On Models and Modeling

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ABSTRACT

The argument is made that biological modeling should recognize limitation simultation and reductionism.

1. INTRODUCTION

In my days as a graduate student at the University of Chicago, its Department of Mathematics was one of the best in the country if not in the world.

But it was a department of *pure* mathematics. Every once in a while, the Department would establish a committee to study whether there should be more applied mathematics done in the Department. These committees, as I recall, were always chaired by Saunders MacLane. They would work very hard, and always came up with the same recommendation; namely, that the mix of pure and applied mathematics being done in the Department was already optimal. Hence, the *status quo* was maintained.

As far as I am concerned, the only real difference between "pure" and "applied" mathematics lies in the fact that applications of formalisms presume some kind of referent external to the formalism itself. As we shall see, it is the judicious association of a formalism with such external referents that is the essence of a (mathematical) model. From this point of view, a great deal of what passes for pure mathematics is really applied mathematics; it is essentially modelling in the above sense, except that the external referents assigned to a particular formalism are themselves mathematical in character. In this sense, everything from analytic geometry to algebraic topology is applied mathematics. Indeed, people do not, in general, recognize just how much modelling goes on within the precincts of pure mathematics itself, and

APPLIED MATHEMATICS AND COMPUTATION 56:359-372 (1993)

© Elsevier Science Publishing Co., Inc., 1993 655 Avenue of the Americas, New York, NY 10010 how much can be learned about the modelling enterprise from this recognition.

One attempt to systematize this kind of modelling experience within mathematics is today embodied in the Theory of Categories. This theory grew directly out of algebraic topology, which itself involves the assignment of algebraic referents to topological or geometric structures, and *vice versa*. The Theory of Categories is thus, in a sense, a kind of general theory of modelling, and one of its fathers was none other than Saunders MacLane. Thus, perhaps he knew whereof he spoke when he said that his Department was already doing "enough" applied mathematics; it was, in fact, doing quite a lot. Indeed, the lessons I indirectly learned from him about modelling in general, under the peculiar guise of Category Theory, were among the most valuable I ever learned.

In the present article, we shall be concerned with just this process of assigning external referents to formalisms, which constitutes the making of models. As we shall see, this is a process that is in the nature of an art, and not a science; there is nothing in either the formalisms or the referents that mandates or entails how it is to be done. If it is not done carefully, the process itself creates *artifacts*; we will exhibit a few examples of these. Finally, we shall briefly consider the Theory of Categories as both exemplar and tool of the modelling enterprise by briefly considering what the structure of the category of models of a system tells us about the system itself.

2. GOOD MATHEMATICS, BAD MODELS

As we have seen, pure mathematics is in a paradoxical situation when it comes to modelling. One the one hand, a great deal of modelling is done entirely within its precincts. On the other hand, its rejection of extramathematical referents is proverbial and amounts almost to an immune response. Indeed, the need to make allowances for alien extra-mathematical referents imposes a severe handicap on pure mathematicians when it comes to modelling; a handicap almost as severe, although for an opposite reason, is that faced by pure empiricists ignorant of formalisms. Thus, good mathematicians often make bad modellers.

Let me illustrate this paradox, with a typical example drawn from current literature. Names will be withheld to protect the guilty. As we will see, the example is interesting in itself; we will present it first, and then, in subsequent sections, trace its sources.

Vito Volterra was a good mathematician who also was a good modeller. Volterra had been a pioneer in what is nowadays called functional analysis, especially in connection with integral equations. Rather late in life, he turned to the studying of interacting biological populations, which he came to describe by means of systems of ordinary differential equations, kinetic equations of mass-action type:

$$dx_i/dt = a_i x_i + \sum_{j=1}^N b_{ij} x_i x_j, \qquad i = 1, \dots, N.$$
 (1)

Just about everything in current mathematical ecology stems from these equations in one way or another.

The extra-mathematical referents here pertain to the populations that these equations are intended to describe. The "state variables" x_i are thus interpreted as population sizes or population densities. Obviously, these facts translate at least into the purely formal conditions

$$x_i(t) \ge 0$$

even though the equations in (1) are formally defined for other situations as well. Consequently, no one cares what these equations do when the variables are negative. So far, so good.

The equations in (1) have a lot of nice properties, most of which were already known to Volterra. For one thing, a corollary of them is the so-called Principle of Competitive Exclusion (cf. [1]), which refers to the *persistence* of species in a given population. This is clearly a question of great interest to population biologists; given a population of interacting species, which will persist, and which will go extinct? That is, for which x_i in (1) will we have

$$\lim_{t\to\infty}x_i(t)\to 0$$

under a given set of initial conditions?

On the other hand, formal objects like (1) have been the subject of deep (pure) mathematical study over the past three or four decades under the rubric of *dynamical systems*. There are now a lot of general theorems about them; application of these to (1) should presumably tell us a lot about biological populations. The problem of extinction and persistence, for instance, devolves on whether or not there are attractors of (1) lying on the hyperplanes $x_i = 0$ that bound the first orthant of the N-dimensional state space on which (1) is defined.

This is now, apparently, a purely formal, mathematical problem, which pure mathematicians can happily attack without worrying further about the external biological referents that gave rise to it. And indeed, there are a substantial number of papers that investigate precisely this problem—papers that study the existence of such attractors and the details of how trajectories approach them. Good, subtle mathematics here, but very poor modelling.

Why? Simply because, when population sizes get *small*, the rate equations in (1) progressively lose their meaning; they lose their contact with the external referents they are supposed to describe. The use of such systems of differential equations, and of all the tools of analysis that come with them, are tacitly predicated on a hypothesis, namely, that population sizes are large enough to justify it. When this hypothesis is not satisfied, as it is not whenever we are close to the bounding hyperplanes of the first orthant, the properties of (1) are utterly *artifactual* as far as population biology is concerned.

In fact, the deterministic rate equations in (1) are themselves an *approxi*mation to something else—an approximation that is only good under certain conditions, and no good otherwise. We may look upon them as a macroscopic version of underlying microscopic processes, which are not themselves governed by those equations. Intuitively, by forcing population sizes to become small, we correspondingly force the underlying microscopic properties to become more and more prominent until they simply swamp everything else.

It was precisely this kind of situation that occurred with the birth of quantum theory. In that case, again, we had systems of rate equations like (1), coming from Newton's Laws, which were thought to be universally applicable. They did, indeed, work very well for matter in bulk, but became increasingly wronger as we approach the atomic level. Bohr's "old quantum theory" proposed a whole new set of rules that completely changed the game for microscopic phenomena, *subject to* what he called the *Correspondence Principle*—roughly, that when we had "enough" microscopic phenomena, their aggregate had to behave in a way describable by the old macroscopic rules.

If we suppose that what happens at the microscopic level is governed by *stochastics* (i.e., by some kind of Master Equation), then we are in a world of means and variances. The Correspondence Principle says that when variances are small enough, we only have to worry about the means, and then these means are governed by deterministic equations like (1). In other words, the equations in (1) are approximations based on the hypothesis that variances are *negligible*. And, of course, in the present situation, that translates into large population sizes.

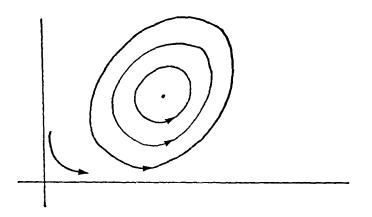
Thus, it is no accident that population dynamics exhibits many quantum-like phenomena when population sizes get small. Just for fun, let us look at a few of them in a very familiar special case, where our population consists of one predator species y, and one prey species x. The equations in (1) thus assume the form

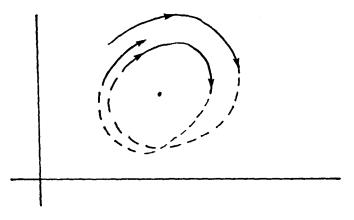
$$dx/dt = a_1 x - b_1 xy$$

$$dy/dt = -a_2 y + b_2 xy$$
 (2)

with the familiar phase portrait shown in Figure 1, consisting of neutrally stable closed trajectories. There is even a conserved quantity, and the whole thing can be put into a Hamiltonian form (cf., [4]).

However, as we have indicated, close enough to the lines x = 0, y = 0, these rate equations, and hence the phase portrait they determine, become increasingly wronger when compared with the actual behavior of the real population. Let us schematically follow one actual trajectory of such a population over a few cycles. We would see something like Figure 2. Here, the solid parts of the trajectory are those governed by (2), the deterministic, macroscopic equations. The dotted parts represent population sizes small enough so that these equations no longer hold, e.g., where variances or "fluctuations" become dominant. Even supposing that the dotted curves swing around as indicated, we will, in general, come back into the macroscopic region on a different trajectory than we left it. That is, we have violated the conservation law; we have "tunneled" to a different value of the conserved quantity. Indeed, we may even "tunnel" to extinction of the predator, or of the entire population.







All of this arises because the rate equations (1) or (2) are being employed under conditions where the appropriate Correspondence Principle, which attaches meaning to them, is being violated. We can still *formally* study those rate equations, but they no longer need approximate what the populations themselves are actually doing. We have lost the external referents, and hence are left with a bad model, indeed, not a model at all.

3. COGNATE SITUATIONS IN PURE MATHEMATICS

Situations like that sketched in the preceding section are not, unfortunately, all that uncommon. I chose this one to begin to illustrate a basic point, because it is fairly transparent what is happening here. Namely, we have replaced a system of interest (a biological population) by a mathematical object (a system of rate equations), without sufficiently noting the conditions that allow it, conditions coming both from the mathematical model *and* from the external referent it is supposed to describe.

Can such a thing happen within the precincts of pure mathematics itself? Of course it can, and, indeed, it has happened many times. It happened to Pythagoras, who tried to replace arbitrary numbers by ratios of integers. It happened to everyone who tried to follow in the footsteps of Euler and the Bernoullis, and ended up trying to sum a divergent series. As we shall soon see, it happened not too long ago to Hilbert himself.

Instead of looking at any of these historical cases, we shall look rather at one place where perhaps it did not happen, but could have happened. This field is topology, as pure a part of mathematics as there is, but one which has always been rife with models of various kinds. Indeed, it is out of the relation between the objects of topology, the topological spaces, and their various models that the theory of categories, to which we have already alluded, historically grew. That is the reason we choose these examples.

Everyone knows that the first conscious steps towards topology were taken by Euler. Everyone knows about the Seven Bridges of Koenigsberg, and how Euler solved the problem they posed by what we nowadays call graphtheoretic methods. But these graph-theoretic models led Euler much further. By means of such ideas, he was led to his famous Formula, connecting the number of vertices, edges, and faces of an arbitrary convex polyhedron in space:

vertices
$$- edges + faces = 2$$
.

This is, by itself, an amazing relation, but its true depth was not perhaps fully realized until the time of Poincaré. By itself, it seems to be a property of *polyhedra*, or more generally, to the graphs (arrays of vertices and edges) to which they give rise. But from a more general perspective, the Euler Formula expresses a property, not of these graphs, but of the space in which they are drawn. In this sense, the graph is a *model* of that space.

In thinking of a graph as a model of a larger thing, of a topological space, we must *interpret* the vertices of the graph as points of the space (i.e., as a discrete, finite subspace) and the edges of the graph as arcs or curves lying in that space and bounded by the appropriate vertices. These are the external referents. Then it is a theorem that every graph can be so interpreted, as defining a "polyhedron" in an appropriate space (one of sufficiently high genus, or with "enough holes"), and under such circumstances, the appropriate Euler Formula defines a *topological invariant* of that space. That is, the Euler number, or Euler Characteristic, is obviously invariant under topological homeomorphisms of the whole space. In particular, two topological spaces whose Euler characteristics are different *cannot* be homeomorphic.

In all of this, the external referents, the topological interpretations given to abstract graph-theoretic structures play an absolutely essential role. As noted, we must think of *vertices* as points of a topological space, and *edges* as arcs (1-dimensional subsets of the space) connecting them. The property of the external topological referent (namely, that edges can only intersect in vertices and not elsewhere), is precisely what allows us to talk about higherdimensional faces in graph-theoretic terms; these, in turn, are precisely what get counted up in the Euler Formula.

It should be evident that this process of associating a graph with a topological space, in such a way that properties of the graph (e.g., the Euler

characteristic) tell us something about the space, is very like associating a system of rate equations with a biological population; they are all instances of modelling. However, it is clear in the topological situation that one cannot generally replace the original space by such a graph, i.e., pretend that the graph tells us *all* about the space to which it is related. So we are not easily prone to the same kind of error we made with the population.

The relation we have established between the space and the graph tells us something about modelling itself, out where we can see it clearly, unencumbered by the thick epistemological veils that permeate the sciences. We will accordingly push this purely mathematical situation, which we have introduced with the Euler Characteristic, a little further, not because we are interested in topology, but because we are interested in modelling. In a way, we are going to try our hand at making models of modelling, turning the process on itself.

4. ALGEBRAIC TOPOLOGY

In the preceding section, we sketched how to associate with a topological space X a graph G(X) drawn in that space in such a way that G(X) tells us something about X. This association is established by making G(X) refer to X, by encoding properties of X into G(X), and by decoding properties of G(X) back to X.

The rule G that associates a space X with a graph G(X) pertains not only to the spaces themselves, but to the continuous mappings that compare them. Thus, if $f: X \to Y$ is a continuous map between topological spaces, there is a map $G(f): G(X) \to G(Y)$ that compares their graphs. In particular, we have already seen that if f is a homeomorphism of topological spaces, then G(f) is an isomorphism of graphs. More generally, we would expect that *any* kind of relation between X and Y (e.g., that X is a subspace of Y) would express itself as a corresponding relation between their models G(X) and G(Y).

This kind of rule G, in this case from spaces to graphs, is an example of a *functor*. It is obviously one way of talking about the relation between a model G(X) and its referent X. That relation itself has referent, which pertains to modelling and not specifically to topology.

The reasoning that led from spaces to graphs, and which is embodied in the Euler Characteristic, is just the tip of an enormous iceberg, which first began to be fathomed by Poincaré. Nowadays we talk of them in terms of words like homology, cohomology, homotopy and the like, studied successively under the rubrics of Analysis Situs, combinatorial topology, and algebraic topology. At root, they involve relatively straightforward enlargements on those same ideas embodied in the Euler Characteristic.

There are two basic underlying ideas here. The first is to "approximate" to

a topological space X, not by a single polyhedron, but by a sufficiently large family of them: a *complex*. Then, in the individual polyhedra (*simplexes*) which make up the complex, to introduce an idea of *orientation* or sense, which allow us to add faces (an algebraic operation) and to interpret this addition in terms of navigating through the complex itself. This leads to the idea of groups of *chains* of various dimensions. The simple intuitive notion of *boundary* turns out to induce homomorphisms between these groups of chains of each dimension, with the nice property that the image of any one of them is contained in the kernel of the next (exactness); hence, the boundary of a boundary is zero. The quotient groups of kernels modulo images are the homology groups of the complex, and, hence, if we are careful, of the space X to which the complex "approximates."

When we are all done, we have assigned to a topological space X a whole family $H_q(X)$ of commutative groups, the q-dimensional homology groups, for q = 0, 1, 2, ... And just as before, if $f: X \to Y$ is a continuous mapping between topological spaces, we find induced group homomorphisms $H_q(f)$ between the homology groups. Each of these homology groups provides a *model* of the space X, just as did the graph we had before. Indeed, the graph is subsumed into these group-theoretic models in a way that generalizes the Euler Formula we spoke of earlier.

These concepts can be dualized, in a way familiar from the dual spaces of Euclidean vector spaces. We pass, via this duality, to a new family $H^q(X)$ of group-theoretic models of X, the cohomology groups. Their advantage is that they admit additional structures, which also turn out to represent aspects of the topology of X; for instance, there is a multiplication (cup product) that turns the family of cohomology groups into a kind of graded ring. There are additional *cohomology operations*, which provide a still more elaborate algebraic structure.

Of course, we cannot enter into details here. But the goal, or animating faith, of algebraic topology is that there are "enough" of these algebraic models to faithfully capture every aspect of the topology of a space X, and, hence, to answer every topological question about X in purely algebraic terms. In particular, the faith is that there are "enough" such models to answer the basic question of (algebraic) topology: when are two topological spaces X, Y homeomorphic? (the classification problem).

Let us examine this article of faith for a moment. Suppose that X is a topological space. We have, as we have seen, a rather large spectrum of algebraic, group-theoretic models of X, namely the $H_q(X)$ and $H^q(X)$, together with certain relations between them. Suppose that these were "enough" to answer every topological question about X (in fact, they are not "enough" in general). Then we could, in fact, simply forget about X entirely; X could be effectively reconstructed (up to homeomorphism anyway) from its algebraic models. We would thus no longer need the external referent X of

these models; X has been entirely internalized into the models themselves and the relations between them.

Thus, the faith of algebraic topology, and indeed of modelling in general, is that we can replace a topological space X by a sufficiently comprehensive set of functorial images of X, more generally, that we can capture every aspect of reality in a natural system in an appropriate set of models. A corollary of this faith is, as we have seen, that we can dispense with the external referents entirely, for we have effectively internalized them into this *category* of functorial images. In this category, where everything we can know about the original system or space X has been internalized, we will never make the kind of simple-minded mistakes we spoke of earlier.

The question then becomes: how far is such a faith justified? When can we justify it? In what follows, we shall explore a couple of ramifications of this question.

5. SYNTAX, SEMANTICS, AND FORMALIZATION

Any language, including mathematics, must possess two distinct aspects, which we may refer to as syntax and semantics. Syntax pertains roughly to the internal rules governing the structure of the language itself; semantics pertains to meanings, and hence to external referents.

David Hilbert, goaded by the perceived need to defend mathematics in the face of the paradoxes of "naive" set theory, thought he could accomplish this task by expunging semantics from mathematics entirely. He argued in effect that, at least within mathematics itself, semantics could always be effectively replaced by more syntax. He called this process *formalization*. He believed that mathematical consistency could be assured, and all paradoxes eliminated, by replacing conventional mathematics by a game of pattern generation, played according to fixed rules, with meaningless symbols and combinations of them.

Such ideas are, of course, closely related to what we have been talking about. So it is instructive to see what has happened to Hilbert's plan to cut mathematics off from all referents, to completely expunge semantics from mathematics and replace it with pure syntax, i.e., with symbol manipulation and word processing.

What happened was basically the Gödel Incompleteness Theorem of 1931, which laid waste to the whole formalist program. The conclusion of this theorem is that Number Theory could not thus be formalized—unless it was inconsistent to begin with.

Gödel's Theorem can be viewed in many ways. One of them is this: one cannot forget that number theory is about numbers. No matter how we try to formalize it, or to convert it to pure syntax, we miss most of the truths of number theory thereby. Seen in this light, Gödel's result is a kind of cardinality argument; the set of theorems of number theory (or more precisely, the set of entailments which relate them) are of strictly higher cardinality than those coming from syntax along.

Stated in yet another way, the relation between number theory and any hypothetical formalization (i.e., syntactization) of it is essentially that of system to model; it is the same relation as that obtaining between topological space X and the q^{th} homology group $H_q(X)$. Gödel's Theorem shows that no such model of number theory will suffice, indeed, that no countable family of such models will suffice.

One can happily spend one's entire life within the precincts of such a formalization. One can even claim that he or she is doing number theory. But, as Gödel's Theorem makes clear, one is thereby trapped into, at best, an infinitesmal sliver of number theory. If we insist on having the formalistic cake and eating it too, most of number theory is thereby rendered (to borrow a term from Metaphysics) *noumenal*. Not to put too fine a point on it, we see that, at least in this context, the relation between noumenon and phenomenon is bound up with semantics (i.e., with external referents) and not with internal syntax.

Lurking in the background of Gödel's Theorem is, thus, an assertion of the form: the category of all formalizations of number theory is not number theory. Or, there exist models of number theory that are not formalizations. Such models must obviously manifest an inherent semantic character.

6. SIMULATIONS AND MODELING

People have been trying for a long time to move Gödel's Theorem from mathematics to science. The circle of ideas relating this theorem to modelling, which were briefly sketched in the preceding section, indicate one way in which this can be done.

As we have seen, formalizations are very special kinds of mathematical systems; they are systems governed by syntax alone. This fact severely limits the entailments they can manifest; indeed, Gödel's Theorem says that, compared with other mathematical systems (e.g., with number theory) formalizations are *impoverished*. They rely entirely on symbol manipulation, according to a finite family of syntactical rules.

Hence, the close tie between such formalizations and the concept of *algorithm*, and the concept of (mathematical) *machine*, already studied in great detail by Church, Tarski, Turing, and others, in the 1930's. It was already shown in those days that all these ideas are equivalent, hence the pervasive interest in the *kind* of mathematics that could be done with the aid

of them alone, i.e., the kind of mathematics that we could "program a machine" to do, or better, to *simulate*.

For some unfathomable reason, mathematical processes that could be thus simulated were called *effective*. As we have seen, effective processes in this sense are vanishingly sparse in mathematics. Nevertheless, the identification of "simulable" with "effective" has long been referred to as *Church's Thesis*. We repeat that effectiveness, or simulability, is property of a mathematical system, pertaining to the replacement of semantics (external referents) by syntax. Accordingly, and we cannot stress this too strongly, *simulation is not modelling*.

In any event, it makes perfect sense to ask of a mathematical system whether it is simulable (formalizable) or not. As we have seen, the answer is almost always "no." In particular, we may ask of a mathematical system *which is already a model* whether it is simulable or not. If it is, then it is natural to impute the limitations that make it simulable back to the causal processes which the model is supposed to represent. In fact, in this way a simulation of the model becomes a simulation of that (natural) system.

In this way, Church's Thesis can be transmuted into an assertion, not just about mathematics, but about the material world itself. In essence, it asserts that *every model of a material system must be simulable*. In this form, it becomes itself a law of nature, like the Second Law of Thermodynamics.

If true in this context, the implications of Church's Thesis are truly awesome. But on the face of it, the thesis does not look very startling. After all, are we not used to representing what goes on in the world by differential equations, which are always simulable?

Indeed, it can be shown that the material world mandated by Church's Thesis in this form is very like the world we know from contemporary physics, i.e., a very syntactic world of (structureless) particles and their configurations. If we look at the category of all models of a system in such a world, it has a very detailed structure. In a precise sense, there is a unique largest model, and a finite spectrum of smallest models (atoms). We can construct the largest model from the smallest, and conversely, and the same with every model in between. The material world is thus converted, by Church's Thesis, into the reductionist's dream.

7. COMPLEX SYSTEMS

Let us call a system satisfying Church's Thesis (i.e., such that every model is simulable) a *simple system* or *mechanism*.

As we saw above, Gödel's Theorem shows that number theory is not simple. It does not satisfy Church's Thesis in this form. Most of what goes on in number theory is ineffective: nonsimulable, nonalgorithmic, nonsyntactic.

On Models and Modeling

Is the same true in science? Are there material systems that possess nonsimulable models? Is Church's Thesis, so patently false in mathematics, nevertheless true in the material world? Is it the case that *causal* entailments between events or phenomena are sufficiently impoverished to allow the thesis to hold? In a word, are there, or are there not, material systems that are not simple, not mechanisms? Are there material systems that are *complex*, as number theory is complex in mathematics?

I would argue that the answer to this last question is yes, and that, in particular, biology is replete with them.

If so, then complexity in this sense is intimately tied up with the structure of the category of all models. In particular, there is, in general, no largest model in such a category, and, in general, no smallest models either. We cannot get away merely with models that are simulable, e.g., with differential equations that can be isolated from all external referents; to try to do so would be to commit precisely the error we discussed in Section 2 above. Above all, we must give up reductionism as a universal strategy for studying the material world.

But what can we do in a material world of complex systems if we must give up every landmark that has heretofore seemed to govern our relation to that world? I can give an optimistic answer to that question, beginning with the observation that we do not give up number theory simply because it is not formalizable. Gödel's Theorem pertains to the limitations of formalizability, not of mathematics. Likewise, complexity in the material world is not a limitation on science, but on certain ways of doing science.

Indeed, category theory itself suggests what we must do. A complex system still admits a category of models. In it, there will be a proper subcategory of simulable models. We can take limits in that subcategory; if we do it properly, the limit of a family of simulable models will still be a model, but not, in general, itself simulable. We can thus extract ourselves from the limitations of simulability, and enter thereby into a whole new world of modelling. In fact, modelling offers the only way into such a world of complex systems. It cannot be reached empirically, through data, any more than Gödel's Theorem expresses data about numbers.

Thus, we will conclude with the same assertion with which we started, though at a far more general level. One cannot forget the external referents. Modelling contains ineluctable semantic aspects, which inherently defy formalization. That is why modelling is, and will always remain, an art.

8. IN LIEU OF REFERENCES

The circle of ideas sketched in the text of the present paper has been germinating in my mind for a long time. I have talked about bits and pieces of it, from various points of view, for about three decades now, but the full picture is relatively recent. In what follows, I will sketch the sources of its various elements; the reader is referred to these for more details, and for fuller background and references.

I believe I was the first to suggest that category theory had important roles to play in the sciences [7]. The realization that this was so actually began dawning on me a couple of years earlier. I remember well my suggesting this, with a great deal of diffidence, to Samuel Eilenberg, from whom I first learned category theory. This was in 1958, when Eilenberg was in residence for a quarter at the University of Chicago. I will never forget his two-word response: "Oh, no." At this point, I realized there would be no help from this quarter, and that I was on my own.

My first discussion of Church's Thesis as a hypothesis about the material world dates from three years later [3]. As far as I can recall, my earliest treatment of complexity, in terms of the set of models that could be made of a material system, dates from 1973 [8]. I have returned to these matters repeatedly (cf. especially [2, 5, 6]. They are dealt with at greatest length in a monograph manuscript currently being prepared for publication.

REFERENCES

- 1 A. Rescigno and I. W. Richardson, The deterministic theory of population dynamics, in *Foundations of Mathematical Biology*, Vol. III, (R. Rosen, Ed.), Academic Press, New York, 1973, pp. 283-360.
- 2 R. Rosen, Anticipatory Systems, Pergamon Press, Oxford, 1985.
- 3 R. Rosen, Church's thesis and its relation to the concept of realizability in biology and physics, *Bulletin of Mathematics and Biophysics* 24:375-393 (1962).
- 4 R. Rosen, Dynamical System Theory in Biology, Wiley Interscience, New York, 1970.
- 5 R. Rosen, Effective processes and natural law in *The Universal Turing Machine—A Half-Century Survey*, (R. Herken, Ed.), Kammerer and Unverzagt, Hamburg-Berlin, 1988, pp. 523-537.
- 6 R. Rosen, Fundamentals of Measurement and Representation of Natural Systems, American Elsevier, New York, 1978.
- 7 R. Rosen, The representation of biological systems from the standpoint of the theory of categories, Bulletin of Mathematics and Biophysics 21:71-96 (1959).
- 8 R. Rosen, On the generation of metabolic novelties in evolution, in *Biogenesis-Evolution-Homeostasis*, Springer-Verlag, New York, 1973.