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The Institute of Protein Research of the Russian Academy of Sciences Is 50 Years Old

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Abstract—Here I introduce collection of review articles written by members of the Institute of Protein Research of the Russian Academy of Sciences. This collection commemorates the 50th anniversary of the Institute. The review articles cover a broad range of problems concerning the spatial structure of protein molecules, including the state of the molten globule, protein–RNA interactions, polysome and ribosome structure, the molecular colony method, and the original methods for studying the structure of proteins. Several of the reviews consider the practical use of knowledge about the structure of proteins and protein polymers. They reflect both the long experience of the authors and contemporary scientific data.

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The Institute of Protein Research of the Academy of Sciences of the USSR (now the Institute of Protein Research of the Russian Academy of Sciences) was established on June 9, 1967, by a decree of the USSR Academy of Sciences. The purpose of the Institute was to strengthen and develop scientific research in the field of molecular and physicochemical biology, especially studies on the structure and functions of proteins. The main directions in the work of the Institute were then and now remain studies of mechanisms of genetic information processing on the translation level, structural and functional investigations of components of the protein-synthesizing system, development of theory of structural organization of proteins, studies on the structural bases of the RNA–protein recognition and stability of RNA–protein complexes, and investigations of replication and recombination of RNA [1]. Over the past 50 years, the World progress in all these areas of science has been very remarkable, and members of the Institute significantly contributed to it. Besides achievements in academic fundamental science, researchers of the Institute have developed original applied directions, such as creation of therapeutic proteins [2], the molecular colony method for medical diagnostics [3], modification of biopolymer surface for biotechnology [4], the flow cell-free translation system [5], etc.

Long-term study on protein biosynthesis under the guidance of the founder and first director of the Institute of Protein Research, Academician A. S. Spirin, led to creation of a model of the translating ribosome based on the relative mobility of ribosomal subparticles. Structural mobility of the ribosome during translation was first shown experimentally when ribosomes were shown to translate the template in the absence of elongation factors and GTP (factor-free or "nonenzymatic" translation) [6]. Current cryoelectronic tomography studies have revealed various alignments in the polyribosome depending on translation and the course of mRNA in the polyribosome [7]. When the development of flow cell-free systems of translation began more than 35 years ago, it was necessary to synthesize large amounts of RNA. For this purpose, a method with Qβ-replicase (RNA-dependent RNA polymerase of bacteriophage Qβ) was used [3]. Investigation of the properties of Qβ-replicase resulted in some unexpected findings and led to creation of the molecular colony method, which for the first time made possible clonal proliferation of nucleic acids outside living cells. The method is very sensitive and specific, allowing single target molecules to be detected without any previous enrichment of the sample [3]. To improve the molecular colony method, current approaches are being developed to find individual cells with particular properties, e.g. malignant cells, among a large population of heterogenous cells [8]. In nature translation occurs in the cytoplasm, and in eukaryotic cells the translation apparatus has been shown to interact with the cytoskeleton, which regulates the process [9, 10]. For better understanding of protein biosynthesis, it is important

to know the fine structure of the ribosome and the interaction of all of its components. Study of the structure of RNA–protein complexes became an important milestone in the pathway for understanding ribosome organization and general principles of RNA–protein recognition [11].

One of the significant problems in the study of proteins is the mechanism of folding of the protein globule. Investigation of this problem was opened in the works of the organizer of the Laboratory of Protein Physics at the Institute of Protein Research, the founder of the Russian school of protein physics O. B. Ptitsyn (1929-1999). A long and difficult pathway was traveled to understanding the spontaneous self-organization of protein structure, and especially to solving the "Levinthal paradox" – how the most stable structure of a protein globule could be formed spontaneously within a reasonable time among billions of possible structures. A general theory of protein folding was created, opening a path for concrete theories and algorithms for searching for folding nuclei and calculating the rates of protein folding [12]. The existence of a molten globule, i.e. a new physical state of a protein molecule, was predicted theoretically, found experimentally, and characterized in detail; moreover, the participation of the molten protein globule in physiological processes in cells has been confirmed experimentally [13]. A search for new structural motifs in proteins was made, the interrelationship was established between the structure and the amino acid sequence, and 18 structural trees were built for large protein families [14]. Pseudo-chirality was investigated among protein structures that can exist in left and right configurations, but which are not true mirror images of each other [15].

Disorders in protein folding leads to development of various systemic and neurodegenerative diseases, in particular Alzheimer's disease. The study of generation of Aβ peptide fibrils in Alzheimer's disease presents a contribution to the understanding of pathophysiological mechanisms of the development of this disease [16]. The study of the ability of a protein to produce fibrils is important for the development of new insulin preparations [2]. It has also been established that modified protein fibrils, such as in flagella of bacteria or archaea, can be used to obtain nanostructural materials with desired properties (electrically conducting, semiconducting, magnetic, catalytic, sorptional) [4].

Studies at the Institute of Protein Research of the Russian Academy of Sciences have been performed using new original methods and devices. In the Institute, together with the L. F. Vereshchagin Institute of High Pressure Physics of the Russian Academy of Sciences, a unique scanning microcalorimeter has been developed and manufactured that can operate at pressures up to 6000 atm. This device makes it possible to start systemic studies on volumetric changes during conformational transformations of biologically important macromolecules [17]. Together with foreign partners, studies have been started with a modern version of the X-ray diffraction analysis – flow X-ray diffraction analysis using femtosecond laser pulses on free electrons [18].

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