Conceptual objectives of the Institute

Institute:
Institute of Biophysics of the CAS
Královopolská 135
61265
Brno

Concept of the Institute – abstract

The Institute of Biophysics of the Czech Academy of Sciences (the IBP) was established in 1955 and has become an important part of the research infrastructure in Czechoslovakia and later in the Czech Republic. Toward the end of the 1950s and in the early 1960s, it was found at the IBP that DNA and RNA may accept and provide electrons during interactions with electrodes and provide electrochemical signals reflecting the changes in DNA structure. This laid the foundation for the emergence of a new scientific field of electrochemistry, which is currently developing successfully. The objective of the IBP scientists is, in particular, to conduct basic research, to transmit the acquired knowledge to the general scientific community, and to use it to educate pre-graduate as well as post-graduate university students. The main mission of the Institute is to research issues from the field of biology, including physical and chemical processes, using a broad spectrum of physical, chemical, biological, and other experimental or theoretical methods that may be used to study matter, from a molecular level up to whole cell systems. In terms of the application potential of the acquired knowledge, many fields of biology and chemistry come together in the study of epigenetic processes, such as DNA methylation, micro-RNA function, or post-translation histone modification, i.e. processes which regulate gene expression, determine DNA/RNA conformation, contribute to DNA repair after it was damaged, and ensure genome integrity. Epigenetic studies, including the analysis of various biomacromolecule interactions, represent one of the major trends in global science in which biophysical approaches may be implemented to a significant extent.

1. Detailed analysis of the Institute professional activities so far

Scientists of the Institute of Biophysics (IBP) pursue basic research in the field of biophysics, more precisely, they research the structure, evolution, function, and dynamics of biological systems (biomolecules, cellular components, cells, and also cell populations) using a broad spectrum of methods (of biophysics, molecular biology, biochemistry, electrochemistry, and bioinformatics). Through their activities, the scientists of the IBP contribute to the increase of the level of knowledge and education in the Czech Republic, to the development of biotechnology, and to the transfer of research results into practice, particularly in the field of diagnostics and treatment of serious illnesses. Within the scope of their activities, the IBP teams of scientists develop international cooperation, including the

organisation of international scientific conferences, seminars, and training of foreign students taking place in laboratories. In their cooperation with universities, the IBP scientists educate postgraduate students and take significant part in the pedagogical activities of several Czech universities. The educational activities are implemented mainly in cooperation with Masaryk University in Brno and Palacký University in Olomouc.

Our goal is also to strengthen our position as a top national centre of excellent research, and we also want to become an important research institute recognised internationally. At the Institute, we largely guarantee the biophysics field, mainly by involving our scientists in the education of biophysics students as well as incorporating the Czech Committee for Biophysics into the IUPAB international association (International Union of Pure and Applied Biophysics). In addition, many of the Institute scientists were or are the main investigators of international projects, such as projects guaranteed by Norwegian Funds, Marie Curie EU grants, COST, or projects guaranteed by the Howard Hughes Medical Institute located in the US. Through these activities we want to create conditions to attract the most scientifically competent people and make breakthrough discoveries in the scientific fields that fall within the concept of the IBP. The best scientists of the Institute are granted academic freedom, as well as extraordinary financial and technical support. The heads of the IBP research teams may use the allocated institutional funds to ensure maximal effectiveness of the research. The amount of these funds is determined by the scientific performance of the team, which is evaluated regularly. The professional activities of individual IBP teams are also reflected in the high citation rate of scientific papers that were created at the Institute.

2. Long-term plan of conceptual and professional development of the Institute

The purpose of the concept is to define the basic research framework for the IBP research departments to serve as a guide for the preparation of research projects and their subsequent implementation. The concept is important for building new investment units and developing cooperation between the Institute departments and other scientific institutions, both domestic and foreign. Also, specification of the concept of the Institute is also important for the education of postgraduate students and other pedagogical activities. Increasing the standard of research and achieving significant results within the international scientific community, particularly in the European Research Area, is among the priorities of all the departments of the Institute. Publication of scientific articles in prestigious journals is a pre-requirement for every department as well as individual employees. The authors of professional articles and scientific results created at the laboratories of the Institute, are rewarded with an extraordinary financial reward. In addition to this, the quality of the scientific output of individual employees is reflected in the overall evaluation of the departments. This regular evaluation serves as a platform for allocation of institutional funds. A significant amount of credit is also given to foreign projects which help to incorporate the IBP laboratories into broader international scientific units. Our priorities also include acquisition of national grants and participation in projects that are a part of various national scientific programmes. An integral part of our scientific work is also qualified involvement in scientific and pedagogical cooperation with universities. The objective of this activity is the acquisition and stabilisation of skilled young scientists. We want to motivate young scientists by the opportunity to use first-class methodology and facilities which should belong to the best ones on international level. Emphasis will also be placed on the continuous popularisation of these top devices and the resulting scientific knowledge, which will eventually be transferred to the practice.

2.1. Main directions of research:

(1) Molecular biophysics and pharmacology: (i) Mechanism of the antitumor effect of metallopharmaceuticals, (ii) DNA interactions with biologically significant substances, (iii) DNA

synthesis and DNA repair, (iv) Raman spectroscopy, circular/linear dichroism spectroscopy and microcalorimetry of nucleic acids and proteins.

(2) Biophysical chemistry and molecular oncology: (i) chemical reactivity, structure, and interactions of biomacromolecules in solution and on electrically charged surfaces, electrochemistry of biopolymers; (ii) new methods for analysing biomacromolecules, including proteins relevant to biomedicine, natural and modified nucleic acids, polysaccharides and glycoproteins; (iii) molecular oncology, interaction of proteins relevant to cancer with DNA and other substances, including protein–protein interactions.

(3) Molecular epigenetics: (i) Epigenetic regulation of gene expression, (ii) biology of ribosomal RNA, (iii) evolutionary genomics.

(4) Molecular cytology and cytometry: Scientists of this department deal with the following issues: (i) the architecture of the cell nucleus and chromatin structure, (ii) epigenetic mechanisms of gene expression regulation and DNA repair with focus on histone code, (iii) cell differentiation, cell transformation, cancer diagnosis, search for diagnostic markers, (iv) high-resolution cytometry, microscopical plot of processes in live cells in time, (v) analysis of histone proteins by methods of advanced confocal microscopy, (vi) study of diffusion and interaction of proteins by biophysical methods of FRAP (Fluorescence Recovery after Phobleaching) and FRET (Fluorescence Resonance Energy Transfer), (vii) study of the effects of ionizing radiation on cell systems.

(5) Cytokinetics: study of cellular, molecular and biophysical mechanisms regulating cell proliferation, differentiation, cell death, intercellular communication, or cellular metabolism aiming to contribute to: (1) the definition of the contribution of environmental factors, in particular toxic organic pollutants, to the formation of cancer and other modern lifestyle diseases; (2) the knowledge of role of signal and structural lipids in the regulation of normal and tumour cell population behaviour; (3) the understanding of mechanisms regulating plasticity and heterogeneity of tumour cell populations; (4) the identification and recognition of the functional properties of specific tumour cell populations contributing to the progression of disease and resistance to therapy; (5) the development of advanced analytical, biophysical, and imaging methodologies for the study of basic cell processes *in situ* and in *in-vivo* models of laboratory organisms.

(6) Biophysics of the immune system: (i) mechanisms leading to the formation of reactive oxygen and nitrogen metabolites by non-specific immune cells; (ii) epigenetic mechanisms in the regulation of immune cell function; (iii) antioxidant properties of bodily fluids, medicaments and natural substances; (iv) microfluidic systems in the study of haemodynamic alternations of the cardiovascular system during pathological processes; (v) the application of organic polymer electronics in scanning and affecting the behaviour and phenotype of cells.

(7) Structure and dynamics of nucleic acids: The department studies a broad range of systems, including, for example, (i) the structural dynamics of canonical and non-canonical DNA molecules; (ii) structural dynamics, catalytic functions, and RNA molecule evolution; (iii) molecular complexes between nucleic acids and proteins; (iv) the chemical processes that led to the creation of life and other processes using an extensive portfolio of theoretical methods, the department actively participates in the development thereof: (v) in classic molecular simulations; (vi) quantum chemistry; (vii) bioinformatics.

(8) CD spectroscopy of nucleic acids: (i) biophysical, particularly structural, characterisation of sequentially dependent DNA configurations; (ii) study of non-standard structures, such as quadruplexes or left-handed DNA in biologically significant areas of genome DNA in relation to their function.

(9) Developmental plant genetics: (i) structure of sex chromosomes, (ii) functions of genes linked to sex chromosomes, (iii) stability and integrity of the cell nucleus. Structural and functional genomics of plants.

(10) Radiobiology and cell biology: (i) effects of radiation on biological systems, (ii) DNA repair after radiation damage.

The main tools for implementing and monitoring the objectives set out in this conceptual objectives will include regular evaluations of results of the individual teams. Particularly, in evaluation of the individual departments of the IBP, publication in highly-regarded international journals and the citation rate of professional works of researchers according to the Web of Science database will be taken in account. Further joining of teams to create research, methodological, or educational centres both inside and outside of the Institute will be supported. Increased institutional support will primarily be provided to teams with good evaluations, but unexpected socio-economic problems which can occur temporarily in scientific teams must also be taken into account.

2.2. Cooperation between IBP and other research institutions and universities

The primary objective is to incorporate teams into the European Research Area. Support will be provided to all forms of international cooperation, particularly projects funded by foreign sources. Attention will be paid to mutual mobility of scientists, and postgraduate student and young scientist exchanges. Activities associated with the organisation of international conferences in the Czech Republic or abroad will be supported in various ways. The main partners of the Institute, especially within Strategy AV21, will be CAS institutes dealing with similar topics (IOCB, IEB, IEM, IACH, JH IPC, IMG, IPMB, ISI, etc.), universities (Masaryk University in Brno, Charles University in Prague, Brno University of Technology and Palacký University in Olomouc), departmental institutes (e.g. Masaryk Memorial Cancer Institute in Brno; MMCI), and the University Hospital in Brno (FNUSA, UHB, etc.). Cooperation with research institutes founded as part of the OP VaVpI (CEITEC, ICRC) is also significant. The cooperation will be realised mainly in the form of joint projects using common devices and common sites but also by participating in the education process, e.g. in educating postgraduate students and attendance at scientific councils of institutions.

2.3. Infrastructure of the Institute

High-quality research in biology is predominantly determined by modern technologies. The facilities of the Institute are currently at a very good level. We have built the Laboratory of Cell Biophysics, which is equipped with two confocal systems (Leica SP5 and Leica SP8) that enable the study of protein interactions using the FLIM–FRET technology. Furthermore, the Laboratory contains a flow cytometer (FASCAria II), which enables sorting of cells according to the selected fluorescent-labelled markers and a common IBP–CEITEC laboratory (equipped with computer clusters for the study of molecular dynamics) or common IBP–ICRC laboratory. A facility for laboratory animal breeding by means of the so-called SPF (Specific Pathogen Free) breeding has also been built. In future, we will continue to devote attention to the development of the Institute facilities (building of central laboratories) using both academic sources and large national or international project (OP VVV) funds. In case of large facilities, we will provide maintenance and usage within the region. Furthermore, we will maintain a computer network at a sufficient level and expand the information resources of the IBP laboratories.

2.4. Popularisation of science

We will support popularisation activities of all employees, particularly by informing the general public about the importance and benefits of research in the fields of biophysics, cell

biology and chemistry. The IBP scientists will continue to regularly participate in the "Open Days" of the Czech Academy of Sciences and support the interest of young people in science through lecturing supplemented by excursions. These activities are intended for students at high schools and secondary schools as well as universities. Our popularisation activities will be implemented by means of social networking sites and popular scientific journals, such as Vesmír or Scientific American. We will participate in the activities of Strategy AV21 within the new programme called "Genetics and Epigenetics: From Theory to Practice".

3. Staffing of planned activities

The Institute structure is very convenient in terms of both, expertise and age-distribution. All department heads are important, internationally recognised, scientists. In addition, the senior scientist of each department has a substitute, and some departments have also established individual research groups, often led by an expert recognised internationally in the given field. Each department has several workers teaching (mainly outside their working hours) students from various Czech universities. The Institute employees provide approximately 60 semestral lectures and specialised courses. This active approach enables recruitment of new young researchers to the IBP laboratories. There are approximately 60 postgraduate students trained at the Institute, of whom the vast majority defend their dissertation works very successfully.

In the upcoming period, the Institute management will seek to continue to maintain the high professional qualifications of the senior researchers and the optimum age structure across the IBP departments. This purpose will be served mainly by actively searching for young talents among postgraduate students and postdoctoral researchers. To this end, we will also use popularisation and motivational tools, which should support the newly-established direction of Strategy AV21. The objective of this programme is genetic and epigenetic research, which is at the forefront of global interest and is currently relatively underdeveloped in the Czech Republic.

4. Involvement of IBP laboratory members in Strategy AV21

The main objective of the proposed direction of Strategy AV21 is to conduct basic research of the genetic and epigenetic processes that take place in various biological processes, such as DNA replication, gene expression, or DNA repair. In addition, we want to identify and characterise genetic and epigenetic changes relevant to clinical applications or applications based on the knowledge of plant biologists dealing with genetic and epigenetic mechanisms. As far as antitumor treatment is concerned, we want to study the effects of combining HDAC inhibitors with a conventional cytostatic – cisplatin. Another goal is to study the influence of environmental factors on the epigenome of normal and tumour cells and the influence of these factors on the reproductive systems of not only humans but also plants. From a theoretical point of view, we will also simulate the influence of the epigenetic factors on the conformation of selected proteins that regulate gene expression and the stability of chromatin domains. We also rely on the hypothesis that individualised therapy and disease prevention in the future will be based on the knowledge of not only the patient's genome but also epigenome. As a contribution to the research trend of functional characterisation of (epi)genetically-conditioned diseases, we propose to create a multidisciplinary team that will actively cooperate. We will also strive to strengthen cooperation not only across the CAS institutes but also across departmental institutes whose research and practical activities are

oriented towards genetics and epigenetics. Within the proposed Strategy AV21 consortium (Genetics and Epigenetics: From Theory to Practice), we will study the following objectives:

(1) We want to define the role of genetics and epigenetics in the progression and diagnosis of cancer.
(2) We will test biophysical effects of some clinically significant medicines based on inhibitors or activators of histone-modifying enzymes and DNA methylation.
(3) We will characterise the epigenetic regulation of the expression of genes which play an important role in reproductive processes, not only in humans but also in laboratory animals and plants.
(4) We will define new, clinically significant candidate genes and pathological variants of these genes.
(5) We will propose and test the effective preparation of cell models for the characterisation of molecular, epigenetic, and pathophysiological mechanisms of the studied diseases.
(6) We will identify genetic and epigenetic biomarkers useful for diagnostics and monitoring of the course of the studied diseases.
(7) We will analyse changes in the genome and epigenome in the context of DNA repair after irradiation and chemotherapy.
(8) We will participate in research aimed at improving the specificity of glycoprotein biomarkers (e.g. PSA) by analysing sugar components thereof. We will attempt to discover the application potential of electrochemical methods in the diagnosis of cancers.

Some IBP laboratories are also involved in Strategy AV21, the Qualitas programme, which is coordinated by colleagues from the Institute of Physiology of the CAS, and the IBP employees attend annually, with their lectures, a conference which is held as part of the implementation of this programme. Finally, the Department of Plant Developmental Genetics is involved in a Strategy AV21 programme called Food for the Future. Within this programme coordinated by our colleagues from the Institute of Experimental Biology in Olomouc, our Institute focuses on modern methods of genome editing.

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doc. RNDr. Eva Bártová, Ph.D.	RNDr. Aleš Kovařík, CSc.
Director of the IBP of the CAS	Head of Institute Board of the IBP of the CAS.