Chapter 8

Concepts of Metabolism

KEY CONCEPTS

1. Almost every chemical reaction that takes place in a cell is catalyzed (accelerated) by a specific enzyme. Each type of enzyme is formed from a unique kind of protein molecule. Some types of enzymes also require special non-protein cofactors to work.

2. Chemical reactions in a cell form a network of interrelated metabolic pathways. The cell controls the synthesis and breakdown of chemicals by regulating the activities of enzymes that catalyze key reactions in the network.

3. Every reaction--and every set of interrelated (coupled) reactions--that proceeds forward spontaneously (with or without enzymatic catalysis) loses free energy. A reaction that gains free energy can be forced to proceed by coupling it to another reaction that loses even more free energy.

4. Two key reactions that lose free energy--the hydrolysis of adenosine triphosphate and the oxidation of nicotinamide adenine dinucleotide--power many of the activities of a cell.

8.1 SWIMMING UPSTREAM

Living organisms have a problem. They consist of highly ordered forms of matter in a universe that favors an ever greater state of disorder. Furthermore, they need a constant supply of ordered, complex molecules to say alive. Similar to salmon swimming upstream, life itself moves against the universe's chaotic tendencies. That it can do so stems from the ability of plants to supply not only themselves but almost all other living organisms with the basic molecules needed for life. To overcome the universal current of disorder, plants use the sun's energy to synthesize carbohydrates, hydrocarbons, and other complex molecules from much simpler molecules. They then reverse the process and use the energy stored in the new molecules to drive various life-sustaining processes. But synthesizing and destroying complex molecules poses another problem: how to orchestrate thousands of chemical reactions so that they fit together in the complex process called metabolism. This chapter describes some of the elegant solutions cells have devised to control the rates of chemical reactions as well as to surmount the energy hurdles to building complex molecules and structures.

8.2 CHEMICAL REACTIONS

Living cells are made of thousands of different chemical compounds. Some of these are small, simple compounds, such as water, sugars, and amino acids; others, such as proteins and nucleic acids, are large, complex molecules. Many of these compounds, especially the complex ones, are used to construct the organelles seen inside a cell.

Some compounds are the building blocks of more complex molecules. Still others have specialized functions in the life of the cell, such as defending against pathogens or herbivores.

Virtually every plant cell synthesizes all the different complex compounds that it contains. These compounds are formed from very simple chemicals containing carbon, hydrogen, oxygen, and nitrogen, as well as smaller amounts of other elements such as sulfur and phosphorus. Water (H_2O), carbon dioxide (CO_2), ammonium (NH_4^+) or nitrate (NO_3^-) ion, sulfate (SO_4^{2-}), and phosphate (PO_4^{3-}) represent the major basic stocks for the production of all the other molecules in the cell. Water, which makes up more than 90% of the weight of the protoplast (the portion of the cell inside the cell wall), is primarily a solvent, but it also is the source of most of the hydrogen atoms and some of the oxygen atoms in organic molecules. Carbon dioxide is the primary source of carbon and is a major source of oxygen. Ammonium and nitrate are the primary sources of nitrogen in proteins and nucleic acids. Sulfate is the source of the sulfur found in some amino acids, and inorganic phosphate is incorporated into nucleotides.

The rearrangement of atoms from their initial positions in certain molecules to new positions in other molecules is called a *chemical reaction*. In cells of biological organisms, the reactions often are called *biochemical reactions*. It is clear that there must be thousands of biochemical reactions in plant cells to produce the thousands of bio-organic molecules found there.

Chemical Reactions Must Overcome Energy Barriers

Although every chemical reaction is different, there are concepts that describe reactions in general. Because a chemical reaction involves the rearrangement of atoms, it must also involve the breaking and re-formation of some of the covalent bonds holding the atoms together. The covalent bonds represent shared pairs of electrons in orbitals that are reasonable stable. To break an existing bond, it is necessary to stretch or bend it. This destabilizes the electrons, enabling them to move to other, even more stable places. Just as it takes energy to stretch or bend a spring, it takes energy to stretch or bend a covalent bond. And just as the energy used to stretch a spring is not lost--it is stored as potential energy--the energy used to stretch a bond also is stored as potential energy. The energy can be recovered as the stretched bond either springs back (and the electrons move back to their original positions) or breaks (and the electrons move to other stable positions.

Figure 8.1 shows the potential energy relationships of the various phases of the following reaction:

$$A + B \rightarrow C + D \quad ,$$

where A and B, the **substrates** (or reactants) of the reaction, collide and rearrange their covalent bonds to form C and D, the products of the reaction. The two molecules, A and B, have a certain amount of potential energy inherent in their separate covalent bonds. As they collide, their bonds bend (that is, the electron orbitals move from their most stable positions), and their potential energy goes up. This distorted, high-energy state is called an *activated complex*. As the activated complex forms, electrons can move to new orbitals, and bonds thus can shift. For instance, the orbitals holding an atom to the other atoms of A can be broken, and new orbitals can form to attach the atom to the atoms of B. At this step, C and D form. As the new bonds shift into their most stable positions, the potential energy of C and D decreases to its normal value. For A and B to react to form C and D, they must attain an increase in potential energy, called the **activation energy**. The activation energy is an energy barrier that must be scaled for the reaction to proceed.

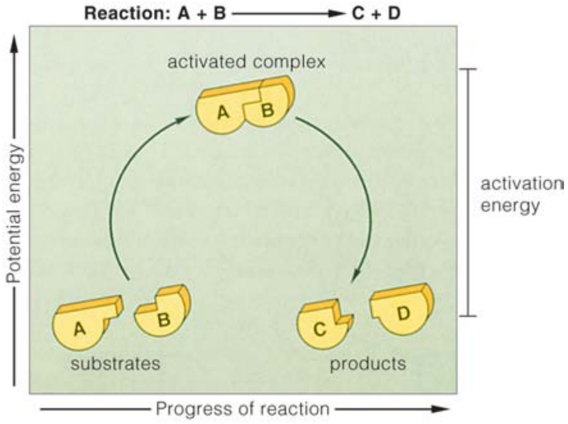


Fig. 8.1. The changes in potential energy of two molecules as they exchange atoms in a chemical reaction.

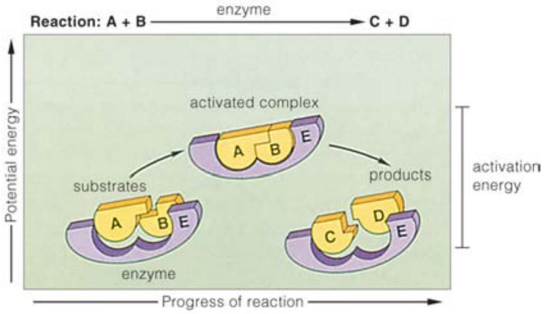


Fig. 8.2. The changes in potential energy of two molecules as they exchange atoms in an enzyme-catalyzed reaction. The activation energy is less than it was in the uncatalyzed reaction shown in Fig. 8.1.

The law of conservation of energy says that energy cannot be created or destroyed in normal chemical reactions. Where does the energy come from to bend the bonds of A and B and form the activated state? That increasing the temperature speeds the reaction suggests that it comes from the energy of motion--the kinetic energy--of the two substrates. The average amount of kinetic energy of a mixture depends on the temperature. The greater the temperature, the faster the molecules in the mixture are moving. In a solution such as the cytoplasm, molecules are closely packed and travel for only short distances before bouncing against other molecules. The means that the molecules of water and other solutes continually collide with the substrate molecules; thus, the kinetic energy of the substrate molecules matches the kinetic energy of the other molecules in the mixture.

Although the temperature determines the average energy of all the molecules, including the substrates, individual molecules have more or less than the average. At a normal temperature, for instance 20°C, only a few A and B pairs will come together with enough kinetic energy to provide the potential energy needed to form the activated complex. This limits the rate at which the reaction can proceed. If the temperate increases, the reaction goes faster because a greater proportion of the A and B pairs will have enough kinetic energy.

A Catalyst Speeds a Reaction by Decreasing the Energy Barrier

The rate of a chemical reaction is important. Each of the thousands of reactions in a cell must proceed at a reasonable rate for the cell to function. There are a few ways to speed up a reaction. Increasing the concentrations of the substrates speeds the reaction by increasing the probability that pairs of substrate molecules will meet. Increasing the temperature increases the rate at which molecules move and thus the frequency with which pairs of molecules will meet. As mentioned earlier, increasing the temperature also speeds the reaction by increasing the probability that substrate molecules will have enough kinetic energy to form an activated complex when they meet.

Although cells can increase the concentrations of specific molecules, they can do so only up to a certain point. Increasing the temperature is not a good strategy for speeding biochemical reactions in a cell because many of a cell's components are harmed by excessive heat. Instead, cells rely on catalysts to speed up reactions. Catalysts are not substrates or products of the reaction. They are neither used up nor formed as the reaction proceeds, although they do interact closely with the substrates. A catalyst can be as simple as the metallic element palladium, or it can be a complex biomolecule. A catalyst is thought to work by forming a temporary complex with one or both substrates, attaching to it (or them) with reversible bonds (bonds that will break after the reactions is completed). The formation of the complex distorts the bonds of the substrate, so that further bond bending or stretching requires less energy.

A diagram showing the effect of a catalyst would look similar to the original energy diagram (compare Fig. 8.2 with Fig. 8.1). Substrates plus catalyst have a certain amount of potential energy. When they come together to form an activated complex (which may be quite different in form from the uncatalyzed activated complex described in Fig. 8.1), they have a high potential energy. As the products are formed and the new bonds relax, the potential energy of the trio decreases again. The difference between the catalyzed and the original, uncatalyzed reaction is that the amount of activation energy needed is less in the catalyzed reaction. Therefore, at a particular temperature, the substrates plus catalyst are more likely than the substrates alone to have enough energy to form an activated complex.

Enzymes Catalyze Specific Reactions

One of the features that characterizes all living cells is the presence of biological catalysts called enzymes. Enzymes catalyze the thousands of reactions in a cell. Enzymes differ from simple catalysts, such as palladium, in their specificity. Each enzyme works on only one set of substrates (or at most, a few related substrates); each enzyme catalyzes one type of reaction. That means that a cell must have thousands of enzymes to catalyze all the reactions it needs.

With few exceptions, enzymes are made of protein molecules. As described in Chapter 2, proteins are large polymeric molecules with complex three-dimensional shapes. Each different type of protein has a different shape. In particular, enzyme proteins have **active sites**, which are grooves or crevices in their surfaces, into which one or both of the substrates can fit (Fig. 8.3). The shape of the active site is almost complementary to that of the substrate--that is, the active site almost fits the substrate as a glove fits a hand. The substrate is held in the active site by hydrogen bonds and other forces that are weak individually but very effective as a group. As the substrate is held in the active site, its bonds are distorted in any of a number of ways. Sometimes pulling the substrate into a slightly misfitting groove distorts the substrate's shape; sometimes the active site changes shape once the substrate is present; sometime electric charges in the active site push and pull the electrons of the substrate; sometimes functional groups (side chains of amino acids) in the active site react (temporarily) with the substrate. In any case, the distortion of the substrate makes it susceptible to the particular reaction catalyzed by the enzyme. If the reaction involves two substrates, the active site might bind both, bringing them close together in the proper orientation to react.

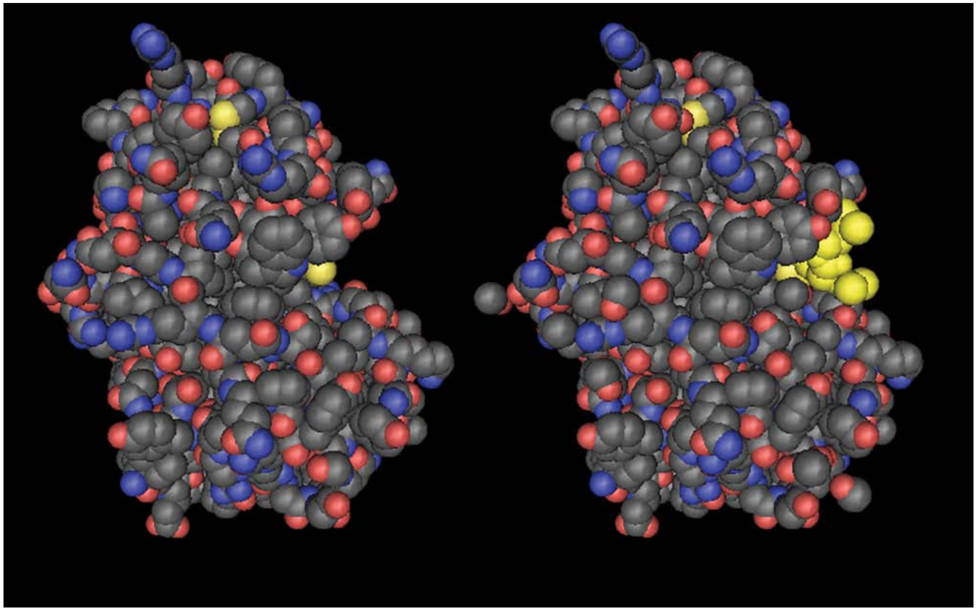


Figure 8.3. Three-dimensional model of an enzyme, papain, from papaya (*Carica papaya*) fruit. The image at the left shows the active site (notch at the right of the molecule). The yellow atom is a sulfur, essential for enzyme activity. The image at the right shows a substrate molecule (yellow-green) in the active site. Papain hydrolyzes the bonds between amino acids in a polypeptide chain. It is used as a meat tenderizer.

Some enzymes depend only on their protein structure for their activity; others cannot function without certain nonprotein substances called *cofactors*. Examples of cofactors include metal ions, such as Fe^{2+} and Fe^{3+}, as well as complex organic molecules without metal ions. Some cofactors are bound to enzymes by covalent bonds. Others are loosely bound and may be removed easily from the enzyme protein. Often, but not always, the cofactors are able to accept or donate electrons in oxidation-reduction reactions. If a cofactor (sometimes called a **coenzyme**) is loosely bound to its enzyme and is capable of accepting and donating electrons (or hydrogen atoms; electrons plus protons), it may serve as a carrier of electrons (or hydrogen atoms) from one reaction to another. Plants require trace amounts of certain metals that serve as cofactors, for instance, iron, copper, and molybdenum, but they make all the bio-organic cofactors they use. Many of the bio-organic cofactors that are common in plants--such as riboflavin, thiamin, niacin, and pantothenic acid--cannot be synthesized by humans. We obtain these compounds from the plants we eat.

The results of some plant enzyme activities are easy to detect. The darkening of an apple fruit after it has been cut or bitten results from the action of the enzyme polyphenol oxidase on chemicals released from the cells. The softening of a tomato fruit as it ripens is caused by the action of several enzymes on the polysaccharides of the cell walls, including cellulase, which breaks down cellulose, and polygalacturonase, which cleaves the pectin chains. Papain, an enzyme from papaya fruit, digests proteins in the fruit as it ripens. It also can be extracted from the fruit and used to tenderize meat quickly before it is cooked.

The Rates of Reactions Can Be Controlled by the Synthesis, Activation, and Inhibition of Enzymes

In a normal cell, the temperature is too low for most essential biochemical reactions to occur at reasonable rates. For cells to function, all the reactions must occur fairly rapidly and in a balanced fashion. In this way, the components of the cells can be synthesized in the proper proportions, and no one material is formed (using up all the substrates) at the expense of all the others. The synthesis of the various organelles must be balanced, and synthetic reactions must be coordinated with the reactions that break down molecules into their component parts.

Cells have several ways of controlling the rates of individual reactions. One method is to synthesize the enzyme that catalyzes a particular reaction when, and only when, that reaction is needed. The formation and germination of a seed provides a good example. A seed contains an embryo with associated tissues that store nutrients used for the growth of the embryo when the seed germinates. The nutrients include starch, and starch is formed in the cells from simple carbohydrate subunits imported in the form of sucrose. Two enzymes (at least) are required to break down sucrose and use the products to form starch; these enzymes increase in amount as the seed is formed. Later, they disappear. When the seed germinates, the starch must be broken down into subunits, and the enzymes that accomplish this are synthesized during the early stages of germination. The synthesis of enzymes is a key aspect of development and is discussed in more detail in Chapter 15. The control of reaction rates by the synthesis and breakdown of enzymes is rather slow and crude. A much quicker and finer control occurs through the regulation of the catalytic activity of already existing enzymes. Such regulation is possible because the catalytic activity of an enzyme depends on its three-dimensional shape, and the shape depends in turn on weak bonds, such as hydrogen bonds, that can be easily broken and reformed. Not all enzymes can be regulated in this way; those that can generally have a special site on their surface that will bind a regulatory molecule. In some cases, a special enzyme attaches a phosphate group to that site covalently. In other cases, some other molecule (there are many possibilities) binds to the site through weak bonds, such as hydrogen or ionic bonds. Binding of the regulatory molecule changes the shape of the enzyme, and that change affects the shape of the active site (Fig. 8.4). The overall result is either (1) to lower the affinity of the active site for the substrate or its catalytic efficiency once the substrate has been bound, in which case the enzyme is inhibited, or (2) to increase the affinity of the active site for the substrate or its catalytic efficiency, in which case the enzyme is activated.

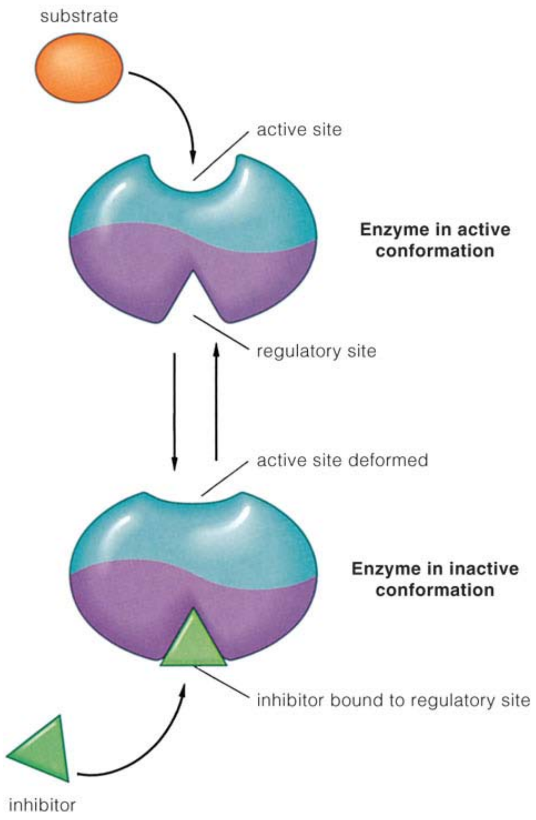


Fig. 8.4. A regulatory enzyme has two sites: an "active" catalytic site and a site at which a regulatory molecule ("inhibitor") can bind. In the presence of the regulatory molecule, the enzyme changes it shape. Substrate binding at the active site may contribute to (or oppose) the shape change.

The regulatory step used depends on the enzyme. It may involve a normal compound found in the cell, perhaps the substrate or product of another chemical reaction. For the regulated enzyme, this compound serves as a signal to turn off or on the reaction it catalyzes. Later in this chapter we show how regulation of an enzyme in this way can maintain a steady concentration of a compound.

8.3 METABOLIC PATHWAYS

Most bio-organic molecules produced in a cell are formed not from a single chemical reaction but from a sequence of reaction, in which the product of one reaction becomes the substrate for the next. A series of such linked reactions in a cell is called a **metabolic pathway**.

Reactions Are Linked When One Reaction's Product Is Another's Substrate

It is not possible to make complex molecules in a single step; it takes a series of simple steps. A single step might be the addition of the components of water to the molecule or a reduction (addition of one or two electrons) or perhaps the removal of a CO_2 group. A series of such steps, each in the correct order, can lead to quite complex compounds, as seen in Chapters 9 and 10.

In a metabolic pathway (Fig. 8.5), the product of the first reaction is the substrate of the second reaction, the product of the second reaction is the substrate of the third, and so forth. Each reaction is catalyzed by a separate enzyme. The products of reactions, other than the final product of a series, are called **intermediates**. For this reason, the collection of all the metabolic pathways in cells is called **intermediary metabolism**. The enzymes that catalyze the reactions are linked: each enzyme depends on the ones before it to provide substrates. Without the substrates, the enzymes cannot function. In the same way, each enzyme depends on those after it to complete the formation of the pathway's product. Without the enzymes for the later reactions, intermediates will accumulate, and no final product will be formed.

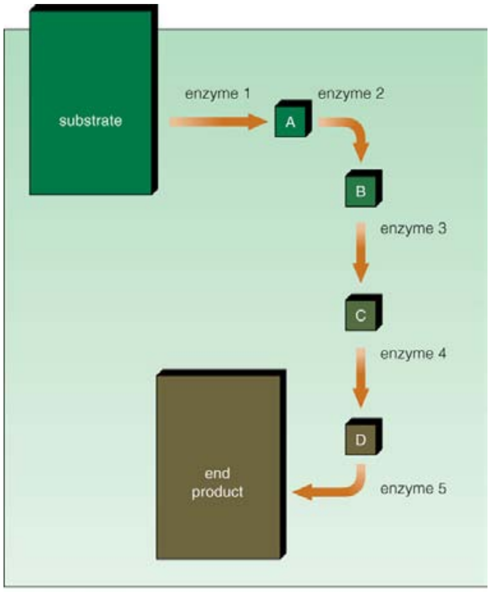


Figure 8.5. A metabolic pathway. Each letter represents a different compound. Each reaction is catalyzed by a different enzyme.

In Cells, Linked Reactions Form a Complex Network

Although Figure 8.5 shows a simple linear pathway, few, if any, pathways in a cell are this simple. In some cases, two or more compounds are needed to form a product. Frequently, one intermediate is used as a substrate by several separate enzymes to produce different products. In this case, the intermediate is called a *branch point* because, diagrammatically, the pathways appear to branch off in different directions (Fig. 8.6). Some intermediate are key compounds in the cell because they serve as substrates for many different reactions.

Figure 8.6 gives a rough idea of the complexity of the metabolic reactions in a typical plant cell. This diagram shows several metabolic pathways linked together, with each arrow representing a separate reaction with a separate enzyme. Each pair of adjacent reactions is connected by an intermediate, although only a few key intermediates are shown.

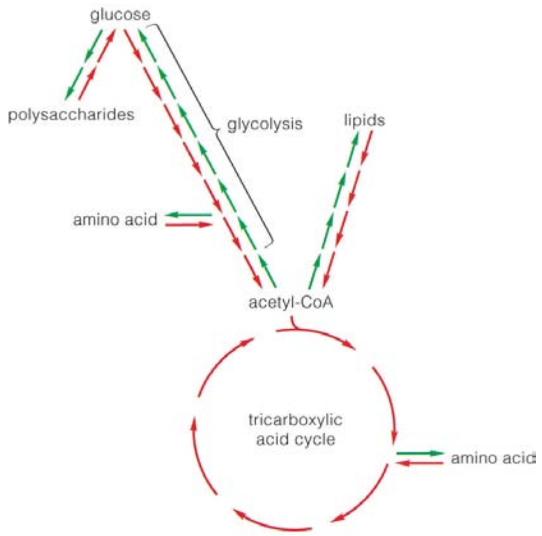


Figure 8.6. A simplified picture of some interacting metabolic pathways in a typical plant cell. The anabolic reactions (*green arrows*) synthesizing substances and the catabolic reactions (*red arrows*) breaking down substances often involve different enzymes. *Glycolysis* and the *tricarboxylic acid cycle* are pathways described in Chapter 9.

The reactions that produce subunits of functional or structural molecules, such as proteins or cellulose, are sometimes called **anabolic** reactions. Reactions that break down damaged or unwanted molecules into their component parts are called **catabolic** reactions. Figure 8.6 indicates these two classes of reactions, with arrows pointed in opposite direction to denote that the synthesis and breakdown of materials generally, but not always, involve different enzymes. In some cells, such as those in meristems, anabolic reactions predominate; in others, such as the cells in ripening fruit, catabolic reactions are most active. In most cells of plants and other organisms, both sets of reactions occur; there is a constant synthesis and breakdown--called a turnover--of cell components.

The Concentration of a Compound Often Controls Its Production in a Cell

Cells cannot afford to allow metabolic pathways to run amok. If pathways operated without any control, materials and energy would be wasted in the formation of unneeded compounds or the breakdown of necessary ones. Certain intermediates might accumulate to toxic levels; others vital to the cell might become scarce. That reactions are organized into pathways immediately suggests an efficient way of controlling the formation of the end product of a pathway. Because each reaction depends on the ones before it to provide substrates, the cell need only shut off the activity of the first enzyme in the pathway to restrict the formation of the final product.

A control mechanism often found in cells is that the first enzyme (*branch-point enzyme*) of a pathway has a regulatory site, and the final product of that pathway serves as its inhibitor (Fig. 8.7). This mechanism keeps the concentration of the product constant. As the product accumulates and its concentration increases, the product inhibits the branch-point enzyme; therefore, its synthesis slows down. As the cells use up the product, its concentration decreases, the inhibition of the branch-point enzyme is released, and synthesis resumes. This type of control is called **feedback inhibition**. It is just one example of the ways in which the control of enzyme activity can be used to orchestrate metabolic reactions.

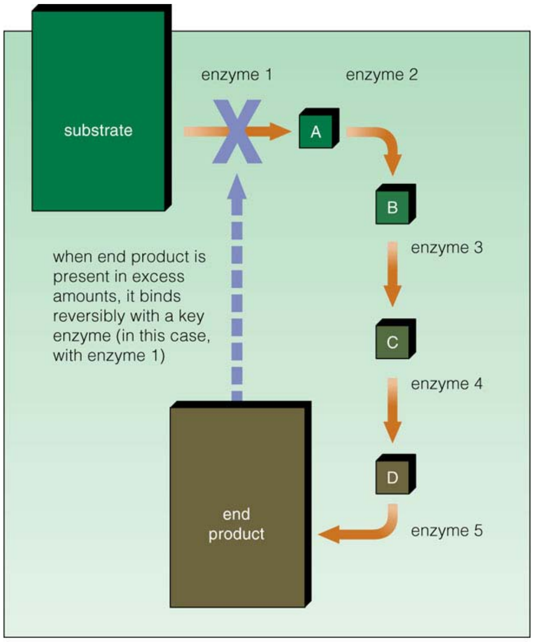


Figure 8.7. Feedback inhibition of a branch-point enzyme stops the formation of the final product of the pathway. The dotted line indicates that the final product of the pathway inhibits the catalytic activity of enzyme 1.

8.4 THE ROLE OF FREE ENERGY IN METABOLISM

Free Energy Determines the Direction a Reversible Reaction will Take

Most chemical and biochemical reactions are reversible, at least in theory, so that:

$$A + B \leftrightarrow C + D$$

This means that the substrates and products of a reaction can be interconverted. Under arbitrary conditions, a reversible reaction generally favors one direction or the other. Therefore, the rate of the forward reaction, $A + B \rightarrow C + D$, often differs initially from that of the reverse reaction, $A + B \leftarrow C + D$. As the forward and reverse reactions proceed, the overall reaction reaches a state of equilibrium. The rates of the forward and reverse reactions become equal, and the concentrations of the substrates and products become constant. Enzymes are thought to reduce the *time* needed to reach equilibrium but not the change the *ratio* of substrates and products at equilibrium.

What determines the direction in which a reaction proceeds? There are several factors: (a) the initial concentrations of substrates and products in the reaction's mixture; (b) the relative stability of the bonds in the substrates and products; (c) the number of substrates and products that participate in the reaction; and (d) the temperature.

Chemists and biochemists group all the above factors into one useful concept: the **free energy**. Every chemical or set of chemicals can be assigned a free energy value. That is, the greater the concentration of substrates in a reaction mixture, the grater their free energy. The more stable the bonds of the substrates, the lower their free energy. The more independent molecules included in the substrates, the lower their free energy. All these statements apply also to the *products* of a reaction.

Every chemical reaction that can be imagined is associated with a change in free energy, which is defined as the difference between the free energies of the products and substrates. The reason that this concept is important is that *every reaction that proceeds forward spontaneously (with or without enzymatic catalysis) loses free energy*. Every reaction that shows no change in free energy is at equilibrium. Every reaction that is associated with an increase in free energy will not occur spontaneously and will need free energy from some source to proceed. These concepts are diagrammed in Figure 8.8. This figure shows why spontaneous reactions, those associated with a decrease in free energy, are sometimes called *downhill reactions* and why reactions that do not proceed spontaneously may be called *uphill reactions*. Note that free energy includes potential energy but also includes other factors; thus the graph in Figure 8.8 is not the same as--and cannot be compared with--the graph in Figure 8.1.

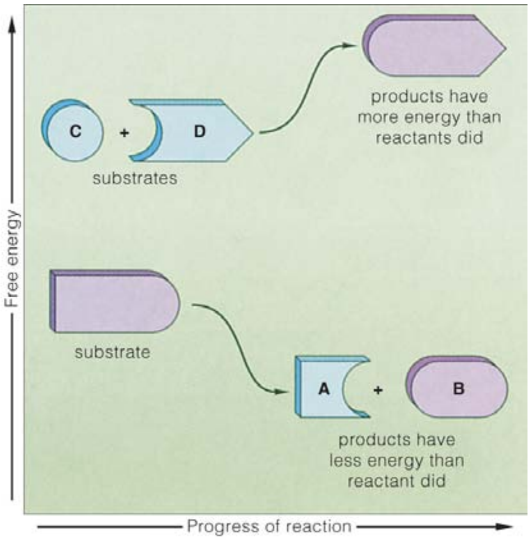


Figure 8.8. Free energy changes in uphill and downhill reactions. Only the downhill reaction will go forward spontaneously. Uphill reactions require an input of free energy from some other source.

The free energy requirements for reactions provide a difficulty for cells because many of the anabolic reactions on which the growth and survival of a cell depend are associated with an increase in free energy. The combination of 100 amino acids into a single protein represents a large increase in free energy, as does the synthesis of a large molecule of RNA or DNA. The reduction of carbon-containing molecules to form the hydrocarbon chains in lipid molecules involves the formation of bonds that are inherently less stable in an oxygen atmosphere--again representing an increase in free energy. Movement, whether it is the whipping of flagella or the separation of chromosomes during mitosis, depends on uphill chemical reactions. The accumulation of nutrients by pumping ions from an area of low concentration to an area of high concentration also depends on reactions that require the input of free energy. Some of the great discoveries in biology have been the ways in which cells provide sources of free energy to force anabolic reactions forward, thus obtaining the materials they need to power growth and reproduction.

In Coupled Reactions, a Downhill Reaction Can Push an Uphill Reaction

When biologists try to unravel the complexities of metabolism, one of the ways in which they simplify the biochemical reactions is to think of partial reactions. In oxidation-reduction reactions, for example, one compound is oxidized (loses electrons), and another is reduced (gains electrons). The oxidation can be written as a separate, but partial, reaction, and so can the reduction. Neither reaction occurs by itself, however, because electrons must be conserved. Because they must occur together, the reactions are said to be *coupled*.

Another example is the transfer of a phosphate group. One compound might lose a phosphate group through a **hydrolysis reaction** (the addition of the components of water, H^+ and OH^-, breaking the bond between the phosphate and the rest of the compound). Another compound might gain a phosphate group through a **condensation reaction** (the opposite of hydrolysis, producing water). These two partial reactions can be coupled so that they occur together. In this case, neither the hydrolysis nor the condensation actually occurs; instead, the phosphate group is transferred from the first compound to the second without ever being independent.

The coupling of the two reactions means that the change in free energy of the overall reaction equals the sum of the changes in free energy of the partial reactions. This is important because if one of the partial reactions is a strong uphill reaction but the other is an even stronger downhill reaction, the overall reaction will be downhill, and both reactions will proceed spontaneously. It is not unreasonable to suggest that the downhill partial reaction has forced the uphill reaction to run forward. If the uphill reaction involves the synthesis of DNA, then the cell has provided free energy, in the form of the substrates of the downhill partial reaction, to make DNA. If the uphill reaction involves the separation of chromosomes in anaphase, then the cell has provided free energy for that process.

Two Downhill Reactions Run Much of the Cell's Machinery

There are a number of downhill reactions that occur in almost all cells and that are coupled to many uphill reactions. Two of the most common of these reactions are described in the following paragraphs.

HYDROLYSIS OF ADENSINE TRIPHOSPHATE The compound adenosine triphosphate (ATP) is found in all cells. It is formed from the nucleotide adenosine--which is composed of the complex organic base adenine, covalently bound to the sugar ribose--plus three phosphate groups (Fig. 8.9a).

The three phosphates hooked together (triphosphate) form a relative unstable assemblage. They can be split apart by hydrolysis (addition of water) to form adenosine diphosphate (ADP) and an independent phosphate group (Fig. 8.9b). This hydrolysis reaction is spontaneous and is associated with a release of free energy of 7 to 12 kcal per mole of ATP, just enough to run any of several uphill reactions in a cell.

The hydrolysis of ATP, for instance, provides energy to pump protons across a membrane, to force the addition of an amino acid to a growing protein, and to extend a cellulose chain by one glucose unit. It also powers the motor proteins that attach to microtubules; these move cilia and flagella and the chromosomes in mitosis. ATP is the quintessential *high-energy compound* or *energy carrier*. That it is formed in the mitochondrion (by a condensation of ADP with phosphate--formally the reverse of the reaction shown in Fig. 8.9b) is the main reason that the mitochondrion is called the "powerhouse of the cell."

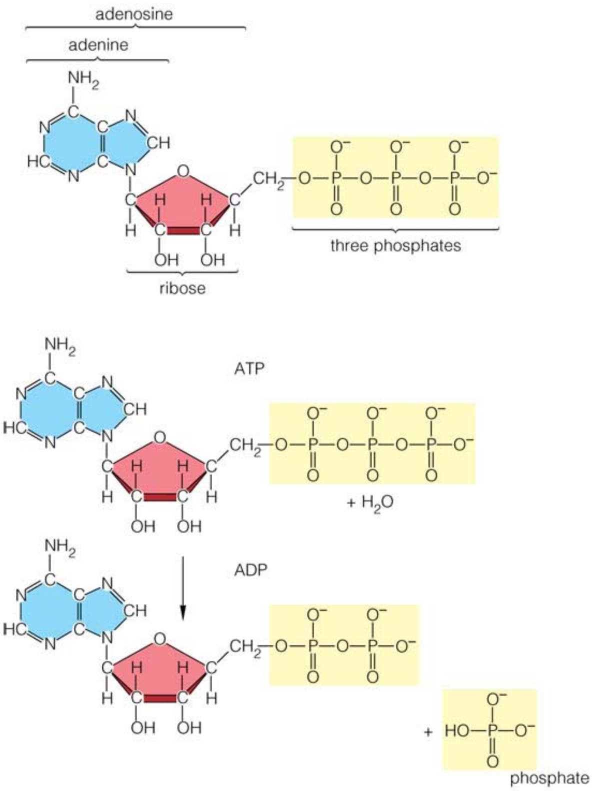


Figure 8.9. Adenosine triphosphate (ATP), the main energy carrier in cells. (a) The structural formula for ATP. (b) The hydrolysis of ATP, a strongly downhill reaction.

OXIDATION OF NICOTINAMIDE ADENINE DINUCLEOTIDE AND NICOTINAMIDE ADENINE DINUCLEOTIDE PHOSPHATE The coenzymes **nicotinamide adenine dinucleotide (NADH)** and **nicotinamide adenine dinucleotide phosphate (NADPH)** are essential molecules in eukaryotic cells. The reactive part of these molecules is their nicotinamide functional group. Our bodies cannot synthesize nicotinamide; we must obtain it in food as the vitamin called *niacin*. Plant cells, however, can synthesize niacin and use it to make NADH and NADPH. NADH is the reduced form of the molecule, which can readily donate electrons to other molecules; the oxidized form, remaining after the electrons have gone, is denoted as NAD^+. The oxidation of NADH by oxygen gas (Fig. 8.10) is associated with the release of 52 kcal per mole of free energy! This is enough free energy to power the formation of several molecules of ATP. In fact, in mitochondria, the oxidation of NADH is coupled to the formation of two to three molecules of ATP. The oxidation of NADPH, a parallel reaction to that of NADH, is used to synthesize fatty acids and some amino acids and, in chloroplasts, carbohydrates.

Of course, the energy locked in the bonds of ATP, NADH, and NADPH does not come without cost. The reactions that form these compounds are uphill reactions, and they occur only when they are coupled to other downhill reactions. The metabolic pathways that provide the energy for the synthesis of these compounds are described in Chapter 9, which discusses cellular respiration, and Chapter 10, which describes photosynthesis.

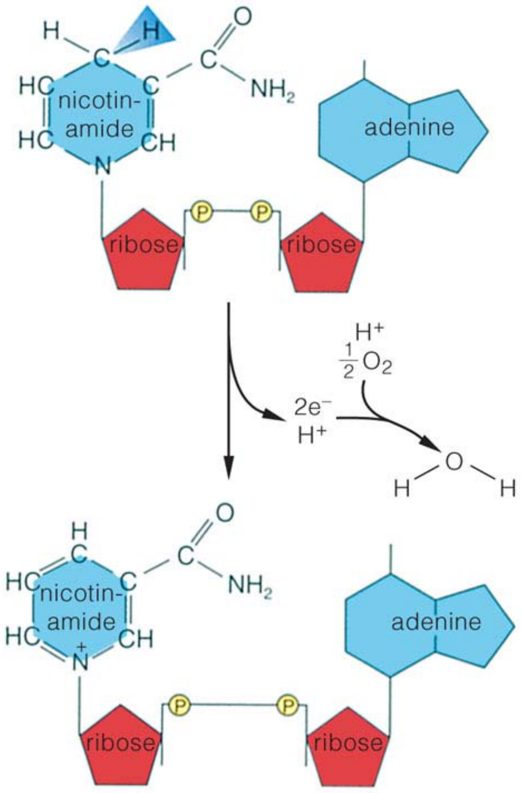


Figure 8.10. The oxidation of nicotinamide adenine dinucleotide (NADH) to NAD$^+$ by oxygen. Notice that the NADH loses one H (hydrogen atom), and one chemical bond between the H and C (carbon), which represents two electrons. The electrons may be transferred to a series of compounds before they reach oxygen.

KEY TERMS

activation energy
active sites
adenosine triphosphate (ATP)
anabolic
catabolic
catalysts
coenzyme
condensation reaction
feedback inhibition
free energy
hydrolysis reaction
intermediary metabolism
intermediates
kinetic energy
metabolic pathway
nicotinamide adenine dinucleotide (NADH)
nicotinamide adenine dinucleotide phosphate (NADPH)
potential energy
substrates

SUMMARY

1. The amount of potential energy needed to force molecules to react together limits the rate of a chemical reaction. Chemical reactions can be speeded up by increasing the concentration of the substrates, increasing the temperature, or adding a catalyst.

2. Enzymes are catalysts made from protein. Most enzymes catalyze a single reaction from a specific substrate or set of substrates. In cells, the rate of a reaction is determined by the amount of enzyme and by the activity of the enzyme that is present.

3. Enzyme-catalyzed reactions can be linked together in metabolic pathways, in which the product of one reaction is the substrate for the next, to produce complex biochemicals. In a cell, the network of metabolic pathways is complex, with a few key compounds being converted into many other compounds.

4. Feedback inhibition of the first enzyme in a pathway by the final product of the pathway enables the cell to control the concentration of that product.

5. The change in free energy of a reaction defines the direction in which it will proceed. The change in free energy is influenced by the initial concentrations of substrates and products in the reaction mixture, the relative stability of the bonds in the substrates and products, the number of independent substrates and products involved in the reaction, and the temperature. A spontaneous reaction always loses free energy.

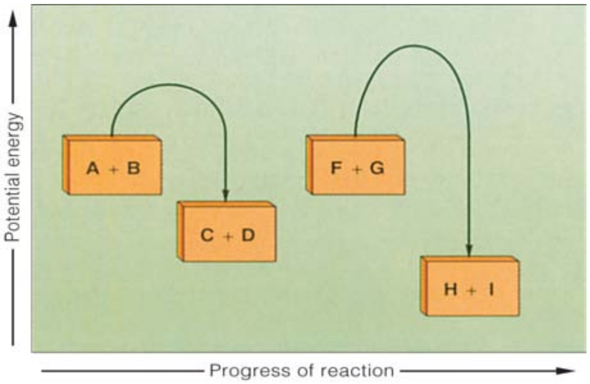
6. If two partial reactions are coupled, the free energy change of the overall reaction is the sum of their separate free energy changes. A downhill reaction can thus force an otherwise uphill reaction to proceed.

7. Two reactions, the hydrolysis of ATP and the oxidation of NADH, are coupled to--and drive--many of the important functions of a cell.

Questions

1. Name the sources of the elements carbon, hydrogen, oxygen, nitrogen, sulfur, and phosphorus that plants use for growth. Why are enzymes needed to convert these sources to bio-organic compounds?

2. The diagram below shows the energy relations for two chemical reactions in which chemical compounds A and B and converted to C and D, and F and G are converted to H and I. Which reaction will proceed faster? Explain.



3. Would increasing the temperature by 5°C change the diagram in Question #2? What would happen to the reactions?

4. Would adding an enzyme that catalyzes the first reaction (A + B → C + D) change the diagram in Question #2? How?

5. Adding a weak acid to a solution containing an enzyme usually inactivates the enzyme, often irreversibly. Boiling the solution does the same thing. Suggest an explanation for these observations.

6. Give an example from your own experience (other than the one in the text) of the action of the enzyme polyphenol oxidase. Do the same for the enzyme polygalacturonase.

7. Assume that three enzyme (E1, E2, and E3) form a metabolic pathway, such as:

$$A \xrightarrow{E1} B \xrightarrow{E2} C \xrightarrow{E3} D$$

Which factors will influence the rate of formation of D?

a. The amount of E1
b. The amount of E2
c. The amount of E3
d. The temperature
e. All of these

8. How are catabolic reactions energetically coupled to anabolic reactions in a cell?

9. In the metabolic pathway described in Question #7, are the reaction catalyzed by E1 and E2 coupled reactions? Explain your answer.

10. List five uphill reaction that occur in a living plant cell.

11. Maltose is formed from two glucose molecules bound together with a covalent bond. The enzyme maltase breaks the two glucoses apart by catalyzing the reaction:

maltose + H_2O → 2 glucose

A solution of maltose alone produces glucose very slowly, but when maltase is added to the solution, glucose appears rapidly. Which of following statements best explain this effect? Explain.

a. The free energy of glucose is much less than that of maltose.
b. The free energy of glucose is much more than that of maltose.
c. Maltase makes the reaction irreversible.
d. Maltase decreases the activation energy for the forward reaction.
e. Maltase increases the activation energy for the reverse reaction.

12. No one ever detects the formation of maltose when maltase is added to a solution of glucose. Which of the statements listed as possible answers to Question #11 best explains why?

13. In the presence of ATP, the enzyme luciferase, an enzyme found in the abdomens of fireflies, together with its cofactor luciferin produces light. Light is energy. Energy cannot be created; therefore the light energy must have come from somewhere. Where does the light energy come from?

a. From the breakdown of the luciferase and luciferin.
b. From the hydrolysis of ATP.
c. From the heat energy in the water molecules.

Figure credits

CO. http://en.wikipedia.org/wiki/Poppy
Fig. 3. Terence M. Murphy