Because ΔG has a positive value, you know that the product of this reaction has more free energy than the reactant. This is an endergonic reaction. It is not spontaneous and does not take place without an energy source.

By contrast, consider the following reaction:

$$(2)\ C \longrightarrow D \qquad \Delta G = -33.5\ \text{kJ/mol}\ (-8\ \text{kcal/mol})$$

The negative value of ΔG tells you that the free energy of the reactant is greater than the free energy of the product. This exergonic reaction proceeds spontaneously.

You can sum up reactions 1 and 2 as follows:

$$(1)\ A \longrightarrow B \qquad \Delta G = +20.9\ \text{kJ/mol}\ (+5\ \text{kcal/mol})$$
$$(2)\ C \longrightarrow D \qquad \Delta G = -33.5\ \text{kJ/mol}\ (-8\ \text{kcal/mol})$$
$$\text{Overall} \qquad \Delta G = -12.6\ \text{kJ/mol}\ (-3\ \text{kcal/mol})$$

Because thermodynamics considers the overall changes in these two reactions, which show a net negative value of ΔG, the two reactions taken together are exergonic.

The fact that scientists can write reactions this way is a useful bookkeeping device, but it does not mean that an exergonic reaction mysteriously transfers energy to an endergonic "bystander" reaction. However, these reactions are coupled if their pathways are altered so a common intermediate links them. Reactions 1 and 2 might be coupled by an intermediate (I) in the following way:

$$(3)\ A + C \longrightarrow I \qquad \Delta G = -8.4\ \text{kJ/mol}\ (-2\ \text{kcal/mol})$$
$$(4)\ I \longrightarrow B + D \qquad \Delta G = -4.2\ \text{kJ/mol}\ (-1\ \text{kcal/mol})$$
$$\text{Overall} \qquad \Delta G = -12.6\ \text{kJ/mol}\ (-3\ \text{kcal/mol})$$

Note that reactions 3 and 4 are sequential. Thus, the reaction pathways have changed, but overall the reactants (A and C) and products (B and D) are the same, and the free-energy change is the same.

Generally, for each endergonic reaction occurring in a living cell there is a coupled exergonic reaction to drive it. Often the exergonic reaction involves the breakdown of ATP. Now let's examine specific examples of the role of ATP in energy coupling.

Review

- Consider the free-energy change in a reaction in which enthalpy decreases and entropy increases. Is ΔG zero, or does it have a positive value or a negative value? Is the reaction endergonic or exergonic?
- Why can't a reaction at equilibrium do work?

7.4 ATP, THE ENERGY CURRENCY OF THE CELL

LEARNING OBJECTIVE

7 Explain how the chemical structure of ATP allows it to transfer a phosphate group and discuss the central role of ATP in the overall energy metabolism of the cell.

In all living cells, energy is temporarily packaged within a remarkable chemical compound called **adenosine triphosphate (ATP),** which holds readily available energy for very short periods. We may think of ATP as the energy currency of the cell. When you work to earn money, you might say your energy is symbolically stored in the money you earn. The energy the cell requires for immediate use is temporarily stored in ATP, which is like cash. When you earn extra money, you may deposit some in the bank; similarly, a cell may deposit energy in the chemical bonds of lipids, starch, or glycogen. Moreover, just as you dare not make less money than you spend, the cell must avoid energy bankruptcy, which would mean its death. Finally, just as you probably do not keep money you earn very long, the cell continuously spends its ATP, which must be replaced immediately.

ATP is a nucleotide consisting of three main parts: adenine, a nitrogen-containing organic base; ribose, a five-carbon sugar; and three phosphate groups, identifiable as phosphorus atoms surrounded by oxygen atoms (**FIG. 7-5**). Notice that the phosphate

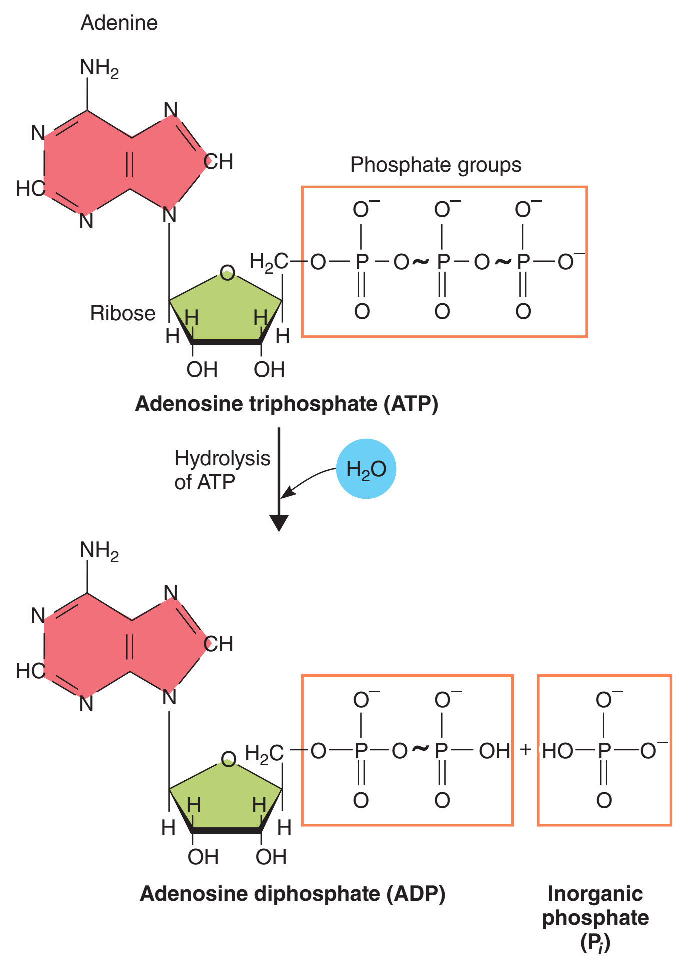

FIGURE 7-5 ***Animated*** **ATP and ADP**

ATP, the energy currency of all living things, consists of adenine, ribose, and three phosphate groups. The hydrolysis of ATP, an exergonic reaction, yields ADP and inorganic phosphate. (The black wavy lines indicate unstable bonds. These bonds allow the phosphates to be transferred to other molecules, making them more reactive.)

groups are bonded to the end of the molecule in a series, rather like three cars behind a locomotive, and, like the cars of a train, they can be attached and detached.

ATP donates energy through the transfer of a phosphate group

When the terminal phosphate is removed from ATP, the remaining molecule is adenosine diphosphate (ADP) (see Fig. 7-5). If the phosphate group is not transferred to another molecule, it is released as inorganic phosphate (P_i). This is an exergonic reaction with a relatively large negative value of ΔG. (Calculations of the free energy of ATP hydrolysis vary somewhat, but range between about −28 and −37 kJ/mol, or −6.8 to −8.7 kcal/mol.)

$$(5)\ \text{ATP} + H_2O \longrightarrow \text{ADP} + P_i \qquad \Delta G = -32\ \text{kJ/mol (or } -7.6\ \text{kcal/mol)}$$

Reaction 5 can be coupled to endergonic reactions in cells. Consider the following endergonic reaction, in which two monosaccharides, glucose and fructose, form the disaccharide sucrose.

$$(6)\ \text{glucose} + \text{fructose} \longrightarrow \text{sucrose} + H_2O \qquad \Delta G = +27\ \text{kJ/mol (or } +6.5\ \text{kcal/mol)}$$

With a free-energy change of −32 kJ/mol (−7.6 kcal/mol), the hydrolysis of ATP in reaction 5 can drive reaction 6, but only if the reactions are coupled through a common intermediate.

The following series of reactions is a simplified version of an alternative pathway that some bacteria use:

$$(7)\ \text{glucose} + \text{ATP} \longrightarrow \text{glucose-P} + \text{ADP}$$

$$(8)\ \text{glucose-P} + \text{fructose} \longrightarrow \text{sucrose} + P_i$$

Recall from Chapter 6 that a **phosphorylation reaction** is one in which a phosphate group is transferred to some other compound. In reaction 7 glucose becomes phosphorylated to form glucose phosphate (glucose-P), the intermediate that links the two reactions. Glucose-P, which corresponds to I in reactions 3 and 4, reacts exergonically with fructose to form sucrose. For energy coupling to work in this way, reactions 7 and 8 must occur in sequence. It is convenient to summarize the reactions thus:

$$(9)\ \text{glucose} + \text{fructose} + \text{ATP} \longrightarrow \text{sucrose} + \text{ADP} + P_i \qquad \Delta G = -5\ \text{kJ/mol}\ (-1.2\ \text{kcal/mol})$$

When you encounter an equation written in this way, remember that it is actually a summary of a series of reactions and that transitory intermediate products (in this case, glucose-P) are sometimes not shown.

ATP links exergonic and endergonic reactions

We have just discussed how the transfer of a phosphate group from ATP to some other compound is coupled to endergonic reactions in the cell. Conversely, adding a phosphate group to adenosine monophosphate, or AMP (forming ADP), or to ADP (forming ATP) requires coupling to exergonic reactions in the cell.

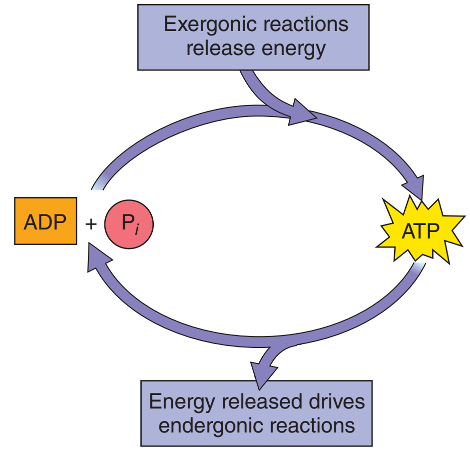

FIGURE 7-6 ATP links exergonic and endergonic reactions
Exergonic reactions in catabolic pathways (*top*) supply energy to drive the endergonic formation of ATP from ADP. Conversely, the exergonic hydrolysis of ATP supplies energy to endergonic reactions in anabolic pathways (*bottom*).

$$\text{AMP} + P_i + \text{energy} \longrightarrow \text{ADP}$$

$$\text{ADP} + P_i + \text{energy} \longrightarrow \text{ATP}$$

Thus, ATP occupies an intermediate position in the metabolism of the cell and is an important link between exergonic reactions, which are generally components of *catabolic pathways,* and endergonic reactions, which are generally part of *anabolic pathways* (**FIG. 7-6**).

The cell maintains a very high ratio of ATP to ADP

The cell maintains a ratio of ATP to ADP far from the equilibrium point. ATP constantly forms from ADP and inorganic phosphate as nutrients break down in cellular respiration or as photosynthesis traps the radiant energy of sunlight. At any time, a typical cell contains more than 10 ATP molecules for every ADP molecule. The fact that the cell maintains the ATP concentration at such a high level (relative to the concentration of ADP) makes its hydrolysis reaction even more strongly exergonic and more able to drive the endergonic reactions to which it is coupled.

Although the cell maintains a high ratio of ATP to ADP, the cell cannot store large quantities of ATP. The concentration of ATP is always very low, less than 1 mmol/L. In fact, studies suggest that a bacterial cell has no more than a 1-second supply of ATP. Thus, it uses ATP molecules almost as quickly as they are produced. A healthy adult human at rest uses about 45 kg (100 lb) of ATP each day, but the amount present in the body at any given moment is less than 1 g (0.035 oz). Every second in every cell, an estimated 10 million molecules of ATP are made from ADP and phosphate, and an equal number of ATPs transfer their phosphate groups, along with their energy, to whatever chemical reactions need them.

Review

- Why do coupled reactions typically have common intermediates?

- Give a generalized example of a coupled reaction involving ATP, distinguishing between the exergonic and endergonic reactions.
- Why is the ATP concentration in a cell about 10 times the concentration of ADP?

7.5 ENERGY TRANSFER IN REDOX REACTIONS

LEARNING OBJECTIVE

8 Relate the transfer of electrons (or hydrogen atoms) to the transfer of energy.

You have seen that cells transfer energy through the transfer of a phosphate group from ATP. Energy is also transferred through the transfer of electrons. As discussed in Chapter 2, oxidation is the chemical process in which a substance loses electrons, whereas reduction is the complementary process in which a substance gains electrons. Because electrons released during an oxidation reaction cannot exist in the free state in living cells, every oxidation reaction must be accompanied by a reduction reaction in which the electrons are accepted by another atom, ion, or molecule. Oxidation and reduction reactions are often called redox reactions because they occur simultaneously. The substance that becomes oxidized gives up energy as it releases electrons, and the substance that becomes reduced receives energy as it gains electrons.

Redox reactions often occur in a series, as electrons are transferred from one molecule to another. These electron transfers, which are equivalent to energy transfers, are an essential part of cellular respiration, photosynthesis, and many other chemical processes. Redox reactions, for example, release the energy stored in food molecules so that ATP can be synthesized using that energy.

Most electron carriers transfer hydrogen atoms

Generally, it is not easy to remove one or more electrons from a covalent compound; it is much easier to remove a whole atom. For this reason, redox reactions in cells usually involve the transfer of a hydrogen atom rather than just an electron. A hydrogen atom contains an electron, plus a proton that does not participate in the oxidation–reduction reaction.

When an electron, either singly or as part of a hydrogen atom, is removed from an organic compound, it takes with it some of the energy stored in the chemical bond of which it was a part. That electron, along with its energy, is transferred to an acceptor molecule. An electron progressively loses free energy as it is transferred from one acceptor to another.

One of the most common acceptor molecules in cellular processes is **nicotinamide adenine dinucleotide (NAD^+)**. When NAD^+ becomes reduced, it temporarily stores large amounts of free energy. Here is a generalized equation showing the transfer of hydrogen from a compound, which we call X, to NAD^+:

$$\underset{\text{Oxidized}}{XH_2} + \underset{\text{Reduced}}{NAD^+} \longrightarrow X + NADH + H^+$$

Notice that the NAD^+ becomes reduced when it combines with hydrogen. NAD^+ is an ion with a net charge of +1. When 2 electrons and 1 proton are added, the charge is neutralized and the reduced form of the compound, **NADH,** is produced (**FIG. 7-7**). (Although the correct way to write the reduced form of NAD^+

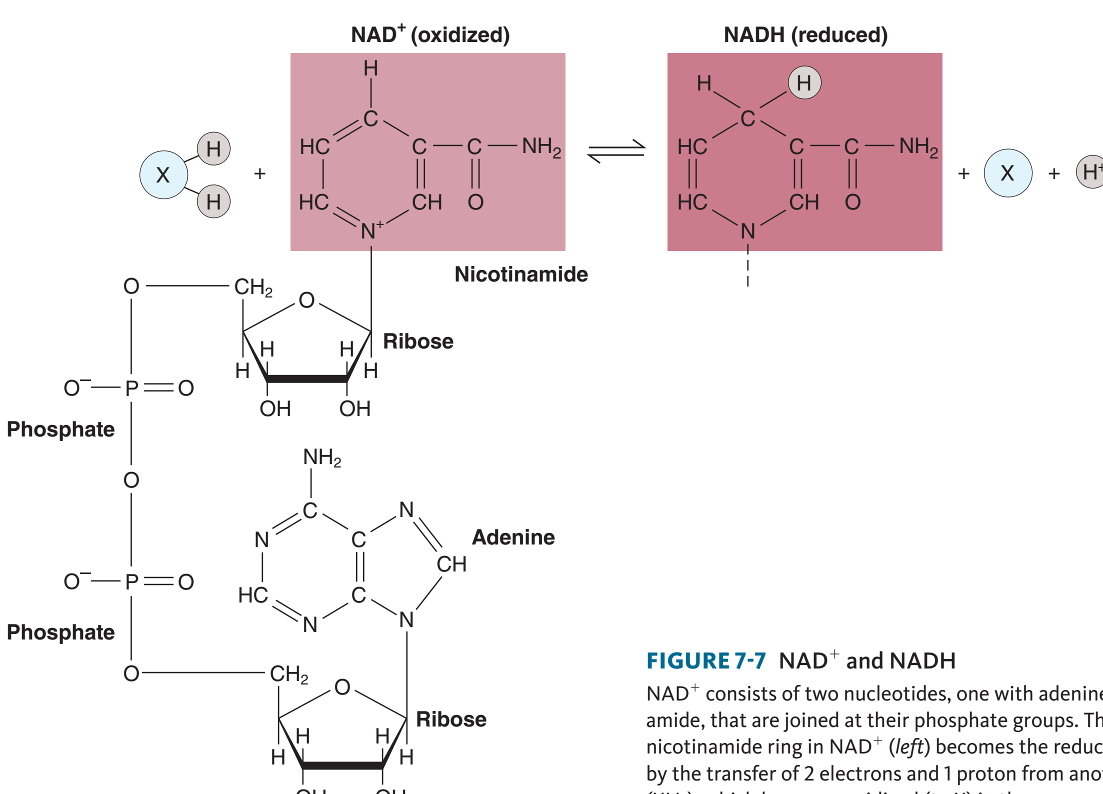

FIGURE 7-7 NAD^+ and NADH

NAD^+ consists of two nucleotides, one with adenine and one with nicotinamide, that are joined at their phosphate groups. The oxidized form of the nicotinamide ring in NAD^+ (*left*) becomes the reduced form in NADH (*right*) by the transfer of 2 electrons and 1 proton from another organic compound (XH_2), which becomes oxidized (to X) in the process.

is NADH + H^+, for simplicity we present the reduced form as NADH in this book.) Some energy stored in the bonds holding the hydrogen atoms to molecule X has been transferred by this redox reaction and is temporarily held by NADH. When NADH transfers the electrons to some other molecule, some of their energy is transferred. This energy is usually then transferred through a series of reactions that ultimately result in the formation of ATP (discussed in Chapter 8).

Nicotinamide adenine dinucleotide phosphate ($NADP^+$) is a hydrogen acceptor that is chemically similar to NAD^+ but has an extra phosphate group. Unlike NADH, the reduced form of $NADP^+$, abbreviated **NADPH,** is not involved in ATP synthesis. Instead, the electrons of NADPH are used more directly to provide energy for certain reactions, including certain essential reactions of photosynthesis (discussed in Chapter 9).

Other important hydrogen acceptors or electron acceptors are FAD and the cytochromes. Flavin adenine dinucleotide (FAD) is a nucleotide that accepts hydrogen atoms and their electrons; its reduced form is $FADH_2$. The cytochromes are proteins that contain iron; the iron component accepts electrons from hydrogen atoms and then transfers these electrons to some other compound. Like NAD^+ and $NADP^+$, FAD and the cytochromes are electron transfer agents. Each exists in a *reduced state,* in which it has more free energy, or in an *oxidized state,* in which it has less. Each is an essential component of many redox reaction sequences in cells.

Review

- Which has the most energy, the oxidized form of a substance or its reduced form? Why?

7.6 ENZYMES

LEARNING OBJECTIVES

9 Explain how an enzyme lowers the required energy of activation for a reaction.

10 Describe specific ways enzymes are regulated.

The principles of thermodynamics help us predict whether a reaction can occur, but they tell us nothing about the speed of the reaction. The breakdown of glucose, for example, is an exergonic reaction, yet a glucose solution stays unchanged virtually indefinitely in a bottle if it is kept free of bacteria and molds and not subjected to high temperatures or strong acids or bases. Cells cannot wait for centuries for glucose to break down, nor can they use extreme conditions to cleave glucose molecules. Cells regulate the rates of chemical reactions with **enzymes,** which are biological **catalysts** that increase the speed of a chemical reaction without being consumed by the reaction. Although most enzymes are proteins, scientists have learned that some types of RNA molecules have catalytic activity as well (catalytic RNA is discussed in Chapter 13).

Cells require a steady release of energy, and they must regulate that release to meet metabolic energy requirements. Metabolic processes generally proceed by a series of steps such that a molecule may go through as many as 20 or 30 chemical transformations before it reaches some final state. Even then, the seemingly completed molecule may enter yet another chemical pathway and become totally transformed or consumed to release energy. The changing needs of the cell require a system of flexible metabolic control. The key directors of this control system are enzymes.

The catalytic ability of some enzymes is truly impressive. For example, hydrogen peroxide (H_2O_2) breaks down extremely slowly if the reaction is uncatalyzed, but a single molecule of the enzyme **catalase** brings about the decomposition of 40 million molecules of hydrogen peroxide per second! Catalase has the highest catalytic rate known for any enzyme. It protects cells by destroying hydrogen peroxide, a poisonous substance produced as a byproduct of some cell reactions. The bombardier beetle uses the enzyme catalase as a defense mechanism (**FIG. 7-8**).

All reactions have a required energy of activation

All reactions, whether exergonic or endergonic, have an energy barrier known as the **energy of activation (E_A),** or **activation energy,** which is the energy required to break the existing bonds and begin the reaction. In a population of molecules of any kind, some have a relatively high kinetic energy, whereas others have a lower energy content. Only molecules with a relatively high kinetic energy are likely to react to form the product.

Even a strongly exergonic reaction, one that releases a substantial quantity of energy as it proceeds, may be prevented from proceeding by the activation energy required to begin the reaction. For example, molecular hydrogen and molecular oxygen can react explosively to form water:

$$2\,H_2 + O_2 \longrightarrow 2\,H_2O$$

Thomas Eisner and Daniel Aneshansley/Cornell University

FIGURE 7-8 Catalase as a defense mechanism

When threatened, a bombardier beetle (*Stenaptinus insignis*) uses the enzyme catalase to decompose hydrogen peroxide. The oxygen gas formed in the decomposition ejects water and other chemicals with explosive force. Because the reaction releases a great deal of heat, the water comes out as steam. (A wire attached by a drop of adhesive to the beetle's back immobilizes it. The researcher prodded its leg with the dissecting needle on the left to trigger the ejection.)