

# Master course in Biotechnology for Neuroscience

## Admission test Syllabus

### General and inorganic chemistry

States of aggregation of matter. Phase transitions. Solutions. Concentration. Colligative properties of solutions.

Chemical thermodynamics. Thermal capacity. First principle. Enthalpy: Hess's law. Entropy: second principle. Gibbs free energy and spontaneity of chemical reactions. Chemical kinetics. Reaction mechanisms. Catalysis. Chemical equilibrium. Equilibrium constants. Le Chatelier's principle.

Acids and Bases. Arrhenius and Bronsted-Lowry theories. Strength of acids and bases. Buffer Solutions. Equilibrium of dissolution / precipitation. Solubility and solubility product.

Electrochemistry: redox reactions. Atomic and molecular mass, minimum and molecular formula, mole concept. Chemical equations - balanced. Weight relationships. Gas systems. Solutions - concept of concentration, colligative properties.

Thermodynamics and Thermochemistry. Chemical equilibrium - equilibrium constants. Displacement of balance. Salt Solutions - Hydrolysis. Concept of pH: solutions of acids and bases. Buffer solutions. Solubility equilibria. Solubility product. Electrochemistry.

### Organic chemistry

Structure, nomenclature, physical properties and reactivity of the following organic compounds: alkanes; cycloalkanes; alkenes; alkynes; aromatic compounds; aromatic heterocycles; alkyl and aryl halides; alcohols; phenols; ethers; aldehydes; ketones; carboxylic acids and their derivatives; amines.

Stereoisomerism. The radical substitution reaction. Electrophilic and radical addition reaction according to Markovnikov and anti-Markovnikov. Aromatic electrophilic substitution reaction. Enantiomerism. Optical activity and chirality. Nucleophilic substitution and elimination.

Carbohydrates: General structure, representation and properties of carbohydrates. Molecular structure and properties of the main mono, di and oligosaccharides.

Lipids: structure, properties and classification of the main hydrolysable and non-hydrolysable lipids.

Amino acids, peptides and proteins: Structure and properties of amino acids. Acidity, basicity and isoelectric pH.

Nucleic acids. Structure and properties of nitrogenous bases, nucleosides and nucleotides. Formation, stability and rupture of the phosphodiester bond.

### Biochemistry

Proteins: Amino acids, Structure of proteins, fibrous and globular proteins. Protein folding and diseases associated to conformational abnormalities.

Enzymes: Characteristics and kinetic properties. The change in free energy of the reactions. Catalytic strategies. Enzyme inhibitors.

Hemoglobin: Structure, allosteric regulation and Bohr effect. Hemoglobinopathies.

Carbohydrates: monosaccharides, disaccharides, polysaccharides (starch, cellulose, glycogen). The bacterial wall. Modified monosaccharides. Glycosaminoglycans, proteoglycans, glycoproteins.

Lipids: fatty acids, triglycerides, phospholipids (glycerophospholipids and sphingolipids). Lipids Ethers (PAF). Glycolipids. Cholesterol and its derivatives: acids steroids and bile acids. Phosphatidylinositols and eicosanoids. Membrane composition.

Biosignaling: general characteristics of the signal transduction. G protein-coupled receptors with tyrosine kinase activity, with guanylyl cyclase activity. Sensory systems: signal transduction in vision, olfaction and taste.

Introduction to energy metabolism: catabolic pathways and energy production: ATP. Coupled reactions. Transfer potential of the phosphoric group. Reducing agents. Coenzyme A.

Energy metabolism of carbohydrates: glycolysis, fermentation, glycolysis regulation, hormonal control (insulin and glucagon). Gluconeogenesis. Coordinated regulation of glycolysis and gluconeogenesis. Glycogen metabolism and its regulation (allosteric and hormonal). Metabolic clustering of glycolytic and glycogenolytic enzymes. The citric acid cycle (TCA). Pyruvate dehydrogenase. TCA regulation. TCA as a source of biosynthetic precursors. Oxidative phosphorylation. Electron carriers. Electron transport coupled to the formation of a proton gradient. Decoupling. The chemiosmotic theory. Experimental verification of the theory. ATP synthase. Transport systems on the mitochondrial membrane. Oxidative phosphorylation regulation.

Photosynthesis: light period, photo-pigments, absorption of light energy and photo-induced charge separation. Photosystems. NADPH and ATP production. The dark phase: Calvin cycle, Rubisco and its regulation. Sucrose and starch production in plants. Photorespiration. Metabolism of C<sub>3</sub>, C<sub>4</sub> and CAM plants.

The pentose cycle: steps. Antioxidant function of NADPH. Genetic deficiency of G6PD.

Fatty acids catabolism: origin of lipids from the diet and from adipose tissue. Apo-lipoproteins (chylomicrons, VLDL, LDL, HDL). Acyl-CoA activation, transport in the mitochondria and beta-oxidation. Oxidation of unsaturated fatty acids and odd chains.

Biosynthetic reactions from acetyl-CoA: ketone bodies and their meaning, fatty acids synthesis. Fatty acids synthesis from carbohydrates. Regulation of synthesis and degradation of fatty acids (allosteric and hormonal). Reactions of elongation and unsaturation. Synthesis of triglycerides and phospholipids.

Cholesterol biosynthesis. Cholesterol synthesis regulation. Transport of cholesterol in the blood plasma: lipoproteins. Mevalonate as a precursor of compounds with isoprene units (Vitamin A, E, K). Farnesylation and geranylation of proteins. Catabolism of cholesterol to bile acids. Steroid hormones: biosynthesis and catabolism of corticosteroids and sex hormones. Vitamin D.

Turnover of proteins and amino acid catabolism. Deamination by transaminase. Pyridoxalphosphate. Desaminazione. Glutamate dehydrogenase. Urea cycle. Genetic deficiencies.

Biosynthesis of amino acids: nitrogen fixation. Nitrogen cycle, insertion of ammonium into amino acids. Gln synthetase regulation. Biosynthesis of amino acids (specific examples). S-adenosyl-methionine, THF. Amino acid derivatives. Synthesis of GSH, dopamine, norepinephrine, epinephrine, GABA, histamine, polyamines.

Biosynthesis and catabolism of purine and pyrimidine nucleotides. Genetic deficiencies. Ribonucleotide reductase. Mechanisms of regulation. Folic coenzyme. DHF reductase inhibitors as anticancer drugs. Uric acid.

## Cell biology

Cell structure and organization: eukaryotic and prokaryotic cells; cellular compartments.

Biological membranes: phospholipids; the organization in double layers; fluidity of the phospholipid bilayer; intrinsic and extrinsic proteins; the cytoskeleton as mechanical support for the lipid bilayer.

Membrane transport of small molecules: characteristics of permeability of the lipid bilayer; channel proteins and carrier proteins: kinetic properties of the two systems and operating methods; glucose transporter; passive transport and active transport; the sodium potassium pump: operating mode; antiport and symport; regulation of channel opening.

Mitochondria and ATP synthesis: general information on the process of glycolysis, pyruvate oxidation and the Krebs cycle; chemo-osmotic ATP synthesis; evolutionary origin of mitochondria.

Endoplasmic reticulum and Golgi apparatus: synthesis of membrane proteins and secretion; glycosylation and maturation of proteins in the Golgi; vesicular traffic: vesicle formation and movement, recognition of the target organelle.

Mechanisms of protein sorting in different cellular compartments: signal sequences and protein localization (entry into the nucleus, the endoplasmic reticulum, the mitochondria).

Receptors: plasma membrane as a communication interface with the outside; receptors: intrinsic protein and the specificity of the receptor-ligand interaction; generation of intracellular messages: activation of protein phosphorylation; kinases and phosphatases; monomeric and trimeric GTPases; receptors associated with Gs and Gi proteins and the cAMP/protein kinase A signaling pathway; Gq protein coupled receptors and PLC/Ca<sup>2+</sup> signaling pathway; tyrosine kinase receptors: MAPK, PI3K, PLC signaling pathways; JAK/STAT signaling pathway; TGF- $\beta$  signaling pathway; amplification of intracellular signaling; inactivation mechanisms: degradation of the ligand; internalization of the receptor; steroid hormones can cross the membrane: cytoplasmic and nuclear receptors.

The cytoskeleton: microfilaments of actin and myosin, and cell movement; intermediate filaments; microtubule and organelle movement; muscle contraction.

The extracellular matrix and the adhesive receptors: collagens, laminin, fibronectin and proteoglycans; extracellular matrix proteins establish multiple interactions; extracellular matrix-cell interaction is mediated by specific receptors: integrins; structure and function of integrins and cadherins.

The cell cycle and mitosis: G<sub>1</sub>, S, G<sub>2</sub> and M cell cycle phases; role of cyclins and cdks in cell cycle progression; cell cycle checkpoints: G<sub>1</sub> check point (Rb/E2F), G<sub>2</sub> check point (p53) and mitotic checkpoint (cdc20/APC).

Apoptosis: intrinsic pathway (p53 and mitochondria); extrinsic pathway (the death receptor)

Cancer: hallmarks of cancer cells; oncogenes and tumor suppressors.

## Genetics

Cell division: an overview of cell cycle; mitosis; meiosis.

Mendelian genetics: principle of segregation; principle of independent assortment; linked genes; linkage maps; X-linked inheritance.

Gene interaction: interactions between the alleles of one gene; gene interaction leads to modified dihybrid ratios; penetrance and expressivity.

Introduction to quantitative genetics; analysis of quantitative traits.

Introduction to population genetics: Darwin's revolution; variation and its modulation; the Hardy-Weinberg principle.

Principles of recombinant DNA technology: making recombinant DNA; DNA electrophoresis; introduction to transgenic animals.

The Structure of Genes and Genomes: the molecular nature of genes and genomes

DNA and Chromosomes: the structure and function of DNA; chromosomal DNA and its packaging in the chromatin fiber; the global structure of chromosomes; changes in chromosome number; chromosomal rearrangements.

DNA replication, repair, and recombination: the maintenance of DNA sequences; DNA replication mechanisms; gene mutations; DNA repair; general and site-specific recombination.

Analysis of gene structure: Nucleic acid hybridization; Restriction enzymes and DNA ligases; Synthetic oligonucleotides; Polymerase Chain Reaction; Production of labeled probes; DNA analysis by Southern blotting; DNA and genomic sequencing; DNA polymorphisms.

Gene cloning: Cloning of DNA fragments in plasmid and phage vectors; Construction of genomic and cDNA libraries; Screening of DNA libraries by hybridization; Reconstruction of full length transcripts; The Human Genome Project and the other genomes.

## Molecular biology

From DNA to protein: from DNA to RNA; from RNA to protein.

Control of gene expression: an overview of gene control; the basics of prokaryotic transcriptional regulation; regulation of the lactose system;

Analysis of gene expression: northern and western blotting; reverse-transcription- (RT)-PCR; real time PCR; in-situ hybridization; microarrays.

The control of gene expression in eukaryotes: histones acetylation-deacetylation and their regulation, the histone code; nucleosome positioning and chromatin remodeling; control of transcription and DNA looping; the core promoter and pre-initiation complex assembly; main features of RNA polymerase II - the CTD; general transcription factors (GTF) and basal transcriptional machinery; specific transcription factors; distinction between transcriptional activators and co-activators; the mediator; structure of transcription factors (DNA binding domain, transcriptional activation domain); mechanisms of transcriptional repression; DNA methylation and its main functions.

Techniques to study transcriptional regulation: reporter assays; EMSA assays; chromatin immunoprecipitation (ChIP).

Mechanisms of post-transcriptional regulation: coordination between transcription, RNA maturation and transport: the gene expression factory; RNA interference and microRNAs: physiological and pathological functions; other-coding RNAs; the long non-coding RNAs.

Recombinant DNA-based technologies: prokaryotic expression systems; Yeasts expression systems; protein expression in insect cells by Baculoviral vectors; expression in mammalian cells: viral and non viral vectors; transgenic animal and plants; conditional expression systems; the yeast two hybrid system.

## Physiology

Basic concepts of Physiology of excitable cells and synaptic transmission

Basic concepts of Physiology of muscle tissue

Basic concepts of Physiology of the autonomous nervous system.

Physiology of cardiovascular system: basis of mechanical and electrical activity of the heart, the heart cycle in experimental species (mouse, rat, rabbit), blood circulation and pressure.

Physiology of the respiratory system: description of the breathing process, gas exchange in the alveoli, gas transport mechanisms. Evaluation of respiration in experimental animals.

Stress Physiology: the hypothalamic-pituitary-adrenal axis, evaluation of hormone response to stress, behavior responses to stressors in mouse, rat and rabbit.

Basic concepts of Physiology of the reproduction.

## Anatomy

Organization of the human body and anatomical nomenclature: Musculoskeletal system (structure and development of bones; organization and mechanics of joints and muscles; general organization of the skeleton and muscle compartments).

Cardiovascular system (structure of the heart and blood vessels; pulmonary and systemic circulation)

Lymphatic system (lymphatic vessels and lymphoid organs).

Respiratory system (organization of the upper and lower airways, structure of the lungs and pleurae).

Digestive system (organization and structure of the digestive tract and accessory glands).

Urinary system (organization and structure of the kidneys and urinary tract).

Male and female reproductive systems (organization and structure of the gonads and the genital tracts, with special emphasis on gametogenesis and the anatomical bases of ovarian and uterine cycles).