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In Memory of
Yuri A. Ovchinnikov

Yuri A. Ovchinnikov
1934–1988

In spite of all efforts to save him, after a two-year struggle with the advancing disease, Yuri Ovchinnikov died on February 17, 1988. He was the Vice President of the USSR Academy of Sciences and a member of the Editorial Board of The Journal of Membrane Biology since 1972.

Yuri Ovchinnikov was born on August 2, 1934, in Moscow. After completing his postgraduate training at the Department of Chemistry of Lomonosov State University in 1960, he entered the laboratory of M. Shemyakin at the Institute for Chemistry of Natural Products (now the Shemyakin Institute of Bioorganic Chemistry) where he worked until his very last day as Director and Head of the laboratory of protein chemistry.

Yuri Ovchinnikov's influence in the development of biology in the USSR has been enormous. To assess his contribution, we should bear in mind that in 1973, when Ovchinnikov was put in charge of chemistry and biology at the Presidium of the USSR Academy of Sciences, biological science had not yet recovered from the disastrous consequences of Lysenkoism. Khruschev's thaw gave way to stagnation. Those were hard days: the laboratories were without personnel, equipment or chemicals. By that time the Iron Curtain had just parted and it became evident that we had failed to keep up with our fellow biologists in the West. Nobody would ever have suspected Yuri Ovchinnikov of jingoism; he realized that science belonged to the world community and had no boundary posts. With a heavy heart he appraised the situation in biology; his energy and efficiency and eventually all his life were devoted to revive biological science in the USSR. Yes, to revive; in the 1920s–1930s our investigators had made it to the highest peaks in the life sciences.

Already in his youth Ovchinnikov recognized that to tackle difficult scientific problems successfully, future specialists would have to work in advanced laboratories, participate in scientific conferences and exchange results through journals. Today all this seems trivial, but many projects then performed were framed by the red-tape system of those times. The point was to avoid conflict with the system's tenets and, within the system, to achieve success. Biology was like Cinderella at a grand occasion where the gifts were distributed among space research and nuclear physics. It was important to convince the Academy's Presidium and the government to support biology. No one but Yuri Ovchinnikov could handle this, and he was a winner.

Much more complicated was the task of raising the research to a level of distinction. Ovchinnikov was quite aware that it was not easy to do this on a national scale, as this would require reforms in economy and management. The time of Gorbachev's drive for perestroika had not yet come. Resources had to be found that would allow a breakthrough in science, and experts had to be found who would support new initiatives. Ovchinnikov gathered well-trained scientists around himself, who shared his ideas and the eager wish to rival the scientifically leading countries in studies of molecular structure. His vision was a biology based on structural studies, where knowledge about cellular function would follow from molecular information. He never lost his optimism and enthusiasm for his vision, and that is why Ovchinnikov had so many ardent followers.

A man of grand ideas, he could crystallize the major points, define the tasks and implement them. The birth of membrane biology in the USSR is an example. He started with research in chemistry of depsipeptides: structures, total syntheses, mechanisms of action, structure-functional relationship of enniatins, sporidesmolides, esperin, angolide, serratamolide, valinomycin. This was followed by the development of mass-spectrometric approaches to the amino acid sequences of peptides. In 1964 Yuri Ovchinnikov spent a year in the laboratory of V. Prelog (Swiss Federal Institute of Technology, Zurich), where he acquired a taste for stereochemical studies of peptides. He was among the pioneers of dynamic conformational studies of peptides in solution by spectroscopic techniques. The above-mentioned depsipeptides, as well as the membrane-active antibiotics gramicidin S, gramicidin A and a large series of linear and cyclic model peptides were objects of these studies. Topochemical approaches to structure-function analysis of peptides were formulated. In 1971 in Pushchino, Ovchinnikov gathered enthusiasts in studies of biological model membranes and ion exchange membranes. Just then the basic principles underlying the function of various membrane systems—transformers of information or energy—were formulated. His monograph "Membrane active complexones" presented a refreshing chemist's view of membrane processes.

The investigation of nerve cells—sensory transduction and membrane bioenergetics—is an example of Ovchinnikov's unusual combination of scientific gifts. For these studies bacteriorhodopsin was a good candidate to start with. This membrane chromoprotein functions as a light-driven proton translocase. The exact details of the mode of action of this unique molecular machine still remain obscure, largely due to the absence of precise data on its tertiary structure. The elegant work of Henderson and Unwin on the membrane packing of bacteriorhodopsin had excited one's fantasy as to the way it acts, leaving unanswered the question of the actual building plan of the protein and the arrangement of the functional groups in the molecule. In 1979 Yuri Ovchinnikov published a paper on the amino acid sequence and membrane disposition of bacteriorhodopsin. Thus, bacteriorhodopsin became the first intrinsic membrane protein for which the primary structure and topography were established. In complete accordance with electron microscopy and electron diffraction data, bacteriorhodopsin turned out to be made of seven transmembrane segments—a motif later seen in several membrane pumps, channels and receptors. The results obtained by Ovchinnikov and his colleagues at the Shemyakin Institute and by Khorana and his group at MIT have opened wide perspectives for further studies on the mode of action of this proton pump. The experience gained from this work was applied by Ovchinnikov to studies of another retinal-containing membrane protein—rhodopsin. This protein is involved in signal amplification in vision. The determination of the amino acid sequence of bovine rhodopsin was the culmination of intensive work by many laboratories over a decade. This was invaluable for our understanding of the structure of a large family of visual pigments and hormone receptors.

Yuri Ovchinnikov's more recent work focused on Na^+,K^+-transporting adenosine triphosphatase. Electron microscopy and computer-aided image processing technique unraveled a three-dimensional structure of the enzyme at a 20-Å resolution. The unit cell is formed by two $\alpha\beta$-promoters which make contact in their central parts. Furthermore, the hydrophilic parts of the smaller (β) subunit were shown to be exposed only on the outer surface. As to the larger (α) subunit, distribution of its hydrophilic parts in cytoplasmic and extracellular surfaces is 3 : 1, which accords well with the results of direct chemical and immunological approaches. Such general ideas of the ion pump organization were defined at the molecular level only by the analysis of complete chemical structures of the subunits.

Ovchinnikov and his colleagues determined the primary structure of both subunits of the pig kidney enzyme by applying protein chemistry and genetic engineering methods. The amino acid sequence determination made possible the direct analysis of the spatial arrangement of Na^+,K^+-ATPase. Models for insertion of both subunits based on proteolysis experiments and hydropathy plots predicted transmembrane segments. Immunochemical approaches together with other methods provided information on the orientation of the C-terminal domain of the α-subunit with respect to the lipid bilayer. A number of catalytic functions of the Na^+,K^+-ATPase are exerted by its α-subunit. The models elaborated by Ovchinnikov and his colleagues and by other groups assign ATP hydrolysis and other functions to distinct parts of the polypeptide chain.

Thus, the way was paved for structure-function studies of the Na^+,K^+-pump, using recombinant DNA techniques and for molecular-genetic analysis of ion transport in human cells. The existence of the families of at least five genes encoding several isoforms of the enzyme catalytic subunit and other still unidentified closely related ion pumps was revealed in the human genome. Evidence was gathered for tissue-specific regulation of the expression level of this gene family. Finally, the complete structure of one of these genes was established, and correlations of the exon-intron structure of the gene and structure-functional domains of the Na^+,K^+-ATPase molecule were discovered. These investigations highlighted a new aspect of active ion transport in biological membranes.

The analysis of Yuri Ovchinnikov's work presented here is, of course, incomplete and does not adequately appraise his talent, for in all he published over 500 papers. Ovchinnikov was not only a brilliant researcher, but he also was an excellent lecturer and speaker, one of the most influential ones among soviet scientists. Following the footsteps of V. Engelghardt and M. Shemyakin, Yuri Ovchinnikov focused his effort to advance physicochemical biology. His innovative work inspired and shaped biological science in the USSR. We enjoyed working with him for many years, and always thought—but now our feeling is so much more acute—that Yuri was truly a grand man.

His words and deeds were never at variance. His "yes" meant that he would exert every effort to tackle the problem. If he disagreed, he did not try to hide behind "probably or maybe"; his answer was, "no." Yuri Ovchinnikov was a man of quite outstanding range and brilliance: extraordinary memory, quick in grasping a meaning, always full of energy. He fascinated people, he had a thirst for life, but his primary interest and, indeed, devotion were always to science—a passion he pursued day and night. Whether outdoors or in a museum, whether among his friends or among colleagues, his thoughts were always of the laboratory and research. Later, after his death, we began to realize that Yuri knew how little time he had and that he cherished his candle of life, terribly short but bright. Probably, he sometimes felt happy, but he was never self-satisfied. Anyway, Yuri had the right to feel happy: he accomplished the aim of his life—to revive the traditions of biological science in his country and to restore its status among other sciences.

Yuri Ovchinnikov was a member of Editorial Boards of several journals, apart from the Journal of Membrane Biology. He chaired the Federation of European Biochemical Societies, was a member of European Committee on Peptide Chemistry, the International Institute for Energy Resources and Ecology, and the European Academy of Arts, Sciences and Humanities.

We all grieve and mourn his loss not only as a great scientist, but also as a dear personal friend.

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