

A. N. Bach – A Revolutionary in Politics and Science (Commemorating the 150th anniversary of Academician A. N. Bach)

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An outstanding scientist who made substantial contributions to the world of science and played an exclusive role in the formation of biochemical studies in our country, Aleksey Nikolaevich Bach was born 150 years ago, on the 17th of March 1857, in the quiet town of Zolotonosha (Poltava guberniya), in a large family of a distillery technician. The family had very modest possibilities, but his parents, respecting science, gave a good education to Aleksey. At the age of 10 he joined the 2nd Kiev gymnasium. Exceptional memory, clear understanding of the subject matter, and well-defined expression of ideas distinguished him among other pupils. He was particularly interested in natural sciences. He also enthusiastically learned French, German, and later English and could freely read fiction published in these languages. Later in expatriation, excellent knowledge of these languages helped him to find his place in science, initially as a translator of scientific papers and then as an experimental biochemist.

In spite of his parents' wishes to see him as a physician, in 1875 A. N. Bach entered the Department of Natural Sciences of the School of Physics and Mathematics, Kiev University. He was an assiduous student and worked in mineralogical and zoological departments, and also in the botanical garden. Among a few students he attended English language lessons (paid for by the students themselves) and together with many friends, Bach had to work for a living allowance as a tutor. Chemistry was his favorite subject, especially those directions which constituted later a new science now known as biochemistry. He attended the lectures delivered by Professor N. A. Bunge and Assistant Professor P. P. Alekseev. Both graduated from Kiev University and continued their education in Germany (with the outstanding

chemists A. Baeyer, G. Kolbe, and F. Wohler). Under Bunge's supervision, Aleksey Bach made studies in electrochemistry and investigated redox processes and technology of sugar preparation.

Everything sharply changed in 1878, when A. N. Bach among 30 students participated in a student's meeting was sent down from the university for three years without rights to enter other higher educational institutions and exiled. Bach spent more than 3.5 years in exile: initially in Belozersk town (Novgorod guberniya) and later in Novomoskovsk and Bakhmut (Ekaterinoslav guberniya), where he was moved due to pulmonary tuberculosis. In January 1882 he returned to Kiev and restored his rights and became a student again. However, he did not finish his course in the university because he joined the Kiev organization of the party Narodnaya Volya and was involved in propagandist work. He was a leader in propaganda of socialistic ideas among workers. In the end of February 1883, Bach went underground. Changing false passports and names, he moved from one city to another and organized underground work. In that year, he wrote his famous brochure "The Tsar-Hunger" [1], which became one of the "table books" of the revolutionary movement. It was highly evaluated by V. I. Lenin, and socialist revolutionaries published millions of copies of this brochure. Bach had great respect and won unquestioned authority among Narodnaya Volya party members and later among socialist revolutionaries due to integrity of his character, crystal honesty, and disinterestedness. He was a member of Central Executive Committee of Narodnaya Volya (last staff) before its defeat in 1882-1883. Due to lucky opportunity or prudence, he avoided arrest. In 1885, he realized the error of his activity in Narodnaya Volya, and his tuberculosis worsened. These prompted him to leave Russia using a false passport. He was 28, and he suggested that he left Russia forever.

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A. N. Bach. 1879

As many other political emigrants, A. N. Bach initially settled in Paris. The first year in emigration was the most difficult. A lonely man in his thirties without profession and future plans, he lived in misery and even starved. So he had to look for any job to get money. He could not continue his education, but science related work appeared soon due to his skill in foreign languages. Bach became a referent at the patent department of the Journal *Moniteur Scientifique*; this work supported him financial-

ly during the period of his emigration and also it gave a possibility to be updated in the latest achievements in applied chemistry in various countries. Later he published papers and reports on his own biochemical studies there. Difficulties of emigration life provoked deterioration of his health and resulted in recurrence of tuberculosis. Physicians strongly recommended medical treatment in Switzerland, and in the spring of 1888 Bach moved there, where he met Alexandra Alexandrovna Cherven-Vodali, a 17-year-old girl from an impoverished family of Bessarabian landlords. In summer 1890, they married and the marriage was registered at the mayorate of the Fifth District of Paris. Then the young couple married in the Orthodox Church at the Romanian Embassy. Their happy marriage with three daughters continued for 56 years.

In Paris, Bach began his scientific activity in the laboratory of Professor Paul Schutzenberger at the Department of Inorganic Chemistry, College de France. The professor liked the young Russian political emigrant, who proposed a reasonable plan for experimental work on the mechanism of carbon assimilation. Thus, a half-educated chemistry student could continue laboratory practice in a higher research institute of France. The College de France had the reputation of a center of free scientific creative work, and many outstanding scientists worked and delivered lectures there: Andre Marie Ampere, Marcelin Berthelot, Claude Bernard, Frederick Joliot-Curie. Traditionally work in the College de France was for free and it did not give right to apply for scientific degrees. Bach worked at College de France from 1890 to 1894.

Doctors strongly recommended that Bach move to Switzerland, and in 1894 the Bach family settled in



A. A. Cherven-Vodali. 1890



A. N. Bach. 1890

Geneva, where they would live for almost a quarter of a century. The Bach family fitted into conservative Geneva society. Alexandra Alexandrovna, an educated medical doctor, was able to get local practice, and A. N. Bach continued his studies in his own house laboratories, which he “organized” in a mansard or store rooms of their Geneva flats. He worked there alone without assistants, and made equipment and washed laboratory glass by himself.

The Geneva period was the most fruitful one in the scientific activity of Bach. During that period, he formulated the most well known ideas and performed the main experiments. In Geneva, he became an internationally distinguished scientist. During 23 years of the Geneva period, Bach published 87 papers in leading international journals. In recognition of his scientific achievements, he was elected as the Chairman of the Geneva Naturalist Society in 1916. In the annual report describing work of this society in 1916 he stated: “In spite of horrible crisis caused by the World War, the number of scientific reports increased compared with the pre-war period. Perhaps, it can be attributed to the fact that at moments of catastrophe people face constant values, and science is one of the most reliable values” [2]. In the beginning of 1917, Lausanne University awarded A. N. Bach the degree of Doctor *honoris causa* in recognition of scientific merit of his works. In a letter of February 9, 1917, A. Shavan, Rector of Lausanne University, wrote to A. N. Bach: “... The University expresses our delight and gratitude to you for your innovative investigations opening the way to theoretical studies of respiration and particularly for your outstanding works on oxidative and reductive enzymes” [2].

Bach belonged to scientists of the thinker type. In his studies, Bach linked the past and the future. In various periods of his life, Bach took interest in various ideas, which completely devoured him; many of his ideas were ahead of his time. He believed that specificity of the living world is determined by various chemical conversions, which constantly occur in living organisms rather than specific features of composition of the living world. His attention was fixed on three key problems of biochemistry: chemistry of carbon assimilation by green plants, representing a basis for organic matter formation in nature, the problem of oxidative processes occurring in a living cell, particularly, chemistry of respiration, and enzymology. In pilot studies on the chemical mechanism of carbon dioxide accumulation by green plants carried out in College de France, he gave a new explanation of sugar formation during carbon dioxide assimilation: he considered carbon assimilation as a coupled redox reaction involving the elements of water. In contrast to the existing viewpoint, Bach proposed that water rather than carbon dioxide is the source of molecular oxygen [3]. His idea on the involvement of coupled redox reactions in the processes of CO₂ assimilation and photosynthesis was not



A. N. Bach in his home laboratory (Champel, Geneva), about 1900

only correct but also predictive. According to modern considerations [4], plants, algae, and most autotrophic microorganisms assimilate carbon dioxide via the reductive pentose phosphate Calvin cycle, which involves ribulose-1,5-bisphosphate carboxylase/oxygenase (RubisCO). This enzyme catalyzes initial stages of cycles of photosynthetic carbon reduction and carbon photooxidation by addition of CO₂ and O₂ to ribulose-1,5-bisphosphate, respectively. Several forms of RubisCO regulated by various effectors have been recognized. Studying action mechanism of tyrosinase, Bach concluded that this is an oxidative rather than a hydrolytic enzyme (as other researchers suggested) [5]. Later it was found that tyrosinase is indeed a monophenol, *o*-diphenol oxidoreductase, a binuclear copper containing enzyme catalyzing two types of reactions: *ortho*-hydroxylation of monophenols (cresolase activity) and oxidation of *o*-diphenols followed by formation of *o*-diquinones (catecholase activity) [6].

Bach's concept that molecular oxygen may be directly involved in processes of biological oxidation is correct for many enzymes. According to modern nomenclature, the whole subclass of oxygenases (1.13.) includes enzymes catalyzing insertion of molecular oxygen into oxidizable substrates such as polyphenols, amino acids, ascorbic acid, unsaturated fatty acids, and carotenoids. These enzymes play a very important role in metabolism. One of these enzymes, cytochrome P450, corresponds well to the description postulated by Bach “as enzymes adding -O-O- groups from unsaturated easily oxidizable substances and transfer activated oxygen on poorly oxidizable substrates”. Now three families of cytochrome

P450 differing in their structure have been recognized. The enzyme is characterized by polymorphism. For example, in man 57 various cytochromes P450 have been found: half of them is involved in metabolism of endogenous compounds (biosynthesis of steroids, prostaglandins, bile components, retinoic acid, fatty acid metabolism), the other half is involved in detoxification of hydrophobic venoms, carcinogens, toxins (including neurotoxins involved into pathogenesis of Alzheimer's disease), and xenobiotics. In contrast to classic enzymes characterized by strict substrate specificity, microsomal cytochromes P450 can bind and metabolize a large number of substrates differing in size, shape, and stereochemistry [7].

A. N. Bach was one of the first scientists who proposed the idea that slow oxidative and respiratory processes are based on peroxide formation. He suggested that the inert state of molecular oxygen might be overcome only by cleavage or loosening of bonds between oxygen atoms (in molecular oxygen) and he considered this as an important precondition for any oxidative process [8]. Formulating his famous theory of peroxidase oxidation, Bach considered already known facts and also his own experimental data (obtained including model systems). According to Bach, energy required for activation of molecular oxygen comes from oxidizable substrates themselves, which represent chemically unsaturated compounds activating oxygen during interaction with it. The oxidative reactions end by cleavage of one of two bonds in the oxygen molecule, and the resultant peroxides bind to the oxidizable substrate. Being unstable and chemically reactive compounds, the reaction products further oxidize other substrates. Bach denominated the added products "peroxide", which can easily donate one or both added oxygen atoms to another molecule of the same or different compound. For evaluation of the novelty of Bach's ideas, one should take into consideration that from the discovery in 1819, hydrogen peroxide had been always considered as a toxic agent. Bach's idea conflicted with generally accepted viewpoint, but he was right. Now there is evidence that hydrogen peroxide (H_2O_2) is an obligate component of cells of aerobic organisms (from prokaryotes to man), and the cells contain not only peroxide sensor(s) [9], but also a regulatory system responsible for maintenance of hydrogen peroxide concentrations at the level required for viability of the organism. Peroxide plays an important protective role (e.g. in phagocytosis); it is involved in degradation of some proteins and also in oxidative biosynthetic reactions. Very recently, it has been also demonstrated that peroxide acts as a second messenger in cell signal transduction, especially in higher organisms [10], as inducer or inactivator of transcription factors, during induction of apoptosis or necrosis, and also in cell-cell interactions.

The latest achievements in studies of the mechanism of cytochrome oxidase functioning underlie the triumph

of Bach's peroxidase theory. Cytochrome oxidase is a terminal component of the aerobic respiratory chain of mitochondria and many prokaryotes. This enzyme catalyzes the four-electron reduction of molecular oxygen; according to modern considerations [11], cytochrome oxidase integrates two sequential redox activities—oxidase and peroxidase. This enzyme can be considered as a proton translocating peroxidase with additional oxidase module activating oxygen; oxidase and peroxidase phases of the catalytic cycle may involve various structural states of cytochrome oxidase.

Developing an idea on the role of peroxides, Bach published a series of studies on oxidative enzymes, catalase, oxidases, and especially peroxidase [12]. He isolated peroxidase from plant sources: juice of white turnip, pumpkin fruits, horseradish roots, mushrooms. His daughter remembered that "he, already a distinguished scientist, shed so many tears in the process of grinding of horseradish in quantities striking imagination; during that time in Geneva, Bach did not have assistants and he carried out all experiments by himself" [2]. According to modern considerations, peroxidases form a large multigene family of heme-containing monomeric glycoproteins utilizing hydrogen peroxide or molecular oxygen for oxidation of various compounds. Reflecting the large number of isoforms and heterogeneous regulation of peroxidase expression, Passardi figuratively said that "peroxidases have more functions than a Swiss army knife" [13].

Bach also investigated catalase, a heme-containing protein catalyzing cleavage of hydrogen peroxide to water and oxygen; he was interested in its ratio with peroxidase, its effect on alcoholic fermentation in yeasts, etc. [12]. Now the primary structure is known for more than 300 catalases from various sources [14, 15], including monofunctional catalases (more than 225), bifunctional catalases/peroxidases (>50), and Mn-containing catalases (>25). Bifunctional catalases/peroxidases are heme proteins, probably originating from doubling of an ancestor gene encoding peroxidase. However, in exact accordance with prediction of Bach's peroxidase theory, under certain conditions the monofunctional catalases may act as peroxidases in peroxide decomposition. Recently it has become evident that catalase together with superoxide dismutases plays an important role in detoxification of superoxide anion, a highly toxic radical formed in eukaryotic cells, mainly in the mitochondrial respiratory chain. It can cause mutations in mitochondrial DNA, and this may result in the development of neurodegenerative diseases as well as such common diseases as diabetes and cancer [16].

Like many scientists of that time, Bach was also involved in studies of laccase (at that time it was known as phenolase) [17]. Laccases are multinuclear copper-containing oxidoreductases catalyzing one-electron oxidation of substrates followed by simultaneous reduction of

molecular oxygen to water [18]. Since it was already known that this was oxidoreductase, he paid much attention to this enzyme and demonstrated its wide specificity with respect to various phenols [17].

Bach was interested in nitrate reduction; he considered this process as one of the most interesting chemical phenomena in plants. In his viewpoint, “its direct result consists in formation of proteins, which are a precondition for any living process” [19]. Studying concepts of nitrate reduction proposed in his time, Bach came to the conclusion that nitrate is converted into nitrite and then into hydroxylamine; the latter interacts with formaldehyde yielding formaldoxime and then formamide. Now it is accepted that nitrate reduction promotes utilization of NO_3^- as the source of nitrogen (nitrate assimilation), formation of metabolite energy during employment of NO_3^- as the terminal electron acceptor (nitrate respiration), and dissipation of excess of reductive energy for maintenance of redox balance (nitrate dissimilation). The two-electron reduction of nitrates to nitrites involves nitrate reductase.

Bach was also interested in problems of molecular nitrogen fixation and formation of ammonia during this process. He considered the idea that, by analogy with fermentation, molecular nitrogen fixation occurs due to the functioning of specific enzymes. So he with his colleagues tried to obtain cell free enzyme preparations from *Azotobacter vinelandii* (a very active nitrogen fixation species), which would catalyze fixation of N_2 and formation of NH_3 . Now it is known that the nitrogenase enzymatic complex consists of two proteins, Mo-Fe-protein and Fe-protein. The latter contains sites for binding and hydrolysis of MgATP. Mo-Fe-protein contains sites for binding and reduction of substrates. During catalysis an electron is transferred from Fe-protein to Mo-Fe protein, and this process is accompanied by hydrolysis of at least two MgATP molecules per one electron transferred. ATP hydrolysis in the nitrogenase complex is controlled by cyclic association/dissociation of components between electron-donor ATPase (Fe-protein) and Mo-Fe protein. Recent achievements in crystallography and spectroscopy revealed details of this process [20].

Results of numerous studies by A. N. Bach on oxidative and other enzymes (more than 100 papers) were published in *Proceedings of the Paris Academy (Academie Royale des Sciences de Paris)*, in the *Journal of German Chemical Society (Zeitschrift fur Deutsche Chemische Gesellschaft)* (Bach was a member of this society), and in other foreign periodical editions. Interestingly, Bach's papers published more than century ago are still cited. According to ISI, Bach's papers published during the Geneva period were cited 120 times during the last 17 years!

In the beginning of 1917, Bach, a 60-year-old man, an internationally distinguished scientist at the top of his scientific glory, the father of a large and friendly family,

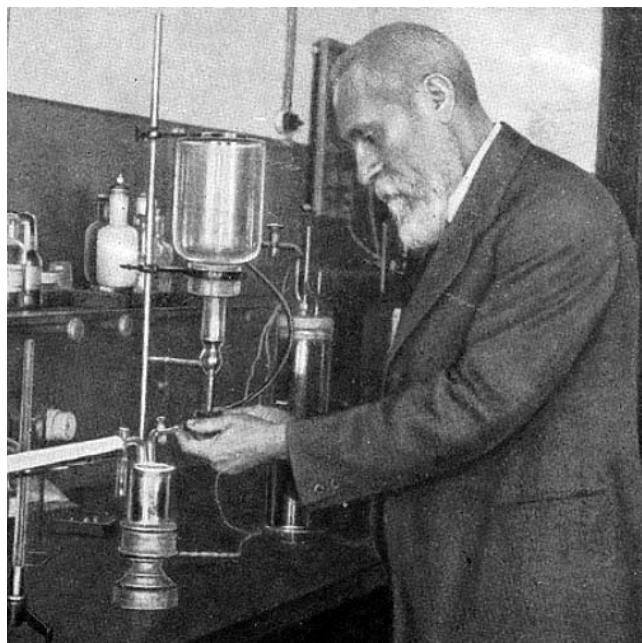
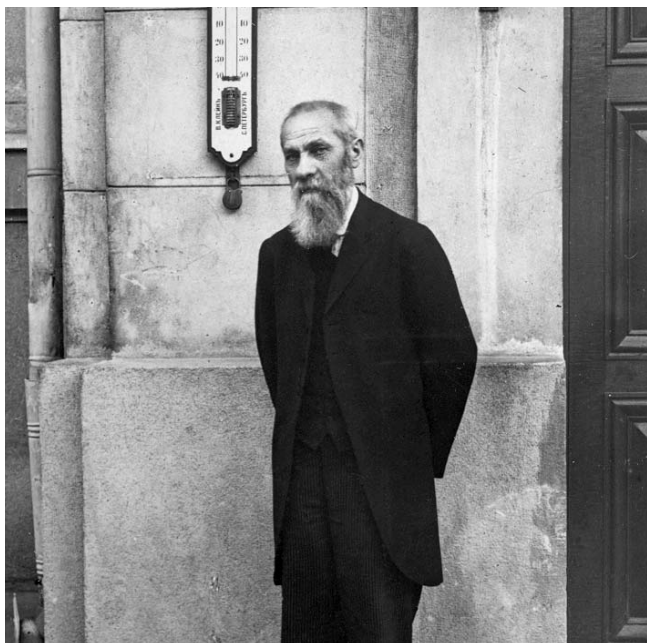


A. N. Bach. 1917

left quiet Switzerland, his laboratory, respectable position in the scientific world, home comfort, and came back to revolutionary Russia after news about the February revolution in his homeland. A new period of his life began. This period discovered its talent as the outstanding organizer of Russian science.

Two weeks after his return Aleksey Nikolaevich together with his wife and daughter went to the settlement of Tikhiey Gory near the town of Elabuga to visit chemical factories. There he met Lev Yakovlevich Karpov, who became a director of chemical factories in Bondug (also in Kama region) in 1915. In friendly discussions, they dreamed about organization of large research institutes in Moscow, which would not only solve theoretical problems but also realize results of theoretical studies in practice of factories. In pre-revolutionary Russia research institutions were private laboratories in some industrial factories. There were only a few medical and biological institutes, but in reality they were just laboratories. Even in the Academy of Sciences, there were only five laboratories and the main studies were carried out in university departments. All research institutions worked separately, uncoordinatedly without plans.

A. N. Bach organized his first institution, the Central Chemical Laboratory (CCL) at the All-Russian Council of National Economy of the Russian Federation, which was the first chemical research institution of the young Soviet State. This happened on the 4th of October 1918, when hunger and economic dislocation were in the country. (Now this Institute is known as L. Ya. Karpov Physico-Chemical Institute.) Bach's flat was on



A. N. Bach in front of the building of the Institute, Narkomzdrav of the USSR, and in the laboratory, 1927

the third floor of the institution building and the door of Bach's office connected his flat with laboratory, where Aleksey Nikolaevich spent many hours as experimental work was the best rest for him. The major task which Bach had set for his assistants and colleagues was to improve chemical industry via innovation and rationalization of existing technologies, and also to develop new industrial processes. A. N. Bach's daughter, L. A. Bach, recalled



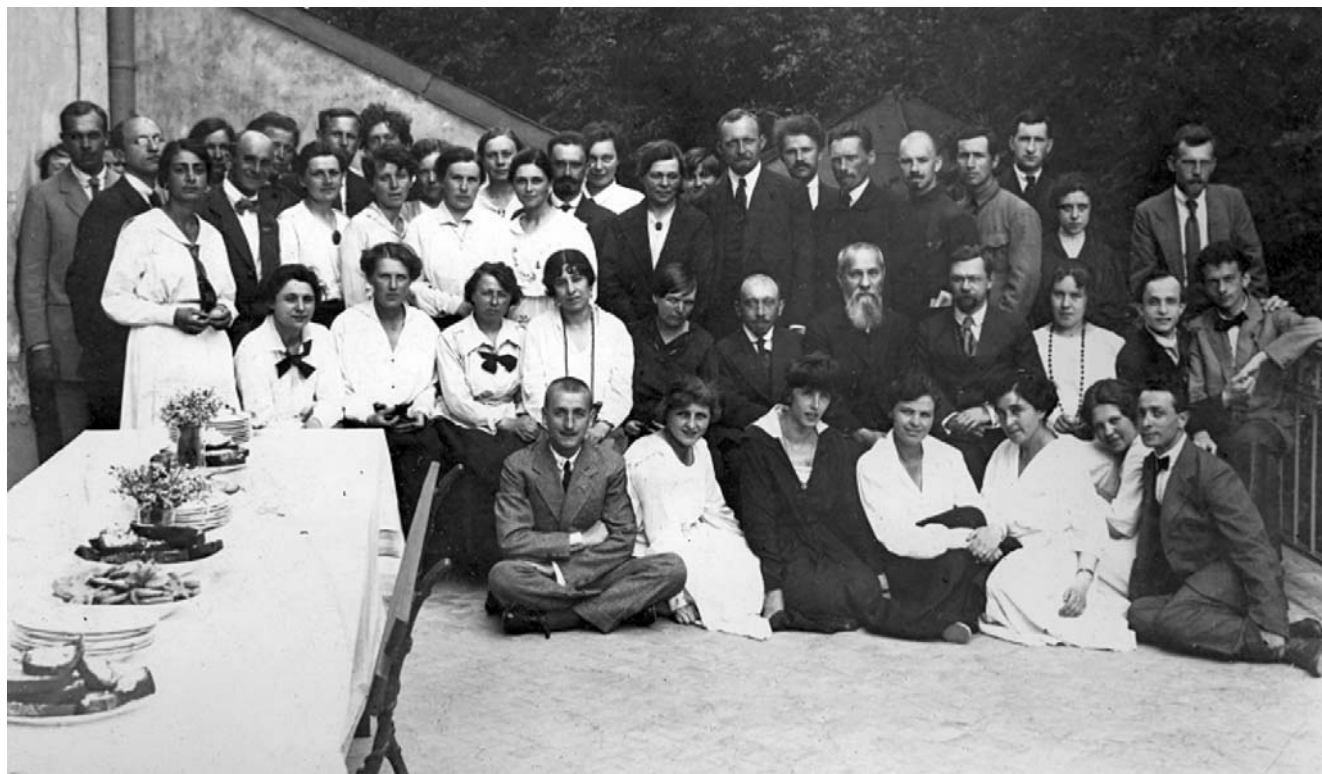
A. N. Bach with his family. Middle 30s

that they had to invent methods for production of castor oil surrogates for aviation, prepare fuel mixtures for internal-combustion engines, to elaborate drying oil substituents from products of oil oxidation (this was needed for painting of railway bridges), to carry out important analyses, and decipher patents. After the organization of the CCL, Aleksey Nikolaevich began his biochemical studies. He directed studies of enzyme formation in germinating seeds and the development of the method of quantitative assay of catalase in a drop of blood. Bach was a director of the Karpov Institute for 28 years up to his death.

Being a member of Central Executive Committee of the All-Russian Council of National Economy, L.Ya. Karpov energetically supported erection of a new building for this institution, which was started in autumn of 1920, and on the 20th of December 1922 there was its solemn opening. This was the first building erected in Moscow after the Revolution.

The Karpov Institute became a "cradle" for many research institutions of the Soviet Union, including the Institute of Coal and Oil Chemistry, Institute of Artificial Fiber, Institute of Plastic Masses, Institute of Sugar Industry, and many others.

Bach's special interest in biochemistry appeared again in 1921, when he initiated organization of the Biochemical Institute (with medical emphasis) of the People's Commissariat of Health (Narkomzdrav). His initiative was supported by N. A. Semashko, the Commissar of Public Health. This was the first biochemical research center in the USSR, where future academician-biochemists A. I. Oparin, V. A. Engelhardt, S. E. Severin,



A. N. Bach among colleagues of the Institute, Narkomzdrav of the USSR, 1927



A. N. Bach among pupils and colleagues, Biochemistry Institute. 1936

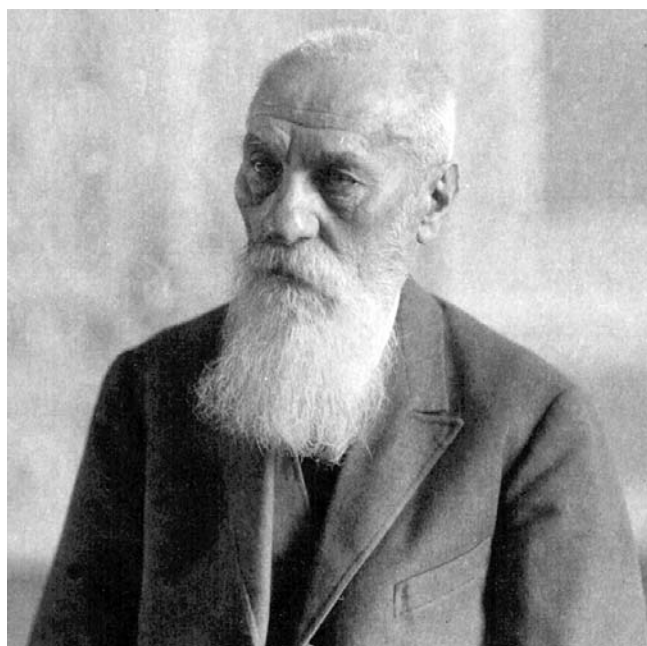


A. N. Bach with colleagues, Biochemistry Institute. Seated from left to right: A. I. Smirnov, A. I. Oparin, A. N. Bach, S. S. Elizarova, Z. V. Ermol'eva. Stand from left to right: V. L. Kretovich, E. M. Popova, N. I. Proskuryakov, N. M. Sisakyan, V. N. Bukin. 1939

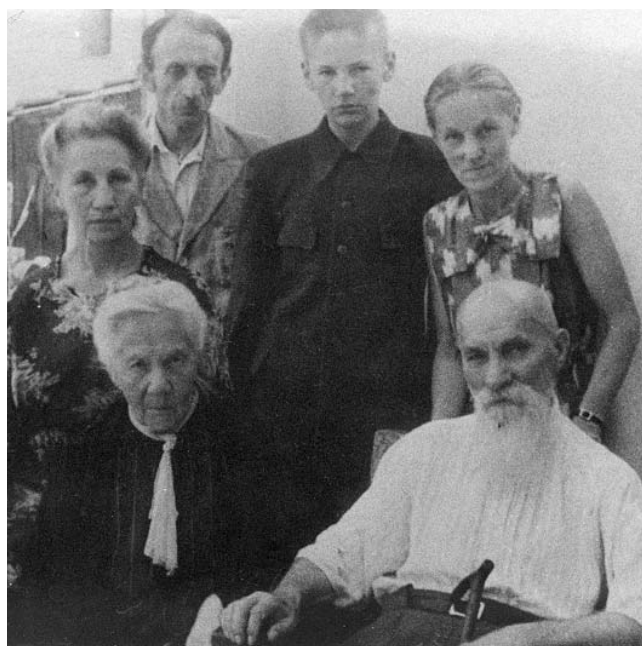
A. E. Braunstein began their ways in science. Characterizing this period of his life, Bach wrote: "I never lived before such full life as now. And this completeness of life, involvement in the grandiose historical process, which has not been experienced by mankind

before, gives me high moral satisfaction, which I would not exchange for all earthly blessings" [21].

In 1935, A. N. Bach and A. I. Oparin organized the Institute of Biochemistry of the Academy of Sciences of the USSR (now Russian Academy of Sciences), which



A. N. Bach. About 1940



A. N. Bach and his family. 40s

became a logic result of the development of science in the USSR. Since 1944, this institute is named after A. N. Bach (a unique case, the institute was named after a scientist who was still alive). Although A. N. Bach was in his 80s, he was able to collect in his institute talented scientists, who subsequently formed the pride and glory of Russian life sciences, many of them became founders of own scientific schools, authors of outstanding discoveries: A. I. Oparin, V. A. Engelhardt, N. M. Sisakyan, A. N. Belozersky, A. N. Terenin, A. A. Baev, A. L. Kursanov, A. A. Krasnovsky, V. N. Bukin, V. L. Kretovich, D. L. Talmud, A. M. Kuzin, A. I. Smirnov. Among several institutes of our country, the Institute of Biochemistry was awarded the highest government award, the Order of Lenin.

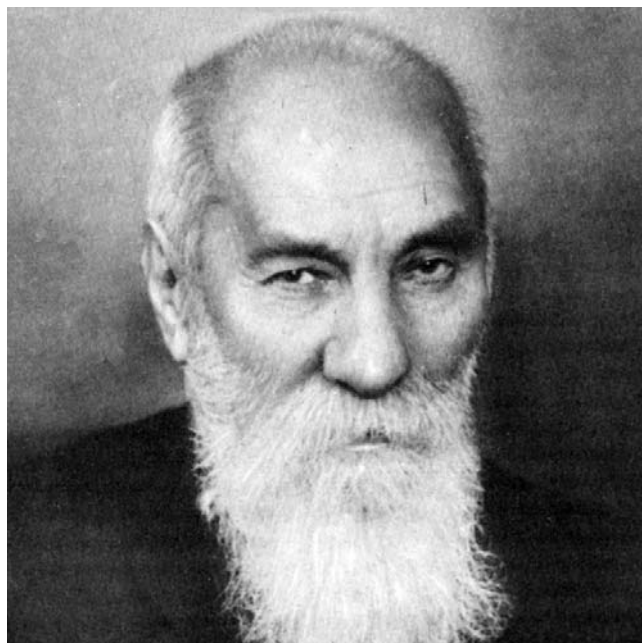
Attempts to link theoretical studies in the fields of chemistry and biological chemistry with practical needs were typical for Bach's scientific activity. Study of enzymes in resting, germinating, and maturing wheat seeds was carried out for the development of biochemical parameters for evaluation of baking quality of the flour and thus for improvement of bakery technology.

In the 30s and 40s, the biochemical bases of tea industry and methods of its control were developed in the USSR under the supervision by A. N. Bach and A. I. Oparin, in close collaboration with representatives of tea factories.

A. N. Bach significantly influenced processes of organization of science in our country. He was one of the persons directing activity of the Academy of Sciences in the pre-war period. In 1935, A. N. Bach was elected as the President of D. I. Mendeleev All-Union Chemical Society. In 1936, the first All-Union journal *Biokhimiya* was organized by Bach's initiative, and he became its Editor-in-Chief. A. N. Bach became the unquestioned leader of Soviet biochemists. He was elected as a deputy of the Supreme Soviet of the USSR, he was Academician-Secretary of the Department of Chemical Sciences, Academy of Sciences of the USSR, and during the Great Patriotic War A. N. Bach was a member of Scientific Technical Council at State Committee of Defense.

A. N. Bach was a director of three institutes: Karpov Institute, Institute of Biochemistry, and Institute of Plant Physiology.

Bach's outstanding contribution to science was recognized by high awards. In 1926 Bach was awarded the V. I. Lenin Prize, and at the general meeting of the Academy of Sciences of the USSR (12 January 1929) he was elected as full member of the Academy (Department of Physico-Chemical Sciences). In 1941 he was a recipient of the State Prize of the 1st degree for his works in biochemistry, on June 10, 1945 Bach was awarded the title Hero of Socialist Labor for his outstanding contribution to biochemistry, particularly for the development of the theory of reactions of slow oxidation and chemistry of enzymes and also for the development of own scientific



A. N. Bach. Last years

biochemical school. He was awarded with four Orders of Lenin and Order of the Red Banner.

In June, 1944, the Department of Biological Sciences of the Academy of Sciences of the USSR organized a special session dedicated to the 50th anniversary of the peroxidase theory of slow oxidation and the role of A. N. Bach in Soviet Biochemistry. The Presidium of the Academy of Sciences of the USSR decided to organize annual scientific readings at his birthday on the main problems of biochemistry. The first Bach Lecture was held in Moscow on March 17, 1945 and A. I. Oparin delivered his lecture "Enzymes in the living cycle of plants". Since that date leading Soviet scientists have delivered Bach lectures: Academicians N. N. Semenov, A. N. Belozersky, V. A. Engelhardt, A. E. Braunstein, M. N. Sisakyan, A. V. Palladin, A. N. Frumkin, A. N. Terenin, A. L. Kursanov, A. A. Baev, A. A. Krasnovsky, I. V. Berezin, N. M. Emanuel, M. M. Shemyakin, Yu. A. Ovchinnikov, S. E. Severin. In 2007, the 63rd Bach Lecture was delivered by Nobel Prize Laureate Professor J. Walker (the full list of speakers one can see at <http://www.inbi.ras.ru/bach/index.html>).

Aleksey Nikolaevich Bach died on the 13th of May, 1946 in his ninetieth year of life. He left a huge heritage after him: organized laboratories, institutions, outstanding school of Russian biochemists. In his studies Bach was far ahead of his time.

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