

8

How Cells Harvest Energy from Food

Chapter-at-a-Glance

An Overview of Cellular Respiration

8.1 Where Is the Energy in Food?

In mitochondria, electrons are stripped from organic molecules to produce NADH and ATP, the reverse of the photosynthesis process in chloroplasts. This occurs in two stages, glycolysis and oxidation.

Respiration Without Oxygen: Glycolysis

8.2 Using Coupled Reactions to Make ATP

In glycolysis, reshuffling the bonds of glucose makes a small amount of ATP. In addition, electrons are transferred to carrier molecules, NAD^+ , forming NADH. NADH carries these electrons to other electron acceptor molecules.

Respiration With Oxygen: The Krebs Cycle

8.3 Harvesting Electrons from Chemical Bonds

Pyruvate, the product of glycolysis, enters the Krebs cycle. In the Krebs cycle, a series of oxidation-reduction reactions strips off energetic electrons and transfers them to NAD^+ and FAD, forming NADH and FADH_2 . These electron carriers ferry the electrons to the electron transport chain.

8.4 Using the Electrons to Make ATP

Electrons harvested from glucose and carried by NADH and FADH_2 pass through a chain of membrane proteins, called the electron transport chain, that use the energy to pump protons across the inner mitochondrial membrane. The proton gradient drives the synthesis of ATP.

Other Sources of Energy

8.5 Glucose Is Not the Only Food Molecule

Molecules other than glucose are consumed by organisms and used in harvesting energy. Macromolecules, such as proteins and lipids, are broken down into their monomers, which enter the oxidative respiration pathway at different points.



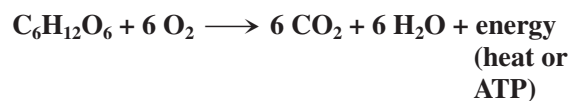
Animals such as this chipmunk depend on the energy stored in the chemical bonds of the food they eat to power their life processes. Their lives are driven by energy. All the activities this chipmunk carries out—climbing trees, chewing on acorns, seeing and smelling and hearing its surroundings, thinking the thoughts that chipmunks think—use energy. But unlike the oak tree that produces the nuts on which this chipmunk is dining, no part of the chipmunk is green. It cannot carry out photosynthesis like an oak tree, and so cannot harvest energy from the sun as the tree does. Instead, it must get its energy secondhand, by consuming organic molecules manufactured by plants. The chemical energy that the oak tree invested in making its molecules is harvested by the chipmunk in a process called cellular respiration. The same processes are used by all animals to harvest energy from molecules—and by plants too. There is no sunlight under the soil where the oak tree's roots penetrate, and like the cells of the chipmunk, these plant root cells obtain the energy to fuel their lives from cellular respiration. In this chapter, we examine cellular respiration up close. As you will see, cellular respiration and photosynthesis have much in common.

8.1 Where Is the Energy in Food?

In both plants and animals, and in fact in almost all organisms, the energy for living is obtained by breaking down the organic molecules originally produced in plants. The ATP energy and reducing power invested in building the organic molecules are retrieved by stripping away the energetic electrons and using them to make ATP. When electrons are stripped away from chemical bonds, the food molecules are being oxidized (remember, oxidation is the loss of electrons). The oxidation of foodstuffs to obtain energy is called **cellular respiration**. Do not confuse the term cellular respiration with the breathing of oxygen gas that your lungs carry out, which is called simply respiration.

The cells of plants fuel their activities with sugars and other fuel molecules, just as yours do; only the chloroplasts carry out photosynthesis. No light shines on roots below the ground, and yet root cells are just as alive as the cells in the stem and leaves. Why would plant cells manufacture organic molecules only to turn around and break them down? The organic molecules produced by plants serve two functions, to build plant tissue and to store energy for future needs. The plant breaks down “storage molecules” during cellular respiration. Nonphotosynthetic organisms eat plants, extracting energy from plant tissue and plant storage molecules in cellular respiration. Other animals, like the lion gnawing with such relish on a giraffe leg in figure 8.1, eat these animals.

In aerobic respiration, which requires oxygen, ATP is formed as electrons are harvested, transferred along an electron transport chain (similar to the electron transport system in photosynthesis), and eventually donated to oxygen gas. Eukaryotes produce the majority of their ATP from glucose in this way. Chemically, there is little difference between this oxidation of carbohydrates in a cell and the burning of wood in a fireplace. In both instances, the reactants are carbohydrates and oxygen, and the products are carbon dioxide, water, and energy:



Cellular respiration is carried out in two stages, illustrated in figure 8.2: The first stage uses coupled reactions to make ATP. This stage, *glycolysis*, takes place in the cell’s cytoplasm, (the blue area in figure 8.2). Importantly, it does not require oxygen. This ancient energy-extracting process is thought to have evolved over 2 billion years ago, when there was no oxygen in the earth’s atmosphere.

The second stage, which requires oxygen, takes place within the mitochondrion (the tan sausage-shaped structure in figure 8.2). The focal point of this stage is the *Krebs cycle*, shown as the dark blue circle, a cycle of chemical reactions



Figure 8.1 Lion at lunch.

Energy that this lion extracts from its meal of giraffe will be used to power its roar, fuel its running, and build a bigger lion.

that harvests electrons from C—H chemical bonds and passes the energy-rich electrons through the electron transport chain, which uses their energy to power the production of ATP. As you see in the figure, the harvested electrons are first transferred to electron carriers, NADH and FADH₂, that then deliver the electrons, indicated by the long red arrow on the left, to the electron transport chain. The harvesting of electrons, a form of *oxidation*, is far more powerful than glycolysis at recovering energy from food molecules, and is how the bulk of the energy used by eukaryotic cells is extracted from food molecules.

8.1 Cellular respiration is the dismantling of food molecules to obtain energy. In aerobic respiration, the cell harvests energy from glucose molecules in two stages, glycolysis and oxidation. Oxygen is the final electron acceptor.

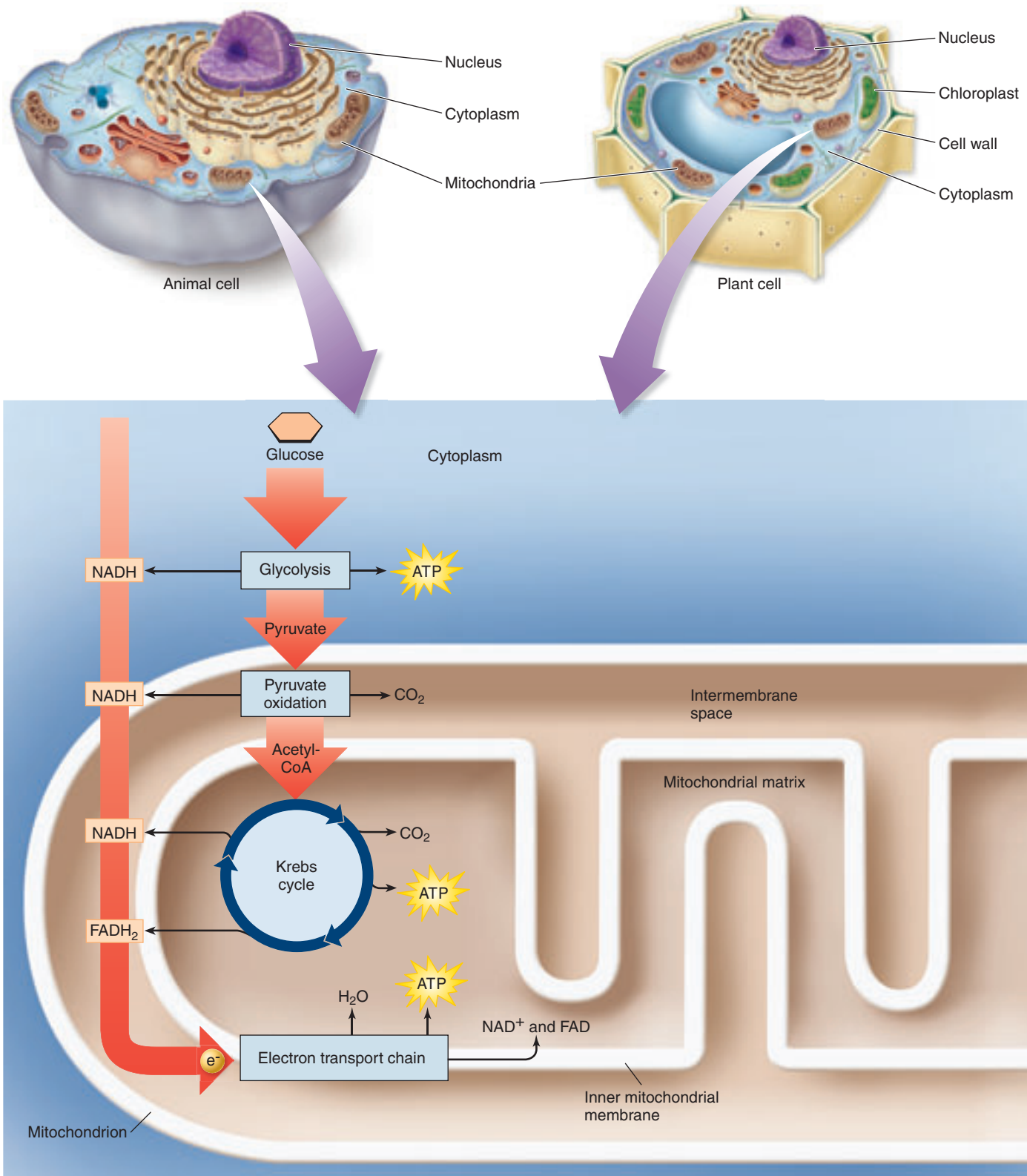


Figure 8.2 An overview of aerobic respiration.

8.2 Using Coupled Reactions to Make ATP

Glycolysis

The first stage in cellular respiration, **glycolysis** is a series of sequential biochemical reactions, a *biochemical pathway*. In 10 enzyme-catalyzed reactions, the six-carbon sugar glucose is cleaved into two three-carbon molecules called pyruvate. Figure 8.3 presents a conceptual overview of the process, while figure 8.4 provides a more detailed look at the series of 10 biochemical reactions. Where is the energy extracted? In each of two “coupled” reactions (steps 7 and 10 in figure 8.4), the breaking of a chemical bond in an exergonic reaction releases enough energy to drive the formation of an ATP

molecule from ADP (an endergonic reaction). This transfer of a high-energy phosphate group from a substrate to ADP is called **substrate-level phosphorylation**. In the process, electrons and hydrogen atoms are extracted and donated to a carrier molecule called NAD^+ . The NAD^+ carries the electrons as NADH to join the other electrons extracted during oxidative respiration, discussed in the following section. Only a small number of ATP molecules are made in glycolysis itself, two for each molecule of glucose, but in the absence of oxygen this is the only way organisms can get energy from food.

Glycolysis is thought to have been one of the earliest of all biochemical processes to evolve. Every living creature is capable of carrying out glycolysis. Glycolysis, although inefficient, was not discarded during the course of evolution but rather was used as the starting point for the further extraction

Overview of Glycolysis

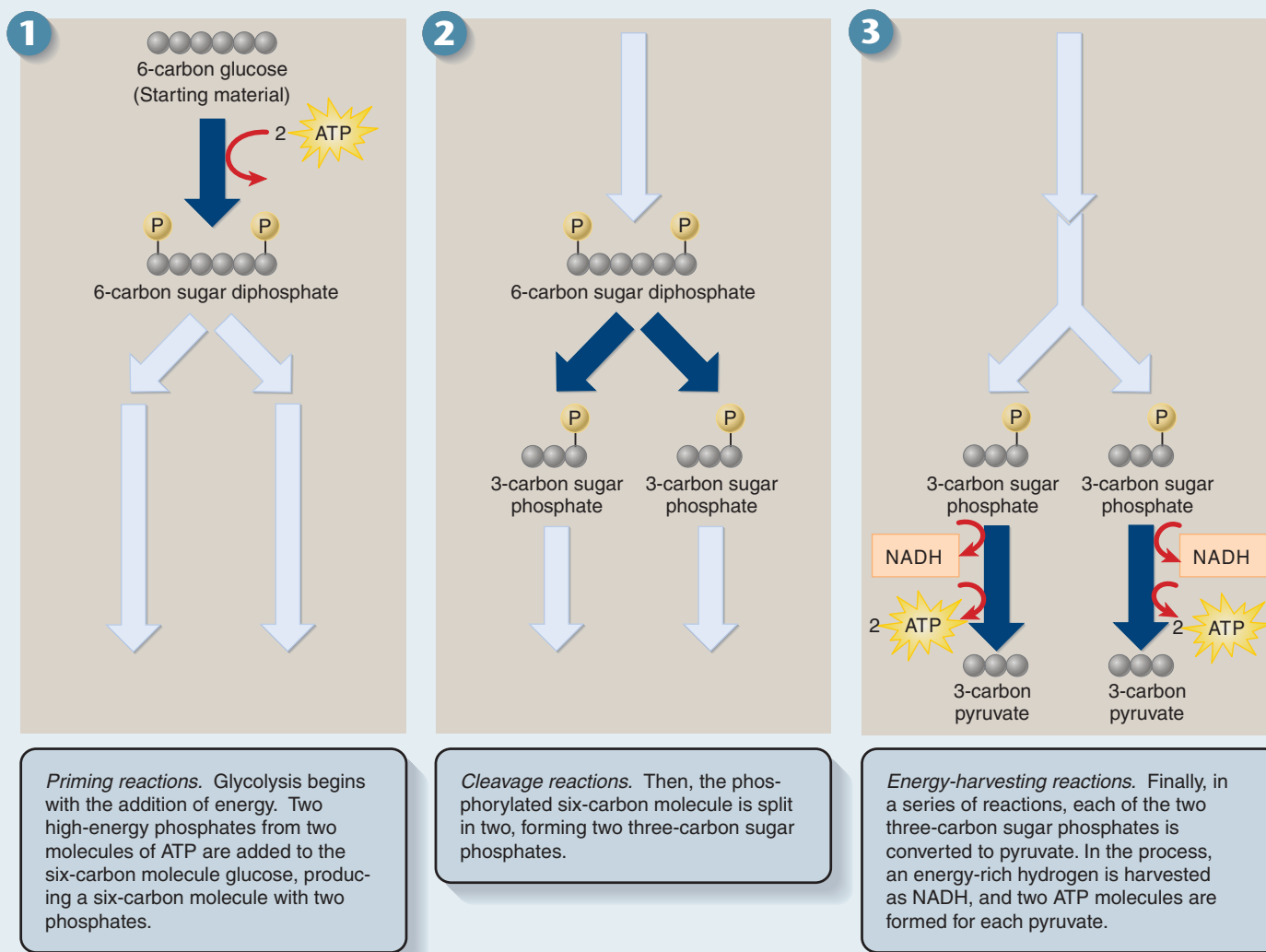


Figure 8.3 How glycolysis works.

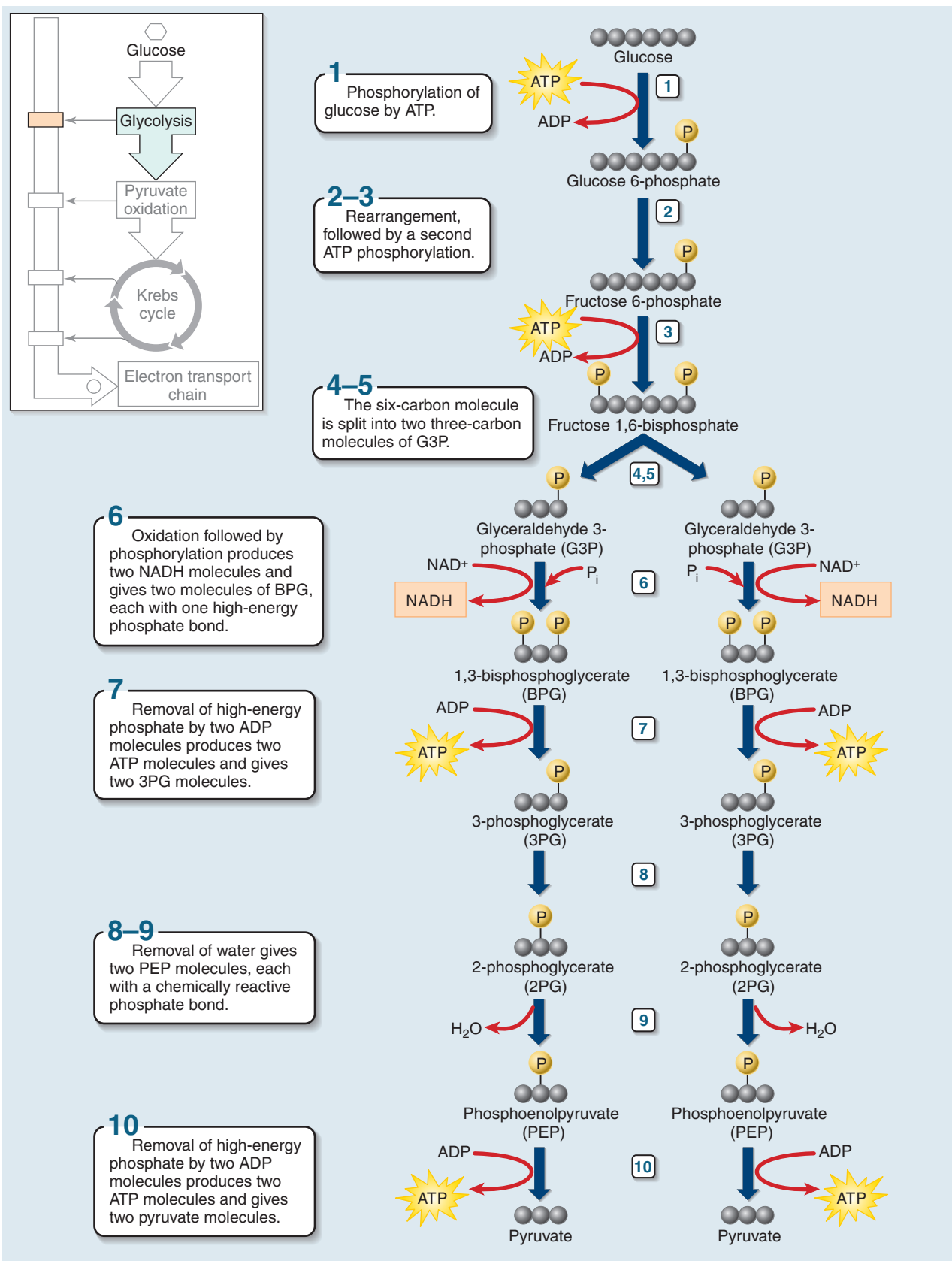


Figure 8.4 The reactions of glycolysis.
The process of glycolysis involves 10 enzyme-catalyzed reactions.

of energy by oxidation. Nature did not, so to speak, go back to the drawing board and design metabolism from scratch. Rather, new reactions, which make up what is called the *Krebs cycle*, were added onto the old, just as renovations to a house build upon what is already there.

Anaerobic Respiration

As explained in section 8.1, aerobic cellular respiration occurs in two stages—coupled reactions to make ATP in glycolysis, and oxidation reactions in the Krebs cycle and electron transport chain to make additional molecules of ATP. Oxygen is the final electron acceptor in the oxidation reactions, accepting the electrons carried by NADH. In the presence of oxygen, cells can use both stages of cellular respiration, because the required oxygen is available for the oxidation reactions. In the absence of oxygen, some organisms can still carry out oxidation reactions to make ATP by using electron acceptors other than oxygen. They are said to respire anaerobically. For example, many bacteria use sulfur, nitrate, or other inorganic compounds as the electron acceptor in place of oxygen. Other organisms use organic molecules as electron acceptors. For example, some eukaryotic cells use pyruvate, the end product of glycolysis, as an electron acceptor.

Methanogens. Among the organisms that practice anaerobic respiration are primitive archaea. A group of archaea called methanogens use CO_2 as the electron acceptor, reducing CO_2 to CH_4 (methane), using hydrogens derived from organic molecules produced by other organisms.

Sulfur Bacteria. A second anaerobic respiratory process is carried out by certain primitive bacteria. In this sulfate respiration, the bacteria derive energy from the reduction of inorganic sulfate (SO_4) to hydrogen sulfide (H_2S). The hydrogen atoms are obtained from organic molecules produced by other organisms. These bacteria thus do the same thing methanogens do, but they use SO_4 as the oxidizing (that is, electron-accepting) agent in place of CO_2 .

Fermentation. In the absence of oxygen, does the pyruvate that is the product of glycolysis and the starting material for oxidative respiration just accumulate in the cytoplasm of aerobic organisms? No. It has a different fate. Recall that during glycolysis energetic electrons are extracted, carried away on protons that are contributed to a carrier molecule called NAD⁺ to form NADH. In the absence of oxygen, these electrons are not used in oxidative reactions, and so soon all the cell's NAD⁺ becomes converted to NADH. With no more NAD⁺ available to carry away electrons, glycolysis cannot proceed. Clearly, to obtain energy from food in the absence of oxygen, a solution to this problem is needed. A home must be found for these electrons, recycling the NADH back to the NAD⁺ needed in glycolysis. Adding the extracted electrons to an organic molecule, as animals and plants do when they have no oxygen to take it, is called **fermentation**.

Two types of fermentation are common among eukaryotes, illustrated in figure 8.5. Animals such as ourselves simply add the extracted electrons to pyruvate (the center arrow in the figure), forming lactate. Later, when oxygen becomes available, the process can be reversed and the electrons used

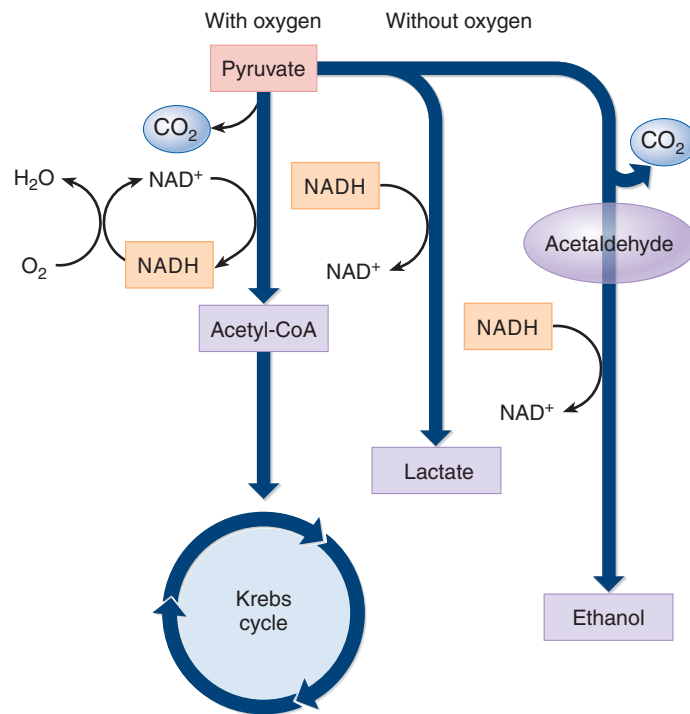


Figure 8.5 Two types of fermentation.

In the presence of oxygen, pyruvate is oxidized to acetyl-CoA and enters the Krebs cycle. In the absence of oxygen, pyruvate is reduced in a process called fermentation. When pyruvate is reduced directly, the product is lactate; when CO_2 is first removed from pyruvate and the remainder is reduced, the product is ethanol.

for energy production. This is why your arm muscles would feel tired if you were to lift this text up and down 100 times rapidly. The muscle cells use up all the oxygen, and so they start running on ATP made by glycolysis, storing the pyruvate and electrons as lactate. This so-called oxygen debt produces the tired, burning feeling in the muscle.

Single-celled fungi called yeasts adopt a different approach to fermentation. First they convert the pyruvate into another molecule called acetaldehyde (the purple oval in figure 8.5), to which they add the electron extracted during glycolysis, producing ethyl alcohol (ethanol). For centuries, humans have consumed ethyl alcohol produced by fermentation in wine and beer. Yeasts conduct this process only in the absence of oxygen, which is why wine is made in closed containers—to keep oxygen in the air away from the crushed grapes.

Although these are two common examples of fermentation, many other organisms carry out the process of fermentation, and many of these organisms are used in industrial applications, producing consumer goods.

8.2 In the first stage of respiration, called glycolysis, cells shuffle chemical bonds so that two coupled reactions can occur, producing ATP by substrate-level phosphorylation. When electrons that are also a product of glycolysis are not donated to oxygen, they are added to inorganic or organic molecules.

Author's Corner

Fad Diets and Impossible Dreams

In my mind I will always weigh 165 pounds, as I did the day I married. The bathroom scale tells a different story, somehow finding another 30 pounds. I did not ask for that weight, do not want it, and am constantly looking for a way to get rid of it. I have not found this to be a lonely search—it seems like everyone I know past the flush of youth is trying to lose weight, too. And, like many, I have been seduced by fad diets, investing hope only to harvest frustration. The much discussed Atkins' diet was the fad diet I tried. As a scientist I should have known better, but so many people seemed to use it—*Dr. Atkins' Diet Revolution* is one of the 10 best-selling books in history, and was (and is) prominently displayed in every bookstore I enter. The reason this diet doesn't deliver on its promise of pain-free weight loss is well understood by science, but not by the general public. Only hope and hype make it a perpetual best seller.



The secret of the Atkins' diet, stated simply, is to avoid carbohydrates. Atkins' basic proposition is that your body, if it does not detect blood glucose (from metabolizing carbohydrates), will think it is starving and start to burn body fat, even if there is lots of fat already circulating in your bloodstream. You may eat all the fat and protein you want, all the steak and eggs and butter and cheese, and you will still burn fat and lose weight—just don't eat any carbohydrates, any bread or pasta or potatoes or fruit or candy. Despite the title of Atkins' book, this diet is hardly revolutionary. A basic low-carbohydrate diet was first promoted over a century ago in the 1860s by William Banting, an English casket maker, in his best-selling book *Letter on Corpulence*. Books promoting low-carbohydrate diets have continued to be best sellers ever since. I even found one on my mother's bookshelf, in the guise of Dr. Herman Taller's 1961 *Calories Don't Count*.

When I tried the Atkins' diet I lost 10 pounds in three weeks. In three months it was all back, and then some. So what happened? Where did the pounds go, and why did they come back? The temporary weight loss turns out to have a simple explanation: because carbohydrates act as water sponges in your body, forcing your body to become depleted of carbohydrates causes your body to lose water. The 10 pounds I lost on this diet was not fat weight but water, quickly regained with the first starchy foods I ate.

The Atkins' diet is the sort of diet the American Heart Association tells us to avoid (all those saturated fats and cholesterol), and it is difficult to stay on. If you do hang in there, you will lose weight, simply because you eat less. Other popular diets these days, *The Zone* diet of Dr. Barry Sears and *The South Beach Diet* of Dr. Arthur Agatston, are also low-carbohydrate diets, although not as extreme as the Atkins' diet. Like the Atkins' diet, they work not for the

bizarre reasons claimed by their promoters, but simply because they are low-calorie diets.

In teaching my students at Washington University about fad diets, I tell them there are two basic laws that no diet can successfully violate:

1. All calories are equal.
2. (calories in) – (calories out) = fat.

The fundamental fallacy of the Atkins' diet, the Zone diet, the South Beach diet, and indeed of all fad diets, is the idea that somehow carbohydrate calories are different from fat and protein calories. This is scientific foolishness. Every calorie you eat contributes equally to your eventual weight, whether it comes from carbohydrate, fat, or protein.

To the extent these diets work at all, they do so because they obey the second law. By reducing calories in, they reduce fat. If that were all there was to it, I'd go out and buy Sears' book. Unfortunately, losing weight isn't that simple, as anyone who has seriously tried already knows. The problem is that your body will not cooperate.

If you try to lose weight by exercising and eating less, your body will attempt to compensate by metabolizing more efficiently. It has a fixed weight, what obesity researchers call a "set point," a weight to which it will keep trying to return. A few years ago, a group of researchers at Rockefeller University in New York, in a landmark study, found that if you lose weight, your metabolism slows down and becomes more efficient, burning fewer calories to do the same work—your body will do everything it can to gain the weight back! Similarly, if you gain weight, your metabolism speeds up. In this way your body uses its own natural weight control system to keep your weight at its set point. No wonder it's so hard to lose weight!

Clearly our bodies don't keep us at one weight all our adult lives. It turns out your body adjusts its fat thermostat—its set point—depending on your age, food intake and amount of physical activity. Adjustments are slow, however, and it seems to be a great deal easier to move the body's set point up than to move it down. Apparently higher levels of fat reduce the body's sensitivity to the leptin hormone that governs how efficiently we burn fat. That is why you can gain weight, despite your set point resisting the gain—your body still issues leptin alarm calls to speed metabolism, but your brain doesn't respond with as much sensitivity as it used to. Thus the fatter you get, the less effective your weight control system becomes.

This doesn't mean that we should give up and learn to love our fat. Rather, now that we are beginning to understand the biology of weight gain, we must accept the hard fact that we cannot beat the requirements of the two diet laws. The real trick is not to give up. Eat less and exercise more, and keep at it. In one year, or two, or three, your body will readjust its set point to reflect the new reality you have imposed by constant struggle. There simply isn't any easy way to lose weight.

8.3 Harvesting Electrons from Chemical Bonds

The first step of oxidative respiration in the mitochondrion is the oxidation of the three-carbon molecule called pyruvate, which is the end product of glycolysis. The cell harvests pyruvate's considerable energy in two steps: first, by oxidizing pyruvate to form acetyl-CoA, and then by oxidizing acetyl-CoA in the Krebs cycle.

Step One: Producing Acetyl-CoA

Pyruvate is oxidized in a single reaction that cleaves off one of pyruvate's three carbons. This carbon then departs as part of the CO_2 molecule shown coming off the pathway with the green arrow in figure 8.6. Pyruvate dehydrogenase, the complex of enzymes that removes CO_2 from pyruvate, is one of the largest enzymes known. It contains 60 subunits! In the course of the reaction, a hydrogen and electrons are removed from pyruvate and donated to NAD^+ to form NADH. Figure 8.7 shows how an enzyme catalyzes this reaction, bringing the substrate (pyruvate) into proximity with NAD^+ . Now focus again on figure 8.6. The two-carbon fragment (called an acetyl group) that remains after removing CO_2 from pyruvate is joined to a cofactor called coenzyme A (CoA) by pyruvate dehydrogenase, forming a compound known as **acetyl-CoA**. If the cell has plentiful supplies of ATP, acetyl-CoA is funneled into fat synthesis, with its energetic electrons preserved for later needs. If the cell needs ATP now, the fragment is directed instead into ATP production through the Krebs cycle.

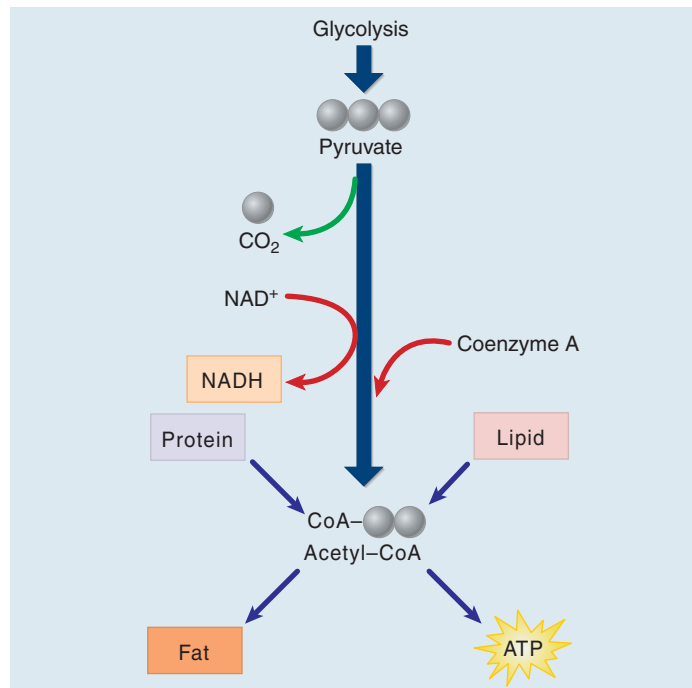


Figure 8.6 Producing acetyl-CoA.

Pyruvate, the three-carbon product of glycolysis, is oxidized to the two-carbon molecule acetyl-CoA, in the process losing one carbon atom as CO_2 and an electron (donated to NAD^+ to form NADH). Almost all the molecules you use as foodstuffs are converted to acetyl-CoA; the acetyl-CoA is then channeled into fat synthesis or into ATP production, depending on your body's needs.

Transferring Hydrogen Atoms

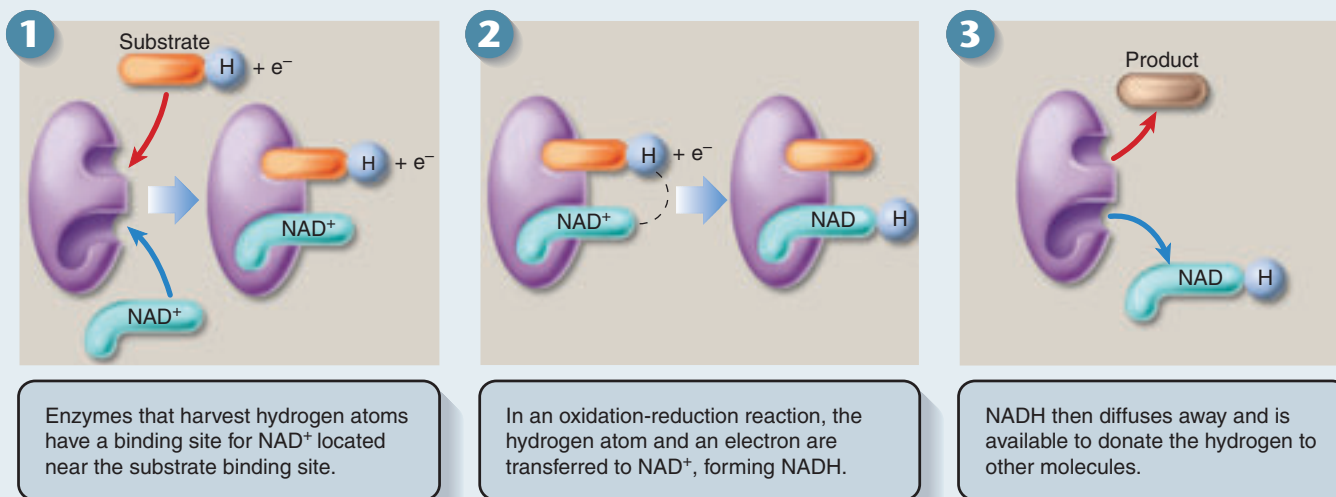


Figure 8.7 How NAD^+ works.

Cells use NAD^+ to carry hydrogen atoms and energetic electrons from one molecule to another. NAD^+ oxidizes energy-rich molecules by acquiring their hydrogens (this proceeds 1 \rightarrow 2 \rightarrow 3) and then reduces other molecules by giving the hydrogens to them (this proceeds 3 \rightarrow 2 \rightarrow 1).

A Closer Look

Metabolic Efficiency and the Length of Food Chains

In the earth's ecosystems, the organisms that carry out photosynthesis are often consumed as food by other organisms. We call these "organism-eaters" *heterotrophs*. Humans are heterotrophs, as no human photosynthesizes.

It is thought that the first heterotrophs were ancient bacteria living in a world where photosynthesis had not yet introduced much oxygen into the oceans or atmosphere. The only mechanism they possessed to harvest chemical energy from their food was glycolysis. Neither oxygen-generating photosynthesis nor the oxidative stage of cellular respiration had evolved yet. It has been estimated that a heterotroph limited to glycolysis, as these ancient bacteria were, captures only 3.5% of the energy in the food it consumes. Hence, if such a heterotroph preserves 3.5% of the energy in the photosynthesizers it consumes, then any other heterotrophs that consume the first heterotroph will capture through glycolysis 3.5% of the energy in it, or 0.12% of the energy available in the original photosynthetic organisms. A very large base of photosynthesizers would thus be needed to support a small number of heterotrophs.

When organisms became able to extract energy from organic molecules by oxidative cellular respiration, this constraint became far less severe, because the efficiency of oxidative respiration is estimated to be about 32%. This increased efficiency results in the transmission of much more energy from one trophic level to another than does glycolysis. (A *trophic level* is a step in the movement of energy through an ecosystem.) The efficiency of oxidative cellular respiration has made possible the evolution of food chains, in which photosynthesizers are consumed by heterotrophs, which are consumed by other heterotrophs, and so on. You will read more about food chains in chapter 20.

Even with this very efficient oxidative metabolism, approximately two-thirds of the available energy is lost at each trophic level, and that puts a limit on how long a food chain can be. Most food chains, like the East African grassland ecosystem illustrated here, involve only three or rarely four trophic levels. Too much energy is lost at each transfer to allow chains to be much longer than that. For example, it would be impossible for a large human population to subsist by eating lions captured from the grasslands of East Africa; the amount of grass available there would not support enough zebras and other herbivores to maintain the number of lions needed to feed the human population. Thus, the ecological complexity of our world is fixed in a fundamental way by the chemistry of oxidative cellular respiration.



Photosynthesizers. The grass under this yellow fever tree grows actively during the hot, rainy season, capturing the energy of the sun and storing it in molecules of glucose, which are then converted into starch and stored in the grass.



Herbivores. These zebras consume the grass and transfer some of its stored energy into their own bodies.



Carnivores. The lion feeds on zebras and other animals, capturing part of their stored energy and storing it in its own body.

Scavengers. This hyena and the vultures occupy the same stage in the food chain as the lion. They are also consuming the body of the dead zebra, which has been abandoned by the lion.



Refuse utilizers. These butterflies, mostly *Precis octavia*, are feeding on the material left in the hyena's dung after the food the hyena consumed had passed through its digestive tract.

A food chain in the savannas, or open grasslands, of East Africa.

At each of these levels in the food chain, only about a third or less of the energy present is used by the recipient.

Step Two: The Krebs Cycle

The next stage in oxidative respiration is called the **Krebs cycle**, named after the man who discovered it. The Krebs cycle (not to be confused with the Calvin cycle in photosynthesis) takes place within the mitochondrion. While a complex process, its nine reactions can be broken down into three stages, as indicated by the overview presented in figure 8.8:

- Stage 1.** Acetyl-CoA joins the cycle, binding to a four-carbon molecule and producing a six-carbon molecule.
- Stage 2.** Two carbons are removed as CO_2 , their electrons donated to NAD^+ , and a four-carbon molecule is left. A molecule of ATP is also produced.
- Stage 3.** More electrons are extracted, forming NADH and FADH_2 ; the four-carbon starting material is regenerated.

To examine the Krebs cycle in more detail, follow along the series of individual reactions illustrated in figure 8.9. The cycle starts when the two-carbon acetyl-CoA fragment produced from pyruvate is stuck onto a four-carbon sugar called oxaloacetate. Then, in rapid-fire order, a series of eight additional reactions occur (steps 2 through 9). When it is all over, two carbon atoms have been expelled as CO_2 , one ATP molecule has been made in a coupled reaction, eight more energetic electrons have been

harvested and taken away as NADH or on other carriers, such as FADH_2 , which serves the same function as NADH , and we are left with the same four-carbon sugar we started with. The process of reactions is a cycle—that is, a circle of reactions. In each turn of the cycle, a new acetyl group replaces the two CO_2 molecules lost, and more electrons are extracted. Note that a single glucose molecule produces *two* turns of the cycle, one for each of the two pyruvate molecules generated by glycolysis.

In the process of cellular respiration, glucose is entirely consumed. The six-carbon glucose molecule is first cleaved into a pair of three-carbon pyruvate molecules during glycolysis. One of the carbons of each pyruvate is then lost as CO_2 in the conversion of pyruvate to acetyl-CoA, and the other two carbons are lost as CO_2 during the oxidations of the Krebs cycle. All that is left to mark the passing of the glucose molecule into six CO_2 molecules is its energy, preserved in four ATP molecules and electrons carried by 10 NADH and two FADH_2 carriers.

8.3 The end product of glycolysis, pyruvate, is oxidized to the two-carbon acetyl-CoA, yielding a pair of electrons plus CO_2 . Acetyl-CoA then enters the Krebs cycle, yielding ATP, many energized electrons, and two CO_2 molecules.

Overview of the Krebs Cycle

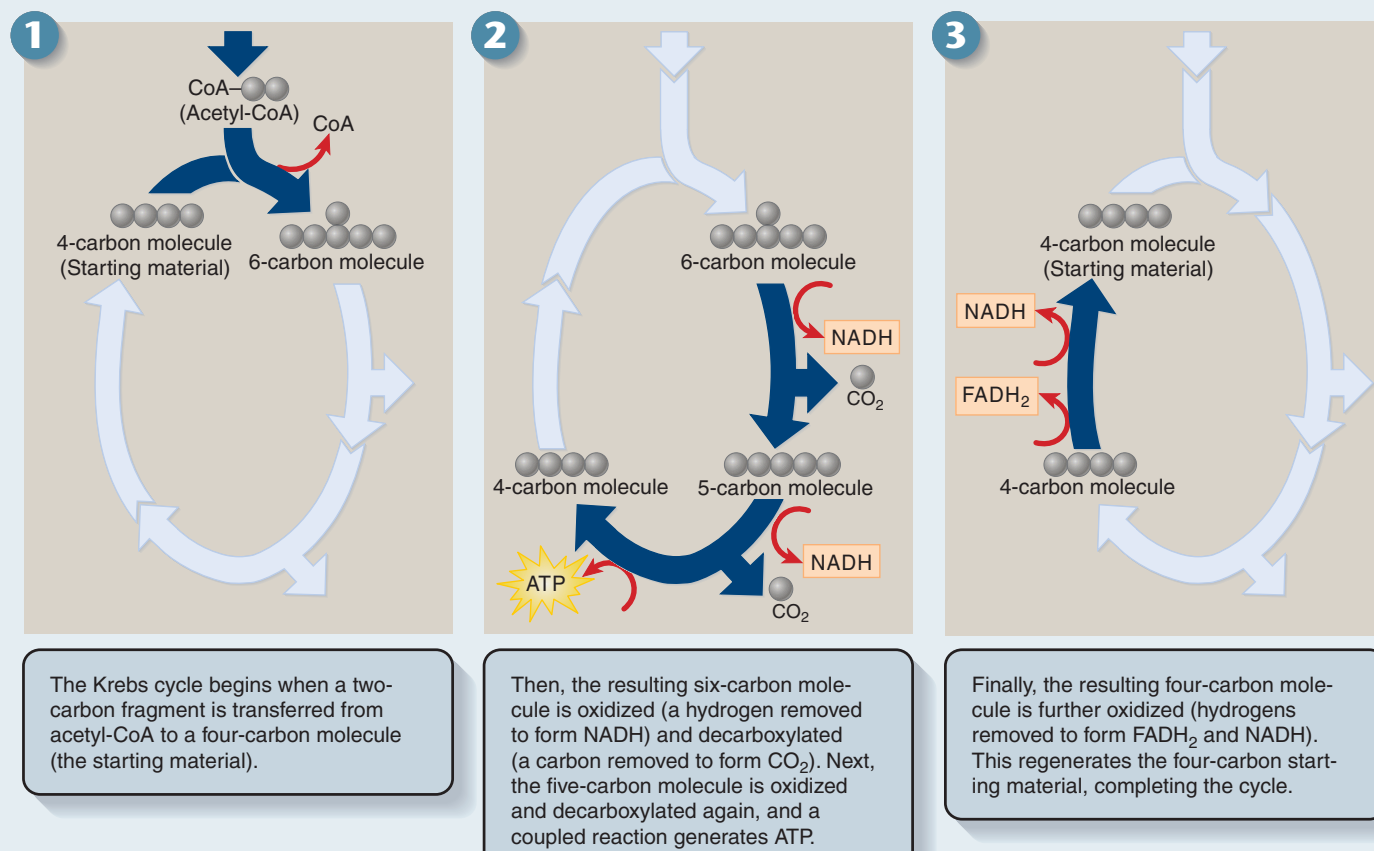


Figure 8.8 How the Krebs cycle works.

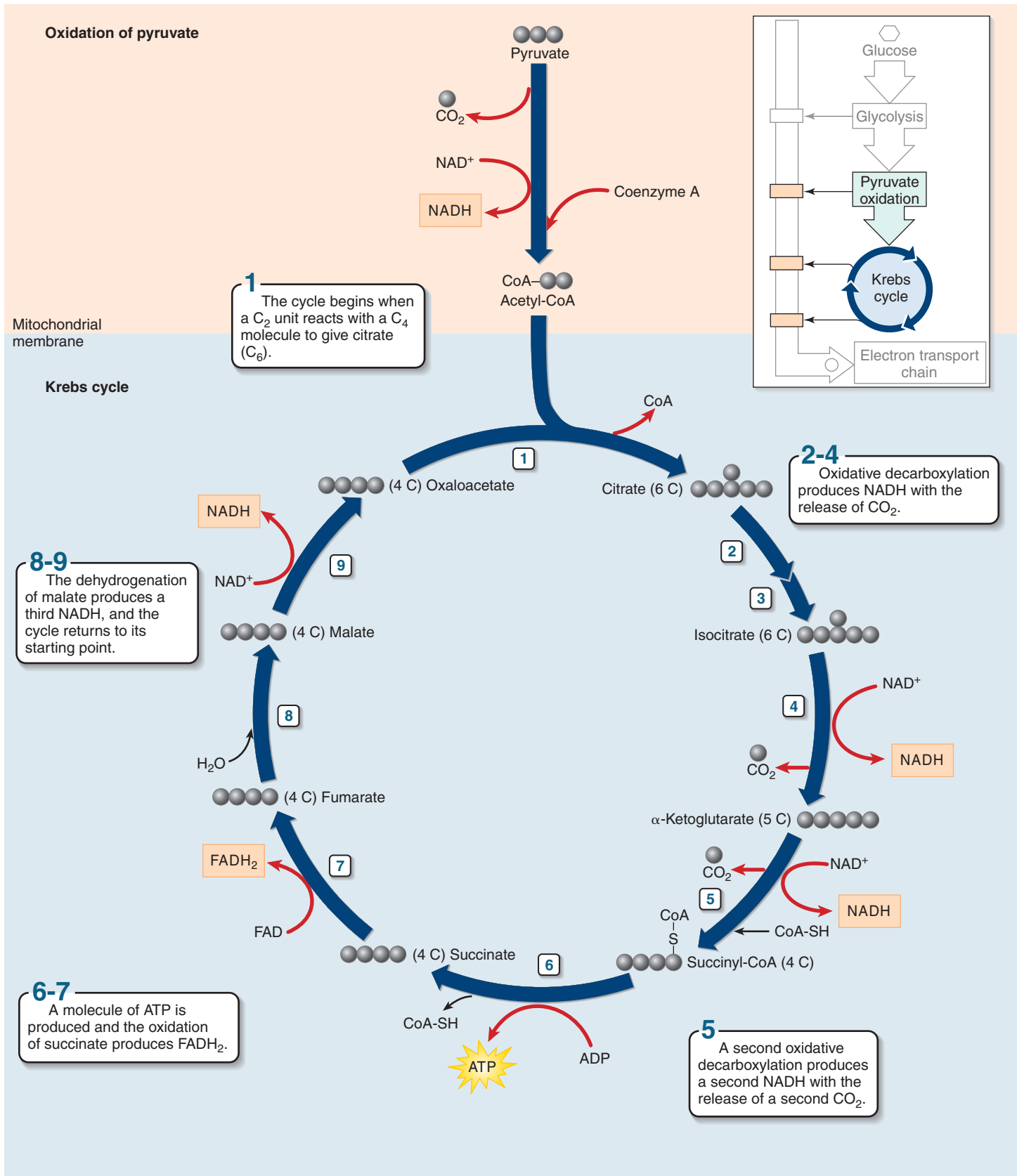


Figure 8.9 The Krebs cycle.

This series of nine enzyme-catalyzed reactions takes place within the mitochondrion.

8.4 Using the Electrons to Make ATP

Mitochondria use chemiosmosis to make ATP in much the same way that chloroplasts do, although their proton pumps transport protons *out of* an enclosed space (the matrix) while the electron transport system in chloroplasts transport protons *into* an enclosed space (the thylakoid). Mitochondria use energetic electrons extracted from food molecules to power proton pumps that drive protons across the inner mitochondrial membrane. As protons become far more scarce inside than outside, the concentration gradient drives protons back in through special ATP synthase channels. Their passage powers the production of ATP from ADP. The ATP then passes out of the mitochondrion through open ATP-passing channels.

Moving Electrons Through the Electron Transport Chain

The NADH and FADH₂ molecules formed during the first stages of aerobic respiration each contain electrons and hydrogens that were gained when NAD⁺ and FAD were reduced (refer back to figure 8.2). The NADH and FADH₂ molecules carry their electrons to the inner mitochondrial membrane (an enlarged area of the membrane is shown in figure 8.10), where they transfer the electrons to a series of membrane-associated molecules collectively called the **electron transport chain**. The electron transport chain

works much as does the electron transport system you encountered in studying photosynthesis.

A protein complex (the pink structure in figure 8.10) receives the electrons and, using a mobile carrier, passes these electrons to a second protein complex (the purple structure). This protein complex, along with others in the chain, operates as a proton pump, using the energy of the electron to drive a proton out across the membrane into the intermembrane space. The arrows indicating the transport of the protons extend up into the top of the figure, which represents the intermembrane space.

The electron is then carried by another carrier to a third protein complex (the light blue structure). This complex uses electrons such as this one to link oxygen atoms with hydrogen ions to form molecules of water.

It is the availability of a plentiful supply of electron acceptor molecules like oxygen that makes oxidative respiration possible. The electron transport chain used in aerobic respiration is similar to, and may well have evolved from, the electron transport system employed in photosynthesis. Photosynthesis is thought to have preceded cellular respiration in the evolution of biochemical pathways, generating the oxygen that is necessary as the electron acceptor in cellular respiration. Natural selection didn't start from scratch and design a new biochemical pathway for cellular respiration; instead, it built on the photosynthetic pathway that already existed, and uses many of the same reactions.

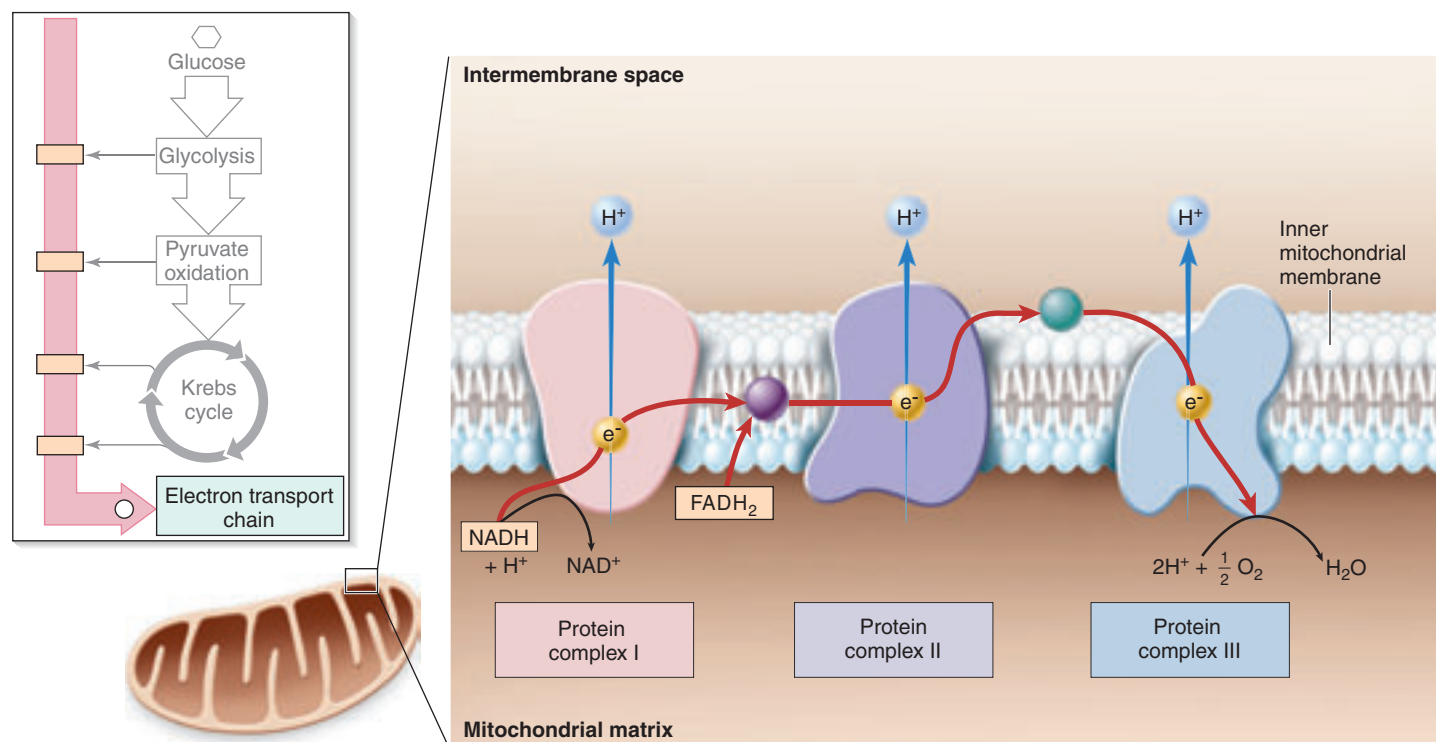


Figure 8.10 The electron transport chain.

High-energy electrons are transported (red arrows) along a chain of electron-carrier molecules. Three of these molecules are protein complexes that use portions of the electrons' energy to pump protons (blue arrows) out of the matrix and into the intermembrane space. The electrons are finally donated to oxygen to form water.

Producing ATP: Chemiosmosis

In eukaryotes, aerobic respiration takes place within the mitochondria present in virtually all cells. The internal compartment, or **matrix**, of a mitochondrion contains the enzymes that carry out the reactions of the Krebs cycle. As described earlier, the electrons harvested by oxidative respiration are passed along the electron transport chain, and the energy they release transports protons out of the matrix and into the outer compartment, sometimes called the **intermembrane space**. Proton pumps in the inner mitochondrial membrane accomplish the transport. The electrons contributed by NADH activate three of these proton pumps, and those contributed by FADH_2 activate two, as indicated in figure 8.10. As the proton concentration in the outer compartment rises above that in the matrix, the concentration gradient induces the protons to reenter the matrix by diffusion through special proton channels. Called ATP synthases, these channels are embedded in the inner mitochondrial membrane, as shown in figure 8.11. As the protons pass through, these channels synthesize ATP from ADP and P_i within the matrix. The ATP is then transported by facilitated diffusion out of the mitochondrion and into the cell's cytoplasm. This ATP synthesizing process is the same chemiosmosis process that you encountered in studying photosynthesis in chapter 7.

Although we have discussed electron transport and chemiosmosis as separate processes, in a cell they are integrated as shown in the overview figure 8.12. The electron transport chain uses electrons harvested in aerobic respiration (red arrows) to pump a large number of protons across the inner mitochondrial membrane (in the upper right). Their subsequent reentry into the mitochondrial matrix drives the synthesis of ATP by chemiosmosis (in the lower right).

8.4 The electrons harvested by oxidizing food molecules are used to power proton pumps that chemiosmotically drive the production of ATP.

Figure 8.12 An overview of the electron transport chain and chemiosmosis.

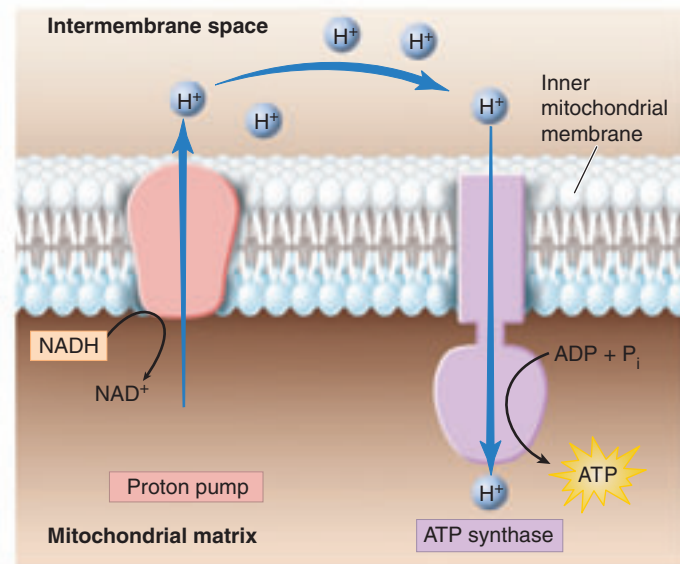
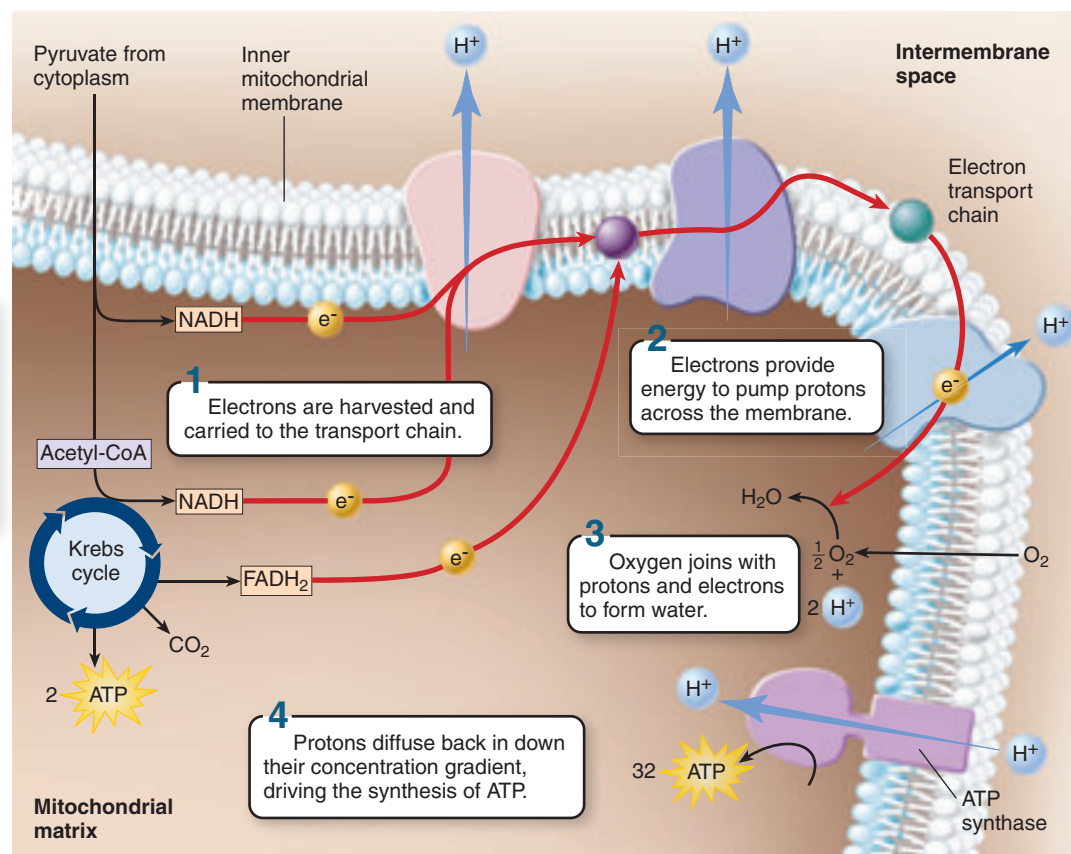


Figure 8.11 Chemiosmosis.

NADH transports high-energy electrons harvested from macromolecules to “proton pumps” that use the energy to pump protons out of the mitochondrial matrix. As a result, the concentration of protons outside the inner mitochondrial membrane rises, inducing protons to diffuse back into the matrix. Many of the protons pass through ATP synthase channels that couple the reentry of protons to the production of ATP.

8.5 Glucose Is Not the Only Food Molecule

We have considered in detail the fate of a molecule of glucose, a simple sugar, in cellular respiration. But how much of what you eat is sugar? As a more realistic example of the food you eat, consider the fate of a fast-food hamburger. The hamburger you eat is composed of carbohydrates, fats, protein, and many other molecules. This diverse collection of complex molecules is broken down by the process of digestion in your stomach and intestines into simpler molecules. Macromolecules are broken down by digestion into their subunits (building blocks). Recall from chapter 4 that carbohydrates are broken down into glucose, fats into fatty acids, and proteins into amino acids. These breakdown reactions produce little or no energy themselves, but prepare the way for cellular respiration—that is, glycolysis and oxidative metabolism.

We have seen what happens to the glucose. What happens to the amino acids and fatty acids? These subunits undergo chemical modifications that convert them into products that feed into cellular respiration. For example, proteins (the second set of arrows in figure 8.13) are first broken down into their individual amino acids. A series of reactions removes the nitrogen side groups and converts the rest of the amino acid into a molecule that takes part in the Krebs cycle. Thus the proteins and fats in the hamburger, like glucose, also become important sources of energy.

8.5 Cells also garner energy from proteins and fats, which are broken down into products that feed into cellular respiration.

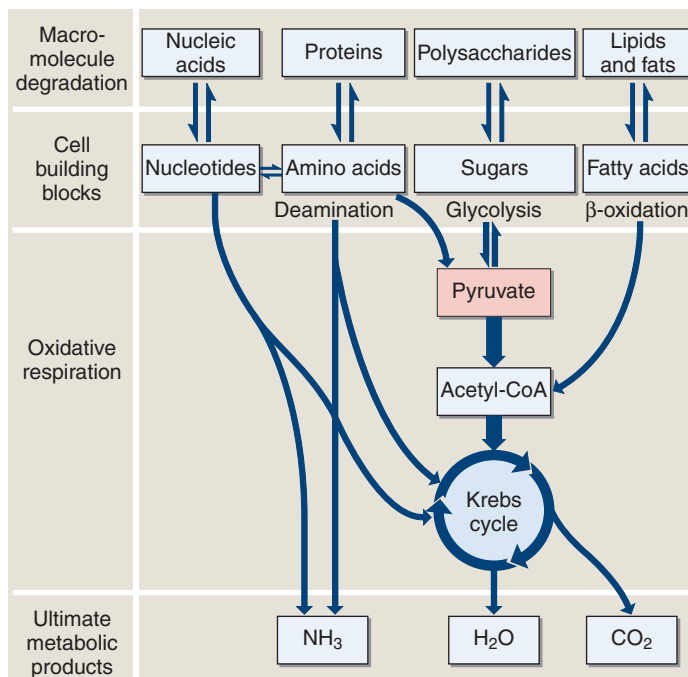


Figure 8.13 How cells obtain energy from foods.

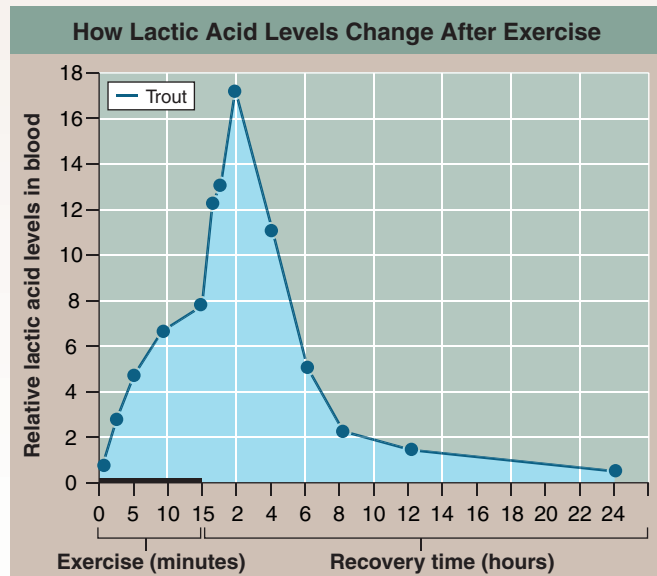
Most organisms extract energy from organic molecules by oxidizing them. The first stage of this process, breaking down macromolecules into their subunits, yields little energy. The second stage, cellular respiration, extracts energy, primarily in the form of high-energy electrons. The subunit of many carbohydrates, glucose, readily enters glycolysis and passes through the biochemical pathways of oxidative respiration. However, the subunits of other macromolecules must be converted into products that can enter the biochemical pathways found in oxidative respiration.

INQUIRY & ANALYSIS

How Do Swimming Fish Avoid Low Blood pH?

During exercise, if oxygen is depleted, muscles use glycolysis to obtain ATP, donating the electrons to pyruvate to form lactic acid. The lactic acid is released into the blood and lowers blood pH. Fish blood has poor buffering capacity, and the experiment in the graph explores how they avoid low blood pH after vigorous exercise for up to 15 minutes.

- 1. Applying Concepts** What is the dependent variable?
- 2. Making Inferences** About how much of the total lactic acid is released after exercise stops? [Hint: notice the x-axis scale changes from minutes to hours, so replot all points to minutes and compare areas under the curve.]
- 3. Drawing Conclusions** Is this result consistent with the hypothesis that fish maintain blood pH levels by delaying the release of lactic acid from muscles? Why might this be beneficial to the fish?



An Overview of Cellular Respiration

8.1 Where Is the Energy in Food?

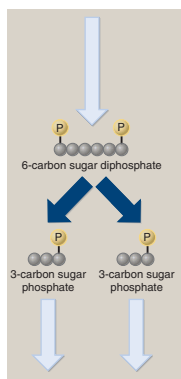
- Cellular respiration is the process of harvesting energy from glucose molecules and storing it as cellular energy in ATP. Cellular respiration is carried out in two stages: glycolysis occurring in the cytoplasm and oxidation occurring in the mitochondria (figure 8.2).



Respiration Without Oxygen: Glycolysis

8.2 Using Coupled Reactions to Make ATP

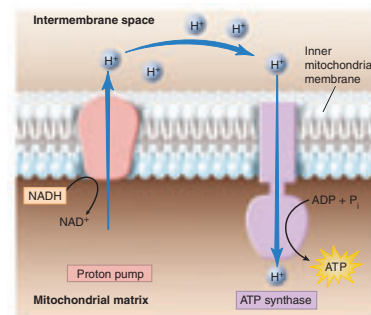
- Glycolysis is a series of 10 chemical reactions in which glucose is broken down into two three-carbon pyruvate molecules. Two exergonic reactions are coupled with a reaction that leads to the formation of ATP. This is called substrate-level phosphorylation (figures 8.3 and 8.4).
- Electrons are extracted from glucose and are donated to a carrier molecule, NAD^+ , which carries electrons and hydrogen as NADH to be used later in oxidative respiration.
- Glycolysis does not require oxygen and is therefore referred to as anaerobic respiration. There are other forms of anaerobic respiration, including fermentation (figure 8.5).
- During fermentation, NAD^+ is recycled by transferring its electrons to a molecule other than oxygen. In animals, the electrons are transferred back to pyruvate and the product is lactate. In yeast, pyruvate is converted to acetaldehyde, which accepts the electrons from NADH , and the product is ethanol or ethyl alcohol.



- Acetyl-CoA enters a series of chemical reactions called the Krebs cycle, where one molecule of ATP is produced and energy is harvested in the form of electrons that are transferred to molecules of NAD^+ and FAD to produce NADH and FADH_2 , respectively (figures 8.8 and 8.9).
- The Krebs cycle makes two turns for every molecule of glucose that is oxidized.

8.4 Using the Electrons to Make ATP

- The energy stored in NADH and FADH_2 is harvested by the electron transport chain to make ATP. NADH and FADH_2 are transported to the inner mitochondrial membrane, where they transfer electrons to the electron transport chain.

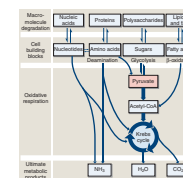


- The electrons are passed along the electron transport chain, a group of proteins embedded in the inner mitochondrial membrane. The energy from the electrons drives proton pumps that pump H^+ across the inner membrane from the matrix to the intermembrane space, creating a H^+ concentration gradient (figure 8.10).
- As in photosynthesis, ATP is formed when H^+ passes back across the membrane through ATP synthase channels, driven by the proton concentration gradient. The energy from the movement of electrons is transferred to the chemical bonds in ATP (figure 8.11). Thus, the energy harvested from glucose is stored in ATP (figure 8.12).

Other Sources of Energy

8.5 Glucose Is Not the Only Food Molecule

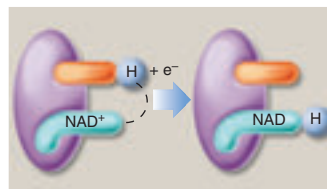
- Food sources other than glucose are also used in oxidative respiration. Macromolecules, such as proteins, lipids, and nucleic acids, are broken down into intermediate products that enter cellular respiration in different reaction steps (figure 8.13).



Respiration With Oxygen: The Krebs Cycle

8.3 Harvesting Electrons from Chemical Bonds

- The two molecules of pyruvate formed in glycolysis are passed into the mitochondrion, where they are converted into two molecules of acetyl-coenzyme A (figure 8.6). Some of the energy in pyruvate is transferred to NAD^+ to produce NADH , which will be used in a later step (figure 8.7).

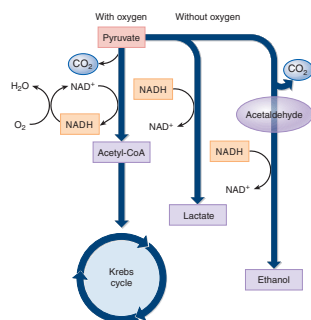


Self-Test

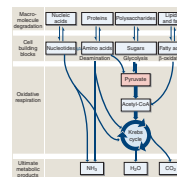
- In animals, the energy for life is obtained by cellular respiration. This involves
 - breaking down the organic molecules that were consumed.
 - capturing photons from plants.
 - utilizing ATP that was produced by plants.
 - breaking down CO_2 that was produced by plants.
- NAD^+ is recycled during
 - glycolysis.
 - fermentation.
 - the Krebs cycle.
 - the formation of acetyl-CoA.
- During glycolysis, ATP forms by
 - the breakdown of pyruvate.
 - chemiosmosis.
 - substrate-level phosphorylation.
 - NAD^+ .
- Which of the following processes can occur in the absence of oxygen?
 - the Krebs cycle
 - glycolysis
 - chemiosmosis
 - all of the above
- Every living creature on this planet is capable of carrying out the rather inefficient biochemical process of glycolysis, which
 - makes glucose, using the energy from ATP.
 - makes ATP by splitting glucose and capturing the energy.
 - phosphorylates ATP to make ADP, using the energy from photons.
 - makes glucose, using oxygen and carbon dioxide and water.
- The electrons generated from the Krebs cycle are transferred to _____ and then are shuttled to _____.
 - NAD^+ , oxygen
 - NAD^+ , electron transport chain
 - NADH , oxygen
 - NADH , electron transport chain
- The final electron acceptor in lactate fermentation is
 - pyruvate.
 - NAD^+
 - lactic acid.
 - O_2 .
- After glycolysis, the pyruvate molecules go to the
 - nucleus of the cell and provide energy.
 - membranes of the cell and are broken down in the presence of CO_2 to make more ATP.
 - mitochondria of the cell and are broken down in the presence of O_2 to make more ATP.
 - Golgi bodies and are packaged and stored until needed.
- The vast majority of the ATP molecules produced within a cell are produced
 - during photosynthesis.
 - during glycolysis.
 - during the Krebs cycle.
 - during the electron transport chain.
- Cells can extract energy from foodstuffs other than glucose because
 - proteins, fatty acids, and nucleic acids get converted to glucose and then enter oxidative respiration.
 - each type of macromolecule has its own oxidative respiration pathway.
 - each type of macromolecule is broken down into its subunits, which enter the oxidative respiration pathway.
 - they can all enter the glycolytic pathway.

Visual Understanding

- Figure 8.5** Soft drinks are artificially carbonated, which is what causes them to fizz. Beer and sparkling wines are naturally carbonated. How does this natural carbonation occur?



- Figure 8.13** Your friend Yevgeny wants to go on a low-carbohydrate diet so that he can lose some of the “baby fat” he’s still carrying. He asks your advice; what do you tell him?



Challenge Questions

- If cellular respiration were the stock market (you’re investing ATPs and getting ATP dividends), where would you get the most return on your investment: glycolysis, the Krebs cycle, or the electron transport chain? Explain your answer.
- How much ATP would be generated in the cells of a person who consumed a diet of pyruvate instead of glucose?
- If you poke a hole in a mitochondrion, can it still perform oxidative respiration? Can fragments of mitochondrion perform oxidative respiration?