6.1 | Energy and Metabolism

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

- Explain metabolic pathways and describe the two major types
- 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 building and breaking down 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 they have used, cells must continually produce more energy to replenish that which the many energy-requiring chemical reactions that constantly take place use. All of the chemical reactions that transpire inside cells, including those that use and release energy, are the cell's **metabolism**.

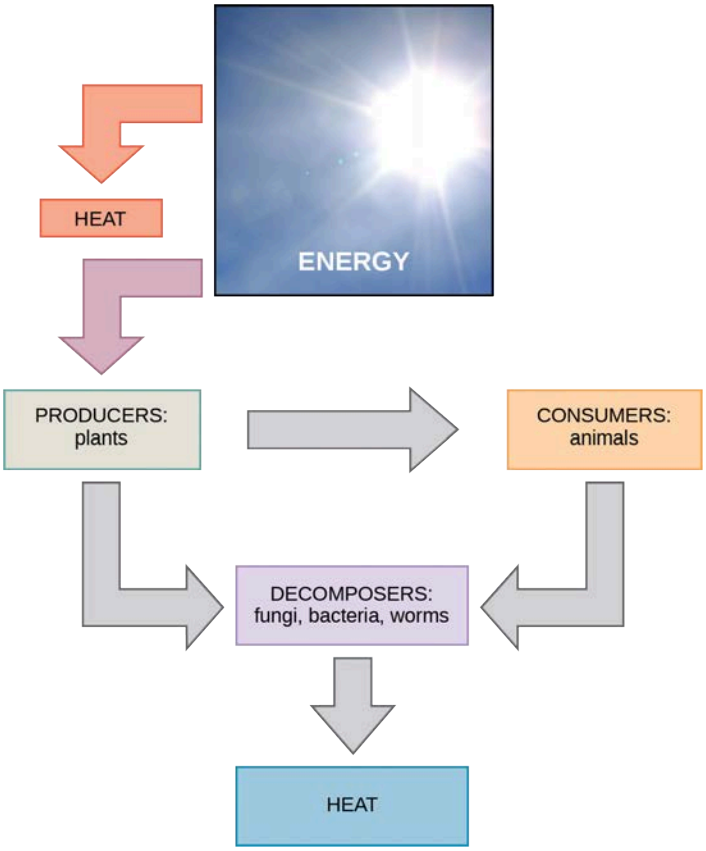

Figure 6.2 Most life forms on earth obtain their energy from the sun. Plants use photosynthesis to capture sunlight, and herbivores eat those plants to obtain energy. Carnivores eat the herbivores, and decomposers digest plant and animal matter.

Carbohydrate Metabolism

Sugar (chemical reactions) metabolism (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 considerable energy stored within their bonds. The following equation describes the breakdown of glucose, a simple sugar:

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

Consumed carbohydrates 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 energy input to proceed. The following equation (notice that it is the reverse of the previous equation) describes the synthesis of glucose:

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

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

Solar energy is required to synthesize a glucose molecule during the photosynthesis reactions. In photosynthesis, light energy from the sun initially transforms into chemical energy that temporally stores itself in the energy carrier molecules ATP and NADPH (nicotinamide adenine dinucleotide phosphate). Photosynthesis later uses the stored energy in ATP and NADPH to build one glucose molecule from six molecules of CO_2. This process is analogous to eating breakfast in the morning to acquire energy for your body that you can use later in the day. Under ideal conditions, energy from 18 molecules of ATP is required to synthesize one glucose molecule during photosynthesis reactions. Glucose molecules can also combine with and convert into other sugar types. When an organism consumes sugars, glucose molecules eventually make their way into each organism's living cell. Inside the cell, each sugar molecule breaks 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 makes high-energy ATP molecules, which perform work, powering many chemical reactions in the cell. The amount of energy needed to make one glucose molecule from six carbon dioxide molecules is 18 ATP molecules and 12 NADPH molecules (each one of which is energetically equivalent to three ATP molecules), or a total of 54 molecule equivalents required for synthesizing one glucose molecule. 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 that plants originally produced. (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. Scientists call these two opposite processes—the first requiring energy and the second producing energy—anabolic (building) and catabolic (breaking down) pathways, respectively. Consequently, building (anabolism) and degradation (catabolism) comprise metabolism.

evolution CONNECTION

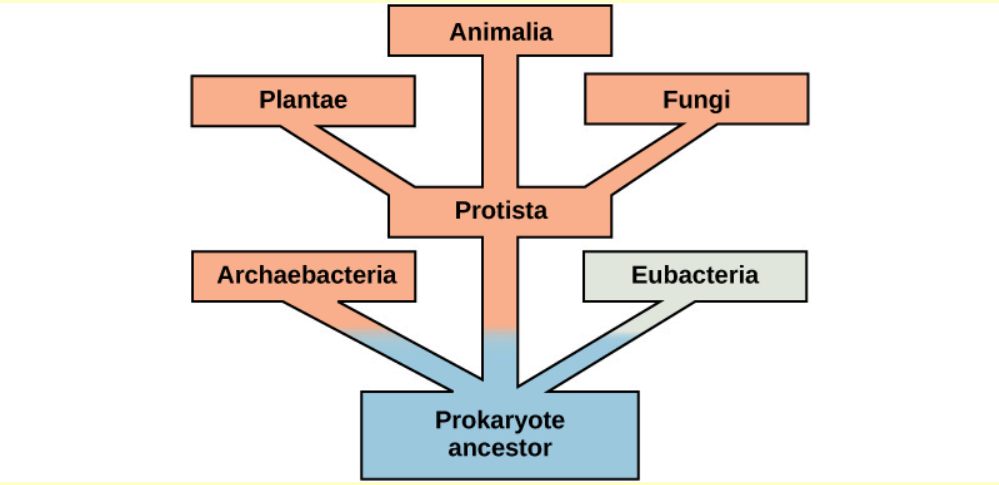

Figure 6.4 This tree shows the evolution of the various branches of life. The vertical dimension is time. Early life forms, in blue, used anaerobic metabolism to obtain energy from their surroundings.

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 (planktonic algae perform the majority of global synthesis) harvest the sun's energy and convert it into carbohydrates. The by-product of photosynthesis is oxygen, which some cells require to carry out cellular respiration. During cellular respiration, oxygen aids in the catabolic breakdown of carbon compounds, like carbohydrates. Among the products 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 synthesizing large proteins from amino acid building blocks, and synthesizing new DNA strands from nucleic acid building blocks. These biosynthetic processes are critical to the cell's life, take place constantly, and demand energy that ATP and other high-energy molecules like NADH (nicotinamide adenine dinucleotide) and NADPH provide (**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 glucose molecule can store enough energy to make a great deal of ATP, 36 to 38 molecules. This is a **catabolic** pathway. Catabolic pathways involve degrading (or breaking down) complex molecules into simpler ones. Molecular energy stored in complex molecule bonds release in catabolic pathways and harvest in such a way that it can produce ATP. Other energy-storing molecules, such as fats, also break down through similar catabolic reactions to release energy and make ATP (**Figure 6.5**).

It is important to know that metabolic pathway chemical reactions do not take place spontaneously. A protein called an enzyme facilitates or catalyzes each reaction step. Enzymes are important for catalyzing all types of biological reactions—those that require energy as well as those that release energy.

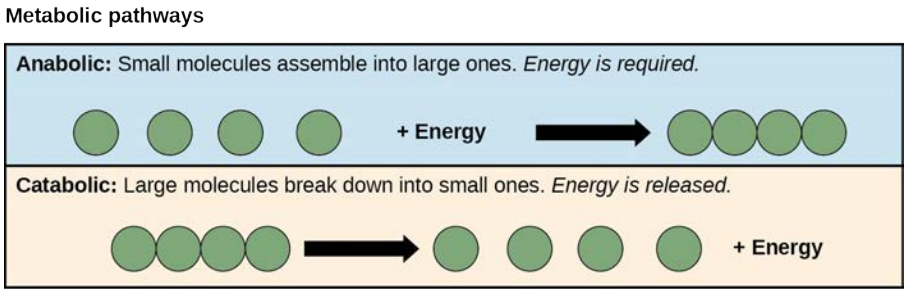

Figure 6.5 Anabolic pathways are those that require energy to synthesize larger molecules. Catabolic pathways are those that generate energy by breaking down larger molecules. Both types of pathways are required for maintaining the cell's energy balance.

6.2 | Potential, Kinetic, Free, and Activation Energy

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

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

We define energy 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 energy types. While these are all familiar energy types that one can see or feel, there is another energy type that is much less tangible. Scientists associate this energy with something as simple as an object 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 energy types that exist in the physical world.

Energy Types

When an object is in motion, there is energy. For example, an airplane in flight produces considerable energy. 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 considerable damage to other objects. However, a wrecking ball that is not in motion is incapable of performing work. Energy with objects in motion is **kinetic energy**. A speeding bullet, a walking person, rapid molecule movement in the air (which produces heat), and electromagnetic radiation like light all have kinetic energy.

What if we lift that same motionless wrecking ball two stories above a car with a crane? If the suspended wrecking ball is unmoving, can we associate energy with it? The answer is yes. The suspended wrecking ball has associated energy that is fundamentally different from the kinetic energy of objects in motion. This energy form results from the *potential* for the wrecking ball to do work. If we release the ball it would do work. Because this energy type refers to the potential to do work, we call it **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 releases, its kinetic energy begins to increase because it builds speed due to gravity. Simultaneously, 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 water's energy held behind a dam (**Figure 6.6**), or a person about to skydive from 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)

We associate potential energy only with the matter's location (such as a child sitting on a tree branch), but also with the matter's structure. A spring on the ground has potential energy if it is compressed; so does a tautly pulled rubber band. The very existence of living cells relies heavily on structural potential energy. On a chemical level, the bonds that hold the molecules' atoms 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 break down. That certain chemical bonds' breakdown can release energy 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 we eventually harness for use. This is because these bonds can release energy when broken. Scientists call the potential energy type that exists within chemical bonds that releases when those bonds break **chemical energy** (Figure 6.7). Chemical energy is responsible for providing living cells with energy from food. Breaking the molecular bonds within fuel molecules brings about the energy's release.

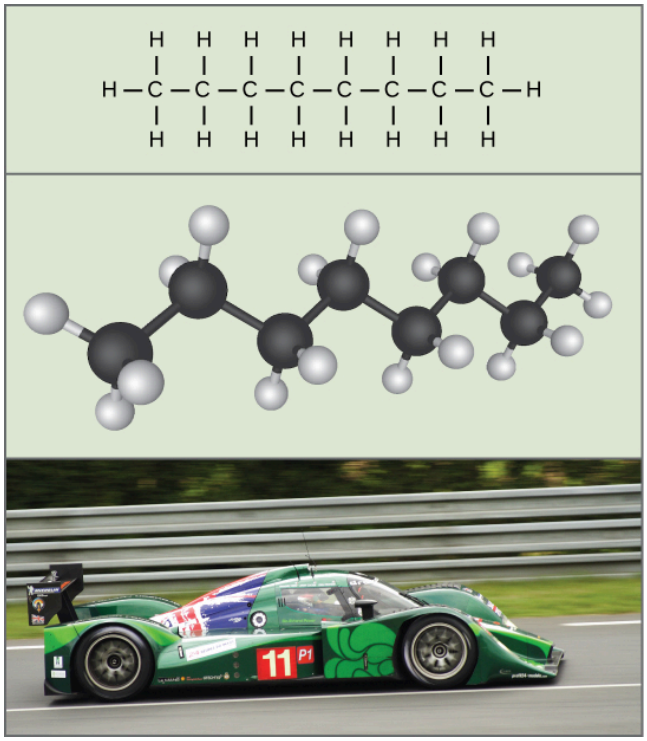

Figure 6.7 The molecules in gasoline contain chemical energy within the chemical bonds. This energy transforms into kinetic energy that allows a car to race on a racetrack. (credit “car”: modification of work by Russell Trow)

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.

Free Energy

After learning that chemical reactions release energy when energy-storing bonds break, an important next question is how do we quantify and express the chemical reactions with the associated energy? How can we compare the energy that releases from one reaction to that of another reaction? We use a measurement of **free energy** to quantitate these energy transfers. Scientists call this free energy 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 losing some energy in an unusable form such as heat, resulting in entropy. Gibbs free energy specifically refers to the energy that takes place with a chemical reaction that is available after we account for entropy. 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). We can calculate the change in free energy 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 system's total energy change. Scientists call this total energy change in the system **enthalpy** and we denote it as ΔH. The formula for calculating ΔG is as follows, where the symbol T refers to absolute temperature in Kelvin (degrees Celsius + 273):

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

We express a chemical reaction's standard free energy change 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. We generally calculate standard pH, temperature, and pressure conditions at pH 7.0 in biological systems, 25 degrees Celsius, and 100 kilopascals (1 atm pressure), respectively. 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 releases 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 reaction's products have less free energy than the reactants, because they gave off some free energy during the reaction. Scientists call reactions that have a negative ΔG and consequently release free energy **exergonic reactions**. Think: *ex*ergonic means energy is *ex*iting the system. We also refer to these reactions as spontaneous reactions, because they can occur without adding 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. We must draw an important distinction 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. Rusting iron is an example of a spontaneous reaction that occurs slowly, little by little, over time.

If a chemical reaction requires an energy input 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, we can think of the reactions' products as energy-storing molecules. We call these chemical reactions **endergonic reactions**, and they are non-spontaneous. An endergonic reaction will not take place on its own without adding free energy.

Let’s revisit the example of the synthesis and breakdown of the food molecule, glucose. Remember that building 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. Alternatively the catabolic process of breaking sugar down into simpler molecules releases energy in a series of exergonic reactions. Like the rust example above, the sugar breakdown involves spontaneous reactions, but these reactions do not 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 This figure shows 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 destruction, 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, 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 studying 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 they reach a state of equilibrium, which is one of the lowest possible free energy and a state of maximal entropy. To push the reactants and products away from a state of equilibrium requires energy. 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 necessary work 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 there is never chemical equilibrium. In this way, living organisms are in a constant energy-requiring, uphill battle against equilibrium and entropy. This constant energy supply ultimately comes from sunlight, which produces nutrients in the photosynthesis process.

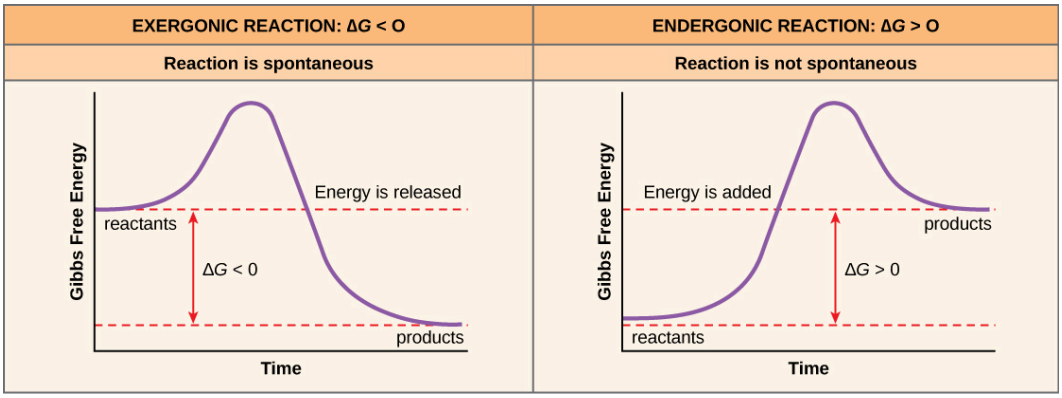

Figure 6.9 Exergonic and endergonic reactions result in changes in Gibbs free energy. Exergonic reactions release energy. Endergonic reactions require energy to proceed.

Activation Energy

There is another important concept that we must consider regarding endergonic and exergonic reactions. Even exergonic reactions require a small amount of energy input before they can proceed with their energy-releasing steps. These reactions have a net release of energy, but still require some initial energy. Scientists call this small amount of energy input necessary for all chemical reactions to occur the **activation energy** (or free energy of activation) abbreviated as 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 break and new ones form. For example, when a glucose molecule breaks down, bonds between the molecule's carbon atoms break. 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 the **transition state**, and it is a high-energy, unstable state. For this reason, reactant molecules do not last long in their transition state, but very quickly proceed to the chemical reaction's next steps. 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.

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

From where does the activation energy that chemical reactants require come? The activation energy's required source 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 molecule's motion, 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 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. The example of iron rusting illustrates an inherently slow reaction. This reaction occurs slowly over time because of its high E_A. Additionally, burning many fuels, which is strongly exergonic, will take place at a negligible rate unless sufficient heat from a spark overcomes their activation energy. However, once they begin to burn, 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**). Scientist refer to this 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 cell's essential components would disintegrate.

visual CONNECTION

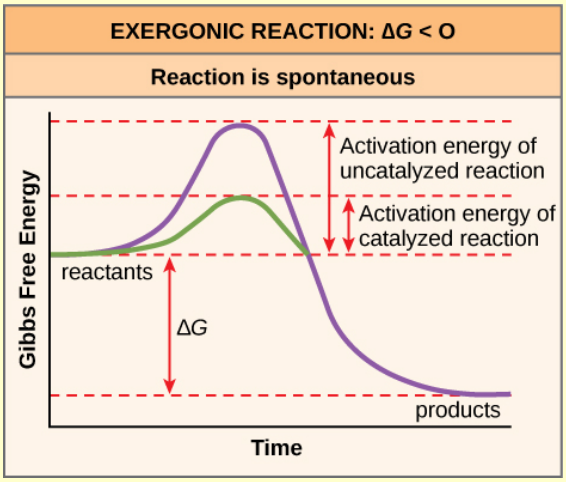

Figure 6.10 Activation energy is the energy required for a reaction to proceed, and it is lower if the reaction is catalyzed. This diagram's horizontal axis describes the sequence of events in time.

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 do the following:

- 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 that system is the surroundings. For instance, when heating a pot of water on the stove, the system includes the stove, the pot, and the water. Energy transfers 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 transfer between the system and its surroundings. The stovetop system is open because it can lose heat into the air. A closed system is one that cannot transfer energy to its surroundings.

Biological organisms are open systems. Energy exchanges 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 transfer from place to place or transform 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 sunlight energy into the chemical energy stored within organic molecules (**Figure 6.2**). **Figure 6.11** examples of energy transformations.

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 transforms through a series of cellular chemical reactions into energy within ATP molecules. 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.

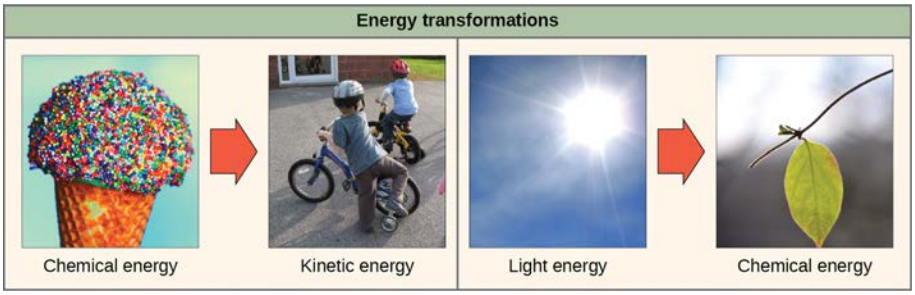

Figure 6.11 Here are two examples of energy transferring from one system to another and transformed from one form to another. Humans can convert the chemical energy in food, like this ice cream cone, into kinetic energy (the energy of movement to ride a bicycle). Plants can convert electromagnetic radiation (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 that we have 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, scientists define **heat energy** as energy that transfers from one system to another that is not doing work. For example, when an airplane flies through the air, it loses some of its energy as heat energy due to friction with the surrounding air. This friction actually heats the air by temporarily increasing air molecule speed. 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 (or randomness). The more energy that a system loses to its surroundings, the less ordered and more random the system. 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, a house's or car's entropy 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 transfers 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 ice's temperature is 0°C. As a result, the system's entropy 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 system's entropy higher or lower? Why?
3. Heat the water to its boiling point. What happens to the system's entropy when the water is heated?

Think of all physical systems of in this way: Living things are highly ordered, requiring constant energy input to maintain themselves 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 are not useful energy sources. This process increases the entropy of the system's surroundings. Since all energy transfers result in losing some usable energy, the second law of thermodynamics states that every energy transfer or transformation increases the universe's entropy. Even though living things are highly ordered and maintain a state of low entropy, the universe's entropy in total is constantly increasing due to losing usable energy with each energy transfer that occurs. Essentially, living things are in a continuous uphill battle against this constant increase in universal entropy.

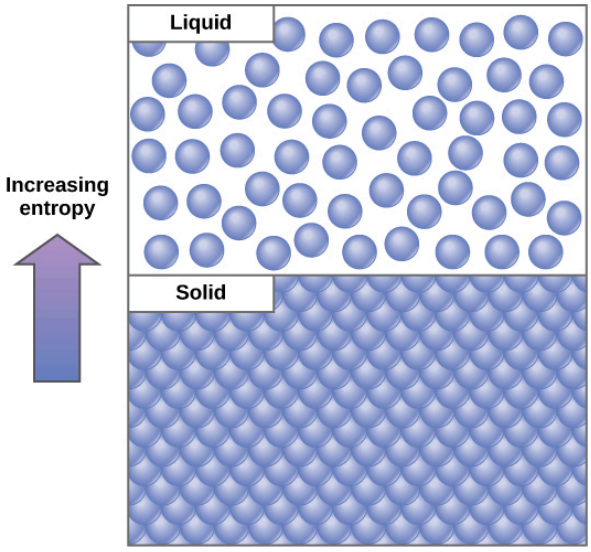

Figure 6.12 Entropy is a measure of randomness or disorder in a system. Gases have higher entropy than liquids, and liquids have higher entropy than solids.

6.4 | ATP: Adenosine Triphosphate

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

- Explain ATP's role as the cellular energy currency
- Describe how energy releases through ATP hydrolysis

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, from where does energy to power such reactions come? The answer lies with an energy-supplying molecule scientists call **adenosine triphosphate**, or **ATP**. This 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. Think of this molecule as the cells' primary energy currency in much the same way that money is the currency that people exchange for things they need. ATP powers the majority of energy-requiring cellular reactions.

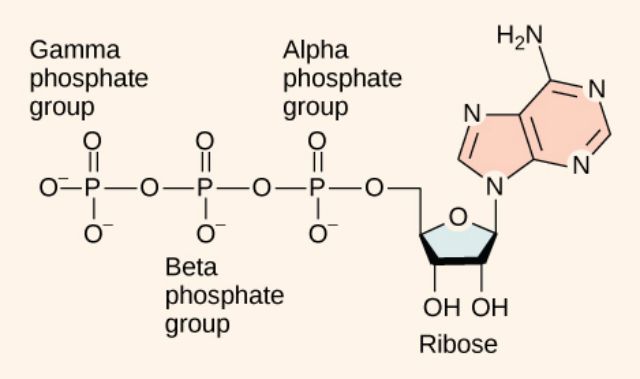

Figure 6.13 ATP is the cell's primary energy currency. It has an adenosine backbone with three phosphate groups attached.

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 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. These bonds are “high-energy” 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 using a water molecule, it is a hydrolysis reaction. In other words, ATP hydrolyzes 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, ATP to ADP hydrolysis is reversible. The reverse reaction regenerates ATP from ADP + P_i. Cells rely on ATP regeneration just as people rely on regenerating spent money through some sort of income. Since ATP hydrolysis releases energy, ATP regeneration must require an input of free energy. This equation expresses ATP formation:

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

Two prominent questions remain with regard to using ATP as an energy source. Exactly how much free energy releases with ATP hydrolysis, and how does that free energy do cellular work? The calculated ΔG for the hydrolysis of one ATP mole into ADP and P_i is −7.3 kcal/mole (−30.5 kJ/mol). Since this calculation is true under standard conditions, one would expect a different value exists under cellular conditions. In fact, the ΔG for one ATP mole's hydrolysis 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 we posed above discusses how ATP hydrolysis energy release performs work inside the cell. This depends on a strategy scientists call energy coupling. Cells couple the ATP hydrolysis' exergonic reaction 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 powers this pump, because cellular processes bring considerable sodium into the cell and potassium out of it. 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 ATP molecule must hydrolyze. When ATP hydrolyzes, its gamma phosphate does not simply float away, but it actually transfers onto the pump protein. Scientists call this process of a phosphate group binding to a molecule phosphorylation. As with most ATP hydrolysis cases, a phosphate from ATP transfers 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 cell's outside. It then binds extracellular K^+, which, through another conformational change, causes the phosphate to detach from the pump. This phosphate release triggers the K^+ to release to the cell's inside. Essentially, the energy released from the ATP hydrolysis couples 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

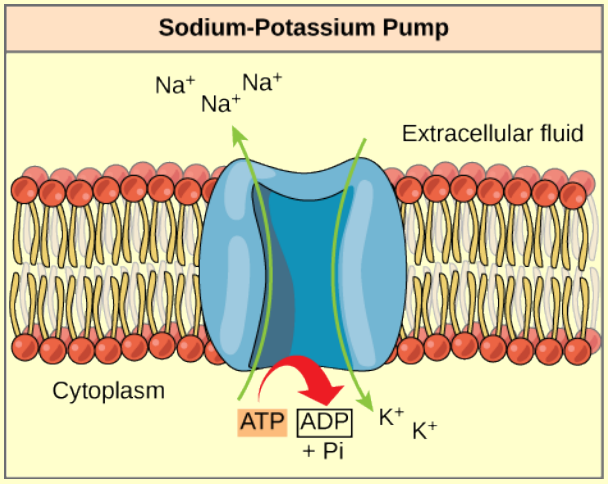

Figure 6.14 The sodium-potassium pump is an example of energy coupling. The energy derived from exergonic ATP hydrolysis pumps sodium and potassium ions across the cell membrane.

One ATP molecule's hydrolysis 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 one ATP molecule's hydrolysis move?

Often during cellular metabolic reactions, such as nutrient synthesis and breakdown, certain molecules must alter 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 sugar glucose molecule breaks down in the process of glycolysis. In the first step, ATP is required to phosphorylze glucose, creating a high-energy but unstable intermediate. This phosphorylation reaction powers a conformational change that allows the phosphorylated glucose molecule to convert to the phosphorylated sugar fructose. Fructose is a necessary intermediate for glycolysis to move forward. Here, ATP hydrolysis' exergonic reaction couples 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 phosphorylyzing 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 do the following:

- 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 enzymes. Almost all enzymes are proteins, comprised of amino acid chains, 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 do not change the reaction's ΔG. In other words, they do not change whether a reaction is exergonic (spontaneous) or endergonic. This is because they do not change the reactants' or products' free energy. They only reduce the activation energy required to reach the transition state (**Figure 6.15**).

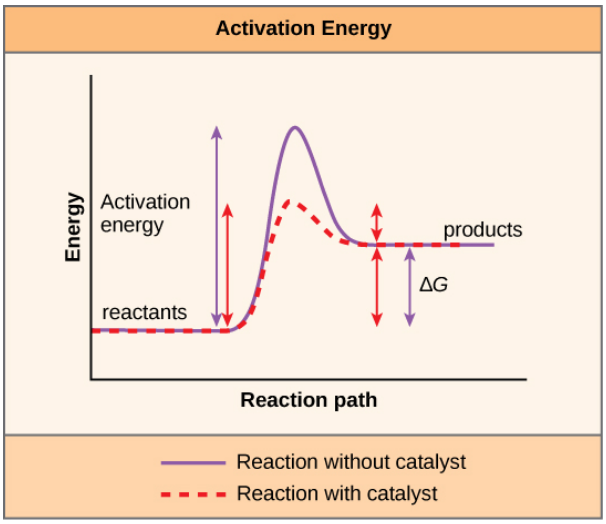

Figure 6.15 Enzymes lower the reaction's activation energy but do not change the reaction's free energy.

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 breaks 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 the enzyme's **active site**. This is where the "action" happens. Since enzymes are proteins, there is a unique combination of amino acid residues (also side chains, or R groups) within the active site. Different properties characterize each residue. These 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 local enviromental influences. 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 substance's natural properties. Likewise, the local environment's pH 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 environmental pH values (acidic or basic) 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 scientists call **induced fit** (**Figure 6.16**). This 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 substrate's transition state. This ideal binding maximizes the enzyme’s ability to catalyze its reaction.

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

When an enzyme binds its substrate, it forms an enzyme-substrate complex. This complex lowers the reaction's activation energy 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 other molecule's appropriate region with which it must react. Another way in which enzymes promote substrate reaction 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 have 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 reaction's completion. One of enzymes' hallmark properties is that they remain ultimately unchanged by the reactions they catalyze. After an enzyme catalyzes a reaction, it releases its product(s).

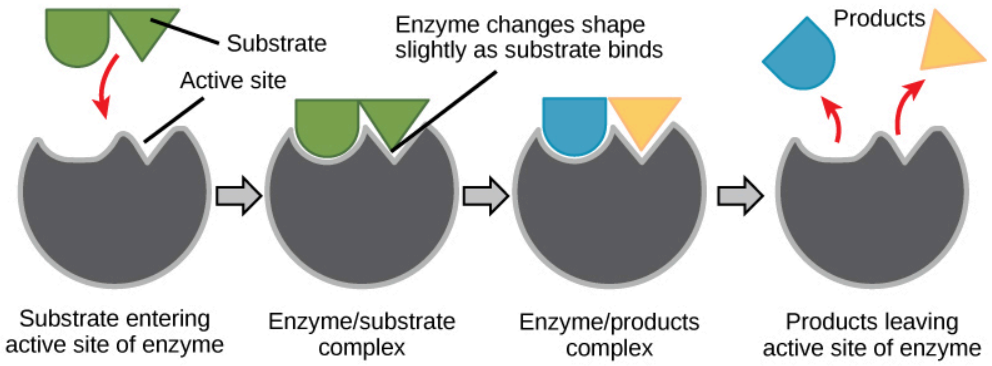

Figure 6.16 According to the induced-fit model, both enzyme and substrate undergo dynamic conformational changes upon binding. The enzyme contorts the substrate into its transition state, thereby increasing the reaction's rate.

Metabolism Control Through Enzyme Regulation

It would seem ideal to have a scenario in which all the encoded enzymes 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, environmental factors like pH and temperature partly control enzyme activity. There are other mechanisms through which cells control enzyme activity and determine the rates at which various biochemical reactions will occur.

Molecular Regulation of Enzymes

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. For example, in some cases of enzyme inhibition, 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**). Alternatively, in noncompetitive inhibition, an inhibitor molecule binds to the enzyme in a location other than an allosteric site, a binding site away from the active site, and still manages to block substrate binding to the active site.

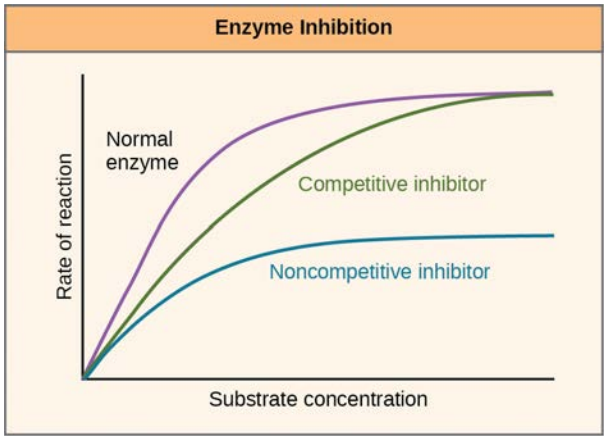

Figure 6.17 Competitive and noncompetitive inhibition affect the reaction's rate differently. Competitive inhibitors affect the initial rate but do not affect the maximal rate; whereas, noncompetitive inhibitors affect the maximal rate.

Some inhibitor molecules bind to enzymes in a location where their binding induces a conformational change that reduces the enzyme's affinity for its substrate. This type of inhibition is an **allosteric inhibition** (**Figure 6.18**). More than one polypeptide comprise most allosterically regulated enzymes, meaning that they have more than one protein subunit. When an allosteric inhibitor binds to an enzyme, all active sites on the protein subunits change 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).

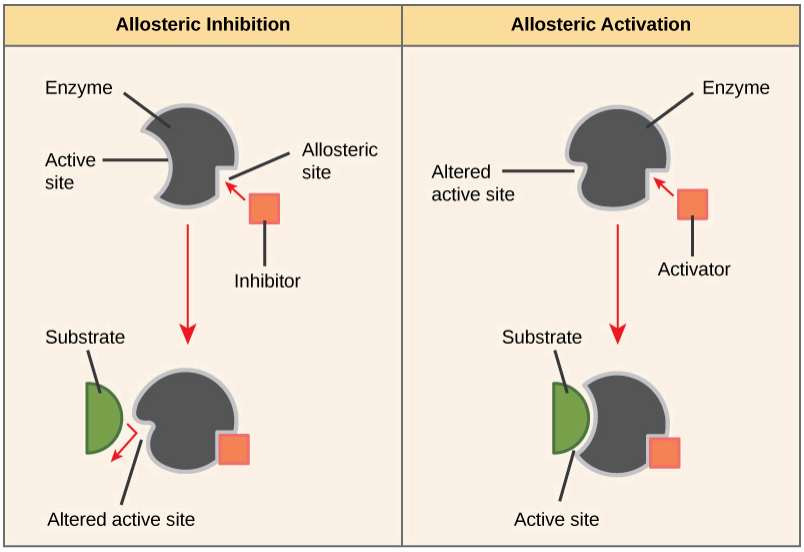

Figure 6.18 Allosteric inhibitors modify the enzyme's active site so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the enzyme's active site so that the affinity for the substrate increases.

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 developing many 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 a 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 drug reduces cholesterol levels synthesized in the body. 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), scientists still do not completely understand its mechanism of action.

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. Researchers identify targets 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 researchers identify the target and the pathway, then the actual drug design process 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 obtain 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 a bound zinc ion (Zn++) to function. Coenzymes are organic helper molecules, with a basic atomic structure comprised 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 breaking down glucose to yield energy is catalysis by a multi-enzyme complex scientists call 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 the diets of most organisms supply.

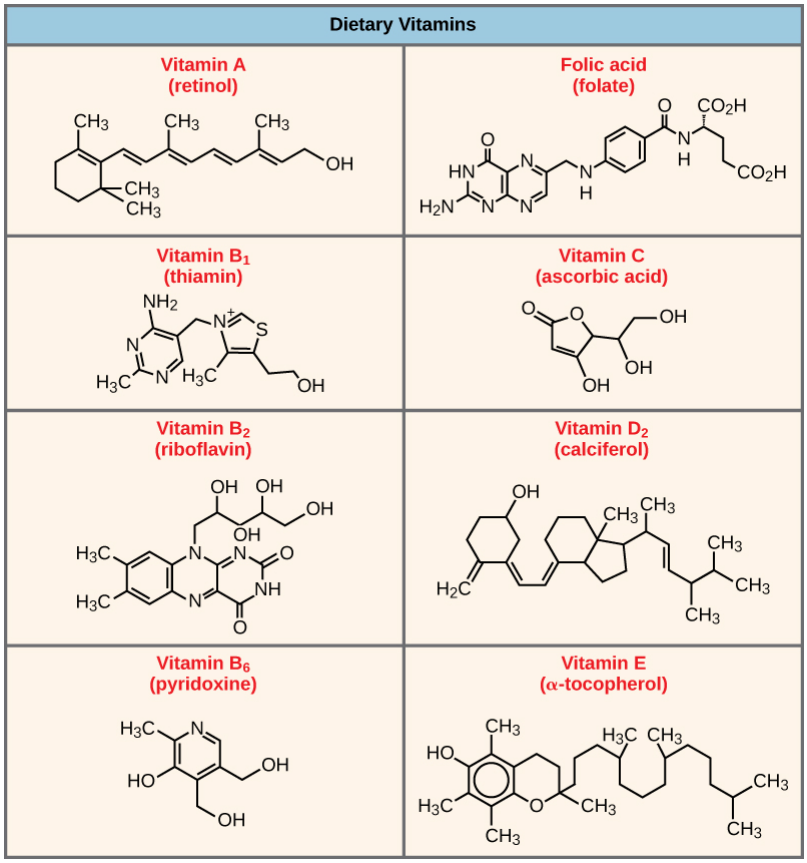

Figure 6.20 Vitamins are important coenzymes or precursors of coenzymes, and are required for enzymes to function properly. Multivitamin capsules usually contain mixtures of all the vitamins at different percentages.

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 are sometimes 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 digesting cellular debris and foreign materials, located within lysosomes.

Feedback Inhibition in Metabolic Pathways

Molecules can regulate enzyme function in many ways. However, a major question remains: What are these molecules and from where do they come? Some are cofactors and coenzymes, ions, and organic molecules, as you have 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 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 cellular metabolic reaction products themselves. In a most efficient and elegant way, cells have evolved to use their own reactions' products for feedback inhibition of enzyme activity. **Feedback inhibition** involves using 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 that we described above.

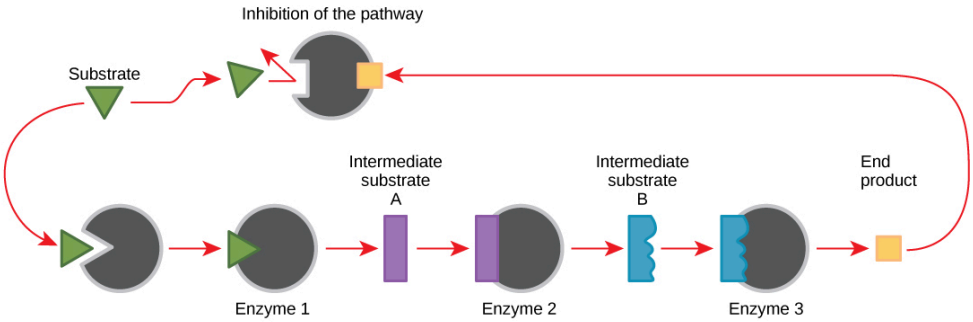

Figure 6.21 Metabolic pathways are a series of reactions that multiple enzymes catalyze. Feedback inhibition, where the pathway's end product inhibits an upstream step, is an important regulatory mechanism in cells.

Producing both amino acids and nucleotides is controlled through feedback inhibition. Additionally, ATP is an allosteric regulator of some of the enzymes involved in sugar's catabolic breakdown, 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. Alternatively, ADP serves as a positive allosteric regulator (an allosteric activator) for some of the same enzymes that ATP inhibits. Thus, when relative ATP levels are high compared to ATP, the cell is triggered to produce more ATP through sugar catabolism.