

## *Biological and Biochemical Foundations of Living Systems*

### **Foundational Concept 1**

Biomolecules have unique properties that determine how they contribute to the structure and function of cells, and how they participate in the processes necessary to maintain life.

The unique chemical and structural properties of biomolecules determine the roles they play in cells. The proper functioning of a living system depends on the many components acting harmoniously in response to a constantly changing environment. Biomolecules are constantly formed or degraded in response to the perceived needs of the organism.

#### **Content Categories**

- *Category 1A* focuses on the structural and functional complexity of proteins, which is derived from their component amino acids, the sequence in which the amino acids are covalently bonded, and the three-dimensional structures the proteins adopt in an aqueous environment.
- *Category 1B* focuses on the molecular mechanisms responsible for the transfer of sequence-specific biological information between biopolymers which ultimately results in the synthesis of proteins.
- *Category 1C* focuses on the mechanisms that function to transmit the heritable information stored in DNA from generation to generation.
- *Category 1D* focuses on the biomolecules and regulated pathways involved in harvesting chemical energy stored in fuel molecules, which serves as the driving force for all of the processes that take place within a living system.

With these building blocks, medical students will be prepared to learn how the major biochemical energy production pathways are regulated, how the synthesis and degradation of macromolecules functions to maintain health, and how various forms of biochemical dysfunction result in disease.

### ***Content Category 1A: Structure and function of proteins and their constituent amino acids***

Macromolecules formed from amino acids adopt well-defined, three-dimensional structures with chemical properties that are responsible for their participation in virtually every process occurring within and between cells. The three-dimensional structure of proteins is a direct consequence of the nature of the covalently-bonded sequence of amino acids, their chemical and physical properties, and the way in which the whole assembly interacts with water.

Enzymes are proteins that interact in highly regio- and stereo-specific ways with dissolved solutes. They either facilitate the chemical transformation of these solutes, or allow for their transport innocuously. Dissolved solutes compete for protein-binding sites, and protein conformational dynamics give rise to mechanisms capable of controlling enzymatic activity.

The infinite variability of potential amino acid sequences allows for adaptable responses to pathogenic organisms and materials. The rigidity of some amino acid sequences makes them suitable for structural roles in complex living systems.

Content in this category covers a range of protein behaviors which originate from the unique chemistry of amino acids themselves. Amino acid classifications and protein structural elements are covered. Special emphasis is placed on enzyme catalysis, including mechanistic considerations, kinetics, models of enzyme-substrate interaction, and regulation. The topics and subtopics in this category are the following:

#### **Amino Acids (BC, OC)**

- Description
  - Absolute configuration at the  $\alpha$  position
  - Amino acids as dipolar ions
  - Classifications
    - Acidic or basic
    - Hydrophobic or hydrophilic
- Reactions
  - Sulfur linkage for cysteine and cysteine
  - Peptide linkage: polypeptides and proteins
  - Hydrolysis

#### **Please Note**

Topics that appear on multiple content lists will be treated differently. Questions will focus on the topics as they are described in the narrative for the content category.

#### **Protein Structure (BIO, BC, OC)**

- Structure
  - 1° structure of proteins
  - 2° structure of proteins
  - 3° structure of proteins; role of proline, cystine, hydrophobic bonding
  - 4° structure of proteins (BIO, BC)
- Conformational stability
  - Denaturing and folding
  - Hydrophobic interactions
  - Solvation layer (entropy) (BC)
- Separation techniques
  - Isoelectric point

- Electrophoresis

### **Non-Enzymatic Protein Function (BIO, BC)**

- Binding (BC)
- Immune system
- Motors

### **Enzyme Structure and Function (BIO, BC)**

- Function of enzymes in catalyzing biological reactions
- Enzyme classification by reaction type
- Reduction of activation energy
- Substrates and enzyme specificity
- Active Site Model
- Induced-fit Model
- Mechanism of catalysis
  - Cofactors
  - Coenzymes
  - Water-soluble vitamins
- Effects of local conditions on enzyme activity

### **Control of Enzyme Activity (BIO, BC)**

- Kinetics
  - General (catalysis)
  - Michaelis–Menten
  - Cooperativity
- Feedback regulation
- Inhibition – types
  - Competitive
  - Non-competitive
  - Mixed (BC)
  - Uncompetitive (BC)
- Regulatory enzymes
  - Allosteric enzymes
  - Covalently-modified enzymes
  - Zymogen

### ***Content Category 1B: Transmission of genetic information from the gene to the protein***

Biomolecules and biomolecular assemblies interact in specific, highly-regulated ways to transfer sequence information between biopolymers in living organisms. By storing and transferring biological information, DNA and RNA enable living organisms to reproduce their complex components from one generation to the next. The nucleotide monomers of these biopolymers, being joined by phosphodiester linkages, form a polynucleotide molecule with a “backbone” composed of repeating sugar-phosphate units and “appendages” of nitrogenous bases. The unique sequence of bases in each gene provides specific information to the cell.

DNA molecules are composed of two polynucleotides that spiral around an imaginary axis, forming a double helix. The two polynucleotides are held together by hydrogen bonds between the paired bases and van der Waals interactions between the stacked bases. The pairing between the bases of two polynucleotides is very specific, and its complementarity allows for a precise replication of the DNA molecule.

The DNA inherited by an organism leads to specific traits by dictating the synthesis of the biomolecules (RNA molecules and proteins) involved in protein synthesis. While every cell in a multicellular organism inherits the same DNA, its expression is precisely regulated such that different genes are expressed by cells at different stages of development, by cells in different tissues, and by cells exposed to different stimuli.

The topics included in this category concern not only the molecular mechanisms of the transmission of genetic information from the gene to the protein (*transcription* and *translation*), but also the biosynthesis of the important molecules and molecular assemblies that are involved in these mechanisms. The control of gene expression in prokaryotes and eukaryotes is also included.

Broadly speaking, the field of biotechnology uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use. The biotechnological techniques emphasized in this category, however, are those that take advantage of the complementary structure of double-stranded DNA molecules to synthesize, sequence, and amplify them, and to analyze and identify unknown polynucleotide sequences. Included within this treatment of biotechnology are those practical applications which directly impact humans, such as medical applications, human gene therapy, and pharmaceuticals.

Content in this category covers the biopolymers, including ribonucleic acid (RNA), deoxyribonucleic acid (DNA), proteins, and the biochemical processes involved in carrying out the transfer of biological information from DNA. The topics and subtopics in this category are the following:

#### **Nucleic Acid Structure and Function (BIO, BC)**

- Description
- Nucleotides and nucleosides
  - Sugar phosphate backbone
  - Pyrimidine, purine residues
- Deoxyribonucleic acid (DNA): double helix, Watson–Crick model of DNA structure
- Base pairing specificity: A with T, G with C
- Function in transmission of genetic information (BIO)

- DNA denaturation, reannealing, hybridization

### **DNA Replication (BIO)**

- Mechanism of replication: separation of strands, specific coupling of free nucleic acids
- Semi-conservative nature of replication
- Specific enzymes involved in replication
- Origins of replication, multiple origins in eukaryotes
- Replicating the ends of DNA molecules

### **Repair of DNA (BIO)**

- Repair during replication
- Repair of mutations

### **Genetic Code (BIO)**

- Central Dogma: DNA → RNA → protein
- The triplet code
- Codon–anticodon relationship
- Degenerate code, wobble pairing
- Missense, nonsense codons
- Initiation, termination codons
- Messenger RNA (mRNA)

### **Transcription (BIO)**

- Transfer RNA (tRNA); ribosomal RNA (rRNA)
- Mechanism of transcription
- mRNA processing in eukaryotes, introns, exons
- Ribozymes, spliceosomes, small nuclear ribonucleoproteins (snRNPs), small nuclear RNAs (snRNAs)
- Functional and evolutionary importance of introns

### **Translation (BIO)**

- Roles of mRNA, tRNA, rRNA
- Role and structure of ribosomes
- Initiation, termination co-factors
- Post-translational modification of proteins

### **Eukaryotic Chromosome Organization (BIO)**

- Chromosomal proteins
- Single copy vs. repetitive DNA
- Supercoiling
- Heterochromatin vs. euchromatin
- Telomeres, centromeres

### **Control of Gene Expression in Prokaryotes (BIO)**

- Operon Concept, Jacob–Monod Model

- Gene repression in bacteria
- Positive control in bacteria

### **Control of Gene Expression in Eukaryotes (BIO)**

- Transcriptional regulation
- DNA binding proteins, transcription factors
- Gene amplification and duplication
- Post-transcriptional control, basic concept of splicing (introns, exons)
- Cancer as a failure of normal cellular controls, oncogenes, tumor suppressor genes
- Regulation of chromatin structure
- DNA methylation
- Role of non-coding RNAs

### **Recombinant DNA and Biotechnology (BIO)**

- Gene cloning
- Restriction enzymes
- DNA libraries
- Generation of cDNA
- Hybridization
- Expressing cloned genes
- Polymerase Chain Reaction
- Gel Electrophoresis and Southern Blotting
- DNA sequencing
- Analyzing gene expression
- Determining gene function
- Stem cells
- Practical applications of DNA technology: medical applications, human gene therapy, pharmaceuticals, forensic evidence, environmental cleanup, agriculture
- Safety and ethics of DNA technology

***Content Category 1C: Transmission of heritable information from generation to generation and the processes that increase genetic diversity***

The information necessary to direct life functions is contained within discrete nucleotide sequences transmitted from generation to generation by mechanisms that, by nature of their various processes, provide the raw materials for evolution by increasing genetic diversity. Specific sequences of deoxyribonucleic acids store and transfer the heritable information necessary for the continuation of life from one generation to the next. These sequences, called *genes* — being part of longer DNA molecules — are organized, along with various proteins, into biomolecular assemblies called *chromosomes*.

Chromosomes pass from parents to offspring in sexually-reproducing organisms. The processes of *meiosis* and *fertilization* maintain a species' chromosome count during the sexual life cycle. Because parents pass on discrete heritable units that retain their separate identities in offspring, the laws of probability can be used to predict the outcome of some, but not all, genetic crosses.

The behavior of chromosomes during meiosis and fertilization is responsible for most of the genetic variation that arises each generation. Mechanisms that contribute to this genetic variation include independent assortment of chromosomes, crossing over, and random fertilization. Other mechanisms, such as mutation, random genetic drift, bottlenecks, and immigration, exist with the potential to affect the genetic diversity of individuals and populations. Collectively, the genetic diversity that results from these processes provides the raw material for evolution by natural selection.

The content in this category covers the mechanisms by which heritable information is transmitted from generation to generation, and the evolutionary processes that generate and act upon genetic variation.

The topics and subtopics in this category are the following:

**Evidence that DNA is Genetic Material (BIO)**

**Mendelian Concepts (BIO)**

- Phenotype and genotype
- Gene
- Locus
- Allele: single and multiple
- Homozygosity and heterozygosity
- Wild-type
- Recessiveness
- Complete dominance
- Co-dominance
- Incomplete dominance, leakage, penetrance, expressivity
- Hybridization: viability
- Gene pool

**Meiosis and Other Factors Affecting Genetic Variability (BIO)**

- Significance of meiosis

- Important differences between meiosis and mitosis
- Segregation of genes
  - Independent assortment
  - Linkage
  - Recombination
    - Single crossovers
    - Double crossovers
    - Synaptonemal complex
    - Tetrad
  - Sex-linked characteristics
  - Very few genes on Y chromosome
  - Sex determination
  - Cytoplasmic/extranuclear inheritance
- Mutation
  - General concept of mutation — error in DNA sequence
  - Types of mutations: random, translation error, transcription error, base substitution, inversion, addition, deletion, translocation, mispairing
  - Advantageous vs. deleterious mutation
  - Inborn errors of metabolism
  - Relationship of mutagens to carcinogens
- Genetic drift
- Synapsis or crossing-over mechanism for increasing genetic diversity

### **Analytic Methods (BIO)**

- Hardy–Weinberg Principle
- Testcross (Backcross; concepts of parental, F1, and F2 generations)
- Gene mapping: crossover frequencies
- Biometry: statistical methods

### **Evolution (BIO)**

- Natural selection
  - Fitness concept
  - Selection by differential reproduction
  - Concepts of natural and group selection
  - Evolutionary success as increase in percent representation in the gene pool of the next generation
- Speciation
  - Polymorphism
  - Adaptation and specialization
  - Inbreeding
  - Outbreeding
  - Bottlenecks
- Evolutionary time as measured by gradual random changes in genome



### ***Content Category 1D: Principles of bioenergetics and fuel molecule metabolism***

Living things harness energy from fuel molecules in a controlled manner in order to sustain all of the processes responsible for maintaining life. Cell maintenance and growth is energetically costly. Cells harness the energy stored in fuel molecules, such as carbohydrates and fatty acids, and convert it into smaller units of chemical potential known as *adenosine triphosphate* (ATP).

The hydrolysis of ATP provides a ready source of energy for cells that can be coupled to other chemical processes in order to make them thermodynamically favorable. Fuel molecule mobilization, transport, and storage are regulated according to the needs of the organism.

The content in this category covers the principles of bioenergetics and fuel molecule catabolism. Details of oxidative phosphorylation including the role of chemiosmotic coupling and biological electron transfer reactions are covered, as are the general features of fatty acid and glucose metabolism. Additionally, regulation of these metabolic pathways, fuel molecule mobilization, transport, and storage are covered. The topics and subtopics in this category are the following:

#### **Principles of Bioenergetics (BC, GC)**

- Bioenergetics/thermodynamics
  - Free energy/ $K_{eq}$ 
    - Equilibrium constant
    - Relationship of the equilibrium constant and  $\Delta G^\circ$
  - Concentration
    - Le Châtelier's Principle
  - Endothermic/exothermic reactions
  - Free energy:  $G$
  - Spontaneous reactions and  $\Delta G^\circ$
- Phosphoryl group transfers and ATP
  - ATP hydrolysis  $\Delta G \ll 0$
  - ATP group transfers
- Biological oxidation-reduction
  - Half-reactions
  - Soluble electron carriers
  - Flavoproteins

#### **Carbohydrates (BC, OC)**

- Description
  - Nomenclature and classification, common names
  - Absolute configuration
  - Cyclic structure and conformations of hexoses
  - Epimers and anomers
- Hydrolysis of the glycoside linkage
- Monosaccharides
- Disaccharides
- Polysaccharides

### **Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway (BIO, BC)**

- Glycolysis (aerobic), substrates and products
  - Feeder pathways: glycogen, starch metabolism
- Fermentation (anaerobic glycolysis)
- Gluconeogenesis (BC)
- Pentose phosphate pathway (BC)
- Net molecular and energetic results of respiration processes

### **Principles of Metabolic Regulation (BC)**

- Regulation of metabolic pathways (BIO, BC)
  - Maintenance of a dynamic steady state
- Regulation of glycolysis and gluconeogenesis
- Metabolism of glycogen
- Regulation of glycogen synthesis and breakdown
  - Allosteric and hormonal control
- Analysis of metabolic control

### **Citric Acid Cycle (BIO, BC)**

- Acetyl-CoA production (BC)
- Reactions of the cycle, substrates and products
- Regulation of the cycle
- Net molecular and energetic results of respiration processes

### **Metabolism of Fatty Acids and Proteins (BIO, BC)**

- Description of fatty acids (BC)
- Digestion, mobilization, and transport of fats
- Oxidation of fatty acids
  - Saturated fats
  - Unsaturated fats
- Ketone bodies (BC)
- Anabolism of fats (BIO)
- Non-template synthesis: biosynthesis of lipids and polysaccharides (BIO)
- Metabolism of proteins (BIO)

### **Oxidative Phosphorylation (BIO, BC)**

- Electron transport chain and oxidative phosphorylation, substrates and products, general features of the pathway
- Electron transfer in mitochondria
  - NADH, NADPH
  - Flavoproteins
  - Cytochromes
- ATP synthase, chemiosmotic coupling
  - Proton motive force
- Net molecular and energetic results of respiration processes

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- Regulation of oxidative phosphorylation
- Mitochondria, apoptosis, oxidative stress (BC)

**Hormonal Regulation and Integration of Metabolism (BC)**

- Higher level integration of hormone structure and function
- Tissue specific metabolism
- Hormonal regulation of fuel metabolism
- Obesity and regulation of body mass

## *Biological and Biochemical Foundations of Living Systems*

### **Foundational Concept 2**

Highly-organized assemblies of molecules, cells, and organs interact to carry out the functions of living organisms.

Cells are the basic unit of structure in all living things. Mechanisms of cell division provide not only for the growth and maintenance of organisms, but also for the continuation of the species through asexual and sexual reproduction. The unique micro-environment to which a cell is exposed during development and division determines the fate of the cell by impacting gene expression and ultimately the cell's collection and distribution of macromolecules, and its arrangement of subcellular organelles.

In multicellular organisms, the processes necessary to maintain life are executed by groups of cells that are organized into specialized structures with specialized functions — both of which result from the unique properties of the cells' component molecules.

#### **Content Categories**

- *Category 2A* focuses on the assemblies of molecules, cells, and groups of cells within single cellular and multicellular organisms that function to execute the processes necessary to maintain life.
- *Category 2B* focuses on the structure, growth, physiology, and genetics of prokaryotes, and the structure and life cycles of viruses.
- *Category 2C* focuses on the processes of cell and nuclear division, and the mechanisms governing cell differentiation and specialization.

With these building blocks, medical students will be prepared to learn about the morphological and biochemical events that occur when somatic or germ cells divide, the mechanisms that regulate cell division and cell death, and the characteristics that distinguish normal from abnormal growth and development. These building blocks also prepare them to learn about the micro- and macroscopic structures of cells, tissues, and organs that lead to their unique and integrated functions, and how perturbations contribute to disease.

***Category 2A: Assemblies of molecules, cells, and groups of cells within single cellular and multicellular organisms***

The processes necessary to maintain life are executed by assemblies of molecules, cells, and groups of cells, all of which are organized into highly-specific structures as determined by the unique properties of their component molecules. The processes necessary to maintain life require that cells create and maintain internal environments within the cytoplasm and within certain organelles that are different from their external environments.

Cell membranes separate the internal environment of the cell from the external environment. The specialized structure of the membrane, as described in the fluid mosaic model, allows the cell to be selectively permeable and dynamic, with homeostasis maintained by the constant movement of molecules across the membranes through a combination of active and passive processes driven by several forces, including electrochemical gradients.

Eukaryotic cells also maintain internal membranes that partition the cell into specialized regions. These internal membranes facilitate cellular processes by minimizing conflicting interactions and increasing surface area where chemical reactions can occur. Membrane-bound organelles localize different processes or enzymatic reactions in time and space.

Through interactions between proteins bound to the membranes of adjacent cells, or between membrane-bound proteins and elements of the extracellular matrix, cells of multicellular organisms organize into tissues, organs, and organ systems. Certain membrane-associated proteins also play key roles in providing identification of tissues or recent events in the cell's history for purposes of recognition of "self" versus foreign molecules.

The content in this category covers the composition, structure, and function of cell membranes; the structure and function of the membrane-bound organelles of eukaryotic cells; and the structure and function of the major cytoskeletal elements. It covers the energetics of and mechanisms by which molecules, or groups of molecules, move across cell membranes. It also covers how cell-cell junctions and the extracellular matrix interact to form tissues with specialized functions. Epithelial tissue and connective tissue are covered in this category. The topics and subtopics in this category are the following:

**Plasma Membrane (BIO, BC)**

- General function in cell containment
- Composition of membranes
  - Lipid components (BIO, BC, OC)
    - Phospholipids (and phosphatids)
    - Steroids
    - Waxes
  - Protein components
  - Fluid mosaic model
- Membrane dynamics
- Solute transport across membranes
  - Thermodynamic considerations

- Osmosis
  - Colligative properties; osmotic pressure (GC)
- Passive transport
- Active transport
  - Sodium/potassium pump
- Membrane channels
- Membrane potential
- Membrane receptors
- Exocytosis and endocytosis
- Intercellular junctions (BIO)
  - Gap junctions
  - Tight junctions
  - Desmosomes

### **Membrane-Bound Organelles and Defining Characteristics of Eukaryotic Cells (BIO)**

- Defining characteristics of eukaryotic cells: membrane bound nucleus, presence of organelles, mitotic division
- Nucleus
  - Compartmentalization, storage of genetic information
  - Nucleolus: location and function
  - Nuclear envelope, nuclear pores
- Mitochondria
  - Site of ATP production
  - Inner and outer membrane structure (BIO, BC)
  - Self-replication
- Lysosomes: membrane-bound vesicles containing hydrolytic enzymes
- Endoplasmic reticulum
  - Rough and smooth components
  - Rough endoplasmic reticulum site of ribosomes
  - Double membrane structure
  - Role in membrane biosynthesis
  - Role in biosynthesis of secreted proteins
- Golgi apparatus: general structure and role in packaging and secretion
- Peroxisomes: organelles that collect peroxides

### **Cytoskeleton (BIO)**

- General function in cell support and movement
- Microfilaments: composition and role in cleavage and contractility
- Microtubules: composition and role in support and transport
- Intermediate filaments, role in support
- Composition and function of cilia and flagella
- Centrioles, microtubule organizing centers

### **Tissues Formed From Eukaryotic Cells (BIO)**

- Epithelial cells

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- Connective tissue cells

***Content Category 2B: The structure, growth, physiology, and genetics of prokaryotes and viruses***

The highly-organized assembly of molecules that is the cell represents the fundamental unit of structure, function, and organization in all living organisms. In the hierarchy of biological organization, the cell is the simplest collection of matter capable of carrying out the processes that distinguish living organisms. As such, cells have the ability to undergo metabolism; maintain homeostasis, including ionic gradients; the capacity to grow; move in response to their local environments; respond to stimuli; reproduce; and adapt to their environment in successive generations.

Life at cellular levels arises from structural order and its dynamic modulation. It does so in response to signals, thereby reflecting properties that result from individual and interactive features of molecular assemblies, their compartmentalization, and their interaction with environmental signals at many spatial and temporal scales.

The content in this category covers the classification, structure, growth, physiology, and genetics of prokaryotes, and the characteristics that distinguish them from eukaryotes. Viruses are also covered here. The topics and subtopics in this category are the following:

**Cell Theory (BIO)**

- History and development
- Impact on biology

**Classification and Structure of Prokaryotic Cells (BIO)**

- Prokaryotic domains
  - Archaea
  - Bacteria
- Major classifications of bacteria by shape
  - Bacilli (rod-shaped)
  - Spirilli (spiral-shaped)
  - Cocci (spherical)
- Lack of nuclear membrane and mitotic apparatus
- Lack of typical eukaryotic organelles
- Presence of cell wall in bacteria
- Flagellar propulsion, mechanism

**Growth and Physiology of Prokaryotic Cells (BIO)**

- Reproduction by fission
- High degree of genetic adaptability, acquisition of antibiotic resistance
- Exponential growth
- Existence of anaerobic and aerobic variants
- Parasitic and symbiotic
- Chemotaxis

**Genetics of Prokaryotic Cells (BIO)**

- Existence of plasmids, extragenomic DNA



- Transformation: incorporation into bacterial genome of DNA fragments from external medium
- Conjugation
- Transposons (also present in eukaryotic cells)

### **Virus Structure (BIO)**

- General structural characteristics (nucleic acid and protein, enveloped and nonenveloped)
- Lack organelles and nucleus
- Structural aspects of typical bacteriophage
- Genomic content — RNA or DNA
- Size relative to bacteria and eukaryotic cells

### **Viral Life Cycle (BIO)**

- Self-replicating biological units that must reproduce within specific host cell
- Generalized phage and animal virus life cycles
  - Attachment to host, penetration of cell membrane or cell wall, and entry of viral genetic material
  - Use of host synthetic mechanism to replicate viral components
  - Self-assembly and release of new viral particles
- Transduction: transfer of genetic material by viruses
- Retrovirus life cycle: integration into host DNA, reverse transcriptase, HIV
- Prions and viroids: subviral particles

## ***Content Category 2C: Processes of cell division, differentiation, and specialization***

The ability of organisms to reproduce their own kind is the characteristic that best distinguishes living things. In sexually reproducing organisms, the continuity of life is based on the processes of cell division and meiosis.

The process of cell division is an integral part of the cell cycle. The progress of eukaryotic cells through the cell cycle is regulated by a complex molecular control system. Malfunctions in this system can result in unabated cellular division, and ultimately the development of cancer.

In the embryonic development of multicellular organisms, a fertilized egg gives rise to cells that differentiate into many different types of cells, each with a different structure, corresponding function, and location within the organism. During development, spatial–temporal gradients in the interactions between gene expression and various stimuli result in the structural and functional divergence of cells into specialized structure, organs, and tissues. The interaction of stimuli and genes is also explained by the progression of stem cells to terminal cells.

The content in this category covers the cell cycle; the causes, genetics, and basic properties of cancer; the processes of meiosis and gametogenesis; and the mechanisms governing cell specialization and differentiation. The topics and subtopics in this category are the following:

### **Mitosis (BIO)**

- Mitotic process: prophase, metaphase, anaphase, telophase, interphase
- Mitotic structures
  - Centrioles, asters, spindles
  - Chromatids, centromeres, kinetochores
  - Nuclear membrane breakdown and reorganization
  - Mechanisms of chromosome movement
- Phases of cell cycle: G<sub>0</sub>, G<sub>1</sub>, S, G<sub>2</sub>, M
- Growth arrest
- Control of cell cycle
- Loss of cell cycle controls in cancer cells

### **Biosignalling (BC)**

- Oncogenes, apoptosis

### **Reproductive System (BIO)**

- Gametogenesis by meiosis
- Ovum and sperm
  - Differences in formation
  - Differences in morphology
  - Relative contribution to next generation
- Reproductive sequence: fertilization; implantation; development; birth

### **Embryogenesis (BIO)**

- Stages of early development (order and general features of each)

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- Fertilization
- Cleavage
- Blastula formation
- Gastrulation
  - First cell movements
  - Formation of primary germ layers (endoderm, mesoderm, ectoderm)
- Neurulation
- Major structures arising out of primary germ layers
- Neural crest
- Environment–gene interaction in development

**Mechanisms of Development (BIO)**

- Cell specialization
  - Determination
  - Differentiation
  - Tissue types
- Cell–cell communication in development
- Cell migration
- Pluripotency: stem cells
- Gene regulation in development
- Programmed cell death
- Existence of regenerative capacity in various species
- Senescence and aging

## *Biological and Biochemical Foundations of Living Systems*

### **Foundational Concept 3**

Complex systems of tissues and organs sense the internal and external environments of multicellular organisms, and through integrated functioning, maintain a stable internal environment within an ever-changing external environment.

As a result of the integration of a number of highly specialized organ systems, complex living things are able to maintain homeostasis while adapting to a constantly changing environment and participating in growth and reproduction. The interactions of these organ systems involves complex regulatory mechanisms that help maintain a dynamic and healthy equilibrium, regardless of their current state and environment.

#### **Content Categories**

- *Category 3A* focuses on the structure and functions of the nervous and endocrine systems, and the ways in which the systems work together to coordinate the responses of other body systems to both external and internal stimuli.
- *Category 3B* focuses on the structure and functions of the organ systems — circulatory, respiratory, digestive, immune, lymphatic, muscular, skeletal, and reproductive — and the ways these systems interact to fulfill their concerted roles in the maintenance and continuance of the living organism.

With these building blocks, medical students will be prepared to learn how the coordinated interactions of organ systems explain how the human body functions in health and in disease. They will also be prepared to learn how the principles of feedback control explain homeostatic and reproductive systems' maintenance of the internal environment, how perturbations in these systems may result in disease, and how homeostasis can be changed by disease.

***Content Category 3A: Structure and functions of the nervous and endocrine systems and ways in which these systems coordinate the organ systems***

The nervous and endocrine systems work together to detect external and internal signals, transmit and integrate information, and maintain homeostasis. They do all of this by producing appropriate responses to internal and external cues and stressors. The integration of these systems both with one another, and with the other organ systems, ultimately results in the successful and adaptive behaviors that allow for the propagation of the species.

Animals have evolved a nervous system that senses and processes internal and external information that is used to facilitate and enhance survival, growth, and reproduction. The nervous system interfaces with sensory and internal body systems to coordinate physiological and behavioral responses ranging from simple movements and small metabolic changes to long-distance migrations and social interactions. The physiological processes for nerve signal generation and propagation involve specialized membranes with associated proteins that respond to ligands and/or electrical field changes, signaling molecules and, by extension, the establishment and replenishment of ionic electrochemical gradients requiring ATP.

The endocrine system of animals has evolved to produce chemical signals that function internally to regulate stress responses, reproduction, development, energy metabolism, growth, and various individual and interactive behaviors. The integrated contributions of the nervous and endocrine systems to bodily functions are exemplified by the process whereby the signaling of neurons regulates hormone release, and by the targeting of membrane or nuclear receptors on neurons by circulating hormones.

The content in this category covers the structure, function, and basic aspects of nervous and endocrine systems, and their integration. The structure and function of nerve cells is also included in this category. The topics and subtopics in this category are the following:

**Nervous System: Structure and Function (BIO)**

- Major Functions
  - High level control and integration of body systems
  - Adaptive capability to external influences
- Organization of vertebrate nervous system
- Sensor and effector neurons
- Sympathetic and parasympathetic nervous systems: antagonistic control
- Reflexes
  - Feedback loop, reflex arc
  - Role of spinal cord and supraspinal circuits
- Integration with endocrine system: feedback control

**Nerve Cell (BIO)**

- Cell body: site of nucleus, organelles
- Dendrites: branched extensions of cell body
- Axon: structure and function
- Myelin sheath, Schwann cells, insulation of axon
- Nodes of Ranvier: propagation of nerve impulse along axon
- Synapse: site of impulse propagation between cells

- Synaptic activity: transmitter molecules
- Resting potential: electrochemical gradient
- Action potential
  - Threshold, all-or-none
  - Sodium/potassium pump
- Excitatory and inhibitory nerve fibers: summation, frequency of firing
- Glial cells, neuroglia

### **Electrochemistry (GC)**

- Concentration cell: direction of electron flow, Nernst equation

### **Biosignalling (BC)**

- Gated ion channels
  - Voltage gated
  - Ligand gated
- Receptor enzymes
- G protein-coupled receptors

### **Lipids (BC, OC)**

- Description; structure
  - Steroids
  - Terpenes and terpenoids

### **Endocrine System: Hormones and Their Sources (BIO)**

- Function of endocrine system: specific chemical control at cell, tissue, and organ level
- Definitions of endocrine gland, hormone
- Major endocrine glands: names, locations, products
- Major types of hormones
- Neuroendocrinology — relation between neurons and hormonal systems

### **Endocrine System: Mechanisms of Hormone Action (BIO)**

- Cellular mechanisms of hormone action
- Transport of hormones: blood supply
- Specificity of hormones: target tissue
- Integration with nervous system: feedback control
- Regulation by second messengers

### ***Category 3B: Structure and integrative functions of the main organ systems***

Animals use a number of highly-organized and integrated organ systems to carry out the necessary functions associated with maintaining life processes. Within the body, no organ system is an island. Interactions and coordination between organ systems allow organisms to engage in the processes necessary to sustain life. For example, the organs and structures of the circulatory system carry out a number of functions, such as transporting:

- nutrients absorbed in the digestive system;
- gases absorbed from the respiratory system and muscle tissue;
- hormones secreted from the endocrine system; and
- blood cells produced in bone marrow to and from cells in the body to help fight disease.

The content in this category covers the structure and function of the major organ systems of the body including the respiratory, circulatory, lymphatic, immune, digestive, excretory, reproductive, muscle, skeletal, and skin systems. Also covered in this category is the integration of these systems and their control and coordination by the endocrine and nervous systems. The topics and subtopics in this category are the following:

#### **Respiratory System (BIO)**

- General function
  - Gas exchange, thermoregulation
  - Protection against disease: particulate matter
- Structure of lungs and alveoli
- Breathing mechanisms
  - Diaphragm, rib cage, differential pressure
  - Resiliency and surface tension effects
- Thermoregulation: nasal and tracheal capillary beds; evaporation, panting
- Particulate filtration: nasal hairs, mucus/cilia system in lungs
- Alveolar gas exchange
  - Diffusion, differential partial pressure
  - Henry's Law (GC)
- pH control
- Regulation by nervous control
  - CO<sub>2</sub> sensitivity

#### **Circulatory System (BIO)**

- Functions: circulation of oxygen, nutrients, hormones, ions and fluids, removal of metabolic waste
- Role in thermoregulation
- Four-chambered heart: structure and function
- Endothelial cells
- Systolic and diastolic pressure
- Pulmonary and systemic circulation

- Arterial and venous systems (arteries, arterioles, venules, veins)
  - Structural and functional differences
  - Pressure and flow characteristics
- Capillary beds
  - Mechanisms of gas and solute exchange
  - Mechanism of heat exchange
  - Source of peripheral resistance
- Composition of blood
  - Plasma, chemicals, blood cells
  - Erythrocyte production and destruction; spleen, bone marrow
  - Regulation of plasma volume
- Coagulation, clotting mechanisms
- Oxygen transport by blood
  - Hemoglobin, hematocrit
  - Oxygen content
  - Oxygen affinity
- Carbon dioxide transport and level in blood
- Nervous and endocrine control

### **Lymphatic System (BIO)**

- Structure of lymphatic system
- Major functions
  - Equalization of fluid distribution
  - Transport of proteins and large glycerides
  - Production of lymphocytes involved in immune reactions
  - Return of materials to the blood

### **Immune System (BIO)**

- Innate (non-specific) vs. adaptive (specific) immunity
- Adaptive immune system cells
  - T-lymphocytes
  - B-lymphocytes
- Innate immune system cells
  - Macrophages
  - Phagocytes
- Tissues
  - Bone marrow
  - Spleen
  - Thymus
  - Lymph nodes
- Concept of antigen and antibody
- Antigen presentation
- Clonal selection
- Antigen-antibody recognition
- Structure of antibody molecule



- Recognition of self vs. non-self, autoimmune diseases
- Major histocompatibility complex

### Digestive System (BIO)

- Ingestion
  - Saliva as lubrication and source of enzymes
  - Ingestion; esophagus, transport function
- Stomach
  - Storage and churning of food
  - Low pH, gastric juice, mucal protection against self-destruction
  - Production of digestive enzymes, site of digestion
  - Structure (gross)
- Liver
  - Structural relationship of liver within gastrointestinal system
  - Production of bile
  - Role in blood glucose regulation, detoxification
- Bile
  - Storage in gall bladder
  - Function
- Pancreas
  - Production of enzymes
  - Transport of enzymes to small intestine
- Small Intestine
  - Absorption of food molecules and water
  - Function and structure of villi
  - Production of enzymes, site of digestion
  - Neutralization of stomach acid
  - Structure (anatomic subdivisions)
- Large Intestine
  - Absorption of water
  - Bacterial flora
  - Structure (gross)
- Rectum: storage and elimination of waste, feces
- Muscular control
  - Peristalsis
- Endocrine control
  - Hormones
  - Target tissues
- Nervous control: the enteric nervous system

### Excretory System (BIO)

- Roles in homeostasis
  - Blood pressure
  - Osmoregulation

- Acid–base balance
- Removal of soluble nitrogenous waste
- Kidney structure
  - Cortex
  - Medulla
- Nephron structure
  - Glomerulus
  - Bowman's capsule
  - Proximal tubule
  - Loop of Henle
  - Distal tubule
  - Collecting duct
- Formation of urine
  - Glomerular filtration
  - Secretion and reabsorption of solutes
  - Concentration of urine
  - Counter-current multiplier mechanism
- Storage and elimination: ureter, bladder, urethra
- Osmoregulation: capillary reabsorption of H<sub>2</sub>O, amino acids, glucose, ions
- Muscular control: sphincter muscle

### Reproductive System (BIO)

- Male and female reproductive structures and their functions
  - Gonads
  - Genitalia
  - Differences between male and female structures
- Hormonal control of reproduction
  - Male and female sexual development
  - Female reproductive cycle
  - Pregnancy, parturition, lactation
  - Integration with nervous control

### Muscle System (BIO)

- Important functions
  - Support: mobility
  - Peripheral circulatory assistance
  - Thermoregulation (shivering reflex)
- Structure of three basic muscle types: striated, smooth, cardiac
- Muscle structure and control of contraction
  - T-tubule system
  - Contractile apparatus
  - Sarcoplasmic reticulum
  - Fiber type
  - Contractile velocity of different muscle types
- Regulation of cardiac muscle contraction

- Oxygen debt: fatigue
- Nervous control
  - Motor neurons
  - Neuromuscular junction, motor end plates
  - Sympathetic and parasympathetic innervation
  - Voluntary and involuntary muscles

### Specialized Cell - Muscle Cell (BIO)

- Structural characteristics of striated, smooth, and cardiac muscle
- Abundant mitochondria in red muscle cells: ATP source
- Organization of contractile elements: actin and myosin filaments, crossbridges, sliding filament model
- Sarcomeres: “I” and “A” bands, “M” and “Z” lines, “H” zone
- Presence of troponin and tropomyosin
- Calcium regulation of contraction

### Skeletal System (BIO)

- Functions
  - Structural rigidity and support
  - Calcium storage
  - Physical protection
- Skeletal structure
  - Specialization of bone types, structures
  - Joint structures
  - Endoskeleton vs. exoskeleton
- Bone structure
  - Calcium/protein matrix
  - Cellular composition of bone
- Cartilage: structure and function
- Ligaments, tendons
- Endocrine control

### Skin System (BIO)

- Structure
  - Layer differentiation, cell types
  - Relative impermeability to water
- Functions in homeostasis and osmoregulation
- Functions in thermoregulation
  - Hair, erectile musculature
  - Fat layer for insulation
  - Sweat glands, location in dermis
  - Vasoconstriction and vasodilation in surface capillaries
- Physical protection
  - Nails, calluses, hair
  - Protection against abrasion, disease organisms

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- Hormonal control: sweating, vasodilation, and vasoconstriction