

# Integrative course “Life Sciences”

(physiology, biochemistry, molecular biology, biophysics, bioenergetics)

100 h lectures, 50 h seminars, 30 h self-study, 180 h in total

## General description

This is an integrated course that consists of five blocks: physiology, biochemistry, molecular biology, biophysics, bioenergetics. As the disciplines and topics are interconnected, the blocks will be taught in parallel. Total duration of each block will be detailed in the course certificates.

Off-class study include preparation for seminars, individual practical assignments, which students will present at seminars as well as preparation for intermediate and final examinations.

All lectures and seminars of this course are 2 h. For seminars students will be divided into 3 groups.

All classes will be given in Ukrainian

## Physiology

26h lectures, 10h seminars

Lectures: **Volodymyr Manko, Olga Garaschuk**

Seminars: **Volodymyr Merlavsky**

### Lectures

1. **Bioelectric potentials.** Structure, properties and functions of the plasma membrane. Resting membrane potential. Action potential, its physiological role and mechanisms of generation. Direct and indirect mechanism of action of primary messengers. Ionotropic and metabotropic receptors. The role of G-proteins in physiological signal transduction.
2. **Synaptic excitation transduction.** Electrical and chemical synapses. Mechanism of excitation transduction via chemical synapse. Exocytosis. General scheme and role of membrane proteins. Synaptic mediators. Properties, mechanism of action and inactivation. Fast and slow postsynaptic processes. The role of ionotropic and metabotropic receptors. Presynaptic and postsynaptic inhibition.
3. **Muscle physiology.** Skeletal muscles. Muscle fiber. Sarcomere. Physiological properties and mechanism of skeletal muscle contraction. Slow and fast neuromotor units. Energy of muscle contraction. Work, strength and muscle fatigue. Structural features and electrophysiological properties of smooth muscle cells. Classification of smooth muscles. The mechanism of contraction and relaxation of smooth muscle. The mechanism of regulation of smooth muscle contraction involving Gq- and Gs-proteins.
4. **Sensory systems.** General description, role and mechanisms of transduction, transformation and transmission of sensory information in sensory systems. Sensory network. Classification of sensory systems and receptors. Visual sensory system. Optical system of the eye and its significance. Architecture of the receptor apparatus of the eye. Structure of retinal photoreceptors and mechanism of transduction. Architecture of receptor fields of retinal ganglion cells. Transformation of receptor potential into a sequence of action potentials. Auditory sensory system, components and functioning. Gustatory and olfactory sensory systems, components and functioning. Somatosensory system and pain sensing.

5. **Motor functions of the nervous system.** Spinal reflexes. Spinal shock and hyperreflexia. Decerebrate rigidity. Descending and ascending pathways of the spinal cord. Motor functions of the medulla oblongata and pons. The role of the substantia nigra and red nuclei of the midbrain legs in the regulation of skeletal muscle tone and phase contractions. Reflex arc and physiological significance of four-humped reflexes of the midbrain. Motor functions of the cerebellum. Disorders that occur due to removal or damage of the cerebellum. Motor functions of the basal ganglia of the cortex of the large hemispheres. Motor zones of the cortex of the large hemispheres. Cortical representation of muscles in the primary motor area. Premotor and secondary motor zones of the cortex of the large hemispheres.
6. **Functions of the autonomic nervous system. General characteristics of humoral regulation. Stress.** Peculiarities of the autonomic nervous system organization. Features of the vegetative reflex arc. Mediators of the autonomic nervous system and their mechanism of transduction. Comparative characteristics of the sympathetic and parasympathetic nervous systems. The role of the sympatho-adrenal system, cortisol and endogenous opiates. General characteristics of endocrine glands. Properties of hormones and their classification. Hypothalamic-pituitary connection.
7. **Blood system.** Composition, functions and physicochemical properties of blood. Structure and functions of erythrocytes. Hematopoiesis. Respiratory function of blood. Blood groups. System ABO and Rh. General characteristics, classification and functions of leukocytes. Immunity. Nonspecific and specific mechanisms. Congenital and acquired. Allergy. Platelets. Vascular-platelet and coagulation hemostasis. The role of plasma coagulation factors. Fibrin clot retraction.
8. **Physiological properties of the heart.** Properties of the heart muscle. Automation of the heart. Regulation of heart activity. Frank-Starling's law. Electrical conduction system analysis. Propagation of excitement in the heart. Cardiac cycle. Electrocardiogram. Arterial pulse. Structure and types of vessels. Basic principles of hemodynamics. Pressure in different parts of the big circle of blood circulation. Blood pressure. Laminar and turbulent blood flow. Volumetric and linear blood flow rate. The rate of blood flow in different parts of the big circle of blood circulation. Nervous and humoral regulation of blood vessel tone.
9. **Physiology of respiration and excretion.** The main stages of respiration. Mechanism of inhalation and exhalation. The role of the respiratory muscles. Intrapleural pressure and elasticity of the lungs and their role in respiration. Surfactant. Lung volumes. The composition of inhaled, exhaled and alveolar air. Gas exchange in the lungs and tissues. Partial pressure and tension of gases. Blood gas transport. Nervous and humoral regulation of respiration. Respiratory center of the medulla oblongata.
10. **Kidneys:** structure and blood supply of the nephron. Composition and properties of primary and secondary urine. The mechanism of formation of primary and secondary urine. Regulation of renal function.
11. **Physiology of digestion and absorption.** Secretion and secretory cells. Classifications of exocrine glands. Basal and stimulated secretion. The mechanism of fluid secretion. Digestion in the mouth. Regulation of salivary secretion. Swallowing. Digestion in the stomach and small intestine. Intestinal juice. Secretion and composition of pancreatic juice. Regulation of pancreatic activity. Liver. Gallbladder. Bile. Composition and functions of bile. Enterohepatic circulation of bile acids. Digestion in the colon. The role of symbiotic microorganisms. Mechanisms of absorption of nutrients, water and mineral salts in different parts of the gastrointestinal tract.
12. **Higher nervous activity.** Congenital and acquired forms of behavior. Memory formation. Forms of learning. Circadian rhythm and sleeping. Physiological fundamentals of motivation and emotions.
13. **Neural fundamentals of speech.** Human and animal language. Mirror neurons. Mind and its manifestations in the animal world.

### **Practical training**

1. **They have different specializations but work in the same way.** Basic principles of cellular physiology. Cellular mechanisms of signal transduction. Generation of bioelectric potentials. Contraction. Secretion.
2. **How do we see and hear?** Physiological properties and mechanisms of visual and auditory sensory systems.
3. **Why are defibrillators placed in the Kyiv subway?** Basic principles of cardiovascular physiology.
4. **Why do we suffocate during Covid-19?** Gas exchange in the lungs and transportation of gases in the blood.
5. **We are afraid!** Or not? Physiology of emotions. The basic principles of the stress physiology, and its advantages in the formation of the adaptation potential of the body.

### **Self-study**

1. Solving tasks in electrophysiology.
2. Solving tasks for work and muscle contraction.
3. Solving tasks in the physiology of sensory systems.
4. Solving tasks in the physiology of the blood system and circulatory system.
5. Characteristics of the ECG recording in the II standard lead

### **Digital materials preparation**

1. Development of calculation tasks and tests.
2. Recording of the video clip "Registration and analysis of tremor in humans".

# Biochemistry

30h lectures, 16h seminars

Lectures: **Halyna Semchyshyn, Galyna Ushakova**

Seminars: **Galyna Ushakova, Oleksandra Abrat, Halyna Semchyshyn**

In the course presented here, we discuss the molecular basis of biological system functioning and main biochemical processes underlying general metabolism of carbohydrates, proteins, lipids and nucleic acids. A special attention is focused on coordination of metabolism of different biological compounds and its regulation by vitamins and hormones. Besides the classic enzymatic metabolism, this course is complemented by our modern understanding of non-enzymatic processes in biological systems and their role in the functioning of living organisms.

## Lectures

### 1. Energy and Metabolism.

General aspects of metabolism: anabolism and catabolism. Thermodynamic bases of metabolism. The first and second laws of thermodynamics. Endergonic and exergonic reactions. Metabolic Pathways. Oxidation and reduction reactions. Redox potential. The Nernst equation. Biological oxidation. High energy phosphates. Chemical structure and biological role of ATP.

### 2. Energy and metabolism of carbohydrates.

Carbohydrates: general characteristics and their role in metabolism and energy of organism. Metabolism of glycogen: chemistry, biological sense and reciprocal regulation of glycogen metabolism by cyclic AMP. Biological role and chemistry of the glycolytic pathway. Fate of pyruvate after glycolysis.

### 3. Aerobic cellular respiration.

General aspects of aerobic cellular respiration. Chemistry and biological significance of oxidative decarboxylation of pyruvate and tricarboxylic acid cycle (TCA). Their regulation. Substrate-level phosphorylation. Energy balance of complete glucose oxidation. Modified TCA pathways.

### 4. Electron transport chain and oxidative phosphorylation.

General characteristics and principle of functioning of the mitochondrial electron transport chain. Mechanism of oxidative phosphorylation. Chemi-osmotic theory. ATP synthase. Regulation of oxidative phosphorylation. Mitochondrial electron transport chain is a source of free radicals. General aspects and biological significance of non-mitochondrial electron transport chains.

### 5. Metabolic pathways of carbohydrates: gluconeogenesis and its interplay with glycolysis.

Gluconeogenesis: chemistry and biological sense. Entrance of lactate, glycerol, alanine, and propionate in gluconeogenesis. Interplay between glycolysis and gluconeogenesis. Cori cycle. Reciprocal regulation of glycolysis and gluconeogenesis. Futile cycles.

### 6. Metabolic pathways of carbohydrates: pentose phosphate and polyol pathways, interconversion of hexoses and their entrance in glycolysis.

Pentose phosphate pathway: chemistry, regulation and biological sense. Interplay between pentose phosphate pathway and glycolysis. Polyol pathway, chemistry and its biological role. Entrance of fructose and galactose in glycolysis. Metabolism of alcohol.

### 7. Metabolic pathways of lipids: catabolism.

Lipids: general characteristics and their role in metabolism and energy of organism. Catabolism of triacylglycerides: the role of hormones. Fatty acid oxidation: activation and transport across the mitochondrial membrane.  $\beta$ -oxidation of saturated fatty acids with an even number of carbon atoms. Energy balance of complete oxidation of palmitic acid. Oxidation of unsaturated fatty acids. Oxidation of fatty acids with an odd number of carbon atoms.  $\alpha$ - and  $\omega$ -oxidation of fatty acids.

### **8. Metabolic pathways of lipids: anabolism (biosynthesis of fatty acids).**

Biosynthesis of fatty acids: shuttle mechanism of acetyl-CoA transportation across the mitochondrial membrane, formation of malonyl-CoA. Biosynthesis of saturated and unsaturated fatty acids. Regulation of oxidation and synthesis of fatty acids. Biosynthesis of triacylglycerides and phospholipids.

### **9. Metabolic pathways of lipids: cholesterol, ketone bodies, eicosanoids.**

Biological role, chemistry and regulation of cholesterol biosynthesis. Inhibitors of the process, statins. Biotransformation and degradation of cholesterol. General characteristics, biological role and metabolism of ketone bodies and eicosanoids.

### **10. Metabolic pathways of proteins and amino acids: general catabolic pathways.**

Proteins and amino acids: general characteristics and their role in metabolism and energy of organism. General pathways of catabolism of amino acids. The role of vitamins. Deamination of amino acids: types and general characteristics. Oxidative deamination of amino acids: role of glutamic acid. Transamination of amino acids: mechanism and biological significance. Non-direct deamination. The role of glutamic and aspartic acids. Transamination. Synthesis of non-essential amino acids. Decarboxylation of amino acids and their derivatives. Biogenic amines.

### **11. Metabolic pathways of proteins and amino acids: ammonia metabolism, urea cycle, specific pathways of amino acids.**

Ammonia binding, transportation, and detoxification. Ammonia metabolism in animals. Urea biosynthesis. Relationship between tricarboxylic acids and the ornithine cycles (Krebs bicycle).

### **12. Metabolic pathways of nucleotides.**

Nucleic acids: general characteristics, structure, and functions. Degradation and biosynthesis of purine and pyrimidine nucleotides. General characteristics, chemistry, biological role and regulation of the processes. Disturbance of nucleotide metabolism.

### **13. Integration of metabolism.**

Coordination of carbohydrate, lipid, and protein metabolism. Involvement of vitamins and hormone in the metabolism regulation.

### **14. Non-enzymatic processes in biological systems: free radical oxidation and glycation.**

General characteristics of free radicals and reactive oxygen species and their reactions. Non-enzymatic glycosylation (glycation). General characteristics of reactive carbonyl species and advanced glycation end products. Generation of reactive oxygen and carbonyl species in living systems, their reaction with cellular constituents. Mechanisms of protection against the reactive forms. Glycooxidation. "Useful" role of reactive species: signaling and involvement in immune response.

### **15. Non-enzymatic processes in biological systems: free radical and glycation aging theories.**

Analysis of the theories of "chemical damage" of biomolecules. General aspects of the theory of oxidative/carbonyl stress. Chronic and acute oxidative/carbonyl stress. "Aging" of biomolecules and defensive systems against reactive oxygen and carbonyl species.

### **Practicals (seminars)**

1. Carbohydrate metabolism and its regulation.
2. Lipid metabolism and its regulation.
3. Carbohydrate and lipid metabolism disorders.
4. Metabolism of proteins and amino acids and regulation.
5. Metabolism of nucleotides and its regulation.
6. Protein and nucleotide metabolism disorders.
7. Integration of metabolism.
8. Non-enzymatic processes in biological systems.

# Molecular biology

18h lectures, 10h seminars

Lectures: **Volodymyr Lushchak, Andriy Luzhetskyi**

Seminars: **Dmytro Gospodaryov, Volodymyr Lushchak, Anastasia Shkuropat**

The purpose of the block is to provide in-depth knowledge of the structure of nucleic acids and nucleoprotein complexes, the peculiarities of genetic information flow (DNA replication) in prokaryotes and eukaryotes; to give an idea on gene expression at different levels (transcription, RNA processing, translation, post-translational modification of proteins), to familiarize with the mechanisms of gene expression regulation in prokaryotes and eukaryotes; to get acquainted with the molecular mechanisms involved in the adaptation of living organisms to the action of adverse environmental factors, in particular to the action of oxidative stress; to provide students with the theoretical basis of the main methods used by modern molecular biology to detect hereditary pathologies and infectious diseases, genome editing to correct hereditary disorders, and the generation of genetically modified organisms with beneficial properties for humans.

## Lectures

### **1. The flow of genetic information and principles of its regulation.**

The main dogma of molecular biology. The flow of genetic information in pro- and eukaryotes and the basic principles of its regulation.

### **2. DNA biosynthesis - replication.**

DNA replication — initiation, elongation, termination. Formation of phosphodiester bonds. DNA replication in *E. coli*. DNA replication in eukaryotes. Replication at the ends of linear chromosomes.

### **3. DNA repair.**

Terminology. Repair in *E. coli* by excision. Repair during replication. Reversal of damages. SOS repair.

### **4. Transcription.**

Initiation and elongation. Termination. RNA polymerases of pro-, eukaryotes and archaeobacteria. RNA processing. Ribozymes.

### **5. Translation.**

Activation of amino acids. Initiation, elongation and termination of protein biosynthesis. Regulation of translation.

### **6. Molecular bases of mutagenesis.**

Types of mutations. Chemical modification. Radiation damage. Errors of DNA polymerase and repair systems. Stretching the double helix. Biological mutagenesis. Directed mutagenesis.

### **7. Regulation of gene expression.**

General principles. Repression and induction. Operons and regulons. Peculiarities of gene expression in pro- and eukaryotes. Positive and negative control. Lactose and tryptophan operons. Catabolite repression. DNA protection.

### **8. Regulation of gene expression by active forms in prokaryotes and eukaryotes.**

Active forms oxygen in biological systems. Oxidative/reductive stress. Bacterial regulons OxyR and SoxRS. Yap1 stimulon in yeasts. The Keap1/Nrf2 system in animals.

### **9. Use of molecular biology methods in medicine and biotechnology.**

Polymerase chain reaction. Detection of hereditary pathologies and infectious diseases by the PCR method. Genome editing to correct hereditary disorders. Genetically modified and transgenic organisms.

**Practicals (seminars)**

1. The flow of genetic information and its regulation in pro- and eukaryotes.
2. Replication, mutagenesis and repair.
3. Transcription and translation and their regulation.
4. Regulation of gene expression.
5. Biomedical and biotechnological use of molecular biological approaches.

# Biophysics

12 h lectures, 8 h seminars

Lecturer: **Volodymyr Shvadchak**

This block introduces physical aspects of the interactions of biological molecules and some cellular processes. It will also provide understanding how composition determines the structure and properties of proteins, DNA, and RNA and membranes. Practical classes will be focused on design of peptides and oligonucleotides with desirable properties, skills to use specialized software and web services, investigation of mechanisms of biological processes with special attention to the issues that arise in drug development.

## Lectures

### 1. Thermodynamics.

Reversible and irreversible processes. Laws of Thermodynamics. Heat and reaction enthalpy. Entropy.  $\Delta G$ . Nernst equation. Hess law. Equilibrium constants. Determining  $K_d$  and stoichiometry of protein interactions.

### 2. Kinetics.

First-order reactions. Two-stage reactions. Reversible reaction rates and equilibrium constants. Second order reaction. Kinetics in complex systems. Basics of kinetic modeling. Modeling of epidemics development. Catalysis. Kinetics of fermentative reactions. Inhibition. Kinetics in studies of reaction mechanisms.

### 3. Structure of proteins.

Covalent, hydrogen, ionic bonds. Individual molecules and biopolymers. Diffusion and size of molecules. Primary, secondary, tertiary structure of proteins. Disulfide bonds. Relationship between amino acid sequence and secondary structure. CD spectroscopy.

### 4. DNA and RNA.

Complementarity. Helix. Hairpins. tRNA. Annealing. UV absorbance to monitor dsDNA-ssDNA transition. Atypical conformations. Viral and non-coding RNA. RNAzymes. Software for protein and DNA structure visualization.

### 5. Membrane.

Lipid bilayer. Model membranes. Membrane phase. Structure and composition of cell membrane. Proteins and membranes. Membrane permeability. Membrane asymmetry. Transmembrane potential. Channels.

### 6. Molecular machines and transport in cells.

ATP-synthase. Bacterial flagella. Tubulin microtubules. Kinesin and dynein. Actin microfilaments and myosin.

## Seminars

1. Calculations of binding and dissociation constants. Equilibria in solution. Methods to study protein interactions.

2. Design of peptides with desirable properties. DNA hairpins. Online properties calculators for peptides and oligonucleotides. Model membranes.

3. Kinetics of protein interactions. Inhibition mechanism on kinetic level. Simulation of complex reaction kinetics in Excel.

4. VMD software for protein structure visualization. Channels. Molecular machines. Motor proteins.



# Bioenergetics

14 h lectures, 6 h seminars

Lectures: **Andriy Babsky, Dmytro Gospodaryov**

Seminars: **Oksana Ikkert**

This block deals with energy metabolism in cells, and function of mitochondria.

## Lectures

- 1. Structure and functions of mitochondria.** Localization of mitochondria in the cell. The structure of mitochondria. Connection with the endoplasmic reticulum. Features of mitochondrial DNA.
- 2. Forms of energy storage in the cell.** ATP as a universal source of energy. Energetic and regulatory role of adenylate kinase and AMP-dependent kinase. Other macroergic compounds. Redox reactions in biological systems. The role of pyridine and flavin nucleotides in redox reactions. The role of mitochondria in "switching" from catabolism to anabolism and vice versa.
- 3. Energy sources in cells.** Glycolysis and energy metabolism. Energetics of fat metabolism. Catabolism of amino acids. Role in the biological evolution, effectiveness and feasibility of use. Krebs cycle. Pyruvate dehydrogenase complex. Energy-dependent reactions of the cycle. Does the cycle always work "completely"? "Amber" energy.
- 4. Structure and functions of the mitochondrial respiratory chain and ATP synthesis.** Proton gradient as a form of energy storage. Theories of the coupling of respiration and oxidative phosphorylation. Rotational catalysis of ATP synthesis. The ratio between consumed  $O_2$  and synthesized ATP. R/O: 3 and 2, or 2.5 and 1.5?
- 5. Mitochondria and active forms of oxygen.** Processes of lipid peroxidation and antioxidant protection of the cell. Why do we age?
- 6. Transport systems of mitochondria.** Active and passive transport of substances through biological membranes. What is the role of mitochondria in regulating the level of  $Ca^{2+}$  in the cell?
- 7. The role of mitochondria in physiological processes and pathologies.** Physiology of muscles. Secretion of insulin and hydrochloric acid. Hereditary mitochondrial diseases. Ischemia, diabetes, stroke, etc.

## Seminars

- Mitochondria and diseases: role of mitochondria in heart diseases, neurodegenerative diseases, autoimmune diseases.
- Antioxidants in our life: aging, dermatology, food. Succinic bioenergetics: the role of succinate in medicine, food industry, sports. Is succinate doping or not?
- Methods of studying mitochondrial respiration. Polarography; mitochondrial functional states. Various experimental protocols for assessing the mitochondria functional states.