6 | METABOLISM

Figure 6.1 A hummingbird needs energy to maintain prolonged periods of flight. The bird obtains its energy from taking in food and transforming the nutrients into energy through a series of biochemical reactions. The flight muscles in birds are extremely efficient in energy production. (credit: modification of work by Cory Zanker)

Chapter Outline

Introduction

Virtually every task performed by living organisms requires energy. Energy is needed to perform heavy labor and exercise. Humans also use a great deal of energy while thinking and even during sleep. In fact, the living cells of every organism constantly use energy. Nutrients and other molecules are imported, metabolized (broken down), synthesized into new molecules, modified if needed, transported around the cell, and, in some cases, distributed to the entire organism. For example, the large proteins that make up muscles are actively built from smaller molecules. Complex carbohydrates are broken down into simple sugars that the cell uses for energy. Just as energy is required to both build and demolish a building, energy is required for both the synthesis and breakdown of molecules. Additionally, signaling molecules such as hormones and neurotransmitters are actively transported between cells. Pathogenic bacteria and viruses are ingested and broken down by cells. Cells must also export waste and toxins to stay healthy. Many cells swim or move surrounding materials via the beating motion of cellular appendages such as cilia and flagella.

All of the cellular processes listed above require a steady supply of energy. From where, and in what form, does this energy come? How do living cells obtain energy and how do they use it? This chapter will discuss different forms of energy and the physical laws that govern energy transfer.

How enzymes lower the activation energy required to begin a chemical reaction in the body will also be discussed in this chapter. Enzymes are crucial for life; without them the chemical reactions required to survive would not happen fast enough for an organism to survive. For example, in an individual who lacks one of the enzymes needed to break down a type of carbohydrate known as a mucopolysaccharide, waste products accumulate in the cells and cause progressive brain damage. This deadly genetic disease is called Sanfilippo Syndrome type B or Mucopolysaccharidosis III. Previously incurable, scientists have now discovered a way to replace the missing enzyme in the brain of mice. Read more about the scientists' research **here (http://openstaxcollege.org/l/32mpsiiib)** .

6.1 | Energy and Metabolism

In this section, you will explore the following questions:

- What are metabolic pathways?
- What are the differences between anabolic and catabolic pathways?
- How do chemical reactions play a role in energy transfer?

Connection for AP® Courses

All living systems, from simple cells to complex ecosystems, require free energy to conduct cell processes such as growth and reproduction.

Organisms have evolved various strategies to capture, store, transform, and transfer free energy. A cell's metabolism refers to the chemical reactions that occur within it. Some metabolic reactions involve the breaking down of complex molecules into simpler ones with a release of energy (catabolism), whereas other metabolic reactions require energy to build complex molecules (anabolism). A central example of these pathways is the synthesis and breakdown of glucose.

The content presented in this section supports the Learning Objectives outlined in Big Idea 1 and Big Idea 2 of the AP® Biology Curriculum Framework listed below. The AP® Learning Objectives merge Essential Knowledge content with one or more of the seven Science Practices. These objectives provide a transparent foundation for the AP® Biology course, along with inquiry-based laboratory experiences, instructional activities, and AP® exam questions.

Big Idea 1	The process of evolution drives the diversity and unity of life.
Enduring Understanding 1.B	Organisms are linked by lines of descent from common ancestry.
Essential Knowledge	**1.B.1** Organisms share many conserved core processes and features that evolved and are widely distributed among organisms today.
Science Practice	**3.1** The student can pose scientific questions.
Learning Objective	**1.14** The student is able to pose scientific questions that correctly identify essential properties of shared, core life processes that provide insight into the history of life on Earth.
Essential Knowledge	**1.B.1** Organisms share many conserved core processes and features that evolved and are widely distributed among organisms today.
Science Practice	**7.2** The student can connect concepts in and across domain(s) to generalize or extrapolate in and/or across enduring understandings and/or big ideas.
Learning Objective	**1.15** The student is able to describe specific examples of conserved core biological processes and features shared by all domains or within one domain of life, and how these shared, conserved core processes and features support the concept of common ancestry for all organisms.
Essential Knowledge	**1.B.1** Organisms share many conserved core processes and features that evolved and are widely distributed among organisms today.
Science Practice	**6.1** The student can justify claims with evidence.
Learning Objective	**1.16** The student is able to justify the scientific claim that organisms share many conserved core processes and features that evolved and are widely distributed among organisms today.

Big Idea 2	Biological systems utilize free energy and molecular building blocks to grow, to reproduce, and to maintain dynamic homeostasis.
Enduring Understanding 2.A	Growth, reproduction and maintenance of living systems require free energy and matter.
Essential Knowledge	**2.A.1** All living systems require a constant input of free energy.
Science Practice	**6.2** The student can construct explanations of phenomena based on evidence produced through scientific practices.
Learning Objective	**2.1** The student is able to explain how biological systems use free energy based on empirical data that all organisms require constant energy input to maintain organization, to grow and to reproduce.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.1][APLO 2.3][APLO 4.3][APLO 4.15][APLO 4.17][APLO 2.21]

Scientists use the term **bioenergetics** to discuss the concept of energy flow (Figure 6.2) through living systems, such as cells. Cellular processes such as the building and breaking down of complex molecules occur through stepwise chemical reactions. Some of these chemical reactions are spontaneous and release energy, whereas others require energy to proceed. Just as living things must continually consume food to replenish what has been used, cells must continually produce more energy to replenish that used by the many energy-requiring chemical reactions that constantly take place. All of the chemical reactions that take place inside cells, including those that use energy and those that release energy, are the cell's **metabolism**.

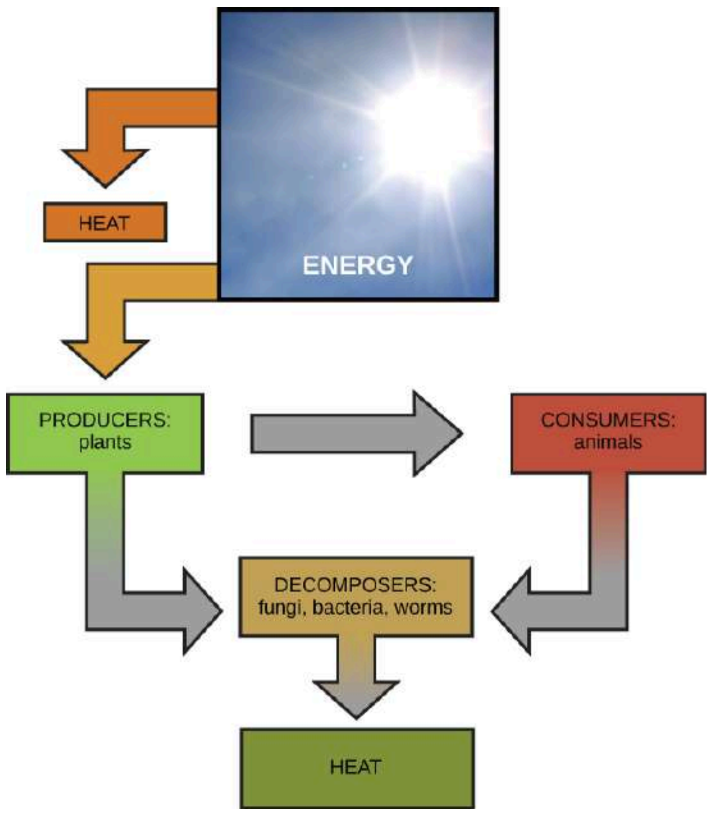


Figure 6.2 Most life forms on earth get their energy from the sun. Plants use photosynthesis to capture sunlight, and herbivores eat those plants to obtain energy. Carnivores eat the herbivores, and decomposers digest plant and animal matter.

Metabolism of Carbohydrates

The metabolism of sugar (a simple carbohydrate) is a classic example of the many cellular processes that use and produce energy. Living things consume sugar as a major energy source, because sugar molecules have a great deal of energy stored within their bonds. The breakdown of glucose, a simple sugar, is described by the equation:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{energy}$$

Carbohydrates that are consumed have their origins in photosynthesizing organisms like plants (**Figure 6.3**). During photosynthesis, plants use the energy of sunlight to convert carbon dioxide gas (CO_2) into sugar molecules, like glucose ($C_6H_{12}O_6$). Because this process involves synthesizing a larger, energy-storing molecule, it requires an input of energy to proceed. The synthesis of glucose is described by this equation (notice that it is the reverse of the previous equation):

$$6CO_2 + 6H_2O + \text{energy} \rightarrow C_6H_{12}O_6 + 6O_2$$

During the chemical reactions of photosynthesis, energy is provided in the form of a very high-energy molecule called ATP, or adenosine triphosphate, which is the primary energy currency of all cells. Just as the dollar is used as currency to buy goods, cells use molecules of ATP as energy currency to perform immediate work. The sugar (glucose) is stored as starch or glycogen. Energy-storing polymers like these are broken down into glucose to supply molecules of ATP.

Solar energy is required to synthesize a molecule of glucose during the reactions of photosynthesis. In photosynthesis, light energy from the sun is initially transformed into chemical energy that is temporally stored in the energy carrier molecules ATP and NADPH (nicotinamide adenine dinucleotide phosphate). The stored energy in ATP and NADPH is then used later in photosynthesis to build one molecule of glucose from six molecules of CO_2. This process is analogous to eating breakfast in the morning to acquire energy for your body that can be used later in the day. Under ideal conditions, energy from 18 molecules of ATP is required to synthesize one molecule of glucose during the reactions of photosynthesis. Glucose molecules can also be combined with and converted into other types of sugars. When sugars are consumed, molecules of glucose eventually make their way into each living cell of the organism. Inside the cell, each sugar molecule is broken down through a complex series of chemical reactions. The goal of these reactions is to harvest the energy stored inside the sugar molecules. The harvested energy is used to make high-energy ATP molecules, which can be used to perform work, powering many chemical reactions in the cell. The amount of energy needed to make one molecule of glucose from six molecules of carbon dioxide is 18 molecules of ATP and 12 molecules of NADPH (each one of which is energetically equivalent to three molecules of ATP), or a total of 54 ATP molecule equivalents required for the synthesis of one molecule of glucose. This process is a fundamental and efficient way for cells to generate the molecular energy that they require.

Figure 6.3 Plants, like this oak tree, use energy from sunlight to make sugar and other organic molecules. Both plants and animals, like this squirrel, use cellular respiration to derive energy from the organic molecules originally produced by plants.

Metabolic Pathways

The processes of making and breaking down sugar molecules illustrate two types of metabolic pathways. A metabolic pathway is a series of interconnected biochemical reactions that convert a substrate molecule or molecules, step-by-step, through a series of metabolic intermediates, eventually yielding a final product or products. In the case of sugar metabolism, the first metabolic pathway synthesized sugar from smaller molecules, and the other pathway broke sugar down into smaller molecules. These two opposite processes—the first requiring energy and the second producing energy—are referred to as anabolic (building) and catabolic (breaking down) pathways, respectively. Consequently, metabolism is composed of building (anabolism) and degradation (catabolism).

evolution CONNECTION

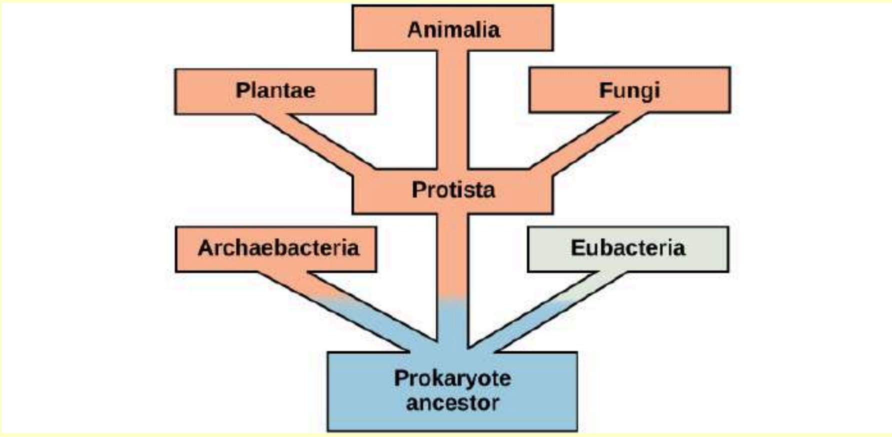


Figure 6.4 This tree shows the evolution of the various branches of life. The vertical dimension is time. Early life forms, in blue, used anaerobic metabolism to obtain energy from their surroundings.

Evolution of Metabolic Pathways

There is more to the complexity of metabolism than understanding the metabolic pathways alone. Metabolic complexity varies from organism to organism. Photosynthesis is the primary pathway in which photosynthetic organisms like plants (the majority of global synthesis is done by planktonic algae) harvest the sun's energy and convert it into carbohydrates. The by-product of photosynthesis is oxygen, required by some cells to carry out cellular respiration. During cellular respiration, oxygen aids in the catabolic breakdown of carbon compounds, like carbohydrates. Among the products of this catabolism are CO_2 and ATP. In addition, some eukaryotes perform catabolic processes without oxygen (fermentation); that is, they perform or use anaerobic metabolism.

Organisms probably evolved anaerobic metabolism to survive (living organisms came into existence about 3.8 billion years ago, when the atmosphere lacked oxygen). Despite the differences between organisms and the complexity of metabolism, researchers have found that all branches of life share some of the same metabolic pathways, suggesting that all organisms evolved from the same ancient common ancestor (**Figure 6.4**). Evidence indicates that over time, the pathways diverged, adding specialized enzymes to allow organisms to better adapt to their environment, thus increasing their chance to survive. However, the underlying principle remains that all organisms must harvest energy from their environment and convert it to ATP to carry out cellular functions.

The early atmosphere lacked oxygen. Why do you think this is the case?

a. Oxygen is a byproduct of photosynthesis, so there was very little oxygen in the atmosphere until photosynthetic organisms evolved.

b. Oxygen is a byproduct of anaerobic respiration, so there was very little oxygen in the atmosphere until anaerobic organisms evolved.

c. Oxygen is a byproduct of fermentation, so there was very little oxygen in the atmosphere until fermentative organisms evolved.

Anabolic and Catabolic Pathways

Anabolic pathways require an input of energy to synthesize complex molecules from simpler ones. Synthesizing sugar from CO_2 is one example. Other examples are the synthesis of large proteins from amino acid building blocks, and the synthesis of new DNA strands from nucleic acid building blocks. These biosynthetic processes are critical to the life of the cell, take place constantly, and demand energy provided by ATP and other high-energy molecules like NADH (nicotinamide adenine dinucleotide) and NADPH (**Figure 6.5**).

ATP is an important molecule for cells to have in sufficient supply at all times. The breakdown of sugars illustrates how a single molecule of glucose can store enough energy to make a great deal of ATP, 36 to 38 molecules. This is a **catabolic** pathway. Catabolic pathways involve the degradation (or breakdown) of complex molecules into simpler ones. Molecular energy stored in the bonds of complex molecules is released in catabolic pathways and harvested in such a way that it can be used to produce ATP. Other energy-storing molecules, such as fats, are also broken down through similar catabolic reactions to release energy and make ATP (**Figure 6.5**).

It is important to know that the chemical reactions of metabolic pathways don’t take place spontaneously. Each reaction step is facilitated, or catalyzed, by a protein called an enzyme. Enzymes are important for catalyzing all types of biological reactions—those that require energy as well as those that release energy.

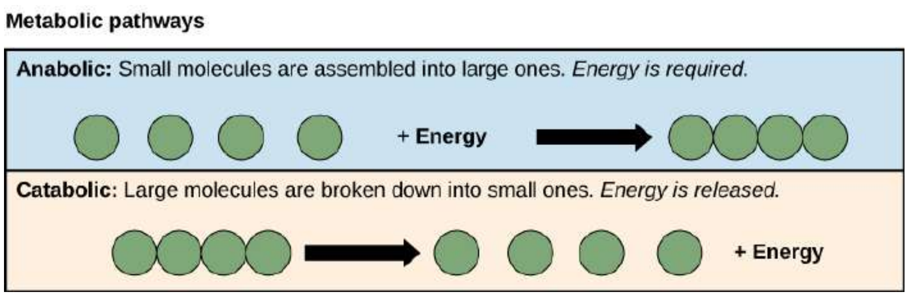


Figure 6.5 Anabolic pathways are those that require energy to synthesize larger molecules. Catabolic pathways are those that generate energy by breaking down larger molecules. Both types of pathways are required for maintaining the cell’s energy balance.

science practices CONNECTION for AP® Courses

Think About It

Describe two different cellular functions in different organisms that require energy that parallel human energy-requiring functions such as physical exercise.

Section Summary

Cells perform the functions of life through various chemical reactions. A cell’s metabolism refers to the chemical reactions that take place within it. There are metabolic reactions that involve the breaking down of complex chemicals into simpler ones, such as the breakdown of large macromolecules. This process is referred to as catabolism, and such reactions are associated with a release of energy. On the other end of the spectrum, anabolism refers to metabolic processes that build complex molecules out of simpler ones, such as the synthesis of macromolecules. Anabolic processes require energy. Glucose synthesis and glucose breakdown are examples of anabolic and catabolic pathways, respectively.

6.2 | Potential, Kinetic, Free, and Activation Energy

In this section, you will explore the following questions:

- What is “energy”?
- What is the difference between kinetic and potential energy?
- What is free energy, and how does free energy related to activation energy?
- What is the difference between endergonic and exergonic reactions?

Connection for AP® Courses

Although cells and organisms require free energy to survive, they cannot spontaneously create energy, as stated in the Law of Conservation of Energy. Energy is available in different forms. For example, objects in motion possess kinetic energy, whereas objects that are not in motion possess potential energy. The chemical energy in molecules, such as glucose, is potential energy because when bonds break in chemical reactions, free energy is released. Free energy is a measure of energy that is available to do work. The free energy of a system changes during energy transfers such as chemical reactions, and this change is referred to as ΔG or Gibbs free energy. The ΔG of a reaction can be negative or positive, depending on whether the reaction releases energy (exergonic) or requires energy input (endergonic). All reactions require an input of energy called activation energy in order to reach the transition state at which they will proceed. (In another section, we will explore how enzymes speed up chemical reactions by lowering activation energy barriers.)

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined in Big Idea 2 of the AP® Biology Curriculum Framework. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® Exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 2	Biological systems utilize free energy and molecular building blocks to grow, to reproduce, and to maintain dynamic homeostasis.
Enduring Understanding 2.A	Growth, reproduction and maintenance of living systems require free energy and matter.
Essential Knowledge	**2.A.1** All living systems require constant input of free energy.
Science Practice	**6.2** The student can construct explanations of phenomena based on evidence produced through scientific practices.
Learning Objective	**2.1** The student is able to explain how biological systems use free energy based on empirical data that all organisms require constant energy input to maintain organization, to grow, and to reproduce.
Essential Knowledge	**2.A.1** All living systems require constant input of free energy.
Science Practice	**6.2** The student can justify claims with evidence.
Learning Objective	**2.2** The student is able to justify a scientific claim that free energy is required for living systems to maintain organization, to grow or to reproduce, but that multiple strategies exist in different living systems.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.5]

Energy is defined as the ability to do work. As you've learned, energy exists in different forms. For example, electrical energy, light energy, and heat energy are all different types of energy. While these are all familiar types of energy that one can see or feel, there is another type of energy that is much less tangible. This energy is associated with something as simple as an object held above the ground. In order to appreciate the way energy flows into and out of biological systems, it is important to understand more about the different types of energy that exist in the physical world.

Types of Energy

When an object is in motion, there is energy associated with that object. In the example of an airplane in flight, there is a great deal of energy associated with the motion of the airplane. This is because moving objects are capable of enacting a change, or doing work. Think of a wrecking ball. Even a slow-moving wrecking ball can do a great deal of damage to other objects. However, a wrecking ball that is not in motion is incapable of performing work. Energy associated with objects in motion is called **kinetic energy**. A speeding bullet, a walking person, the rapid movement of molecules in the air (which produces heat), and electromagnetic radiation like light all have kinetic energy.

Now what if that same motionless wrecking ball is lifted two stories above a car with a crane? If the suspended wrecking ball is unmoving, is there energy associated with it? The answer is yes. The suspended wrecking ball has energy associated with it that is fundamentally different from the kinetic energy of objects in motion. This form of energy results from the fact that there is the *potential* for the wrecking ball to do work. If it is released, indeed it would do work. Because this type of energy refers to the potential to do work, it is called **potential energy**. Objects transfer their energy between kinetic and potential in the following way: As the wrecking ball hangs motionless, it has 0 kinetic and 100 percent potential energy. Once it is released, its kinetic energy begins to increase because it builds speed due to gravity. At the same time, as it nears the ground, it loses potential energy. Somewhere mid-fall it has 50 percent kinetic and 50 percent potential energy. Just before it hits the ground, the ball has nearly lost its potential energy and has near-maximal kinetic energy. Other examples of potential energy include the energy of water held behind a dam (**Figure 6.6**), or a person about to skydive out of an airplane.

Figure 6.6 Water behind a dam has potential energy. Moving water, such as in a waterfall or a rapidly flowing river, has kinetic energy. (credit "dam": modification of work by "Pascal"/Flickr; credit "waterfall": modification of work by Frank Gualtieri)

Potential energy is not only associated with the location of matter (such as a child sitting on a tree branch), but also with the structure of matter. A spring on the ground has potential energy if it is compressed; so does a rubber band that is pulled taut. The very existence of living cells relies heavily on structural potential energy. On a chemical level, the bonds that hold the atoms of molecules together have potential energy. Remember that anabolic cellular pathways require energy to synthesize complex molecules from simpler ones, and catabolic pathways release energy when complex molecules are broken down. The fact that energy can be released by the breakdown of certain chemical bonds implies that those bonds have potential energy. In fact, there is potential energy stored within the bonds of all the food molecules we eat, which is eventually harnessed for use. This is because these bonds can release energy when broken. The type of potential energy that exists within chemical bonds, and is released when those bonds are broken, is called **chemical energy** (**Figure 6.7**). Chemical energy is responsible for providing living cells with energy from food. The release of energy is brought about by breaking the molecular bonds within fuel molecules.

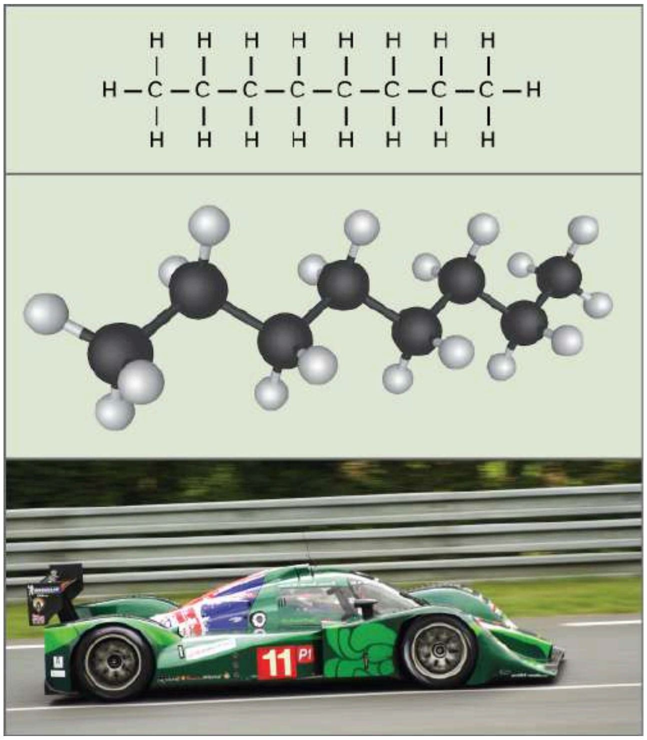


Figure 6.7 The molecules in gasoline (octane, the chemical formula shown) contain chemical energy within the chemical bonds. This energy is transformed into kinetic energy that allows a car to race on a racetrack. (credit “car”: modification of work by Russell Trow)

LINK TO LEARNING

Visit this site (http://openstaxcollege.org/l/simple_pendulum) and select “A simple pendulum” on the menu (under “Harmonic Motion”) to see the shifting kinetic (K) and potential energy (U) of a pendulum in motion.

Explain how the potential and kinetic energy shown in the pendulum model (http://openstaxcollege.org/l/simple_pendulum) relates to a child swinging on a swing set.

a. Kinetic energy increases when the child swings downward, potential energy increases when the child swings upward.

b. Kinetic energy decreases when the child swings downward, potential energy decreases when the child swings upward.

c. Kinetic energy increases when the child swings upward, potential energy increases when the child swings downward.

d. Kinetic energy increases when child swings downward, potential energy increases when the child swings downward.

Free Energy

After learning that chemical reactions release energy when energy-storing bonds are broken, an important next question is how is the energy associated with chemical reactions quantified and expressed? How can the energy released from one reaction be compared to that of another reaction? A measurement of **free energy** is used to quantitate these energy transfers. Free energy is called Gibbs free energy (abbreviated with the letter G) after Josiah Willard Gibbs, the scientist who developed the measurement. Recall that according to the second law of thermodynamics, all energy transfers involve the loss of some amount of energy in an unusable form such as heat, resulting in entropy. Gibbs free energy specifically refers to the energy associated with a chemical reaction that is available after entropy is accounted for. In other words, Gibbs free energy is usable energy, or energy that is available to do work.

Every chemical reaction involves a change in free energy, called delta G (ΔG). The change in free energy can be calculated for any system that undergoes such a change, such as a chemical reaction. To calculate ΔG, subtract the amount of energy lost to entropy (denoted as ΔS) from the total energy change of the system. This total energy change in the system is called **enthalpy** and is denoted as ΔH . The formula for calculating ΔG is as follows, where the symbol T refers to absolute temperature in Kelvin (degrees Celsius + 273):

$$\Delta \mathrm{G} = \Delta \mathrm{H} - \mathrm{T}\Delta \mathrm{S}$$

The standard free energy change of a chemical reaction is expressed as an amount of energy per mole of the reaction product (either in kilojoules or kilocalories, kJ/mol or kcal/mol; 1 kJ = 0.239 kcal) under standard pH, temperature, and pressure conditions. Standard pH, temperature, and pressure conditions are generally calculated at pH 7.0 in biological systems, 25 degrees Celsius, and 100 kilopascals (1 atm pressure), respectively. It is important to note that cellular conditions vary considerably from these standard conditions, and so standard calculated ΔG values for biological reactions will be different inside the cell.

Endergonic Reactions and Exergonic Reactions

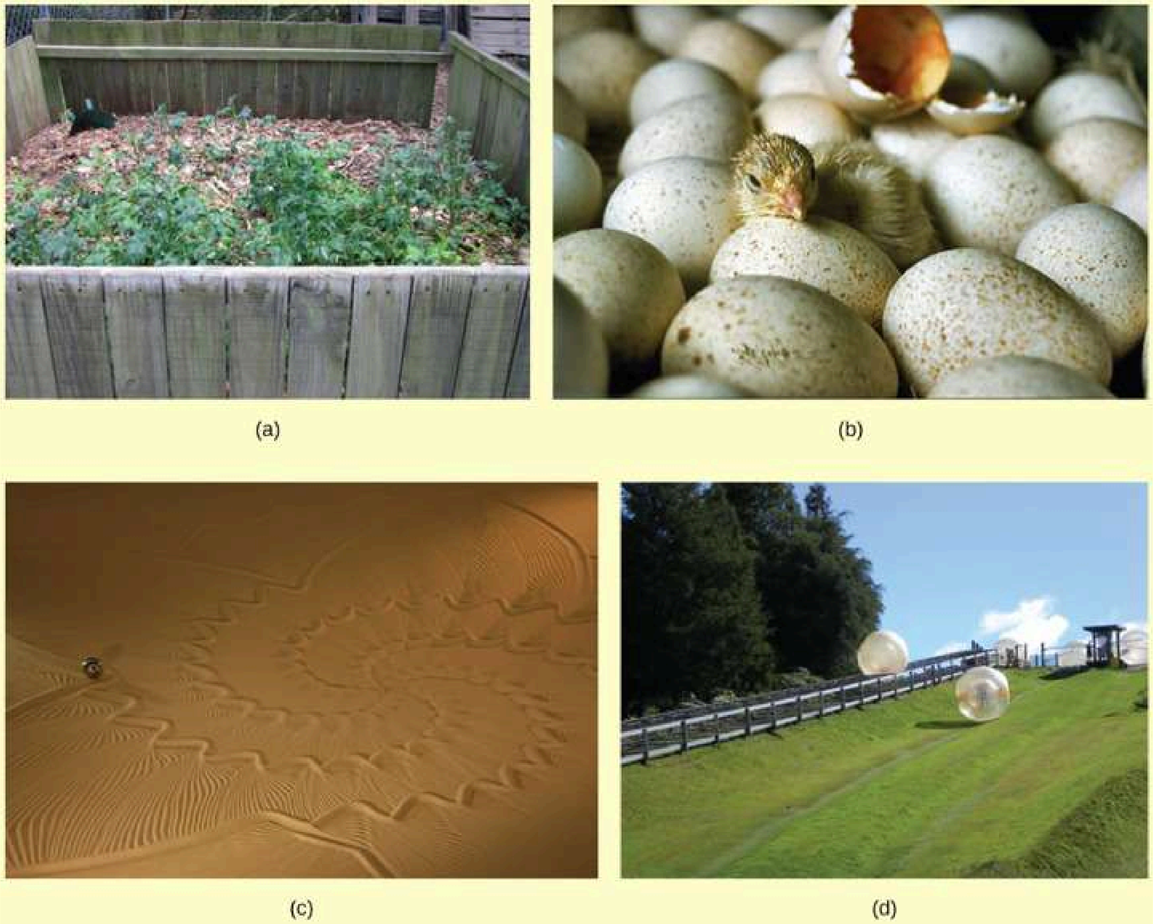
If energy is released during a chemical reaction, then the resulting value from the above equation will be a negative number. In other words, reactions that release energy have a $\Delta G < 0$. A negative ΔG also means that the products of the reaction have less free energy than the reactants, because they gave off some free energy during the reaction. Reactions that have a negative ΔG and consequently release free energy are called **exergonic reactions**. Think: *ex*ergonic means energy is *ex*iting the system. These reactions are also referred to as spontaneous reactions, because they can occur without the addition of energy into the system. Understanding which chemical reactions are spontaneous and release free energy is extremely useful for biologists, because these reactions can be harnessed to perform work inside the cell. An important distinction must be drawn between the term spontaneous and the idea of a chemical reaction that occurs immediately. Contrary to the everyday use of the term, a spontaneous reaction is not one that suddenly or quickly occurs. The rusting of iron is an example of a spontaneous reaction that occurs slowly, little by little, over time.

If a chemical reaction requires an input of energy rather than releasing energy, then the ΔG for that reaction will be a positive value. In this case, the products have more free energy than the reactants. Thus, the products of these reactions can be thought of as energy-storing molecules. These chemical reactions are called **endergonic reactions**, and they are non-spontaneous. An endergonic reaction will not take place on its own without the addition of free energy.

Let’s revisit the example of the synthesis and breakdown of the food molecule, glucose. Remember that the building of complex molecules, such as sugars, from simpler ones is an anabolic process and requires energy. Therefore, the chemical reactions involved in anabolic processes are endergonic reactions. On the other hand, the catabolic process of breaking sugar down into simpler molecules releases energy in a series of exergonic reactions. Like the example of rust above, the breakdown of sugar involves spontaneous reactions, but these reactions don’t occur instantaneously. **Figure 6.8** shows some other examples of endergonic and exergonic reactions. Later sections will provide more information about what else is required to make even spontaneous reactions happen more efficiently.

visual CONNECTION

Figure 6.8 Shown are some examples of endergonic processes (ones that require energy) and exergonic processes (ones that release energy). These include (a) a compost pile decomposing, (b) a chick developing from a fertilized egg, (c) sand art being destroyed, and (d) a ball rolling down a hill. (credit a: modification of work by Natalie Maynor; credit b: modification of work by USDA; credit c: modification of work by "Athlex"/Flickr; credit d: modification of work by Harry Malsch)



Look at each of the processes shown, and decide if it is endergonic or exergonic. In each case, does enthalpy increase or decrease, and does entropy increase or decrease?

a. Compost pile decomposition is endergonic, enthalpy increases and entropy increases. A baby developing from egg is an endergonic process, enthalpy decreases and entropy decreases. Sand art being destroyed is exergonic, no change in enthalpy and entropy increases. A ball rolling downhill is exergonic process, enthalpy decreases and no change in entropy.

b. Compost pile decomposition is exergonic, enthalpy increases and entropy increases. A baby developing from egg is an endergonic process, enthalpy decreases and entropy decreases. Sand art being destroyed is exergonic, no change in enthalpy and entropy decreases. A ball rolling downhill is exergonic process, enthalpy decreases and no change in entropy.

c. Compost pile decomposition is exergonic, enthalpy increases and entropy increases. A baby developing from egg is an endergonic process, enthalpy decreases and entropy decreases. Sand art being destroyed is exergonic, no change in enthalpy and entropy increases. A ball rolling downhill is exergonic process, enthalpy decreases and entropy increases.

d. A ball rolling down the hill doesn't affect the order of system; therefore, the entropy would remain unchanged.

An important concept in the study of metabolism and energy is that of chemical equilibrium. Most chemical reactions are reversible. They can proceed in both directions, releasing energy into their environment in one direction, and absorbing it from the environment in the other direction (**Figure 6.9**). The same is true for the chemical reactions involved in cell metabolism, such as the breaking down and building up of proteins into and from individual amino acids, respectively. Reactants within a closed system will undergo chemical reactions in both directions until a state of equilibrium is reached. This state of equilibrium is one of the lowest possible free energy and a state of maximal entropy. Energy must be put into the system to push the reactants and products away from a state of equilibrium. Either reactants or products must be added, removed, or changed. If a cell were a closed system, its chemical reactions would reach equilibrium, and it would die because there would be insufficient free energy left to perform the work needed to maintain life. In a living cell, chemical reactions are constantly moving towards equilibrium, but never reach it. This is because a living cell is an open system. Materials pass in and out, the cell recycles the products of certain chemical reactions into other reactions, and chemical equilibrium is never reached. In this way, living organisms are in a constant energy-requiring, uphill battle against equilibrium and entropy. This constant supply of energy ultimately comes from sunlight, which is used to produce nutrients in the process of photosynthesis.

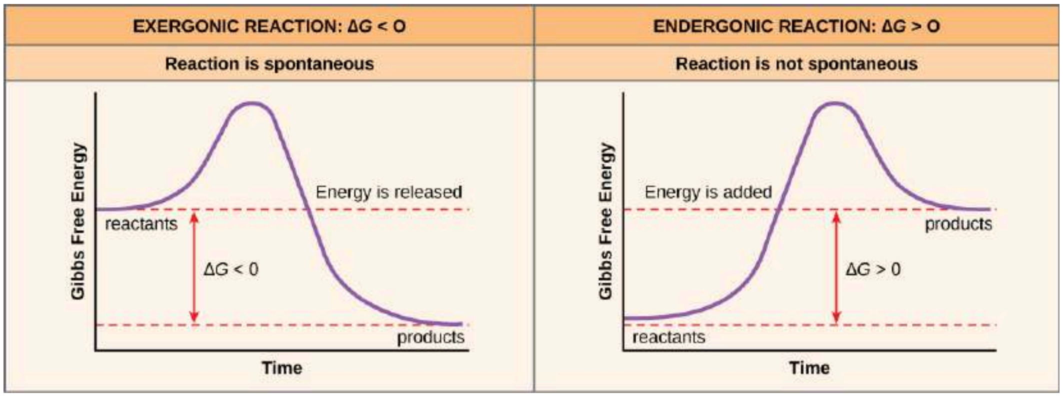


Figure 6.9 Exergonic and endergonic reactions result in changes in Gibbs free energy. Exergonic reactions release energy; endergonic reactions require energy to proceed.

Activation Energy

There is another important concept that must be considered regarding endergonic and exergonic reactions. Even exergonic reactions require a small amount of energy input to get going before they can proceed with their energy-releasing steps. These reactions have a net release of energy, but still require some energy in the beginning. This small amount of energy input necessary for all chemical reactions to occur is called the **activation energy** (or free energy of activation) and is abbreviated E_A (**Figure 6.10**).

Why would an energy-releasing, negative ΔG reaction actually require some energy to proceed? The reason lies in the steps that take place during a chemical reaction. During chemical reactions, certain chemical bonds are broken and new ones are formed. For example, when a glucose molecule is broken down, bonds between the carbon atoms of the molecule are broken. Since these are energy-storing bonds, they release energy when broken. However, to get them into a state that allows the bonds to break, the molecule must be somewhat contorted. A small energy input is required to achieve this contorted state. This contorted state is called the **transition state**, and it is a high-energy, unstable state. For this reason, reactant molecules don't last long in their transition state, but very quickly proceed to the next steps of the chemical reaction. Free energy diagrams illustrate the energy profiles for a given reaction. Whether the reaction is exergonic or endergonic determines whether the products in the diagram will exist at a lower or higher energy state than both the reactants and the products. However, regardless of this measure, the transition state of the reaction exists at a higher energy state than the reactants, and thus, E_A is always positive.

LINK TO LEARNING

Watch an animation of the move from free energy to transition state at **this (http://openstaxcollege.org/l/energy_reaction)** site.

Explain why transitional states are unstable.

a. Molecules have relaxed molecular structure with low energy.

b. Molecules have strained molecular structure with high energy.

c. Molecules have relaxed molecular structure with high energy.

d. Molecules have strained molecular structure with low energy.

Where does the activation energy required by chemical reactants come from? The source of the activation energy needed to push reactions forward is typically heat energy from the surroundings. **Heat energy** (the total bond energy of reactants or products in a chemical reaction) speeds up the motion of molecules, increasing the frequency and force with which they collide; it also moves atoms and bonds within the molecule slightly, helping them reach their transition state. For this reason, heating up a system will cause chemical reactants within that system to react more frequently. Increasing the pressure on a system has the same effect. Once reactants have absorbed enough heat energy from their surroundings to reach the transition state, the reaction will proceed.

The activation energy of a particular reaction determines the rate at which it will proceed. The higher the activation energy, the slower the chemical reaction will be. The example of iron rusting illustrates an inherently slow reaction. This reaction occurs slowly over time because of its high E_A. Additionally, the burning of many fuels, which is strongly exergonic, will take place at a negligible rate unless their activation energy is overcome by sufficient heat from a spark. Once they begin to burn, however, the chemical reactions release enough heat to continue the burning process, supplying the activation energy for surrounding fuel molecules. Like these reactions outside of cells, the activation energy for most cellular reactions is too high for heat energy to overcome at efficient rates. In other words, in order for important cellular reactions to occur at appreciable rates (number of reactions per unit time), their activation energies must be lowered (**Figure 6.10**); this is referred to as catalysis. This is a very good thing as far as living cells are concerned. Important macromolecules, such as proteins, DNA, and RNA, store considerable energy, and their breakdown is exergonic. If cellular temperatures alone provided enough heat energy for these exergonic reactions to overcome their activation barriers, the essential components of a cell would disintegrate.

visual CONNECTION

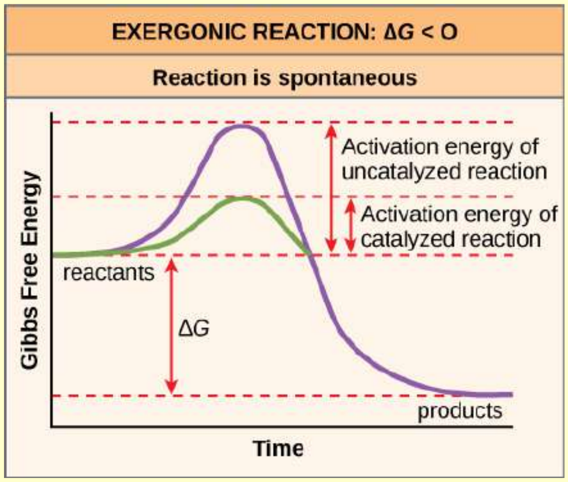


Figure 6.10 Activation energy is the energy required for a reaction to proceed, and it is lower if the reaction is catalyzed. The horizontal axis of this diagram describes the sequence of events in time.

How does the change in Gibbs free energy (ΔG) differ between the catalyzed versus uncatalyzed reaction?

a. ΔG is greater for the forward direction than for the reverse direction.

b. ΔG is greater for the uncatalyzed than the catalyzed reaction.

c. ΔG is greater for the catalyzed than the uncatalyzed reaction.

d. ΔG is the same for the catalyzed and uncatalyzed reactions.

science practices CONNECTION for AP® Courses

Think About It

All plants use water, carbon dioxide, and energy from the sun to make sugars. Think about what would happen to plants that do not have sunlight as an energy source or sufficient water. What would happen to organisms that depend on those plants for their own survival? How does depletion or destruction of forests by human activity affect free energy availability to organisms living in the rain forest? What measures can be taken to try and restore the free energy to an acceptable level?

Section Summary

Energy comes in many different forms. Objects in motion do physical work, and kinetic energy is the energy of objects in motion. Objects that are not in motion may have the potential to do work, and thus, have potential energy. Molecules also have potential energy because the breaking of molecular bonds has the potential to release energy. Living cells depend on the harvesting of potential energy from molecular bonds to perform work. Free energy is a measure of energy that is available to do work. The free energy of a system changes during energy transfers such as chemical reactions, and this change is referred to as ΔG.

The ΔG of a reaction can be negative or positive, meaning that the reaction releases energy or consumes energy, respectively. A reaction with a negative ΔG that gives off energy is called an exergonic reaction. One with a positive ΔG that requires energy input is called an endergonic reaction. Exergonic reactions are said to be spontaneous, because their products have less energy than their reactants. The products of endergonic reactions have a higher energy state than the reactants, and so these are nonspontaneous reactions. However, all reactions (including spontaneous –ΔG reactions) require an initial input of energy in order to reach the transition state, at which they'll proceed. This initial input of energy is called the activation energy.

6.3 | The Laws of Thermodynamics

In this section, you will explore the following questions:

- What is entropy?
- What is the difference between the first and second laws of thermodynamics?

Connection for AP® Courses

In studying energy, scientists use the term system to refer to the matter and its environment involved in energy transfers, such as an ecosystem. Even single cells are biological systems and all systems require energy to maintain order. The more ordered a system is, the lower its entropy. Entropy is a measure of the disorder of the system. (Think of your bedroom as a system. On Sunday evening, you throw dirty clothes in the laundry basket, put books back on the shelves, and return dirty dishes to the kitchen. Cleaning your room requires an input of energy. What gradually happens as the week progresses? You guessed it: entropy.) All biological systems obey the laws of chemistry and physics, including the laws of thermodynamics that describe the properties and processes of energy transfer in systems. The first law states that the total amount of energy in the universe is constant; energy cannot be created or destroyed, but it can be transformed and transferred. The second law states that every energy transfer involves some loss of energy in an unusable form, such as heat energy, resulting in a more disordered system (e.g., your bedroom over the course of a week). Thus, no energy transfer is completely efficient. (We will explore how free energy is stored, transferred, and used in more detail when we study photosynthesis and cellular respiration.)

Information presented and the examples highlighted in the section, support concepts and Learning Objectives outlined in Big Idea 2 of the AP® Biology Curriculum Framework. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® Exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 2	Biological systems utilize free energy and molecular building blocks to grow, to reproduce, and to maintain dynamic homeostasis.
Enduring Understanding 2.A	Growth, reproduction and maintenance of living systems require free energy and matter.
Essential Knowledge	**2.A.1** All living systems require constant input of free energy.
Science Practice	**6.2** The student can construct explanations of phenomena based on evidence produced through scientific practices.
Learning Objective	**2.1** The student is able to explain how biological systems use free energy based on empirical data that all organisms require constant energy input to maintain organization, to grow, and to reproduce.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.1][APLO 2.2][APLO 2.4][APLO 4.16][APLO 2.3]

Thermodynamics refers to the study of energy and energy transfer involving physical matter. The matter and its environment relevant to a particular case of energy transfer are classified as a system, and everything outside of that system is called the surroundings. For instance, when heating a pot of water on the stove, the system includes the stove, the pot, and the water. Energy is transferred within the system (between the stove, pot, and water). There are two types of systems: open and closed. An open system is one in which energy can be transferred between the system and its surroundings. The stovetop system is open because heat can be lost into the air. A closed system is one that cannot transfer energy to its surroundings.

Biological organisms are open systems. Energy is exchanged between them and their surroundings, as they consume energy-storing molecules and release energy to the environment by doing work. Like all things in the physical world, energy is subject to the laws of physics. The laws of thermodynamics govern the transfer of energy in and among all systems in the universe.

The First Law of Thermodynamics

The first law of thermodynamics deals with the total amount of energy in the universe. It states that this total amount of energy is constant. In other words, there has always been, and always will be, exactly the same amount of energy in the universe. Energy exists in many different forms. According to the first law of thermodynamics, energy may be transferred from place to place or transformed into different forms, but it cannot be created or destroyed. The transfers and transformations of energy take place around us all the time. Light bulbs transform electrical energy into light energy. Gas stoves transform chemical energy from natural gas into heat energy. Plants perform one of the most biologically useful energy transformations on earth: that of converting the energy of sunlight into the chemical energy stored within organic molecules, as shown in **Figure 6.2**. Some examples of energy transformations are shown in **Figure 6.11**.

The challenge for all living organisms is to obtain energy from their surroundings in forms that they can transfer or transform into usable energy to do work. Living cells have evolved to meet this challenge very well. Chemical energy stored within organic molecules such as sugars and fats is transformed through a series of cellular chemical reactions into energy within molecules of ATP. Energy in ATP molecules is easily accessible to do work. Examples of the types of work that cells need to do include building complex molecules, transporting materials, powering the beating motion of cilia or flagella, contracting muscle fibers to create movement, and reproduction.

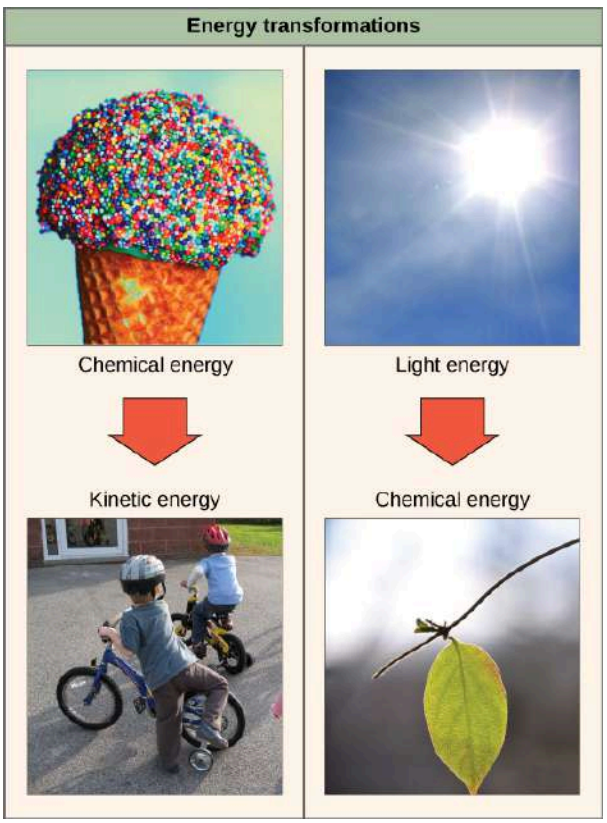


Figure 6.11 Shown are two examples of energy being transferred from one system to another and transformed from one form to another. Humans can convert the chemical energy in food, like this ice cream cone, into kinetic energy (the energy of movement to ride a bicycle). Plants can convert electromagnetic radiation (light energy) from the sun into chemical energy. (credit “ice cream”: modification of work by D. Sharon Pruitt; credit “kids on bikes”: modification of work by Michelle Riggen-Ransom; credit “leaf”: modification of work by Cory Zanker)

The Second Law of Thermodynamics

A living cell’s primary tasks of obtaining, transforming, and using energy to do work may seem simple. However, the second law of thermodynamics explains why these tasks are harder than they appear. None of the energy transfers we've discussed, along with all energy transfers and transformations in the universe, is completely efficient. In every energy transfer, some amount of energy is lost in a form that is unusable. In most cases, this form is heat energy. Thermodynamically, **heat energy** is defined as the energy transferred from one system to another that is not doing work. For example, when an airplane flies through the air, some of the energy of the flying plane is lost as heat energy due to friction with the surrounding air. This friction actually heats the air by temporarily increasing the speed of air molecules. Likewise, some energy is lost as heat energy during cellular metabolic reactions. This is good for warm-blooded creatures like us, because heat energy helps to maintain our body temperature. Strictly speaking, no energy transfer is completely efficient, because some energy is lost in an unusable form.

An important concept in physical systems is that of order and disorder (also known as randomness). The more energy that is lost by a system to its surroundings, the less ordered and more random the system is. Scientists refer to the measure of randomness or disorder within a system as **entropy**. High entropy means high disorder and low energy (**Figure 6.12**). To better understand entropy, think of a student's bedroom. If no energy or work were put into it, the room would quickly become messy. It would exist in a very disordered state, one of high entropy. Energy must be put into the system, in the form of the student doing work and putting everything away, in order to bring the room back to a state of cleanliness and order. This state is one of low entropy. Similarly, a car or house must be constantly maintained with work in order to keep it in an ordered state. Left alone, the entropy of the house or car gradually increases through rust and degradation. Molecules and chemical reactions have varying amounts of entropy as well. For example, as chemical reactions reach a state of equilibrium, entropy increases, and as molecules at a high concentration in one place diffuse and spread out, entropy also increases.

scientific method CONNECTION

Transfer of Energy and the Resulting Entropy

Set up a simple experiment to understand how energy is transferred and how a change in entropy results.

1. Take a block of ice. This is water in solid form, so it has a high structural order. This means that the molecules cannot move very much and are in a fixed position. The temperature of the ice is 0°C. As a result, the entropy of the system is low.
2. Allow the ice to melt at room temperature. What is the state of molecules in the liquid water now? How did the energy transfer take place? Is the entropy of the system higher or lower? Why?
3. Heat the water to its boiling point. What happens to the entropy of the system when the water is heated?

All physical systems can be thought of in this way: Living things are highly ordered, requiring constant energy input to be maintained in a state of low entropy. As living systems take in energy-storing molecules and transform them through chemical reactions, they lose some amount of usable energy in the process, because no reaction is completely efficient. They also produce waste and by-products that aren't useful energy sources. This process increases the entropy of the system's surroundings. Since all energy transfers result in the loss of some usable energy, the second law of thermodynamics states that every energy transfer or transformation increases the entropy of the universe. Even though living things are highly ordered and maintain a state of low entropy, the entropy of the universe in total is constantly increasing due to the loss of usable energy with each energy transfer that occurs. Essentially, living things are in a continuous uphill battle against this constant increase in universal entropy.

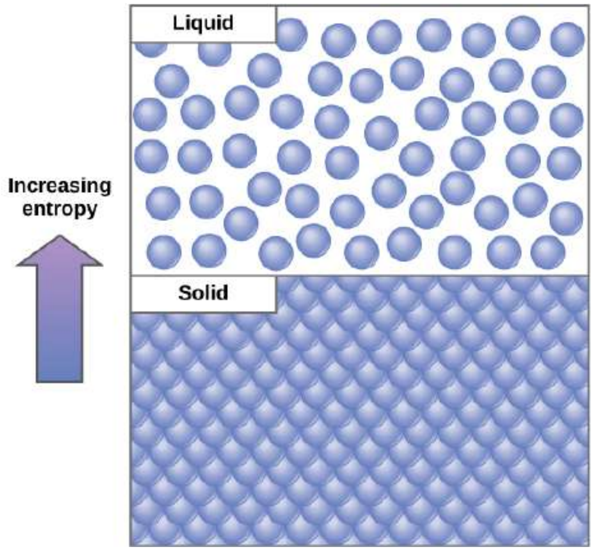


Figure 6.12 Entropy is a measure of randomness or disorder in a system. Gases have higher entropy than liquids, and liquids have higher entropy than solids.

science practices CONNECTION for AP® Courses

Think About It

- Imagine a large ant colony with an elaborate nest, containing many tunnels and passageways. Now imagine that an earthquake shakes the ground and demolishes the nest. Did the ant nest have higher entropy before or after the earthquake? What can the ants do to restore their nest to close to its original amount of entropy? Explain your answers.
- Energy transfers take place constantly in everyday activities. Think of two scenarios: cooking on a stove and driving a car. Explain how the second law of thermodynamics applies to these two scenarios.

Section Summary

In studying energy, scientists use the term “system” to refer to the matter and its environment involved in energy transfers. Everything outside of the system is called the surroundings. Single cells are biological systems. Systems can be thought of as having a certain amount of order. It takes energy to make a system more ordered. The more ordered a system is, the lower its entropy. Entropy is a measure of the disorder of a system. As a system becomes more disordered, the lower its energy and the higher its entropy become.

A series of laws, called the laws of thermodynamics, describe the properties and processes of energy transfer. The first law states that the total amount of energy in the universe is constant. This means that energy can’t be created or destroyed, only transferred or transformed. The second law of thermodynamics states that every energy transfer involves some loss of energy in an unusable form, such as heat energy, resulting in a more disordered system. In other words, no energy transfer is completely efficient and tends toward disorder.

6.4 | ATP: Adenosine Triphosphate

In this section, you will explore the following questions:

- Why is ATP considered the energy currency of the cell?
- How is energy released through the hydrolysis of ATP?

Connection for AP® Courses

Adenosine triphosphate or ATP is the energy “currency” or carrier of the cell. When cells require an input of energy, they use ATP. An ATP nucleotide molecule consists of a five-carbon sugar, the nitrogenous base adenine, and three phosphate groups. (Do not confuse ATP with the nucleotides of DNA and RNA, although they have structural similarities.) The bonds that connect the phosphate have high-energy content, and the energy released from the hydrolysis of ATP to ADP + P_i (Adenosine Diphosphate + Pyrophosphate) is used to perform cellular work, such as contracting a muscle or pumping a solute across a cell membrane in active transport. Cells use ATP by coupling the exergonic reaction of ATP hydrolysis with endergonic reactions, with ATP donating its phosphate group to another molecule via a process called phosphorylation. The phosphorylated molecule is at a higher energy state and is less stable than its unphosphorylated form and free energy is released to substrates to perform work during this process. Phosphorylation is an example of energy transfer between molecules.

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined in Big Idea 2 of the AP® Biology Curriculum Framework. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® Exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 2	Biological systems utilize free energy and molecular building blocks to grow, to reproduce, and to maintain dynamic homeostasis.
Enduring Understanding 2.A	Growth, reproduction and maintenance of living systems require free energy and matter.
Essential Knowledge	**2.A.1** All living systems require constant input of free energy.
Science Practice	**6.2** The student can construct explanations of phenomena based on evidence produced through scientific practices.
Learning Objective	**2.1** The student is able to explain how biological systems use free energy based on empirical data that all organisms require constant energy input to maintain organization, to grow, and to reproduce.

The Science Practices Assessment Ancillary contains additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.2][APLO 4.14][APLO 2.7][APLO 2.35]

Even exergonic, energy-releasing reactions require a small amount of activation energy in order to proceed. However, consider endergonic reactions, which require much more energy input, because their products have more free energy than their reactants. Within the cell, where does energy to power such reactions come from? The answer lies with an energy-supplying molecule called **adenosine triphosphate**, or **ATP**. ATP is a small, relatively simple molecule (**Figure 6.13**), but within some of its bonds, it contains the potential for a quick burst of energy that can be harnessed to perform cellular work. This molecule can be thought of as the primary energy currency of cells in much the same way that money is the currency that people exchange for things they need. ATP is used to power the majority of energy-requiring cellular reactions.

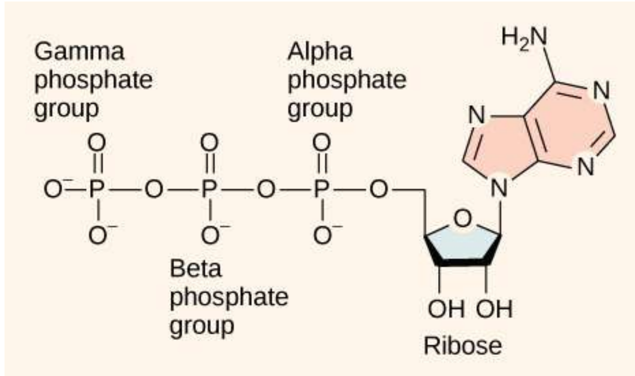


Figure 6.13 ATP is the primary energy currency of the cell. It has an adenosine backbone with three phosphate groups attached.

As its name suggests, adenosine triphosphate is comprised of adenosine bound to three phosphate groups (Figure 6.13). Adenosine is a nucleoside consisting of the nitrogenous base adenine and a five-carbon sugar, ribose. The three phosphate groups, in order of closest to furthest from the ribose sugar, are labeled alpha, beta, and gamma. Together, these chemical groups constitute an energy powerhouse. However, not all bonds within this molecule exist in a particularly high-energy state. Both bonds that link the phosphates are equally high-energy bonds (**phosphoanhydride bonds**) that, when broken, release sufficient energy to power a variety of cellular reactions and processes. These high-energy bonds are the bonds between the second and third (or beta and gamma) phosphate groups and between the first and second phosphate groups. The reason that these bonds are considered “high-energy” is because the products of such bond breaking—adenosine diphosphate (ADP) and one inorganic phosphate group (P_i)—have considerably lower free energy than the reactants: ATP and a water molecule. Because this reaction takes place with the use of a water molecule, it is considered a hydrolysis reaction. In other words, ATP is hydrolyzed into ADP in the following reaction:

$$\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_\text{i} + \text{free energy}$$

Like most chemical reactions, the hydrolysis of ATP to ADP is reversible. The reverse reaction regenerates ATP from ADP + P_i. Indeed, cells rely on the regeneration of ATP just as people rely on the regeneration of spent money through some sort of income. Since ATP hydrolysis releases energy, ATP regeneration must require an input of free energy. The formation of ATP is expressed in this equation:

$$\text{ADP} + \text{P}_\text{i} + \text{free energy} \rightarrow \text{ATP} + \text{H}_2\text{O}$$

Two prominent questions remain with regard to the use of ATP as an energy source. Exactly how much free energy is released with the hydrolysis of ATP, and how is that free energy used to do cellular work? The calculated ΔG for the hydrolysis of one mole of ATP into ADP and P_i is −7.3 kcal/mole (−30.5 kJ/mol). Since this calculation is true under standard conditions, it would be expected that a different value exists under cellular conditions. In fact, the ΔG for the hydrolysis of one mole of ATP in a living cell is almost double the value at standard conditions: -14 kcal/mol (−57 kJ/mol).

ATP is a highly unstable molecule. Unless quickly used to perform work, ATP spontaneously dissociates into ADP + P_i, and the free energy released during this process is lost as heat. The second question posed above, that is, how the energy released by ATP hydrolysis is used to perform work inside the cell, depends on a strategy called energy coupling. Cells couple the exergonic reaction of ATP hydrolysis with endergonic reactions, allowing them to proceed. One example of energy coupling using ATP involves a transmembrane ion pump that is extremely important for cellular function. This sodium-potassium pump (Na^+/K^+ pump) drives sodium out of the cell and potassium into the cell (Figure 6.14). A large percentage of a cell’s ATP is spent powering this pump, because cellular processes bring a great deal of sodium into the cell and potassium out of the cell. The pump works constantly to stabilize cellular concentrations of sodium and potassium. In order for the pump to turn one cycle (exporting three Na+ ions and importing two K^+ ions), one molecule of ATP must be hydrolyzed. When ATP is hydrolyzed, its gamma phosphate doesn’t simply float away, but is actually transferred onto the pump protein. This process of a phosphate group binding to a molecule is called phosphorylation. As with most cases of ATP hydrolysis, a phosphate from ATP is transferred onto another molecule. In a phosphorylated state, the Na^+/K^+ pump has more free energy and is triggered to undergo a conformational change. This change allows it to release Na^+ to the outside of the cell. It then binds extracellular K^+, which, through another conformational change, causes the phosphate to detach from the pump. This release of phosphate triggers the K^+ to be released to the inside of the cell. Essentially, the energy released from the hydrolysis of ATP is coupled with the energy required to power the pump and transport Na^+ and K^+ ions. ATP performs cellular work using this basic form of energy coupling through phosphorylation.

visual CONNECTION

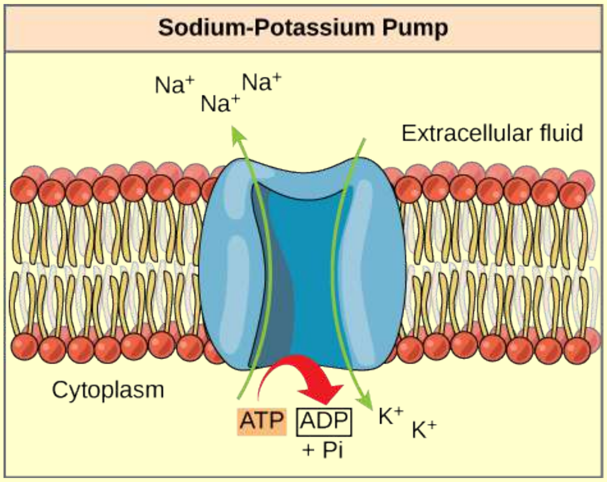


Figure 6.14 The sodium-potassium pump is an example of energy coupling. The energy derived from exergonic ATP hydrolysis is used to pump sodium and potassium ions across the cell membrane.

The hydrolysis of one ATP molecule releases $7.3\ \text{kcal/mol}$ of energy ($\Delta G = -7.3\ \text{kcal/mol}$ of energy). If it takes $2.1\ \text{kcal/mol}$ of energy to move one Na^+ across the membrane ($\Delta G = +2.1\ \text{kcal/mol}$ of energy), what is the maximum number of sodium ions that could be moved by the hydrolysis of one ATP molecule?

a. five
b. four
c. three
d. two

Often during cellular metabolic reactions, such as the synthesis and breakdown of nutrients, certain molecules must be altered slightly in their conformation to become substrates for the next step in the reaction series. One example is during the very first steps of cellular respiration, when a molecule of the sugar glucose is broken down in the process of glycolysis. In the first step of this process, ATP is required for the phosphorylation of glucose, creating a high-energy but unstable intermediate. This phosphorylation reaction powers a conformational change that allows the phosphorylated glucose molecule to be converted to the phosphorylated sugar fructose. Fructose is a necessary intermediate for glycolysis to move forward. Here, the exergonic reaction of ATP hydrolysis is coupled with the endergonic reaction of converting glucose into a phosphorylated intermediate in the pathway. Once again, the energy released by breaking a phosphate bond within ATP was used for the phosphorylation of another molecule, creating an unstable intermediate and powering an important conformational change.

LINK TO LEARNING

See an interactive animation of the ATP-producing glycolysis process at this **site (http://openstaxcollege.org/l/glycolysis_stgs)** .

Explain why the lock-and-key model does not adequately represent the relationship between hexokinase and glucose.

a. Hexokinase changes conformation in presence of glucose

b. Hexokinase induces change in the glucose structure

c. Hexokinase requires an effector molecule to bind at allosteric site

d. Hexokinase binds glucose without any conformational change

science practices CONNECTION for AP® Courses

Think About It

The hydrolysis of one ATP molecules releases 7.3 kcal/mol of energy (ΔG = –7.3 kcal/mol energy). If it takes 2.1 kcal/mol of energy to move one Na^+ across the membrane (ΔG = +2.1 kcal/mol of energy), how many sodium ions could be moved by the hydrolysis of one ATP molecule?

Section Summary

ATP is the primary energy-supplying molecule for living cells. ATP is made up of a nucleotide, a five-carbon sugar, and three phosphate groups. The bonds that connect the phosphates (phosphoanhydride bonds) have high-energy content. The energy released from the hydrolysis of ATP into ADP + P_i is used to perform cellular work. Cells use ATP to perform work by coupling the exergonic reaction of ATP hydrolysis with endergonic reactions. ATP donates its phosphate group to another molecule via a process known as phosphorylation. The phosphorylated molecule is at a higher-energy state and is less stable than its unphosphorylated form, and this added energy from the addition of the phosphate allows the molecule to undergo its endergonic reaction.

6.5 | Enzymes

In this section, you will explore the following questions:

- What is the role of enzymes in metabolic pathways?
- How do enzymes function as molecular catalysts?

Connection for AP® Courses

Many chemical reactions in cells occur spontaneously, but happen too slowly to meet the needs of a cell. For example, a teaspoon of sucrose (table sugar), a disaccharide, in a glass of iced tea will take time to break down into two monosaccharides, glucose and fructose; however, if you add a small amount of the enzyme sucrase to the tea, sucrose breaks down almost immediately. Sucrase is an example of an enzyme, a type of biological catalyst. Enzymes are macromolecules—most often proteins—that speed up chemical reactions by lowering activation energy barriers. Enzymes are very specific for the reactions they catalyze; because they are polypeptides, enzymes can have a variety of shapes attributed to interactions among amino acid R-groups. One part of the enzyme, the active site, interacts with the substrate via the induced fit model of interaction. Substrate binding alters the shape of the enzyme to facilitate the chemical reaction in several different ways, including bringing substrates together in an optimal orientation. After the reaction finishes, the product(s) are released, and the active site returns to its original shape.

Enzyme activity, and thus the rate of an enzyme-catalyzed reaction, is regulated by environmental conditions, including the amount of substrate, temperature, pH, and the presence of coenzymes, cofactors, activators, and inhibitors. Inhibitors, coenzymes, and cofactors can act competitively by binding to the enzyme's active site, or noncompetitively by binding to the enzyme's allosteric site. An allosteric site is an alternate part of the enzyme that can bind to non–substrate molecules. Enzymes work most efficiently under optimal conditions that are specific to the enzyme. For example, trypsin, an enzyme in the human small intestine, works most efficiently at pH 8, whereas pepsin in the stomach works best under acidic conditions. Sometimes environmental factors, especially low pH and high temperatures, alter the shape of the active site; if the shape cannot be restored, the enzyme denatures. The most common method of enzyme regulation in metabolic pathways is via feedback inhibition.

How can various factors, such as feedback inhibition, regulate enzyme activity?

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined in Big Idea 4 of the AP® Biology Curriculum Framework. The learning objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® Exam questions. A Learning Objective merges required content with one or more of the seven science practices.

Big Idea 4	Biological systems interact, and these systems and their interactions possess complex properties.
Enduring Understanding 4.B	Competition and cooperation are important aspects of biological systems.
Essential Knowledge	**4.B.1** Interactions between molecules affect their structure and function.
Science Practice	**5.1** The student can analyze data to identify patterns or relationships.
Learning Objective	**4.17** The student is able to analyze data to identify how molecular interactions affect structure and function.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.15][APLO 4.8][APLO 2.16]

A substance that helps a chemical reaction to occur is a catalyst, and the special molecules that catalyze biochemical reactions are called enzymes. Almost all enzymes are proteins, made up of chains of amino acids, and they perform the critical task of lowering the activation energies of chemical reactions inside the cell. Enzymes do this by binding to the reactant molecules, and holding them in such a way as to make the chemical bond-breaking and bond-forming processes take place more readily. It is important to remember that enzymes don't change the ΔG of a reaction. In other words, they don't change whether a reaction is exergonic (spontaneous) or endergonic. This is because they don't change the free energy of the reactants or products. They only reduce the activation energy required to reach the transition state (**Figure 6.15**).

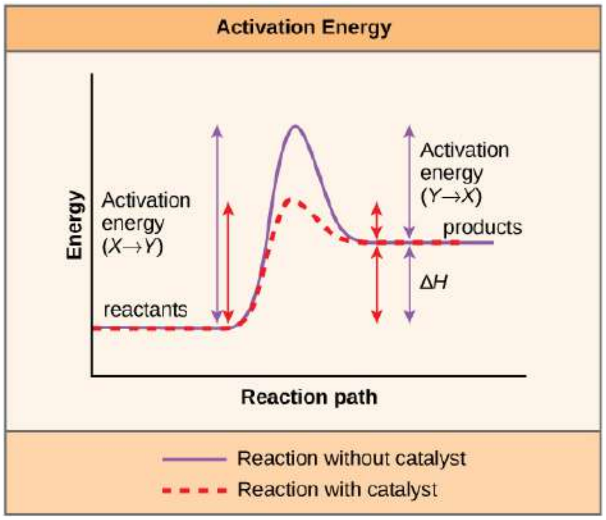


Figure 6.15 Enzymes lower the activation energy of the reaction but do not change the free energy of the reaction.

Enzyme Active Site and Substrate Specificity

The chemical reactants to which an enzyme binds are the enzyme's **substrates**. There may be one or more substrates, depending on the particular chemical reaction. In some reactions, a single-reactant substrate is broken down into multiple products. In others, two substrates may come together to create one larger molecule. Two reactants might also enter a reaction, both become modified, and leave the reaction as two products. The location within the enzyme where the substrate binds is called the enzyme's **active site**. The active site is where the "action" happens, so to speak. Since enzymes are proteins, there is a unique combination of amino acid residues (also called side chains, or R groups) within the active site. Each residue is characterized by different properties. Residues can be large or small, weakly acidic or basic, hydrophilic or hydrophobic, positively or negatively charged, or neutral. The unique combination of amino acid residues, their positions, sequences, structures, and properties, creates a very specific chemical environment within the active site. This specific environment is suited to bind, albeit briefly, to a specific chemical substrate (or substrates). Due to this jigsaw puzzle-like match between an enzyme and its substrates (which adapts to find the best fit between the transition state and the active site), enzymes are known for their specificity. The "best fit" results from the shape and the amino acid functional group's attraction to the substrate. There is a specifically matched enzyme for each substrate and, thus, for each chemical reaction; however, there is flexibility as well.

The fact that active sites are so perfectly suited to provide specific environmental conditions also means that they are subject to influences by the local environment. It is true that increasing the environmental temperature generally increases reaction rates, enzyme-catalyzed or otherwise. However, increasing or decreasing the temperature outside of an optimal range can affect chemical bonds within the active site in such a way that they are less well suited to bind substrates. High temperatures will eventually cause enzymes, like other biological molecules, to **denature**, a process that changes the natural properties of a substance. Likewise, the pH of the local environment can also affect enzyme function. Active site amino acid residues have their own acidic or basic properties that are optimal for catalysis. These residues are sensitive to changes in pH that can impair the way substrate molecules bind. Enzymes are suited to function best within a certain pH range, and, as with temperature, extreme pH values (acidic or basic) of the environment can cause enzymes to denature.

Induced Fit and Enzyme Function

For many years, scientists thought that enzyme-substrate binding took place in a simple "lock-and-key" fashion. This model asserted that the enzyme and substrate fit together perfectly in one instantaneous step. However, current research supports a more refined view called **induced fit** (**Figure 6.16**). The induced-fit model expands upon the lock-and-key model by describing a more dynamic interaction between enzyme and substrate. As the enzyme and substrate come together, their interaction causes a mild shift in the enzyme's structure that confirms an ideal binding arrangement between the enzyme and the transition state of the substrate. This ideal binding maximizes the enzyme's ability to catalyze its reaction.

LINK TO LEARNING

View an animation of induced fit at **this website (http://openstaxcollege.org/l/hexokinase)** .

Phosphofructokinase deficiency occurs when a person lacks an enzyme needed to perform glycolysis in skeletal muscles. What effect could this have on the body?

a. Production of energy by glycolysis will occur, skeletal muscles will function properly

b. Production of energy by glycolysis will not occur, skeletal muscles will function properly

c. Production of energy by glycolysis will occur, skeletal muscles will not function properly

d. Production of energy will not occur, skeletal muscles will not function properly

When an enzyme binds its substrate, an enzyme-substrate complex is formed. This complex lowers the activation energy of the reaction and promotes its rapid progression in one of many ways. On a basic level, enzymes promote chemical reactions that involve more than one substrate by bringing the substrates together in an optimal orientation. The appropriate region (atoms and bonds) of one molecule is juxtaposed to the appropriate region of the other molecule with which it must react. Another way in which enzymes promote the reaction of their substrates is by creating an optimal environment within the active site for the reaction to occur. Certain chemical reactions might proceed best in a slightly acidic or non-polar environment. The chemical properties that emerge from the particular arrangement of amino acid residues within an active site create the perfect environment for an enzyme’s specific substrates to react.

You’ve learned that the activation energy required for many reactions includes the energy involved in manipulating or slightly contorting chemical bonds so that they can easily break and allow others to reform. Enzymatic action can aid this process. The enzyme-substrate complex can lower the activation energy by contorting substrate molecules in such a way as to facilitate bond-breaking, helping to reach the transition state. Finally, enzymes can also lower activation energies by taking part in the chemical reaction itself. The amino acid residues can provide certain ions or chemical groups that actually form covalent bonds with substrate molecules as a necessary step of the reaction process. In these cases, it is important to remember that the enzyme will always return to its original state at the completion of the reaction. One of the hallmark properties of enzymes is that they remain ultimately unchanged by the reactions they catalyze. After an enzyme is done catalyzing a reaction, it releases its product(s).

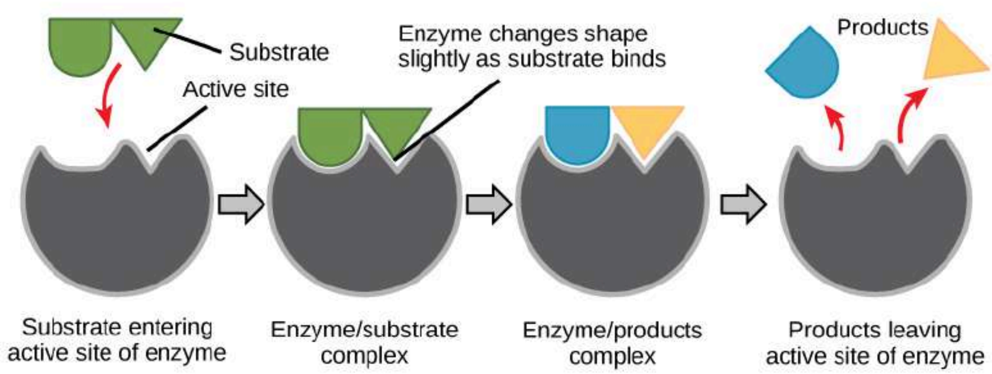


Figure 6.16 According to the induced-fit model, both enzyme and substrate undergo dynamic conformational changes upon binding. The enzyme contorts the substrate into its transition state, thereby increasing the rate of the reaction.

science practices CONNECTION for AP® Courses

Activity

AP Biology Investigation 13: Enzyme Activity. This investigation allows you to design and conduct experiments to explore the effects of environmental variables, such as temperature and pH, on the rates of enzymatic reactions.

Control of Metabolism Through Enzyme Regulation

It would seem ideal to have a scenario in which all of the enzymes encoded in an organism's genome existed in abundant supply and functioned optimally under all cellular conditions, in all cells, at all times. In reality, this is far from the case. A variety of mechanisms ensure that this does not happen. Cellular needs and conditions vary from cell to cell, and change within individual cells over time. The required enzymes and energetic demands of stomach cells are different from those of fat storage cells, skin cells, blood cells, and nerve cells. Furthermore, a digestive cell works much harder to process and break down nutrients during the time that closely follows a meal compared with many hours after a meal. As these cellular demands and conditions vary, so do the amounts and functionality of different enzymes.

Since the rates of biochemical reactions are controlled by activation energy, and enzymes lower and determine activation energies for chemical reactions, the relative amounts and functioning of the variety of enzymes within a cell ultimately determine which reactions will proceed and at which rates. This determination is tightly controlled. In certain cellular environments, enzyme activity is partly controlled by environmental factors, like pH and temperature. There are other mechanisms through which cells control the activity of enzymes and determine the rates at which various biochemical reactions will occur.

Regulation of Enzymes by Molecules

Enzymes can be regulated in ways that either promote or reduce their activity. There are many different kinds of molecules that inhibit or promote enzyme function, and various mechanisms exist for doing so. In some cases of enzyme inhibition, for example, an inhibitor molecule is similar enough to a substrate that it can bind to the active site and simply block the substrate from binding. When this happens, the enzyme is inhibited through **competitive inhibition**, because an inhibitor molecule competes with the substrate for active site binding (**Figure 6.17**). On the other hand, in noncompetitive inhibition, an inhibitor molecule binds to the enzyme in a location other than an allosteric site and still manages to block substrate binding to the active site.

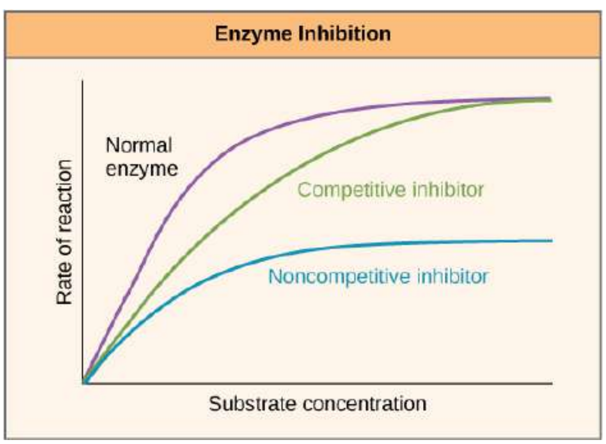


Figure 6.17 Competitive and noncompetitive inhibition affect the rate of reaction differently. Competitive inhibitors affect the initial rate but do not affect the maximal rate, whereas noncompetitive inhibitors affect the maximal rate.

Some inhibitor molecules bind to enzymes in a location where their binding induces a conformational change that reduces the affinity of the enzyme for its substrate. This type of inhibition is called **allosteric inhibition** (**Figure 6.18**). Most allosterically regulated enzymes are made up of more than one polypeptide, meaning that they have more than one protein subunit. When an allosteric inhibitor binds to an enzyme, all active sites on the protein subunits are changed slightly such that they bind their substrates with less efficiency. There are allosteric activators as well as inhibitors. Allosteric activators bind to locations on an enzyme away from the active site, inducing a conformational change that increases the affinity of the enzyme's active site(s) for its substrate(s).

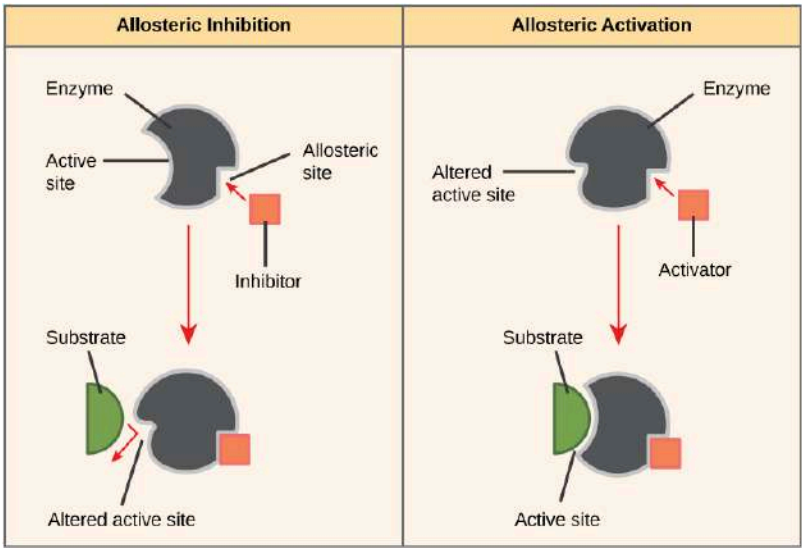


Figure 6.18 Allosteric inhibitors modify the active site of the enzyme so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the active site of the enzyme so that the affinity for the substrate increases.

everyday CONNECTION

Figure 6.19 Have you ever wondered how pharmaceutical drugs are developed? (credit: Deborah Austin)

Drug Discovery by Looking for Inhibitors of Key Enzymes in Specific Pathways

Enzymes are key components of metabolic pathways. Understanding how enzymes work and how they can be regulated is a key principle behind the development of many of the pharmaceutical drugs (**Figure 6.19**) on the market today. Biologists working in this field collaborate with other scientists, usually chemists, to design drugs.

Consider statins for example—which is the name given to the class of drugs that reduces cholesterol levels. These compounds are essentially inhibitors of the enzyme HMG-CoA reductase. HMG-CoA reductase is the enzyme that synthesizes cholesterol from lipids in the body. By inhibiting this enzyme, the levels of cholesterol synthesized in the body can be reduced. Similarly, acetaminophen is an inhibitor of the enzyme cyclooxygenase. While it is effective in providing relief from fever and inflammation (pain), its mechanism of action is still not completely understood.

How are drugs developed? One of the first challenges in drug development is identifying the specific molecule that the drug is intended to target. In the case of statins, HMG-CoA reductase is the drug target. Drug targets are identified through painstaking research in the laboratory. Identifying the target alone is not sufficient; scientists also need to know how the target acts inside the cell and which reactions go awry in the case of disease. Once the target and the pathway are identified, then the actual process of drug design begins. During this stage, chemists and biologists work together to design and synthesize molecules that can either block or activate a particular reaction. However, this is only the beginning: both if and when a drug prototype is successful in performing its function, then it must undergo many tests from *in vitro* experiments to clinical trials before it can get FDA approval to be on the market.

Statins reduce the level of cholesterol in the blood. Based on the everyday connection, which of the following might also reduce cholesterol levels in the blood?

a. a drug that increases HMG-CoA reductase levels
b. a drug that reduces cyclooxygenase levels
c. a drug that reduces lipid levels in the body
d. a drug that blocks the action of acetaminophen

Many enzymes don’t work optimally, or even at all, unless bound to other specific non-protein helper molecules, either temporarily through ionic or hydrogen bonds or permanently through stronger covalent bonds. Two types of helper molecules are **cofactors** and **coenzymes**. Binding to these molecules promotes optimal conformation and function for their respective enzymes. Cofactors are inorganic ions such as iron (Fe^{++}) and magnesium (Mg^{++}). One example of an enzyme that requires a metal ion as a cofactor is the enzyme that builds DNA molecules, DNA polymerase, which requires a bound zinc ion (Zn^{++}) to function. Coenzymes are organic helper molecules, with a basic atomic structure made up of carbon and hydrogen, which are required for enzyme action. The most common sources of coenzymes are dietary vitamins (**Figure 6.20**). Some vitamins are precursors to coenzymes and others act directly as coenzymes. Vitamin C is a coenzyme for multiple enzymes that take part in building the important connective tissue component, collagen. An important step in the breakdown of glucose to yield energy is catalysis by a multi-enzyme complex called pyruvate dehydrogenase. Pyruvate dehydrogenase is a complex of several enzymes that actually requires one cofactor (a magnesium ion) and five different organic coenzymes to catalyze its specific chemical reaction. Therefore, enzyme function is, in part, regulated by an abundance of various cofactors and coenzymes, which are supplied primarily by the diets of most organisms.

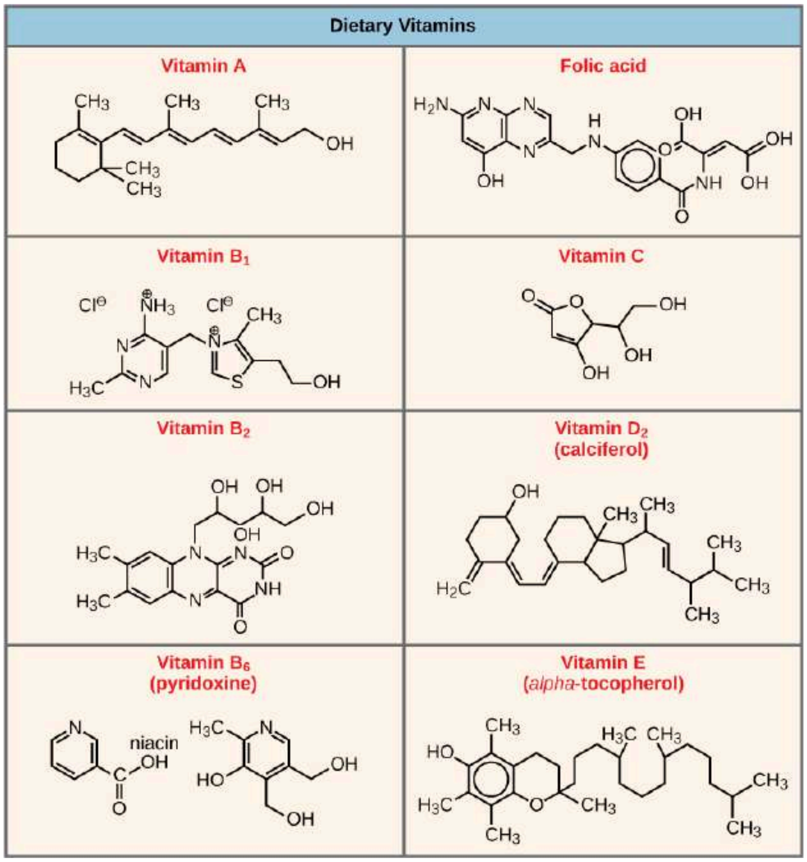


Figure 6.20 Vitamins are important coenzymes or precursors of coenzymes, and are required for enzymes to function properly. Multivitamin capsules usually contain mixtures of all the vitamins at different percentages.

Enzyme Compartmentalization

In eukaryotic cells, molecules such as enzymes are usually compartmentalized into different organelles. This allows for yet another level of regulation of enzyme activity. Enzymes required only for certain cellular processes can be housed separately along with their substrates, allowing for more efficient chemical reactions. Examples of this sort of enzyme regulation based on location and proximity include the enzymes involved in the latter stages of cellular respiration, which take place exclusively in the mitochondria, and the enzymes involved in the digestion of cellular debris and foreign materials, located within lysosomes.

Feedback Inhibition in Metabolic Pathways

Molecules can regulate enzyme function in many ways. A major question remains, however: What are these molecules and where do they come from? Some are cofactors and coenzymes, ions, and organic molecules, as you've learned. What other molecules in the cell provide enzymatic regulation, such as allosteric modulation, and competitive and noncompetitive inhibition? The answer is that a wide variety of molecules can perform these roles. Some of these molecules include pharmaceutical and non-pharmaceutical drugs, toxins, and poisons from the environment. Perhaps the most relevant sources of enzyme regulatory molecules, with respect to cellular metabolism, are the products of the cellular metabolic reactions themselves. In a most efficient and elegant way, cells have evolved to use the products of their own reactions for feedback inhibition of enzyme activity. **Feedback inhibition** involves the use of a reaction product to regulate its own further production (**Figure 6.21**). The cell responds to the abundance of specific products by slowing down production during anabolic or catabolic reactions. Such reaction products may inhibit the enzymes that catalyzed their production through the mechanisms described above.

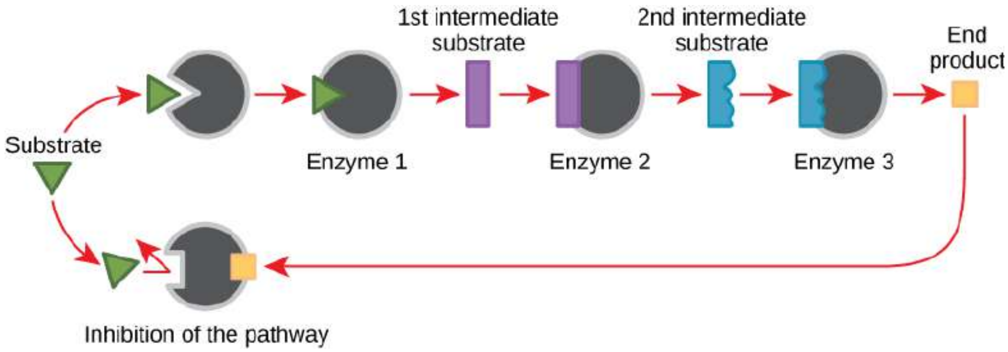


Figure 6.21 Metabolic pathways are a series of reactions catalyzed by multiple enzymes. Feedback inhibition, where the end product of the pathway inhibits an upstream step, is an important regulatory mechanism in cells.

The production of both amino acids and nucleotides is controlled through feedback inhibition. Additionally, ATP is an allosteric regulator of some of the enzymes involved in the catabolic breakdown of sugar, the process that produces ATP. In this way, when ATP is abundant, the cell can prevent its further production. Remember that ATP is an unstable molecule that can spontaneously dissociate into ADP. If too much ATP were present in a cell, much of it would go to waste. On the other hand, ADP serves as a positive allosteric regulator (an allosteric activator) for some of the same enzymes that are inhibited by ATP. Thus, when relative levels of ADP are high compared to ATP, the cell is triggered to produce more ATP through the catabolism of sugar.

Section Summary

Enzymes are chemical catalysts that accelerate chemical reactions at physiological temperatures by lowering their activation energy. Enzymes are usually proteins consisting of one or more polypeptide chains. Enzymes have an active site that provides a unique chemical environment, made up of certain amino acid R groups (residues). This unique environment is perfectly suited to convert particular chemical reactants for that enzyme, called substrates, into unstable intermediates called transition states. Enzymes and substrates are thought to bind with an induced fit, which means that enzymes undergo slight conformational adjustments upon substrate contact, leading to full, optimal binding. Enzymes bind to substrates and catalyze reactions in four different ways: bringing substrates together in an optimal orientation, compromising the bond structures of substrates so that bonds can be more easily broken, providing optimal environmental conditions for a reaction to occur, or participating directly in their chemical reaction by forming transient covalent bonds with the substrates.

Enzyme action must be regulated so that in a given cell at a given time, the desired reactions are being catalyzed and the undesired reactions are not. Enzymes are regulated by cellular conditions, such as temperature and pH. They are also regulated through their location within a cell, sometimes being compartmentalized so that they can only catalyze reactions under certain circumstances. Inhibition and activation of enzymes via other molecules are other important ways that enzymes are regulated. Inhibitors can act competitively, noncompetitively, or allosterically; noncompetitive inhibitors are usually allosteric. Activators can also enhance the function of enzymes allosterically. The most common method by which cells regulate the enzymes in metabolic pathways is through feedback inhibition. During feedback inhibition, the products of a metabolic pathway serve as inhibitors (usually allosteric) of one or more of the enzymes (usually the first committed enzyme of the pathway) involved in the pathway that produces them.

KEY TERMS

activation energy energy necessary for reactions to occur

active site specific region of the enzyme to which the substrate binds

allosteric inhibition inhibition by a binding event at a site different from the active site, which induces a conformational change and reduces the affinity of the enzyme for its substrate

anabolic (also, anabolism) pathways that require an input of energy to synthesize complex molecules from simpler ones

ATP adenosine triphosphate, the cell's energy currency

bioenergetics study of energy flowing through living systems

catabolic (also, catabolism) pathways in which complex molecules are broken down into simpler ones

chemical energy potential energy in chemical bonds that is released when those bonds are broken

coenzyme small organic molecule, such as a vitamin or its derivative, which is required to enhance the activity of an enzyme

cofactor inorganic ion, such as iron and magnesium ions, required for optimal regulation of enzyme activity

competitive inhibition type of inhibition in which the inhibitor competes with the substrate molecule by binding to the active site of the enzyme

denature process that changes the natural properties of a substance

endergonic describes chemical reactions that require energy input

enthalpy total energy of a system

entropy (S) measure of randomness or disorder within a system

exergonic describes chemical reactions that release free energy

feedback inhibition effect of a product of a reaction sequence to decrease its further production by inhibiting the activity of the first enzyme in the pathway that produces it

free energy Gibbs free energy is the usable energy, or energy that is available to do work.

heat energy energy transferred from one system to another that is not work (energy of the motion of molecules or particles)

heat energy total bond energy of reactants or products in a chemical reaction

induced fit dynamic fit between the enzyme and its substrate, in which both components modify their structures to allow for ideal binding

kinetic energy type of energy associated with objects or particles in motion

metabolism all the chemical reactions that take place inside cells, including anabolism and catabolism

phosphoanhydride bond bond that connects phosphates in an ATP molecule

potential energy type of energy that has the potential to do work; stored energy

substrate molecule on which the enzyme acts

thermodynamics study of energy and energy transfer involving physical matter

transition state high-energy, unstable state (an intermediate form between the substrate and the product) occurring during a chemical reaction

CHAPTER SUMMARY

6.1 Energy and Metabolism

Cells perform the functions of life through various chemical reactions. A cell's metabolism refers to the chemical reactions that take place within it. There are metabolic reactions that involve the breaking down of complex chemicals into simpler ones, such as the breakdown of large macromolecules. This process is referred to as catabolism, and such reactions are associated with a release of energy. On the other end of the spectrum, anabolism refers to metabolic processes that build complex molecules out of simpler ones, such as the synthesis of macromolecules. Anabolic processes require energy. Glucose synthesis and glucose breakdown are examples of anabolic and catabolic pathways, respectively.

6.2 Potential, Kinetic, Free, and Activation Energy

Energy comes in many different forms. Objects in motion do physical work, and kinetic energy is the energy of objects in motion. Objects that are not in motion may have the potential to do work, and thus, have potential energy. Molecules also have potential energy because the breaking of molecular bonds has the potential to release energy. Living cells depend on the harvesting of potential energy from molecular bonds to perform work. Free energy is a measure of energy that is available to do work. The free energy of a system changes during energy transfers such as chemical reactions, and this change is referred to as ΔG.

The ΔG of a reaction can be negative or positive, meaning that the reaction releases energy or consumes energy, respectively. A reaction with a negative ΔG that gives off energy is called an exergonic reaction. One with a positive ΔG that requires energy input is called an endergonic reaction. Exergonic reactions are said to be spontaneous, because their products have less energy than their reactants. The products of endergonic reactions have a higher energy state than the reactants, and so these are nonspontaneous reactions. However, all reactions (including spontaneous $-\Delta G$ reactions) require an initial input of energy in order to reach the transition state, at which they'll proceed. This initial input of energy is called the activation energy.

6.3 The Laws of Thermodynamics

In studying energy, scientists use the term "system" to refer to the matter and its environment involved in energy transfers. Everything outside of the system is called the surroundings. Single cells are biological systems. Systems can be thought of as having a certain amount of order. It takes energy to make a system more ordered. The more ordered a system is, the lower its entropy. Entropy is a measure of the disorder of a system. As a system becomes more disordered, the lower its energy and the higher its entropy become.

A series of laws, called the laws of thermodynamics, describe the properties and processes of energy transfer. The first law states that the total amount of energy in the universe is constant. This means that energy can't be created or destroyed, only transferred or transformed. The second law of thermodynamics states that every energy transfer involves some loss of energy in an unusable form, such as heat energy, resulting in a more disordered system. In other words, no energy transfer is completely efficient and tends toward disorder.

6.4 ATP: Adenosine Triphosphate

ATP is the primary energy-supplying molecule for living cells. ATP is made up of a nucleotide, a five-carbon sugar, and three phosphate groups. The bonds that connect the phosphates (phosphoanhydride bonds) have high-energy content. The energy released from the hydrolysis of ATP into ADP + P_i is used to perform cellular work. Cells use ATP to perform work by coupling the exergonic reaction of ATP hydrolysis with endergonic reactions. ATP donates its phosphate group to another molecule via a process known as phosphorylation. The phosphorylated molecule is at a higher-energy state and is less stable than its unphosphorylated form, and this added energy from the addition of the phosphate allows the molecule to undergo its endergonic reaction.

6.5 Enzymes

Enzymes are chemical catalysts that accelerate chemical reactions at physiological temperatures by lowering their activation energy. Enzymes are usually proteins consisting of one or more polypeptide chains. Enzymes have an active site that provides a unique chemical environment, made up of certain amino acid R groups (residues). This unique environment is perfectly suited to convert particular chemical reactants for that enzyme, called substrates, into unstable intermediates called transition states. Enzymes and substrates are thought to bind with an induced fit, which means that enzymes undergo slight conformational adjustments upon substrate contact, leading to full, optimal binding. Enzymes bind to substrates and catalyze reactions in four different ways: bringing substrates together in an optimal orientation, compromising the bond structures of substrates so that bonds can be more easily broken, providing optimal environmental conditions for a reaction to occur, or participating directly in their chemical reaction by forming transient covalent bonds with the substrates.

Enzyme action must be regulated so that in a given cell at a given time, the desired reactions are being catalyzed and the undesired reactions are not. Enzymes are regulated by cellular conditions, such as temperature and pH. They are also regulated through their location within a cell, sometimes being compartmentalized so that they can only catalyze reactions under certain circumstances. Inhibition and activation of enzymes via other molecules are other important ways that enzymes are regulated. Inhibitors can act competitively, noncompetitively, or allosterically; noncompetitive inhibitors are usually allosteric. Activators can also enhance the function of enzymes allosterically. The most common method by which cells regulate the enzymes in metabolic pathways is through feedback inhibition. During feedback inhibition, the products of a metabolic pathway serve as inhibitors (usually allosteric) of one or more of the enzymes (usually the first committed enzyme of the pathway) involved in the pathway that produces them.

REVIEW QUESTIONS

1. Energy can be taken in as glucose, then has to be converted to a form that can be easily used to perform work in cells. What is the name of the latter molecule?

a. anabolic molecules
b. cholesterol
c. electrolytes
d. adenosine triphosphate

2. When cellular respiration occurs, what is the primary molecule used to store the energy that is released?

a. AMP
b. ATP
c. mRNA
d. phosphate

3. DNA replication involves unwinding two strands of parent DNA, copying each strand to synthesize complementary strands and releasing the resulting two semi-conserved strands of DNA. Which of the following accurately describes this process?

a. This is an anabolic process.
b. This is a catabolic process.
c. This is both an anabolic and a catabolic process.
d. This is a metabolic process, but is neither anabolic nor catabolic.

4. Which of the following is a catabolic process?

a. digestion of sucrose
b. dissolving sugar in water
c. DNA replication
d. RNA translation

5. What food molecule used by animals for energy and obtained from plants is most directly related to the use of sun energy?

a. glucose
b. protein
c. triglycerides
d. tRNA

6. What reaction will release the largest amount of energy to help power another reaction?

a. AMP to ATP
b. ATP to ADP
c. DNA to proteins
d. glucose to starch

7. Consider a pendulum swinging. Which type(s) of energy is/are associated with the pendulum in the following instances:

1. the moment at which it completes one cycle, just before it begins to fall back towards the other end
2. the moment that it is in the middle between the two ends
3. just before it reaches the end of one cycle (before step 1)

a. 1. potential and kinetic
   2. potential and kinetic
   3. kinetic
b. 1. potential
   2. potential and kinetic
   3. potential and kinetic
c. 1. potential
   2. kinetic
   3. potential and kinetic
d. 1. potential and kinetic
   2. kinetic
   3. kinetic

8. Which of the following best describes energy?

a. the transfer of genetic information
b. the ability to assemble a large number of functional catalysts
c. the ability to store solar output
d. the ability to do work

9. What is the ultimate source of energy on this planet?

a. glucose
b. plants
c. metabolic pathways
d. the sun

10. Which of the following molecules is likely to have the most potential energy?

a. ATP
b. ADP
c. glucose
d. sucrose

11. Which of the following is the best way to judge the relative activation energies between two given chemical reactions?

a. Compare the ΔG values between the two reactions.
b. Compare their reaction rates.
c. Compare their ideal environmental conditions.
d. Compare the spontaneity between the two reactions.

12. Which of the terms in the Gibbs free energy equation denotes enthalpy?

a. ΔG
b. ΔH
c. ΔS
d. ΔT

13. Which chemical reaction is more likely to occur?

a. dehydration synthesis
b. endergonic
c. endothermic
d. exergonic

14. Which of the following comparisons or contrasts between endergonic and exergonic reactions is false?

a. Both endergonic and exergonic reactions require a small amount of energy to overcome an activation barrier.
b. Endergonic reactions have a positive ΔG and exergonic reactions have a negative ΔG.
c. Endergonic reactions consume energy and exergonic reactions release energy.
d. Endergonic reactions take place slowly and exergonic reactions take place quickly.

15. Label each of the following systems as high or low entropy:

1. perfume the instant after it is sprayed into the air
2. an unmaintained 1950s car compared with a brand new car
3. a living cell compared with a dead cell

a. 1. low
   2. high
   3. low
b. 1. low
   2. high
   3. high
c. 1. high
   2. low
   3. high
d. 1. high
   2. low
   3. low

16. What counteracts entropy?

a. energy release
b. endergonic reactions
c. input of energy
d. time

17. Which of the following is the best example of the first law of thermodynamics?

a. a body getting warmer after exercise
b. a piece of fruit spoiling in the fridge
c. a power plant burning coal and producing electricity
d. an exothermic chemical reaction

18. What is the difference between the first and second laws of thermodynamics?

a. The first law involves creating energy while the second law involves expending it.
b. The first law involves expending energy while the second involves creating it.
c. The first law involves conserving energy while the second law involves the inability to recapture energy.
d. The first law discusses creating energy while the second law discusses the energy requirement for reactions.

19. Which best describes the effect of inputting energy into a living system?

a. It decreases entropy within the system.
b. It fuels catabolic reactions.
c. It causes enthalpy.
d. The energy is used to produce carbohydrates.

20. Why is ATP considered the energy currency of the cell?

a. It accepts energy from chemical reactions.
b. It holds energy at the site of release from substrates.
c. It is a protein.
d. It can transport energy to locations within the cell.

21. What is ATP made from?

a. adenosine + high energy electrons
b. ADP + pyrophosphate
c. AMP + ADP
d. the conversion of guanine to adenosine

22. What is true about the energy released by the hydrolysis of ATP?

a. It is equal to $-57\,\text{kJ/mol}$.
b. The cell harnesses it as heat energy in order to perform work.
c. It is primarily stored between the alpha and beta phosphates.
d. It provides energy to coupled reactions.

23. What part of ATP is broken to release energy for use in chemical reactions?

a. the adenosine molecule
b. the bond between the first and second phosphates
c. the bond between the first phosphate and the adenosine molecule
d. the bond between the second and third phosphates

24. An allosteric inhibitor does which of the following?

a. binds to an enzyme away from the active site and changes the conformation of the active site, increasing its affinity for substrate binding
b. binds to an active site and blocks it from binding substrate
c. binds to an enzyme away from the active site and changes the conformation of the active site, decreasing its affinity for the substrate
d. binds directly to the active site and mimics the substrate

25. What happens if an enzyme is not functioning in a chemical reaction in a living organism that needs it?

a. The reaction stops.
b. The reaction proceeds, but much more slowly.
c. The reaction proceeds faster without the interference.
d. There is no change in the reaction rate.

26. Which of the following is not true about enzymes?

a. They increase the ΔG of reactions.
b. They are usually made of amino acids.
c. They lower the activation energy of chemical reactions.
d. Each one is specific to the particular substrate, or substrates, to which it binds.

27. Which of the following analogies best describe the induced-fit model of enzyme-substrate binding?

a. a hug between two people
b. a key fitting into a lock
c. a square peg fitting through the square hole and a round peg fitting through the round hole of a children’s toy
d. the fitting together of two jigsaw puzzle pieces

28. What is the function of enzymes?

a. to increase the ΔG of reactions
b. to increase the ΔH of reactions
c. to lower the entropy of the chemicals in the reaction
d. to lower the activation energy of a reaction

CRITICAL THINKING QUESTIONS

29. Describe the connection between anabolic and catabolic chemical reactions in a metabolic pathway.

a. Catabolic reactions produce energy and simpler compounds, whereas anabolic reactions involve the use of energy to make more complex compounds.
b. Catabolic reactions produce energy and complex compounds are formed, whereas in anabolic reactions free energy is utilized by complex compounds to make simpler molecules.
c. Catabolic reactions utilize energy and gives simpler compounds, whereas in anabolic reactions reactions, energy is produced and simpler compounds are used to make complex molecules.
d. Catabolic reactions produce energy and water molecules, whereas in anabolic reactions this free energy is utilized by simpler compounds to make only proteins and nucleic acids.

30. Does physical exercise involve anabolic processes, catabolic processes, or both? Give evidence for your answer.

a. Physical exercise involves both catabolic and anabolic processes. Glucose is broken down into simpler compounds during physical activity. The simpler compounds are then used to provide energy to the muscles for contraction by the anabolic pathway.
b. Physical exercise is just a catabolic process. Glucose is broken down into simpler compounds during physical activity and the simpler compounds are then used to provide energy to the muscles for contraction.
c. Physical activity involves only anabolic processes. Glucose is broken down into simpler compounds during physical activity and the simpler compounds are then used to provide energy to the muscles for contraction by anabolic pathways.
d. Physical exercise involves both anabolic and catabolic processes. Cellulose is broken down into simpler compounds during physical activity. The simpler compounds are then used to provide energy to the muscles for contraction by anabolic pathways.

31. How do chemical reactions play a role in energy transfer?

a. Energy from the breakdown of glucose and other molecules in animals is released as ATP, which transfer energy to other reactions.
b. Energy from the breakdown of glucose and other molecules in animals is released in the form of NADP, which transfers energy to other reactions.
c. Energy is released in the form of glucose from the breakdown of ATP molecules. These ATP molecules transfer energy from one reaction to other.
d. Energy is released in the form of water from the breakdown of glucose. These molecules transfer energy from one reaction to other.

32. Name two different cellular functions that require energy.

a. Phagocytosis helps amoebae take up nutrients and pseudopodia help the amoebae move.
b. Phagocytosis allows amoebae to move and pseudopodia help in the uptake of nutrients.
c. Phagocytosis helps amoebae to take up nutrients and cilia help amoebae move.
d. Phagocytosis helps amoebae in cell division and pseudopodia help amoebae move.

33. Explain the conversion of energy that takes place when the sluice of a dam is opened.

a. Potential energy stored in the water held by the dam will convert to kinetic energy when it falls through the opening of the sluice.
b. Kinetic energy stored in the water held by the dam will convert to potential energy when it falls through the opening of the sluice.
c. Potential energy stored in the water held by the dam will convert to electrical energy, when it falls through the opening of the sluice.
d. Hydrothermal energy stored in the water held by the dam will convert to kinetic energy, when it falls through the opening of the sluice.

34. Explain in your own words the difference between a spontaneous reaction and one that occurs instantaneously.

a. A spontaneous reaction is one which releases free energy and moves to a more stable state. Instantaneous reactions occur rapidly with sudden release of energy.
b. A spontaneous reaction is one which utilizes free energy and moves to a more stable state. Instantaneous reactions occur rapidly with sudden release of energy.
c. A spontaneous reaction is one which releases free energy and moves to a more stable state. Instantaneous reactions occur rapidly within a system by uptake of energy.
d. A spontaneous reaction is one in which the reaction occurs rapidly with sudden release of energy. Instantaneous reaction releases free energy and moves to a more stable state.

35. Describe the position of the transition state on a vertical energy scale, from low to high, relative to the position of the reactants and products, for both endergonic and exergonic reactions.

a. The transition state of the reaction exists at a lower energy level than the reactants. Activation energy is always positive regardless of whether the reaction is exergonic or endergonic.
b. The transition state of the reaction exists at a higher energy level than the reactants. Activation energy is always positive regardless of whether the reaction is exergonic or endergonic.
c. The transition state of the reaction exists at a lower energy level than the reactants. Activation energy is always negative regardless of whether the reaction is exergonic or endergonic.
d. The transition state of the reaction exists at an intermediate energy level than that of the reactants. Activation energy is always positive regardless of whether the reaction is exergonic or endergonic.

36. Imagine an elaborate ant farm with tunnels and passageways through the sand where ants live in a large community. Now imagine that an earthquake shook the ground and demolished the ant farm. In which of these two scenarios, before or after the earthquake, was the ant farm system in a state of higher or lower entropy? Why?

a. The ant farm is in the state of high entropy after the earthquake and energy must be spent to bring the system to low entropy.
b. The ant farm is in the state of lower entropy after the earthquake and energy must be spent to bring the system to high entropy.
c. The ant farm is in the state of higher entropy before the earthquake and energy is given out of the system after the earthquake.
d. The ant farm is in the state of lower entropy before the earthquake and energy is given out of the system after the earthquake.

37. Energy transfers take place constantly in every day activities. Think of two scenarios: cooking on a stove and driving. Explain how the second law of thermodynamics applies to these scenarios.

a. Heat is lost into the room while cooking and into the metal of the engine during gasoline combustion.
b. Heat gained while cooking helps to make the food and heat released due to gasoline combustion helps the car accelerate.
c. The energy given to the system remains constant during cooking and more energy is added to the car engine when the gasoline combusts.
d. The energy given to the system for cooking helps to make food and energy in the car engine remains conserved when gasoline combustion takes place.

38. What does it mean for a system to be in a higher level of entropy? How can it be reduced?

a. Higher level of entropy refers to higher state of disorder in the system and it can be reduced by input of energy to lower the entropy.
b. Higher level of entropy refers to higher state of symmetry in the system and it can be reduced by release of energy to lower the entropy.
c. Higher level of entropy refers to low disorder in the system and it can be reduced by input of energy to increase the entropy.
d. Higher level of entropy refers to higher state of disorder in the system and it can be reduced by providing a catalyst to lower the entropy.

39. When the air temperature drops and rain turns to snow, which law of thermodynamics is exhibited?

a. first law of thermodynamics
b. second law of thermodynamics
c. third law of thermodynamics
d. zeroth law of thermodynamics

40. How does ATP supply energy to chemical reactions?

a. ATP dissociates and the energy released by breaking of a phosphate bond within ATP is used for phosphorylation of another molecule. ATP hydrolysis also provides energy to power coupling reactions.

b. ATP utilizes energy to power exergonic reactions by hydrolysis of ATP molecule. The free energy released as a result of ATP breakdown is used to carry out metabolism of products.

c. ATP utilizes energy to power endergonic reactions by dehydration of ATP molecule. The free energy released as a result of ATP breakdown is used to carry out metabolism of products.

d. ATP utilizes the energy released from the coupling reactions and that energy is used to power the endergonic and exergonic reactions.

41. Is the E_A for ATP hydrolysis relatively low or high? Explain your reasoning.

a. E_A for ATP hydrolysis is high because considerable energy is released.

b. E_A for ATP hydrolysis is low because considerable energy is released.

c. E_A for ATP hydrolysis is intermediate because considerable energy is released.

d. E_A for ATP hydrolysis is high because a low amount of energy is released.

42. What is phosphorylation as it occurs in chemical reactions?

a. Phosphorylation refers to the attachment of a phosphate to another molecule to facilitate a chemical reaction.

b. Phosphorylation is the uptake of a phosphorous molecule by an ATP molecule to power chemical reactions.

c. Phosphorylation is the release of a third phosphorous molecule of ATP during hydrolysis.

d. Phosphorylation is the breakdown of a pyrophosphate molecule which gives phosphate ions.

43. If a chemical reaction could occur without an enzyme, why is it important to have one?

a. Enzymes are important because they give the desired products only from the reaction.

b. Enzymes are important because the products are obtained consistently with time.

c. Enzymes are important because it does not disturb the concentration of the products.

d. Enzymes are important because energy remains conserved and no loss of energy occurs.

44. How does enzyme feedback inhibition benefit a cell?

a. Feedback inhibition benefits the cell by blocking the production of the products by changing the configuration of enzymes. This will prevent the cells from becoming toxic.

b. Feedback inhibition benefits the cell by blocking the production of the reactants by changing the configuration of enzymes. This will prevent the cells from becoming toxic.

c. Feedback inhibition benefits the cell by blocking the production of the products by changing the configuration of reactants. This will prevent the cells from becoming toxic.

d. Feedback inhibition benefits the cell by blocking the production of the products by reducing the reactants. This will prevent the cells from becoming toxic.

45. What type of reaction allows chemicals to be available for an organism’s growth and maintenance in a timely manner?

a. enzymatically facilitated reactions

b. redox reactions

c. catabolic reactions

d. hydrolysis of ATP

TEST PREP FOR AP® COURSES

46. Cell metabolism is a complex process that uses many types of chemicals in a variety of processes. Which of the following statements is true?

a. A loss of free nucleotides would result in cancer.

b. A loss of assorted carbohydrates would result in mitosis.

c. A loss of triglycerides would result in cell death.

d. A loss of enzymes would result in cell death.

47. Which pair of descriptors of chemical reactions go together?

a. anabolic and exergonic
b. exergonic and dehydration synthesis
c. endergonic and catabolic
d. hydrolysis and exergonic

48. What is the underlying principle that supports the idea that all living organisms share the same core processes and features?

a. All organisms must harvest energy from their environment and convert it to ATP to carry out cellular functions.
b. Plants produce their own energy and pass it on to animals.
c. Herbivores, carnivores, and omnivores coexist for the survival of all.
d. Glucose is the primary source of energy for all cellular functions.

49. It has been accepted that life on the Earth started out as single celled, simple organisms, which then evolved into complex organisms. How did evolution proceed to produce such a wide variety of living organisms from a simple ancestor?

a. Prokaryotes produced the fungi, then the protists which then branches to plants and animals.
b. Protists evolved first, then the prokaryotes, which branched into the fungi, plants, and animals
c. Prokaryotes produced the protists, which branched into the fungi, plants, and animals.
d. Prokaryotes produced the protists, then the fungi, which branched into the plants and animals.

50. Plants make glucose through a pathway called photosynthesis. The amount of energy captured from light can be expressed as the number of energy containing molecules used to make one molecule of glucose. Which of the following best states the number of each molecule needed?

a. 54 molecules of ATP and 18 molecules of nicotinamide adenine dinucleotide phosphate (NADPH)
b. 18 molecules of ATP and 12 molecules of NADPH
c. 24 molecules of ATP and 18 molecules of NADPH
d. 12 molecules of ATP and 18 molecules of NADPH

51. What is an anabolic pathway? Which of these is an example of an anabolic pathway used by cells in their metabolism?

a. Anabolic pathways involve the breakdown of nutrient molecules into usable forms. An example is the harvesting of amino acids from dietary proteins.
b. Anabolic pathways involve the breakdown of nutrient molecules into useable forms. An example is the use of glycogen by the liver to maintain blood glucose levels.
c. Anabolic pathways build new molecules out of the products of catabolic pathways. An example is the separation of fatty acids from triglycerides to satisfy energy needs.
d. Anabolic pathways build new molecules out of the products of catabolic pathways. An example is the linkage of nucleotides to form a molecule of mRNA.

52. If glucose is broken down through aerobic respiration, a number of ATP can be made from the energy extracted. How many ATP are possible?

a. 2 to 4
b. 36 to 38
c. 10 to 12
d. 24 to 30

53. Plants must have adequate resources to complete their functions. If they do not have what they need, there are changes in the organism's metabolism. What happens to the metabolism of a plant that does not have adequate sunlight?

a. Photosynthesis slows and less glucose is produced for energy use.
b. The plant switches to anaerobic metabolism.
c. The plant goes into a dormant state until the sunlight returns.
d. The plant flowers quickly to reproduce while it can.

54. Water deficiency is arguably the easiest deficiency to detect in plants. This is because plants that are lacking water will wilt, as water within the plant's cells helps to supports the plant's weight. Plant cells become water deficient because their cells use the water for metabolic processes. What happens to the metabolism of a plant that does not have adequate water?

a. Photosynthesis is inhibited, less glucose is produced, and water used by the cells is not replaced.
b. The plant increases its breakdown of glucose to create more water at the end of the process.
c. The plant will stop photosynthesizing for long periods of time until it has enough water to do so.
d. The cell will bring in more CO_2, to compensate for the lack of water, allowing glucose synthesis to continue.

55. Enzymes facilitate chemical reactions that result in changes to a substrate. How does the induced fit model of enzymes and substrates explain their function?

a. Both enzyme and substrate undergo dynamic changes, inducing the transitions state of the substrate.
b. The enzyme induces a change in the substrate, but is not changed itself during the reaction.
c. The substrates attach to the enzyme and the chemical reaction proceeds.
d. The enzyme changes shape to fit the substrate causing the transition state to occur.

56. Enzyme inhibitors play an important part in the control of enzyme functions, allowing them to continue, or inhibiting them for a period of time. Which inhibitor affects the initial rate but do not affect the maximal rate?

a. allosteric
b. competitive
c. non-competitive
d. uncompetitive

SCIENCE PRACTICE CHALLENGE QUESTIONS

57. Activation energy is required for a reaction to proceed, and it is lower if the reaction is catalyzed. Sucrose (table sugar) is a disaccharide. When we eat sucrose it is converted to carbon dioxide and water, as with other carbohydrates.

1. **Identify** if the breakdown of sucrose is endergonic or exergonic. **Explain** the reasoning for your identification.
2. Based on your identification, **explain** if cubes of sugar can be stored in a sugar bowl by creating a diagram similar to **Figure 6.10**.
3. If table sugar is placed in a spoon held over a high flame, the sugar is charred and becomes a blackened mixture composed primarily of carbon. **Create a visual representation** that includes a chemical equation to **explain** the role of the flame in this process.
4. In terms of your answers to questions 1-3, **predict** if sugar cubes in a bowl placed in a dish of water can be stored on a table, and **justify** your prediction.
5. **[Extension]** The energy of activation of a chemical reaction can be determined by measurement of the effect of temperature on reaction rate. The natural logarithm of the reaction rate constant is a linear function of the inverse of the temperature in Kelvin degrees. The negative of the slope of that graph is the energy of activation divided by the universal ideal gas constant, R = 8.314 J/Kmol. Using the following data (R. Wolfenden and Yang Yean, *Journal of the American Chemical Society*, 2008 Jun 18; 130(24): 7,548–7,549) evaluate the energy of activation of the following reaction.

$$\text{sucrose} \rightarrow \text{fructose} + \text{glucose}$$

Temperature (K)	ln(rate)
440	-3.8
423	-4.5
403	-5
388	-6

Table 6.1

(a) **Construct a graph** of ln(rate) versus 1/T(K) and determine the energy of activation for the uncatalyzed reaction.

(b) Based on the data, **explain** the importance of enzymes for time scales characteristic of living systems on Earth—that is to say, life as we know it.

The time scale required for half of the molecules of initial sucrose to remain can be estimated. The relationship between the half-life and the activation energy is:

$$t_{1/2} = 0.69 \times 10^{E_A / 2.3RT}$$

At a temperature of 300K, approximately room temperature, RT is equal to 2,494 J/mole.

58. Physical exercise involves both anabolic and catabolic processes. For each process, **explain** an expected outcome and **describe** an example of a specific exercise that can lead to the expected outcome.

59. Explanations in science are often constructed by analogy. Explanations of the behavior of a poorly understood phenomenon can often be constructed by analogy to a phenomenon that is well understood. For each of the following cellular functions that require free energy, **describe** a parallel human activity and **identify** a source of free energy for that activity. For example, the synthesis of proteins can be expected to proceed as an assembly of a small set of sub-components, just as the construction of a building is accomplished by gathering and joining materials. It is consistent with our analogy to expect that there must be a free-energy resource that is consumed in the synthesis of proteins, just as hydrocarbon fuels are a source of energy for the construction of a building.

60. Look at each of the processes shown in **Figure 6.8** that show examples of endergonic and exergonic processes.

1. For each process, **identify** if it is endergonic or exergonic, and **provide reasoning** for your identification that includes your definition of the system.
2. For each process, does entropy increase or decrease? **Explain** your reasoning in terms of changes in the amount of order within the system.
3. For each process, is there an input of energy? **Explain** your reasoning in terms of (a) the source of the energy input into the system and (b) the interaction between the system and its environment that provides that input of energy.

61. Energy transfers occur constantly in daily activities. Think of two scenarios: cooking on a stove and driving a car. For each scenario, **describe** the system and **explain** how the second law of thermodynamics applies to the system in terms of energy input and change in entropy.

62. Consider a simple process that illustrates the change in entropy when energy is transferred.

1. Take a block of ice as a system with a temperature of 0°C. This is water as a solid, so it has a high structural order. This means that the molecules are in a fixed position. As a result, the entropy of the system is low.
2. Allow the ice to melt at room temperature. **Describe** changes in the motion and interactions of water molecules before and after melting. **Explain** where the energy came from whose transfer produced melting. **Predict** the effect of the energy transfer on the entropy on the system, and **justify** your prediction.
3. Heat the water until the temperature reaches boiling point. **Explain** what happens to the entropy of the system when the water is heated.
4. Continue to heat the water at the constant temperature of the boiling point. **Describe** changes in the motion and interactions of water molecules before and after boiling. **Predict** the effect of the energy transfer on the entropy of the system, and **justify** your prediction.
5. **[Extension/Connection]** Molecules of water have simple responses to heating: The molecules move faster and interact less strongly with other neighboring molecules. Consider the primary producers of an aquatic ecosystem in summer. **Describe** the source of energy transfer to the system of photosynthetic plants and algae. **Predict** changes in the system in response. **Explain** what happens to the entropy of this trophic level when energy transfer occurs. Now consider the primary producers and their aqueous environment as the system. **Explain** what happens to the entropy of this system composed of photosynthetic organisms and their abiotic environment.
6. **Predict** the change in entropy of the system when both autotrophs and their abiotic environment are considered. **Justify** your prediction. **Predict** the signs of the entropy changes in both biotic and abiotic components of this system. **Predict** the relative magnitudes of these entropy changes, and justify your prediction.

63. The sodium-potassium pump is an example of free-energy coupling. The free energy derived from exergonic ATP hydrolysis is used to pump sodium and potassium ions across the cell membrane. The hydrolysis of one ATP molecule releases 7.3 kcal/mol of free energy (ΔG = -7.3 kcal/mol). If it takes 2.1 kcal/mol of free energy to move one Na^+ across the membrane (ΔG = +2.1 kcal/mol), how many sodium ions could be moved by the hydrolysis of one ATP molecule? **Show your calculations to provide reasoning for your answer.**

64. Is the E_A for ATP hydrolysis in cells likely relatively low or high compared to the E_A for the combustion of gasoline in an internal combustion engine?

1. **Explain** your reasoning in terms of the relative stabilities of ATP and gasoline compared to air in which no catalysts are present.
2. **Describe** how the role of the enzyme ATPase in the hydrolysis of ATP in a cell differs from a spark in the cylinder of an internal combustion engine.
3. **Describe** a strategy for collecting data that can be used to measure the energies of activation (E_A) of each of these two processes with instruments that can measure concentrations of reactions produced in each system.

65. Vitamin B_{12} is a co-enzyme involved in a wide variety of cellular processes. Synthesis of vitamin B_{12} occurs only in bacteria; in animals, these bacteria populate anaerobic environments in the gut. Consequently, vegan diets in developing nations and diets common to developing nations provide no source of B_{12}. Researchers (Ghosh et al. http://dx.doi.org/10.3389/fnut.2016.00001]) found that rats whose diets contained limited (L) and no (N) B_{12} displayed symptoms that were not observed in the control group (C) whose diet included B_{12} and was otherwise identical. Chemical analysis of adipocytokines in the plasma after feeding periods of 4 and 12 weeks are shown in the following table.

Adipocytokines Tissue of origin	Feeding duration (weeks)	C	L	N
Leptin (pg/L)	4	5.7± 0.21	5.8± 0.25	6.1± 0.25
Adipose	12	5.8± 0.39	6.5± 0.36	9.9± 0.68
MCP-1 (mg/L)	4	43.0± 1.18	44.4± 1.95	46.9± 2.08
Monocytes	12	43.2± 2.47	45.3± 3.02	49.5± 1.27
IL-6 (mg/L)	4	150± 3.2	154± 4.5	184± 8.0
Monocytes	12	151± 6.7	176± 11.0	185± 8.2

Table 6.2

The sample size for these data are small: n = 6, within each group. Also shown in the table are cells in which these cytokine messages originate. Adipose cells store fats. Monocytes are white blood cells of the immune system. Over the 12 weeks of feeding, the weights of all three groups were equivalent, while the percent of body fat increased relative to the control for the rats fed a diet of limited and no B_{12}: 40% (N) and 20% (L), respectively.

a. **Identify** which adipocytokines show significant increases, relative to the control group, after only 4 weeks of treatment. **Justify** your identification.
b. **Identify** which adipocytokines show only significant increases, relative to the control group, after 12 weeks of treatment. **Justify** your identification.
c. **Identify** which adipocytokines show significant increases, relative to the control group, after 4 weeks of treatment but no further increase after 12 weeks. **Justify** your identification.

Adipocytokines are chemical messengers that regulate metabolism and blood vessel production and dilation. High concentrations of adipocytokines are commonly found among individuals with abnormal autoimmune response. Monocyte chemoattractant protein 1 (MCP-1) is involved in the trafficking or guiding of monocytes to damaged tissue, as in a wound. In mice, leptin receptors of cells in the hypothalamus suppress hunger. Interleukin (IL-6) is released to initiate and then regulate inflammation in response to an infection. The mice in this study were not infected or wounded.

d. **Construct an explanation**, with reasoning based on the evidence provided by these data, for the observed variations in adipocytokines.

Many noncommunicable diseases are associated with abnormal autoimmune responses, and the number of diseases that involve abnormal autoimmune response is increasing. Many autoimmune diseases, such as diabetes and heart disease, occur in developed nations at a much higher frequency than in developing nations.

e. **Evaluate**, based on these data concerning the effect of restrictions on the availability of B_{12}, the following question: Does the increased lack of exposure to pathogens in developed nations lead to reduced or abnormal immune response?

66. Using an example, **explain** how enzyme feedback inhibition regulation regulates a cellular process.