

## What will the Chemical and Physical Foundations of Biological Systems section test?

The Chemical and Physical Foundations of Biological Systems section asks you to solve problems by combining your knowledge of chemical and physical foundational concepts with your scientific inquiry and reasoning skills. This section tests your understanding of the mechanical, physical, and biochemical functions of human tissues, organs, and organ systems. It also tests your knowledge of the basic chemical and physical principles that underlie the mechanisms operating in the human body and your ability to reason about and apply your understanding of these basic chemical and physical principles to living systems.

This section is designed to:

- test introductory-level biology, organic and inorganic chemistry, and physics concepts;
- test biochemistry concepts at the level taught in many colleges and universities in first-semester biochemistry courses;
- test molecular biology topics at the level taught in many colleges and universities in introductory biology sequences and first-semester biochemistry courses;
- test basic research methods and statistics concepts described by many baccalaureate faculty as important to success in introductory science courses; and
- require you to demonstrate your scientific inquiry and reasoning, research methods, and statistics skills as applied to the natural sciences.

Test Section	Number of Questions	Time
Chemical and Physical Foundations of Biological Systems	59 (note that questions are a combination of passage-based and discrete questions)	95 minutes

## Scientific Inquiry and Reasoning Skills

As a reminder, the scientific inquiry and reasoning skills that you will be asked to demonstrate on this section of the exam are:

### Knowledge of Scientific Concepts and Principles

- Demonstrating understanding of scientific concepts and principles
- Identifying the relationships between closely-related concepts

### Scientific Reasoning and Problem Solving

- Reasoning about scientific principles, theories, and models
- Analyzing and evaluating scientific explanations and predictions

### Reasoning about the Design and Execution of Research

- Demonstrating understanding of important components of scientific research
- Reasoning about ethical issues in research

### Data-Based and Statistical Reasoning

- Interpreting patterns in data presented in tables, figures, and graphs
- Reasoning about data and drawing conclusions from them

**General Mathematical Concepts and Techniques**

It's important for you to know that questions on the natural, behavioral, and social sciences sections will ask you to use certain mathematical concepts and techniques. As the descriptions of the scientific inquiry and reasoning skills suggest, some questions will ask you to analyze and manipulate scientific data to show that you can

- Recognize and interpret linear, semilog, and log-log scales and calculate slopes from data found in figures, graphs, and tables
- Demonstrate a general understanding of significant digits and the use of reasonable numerical estimates in performing measurements and calculations
- Use metric units, including converting units within the metric system and between metric and English units (conversion factors will be provided when needed), and dimensional analysis (using units to balance equations)
- Perform arithmetic calculations involving the following: probability, proportion, ratio, percentage, and square-root estimations
- Demonstrate a general understanding (Algebra II-level) of exponentials and logarithms (natural and base 10), scientific notation, and solving simultaneous equations
- Demonstrate a general understanding of the following trigonometric concepts: definitions of basic (sine, cosine, tangent) and inverse ( $\sin^{-1}$ ,  $\cos^{-1}$ ,  $\tan^{-1}$ ) functions; sin and cos values of  $0^\circ$ ,  $90^\circ$ , and  $180^\circ$ ; relationships between the lengths of sides of right triangles containing angles of  $30^\circ$ ,  $45^\circ$ , and  $60^\circ$
- Demonstrate a general understanding of vector addition and subtraction and the right-hand rule (knowledge of dot and cross products is not required)

Note also that an understanding of calculus is *not* required, and a periodic table will be provided during the exam.

## References

During the actual exam, you will have access to the periodic table below while answering questions in this section of the exam.

1 <b>H</b> 1.0																	2 <b>He</b> 4.0
3 <b>Li</b> 6.9	4 <b>Be</b> 9.0											5 <b>B</b> 10.8	6 <b>C</b> 12.0	7 <b>N</b> 14.0	8 <b>O</b> 16.0	9 <b>F</b> 19.0	10 <b>Ne</b> 20.2
11 <b>Na</b> 23.0	12 <b>Mg</b> 24.3											13 <b>Al</b> 27.0	14 <b>Si</b> 28.1	15 <b>P</b> 31.0	16 <b>S</b> 32.1	17 <b>Cl</b> 35.5	18 <b>Ar</b> 39.9
19 <b>K</b> 39.1	20 <b>Ca</b> 40.1	21 <b>Sc</b> 45.0	22 <b>Ti</b> 47.9	23 <b>V</b> 50.9	24 <b>Cr</b> 52.0	25 <b>Mn</b> 54.9	26 <b>Fe</b> 55.8	27 <b>Co</b> 58.9	28 <b>Ni</b> 58.7	29 <b>Cu</b> 63.5	30 <b>Zn</b> 65.4	31 <b>Ga</b> 69.7	32 <b>Ge</b> 72.6	33 <b>As</b> 74.9	34 <b>Se</b> 79.0	35 <b>Br</b> 79.9	36 <b>Kr</b> 83.8
37 <b>Rb</b> 85.5	38 <b>Sr</b> 87.6	39 <b>Y</b> 88.9	40 <b>Zr</b> 91.2	41 <b>Nb</b> 92.9	42 <b>Mo</b> 95.9	43 <b>Tc</b> (98)	44 <b>Ru</b> 101.1	45 <b>Rh</b> 102.9	46 <b>Pd</b> 106.4	47 <b>Ag</b> 107.9	48 <b>Cd</b> 112.4	49 <b>In</b> 114.8	50 <b>Sn</b> 118.7	51 <b>Sb</b> 121.8	52 <b>Te</b> 127.6	53 <b>I</b> 126.9	54 <b>Xe</b> 131.3
55 <b>Cs</b> 132.9	56 <b>Ba</b> 137.3	57 <b>La*</b> 138.9	72 <b>Hf</b> 178.5	73 <b>Ta</b> 180.9	74 <b>W</b> 183.9	75 <b>Re</b> 186.2	76 <b>Os</b> 190.2	77 <b>Ir</b> 192.2	78 <b>Pt</b> 195.1	79 <b>Au</b> 197.0	80 <b>Hg</b> 200.6	81 <b>Tl</b> 204.4	82 <b>Pb</b> 207.2	83 <b>Bi</b> 209.0	84 <b>Po</b> (209)	85 <b>At</b> (210)	86 <b>Rn</b> (222)
87 <b>Fr</b> (223)	88 <b>Ra</b> (226)	89 <b>Ac†</b> (227)	104 <b>Rf</b> (261)	105 <b>Db</b> (262)	106 <b>Sg</b> (266)	107 <b>Bh</b> (264)	108 <b>Hs</b> (277)	109 <b>Mt</b> (268)	110 <b>Ds</b> (281)	111 <b>Rg</b> (280)	112 <b>Cn</b> (285)	113 <b>Uut</b> (284)	114 <b>Fl</b> (289)	115 <b>Uup</b> (288)	116 <b>Lv</b> (293)	117 <b>Uus</b> (294)	118 <b>Uuo</b> (294)

58 <b>Ce</b> 140.1	59 <b>Pr</b> 140.9	60 <b>Nd</b> 144.2	61 <b>Pm</b> (145)	62 <b>Sm</b> 150.4	63 <b>Eu</b> 152.0	64 <b>Gd</b> 157.3	65 <b>Tb</b> 158.9	66 <b>Dy</b> 162.5	67 <b>Ho</b> 164.9	68 <b>Er</b> 167.3	69 <b>Tm</b> 168.9	70 <b>Yb</b> 173.0	71 <b>Lu</b> 175.0
90 <b>Th</b> 232.0	91 <b>Pa</b> (231)	92 <b>U</b> 238.0	93 <b>Np</b> (237)	94 <b>Pu</b> (244)	95 <b>Am</b> (243)	96 <b>Cm</b> (247)	97 <b>Bk</b> (247)	98 <b>Cf</b> (251)	99 <b>Es</b> (252)	100 <b>Fm</b> (257)	101 <b>Md</b> (258)	102 <b>No</b> (259)	103 <b>Lr</b> (260)

## **Chemical and Physical Foundations of Biological Systems Distribution of Questions by Discipline, Foundational Concept, and Scientific Inquiry and Reasoning Skill**

You may wonder how much chemistry you'll see on this section of the MCAT exam, how many questions you'll get about a particular foundational concept, or how the scientific inquiry and reasoning skills will be distributed on your exam. The questions that you see are likely to be distributed in the ways described below. These are the approximate percentages of questions you'll see on a test for each discipline, foundational concept, and scientific inquiry and reasoning skill.\*

### **Discipline:**

- First-semester biochemistry, 25%
- Introductory biology, 5%
- General chemistry, 30%
- Organic chemistry, 15%
- Introductory physics, 25%

### **Foundational Concept:**

- Foundational Concept 4, 40%
- Foundational Concept 5, 60%

### **Scientific Inquiry and Reasoning Skill:**

- Skill 1, 35%
- Skill 2, 45%
- Skill 3, 10%
- Skill 4, 10%

\*These percentages have been approximated to the nearest 5% and will vary from one test to another for a variety of reasons. These reasons include, but are not limited to, controlling for question difficulty, using groups of questions that depend on a single passage, and using unscored field-test questions on each test form.

## Chemical and Physical Foundations of Biological Systems Framework of Foundational Concepts and Content Categories

**Foundational Concept 4:** *Complex living organisms transport materials, sense their environment, process signals, and respond to changes using processes understood in terms of physical principles.*

The content categories for this foundational concept include

- 4A. Translational motion, forces, work, energy, and equilibrium in living systems
- 4B. Importance of fluids for the circulation of blood, gas movement, and gas exchange
- 4C. Electrochemistry and electrical circuits and their elements
- 4D. How light and sound interact with matter
- 4E. Atoms, nuclear decay, electronic structure, and atomic chemical behavior

**Foundational Concept 5:** *The principles that govern chemical interactions and reactions form the basis for a broader understanding of the molecular dynamics of living systems.*

The content categories for this foundational concept include

- 5A. Unique nature of water and its solutions
- 5B. Nature of molecules and intermolecular interactions
- 5C. Separation and purification methods
- 5D. Structure, function, and reactivity of biologically-relevant molecules
- 5E. Principles of chemical thermodynamics and kinetics

## How Foundational Concepts and Content Categories Fit Together

The MCAT exam asks you to solve problems by combining your knowledge of concepts with your scientific inquiry and reasoning skills. Figure 1 illustrates how foundational concepts, content categories, and scientific inquiry and reasoning skills intersect to create test questions.

	Foundational Concept 1			Foundational Concept 2		
	Content Category 1A	Content Category	Content Category	Content Category	Content Category	Content Category
Skill 1						
Skill 2						
Skill 3						
Skill 4						

- Each cell represents the point at which foundational concepts, content categories, and scientific inquiry and reasoning skills cross.
- Test questions are written at the intersections of the knowledge and skills.

## Understanding the Foundational Concepts and Content Categories in the Chemical and Physical Foundations of Biological Systems Outline

The following are detailed explanations of each foundational concept and related content categories tested in this section. As with the Biological and Biochemical Foundations of Living Systems section, lists describing the specific topics and subtopics that define each content category for this section are provided. The same content list is provided to item writers who develop the content of the exam. Here is an excerpt from the content list.

### EXCERPT FROM THE CHEMICAL AND PHYSICAL FOUNDATIONS OF BIOLOGICAL SYSTEMS OUTLINE

Separations and Purifications (OC, BC) ←	Topic
<ul style="list-style-type: none"> <li>▪ Extraction: distribution of solute between two immiscible solvents ← Subtopic</li> <li>▪ Distillation</li> <li>▪ Chromatography: Basic principles involved in separation process               <ul style="list-style-type: none"> <li>○ Column chromatography                   <ul style="list-style-type: none"> <li>▪ Gas-liquid chromatography</li> <li>▪ High pressure liquid chromatography</li> </ul> </li> <li>○ Paper chromatography</li> <li>○ Thin-layer chromatography</li> </ul> </li> <li>▪ Separation and purification of peptides and proteins (BC)               <ul style="list-style-type: none"> <li>○ Electrophoresis</li> <li>○ Quantitative analysis</li> <li>○ Chromatography                   <ul style="list-style-type: none"> <li>▪ Size-exclusion</li> <li>▪ Ion-exchange</li> <li>▪ Affinity</li> </ul> </li> </ul> </li> <li>▪ Racemic mixtures, separation of enantiomers (OC)</li> </ul>	

The abbreviations found in parentheses indicate the course(s) in which undergraduate students at many colleges and universities learn about the topics and associated subtopics. The course abbreviations are

- BC: first semester of biochemistry
- BIO: two-semester sequence of introductory biology
- GC: two-semester sequence of general chemistry
- OC: two-semester sequence of organic chemistry
- PHY: two-semester sequence of introductory physics

In preparing for the MCAT exam, you will be responsible for learning the topics and associated subtopics at the levels at which they are taught at many colleges and universities in the courses listed in parentheses. A small number of subtopics have course abbreviations indicated in parentheses. In those cases, you are responsible only for learning the subtopics as they are taught in the course(s) indicated.



Using the excerpt above as an example:

- You are responsible for learning about the topic Separations and Purifications at the level at which it is taught in a typical two-semester organic chemistry sequence *and* in a typical first-semester biochemistry course.
- You are responsible for learning about the subtopic Separation and purifications of peptides and proteins (and sub-subtopics) *only* at the level at which it is taught in a first-semester biochemistry course.
- You are responsible for learning about the subtopic Racemic mixtures, separation of enantiomers *only* at the level at which it is taught in a two-semester organic chemistry course.

Remember that course content at your school may differ from course content at other colleges and universities. The topics and subtopics described in this chapter may be covered in courses with titles that are different from those listed here. Your pre-health advisor and faculty are important resources for your questions about course content.

## *Chemical and Physical Foundations of Biological Systems*

### **Foundational Concept 4**

Complex living organisms transport materials, sense their environment, process signals, and respond to changes using processes that can be understood in terms of physical principles.

The processes that take place within organisms follow the laws of physics. They can be quantified with equations that model the behavior at a fundamental level. For example, the principles of electromagnetic radiation, and its interactions with matter, can be exploited to generate structural information about molecules or to generate images of the human body. So, too, can atomic structure be used to predict the physical and chemical properties of atoms, including the amount of electromagnetic energy required to cause ionization.

#### **Content Categories**

- *Category 4A* focuses on motion and its causes, and various forms of energy and their interconversions.
- *Category 4B* focuses on the behavior of fluids, which is relevant to the functioning of the pulmonary and circulatory systems.
- *Category 4C* emphasizes the nature of electrical currents and voltages; how energy can be converted into electrical forms that can be used to perform chemical transformations or work; and how electrical impulses can be transmitted over long distances in the nervous system.
- *Category 4D* focuses on the properties of light and sound; how the interactions of light and sound with matter can be used by an organism to sense its environment; and how these interactions can also be used to generate structural information or images.
- *Category 4E* focuses on sub-atomic particles, the atomic nucleus, nuclear radiation, the structure of the atom, and how the configuration of any particular atom can be used to predict its physical and chemical properties.

With these building blocks, medical students will be able to utilize core principles of physics to learn about the physiological functions of the respiratory, cardiovascular, and neurological systems in health and disease.

### ***Content Category 4A: Translational motion, forces, work, energy, and equilibrium in living systems***

The motion of any object can be described in terms of displacement, velocity, and acceleration. Objects accelerate when subjected to external forces and are at equilibrium when the net force and the net torque acting upon them are zero. Many aspects of motion can be calculated with the knowledge that energy is conserved, even though it may be converted into different forms. In a living system, the energy for motion comes from the metabolism of fuel molecules, but the energetic requirements remain subject to the same physical principles.

The content in this category covers several physics topics relevant to living systems including translational motion, forces, work, energy, and equilibrium. The topics and subtopics in this category are the following:

#### **Translational Motion (PHY)**

- Units and dimensions
- Vectors, components
- Vector addition
- Speed, velocity (average and instantaneous)
- Acceleration

#### **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.

#### **Force (PHY)**

- Newton's First Law, inertia
- Newton's Second Law ( $F = ma$ )
- Newton's Third Law, forces equal and opposite
- Friction, static and kinetic
- Center of mass

#### **Equilibrium (PHY)**

- Vector analysis of forces acting on a point object
- Torques, lever arms

#### **Work (PHY)**

- Work done by a constant force:  $W = Fd \cos\theta$
- Mechanical advantage
- Work Kinetic Energy Theorem
- Conservative forces

#### **Energy of Point Object Systems (PHY)**

- Kinetic Energy:  $KE = \frac{1}{2}mv^2$ ; units
- Potential Energy
  - $PE = mgh$  (gravitational, local)
  - $PE = \frac{1}{2}kx^2$  (spring)
- Conservation of energy
- Power, units

### **Periodic Motion (PHY)**

- Amplitude, frequency, phase
- Transverse and longitudinal waves: wavelength and propagation speed

### ***Content Category 4B: Importance of fluids for the circulation of blood, gas movement, and gas exchange***

Fluids are featured in several physiologically important processes, including the circulation of blood, gas movement into and out of the lungs, and gas exchange with the blood. The energetic requirements of fluid dynamics can be modeled using physical equations. A thorough understanding of fluids is necessary to understand the origins of numerous forms of disease.

The content in this category covers hydrostatic pressure, fluid flow rates, viscosity, the Kinetic Molecular Theory of Gases, and the Ideal Gas Law. The topics and subtopics in this category are the following:

#### **Fluids (PHY)**

- Density, specific gravity
- Buoyancy, Archimedes' Principle
- Hydrostatic pressure
  - Pascal's Law
  - Hydrostatic pressure;  $P = \rho gh$  (pressure vs. depth)
- Viscosity: Poiseuille Flow
- Continuity equation ( $A \cdot v = \text{constant}$ )
- Concept of turbulence at high velocities
- Surface tension
- Bernoulli's equation
- Venturi effect, pitot tube

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

- Arterial and venous systems; pressure and flow characteristics

#### **Gas Phase (GC, PHY)**

- Absolute temperature, (K) Kelvin Scale
- Pressure, simple mercury barometer
- Molar volume at 0°C and 1 atm = 22.4 L/mol
- Ideal gas
  - Definition
  - Ideal Gas Law:  $PV = nRT$
  - Boyle's Law:  $PV = \text{constant}$
  - Charles' Law:  $V/T = \text{constant}$
  - Avogadro's Law:  $V/n = \text{constant}$
- Kinetic Molecular Theory of Gases
  - Heat capacity at constant volume and at constant pressure (PHY)
  - Boltzmann's Constant (PHY)
- Deviation of real gas behavior from Ideal Gas Law
  - Qualitative
  - Quantitative (Van der Waals' Equation)
- Partial pressure, mole fraction
- Dalton's Law relating partial pressure to composition

### ***Content Category 4C: Electrochemistry and electrical circuits and their elements***

Charged particles can be set in motion by the action of an applied electrical field, and can be used to transmit energy or information over long distances. The energy released during certain chemical reactions can be converted to electrical energy, which can be harnessed to perform other reactions or work.

Physiologically, a concentration gradient of charged particles is set up across the cell membrane of neurons at considerable energetic expense. This allows for the rapid transmission of signals using electrical impulses — changes in the electrical voltage across the membrane — under the action of some external stimulus.

The content in this category covers electrical circuit elements, electrical circuits, and electrochemistry. The topics and subtopics in this category are the following:

#### **Electrostatics (PHY)**

- Charge, conductors, charge conservation
- Insulators
- Coulomb's Law
- Electric field **E**
  - Field lines
  - Field due to charge distribution
- Electrostatic energy, electric potential at a point in space

#### **Circuit Elements (PHY)**

- Current  $I = \Delta Q / \Delta t$ , sign conventions, units
- Electromotive force, voltage
- Resistance
  - Ohm's Law:  $I = V/R$
  - Resistors in series
  - Resistors in parallel
  - Resistivity:  $\rho = R \cdot A / L$
- Capacitance
  - Parallel plate capacitor
  - Energy of charged capacitor
  - Capacitors in series
  - Capacitors in parallel
  - Dielectrics
- Conductivity
  - Metallic
  - Electrolytic
- Meters

#### **Magnetism (PHY)**

- Definition of magnetic field **B**
- Motion of charged particles in magnetic fields; Lorentz force

### **Electrochemistry (GC)**

- Electrolytic cell
  - Electrolysis
  - Anode, cathode
  - Electrolyte
  - Faraday's Law relating amount of elements deposited (or gas liberated) at an electrode to current
  - Electron flow; oxidation, and reduction at the electrodes
- Galvanic or Voltaic cells
  - Half-reactions
  - Reduction potentials; cell potential
  - Direction of electron flow
- Concentration cell
- Batteries
  - Electromotive force, Voltage
  - Lead-storage batteries
  - Nickel-cadmium batteries

### **Specialized Cell - Nerve Cell (BIO)**

- Myelin sheath, Schwann cells, insulation of axon
- Nodes of Ranvier: propagation of nerve impulse along axon

### **Content Category 4D: How light and sound interact with matter**

Light is a form of electromagnetic radiation — waves of electric and magnetic fields that transmit energy. The behavior of light depends on its frequency (or wavelength). The properties of light are exploited in the optical elements of the eye to focus rays of light on sensory elements. When light interacts with matter, spectroscopic changes occur that can be used to identify the material on an atomic or molecular level. Differential absorption of electromagnetic radiation can be used to generate images useful in diagnostic medicine. Interference and diffraction of light waves are used in many analytical and diagnostic techniques. The photon model of light explains why electromagnetic radiation of different wavelengths interacts differently with matter.

When mechanical energy is transmitted through solids, liquids, and gases, oscillating pressure waves known as “sound” are generated. Sound waves are audible if the sensory elements of the ear vibrate in response to exposure to these vibrations. The detection of reflected sound waves is utilized in ultrasound imaging. This non-invasive technique readily locates dense subcutaneous structures, such as bone and cartilage, and is very useful in diagnostic medicine.

The content in this category covers the properties of both light and sound and how these energy waves interact with matter. The topics and subtopics in this category are the following:

#### **Sound (PHY)**

- Production of sound
- Relative speed of sound in solids, liquids, and gases
- Intensity of sound, decibel units, log scale
- Attenuation (Damping)
- Doppler Effect: moving sound source or observer, reflection of sound from a moving object
- Pitch
- Resonance in pipes and strings
- Ultrasound
- Shock waves

#### **Light, Electromagnetic Radiation (PHY)**

- Concept of Interference; Young Double-slit Experiment
- Thin films, diffraction grating, single-slit diffraction
- Other diffraction phenomena, X-ray diffraction
- Polarization of light: linear and circular
- Properties of electromagnetic radiation
  - Velocity equals constant  $c$ , *in vacuo*
  - Electromagnetic radiation consists of perpendicularly oscillating electric and magnetic fields; direction of propagation is perpendicular to both
- Classification of electromagnetic spectrum, photon energy  $E = hf$
- Visual spectrum, color



### Molecular Structure and Absorption Spectra (OC)

- Infrared region
  - Intramolecular vibrations and rotations
  - Recognizing common characteristic group absorptions, fingerprint region
- Visible region (GC)
  - Absorption in visible region gives complementary color (e.g., carotene)
  - Effect of structural changes on absorption (e.g., indicators)
- Ultraviolet region
  - $\pi$ -Electron and non-bonding electron transitions
  - Conjugated systems
- NMR spectroscopy
  - Protons in a magnetic field; equivalent protons
  - Spin-spin splitting

### Geometrical Optics (PHY)

- Reflection from plane surface: angle of incidence equals angle of reflection
- Refraction, refractive index  $n$ ; Snell's law:  $n_1 \sin \theta_1 = n_2 \sin \theta_2$
- Dispersion, change of index of refraction with wavelength
- Conditions for total internal reflection
- Spherical mirrors
  - Center of curvature
  - Focal length
  - Real and virtual images
- Thin lenses
  - Converging and diverging lenses
  - Use of formula  $1/p + 1/q = 1/f$ , with sign conventions
  - Lens strength, diopters
- Combination of lenses
- Lens aberration
- Optical Instruments, including the human eye

**Content Category 4E: Atoms, nuclear decay, electronic structure, and atomic chemical behavior**

Atoms are classified by their *atomic number*: the number of protons in the atomic nucleus, which also includes neutrons. Chemical interactions between atoms are the result of electrostatic forces involving the electrons and the nuclei. Because neutrons are uncharged, they do not dramatically affect the chemistry of any particular type of atom, but do affect the stability of the nucleus itself.

When a nucleus is unstable, decay results from one of several different processes, which are random, but occur at well-characterized average rates. The products of nuclear decay (alpha, beta, and gamma rays) can interact with living tissue, breaking chemical bonds and ionizing atoms and molecules in the process.

The electronic structure of an atom is responsible for its chemical and physical properties. Only discrete energy levels are allowed for electrons. These levels are described individually by quantum numbers. Since the outermost, or *valence*, electrons are responsible for the strongest chemical interactions, a description of these electrons alone is a good first approximation to describe the behavior of any particular type of atom.

Mass spectrometry is an analytical tool that allows characterization of atoms or molecules, based on well recognized fragmentation patterns and the charge to mass ratio ( $m/z$ ) of ions generated in the gas phase.

The content in this category covers atomic structure, nuclear decay, electronic structure, and the periodic nature of atomic chemical behavior. The topics and subtopics in this category are the following:

**Atomic Nucleus (PHY, GC)**

- Atomic number, atomic weight
- Neutrons, protons, isotopes
- Nuclear forces, binding energy
- Radioactive decay
  - $\alpha$ ,  $\beta$ ,  $\gamma$  decay
  - Half-life, exponential decay, semi-log plots
- Mass spectrometer
- Mass spectroscopy

**Electronic Structure (PHY, GC)**

- Orbital structure of hydrogen atom, principal quantum number  $n$ , number of electrons per orbital (GC)
- Ground state, excited states
- Absorption and emission line spectra
- Use of Pauli Exclusion Principle
- Paramagnetism and diamagnetism
- Conventional notation for electronic structure (GC)
- Bohr atom
- Heisenberg Uncertainty Principle
- Effective nuclear charge (GC)
- Photoelectric effect

### **The Periodic Table - Classification of Elements into Groups by Electronic Structure (GC)**

- Alkali metals
- Alkaline earth metals: their chemical characteristics
- Halogens: their chemical characteristics
- Noble gases: their physical and chemical characteristics
- Transition metals
- Representative elements
- Metals and non-metals
- Oxygen group

### **The Periodic Table - Variations of Chemical Properties with Group and Row (GC)**

- Valence electrons
- First and second ionization energy
  - Definition
  - Prediction from electronic structure for elements in different groups or rows
- Electron affinity
  - Definition
  - Variation with group and row
- Electronegativity
  - Definition
  - Comparative values for some representative elements and important groups
- Electron shells and the sizes of atoms
- Electron shells and the sizes of ions

### **Stoichiometry (GC)**

- Molecular weight
- Empirical versus molecular formula
- Metric units commonly used in the context of chemistry
- Description of composition by percent mass
- Mole concept, Avogadro's number  $N_A$
- Definition of density
- Oxidation number
  - Common oxidizing and reducing agents
  - Disproportionation reactions
- Description of reactions by chemical equations
  - Conventions for writing chemical equations
  - Balancing equations, including redox equations
  - Limiting reactants
  - Theoretical yields

## *Chemical and Physical Foundations of Biological Systems*

### **Foundational Concept 5**

The principles that govern chemical interactions and reactions form the basis for a broader understanding of the molecular dynamics of living systems.

The chemical processes that take place within organisms are readily understood within the framework of the behavior of solutions, thermodynamics, molecular structure, intermolecular interactions, molecular dynamics, and molecular reactivity.

#### **Content Categories**

- *Category 5A* emphasizes the nature of solution formation, factors that affect solubility, and the properties and behavior of aqueous solutions, with special emphasis on the acid-base behavior of dissolved solutes.
- *Category 5B* focuses on molecular structure and how it affects the strength of intermolecular interactions.
- *Category 5C* emphasizes how differential intermolecular interactions can be used to effect chemical separations.
- *Category 5D* emphasizes the varied nature of biologically-relevant molecules, and how patterns of covalent bonding can be used to predict the chemical reactivity of these molecules and their structure and function within a living system.
- *Category 5E* emphasizes how relative energy dictates the overall favorability of chemical processes and the rate at which these processes can occur.

With these building blocks, medical students will be able to utilize core principles of human chemistry to learn about molecular and cellular functions in health and disease.

### ***Content Category 5A: Unique nature of water and its solutions***

In order to fully understand the complex and dynamic nature of living systems, it is first necessary to understand the unique nature of water and its solutions. The unique properties of water allow it to strongly interact with and mobilize many types of solutes, including ions. Water is also unique in its ability to absorb energy and buffer living systems from the chemical changes necessary to sustain life.

The content in this category covers the nature of solutions, solubility, acids, bases, and buffers. The topics and subtopics in this category are the following:

#### **Acid/Base Equilibria (GC, BC)**

- Brønsted–Lowry definition of acid, base
- Ionization of water
  - $K_w$ , its approximate value ( $K_w = [\text{H}^+][\text{OH}^-] = 10^{-14}$  at 25°C, 1 atm)
  - Definition of pH: pH of pure water
- Conjugate acids and bases (e.g.,  $\text{NH}_4^+$  and  $\text{NH}_3$ )
- Strong acids and bases (e.g., nitric, sulfuric)
- Weak acids and bases (e.g., acetic, benzoic)
  - Dissociation of weak acids and bases with or without added salt
  - Hydrolysis of salts of weak acids or bases
  - Calculation of pH of solutions of salts of weak acids or bases
- Equilibrium constants  $K_a$  and  $K_b$ :  $\text{p}K_a$ ,  $\text{p}K_b$
- Buffers
  - Definition and concepts (common buffer systems)
  - Influence on titration curves

#### **Ions in Solutions (GC, BC)**

- Anion, cation: common names, formulas and charges for familiar ions (e.g.,  $\text{NH}_4^+$  ammonium,  $\text{PO}_4^{3-}$  phosphate,  $\text{SO}_4^{2-}$  sulfate)
- Hydration, the hydronium ion

#### **Solubility (GC)**

- Units of concentration (e.g., molarity)
- Solubility product constant; the equilibrium expression  $K_{\text{sp}}$
- Common-ion effect, its use in laboratory separations
  - Complex ion formation
  - Complex ions and solubility
  - Solubility and pH

#### **Titration (GC)**

- Indicators
- Neutralization
- Interpretation of the titration curves
- Redox titration

### ***Content Category 5B: Nature of molecules and intermolecular interactions***

Covalent bonding involves the sharing of electrons between atoms. If the result of such interactions is not a network solid, then the covalently bonded substance will be discrete and molecular.

The shape of molecules can be predicted based on electrostatic principles and quantum mechanics since only two electrons can occupy the same orbital. Bond polarity (both direction and magnitude) can be predicted based on knowledge of the valence electron structure of the constituent atoms. The strength of intermolecular interactions depends on molecular shape and the polarity of the covalent bonds present. The solubility and other physical properties of molecular substances depend on the strength of intermolecular interactions.

The content in this category covers the nature of molecules and includes covalent bonding, molecular structure, nomenclature, and intermolecular interactions. The topics and subtopics in this category are the following:

#### **Covalent Bond (GC)**

- Lewis Electron Dot formulas
  - Resonance structures
  - Formal charge
  - Lewis acids and bases
- Partial ionic character
  - Role of electronegativity in determining charge distribution
  - Dipole Moment
- $\sigma$  and  $\pi$  bonds
  - Hybrid orbitals:  $sp^3$ ,  $sp^2$ ,  $sp$  and respective geometries
  - Valence shell electron pair repulsion and the prediction of shapes of molecules (e.g.,  $\text{NH}_3$ ,  $\text{H}_2\text{O}$ ,  $\text{CO}_2$ )
  - Structural formulas for molecules involving H, C, N, O, F, S, P, Si, Cl
  - Delocalized electrons and resonance in ions and molecules
- Multiple bonding
  - Effect on bond length and bond energies
  - Rigidity in molecular structure
- Stereochemistry of covalently bonded molecules (OC)
  - Isomers
    - Structural isomers
    - Stereoisomers (e.g., diastereomers, enantiomers, cis/trans isomers)
    - Conformational isomers
  - Polarization of light, specific rotation
  - Absolute and relative configuration
    - Conventions for writing *R* and *S* forms
    - Conventions for writing *E* and *Z* forms

**Liquid Phase - Intermolecular Forces (GC)**

- Hydrogen bonding
- Dipole Interactions
- Van der Waals' Forces (London dispersion forces)

### ***Content Category 5C: Separation and purification methods***

Analysis of complex mixtures of substances — especially biologically relevant materials — typically requires separation of the components. Many methods have been developed to accomplish this task, and the method used is dependent on the types of substances which comprise the mixture. All of these methods rely on the magnification of potential differences in the strength of intermolecular interactions.

The content in this category covers separation and purification methods including: extraction, liquid and gas chromatography, and electrophoresis. The topics and subtopics in this category are the following:

#### **Separations and Purifications (OC, BC)**

- Extraction: distribution of solute between two immiscible solvents
- Distillation
- Chromatography: Basic principles involved in separation process
  - Column chromatography
    - Gas-liquid chromatography
    - High pressure liquid chromatography
  - Paper chromatography
  - Thin-layer chromatography
- Separation and purification of peptides and proteins (BC)
  - Electrophoresis
  - Quantitative analysis
  - Chromatography
    - Size-exclusion
    - Ion-exchange
    - Affinity
- Racemic mixtures, separation of enantiomers (OC)



### ***Content Category 5D: Structure, function, and reactivity of biologically-relevant molecules***

The structure of biological molecules forms the basis of their chemical reactions including oligomerization and polymerization. Unique aspects of each type of biological molecule dictate their role in living systems, whether providing structure or information storage, or serving as fuel and catalysts.

The content in this category covers the structure, function, and reactivity of biologically-relevant molecules including the mechanistic considerations that dictate their modes of reactivity. The topics and subtopics in this category are the following:

#### **Nucleotides and Nucleic Acids (BC, BIO)**

- Nucleotides and nucleosides: composition
  - Sugar phosphate backbone
  - Pyrimidine, purine residues
- Deoxyribonucleic acid: DNA; Ribonucleic acid: RNA; Double helix; RNA structures
- Chemistry (BC)
- Other functions (BC)

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

- Amino acids: description
  - Absolute configuration at the  $\alpha$  position
  - Dipolar ions
  - Classification
    - Acidic or basic
    - Hydrophilic or hydrophobic
  - Synthesis of  $\alpha$ -amino acids (OC)
    - Strecker Synthesis
    - Gabriel Synthesis
- Peptides and proteins: reactions
  - Sulfur linkage for cysteine and cystine
  - Peptide linkage: polypeptides and proteins
  - Hydrolysis (BC)
- General Principles
  - Primary structure of proteins
  - Secondary structure of proteins
  - Tertiary structure of proteins
  - Isoelectric point

#### **The Three-Dimensional Protein Structure (BC)**

- Conformational stability
  - Hydrophobic interactions
  - Solvation layer (entropy)
- Quaternary structure
- Denaturing and Folding

### Non-Enzymatic Protein Function (BC)

- Binding
- Immune system
- Motor

### Lipids (BC, OC)

- Description, Types
  - Storage
    - Triacyl glycerols
    - Free fatty acids: saponification
  - Structural
    - Phospholipids and phosphatids
    - Sphingolipids (BC)
    - Waxes
  - Signals/cofactors
    - Fat-soluble vitamins
    - Steroids
    - Prostaglandins (BC)

### Carbohydrates (OC)

- Description
  - Nomenclature and classification, common names
  - Absolute configuration
  - Cyclic structure and conformations of hexoses
  - Epimers and anomers
- Hydrolysis of the glycoside linkage
- Keto-enol tautomerism of monosaccharides
- Disaccharides (BC)
- Polysaccharides (BC)

### Aldehydes and Ketones (OC)

- Description
  - Nomenclature
  - Physical properties
- Important reactions
  - Nucleophilic addition reactions at C=O bond
    - Acetal, hemiacetal
    - Imine, enamine
    - Hydride reagents
    - Cyanohydrin
  - Oxidation of aldehydes
  - Reactions at adjacent positions: enolate chemistry
    - Keto-enol tautomerism ( $\alpha$ -racemization)
    - Aldol condensation, retro-aldol
    - Kinetic versus thermodynamic enolate

- General principles
  - Effect of substituents on reactivity of C=O; steric hindrance
  - Acidity of  $\alpha$ -H; carbanions

### Alcohols (OC)

- Description
  - Nomenclature
  - Physical properties (acidity, hydrogen bonding)
- Important reactions
  - Oxidation
  - Substitution reactions:  $S_N1$  or  $S_N2$
  - Protection of alcohols
  - Preparation of mesylates and tosylates

### Carboxylic Acids (OC)

- Description
  - Nomenclature
  - Physical properties
- Important reactions
  - Carboxyl group reactions
    - Amides (and lactam), esters (and lactone), anhydride formation
    - Reduction
    - Decarboxylation
  - Reactions at 2-position, substitution

### Acid Derivatives (Anhydrides, Amides, Esters) (OC)

- Description
  - Nomenclature
  - Physical properties
- Important reactions
  - Nucleophilic substitution
  - Transesterification
  - Hydrolysis of amides
- General principles
  - Relative reactivity of acid derivatives
  - Steric effects
  - Electronic effects
  - Strain (e.g.,  $\beta$ -lactams)

### Phenols (OC, BC)

- Oxidation and reduction (e.g., hydroquinones, ubiquinones): biological  $2e^-$  redox centers

### Polycyclic and Heterocyclic Aromatic Compounds (OC, BC)

- Biological aromatic heterocycles

### ***Content Category 5E: Principles of chemical thermodynamics and kinetics***

The processes that occur in living systems are dynamic, and they follow the principles of chemical thermodynamics and kinetics. The position of chemical equilibrium is dictated by the relative energies of products and reactants. The rate at which chemical equilibrium is attained is dictated by a variety of factors: concentration of reactants, temperature, and the amount of catalyst (if any).

Biological systems have evolved to harness energy, and utilize it in very efficient ways to support all processes of life, including homeostasis and anabolism. Biological catalysts, known as *enzymes*, have evolved to allow all of the relevant chemical reactions required to sustain life to occur both rapidly and efficiently, and under the narrow set of conditions required.

The content in this category covers all principles of chemical thermodynamics and kinetics including enzymatic catalysis. The topics and subtopics in this category are the following:

#### **Enzymes (BC)**

- Classification by reaction type
- Mechanism
  - Substrates and enzyme specificity
  - Active site model
  - Induced-fit model
  - Cofactors, coenzymes, and vitamins
- Kinetics
  - General (catalysis)
  - Michaelis–Menten
  - Cooperativity
  - Effects of local conditions on enzyme activity
- Inhibition
- Regulatory enzymes
  - Allosteric
  - Covalently modified

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

- Bioenergetics/thermodynamics
  - Free energy/ $K_{eq}$
  - Concentration
- Phosphorylation/ATP
  - ATP hydrolysis  $\Delta G \ll 0$
  - ATP group transfers
- Biological oxidation–reduction
  - Half-reactions
  - Soluble electron carriers
  - Flavoproteins

### Energy Changes in Chemical Reactions – Thermochemistry, Thermodynamics (GC, PHY)

- Thermodynamic system – state function
- Zeroth Law – concept of temperature
- First Law – conservation of energy in thermodynamic processes
- *PV* diagram: work done = area under or enclosed by curve (PHY)
- Second Law – concept of entropy
  - Entropy as a measure of “disorder”
  - Relative entropy for gas, liquid, and crystal states
- Measurement of heat changes (calorimetry), heat capacity, specific heat
- Heat transfer – conduction, convection, radiation (PHY)
- Endothermic/exothermic reactions (GC)
  - Enthalpy,  $H$ , and standard heats of reaction and formation
  - Hess' Law of Heat Summation
- Bond dissociation energy as related to heats of formation (GC)
- Free energy:  $G$  (GC)
- Spontaneous reactions and  $\Delta G^\circ$  (GC)
- Coefficient of expansion (PHY)
- Heat of fusion, heat of vaporization
- Phase diagram: pressure and temperature

### Rate Processes in Chemical Reactions - Kinetics and Equilibrium (GC)

- Reaction rate
- Dependence of reaction rate on concentration of reactants
  - Rate law, rate constant
  - Reaction order
- Rate-determining step
- Dependence of reaction rate upon temperature
  - Activation energy
    - Activated complex or transition state
    - Interpretation of energy profiles showing energies of reactants, products, activation energy, and  $\Delta H$  for the reaction
  - Use of the Arrhenius Equation
- Kinetic control versus thermodynamic control of a reaction
- Catalysts
- Equilibrium in reversible chemical reactions
  - Law of Mass Action
  - Equilibrium Constant
  - Application of Le Châtelier's Principle
- Relationship of the equilibrium constant and  $\Delta G^\circ$