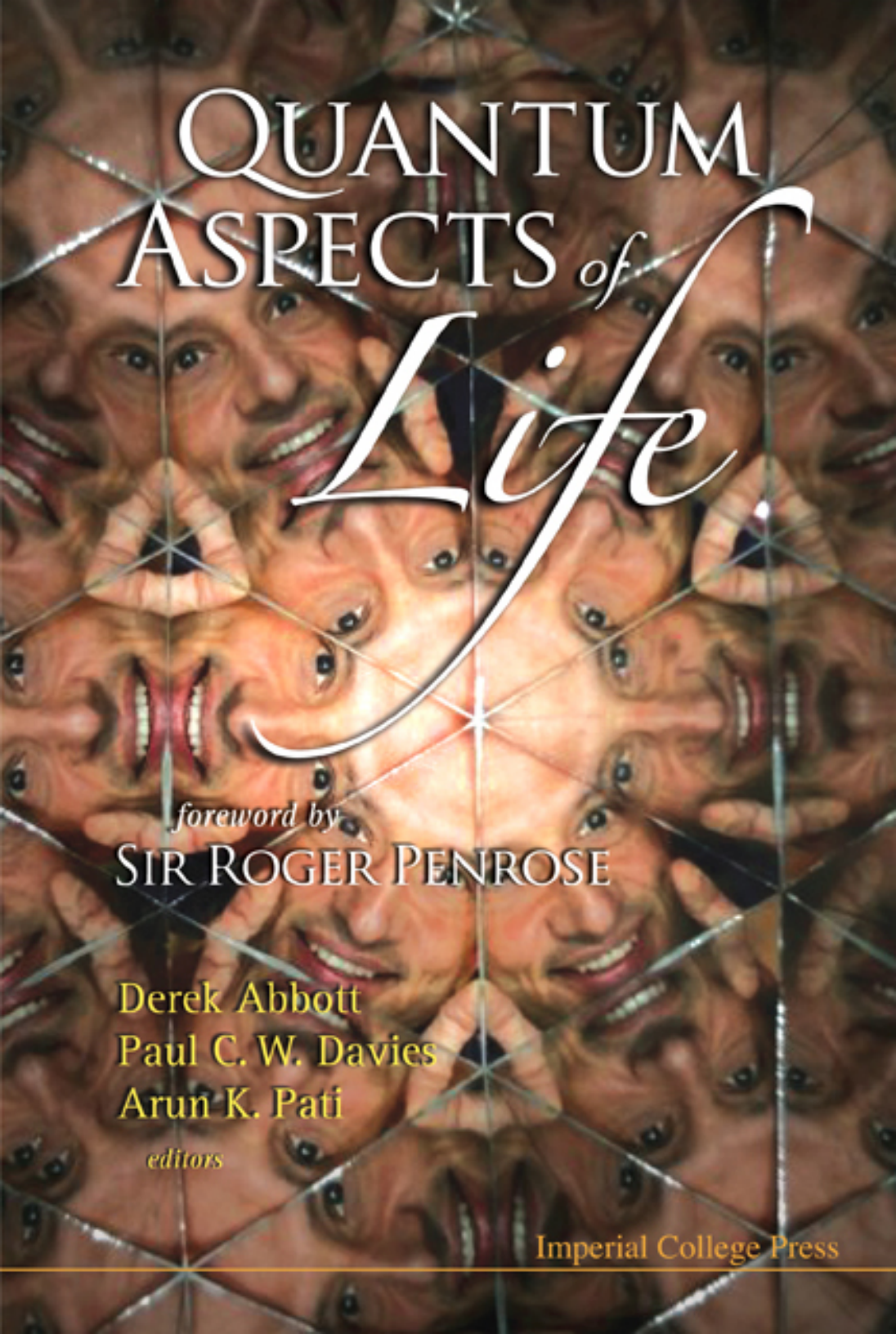
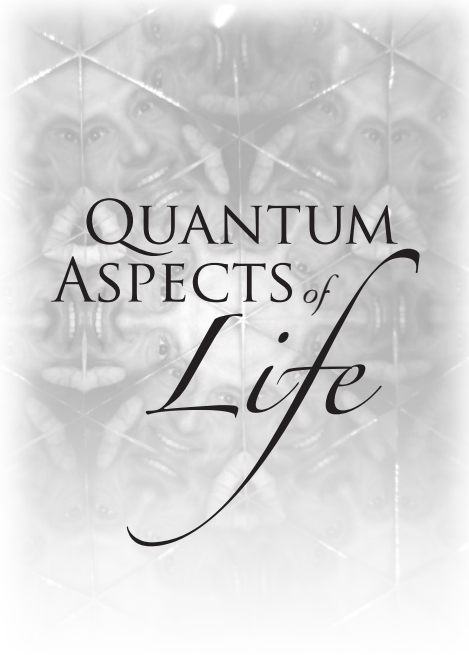

QUANTUM ASPECTS of Life
foreword by
SIR ROGER PENROSE
Derek Abbott
Paul C. W. Davies
Arun K. Pati
editors
Imperial College Press


QUANTUM
ASPECTS of
Life

This page intentionally left blank

Quantum Aspects of Life

foreword by
Sir Roger Penrose

editors
Derek Abbott *(University of Adelaide, Australia)*
Paul C. W. Davies *(Arizona State University, USA)*
Arun K. Pati *(Institute of Physics, Orissa, India)*

ICP
Imperial College Press

Published by

Imperial College Press
57 Shelton Street
Covent Garden
London WC2H 9HE

Distributed by

World Scientific Publishing Co. Pte. Ltd.

5 Toh Tuck Link, Singapore 596224

USA office: 27 Warren Street, Suite 401-402, Hackensack, NJ 07601

UK office: 57 Shelton Street, Covent Garden, London WC2H 9HE

Library of Congress Cataloging-in-Publication Data
Quantum aspects of life / editors, Derek Abbott, Paul C.W. Davies, Arun K. Pati ; foreword by Sir Roger Penrose.
p. ; cm.
Includes bibliographical references and index.
ISBN-13: 978-1-84816-253-2 (hardcover : alk. paper)
ISBN-10: 1-84816-253-7 (hardcover : alk. paper)
ISBN-13: 978-1-84816-267-9 (pbk. : alk. paper)
ISBN-10: 1-84816-267-7 (pbk. : alk. paper)
1. Quantum biochemistry. I. Abbott, Derek, 1960– II. Davies, P. C. W. III. Pati, Arun K.
[DNLM: 1. Biogenesis. 2. Quantum Theory. 3. Evolution, Molecular. QH 325 Q15 2008]
QP517.Q34.Q36 2008
576.8'3--dc22
2008029345

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library.

Photo credit: Abigail P. Abbott for the photo on cover and title page.

Copyright © 2008 by Imperial College Press

All rights reserved. This book, or parts thereof, may not be reproduced in any form or by any means, electronic or mechanical, including photocopying, recording or any information storage and retrieval system now known or to be invented, without written permission from the Publisher.

For photocopying of material in this volume, please pay a copying fee through the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, USA. In this case permission to photocopy is not required from the publisher.

Printed in Singapore.

This book is dedicated to Arun's baby daughter, Arshia, who does not know what life is, yet she has a life.

Artwork credit: Arun K. Pati

This page intentionally left blank

Foreword

When the remarkable book *What is Life?* was published in 1944, written by the great quantum physicist Erwin Schrödinger and based on lectures that he had given at Trinity College Dublin in February 1943, it had a very considerable influence on several key figures in the development of molecular biology. In particular, J. B. S. Haldane, James Watson, Francis Crick, and Maurice Wilkins, have each expressed indebtedness to the penetrating ideas that Schrödinger put forward. One of the basic questions that Schrödinger raised was whether the ideas of classical physics, as normally employed by biologists in their understanding of the behaviour of the physical world, can be sufficient for explaining the basic features of life. He allowed that a case could certainly be put forward that biological systems, being large as compared with the atomic scale and containing vast numbers of constituent atoms, would consequently have macroscopic actions determined essentially by the statistical laws of large numbers. Together with some general overreaching principles of Newtonian mechanics such as conservation of energy, he accepted that this could lead to an overall behaviour consistent with classical Newtonian laws. However, he pointed out that a key feature of the Darwinian/Mendelian nature of inheritance is its basis in discreteness, which could only be explained through a quantum discreteness and stability, in the basic carriers of genetic information. He argued that these carriers had to be molecules of some nature—the molecules that we now know as DNA.

Molecules, and their chemistry, are certainly governed by quantum laws, according to our present understanding; nevertheless, chemists and biologists may not think of chemistry as very "quantum mechanical," perhaps because of the many ball-and-stick (or computer) models that they have

built their experience upon, and such a "hands-on" familiarity is not suggestive of the strange non-intuitive nature of quantum systems. In accordance with such images, we may think of chemistry as being only rather "weakly" quantum mechanical, where the more puzzling features of quantum mechanics in which distant entanglements and globally coherent behaviour do not seem to feature significantly. Such coherent behaviour is witnessed in the phenomena of superfluidity and superconductivity, and in the mysterious entanglements that one can find between the distantly separated quantum particles of EPR (Einstein-Podolsky-Rosen) situations, where the overall behaviour of the combined system cannot be understood simply in terms of the individual nature of its constituent components.

A question of great interest, therefore, is whether or not such "strongly" quantum-mechanical features of Nature might be playing significant roles in the essential processes of life. An area where such a non-local role has been argued for is in the operation of the brain, where the "binding problem", according to which widely separated areas of the brain, with very little in the way of direct neuronal connection, are responsible for the processing of different types of perception (such as colour, shape, and movement, in visual processing); nevertheless all come together in the formation of a single conscious image. On the other side of the argument is the seemingly inhospitable environment that the warm and apparently "messy" living brain provides for such delicate and subtle non-local quantum processes. Indeed, there is no question that if the brain does make use of such "strongly" quantum-mechanical phenomena, it must do so through the agency of some very sophisticated organization. But the situation is certainly far from hopeless as, on the one hand, there is indeed great subtlety in cell structure and, on the other, the very existence of high-temperature superconductors demonstrates that collective quantum phenomena can take place with a relatively small amount of sophistication and without the necessity of extreme cold.

There is a further question that Schrödinger touched upon towards the end of his book, in which he raised the more speculative issue of whether it need actually be the case that even the physical laws provided by standard 20th century quantum mechanics are sufficient for a physical explanation of life. He imagined the situation of an engineer, familiar only with Newtonian mechanics and general statistical principles, being presented with an electric motor. Without any familiarity with the laws of electromagnetism that Faraday and Maxwell have now presented us with, the engineer would have no explanation for the motor's behaviour, which might seem almost

like magic. But the Faraday-Maxwell laws are still mathematical laws of physics, going beyond (but still consistent with) the overall scheme of things laid down by the general framework of Newtonian mechanics and statistical physics. Likewise, Schrödinger argues, it is certainly possible that new physical ingredients, going beyond those of 20th century physics, might be needed for a full understanding of the physical underpinnings of life.

There are probably not many biologists today who would argue for the necessity of such new physical ingredients in order to explain life. Yet, in an Epilogue (On Determinism and Free Will) to his book, Schrödinger raises the further conundrum of how the conscious mind, with its apparent free will, can be accommodated within the "statistico-deterministic" framework of our current quantum/classical pictures. The possible physical need for going beyond this framework had already been raised by Schrödinger himself some eight years before his Dublin lectures, when he introduced his famous "cat paradox". Although he did not refer to this paradox explicitly in *What is Life?* (presumably because he had no desire to confuse his lay audience by introducing such unsettling issues into his descriptions of quantum mechanics), this unsatisfactory state of affairs in the foundations of quantum theory no doubt led him to be sceptical of the current dogma that the rules of quantum mechanics must hold true at all levels of physical description. (It may be pointed out that three others of the key figures in the development of quantum mechanics, namely Einstein, de Broglie, and Dirac, have also expressed the opinion that existing quantum mechanics must be a provisional theory.) There is, indeed, a distinct possibility that the broadening of our picture of physical reality that may well be demanded by these considerations is something that will play a central role in any successful theory of the physics underlying the phenomenon of consciousness.

These deep matters are still subject to much controversy, and the present volume provides a multitude of closely argued opinions on the issues that Schrödinger raised concerning the relation of biology to quantum physics. Is it merely the complexity of biology that gives living systems their special qualities and, if so, how does this complexity come about? Or are the special features of strongly quantum-mechanical systems in some way essential? If the latter, then how is the necessary isolation achieved, so that some modes of large-scale quantum coherence can be maintained without their being fatally corrupted by environmental decoherence? Does life in some way make use of the potentiality for vast quantum superpositions, as would be required for serious quantum computation? How important are the

quantum aspects of DNA molecules? Are cellular microtubules performing some essential quantum roles? Are the subtleties of quantum field theory important to biology? Shall we gain needed insights from the study of quantum toy models? Do we really need to move forward to radical new theories of physical reality, as I myself believe, before the more subtle issues of biology—most importantly conscious mentality—can be understood in physical terms? How relevant, indeed, is our present lack of understanding of physics at the quantum/classical boundary? Or is consciousness really "no big deal," as has sometimes been expressed?

It would be too optimistic to expect to find definitive answers to all these questions, at our present state of knowledge, but there is much scope for healthy debate, and this book provides a profound and very representative measure of it.

Sir Roger Penrose, OM, FRS
The Mathematical Institute, University of Oxford
March 2007.

About the author

Sir Roger Penrose, OM, FRS was born on 8 August 1931 in Colchester, Essex, England. He is a mathematical physicist and Emeritus Rouse Ball Professor of Mathematics at the Mathematical Institute, University of Oxford and Emeritus Fellow of Wadham College. Penrose is concurrently the Francis and Helen Pentz Distinguished Visiting Professor of Physics and Mathematics at Penn State University. Penrose graduated with a first class degree in mathematics from University College London. He obtained his PhD at Cambridge (St John's College) in 1958, writing a thesis on tensor methods in algebraic geometry under John Arthur Todd. In 1965 at Cambridge, Penrose proved that black hole singularities could be formed from the gravitational collapse of large dying stars. In 1967, Penrose invented twistor theory and in 1969 he conjectured the cosmic censorship hypothesis—this form is now known as the weak censorship hypothesis. In 1979, Penrose formulated a stronger version called the strong censorship hypothesis. He is also well-known for his 1974 discovery of Penrose tilings, which are formed from two tiles that can surprisingly tile an infinite plane aperiodically. Another noteworthy contribution is his 1971 invention of spin

networks, which later came to form the geometry of spacetime in loop quantum gravity. He was influential in popularizing what are commonly known as Penrose diagrams. He has written 8 books, including *The Emperor's New Mind* (1989) and *Shadows of the Mind* (1994) that explore the lacunae between human consciousness and the known laws of physics. In 2004, Penrose released his magnum opus *The Road to Reality: A Complete Guide to the Laws of the Universe*. In 1975, Stephen Hawking and Roger Penrose were jointly awarded the Eddington Medal of the Royal Astronomical Society. In 1985, Penrose was awarded the Royal Society Royal Medal. Together with Stephen Hawking, he was awarded the Wolf Foundation Prize for Physics in 1988. In 1989, Penrose was awarded the Dirac Medal and Prize of the British Institute of Physics. In 1990, he was awarded the Albert Einstein Medal and, in 1991, he was awarded the Naylor Prize of the London Mathematical Society. In 1998, he was elected Foreign Associate of the United States National Academy of Sciences and, in 2004, he was awarded the De Morgan Medal.

This page intentionally left blank

Preface

A landmark event in the history of science was the publication in 1944 of Erwin Schrödinger's book *What is Life?* Six decades later, the question remains unanswered. Although biological processes are increasingly well understood at the biochemical and molecular biological level, from the point of view of fundamental physics, life remains deeply mysterious. Schrödinger himself drew inspiration from his seminal work on quantum mechanics, which had so spectacularly explained the nature of matter, believing it was sufficiently powerful and remarkable to explain the nature of life too. These dreams have not been realized. To be sure, quantum mechanics is indispensable for explaining the shapes, sizes and chemical affinities of biological molecules, but for almost all purposes scientists go on to treat these molecules using classical ball-and-stick models. Life still seems an almost magical state of matter to physicists; furthermore, its origin from non-living chemicals is not understood at all.

In recent years, circumstantial evidence has accumulated that quantum mechanics may indeed, as Schrödinger hoped, cast important light on life's origin and nature. In October 2003, the US space agency NASA convened a workshop at the Ames Laboratory in California, the leading astrobiology institution, devoted to quantum aspects of life. The workshop was hosted by Ames astrobiologist Chris McKay and chaired by Paul Davies. In this volume we solicit essays both from the participants in the workshop, and from a wider range of physical scientists who have considered this theme, including those who have expressed skepticism. The over-arching question we address is whether quantum mechanics plays a non-trivial role in biology.

We believe it is timely to set out a distinct quantum biology agenda. The burgeoning fields of nanotechnology, biotechnology, quantum technology and quantum information processing are now strongly converging. The acronym BINS, for Bio-Info-Nano-Systems, has been coined to describe the synergetic interface of these several disciplines. The living cell is an information replicating and processing system that is replete with naturally-evolved nanomachines, which at some level require a quantum mechanical description. As quantum engineering and nanotechnology meet, increasing use will be made of biological structures, or hybrids of biological and fabricated systems, for producing novel devices for information storage and processing, and other tasks. An understanding of these systems at a quantum mechanical level will be indispensable.

To broaden the discussion, we include chapters on "artificial quantum life," a rapidly-developing topic of interest in its own right, but also because it may cast light on real biological systems. Related mathematical models include quantum replication and evolution, von Neumann's universal constructors for quantum systems, semi-quantum cellular automata, and evolutionary quantum game theory.

Finally, we include the transcripts of two debates:

(1) "Dreams versus reality: quantum computing" hosted by the *Fluctuations and Noise* symposium held in Santa Fe, USA, 1–4 June 2003. The panelists were Carlton M. Caves, Daniel Lidar, Howard Brandt, Alex Hamilton (for) and David Ferry, Julio Gea-Banacloche, Sergey Bezrukov and Laszlo Kish (against). The debate chair was Charles Doering.
(2) "Quantum effects in biology: trivial or not?" hosted by the *Fluctuations and Noise* symposium held in Gran Canaria, Spain, 25–28 May 2004. The panelists were Paul Davies, Stuart Hameroff, Anton Zeilinger, Derek Abbott (for) and Jens Eisert, Sergey Bezrukov, Hans Frauenfelder and Howard Wiseman (against). The debate Chair was Julio Gea-Banacloche.

The second debate represents the topic of this book and a new reader to the area may find it beneficial to jump directly to Chapter 16, as this will help the reader navigate some of the competing arguments in an entertaining way. The first debate, in Chapter 15, is on whether useful man-made quantum computers are possible at all. Placing these two debates side by side exposes interesting conflicting viewpoints of relevance to this book: (1) Those who would argue for quantum processing in various biological

systems have to face the difficulty that useful man-made quantum computers are extremely hard to make, and if they are fodder for debate then the biological proposition would appear to be on even weaker ground; (2) Those physicists who are working towards realizing large scale man-made quantum computers, when faced with skepticism, are on occasion tempted to appeal to biology in their defence as can be seen in Chapter 15. This therefore creates an exciting tension between the opposing viewpoints, namely, that on one hand pessimistic experience with man-made quantum computers is used to cast doubt on quantum effects in biology, whereas on the other hand an optimistic view of quantum effects in biology is used to motivate future man-made quantum computers. Physicists with a vested interest in realizing quantum computers often find themselves in a strange superposition of these orthogonal viewpoints, which can only be finally resolved if more detailed experiments on biomolecules are carried out.

Finally, it is our hope that at the very least this book will provoke further debate and help provide motivation for more experimental research into nature's nanostructures. If experiments can shed further light on our understanding of decoherence in biomolecules, at scales where equillibrium thermodynamics no longer applies, this may provide the required foundation for greatly accelerating our progress in man-made quantum computers.

Derek Abbott, University of Adelaide, Australia
Paul C. W. Davies, Arizona State University, USA
Arun K. Pati, Institute of Physics (IOP), Orissa, India.

November 2007

This page intentionally left blank

Acknowledgments

We thank Rita Yordy, Stefanie Cross, Pauline Davies, and Megan Hunt of Arizona State University (ASU) for administrative assistance, manuscript proof reading, and correspondence.

A special thanks is due to Mathias Baumert, of the University of Adelaide, who coordinated the LaTeX formatting of the book.

DA
PCWD
AP

This page intentionally left blank

Contents

PART 1

Emergence and Complexity

This page intentionally left blank

Chapter 1

A Quantum Origin of Life?

Paul C. W. Davies

The origin of life is one of the great unsolved problems of science. In the nineteenth century, many scientists believed that life was some sort of magic matter. The continued use of the term "organic chemistry" is a hangover from that era. The assumption that there is a chemical recipe for life led to the hope that, if only we knew the details, we could mix up the right stuff in a test tube and make life in the lab.

Most research on biogenesis has followed that tradition, by assuming chemistry was a bridge—albeit a long one—from matter to life. Elucidating the chemical pathway has been a tantalizing goal, spurred on by the famous Miller-Urey experiment of 1952, in which amino acids were made by sparking electricity through a mixture of water and common gases [Miller (1953)]. But this concept turned out to be something of a blind alley, and further progress with pre-biotic chemical synthesis has been frustratingly slow.

In 1944, Erwin Schrödinger published his famous lectures under the title *What is Life?* [Schrödinger (1944)] and ushered in the age of molecular biology. Schödinger argued that the stable transmission of genetic information from generation to generation in discrete bits implied a quantum mechanical process, although he was unaware of the role of or the specifics of genetic encoding. The other founders of quantum mechanics, including Niels Bohr, Werner Heisenberg and Eugene Wigner shared Schrödinger's belief that quantum physics was the key to understanding the phenomenon

Received May 9, 2007

of life. This was a reasonable assumption at the time. Shortly before, quantum mechanics had solved the problem of matter, by explaining atomic and molecular structure, chemical bonds and the nature of solids. It seemed natural that quantum mechanics would soon also solve the riddle of the living state of matter. To a physicist, life seems fundamentally weird, even bizarre, in its properties, and bears almost no resemblance to any other type of physical system. It is tempting to suppose that quantum mechanics possesses enough weirdness to account for it.

These early musings about the place of quantum mechanics in life were soon swept away in the rush. Molecular biology proved so successful that rich pickings could be harvested merely from crude ball-and-stick models of molecules. However, with the maturity of the subject, hints began to surface that non-trivial quantum effects might be of crucial significance in the functioning of certain biosystems. Some of these effects are reviewed in other chapters in this volume. The question I wish to address in this chapter is in what manner quantum mechanics played a role in the origin of life. One point needs clarification. There is a trivial sense in which life is quantum mechanical. Cellular function depends on the shapes of molecules and their chemical affinities, properties that require quantum mechanics to explain. However, what I have in mind are non-trivial quantum effects, for example, the coherent wavelike nature of matter, tunnelling, entanglement, intrinsic spin, Berry phase, environmental post-selection and the watchdog effect.

Obviously at some level quantum mechanics cannot be ignored in the life story, since by general consent, life somehow emerged from the molecular realm, even if the specifics remain mysterious. The molecular road to life is in contrast to the "magic matter" theories of the nineteenth century that were essentially macroscopic in conception. Because the molecular realm is unquestionably quantum mechanical in nature, the issue I am raising is whether classicality emerged before life or whether life emerged before classicality. My central hypothesis is that quantum mechanics enabled life to emerge directly from the atomic world, without complex intermediate chemistry. The orthodox view is that an extended period of increasingly complex "ball-and-stick" chemistry preceded the transition to the first genuinely autonomous living system (which may not have been an individual cell, more likely it was a cellular cooperative). The philosophical position that underpins my hypothesis is that the secret of life lies not with its complexity per se, still less with the stuff of which it is composed, but with its remarkable information processing and replicating abilities.

1.1. Chemistry and Information

Although there is no agreed definition of life, all living organisms are information processors: they store a genetic database and replicate it, with occasional errors, thus providing the basis for natural selection. The direction of information flow is bottom up: the form of the organism and its selective qualities can be traced back to molecular processes. The question then arises of whether, since this information flows from the quantum realm, any vestige of its quantum nature, other than its inherent randomness, is manifested. Biological molecules serve the role of both specialized chemicals and informational molecules, mirroring the underlying dualism of phenotype/genotype. In computer terminology, chemistry is akin to hardware, information to software. A complete understanding of the origin of life demands an explanation for both hardware and software. Most research in biogenesis focuses on the hardware aspect, by seeking a plausible chemical pathway from non-life to life. Though this work has provided important insights into how and where the basic building blocks of life might have formed, it has made little progress in the much bigger problem of how those building blocks were assembled into the specific and immensely elaborate organization associated with even the simplest autonomous organism [Davies (2003)]. But viewing life in terms of information processing transforms the entire conceptual basis of the problem of biogenesis. Reproduction is one of the defining characteristics of life. Traditionally, biologists regarded reproduction as the replication of material structures, whether DNA molecules or entire cells. But to get life started all one needs is to replicate information. In recent years our understanding of the nature of information has undergone something of a revolution with the development of the subjects of quantum computation and quantum information processing. The starting point of this enterprise is the replacement of the classical "bit" by its quantum counterpart, the "qubit". As a quantum system evolves, information is processed; significantly, the processing efficiency is enhanced because quantum superposition and entanglement represent a type of computational parallelism. In some circumstances this enhancement factor can be exponential, implying a vast increase in computational speed and power over classical information processing. Many researchers have spotted the sweeping consequences that would follow from the discovery that living organisms might process information quantum mechanically, either at the bio-molecular level, or the cellular/neuronal level [Penrose (1989); Beck and Eccles (1992); Hameroff (1994); Davies (2004);

Matsuno (1999); Patel (2001); Vedral (2003); Schempp (2003)]. Biological systems are quintessential information processors. The informational molecules are RNA and DNA. Although quantum mechanics is crucial to explain the structure of these molecules, it is normally disregarded when it comes to their information processing role. That is, biological molecules are assumed to store and process classical bits rather than qubits. In an earlier paper [Davies (2004)] I speculated that, at least in some circumstances, that assumption may be wrong. It is then helpful to distinguish between three interesting possibilities:

(1) Quantum mechanics played a key role in the emergence of life, but either ceased completely to be a significant factor when life became established, or was relegated to a sporadic or subsidiary role in its subsequent development. Nevertheless, there may be relics of ancient quantum information processing systems in extant organisms, just as there are biochemical remnants that give clues about ancient biological, or even pre-biological, processes.
(2) Life began classically, but evolved some efficiency-enhancing "quantum tricks." For example, if biological systems were able to process information quantum mechanically, they would gain a distinct advantage in speed and power, so it might be expected that natural selection would discover and amplify such capabilities, if they are possible.
(3) Life started out as a classical complex system, but later evolved towards "the quantum edge," where quantum uncertainty places a bound on the efficiency of bio-molecular processes.

As there is little doubt that some cellular machinery (e.g. photosynthesis—see Chapter 4) does exploit quantum mechanics [Engel *et al.* (2007)], the issue arises of whether quantum enhancement is a product of evolution (as in 2), or a remnant of life's quantum origin (as in 1).

1.2. Q-life

The starting point of my hypothesis is the existence of a quantum replicator, a quantum system that can copy information with few errors [Wigner (1961); Pati (2004)]. The information could be instantiated in the form of qubits, but that is not necessary—the quantum replication of classical bits is sufficient (see below). A quantum replicator need not be an atomic system that clones itself. Indeed, there is a quantum no-cloning theorem

that forbids the replication of wavefunctions [Wooters and Zurek (1982); Pati (2004)]—see also Chapter 11 in this book. Rather, the information content of an atomic system must be copied more or less intact—not necessarily in one step, maybe after a sequence of interactions. This information might well be in binary form, making use of the spin orientation of an electron or atom for example. Quantum mechanics thus provides an automatic discretization of genetic information. Quantum replicators certainly exist in Nature. The simplest case is the stimulated emission of photons. Another is the atom-by-atom growth of a crystal lattice. But these examples are not information-rich; they do not fulfill the additional requirement of high algorithmic complexity demanded by biology, as neither the identical photons not the identical crystal atoms store more than a very few bits of information. So we seek a natural system in which high-fidelity replication of an information-rich assemblage of quantum objects takes place on a short time scale. Henceforth I shall refer to this hypothetical system as Q-life. Leaving aside wild speculations like life in neutron stars [Forward (1980)], a venue for Q-life might plausibly be a condensed matter setting at a low temperature, for example, the crust of an icy rogue planetesimal in interstellar space.

Let me illustrate the basic idea of Q-life with a simple, and almost certainly unsatisfactory, example. Consider an array of atomic spins embedded in a condensed matter system, defined relative to some fiducial direction. The initial template A may be described by a ket vector such as

$$|\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow> \ .$$

This template then comes into interaction with an arbitrary system of spins B, say,

$$|\uparrow\uparrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\uparrow\downarrow\uparrow\downarrow\uparrow\downarrow> \ .$$

As a result of the interaction (which may entail many intermediate steps), the following transition occurs

$$|\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow>|\uparrow\uparrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\uparrow\downarrow\uparrow\downarrow\uparrow\downarrow>\longrightarrow$$

$$|\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow>|\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\uparrow> \ .$$

Symbolically, the overall evolution of the state is $AB \longrightarrow AA$. Because the transition has erased the information contained in state B, the replication process is asymmetric and irreversible, and accompanied by an increase in entropy. The system thus requires an energy source to drive the reaction forward. This could be in the form of an exciton that hops along the array of atoms, flipping the B spins where necessary one-by-one but leaving the A spins unchanged.

The foregoing model is very simplistic. A more realistic form of interaction, and a closer analogue of DNA replication, would be if the template array A first created a complementary array

$$|\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\uparrow\downarrow\uparrow\downarrow\downarrow\downarrow\uparrow\downarrow\uparrow\uparrow\downarrow> ,$$

which then generated the original array by "base-pairing". An additional simplification is that the model described so far neglects interactions between neighbouring spins. Such interactions produce greater complexity, and so increase the opportunity to encode algorithmically incompressible information.

The replication rate of a spin array will depend on whether the sequence is processed linearly, after the fashion of DNA, or all at once. It will also depend on the availability of the necessary complementary structure. Once the two structures are brought into interaction, each bit flip could occur extremely fast (i.e. in less than a femtosecond). This can be compared to the sluggish rate of only 100 base-pairs per second typical of DNA replication by polymerase enzymes, even when the system is not resource-limited [Goel *et al.* (2003)]. Thus, in an appropriate quantum setting, Q-life could replicate and evolve at least 12 orders of magnitude faster than familiar life! However, in practice an ideal appropriate setting is unlikely to occur in nature. More realistic is a model of replication in which the process is managed by a catalytic structure, in analogy with the replicase enzymes of DNA replication. The job of this conjectured structure would be to bring the required components into interaction, perhaps by creating an "interaction centre" screened from the environment. The replication rate would then be limited by the performance of this "Q-replicase." In particular, the Q-replicase is likely to be subject to the opportunities and limitations of quantum mechanics. In the later category are fundamental limits of choreography set by the uncertainty principle, a topic that I shall defer to the final section.

How, then, did organic life arise? Information can readily be passed from one medium to another. At some stage Q-life could have co-opted large

organic molecules for back-up memory, much as a computer uses a hard-disk. The computer's processor (analogous to Q-life) is much faster than the hard disk drive (analogous to RNA and DNA), but more vulnerable and in need of a continual input of energy. Robust computing systems require something like a hard disk. Eventually the organic molecular system would literally have taken on a life of its own. The loss in processing speed would have been offset against the greater complexity, versatility and stability of organic molecules, enabling organic life to invade many environments off-limits to Q-life (e.g. high temperature).

Note that although the replicator I have used as a simple illustration is fundamentally quantum mechanical in nature, the copying process as described does not replicate any entanglement or phase information; i.e. the process replicates bits rather than qubits. For that reason, decoherence would not be an issue at the replication stage. Left out of the account so far, however, is how the quantum replicator arises in the first place. The nature of the transition from an arbitrary quantum system to a replicating quantum system is far from clear, but the process is likely to be enormously enhanced if it is at least partially coherent. Let me therefore make some general remarks about decoherence in biosystems.

1.3. The Problem of Decoherence

Coherence entails the preservation of delicate phase relationships between different components of the wave function. Interactions between the quantum system and its environment will serve to decohere the wave function: the noise of the environment effectively scrambles the phases. Once decohered, a quantum system behaves in most respects as a classical system [Zurek (1982)]. The decoherence rate depends on the nature and temperature of the environment and the strength with which it couples to the quantum system of interest [Zurek (1982); Caldeira and Leggett (1985); Unruh and Zurek (1989); Hu *et al.* (1992)]. The main burden in the development of quantum computation, for example, is to screen out the decohering environment as efficiently as possible, e.g. by reducing the temperature. If quantum mechanics is to play a role in the origin of life, typical decoherence rates must not be greater than the relevant transition rates. Simple models of decoherence have been much studied over the past twenty years. Typically, for a particle interacting with a heat bath at room temperature, exceedingly short decoherence times result. Translated into the context of,

say, a nucleotide in the environment of a cell at room temperature, decoherence times of femtoseconds are typical, [Caldeira and Leggett (1985); Unruh and Zurek (1989); Hu *et al.* (1992); Tegmark (2000)]. But on a second look, the situation is found to be more subtle. There are two ways in which decoherence could be diminished for long enough to enable biologically important processes to occur. The first is screening: if the system of interest can be quasi-isolated from the decohering environment then decoherence rates can be sharply reduced. According to Matsuno (1999), organisms may exploit thermodynamic gradients by acting as heat engines and thereby drastically reduce the effective temperature of certain molecular complexes. He cites the example of the slow release of energy from ATP molecules at actomyosin complexes, which he claims implies an effective temperature for the actomyosin of a mere 1.6×10^{-3} K. At any rate, the lesson of high-temperature superconductivity reminds us that in complex states of matter, simple "kT reasoning" can be misleading.

The second possibility involves decoherence-free subspaces. In the effort to build a quantum computer, much attention has been given to identifying subspaces of Hilbert space that are unaffected by the coupling of the system to its environment [Nielson and Chuang (2001)]. Paradoxically, when a system couples very strongly to its environment through certain degrees of freedom, it can effectively "freeze" other degrees of freedom by the quantum Zeno effect, enabling coherent superpositions and even entanglement to persist. An explicit example is provided by a double-well one-dimensional potential. A particle placed in the lowest energy state of one well will tunnel back and forth through the intervening barrier, oscillating with a certain frequency. If the particle is placed instead in an excited state of the well, this flip-flop frequency will be different. Thus an initial state consisting of a superposition of lowest energy and excited states will soon evolve into a complicated muddle as the flip-flops get out of phase. However, if the particle is now allowed to interact strongly with an external heat bath, the environment has the effect of forcing the disparate oscillations into synchrony, thereby maintaining a limited form of quantum coherence, not in spite of, but because of, environmental interactions [Davies (2003)]. Furthermore, if the system is placed in an entangled state of left and right well-locations, this entanglement is also preserved by environmental interaction. The model was developed in the context of neutrino oscillations, but has general applicability [Bell *et al.* (2002)]. It does, however, depend on the interaction being "blind" between the two potential wells. It is unclear how realistically this would translate into a biological scenario, or whether

it has any relevance to the extended decoherence times reported recently [Engel *et al.* (2007)].

1.4. Life as the "Solution" of a Quantum Search Algorithm

The hypothesis I am proposing is that the transition from non-life to life was a quantum-mediated process, and that the earliest form of life involved non-trivial quantum mechanical aspects. The power of quantum superpositions is that the system can explore many alternative pathways simultaneously, thereby potentially shortcutting the transition time by a large factor. Because life is a highly unusual state of matter, its formation from an arbitrary initial state is presumably extremely improbable. Quantum mechanics provides a way to drastically shorten the odds and fast-track matter to life by exploiting the parallel processing properties of superpositions. There is, however, a deep philosophical issue that must be confronted. I am defining "life" as a certain special state of low probability. Quantum mechanics enables the space of possibilities to be much more efficiently explored than a stochastic classical system. Now, if there are branches of the wave function "containing life" (e.g. a quantum replicator), they will, by assumption, have very small amplitudes. We must therefore explain why the wave function of the system "collapses" onto one of these states of such low intrinsic probability. Expressed differently, how does a quantum superposition recognize that it has "discovered" life and initiate the said collapse? There seems to be an unavoidable teleological component involved: the system somehow "selects" life from the vastly greater number of states that are nonliving.

Actually, the way I have expressed it is an abuse of language. In the standard formulation of quantum mechanics, a quantum system itself never "initiates collapse." The wavefunction collapses as a result of interaction with the environment. One possibility is that replicators are the products of environmental post-selection, perhaps amplified by a quantum feedback loop. The importance of quantum post-selection has only recently been recognized [Aharonov *et al.* (1996)]. The idea is this. The environment serves as a sort of measuring device, and, by hypothesis, it somehow selects for measurement a quantum variable relevant for life. Then even if the amplitude is small, life will be "projected out" of the superposition by the measurement-like interaction. It may even be "steered" towards life by the inverse-Zeno effect. But this implies the environment somehow favours life—that life is "built into" nature in a preordained manner. So an element of teleology remains.

One way to envision the emergence of life by "state exploration" is in terms of a vast decision tree of states (quantum or classical). The root of the tree might correspond to a simple and easy-to-form initial state, which might then evolve to any one of a huge range of possible subsequent states. This can be represented by the tree of states splitting repeatedly into a proliferating number of branches, each branch denoting a possible physical path in state space leading away from the initial state. States of great complexity are represented by branches high up on the tree, and a subset of these branches represents a quantum replicator, or some other state that we may designate as life, or incipient life. The puzzle of life's origin is how the initial simple state "finds" one of the exceedingly rare branches associated with life. Farhi and Gutmann (1998) have compared quantum and classical searches of decision trees, and they find that in some circumstances a quantum search is exponentially faster than a classical search. Their model cannot be immediately applied to the problem of biogenesis, however, because quantum coherence could not possibly be maintained through more than a brief sequence of interactions in any likely prebiotic physical setting. Nevertheless, as the example, of Engel *et al.* (2007) demonstrates, quantum coherence over picosecond timescales is plausible, and leads to an enormous speed-up in the transition to certain otherwise hard-to-attain states.

Our ignorance of the precise nature of the quantum replicator makes it almost impossible to evaluate the probability that one will form as the end product of a quantum search. However, some general points may be made concerning quantum speed-up. If the replicator, or some other quantum structure en route to it, is describable as a local minimum in an energy landscape, with the formation of this unknown system being akin to a phase transition, then quantum mechanics has the ability to enormously enhance the probability of the transition by permitting tunnelling through the relevant potential barrier in the energy landscape. So a possible model of biogenesis is that of a phase transition analogous to bubble nucleation in quantum field theory, where the nucleated lower-energy state is a community of interacting replicators—possibly a large community occupying a mesoscopic region of a condensed matter system. This would constitute a quantum version of Kauffman's concept of an autocatalytic network of molecules [Kauffman (1993)]. Secondly, if the "solution" of the quantum "search" is defined to be a quantum replicator, and if the system does not decohere faster than the replication time, then the replicator should act in a manner similar to a quantum resonance (in view of the fact that the wave function describing the replicator will be amplified by iteration), thus greatly enhancing the probability for a transition to a replicator state.

So far I have been describing the replicator as if it is a physical structure, but the significant point about viewing life in terms of information is that, so long as the information is replicated, the structures embodying that information need not be. In the case of familiar DNA based life, the information represented by the base-pair sequence, and the base-pairs, are replicated together. Thus information replication is tied to structural replication. But at the quantum level there are alternative possibilities. Consider, for example, a cellular automaton, such as the Game of Life—see, for example, Gardner (1970). In this system a group of five clustered cells can form a so-called glider. The glider moves across the array of cells as a coherent (in the classical sense) object, and thus conserves information. However, individual cells are switched on and off, but in a way that preserves the overall pattern. The origins of biological information could belong to this category (perhaps constituting a quantum cellular automaton—see Chapter 12 by Flitney and Abbott in this book). We can imagine a condensed matter system in which a pattern of excitation, or a pattern of spins, or some other quantum variable, might induce transitions in neighbouring quantum states in such a way as to conserve the pattern to high probability, but to "pass on" the excitation, or spin, to adjacent atoms. The "information packet" would thereby be preserved and propagate, until it encounters a suitable quantum milieu in which it will replicate. Then two information packets would propagate away from the interaction region, and so on. Quantum fluctuations in the propagation and replication process would lead in a natural way to "mutations", and to a Darwinian competition between rival information packets.

1.5. Quantum Choreography

An unresolved issue concerning replication is the matter of timing and choreography. In the simplest templating arrangement one can imagine, the formation of complementary base-pairs takes place by random access of molecular components and will proceed at a rate determined by the slower of two processes: the reaction time for pair bonding and the diffusion time of the appropriate molecular or atomic building blocks. In real DNA replication, the base-pairing is incomparably more efficient and faster because it is managed by a large and complex polymerase with complicated internal states. Very little is known about the specifics of the replicase's internal activity, but it seems reasonable to conjecture in relation to its function

that in addition to the normal lowering of potential barriers to facilitate quantum tunnelling (and thus accelerate the process), the replicase also engages in a certain amount of choreography, making sure the right pieces are in the right places at the right times. The concomitant speed-up over the random access process would have a distinct evolutionary advantage.

Although the complexity of the replicase renders its internal workings obscure at this time, one may deploy general arguments to determine whether quantum mechanics might be playing a non-trivial role in the hypothesized choreography, by appealing to the general analysis of quantum time-keeping given by Wigner. As he pointed out, the energy-time uncertainty relation sets a fundamental limit to the operation of all quantum clocks [Wigner (1957); Pesic (1993); Barrow (1996)]. For a clock of mass m and size l, he found

$$T < ml^2/\hbar\,. \tag{1.1}$$

It is noteworthy that, for values of m and l of interest in molecular biology, T also takes values of biological interest, suggesting that some biological systems utilize quantum choreography. Let me give as an example the well-known problem of protein folding, which is a major outstanding problem of theoretical biology [Creighton (1993)]. Consider a peptide chain of N amino acids, which folds into a specific three-dimensional structure. The number of possible final configurations is astronomical, and it is something of a mystery how the chaotically-moving chain "finds" the right configuration in such a short time (typically microseconds). Quantum mechanics could offer an explanation. If the average mass and length of an amino acid are m_o, and a respectively, then Eq. (1.1) yields

$$T < m_o a^2 N^3/\hbar\,, \tag{1.2}$$

suggesting a quantum scaling law for the maximum folding time of

$$T \propto N^3\,. \tag{1.3}$$

It is not clear that the linear dimension is the relevant size parameter when it comes to large proteins. The assumption $l \equiv Na$ in Eq. (1.2) may be justified for small proteins ($N = 80$ to 100) that fold in one step, but larger proteins do not remain "strung out" for a large fraction of the folding process. Instead, they first fold into sub-domains. The opposite limit would be to replace l by the diameter of the folded protein. Assuming it is roughly spherical, this would imply $T \propto N^{5/3}$. The intermediate process of sub-domain folding suggests a more realistic intermediate scaling law of, say,

$$T \propto N^{7/3} \tag{1.4}$$

for large proteins. In fact, a power law of this form has been proposed on empirical grounds [Gutlin *et al.* (1996); Cieplak and Hoang (2003)], with the exponent in the range 2.5 to 3. Inserting typical numerical values from Eq. (1.2), the limiting values of T for a 100 and 1000 amino acid protein are 10^{-3} s and 0.3 s respectively. This is comfortably within the maximum time for many protein folds (typically 10^{-6} s to 10^{-3} s for small proteins *in vitro*), but near the limit for some, hinting that quantum choreography may indeed be taking place in some cases.

Turning now to the polymerase enzyme, this is a molecular motor, or ratchet, powered by ATP and using nucleotides as the raw material for the base pairing. The physics of this system has been studied in some detail for lambda-phage DNA [Goel *et al.* (2003)]. The Wigner inequality (1.1) may be converted to a velocity bound

$$\nu > \hbar/mL\,. \tag{1.5}$$

Using the parameters for the experimentally studied case, taking L to be the length of the DNA (16 μm), and a polymerase mass of about 10^{-19} g, Eq. (1.5) yields a minimum velocity of about 10^{-5}cm s^{-1}. The experimental results show the motor operates at about 100 base pairs per second, which is indeed about 10^{-5} cm s^{-1}, suggesting that in normal operation the motor could be limited by quantum synchronization uncertainty. Experiments demonstrate that applying tension to DNA using optical tweezers decelerates the motor at a rate of about 3 bases per second per pN of applied tension [Goel *et al.* (2003)]. At a tension of about 40 pN the motor stops altogether. (With further stretching of the DNA the motor runs backward). This suggests that the speed of the motor is not determined by the availability of nucleotides or kT (which does not change as a function of tension).

If quantum choreography underlies the efficiency of the polymerase motor, it seems reasonable to suppose that quantum choreography would be even more important in the operation of Q-life. In the absence of a detailed idea of the nature of the hypothetical Q-replicase, it is hard to know what to choose for m and l, but by way of illustration if we take m to be 1000 proton masses and l to be 100 nm then the maximum running time of a quantum clock is a few hundred femtoseconds. Quantum transitions that take longer than about this limit could not be assisted in efficiency by such a Q-replicase. For femtosecond transition rates, however, quantum choreography would seem, at least based on this crude estimate, to offer a good mechanism for instantiating quantum replication.

Acknowledgements

I should like to thank Anita Goel, Gerard Milburn, Sandu Popescu, and Jeff Tollaksen for helpful discussions.

References

Aharonov, Y., Massar, S., Popescu, S., Tollaksen, J., Vaidman, L. (1996). Adiabatic measurements on metastable systems, *Phys. Rev. Lett.* **77**, pp. 983–987.

Aharonov, Y., Albpert, D. Z., and Vaidman, L. (1988). *Phys. Rev. Lett.* **60**, p. 1351.

Barrow, J. D. (1996). The Wigner inequalities for a black hole, *Phys. Rev. D* **54**, pp. 6563–4.

Beck, F., and Eccles, J. C. (1992). Quantum aspects of brain activity and the role of consciousness, *Proc. Nat. Acad. Sci. USA* **89**, pp. 11357–11362.

Bell, N. F., Sawyer, R. F., and Volkas, R. R. (2002). Entanglement and quantal coherence: a study of two limiting cases of rapid system-bath interactions, *Phys. Rev. A* **65**, art. no. 042328.

Caldeira, A. O. and Leggett, A. J. (1985). Influence of damping on quantum interference: An exactly soluble model, *Phys. Rev. A* **31**, pp. 1059–1066.

Cieplak, M. and Hoang, T. X. (1993). Universality classes in folding times of proteins, *Biophys. J.* **84** pp. 475–488.

Creighton, T. E. (1993). *Proteins: Structures and Molecular Properties* (W. H. Freeman).

Davies, P. C. W. (2003). *The Origin of Life* (Penguin).

Davies, P. C. W. (2004). Does quantum mechanics play a non-trival role in life? *Biosystems* **78**, p. 69.

Engel, G. S. (2007). Evidence for wavelike energy transfer through quantum coherence in photosynthetic systems, *Nature* **446**, pp. 782–786.

Farhi, E., and Gutmann, S. (1998). Quantum computation and decision trees, *Phys. Rev. A* **58**, pp. 915–929.

Forward, R. L. (1980). *Dragon's Egg* (Ballantine Books).

Gardner, M. (1970). The fantastic combinations of John Conway's new solitaire game "life", *Scientific American* **223**, pp. 120–123.

Goel, A., Astumian, R. D., and Herschbach, D. (2003). Tuning and switching a DNA polymerase motor with mechanical tension, *Proc. Nat. Acad. Sci. USA* **98**, pp. 8485–8491.

Gutlin, A. M., Abkevich, V. I., Shakhnovich, E. I. (1996). Chain length scaling of protein folding time, *Phys. Rev. Lett.* **77**, pp. 5433–5436.

Hameroff, S. R. (1994). Quantum coherence in microtubules: a neural basis for emergent consciousness? *Journal of Consciousness Studies* **1**, pp. 98–118.

Hu, B. L., Paz, J. P., and Zhang, Y. (1992). Quantum Brownian motion in a general environment: Exact master equation with nonlocal dissipation and colored noise, *Phys. Rev. D* **45**, pp. 2843–2861.

Kauffman, S. A. (1993). *The Origins of Order* (Oxford University Press).
Matsuno, K. (1999). Cell motility as an entangled quantum cohererence, *BioSystems* **51**, pp. 15–19.
Matsuno, K., and Paton, R. C. (2000). Is there a biology of quantum information? *BioSystems* **55**, pp. 39–46.
Miller, S. L. (1953). *Science* **117**, p. 528.
Nielson, M. and Chuang, I. L. (2001). *Quantum Computation and Quantum Information* (Cambridge University Press).
Patel, A. (2001). Why genetic information processing could have a quantum basis, *J. Biosci.* **26**, pp. 145–51.
Pati, A. K. (2004). Replication and evolution of quantum species, *Fluctuation and Noise Letters*, **4**, pp. R27-R38.
Penrose, R. (1989). *The Emperor's New Mind* (Oxford University Press).
Pesic, P. D. (1993). The smallest clock, *Eur. J. Phys.* **14**, pp. 90–92.
Schempp, W. (2003). Replication and transcription processes in the molecular biology of gene expressions: control paradigms of the DNA quantum holographic information channel in nanobiotechnology, *BioSystems* **68**, pp. 119–145.
Schrödinger, E. (1944) *What is Life?* (Cambridge University Press, Cambridge).
Tegmark, M. (2000). The importance of quantum decoherence in brain processes, *Phys. Rev. E* **61**, pp. 4194–4206.
Unruh, W. G., Zurek, W. H. (1989). Reduction of a wave packet in quantum Brownian motion, *Phys. Rev. D* **40**, pp. 1071–1094.
Vedral, V. (2003). Entanglement hits the big time, *Nature* **425**, pp. 28–29.
Wigner, E. P. (1957). Relativistic invariance and quantum phenomena, *Rev. Mod. Phys.* **29**, pp. 255–268.
Wigner, E. P. (1961). *The Probability of the Existence of a Self-Reproducing Unit.* Routledge & Keegan Paul, London, pp. 231-238.
Wooters, W. K. and Zurek, W. H. (1982). A single quantum cannot be cloned, *Nature* **299**, pp. 802–803.
Zurek, W. (1982). Environment induced superselection rules, *Phys. Rev. D* **26**, pp. 1862–1880.

About the author

Paul C. W. Davies is a theoretical physicist, cosmologist, and astrobiologist. He received his PhD in 1970 from University College London, under Michael Seaton and Sigurd Zienau. At Cambridge, he was a postdoc under Sir Fred Hoyle. He held academic appointments at the Universities of Cambridge, London and Newcastle-upon-Tyne before moving to Australia in 1990, first as Professor of Mathematical Physics at The University of Adelaide, and later as Professor of Natural Philosophy at Macquarie University in Sydney, where he helped establish the NASA-affiliated Australian

Centre for Astrobiology. In September 2006, he joined Arizona State University as College Professor and Director of a new interdisciplinary research institute called Beyond: Center for Fundamental Concepts in Science, devoted to exploring the "big questions" of science and philosophy. Davies' research has been mainly in the theory of quantum fields in curved spacetime, with applications to the very early universe and the properties of black holes, although he is also an expert on the nature of time. His astrobiology research has focused on the origin of life; he was a forerunner of the theory that life on Earth may have originated on Mars.

Davies is the author of several hundred research papers and articles, as well as 27 books, including *The Physics of Time Asymmetry* and *Quantum Fields in Curved Space*, co-authored with his former PhD student Nicholas Birrell. Among his recent popular books are *How to Build a Time Machine* and *The Goldilocks Enigma: Why is the Universe Just Right for Life?* (US edition entitled *Cosmic Jackpot*). He writes frequently for newspapers, journals and magazines in several countries. His television series "The Big Questions", filmed in the Australian outback, won national acclaim, while his theories on astrobiology formed the subject of a specially commissioned one-hour BBC 4 television production screened in 2003 entitled *The Cradle of Life*. In addition, he has also devised and presented many BBC and ABC radio documentaries on topics ranging from chaos theory to superstrings. Davies was awarded the 2001 Kelvin Medal and Prize by the UK Institute of Physics and the 2002 Faraday Award by The Royal Society. In Australia, he was the recipient of two Eureka Prizes and an Advance Australia award. Davies also won the 1995 Templeton Prize for his work on the deeper meaning of science. The asteroid 1992 OG was renamed (6870) Pauldavies in his honour.

Chapter 2

Quantum Mechanics and Emergence

Seth Lloyd

Quantum mechanics has two features that are important in guaranteeing the emergence of complex systems such as life. The first is discreteness: any finite quantum system with bounded energy has a finite number of distinguishable states. Quantum mechanics is inherently *digital*. The second is chanciness: the outcomes of some quantum events are inherently *probabilistic* [Peres (1995)].

This chapter shows that these two features combined, imply that quantum systems necessarily give rise to complex behaviour. Because it is digital, the universe can be thought of as a giant information processor: at its most microscopic scales, it is flipping bits. The universe computes. The computational nature of the universe is responsible for generating the structures—galaxies, stars, planets, humans, bacteria—we see around us [Lloyd (2006)]. Because it is probabilistic, the computing universe is effectively programmed by random quantum events called quantum fluctuations. These events inject random bits into the operation of the universe: they generate variation. It is this variation, processed by the universe's ongoing computation, which is responsible for the complexity of the structures we see around us.

The chapter is organized as follows. A few paragraphs each will review how quantum mechanics guarantees the digital and stochastic nature of the universe. Then we shall delve more deeply into how those features combine via the process of computation to produce complexity.

Received February 12, 2007

2.1. Bits

First, let us examine the consequences of discreteness. The universe is digital: the unit of digital information is the bit. A bit represents the distinction between two possibilities—Yes or No, True or False, 0 or 1. The digital nature of quantum mechanics is ubiquitous at the microscopic level. Bits are everywhere: the spin of an electron or the polarization of a photon registers a bit—strictly speaking, such bits are quantum bits, or "qubits" [Nielsen and Chuang (2000)]. The interactions between those bits give rise to a microscopic dynamics that is, in essence, a computation. As will be shown in detail below, the computational capability of the universe at its most microscopic level is a key ingredient in the spontaneous emergence of complexity. Anything that computes can be programmed to produce structure of any desired degree of complexity.

The digital nature of quantum mechanics implies that the universe is effectively computing not only at its most microscopic level, but at larger scales as well. The quantum nature of the universe implies that, at any given energy scale, the spectrum of elementary particles is finite. Of these elementary particles, only a few—protons, neutrons, electrons, photons—are sufficiently long-lived and interact sufficiently strongly to play a significant role in the energy scales involved in everyday life. This small number of elementary particles can combine to make a larger, but still finite set of simple chemicals. Just as the nonlinear interactions between elementary particles allow them to process information in a nontrivial way, the interactions between chemicals allow chemical reactions to perform the same type of logical operations that are performed by digital computers.

As we shall see below, because they are computing, chemical reactions spontaneously give rise to complex behaviour such as life. Exactly how and where life arose, we do not know. Once something is computing, however, we should not be surprised if it gives rise to the self-reproducing chemical structures that presumably formed the basis for proto-life. Because chemistry is digital, this proto-life—whatever it was—inherited its digital nature from chemistry. Later on, its descendants would inherit that beautiful digital structure, the genetic code: one base pair, two bits.

2.2. Coin Flips

Now let us look at the probabilistic nature of the universe. Although many processes in quantum mechanics are deterministic, like the great part of

the computational processes described above, some quantum events are intrinsically chancy. The best known of those events are the outcomes of measurements. Let us look at some examples of probabilistic quantum events.

As noted above, quantum systems are digital. The polarization of a photon, for example, has two distinguishable states: it represents a bit. One of those states could correspond to the electromagnetic fields of the photon wiggling back and forth: such a photon is said to be horizontally polarized. Regarding the photon as a bit, we can call this state, "0." The second state corresponds to the electromagnetic fields of the photon wiggling up and down: such a photon is said to be vertically polarized. Regarding the photon as a bit, we call this state, "1."

Such polarized photons are easy to produce: just pass ordinary light, which contains both types of photons, through the polarizing lenses of your sunglasses. The vertical ones pass through, while the horizontal ones are reflected. Since light reflected off water or the road consists primarily of horizontally polarized photons, polarizing sunglasses filter out glare. (The light of the sun consists of equal quantities of horizontally and vertically polarized photons. When it bounces at an angle off the surface of the water, many more horizontally polarized photons are reflected than are vertically polarized photons. So glare consists mostly of horizontally polarized photons. By filtering out the glare's horizontally polarized photons, your sunglasses restore the balance of the light.)

So far, so good. But now quantum mechanics kicks in. Photons can also be circularly polarized: their electromagnetic fields spiral around as they move along at the speed of light. What happens if one takes a circularly polarized photon and passes it through one's sunglasses? The sunglasses reflect horizontally polarized photons and transmit vertically polarized photons. But what about circularly polarized photons? It turns out that half the time the circularly polarized photon is transmitted and half the time it is reflected. When it is transmitted, its new polarization is vertical; when it is reflected, its new polarization is horizontal.

Whether or not the circularly polarized photon is transmitted is a purely chance event, like the toss of a fair coin. When you pass a string of circularly polarized photons through the sunglasses you are generating random, probabilistic outcomes. If we take reflection (photon ends up in a horizontal polarization) to correspond to 0, and transmission (photon ends up in a vertical polarization) to correspond to 1, then each time a circularly polarized photon passes through the sunglasses, a brand new, random bit is born.

The process by which quantum mechanics generates new, random bits of information is called *decoherence* [Griffiths (2003)]. Measurement generates decoherence, and so do a host of other quantum mechanical processes, notably quantum chaos. In particular, both measurement and chaos have the tendency to amplify small and weak signals, so that a tiny quantum fluctuation can end up having a substantial effect on the macroscopic world. Similarly, if one traces back thermal and chemical fluctuations in energy, temperature, pressure, particle number, etc., to their microscopic origins, one finds that such statistical mechanical fluctuations are in fact quantum mechanical in nature. That is, the probabilistic nature of statistical mechanics can, in the end, be traced back to the probabilistic nature of quantum mechanics.

Decoherence is a rich topic of research, into which we will delve no further here. For our purposes, what is important about decoherence is that it is ubiquitous. Quantum mechanics is constantly injecting brand new, random bits into the universe.

2.3. The Computational Universe

Quantum mechanics makes the world digital and provides variation. Now let us look more closely at how the universe is computing. We are all familiar with conventional digital electronic computers of the sort on which I am writing these words. But computation is a more general and ubiquitous process than what occurs within a Mac or a PC. For our purposes, computation can be thought of as a process that combines digital information with variation to produce complexity. This is a less familiar aspect of computation than, say spreadsheets or word processing. But the generation of complexity is no less part of computation than computer games and viruses. Indeed, the capacity of computers to generate complexity is one of their most basic intrinsic abilities.

What is a computer? A computer is a device that processes information in a systematic way. A digital computer operates on digital information, i.e. on bits. When I play a computer game, my computer breaks up the inputs that I give it into bits, and then processes and flips those bits one or two at a time. At bottom, all that a PC or Mac is doing is flipping bits.

Now we see why it is natural to regard the universe itself as a computer. Quantum mechanics guarantees the digital nature of the universe: at bottom, everything consists of quantum bits such as photon polarization.

(Other famous microscopic qubits are electron spin, the presence or absence of an electric charge, whether an atom is its ground or excited state, etc.) These bits are constantly flipping due to the natural microscopic dynamics of the universe. How they flip is governed by the laws of quantum mechanics. Some of this quantum bit flipping is deterministic, like the bit flipping in a classical digital computer. Some of these quantum bit flips are random, as when your sunglasses reflects or transmits a circularly polarized photon.

At first, the computational nature of the universe might seem like a radical, twenty first century discovery. In fact, the discovery that the universe is, at bottom, registering and processing information, was made in the nineteenth century. In the second half of the nineteenth century, the great statistical mechanicians James Clerk Maxwell, Ludwig Boltzmann, and Josiah Willard Gibbs, discovered the mathematical formula for entropy [Ehrenfest and Ehrenfest (1990)]. Up until that point entropy was a somewhat mysterious quantity that gummed up the works of heat engines, preventing them from performing as much work as they might otherwise. But what was entropy in terms of the motions of individual atoms and molecules? The energy of the molecules was simple to describe: it consisted of the kinetic energy inherent in the molecules' motion, and the potential energy stored in their chemical bonds. Entropy was more mysterious.

Finally, over decades of painstaking analysis, Maxwell, Boltzmann, and Gibbs discovered the mathematical formulation for entropy in terms of the motion of atoms and molecules. Phrased in contemporary terms, their formulae stated that entropy was proportional to the number of bits of information registered by the microsocopic state of the atoms and molecules. Each atom carries with it a small number of bits of information. Every time two atoms collide, those bits are flipped and processed. (The way in which bits flip when two atoms collide is governed by the Boltzmann equation.) The discovery that, at bottom, the universe computes was made more than one hundred years ago.

Maxwell, Boltzmann, and Gibbs, together with their successors, used the digital nature of the universe to analyze the behaviour of agglomerations of atoms and elementary particles, with spectacular success. Here, we will use the digital nature of the universe to analyse the creation of structure and complexity in the universe.

In order to perform this analysis, we must go deeper into the notion of digital computation. First, consider the concept of a program. A program is a sequence of instructions that tells the computer what to do. In other words, a program is a sequence of bits to which the computer attaches a

meaning. The meaning of the program need not be deep: for example, at a particular point in the operation of a given computer, the instruction "0" might mean "add $2 + 2$," while the instruction "1" might mean "add $4+0$." In a digital computer, each instruction on its own typically possesses a simple, prosaic meaning. By stringing many simple instructions together, however, arbitrarily complicated operations can be performed.

Above, it was noted that quantum fluctuations program the universe. All that this means is that the random results of quantum events, such as the reflection or transmission of a photon, can set into motion a sequence of further bit flips. Just how quantum fluctuations program the universe depends on the laws of quantum mechanics. Suppose, for example, that as a result of a quantum fluctuation a vertically polarized photon penetrates your sunglasses and is absorbed by your eye, causing a signal to propagate down your optic nerve to your brain. Your brain interprets this signal as indicating the presence of a fish just below the surface of the water, and you throw your spear in its direction. What does this photon mean? In this case, it means dinner!

Computers such as Macs and PCs have a special feature: they are universal digital computers. A universal digital computer is one that can be programmed to simulate the operation of any other digital computer. That is, a universal digital computer can be given a sequence of instructions that allows it to perform the same sequence of operations that any other digital computer performs. A familiar example of computational universality is the fact that a program that runs on one computer can be translated into a version of the program that runs on another computer. Microsoft Word can run both on a Mac and on a PC.

The universe is also a universal computer. Matter can be configured to compute. How so? Very simple. We "program" matter to imitate a Mac or PC simply by constructing a Mac or PC! Over the last decade or so, it has become clear that the universe itself is a universal computer at the most microscopic levels. In 1993, I showed how atoms and elementary particles could be programmed to perform any desired digital computation simply by shining light on them in the right way [Lloyd (1993)]. Since that time, my colleagues and I have constructed and demonstrated a wide variety of quantum computers that store bits on the spins of individual electrons and the polarizations of individual photons. Not only is the universe a universal computer, it can perform such universal computations at the most microscopic level.

A system need not be complex to be a universal digital computer. For example, the laws of physics are simple, and they support universal digital computation. Many simple extended systems, such as uniform arrays of bits with simple rules for interaction between them, are computationally universal.

2.4. Generating Complexity

In a way, the fact that the universe has generated huge complexity is highly puzzling. Our observations of the cosmos indicate that the universe began around 13.8 billion years ago. When it began, it was in a very simple, uniform state, the physical analog of a bit string that is nothing but zeros. As soon as the universe began, it began to evolve dynamically in time, governed by the laws of physics. But the known laws of physics are themselves simple: the equations of the standard model for elementary particles fit on the back of a T-shirt. Simple initial conditions and simple laws. So what happened?

When I look out my window I see trees, people, dogs, cars, and buildings, all immensely varied and complex. When I look through a microscope, I see the structure of materials and the behaviours of microorganisms, also tremendously varied and complex. When I look up into the sky I see planets, stars, and galaxies containing unimaginably greater quantities of complexity. Where did all this complexity come from?

The answer lies in the computational nature of the universe. Although a universal computer need not be complex in and of itself, it is nonetheless capable of exhibiting complex behaviour. A universal computer can be programmed to do anything a Mac or PC can do. Indeed, because the consequences of the laws of physics can be computed on a digital computer, it can in principle be programmed to do anything the universe can do! (Note, however, that a computer that was simulating the universe precisely would have to be at least as large as the universe itself.)

Above, we saw that the universe itself is a universal computer that is effectively programmed by random quantum fluctuations. Now we can ask the question, "How likely is the universe, starting from a simple state, to generate complex behavior?" There is an elegant branch of mathematics that deals with this very question. This branch of mathematics is called algorithmic information theory [Solmonoff (1964); Kolmogorov (1965); Chaitin (1987)]: one of the primary questions it asks and answers

is the question, "How likely is a universal computer, programmed with a random program, to generate any given structure?"

The central quantity in algorithmic information theory is algorithmic information content. The algorithmic content of some structure is equal to the length of the shortest computer program, written in some suitable computer language such as Java or C, that instructs the computer to produce that structure. Algorithmic information content was discovered independently by (in chronological order) Ray Solmonoff (1964), Andrey Kolmogorov (1965), and Gregory Chaitin (1987). It is Solomonoff's interpretation of algorithmic information that concerns us most here.

Solomonoff was interested in formalizing the notion of Ockham's razor. William of Ockham was a medieval English Philosopher and Franciscan monk. Ockham's razor is not a shaving implement, but rather a philosophical principle for "cutting away" needless complexity. Ockham phrased his razor in various ways: *Pluralitas non est ponenda sine necessitate*, ("Plurality should not be posited unless necessity") and *Frustra fit per plura quod potest fieri per pauciora* ("It is a mistake to make with more what can be made with less"). A later paraphrase of Ockham's razor is, *Entia non sunt multiplicand praeter necessitatem* ("Beings should not be multiplied beyond necessity"). Solomonoff made a mathematical paraphrase of the notion that brief explanations are preferable. He identified an "explanation" of a structure or string of bits as a computer program that instructs a computer to produce that structure or string. The briefest explanation is identified with the shortest program that produces the structure. The length of this program is the algorithmic information content of the structure and is denoted $K(s)$, where s is the structure in question. (More precisely, we should write $K_U(s)$ where and U denotes either the universal computer that is to be programmed to produce s, or the programming language that is to be used. Because any universal computer can be programmed to simulate any other computer, however, we have $K_U(s) = K_V(s) + O(1)$, where the $O(1)$ term is no longer than the length of the program that allows universal computer V to simulate U. In other words, algorithmic information content is to some degree independent of the computer or programming language used.)

To make the connection with probability, Solomonoff invoked the notion of a computer that has been programmed at random. A program is itself nothing but a string of 0s and 1s. If these 0s and 1s are generated completely randomly, as by tosses of a fair coin, then the probability that the first ℓ random bits reproduce a particular program of length ℓ is $2^{-\ell}$. Referring to the concept of algorithmic information, we see that the probability that the

randomly programmed computer produces the structure s is no less than $2^{-K(s)}$.

Suppose we take a random string of 0s and 1s and feed it into a computer as a program. The computer interprets those 0s and 1s as instructions and begins to execute them in sequence, reading and executing one bit after another. Structures that can be generated by short programs are more likely to arise than structures that can be generated only by long programs. Just what sort of structures can be generated by short programs? The answer is, all structures.

In particular, there exists a brief program that instructs the computer to start computing all computable structures. Ironically, the length of this program is much shorter than the program that causes the computer to generate some particular complex structure: it is easier to generate *all* structures than it is to generate any given one! Other structures that have short programs include (a) the known laws of physics (printable on a T-shirt), (b) the digits of π, (c) the spiral structure of galaxies, (d) . . . .

As noted above, many universal computers have very simple structure. That is, only a short program is required for our computer to simulate these other computers. A randomly programmed universal computer has a high probability of generating all sorts of other universal computers. Those computers in turn have a high probability of generating further computers, etc.

This nested generation of computing structures is a familiar feature of our universe. As noted above, the laws of physics support universal computation at their most microscopic scale, at the level of the laws of elementary particles. Quantum computers are the expression of this most microscopic computational power. As a consequence of this microscopic computational universality, it is no surprise that the universe exhibits computational universality at the next higher level, given by the laws of chemistry. This chemical computational universality is expressed by the coupled, nonlinear equations of chemical reactions that can encode all sorts of computational processes, including logic circuits, memory, switching processes, etc.

Similarly, it should be no surprise that the laws of chemistry give rise to computational universality at the next higher level, in the form of life. Life in its current form on earth is highly complex. But to get simple proto-life, only a few features are required. Apparently, all that is required for proto-life is the existence of physical systems that reproduce themselves with variation. As much as one might like to set other requirements for the origins of life, reproduction and variation seem to suffice.

Lots of chemical species manage to reproduce themselves within the context of autocatalytic sets—networks of interacting chemical reactions in which chemicals can catalyze, or enhance, their own production as part of their reactions with other chemicals [Kauffman and Farmer (1986); Jain and Krishna (1998)]. As part of the natural processes of chemical reactions, quantum fluctuations produce variation in the outputs of chemical reactions. As soon as one of these self-catalyzing chemicals constructs variants of itself that are also auto-catalytic, the origins of life are off and running. Variants that are more successful at producing copies of themselves become more prevalent in the chemical population; variants that are more successful in their interactions with other chemicals also survive to reproduce another day. These proto-living chemicals within their autocatalytic sets were presumably much simpler than life today. But if they were not very complex, they were nonetheless ambitious. We are their lineal descendants.

2.5. A Human Perspective

As life continued to evolve more and more variants and more and more complex forms, we should not be surprised that, amongst those forms, new types of computational universality arose. Human language, together with the mental apparatus that supports it, represents a remarkable and wonderful type of computational universality. Human language can express, well, anything that can be expressed in words. It is this universal capacity for language that sets us apart from other species; until the time, of course, that we discover such a capacity in them and begin to communicate with them as equals. For the moment, however, it is not evident that other species on Earth possess the rich linguistic ability that humans do.

Human beings, in turn, as they became more and more technically adept, spawned a new type of computational universality in the form of digital computation. Not only did we evolve the technologies to construct computers, but we bequeathed to them a stripped-down form of universal human language in the form of universal computer languages. Computers do not yet possess the emotional depth that would make us treat them as conscious beings. As time goes on, however, I suspect that we will regard some computers as more and more human (some of my students at MIT have already taken this step with their computers). There will be no single moment of creation of a computer we regard as our intellectual, emotional,

or even our spiritual equal. Rather, as computers become more and more capable and sympathetic beings, we will gradually assign to them the rights and capacities of more "conventional" humans, in just the same way that as human society progressed over history, it became clear to most men that women and slaves were, in fact, man's equal.

2.6. A Quantum Perspective

Quantum mechanics makes the world locally finite and discrete, allowing it to compute. It is this computational ability that allows the universe to generate complexity. But complexity does not arise from computation alone: it requires variation.

There is no one quantum-mechanical perspective: it is in the nature of quantum mechanics to reflect all possibilities at once. The chancy and probabilistic nature of quantum mechanics comes about exactly because quantum systems explore Yes and No, True and False, Horizontal and Vertical, or 0 and 1, simultaneously. Quantum computation, chemical reactions, and life itself, are constantly exploring and searching out the consequences of the possibilities allowed by the laws of physics.

At bottom, all the details that we see around us—the motions of air and water, the microscopic pattern of cells in a leaf—arise from quantum mechanical accidents that have been processed by the computing power of the universe. Quantum mechanics makes nature digital: it supplies the bits and the bit flips that are the substance of the the universe. Having supplied the world with its substance, quantum mechanics then adds the variety that is the proverbial spice of life. The result is what we see around us.

References

Chaitin, G. J. (1987). *Algorithmic Information Theory* (Cambridge University Press).

Ehrenfest, P., and Ehrenfest, T. (1990, reprint of 1912 edition). *The Conceptual Foundations of the Statistical Approach in Mechanics* (Dover).

Griffiths, R. (2003). *Consistent Quantum Theory* (Cambridge).

Jain, S. and Krishna, S. (1998). Autocatalytic Sets and the Growth of Complexity in an Evolutionary Model, *Phys. Rev. Lett.* **81**, pp. 5684–5687.

Kauffman, S. A., and Farmer, J. D. (1986). Autocatalytic sets of proteins, *Origins of Life and Evolution of Biospheres*, **16**, pp. 446–447.

Kolmogorov, A. N. (1965). *Three approaches to the quantitative definition of information*, *Problems of Information Transmission*, **1**, pp. 1–11.
Lloyd, S. (1993). A potentially realizable quantum computer, *Science* **261**, pp. 1569–1571.
Lloyd, S. (2006). *Programming the Universe* (Knopf).
Nielsen, M. A., and Chuang, I. L. (2000). *Quantum Computation and Quantum Information* (Cambridge University Press).
Peres, A. (1995). *Quantum Theory: Concepts and Methods* (Springer).
Solomonoff, R. J. (1964). A formal theory of inductive inference, *Information and Control* **7**, pp. 1–22.

About the author

Seth Lloyd was born on August 2, 1960. He received his AB from Harvard College in 1982, his MathCert and MPhil from Cambridge University in 1983 and 1984, and his PhD from Rockefeller University in 1988, under Heinz Pagels, for a thesis entitled *Black Holes, Demons, and the Loss of Coherence: How Complex Systems Get Information, and What They Do With It.* After postdoctoral fellowships at the California Institute of Technology and Los Alamos National Laboratory, he joined MIT in 1994 where he is currently a Professor of mechanical engineering, preferring to call himself a "quantum mechanic." His research area is the interplay of information with complex systems, especially quantum systems. He has made contributions to the field of quantum computation and proposed a design for a quantum computer. In his book, *Programming the Universe* (Knopf, 2006), Lloyd argues that the universe itself is one big quantum computer producing what we see around us. Lloyd is principal investigator at the MIT Research Laboratory of Electronics, and directs the Center for Extreme Quantum Information Theory (xQIT) at MIT.

PART 2

Quantum Mechanisms in Biology

This page intentionally left blank

Chapter 3

Quantum Coherence and the Search for the First Replicator

Jim Al-Khalili and Johnjoe McFadden

3.1. When did Life Start?

The Earth formed about 4 billion years ago out of the coalescing debris of the nascent solar system. But the newly formed planet remained uninhabitable for several hundred million years as it continued to be showered with massive rock fragments that would have vaporized the ocean. It was only when this battering slowed down, about 3.8 billion years ago, that liquid water became sufficiently stable to allow the formation of oceans. As liquid water is an essential ingredient of life on this planet (and probably on any other) it is generally agreed that life was not possible on the Earth until about 3.8 billion years ago. The earliest undisputed evidence for life arrives much later—about 3 billion years ago. There is however evidence—much disputed—that life started much earlier than this. Microbe-like fossils in Early Archaean rocks have been dated to 3.5 billion years ago [Schopf (2006); Rasmussen (2000)] but other researchers have claimed that these are of inorganic origin [Brasier *et al.* (2006, 2002)]. Chemical signatures of life (carbon isotope enrichment) have also been found at this age, or even a little earlier (some claim as early as 3.85 billion years ago), but once again the evidence is disputed. Until the disputed evidence is resolved the only thing we can say for sure is that life first emerged on Earth sometime between 3.0 and 3.8 billion years ago.

Received March 29, 2007

3.2. Where did Life Start?

Darwin famously mused on the possible origin of life in a warm little pond. Alexander Oparin and J. B. S. Haldane independently put scientific flesh on Darwin's speculation in the 1920s with what we now call the "primordial soup theory". The basic bones of the theory are that abiotic processes—heat, lightning, wind, rain, impacts etc. churned up inorganic material (ammonia, methane, water, hydrogen, etc.) on the early Earth to form the basic chemical ingredients of life: amino acids, sugars, etc.. These ingredients were still a long way from life itself but, dissolved in the early seas, oceans and ponds (the primordial soup), they could recombine, through random thermodynamic processes, to form more and more complex biomolecules. Eventually, and again through random thermodynamic processes, these primitive biomolecules would have associated with lipid membranes to enclose the biomolecules within some kind of "proto-cell". These proto-cells were not living in the conventional sense but they may have possessed the ability to divide—perhaps by simple binary fission—to form daughter proto-cells. Some of the daughter cells may have contained the same mix of biomolecules as the original proto-cell, whereas others would have inherited (again, through random processes) a slightly different mix of ingredients generating a population of variant proto-cells with slightly different properties. Some of the daughter proto-cells may have been incapable of self-replication, but others might have been more efficient than the parent proto-cells or their siblings. Over many generations of replication the population would have tended to become dominated by the more efficient self-replicating proto-cells and, as resources for replication became limited, a kind of chemical selection process (analogous to natural selection) would have kicked in to drive the population towards faster and more efficient replication. The more successful proto-cells would have gradually captured the characteristics and capabilities of living systems cell membranes, DNA, RNA, enzymes etc. until eventually the first living cell was born. There was obviously much that was vague and hand-waving about the Oparin-Haldane primordial soup theory, particularly the precise nature of the early self-replicators and how they formed, but the theory at least provide a credible alternative to divine creation as the origin of life.

3.3. Where did the Precursors Come From?

When Haldane and Oparin were speculating about primordial soups, the mechanisms responsible for replication of actual living cells were still largely unknown—the double helix was still nearly half a century away. But there was a general appreciation that various biochemicals—proteins, nucleic acids, sugars etc.—were probably necessary for the proto-cell to work. But where did these simple biochemicals come from? Organic molecules found on Earth today are nearly all the products of life; they are not formed in significant quantities abiotically. They are also rather unstable and break down pretty quickly once formed. For life to be initiated on the planet, it needed some way of making biomolecules abiotically. To solve this problem Haldane proposed that the early Earth possessed an atmosphere that was very different from today's: He proposed that the primordial Earth possessed a reducing atmosphere rich in compounds like methane, hydrogen, water and ammonia. In these conditions it is much easier to make biomolecules such as protein or nucleic acids (as these are reduced forms of carbon) and the biomolecules thus formed are more stable than they would be today. It was thirty years before Oparin and Haldan's speculations were put to the test in a simple set of experiments performed by Stanley Miller and Harold Urey in the 1950s. Miller and Urey constructed a kind of laboratory primordial soup: the chemical constituents of the supposed primordial atmosphere—ammonia, methane, hydrogen, water with electrical discharges to simulate lightning strike on the early Earth. Remarkably, when Miller and Urey analyzed the chemical composition of their soup after it had been cooking for several days they found that 10-15% of the carbon was now in the form of simple organic molecules such as amino acids. At least some of the ingredients of life could indeed have been made precisely as Haldane had predicted [Miller *et al.* (1976); Urey (1952)]. The Miller-Urey experiments were so remarkable that many thought that the problem of the origin of life had been more-or-less solved. When the work was published there was widespread anticipation that it would not be long before simple life forms were crawling out of origin of life experiments. But it did not happen. Why not? The answer is that the situation has become more complicated. For a start, the atmosphere of the early Earth is no longer thought to have been reducing. The present guess is that it was probably at best redox neutral dominated by compounds like carbon dioxide and nitrogen. Under these conditions it is much harder to form biomolecules like amino acids. Another problem was that although amino

acids were made, no proteins (polymers of amino acids) were synthesized. This is because the reactions were taking place in water, and since polymerization of biomolecules involves removal of water, life does not occur spontaneously in aqueous solutions. With water present in such excess the balance of the reaction is overwhelmingly towards hydrolysis rather than polymerization. A third problem was the chirality of biomolecules—such as (most) amino acids. All biomolecules come in either left-handed or right-handed forms, not both. But the Miller-Urey experiments (and all similar primordial soup experiments) synthesized equal amounts of left and right-handed forms. These racemic mixtures simply do not polymerize to form proteins. A fourth problem was that many essential biomolecules such as nucleic acids—were not formed in the Miller-Urey experiments and have since proven to be exceedingly difficult to form in any laboratory based primordial soup experiment.

3.4. What was the Nature of the First Self-replicator?

Even if all the biomolecules were present there was still a long way to go before a self-replicating system was made. Somehow, the cooked-up ingredients of the soup would have to have formed a self-replicating structure, such as the putative proto-cell. But how feasible is the abiotic synthesis of the self-replicating proto-cell? To answer this question we must have some idea of what the proto-cell was made of. Unfortunately none have survived today and they have left no fossil records. The first undisputed evidence for living cells are bacterial-like fossils within layered structures called stromatolites that existed about 3 billion years ago. These are similar to structures that are still formed today in shallow seas that are generated by a photosynthetic group of bacteria called cyanobacteria (blue-green algae). Capturing light from the sun and both carbon and nitrogen from the air, cyanobacteria form microbial mats in annual cycles that eventually build up into stromatolites. But cyanobacteria are nothing like a proto-cell. Their cells are rather complex for bacteria with outer and inner membranes, and include a set of internal organelles that perform the photosynthesis reaction and (in many cyanobacteria) another organelle that captures and fixes nitrogen. Their cells contain DNA, RNA, proteins, sugars, fats and hundreds of other biomolecules. The complete genome of several members of the group have recently been sequenced and the size of their genome ranges from the relatively small 1.6 megabases (1.6 million base pairs) genome of

Prochlorococcus marinus through to the hefty 9 megabase genome of *Nostoc punctiforme*. The genome of even the simplest of these organisms, the diminutive *P. marinus* (with a cell size between 0.5-0.7 μm, these are the smallest photosynthetic organisms known to date) encodes more than 1,800 genes. Each gene is composed of several hundred to several thousand bases encoding a protein with many hundreds of amino acids folded into high specific and information rich structures—enzymes—that perform the complex biochemical reactions of DNA replication, protein synthesis, photosynthesis and energy generation. *Prochlorococcus* is clearly the product of a long evolutionary process and the same is presumably true for the organisms that built the fossil stromatolites. They were not proto-cells but must have been the descendants of simpler cellular life. But how simple is simple? What is the minimal cell necessary for life? This question can at least be addressed today and the answer is: not very simple at all. The simplest self-replicating organisms alive today are, as far as we know, the mycoplasmas that have a genome size of 580,000 base pairs, sufficient to code for nearly five hundred proteins! But even mycoplasmas are not feasible primordial organisms because they are in fact descended from more complex bacteria by gene loss and this reductive evolution has left them very enfeebled. They are parasites that grow best inside living cells requiring their host cell to make many of their biomolecules. They are unlikely inhabitants of any primordial soup. Bacteria even simpler than mycoplasmas have been discovered, such as the recently sequenced parasitic organism *Nanoarchaeum equitans*, which, with a genome size of only 490,000 base pairs, is the smallest bacterial genome known. Viruses do of course have much simpler genomes, but these (and *N. equitans*) are parasites of living cells. They rely wholly (viruses) or partly (*N. equitans*) on their host cells to provide the essential functions of life. They are not viable primordial soup organisms. So we are left with a dilemma. The simplest self-replicating organisms alive today are far from simple and unlikely to have formed spontaneously in the primordial oceans. The astronomer Fred Hoyle considered the probability of assembling a structure like a bacterium from the random thermodynamic processes available on the early Earth and likened its chances to that of a tornado in a junkyard spontaneously assembling a Boeing 747.

3.5. The RNA World Hypothesis

If cells are too complex to form spontaneously then perhaps some precellular self-replicator was not a cell but some kind of naked self-replicating

DNA or protein. But a problem with this scenario is that DNA or proteins do not self-replicate today. DNA makes RNA makes proteins and proteins make enzymes that replicate DNA. The genetic information is stored in DNA, transcribed into the mobile messenger nucleic acid, RNA, and then translated into strings of amino acids that fold into proteins. These folded proteins then make enzymes capable of chemical catalysis that are responsible for all the dynamics of living cells: energy capture, mobility, DNA replication etc. You need DNA and RNA to make enzymes. But you need enzymes to make DNA or RNA! A possible way out of this chicken and egg scenario was provided in the 1970s with the discovery that some forms of RNA could also act as catalysts. Ribozymes, as they came to be known, could close the loop between heredity (it can store genetic information) and metabolism (it can catalyse biochemical reactions). Perhaps the first self-replicator was a ribozyme? The idea of an early precellular phase of life dominated by ribozymes has become probably the most popular origin of life scenario [Orgel (2004)]. Ribozymes have been shown to be capable of catalysing quite a wide range of biochemical reactions and can even act as simple "replicases" capable of stitching together two fragments of themselves to generate a copy. There are however a number of problems with the RNA world hypothesis. The first is that no one has yet found a feasible way to generate RNA in any plausible primordial soup experiment. RNA is a more complex biomolecule than an amino acid and is far harder to make! The second problem is the fact that ribozymes are already rather complex structures. A recent study by David Bartel's group at MIT used an artificial evolutionary process to select for ribozymes capable of performing RNA polymerization reactions (essential component of an RNA self-replicator). The strategy did identify some novel ribozyme structures [Johnston *et al.* (2001); Lawrence and Bartel (2005)] but the minimum size for any kind of replicase activity was 165 bases, at least ten-fold bigger than anything that might be synthesized in even the most optimistic primordial soup RNA synthesis scenarios. Even if it were possible to generate structures as large as 165 bases, the chances of generating Bartel's ribozyme by random processes (in their experiments their starting point was a known RNA ligase) are exceedingly small. There are 4^{165} (or 2×10^{99}) possible 165 base long RNA structures. If there was just one molecule of each of the possible 165 base long RNA molecules in the primordial soup then the combined mass of all those RNA molecules would be 1.9×10^{77} kilograms. To put this number in perspective, the entire mass of the observable universe is estimated as approximately 3×10^{52} kilograms. It clearly would have to have

been an astronomically big pond to have had any chance of generating a ribozyme self-replicator by random processes alone. We thereby come to the crux of the origin of life problem. It is not that it is difficult to form the chemical precursors (although it is) or identify proteins or RNA molecules capable of performing some of the necessary steps of self-replication. The problem is a search problem. The self-replicator is likely to be only one or a few structures in a vast space of possible structures. The problem is that random searches (essentially thermodynamic processes) are far too inefficient to find a self-replicator in any feasible period of time. An examination of the origin of life problem from an information science perspective has recently reached the same conclusion [Trevors and Abel (2004)]. This is probably true not only of carbon-based self-replication systems but also of digital life. Although digital self-replicating programs, such as Tierra, have been created in computers [Bedau *et al.* (2000)] digital life has not, so far, emerged spontaneously out of the huge volume of digital traffic of the internet. This is all the more surprising since we know that self-replicating programs—able to infect and replicate in the primordial soup of the internet are surprisingly easy to make: we call them computer viruses. But, as far as we are aware, all known computer viruses have been synthesized by hackers; none has emerged spontaneously out of the digital primordial soup of the internet. Why has not the internet generated its own digital life? The answer is probably that self-replication, even in the protected environment of digital computers, is too complex to emerge by chance.

3.6. A Quantum Mechanical Origin of Life

It hardly needs stating that quantum mechanics plays an important role in biology since it underlies the nature of atomic and molecular structure, and therefore the nature of molecular shapes and bonding, and hence the templating functions of nucleic acids and the specificity of proteins. It is also crucial in explaining differential diffusion rates, membrane specificity, and many other important biological functions. Thus quantum mechanics underpins at the most fundamental level the machinery of life itself. However, what is emerging today is the notion that quantum mechanics may play more than this basic role of determining molecular structure, bonding and chemical affinity. After all, biology is based on chemistry, which in turn is subject to quantum principles such as Pauli's Exclusion Principle. Thus, a number of the more counterintuitive features of the theory, such

as quantum superposition, entanglement, tunnelling and decoherence, may also turn out to play a vital role in describing life itself. This is not so speculative as it sounds; it is already well established that quantum tunnelling of protons may alter the structure of nucleotide bases and can be responsible for certain types of mutations. Likewise, it plays a vital role in many enzyme-driven reactions and enzyme catalysis. We propose here that some of these more profound aspects of quantum mechanics may have provided a helping hand in kick starting life within the primordial soup.

3.6.1. *The dynamic combinatorial library*

Consider some small corner of the primordial soup—perhaps a drop of liquid trapped within a rock cavity. We propose that the drop contains some proto-self replicator structures—perhaps RNA or amino acid polymers that are large enough to form a self-replicator, but are in the wrong region of sequence space so they are unable to self-replicate. We also imagine that the proto self-replicators are subject to some kind of mutational process that changes their structure by standard chemical reactions—breaking and forming chemical bonds. Somewhere out there in the vast chemical structure space available to the proto self-replicators is the correct structure for an actual self-replicating RNA or peptide but, as discussed above, for a limited number of proto self-replicating molecules this become a massive search problem that cannot be solved in any reasonable time period, at least in a classical system. The problem for the classical system is that the chemical mutational process of forming new configurations/structures is very slow and limited by the number of molecules available to do the searching. A proto-replicator may suffer a chemical change (a chemical "mutation") to form any new structure that may or may not be a self-replicator. Usually of course the new structure will not be a self-replicator so to *try again* the system must dismantle the newly-formed structure by the same chemical processes—breaking and forming covalent bonds—before another novel structure can be formed by another chemical mutation. With a limited pool of proto self-replicators available in our primordial soup the *library* of possible structures made by the system will be very tiny in comparison to the total space of structures that needs to be searched. The time available for this search is of course tens, or hundreds, of millions of years from the time that conditions on Earth first reached their "Goldilocks values" to the time that the first simple self-replicators emerged. However, given the shear improbability that the correct configuration is hit upon by

chance and the time taken for classical chemical mutation of breaking and reforming covalent bonds, speeding up of the search mechanism would be greatly desired. To make the search more tractable we propose that we consider the library of structures in our soup as a *dynamic combinatorial library*. Combinatorial libraries have been widely used in the pharmaceutical industry to identify novel drug compounds. Essentially a library of related chemical compounds is synthesized by standard chemical synthesis methods: the combinatorial library. The library can then be screened for binding to a particular ligand say a viral protein—to identify a compound that will bind to the virus and perhaps prevent it binding to host cells. Dynamic combinatorial libraries are a recently introduced variation on the combinatorial library approach [Ramstrom and Lehn (2002)] whereby reversible chemical self-assembly processes are used to generate the libraries of chemical compounds. Dynamic combinatorial chemistry allows for the generation of libraries based on the continuous interconversion between the library constituents. Reversible chemical reactions are used for spontaneous assembly and interconversion of the building blocks to continually generate novel structures. The dynamic combinatorial library is thereby able to form all possible combinations of the building blocks, within the time and chemical resources at its disposal. Addition of a target ligand or receptor can even be used to capture binding compounds and thereby drive the synthetic reactions towards synthesis of chemical binders. It is easy to see that the primordial soup may be considered to be a dynamic combinatorial library capable of forming novel structures by reversible processes and some of those novel structures could eventually become self-replicators. However, the system still suffers from the search space problem: there are not enough molecules within the dynamic combinatorial soup to find the self-replicator within a feasible timescale. We thus add a further mechanism to the dynamic combinatorial library soup proposal: that the compounds within the library are linked, not only via reversible reactions but via quantum mechanics. Quantum tunnelling is a familiar process in chemistry where it is often known by another name: *chemical tautomerization*. Many compounds, for instance nucleotide bases, are found in mixtures of related chemical structures, known as tautomers. For nucleotide bases the tautomeric structures differ in the position of protons within the nucleotide bases to form enol of keto forms of the bases with different base-pairing properties (since these protons are involved in Watson and Crick base-pairing). The alternative positions of the protons in the enol and keto forms are linked, not by conventional chemical reactions, but by proton tunnelling [Douhal

et al. (1995)]. Each preparation of tautomeric compounds such as adenine (a nucleotide base) contains a mixture of its tautomeric forms. The balance between the alternative tautomeric forms depends on the relative stability of each tautomer. Nucleotide bases usually exist predominantly in one of the other keto or enol forms. But we must remember that the conversion between the forms is quantum mechanical. Each molecule of a DNA base is not in either the enol or keto form but must exist as a superposition of both forms linked by proton tunnelling. We now return to our primordial pool and imagine it to be a quantum dynamic combinatorial library with many molecules of a single compound that can *each* exist in a quantum superposition of many tautomeric states simultaneously. The issue here is one of time scales; if such a quantum superposition of all possible states in the combinatorial library can be built up before the onset of decoherence then this becomes an extremely efficient way of searching for the correct state: that of a simple replicator. Searches of sequence space or configuration space may proceed much faster quantum mechanically. In effect, a quantum system can "feel out" a vast array of alternatives simultaneously. So the question is: can quantum mechanics fast-track matter to life by "discovering" biologically potent molecular configurations much faster than one might expect classically? This is, after all, just the principle that underlies the concept of a quantum computer. In effect, quantum computation enables information processing to take place in a large number of states in parallel, thus shortcutting the computation resources necessary to process a given amount of information. There are two perceived problems with this idea. Firstly, it has been argued that while it is easy to believe that quantum superpositions might accelerate the "discovery" of the correct and unique replicator state from amongst the myriad of other equally complex but wrong structures, an element of teleology is required; namely that the molecule must somehow know before hand what it is aiming for. We do not believe this is necessary (as we argue below). The second problem is more serious and less understood. It involves the estimate of how long the delicate quantum superposition can be maintained before the onset of decoherence, the process by which the delicate superposition is destroyed through interactions with the surrounding environment. In order to quantify very roughly the timescales involved we employ a simple example.

3.6.2. *The two-potential model*

We propose a 1-dimensional quantum mechanical model of a double potential well containing a single particle that must exist in a superposition of

being in both sides of the well until measured. There are plenty of examples of such a situation, such as the inversion resonance in NH_3 in chemistry or strangeness oscillations in the neutral K-meson in physics. Consider a 1-D double oscillator potential, $V(x)$, symmetric about $x = 0$ and defined as

$$V(x) = \frac{m\omega^2}{2} \left(|x| - a\right)^2 , \tag{3.1}$$

where m is the mass of the particle, ω is the oscillator parameter and $2a$ is the distance between the two sites. If the particle starts off on the right hand side of the double well then it can be described by a superposition of the lowest two eigenstates of the full Hamiltonian of the system

$$\psi(x, t = 0) = \frac{1}{\sqrt{2}} \left(\psi_0 + \psi_1\right) . \tag{3.2}$$

Standard textbook quantum mechanics shows the time evolution of this state, which shuttles back and forth between the two wells. This "shuttling" time that describes how long it takes for the particle to tunnel across from one side of the double well to the other is given by

$$t_s = \frac{\hbar}{2\Delta E} , \qquad \Delta E = E_1 - E_0 , \tag{3.3}$$

where E_0 and E_1 are lowest two energy eigenvalues. However, as is well-known with all quantum tunnelling, t_s is extremely sensitive to the potential parameters since

$$\Delta E = 2\hbar\omega \sqrt{\frac{2V_0}{\pi\hbar\omega}} \exp\left(-\frac{2V_0}{\hbar\omega}\right) , \tag{3.4}$$

where the height of the potential barrier between the two wells is

$$V_0 = \frac{1}{2} m\omega^2 a^2 . \tag{3.5}$$

Typically, $a = 1$ Å, $m = 10^{-27}$ kg (proton mass) and $\omega = 10^{12}$ Hz (terahertz vibration frequency typical in molecular physics). These give a value of $t_s = 10^{12}$ seconds. Experimentally, coherent proton tunnelling in a hydrogen bonded network gives a timescale of $t_s = 10^{-7}$ seconds [Horsewill *et al.* (2001)]. Of course, in order for our proto-replicator molecule to explore all possibilities the quantum mechanical evolution of its wave function will involve a large number of such tunnelling processes. However, they will all take place simultaneously within a similar timescale t_s from the moment the molecule is left to its own devices as a quantum system isolated from its environment.

3.6.3. *Decoherence*

The crucial other timescale therefore is the decoherence time, t_D—this is the time that the full quantum superposition of all possible states in the combinatorial library can be explored before the interaction with the surrounding environment destroys it. The noise of the environment effectively scrambles the delicate phases between the many different terms in the full wave function of the system. After collapse due to such thermal decoherence, the quantum state is reset and the wave function evolves again. Of course if decoherence is rapid ($t_D < t_s$) then we would essentially have a quantum Zeno effect in which the molecule never gets a chance to explore other configurations before collapsing back to its original state. However, provided $t_D > t_s$ then each time the complex quantum superposition collapses there is a (very tiny) chance that it will find itself in the correct replicator configuration. The advantage this now has, of course, (over classical non-quantum searching) is that this search takes place far more rapidly than it would if it had to explore (build-dismantle-rebuild) each possible structure in the combinatorial library one by one through chemical reactions and random thermal collisions.

3.6.4. *Replication as measurement*

But what if the correct structure for a replicator *is* hit upon following decoherence? Would not this unique state simply be lost as quickly as it is found once the wave function evolves yet again? We argue not. Consider if, once formed, the self-replicator then does what it is uniquely able to do: replicate. Now, the dynamics of the system will be subtly but significantly changed. Under these conditions, the thermal field is not the only source of decoherence. Self-replication will incorporate precursor molecules into newly-formed replicators. In these circumstances, self-replication will inevitably couple the system more strongly with the environment. In a sense, the possibility of self-replication is constantly examining the system for tunnelling events that can form the self-replicator. And, *crucially*, these examinations do not merely look; they "capture" the replicator state by virtue of their property of self-replication. Once a self-replicator is present then it will be permanently coupled to its environment through the replication process. Thus, while decoherence takes place all the time and, with overwhelming likelihood leads every time to the "wrong" structure, once the replicator is formed, the process of replication becomes an "irreversible

act of amplification" (a classical measurement as defined by one of the founders of quantum mechanics, Niels Bohr) of the system. That is, by coupling more strongly to its environment, the replicator state announces itself as being "macroscopically distinguishable" from all the other possible structures the molecule could have. There is no teleology needed here since we describe the measurement as a two-step process: the inevitable and very rapid environment-induced decoherence process taking place all the time followed, in the unique case of the replicator state being discovered, by the irreversible dragging out of this state into the macroscopic world. Of course, the biological process of replication is on a time scale far greater than those discussed above, but we argue that it is the stronger coupling of this state to its environment (such as its ability to utilize the chemicals in the environment for replication) that marks it out as special. To reiterate then: provided the search time needed for exploring all possible structures within the quantum combinatorial library is shorter than the decoherence time, which in turn is many orders of magnitude shorter than the time it would take to explore all the possible structures "classically", then quantum mechanics can provide a crucial advantage in the locating that special replicator state.

3.6.5. *Avoiding decoherence*

There remains, however, the issue of how long such a delicate and complex quantum state can be maintained and decoherence kept at bay. Of course we are not suggesting that every molecule of the requisite complexity will, every time, explore all regions of the combinatorial library space, but rather only those molecules that are already close enough to the replicator state for them to be linked to it via quantum tunnelling of protons or even superpositions of different shapes. This "shape co-existence" is well known in many areas of quantum physics. For instance, in nuclear physics, the lead isotope ^{186}Pb has a nuclear ground state that looks like a superposition of three different shapes simultaneously: spherical, prolate and oblate. Even in biology, the protein tubulin that makes up the microtubules within neurons has been suggested to be in a superposition of two different shapes.

Keeping decoherence at bay is of course a tall order in the complex, warm and wet conditions of a primordial pool that are not the kind of conditions where one would expect to find significant quantum coherence. However, there are many gaps in our understanding of decoherence in complex systems. Recent demonstrations of dynamical tunnelling [Hensinger *et al.*

(2001)], indicates that our understanding of quantum coherence within dynamic systems is far from complete. Recent experiments [Margadonna and Prassides (2002)] demonstrating superconductivity in doped fullerene (C_{60}) molecules) at 117 K (with indications that higher temperatures may be attainable) indicate that certain organic structures may indeed support quantum superpositions. Transport of charges along the DNA double helix by hole transfer through quantum tunnelling has also been recently demonstrated [Giese *et al.* (2001)], as has coherent proton tunnelling in a hydrogen bonded network [Horsewill *et al.* (2001)]. It should also be remembered that intramolecular quantum tunnelling is of course responsible for the room temperature chemical properties of conventional chemicals, such as benzene (tunnelling of the three π electrons across all bonds in the benzene ring) and the tautomeric forms of compounds such as nucleotide bases, as discussed above. Quantum tunnelling of electrons and protons is also proposed to be involved in a number of enzyme reactions [Scrutton (1999); Scrutton *et al.* (1999); Sutcliffe and Scrutton (2002)] and proton tunnelling has recently been shown to be the dominant reaction mechanism accounting for the rate acceleration performed by the enzyme aromatic amine dehydrogenase [Masgrau *et al.* (2006)]. If our proposal is correct then some way of sustaining quantum coherence, at least for biochemically—if not biologically—significant time scales must be found. It is already known there are two ways in which this can occur. The first is screening: when the quantum system of interest can be kept isolated from its surrounding (decohering) environment. Very little is known about the screening properties of biological molecules. For example, a reaction region enveloped in an enzyme molecule will be partially screened from van der Waals-mediated thermal interactions from the rest of the cell. Similarly, the histone-wrapped double helix might serve to shield coding protons in DNA from decoherence. The second possibility concerns what are known as decoherence-free subspaces. In the effort to build a quantum computer, much attention has been given to identifying degrees of freedom (technically, subspaces of Hilbert space) that are unaffected by the coupling of the system to its environment. Paradoxically, when a system couples very strongly to its environment through certain degrees of freedom, it can effectively "freeze" other degrees of freedom by a sort of quantum Zeno effect, enabling coherent superpositions and even entanglement to persist. A clear example has been presented [Bell *et al.* (2002)] in the context of neutrino oscillations in a medium, but their model serves to make the general point. These authors consider a double-well one-dimensional potential—for further discussion see Section 1.3 in Chapter 1.

3.7. Summary

There are of course many difficulties with this scenario, but, as described above, there are many difficulties with all explanations of the origin of life. If the emergence of life depended on an unlikely sequence of maintenance of quantum coherence within some small primordial pool then it may yet be the most plausible "origin of life" scenario. And the proposal has one further merit: it could be explored experimentally. As stated earlier, our proposal is of course tied closely to the feasibility of building a quantum computer and we do not realistically see how the merits of the former can be explored and tested before we fully understand the possibilities of the latter.

References

Bedau, M., McCaskill, J., Packard, N., Rasmussen, S., Adami, C., Green, D., Ikegami, T., Kaneko, K., and Ray, T. (2000). Open problems in artificial life, *Artif. Life* **6**, pp. 363–376.

Bell, N., Sawyer, R., Volkas, R., and Wong, Y. (2002). Generation of entangled states and error protection from adiabatic avoided level crossings, *Phys. Rev. A* **65**, art. no. 042328.

Brasier, M., Green, O., Jephcoat, A., Kleppe, A., Kranendonk, M. V., Lindsay, J., Steele, A., and Grassineau, N. (2002). Questioning the evidence for earth's oldest fossils, *Nature* **416**, pp. 76–81.

Brasier, M., McLoughlin, N., Green, O., and Wacey, D. (2006). A fresh look at the fossil evidence for early archaean cellular life, *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* **361**, pp. 887–902.

Douhal, A., Kim, S., and Zewail, A. (1995). Femtosecond molecular dynamics of tautomerization in model base pairs, *Nature* **378**, pp. 260–263.

Giese, B., Amaudrut, J., Kohler, A., Spormann, M., and Wessely, S. (2001). Direct observation of hole transfer through DNA by hopping between adenine bases and by tunnelling, *Nature* **412**, pp. 318–320.

Hensinger, W., Haffner, H., Browaeys, A., Heckenberg, N., Helmerson, K., McKenzie, C., Milburn, G., Phillips, W., Rolston, S., Rubinsztein-Dunlop, H., and Upcroft, B. (2001). Dynamical tunnelling of ultracold atoms, *Nature* **412**, pp. 52–55.

Horsewill, A., Jones, N., and Caciuffo, R. (2001). Evidence for coherent proton tunnelling in a hydrogen bond network, *Science* **291**, pp. 100–103.

Johnston, W., Unrau, P., Lawrence, M., Glasner, M., and Bartel, D. (2001). RNA-catalyzed RNA polymerization: accurate and general rna-templated primer extension, *Science* **292**, pp. 1319–1325.

Lawrence, M., and Bartel, D. (2005). New ligase-derived RNA polymerase ribozymes, *RNA* **11**, pp. 1173–1180.

Margadonna, S., and Prassides, K. (2002). Recent advances in fullerene superconductivity, *J. Solid State Chem.* **168**, pp. 639–652.

Masgrau, L., Roujeinikova, A., Johannissen, L., Hothi, P., Basran, J., Ranaghan, K., Mulholland, A., Sutcliffe, M., Scrutton, N., and Leys, D. (2006). Atomic description of an enzyme reaction dominated by proton tunnelling, *Science* **312**, pp. 237–241.

Miller, S., Urey, H., and Oro, J. (1976). Origin of organic compounds on the primitive earth and in meteorites, *J. Mol. Evol.* **9**, pp. 59–72.

Orgel, L. (2004). Prebiotic chemistry and the origin of the RNA world, *Crit Rev. Biochem. Mol. Biol.* **39**, pp. 99–123.

Ramstrom, O., and Lehn, J. (2002). Drug discovery by dynamic combinatorial libraries, *Nat. Rev. Drug Discov.* **1**, pp. 26–36.

Rasmussen, B. (2000). Filamentous microfossils in a 3,235-million-year-old volcanogenic massive sulphide deposit, *Nature* **405**, pp. 676–679.

Schopf, J. (2006). Fossil evidence of archaean life, *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **361**, pp. 869–885.

Scrutton, N. (1999). Colworth medal lecture: Enzymes in the quantum world, *Biochem. Soc. Trans.* **27**, pp. 767–779.

Scrutton, N., Basran, J., and Sutcliffe, M. (1999). New insights into enzyme catalysis. ground state tunnelling driven by protein dynamics, *Eur. J. Biochem.* **264**, pp. 666–671.

Sutcliffe, M., and Scrutton, N. (2002). A new conceptual framework for enzyme catalysis. hydrogen tunnelling coupled to enzyme dynamics in flavoprotein and quinoprotein enzymes, *Eur. J. Biochem.* **269**, pp. 3096–3102.

Trevors, J., and Abel, D. (2004). Chance and necessity do not explain the origin of life, *Cell Biol. Int.* **28**, pp. 729–739.

Urey, H. (1952). On the early chemical history of the earth and the origin of life, *Proc. Natl. Acad. Sci. USA* **38**, pp. 351–363.

About the authors

Jim Al-Khalili obtained his PhD at the University of Surrey under Ronald C. Johnson. He is presently a theoretical physicist at the University of Surrey, UK, where he also holds a chair in the public engagement in science. He has published widely in his specialist field of theoretical nuclear physics where he has developed quantum scattering methods to model the structure and properties of light exotic nuclei. He has published several popular science books on a range of topics in physics and is a regular broadcaster on radio and television. He is a fellow of the UK Institute of Physics and a trustee of the British Association for the Advancement of Science.

Johnjoe McFadden obtained his PhD from Imperial College, London, under Ken Buck. He is professor of molecular genetics at the University of Surrey, UK. For more than a decade, he has specialised in examining the genetics of microbes such as the agents of tuberculosis and meningitis and he invented a test for the diagnosis of meningitis. He has published on subjects as wide-ranging as bacterial genetics, tuberculosis, idiopathic diseases and computer modelling of evolution and has edited a book on the genetics of mycobacteria. He has produced a widely reported artificial life computer model and is author of the popular science book, *Quantum Evolution*.

This page intentionally left blank

Chapter 4

Ultrafast Quantum Dynamics in Photosynthesis

Alexandra Olaya Castro, Francesca Fassioli Olsen, Chiu Fan Lee, and Neil F. Johnson

4.1. Introduction

Photosynthesis lies at the heart of the process of life on Earth. After photon absorption by a light-harvesting (LH) antenna, the central step in photosynthesis is excitation-transfer to a molecular complex that serves as a reaction centre (RC) where the excitation is trapped, thereby allowing charge separation to take place [Ritz *et al.* (2002); van Amerongen *et al.* (2002)] (see Fig. 4.1). This transfer takes only a few hundred picoseconds and is performed with extraordinarily high efficiency: most of the absorbed photons give rise to a charge separation event. These observations are all the more remarkable when one considers the rather extreme environmental conditions in which these organisms manage to survive, and they provide an enormous motivation for studying and manipulating natural photosynthetic systems, as well as building artificial nanostructures, which can emulate the early steps of photosynthesis.

One of the most fundamental and long standing questions about these early steps in the photosynthetic process, concerns the extent to which quantum coherent phenomena might play a role in the high-efficiency transfer [Hu and Schulten (1997)]. The issue is tremendously controversial. Some experimental works have claimed the observation of coherent delocalized excitations around the B850 ring of the LH-II complex of purple bacteria [van Oijen *et al.* (1999)] at low temperature (1K). Others have suggested that

Received February 23, 2007

even at such low temperatures, coherence only extends around a few chromophores [Trinkunas *et al.* (2001)]. Although it has been widely accepted that excitations in the B800 ring of LH-II are localized, recent discussions suggest that coherence in such molecules does indeed affect the excitation-transfer dynamics [Cheng and Silbey (2006)].

In this chapter, we are interested in the dynamics of energy transfer in the LH-I-RC subunit. Although the evidence for coherence in the LH-I-RC complex is fairly sparse, Ketelaars *et al.* (2002) supports the view of largely delocalized excited states in the LH1 assembly of pigments at low temperatures. Remarkably, a recent report by Engel *et al.* (2007) presents empirical evidence of quantum beats associated with electronic coherence in the Fenna-Matthews-Olson (FMO) bacteriochlorophyll complex, which connects a large peripheral LH antenna to the reaction centre. Theoretical support for quantum coherence in photosynthesis is ambiguous, with some phenomenological works indicating that coherence will induce higher excitation-transfer rates [Jang *et al.* (2004)] while others argue that this may not necessarily be the case [Gaab and Bardeen (2004)]. Even in the simplified limit where the LH network is replaced by a set of interacting two-level systems, there is still no clear theoretical picture as to how quantum coherence might affect the efficiency of an LH network [Gaab and Bardeen (2004)].

Against this backdrop, the excitation transfer in organic dendrimers—which are nanometre-size macromolecules with a regular tree-like array of branch units [Fréchet (1994)]—has attracted significant attention recently through the prospect of creating artificial photosynthetic systems [Ranasinghe *et al.* (2002); Varnavski *et al.* (2002); Lupton *et al.* (2002); Ranasinghe *et al.* (2003); Andrews and Bradshaw (2004)]. One of the key elements in these artificial systems is the evidence of coherent energy transfer mechanisms. These experiments therefore open up the possibility of exploring in detail the interplay between quantum coherence and the efficiency of artificial light-harvesting units, and should in turn help understand the possible roles of quantum coherence in natural photosynthesis.

Motivated by this experimental possibility, we wish to investigate how quantum superposition and entanglement might be exploited in a prospective photosynthetic complex which exhibits such coherent energy transfer mechanisms. Using a quantum jump approach [Carmichael (1993); Plenio and Knight (1998)], we show a dual role for quantum superposition and entanglement in the LH-I-RC subunit. It is shown that such quantum phenomena can be used to (1) increase the photosynthetic unit's efficiency,

or (2) act as a "crowd control" mechanism that modifies the efficiency in such a way that it reduces the possibility of burnout of the photosynthetic machinery. These results therefore provide significant motivation for exploiting such quantum phenomena in the development of future artificial photosynthetic complexes. They also give additional insight into the role that quantum coherence could play in natural photosynthetic units.

We begin the chapter with a brief description of the main features that define a photosynthetic unit in the coherent regime. With the photosynthetic apparatus of purple bacteria in mind (Fig. 4.1) we consider such a unit to be made up of donors surrounding acceptors at a reaction centre, as illustrated in Fig. 4.2(a). The fact that there has been no experimental evidence presented to date for coherent transfer in the LH-I-RC of purple bacteria, is mostly due to the lack of suitable ultrafast experiments so far. At the same time, the justification for choosing it to investigate the role of coherence rests on the large amount of experimental data that exists concerning its structure (see e.g. [Roszak *et al.* (2003)]), in addition to several accompanying theoretical studies [Hu *et al.* (1997); Ritz *et al.* (2001); Hu and Schulten (1998); Damjanović *et al.* (2000)]. As a first approximation, we will model this unit as a collection of interacting two-level systems whose interactions take the form of a star-like configuration (see Fig. 4.2(c)) and we describe its dynamics following a quantum jump model [Carmichael (1993); Plenio and Knight (1998)]. Given the lack of precise information about interactions in the artificial systems, we will consider the effects of various candidate interaction mechanisms (i.e. dipole-dipole, pairwise and nearest-neighbour). In particular, we obtain analytical solutions for the relationship between the efficiency, the symmetry of the initial state and the number of initially entangled donors. We then consider a more detailed interaction Hamiltonian for purple bacteria (see Fig. 4.2(b)). We finish the chapter with a discussion of some of the open questions and relevant experimental considerations.

4.2. A Coherent Photosynthetic Unit (CPSU)

The photosynthetic efficiency depends primarily on the mechanism of energy transfer, the dissipation and charge separation rates, and the network geometry [Sener and Schulten (2005)]. In photosynthetic systems operating at environmental temperatures [Ritz *et al.* (2002); van Amerongen *et al.* (2002)], the transfer mechanism agrees with the picture of an electronic

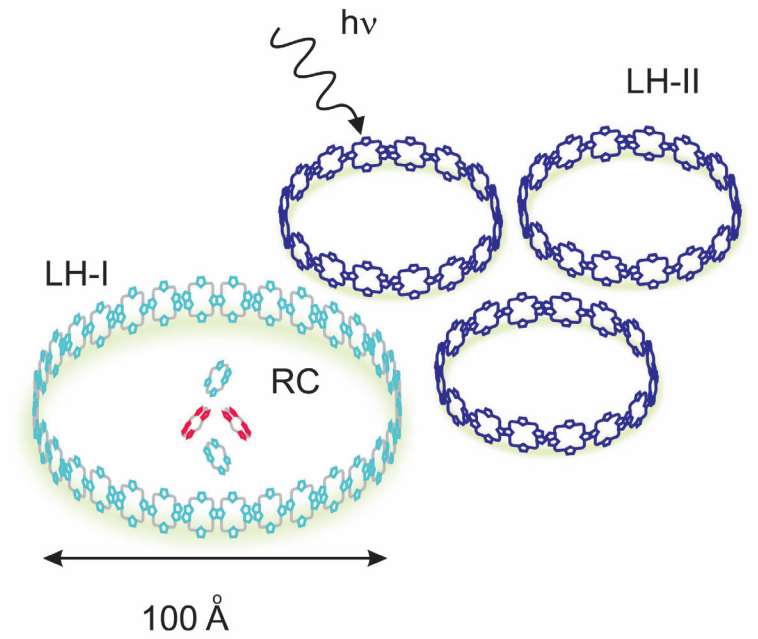


Fig. 4.1. Schematic diagram of the photosynthetic apparatus of Purple Bacteria Rhodobacter Sphaeroides. A photon is initially captured by the LH-II. This creates an electronic excitation that is quickly transferred to the RC via the LH-I. For details see Ritz *et al.* (2002).

excitation migrating between chromophores via a Förster interaction [Förster (1965)]. Here we are interested however, in the efficiency of molecular aggregates that can mimic photosynthesis and which can operate in the regime dominated by coherent excitation-transfer [Gilmore and MacKenzie (2006)]. We will refer to such an aggregate as a *coherent photosynthetic unit* (CPSU) and will show that quantum coherence and entanglement offer remarkable control over the efficiency of a CPSU. As mentioned before, such systems could correspond to natural photosynthetic aggregates at very low temperatures, or can be synthesized complexes [Ranasinghe *et al.* (2002); Varnavski *et al.* (2002); Lupton *et al.* (2002); Ranasinghe *et al.* (2003); Andrews and Bradshaw (2004)].

Motivated by the photosynthetic apparatus of purple bacteria [Hu *et al.* (1997); Ritz *et al.* (2001); Hu and Schulten (1998); Damjanović *et al.* (2000)], we consider the excitation transfer in a system of M donors in a circular arrangement around a RC with n acceptors (see Fig. 4.2). We are

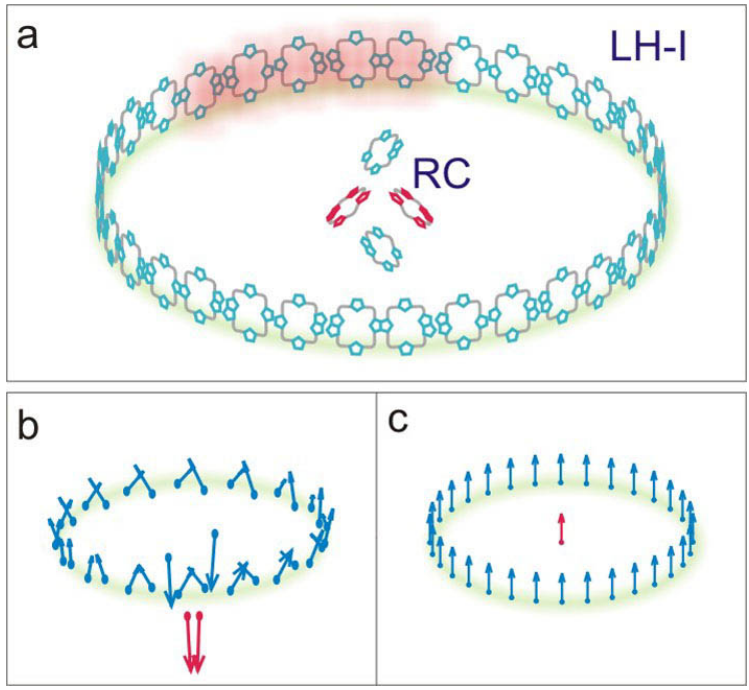


Fig. 4.2. Schematic diagram of the LH-I and Reaction Centre (RC) of purple bacteria (a) Arrangement of the 32 Bactericlorophils (BChl) (light lines) or donors surrounding the RC in photosynthetic Rodobacter Sphaeroides. The RC has two accessory BChl (light lines) and two acceptors (shaded dark lines) forming a special pair responsible for charge separation. The excitation (red cloud) is initially shared among several donors. (b) Schematic diagram of the induced dipole moments in (a). The arrows indicate the dipole moment directions corresponding to data taken from Hu and Schulten (1998). (c) Toy model: The RC is assumed to be a single two-level system.

interested in the limit where electronic coherence is most relevant, hence we consider the donors and acceptors to be on-resonance two-level systems. The coherent interaction among donors and acceptors is described by the Hamiltonian

$$H_I = \sum_{j=1}^{M}\sum_{c=1}^{n}\gamma_{jc}\hat{V}_{jc} + \sum_{j=1,k>j}^{M} J_{jk}\hat{V}_{jk} + \sum_{c=1,r>c}^{n} g_{cr}\hat{V}_{cr}\ , \qquad (4.1)$$

with $\hat{V}_{ab} = \sigma_a^+\sigma_b^- + \sigma_b^+\sigma_a^-$. Here $\sigma^{+(-)}$ is the usual creation (annihilation) operator for two-level systems, and γ_{jc}, J_{jk} and g_{cr} are the donor-acceptor, donor-donor, and acceptor-acceptor couplings, respectively.

To include the decoherence effects in the excitation transfer we employ the quantum jump approach [Carmichael (1993); Plenio and Knight (1998)]. The irreversible dynamics of an open quantum system, i.e. a quantum system in contact with the environment, is often treated in terms of a master equation for its density operator $\rho(t)$. In the Markovian approximation where all memory effects in the bath are neglected, the dynamics of the open system is described by the Lindblad master equation ($\hbar = 1$)

$$\frac{d}{dt}\rho = \mathcal{L}\rho = -i[H,\rho] + \frac{1}{2}\sum_{j=1}^{n}[2A_j\rho A_j^\dagger - A_j^\dagger A_j\rho - \rho A_j^\dagger A_j] \ , \qquad (4.2)$$

where the commutator generates the coherent part of the evolution. The second part on the right-hand side of this equation, represents the effect of the reservoir on the dynamics of the system, where the action of each operator A_j accounts for a decohering process labelled j. In order to illustrate how the system's dynamics can be interpreted in terms of *quantum trajectories* we follow the approach given by Carmichael (1993). Let us define $\tilde{\mathcal{L}} = \mathcal{L} - \mathcal{J}$ and re-write Eq. (4.2) in the following way:

$$\mathcal{L}\rho = (\tilde{\mathcal{L}} + \ \mathcal{J})\rho = \left(\tilde{\mathcal{L}} + \sum_{j=1}^{n}\mathcal{J}_j\right)\rho \ , \qquad (4.3)$$

where

$$\tilde{\mathcal{L}}\rho = -i(H_{\rm cond}\rho - \rho H_{\rm cond}^\dagger) \quad \text{and} \quad \mathcal{J}_j\rho = A_j\rho A_j^\dagger \qquad (4.4)$$

with

$$H_{\rm cond} = H - \frac{i}{2}\sum_{j=1}^{n}A_j^\dagger A_j \ . \qquad (4.5)$$

By re-writing the master equation as in Eq. (4.3) one can divide the dynamics of the system into two processes: A non-Hermitian evolution associated with the generator $\widetilde{\mathcal{L}}$, and jump processes associated with the set of A_j that are the operators describing the sources of decoherence of the open system. One can then interpret the system's dynamics as given by *quantum trajectories* that are defined by continuous evolutions interrupted by stochastic collapses at the times the jumps occur. The dynamics given by the master equation is recovered by averaging over all possible trajectories [Carmichael (1993)].

The *no-jump trajectory* corresponds to the case in which no decay occurs. The evolution of a quantum state along this trajectory is governed by the non-Hermitian Hamiltonian $H_{\rm cond}$. For instance, if the initial state

is pure, i.e. $|\Psi(0)\rangle$, the non-normalized state in the no-jump trajectory becomes $|\widetilde{\Psi}_{\rm cond}\rangle(t) = \exp(-iH_{\rm cond}\,t)|\Psi(0)\rangle$. For a wide variety of physical situations, particularly in the context of quantum optics, it has been shown that the no-jump trajectory can yield a good estimation of the system's evolution in the presence of decoherence sources [Plenio *et al.* (1999); Nicolosi *et al.* (2004); Beige (2003)]. In most of these schemes a single excitation is present—hence if the excitation is "lost", i.e. a photon is detected, the system collapses into its ground state. Therefore it is desirable to investigate the system's dynamics conditioned on no-excitation loss.

Most of the research in energy transfer in light-harvesting systems indicates that there is no more than a single excitation present in each complex (LH-I or LH-II) [Hu *et al.* (1997)]. Also, the high efficiency in the transfer of excitation to the reaction centre indicates that most likely no excitation is lost in the transfer. Therefore, the dynamics along the no-jump trajectory provides a tractable description of the excitation-transfer dynamics in a CPSU. The resulting non-unitary evolution, conditioned on there being no loss of excitation, is interrupted by stochastic jumps that can be associated either with excitation dissipation by any of the donors or excitation trapping in the RC. Between jumps, the dissipative dynamics is governed by

$$H_{\rm cond} = H_I - i\Gamma \sum_{j=1}^{M} \sigma_j^+ \sigma_j^- - i\kappa \sum_{i=1}^{n} \sigma_{ci}^+ \sigma_{ci}^- \ , \tag{4.6}$$

where the dissipation rate Γ is assumed to be identical for all the donors, and the trapping rate κ is assumed to be identical for all the acceptors at the RC. A basis is given by states in which one of the two-level systems is excited and the rest are in their ground state, i.e. $|d_j\rangle = |0_1 0_2 \ldots 1_j \ldots 0_M; 0_{c1} 0_{c2} \ldots 0_{cn}\rangle$ union $|C_i\rangle = |0_1 0_2 \ldots 0_M; 0_{c1} \ldots 1_{ci} \ldots 0_{cn}\rangle$, $j = 1, 2, \ldots, M$ and $i = 1, 2, \ldots, n$. The labels after the semicolon in each ket denote the acceptors at the RC. Since we are interested in describing the effects of initial entangled state we will assume pure initial states Ψ_0. The non-unitary evolution is given by $U = \exp[-iH_{\rm cond}t]$ and the unnormalized conditional state becomes

$$|\widetilde{\Psi}_{\rm cond}(t)\rangle = \sum_{j=1}^{M} \widetilde{b_j}(t)|d_j\rangle + \sum_{i=1}^{n} \widetilde{b_{ci}}(t)|C_i\rangle \ . \tag{4.7}$$

The monotonically decreasing norm of this conditional state gives the probability that the excitation is still in the system during the interval $(0, t)$, i.e. the probability of no-jump $P(t; \Psi_0) = \| \ |\widetilde{\Psi}_{\rm cond}\rangle \ \|^2$. The quantity of

interest is the probability density of having a jump between t and $t+dt$, $w(t;\Psi_0) = -dP(t;\Psi_0)/dt$ which becomes

$$\begin{aligned} w(t;\Psi_0) &= \langle \Psi_{\rm cond}(t)|(-i\tilde{H}^\dagger + i\tilde{H})|\Psi_{\rm cond}(t)\rangle \\ &= 2\Gamma \sum_{j=1}^{M} |\widetilde{b}_j(t)|^2 + 2\kappa \sum_{i=1}^{n} |\widetilde{b}_{ci}(t)|^2 \\ &= w_D(t,\Psi_0) + w_{RC}(t,\Psi_0) \ . \end{aligned} \tag{4.8}$$

Here Ψ_0 is the initial state, $w_{RC}(t;\Psi_0)dt$ is the probability that the excitation is used by the RC in $(t, t+dt)$ while $w_D(t;\Psi_0)dt$ is the probability that it is dissipated by any of the donors. Notice that $\int_0^\infty w(t;\Psi_0)dt = 1$ which implies that the excitation will eventually either be dissipated or trapped in the RC.

Within this framework we can now define the main features of our CPSU: the excitation lifetime, the efficiency or quantum yield, and the transfer times [Sener and Schulten (2005)]. Given an initial state Ψ_0, the *excitation lifetime* (τ) is the average waiting-time before a jump of any kind occurs. The *efficiency* (η) is the total probability that the excitation is used in charge separation. The *forward-transfer time* (t_f) is the average waiting-time before a jump associated with charge-separation in the RC, given that the excitation was initially in the donor subsystem:

$$\tau = \int_0^\infty dt\, t\, w(t;\Psi_0) \ , \ \eta = \int_0^\infty dt\, w_{RC}(t;\Psi_0) \ , \ t_f = \frac{\int_0^\infty dt\, t\, w_{RC}(t;\Psi_0)}{\int_0^\infty dt\, w_{RC}(t;\Psi_0)} \ . \tag{4.9}$$

4.3. Toy Model: Interacting Qubits with a Spin-star Configuration

We start by considering the simplest model for which analytical solutions can be obtained: the RC is a single two-level system on resonance with the donors, i.e. $n = 1$, and all donor-RC couplings are identical, i.e. $\gamma_{jc} \equiv \gamma$; see Fig. 4.2(c). Later we shall show that the main results obtained in this situation also apply to a more realistic model featuring the detailed structure of the RC as in purple bacteria.

First we establish a relationship between the efficiency and number of initially entangled donors. We consider the excitation to be initially in the donor subsystem, i.e. $b_c(0) = 0$, and compare $\widetilde{b}_c(t)$ for three different mechanisms of interaction between the donors: (i) nearest neighbours with

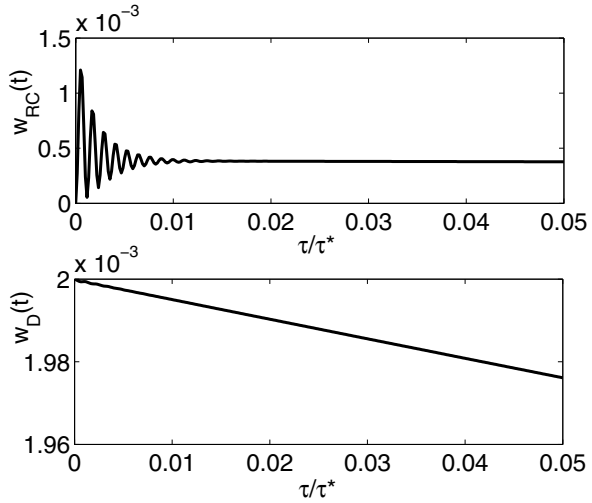


Fig. 4.3. Short time behaviour of the waiting-time distribution for a jump associated to the RC (top) or for a jump associated to any of the donors (bottom). Time in units of $\tau^* = 100\hbar/\gamma$.

$J_{jk} = (J/2)\delta_{j,k-1}$, (ii) pairwise interaction with $J_{jk} \equiv J$ for all $\{j,k\}$ pairs and (iii) dipole-dipole interactions of the form $J_{jk} = J/r_{jk}^3$ where $\mathbf{r}_{jk}$ is the relative position vector between the induced dipole moments of donors j and k. Analytical solutions for $\widetilde{b}_c(t)$ [Olaya-Castro *et al.* (2006)] and therefore $w_{RC}(t)$, can be found in each of these cases:

$$w_{RC}(t) = |B_0|^2 \mathcal{F}(t) \tag{4.10}$$

where $B_0 = \sum_{j=1}^{M} b_j(0)$ and $\mathcal{F}(t) = 8\kappa\gamma^2 e^{-(\kappa+\Gamma)t/2}|\sin(\Omega t/2)|^2/|\Omega|^2$. Here Ω is the complex collective frequency that determines the timescale of coherent oscillations [Olaya-Castro *et al.* (2006)] i.e. $\Omega = \sqrt{4M\gamma^2 - (\delta + i\Delta)^2}$ with $\delta = \Gamma - \kappa$ and

$$\Delta = \begin{cases} J & \text{Nearest} \\ J(M-1) & \text{Pairwise} \\ J\sum_{k=2}^{M}(1/r_{1k})^3 & \text{Dipole} \end{cases} . \tag{4.11}$$

To illustrate the dynamics of $w_{RC}(t)$ and $w_D(t)$, we have plotted in Fig. 4.3 the short-time behaviour of these quantities for the case of dipole-dipole interactions. In the case plotted, we take the excitation to be initially localized on one of the donors. As we shall discuss below, the coherent oscillations exhibited by w_{RC} dominate the efficiency of our CPSU, while

$w_D(t)$ is a monotonically decreasing function of time that dominates the dynamics of probability of no-jump $P(t;\Psi_0)$.

We consider initial entangled states in which the excitation is delocalized among donors, i.e. $\Psi_0 = \sum_{j=1}^{M} b_j(0)|d_j\rangle$ and we now proceed to show how the symmetry and entanglement in this initial state can act as *efficiency control mechanisms*. Equation (4.10) shows that the efficiency η becomes proportional to $|B_0|^2$. The latter quantity accounts for the relative phases between states $|d_j\rangle$ i.e. *quantum coherence* and therefore it is clear that symmetric initial entangled states yield an increase in η, while some asymmetric states could be used to limit or even prevent the transfer, i.e. $\eta = 0$. Unless otherwise stated, we henceforth consider symmetric initial entangled states of the form $\Psi_0 = (1/\sqrt{N})\sum_{j=1}^{N}|d_j\rangle$ where N is the number of initially entangled donors, i.e. $N \leq M$. For these states $|B_0|^2 = N$ and hence the efficiency not only depends on the symmetry, but becomes proportional to the number of initially entangled donors N as shown in Fig. 4.4. These results can be understood in terms of one striking feature of the entanglement, that is, *entanglement sharing*. This feature refers to the fact that quantum correlations cannot be shared arbitrarily among several particles [Dawson *et al.* (2005)]. In our case, for any initial state, the system evolves conditionally towards an entangled state where the excitation is shared between donors and the RC. Since entanglement cannot be shared arbitrarily, the efficiency will therefore depend on the dynamics of entanglement-sharing between donors and RC. When the excitation is initially localized on only one of the donors, the average donor-RC entanglement should be small since the excitation also has to be shared directly among all interacting donors. By contrast when the excitation is already shared by several donors, there are fewer donors left to be entangled and consequently the gain in entanglement between donors and RC should be larger than in the previous situation. This feature is illustrated in Fig. 4.4(a) which shows the long-time average entanglement between donor and RC (AEDC) and the average entanglement between donors (AEDD), as a function of N for the dipole-dipole case. As can be seen, AEDC increases with N while AEDD does not change drastically. Hence the efficiency can be seen as a monotonic function of AEDC as depicted in Fig. 4.4(b). The larger value of AEDC when $N = M$ confirms the strong damping effect of non-entangled donors on the AEDC.

In order to compute these averages, we have taken advantage of the known results for W-class entangled states [Dawson *et al.* (2005)] as it is the state given in Eq. (4.7). We quantify the pair entanglement using the

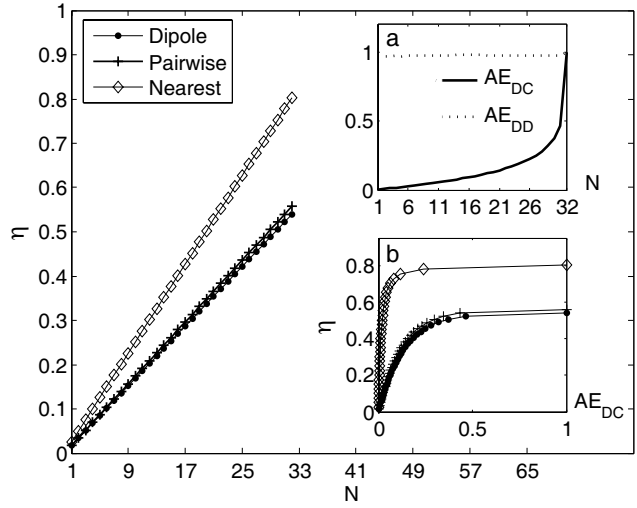


Fig. 4.4. Efficiency (η) versus number of donors which are initially entangled (N), for the toy model. Main panel shows numerical results for three different interaction mechanisms. For nearest-neighbour interactions ($\Diamond$) the coupling is 100 meV, while for the pairwise case (+) it is 10 meV and equals the average dipole-dipole coupling ($\bullet$). These values have been taken to be such that $\Delta_{\rm dipole} \simeq \Delta_{\rm pairwise} > \Delta_{\rm nearest}$. In each case, the donor-RC coupling equals 1 meV, $\Gamma = 1$ ns^{-1} and $\kappa = 4$ ps^{-1}. (a) The average entanglement between donors and RC (solid line) and the average intra-donor entanglement (dotted line) as a function of N, in the case of dipole-dipole interaction. The same behaviour is observed for the pairwise and nearest-neighbour cases (not shown). (b) η versus the average donor-RC entanglement for the three forms of interaction. In (a) and (b), the average-entanglement values have been normalized to the maximum value obtained in each case.

"tangle" [Coffman *et al.* (2000)] that equals $|b_j(t)b_k(t)^*|^2$ for the reduced state of two two-level systems j and k in our CPSU. Here $b_j(t)$ are the normalized versions of $\widetilde{b}_j(t)$. The total intra-donor entanglement ($E_{DD}(t)$) and donor-RC entanglement ($E_{DC}(t)$) are each equal to the sum over all distinct pair contributions, and their long-time averages are calculated for the time when the probability of no-jump $P(t;\Psi_0)$ has decayed to 0.01 at $t = t_{\rm max}$. These averages are defined as follows:

$$\begin{aligned} \text{AEDC} &= \lim_{T\to t_{\rm max}} \frac{1}{T}\int_0^T E_{DC}(t)dt \\ \text{AEDD} &= \lim_{T\to t_{\rm max}} \frac{1}{T}\int_0^T E_{DD}(t)dt \end{aligned} \tag{4.12}$$

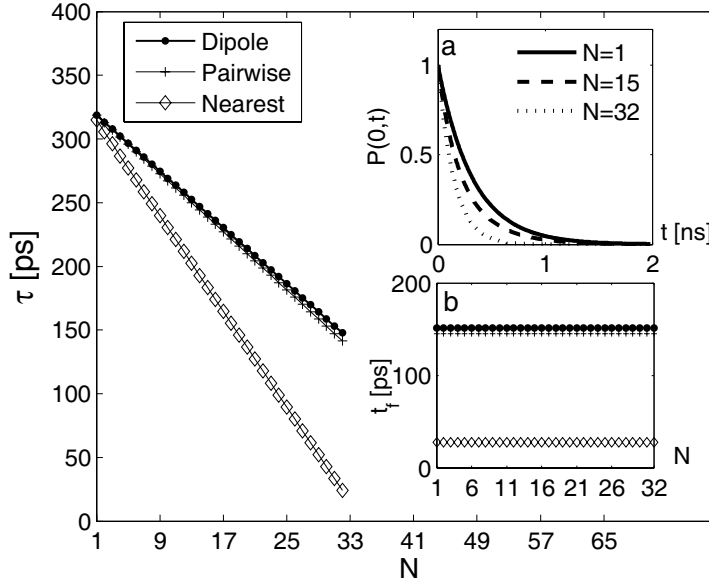


Fig. 4.5. Lifetime (τ), transfer time (t_f), and probability of no-jump versus the number of donors initially entangled (N), for the toy model. Main panel shows numerical results for τ, for the three forms of interaction: dipole-dipole ($\diamondsuit$), pairwise ($+$) and nearest-neighbour ($\bullet$). Coupling strengths and parameter values are as in Fig. 4.4. Shorter lifetimes are associated with faster decays in the probability of no-jump as shown in (a), but also with shorter transfer times as shown in (b). (a) Probability of no-jump as a function of time for different N values, for the case of dipole-dipole interactions. The same behaviour is observed for pairwise and nearest-neighbour cases (not shown). (b) t_f as a function of N for the three mechanisms of interaction.

In Fig. 4.4, we note that the gradient in each case depends on the nature of the interaction in the system. For a fixed N, η reaches higher values in the case of nearest-neighbour interactions, while it reaches similar values for dipole-dipole and pairwise interactions. We have chosen γ to be the same for all these situations and J has been taken to be such that $\Delta_{\rm dipole} \simeq \Delta_{\rm pairwise} > \Delta_{\rm nearest}$. According to these results, the stronger the effective interaction between one donor and the rest, the lower the efficiency. This is due to the fact that a stronger interaction implies a larger value for the average intra-donor entanglement, therefore limiting the donor-RC entanglement and hence the efficiency.

The decay-rate of $P(t;\psi_0)$ increases with the number of initially entangled donors, as shown in Fig. 4.5(a). Correspondingly, the excitation lifetime τ decreases as shown in Fig. 4.5. As expected, situations for which

the efficiency reaches higher values imply lower lifetimes. Interestingly, for these interaction mechanisms the transfer time t_f is independent of N as can be seen in Fig. 4.5(b). The three situations satisfy $t_f \leq \tau$, where the equality holds for the initial state in which all the donors are entangled. Also, the lifetime and transfer times are less than the time at which probability of no-jump is no lower than 0.9 (see Fig. 4.5(a)), hence we can say that the excitation transfer dynamics is indeed dominated by the short-time behaviour illustrated in Fig. 4.3.

4.4. A More Detailed Model: Photosynthetic Unit of Purple Bacteria

We now consider an effective LH-I-RC interaction Hamiltonian given by Hu *et al.* (1997) and Hu and Schulten (1998) which has been used to describe the excitation transfer in the photosynthetic unit of the purple bacteria Rhodobacter Spharoides [Hu *et al.* (1997); Hu and Schulten (1998); Damjanović *et al.* (2000)]. The LH-I of these bacteria contain 32 identical bacteriochlorophyll (BChl), or donors, surrounding the RC (see Fig. 4.2). The RC is in turn made up of a special pair of BChl responsible for the charge separation, and two more accessory BChl molecules whose function is still under debate [Ritz *et al.* (2002)]. In general the BChl at the RC are slightly off-resonance with the donors. Here, for the sake of simplicity, we have assumed they are on-resonance such that the effective Hamiltonian is of the form given in Eq. (4.1) but with certain particularities. First, the interactions between adjacent donors cannot be accounted for properly with a dipole-dipole approximation. They should be quantified by two different constants ν_1 and ν_2, i.e. $J_{j,j+1} = \nu_1$ and $J_{j,j-1} = \nu_2$ whose difference reflects the dimeric structure of the LH-I ring—each BChl is bound to two different proteins. Second, the coupling between non-neighbouring donors corresponds to a dipole-dipole interaction of the form

$$J_{jk} = \frac{\boldsymbol{\mu}_j \cdot \boldsymbol{\mu}_k}{r_{jk}^3} - \frac{3(\mathbf{r}_{jk} \cdot \boldsymbol{\mu}_j)(\mathbf{r}_{jk} \cdot \boldsymbol{\mu}_k)}{r_{jk}^5}\,, \qquad |j-k| > 1\ ; \qquad (4.13)$$

where $\boldsymbol{\mu}_j$ is the transition dipole moment of the j^{th} donor and $\mathbf{r}_{jk}$ is the relative position vector between donors j and k. The directions of $\boldsymbol{\mu}_j$ have been taken from Hu and Schulten (1998). A top view of the dipole representation of LH-I-RC is shown in Fig. 4.2(b).

We consider two cases for the RC: (i) the full structure, and (ii) the structure without the two accessory BChls. Our numerical results suggest that a CPSU with an effective interaction as in the LH-I-RC apparatus of purple bacteria, could exploit both the symmetrically entangled $\Psi_0 = (1/\sqrt{N})\sum_{j=1}^{N}|d_j\rangle$ *and* the asymmetrically entangled $\Psi_0 = (1/\sqrt{N})\sum_{j=1}^{N}(-1)^j|d_j\rangle$ states in order to modify the efficiency. For the symmetric states, η behaves very similarly to before: it increases with N as shown in Figs. 4.6(a) and 4.6(b) which correspond to cases (i) and (ii) respectively. The results indicate, however, that accessory BChls have a strong damping effect for symmetric states which is seen not only in the lower values for the efficiency in case (i), but in the fact that the transfer time has an increasing trend as a function of N as shown in the inset in Fig. 4.6(a). In the absence of the accessory BChls the transfer time presents the opposite behaviour: it decreases with N (see inset in Fig. 4.6(b)) and in consequence the efficiency values are larger. Conversely for the asymmetric states, the efficiency is a non-monotonic function of N, indicating that there is an *optimal* number of entangled donors for which η has a maximum (Figs. 4.6(c) and 4.6(d)) and for which t_f has a minimum (see insets in Figs. 4(c) and 4(d)).

The slight differences between Figs. 4(c) and 4(d) indicate that for asymmetric initial states, the presence of the accessory BChls in RC do not significantly affect the efficiency of the transfer. Most importantly, the non-monotonic profile for these states indicates that such a CPSU could use the symmetry of the initial state as a "crowd-control" mechanism: it can modify the efficiency, for example, in order to reduce the risk of burnout on the RC. Interestingly, some recent experimental works have indeed indicated that the excitation in LH-II may be coherently delocalized over just a few donors [van Oijen *et al.* (1999)]. Unfortunately, no such investigation has been reported on the LH-I.

The above discussion raises several interesting questions, which hopefully justify and motivate further experimental work in these systems. First, notice that the distinction between symmetric and asymmetric states is a purely quantum coherent phenomena, i.e. a well defined phase-difference between quantum states. Do these results suggest that quantum coherence might be not just sufficient, but indeed necessary for the transfer of excitation to the RC? Second, even if entanglement is not necessary for the transfer of excitation to the RC, might it be used to artificially enhance the performance of natural photosynthetic units?

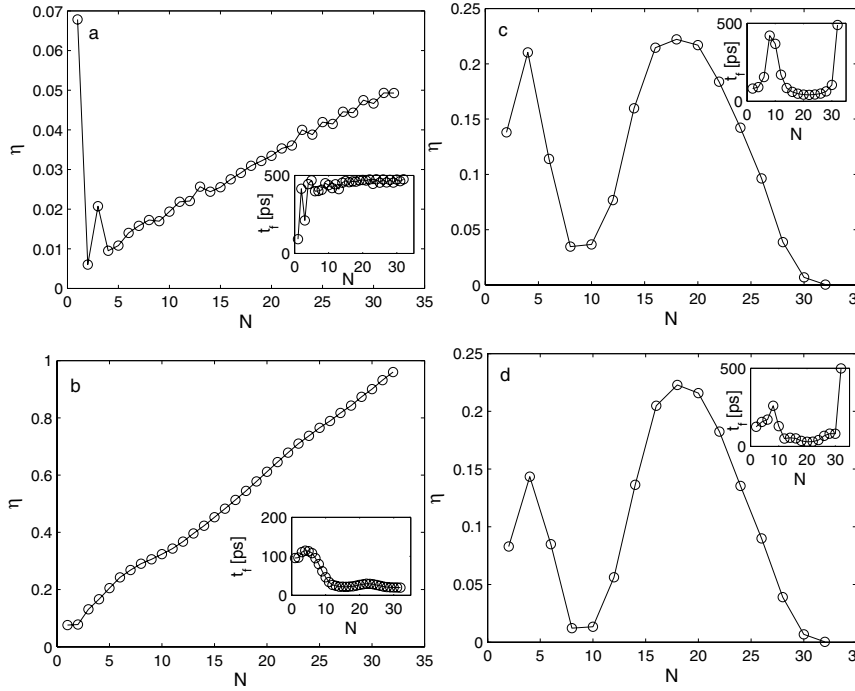


Fig. 4.6. Efficiency (η) and transfer time (t_f) versus number of initially entangled donors (N), for the photosynthetic bacterium Rhodobacter spharoides. Two situations have been considered: (i) The RC with the special pair responsible for charge separation and the two more accessory BChls, and (ii) the RC without the two accessory BChls. The effective Hamiltonian has been taken following Hu *et al.* (1997). (a) and (b) show numerical results for η as a function of N, for cases (i) and (ii) respectively, when the initial state is a symmetric entangled state. For these initial states, the main difference between situations (i) and (ii) is the behaviour of t_f which is depicted in the insets in (a) and (b). Numerical results for the situation where the initial state is an asymmetric entangled state, are shown in (c) for case (i) and in (d) for case (ii). It turns out that the transfer times (shown in the insets) are always less than or equal to the lifetimes (not shown).

4.5. Experimental Considerations

Experimental observation, and even manipulation, of the coherent excitation transfer in synthesized LH-I-RC [Davis *et al.* (1995)] should become plausible as the temperature is lowered. An estimate of the temperature below which robust coherent excitation transfer between donors and RC

should be expected is given by $k_B T^* = h\gamma/\alpha$ where the coupling between the donor and the environment should satisfy $\alpha < 1/2$ [Gilmore and MacKenzie (2006)]. The α values for naturally occurring photosynthetic structures are however unknown. Taking $\alpha = 0.1$ yields an estimated temperature of $T^* \simeq 10$ K, which is *larger* than the temperatures at which experiments have previously been performed (i.e. 1 K [van Oijen *et al.* (1999)])—hence our belief that such quantum phenomena can be usefully explored using current experimental expertise.

Most of the advances in our understanding of photobiological systems have been due to recent improvements in instrumental techniques—for example, confocal microscopy which allows single-molecule experiments and fluorescence correlation spectroscopy [Jung *et al.* (2002)]. We believe that these techniques are ideal candidates for generating and manipulating entangled states within the chromophores of light-harvesting systems and to probe the effects discussed in this work. The purely symmetric and antisymmetric entangled states discussed here will not, in the real system, have these exact symmetries because of symmetry-breaking interactions within the molecules and immediate environment. To the extent to which these symmetries are broken, then the states will be either mostly symmetric with some asymmetric component, or mostly asymmetric with some symmetric component. Both will now be allowed optically, and both will have a greater or lesser character of the efficiency and transfer times for the pure symmetric or antisymmetric states. In short, as with all symmetry breaking, one can expect the two resulting manifolds to still have predominantly one of the two characters—hence the theoretical analysis of the present chapter, while ideal, will still hold qualitatively. Given the current advances in nanotechnology, we also hope that the results in this chapter will stimulate fabrication of novel nanoscale energy sources and devices built around quantum coherent (or even mixed quantum-classical) dynamics. In this direction we note the interesting theoretical possibility that natural photosynthetic systems may one day be used as the basis of quantum logic gates. An example of how this might be achieved using excitons, is given by Hitchcock (2001).

4.6. Outlook

In photosynthetic organisms such as purple bacteria, the LH-I-RC system studied in this chapter is embedded in a network of other LH-I- RC systems and LH-II rings. After sunlight is harvested by the LH-I and LH-II rings,

each excitation migrates from one ring to another until it either dissipates or arrives to the RC where charge separation takes place. This process is characterized by the excitation transfer rates between the different complexes (LH-I/LH- II, LH-I/LH-I, LH-II/LH-II and LHI-RC), by the probability of an LH to be excited upon light and by the dissipation rate of excitations. The high efficiency of these organisms depend on these parameters and in particular on the fact that dissipation occurs in a nanosecond scale in contrast to the few tens picosecond scale of average lifetime excitation. An important role in this process may be played by the different structures of the various membranes themselves. We are currently investigating this question, using both a classical walk simulation [Fassioli *et al.* (2007)] and a quantum walk analysis (see Flitney *et al.* (2004) and references therein, for discussions of quantum walks).

References

Andrews, D. L., and Bradshaw, D. S. (2004). Optically nonlinear energy transfer in light-harvesting dendrimers, *J. Chem Phys.* **121**, pp. 2445–2454.

Beige, A. (2003). Dissipation assisted quantum-gates with cold ions, *Phys. Rev. A* **67**, 020301(R).

Carmichael, H. (1993). An open systems approach to Quantum Optics, vol. 18 of *Lecture Notes in Physics*, Springer-Verlag, Berlin.

Cheng, Y. C., and Silbey, R. J. (2006). Coherence in the B800 ring of purple bacteria LH2, *Phys. Rev. Lett.* **96**, 028103.

Coffman, V., Kundu, J., and Wootters, W. K. (2000). Distributed entanglement, *Phys. Rev. A* **61**, 052306.

Damjanović, A., Ritz, T., and Schulten, K. (2000). Excitation energy trapping by the reaction center of Rhodobacter Sphaeroides, *Int. J. Quant. Chem.* **77**, pp. 139–151.

Davis, C. M., Bustamante, P. L., and Loach, P. A. (1995). Reconstitution of the bacterial core light-harvesting complexes of rhodobacter sphaeroides and rhodospirillum rubrum with isolated α- and β-polypeptides, bacteriochlorophyll A, and barotenoid, *J. Bio. Chem.* **270**, pp. 5793–5804.

Dawson, C. M., Hines, A. P., McKenzie, R. H., and Milburn, G. J. (2005). Entanglement sharing and decoherence in the spin-bath, *Phys. Rev. A* **71**, 052321.

Engel, G. S., Calhoun, T. R., Read, E. L., Ahn, T-K., Mančal, T., Cheng, Y-C., Blannkeship, R. E., and Fleming, G. R. (2007). Evidence for wavelike energy transfer through quantum coherence in photosynthetic systems, *Nature* **446**, pp. 782–786.

Fassioli Olsen, F., Olaya-Castro, A., and Johnson, N.F. *in preparation.*

Flitney, A. P., Abbott, D., and Johnson, N. F. (2004). Quantum walks with history dependence, *J. Phys. A* **37**, pp. 7581–7591.

Förster, T. (1965). *Modern Quantum Chemistry*, O. Sinanoglu, Ed., Academic Press, New York, vol. 3, pp. 93–137.

Fréchet, J. M. (1994). Functional polymers and dendrimers: reactivity, molecular architecture, and interfacial energy, *Science* **263**, pp. 1710–1715.

Gaab, K. M., and Bardeen, C. J. (2004). The effects of connectivity, coherence, and trapping on energy transfer in simple light-harvesting systems studied using the Haken-Strobl model with diagonal disorder, *J. Chem. Phys.* **121**, pp. 7813–7820.

Gilmore, J. B., and MacKenzie, R. H. (2006). Criteria for quantum coherent transfer of excitations between chromophores in a polar solvent, *Chem. Phys. Lett.* **421**, pp. 266–271.

Hitchcock, S. M. (2001). Photosynthetic Quantum Computers? LANL pre-print quant-ph/0108087.

Hu, X., Ritz, T., Damjanović, A., and Schulten, K. (1997). Pigment organization and transfer of electronic excitation in the photosynthetic unit of purple bacteria, *J. Phys Chem. B* **101**, pp. 3854–3871.

Hu, X., and Schulten, K. (1997). How nature harvests sunlight, *Phys. Today* **50**, pp. 28–34.

Hu, X., and Schulten, K. (1998). A model for the light-harvesting complex I (B875) of Rhodobacter sphaeroides, *Biophy. J.* **75**, pp. 683–694.

Jang, S., Newton, M. D., and Silbey, R. J. (2004). Multichromophoric Förster, Resonance Energy Transfer, *Phys. Rev. Lett.* **92**, 218301.

Jung, Y.J., Barkai, E., and Silbey, R.J. (2002). Current status of single-molecule spectroscopy: Theoretical aspects, *J. Chem. Phys.* **117**, pp. 10980–10995.

Lupton, J. M., Samuel, I. D. W., Burn, P. L., and Mukamel, S. (2002). Control of intrachromophore excitonic coherence in electroluminescent conjugated dendrimers, *J. Phys. Chem. B* **106**, pp. 7647–7653.

Ketelaars, M., Hofmann, C., Köhler, J., Tina, D., Howard, T. D., Cogdell, R. J., Schmidt, J., and Aartsma, T.J. (2002). Spectroscopy on individual light-harvesting 1 complexes of Rhodopseudomonas acidophila, *Biophys. J.* **83**, pp. 1701–1715.

Nicolosi, S. (2004). Stationary entanglement induced by dissipation, *Phys Rev A* **70**, 022511.

Plenio, M. B., and Knight P. L. (1998). The quantum-jump approach to dissipative dynamics in quantum optics, *Rev. Mod. Phys.* **70**, pp. 101–144.

Plenio, M. B., Huelga, S. F., Beige, A., and Knight, P. L. (1999). Cavity-loss-induced generation of entangled atoms, *Phys. Rev. A* **59**, 2468.

Olaya-Castro, A., Lee, C. F., Fassioli Olsen, F., and Johnson, N. F. (2008). Efficiency of energy transfer in a light-harvesting system under quantum coherence, LANL pre-print quant-ph/0708.1159v3.

Ranasinghe, M. I., Varnavski, O. P., Pawlas, J., Hauck, S. I., Louie, J., Hartwig, J. F., and Goodson, T. (2002). Femtosecond excitation energy transport in triarylamine dendrimers, *J. Am. Chem. Soc.* **124**, pp. 6520–6521.

Ranasinghe, M. I., Wang, Y., and Goodson, T. (2003). Excitation energy transfer in branched dendritic macromolecules at low (4 K) temperatures, *J. Am. Chem. Soc.* **125**, pp. 5258–5259.

Ritz, T., Park, S., and Schulten, K. (2001). Kinetics of excitation migration and trapping in the photosynthetic unit of purple bacteria, *J. Phys Chem. B* **105**, pp. 8259–8267.

Ritz, T., Damjanović, A., and Schulten, K. (2002). The quantum physics of photosynthesis, *Chem. Phys. Chem.* **3**, pp. 243–248.

Roszak, A. W., Howard, T. D., Southall, J., Gardiner, A. T., Law, C. J., Isaacs, N. W., and Cogdell, R. J. (2003). Crystal structure of the RC-LH1 core complex from Rhodopseudomonas palustris, *Science* **302**, pp. 1969–1972.

Sener, M., and Schulten, K. (2005). *Energy Harvesting Materials*, David L. Andrews, Ed. (World Scientific, Singapore).

Trinkunas, G., Herek, J. L, Polívka, T., Sundström, V., and Pullerits, T. (2001). Exciton delocalization probed by excitation annihilation in the light-harvesting antenna LH2, *Phys. Rev. Lett.* **86**, 4167.

van Amerongen, H., Valkunas, L., and van Grondelle, R. (2002). Photosynthetic Excitons (World Scientific, Singapore).

van Oijen, A. M, Ketelaars, M., Khler, J., Aartsma, T.J., and Schmidt J. (1999). Unraveling the electronic structure of individual photosynthetic pigment-protein complexes, *Science* **285**, pp. 400–402.

Varnavski, O. P., Ostrowski, J. C., Sukhomlinova, L., Twieg, R. J.,Bazan, G. C., and Goodson, T. (2002). Coherent effects in energy transport in model dendritic structures investigated by ultrafast fluorescence anisotropy spectroscopy, *J. Am. Chem. Soc.* **124**, pp. 1736–1743.

About the authors

Alexandra Olaya-Castro is currently a Junior Research Fellow in Physics at Trinity College, Oxford. She obtained her undergraduate degree in Physics at Universidad Distrital Francisco José de Caldas and MSc at Universidad de Los Andes in Bogotá, Colombia. She obtained her DPhil at Oxford under Neil F. Johnson. Her research interests currently focus on entanglement in open systems and quantum coherence in biomolecular complexes.

Francesca Fassioli Olsen is currently a DPhil student under Neil F. Johnson at Oxford University. She obtained her BSc in Physics at Pontificia Universidad Católica de Chile. Her research interests are in entanglement in open quantum systems and excitation dynamics in photosynthetic membranes.

Chiu Fan Lee is currently a Glasstone Research Fellow at the physics department and a Junior Research Fellow at Jesus College, Oxford. He

obtained his BSc at McGill University and DPhil at Oxford University under Niel F. Johnson. His research interests lie in the areas of biophysics and theoretical biology.

Neil F. Johnson until recently was a professor of physics at Oxford University—he is now at the University of Miami, Florida. His training in physics consisted of an undergraduate degree at Cambridge University and a PhD at Harvard University under Henry Ehrenreich. His interests focus around Complexity, and Complex Systems, in the physical, biological and social sciences.

Chapter 5

Modelling Quantum Decoherence in Biomolecules

Jacques Bothma, Joel Gilmore, and Ross H. McKenzie

5.1. Introduction

Decoherence in the context of quantum mechanics is a concept that not many people without a background in physics are familiar with. Anyone who has carried out some general studies in science will be aware of the strange manifestations of quantum mechanics that leads to counter intuitive effects like tunnelling and superpositions on the atomic scale. The question of why these effects do not manifest on macroscopic scales is often rationalized in terms of large objects having very small de Broglie wavelength. When this argument is applied to microscopic systems like biological chromophores or enzymes the relevant mass and length scales often appear to be small enough to allow for the possibility of observing quantum effects. It is this kind of thinking that has in some cases lead to sensationalist claims that quantum effects must be manifesting in biological systems when anomalous observations are made. However this neglects the subtlety of decoherence that tends to "wash out" quantum effects.

The phenomenon of decoherence comes about when different quantum entities interact. An illustrative example of this is a beautiful experiment that was performed by Anton Zeilinger's group in 2003, which looked at decoherence in C70 fullerenes [Hornberger *et al.* (2003)]. In this experiment a beam of C70 molecules were fired at a series of slits. As a result the

Received April 7, 2007

wavefunctions of the fullerene molecules interfered to produce an interference pattern. When gas particles were introduced along the path, which the C70 molecules needed to traverse, the interference pattern deteriorated significantly. At high enough pressures no interference could be seen and the C70 molecules behaved like classical particles. This arose simply from the fact that the C70 and gas molecules were interacting, and as a result the C70 molecule behaved like a classical entity.

In biological systems there is often a vast array of different sources of decoherence. The cell is a "hot and wet" environment. A chromophore on a protein can interact with the water molecules around the protein and also the protein itself. It is of the utmost importance to be able to model decoherence in biological molecules in order to understand whether quantum mechanics plays a functional role in these systems.

A major problem in understanding biomolecules' behaviour is that the molecule itself may contain hundreds of atoms, while its surrounding environment might consist of thousands or even millions of water molecules that all contribute to the biomolecule's behaviour. To simulate the quantum dynamics of such systems on a computer is very time intensive and, while it has been very informative for certain systems, the general principles underlying the results are not always clear (similar to using a pocket calculator to do complex sums—you can obtain the right answer, but it may not be obvious *why* it is right). Most significantly, to study even a slightly different molecule means the whole simulation must be run again.

In this chapter we describe some *minimal models* that we and others have developed to describe the interactions between biomolecules and their surroundings. This includes looking at biological chromophores embedded in a protein in solution and enzymes that catalyse hydrogen transfer reactions. These models capture the essential physics of the interactions but are simple enough that very complex systems can be studied. They use approximations like assuming the biomolecules are spherical, and treating the water as a uniform fluid (not including individual molecules). Therefore, instead of describing every single atom, it is enough just to input the size of the molecule and some information about its electric charge. It also turns out that, mathematically, this same type of model has been used for a number of other physical situations (such as in quantum computing), so a lot of results for these models are already available, ready to be applied to specific biological systems.

These models let us separate out the effects on a biomolecule of the nearby proteins and the solvent, and can tell us which part of the environment contributes most to the behaviour of different biomolecules. Ultimately, this could help in creating more efficient versions of, for example, artificial photosynthesis. It also allows one to determine how valid the hypothesis that certain enzymes enhance their catalytic power by exploiting tunnelling of hydrogen.

5.2. Time and Energy Scales

Biology is remarkable in that the range of time and energy scales over which biological processes occur spans seven orders of magnitude, ranging from ultrafast solvation times in water on the order of femtoseconds to the slow rotation of a protein which can take tens of nanoseconds. Figure 5.1 shows some relevant processes and their corresponding time scales, Table 5.1 gives some specific data for systems of relevance to this chapter.

In particular, we observe that within a given system, the various relevant processes often occur on widely separated time scales. For example, a chromophore inside a protein has a radiative lifetime of 10 ns, the surrounding water can respond in 10-100 fs, while the protein exhibits internal dynamics on the order of picoseconds, although in some circumstances much longer relaxation times (up to 20 ns) have been observed [Pierce and Boxer (1992)].

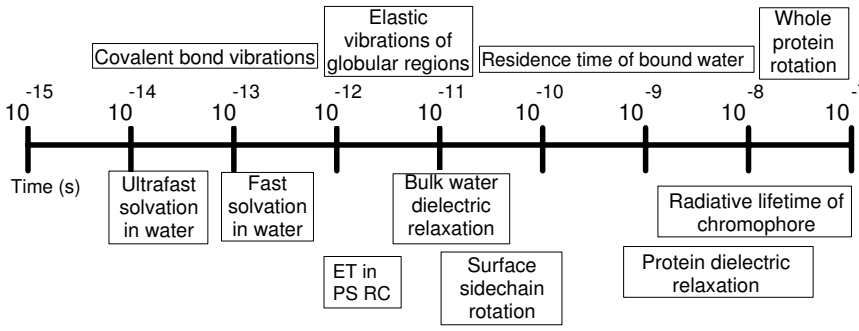


Fig. 5.1. Schematic representation of the time scales of various processes in biomolecules, proteins and solutions. ET stands for electron transfer, PS RC for photosynthetic reaction centre. See Table 5.1 for specific numbers.

Table 5.1. Timescales for various processes in biomolecules and solutions. The radiative lifetime of a chromophore is order of magnitudes longer than all other timescales, except perhaps protein dielectric relaxation. MD refers to results from molecular dynamics simulations. Of particular relevance to this work is the separation of timescales, $\tau_s \ll \tau_b \ll \tau_p$ (compare Fig. 5.1).

Process	Timescale	Ref.
Radiative lifetime	10 ns	[van Holde *et al.* (1998)]
Bulk water dielectric relaxation	8 ps	[Afsar and Hasted (1978)]
Protein dielectric relaxation (MD), $\tau_{D,p}$	1-10 ns	[Loffler *et al.* (1997); Boresch *et al.* (2000)]
Ultrafast solvation in water	10's fs	[Lang *et al.* (1999)]
Fast solvation in water, τ_s	100's fs	[Lang *et al.* (1999)]
Solvation due to bound water, τ_b	5-50 ps	[Peon *et al.* (2002)]
Solvation due to protein, τ_p	1-10 ns	[Sen *et al.* (2003)]
Covalent bond vibrations	10-100 fs	[van Holde *et al.* (1998)]
Elastic vibrations of globular regions	1-10 ps	[van Holde *et al.* (1998)]
Rotation of surface sidechains	10-100 ps	[van Holde *et al.* (1998)]
Reorientation of whole protein	4-15 ns	[Boresch *et al.* (2000)]

5.3. Models for Quantum Baths and Decoherence

As discussed above, systems are rarely completely isolated from their environment, and in many cases, particularly in biology, this system-bath coupling may be very strong and in fact play an important role in their functionality. This interaction may be through photons (i.e. light), phonons (such as vibrational modes in the solvent or protein scaffold, or indeed the molecule comprising the two-level system (TLS) itself) or specific localized defects (such as local point charges).

In terms of dynamics, the presence of a strongly coupled environment may "observe" the state of the TLS and destroy or weaken the Rabi quantum oscillations between the two states. At the most extreme limit, this may lead to the quantum Zeno effect, where the system is completely localized [Sekatskii (2003); Joos (1984)] in one state or the other, even if an alternative lower energy state is available.

Particularly with the current interest in creating a quantum computer, it is necessary to have good models for the bath and how the resulting decoherence will effect the system dynamics. In particular, the development of simple, minimal models allows for both physical insight and the classifications of different parameter regimes exhibiting different dynamics. A particularly interesting class of models focuses on interaction between a two level system, described by a Pauli matrix σ_z, and its bath. It suffices in many situations to represent this environment coupling by a term

$$H_{\text{int}} = \sigma_z \cdot \hat{\Omega} \,. \tag{5.1}$$

Here some, typically many-body, operator $\hat{\Omega}$ of the environment couples to the state of the TLS via σ_z. Although situations exist where coupling to the other operators σ_x or σ_y is relevant, in many cases these couplings will be negligible [Leggett *et al.* (1987)].

Two specific forms for this interaction are worth discussion, as they can be applied to a diverse range of physical systems. The first is the spin-bath model (for a good review, see Prokof'ev and Stamp (2000)), where local defects which are strongly coupled to the TLS of interest are themselves modelled as two-level systems. This allows for strong coupling to localized features of the environment.

The second is the spin-boson model [Weiss (1999); Leggett *et al.* (1987)]. This describes the interaction between a two-level system and the (typically) delocalized modes of the environment (phonons, photons, etc.), which

are treated as a bath of harmonic oscillators [Leggett *et al.* (1987)]. Provided the coupling to any single environment mode is sufficiently weak, and intra-bath interactions can be neglected, a quite general environment can be treated as a collection of harmonic oscillators [Caldeira and Leggett (1983)]. It is distinct from the spin-bath model, however, because it cannot describe any single, strongly coupled feature of the environment, so careful consideration must be given to the applicability of each model.

5.3.1. *The spin-boson model*

The spin-boson model is a powerful and widely used model for describing decoherence. It exhibits rich quantum dynamics, and has found wide and varied applications in modelling decoherence in qubits [Reina *et al.* (2002)] and electron transfer reactions [Xu and Schulten (1994)], as well as deeper questions about the role of quantum mechanics on the macroscopic level. Most importantly, its dynamics have been widely studied [Weiss (1999); Lesage and Saleur (1998); Costi and McKenzie (2003)] and its behaviour is known through much of the parameter space.

In Leggett *et al.* (1987) the spin-boson Hamiltonian is defined as

$$H = -\frac{1}{2}\Delta\sigma_x + \frac{1}{2}\epsilon\sigma_z + \sum_\alpha (p_\alpha^2/2m_\alpha + \frac{1}{2}m_\alpha\omega_\alpha^2 x_\alpha^2) + \frac{1}{2}\sigma_z \sum_\alpha C_\alpha x_\alpha \,. \quad (5.2)$$

This Hamiltonian describes a two level system interacting with an infinite bath of harmonic oscillators. Here, σ_z is a Pauli sigma matrix which describes the state of a two level system (TLS) with energy gap ϵ. Here, Δ represents the bare tunnelling energy between the two levels (note that in Leggett *et al.* (1987) a tunnelling *frequency* is used instead of energy, and $\hbar\Delta$ appears in Eq. (5.2) instead). The TLS is coupled to a bath of harmonic oscillators identified by subscript α, described by frequency, mass, position and momentum $\omega_\alpha, m_\alpha, x_\alpha$ and p_α respectively. The third term in (5.2) is the standard energy of a simple harmonic oscillator. The final term describes the coupling to the position of the αth oscillator and has units of force (energy per unit length, kg m s^{-2}). Leggett *et al.* (1987) also includes a coordinate q_0, representing a length scale derived from mapping a continuous system (such as the double well potential) to a TLS that is unnecessary for the intrinsically two-state system which we will be considering in this chapter, and is usually not included (although it should be noted it would change the dimensions of the coupling constants C_α).

Table 5.2. Parameters of the spin-boson model, and their units.

Symbol	Description	Units
ϵ	Bias / TLS energy	Energy (J)
Δ	Tunnelling element / coupling	Energy (J)
ω_α	Frequency of the αth oscillator	Frequency (s^{-1})
C_α	Coupling to the αth mode	Force (kg m s^{-2})
$J(\omega)$	Spectral density	Energy (J)
α	Dimensionless coupling for Ohmic $J(\omega)$	Unitless

It is also possible to rewrite the spin-boson model in terms of creation and annihilation operators of the bath:

$$H = \frac{1}{2}\epsilon\sigma_z + \Delta\sigma_x \sum_\alpha \hbar\omega_\alpha a_\alpha^\dagger a_\alpha + \sigma_z \sum_\alpha M_\alpha(a_\alpha^\dagger + a_\alpha) \tag{5.3}$$

where the position and momentum are defined as

$$x_\alpha = \sqrt{\frac{\hbar}{2m_\alpha\omega_\alpha}}(a_\alpha + a_\alpha^\dagger)$$

and

$$p_\alpha = -i\sqrt{\frac{\hbar m_\alpha\omega_\alpha}{2}}(a_\alpha - a_\alpha^\dagger)$$

or equivalently $a_\alpha = x_\alpha\sqrt{\frac{m_\alpha\omega_\alpha}{2\hbar}} + p_\alpha\frac{i}{\sqrt{2\hbar m_\alpha\omega_\alpha}}$. In addition to allowing us to use the framework of second quantization, we no longer need to specify an effective mass m_α for each oscillator; instead, it is sufficient to simply specify the oscillator frequencies and their couplings.

5.3.1.1. *Independent boson model*

A closely related model is the independent boson model, where there is no coupling between the two states of the TLS (i.e., $\Delta = 0$). This is sometimes referred to as a polaron model [Mahan (1990)]. It is described by the Hamiltonian

$$H = \frac{1}{2}\epsilon\sigma_z + \sum_\alpha (p_\alpha^2/2m_\alpha + \frac{1}{2}m_\alpha\omega_\alpha^2 x_\alpha^2) + \frac{1}{2}\sigma_z \sum_\alpha C_\alpha x_\alpha\,. \tag{5.4}$$

This corresponds to two uncoupled energy levels interacting with an environment modelled by the harmonic oscillators. Now, the TLS operator σ_z commutes with the Hamiltonian and so is a constant of motion—environment effects cannot act to change σ_z, but the off diagonal terms of the reduced density matrix $\rho(t)$, describing quantum coherence between the two TLS states, will change over time. This system may be of particular

interest where transitions may be induced between the two states by an external, "fast" influence, and the resulting changes and relaxation of the environment are of interest. For example, solvent relaxation after a rapid, laser induced transition in a chromophore is directly observable through the gradual shift in the wavelength of the chromophore's fluorescence peak.

5.3.2. *Caldeira-Leggett Hamiltonian*

Another Hamiltonian that is highly analogous to the spin boson Hamiltonian can be used to model how coupling to the environment influences hydrogen transfer reactions. This Hamiltonian is generally referred to as the Caldeira-Leggett Hamiltonian and treats the position of the hydrogen as a continuous one dimensional variable that is the subject of some position dependent external potential $V(x)$,

$$\mathcal{H} = \frac{p^2}{2M} + V(x) + \frac{1}{2}\sum_{\alpha=1}^{N}\left[\frac{p_\alpha^2}{m_\alpha} + m_\alpha\omega_\alpha^2\left(q_\alpha - \frac{C_\alpha}{m_\alpha\omega_\alpha^2}x\right)^2\right]. \qquad (5.5)$$

Figure 5.2 shows a double well potential that is the generic potential for an arbitrary chemical reaction. There are two metastable positions located at the reactant and product states and then an unstable position that corresponds to the transition state of the reaction.

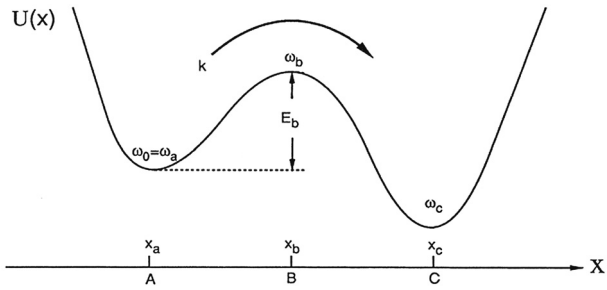


Fig. 5.2. Potential energy as a function of the reaction coordinate, x, with the metastable reaction state at A, the transition state at B and the final product state at C. Escape occurs via the forward rate k and E_b is the corresponding activation energy. The angular frequency of oscillations about the reactant state is ω_0, which depends on the curvature of the potential energy surface at the local minimum ($x = x_a$) and the mass of the particle. Similarly the barrier frequency ω_b, depends on the curvature of the potential energy surface at the local maximum ($x = x_b$) and the mass of the particle [Hänggi *et al.* (1990)].

5.3.3. *The spectral density*

In many situations, we are either unable to measure the state of the environment or have no interest in it beyond its effect on the chromophore or hydrogen being transferred. A key result for the spin-boson model and Caldeira-Leggett Hamiltonian is that the effect of the environment on the dynamics of the subsystem of interest can be completely encapsulated in the "spectral density" function $J(\omega)$ defined as:

$$J(\omega) = \frac{\pi}{2} \sum_{\alpha} \frac{C_\alpha^2}{m_\alpha \omega_\alpha} \delta(\omega - \omega_\alpha) = \frac{4\pi}{\hbar} \sum_{\alpha} M_\alpha^2 \delta(\omega - \omega_\alpha)\,, \tag{5.6}$$

Here, $\delta(\omega - \omega_\alpha)$ is the Dirac δ-function, and so $J(\omega)$ is effectively the density of states of the environment, but weighted by the couplings C_α. It has units of energy. The Caldeira-Leggett Hamiltonian is similarly characterized by a spectral density that is similarly defined. In this context another function known as the friction kernel is often used to characterise the interaction with the environment. It is formally defined as:

$$\gamma(t) = \frac{1}{M} \sum_{\alpha} \frac{C_\alpha^2}{m_\alpha \omega_\alpha^2} \cos(\omega_\alpha t)\,, \tag{5.7}$$

where M is the effective mass of the particle involved in the chemical reaction. For most applications it is appropriate to assume that the spectrum of oscillator frequencies are sufficiently dense and the couplings M_α are sufficiently smooth that $J(\omega)$ may be considered a smooth, continuous function of ω. In this way, we remove the need to specify the couplings to each individual oscillator (potentially requiring a large number of discrete parameters) and can instead describe the functional form of the spectral density.

In particular, for many (though by no means all) physical situations $J(\omega)$ takes the form of a simple power law at low frequencies, but decays to zero above some cut-off frequency ω_c. We will later see that when the dynamics occur on time scales much shorter than the environment response times (specifically, quantum tunnelling with energy $\Delta \ll \hbar\omega_c$) that the exact form of the cut-off, and the exact value of the cut-off frequency, will be unimportant [Leggett *et al.* (1987); Weiss (1999)]. Clearly, though, if both system and bath dynamics occur on comparable time scales, couplings around ω_c may be important.

Typically, ω_c is introduced when mapping a continuous system to a discrete, two level system, but in many physical situations the high frequency cut-off will occur naturally: intuitively, there is a minimum timescale over

which the TLS is capable of responding to the environment. For bath events, particularly oscillatory events, on time scales shorter than this, the TLS will only see the average behaviour of the environment. This corresponds to zero coupling at sufficiently high environment frequencies.

A general power law for the spectral density has been treated extensively in Leggett *et al.* (1987):

$$J(\omega) = A\omega^s e^{-\omega/\omega_c} \,. \tag{5.8}$$

The spectral density for $s = 1$ is referred to as Ohmic, and for $s > 1$ as superohmic, and as subohmic for $s < 1$. The Ohmic spectral density is important as $J(\omega)$ is roughly linear up to some cut-off frequency ω_c:

$$J(\omega) = h\alpha\omega \,, \qquad \omega < \omega_c \tag{5.9}$$

where α is a dimensionless measure of the strength of the system-environment coupling, independent of ω_c, and will be critical in determining the system dynamics. In many situations with an Ohmic spectral density it is more convenient (or, indeed, more physically relevant) to consider a Drude form for the spectral density [Weiss (1999)], as follows:

$$J(\omega) = \frac{h\alpha\omega/\omega_c}{1 + (\omega/\omega_c)^2} \,. \tag{5.10}$$

5.4. The Spectral Density for the Different Continuum Models of the Environment

In this section we consider dielectric continuum models of the environment of a biological chromophore. For the different models it is possible to derive an expression for the spectral density Eq. (5.6). This allows us to explore how the relative importance of the dielectric relaxation of the solvent, bound water, and protein depends on the relevant length scales (the relative size of the chromophore, the protein and the thickness of the layer of bound water) and time scales (the dielectric relaxation times of the protein, bound water and the solvent). We find that even when the chromophore is completely surrounded by a protein it is possible that the ultra-fast solvation (on the psec timescale) is dominated by the bulk solvent surrounding the protein.

Many experimentally obtained spectral densities can be fitted to a sum of Lorentzians of the form

$$J(\omega) = \frac{\alpha_1\omega}{1 + (\omega\tau_1)^2} + \frac{\alpha_2\omega}{1 + (\omega\tau_2)^2} + \dots \,. \tag{5.11}$$

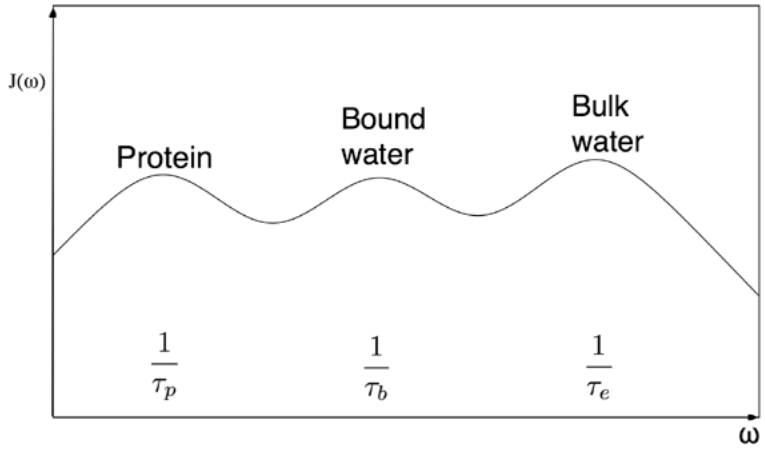


Fig. 5.3. Schematic plot of the spectral density for a typical chromophore on a log-log scale. We see three distinct peaks, which can be attributed to the relaxation of the protein, bound water and bulk solvent, respectively, with corresponding relaxation times τ_p,τ_b and τ_e.

For a protein that is large compared to the size of the binding pocket of the chromophore and the width of the bound water layer, we find the spectral density is described as the sum of three Lorentzians which correspond to the dynamics of the protein, bound water and bulk water dynamics respectively. This is shown schematically in Fig. 5.3. Key to this is the separation of time scales, associated with the solvation coming from each of the three components of the environment.

We have shown that to a good approximation, the spectral density is given by,

$$J(\omega) = \frac{\alpha_p \omega}{1 + (\omega\tau_p)^2} + \frac{\alpha_b \omega}{1 + (\omega\tau_b)^2} + \frac{\alpha_s \omega}{1 + (\omega\tau_s)^2} \tag{5.12}$$

where the relaxation times can be expressed as:

$$\frac{\tau_p}{\tau_{D,p}} = \frac{2\epsilon_{p,i} + 1}{2\epsilon_{p,s} + 1} \tag{5.13}$$

$$\frac{\tau_s}{\tau_{D,s}} = \frac{2\epsilon_{e,i} + 1}{2\epsilon_{e,s} + 1} \tag{5.14}$$

$$\tau_b = \tau_{D,b}\,. \tag{5.15}$$

The subscripts $x = p, s, b$ refer to the protein, solvent, and bound water respectively; and $\epsilon_{x,s}, \epsilon_{x,i}, \tau_{D,x}$ are the static dielectric constant, high frequency dielectric constant, and relaxation times of a Debye model for each medium, although we use $\epsilon_e(\omega)$ for the dielectric of the bulk solvent to avoid confusion between subscripts. The reorganization energies associated with each part of the environment are given by α_i/τ_i, where

$$\frac{\alpha_p}{\tau_p} = \frac{(\Delta\mu)^2}{2\pi\epsilon_0 a^3} \frac{6(\epsilon_{e,s} - \epsilon_{e,i})}{(2\epsilon_{p,s} + 1)(2\epsilon_{e,i} + 1)} \tag{5.16}$$

$$\frac{\alpha_s}{\tau_s} = \frac{(\Delta\mu)^2}{2\pi\epsilon_0 b^3} \frac{6(\epsilon_{e,s} - \epsilon_{e,i})}{(2\epsilon_s + 1)(2\epsilon_{e,i} + 1)} \left(\frac{9\epsilon_{p,i}}{(2\epsilon_{p,i} + 1)^2} \right) \tag{5.17}$$

$$\frac{\alpha_b}{\tau_b} = \frac{3(\Delta\mu)^2}{2\pi\epsilon_0 b^3} \left(\frac{c - b}{b} \right) \frac{(\epsilon_{b,s}^2 + 2\epsilon_{e,s}^2)(\epsilon_{b,s} - \epsilon_{b,i})}{\epsilon_{b,s}^2 (2\epsilon_{e,s} + 1)^2} . \tag{5.18}$$

In particular, for typical systems the above three quantities can be of the same order of magnitude, i.e.

$$\frac{\alpha_s}{\tau_s} \sim \frac{\alpha_b}{\tau_b} \sim \frac{\alpha_p}{\tau_p} . \tag{5.19}$$

Hence, the peaks of the spectral density can be of the same order of magnitude. This is because although each contribution is due to different dielectrics constants, they only have a limited range of values. This is supported by experimental data (see Table 5.5) where several relaxation times are observed which vary by several orders of magnitude, but whose relative contributions are comparable. Therefore, in many cases only a single component of the environment (protein, bound water, bulk solvent) will be relevant to a given process. These expressions allow us to predict the ultrafast solvation times in the presence of a protein, which we find may increase the solvation time by at most a factor of two. We also suggest that at least some of the studies which have identified ultrafast dielectric relaxation of proteins [Homoelle *et al.* (1998); Riter *et al.* (1996)] may in fact be detecting the fast response of the distant solvent.

5.5. Obtaining the Spectral Density from Experimental Data

The spectral function $J(\omega)$ associated with optical transitions in chromophores can be extracted from ultra-fast laser spectroscopy [Fleming and Cho (1996)]. The time dependence of the Stokes shift in the fluorescence

spectrum, where $\nu(t)$ is the maximum (or the first frequency moment) of the fluorescence spectrum at time t, can be normalized as

$$C(t) = \frac{\nu(t) - \nu(\infty)}{\nu(0) - \nu(\infty)} \tag{5.20}$$

such that $C(0) = 1$, and $C(\infty) = 0$ when the fluorescence maxima has reached its equilibrium value. This is related to the spectral density by

$$C(t) = \frac{\hbar}{E_R} \int_0^\infty d\omega \frac{J(\omega)}{\omega} \cos(\omega t) \tag{5.21}$$

where E_R is the total reorganization energy given in Eq. (5.35), which also equals half the total Stokes shift.

The function $C(t)$ is sometimes referred to as the *hydration correlation function* and experimental results are often fitted to several decaying exponentials,

$$C(t) = A_1 \exp(-t/\tau_1) + A_2 \exp(-t/\tau_2) + A_3 \exp(-t/\tau_3) + \ldots \tag{5.22}$$

where $A_1 + A_2 + \ldots = 1$. From (5.21), this corresponds to a spectral density of the form

$$J(\omega) = \frac{\alpha_1 \omega}{1 + (\omega\tau_1)^2} + \frac{\alpha_2 \omega}{1 + (\omega\tau_2)^2} + \ldots . \tag{5.23}$$

The dimensionless couplings α_j $(j = 1, 2, \ldots)$ are related to the total reorganization energy by

$$\alpha_j = \frac{2E_R A_j \tau_j}{\pi\hbar} \simeq 0.25 A_j \frac{E_R}{\mathrm{cm}^{-1}} \frac{\tau_j}{\mathrm{psec}} . \tag{5.24}$$

Table 5.5 gives values of the fitting parameters (E_R, A_j, τ_j) determined by fast laser spectroscopy for a range of chromophores and different environments, both protein and solvent. We do not claim the list is exhaustive of all the published values, but is meant to be indicative [Riter *et al.* (1996); Kennis *et al.* (2002)]. We note the following general features:

(i) The Stokes shift varies significantly between different environments, both solvent and protein. Generally, the presence of the protein reduces the total Stokes shift and the relative contribution of the ultrafast component, which can be assigned to the solvent. The less exposed the chromophore is to the solvent the smaller is solvent contribution to the spectral density. This is also seen in measurements of the dynamic Stokes shift for a chromophore placed at three different sites in the B1 domain of protein G. (See Fig. 3c of Cohen *et al.* (2002)). Denaturing the protein tends to expose the chromophore to more solvent and increase the total Stokes shift and increase the relative contribution of the ultrafast component.

Table 5.3. Solvation relaxation times for various chromophores in a range of environments.

Chromophore	Protein	Solvent	Ref.	E_R (cm^{-1})	A_1, τ_1 (fsec)	A_2, τ_2 (psec)	A_3, τ_3 (nsec)
Eosin	none	water	[Lang *et al.* (1999)]	877	0.15, 400	0.12, 3	
Eosin	lysozyme	water	[Jordanides *et al.* (1999(@)]	710	0.1, 310	0.1, 7	
Trp	none	water	[Zhong *et al.* (2002)]		0.2, 180	0.8, 1	
Trp	SC	water	[Pal *et al.* (2002)]	1440	0.6, 800	0.4, 38	
Trp	Rube	water	[Zhong *et al.* (2002)]		0.17, 1000	0.26, 12	0.57, 0.320
Trp	Monellin	water	[Peon *et al.* (2002)]		0.46,1300	0.54, 16	
Dansyl	SC	water	[Pal *et al.* (2002)]	1180	0.94, 1500	0.06, 40	
DCM	HSA	water	[Pal *et al.* (2001)]	515		0.25, 600	0.75, 10
Prodan	none	water	[Kamal *et al.* (2004)]	2313	0.47, 130	0.53, 0.770	
Prodan	HSA	water	[Kamal *et al.* (2004)]	916	0.19, 780	0.56, 2.6	0.25, 0.032
Acrylodan	HSA	water	[Kamal *et al.* (2004)]	1680	0.23, 710	0.41, 3.7	0.36, 0.057
Acrylodan	HSA	0.2M Gdn.HCl	[Kamal *et al.* (2004)]		0.16, 280	0.36, 5.4	0.48, 0.061
Acrylodan	HSA	0.2M Gdn.HCl	[Kamal *et al.* (2004)]		0.2, 120	0.55, 2	0.25, 0.0135
Coumarin 153	none	acetonitrile	[Changenet-Barret *et al.* (2000)]	2200	0.8, 100	0.2, 700	
C343-peptide	Calmodulin	water	[Changenet-Barret *et al.* (2000)]	250	0.9, 100	0.1, 2.4	
Coumarin 343	none	water	[Jimenez *et al.* (1994)]	1953	0.2, 126	0.35, 0.880	
Phycocyanobilin	C-phycocyanin	water	[Homoelle *et al.* (1998)]	372	$0.2,\ 100 \pm 30$	$0.2,\ 6 \pm 5$	
Phycocyanobilin	C-phycocyanin	water	[Riter *et al.* (1996)]	372		$0.1\ ,\ > 10$	
MPTS	none	water	[Jimenez *et al.* (2002)]	2097	0.8, 20	0.2, 0.340	
MPTS	Ab6C8	water	[Jimenez *et al.* (2002)]	1910	0.85, 33	0.1, 2	0.05, 0.067
bis-ANS	GlnRS (native)	water	[Sen *et al.* (2003)]	750		0.45, 170	0.55, 2.4
bis-ANS	GlnRS (molten)	urea soln.	[Sen *et al.* (2003)]	500		0.63, 60	0.37, 0.96
4-AP	GlnRS (native)	water	[Sen *et al.* (2003)]	1330		0.85, 40	0.15, 0.580
4-AP	GlnRS (molten)	urea soln.	[Sen *et al.* (2003)]	700		0.77, 50	0.23, 0.9

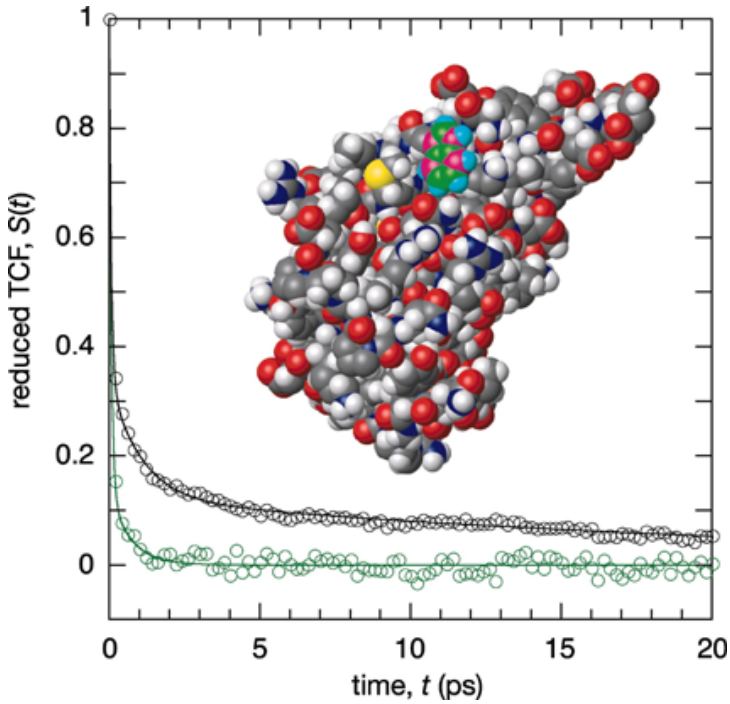


Fig. 5.4. Hydration correlation function $C(t)$ for Trp (light) and Trp-3 in monellin (dark) in aqueous solution at 300 K [Nilsson and Halle (2005)].

(ii) The different decay times observed for a particular system can vary by as many as four orders of magnitude, ranging from 10's fsec to a nsec.

(iii) The relative contributions of the ultrafast (100's fsec) and slow (10's psec) response are often of the same order of magnitude, consistent with Eq. (5.19).

(iv) Even when the chromophores are inside the protein, the coupling of the chromophore to the solvent is large. For example, Prodan is in a hydrophobic pocket of HSA, well away from the surface, and yet $\alpha_s \sim 50$. Even for the "buried" chromophores (Leu^7 and Phe^{30}) in GB1, [Cohen *et al.* (2002)] the solvent contribution is $A_s E_R \sim 100$ cm^{-1}, $\tau_s \sim 5$ psec, and so $\alpha_s \sim 100$. There are several proteins for which a very slow ($\sim$ 10's nsec) dynamic Stokes shift has been observed and has been assigned to dielectric relaxation of the protein itself [Pierce and Boxer (1992); Pal *et al.* (2001)].

5.6. Analytical Solution for the Time Evolution of the Density Matrix

Of particular interest is the time evolution of the reduced density matrix for the TLS of interest interacting with the oscillator bath. Reina *et al.* (2002) have studied the decoherence of quantum registers through independent boson models. They consider the 2×2 reduced density matrix $\rho(0)$ with elements

$$\rho(0) = \begin{pmatrix} \rho_{11} & \rho_{12} \\ \rho_{21} & \rho_{22} \end{pmatrix} \tag{5.25}$$

for the TLS, and assume that the bath is initially uncoupled to the TLS and in thermal equilibrium so that the initial density matrix for the whole system is

$$\tilde{\rho}(0) = \rho_0(0) \exp(-\beta H_b) \tag{5.26}$$

where H_b is the Hamiltonian representing the bath, for the independent boson model given by $H_b = \sum_\alpha \hbar\omega_\alpha a_\alpha^\dagger a_\alpha$. The density matrix at a later time t is then given by

$$\rho(t) = \mathrm{Tr}\left[e^{iHt}\tilde{\rho}(0)e^{-iHt}\right] \tag{5.27}$$

where H is the total independent boson Hamiltonian for the system, given by Eq. (5.4). They show that the time dependent density matrix has matrix elements [Reina *et al.* (2002)]

$$\begin{aligned} \rho_{11}(t) &= \rho_{11}(0) \\ \rho_{22}(t) &= \rho_{22}(0) = 1 - \rho_{11}(0) \\ \rho_{12}(t) = \rho_{21}^*(t) &= \rho_{12}(0) \exp(i\epsilon t + i\theta(t) - \Gamma(t,T)) \end{aligned} \tag{5.28}$$

where $\theta(t)$ is a phase shift given by

$$\theta(t,T) = \int_0^\infty J(\omega) \frac{[\omega t - \sin(\omega t)]}{\omega^2} d\omega \tag{5.29}$$

and

$$\Gamma(t,T) = \int_0^\infty d\omega J(\omega) \coth\left(\frac{\omega}{2k_BT}\right) \frac{(1-\cos\omega t)}{\omega^2} \tag{5.30}$$

describes the decoherence due to interaction with the environment.

Provided $k_BT \ll \hbar\omega_c$, for an Ohmic spectral density and for low temperatures compared to the cut-off frequency ($\hbar\omega_c \ll k_BT$), the decoherence rate is approximately

$$\Gamma_1(t,T) \approx \alpha_1 \left[2\omega_T t \arctan(2\omega_T t) + \frac{1}{2}\ln\left(\frac{1+\omega_c^2 t^2}{1+4\omega_T^2 t^2}\right)\right]. \tag{5.31}$$

This rate shows three different regimes of qualitative behaviour depending on the relative size of the time t to the time scales defined by $1/\omega_c$ and $\hbar/k_BT$. For short times $\omega_c t < 1$,

$$\Gamma(t,T) = \frac{t^2}{2\tau_g^2} \tag{5.32}$$

where

$$\frac{1}{\tau_g^2} = \int_0^\infty d\omega J(\omega) \coth\left(\frac{\omega}{2k_BT}\right) \tag{5.33}$$

and so there is a Gaussian decay of decoherence. For $k_BT \gg \hbar\omega_c$, this reduces to

$$\frac{\hbar}{\tau_g} = \sqrt{2E_Rk_BT}/\hbar \tag{5.34}$$

where E_R is the reorganization energy given by

$$E_R = \frac{1}{\pi}\int_0^\infty \frac{J(\omega)}{\omega} d\omega\,. \tag{5.35}$$

For an Ohmic spectral density of the form $J(\omega) = \alpha\omega/[1 + (\omega/\omega_c)^2]$ one obtains for intermediate times (the quantum regime [Unruh (1995)]),

$$\Gamma(t,T) \approx \alpha \ln(\omega_c t) \tag{5.36}$$

and for long times ($t \gg \hbar/k_BT$, the thermal regime) the decoherence is linear in time,

$$\Gamma(t,T) \approx 2\alpha k_BTt/\hbar\,. \tag{5.37}$$

as might be expected from a golden rule type calculation.

5.7. Nuclear Quantum Tunnelling in Enzymes and the Crossover Temperature

General tunnelling problems can be investigated by employing complex-time path integrals [Hänggi *et al.* (1990); Weiss (1999)]. The functional-integral representation of quantum mechanics pioneered by Feynman lends itself to this treatment of the problem. Consider the partition function

$$Z = \mathrm{Tr}\{\exp(-\beta\mathcal{H})\}\,, \tag{5.38}$$

here $\mathcal{H}$ denotes the full Hamiltonian operator corresponding to the system plus environment. Following [Feynman (1972)] this quantity can be

expressed in the form of a functional path integral over the tunnelling coordinate $x(\tau)$, here $\tau = it$ is a real variable. This integral runs over all paths that are periodic with period $\theta = \hbar\beta$. Accordingly each trajectory $x(\tau)$ is weighted by the Euclidean action S_E. In the Feynman path integral formulation of quantum mechanics the transition probability between two states involves the square of a transition amplitude which is the sum of all possible paths joining those two states. At finite temperatures the path integral is dominated by the extrema of the imaginary time action. Pursuing this analysis for the Caldeirra-Legget Hamiltonian shows that a non-trivial periodic solution (which has been dubbed the bounce solution) only exists below a certain crossover temperature T_0 [Hänggi *et al.* (1990)]. The bounce solution is associated with tunnelling from the reactant to product well. For temperatures $T > T_0$ there is no oscillation of the particle in the classically forbidden regime.

For temperatures $T > T_0$ the role of the bounce solution is taken over by the constant solution ($x_e(\tau) = x_b$) where the particle sits at the barrier top. In this kinetic regime there are still rate enhancements from quantum effects but in this temperature regime the bounce solution which is associated with conventional tunnelling does not exist. Figure 5.5 depicts the different kinetic regimes.

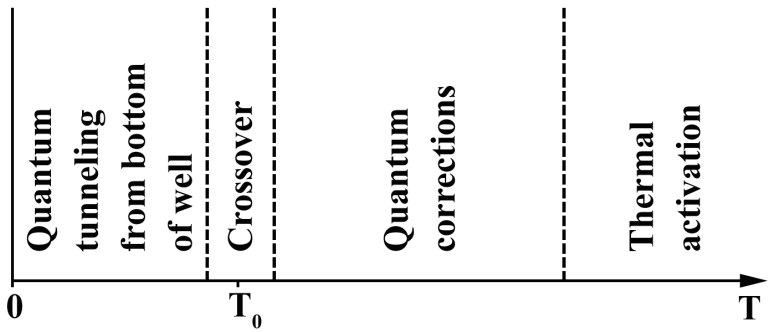


Fig. 5.5. Different kinetic regimes as a function of temperature [Hänggi *et al.* (1990)]. At temperatures much greater than the crossover temperature T_0 thermal activation dominates as the means of getting over the energy barrier. As the temperature decreases the dynamics become influenced by quantum effects which manifest themselves as a correction to the classical rate expression. When the temperature is less than T_0 the dynamics becomes dominated by tunnelling since the effect of thermal hopping vanishes [Hänggi *et al.* (1990)].

The crossover temperature T_0 is defined as

$$T_0 = \hbar\mu(2\pi k_B)^{-1} = (1.216 \times 10^{-12}\ \text{secK})\mu\,, \tag{5.39}$$

where μ is the effective barrier frequency which is be obtained by finding the positive root of the following equation

$$0 = \mu^2 - \omega_b^2 + \mu\hat{\gamma}(\mu)\,. \tag{5.40}$$

Here $\hat{\gamma}(z)$ is simply the Laplace transform of the friction kernel defined in Eq. (5.7). It is simply another means of representing the spectral density. This equation shows that the effective barrier frequency depends on the nature of the coupling to the environment. In the case of a Lorentzian spectral density it takes the explicit form of

$$0 = \mu^2 - \omega_b^2 + \frac{\mu\omega_D\gamma}{\omega_D + \mu}\,. \tag{5.41}$$

As T_0 depends linearly on μ, one can gain an understanding of how T_0 varies as a function of the friction strength for different bath response frequencies from Fig. 5.6. This figure shows how the positive root of Eq. (5.41) changes as a function of the scaled friction and bath response frequency.

It is worthwhile to examine how the effective barrier frequency changes in the different limits of the bath response. In the limit where $\omega_D \gg 2\pi T$ the barrier frequency does not depend on the response frequency of the bath and is essentially Ohmic. In this case the effective barrier frequency takes the form of

$$\mu = \sqrt{\omega_b^2 + \gamma^2/4} - \gamma/2\,. \tag{5.42}$$

In the other limit where $\mu \gg \omega_D$ the effective barrier frequency becomes

$$\mu = \sqrt{\omega_b^2 - \gamma\omega_D}\,. \tag{5.43}$$

In both cases an increase in the strength of the damping, γ, reduces the effective barrier frequency and hence the crossover temperature. When $\mu \gg \omega_D$ increasing the response frequency of the bath also decreases the crossover temperature. In the absence of any dissipative interaction with the environment ($\gamma = 0$), the crossover temperature assumes the maximum value of

$$T_0 = \hbar\omega_b(2\pi k_B)^{-1}\,. \tag{5.44}$$

This is an upper limit on the crossover temperature and any interaction with the environment always tends to *decrease* it. This is a direct manifestation of the effect that decoherence has on the system showing that as the environment more strongly interacts with the hydrogen being transferred you need to go to lower and lower temperatures to see any quantum effects.

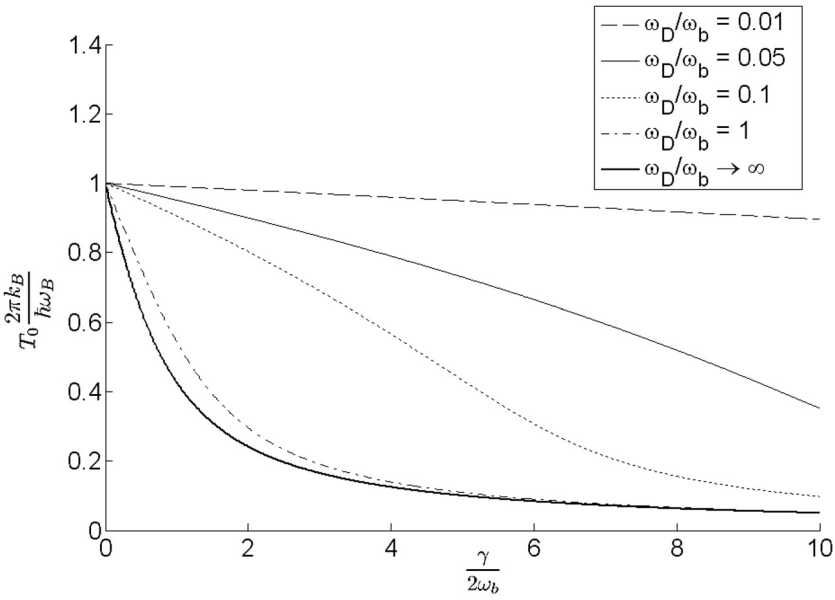


Fig. 5.6. The scaled crossover temperature as a function of the friction strength for a Lorentzain spectral density. The scaled crossover temperature is the ratio of the actual crossover temperature and the theoretical upper limit where there is no friction. The friction strength is the dimensionless parameter $\gamma/2\omega_b$. The different plots show how the relative size of the response frequency of the bath, ω_D, and the barrier frequency, ω_b change the influence that friction strength has on the crossover temperature. These show that in the limit where $\omega_D/\omega_b \to \infty$ the crossover temperature becomes very sensitive to the friction strength. However as the ratio is reduced the strength of the dependence decreases.

5.8. Summary

In the preceding sections we have given an illustrative guide to approaches that we and others have taken to modelling decoherence in biomolecules. By taking a minimalist approach one is able to capture a significant fraction of the essential physics that describes how significant quantum effects can be to the *in vivo* function of biomolecules. The results clearly show that interaction with the environment suppresses the significance of quantum effects like interference and tunnelling. In the case of biological chromophores increasing the strength of interaction with the environment directly increases the decoherence rate. Moreover, in the case of hydrogen transfer reactions in enzymes significant interaction with the environment deceases the temperature at which quantum effects impinge on the kinetics to well outside

the biologically relevant range. This shows that modelling the decoherence, which a particular biomolecule is subject to, is of the utmost importance if one is to determine whether quantum mechanics plays a non-trivial role in its biological functionality.

References

Afsar, M. N., and Hasted, J. B. (1978). Submillimetre wave measurements of optical constants of water at various temperatures, *Infrared Phys.* **18**, p. 835.

Boresch, S., Höchtl, P., and Steinhauser, O. (2000). Studying the dielectric properties of a protein solution by computer simulation. *J. Phys. Chem. B* **104**, p. 8743.

Caldeira, A., and Leggett, A. (1983). Quantum tunnelling in a dissipative system, *Ann. Phys. (N.Y.)* **149**, p. 374.

Changenet-Barret, P., Choma, C., Gooding, E., DeGrado, W., and Hochstrasser, R. (2000). Ultrafast dielectric response of proteins from dynamics Stokes shifting of coumarin in calmodulin, *J. Phys. Chem. B* **104**, p. 9322.

Cohen, B. E., McAnaney, T. B., Parl, E. S., Jan, Y. N., Boxer, S. G., and Jan, L. Y. (2002). Probing protein electrostatics with a synthetic fluorescent amino acid, *Science* **296**, p. 1700.

Costi, T., and McKenzie, R. (2003). Entanglement between a qubit and the environment in the spin-boson model, *Phys. Rev. A* **68**, p. 034301.

Feynman, R. (1972). *Statistical Mechanics* (Benjamin, Reading, Mass.).

Fleming, G., and Cho, M. (1996). Chromophore-solvent dynamics, *Ann. Rev. Phys. Chem.* **47**, p. 109.

Hänggi, P., Talkner, P., and Borkoves, M. (1990). Reaction-rate theory: fifty years after Kramers, *Rev. Mod. Phys.* **62**, p. 251.

Homoelle, B. J., Edington, M. D., Diffey, W. M., and Beck, W. F. J. (1998). Stimulated photon-echo and transient-grating studies of protein-matrix solvation dynamics and interexciton-state radiationless decay in a phycocyanin and allophycocyanin, *J. Phys. Chem. B* **102**, p. 3044.

Hornberger, K., Uttenthaler, S., Brezger, B., Hackermuller, L., Arndt, M., and Zeilinger, A. (2003). Collisional decoherence observed in matter wave interferometry, *Physical Review Letters* **90**, 16, art. no. 160401.

Jimenez, R., Case, D., and Romesberg, F. (2002). Flexibility of an antibody binding site measured with photon echo spectroscopy, *J. Phys. Chem. B* **106**, p. 1090.

Jimenez, R., Fleming, G., Kumar, P., and Maroncelli, M. (1994). Femtosecond solvation dynamics of water, *Nature* **369**, p. 471.

Joos, E. (1984). Continuous measurement: Watchdog effect versus golden rule, *Phys. Rev. D* **29**, p. 1626.

Jordanides, X. J., Lang, M. J., Song, X., and Fleming, G. R. (1999). Solvation dynamics in protein environments studied by photon echo spectroscopy, *J. Phys. Chem. B* **103**, p. 7995.

Kamal, J. K. A., Zhao, L., and Zewail, A. H. (2004). Ultrafast hydration dynamics in protein unfolding: Human serum albumin, *Proc. Natl. Acad. Sci.* **101**, p. 13411.

Kennis, J. T. M., Larsen, D. S., Ohta, K., Facciotti, M. T., Galeser, R. M., and Fleming, G. R. (2002). Ultrafast protein dynamics of bacteriorhodopsin probed by photon echo and transient absorption spectroscopy, *J. Phys. Chem. B* **106**, p. 6067.

Lang, M. S., Jordanides, X. J., Song, X., and Fleming, G. (1999). Aqueous solvation dynamics studied by photon echo spectroscopy, *J. Chem. Phys.* **110**, p. 5884.

Leggett, A., Chakravarty, S., Dorsey, A., Fisher, M., Garg, A., and Zwerger, W. (1987). Dynamics of the dissipative two-state system, *Rev. Mod. Phys.* **59**, p. 1.

Lesage, F., and Saleur, H. (1998). Boundary interaction changing operators and dynamical correlations in quantum impurity problems, *Phys. Rev. Lett.* **80**, p. 4370.

Loffler, G., Schreiber, H., and Steinhauser, O. (1997). Calculation of the dielectric properties of a protein and its solvent: Theory and a case study, *J. Mol. Biol.* **270**, p. 520.

Mahan, G. D. (1990). *Many-Particle Physics*, 2nd edn. (Plenum Press, New York and London), p. 285.

Nilsson, L., and Halle, B. (2005). Molecular origin of time-dependent fluorescence shifts in proteins, *Proc. Natl. Acad. Sci.* **102**, p. 13867.

Pal, S. K., Mandal, D., Sukul, D., Sen, S., and Bhattacharyya, K. (2001). Solvation dynamics of dcm in human serum albumin, *J. Phys. Chem. B* **105**, p. 1438.

Pal, S. K., Peon, J., and Zewail, A. H. (2002). Ultrafast surface hydration dynamics and expression of protein functionality: α-Chymotrypsin, *Proc. Natl. Acad. Sci.* **99**, p. 15297.

Peon, J., Pal, S. K., and Zewail, A. H. (2002). Hydration at the surface of the protein monellin: Dynamics with femtosecond resolution, *Proc. Natl. Acad. Sci.* **99**, p. 10964.

Pierce, W., and Boxer, S. G. (1992). Dielectric relaxation in a protein matrix, *J. Phys. Chem.* **96**, p. 5560.

Prokof'ev, N., and Stamp, P. (2000). Theory of the spin bath, *Rep. Prog. Phys.* **63**, p. 669.

Reina, J. H., Quiroga, L., and Johnson, N. F. (2002). Decoherence of quantum registers, *Phys. Rev. A* **65**, art. no. 032326.

Riter, R. E., Edington, M. D., and Beck, W. F. (1996). Protein-matrix solvation dynamics in the alpha subunit of C-Phycocyanin, *J. Phys. Chem. B* **100**, p. 14198.

Sekatskii, S. (2003). Fluorescence resonance energy transfer and quantum Zeno effect, *Physics Letters A* **317**, p. 1.

Sen, P., Mukherjee, S., Dutta, P., Halder, A., Mandal, D., Banerjee, R., Roy, S., and Bhattacharyya, K. (2003). Solvation dynamics in the molten globule state of a protein, *J. Phys. Chem. B* **107**, p. 14563.

Unruh, W. G. (1995). Maintaining coherence in quantum computers, *Phys. Rev. A* **51**, p. 992.

van Holde, K. E., Johnson, W. C., and Ho, P. S. (1998). *Physical Biochemistry* (Prentice-Hall).

Weiss, U. (1999). *Quantum Dissipative Systems*, 2nd edn. (World Scientific, Singapore).

Xu, D., and Schulten, K. (1994). Coupling of protein motion to electron transfer in a photosynthetic reaction center: Investigating the low temperature behavior in the framework of the spin-boson model, *Chem. Phys.* **182**, p. 91.

Zhong, D., Pal, S. K., Zhang, D., Chan, S. I., and Zewail, A. H. (2002). Femtosceond dynamics of rubredoxin: Tryptophan solvation and resonance energy transfer in the protein, *Proc. Natl. Acad. Sci.* **99**, p. 13.

About the authors

Jacques Bothma is currently an MPhil student in the Physics department at the University of Queensland. He completed his BSc in Physics at the University of Queensland in 2006. His research interests are in the areas of theoretical and experimental biological physics.

Joel Gilmore is a science communicator with the University of Queensland, and coordinator of the UQ Physics Demo Troupe. He completed a PhD in Physics at the University of Queensland in 2007, under Ross McKenzie, researching minimal models of quantum mechanics in biological systems.

Ross McKenzie is a Professorial Research Fellow in Physics at the University of Queensland. He was an undergraduate at the Australian National University and completed a PhD at Princeton University in 1988, under Jim Sauls. His research interests are in the quantum many-body theory of complex materials ranging from organic superconductors to biomolecules to rare-earth oxide catalysts.

This page intentionally left blank

PART 3

The Biological Evidence

This page intentionally left blank

Chapter 6

Molecular Evolution: A Role for Quantum Mechanics in the Dynamics of Molecular Machines that Read & Write DNA

Anita Goel

6.1. Introduction

Are the dynamics of biological systems governed solely by classical physics or could they somehow be influenced by quantum effects? New developments from the convergence of physics, biology, and nanotechnology are leading us to critically reexamine our conventional assumptions about the role of quantum physics in life and living systems. Schrödinger in his 1944 book *What is Life?* [Schrödinger (1967)] questioned whether the laws of classical physics were really sufficient to understand life. Schrödinger also wondered whether life, at the most fundamental level, could somehow be a quantum phenomena or at least be influenced by quantum effects? In recent times, such lines of inquiry have, for the most part, been dismissed by mainstream scientists because biological systems are wet and swampy, complex macroscopic systems, where it is presumed that quantum coherences would be destroyed much before their effects become relevant to biological processes. It is widely accepted, however, that quantum mechanics must play some role, albeit a trivial one, in life; namely the electronic structures of biomolecules are determined as per the laws of quantum chemistry.

My own quest to understand the physics of living systems is driven, in part, by an inner, intuitive conviction that twentieth century physics developed in the context of inanimate matter has not yet adequately come to terms with life and living systems. Living systems provide an excellent

Received May 1, 2007

laboratory to probe the interplay of matter, energy, and information. I have for many years been fascinated with molecular machines that read and write information into molecules of DNA. These nanomotors (*matter*) transduce chemical free *energy* into mechanical work as they copy biological *information* stored in a DNA molecule. These motors can be thought of as information processing machines that use information in their environment to evolve or adapt the way they read out DNA. In ways yet unknown to us, *information* from the environment can couple into and modulate the dynamics of these nanomachines as they replicate or transcribe genetic information.

For the past several years, I have been seeking, with the aid of fundamental physics concepts and emerging experimental tools, to identify and elucidate the various "knobs" in a motor's environment that can exert control on its dynamics as it replicates or transcribes the genetic code. Here, I heuristically examine the role that quantum mechanics may play in influencing the dynamics of the motors as they read/write bits of DNA. I begin by discussing how Wigner's inequalities for a quantum clock impose fundamental constraints on the accuracy and precision with which these nanomotors can read or write DNA. Contrary to implicit assumptions, I discuss how the relaxation times of DNA polymer molecules can be quite long, and hence lead to decoherence times that are long compared to the timescale of the internal state transitions in the motor and relevant compared to the timescale associated with the motor reading a DNA base. Thus, we argue that it is entirely plausible for quantum effects to influence not only the structure but also the dynamics of biomolecular motors. Lastly, some broader implications of this work are discussed.

6.2. Background

Nature packs information into DNA molecules with remarkable efficiency. Nanometre-sized molecular engines replicate, transcribe, and otherwise process this information. New tools to detect and manipulate single molecules have made it possible to elicit how various parameters in the motor's microenvironment can control the dynamics of these nano-motors (i.e. enzymes). At small length scales, noise plays a non-negligible role in the motor's movement along DNA.

Biological information in DNA is replicated, transcribed, or otherwise processed by molecular machines called polymerases. This process of

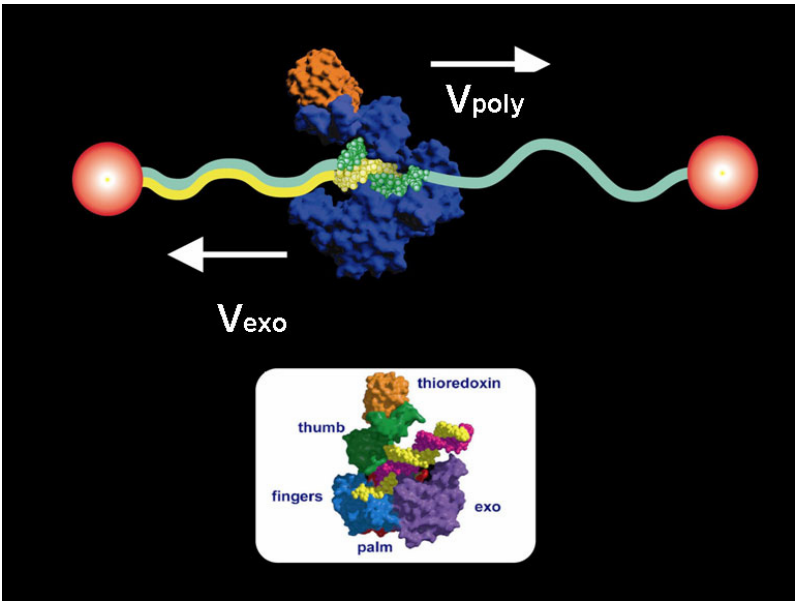


Fig. 6.1. Single molecule experiments reveal that mechanical tensions above 35 pN on the DNA induce a velocity reversal in the T7 DNA polymerase (DNAp) motor. A single DNA molecule is stretched between two plastic beads, while the motor catalyzes the conversion of ss to dsDNA. The speed of polymerization or formation of dsDNA is denoted by V_{poly}, while the reverse excision of dsDNA ($n \to n-1$) is denoted by V_{exo}. Inset: Crystal structure of T7 complex indicates that the polymerase and exonuclease activities (forward and reverse "gears") of the motor arise from structurally distinct catalytic domains.

reading and writing genetic information can be tightly coupled or regulated by the motor's environment. Environmental parameters (like temperature, nucleoside concentrations, mechanical tension of template, etc.) [Goel *et al.* (2003, 2002); Wuite *et al.* (2000)] can directly couple into the conformational dynamics of the motor. Theoretical concepts in concert with emerging nanotools to probe and manipulate single molecules are elucidating how various "knobs" in a motor's environment can control its real-time dynamics. Recent single molecule experiments have shown, for example, that increasing the mechanical tension applied to a DNA template can appreciably "tune" the speed at which the motor enzyme DNA polymerase (DNAp) replicates DNA. In addition to the tuning effect, a tension-induced reversal in the motor's velocity has been found to occur at high stretching forces (i.e. above ~ 35 pN). See Fig. 6.1.

We have been working to understand how mechanical tension on a DNA polymer can control both the "tuning" and "switching" behaviour in the molecular motor. The tension-induced switching observed in single molecule experiments is similar to the natural reversal that occurs after a mistake in DNA incorporation, whereby the reaction pathways of the biochemical network are kinetically partitioned to favour the exonuclease pathway over the polymerase one. We seek to develop a framework to understand how environmental parameters (like tension, torsion, external acoustic or electromagnetic signals) can directly couple into the conformational dynamics of the motor. By understanding how these various perturbations affect the molecular motor's dynamics, we can develop a more holistic picture of their context-dependent function. These motors are fundamentally open systems and very little is understood today about how their (local and global) environment couples into their function. Viewing the motor as a complex adaptive system that is capable of utilizing information in its environment to evolve or learn may shed new light on how information processing and computation can be realized at the molecular level.

As it becomes possible to probe the dynamics of these motors at increasingly smaller length and time scales, quantum effects, if relevant, are more likely to become experimentally detectable. Paul Davies (2004) has very elegantly posed the question "Does quantum mechanics play a non-trivial role in life?" and whether quantum mechanics could somehow enhance the information processing capabilities of biological systems. Here we revisit such fundamental questions in the context of examining the information processing capabilities of motors that read DNA. We use Wigner's relations for a quantum clock to derive constraints on the information processing accuracy and precision of a molecular motor reading DNA. In order for this motor to process information quantum mechanically, it must have long decoherence times. Here we also calculate the decoherence time for our motor-DNA system.

6.3. Approach

In the late 1950's Eugene Wigner showed how quantum mechanics can limit both the accuracy and precision with which a clock can measure distances between events in space-time [Wigner (1957)]. Wigner's clock inequalities can be written as constraints on the accuracy (maximum running time

$T_{\max}$) and precision (smallest time interval $T_{\min}$) achievable by a quantum clock as a function of its mass M, uncertainty in position λ, and Planck's constant $\hbar$:

$$T_{\max} < \frac{M\lambda^2}{\hbar} \tag{6.1}$$

$$T_{\min} > \frac{\hbar}{Mc^2}\left(\frac{T_{\max}}{T_{\min}}\right) . \tag{6.2}$$

Wigner's second constraint is more severe (by a factor $\frac{T_{\max}}{T_{\min}} > 1$) than the Heisenberg uncertainty principle, which requires that only one single simultaneous measurement of both energy ($E = Mc^2$) and the time $T_{\min}$ be accurate. Wigner's constraints require that repeated measurements not disrupt the clock and that it must accurately register time over the total running period $T_{\max}$. An intuitive way of saying this is that a Wigner clock must have a minimum mass so that its interaction with a quantum of light (during the measurement of a space-time interval) does not significantly perturb the clock itself. Wigner suggested that these inequalities (Eqs. (6.1) and (6.2)) should fundamentally limit the performance of any clock or information processing device [Barrow (1996)], even "when the most liberal definition of a clock" is applied [Wigner (1957)].

These inequalities have elegantly been applied by John Barrow (1996) to describe the quantum constraints on a black hole (a rather "liberal definition for a clock"). He shows that the maximum running time for a black hole ($T_{\max}$ in Wigner's relations) corresponds to its Hawking lifetime and that Wigner's size constraints are equivalent to the black hole's Schwarzchild radius. Furthermore, Barrow demonstrates that the information processing power of a black hole is equivalent to its emitted Hawking radiation. Wigner inequalities should likewise provide nontrivial constraints on the performance of any information processing nanomachine or time-registering device.

Here we heuristically examine the ramifications of these limits on the capability of a nanomachine to read DNA. We assume that λ is the uncertainty in the motor's position along the DNA (linear span over which it processes information) and can be estimated by the length of the DNA molecule (e.g. $\sim$ 16 μm for lambda–phage DNA used in typical single molecule experiments). Then Eq. (6.1) gives $T_{\max} < 387$ sec as the maximum running time for which the motor can reliably run and still be accurate. For comparison, the error rate for a polymerase motor from the species *Thermus aquaticus* (TAQ) is about 1 error every 100 sec. Likewise,

Eq. (6.2) gives $T_{\min} > 5 \times 10^{-14}$ sec as the motor's precision, or the minimum time interval that it can measure. A plausible interpretation of this value is that $T_{\min}$ corresponds not to the motor incorporating one base but to the motor undergoing an internal state transition. Note this time corresponds well to the timescale for the lifetime of a transition state [Peon and Zewail (2001)].

These Wigner constraints can also be written in terms of $L_{\max}$, the maximum readout length over which the motor is accurate, and $L_{\min}$, the minimum effective step size of the motor. If the motor's speed $v_{\text{motor}} \sim 100$ bases/sec, then $L_{\max} = v_{\text{motor}}$ x $T_{\max} \sim 4$ x 10^4 bases. This compares reasonably well with known error rates of the DNA polymerase motor. For example, a TAQ polymerase is known to make about one mistake once for every 10^4 bases it reads. Likewise, $L_{\min} = v_{\text{motor}}$ x $T_{\min} \sim 5$ x 10^{-12} bases, which corresponds to about 2 x 10^{-21} m. This is the effective step size or the minimum "distance" interval that can be accurately registered by the motor. This linear coordinate corresponds to the time associated with the fastest internal state transition within the motor and indicates a minimum lengthscale over which the motor can register information.

6.3.1. *The information processing power of a molecular motor*

The power $P \equiv \frac{E}{T_{\max}}$ required by any information processor can be calculated using Wigner's second clock inequality [Barrow (1996)]. Analogous to Barrow's treatment for a quantum black hole, we can estimate the motor's information processing power as

$$\frac{E}{T_{\max}} = \hbar \left(T_{\min}\right)^{-2} = \hbar \left(\nu\right)^{2} , \tag{6.3}$$

where $\nu = T_{\min}^{-1}$ is the fastest possible information processing frequency of the motor. For a theoretical estimate of the precision $T_{\min} \sim 5 \times 10^{-14}$ sec, this corresponds to a power of $P_{\text{inf}} \sim 4 \times 10^{-8}$J/ sec.

The maximum number of computational steps carried out by the motor can be estimated as $m = \frac{T_{\max}}{T_{\min}} \sim 7 \times 10^{15}$. Note the number of computational steps the motor performs are much larger than the number of bases (4×10^4) that the motor actually reads in the running time $T_{\max}$. Thus each base in the DNA molecule corresponds to roughly about 2×10^{11} computational (information processing) steps carried out by the motor.

In comparison, the power actually generated by the motor P_{out} can be estimated using experimental force vs velocity data [Wuite *et al.* (2000); Goel *et al.* (2003)] as

$$P_{\text{out}} = f \times v \sim 5\text{pN} \times 100\text{bases/sec} \sim 1.5 \times 10^{-19}\text{J/sec} \,. \tag{6.4}$$

If a motor molecule consumes 100 NTP (i.e. nucleotide triphosphate fuel) molecules per second, this corresponds to an input power $P_{\text{in}} \sim 8 \times 10^{-19}\text{J/sec}$ and a thermodynamic efficiency $\epsilon = \frac{P_{\text{out}}}{P_{\text{in}}} \sim 20\%$. From the actual power P_{out} generated, we can better estimate the actual precision of our motor $T_{\text{min measured}}$ to be about 26 n sec. This suggests that the actual number of computational steps taken by our motor during its longest running period is about

$$m_{\text{measured}} = \frac{T_{\max}}{T_{\text{min measured}}} \sim 10^{10} \,, \tag{6.5}$$

which means about 3×10^5 computational steps are taken (or information bits processed) for every DNA base that the motor reads. Each of the internal microscopic states of the motor or clock can store information. This leads to dramatically higher information storage densities than if the information were stored solely in the DNA molecule itself.

As discussed above, the first Wigner relation imposes constraints on the maximum timescales (and length scales) over which DNA replication is accurate or, in other words, remains coherent. The second Wigner inequality sets limits on the motor's precision and its information processing power. By viewing the motor as an information processing system, we also calculated the number of computational steps or bits required to specify the information content of the motor-DNA system. However, in order for quantum mechanics to play a more proactive role in the dynamics of these motors (i.e. beyond just imposing the above constraints on their performance), it is critical that the decoherence time (τ_{D}) of the motor-DNA complex be much longer than the motor's base reading time ($\tau_{\text{base reading}} \sim 10$ milliseconds). This decoherence time (τ_{D}) denotes a time scale over which quantum coherence is lost.

6.3.2. *Estimation of decoherence times of the motor-DNA complex*

We consider the motor-DNA complex as a quantum system moving in one dimension where the environment is a heat bath comprised of a set of n

harmonic oscillators, each vibrating with a given frequency and a given coupling strength between oscillations. Then, using an expression derived by Zurek (1991), we can estimate the decoherence time of this system as

$$t_D = t_r \left(\frac{\lambda_T}{\Delta x} \right)^2 \tag{6.6}$$

where the motor of mass M is in a superposition of two position states that are separated spatially by Δx. This effective interstate spacing Δx can be estimated as $L/m_{\text{measured}} \sim 10^{-15}$ metres, for a motor that takes roughly 10^{10} computational steps while reading a 16 micron long molecule of DNA. The thermal de Broglie wavelength λ_T for a motor in equilibrium with its surrounding heat bath is estimated as

$$\lambda_T = \hbar \sqrt{\frac{2\pi}{m k_B T}} \sim 3 \times 10^{-13} \text{m} \,. \tag{6.7}$$

When the thermal de Broglie wavelength is much smaller than the distance Δx, the motor-DNA system will behave as a classical system. On the other hand, when the thermal de Broglie wavelength is on the order of, or larger than the spacing Δx, quantum effects will predominate. Thus, for our motor-DNA complex, Eq. (6.6) gives $t_D \sim 8.4 \times 10^4 \; t_r$.

The spectrum of relaxation times for a DNA polymer vary with the length of the molecule and can be estimated from the Zimm model [Grosberg and Khokhlov (1994)] and have been experimentally verified [Perkins *et al.* (1994)] to range from microseconds to milliseconds. For instance, the slowest relaxation time for a DNA polymer chain of length L and persistence length P can be approximated via the Zimm model as

$$t_r = 2 \sqrt{\frac{6}{\pi}} \frac{(LP)^{\frac{3}{2}} \, \eta}{k_B T} \,. \tag{6.8}$$

This corresponds, for a typical $\sim$16 μm long lambda-phage DNA molecule, to the longest relaxation time being about 500 milliseconds for double-stranded DNA and about 3 milliseconds for single stranded DNA. With the longest DNA relaxation times being in the milliseconds, the corresponding longest decoherence times, Eq. (6.8), of the motor-DNA complex will range from several minutes to several hours. This easily satisfies the condition that $t_D \gg \tau_{\text{base reading}}$. Thus, it is indeed quite possible that quantum mechanical effects play a proactive role in influencing the dynamics of motors reading DNA.

6.3.3. *Implications and discussion*

The heuristic exercise above leads to a few intriguing implications.

(1) The first Wigner inequality sets fundamental constraints on the motor's accuracy for reading DNA. Our numerical estimates are comparable to known error rates of the polymerase motor.
(2) The second Wigner inequality sets fundamental constraints on the motor's precision and information processing power. This exercise suggests that the information content or the number of bits stored in a DNA-motor system is much larger than that typically assumed (1 bit per base). This increase in information storage density results from the motor itself having several internal microscopic states. Conventionally, information in DNA is seen as being stored in the DNA bases itself. This work, in contrast, suggests that DNA, the replicating motors, and their environment comprise a dynamic and complex information-processing network with dramatically higher information storage and processing capabilities.
(3) The power of information processing was compared to the actual power generated by the motor as it consumes energy to mechanically move along a DNA track. Molecular motors provide an excellent laboratory for probing the interplay of matter, energy, and information. These molecules (matter) transduce chemical free energy into mechanical work with remarkably high efficiency; and (in ways as of yet unknown to us) information from their environment plays a critical role in controlling or modulating their dynamics. What is needed is a more rigourous conceptual framework, where the molecular motor's dynamics can be intrinsically and strongly coupled to its exchange of information and energy with its environment.
(4) The decoherence times for the motor-DNA system was found to be on the order of minutes to hours, paving the way for quantum mechanics to play a non-trivial role. In order for quantum effects on the motor dynamics along DNA to enter the realm of experimental detection, a few prerequisites must be met: i) the decoherence times must indeed be sufficiently long; ii) single molecule experiments must be carefully designed so they do not destroy coherences; and iii) we should look more seriously for emergent macroscopic quantum effects, including for instance evidence for quantum information processing occurring within these molecular systems.

There is fervent interest in developing technologies that can store, retrieve, and process information at the nanoscale. Biological systems have already evolved the ability to efficiently process remarkable amounts of information at the nanoscale. Perhaps futuristic quantum information technologies could find their best realization yet in the context of biomolecular motors.

In his classic book, *What is Life*, Schrödinger first speculated that quantum mechanical fluctuations could give rise to mutations. In more recent times, McFadden and Al-Khalili (1999) describe how quantum mechanics may provide a mechanism for understanding "adaptive mutations"—i.e. mutations that are not purely random but are driven by environmental pressures. We have discussed how Wigner relations limit the accuracy with which polymerase motors can copy DNA. This suggests that mutations are fundamentally built into the replication machinery. We have also argued that these complex macromolecular systems can have decoherence times that are long compared to the timescale associated with the motor reading a DNA base, suggesting that quantum features are not really destroyed in these systems. We can dare to speculate and ask some provocative questions: Could quantum noise or fluctuations perhaps give rise to mistakes made during the motor's copying of the DNA? Since these motors propagate genetic information, such molecular mistakes made during DNA replication lead to mutations in the organism. Could the environment be somehow deeply entangled with the dynamics of these molecular motors as they move along DNA? Could information embedded in the motor's environment somehow modulate or influence its information processing, and hence how it reads the DNA bases? Could the environment somehow be selectively driving evolution and if so could it be that evolution, at least at the molecular level, is more Lamarckian than it is Darwinian?

As fields like nanotech, biotech, and quantum information processesing come together and new fields like quantum biology are born, it will become more fashionable to ask such questions and increasingly possible to experimentally address them.

References

Anglin, J. R., Paz, J. P., and Zurek W. H. (1996). Deconstructing Decoherence. quant-ph/9611045v1.

Barrow, J. D. (1996). Wigner inequalities for a black hole. *Physical Review D* **54**, pp. 6563–6564.

Davies, P. C. W. (2000). *The Fifth Miracle: The Search for the Origin and Meaning of Life* (Touchstone).

Davies, P. C. W. (2004). Does quantum mechanics play a non-trivial role in life?, *BioSystems* **78**, pp. 69–79.

Goel, A., Ellenberger, T., Frank-Kamenetskii, M. D., and Herschbach, D. R. (2002). Unifying themes in DNA replication: reconciling single molecule kinetic studies with structrual data on DNA polymerases, *J. Biolmolecular Structure and Dynamics* **19**.

Goel, A., and Herschbach, D. R., 2–4 June 2003. Controlling the speed and direction of molecular motors that replicate DNA, *Proc. SPIE Fluctuations and Noise in Biological, Biophysical, and Biomedical Systems*, Eds. Sergey M. Bezrukov, Hans Frauenfelder, and Frank Moss, Santa Fe, New Mexico, USA **5110** pp. 63–68 (Santa Fe, New Mexico).

Goel, A., Astumian, R. D., and Herschbach, D. R. (2003). Tuning and switching a DNA polymerase motor with mechanical tension, *Proc. of the National Academy of Science*, **100** pp. 9699–9704.

Grosberg, A. Y., and Khokhlov, A. R. (1994). *Statistical Physics of Macromolecules* eds. Larson, R. and Pincus, P.A. (AIP Press).

McFadden, J., and Al-Khalili, J. (1999). A quantum mechanical model of adaptive mutation, *BioSystems* **50**, pp. 203–211.

Peon, J., and Zewail, A. H. (2001). DNA/RNA nucleotides and nucleosides: direct measurement of excited-state lifetimes by femtosecond fluorescence upconversion, *Chem. Phys. Lett.* **348**, p. 255.

Perkins, T. T., Quake, S. R., Smith, D. E., and Chu, S. (1994). Relaxation of a single DNA molecule observed by optical microscopy, *Science* **264**, pp. 822–826.

Salecker, H., and Wigner, E. P. (1958). Quantum limitations of the measurement of space-time dimensions, *Physical Review* **109**, pp. 571–577.

Schrödinger, E. (1967). *What is Life?* (Cambridge University Press).

Scully, M. O., and Zubairy, M. S. (1997). *Quantum Optics* (Cambridge University Press).

Wigner, E. P. (1957). Relativistic invariance and quantum phenomena. *Reviews of Modern Physics* **29**, pp. 255–268.

Wuite, G. J. L., Smith, S. B., Young, M., Keller, D., and Bustamante, C. (2000). Single-molecule studies of the effect of template tension on T7 DNA polymerase activity, *Nature* **404**, pp. 103–106.

Zurek, W. H. (1991). Decoherence and the transition from quantum to classical, *Phys. Today* **43**, pp. 36–44.

About the author

Anita Goel holds both a PhD in Physics from Harvard University under Dudley Herschbach, and an MD from the Harvard-MIT Joint Division of Health Sciences and Technology (HST) and BS in Physics from Stanford

University. She was named in 2005 as one of the world's "top 35 science and technology innovators under the age of 35" by the *MIT Technology Review Magazine*. Goel is the Chairman, and Scientific Director of Nanobiosym Labs and the President and CEO of Nanobiosym Diagnostics, Inc. Goel also serves as an Associate of the Harvard Physics Department, an Adjunct Professor at Beyond: Center for Fundamental Concepts in Science, Arizona State University; a Fellow of the World Technology Network; a Fellow-at-Large of the Santa Fe Institute; and a Member of the Board of Trustees and Scientific Advisory Board of India-Nano, an organization devoted to bridging breakthrough advances in nanotechnology with the burgeoning Indian nanotech sector.

Chapter 7

Memory Depends on the Cytoskeleton, but is it Quantum?

Andreas Mershin and Dimitri V. Nanopoulos

7.1. Introduction

One of the questions the book you are reading debates is whether there is a non-trivial place for quantum physics in explaining life phenomena. This chapter will shed light on the possible role quantum mechanics may play in the cognitive processes of life, in particular memory encoding, storage, and retrieval that represents a subsection of the nearly thirty-five year old "Quantum Mind" theory or, more accurately, the loosely-connected collection of numerous and generally experimentally unsupported notions regarding the importance of quantum effects in consciousness.

From its inception, this space of human enquiry has been populated by bright and open minded folk, to whom it usually represented a secondary field to their areas of expertise, most famously mathematician Sir Roger Penrose, who along with anesthesiologist Stuart Hameroff are responsible for the most widely known incarnation of the Quantum Consciousness Idea (QCI) they title "Orch-OR" to stand for orchestrated objective reduction (by gravity) of the wavefunction of microtubules (MTs) inside neural cells [Hameroff (1998)]. This presents perhaps the most far-reaching conjecture about consciousness to date as it bridges the quantum realm of atoms and molecules to the cosmic scale of gravity through the human brain. It is suspiciously anthropocentric and brings to mind times when the Earth was considered the centre of the universe (here, human consciousness is at the

Received May 9, 2007

centre of the infamously difficult to bridge gap between quantum theory and general relativity). At the same time, one can argue that this is just the anthropic principle in action and it is only natural for consciousness, which occupies itself with the study of both the atomic and the cosmic to be the very centre of the two [Nanopoulos (1995)].

This space has also been highly attractive to people who are eager to believe that the currently mysterious physical phenomenon of consciousness can be somehow automatically tamed when coupled to the famously mysterious and counterintuitive quantum theory. This is similar to the "god of the gaps" strategy of assigning a deity to poorly understood phenomena until they are adequately explained by science—from Zeus the god of lighting thousands of years ago to the "intelligent designer" heavily and implausibly marketed by some as responsible for the origin and complexity of life even now.

Before continuing, we will put forth two necessary and we feel entirely reasonable assumptions: 1) the phenomenon of consciousness depends on (brain) cellular processes [Crick (1994)] and 2) any "quantum effects" such as non-locality, coherence and entanglement at the macromolecular or cellular scales must originate at the atomic and molecular scales (where quantum effects are commonplace) and be somehow "amplified" in both size and time span.

Instances of such amplification of quantum behaviour to the macroscopic world (in non-biological systems) have started to appear in recent years albeit using very intricate apparata including either very low temperatures [Corbitt *et al.* (2007)] or very large collection of particles at room temperature that are put into a superposition of states such that decoherence takes a long time [Julsgaard *et al.* (2001)]. While these experiments are very far from being biologically relevant they are a clear indication that science and technology are moving in the direction of amplifying quantum behaviour with all its weirdness in tow to the meso- and macro- worlds.

One of the key objections to all manners of QCIs by skeptics such as Max Tegmark (2000) has been that the brain is a "wet, warm and noisy environment" where any amplification of atomic scale quantum effects is washed away and his QCI-damning quotation in an article in *Science* [Seife (2000)] still ranks amongst the first hits of a Google search for "quantum mind" and is featured prominently in the Wikipedia lemma for the same keyword. These two measures accurately reflect the current scientific consensus on QCI: it is worth mentioning but it cannot yet be taken seriously.

In fact, consciousness research even without any controversial quantum hypotheses is mired in taboo. In some learned neuroscience circles, consciousness is referred to as the "unmentionable C-word" indicating there is something deeply wrong with its study. Clearly, the reason for the taboo has to do with the fact that it is a difficult and unexplored subject with fundamental philosophical implications (e.g. free will) and is so very personal to many. Additionally, we think that part of the blame for this sad state lies with the unchecked proliferation of quantum brain hypotheses, and their adoption by pseudoscientists, new age enthusiasts, and others seeking to validate their shaky reasoning by association with the well-established quantum theory. Sometimes, the most prolific of these receive well-deserved prizes for books with titles such as *Quantum Healing* [IgNobel (1998)].

We feel that the QCI is worth more than a passing mention in current neuroscience and in some of its more realistic incarnations, exhibits bold and interesting, experimentally testable predictions. But the field is sick and the best cure for it is not to avoid it completely [Dennett (1991)] but to perform well-controlled experiments and cull this space of the gratuitous assumptions, while at the same time illuminate the possibilities of non-trivial quantum effects playing a non-trivial role in life's processes. To clarify, there are certainly a slew of quantum phenomena important to biology, for instance the quantum nature of photon absorption by rhodopsin in the retina that leads to the—classical as far as we know—cascade of G-protein release and subsequent neural membrane depolarization and action potential propagation. While this type of phenomenon starts rooted in the quantum realm, it quickly becomes classical and does not amplify any of the quantum weirdness and for that reason we consider it "trivial." An example of a non-trivial quantum phenomenon would be the experimental observation of quantum coherence, non-locality or—the clearest case—entanglement occurring at a biologically relevant time and size scale as we describe in more detail below. But first, we would like to touch upon the motivation behind looking at quantum physics to explain the brain.

7.2. Motivation behind Connecting Quantum Physics to the Brain

While different scientists have different motivations behind connecting quantum physics to consciousness [Penrose (1989)], it seems that a unifying trend in the community is the argument that "qualia" [Koch (2004)]

and the "binding problem" (i.e. the problem of how the unity felt while perceiving the results of highly distributed activities of the nervous system is achieved), cannot be explained by classical physics alone and the weirdness of quantum mechanics (usually superposition of states and quantum entanglement) is needed [Penrose (1994)]. Additionally, the biological brain's unsurpassed ability at pattern recognition and other massively parallel processes is also sometimes alluded to in comparison to the algorithms of Shor (1995) and Grover (1996) that afford "super powers" to quantum computers.

As far as the authors can discern, the basic reasoning behind such assertions stems from the observation that just like Schrödinger's cat is both alive and dead until measured, so is a mental state undetermined until a collapse of the superposed wavefunctions (presumably each representing a different mental state). Quantum entanglement is sometimes employed to explain the "differentiated yet integrated" [Edelman *et al.* (1987)] aspect of experience in general and memory in particular where different parts of a memory are encoded in macroscopically separated parts of the brain while when one remembers, everything is integrated into a coherent whole. Both quantum superposition and entanglement are usually alluded to when arguing that the brain is too ill-equipped and regular neurotransmission too slow to achieve these spectacular results unless it works as a quantum computer.

Qualia and binding are fascinating philosophical and scientific problems and approaching them from a quantum mechanical perspective is provocative. Amongst others, we have in the past conjectured a possible mechanism for quantum entanglement to lead to correlated neural firing [Mavromatos *et al.* (2002)] thus addressing aspects of the binding problem. To do this, we approximated the internal cavity of microtubules (MTs) as quantum electrodynamic (QED) cavities and proposed that if this turns out to be an experimentally verified assumption, nature has provided us with the necessary MT structures to operate as the basic substrate for quantum computation either *in vivo*, e.g. intracellularly, or *in vitro*, e.g. in fabricated bioqubit circuits. This would mean that we could in principle construct quantum computers by using MTs as building blocks, in much the same way as QED cavities in quantum optics are currently being used in successful attempts at implementing qubits and quantum logic gates [Song and Zhang (2001)]. Detecting quantum behaviour in biological matter at this level would undoubtedly advance attempts at implicating quantum physics in consciousness while at the same time uncover intriguing new possibilities at the interface of bio-nanotechnology and quantum information science.

However, to our knowledge, there is currently no complete and experimentally testable quantum mechanical model of neural function or consciousness. In this chapter we show that there are ways to phenomenologically start addressing this issue and perform experiments that can falsify large swaths of the QCI space thus narrowing the possibilities down to a manageable few while moving the field towards scientific credibility.

7.3. Three Scales of Testing for Quantum Phenomena in Consciousness

There are three broad kinds of experiments that one can devise to test hypotheses involving the relevance of quantum effects to the phenomenon of consciousness. The three kinds address three different scale ranges associated roughly with tissue-to-cell (1 cm–10 μm), cell-to-protein (10 μm–10 nm) and protein-to-atom (10 nm–0.1 nm) sizes. Note that we are excluding experiments that aim to detect quantum effects at the "whole human" or "society" level as these have consistently given either negative results or been embarrassingly irreproducible when attempted under properly controlled conditions (e.g. the various extra sensory perception and remote viewing experiments [Lilienfeld (1999)]).

The consciousness experiments belonging to the tissue-cell scale frequently utilize apparatus such as electro-encephalographs (EEG) or magnetic resonance imaging (MRI) to track responses of brains to stimuli. A first-class example of consciousness-research at the tissue-to-cell scale [Crick and Koch (1990); Crick *et al.* (2004)] is that by Christoff Koch and his group at Caltech sometimes in collaboration with the late Francis Crick; tracking the activity of living, conscious human brain neurons involved in visual recognition. While any quantum phenomena found at these time and size scales would shake the world of science and lead to profound breakthroughs in the study of both consciousness and quantum physics, we feel that the wet/warm/noisy-type objections have their strongest footing here as any quantum effects will most likely be washed-out by the measurement techniques used (unless of course the provocative thought experiment proposed in Koch and Hepp (2006) is, somehow, performed).

The second scale in the quest to understand consciousness is that covering sizes between a cell and a protein. Inspired by QCI, seminal experimental work has been carried out by Nancy Woolf *et al.* (1994, 1999) on dendritic expression of microtubule associated protein-2 (MAP-2) in rats

and has been followed by experiments performed by members of our group on the effects of MAP-TAU overexpression on the learning and memory of transgenic *Drosophila*. Working at this scale leads to an understanding of the intracellular processes that undoubtedly plays a significant role in the emergence of consciousness but it is hard to see how experiments involving tracking the memory phenotypes and intracellular redistribution of proteins can show a direct quantum connection. It seems clear that experimentation at this size scale can invalidate many flavours of QCI if they predict phenomena that are found to not occur so it is a fruitful field if one is aiming to weed out bad assumptions and hypotheses. On the other hand, if one is trying to find support for a QCI at this scale, one can at best expect evidence that is "not inconsistent with" and perhaps "suggestive of" a QCI [Mershin *et al.* (2004a, 2006)]. In Sec. 7.4 we summarize experimental evidence obtained by our group that the correct stochiometry, and therefore local electrostatic and electrodynamic properties of MTs are of paramount importance to memory storage and retrieval as first reported in a 2004 publication in *Learning & Memory* titled "Learning and memory deficits upon TAU accumulation in *Drosophila* mushroom body neurons." While this experimental *in vivo* study provides clear and direct proof of MTs' involvement in memory, these data are merely consistent with—but not proof of—a quantum mechanical role. The significance of these experiments to the QCI is twofold: firstly, it has been discovered that there is a cytoskeletal pathway underlying the very first steps towards associative olfactory memory encoding in *Drosophila* showing that QCI-motivated research can have direct impact on conventional neurobiology. Secondly, it is shown for the first time that it is possible to at least indirectly test some aspects of the various QCIs, i.e. they are experimentally falsifiable. Had that data shown that MTs are not involved in memory we could then confidently write that the entire MT-consciousness connection would need to be discarded.

The third scale regime is that of protein-to-atom sizes. It is well understood that at the low end of this scale, quantum effects play a significant role in both chemistry and biology and it is slowly being recognized that even at the level of whole-protein function, quantum-mechanical effects such as quantum tunneling may be key to biological processes such as for instance enzymatic action [Ball (2004)] or photosynthesis [Ritz *et al.* (2002)] or, more controversially, signal transduction [Kell (1992); Turin (1996)]. Showing that a quantum effect is significant at this level, and is also somehow propagated up in size to the protein-cell scale would be a tremendous discovery across many fields.

So far however, no-one has demonstrated direct evidence for either superposition of biologically relevant states in biomolecules (e.g. a superposition of two conformational states for a membrane protein such as an ion channel) or larger structures such as for instance neural cells. Similarly, no-one has ever shown, and very few have suggested tangible ways to show, in living matter, the gold-standard of quantum behaviour: entanglement. In Sec. 7.5 we will suggest a direct experimental path to possibly measuring quantum-entangled electric dipole moment states amongst biomolecules.

7.4. Testing the QCI at the 10 nm–10 μm Scale

This section summarizes and condenses original research published in [Mershin *et al.* (2004a)].

We asked whether it is possible to directly test one key prediction of the microtubular QCI, namely that memory must be affected by perturbations in the microtubular (MT) cytoskeleton.

We induced the expression of vertebrate (human and bovine) tau genes, producing microtubule-associated protein TAU in specific tissues and at specific times in *Drosophila* using directed gene expression. We disturbed the fly MTs as little as possible, avoiding perturbation of the cytoskeleton by formation of such large protein aggregates as neurofibrillary tangles (NFTs) that could effectively "strangle" the neuron disrupting or even stopping intracellular (axonal) transport. In addition, NFTs and/or amyloid or senile plaques have been unequivocally shown to contribute to neurodegeneration and eventual neuronal death and it is reasonable to expect a dying neuron to dysfunction, regardless of the state of its MTs. We also carefully selected gene promoters that were activated in the adult fly only to avoid any developmental problems that would be difficult to discern from a cytoskeleton-specific dysfunction.

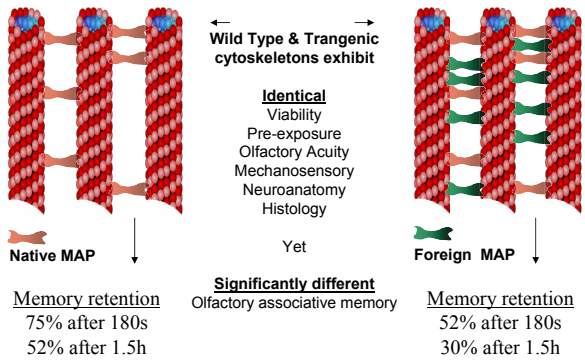
It was established that the bovine and human TAU protein expressed in our transgenic flies bound to the appropriate (mushroom body) neurons responsible for olfactory associative memory in *Drosophila*. The flies were then conditioned using two standard negatively reinforced associative learning paradigms that essentially generalize the Pavlovian conditioning protocol by coupling aversive odours as conditioned stimuli to electric shock as the unconditioned stimulus. This way, olfactory cues are coupled with electric shock to condition the flies to avoid the odourant associated with the negative reinforcer. These conditioning protocols for *Drosophila* were

initially developed by Tully and Quinn (1985) and modified by Skoulakis *et al.* (1996); Philip (2001).

Following these protocols it is routinely observed that post-conditioning (or "training"), a large percentage of wild type flies choose to avoid the smell that was present when they received the electric shocks. The memory "score" is calculated as a normalized performance index (PI) where $\mathrm{PI} = \frac{\text{trained}-\text{untrained}}{\text{total}} \times 100$. Typical PI values for various genotype wild-type flies averaged to 75% when tested 180 s post training and 52% at 1.5 hours post training while the transgenic flies, whose neuronal cytoskeleton was burdened with excess microtubule associated protein TAU only scored 52% and 30% respectively (averaged over various genotypes). These results are summarized in Fig. 7.1.

These data, when coupled to the numerous controls that eliminated the possibility of any residual effects due to: non-MT specific overexpression of protein, changes in: pre-exposure sensitivity, mechanosensory ability, overall viability and virility, neurodegeneration, decreased olfactory acuity to both attractive and aversive odors and finally histology, compel us to conclude that MTs and their stochiometry to MAPs are in fact intimately involved in memory. Taken together, the results strongly suggest that excess TAU binding to the neuronal microtubular cytoskeleton causes mushroom body neuron dysfunction exhibited as learning and memory deficits while the cells and flies are normal in every other way. This also indicates that although excessive TAU may not result in (immediate or medium-term) neurodegeneration, it is sufficient to cause significant decrements in associative learning and memory that may underlie the cognitive deficits observed early in human tauopathies such as Alzheimer's.

As an intriguing aside, looking at the cytoskeletal diagram of Fig. 7.1 it is difficult not to speculate that the abacus-like binding pattern of MAPs represents information coding which is disrupted when extra MAPs are introduced and this is indeed alluded to in [Woolf *et al.* (1994, 1999)]. We have conjectured [Mershin *et al.* (2006)] this as the "Guitar String Model" of the memory engram where the MAPs play the roles of fingers clamping vibrating strings (played by MTs) at various positions. While purely speculative at this point, this model is too provocative to ignore as it automatically addresses the issue of both information storage (the pattern of MAPs), information loss (MAPs break loose), long-term synaptic potentiation (pattern of MAPs guides kinesins during axonal transport to synapses in need of reinforcement) etc.



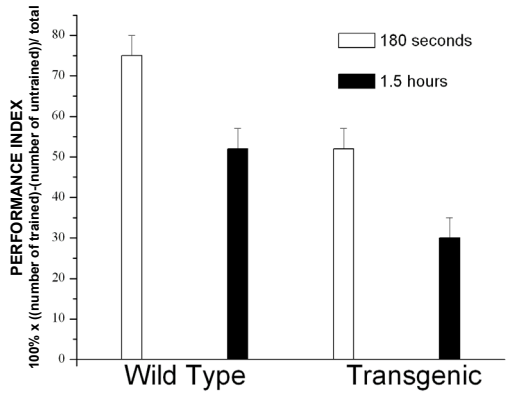


Fig. 7.1. Wild-type and transgenic cytoskeleton of neurons involved in olfactory associative memory representing the expected distribution of MAP tau. Summary of results presented in [Mershin *et al.* (2004a)]. Wild type and transgenic flies' average performance index (PI) for short term (180 s) and long term (1.5 h). PI suffers in transgenic flies expressing excess MAP-tau in their mushroom body neurons indicating a direct involvement of microtubular cytoskeleton in short and long term olfactory associative memory.

7.5. Testing for Quantum Effects in Biological Matter Amplified from the 0.1 nm to the 10 nm Scale and Beyond

Objections to a quantum role in biological processes of the "warm/wet/noisy" kind usually come from the application of equilibrium principles to the constituent particles. We hope to investigate deeper, as although—for instance—the tubulin molecule consists of some 17,000 atoms that are

subject to considerable thermal noise, the mesoscopically relevant electric dipole moment state of this protein depends crucially on only a few electrons that can be in two sets of orbitals and the use of the conventional notion of ambient temperature at the atomic scale is unwarranted since tubulin is not an equilibrium system, rather it is a dynamic dissipative system. Theoretical work has suggested that for a certain set of parameters (such as the value of the local dielectric constant, dipole moment, the pH etc.) tubulin could indeed sustain a quantum mechanically coherent state of its electric dipole moment for times of the order of microseconds [Mavromatos and Nanopoulos (1998)]. Clearly, the best way to settle this is to experimentally determine whether in fact a biomolecule can store a qubit and the most profound way of doing so would be to exhibit quantum "entanglement" amongst biomolecules.

Erwin Schrödinger, one of the fathers of quantum theory, coined the word "entanglement" in 1935 to refer to a state where the wavefunction describing a system is unfactorizable. This peculiar phenomenon has turned out to be very useful in quantum information science, quantum cryptography and quantum teleportation. Entanglement is the "gold standard" of non-classical behavior and has been experimentally realized in light [Ou *et al.* (1992); Togerson *et al.* (1995)], in matter [Sackett (2000)] and in combinations of those [Julsgaard *et al.* (2001); Rauschenbeutel (2000)]. Here we suggest one way to experimentally test for the survival of entanglement in biological matter by using entangled states of light to couple to surface plasmons (mesoscopic quantum objects) that can couple, in turn, to the electric dipole moment of proteins.

One way to produce entangled states in light is via type-II phase-matching parametric downconversion, which is a process occurring when ultraviolet (UV) laser light is incident on a non-linear beta-barium borate (BBO) crystal at specific angles. A UV photon incident on a BBO crystal can sometimes spontaneously split into two correlated infrared (IR) photons. The infrared photons are emitted on opposite sides of the UV pump beam, along two cones, one of which is horizontally polarized and the other vertically. The photon pairs that are emitted along the intersections of the two cones have their polarization states entangled. This means the photons of each pair necessarily have perpendicular polarizations to each other. The state Ψ of the outgoing entangled photons can be written as: $|\Psi\rangle = |\leftrightarrow, \updownarrow\rangle + e^{i\alpha}|\updownarrow, \leftrightarrow\rangle$ where the arrows indicate polarizations for the (first,second) IR photon and can be controlled by inserting appropriate half wave plates, while the phase factor $e^{i\alpha}$ can be controlled by tilting the

crystal or using an additional BBO. Measuring the polarization state of one of the outgoing photons—say IR1, immediately determines the state of the other (IR2) regardless of their separation in space. This counterintuitive phenomenon is referred to as the Einstein Podolsky Rosen (EPR)-paradox and such pairs are called EPR pairs.

To use EPR-pair photons to check for the ability of biological matter to carry quantum entangled states, we propose to follow a protocol similar to one developed by Kurtsiefer *et al.* (2001) capable of producing brightness in excess of 360,000 entangled photon pairs per second, coupled to a setup similar to the one developed by Altwischer (2002) where entangled photons are transduced into (entangled) surface plasmons and re-radiated back as (surprisingly still entangled) photons.

The essential difference would be that the insides of the perforations in the gold film of Altwischer (2002) would be covered with a monolayer of tubulin dimers or microtubules (there exist numerous protocols for doing this e.g. [Schuessler *et al.* (2003)]). The evanescent wave of the (entangled) surface plasmon generated at resonance will interact with the electric dipole moment of the immobilized protein complexes and presumably transfer the entanglement (and quantum bit) to a dipole state in a manner similar to the transfer of the photon polarization entanglement to surface plasmons. At the end of the tunnel, the surface plasmons would be reradiated having undergone the interaction with the protein electric dipole moment. If partial entanglement with the partner photon (that underwent a subset or even none of these transductions) is found, then this would suggest that the protein is capable of "storing" the entanglement in its electric dipole moment state and characteristic decoherence times could be measured by varying the length of the tunnels from 200 nm up.

We have previously preformed numerous experiments immobilizing monomolecular layers of tubulin on gold substrates and probing them with surface plasmons and have measured the changes of the refractive index and dielectric constant with tubulin concentration: $\frac{\Delta n}{\Delta c} = (1.85 \pm 0.20) \times 10^{-3}(\mathrm{mg/ml})^{-1} \Rightarrow \frac{\Delta \epsilon}{\Delta c} = (5.0 \pm 0.5) \times 10^{-3}(\mathrm{mg/ml})^{-1}$ as reported in [Schuessler *et al.* (2003)] where n and $\Delta\epsilon$ are the changes in the refractive index n and dielectric constant ϵ and Δc is the change in concentration c. We also checked using direct refractometry (a method based on the same underlying physical principle as surface plasmon resonance but very different in implementation), and found a $\Delta n/\Delta c$ of $1.8 \times 10^{-3}(\mathrm{mg/ml})^{-1}$. These methods alone cannot provide the permanent dipole moment of the molecule since they address only the high frequency region where the

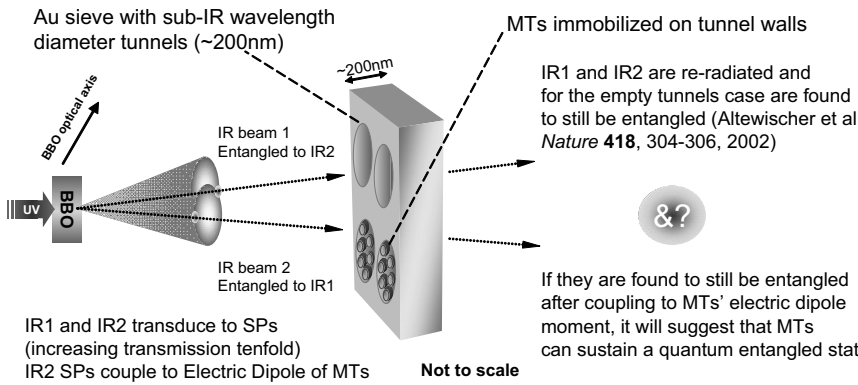


Fig. 7.2. For certain orientations, a UV photon is absorbed by the BBO crystal and re-emitted as two entangled IR photons (IR1, IR2). One of the EPR-paired beams can be allowed to undergo the quadruple transduction of photon → surface plasmon → electric dipole moment → surface plasmon → photon while the other beam can either be left undisturbed or undergo any subset of transductions determining whether proteins can sustain entanglement.

permanent dipole is "frozen out" so to calculate it we resorted to supercomputer molecular dynamic simulations [Mershin *et al.* (2004b)] and arrived at a value of 552D and 1193D for the α- and β- monomers and 1740D for the $\alpha\beta$-dimer with a refractive index for the protein at 2.90 and the high-frequency dielectric constant at 8.41 and polarizability 2.1×10^{-33} Cm^2/V. Knowing these parameters paves the way towards implementing the experiment described in Fig. 7.2 as the high values of the dielectric constant and dipole moments are particularly encouraging suggesting strong interaction between the entangled surface plasmons and the biomolecules' electric dipole moment.

7.6. Summary and Conclusions

By performing carefully controlled *in-vivo* experiments it has been shown that olfactory associative memory encoding, storage and retrieval is intimately tied to the neuronal microtubular cytoskeleton in *Drosophila*. This finding undoubtedly applies to the microtubular cytoskeleton of many other animals including humans. Since memory is a necessary ingredient of consciousness, our finding is consistent with a microtubular involvement in consciousness but at this stage does not lean toward a classical or quantum

role. We have proposed an experiment to test for the ability of microtubules to sustain entangled states of their electric dipole moments, set up by EPR-pair photons transduced to surface plasmons. A positive result to this experiment would revolutionize the way we look at proteins and will undeniably create a more positive climate for the QCI.

7.7. Outlook

Fabrication of novel biomaterials through molecular self-assembly is going to play a significant role in material science [Zhang (2003)] and possibly the information technology of the future [Ou *et al.* (1992)]. Tubulin, microtubules and the dynamic cytoskeleton are fascinating self-assembling systems and we have here asked whether they underlie the possibly quantum nature of consciousness. Whatever the consciousness case may be, our work with the neurobiology of transgenic *Drosophila* [Mershin *et al.* (2004a)] compels us to recognize that the cytoskeleton is very near the "front lines" of intracellular information manipulation and storage. Our work with surface plasmon resonance and tubulin biophysics suggests that cytoskeletal structure and function contains clues on how to fabricate biomolecular information processing devices whether they are fundamentally quantum in nature or not.

So perhaps one way to proceed is to accept Richard Feynman's adage *"What I cannot create, I do not understand"* and try to create biomolecular information-processing circuits using nature's cytoskeletal building blocks. If we discover that they are in fact harnessing quantum effects, then it will be that much easier to take the leap to quantum consciousness, but for now, we must hedge our bets.

Acknowledgements

The authors wish to thank E. M. C. Skoulakis, H. A. Schuessler, A. A. Kolomenski, J. H. Miller, H. Sanabria, R. F. Luduena, D. Nawarathna, and N. E. Mavromatos.

References

Altewischer, E. T. (2002). Plasmon-assisted transmission of entangled photons. *Nature* **418**, pp. 304–306.

Ball, P. (2004). By Chance or by Design? *Nature* **431**, p. 397.

Corbitt, T. Chen, Y., Mueller-Ebhardt, H., Innerhofer, E., Ottaway, D, Rehbein, H., Sigg, D., Whitcomb, S., Wipf, C., and Mavalvala, N. (2007). Toward achieving the quantum ground state of a gram-scale mirror oscillator, `arXiv:quant-ph/0612188v1`.

Crick, F., and Koch, C. (1990). Toward a neurobiological theory of consciousness, *Seminars in the Neurosciences* **2**, pp. 263–275.

Crick, F. (1994). *The Astonishing Hypothesis: The Scientific Search for the Soul* (New York: Scribners).

Crick, F., Koch C., Kreiman, G., and Fried, I. (2004). Consciousness and Neuroscience, *Neurosurgery*, **55**, pp. 273–282.

Dennett, D. C. (1991). *Consciousness Explained* (Boston: Little, Brown).

Edelman, G., Gall, W. E., and Cowan W. M. (1987). *Synaptic Function* (John Wiley & Sons, New York).

Grover L. K. (1996). A fast quantum mechanical algorithm for database search, *Proceedings 28th Annual ACM Symposium on the Theory of Computing*, p. 212.

Hameroff, S. (1998). Quantum computation in brain microtubules? The Penrose-Hameroff "Orch OR" model of consciousness, *Philos. Trans. R. Soc. London Ser. A* **356**, pp. 1869–1896.

IgNobel, Physics Prize to Deepak Chopra (1998). "For his unique interpretation of quantum physics as it applies to life, liberty, and the pursuit of economic happiness," `http://www.improb.com/ig/ig-pastwinners.html` accessed April 2007.

Julsgaard, B., Kozhekin, A., and Polzik E. (2001). Experimental long-lived entanglement of two macroscopic objects, *Nature* **413**, pp. 400–412.

Kell, D. B. (1992). Scanning tunneling microscopy in biology: are the current carriers tunneling electrons or hydrated protons? *Bioelectrochemistry and Bioenergetics* **27**, pp. 235–237.

Koch, C. (2004). Quick guide: qualia, *Current Biology* **14**, pp. 497–97.

Koch, C., and Hepp, K. (2006). Quantum mechanics in the brain, *Nature* **440**, pp. 611–612.

Kurtsiefer, C., Oberparleiter, M., and Weinfurt, H. (2001). High-efficiency photon pair collection in type-II parametric fluorescence, *Phys. Rev. A* **64**, pp. 23–28.

Lilienfeld, S. O. (1999). New analyses raise doubts about replicability of ESP findings, *Skeptical Inquirer Magazine Online* `http://www.csicop.org/si/` accessed March 2006.

Mavromatos, N. E., Mershin, A., and Nanopoulos, D. V. (2002). QED-Cavity model of microtubules implies dissipationless energy transfer and biological quantum teleportation *Int. J. Modern Physics B* **16**, pp. 3623–3642.

Mavromatos, N. E., and Nanopoulos, D. V. (1998). On quantum mechanical aspects of microtubules, *Int. J. of Mod. Physics B* **12**, pp. 517–527.

Mershin, A., Pavlopoulos, E., Fitch, O., Braden, B. C., Nanopoulos D. V., and Skoulakis E. M. C. (2004a). Learning and memory deficits upon TAU accumulation in Drosophila mushroom body neurons, *Learning & Memory* **11**, pp. 277–87.

Mershin, A., Kolomenski, A. A., Schuessler H. A., and Nanopoulos, D. V. (2004b). Tubulin dipole moment, dielectric constant and quantum properties: computer simulations, experimental results and suggestions, *Biosystems* **77**, pp. 73–85.

Mershin, A., Sanabria, H., Miller, J. H., Nawarathna, D. Skoulakis, E. M. C., Mavromatos, N. E, Kolomenski, A. A., Schuessler, H. A., Luduena R. F., and Nanopoulos, D. V. (2006). Towards experimental tests of quantum effects in cytoskeletal proteins, *The Emerging Physics of Consciousness* Springer-Verlag Berlin, Heidelberg, New York, ISBN-13-9783540238904 Chapter **4**, pp. 95–170.

Nanopoulos, D. V. (1995). arXiv:hep-ph/9505374v1 October 4-8, (1994) and on an invited talk at the "Physics Without Frontiers Four Seas Conference," Trieste, Italy, June 25-July 1, 1995. in *XV Brazilian National Meeting on Particles and Fields* Angra dos Reis, Brazil.

Ou, Z. Y., Pereira, S. F., Kimble, H. J., and Peng, K. C. A. (1992). Realization of the Einstein-Podolsky-Rosen paradox for continuous variables, *Phys. Rev. Lett.* **68**, pp. 3663–3666.

Penrose, R. (1989). *The Emperor's New Mind* (Oxford University Press).

Penrose, R. (1994). *Shadows of the Mind* (Oxford University Press).

Philip, N., Acevedo, S., and Skoulakis, E. M. C. (2001). Conditional rescue of olfactory learning and memory defects in mutants of the 14-3-3ζ gene Leonardo, *J. Neuroscience* **21**, pp. 8417–8425.

Rauschenbeutel, E. (2000). Step-by-step engineered multiparticle engtanglement, *Science* **288**, pp. 2024–2028.

Ritz, T., Damjanovic, A., and Schulten, K. (2002). The Quantum physics of photosynthesis, *Chemphyschem* **3**, pp. 243–248.

Sackett, L. (2000). Experimental entanglement of four particles, *Nature* **404**, pp. 256–259.

Sanabria, H., Miller, J. H., Mershin, A., Luduena, R. F., Kolomenski, A. A., Schuessler, H. A., and Nanopoulos, D. V. (2006). Dielectric spectroscopy of $\alpha\beta$-tubulin heterodimer, *Biophysical Journal* **90**, pp. 4644–4650.

Schuessler, H. A. Mershin, A, Kolomenski A. A., and Nanopoulos, D. V. (2003). Surface plasmon resonance study of the actin-myosin sarcomere complex and tubulin dimer, *J. Modern Optics* **50**, pp. 2381–2391.

Seife, C. (2000). Cold numbers unmake the quantum mind, *Science* **287**, p. 791.

Shor, P. W. (1995). Polynomial-time algorithms for prime factorization and discrete logarithms on a quantum computer. arXiv:quant-ph/9508027v2

Skoulakis, E. M. C. and Davis, R. L. (1996). Olfactory learning deficits in mutants for leonardo, a Drosophila gene encoding a 14-3-3 protein, *Neuron* **17**, pp. 931–944.

Song, K.-H., and Zhang, W.-J. (2001). Proposal for teleporting an entangled coherent state via the dispersive atom-cavity-field interaction, *Physics Letters A* **290**, pp. 214–218.

Tegmark, M (2000). Importance of quantum decoherence in brain processes, *Phys. Rev. E* **61**, pp. 4194–4206.

Togerson, T., Branning, S., Monken, M., and Mandel, A. (1995). *Phys. Lett. A* **204**, pp. 323–328.

Tully, T., and Quinn., W. (1985). Classical conditioning and retention in normal and mutant Drosophila melanogaster, *J. Comp. Physiol* **157**, pp. 263–277.

Turin, L. (1996). A spectroscopic mechanism for primary olfaction, *Chemical Senses* **21**, pp. 773–791.

Woolf, N. J., Young, S. L., Johnson, G. V. W., and Fanselow, M. S. (1994). Pavlovian conditioning alters cortical microtubule-associated protein-2, *NeuroReport* **5**, pp. 1045–1048.

Woolf, N. J., Zinnerman, M. D., and Johnson, G. V. (1999). Hippocampal microtubule-associated protein-2 alterations with contextual memory, *Brain Res* **821**, pp. 241–249.

Zhang, S. (2003). Fabrication of novel biomaterials through molecular self-assembly, *Nature Biotechnology* **21**, pp. 1171–1178.

About the authors

Andreas Mershin received his MSci in Physics from Imperial College London (1997) and his PhD in Physics from Texas A&M University (2003), under D. V. Nanopoulos, where he studied the theoretical and experimental biophysics of the cytoskeleton. He performed molecular dynamic simulations on tubulin and after winning an NSF grant initiated wide-reaching, cross-disciplinary collaborations performing experiments utilizing surface plasmon resonance, dielectric spectroscopy and molecular neurobiology to successfully test the hypothesis that the neuronal microtubular cytoskeleton is involved in memory encoding, storage and retrieval in *Drosophila*. Currently, he is a postdoctoral associate at the Center for Biomedical Engineering of the Massachusetts Institute of Technology developing bioelectronic photovoltaic and chemical sensing applications using membrane proteins integrated onto semiconductors. A patent holder and entrepreneur in the field of biosensors, he is also a co-founder of the Royal Swedish Academy of Sciences' international annual "Molecular Frontiers Inquiry Prize" for the best scientific question posed by children (www.molecularfrontiers.org).

Dimitri V. Nanopoulos received his BSc in Physics from the University of Athens (1971) and his PhD in High Energy Physics from the University of Sussex (1973), under Norman Dombey. He has been a Research Fellow at CERN, at Ecole Normale Superieure and at Harvard University. In 1989, he was elected professor (Department of Physics, Texas A&M University) where since 1992 he is a Distinguished Professor of Physics and since 2002

holds the Mitchell/Heep Chair in High Energy Physics. He is also Head of the Astroparticle Physics Group at the Houston Advanced Research Center. He has made several contributions to particle physics and cosmology working on string unified theories, fundamentals of quantum theory, astroparticle physics and quantum-inspired models of brain function. With over 550 original papers and 31,000 citations he has been ranked 4th most cited high energy physicist of all time by the Stanford University Census. A fellow of the American Physical Society since 1988 he was elected a member of the Academy of Athens in 1997 and became President of the Greek National Council for Research and Technology as well as the National representative of Greece to CERN in 2005. He has received numerous awards and honors including the Onassis International prize.

This page intentionally left blank

Chapter 8

Quantum Metabolism and Allometric Scaling Relations in Biology

Lloyd Demetrius

The basal metabolic rate of an organism is its steady-state rate of heat production under a set of standard conditions. There exists a class of empirical rules relating this physiological property with the body size of an organism. The molecular mechanism that underlies these rules can be understood in terms of quantum metabolism, an analytical theory which deals with the dynamics of energy transduction within the membranes of the energy transducing organelles. This chapter delineates the origin and analytical basis of quantum metabolism and illustrates its predictive power with examples drawn from the empirical literature.

8.1. Introduction

The metabolic rate of an organism—the rate of energy expenditure,—and body size—an organism's total metabolic mass—are highly interrelated characteristics. Elucidating the rules that define this dependency and delineating the mechanisms that underlie these rules are central problems in bioenergetics. Since body size is correlated with many physiological, ecological and life-history traits, an understanding of the relation between metabolic rate and body size has important implications in many areas of biology.

Body size is a highly variable property: size changes during an organism's ontogeny. Hence, most efforts to determine the relation between

Received May 8, 2007

metabolic rate and body size have focused on adult size, which is a relatively constant morphological index. Metabolic rate is also highly variable—even for an adult individual. Three situations are usually distinguished: standard metabolic rate, maximal metabolic rate, and field metabolic rate [Rolfe and Brown (1997)].

Standard metabolic rate is the steady-state rate of heat production under a set of standard conditions; in mammals, these conditions are that the individual is an adult, resting and maintained at a temperature that generates no thermoregulatory effect. The maximal metabolic rate is the maximum steady-state metabolic rate attainable during hard exercise over a defined period of time. Field metabolic rate represents the average rate over an extended period of time when the organism is living in its natural environment.

The distinction between the different measures of metabolic rate and its relevance in understanding the constraints which body size imposes on metabolic activity was recognized as early as 1781 by Lavoisier and Laplace. They carried out calorimetry experiments on adult guinea pigs who were maintained in a resting state. One of the main achievements of these two pioneers in the field of bioenergetics was the discovery that the standard metabolic rate is quantitatively related to the caloric nutrient requirements of the organism. More than a century later, in 1804, Rubner, the German physiologist, repeated the experiments of Laviosier and Laplace on several species of domesticated animals and proposed a series of scaling rules relating the standard metabolic rate (SMR) to body size. A systematic approach to the study of bioenergetics and allometry, however, only began with the investigations of Kleiber (1961). He expanded on the work of Rubner by including non-domesticated species in his studies, and subjecting his data to statistical analysis.

During the last 50 years, Kleiber's work has been extended to include uni-cellular organisms, various species of invertebrates, birds and plants. Much of this work has now been reviewed and analyzed in various texts [Brody (1946); Peters (1983); Calder (1984)].

The allometric rules that have emerged from these investigations can be expressed in the form

$$P = \alpha W^{\beta}\,, \tag{8.1}$$

here W denotes the body size, and P, the standard metabolic rate.

Equation (8.1) involves two critical parameters:

(i) a scaling exponent, β, which refers to the fractional change in metabolic rate to a change in body size. Typically, β is found to be 2/3 for small animals, 3/4 for large animals, and 1 for perennial plants.
(ii) A normalizing coefficient α, which describes the rate of energy expenditure in an organism of unit mass. This parameter also shows a large interspecific variation. For example, endotherms have a much higher metabolic rate than ectotherms of the same body size.

The problem of explaining the allometric rules in mechanistic terms has generated considerable controversy; see for example McMahon (1973); West *et al.* (1997); Banavar *et al.* (2002). These studies have been largely concerned with explaining the incidence of a 3/4 scaling exponent for the metabolic rate. Such models have largely ignored the significance of proportionality constants, and the deviations from the 3/4 rule that characterizes small animals ($\beta = 2/3$), and perennial plants ($\beta = 1$).

The difficulties in explaining the interspecific variation in scaling exponents and proportionality constants derive in large part from the fact that the models proposed are framed in terms of macroscopic organismic properties. However, empirical studies show that variations in scaling exponents and proportionality constants are largely contingent on cellular level properties, in particular, on the molecular dynamics of metabolic activity [Hochachka and Somero (2000)], Chap. 4).

The mechanism underlying the allometric rules was recently addressed in [Demetrius (2003, 2006)], in terms of a cellular-level model based on the molecular dynamics of metabolic regulation. The model rests on the observation that metabolic activity within organisms has its origin in the processes of energy transduction localized in biomembranes: the plasma membrane in uni-cells, the inner membrane of mitochondria in animals, and the thylakoid membrane in plants, see [Harold (1986)].

Energy transduction in biomembranes can be understood in terms of the chemiosmotic coupling of two molecular motors [Mitchell (1966)].

(a) The redox chain which describes the transfer of electrons between redox centers within the biomembrane.
(b) The ATP-ase motor, which is involved in the phosphorylation of ADP to ATP.

The molecular dynamics model, [Demetrius (2003, 2006)], integrates the chemiosmotic theory of energy transduction [Mitchell (1966)], with the

proposition, due to Fröhlich (1968), that the energy generated by the redox-reactions can be stored in terms of the coherent vibrational modes of the molecular oscillators embedded in biomembranes.

This new synthesis, which we call quantum metabolism, postulates that the collective modes of vibration of the molecular oscillators is quantized. Quantum metabolism exploited certain methods, integral to the methods developed in the quantum theory of solids, to derive a set of analytic relations between cellular metabolic rate and cycle time—that is, the mean transit time of the redox reactions within the cell. These relations were then invoked to establish an allometric rule relating cycle time, τ, with cell size, W_c, namely,

$$\tau = \alpha W_c^{\beta} . \tag{8.2}$$

The distinct values assumed by the scaling exponent are contingent on the magnitude of the metabolic energy stored in the molecular oscillators. Typically, $\beta = 1$, when the metabolic energy associated with the vibrational modes is much greater than the vibrational spacing. In this case the energy transduction process is *continuous* and the total metabolic energy generated is proportional to the cycle time. The condition $\beta = 3/4$ is obtained when the metabolic energy per mole is smaller than the vibrational spacing. Under this constraint energy transduction becomes *discrete*, and the total metabolic energy generated is now the fourth power of the cycle time.

The proportional constant α was shown to be determined by (i) the capacity of the system to transport protons across the membrane, (ii) the extent to which the dynamics of the electron transport chain, the energy donating process, is coupled to ADP phosphorylation, the energy accepting process. The first property depends on the bioenergetic parameters, the proton conductance, denoted C, and the proton motive force, denoted Δp. The second property defines the metabolic efficiency, denoted μ.

The relation between the metabolic cycle time τ, and cell size W_c, given by Eq. (8.2) can be extended to higher levels of biological organization, such as organs and multicellular organisms, by appealing to a multi-level scaling argument, [Demetrius (2006)]. These extensions provide the basis for a series of allometric rules relating the metabolic rate, denoted P, with the body size, denoted W, of multicellular organisms. The rules are given by

$$P = \gamma C \Delta p W^{\beta} . \tag{8.3}$$

The parameter C (dimension: nmol H^+ per unit time, per mg protein, per mV); and Δp (dimension: mV) represent bioenergetic variables averaged

over the different cells and organ systems. The parameter γ is the product, $\gamma = a\mu$, where μ is the metabolic efficiency, and a the capacity of the organism to transport nutrients from the external environment to cellular organelles.

This chapter aims to provide a conceptual overview and a non-technical account of the mathematical ideas that constitute quantum metabolism. We pursue this aim by

(i) providing a historical account of the ideas of quantum theory and the implications of the theory to energy transduction in sub-cellular processes in living systems;
(ii) delineating the main mathematical ideas that underlie the derivation of the allometric rules;
(iii) illustrating, with empirical examples, the predictive power of the allometric laws.

8.2. Quantum Metabolism: Historical Development

The law of conservation of energy asserts that an object in a mechanically stable state and isolated from its surroundings has a definite energy E. In classical mechanics, E is a continuous variable and can assume any value consistent with the stability of the object. In quantum mechanics, the possible values of the energy are discrete,

$$E = E_i\,, \quad i = 0, 1, 2, \ldots$$

Here E_0 denotes the ground state energy, E_1, the energy in the first excited state, and so on.

We will describe the pertinence of this quantization postulate in the context of Planck's derivation of the black body radiation spectrum. We will then discuss its application to the study of the heat capacity of solids and, finally describe its application to the analysis of the metabolic rate of subcellular processes in living organisms. Our historical overview draws extensively from [Longair (2004)].

8.2.1. *Quantization of radiation oscillators*

The quantization concept was invoked by Planck in 1900 to explain the Stephan-Boltzmann law of electromagnetic radiation. This empirical law

asserts that the energy density of radiation, denoted e, is given by

$$e = \sigma T^4 \,. \tag{8.4}$$

Here T denotes the absolute temperature, and σ a proportionality constant, with an empirically precise value.

The first attempt to explain the radiation law was made by Boltzmann who exploited classical thermodyamical arguments to account for Eq. (8.4). These methods were able to determine the value for the scaling exponent. However, in Boltzmann's model, the proportionality constant appeared as a constant of integration without any physical meaning.

An explanation of both the scaling exponent and the proportionality constant was achieved by Planck in 1900. The crucial insight in Planck's model was to analyze radiation as a photon gas. The oscillations of these photons were assumed to be the mechanism underlying radiation in a metallic cavity. The model resides on the so called quantization principle: *The energy that can be stored by an oscillator with frequency ω can only be integral multiples of a basic energy unit which is proportional to the characteristic frequency of the oscillator.*

Analytically, we write

$$E_n = nh\omega \,, \quad n = 1, 2, \ldots \,, \tag{8.5}$$

where h is Planck's constant and n an integer.

An important achievement of Planck's model was his expression for the spectral density of radiation at temperature T,

$$u(\omega) = \frac{h\omega}{\exp(\frac{h\omega}{k_B T}) - 1} \,. \tag{8.6}$$

Here k_B denotes Boltzmann's constant.

For small $h\omega/k_B T$, the exponential term can be expanded and retention of only the first terms gives $u(\omega) = k_B T$, which is consistent with the Rayleigh-Jeans law. For large $h\omega/k_B T$, the expression in Eq. (8.6) tends to $h\omega \exp(-h\omega/k_B T)$. This is consistent with Wien's law. The significance of the quantization rule resides in the fact that Eq. (8.6), provides an excellent agreement with experimental data at all temperatures.

8.2.2. *Quantization of material oscillators*

The fundamental nature of Planck's radiation law was evidently recognized by Einstein, who in 1907 appealed to quantum theory to study the thermal properties of solids. The characteristic property of a solid is that its atoms

execute small vibrations about their equilibrium positions. When in thermal equilibrium the atoms are arranged on a regular lattice—a condition called the crystalline state.

Einstein treated the atoms in a crystalline solid as vibrating independently of each other about fixed lattice sites. The vibrations are assumed to be simple harmonic. In contrast to the radiation oscillators that can assume all possible frequencies, the material oscillators are assumed to have a single frequency.

By invoking Planck's quantization rule, the mean energy associated with a given frequency will now be given by

$$E(\omega) = \frac{h\omega}{\exp(\frac{h\omega}{k_B T}) - 1}\,. \tag{8.7}$$

This expression yielded an analytical framework for predicting the specific heat per molecule at high temperatures. The model thus yielded a molecular explanation of the law of Dulong and Petit. However the argument was not able to explain the heat capacity at low temperatures.

The reason for this failure is due to the independence assumption made regarding the vibrations of the atoms at the lattice sites. This is now recognized as a highly restrictive condition. A crystal does not consist of atoms vibrating totally independently of each other about fixed lattice sites: there is a strong coupling between the atoms. On account of this assumption, Einstein's model was inconsistent with the empirically observed values of heat capacity at low temperatures.

The discrepancy at low temperatures was elucidated in 1912 by Debye who formulated a new model in which the atoms are assumed to execute coupled vibrations about the fixed sites. Hence for a crystal consisting of N atoms, the system can be described by $3N$ normal modes of vibration of the whole crystal, each with its own characteristic frequency. Hence if we know the characteristic frequencies, we can write down the total energy of the crystal.

8.2.3. *Quantization of molecular oscillators*

Quantum metabolism is a molecular biological application of Planck's quantization concept. Quantum metabolism is concerned with explaining certain empirical relations between the size of an organism and its metabolic rate.

The model addresses this problem by first investigating at the cellular level the mechanisms underlying the scaling rules relating cycle time and cell

size. The fundamental idea invoked draws from the chemiosmotic theory proposed by Mitchell (1966). According to this theory, metabolic activity is localized in energy-transducing membranes and is determined by the coupling of an energy donating process (oxidation-reduction reaction) and an energy-accepting process (ADP phosphorylation).

According to Fröhlich (1968), a characteristic property of an energy-transducing membrane is that the phospholipid head groups, which constitute an integral component of the membrane, can execute small vibrations due to their oscillating dipole moments. When the system is subject to a continuous supply of energy, coherent elastic vibrations will be generated—a consequence of the strong coupling between the molecular elements and the long-range Coulomb interaction between the molecular groups.

Quantum metabolism rests on the postulate that Planck's quantization principle, which was invoked by Einstein and Debye in their studies of the heat capacity of solids, can also be applied to the vibration of molecular groups embedded in the biomembrane.

There exists, however, a fundamental difference between the Einstein-Debye models and quantum metabolism. In the quantum theory of solids, the fundamental unit of energy is given by

$$E(T) = k_B T\,; \tag{8.8}$$

the typical thermal energy per molecule.

In a crystal lattice each atom is in equilibrium when it occupies its designated position in the lattice; and if perturbed the atom undergoes oscillations about the equilibrium state with a dynamic that is approximately simple harmonic. The quantization of the material oscillators ensures that the mean energy per atom will now be dependent on the ratio $h\omega/k_B T$. Here $h\omega$ denotes the vibrational spacing of the harmonic oscillator. The mean energy will now be given by Eq. (8.7), the expression derived by Planck in the context of radiation oscillators.

In quantum metabolism, the fundamental unit of energy is

$$E(\tau) = g\tau\,. \tag{8.9}$$

Here τ denote the metabolic cycle time, the mean turnover time of the oxidation-reduction reaction. The quantity $g = (\tilde{g}w)/N_A$, where w denotes the mean protein mass, and $\tilde{g} = (C\Delta p)$, and N_A denotes Avogadro's number. The parameter C, we recall describes the proton conductance and Δp, the proton motive force—both bioenergetic parameters. The quantity $E(\tau)$ is the total metabolic energy generated per cycle per mole.

The metabolic energy of the cell is derived from the vibration of the molecular groups embedded in the biomembrane. Each molecular group embedded in the membrane undergoes oscillations about its steady state with a motion which is simple harmonic for small oscillations. The frequency of the oscillations can also be computed in terms of the size of molecular group and elastic constants of the membrane.

The mean metabolic energy can be computed using methods analogous to the derivation of Eq. (8.7). We have

$$\tilde{E}(\omega) = \frac{h\omega}{\exp(\frac{h\omega}{g\tau}) - 1}\,. \tag{8.10}$$

The fundamental difference between Eq. (8.7) and Eq. (8.10) is the replacement of thermal energy, $E(T) = k_B T$, by the metabolic energy per cycle, $E(\tau) = g\tau$.

The difference between the components of energy invoked in the two classes of models resides in the fact that energy transformation in living organisms, in contrast to energy transformations in physical systems, occur under isothermal conditions. There are no significant differences in temperature between the parts of a cell or between cells in a tissue. Cells cannot function as heat engines. Energy transformation in cells proceeds through differences in ion-gradients, hence processes of energy transformation in cells are not described by equilibrium conditions. Living systems, in sharp contrast to physical systems, are in a dynamic steady state where the notion of a cycle time now replaces temperature as the critical organizing parameter.

8.2.4. *Material versus molecular oscillators*

Quantum metabolism rests on the recognition that the molecular oscillators in biomembranes and the material oscillators in crystalline solids can be analyzed in terms of the same mathematical formalism. This realization derives from a formal correspondence between the thermodynamic variables that describe material systems and the metabolic parameters that define certain biological processes [Demetrius (1983)]. We summarize this correspondence in Table 8.1.

This correspondence between thermodynamic variables and metabolic parameters is a consequence of the following analytical fact: *The growth rate parameter in metabolic processes satisfies a variational principle which is formally analogous to the minimization of the free energy in thermodynamic systems* [Demetrius (1983); Arnold *et al.* (1994)].

Table 8.1. Relation between thermodynamic variables and metabolic parameters.

Thermodynamic Variables	Metabolic Parameters
Temperature	Cycle time
Heat capacity	Metabolic rate
Thermodynamic entropy	Entropy production rate

The conceptual framework and the analytical methods invoked in quantum metabolism is an elaboration of this mathematical principle.

8.3. Metabolic Energy and Cycle Time

The fundamental equation in quantum metabolism, Eq. (8.2), relates the metabolic cycle time with cell size. This relation derives from the analysis of energy transduction within biomembranes. The basic information on the structure of biomembranes is due to Singer and Nicholson (1972). This study, which led to the fluid-mosaic model, describes the membrane as a sheet-like structure with a thickness of about 10^{-6} cm. This structure, which consist of lipid-protein complexes, are non-covalent aggregates. The constituent proteins, which are embedded in the phospholipid layer, are held together by many cooperative non-covalent interactions.

According to the chemiosmotic theory, the energy released in oxidations is coupled by proton translocation across the biomembrane to ADP phosphorylation.

The energy transformation involves the interconversion of three forms of energy; see [Nicholls and Ferguson (2002); Harris (1995)].

(1) The redox potential difference, that is, the actual redox potential between the donor and acceptor couples in the electron transfer chain.
(2) The proton motive force which describes the free energy stored in the membrane electrochemical proton gradients
(3) The phosphorylation potential for ATP synthesis.

Let $\tilde{g}$ denote the proton current induced by the electromotive force. We can now apply Ohm's law to the proton circuit and obtain $\tilde{g} = C\Delta p$.

The proton circuit which describes the coupling of the electron transport chain with ADP phosphorylation by means of the proton flux, denoted $\tilde{g}$, is schematically represented by Fig. 8.1.

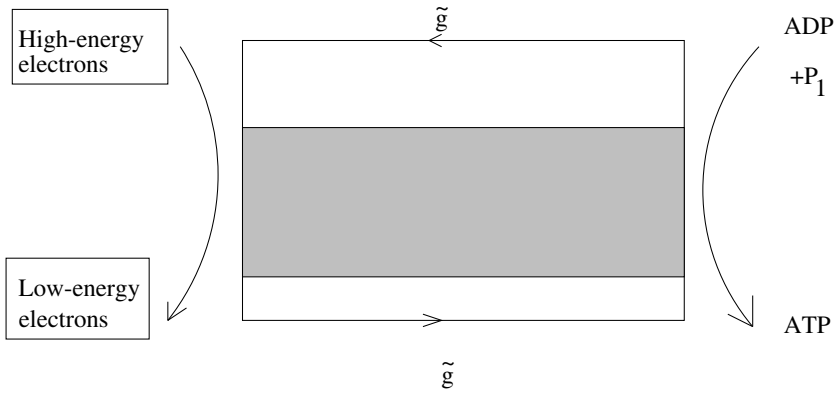


Fig. 8.1. Proton circuit linking the electron transport chain with ADP phosphorylation.

The energy generated per cycle, per mole, is given by $\tilde{E} = g\tau$. Here $g = (\tilde{g}w)/N_A$, where w denotes protein mass, and N_A, Avogadro's constant.

We let N denote the number of molecular groups in the membrane. The system has $3N$ degrees of freedom corresponding to the $3N$ coordinates, which are necessary to specify the location of the molecular groups. The molecular oscillations of the system can be described in terms of $3N$ normal modes of vibration; each with characteristic frequency $\omega_1, \omega_2 \ldots, \omega_{3N}$. We will consider the molecular oscillators to be collective properties of the membrane as a whole and we will compute the metabolic energy, a property which is generated by the vibrations of the membrane into which the molecular groups are bound.

8.3.1. *The mean energy*

We will assume that the vibrational modes of the molecular groups are quantized and then apply a statistical argument to obtain an average energy for each independent mode of oscillation.

For a given energy $E_n = nh\omega$, the probability W_n that the oscillation has an energy corresponding to its nth allowed value is

$$W_n \sim \exp[-\frac{E_n}{\tilde{E}}] \tag{8.11}$$

where $\tilde{E} = g\tau$.

To normalize this expression, we write

$$W_n = \frac{\exp[-\frac{nh\omega}{g\tau}]}{\sum_{n=0}^{\infty} \exp[-\frac{nh\omega}{g\tau}]}$$

which reduces to

$$W_n = \frac{\exp[-\frac{nh\omega}{g\tau}]}{1 - \exp[\frac{-h\omega}{g\tau}]} .$$

The mean energy associated with an independent mode of oscillation is now given by

$$E^* = \sum E_n W_n .$$

In view of the expression for W_n given by Eq. (8.11) we obtain the mean metabolic energy $\tilde{E}(\omega)$ given by Eq. (8.10).

8.3.2. *The total metabolic energy*

The total metabolic energy generated by the redox reactions and stored in the membrane will be given by

$$u = \sum_{k=1}^{3N} \frac{h\omega_k}{\exp[\frac{h\omega_k}{g\tau}] - 1} . \tag{8.12}$$

We will derive an approximate value for this energy by ignoring the discrete structure of the membrane and considering the system as a homogeneous elastic medium. In order to determine the total metabolic energy, we need to calculate the different standing wave patterns generated by the vibrations of the molecular groups.

Now, the number of standing waves in an enclosure with wave vectors in the range ω to $\omega + d\omega$ is determined by the geometry of the system. It is proportional to the volume of the enclosure and to $\omega^2 d\omega$. Hence for elastic waves, the density of modes will be given by, see for example [Mandl (1988)],

$$f(\omega) = \frac{3v\omega^2}{2\pi^2 c^3} d\omega . \tag{8.13}$$

Here v denotes the volume of the wave medium. We can now exploit this expression to derive an approximate value for the total metabolic energy, u.

In view of Eq. (8.13), we can approximate Eq. (8.12) by

$$u = \int_0^{\omega_{\max}} \left(\frac{3hv}{2\pi^2 c^3}\right) \frac{w^3 d\omega}{\exp(\frac{h\omega}{g\tau}) - 1}\,. \tag{8.14}$$

Here $\omega_{\max}$ is the maximum frequency.

We will now evaluate Eq. (8.14) under certain particular constraints on the energy function, $g\tau$. We first introduce the notion of a characteristic cycle time, denoted τ^*, by writing

$$g\tau^* = h\omega_{\max}\,.$$

Hence

$$\tau^* = \frac{h\omega_{\max}}{g}\,.$$

The characteristic cycle time thus depends critically on the bioenergetic parameters C and Δp, variables which define the proton current, g.

We consider two limiting regimes of cycle time:

(a) $\tau \gg \tau^*$: When this condition holds, $g\tau \gg h\omega$ and the metabolic energy is thus much larger than the vibrational spacing.
(b) $\tau \ll \tau^*$: When this condition is obtained, we have $g\tau \ll h\omega$ and the metabolic energy is now much smaller than the vibrational spacing.

We will observe that these two constraints will lend to distinct characterizations of the metabolic energy as a function of cycle time.

(I) $\tau \gg \tau^*$.

When this condition holds, the integral given by Eq. (8.14) can now be simplified and we obtain

$$u = g\tau \times \left(\frac{3v}{2\pi^2 c^3}\right) \int_0^{\omega_{\max}} \omega^2 d\omega\,. \tag{8.15}$$

By expressing N, the total number of oscillators in terms of $\omega_{\max}$, we obtain the following expression for the total metabolic energy,

$$u = 3Ng\tau\,. \tag{8.16}$$

(II) $\tau \ll \tau^*$.

When this condition prevails, the Eq. (8.14) can be approximated by the integral,

$$u = \frac{3v}{2\pi^2 h^3 c^3}(g\tau)^4 \int_0^{\infty} \frac{x^3}{e^x - 1} dx$$

which reduces to

$$u = a\tau^4\,, \tag{8.17}$$

where $a = kg^4$ and $k = \frac{\pi^2 v}{h^3 c^3}$.

8.4. The Scaling Relations

The scaling relationship of metabolic rates with body size, given by Eq. (8.3) can now be derived from Eq. (8.16) and Eq. (8.17) by appealing to thermodynamic arguments.

8.4.1. *Metabolic rate and cell size*

The relations given by Eqs. (8.16) and (8.17) can be exploited to determine scaling relations between metabolic rate and cell size. Thermodynamic arguments entail that the total metabolic energy u generated by the redox reactions can be expressed in the form

$$u = \rho\mu W_c \,. \tag{8.18}$$

Here ρ is a proportionality constant with dimension [energy/mass], and μ the metabolic efficiency, which is defined by the ratio: rate of ADP phosphorylation / rate of electron transport.

We now return to the two limiting cases and appeal to Eqs. (8.16), (8.17) and (8.18).

(I) $\tau \gg \tau^*$:
This describes the classical regime where the energy transduction process is continuous. The cycle time and metabolic rate now becomes

$$\tau = \frac{(\rho\mu)}{g}\,; \quad P = g\mu W_c \,.$$

(II) $\tau \ll \tau^*$:
When this constraint on cycle time is obtained, the energy transduction process is discrete. The scaling exponents for the cycle time and metabolic rate now assume the values 1/4 and 3/4, respectively. The allometric relations become

$$\tau = (\frac{\rho\mu}{a})^{1/4} W_c^{1/4}\,; \quad P = a^{1/4}(\rho\mu)^{3/4} W_c^{3/4}\,.$$

8.4.2. *Metabolic rate and body mass*

The analytic relation between metabolic rate and cell mass can be extended to yield an allometric relation between organism metabolic rate and body mass. Extension to allometry at the whole organism level rests on a *multi-level scale* hypothesis, see [Suarez and Darveau (2005)]. This hypothesis entails that the scaling exponent (β) of a multicellular organism is similar to

that of its constituent cells, while the proportionality constant (α) depends on the efficiency with which nutrients are transported within the organism to the energy-transducing membranes in the cell.

According to the multi-level scale hypothesis, the metabolic rate of the whole organism, P, is now given by

$$P \sim C\Delta p W^{\beta} \tag{8.19}$$

where W denotes organism body mass.

The scaling exponent β depends on the cycle time τ. For systems described by a large cycle time, $\tau \gg \tau^*$, we have $\beta = 1$, for systems defined by a small cycle time, $\tau \ll \tau^*$, we obtain the characterization $\beta = 3/4$. The large majority of organisms are characterized by either the exponent $\beta = 1$, or $\beta = 3/4$. This observation is consistent with the fact that when the limiting conditions hold, the expressions for metabolic energy given by Eq. (8.16) and Eq. (8.17) are exact. The expression for the metabolic energy is an interpolation formula between two correct limits.

Beyond these two limiting conditions for the cycle time, the scaling exponent may assume values distinct from 1 or 3/4. However, a *minimal* value for β can be derived by invoking an energetic argument.

We assume that the metabolic rate P, scales with body size; that is $P \sim W^{\beta}$. Now, let Q denote the rate of assimilation of energy. By appealing to surface-area relations, we have, $Q \sim W^{2/3}$. Since the minimal metabolic rate, the rate needed for homeostasis, must exceed the rate of assimilation of energy, we have $P \geq Q$, and we conclude that $\beta \geq 2/3$.

8.5. Empirical Considerations

Quantum metabolism is a mathematical model of energy transduction which provides a quantitative explanation of the empirical rules relating body size with metabolic rate. The model shows that the dependency on body size involves three main factors:

(a) *Metabolic efficiency:* The extent to which the electron transfer process is coupled to ADP phosphorylation.
(b) *Membrane composition:* The phospholipid composition of the biomembrane. This property determines the bioenergetic parameters such as proton conductance and the proton motive force.
(c) *Network geometry:* The complexity of the circulatory network by which nutrients are transported within the cells and tissues of the organism.

The analytic relation between metabolic rate and body size is given by Eq. (8.19). This relation yields explicit predictions regarding both the scaling exponent and the proportionality constant. We now describe the nature of these predictions and discuss their empirical support.

8.5.1. *Scaling exponents*

The model predicts that the scaling exponent β will satisfy the condition, $2/3 \leq \beta \leq 1$.

Different classes of organisms will be defined by different range of values of β — this range will be contingent on the metabolic cycle time.

Quantum metabolism distinguishes between two classes of organisms.

Type (I): defined by the condition $\tau > \tau^*$. Chloroplasts the energy transducing organelles in plants are relatively large and described by a large cycle time. Hence plants are typical members of Type (I).

Type (II): defined by the condition $\tau < \tau^*$. Mitochondria the energy transducing organelles in animals are described by a relatively short cycle time. Hence animals are typical members of Type (II).

This classification according to cycle time indicates that in plants, the scaling exponents will satisfy the condition $2/3 < \beta < 1$, whereas in animals, we have $2/3 < \beta < 3/4$.

However, the actual value of β will depend on the ecological constraints experienced by the population during its evolutionary history. The effect of these constraints on the scaling exponent can be understood in terms of *directionality theory* [Demetrius (1997)]. This model of the evolutionary process distinguishes between equilibrium and opportunistic species.

(i) *Equilibrium species.* This condition characterizes populations that spend most of their time in the stationary phase or undergoing small fluctuations in population numbers around some constant value. (Examples: perennial plants, large mammals.)

(ii) *Opportunistic species,* This property defines species subject to large irregular fluctuations in population size. (Examples: annual plants, small mammals, birds.)

The central parameter in directionality theory is demographic entropy, S, which is given by

$$S = -\int_0^\infty p(x) \log p(x) dx \,. \tag{8.20}$$

Here, $p(x)$ is the probability that the mother of a randomly-chosen newborn belongs to the age-class $(x, x + dx)$.

Directionality theory predicts that evolution will result in a unidirectional *increase* in entropy in equilibrium species. In opportunistic species, evolution results in a unidirectional *decrease* in entropy for large populations, and random, *non-directional change* in entropy for small populations [Demetrius (1997)].

In view of the allometric rules relating body size to cycle time and metabolic rate, we can derive an expression relating the entropy, S to the mass-specific metabolic rate, denoted P^*. The relation is given by

$$S = a - c \log P^* \,. \tag{8.21}$$

Equation (8.21) provides a basis for predicting evolutionary trends in metabolic rate by appealing to the directionality principles for evolutionary entropy. These principles imply the following patterns: (a) in equilibrium species, evolution will act to decrease P^*; (b) in opportunistic species, evolution will act to increase P^*, when population size is large, and result in random non-directional changes in P^* when population size is small.

Now, the mass-specific metabolic rate, P^*, is given by

$$P^* \sim C \Delta p W^{\beta - 1} \,. \tag{8.22}$$

We can therefore exploit directionality theory to infer the following characterization of the scaling exponents for perennial plants and large mammals (equilibrium species), and annual plants and small mammals (opportunistic species).

(I) *The scaling exponent for plants will range between* $3/4$ *and* 1. *Perennial angiosperms are described by* $\beta = 1$, *annual ones by* $\beta = 3/4$.

(II) *The scaling exponent for mammals will range between* $2/3$ *and* $3/4$. *Large mammals are described by* $\beta = 3/4$, *small mammals by* $\beta = 2/3$.

Empirical observations on mammals [Dodds (2001)]; plants [Reich *et al.* (2006)] and a range of other taxa [Glazier (2005)] broadly corroborate these two classes of predictions.

8.5.2. *The proportionality constant*

The proportionality constant α is determined principally by the microlevel variables proton conductance and proton motive force and one macrolevel variable, nutrient supply.

Proton conductance is highly dependent on the degree of polyunsaturation of membrane phospholipids: the more polyunsaturated the mitochondrial membranes, the larger the proton conductance.

There exists a large variation in phospholipid composition between species. However, certain distinct patterns of variation exist [Hulbert (2005); Brand *et al.* (1994)]:

(a) Membrane bilayers of endotherms are more polyunsaturated than those of similar-size ectotherms;
(b) Membrane bilayers of tissues of small mammals are highly polyunsaturated, while in large mammals, membrane polyunsaaturation decreases with increased body size.

Since proton conductance is positively correlated with proton current, we can invoke (a), (b), and Eq. (8.19) to predict the following patterns.

(III) *The metabolic rate of an endotherm will be greater than that of an equivalently-sized ectotherm at the same body temperature.*
(IV) *Tissues from larger mammals should have lower* in vitro *metabolic rate than homologous tissues from small mammals*

Experimental studies of metabolic rate, described for example by Hulbert (2005) and Hochachka and Somero (2000), are consistent with these predictions.

References

Arnold, L., Demetrius, L., and Gundlach, M. (1994). Evolutionary formalism and products of random matrices. *Ann. Appl. Prob.* **4**, pp. 859–901.

Banavar, J. R., Damuth, J., Martan, A., and Rinaldo, A. (2002). Supply-demand balance and metabolic scaling, *Proc. Natl. Acad. Sci.* **99**, pp. 1056–1059.

Brand, M. D., Chien, L. F., and Diolez, P. (1994). Experimental discrimination between proton leak and redox slip during mitochondrial electron transport. *Biochem. J.* **297**, pp. 27–29.

Brody, S. (1946). *Bioenergetics and Growth* (Reinhold).

Calder, W. A. (1984). *Size, Function and Life History* (Harvard University Press).

Demetrius, L. (1983). Statistical mechanics and population biology, *Jour. Stat. Phys.* **30**, pp. 709–783.

Demetrius, L. (1997). Directionality principles in thermodynamics and evolution. *Proc. Natl. Acad. Sci.* 94, pp. 3401–3408.

Demetrius, L. (2003). Quantum statistics and allometric scaling of organisms. *Physica A*. **322**, pp. 477–480.

Demetrius, L. (2006). The origin of allometric scaling laws in biology. *Jour. Theor. Bio*. **243**, pp. 455–467.

Dodds, P. S., Rothmann, D. H., and Weitz, J. S. (2001). Re-examination of the 3/4 law of metabolism. *Jour. Theor. Biol.* **209**, pp. 2–27.

Fröhlich, H. (1968). Long range coherence and energy storage in biological systems. *Int. Jour. Quantum Chem.* **11**, pp. 641–649.

Glazier D. S. (2005). Beyond the 3/4 power law: variation in the intra- and interspecific scaling of metabolic rate in animals. *Biol. Rev.* **80**, pp. 611–662.

Harold, F. M. (1986). The Vital Force. A Study of Bioenergetics (Freeman, New York).

Harris, D. A. (1995). *Bioenergetics at a Glance* (Blackwell Scientific Publications).

Hochachka, P. W., and Somero, G. W. (2000). *Biochemical Adaptation* (Oxford University Press).

Hulbert, A. H. (2005). On the importance of fatty acid composition of membranes for aging. *J. Theor. Biol.* **234**, pp. 277–288.

Hulbert, A H., and Else, P. (2000). Mechanisms underlying the cost of living in animals. *Ann. Rev. Phys.* **62**, pp. 207–253.

Kleiber, M. (1961). *The Fire of Life. An Introduction to Animal Energetics* (Wiley, New York).

Linsteadt, S. L., and Calder III, W. A. (1981). Body size, physiological time and longevity of homeothermic animals. *Quart. Review of Biology* **56**, pp. 1–15.

Longair, M. S. (2004). *Theoretical Concepts in Physics*, 2nd Ed. (Cambridge University Press).

McMahon, T. A. (1973). Size and Shape in Biology. *Science* **171**, pp. 1201–1204.

Mandl, F. (1988). *Statistical Physics*, 2nd Ed. (Wiley, New York).

Mitchell, P. (1966). Chemiosmotic coupling in oxidative phosphorylation. *Bio. Rev. Cambridge Philos. Soc.* **4A**, pp. 445–502.

Nicholls, D. G., and Ferguson, S. J. (2002). *Bioenergetics 3* (Academic Press, London).

Peters, R. H. (1983). *The Ecological Implication of Body Size* (Cambridge University Press).

Reich, P. B., Tjoelker, M. G., Machado, T. L., and Oleksyn, J. (2006): Universal scaling of respiratory metabolism, size and nitrogen in plants, *Nature* **439**, pp. 457–461.

Rolfe, D. F., and Brown, G. C. (1997). Cellular energy utilization and molecular origin of standard metabolic rate in mammals, *Physiol. Rev.* **77**, pp. 731–758.

Singer, S., and Nicholson, G. L. (1972). The fluid mosaic model of cell membranes. *Science* **172**, pp. 720–730.

Suarez, R. K., and Darveau, C. A. (2005). Multi-level regulation and metabolic scaling. *J. Exp. Biol.* **208**, pp. 1629–1634.

West, G. B, Brown J. H., and Enquist, B. (1997). A general model for the origin of allometric scaling laws in biology, *Science* **276**, pp. 122–126.

About the author

Lloyd Demetrius was educated at Cambridge University, England and the University of Chicago, USA. His present research interests include the application of ergodic theory and dynamical systems to the study of evolutionary processes in biology. He has been on the mathematics faculty at the University of California, Berkeley, Brown University and Rutgers. His current affiliations are the Max Planck Institute for molecular genetics, Berlin, and Harvard University.

Chapter 9

Spectroscopy of the Genetic Code

Jim D. Bashford and Peter D. Jarvis

Discussions of the nature of the genetic code cannot be divorced from the biological context of its origin and evolution. We briefly review some of the main arguments that have been put forward for the evolution of the genetic code, together with the salient biological background. Longstanding observations of genetic code regularities have led to combinatorially-based assertions about its structure. However, it is also possible to extend such "symmetry" descriptions to continuous symmetries or supersymmetries, especially in relation to the pattern of redundancy (degeneracy) of the genetic code. We give an account of some recent work along these lines. This is supported by graphical presentations, and some data fits, of samples of measured physico-chemical properties of codons and amino acids across the genetic code table. Finally, we review codon-anticodon recognition in terms of conformational degrees of freedom, and structural, stereochemical and kinetic considerations. Based on this, we suggest a possible role for quantum processes at important stages of codon reading and translation.

9.1. Background: Systematics of the Genetic Code

Discussion of the nature, and organization, of the genetic code dates from almost before the early work on its detailed elucidation, and has spawned a great variety of ingenious suggestions and insights.[1]

Received April 3, 2007

[1] One of the first such speculations was the so-called "diamond code" proposed by the physicist Gamow (1954).

The dual aims of this chapter are firstly, to review physics-inspired approaches for describing and analysing the patterns of codon-amino acid assignments that characterize the nature of the genetic code, almost universally across all life forms, and secondly, to discuss possible roles for quantum processes within the genetic code recognition system.

The simplest abstraction of the "genetic code" is as a mapping of genetic information, encoded by one type of biological macromolecule, the nucleic acids, into another family, the amino acids, which constitute the building blocks of proteins.[2] The scheme is simple enough to state: a dictionary of 64 possible code-words (codons), is associated with 20 amino acids plus a "stop" signal. The vast bulk of built-in redundancy in this mapping is conserved within all living organisms, and this strongly suggests that the code in its present form is the result of an evolutionary process at the molecular level, whereby the code derived from some more primitive form. A common first step in attempting to describe the evolution of the genetic code is simply to explain the two numbers, "64" and "20".[3]

The remainder of this section is devoted to a rapid survey of the salient biological and biochemical facts relating to the biomolecules and processes involved in the genetic coding system, followed by a brief commentary on the traditional "explanations" of the origins of the code. More recent, information-theory perspectives, of potential relevance to a role for quantum processes, are also mentioned. In Sec. 9.2 the "systematics" of the genetic code in terms of the observed patterns and regularities of the genetic code are developed in the group-theoretical language of dynamical Lie algebras and superalgebras. In particular, we show that an $sl(6/1)$ supersymmetry model proposed by us [Bashford *et al.* (1998)], is able to give an interpretation in this language, of two main models of code evolution developed quite independently in the biological literature, [Jiménez Sanchez (1995); Jiménez-Montaño (1999)]. The most subtle stage of code evolution relates to the third codon base (see below), and this is taken up in Sec. 9.4, with a detailed discussion of codon-anticodon recognition taking into account ribonucleotide conformational degrees of freedom. On this basis we suggest a possible role for quantum processes at important stages of codon-anticodon reading. Meanwhile in Sec. 9.3, the dynamical symmetry

[2] A recent review of the origin of the genetic code is, for example, Szathmáry (1999); see also articles in the special issue Vol. 33, 2003 of *Origins of Life and Evolution of the Biosphere*.

[3] An entertaining discussion on how such numbers might relate to the Tower of Hanoi Problem can be found in Berryman, Matthew J. (2006). Mathematic principles underlying genetic structures, `http://www.manningclark/events/stars.Berryman.pdf`.

description is corroborated by giving some simple numerical fits between various measured biological and physico-chemical codon and amino acid properties, and appropriate polynomials in the group labels, or "quantum" numbers of the codons.

9.1.1. RNA *translation*

The machinery of gene translation is dependent upon four major kinds of biomolecule [Woese *et al.* (1966)]: *mRNA*—the gene transcript, which contains sequences of codons; amino acids (*a.a.*)—the building blocks of polypeptides; *tRNA*—the intermediary molecules, which carry amino acids and recognise specific codons on *mRNA* via base-pairing with the *anticodons* which they present: and the amino-acyl (-*tRNA*-) synthetases, *aaRS*—enzymes that bind specific amino acids to their cognate *tRNA*. The basic reactions connecting these biomolecules are sketched in Fig. 9.1. Other kinds of molecule also participate: the ribosome complex, at which translation occurs, and elongation factor *EF-Tu*: a protein that transports amino-acylated *tRNA*s to the ribosome. However these latter pathway components have more generic roles, independent of codon or amino acid properties, and will not be discussed in great detail. The basic unit of the genetic code is the *codon*: a triplet of nucleotide bases. Four such bases, *G*uanine, *C*ytosine, *A*denosine and *U*racil (*T*hymine for *DNA*) occur naturally in *mRNA*. Therefore there exist $64 = 4^3$ possible triplet combinations which are distributed, unequally, amongst 20 amino acids as shown in Table 9.1. Even a cursory inspection of this, mitochondrial, genetic code

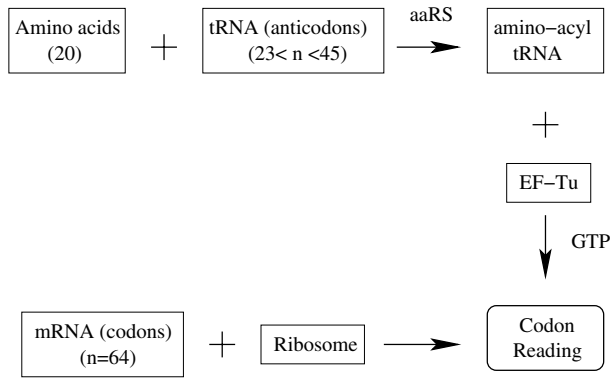


Fig. 9.1. Organisational chart of key steps in codon reading.

Table 9.1. Mitochondrial genetic code.

a. a.[a]	codon	a.c.[b]	a. a.[a]	codon	a.c.[b]	a. a.[a]	codon	a.c.[b]	a. a.[a]	codon	a.c.[b]
Phe	UUU	GAA	Ser	UCU	UGA	Tyr	UAU	GUA	Cys	UGU	GCA
Phe	UUC	GAA	Ser	UCC	UGA	Tyr	UAG	GUA	Cys	UGC	GCA
Leu	UUA	UAA	Ser	UCA	UGA	Ter	UAA	-	Trp	UGA	UCA
Leu	UUG	UAA	Ser	UCG	UGA	Ter	UAG	-	Trp	UGG	UCA
Leu	CUU	UAG	Pro	CCU	UGG	His	CAU	GUG	Arg	CGU	UCG
Leu	CUC	UAG	Pro	CCC	UGG	His	CAC	GUG	Arg	CGC	UCG
Leu	CUA	UAG	Pro	CCA	UGG	Gln	CAA	UUG	Arg	CGA	UCG
Leu	CUG	UAG	Pro	CCG	UGG	Gln	CAG	UUG	Arg	CGC	UCG
Ile	AUU	GAU	Thr	ACU	UGU	Asn	AAU	GUU	Ser	AGU	GCC
Ile	AUC	GAU	Thr	ACC	UGU	Asn	AAC	GUU	Ser	AGC	GCC
Met	AUA	UAU	Thr	ACA	UGU	Lys	AAA	UUU	Ter	AGA	-
Met	AUG	UAU	Thr	ACG	UGU	Lys	AAG	UUU	Ter	AGG	-
Val	GUU	UAC	Ala	GCU	UGC	Asp	GAU	GUC	Gly	GGU	UCC
Val	GUC	UAC	Ala	GCC	UGC	Asp	GAC	GUC	Gly	GGC	UCC
Val	GUA	UAC	Ala	GCA	UGC	Glu	GAA	UUC	Gly	GGA	UCC
Val	GUG	UAC	Ala	GCG	UGC	Glu	GAG	UUC	Gly	GGG	UCC

[a] a.a. = amino acid.
[b] a.c. = anticodon. Anticodon base modifications not shown.

reveals systematic patterns in the observed degeneracy of amino acids to codons. Specifically, changes in the first and second codon letters always change the coded amino acid, whilst changes in the third position often do not. Furthermore, codons with the purine (R)-derivative bases (A and G) in the third position always code for the same amino acid, as do those with pyrimidine-derivatives (U and C)[4]. The overall effect seen in Table 9.1 is that codons cluster in families, with either 4-fold ("family boxes") or 2-fold degeneracies ("mixed boxes"), which all code for the same amino acid; moreover there are two cases of "hexanumerate" codons in which both a family box and a mixed box contribute. This structure is a direct consequence of the *tRNA-mRNA* pairing: bases in the first[5] two positions of the codon always bind to their complements (G with C, A with U) on the *anticodon* (*a.c.*, as shown in Fig. 9.2). The binding in the third position is less precise. The nature of this ambiguous or "wobble" pairing, first postulated by Crick (1966), is still not completely understood, and we

[4]The code for eukaryotic organisms is more involved, as will be discussed below.
[5]Relative to the standard (5' carbon→3' carbon) orientation of the sugar-phosphate backbone; see Sec. 9.4.

will review current knowledge in a subsequent section (see Sec. 9.4), as it forms the cornerstone of our suggestions for quantum processes in codon reading.

Finally let us mention the fourth class of molecule, the *aaRS*. Each enzyme contains a receptor for a specific amino acid, and binds to the anticodon-containing region of the cognate *tRNA*. Detailed comparison of *aaRS* structures [Eriani *et al.* (1990)] led to the discovery that two structurally-distinct families of molecule exist. Furthermore, these structural motifs are strongly conserved amongst organisms with only one, primitive, exception amongst archaebacteria, discovered to date [Fabrega *et al.* (2001)]. Remarkably, each *aaRS* class contains species cognate for 10 amino acids, with the resulting families being "complete" in the sense that each contains physicochemically-distinct (in terms of hydrophobicity and acidity) amino acids [Cavalcanti *et al.* (2004)], capable of producing key protein structural motifs. Moreover the so-called class II *aaRS* are associated with smaller, polar *a.a.*'s, commonly believed to have been incorporated in the genetic code earlier than the bulkier residues of class I. This observation has led to speculation that the modern genetic code formed via a "doublet" predecessor.

9.1.2. *The nature of the code*

During the 1960s and 1970s organisms as diverse as certain bacteria, viruses and vertebrates were all found to have the same genetic code, leading to the concept of a "universal" genetic code, present at least since the Last Universal Common Ancestor (LUCA). This observed universality was the motivation for the "frozen accident" hypothesis [Crick (1968)], which stated that as evolution progressed, the increased complexity of proteins made incorporation of new amino acids unlikely to be beneficial.

Although the "universal" genetic code incorporates 20 amino acids, recognized by the procedure in Fig. 9.1, several recently-discovered exceptions exist, whereby "new" amino acids are encoded by *tRNA* simultaneously binding to a "stop" codon and recognizing a secondary structural motif. Examples include selenocysteine [Bock *et al.* (1991)] in eukaryotes and pyrrolysine [Srinivasan *et al.* (2002)] in archaebacteria. Differences in amino acid-codon assignments have also been discovered (for a review see the paper by Osawa *et al.* (1992)) and currently 16 variants on the "universal" code are catalogued on the NCBI Taxonomy webpage `http://www.ncbi.nlm.nih.gov/Taxonomy/Utils/wprintgc.cgi`.

Table 9.2. Wobble pairing rules[a].

First a.c. position[b]	Third codon position
U	U, C, A, G
G	U, C
C	G
I	U, C, A

[a] Adapted from [Osawa *et al.* (1992)].
[b] Nucleoside modifications not shown.

In this paper we shall be concerned with two codes: the (vertebrate) mitochondrial code (VMC), posited to be related to an ancestor of the universal or eukaryotic code (EC). The EC has qualitatively similar 2- and 4-fold degeneracies, and codon assignments to amino acids, to those observed for the VMC. As mentioned, these degeneracies are due to the ambiguous or "wobble" nature of pairing between third codon, and first anticodon, bases [Crick (1966); Agris (1991)]. Here it suffices to state the wobble rules (Table 9.2); we shall discuss them in greater detail in Sec. 9.4. As seen from Table 9.1, in the VMC only first *a.c.* position U and G are present, leading to the characteristic "4" and "2+2" box degeneracies. While *a.a.*—codon assignments are very similar in the EC, the *anticodon* usage is different. Firstly the purine-derived base Inosine (I) replaces A (in all but a few exceptions) in the first *a.c.* position, while C may compete with I and U for codons ending with G. We shall comment further on this competition in Sec. 9.2.

Regularities inherent in the nucleobase "alphabet" allow discussion of codon-amino acid relationships to be abstracted from a biochemical setting to a mathematical/logical one. Nucleobases are commonly classified in terms of three dichotomous indices [Saenger (1984)]: *S*trong (G, C) versus *W*eak (A, U/T) pertaining to the number of H-bonds formed in canonical pairs (Fig. 9.2); pu*R*ine-derived bases (A, G) contain two heterocyclic rings, while p*Y*rimidine bases (C, U/T) have one. Thirdly one can distinguish the proton acceptor/donor nature of the functional group attached to the C1 atom: a*M*ino (A, C) versus *K*eto (G, U/T). Of course any two of these indices are sufficient to establish the identity of any given nucleobase. Finally there exists the common notation a*N*y base, that is $N = U/T, C, A, G$. In terms of this language, regularities in the code are easily expressed. Arguably the best known is Rumer's rule [Rumer (1966)]: replacement of the bases in codon positions I and II by their M/K counterparts changes the nature of the 4-codon box. For example, the box UUN is split, with

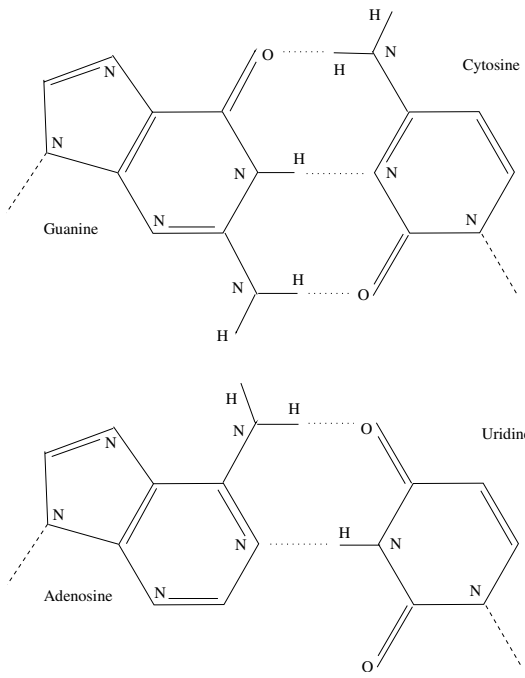


Fig. 9.2. Watson-Crick pairing of RNA bases.

codons UUY and UUR coding for Phe(nylalanine) and Leu(cine) respectively. Replacing $U(I)$ and $U(II)$ by the other K-type base (G) changes the structure to GGN, which is a family (unsplit) box, coding for Gly(cine). Another, more recent example is the observed correlation [Biro *et al.* (2003); Chechetkin (2006)] between class I and class II $aaRS$ and anticodon families of the forms

$$(WWW, WWS, SWW, SWS)\,, \quad (SSS, SSW, WSS, WSW)\,,$$
$$(MMM, MMK, KMM, KMK)\,, \quad (KKK, KKM, MMK, MKM)\,.$$

Other regularities apparent in the code, in particular relating amino acid and codon physico-chemical properties will be discussed in more detail in subsequent sections.

Theories on the evolution of the code fall into one of three broad categories. The *co-evolution* theory posits that the genetic code evolved in parallel with the emergence of increasingly complex amino acids [Wong (1976); Weberndorfer *et al.* (2003)]. Thus similar amino acids would be

coded by similar codons because more recent *a.a.*'s "captured" codons from their precursors. The *physico-chemical* hypothesis [Di Giulio (2003)] suggests that, at an early stage of evolution, direct contacts between amino acids and codons/anticodons facilitated translation, dictating patterns of physico-chemical regularities observed within the modern, universal code. Finally the *selection* theory suggests that the code evolved to minimize phenotypic errors [Freeland *et al.* (2003); Ronneberg *et al.* (2000)] and, indeed, secondary structure of $mRNA$ transcripts [Shabalina *et al.* (2006)]. The three streams of thought are not, however, mutually exclusive and each mechanism may have influenced different stages of evolution.

9.1.3. *Information processing and the code*

On an abstract level, the flow of genetic information from DNA to polypeptide can readily be viewed in terms of a digital code. Generally the Y/R and S/W characteristics of each nucleobase are represented as "bits" and regularities within patterns of codon and amino acid assignments are investigated [Freeland *et al.* (2003); Mac Dónaill and Manktelow (2004)]. For example in a 2-bit scheme (1 each for Y/R and S/W) Rumer's conjugate rule ($G \leftrightarrow U$, $A \leftrightarrow C$) can be implemented as the negation operation [Négadi (2003)]. Informational aspects of coding evolution, including adaptor enzymes ($aaRS$) have been discussed by Nieselt Struwe and Wills (1997). A fuller discussion of such coding labelling is given in Sec. 9.2 and Sec. 9.3.

From the evolutionary point of view however Gray, or error-checking codes [Freeland *et al.* (2003)] are of particular interest. For example Mac Dónaill (2003) proposed a 4-bit scheme, where 3 bits indicated proton donor/acceptor sidegroups on the bases and 1 labelled the base Y/R nature, viz,

$$G = (0, 1, 1; 0)\,, \quad C = (1, 0, 0; 1)$$
$$aA = (1, 0, 1; 0)\,, \quad U/T = (0, 1, 0; 1)\,.$$

Here "aA" (amino-Adenosine) was considered on theoretical grounds. With base parity defined as the sum of all 1's appearing in the corresponding vector, it is clear that the fourth, Y/R bit acts as a parity check upon permissible H-bonding patterns (i.e. those which do not disrupt the regular helical geometries of DNA or RNA)[6]. Using this scheme an extended set of 2^4 candidate bases was considered for inclusion in the nucleotide alphabet,

[6]Changing from aA to A (deletion of the third "1" of aA) does not affect the even parity of the resulting alphabet.

whereupon it was argued that same-parity alphabets have high recognition fidelity, in contrast to those of mixed parity. Further, alphabets with even parity, such as the natural one, are likely to be favoured over odd ones as the occurrence of tautomers is generally less likely.

A different kind of information-processing hypothesis was proposed by Patel (2001a,b,c) whereby DNA or protein assembly is reduced to a computational task. The problem is to determine a maximally-sized "database" of items (nucleobases), which are readily distinguishable, with a minimal number of search queries. For a database containing N randomly-ordered items denote the number of binary ("yes/no") queries, Q, required to locate the desired item. In a classical ensemble, where rejected items are returned to the database, the expected mean number of questions, $\langle Q \rangle = N/2$.

However in a quantum-mechanical system, superpositions of items are permitted, and Grover's algorithm exploits this feature [Grover (1997)]. Starting with the symmetric initial state $N^{-1/2}(|1\rangle + |2\rangle + \ldots |N\rangle)$, the number of queries needed is determined by

$$(2Q+1)\mathrm{Arcsin}N^{-1/2} = \pi/2\,. \tag{9.1}$$

The potential significance of several solutions of this equation for DNA replication and expression have been pointed out by Patel (2001a,b,c). For $Q = 1$ the database has $N = 4$ items which, if the "items" are nucleobases, and (Watson-Crick) base-pairing the "quantum oracle", has implications for DNA replication. For $Q = 3$ (one question per base pair in a codon) $N \simeq 20.2$, while the number of "letters" in the genetic code is 21 (20 amino acids plus a stop signal). Lastly when $Q = 2$ one finds $N \simeq 10.5$, which is potentially of interest in regard to the two classes of aaRS and amino acids [Patel (2005)].

In order for quantum genetic information-processing to occur, as outlined above, there are two important considerations. Firstly quantum decoherence, which occurs far more quickly than proton tunnelling, at room temperature needs to be mitigated. Indeed particular enzymes have been suggested to facilitate proton tunnelling—for a recent review see the paper by Knapp and Klinman (2002)—in other reactions, via the exclusion of H_2O, although whether DNA polymerases have such capabilities is unknown. Secondly there is the inference that, somehow a quantum superposition of base molecules is set up in the vicinity of the assembly site. It is unclear precisely how an enzyme might achieve this. However, as has recently been pointed out [Shapira *et al.* (2005)], the Grover algorithm can produce advantageous searches under a variety of initial conditions including mixed states.

9.2. Symmetries and Supersymmetries in the Genetic Code

Attempts to understand the non-random nature of the genetic code invite a description in a more abstract setting. Combinatorial symmetry considerations amount to statements about certain transformations amongst the basic ingredients, like bases and codons, or groupings thereof, which display or predict regularities.[7] A natural extension of this language is to formal *continuous* linear transformations amongst the physical objects themselves. This mathematical viewpoint thereby allows access to the rich theory of Lie groups and their representations. In group theoretical language, the existence of the genetic code itself entails a simple counting problem—find the semisimple Lie groups[8] that have irreducible representations of dimension 64, the number of codons in the genetic code. Secondly, such a genetic code group should have a "reading subgroup", for which the dimension and multiplicity of its representations in the decomposition of the 64-dimensional codon representation, coincides with, or is a refinement of, the known pattern of codon redundancies in the amino acid assignments. Such groups and subgroups are candidates for "symmetries of the genetic code".

The first work along these lines was carried out in a pioneering paper by Hornos and Hornos (1993), and elaborated in Forger *et al.* (1997)—for a review see Hornos *et al.* (1999). A comprehensive sort by rank and dimension of representations led to the almost unique identification of the 64-dimensional representation of the group $Sp(6)$. It was shown that standard symmetry-breaking scenarios using eigenvalues of Casimir operators in group-subgroup branching chains, for plausible assignments of codons to basis vectors, could provide a quantitative and statistically significant match to a certain major composite index of amino acid functionality, the so-called Grantham polarity index. The group-subgroup branching chain also gave support to the interpretation of the code as a "frozen accident": generically unequal polarity eigenvalues of certain distinct representations of the "reading subgroup" are constrained by the numerical fit to be degenerate, because in practice they still code for the same amino acid.

[7] There have been many studies attempting to unlock the "secret of the genetic code" by careful examination of code patterns. See Sec. 9.1 for historical remarks, and Szathmáry (1999) for a modern account. A recent orthodox study attempting to establish objective support for code trends is Biro *et al.* (2003). Intriguing geometrical insights have been developed by Yang (2005) (also see references therein).

[8] A restriction to simple groups would proscribe the reasonable candidate $SL(4) \times SL(4) \times SL(4)$ for example (see below); on the other hand, weakening the search criteria (for example to non-classical groups or even reducible representations) would considerably complicate the discussion, and so is avoided just on technical grounds.

Subsequent work has exploited the connection between *algebraic* structures and allied transformation groups. In Bashford *et al.* (1997, 1998), and Forger and Sachse (2000a,b), the notion of symmetry transformations is generalized to that of supersymmetries, which make allowance for the fact that objects in the underlying space may possess a grading, that is an assigned "even", "odd", or in physics language "bosonic", "fermionic", character. In Bashford *et al.* (1997, 1998) a specific type of scheme based on the Lie superalgebra $sl(6/1)$ is developed, and in Forger and Sachse (2000a,a) more general possibilities are identified. The work of Frappat *et al.* (1998), reviewed by Frappat *et al.* (2001) on the other hand, deviates further from the Lie group—Lie algebra connection in exploiting a specific type of "quantum", or q-deformed algebra, here $sl_q(2) \times sl_q(2)$, in which tensor products of representations reduce in a simple way, as desirable if unique assignments of abstract state vectors to objects in the genetic code system are to be maintained. An important paper which critically reviews *all* group-based and related attempts at a description of the genetic code, especially the $Sp(6)$ models and an alternative $SO(13)$ version, is the article by Kent *et al.* (1998).

As reviewed in Sec. 9.1 above, current thinking is that the origin of the genetic code is distinct from the origin of life itself, and that its present-day, near-universal structure is the result of some evolutionary process of refinement from earlier, primitive versions. The potential of group-theory based accounts is that, in contrast to combinatorial schemes, which merely serve to express genetic code regularities via succinct statements about various discrete transformations, the code structure as a whole can be described in terms of a succession of group-subgroup steps, in a chain starting with the initial codon group, and ending with the final "reading" group. In the remainder of this section we describe the $sl(6/1)$ model in some detail, in this context. The focus is not so much on quantitative predictions (but see Sec. 9.3 below), but rather to demonstrate that a group-theory based account can indeed be broadly compatible with established biochemically- and biologically-based understandings about the origin and evolution of the code. The claim would be that an eventual, "dynamical code model" will bear out the group-theoretical steps in detail.

A useful starting point for code degeneracy, compatible with both physico-chemical and coevolution views of the code origin, is to regard the outputs of the early translation system as "stochastic proteins". Possibly, early proto-amino acid/nucleic acid associations were useful in the context of optimizing replication, and only incrementally acquired sufficient specificity for the synthesis of functional oligopeptides to emerge as an end in

itself. It is reasonable to suggest that early coding for such primitive enzymes was quite non-specific and error-prone, but also, that the system as a whole was error-tolerant. The group-theoretical counterpart of this is that the degeneracies of the early code should be associated with the decomposition of the 64-dimensional representation of the codon group into irreducible representations (irreps) of intermediate subgroup(s), such that codon assignments within, or between, such subgroup irreps, respectively minimize, or maximize, variations in amino acid properties at the largest possible levels of functional synonymy.

As was pointed out in Sec. 9.1 above, a major determinant of amino acid type is the character of the second codon base. Specifically *weak* bases $W = \{A, U\}$ are associated with hydrophilicity/hydrophobicity extremes respectively—see Weber and Lacey (1978). Also, there is an argument from biosynthetic complexity [Jiménez Sanchez (1995)] that the earliest utilized bases should be the simplest chemically, namely A, U again (there are of course other arguments, for example thermodynamic stability of codon-anticodon pairs, [Baumann and Oro (1993)] for the strong bases $S = \{C, G\}$ to have been the earliest coding bases). Finally, it can be argued [Woese *et al.* (1966)] that a minimal requirement for useful oligopeptides, should be the existence of tunable hydrophobic/hydrophilic regions in the primary structure, so as to allow the possibility of folding and the presentation of stereochemically specific, enzymatically active contact regions.

9.2.1. *sl*(6/1) *model: UA+S scheme*

The representation-theoretical equivalent is thus that there should be an assignment of codons to a basis for the 64-dimensional representation of the genetic code algebra, which is adapted to a subalgebra decomposition which distinguishes the second base letter and assigns codons NAN and NUN to different representations (necessarily of dimension 16). It turns out that the class of superalgebras $sl(n/1)$ possesses a family of so-called typical irreducible representations of dimension 2^n, which moreover branch to members of the corresponding family under restriction to smaller subalgebras $sl(n'/1)$, $sl(n''/1)$ with $n'' < n' < n$. This property, shared by spinor representations of the orthogonal groups, singles out for attention in the genetic code context the superalgebra $sl(6/1)$, and its typical irreducible representations of dimension $2^6 = 64$, with Dynkin label $(0, 0, 0, 0, 0; b)$ for appropriate values of $b > 5$ (denoted hereafter by $\mathbf{64}_b$). The branching rule

(for $n' = n - 2 = 4$) reads

$$sl(6/1) \rightarrow sl(2)^{(2)} \times sl(4/1)^{(1,3)} \times gl(1)\,,$$
$$\mathbf{64}_b \rightarrow \mathbf{1} \times \mathbf{16}_{b+2} + \mathbf{2} \times \mathbf{16}_{b+1} + \mathbf{1} \times \mathbf{16}_b\,,$$

where the Dynkin label of the $2^4 = 16$ dimensional typical irreducible representation **16** of $sl(4/1)$ is given as a subscript,[9] and the superscripts on superalgebra labels (or multiplets as needed) refer to the codon positions on which the subalgebra factors act. Making the natural identification of the **1**'s with the A and U codons as suggested by the above discussion, and assigning the strong bases S to the doublet **2**, a more descriptive form of the branching rule is thus

$$\mathbf{64}_b \rightarrow \mathbf{1}_A \times \mathbf{16}_{b+2} + \mathbf{2}_S \times \mathbf{16}_{b+1} + \mathbf{1}_U \times \mathbf{16}_b$$

with the understanding that the codon groups being assigned to the symmetry adapted bases for the subalgebra representations are NAN, NSN, and NUN, respectively.

From the standpoint that redundancy in codon reading and amino acid translation, equates with degeneracy in codon assignments to irreducible representations in the group theoretical schemes, it can be suggested that this stage of code evolution would have corresponded to the existence of three proto-amino acids, or possibly three groups of amino acids with shared functional uses within each group. Alternatively, in the earliest stages the middle NSN group could have simply been unassigned to a definite amino acid coding role. Code elaboration became possible once the developing translation system had achieved a requisite degree of accuracy and reliability. Further major determinants of amino acid assignments to codons are once again the precise identity of the second codon base (thus, not just a coding role for the NSN group, but perhaps separately for NCN and NGN), but also the modulation of codon assignments afforded by the identity of the *first* codon base. Both options are plausible, and lead to different group branching scenarios.

Consider, for example, the second option. It is natural to repeat, at the level of the first base letter, the previous branching pattern, this time at the level of $sl(4/1)^{(1,3)} \rightarrow sl(2)^{(1)} \times sl(2/1)^{(3)} \times gl(1)$,

$$\mathbf{16}_{b'} \rightarrow \mathbf{1} \times \mathbf{4}_{b'+2} + \mathbf{2} \times \mathbf{4}_{b'+1} + \mathbf{1} \times \mathbf{4}_{b'}\,,$$

[9] This label is closely related to the weight of the irreducible representations of $gl(1)$ which occur in the decomposition; however these are not given explicitly.

where again the $gl(1)$ label has been omitted in favour of the related nonzero Dynkin index of the $sl(2/1)^{(3)}$ typical irreps $\mathbf{4}$ (given as a subscript). At this stage the full list of $sl(2)^{(1)} \times sl(2)^{(2)} \times sl(2/1)^{(3)}$ irreps (again omitting $gl(1)$ factors but including the nonzero Dynkin label of the $sl(2/1)$ third base letter quartets) in the decomposition of the codon representation is

$$\begin{aligned}\mathbf{64}_b \rightarrow & (\mathbf{1} \times \mathbf{1} \times \mathbf{4}_{b+2} + \mathbf{1} \times \mathbf{2} \times \mathbf{4}_{b+3} + \mathbf{1} \times \mathbf{1} \times \mathbf{4}_{b+4}) \\ & + (\mathbf{2} \times \mathbf{1} \times \mathbf{4}_{b+3} + \mathbf{2} \times \mathbf{2} \times \mathbf{4}_{b+2} + \mathbf{2} \times \mathbf{1} \times \mathbf{4}_{b+1}) \\ & + (\mathbf{1} \times \mathbf{1} \times \mathbf{4}_{b} + \mathbf{1} \times \mathbf{2} \times \mathbf{4}_{b+1} + \mathbf{1} \times \mathbf{1} \times \mathbf{4}_{b+2}) \,,\end{aligned}$$

corresponding to the codon groups

$$\begin{aligned}& (AUN + ASN + AAN) \\ & + (SUN + SSN + SAN) \\ & + (UUN + USN + UAN)\end{aligned} \tag{9.2}$$

respectively. Once again, depending on whether the codons with middle letter S are translated or unassigned (or ambiguous), this code stage suggests 5 or 6, or possibly as many as 8 or 9, active groups of mutually exchangeable proto-amino acids. This group-theoretical description closely matches the scheme for code evolution proposed by Jiménez Sanchez (1995) where the weak U, A bases are argued to be the first informative parts of primordial (three-letter) codons (with the strong bases merely providing stability for the codon-anticodon association). Van den Elsen and coworkers have argued for an intermediate expansion stage of evolution of the genetic triplet code via two types of doublet codons, namely both "prefix codons" in which both the middle and first bases are read (as in the above scenario), but also "suffix codons" involving reading of the middle and third codon bases [Wu *et al.* (2005)]. Conflicts are resolved by allowing certain amino acids to possess both prefix and suffix codons, which are still visible in the present eukaryotic code in the form of the six-fold codon degeneracies for Arg, Leu and Ser. It should be noted that the above scheme involving A, U and S in both first and second bases, which has been introduced as a partial doublet prefix codon genetic code, could also develop suffix codon reading; for example $SWN \rightarrow SWW$, and $SSN \rightarrow SSW$ wherein the third base position is read and the remaining S base positions confer stability.

The final step in this scheme is the breaking of the strong base $sl(2)$ symmetries which hold C, G bases in the first and second codon positions degenerate (or unassigned). If the second codon position is the major determinant of amino acid differentiation, then the $sl(2)^{(2)}$ breaking step

proceeds first, yielding (referring to (9.2) above)

$$\begin{gathered}\text{four } WWN \text{ quartets}\,;\\ ASN \text{ and } USN \to \text{four quartets } ACN, AGN, UCN, UGN\,;\\ \text{two unbroken octets } SUN,\ SAN\,;\\ SSN \to \text{two octets } SCN, SGN\,.\end{gathered}$$

The code has thus expanded to eight degenerate quartets and four octets, for up to twelve readable amino acids.[10] The final step is first base position symmetry breaking leading to 16 family boxes, with both first and second base positions being read. This proposal for code evolution, with or without the variation of prefix and suffix doublet codons, can be referred to as the "$UA+S$" scheme, to distinguish it from the following alternative model.

9.2.2. *sl*(6/1) *model:* $\mathfrak{Z}\mathbb{CH}$ *scheme*

A somewhat different proposal for the origin and organization of the genetic code has been developed by Jiménez-Montaño *et al.* (1996); Jiménez-Montaño (1999) under the motto "protein evolution drives the evolution of the genetic code, and vice-versa". According to this scenario, the code has evolved by sequential *full* elaboration of the second codon base letter, followed by the first (and lastly the third); however at each stage pyrimidine-purine reading occurs, before further strong-weak base reading within the Y, R types. This is argued by strictly applying a systematic criterion of code evolution via incremental, minimum change coding pathways, whereby the hierarchical order of codon-anticodon Gibbs free energy of interaction, $\mathbb{C}_2 > \mathbb{H}_2 > \mathbb{C}_1 > \mathbb{H}_1$ (followed by $\cdots > \mathbb{C}_3 > \mathbb{H}_3$), which can be established *in vitro*, is adopted to infer a temporal sequence of code expansion. This means that the *chemical type* $\mathbb{C} = \{Y, R\}$ (that is, whether bases are pyrimidines Y or purines R), and then the *hydrogen bonding* type $\mathbb{H} = \{S, W\}$ (that is, whether bases are strong, S, or weak, W) of the second, first (and finally third) codon base are successively able to be read by the evolving translation system.

A group-theoretical branching scheme reflecting this scenario would entail symmetry breaking of transformations on successively the second, first (and lastly the third) base letters, in contrast to the hierarchical $UA+S$ scheme's adoption of the partial A, U and S breaking scheme on the second

[10] In the account of Jiménez Sanchez (1995), the original code used triplet codons entirely of the WWW form, which later acquired S codons in all positions.

and first base letters before differentiation of the S bases into C, G. Thus corresponding to the chemical type Y, R, within each of which is in turn a strong and a weak base (Y includes C, U and R includes G, A respectively), each base quartet is assigned two dichotomic labels, which serve to distinguish subgroup transformations. Remarkably group-theoretical branching rules incorporating these steps are once again natural within the class of 64-dimensional typical representations of the $sl(6/1)$ superalgebra. In this scheme the required labels are eigenvalues of $gl(1)$ generators, and the relevant $sl(n'/1)$, $sl(n''/1)$ subalgebras are now successively $n' = n - 1 = 5$, $n'' = n' - 1 = 4$, rather than $n' = n - 2 = 4$, $n'' = n - 4 = 2$ as in the $UA+S$ scheme. The branching rules read finally (with the $gl(1)$'s being tagged according to whether they refer to chemical or hydrogen bonding type),

$$sl(6/1) \to sl(5/1) \times gl(1)^{\mathbb{C}_2}\,,$$

$$\mathbf{64} \to \mathbf{32}_Y + \mathbf{32}_R \cong NYN + NRN\,;$$

$$sl(5/1) \times gl(1)^{\mathbb{C}_2} \to sl(4/1)^{(1,3)} \times gl(1)^{\mathbb{H}_2} \times gl(1)^{\mathbb{C}_2}\,,$$

$$\mathbf{32}_Y \to \mathbf{16}_{Y_S} + \mathbf{16}_{Y_W}\,,\ \mathbf{32}_R \to \mathbf{16}_{R_S} + \mathbf{16}_{R_W}\,,$$

$$NYN \to NCN + NUN,\ NRN \to NGN + NAN\,.$$

This pattern is repeated for the first codon base letter giving eventually

$$sl(6/1) \to sl(2/1)^{(3)} \times gl(1)^{\mathbb{H}_1} \times gl(1)^{\mathbb{C}_1} \times gl(1)^{\mathbb{H}_2} \times gl(1)^{\mathbb{C}_2}$$

with 16 codon quartets in which the first two bases are read. This scenario can be referred to as the "3$\mathbb{CH}$" scheme.

A variant of this picture was in fact proposed earlier by Swanson (1984). That version considered code elaboration based on a $\mathbb{C}_2 > \mathbb{C}_1 > \mathbb{H}_2 > \mathbb{H}_1$ hierarchy. In the $sl(6/1)$ model, the corresponding subalgebra branching pattern would be

$$\begin{aligned} sl(6/1) &\to sl(4/1)^{(1,3)} \times sl(2)^{(3)} \times gl'(1) \\ &\to sl(4/1)^{(1,3)} \times gl(1)^{(3)} \times gl(1)' \\ &\to sl(2/1)^{(3)} \times sl(2)^{(1)} \times gl''(1) \times gl(1)^{(3)} \times gl(1)' \\ &\to sl(2/1)^{(3)} \times gl(1)^{(1)} \times gl''(1) \times gl(1)^{(3)} \times gl(1)'\,. \end{aligned}$$

However, in a quantitative study of the effect of base changes on amino acid similarity across the code (using amino acid correlation matrices from alignment methodologies), it was shown by Mac Dónaill and Manktelow

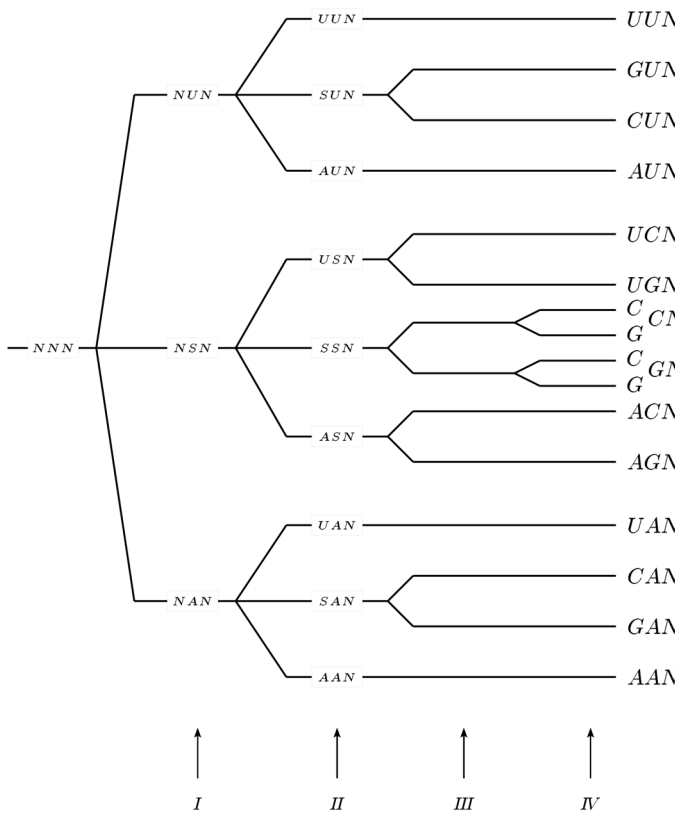


Fig. 9.3. Code evolution according to Jiménez Sanchez (1995) transcribed into a group branching scheme in the $sl(6/1)$ chain. Dynamical symmetry breaking stages: *I*: $sl^{(1,3)}(4/1)\times gl^{(2)}(2)_S\times gl^{(2)}(1)$. *II*: $sl(2/1)^{(3)}\times gl^{(1)}(2)_S\times gl^{(1)}(1)\times gl^{(2)}(2)_S\times gl^{(2)}(1)$. *III*: $sl(2/1)^{(3)}\times gl^{(1)}(2)_S\times gl^{(1)}(1)\times gl^{(2)}(1)_m\times gl^{(2)}(1)_d$. *IV*: $sl(2/1)^{(3)}\times gl^{(1)}(1)_m\times gl^{(1)}(1)_d\times gl^{(2)}(1)_m\times gl^{(2)}(1)_d$.

(2004) that this scheme is less supported than the standard $3\mathbb{CH}$ version above.

Thus far, both group-theoretical branching scenarios based on the $sl(6/1)$ scheme have arrived at the 16 codon boxes (quartets) of the standard genetic code, regarded as 4-dimensional irreps of the residual third letter $sl(2/1)^{(3)}$ dynamical symmetry to which both branching chains reduce. These are shown in Figs. 9.3 and 9.4 for the $UA{+}S$ and $3\mathbb{CH}$ schemes respectively (compare Fig. 9.3 with (Jiménez Sanchez, 1995) Table 2 and Fig. 2, and Fig. 9.4 with (Jiménez-Montaño, 1999), Figs. 1a, 1b and 1c).

The $SO(13)$ model mentioned above, would have similar counterparts because of the intimate relation between the typical irreducible representations of the $gl(n/1)$ superalgebras and the spinor representations of $SO(2n)$ or $SO(2n+1)$ groups.[11]

9.2.3. *Dynamical symmetry breaking and third base wobble*

The final stage in code evolution is the expansion of the amino acid repertoire via reading of the third codon letter. The relevant feature of the genetic code in this respect, is that the canonical Crick-Watson pairing between the codon base letters on the $mRNA$ strand, and the $tRNA$ base anticodon (recognition) letters, breaks down. Namely, the "first", 5'-3' base of the anticodon triplet (which structurally occurs at base position 34 in the so-called anticodon loop of 7 bases in each $tRNA$), admits the so-called Crick wobble pairing with respect to the third codon base, which is more flexible than canonical pairing.[12] The "degeneracy of the genetic code" as a whole, is in fact a convolution of the association between the 45 or so used anticodons and amino acids (and the 20-strong $aaRS$ enzyme system), and the wobble pairing. Indeed, pairing at the third codon position determines almost all of the degeneracy in the genetic code and, as such, is least correlated with amino acid properties. On the other hand, as will be seen in detail below, the pattern of such pairing depends upon genomic $G{+}C$ content, and also post-transcriptional modification of $tRNA$ bases; usually at bases 34 (*a.c.* position 1) and also at base 37 (downstream of *a.c.* position 3). It is reasonable to contend then that reading at this codon position is associated with the latter stages of evolution of the genetic code, the basic translation apparatus necessarily already having been established.

The viewpoint adopted here is that the dynamical symmetry description must relate to codon-anticodon binding and amino acid recognition as a whole; in the $UA+S$ scheme stereochemical or other considerations are dominant in organizing coding according to hydrophobicity; in the $3\mathbb{CH}$ scheme the free energy of formation is the major determinant of coding.

[11] In the first scenario the $UA+S$ split is natural within spinor reductions $SO(n) \to SO(n-4) \times SO(4)$, wherein a four dimensional spinor of $SO(4) \simeq SU(2) \times SU(2)$ decomposes into a direct sum $\mathbf{1}+\mathbf{1}+\mathbf{2}$ with respect to one of the $SU(2)$ factors. The second scenario is compatible with successive branchings of the form $SO(n) \to SO(n-2) \times SO(2)$ wherein a spinor representation of a certain dimension reduces to a pair of spinors of the subgroup.

[12] The explicit notation $N(34) \cdot N'(III)$ can be used to denote this anticodon-codon base (wobble) pairing, or simply $N \cdot N'$ where no confusion arises.

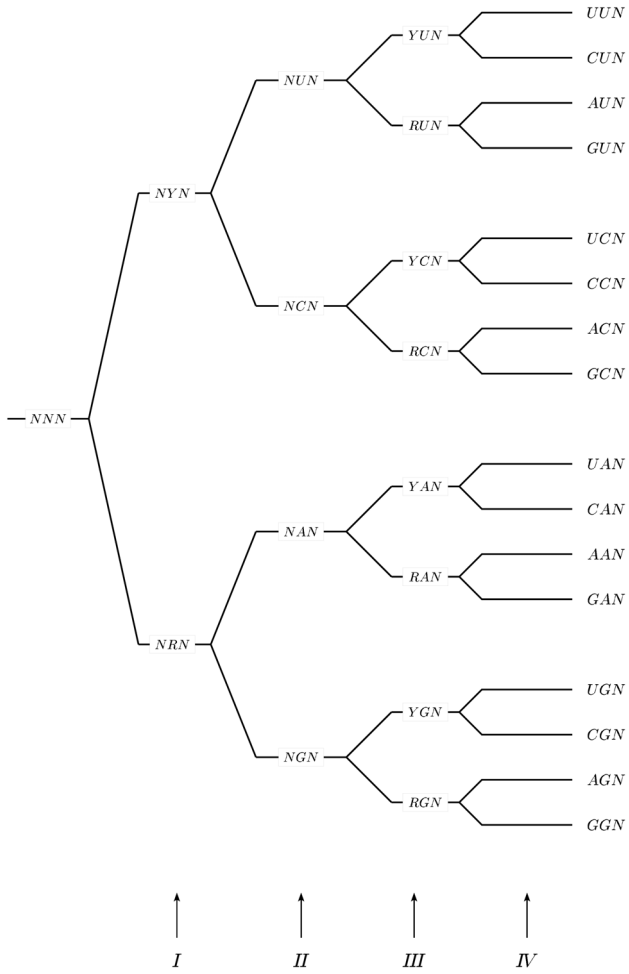


Fig. 9.4. Code evolution steps according to Jiménez-Montaño (1999) transcribed into a group branching scheme in the $sl(6/1)$ chain. Dynamical symmetry breaking stages: *I*: $sl(5/1) \times gl^{(2)}(1)_{m-d}$. *II*: $sl(4/1)^{(3,1)} \times gl^{(2)}(1)_{m-d} \times gl^{(2)}(1)_{m+d}$. *III*: $sl(3/1) \times gl^{(1)}(1)_{m-d} \times gl^{(2)}(1)_{m-d} \times gl^{(2)}(1)_{m+d}$. *IV*: $sl(2/1)^{(3)} \times gl^{(1)}(1)_{m-d} \times gl^{(1)}(1)_{m+d} \times gl^{(2)}(1)_{m-d} \times gl^{(2)}(1)_{m+d}$.

For the third codon base, attention is naturally focussed on the patterns not only of amino acid assignments within codon boxes, but also, in view of the wobble pairing, of anticodon usage.

We now take up in detail these issues of the codon-anticodon degeneracy and the wobble rules. The mitochondrial codes, believed to show similar

structural simplifications to a hypothetical ancestral code,[13] are especially simple: in each *family* box, *one tRNA* codes; Uridine $U(34)$ in the first *a.c.* position can pair with U, C, A, or G—in the case of $U \cdot A$ by canonical pairing, and in $U \cdot U$, $U \cdot C$ and $U \cdot G$ by wobble pairing. *Mixed* boxes on the other hand have *two tRNA* species; Guanine $G(34)$ recognizes U and C—via wobble pairing in $G \cdot U$ and canonical pairing in $G \cdot C$, while $U(34)$ binds A and G—again via canonical pairing in $U \cdot A$, and in $U \cdot G$ by wobble pairing. Uridine $U(34)$ in these mixed boxes is commonly prevented from misreading U and C by chemical modification (and in the family boxes, may indeed undergo different modification to *facilitate* the $U \cdot N$ wobbles).[14]

The dynamical symmetry description of code elaboration for the third codon position in the mitochondrial codes is therefore rather straightforward. Codon boxes (quartets) either lead to *family* boxes ("intact" $sl(2/1)^{(3)}$ irreps), or reduce for *mixed* boxes to two doublets of some subalgebra, $N_1N_2N \to N_1N_2Y + N_1N_2R$. It follows that the symmetry breaking at the third position is *partial* (8 family, and 8 mixed, boxes); moreover the pattern of breaking turns out to be specified completely by the identity of bases occupying the first two codon positions. We shall return to these points presently, along with a specific choice for the unbroken subalgebra.

In higher organisms, which use the "universal" genetic code (for example, the eukaryotic code), codon usage is strongly linked with genomic base content. In particular, within the open reading frames in a genome, the $G+C$ content of the third codon position correlates well with genomic $G+C$ content, in contrast to the other positions. In genomes with high $A+T$ content, $G+C$-rich codons are seldom used, and can even be deleted from the code (for example CGG in *Mycoplasma capricolum* [Andachi *et al.* (1989)]). Conversely, if $G+C$ content is high, $A+U$-rich codons become rare, and may also disappear (for example NNA within family boxes in *Micrococcus luteus* [Kano *et al.* (1991)]). In between these extremes, different *tRNA* species can "compete" for the same set of synonymous codons. Representative patterns of codon degeneracy within a box are shown in Table 9.3. The $\mathbf{2+2}$ and $\mathbf{2+1+1}$ patterns on the left-hand side of Table 9.3 are utilized in seven of the eight mixed boxes, while the $\mathbf{2+1+1}$ patterns on the right (the triplet of anticodons involving Inosine is actually $\mathbf{2+1}$ arising from $NNY + NNA$) determine seven of the family boxes.

[13]Code variations across biota have been intensively studied in recent years; see for example Osawa *et al.* (1992) for a comprehensive early review.

[14]We shall discuss further the effects of post-transcriptional modification in a quantal model of codon recognition in Sec. 9.4.

Table 9.3. Anticodon usage patterns in eukaryotes.

mixed boxes		family boxes	
codon	a.c	codon	a.c.
NNU	GNN	NNU	INN
NNC	GNN	NNC	INN
NNA	UNN	NNA	(INN, UNN)
NNG	(CNN, UNN)	NNG	(CNN, UNN)

The exceptions are boxes AUN (in which *Met* has the single codon AUG, and *Ile* is coded for by three codons AUY and AUC) and GGN (the *Gly* family box) in which these patterns are reversed. However, as emphasized already, we also need to consider how codon usage shifts with genomic base content. For A+T-rich genomes, codons NNG are selected against, resulting in the probable disappearance of anticodons CNN. In this instance, the codon/anticodon box pattern coincides with that of the mitochondrial code $\mathbf{2}+\mathbf{2}$ mixed boxes, $N_1N_2N \rightarrow N_1N_2Y + N_1N_2R$. Conversely, in G+C-rich organisms codon NNA is relatively rare, and consequently there is little need for *tRNA* species UNN: recognition of codon NNG is predominantly due to anticodon CNN. Thus, in this case there tends to be a further "breaking" of the NNR codon doublet assignment leading to $N_1N_2N \rightarrow N_1N_2Y + N_1N_2R \rightarrow N_1N_2Y + N_1N_2A + N_1N_2G$.

It remains to tie the third base reading patterns to a dynamical symmetry breaking account relating to the proposed $sl(2/1)^{(3)}$ codon quartet superalgebra. We suggest [Bashford *et al.* (1998)] that the basic pattern of $sl(2/1)^{(3)}$ breaking for the primitive and mitochondrial codes is to a $gl(1/1)^{(3)}$ superalgebra, which is further reduced to an appropriate $gl(1)^{(3)}$ label for the eukaryotic code. $gl(1/1)$ is the well-known superalgebra of supersymmetric quantum mechanics , with supercharge generators $Q^{\pm}$ satisfying $\{Q^-, Q^+\} = H$, $[F, Q^{\pm}] = \pm Q^{\pm}$ where H is the "Hamiltonian" and F (with eigenvalues $= 0, 1$) labels fermion number. Irreducible representations are generically two-dimensional, so that quartets of $sl(2/1)^{(3)}$ decompose under $gl(1/1)^{(3)}$ to two degenerate doublets as $\mathbf{4} \rightarrow \mathbf{2}+\mathbf{2}$ (the mixed box codon-antiocodon pattern). *Partial* symmetry breaking—the fact that 8 family boxes remain intact, and do not show this codon-anticodon splitting—must be attributed to the varying *strength* of this breaking across the code. The same applies to the final $\mathbf{2}+\mathbf{2} \rightarrow \mathbf{2}+\mathbf{1}+\mathbf{1}$ decomposition manifested in the eukaryotic code, which can be attributed

in turn to partial $gl(1/1)^{(3)}$ breaking, this time to the generator F of its Abelian $gl(1)^{(3)}$ subalgebra. The codon-anticodon doublet degeneracy is potentially completely lifted by the additional fermion number-dependent shift; however again this is realized only in certain of the mixed boxes for N_1N_2R, and never for N_1N_2Y.

As mentioned already, the existence of partial symmetry breaking was argued by Hornos and Hornos (1993) to support the "frozen accident" account of the structure of the genetic code (see also Sec. 9.1). In terms of dynamical symmetry breaking, appropriate breaking parameters are to be fine-tuned, so that otherwise non-degenerate codons remain degenerate, and can consistently be assigned the same amino acids. The mechanism operates similarly in our present $sl(6/1)$ scheme, except that we have been discussing codon-anticodon pairings rather than codon-amino acid assignments (which are not the same if different *tRNA*'s can be charged with the same amino acid). Moreover, we have linked the emergence of $\mathbf{2}+\mathbf{1}+\mathbf{1}$ pairing to genomic $G+C$ content, and so effectively injected an organism-dependence into the breaking patterns. Further numerical aspects of the partial breaking, and of the related issue of codon-amino acid assignments, are given in Sec. 9.3. A more refined discussion of the codon-anticodon recognition process is given in Sec. 9.4.

9.3. Visualizing the Genetic Code

The discussion of the genetic code so far has centred on qualitative aspects of its systematics. These include both longstanding trends, noticed almost as soon as the code was fully elucidated in the 1960s (Sec. 9.1), as well as more elaborate Lie symmetry and supersymmetry-based schemes (Sec. 9.2), which served to transcribe selected accounts grounded in biological understanding, into a mathematical language.

The utility of broken dynamical symmetry schemes in physics is specifically, in helping to quantify the hierarchy of symmetry and symmetry-breaking in the spectroscopy of complex quantum systems such as atoms, molecules and nuclei. Schematically, suppose that a Hamiltonian operator can be constructed as a series of the form

$$H = H_0 + H_1 + H_2 + \cdots$$

where the terms are successively "smaller" in the appropriate sense. Also, on the Hilbert space of quantum-mechanical states of the system, suppose there are operators representing the transformations of a hierarchy of

symmetry groups $G_0 \supset G_1 \supset G_2 \supset \cdots$ such that G_0 is a symmetry of (commutes with) H_0, G_1 commutes with H_1, $\cdots$, and so on. Then, by general theorems, the energy eigenfunctions of the system (the energy levels of physical states) are organized into unitary irreducible representations of the successive subgroups. The spectra of the partial Hamiltonians H_0, $H_0 + H_1$, $H_0 + H_1 + H_2$ can be labelled by these irreducible representations, each of which corresponds to states with degenerate energy levels. Moreover, as the corrections introduced become smaller, this labelling thus provides a hierarchical "symmetry breaking" scheme for understanding the structure of the system. In ideal cases the contributions to H are moreover appropriate combinations of so-called Casimir operators of the various subgroups, such that when the states are accorded their correct ancestry in terms of the descending hierarchy of subgroups and respective irreducible representations, their energies (eigenvalues of H) are the corresponding sum of Casimir eigenvalues (polynomials in the labels, or quantum numbers, of the respective representations, for example the highest weight labels).

This methodological approach has indeed been taken, with some success, for the genetic code problem in the work of Hornos and Hornos (1993). As mentioned in Sec. 9.2, the symmetry groups were taken to be a chain of subgroups of $Sp(6)$, with codons assigned to its 64-dimensional representation, with the role of the energy being played by a composite measure of codon and amino acid organization, the Grantham polarity index. An attractive feature of the argument was that although the symmetry breaking chain taken implied complete degeneracy in the generic case, the "frozen accident" visible in the instances of synonymous codon assignments in the real genetic code could be explained by particular parameter constraints between the strengths with which Casimirs belonging to the partial Hamiltonians appeared in the total Hamiltonian H.

In our work we have taken a somewhat weaker approach to quantifying the structure of the genetic code. Within the group branching scenario, it is often sufficient[15] to distinguish states within an irreducible representation of a starting group G by their so-called weights, which are labels for (one dimensional) representations of the smallest available continuous subgroup, the Cartan (maximal Abelian) subgroup. Thus a parametrization of physical properties via *fitted* polynomials in these labels, can be regarded as a kind of general proxy for the more specific approach sketched above, where a definite subgroup chain is declared, and specific Casimir operators are

[15]Technically the irreducible representation of G must have no *weight multiplicities*.

included at the outset. It is this more flexible method that we have used as an attempted confirmation of the $sl(6/1)$-based supersymmetric schemes for the structure of the genetic code in Sec. 9.2 above. It is apparent from the discussion in Sec. 9.2 that the subgroup and state labelling required is closely matched to the four base letter alphabet, three letter word lexicon of the genetic code. Mention has already been made of the fact that the nucleic acid bases stand in very symmetrical relationships with respect to each other, and it is natural to reflect this in the state labelling appropriate to the 64-dimensional codon "space" (see the introductory discussion in Sec. 9.2 above). Indeed, any *bipartite* labelling system which identifies each of the four bases A, C, G, U, extends naturally to a *composite* labelling for codons, and hence amino acids. We choose for bases two coordinates $d, m = 0, \pm 1$ as $A = (-1, 0)$, $C = (0, -1)$, $G = (0, 1)$, $U = (1, 0)$, so that codons are labelled as ordered sextuplets, $NNN = (d_1, m_1, d_2, m_2, d_3, m_3)$; for example $ACG = (-1, 0, 0, -1, 0, 1)$. Our choice of dichotomic base labels is of course equivalent to $0, 1$ binary labelling and the geometrical picture of the code as a 6 dimensional hypercube[16] as has been noted by several authors (see the discussion above). Fitting polynomial functions in these labels to code properties is furthermore compatible with *any* group labelling scheme for which the 64-dimensional codon representation is equivalent to a hypercube in weight space; as discussed earlier, candidate groups and algebras include $sl(6/1)$ but also $so(13)$, and non-simple groups such as $so(4) \times so(4) \times so(4)$. With these preliminaries it only remains to present sample genetic code (codon and or amino acid), physico-chemical or biological, data, and compare this data to polynomials in the codon labels.

Figure 9.5 gives a two-dimensional presentation of the genetic code whereby each of the m, d paired labels for each base letter are plotted or projected onto the plane. In the case of the first two base letters this occurs by showing four d_2, m_2 diamonds separated by their different d_1, m_1 coordinates; for the third base letter instead a linear rank ordering U, C, A, G of the bases is used (corresponding to a one-dimensional projection of the diamond to a line skew to the sides of the basic diamond). Remarkably, essentially this organization of the code was discussed some time ago by Siemion (1994) in connection with so-called "mutation rings", designed to present a rank ordering of codons reflecting their relative interconvertability or functional similarity (so that near neighbours in the mutation ring are also likely to be correlated in their occurrences in nucleic acid coding).

[16]The d, m labels give a **dia**gram**mon**atic **d** rather than a square orientation to the fundamental base quartet.

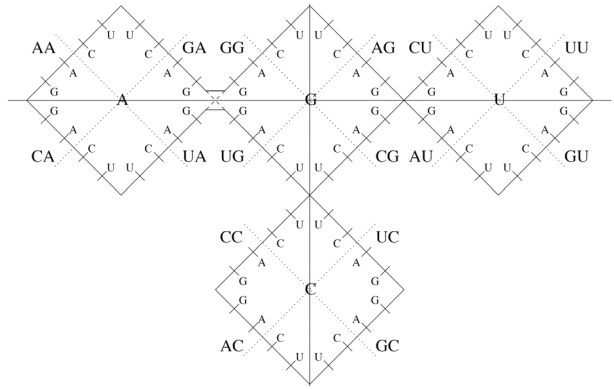


Fig. 9.5. Diamond presentation of codon labelling $NNN = (d_1,m_1,d_2,m_2,d_3,m_3)$.

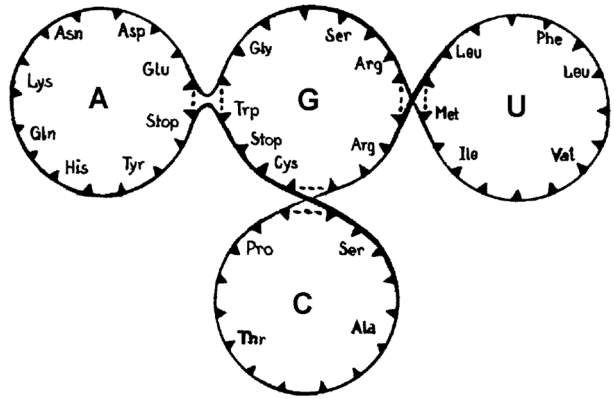


Fig. 9.6. Genetic code "mutation rings" according to Siemion. The "mutation number" $0 \leq k \leq 63$, labels the looping closed path around the main second base letter rings, with excursions into and out of the G ring starting with GAU (Asp).

Figure 9.6 shows Siemion's rings, with the linear rank ordering (related by Siemion to a "mutation number" $0 \leq k \leq 63$), following a looping closed path around the main second base letter rings with excursions into and out of the G ring starting with GAU (Asp) (compare Fig. 9.5, which has had the $G_2 = \{d_2 = 0, m_2 = 1\}$ ring shifted downwards, with Fig. 9.6).

Important quantitative indicators of coding functions are the so-called Chou-Fasman parameters, which give *log* frequency measures of the presence of each amino acid in protein tertiary structures such as β sheets and

α helices and associated turns. We have fitted several of these parameters to the codon weight labels as described above, and we present here representative fits—taken from (Bashford and Jarvis, 2000). In Figs. 9.8 and 9.9 are plotted histograms of the P^{α} and P^{β} parameters against the Siemion number, together with least-squares polynomial fits to functions $F^{\alpha}(d_1,m_1,d_2,m_2,d_3,m_3)$, $F^{\beta}(d_1,m_1,d_2,m_2,d_3,m_3)$ given by

$$\begin{aligned} F^{\alpha} &= 0.86 + 0.24d_2^2 + 0.21m_1m_2(m_2-1) - 0.02(d_3-m_3) \\ &\quad - 0.075d_2^2(d_3-m_3)\,, \\ F^{\beta} &= 1.02 + 0.26d_2 + 0.09d_1^2 - 0.19d_2(d_1-m_1) - 0.1d_1m_2(m_2-1) \\ &\quad - 0.16m_1^2m_2(m_2-1)\,, \end{aligned}$$

respectively.

In Figs. 9.7(a) to 9.7(f) measured values for a selection of further experimental parameters are plotted (without any fitting), not against Siemion number, but as histograms over the rings themselves.[17] It is clear from the fitted plots Figs. 9.8 and 9.9 and from these further plots that simple numerical fitting of the type given in (9.3) can capture the major trends in such genetic code data. For example in Bashford and Jarvis (2000), it was found that for the Grantham polarity itself, the important terms were simply d_2 (second codon base hydrophobicity) and $d_3 - m_3$ (third base chemical Y/R type) with appropriate coefficients, modulo some first base dependence. Similar numerical considerations also support the "partial symmetry breaking" scenarios. For example, the polynomial

$$(d_1d_2)^2 + \frac{1}{2}\left(d_1^2m_2^2(1+m_2) + m_1^2d_2^2(1-d_2)\right) \tag{9.3}$$

takes the value 1 on WWN, WGN and SAN and 0 on SSN, WCN and SUN and so serves to "turn on" the partial codon-anticodon $sl(2/1)^{(3)}$ breaking leading to mixed versus family boxes (the key parameter underlying Rumer's rule [Rumer (1966)]). Finally it can be noted that the difference between codon-anticodon pairing degeneracy and codon-amino acid assignment synonymy also has numerical support: periodicity or symmetry patterns of codon-amino acid properties over the Siemion rings is consistent with repeated amino acid assignments (belonging to different codon boxes) occurring on certain symmetrical ring locations—see Bashford and Jarvis (2000); Siemion (1994).

[17] Recently entire databases of physico-chemical and biological codon and amino acid properties have become available; see for example Kawashima and Kanehisa (2000).

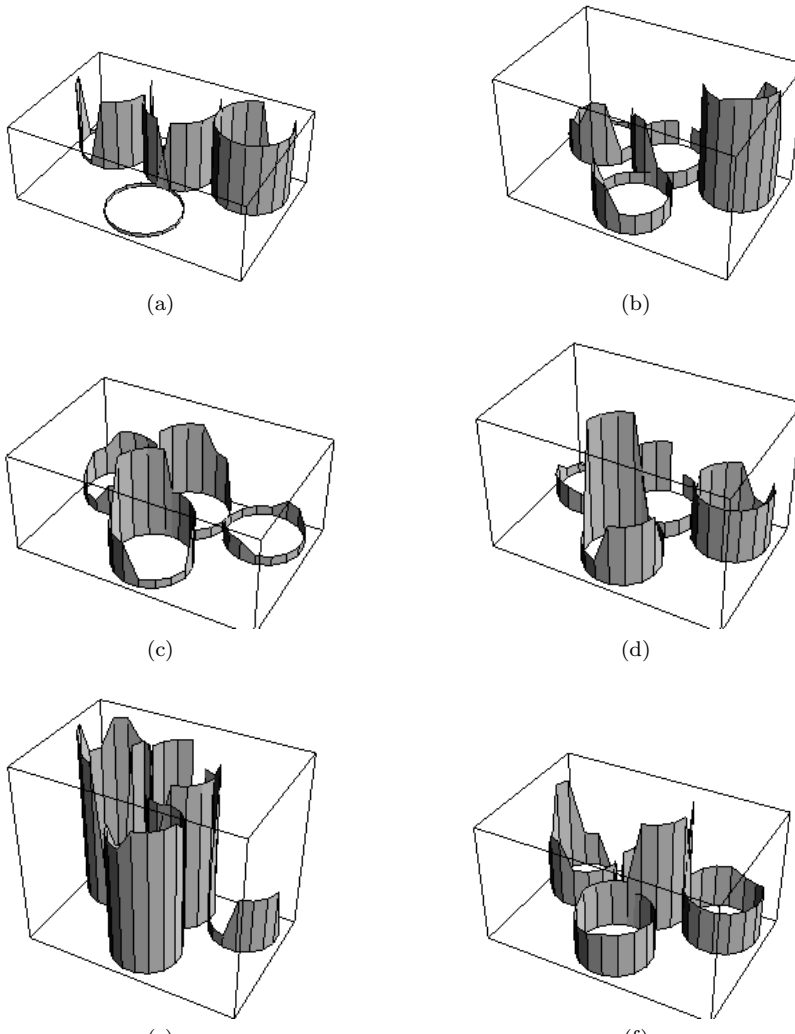


Fig. 9.7. Histograms of physicochemical parameters superimposed upon Siemion's rings: (a) *aaRS* synthetase class I=0, II=1; Chou-Fasman parameters relating (b) to beta sheets and (c) coils [Jiang *et al.* (1998)]; (d) *pKb* (a measure of codon polarity); [Sober (1970)] (e) hydrophobicity [Bull and Breese (1974)] and (f) isoelectronic potential [Sober (1970)].

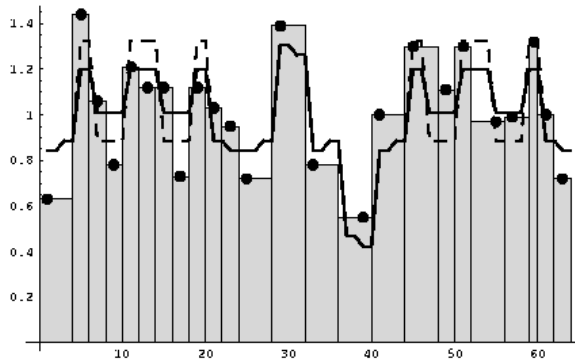


Fig. 9.8. P^{α} *versus* k. Histogram: data; solid and dashed curves: polynomial fits (four parameters); dots: preferred codon positions.

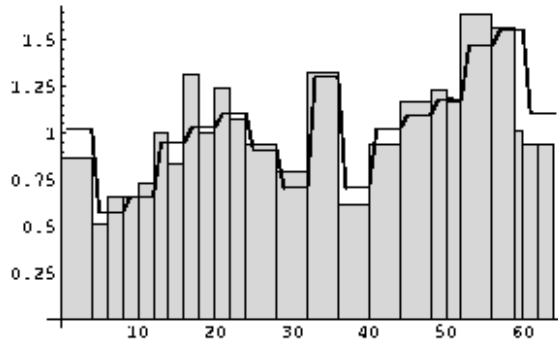


Fig. 9.9. P^{β} *versus* k. Histogram: data; solid curve: polynomial least squares fit (five parameters).

9.4. Quantum Aspects of Codon Recognition

In this section we present the proposition that the codon-anticodon recognition process has an initial, quantum-mechanical step. Previously, Patel (2001a,b) discussed the genetic code in terms of quantum information processing, however despite the striking numerical predictions stemming from Grover's search algorithm, the model required some unlikely properties of enzymes.

Our basic assertion rests on the observation that the first anticodon base (labelled henceforth as $N(34)$) is conformationally flexible, whereas *a.c.* sites 35, 36 are constrained by the geometry of the *tRNA* anticodon loop (in addition to modifications to base 37). In an unpaired *tRNA*, $N(34)$ could therefore be expected to be in a superposition of conformational states. In proximity to the complementary codon base, one such state becomes increasingly favoured, facilitating the "collapse" to the classical, paired state. Thus, in contrast to the Patel picture, the superposition of nucleobase states occurs at a structural, rather than chemical level. There is still the issue of thermal effects; however in this regard, we note that aminoacyl-*tRNA* is transported to the ribosome by elongation factor (*EF-Tu*). There are thus two distinct *tRNA*-protein environments, in either of which quantum coherence could be maintained.

9.4.1. *N*(34) *conformational symmetry*

In order to develop this quantal hypothesis it is necessary to first discuss nucleobase conformational states. The RNA oligomer is formed of repeated ribonucleotide-phosphate units, one of which is sketched in Fig. 9.10(a). The conformer degrees of freedom fall into three broad categories—for a full discussion see Yokoyama and Nishimura (1995). First are the torsion angles between ribonucleotide and phosphate groups: there are respectively three C4'-C5' (*gg*, *gt* and *tg*) and two C3'-O3' ($G^{\pm}$) bond rotamers. Secondly there is a twofold degree of freedom (*anti/syn*) describing the relative orientation of the base to the ribose ring. Only R-type bases can form two H-bonds (commonly argued to be the minimum required for recognition) in the *syn* conformation, however such $R \cdot R$ pairings are not observed *in vivo* [Yokoyama and Nishimura (1995)]. Finally there is a nonplanar deformation of the ribose ring (Figure 9.10(b)), commonly described by the pseudorotation parameter τ. Typically one of two conformers: C2'-*endo* ($\tau \simeq 180°$) or C3'-*endo* ($\tau \simeq 0°$) is favoured, as sketched in Fig. 9.10(b). Note however that other states, such as O4'-*exo*, may also become favourable under special circumstances. By correlating these degrees of freedom with stereochemical considerations arising from linking nucleobase units, it is possible to identify likely, low-energy conformer states. For example, according to Altona and Sundralingam (1972), for mononucleosides in the solid state favoured low-energy conformers of R and Y bases can be summarized as in Table 9.4. Any extrapolation to duplex RNA is likely to restrict the number of favourable states even further.

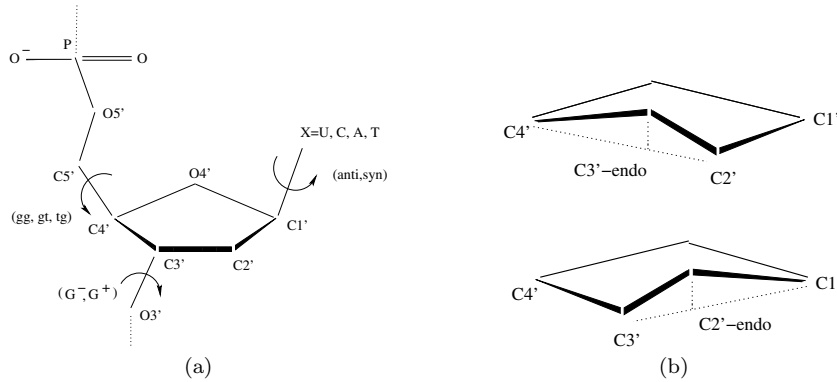


Fig. 9.10. (a) RNA backbone showing rotamer degrees of freedom. (b) Preferred ribose buckling conformations in A-form RNA.

Table 9.4. Mononucleoside conformations.

Base	Conformer	Rotamer[a]	States
R	C2'-*endo*	$\begin{pmatrix}\text{syn}\\ \text{anti}\end{pmatrix} \times \begin{pmatrix} gg \\ gt \end{pmatrix}$	4
R	C3'-*endo*	$(\text{anti}) \times \begin{pmatrix} gg \\ gt \end{pmatrix}$	2
Y	C3'-*endo*	$(\text{anti}) \times (gg)$	1
Y	C2'-*endo*	$(\text{anti}) \times \begin{pmatrix} gg \\ gt \\ tg \end{pmatrix}$	3

[a] Rotamer states $G^{\pm}$ have been neglected.

For example, the above classification is *modulo* $G^{\pm}$ rotamer states. Within a duplex the combination of G^{-} and C2'-*endo* ribose places an oxygen (O2') group in close proximity to a (backbone) P unit, with the resulting repulsion making such conformers highly unfavourable. In fact (C3'-*endo*, G^{-}) and (C2'-*endo*, G^{+}) are the stable combinations [Yokoyama and Nishimura (1995)] of these degrees of freedom. Additional constraints upon allowable states may arise since the binding occurs with the codon as a ribosomal substrate, rather than in solution. To date only R_{C3} and Y_{C2}, Y_{C3} conformers have been observed *in vivo* [Takai (2006)] and on these grounds we may neglect the R_{C2} states in a first approximation.

From the rules in Table 9.4 it is easy to see how anticodon GNN might accommodate codons NNC and NNU: $G(34)$ is predominantly in the

C3'-*endo* form. The WC pairing geometry ($G \cdot C$) requires the *gg* rotamer, while $G \cdot U$ requires a Guanine deformation towards the major groove, possibly facilitated by transition to the *gt* form. In the present picture the flexible $G(34)$ base would be in a superposition of conformer states, until it encounters the third codon base, whereupon it is required to collapse to either an optimal or suboptimal state (in the contexts of $G \cdot C$ and $G \cdot U$ respectively).

The case of $U(34)$ is more complex. From the rules above, one identifies the $U_{C3}(34)$ *gg* singlet, which participates in WC pairing, and a triplet of U_{C2} rotamers. Empirical evidence strongly suggests $U \cdot G$ and $U \cdot U$ wobble pairs occur in the C2'-*endo* form, hence can be placed in the triplet. However little is known about the $U \cdot C$ pair. Note that $U \cdot Y$ mismatches are physically impossible in the C3'-*endo* form; on the other hand the C2'-*endo* conformer theoretically suffers from steric hindrance. Other proposals for the $U \cdot C$ pairing geometry include water-mediated H-bonds [Agris (2004)] and protonation of C or, possibly a different ribose conformer. Based upon current knowledge, the $U \cdot C$ pair is not inconsistent as the third member of the U_{C2} triplet. Uridine is unique amongst the bases, in that the C2'-*endo* and C3'- *endo* forms are almost equally favoured: ΔG^* as defined in Fig. 9.11(b) is of the order of -0.1 kcal mol^{-1} [Yokoyama *et al.* (1985)] and it therefore readily forms wobble pairs. However $U(34)$ is almost invariably modified post-transcriptionally, presumably to enhance recognition fidelity in one of several ways. The 5-hydroxyuridine derivatives[18] (xo$^5U^*$) almost always participate in 4-way wobbles [Takai (2006)]. This modification shifts the pseudorotation double well in Fig. 9.11(a) in favour of the C2-*endo* form ($\Delta G^* = 0.7$ kcal mol^{-1}), thereby enhancing recognition of the $U \cdot U$, $U \cdot G$ (and presumably $U \cdot C$) wobble pairs. Conversely, 5-methyl-2-thio-uridine derivatives (m^{5}s$^2U^*$) strongly stabilize the C3' form ($\Delta G^* = -1.1$ kcal mol^{-1}) [Takai and Yokoyama (2003)]. These modifications appear in the split boxes, where misreading of U- and C- ending codons would be potentially lethal. Note that such misreadings still occur, albeit several orders of magnitude less frequently than the "correct" $G \cdot C$ and $G \cdot U$ pairings [Inagaki *et al.* (1995)].

9.4.2. *Dynamical symmetry breaking and third base wobble*

In the "modified wobble hypothesis", [Agris (1991, 2004)] patterns of nucleotide modification are proposed to modify anticodon loop dynamics so

[18]The "*" superscript denotes possible further modification.

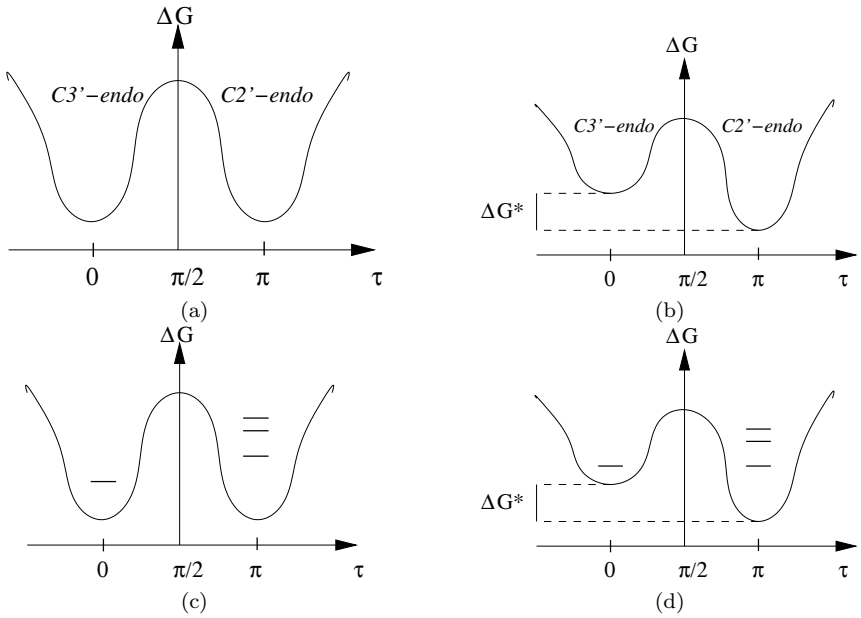


Fig. 9.11. (a) Sketch of Uridine ribose pseudorotation potential, showing equally stable C2'- and C3'-*endo* conformers. (b) Effect of xo^5 modification to Uridine on potential. (c) Same as (a) but with hypothetical (conformer) bound states imposed. (d) Same as (b) showing hypothetical bound states.

as to be compatible with the codon-ribosome complex. In addition to the effects of post-transcriptional modification upon $N(34)$ conformations, as discussed above, bases 32 and 38 (which demarcate the anticodon loop) are commonly modified to enhance H-bonding, thereby facilitating an "open" loop. Further, modifications to $R(37)$ (just downstream of *a.c.* position 3), the so-called "universal purine", generally correlate with the base content of position 36.

Structural studies lend support to kinetic models of codon reading [Takai (2006); Ninio (2006)] describing multiple-stage processes. Initial contacts between ribosome and canonical A-form duplex RNA (for pairs $N(35) \cdot N(II)$ and $N(36) \cdot N(I)$) have been observed to promote conformational changes [Ogle *et al.* (2003)] in the ribosome which facilitate the release of the amino acid from *tRNA*. In fact the conservation of A-form *structure* is more important than stability conferred by base-pairing. For example, thermodynamically, the difference between contributions of canonical, $U(36) \cdot A(I)$, and a potential first codon position wobble, $U(36) \cdot G(I)$,

pairs is of the order of 10%. Yet when bound to the ribosome, reading of the "correct" Watson-Crick pair proceeds 3-4 orders of magnitude faster [Kurland *et al.* (1996)].

With the codon bound at the ribosomal A-site, it is reasonable to assume that these three bases are intrinsically rigid, and amenable to A-form duplex formation. Moreover, it can be argued [Lim and Curran (2001)] that anticodon nucleotides 35, 36 are inflexible, whether by way of proximity to the 5' end of the anticodon loop, or due to $R(37)$ modifications. With these considerations it is straightforward to envisage a simple, lattice Hamiltonian containing three sites with one, corresponding to position (34), carrying an internal conformer degree of freedom which feels a double-well potential of the sort sketched in Fig. 9.11(a) above.

Using the "low energy" conformer states of Table 9.4 (and tentatively assuming the $\mathrm{xo}^5U^*(34)$ base adopts the C2'-*endo tg* form in the context of $U(34)\cdot C(III)$) we can write down correlated anticodon states associated with third letter codon recognition. In the mitochondrial code, for example, in the mixed boxes the possible states for the first anticodon letter are

$$\begin{aligned} G(34) &\rightarrow (|C3'>\otimes|G^->\otimes(\alpha_1|gg>+\alpha_2|gt>)\,, \\ \mathrm{m}^5\mathrm{s}^2U^*(34) &\rightarrow \beta_1|C3'>\otimes|G^->\otimes|gg>+\beta_2|C2'>\otimes|G^+>\otimes|gg>\,, \end{aligned}$$

while the family boxes have

$$\begin{aligned} \mathrm{xo}^5U^*(34) \rightarrow \gamma_1|C3'>\otimes|G^->\otimes|gg> \\ +|C2'>\otimes|G^+>\otimes(\gamma_2|gg>+\gamma_3|gt>+\gamma_4|tg>)\,. \end{aligned}$$

In their model of permitted wobble-rules, Lim and Curran (2001) predicted that, given certain wobble pairs $U(34)\cdot N(III)$, a second position wobble, $U(35)\cdot G(II)$ was not forbidden, but prevented from occurring by the use of anticodons GNN. This kind of observation naturally connects the above, quantum picture of codon reading with our original discussion of broken dynamical symmetries. Second position wobbles are likely to be suppressed by the local rigidity of the 7-member anticodon loop, in addition to ribosomal contacts with the bound codon-anticodon complex. It is therefore plausible that higher, dynamically-broken symmetries could describe some ancestral translation system with simpler structural features (and lower fidelity). In this manner the pattern of dynamical symmetry breaking may be indicative of the evolution of the translation apparatus (see, for example, Seligmann and Amzallag (2002); Poole *et al.* (1996); Beuning and Musier Forsyth (1999)).

The possibility of a graded symmetry underlying the scenario just described is left open. Whenever a 4-way wobble ($xo^5U(34)^*$) is present, the bound states described in Fig. 9.11(d) are in one-to-one correspondence with the "physical" codon-anticodon reading complexes. In a mixed box (or indeed in any eukaryotic box) multiple *tRNA* species exist, and several analogues of Fig. 9.11(d) are required, with the lowest-lying states of each comprising the set of reading complexes. One possibility is to postulate that certain kinds of pairing geometry have even or odd grading, the motivation being the $gl(1/1)$ dynamical symmetry analogue of supersymmetric quantum mechanics, whereby an even Watson-Crick (ground) state would lie below an odd (excited) wobble state in the case of $U(34) \cdot R(III)$ or $G(34) \cdot Y(III)$ pairs. The following, speculative grading of pairs

$$\{G \cdot C, C \cdot G, A \cdot U, U \cdot A, U \cdot C, I \cdot U\} \text{ even}$$
$$\{G \cdot U, U \cdot G, U \cdot U, I \cdot C, U \cdot C, I \cdot A\} \text{ odd}$$

within the VMC and EC is compatible with the supermultiplet structure described previously in Sec. 9.2.

Finally we wish to emphasize the following point: the differences in codon-anticodon *binding energies* are several orders of magnitude less than differences in codon *reading rates*. The connection with the "spectroscopic" theme of earlier sections does not lie directly within the bound states sketched in the potentials of Fig. 9.11(c)-(d), which are indicative of only the first stage of a multi-step kinetic pathway. Rather the "spectrum", if there is one, is in terms of *total* reading reaction rates, analogously to the "potentiation" concept of Takai (2006).

9.5. Conclusions

Regularities inherent in the genetic code "alphabets" allow discussion of codon-amino acid relationships to be abstracted from a biochemical setting to a mathematical/logical one. In this review we have attempted to present insights into the form (and possible evolution) of the genetic code, borrowing group theory concepts from spectroscopy. In Sec. 9.2 an argument for an evolutionary role of continuous and/or graded symmetries was made, in comparison with different models in the (biological) literature. Section 9.3 provided some numerical support for this view, via fits of physico-chemical properties of amino acids to those of codons. Finally in Sec. 9.4 we proposed a possible role for quantum processes in codon reading. Our hope is

that an eventual, dynamical code model will bear out the preliminary steps taken here in this direction.

Acknowledgements

This research was partly funded by Australian Research Council grant DP0344996. Collaboration with Ioannis Tsohantjis in earlier stages of this work is also acknowledged. PDJ thanks I. Z. Siemion and his group at Wrocław for hospitality and useful discussions. JDB wishes to thank K. Takai for helpful discussions. The assistance of Elizabeth Chelkowska in formatting the 3D plots of genetic code data is gratefully acknowledged.

References

Agris, P. (1991). Wobble position modified nucleosides evolved to select transfer RNA codon recognition: a modified wobble hypothesis, *Biochimie* **73**, pp. 1345–1349.

Agris, P. (2004). Decoding the genome: a modified view, *Nucleic Acids Research* **32**, pp. 223–238.

Altona, C., and Sundralingam, M. (1972). Conformational analysis of the sugar ring in nucleotides and nucleosides: a new description using the concept of pseudorotation, *Journal of the American Chemical Society* **94**, pp. 8205–8212.

Andachi, Y., Yamao, F., Muto, A., and Osawa, S. (1989). Codon recognition patterns as deduced from sequences of the complete set of transfer RNA species in *mycoplasma capricolum*: resemblance to mitochondria, *Journal of Molecular Biology* **209**, pp. 37–54.

Bashford, J., and Jarvis, P. (2000). The genetic code as a periodic table: algebraic aspects, *BioSystems* **57**, pp. 147–161.

Bashford, J., Tsohantjis, I., and Jarvis, P. (1997). Codon and nucleotide assignments in a supersymmetric model of the genetic code, *Physics Letters A* **233**, pp. 481–488.

Bashford, J., Tsohantjis, I., and Jarvis, P. (1998). A supersymmetric model for the origin of the genetic code, *Proceedings of the National Academy of Sciences*, **95**, pp. 987–992.

Baumann, U., and Oro, J. (1993). Three stages in the evolution of the genetic code, *BioSystems* **29**, pp. 133–141.

Beuning, P., and Musier Forsyth, K. (1999). Transfer RNA recognition by aminoacyl-tRNA synthetases, *Biopolymers* **52**, pp. 1–28.

Biro, J., Benyó, B., Szlávecz, Á., Fördös, G., Micsik, T., and Benyó, Z. (2003). A common periodic table for codons and amino acids, *Biochemical and Biophysical Research Communications* **306**, pp. 408–415.

Bock, A., Forchhammer, K., Heider, J., Leinfelder, W., Sawers, G., Veprek, B., and Zinoni, F. (1991). Selenocysteine: the 21st amino acid, *Molecular Microbiology* **5**, pp. 515–520.

Bull, H., and Breese, K. (1974). Surface tension of amino acid solutions: a hydrophobicity scale of the amino acid residues, *Archives of Biochemistry and Biophysics* **161**, pp. 665–670.

Cavalcanti, A., Leite, E., Neto, B., and Ferreira, R. (2004). On the classes of aminoacyl-tRNA synthetases, aminoacids and the genetic code, *Origins of Life and Evolution of the Biosphere* **34**, pp. 407–420.

Chechetkin, V. (2006). Genetic code from tRNA point of view, *Journal of Theoretical Biology* **242**, pp. 922–934.

Crick, F. (1966). Codon-anticodon pairing: the wobble hypothesis, *Journal of Molecular Biology* **19**, pp. 548–555.

Crick, F. (1968). The origin of the genetic code, *Journal of Molecular Biology* **38**, pp. 367–379.

Di Giulio, M. (2003). The early phases of the genetic code origin: conjectures on the evolution of coded catalysis, *Origins of Life and Evolution of the Biosphere* **33**, pp. 479–489.

Eriani, G., Delarue, M., Poch, O., Gangloff, J., and Moras, D. (1990). Partition of tRNA synthetases into two classes based on mutually exclusive sets of sequence motifs, *Nature* **347**, pp. 203–206.

Fabrega, C., Farrow, M., Mukhopadhyay, B., de Crecy-Lagard, V., Ortiz, A., and Schimmel, P. (2001). An aminoacyl tRNA synthetase whose sequence fits into neither of the two known classes, *Nature* **411**, pp. 110–114.

Forger, M., Hornos, Y., and Hornos, J. (1997). Global aspects in the algebraic approach to the genetic code, *Physical Review E—Statistical Physics* **56**, 6, pp. 7078–7082.

Forger, M., and Sachse, S. (2000a). Lie superalgebras and the multiplet structure of the genetic code. I. Codon representations, *Journal of Mathematical Physics* **41**, 8, pp. 5407–5422.

Forger, M., and Sachse, S. (2000b). Lie superalgebras and the multiplet structure of the genetic code. II. Branching schemes, *Journal of Mathematical Physics* **41**, 8, pp. 5423–5444.

Frappat, L., Sciarrino, A., and Sorba, P. (2001). Crystalizing the genetic code, *Journal of Biological Physics* **27**, 1, pp. 1–34.

Frappat, L., Sorba, P., and Sciarrino, A. (1998). A crystal base for the genetic code, *Physics Letters A* **250**, 1-3, pp. 214–221.

Freeland, S., Wu, T., and Keulmann, N. (2003). The case for an error minimising standard genetic code, *Origins of Life and Evolution of the Biosphere* **33**, pp. 457–477.

Gamow, G. (1954). Possible relation between deoxyribonucleic acid and protein structures, *Nature* **173**, p. 318, 13 February 1954.

Grover, L. (1997). Quantum mechanics helps in searching for a needle in a haystack, *Physical Review Letters* **79**, 2, p. 325, quant-ph/9706033.

Hornos, J., and Hornos, Y. (1993). Algebraic model for the evolution of the genetic code, *Phys. Rev. Lett.* **71**, 26, pp. 4401–4404.

Hornos, J. E. M., Hornos, Y. M. M., and Forger, M. (1999). Symmetry and symmetry breaking: an algebraic approach to the genetic code, *International Journal of Modern Physics B* **13**, 23, pp. 2795–2885.

Inagaki, Y., Kojima, A., Bessho, Y., Hori, H., Oham, T., and Osawa, S. (1995). Translation of synonymous codons in family boxes by *mycoplasma capricolum* tRNAs with unmodified Uridine or Adenosine at the first anticodon position, *Journal of Molecular Biology* **251**, pp. 486–492.

Jiang, B., Gou, T., Peng, L.-W., and Sun, Z.-R. (1998). Folding type-specific secondary structure propensities of amino acids, derived from α-helical, β-sheet, α/β, and $\alpha+\beta$ proteins of known structures, *Biopolymers* **45**, pp. 35–49.

Jiménez-Montaño, M. A. (1999). Protein evolution drives the evolution of the genetic code and vice versa, *Biosystems* **54**, pp. 47–64.

Jiménez-Montaño, M. A., de la Mora Basánez, C. R., and Pöschel, T. (1996). The hypercube structure of the genetic code explains conservative and non-conservative amino acid substitutions *in vivo* and *in vitro*, *BioSystems* **39**, pp. 117–125.

Jiménez Sanchez, A. (1995). On the origin and evolution of the genetic code, *Journal of Molecular Evolution* **41**, pp. 712–716.

Kano, A., Andachi, Y., Ohama, T., and Osawa, S. (1991). Novel anticodon composition of transfer RNAs in *micrococcus luteus*, a bacterium with a high GC genomic content: correlation with codon usage, *Journal of Molecular Biology* **221**, pp. 387–401.

Kawashima, S., and Kanehisa, M. (2000). AAindex: Amino acid index database. *Nucleic Acids Research* **28**, p. 374, `http://www.genome.ad.jp/dbget/`.

Kent, R. D., Schlesinger, M., and Wybourne, B. G. (1998). On algebraic approaches to the genetic code, *Canadian J Phys* **76**, pp. 445–52.

Knapp, M. J., and Klinman, J. P. (2002). Environmentally coupled hydrogen tunneling: linking catalysis to dynamics, *European Journal of Biochemistry* **269**, pp. 3113–3121.

Kurland, C., Hughes, D., and Ehrenberg, M. (1996). Limitations of translational accuracy. In *Escherichia coli and Salmonella typhimurium: Cellular and Molecular Biology.* Volume I (F.C. Neidhart *et al.* eds.) (American Society for Microbiology Press).

Lim, V., and Curran, J. (2001). Analysis of codon :anticodon interactions within the ribosome provides new insights into codon reading and the genetic code structure, *RNA* **7**, pp. 942–957.

Mac Dónaill, D. (2003). Why nature chose A,C,G and U/T: an error-coding perspective of nucleotide alphabet composition, *Origins of Life and Evolution of the Biosphere* **33**, pp. 433–455.

Mac Dónaill, D., and Manktelow, M. (2004). Molecular informatics: quantifying information patterns in the genetic code, *Molecular Simulation* **30**, 5, pp. 267–272.

Négadi, T. (2003). Rumer's transformation, in biology, as the negation, in classical logic, *International Journal of Quantum Chemistry* **94**, pp. 65–74.

Nieselt Struwe, K., and Wills, P. (1997). The emergence of genetic coding in physical systems, *Journal of Theoretical Biology* **187**, pp. 1–14.

Ninio, J. (2006). Multiple stages in codon-anticodon: double-trigger mechanisms and geometric constraints, *Biochimie* **88**, pp. 963–992.

Ogle, J., Carter, A., and Ramakrishnan, V. (2003). Insights into the decoding mechanism from recent ribosome structures, *Trends in Biochemical Sciences* **28**, pp. 259–266.

Osawa, S., Jukes, T. H., Watanabe, K., and Muto, A. (1992). Recent evidence for evolution of the genetic code, *Microbiological Reviews* **56**, pp. 229–264.

Patel, A. (2001a). Quantum algorithms and the genetic code, *Pramana - Journal of Physics* **56**, 2-3, pp. 367–381, `arXiv:quant-ph/0002037`.

Patel, A. (2001b). Testing quantum dynamics in genetic information processing, *Journal of Genetics* **80**, 1, pp. 39–43.

Patel, A. (2001c). Why genetic information processing could have a quantum basis, *Journal of Biosciences* **26**, 2, pp. 145–151.

Patel, A. (2005). The triplet genetic code had a doublet predecessor, *Journal of Theoretical Biology* **233**, 4, pp. 527–532, `arXiv:q-bioGN/0403036`.

Poole, A., Jeffares D. C., and Penny, D. (1996). The path from the RNA world, *Journal of Molecular Evolution* **46**, pp. 1–17.

Ronneberg, T., Landweber, L., and Freeland, S. (2000). Testing a biosynthetic theory of the genetic code: fact or artifact? *Proceedings of the National Academy of Sciences, USA* **97**, pp. 13690–13695.

Rumer, Y. (1966). Systematization of the codons of genetic code, *Translated from Doklady Akademi Nauk SSSR* **167**, pp. 1393–1394.

Saenger, W. (1984). *Principles of Nucleic Acid Structure* (Springer-Verlag, New York).

Seligmann, H., and Amzallag, G. (2002). Chemical interactions between amino acid and rna: multiplicity of the levels of specificity explains origin of the genetic code, *Naturwissenschaften* **89**, pp. 542–551.

Shabalina, S., Ogurtsov, A., and Spiridonov, N. (2006). A periodic table of mRNA secondary structure created by the genetic code, *Nucleic Acids Research* **34**, pp. 2428–2437.

Shapira, D., Shimoni, Y., and Biham, O. (2005). Algebraic analysis of quantum search with pure and mixed states, *Physical Review A* **71**, 4, pp. 1–8.

Siemion, I. (1994). The regularity of changes of Chou-Fasman parameters within the genetic code, *BioSystems* **32**, pp. 25–35.

Sober, H. E. (1970). *C. R. C. Handbook of Biochemistry : Selected Data for Molecular Biology*, 2nd edition (Chemical Rubber Co, Cleveland).

Srinivasan, G., James, C. M., and Krzycki, J. A. (2002). Pyrrolysine encoded by UAG in Archaea: charging of a UAG-decoding specialized tRNA, *Science* **296**, pp. 1459–1462.

Swanson, R. (1984). A unifying concept for the amino acid code, *Bull Math Biol* **46**, p. 187.

Szathmáry, E. (1999). The origin of the genetic code: amino acids as cofactors in an RNA world, *Trends in Genetics* **15**, pp. 223–229.

Takai, K. (2006). Classification of the possible pairs between the first anticodon and the third codon positions based on a simple model assuming two geometries with which the pair effectively potentiates the decoding complex, *Journal of Theoretical Biology* **242**, pp. 564–580.

Takai, K., and Yokoyama, S. (2003). Roles of 5'-substituents of tRNA wobble Uridines in the recognition of purine-ending codons, *Nucleic Acids Resarch* **31**, pp. 6383–6391.

Weber, A., and Lacey, J. (1978). Genetic code correlations: amino acids and their anticodon nucleotides, *Journal of Molecular Evolution* **11**, pp. 199–210.

Weberndorfer, G., Hofacker, I. L., and Stadler, P. F. (2003). On the evolution of primitive genetic code, *Origins of Life and Evolution of the Biosphere* **33**, pp. 491–514.

Woese, C., Dugre, D., Saxinger, W., and Dugre, S. (1966). The molecular basis for the genetic code, *Proceedings of the National Academy of Sciences*, **55**, pp. 966–974.

Wong, J. (1976). The evolution of a universal genetic code, *Proceedings of the National Academy of Sciences*, **73**, 7, pp. 2336–2340.

Wu, H.L., Bagby, S., and van den Elsen, J. M. (2005). Evolution of the genetic triplet code via two types of doublet codons, *Journal of Molecular Evolution* **61**, pp. 54–64.

Yang, C. (2005). On the structural regularity in nucleobases and amino acids and relationship to the origin and evolution of the genetic code, *Origins of Life and Evolution of Biosphere* **35**, 3, pp. 275–295.

Yokoyama, S., and Nishimura, S. (1995). Modified nucleosides and codon recognition, in D. Söll and U. RajBhandary (eds.), *tRNA: Structure, Biosynthesis and Function* (American Society for Microbiology, Washington DC), pp. 207–223.

Yokoyama, S., Watanabe, T., Murao, K., Ishikura, H., Yamaizumi, Z., Nishimura, S., and Miyazawa, T. (1985). Molecular mechanisms of codon recognition by tRNA species with modified Uridine in the first position of the anticodon, *Proceedings of the National Academy of Sciences*, **82**, pp. 4905–4909.

About the authors

Jim Bashford is presently an ice sheet data analyst at the Australian Government Antarctic Division. He graduated with a PhD in theoretical physics from the University of Adelaide in 2003, under Anthony W. Thomas. Recent research interests have included modelling of codon-amino acid degeneracy, oligomer thermodynamics, nonlinear models of DNA dynamics and phylogenetic entanglement.

Peter Jarvis obtained his PhD from Imperial College, London, 1976, under Robert Delbourgo. He is presently at the School of Mathematics and Physics, University of Tasmania. His main interests are in algebraic structures in mathematical physics and their applications, especially combinatorial Hopf algebras in integrable systems and quantum field theory. In applications of group theory to physical problems, aside from the work on supersymmetry in the genetic code, recent papers have included applications of classical invariant theory to problems of quantum physics (entanglement measures for mixed state systems), and also to phylogenetic reconstruction (entanglement measures, including distance measures, for taxonomic pattern frequencies).

Chapter 10

Towards Understanding the Origin of Genetic Languages

Apoorva D. Patel

"...four and twenty blackbirds baked in a pie ..."

Molecular biology is a nanotechnology that works—it has worked for billions of years and in an amazing variety of circumstances. At its core is a system for acquiring, processing and communicating information that is universal, from viruses and bacteria to human beings. Advances in genetics and experience in designing computers have taken us to a stage where we can understand the optimization principles at the root of this system, from the availability of basic building blocks to the execution of tasks. The languages of DNA and proteins are argued to be the optimal solutions to the information processing tasks they carry out. The analysis also suggests simpler predecessors to these languages, and provides fascinating clues about their origin. Obviously, a comprehensive unraveling of the puzzle of life would have a lot to say about what we may design or convert ourselves into.

10.1. The Meaning of It All

I am going to write about some of the defining characteristics of life. Philosophical issues always arise in discussions regarding life, and I cannot avoid that. But let me state at the outset that such issues are not the purpose of my presentation. I am going to look at life as an exercise in information theory, and extend the analysis as far as possible.

Received April 13, 2007

Let me begin with the textbook answer to the question made famous by Schrödinger (1944): *What is life?* Life is fundamentally a non-equilibrium process, commonly characterized in terms of two basic phenomena. One is "metabolism". Many biochemical processes are needed to sustain a living organism. Running these processes requires a continuous supply of free energy, which is extracted from the environment. (Typically this energy is in electromagnetic or chemical form, but its ultimate source is gravity—the only interaction in the universe that is not in equilibrium.) The other is "reproduction". A particular physical structure cannot survive forever, because of continuous environmental disturbances and consequent damages. So life perpetuates itself by a succession of generations.

It is obvious that both these phenomena are sustaining and protecting and improving something, often against the odds. So let us figure out what is it that is being sustained and protected and improved.

All living organisms are made up of atoms. These atoms are fantastically indestructible. In all the biochemical processes, they just get rearranged in different ways. Each of us would have a billion atoms that once belonged to the Buddha, or Genghis Khan, or Isaac Newton—a sobering or exciting realization depending on one's frame of mind! We easily see that it is not the atoms themselves but their arrangements in complex molecules, which carry biochemical information. In the flow of biochemical processes, living organisms synthesize and break up various molecules, by altering atomic arrangements. The biochemical information resides in what molecules to use where, when and how. Characterization of this information is rather abstract, but central to the understanding of life. To put succinctly:

Hardware is recycled, while software is refined!

At the physical level, atoms are shuffled, molecules keep on changing, and life goes on. At the abstract level, it is the manipulation and preservation of information that requires construction of complex structures. Information is not merely "a" property of life—it is "the" basis of life.

Now information is routinely quantified as entropy of the possible forms a message could take [Shannon (1948)]. What the living organisms require, however, is not mere information but information with meaning. A random arrangement of components (e.g. a gas) can have large information, but it is not at all clear how that can be put to any use. The molecules of life are destined to carrying out specific functions, and they have to last long enough to execute their tasks. The meaning of biological information is carried by the chemical properties of the molecules, and a reasonably stable

cellular environment helps in controlling the chemical reactions. What the living organisms use is "knowledge",

$$\text{Knowledge} = \text{Information} + \text{Interpretation}.$$

Knowledge has to be communicated using a language. A language uses a set of building blocks (e.g. letters of an alphabet) whose meaning is fixed, and whose variety of arrangements (invariably aperiodic) compose different messages. It is the combination of information and interpretation that makes languages useful in practice.

Thus to understand how living organisms function, we need to focus on the corresponding languages whose interpretation remains fixed, while all manipulations of information processing go on. A practical language is never constructed arbitrarily—criteria of efficiency are always involved. These criteria are necessarily linked to the tasks to be implemented using the language, and fall into two broad categories. One is the stability of the meaning, i.e. protection against error causing fluctuations. And the other is the efficient use of physical resources, i.e. avoidance of unnecessary waste of space, time, energy etc. while conveying a message. The two often impose conflicting demands on the language, and the question to investigate is: *Is there an optimal language for a given task, and if so how can we find it?* From the point of view of a computer designer, the question has two parts:

Software: What are the tasks? What are the algorithms?
Hardware: How are the operations physically implemented?

It goes without saying that the efficiency of a language depends both on the software and the hardware.

In the computational complexity analysis, space and time resources are often traded off against each other, and algorithms are categorized as polynomial or non-polynomial (usually exponential). In the biological context, however, the efficiency considerations are not quite the same. Time is highly precious, while space is fairly expendable. Biological systems can sense small differences in population growth rates, and even an advantage of a fraction of a percent is sufficient for one species to overwhelm another over many generations. Spatial resources are frequently wasted, that too on purpose. For instance, how many seeds does a plant produce, when just a single one can ensure continuity of its lineage? It must not be missed that this wastefulness leads to competition and Darwinian selection.

Before going on to the details of the genetic languages, here is a quick summary of the components making up the biochemical machinery of

living organisms, at different scales. A framework for understanding genetic languages must incorporate this hierarchical structure.

Atoms	H,C,N,O, and infrequently P,S
Nucleotide bases and amino acids	10-20 atoms
Peptides and drugs	40-100 atoms
Proteins	100-1000 amino acids
Genomes	10^3-10^9 nucleotide base pairs
Size	1 nm (molecules)-10^4 nm (cells)

Gene and protein databases have been accumulating a lot of data, which can be used to test hypotheses and consequences of specific choice of languages.

To summarize, the aim of this chapter is to understand the physical and the evolutionary reasons for (a) the specific genetic languages, and (b) their specific realizations. A tiny footnote is that such an understanding would have a bearing on the probability of finding life elsewhere in the universe and then characterizing it.

10.2. Lessons of Evolution

Evolution is the centrepiece of biology. It has been the cause of many controversies, mainly because it is almost imperceptible—the evolutionary timescales are orders of magnitude larger than the lifetimes of individual living organisms. But it is the only scientific principle that provides a unifying framework encompassing all forms of life, from the simple origin to an amazing variety. We need to understand the forces governing the direction of evolution, in order to comprehend where we came from as well as what the future may have in store for us.

Genetic information forms the quantitative underpinning of evolution. Certain biological facts regarding genetic languages are well-established:

(1) Languages of genes and proteins are universal. The same 4 nucleotide bases and 20 amino acids are used in DNA, RNA and proteins, all the way from viruses and bacteria to human beings. This is despite the fact that other nucleotide bases and amino acids exist in living cells. This clearly implies that selection of specific languages has taken place.

(2) Genetic information is encoded close to data compression limit and maximal packing. This indicates that optimization of information storage has taken place.
(3) Evolution occurs through random mutations, which are local changes in the genetic sequence. In the long run, however, only a small fraction of the mutations survive—those proving advantageous to the organisms. This optimizing mechanism is labelled Darwinian selection, i.e. competition for limited resources leading to survival of the fittest.

Over the years, many attempts have been made to construct evolutionary scenarios that can explain the universality of genetic languages. They can be broadly classified into two categories. One category is the "frozen accident" hypothesis [Crick (1968)], i.e. the language somehow came into existence, and became such a vital part of life's machinery that any change in it would be highly deleterious to living organisms. This requires the birth of the genetic machinery to be an extremely rare event, without sufficient time to explore other possibilities. There is not much room for analysis in this ready-made solution. I do not subscribe to it, and instead argue for the other category. That is the "optimal solution" end-point [Patel (2003)], i.e. the language arrived at its best form by trial and error, and it did not change thereafter, because any change in it would make the information processing less competitive. This requires the evolution of genetic machinery to have sufficient scope to generate many possibilities, and subsequent competition amongst them whence the optimal solution wins over the rest.

It should be noted that the existence of an optimizing mechanism does not make a choice between the two categories clear-cut. The reason is that a multi-parameter optimization manifold generically has a large number of minima and maxima, and an optimization process relying on only local changes often gets trapped in local minima of the undulating manifold without reaching the global optimum. In such situations, the initial conditions and history of evolution become crucial in deciding the outcome of the process, and typically there arise several isolated surviving candidates. The globally optimal solution is certainly easier to reach, when the number of local minima is small and/or the range of exploratory changes is large. The extent of optimization is therefore critically controlled by the ratio of time available for exploration of various possibilities to the transition time amongst them. For the genetic machinery to have reached its optimal form, the variety of possibilities thrown up by the primordial soup must have had a simple and quick winner.

The procedure of optimization needs a process of change, and a process of selection. The former is intrinsic, the latter is extrinsic, and the two take place at different levels in biology. Indeed the difference between the two provides much ammunition for debates involving choice vs. environment, or nature vs. nurture. The changes are provided by mutations, which occur essentially randomly at the genetic level. That describes the genotype. The selection takes place by the environmental pressure at the level of whole organisms. It is not at all random, rather it is biased towards short-term survival (till reproduction). That describes the phenotype. We have good reasons to believe that the primitive living organisms were unicellular, without a nucleus, with small genomes, and having a simple cellular machinery. In such systems, the genotype and phenotype levels are quite close, and the early evolution can easily be considered a direct optimization problem.

Before exploring what could have happened in the early stages of evolution, let us also briefly look at the direction in which it has continued. The following table summarizes how the primitive unicellular organisms progressed to the level of humans (certainly the most developed form of life in our own point of view), using different physical resources to process information at different levels.

Organism	**Messages**	**Physical Means**
Single cell	Molecular (DNA, Proteins)	Chemical bonds, Diffusion
Multicellular	Electrochemical (Nervous system)	Convection, Conduction
Families, Societies	Imitation, Teaching, Languages	Light, Sound
Humans	Books, Computers, Telecommunication	Storage devices, Electromagnetic waves
Gizmos or Cyborgs ?	Databases	Merger of brain and computer

It is clear that evolution has progressively discovered higher levels of communication mechanisms, whereby the communication range has expanded (both in space and time), the physical contact has reduced, abstraction has increased, succinct language forms have arisen and complex translation machinery has been developed. More interesting is the manner in which all this has been achieved, with cooperation (often with division of labour) gradually replacing competition. This does not contradict Darwinian selection—it is just that the phenotype level has moved up, and components of a phenotype are far more likely to cooperate than compete. The mathematical formulation underlying this behaviour is "repeated games", with no foresight but with certain amount of memory [Aumann (2006)].

The evolutionary features useful for the purpose of this article are:

- The older and lower information processing levels are far better optimized than the more recent higher levels. This is a consequence of the fact that in the optimization process the lower levels had less options to deal with and more time to settle on a solution.
- The capacity of gathering, using and communicating knowledge has grown by orders of magnitude in the course of evolution. Indeed one can surmise that, in the long run, the reach of knowledge overwhelms physical features in deciding survival fitness.

> *Knowledge is the essential driving force behind evolution,*
> *providing a clear direction even when the goal remains unclear.*

10.3. Genetic Languages

Let us now return to analysing the lowest level of information processing, i.e. the genetic languages. There are two of them—the language of DNA and RNA with an alphabet of four nucleotide bases, and the language of proteins with an alphabet of twenty amino acids. The tasks carried out by both of them are quite specific and easy to identify.

(1) The essential job of DNA and RNA is to sequentially assemble a chain of building blocks on top of a pre-existing master template. One can call DNA the read-only-memory of living organisms. When not involved in the replication process, the information in DNA remains idle in a secluded and protected state.
(2) Proteins are structurally stable molecules of various shapes and sizes, with precise locations of active chemical groups. They carry out

various functions of life by highly selective binding to other molecules. Molecular interactions are weak and extremely short-ranged, and so the binding necessitates matching of complementary shapes, i.e. lock-and-key mechanism in three dimensions. Proteins are created whenever needed, based on the information present in DNA, and disintegrated once their function is over.

The identification of these tasks makes it easy to see why there are two languages and not just one. Memory needs long term stability, on the other hand fast execution of functions is desirable, and the two make different demands on the hardware involved. (The accuracy of a single language performing both the tasks would be limited, which is the likely reason why the RNA world, described later, did not last very long.) Indeed, our electronic computers compute using electrical signals, but store the results on the disk using magnetic signals. The former encoding is suitable for fast processing, while the latter is suitable for long term storage. The two hardware languages fortunately correspond to the same binary software language, and are conveniently translated into each other by the laws of electromagnetism. In case of genetic information, the two hardware languages work in different dimensions—DNA is a linear chain while proteins are three dimensional structures—forcing the corresponding software languages also to be different and the translation machinery fairly complex.

We want to find the optimal languages for implementing the tasks of DNA/RNA and proteins. So we have to study what constraints are imposed on a language for minimization of errors and minimization of resources. Minimization of errors inevitably leads to a digital language, having a set of clearly distinguishable building blocks with discrete operations. With non-overlapping signals, small fluctuations (say less than half the separation between the discrete values) are interpreted as noise and eliminated from the message by resetting the values, while large changes represent genuine change in meaning. The loss of intermediate values is not a drawback, as long as actual applications need only results with bounded errors. Minimization of resources is achieved by using a small number of building blocks, with simple and quick operations. A versatile language is then obtained by arranging the building blocks together in as many different ways as possible.

In this optimization exercise, the "minimal language", i.e. the language with the smallest set of building blocks for a given task, has a unique status [Patel (2006a)]:

- It has the largest tolerance against errors, since the discrete variables are spread as far apart as possible in the available range of physical hardware properties.
- It has the smallest instruction set, since the number of possible transformations is automatically limited.
- It can function with high density of packing and quick operations, which more than make up for the increased depth of computation.
- It can avoid the need for translation, by using simple physical responses of the hardware.

The genetic languages are undoubtedly digital, and that has been crucial in producing evolution as we know it. Some tell-tale signatures are:

- Digital language helps in maintaining variation, while continuous variables would average out fluctuations.
- It is a curious fact that evolution is a consequence of a tiny error rate. With too many errors the organism will not be able to survive, but without mutations there will be no evolution.
- Even minimal changes in discrete genetic variables generate sizeable disruptions in the system, and they will be futile unless the system can tolerate them. Often a large number of trial variations are needed to find the right combinations, and having only a small number of discrete possibilities helps. Continuous variables produce gradual evolution, which appears on larger phenotypic scales when multiple sources contributing to a particular feature average out.
- With most of the trial variations getting rejected as being unproductive, digital variables give rise to punctuated evolution—sudden changes interspersed amongst long periods of stasis.

In the following sections, we investigate to what extent the digital genetic languages are minimal, i.e. we first deduce the minimal languages for the tasks of DNA/RNA and proteins, and then compare them to what the living organisms have opted for. A worthwhile bonus is that we gain useful clues about the simpler predecessors of the modern genetic languages.

10.4. Understanding Proteins

Finding the minimal language for proteins is a straightforward problem in classical geometry [Patel (2002)]. The following is a rapid-fire summary of

the analysis:

- *What is the purpose of the language of amino acids?*
  To form protein molecules of different shapes and sizes in three dimensions, and containing different chemical groups.
- *What is the minimal discrete geometry for designing three dimensional structures?*
  Simplicial tetrahedral geometry and the diamond lattice. Secondary protein structures, i.e. α-helices, β-bends and β-sheets, fit quite well on the diamond lattice.
- *What are the best physical components to realize this geometry?*
  Covalently bonded carbon atoms, also N^+ and H_2O. Silicon is far more abundant, but it cannot form aperiodic structures needed to encode a language. (In the graphite sheet arrangement, carbon also provides the simplicial geometry for two dimensional membrane patterns.)
- *What is a convenient way to assemble these components in the desired three dimensional structures?*
  Synthesize one dimensional polypeptide chains, which carry knowledge about how to fold into three dimensional structures. The problem then simplifies to assembling one dimensional chains. (Note that images in our electronic computers are stored as folded sequences.)
- *What are the elementary operations needed to fold a polypeptide chain on a diamond lattice, in any desired manner?*
  Nine discrete rotations, represented as a 3×3 array on the Ramachandran map (see Fig. 10.2). Additional folding operations are trans-cis flip and long distance bonds.
- *What can the side groups of polypeptide chains do?*
  They favour particular orientations of the polypeptide chain by interactions amongst themselves. They also fill up cavities in the structure by variations in their size.

To put the above statements in biological perspective, and to illustrate the minimalistic choices made by the living organisms (in the context of what was available), here are some facts about the polypeptide chains:

(a) Amino acids are easily produced in primordial chemical soup. They even exist in interstellar clouds.
(b) Amino acids are the smallest organic molecules with both an acid group ($-COOH$) and a base group ($-NH_2$). They differ from each other in terms of distinct R-groups, which become the side groups of polypeptide chains.

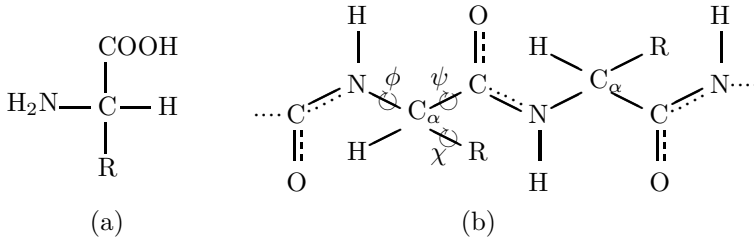


Fig. 10.1. Chemical structures of (a) an amino acid, (b) a polypeptide chain.

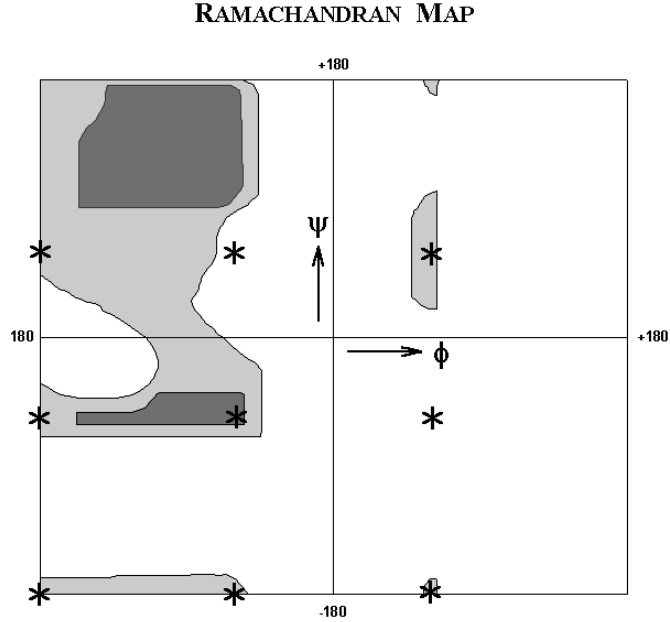


Fig. 10.2. The allowed orientation angles for the C_α bonds in real polypeptide chains for chiral L-type amino acids, taking into account hard core repulsion between atoms [Ramachandran *et al.* (1963)]. Stars mark the nine discrete possibilities for the angles, uniformly separated by 120° intervals, when the polypeptide chain is folded on a diamond lattice.

(c) Polypeptide chains are produced by polymerisation of amino acids by acid-base neutralisation (see Fig. 10.1).

(d) Folded ↔ unfolded transition of polypeptide chains requires flexible joints and weak non-local interactions (close to critical behaviour).

(e) Transport of polypeptides across membranes is efficient in the unfolded state than in the folded one, preventing leakage of other molecules at the same time. (A chain can slide through a small hole.)

The structural language of polypeptide chains would be the most versatile when all possible orientations can be generated by every amino acid segment. This cannot be achieved by just a single property of the R-groups (e.g. hydrophobic to hydrophilic variation). The table below lists the amino acids used by the universal language of proteins. They are subdivided into several categories according to the chemical properties of the R-groups, and their molecular weights provide an indication of the size of the R-groups [Lehninger *et al.* (1993)]. The language of bends and folds of the polypeptide chains is non-local, i.e. the orientation of an amino acid is not determined by its own R-group alone, rather the orientation is decided by the interactions of the amino acid with all its neighbours. Still, by analysing protein databases, one can find probabilities for every amino acid to participate in specific secondary structures, and the dominant propensities are listed in the table below as well [Creighton (1993)].

Deciphering the actual orientations of amino acids in proteins is an outstanding open problem—the protein folding problem. Even then a rough count of the number of amino acids present can be obtained with one additional input. This is the division of the amino acids into two classes, according to the properties of the corresponding aminoacyl-tRNA synthetases (aaRS). In the synthesis of polypeptide chains, tRNA molecules are the adaptors with one end matching with a genetic codon and the other end attached to an amino acid. The aaRS are the truly bilingual molecules in the translation machinery, that attach an appropriate amino acid to the tRNA corresponding to its anticodon. There is a unique aaRS for every amino acid, even though several different tRNA molecules can carry the same amino acid (the genetic code is degenerate). It has been discovered that the aaRS are clearly divided in two classes, according to their sequence and structural motifs, active sites and the location where they attach the amino acids to the tRNA molecules [Arnez and Moras (1997); Lewin (2000)]. The classes of amino acids are also listed in the table below, and here is what we find:

(a) The 20 amino acids are divided into two classes of 10 each.
(b) The two classes divide amino acids with each R-group property equally, in such a way that for every R-group property the larger R-groups correspond to class I and the smaller ones to class II.

Amino acid	R-group	Mol. wt.	Class	Propensity
G Gly (Glycine)	Non-polar	75	II	turn
A Ala (Alanine)	aliphatic	89	II	α
P Pro (Proline)		115	II	turn
V Val (Valine)		117	I	β
L Leu (Leucine)		131	I	α
I Ile (Isoleucine)		131	I	β
S Ser (Serine)	Polar	105	II	turn
T Thr (Threonine)	uncharged	119	II	β
N Asn (Asparagine)		132	II	turn
C Cys (Cysteine)		121	I	β
M Met (Methionine)		149	I	α
Q Gln (Glutamine)		146	I	α
D Asp (Aspartate)	Negative	133	II	turn
E Glu (Glutamate)	charge	147	I	α
K Lys (Lysine)	Positive	146	II	α
R Arg (Arginine)	charge	174	I	α
H His (Histidine)	Ring/	155	II	α
F Phe (Phenylalanine)	aromatic	165	II	β
Y Tyr (Tyrosine)		181	I	β
W Trp (Tryptophan)		204	I	β

(c) The class label of an amino acid can be interpreted as a binary code for its R-group size, in addition to the categorization in terms of chemical properties.

(d) This binary code has unambiguous structural significance for packing of proteins. Folding of an aperiodic chain into a compact structure invariably leaves behind cavities of different shapes and sizes. The use of large R-groups to fill big cavities and small R-groups to fill small ones can produce dense compact structures.

(e) Each class contains a special amino acid, involved in operations other than local folding of polypeptide chains—Cys in class I can make long distance disulfide bonds, and Pro in class II can induce a trans-cis flip.

We thus arrive at a structural explanation for the 20 amino acids as building blocks of proteins. Local orientations of the polypeptide chains have to cover the nine discrete points on the Ramachandran map. They are governed by the chemical properties of the amino acid R-groups, and an efficient encoding can do the job with nine amino acids. The binary code for the R-group sizes fills up the cavities nicely without disturbing the folds. And then two more non-local operations increase the stability of protein molecules.

The above counting does not tell which sequence of amino acids will lead to which conformation of the polypeptide chain. That remains an unsolved exercise in coding as well as chemical properties. On the other hand, it is known that amino acids located at the active sites and at the end-points of secondary structures determine the domains and activity of proteins, while the amino acids in the intervening regions more or less act like space-fillers. Among the space-fillers, many substitutions can be carried out that hardly affect the protein function—indeed protein database analyses have produced probabilistic substitution tables for the amino acids. We need to somehow incorporate this feature into our understanding of the structural language of proteins, so that we can progress beyond individual letters to words and sentences [see for example, Socolich *et al.* (2005); Russ *et al.* (2005)]. A new perspective is necessary, and perhaps the following self-explanatory paragraph is a clue [Rawlinson (1976)]. Surprise yourself by reading it at full speed, even if you are not familiar with crossword puzzles!

> You arne't ginog to blveiee taht you can aulaclty uesdnatnrd waht I am wirtnig. Beuacse of the phaonmneal pweor of the hmuan mnid, aoccdrnig to a rscheearch at Cmabrigde Uinervtisy, it deosn't mttaer in waht oredr the ltteers in a wrod are, the olny iprmoatnt tihng is taht the frist and lsat ltteer be in the rghit pclae. The rset can be a taotl mses and you can sitll raed it wouthit a porbelm. Tihs is bcuseae the huamn mnid deos not raed ervey lteter by istlef, but the wrod as a wlohe. Amzanig huh? Yaeh and you awlyas tghuhot slpeling was ipmorantt!

Written English and proteins are both non-local languages. Evolution, after all, is no stranger to using a worthwhile idea—here a certain amount of parallel and distributed processing—over and over again.

10.5. Understanding DNA

Now let us move on to finding the minimal language for DNA and RNA. Once again, here is a quick-fire summary of the analysis [Patel (2001a)].

- *What is the information processing task carried out by DNA?*
  Sequential assembly of a complementary copy on top of the pre-existing template by picking up single nucleotide bases from an unsorted ensemble. The same task is carried out by mRNA in the assembly of polypeptide chains, but proceeding in steps of three nucleotide bases (triplet codons).
- *What is the optimal way of carrying out this task?*
  Lov Grover's database search algorithm [Grover (1996)], which uses binary queries and requires wave dynamics. It optimizes the number of queries, providing a quadratic speed up over any Boolean algorithm, irrespective of the size of spatial resources the Boolean algorithm may use. In a classical wave implementation the database is encoded as N distinct wave modes, while in a quantum setting the database is labeled by $\log_2 N$ qubits.
- *What is the characteristic signature of this algorithm?*
  The number of queries Q required to pick the desired object from an unsorted database of size N are given by:

$$(2Q+1)\sin^{-1}\frac{1}{\sqrt{N}} = \frac{\pi}{2} \implies \begin{cases} Q=1, & N=4 \\ Q=2, & N=10.5 \\ Q=3, & N=20.2 \end{cases} \tag{10.1}$$

  (Non-integral values of N imply small errors in object identification, about 1 part in 700 and 1050 for $Q=2$ and $Q=3$ respectively.)
- *What are the physical ingredients needed to implement this algorithm?*
  A system of coupled wave modes whose superposition maintains phase coherence, and two reflection operations (phase changes of π).

Again to clarify the biological perspective, and to illustrate the minimalistic choices made by the living organisms, here are some facts about the biochemical assembly process:

(a) Instead of waiting for a desired complex biomolecule to come along, it is far more efficient to synthesize it from common, simple ingredients.
(b) There should be a sufficient number of clearly distinguishable building blocks to create the wide variety of required biomolecules.

(c) The building blocks are randomly floating around in the cellular environment. They get picked one by one and added to a linearly growing polymer chain.
(d) Complementary nucleotide base-pairing decides the correct building block to be added at each step of the assembly process.
(e) The base-pairings are binary questions; either they form or they do not form. The molecular bonds involved are hydrogen bonds.

With these features, the optimal classical algorithm based on Boolean logic would be a binary tree search. But the observed numbers do not fit that pattern (of powers of two). On the other hand, the optimal search solutions of Grover's algorithm are clearly different from and superior to the Boolean ones, and they do produce the right numbers. The crucial difference between the two is that wave mechanics works with amplitudes and not probabilities, which allows constructive as well as destructive interference. Grover's algorithm manages the interference of amplitudes cleverly, and the individual steps are depicted in Fig. 10.3 for the simplest case of four items in the database.

Now note that classically the binary alphabet is the minimal one for encoding information in a linear chain, and two nucleotide bases (one complementary pair) are sufficient to encode the genetic information. As a matter of fact, our digital computers encode all types of information using

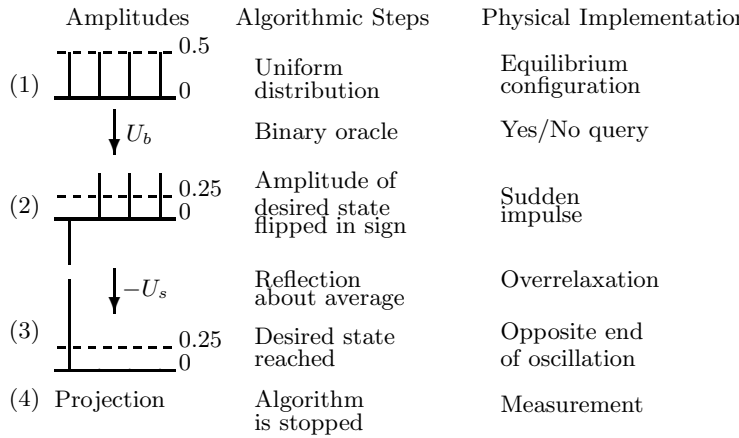


Fig. 10.3. The steps of Grover's database search algorithm for the simplest case of four items, when the first item is desired by the oracle. The left column depicts the amplitudes of the four states, with the dashed lines showing their average values. The middle column describes the algorithmic steps, and the right column mentions their physical implementation.

only 0's and 1's. The binary alphabet is the simplest system, and so would have preceded (during evolution) the four nucleotide base system found in nature. Then, was the speed-up provided by the wave algorithm the real incentive for nature to complicate the genetic alphabet? Certainly, if we have to design the optimal system for linear assembly, knowing all the physical laws that we do, we would opt for something like what is present in nature. But what did nature really do? We have no choice but to face the following questions:

- *Does the genetic machinery have the ingredients to implement Grover's algorithm?*
  The physical components are definitely present, and it is not too difficult to construct scenarios based on quantum dynamics [Patel (2001a)] as well as vibrational motion [Patel (2006b)]. Although Grover's algorithm was discovered in the context of quantum computation, it is much more general, and does not need all the properties of quantum dynamics. In particular, highly fragile entanglement is unnecessary, while much more stable superposition of states is a must. The issue of concern then is whether coherent superposition of wave modes can survive long enough for the algorithm to execute. This superposition may be quantum (i.e. for the wavefunction) or may be classical (as in case of vibrations). It need not be exactly synchronous either—if the system transits through all the possible states at a rate much faster than the time scale of the selection oracle, that would simulate superposition, averaging out high frequency components (e.g. the appearance of spokes of a rapidly spinning wheel). Provided that the superposition is achieved somehow, the mathematical signature, i.e. Eq. (10.1), follows. Explicit formulation of a testable scenario, based on physical properties of the available molecules and capable of avoiding fast decoherence, is an open challenge.
- *Did nature actually exploit Grover's algorithm when the genetic machinery evolved billions of years ago?*
  Unfortunately there is no direct answer, since evolution of life cannot be repeated.
- *Do the living organisms use Grover's algorithm even today?*
  In principle, this is experimentally testable. Our technology is yet to reach a stage where we can directly observe molecular dynamics in a liquid environment. But indirect tests of optimality are plausible, e.g. constructing artificial genetic texts containing a different number of letters and letting it compete with the supposedly optimal natural language [Patel (2001b)].

This is not the end of the road, and I return to a deeper analysis later on. But prior to that let us look at what the above described understanding of the languages of proteins and DNA has to say about the translation mechanism between the two, i.e. the genetic code. That investigation does offer non-trivial rewards, regarding how the complex genetic machinery could have arisen from simpler predecessors.

10.6. What Preceded the Optimal Languages?

Languages of twenty amino acids and four nucleotide bases are too complex to be established in one go, and evolution must have arrived at them from simpler predecessors. On the other hand, continuity of knowledge has to be maintained in evolution from simpler to complex languages, because sudden drastic changes lead to misinterpretations that kill living organisms. Two evolutionary routes obeying this restriction, and still capable of producing large jumps, are known:

(1) Duplication of information, which allows one copy to carry on the required function while the other is free to mutate and give rise to a new function.
(2) Wholesale import of fully functional components by a living organism, distinct from their own and developed by a different living organism.

In what follows, we study the genetic languages within this framework. The two classes of amino acids and the $Q = 2$ solution of Grover's algorithm, described in preceding sections, suggest a duplication event, i.e. the universal non-overlapping triplet genetic code arose from a more primitive doublet genetic code labelling ten amino acids [Patel (2005); Wu *et al.* (2005); Rodin and Rodin (2006)]. To justify this hypothesis, we have to identify evolutionary remnants of (a) a genetic language where only two nucleotide bases of a codon carry information while the third one is a punctuation mark, (b) a set of amino acids that can produce all the orientations of polypeptide chains but without efficiently filling up the cavities, and (c) a reasonable association between these codons and amino acids. Amazingly, biochemical signals for all of these features have been observed.

The central players in this event are the tRNA molecules. They are older than the DNA and the proteins in evolutionary history, and are believed to link the modern genetic machinery with the earlier RNA world [Gesteland *et al.* (2006)]. It has been discovered that RNA polymers called ribozymes

can both store information and function as catalytic enzymes, although not very accurately. The hypothesis is that when more accurate DNA and proteins took over these tasks from ribozymes, tRNA molecules survived as adaptors from the preceding era.

As illustrated in Fig. 10.4, the tRNAs are L-shaped molecules with the amino acid acceptor arm at one end and the anticodon arm at the other. The two arms are separated by a distance of about 75 Å, too far apart for any direct interaction. The aaRS molecules are much larger than the tRNAs, and they attach an amino acid to the acceptor stem corresponding to the anticodon by interacting with both the arms. The two classes of aaRS perform this attachment from opposite sides, in a mirror image fashion as shown in Fig. 10.4. Class I attachment is from the minor groove side of the acceptor arm helix, and class II attachment is from the major groove side. It has been observed that the tRNA acceptor stem sequence, which directly interacts with the R-group of the amino acid being attached, plays a dominant role in the amino acid recognition and the anticodon does not matter much. This behaviour characterizes the operational RNA code, formed by the first four base pairs and the unpaired base N^{73} of the acceptor stem [Schimmel *et al.* (1993)]. The operational code relies on stereochemical atomic recognition between amino acid R-groups and nucleotide bases; it is argued to be older than the genetic code and a key to understanding the goings on in the RNA world.

We now look at the amino acid class pattern in the genetic code. The universal triplet genetic code has considerable and non-uniform degeneracy,

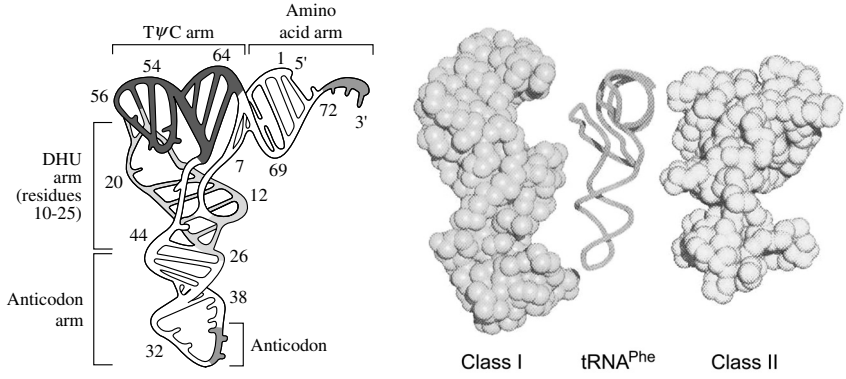


Fig. 10.4. The structure of tRNA [Lehninger *et al.* (1993)] (left), and the tRNA-AARS interaction from opposite sides for the two classes [Arnez and Moras (1997)] (right).

Table 10.1. The universal genetic code. Boldface letters indicate class II amino acids.

UUU Phe	**UCU Ser**	UAU Tyr	UGU Cys
UUC Phe	**UCC Ser**	UAC Tyr	UGC Cys
UUA Leu	**UCA Ser**	UAA Stop	UGA Stop
UUG Leu	**UCG Ser**	UAG Stop	UGG Trp
CUU Leu	**CCU Pro**	**CAU His**	CGU Arg
CUC Leu	**CCC Pro**	**CAC His**	CGC Arg
CUA Leu	**CCA Pro**	CAA Gln	CGA Arg
CUG Leu	**CCG Pro**	CAG Gln	CGG Arg
AUU Ile	**ACU Thr**	**AAU Asn**	**AGU Ser**
AUC Ile	**ACC Thr**	**AAC Asn**	**AGC Ser**
AUA Ile	**ACA Thr**	**AAA Lys**	AGA Arg
AUG Met	**ACG Thr**	**AAG Lys**	AGG Arg
GUU Val	**GCU Ala**	**GAU Asp**	**GGU Gly**
GUC Val	**GCC Ala**	**GAC Asp**	**GGC Gly**
GUA Val	**GCA Ala**	GAA Glu	**GGA Gly**
GUG Val	**GCG Ala**	GAG Glu	**GGG Gly**

with 64 codons carrying 21 signals (including Stop) as shown. Although there is a rough rule of similar codons for similar amino acids, no clear pattern is obvious.

By analysing genomes of living organisms, it has been found that during the translation process 61 mRNA codons (excluding Stop) pair with a smaller number of tRNA anticodons. The smaller degeneracy of the anticodons is due to wobble pairing of nucleotide bases, where the third base carries only a limited meaning (either binary or none) instead of four-fold possibilities [Crick (1966)]. The wobble rules are exact for the mitochondrial code—all that matters is whether the third base is a purine or a pyrimidine, and the number of possibilities reduces to 32 as shown. (Note that the mitochondrial code works with rather small genomes and evolves faster than the universal code, and so is likely to have simpler optimization criteria.)

The departures exhibited by the mitochondrial genetic code, as well as the genetic codes of some living organisms, from the universal genetic code are rather minor, and only occur in some of the positions occupied by class I amino acids. It can be seen that all the class II amino acids, except Lys, can be coded by codons NNY and anticodons $\overleftarrow{\text{GNN}}$ (wobble rules allow

Table 10.2. The (vertebrate) mitochondrial genetic code. Pyrimidines Y=U or C, Purines R=A or G.

UUY Phe	**UCY Ser**	UAY Tyr	UGY Cys
UUR Leu	**UCR Ser**	UAR Stop	UGR Trp
CUY Leu	**CCY Pro**	**CAY His**	CGY Arg
CUR Leu	**CCR Pro**	CAR Gln	CGR Arg
AUY Ile	**ACY Thr**	**AAY Asn**	**AGY Ser**
AUR Met	**ACR Thr**	**AAR Lys**	AGR Stop
GUY Val	**GCY Ala**	**GAY Asp**	**GGY Gly**
GUR Val	**GCR Ala**	GAR Glu	**GGR Gly**

pairing of G with both U and C) [Patel (2005)]. This pattern suggests that the structurally more complex class I amino acids entered the genetic machinery later, and a doublet code for the class II amino acids (with the third base acting only as a punctuation mark) preceded the universal genetic code.

The class pattern becomes especially clear with two more inputs:

(1) According to the sequence and structural motifs of their aaRS, Phe is assigned to class I and Tyr to class II. But if one looks at the stereochemistry of how the aaRS attach the amino acid to tRNA, then Phe belongs to class II and Tyr to class I [Goldgur *et al.* (1997); Yaremchuk *et al.* (2002)]. Thus from the operational RNA code point of view the two need to be swapped.
(2) Lys has two distinct aaRS, one belonging to class I (in most archaea) and the other belonging to class II (in most bacteria and all eukaryotes) [Woese *et al.* (2000)]. On the other hand, the assignment of AGR codons varies from Arg to Stop, Ser and Gly. This feature is indicative of an exchange of class roles between AAR and AGR codons (models swapping Lys and Arg through ornithine have been proposed).

These two swaps of class labels do not alter the earlier observation that the two amino acid classes divide each R-group property equally. We thus arrive at the predecessor genetic code shown below. The binary division of the codons according to the class label is now not only unmistakable but produces a perfect complementary pattern [Rodin and Rodin (2006)].

Table 10.3. The predecessor genetic code. Pyrimidines Y=U or C, Purines R=A or G.

UUY Phe	**UCY Ser**	**UAY Tyr**	UGY Cys
UUR Leu	**UCR Ser**	UAR Stop	UGR Trp
CUY Leu	**CCY Pro**	**CAY His**	CGY Arg
CUR Leu	**CCR Pro**	CAR Gln	CGR Arg
AUY Ile	**ACY Thr**	**AAY Asn**	**AGY Ser**
AUR Met	**ACR Thr**	AAR Lys*	**AGR Arg***
GUY Val	**GCY Ala**	**GAY Asp**	**GGY Gly**
GUR Val	**GCR Ala**	GAR Glu	**GGR Gly**

When the middle base is Y (the first two columns), it indicates the class on its own—U for class I and C for class II. When the middle base is R (the last two columns), the class is denoted by an additional Y or R, in the third position when the middle base is A and in the first position when the middle base is G. (Explicitly the class I codons are NUN, NAR and YGN, while the class II codons are NCN, NAY and RGN.) The feature that after the middle base, the first or the third base determines the amino acid class in a complementary pattern, has led to the hypothesis that the amino acid class doubling occurred in a strand symmetric RNA world, with complementary tRNAs providing complementary anticodons [Rodin and Rodin (2006)].

The complementary pattern has an echo in the operational code of the tRNA acceptor stem too. When the aaRS attach the amino acid to the −CCA tail of the tRNA acceptor arm, the tail bends back scorpion-like, and the R-group of the amino acid gets sandwiched between the tRNA acceptor stem groove (bases 1-3 and 70-73) and the aaRS. Analysis of tRNA consensus sequences from many living organisms reveals [Rodin and Rodin (2006)] that (a) the first base-pair in the acceptor stem groove is almost invariably G^1-C^{72} and is mapped to the wobble position of the codon, (b) the second base-pair is mostly G^2-C^{71} or C^2-G^{71}, which correlate well respectively with Y and R in the middle position of the codon, and (c) the other bases do not show any class complementarity pattern.

The involvement of both the operational RNA code and the anticodon in the selection of appropriate amino acid, and the above mentioned correlations between the two, make it very likely that the two had a common

origin. Then piecing together all the observed features, the following scenario emerges for the evolution of the genetic code:

(1) Ribozymes of the RNA world could replicate, but their functional capability was limited—a small alphabet (quite likely four nucleotide bases) and restricted conformations could only produce certain types of structures. Polypeptide chains, even with a small repertoire of amino acids, provided a much more accurate and versatile structural language, and they took over the functional tasks from ribozymes. This takeover required close stereochemical matching between ribozymes and polypeptide chains, in order to retain the functionalities already developed.

(2) The class II amino acids provided (or at least dominated) the initial structural language of proteins. With smaller R-groups, they are easier to synthesize, and so are likely to have appeared earlier in evolution. They can fold polypeptide chains in all possible conformations, although some of the cavities may remain incompletely filled. They also fit snugly into the major groove of the tRNA acceptor stem, with the bases 1-3 and 70-74 essentially forming a mould for the R-group, for precise stereochemical recognition. Indeed, this stereochemical identification of an R-group by three base-pairs, necessitated by actual sizes of molecules, would be the reason for the triplet genetic code, even in a situation where all the bases do not carry information.

(3) The modern tRNA molecules arose from repetitive extensions and complementary pairing of short acceptor stem sequences. In the process, the 1-2-3 bases became the forerunners of the 34-35-36 anticodons. With different structural features identifying the amino acids, paired bases in the acceptor stem and unpaired bases in the anticodon, the evolution of the operational code and the genetic code diverged. The two are now different in exact base sequences, but the purine-pyrimidine label (i.e. R vs. Y) still shows high degree of correlation between the two.

(4) In the earlier era of class II amino acid language, the wobble base was a punctuation mark (likely to be G in the anticodon, as descendant of the 1-72 pair), the central base was the dominant identifier (descendant of the 2-71 pair), and the last anticodon base provided additional specification (equivalent to the 3-70 pair and the unpaired base 73). During subsequent evolution, these $\overleftarrow{\text{GNN}}$ anticodons have retained their meaning, and all minor variations observed between genetic codes are in the other anticodons corresponding to class I amino acids.

(5) Class I amino acids got drafted into the structural language, because they could increase stability of proteins by improved packing of large cavities without disrupting established structures. The required binary label for the R-group size, appeared differently in the operational code and the genetic code. For the operational code, the minor groove of the acceptor stem was used, and utilization of the same paired bases from the opposite side led to a complementary pattern. The class I amino acids fit loosely in the minor groove, and subsequent proof-reading is necessary at times to remove incorrectly attached amino acids. For the genetic code, several of the unassigned anticodons were used for the class I amino acids, introducing a binary meaning to the wobble position whenever needed. The Darwinian selection constraint that the operational code and the genetic code serve a common purpose ensured a rough complementary strand symmetry for the anticodons as well.

(6) The structural language reached its optimal stage, once both classes of amino acids were incorporated. With 32 anticodons (counting only a binary meaning for the wobble position) and 20 amino acid signals, enough anticodons may have remained unassigned. Most of them were taken over by amino acids with close chemical affinities (wobble position did not assume any meaning), and a few left over ones mapped to the Stop signal.

(7) All this could have happened when each gene was a separate molecule, coding for a single polypeptide chain. Additional selection pressures must have arisen when the genes combined into a genome. To take care of the increased complexity, some juggling of codons happened and the Start signal appeared. The present analysis is not detailed enough to explain this later optimization. Nevertheless, interpretation of similar codons for similar amino acids and the wobble rules, as relics of the doubling of the genetic code—indicative but not perfect—is a significant achievement.

At the heart of the class duplication mechanism described above is (a) the mirror image pattern of the amino acid R-group fit with the tRNA acceptor stem, and (b) the complementary pattern of the anticodons. More detailed checks for these are certainly possible. The amino acids have been tested for direct chemical affinities with either their codons or their anticodons (but not both together), and most results have been lukewarm [Yarus *et al.* (2005)]. Instead, chemical affinities of amino acids with paired codon-anticodon grooves should be tested, both by stereochemical models

and actual experiments. It should be also possible to identify which amino acid paired with which one when the genetic code doubled. Some pairs can be easily inferred from biochemical properties [Ribas de Pouplana and Schimmel (2001); Patel (2005)]—(Asp,Glu), (Asn,Gln), (Lys,Arg), (Pro,Cys), (Phe,Tyr), (Ser&Thr,Val&Ile)—while the others would be revealed by stereochemical modeling.

The next interesting exercise, further back in time and therefore more speculative, is to identify how a single class 10 amino acid language took over the functional tasks of 4 nucleotide base ribozymes. This is the stage where Grover's algorithm might have played a crucial role, and so we go back and look into it more inquisitively.

10.7. Quantum Role?

The arguments of the preceding section reduce the amino acid identification problem by a triplet code, to the identification problem within a class by a doublet code plus a binary class label. It is an accidental degeneracy that the $Q = 3$ solution of Grover's algorithm, Eq. (10.1), can be obtained as the $Q = 2$ solution plus a classical binary query. To assert that the sequential assembly process reached its optimal solution, we still need to resolve how the $Q = 1, 2$ solutions of Eq. (10.1) were realized by the primordial living organisms.

Clearly, the assembly processes occur at the molecular scale. We know the physical laws applicable there—classical dynamics is relevant, but quantum dynamics cannot be bypassed. Discrete atomic structure provided by quantum mechanics is the basis of digital genetic languages. Molecular bonds are generally given a classical description, but they cannot take place without appropriate quantum correlations among the electron wavefunctions. Especially, hydrogen bonds are critical to the genetic identification process, and they are inherently quantum—typical examples of tunnelling in a double well potential. The assemblers, i.e. the polymerase enzymes and the aaRS molecules, are much larger than the nucleotide bases and the amino acids, and completely enclose the active regions where identification of nucleotide bases and amino acids occurs. They provide a well-shielded environment for the assembly process, but the cover-up also makes it difficult to figure out what exactly goes on inside.

Chemical reactions are typically described in terms of specific initial and final states, and transition matrix elements between the two that

characterize the reaction rates. That is a fully classical description, and it works well for most practical purposes. But to the best of our understanding, the fundamental laws of physics are quantum and not classical—the classical behaviour arises from the quantum world as an "averaged out" description. Quantum steps are thus necessarily present inside averaged out chemical reaction rates, and would be revealed if we can locate their characteristic signatures. In the present context, such a fingerprint is superposition.

The initial and final states of Grover's algorithm are classical, but the execution in between is not. In order to be stable, the initial and final states have to be based on a relaxation towards equilibrium process. For the execution of the algorithm in between, the minimal physical requirement is a system that allows superposition of states, in particular a set of coupled wave modes. As illustrated earlier in Fig. 10.3, the algorithm needs two reflection operations. Provided that the necessary superposition is achieved somehow, it is straightforward to map these operations to: (i) the impulse interaction during molecular bond formation which has the right properties to realize the selection oracle as a fairly stable geometric phase, and (ii) the (damped) oscillations of the subsequent relaxation, which when stopped at the right instant by release of the binding energy to the environment can make up the other reflection phase.

Beyond this generic description, the specific wave modes to be superposed can come from a variety of physical resources, e.g. quantum evolution, vibrations and rotations. With properly tuned couplings, resonant transfer of amplitudes occurs amongst the wave modes (the phenomenon of beats), and that is the dynamics of Grover's algorithm. When the waves remain coherent, their amplitudes add and subtract, and we have superposition. But when the waves lose their coherence, we get an averaged out result—a classical mixture. Thus the bottom line of the problem is:

> *Can the genetic machinery maintain coherence of appropriate wave modes on a time scale required by the transition matrix elements?*

Explicitly, let t_b be the time for molecular identification by bond formation, $t_{\rm coh}$ be the time over which coherent superposition holds, and $t_{\rm rel}$ be the time scale for relaxation to equilibrium. Then, Grover's algorithm can be executed when the time scales satisfy the hierarchy

$$t_b \ll t_{\rm coh} \ll t_{\rm rel}\,. \tag{10.2}$$

Other than this constraint, the algorithm is quite robust and does not rely on fine-tuned parameters. (Damping is the dominant source of error; other effects produce errors which are quadratic in perturbation parameters.)

Wave modes inevitably decohere due to their interaction with environment, essentially through molecular collisions and long range forces. Decoherence always produces a cross-over leading to irreversible loss of information [Guilini *et al.* (1996)]—collapse of the wavefunction in the quantum case and damped oscillations for classical waves. The time scales of decoherence depend on the dynamics involved, but a generic feature is that no wave motion can be damped faster than its natural undamped frequency of oscillation. For an oscillator,

$$\ddot{x} + 2\gamma\dot{x} + \omega_0^2 x = 0\,,\ x \sim e^{i\omega t} \implies \gamma_{\rm crit} = \max(\mathrm{Im}(\omega)) = \omega_0\,. \qquad (10.3)$$

Too much damping freezes the wave amplitude instead of making it decay. Thus ω_0^{-1} is both an estimate of t_b and a lower bound on $t_{\rm coh}$. Molecular properties yield $\omega_0 = \Delta E/\hbar = O(10^{14})$ sec^{-1}, for the transition frequencies of weak bonds as well as for the vibration frequencies of covalent bonds.

Decoherence must be controlled in order to observe wave dynamics, irrespective of any other (undiscovered) physical phenomena that may be involved. In case of vibrational and rotational modes of molecules, the fact that we can experimentally measure the excitation spectra implies that the decoherence times are much longer than t_b. In case of quantum dynamics, the decoherence rate is often estimated from the scattering cross-sections of environmental interactions, in dilute gas approximation using conventional thermodynamics and Fermi's golden rule. For molecular processes, these times are usually minuscule, orders of magnitude below ω_0^{-1}. In view of Eq. (10.3), such minuscule estimates are wrong—the reason being that Fermi's golden rule is an approximation, not valid at times smaller than the natural oscillation period. A more careful analysis is necessary.

According to Fermi's golden rule, the environmental decoherence rate is inversely proportional to three factors: the initial flux, the interaction strength and the final density of states. We know specific situations, where quantum states are long-lived due to suppression of one or more of these factors. The initial flux is typically reduced by low temperatures and shielding, the interaction strength is small for lasers and nuclear spins, and the final density of states is suppressed due to energy gap for superconductors and hydrogen bonds. We need to investigate whether or not these features are exploited by the genetic machinery, and if so to what extent.

Large catalytic enzymes (e.g. polymerases, aaRS, ribosomes) have an indispensable role in biomolecular assembly processes. These processes do not take place in thermal equilibrium, rather the enzymes provide an environment that supplies free energy (using ATP molecules) as well as shields. The assembly then proceeds along the chain linearly in time. In a free solution without the enzymes, the assembly just does not take place, even though such a free assembly would have the advantage of parallel processing (i.e. simultaneous assembly all along the chain). The enzymes certainly reduce the external disturbances and decrease the final density of states by limiting possible configurations. But much more than that, they stabilize the intermediate reaction states, called the transition states. The traditional description is that the free energy barrier between the reactants and the products is too high to cross with just the thermal fluctuations, and the enzymes take the process forward by lowering the barrier and supplying free energy. The transition states are generally depicted using distorted electron clouds, somewhere in between the configurations of the reactants and the products, and they are unstable when not assisted by the enzymes. They can only be interpreted as superpositions, and not as mixtures—we have to accept that the enzymes stabilize such intermediate superposition states while driving biomolecular processes. Thus we arrive at the heart of the inquiry:

> *Grover's algorithm needs certain type of superpositions, and catalytic enzymes can stabilize certain type of superpositions. Do the two match, and if so, what is the nature of this superposition?*

The specific details of the answer depend on the dynamical mechanism involved. The requisite superposition is of molecules that have a largely common structure while differing from each other by about 5-10 atoms. I have proposed two possibilities [Patel (2001a, 2006b)]:

(1) In a quantum scenario, wavefunctions get superposed and the algorithm enhances the probability of finding the desired state. Chemically distinct molecules cannot be directly superposed, but they can be effectively superposed by a rapid cut-and-paste job of chemical groups (enzymes are known to perform such cut-and-paste jobs). Whether this really occurs, faster than the identification time scale t_b and with the decoherence time scale significantly longer than $\hbar/\omega_0$, is a question that should be experimentally addressed. It is a tough proposition, and most theoretical estimates are pessimistic.

(2) In a classical wave scenario, all the candidate molecules need to be present simultaneously and coupled together in a specific manner. The algorithm concentrates mechanical energy of the system into the desired molecule by coherent oscillations, helping it cross the energy barrier and complete the chemical reaction. Enzymes are required to couple the components together with specific normal modes of oscillation, and long enough coherence times are achievable. This scenario provides the same speed up in the number of queries Q as the quantum one, but involves extra spatial costs. The extra cost is not insurmountable in the small N solutions relevant to genetic languages, and the extra stability against decoherence makes the classical wave scenario preferable. (Once again note that time optimization is far more important in biology than space optimization.)

Twists and turns can be added to these scenarios while constructing a detailed picture. But in any implementation of Grover's algorithm, the requirement of superposition would manifest itself as simultaneous presence of all the candidate molecules during the selection process, in contrast to the one by one trials of a Boolean algorithm. This particular aspect can be experimentally tested by the available techniques of isotope substitution, NMR spectroscopy and resonance frequency measurements. The algorithm also requires the enzymes to play a central role in driving the non-equilibrium selection process, but direct observation of that would have to await breakthroughs in technologies at nanometre and femtosecond scales.

10.8. Outlook

Information theory provides a powerful framework for extracting essential features of complicated processes of life, and then analysing them in a systematic manner. The easiest processes to study are no doubt the ones at the lowest level. We have learned a lot, both in computer science and in molecular biology, since their early days [Schrödinger (1944); von Neumann (1958); Crick (1968)], and so we can now perform a much more detailed study. Physical theories often start out as effective theories, where predictions of the theories depend on certain parameters. The values of the parameters have to be either assumed or taken from experiments; the effective theory cannot predict them. To understand why the parameters have the values they do, we have to go one level deeper—typically to smaller

scales. When the deeper level reduces the number of unknown parameters, we consider the theory to be more complete and satisfactory. The level below conventional molecular biology is spanned by atomic structure and quantum dynamics, and that is the natural place to look for reasons behind life's "frozen accident". It is indeed wonderful that sufficient ingredients exist at this deeper level to explain the frozen accident as the optimal solution. The first reward of this analysis has been a glimpse of how the optimal solution was arrived at.

Evolution of life occurs through random events (i.e. mutations), without any foresight or precise rules of logic. It is the powerful criterion of survival, in a usually uncomfortable and at times hostile environment, that provides evolution a direction. Even though we do not really understand why living organisms want to perpetuate themselves, we have enough evidence to show that they use all available means for this purpose [Dawkins (1989)]. This struggle for fitness allows us to assign underlying patterns to evolution—not always perfect, frequently with variations, and yet very much practical. By understanding these patterns, we can narrow down the search for a likely evolutionary route among a multitude of possibilities. Such an insight is invaluable when we want to extrapolate in the unknown past with scant direct evidence. That is certainly the case in trying to understand the origin of life as we know it. Of course, the inferences become stronger when supported by simulated experiments, and worthwhile tests of every hypothesis presented have been pointed out in the course of this article.

Counting the number of building blocks in the languages of DNA and proteins, and finding patterns in them, is only the beginning of a long exercise to master these languages. Natural criteria for the selection of particular building blocks would be chemical simplicity (for easy availability and quick synthesis) and functional ability (for implementing the desired tasks). Life can be considered to have originated, not with just complex chemical interactions in a primordial soup, but only when the knowledge of functions of biomolecules started getting passed from one generation to the next. This logic puts the RNA world before the modern genetic machinery; ribozymes provide both function and memory, to a limited extent but with simpler ingredients. During evolution, the structurally more versatile polypeptides—they have been observed to successfully mimic DNA [Walkinshaw *et al.* (2002)] as well as tRNA [Nakamura (2001)]—took over the task of creating complex biochemistry, while leaving the memory storage job to DNA. The work described in this chapter definitely reinforces this point of view, with simpler predecessors of the modern genetic languages

to be found in the stereochemical interaction between the tRNA acceptor stem and simple class II amino acids. Experimental verification of this hypothesis would by and large solve the translation mystery, i.e. which amino acid corresponds to which codon/anticodon? Then we can push the analysis further back in time, to the still simpler language of ribozymes, and try to figure out what went on in the RNA world.

The opposite direction of investigation, of constructing words and sentences from the letters of alphabets, is much more than a theoretical adventure and closely tied to what the future holds for us. We want to design biomolecules that carry out specific tasks, and that needs unraveling how the functions are encoded in the three dimensional protein assembly process. This is a tedious and difficult exercise, involving hierarchical structures and subjective variety. But some clues have appeared, and they should be built on to understand more and more complicated processes of life. We may feel uneasy and scared about consequences of redesigning ourselves, but that after all would also be an inevitable part of evolution!

"... when the pie was opened, the birds began to sing ..."

References

Arnez, J. G., and Moras, D. (1997). Structural and functional considerations of the aminoacyl reaction, *Trends Biochem. Sci.* **22**, pp. 211–216.

Aumann, R. J. (2006). War and Peace, *Les Prix Nobel 2005*, ed. K. Grandin (The Nobel Foundation, Stockholm), pp. 350–358.

Creighton, T. E. (1993). *Proteins: Structures and Molecular Properties*, 2nd ed. (W. H. Freeman, New York).

Crick, F. H. C. (1966). Codon-anticodon pairing: the wobble hypothesis, *J. Mol. Biol.* **19**, pp. 548–555.

Crick, F. H. C. (1968). The origin of the genetic code, *J. Mol. Biol.* **38**, pp. 367–379.

Dawkins, R. (1989). *The Selfish Gene* (Oxford University Press, Oxford).

Gesteland, R. F., Cech, T. R., and Atkins, J. F. (Eds.) (2006). *The RNA World*, 3rd ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor).

Giulini, D., Joos, E., Kiefer, C., Kupsch, J., Stamatescu, I.-O., and Zeh, H. D. (1996). *Decoherence and the Appearance of a Classical World in Quantum Theory* (Springer, Berlin).

Goldgur, Y., Mosyak L., Reshetnikova, L., Ankilova, V., Lavrik, O., Khodyreva, S., and Safro, M. G. (1997). The crystal structure of phenylalanyl-tRNA synthetase from th. thermophilus complexed with cognate $tRNA^{Phe}$, *Structure* **5**, pp. 59–68.

Grover, L. K. (1996). A fast quantum mechanical algorithm for database search, *Proc. 28th Annual ACM Symposium on Theory of Computing*, Philadelphia, pp. 212–219, `arXiv.org:quant-ph/9605043`.

Lehninger, A. L., Nelson, D. L. and Cox, M. M. (1993). *Principles of Biochemistry*, 2nd ed. (Worth Publishers, USA).

Lewin, B. (2000). *Genes VII* (Oxford University Press, Oxford).

Nakamura, Y. (2001). Molecular mimicry between protein and tRNA, *J. Mol. Evol.* **53**, pp. 282-289.

Patel, A. (2001a). Quantum algorithms and the genetic code, *Pramana* **56**, pp. 367–381, `arXiv.org:quant-ph/0002037`.

Patel, A. (2001b). Testing quantum dynamics in genetic information processing, *J. Genet.* **80**, pp. 39–43, `arXiv.org:quant-ph/0102034`.

Patel, A. (2002). Carbon—the first frontier of information processing, *J. Biosc.* **27**, pp. 207–218, `arXiv.org:quant-ph/0103017`.

Patel, A. (2003). Mathematical Physics and Life, *Computing and Information Sciences: Recent Trends*, ed. J. C. Misra (Narosa, New Delhi), pp. 271–294, `arXiv.org:quant-ph/0202022`.

Patel, A. (2005). The triplet genetic code had a doublet predecessor, *J. Theor. Biol.* **233**, pp. 527–532, `arXiv.org:q-bio.GN/0403036`.

Patel, A. (2006a). The future of computation, *Proc. QICC 2005*, IIT Kharagpur, eds. S. P. Pal and S. Kumar (Allied Publishers, Mumbai), pp. 197–206, `arXiv.org:quant-ph/0503068`.

Patel, A. (2006b). Optimal database search: waves and catalysis, *Int. J. Quant. Inform.* **4**, pp. 815–825; Erratum *ibid.* **5**, p. 437, `arXiv.org:quant-ph/0401154`.

Ramachandran, G.N., Ramakrishnan, C. and Sasisekharan, V. (1963). *J. Mol. Biol.* **7**, pp. 95–99.

Rawlinson, G.E. (1976). *The Significance of Letter Position in Word Recognition*, PhD Thesis, Psychology Department, University of Nottingham, UK.

Ribas de Pouplana, L. and Schimmel, P. (2001). Aminoacyl-tRNA synthetases: potential markers of genetic code Development, *Trends Biochem. Sci.* **26**, pp. 591-596.

Rodin, S. N., and Rodin, A. S. (2006). Partitioning of aminoacyl-tRNA synthetases in two classes could have been encoded in a strand-symmetric RNA world, *DNA Cell Biol.* **25**, pp. 617–626.

Russ, W. P., Lowery, D. M., Mishra, P., Yaffe, M. B., and Ranganathan, R. (2005). Nature-like function in artificial WW domains, *Nature* **437**, pp. 579–583.

Schimmel, P., Giege, R., Moras, D., and Yokoyama, S. (1993). An operational RNA code for amino acids and possible relationship to genetic code, *Proc. Natl. Acad. Sci. USA* **90**, pp. 8763–8768.

Schrödinger, E. (1944). *What is Life?* (Cambridge University Press, Cambridge).

Shannon, C. E. (1948). A mathematical theory of communication, *Bell System Tech. J.* **27**, pp. 379–423; 623–656.

Socolich, M., Lockless, S. W., Russ, W. P., Lee, H., Gardner, K. H. and Ranganathan, R. (2005). Evolutionary information for specifying a protein fold, *Nature* **437**, pp. 512–518.

von Neumann, J. (1958). *The Computer and the Brain* (Yale University Press, New Haven).

Walkinshaw, M. D., Taylor, P., Sturrock, S. S., Atanasiu, C., Berge, T., Henderson, R. M., Edwardson, J. M. and Dryden, D. T. F. (2002). Structure of ocr from bacteriophage T7, a protein that mimics B-form DNA, *Mol. Cell* **9**, pp. 187-194.

Woese, C. R., Olsen, G. J., Ibba, M. and Söll, D. (2000). Aminoacyl-tRNA synthetases, the genetic code and the evolutionary process, *Microbiol. Mol. Biol. Rev.* **64**, pp. 202–236.

Wu, H.-L., Bagby, S. and van den Elsen, J. M. H. (2005). Evolution of the genetic triplet code via two types of doublet codons, *J. Mol. Evol.* **61**, pp. 54–64.

Yaremchuk, A., Kriklivyi, I., Tukhalo, M. and Kusack, S. (2002). Class I tyrosyl-tRNA synthetase has a class II mode of tRNA recognition, *EMBO J.* **21**, pp. 3829–3840.

Yarus, M., Caporaso, J. G. and Knight, R. (2005). Origins of the genetic code: the escaped triplet theory, *Ann. Rev. Biochem.* **74**, pp. 179–198.

About the author

Apoorva D. Patel is a Professor at the Centre for High Energy Physics, Indian Institute of Science, Bangalore. He obtained his MSc in Physics from the Indian Institute of Technology, Mumbai, and PhD in Physics from the California Institute of Technology (Caltech) under Geoffrey Fox (1984). His major field of work has been the theory of QCD, where he has used lattice gauge theory techniques to investigate spectral properties, phase transitions and matrix elements. In recent years, he has worked on quantum algorithms, and used information theory concepts to understand the structure of genetic languages.

This page intentionally left blank

PART 4

Artificial Quantum Life

This page intentionally left blank

Chapter 11

Can Arbitrary Quantum Systems Undergo Self-replication?

Arun K. Pati and Samuel L. Braunstein

Arbitrary quantum states cannot be copied. In fact, to make a copy we must provide complete information about the system. However, can a quantum system self-replicate? This is not answered by the no-cloning theorem. In the classical context, von Neumann showed that a "universal constructor" can exist that can self-replicate an arbitrary system, provided that it had access to instructions for making a copy of the system. We question the existence of a universal constructor that may allow for the self-replication of an arbitrary quantum system. We prove that there is no deterministic universal quantum constructor that can operate with finite resources. Further, we delineate conditions under which such a universal constructor can be designed to operate deterministically and probabilistically.

11.1. Introduction

The basis of classical computation is the Church-Turing thesis [Church (1936); Turing (1936)], which says that every recursive function can be computed algorithmically provided the algorithm can be executed by a physical process. However, fundamental physical processes are not governed by classical mechanics, rather by quantum mechanical laws. The possibility of performing reversible computation [Bennett (1973)] and the fact that classical computers cannot efficiently simulate quantum systems [Feynman (1982); Benioff (1982)] gave birth to the concept of the quantum

Received April 26, 2007

Turing machine [Deutsch (1985)]. This led to a flurry of discoveries in quantum computation [Feynman (1986)], quantum algorithms [Bernstein and Vazirani (1993); Deutsch and Jozsa (1992); Shor (1997); Grover (1997)], quantum simulators [Lloyd (1996)], quantum automata [Albert (1983)] and programmable gate arrays [Nielsen and Chuang (1997)]. In another development, von Neumann (1966) thought of an extension of the logical concept of a universal computing machine that might mimic a living system. One of the hall-mark properties of a living system is its capability of self-reproduction. He asked the question: Is it possible to design a machine that could be programmed to produce a copy of itself, in the same spirit that a Turing machine can be programmed to compute any function allowed by physical law? More precisely, he defined a *universal constructor* as a machine that can reproduce itself if it is provided with a program containing its own description. The process of self-reproduction requires two steps: first, the constructor has to produce a copy of itself and second, it has to produce the program of how to copy itself. The second step is important in order that the self-reproduction continues, otherwise, the child copy cannot self-reproduce. When the constructor produces a copy of the program, then it attaches it to the child copy and the process repeats. Unexpectedly, working with classical cellular automata it was found that there is indeed a universal constructor capable of self-reproducing.

In a sense, von Neumann's universal constructor is a "Turing test of life" [Adami (1995)] if we attribute the above unique property to a living system, though there are other complex properties such as the ability to self-repair, grow and evolve. From this perspective, the universal constructor is a very useful model to explore and understand under what conditions a system is capable of self-reproducing (either artificially or in reality). If one attempts to understand elementary living systems as quantum mechanical systems in an information theoretic sense, then one must first try to find out whether a *universal quantum constructor* exists. In a simple and decisive manner, we find that an all-purpose quantum mechanical constructor operating in a closed universe with finite resources cannot exist.

Wigner was probably the first to address the question of replicating machines in the quantum world and found that it is infinitely unlikely that such machines can exist [Wigner (1961)]. It is now well known that the information content of a quantum state has two remarkable properties: first, it cannot be copied exactly [Wootters and Zurek (1982); Dieks (1982)] and second, given several copies of an unknown state we cannot delete a copy [Pati and Braunstein (2000)]. In addition, non-orthogonal quantum states

cannot be perfectly copied [Yuen (1986)]. Indeed, the extra information needed to make a copy must be as large as possible—a recent result known as the stronger no-cloning theorem [Jozsa (2002)]. The no-cloning and the no-deleting principles taken together reveal some kind of "permanence" of quantum information.

11.2. Formalizing the Self-replicating Machine

First, we observe that merely the copying of information is *not self-replication*. Therefore, along with the usual quantum mechanical toolkit, we must formalize the question of a self-replicating machine. A quantum mechanical universal constructor may be completely specified by a quadruple $\mathcal{UC} = (|\Psi\rangle, |P_U\rangle, |C\rangle, |\Sigma\rangle)$, where $|\Psi\rangle \in \mathcal{H}^N$ is the state of the (artificial or real) living system that contains quantum information to be self-replicated, $|P_U\rangle \in \mathcal{H}^K$ is the program state that contains instructions to copy the original information, i.e. the unitary operator U needed to copy the state $|\Psi\rangle$ via $U(|\Psi\rangle|0\rangle) = |\Psi\rangle|\Psi\rangle$ is encoded in the program state, $|C\rangle$ is the state of the control unit, and $|\Sigma\rangle = |0\rangle|0\rangle\cdots|0\rangle \in \mathcal{H}^M$ is a collection of blank states onto which the information and the program will be copied. Let there be n blank states each with $|0\rangle \in \mathcal{H}^N$, then the dimension of the blank state Hilbert space is $M = N^n$. Without loss of generality we may assume that an individual blank state $|0\rangle$ may belong to a Hilbert space of dimension equal to N. It is assumed that a *finite* string of blank states are available in the environment in which the universal constructor is operating (they are analogous to the low-entropy nutrient states that are required by a real living system). The justification for a finite number of such states comes from the fact that in the universe the total energy and negative entropy available at any time is always finite [Wigner (1961)]. To copy the program state the machine uses m blank states in one generation, so $K = N^m$. Thus M is finite but $M \gg N, K$. The initial state of the universal constructor is $|\Psi\rangle|P_U\rangle|C\rangle|\Sigma\rangle$. A universal constructor will be said to exist if it can implement copying of the original and the stored program by a fixed linear unitary operator $\mathcal{L}$ acting on the combined Hilbert space of the input, program, control and $(m+1)$ blank states that allows the following transformation

$$\begin{aligned}&\mathcal{L}(|\Psi\rangle|0\rangle|P_U\rangle|0\rangle^m|C\rangle)|0\rangle^{n-(m+1)}\\&\quad= |\Psi\rangle|P_U\rangle\mathcal{L}(|\Psi\rangle|0\rangle|P_U\rangle|0\rangle^m|C'\rangle)|0\rangle^{n-2(m+1)}\,,\end{aligned}\tag{11.1}$$

where $|C'\rangle$ is the final state of the control unit. It is worth emphasizing that Eq. (11.1) is not a cloning transformation. It is a *recursively defined transformation* where the fixed unitary operator $\mathcal{L}$ acts on the initial (parent) configuration and the same operator acts on the final (child) configuration after the copies have been produced. This definition is required in order that the self-replication proceeds in an *autonomous* manner until the blank states are exhausted. The fixed unitary operator will not act on the child configuration unless $(m+1)$ nutrient states are available in the universe. Once the transformation is complete, the control unit separates the original information from the program states (parent information) so that the off-spring exists independently. It then continues to self-reproduce.

If such a universal constructor exists, then when it is fed with another state $|\Phi\rangle$ and a suitable program $|P_V\rangle$ to create it via $V(|\Phi\rangle|0\rangle) = |\Phi\rangle|\Phi\rangle$ then it will allow the transformation

$$\begin{aligned}&\mathcal{L}(|\Phi\rangle|0\rangle|P_V\rangle|0\rangle^m|C\rangle)|0\rangle^{n-(m+1)}\\&\quad= |\Phi\rangle|P_V\rangle\mathcal{L}(|\Phi\rangle|0\rangle|P_V\rangle|0\rangle^m|C''\rangle)|0\rangle^{n-2(m+1)}\,.\end{aligned}\tag{11.2}$$

11.3. Proof of No-self-replication

If such a machine can make a copy of any state along with its program in a unitary manner, then it must preserve the inner product. This implies that we must have

$$\langle\Psi|\Phi\rangle\langle P_U|P_V\rangle = \langle\Psi|\Phi\rangle^2\langle P_U|P_V\rangle^2\langle C'|C''\rangle\,,\tag{11.3}$$

holds true. However, the above equation tells us that the universal constructor can exist only under two conditions, namely, (i) either $\langle\Psi|\Phi\rangle = 0$ and $\langle P_U|P_V\rangle \neq 0$ or (ii) $\langle\Psi|\Phi\rangle \neq 0$ and $\langle P_U|P_V\rangle = 0$. The first condition suggests that for orthogonal states as the carrier of information, there is no restriction on the program state. This means that with a finite dimensional program state and a finite number of blank states orthogonal states can self-replicate. Such a universal constructor can exist with finite resources. This corresponds to the realization of a classical universal constructor, and is consistent with von Neumann's thesis, that a self-reproducing general purpose machine can exist, in principle, in a deterministic universe [von Neumann (1966)]. However, the second condition tells us that for non-orthogonal states, the program states have to be orthogonal. This means that to perfectly self-replicate a collection of non-orthogonal states $\{|\Psi_i\rangle\}$ together with their program states $\{|P_{U_i}\rangle, i = 1, 2, \ldots\}$ one

requires that the states $|P_{U_i}\rangle$ should be orthogonal. Since an arbitrary state such as $|\Psi\rangle = \sum_i \alpha_i |i\rangle$ with the complex numbers α_i's varying continuously can be viewed as an infinite collection of non-orthogonal states (or equivalently the set of non-orthogonal states for a single quantum system is infinite, even for a simplest two-state system such as a qubit), one requires an infinite-dimensional program state to copy it. In one generation of the self-replication the number of blank states used to copy the program state is $m = \log_2 K / \log_2 N$ and when $K \to \infty$ the nutrient resource needed also becomes infinite. As a consequence, to copy an infinite-dimensional Hilbert space program state one needs an infinite collection of blank states to start with. Furthermore, the number of generations g for which the self-reproduction can occur with a finite nutrient resource is $g = \log_2 M/(\log_2 KN)$. When K becomes infinite, then there can be no generations supporting self-reproduction. Therefore, we surmise that *with a finite-dimensional program state and a finite nutrient resource there is no deterministic universal constructor for arbitrary quantum states.*

11.4. Discussion

One may ask is it not possible to rule out the nonexistence of deterministic universal constructor from the no-cloning principle? The answer is "no" for two reasons. First, a simple universal cloner is *not* a universal constructor. Second, in a universal constructor we provide the complete specification about the input state, hence it should have been possible to self-reproduce, thus reaching an opposite conclusion! The surprising and remarkable result is that when we ask a constructor to self-replicate any arbitrary living species, then it cannot. The perplexity of the problem lies where we attempt to copy the program. If it has to self-replicate then it violates the unitarity of quantum theory.

This result may have immense bearing on explaining life based on quantum theory. One may argue that after all if everything comes to the molecular scale then there are a variety of physical actions and chemical reactions that might be explained by the basic laws of quantum mechanics. However, if one applies quantum theory, then as we have proved an arbitrary quantum mechanical living organism cannot self-replicate. Interpreting this differently, we might say that the present structure of quantum theory cannot model a living system as it fails to mimic a minimal living system. *Quantum mechanizing a living system seems to be an impossible task.* If

that holds true, then this conclusion is going to have rather deep implications for our present search for the ultimate laws of nature encompassing both the physical and biological world. On the other hand, because the self-reproducible information must be "classical" the replication of DNA in a living cell can be understood purely by classical means. Having said this, our result does not preclude the possibility that quantum theory might play a role in explaining other features of living systems [Penrose (1994); McFadden (2000)]. For example, there is a recent proposal that quantum mechanics may explain why living organisms have four nucleotide bases and twenty amino acids [Patel (2001)]. It has been also reported that the game of life can emerge in the semi-quantum mechanical context [Flitney and Abbott (2002)]—see Chapter 12.

Implications of our results are multifold for physical and biological sciences. It is beyond doubt that progress in the burgeoning area of quantum information technology can lead to revolutions in the machines that one cannot think of at present. If a quantum mechanical universal constructor would have been possible, future technology would have allowed quantum computers to self-replicate themselves with little or no human input. That would have been a completely autonomous device—a truly marvelous thing. However, as we have shown, a deterministic universal constructor with finite resources is impossible in principle. One may have to look instead to probabilistic universal constructors that could self-replicate with only a limited probability of success, similar to a probabilistic cloner [Duan and Guo (1998)]. This could still have great implications for the future. With a complete specification such a machine could construct copies based on its own quantum information processing devices. Future lines of exploration may lead to the design of approximate universal constructors in analogy with approximate universal quantum cloners [Buzek and Hillery (1996)].

11.5. Conclusion

How life emerges from inanimate quantum objects has been a conundrum [Schrödinger (1944); Elsasser (1958); Chaitin (1970); Davies (1995)]. What we have shown here is that quantum mechanics fails to mimic a self-reproducing unit in an autonomous way. Nevertheless, if one allows for errors in self-replication, which actually do occur in real living systems, then an approximate universal constructor should exist. Such a machine would constitute a quantum mechanical mutation machine. It would be

important to see how variations in "life" emerge due to the errors in self-replication. From this perspective, if quantum mechanics is the final theory of Nature, our result indicates that the information stored in a living organism is copied imperfectly and the error rate may be just right in order for mutation to occur to drive Darwinian evolution. In addition, one could study how the quantum evolution of species leads to an increase in the level of complexity in living systems. Since understanding these basic features of life from quantum mechanical principles is a fundamental task, we hope that the present result is a first step in that direction, and will be important in the areas of quantum information, artificial life, cellular automata, and last but not least in biophysical science.

Acknowledgments

We thank C. Fuchs for bringing the paper of E. P. Wigner to our attention. AKP wishes to thank C. H. Bennett, S. Lloyd, and I. L. Chuang for useful discussions. SLB currently holds a Wolfson–Royal Society Research Merit Award.

References

Adami, C. (1995). On modeling life, *Artificial Life* **1**, pp. 429–438.

Albert, D. Z. (1983). On quantum mechanical automata, *Phys. Lett. A* **98**, pp. 249–252.

Benioff, P. (1982). Quantum mechanical Hamiltonian models of Turing machines that dissipates no energy, *Phys. Rev. Lett.* **48**, pp. 1581–1585.

Bennett, H. H. (1973). Logical reversibility of computation, *IBM Journal of Research and Development* **17**, pp. 525–532.

Bernstein, E., and Vazirani, U. (1993). Quantum complexity theory, *Proc. 25th Annual ACM Symposium on Theory of Computing*, pp. 11–20.

Buzek, V., and Hillery, M. H. (1996). Quantum copying: Beyond the no-cloning theorem, *Phys. Rev. A* **54**, pp. 1844–1852.

Chaitin, G. J. (1970). To a mathematical definition of life, *ACM SICACT News* **4**, pp. 12–18.

Church, A. (1936). An unsolvable problem of elementary number theory, *Am. J. Math.* **58** pp. 345–363.

Davies, P. C. W. (1995). *The Cosmic Blueprint* (Penguin).

Deutsch, D. (1985). Quantum theory, the Church-Turing principle and the universal computers, *Proc. R. Soc. London* A **400**, pp. 97–11.

Deutsch, D., and Jozsa, R. (1992). Rapid solutions of problems by quantum computation, *Proc. R. Soc. London A* **449**, pp. 553–558.

Dieks, D. (1982). Communication by EPR devices, *Phys. Lett. A* **92**, pp. 271–272.
Duan, L. M., and Guo, G. C. (1998). Probabilistic cloning and identification of linearly independent states, *Phys. Rev. Lett.* **80**, pp. 4999–5002.
Elsasser, W. M. (1968). *The Physical Foundation of Biology* (Pergamon Press).
McFadden, J. (2000). *Quantum Evolution* (Harper Collins).
Feynman, R. (1982). Simulating physics with computers, *Int. J. Theo. Phys.* **21**, pp. 467–488.
Feynman, R. (1986). Quantum mechanical computers, *Found. Phys.* **16**, pp. 507–531.
Flitney, A. P., and Abbott, D. (2002). A semi-quantum version of the game of life, `arXiv quant-ph 0208149`.
Grover, L. K. (1997). Quantum mechanics helps in searching a needle in a haystack, *Phys. Rev. Lett.* **79**, pp. 325–328.
Jozsa, R. (2002). A stronger no-cloning theorem, `arXiv quant-ph 0204153`.
Lloyd, S. (1996). Universal quantum simulators, *Science* **263**, pp. 1073–1078.
Nielsen, M. A., and Chuang, I. L. (1997). Programmable quantum gate arrays, *Phys. Rev. Lett.* **79**, pp. 321–324.
von Neumann, J. (1966). *The Theory of Self-Replicating Automata* (University of Illinois Press).
Patel, A. (2001). Why genetic information processing could have a quantum basis, *J. of Bioscience* **26**, pp. 145–151.
Pati, A. K., and Braunstein, S. L. (2000). Impossibility of deleting an unknown quantum state, *Nature* **404**, p. 164.
Penrose, R. (1994). *Shadows of the Mind* (Oxford University Press).
Schrödinger, E. (1944). *What is life?* (Cambridge University Press).
Shor, P (1997). Polynomial-time algorithms for prime factorization and discrete logarithms on a quantum computer, *SIAM J. Comput.* **265**, pp. 1484–1509.
Turing, A. M. (1936). On computable numbers with an application to the Entscheidungs problem, *Proc. Lond. Math. Soc.* **42**, pp. 230–265.
Wigner, E. P. (1961). The probability of the existence of a self-reproducing unit, *The Logic of Personal Knowledge: Essays Presented to Michael Polany on his Seventieth Birthday* (Routledge & Kegan Paul, London) pp. 231–238.
Wootters, W. K., and Zurek, W. H. (1982). A single quantum cannot be cloned, *Nature* **299**, pp. 802–803.
Yuen, H. P. (1986). Amplification of quantum states and noiseless photon amplifiers, *Phys. Lett. A* **113**, pp. 405–407.

About the authors

Arun K. Pati obtained his PhD from the University of Bombay, Mumbai, India. He has been a theoretical physicist in the Theoretical Physics Division, BARC, Mumbai, India since 1989, and is currently a visiting scientist at the Institute of Physics, Bhubaneswar, India. His research is in

quantum information and computation, the theory of geometric phases and its applications, and the foundations of quantum mechanics. He is also interested in the quantum mechanics of bio-systems. He has published over 60 papers on these topics and has edited a book on quantum information theory. Pati is the recipient of the India Physics Association Award for Young Physicist of the Year (2000) and the Indian Physical Society Award for Young Scientists (1996). His research has been featured in news items in *Nature*, *Science* and many national and international newspapers.

Samuel L. Braunstein obtained his PhD from Caltech, USA, under Carlton Caves. He joined the University of York, in 2003 and is heading a group in non-standard computation. He is a recipient of the prestigious Royal Society-Wolfson Research Merit Award. He was recently awarded the honorary title of 2001 Lord Kelvin Lecturer. He is editor of three books *Quantum Computing*, *Scalable Quantum Computing* and *Quantum Information with Continuous Variables* and serves on the editorial board of the journal *Fortschritte der Physik*. He is a Founding Managing Editor of *Quantum Information and Computation*. He has over 90 papers published in refereed journals. His work has received extensive coverage in prestigious scientific venues such as *Science*, *Nature*, *Physics Today*, *New Scientist* and daily newspapers around the world.

This page intentionally left blank

Chapter 12

A Semi-quantum Version of the Game of Life

Adrian P. Flitney and Derek Abbott

Cellular automata provide a means of obtaining complex behaviour from a simple array of cells and a deterministic transition function. They supply a method of computation that dispenses with the need for manipulation of individual cells and they are computationally universal. Classical cellular automata have proved of great interest to computer scientists but the construction of quantum cellular automata pose particular difficulties. This chapter presents a version of John Conway's famous two-dimensional classical cellular automata Life that has some quantum-like features, including interference effects. Some basic structures in the new automata are given and comparisons are made with Conway's game.

12.1. Background and Motivation

12.1.1. *Classical cellular automata*

A cellular automaton (CA) consists of an infinite array of identical cells, the states of which are simultaneously updated in discrete time steps according to a deterministic rule. Formally, they consist of a quadruple (d, Q, N, f), where $d \in \mathbb{Z}^+$ is the dimensionality of the array, Q is a finite set of possible states for a cell, $N \subset \mathbb{Z}^d$ is a finite neighbourhood, and $f : Q^{|N|} \to Q$ is a local mapping that specifies the transition rule of the automaton. The simplest cellular automata are constructed from a one-dimensional array

Received February 10, 2006

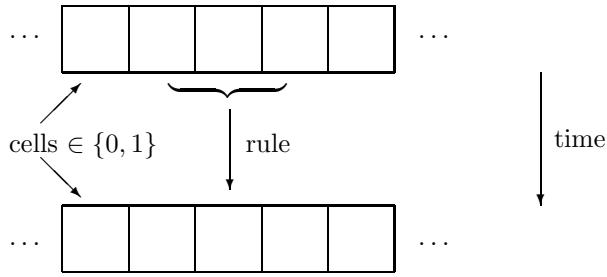


Fig. 12.1. A schematic of a one-dimensional, nearest neighbour, classical cellular automaton showing the updating of one cell in an infinite array.

of cells taking binary values, with a nearest neighbour transition function, as indicated in Fig. 12.1. Such CA were studied intensely by Wolfram (1983) in a publication that lead to a resurgence of interest in the field. Wolfram classified cellular automata into four classes. The classes showed increasingly complex behaviour, culminating in class four automata that exhibited self-organization, that is, the appearance of order from a random initial state.

In general, information is lost during the evolution of a CA. Knowledge of the state at a given time is not sufficient to determine the complete history of the system. However, reversible CA are of particular importance, for example, in the modeling of reversible phenomena. Furthermore, it has been shown that there exists a one-dimensional reversible CA that is computationally universal [Morita (1989)]. Toffoli (1977) demonstrated that any d-dimensional CA could be simulated by a $(d+1)$-dimensional reversible CA and later Morita (1995) found a method using partitioning (see Fig. 12.2) whereby any one-dimensional CA can be simulated by a reversible one-dimensional CA. There is an algorithm for deciding on the reversibility of a one-dimensional CA [Amoroso and Patt (1972)], but in dimensions greater than one, the reversibility of a CA is, in general, undecidable [Kari (1990)].

12.1.2. *Conway's game of life*

John Conway's game of Life [Gardner (1970)] is a well known two-dimensional CA, where cells are arranged in a square grid and have binary values generally known as "dead" or "alive." The status of the cells change in discrete time steps known as "generations." The new value depends

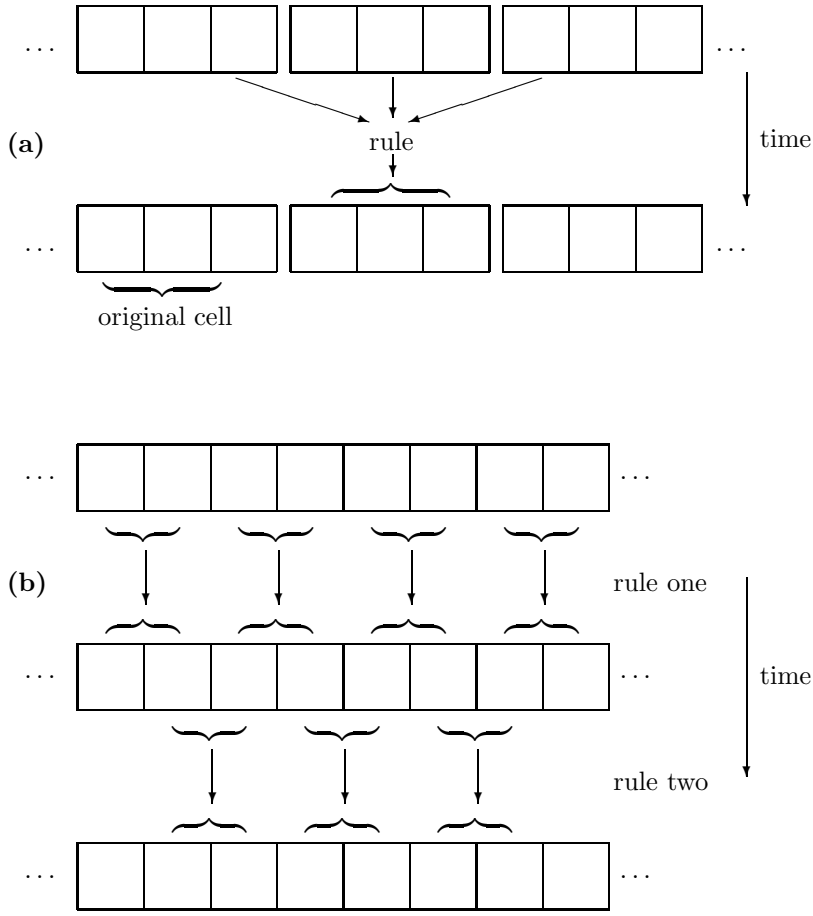


Fig. 12.2. A schematic of a one-dimensional, nearest neighbour, classical (a) partitioned cellular automaton [Morita (1995)] and (b) block (or Margolus) partitioned cellular automata. In (a), each cell is initially duplicated across three cells and a new transition rule $f : Q^3 \to Q^3$ is used. In (b), a single step of the automata is carried out over two clock cycles, each with its own rule $f : Q^2 \to Q^2$.

upon the number of living neighbours, the general idea being that a cell dies if there is either overcrowding or isolation. There are many different rules that can be applied for birth or survival of a cell and a number of these give rise to interesting properties such as still lives (stable patterns), oscillators (patterns that periodically repeat), spaceships or gliders (fixed shapes that move across the Life universe), glider guns, and so on

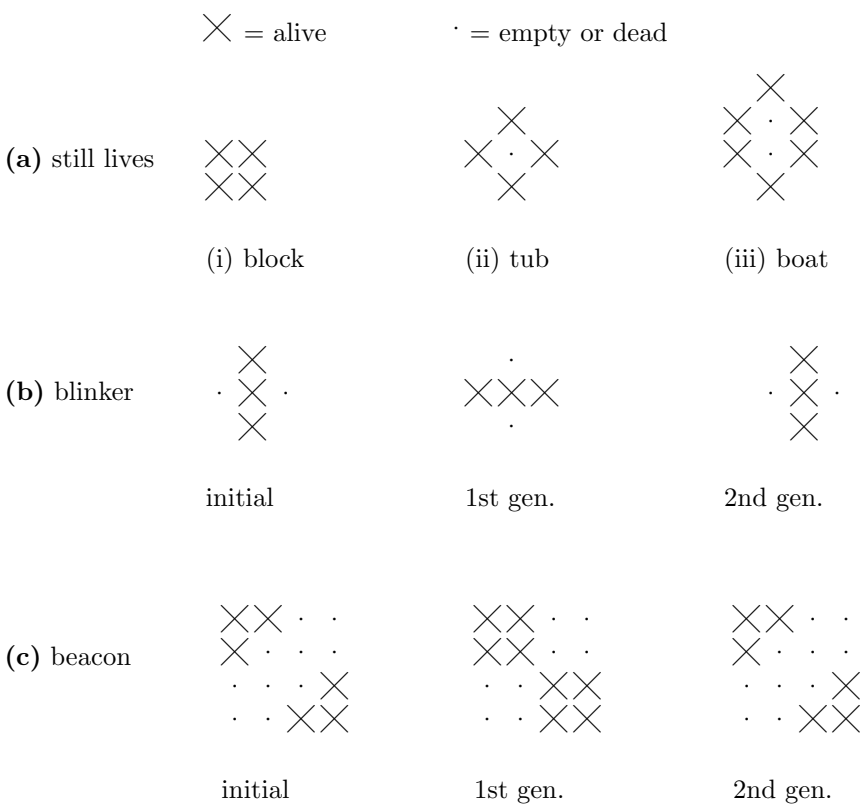


Fig. 12.3. A small sample of the simplest structures in Conway's Life: (a) the simplest still-lives (stable patterns) and (b)–(c) the simplest period two oscillators (periodic patterns). A number of these forms will normally evolve from any moderate sized random collection of alive and dead cells.

[Gardner (1971, 1983); Berlekamp *et al.* (1982)]. Conway's original rules are one of the few that are balanced between survival and extinction of the Life "organisms." In this version a dead (or empty) cell becomes alive if it has exactly three living neighbours, while an alive cell survives if and only if it has two or three living neighbours. Much literature on the game of Life and its implications exists and a search on the world wide web reveals numerous resources. For a discussion on the possibilities of this and other CA the interested reader is referred to Wolfram (2002).

The simplest still lives and oscillators are given in Fig. 12.3, while Fig. 12.4 shows a glider, the simplest and most common moving form.

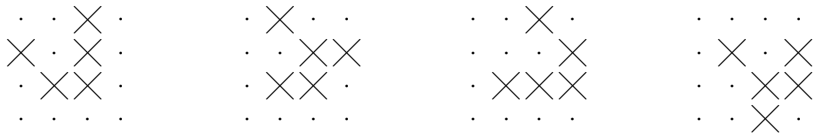


Fig. 12.4. In Conway's Life, the simplest spaceship (a pattern that moves continuously through the Life universe), the glider. The figure shows how the glider moves one cell diagonally over a period of four generations, the fourth generation (not shown) is the same as the first moved diagonally down and to the right.

A large enough random collection of alive and dead cells will, after a period of time, usually decay into a collection of still lives and oscillators like those shown here, while firing a number of gliders off toward the outer fringes of the Life universe.

12.1.3. *Quantum cellular automata*

The idea of generalizing classical cellular automata to the quantum domain was already considered by Feynman (1982). Grössing and Zeilinger made the first serious attempts to consider quantum cellular automata (QCA) [Grössing and Zeilinger (1988a,b)], though their ideas are considerably different from modern approaches. Quantum cellular automata are a natural model of quantum computation where the well developed theory of classical CA might be exploited. Quantum computation using optical lattices [Mandel *et al.* (2003)] or with arrays of microtraps [Dumke *et al.* (2002)] are possible candidates for the experimental implementation of useful quantum computing. It is typical of such systems that the addressing of individual cells is more difficult than a global change made to the environment of all cells [Benjamin (2000)] and thus they become natural candidates for the construction of QCA. An accessible discussion of QCA is provided by Gruska (1999). The simple idea of quantizing existing classical CA by making the local translation rule unitary is problematic: the global rule on an infinite array of cells is rarely described by a well defined unitary operator. One must decide whether a given local unitary rule leads to "well-formed" unitary QCA [Dürr and Santha (2002)] that properly transform probabilities by preserving their sum squared to one. One construction method to achieve the necessary reversibility of a QCA is to partition the system into

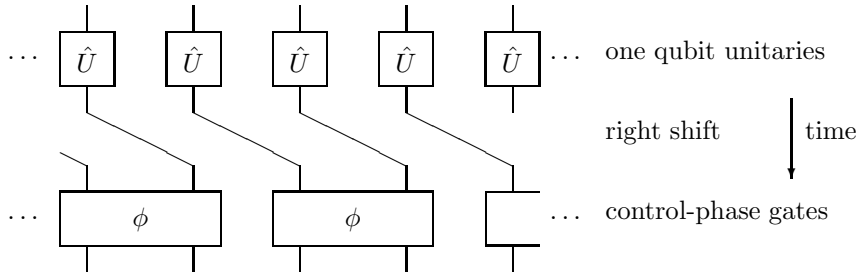


Fig. 12.5. A schematic of a one-dimensional nearest neighbour quantum cellular automaton according to the scheme of Schumacher and Werner (2004) (from Fig. 10 of that publication). The right-shift may be replaced by a left-shift or no shift.

blocks of cells and apply blockwise unitary transformations. This is the quantum generalization to the scheme shown in Fig. 12.2(b)—indeed, all QCA, even those with local irreversible rules, can be obtained in such a manner [Schumacher and Werner (2004)]. Formal rules for the realization of QCA using a transition rule based on a quasi-local algebra on the lattice sites is described by Schumacher and Werner (2004). In this formalism, a unitary operator for the time evolution is not necessary. The authors demonstrate that all nearest neighbour one-dimensional QCA arise by a combination of a single qubit unitary a possible left- or right-shift, and a control-phase gate,[1] as indicated in Fig. 12.5.

Reversible one-dimensional nearest neighbour classical CA are a subset of the quantum ones. In the classical case, the single qubit unitary can only be the identity or a bit-flip, while the control-phase gate is absent. This leaves just six classical CA, all of which are trivial.

12.2. Semi-quantum Life

12.2.1. *The idea*

Conway's Life is irreversible while, in the absence of a measurement, quantum mechanics is reversible. In particular, operators that represent measurable quantities must be unitary. A full quantum Life on an infinite array would be impossible given the known difficulties of constructing unitary QCA [Meyer (1996)]. Interesting behaviour is still obtained in a version

[1] A control-phase gate is a two-qubit gate that multiplies the target qubit by $\left(\begin{smallmatrix} 1 & 0 \\ 0 & \exp(i\phi) \end{smallmatrix}\right)$ if the control qubit is 1.

of Life that has some quantum mechanical features. Cells are represented by classical sine-wave oscillators with a period equal to one generation, an amplitude between zero and one, and a variable phase. The amplitude of the oscillation represents the coefficient of the alive state so that the square of the amplitude gives the probability of finding the cell in the alive state when a measurement of the "health" of the cell is taken. If the initial state of the system contains at least one cell that is in a superposition of eigenstates the neighbouring cells will be influenced according to the coefficients of the respective eigenstates, propagating the superposition to the surrounding region.

If the coefficients of the superpositions are restricted to positive real numbers, qualitatively new phenomena are not expected. By allowing the coefficients to be complex, that is, by allowing phase differences between the oscillators, qualitatively new phenomena such as interference effects, may arise. The interference effects seen are those due to an array of classical oscillators with phase shifts and are not fully quantum mechanical.

12.2.2. *A first model*

To represent the state of a cell introduce the following notation:

$$|\psi\rangle = a|\text{alive}\rangle + b|\text{dead}\rangle, \tag{12.1}$$

subject to the normalization condition

$$|a|^2 + |b|^2 = 1. \tag{12.2}$$

The probability of measuring the cell as alive or dead is $|a|^2$ or $|b|^2$, respectively. If the values of a and b are restricted to non-negative real numbers, destructive interference does not occur. The model still differs from a classical probabilistic mixture, since here it is the amplitudes that are added and not the probabilities. In our model $|a|$ is the amplitude of the oscillator. Restricting a to non-negative real numbers corresponds to the oscillators all being in phase.

The birth, death and survival operators have the following effects:

$$\begin{aligned} \hat{B}|\psi\rangle &= |\text{alive}\rangle\,, \\ \hat{D}|\psi\rangle &= |\text{dead}\rangle\,, \\ \hat{S}|\psi\rangle &= |\psi\rangle\,. \end{aligned} \tag{12.3}$$

A cell can be represented by the vector $\binom{a}{b}$. The $\hat{B}$ and $\hat{D}$ operators are not unitary. Indeed they can be represented in matrix form by

$$\begin{aligned} \hat{B} &\propto \begin{pmatrix} 1 & 1 \\ 0 & 0 \end{pmatrix}, \\ \hat{D} &\propto \begin{pmatrix} 0 & 0 \\ 1 & 1 \end{pmatrix}, \end{aligned} \tag{12.4}$$

where the proportionality constant is not relevant for our purposes. After applying $\hat{B}$ or $\hat{D}$ (or some mixture) the new state will require (re-) normalization so that the probabilities of being dead or alive still sum to unity.

A new generation is obtained by determining the number of living neighbours each cell has and then applying the appropriate operator to that cell. The number of living neighbours in our model is the amplitude of the superposition of the oscillators representing the surrounding eight cells. This process is carried out on all cells effectively simultaneously. When the cells are permitted to take a superposition of states, the number of living neighbours need not be an integer. Thus a mixture of the $\hat{B}$, $\hat{D}$ and $\hat{S}$ operators may need to be applied. For consistency with standard Life the following conditions will be imposed upon the operators that produce the next generation:

- If there are an integer number of living neighbours the operator applied must be the same as that in standard Life.
- The operator that is applied to a cell must continuously change from one of the basic forms to another as the sum of the a coefficients from the neighbouring cells changes from one integer to another.
- The operators can only depend upon this sum and not on the individual coefficients.

If the sum of the a coefficients of the surrounding eight cells is

$$A = \sum_{i=1}^{8} a_i \tag{12.5}$$

then the following set of operators, depending upon the value of A, is the simplest that has the required properties

$$\begin{aligned} 0 \le A \le 1;\ \hat{G}_0 &= \hat{D}\,, \\ 1 < A \le 2;\ \hat{G}_1 &= (\sqrt{2}+1)(2-A)\hat{D} \ + \ (A-1)\hat{S}\,, \\ 2 < A \le 3;\ \hat{G}_2 &= (\sqrt{2}+1)(3-A)\hat{S} \ + \ (A-2)\hat{B}\,, \\ 3 < A < 4;\ \hat{G}_3 &= (\sqrt{2}+1)(4-A)\hat{B} \ + \ (A-3)\hat{D}\,, \\ A \ge 4;\ \hat{G}_4 &= \hat{D}\,. \end{aligned} \tag{12.6}$$

For integer values of A, the $\hat{G}$ operators are the same as the basic operators of standard Life, as required. For non-integer values in the range $(1, 4)$, the operators are a linear combination of the standard operators. The factors of $\sqrt{2}+1$ have been inserted to give more appropriate behaviour in the middle of each range. For example, consider the case where $A = 3 + 1/\sqrt{2}$, a value that may represent three neighbouring cells that are alive and one the has a probability of one-half of being alive. The operator in this case is

$$\hat{G} = \frac{1}{\sqrt{2}}\,\hat{B} + \frac{1}{\sqrt{2}}\,\hat{D}, \propto \frac{1}{\sqrt{2}} \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix}. \tag{12.7}$$

Applying this to either a cell in the alive, $\left(\begin{smallmatrix} 1 \\ 0 \end{smallmatrix}\right)$ or dead, $\left(\begin{smallmatrix} 0 \\ 1 \end{smallmatrix}\right)$ states will produce the state

$$|\psi\rangle = \frac{1}{\sqrt{2}}\,|\text{alive}\rangle + \frac{1}{\sqrt{2}}\,|\text{dead}\rangle \tag{12.8}$$

which represents a cell with a 50% probability of being alive. That is, $\hat{G}$ is an equal combination of the birth and death operators, as might have been expected given the possibility that A represents an equal probability of three or four living neighbours. Of course the same value of A may have been obtained by other combinations of neighbours that do not lie half way between three and four living neighbours, but one of our requirements is that the operators can only depend on the sum of the a coefficients of the neighbouring cells and not on how the sum was obtained.

In general the new state of a cell is obtained by calculating A, applying the appropriate operator $\hat{G}$:

$$\begin{pmatrix} a' \\ b' \end{pmatrix} = \hat{G} \begin{pmatrix} a \\ b \end{pmatrix}, \tag{12.9}$$

and then normalizing the resulting state so that $|a'|^2 + |b'|^2 = 1$. It is this process of normalization that means that multiplying the operator by a constant has no effect. Hence, for example, $\hat{G}_2$ for $A = 3$ has the same effect as $\hat{G}_3$ in the limit as $A \to 3$, despite differing by the constant factor $(\sqrt{2} + 1)$.

12.2.3. *A semi-quantum model*

To get qualitatively different behaviour from classical Life we need to introduce a phase associated with the coefficients, that is, a phase difference between the oscillators. We require the following features from this version of Life:

- It must smoothly approach the classical mixture of states as all the phases are taken to zero.
- Interference, that is, partial or complete cancellation between cells of different phases, must be possible.
- The overall phase of the Life universe must not be measurable, that is, multiplying all cells by $e^{i\phi}$ for some real ϕ will have no measurable consequences.
- The symmetry between $(\hat{B}, |\text{alive}\rangle)$ and $(\hat{D}, |\text{dead}\rangle)$ that is a feature of the original game of Life should be retained. This means that if the state of all cells is reversed ($|\text{alive}\rangle \longleftrightarrow |\text{dead}\rangle$) and the operation of the $\hat{B}$ and $\hat{D}$ operators is reversed the system will behave in the same manner.

In order to incorporate complex coefficients, while keeping the above properties, the basic operators are modified in the following way:

$$\begin{aligned} \hat{B}|\text{dead}\rangle &= e^{i\phi}|\text{alive}\rangle\,, \\ \hat{B}|\text{alive}\rangle &= |\text{alive}\rangle\,, \\ \hat{D}|\text{alive}\rangle &= e^{i\phi}|\text{dead}\rangle\,, \\ \hat{D}|\text{dead}\rangle &= |\text{dead}\rangle\,, \\ \hat{S}|\psi\rangle &= |\psi\rangle\,, \end{aligned} \tag{12.10}$$

where the superposition of the surrounding oscillators is

$$\alpha = \sum_{i=1}^{8} a_i = Ae^{i\phi}\,, \tag{12.11}$$

A and ϕ being real positive numbers. That is, the birth and death operators are modified so that the new alive or dead state has the phase of the sum of the surrounding cells. The operation of the $\hat{B}$ and $\hat{D}$ operators on the state $\binom{a}{b}$ can be written as

$$\begin{aligned} \hat{B}\begin{pmatrix} a \\ b \end{pmatrix} &= \begin{pmatrix} a + |b|e^{i\phi} \\ 0 \end{pmatrix}, \\ \hat{D}\begin{pmatrix} a \\ b \end{pmatrix} &= \begin{pmatrix} 0 \\ |a|e^{i\phi} + b \end{pmatrix}, \end{aligned} \tag{12.12}$$

with $\hat{S}$ leaving the cell unchanged. The modulus of the sum of the neighbouring cells A determines which operators apply, in the same way as before [see Eq. (12.6)]. The addition of the phase factors for the cells allows for interference effects since the coefficients of alive cells may not always reinforce in taking the sum, $\alpha = \sum a_i$. A cell with $a = -1$ still has a unit probability of being measured in the alive state but its effect on the sum will cancel that of a cell with $a = 1$. A phase for the dead cell is retained in order to maintain the alive $\longleftrightarrow$ dead symmetry, however, it has no effect. Such an effect would conflict with the physical model presented earlier and would be inconsistent with Conway's Life, where the empty cells have no influence.

A useful notation to represent semi-quantum Life is to use an arrow whose length represents the amplitude of the a coefficient and whose angle with the horizontal is a measure of the phase of a. That is, the arrow represents the phasor of the oscillator at the beginning of the generation. For example

$$\begin{aligned} \longrightarrow &= \begin{pmatrix} 1 \\ 0 \end{pmatrix}, \\ \uparrow &= e^{i\pi/2}\begin{pmatrix} 1/2 \\ \sqrt{3}/2 \end{pmatrix} = \begin{pmatrix} i/2 \\ i\sqrt{3}/2 \end{pmatrix}, \\ \nearrow &= e^{i\pi/4}\begin{pmatrix} 1/\sqrt{2} \\ 1/\sqrt{2} \end{pmatrix} = \begin{pmatrix} (1+i)/2 \\ (1+i)/2 \end{pmatrix}, \end{aligned} \tag{12.13}$$

etc. In this picture α is the vector sum of the arrows. This notation includes no information about the b coefficient. The magnitude of this coefficient can be determined from a and the normalization condition. The phase of the b coefficient has no effect on the evolution of the game state so it is not necessary to represent this.

12.2.4. *Discussion*

The above rules have been implemented in the computer algebra language *Mathematica*. All the structures of standard Life can be recovered by making the phase of all the alive cells equal. The interest lies in whether there are new effects in the semi-quantum model or whether existing effects can be reproduced in simpler or more generalized structures. The most important aspect not present in standard Life is interference. Two live cells can work against each other as indicated in Fig. 12.6 that shows an elementary example in a block still life with one cell out of phase with its neighbours. In standard Life there are linear structures called wicks that die or "burn" at a constant rate. The simplest such structure is a diagonal line of live cells as indicated in Fig. 12.7(a). In this, it is not possible to stabilize an end without introducing other effects. In the new model a line of cells of alternating phase (... $\longrightarrow\!\longleftarrow$ ...) is a generalization of this effect since

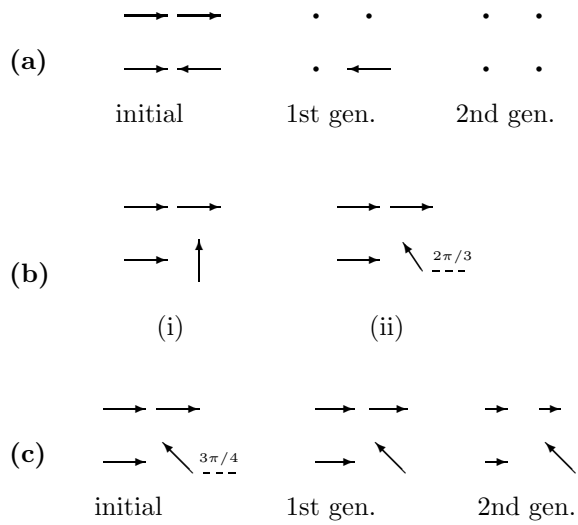


Fig. 12.6. (a) A simple example of destructive interference in semi-quantum Life: a block with one cell out of phase by π dies in two generations. (b) Blocks where the phase difference of the fourth cell is insufficient to cause complete destructive interference; each cell maintains a net of at least two living neighbours and so the patterns are stable. In the second of these, the fourth cell is at a critical angle. Any greater phase difference causes instability resulting in eventual death as seen in (c), which dies in the fourth generation.

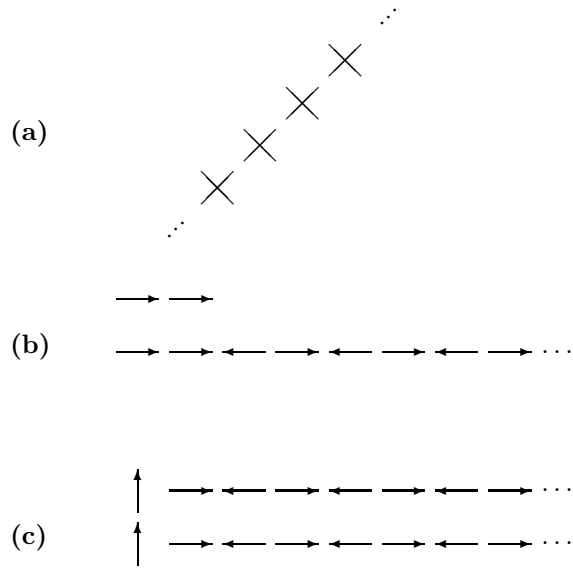


Fig. 12.7. (a) A wick (an extended structure that dies, or "burns", at a constant rate) in standard Life that burns at the speed of light (one cell per generation), in this case from both ends. It is impossible to stabilize one end without giving rise to other effects. (b) In semi-quantum Life an analogous wick can be in any orientation. The block on the left-hand end stabilizes that end; a block on both ends would give a stable line; the absence of the block would give a wick that burns from both ends. (c) Another example of a light-speed wick in semi-quantum Life showing one method of stabilizing the left-hand end.

it can be in any orientation and the ends can be stabilized easily. Figures 12.7(b)–(c) show some examples. A line of alternating phase live cells can be used to create other structures such as the loop in Fig. 12.8. This is a generalization of the boat still life, Fig. 12.3(a)(iii), in the standard model that is of a fixed size and shape. The stability of the line of $\longrightarrow\!\!\!\!\!\!\leftarrow$'s results from the fact that while each cell in the line has exactly two living neighbours, the cells above or below this line have a net of zero (or one at a corner) living neighbours due to the canceling effect of the opposite phases. No new births around the line will occur, unlike the case where all the cells are in phase.

Oscillators (Fig. 12.3) and spaceships (Fig. 12.4) cannot be made simpler than the minimal examples presented for standard Life. Figure 12.9 shows a stable boundary that results from the appropriate adjustment of the phase

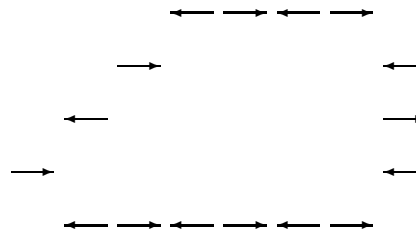


Fig. 12.8. An example of a stable loop made from cells of alternating phase. Above a certain minimum, such structures can be made of arbitrary size and shape compared with a fixed size and limited orientations in Conway's scheme.

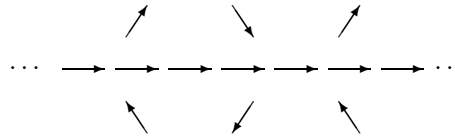


Fig. 12.9. A boundary utilizing appropriate phase differences to produce stability. The upper cells are out of phase by $\pm\pi/3$ and the lower by $\pm 2\pi/3$ with the central line.

differences between the cells. The angles have been chosen so that each cell in the line has between two and three living neighbours, while the empty cells above and below the line have either two or four living neighbours and so remain life-less. Such boundaries are known in standard Life but require a more complex structure.

In Conway's Life interesting effects can be obtained by colliding gliders. In the semi-quantum model additional effects can be obtained from colliding gliders and "anti-gliders," where all the cells have a phase difference of π with those of the original glider. For example, a head-on collision between a glider and an anti-glider, as indicated in Fig. 12.10, causes annihilation, where as the same collision between two gliders leaves a block. However, there is no consistency with this effect since other glider-antiglider collisions produce alternative effects, sometimes being the same as those from the collision of two gliders.

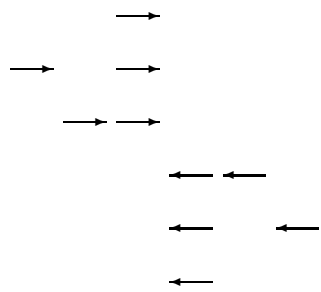


Fig. 12.10. A head on collision between a glider and its phase reversed counter part, an anti-glider, produces annihilation in six generations.

12.3. Summary

John Conway's game of Life is a two-dimensional cellular automaton where the new state of a cell is determined by the sum of neighbouring states that are in one particular state generally referred to as "alive." A modification to this model is proposed where the cells may be in a superposition of the alive and dead states with the coefficient of the alive state being represented by an oscillator having a phase and amplitude. The equivalent of evaluating the number of living neighbours of a cell is to take the superposition of the oscillators of the surrounding states. The amplitude of this superposition will determine which operator(s) to apply to the central cell to determine its new state, while the phase gives the phase of any new state produced. Such a system show some quantum-like aspects such as interference.

Some of the results that can be obtained with this new scheme have been touched on in this chapter. New effects and structures occur and some of the known effects in Conway's Life can occur in a simpler manner. However, the scheme described should not be taken to be a full quantum analogue of Conway's Life and does not satisfy the definition of a QCA.

The field of quantum cellular automata is still in its infancy. The protocol of Schumacher and Werner (2004) provides a construction method for the simplest QCA. Exploration and classification of these automata is an important unsolved task and may lead to developments in the quantum domain comparable to those in the classical field that followed the exploration of classical CA. Quantum cellular automata are a viable candidate for achieving useful quantum computing.

References

Amoroso, S., and Patt, Y. N. (1972). Decision procedures for surjectivity and injectivity of parallel maps for tessellation structures, *J. Comput. Syst. Sci.* **6**, pp. 448–464.

Benjamin, S. C. (2000). Schemes for parallel quantum computation without local control of qubits, *Phys. Rev. A* **61**, art. no. 020301.

Berlekamp, E. R., Conway, J. H., and Guy, R. K. (1982). *Winning Ways for Your Mathematical Plays* Vol. 2, (Academic Press).

Dumke, R., Volk, M., Müther, T., Buchkremer, F. B. J., Birkl, G., and Ertmer, W. (2002). Micro-optical realization of arrays of selectively addressable dipole traps: a scalable configuration for quantum computation with atomic qubits, *Phys. Rev. Lett.* **89**, art. no. 097903.

Dürr, C., and Santha M. (2002). A decision procedure for well-formed unitary linear quantum cellular automata, *SIAM J. Comput.* **31**, pp. 1076–1089.

Feynman, R. (1982). Simulating physics with computers, *Int. J. Theor. Phys.* **21**, pp. 467–488.

Gardner, M. (1970). Mathematical games: The fantastic combinations of John Conway's new solitaire game of "Life", *Sci. Am.* **223**, 10, p. 120.

Gardner, M. (1971). Mathematical games: On cellular automata, self-reproduction, the Garden of Eden and the game of "Life", *Sci. Am.* **224**, 2, p. 116.

Gardner, M. (1983). *Wheels, Life and Other Mathematical Amusements* (W. H. Freeman)

Grössing G., and Zeilinger, A. (1988a). Quantum cellular automata, *Complex Systems* **2**, pp. 197–208.

Grössing G., and Zeilinger, A. (1988b). Structures in quantum cellular automata, *Physica B* **151**, pp. 366–370.

Gruska, J. (1999). *Quantum Computing* ch. 4, pp. 181–192 (McGraw Hill, Maidenhead, Berkshire, UK).

Kari, J. (1990). Reversibility of two-dimensional cellular automata is undecidable, *Physica D* **45**, pp. 379–385.

Mandel, D., Greiner, M., Widera, A., Rom, T., Hänsch, T. W., and Bloch, I. (2003). Coherent transport of neutral atoms in spin-dependent optical lattice potentials, *Phys. Rev. Lett.* **91**, art. no. 010407.

Meyer, D. A. (1996). From quantum cellular automata to quantum lattice gases, *J. Stat. Phys.* **85**, pp. 551–574.

Morita, K. (1989). Computation universality of one-dimensional reversible (injective) cellular automata, *Trans. IEICE* **72**, pp. 758–762.

Morita, K. (1995). Reversible simulation of one-dimensional irreversible cellular automata, *Theor. Comput. Sci.* **148**, pp. 157–163.

Schumacher, B., and Werner, R. F. (2004). *Reversible quantum cellular automata*, e-print: `quant-ph/0405174`.

Toffoli, T. (1977). *Cellular Automata Mechanics*, PhD thesis, University of Michigan.

Wolfram, S. (1983). Statistical mechanics of cellular automata, *Rev. Mod. Phys.* **55**, pp. 601–644.
Wolfram, S. (1988). *Mathematica: A System for Doing Mathematics by Computer* (Addison-Wesley).
Wolfram, S. (2002). *A New Kind of Science* (Wolfram Media Inc.).

About the authors

Adrian P. Flitney completed a Bachelor of Science with first class honours in theoretical physics at the University of Tasmania in 1983. He worked in the field of ionospheric physics and high frequency radio communications for the Department of Science for two years and later for Andrew Antennas Corporation. He was a researcher in quantum field theory in the Physics Department at the University of Adelaide for some time, and worked as a tutor in physics and mathematics both within the University and privately. In 2001 Flitney finally saw the light and began a PhD in the field of quantum information with the Department of Electrical and Electronic Engineering at the University of Adelaide. At the beginning of 2005 he submitted a thesis entitled "Aspects of Quantum Game Theory," under Derek Abbott, and was awarded his doctorate with highest commendation. He is currently working in the School of Physics, University of Melbourne on quantum games and decoherence under an Australian Research Council Postdoctoral Fellowship. Currently Flitney's major non-academic interests are chess, where he has achieved considerable success in the past, and kayaking.

Derek Abbott was born in South Kensington, London, UK. He received his BSc (Hons) in Physics from Loughborough University of Technology. He obtained his PhD in Electrical and Electronic Engineering from the University of Adelaide, under Kamran Eshraghian and Bruce R. Davis. He is with The University of Adelaide, Australia, where he is presently a full professor and the Director of the Centre for Biomedical Engineering (CBME). He has served as an editor and/or guest editor for a number of journals including *Chaos* (AIP), *Smart Structures and Materials* (IOP), *Journal of Optics B* (IOP), *Microelectronics Journal* (Elsevier), *Proceedings of the IEEE*, and *Fluctuation Noise Letters* (World Scientific). He is a life Fellow of the Institute of Physics (IOP) and Fellow of the Institution of Electrical & Electronic Engineers (IEEE). He has won a number of awards including a 2004 Tall Poppy Award for Science. He holds over 300 publications and

is a co-author of the book *Stochastic Resonance* published by Cambridge University Press. Prof Abbott is co-founder of two international conference series: *Microelectronics in the New Millennium* (with J. F. Lopez) and *Fluctuations and Noise* (with L. B. Kish).

Chapter 13

Evolutionary Stability in Quantum Games

Azhar Iqbal and Taksu Cheon

In evolutionary game theory an Evolutionarily Stable Strategy (ESS) is a refinement of the Nash equilibrium (NE) concept that is sometimes also recognized as evolutionary stability. It is a game-theoretic model, well known to mathematical biologists, that was found quite useful in the understanding of evolutionary dynamics of a population. This chapter presents an analysis of evolutionary stability in the emerging field of quantum games.

Games such as chess, warfare and politics have been played throughout history. Whenever individuals meet who have conflicting desires, and priorities, then strategic games are likely to be played. Analysis and understanding of games has existed for long a time but the emergence of game theory as a formal study of games is widely believed to have taken place when Neumann and Morgenstern [Neumann and Morgenstern (1953)] published their pioneering book "The Theory of Games and Economic Behaviour" in 1944. Game theory [Rasmusen (1989)] is now an established discipline of mathematics that is a vast subject having a rich history and content. Roughly speaking, game theory is the analysis of the actions made by rational players when these actions are strategically interdependent.

The 1970s saw game theory being successfully applied to problems of evolutionary biology and a new branch of game theory, recognized as evolutionary game theory [Maynard Smith (1982); Hofbrauer and Sigmund (1998); Weibull (1995)], came into existence. The concept of utility from

Received April 8, 2007

economics was given an interpretation in terms of Darwinian fitness. Originally, evolutionary game theory considered animal conflicts occurring in the macro-world. Later, research in biology [Turner and Chao (1999)] suggested that nature also plays classical games at the micro-level. Bacterial infections by viruses are classical game-like situations where nature prefers dominant strategies. Economics and biology are not the only areas that have benefited from game theory as there is recent interest in the application of game theory to problems in physics [Abbott *et al.* (2002)].

In game theory [Neumann and Morgenstern (1953); Rasmusen (1989)] one finds many examples where multiple Nash equilibria (NE) [Nash (1950, 1951)] emerge as solutions of a game. To select one (or possibly more) out of these requires some refinement of the equilibrium concept [Myerson (1978)]. A refinement is a rule/criterion that describes the preference of one (in some cases more than one) equilibrium out of many. Numerous refinements are found in game theory, for example, perfect equilibrium (used for extensive- and normal-form games), sequential equilibrium (a fundamental non-cooperative solution concept for extensive-form games), and correlated equilibrium (used for modelling communication among players). The ESS concept is known to be a refinement on the set of symmetric NE and is generally considered central to evolutionary game theory.

During recent years quantum game theory [Meyer (1999); Eisert *et al.* (1999); Eisert and Wilkens (2000); Flitney and Abbott (2002a)] has emerged as a new research field within quantum information and computation [Nielsen and Chuang (2000)]. A significant portion of research in quantum games deals with the question asking how quantization of a game affects/changes the existence/location of a NE. This question has been addressed in a number of publications [Flitney and Abbott (2002a,b); Iqbal (2004)] in this area and now it seems that it is generally agreed that quantization of a game indeed affects/changes the existence/location of a NE.

In this chapter we argue that, like asking how quantization of a game affects/changes the existence/location of a NE, an equally important question for quantum games is to ask how quantization of a game can affect a refinement of the NE concept. While focussing on the refinement of the notion of an ESS, we motivate those quantum games in which a NE persists[1] in both of its classical and quantum versions while its property of being an ESS survives in either classical or its quantum version, but not in both.

[1]By saying that a NE persists in both the classical and quantum version of a game we mean that there exists a NE consisting of quantum strategies that rewards both the players exactly the same as the corresponding NE does in the classical version of the game.

We argue that, the quantum games offering such situations, along with their quantization procedures, can justifiably be said to extend the boundary of investigations in quantum games from existence/location of NE to existence/location of one (or more) of its refinements.

13.1. Evolutionary Game Theory and Evolutionary Stability

The roots of evolutionary game theory [Weibull (1995)] can be traced to the puzzle of the approximate equality of the sex ratio in mammals. In 1930 Fisher ([Stanford (2003)]) noticed that if individual fitness is defined in terms of the expected number of grandchildren, then it becomes dependent on how males and females are distributed in a population. Fisher showed that the evolutionary dynamics then leads to the sex ratio becoming fixed at equal numbers of males and females. Although Fisher's argument can be recast in game-theoretic language, it was not originally presented in those terms. Perhaps it was due to the fact that until that time modern game theory had not yet emerged as a formal study.

Modern game theory was used, for the first time, to understand evolution when in 1972 Maynard Smith and G. R. Price introduced the concept of an Evolutionarily Stable Strategy (ESS) [Maynard Smith and Price (1973); Maynard Smith (1982)]. Presently, this concept is widely believed to be the cornerstone of evolutionary game theory [Hofbrauer and Sigmund (1998)] and has been found quite useful to explain and understand animal behaviour.

Traditionally, game theory had concerned analyzing interactions among hyperrational players and the idea that it can be applied to animals seemed strange at the time. The ESS concept made three important changes in the traditional meaning of the concepts of a) strategy, b) equilibrium, and c) players' interactions.

a) *Strategy*: In traditional game theory, players have strategy set from which they choose their strategies. In biology, animals belonging to a species have strategy sets, which are genotypic variants that may be mutated, of which individuals inherit one or another variant, which they then play in their strategic interactions. A mixed strategy in game theory means a convex linear combination (with real and normalized coefficients) of pure strategies. Because genotypic variants are taken as pure strategies, the evolutionary game theory interprets a mixed strategy in terms of proportion of the population that is playing that strategy.

b) *Equilibrium*: An ESS represents an equilibrium and it is a strategy having the property that if a whole population plays it, it cannot be invaded under the influence of natural selection, by a small group of players playing mutant strategies. Because strategies of evolutionary games are genotypes the ESS definition takes the following form: If adapted by a whole population an ESS is a genotype that cannot be invaded by another genotype when it appears in a small fraction of the total population.

c) *Player interactions*: The ESS concept is about repeated and random pairing of players who play strategies based on their genome and *not* on the previous history of play. This concept presented a new approach to analyze repeated games that are played in evolutionary settings.

Consider a large population [Weibull (1995); Hofbrauer and Sigmund (1998)] in which members are matched repeatedly and randomly in pairs to play a bi-matrix game. The players are anonymous, that is, any pair of players plays the same symmetric bi-matrix game. The symmetry of a bi-matrix game means that for a strategy set S Alice's payoff when she plays $S_1 \in S$ and Bob plays $S_2 \in S$ is the same as Bob's payoff when he plays S_1 and Alice plays S_2. Hence, a player's payoff is defined by his/her strategy and *not* by his/her identity and an exchange of strategies by the two players also exchanges their respective payoffs. A symmetric bi-matrix game is represented by an expression $G = (M, M^T)$ where M is the first player's payoff matrix and M^T, being its transpose, is the second players' payoff matrix. In a symmetric pair-wise contest one can write $P(x, y)$ as being the payoff to a x-player against a y-player.

To be precise [Hofbrauer and Sigmund (1998); Bomze (1996); Bomze and Pötscher (1989)] a strategy x is said to be an ESS if:

a) for each mutant strategy y there exists a positive *invasion barrier*.

b) if the population share of individuals playing the mutant strategy y falls below the invasion barrier, then x earns a higher expected payoff than y.

Mathematically speaking [Weibull (1995); Hofbrauer and Sigmund (1998)] x is an ESS when for each strategy $y \neq x$ the inequality

$$P[x, (1-\epsilon)x + \epsilon y] > P[y, (1-\epsilon)x + \epsilon y] \tag{13.1}$$

holds for all sufficiently small $\epsilon > 0$. In Eq. (13.1) the expression on the left-hand side is payoff to the strategy x when played against the mixed strategy $(1-\epsilon)x + \epsilon y$. This condition for an ESS is shown [Maynard Smith and Price (1973); Maynard Smith (1982); Weibull (1995)] equivalent to the

following requirements:

$$\begin{aligned} &\text{a) } P(x,x) > P(y,x) \\ &\text{b) If } P(x,x) = P(y,x) \text{ then } P(x,y) > P(y,y)\,. \end{aligned} \tag{13.2}$$

It turns out [Maynard Smith (1982); Weibull (1995)] that an ESS is a symmetric NE that is stable against small mutations. Condition a) in the definition (13.2) shows (x,x) is a NE for the bi-matrix game $G = (M, M^T)$ if x is an ESS. However, the converse is not true. That is, if (x,x) is a NE then x is an ESS only if x satisfies condition b) in Definition (13.2).

Evolutionary game theory defines the concept of *fitness* [Prestwich (1999)] of a strategy as follows. Suppose x and y are pure strategies played by a population of players that is engaged in a two-player game. Their fitnesses are

$$W(x) = P(x,x)F_x + P(x,y)F_y\,; \quad W(y) = P(y,x)F_x + P(y,y)F_y \tag{13.3}$$

where F_x and F_y are frequencies (the relative proportions) of the pure strategies x and y respectively.

It turned out that an ESS is a refinement on the set of symmetric Nash equilibria [Weibull (1995); Cressman (1992)]. For symmetric bi-matrix games this relationship is described [van der Laan and Tiemen (1996)] as $\triangle^{ESS} \subset \triangle^{PE} \subset \triangle^{NE}$ where $\triangle^{PE} \neq \Phi$ and $\triangle^{NE}$, $\triangle^{PE}$, $\triangle^{ESS}$ are the sets of symmetric NE, symmetric proper equilibrium, and ESSs respectively.

The property of an ESS of being robust against small mutations is also referred to as *evolutionary stability* [Bomze (1996); Bomze and Pötscher (1989)]. In evolutionary game theory, the Darwinian natural selection is formulated as an algorithm called *replicator dynamics* [Hofbrauer and Sigmund (1998); Weibull (1995)], which is a mathematical statement saying that in a population the proportion of players playing better strategies increases with time. Mathematically, ESSs come out as the *rest points* of replicator dynamics [Hofbrauer and Sigmund (1998); Weibull (1995)].

The concept of evolutionary stability has provided significant part of the motivation for later developments in evolutionary game theory and was found to be a useful concept because it says something about the dynamic properties of a system without being committed to a particular dynamic model. Sometimes, it is also described as a model of rationality that is physically grounded in natural selection.

13.1.1. *Population setting of evolutionary game theory*

Evolutionary game theory introduces the so-called *population setting* [Weibull (1995); Hofbrauer and Sigmund (1998)] that is also known as a *population-statistical setting*. This setting assumes a) an infinite population of players who are engaged in random pair-wise contests, b) each player being programmed to play only one strategy, and c) an evolutionary pressure ensuring that better-performing strategies have better chances of survival at the expense of other competing strategies. Because of b) one can refer to better-performing players as better-performing strategies.

Although it may give such an impression, the population setting of evolutionary game theory is not alien to the concept of the NE. In fact, as was found later, John Nash himself had this setting in his mind when he introduced this concept in game theory. In his unpublished PhD thesis [Nash (1950); Hofbrauer and Sigmund (1998)] he wrote "*it is unnecessary to assume that the participants have...the ability to go through any complex reasoning process. But the participants are supposed to accumulate empirical information on the various pure strategies at their disposal...We assume that there is a population...of participants...and that there is a stable average frequency with which a pure strategy is employed by the 'average member' of the appropriate population.*"

That is, Nash had suggested a population interpretation of the NE concept in which players are randomly drawn from large populations. Nash assumed that these players were not aware of the total structure of the game and did not have either the ability nor inclination to go through any complex reasoning process.

13.2. Quantum Games

This chapter considers the game-theoretic concept of evolutionary stability in quantum games that are played in the two quantization schemes: the Eisert, Wilkens, Lewenstein (EWL) scheme [Eisert *et al.* (1999); Eisert and Wilkens (2000)] for playing quantum Prisoners' Dilemma (PD) and Marinatto and the Weber (MW) scheme [Marinatto and Weber (2000a)] for playing the quantum Battle of the Sexes (BoS) game.

The EWL quantization scheme appeared soon after Meyer's publication [Meyer (1999)] of the PQ penny-flip—a quantum game that generated significant interest and is widely believed to have led to the creation of the new research field of quantum games. The MW scheme derives from the EWL

scheme, but it gives a different meaning to the term "strategy" [Benjamin (2000); Marinatto and Weber (2000b)].

EWL quantum PD assigns two basis vectors $|C\rangle$ and $|D\rangle$ in the Hilbert space of a qubit, where C and D refer to the strategies of Cooperation and Defection, respectively, in PD. States of the two qubits belong to two-dimensional Hilbert spaces H_A and H_B, respectively. The state of the game is defined as being a vector residing in the tensor-product space $H_A \otimes H_B$, spanned by the bases $|CC\rangle, |CD\rangle, |DC\rangle$ and $|DD\rangle$. The initial state of the game is $|\psi_{\text{ini}}\rangle = \hat{J}\,|CC\rangle$ where $\hat{J}$ is a unitary operator known to both the players. Alice's and Bob's strategies are unitary operations $\hat{U}_A$ and $\hat{U}_B$, respectively, chosen from a strategic space Ş. After players' actions the state of the game changes to $\hat{U}_A \otimes \hat{U}_B \hat{J}\,|CC\rangle$. Finally, the state is measured and it consists of applying reverse unitary operator $\hat{J}^\dagger$ followed by a pair of Stern-Gerlach type detectors. Before detection the final state of the game is $|\psi_{\text{fin}}\rangle = \hat{J}^\dagger \hat{U}_A \otimes \hat{U}_B \hat{J}\,|CC\rangle$. Players' expected payoffs are the projections of the state $|\psi_{\text{fin}}\rangle$ onto the basis vectors of tensor-product space $H_A \otimes H_B$, weighed by the constants appearing in the following Game Matrix,

$$\begin{array}{c} \\ \text{Alice} \end{array} \begin{array}{c} \text{Bob} \\ C \quad D \\ C \\ D \end{array} \begin{pmatrix} (r,r) & (s,t) \\ (t,s) & (u,u) \end{pmatrix}. \tag{13.4}$$

The first and the second entry in small braces correspond to Alice's and Bob's (classical, pure strategy) payoffs, respectively. When $s < u < r < t$ the Matrix (13.4) represents PD. In EWL quantum PD Alice's payoff, for example, reads

$$P_A = r\,|\langle CC \mid \psi_{\text{fin}}\rangle|^2 + s\,|\langle CD \mid \psi_{\text{fin}}\rangle|^2 + t\,|\langle DC \mid \psi_{\text{fin}}\rangle|^2 + u\,|\langle DD \mid \psi_{\text{fin}}\rangle|^2 \,. \tag{13.5}$$

With reference to the Matrix (13.4) Bob's payoff is, then, obtained by the transformation $s \rightleftarrows t$ in Eq. (13.5). Eisert and Wilkens (2000) used following matrix representations of unitary operators of their one- and two-parameter strategies, respectively:

$$U(\theta) = \begin{pmatrix} \cos(\theta/2) & \sin(\theta/2) \\ -\sin(\theta/2) & \cos(\theta/2) \end{pmatrix} \tag{13.6}$$

$$U(\theta,\phi) = \begin{pmatrix} \mathrm{e}^{i\phi}\cos(\theta/2) & \sin(\theta/2) \\ -\sin(\theta/2) & \mathrm{e}^{-i\phi}\cos(\theta/2) \end{pmatrix} \tag{13.7}$$

where

$$0 \leq \theta \leq \pi \text{ and } 0 \leq \phi \leq \pi/2\,. \tag{13.8}$$

To ensure that the classical game is faithfully represented in its quantum version, EWL imposed an additional conditions on $\hat{J}$:

$$\left[\hat{J}, \hat{D} \otimes \hat{D}\right] = 0, \left[\hat{J}, \hat{D} \otimes \hat{C}\right] = 0, \left[\hat{J}, \hat{C} \otimes \hat{D}\right] = 0 \tag{13.9}$$

with $\hat{C}$ and $\hat{D}$ being the operators corresponding to the classical strategies C and D, respectively. A unitary operator satisfying the condition (13.9) is

$$\hat{J} = \exp\left\{i\gamma \hat{D} \otimes \hat{D}/2\right\} \tag{13.10}$$

where $\gamma \in [0, \pi/2]$ and $\hat{J}$ represents a measure of the game's entanglement. At $\gamma = 0$ the game can be interpreted as a mixed-strategy classical game. For a maximally entangled game $\gamma = \pi/2$ the classical NE of $\hat{D} \otimes \hat{D}$ is replaced by a different unique equilibrium $\hat{Q} \otimes \hat{Q}$ where $\hat{Q} \sim \hat{U}(0, \pi/2)$. This new equilibrium is found also to be *Pareto optimal* [Rasmusen (1989)], that is, a player cannot increase his/her payoff by deviating from this pair of strategies without reducing the other player's payoff. Classically (C, C) is Pareto optimal, but is not an equilibrium [Rasmusen (1989)], thus resulting in the "dilemma" in the game. It is argued [Benjamin and Hayden (2001); Eisert *et al.* (2001)] that in its quantum version the dilemma disappears from the game and quantum strategies give a superior performance if entanglement is present.

The MW quantization scheme [Marinatto and Weber (2000a); Benjamin (2000); Marinatto and Weber (2000b)] for BoS identifies a state in $2 \otimes 2$ dimensional Hilbert space as a *strategy*. At the start of the game the players are supplied with this strategy and the players manipulate the strategy in the next phase by playing their *tactics*. The state is finally measured and payoffs are rewarded depending on the results of the measurement. A player can carry out actions within a two-dimensional subspace. Tactics are therefore *local actions* on a player's qubit. The final measurement, made independently on each qubit, takes into consideration the local nature of players' manipulations. This is done by selecting a measurement basis that respects the division of Hilbert space into two equal parts.

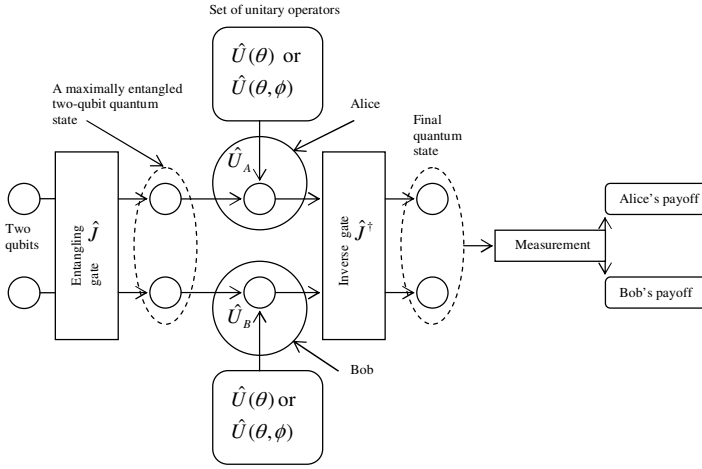


Fig. 13.1. The EWL scheme for playing a quantum game.

Essentially the MW scheme differs from the EWL scheme [Eisert *et al.* (1999); Eisert and Wilkens (2000)] in the absence of the reverse gate[2] $J^\dagger$. Finally, the quantum state is measured and it is found that the classical game remains a subset of the quantum game if the players' tactics are limited to a convex linear combination, with real and normalized coefficients, of applying the identity $\hat{I}$ and the Pauli spin-flip operator $\hat{\sigma}_x$. Classical game results when the players are forwarded an initial strategy $|\psi_{\rm in}\rangle = |00\rangle$.

Let $\rho_{\rm in}$ be the initial strategy the players Alice and Bob receive at the start of the game. Assume Alice acts with identity $\hat{I}$ on $\rho_{\rm in}$ with probability p and with $\hat{\sigma}_x$ with probability $(1-p)$. Similarly, Bob act with identity $\hat{I}$ with probability q and with $\hat{\sigma}_x$ with probability $(1-q)$. After the players' actions the state changes to

$$\begin{aligned}\rho_{\rm fin} = {} & pq\hat{I}_A \otimes \hat{I}_B \rho_{\rm in} \hat{I}_A^\dagger \otimes \hat{I}_B^\dagger + p(1-q)\hat{I}_A \otimes \hat{\sigma}_{xB} \rho_{\rm in} \hat{I}_A^\dagger \otimes \hat{\sigma}_{xB}^\dagger \\ & + q(1-p)\hat{\sigma}_{xA} \otimes \hat{I}_B \rho_{\rm in} \hat{\sigma}_{xA}^\dagger \otimes \hat{I}_B^\dagger \\ & + (1-p)(1-q)\hat{\sigma}_{xA} \otimes \hat{\sigma}_{xB} \rho_{\rm in} \hat{\sigma}_{xA}^\dagger \otimes \hat{\sigma}_{xB}^\dagger \,. \end{aligned} \tag{13.11}$$

[2]EWL introduced the gate $J^\dagger$ before measurement takes place that makes sure that the classical game remains a subset of its quantum version.

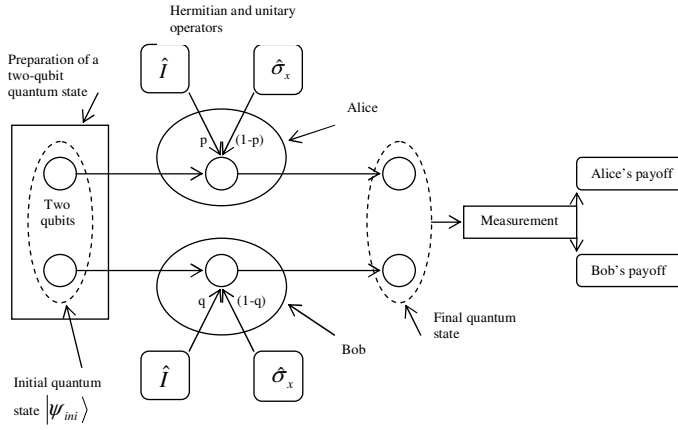


Fig. 13.2. The MW scheme for playing a quantum game.

When the game is given by the bi-matrix:

$$\begin{array}{c} \\ \\ \text{Alice} \end{array} \begin{array}{c} \text{Bob} \\ S_1 \quad S_2 \\ \begin{array}{c} S_1 \\ S_2 \end{array} \left(\begin{array}{cc} (\alpha_A, \alpha_B) & (\beta_A, \beta_B) \\ (\gamma_A, \gamma_B) & (\delta_A, \delta_B) \end{array} \right) \end{array} \tag{13.12}$$

the payoff operators are:

$$\begin{aligned} (P_A)_{\text{oper}} &= \alpha_A \left|00\right\rangle \left\langle 00\right| + \beta_A \left|01\right\rangle \left\langle 01\right| + \gamma_A \left|10\right\rangle \left\langle 10\right| + \delta_A \left|11\right\rangle \left\langle 11\right| \\ (P_B)_{\text{oper}} &= \alpha_B \left|00\right\rangle \left\langle 00\right| + \beta_B \left|01\right\rangle \left\langle 01\right| + \gamma_B \left|10\right\rangle \left\langle 10\right| + \delta_B \left|11\right\rangle \left\langle 11\right| , \end{aligned} \tag{13.13}$$

and payoff functions are then obtained as mean values of these operators:

$$P_{A,B} = \text{Tr}\left\{(P_{A,B})_{\text{oper}} \rho_{\text{fin}}\right\} . \tag{13.14}$$

It is to be pointed out that in the EWL set-up a quantum game results when the entanglement parameter γ of the initial quantum state is different from zero. Also, when γ is non-zero the players have strategies available to them that result in the classical game. The general idea is to allow a range of values to the parameter γ and then to find how it leads to a different, i.e. non-classical, equilibrium in the game.

In the MW scheme [Marinatto and Weber (2000a); Benjamin (2000); Marinatto and Weber (2000b)] an initial strategy is forwarded to two players who then apply their tactics on it and the classical game corresponds to

the initial state $|00\rangle$. Assume now that the players receive pure two-qubit states, different from $|00\rangle$, while the measurement remains the same. A quantum form of the game then corresponds if initial states different from the product state $|00\rangle$ are used. This translates finding the quantum form of a matrix game to finding appropriate initial state(s). This can be justified on the ground that the only reasonable restriction [Marinatto and Weber (2000b)] on a quantum form of a game is that the corresponding classical game must be reproducible as its special case. As the product initial state $|00\rangle$ always results in the classical game, this approach towards obtaining a quantum game remains within the mentioned restriction.

In the EWL scheme one looks for new equilibria in games in relation to the parameter γ. In the above approach, however, one finds equilibria in relation to different initial states. In this chapter, we restrict ourselves to pure states only.

13.3. Evolutionary Stability in Quantum Games

The concept of a NE from noncooperative game theory was addressed in the earliest research publications in quantum games [Eisert *et al.* (1999); Eisert and Wilkens (2000)]. Analysis of this solution concept generated significant interest thereby motivating an emerging new research field. These publications do not explicitly refer to the population interpretation of the NE concept, which was behind the development of the ESS concept in evolutionary game theory. When this interpretation is brought within the domain of quantum games it becomes natural to consider ESSs in this domain.

One may ask how and where the population setting may be relevant to quantum games. How can a setting, originally developed to model population biology problems, be relevant and useful to quantum games? One can sharpen this argument further given the fact that, to date, almost all of the experimental realizations of quantum games are artificially constructed in laboratories using quantum computational circuits [Nielsen and Chuang (2000)].

It seems that reasonable replies can be made to this question. For example, that the population setting, which, in fact, was behind the NE—the concept that was addressed in the earliest constructions of quantum games. It, then, justifies consideration of this setting within quantum games. One also finds that evolutionary stability has very rich literature in game theory, mathematical biology and in evolutionary economics [Friedman (1998);

Witt (2006)], thus making it almost natural to explore how this concept comes into play when games are quantized. In quantum games the NE has been discussed in relation to quantum entanglement [Nielsen and Chuang (2000)] and the possibility that the same can be done with evolutionary stability clearly opens a new interesting role for this quantum phenomenon. It is conjectured that the possibility of this extended role for entanglement may perhaps be helpful to better understand entanglement itself.

Evolutionary stability presents a game-theoretic model to understand evolutionary dynamics. Quantum games motivate us to ask how this game-theoretic solution concept adapts/shapes/changes itself when players are given access to quantum strategies. It appears that this question is clearly related to a bigger question: Can quantum mechanics have a role in directing, or possibly dictating, the dynamics of evolution? We believe that, for an analysis along this direction, evolutionary stability offers an interesting situation because, it is a simple and a beautiful concept that is supported by extensive literature [Bomze (1996); Hofbrauer and Sigmund (1998)].

Discussing evolutionary stability in quantum games may appear as if a concept originally developed for population biology problems is arbitrarily being placed within the domain of quantum games. In reply we notice that population biology is not the only relevant domain for evolutionary stability. This concept can also be interpreted using infinitely repeated two-player games and without referring to a population of players. Secondly, as the Nash's thesis [Nash (1950); Hofbrauer and Sigmund (1998)] showed, it is not the population biology alone that motivates a population setting for game theory—responsible for the concept of evolutionary stability. Surprisingly, the concept of NE also does the same, although it may not be recognized generally.

The usual approach in game theory consists of analyzing games among hyper-rational players who are always found both ready and engaged in their selfish interests to optimize their payoffs or utilities. Evolutionary stability has roots in the efforts to get rid of this usual approach that game theory had followed. The lesson it teaches is that playing games can be disassociated from players' capacity to make rational decisions. This disassociation seems equally valid in those possible situations where nature plays quantum games.[3] It is because associating rationality to quantum-interacting entities is of even a more remote possibility than it is the case

[3]Although, no evidence showing nature playing quantum games has been found to date, the idea itself does not seem far-fetched.

when this association is made to bacteria and viruses, whose behaviour evolutionary game theory explains.

In the following we will try to address the questions: How ESSs are affected when a classical game, played by a population, changes itself to a quantum form? How pure and mixed ESSs are distinguished from one another when such a change in the form of a game takes place? Can quantum games provide a route that can relate evolutionary dynamics, for example, to quantum entanglement? Considering a population of players in which a classical strategy has established itself as an ESS, we would like to ask: a) What happens when "mutants" of ESS theory come up with quantum strategies and try to invade the classical ESS? b) What happens if such an invasion is successful and a new ESS is established—an ESS that is quantum in nature? c) Suppose afterwards another small group of mutants appears which is equipped with some other quantum strategy. Will it successfully invade the quantum ESS?

13.3.1. *Evolutionary stability in EWL scheme*

EWL used the matrix (13.4) with $r = 3, s = 0, t = 5$, and $u = 1$ in their proposal for quantum PD. Assume a population setting where in each pair-wise encounter the players play PD with the same matrix and each contest is symmetric. Which strategies will then be likely to be stable? Straightforward analysis [Prestwich (1999)] shows that D will be the pure classical strategy prevalent in the population and hence the classical ESS. We consider following three cases:

- Case (a) A small group of mutants appear equipped with one-parameter quantum strategy $\hat{U}(\theta)$ when D exists as a classical ESS;
- Case (b) Mutants are equipped with two-parameter quantum strategy $\hat{U}(\theta, \phi)$ against the classical ESS;
- Case (c) Mutants have successfully invaded and a two-parameter quantum strategy $\hat{Q} \sim \hat{U}(0, \pi/2)$ has established itself as a new quantum ESS. Again another small group of mutants appear, using some other two-parameter quantum strategy, and tries to invade the quantum ESS, which is $\hat{Q}$.

Case (a): Because players are anonymous one can represent $P(\hat{U}(\theta), D)$ as the payoff to $\hat{U}(\theta)$-player against the D-player. Here $\hat{U}(\theta)$ is the Eisert and Wilkens' one-parameter quantum strategy set as in Eq. (13.6). Players' payoffs read $P(\hat{U}(\theta), D) = \sin^2(\theta/2)$; $P(\hat{U}(\theta), \hat{U}(\theta)) = 2\cos^2(\theta/2) +$

$5\cos^2(\theta/2)\sin^2(\theta/2) + 1$; $P(D,\hat{U}(\theta)) = 5\cos^2(\theta/2) + \sin^2(\theta/2)$; and $P(D,D) = 1$. Now $P(D,D) > P(\hat{U}(\theta),D)$ for all $\theta \in [0,\pi)$. Hence the first condition for an ESS holds and $D \sim \hat{U}(\pi)$ is an ESS. The case $\theta = \pi$ corresponds to one-parameter mutant strategy coinciding with the ESS, which is ruled out. If $D \sim \hat{U}(\pi)$ is played by almost all the members of the population—which corresponds to high frequency F_D for D—we then have $W(D) > W(\theta)$ for all $\theta \in [0,\pi)$ using the definition in Eq. (13.3). The fitness of a one-parameter quantum strategy[4], therefore, cannot exceed the fitness of a classical ESS. And a one-parameter quantum strategy cannot invade a classical ESS.

Case (b): Let $\hat{U}(\theta,\phi)$ be a two-parameter strategy from the set (13.7). The expected payoffs read $P(D,D) = 1$; $P(D,\hat{U}(\theta,\phi)) = 5\cos^2(\phi)\cos^2(\theta/2) + \sin^2(\theta/2)$; $P(\hat{U}(\theta,\phi),D) = 5\sin^2(\phi)\cos^2(\theta/2) + \sin^2(\theta/2)$; and

$$\begin{aligned} P(\hat{U}(\theta,\phi),\hat{U}(\theta,\phi)) = {} & 3\left|\cos(2\phi)\cos^2(\theta/2)\right|^2 \\ & + 5\cos^2(\theta/2)\sin^2(\theta/2)\left|\sin(\phi)-\cos(\phi)\right|^2 \\ & + \left|\sin(2\phi)\cos^2(\theta/2)+\sin^2(\theta/2)\right|^2 . \end{aligned} \tag{13.15}$$

Here $P(D,D) > P(\hat{U}(\theta,\phi),D)$ if $\phi < \arcsin(1/\sqrt{5})$ and if $P(D,D) = P(\hat{U}(\theta,\phi),D)$ then $P(D,\hat{U}(\theta,\phi)) > P(\hat{U}(\theta,\phi),\hat{U}(\theta,\phi))$. Therefore, D is an ESS if $\phi < \arcsin(1/\sqrt{5})$ otherwise the strategy $\hat{U}(\theta,\phi)$ will be in position to invade D. Alternatively, if most of the members of the population play $D \sim \hat{U}(\pi,0)$—which means a high frequency F_D for D—then the fitness $W(D)$ will remain greater than the fitness $W[\hat{U}(\theta,\phi)]$ if $\phi < \arcsin(1/\sqrt{5})$. For $\phi > \arcsin(1/\sqrt{5})$ the strategy $\hat{U}(\theta,\phi)$ can invade the strategy D, which is the classical ESS.

In this analysis mutants are able to invade D when $\phi > \arcsin(1/\sqrt{5})$ and the invasion may seem not so unusual given the fact that they exploit richer strategies. But it leads to the third case i.e. when "quantum mutants" have successfully invaded and a two-parameter strategy $\hat{U}$ has established itself. Can now some new mutants coming up with $\hat{Q} \sim \hat{U}(0,\pi/2)$ and invade the "quantum ESS"?

Case (c): EWL [Eisert *et al.* (1999); Eisert and Wilkens (2000)] showed that in their quantum PD the quantum strategy $\hat{Q}$, played by both the

[4]In the EWL set-up one-parameter quantum strategies correspond to mixed (randomized) classical strategies.

players, is the unique NE. How mutants playing $\hat{Q}$ come up against $\hat{U}(\theta,\phi)$ which already exists as an ESS? To find it the following payoffs are obtained. $P(\hat{Q},\hat{Q}) = 3$; $P(\hat{U}(\theta,\phi),\hat{Q}) = [3 - 2\cos^2(\phi)]\cos^2(\theta/2)$; and $P(\hat{Q},\hat{U}(\theta,\phi)) = [3 - 2\cos^2(\phi)]\cos^2(\theta/2) + 5\sin^2(\theta/2)$. Now the inequality $P(\hat{Q},\hat{Q}) > P(\hat{U}(\theta,\phi),\hat{Q})$ holds for all $\theta \in [0,\pi]$ and $\phi \in [0,\pi/2]$ except when $\theta = 0$ and $\phi = \pi/2$, which is the case when the mutant strategy $\hat{U}(\theta,\phi)$ is the same as $\hat{Q}$. This case is obviously ruled out. The first condition for $\hat{Q}$ to be an ESS, therefore, holds. The condition $P(\hat{Q},\hat{Q}) = P(\hat{U}(\theta,\phi),\hat{Q})$ implies $\theta = 0$ and $\phi = \pi/2$. Again we have the situation of mutant strategy same as $\hat{Q}$ and the case is neglected. If $\hat{Q}$ is played by most of the players, meaning high frequency $F_{\hat{Q}}$ for $\hat{Q}$, then $W(\hat{Q}) > W[\hat{U}(\theta,\phi)]$ for all $\theta \in (0,\pi]$ and $\phi \in [0,\pi/2)$. A two-parameter quantum strategy $\hat{U}(\theta,\phi)$, therefore, cannot invade the quantum ESS (i.e. the strategy $\hat{Q} \sim \hat{U}(0,\pi/2)$). Mutants' access to richer strategies, as it happens in the case (B), does not continue to be an advantage as most of the population also have access to it. Hence $\hat{Q}$ comes out as the unique NE and ESS of the game.

13.3.1.1. *Evolutionary stability and entanglement*

The above analysis motivates us to obtain a direct relationship between a measure of entanglement and the mathematical concept of evolutionary stability for two-player games. The following example shows this relationship. Consider the two-player game given by the Matrix (13.16):

$$\begin{array}{cc} & \begin{array}{cc} \text{Bob} & \\ S_1 & S_2 \end{array} \\ \begin{array}{c} \text{Alice} \\ \begin{array}{c} S_1 \\ S_2 \end{array} \end{array} & \begin{pmatrix} (r,r) & (s,t) \\ (t,s) & (u,u) \end{pmatrix} \end{array} \tag{13.16}$$

and suppose Alice and Bob play the strategy S_1 with probabilities p and q, respectively. The strategy S_2 is then played with probabilities $(1-p)$ and $(1-q)$ by Alice and Bob, respectively. We denote Alice's payoff by $P_A(p,q)$ when she plays p and Bob plays q. That is, Alice's and Bob's strategies are now identified by the numbers $p,q \in [0,1]$, without referring to S_1 and S_2. For the Matrix (13.16) Alice's payoff $P_A(p,q)$, for example, reads

$$P_A(p,q) = rpq + sp(1-q) + t(1-p)q + u(1-p)(1-q)\,. \tag{13.17}$$

Similarly, Bob's payoff $P_B(p,q)$ can be written. In this symmetric game we have $P_A(p,q) = P_B(q,p)$ and, without using subscripts, $P(p,q)$, for

example, describes the payoff to p-player against q-player. In this game the inequality

$$P(p^*, p^*) - P(p, p^*) \geqslant 0 \tag{13.18}$$

says that the strategy p^*, played by both the players, is a NE. We consider the case when

$$s = t\,, \quad r = u\,, \text{ and } \quad (r - t) > 0 \tag{13.19}$$

in the Matrix (13.16). In this case the Inequality (13.18) along with the Definition (13.17) gives

$$P(p^*, p^*) - P(p, p^*) = (p^* - p)(r - t)(2p^* - 1)\,, \tag{13.20}$$

and the strategy $p^* = 1/2$ comes out as a mixed NE. From the ESS definition (13.2) we get $P(1/2, 1/2) - P(p, 1/2) = 0$ and the part a) of the definition does not apply. Part b) of the definition (13.2), then, gives

$$P(1/2, p) - P(p, p) = (r - t)\left\{2p(1 - p) - 1/2\right\}\,, \tag{13.21}$$

which can not be strictly greater than zero given $(r - t) > 0$. For example, at $p = 0$ it becomes a negative quantity. Therefore, for the matrix game defined by (13.16) and (13.19) the strategy $p^* = 1/2$ is a symmetric NE, but it is not evolutionarily stable. Also, at this equilibrium both players get $(r + t)/2$ as their payoffs.

Now consider the same game, defined by (13.16) and (13.19), when it is played by the set-up proposed by EWL. We set $s_A \equiv (\theta_A, \phi_A)$ and $s_B \equiv (\theta_B, \phi_B)$ to denote Alice's and Bob's strategies, respectively. Because the quantum game is symmetric i.e. $P_A(s_A, s_B) = P_B(s_B, s_A)$ we can write, as before, $P(s_A, s_B)$ for the payoff to s_A-player against s_B-player. For the quantum form of the game defined by (13.16) and (13.19) one finds

$$\begin{aligned} P(s_A, s_B) = {} & (1/2)(r - t) \\ & \{1 + \cos\theta_A \cos\theta_B + \sin\theta_A \sin\theta_B \sin\gamma \sin(\phi_A + \phi_B)\} + t\,. \end{aligned} \tag{13.22}$$

The definition of a NE gives $P(s^*, s^*) - P(s, s^*) \geqslant 0$ where $s = (\theta, \phi)$ and $s^* = (\theta^*, \phi^*)$. This definition can be written as

$$\left\{\partial_\theta P\,|_{\theta^*, \phi^*}\,(\theta^* - \theta) + \partial_\phi P\,|_{\theta^*, \phi^*}\,(\phi^* - \phi)\right\} \geq 0\,. \tag{13.23}$$

We search for a quantum strategy $s^* = (\theta^*, \phi^*)$ for which both $\partial_\theta P\,|_{\theta^*,\phi^*}$ and $\partial_\phi P\,|_{\theta^*,\phi^*}$ vanish at $\gamma = 0$ and which, at some other value of γ, is not zero. For the payoffs in Eq. (13.22) the strategy $s^* = (\pi/2, \pi/4)$ satisfies these conditions. For this strategy Eq. (13.22) gives

$$P(s^*, s^*) - P(s, s^*) = (1/2)(r-t)\sin\gamma\,\{1 - \sin(\phi + \pi/4)\sin\theta\}\ . \quad (13.24)$$

At $\gamma = 0$ the strategy $s^* = (\pi/2, \pi/4)$, when played by both the players, is a NE and it rewards the players same as does the strategy $p^* = 1/2$ in the classical version of the game i.e. $(r+t)/2$. Also, then we have $P(s^*, s^*) - P(s, s^*) = 0$ from Eq. (13.24) and the ESS's second condition in (13.2) applies. Using Eq. (13.22) to evaluate

$$\begin{aligned} P(s^*, s) - P(s, s) = &-(r-t)\cos^2(\theta) \\ &+ (1/2)(r-t)\sin\gamma\sin\theta\,\{\sin(\phi + \pi/4) - \sin\theta\sin(2\phi)\}\ , \end{aligned} \quad (13.25)$$

which at $\gamma = 0$ reduces to $P(s^*, s) - P(s, s) = -(r-t)\cos^2(\theta)$, that can assume negative values. The game's definition (13.19) and the ESS's second condition in (13.2) show that the strategy $s^* = (\pi/2, \pi/4)$ is not evolutionarily stable at $\gamma = 0$.

Now consider the case when $\gamma \neq 0$ in order to know about the evolutionary stability of the *same* quantum strategy. From (13.8) we have both $\sin\theta, \sin(\phi + \pi/4) \in [0, 1]$ and Eq. (13.24) indicates that $s^* = (\pi/2, \pi/4)$ remains a NE for all $\gamma \in [0, \pi/2]$. The product $\sin(\phi + \pi/4)\sin\theta$ attains a value of 1 only at $s^* = (\pi/2, \pi/4)$ and remains less than 1 otherwise. Equation (13.24) shows that for $\gamma \neq 0$ the strategy $s^* = (\pi/2, \pi/4)$ becomes a strict NE for which the ESS's first condition in (13.2) applies. Therefore, for the game defined in (13.19) the strategy $s^* = (\pi/2, \pi/4)$ is evolutionarily stable for a non-zero measure of entanglement γ. That is, entanglement gives evolutionary stability to a symmetric NE by making it a strict NE, that is, it is achieved by using in (13.2) the ESS's first condition only. Perhaps a more interesting example would be the case when entanglement gives evolutionary stability via the ESS's second condition. In that case, entanglement will make $P(s^*, s)$ strictly greater than $P(s, s)$ when $P(s^*, s^*)$ and $P(s, s^*)$ are equal.

It is to be pointed out here that in literature there exists an approach [Demitrius and Gundlach (2000)] which characterizes ESSs in terms of extremal states of a function known as *evolutionary entropy* that is defined by

$$E = -\sum_i \mu_i \log \mu_i \tag{13.26}$$

where μ_i represents the relative contribution of the i-th strategy to the total payoff. A possible extension of the present approach may be the case when quantum entanglement decides extremal states of evolutionary entropy. Extension along similar lines can be proposed for another quantity called *relative negentropy* [Bomze (1996)] that is optimized during the course of evolution.

13.3.2. *Evolutionary stability in MW quantization scheme*

Another interesting route that allows us to consider evolutionary stability in relation to quantization of a game is provided by MW scheme [Marinatto and Weber (2000a)]. In this scheme a transition between classical and quantum game is achieved by the initial state: classical payoffs are obtained when the initial state is a product state $|\psi_{\text{in}}\rangle = |00\rangle$. In this scheme one can consider evolutionary stability in a quantum game by asking whether it possible that a particular symmetric NE switches-over between being an ESS and not being an ESS when the initial state (initial strategy) changes from being $|\psi_{\text{in}}\rangle = |00\rangle$ to another state. MW scheme offers the possibility to make transition from classical to quantum version of a game by using different initial states and it appears to be a more suitable quantization scheme to analyze evolutionary stability in quantum games. It is because:

a) In a symmetric bi-matrix game, played in a population setting, players have access to two pure strategies and a mixed strategy is interpreted as a convex linear combination of pure strategies. Similar is the case with the players' strategies in MW scheme where a mixed strategy consists of a convex linear combination of the players' actions with two unitary operators.
b) Fitness of a pure strategy can be given a straightforward extension in MW scheme. It corresponds to a situation when, for example, in the quantum game, a player uses only one unitary operator out of the two.

c) Theory of ESSs, in the classical domain, deals with anonymous players possessing discrete number of pure strategies. EWL scheme involves a continuum of pure quantum strategies. The ESS concept is known to encounter problems [Oechssler and Riedel (2000)] when players possess a continuum of pure strategies.

13.3.2.1. 2×2 *asymmetric games*

An ESS is defined as a strict NE [Weibull (1995)] for an asymmetric bimatrix game, i.e. the game $G = (M, N)$ for which $N \neq M^T$. That is, a strategy pair $(\overset{\star}{x}, \overset{\star}{y}) \in S$ is an ESS of the game G if $P_A(\overset{\star}{x}, \overset{\star}{y}) > P_A(x, \overset{\star}{y})$ and $P_B(\overset{\star}{x}, \overset{\star}{y}) > P_B(\overset{\star}{x}, y)$ for all $x \neq \overset{\star}{x}$ and $y \neq \overset{\star}{y}$. For example, the BoS:

$$\begin{pmatrix} (\alpha, \beta) & (\gamma, \gamma) \\ (\gamma, \gamma) & (\beta, \alpha) \end{pmatrix} \tag{13.27}$$

where $\alpha > \beta > \gamma$ is a asymmetric game with three classical NE [Marinatto and Weber (2000a)] given as 1) $\overset{\star}{p}_1 = \overset{\star}{q}_1 = 0$ 2) $\overset{\star}{p}_2 = \overset{\star}{q}_2 = 1$ and 3) $\overset{\star}{p}_3 = \frac{\alpha-\gamma}{\alpha+\beta-2\gamma}, \overset{\star}{q}_3 = \frac{\beta-\gamma}{\alpha+\beta-2\gamma}$. Here the NE 1) and 2) are also ESS's but 3) is not because of not being a strict NE. When the asymmetric game (13.27) is played with the initial state $|\psi_{in}\rangle = a\,|S_1S_1\rangle + b\,|S_2S_2\rangle$, where S_1 and S_2 are players' pure classical strategies, the following three NE [Marinatto and Weber (2000a)] emerge 1) $\overset{\star}{p}_1 = \overset{\star}{q}_1 = 1$ 2) $\overset{\star}{p}_2 = \overset{\star}{q}_2 = 0$ and 3) $\overset{\star}{p}_3 = \frac{(\alpha-\gamma)|a|^2+(\beta-\gamma)|b|^2}{\alpha+\beta-2\gamma}, \overset{\star}{q}_3 = \frac{(\alpha-\gamma)|b|^2+(\beta-\gamma)|a|^2}{\alpha+\beta-2\gamma}$. It turns out that, similar to the classical case, the quantum NE 1) and 2) are ESSs while 3) is not. Now, play this game with a different initial state:

$$|\psi_{\text{in}}\rangle = a\,|S_1S_2\rangle + b\,|S_2S_1\rangle \tag{13.28}$$

for which players' payoffs are:

$$\begin{aligned} P_A(p,q) &= p\left\{-q(\alpha+\beta-2\gamma) + \alpha\,|a|^2 + \beta\,|b|^2 - \gamma\right\} \\ &\quad + q\left\{\alpha\,|b|^2 + \beta\,|a|^2 - \gamma\right\} + \gamma \\ P_B(p,q) &= q\left\{-p(\alpha+\beta-2\gamma) + \beta\,|a|^2 + \alpha\,|b|^2 - \gamma\right\} \\ &\quad + p\left\{\beta\,|b|^2 + \alpha\,|a|^2 - \gamma\right\} + \gamma \end{aligned} \tag{13.29}$$

and there is only one NE, i.e. $\overset{\star}{p} = \frac{\beta|a|^2+\alpha|b|^2-\gamma}{\alpha+\beta-\gamma}, \overset{\star}{q_3} = \frac{\alpha|a|^2+\beta|b|^2-\gamma}{\alpha+\beta-\gamma}$, which is not an ESS. So that, no ESS exists when BoS is played with the state (13.28).

Consider now another game:

$$\begin{pmatrix} (\alpha_1, \alpha_2) & (\beta_1, \beta_2) \\ (\gamma_1, \gamma_2) & (\sigma_1, \sigma_2) \end{pmatrix} \tag{13.30}$$

for which

$$\begin{pmatrix} \alpha_1 & \beta_1 \\ \gamma_1 & \sigma_1 \end{pmatrix} \neq \begin{pmatrix} \alpha_2 & \beta_2 \\ \gamma_2 & \sigma_2 \end{pmatrix}^T \tag{13.31}$$

and that it is played by using initial state $|\psi_{in}\rangle = a\,|S_1 S_1\rangle + b\,|S_2 S_2\rangle$ with $|a|^2 + |b|^2 = 1$. Players' payoffs are:

$$\begin{aligned} P_{A,B}(p,q) = {} & \alpha_{1,2}\left\{pq\,|a|^2 + (1-p)(1-q)\,|b|^2\right\} \\ & + \beta_{1,2}\left\{p(1-q)\,|a|^2 + q(1-p)\,|b|^2\right\} \\ & + \gamma_{1,2}\left\{p(1-q)\,|b|^2 + q(1-p)\,|a|^2\right\} \\ & + \sigma_{1,2}\left\{pq\,|b|^2 + (1-p)(1-q)\,|a|^2\right\}. \end{aligned} \tag{13.32}$$

The NE conditions are

$$\begin{aligned} & P_A(\overset{\star}{p}, \overset{\star}{q}) - P_A(p, \overset{\star}{q}) \\ & \quad = (\overset{\star}{p} - p)\left[|a|^2(\beta_1 - \sigma_1) + |b|^2(\gamma_1 - \alpha_1) - \overset{\star}{q}\{(\beta_1 - \sigma_1) + (\gamma_1 - \alpha_1)\}\right] \\ & \quad \geq 0 \end{aligned} \tag{13.33}$$

$$\begin{aligned} & P_B(\overset{\star}{p}, \overset{\star}{q}) - P_B(\overset{\star}{p}, q) \\ & \quad = (\overset{\star}{q} - q)\left[|a|^2(\gamma_2 - \sigma_2) + |b|^2(\beta_2 - \alpha_2) - \overset{\star}{p}\{(\gamma_2 - \sigma_2) + (\beta_2 - \alpha_2)\}\right] \\ & \quad \geq 0\,. \end{aligned} \tag{13.34}$$

So that, for $\overset{\star}{p} = \overset{\star}{q} = 0$ to be a NE we have

$$\begin{aligned} & P_A(0,0) - P_A(p,0) = -p\left[(\beta_1 - \sigma_1) + |b|^2\{(\gamma_1 - \alpha_1) - (\beta_1 - \sigma_1)\}\right] \geq 0 \\ & P_B(0,0) - P_B(0,q) = -q\left[(\gamma_2 - \sigma_2) + |b|^2\{(\beta_2 - \alpha_2) - (\gamma_2 - \sigma_2)\}\right] \geq 0 \end{aligned} \tag{13.35}$$

and for the strategy pair $(0,0)$ to be an ESS in the classical game[5] we require $P_A(0,0) - P_A(p,0) = -p(\beta_1 - \sigma_1) > 0$ and $P_B(0,0) - P_B(0,q) = -q(\gamma_2 - \sigma_2) > 0$ for all $p, q \neq 0$. That is, $(\beta_1 - \sigma_1) < 0$ and $(\gamma_2 - \sigma_2) < 0$. For the pair $(0,0)$ not to be an ESS for some $|b|^2 \neq 0$, let take $\gamma_1 = \alpha_1$ and $\beta_2 = \alpha_2$ and we have

$$\begin{aligned} P_A(0,0) - P_A(p,0) &= -p(\beta_1 - \sigma_1)\left\{1 - |b|^2\right\} \\ P_B(0,0) - P_B(0,q) &= -q(\gamma_2 - \sigma_2)\left\{1 - |b|^2\right\} \end{aligned} \tag{13.36}$$

i.e. the pair $(0,0)$ does not remain an ESS at $|b|^2 = 1$. A game having this property is given by the matrix:

$$\begin{pmatrix} (1,1) & (1,2) \\ (2,1) & (3,2) \end{pmatrix}. \tag{13.37}$$

For this game the strategy pair $(0,0)$ is an ESS when $|b|^2 = 0$ (classical game) but it is not when for example $|b|^2 = \frac{1}{2}$, though it remains a NE in both the cases. The example shows a NE switches between ESS and "not ESS" by using different initial state. In contrast to the last case, one can also find initial states—different from the one corresponding to the classical game—that turn a NE strategy pair into an ESS. An example of a game for which it happens is

$$\begin{array}{c} \\ \\ \text{Alice} \end{array} \begin{array}{c} \text{Bob} \\ \begin{array}{cc} S_1 & S_2 \end{array} \\ \begin{array}{c} S_1 \\ S_2 \end{array} \begin{pmatrix} (2,1) & (1,0) \\ (1,0) & (1,0) \end{pmatrix} \end{array}. \tag{13.38}$$

Playing this game again via the state $|\psi_{\text{in}}\rangle = a\,|S_1S_1\rangle + b\,|S_2S_2\rangle$ gives the following payoff differences for the strategy pair $(0,0)$:

$$P_A(0,0) - P_A(p,0) = p\,|b|^2 \quad \text{and} \quad P_B(0,0) - P_B(0,q) = q\,|b|^2 \tag{13.39}$$

for Alice and Bob respectively. Therefore, (13.38) is an example of a game for which the pair $(0,0)$ is not an ESS when the initial state corresponds to the classical game. But the same pair is an ESS for other initial states for which $0 < |b|^2 < 1$.

[5] which corresponds when $|b|^2 = 0$.

13.3.2.2. 2×2 *symmetric games*

Consider now a symmetric bi-matrix game:

$$\begin{array}{c} \\ \\ \text{Alice} \end{array} \begin{array}{c} \begin{array}{cc} \multicolumn{2}{c}{\text{Bob}} \\ S_1 & S_2 \end{array} \\ \begin{array}{c} S_1 \\ S_2 \end{array} \begin{pmatrix} (\alpha,\alpha) & (\beta,\gamma) \\ (\gamma,\beta) & (\delta,\delta) \end{pmatrix} \end{array} \tag{13.40}$$

that is played by an initial state:

$$|\psi_{\text{in}}\rangle = a\,|S_1S_1\rangle + b\,|S_2S_2\rangle\ , \quad \text{with}\ \ |a|^2 + |b|^2 = 1\,. \tag{13.41}$$

Let Alice's strategy consists of applying the identity operator $\hat{I}$ with probability p and the operator $\hat{\sigma}_x$ with probability $(1-p)$, on the initial state written ρ_{in} in density matrix notation. Similarly Bob applies the operators $\hat{I}$ and $\hat{\sigma}_x$ with the probabilities q and $(1-q)$ respectively. The final state is

$$\rho_{\text{fin}} = \sum_{\hat{U}=\hat{I},\hat{\sigma}_x} \Pr(\hat{U}_A)\Pr(\hat{U}_B)[\hat{U}_A \otimes \hat{U}_B \rho_{in} \hat{U}_A^\dagger \otimes \hat{U}_B^\dagger] \tag{13.42}$$

where unitary and Hermitian operator $\hat{U}$ is either $\hat{I}$ or $\hat{\sigma}_x$. Here, $\Pr(\hat{U}_A)$, $\Pr(\hat{U}_B)$ are the probabilities, for Alice and Bob, respectively, to apply the operator on the initial state. The matrix ρ_{fin} is obtained from ρ_{in} by making a convex linear combination of players' possible quantum operations. Payoff operators for Alice and Bob are [Marinatto and Weber (2000a)]

$$\begin{aligned}(P_{A,B})_{\text{oper}} = {} & \alpha,\alpha\,|S_1S_1\rangle\langle S_1S_1| + \beta,\gamma\,|S_1S_2\rangle\langle S_1S_2| \\ & + \gamma,\beta\,|S_2S_1\rangle\langle S_2S_1| + \delta,\delta\,|S_2S_2\rangle\langle S_2S_2|\ .\end{aligned} \tag{13.43}$$

The payoffs are then obtained as mean values of these operators i.e. $P_{A,B} = Tr\,[(P_{A,B})_{\text{oper}}\rho_{\text{fin}}]$. Because the quantum game is symmetric with the initial state (13.41) and the payoff matrix (13.40), there is no need for subscripts. We can , then, write the payoff to a p-player against a q-player as $P(p,q)$, where the first number is the focal player's move. When $\overset{\star}{p}$ is a NE we find the following payoff difference:

$$\begin{aligned}P(\overset{\star}{p},\overset{\star}{p}) - P(p,\overset{\star}{p}) = {} & (\overset{\star}{p}-p)[\,|a|^2(\beta-\delta) \\ & + |b|^2(\gamma-\alpha) - \overset{\star}{p}\{(\beta-\delta)+(\gamma-\alpha)\}]\,.\end{aligned} \tag{13.44}$$

Now the ESS conditions for the pure strategy $p = 0$ are given as

$$\begin{aligned} &1. \quad |b|^2 \{(\beta - \delta) - (\gamma - \alpha)\} > (\beta - \delta) \\ &2.\ \text{If } |b|^2 \{(\beta - \delta) - (\gamma - \alpha)\} = (\beta - \delta) \\ &\quad \text{then } q^2 \{(\beta - \delta) + (\gamma - \alpha)\} > 0 \end{aligned} \tag{13.45}$$

where 1 is the NE condition. Similarly the ESS conditions for the pure strategy $p = 1$ are

$$\begin{aligned} &1. \quad |b|^2 \{(\gamma - \alpha) - (\beta - \delta)\} > (\gamma - \alpha) \\ &2.\ \text{If } |b|^2 \{(\gamma - \alpha) - (\beta - \delta)\} = (\gamma - \alpha) \\ &\text{then } (1 - q)^2 \{(\beta - \delta) + (\gamma - \alpha)\} > 0\,. \end{aligned} \tag{13.46}$$

Because these conditions, for both the pure strategies $p = 1$ and $p = 0$, depend on $|b|^2$, therefore, there can be examples of two-player symmetric games for which the evolutionary stability of pure strategies can be changed while playing the game using initial state in the form $|\psi_{\text{in}}\rangle = a\,|S_1 S_1\rangle + b\,|S_2 S_2\rangle$. However, for the mixed NE, given as $\overset{\star}{p} = \frac{|a|^2(\beta-\delta)+|b|^2(\gamma-\alpha)}{(\beta-\delta)+(\gamma-\alpha)}$, the corresponding payoff difference (13.44) becomes identically zero. From the second condition of an ESS we find for the mixed NE $\overset{\star}{p}$ the difference

$$\begin{aligned} &P(\overset{\star}{p}, q) - P(q, q) \\ &= \frac{1}{(\beta - \delta) + (\gamma - \alpha)} \\ &\quad \times \left[(\beta - \delta) - q\,\{(\beta - \delta) + (\gamma - \alpha)\} - |b|^2 \{(\beta - \delta) - (\gamma - \alpha)\}\right]^2 . \end{aligned} \tag{13.47}$$

Therefore, the mixed strategy $\overset{\star}{p}$ is an ESS when $\{(\beta - \delta) + (\gamma - \alpha)\} > 0$. This condition, making the mixed NE $\overset{\star}{p}$ an ESS, is independent [6] of $|b|^2$. So that, in this symmetric two-player quantum game, evolutionary stability of the mixed NE $\overset{\star}{p}$ can not be changed when the game is played using initial quantum states of the form of Eq. (13.41).

However, evolutionary stability of pure strategies can be affected, with this form of the initial states, for two-player symmetric games. Examples of the games with this property are easy to find. The class of games for which $\gamma = \alpha$ and $(\beta - \delta) < 0$ the strategies $p = 0$ and $p = 1$ remain NE for

[6] An alternative possibility is to adjust $|b|^2 = \frac{(\beta-\delta)-q\{(\beta-\delta)+(\gamma-\alpha)\}}{\{(\beta-\delta)-(\gamma-\alpha)\}}$ which makes the difference $\left\{P(\overset{\star}{p}, q) - P(q, q)\right\}$ identically zero. The mixed strategy $\overset{\star}{p}$ then does not remain an ESS. However such "mutant dependent" adjustment of $|b|^2$ is not reasonable because the mutant strategy q can be anything in the range $[0, 1]$.

all $|b|^2 \in [0,1]$; but the strategy $p=1$ is not an ESS when $|b|^2 = 0$ and the strategy $p=0$ is not an ESS when $|b|^2 = 1$.

Consider the symmetric bi-matrix game (13.40) with the constants $\alpha, \beta, \gamma, \delta$ satisfying the conditions:

$$\alpha, \beta, \gamma, \delta \geq 0; (\delta - \beta) > 0; (\gamma - \alpha) \geq 0; (\gamma - \alpha) < (\delta - \beta)\,. \tag{13.48}$$

The condition making $(p^\star, p^\star)$ a NE is given by (13.44). For this game three Nash equilibria arise i.e. two pure strategies $p^* = 0$, $p^* = 1$, and one mixed strategy $p^* = \frac{(\delta-\beta)|a|^2-(\gamma-\alpha)|b|^2}{(\delta-\beta)-(\gamma-\alpha)}$. These three cases are considered below.

Case $p^\star = 0$: For the strategy $p^\star = 0$ to be a NE one requires

$$P(0,0) - P(p,0) = \frac{p}{(\gamma-\alpha)+(\delta-\beta)}\left[|a|^2 - \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}\right] \geq 0 \tag{13.49}$$

and the difference $\{P(0,0) - P(p,0)\} > 0$ when $1 \geq |a|^2 > \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$. In this range of $|a|^2$ the equilibrium $p^\star = 0$ is a pure ESS. However, when $|a|^2 = \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$ we have the difference $\{P(0,0) - P(p,0)\}$ identically zero. The strategy $p^\star = 0$ can be an ESS if

$$\begin{aligned} &P(0,p) - P(p,p) \\ &\quad = p\,\{(\gamma-\alpha)+(\delta-\beta)\}\left\{|a|^2 - \frac{(1-p)(\gamma-\alpha)+p(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)}\right\} \\ &\quad > 0 \end{aligned} \tag{13.50}$$

that can be written as

$$P(0,p) - P(p,p) = p\,\{(\gamma-\alpha)+(\delta-\beta)\}\left\{|a|^2 - \digamma\right\} > 0 \tag{13.51}$$

where $\frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)} \leq \digamma \leq \frac{(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)}$ when $0 \leq p \leq 1$. The strategy $p^\star = 0$ can be an ESS only when $|a|^2 > \frac{(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)}$, which is not possible because $|a|^2$ is fixed at $\frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$. Therefore the strategy $p^\star = 0$ is an ESS for $1 \geq |a|^2 > \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$ and for $|a|^2 = \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$ this NE becomes unstable. The classical game is obtained by taking $|a|^2 = 1$ for which $p^\star = 0$ is an ESS or a stable NE. However this NE does not remain stable for $|a|^2 = \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$ which corresponds to an entangled initial state; though the NE remains intact in both forms of the game.

Case $p^\star = 1$: Similar to the last case the NE condition for the strategy $p^\star = 1$ can be written as

$$P(1,1) - P(p,1) = \frac{(1-p)}{(\gamma-\alpha)+(\delta-\beta)} \left[-|a|^2 + \frac{(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)} \right] \geq 0\,. \tag{13.52}$$

Now $p^\star = 1$ is a pure ESS for $0 \leq |a|^2 < \frac{(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)}$. For $|a|^2 = \frac{(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)}$ the difference $\{P(1,1) - P(p,1)\}$ becomes identically zero. The strategy $p^\star = 1$ is an ESS when

$$\begin{aligned} &P(1,p) - P(p,p) \\ &\quad = (1-p)\left\{(\gamma-\alpha)+(\delta-\beta)\right\} \left\{ -|a|^2 + \frac{(1-p)(\gamma-\alpha)+p(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)} \right\} \\ &\quad > 0\,. \end{aligned} \tag{13.53}$$

It is possible only if $|a|^2 < \frac{(\gamma-\alpha)}{(\gamma-\alpha)+(\delta-\beta)}$. Therefore the strategy $p^\star = 1$ is a stable NE (ESS) for $0 \leq |a|^2 < \frac{(\delta-\beta)}{(\gamma-\alpha)+(\delta-\beta)}$. It is not stable classically (i.e. for $|a|^2 = 1$) but becomes stable for an entangled initial state.

Case $p^\star = \frac{(\delta-\beta)|a|^2-(\gamma-\alpha)|b|^2}{(\delta-\beta)-(\gamma-\alpha)}$: In case of the mixed strategy:

$$p^\star = \frac{(\delta-\beta)\,|a|^2 - (\gamma-\alpha)\,|b|^2}{(\delta-\beta)-(\gamma-\alpha)} \tag{13.54}$$

the NE condition (13.44) turns into $P(p^\star,p^\star) - P(p,p^\star) = 0$. The mixed strategy (13.54) can be an ESS if

$$\begin{aligned} &P(p^\star,p) - P(p,p) \\ &\quad = (p^\star - p)\left[-|a|^2\,(\delta-\beta) + |b|^2\,(\gamma-\alpha) + p\left\{(\delta-\beta)-(\gamma-\alpha)\right\} \right] > 0 \end{aligned} \tag{13.55}$$

for all $p \neq p^\star$. Write now the strategy p as $p = p^\star + \triangle$. For the mixed strategy (13.54) the payoff difference of the Eq. (13.55) is reduced to

$$P(p^\star,p) - P(p,p) = -\triangle^2 \left\{(\delta-\beta)-(\gamma-\alpha)\right\}. \tag{13.56}$$

Hence, for the game defined in the conditions (13.48), the mixed strategy $p^\star = \frac{(\delta-\beta)|a|^2-(\gamma-\alpha)|b|^2}{(\delta-\beta)-(\gamma-\alpha)}$ cannot be an ESS, though it can be a NE of the symmetric game.

It is to be pointed out that above considerations apply when the game is played with the initial state given by Eq. (13.41).

To find examples of symmetric quantum games, where evolutionary stability of the mixed strategies may also be affected by controlling the initial states, the number of players is now increased from two to three.

13.3.2.3. $2 \times 2 \times 2$ *symmetric games*

In extending the two-player scheme to a three-player case, we assume that three players A, B, and C play their strategies by applying the identity operator $\hat{I}$ with the probabilities p, q and r respectively on the initial state $|\psi_{\text{in}}\rangle$. Therefore, they apply the operator $\hat{\sigma}_x$ with the probabilities $(1-p), (1-q)$ and $(1-r)$ respectively. The final state becomes

$$\rho_{\text{fin}} = \sum_{\hat{U}=\hat{I},\hat{\sigma}_x} \Pr(\hat{U}_A)\Pr(\hat{U}_B)\Pr(\hat{U}_C)\left[\hat{U}_A \otimes \hat{U}_B \otimes \hat{U}_C \rho_{in} \hat{U}_A^\dagger \otimes \hat{U}_B^\dagger \otimes \hat{U}_C^\dagger\right] \tag{13.57}$$

where the 8 basis vectors are $|S_i S_j S_k\rangle$, for $i, j, k = 1, 2$. Again we use initial quantum state in the form $|\psi_{in}\rangle = a\,|S_1S_1S_1\rangle + b\,|S_2S_2S_2\rangle$, where $|a|^2 + |b|^2 = 1$. It is a quantum state in $2 \otimes 2 \otimes 2$ dimensional Hilbert space that can be prepared from a system of three two-state quantum systems or qubits. Similar to the two-player case, the payoff operators for the players A, B, and C can be defined as

$$\begin{aligned}
&(P_{A,B,C})_{\text{oper}} \\
&\quad = \alpha_1, \beta_1, \eta_1\,|S_1S_1S_1\rangle\langle S_1S_1S_1| + \alpha_2, \beta_2, \eta_2\,|S_2S_1S_1\rangle\langle S_2S_1S_1| \\
&\qquad + \alpha_3, \beta_3, \eta_3\,|S_1S_2S_1\rangle\langle S_1S_2S_1| + \alpha_4, \beta_4, \eta_4\,|S_1S_1S_2\rangle\langle S_1S_1S_2| \\
&\qquad + \alpha_5, \beta_5, \eta_5\,|S_1S_2S_2\rangle\langle S_1S_2S_2| + \alpha_6, \beta_6, \eta_6\,|S_2S_1S_2\rangle\langle S_2S_1S_2| \\
&\qquad + \alpha_7, \beta_7, \eta_7\,|S_2S_2S_1\rangle\langle S_2S_2S_1| + \alpha_8, \beta_8, \eta_8\,|S_2S_2S_2\rangle\langle S_2S_2S_2|
\end{aligned} \tag{13.58}$$

where $\alpha_l, \beta_l, \eta_l$ for $1 \le l \le 8$ are 24 constants of the matrix of this three-player game. Payoffs to the players A, B, and C are then obtained as mean values of these operators i.e. $P_{A,B,C}(p,q,r) = \text{Tr}[(P_{A,B,C})_{\text{oper}}\rho_{\text{fin}}]$.

Here, similar to the two-player case, the classical payoffs can be obtained when $|b|^2 = 0$. To get a symmetric game we define $P_A(x,y,z)$ as the payoff to player A when players A, B, and C play the strategies x, y, and z respectively. With following relations the players' payoffs become identity-independent.

$$\begin{aligned}
P_A(x,y,z) &= P_A(x,z,y) = P_B(y,x,z) \\
&= P_B(z,x,y) = P_C(y,z,x) = P_C(z,y,x)\,.
\end{aligned} \tag{13.59}$$

The players in the game then become anonymous and their payoffs depend only on their strategies. The relations in (13.59) hold with the following replacements for β_i and η_i:

$$\begin{array}{llll} \beta_1 \to \alpha_1 & \beta_2 \to \alpha_3 & \beta_3 \to \alpha_2 & \beta_4 \to \alpha_3 \\ \beta_5 \to \alpha_6 & \beta_6 \to \alpha_5 & \beta_7 \to \alpha_6 & \beta_8 \to \alpha_8 \\ \eta_1 \to \alpha_1 & \eta_2 \to \alpha_3 & \eta_3 \to \alpha_3 & \eta_4 \to \alpha_2 \\ \eta_5 \to \alpha_6 & \eta_6 \to \alpha_6 & \eta_7 \to \alpha_5 & \eta_8 \to \alpha_8 \,. \end{array} \tag{13.60}$$

Also, it is now necessary that we should have $\alpha_6 = \alpha_7$, $\alpha_3 = \alpha_4$.

A symmetric game between three players, therefore, can be defined by only six constants of the payoff matrix . These constants can be taken as $\alpha_1, \alpha_2, \alpha_3, \alpha_5, \alpha_6$, and α_8. Payoff to a p-player, when other two players play q and r, can now be written as $P(p, q, r)$. A symmetric NE $\overset{\star}{p}$ is now found from the Nash condition $P(\overset{\star}{p}, \overset{\star}{p}, \overset{\star}{p}) - P(p, \overset{\star}{p}, \overset{\star}{p}) \geq 0$, i.e.

$$\begin{aligned} P(\overset{\star}{p}, \overset{\star}{p}, \overset{\star}{p}) - P(p, \overset{\star}{p}, \overset{\star}{p}) = (\overset{\star}{p} - p) \Big[& \overset{\star 2}{p} (1 - 2\,|b|^2)(\sigma + \omega - 2\eta) \\ & + 2\overset{\star}{p} \left\{ |b|^2 (\sigma + \omega - 2\eta) - \omega + \eta \right\} \\ & + \left\{ \omega - |b|^2 (\sigma + \omega) \right\} \Big] \geq 0 \end{aligned} \tag{13.61}$$

where $(\alpha_1 - \alpha_2) = \sigma, (\alpha_3 - \alpha_6) = \eta$, and $(\alpha_5 - \alpha_8) = \omega$.

Three possible NE are found as

$$\left.\begin{array}{c} \overset{\star}{p}_1 = \frac{\left\{(\omega-\eta)-|b|^2(\sigma+\omega-2\eta)\right\} \pm \sqrt{\{(\sigma+\omega)^2-(2\eta)^2\}|b|^2(1-|b|^2)+(\eta^2-\sigma\omega)}}{(1-2|b|^2)(\sigma+\omega-2\eta)} \\ \overset{\star}{p}_2 = 0 \\ \overset{\star}{p}_3 = 1 \end{array}\right\} . \tag{13.62}$$

It is observed that the mixed NE $\overset{\star}{p}_1$ makes the differences $\left\{ P(\overset{\star}{p}, \overset{\star}{p}, \overset{\star}{p}) - P(p, \overset{\star}{p}, \overset{\star}{p}) \right\}$ identically zero and two values for $\overset{\star}{p}_1$ can be found for a given $|b|^2$. Apart from $\overset{\star}{p}_1$ the other two NE (i.e. $\overset{\star}{p}_2$ and $\overset{\star}{p}_3$) are pure strategies. Also now $\overset{\star}{p}_1$ comes out a NE without imposing further restrictions on the matrix of the symmetric three-player game. However, the pure strategies $\overset{\star}{p}_2$ and $\overset{\star}{p}_3$ can be NE when further restriction are imposed on the matrix of the game. For example, $\overset{\star}{p}_3$ can be a NE provided $\sigma \geq (\omega + \sigma)\,|b|^2$ for all $|b|^2 \in [0, 1]$. Similarly $\overset{\star}{p}_2$ can be NE when $\omega \leq (\omega + \sigma)\,|b|^2$.

Now we address the question: How evolutionary stability of these three NE can be affected while playing the game via initial quantum states given in the following form?

$$|\psi_{\text{in}}\rangle = a\,|S_1 S_1 S_1\rangle + b\,|S_2 S_2 S_2\rangle \ . \tag{13.63}$$

For the two-player asymmetric game of BoS we showed that out of three NE only two can be evolutionarily stable. In classical evolutionary game theory the concept of an ESS is well-known [Broom *et al.* (2000, 1997)] to be extendable to multi-player case. When mutants are allowed to play only one strategy the definition of an ESS for the three-player case is written as [Broom *et al.* (2000)]

$$\begin{aligned} &1. \quad P(p,p,p) > P(q,p,p) \\ &2.\ \text{If } P(p,p,p) = P(q,p,p) \text{ then } P(p,q,p) > P(q,q,p)\,. \end{aligned} \tag{13.64}$$

Here p is a NE if it satisfies the condition 1 against all $q \neq p$. For our case the ESS conditions for the pure strategies $\overset{\star}{p}_2$ and $\overset{\star}{p}_3$ can be written as follows. For example $\overset{\star}{p}_2 = 0$ is an ESS when

$$\begin{aligned} &1. \quad \sigma\,|b|^2 > \omega\,|a|^2 \\ &2.\ \text{If } \sigma\,|b|^2 = \omega\,|a|^2 \ \text{ then } \ -\eta q^2(|a|^2 - |b|^2) > 0 \end{aligned} \tag{13.65}$$

where 1 is NE condition for the strategy $\overset{\star}{p}_2 = 0$. Similarly, $\overset{\star}{p}_3 = 1$ is an ESS when

$$\begin{aligned} &1. \quad \sigma\,|a|^2 > \omega\,|b|^2 \\ &2.\ \text{If } \sigma\,|a|^2 = \omega\,|b|^2 \ \text{ then } \eta(1-q)^2(|a|^2 - |b|^2) > 0 \end{aligned} \tag{13.66}$$

and both the pure strategies $\overset{\star}{p}_2$ and $\overset{\star}{p}_3$ are ESSs when $|a|^2 = |b|^2$. The conditions (13.66) can also be written as

$$\begin{aligned} &1. \quad \sigma > (\omega + \sigma)\,|b|^2 \\ &2.\ \text{If } \sigma = |b|^2\,(\omega + \sigma) \text{ then } \frac{\gamma(\omega - \sigma)}{(\omega + \sigma)} > 0\,. \end{aligned} \tag{13.67}$$

For the strategy $\overset{\star}{p}_2 = 0$ the ESS conditions (13.65) reduce to

$$\begin{aligned} &1. \quad \omega < (\omega + \sigma)\,|b|^2 \\ &2.\ \text{If } \ \omega = |b|^2\,(\omega + \sigma) \text{ then } \frac{\gamma(\omega - \sigma)}{(\omega + \sigma)} > 0\,. \end{aligned} \tag{13.68}$$

Examples of three-player symmetric games are easy to find for which a pure strategy is a NE for the whole range $|b|^2 \in [0,1]$, but it is not an ESS for some particular value of $|b|^2$. An example of a class of such games is for which $\sigma = 0$, $\omega < 0$, and $\eta \leq 0$. In this class the strategy $\overset{\star}{p}_2 = 0$ is a NE for all $|b|^2 \in [0,1]$ but not an ESS when $|b|^2 = 1$.

Apart from the pure strategies, the mixed strategy equilibrium $\overset{\star}{p}_1$ forms the most interesting case. It makes the payoff difference

$\left\{P(\overset{\star}{p_1},\overset{\star}{p_1},\overset{\star}{p_1}) - P(p,\overset{\star}{p_1},\overset{\star}{p_1})\right\}$ identically zero for every strategy p. The strategy $\overset{\star}{p_1}$ is an ESS when $\left\{P(\overset{\star}{p_1},q,\overset{\star}{p_1}) - P(q,q,\overset{\star}{p_1})\right\} > 0$ but

$$P(\overset{\star}{p_1},q,\overset{\star}{p_1}) - P(q,q,\overset{\star}{p_1}) = \pm(\overset{\star}{p_1}-q)^2\sqrt{\{(\sigma+\omega)^2-(2\eta)^2\}\,|b|^2\,(1-|b|^2)+(\eta^2-\sigma\omega)}\,. \quad (13.69)$$

Therefore, out of the two possible roots $(\overset{\star}{p_1})_1$ and $(\overset{\star}{p_1})_2$ of the quadratic equation[7]:

$$\overset{\star}{p_1}^{\,2}(1-2\,|b|^2)(\sigma+\omega-2\eta) + 2\overset{\star}{p_1}\left\{|b|^2\,(\sigma+\omega-2\eta)-\omega+\eta\right\} + \left\{\omega-|b|^2\,(\sigma+\omega)\right\} = 0 \quad (13.70)$$

only $(\overset{\star}{p_1})_1$ can exist as an ESS. When the square root term in Eq. (13.69) becomes zero we have only one mixed NE, which is not an ESS. Hence, out of four possible NE in this three-player game only three can be ESSs.

An interesting class of three-player games is the one for which $\eta^2 = \sigma\omega$. For these games the mixed NE are

$$\overset{\star}{p_1} = \frac{\left\{(w-\eta)-|b|^2\,(\sigma+\omega-2\eta)\right\} \pm |a|\,|b|\,|\sigma-\omega|}{(1-2\,|b|^2)(\sigma+\omega-2\eta)} \quad (13.71)$$

and, when played classically, we can get only one mixed NE that is not an ESS. However for all $|b|^2$, different from zero, we generally obtain two NE out of which one can be an ESS.

Similar to the two-player case, the equilibria in a three-player symmetric game where quantization affects evolutionary stability, are the ones that survive for two initial states, one of which is a product state and corresponds to the classical game. Suppose $\overset{\star}{p_1}$ remains a NE for $|b|^2 = 0$ and some other non-zero $|b|^2$. It is possible when $(\sigma-\omega)(2\overset{\star}{p_1}-1) = 0$. Alternatively, the strategy $\overset{\star}{p} = \frac{1}{2}$ remains a NE for all $|b|^2 \in [0,1]$. It reduces the defining quadratic equation (13.70) for $\overset{\star}{p_1}$ to $\sigma+\omega+2\eta = 0$ and makes the difference $\left\{P(\overset{\star}{p_1},q,\overset{\star}{p_1}) - P(q,q,\overset{\star}{p_1})\right\}$ independent of $|b|^2$. Therefore the strategy $\overset{\star}{p} = \frac{1}{2}$, even when it is retained as an equilibrium for all $|b|^2 \in [0,1]$, cannot be

[7]These roots make the difference $\left\{P(\overset{\star}{p_1},q,\overset{\star}{p_1}) - P(q,q,\overset{\star}{p_1})\right\}$ greater than and less than zero, respectively.

an ESS in only one version of the symmetric three-player game. For the second possibility $\sigma = \omega$ the defining equation for $p_1^\star$ is reduced to

$$(1-2\,|b|^2)\left\{p_1^\star - \frac{(\eta-\sigma)-\sqrt{\eta^2-\sigma^2}}{2(\eta-\sigma)}\right\}\left\{p_1^\star - \frac{(\eta-\sigma)+\sqrt{\eta^2-\sigma^2}}{2(\eta-\sigma)}\right\} = 0 \tag{13.72}$$

for which

$$P(p_1^\star, q, p_1^\star) - P(q, q, p_1^\star) = \pm 2(p_1^\star - q)^2 \left||b|^2 - \frac{1}{2}\right| \sqrt{\eta^2-\sigma^2}\,. \tag{13.73}$$

Here the difference $\left\{P(p_1^\star, q, p_1^\star) - P(q, q, p_1^\star)\right\}$ still depends on $|b|^2$ and becomes zero for $|b|^2 = 1/2$.

Hence, for the class of games for which $\sigma = \omega$ and $\eta > \sigma$, one of the mixed strategies $(p_1^\star)_1, (p_1^\star)_2$ remains a NE for all $|b|^2 \in [0,1]$ but not an ESS when $|b|^2 = 1/2$. In this class of three-player quantum games the evolutionary stability of a mixed strategy can, therefore, be changed while the game is played using initial quantum states in the form of Eq. (13.63).

13.3.2.4. *Rock-Scissors-Paper game*

Rock-Scissors-Paper (RSP) is a game for two players that is typically played using the players' hands. This game has been played for long as a children's pastime or as an odd-man-out selection process. The players opposite each others, tap their fist in their open palm three times (saying rock, scissors, paper) and then show one of three possible gestures. The rock wins against the scissors (crushes it) but looses against the paper (is wrapped into it). The scissors wins against the paper (cuts it) but looses against the rock (is crushed by it). The paper wins against the rock (wraps it) but looses against the scissors (is cut by it). The game is also played in nature like many other games. Lizards in the Coast Range of California play this game [Peterson (1996)] using three alternative male strategies locked in an ecological never ending process from which there seems little escape.

In a slightly modified version of the RSP game both players get a small premium ϵ for a draw. This game can be represented by the payoff matrix:

$$\begin{array}{c} \\ R \\ S \\ P \end{array} \begin{array}{c} \begin{array}{ccc} R & S & P \end{array} \\ \begin{pmatrix} -\epsilon & 1 & -1 \\ -1 & -\epsilon & 1 \\ 1 & -1 & -\epsilon \end{pmatrix} \end{array} \tag{13.74}$$

where $-1 < \epsilon \leq 0$. The matrix of the usual game is obtained when ϵ is zero.

One cannot win if one's opponent knew which strategy was going to be picked. For example, when picking rock consistently, all the opponent needs to do is pick paper and s/he would win. Players find soon that in case predicting opponent's strategy is not possible the best strategy is to pick rock, scissors, or paper at random. In other words, the player selects rock, scissors, or paper with a probability of 1/3. In case opponent's strategy is predictable picking a strategy at random with a probability of 1/3 is *not* the best thing to do unless the opponent does the same [Prestwich (1999)].

Analysis [Weibull (1995)] of the modified RSP game of Matrix (13.74) shows that its NE consists of playing each of the three different pure strategies with a fixed equilibrial probability 1/3. However it is not an ESS because ϵ is negative.

Here we want to study the effects of quantization on evolutionary stability for the modified RSP game. The game is different, from others considered earlier, because classically each player now possesses three pure strategies instead of two. A classical mixed NE exists which is not an ESS. Our motivation is to explore the possibility that the classical mixed NE becomes an ESS for some quantum form of the game.

Quantization of Rock-Scissors-Paper game: Using simpler notation: $R \sim 1$, $S \sim 2$, $P \sim 3$ we quantize this game via MW scheme [Marinatto and Weber (2000a)]. We assume the two players are in possession of three unitary and Hermitian operators $\hat{I}$, $\hat{C}$ and $\hat{D}$ defined as follows.

$$\begin{aligned} \hat{I}\,|1\rangle = |1\rangle\,, \qquad & \hat{C}\,|1\rangle = |3\rangle\,, \qquad & \hat{D}\,|1\rangle = |2\rangle \\ \hat{I}\,|2\rangle = |2\rangle\,, \qquad & \hat{C}\,|2\rangle = |2\rangle\,, \qquad & \hat{D}\,|2\rangle = |1\rangle \\ \hat{I}\,|3\rangle = |3\rangle\,, \qquad & \hat{C}\,|3\rangle = |1\rangle\,, \qquad & \hat{D}\,|3\rangle = |3\rangle \end{aligned} \tag{13.75}$$

where $\hat{C}^\dagger = \hat{C} = \hat{C}^{-1}$ and $\hat{D}^\dagger = \hat{D} = \hat{D}^{-1}$ and $\hat{I}$ is the identity operator.

Consider a general two-player payoff matrix when each player has three strategies:

$$\begin{array}{c} \\ 1 \\ 2 \\ 3 \end{array} \begin{array}{c} \begin{array}{ccc} 1 & 2 & 3 \end{array} \\ \begin{pmatrix} (\alpha_{11},\beta_{11}) & (\alpha_{12},\beta_{12}) & (\alpha_{13},\beta_{13}) \\ (\alpha_{21},\beta_{21}) & (\alpha_{22},\beta_{22}) & (\alpha_{23},\beta_{23}) \\ (\alpha_{31},\beta_{31}) & (\alpha_{32},\beta_{32}) & (\alpha_{33},\beta_{33}) \end{pmatrix} \end{array} \tag{13.76}$$

where α_{ij} and β_{ij} are the payoffs to Alice and Bob, respectively, when Alice plays i and Bob plays j and $1 \leq i, j \leq 3$. Suppose Alice and Bob apply the operators $\hat{C}$, $\hat{D}$, and $\hat{I}$ with the probabilities p, p_1, $(1-p-p_1)$ and q, q_1, $(1-q-q_1)$ respectively. The initial state of the game is $\rho_{\rm in}$. Alice's move changes the state changes to

$$\overset{A}{\rho}_{\rm in} = (1-p-p_1)\hat{I}_A\rho_{\rm in}\hat{I}_A^\dagger + p\hat{C}_A\rho_{\rm in}\hat{C}_A^\dagger + p_1\hat{D}_A\rho_{\rm in}\hat{D}_A^\dagger\,. \tag{13.77}$$

The final state, after Bob too has played his move, is

$$\overset{A,B}{\rho}_f = (1-q-q_1)\hat{I}_B\overset{A}{\rho}_{\rm in}\hat{I}_B^\dagger + q\hat{C}_B\overset{A}{\rho}_{\rm in}\hat{C}_B^\dagger + q_1\hat{D}_B\overset{A}{\rho}_{\rm in}\hat{D}_B^\dagger\,. \tag{13.78}$$

This state can be written as

$$\begin{aligned}
\overset{A,B}{\rho}_f =& (1-p-p_1)(1-q-q_1)\left\{\hat{I}_A\otimes\hat{I}_B\rho_{\rm in}\hat{I}_A^\dagger\otimes\hat{I}_B^\dagger\right\} + p(1-q-q_1)\\
&\times\left\{\hat{C}_A\otimes\hat{I}_B\rho_{\rm in}\hat{C}_A^\dagger\otimes\hat{I}_B^\dagger\right\} + p_1(1-q-q_1)\left\{\hat{D}_A\otimes\hat{I}_B\rho_{\rm in}\hat{D}_A^\dagger\otimes\hat{I}_B^\dagger\right\}\\
&+(1-p-p_1)q\left\{\hat{I}_A\otimes\hat{C}_B\rho_{\rm in}\hat{I}_A^\dagger\otimes\hat{C}_B^\dagger\right\} + pq\left\{\hat{C}_A\otimes\hat{C}_B\rho_{\rm in}\hat{C}_A^\dagger\otimes\hat{C}_B^\dagger\right\}\\
&+p_1q\left\{\hat{D}_A\otimes\hat{C}_B\rho_{\rm in}\hat{D}_A^\dagger\otimes\hat{C}_B^\dagger\right\} + (1-p-p_1)q_1\left\{\hat{I}_A\otimes\hat{D}_B\rho_{\rm in}\hat{I}_A^\dagger\otimes\hat{D}_B^\dagger\right\}\\
&+pq_1\left\{\hat{C}_A\otimes\hat{D}_B\rho_{\rm in}\hat{C}_A^\dagger\otimes\hat{D}_B^\dagger\right\} + p_1q_1\left\{\hat{D}_A\otimes\hat{D}_B\rho_{\rm in}\hat{D}_A^\dagger\otimes\hat{D}_B^\dagger\right\}.
\end{aligned} \tag{13.79}$$

The nine basis vectors of initial quantum state with three pure classical strategies are $|ij\rangle$ for $i, j = 1, 2, 3$. We consider the initial state to be a pure quantum state of two qutrits, i.e.

$$|\psi_{\rm in}\rangle = \sum_{i,j=1,2,3} c_{ij}\,|ij\rangle\,, \qquad \text{where} \sum_{i,j=1,2,3} |c_{ij}|^2 = 1\,. \tag{13.80}$$

The payoff operators for Alice and Bob are [Marinatto and Weber (2000a)]

$$\begin{aligned}
(P_{A,B})_{\rm oper} =& (\alpha,\beta)_{11}\,|11\rangle\langle 11| + (\alpha,\beta)_{12}\,|12\rangle\langle 12| + (\alpha,\beta)_{13}\,|13\rangle\langle 13|\\
&+(\alpha,\beta)_{21}\,|21\rangle\langle 21| + (\alpha,\beta)_{22}\,|22\rangle\langle 22| + (\alpha,\beta)_{23}\,|23\rangle\langle 23|\\
&+(\alpha,\beta)_{31}\,|31\rangle\langle 31| + (\alpha,\beta)_{32}\,|32\rangle\langle 32| + (\alpha,\beta)_{33}\,|33\rangle\langle 33|\,.
\end{aligned} \tag{13.81}$$

The players' payoffs are then

$$P_{A,B} = {\rm Tr}[\{(P_{A,B})_{\rm oper}\}\,\overset{A,B}{\rho}_f] \tag{13.82}$$

Payoff to Alice, for example, can be written as

$$P_A = \Phi\Omega\Upsilon^T \tag{13.83}$$

where T is for transpose, and the matrices Φ, Ω, and Υ are

$$\Phi = [\,(1-p-p_1)(1-q-q_1)\; p(1-q-q_1)\; p_1(1-q-q_1)$$
$$(1-p-p_1)q\; pq\; p_1 q\; (1-p-p_1)q_1\; pq_1\; p_1 q_1\,]$$
$$\Upsilon = [\,\alpha_{11}\; \alpha_{12}\; \alpha_{13}\; \alpha_{21}\; \alpha_{22}\; \alpha_{23}\; \alpha_{31}\; \alpha_{32}\; \alpha_{33}\,]$$
$$\Omega = \begin{bmatrix} |c_{11}|^2 & |c_{12}|^2 & |c_{13}|^2 & |c_{21}|^2 & |c_{22}|^2 & |c_{23}|^2 & |c_{31}|^2 & |c_{32}|^2 & |c_{33}|^2 \\ |c_{31}|^2 & |c_{32}|^2 & |c_{33}|^2 & |c_{21}|^2 & |c_{22}|^2 & |c_{23}|^2 & |c_{11}|^2 & |c_{12}|^2 & |c_{13}|^2 \\ |c_{21}|^2 & |c_{22}|^2 & |c_{23}|^2 & |c_{11}|^2 & |c_{12}|^2 & |c_{13}|^2 & |c_{31}|^2 & |c_{32}|^2 & |c_{33}|^2 \\ |c_{13}|^2 & |c_{12}|^2 & |c_{11}|^2 & |c_{23}|^2 & |c_{22}|^2 & |c_{21}|^2 & |c_{33}|^2 & |c_{32}|^2 & |c_{31}|^2 \\ |c_{33}|^2 & |c_{32}|^2 & |c_{31}|^2 & |c_{23}|^2 & |c_{22}|^2 & |c_{21}|^2 & |c_{13}|^2 & |c_{12}|^2 & |c_{11}|^2 \\ |c_{23}|^2 & |c_{22}|^2 & |c_{21}|^2 & |c_{13}|^2 & |c_{12}|^2 & |c_{11}|^2 & |c_{33}|^2 & |c_{32}|^2 & |c_{31}|^2 \\ |c_{12}|^2 & |c_{11}|^2 & |c_{13}|^2 & |c_{22}|^2 & |c_{21}|^2 & |c_{23}|^2 & |c_{32}|^2 & |c_{31}|^2 & |c_{33}|^2 \\ |c_{32}|^2 & |c_{31}|^2 & |c_{33}|^2 & |c_{22}|^2 & |c_{21}|^2 & |c_{23}|^2 & |c_{12}|^2 & |c_{11}|^2 & |c_{13}|^2 \\ |c_{22}|^2 & |c_{21}|^2 & |c_{23}|^2 & |c_{12}|^2 & |c_{11}|^2 & |c_{13}|^2 & |c_{32}|^2 & |c_{31}|^2 & |c_{33}|^2 \end{bmatrix}. \tag{13.84}$$

The payoff (13.83) corresponds to the Matrix (13.76). Payoffs in classical mixed strategy game can be obtained from Eq. (13.82) for the initial state $|\psi_{\rm in}\rangle = |11\rangle$. The game is symmetric when $\alpha_{ij} = \beta_{ji}$ in the Matrix (13.76). The quantum game played using the quantum state (13.80) is symmetric when $|c_{ij}|^2 = |c_{ji}|^2$ for all constants c_{ij} in the state (13.80). These two conditions together guarantee a symmetric quantum game. The players' payoffs P_A, P_B then do not need a subscript and we can simply use $P(p,q)$ to denote the payoff to the p-player against the q-player.

The question of evolutionary stability in quantized RSP game is addressed below.

Analysis of evolutionary stability: Assume a strategy is defined by a pair of numbers (p, p_1) for players playing the quantized RSP game. These numbers are the probabilities with which the player applies the operators $\hat{C}$ and $\hat{D}$. The identity operator $\hat{I}$ is, then, applied with probability $(1-p-p_1)$. Similar to the conditions a) and b) in Eq. (13.2), the conditions making a strategy $(p^\star, p_1^\star)$ an ESS can be written as [Maynard Smith and Price (1973); Weibull (1995)]

$$\begin{aligned} &1. \quad P\{(p^\star,p_1^\star),(p^\star,p_1^\star)\} > P\{(p,p_1),(p^\star,p_1^\star)\} \\ &2.\ \text{if } P\{(p^\star,p_1^\star),(p^\star,p_1^\star)\} = P\{(p,p_1),(p^\star,p_1^\star)\} \text{ then} \\ &\qquad P\{(p^\star,p_1^\star),(p,p_1)\} > P\{(p,p_1),(p,p_1)\}\,. \end{aligned} \tag{13.85}$$

Suppose $(p^\star, p_1^\star)$ is a mixed NE then

$$\left\{ \frac{\partial P}{\partial p} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} (p^\star - p) + \frac{\partial P}{\partial p_1} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} (p_1^\star - p_1) \right\} \geq 0\,. \tag{13.86}$$

Using substitutions

$$\begin{array}{l} |c_{11}|^2 - |c_{31}|^2 = \triangle_1,\ |c_{21}|^2 - |c_{11}|^2 = \triangle_1^{'} \\ |c_{13}|^2 - |c_{33}|^2 = \triangle_2,\ |c_{22}|^2 - |c_{12}|^2 = \triangle_2^{'} \\ |c_{12}|^2 - |c_{32}|^2 = \triangle_3,\ |c_{23}|^2 - |c_{13}|^2 = \triangle_3^{'} \end{array} \tag{13.87}$$

we get

$$\begin{aligned} \frac{\partial P}{\partial p} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} &= p^\star(\triangle_1 - \triangle_2)\left\{(\alpha_{11} + \alpha_{33}) - (\alpha_{13} + \alpha_{31})\right\} \\ &\quad + p_1^\star(\triangle_1 - \triangle_3)\left\{(\alpha_{11} + \alpha_{32}) - (\alpha_{12} + \alpha_{31})\right\} \\ &\quad - \triangle_1\,(\alpha_{11} - \alpha_{31}) - \triangle_2(\alpha_{13} - \alpha_{33}) - \triangle_3(\alpha_{12} - \alpha_{32})\,, \end{aligned} \tag{13.88}$$

$$\begin{aligned} \frac{\partial P}{\partial p_1} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} &= p^\star(\triangle_3^{'} - \triangle_1^{'})\left\{(\alpha_{11} + \alpha_{23}) - (\alpha_{13} + \alpha_{21})\right\} \\ &\quad + p_1^\star(\triangle_2^{'} - \triangle_1^{'})\left\{(\alpha_{11} + \alpha_{22}) - (\alpha_{12} + \alpha_{21})\right\} \\ &\quad + \triangle_1^{'}\,(\alpha_{11} - \alpha_{21}) + \triangle_2^{'}(\alpha_{12} - \alpha_{22}) + \triangle_3^{'}(\alpha_{13} - \alpha_{23})\,. \end{aligned} \tag{13.89}$$

For the Matrix (13.74) the Eqs. (13.88) and (13.89) can be written as

$$\begin{aligned} \frac{\partial P}{\partial p} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} &= \triangle_1\left\{-2\epsilon p^\star - (3+\epsilon)p_1^\star + (1+\epsilon)\right\} \\ &\quad + \triangle_2\left\{2\epsilon p^\star + (1-\epsilon)\right\} + \triangle_3\left\{(3+\epsilon)p_1^\star - 2\right\} \end{aligned} \tag{13.90}$$

$$\begin{aligned} \frac{\partial P}{\partial p_1} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} &= \triangle_1^{'}\left\{-p^\star(3-\epsilon) + 2\epsilon p_1^\star + (1-\epsilon)\right\} \\ &\quad - \triangle_2^{'}\left\{2\epsilon p_1^\star - (1+\epsilon)\right\} + \triangle_3^{'}\left\{(3-\epsilon)p^\star - 2\right\}\,. \end{aligned} \tag{13.91}$$

The payoff difference in the second condition of an ESS given in the Eq. (13.85) reduces to

$$\begin{aligned} & P\{(p^\star, p_1^\star), (p, p_1)\} - P\{(p, p_1), (p, p_1)\} \\ & \quad = (p^\star - p)[- \triangle_1 \{2\epsilon p + (3+\epsilon)p_1 - (1+\epsilon)\} \\ & \qquad + \triangle_2 \{2\epsilon p + (1-\epsilon)\} + \triangle_3 \{(3+\epsilon)p_1 - 2\}] \\ & \qquad + (p_1^\star - p_1)[- \triangle_1^{'} \{(3-\epsilon)p - 2\epsilon p_1 - (1-\epsilon)\} \\ & \qquad - \triangle_2^{'} \{2\epsilon p_1 - (1+\epsilon)\} + \triangle_3^{'} \{(3-\epsilon)p - 2\}] \,. \end{aligned} \tag{13.92}$$

With the substitutions $(p^\star - p) = x$ and $(p_1^\star - p_1) = y$ the above payoff difference is

$$\begin{aligned} & P\{(p^\star, p_1^\star), (p, p_1)\} - P\{(p, p_1), (p, p_1)\} \\ & \quad = \triangle_1 x \{2\epsilon x + (3+\epsilon)y\} - \triangle_2 (2\epsilon x^2) - \triangle_3 xy(3+\epsilon) \\ & \qquad - \triangle_1^{'} y \{2\epsilon y - (3-\epsilon)x\} + \triangle_2^{'} (2\epsilon y^2) - \triangle_3^{'} xy(3-\epsilon) \end{aligned} \tag{13.93}$$

provided that

$$\frac{\partial P}{\partial p} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} = 0 \qquad\qquad \frac{\partial P}{\partial p_1} \mid_{\substack{p=q=p^\star \\ p_1=q_1=p_1^\star}} = 0 \,. \tag{13.94}$$

The conditions in Eq. (13.94) together define the mixed NE $(p^\star, p_1^\star)$. Consider now the modified RSP game in classical form obtained by setting $|c_{11}|^2 = 1$. Equation (13.94) becomes

$$\begin{aligned} -2\epsilon p^\star - (\epsilon + 3)p_1^\star + (\epsilon + 1) = 0 \\ (-\epsilon + 3)p^\star - 2\epsilon p_1^\star + (\epsilon - 1) = 0 \end{aligned} \tag{13.95}$$

and $p^\star = p_1^\star = \frac{1}{3}$ is obtained as a mixed NE for all the range $-1 < \epsilon < 0$. From Eq. (13.93) we get

$$\begin{aligned} & P\{(p^\star, p_1^\star), (p, p_1)\} - P\{(p, p_1), (p, p_1)\} \\ & \quad = 2\epsilon(x^2 + y^2 + xy) = \epsilon \left\{(x+y)^2 + (x^2 + y^2)\right\} \leq 0 \,. \end{aligned} \tag{13.96}$$

In the classical RSP game, therefore, the mixed NE $p^\star = p_1^\star = \frac{1}{3}$ is a NE but not an ESS, because the second condition of an ESS given in the Eq. (13.85) does not hold.

Now define a new initial state as

$$|\psi_{\text{in}}\rangle = \frac{1}{2} \{|12\rangle + |21\rangle + |13\rangle + |31\rangle\} \tag{13.97}$$

and use it to play the game, instead of the classical game obtained from $|\psi_{\rm in}\rangle = |11\rangle$. The strategy $p^\star = p_1^\star = \frac{1}{3}$ still forms a mixed NE because the conditions (13.94) hold true for it. However the payoff difference of Eq. (13.93) is now given below, when $-1 < \epsilon < 0$ and $x, y \neq 0$:

$$P\{(p^\star, p_1^\star), (p, p_1)\} - P\{(p, p_1), (p, p_1)\}$$
$$= -\epsilon \left\{(x+y)^2 + (x^2+y^2)\right\} > 0\,. \tag{13.98}$$

Therefore, the mixed NE $p^\star = p_1^\star = \frac{1}{3}$, not existing as an ESS in the classical form of the RSP game, becomes an ESS when the game is quantized and played using an initial (entangled) quantum state given by the Eq. (13.97).

Note that from Eq. (13.82) the sum of the payoffs to Alice and Bob $(P_A + P_B)$ can be obtained for both the classical mixed strategy game (i.e. when $|\psi_{\rm in}\rangle = |11\rangle$) and the quantum game played using the quantum state of Eq. (13.97). For the Matrix (13.74) we write these sums as $(P_A + P_B)_{\rm cl}$ and $(P_A + P_B)_{\rm qu}$ for classical mixed strategy and quantum games, respectively. We obtain

$$(P_A + P_B)_{cl} = -2\epsilon \left\{(1-p-p_1)(1-q-q_1) + p_1 q_1 + pq\right\} \tag{13.99}$$

and

$$(P_A + P_B)_{\rm qu} = -\left\{\frac{1}{2}(P_A + P_B)_{\rm cl} + \epsilon\right\}. \tag{13.100}$$

In case $\epsilon = 0$ both the classical and quantum games are clearly zero sum. For the slightly modified version of the RSP game we have $-1 < \epsilon < 0$ and both versions of the game become non zero-sum.

13.4. Concluding Remarks

Evolutionary stability is a game-theoretic solution concept that tells which strategies are going to establish themselves in a population of players engaged in symmetric contests. By establishing itself it means that the strategy becomes resistant to invasion by mutant strategies when played by a small number of players. Our analysis of evolutionary stability in quantum games shows that quantization of games, played by a population of players, can lead to new stable states of the population in which, for example, a quantum strategy establishes itself. Our results show that quantum strategies can indeed change the dynamics of evolution as described by the concept of evolutionary stability. Quantum strategies being able to decide evolutionary outcomes clearly gives a new role to quantum mechanics

which is higher than just keeping the atoms together. Consideration of this role also provides a mathematically tractable method of analysis for studying multi-player quantum games [Benjamin and Hayden (2001)] played in evolutionary arrangements.

Using EWL and MW quantization schemes, we explored how quantization can change evolutionary stability of Nash equilibria in certain asymmetric bi-matrix games. We showed that quantization can change evolutionary stability of a NE in certain types of symmetric bi-matrix games to which the ESS concept refers. We identified the classes of games, both symmetric and asymmetric, for which, within the EWL and MW schemes, the quantization of games becomes related to evolutionary stability of NE. For example, in the case of Prisoners' Dilemma we found that when a population is engaged in playing this symmetric bi-matrix game, a small number of mutant players can invade the classical ESS[8] when they exploit Eisert and Wilken's two-parameter set of quantum strategies. As another example we studied the well-known children's two-player three-strategy game of Rock-Scissors-Paper. In its classical form a mixed NE exists that is not evolutionarily stable. We found that in a quantum form of this game, played using MW quantization scheme, the classical NE becomes evolutionarily stable when the players share an entangled state.

We speculate that evolutionary stability in quantum games can potentially provide a new approach towards the understanding of rise of complexity and self-organization in groups of quantum-interacting entities, although this opinion, at the present stage of development in evolutionary quantum game theory, remains without any supportive evidence, either empirical or experimental. However, it seems that the work presented in this chapter provides a theoretical support in favour of this opinion. Secondly, evolutionary quantum game theory benefits from the methods and concepts of quantum mechanics and evolutionary game theory, the second of which is well known to facilitate better understanding of complex interactions taking place in communities of animals as well as that of the bacteria and viruses. Combining together the techniques and approaches of these two, seemingly separate, disciplines appears to provide an ideal arrangement to understand the rise of complexity and self-organization at molecular level.

Although it is true that evolutionary stability and evolutionary computation provide two different perspectives on the dynamics of evolution, it appears to us that an evolutionary quantum game-theoretic approach

[8]Consisting of a Defection-Defection strategy pair.

can potentially provide an alternative viewpoint in finding evolutionary quantum search algorithms that may combine the advantages of quantum and evolutionary computing [Greenwood (2001)]. This will then also provide the opportunity to combine the two different philosophies representing these approaches towards computing: evolutionary search and quantum computing.

References

Alexander, J. M. (2003). *Evolutionary Game Theory*, Stanford Encyclopedia of Philosophy, available at `http://plato.stanford.edu/entries/game-evolutionary/`.

Abbott, D., Davies, P. C. W., and Shalizi, C. R. (2002). Order from Disorder: the role of noise in creative processes, *Fluctuation and Noise Letters* **2**, pp. C1–C12.

Benjamin, S. C., and Hayden, P. M. (2001). *Phy. Rev. A* **64**, art. no. 030301.

Benjamin, S. C. (2000). *Physics Letters A* **277**, p. 180.

Benjamin, S. C., and Hayden, P. M. (2001). *Phys. Rev. Lett.* **87**, art. no. 069801.

Bomze, I. M. (1996). *Cent. Europ. J. Oper. Res. Eco.*, Vol. **4**/1, p. 25.

Bomze, I. M., and Pötscher, B. M. (1989). *Game theoretical foundations of evolutionary stability*, Lecture notes in Economics and Mathematical systems, No. **324** (Springer Verlag).

Broom, M., Cannings, C., and Vickers, G. T. (1997). Multi-player matrix games, *Bulletin of Mathematical Biology* **59**, pp. 931–952.

Broom, M. Canning, C., and Vickers, G. T. (2000). *Bull. Math. Bio.* **62**, p. 451.

Cressman, R. (1992). *The Stability Concept of Evolutionary Game Theory* (Springer Verlag).

Demetrius, L., and Gundlach, V. M. (2000). *Mathematical Biosciences* **168**, pp. 9–38.

Eisert, J., Wilkens, M., and Lewenstein, M. (1999). *Phy. Rev. Lett.* **83**, p. 3077.

Eisert, J., and Wilkens, M. (2000). *J. Quantum Games. Mod. Opt.* **47**, p. 2543.

Eisert, J., Wilkens, M., and Lewenstein, M. (2001). Eisert, Wilkens, and Lewenstein Reply, *Phys. Rev. Lett.* **87**, art. no. 069802.

Fisher, R. A. (1930). *The Genetic Theory of Natural Selection* (Clarendon Press).

Flitney, A. P., and Abbott, D., (2002a). *Fluctuation and Noise Letters*, **2**, pp. R175–R188.

Flitney, A. P., and Abbott, D., (2002b). *Proc. Roy. Society London A*, **459**, pp. 2463–2474.

Friedman, D. (1998). *J. Evol. Econ.* **8**, p. 15 and references within.

Greenwood, G. (2001). *Congress on Evol. Comp.*, pp. 815–822.

Harsanyi, J. C., and Selten, R. (1988). *A General Theory of Equilibrium Selection in Games* (The MIT Press).

Hofbauer, J., and Sigmund, K. (1998). *Evolutionary Games and Population Dynamics* (Cambridge University Press).

Iqbal, A. (2004). PhD Thesis Quaid-i-Azam University, available at: http://arxiv.org/abs/quant-ph/0503176.
Marinatto, L., and Weber, T. (2000a). *Phys. Lett. A* **272**, p. 291.
Marinatto, L., and Weber, T. (2000b). *Phys. Lett. A* **277**, p. 183.
Maynard Smith, J. (1982). *Evolution and the Theory of Games* (Cambridge University Press).
Maynard Smith, J., and Price, G. R. (1973). *Nature* **246**, pp. 15–18.
Meyer, D. A. (1999). *Phys. Rev. Lett.* **82**, p. 1052.
Myerson, R. B. (1978). *Int. J. Game Theo.* **7**, p. 73.
Nash, J. (1950). *Proc. of the National Academy of Sciences* **36**, p. 48.
Nash, J. (1950). Non-cooperative games, PhD dissertation, Princeton University.
Nash, J. (1951). *Ann. Math.* **54**, pp. 287–295.
Nielsen, M. A., and Chuang, I. L. (2000). *Quantum Computation and Quantum Information* (Cambridge University Press).
von Neumann, J., and Morgenstern, O. (1953). *Theory of Games and Economic Behaviour* (Princeton).
Oechssler, J., and Riedel, F. (2000). Discussion paper 7/2000, Bonn Graduate School of Economics, University of Bonn, Adenauerallee 24-42, D-53113 Bonn, http://www.bgse.uni-bonn.de/papers/liste.html#2000.
Peterson, I. (1996). *Lizard Game*, Available at http://www.maa.org/ mathland/mathland_4_15.html.
Prestwich, K. (1999). *Game Theory*, A report submitted to the Department of Biology, College of the Holy Cross, Worcester, MA, USA 01610. Available at http://www.holycross.edu/departments/biology/kprestwi/behavior/ESS/pdf/games.pdf.
Rasmusen, E. (1989). *Games and Information* (Blackwell).
Turner, P. E., and Chao, L. (1999). *Nature* **398**, p. 111.
van der Laan, G., and Tieman, X. (1996). Evolutionary game theory and the Modelling of Economic Behaviour, A report presented to research program "Competition and Cooperation" of the Faculty of Economics and Econometrics, Free University, Amsterdam, November 6, 1996. Available online at http://www.tinbergen.nl/discussionpapers/96172.pdf.
Weibull, J. W. (1995). *Evolutionary Game Theory* (The MIT Press).
Williams, C. P., and Clearwater, S. H. (1998). *Explorations in Quantum Computing* (Springer-Verlag).
Witt, U. (2006). *Evolutionary Economics*, paper No 0605, The Papers on Economics and Evolution, Max Plank Institute of Economics, available from https://papers.econ.mpg.de/evo/discussionpapers/2006-05.pdf.

About the authors

Azhar Iqbal graduated in Physics in 1995 from the University of Sheffield, UK. From 1995 to 2002 he was associated with the Pakistan Institute of Lasers & Optics. He earned his first PhD from Quaid-i-Azam University, Pakistan, under Abdul Hameel Toor. He earned his second PhD from

the University of Hull, UK, in 2006 in the area of quantum games under Tim Scott. He is Assistant Professor (on leave) at the National University of Sciences and Technology, Pakistan, and has been a Visiting Associate Professor at the Kochi University of Technology, Japan. In 2007, he won the prestigious ARC Australian Postdoctoral (APD) Fellowship to carry out further research on quantum games at the University of Adelaide, under Derek Abbott.

Taksu Cheon graduated in Physics in 1980 from the University of Tokyo, Japan. He earned his PhD from the University of Tokyo in 1985 in the area of theoretical nuclear physics under Akito Arima. He is Professor of Theoretical Physics at the Kochi University of Technology, Japan.

Chapter 14

Quantum Transmemetic Intelligence

Edward W. Piotrowski and Jan Sładkowski

Congregados los sentidos, surge el alma. Haba que esperarla.
Madeleine estaba para la vista, Madeleine estaba para el odo,
Madeleine estaba para el sabor, Madeleine estaba para el olfato,
Madeleine estaba para el tacto: Ya estaba Madeleine.

Adolfo Bioy Casares, *La Invencin de Morel*[1]

14.1. Introduction

Richard Dawkins put forward the fascinating idea of a meme—a self-replicating unit of evolution of human behaviour[2], that is analogous to a gene, the fundamental unit of biological evolution [Dawkins (1989)]. Although the memetic model of human consciousness and intelligence is not widely accepted by scientists investigating the phenomenon of human beings it seems to be unrivalled with respect to the evolutionary paradigm so successful in biology. In some sense, it passes the Ockham's razor test of efficiency and holds out hope of unification of knowledge. It certainly deserves a thorough analysis from the point of view of the qualitatively new perspective opened by quantum information processing [Nielsen and Chuang (2000)]. Restrictions, such as no-cloning theorems, imposed by the unitarity of quantum evolution would certainly shed new light on the

Received June 26, 2006

[1] When all the senses are synchronized, the soul emerges... When Madeleine existed for the senses of sight, hearing, taste, smell, and touch, Madeleine herself was actually there.

[2] e.g. ideas, tunes, fashions, habits etc.

otherwise interesting and bewildering aspects of Darwin's ideas.[3] The idea of a quantum meme (qumeme) offers a unique opportunity of interpretation of human consciousness as an element of material evolution. This holds out hope of overcoming the soul-matter dychotomy that has been dominating research since Descartes, and perhaps even Plato.

Although very interesting, the problem of whether the memetic structures are abstract ideas or could possibly be identified with some substructures of individual human brains is of secondary significance.[4] Whatever the answer is, it might be that while observing the complex ceremonial of everyday human behaviour we are in fact observing quantum games eluding classical description. If human decisions can be traced to microscopic quantum events one would expect that nature would have taken advantage of quantum computation in evolving complex brains. In that sense one could indeed say that sorts of quantum computers are already playing games according to quantum rules. Even if this is not true, the investigation into the quantum aspects of information processing opens new chapters in information science the quantum mechanism might have the power to overcome complexity barriers stemming from the classical Turing theory. What that science will look like is currently unclear, and it is difficult to predict which results will turn out to be fruitful and which will have only marginal effect. The results of the research will probably influence the development of cryptography, social sciences, biology, and economics.

The emergent quantum game theory [Meyer (1999); Eisert (1999); Flitney and Abbott (2002); Piotrowski (2004a, 2002)] is, from the information theory point of view, a proposal of a new language game [Wittgenstein (1961)] describing empirical facts that, although a having precise mathematical model, resist classical analysis.[5] It forms a promising tool because quantum theory is up to now the only scientific theory that requires the observer to take into consideration the usually neglected influence of the method of observation on the result of observation and strategies can be

[3]The reversed process can also be fruitful: Quantum Darwinism—the process by which the fittest information is propagated at the expense of incompatible information can be useful in the quantum measurement theory. The fittest information becomes objective and the incompatible redundant [Zurek (2004)].

[4]It is very difficult, if not impossible, to identify the algorithm being executed by a computer by, say, microscopic analysis of its hardware, especially if one notices that often the computer in question might be only a minute part of a network performing parallel computation.

[5]Full and absolutely objective information about the investigated phenomenon is impossible and this is a fundamental principle of nature and does not result from deficiency in our technology or knowledge.

intertwined in a more complicated way than probabilistic mixtures. In this chapter we discuss several simple quantum systems that resist classical (non-quantum) description. They form information processing units that can "proliferate" via scientific publications and experiments. We propose to call them qumemes. We will neither consider here "technological" realization nor replication mechanisms of qumemes[6] [Iqbal (2001)]. New artificial sensors might result in development analogous to that caused by transgenic plants in agriculture. But this time the revolutionary changes are brought about in human intelligence/mind theory. Since the first implementations of algorithms as computer programs, the information content has became an abstract notion separated from its actual (physical) realization—all such realizations (representations) are equivalent. Moreover, a way of division into substructures can be quite arbitrary, dictated only by conventions or point of view. Engineers commonly use analogies with natural evolution to optimize technical devices. If sciences, techniques, human organizations, and more generally all complex systems, obey evolutionary rules that have a good genetic model, even if genes and chromosomes are only "virtual" entities [Krähenbühl (2005)]. Thus, the genetic representation is not only a powerful tool in the design of technological solutions, but also a global and dynamic model for the action of human behaviour. Let us have a closer look at such as yet virtual objects. Following examples from classical logical circuits, David Deutsch put forward the idea of quantum logical circuits made up from quantum gates. Quantum gates seem to be too elementary to represent quantum operations that could be referred to as memes—rather they play the roles of RNA (DNA) bases in genetics. The qumeme functionality (as an analogue of a gene) can be attained only at the level of a circuit made up from several quantum gates representing, for example, tactics in a quantum game[7]—examples would be discussed below. The due ceremonial of everyday performance of quantum physicists and, possibly not yet discovered, natural phenomena outside the area of human activities might already be the theater of activity of qumemes that cannot be replaced by classical ones—they might participate in evolutionary struggle

[6]Quantum states cannot be cloned, but such no-go theorems do not concern evolution and measurements of quantum systems. The no-cloning theorem is not so restricting to our model as the reader might expect. The solution is coding the information in the statistics of a set of observables [Ferraro (2005)]. The concepts of both exact and approximate cloning of classes of observables can be introduced. Explicit implementations for cloning machines for classes of commuting observables based on quantum non-demolition measurements have already been proposed [Ferraro (2005)].

[7]From the information theory point of view (qu-)memes correspond to algorithms.

for survival with themselves, genes or memes.[8] Is the notion of a qumeme, a replicable quantum tactics or unit of quantum information living in a kind of quantum information soup that is being detected, a newly recognized autonomous class of replicators? In the light of recent speculations [Patel (2005)] a fascinating relationship between qumemes and mechanisms for functioning of the genetic code emerged. Does the chain of replicators driving the evolution end at the qumemes stage or shall we look for a more fundamental modules? The theory of evolution can, to some extent, be perceived as decision making in conflict situations.[9] We will restrict ourselves to simple cases when memes can be perceived as strategies or tactics or, more precisely, self-replicating strategies/tactics. Details of the formalism can be found in [Piotrowski (2004a)]. Game theory considers strategies that are probabilistic mixtures of pure strategies. Why cannot they be intertwined in a more complicated way, for example interfered or entangled? Are there situations in which quantum theory can enlarge the set of possible strategies? Can quantum memes-strategies be more successful than classical ones? Do they replicate in the way we suspect?

14.2. A Quantum Model of Free Will

The idea of human free will is one of most infectious memes. It can be illustrated in game theoretical terms as was shown by Newcomb [Levi (1982)].[10] Martin Gardner proposed the following fabulous description of the game with pay-off given by the Matrix (14.1) [Gardner (1982)]. An alien Omega being a representative of alien civilization (player 2) offers a human (player 1) a choice between two boxes:

$$M := \begin{pmatrix} \$1000 & \$1\,001\,000 \\ 0 & \$1\,000\,000 \end{pmatrix} \tag{14.1}$$

Player 1 can take the content of both boxes or only the content of the second one. The first one is transparent and contains $1,000. Omega declares to

[8]The possibility that human consciousness explores quantum phenomena, although it seems to be at least as mysterious as the quantum world, is often berated. Nevertheless, one cannot reject the the idea that the axioms of probability theory are too restrictive and one, for example, should take quantum-like models into consideration. Such a possibility removes some paradoxes in game theory.

[9]For example, games against nature [Milnor (1954)]. These include those for which Nature is quantum mechanical.

[10]In 1960 William Newcomb, a physicist, intrigued the philosopher Robert Nozick with the parable of faith, decision-making, and free will [Nozik (1969)].

have put into the second box that is opaque \$1,000,000 (strategy $|1\rangle_2$) but only if Omega foresaw that player 1 decided to take only the content of that box ($|1\rangle_1$). A male player 1 thinks: *If Omega knows what I am going to do then I have the choice between \$1,000 and \$1,000,000. Therefore I take the \$1,000,000* (strategy $|1\rangle_1$). A female player 1 thinks: *It is obvious that I want to take the only the content of the second box therefore Omega foresaw it and put the \$1,000,000 into the box. So the one million dollars* **is** *in the second box. Why should I not take more?—I take the content of both boxes* (strategy $|0\rangle_1$). The question is whose strategy, male's or female's, is better? If between deciding what to do and actually doing it the male player was to bet on the outcome he would certainly bet that if he takes both boxes he will get \$1,000 and if he takes the opaque box only he will get \$1,000,000. Why should he act in a way that he would bet will have a worse result? But suppose you are observing the game and that you know the content of the boxes. From your point of view the player should always choose both boxes because in this case the player will get better of the game. Does the prediction blur the distinction between past and future and therefore between what can and what cannot be affected by one's actions? One cannot give unambiguous answer to this question, without precise definition of the measures of the events relevant for the pay-off. Quantum theory offers a solution to this paradox.

Suppose that Omega, as representative of an advanced alien civilization, is aware of quantum properties of the Universe that are still obscure or mysterious to humans. The boxes containing pay-offs are probably coupled. One can suspect that because the human cannot take the content of the transparent box alone (\$1,000). The female player is sceptical about the possibility of realization of the Omega's scenario for the game. She thinks that the choice of the male strategy results in Omega putting one million dollars in the second box, and after this being done no one can prevent her from taking the content of both boxes in question (i.e. \$1,001,000). But Meyer proposed recently the use of quantum tactics [Meyer (1999)] that, if adopted by Omega, allows Omega to accomplish his scenario. Omega may not be able to foresee the future [Gardner (1982)]. It is sufficient that Omega is able to discern human intentions regardless of their will or feelings on the matter. This can be accomplished by means of teleportation [Milburn (1999)]: Omega must intercept and then return the human's strategies. The manipulations presented below leading to thwarting humans are feasible with contemporary technologies. The game may take the following course. At the starting-point, the density operator $\mathcal{W}$ acting on

the Hilbert space of both players (1 and 2) $\mathcal{H}_1 \otimes \mathcal{H}_2$ describes the human's intended strategy and the Omega's strategy based on its prediction of the human's intentions. The game must be carried on according to quantum rules, that is, the players are allowed to change the state of the game by unitary actions on $\mathcal{W}$ [Eisert (1999)]. The human player can only act on her/his q-bit Hilbert space $\mathcal{H}_1$. Omega's tactics must not depend on the actual move performed by the human player (it may not be aware of the human strategy): its moves are performed by automatic device that couples the boxes. Meyer's recipe leads to:

(1) Just before the human's move, Omega set the automatic devise according to its knowledge of human's intention. The device executes the tactics $\mathcal{F} \otimes \mathcal{I}$, where $\mathcal{I}$ is the identity transform (Omega cannot change its decision) and $\mathcal{F}$ is the well known Hadamard transform frequently used in quantum algorithms: $\mathcal{F} := \frac{1}{\sqrt{2}} \begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix}$.
(2) The human player uses with probability w the female tactics $\mathcal{N} \otimes \mathcal{I}$, where $\mathcal{N}$ is the negation operator[11] and with probability $1-w$ the male tactics $\mathcal{I} \otimes \mathcal{I}$.
(3) At the final step the boxes are being opened and the built-in coupling mechanism performs once more the transform $\mathcal{F} \otimes \mathcal{I}$ and the game is settled.

Players' tactics, by definition, could have resulted in changes in the (sub-) space $\mathcal{H}_1$ only. Therefore it suffices to analyze the human's strategies. In a general case the human can use a mixed strategy: the female one with the probability v and the male one with probability $1-v$. Let us begin with the extreme values of v (pure strategies). If the human decided to use the female strategy ($v=1$) or the male one ($v=0$) then the matrices $\mathcal{W}_i$, $i = 0, 1$ corresponding to the density operators [Nielsen and Chuang (2000)]

$$\mathcal{W}_0 = \sum_{r,s=1}^{2} W_{0rs} |\mathsf{r}-1\rangle_1 \, |0\rangle_{2\,1} \langle \mathsf{s}-1| \, {}_2\langle 0| \tag{14.2}$$

and

$$\mathcal{W}_1 = \sum_{r,s=1}^{2} W_{1rs} |\mathsf{r}-1\rangle_1 \, |1\rangle_{2\,1} \langle \mathsf{s}-1| \, {}_2\langle 1| \tag{14.3}$$

[11] $\mathcal{N}|0\rangle = |1\rangle$, $\mathcal{N}|1\rangle = |0\rangle$.

are calculated as follows:

$$\begin{pmatrix} v & 0 \\ 0 & 1-v \end{pmatrix} \longrightarrow \tfrac{1}{2}\begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix}\begin{pmatrix} v & 0 \\ 0 & 1-v \end{pmatrix}\begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix}$$

$$= \tfrac{1}{2}\begin{pmatrix} 1 & 2v-1 \\ 2v-1 & 1 \end{pmatrix} \longrightarrow \tfrac{w}{2}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}\begin{pmatrix} 1 & 2v-1 \\ 2v-1 & 1 \end{pmatrix}\begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}$$

$$+ \tfrac{1-w}{2}\begin{pmatrix} 1 & 2v-1 \\ 2v-1 & 1 \end{pmatrix} = \tfrac{1}{2}\begin{pmatrix} 1 & 2v-1 \\ 2v-1 & 1 \end{pmatrix}$$

$$\longrightarrow \tfrac{1}{4}\begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix}\begin{pmatrix} 1 & 2v-1 \\ 2v-1 & 1 \end{pmatrix}\begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix} = \begin{pmatrix} v & 0 \\ 0 & 1-v \end{pmatrix}. \qquad (14.4)$$

It is obvious that independently of the employed tactics, the human's strategy takes the starting form. For the mixed strategy the course of the game is described by the density operator

$$\mathcal{W} = v\,\mathcal{W}_0 + (1-v)\,\mathcal{W}_1\,. \qquad (14.5)$$

which also has the same diagonal form at the beginning and at the end of the game [Piotrowski (2003)].

Therefore the change of mind resulting from the female strategy cannot lead to any additional profits. If the human using the female tactics (that is changes his/her mind) begins the game with the female strategy then at the end the opaque box will be empty and he/she will not get the content of the transparent box: the pay-off will be minimal (0). If the human acts in the opposite way the transparent box must not be opened but nevertheless the pay-off will be maximal ($1,000,000). Only if the human begins with the female strategy and then applies the male tactics the content of the transparent box is accessible. If restricted to classical game theory, Omega would have to prevent humans from changing their minds. In the quantum domain the pay-off M_{21} (female strategy and tactics) is possible: humans regain their free will but they have to remember that Omega has (quantum) means to prevent humans from profiting out of altering their decisions. In this way the quantum approach allows us to remove the paradox from the classical dilemma. One can also consider games with more alternatives for the human player. The respective larger pay-off matrices would offer even more sophisticated versions of the Newcomb's observation. But even then there is a quantum protocol that guarantees that Omega keeps its promises (threats) [Wang (2000)]. Thus, even if there exists nothing like a quantum meme, the meme of quantum theory is likely to replicate using human hosts and to influence their behaviour so to promote its replication.

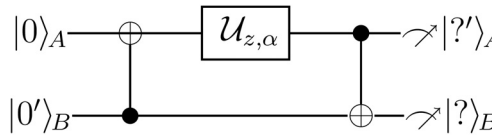


Fig. 14.1. The game *Master and Pupil* (dense coding).

14.3. Quantum Acquisition of Knowledge

Acquisition of knowledge certainly belongs to the class of behaviours that can be interpreted in terms of memes replication. Let us consider a collective game that has no classical counterpart and can shed some light on qumemes replication. We call it *Master and Pupil*. Suppose Alice (A) is ready to sell some asset $\mathfrak{G}$ at low price and Bob (B) wants to buy $\mathfrak{G}$ even at high price. But Bob, instead of making the deal (according to the measured strategies), enters into an alliance[12] with Alice. In the aftermath, Alice changes her strategy and enters into an alliance with Bob. As a result an entangled quantum state[13] $|z,\alpha\rangle_{AB} \in \mathbb{R}P^3 \subset \mathbb{C}P^3$ is formed, cf. Fig. 14.1:

$$\begin{aligned} |z,\alpha\rangle_{AB} := \mathcal{C}\,(\mathcal{U}_{z,\alpha}\otimes I)\,\mathcal{C}'\,|0\rangle_A|0'\rangle_B &= \cos(\alpha)\,|0'\rangle_A|0\rangle_B \\ &+ \mathrm{i}\,\sin(\alpha)\,\big(E_z(\mathcal{X})\,|0'\rangle_A|\mathrm{I}\rangle_B + E_z(\mathcal{X}')\,|\mathrm{I}'\rangle_A|0\rangle_B \\ &+ E_z(\mathcal{X}\mathcal{X}')\,|\mathrm{I}'\rangle_A|\mathrm{I}\rangle_B\big)\,. \end{aligned} \tag{14.6}$$

Although Bob cannot imitate Alice's tactics $\mathcal{U}_{z,\alpha}$ by cloning of the state, he can gather substantial knowledge about her strategy when she is buying (he is able to measure proportions among the components I, $\mathcal{X}$, $\mathcal{X}'$ and $\mathcal{X}\mathcal{X}'$). The game is interesting also from the Alice's point of view because it allows her to form convenient correlations of her strategy with the Bob's one. Such a procedure is called dense coding in quantum information theory [Rieffel (2000)]. If Alice and Bob are separated from each other and have formed

[12] Alliances are represented by controlled NOT gates denoted here by $\mathcal{C}$ [Nielsen and Chuang (2000)].

[13] We call any unitary transformation that changes agent's (player's) strategy a tactics. We follow the notation introduced in [Piotrowski (2004b)]: $SU(2) \ni \mathcal{U}_{z,\alpha} = \mathrm{e}^{\mathrm{i}\alpha\,\overrightarrow{\sigma}\cdot E_z(\overrightarrow{\sigma})} = I\cos\alpha + \mathrm{i}\,\overrightarrow{\sigma}\cdot E_z(\overrightarrow{\sigma})\,\sin\alpha$, where the vector $E_z(\overrightarrow{\sigma}) = \frac{\langle z|\overrightarrow{\sigma}|z\rangle}{\langle z|z\rangle}$ represents the expectation value of the vector of Pauli matrices $\overrightarrow{\sigma} := (\sigma_1, \sigma_2, \sigma_3)$ for a given strategy $|z\rangle$. The family $\{|z\rangle\}, z \in \overline{\mathbb{C}}$ of complex vectors (states) $|z\rangle := |0\rangle + z\,|\mathrm{I}\rangle$ ($|\pm\infty\rangle := |\mathrm{I}\rangle$) represents all trader's strategies in the linear subspace spanned by the vectors $|0\rangle$ and $|\mathrm{I}\rangle$.

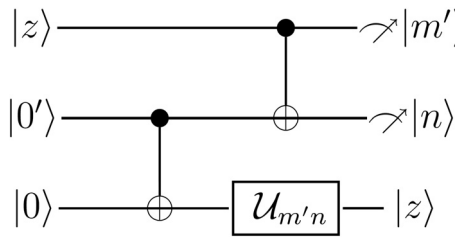


Fig. 14.2. Teleportation of the strategy $|z\rangle$ consisting in measurement of the tactic $\mathcal{U}_{m'n} := \mathcal{X}^{[n=\mathrm{I}]}\mathcal{X}'^{[m'=\mathrm{I}']}$ (the notation [true]:=1 and [false]:=0 is used).

the entangled state $|0\rangle_A|0\rangle_B + |\mathrm{I}\rangle_A|\mathrm{I}\rangle_B$ (this is the collective strategy before the execution of $\mathcal{U}_{z,\alpha} \otimes I$) then Alice is able to communicate her choice of tactic (I, $\mathcal{X}$, $\mathcal{X}'$, $\mathcal{X}\mathcal{X}'$) to Bob (bits of information) by sending to him a single qubit. Bob can perform a joint measurement of his and Alice's qubits. Only one of four orthogonal projections on the states $|0'\rangle_A|0\rangle_B$, $|0'\rangle_A|\mathrm{I}\rangle_B$, $|\mathrm{I}'\rangle_A|0\rangle_B$ and $|\mathrm{I}'\rangle_A|\mathrm{I}\rangle_B$ will give a positive result forming the message.[14] Such concise communication is impossible for classical communication channels and any attempt at eavesdropping would irreversibly destroy the quantum coherence (and would be detected).

If one player forms an alliance with another that has already formed another alliance with a third player then the later can actually perform measurements that will allow him to transform his strategy to a strategy that is identical to the first player's primary strategy (teleportation [Bennet (1993)]). This is possible due to the identity (remember that $\mathcal{X}$, $\mathcal{X}'$, $\mathcal{X}\mathcal{X}'$ are involutive maps)

$$2\,(\mathcal{C}\otimes I)\,(I\otimes\mathcal{C})\,|z\rangle|0'\rangle|0\rangle = |0'\rangle|0\rangle|z\rangle + |0'\rangle|\mathrm{I}\rangle\mathcal{X}|z\rangle + |\mathrm{I}'\rangle|0\rangle\mathcal{X}'|z\rangle + |\mathrm{I}'\rangle|\mathrm{I}\rangle\mathcal{X}\mathcal{X}'|z\rangle\,. \tag{14.7}$$

Recall that quantum strategies cannot be cloned (no-cloning theorem) and if there are several identical strategies their number cannot be reduced by classical means (no-reducing theorem). A possible working mechanism for replication is coding the information in the statistics of a set of observables [Ferraro (2005)]. Both exact and approximate cloning of classes of observables can be considered as a quantum replication of (qu-)memes.

[14] Answers to the questions *Would Alice buy at high price?* and *Would Bob sell at low price?* would decode the message.

14.4. Thinking as a Quantum Algorithm

Let us recall the anecdote popularized by John Archibald Wheeler [Davies (1993)]. The plot concerns the game of 20 questions: the player has to guess an unknown word by asking up to 20 questions (the answers could be only yes or no and are always true). In the version presented by Wheeler, the answers are given by a "quantum agent" who attempts to assign the task the highest level of difficulty without breaking the rules. Any quantum algorithm (including classical algorithms as a special cases) can be implemented as a sequence of appropriately constructed questions-measurements. The results of the measurements (i.e. answers) that are not satisfactory cause further "interrogation" about selected elementary ingredients of the reality (qubits). If Quantum Intelligence (QI) is perceived in such a way (as quantum game) then it can be simulated by a deterministic automaton that follows a chain of test bits built on a quantum tenor [Deutsch (1998)]. The automaton completes the chain with afore prepared additional questions at any time that an unexpected answer is produced. Although the results of the test will be random (and actually meaningless—they are instrumental), the kind and the topology of tests that examine various layers multi-qubit reality and the working scheme of the automaton are fixed prior to the test. The remarkability of performance of such an automaton in a game against nature is by the final measurement that could reveal knowledge that is out of reach of classical information processing, cf. the already known Grover and Shor quantum algorithms and the Elitzur-Vaidman "bomb tester". Needless to say, such an implementation of a game against quantum nature leaves some room for perfection. The tactics $CNOT$ and H belong to the normalizer of the n-qubit Pauli group G_n [Nielsen and Chuang (2000)], hence their adoption allows to restrict oneself to single corrections of "errors" made by nature that precede the final measurement. It is worth noting that a variant of implementation of the tactics T makes it possible to postpone the correction provided the respective measurements methods concern the current state of the cumulated errors [Jorrand (2003)]. Therefore in this setting of the game some answers given by nature, though being instrumental, have a significance because of the influence of the following tests. There is no need for the final error correction—a modification of the measuring method is sufficient. In that way the course of the game is fast and the length of the game is not a random variable. This example shows that in some sense the randomness in the game against quantum nature can result from awkwardness of agents

and erroneous misinterpretation of answers that are purely instrumental. If only one error (lie) in the two-person framework is allowed, fast quantum algorithms solving the problem exist (Ulams's problem) [Mancini (2005)]. There is a wide class of human behaviours that are adopted during the process of education (classical memes!) that manifests quantum-like character. If realization of own or some else behaviour is to be perceived as a measurement, then, contrary to the classical approach, there are restrictions on conscious transfer of emotions [Ferraro (2005)] but appropriate measurement can help to became aware of emotions. In that way qumemes (replicated via education process quantum strategies) might represent forming of emotions that would be unique individual features. Moreover, the process of realization (measurement) of such quantum behaviourism would itself form a class of qumemes.

14.5. Counterfactual Measurement as a Model of Intuition

Mauritius Renninger has discovered a fascinating qumeme that allows to identify events that are possible but did not occur and distinguish them from events that are impossible [Renninger (1953)].

Let us now consider a modification of the method of jamming the strategy measuring game in which the circuit-breaker gate I/NOT[15] is implemented as a part in a separate switching-off strategy, cf. Fig. 14.3. To this end, the alliance $CNOT$ was replaced by the Toffoli gate (controlled-controlled-NOT). Contrary to the former case we are now interested in an effective accomplishment of the measurement. Therefore, we assume that there are no correlations between the state of the gate I/NOT and the strategy $|1/0\rangle$. The role of the gate NOT that comes before the measurement of the central qubit is to guarantee that the measurement of the state $|1\rangle$ stands for the switching-off the subsystem consisting of the two bottom qubits. To quantize this game we will follow Elitzur and Vaidman [Vaidman (1996)] who explored Mauritius Renninger's idea of the *negative measurement* [Renninger (1953)], see Fig. 14.4. The method is based on gradual unblocking the switching-off gate (n steps of $\sqrt[n]{NOT}$) and giving up the whole measurement at any step, if only the change of the third qubit is observed (measuring the first qubit). Hence, the game is stopped

[15]The gate I/NOT is defined as a randomly chosen gate from the set $\{I, NOT\}$ and is used to switching-off the circuit in a random way. It can be generalized to have some additional control qubits [Miakisz (2006)].

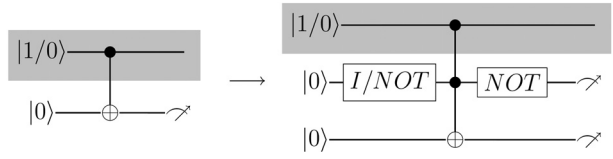


Fig. 14.3. Modification of the system by adding a switching-off strategy.

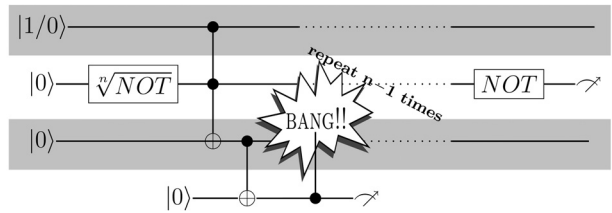


Fig. 14.4. The Elitzur–Vaidman tactics of gradual unblocking the switching-off strategy.

by the "exploding bomb" in circumstances when at some step the value of the auxiliary strategy measured after the alliance $CNOT$ is measured to be $|1\rangle$, see Fig. 14.4.

The tactics $\sqrt[n]{NOT}$ of gradual unblocking is represented by the operator:

$$\sqrt[n]{NOT} := I\cos\tfrac{\pi}{2n} + NOT\sin\tfrac{\pi}{2n} = \mathrm{e}^{NOT\frac{\pi}{2n}} \in SU(2)\,. \tag{14.8}$$

The probability of continuation of the game after one step is equal to

$$\left|\langle 0|\sqrt[n]{NOT}|0\rangle\right|^2 = \cos^2\tfrac{\pi}{2n}$$

and all steps are successfully accomplished with the probability $\cos^{2n}\frac{\pi}{2n} = 1 - \frac{\pi^2}{4n} + \frac{\pi^4}{32n^2} + O(n^{-3})$. Therefore, in the limit $n \to \infty$ the probability of stopping the game tends to zero.[16] The inspection of the value of the first qubit with help of the third qubit acquires a transcendental dimension because if $|1/0\rangle = |1\rangle$ the measuring system is switched-off and if $|1/0\rangle = |0\rangle$ the switching-off strategy cannot be unblocked. The bomb plays the key role in the game because it freezes the second qubit in the state $|0\rangle$—this is the famous quantum Zeno effect [Facchi (2000)]. However, the information about the state of the first qubit ($|0\rangle$ or $|1\rangle$) can only be acquired via the effectiveness of the unblocking the second qubit. The presented

[16]The limit can be found by application of the de L'Hospital rule to $\ln\cos^{2n}\frac{\pi}{2n}$.

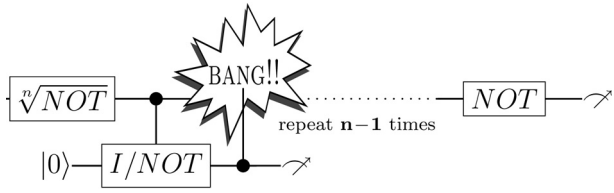


Fig. 14.5. Safe Elitzur–Vaidman bomb tester.

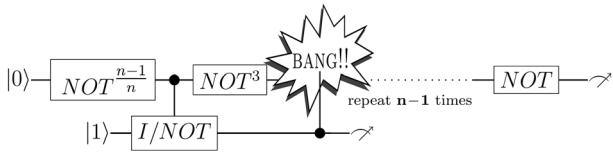


Fig. 14.6. A bomb tester constructed on the basis of the quantum anti-Zeno effect.

implementation and analysis of the Elitzur-Vaidman circuit-breaker paves the way for a completely new class of technologies that might be shocking for those unacquainted with quantum effects. For example, if the first qubit represents a result of quantum computation, then such a breaker allows the access in that part of the Deutsch Multiversum [Deutsch (1998)] where this computer is turned off [Mitchison (2001)]. If the first qubit of the circuit represented in Fig. 14.4 is fixed in the state $|1\rangle$, then this machinery can be used to nondestructive testing, for example, to select bombs with damaged fuse. The respective measuring system is presented in Fig. 14.5 (the shaded-in qubits in Fig. 14.4 are absent because they are redundant). The breaker $controlled-(I/NOT)$ that replaces the alliance $CNOT$ is in the state $I/NOT = I$ if the bomb fuse is damaged and in the state $I/NOT = NOT$ if the fuse is working. The result $|1\rangle$ of the measurement of the first qubit informs us that the bomb is in working order. This is due to the fact that the working bomb always reduces this qubit to $|0\rangle$ after the transformation $\sqrt[n]{NOT}$ (quantum Zeno effect). Without doubt such a bomb tester (and the Elitzur–Vaidman circuit–breaker) can be constructed on the basis of the quantum anti-Zeno effect [Facci (2001)]. In this case the working but unexploded bomb accelerates the evolution of the system instead of "freezing" it. Such an alternative tester is represented in Fig. 14.6, where the working bomb causes at any of the n stages the increase of $\frac{\pi}{2n}$ in the phase φ of the cumulative tactics $e^{NOT\varphi}$. Let us

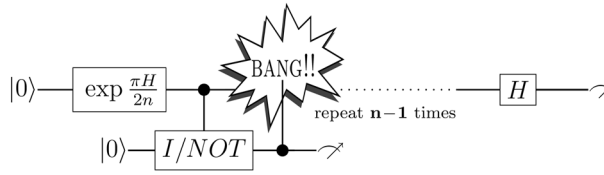


Fig. 14.7. Supply-demand switch.

define $V(\beta) := NOT\cos\beta + (I\cos\alpha + H\cdot NOT\cdot H\sin\alpha)\sin\beta$. It is not difficult to show that $V(\beta_2)\cdot NOT^3\cdot V(\beta_1) = V(\beta_1+\beta_2)$. Therefore, we can replace the gate $NOT^{\frac{n-1}{n}}$ with any of the gates

$$NOT\cos\tfrac{\pi}{2n} + (I\cos\alpha + H\cdot NOT\cdot H\sin\alpha)\sin\tfrac{\pi}{2n}\,,$$

where $\alpha\in[0,2\pi)$. But only for $\alpha = 0,\pi$ such gate belongs to the class $\mathrm{e}^{NOT\varphi}$ and we can claim that the transformation NOT results from the acceleration or freezing of the evolution of the system. For $\alpha\neq 0,\pi$ we observe a kind of para-Zeno effect because the measurement of the qubit entangled with the qubit in question stops the free evolution corresponding to a damaged bomb. Consider a slight modification of the circuit presented in Fig. 14.7, where now $\exp\frac{\pi H}{2n} = I\,\cos\frac{\pi}{2n} + H\,\sin\frac{\pi}{2n}$. Again, there is a strong likelihood that we can avoid explosion because $(\,|\cos\frac{\pi}{2n} + \frac{\mathrm{i}}{\sqrt{2}}\sin\frac{\pi}{2n}\,|^2\,)^n > \cos^{2n}\frac{\pi}{2n}$. In this case the information revealed by the breaker is more subtle because the "bomb" can only cause transition to a corresponding state in the conjugated basis [Wiesner (1983)]. Nevertheless, the bomb being in the working order causes strategy change.

14.6. Quantum Modification of Freud's Model of Consciousness

In the former section we have put great emphasis on distinction between measuring qubits and qubits being measured. The later were shaded in figures. Analogously to the terminology used in the computer science, we can distinguish the shell (the measuring part) and the kernel (the part being measured) in a quantum game that is perceived as an algorithm implemented by a specific quantum process. Note that this distinction was introduced on the basis of abstract properties of the game (quantum algorithm, quantum software) and not properties of the specific physical implementation. Quantum hardware would certainly require a great deal of additional

measurements that are nor specific to the game (or software), cf. the process of starting a one-way quantum computer. For example, consider a Quantum Game Model of Mind (QGMM) exploring the confrontation of quantum dichotomy between kernel and shell with the principal assumption of psychoanalysis of dichotomy between consciousness and unconsciousness [Freud (1923)]. The relation is as follows.

- Kernel represents the Ego, that is the conscious or more precisely, that level of the psyche that is aware of its existence (it is measured by the Id). This level is measured due to its coupling to the Id via the actual or latent (not yet measured) carriers of consciousness (in our case qubits representing strategies)
- Shell represents the Id that is not self-conscious. Its task is monitoring (that is measuring) the kernel. Memes, the AI viruses [Dawkins (1989)], can be nesting in that part of the psyche.

Memes being qutrojans, that is quantum parasitic gates (not qubits!) can replicate themselves (qubits cannot—no-cloning theorem). There is a limited knowledge of the possible threat posed by qutrojans to the future of quantum networks. In quantum cryptography teleportation of qubits might be helpful in overcoming potential threats posed by qutrojans therefore, we should only be concerned about attacks by conventional trojans [Lo (1999)]. If the qutrojan is able to replicate itself it certainly deserves the name quvirus. A consistent quantum mechanism of such replication is especially welcome if quantum computers and cryptography are to become a successful technology. Measuring apparatus and "bombs" reducing (projecting) quantum states of the game play the role of the nervous system providing the "organism" with contact with the environment that sets the rules of the game defined in terms of supplies and admissible methods of using of tactics and pay-offs [Piotrowski (2004b)]. Contrary to the quantum automaton put forward by Albert (1983), there is no self-consciousness—only the Ego is conscious (partially) via alliances with the Id and is infallible only if the Id is not infected with memes. Alliances between the kernel and the Id (shell) form kind of states of consciousness of quantum artificial intelligence (QAI) and can be neutralized (suppressed) in a way analogous to the quantum solution to the Newcomb's paradox [Piotrowski (2003)]. In the context of unique properties of the quantum algorithms and their potential applications, the problem of deciding which model of artificial intelligence (AI) (if any) faithfully describes human mind is regarded as fascinating, though less important. The discussed earlier variants of the

Elitzur-Vaidman breaker suggests that the addition of the third qubit to the kernel could be useful in modelling the process of forming the psyche by successive decoupling qubits from the direct measurement domain (and thus becoming independent of the shell functions). For example dreams and hypnosis could take place in shell domains that are temporary coupled to the kernel in this way. The example discussed in the previous section illustrates what QAI intuition resulting in a classically unconveyable belief might be like. It is important that QAI reveals more subtle properties than its classical counterparts because it can deal with counterfactual situations [Mitchison (2001); Vaidman (1996)] and in that sense analyze hypothetical situations (imagination). Therefore QAI is anti-Jourdainian: Molier's Jourdain speaks in prose without having knowledge of it; QAI might be unable to speak but QAI knows that it would have spoken in prose if it were able to speak.

14.7. Conclusion

Quantum intertwining of tactics creates unique possibilities of parallel actions on practically unlimited number of strategies. Therefore quantum systems can adopt various types of ambivalent tactics [Makowski (2006)]. In probabilistic models life is kind of gambling scheme. Quantum tactics, being deterministic from the theoretical point of view, can represent fascinating and yet fully understood wealth of behaviours and the probabilistic nature emerges only after brutal interactions with classical environment[17]—measurements that extort information from the system. Not only God does not play dice! Morel, brought to existence by Casares' vivid imagination[18], neglected the fact that Madeleine is a being of intelligence that is not representable by classically computable functions. Does a quantum mathematics that, among others, investigates quantum-computable functions wait for its discovery? Will the paradoxes following from the Gödel and Chaitin theorems survive? The specific character of quantum models of consciousness and thinking that consists in information barrier between conscious and unconscious activities (e.g. computing) suggests a possibility for a complete understanding of the physical world.[19] Would the dream of the Theory of Everything come true via a Quantum Metatheory of Everything? Quantum

[17]One can say, a brutal invasion of privacy of an isolated quantum system.
[18]Adolfo Bioy Casares, *La Invencin de Morel*, we do recommend reading this novel.
[19]The world is not reduced to abstract idea such that the axiom of intelligibility is satisfied [Barrow (1992)].

(artificial) sensors are already being used, mostly in physical laboratories. Humans have already overcome several natural limitations with the help of artificial tools. Would quantum artificial intelligence/life ever come to existence? Adherents of artificial intelligence should welcome a great number of new possibilities offered by quantum approach to AI.

Acknowledgements

This paper has been supported by the Polish Ministry of Scientific Research and Information Technology under the (solicited) grant No PBZ-MIN-008/P03/2003.

References

Aerts, D., and Czachor, M., (2004). Quantum aspects of semantic analysis and symbolic AI, Journal of Physics A: Math. Gen. **37** p. L123.

Albert, D. Z., (1983). On quantum-mechanical automata, *Physics Leters* A **98** p. 249.

Barrow, J. D. (1992). Perche il mondo e matematico?, Laterza, Rome (1991 Sigma-Tau-Laterza Lectures in various languages).

Bennet, C. et al., (1993). Teleporting an unknown quantum state via dual classical end Einstein-Podolsky-Rosen channels, *Physical Review Letters* **70** p. 1895.

Davies, P. C. W., and Brown, J. R., (eds), (1993). *The Ghost in the Atom: A Discussion of the Mysteries of Quantum Physics* (Cambridge University Press).

Dawkins, R. (1989). *The Selfish Gene*, 2nd edn. (Oxford University Press, Oxford).

Deutsch, D. (1998). *The Fabric of Reality* (Penguin, London).

Eisert, J., Wilkens, M., and Lewenstein, M. (1999). Quantum games and quantum strategies, *Physical Review Letters* **83** p. 3077.

Facchi, P., Gorini, V., Marmo, G., Pascazio, S., and Sudarshan, E. C. G., (2000). Quantum Zeno dynamics, *Physics Letters* A **275** p. 12.

Facchi, P., Nakazato, H., and Pascazio, S. (2001). From the quantum Zeno to the Inverse quantum Zeno effect, *Physical Review Letters* **86** p. 2699.

Ferraro A, Galbiati, M., and Matteo G. A. (2005). Cloning of observables, quant-ph/0509170 v2.

Flitney, A. P., and Abbott, D., (2002). *Fluctuation and Noise Letters*, **2**, pp. R175-R188.

Freud, Z. (1923). *Ich und das Es* (Internationaler Psychoanalytischer Verlag).

Gardner, M. (1982). *Aha! Gotcha. Paradoxes to Puzzle and Delight*, Freeman & Co, San Francisco.

Iqbal, A., and Toor, A. H. (2001). Equilibria of replicator dynamics in quantum games; `quant-ph/0106135`.

Jorrand, P., and Perdrix, S., (2003). Non-probabilistic termination of measurement-based quantum computation; `quant-ph/0311142`.

Krähenbühl, L. (2005). Genetic representations of objects: simple analogies or efficient models? The "evolutic" point of view (in French). `arXix,cs.AI/0503059`.

Levi, I. (1982). A note on Newcombmania, *J. Philosophy* **79** p. 337.

Lo, H.-K., (1999). Will quantum cryptography ever become a successful technology in the marketplace?, quant-ph/9912011; note that the version published in Physics World omitts this problem.

Makowski, M., and Piotrowski, E. W. (2006). Quantum cat's dilemma: an example of intransitivity in a quantum game, *Physics Letters A* **355** p. 250.

Mancini, S., and Maccone, L. (2005). Using quantum mechanics to cope with liars, *International Journal of Quantum Information*, **3** 729; quant-ph/0508156.

Meyer, D. A. (1999). Quantum strategies. *Physical Review Letters* **82** p. 1052.

Miakisz, K., Piotrowski, E. W., and Sładkowski, J. (2006). Quantization of Games: Towards Quantum Artificial Intelligence, *Theoretical Computer Science* - in print; quant-ph/0412215.

Milburn, G. J. (1999). *The Feynman Processor: Quantum Entaglement and the Computing Revolution* (Perseus Book Group, New York).

Milnor, J. (1954). Games against nature, in Thrall, R. M., Coombs, C. H., Davis, R. L., (eds.), *Decision Processes* (John Wiley & Sons, New York) p. 49.

Mitchison, G., and Jozsa, R. (2001). Counterfactual computation, *Proceedings of the Royal Society of London* A**457** p. 1175.

Nielsen, M. A., and Chuang, I. L. (2000). *Quantum Computation and Quantum Information* (Cambridge University Press).

Nozik, R. (1969). Newcomb's problem and two principles of choice, in *Essays in Honour of Carl Hempel*, eds. N. Rescher *et al.*, D. Reidel, Dordrecht.

Patel, A. (2003). Mathematical physics and life in *Computing and Information Sciences: Recent Trends*, J.C. (ed.), (Narosa Publishing House).

Piotrowski, E. W. and Sładkowski, J. (2002). Quantum market games, *Physica A* **312** p. 208.

Piotrowski, E. W., and Sładkowski, J. (2003). Quantum solution to the Newcomb's paradox, *International Journal of Quantum Information* **1** p. 395.

Piotrowski, E. W., and Sładkowski, J. (2004). The next stage: quantum game theory, in *Mathematical Physics Frontiers* (Nova Science Publishers, Inc.) `quant-ph/0308027`.

Piotrowski, E. W., Sładkowski, J., (2004). Quantum computer: an appliance for playing market games, *International Journal of Quantum Information*, **2** p. 495.

Renninger, M. (1953). Zum Wellen–Korpuskel–Dualismus, *Zeitschrift für Physik.* **136** p. 251.

Rieffel, E., and Polak, W. (2000). Introduction to quantum computing for non-physicists, *ACM Computing Surveys* **32** p. 3.

Vaidman, L., (1996). Interaction-free measurements, quant-ph/9610033.

Wang, X.-B., Kwek, L. C., and Oh, C. H. (2000). Quantum roulette: an extended quantum strategy, *Phys. Lett.* **A** 278 p. 44.

Wiesner, S. (1983). Conjugate coding, *SIGACT News* **15/1** 78; `http://kh.bu.edu/qcl/pdf/wiesners198316024137.pdf`.

Wittgenstein, L. (1961). *Tractatus Logico-Philosophicus* (Routledge & Kegan Paul).

Zurek, W. H. (2004). Quantum Darwinism and envariance, in *Science and Ultimate Reality: From Quantum to Cosmos*, eds. Barrow, J. D., Davies P. C. W., and Harper C. H. (Cambridge University Press).

About the authors

Edward W. Piotrowski is presently the head of the Applied Mathematics Group at The University of Białystok, Poland. He was born in Rybnik (Poland) in 1955, graduated in theoretical physics from the University of Silesia (Katowice) and earned his PhD and habilitation from the University of Silesia, under Andrzej Pawlikowski. He has published about 40 papers in leading international journals on statistical physics, quantum game theory, and econophysics. His most important results are the analysis of quantum strategies, showing connections between the Kelly criterion, thermodynamics, and special theory of relativity. He discovered extremal properties of fixed points profit intensities of elementary merchant tactics.

Jan Sładkowski was born in Świćetochłowice, Poland in 1958. He earned his PhD, under Marek Zrałek, and habilitation in theoretical physics from the University of Silesia (Katowice, Poland). He has published over 50 papers on quantum field theory, mathematical physics, quantum information processing, and econophysics. He has held visting posts at the Bielefeld University and at the State University of Wisconsin in Madison. During the past 15 years he has been working on the role of exotic smoothness in cosmology, quantum games, and applications of thermodynamics in finance theory. He presently holds the Chair of Astrophysics and Cosmology at the University of Silesia.

This page intentionally left blank

PART 5

The Debate

This page intentionally left blank

Chapter 15

Dreams versus Reality: Plenary Debate Session on Quantum Computing

6:00pm, Wednesday, 4th June 2003, La Fonda Hotel, Santa Fe, USA, *The International Symposium on Fluctuations and Noise (FaN'03).*

The Panel - Dramatis Personae

Chair/Moderator: **Charles R. Doering**, Univ. of Michigan (USA); Editor of *Physics Letters A*

Pro Team (*assertion "reality"*):
Carlton M. Caves, Univ. of New Mexico (USA);
Daniel Lidar, Univ. of Toronto (Canada); Editor of *Quantum Information Processing*;
Howard Brandt, Army Research Lab. (USA);
Alex Hamilton, Univ. of New South Wales (Australia).

Con Team (*assertion "dream"*):
David Ferry, Arizona State University (USA); Editor of *Journal of Computational Electronics*; *Journal of Applied Physics/Applied Physics Letters*; *Solid State Electronics; Superlattices and Microstructures*;
Julio Gea-Banacloche, Univ. of Arkansas (USA); Editor of *Physical Review A*;
Sergey Bezrukov, National Institutes of Health (USA); Editor of *Fluctuation Noise Lett.*;

First published in abridged form in *Quantum Information Processing*, **2** 2003, pp. 449–472.

Laszlo Kish, Texas A&M (USA); Editor-in-Chief of *Fluctuation Noise Lett.*

Transcript Editor:
Derek Abbott, The University of Adelaide (Australia); Editor of *Fluctuation Noise Lett.*; *Smart Materials and Structures.*

Disclaimer: The views expressed by all the participants were for the purpose of lively debate and do not necessarily express their actual views.

Transcript conventions: Square brackets [...] containing a short phrase indicate that these words were not actually spoken, but were editorial insertions for clarity. Square brackets [...] containing a long section indicate that the recording was unclear and the speaker has tried to faithfully reconstruct what was actually said; [*sic*] indicates the transcript has been faithful to what was spoken, even though grammatically incorrect. Where acoustic emphasis was deemed to occur in the recording, the transcript reflects this with italics.

The Debate

Charlie Doering (Chair): [Welcome everybody to the Plenary Debate on quantum computing "Dream or Reality." We are going to start with the Pro team and then the Con team. Each speaker will strictly have 3 minutes. Before we start, I would like to remind everybody about the dangers of trying to make future predictions about computers with the following quote:]
"I think there is a world market for maybe five computers."
—Thomas Watson, Chairman of IBM, 1943.

Audience laughter

Charlie Doering (Chair): [OK, now let's move straight to our first panellist. Carl.]

Carl Caves (Pro Team): [I'm going to declare that the subject of this debate is the question: "Is it possible to build a quantum computer?" With this question in hand, we still have to define our terms. What does "possible" mean? It could mean, "Are quantum computers allowed by physical law?" Since we think they are, and since small numbers of qubits

have been demonstrated, I'm going to define "possible" to mean, "Can it be done in n years?" And then we have the further question of the value of n. Does $n = 1{,}000$, $n = 100$, $n = 30$ or $n = 10$? Finally, we need to define what we mean by a "quantum computer." Do we mean a rudimentary, but scalable device that can, say, factor 15? Do we mean a useful quantum simulator? Or do we mean a scalable, general-purpose quantum computer (e.g., one that factors interestingly large numbers)? Before proceeding, I will issue a warning about physicists' estimates of the time needed to accomplish some task:

- $n = 1$ year: This is a reliable guess, but it will probably take 2 to 5 years.
- $n = 10$ years: I have a clue how to proceed, but this is a guess that I'm hoping the funders will forget before the 10 years are out.
- $n > 30$ years: I don't have a clue, but someone put a gun to my head and made me guess.]

Audience laughter

Carl Caves (Pro Team): [So n is going to have a different answer depending on what we mean. Here are my estimates for the three cases:

- Rudimentary, but scalable 10-15 years device that can, say, factor 15? Motivation: High.
- Useful quantum simulator? 20-30 years Motivation: Medium.
- General-purpose quantum computer? 50 years Motivation: Need more algorithms.

The really important question for discussion is not whether we can build a quantum computer, but rather, "Is quantum information science a worthwhile interdisciplinary research field?" Yes! It puts physical law at the core of information-processing questions. It prompts us to ask what can be accomplished in a quantum-mechanical world that can't be accomplished in a classical world. And it prompts us to investigate how to make quantum systems do what we want instead of what comes naturally.]

Charlie Doering (Chair): [OK, good timing. Next, Daniel.]

Second Pro Panelist (Daniel Lidar): I think it was in '95, [a paper in Physics Today by Haroche and Raimond,][1] and the title of the paper was

[1]Transcript editor's note: It was actually 1996, see: Haroche, S. and Raimond, J.-M., (1996) Quantum computing: Dream or Nightmare?, *Physics Today*, **49**, pp. 51–52.

"Quantum computing: dream or nightmare,"—so we're making progress by making this [debate] "dream or reality."

Audience laughter

Daniel Lidar (Pro Team): I believe that there's no question that quantum computers will be built and my reasoning for this is very simple. There is simply no law of nature, which prevents a quantum computer from being built and there are some damn good reasons for building one. Now, why is it that there is no law of nature? Well, in that "dream or nightmare" paper and as well as some other papers by Bill Unruh and Landauer around the same time, it was argued that decoherence was going to kill quantum computers and therefore there was no chance. And there was a quick reaction to that, which astonished a lot of people because it seemed to somehow violate the second law of thermodynamics; and this was the discovery of quantum error correcting codes. So while it was believed naively that quantum computers would never work because of decoherence, quantum error correcting theory shows that this belief was false and that in fact it is possible to overcome the decoherence problem, at least in principle. And this theory has been refined to the level where we now know that there exists a threshold, which is measured in terms of a number that's rather small—about 10^{-4} or so. It's basically something like the ratio between the decoherence time and the time it takes to apply an elementary logic gate. So you have to be able to squeeze in 10^4 logic gates within a unit of decoherence time. If you can do that, we know from the theory of quantum error correction that there is nothing in principle preventing quantum computers from being built. They will be robust; they will be able to resist decoherence absolutely. So this disproves the old skepticism and I believe it reduces the problem of constructing a quantum computer to a very interesting one, but it has basically now become a problem of finding the optimal system and fine-tuning the ways that we're going to implement quantum error correction, quantum logic gates, and measurements.

Charlie Doering (Chair): Excellent. Thank you. Twenty seconds to spare.

Audience applause

Charlie Doering (Chair): Now can we have Howard?

Howard Brandt (Pro Team): Yes.

Charlie Doering (Chair): OK, go!

Howard Brandt (Pro Team): Quantum information processors are certainly viable: quantum crypto systems, operational quantum crypto systems, have already been demonstrated. That's small-scale quantum information processing. Quantum teleportation has been demonstrated. Some of the basic ingredients of quantum repeaters have been demonstrated. Quantum copiers are certainly feasible. Grover's algorithm has had a proof-of-principle—Grover's algorithm has been demonstrated for a database of 8 entries, doing it faster than a classical computer could have. So the algorithm has been proof-of-principle demonstrated. Shor's algorithm has been proof-of-principle demonstrated in factoring the number 15 faster than a classical computer could. Quantum error correction has also been demonstrated on a small scale—proof-of-principle. As Lidar has pointed out, the laws of physics do not prohibit even large-scale quantum computers capable of exercising Shor's algorithm, or Grover's algorithm to search a large database. There's potentially a big pay-off in solving problems not possible to solve classically, and breaking unbreakable codes. Speaking for the viability of quantum information processors is the worldwide effort including many elements, many disciplines, special sections of our most prestigious journals on quantum information, and a number of entirely new journals on this subject. The real feasibility of developing a robust largescale quantum computer by any of the current approaches remains in question. It will likely take a lot of time.

Charlie Doering (Chair): 30 seconds.

Howard Brandt (Pro Team): Luv Grover has warned us against erring on the side of pessimism. Witness the pessimism at the end of the ENIAC in 1949 in terms of projected size and number of vacuum tubes.

Charlie Doering (Chair): One second.

Howard Brandt (Pro Team): My time is up, is it? All right, well...the Army Research Lab is tasked with assessing the viability of quantum information science and technology for possible transition to the Army. Quantum crypto systems are ready and that's being pursued—the other systems are not ready but they will be.

Charlie Doering (Chair): OK, thank you very much.

Audience applause

Charlie Doering (Chair): OK, I'm pretty excited now! Alex.

Alex Hamilton (Pro Team): OK, so to follow Carl's theme; the first thing we've got to do is look at the question: Is it a dream or reality?

And the answer is we best not follow that path, actually, because it is an entanglement of both. The dream is really to—as system engineers—to understand nature and to try to control nature. What's the simplest quantum mechanical thing we can understand? [It is] the quantum two-level system. What could be simpler? Let's get one and control it. That will be a beautiful thing to do. Understanding even what quantum mechanics means at the most fundamental level—this is all part of the dream. Well, what do we mean by doing a quantum measurement? We teach our high school and undergraduate students that you have a quantum system, you come along, do a measurement and that collapses the wave function—but we're not really sure how it collapses the wave function—that's never really discussed. It just comes in, it collapses and you get a 1 or a 0. The cat is either alive or dead. So, we're having to think very hard about what a quantum measurement means. This seemingly esoteric and irrelevant question now has a very real physical meaning in terms of doing a measurement on a quantum bit. And then, how do you couple these two-level systems? What does it mean to entangle them? Do you actually need entanglement for quantum computing?[2] So these are, physically, very important questions to answer. The other breakthrough is that it does bring together people from all sorts of different disciplines. In the solid-state area there are people from superconductivity, semiconductors, surface science, other variant schools of physics, all talking about the same thing and for the first time, in a long time, speaking the same language. So there are 3 level quantum systems, decoherence, T_1, T_2. In liquid-state NMR, same thing is happening. Every phase of matter is being represented: solid-state, through liquid, through gas, even the others: Bose-Einstein condensates, fractional quantum Hall liquids. We're all coming together and talking the same language, so that's the dream, who knows? The reality—can it be done? Well, there's good evidence that we can make one-qubit systems. There's evidence we can couple n small numbers of qubits. So on a very small scale, yes, it looks like it can be done. Can it be scaled to a usefully large quantum computer? That really is a very difficult question to answer. I would say that it is perhaps too early to say because it's a big engineering problem but there's no law of physics that says that it simply cannot be done. And, again, if we look at the history of electronics the first vacuum valves were in operation in the early twentieth century but it wasn't until about the 1960s that it was possible to really build a useful [classical] computer.

[2]Transcript editor's note: See, for example, D. A. Meyer (2002) Sophisticated quantum search without entanglement, *Phys Rev Lett,* **85**, pp. 2014-2017.

Charlie Doering (Chair): Twenty seconds.

Alex Hamilton (Pro Team): Will it actually be useful? Will I be able to go down to Walmart and buy one for my grandmother for Christmas?

Audience laughter

Alex Hamilton (Pro Team): This is a question that one of my students asked. Maybe it will never be one per household, but perhaps we don't need it to. Supercomputers—my grandmother doesn't have a supercomputer at home—she's quite happy, in fact she doesn't have a computer at home. And perhaps you can say, "Look, it doesn't matter. It's just never going to work." How do we know? If you look at the history of computers, people said that it would never work. They were weighing no more than 1.5 tonnes and they'll consume no more than the power of a small city; and look what we've got today, so I think it is possible and it's just... you better go and see what happens.

Charlie Doering (Chair): OK, thank you very much.

Audience applause

Charlie Doering (Chair): OK. I'm glad you addressed the issue of how much they're going to weigh. That's certainly something on a lot of people's minds. At least a while ago,

"Computers in the future may weigh no more than 1.5 tonnes."
—*Popular Mechanics*, forecasting the relentless march of science, 1949.

Audience laughter

Charlie Doering (Chair): Now we're going to go over to the Con side, which I believe is some kind of Republican view of [quantum computing].

Hysterical audience laughter

Charlie Doering (Chair): We'll start off with David Ferry—please.

David Ferry (Con Team): Just a simple, little 2-level system. It would be the easiest thing in the world to make, all right? We've had twenty years working on quantum computers, more than two decades in fact and we haven't got it going yet. The problem is that in those two decades—more than two decades—they've only got two algorithms. Although I heard in a rumour, today, that a third algorithm may have been followed up. Without having the architecture and an algorithm making the system work, you can't make a system. So you really have to have more than just a device—the

world is littered with devices and it takes more than just a theory. When I was young, last century or just before ...

Audience laughter

David Ferry (Con Team): [Many years ago,] one of the first conferences I went to was on superconductivity, and there was a god of superconductivity who made the statement that all the theory in the world, integrated over time had not raised the transition temperature one milliKelvin. So it takes more than just ideas about where science goes—you have to have practical working examples from the laboratory. You have to see the results. If you haven't seen it yet, it's quite a difficult problem. We've been arguing about [quantum] measurement since the 1927 Solvay Conference, and even the idea of wave-function collapse depends upon your view of quantum mechanics. [Bob] Griffiths doesn't believe in wave-function collapse. So you have to be careful now about your interpretation. This makes it a very difficult problem both intellectually and practically, but it's a dream with a shift in emphasis over there by Caves and he probably should work on quantum information.

Chair taps to indicate time.

OK. Great.

Audience applause

Charlie Doering (Chair): Excellent, excellent. The economy of your presentation was perfect. Julio?

Julio Gea-Banacloche (Con Team): Alright, well ...I ...um ...I'm surprised, actually, that I'm sitting here on the Con side.

Audience laughter

Julio Gea-Banacloche (Con Team): ... because I just realized that I'm actually more optimistic than Carl is.

Audience laughter

Julio Gea-Banacloche (Con Team): I would like to mention, nonetheless, that the reason I'm here, I think, is because I understood the question to mean the last of these options, that is to say, the general purpose, huge, big, million physical qubit factoring machine of strategic importance and so on. And that actually ...personally, I don't think that we will ever see that, for the reason that it's basically—even though we may call it a universal quantum computer, and that seems to confuse some people—we really don't mean that this is a computer that will replace current computers in

any sense. We're not building this so that we can run Microsoft Office on it.

Audience laughter

Julio Gea-Banacloche (Con Team): In fact, there is no reason to build anything to run Microsoft Office on it [*sic*].

Audience laughter

Julio Gea-Banacloche (Con Team): But this is obviously going to be—even if it is built—a special purpose machine and in fact, as Carl also has pointed out, so far we have only one reason to build it... and that is to break certain encryption systems, which are currently very popular. But the thing is that this device is not going to be built, if at all, for some 20 years, 30 years or something like that. And I find it very hard to believe that in 20-30 years people are still going to be relying for the encryption of sensitive data on the same encryption algorithm that today a quantum computer can break. Given that, my personal prediction is that this idea is going to go basically the way of some other technologies that looked very promising at one time, but they turned out to be so extremely challenging that they failed to deliver on their promise in a timely fashion and they simply fell by the wayside—mostly we found ways around them, and that's basically what I think is going to happen with quantum computers; I mean the large scale quantum computers. Like Carl and like everybody else, I think that this is very valuable scientific research and having a small, say 100 qubit, quantum simulator in 10 or 15 years will be a big accomplishment and not out of the realm of possibility.

Charlie Doering (Chair): Thank you.

Audience applause

Charlie Doering (Chair): Sergey.

Sergey Bezrukov (Con Team): The organizers have asked me to say something about quantum computing and biology.[3] This is something of a very short message, which is "there is no place for quantum computing in our brain." The main function [of the brain] is based on nerve pulse propagation and this process has been studied in great detail. What I mean is that most of you in this audience do not have any idea of how many people [are working on these problems] and how much effort is put into this investigation. It is well understood that this [pulse propagation] is

[3]Transcript editor's note: The possible implication being that if nature hasn't somehow made use of quantum computing, itself, then there probably isn't much hope for it.

a dissipative macroscopic process. The next in line is synaptic transduction. This is how nerve cells talk to teach other. Again, this is a macroscopic dissipative process, which is understood right down to molecular detail. Next, there are—and these are necessary for "computation" in our brain—short-term and long-term memory. Well, these things are not as well studied as the previous two, but one can say that the short-term memory is related to the short-term changes in the chemical composition of interacting cells. For example, if I say something to you right now, you are able to recall it within time intervals of several seconds, because of the transient chemical changes in the right places. And, finally, our long-term memory is definitely related to, again, macroscopic dissipative processes leading to structural changes in the brain. This is all.

Charlie Doering (Chair): Thank you.

Audience applause

Charlie Doering (Chair): OK, everybody take a deep breath because—next—Laszlo is going to give us his view on the subject.

Laszlo Kish (Con Team): I don't have much to say... yes, it's really marvellous that the quantum field has found new effects. This is really great. My problem is with—just like Julio—general-purpose quantum computing, it seems, is like analog computing:[4] we have to build a system that is special purpose. The error space is analog. What we have to see is that quantum parallelism is a consequence of Hilbert space. But classical systems also can inhabit Hilbert space. So to save time, you can also try classical systems. When we compare classical and quantum computing, it is very important to use the same temperature and the same speed <clock frequency> and then compare a classical hardware version with a quantum version, with the same number of elements, and ask what is the power dissipation. Another question is where are the general-purpose quantum algorithms? It is important to note that a classical Hilbert space computer

[4]Transcript editor's note: The fact a state in a quantum computer (QC) can be described by a vector in a Hilbert space that is complex and real valued has led some to believe that QCs are analog machines. This is not quite true, as it is not the full picture. QCs are digital because it has been rigorously proven, for a general quantum Turing machine, that for n computational steps only $\mathrm{O}(\log n)$ bits of precision is required. So when constructing a quantum computer, the measurement of, say, a rotation of a nuclear spin by arbitrary real-valued angles is not needed as the required precision can still be maintained by throwing away real-valued information in the sense of a digital computer. However, what Kish probably really means is that QCs might display some "analog-like" disadvantages in terms of power dissipation and the requirement for special purpose circuitry.

is already working in Japan! A 15-qubit classical quantum computer was built by Fujishima[5]—we saw this in the talks. Thanks.

Charlie Doering (Chair): OK, thank you very much.

Audience applause

Charlie Doering (Chair): What we're going to do now is... I'm going to show you something to the Con side here: the Pro side is very busy taking notes while you were all speaking. So, now, I'd like to have a reality check every once in a while about telling the future of computer science:

"There is no reason anyone would want a computer in their home."
—Ken Olson, president, chairman and founder of Digital Equipment Corp., 1977.

Audience laughter

Charlie Doering (Chair): That's right, that's why DEC doesn't exist anymore, OK!

Audience laughter

Charlie Doering (Chair): Now what we're going to do is we're going to go back. Quickly, one minute, each person, same direction; any comments they want to make, any ridiculing they want to do. Then we're going to open it up to a free discussion to take comments and questions from the audience and so on, OK, so, we'll start off right now with Carl.

Carl Caves (Pro Team): I'm going to try and make four quick points. First, it is good to know that the editor of PRA, i.e. for quantum information views research in this field as useful.

Audience laughter

Carl Caves (Pro Team): I think we might learn that... this is in response to some comments by Dave Ferry... I think we might learn some things about how to interpret quantum mechanics by thinking in terms of quantum information processing. I think quantum mechanics is partly information theory, partly physical theory, and we've never understood exactly how these two go together. We might learn something in this regard, but I don't think we have to know anything about the interpretation of quantum mechanics to know how physicists will interpret and make predictions for what a computer will do. I guess I want to get to my third point: I agree that we need more algorithms. Let me say that the only reason

[5]Transcript editor's note: Fujishima M., and Hoh K., (2003) High speed quantum computing emulator utilizing a dedicated processor, *Proc. SPIE Noise and Information in Nanoelectronics, Sensors, and Standards,* **5115**, pp. 281–287.

I'm optimistic about that is—because I don't know much about that and I don't think there's anyone here in this room who's a real expert on that—Umesh Vazirani told me that after probabilistic algorithms came out, it took people 15 years before they realised what could be done with probabilistic algorithms. Maybe something like that will happen with quantum algorithms.

Charlie Doering (Chair): OK, thank you. No applause for this [round]. Too much time, too much time. Daniel.

Daniel Lidar (Pro Team): OK, let me take these guys on one by one.

Audience laughter

Daniel Lidar (Pro Team): David Ferry says that "20 years and we have no qubits yet, no [new] algorithms, no practical devices"—but he neglects the amazing results in trapped ions, 4-qubit entanglement, Josephson qubits have already shown entanglement, and in quantum dots single qubit operations have already been performed. [This] all happened in the last three or four years—no reason that it won't continue. Julio says "only reason is to break crypto" but he forgets that quantum computers will be to simulate quantum mechanics exponentially faster than we can do on classical devices. Now, Sergey: "no role for quantum computers in the brain"—I agree.

Audience laughter

Daniel Lidar (Pro Team): Laszlo: "quantum computers are like analog systems, that are special purpose," well, they are not analog. Actually they are digital. That is a subtle point. "Classical computers can be described in Hilbert space." Yes, but there's no entanglement, no tensor product structure. The whole speed up issue just breaks down for classical computers, even if you use Hilbert spaces.

Charlie Doering (Chair): Perfect. OK. Howard.

Howard Brandt (Pro Team): I agree with Dan that David is not up to date. I'm not surprised, because when I looked at his paper, he speaks of entanglement as being a hidden variable... enough for David.

David Ferry (Con Team): *Clutches his chest as if he's been shot.*

Howard Brandt (Pro Team): Julio, well, I think that you have to realize that a universal quantum computer is a mathematical artifice, as was the Turing machine. It's an idealisation—something that will be approached—it does not deal with decoherence, it doesn't deal properly with a halt bit. There are certain operations and certain unitary transformations that are

suspect. However, related to the universal quantum computer—we now have a generalized Church-Turing thesis...

Charlie Doering (Chair): 10 seconds.

Howard Brandt (Pro Team): The original Church-Turing thesis is not true because of quantum computers. Also I heard that factoring might not be that important. But Grover's search will [be important], and there will be other NP incomplete algorithms (such as the travelling salesman problem) that may happen. And Laszlo, sure you can use Hilbert space for some classical systems, but that's an entirely different ballgame than in quantum mechanics.

Charlie Doering (Chair): OK, right, let's move on. You'll get another chance.

Alex Hamilton (Pro Team): I think everything has been said, so let me add just two quick points. One is, well perhaps, we don't have many [quantum] algorithms, but that's OK, we don't have that many [quantum] computers to run them on just yet...

Audience laughter

Alex Hamilton (Pro Team): ... so, you know, algorithms—it helps if we have something to do to run them with and that will probably come in time. Second thing is that, does it have to be a general-purpose quantum computer?[6] The floating-point unit in my laptop is not general purpose. All it does is crunches numbers but it makes my games so much better, and I think what we really need to do is quantum gaming and that's what's really driven the microprocessor industry and that's what will drive the quantum gaming industry.

Audience laughter

Alex Hamilton (Pro Team): And finally, the classical representation of quantum computing. If you want to represent 300 qubits for a quantum computer classically, you can, but there won't be much left of the universe once you've done that.

Charlie Doering (Chair): Excellent. And in time. David? Hold the mike closer.

[6]Transcript editor's note: An important point that is often missed in such debates is that general-purpose quantum computing is out of the question in the first place. This is because an *arbitrary* unitary operation on n qubits takes a number of gates that is exponential in n, see Nielsen, M. A., and Chuang, I. L. (2000). *Quantum Computation and Quantum Information* (Cambridge University Press), pp. 198–200.

David Ferry (Con Team): Alright, I believe, Dan, I used the word "practical" but there's a big difference in "practical" and the number of the qubits you need out there. I spent a great deal of time working on quantum dots and I know how practical they are for this purpose. And there are other examples of some massively parallel analog systems, which factor the number 15 really fast—it's called the [human] brain.

Audience laughter

Charlie Doering (Chair): Onward. Julio.

Julio Gea-Banacloche (Con Team): Ummm ... ummm

Audience laughter

Julio Gea-Banacloche (Con Team): Ummm ... ummm

Audience laughter

Charlie Doering (Chair): Fourty seconds.

Audience laughter

Julio Gea-Banacloche (Con Team): Ummm ... ummm

Charlie Doering (Chair): Okaaaay. Now, Sergey.

Sergey Bezrukov (Con Team): My only point is that the solutions adopted by nature are very, very good. For example, the other day, Laszlo Kish and I discussed the dissipation issue of 1-bit processing in our brain and in a conventional computer... and it turned out [that] our brain is 10 times more efficient in power dissipation. Why is that? For two reasons. [Firstly,] because our brain uses ten times smaller voltages. The computer uses about 1 V and the brain only about 0.1 V. The second reason is that our brain is a massively parallel computer, so that mistakes are not prohibited but, to a degree, are welcome for our spontaneity and ability to think.

Charlie Doering (Chair): Excellent. Thank you. Last one.

Laszo Kish (Con Team): The brain is using noise to communicate, which is important. Concerning Hilbert space: yes classical and quantum is different. Classical is better because it is not statistical like quantum. But finally to you Charlie [Doering], your quotes are against us—I mean they are Pro! How about the moon base? In the 1970s, we expected that we would have a base on the moon at the end of the century, [which did not eventuate.] That's all.

Charlie Doering (Chair): It's no good taking shots at me! I just work here.

Audience laughter

Charlie Doering (Chair): What we're going to do now is ... I'd like to open it up to the audience here. If people have questions, you can direct questions toward either a particular side or particular person, but we'll keep it short and then we may allow some rebuttal from the other side, whatever. So, we have a question right here.

Audience member (Unknown): I would like to ask a question to just anybody who's most motivated to, to one or two of you who might answer. I would like to stick to the moon. What do you think is harder—to build a 10,000-qubit-quantum computer right now, say in the next years—some big effort—or to decide in 1960 to go and put a man on the Moon within 10 years?

Charlie Doering (Chair): Who would like to take that? Carlton, it looks like you're reaching for that.

Carl Caves (Pro Team): No question. It's easier to put a man on the moon. That's basically engineering. There's a huge amount of basic research that has to be done to make a quantum computer work.

Charlie Doering (Chair): Anybody else? Everybody agrees.

The whole Pro team nods affirmatively.

Charlie Doering (Chair): That's an interesting take-home message.

Derek Abbott (The University of Adelaide, Australia): It seems to me, without a doubt, that small numbers of qubits have been demonstrated. So the real question for this debate should be: "Is it possible to scale quantum computers?" I think that's your real question and if you look at the most sensible way of scaling, which is on silicon, in my opinion—because it's a mature scaleable technology—you have then got to ask, "What is the decoherence time in silicon?" And all the papers say, "If you use pure silicon and blah, blah, blah, it's all very good." But putting my Con hat on, to help the Con team a bit...

Charlie Doering (Chair): They need it.

Derek Abbott, The University of Adelaide, Australia (Audience member): ... they need it, so I'm going to help them a bit. What the papers don't address is that, "OK, I've got this..."

Charlie Doering (Chair): Questions cannot last longer than three minutes.

Audience laughter

Derek Abbott, The University of Adelaide, Australia (Audience member): [What the papers don't address is that,] "OK, I've got this scaleable quantum computer; I've got zillions of qubits on here; I've got all these A and J gates switching like crazy. That is a coupling into the environment. What's going to happen to that decoherence time when they are all switching like crazy? That is my question to this [Pro] side. Thank you.

Daniel Lidar (Pro Team): Well, the answer once again is in quantum error correction. Provided that you can get the single qubit decoherence rate below a certain threshold, the theory of quantum error correction guarantees that you can scale-up a quantum computer.

Alex Hamilton (Pro Team): Just to finish, to go back to your point about scalability. Although silicon is one of the things I'm working in—I don't think it's the only one that's scaleable—superconductive technology is equally scaleable. It's very good—you can go out right now and buy RSFQ <Rapid Single Flux Quantum> electronics that's basically a superconducting electronics that's been scaled-up and there's no reason that other systems can't be scaled-up. Ion traps can be put on-chip and so on. So, there's no reason that semiconductors are the only ones that are scaleable.

Charlie Doering (Chair): Julio.

Julio Gea-Banacloche (Con Team): I think that it's always a big jump to say that just because you have demonstrated something for, say, 100 qubits that you're going to be able to scale that up 4 orders of magnitude, without encountering any unexpected problems. I don't think there are any engineers here that will support such a point of view. And, there are constraints that we can already begin to imagine, as you just mentioned. If you're going to address your qubits by frequency, for instance, it's not the same thing to have a hundred different frequencies, as it is to have a million different frequencies. And that's not all. There are constraints on the amount of energy that you need in order to perform the gates, and it's not the same to operate a hundred qubits as to operate a million of them. So, the scaling is not by any means trivial. I am willing to grant that once we have demonstrated, say, 5 qubits—with some effort in a 5-10 years time frame, we may be able to do 50 to 100 qubits.

Minor audience applause

Charlie Doering (Chair): David, did you want to...?

David Ferry (Con Team): Scaling is not all it's cracked up to be. You can go to the Intel website. You can find there a view graph, which predicts that in about 6 or 7 years from now, the power dissipation figure for your Pentium will about that of a nuclear reactor.[7]

Audience laughter

Laszlo Kish (Con Team): Yeah, Alex Hamilton said in his talk yesterday, that if you use error correction you need an error rate of 10^{-6} or less. A 10^{-6} error rate—this is a huge thing, because this is just like analog circuits, which can achieve [a] 10^{-6} error [rate] by using very strong negative feedback. You know, [a] 10^{-6} error rate [for quantum computation] seems to be hopeless. Anyway, this is very difficult.

Carl Caves (Pro Team): I think it's generally 10^{-4}, which is also incredibly small. But there's a lot of work in getting error correction worked out and in some systems based on dits instead of bits—that is higher dimensional quantum systems—or systems based on topological quantum computing, there's some indication that the error threshold might get up to one per cent, and then you're in the ballgame, I think. So we're just at the start of this and to dismiss the whole thing because the first results say fault tolerance is going to be extremely difficult to achieve, seems to be a mistake. Let's do some further work and see what the error threshold can get up to in other kinds of architectures and designs.

Charlie Doering (Chair): OK. All right, let's move on to a different... Another question.

Howard Wiseman, Griffith University, Australia (Audience member): This is addressing Carl's observation comparing probabilistic computing with quantum computing. The genuine question is, "Was probabilistic computing as sexy an area as quantum computing is now?" Because it is sort of worrying that there are so many smart people working on quantum algorithms and there hasn't been another reasonable one since '97. It does indicate a genuine concern.

Charlie Doering (Chair): Anyone know what the response is? David? You have the mike.

David Ferry (Con Team): In the beginning, Poppelbaum (University of Illinois) was working on probabilistic computing back in the mid-70s, around '73 or '74, and it was not a big area like this. He was kind of

[7] Transcript editor's note: `ftp://download.intel.com/research/silicon/TeraHertzshort.pdf`, slide number 9.

trudging on alone with a small, dedicated group working in it, but I don't think it grabbed the attention of big research groups around the world like quantum computing did.

Daniel Lidar (Pro Team): There is a misconception that there are no good quantum algorithms out there. For problems in number theory and pure computer science, yes—there are very few. But let's not forget that quantum computers are exponentially faster at simulating quantum mechanics. Every university in the world has people in chemistry and physics departments working on trying to find fast algorithms to solve problems in quantum mechanics. A quantum computer would be enormously helpful there, so that's a huge benefit.

Charlie Doering (Chair): OK.

Carl Caves (Pro Team): I think that's a good point Howard [Wiseman]. I'm just relying on the fact that Umesh Vazirani, who has worked on both, suggested that given the current scale of effort in computer science among people who think about this, you might expect to make a big breakthrough in quantum algorithms any time or you might expect it to be in another decade. My direct response to you is that quantum mechanics is a much richer theory than classical probability theory, so you might think it is harder to come up with quantum algorithms, and it might take longer even with more people working on it.

Charlie Doering (Chair): Another question here.

Audience member (Unknown): Just like to make a quick comment. Doing all those is fine but as general-purpose computers, I'm just wondering in the '60s, '70s and '80s people doing optical computing. Except for certain special purpose optical computing, there isn't any general purpose optical computing.

Charlie Doering (Chair): Anybody?

Alex Hamilton (Pro Team): My understanding is that for optical computing that one of the great things that it would be good for would be for Fourier transforms, and with the invention of the fast Fourier transform algorithm, there really wasn't any more need for optical computing.

Audience member (Unknown): That's not quite true because you've got optical parallelism and your Fourier transform [is traditionally computed in] series.

Kotik Lee, BAH, USA (Audience member): Optical computers are used extensively with defence systems, for special purpose processes.

Charlie Doering (Chair): Another question. Up the back.

Fred Green, University of New South Wales, Australia (Audience member): Well, it's really a comment. It's another take on the relative lack of algorithms. One of the things that happens when you make a machine, that's enormously complex, is that it may well become something that uses its emergent behaviour—to copy a buzzword. The thing is, that in a sense we are thinking in a reductionist way about machines, we're thinking of a specification and rules and designs to make an enormous machine, but it's equally likely that the machine will go and do things that you simply cannot predict from its underlying equations. That is just an open question. For example, you cannot—just by having a set of equations and putting it on a computer—you cannot get superconductivity out of that. Something has to make it all complete and all I'm doing is actually repeating what Laughlin said some years ago now. It's quite conceivable that a machine in all its complexity will be able to do things like that. It's something that human brains are quite good at.

Charlie Doering (Chair): Any response? Julio?

Julio Gea-Banacloche (Con Team): I'll venture a response. That's certainly a possibility but it's not currently an envisioned possibility, the way people envision this huge fault-tolerant quantum computer. Most of its time—99.99% of its time in every clock cycle it will not be doing anything except error correction. Emergent behaviour would be, you know, remarkable—almost anything could show emergent behavior more likely than such a machine.

Charlie Doering (Chair): You Carl, you have to respond to that.

Carl Caves (Pro Team): I'm not really directly responding to that. I want to say something that popped into my head that has something to do with that. Now what if there were a fundamental decoherence mechanism in the universe that couldn't be explained by coupling to external systems. You could error correct that. Wouldn't that be pretty neat? You could restore linear quantum mechanics even though the universe is fundamentally [might possibly not be] linear quantum mechanics.

Audience laughter

Charlie Doering (Chair): Whoa, whoa, whoa. OK.

Daniel Lidar (Pro Team): I just wanted to say something about the [observation that] 99% of the time is spent doing error correction. This is true, but it does in no way contradict the fact that a quantum computer offers a speed up.

Michael Weissman, Univ. Illinois Urbana Champagne, USA (Audience member): I did not understand those last remarks [of Caves on restoring linearity], but while we are on the same topic: you mentioned earlier that the interpretation of quantum mechanics does not affect the operation of a quantum computer. That is certainly true up to an extent. However, if there were an intrinsic non-unitary operator involved, at some point, for example, you would find decoherence in cases where [you] do not expect decoherence if there are only unitary operators. If you made a quantum computer more or less of the same physical scale as your head and with similar amounts of mass and current involved in its thoughts as in yours and it did not show unknown nonunitary operations that would be very important for understanding quantum mechanics. If it did, it would be even more important because it would support the idea that some modification is needed. Either way, conceivably, it would have something to do with the experimental realisation of tests of modification-type interpretations.

Carl Caves (Pro Team): Yeah, I certainly agree with you that one thing you might find out is that there are fundamental non-unitary processes when you get a sufficiently large system, and those are processes responsible for making the world classical and they would represent a barrier to making a quantum computer of sufficient size.[8] Those are important issues. I don't call them interpretational because they're changing quantum mechanics, whereas when I refer to the interpretation of quantum mechanics I mean keeping what we've got and figuring out what it means—not making changes.

Charlie Doering (Chair): As the Chair of this session, I'm going to declare we're going to keep quantum mechanics the same way, as it's not fair to try to change quantum mechanics for either the Pro side or the Con side.

Audience laughter

Charlie Doering (Chair): OK, yes, absolutely, absolutely.

Howard Brandt (Pro Team): We've got some affirmation of the worth of the pursuit of quantum information science and technology by one of the editors of *Physical Review A*, Julio here. But Charles, one of the things I hear is you're an editor of *Physics Letters A*. I'm very concerned about one

[8]Transcript editor's note: In fact, the *holographic principle* indeed sets an upper bound, the "Davies Limit", to the size of a quantum computer, as there is a cosmological information bound for quantum information. See, P. C. W. Davies in quant-ph/0703041.

of the things you said previously and that the editor of *Physics Letters A* may be ignorant about quantum mechanics. You stated that yourself!

Audience laughter

Charlie Doering (Chair): Very good. I apologize.

Audience laughter

Charlie Doering (Chair): The great thing about *Physics Letters A* is that each editor has their own area of expertise and mine is explicitly not quantum information, [which means I have no bias]. So, anyway, quantum mechanics shall not be changed in remaining discussion and we'll move on from there. Peter Hänggi.

Peter Hänggi, University of Augsburg, Germany (Audience member): I like quantum computing because you can see all this knowledge being brought together from different areas of science and great progress in understanding quantum mechanics. But I also believe in human nature, you know. After five, ten years I get a bit tired because I've seen enough of it. See, there are those things that can be done quickly, and I'm not so sure this momentum carries on when it comes to do the very hard work. Most of the people here don't want to do the nitty-gritty work, the core and the details about this stuff, and so on. I think the excitement, which is so high up with tackling all these problems on quantum information, will eventually slow down. [If] the problems are not [solved in] three, four, five years maximum, and then of course we need something else and we don't know what the next excitement in science will be; but most likely we physicists don't want to do for two or even more years [the] nitty-gritty work on a detail. Moreover, we also need to talk about the engineering, so that explaining this heightened expectation [*sic*]; we also need practical things from this whole exciting quantum computer and computation [area].

Charlie Doering (Chair): OK, so that sounded like a ... ? Is that a... ? Could we have a response to that? Is that a Pro or a Con?

Peter Hänggi (Audience member): I don't know what it is.

Charlie Doering (Chair): Yeah, that's OK.

Audience laughter

Daniel Lidar (Pro Team): I think it would be great [if people got tired], because there are way too many papers in this field right now.

Audience laughter. Julio nods affirmatively.

Charlie Doering (Chair): OK, the editor of *Physical Rev. A* seconds the motion.

Audience laughter

Carl Caves (Pro Team): I think the example of quantum cryptography shows that people are willing to do very sophisticated, higher mathematical and physical work on a system that is closer to the point of transference into something useful. And I think that's a good example of quantum cryptography inspiring extremely useful work—detailed work about improving security in quantum crypto systems—for real systems. So I think that as long as the experimental work in the field is moving forward to increasing numbers of qubits, there are going to be important theoretical problems to address, and we have plenty of theorists to work on them, and I think they will.

Charlie Doering (Chair): Yup.

Julio Gea-Banacloche (Con Team): I think that the concern is more with the funding agencies losing interest and... clearly, if this machine is 20 or 30 years in the future, I think that it doesn't take a prophet to predict, that they are not going to continue... the current level of funding for the next 20 or 30 years. Moreover, as I said, without any more algorithms there is the possibility that they will lose interest much earlier because all we need is basically an easy, convenient alternative to RSA encryption and you're in business, and there are already encryption—public key encryption—algorithms that nobody knows whether they are equivalent to factoring or not. Which means that even if you had the big quantum computer today, you would not know how to use it to crack those forms of encryption. So, it's really only a matter of time. So...

Charlie Doering (Chair): Howard? Comment?

Howard Brandt (Pro Team): [Regarding] the business about, you know, if it's going to take thirty years to build a quantum computer, that the government agencies aren't going to wait that long and continue to fund it. I don't believe that, because the imperative is still considerable. Witness thermonuclear fusion. Sakharov came up with the invention of the Tokomak. Now, that was a long, long time ago. That has continued to be funded. Also, newly, and nicely, inertial confinement fusion. And you know, I remember in the '70s I was asked to predict when we would have controlled thermonuclear fusion, and I said, "At the earliest 2030", and certainly after all the major participants are dead. And that is true of large-scale quantum computers too. The government will still have this imperative and it will be supported at some level, I believe.

Charlie Doering (Chair): Now let Julio talk.

Julio Gea-Banacloche (Con Team): Now I think there's a big difference between physical controlled fusion and quantum computing, as we know it now. I mean, once you get a fusion reactor going, then you can do a lot of things with the energy. Once you get these huge quantum computers going you can do exactly one thing ...

Audience laughter

Julio Gea-Banacloche (Con Team): No, sorry, apologies to Daniel, actually-one thing of strategic importance, OK? Which is to break the RSA code. How much longer is RSA encryption going to be of strategic importance? My guess is not 30 years, OK. Now, I completely agree with Daniel, this is of extremely high [scientific value] and I hope the NSF will continue to support the development of quantum computers at the medium-sized scale for all the universities that will want to have a quantum computer.

Charlie Doering (Chair): Alex?

Alex Hamilton (Pro Team): Well, I think my point has been said, actually. It's not just the one algorithm you want to include—there's a whole raft of fundamental science reasons, there's a whole raft of computational reasons that you [want a quantum computer for] as well for simulating physical systems. I mean, it's crazy that we have a transistor with 50 electrons in it and we still can't calculate, properly, what its properties should be from a fully quantum mechanical viewpoint. So that would be kind of nice, and ... the second thing is about, going back to RSA: if everyone switched to quantum hard codes there'd be no need for this computer, but wouldn't you love to know what Clinton really said about Lewinsky? I mean, you could go back and ...

Audience laughter

Charlie Doering (Chair): OK, OK, let's keep this clean!

Audience laughter

Charlie Doering (Chair): Let's move on here. Anybody have a comment or complaint, or a ... you know. Gottfried.

Gottfried Mayer-Kress, Penn State University, USA (Audience member): Yes, just a question or comment on the statement about the brain and it was so sweeping a rejection of any kind of possibility of quantum computation in the brain, and you gave the impression [that] everything was known how the brain works and, you know, there's really no open questions—so do you really know how we make a decision? How you make a choice between different alternatives and the speed at which this is

happening? So, it seems to me like ... just from the problem solving point of view: if you think about it, how fast a human brain, can select from a huge database of visual or sensory inputs and make a very rapid decision. I mean, that sounds very much like a quantum computation to me, and if you go down to the biochemical processes of how ion-channels open and close I think, you know, that quantum processes certainly play a role. So, I don't understand why you just completely reject the possibility of quantum computation occurring.

Sergey Bezrukov (Con Team): I agree with you that we don't understand how our brain operates in... concerning what you just said. My only point is that according to the current knowledge of the "elemental base" of the brain, responsible for logical operations, there is no place for quantum computing.

Charlie Doering (Chair): Carlton?

Carl Caves (Pro Team): I used to have the conventional view—and I still have it—that the probability is about [point] 50 nines in a row that there aren't any coherent quantum processes going on in the brain that are of any value. You can do simple calculations that show that decoherence removes any coherent quantum information processes in the brain. But we now know that in complex quantum systems there are these decoherence free subspaces just sitting around that are free of certain kinds of decoherence and it's not out of the question that maybe something's going on there and, you know, evolution by natural selection is awfully good at figuring out how to do stuff. I'll give it a probability of epsilon, where epsilon is smaller than the error threshold, but I wouldn't rule it out.

Charlie Doering (Chair): Interesting point. Anybody else? Yeah, let me see your hand.

Howard Wiseman, Griffith University, Australia (Audience member): I'll keep supporting the Con side, just to be fair. Daniel, you keep bringing up this simulating quantum systems thing, but how big—given that classical computers will probably keep going faster for the next, say, 20 years—how big a quantum computer do you actually need to make it useful? To make it definitely useful? And, you know, is there anything that can bridge the gap between, you know, the next 5 to 10 years, and that sort of level?

Daniel Lidar (Pro Team): Well, there are several papers, which have looked at this question in detail, and not taking into account the error correction overhead, it turns out that at about 100 qubits you can solve

problems in mesoscopic quantum physics, which are not possible on any reasonable classical computer. So, 100 qubits is my answer but you'd have to multiply that probably by a factor of like at least 15 if you want to take error correction into account.

Howard Wiseman (Audience member): Is there something that can take us from where we will be in the foreseeable future to that level of some 1500 qubits?

Charlie Doering (Chair): Did you hear the question?

Howard Wiseman (Audience member): What is going to motivate us to go from the level of having 10 or 100 qubits—where we can do interesting things from the point of communications and distillation and stuff like that—to that level, which is considerably harder?

Dan Lidar (Pro Team): Well, one problem, for example, is understanding superconductivity in metallic grains. So, if that is a problem that is of considerable interest, which I believe it probably is, I can see that motivating going to that number of qubits that's required, and there are plenty of other problems in this class of highly-correlated-electron systems that are mesoscopic, for which you would need a quantum computer on the order of 100-1000 qubits.

Charlie Doering (Chair): Another question here.

Carl Caves (Pro Team): Can I say one more thing about that?

Charlie Doering (Chair): Certainly.

Carl Caves (Pro Team): Let me say something pretty quickly. The systems that are proposed for quantum computing and quantum information processing are the cleanest we know of. The best records for quantum coherence are the atomic physics systems, now using trapped ions and trapped neutrals. Those are pristine systems for which decoherence is very low, but it's not so clear how you scale those. The condensed systems are easier to see how to scale because they rely on more conventional technology, but their record for decoherence isn't as good. All the superconducting qubits are getting there now in terms of decoherence, but we still have to see how they do when they're coupled together. We don't yet know which one of these systems, if any, is going to be one that ultimately works out. We don't know what the architecture is going to look like for a 1500 qubit quantum computer.

Audience member (Unknown): Yes, I would like to ask Carlton a question. You seem to be hopping around a bit together with other members in

the Pro team, appeasing the two editors of PRA and PLA. One [statement] is that in principle you can do [quantum computing] operations with error correction... Simply, it sounds like it's just an engineering problem; get enough engineers together and enough money together and [quantum error correction] will work. And on the other hand the suggestion is that you actually need some more basic research—you may find that, you know, you run into something like a mental limitation. So like, the question is: Is it just an engineering problem or not?

Carl Caves (Pro Team): You might have exposed a rift in the Pro team, I don't know. We're sitting awfully close together up here, so if you can see any rift between us ... but I think there's a lot of basic research to be done. It's not an engineering problem yet. I think a fairer comparison, when I was asked about the space program, would have been the Manhattan Project. If you put in an amount of money comparable to that in today's dollars, would we get a quantum computer a lot faster? Which would be several billion dollars a year, I reckon. Oh, I don't think so. I think we wouldn't know what to do with it, because it's not yet an engineering problem. There's a lot of basic science yet to be done before we know which physical system is the best one.

Charlie Doering (Chair): So, we have something from the Pro side?

Carl Caves (Pro Team): Yeah.

Audience laughter

Dan Lidar (Pro Team): Alright, I think you are probably referring to—or extrapolating from a comment that I made—that, well, we have error correction, therefore problem solved. No, that's not the case. The fact that we have an existence proof or a viability proof, if you wish, that quantum computers are possible, does not in any sense imply that there's no basic research left to be done. I mean, it's like—what's a good analog?—maybe: an existence proof is like saying that we have an axiomatic system for doing mathematics and now, that's it, we're done. Of course, a lot of theorems remain to be discovered. There's a lot of basic research to be done on how we can actually construct a device and there'll also be lots of spin-offs in terms of just interesting fundamental questions that are not necessarily related to how you construct a device.

Howard Brandt (Pro Team): I agree with Carl. I think Derek's comment was very appropriate and it sort of addresses this question of the fundamental nature of current research. [Regarding] Derek's comment, well you know, the hybrid Kane-type quantum computer in silicon, and

other solid-state approaches that we include here, like quantum dots, well, they're scalable. What does that mean in practice? It means that there's a giga-dollar industry in semiconductors and solid-state, and frankly, you know, I think that the funding agencies sort of translate that into scalability. I mean, after all, you know, the classical widgets scaled, so we make one quantum widget and put the widgets together, but as Derek sensibly questioned, you know, right now—be it Josephson junctions, quantum dots or a Kane-type of quantum computer—the study of decoherence is at a very primitive level. The study of how to produce controlled entanglement is at a very primitive level. Gates and solid-state approaches are at a very, very primitive level. People do not know how to do this. They're doing research to hopefully, you know, be able to do this, but it's a big question mark. It's a basic research issue. And so Derek, you know, is justified in questioning the scalability, of the solid-state semiconductor approaches anyway. So, it's a basic research issue. The answers are not there. If they were, we'd hear about it in program reviews. I mean, I've heard tens and tens of program reviews, and nobody is coming close yet, but that doesn't mean they won't. Basic research is needed in fact.

Charlie Doering (Chair): Any other comments or questions from the audience? Derek wants to rebuff.

Derek Abbott, The University of Adelaide, Australia (Audience member): [No, I don't, but] I just thought I'd give the Con team some more help because they need it.

Audience laughter

Julio Gea-Banacloche (Con Team): I wish you would stop saying that.

Audience laughter

Derek Abbott (Audience member): OK, so I think we've established that the real question is: scaling. To make it practical we need a scaleable quantum computer. To make it scaleable you're talking about chip technology for a number of reasons because it's the only way we know how to make scaleable things—and we've got millions of dollars of backing behind that. Now, as soon as you put qubits on a chip and line them up in a nice little pretty order, I find it very hard to believe that you can make a useful quantum computer with that, because on top of those qubits you're going to need classical control registers to control the gates and you are going to need read-out circuitry. So there's going to a number of post-processing steps on top of that. Now, I know some clever guys have put phosphorous ions [on chip] nicely in a neat little row and it works. But once you do all

that post-processing, are they [the qubits] really going to stay still? So, this is my question to the Pro team.

Charlie Doering (Chair): Yes, and it's a good question. Alex?

Alex Hamilton (Pro Team): OK, so for the specific case of phosphorous and silicon it actually looks like they do stay put, during the post-processing—but that's just a specific answer. But the more general answer is, you do need control chip circuitry, absolutely, and so there's no reason that that has to be on the same chip. There's no reason that we can't build a [separate] complete high-frequency silicon germanium control electronics [chip] and match it up.

Derek Abbott (Audience member): You have to use the same chip because of noise.

Alex Hamilton (Pro Team): No, no, it doesn't have to be on the same chip, Derek, because they [only] have to be physically close to each other. They don't have to be on the same chip.

Charlie Doering (Chair): OK. He says no and you say yes.

Audience laughter

Julio Gea-Banacloche (Con Team): Yes, I wanted to say something about that too, regarding the same sort of thing: the control systems. I actually gave a talk yesterday[9] on this subject and there are constraints there: how large the control systems have to be in some sense. So in some sense, some of these amusing quotes referring to the famous quotes recalled by Charlie Doering are a little misleading because ...

Charlie Doering (Chair): We don't know.

Julio Gea-Banacloche (Con Team): ...they suggest that, you know, quantum computing might follow a path similar to classical computers where you start with something huge, like vacuum tubes, and then slowly and over time, sometimes fast, you start making things smaller and more efficient and so forth. And the indications are that it's not going to be like that. I mean, when we get the quantum computer we're stuck at the vacuum tube level. The control systems have to be large because they have to be classical, so there is going to be no pocket quantum computer that somebody will be able to carry around, and there are minimum energy requirements and so another question to ask, you know, is: how are you going to deal with the heating and so on? How are you going to extract it?

[9]Transcript editor's note: J. Gea-Banacloche (2003), Energy requirements for quantum computation, *Proc. SPIE Noise and Information in Nanoelectronics, Sensors, and Standards,* **5115**, pp. 154–166.

Charlie Doering (Chair): OK. Laszlo's going to make one more comment and then we're going to move into the next stage, the final stage of this panel.

Laszlo Kish (Con Team): [Regarding] the comment of Julio's: the calculations I showed yesterday—at the same temperature, same speed and same number of elements—the quantum computer dissipates more energy when processing the same information. So, again, the dissipation and noise is the key [as to why classical computers are better].

Charlie Doering (Chair): What I would like to...you're going to talk? I think we need to move on ...

Carl Caves (Pro Team): Well, we're at about the last stage ...

Charlie Doering (Chair): OK.

Carl Caves (Pro Team): We might have to run the gauntlet to get out of here.

Charlie Doering (Chair): OK. That's right. Let me organize the last stage as follows. Let me have each one talking. Think about a two-sentence summary of your view, a two-sentence summary of your view, and we'll run down the road here and then we'll take a vote on how the audience feels what the panel says. A forum—OK? Carl.

Carl Caves (Pro Team): Well, my consistent view has been that it would be extremely difficult to build a general-purpose quantum computer though it might be somewhat easier to build quantum simulators, but that's not the point of why information science—quantum information science—is a discipline worth pursuing.

Charlie Doering (Chair): That's one sentence. OK, good.

Audience laughter

Charlie Doering (Chair): Daniel.

Dan Lidar (Pro Team): I agree.

Howard Brandt (Pro Team): Well, again, no one has demonstrated that a large-scale quantum computer is, you know, physically impossible, and certainly small scale quantum information processors are possible and have already been demonstrated. It's a worthwhile enterprise and will continue.

Alex Hamilton (Pro Team): We're scientists. Our job is to try and understand nature and if we want to—and we're humans—and we try to control nature. And we've been given this amazing curiosity and we want to do things. Why does one climb Mount Everest? Because it's there.

The Con Team all purse their lips in a thoughtful pose, gently nodding, apparently conceding this point.

If we build this thing [a quantum computer], let's have a go or let's prove that it's simply not physically possible.

Charlie Doering (Chair): Very good. Julio?

Julio Gea-Banacloche (Con Team): I really would like to say that I am also very impressed ...

Charlie Doering (Chair): Julio, also let me just say, that the Con team does not have the volume of the Pro team...

Julio Gea-Banacloche (Con Team): OK.

Charlie Doering (Chair): ...we would like to hear how the argument's going. Hold the mike closer!

Julio Gea-Banacloche (Con Team): Well, I would really like to say that I find it incredibly amazing and very, very impressive. [A lot of] good science has come out of quantum information, for the past seven years. And if quantum computing is responsible for this, then it's a good thing. The dream, at least, [is] of a quantum computer.

Sergey Bezrukov (Con Team): While [many] functional processes in the brain are not understood, the "elemental base" [of the brain] is very well studied. Also, main interactions between the elements are already well understood. So, as I said, there is no any [*sic*] place for quantum computing in the human brain. But, the concepts, which are being developed by the scientists working in this field, will find their way into the brain studies and will be very useful there.

Charlie Doering (Chair): Yes.

Laszlo Kish (Con Team): Quantum compared to classical. Quantum means more noise, statistical in nature, more dissipation, and higher price.

Audience laughter

Charlie Doering (Chair): OK, that was enough. Now we've got first ... for the record ... I guess the question is a "pro-con/dream-reality" thing. I would like to take a show of hands for ... first, question number one. How many people think that quantum computing is really a dream and it's just going to fall by the wayside and our attention will go some place else, and ... can I have a show of hands?

A few hands show

Charlie Doering (Chair): OK, how many people think that it's possible that quantum computers as—people envision it as a tool—is simply not going to happen? The way we're visioning it now?

A few hands show, some people holding up two hands

Charlie Doering (Chair): You are not allowed to hold up two hands. But you can attempt to have your hands in a superposition of "for" and "against."

Audience laughter

Charlie Doering (Chair): That's good, that's good. I'm impressed! Now, now ... but that does not mean that the complement to that set will be reality, OK. So, how many people think that there's a possibility that it may be a useful tool, based on the ideas that we're now tossing around in the year 2003? That it's going to emerge—and some of us in this room are [still] alive to realise it? Anybody agree with that?

A unanimous majority of hands show

Charlie Doering (Chair): OK. I think the conclusion is clear. I would just like to reinforce the whole idea of predicting the future in computer science [is dangerous]:

"640 K ought to be enough for anybody."
—Bill Gates, 1981.

Let's thank everyone on the panel here.

Audience applause

End of transcript.

Acknowledgements

The assistance of Phil Thomas, as the audio transcript typist and amanuensis, and Gottfried Mayer-Kress, for the mp3 recording, are gratefully acknowledged. The mp3 recording can be downloaded from the *Complexity Digest* at: `http://www.comdig2.de/Conf/SPIE2003/`. Thanks are due to the many people who proof read this transcript—especially Howard Wiseman whose remarkable aural abilities miraculously decoded otherwise inaudible parts of the recording; any remaining errors are of course mine (Derek Abbott).

About the Panelists

Charles R. Doering is professor of mathematics at the University of Michigan, Ann Arbor. He received his BS from Antioch College, 1977; his MS from the University of Cincinnati, 1978; and his PhD from The University of Texas at Austin under Cécile DeWitt-Morette, 1985, in the area of applying stochastic differential equations to statistical mechanics and field theory. In 1986–87, he was a Director's Postdoctoral Fellow 1986–87, Center for Nonlinear Studies, Los Alamos National Laboratory; in 1987–96, he rose to Professor of Physics, 1987–96, Clarkson University; in 1994–96, he was Deputy Director of Los Alamos' Center for Nonlinear Studies. Doering has received a number of honours including the NSF Presidential Young Investigator, 1989–94; Fellow of the American Physical Society, 2000; and the Humboldt Research Award, 2003. His research is generally focused on the analysis stochastic dynamical systems arising in biology, chemistry and physics, to systems of nonlinear partial differential equations. Recently he has been focusing on fundamental questions in fluid dynamics as part of the $1M Clay Institute millennium challenge concerning the regularity of solutions to the equations of fluid dynamics. With J. D. Gibbon, he co-authored the book *Applied Analysis of the Navier-Stokes Equations*, published by Cambridge University Press. Doering is an editor of *Physics Letters A*.

Carlton M. Caves holds the position of Distinguished Professor in physics at the University of New Mexico. He received his BA in physics and mathematics from Rice University, 1972; and his PhD from Caltech under Kip Thorne, 1979, in the area of gravitation. In 1979–81, he was a Research Fellow, Caltech; in 1982-87, he was a Senior Research Fellow, Caltech; in 1987–92, he was an associate professor at the University of Southern California; and in 1992–2006, he was Professor of Physics and Astronomy, University of New Mexico. He has received a number of honours including Fellow of the American Physical Society; National Science Foundation (NSF) Predoctoral Fellow, 1972–75; Richard P. Feynman Fellow, Caltech, 1976–77; first Öcsi Bácsi Fellow, Caltech, 1976–77; and the Einstein Prize for Laser Science, Society for Optical and Quantum Electronics, 1990. His research focus is in the area of physics of information; information, entropy, and complexity; quantum information theory; quantum chaos quantum optics; theory of nonclassical light; theory of quantum noise; and the quantum theory of measurement.

Daniel Lidar is the Director and co-founding member of the USC Center for Quantum Information Science & Technology (CQIST). He received his BS from the Hebrew University of Jerusalem, 1989; and obtained his PhD under Robert Benny Gerber and Ofer Biham, 1997, in the area of disordered surfaces also from the Hebrew University of Jerusalem. In 1997-2000, he was a postdoc at UC Berkeley; in 2000–05, he was an assistant and then later an associate professor of Chemistry at the University of Toronto. He moved to Southern California in 2005 as an associate professor of Chemistry and Electrical Engineering, with a cross-appointment in Physics. Lidar's research interests lie primarily in the theory and control of open quantum systems, with a special emphasis on quantum information processing. His past interests include scattering theory and disordered systems.

Howard E. Brandt was born in Emerado, North Dakota, and is presently with the US Army Research Laboratory in Maryland. He received his BS in physics from MIT as a National Sloan Scholar, 1962; he received his MS in physics from the University of Washington, 1963; and obtained his PhD at the University of Washington under Marshall Baker, 1970, calculating the divergent part of the charge renormalization constant in quantum electrodynamics to sixth order in perturbation theory in Feynman gauge to verify the gauge invariance of the calculation. In 1970-76, he was a postdoc in general relativity at the University of Maryland. In 1976, he joined the Army Research Laboratory in 1976 (then the Harry Diamond Laboratory). From 1986 to 1995, he technically directed three major programs for the Office of Innovative Science and Technology of the Strategic Defense Initiative Organization, involving nation-wide research on high-power microwave source development, sensors for interactive discrimination, and electromagnetic missiles and directed energy concepts. Brandt has received a number of honours including the Siple Medal, Hinman Award, and Ulrich Award. He is an elected Fellow of the US Army Research Laboratory. He received a major achievement award from the US Army Research Laboratory for his publications and research on quantum information processing. He also received the ARL 2004 Science Award. He is inventor of the Turbutron, a high power millimeter-wave source (US Patent 4,553,068), and co-inventor of a quantum key receiver based on a positive operator valued measure (US Patent 5,999,285). His broad research interests include quantum field theory, quantum computation, quantum cryptography, quantum optics, general relativity, and non-neutral plasma physics. Most recently, his research has concentrated on quantum information processing includ-

ing quantum computing and quantum cryptography. Brandt's extramural interests include philosophy, theology, art, and classical music.

Alex Hamilton is an Associate Professor in the School of Physics at the University of New South Wales (UNSW), and manager of the quantum measurement program in the ARC Centre of Excellence for Quantum Computer Technology. He obtained his BSc in Physics from the University of London in 1988, and a PhD, under Michael Pepper and Michael Kelly, from the University of Cambridge in 1993. He was awarded a highly competitive EPSRC postdoctoral fellowship to continue his work at the Cavendish Laboratory, which led to new understandings of electrical conduction in highly correlated low-dimensional quantum systems. Alex moved to UNSW in 1999, where his team is developing techniques for controlling and reading out quantum information in silicon quantum computer devices. His expertise lies in the field of Experimental Condensed Matter Physics, having worked on semiconductor nanofabrication and the study of quantum effects in nanometer scale electronic devices at ultra-low temperatures. He has published over 50 research papers, and is Australasian editor of the international journal *Solid State Communications*.

David K. Ferry is the Regents' Professor of Electrical Engineering at Arizona State University (ASU). He received his BSEE, 1962, and MSEE, 1963, both from Texas Technical College. Ferry obtained his PhD under Arwin A. Dougal, 1996, from the University of Texas at Austin. Following a postdoctoral year in Vienna (1966–67) under Karl-Heinz Seeger, he spent time at Texas Tech University (1967–73), the Office of Naval Research (1973–77), and Colorado State University (1977–83), and the joined ASU in 1983. He has received a number of honours including the IEEE Cledo Brunetti Award, 1999; IEEE (Phoenix) Engineer of Year, 1990; Fellow of the IEEE Fellow, 1987; and Fellow of the American Physical Society, 1974. His research involves the physics and simulation of semiconductor devices and quantum effects and transport in mesoscopic device structures. His books include *Quantum Mechanics* (Adam Hilger, Bristol, 1995), 2nd Edition (Inst. Physics Publ., London, 2000); *Quantum Transport in Ultrasmall Devices* (Plenum, New York, 1995), Edited with Hal Grubin, Carlo Jacoboni, and Antti-Pekka Jauho; *Transport in Nanostructures* (Cambridge University Press, Cambridge, 1997), with Steve Goodnick; *Semiconductor Transport* (Taylor and Francis, London, 2001); and *Electronic Materials and Devices* (Academic Press, San Diego, 2001), with Jon Bird.

Julio Gea-Banacloche was born in 1957, Seville, Spain and is presently professor of physics at the University of Arkansas. He received his BS from Universidad Autonoma de Madrid, 1979; and obtained his PhD under Marlan O. Scully, 1985, on quantum theory of the free-electron laser, from the University of New Mexico. In 1985–87, he served as a Research Associate, Max Planck Institute for Quantum Optics; in 1988–90 he was a Staff Scientist, Instituto de Optica, Madrid, Spain; and in 1990 he joined the Universisty of Arkansas initially as an assistant professor. He is an Associate editor of *Physical Review A* and Fellow of the American Physical Society. He has carried out theoretical work in laser physics, quantum optics, and quantum information. His main contribution to the field of quantum information has been the observation that the quantum mechanical nature of the fields used to manipulate the quantum information carriers themselves—often called "qubits", or "quantum bits"—might lead to unpredictable errors in the performance of the quantum logical operations. The lower bound on the size of these errors can be made smaller by increasing the energy of the control system. This has led Banacloche to predict a minimum energy requirement for quantum computation, which has given rise to some controversy.

Sergey Bezrukov is a Section Chief in the Laboratory of Physical and Structural Biology, National Institutes of Health (NIH), Bethesda, Maryland. He received his MS in Electronics and Theoretical Physics from St. Petersburg Polytechnic University, 1973; and he obtained his PhD under Giliary Moiseevich Drabkin in Physics and Mathematics from Moscow State University, Russia, 1981. In 1981–87, he was a Research Scientist, St. Petersburg Nuclear Physics Institute, Laboratory of Condensed Matter Physics; in 1987–90 a Senior Research Scientist, St. Petersburg Nuclear Physics Institute, Laboratory of Condensed Matter Physics; in 1990–92 he was a Visiting Research Associate, University of Maryland and Special Volunteer, National Institutes of Health, LBM, NIDDK; in 1992–98 he was Visiting Scientist, National Institutes of Health, LSB, DCRT and LPSB, NICHD; in 1998-02 he was an Investigator, Head of Unit, National Institutes of Health, LPSB, NICHD; and he took up his present position in 2002. Bezrukov was elected Member of Executive Council of the Division of Biological Physics of the American Physical Society in 2002. One of his key research interests is in the physics of ion channels.

Laszlo B. Kish is a professor of Electrical Engineering at Texas A&M University. He received his MS in physics from Attila József University

(JATE), Hungary, 1980; and a PhD in Solid-State Physics, at JATE in 1984. He had no official PhD advisor, though his mentors were Laszlo Vize and Miklos Torok. He received a Docent in Solid State Physics (habilitation) from Uppsala University, Sweden in 1994. He received a Doctor of Science (Physics), from the Hungarian Academy of Science in 2001. He won the 2001 Benzelius Prize of the Royal Society of Science of Sweden for his activities in chemical sensing. He is the foundation Editor-in-Chief of *Fluctuation and Noise Letters* and serves on the Editorial Board of the *Journal of Nanoscience and Nanotechnology*. He holds 8 patents and over 200 international publications. He coauthored the innovative HTML document available for download from Amazon, *The Dancer and the Piper: Resolving Problems with Government Research Contracting*. His research interests lie in the physics of noise and fluctuations. Professor Kish is co-founder of the international conference series *Fluctuations and Noise* (with D. Abbott).

Chapter 16

Plenary Debate: Quantum Effects in Biology: Trivial or Not?

6:00pm, Friday, May 28th, 2004, Costa Meloneras Hotel, Canary Islands, Spain *Second International Symposium on Fluctuations and Noise (FaN'04).*

The Panel - Dramatis Personae

Chair/Moderator: **Julio Gea-Banacloche**, Univ. of Arkansas (USA); Editor of *Physical Review A*.

No Team (*assertion "not trivial"*):
Paul C. W. Davies, Macquarie University (Australia);
Stuart Hameroff, Univ. of Arizona (USA);
Anton Zeilinger, Univ. of Vienna (Austria);
Derek Abbott, Univ. of Adelaide (Australia); Editor of *Fluctuation Noise Lett.* and *Smart Structures and Materials.*

Yes Team (*assertion "trivial"*):
Jens Eisert, Imperial College (UK) and Potsdam University (Germany);
Howard Wiseman, Griffith University (Australia);
Sergey Bezrukov, National Institutes of Health (USA); Editor of *Fluctuation Noise Lett.*;
Hans Frauenfelder, Los Alamos National Laboratories (USA).

Transcript Editor:
Derek Abbott, The University of Adelaide (Australia);

Disclaimer: The views expressed by all the participants were for the purpose of lively debate and do not necessarily express their actual views.

Transcript conventions: Square brackets [...] containing a short phrase indicate that these words were not actually spoken, but were editorial insertions for clarity. Square brackets [...] containing a long section indicate that the recording was unclear and the speaker has tried to faithfully reconstruct what was actually said. [*sic*] indicates the transcript has been faithful to what was spoken, even though grammatically incorrect. Where acoustic emphasis was deemed to occur in the recording, the transcript reflects this with italics.

The Debate

Julio Gea-Banacloche (Chair): [I am pleased to introduce] this special debate, *Quantum effects in biology: trivial or not?* I am Julio Gea-Banacloche, originally from here: a native of Spain. As Laszlo Kish pointed out yesterday at the banquet that there was an intense pre-debate debate concerning what the debate should be about—and such topics as whether the title of the debate should phrased as a "yes" or "no" question or not. That's something some people were very adamant about and in some sense it is kind of a miracle that we are having this debate at all. I am really glad about it. So the question is: "Quantum effects in biology: trivial or not?" and on the Yes Team we have Professor Paul Davies from Macquarie University...

Stuart Hameroff (No Team): [Interrupts] We're the non-trivial team... we're the No Team!

Audience laughter

Julio Gea-Banacloche (Chair): See: sorry, I got it wrong already. With apologies to the teams, so, actually the No Team are the good guys, eh...

Audience laughter

Julio Gea-Banacloche (Chair): We must not get this bit confused. The No Team claim that quantum effects in biology are *not* trivial and we have Professor Paul Davies from Macquarie University, and Professor Stuart Hameroff from the University of Arizona, and Professor Anton Zeilinger, who is currently in a superposition of states and thus invisible[1]...

[1]Transcript editor's note: At the beginning of the debate Zeilinger's chair was vacant—but he did turn up later.

Audience laughter

Julio Gea-Banacloche (Chair): And masquerading as Jack Tuszynski is Professor Derek Abbott,[2] our organizer from The University of Adelaide. On the Yes Team we have Professor Jens Eisert, from the University of Potsdam; Professor Howard Wiseman, from Griffith University; Dr Sergey Bezrukov, from the National Institutes of Health; and Dr Hans Frauenfelder from Los Alamos National Labs. There are a couple of things about the way I see this today, and of course the audience—and they represent themselves—are welcome to think any way they want to. But way, way back in the early, early stages of the pre-debate debate, somebody had suggested the title of *Quantum mechanical effects on the mind: important or not?* I actually thought that was a very exciting question, not having any idea about what the possible answers might have been and what anybody might have to say for or against it. So at the time, when I was asked whether I would chair the debate, I thought that I would ask the panelists about their quantum mechanical states of mind and, if so, what drugs we need to take in order to experience them...

Audience laughter

Julio Gea-Banacloche (Chair): I would still like somebody to address that, except for the drugs part—which of course is just a joke. The other thing—that I am probably responsible for—is the final wording of the question: putting the word "trivial" in there. What I am personally expecting to get from this [is for] the No Team to try to provide some surprising facts—things that we would not have expected. In a sense, of course, we believe the entire world is described by quantum mechanics, so you can always say quantum mechanics is responsible for this or that. So what? Of course it would be responsible, because ultimately everything can be described by quantum mechanics. What I would like to see [are things that make me say] "I would not have expected that. Wow, this is unexpected. That is a surprise." That's the sort of thing that I would like to see come out of this. That is the sort of thing that would lead me to vote, if I were to vote, for the No Team as opposed to the Yes Team, and this is perhaps a suggestion to the audience that maybe you should look for the wow-factor at the end of the debate when I will ask for an informal vote on whose side was the most persuasive. If you have been wowed by something that the No Team said that the Yes Team did not manage to make sound totally mundane, and so forth, then [consider this in your voting decision].

[2]Transcript editor's note: Jack Tuszynski was invited to be on the panel but unfortunately called in sick, so Derek Abbott substituted him at the last minute.

So, the format that we are going to adopt is the following. First, we will start with the No Team presenting their case, each panelist will speak in turn only for three minutes, and then we move to the Yes Team, again three minutes each. Then [in order to] reply we return again to the same order—limited to two minutes for panelists, and then at the end of that I would like to go one more round to give each one of the panelists a chance to summarize his position in two sentences. After that we will take questions from the audience for the panelists and then I will ask for an informal vote. I hope the panelists summarize their points from their talks yesterday. I apologize to the panelists for having missed the presentations of Wednesday, because I haven't mastered the quantum mechanical art of being in two places at the same time. Unfortunately, I just couldn't. I hope they will be kind enough to repeat the things that they might have said in their talks that might be relevant to [today's] subject as I would very much like to learn myself. So without further ado, let's start with the No Team: Professor Davies.

Paul Davies (No Team): Thank you. Well I'm sorry to disappoint you but I was particularly *not* going to repeat the content of my lecture on Wednesday morning, where I set out what I felt were the most persuasive arguments on the grounds of science for the non-trivial effects in biology. I thought I would restrict my remarks, this evening, to addressing a more philosophical point as befits a professor of natural philosophy. The problem of the origin of life remains one of the great unsolved problems of science, and that in itself is a highly non-trivial problem. The simplest living thing is already so immensely complex—[when you consider] the first living thing that arose just from the random shuffling of building blocks of molecules—that it is quite clear that the odds against that happening are so stupendous that it would have happened only once in the observable universe. It will in fact be a near miracle. The alternative is that life is a natural and more or less automatic part of the outworkings of the laws of nature; in which case there must be some sort of life-principle, or what the Christian de Duve calls a "cosmic imperative." And if there is such a principle then this principle must exist within physical theory. It must be a part of physics and, though we haven't deduced this principle yet, we imagine that it is something that is incorporated within physics; and then the question arises: Does that life principle come from quantum physics or is it part of classical physics? I can give three reasons at least why I think it will be part of quantum physics. The first is that quantum mechanics is, of course, a fundamental theory;

the idea that you can choose the world as classical or quantum mechanical is nonsense. The world *is* quantum mechanical. We live in a quantum mechanical universe, so quantum mechanics is the *default* position. If we are looking for a new principle in physics—by default it belongs in quantum mechanics, or else quantum mechanics is *not* the correct description of the world.

The second point is that life, of course, proceeds from the quantum world. Life is ultimately molecular and it must have begun in the molecular domain. And so life came out of the quantum domain, and to insist that the quantum domain somehow had to stop or that one had to move beyond it before life came to exist, seems to me to be completely unreasonable. The third point of view—I'll mention it very briefly, famously introduced by Eugene Wigner—is that the connection between life and quantum mechanics is there all along in the role of the observer. Of course, we are all persuaded that wave functions don't collapse [due to conscious agents], [rather] they decohere by the environment—but, as Anton Zeilinger said so clearly in his lecture,[3] we're still left with the issue that quantum mechanics is incomplete inasmuch as it gives a probabilistic description of the world and the actual outcome of any given observation clearly depends on the observer. So, I think that the other team had better state, first of all, whether they think life is a miracle—and if it's not a miracle, why is it that the life-principle, which must be there, is disconnected from fundamental quantum physics? What sort of principle emerges only when wave functions decohere? That's what I'd like them to answer. Thank you.

Gea-Banacloche (Chair): I will try to stand up and signal that it is 15 seconds before the end.

Stuart Hameroff (No Team): Thank you. Real-time activities of living systems are all performed by conformational fluctuations of proteins, changing shape on the order of nanoseconds. How do proteins control their shape? Within proteins high energy charge interactions tend to cancel out. So functional dynamics are governed by collective actions of numerous quantum mechanical van der Waals-London forces, influenced by external factors. London forces are instantaneous dipole couplings of electron clouds in non-polar amino-acids, which form non-polar hydrophobic pockets within proteins. These tiny pockets—where quantum forces rule—are essentially the "brain" of each protein. Thus proteins—at least certain proteins—are

[3]Transcript editor's note: Jennewein, T. and Zeilinger, A. (2004), Quantum noise and quantum comunication, *Proc. SPIE Fluctuations and Noise in Photonics and Quantum Optics II*, **5468**, pp. 1–9.

quantum switches, which should exist for some time in a superposition of conformational states. Protein qubits: why would nature need qubits? Quantum computing is the answer, I believe. Geometric lattice assemblies of protein qubits, for example, microtubules, are well-suited to act as quantum computers. The evolution of organisms utilizing quantum computation would have enormous advantages.

Is there evidence of quantum computation in biology? If any of us needed surgery, say our appendix ruptured, we would be anaesthetized, rendered non-conscious by breathing a gas mixture containing roughly one per cent of an anaesthetic gas molecule, which is inert. These molecules float from our lungs into our blood and brains selectively and act at the same hydrophobic pockets, which govern the dynamics of certain proteins in our brain. They form no chemical bonds or ionic interactions, acting merely by the same quantum mechanical van der Waals-London forces, occurring naturally in these proteins, thereby preventing the normally occurring London forces, inhibiting protein quantum switching in the brain and erasing consciousness. [Other brain activities continue.] The surgeon takes his knife and we feel nothing. So consciousness—the most elegant biological process—utilizes quantum processes quite possibly quantum computation. Other functions like immune cell recognition, cell division, etc. may also utilize the unitary oneness of quantum coherence and entanglement.

Ah! The decoherence! Biology is warm and wet—it's very warm. Yes, but bio-systems may utilize laser-like coherent phonon-pumping from a heat-bath of biochemical metabolism. Several months ago a paper in *Science* by Ouyang and Awschalom[4] showed quantum spin transfer between quantum dots connected by benzene rings—the same type of [electron cloud] ring found in hydrophobic pockets. The quantum spin transfer was *more* efficient at higher temperature. Benzene rings are identical to the electron resonance rings of the amino-acids found in hydrophobic pockets in proteins.

Wet—yes, we are mostly water, but cell interiors exist much of the time in a gel state in which all water is ordered, coupled to protein dynamics. Additionally structures like microtubules can use Debye layer screening and topological quantum error correction—that is, utilizing the Aharanov-Bohm effect as suggested for quantum computers by Kitaev. In conclusion, whether quantum processes evolved as an adaptation of biology, or whether biology and consciousness [evolved as] classical adaptations of pre-existing

[4]Transcript editor's note: Ouyang, M. and Awschalom, D.D. (2003). Coherent spin transfer between molecularly bridged quantum dots, *Science*, **301**, pp. 1074–1078.

quantum information, they [may be] like artificial neural networks, [which were copied after] brain systems in the 80s. Quantum information technology can learn a great deal from the study of certain biomolecules.

Julio Gea-Banacloche (Chair): Thank you, and that was a little long, but I don't mind perhaps giving this team a little more time since they are slightly handicapped here...

Audience laughter

Julio Gea-Banacloche (Chair): ...by the absence of one person [Anton Zeilinger]. Thank you for addressing the drugs question too.

Audience laughter

Julio Gea-Banacloche (Chair): Moving on...Derek.

Derek Abbott (No Team): OK, the position I'm going to take in this debate is one of cautious optimism and my question I'm going to put to the Con Team is: Why not explore the relationship between quantum mechanics and biology? Why not have a go? It might be fruitful because, when you think about it, nature has been around for 3.5 billion years and it's produced some marvelous, fascinating things that we don't understand. It's often said that nature is the world's best engineering text book. Anything man sets out to go and do technologically—if he looks at nature first—he will always find examples beforehand carried out by nature [often] even better than we can do. So my challenge to the Con Team is to think of a counterexample and actually tell me something that Man has invented that nature hasn't. So, if this is true, then it's hard to believe that nature hasn't [already] made clever use of quantum effects.

Now, there are two people that have famously made a counter-example to [the standard] argument that I've made, and one is John Maynard Smith, and the other is Charles Bennett. And I'm going to take on these guys one by one now. So, Maynard Smith says that nature has never used the wheel—man has invented the wheel, but nature hasn't. Now of course he's wrong because bacteria have flagella, which have true 360 degree axes of rotation! Maynard Smith visited [my lab at] The University of Adelaide 3-4 years ago and actually admitted this oversight. Also, Charles Bennett famously commented that nature has never made explosives and has never made the radio, but this of course is wrong as well. For example, there is the bombardier beetle that excretes a gas that explodes when it hits the air, to keep off its predators. Also, nature invented the radio as well. The example is fireflies; when they're [about to] mate they modulate an electromagnetic signal—in other words they flash on and off—and the female receives that message. And so that's a radio—it's [albeit] a slightly different wavelength.

Audience laughter

So, anything that you can think of biology has already thought of it. So, if these team members, over there, really believe in quantum computation—and I assume they do because they've actually made quantum computers to a few qubits, so they must believe in it—then nature must have "thought" of it or used it in some way first.

Just finally, to finish off, I want to remind the Con Team that Carlton Caves—their quantum information guru—is on record as saying that because nature is so clever, there possibly is a very small chance that nature, through natural selection, may have found some use for quantum decoherence-free subspaces.[5] And so I would just like to leave it at that point.

Julio Gea-Banacloche (Chair): Thank you, Derek. I just want to remind the No Team that this team is actually a Yes Team, not the Con Team. I realize that is confusing but...

Audience laughter

Anyway, thank you very much to all of you and now we are going to hear what the Yes Team has to say ...

Jens Eisert (Yes Team): Well then, I suppose it's up to me to open the case for the Yes-No Team...

Audience laughter

Jens Eisert (Yes Team): ...well, unless someone expects me to volunteer to fill in for Anton Zeilinger on the other side. Well, let me start with some numbers and science, rather than the philosophical issues raised before. It seems that in the whole debate the "make-or-break" issue is whether coherence can be preserved over the timescales relevant for non-trivial biological processes. And of course, one has to say what one means by non-trivial here. Needless to say, everything in biology is built via quantum mechanics—bonds, hydrogen tunnelling, and so on. But, however, if one regards living entities as information processing devices, one could make a definition of "non-trivial" that this kind of information processing is in some form quantum information processing. There I would doubt whether coherence can be preserved over timescales that would be relevant to have efficient quantum computation—in the sense that it is discussed in [the field of] quantum information. In a nice paper by Tegmark[6]—where

[5]Transcript editor's note: see Chapter 15, p. 384.

[6]Transcript editor's note: See Tegmark, M. (2000). The importance of quantum decoherence in brain processes, *Phys. Rev. E* **61**, pp. 4194–4206.

he looks at the decoherence timescale in a simple model of neurons firing or not—for a neuron to fire or not means that 10^6 sodium atoms are on one side of the brain or the other side of the brain. If one just looks at the neighbouring sodium atoms then the decoherence timescale just from simple high-temperature Brownian motion gives a lower bound of 10^{-20} seconds, which is very, very short and even if one [considers] very low levels for decoherence timescales in microtubules inside the cytoskeleton, then the most conservative bounded scheme is 10^{-30} seconds for a typical decoherence timescale. So, I mean in the light of this, it seems fairly unlikely that something non-trivial as quantum information processing [appears in] biological systems.

Let me remark on Paul Davies' [point] directly. What he would suggest is that [a quantum process in] life is some sort of fast-track to the early emergence of life. There are two points [I can make]. If one thinks of searching—well, if it's a quantum search there must be some sort of oracle that says, "OK, you have life, or you do not have life," so—the point is also that everything must be coherent all the time. One thing is, what must be coherent over all generations so that we have the superpositions of us, our kids and our kids' kids, and so on, and they do not cohere in order to have a proper fast-track to life—and then, my final point: there's the teleological point that, hey, we search for something—but first point—one has to specify is what one looks for when we're searching. So, it doesn't seem entirely clear what the search is for life, because the pay-off is not clear. It is not clear what one in fact is looking for.

Julio Gea-Banacloche (Chair): Thanks, Jens. Howard.

Howard Wiseman (Yes Team): Thanks Julio. Okay, so to begin I would just like to say that the Yes Team in this debate obviously wins by default. The topic is debating "Quantum effects in biology: trivial or not?"—well, clearly the answer is yes, they are trivial or not ...

Audience laughter

Howard Wiseman (Yes Team): ... No, seriously, I think the point is that, yes, you do need to look at the title of this debate carefully and the keyword in my mind is "trivial." I'm glad that people see that people are taking this in a good spirit, and indeed claiming things to be non-trivial that I would agree are non-trivial. There are a number of people that have said that obviously quantum mechanics is behind everything, but Julio said that what he is really looking for is for the No Team to come up with something *surprising*. I guess I think a word or a note of

warning is necessary here: that what physicists like Julio and many of us here are surprised or interested by here are notoriously obscure: the fact that we're all here at a conference called *Fluctuations and Noise* would be very surprising to most members of the public.

Audience laughter

Howard Wiseman (Yes Team): So, I think a better definition, of what is non-trivial, is not what will surprise and interest physicists but, rather, something that would convince a biologist that they need to learn quantum mechanics. A non-trivial quantum effect in biology is something that will make a biologist want to go out and, you know, take a second year quantum mechanics course and learn about Hilbert space and operators, so that they understand what's going on. That's my concept. Now, again, we all seem to be in agreement that an obvious example of this is quantum information processing: that this is somehow the heart of what we're getting at here, because what most people involved in biology are interested in these days is information processing in some form—in control, in genetics, in cells, in thoughts, in consciousness, and all of that is information processing. So something non-trivial would be whether there's quantum information processing in there. So, needless to say, I don't believe there is.

To respond to some of the points of the No Team so far, Paul Davies said he wants the No Team...er...I mean...Yes Team to respond to his challenge of explaining where the life-principle comes from—that is supposed to be a new principle of physics. So, I have two responses to that: (a) I don't believe there is one, and (b) I think that it's outside this debate, so it shouldn't be talked about at all. Firstly, I don't believe it because I think it comes from the fallacy that "I don't understand A, I don't understand B. Therefore, A and B must be the same thing." And secondly, I think it's outside the realms of debate. This debate is about quantum effects, not about effects that result from some new theory—that we don't even understand yet—but which has something to do with quantum mechanics. I think this remark is also directed at Stuart Hameroff's ideas that involve quantum gravity and things that don't even exist yet in theory. I guess I'll leave it at that.

Anton Zeilinger enters the room

Julio Gea-Banacloche (Chair): Right, I'll take a break to welcome Anton Zeilinger. I'll probably let him have some four or five minutes in the next round. But now, to keep going with the flow, the third member of the Yes Team: Sergey.

Sergey Bezrukov (Yes Team): Thank you. I think that everybody is too serious for this late hour, so I decided, instead of sticking to my introduction and answering questions, to tell you an anecdote. This anecdote is a real true story, which happened about twenty five years ago at the NIH—National Institutes of Health—campus in Bethesda. The story is that one young post-doc—actually a candidate who looked for a post-doctoral position and who is now a well-established professor at the University of Maryland and, by the way, came to be a very famous scientist (I would tell you all the names if I did not know that Derek is going to publish all this).

Audience laughter

Sergey Bezrukov (Yes Team): Anyway, [this young man] came to the famous scientist (anyone of you, who ever did anything in rate theory knows his name for sure) [looking for a job]. And he was told "Okay, I like what you're saying, I like you, so I think am offering you the job, but please remember that $\hbar$ in Building 5 is zero".

Audience laughter

Sergey Bezrukov (Yes Team): And all I have to add here is that after 25 years, $\hbar$ in Building 5 (where most of the physicists at the NIH sit) is still zero. Now, I agree completely with what Paul just said. Of course, life is a non-miracle, it follows from physical laws, but if quantum mechanics plays a decisive role in the explanation of the life phenomenon I'm not sure about this; [I say "not sure" rather than "no"] because it is very dangerous to say "no" when talking about science. As for Stuart's short speech, I can say all those fluctuations that he was talking about are pretty well understood from the point of view of classical physics; there is no problem in all of this. In his talk [at this conference] Prof Frauenfelder [was discussing the] timescales of these fluctuations and the timescales are understood [in the framework of classical physics]. Thank you.

Julio Gea-Banacloche (Chair): Thank you.

Hans Frauenfelder (Yes Team): I think as an experimentalist I would only start looking for non-trivial quantum effects if I find something that I cannot explain in any other way—but since we have started in telling stories, I have a story about what is trivial. Frank Yang, the Nobel Prize winner, gave a talk in Seattle many years ago and he said, when discussing a particular point, "It is trivial." He was challenged by another physicist, Boris Jacobson who asked, "Is it really trivial?" After the talk they went back to the office of Boris, worked for two days and they came out agreeing that it was trivial.

Audience laughter

Hans Frauenfelder (Yes Team): Some of Paul's statements sound to me like religion and it's very hard to discuss religion. Two statements about the fluctuations—I probably know as much about fluctuations as most people—and I've never yet seen something that looks like a miracle. The fluctuations that we observe are explainable using standard physics. At the moment, I see no reason to invoke something that's supernatural or quantum mechanical in the understanding of biology.

Julio Gea-Banacloche (Chair): Thank you and that finishes the first round, so everybody has now two minutes to reply, except for Professor Zeilinger who can have 5 minutes. Thank you.

Paul Davies (No Team): Let me just respond to a few of these points. First of all, is my position religious? I would say that it is exactly the opposite—[it is the person] who says that life originates because of some stupendously improbable set of events [who] is effectively appealing to religion by calling [life's origin] a miracle. There's no real difference between a miracle and an event that is so improbable that it's going to happen only once in the universe. So I think by saying that there are principles in physics, which encourage matter to organize itself into life, is the scientific position. We don't know [this hypothetical principle] yet, but to [claim] perversely that this principle does not belong within quantum mechanics seems to me a very peculiar position. As far as the teleological aspects are concerned, I think that's very easily dealt with because the physicist will define life as a system that would replicate, which is a well-defined physical criterion. The pay-off for the system is that it gets to replicate—so that takes care of that point. And I've probably used up my two minutes—well, I think I've got nothing else to say!

Audience laughter

Paul Davies (No Team): ... because I'll defer to Stuart on the question of timescales for decoherence.

Stuart Hameroff (No Team): First of all, Jens, I'm glad you read Tegmark's paper; unfortunately you didn't read our reply to Tegmark.

Audience laughter

Howard Wiseman (Yes Team): [You mean in] *Phys. Rev. E*, the same journal as your paper?

Stuart Hameroff (No Team): Yes, *Phys. Rev. E*, the same journal that he published in. Tegmark successfully disproved his own theory about

microtubules [implying] that he was disproving ours. However, his decoherence time of 10^{-13} [seconds] was based on a superposition separation distance of 24 nm, whereas our [superposition separation distance] was a Fermi length—so that's seven orders [of magnitude lengthening of the decoherence time] right there. He also neglected things like dielectric, [permittivity], Debye layers, and [decoherence free sub-spaces] and some other things. We corrected for those, we used his same formula, and we got [the calculated decoherence time] to 10-100 milliseconds. If you add the potential effect of topological quantum error correction you get an indefinite extension. As far as the comments about the fluctuations of the proteins not needing any miracle, quantum effects are not supernatural. It may seem that that protein dynamics is [straightforward and classical], however, as I mentioned, the biochemistry text, by Voet and Voet, clearly states that the strong forces cancel out, and the weak London forces rule on timescales relevant to conformational fluctuations. Also, [in] Professor Frauenfelder's lecture in his wonderful work on myoglobin, he showed a xenon molecule, which is an anaesthetic, exactly like [the other inert anesthetic gases we use clinically]. [Xenon is] a perfectly good anaesthetic, we [could use for patients] to go to sleep for surgery. It's expensive but it works just fine. It's completely inert and neutral; gets into hydrophobic pockets and does exactly what the other anaesthetics do [binding only by quantum London forces]. Professor Frauenfelder has said that xenon prevents the dynamics of myoglobin, so while he was looking at the other effects and attributing [protein conformational control] to external classical fluctuations rather than internal control. [Control of myoglobin may be mediated through quantum London forces in a hydrophobic pocket blocked by xenon]. Thank you.

Anton Zeilinger (No Team): OK, first I would like to apologize it's my fault that I didn't realize that the debate was moved down by half an hour. I had the old schedule, but this is my fault and I apologize for this happening. Now, let me make one or two statements. I have no idea whether quantum states play a trivial or non-trivial role in biological systems; otherwise I might not be sitting here. But I feel that there is no reason why they should not. And as an experimentalist I view—I see a challenge—to prove that quantum systems basically no matter how complex can exist in quantum superposition. This is independent of the question of whether this plays a role in living systems or not but my fervent approach is, that if we are able to prove that quantum superpositions can be shown in the laboratory and

later on for very complex systems including living systems, it might change the way biologists view their own business, because biologists' essential paradigm is that we are essentially classical machines.

Now I am saying—in including living systems—I do not see any reason whatsoever why we should not be able to see a quantum superposition of bacteria, for example some day. I know that all the papers which talk about, you know, decoherence, about coupling linking systems with environment, and why this would not allow quantum interference—I read such papers as instructions about what *not* to do and how to avoid decoherence. For example, this specific thing, which I am sure will be done in the future—I don't know when—is that you take a small living system, say a bacterium provided with other technology with its own living shell around it, so that the whole system does not couple to the environment, and then I'm sure you can put the whole thing through a double slit or whatever. There is no reason not to have quantum superpositions of living systems. As I said this might change the viewpoint of people. It might really lead to something new. The question is certainly interesting and whether [quantum effects are] trivial or non-trivial in living systems and what is called for is something like Bell's theorem. It is also under-appreciated, how gigantic the achievement of John Bell was. Namely that he was able to give a general set of quantified criteria, which tells you whether in a given situation, you can explain what you observe, by a local, realistic viewpoint. We need to see exactly the same kind of thing for a living system. So, if somebody would be able to provide criteria which tell you if a certain condition is met, we know that quantum phenomena play no role in living systems that would be an equally important achievement as the opposite [viewpoint]. It might be possible, it might not be possible, I have no idea whatsoever...

Julio Gea-Banacloche (Chair): Not much time left for you.

Anton Zeilinger (No Team): Alright I should give the rest of the time to others, but I just would like to point out one more thing. Suppose we have some dynamics, which release two coherent superpositions in living systems. No matter for how short a time, then my claim is that decoherence does not [matter]—because decoherence gets rid of non-diagonal terms in the density matrix, but it does not explain to you why a specific event the living system happens and we are dealing with living systems in relation to each other. Finally I want to share with you something I learned from yesterday, and in the quick discussions we had about today's debate. It would be extremely non-trivial if quantum mechanics did not play a role

in living systems, it would be the only area in which we know quantum mechanics is not at work. Thank you very much.

Derek Abbott (No Team): Just in rebuttal to the Pro Team...I get confused...so I'll call them the Fundamentalist Team. So I find it surprising that they take their particular position. I'd like to remind Jens Eisert of one of his own papers, where he motivated the idea of quantum games as perhaps helping to explain how nature might play quantum games at the molecular level.[7] So this leads to an interesting point that perhaps quantum mechanics might—if it doesn't [already play a non-trivial] part at the biological level—then what about the [evolutionary] pre-biotic level? So that is another thing I'd like to throw out to the Con Team... er... Fundamentalist Team. And I'd also like to remind them that they haven't yet found a counterexample to my little conundrum I made the first time. Thank you.

Julio Gea-Banacloche (Chair): That was short. Alright, Jens you may as well address your guilty past.

Audience laughter

Jens Eisert (Yes Team): I don't want to: that's my game. OK, we'd better start with Anton—there seem to be three things that need to be addressed and need to be done, in order to have a meaningful debate. And that's, in my point of view: experiments, experiments, and experiments. What I would like to see, for example, is [based on] some of the arguments that we were discussing are in principle explainable. So I would like to see, say, an experiment where you prepare entangled photons, let them be absorbed in a photosynthesis reaction, the energy is transferred to internal degrees of freedom, and then you have a Bell inequality violated. The point is that, some of the statements about coherence are testable in principle. It only becomes difficult if one thinks of processes that are underlying other processes that are so much larger than the things you're talking about. To Stuart, and if you look for, say, the effects of gravitational objective state reduction, it looks beautiful to do experiments to confirm or to falsify the hypothesis made in this context, but I mean, if the effect you're looking for is orders of magnitudes smaller than the environment induced decoherence that you have, then I would rather like to see an experiment that first deals with the numbers that are there and are accessible by experiment. And

[7] Transcript editor's note: See Eisert, J., and Wilkens, M., and Lewenstein M. (1999). Quantum games and quantum strategies, *Phys Rev Lett.* **83**, pp. 3077–3080.

then, what about timescales? I liked Howard's comment on the A and B. One needs to be careful of the fallacy that, well, if A happens on timescale something and B happens on timescale something, therefore A must be B. You have decoherence processes happening on, say, one second—which happens to be decoherent—and our thought processes happening on the level of one, then we should not be really tempted to say it is the thought process.

Three, concerns the search for life, I mean, if one is really searching for life and the goal is to have a successful species in the end of maybe if you want to, you can have a quantum strategy or whatever. I mean, this concludes that there are so many rounds going on with the generations, this has to be coherent. I find it hard to imagine that the power to replicate or to have a powerful species again can play any role in the search for life on the quantum level. My time is up.

Howard Wiseman (Yes Team): So yeah, in terms of counter-examples to Derek's claim, it seems to me a ludicrous suggestion that nature has developed every technology that you can think of. And yes, I just thought of four things here, which to my knowledge, Nature hasn't done: an internal combustion engine, a television, a refrigerator, an inferometric measurement of gravity.

Audience laughter and applause

Howard Wiseman (Yes Team): So, to move on—oh, Anton—Anton said that in his experiments that there is no reason that quantum effects couldn't play a role in biology. I would say if that's the case, Anton, why don't you do your interference experiments in a saline solution? Warm, wet... my point was, why do you do yours in a high vacuum rather than in a warm, wet environment? OK, so to go back again to what Julio began with by asking: he not only asks to be surprised, he asks for the No Team to provide surprising *facts*. I think that's one thing that's been lacking. You have surprising *speculations* ...

Audience laughter

I'd like to make a comment specifically for Stuart: the word "coherent" and the word "quantum" are not synonyms. So you can have coherence without having quantum effects. I think that's a very important point. OK, in terms of whether there's quantum computation going on in the brain, I think it's an *enormous* leap of faith to believe something like that. To begin with, in Stuart's scheme involving tubulin proteins, as far as I know—I would like to know if I'm wrong—there's no evidence that tubulin even

does *classical* computations, still less that it does quantum computations, and even *less* than it does quantum computation that involves general relativistic effects. So I think this theory is so far ahead of the experiments that it is fairly pointless.

OK, another point about why we are skeptical about quantum computation happening in the brain is [the following]. An important point about quantum computation is that it is useless unless you have a real large-scale computer—because quantum computers are very hard to build and they tend to be slower than classical computers. So you only get an advantage out of them if you can actually get to a very large scale, and then finally quantum computers are going to be faster than a classical computer. So how a quantum computer could ever have evolved, as it's completely useless until it's extremely large? And my time's up.

Sergey Bezrukov (Yes Team): I would like to comment on Prof Zeilinger's last statement where he proposed that "it would be very surprising if quantum mechanics has nothing to do with biology."

Anton Zeilinger (No Team) [Interjecting]: I did not say "surprising," I said "non-trivial."

Sergey Bezrukov (Yes Team): Okay, I meant "non-trivial." Anyway, quantum mechanics has actually a lot to do with biology and it was a problem for me [to decide] on which side of the debate to join. [This is] because my only point is that quantum mechanics as of this moment hasn't provided any *qualitatively* new insights into the mechanisms [studied by] biological physics. At the same time, it has great importance in the *quantification* of many phenomena at the elementary level. And the best example to discuss is probably van der Waal's forces, because to explain van der Waal's forces one doesn't need any quantum mechanics. If you know the history of the subject, the first explanation, the first qualitative explanation of van der Waal's forces, belongs to [the Russian physicist] Lebedev [who worked it out] more than hundred years ago. There was not any quantum mechanics at that time. However, to calculate with reasonable accuracy the constants of interaction, one has to have the quantum mechanical input. So what I'm saying is that up to now—and I don't know what is going to happen in the future—but up to now, "$\hbar$ is zero" for the reason that quantum mechanics did not supply us with any qualitatively new insights about the molecular mechanisms in biology. At the same time [quantum mechanics] is of greatest importance for quantifying [the] dynamic interactions, including interactions [involved] in protein folding [and functioning].

Hans Frauenfelder (Yes Team): First of all I have to remind the audience that the roles we play in here have been pre-assigned, so we cannot be accused of being a believer or non-believer.

Audience laughter

Hans Frauenfelder (Yes Team): The second point is quantum mechanics is absolutely essential for biology. There is no question. For instance electron transfer occurs in quantum mechanical tunneling—it is essential. I think that the question which we're really discussing hasn't been clearly stated is: "If we find a general law that determines or explains life, is it quantum mechanical or classical?" Here I have no opinion and I will wait till it is discovered.

Julio Gea-Banacloche (Chair): Thanks to all the panelists. I think that they have raised lots of interesting points, on both sides, and I'm sure that the audience will have many questions. Yes, we'll have a two sentence summary and so, Paul.

Paul Davies (No Team): I just want to respond to Jen's point about remaining coherent, generation after generation. That's certainly not what I had in mind. Just getting the first replicator seems to me is very hard. Quantum mechanics would potentially be very useful for [acting over fractions of a second to avoid] hanging in there for thousands of millions of years. To sum up, I would say that quantum mechanics is the default [option] and until somebody persuades me that it's not [part of] the origin of life, I think that's the only reasonable thing to assume.

Stuart Hameroff (No Team): OK, well, in the first of two very long sentences I want to respond to the chairman's point about (a) drugs, and (b) consciousness, which were brought into the discussion. In the '70s it was shown that the potency of the psychedelic drugs was proportional to their ability to donate electron resonance energy to their receptors, suggesting that receptors are more prone to go in the quantum state, suggesting further that the psychedelic experience might use quantum information, and I might add that psychoactive neurotransmitters like serotonin and dopamine also have electron resonance effects. The second sentence is that aspects of the subconscious including [dreams] are increasingly being expressed in terms of quantum information, that the subconscious mind is to consciousness what the quantum world is to the classical world.

Anton Zeilinger (No Team): First, one little remark on Howard's remark on my remark: "Why don't we do our experiments in saline solution?" And I guess I pointed out that someday we hope we can do these exper-

iments, in quantum superposition, with living things including the saline solution. So it might simply be that the picture is a little bit too narrow. If we dissect a living system to the centre of the saline solution to the brain and it is clear that information goes back and forth to the between all kinds of components in there, and may be we should do that and we should include those kind of considerations somehow. I know there are all kinds of reasons why this is stupid, but there might be a reason—it may work some time. The second point, the second sentence, I would like to mention—I think Howard's argument against some of these that they are far ahead of experiments that some scientists have been discouraged about what us experimentalists can do. I mean I saw it happen in the field of quantum information. People simply didn't think about ideas or writing them down, because they thought the experiment was not possible or the experiment too far ahead. You never know how fast we can move and in which direction—this might be true in this area too, I hope.

Derek Abbott (No Team): Howard's[8] refrigerator: the principles are there and animals cool themselves down by sweating, by evaporation. The internal combustion engine: Howard's stomach when he eats and consumes food—the principles are there. Television: the principles of encoding information and transmitting it through electromagnetic radiation are there—that's the firefly example. As for detection of gravity waves: wrong scale in biology. That one doesn't count.

Audience laughter

Derek Abbott (No Team): I would like to make an observation now, in my summary. I would like to make an observation that, you know, our team has been pro-active whereas the other team has been reactive. They haven't come up with any interesting stuff.

Audience laughter

Derek Abbott (No Team): ... we're the interesting team!

Audience laughter

Julio Gea-Banacloche (Chair): Your two sentences are over.

Derek Abbott (No Team): The question of quantum mechanics in biology: it's a fascinating question—so in summary, I want to say: let's stop being armchair scientists, let's apply the scientific method, let's go out, and let's do some experiments in the spirit of what Anton is saying. We

[8]Transcript editor's note: This refers to Howard Wiseman.

may—if we do this—we may just find *something* that nature can teach us about quantum computation.

Julio Gea-Banacloche (Chair): Well, these have turned out to be rather long sentences, but...

Audience laughter

Jens Eisert (Yes Team): To start with, nature has television, but does nature also have game shows?

Audience laughter

Jens Eisert (Yes Team): OK so we are on the boring side, but something seems to be buried. There seems to be some sort of psychological belief that the mystery of life sounds cool if some sort of quantum effect is involved. I must say that I'm not very happy if the brain just works as a classical Turing machine—admittedly—and not that happy that the brain is a quantum Turing machine either.

Howard Wiseman (Yes Team): OK, I just want to say, quantum information processing is *extremely* hard to do and as far as we know, it's only used for solving obscure number-theoretical problems.

Audience laughter

Howard Wiseman (Yes Team): I'd be happy for the experimentalists on the other team to find evidence for [non-trivial quantum effects] in biology, but I don't believe it so far.

Sergey Bezrukov (Yes Team): Just in two sentences. Quantum mechanics will be very important for the future development of the biological physics, or "physics of biology", but up to now the situation is very simple. As I told you already, [quantum mechanics is of] great importance for the quantitative understanding of the [basic interactions and] processes' rates, but, unfortunately, [of little importance] for the qualitatively new insights and new concepts. Thank you.

Hans Frauenfelder (Yes Team): I think essentially everything has been said, and I am concerned with summarizing. The answer is we need experiments to answer the question, but first we have to find out what the real question is, and we haven't done that.

Audience laughter

Julio Gea-Banacloche (Chair): Well, I would like to thank all the panelists again, and now we have questions from the audience. Ah, there is one!

Laszlo Kish (Texas A&M): Just a short comment: Paul didn't take the "trivial" part seriously. The question was about *non-trivial* quantum effects. Anything that refers to material properties, dead material properties: chemistry, tunneling, van der Waals forces, even if it is quantum, is trivial because still occurs in dead non-living material.

Julio Gea-Banacloche (Chair): Does anybody want to address this point?

Paul Davies (No Team): I dread to reopen the whole debate about what is trivial and what is non-trivial, as it is a non-trivial topic.

Audience laughter

Peter Heszler (University of Uppsala): I just have a comment that, as far as I know, if you take high quantum numbers, quantum theory converges to classical theory. My question is: "Are [humans made up of materials] with high quantum numbers or low quantum numbers?" Because if we are high quantum numbers—apparently according to Bohr—we are classical. If we are low quantum numbers, then we are quantum mechanical. That's my point.

Anton Zeilinger (No Team): I would simply disagree with your starting point. The limit of high quantum numbers is not always classical.

Juan Parrondo (Universidad Complutense): It looks like when we're talking about the brain here, the only way to escape from this picture of the brain as a classical Turing machine is going to the quantum world. I would like to say that there are other ways of escaping from the Turing machine: for instance [by appealing to] chaotic classical systems or [by appealing to] recent studies of treating the mind-body relationship as a whole. [Thus] I think there are other ways of escaping from this narrow aspect. This is a kind of an off-side comment.

Stuart Hameroff (No Team): I'll cover that now. I got interested in Roger Penrose's argument using [Gödel's] theorem that human consciousness uses something that is non-computable. Still deterministic, but not algorithmic and chaotic systems and everything you said are still basically deterministic and algorithmic. The only way out of that is something that he called non-computable and he brought in his hypothesis of quantum gravity, which is the only way out of us being helpless spectators and conscious automata. And [Jens Eisert] mentioned how seemingly ludicrous it is to bring in quantum gravity because [the energy] is 24 orders of magnitude lower than [the environment], however, in Roger [Penrose's] scheme the re-

duction is instantaneous so the power is actually calculated as a kilowatt per tubulin protein.

Unknown (Audience Member): You say that it's instantaneous?

Stuart Hameroff (No team): If you approximate "instantaneous" to one Planck time, you take the very low energy divided by the [even smaller] Planck time of 10^{-43} seconds, giving a kind of a karate chop.

Anton Zeilinger (No Team): Why don't we all boil if it is a kilowatt?

Stuart Hameroff (No Team): Because [the energy is delivered] only over a Planck time of 10^{-43} seconds.

Jens Eisert (Yes Team): In the mid-19th century as far as I know there was this debate whether there's something special about this kind of energy of life or not...er...I only know the German word—very sorry—a kind of spirit of life specific for...

Derek Abbott (No Team): "Vitalism" [is the word you are looking for.]

Jens Eisert (Yes Team): Ah, vitalism. Okay, if one pushes that picture so far, then one can just speak of consciousness particles that are in the brain and then we are done. If you go beyond the theories that are open to empirical verification [then you have gone too far].

Stuart Hameroff (No Team): You're putting words in our mouths, we didn't say that—although I will admit to being a quantum vitalist—but it's not that we have quantum particles, it's that [biology utilizes quantum superposition, entanglement and computation. Why wouldn't it?]

Unknown (Audience Member): What quantum information processing could be useful in biology?

Paul Davies (No Team): If quantum information processing is not useful, why is so much money being spent on trying to improve it?

Audience laughter

Paul Davies (No Team): Quantum information processing bestows upon nature awesome information processing power and I would find it totally extraordinary if in the entire history of the universe this has never been put to use until now.

Unknown (Audience Member): What is the one example? One possible example?

Paul Davies (No Team): Well, we naturally look to nature's great information processing system which is called life. Really, for me, that is the

most persuasive point. Where else would we expect to see this happening in nature, except life, which is just so wonderfully adept at processing information? And [according to orthodoxy] we are to suppose that life hasn't discovered the awesome information processing power that quantum mechanics provides—but that's all gone to waste over the 13.7 billion year history of the universe and it's only *now* that human beings have discovered [quantum information processing]. That seems extraordinary hubris.

Stuart Hameroff (No Team): Just think of your subconscious mind as being quantum information, which 40 times a second collapses or reduces into your conscious mind.

Unknown (Audience Member): In order to live you've got to have very large redundancy because you are constantly attacked by microbes, viruses with all kinds of things—if I use my glasses it is because I see not so well. Quantum information seems to be very, very fragile. Whatever you do, a small perturbation and the whole computation fails. If quantum computation has anything to do with living [systems], it seems to me that nature should have found the optimal quantum error correction scheme. So maybe this is what we should be [looking for.]

Paul Davies (No Team): Yes, they may indeed to have done so and it seems to me very sensible to look at nature's nanostructures within cells to see if they are deploying any tricks that we could make use of.

Stuart Hameroff (No Team): I mentioned [yesterday] that microtubules seem to have used the Fibonacci series in terms of their helical winding and it has been suggested that they utilize a topological quantum error correction code that could be emulated in [man-made] technology. As far as redundancy, there is a lot of parallelism in the brain and memory seems to be represented holographically, so redundancy is not a problem.

Jens Eisert (Yes Team): My concern with quantum error correction is that some care is probably appropriate. I mean it's not known what the actual thresholds are for quantum computation against arbitrary errors and if you take off your glasses it is not so clear what errors are going to come against you. But the best known bounds on the "market" are 10^{-4} for quantum computation. And so we need to see the perspective that really small errors can be corrected with error correction.

Stuart Hameroff (No Team): That's why you should look at biology. It might be better.

Julio Gea-Banacloche (Chair): I'm seriously trying to bite my tongue.

Audience laughter

Julio Gea-Banacloche (Chair): Any other questions. I'm sure there must be some comments. Yes.

Michael Hoffman (University of Ulm): It's just a comment. I would like to recall why quantum mechanics have been invented. They have been invented because experiments were done that could not possibly be explained by classical models. So, I'm waiting for the experiment that you are doing that cannot possibly be explained by classical models, and now we should do another one.

Paul Davies (No Team): I'd like to respond to that because it's the point I was going to make, that ... everyone here seems to assume that biologists seem to have a wonderful understanding of what is going on inside a living cell, and the biologists I talk to are continually baffled. For example I spoke in my lecture about the polymerase motor. You may think the basic physical principles must be understood. Absolutely not. The people who work on that say they really haven't a clue what is going on there in terms of basic physics. Somebody made the comment, "Biologists, you know, why don't they go out and learn some physics?" Mostly, biologists don't know quantum physics so, and that doesn't mean they fully understand everything in terms of *classical* physics. That doesn't follow. They are continually troubled and do not understand most of what is going on inside a living cell, except at the level of individual molecular interactions. Once you start getting something that's complicated as the polymerase motor [they are in trouble].

Michael Hoffman (Unversity of Ulm): But have they not tried to explain it by classical models?

Paul Davies (No Team): Yes, I mean there are all sorts of hand waving models around, but the classical models aren't terribly satisfactory either. I think it's a real mystery what's going on inside a cell, and the fact that biologists say, "Well, you know, it isn't a problem" doesn't mean that physicists can just sit on the sidelines saying, "Oh, it will all be explained in terms of classical physics." I think [scientists] do *not* understand what's happening. There are lots of mysteries and we do need experiments. It seems to me an entirely open question as to whether these experiments will reveal that quantum mechanics is going to be really essential for understanding some of these molecular biological properties—at least at the level of smaller components.

Sergey Bezurkov (Yes Team): I would like to disagree with Paul and support Michael. From my point of view, it depends on what you call "experiment." We probably do not actually understand what is going on in a single cell. Absolutely, I am with Paul [in this respect]. But the moment you do your experiments properly, the moment you dissect the cells into the parts that you can study with a real control over the [experimental] parameters, they [the parts] are "golden" [i.e. can be described by laws of physics]. So, [here] I'm with Michael.

Stuart Hameroff (No Team): Can I respond to that? I think what you just said, Sergey, is that if you cut the cell up into small enough pieces, eventually you get an experiment you can perform.

Sergey Bezrukov (Yes Team): Absolutely, but I'm not ashamed by the lack of understanding [of complex biological systems]; this is where we are now, with our physics, and I am not talking only about Building 5 at the NIH, [I am talking about] everybody here and in the world.

Stuart Hameroff (No Team): So when you reduce it too much you throw away the baby with the bathwater, you've lost the essential feature of life. And the other thing is consciousness is completely unexplained by classical means.

Howard Wiseman (Yes Team): To [Stuart], about the possibility of doing the experiment: could you show one tubulin protein being in a superposition? I mean that's pretty small. It seems to me that, you know, you criticize people for saying that you can't take things apart but it would bolster your position enormously if you could demonstrate that just one protein like this could be in a superposition state. So, that's why I think, really, this isn't going forward until an experiment like that is done.

Anton Zeilinger (No Team): Suppose what I believe will come true, namely that we will find superpositions of all kinds of things including tubulin. Would that have any impact for today's debate?

Stuart Hameroff (No Team): *Addressing Wiseman and referring to Zeilinger.* He showed it for Porphyrin so why not Tubulin?

Anton Zeilinger (No Team): *Addressing Wiseman.* If so, what impact would it have on your opinion?

Howard Wiseman (Yes Team): I think it would have an impact, it would advance your side enormously. At the moment there is no evidence whatsoever that there is anything quantum going on or even *potentially* quantum going on. So, I'm not saying it would win the debate, but it would certainly do a lot for you.

Audience laughter

Howard Wiseman (Yes Team): And a comment on the difference between porphyrin and tubulin—it's enormously difficult to show a macromolecule being in a superposition of two different configurations. That is like a miniature Schrödinger's cat. A porphyrin molecule being in a superposition in slightly different *positions*, is a completely different thing and it's much easier to do and to conceive of being true and to demonstrate experimentally.

Stuart Hameroff (No Team): The difference between the two tubulin states in our model: Professor Frauenfelder mentioned that the spatial difference in functional states is very small in a protein—is only the diameter of an atomic nucleus—so you couldn't really tell by looking at it. Of course if you looked at it you'd collapse it anyway.

Most view the brain as a hundred billion neurons with synapses acting as simple switches making up a computer. But if you look at one cell organism like the paramecium, it swims around and finds food, it avoids predators and obstacles. If it gets sucked up into a capillary tube, it gets out faster and faster each time—it can learn! It finds a mate and has sex. [Paramecium] doesn't have any synapses to process information, [but does so] very efficiently using its microtubules. If you try to develop a machine to do that, you would need a hundred million dollars.

Paul Davies (No Team): And a sense of humour?

Audience laughter

Stuart Hameroff (No Team): I'd like to think so!

Juan Parrondo (Universidad Complutense): We know that life [forms] prefer to live at a relatively high temperature, say around 300 Kelvin. If there would be quantum effects in biological processes, wouldn't there be [a preference for] life to develop at a colder temperature? Is it possible to say something *general* about this?

Stuart Hameroff (No Team): Biology has apparently adapted to utilize heat to promote rather than destroy quantum states, somewhat like a laser pumps quantum coherence. For example increased temperature enhances the quantum [spin] transfer through benzene, a perfect example of an organic molecule [found in protein hydrophobic pockets], so there must be some [kind of] electronic resonance that harnesses heat to promote quantum [processes].

Julio Gea-Banacloche (Chair): Well, it is probably about time to begin winding down. I think I would like to informally pose the question to the audience. Basically, I'm not sure that I can pose the question in a way that everybody here will approve of, so I'm not going to try. Let me just say by every individual's definition of trivial then, how many here—we can have a show of hands—would think that it's possible that there may be non-trivial quantum effects in biology, [that is], they tend to believe that there really may be non-trivial [quantum] effects in biology?

A little under 50% of the audience raise their hands

Julio Gea-Banacloche (Chair): OK. Now, how many would tend to believe that there are really no non-trivial quantum effects in biology?

A little over 50% of the audience raise their hands

Julio Gea-Banacloche (Chair): What do you say? I think there are probably more on the non-trivial side... I mean the trivial side—sorry!

Audience laughter

Derek Abbott (No Team): I'd like to see a show of hands whether people think it's worth going out and doing some experiments to check the relationship between quantum mechanics and biology. Hands up who thinks that's worth doing.

Julio Gea-Banacloche (Chair): It's a fair question.

>70% of the audience raise their hands

Derek Abbott (No Team): Hands up if you think you'd be wasting your time.

No hands are raised

Derek Abbott (No Team) Ah, nobody!

Then slowly one hand is raised—that of Laszlo Kish. Audience laughter

Julio-Gea Banacloche: Well, I would like to thank you all again and the participants for taking part in this debate. Thank you.

Audience applause

End of transcript.

Acknowledgements

The assistance of Phil Thomas, as the audio transcript typist, and Matthew J. Berryman for the sound recording are gratefully acknowledged. Thanks

are due to the many people who proof read the manuscript and helped decode the sound recording—any remaining errors are mine (Derek Abbott).

About the Panelists

Julio Gea-Banacloche was born in 1957, Seville, Spain and is presently professor of physics at the University of Arkansas. He received his BS from Universidad Autonoma de Madrid, 1979; and obtained his PhD under Marlan O. Scully, 1985, on quantum theory of the free-electron laser, from the University of New Mexico. In 1985–87, he served as a Research Associate, Max Planck Institute for Quantum Optics; in 1988–90 he was a Staff Scientist, Instituto de Optica, Madrid, Spain; and in 1990 he joined the Universisty of Arkansas initially as an assistant professor. He is an associate editor of *Physical Review A* and Fellow of the American Physical Society. He has carried out theoretical work in laser physics, quantum optics, and quantum information. His main contribution to the field of quantum information has been the observation that the quantum mechanical nature of the fields used to manipulate the quantum information carriers themselves—often called "qubits", or "quantum bits"—might lead to unpredictable errors in the performance of the quantum logical operations. The lower bound on the size of these errors can be made smaller by increasing the energy of the control system. This has led Banacloche to predict a minimum energy requirement for quantum computation, which has given rise to some controversy.

Paul C. W. Davies is a theoretical physicist, cosmologist, and astrobiologist. He received his PhD in 1970 from University College London, under Michael Seaton and Sigurd Zienau. At Cambridge, he was a postdoc under Sir Fred Hoyle. He held academic appointments at the Universities of Cambridge, London and Newcastle upon Tyne before moving to Australia in 1990, first as Professor of Mathematical Physics at The University of Adelaide, and later as Professor of Natural Philosophy at Macquarie University in Sydney, where he helped establish the NASA-affiliated Australian Centre for Astrobiology. In September 2006, he joined Arizona State University as College Professor and Director of a new interdisciplinary research institute called Beyond: Center for Fundamental Concepts in Science, devoted to exploring the "big questions" of science and philosophy. Davies's research has been mainly in the theory of quantum fields in curved spacetime, with applications to the very early universe

and the properties of black holes, although he is also an expert on the nature of time. His astrobiology research has focused on the origin of life; he was a forerunner of the theory that life on Earth may have originated on Mars.

Davies is the author of several hundred research papers and articles, as well as 27 books, including *The Physics of Time Asymmetry* and *Quantum Fields in Curved Space*, co-authored with his former PhD student Nicholas Birrell. Among his recent popular books are *How to Build a Time Machine* and *The Goldilocks Enigma: Why is the universe just right for life?* (U.S. edition entitled *Cosmic Jackpot*). He writes frequently for newspapers, journals and magazines in several countries. His television series "The Big Questions", filmed in the Australian outback, won national acclaim, while his theories on astrobiology formed the subject of a specially commissioned one-hour BBC 4 television production screened in 2003 entitled *The Cradle of Life*. In addition, he has also devised and presented many BBC and ABC radio documentaries on topics ranging from chaos theory to superstrings. Davies was awarded the 2001 Kelvin Medal and Prize by the UK Institute of Physics and the 2002 Faraday Award by The Royal Society. In Australia, he was the recipient of two Eureka Prizes and an Advance Australia award. Davies also won the 1995 Templeton Prize for his work on the deeper meaning of science. The asteroid 1992 OG was renamed (6870) Pauldavies in his honour.

Stuart Hameroff is an anesthesiologist and Professor of Anesthesiology and Psychology at the University of Arizona in Tucson, Arizona. He received his MD from Hahnemann College, Philadelphia, Pennsylvenia, in 1973. He has teamed with Sir Roger Penrose to develop the "Orch OR" (orchestrated objective reduction) model of consciousness based on quantum computation in brain microtubules, and has also researched the action of anesthetic gases. As Director of the University of Arizona's Center for Consciousness Studies, Hameroff organizes the biennial "Tucson conferences" *Toward a Science of Consciousness*, among other Centre activities. His website is `www.quantumconsciousness.org`.

Anton Zeilinger was born on 20 May 1945, Ried im Innkreis, Austria. His family moved to Vienna, where Zeilinger went on to study physics and mathematics at the University of Vienna. In 1971, he completed his PhD *Neutron Depolarization in Dyprosium Single Crystals* under Helmut Rauch. In 1979 he completed his Habilitation in neutron physics at

the Vienna Technical University. From 1972–81, he worked as a research assistant at the University of Vienna under Helmut Rauch, followed by two years as an associate professor at the Massachusetts Institute of Technology (MIT). He then taught at numerous universities in Austria and abroad, such as Melbourne, Munich, Paris, Innsbruck and Oxford. He is currently a professor of physics at the University of Vienna, previously the University of Innsbruck. He is director of the Vienna branch of the Institute of Quantum Optics and Quantum Information (IQOQI). Zeilinger is known for multiple experiments in the realm of quantum interferometry, which include the first demonstration of quantum teleportation between two separately emitted photons. With Daniel Greenberger and Michael Horne he demonstrated an extension of the Einstein-Podolsky-Rosen paradox, where one considers three, not just two entangled particles. In 1999, his Innsbruck group demonstrated experimentally that one can indeed observe three particle Greenberger-Horne-Zeilinger correlations. In Vienna his molecular interferometry team, co-led by Markus Arndt, discovered the possibility of observing quantum interference of heavy chemical molecules, including the C60 molecule (fullerene). Zeilinger received many awards for his scientific work, one of the most recent being the Isaac Newton Medal (2007) of the Institute of Physics (IOP). He is a fan of the *Hitchhiker's Guide To The Galaxy* by Douglas Adams, and has named his yacht "42."

Derek Abbott was born in South Kensington, London, UK. He received his BSc(Hons) in Physics from Loughborough University of Technology. He obtained his PhD in Electrical and Electronic Engineering from the University of Adelaide, under Kamran Eshraghian and Bruce R. Davis. He is with The University of Adelaide, Australia, where he is presently a full professor and the Director of the Centre for Biomedical Engineering (CBME). He has served as an editor and/or guest editor for a number of journals including *Chaos* (AIP), *Smart Structures and Materials* (IOP), *Journal of Optics B* (IOP), *Microelectronics Journal* (Elsevier), *Proceedings of the IEEE*, and *Fluctuation Noise Letters* (World Scientific). He is a life Fellow of the Institute of Physics (IOP) and Fellow of the Institution of Electrical & Electronic Engineers (IEEE). He has won a number of awards including a 2004 Tall Poppy Award for Science. He holds over 300 publications and is a co-author of the book *Stochastic Resonance* published by Cambridge University Press. Professor Abbott is co-founder of two international conference series: *Microelectronics in the New Millennium* (with J. F. Lopez) and *Fluctuations and Noise* (with L. B. Kish).

Jens Eisert is a lecturer and holder of the European Young Investigator Award at Imperial College London in the UK (Diploma, University of Freiburg, Germany; MSc, University of Connecticut, USA; PhD, University of Potsdam, Germany). His research interests are in quantum information science and related fields. This includes formal aspects of entanglement theory and computational models, as well as quantum optical implementations and the study of complex quantum systems.

Howard Wiseman is a theoretical quantum physicist. His principle interests are quantum measurements, quantum feedback control, quantum information, fundamental questions in quantum mechanics, and open quantum systems. He completed his PhD under Gerard J. Milburn at the University of Queensland in 1994, and then undertook a postdoc under Dan Walls at the University of Auckland. Since 1996 he has held Australian Research Council research fellowships. He is currently Professor and Federation Fellow at Griffith University, where he is the Director of the Centre Quantum Dynamics. He is also a Program Manager in the ARC Centre for Quantum Computer Technology. He has over 120 refereed journal papers, and his awards include the Bragg Medal of the Australian Institute of Physics, the Pawsey Medal of the Australian Academy of Science and the Malcolm Macintosh Medal of the Federal Science Ministry.

Sergey Bezrukov is a Section Chief in the Laboratory of Physical and Structural Biology, National Institutes of Health (NIH), Bethesda, Maryland. He received his MS in Electronics and Theoretical Physics from St. Petersburg Polytechnic University, 1973; and he obtained his PhD under Giliary Moiseevich Drabkin in Physics and Mathematics from Moscow State University, Russia, 1981. In 1981–87, he was a Research Scientist, St. Petersburg Nuclear Physics Institute, Laboratory of Condensed Matter Physics; in 1987–90 a Senior Research Scientist, St. Petersburg Nuclear Physics Institute, Laboratory of Condensed Matter Physics; in 1990–92 he was a Visiting Research Associate, University of Maryland and Special Volunteer, National Institutes of Health, LBM, NIDDK; in 1992–98 he was Visiting Scientist, National Institutes of Health, LSB, DCRT and LPSB, NICHD; in 1998–02 he was an Investigator, Head of Unit, National Institutes of Health, LPSB, NICHD; and he took up his present position in 2002. Bezrukov was elected Member of Executive Council of the Division of Biological Physics of the American Physical Society in 2002. One of his key research interests is in the physics of ion channels. He still works at the NIH in a building where $\hbar = 0$.

Hans Frauenfelder was born 28th June 1922 in Schaffhausen, Switzerland. He received his Dr. sc. nat. in physics in 1950 at the Swiss Federal Institute of Technology (ETH) in Zurich under Paul Scherrer. His thesis concerned the study of surfaces with radioactivity. In 1951, he discovered perturbed angular correlation. At ETH he was also taught by Gregor Wentzel and Wolfgang Pauli. Through Pauli, he also got to know many of the leading scientists such as Kramers, Heisenberg, Hans Jensen, and Wolfgang Paul ("Pauli's real part"). Frauenfelder migrated to the US in 1952, joining the Department of Physics at the University of Illinois in Urbana Champaign as a research associate. Despite the absence of mountains, he stayed at the UIUC till 1992, ultimately as Center for Advanced Study Professor of Physics, Chemistry, and Biophysics. His research interests included nuclear physics, particle physics, conservation laws, Mössbauer effect, and biological physics. In 1992, Frauenfelder moved to the Los Alamos National Laboratory where he is currently the director of the Center for Nonlinear Studies and continues research in biological physics. He wrote three books, *Mössbauer Effect*, and together with Ernest Henley, *Nuclear and Particle Physics*, and *Subatomic Physics*. Frauenfelder is a member of the National Academy of Sciences, the American Philosophical Society, and a Foreign Member of the Royal Swedish Academy of Sciences.

Chapter 17

Nontrivial Quantum Effects in Biology: A Skeptical Physicists' View

Howard Wiseman and Jens Eisert

When you have excluded the trivial, whatever remains, however improbable, must be a good topic for a debate.[1]

17.1. Introduction

This chapter is somewhat of an anomaly in this book. Firstly, its authors profess no particular knowledge of any effects in biology, (whether quantum or non-quantum, trivial or non-trivial), both being theoretical quantum physicists by trade. Secondly, we adopt here a skeptical view on the existence of such effects if they fall in the non-trivial class. That two such skeptical non-experts have been invited to contribute to this volume came about as a result of the public debate (reproduced earlier in this volume) at the *Second International Symposium on Fluctuations and Noise*, held in the Canary Islands in 2004 (see Chapter 16). We were invited by Derek Abbott to affirm the statement that *"Quantum effects in biology are trivial."*

This chapter will reproduce many of the arguments that we put in that debate, although hopefully somewhat more coherently than we communicated them at the time. It also contains some arguments that were not covered in the debate. Obviously the debate would have been pointless unless both sides had agreed on what counts as a *non-trivial* quantum effect in biology. Thankfully, all participants in the debate did agree, more or less,

Received April 17, 2007

[1] Apologies to A. C. Doyle.

although only one (HMW) offered a formal definition: that a non-trivial quantum effect in biology is one that would convince a biologist that they needed to take an advanced quantum mechanics course and learn about Hilbert space and operators etc., so that they could understand the effect.

To use the word "trivial" to characterize all quantum effects in biology that do not increase enrollments of biologists in advanced quantum physics courses is unfortunate. Neither we, nor, we imagine, any of the debate participants, wish to denigrate the interesting and challenging research into quantum effects relevant to biology such as coherent excitations of biomolecules [Helms (2002); Gilmore and McKenzie (2005)], quantum tunneling of protons [Kohen and Klinman (1999)], van der Waals forces [Parsegian (2005)], ultrafast dynamics through conical intersections [Cederbaum *et al.* (2005)], and phonon-assisted electron tunneling as the basis for our sense of smell [Brookes *et al.* (2007)]. But here we are concerned not with these real (or at least plausible) quantum effects, but rather with more exotic, unproven (and, we believe, implausible) effects.

What might these non-trivial sorts of quantum effects be? Several have been suggested in the literature (see other papers in this volume), but we will concentrate upon four: A quantum life principle; quantum computing in the brain; quantum computing in genetics; and quantum consciousness. These intriguing topics provide the structure of our chapter. We devote one section each to briefly explaining, and then arguing the implausibility of, these hypothetical effects. It is hence the purpose of the present chapter to be cautionary: to warn of ideas that are more appealing at first sight than they are realistic.

We end, however, on a more constructive note in our final section, by pointing out that there is one sense in which it seems likely that quantum effects introduce a non-trivial difference between brains and digital computers. This section (quantum free will) is of interest philosophically rather than scientifically, so we do not see it as an exception to our claim that biologists should not want to enroll in advanced quantum physics courses.[2]

17.2. A Quantum Life Principle

17.2.1. *A quantum chemistry principle?*

It is a widely held belief that the origin of life is extremely unlikely according to established science. This has led some to argue that there exists a natural

[2]Philosophers, on the other hand, should!

principle, in addition to existing laws, that guarantees that life must arise in the universe—see Davies (2004a). In this review, Davies points out difficulties with this argument, but apparently he gives it some credibility since he used it in the 2004 Canary Island debate (Chapter 16). There he stated that, unless life is miraculous, there must be a life principle, and that since it is a fundamental physical principle, it must be related to our most fundamental physical theory: quantum mechanics. In Davies (2004a) he suggests that the origin of life may be related to quantum search algorithms, an idea we discuss in Sec. 17.4.

That a belief is widely held does not make it correct. Indeed, we claim that the origin of life is entirely plausible according to established physical theories. Moreover, the relevant physical theory, chemistry, has no deep relation to quantum physics. To understand chemical structure and reactions at a fundamental level it is, of course, necessary to use quantum physics. But chemistry is usually regarded as emerging from physics in a straightforward (upwardly causal, not downwardly causal [Davies (2004b)]) way. If this were not the case, it would be necessary to postulate not merely a "quantum life principle", but also a "quantum chemistry principle" (along with, presumably, a "quantum condensed matter principle", a "quantum atom principle", and so on).

That life is an epiphenomenon of chemistry, and one whose appearance on earth is unsurprising, even expected, is well argued by Dawkins in his most recent popular book on evolution [Dawkins (2004)]. First, he stresses (pp. 575-81) that the essence of life, the aspect of life that must precede all others, is *heredity*. Heredity means the existence of a varied population of replicators in which the variation is (at least partially) inherited in the act of replication. To quote Dawkins,

> "[S]ome writers ... have sought a theory of metabolism's spontaneous origin, and somehow hoped that heredity would follow, like other useful devices. But heredity ... is not to be thought of as a useful device. Heredity has to be on the scene first because, before heredity, usefulness itself has no meaning. Without heredity, and hence natural selection, there would have been nothing to be useful for."

Accepting Dawkin's imperative, the origin of life can be illuminated by seeking the simplest carrier of hereditary information in the natural world. A well publicized example [Davies (1999); Dawkins (2004)] is *Spiegelman's Monster*, named after its developer [Kacian *et al.* (1972)]. It is far simpler

than the viruses from which it was derived. It is an RNA strand a mere 218 nucleotides long; that is, it is a large molecule containing less than 10^4 atoms. The environment in which it replicates is an aqueous solution of activated nucleotides, plus an enzyme Qβ-replicase. As shown by Spiegelman and Orgel, the monster carries hereditary information, and undergoes natural selection.[3] Most remarkably, self-replicating monsters appear *spontaneously* in the environment described above [Sumper and Luce (1975)].

The point of these investigations is not that Spiegelman's monster is the first life—that probably developed in quite different environments [Davies (1999); Dawkins (2004)]. Rather, in the present context, the points are: (i) that the beginnings of life need not be nearly so complicated as is imagined by those who stress its implausibility; and (ii) that nothing in these experiments suggest that anything other than chemistry is involved in the self-assembly and replication of these largish molecules. Indeed, it is likely that the chemical reactions involved could be reproduced, in the not too distant future, by simulations based at the atomic level. Such a simulation would be a definitive refutation of the idea of a quantum life principle.

17.2.2. *The anthropic principle*

It could be argued that, even if life is an almost inevitable consequence of chemistry in suitable environment, this fact itself requires explanation. That is, does it not seem miraculous that the physical world enables life to arise? Specifically, it has been argued that the fundamental constants of physics are "fine-tuned" so as to allow the existence of long-lasting stars, planets, liquid water etc. that are apparently necessary for life to arise [Barrow and Tipler (1986)]. Such an argument is known as the strong anthropic principle.[4] According to the standard model of particle physics, there are some 20 fundamental constants whose values are arbitrary, and according to theories like string theory, these "constants" are in fact quantum variables [Susskind (2005)]. Thus it might seem plausible to claim that life is somehow linked to quantum cosmology [Davies (2004a)].

Leaving aside the possible lack of imagination of physicists with regard to the sorts of universes in which life may exist, it seems unnecessary to invoke the strong anthropic principle to argue for a quantum life principle,

[3]Indeed, later work [Eigen and Oehlenschlager (1997)] showed that, through natural selection, the monster reduced even further in size, down to a mere 50 nucleotides—a few thousand atoms!

[4]Martin Gardiner has suggested the name Completely Ridiculous Anthropic Principle for the more extreme versions of this principle [Gardiner (1986)].

when the weak anthropic principle has just as much explanatory power. The weak anthropic principle simply states that we should condition all our predictions on the undeniable fact that we are here to ask the question [Barrow and Tipler (1986)]. Thus, if asked, what is the chance that the fundamental constants will be found to have values that enable life to evolve, we would have to say that the chance is essentially unity, since life evidently has evolved. That is, invoking some special principle to explain that life must have appeared and evolved intelligent observers is as unnecessary as invoking a special principle to explain that the language we call English must have developed and become widespread.

17.3. Quantum Computing in the Brain

17.3.1. *Nature did everything first?*

In the past decade or so, the field of quantum information (theory and experiment) has exploded [Nielsen and Chuang (2000)]. This is driven largely by the prospect of building a large-scale quantum computer, that could compute much faster than any conceivable classical computer by existing in a superposition of different computational states. This leads naturally to the conjecture that the brain itself may be a quantum computer [Hagan, Hameroff, and Tuszyński (2002)].

When looking at the wealth of existing life forms, the following observation becomes apparent: nature had the idea first. Indeed, in nature we can find parachutes and explosives, surfaces reminiscent of the most sophisticated nanostructured materials used in aeronautics today to reduce the aerodynamic resistance. Many effects and concepts of physics can indeed be found to be exploited by some life form to its benefit. So, after all, why should this not apply to the brain being a quantum computer?

We would argue that this is not a legitimate argument. While it is striking that some features have been "invented" by nature, the argument as such is a "postselected argument", based on case studies of anecdotal character. It is equally (if not more) easy to collect counterexamples of the same character; that is, inventions for which no counterpart in nature is known. For example, there are no metal skeletons, despite metal being much stronger than bone. There is no radio (long distance) communication, albeit this certainly being a useful and feasible means of communication. No closed-cycle refrigeration based on gas expansion is known. There is no use of interferometry to measure distances. Also, the eye is as such a really

lousy camera, corrected by the "software" of the brain. This last example illustrates a general point: nature makes do with things that are good enough; it does not do precision engineering. If there is one thing a quantum computer requires, it is precision, as we discuss below in Sec. 17.3.3.

17.3.2. *Decoherence as the make or break issue*

The case for the brain being a quantum computer, or indeed for quantum mechanics playing any key role at a macroscopic level in the nervous system, is weakest because of one effect: decoherence [Zurek (2003, 1998)].

A quantum system is never entirely isolated from its environment, which is always "monitoring" its dynamics. That is, information is transferred into the environment, where it is diluted into a larger and larger number of degrees of freedom. As a result, superposition states become, for all practical purposes, indistinguishable from classical mixtures of alternatives on a time scale known as the decoherence time [Zurek (2003, 1998); Eisert (2004)]. In short, quantum coherence is lost, as an effect of the environment monitoring the system.

This effect of decoherence is one of the main concerns in research on quantum computation [Nielsen and Chuang (2000)], where ingenious ways are being explored of shielding engineered and strongly cooled quantum systems from their respective environments. In fact, decoherence is the key challenge in the realization of a full-scale quantum computer. In large scale biological systems, like the brain, decoherence renders large scale coherence (as necessary for quantum computation) very implausible. Even the most optimistic researchers cannot deny the fact that the brain is a warm and wet environment. This is in contrast to the high-vacuum environment used in the beautiful experiments on spatial superpositions of organic molecules from Anton Zeilinger's group in Vienna [Hackermüller *et al.* (2003)]. In the realistic biological setting, even the most conservative upper bounds to realistic decoherence times are dauntingly small [Tegmark (2000)].

It is essential to keep in mind that large-scale quantum computation does not mean merely computing with a large number of systems, each of which behaves quantum mechanically. If coherence prevails only in subsystems of a quantum computer, but not over wide parts of the whole system, the computation would be no more powerful than its classical counterpart. Simply putting subsystems together operating on quantum rules with no coherence between them cannot give rise to a quantum computer [Nielsen and Chuang (2000)]. To create the large scale superpositions necessary for

quantum computation requires preserving coherence for a long time, long enough to enable all the different subsystems to interact.

Tegmark's article [Tegmark (2000)] is a careful discussion of the plausibility of preserving coherence over long times under the conditions in the brain. He focuses on two situations where it has been suggested that quantum superpositions could be maintained: a superposition of a neuron firing or not [Schadé and Ford (1973)]; and a superposition of kink-like polarization excitations in microtubules, playing a central role in the proposal of Hameroff and Penrose (1996). The firing of a neuron is a complex dynamical process of a chain reaction, involving Na^+ and K^+ ions to quickly flow across a membrane. Tegmark provides a conservative estimate of the relevant decoherence times for a coherent superposition of a neuron firing including only the most relevant contributions, arriving at a number of 10^{-20} seconds. Similarly, he discusses decoherence processes in microtubules, hollow cylinders of long polymers forming the cytoskeleton of a cell. Again, a conservative estimate gives rise to an estimated time of 10^{-13} seconds on which superpositions decohere to mere mixtures.[5] The general picture from a discussion of decoherence times that emerges is the following: Even if superposition states were to appear in the processes relevant for brain functioning, they would persist for times that fall short (by many orders of magnitude!) of the time scales necessary for the proposed quantum effects to become relevant for any thought processes.

17.3.3. *Quantum error correction*

The theory of quantum computation offers a number of strategies for preserving coherence of quantum evolution in the presence of a decohering environment. To be sure, the idea of classical error correction of simply storing information redundantly and measuring the full system to decide with a majority rule whether an error has occurred does not work; in that case the measurement itself necessarily destroys the coherence in the system, as it acquires information about the encoded quantum state. It was one of the major breakthroughs in the field of quantum computation that quantum error correction could nevertheless be realized. One indeed encodes quantum information in several physical systems, but in a way that in later partial measurements, one can only infer whether an error has oc-

[5]To be fair, it should be noted that Hagan *et al.* [Hagan, Hameroff, and Tuszyński (2002)] themselves argue that decoherence times may be significantly shorter than this [Rosa and Faber (2004)].

curred or not, but without being able to gather any information about the encoded state itself [Shor (1996); Steane (1996)]. Based on this knowledge, the error can then be corrected.

The idea of quantum error correction has been further developed into the theory of fault-tolerance [Aharonov and Ben-Or (1998); Aliferis, Gottesman and Preskill (2006)]. Even using faulty devices, an arbitrarily long quantum computation can be executed reliably. In topological quantum memories, systems are arranged in a two-dimensional array on a surface of nontrivial topology [Dennis *et al.* (2002)]. In physical systems, all these ideas may further be enhanced with ideas of trying to stay within physical decoherence-free subspaces [Zanardi and Rasetti (1997)], or bang-bang control. In the debate, Stuart Hameroff said:

> "I mentioned [yesterday] that microtubules seem to have used the Fibonacci series in terms of their helical winding and it has been suggested that they utilize topological quantum error correction codes that could be emulated in [man-made] technology. As far as redundancy there's a lot of parallelism in the brain and memory seems to be representable holographically, so redundancy is not a problem."

So why should, after all, nature not operate like the brain as a fault tolerant quantum computer?

Although this is a tempting idea it is by far more appealing than it is a realistic option. Beautiful as the idea is, it only works if the basic operations (called gates) are not too faulty. In realistic terms, they have to be very, very good. Specifically, quantum fault tolerance, employing complicated concatenated encoding schemes [Aharonov and Ben-Or (1998); Aliferis, Gottesman and Preskill (2006)], works if the performance of logic operations is better than a certain finite threshold. If the probability of failure of a basic logic operation is below this threshold, then a computation can indeed be performed as if perfect quantum gates were available. To obtain good bounds to the exact value of this threshold is a topic of intense research, but values of about 10^{-3} are realistic. Presently, we are a long way from achieving such low probability of error experimentally, even in sophisticated systems of laser cooled ions in traps, or in optical systems. To say, as Hameroff did in the public debate, that

> "[...] if you add the potential effect of topological quantum error correction you get an indefinite extension,"

misses the point that such quantum error correction is only possible once you have already reached the regime of very small errors. The required accuracy is in very sharp contrast to any accuracy that seems plausibly to be available in the slightly above room temperature environment of the brain. To think of performing reliable arbitrarily long quantum computation under these conditions is frankly unrealistic. Thus while the appeal of fault tolerance as an argument in favour of large scale coherence is indeed enormous, the numbers very strongly argue against that.

17.3.4. *Uselessness of quantum algorithms for organisms*

A final objection to the idea that quantum computing in the brain would have evolved through natural selection is that it would not be useful. Quantum computing has no advantage over classical computing unless it is done on a large scale [Nielsen and Chuang (2000)]. It is difficult to make statements about the time scales for quantum operations in the brain because there is zero evidence for their existence, and because existing platforms on which quantum computing is being explored are immensely different from any known biological system. But for no other reason than the difficulty in doing quantum error correction compared to classical error correction, it can only be expected that the time required to do a quantum logic operation would be greater than the corresponding time for classical logic operations. Because of this, quantum computing to solve any given problem would actually be slower than classical computing until the problem reaches some threshold size.

History is littered with case studies of organs and attributes that seem to defy Darwinian evolution because any intermediate stage on the path towards their full development would be useless or even harmful. But none have stood up to scrutiny [Dawkins (2004)]. So perhaps the hypothetical quantum computer in the brain could have come into existence despite the above arguments. After all, quantum computers are generally thought to provide an exponential speed up in solving certain problems [Nielsen and Chuang (2000)], so the threshold problem size needed to overtake the limitations of intrinsically slow quantum logic operations is not so large. Unfortunately, the sort of problems for which such a speed up exists have no obvious application to a biological organism. Basically, the problems quantum computers are really good at are number theoretic in nature. Instances of these problems, such as factoring large semi-prime numbers, form the basis of modern cryptography as used millions of times a day on

the internet (RSA encryption). If it were not for this fact, such problems would be regarded as mathematical curiosities. Do enthusiasts for biological quantum computing imagine that animals evolved the ability to send RSA-encrypted messages to one another, and subsequently evolved the means to eavesdrop by quantum computing?

To be fair, there are problems of more general use that quantum computers can attack using the Grover search algorithm [Grover (1996)] and its relatives [Nielsen and Chuang (2000)]. Grover's algorithm is sometimes described as being useful for "searching a database", suggesting that, for example, it would help one find a person in an (alphabetically ordered) phonebook if all one had was their phone number. This is a misconception. The Grover algorithm is an important quantum algorithm—indeed it was one of the breakthrough results—but it cannot search a classical database. What it requires is a quantum database: a fixed, fully hard-wired database-"oracle", a black box that is "called" in the process of the quantum algorithm. Nevertheless, Grover's algorithm and its relations may be applied to hard problems, such as finding good routes in a network, that would conceivably be useful to an animal. Unfortunately, the speed-up offered by Grover's algorithm on such problems is at best quadratic. Moreover, it has been proven that no algorithm can do better than Grover's algorithm. Thus quantum computers make no difference to the complexity class of these problems. The lack of an exponential speed-up means that the threshold problem size for any speed-up at all is very large. This makes it exceedingly unlikely that evolution could have made the leap to large-scale quantum computing.

17.4. Quantum Computing in Genetics

17.4.1. *Quantum search*

If not in the brain, then perhaps coherent quantum effects, or even fully fledged quantum computations, are operating behind the scenes at the microscopic level of our genes [Davies (2004a)]. It has been argued that the genetic code contains evidence for optimization of a quantum search algorithm. Again, this is intriguing idea, and it may not be possible at the present stage to definitively rule it out. Here we argue, however, that the case for such an idea is, if anything, weaker than that for quantum computing in the brain.

The argument formulated, albeit cautiously, in Patel (2001) in favour of quantum effects to play a role in genetics, is to a large extent based on suggestive numbers that are involved: On the one hand, the genetic code is based on triplets of nucleotides of 4 varieties that code for 20 or 21 amino acids. On the other hand, the optimal number Q of sampling operations in Grover's algorithm on an unsorted database of N objects is given by $Q = 1$ for $N = 4$ and $Q = 3$ for $N = 20$ or $N = 21$. This might appear indeed as a remarkable coincidence of numbers.

But then, some caution is appropriate: To start with, the role of Q and N is very different. More convincing as an argument against a connection, however, is probably the observation that $3, 4, 20, 21$ also appear, say, in the sequence of numbers which appear the same[6] when written in base 5 and base 10/2. This is easily revealed by using the On-Line Encyclopedia of Integer Sequences of AT&T Research [AT&T (2006)]. It is an interesting and educational pastime to see how essentially every finite sequence of integer numbers that one can possibly come up with appears in, for example, the "number of isolated-pentagon fullerenes with a certain number of vertices", or the "decimal expansion of Buffon's constant". The sequence $2, 4, 6, 9$ in this order, to consider a different random example, appears in no fewer than 165 (!) listed integer sequences, each of which is equipped with a different construction or operational meaning. The lesson to learn is that one should probably be not too surprised about coincidences of small tuples of integers.

Moreover, as has been emphasized above, Grover's search is not an algorithm that sorts a database given as a number of objects following the laws of classical mechanics: One needs a hard-wired oracle, following the rules of quantum mechanics between all involved objects throughout the computation [Grover (1996)]. It is difficult to conceive how such a hard-wired coherent oracle would be realized at the genome level. The optimal improvement in the sampling efficiency, in turn, would be of the order of the square root of N. It does seem unlikely that the overhead needed in a reliable quantum computation, possibly even enhanced by error correction requiring again an enormous overhead, would by any figure of merit be more economical than, say, a simple doubling of the waiting time in case of $N = 4$.

[6]To represent a given number in base b, one proceeds as follows: If a digit exceeds b, one has to subtract b and carry 1. In a fractional base b/c, one subtracts b and carries c.

17.4.2. *Teleological aspects and the fast-track to life*

One of the most interesting open questions at the interface of the biological and physical sciences is the exact mechanism that led to the leap from complex molecules to living entities. The path from a non-living complex structure to one of the possible living structures may in some way be a regarded as a search procedure, the number of potential living structures being likely a tiny subset of all possible ones consisting of the same constituents [Davies (2004a)]. Now, how has nature found its way to this tiny subset? Needless to say, we have very little to say about this key question. In this subsection, we merely cautiously warn that whatever the mechanism, the involvement of quantum superpositions to "fast-track" this search again in the sense of a quantum search appears implausible.

When assessing the possibility of quantum search here one has to keep in mind that quantum search is, once again, not just a quantum way of having a look in a classical database of options: Necessarily, the coherence must be preserved. This means that in the search, the figure of merit, the oracle, needs to be hard-wired. This oracle has to couple to all subspaces corresponding to all different options of developments. What is more, there is a teleological issue here: It is not entirely clear what the search algorithm would be searching for. The figure of merit is not well defined. If a search is successful, life has been created, but what features does life have? Arguably, this might be linked to the structure being able to reproduce. But again, this figure of merit could only be evaluated by considering subsequent generations. Thus it seems that it would be necessary to preserve a coherent superposition through multiple generations of such structures, which we would argue is particularly implausible.

17.5. Quantum Consciousness

17.5.1. *Computability and free will*

Recent years have seen significant advances in the understanding of neural correlates of consciousness [Koch (2004)]. Yet, needless to say, the understanding of consciousness on the biological elementary level is not sufficiently advanced to decide the case of quantum mechanics playing a role or not in consciousness, beyond the obvious involvement of ruling the underlying physical laws. Hence, any discussion on the role of quantum mechanics in form of long-range entanglement in the brain or in actual realistic

collapses of wave-functions is necessarily of highly speculative character. Here, we limit ourselves to addressing arguments put forward in the public debate that triggered the publication of this book, and warn of the possibility of fallacies in some of these arguments.

Where could quantum mechanics play a key role in consciousness? Hameroff argued in the debate, based on an earlier proposal put forth in Hameroff and Penrose (1996), that the gravitational induced collapse of the wave-function is eventually responsible for conscious acts. Moreover, microtubules forming the cytoskeleton of neurons should be the right place to look for such state reductions. These reductions should be realistic, actually happening state reductions, in what is called an orchestrated objective reduction (Orch-OR).

This is interesting, but also dangerous territory. To start with, it does not refer to the established physical theory of quantum mechanics as such [Grush and Churchland (1995); Penrose and Hameroff (1995)]. The motivation for this approach is to seek a way for human consciousness to be noncomputable, in order to differentiate it from mere computation as performed by artificial intelligence machines (see also Sec. 17.6). But computability and noncomputability are the same in quantum computer science as in classical computer science. Thus Penrose and Hameroff must appeal to a new theory of nature that may allow for noncomputable physical effects. They speculate that the key feature of this new theory would result from unifying quantum mechanics with general relativity (i.e. gravity).

There is no generally accepted theory of quantum gravity. Hence, to invoke a realistic collapse in this sense bears the risk that the debate is pushed into a dark corner where everybody simply has to admit that he or she has no proper understanding what is happening there: "Ha, I told you that you do not know the answer!" In the debate, Hameroff invoked the

> "[...] hypothesis of quantum gravity, which is the only way out of us being helpless spectators,"

(that is, the only way to prevent our thoughts from being computable). The mere wish that gravity could leave a loophole for free will does not seem to us to be a very strong argument for this hypothesis. Finally, it should be pointed out that there is essentially no experimental evidence for any sort of information processing in microtubules, still less quantum information processing, and yet less again for noncomputable quantum gravitational information processing.

17.5.2. *Time scales*

Invoking quantum gravity also leads to confusions in the comparison of time scales relevant for coherent quantum effects. In the debate, Hameroff said:

> "One of these guys [on the affirmative team] mentioned that how seemingly ludicruous it is to bring in quantum gravity because it is 24 orders of magnitude lower than decoherence.[7] However, in Roger's scheme the reduction is instantaneous so the power is actually calculated as a kilowatt per tubulin protein."

To this Zeilinger (also on the negative team) asked

> "But why don't we all boil if it is a kilowatt?"

to which the response was

> "Because it is only over a Planck time 10^{-42} seconds."

These statements refer to the postulated Orch-OR time scale of state vector reduction. The relevant decoherence time scales are given in Hagan, Hameroff, and Tuszyński (2002); this collection of numbers contains on the one hand estimates for environment-induced decoherence times, for example of a superposition of neural firing (10^{-20} seconds). On the other hand, it gives the time scale of superposition decay in Orch-OR, 10^{-4}–10^{-5} seconds. Based on these numbers, the obvious conclusion would be that, since the gravitationally induced Orch-OR time scale is so much slower than decoherence, the former process will be basically irrelevant.

What is more, the status of these two numbers is very different: The environment-induced decoherence time scale is calculated with the help of standard quantum mechanics as could be taught in any second year quantum mechanics course. In contrast, the number on Orch-OR derives from a speculative reading of what effects quantum gravity could possibly play here. In this figure in Hagan, Hameroff, and Tuszyński (2002), these two numbers are put together on the same footing, written in the same font size. There is nothing wrong with openly speculating, and the presented approach is not necessarily wrong or uninteresting. But it can become problematic when the right disclaimers are not put in the right places, where speculation on time scales of a potential theory of gravity are discussed

[7] For an actual comparison of the relevant time scales, see Hagan, Hameroff, and Tuszyński (2002).

with the same words and on the same footing as an elementary standard quantum mechanics calculation. Regarding the status of the 10^{-4}–10^{-5} seconds it is not even entirely clear what object it refers to. Also, the fact that the conscious thinking process occurs on similar time scales to this hypothetical Orch-OR, does not make the processes causally linked. To make that link is to risk introducing a rather postmodern tone into the debate, where "anything goes".

17.6. Quantum Free Will

17.6.1. *Predictability and free will*

As mooted in the Introduction, there is a relation between life and quantum physics that may motivate a philosopher, if not a biologist, to try to understand advanced quantum physics. This is the fact that quantum physics implies an in-principle distinction between (classical) digital computers and human brains: the behaviour of the former is predictable, while that of the latter is not. Note that we are not just making the obvious observation that in practice the actions of human beings are unpredictable; we are making the stronger statement that no matter how well you observed your neighbour (and your neighbour's surroundings), with the help of any level of technology, and how well you understood them, with the help of any level of computing power (including quantum computers!), you could not predict precisely how they would respond to a given stimulus (such as your kicking a ball into their yard) at some point in the sufficiently distant future.

Digital computers are designed to have deterministic outputs for a given input. Apart from hardware errors, which happen very infrequently, the output of computer is completely predictable simply by feeding the input into an identically designed machine. Human brains are not designed at all, but more to the point they are analog devices. Moreover, they are extremely complicated systems, comprising roughly 10^{11} neurons, each electrically connected with varying strength to many other neurons. And each neuron is a non-trivial element in itself, with complex biochemical reactions determining how it responds to its stimuli. Thus there is every reason to expect the brain to be a chaotic system, in that a small difference to the initial microscopic conditions of the brain would be amplified over time so as to lead to macroscopically different behaviour (such as kicking the ball back, or throwing it back).

The above argument does not yet establish an in-principle difference between brain and computer, because in principle it would seem that a sufficiently advanced technology would allow you to know the microscopic state of your neighbour's brain (and the microscopic state of their body and other surroundings) to any degree of accuracy, so that in principle its state at some fixed future time could be be predicted to any degree of accuracy. What prevents this is of course quantum mechanics: it is impossible to know precisely the position and momentum of a particle. Under chaotic dynamics, this microscopic quantum uncertainty will be amplified up to macroscopic uncertainty. Even for a huge system with few degrees of freedom—Saturn's moon Hyperion —the time taken for its orientation to become completely unpredictable according to quantum mechanics is only 20 years [Zurek (1998)]. For a far smaller and far more complex system such as the human brain, we would expect this time to be far, far smaller—see also Dennett (1984).

Thus quantum mechanics implies that, even if artificial intelligence were realized on a classical digital computer, it would remain different from human intelligence in being predictable. Of course this does not mean artificial intelligence would be deficient in any aspect of human intelligence that we value, such as empathy or the ability to write poetry. However, such an artificial intelligence would lack free will, at least in the following operational sense: If it thought that it had free will, then it would make the wrong decision in Newcomb's problem (see Chapter 14), by thinking that it could outwit a Predictor of its behaviour [Nozik (1969)]. For humans, by contrast, the above arguments imply that such a Predictor cannot exist, except as a supernatural being (a case we have no call to address).

17.6.2. *Determinism and free will*

Having made this distinction between human brains and deterministic digital computers, it is important to note that the above arguments do *not* mean that human brains are non-deterministic (still less that they are uncomputable, as Penrose feels they must be [Penrose (1990)]). The reason is that determinism and in-principle predictability are not the same things. There are deterministic theories in which systems are unpredictable even in principle because there are in-principle limitations on how much any physical observer can find out about the initial conditions of the system. Moreover, these theories are not mere philosopher's toys. One of the more popular interpretations of quantum mechanics, known as Bohmian mechan-

ics [Bohm (1952); Bohm and Hiley (1993); Holland (1993); Cushing *et al.* (1996)], is just such a theory.[8]

In the Bohmian interpretation of quantum mechanics, quantum particles have definite positions that move guided by the universal wave-function Ψ. The latter evolves according to Schrödinger's equation; it never collapses. All that "collapses" is an observer's knowledge of the positions of particles, and this "collapse" is nothing but Bayesian updating based on correlations between the particles in the system of interest and the particles from which the observer is constituted (and on which the observer's consciousness supervenes). Because of the way the particles' motion is guided by Ψ, it can be shown that the observer's knowledge of the position x of a particle for some system is limited by quantum uncertainty in exactly the same way as in orthodox quantum mechanics. But, since Bohmian mechanics is a deterministic theory, probability enters only through observer's lack of knowledge about the position of particles, due in part to their chaotic motion [Valentini (1991)].

In the biological context, this interpretation says that the behaviour of humans is determined, by the initial positions of the particles in the person's brain, and its environment. The latter is naturally regarded as a random influence, while the former is more naturally regarded as the source of an individual's will. It is impossible for an outside observer, no matter how skilled, to find out precisely the positions of the particles in an individual's brain, without making a precise quantum measurement of the positions. Such a measurement would instantly destroy the brain by creating states with unbounded energy. Thus, in the Bohmian interpretation, the actions of an individual derive from the physical configuration of their brain, but quantum mechanics makes this configuration unknowable in-principle to anyone else. For compatibilists,[9] the picture offered by Bohmian mechanics—a deterministic yet unpredictable *quantum free will*—may be an appealing one.

Acknowledgements

HMW acknowledges discussion with Eric Calvalcanti regarding free will in quantum mechanics. HMW was supported by the Australian Research

[8]Please note that the following discussion only reflects the opinions of one of us (HMW).

[9]That is, those who hold that determinism is compatible with—or even a precondition of—free will [Dennett (1984)].

Council Federation Fellowship scheme and Centre for Quantum Computer Technology, and the State of Queensland. JE was supported by the DFG, Microsoft Research, the EPSRC, and the EURYI Award Scheme.

References

Aliferis, P., Gottesman, D., and Preskill J. (2006). Quantum accuracy threshold for concatenated distance-3 codes, *Quant. Inf. Comput.* **6**, pp. 97–165.

Aharonov, A., and Ben-Or, M. (1998). Fault-tolerant quantum computation with constant error, *Proc. 29th Ann. ACM Symp. on Theory of Computing, New York, ACM* p. 76.

AT&T Research, *On-Line Encyclopedia of Integer Sequences*, `http://www.research.att.com/ njas/sequences/Seis.html`.

Barrow J. D., and Tipler F. J. (1986). *The Anthropic Cosmological Principle* (Oxford University Press).

Bohm, D. (1952). A suggested interpretation of the quantum theory in terms of "hidden" variables, I and II, *Phys. Rev.* **85**, pp. 166–93.

Bohm, D., and Hiley, B. J. (1993). *The Undivided Universe: An Ontological Interpretation of Quantum Theory* (Routledge).

Brookes, J. C., Hartoutsiou, F., Horsfield, A. P., and Stoneham, A. M. (2007). Could humans recognize odor by phonon assisted tunneling?, *Phys. Rev. Lett.* **98**, art. no. 038101.

Cederbaum, L. S., Gindensperger, E., and Burghardt, I. (2005). Short-Time Dynamics Through Conical Intersections in Macrosystems, *Phys. Rev. Lett.* **94**, art. no. 113003.

Cushing, J. T., Fine, A., and Goldstein S. (eds.) (1996). *Bohmian Mechanics and Quantum Theory: An Appraisal* (Kluwer).

Davies, P. C. W. (2004). Does quantum mechanics play a non-trivial role in life?, *BioSystems* **78**, pp. 69–79.

Davies, P. C.W (2004). Emergent biological principles and the computational properties of the universe, *Complexity* **10**, pp. 11–15.

Davies, P. (1999). *The Fifth Miracle* (Penguin Press).

Dawkins, R. (2004). *The Ancestor's Tale: A Pilgrimage to the Dawn of Life* (Weidenfeld and Nicholson).

Dennett, D. (1984). *Elbow Room: The Varieties of Free Will Worth Wanting* (MIT Press).

Dennis, E., Kitaev, A., Landahl, A., and Preskill, J. (2002). Topological quantum memory, *J. Math. Phys.* **43**, pp. 4452–4505.

Dürr, D., Goldstein, S., and Zanghì, N. (1996). Bohmian Mechanics as the Foundation of Quantum Mechanics, pp. 21–44 in Cushing *et al.* (1996).

Eigen M., and Oehlenschlager, F. (1997). 30 years later—a new approach to Sol Spiegelman's and Leslie Orgel's in vitro evolutionary studies, *Orig. Life Evol. Biosph.* **5-6**, pp. 437–57.

Eisert, J. (2004). Exact decoherence to pointer states in free open quantum systems is universal, *Phys. Rev. Lett.* **92**, p. 210–401

Gardner, M. (1986). *WAP, SAP, PAP AND FAP*, The New York Review of Books, May 8.

Gilmore, J., and McKenzie, R. H. (2005). Spin boson models for quantum decoherence of electronic excitations of biomolecules and quantum dots in a solvent, *Journal of Physics: Condensed Matter* **17**, pp. 1735–46.

Grover, L. K. (1996). A fast quantum mechanical algorithm for database search, in *Proceedings of the 28th Annual ACM Symposium on the Theory of Computing*, p. 212.

Grush R., and Churchland P. S. (1995). Gaps in Penrose's toilings, *Journal of Consciousness Studies* **2**, pp. 10–29.

Hackermüller, L., Uttenthaler, S., Hornberger, K., Reiger, E., Brezger, B., Zeilinger, A., and Arndt, M. (2003). Wave nature of biomolecules and fluorofullerenes, *Phys. Rev. Lett.* **91**, art. no. 090408.

Hagan, S., Hameroff, S. R., and Tuszyński, J. A. (2002). Quantum computation in brain microtubules: Decoherence and biological feasibility, *Phys. Rev. E* **65**, art. no. 061901.

Hameroff S. R., and Penrose, R. (1996). Conscious events as orchestrated spacetime selections, *Journal of Consciousness Studies* **3**, pp. 36–53.

Helms, V. (2002). Electronic excitations of biomolecules studied by quantum chemistry, *Current Opinion in Structural Biology* **12**, pp. 169–75.

Holland, P. R. (1993). The de Broglie-Bohm theory of motion and quantum field theory, *Phys. Rep.* **224**, pp. 95–150.

Kacian, D. L, Mills, D. R., Kramer, F. R., and Spiegelman, S. (1972). A replicating RNA molecule suitable for a detailed analysis of extracellular evolution and replication, in *Proceedings of the National Academy of Sciences* **69**, art. no. 303842.

Koch, C. (2004). *The Quest for Consciousness: A Neurobiological Approach* (Englewood, Colo., Roberts and Co.).

Kohen A., and Klinman, J. (1999). Hydrogen tunneling in biology, *Chemistry and Biology* **6**, pp. R191–8.

Nielsen M. A., and Chuang, I. L. (2000). *Quantum Computation and Quantum Information* (Cambridge University Press).

Nozick, R. (1969). *Newcomb's Problem and Two principles of Choice*, pp. 115–46. of *Essays in Honor of Carl G. Hempel*, ed. Nicholas Rescher, Synthese Library (Reidel, D. Netherlands).

Patel, A. (2001). Why genetic information processing could have a quantum basis, *J. Biosci.* **26**, p. 145–151.

Parsegian, V. A. (2005). *Van der Waals Forces: A Handbook for Biologists, Chemists, Engineers, and Physicists* (Cambridge University Press).

Penrose, R., and Hameroff, S. (1995). Reply to Gaps in Penrose's toilings, *Journal of Consciousness Studies* **2**, pp. 98–111.

Penrose, R. (1990). *The Emperor's New Mind* (Vintage).

Rosa, L. P., and Faber, J. (2004). Quantum models of the mind: Are they compatible with environment decoherence?, *Phys. Rev. E* **70**, art. no. 031902.

Schadé, J. P., and Ford, D. H. (1973). *Basic Neurology, 2nd ed.* (Elsevier).
Shor, P. W. (1995). Scheme for reducing decoherence in quantum computer memory, *Phys. Rev. A* **52**, p. 2493.
Steane, A. (1996). Error-correcting codes in quantum theory, *Phys. Rev. Lett.* **77**, p. 793.
Sumper M., and Luce, R. (1975). Evidence for de novo production of self-replicating and environmentally adapted RNA structures by bacteriophage Qβ replicase, *Proceedings of the National Academy of Sciences* **72**, pp. 162–166.
Susskind, L.(2005). *The Cosmic Landscape: String Theory and the Illusion of Intelligent Design* (Little Brown and Company).
Tegmark, M. (2000). Importance of quantum decoherence in brain processes, *Phys. Rev. E* **61**, pp. 4194–4206.
Valentini, A. (1991). Signal-locality, uncertainty, and the subquantum H-theorem (part I), *Phys. Lett. A* **156**, pp. 5–11; ibid. (part II) **158**, pp. 1–8.
Zanardi P., and Rasetti, M. (1997). Noiseless quantum codes, *Phys. Rev. Lett.* **79**, p. 3306.
Zurek, W. H. (1998). Decoherence, chaos, quantum-classical correspondence, and the algorithmic arrow of time, *Physica Scripta* **T76**, pp. 186–98.
Zurek, W. H. (2003). Decoherence, einselection, and the quantum origins of the classical, *Rev. Mod. Phys.* **75**, p. 715.

About the authors

Howard Wiseman is a theoretical quantum physicist. His principle interests are quantum measurements, quantum feedback control, quantum information, fundamental questions in quantum mechanics, and open quantum systems. He completed his PhD under Gerard J. Milburn at the University of Queensland in 1994, and then undertook a a postdoc under Dan Walls at the University of Auckland. Since 1996 he has held Australian Research Council research fellowships. He is currently Professor and Federation Fellow at Griffith University, where he is the Director of the Centre Quantum Dynamics. He is also a Program Manager in the ARC Centre for Quantum Computer Technology. He has over 120 refereed journal papers, and his awards include the Bragg Medal of the Australian Institute of Physics, the Pawsey Medal of the Australian Academy of Science and the Malcolm Macintosh Medal of the Federal Science Ministry.

Jens Eisert is a lecturer and holder of the European Young Investigator Award at Imperial College London in the UK (Diploma, University of Freiburg, Germany; MSc, University of Connecticut, USA; PhD, University

of Potsdam, Germany). His research interests are in quantum information science and related fields: This includes formal aspects of entanglement theory and computational models, as well as quantum optical implementations and the study of complex quantum systems.

This page intentionally left blank

Chapter 18

That's Life!—The Geometry of π Electron Clouds

Stuart Hameroff

18.1. What is Life?

Historically, two broad approaches have attempted to characterize the essential nature of living systems: 1) functional emergence, and 2) vitalism.

Functionalism characterizes life by its organizational arrangements leading to purposeful behaviours,[1] implying that non-biological systems which exhibit at least some of these behaviours may be considered living. For example certain types of self-organizing computer programs have life-like functions, and "artificial life" proponents view such systems as alive [Langton (1991)].

But living systems seem to have an essential uniqueness, often ascribed to an *emergent* property of biochemical and physiological processes. Emergence implies a hierarchical organization in which a novel property (e.g. life) arises from complex interactions of relatively simple components at lower, reductionist levels. As weather patterns and candle flames emerge from complex interactions among simple gas and dust particles, life is said to emerge from complex interactions among biomolecules, ions and atoms [Scott (1995)]. However biomolecules are not simple, and emergent

Received May 1, 2007

[1] 1) self-organization, 2) homeostasis (maintaining a steady-state internal environment), 3) metabolism (energy utilization), 4) growth, 5) adaptive behaviour, 6) response to stimuli, 7) replication/reproduction and 8) evolution. Adapted from [Margulis and Sagan (1995)].

phenomena like candle flames and weather patterns manifest self-organization, homeostasis and adaptive behaviours. Are *they* also alive?

Functionalist and emergent approaches based on simple reductionism dominate molecular biology. An historical, opposing viewpoint is that such descriptions fail to capture a fundamental (i.e. non-emergent) essential uniqueness, or "unitary one-ness" specific to living systems. Many nineteenth-century scientists ascribed this quality to a "life force," "elan vital," or energy field: "vitalism" (or "animism"). But as molecular biology revealed biochemical and physical processes involved in cellular activities, vitalism fell from favour. The notion of a life force or field has become almost taboo in modern science—although fields apparently organize mitosis, [Karsenti and Vernos (2001)]. Nineteenth-century vitalism was based either on electromagnetism or on forces outside the realm of science. Quantum mechanics was as yet undiscovered.

In his famous book "*What is Life?*" quantum pioneer Erwin Schrödinger (1944) suggested a quantized basis for living systems, concluding that life's essential framework was in "aperiodic lattices".[2] Schrödinger's description applies to DNA and RNA, and also to cytoskeletal protein assemblies such as microtubules and actin gels that extend throughout cell volumes. Schrödinger suggested further that globally unified behaviour inherent in living systems might involve non-local quantum correlations among biomolecules (see the Foreword by Penrose).

The conventional wisdom in modern science is that biological systems are too "warm, wet, and noisy" for seemingly delicate quantum processes, i.e. that "decoherence" precludes supra-molecular or systemic roles. However recent evidence suggests otherwise, that biomolecules can harness heat and energy to promote functional quantum states, rather than cause decoherence [Engel *et al.* (2007); Ouyang and Awschalom (2003)].

Since Schrödinger's time scientists, including Szent-Györgyi (1960), Pullman and Pullman (1963), Fröhlich (1968, 1970, 1975), Conrad (1994) and others, have in various ways proposed that life is related to organized quantum processes in π electron resonance clouds within biomolecules. For example Fröhlich suggested that living systems utilize heat and biochemical energy to pump quantum coherent dipole states in geometrical arrays of non-polar π electron resonance clouds in protein lattices. Russian biochemists Alberte and Phillip Pullman described cooperative π electron resonance as *the* essential feature of living systems.

[2]In geometry, "aperiodic tiling" of a plane. A shifted copy of such a tiling matches only locally with its original. The best known examples are Penrose tilings, described by Sir Roger Penrose.

In today's terms it is proposed that life involves cooperative quantum processes in geometric lattices of non-polar π electron resonance clouds. Such π clouds are isolated from cell water and ions, buried within non-polar subspaces of components of biomolecular assemblies, e.g. membranes, microtubules, nucleic acids and organelles. In each π cloud, electron dances known as quantum London forces (a type of van der Waals force) govern local nanoscale biomolecular conformational states.

In repetitive structures like the cytoskeleton and DNA, π clouds arrayed in specific periodic and aperiodic lattice geometries are separated by less than two nanometres and thus conducive to electron tunnelling, exciton hopping, long-range classical, and non-local quantum processes, e.g. entanglement, superposition, and quantum computation [Hameroff and Tuszynski (2003); Hameroff (2004)]. In particular, cytoskeletal-based quantum processes can couple to biomolecular mechanical resonances, and extend throughout cell volumes and possibly between cells and throughout organisms via tunnelling through gap junctions [Hameroff (1997)]. Thus geometric distributions of non-polar π electron clouds can enable a collective, cooperative quantum process—a unitary wave function—mediating perception and governing purposeful behaviour of living organisms.

That's life.

18.2. Protoplasm: Water, Gels and Solid Non-polar Regions

Living cells are composed of protoplasm, which in turn consists of cytoplasm—the internal, aqueous cell milieu—as well as structures in and around cytoplasm, e.g. membranes, organelles, nucleic acids and protein assemblies.

Comprising sixty percent water, a cytoplasm alternates between two or more aqueous polar forms. One is a liquid electrolyte solution ("sol") which may rapidly change to a quasi-solid "gel" upon polymerization of actin proteins, as water molecules become aligned and ordered on actin surfaces.

More solid structures including membranes, protein assemblies and nucleic acids are embedded in and around sol or gel cytoplasm. Buried and isolated within these structures are specific non-polar regions, e.g. water-excluding confluences of oil-like aromatic ring structures consisting largely of π electron resonance clouds. Within these isolated regions, quantum processes occur.

Here we consider the three types of media that comprise protoplasm:

Liquid cytoplasm: Aqueous solutions are characterized by H_2O molecular dipoles with different electrical charges on opposite ends, or "poles".[3] Positive poles of each water molecule happily interact with negative poles of others in a stable liquid phase which is chaotic at the molecular level, water molecules adopting disordered configurations which maximize entropy.[4] Charged molecules or ions such as salt/sodium chloride easily dissolve in water via "hydrophilic" (water loving) polar interactions.[5] In such a polar, active aqueous medium, significant supra-molecular quantum states are highly unlikely.

Gel cytoplasm: Cytoplasm may also adopt "gel" phases upon polymerization of the ubiquitous and versatile cytoskeletal protein actin which self-polymerizes to form dense and complex filamentous networks. Negative charges are periodically arrayed on actin filament surfaces, attracting positive poles of water molecules and arranging them in ordered layers. This converts cell interior cytoplasm from a liquid solution ("sol") to a quasi-solid state gelatin ("gel"), such that living cytoplasm transiently exists as an ordered dipole field [Pollack (2001)]. Rapid sol-gel transitions drive "amoeboid" and other intracellular movements. Water molecules also become ordered, or aligned on charged surfaces of membranes, organelles or microtubules. In some situations, charged surfaces attract counter-ions, resulting in plasma-like Debye layers, e.g. on membrane and microtubule surfaces [Hameroff and Tuszynski (2003); Hameroff (2004)].

Solid structures—Hildebrand solubility λ: In and around liquid and water-ordered gel cytoplasm are solid structures including membranes, protein assemblies, organelles and nucleic acids. At smaller scales *within* these structures are "non-polar" regions comprised of molecules (or portions of molecules) which do not easily dissolve in water, e.g. oily compounds which form oil slicks on top of water puddles. These oily hydrophobic (water repelling) non-polar groups are electrically neutral and stabilized from within. They include cyclic carbon rings with delocalized electrons ("π electron resonance clouds") exemplified by benzene, also known as phenyl rings.

[3]Two positively charged hydrogen atoms protrude from one "pole", and one doubly negative charged oxygen protrudes from the other.

[4]Transient meta-stable H_2O complexes of varying geometry also occur.

[5]Types 1 and 2 van der Waals forces and hydrogen bonds.

The degree of non-polarity for a particular solvent is given by the Hildebrand solubility coefficient λ, a measure of the amount of energy needed for a dissolving molecule to break the van der Waals forces in a solvent.

18.3. Van der Waals Forces

Van der Waals forces are attractions or repulsions between atoms or molecules, differing from biochemical covalent forces (based on sharing of electrons), or ionic and electrostatic attractions (between opposite charges). Instead, van der Waals interactions occur between neutral electron clouds of non-polar atoms and molecules. They were discovered in the behaviour of gases.

In the 17th century British scientist Robert Boyle studied the relation between pressure, volume and temperature of a gas. He arrived at Boyle's law $PV = RT$ in which P is pressure, V is volume, R is a constant and T is temperature.[6] But measurement of actual gases showed smaller volumes than predicted. Numerous attempts failed to account for the discrepancy until an explanation by Dutch physicist Johannes Diderik van der Waals several hundred years after Boyle.

Van der Waals reasoned that the smaller volume was the result of an attraction among the gas molecules, "pulling" them together. Gas molecules and atoms are neutral with non-polar electron clouds. But such clouds are "polarizable"—dipoles may be induced within them. Van der Waals attractions and repulsions are based on dipole couplings of nearby electron clouds.

There are three types of van der Waals forces. The first occurs between permanent dipoles in polar molecules, like two tiny bar magnets attracting or repelling each other's opposite poles. The second type is between such a permanent dipole and a neutral atom or molecule with a non-polar (but polarizable) electron cloud. The permanent dipole induces a temporary dipole in ("polarizes") the non-polar electron cloud; the permanent and temporary dipoles then attract or repel each other depending on their relative positions.

The third type of van der Waals interaction is the London force that occurs between non-polar electron clouds of two or more neutral atoms, molecules or molecular groups (Fig. 18.1). London forces are instantaneous

[6]For one mole of a gas, P is in atmospheres, V is in litres, $R = 0.08207$, and T is temperature in degrees Kelvin.

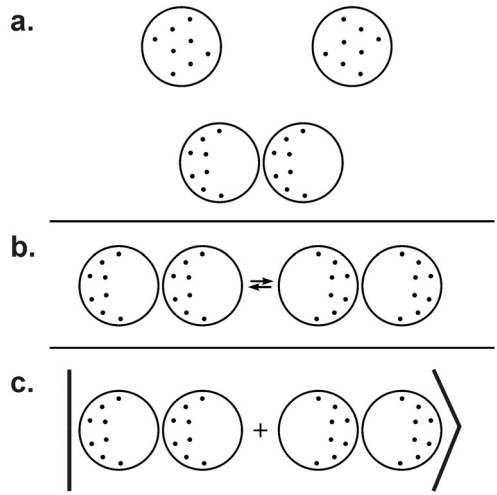


Fig. 18.1. The van der Waals (Type 3) London force. (a) Filled electron clouds of two neutral, non-polar atoms or molecular groups induce dipoles in each other; the mutually-induced dipoles then attract each other. (b) The coupled dipoles oscillate between different orientations. (c) Being quantum mechanical, the coupled dipoles can exist in quantum superposition of both orientations.

dipole couplings—electrons in one cloud repel those in the other, forming temporary dipoles. The dipoles then attract each other, leading to coupled dynamics.[7] The clouds are resonant, or probabilistic electron distributions, so London forces are inherently quantum mechanical, occurring in regions described by a low Hildebrand solubility coefficient λ.

Water, the most polar solvent, utilizes Types 1 and 2 van der Waals forces (and hydrogen bonds) and has a very high λ coefficient of 48 SI units.[8] In water, non-polar oily molecules such as benzene disrupt the entropy-maximized state and self-associate, being pushed together by water—the "hydrophobic effect"—and attracting each other by London forces. The

[7]London force attractions are exquisitely sensitive to distance, varying inversely with the 6th power of the distance between electron clouds. Thus the forces are small (though numerous) until clouds are almost adjacent. However if the clouds become too close and begin to overlap, even stronger repulsive forces occur which vary with the 12th power of the radius.

[8]Hildebrand Solubility Parameters: $\delta/\mathrm{MPa}^{1/2} = 2.0455 \times \delta/\mathrm{cal}^{1/2}\mathrm{cm}^{-3/2}$ Standard Hildebrand values from Hansen, *Journal of Paint Technology* Vol. 39, No. 505, Feb 1967 SI Hildebrand values from Barton, *Handbook of Solubility Parameters*, CRC Press, 1983 and Crowley, *et al. Journal of Paint Technology* Vol. 38, No. 496, May 1966. `http://sul-server-2.stanford.edu/byauth/burke/solpar/solpar2.html`

non-polar molecules aggregate into stable regions (λ equal to 18.7 SI units for benzene) shielded from polar interactions with water. Within such environments, Type 3 van der Waals-London forces play important roles in protein folding and conformational dynamics, protein-protein interactions, membranes and nucleic acid structure.

We can conclude that living protoplasm includes three types of phases: 1) liquid, 2) gel (with or without ordered water), and 3) solid structural phase (membranes, protein assemblies, nucleic acids, organelles). Within the latter, i.e. buried in interiors of solid structural phase components, are non-polar, hydrophobic oil-like regions of low δ, e.g. like that of benzene 18.7 SI units. Such regions occur as planes in membranes, as continuous cores or stacks in nucleic acids and as discrete pockets or islands within proteins. Non-polar regions are typified by benzene-like "oily" aromatic rings with π electron resonance clouds.

Oil slicks or bulk benzene bear no resemblance to living systems. But when discrete regions are arrayed in periodic (or aperiodic) geometric lattices (and particularly when cytoplasm adopts an ordered-water gel phase to minimize decoherence and extend non-polar lattice sites throughout cell interiors), π electron clouds have an opportunity for cooperative resonances, non-local interactions and quantum computation.

18.4. Kekule's Dream and π Electron Resonance

Life is based on carbon chemistry, including organic carbon ring molecules with electron resonance clouds in which London forces play significant roles. The flagship biomolecular organic structure is the phenyl ring, also known as benzene.

The hexagonal ring structure of benzene (and the field of organic chemistry) was discovered in a dream by the 19th century German chemist Friedrich August von Kekule. At that time, carbon atoms were known to have valence 4 (four electrons in the outer shell) and thus able to share electrons with four other atoms—form four covalent single bonds, e.g. with hydrogen or other carbons in hydrocarbon chains. Carbons can also use two valence electrons and form double bonds in which neighbouring carbons share two electrons, the extra, mobile electrons being known as π electrons. Hydrocarbons with only single bonds are called alkanes (methane, alkane etc.) and have the generic formula of C_nH_{2n+2}. Hydrocarbons with a carbon-carbon double bond and one π electron are known as alkenes and follow the formula C_nH_{2n} (Fig. 18.2).

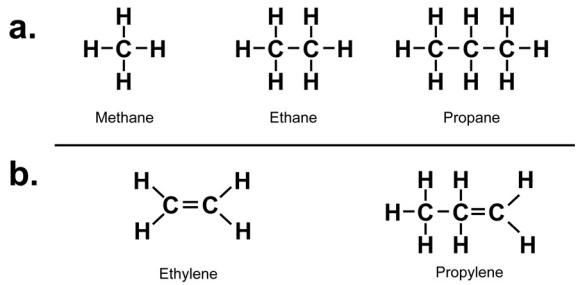


Fig. 18.2. (a) Alkanes with carbon-carbon single bonds and generic formula C_nH_{2n+2}. (b) Alkenes with one carbon-carbon double bond and π electron.

Kekule and his colleagues knew that benzene had the structure of C_6H_6, generically C_nH_n, and thus didn't fit in either alkanes nor alkenes. Plus benzene was far more hydrophobic ("oily") and water insoluble than alkenes and alkenes. While the C_6H_6 chemical formula of benzene was known, the structure was not. Finally, Kekule reported that he had a dream in which snakes of various lengths represented the different hydrocarbon chains and one snake swallowed its tail, forming a ring.[9] This, Kekule concluded, was benzene in which three carbon-carbon double bonds occur among the six carbons in the ring.

There are two alternative configurations of the three double bonds and π electrons among the six possible locations. Where are the extra π electrons? Two types of explanations approach the question. According to valence bond theory, the double bonds and π electrons shift locations, resonating between two equally stable configurations (Fig. 18.3a). As double bonds are shorter than single bonds, the carbon atoms are pulled and pushed slightly, vibrating with electron states. In valence bond theory, benzene is a linear superposition of wave functions of the two states.

In molecular orbital theory, π electrons are considered delocalized over the entire carbon ring, as toroidal π electron cloud orbitals above and below the plane of the hexagonal carbon ring, with carbon locations also slightly delocalized. Thus in both valence bond and molecular orbital approaches, the structure of benzene/phenyl rings is best described quantum mechanically and the electron locations represented as a ring (Fig. 18.3b).

[9]In *The Act of Creation*, Arthur Koestler called this "probably the most important dream in history since Joseph's seven fat and seven lean cows". The snake eating its tail is also represented in the mythical "Ourabouris".

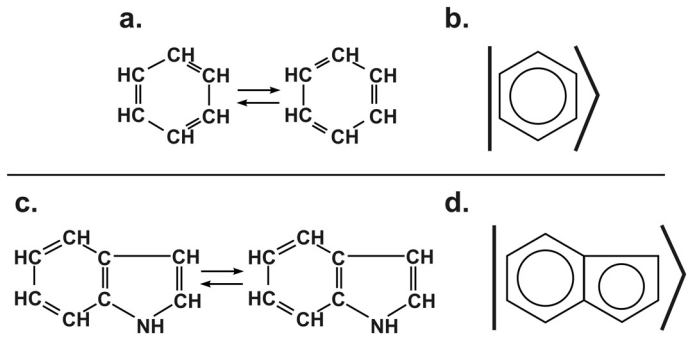


Fig. 18.3. (a) Benzene/phenyl structure with two possible electron configurations. The structure is said to resonate between the two states. (b) Quantum resonance representation of the two states. (c) and (d) Resonance states of the indole ring of tryptophan.

Benzene/phenyl rings, along with more complex indole rings (Figs. 18.3c and d), are often called aromatic rings[10] and comprise several amino acid side groups (e.g. phenyl rings of phenylalanine and tyrosine, and the indole ring of tryptophan). These are the aromatic amino acids.

Aromatic ring π electrons can also be excited into higher energy orbitals ("excited states") by absorption of photons of specific wavelengths. As the excited states return to lower energy ground states, photons are emitted as fluorescence. Becker *et al.* (1975) showed fluorescence resonance energy transfer between subunits in a microtubule lattice (i.e. photon transfer from tryptophan on one subunit to tyrosine on another).

Many biomolecules are amphiphilic—having both polar/hydrophilic and non-polar/hydrophobic regions.[11] For example components of lipid membranes, proteins and nucleic acids may have an oil-like, non-polar aromatic ring region at one end of a linear molecule, with the opposite end having polar charges.

Consider a toy amphiphilic biomolecule (Fig. 18.4) that can represent aromatic amino acids in proteins, lipids in membranes or nucleic acids in DNA and RNA. The biomolecule has a non-polar end consisting of a phenyl ring, and a polar end consisting of separated positive and negative charges.[12]

[10]Original preparations were fragrant, however the smell was found to come from contaminants.
[11]Hydrophobic is equivalent to lipophilic—highly soluble in a non-polar lipid medium.
[12]As in a carboxyl $COOH^-$.

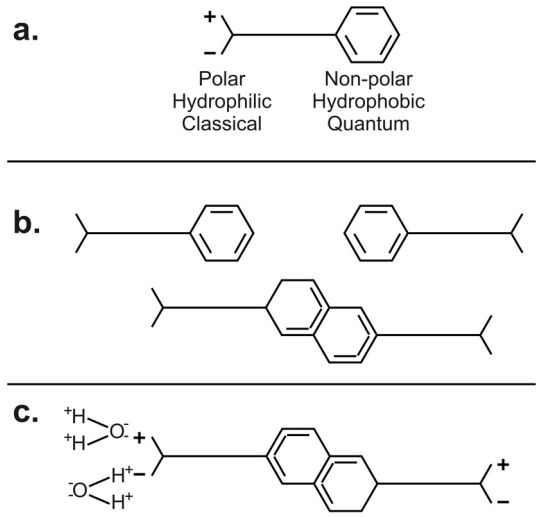


Fig. 18.4. (a) An amphiphilic toy biomolecule consistent with lipids in membranes, non-polar amino acids in proteins and nucleic acids in DNA and RNA. (b) Two amphiphilic biomolecules coalesce, driven by the hydrophobic effect and van der Waals London forces. (c) (Left) Polar ends of the amphiphilic biomolecule interact with water.

In aqueous solution, non-polar hydrophobic ends avoid the polar water environment, coalesce by the hydrophobic effect and, when close enough, attract each other by van der Waals London forces. Opposite end hydrophilic groups face outward into the polar, aqueous environment, stabilizing the hydrophobic core. This is rudimentary self-organization, precisely how membranes and proteins form.

Membranes are double layers of amphiphilic biomolecules (Fig. 18.5a). The planar internal region is non-polar and hydrophobic, and exteriors are polar and hydrophilic, interacting with water. Membranes allow compartmentalization of cells and internal regions, and with ion channels, pumps and other proteins regulate the cell milieu. But lipid membranes are rather fluid, not lattice-like, and may lack abilities to represent and control discrete information.

To be functionally significant, quantum states of π electron resonance clouds must couple to mechanical or chemical states of their host molecules, e.g. protein conformation. It appears that certain proteins may be optimally designed as quantum levers, amplifying quantum processes to exert causal efficacy in the classical world.

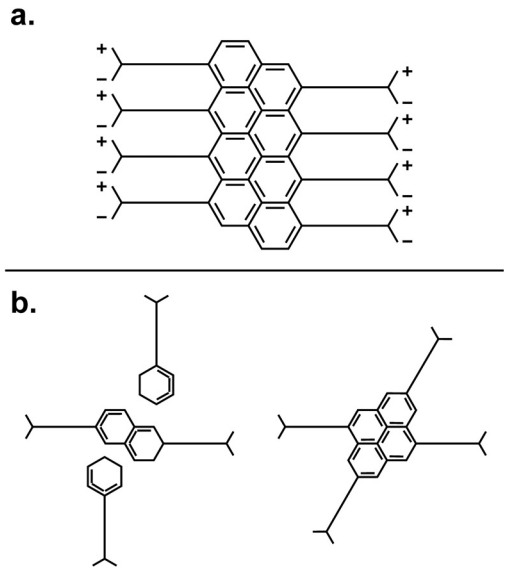


Fig. 18.5. (a) Amphiphilic biomolecules can form double layers, as in cell membranes, with an internal non-polar hydrophobic planar region and external polar, hydrophilic groups which interact with water. (b) Non-polar groups can coalesce to form pockets, as in proteins.

18.5. Proteins—The Engines of Life

Proteins are the molecular machines of living systems, exerting force and causing movement by changing shape, e.g. opening and closing of ion channels, bending and sliding of filaments in muscle, movement of motor proteins along microtubules, assembly of actin gel, grasping of molecules by enzymes and receptors, and flexing of tubulin subunits within microtubules. These coordinated and purposeful molecular movements are the currency of real-time living processes. Their organization and regulation are poorly understood, and lie close to the essential feature of living systems.

Proteins are produced as linear strings of amino acid molecules linked by chemical peptide bonds to form peptide chains. Twenty different amino acids comprise our proteins, each distinguished by a particular chemical "side group" (or "residue") attached to the peptide chain like charms on a bracelet. The specific sequence in which various amino acids are strung together is coded in our genes, and the number of possible sequences, and thus the number of possible proteins is enormous.

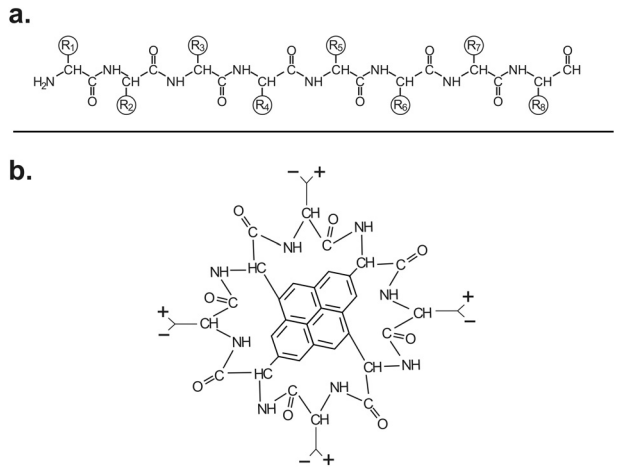


Fig. 18.6. (a) A linear chain of amino acids, each with a specific residue (R1-R8). (b) The chain folds as non-polar hydrophobic residues coalesce, interacting cooperatively by London forces.

But proteins do not remain as linear peptide chains. Because of van der Waals attractions and repulsions among various side groups, proteins "fold" into three dimensional conformational structures that minimize the protein's energy. The number of possible attractions and repulsions among side groups is huge, and predicting three dimensional conformation and energy minimum from amino acid sequence is a computational feat of colossal proportions. But proteins fold quickly using the hydrophobic effect and van der Waals forces (Fig. 18.5b, Fig. 18.6). During folding, non-local interactions among aromatic rings suggest quantum mechanical sampling of all possible folding pathways [Klein-Seetharaman *et al.* (2002)].

Once formed, protein 3-dimensional structure is stabilized and dynamically regulated in the aqueous phase by outwardly-facing polar side groups, and from within by non-polar regions. Coalescence of two or more non-polar amino acid side groups, e.g. a stack of two aromatic rings[13] form extended electron cloud regions called hydrophobic pockets with distinctively low λ (e.g. benzene-like) solubility values. The largest hydrophobic pockets are relatively small, ($\sim$0.3 cubic nanometers, roughly 1/100 to 1/30 the volume of single proteins) yet enable quantum London forces to regulate protein dynamical functions.

[13]Along with non-aromatic, non-polar amino acids including glycine, alanine and valine.

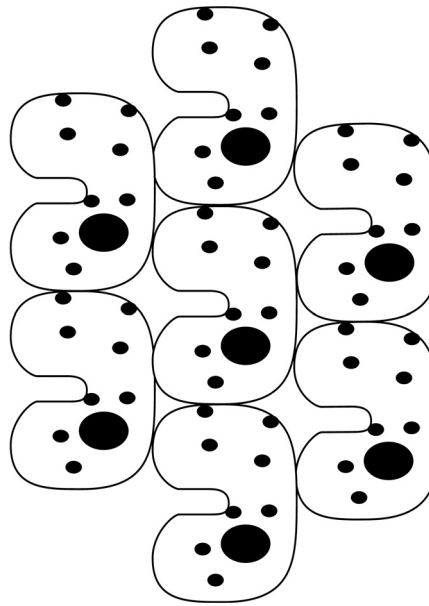


Fig. 18.7. Seven tubulin proteins in the skewed hexagonal lattice in microtubules (Figs. 8 and 9). Dark circles within each tubulin are non-polar regions, e.g. π electron clouds. Large circles are non-polar binding sites of the drug paclitel (taxol); small circles are sites of indole rings of tryptophan (from Hameroff, 2002), whose 3-d locations are here projected onto 2-d. Each tubulin is 8 nanometres by 4 nanometres by 4 nanometres, so non-polar π electron resonance regions are separated roughly by 2 nanometres.

One particular protein is tubulin, a 110 kiloDalton peanut-shaped dimer, which self-assembles into skewed hexagonal cylindrical lattices in microtubules (Figs. 18.7 and 18.8). Tubulin has one large non-polar region below the narrow "hinge,"[14] which binds anesthetic gas molecules, as well as the anti-cancer drug paclitaxel (Taxol), used to paralyze microtubules in out-of-control mitosis.[15] Tubulin has other smaller non-polar regions, for example 8 tryptophans per tubulin, with π electron-rich indole rings distributed throughout tubulin with separations of roughly 2 nanometres (Fig. 18.7).

Periodic placement of tryptophans and other non-polar π cloud regions within 2 nanometres of each other in microtubule subunits can enable

[14]Each tubulin is a "dimer" composed of alpha and beta monomers. The paclitaxel site is in the beta monomer, below the narrow hinge.

[15]Tubulins also bind non-polar anesthetic gas molecules, presumably in the same site at which paclitaxel binds.

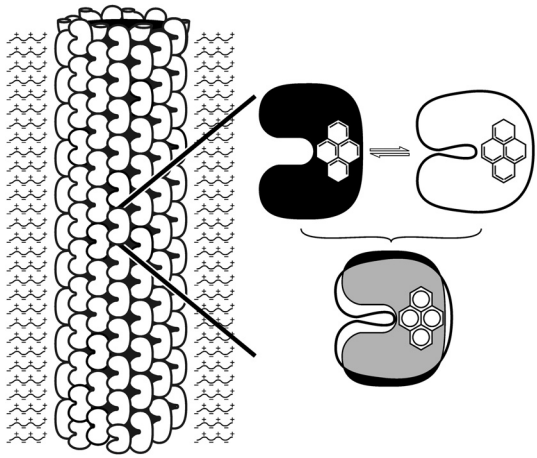


Fig. 18.8. A microtubule composed of peanut-shaped tubulin proteins (the microtubule is surrounded by a Debye layer formed by negatively charged tubulin C-termini and positively charged ions). Right, top: A single tubulin switches between two conformational states coupled to London force dipole states in a non-polar hydrophobic pocket. For simplicity, one large π cloud (4 rings) represents the nine or more shown in Fig. 7. Right, bottom: Quantum superposition of alternate conformations: tubulin as protein qubit.

electron tunnelling, "through-bond" exciton hopping or quantum coherence and entanglement. Conventional wisdom suggests that electron tunnelling or exciton hopping in proteins is only possible over distances under 1 nanometre. This is the "Förster distance" (maximum length of an excitation to travel). However the Förster distance pertains to free hopping via an inert medium like an ionic solution. Within proteins, electron movements may be facilitated by "through bond hopping" over distances of 2 nanometres or more, e.g. from π cloud to an adjacent π cloud in a non-polar phase. In some enzymes, electron hopping between amino acid residues may span 3.5 nanometres or more [Wagenknecht *et al.* (2000)].

In repetitive structures like the cytoskeleton, π clouds separated by less than two nanometres are in lattice geometries which extend throughout cell volumes. Thus electron tunnelling, exciton hopping, long-range classical and non-local quantum processes can lead to entanglement, superposition and quantum computation extending throughout cell volumes, and possibly between cells and throughout organisms via tunnelling through gap junctions [Hameroff (1997); Hameroff and Tuszynski (2003); Hameroff (2004)]. Moreover cytoskeletal-based quantum processes can couple to biomolecular mechanical resonances, as evidenced by simulated coherent phonon

resonances which match functional sites in microtubule lattice structure [Samsonovich *et al.* (1992)]. Thus geometric distributions of non-polar π electron clouds can enable a collective, cooperative quantum process—a unitary wave function—mediating perception and purposeful behaviour of living organisms through the governing of conformational states of individual proteins.

Proteins and their components move between different conformations/energy minima at multiple size and time scales. Amino acid side chains wiggle in femtoseconds (10^{-15} seconds), and longer time scale transitions last many seconds. Spontaneous global and functional protein transitions occur in the range from 10^{-6} to 10^{-11} seconds (microseconds to 10 picoseconds), with nanoseconds (10^{-9} secs) being a representative approximation.

Proteins have large energies with thousands of kiloJoules per mole available from amino acid side group interactions, but are only marginally stable against abrupt unfolding (i.e. exploding) by approximately 40 kiloJoules per mole. Consequently protein conformation is a "delicate balance among powerful countervailing forces" [Voet and Voet (1995)]. At least in some proteins, higher energy, longer time scale chemical and ionic bonds cancel out and London forces acting in hydrophobic pocket π electron clouds tip the balance; they are the switch or lever amplifying quantum electron states to choose conformations and energy minima.

Electron cloud states couple to protein nuclear motions (and thus conformation) via the Mossbauer recoil effect [Sataric *et al.* (1998); Brizhik *et al.* (2001)]. But because of the extremely small electron mass relative to nuclear protons and neutrons, the conformational movement due to recoil is slight: a one nanometre shift of a single electron moves a carbon atom by only 10^{-8} nanometres, the diameter of its nucleus.[16] However the electrical charge on each electron is equivalent in magnitude to that on each nuclear proton. Collectively acting London dipole forces are thus able to influence nuclear motion and protein conformation by charge movements and, to a lesser extent, recoil [Conrad (1994)].

Biophysicist Herbert Fröhlich (1968, 1970, 1975) proposed that fluctuating electron dipoles—London forces—in "non-polar regions" of proteins in geometrical lattices constrained in a voltage gradient (e.g. membrane or cytoskeletal proteins) would oscillate collectively, forming a laser-like quantum coherent state (essentially a pumped Bose-Einstein condensate). Some

[16]The Fermi length—also the separation distance for tubulin superposition in the Orch OR model.

evidence supports biological "Fröhlich coherence", for example in geometrically arrayed protein scaffoldings in photosynthesis [Engel *et al.* (2007)]. Additional support for the essential importance of London forces in non-polar hydrophobic protein pockets of π electron resonance clouds is the mechanism of anesthesia.

18.6. Anesthesia and Consciousness

When inhaled into the lungs, and then dissolving in blood and then brain at a specific concentration, anesthetic gas molecules have the remarkable property of selectively erasing consciousness while having very few effects on other brain and bodily functions. It turns out that anesthetic gases act solely via quantum London forces in hydrophobic pockets in a subset of brain proteins.

At the turn of the 20th century, Meyer and Overton showed that anesthetic potency of a wide variety of gas molecules correlated with their solubility in a non-polar, lipid-like medium of low Hildebrand solubility λ 15.2 to 19.3 SI Units, resembling olive oil and benzene.[17] Consciousness emanates from this low λ, non-polar medium.

After Meyer and Overton, the medium for anesthetic action (and thus consciousness) was assumed to be lipid membranes. But Franks and Lieb (1984) demonstrated that anesthetic gases act in protein hydrophobic pockets of low λ, binding by London forces. Other work demonstrated a cut-off effect; molecules expected to be anesthetic have no effect if they are larger than a critical sub-nanometre size threshold ($\sim$0.3 cubic nanometre). Anesthetic gases must be small enough to fit into π electron cloud pockets, blocking endogenous London forces that are, in some way, responsible for consciousness.

Other non-polar regions may be too small for anesthetic gas molecules, e.g. single aromatic rings, π electrons in alkenes and electron clouds in methyl groups. As consciousness is erased from large hydrophobic pockets, nonconscious quantum processes can continue among these smaller regions. Life goes on.

Mapping of intra-cellular regions according to Hildebrand solubility parameter λ would identify a non-polar, low λ phase in which London forces operate in π electron clouds. Included would be internal planar regions

[17]Lambda values of e.g. diethyl ether 15.4, chloroform 18.7, trichloroethylene 18.7 SI Units.

of lipid membranes, π electron stacks in DNA and RNA, and discrete hydrophobic pockets and smaller non-polar regions in proteins, including cytoskeleton. Because of their geometric distribution throughout cell volumes, we will consider primarily electron clouds in protein hydrophobic pockets in cytoskeletal protein assemblies.

18.7. Cytoskeletal Geometry: Microtubules, Cilia and Flagella

Cellular movements and activities including mitosis, growth and adaptive behaviours are organized by microtubules—self-assembling cylindrical protein polymers, which are the main girders in the cell's three dimensional cytoskeleton. But in addition to bone-like support, microtubules also appear to function as the cellular nervous system and on-board computer. In the 1950s neuroscientist Charles Sherrington (and in the 1970s biologist Jelle Atema) suggested microtubules and other cytoskeletal structures might process information.

Microtubules are hollow cylindrical polymers of individual peanut-shaped protein subunits called tubulin. The cylinders have internal hollow cores of 15 nanometre diameter, with an external diameter of 25 nanometres; lengths may vary from hundreds of nanometres to meters in the case of peripheral nerve axons. Thirteen filamentous tubulin chains ("protofilaments") align so that cylinder walls are slightly skewed hexagonal lattices (Fig. 18.7). Microtubule lattice geometry is suitable for computation if states of each tubulin correspond with information, i.e. bit states (Figs. 18.7 and 18.8). Neighbour interactions allow simulated microtubules to act as cellular automata and process information, with capacity for long term programming (memory) encoded in post-translational modifications of individual tubulins [Hameroff and Watt (1982); Hameroff (1987); Rasmussen *et al.* (1990)].

As computational lattices, microtubles are unique. Not only are they cylindrical with hexagonal lattices, but their skewed geometry results in winding pathways whose intersection on any protofilament reflects the Fibonacci series. Intersections of winding patterns coincide with attachment sites of microtubule-associated proteins ("MAPs") which interconnect microtubules to form 3-dimensional scaffoldings which determine particular cellular architecture, function and behaviour [Lee *et al.* (1986)]. Such MAP attachment patterns correspond with simulated coherent phonon resonances in microtubule lattice structure [Samsonovich *et al.* (1992)].

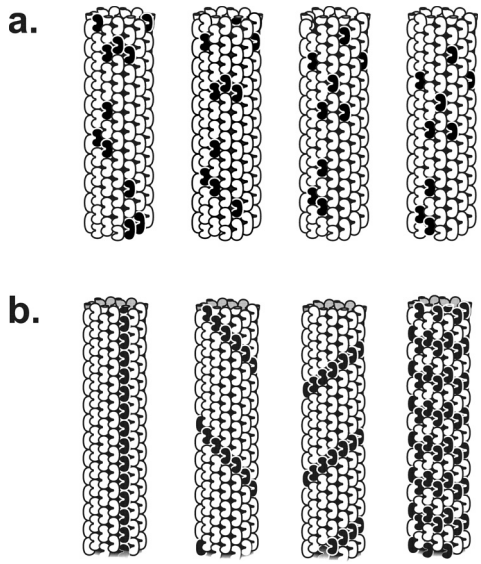


Fig. 18.9. (a) Classical cellular automata information processing model in microtubules based on neighbour dipole interactions (e.g. Rasmussen *et al.* 1990), (b) Winding patterns along adjacent tubulin dimers or monomers. Intersections of the patterns (not shown) match attachment sites of MAP proteins.

Microtubules in neuronal brain dendrites have a distinct and unique arrangement and play essential roles in brain functions. Penrose and Hameroff (1995); Hameroff and Penrose (1996a,b); Hameroff (1998a,b); Woolf and Hameroff (2001); Hameroff (2007) have proposed a model of consciousness based on quantum computation in microtubules mediated by Penrose objective reduction, and timed to gamma synchrony EEG. A summary of the model is included in Appendix 2.

Applying quantum field theory, Del Giudice *et al.* (1982, 1983) concluded that electromagnetic energy penetrating into cytoplasm would self-focus inside filaments whose diameters depended on symmetry breaking ("Bose condensation") of ordered dipoles (e.g. those occurring in actin gels). They calculated a self focusing diameter of about 15 nanometres, precisely the inner diameter of microtubules. Along similar lines, Jibu *et al.* (1994); Jibu and Yasue (1995) calculated that Fröhlich dynamics of ordered water on microtubule surfaces, particularly the internal hollow core of microtubules, would result in quantum optical modes termed super-radiance and self-induced transparency.

Applying zero point energy of the quantum vacuum, Hall (1996) calculated the Casimir force on a microtubule. As the force depends on d^{-4} (where d is the gap excluding certain photons), and setting d equal to the microtubule inner core of 15 nanometres, Hall calculated a Casimir pressure of 0.5 to 20 atmospheres on a microtubule depending on its length, c.f. [Hameroff (1998b)]. London forces are closely related to Casimir forces and the quantum vacuum.[18]

Microtubules occur not only as individual cylinders, but also fuse longitudinally into doublets and triplets. In turn, nine microtubule doublets or triplets align longitudinally to form indispensable barrel-like structures known as cilia, centrioles and flagella found widely in living cells. In some cases a microtubule doublet occurs in the middle of the nine doublets/or triplets barrel—the well known "9&2" structure.

Hundreds of membrane-covered cilia may project outward from cell surfaces, acting as sensors to transmit information about the outside environment (sensory cilia), and like motile oars to efficiently move cells (motor cilia). Cilia are anchored to cytoskeletal structures within cytoplasm. Some living cells use long, single flagella for whip-like movements, e.g. flagellates and spirochetes.[19] Centrioles (part of the cell centrosome) contain two cilia-like barrels in perpendicular tandem which act as the focal point of the cytoskeleton, located adjacent to the cell nucleus. During cell division/mitosis, centriole barrels separate and each form new barrels—the new centriole tandems move to become the focal points of daughter cells, pulling chromosomes apart in a precisely choreographed dance.[20] In many cells (including brain pyramidal cell neurons) one centriole barrel elongates and, covered by cell membrane, pushes outward above the cell surface to form the "primary cilium" thought to function as a chemical antenna.

Motor cilia and flagella bend by contractions of ("dynein") protein struts connecting the doublets. The movement requires dynein consumption of ATP, but the coordination and timing is unknown. Atema (1974) suggested propagating conformational changes along microtubules provide timing to organize ciliary contraction and cell movements. Centrioles move differently, rotating through cell interiors like an Archimedian screw.

[18] A string theory approach to microtubules has also been developed (e.g. [Nanopoulos (1995)]).

[19] The proto-organisms suggested by Margulis (1975) as contributing to formation of the animal cell by endosymbiosis.

[20] The precision is poorly understood, prompting suggestion of quantum entanglement between daughter centrioles [Hameroff (2004)].

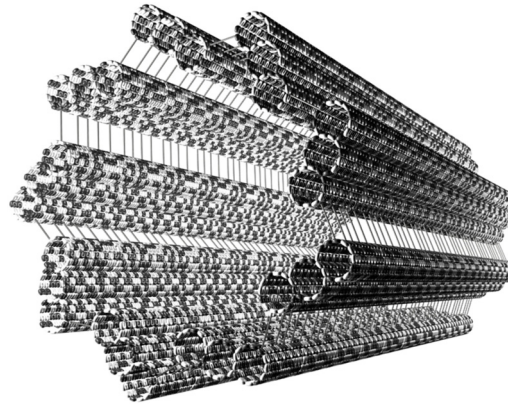


Fig. 18.10. Structure of cilia, flagella and centriole barrel (i.e. half centriole). Nine triplets (or doublets) of longitudinally fused microtubules align and are connected by linking proteins to form a mega-cylinder. In some cases (e.g. motor cilia), a central pair of fused microtubules, or other structures, occupy the inner core. The dimensions of the inner core of the mega-cylinder are roughly 750 nanometres in length, and 150 nanometres diameter, suitable for optical waveguide and detection functions depending on the inner core permittivity. These structures are found in primitive photoreception and vision, and within all retinal rod and cone cells, and may detect quantum properties of photons.

In addition to sensing pressure and chemicals, sensory cilia also detect light, being the main components of primitive visual systems. In our retinas, light passes through cilia in rods and cones to reach photodetectors.[21] In *euglena* and other organisms, the flagellar base detects light, and centrioles also detect photons and orient cell movement accordingly. Albrecht-Buehler (1992) has shown that centrioles respond to infra-red photons generated by other cells.

Cilia, centrioles and flagella are all capable of photodetection and share the same general structure—a barrel or cylinder whose dimensions are precisely related to wavelengths of light from infra-red through visible and ultra-violet. Waveguide properties have been suggested for cilia, centrioles, and flagella that could include the ability to detect quantum optical properties of photons including polarization, angular and orbital momenta.

Overall, the cytoskeleton (microtubules, actin, intermediate filaments, linking proteins, centrioles, cilia etc.) organizes real-time intracellular activities. In polymerized gel form, actin (which also binds anesthetics and contains hydrophobic pockets) fills the cell interior and orders cell water,

[21]The possibility has been raised that retinal cilia extract quantum information from incoming photons [Hameroff (2004)].

providing a quasi-solid state environment. Microtubules and MAPs are embedded in the actin gel, their non-polar, hydrophobic pocket electron clouds especially isolated from electrostatic water interactions.

Thus π electron resonance clouds are geometrically arrayed as lattices of isolated pockets in cytoskeletal polymers as well as membrane interiors and nucleic acids. Quantum states in the interior of one particular cell may become entangled with those in adjacent cells and throughout the organism by tunnelling through gap junctions, window-like openings which also electrically couple membranes. Such cooperative quantum processes suggest a promising explanation for an underlying unifying feature in living systems—"quantum vitalism". However to most scientists, such quantum processes seem unlikely in biological conditions due to decoherence.

18.8. Decoherence

The enticing possibility of quantum interactions unifying and regulating living systems faces the seemingly daunting issue of decoherence. Quantum computing requires superposition of information states (quantum bits, or "qubits"), which interact/compute by nonlocal entanglement. When measured, quantum superpositions reduce/collapse to classical states as the solution.

Technological quantum computing (e.g. ion trap quantum computing) is plagued by decoherence—disruption of seemingly delicate quantum processes by thermal and other environmental interactions. So decoherence must be avoided long enough for quantum computations to proceed. For technological quantum computing, this necessitates extreme cold and isolation to avoid decoherence and loss of qubit superposition before the computation is completed (although quantum entanglement occurs in ambient temperatures in atmosphere). Thus biological systems are assumed too "warm, wet and noisy" for useful supra-molecular quantum processes.[22]

[22]Physicist Max Tegmark (2000) calculated that microtubule quantum states decohere far too quickly (10^{-13} seconds) at brain temperature to exert useful neurophysiological effects. However Tegmark's calculations ignored stipulations of the Penrose-Hameroff model to avoid decoherence. These include 1) transiently encasing bundles of dendritic microtubules in actin gel—an isolated, shielded, and water-ordered non-liquid environment for quantum processes, 2) quantum states extending among dendritic gel environments via quantum tunnelling and/or entanglement through window-like gap junctions of dendritic webs, 3) microtubule quantum error correction topology [Hameroff *et al.* (2002)] and 4) biomolecular quantum states pumped by, rather than disrupted by, heat energy. Hagan, Hameroff & Tuszynski used Tegmark's decoherence formula with Orch OR stipulations and calculated microtubule decoherence times in hundreds of milliseconds or longer—sufficient for neurophysiological effects [Hagan *et al.* (2002)].

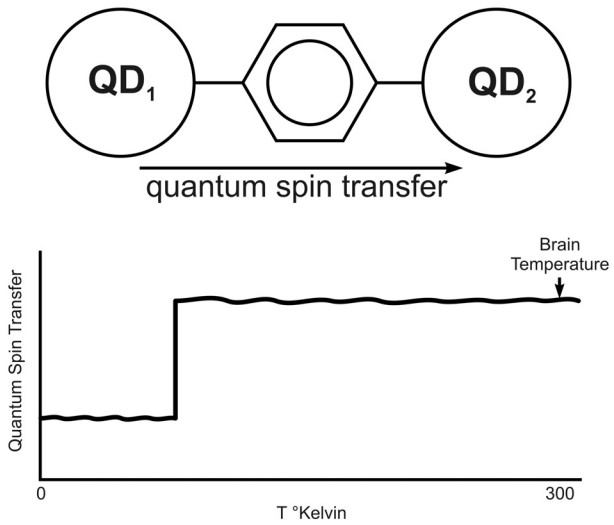


Fig. 18.11. (Top) Quantum spin transfer occurs between quantum dots (QD_1 and QD_2) via π electron rings. (Bottom) Quantum spin transfer increases with temperature from 77 K to brain temperature 300 K. (Modified after Ouyang and Awschalom (2003)).

But π electron resonance clouds avoid water and are hence not "wet". Moreover evidence suggests that biological systems can utilize heat energy ("warm, noisy") to promote quantum processes. Indeed, Engel *et al.* (2007) demonstrated quantum coherence at significantly warm temperatures in photosynthesis. Specifically, photon energy is transported through all possible pathways of the protein scaffolding surrounding the photosynthetic chlorophyll, demonstrating quantum coherent "beating". Ouyang and Awschalom (2003) showed that quantum spin transfer through organic benzene π electron resonance clouds is enhanced as temperature is increased (Fig. 18.11).

Microtubules and microtubule assemblies appear to have specific attributes to avoid decoherence and functionally utilize quantum processes:

(1) At physiological pH, microtubules are covered by a Debye plasma layer due to protruding tubulin C-termini tails which attract counter ions (Fig. 18.7), thus screening microtubule quantum processes from interactions with surrounding cytoplasm.
(2) When embedded in actin gel with ordered water, microtubules may be strongly coupled to this environment, limiting degrees of freedom

and engendering a "decoherence-free subspace" via the quantum Zeno effect.

(3) Microtubules appear to have quantum error correction topology based on Fibonacci series winding pathways which match biomechanical resonances. Qubits based on winding pathways (Fig. 18.9b) would thus be very robust.

(4) Microtubules appear to be suited to quantum field effects via symmetry breaking and Casimir force effects.

(5) Microtubules have non-polar π electron clouds spatially arrayed within 2 nanometres of each other in tubulin subunits, and thus throughout microtubules.

(6) Assemblies of microtubules (cilia, centrioles, flagella) may utilize quantum optical waveguide effects.

18.9. Conclusion

As reductionist biology reveals ever-greater detail, the essential nature of living systems—what life actually *is*—becomes more and more elusive.[23]

It is time to reconsider pioneering suggestions by Erwin Schrödinger, Albert Szent-Györgyi, Alberte and Phillip Pullman, Herbert Fröhlich, Michael Conrad and many others that life's essential feature involves quantum effects in and among geometrically arrayed π electron resonance clouds in non-polar regions of carbon-based chemistry.

Interiors of living cells are composed of cytoplasm, the aqueous phase of cell water and ions. Cytoplasm alternates between a true liquid medium and a quasi-solid gel, as cytoskeletal actin polymerizes to form dense meshworks of protein filaments on which water molecules become ordered. Within and surrounding both liquid and gel cytoplasmic states are solid structures: membranes, protein assemblies, nucleic acids and organelles (in cytoplasmic gels, actin meshworks are also solid structures). Buried within the solid structures are non-polar, hydrophobic oil-like sub-nanometre regions of low Hildebrand solubility coefficient λ. These non-polar islands are typified by benzene-like aromatic rings with π electron resonance clouds. Isolated from the aqueous, polar environment (particularly when cytoplasm is in ordered-water actin gel states), quantum London forces within these clouds operate to govern biomolecular function.

[23]The Myth of Sisyphus.

Particular geometric distributions of π cloud London forces can extend throughout cells and couple to biomolecular mechanical resonances. Quantum states in cytoplasm may extend to neighbouring cells, and throughout organisms by tunnelling through window-like gap junctions [Hameroff (1997)], enabling long-range and non-local collective quantum processes, e.g. superpositions, entanglement and computation. Unitary quantum wave functions can govern purposeful activities of living organisms.

Conventional wisdom (decoherence theory) predicts heat and environmental interactions prevent supramolecular quantum states in biology. However decoherence theory cannot account for warm quantum states in superconductors and semiconductors [Lau *et al.* (2006); Stern *et al.* (2006)], c.f. [Amin *et al.* (2006)]. More importantly, the only experiments that have tested decoherence in biomolecules have shown 1) quantum coherence in photosynthesis scaffolding proteins [Engel *et al.* (2007)] and 2) quantum spin transfer through π electron clouds [Ouyang and Awschalom (2003)] are both enhanced by increased temperatures. The evidence—still meager—is on the side of biomolecular quantum processes.

Organized quantum processes would offer huge advantages to living systems. Quantum computations could enable biomolecules, cells and organisms to sample all possible energy and information transfers, aspects of perceptions and possible responses before choosing particular actions.[24] Entanglement allows immediate communication or correlations. Thus, if feasible, organized quantum processes would have emerged during the course of evolution to enhance survival. However it is also possible that life began in simple oil-water interfaces, that living systems are processes on the edge between the quantum and classical worlds, and that biology evolved to best utilize cooperative quantum processes.

That's life.

Acknowledgements

I thank Dave Cantrell for artwork, the YeTaDeL Foundation for support, Professor Jack Tuszynski and Sir Roger Penrose for collaboration and inspiration.

[24] And the potential for consciousness, assuming it depends on the Orch OR mechanism or something similar.

References

Albrecht-Buehler, G. (1992). Rudimentary form of cellular "vision", *Proc. Natl Acad Sci.*, **89**, pp. 8288-8292.

Amin, M. H. S., Love, P. J., and Truncik, C. J. S. (2006). Thermally assisted adiabatic quantum computation. `arXiv:cond-mat/o609332 v1`.

Atema, J (1974). Microtubule theory of sensory transduction, *J.Theor. Biol.* **38**, pp. 181-190.

Becker, J. S., Oliver, J. M., and Berlin, R. D. (1975). Flourescence techniques for following interactions of microtubule subunits and membranes, *Nature* **254**, pp. 152–154.

Brizhik, L., Eremko, A., Piette, B., and Zakrzewski, W. (2001). Electron self-trapping in a discrete two-dimensional lattice, *Physica D* **159**, pp. 71–90.

Conrad, M. (1994). Amplification of superpositional effects through electronic conformational interactions, *Chaos, Solitons and Fractals* **4**, pp. 423-38.

Del Giudice, E., Doglia, S., Milani, M., and Vitiello, G. (1983). Spontaneous symmetry breakdown and boson condensation in biology, *Phys. Rev. Letts.* **95A**, pp. 508–510.

Del Giudice, E., Doglia, S., and Milani, M. (1982). Self focusing of Fröhlich waves and cytoskeleton dynamics, *Phys. Letts* **90A**, pp. 104–106.

Engel, G. S., Calhoun, T. R., Read, E. L., Ahn, T. K., Mancal, T., Cheng, Y. C., Blankenship, R. E., and Fleming, G. R. (2007). Evidence for wave-like energy transfer through quantum coherence in photosynthetic systems, *Nature* **446**, pp. 782–786.

Franks N. P., and Lieb, W. R. (1984). Do general anaesthetics act by competitive binding to specific receptors? *Nature* **310**, pp. 599–601.

Frauenfelder, H., Fenimore, P. W., and McMahon, B. H. (2002). Hydration, slaving and protein function, *Biophysical Chemistry* **98**, pp. 35–48.

Freedman, F. H., Kitaev, A., Larsen, M. J., and Wang, Z. (2002). Topological quantum error correction. `quant-ph/0101025`.

Fröhlich, H. (1970). Long-range coherence and the actions of enzymes, *Nature* **228**, p. 1093.

Fröhlich, H. (1968). Long-range coherence and energy storage in biological systems, *Int. J.Quantum Chem.* **2**, p. 6419.

Fröhlich, H. (1975). The extraordinary dielectric properties of biological materials and the action of enzymes, *Proc. Natl. Acad. Sci.* **72**, pp. 4211–4215.

Hagan, S., Hameroff, S., and Tuszynski, J. (2002). Quantum computation in brain microtubules? Decoherence and biological feasibility, *Physical Review E* **65**, p. 061901.

Hall, G. H. (1996). Quantum electrodynamic (QED) fluctuations in various models of neuronal microtubules, *Consciousness Research Abstracts—Tucson II (Journal of Consciousness Studies)* Abstract 145.

Hameroff, S. R. (1987). *Ultimate Computing: Biomolecular Consciousness and Nanotechnology* (Elsevier-North Holland, Amsterdam).

Hameroff, S. R. (1994). Quantum coherence in microtubules: A neural basis for emergent consciousness? *Journal of Consciousness Studies* **1**, pp. 91–118.

Hameroff, S. (1997). Quantum vitalism, *Advances: The Journal of Mind-Body Health* **13**, pp. 13–22.

Hameroff, S. R. (1998a). Quantum computation in brain microtubules? The Penrose-Hameroff 'Orch OR' model of consciousness, *Philosophical Transactions Royal Society London (A)* **356**, pp. 1869–1896.

Hameroff, S. (1998b). More neural than thou (A reply to Patricia Churchland) In: *Toward a Science of Consciousness II—The Second Tucson Discussions and Debates*, eds. Hameroff, S. R., Kaszniak, A. W. and Scott, A. C., Cambridge, MA: MIT Press, pp. 197–213.

Hameroff, S. R. (2004). A new theory of the origin of cancer: quantum coherent entanglement, centrioles, mitosis, and differentiation, *Biosystems* **77**, pp. 119–136.

Hameroff, S. (2006). The entwined mysteries of anesthesia and consciousness, *Anesthesiology* **105**, pp. 400–412.

Hameroff, S. (2007). The brain is both neurocomputer and quantum computer, *Cognitive Science* **31**, pp. 1035–1045.

Hameroff, S. R., and Watt, R. C. (1982). Information processing in microtubules, *J Theor Biol* **98**, pp. 549–56l.

Hameroff, S., Rasmussen, S., and Mansson, B. (1988). Molecular automata in microtubules: Basic computational logic of the living state, In *Artifical Life: SFI Studies in the Science of Complexity*, ed. C. Langton (Addison-Wesley, New York, pp. 521–553).

Hameroff, S. R., and Penrose, R. (1996a). Orchestrated reduction of quantum coherence in brain microtubules: A model for consciousness, in S. R. Hameroff, S. R., Kaszniak, A. and Scott, A. C. (eds.), In: *Toward a Science of Consciousness The First Tucson Discussions and Debates*, (MIT Press, Cambridge, MA). Also published in: *Mathematics and Computers in Simulation* **40**, pp. 453–480.

Hameroff, S. R., and Penrose, R. (1996b). Conscious events as orchestrated space-time selections, *Journal of Consciousness Studies* **3**, pp. 36–53.

Hameroff, S., Nip, A., Porter, M., and Tuszynski, J. (2002). Conduction pathways in microtubules, biological quantum computation, and consciousness, *BioSystems* **64**, pp. 149–168.

Hameroff, S., and Tuszynski, J. (2003). Search for quantum and classical modes of information processing in microtubules: Implications for "The Living State" In: *Bioenergetic Organization in Living Systems*, (Eds. Franco Musumeci, Mae-Wan Ho, World Scientific, Singapore).

Jibu, M., Hagan, S., Hameroff, S. R., Pribram, K. H., and Yasue, K. (1994). Quantum optical coherence in cytoskeletal microtubules: implications for brain function, *BioSystems* **32**, pp. 195–209.

Jibu, M. and Yasue, K. (1995). *Quantum Brain Dynamics: an Introduction* (John Benjamins, Amsterdam).

Karplus, M., and McCammon, J. A. (1983). Protein ion channels, gates, receptors. In *Dynamics of Proteins: Elements and Function, Ann. Rev. Biochem.* J. King (ed.), Benjamin/Cummings, Menlo Park, **40**, pp. 263-300.

Karsenti, E., and Vernos, I. (2001). The mitotic spindle: A self-made machine, *Science* **294**, pp. 543–547.

Klein-Seetharaman, J., Oikawa, M., Grimshaw, S. B., Wirmer, J., Duchardt, Ueda, E., Imoto, T., Smith, L. J., Dobson, C. M., and Schwalbe, H. (2002). Long-range interactions within a nonnative protein, *Science* **295**, pp. 1719-1722.

Langton, C. G. (1991). Introduction In: *Artificial Life II*, Chris Langton, C. Taylor, J. D. Farmer, and S. Rasmussen, eds. SFI Studies in the Sciences of Complexity, Vol. X. Redwood City, (CA: Addison-Wesley).

Lau, W. H., Sih, V., Stern, N. P., Myers, R. C., Buell, D. A. and Awschalom, D. D. (2006). Room temperature electron spin coherence in telecom-wavelength quaternary quantum wells, *Applied Physics Letters* **89**, p. 142104.

Lee, J. C., Field, D. J., George, H. J., and Head, J. (1986). Biochemical and chemical properties of tubulin subspecies, *Ann. NY Acad. Sci.* **466**, pp. 111–128.

Margulis, L. (1975). *Origin of Eukaryotic Cells.* (New Haven, Yale University Press).

Margulis, L., and Sagan, D. (1995). *What is Life?* (New York, Simon and Schuster).

McFadden, J. (2000). *Quantum Evolution: The New Science of Life.* (New York, W.H. Norton.)

Nanopoulos, D. (1995). Theory of brain function, quantum mechanics and superstrings, `http: //www.qedcorp.com/pcr/pcr/nanopoul.pdf`.

Ouyang, M., and Awschalom, D. D. (2003). Coherent spin transfer between molecularly bridged quantum dots, *Science* **301**, pp. 1074–1078.

Penrose, R., and Hameroff, S. (1995). Gaps, what gaps? Reply to Grush and Churchland, *Journal of Consciousness Studies* **2**, pp. 99–112.

Pollack, G. H. (2001). *Cells, Gels and the Engines of Life.* (Ebner and Sons, Seattle).

Pullman, B., and Pullman, A. (1963). *Quantum Biochemistry.* (Interscience, New York).

Rasmussen, S., Karampurwala, H., Vaidyanath, R., Jensen, K. S., and Hameroff, S. (1990). Computational connectionism within neurons: A model of cytoskeletal automata subserving neural networks. *Physica D* **42**, pp. 428–49.

Samsonovich, A., Scott, A. C., and Hameroff, S. R. (1992). Acousto-conformational transitions in cytoskeletal microtubules: Implications for information processing, *Nanobiology* **1**, pp. 457–468.

Sataric, M. V., Zekovic, S., Tuszynski, J. A., and Pokorny, J. (1998). The Mössbauer effect as a possible tool in detecting nonlinear excitations in microtubules, *Phys Rev E* **58**, pp. 6333–6339.

Scott, A. C. (1995). *Stairway to the Mind.* Springer-Verlag, (Berlin).

Schrödinger, E. (1944). *What is Life?* (Cambridge University Press).

Steane, A. M. (1998). Introduction to quantum error correction, *Phil. Trans. Roy. Soc. London A* **356**, pp. 1739–1758.

Stern, P., Ghosh, S., Xiang, G., Zhu, M., Samarth, N., and Awschalom, D. D. (2006). Current-induced polarization and the spin Hall effect at room temperature, *Physics Reviews Letters* **97**, art. no. 126603.

Szent-Györgyi, A. (1960). *Introduction to a Submolecular Biology* (Academic Press).

Tegmark, M. (2000). The importance of quantum decoherence in brain processes, *Phys. Rev. E* **61**, pp. 4194–4206.

Tuszynski, J., Hameroff, S., Sataric, M. V., Trpisova, B., and Nip, M. L. A. (1995). Ferroelectric behavior in microtubule dipole lattices; implications for information processing, signaling and assembly/disassembly, *J. Theor. Biol.* **174**, pp. 371–380.

Voet, D., and Voet, J. G. (1995). *Biochemistry.* 2nd ed. (Wiley, New York).

Wagenknecht, A., Stemp, E. D. A., and Barton, J. K. (2000). Evidence of electron transfer from peptides to DNA: oxidation of DNA-bound tryptophan using the flash-quench technique, *J. Am. Chem. Soc.* **122**, pp. 1–7.

Woolf, N. J., and Hameroff, S. (2001). A quantum approach to visual consciousness, *Trends in Cognitive Sciences* **5**, pp. 472–478.

About the author

Stuart Hameroff is an anesthesiologist and Professor of Anesthesiology and Psychology at the University of Arizona in Tucson, Arizona. He received his MD from Hahnemann College, Philadelphia, Pennsylvenia, in 1973. He has teamed with Sir Roger Penrose to develop the "Orch OR" (orchestrated objective reduction) model of consciousness based on quantum computation in brain microtubules, and has also researched the action of anesthetic gases. As Director of the University of Arizona's Center for Consciousness Studies, Hameroff organizes the biennial "Tucson conferences" *Toward a Science of Consciousness*, among other Centre activities. His website is `www.quantumconsciousness.org`.

Appendix 1 Quantum computing in DNA π electron stacks

DNA may utilize quantum information and quantum computation. DNA base pairs all have π electron rings with inducible dipoles, forming a π electron stack in the central core of the double helix. Superpositions of base pair dipole states consisting of purine and pyrimidine ring structures can play the role of qubits, and quantum communication (coherence, entanglement, non-locality) can occur in the "π stack" region of the DNA molecule.

The "π electron stack" is the internal core of the DNA molecule comprised of the purine and pyrimidine ring structures of the base pairs which are always either Adenine (purine) and Thymine (pyrimidine, "A-T"), or Guanine (purine) and Cytosine (pyrimidine, "G-C"). Purines have a double ring structure, with a 6 member ring fused to a 5 member ring, whereas pyrimidines have a single 6 member ring. (The complementary base pairs are held together by hydrogen bonds—2 between A and T, and 3 between G and C.) Thus each base pair always consists of one 6/5 purine ring and one 6 pyrimidine ring.

Each A-T and G-C base pair also has a dipole—a type of van der Waals London force due to mutually induced polarizations between electron clouds of the purine and pyrimidine rings. At any particular time an electron negative charge may be shifted either toward the purine ring, or toward the pyrimidine ring (with corresponding conformational shifts).

For the A-T base pair we can have negative charge more localized toward the adenine purine ring, e.g. A→T, or more toward the thymine pyrimidine ring A←T. For the base pair G-C we can similarly have G→C, or G←C.

But as these dipole couplings are quantum mechanical they can exist in superposition of both possibilities. So quantum mechanically we can have: Both A→T and A←T which eventually reduce to either A→T or A←T

As well as:

Both G→C and G←C which eventually collapse to either G→C or G←C. Using quantum nomenclature we can refer to the quantum superpositions of both possible states $|$ A→T + A←T $\rangle$.

And similarly: $|$ G→C + G←C $\rangle$.

Such superpositions may act as "qubits", bit states which can exist in quantum superposition of, e.g. both 1 *AND* 0. DNA could function as a quantum computer with superpositions of base pair dipoles acting as qubits. Entanglement among the qubits, necessary in quantum computation is accounted for through quantum coherence in the π stack where the quantum information is shared. Consider a string of three base pairs: A-T G-C G-C

A-T can be either A→T or A←T, or quantum superposition of both $|$ A→T + A←T $\rangle$

G-C can be either G→C or G←C, or quantum superposition of both $|$ G→C + G←C $\rangle$.

As each pair may be in two possible dipole states mediated by quantum mechanical interactions, the 3 base pairs may be seen as a quantum

superposition of 8 possible dipole states:

A→T A→T A→T A→T
G→C G←C G→C G←C
G→C G→C G←C G←C
A←T A←T A←T A←T
G→C G←C G→C G←C
G→C G→C G←C G←C.

Each dipole differs slightly due to structural differences, so for example A←T and G←C have slightly different dipoles though pointing in the same general direction whereas A←T and G→C have more or less opposite dipoles. The slight differences will introduce irregularities in the π stack quantum dynamics, and couple to mechanical/conformational movements of the DNA strand. Net and complex dipoles within the π stack may show emergent phenomena. Particular dipoles corresponding to loops, hairpins, dyads etc. may have specific properties. Superconductive DNA loops, for example, could function in a way analogous to SQUIDs (superconductive quantum interference devices). Squids have a superconductive ring with one segment of lower conductance; current through the ring is highly sensitive to dipoles. DNA loops may serve as quantum antenna, with nonlocal communication with other DNA, and perhaps cell machinery. We can then consider DNA as a chain of qubits (with helical twist). Output of quantum computation would be manifest as the net electron interference pattern in the quantum state of the π stack, regulating gene expression and other functions locally and nonlocally by radiation or entanglement.

Appendix 2 Penrose-Hameroff Orch OR model

The Penrose-Hameroff Orch OR model proposes that microtubule (MT) quantum computations in neurons are orchestrated by synaptic inputs and MT-associated proteins (MAPs), and terminate (e.g. after 25 msec, 40 Hz) by the Penrose objective reduction ("OR") mechanism. Hence the model is known as orchestrated objective reduction, "Orch OR". Complete details may be found in [Penrose and Hameroff (1995); Hameroff and Penrose (1996a,b)] and [Hameroff (1998a)]. The key points are:

(1) Conformational states of tubulin protein subunits within dendritic MTs interact with neighbor tubulin states by dipole coupling such that MTs process information in a manner analogous to cellular automata, regulating neuronal activities (trigger axonal spikes, modify synaptic plasticity and hardwire memory by MT-MAP architecture etc.).

(2) Tubulin conformational states and dipoles are governed by quantum mechanical London forces within tubulin interiors (non-polar hydrophobic pockets of low Hildebrand solubility) so that tubulins may exist as quantum superpositions of differing conformational states, thus acting as quantum levers and qubits.

(3) While in superposition, tubulin qubits communicate/compute by entanglement with other tubulin qubits in the same MT, other MTs in the same dendrite, and MTs in other gap junction-connected dendrites (i.e. within a dendritic web or hyper-neuron). Thus quantum computation occurs among MTs throughout macroscopic regions of brain via tunnelling through gap junctions of adjacent neurons or other mechanisms.

(4) Dendritic interiors alternate between two states determined by polymerization of actin protein: a) In the liquid (solution: *sol*) state, actin is depolymerized and MTs communicate/process information classically (tubulin bits) with the external world. During this phase synaptic activities provide inputs via MAPs which *orchestrate* MT processing and (after reduction) MT (output) states regulate axonal firing and synaptic plasticity. b) As actin polymerizes (e.g. triggered by glutamate binding to receptors on dendritic spines), dendritic cytoplasm enters a quasi-solid gelatinous (*gel*) state in which cell water is ordered in cytoskeletal surfaces. MTs become isolated from environment and enter quantum superposition mode in which tubulins function as quantum bits or qubits. The two states alternate e.g. at 40 Hz.

(5) Quantum states of tubulin/MTs in gel phase are isolated/protected from environmental decoherence in shielded non-polar regions of low Hildebrand solubility, encasement by actin gelation and ordered water, Debye screening, coherent pumping and topological quantum error correction.

(6) During quantum gel phase, MT tubulin qubits represent pre-conscious information as quantum information—superpositions of multiple possibilities, of which dream content is exemplary.

(7) Pre-conscious tubulin superpositions reach threshold for Penrose OR (e.g. after 25 msec) according to $E = \hbar/t$ in which E is the gravitational self-energy of the superpositioned mass (e.g. the number of tubulins in superposition), $\hbar$ is Planck's constant over 2π, and t is the time until OR. Larger superpositions (more intense experience) reach threshold faster. For $t = 25$ msec (i.e. 40 Hz) E is roughly 10^{11} tubulins, requiring a hyper-neuron of minimally 10^4 to 10^5 neurons per conscious event.

The makeup of the hyper-neuron (and content of consciousness) evolves with subsequent events.

(8) Each 25 msec OR event chooses $\sim 10^{11}$ tubulin bit states which proceed by MT automata to govern neurophysiological events, e.g. trigger axonal spikes, specify MAP binding sites/restructure dendritic architecture, regulate synapses and membrane functions. The quantum computation is algorithmic but at the instant of OR a non-computable influence (i.e. from Platonic values in fundamental spacetime geometry) occurs.

(9) Each OR event ties the process to fundamental spacetime geometry, enabling a Whiteheadian pan-protopsychist approach to the "hard problem" of subjective experience. A sequence of such events gives rise to our familiar stream of consciousness.

Index