

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

- 6.1: Energy and Metabolism
- 6.2: Potential, Kinetic, Free, and Activation Energy
- 6.3: The Laws of Thermodynamics
- 6.4: ATP: Adenosine Triphosphate
- 6.5: Enzymes

Introduction

Virtually every task performed by living organisms requires energy. Energy is needed to perform heavy labor and exercise, but 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) and possibly synthesized into new molecules, modified if needed, transported around the cell, and may be 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 transported between cells. Pathogenic bacteria and viruses are ingested and broken down by cells. Cells must also export waste and toxins to stay healthy, and many cells must swim or move surrounding materials via the beating motion of cellular appendages like cilia and flagella.

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. This chapter will also describe how cells use energy and replenish it, and how chemical reactions in the cell are performed with great efficiency.

6.1 | Energy and Metabolism

By the end of this section, you will be able to:

- Explain what metabolic pathways are and describe the two major types of metabolic pathways
- Discuss how chemical reactions play a role in energy transfer

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**.

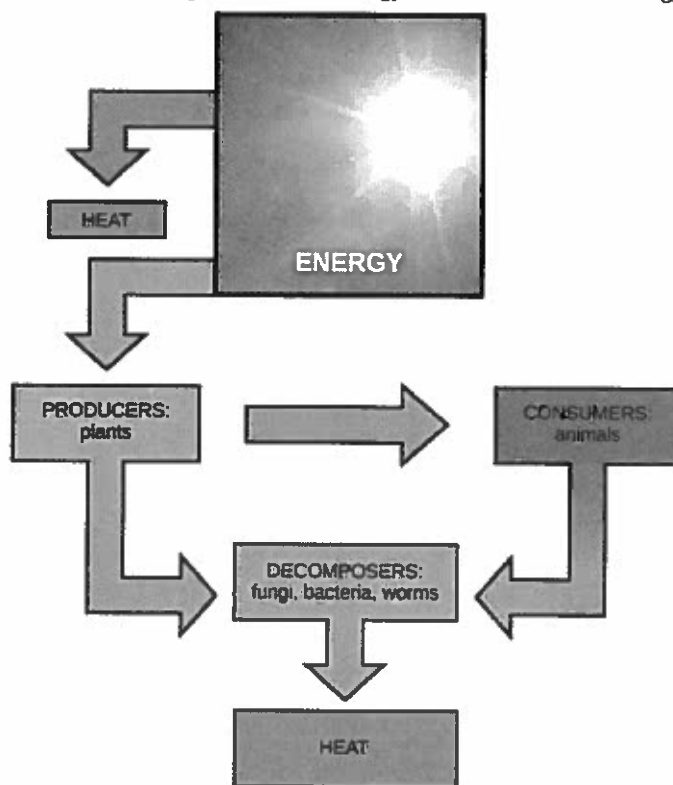


Figure 6.2 Most life forms on earth get their energy from the sun. Plants use photosynthesis to capture sunlight, and herbivores eat those plants to obtain energy. Carnivores eat the herbivores, and decomposers digest plant and animal matter.

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:



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 ($\text{C}_6\text{H}_{12}\text{O}_6$). 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):



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 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.

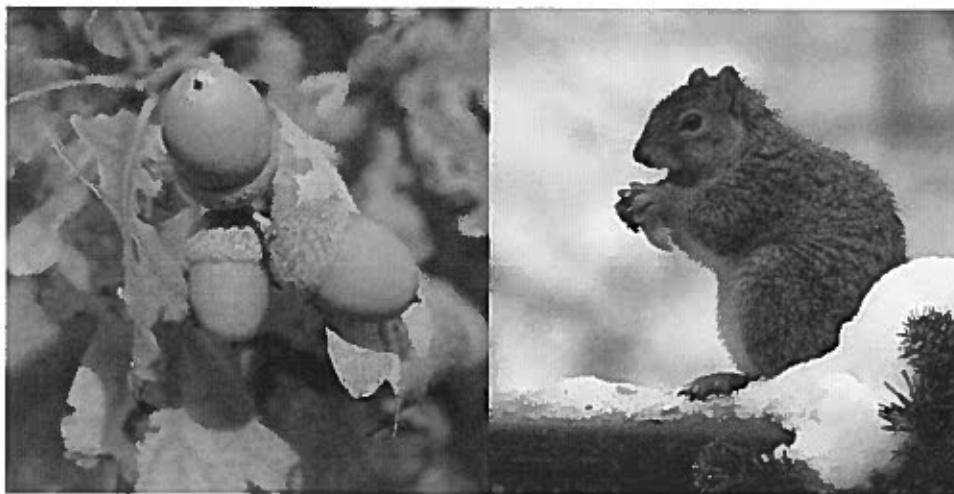


Figure 6.3 Plants, like this oak tree and acorn, use energy from sunlight to make sugar and other organic molecules. Both plants and animals (like this squirrel) use cellular respiration to derive energy from the organic molecules originally produced by plants. (credit "acorn": modification of work by Noel Reynolds; credit "squirrel": modification of work by Dawn Huczek)

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).

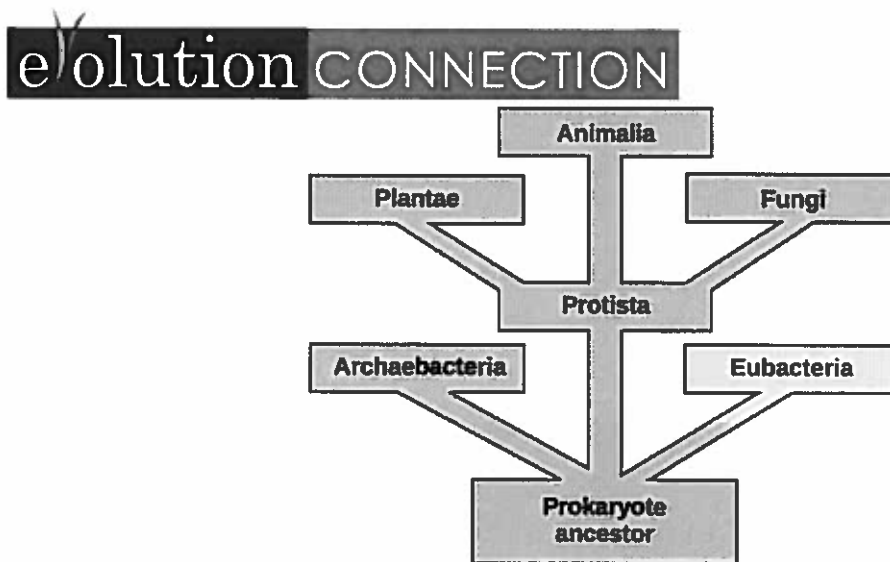


Figure 6.4 This tree shows the evolution of the various branches of life. The vertical dimension is time. Early life forms, in blue, used anaerobic metabolism to obtain energy from their surroundings.

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.

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.

Metabolic pathways

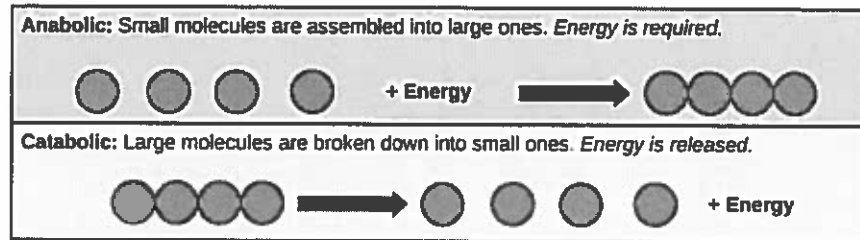


Figure 6.5 Anabolic pathways are those that require energy to synthesize larger molecules. Catabolic pathways are those that generate energy by breaking down larger molecules. Both types of pathways are required for maintaining the cell's energy balance.

6.2 | Potential, Kinetic, Free, and Activation Energy

By the end of this section, you will be able to:

- Define “energy”
- Explain the difference between kinetic and potential energy
- Discuss the concepts of free energy and activation energy
- Describe endergonic and exergonic reactions

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.

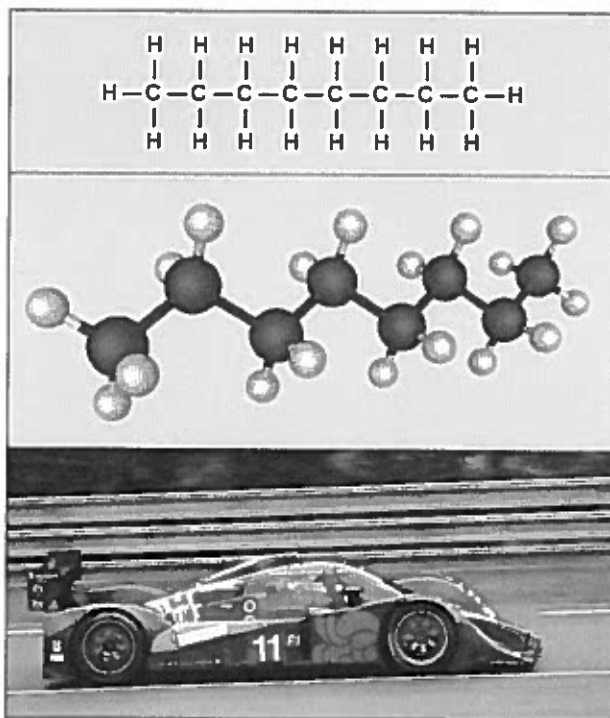


Figure 6.7 The molecules in gasoline (octane, the chemical formula shown) contain chemical energy within the chemical bonds. This energy is transformed into kinetic energy that allows a car to race on a racetrack. (credit "car": modification of work by Russell Trow)



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.

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):

$$\Delta G = \Delta H - T\Delta S$$

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: exergonic means energy is exiting 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.

art CONNECTION

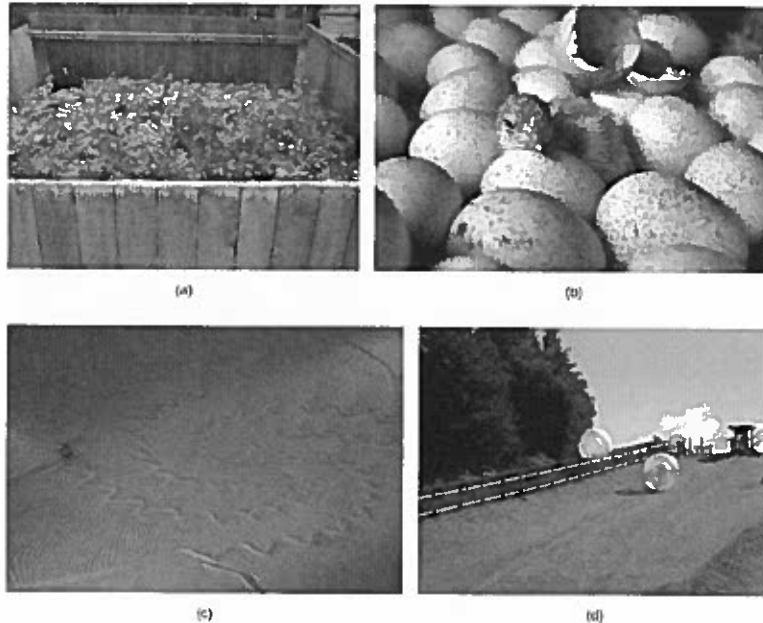


Figure 6.8 Shown are some examples of endergonic processes (ones that require energy) and exergonic processes (ones that release energy). These include (a) a compost pile decomposing, (b) a chick hatching from a fertilized egg, (c) sand art being destroyed, and (d) a ball rolling down a hill. (credit 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?

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.

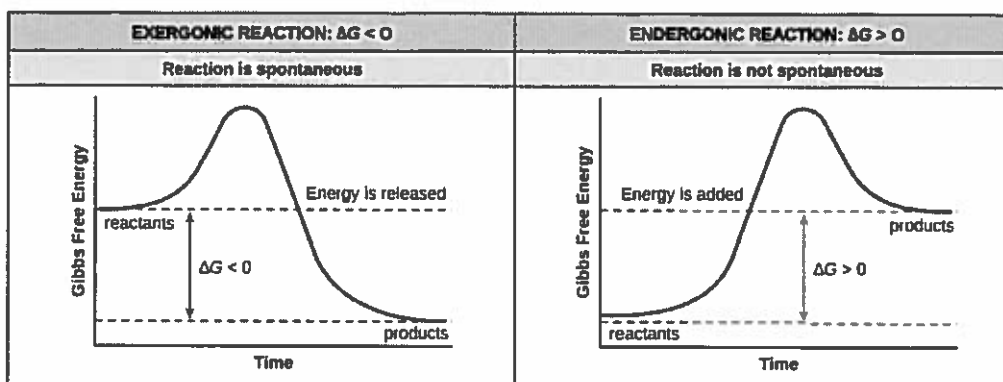


Figure 6.9 Exergonic and endergonic reactions result in changes in Gibbs free energy. Exergonic reactions release energy; endergonic reactions require energy to proceed.

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.

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.

art CONNECTION

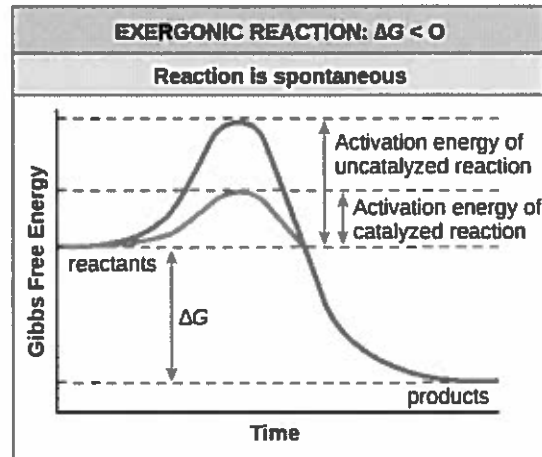


Figure 6.10 Activation energy is the energy required for a reaction to proceed, and it is lower if the reaction is catalyzed. The horizontal axis of this diagram describes the sequence of events in time.

If no activation energy were required to break down sucrose (table sugar), would you be able to store it in a sugar bowl?

6.3 | The Laws of Thermodynamics

By the end of this section, you will be able to:

- Discuss the concept of entropy
- Explain the first and second laws of thermodynamics

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 (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.

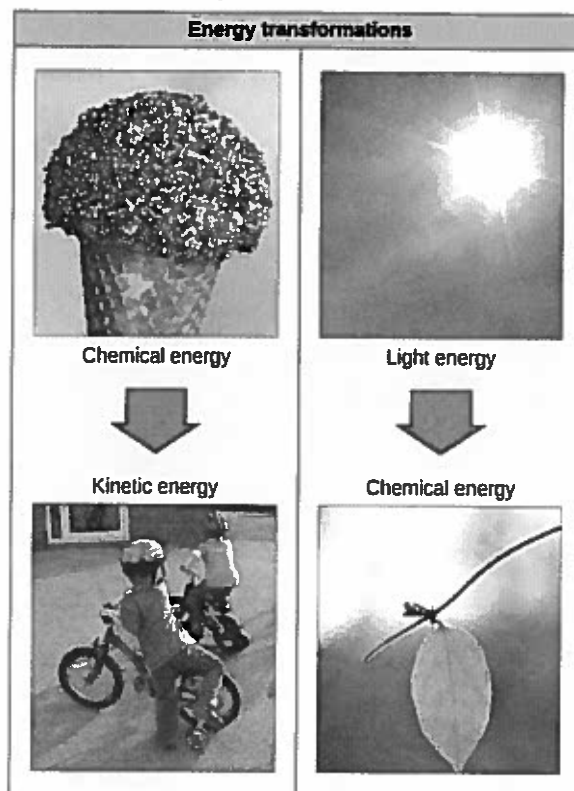


Figure 6.11 Shown are two examples of energy being transferred from one system to another and transformed from one form to another. Humans can convert the chemical energy in food, like this ice cream cone, into kinetic energy (the energy of movement to ride a bicycle). Plants can convert electromagnetic 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 Rigger-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.

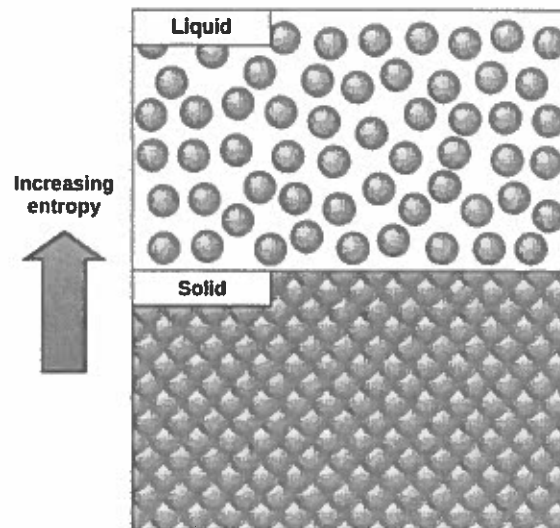


Figure 6.12 Entropy is a measure of randomness or disorder in a system. Gases have higher entropy than liquids, and liquids have higher entropy than solids.

6.4 | ATP: Adenosine Triphosphate

By the end of this section, you will be able to:

- Explain the role of ATP as the cellular energy currency
- Describe how energy is released through hydrolysis of ATP

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.

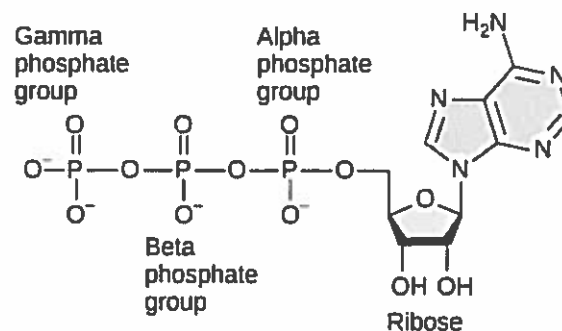


Figure 6.13 ATP is the primary energy currency of the cell. It has an adenosine backbone with three phosphate groups attached.

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:



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:



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.

art CONNECTION

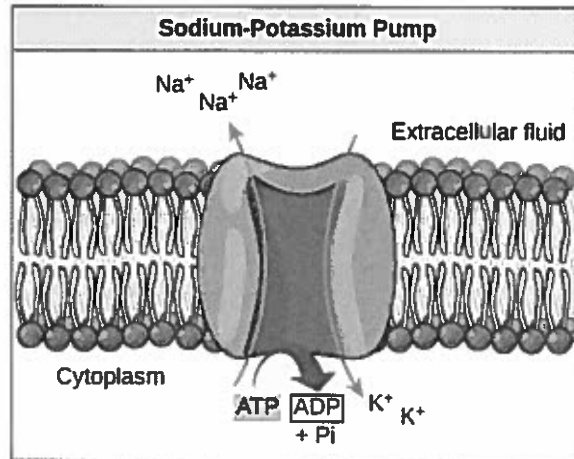


Figure 6.14 The sodium-potassium pump is an example of energy coupling. The energy derived from exergonic ATP hydrolysis is used to pump sodium and potassium ions across the cell membrane.

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

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).

6.5 | Enzymes

By the end of this section, you will be able to:

- Describe the role of enzymes in metabolic pathways
- Explain how enzymes function as molecular catalysts
- Discuss enzyme regulation by various factors

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).

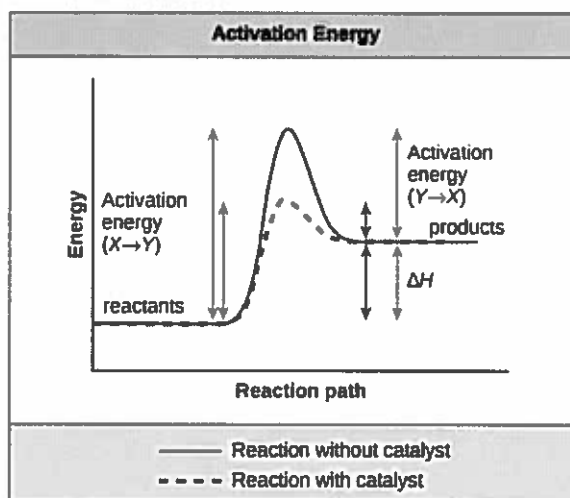


Figure 6.15 Enzymes lower the activation energy of the reaction but do not change the free energy of the reaction.

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>).

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).

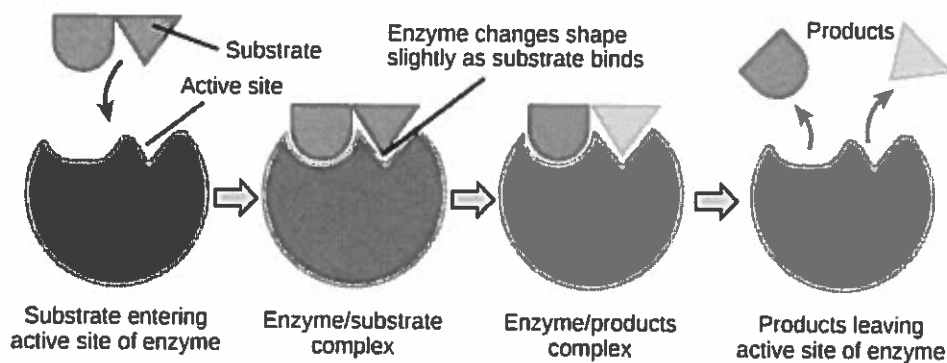


Figure 6.16 According to the induced-fit model, both enzyme and substrate undergo dynamic conformational changes upon binding. The enzyme contorts the substrate into its transition state, thereby increasing the rate of the reaction.

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.

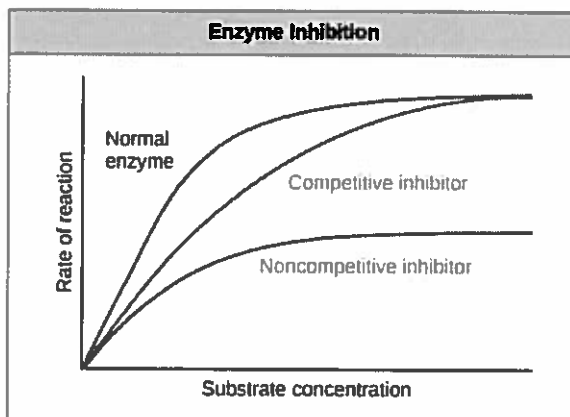


Figure 6.17 Competitive and noncompetitive inhibition affect the rate of reaction differently. Competitive inhibitors affect the initial rate but do not affect the maximal rate, whereas noncompetitive inhibitors affect the maximal rate.

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).

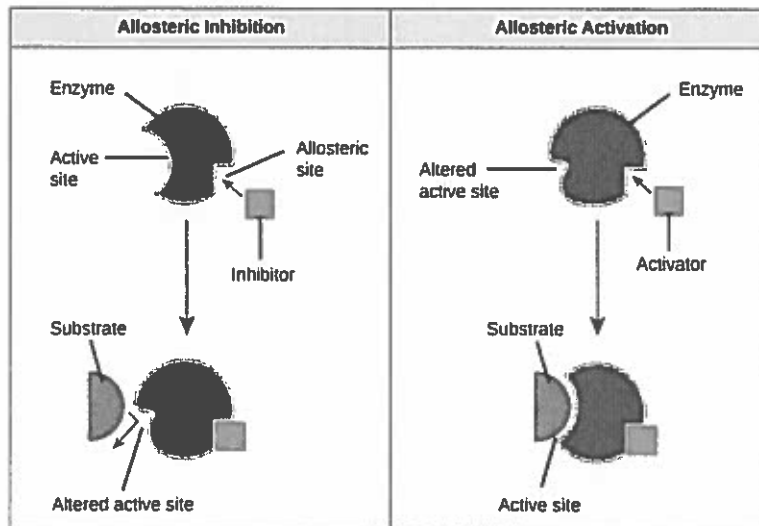


Figure 6.18 Allosteric inhibitors modify the active site of the enzyme so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the active site of the enzyme so that the affinity for the substrate increases.

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, popularly marketed under the brand name Tylenol, 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.

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 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.

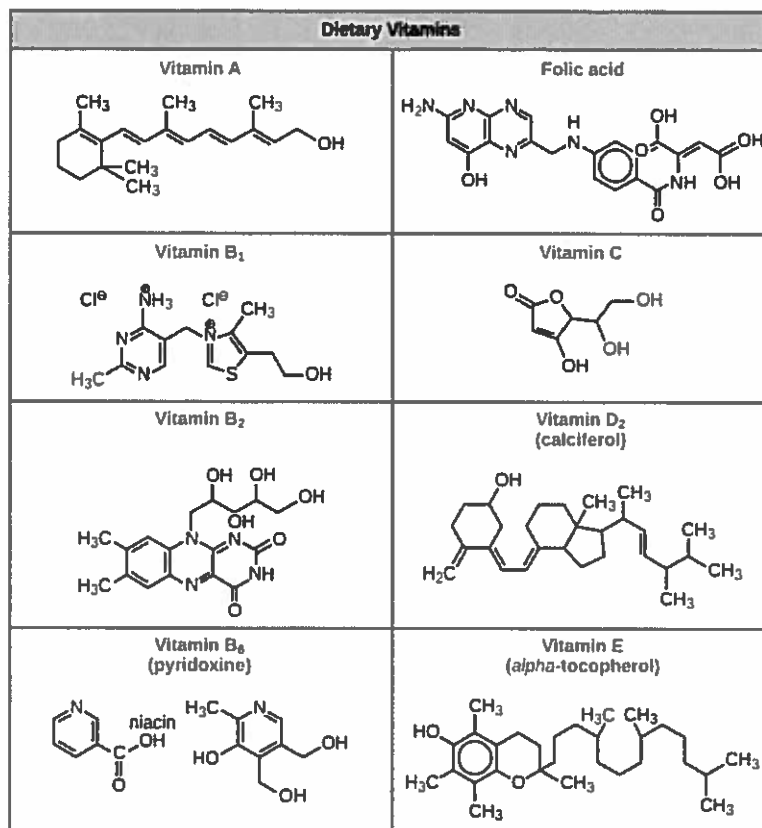


Figure 6.20 Vitamins are important coenzymes or precursors of coenzymes, and are required for enzymes to function properly. Multivitamin capsules usually contain mixtures of all the vitamins at different percentages.

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.

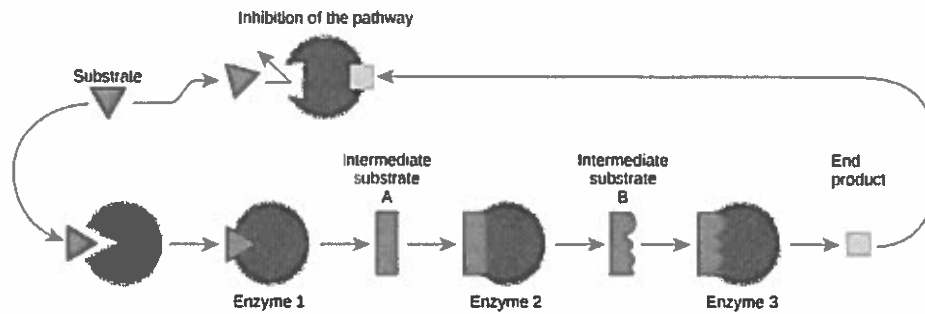


Figure 6.21 Metabolic pathways are a series of reactions catalyzed by multiple enzymes. Feedback inhibition, where the end product of the pathway inhibits an upstream step, is an important regulatory mechanism in cells.

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.

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.

ART CONNECTION QUESTIONS

- Figure 6.8** 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?
- Figure 6.10** If no activation energy were required to break down sucrose (table sugar), would you be able to store it in a sugar bowl?
- Figure 6.14** The hydrolysis of one ATP molecule releases 7.3 kcal/mol of energy ($\Delta G = -7.3$ kcal/mol of energy). If it takes 2.1 kcal/mol of energy to move one Na^+ across the membrane ($\Delta G = +2.1$ kcal/mol of energy), how many sodium ions could be moved by the hydrolysis of one ATP molecule?

REVIEW QUESTIONS

- Energy is stored long-term in the bonds of _____ and used short-term to perform work from a(n) _____ molecule.
 - ATP : glucose
 - an anabolic molecule : catabolic molecule
 - glucose : ATP
 - a catabolic molecule : anabolic molecule
- DNA replication involves unwinding two strands of parent DNA, copying each strand to synthesize complementary strands, and releasing the parent and daughter DNA. Which of the following accurately describes this process?
 - This is an anabolic process
 - This is a catabolic process
 - This is both anabolic and catabolic
 - This is a metabolic process but is neither anabolic nor catabolic
- Consider a pendulum swinging. Which type(s) of energy is/are associated with the pendulum in the following instances: i. the moment at which it completes one cycle, just before it begins to fall back towards the other end, ii. the moment that it is in the middle between the two ends, iii. just before it reaches the end of one cycle (just before instant i.).
 - i. potential and kinetic, ii. potential and kinetic, iii. kinetic
 - i. potential, ii. potential and kinetic, iii. potential and kinetic
 - i. potential, ii. kinetic, iii. potential and kinetic
 - i. potential and kinetic, ii. kinetic iii. kinetic
- Which of the following comparisons or contrasts between endergonic and exergonic reactions is false?
 - Endergonic reactions have a positive ΔG and exergonic reactions have a negative ΔG
 - Endergonic reactions consume energy and exergonic reactions release energy
 - Both endergonic and exergonic reactions require a small amount of energy to overcome an activation barrier
 - Endergonic reactions take place slowly and exergonic reactions take place quickly
- Which of the following is the best way to judge the relative activation energies between two given chemical reactions?
 - Compare the ΔG values between the two reactions
 - Compare their reaction rates
 - Compare their ideal environmental conditions
 - Compare the spontaneity between the two reactions
- Which of the following is not an example of an energy transformation?
 - Turning on a light switch
 - Solar panels at work
 - Formation of static electricity
 - None of the above
- Label each of the following systems as high or low entropy: i. the instant that a perfume bottle is sprayed compared with 30 seconds later, ii. an old 1950s car