

Levels of learning goals are categorized as introductory, intermediate and upper.

## **ENERGY: Energy is required by and transformed in biological systems.**

### **Core concepts of energy and matter transformation**

#### **1. The nature of biological energy**

Many forms of energy are involved in biological processes: light, chemical, conformational, mechanical and gradients. These forms can be understood in terms of the principles of thermodynamics. Energy is utilized for diverse purposes, such as the work required to synthesize biomolecules, create electrical and chemical gradients, perform mechanical work or stored within biomolecules.

##### *Associated learning goals*

- Students should be able to compare and contrast biologically relevant forms of energy (e.g. kinetic energy versus potential energy, energy stored in bonds versus potential energy of concentration gradients).
- Students should be able to identify and explain instances when energy is converted from one form to another.
- Students should be able to write a general chemical reaction and the corresponding mathematical expression that approximates its equilibrium constant ( $K_{eq}$ ).
- Students should be able to explain the relationship between equilibrium constants and reaction rate constants.
- Students should be able to apply their knowledge of basic chemical thermodynamics to biologically catalyzed systems.
- Students should be able to account for energy changes in the intermediate steps that define a biological process and predict the spontaneity of the overall process or an intermediate step.
- Students should be able to explain the properties of biomolecules with high-energy transfer potential that make them suitable as energy currency.

#### **2. Catalysis**

Enzymes, which can be proteins or RNA, are macromolecules with catalytic functions. They do not alter reaction equilibria; instead, they lower the activation energy barrier of a particular reaction allowing it to proceed more rapidly. Key concepts of enzyme kinetics are typically defined in terms of the initial rate of product formation,  $V_o$ , and various catalytic kinetic parameters, such as  $V_{max}$  or  $K_{cat}$  and  $K_m$ , which are either mathematically defined for enzymes that follow Michaelis-Menten kinetics or defined empirically for more complicated enzyme models.

##### *Associated learning goals*

- Students should be able to identify the factors contributing to the activation energy of a reaction.
- Students should be able to explain transition state stabilization.
- Students should be able to calculate the rate enhancement of an enzyme-catalyzed reaction.
- Students should be able to explain what a substrate is in terms of being a reactant.
- Students should differentiate between the activation energy, the free energy and standard free energy of a reaction.
- Students should be able to use kinetic parameters to compare enzymes.
- Students should be able to distinguish the different forms of catalytic inhibition and explain how and why they differ.
- Students should be able to quantitatively model how catalyzed reactions occur and calculate kinetic parameters of enzymes from experimental data.
- Students should be able to explain how catalytic parameters vary as one varies substrate or enzyme concentration.

- Students should be able to interpret the physical meaning of various kinetic parameters and describe the underlying assumptions and conditions (such as steady state or equilibrium) on which different parameters depend.

### 3. Energetic coupling of chemical processes in metabolic pathways

Biochemical systems couple energetically unfavorable reactions with energetically favorable reactions. These reactions can be part of catabolic pathways where complex substances are broken into simpler ones with the release of energy or anabolic pathways where complex molecules are synthesized with an input of energy.

#### *Associated learning goals*

- Students should be able to discuss the concept of Gibbs free energy and how to apply it to chemical transformations.
- Students should be able to explain how endergonic and exergonic pathways can be coupled and how this applies to metabolism.
- Students should be able to calculate the overall  $\Delta G$  for a coupled reaction given the  $\Delta G$  values for the component reactions.
- Students should be able to explain the simplifying assumptions made in biochemistry that are consistent with physiological conditions and make "biochemical standard conditions" (steady state) different from the standard conditions (equilibrium conditions) normally referred to in chemistry.
- Students should be able to predict how perturbing a system affects the actual free energy (both mathematically and conceptually).
- Students should be able to explain evolutionary conservation of key metabolic pathways.
- Students should be able to explain differences in energy use and production in different cells and different biological systems.
- Students should be able to explain the role of gene duplication in the evolution of energy production and utilization by different organisms.

## **STRUCTURE & FUNCTION: Macromolecular structure determines function and regulation.**

### **Core concepts of macromolecular structure and function**

#### **1. Biological macromolecules are large and complex**

Macromolecules are made up of basic molecular units. They include the proteins (polymers of amino acids), nucleic acids (polymers of nucleotides), carbohydrates (polymers of sugars) and lipids (with a variety of modular constituents). The biosynthesis and degradation of biological macromolecules involves linear polymerization, breakdown steps (proteins, nucleic acids and lipids) and may also involve branching/debranching (carbohydrates). These processes may involve multi-protein complexes (e.g. ribosome, proteasome) with complex regulation.

#### *Associated learning goals*

- Students should be able to discuss the diversity and complexity of various biologically relevant macromolecules and macromolecular assemblies in terms of evolutionary fitness.
- Students should be able to describe the basic units of the macromolecules and the types of linkages between them.
- Students should be able to compare and contrast the processes involved in the biosynthesis of the major types of macromolecules (proteins, nucleic acids and carbohydrates).
- Students should be able to compare and contrast the processes involved in the degradation of the major types of macromolecules (proteins, nucleic acids and carbohydrates).
- Students should understand that proteins are made up of domains and be able to discuss how the protein families arise from duplication of a primordial gene.

## 2. Structure is determined by several factors

Covalent and non-covalent bonding govern the three dimensional structures of proteins and nucleic acids which impacts function. The amino acid sequences observed in nature are highly selected for biological function but do not necessarily adopt a unique folded structure. The structure (and hence function) of macromolecules is governed by foundational principles of chemistry such as: covalent bonds and polarity, bond rotations and vibrations, non-covalent interactions, the hydrophobic effect and dynamic aspects of molecular structure. The sequence (and hence structure and function) of proteins and nucleic acids can be altered by alternative splicing, mutation or chemical modification. Sequences (and hence structure and function) of macromolecules can evolve to create altered or new biological activities.

### *Associated learning goals*

- Students should be able to recognize the repeating units in biological macromolecules and be able to discuss the structural impacts of the covalent and noncovalent interactions involved.
- Students should be able to discuss the composition, evolutionary change and hence structural diversity of the various types of biological macromolecules found in organisms.
- Students should be able to discuss the chemical and physical relationships between composition and structure of macromolecules.
- Students should be able to compare and contrast the primary, secondary, tertiary and quaternary structures of proteins and nucleic acids.
- Students should be able to use various bioinformatics approaches to analyze macromolecular primary sequence and structure.
- Students should be able to compare and contrast the effects of chemical modification of specific amino acids on a three dimensional structure of a protein.
- Students should be able to compare and contrast the ways in which a particular macromolecule might take on new functions through evolutionary changes.
- Students should be able to use various bioinformatics and computational approaches to compare primary sequences and identify the impact of conservation and/or evolutionary change on the structure and function of macromolecules.
- Students should be able to predict the effects of mutations on the activity, structure or stability of a protein and design appropriate experiments to assess the effects of mutations.
- Students should be able to propose appropriate chemical or chemical biology approaches to explore the localization and interactions of biological macromolecules.
- Students should be able to discuss how mutations of a duplicated gene generate functional diversity.
- Students should be able to evaluate chemical and energetic contributions to the appropriate levels of structure of the macromolecule and predict the effects of specific alterations of structure on the dynamic properties of the molecule.

## 3. Structure and function are related

Macromolecules interact with other molecules using a variety of non-covalent interactions. The specificity and affinity of these interactions are critical to biological function. Some macromolecules catalyze chemical reactions or facilitate physical processes (e.g. molecular transport), allowing them to proceed in ambient conditions. These processes can be quantitatively described by rate laws and thermodynamic principles, (e.g. collision theory, transition state theory, rate laws and equilibria, the effects of temperature and structure and chemical reactivity, Coulomb's Law, Newton's laws of motion, energy and stability, friction, diffusion, thermodynamics, and the concept of randomness and probability).

### *Associated learning goals*

- Students should be able to use mechanistic reasoning to explain how an enzyme or ribozyme catalyzes a particular reaction.
- Students should be able to discuss the basis for various types of enzyme mechanisms.
- Students should be able to calculate enzymatic rates and compare these rates and relate these rates back to cellular or organismal homeostasis.

- Students should be able to discuss various methods that can be used to determine affinity and stoichiometry of a ligand-macromolecule complex and relate the results to both thermodynamic and kinetic data.
- Students should be able to critically assess contributions to specificity in a ligand-macromolecule complex and design experiments to both assess contributions to specificity and test hypotheses about ligand specificity in a complex.
- Students should be able to predict the biological and chemical effects of either mutation or ligand structural change on the affinity of binding and design appropriate experiments to test their predictions.

#### 4. Macromolecular interactions

The interactions between macromolecules and other molecules rely on the same weak, noncovalent interactions that play the major role in stabilizing the three-dimensional structures of the macromolecules themselves. The hydrophobic effect, ionic interactions and hydrogen bonding interactions are prominent. The structural organization of interacting chemical groups in a binding site or an active site lends a high degree of specificity to these interactions. The specificity and affinity of these interactions are critical to biological function.

##### *Associated learning goals*

- Students should be able to discuss the impact of specificity or affinity changes on biological function and any potential evolutionary impact.
- Students should be able to discuss the various methods that can be used to determine affinity and stoichiometry for a ligand-macromolecule complex and relate the results to both thermodynamic and kinetic data.
- Students should be able to discuss the interactions between a variety of biological molecules (including proteins, nucleic acids, lipids, carbohydrates and small organics, etc.) and describe how these interactions impact specificity or affinity leading to changes in biological function.
- Students should be able to predict the effects of either mutation or ligand structural change on the affinity of binding and design appropriate experiments to test their predictions.
- Students should be able to discuss the relationship between the temperature required for denaturation ( $T_m$ ) and macromolecular structure.

#### 5. Macromolecular Structure is dynamic

Macromolecular structure is dynamic over a wide range of time scales, and the dynamic structural changes, large and small, are often critical for biological function. Small changes can come in the form of localized molecular vibrations that can facilitate the access of small molecules to interior portions of the macromolecule. Large conformational changes can come in the form of the motions of different macromolecular domains relative to each other to facilitate catalysis or other forms of work. Proteins can contain intrinsically unstructured domains. The lack of structure in solution may facilitate a function in which interactions must occur promiscuously with several other molecules. The dynamic structure of macromolecules enables rapid changes that impact the homeostasis of biochemical and molecular biological processes

##### *Associated learning goals*

- Students should be able to discuss the time scales of various conformational effects in biological macromolecules and design appropriate experiments to investigate ligand induced changes in conformation and dynamics.
- Students should be able to discuss the structural basis for the dynamic properties of macromolecules and predict the effects of changes in dynamic properties that might result from alteration of primary sequence.
- Students should be able to predict whether a sequence is ordered or disordered and discuss potential roles for disordered regions of proteins.
- Students should be able to critically discuss the evidence for and against the roles of dynamics in macromolecular function.

## 6. The biological activity of macromolecules is often regulated

The biological activity of macromolecules is often regulated in one or more of a variety of hierarchical ways (e.g. inhibitors, activators, modifiers, synthesis, degradation and compartmentalization).

### *Associated learning goals*

- Students should be able to compare and contrast various mechanisms for regulating the function of a macromolecule or an enzymatic reaction or pathway.
- Students should be able to discuss the advantages and disadvantages of regulating a reaction allosterically.
- Students should be able to discuss examples of allosteric regulation, covalent regulation and gene level alterations of macromolecular structure-function.
- Students should be able to use experimental data to assess the type of regulation in response to either homotropic or heterotropic ligands on a macromolecule.
- Students should be able to design a model to explain the regulation of macromolecule structure-function.
- Students should be able to describe how evolution has shaped the regulation of macromolecules and processes.
- Students should be able to describe how changes in cellular homeostasis affect signaling and regulatory molecules and metabolic intermediates.

## 7. The structure (and hence function) of macromolecules is governed by foundational principles of chemistry and physics

The structure (and hence function) of macromolecules is governed by the foundational principles of chemistry (including covalent bonds and polarity; bond rotations and vibrations; hydrogen bonds and non-covalent interactions; the hydrophobic effect; dynamic aspects of molecular structure; collision theory; transition state theory; rate laws and equilibria; the effects of temperature and structure and chemical reactivity) and physics (including Coulomb's Law; Newton's laws of motion; energy and stability; friction; diffusion; thermodynamics; and the concept of randomness and probability).

### *Associated learning goals*

- Students should be able to relate basic principles of rate laws and equilibria to reactions and interactions and calculate appropriate thermodynamic parameters for reactions and interactions.
- Students should be able to explain how a ligand, when introduced to a solution containing a macromolecule to which it can bind, interacts with the macromolecule.
- Students should be able to explain, using basic principles, the effects of temperature on an enzyme catalyzed reaction.
- Students should be able to discuss the dynamic properties of a macromolecule using foundational principles of physics.

## 8. A variety of experimental and computational approaches can be used to observe and quantitatively measure the structure, dynamics and function of biological macromolecules

A variety of experimental and computational approaches can be used to observe and quantitatively measure the structure, dynamics and function of biological macromolecules. Equations can be derived from models and used to predict outcomes or analyze data. Data can be analyzed statistically to assess the correctness of the model and the reliability of the data.

### *Associated learning goals*

- Students should be able to propose a purification scheme for a particular molecule in a mixture given the biophysical properties of the various molecules in the mix.
- Students should be able to either propose experiments that would determine the quaternary structure of a molecule or be able to interpret data pertaining to tertiary and quaternary structure of molecules.
- Students should be able to explain how computational approaches can be used to explore protein-ligand interactions and discuss how the results of such computations can be explored experimentally.

- Students should be able to compare and contrast the computational approaches available to propose a three dimensional structure of a macromolecule and discuss how the proposed structure could be validated experimentally.
- Students should be able to analyze kinetic or binding data to derive appropriate parameters and assess the validity of the model used to describe the phenomenon.

## **INFORMATION STORAGE: Information storage and flow are dynamic and interactive.**

### **Core concepts of biological information**

#### **1. The genome**

A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. Some noncoding sequences enable our cells to produce different amounts of proteins at different times. For example, control sequences contain instructions to tell the cell how to switch genes on and off. Other noncoding sequences are part of genes but do not directly code for proteins. These are thought to help the cell generate a number of different proteins from one gene. More than half of the DNA in our genome is made up of repeated sequences, which appear to stabilize chromosomes; noncoding regions may have a role in spacing out the coding sequences so that they can be activated independently.

##### *Associated learning goals*

- Students should be able to define what a genome consists of and how the information in the various genes and other sequence classes within each genome is used to store and express genetic information.
- Students should be able to discuss how the genome is organized and packaged in prokaryotes and eukaryotes.
- Students should be able to discuss tools used to study expression, conservation and structure of an organism at the genome level.
- Students should be able to explain the role of repetitive and non-repetitive DNA and how its relative abundance varies from prokaryotes to eukaryotes.

#### **2. Information in the gene: nucleotide sequence to biological function**

The information contained in the nucleotide sequence of a genome is organized into various elements, including coding regions, which contain three base codons coding for amino acids, which are transcribed to messenger RNA. The messenger RNA is translated to give the primary sequence of a protein and regulatory elements. The transcribed coding region for a given protein may contain introns and exons in eukaryotic cells. The amino acid sequence of a protein gives rise to biological function through stably folded regions and/or intrinsically disordered regions.

##### *Associated learning goals*

- Students should be able to explain the central dogma of biology and relate the commonality of the process to all of life.
- Students should be able to explain the process of gene regulation connecting how extracellular signals can result in a change of gene expression.
- Students should be able to discuss how genes are organized and contrast the different approaches used in prokaryotic and eukaryotic organisms.
- Students should be able to explain how mRNA processing occurs and how splicing affects the diversity of gene products in eukaryotic organisms.

#### **3. Genome transmission from one generation to the next**

The primary concern of cell division is the maintenance of the original cell's genome. The genomic information that is stored in chromosomes must be replicated, and the duplicated genome must be separated cleanly between cells. Somatic cell lines are diploid (2n chromosome complement), and mitotic division normally results in two

daughter cells, each with chromosomes and genes identical to those of the parent cell. Germline cells, called gametes, are haploid (having the *haploid* or the n chromosomal complement) and reproduce by meiosis.

*Associated learning goals*

- Students should be able to explain the differences of mitosis and meiosis and relate them to the process of cellular division.
- Students should be able to illustrate how DNA is replicated and genes are transmitted from one generation to the next in multiple types of organisms including bacteria, eukaryotes, viruses and retroviruses.
- Students should be able to apply the concepts of segregation and independent assortment to traits inherited from parent to offspring and discuss how they increase genetic variation.

#### 4. Genome maintenance

Throughout its lifetime, the DNA in a cell is under constant metabolic and environmental assault leading to damage. The ultraviolet (UV) component of sunlight, ionizing radiation and numerous genotoxic chemicals, including the (by)products of normal cellular metabolism (e.g. reactive oxygen species such as superoxide anions, hydroxyl radicals and hydrogen peroxide), constitute a permanent enemy to DNA integrity. Hydrolysis of nucleotide residues leaves non-instructive abasic sites. Spontaneous or induced deamination of cytosine, adenine, guanine or 5-methylcytosine converts these bases to the miscoding uracil, hypoxanthine, xanthine and thymine, respectively. Left unchecked, the resulting genomic instability initiates cancer and other age-related disorders. Inherited or acquired deficiencies in genome maintenance systems contribute significantly to the onset of cancer. Over time, DNA accumulates changes that activate proto-oncogenes and inactivate tumor-suppressor genes. Cells have evolved nucleotide- and base-excision repair mechanisms, homologous recombination, end joining, mismatch repair and telomere metabolism as mechanisms to maintain the integrity of the genome.

*Associated learning goals*

- Students should be able to state how the cell ensures high fidelity DNA replication and identify instances where the cell employs mechanism for damage repair.
- Students should be able to explain what a mutation is at the molecular level, how it arises and how it could potentially affect the organism from gene expression to fitness.
- Students should be able to construct relationships between chromosome and cellular structures (e.g. telomere, centromeres and centrosomes) and explain how these structures are responsible for and/or involved in genomic stability.
- Students should be able to relate how the cell cycle and genome maintenance are coordinated and how disruptions in this coordination could affect the organism.
- Students should be able to list events that result in genomic instability and explain how the cell responds to restore order and stability.

### **SKILLS: Discovery requires objective measurement, quantitative analysis and clear communication.**

#### 1. Process of science

The process of science combines creative ideas, experimentation and data analysis. Scientists develop a hypothesis and design and conduct appropriate experiments. Experimental results are analyzed and data interpreted using appropriate quantitative modeling and simulation tools.

*Associated learning goals*

- Students should be able to accurately prepare and use appropriate volumes of reagents and perform the required experiments.
- When presented with an experimental observation, students should be able to develop a testable and falsifiable hypothesis.

- When provided with a hypothesis, students should be able to identify the appropriate experimental observations and controllable variables.
- Students should be able to determine averages and standard deviations to relate the significance of experimentally obtained data.
- Students should be able to use appropriate equations to analyze experimental data and obtain parameters.
- Students should be able to use equations and models to predict outcomes of experiments.

## 2. Accessing, comprehending and communicating science

Scientists access, assess and use available information and present data in appropriate contexts in a variety of ways at different levels.

### *Associated learning goals*

- Students should be able to identify, locate and use the primary literature.
- Students should be able to use databases and bioinformatics tools.
- Students, when provided with appropriate background information, should be able to identify consistencies and inconsistencies.
- Students should be able to explain the big picture aspects of current challenges in the molecular life sciences.
- Students should be able to use visual and verbal tools to explain concepts and data.
- Students should be able to translate science into everyday examples.

## 3. Community of practice

Science is interdisciplinary and relies on collaboration, effective teamwork, safety and ethical practices.

### *Associated learning goals*

- Students should explain the importance of and keep an accurate laboratory notebook.
- Given a case study, students should be able to identify both scientific and societal ethical aspects.
- Students should be able to explain cross-disciplinary concepts such as modularity, energy, modeling scientific phenomena, change over time and the differences between stochastic and deterministic phenomena.
- Students should be able to access and interpret safety information and conduct lab work safely and ethically.
- Students should be able to give and take directions to be an effective team member.

# EVOLUTION AND HOMEOSTASIS

## Core Concepts of Evolution

### 1. The significance of evolution

Evolution is genetic change within a population over time. Understanding evolutionary processes and the supporting evidence is an integral part of the molecular life sciences. It explains many present day issues, such as crop availability and pesticide resistance in agriculture, vaccine and drug development in medicine and regulatory mechanisms in cellular, developmental and behavioral biology.

#### *Associated learning goals*

- Students should be able to describe evolution as genetic change in a population over time.
- Students should be able to analyze preexisting and novel data and relate the findings in light of evolution.
- Students should be able to relate evolution to concepts in biochemistry and molecular biology.



## 2. Mechanisms of evolution

Many mechanisms may drive evolution. These include mutation, migration (gene flow), genetic drift (chance changes from generation to generation) and natural selection.

### *Associated learning goals*

- Students should be able to explain how mechanisms of evolution cause variation within a population.
- Students should be able to distinguish between random and nonrandom evolutionary processes.
- Students should be able to demonstrate their understanding of the mechanisms of evolution to relevant issues, such as antibiotic resistance, the occurrence of genetic disorders or cancer therapeutics.

## 3. Natural selection is a key evolutionary mechanism

Evolution by natural selection results from differential reproductive success, where individuals with certain heritable traits are more successful. The fitness of an individual and its genotype is directly determined by its relative reproductive success. The fittest individuals will pass their genes to more offspring, driving the evolution of the population. In this way, the population becomes better-suited (adapted) to its environment. Multiple lines of evidence support evolution by natural selection, including the fossil record, homologies and direct observation in laboratory and field studies.

### *Associated learning goals*

- Students should be able to describe the process of natural selection.
- Students should be able to distinguish between individual fitness and adaptation of populations.
- Students should be able to explain how selection of phenotypes affects genotype transmission.
- Students should be able to synthesize and evaluate supporting evidence for the theory of natural selection.

## 4. The molecular basis of evolution

Organismal traits are determined at the genetic and epigenetic level. Molecular modifications at these levels may determine the RNA and protein expression patterns in a cell, influencing the phenotype of the organism. Genetic modifications can also arise from the acquisition of new genetic material via processes such as horizontal gene transfer, endosymbiosis and viral vector transfer. Transmission of these heritable alterations may lead to changes in the genetic composition of a population, thereby driving evolution.

### *Associated learning goals*

- Students should be able to explain how cells can acquire new genetic material.
- Students should be able to explain how mutations and epigenetic changes influence gene expression, structure and function of gene products and the fitness of an organism.
- Using genetic information, students should be able to categorize organisms and establish phylogenetic relationships.

## Core concepts of homeostasis

### 1. Biological need for homeostasis

Biological homeostasis is the ability to maintain relative stability and function as changes occur in the internal or external environment. Organisms are viable under a relatively narrow set of conditions. As such, there is a need to tightly regulate the concentrations of metabolites and small molecules at the cellular level to ensure survival. To optimize resource use and to maintain conditions, the organism may sacrifice efficiency for robustness. Breakdown of homeostatic regulation can contribute to the cause or progression of disease or lead to cell death.

### *Associated learning goals*

- Students should be able to describe why maintenance of homeostasis is advantageous to an organism.
- Students should be able to define homeostasis in a biochemical context to both scientifically trained and lay audiences.
- Students should be able to describe how homeostatic pathways and mechanisms have been conserved throughout evolution.

- Students should be able to appraise the costs and benefits of different homeostatic mechanisms to an organism.
- Students should be able to relate different environmental factors necessitating homeostasis to a specific adaptation.

## 2. Link steady state processes and homeostasis

A system that is in a steady state remains constant over time, but that constant state requires continual work. A system in a steady state has a higher level of energy than its surroundings. Biochemical systems maintain homeostasis via regulation of gene expression, metabolic flux and energy transformation but are never at equilibrium.

### *Associated learning goals*

- Students should be able to explain that a system at chemical equilibrium (or just equilibrium) is stable over time, but no energy or work is required to maintain that condition.
- Students should be able to apply the principles of kinetics to describe flux through biochemical pathways.
- Students should be able to discuss a metabolic pathway in terms of equilibrium and Le Chatelier's principle.
- Students should be able to relate the laws of thermodynamics to homeostasis and explain how the cell or organism maintains homeostasis.
- Students should be able to model how perturbations to the steady state can result in changes to the homeostatic state.
- Students should be able to propose how resources stored in the homeostatic state can be utilized in times of need.

## 3. Quantifying homeostasis

Multiple reactions with intricate networks of activators and inhibitors are involved in biological homeostasis. Modifications of such networks can lead to activation of previously latent metabolic pathways or even to unpredicted interactions between components of these networks. These pathways and networks can be mathematically modeled and correlated with metabolomics data and kinetic and thermodynamic parameters of individual components to quantify the effects of changing conditions related to either normal or disease states.

### *Associated learning goals*

- Students should be able to describe experiments discussing how signaling and regulatory molecules and metabolic intermediates can be quantitated in the laboratory.
- Students should be able to relate concentrations of key metabolites to steps of metabolic pathways and describe the roles they play in homeostasis.
- Students should be able to calculate enzymatic rates and compare these rates and relate these rates back to cellular or organismal homeostasis.
- Students should explain that organismal homeostasis can be measured in multiple ways and over different time scales (seconds, minutes, hours, days and months).
- Students, given a metabolic network and appropriate data, should be able to predict the outcomes of changes in parameters of the system such as increased concentrations of certain intermediates or the changes in the activity of certain enzymes.

## 4. Control mechanisms

Homeostasis is maintained by a series of control mechanisms functioning at the organ, tissue or cellular level. These control mechanisms include substrate supply, activation or inhibition of individual enzymes and receptors, synthesis and degradation of enzymes, and compartmentalization. The primary components responsible for the maintenance of homeostasis can be categorized as stimulus, receptor, control center, effector and feedback mechanism.

### *Associated learning goals*

- Students should be able to discuss how chemical processes are compartmentalized in the organism, organ and the cell.

- Students should be able to explain why biochemical pathways proceed through the intermediates that they do (gradual oxidation or reduction) and why pathways share intermediates.
- Students should be able to summarize the different levels of control (including reaction compartmentalization, gene expression, covalent modification of key enzymes, allosteric regulation of key enzymes, substrate availability and proteolytic cleavage) and relate these different levels of control to homeostasis.
- Students should be able to compare the temporal aspect of different control mechanisms (e.g. how quickly phosphorylation occurs versus changes in gene expression).
- Students should be able to hypothesize why and how organs evolved with specialized function in metazoans.
- Students should be able to discuss different models of allosteric regulation.
- Students should be able to formulate models relating changes in flux through a pathway to other pathways and overall homeostasis.
- Students should be able to defend why anabolic and catabolic pathways are compartmentalized in the cell.

## 5. Cellular and organismal homeostasis

Homeostasis in an organism or colony of single celled organisms is regulated by secreted proteins and small molecules often functioning as signals. Homeostasis in the cell is maintained by regulation and by the exchange of materials and energy with its surroundings.

### *Associated learning goals*

- Students should be able to describe how the cell and organism store resources (both in terms of stored energy and chemical building blocks) for times of need and how they mobilize these resources.
- Students should be able to integrate homeostasis from the cellular to the organismal level. In other words, students should be able to describe how a complex metazoan can have both a cellular and organismal response to maintain homeostasis.
- Students should be able to compare and contrast homeostasis in different organisms.
- Students should be able to describe homeostasis at the level of the cell, organism or system of organisms and hypothesize how the system would react to deviations from homeostasis.