THEORETICAL BIOPHYSICS. BIOPHYSICS OF COMPLEX SYSTEMS

Kinetics of biological processes and kinetics of enzymatic processes. Mathematical modeling in Biology (2 credits)

Main features of kinetics of biological processes. Description of dynamics of biological processes by using tools of chemical kinetics. Mathematical models. Goals of mathematical modeling in biology. General principles of mathematical modeling of biological systems. The concept of model adequacy to the real object. Dynamical models of biological processes. Linear and non-linear processes.

Kinetics of enzymatic processes. Particular mechanisms of enzymatic reactions. Physical basis of enzymatic catalysis. Effect of modifiers on the kinetics of enzymatic reactions. Application of the graph method to study stationary kinetics of enzymatic reactions. General principles for analysis of complex enzymatic reactions. Temperature effects on reaction rates in biological systems. Relationships between kinetic and thermodynamic parameters. The role of conformational properties of biopolymers.

Integration of data and knowledge. Models and modeling. Databases and data banks. Qualitative (basic) models. Simulation models of specific biological systems. Computer programs. Hierarchy of scales and times in biological systems. Regulatory networks. A block diagram of the model. The fundamental problem of modeling: testing hypotheses about the mechanisms of interaction of system components and mechanisms of regulation of processes. Evaluation of rate constants of elementary reactions. Applied problems of modeling: optimization in biotechnology, drug design.

Thermodynamics of biological processes (1 credit)

Classification of thermodynamic systems. Thermal capacity and compressibility of protein globules. Calculations of energetic effects of reactions in biological systems. Characteristic functions and their usage for the analysis of biological processes. Thermodynamic coupling of reactions; thermal effects in biological systems. Application of the linear thermodynamics in biology. Thermodynamic characteristics of the molecular- energetic processes in biological systems. Non-linear thermodynamics

MOLECULAR BIOPHYSICS

Spatial organization of biopolymers. The dynamic properties of globular proteins (1 credit)

Methods for study the conformational mobility: isotope exchange, luminescence methods, EPR, Mossbauer spectroscopy, high-resolution NMR, pulsed NMR, molecular dynamics methods. Auto-and cross-correlation functions of the torsion angles and interatomic distances. Mapping a free energy levels in peptides. Dynamic properties of globular proteins (continuation). Study of conformational flexibility. Restricted diffusion. Types of protein dynamics. Electronic properties of biopolymers.

BIOPHYSICS OF CELL AND MEMBRANE PROCESSES

Structure and function of biological membranes (2 credits)

Physicochemical basis of membrane processes. "Effects of external electric fields on cells and membranes (cell deformation, electrical breakdown, cell fusion, and dielectrophoresis). Biophysics of membrane transport. Mechanisms for the transport of natural and artificial compounds across biological membranes, the role of electrostatic factors in the penetration of charged substances, methods for modifying permeability, as well as transport-related osmotic and electrokinetic phenomena and bioelectrogenesis. The role of osmosis and capillary raising of fluid in the movement of water in plants, using the method of intracellular pressure sensors (to determine the modulus of cell elasticity, the hydraulic conductivity of membranes and the permeability of membranes for non-electrolytes), the structure of aquaporins. The use of weak bases and acids as probes for determining the pH and pH gradient in cells and organelles. The fundamentals of electrodiffusion theory and electrogenesis, the kinetic description of transport taking into account the effect of the membrane potential on the height of the energy barrier for the passage of ions. The theory and methods for determining the ionic selectivity of channels, the properties of channels based on kinetic models, the active transport system H +, the thermodynamic relationships, the regulation of H

+ -ATPases by the electrochemical proton gradient, and the mechanism and methods for studying Na, K-ATPase and other P-type ATPases.

Biophysics of excitable cells (1 credit)

The role of Na and K ions in generation of action potentials in nerve and muscle fibers; significance of Ca and Cl ions in generation of action potentials in other tissues. Kinetics of ion flux changes upon excitation. Mechanisms of channel activation and inactivation. Molecular mechanisms of non-muscle mobility. Molecular mechanisms of energy coupling. Electron transfer processes in chloroplasts and mitochondria. Localization of electron transport chain in the membrane; structural aspects of functioning of membrane-bound carriers; membrane asymmetry. Basics of the Mitchell theory; electrochemical proton gradient; energized membrane state; role of the H+ - ATPase.

Biophysics of regulatory processes (1 credit)

Combined diffusion reaction control according to Adam & Delbruck (1968) and Axelrod & Wang (1994). Ligand flow, aggregated and dispersed receptors. Binding of ligands to their receptors; Feldman model and its derivatives. Methods of investigation of membrane receptors. Mobility of membrane receptors. cAMP, IP3, Ca^{2+} as second messengers. Concept of diffusion-limited interaction of membrane proteins. Percolation theory and its application to membrane receptors. Fractals, reaction kinetics on fractals. Olfactory reception. Taste reception. Sound reception.

RADIATION BIOPHYSICS (1 credit)

Types of ionizing radiation and general physical properties. Doses of ionizing radiation. Main radiation and biological factors defining radiation effects. Acute radiation syndrome in mammals. Critical organs and tissues. Long-term effects of ionizing radiation. Stochastic and deterministic effects, somatic and genetics effects of ionizing radiation. Survival curves of irradiated cells grown in culture. Target theory of cell death. Multitarget–single-hit and linear–quadratic models of cell inactivation. Direct and indirect action of radiation. Radiolysis of water. Radiation-induced oxidation processes and defense role of antioxidant systems. Chemical modification of radiation response. Oxygen effect. Radiosensitizers. Radioprotectors. Effects of low doses of ionizing radiation. Radiation exposures from natural background and other sources.

Supporting courses

Medical Biophysics. Nuclear medicine (2 credits)

Cell receptors, their types, their effector systems; defects/deficiencies, medical significance. Receptor-mediated transport. Receptor-mediated endocytosis: internalisation, sorting, recycling; mathematical models and kinetic characteristics. Defects/deficiencies, medical significance. Exocytosis. Subcellular transport of macromolecules. Nuclear import/export of proteins. Subcellular localization sequences; nuclear import/export sequences; secretion, mitochondrial, lysosomal, and peroxisomal signals. Cellular machinery participating in targeted subcellular transport; defects/deficiencies, medical significance. Basics of photomedicine. Photodynamic therapy; types of photosensitizers; achievements and problems. Problem of targeted delivery of photosensitisers into their target cells and most sensitive subcellular compartments. Basics of molecular mechanism of atherosclerosis. Basics of molecular oncology. Exploiting cellular transport systems for targeted delivery of anti-cancer agents (general characteristics). Basics of genetic diseases. Gene therapy, aims, achievements, problems. Viral and non-viral delivery of genetic material. Lipolexes. Polyplexes. Methods of in vitro and in vivo transfections.

Brief history of nuclear medicine. Alpha-, beta-/+-decay, electron capture, isomeric transition, internal conversion; Auger- and Coster-Kronig electrons. Nuclear reactions; examples, equations. Radionuclides emitting gamma-rays, beta-/+-, alpha-particles, Auger electrons. Radiation decay, its characteristics, doses; track structure. Basics of dosimetry. Survival of cells irradiated with decaying radionuclides (dividing and non-dividing cells). Basics of DNA repair. Production of radionuclides. Production of radionuclides in reactors; neutron activation. Production of radionuclides in accelerators. Generator radionuclides; secular equilibrium, transient equilibrium. 99mTc generator. Basics of radioisotope diagnostics. Basics of image acquisition in nuclear medicine. Positron emission tomography. Single photon emission tomography. Molecular imaging. Endoradiotherapy with the use of beta-emitters. Endoradiotherapy with the use of alpha-particle emitters. Boron-neutron capture therapy. Brachytherapy. Approaches for enhancement of specificity of radionulcide diagnostics and therapy. Delivery systems. Modular nanotransporters for delivery of radionuclides emitting short-range particles. Methods of nulcear medicine in basic science.

Photobiophysics (1 credit)

A given lecture course intends to overview current knowledge on the structural and functional organization of photosynthetic apparatus, mechanisms of oxidative damage of photosynthetic components, and acclimation of photosynthesis to unfavorable conditions. Mechanisms of photoinhibition, generation and scavenging of the reactive oxygen species, and photosynthetic response to the oxidative stress are discussed. Redox- and pH-dependent regulatory mechanisms in plant photosynthesis are described in details, including non-photochemical quenching, state transition, thioredoxin system, and photosynthetic control. Regulatory role of alternative pathways of electron transport in the chloroplast, including cyclic electron flow around photosystem 2, Mehler reaction, and chlororespiration is described. Attention is paid to the peculiar features of photosynthetic regulation in green algae. Acclimation of green algae to nutrient deficiency and mechanisms of hydrogen photoproduction are presented.

Hybrid photoactive structures and artificial photosynthetic complexes (1 credit)

The heterogeneity of metabolic reactions leads to a non-uniform distribution of temperature in different parts of the living cell. The demand to study normal functioning and pathological abnormalities of cellular processes requires the development of new visualization methods. Some photoswitchable proteins (PP) have a strong temperature dependency of photoconversion rates, and its tertiary structure undergoes significant structural rearrangements upon photoactivation, which makes such proteins a nano-sized temperature sensor. However, determination of PP conversion rates must rely on measurements of fluorescence, since it is suitable for microscopy. In order to solve this problem hybrid protein constructions could be obtained, producing photoactive chimeras. In such chimeras, electronic excitation of the fluorescent protein is effectively quenched by the chromophore of PP. Photoactivation of chimeras triggers conformational rearrangements of complex geometry, permitting measurements of the conversion rates by monitoring changes of fluorescence intensity. This approach allowed us to determine the local temperature of the microenvironment. Future directions of PP-based sensor improvements are discussed.

Neurobiophysics (1 credit)

Course for graduate students on the current state and methods in theoretical and computational neurobiology. Models are considered within the framework of the Hodgkin-Huxley formalism, including modifications and simplifications of these models. Analysis of simple models on the phase plane. Simulation of synaptic transmission and analysis of metabolic limitations on the speed of information processing by the brain. Dynamics of intracellular Ca2 + in neurons and astrocytes, regulation of local blood flow.

Nanostructured materials in biomedical applications (1 credit)

Lectures cover a broad range of various nanostructures that can be used in biomedical research and medical applications. Lectures are devoted to (1) plasmonic silver and gold nanoparticles and nanostructured surfaces that are used for the enhancement of Raman scattering of biomolecules in solutions or inside living cells or isolated functional organelles; (2) plasmonic metallic films to monitor ligand-receptor interactions and (3) nanostructures for the drug delivery and drug penetration through blood-brain barrier. For all types of nanostructures the detailed review is given about the synthesis and characterization of nanostructures, experimental methods that employ nanostructures and examples of biomedical applications.

Modern methods of processing and analyzing experimental data (1 credit)

The course consists of two main sections. In the first section, students will become familiar with the processing of time series on the example of the study of the growth of chlorophyll fluorescence, which occurs when the dark-adapted photosynthetic organisms (plants, algae) are illuminated. Different approaches to building models of primary photosynthesis processes, such as kinetic models and agent models, will be considered. Various minimization algorithms will be considered, allowing the identification of model parameters from experimental data. During the classes, students will create simple Python programs in which the methods in question will be used to analyze real-world experimental data. The second part of the course is devoted to current approaches to image processing and analysis. Upon completion of the course, students will receive basic skills of working with static and dynamic images for solving such tasks as noise reduction, separation (segmentation) of images into an object and background, representation of images in the transformation space (Fourier and wavelet), selection of cooperative modes of dynamics in video.

Molecular modeling of proteins (1 credit)

The course includes a series of lectures, during which the theory and numerical methods underlying the methods of molecular mechanical modeling will be analyzed, as well as the main limitations of the method and ways to overcome them. The course also includes a series of practical classes in which students will get acquainted with the GROMACS program package, learn how to create molecular models, carry out calculations and analyze the trajectories obtained.

Redoxbiology (1 credit)

The role of oxygen in biological evolution. The great oxygen event: causes and post-effects. The properties of molecular oxygen. The electronic configuration of singlet and triplet oxygen. Classification of reactive oxygen and nitrogen species. Sources of reactive oxygen species in living cells. The biological significance of ROS in physiological processes. Oxidative stress and oxidative damage. The role of oxidative stress in the pathophysiology of several diseases. Hydrogen peroxide: a Jekyll and Hyde signaling molecule. KEAP1/NRF2/ARE signaling pathway. Redox-dependent transcriptional and posttranscriptional regulation of antioxidants. The antioxidant defense system. Water-soluble antioxidants. Fat-soluble antioxidants. Antioxidant and pro-oxidant activities of some antioxidants in cells. The Biological significance of superoxide dismutase, catalase, and glutathione peroxidase. The catabolism of nitric oxide. Measuring reactive species and oxidative damage in vivo and in cell culture. Biomarkers of oxidative damages.

Dissipative structures in biology and chemistry (1 credit)

The course is dedicated to basic ideas of dissipative structures and applications of principles of self-organization theory to biological systems. Mathematical models, such as Brussellator, Oregonator, and Fitz Hugh Nagumo, are briefly reviewed. Oscillations, different types of waves are classified and discussed on biological and chemical examples. Pattern formation in biology and some well-studied chemical systems (BZ-AOT system) is thoroughly investigated. Turing model is discussed as well as some alternative models from the developmental biology. This course illustrates how dissipative structures of all sorts abound in biological systems.

Nanobiosensors (1 credit)

Introduction to molecular sensors: The fundamental concepts of molecular sensor: capture, recognition and sensor signal transduction mechanisms. Examples of the molecular sensors, their applications and performances. Explanation how recognition agents such as DNAs and antibodies work in a sensing system. The outline of transduction technologies.

Introduction to Nano/Microfabrication: The benefits of system miniaturization by introducing the effect of size and shape in molecular sensing. The basic microfabrication techniques including film deposition, photolithography, and wet and dry etching. The techniques of "soft lithography," where several novel materials including polymers, proteins, DNAs and other nanomaterial are implemented into molecular sensors.

Mechanical transducers: The sensors that utilize mechanical structures for transduction. Two general strategies to detect the binding events: by detecting mechanical deflections induced by molecular binding or by detecting added mass as the change in resonant frequency. The sensors based on a mechanical cantilever as the fundamental building element of many mechanical structures.

Optical transducers: optical molecular sensors and optical spectroscopy: The molecular sensors based on optical transduction. The basics of optical spectroscopy. Optical microscopy and fluorescence spectroscopy. Theory and practical aspects of optical absorption and fluorescence, microscopy techniques. The chlorophyll molecules as natural optical sensors. The approaches and methods to measure chlorophyll fluorescence. Effect of herbicides on photosynthesizing organisms.

Biotechnology for alternative energy sources (1 credit)

The increasing energy demand in the near future will force people to seek environmentally clean alternative energy resources. Solar energy has been seen as a very promising for electrical use. The emergence of nanomaterials in construction of light energy harvesting assemblies has opened up new ways to utilize solar energy. The crucial task is development of non-toxic nanomaterials that will have no adverse effect on an environment. Main topics of the course are natural photosynthesis (primary photosynthetic reactions, energy transfer processes, regulation mechanisms in photosynthetic antennas, electron transport pathways), artificial photosynthesis (artificial antennas for effective energy absorbance, artificial reaction centers, photoelectrochemical cells for water splitting in fuel production), optical methods for investigation of photosynthesis (spectral and luminescence methods – prompt and delayed fluorescence), nanomaterials (material formats, properties and application in solar energy conversion), bioassays for investigation of potential environment risks caused by nanomaterials. Practical tasks involve study of fluorescence methods (fast induction kinetics – OJIP curves, and PAM method) and their application in the investigation mechanisms of photosynthetic reactions in normal conditions and under the effect of environmental factors including nanomaterials.

Mechanical properties of cellular membranes (1 credit)

The course concerns cell shape and mechanisms of maintaining and changing the shape of animal cells on the example of mammalian erythrocytes. The basic principles of maintaining and changing the shape of cells, including the participation of the lipid component of the membrane, transmembrane proteins, polymerization of the cytoskeleton, the direct or indirect effect of cage-forming proteins, the incorporation of amphiphilic protein fragments will be considered. Comparison of cells with a developed cytoskeleton and erythrocytes specialized for movement in the fluid flow was carried out. Considered a variety of mechanisms involved in changing the shape of the red blood cell. Pathologies associated with changes in the shape of red blood cells.

Dynamic fluctuations of the erythrocyte membrane. The phenomenon of dynamic fluctuations of the erythrocyte membrane, erythrocyte flicker, will be considered. Possible mechanisms of its occurrence, connection with the mechanical properties of the erythrocyte membrane (membrane elasticity), physiological significance. The main methodological approaches for the study of this phenomenon will be presented. Possible relationship of flicker and mechanisms of mechanosensing. Mechanisms of cell mechanosensing. Methods to study mechanical properties of cells: AFM. Features of the method, modern applications. Force spectroscopy, the method of force curves.