B P Belousov and his reaction

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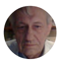

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Perspectives

B P Belousov and his reaction[1]

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The generation to which Boris Pavlovich Belousov (1893–1976) belonged has almost disappeared. The archives hold only a few documents about his life and basically secret research. This article is a brief biography of Belousov and attempts to reconstruct what lay behind his famous discovery of the oscillatory homogeneous chemical reaction named after him.

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1. Introduction

Boris Pavlovich Belousov (figure 1) is famous for discovering a chemical reaction that spontaneously exhibits temporal periodicity, a 'chemical clock'. Later elaborations by A M Zhabotinsky gave it the name 'Belousov-Zhabotinsky' (BZ) reaction. In one of his last interviews, Ilya Prigogine called the BZ reaction 'one of the most important discoveries of the century' (Hargittai 2003, p. 426). He considered it as important as the discovery of quarks or black holes. Every such evaluation of a scientific result can be condemned as an exaggeration. Nevertheless, the BZ reaction contributed substantially to Prigogine's non-linear thermodynamics by creating its experimental basis and visible chemical image. The BZ reaction is a striking example of what Prigogine named a dissipative structure, which operates far from thermodynamic equilibrium in an open system.

In his *Synergetics*, Hermann Haken uses the BZ reaction as a paradigmatic example to explain his concept of the parameters of order and slaving (Haken 1977). This reaction is a standard example of complex behaviour in textbooks on non-linear dynamics and the theory of non-linear oscillations.

Figure 1. B P Belousov (1893–1976).

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The dramatic history of the BZ reaction is roughly known to scientists who deal with non-equilibrium thermodynamics and non-linear dynamics. In fact, this history has been incorporated into scientific folklore. Besides, several essays on it have been published. In 1984, V Poleshchuk, a historian and journalist, published an essay on B P Belousov's discovery in the famous Soviet literary journal *Novy Mir*. S E Shnol, the university research teacher of A M Zhabotinsky, wrote two reminiscences concerning Belousov's discovery of the reaction for which he subsequently became well-known and about the early stage of Zhabotinsky's further development of that work (Shnol 1997, 2001). The prominent biologist A Winfree wrote an essay on the Belousov discovery based on his rich scientific experience and on conversations with Russian colleagues (Winfree 1984). Finally, Zhabotinsky himself wrote a couple of papers on how he further developed Belousov's discovery, first under S E Shnol and later independently (Zhabotinsky 1985, 1991).

The history of the BZ reaction presents a double challenge to the history and philosophy of science. The essays mentioned above report that Belousov's original paper, in which he described discovery of a homogeneous oscillatory reaction and proposed a tentative mechanism for that process, was rejected by two main Soviet chemical journals (*Zhurnal obshchey khimii* [The journal of general chemistry] and *Kinetika i kataliz* [Kinetics and catalysis]) in 1951 and in 1955 respectively. Belousov finally managed to publish a brief abstract in the obscure Proceedings issued by the Institute where he was employed as head of a laboratory (Institute of Biophysics at the Ministry of Public Health) (Belousov 1959). Belousov died in 1976. His full paper was only posthumously published in 1981 (Belousov, 1981). This happened after awarding the Lenin Prize to Zhabotinsky, Director of Institute where he was employed, two other researches of that institute, and B P Belousov (1980). The Lenin Prize was essentially the Soviet Nobel Prize. The government had the State Prize to encourage outstanding scientific results, and awarded the Lenin Prize for exceptional results.

An English translation of the 1951 version of his paper appeared in 1985 (Belousov 1985). In an article (Pechenkin 2004) I tried to explain why the Belousov reaction was rejected by the scientific community of the 1950s, but was accepted in Zhabotinsky's version in the mid-1960s. The Kuhnian concept of paradigm was used in that article.

The present essay concentrates on Belousov's personal trajectory and attempts an explanation of what could have induced Belousov's discovery in his routine work on applied and industrial chemistry. The second section describes Belousov's reaction as it is presented in the above-mentioned small paper published in the Proceedings issued by the Institute where he was employed (1959) [This book (collection of abstracts) was published in 1959, but in the book series it is dated 1958.] This is the only paper that Belousov was able to publish on his reaction during his lifetime.

Certainly it has not been updated. At the end of the 1960s, A M Zhabotinsky and coworkers proposed their mechanism of Belousov's reaction. In 1972–1974, R J Field, E Körös and R M Noyes proposed their mechanism which became standard (*see* Field and Burger 1985 pp 75–116). However, Belousov's report allows us to connect his discovery with his routine work on applied and industrial chemistry.

The third section represents Belousov's biography. In contrast to the biographies available on different websites, this biography is strongly documented.

The fourth section is dedicated to a discussion of Belousov's biography in view of his paper representing his reaction. I have tried to find the prerequisites for Belousov's discovery through his research in toxicology and radiational medicine.

This article uses archival material (the *Archive of Medical and Biological Extreme Problems*) and interviews conducted by me with Belousov's colleagues.

2. The Belousov reaction

In his small, two-page paper (Belousov 1959), Belousov describes a homogeneous reaction connected with a periodic change in colour of an entire reaction mixture: from colourless to yellow and back to colourless, etc. (figure 2). This reaction was the oxidation of citric acid by bromate ion, which is a well known oxidant. As Belousov explained, usually the oxidation reaction of citric acid by bromate is very slow. The rate of oxidation is increased if cerium cation

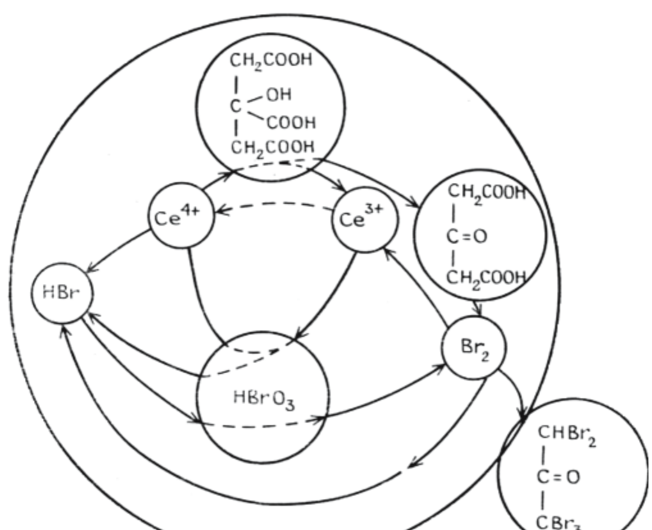

Figure 2. Belousov's scheme of his reaction.

is used as a transmitter of oxidation. Bromate ion oxidises Ce^{3+} to Ce^{4+} and, in turn, Ce^{4+} oxidizes citric acid and cerium is reduced to Ce^{3+}. Since the solution that contains Ce^{3+} is colourless, and the one that contains Ce^{4+} is yellow, the reaction undergoes a periodic change in colour.

Belousov describes the mechanism of his reaction as follows. First of all, the oxidation of citric acid by quadrivalent cerium takes place. This reaction results in the disappearance of yellow colour and accumulation of Ce^{3+}.

The next stage is the oxidation of Ce^{3+} by bromate to Ce^{4+}. The oxidation of citric acid by Ce^{4+} occurs slowly, but the oxidation of Ce^{3+}, which is a product of the first reaction, proceeds even more slowly. As a result, newly formed quadrivalent cerium could be re-reduced in the former reaction. Quadrivalent cerium does not influence the colour of the reaction mixture.

However, the oxidation of Ce^{3+} to Ce^{4+} becomes rapid in the course of time. The reason is as follows. This reaction produces bromide, which accumulates in the reaction mixture. However, this bromide reacts with bromate. This reaction is rapid. The following reactions which produce bromine proceed even faster. This bromine is immediately captured by hydroxyl acid (acetonedicarboxylic acid) that comes from the oxidation of citric acid by Ce^{4+}. As a result, inactive penta bromacetone is formed. The removal of bromine leads to an acceleration of the reaction which forms quadrivalent cerium.

Belousov outlined the following chain of reactions:

$$C_6O_7H_8 \ (\textit{citric acid}) + Ce^{4+} \rightarrow C_5O_5H_6 + Ce^{3+} + CO_2 + H_2O$$

$$BrO_3^- + Ce^{3+} \xrightarrow{H^+} Ce^{4+} + Br^-$$

$$Br^- + 2H^+ + BrO_3^- \rightarrow HBrO + HBrO_2$$

$$H^+ + Br^- + HBrO \rightarrow 2Br^- + 2H_2O$$

$$3H^- + 3Br^- + HBrO_2 \rightarrow 2Br_2 + 2H_2O$$

$$C_5O_5H_6 (\textit{acetonedic arboxylic acid}) + 5Br_2 \rightarrow C_3OHBr_5 \ (\textit{penta bromeacetone}) + 5Br^- + 2CO_2 + 5H^+$$

After disappearance of Ce^{3+} the colour of the mixture is determined by Ce^{4+}; as a result the mixture is again yellow.

Belousov also assumed the release of free bromine. According to Belousov, acetonedicarboxylic acid is quickly consumed because the rate of its production is very slow. As a result, the liberation of free bromine takes place and the colour of the mixture suddenly becomes yellow. Then bromine is 'gradually but at a definite rate' consumed to form Ce^{4+}.

Because of the above processes the reaction mixture consists of citric acid and bromate, Ce^{4+} and inactive pentabromacetone. The processes start again. The reaction will stop when the amount of citric acid and bromate is exhausted.

In his early writings, A M Zhabotinsky showed that the liberation of free bromine was not essential for the Belousov reaction.

Belousov felt that he had discovered a significant phenomenon. 'The reaction described here is remarkable because during its occurrence there is a complex ordered sequence of oxidation–reduction processes, one which is periodically revealed by a temporary change in the colour of the entire reaction mixture' (Belousov 1959, p.145).

3. Who was Belousov?

Boris Pavlovich Belousov was born in Moscow in 1893. In 1908, his parents took him to Zurich where he was a student of the Real Gymnasium and then of the Technical University. Belousov wrote that he graduated from the University in 1915. However, his personal record does not contain any certificate to confirm this. There is just a paper of the Soviet Union Ministry of Public Health which confirms that he underwent studies at this University.

In 1916 Belousov returned to Moscow. He started to work for the chemical laboratory of metallography. In 1919, he began to teach chemistry at high school and the People's University. At the beginning of the 1920s, he started to work for the Higher Military Chemical School of the Red Army (the original name of the Soviet Army). He taught the course on general chemistry and chemical warfare. At the same time, he conducted research on chemical warfare.

In 1935, he left the staff of the Red Army and began to work for the All-Union (All-Union means National) Institute of Sanitation and Chemistry. This allowed him to concentrate on research. As a researcher at the All-Union Institute of Sanitation and Chemistry, Belousov wrote the following reports: 'Studies in dosed micro-amounts of chlorine' (1936), 'Research in the field of detectors of mustard gas and Lewisite' (1935) and 'Studies on the reaction of *ββ*'dichlordiethyl sulphide with xxx' (1939). Secret substances were indicated as xxx in his list of scientific results.

During World War II, the Institute of Sanitation and Chemistry, where Belousov had been employed since 1935, was transformed into the Institute of Pathology and Therapy of Intoxications. In 1952, the Institute and Radiation Laboratory of the Ministry of Public Health formed the basis of the new Institute of Biophysics (see: *Piat'desiat let sluzheniu, 2001)* (figures 3, 4).

This institute should not be confused with the Institute of Biophysics under the Soviet Academy of Sciences. The latter was also established at the beginning of the 1950s in Moscow. At the beginning of the 1960s, it moved to the small city of Pushino-na-Oke in the Moscow region.

Figure 3. Lev Mikhailovich Rozhdestvensky, who worked with Belousov in the 1960s, in his Laboratory at Institute of Biophysics (photo: 2003).

Zhabotinsky was employed there after graduating from Lomonosov Moscow State University.

During World War II, Belousov conducted research in the area of antiburn remedies. For his contribution to this area, he was decorated with the Order of Lenin, the highest Soviet Order.

In 1941, Belousov wrote a paper entitled 'A new chemical for the deactivation of phosphorus'; in 1942 he wrote a paper entitled 'A new chemical for deactivation of phosphorus and light metals'. In the summary of the former paper he wrote: 'A new remedy (VIP-17) containing a compound xxx with a touch of catalysis has been worked up. This substance rapidly and completely interacts with phosphorus and its solutions. The application of gauze tampons impregnated by salts with a touch of catalysis and hygroscopic compounds was proposed (VIP-19)'. VIP is an abbreviation for *Vsesoiuznyi Institut Patologii* (All-Union Institute of Pathology).

At the beginning of the 1950s, the problem of radiation protection became one of the main problems for the Institute of Biophysics. The Soviet Union began to prepare itself for possible nuclear war.

Belousov was charged with the problem of radioprotection and later his concern extended to the problem of excretion of radionuclides from a human being. True, Belousov and his colleagues did not speak about 'radionuclides'; they used the term 'radioactive heavy metals' in this connection.

Belousov's endeavours in the area of radioprotection are partially represented in the 1963 book entitled *The radioprotective action of cyanic compounds* (Rogozkin *et al*. 1963). The basic idea is expressed as follows: 'The chemicals which are able to suppress the oxidation processes in an organism immediately before irradiation help the organism to resist the radiation injury' (p. 10).

Belousov wrote a chapter on the production and chemical properties of amigdalin (mandelonitril-beta-gentobiozide), a chemical containing a cyanogen group.

According to commemorations, Belousov's main idea was to use chitosan as a radioprotectant. Chitosan is a linear polysaccharide that is found in the crustacean exoskeleton and insect cuticles. Dr L M Rozhdestvensky (figure 3), who collaborated with Belousov on the chitosan project at the beginning of the 1960s and still works for the Institute of Biophysics, said that it was an important step in the development of radioprotectants. Although chitosan did not justify the hopes, it brought a new methodology to radioprotection. In the 1950s low-molecular sulphydril-containing compounds such as Cystamine and cysteamine were commonly used as radioprotectants. The efficiency of

Figure 4. Institute of Biophysics (photo: 2005).

protection was low and it required prior injection at high doses that resulted in deleterious side effects including hepatotoxicity, possibly due to formation of mixed disulphides with cysteins in proteins. In turn, chitosan was a high molecular compound and its action consisted basically in activating host defences. Like the generation of radioprotectors that followed (for example, interleukin-1), chitosan induces the production of endogenous substances that are able to pass ahead of the harmful action of penetrating radiation.

Although Belousov never published articles on chitosan, he ran the chitosan project (this protector was named RS-10) and, according to some of commemorations, his retirement in 1970 was due to the failure of the chitosan project.

Belousov, who was a chemist by training, went deeper into advanced biochemical problems. As a matter of fact, he had approached biochemistry earlier, when he conducted research in chemical warfare. In his autobiography, he mentions his theory of intoxication, but this theory is not represented in the available documents. One can judge Belousov's approach to toxicology by his unpublished manuscript: 'On chemical presumptions concerning the foundations of the effective action of the remedies that are tested in the therapy of radiation damage'. In this manuscript, he referred to his hypothesis based on his experience in chemical warfare. The hypothesis, which is apparently out of date now, proposed a chain of biochemical processes. Belousov emphasized that an amino acid, histidine, which is formed 'as a result of autolysis of tissue proteins' can, under the influence of oxidants change into toxic compounds.

In his autobiography, Belousov wrote that in connection with his work on the removal of toxic substances from the human organism, he had shown the importance of some biochemical cycles. He mentioned the tricarboxylic acid cycle in the cited manuscript.

Belousov continued his research in analytical chemistry. In the issue where his paper on the periodic reaction was published, he with his collaborator A P Safronov published a small article entitled 'New approaches to the qualitative analysis of cations from the point of view of a selected theory of chromaticity'. However, in the list of his scientific results Belousov mentioned his manuscript with Safronov similarly entitled and dated by 1947. Apparently his with Safronov 1959 article was an outcome of the project launched before his first attempt to publish an article about the oscillatory reaction and ideologically connected with that article.

The authors wrote: ‘In the course of search for reagents for qualitative determination of uranyl-ions we considered analytical colour reaction of a number of heavy metals with organic and inorganic compounds.

‘By reviewing the corresponding literature we came to the opinion about the essence of the processes which result in the formation of colouration in some colour reactions. We also proposed a classification of some analytical reagents according to their reactions with the ions under consideration’.

‘Our classification is based on the principle of the intermolecular reversibility of the charge transfer between the atoms of metals which occur in the states of higher and lowest valency in a molecule’.

‘The “mineral blues” provide the simplest example. Their chromaticity is explained by isoatomic charge transfer’ (Belousov and Safronov 1958, p. 147)’.

Say, wolfram blue has the formula: $WO_2 \bullet WO_3$. Due to the charge transfer 4↔6, we have a colour mixing grey (the colour of WO_2) and lemon yellow (the colour of WO_3).

In touching on the ‘heteroatomic’ charge transfer the authors wrote about ‘electron oscillations’.

According to recollections, Belousov was familiar with cultural events and sometimes tended to speak about art with friends. His wife was an actress, but they got divorced. Like the majority of his contemporaries, he avoided any political discussions.

As mentioned, Belousov retired in 1970 and died in 1976. He was posthumously awarded the Lenin prize in 1980.

4. Discussion

So, in which way did a researcher whose occupation was applied and industrial chemistry (let us recall ‘gauze tampons impregnated by salts’ mentioned above) come to the fundamental result regarding an oscillatory homogeneous reaction? Does Belousov’s applied research contain analogies of those processes which form his reaction? Does it contain grounds for the construction of such an analogy? The following discussion of this question should be treated as tentative as it is based on a restricted body of historical documents.

Quadrivalent cerium – $Ce(SO_4)_2$ – was at hand in Belousov’s laboratory, literally and figuratively. Cerate oxidimetry was broadly used in chemical analysis, in particular for oxidimetric titration of uranium (4+). This procedure is based on the equation

$$2Ce^{4+} + U^{4+} \longrightarrow 2Ce^{3+} + U^{6+},$$

where Ce^{4+} is converted into Ce^{3+}, as in the Belousov reaction. Thus, for Belousov, it was a routine chemical reagent that he could take off the shelf at any time. As a radiation toxicologist, Belousov and his collaborators had extensive experience and expertise in the chemistry of heavy metals .

It is not known if Belousov worked with bromates. However, the method of bromatometry is a part of analytical chemistry.

The main thrust came from the idea of the tricarboxylic acid (citric acid) cycle. In his posthumously published paper, Belousov himself wrote that the ‘peculiar behaviour of citric acid in relation to some oxidants lies at the foundation of the periodic reaction,’ (Belousov 1985, p. 607). He characterized his reaction as a ‘cycle’.

The American biologist Arthur Winfree, who was mentioned in the first section as the author of a historical essay about Belousov’s discovery, wrote the following:

‘His interest included biochemistry, and 1950 found him endeavoring to model catalysis in the Krebs cycle using the metal ions cerium instead of the protein-bound metal ions common in the enzymes of living cells. The Krebs cycle is a universal part of metabolism by which acetyl residues are oxidized to carbon dioxide in mitochondria. It is called a “cycle” not because it oscillates in time, but just because the reaction sequence leads in a circle, much as any geochemical cycle. Much to Belousov’s surprise, his test-tube caricature, a solution of citric in water with acidified bromate as oxidant and yellow ceric ion as catalyst, turned colourless and returned to yellow periodically for as long as an hour (at room temperature) while effervescing carbon dioxide!’ (Winfree 1984, p. 661).

Winfree had in mind catalytic reactions that were outlined by A Szent-Györgyi as early as 1935. They were included in the network of metabolic pathways and studied by Hans Krebs in connection with the research that led him to the cycle of citric acid (the Krebs cycle). These reactions provided the proton transfer suggested by the Krebs cycle. The catalyst was typically an iron ion bound to the porphyrin ring of the haem group of oxidation enzymes. The mechanism may be represented as follows:

$$Malate + 2Fe^{+++} + 2H^{+} \longrightarrow oxalocetate + 2Fe^{++} + 2H^{+},$$

$$2Fe^{++} + 2H^{+} + ½\ O_2 \longrightarrow 2Fe^{+++} + H_2 0.$$

The conversion of Fe^{+++} into Fe^{++} and again into Fe^{+++} is not a periodic process. Winfree emphasized this. However, it is a cyclical process which could induce the idea of a periodic reaction.

The idea of biochemical cycles was rather popular at the turn of the 1950s. In 1951, the first textbook on biochemistry appeared in Russia (Zbarsky). In this textbook, the Krebs cycle was represented.

It is possible that Belousov’s reaction was stimulated by his reflections on chromaticity in analytical chemistry. As noted, Belousov reviewed the theories of chromaticity and paid attention to the intermolecular reversibility of charge transfer between the atoms of metals. This was stated in his article with Safronov of 1959 published after his basic article on chemical oscillations (1951) and representing an outcome of their 1947 project.

Belousov's reaction did not have any practical application for a long time. However, it is genetically connected with his work on applied and industrial chemistry.

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