Evolution, the Themes of Biology, and Scientific Inquiry

1

Figure 1.1 What can this beach mouse (*Peromyscus polionotus*) teach us about biology?

KEY CONCEPTS

An inland mouse of the species *Peromyscus polionotus*. This mouse has a much darker back, side, and face than mice of the same species that inhabit sand dunes.

Inquiring About Life

There are few hiding places for a mouse among the sparse clumps of beach grass that dot the brilliant white sand dunes along the Florida seashore. However, the beach mice that live there have light, dappled fur, allowing them to blend into their surroundings **(Figure 1.1)**. Mice of the same species (*Peromyscus polionotus*) also inhabit nearby inland areas. These mice are much darker in color, as are the soil and vegetation where they live (see smaller photo). For both beach mice and inland mice, the close color match of coat (fur) and environment is vital for survival, since hawks, herons, and other sharp-eyed predators periodically scan the landscape for prey. How has the color of each group of mice come to be so well matched, or *adapted*, to the local background?

An organism's adaptations to its environment, such as the mouse's protective camouflage, are the result of *evolution*, the process of change over time that has resulted in the astounding array of organisms found on Earth. Evolution is the fundamental principle of biology and the core theme of this book.

Although biologists know a great deal about life on Earth, many mysteries remain. Posing questions about the living world and seeking answers through scientific inquiry are the central activities of **biology**, the scientific study of life. Biologists' questions can be ambitious. They may ask how a single tiny cell

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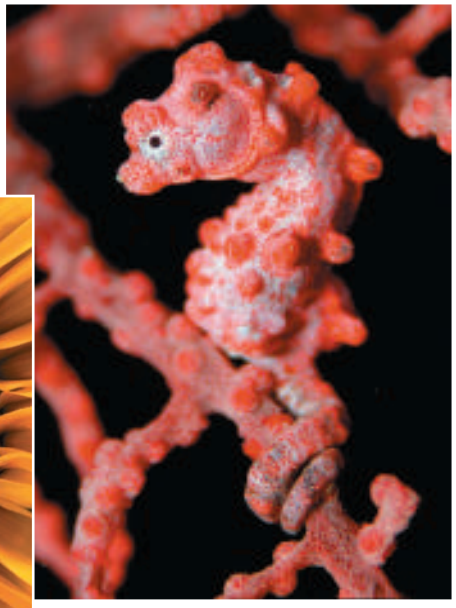
becomes a tree or a dog, how the human mind works, or how the different forms of life in a forest interact. When questions occur to you as you observe the natural world, you are thinking like a biologist. More than anything else, biology is a quest, an ongoing inquiry about the nature of life.

At the most fundamental level, we may ask: What is life? Even a child realizes that a dog or a plant is alive, while a rock or a car is not. Yet the phenomenon we call life defies a simple, one-sentence definition. We recognize life by what living things do. **Figure 1.2** highlights some of the properties and processes we associate with life.

While limited to a handful of images, Figure 1.2 reminds us that the living world is wondrously varied. How do biologists make sense of this diversity and complexity? This opening chapter sets up a framework for answering this question. The first part of the chapter provides a panoramic view of the biological "landscape," organized around some unifying themes. We then focus on biology's core theme, evolution, which accounts for life's unity and diversity. Next, we look at scientific inquiry—how scientists ask and attempt to answer questions about the natural world. Finally, we address the culture of science and its effects on society.

Figure 1.2 Some properties of life.

▼ **Order.** This close-up of a sunflower illustrates the highly ordered structure that characterizes life.



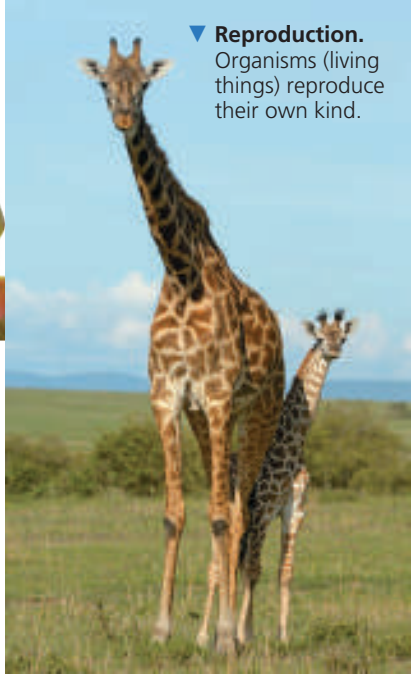
▲ **Evolutionary adaptation.** The overall appearance of this pygmy sea horse camouflages the animal in its environment. Such adaptations evolve over countless generations by the reproductive success of those individuals with heritable traits that are best suited to their environments.

▲ **Regulation.** The regulation of blood flow through the blood vessels of this jackrabbit's ears helps maintain a constant body temperature by adjusting heat exchange with the surrounding air.

▲ **Energy processing.** This butterfly obtains fuel in the form of nectar from flowers. The butterfly will use chemical energy stored in its food to power flight and other work.

▲ **Growth and development.** Inherited information carried by genes controls the pattern of growth and development of organisms, such as this oak seedling.

▲ **Response to the environment.** The Venus flytrap on the left closed its trap rapidly in response to the environmental stimulus of a grasshopper landing on the open trap.



▼ **Reproduction.** Organisms (living things) reproduce their own kind.

Animation: Signs of Life
Video: Sea Horse Camouflage

CONCEPT 1.1

The study of life reveals unifying themes

Biology is a subject of enormous scope, and exciting new biological discoveries are being made every day. How can you organize into a comprehensible framework all the information you'll encounter as you study the broad range of topics included in biology? Focusing on a few big ideas will help.

Here are five unifying themes—ways of thinking about life that will still hold true decades from now.

- Organization
- Information
- Energy and Matter
- Interactions
- Evolution

In this section and the next, we'll briefly define and explore each theme.

▼ Figure 1.3 Exploring Levels of Biological Organization

◄ 1 The Biosphere

Even from space, we can see signs of Earth's life—in the green mosaic of the forests, for example. We can also see the entire **biosphere**, which consists of all life on Earth and all the places where life exists: most regions of land, most bodies of water, the atmosphere to an altitude of several kilometers, and even sediments far below the ocean floor.

◄ 2 Ecosystems

Our first scale change brings us to a North American mountain meadow, which is an example of an ecosystem, as are tropical forests, grasslands, deserts, and coral reefs. An **ecosystem** consists of all the living things in a particular area, along with all the nonliving components of the environment with which life interacts, such as soil, water, atmospheric gases, and light.

► 3 Communities

The array of organisms inhabiting a particular ecosystem is called a biological **community**. The community in our meadow ecosystem includes many kinds of plants, various animals, mushrooms and other fungi, and enormous numbers of diverse microorganisms, such as bacteria, that are too small to see without a microscope. Each of these forms of life belongs to a *species*—a group whose members can only reproduce with other members of the group.

► 4 Populations

A **population** consists of all the individuals of a species living within the bounds of a specified area. For example, our meadow includes a population of lupine (some of which are shown here) and a population of mule deer. A community is therefore the set of populations that inhabit a particular area.

▲ 5 Organisms

Individual living things are called **organisms**. Each plant in the meadow is an organism, and so is each animal, fungus, and bacterium.

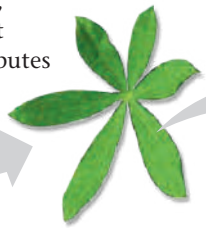
Theme: New Properties Emerge at Successive Levels of Biological Organization

ORGANIZATION The study of life on Earth extends from the microscopic scale of the molecules and cells that make up organisms to the global scale of the entire living planet. As biologists, we can divide this enormous range into different levels of biological organization. In **Figure 1.3**, we zoom in from space to take a closer and closer look at life in a mountain meadow. This journey, depicted as a series of numbered steps, highlights the hierarchy of biological organization.

Zooming in through the levels of the biological hierarchy at ever-finer resolution illustrates an approach called *reductionism*. This method is so named because it reduces complex systems to simpler components that are more manageable to study. Reductionism is a powerful strategy in biology. For example, by studying the molecular structure of DNA that had been extracted from cells, James Watson and Francis Crick inferred the chemical basis of biological inheritance. Reductionism has propelled many major discoveries, but it provides a necessarily incomplete view of life on Earth, as we'll discuss next.

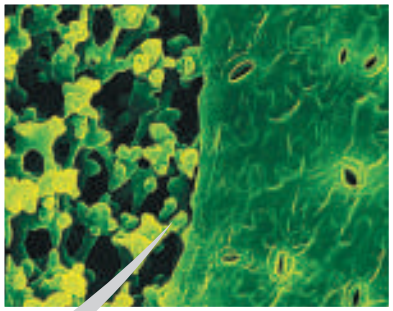
▼6 Organs

The structural hierarchy of life continues to unfold as we explore the architecture of a complex organism. A leaf is an example of an **organ**, a body part that is made up of multiple tissues and has specific functions in the body. Leaves, stems, and roots are the major organs of plants. Within an organ, each tissue has a distinct arrangement and contributes particular properties to organ function.



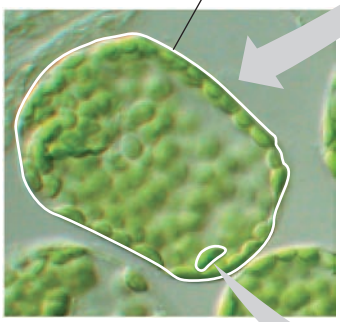
▼7 Tissues

Viewing the tissues of a leaf requires a microscope. Each **tissue** is a group of cells that work together, performing a specialized function. The leaf shown here has been cut on an angle. The honeycombed tissue in the interior of the leaf (left side of photo) is the main location of photosynthesis, the process that converts light energy to the chemical energy of sugar. The jigsaw puzzle–like "skin" on the surface of the leaf is a tissue called epidermis (right side of photo). The pores through the epidermis allow entry of the gas CO_2, a raw material for sugar production.



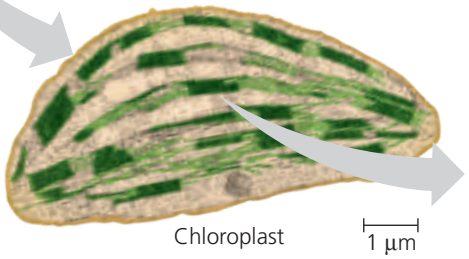
▶8 Cells

The **cell** is life's fundamental unit of structure and function. Some organisms consist of a single cell, which performs all the functions of life. Other organisms are multicellular and feature a division of labor among specialized cells. Here we see a magnified view of a cell in a leaf tissue. This cell is about 40 micrometers (µm) across—about 500 of them would reach across a small coin. Within these tiny cells are even smaller green structures called chloroplasts, which are responsible for photosynthesis.



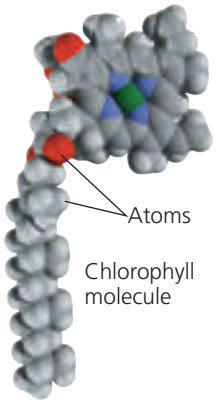
▼9 Organelles

Chloroplasts are examples of **organelles**, the various functional components present in cells. The image below, taken by a powerful microscope, shows a single chloroplast.



▼10 Molecules

Our last scale change drops us into a chloroplast for a view of life at the molecular level. A **molecule** is a chemical structure consisting of two or more units called atoms, represented as balls in this computer graphic of a chlorophyll molecule. Chlorophyll is the pigment that makes a leaf green, and it absorbs sunlight during photosynthesis. Within each chloroplast, millions of chlorophyll molecules are organized into systems that convert light energy to the chemical energy of food.



Emergent Properties

Let's reexamine Figure 1.3, beginning this time at the molecular level and then zooming out. This approach allows us to see novel properties emerge at each level that are absent from the preceding one. These **emergent properties** are due to the arrangement and interactions of parts as complexity increases. For example, although photosynthesis occurs in an intact chloroplast, it will not take place in a disorganized test-tube mixture of chlorophyll and other chloroplast molecules. The coordinated processes of photosynthesis require a specific organization of these molecules in the chloroplast. Isolated components of living systems—the objects of study in a reductionist approach—lack a number of significant properties that emerge at higher levels of organization.

Emergent properties are not unique to life. A box of bicycle parts won't transport you anywhere, but if they are arranged in a certain way, you can pedal to your chosen destination. Compared with such nonliving examples, however, biological systems are far more complex, making the emergent properties of life especially challenging to study.

To fully explore emergent properties, biologists today complement reductionism with **systems biology**, the exploration of a biological system by analyzing the interactions among its parts. In this context, a single leaf cell can be considered a system, as can a frog, an ant colony, or a desert ecosystem. By examining and modeling the dynamic behavior of an integrated network of components, systems biology enables us to pose new kinds of questions. For example, how do networks of molecular interactions in our bodies generate our 24-hour cycle of wakefulness and sleep? At a larger scale, how does a gradual increase in atmospheric carbon dioxide alter ecosystems and the entire biosphere? Systems biology can be used to study life at all levels.

Structure and Function

At each level of the biological hierarchy, we find a correlation of structure and function. Consider a leaf in Figure 1.3: Its thin, flat shape maximizes the capture of sunlight by chloroplasts. Because such correlations of structure and function are common in all forms of life, analyzing a biological structure gives us clues about what it does and how it works. Conversely, knowing the function of something provides insight into its structure and organization. Many examples from the animal kingdom show a correlation between structure and function. For example, the hummingbird's anatomy allows the wings to rotate at the shoulder, so hummingbirds have the ability, unique among birds, to fly backward or hover in place. While hovering, the birds can extend their long, slender beaks into flowers and feed on nectar. The elegant match of form and function in the structures of life is explained by natural selection, which we'll explore shortly.

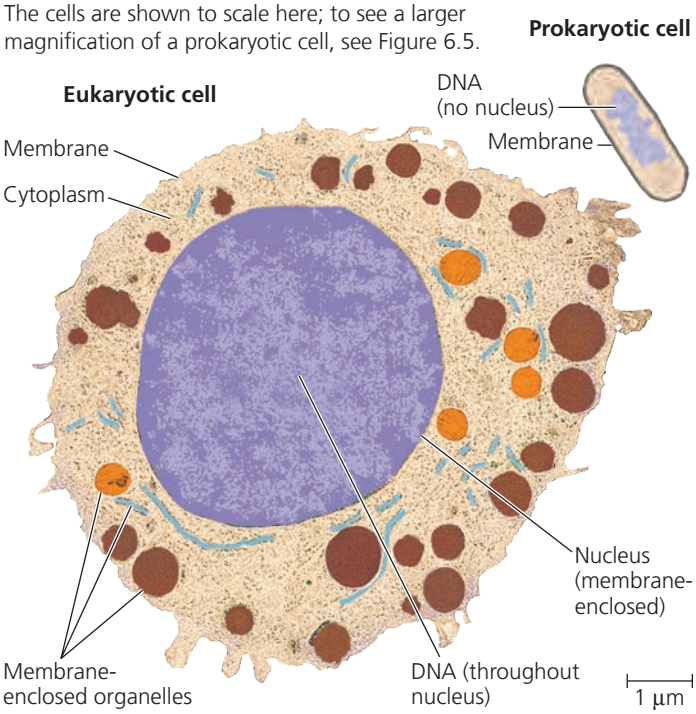
The Cell: An Organism's Basic Unit of Structure and Function

In life's structural hierarchy, the cell is the smallest unit of organization that can perform all activities required for life. The so-called Cell Theory was first developed in the 1800s, based on the observations of many scientists. The theory states that all living organisms are made of cells, which are the basic unit of life. In fact, the actions of organisms are all based on the functioning of cells. For instance, the movement of your eyes as you read this sentence results from the activities of muscle and nerve cells. Even a process that occurs on a global scale, such as the recycling of carbon atoms, is the product of cellular functions, including the photosynthetic activity of chloroplasts in leaf cells.

All cells share certain characteristics. For instance, every cell is enclosed by a membrane that regulates the passage of materials between the cell and its surroundings. Nevertheless, we distinguish two main forms of cells: prokaryotic and eukaryotic. The cells of two groups of single-celled microorganisms—bacteria (singular, *bacterium*) and archaea (singular, *archaean*)—are prokaryotic. All other forms of life, including plants and animals, are composed of eukaryotic cells.

A **eukaryotic cell** contains membrane-enclosed organelles **(Figure 1.4)**. Some organelles, such as the DNA-containing nucleus, are found in the cells of all eukaryotes; other organelles

Figure 1.4 Contrasting eukaryotic and prokaryotic cells in size and complexity.
The cells are shown to scale here; to see a larger magnification of a prokaryotic cell, see Figure 6.5.



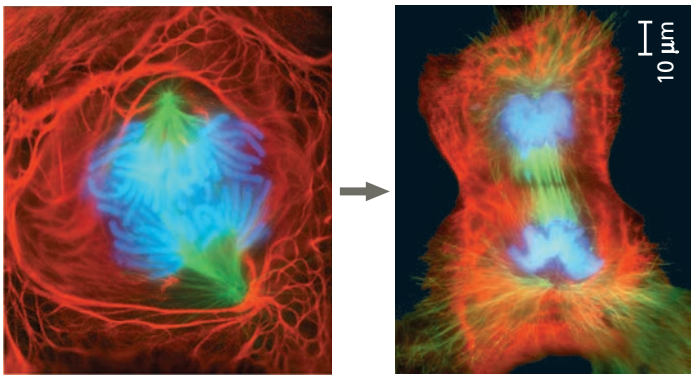
VISUAL SKILLS ➤ *Measure the scale bar and use its length to estimate the length of the prokaryotic cell and the longest dimension of the eukaryotic cell.*

are specific to particular cell types. For example, the chloroplast in Figure 1.3 is an organelle found only in eukaryotic cells that carry out photosynthesis. In contrast to eukaryotic cells, a **prokaryotic cell** lacks a nucleus or other membrane-enclosed organelles. Furthermore, prokaryotic cells are generally smaller than eukaryotic cells, as shown in Figure 1.4.

Theme: Life's Processes Involve the Expression and Transmission of Genetic Information

INFORMATION Within cells, structures called chromosomes contain genetic material in the form of **DNA (deoxyribonucleic acid)**. In cells that are preparing to divide, the chromosomes may be made visible using a dye that appears blue when bound to the DNA **(Figure 1.5)**.

Figure 1.5 A lung cell from a newt divides into two smaller cells that will grow and divide again.



DNA, the Genetic Material

Before a cell divides, the DNA is first replicated, or copied, and each of the two cellular offspring inherits a complete set of chromosomes, identical to that of the parent cell. Each chromosome contains one very long DNA molecule with hundreds or thousands of **genes**, each a section of the DNA of the chromosome. Transmitted from parents to offspring, genes are the units of inheritance. They encode the information necessary to build all of the molecules synthesized within a cell, which in turn establish that cell's identity and function. You began as a single cell stocked with DNA inherited from your parents. The replication of that DNA prior to each cell division transmitted copies of the DNA to what eventually became the trillions of cells of your body. As the cells grew and divided, the genetic information encoded by the DNA directed your development **(Figure 1.6)**.

The molecular structure of DNA accounts for its ability to store information. A DNA molecule is made up of two long chains, called strands, arranged in a double helix. Each chain is made up of four kinds of chemical building blocks called nucleotides, abbreviated A, T, C, and G **(Figure 1.7)**. Specific sequences of these four nucleotides encode the information

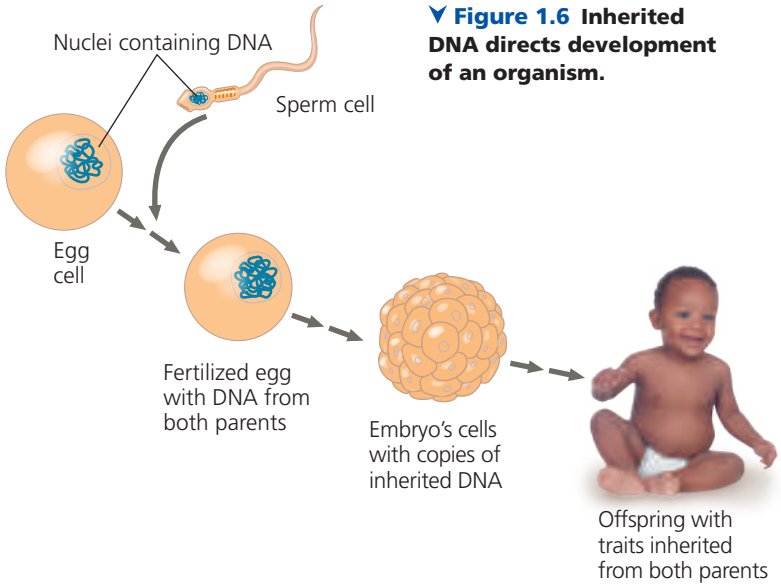


Figure 1.6 Inherited DNA directs development of an organism.

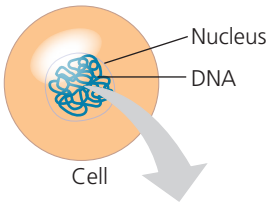
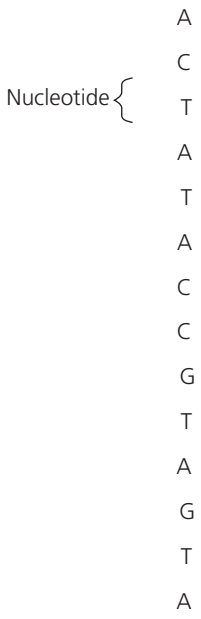


Figure 1.7 DNA: The genetic material.



(a) DNA double helix. This model shows the atoms in a segment of DNA. Made up of two long chains (strands) of building blocks called nucleotides, a DNA molecule takes the three-dimensional form of a double helix.

(b) Single strand of DNA. These geometric shapes and letters are simple symbols for the nucleotides in a small section of one strand of a DNA molecule. Genetic information is encoded in specific sequences of the four types of nucleotides. Their names are abbreviated A, T, C, and G.

Animation: Heritable Information: DNA

in genes. The way DNA encodes information is analogous to how we arrange the letters of the alphabet into words and phrases with specific meanings. The word *rat*, for example, evokes a rodent; the words *tar* and *art*, which contain the same letters, mean very different things. We can think of nucleotides as a four-letter alphabet.

For many genes, the sequence provides the blueprint for making a protein. For instance, a given bacterial gene may specify a particular protein (an enzyme) required to break down a certain sugar molecule, while a human gene may denote a different protein (an antibody) that helps fight off infection. Overall, proteins are major players in building and maintaining the cell and carrying out its activities.

Protein-encoding genes control protein production indirectly, using a related molecule called RNA as an intermediary **(Figure 1.8)**. The sequence of nucleotides along a gene is transcribed into mRNA, which is then translated into a linked series of protein building blocks called amino acids. Once completed, the amino acid chain forms a specific protein with a unique shape and function. The entire process by which the information in a gene directs the manufacture of a cellular product is called **gene expression**.

In carrying out gene expression, all forms of life employ essentially the same genetic code: A particular sequence of nucleotides says the same thing in one organism as it does in another. Differences between organisms reflect differences between their nucleotide sequences rather than between their genetic codes. This universality of the genetic code is a strong piece of evidence that all life is related. Comparing the sequences in several species for a gene that codes for a particular protein can provide valuable information both about the protein and about the relationship of the species to each other.

The mRNA molecule in Figure 1.8 is translated into a protein, but other cellular RNAs function differently. For example, we have known for decades that some types of RNA are actually components of the cellular machinery that manufactures proteins. Recently, scientists have discovered whole new classes of RNA that play other roles in the cell, such as regulating the functioning of protein-coding genes. Genes specify all of these RNAs as well, and their production is also referred to as gene expression. By carrying the instructions for making proteins and RNAs and by replicating with each cell division, DNA ensures faithful inheritance of genetic information from generation to generation.

Genomics: Large-Scale Analysis of DNA Sequences

The entire "library" of genetic instructions that an organism inherits is called its **genome**. A typical human cell has two similar sets of chromosomes, and each set has approximately 3 billion nucleotide pairs of DNA. If the one-letter abbreviations for the nucleotides of a set were written in letters the

Figure 1.8 Gene expression: Cells use information encoded in a gene to synthesize a functional protein.

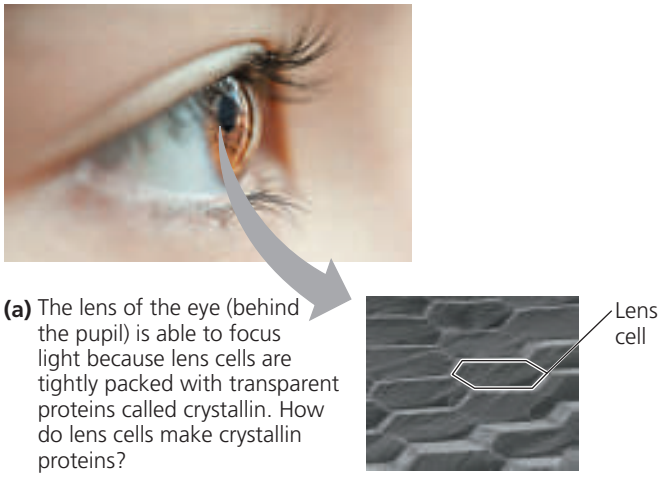


Figure Walkthrough

size of those you are now reading, the genomic text would fill about 700 biology textbooks.

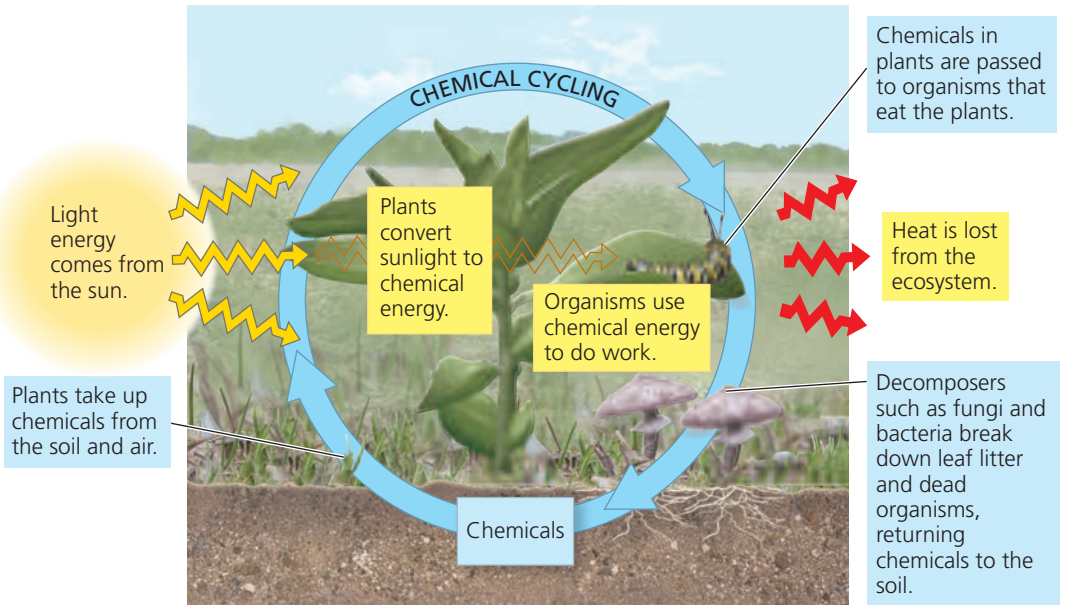
Since the early 1990s, the pace at which researchers can determine the sequence of a genome has accelerated at an astounding rate, enabled by a revolution in technology. The genome sequence—the entire sequence of nucleotides for a representative member of a species—is now known for humans and many other animals, as well as numerous plants, fungi, bacteria, and archaea. To make sense of the deluge of data from genome-sequencing projects and the growing catalog of known gene functions, scientists are applying a systems biology approach at the cellular and molecular levels. Rather than investigating a single gene at a time, researchers study whole sets of genes (or other DNA) in one or more species—an approach called **genomics**. Likewise, the term **proteomics** refers to the study of sets of proteins and their properties. (The entire set of proteins expressed by a given cell, tissue, or organism is called a **proteome**).

Three important research developments have made the genomic and proteomic approaches possible. One is "high-throughput" technology, tools that can analyze many biological samples very rapidly. The second major development is **bioinformatics**, the use of computational tools to store, organize, and analyze the huge volume of data that results from high-throughput methods. The third development is the formation of interdisciplinary research teams—groups of diverse specialists that may include computer scientists, mathematicians, engineers, chemists, physicists, and, of course, biologists from a variety of fields. Researchers in such teams aim to learn how the activities of all the proteins and RNAs encoded by the DNA are coordinated in cells and in whole organisms.

Theme: Life Requires the Transfer and Transformation of Energy and Matter

ENERGY AND MATTER A fundamental characteristic of living organisms is their use of energy to carry out life's activities. Moving, growing, reproducing, and the various cellular activities of life are work, and work requires energy. The input of energy, primarily from the sun, and the transformation of energy from one form to another make life possible **(Figure 1.9)**. When a plant's leaves absorb sunlight, molecules within the leaves convert the energy of sunlight to the chemical energy of food, such as sugars, in the process of photosynthesis. The chemical energy in the food molecules is then passed along by plants and other photosynthetic organisms (**producers**) to consumers. **Consumers** are organisms, such as animals, that feed on other organisms or their remains.

When an organism uses chemical energy to perform work, such as muscle contraction or cell division, some of that energy is lost to the surroundings as heat. As a result, energy *flows through* an ecosystem in one direction, usually entering as light and exiting as heat. In contrast, chemicals *cycle within* an ecosystem, where they are used and then recycled (see Figure 1.9). Chemicals that a plant absorbs from the air or soil may be incorporated into the plant's body and then passed to an animal that eats the plant. Eventually, these chemicals will be returned to the environment by decomposers such as bacteria and fungi that break down waste products, leaf litter, and the bodies of dead organisms. The chemicals are then available to be taken up by plants again, thereby completing the cycle.



➤ Figure 1.9 Energy flow and chemical cycling. There is a one-way flow of energy in an ecosystem: During photosynthesis, plants convert energy from sunlight to chemical energy (stored in food molecules such as sugars), which is used by plants and other organisms to do work and is eventually lost from the ecosystem as heat. In contrast, chemicals cycle between organisms and the physical environment.

Theme: From Molecules to Ecosystems, Interactions Are Important in Biological Systems

INTERACTIONS At any level of the biological hierarchy, interactions between the components of the system ensure smooth integration of all the parts, such that they function as a whole. This holds true equally well for molecules in a cell and the components of an ecosystem; we'll discuss both as examples.

Molecules: Interactions Within Organisms

At lower levels of organization, the interactions between components that make up living organisms—organs, tissues, cells, and molecules—are crucial to their smooth operation. Consider the regulation of blood sugar levels, for instance. Cells in the body must match the supply of fuel (sugar) to demand, regulating the opposing processes of sugar breakdown and storage. The key is the ability of many biological processes to self-regulate by a mechanism called feedback.

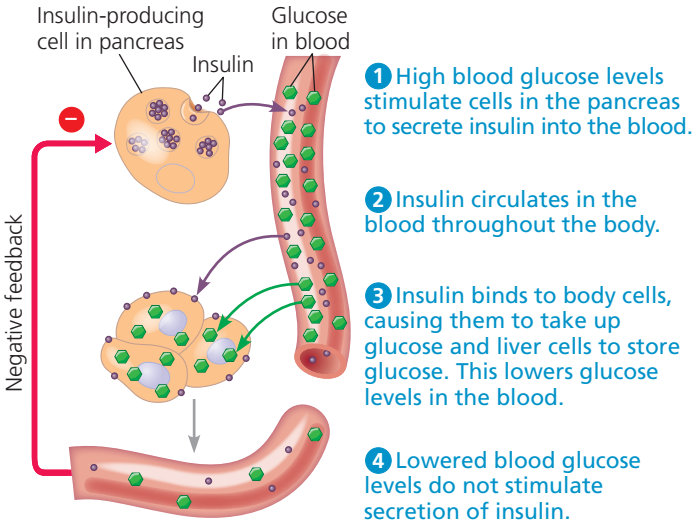
In **feedback regulation**, the output or product of a process regulates that very process. The most common form of regulation in living systems is *negative feedback*, a loop in which the response reduces the initial stimulus. As seen in the example of insulin signaling **(Figure 1.10)**, after a meal the level of the sugar glucose in your blood rises, which stimulates cells of the pancreas to secrete insulin. Insulin, in turn, causes body cells to take up glucose and liver cells to store it, thus decreasing blood glucose levels. This eliminates the stimulus for insulin secretion, shutting off the pathway. Thus, the output of the process negatively regulates that process.

Though less common than processes regulated by negative feedback, there are also many biological processes regulated by *positive feedback*, in which an end product *speeds up* its own production. The clotting of your blood in response to injury is an example. When a blood vessel is damaged, structures in the blood called platelets begin to aggregate at the site. Positive feedback occurs as chemicals released by the platelets attract *more* platelets. The platelet pileup then initiates a complex process that seals the wound with a clot.

Ecosystems: An Organism's Interactions with Other Organisms and the Physical Environment

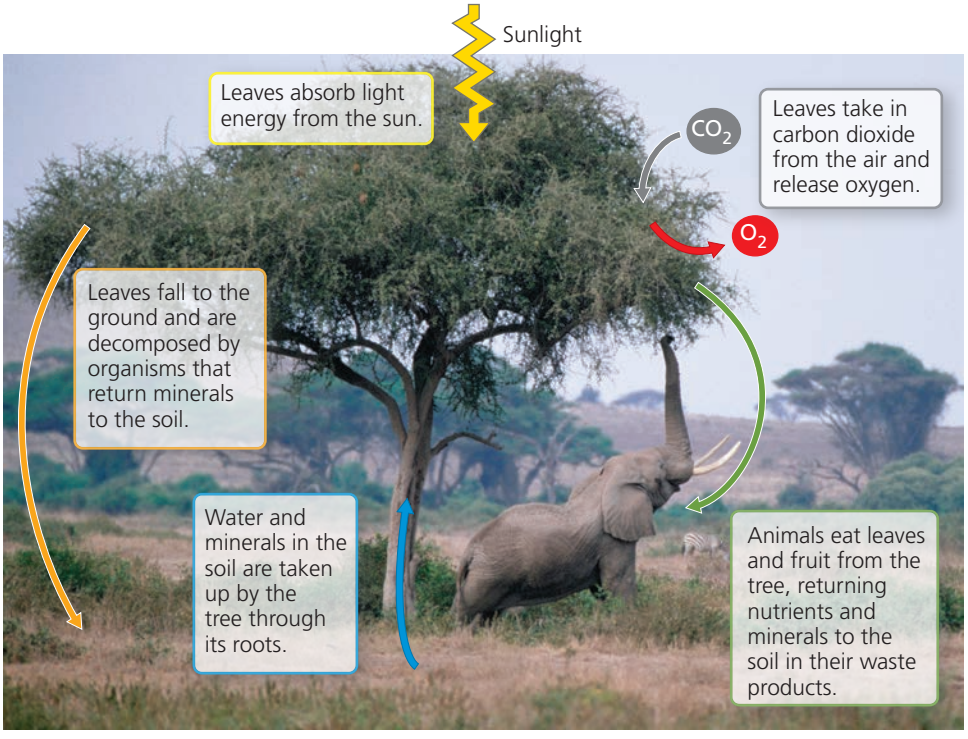
At the ecosystem level, every organism interacts with other organisms. For instance, an acacia tree interacts with soil microorganisms associated with its roots, insects that live on it, and animals that eat its leaves and fruit **(Figure 1.11)**. Interactions between organisms include those that are mutually beneficial (as when "cleaner fish" eat small parasites on a turtle), and those in which one species benefits and the other is harmed (as when a lion kills and eats a zebra). In some interactions between species, both are harmed—for example, when two plants compete for a soil resource that is in short supply.

Figure 1.10 Feedback regulation. The human body regulates use and storage of glucose, a major cellular fuel. This figure shows negative feedback: The response to insulin reduces the initial stimulus.



VISUAL SKILLS ➤ *In this example, what is the response to insulin? What is the initial stimulus that is reduced by the response?*

Figure 1.11 Interactions of an African acacia tree with other organisms and the physical environment.



Interactions among organisms help regulate the functioning of the ecosystem as a whole.

Each organism also interacts continuously with physical factors in its environment. The leaves of a tree, for example, absorb light from the sun, take in carbon dioxide from the air, and release oxygen to the air (see Figure 1.11). The environment is also affected by organisms. For instance, in addition to taking up water and minerals from the soil, the roots of a plant break up rocks as they grow, contributing to the formation of soil. On a global scale, plants and other photosynthetic organisms have generated all the oxygen in the atmosphere.

Like other organisms, we humans interact with our environment. Our interactions sometimes have dire consequences: For example, over the past 150 years, humans have greatly increased the burning of fossil fuels (coal, oil, and gas). This practice releases large amounts of carbon dioxide (CO_2) and other gases into the atmosphere, causing heat to be trapped close to the Earth's surface (see Figure 56.29). Scientists calculate that the CO_2 that human activities have added to the atmosphere has increased the average temperature of the planet by about 1°C since 1900. At the current rates that CO_2 and other gases are being added to the atmosphere, global models predict an additional rise of at least 3°C before the end of this century.

This ongoing global warming is a major aspect of **climate change**, a directional change to the global climate that lasts for three decades or more (as opposed to short-term changes in the weather). But global warming is not the only way the climate is changing: Wind and precipitation patterns are also shifting, and extreme weather events such as storms and droughts are occurring more often. Climate change has already affected organisms and their habitats all over the planet. For example, polar bears have lost much of the ice platform from which they hunt, leading to food shortages and increased mortality rates. As habitats deteriorate, hundreds of plant and animal species are shifting their ranges to more suitable locations—but for some, there is insufficient suitable habitat, or they may not be able to migrate quickly enough. As a result, the populations of many species are shrinking in size or even disappearing **(Figure 1.12)**. This trend can result in extinction, the permanent loss of a species. As we'll discuss in greater detail in Concept 56.4, the consequences of these changes for humans and other organisms may be profound.

➤ Figure 1.12 Threatened by global warming. A warmer environment causes lizards in the genus *Sceloporus* to spend more time in refuges from the heat, reducing time for foraging. Their food intake drops, decreasing reproductive success. Surveys show that 12% of the 200 populations in Mexico have disappeared since 1975. For more examples of climate change affecting life on Earth, see Make Connections Figure 56.30.

Having considered four of the unifying themes (organization, information, energy and matter, and interactions), let's now turn to evolution. There is consensus among biologists that evolution is the core theme of biology, and it is discussed in detail in the next section.

CONCEPT CHECK 1.1

1. Starting with the molecular level in Figure 1.3, write a sentence that includes components from the previous (lower) level of biological organization, for example: "A molecule consists of *atoms* bonded together." Continue with organelles, moving up the biological hierarchy.
2. Identify the theme or themes exemplified by (a) the sharp quills of a porcupine, (b) the development of a multicellular organism from a single fertilized egg, and (c) a hummingbird using sugar to power its flight.
3. **WHAT IF? ➤** For each theme discussed in this section, give an example not mentioned in the text.

For suggested answers, see Appendix A.

CONCEPT 1.2

The Core Theme: Evolution accounts for the unity and diversity of life

EVOLUTION Evolution is the one idea that makes logical sense of everything we know about living organisms. As the fossil record clearly shows, life has been evolving on Earth for billions of years, resulting in a vast diversity of past and present organisms. But along with the diversity there is also unity, in the form of shared features. For example, while sea horses, jackrabbits, hummingbirds, and giraffes all look very different, their skeletons are organized in the same basic way.

The scientific explanation for the unity and diversity of organisms—as well as for the adaptation of organisms to their particular environments—is **evolution**: the concept that the organisms living on Earth today are the modified descendants of common ancestors. As a result of descent with modification, two species share certain traits (unity) simply because they have descended from a common ancestor. Furthermore, we can account for differences between two species (diversity) with the idea that certain heritable changes occurred after the two species diverged from their common ancestor. An abundance of evidence of different types supports the occurrence of evolution and the theory that describes how it takes place, which we'll discuss in detail in Chapters 22–25. To quote one of the founders of modern evolutionary theory, Theodosius Dobzhansky, "Nothing in biology makes sense except in the light of evolution." To understand Dobzhansky's statement, we need to discuss how biologists think about the vast diversity of life on the planet.

Classifying the Diversity of Life

Diversity is a hallmark of life. Biologists have so far identified and named about 1.8 million species of organisms. Each species is given a two-part name: The first part is the name of the genus (plural, *genera*) to which the species belongs, and the second part is unique to the species within the genus. (For example, *Homo sapiens* is the name of our species.)

To date, known species include at least 100,000 species of fungi, 290,000 plant species, 57,000 vertebrate species (animals with backbones), and 1 million insect species (more than half of all known forms of life)—not to mention the myriad types of single-celled organisms. Researchers identify thousands of additional species each year. Estimates of the total number of species range from about 10 million to over 100 million. Whatever the actual number, the enormous variety of life gives biology a very broad scope. Biologists face a major challenge in attempting to make sense of this variety.

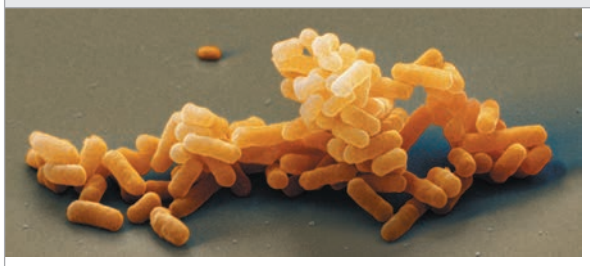
The Three Domains of Life

Historically, scientists have classified the diversity of life-forms into species and broader groupings by careful comparisons of structure, function, and other obvious features. In the last few decades, new methods of assessing species relationships, such as comparisons of DNA sequences, have led to a reevaluation of the classification of life. Although this reevaluation is ongoing, biologists currently divide all organisms into three groups called domains: Bacteria, Archaea, and Eukarya **(Figure 1.13)**.

The organisms making up two of the three domains—**Bacteria** and **Archaea**—are prokaryotic. All the eukaryotes (organisms with eukaryotic cells) are in domain **Eukarya**. This domain includes four subgroups: kingdom Plantae, kingdom Fungi, kingdom Animalia, and the protists. The three kingdoms are distinguished partly by their modes of nutrition: Plants produce their own sugars and other food molecules by photosynthesis, fungi absorb nutrients in

Figure 1.13 The three domains of life.

(a) Domain Bacteria



Bacteria are the most diverse and widespread prokaryotes and are now classified into multiple kingdoms. Each rod-shaped structure in this photo is a bacterial cell.

(b) Domain Archaea

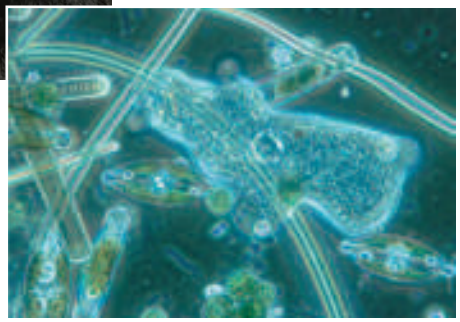
Domain Archaea includes multiple kingdoms. Some of the prokaryotes known as **archaea** live in Earth's extreme environments, such as salty lakes and boiling hot springs. Each round structure in this photo is an archaeal cell.

(c) Domain Eukarya

▲ **Kingdom Plantae** (land plants) consists of terrestrial multicellular eukaryotes that carry out photosynthesis, the conversion of light energy to the chemical energy in food.

▶ **Kingdom Fungi** is defined in part by the nutritional mode of its members (such as this mushroom), which absorb nutrients from outside their bodies.

◀ **Kingdom Animalia** consists of multicellular eukaryotes that ingest other organisms.



▶ **Protists** are mostly unicellular eukaryotes and some relatively simple multicellular relatives. Pictured here is an assortment of protists inhabiting pond water. Scientists are currently debating how to classify protists in a way that accurately reflects their evolutionary relationships.

dissolved form from their surroundings, and animals obtain food by eating and digesting other organisms. Animalia is, of course, the kingdom to which we belong.

The most numerous and diverse eukaryotes are the protists, which are mostly single-celled organisms. Although protists were once placed in a single kingdom, they are now classified into several groups. One major reason for this change is the recent DNA evidence showing that some protists are less closely related to other protists than they are to plants, animals, or fungi.

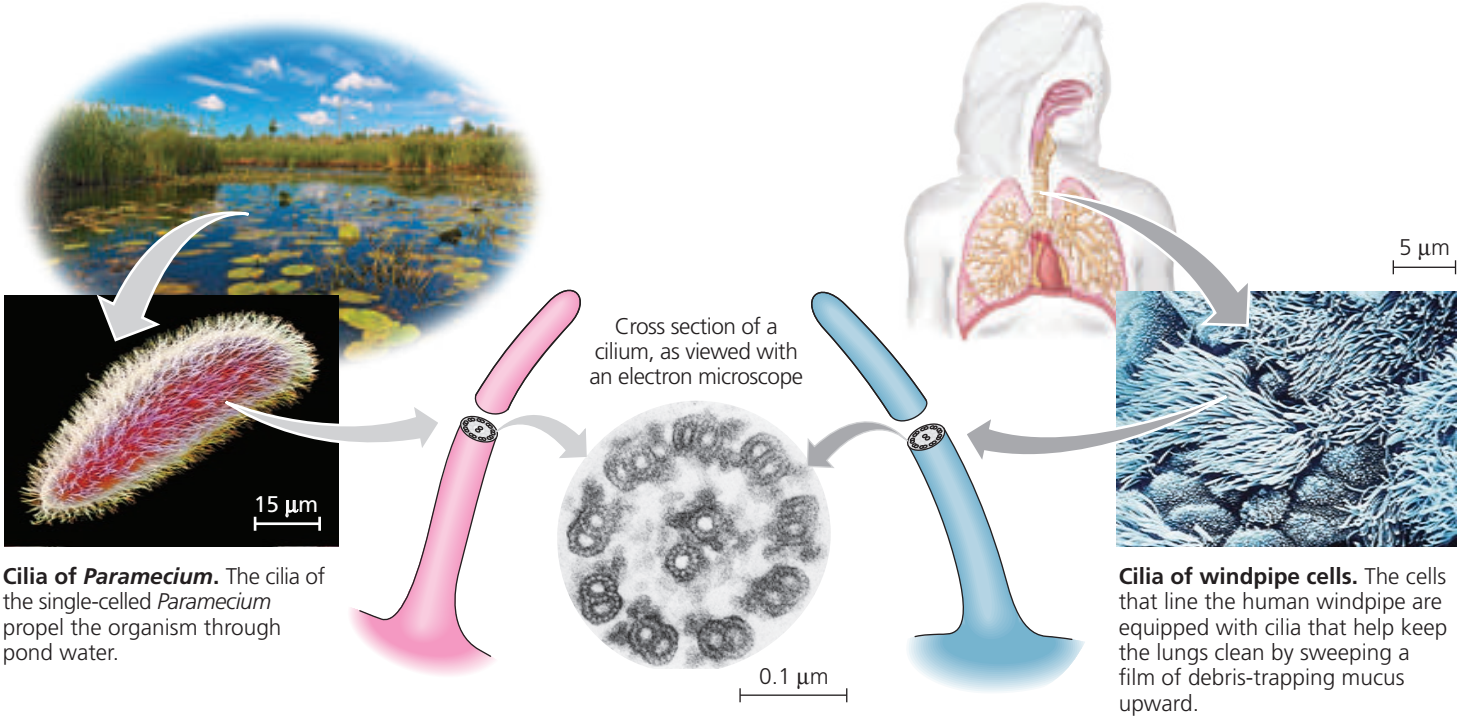
Unity in the Diversity of Life

As diverse as life is, it also displays remarkable unity. Consider, for example, the similar skeletons of different animals and the universal genetic language of DNA (the genetic code), both mentioned earlier. In fact, similarities between organisms are evident at all levels of the biological hierarchy. For example, unity is obvious in many features of cell structure, even among distantly related organisms **(Figure 1.14)**.

How can we account for life's dual nature of unity and diversity? The process of evolution, explained next, illuminates both the similarities and differences in the world of life. It also introduces another important dimension of biology: the passage of time. The history of life, as documented by fossils and other evidence, is the saga of a changing Earth billions of years old, inhabited by an evolving cast of living forms **(Figure 1.15)**.

Figure 1.15 Digging into the past. Paleontologists carefully excavate the hind leg of a long-necked dinosaur (*Rapetosaurus krausei*) from rocks in Madagascar.

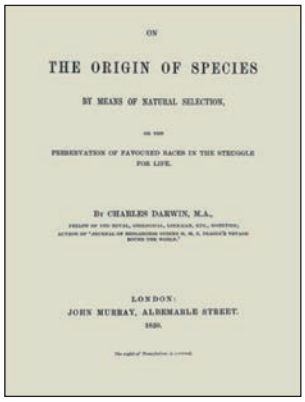
Figure 1.14 An example of unity underlying the diversity of life: the architecture of cilia in eukaryotes. Cilia (singular, *cilium*) are extensions of cells that function in locomotion. They occur in eukaryotes as diverse as *Paramecium* (found in pond water) and humans. Even organisms so different share a common architecture for their cilia, which have an elaborate system of tubules that is striking in cross-sectional views.



Cilia of *Paramecium*. The cilia of the single-celled *Paramecium* propel the organism through pond water.

Cilia of windpipe cells. The cells that line the human windpipe are equipped with cilia that help keep the lungs clean by sweeping a film of debris-trapping mucus upward.

Figure 1.16 Charles Darwin as a young man. His revolutionary book *On the Origin of Species* was first published in 1859.



MB ABC News Video: Exploring Evolution in the Solomon Islands

Charles Darwin and the Theory of Natural Selection

An evolutionary view of life came into sharp focus in November 1859, when Charles Darwin published one of the most important and influential books ever written, *On the Origin of Species by Means of Natural Selection* **(Figure 1.16)**. *The Origin of Species* articulated two main points. The first point was that contemporary species arose from a succession of ancestors that differed from them. Darwin called this process "descent with modification." This insightful phrase captured the duality of life's unity and diversity—unity in the kinship among species that descended from common ancestors and diversity in the modifications that evolved as species branched from their common ancestors **(Figure 1.17)**. Darwin's second main point was his proposal that "natural selection" is a primary cause of descent with modification.

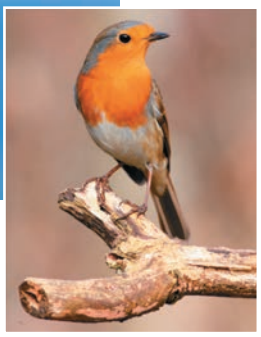
Darwin developed his theory of natural selection from observations that by themselves were neither new nor profound. However, although others had described the pieces of the puzzle, it was Darwin who saw how they fit together. He started with the following three observations from nature: First, individuals in a population vary in their traits, many of which seem to be heritable (passed on from parents to offspring). Second, a population can produce far more offspring than can survive to produce offspring of their own. With more individuals than the environment is able to support, competition is inevitable. Third, species generally are suited to their environments—in other words, they are adapted to their circumstances. For instance, a common adaptation among birds that eat mostly hard seeds is an especially strong beak.

By making inferences from these three observations, Darwin arrived at his theory of evolution. He reasoned that individuals with inherited traits that are better suited to the local environment are more likely to survive and reproduce than less well-suited individuals. Over many generations, a higher and higher proportion of individuals in a population will have the advantageous traits. Evolution occurs as the unequal reproductive success of individuals ultimately leads to adaptation to their environment, as long as the environment remains the same.

Darwin called this mechanism of evolutionary adaptation **natural selection** because the natural environment consistently "selects" for the propagation of certain traits among naturally occurring variant traits in the population. The example in **Figure 1.18** illustrates the ability of natural selection to "edit" a population's heritable variations in color. We see the products of natural selection in the exquisite adaptations of various organisms to the special circumstances of their way of life and their environment. The wings of the bat shown in **Figure 1.19** are an excellent example of adaptation.

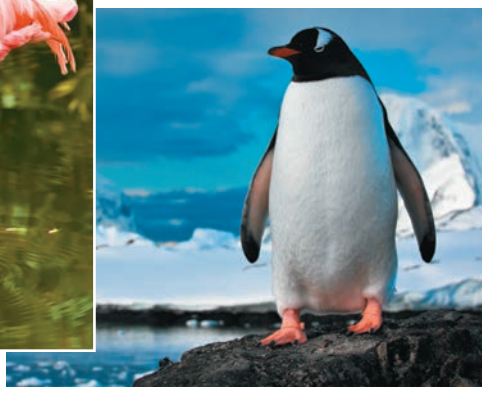
Figure 1.17 Unity and diversity among birds. These four birds are variations on a common body plan. For example, each has feathers, a beak, and wings. However, these common features are highly specialized for the birds' diverse lifestyles.

▼ Red-shouldered hawk



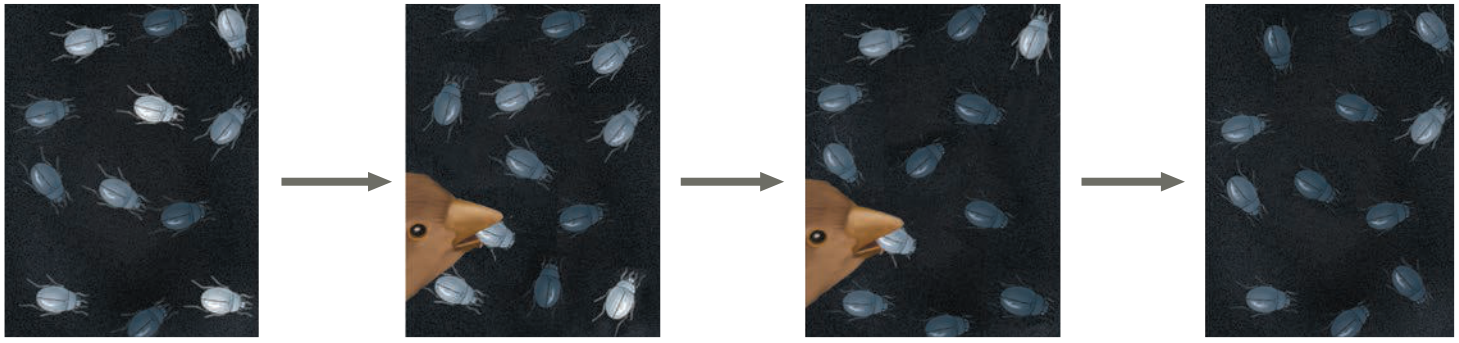
▲ European robin

▼ American flamingo



▲ Gentoo penguin

Figure 1.18 Natural selection. This imaginary beetle population has colonized a locale where the soil has been blackened by a recent brush fire. Initially, the population varies extensively in the inherited coloration of the individuals, from very light gray to charcoal. For hungry birds that prey on the beetles, it is easiest to spot the beetles that are lightest in color.



1 Population with varied inherited traits

2 Elimination of individuals with certain traits

3 Reproduction of survivors

4 Increased frequency of traits that enhance survival and reproductive success

DRAW IT ➤ *Over time, the soil will gradually become lighter in color. Draw another step to show how the soil, when lightened to medium color, would affect natural selection. Write a caption for this new step. Then explain how the population would change over time as the soil becomes lighter.*

MB **HHMI Video: The Making of The Fittest: Natural Selection and Adaptation (Rock Pocket Mouse)**

hhmi BioInteractive

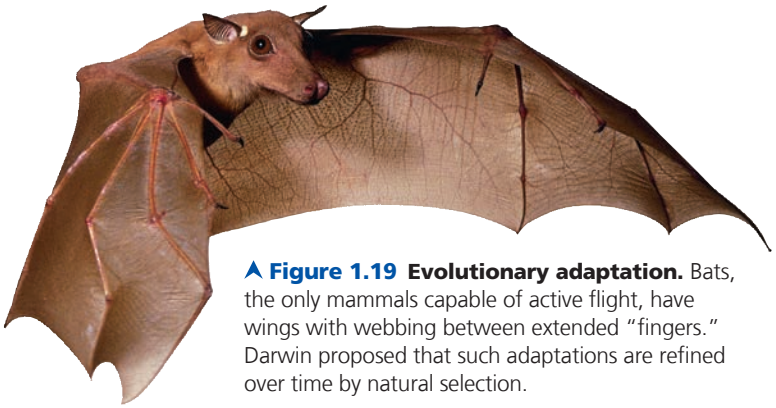


Figure 1.19 Evolutionary adaptation. Bats, the only mammals capable of active flight, have wings with webbing between extended "fingers." Darwin proposed that such adaptations are refined over time by natural selection.

The Tree of Life

Take another look at the skeletal architecture of the bat's wings in Figure 1.19. These wings are not like those of feathered birds; the bat is a mammal. The bat's forelimbs, though adapted for flight, actually have all the same bones, joints, nerves, and blood vessels found in other limbs as diverse as the human arm, the foreleg of a horse, and the flipper of a whale. Indeed, all mammalian forelimbs are anatomical variations of a common architecture. According to the Darwinian concept of descent with modification, the shared anatomy of mammalian limbs reflects inheritance of the limb structure from a common ancestor—the "prototype" mammal from which all other mammals descended. The diversity of mammalian forelimbs results from modification by natural selection operating over millions of years in different environmental contexts. Fossils and other evidence corroborate anatomical unity in supporting this view of mammalian descent from a common ancestor.

Darwin proposed that natural selection, by its cumulative effects over long periods of time, could cause an ancestral species to give rise to two or more descendant species. This could occur, for example, if one population fragmented into several subpopulations isolated in different environments. In these separate arenas of natural selection, one species could gradually radiate into multiple species as the geographically isolated populations adapted over many generations to different sets of environmental factors.

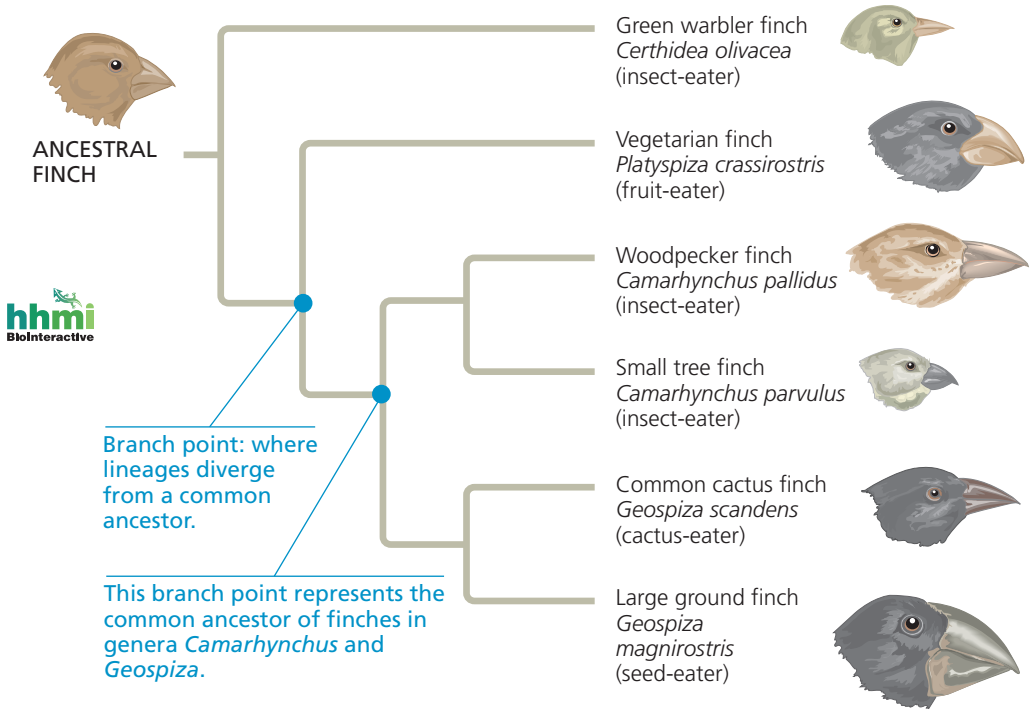
The Galápagos finches are a famous example of the process of radiation of new species from a common ancestor. Darwin collected specimens of these birds during his 1835 visit to the remote Galápagos Islands, 900 kilometers (km) off the Pacific coast of South America. These relatively young volcanic islands are home to many species of plants and animals found nowhere else in the world, though many Galápagos organisms are clearly related to species on the South American mainland. The Galápagos finches are believed to have descended from an ancestral finch species that reached the archipelago from South America or the Caribbean. Over time, the Galápagos finches diversified from their ancestor as populations became adapted to different food sources on their particular islands. Years after Darwin collected the finches, researchers began to sort out their evolutionary relationships, first from anatomical and geographic data and more recently with the help of DNA sequence comparisons.

MB **ABC News Video: Protecting the Galápagos Islands**
Video: Galápagos Biodiversity by Peter and Rosemary Grant

Biologists' diagrams of evolutionary relationships generally take treelike forms, though the trees are often turned sideways

➤ Figure 1.20 Descent with modification: adaptive radiation of finches on the Galápagos Islands. This "tree" illustrates a current model for the evolution of finches on the Galápagos. Note the different beaks, which are adapted to different food sources on the different islands. For example, heavier, thicker beaks are better at cracking seeds, while the more slender beaks are better at grasping insects.

HHMI Video: The Origin of Species: The Beak of the Finch



as in **Figure 1.20**. Tree diagrams make sense: Just as an individual has a genealogy that can be diagrammed as a family tree, each species is one twig of a branching tree of life extending back in time through ancestral species more and more remote. Species that are very similar, such as the Galápagos finches, share a common ancestor. Through an ancestor that lived much farther back in time, finches are related to sparrows, hawks, penguins, and all other birds. Furthermore, finches and other birds are related to us through a common ancestor even more ancient. Trace life back far enough, and we reach the early prokaryotes that inhabited Earth over 3.5 billion years ago. We can recognize their vestiges in our own cells—in the universal genetic code, for example. Indeed, all of life is connected through its long evolutionary history.

CONCEPT CHECK 1.2

1. Explain why "editing" is a metaphor for how natural selection acts on a population's heritable variation.
2. Referring to Figure 1.20, provide a possible explanation for how, over a very long time, the green warbler finch came to have a slender beak.
3. **DRAW IT ➤** The three domains you learned about in Concept 1.2 can be represented in the tree of life as the three main branches, with three subbranches on the eukaryotic branch being the kingdoms Plantae, Fungi, and Animalia. What if fungi and animals are more closely related to each other than either of these kingdoms is to plants—as recent evidence strongly suggests? Draw a simple branching pattern that symbolizes the proposed relationship between these three eukaryotic kingdoms.

For suggested answers, see Appendix A.

CONCEPT 1.3

In studying nature, scientists make observations and form and test hypotheses

Science is a way of knowing—an approach to understanding the natural world. It developed out of our curiosity about ourselves, other life-forms, our planet, and the universe. The word *science* is derived from a Latin verb meaning "to know." Striving to understand seems to be one of our basic urges.

At the heart of science is **inquiry**, a search for information and explanations of natural phenomena. There is no formula for successful scientific inquiry, no single scientific method that researchers must rigidly follow. As in all quests, science includes elements of challenge, adventure, and luck, along with careful planning, reasoning, creativity, patience, and the persistence to overcome setbacks. Such diverse elements of inquiry make science far less structured than most people realize. That said, it is possible to highlight certain characteristics that help to distinguish science from other ways of describing and explaining nature.

Scientists use a process of inquiry that includes making observations, forming logical, testable explanations (*hypotheses*), and testing them. The process is necessarily repetitive: In testing a hypothesis, more observations may inspire revision of the original hypothesis or formation of a new one, thus leading to further testing. In this way,

scientists circle closer and closer to their best estimation of the laws governing nature.

Exploration and Observation

Our innate curiosity often stimulates us to pose questions about the natural basis for the phenomena we observe in the world. For example, what causes the roots of a plant seedling to grow downward? In fine-tuning their questions, biologists rely heavily on the scientific literature, the published contributions of fellow scientists. By reading about and understanding past studies, scientists can build on the foundation of existing knowledge, focusing their investigations on observations that are original and on hypotheses that are consistent with previous findings. Identifying publications relevant to a new line of research is now easier than at any point in the past, thanks to indexed and searchable electronic databases.

In the course of their work, biologists make careful observations. In gathering information, they often use tools such as microscopes, precision thermometers, or high-speed cameras that extend their senses or facilitate careful measurement. Observations can reveal valuable information about the natural world. For example, a series of detailed observations have shaped our understanding of cell structure, and another set of observations is currently expanding our databases of genome sequences from diverse species and databases of genes whose expression is altered in various diseases.

Recorded observations are called **data**. Put another way, data are items of information on which scientific inquiry is based. The term *data* implies numbers to many people. But some data are *qualitative*, often in the form of recorded descriptions rather than numerical measurements. For example, Jane Goodall spent decades recording her observations of chimpanzee behavior during field research in a Tanzanian jungle **(Figure 1.21)**. In her studies, Goodall also enriched the field of animal behavior with volumes of *quantitative* data, such as the frequency and duration of specific behaviors for different members of a group of chimpanzees in a variety of situations. Quantitative data are generally expressed as numerical measurements and often organized into tables and graphs. Scientists analyze their data using a type of mathematics called *statistics* to test whether their results are significant or merely due to random fluctuations. All results presented in this text have been shown to be statistically significant.

Collecting and analyzing observations can lead to important conclusions based on a type of logic called **inductive reasoning**. Through induction, we derive generalizations from a large number of specific observations. "The sun always rises in the east" is an example. And so is "All organisms are made of cells." Careful observations and data analyses, along with generalizations reached by induction, are fundamental to our understanding of nature.

Figure 1.21 Jane Goodall collecting qualitative data on chimpanzee behavior. Goodall recorded her observations in field notebooks, often with sketches of the animals' behavior.

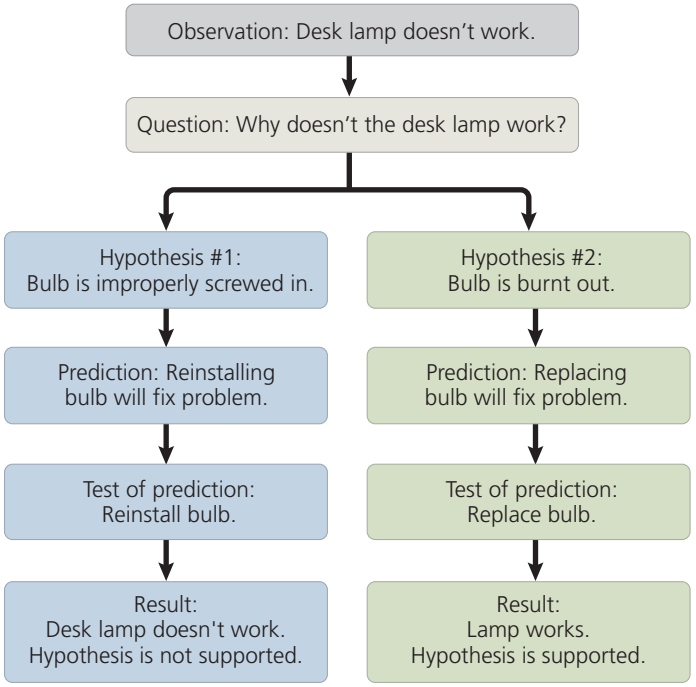
MB **Interview with Jane Goodall: Living with chimpanzees**

Forming and Testing Hypotheses

After carrying out preliminary observations and collecting and analyzing data, scientists begin to form tentative answers to their original questions and to test their hypothetical explanations—that is, their hypotheses. In science, a **hypothesis** is an explanation, based on observations and assumptions, that leads to a testable prediction. Said another way, a hypothesis is an explanation on trial. The hypothesis is usually a rational accounting for a set of observations, based on the available data and guided by inductive reasoning. A scientific hypothesis must lead to predictions that can be tested by making additional observations or by performing experiments. An **experiment** is a scientific test, carried out under controlled conditions.

We all make observations and develop questions and hypotheses in solving everyday problems. Let's say, for example, that your desk lamp is plugged in and turned on but the bulb isn't lit. That's an observation. The question is obvious: Why doesn't the lamp work? Two reasonable hypotheses based on your experience are that (1) the bulb is not screwed in properly or (2) the bulb is burnt out. Each of these alternative hypotheses leads to predictions you can test with experiments. For example, the improperly screwed-in

Figure 1.22 A simplified view of the scientific process. The idealized process sometimes called the "scientific method" is shown in this flow chart, which illustrates hypothesis testing for a desk lamp that doesn't work.



bulb hypothesis predicts that carefully re-installing the bulb will fix the problem. **Figure 1.22** diagrams this informal inquiry. Figuring things out in this way by trial and error is a hypothesis-based approach.

Deductive Reasoning

A type of logic called deduction is also built into the use of hypotheses in science. While induction entails reasoning from a set of specific observations to reach a general conclusion, **deductive reasoning** involves logic that flows in the opposite direction, from the general to the specific. From general premises, we extrapolate to the specific results we should expect if the premises are true. In the scientific process, deductions usually take the form of predictions of results that will be found if a particular hypothesis (premise) is correct. We then test the hypothesis by carrying out experiments or observations to see whether or not the results are as predicted. This deductive testing takes the form of "*If . . . then*" logic. In the case of the desk lamp example: *If* the burnt-out bulb hypothesis is correct, *then* the lamp should work if you replace the bulb with a new one.

We can use the desk lamp example to illustrate two other key points about the use of hypotheses in science. First, one can always devise additional hypotheses to explain a set of observations. For instance, another hypothesis to explain our nonworking desk lamp is that the electrical socket is broken. Although you could design an experiment to test this hypothesis, you can never test all possible hypotheses. Second, we can never *prove* that a hypothesis is true. Based on the experiments shown in Figure 1.22, the burnt-out bulb hypothesis is the most likely explanation, but testing supports that hypothesis *not* by proving that it is correct, but rather by failing to prove it incorrect. For example, even if replacing the bulb fixed the desk lamp, it might have been because there was a temporary power outage that just happened to end while the bulb was being changed.

Although a hypothesis can never be proved beyond the shadow of a doubt, testing it in various ways can significantly increase our confidence in its validity. Often, rounds of hypothesis formulation and testing lead to a scientific consensus—the shared conclusion of many scientists that a particular hypothesis explains the known data well and stands up to experimental testing.

Questions That Can and Cannot Be Addressed by Science

Scientific inquiry is a powerful way to learn about nature, but there are limitations to the kinds of questions it can answer. A scientific hypothesis must be *testable*; there must be some observation or experiment that could reveal if such an idea is likely to be true or false. The hypothesis that a burnt-out bulb is the sole reason the lamp doesn't work would not be supported if replacing the bulb with a new one didn't fix the lamp.

Not all hypotheses meet the criteria of science: You wouldn't be able to test the hypothesis that invisible ghosts are fooling with your desk lamp! Because science only deals with natural, testable explanations for natural phenomena, it can neither support nor contradict the invisible ghost hypothesis, nor whether spirits or elves cause storms, rainbows, or illnesses. Such supernatural explanations are simply outside the bounds of science, as are religious matters, which are issues of personal faith. Science and religion are not mutually exclusive or contradictory; they are simply concerned with different issues.

The Flexibility of the Scientific Process

The desk lamp example of Figure 1.22 traces an idealized process of inquiry sometimes called the *scientific method*. However, very few scientific inquiries adhere rigidly to the sequence of steps that are typically used to describe this approach. For example, a scientist may start to design an experiment, but then backtrack after realizing that more preliminary observations are necessary. In other cases, observations remain too puzzling to prompt well-defined questions until further study provides a new context in which to view those observations. For example, scientists

could not unravel the details of how genes encode proteins until *after* the discovery of the structure of DNA (an event that took place in 1953).

A more realistic model of the scientific process is shown in **Figure 1.23**. The focus of this model, shown in the central circle in the figure, is the forming and testing of hypotheses. This core set of activities is the reason that science does so well in explaining phenomena in the natural world. These activities, however, are shaped by exploration and discovery (the upper circle in Figure 1.23) and influenced by interactions with other scientists and with society more generally (lower circles). For example, the community of scientists influences which hypotheses are tested, how test results are interpreted, and what value is placed on the findings. Similarly, societal needs—such as the push to cure cancer or understand the process of climate change—may help shape what research projects are funded and how extensively the results are discussed.

Now that we have highlighted the key features of scientific inquiry—making observations and forming and testing hypotheses—you should be able to recognize these features in a case study of actual scientific research.

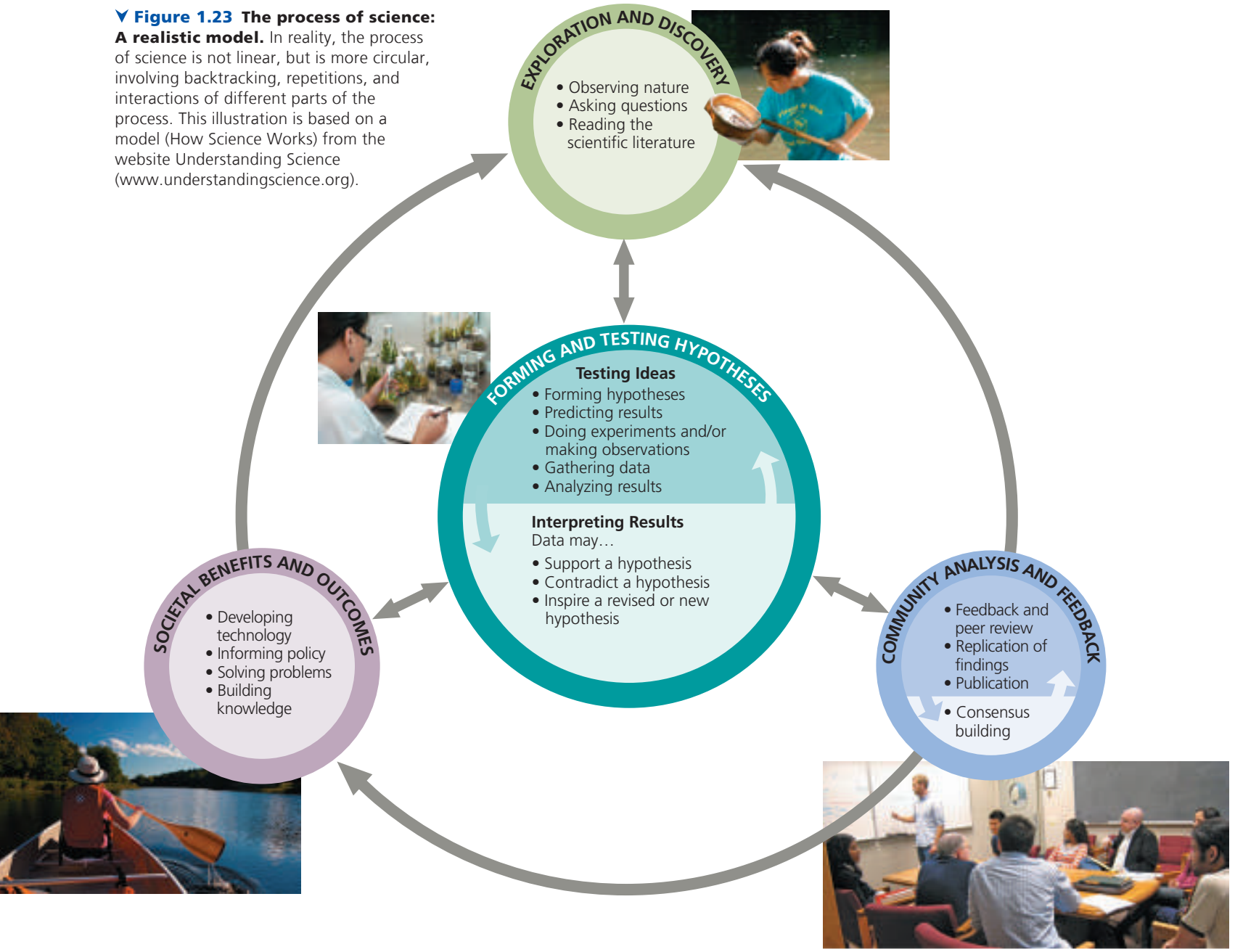


Figure 1.23 The process of science: A realistic model. In reality, the process of science is not linear, but is more circular, involving backtracking, repetitions, and interactions of different parts of the process. This illustration is based on a model (How Science Works) from the website Understanding Science (www.understandingscience.org).

A Case Study in Scientific Inquiry: Investigating Coat Coloration in Mouse Populations

Our case study begins with a set of observations and inductive generalizations. Color patterns of animals vary widely in nature, sometimes even among members of the same species. What accounts for such variation? As you may recall, the two mice depicted at the beginning of this chapter are members of the same species (*Peromyscus polionotus*), but they have different color patterns and reside in different environments. The beach mouse lives along the Florida seashore, a habitat of brilliant white sand dunes with sparse clumps of beach grass. The inland mouse lives on darker, more fertile soil farther inland **(Figure 1.24)**. Even a brief glance at the photographs in Figure 1.24 reveals a striking match of mouse coloration to its habitat. The natural predators of these mice, including hawks, owls, foxes, and coyotes, are all visual hunters (they use their eyes to look for prey). It was logical, therefore, for Francis Bertody Sumner, a naturalist studying populations of these mice in the 1920s, to form the hypothesis that their coloration patterns had evolved as adaptations that camouflage the mice in their native environments, protecting them from predation.

As obvious as the camouflage hypothesis may seem, it still required testing. In 2010, biologist Hopi Hoekstra of Harvard University and a group of her students headed to Florida to test the prediction that mice with coloration that did not match their habitat would be preyed on more heavily than the native, well-matched mice. **Figure 1.25** summarizes this field experiment.

The researchers built hundreds of models of mice and spray-painted them to resemble either beach or inland mice, so that the models differed only in their color patterns. The researchers placed equal numbers of these model mice randomly in both habitats and left them overnight. The mouse models resembling the native mice in the habitat were the *control* group (for instance, light-colored mouse models in the beach habitat), while the mouse models with the non-native coloration were the *experimental* group (for example, darker models in the beach habitat). The following morning, the team counted and recorded signs of predation events, which ranged from bites and gouge marks on some models to the outright disappearance of others. Judging by the shape of the predators' bites and the tracks surrounding the experimental sites, the predators appeared to be split fairly evenly between mammals (such as foxes and coyotes) and birds (such as owls, herons, and hawks).

For each environment, the researchers then calculated the percentage of predation events that targeted camouflaged models. The results were clear-cut: Camouflaged models showed much lower predation rates than those lacking camouflage in both the beach habitat (where light mice were less vulnerable) and the inland habitat (where dark mice were less vulnerable). The data thus fit the key prediction of the camouflage hypothesis.

Experimental Variables and Controls

In carrying out an experiment, a researcher often manipulates one factor in a system and observes the effects of this change. The mouse camouflage experiment described in Figure 1.25 is an example of a **controlled experiment**, one that is designed to compare an experimental group (the non-camouflaged mice models, in this case) with a control group (the camouflaged models). Both the factor that is manipulated and the factor that is subsequently measured are types of experimental **variables**—a feature or quantity that varies in

Figure 1.24 Different coloration in beach and inland populations of *Peromyscus polionotus*.

Beach mice living on sparsely vegetated sand dunes along the coast have light tan, dappled fur on their backs that allows them to blend into their surroundings, providing camouflage.

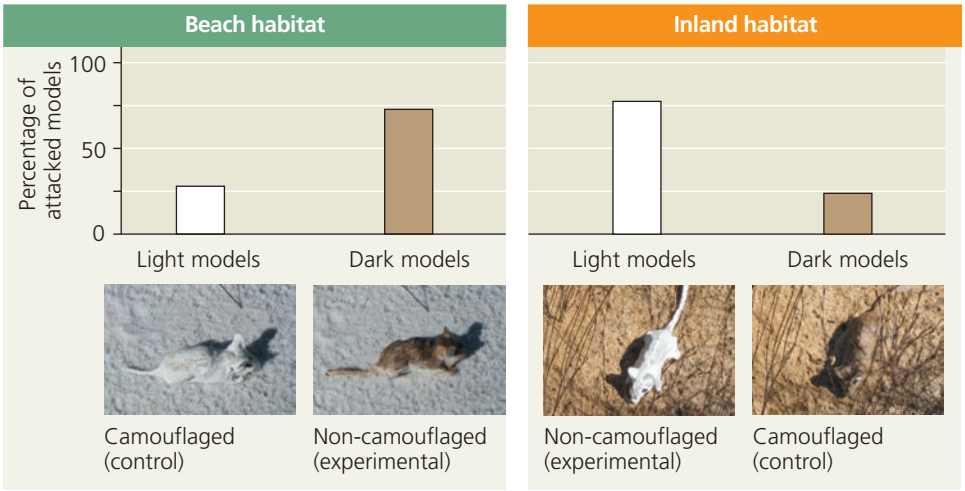
Members of the same species living about 30 km inland have dark fur on their backs, camouflaging them against the dark ground of their habitat.

Figure 1.25

Inquiry **Does camouflage affect predation rates on two populations of mice?**

Experiment Hopi Hoekstra and colleagues tested the hypothesis that coat coloration provides camouflage that protects beach and inland populations of *Peromyscus polionotus* mice from predation in their habitats. The researchers spray-painted mouse models with light or dark color patterns that matched those of the beach and inland mice and placed models with each of the patterns in both habitats. The next morning, they counted damaged or missing models.

Results For each habitat, the researchers calculated the percentage of attacked models that were camouflaged or non-camouflaged. In both habitats, the models whose pattern did not match their surroundings suffered much higher "predation" than did the camouflaged models.



Conclusion The results are consistent with the researchers' prediction: that mouse models with camouflage coloration would be preyed on less often than non-camouflaged mouse models. Thus, the experiment supports the camouflage hypothesis.

Data from S. N. Vignieri, J. G. Larson, and H. E. Hoekstra, The selective advantage of crypsis in mice, *Evolution* 64:2153–2158 (2010).

INTERPRET THE DATA ➤ *The bars indicate the percentage of the attacked models that were either light or dark. Assume 100 mouse models were attacked in each habitat. For the beach habitat, how many were light models? Dark models? Answer the same questions for the inland habitat.*

Interview with Hopi Hoekstra: Investigating the genetics and natural selection of mouse coat color

an experiment. In our example, the color of the mouse model was the **independent variable**—the factor being manipulated by the researchers. The **dependent variable** is the factor being measured that is predicted to be affected by the independent variable; in this case, the researchers measured the predation rate in response to variation in color of the mouse model. Ideally, the experimental and control groups differ in only one independent variable—in the mouse experiment, color.

Without the control group, the researchers would not have been able to rule out other factors as causes of the more frequent attacks on the non-camouflaged mice—such as different numbers of predators or different temperatures in the different test areas. The clever experimental design left coloration as the only factor that could account for the low predation rate on models camouflaged with respect to the surrounding environment.

A common misconception is that the term *controlled experiment* means that scientists control all features of the experimental environment. But that's impossible in field research and can be very difficult even in highly regulated laboratory environments. Researchers usually "control" unwanted variables not by *eliminating* them through environmental regulation, but by *canceling out* their effects by using control groups.

Animation: Introduction to Experimental Design

Theories in Science

"It's just a theory!" Our everyday use of the term *theory* often implies an untested speculation. But the term *theory* has a different meaning in science. What is a scientific theory, and how is it different from a hypothesis or from mere speculation?

First, a scientific **theory** is much broader in scope than a hypothesis. *This* is a hypothesis: "Coat coloration well-matched to their habitat is an adaptation that protects mice from predators." But *this* is a theory: "Evolutionary adaptations arise by natural selection." This theory proposes that natural selection is the evolutionary mechanism that accounts for an enormous variety of adaptations, of which coat color in mice is but one example.

Second, a theory is general enough to spin off many new, testable hypotheses. For example, the theory of natural selection motivated two researchers at Princeton University, Peter and Rosemary Grant, to test the specific hypothesis that the beaks of Galápagos finches evolve in response to changes in the types of available food. (Their results supported their hypothesis; see the introduction to Chapter 23.)

And third, compared to any one hypothesis, a theory is generally supported by a much greater body of evidence. The theory of natural selection has been supported by a vast quantity of evidence, with more being found every day, and has not been contradicted by any scientific data. Those theories that become widely adopted in science (such as the theory of natural selection and the theory of gravity) explain a great diversity of observations and are supported by a vast accumulation of evidence.

In spite of the body of evidence supporting a widely accepted theory, scientists will sometimes modify or even reject theories when new research produces results that don't fit. For example, biologists once lumped bacteria and archaea together as a kingdom of prokaryotes. When new methods for comparing cells and molecules could be used to test such relationships, the evidence led scientists to reject the theory that bacteria and archaea are members of the same kingdom. If there is "truth" in science, it is at best conditional, based on the weight of available evidence.

CONCEPT CHECK 1.3

1. What qualitative observation led to the quantitative study in Figure 1.25?
2. Contrast inductive reasoning with deductive reasoning.
3. Why is natural selection called a theory?
4. **WHAT IF?** ➤ In the deserts of New Mexico, the soils are mostly sandy, with occasional regions of black rock derived from lava flows that occurred about 1,000 years ago. Mice are found in both sandy and rocky areas, and owls are known predators. What might you expect about coat color in these two mouse populations? Explain. How would you use this ecosystem to further test the camouflage hypothesis?

For suggested answers, see Appendix A.

CONCEPT 1.4

Science benefits from a cooperative approach and diverse viewpoints

Movies and cartoons sometimes portray scientists as loners in white lab coats, working in isolated labs. In reality, science is an intensely social activity. Most scientists work in teams, which often include both graduate and undergraduate students. And to succeed in science, it helps to be a good communicator. Research results have no impact until shared with a community of peers through seminars, publications, and websites. And, in fact, research papers aren't published until they are vetted by colleagues in what is called the "peer review" process. The examples of scientific inquiry described in this book, for instance, have all been published in peer-reviewed journals.

Building on the Work of Others

The great scientist Isaac Newton once said: "To explain all nature is too difficult a task for any one man or even for any one age. 'Tis much better to do a little with certainty, and leave the rest for others that come after you. . . ." Anyone who becomes a scientist, driven by curiosity about how nature works, is sure to benefit greatly from the rich storehouse of discoveries by others who have come before. In fact, Hopi Hoekstra's experiment benefited from the work of another researcher, D. W. Kaufman, 40 years earlier. You can study the design of Kaufman's experiment and interpret the results in the **Scientific Skills Exercise**.

Scientific results are continually scrutinized through the repetition of observations and experiments. Scientists working in the same research field often check one another's claims by attempting to confirm observations or repeat experiments. If scientific colleagues cannot repeat experimental findings, this failure may reflect some underlying weakness in the original claim, which will then have to be revised. In this sense, science polices itself. Integrity and adherence to high professional standards in reporting results are central to the scientific endeavor, since the validity of experimental data is key to designing further lines of inquiry.

It is not unusual for several scientists to converge on the same research question. Some scientists enjoy the challenge of being first with an important discovery or key experiment, while others derive more satisfaction from cooperating with fellow scientists working on the same problem.

Cooperation is facilitated when scientists use the same organism. Often it is a widely used **model organism**—a species that is easy to grow in the lab and lends itself particularly well to the questions being investigated. Because all species are evolutionarily related, such an organism may be viewed as a model for understanding the biology of other species and their diseases. For example, genetic studies of the fruit fly *Drosophila melanogaster* have taught us a lot about how genes work in other species, even humans. Some other popular model organisms are the mustard plant *Arabidopsis thaliana*, the soil worm *Caenorhabditis elegans*, the zebrafish *Danio rerio*, the mouse *Mus musculus*, and the bacterium *Escherichia coli*. As you read through this book, note the many contributions that these and other model organisms have made to the study of life.

Biologists may approach interesting questions from different angles. Some biologists focus on ecosystems, while others study natural phenomena at the level of organisms or cells. This text is divided into units that look at biology at different levels and investigate problems through different approaches. Yet any given problem can be addressed from many perspectives, which in fact complement each other. For example, Hoekstra's work uncovered at least one genetic mutation that underlies the differences between beach and inland mouse coloration. Her lab includes biologists specializing in different biological levels, allowing links to be made between the evolutionary adaptations she focuses on and their molecular basis in DNA sequences.

As a biology student, you can benefit from making connections between the different levels of biology. You can develop this skill by noticing when certain topics crop up again and again in different units. One such topic is sickle-cell disease, a well-understood genetic condition that is prevalent among native inhabitants of Africa and other warm regions and their

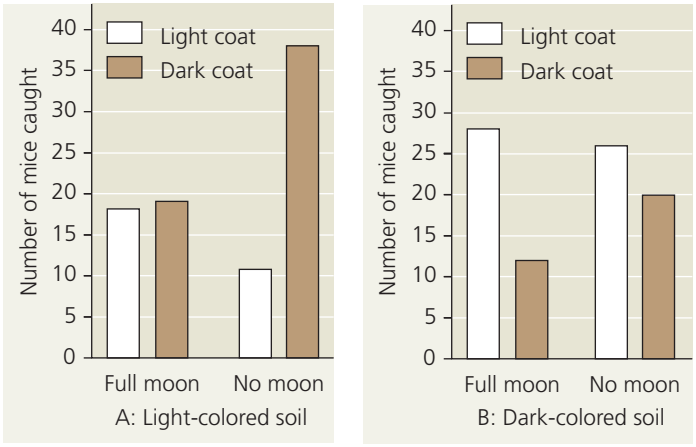
SCIENTIFIC SKILLS EXERCISE

Interpreting a Pair of Bar Graphs

How Much Does Camouflage Affect Predation on Mice by Owls With and Without Moonlight? D. W. Kaufman hypothesized that the extent to which the coat color of a mouse contrasted with the color of its surroundings would affect the rate of nighttime predation by owls. He also hypothesized that the contrast would be affected by the amount of moonlight. In this exercise, you will analyze data from his studies of owl predation on mice that tested these hypotheses.

How the Experiment Was Done Pairs of mice (*Peromyscus polionotus*) with different coat colors, one light brown and one dark brown, were released simultaneously into an enclosure that contained a hungry owl. The researcher recorded the color of the mouse that was first caught by the owl. If the owl did not catch either mouse within 15 minutes, the test was recorded as a zero. The release trials were repeated multiple times in enclosures with either a dark-colored soil surface or a light-colored soil surface. The presence or absence of moonlight during each assay was recorded.

Data from the Experiment



Data from D. W. Kaufman, Adaptive coloration in *Peromyscus polionotus*: Experimental selection by owls, *Journal of Mammalogy* 55:271–283 (1974).

INTERPRET THE DATA

1. First, make sure you understand how the graphs are set up. Graph A shows data from the light-colored soil enclosure and graph B from the dark-colored enclosure, but in all other respects the graphs are the same. (a) There is more than one independent variable in these graphs. What are the independent variables, the variables that were tested by the researcher? Which axis of the graphs has the independent variables? (b) What is the dependent variable, the response to the variables being tested? Which axis of the graphs has the dependent variable?
2. (a) How many dark brown mice were caught in the light-colored soil enclosure on a moonlit night? (b) How many dark brown mice were caught in the dark-colored soil enclosure on a moonlit night? (c) On a moonlit night, would a dark brown mouse be more likely to escape predation by owls on dark- or light-colored soil? Explain your answer.
3. (a) Is a dark brown mouse on dark-colored soil more likely to escape predation under a full moon or with no moon? (b) What about a light brown mouse on light-colored soil? Explain.
4. (a) Under which conditions would a dark brown mouse be most likely to escape predation at night? (b) A light brown mouse?
5. (a) What combination of independent variables led to the highest predation level in enclosures with light-colored soil? (b) What combination of independent variables led to the highest predation level in enclosures with dark-colored soil?
6. Thinking about your answers to question 5, provide a simple statement describing conditions that are especially deadly for either color of mouse.
7. Combining the data from both graphs, estimate the number of mice caught in moonlight versus no-moonlight conditions. Which condition is optimal for predation by the owl? Explain.

Instructors: A version of this Scientific Skills Exercise can be assigned in MasteringBiology.

descendants. Sickle-cell disease will appear in several units of the text, each time addressed at a new level. In addition, we have designed a number of figures that make connections between the content in different chapters, as well as questions that ask you to make the connections yourselves. We hope these features will help you integrate the material you're learning and enhance your enjoyment of biology by encouraging you to keep the big picture in mind.

Science, Technology, and Society

The research community is part of society at large, and the relationship of science to society becomes clearer when we add technology to the picture (see Figure 1.23). Though science and technology sometimes employ similar inquiry patterns, their basic goals differ. The goal of science is to understand natural phenomena, while that of **technology** is to *apply* scientific knowledge for some specific purpose. Biologists and other scientists usually speak of "discoveries," while engineers and other technologists more often speak of "inventions." Because scientists put new technology to work in their research, science and technology are interdependent.

The potent combination of science and technology can have dramatic effects on society. Sometimes, the applications of basic research that turn out to be the most beneficial come out of the blue, from completely unanticipated observations in the course of scientific exploration. For example, discovery of the structure of DNA by Watson and

Figure 1.26 DNA technology and forensics. In 2011, forensic analysis of DNA samples from a crime scene led to the release of Michael Morton from prison after he had served nearly 25 years for a crime he didn't commit, the brutal murder of his wife. The DNA analysis linked another man, also charged in a second murder, to the crime. The photo shows Mr. Morton hugging his parents after his conviction was overturned. The details of forensic analysis of DNA will be described in Chapter 20.

Crick 60 years ago and subsequent achievements in DNA science led to the technologies of DNA manipulation that are transforming applied fields such as medicine, agriculture, and forensics **(Figure 1.26)**. Perhaps Watson and Crick envisioned that their discovery would someday lead to important applications, but it is unlikely that they could have predicted exactly what all those applications would be.

The directions that technology takes depend less on the curiosity that drives basic science than on the current needs and wants of people and on the social environment of the times. Debates about technology center more on "*should* we do it" than "*can* we do it." With advances in technology come difficult choices. For example, under what circumstances is it acceptable to use DNA technology to find out if particular people have genes for hereditary diseases? Should such tests always be voluntary, or are there circumstances when genetic testing should be mandatory? Should insurance companies or employers have access to the information, as they do for many other types of personal health data? These questions are becoming much more urgent as the sequencing of individual genomes becomes quicker and cheaper.

Ethical issues raised by such questions have as much to do with politics, economics, and cultural values as with science and technology. All citizens—not only professional scientists—have a responsibility to be informed about how science works and about the potential benefits and risks of technology. The relationship between science, technology, and society increases the significance and value of any biology course.

The Value of Diverse Viewpoints in Science

Many of the technological innovations with the most profound impact on human society originated in settlements along trade routes, where a rich mix of different cultures ignited new ideas. For example, the printing press, which helped spread knowledge to all social classes, was invented by the German Johannes Gutenberg around 1440. This invention relied on several innovations from China, including paper and ink. Paper traveled along trade routes from China to Baghdad, where technology was developed for its mass production. This technology then migrated to Europe, as did water-based ink from China, which was modified by Gutenberg to become oil-based ink. We have the cross-fertilization of diverse cultures to thank for the printing press, and the same can be said for other important inventions.

Along similar lines, science stands to gain much from embracing a diversity of backgrounds and viewpoints among its practitioners. But just how diverse a population are scientists in relation to gender, race, ethnicity, and other attributes?

The scientific community reflects the cultural standards and behaviors of the society around it. It is therefore not surprising that until recently, women and certain minorities have faced huge obstacles in their pursuit to become professional scientists in many countries around the world. Over the past 50 years, changing attitudes about career choices have increased the proportion of women in biology and some other sciences, so that now women constitute roughly half of undergraduate biology majors and biology Ph.D. students.

The pace has been slow at higher levels in the profession, however, and women and many racial and ethnic groups are still significantly underrepresented in many branches of science and technology. This lack of diversity hampers the progress of science. The more voices that are heard at the table, the more robust, valuable, and productive the scientific interchange will be. The authors of this text welcome all students to the community of biologists, wishing you the joys and satisfactions of this exciting field of science.

CONCEPT CHECK 1.4

1. How does science differ from technology?
2. **MAKE CONNECTIONS ➤** The gene that causes sickle-cell disease is present in a higher percentage of residents of sub-Saharan Africa than among those of African descent living in the United States. Even though this gene causes sickle-cell disease, it also provides some protection from malaria, a serious disease that is widespread in sub-Saharan Africa but absent in the United States. Discuss an evolutionary process that could account for the different percentages of the sickle-cell gene among residents of the two regions. (See Concept 1.2.)

For suggested answers, see Appendix A.

1 Chapter Review

Go to **MasteringBiology**™ for Videos, Animations, Vocab Self-Quiz, Practice Tests, and more in the Study Area.

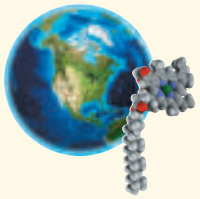
SUMMARY OF KEY CONCEPTS

CONCEPT 1.1

The study of life reveals unifying themes *(pp. 4–11)*

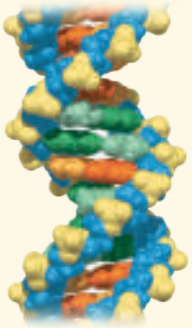
VOCAB SELF-QUIZ goo.gl/6u55ks

Organization Theme: New Properties Emerge at Successive Levels of Biological Organization



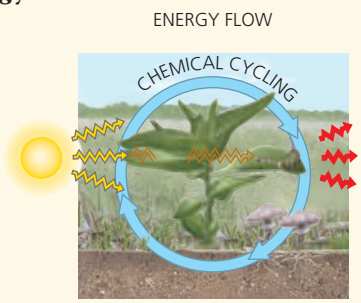
- The hierarchy of life unfolds as follows: biosphere > ecosystem > community > population > organism > organ system > organ > tissue > cell > organelle > molecule > atom. With each step upward from atoms, new **emergent properties** result from interactions among components at the lower levels. In an approach called reductionism, complex systems are broken down to simpler components that are more manageable to study. In **systems biology**, scientists attempt to model the dynamic behavior of whole biological systems by studying the interactions among the system's parts.
- Structure and function are correlated at all levels of biological organization. The cell, an organism's basic unit of structure and function, is the lowest level that can perform all activities required for life. Cells are either prokaryotic or eukaryotic. **Eukaryotic cells** contain membrane-enclosed organelles, including a DNA-containing nucleus. **Prokaryotic cells** lack such organelles.

Information Theme: Life's Processes Involve the Expression and Transmission of Genetic Information



- Genetic information is encoded in the nucleotide sequences of **DNA**. It is DNA that transmits heritable information from parents to offspring. DNA sequences (called **genes)** program a cell's protein production by being transcribed into mRNA and then translated into specific proteins, a process called **gene expression**. Gene expression also produces RNAs that are not translated into protein but serve other important functions. **Genomics** is the large-scale analysis of the DNA sequences of a species (its **genome**) as well as the comparison of genomes between species. **Bioinformatics** uses computational tools to deal with huge volumes of sequence data.

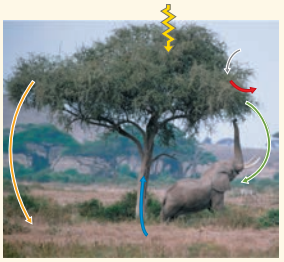
Energy and Matter Theme: Life Requires the Transfer and Transformation of Energy and Matter



- Energy flows through an ecosystem. All organisms must perform work, which requires energy. **Producers** convert energy from sunlight to chemical energy, some of which is then passed on to **consumers**. (The rest is lost from the ecosystem as heat.) Chemicals cycle between organisms and the environment.

Interactions Theme: From Molecules to Ecosystems, Interactions Are Important in Biological Systems

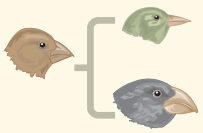
- In **feedback regulation,** a process is regulated by its output or end product. In negative feedback, accumulation of the end product slows its production. In positive feedback, an end product speeds up its own production.
- Organisms interact continuously with physical factors. Plants take up nutrients from the soil and chemicals from the air and use energy from the sun.



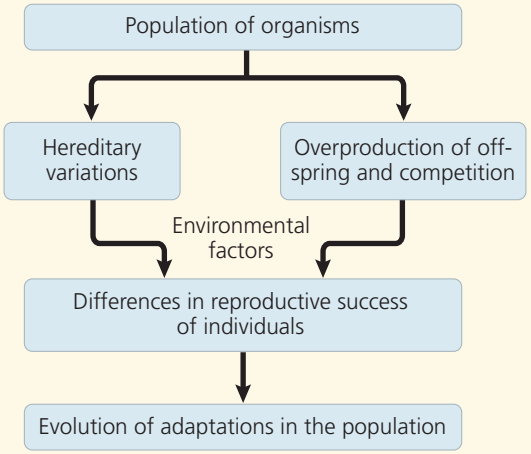
? *Thinking about the muscles and nerves in your hand, how does the activity of text messaging reflect the four themes of biology described in this section?*

CONCEPT 1.2

The Core Theme: Evolution accounts for the unity and diversity of life *(pp. 11–16)*



- **Evolution**, the process of change that has transformed life on Earth, accounts for the unity and diversity of life. It also explains evolutionary adaptation—the match of organisms to their environments.
- Biologists classify species according to a system of broader and broader groups. Domain **Bacteria** and domain **Archaea** consist of prokaryotes. Domain **Eukarya**, the eukaryotes, includes various groups of protists and the kingdoms Plantae, Fungi, and Animalia. As diverse as life is, there is also evidence of remarkable unity, revealed in the similarities between different species.
- Darwin proposed **natural selection** as the mechanism for evolutionary adaptation of populations to their environments. Natural selection is the evolutionary process that occurs when a population is exposed to environmental factors that consistently cause individuals with certain heritable traits to have greater reproductive success than do individuals with other heritable traits.



- Each species is one twig of a branching tree of life extending back in time through more and more remote ancestral species. All of life is connected through its long evolutionary history.

? *How could natural selection have led to the evolution of adaptations such as camouflaging coat color in beach mice?*

CONCEPT 1.3

In studying nature, scientists make observations and form and test hypotheses *(pp. 16–22)*

- In scientific **inquiry**, scientists make and record observations (collect **data**) and use **inductive reasoning** to draw a general conclusion, which can be developed into a testable **hypothesis.** **Deductive reasoning** makes predictions that can be used to

test hypotheses. Hypotheses must be testable; science can address neither the possibility of supernatural phenomena nor the validity of religious beliefs. Hypotheses can be tested by conducting **experiments** or, when that is not possible, by making observations. In the process of science, the core activity is testing ideas. This endeavor is influenced by exploration and discovery, community analysis and feedback, and societal outcomes.

- **Controlled experiments**, such as the investigation of coat color in mouse populations, are designed to demonstrate the effect of one **variable** by testing control groups and experimental groups that differ in only that one variable.
- A scientific **theory** is broad in scope, generates new hypotheses, and is supported by a large body of evidence.

? *What are the roles of gathering and interpreting data in the process of scientific inquiry?*

CONCEPT 1.4

Science benefits from a cooperative approach and diverse viewpoints *(pp. 22–24)*

- Science is a social activity. The work of each scientist builds on the work of others who have come before. Scientists must be able to repeat each other's results, and integrity is key. Biologists approach questions at different levels; their approaches complement each other.
- **Technology** consists of any method or device that applies scientific knowledge for some specific purpose that affects society. The impact of basic research is not always immediately obvious.
- Diversity among scientists promotes progress in science.

? *Explain why different approaches and diverse backgrounds among scientists are important.*

TEST YOUR UNDERSTANDING

Level 1: Knowledge/Comprehension

PRACTICE TEST
goo.gl/CUYGKD

1. All the organisms on your campus make up
   (A) an ecosystem.
   (B) a community.
   (C) a population.
   (D) a taxonomic domain.
2. Systems biology is mainly an attempt to
   (A) analyze genomes from different species.
   (B) simplify complex problems by reducing the system into smaller, less complex units.
   (C) understand the behavior of entire biological systems by studying interactions among its component parts.
   (D) build high-throughput machines for the rapid acquisition of biological data.
3. Which of the following best demonstrates the unity among all organisms?
   (A) emergent properties
   (B) descent with modification
   (C) the structure and function of DNA
   (D) natural selection
4. A controlled experiment is one that
   (A) proceeds slowly enough that a scientist can make careful records of the results.
   (B) tests experimental and control groups in parallel.
   (C) is repeated many times to make sure the results are accurate.
   (D) keeps all variables constant.
5. Which of the following statements best distinguishes hypotheses from theories in science?
   (A) Theories are hypotheses that have been proved.
   (B) Hypotheses are guesses; theories are correct answers.
   (C) Hypotheses usually are relatively narrow in scope; theories have broad explanatory power.
   (D) Theories are proved true; hypotheses are often contradicted by experimental results.

Level 2: Application/Analysis

6. Which of the following is an example of qualitative data?
   (A) The fish swam in a zigzag motion.
   (B) The contents of the stomach are mixed every 20 seconds.
   (C) The temperature decreased from 20°C to 15°C.
   (D) The six pairs of robins hatched an average of three chicks each.
7. Which sentence best describes the logic of scientific inquiry?
   (A) If I generate a testable hypothesis, tests and observations will support it.
   (B) If my prediction is correct, it will lead to a testable hypothesis.
   (C) If my observations are accurate, they will support my hypothesis.
   (D) If my hypothesis is correct, I can expect certain test results.
8. **DRAW IT** With rough sketches, draw a biological hierarchy similar to the one in Figure 1.3 but using a coral reef as the ecosystem, a fish as the organism, its stomach as the organ, and DNA as the molecule. Include all levels in the hierarchy.

Level 3: Synthesis/Evaluation

9. **EVOLUTION CONNECTION** A typical prokaryotic cell has about 3,000 genes in its DNA, while a human cell has almost 21,000 genes. About 1,000 of these genes are present in both types of cells. Based on your understanding of evolution, explain how such different organisms could have this same subset of 1,000 genes. What sorts of functions might these shared genes have?
10. **SCIENTIFIC INQUIRY** Based on the results of the mouse coloration case study, suggest another hypothesis researchers might use to further study the role of predators in the natural selection process.
11. **SCIENTIFIC INQUIRY** Scientists search the scientific literature by means of electronic databases such as PubMed, a free online database maintained by the National Center for Biotechnology Information. Use PubMed to find the abstract of a scientific article that Hopi Hoekstra published in 2015 or later.
12. **WRITE ABOUT A THEME: EVOLUTION** In a short essay (100–150 words), discuss Darwin's view of how natural selection resulted in both unity and diversity of life on Earth. Include in your discussion some of his evidence. (See a suggested grading rubric and tips for writing good essays in the Study Area of MasteringBiology under "Write About a Theme.")
13. **SYNTHESIZE YOUR KNOWLEDGE**

Can you pick out the mossy leaf-tailed gecko lying against the tree trunk in this photo? How is the appearance of the gecko a benefit in terms of survival? Given what you learned about evolution, natural selection, and genetic information in this chapter, describe how the gecko's coloration might have evolved.

For selected answers, see Appendix A.

MB For additional practice questions, check out the **Dynamic Study Modules** in MasteringBiology. You can use them to study on your smartphone, tablet, or computer anytime, anywhere!

Carbon and the Molecular Diversity of Life

4

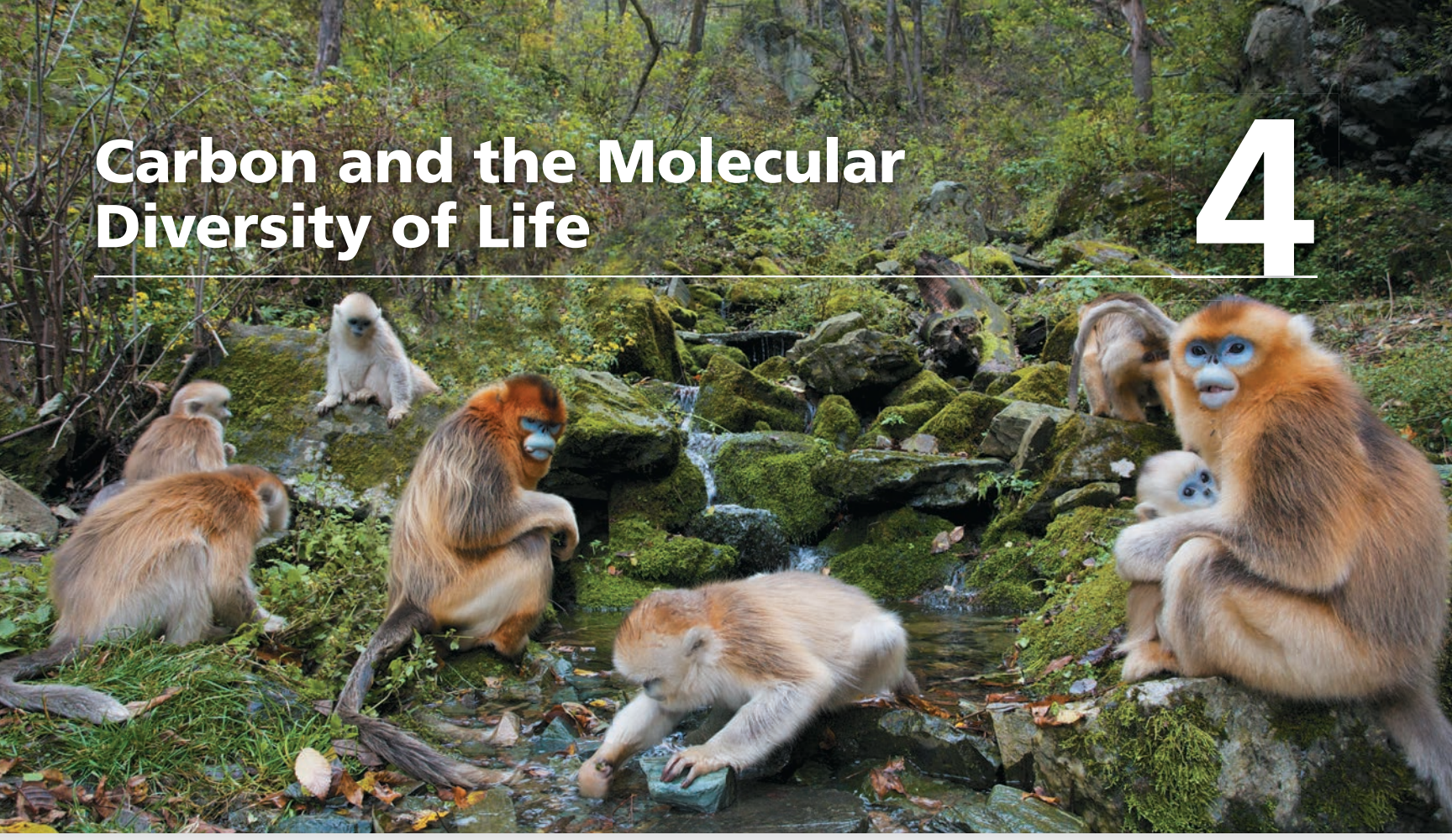
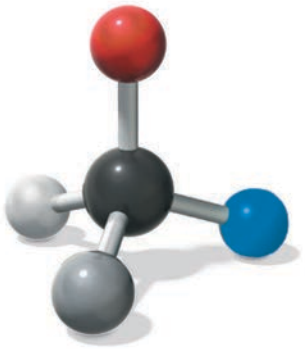


Figure 4.1 **What properties make carbon the basis of all life?**

KEY CONCEPTS



Carbon can bond to four other atoms or groups of atoms, making a large variety of molecules possible.

Carbon: The Backbone of Life

Living organisms, such as the plants and the Qinling golden snub-nosed monkeys shown in **Figure 4.1**, are made up of chemicals based mostly on the element carbon. Carbon enters the biosphere through the action of producers—plants and other photosynthetic organisms that use solar energy to transform atmospheric CO_2 into the carbon-based molecules of life. These molecules are then taken up by consumers, which feed on other organisms.

Of all the chemical elements, carbon is unparalleled in its ability to form molecules that are large, complex, and varied, making possible the diversity of organisms that have evolved on Earth. Proteins, DNA, carbohydrates, and other molecules that distinguish living matter from inanimate material are all composed of carbon atoms bonded to one another and to atoms of other elements. Hydrogen (H), oxygen (O), nitrogen (N), sulfur (S), and phosphorus (P) are other common ingredients of these compounds, but it is the element carbon (C) that accounts for the enormous variety of biological molecules.

Large biological molecules, such as proteins, are the main focus of Chapter 5. In this chapter, we investigate the properties of smaller molecules. We will use these small molecules to illustrate concepts of molecular architecture that help explain why carbon is so important to life, while highlighting the theme that emergent properties arise from the organization of matter in living organisms.

When you see this blue icon, log in to **MasteringBiology** and go to the Study Area for digital resources.

Get Ready for This Chapter

CONCEPT 4.1

Organic chemistry is the study of carbon compounds

For historical reasons, compounds containing carbon are said to be organic, and their study is called **organic chemistry**. By the early 1800s, chemists had learned to make simple compounds in the laboratory by combining elements under the right conditions. Artificial synthesis of the complex molecules extracted from living matter seemed impossible, however. Organic compounds were thought to arise only in living organisms, which were believed to contain a life force beyond the jurisdiction of physical and chemical laws.

Chemists began to chip away at this notion when they learned to synthesize organic compounds in the laboratory. In 1828, Friedrich Wöhler, a German chemist, tried to make an "inorganic" salt, ammonium cyanate, by mixing solutions of ammonium ions (NH_4^+) and cyanate ions (CNO^-). Wöhler was astonished to find that instead he had made urea, an organic compound present in the urine of animals.

The next few decades saw laboratory synthesis of increasingly complex organic compounds, supporting the view that physical and chemical laws govern the processes of life. Organic chemistry was redefined as the study of carbon compounds, regardless of origin. Organic compounds range from simple molecules, such as methane (CH_4), to colossal ones, such as proteins, with thousands of atoms.

Organic Molecules and the Origin of Life on Earth

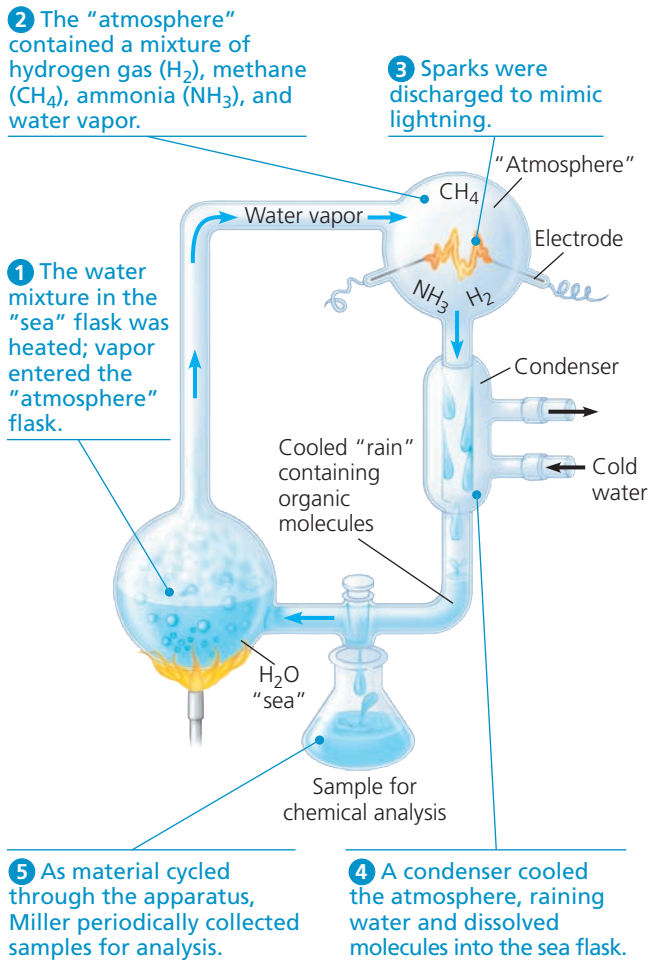
EVOLUTION In 1953, Stanley Miller, a graduate student of Harold Urey at the University of Chicago, helped bring the abiotic (nonliving) synthesis of organic compounds into the context of evolution. Study **Figure 4.2** to learn about his classic experiment. From his results, Miller concluded that complex organic molecules could arise spontaneously under conditions thought at that time to have existed on the early Earth. You can work with the data from a related experiment in the **Scientific Skills Exercise**. These experiments support the idea that abiotic synthesis of organic compounds, perhaps near volcanoes, could have been an early stage in the origin of life (see Figure 25.2).

The overall percentages of the major elements of life—C, H, O, N, S, and P—are quite uniform from one organism to another, reflecting the common evolutionary origin of all life. Because of carbon's ability to form four bonds, however, this limited assortment of atomic building blocks can be used to build an inexhaustible variety of organic molecules. Different species of organisms, and different individuals within a species, are distinguished by variations in the types of organic molecules they make. In a sense, the great diversity

Figure 4.2

Inquiry **Can organic molecules form under conditions estimated to simulate those on the early Earth?**

Experiment In 1953, Stanley Miller set up a closed system to mimic conditions thought at that time to have existed on the early Earth. A flask of water simulated the primeval sea. The water was heated so that some vaporized and moved into a second, higher flask containing the "atmosphere"—a mixture of gases. Sparks were discharged in the synthetic atmosphere to mimic lightning.



Results Miller identified a variety of organic molecules that are common in organisms. These included simple compounds, such as formaldehyde (CH_2O) and hydrogen cyanide (HCN), and more complex molecules, such as amino acids and long chains of carbon and hydrogen known as hydrocarbons.

Conclusion Organic molecules, a first step in the origin of life, may have been synthesized abiotically on the early Earth. Although new evidence indicates that the early Earth's atmosphere was different from the "atmosphere" used by Miller in this experiment, recent experiments using the revised list of chemicals also produced organic molecules. (We will explore this hypothesis in more detail in Concept 25.1.)

Data from S. L. Miller, A production of amino acids under possible primitive Earth conditions, *Science* 117:528–529 (1953).

WHAT IF ➤ *If Miller had increased the concentration of NH_3 in his experiment, how might the relative amounts of the products HCN and CH_2O have differed?*

Interview with Stanley Miller: Investigating the origin of life

SCIENTIFIC SKILLS EXERCISE

Working with Moles and Molar Ratios

Could the First Biological Molecules Have Formed Near Volcanoes on Early Earth? In 2007, Jeffrey Bada, a former graduate student of Stanley Miller, discovered some vials of samples that had never been analyzed from an experiment performed by Miller in 1958. In that experiment, Miller used hydrogen sulfide gas (H_2S) as one of the gases in the reactant mixture. Since H_2S is released by volcanoes, the H_2S experiment was designed to mimic conditions near volcanoes on early Earth. In 2011, Bada and colleagues published the results of their analysis of these "lost" samples. In this exercise, you will make calculations using the molar ratios of reactants and products from the H_2S experiment.

How the Experiment Was Done According to his laboratory notebook, Miller used the same apparatus as in his original experiment (see Figure 4.2), but the mixture of gaseous reactants included methane (CH_4), carbon dioxide (CO_2), hydrogen sulfide (H_2S), and ammonia (NH_3). After three days of simulated volcanic activity, he collected samples of the liquid, partially purified the chemicals, and sealed the samples in sterile vials. In 2011, Bada's research team used modern analytical methods to analyze the products in the vials for the presence of amino acids, the building blocks of proteins.

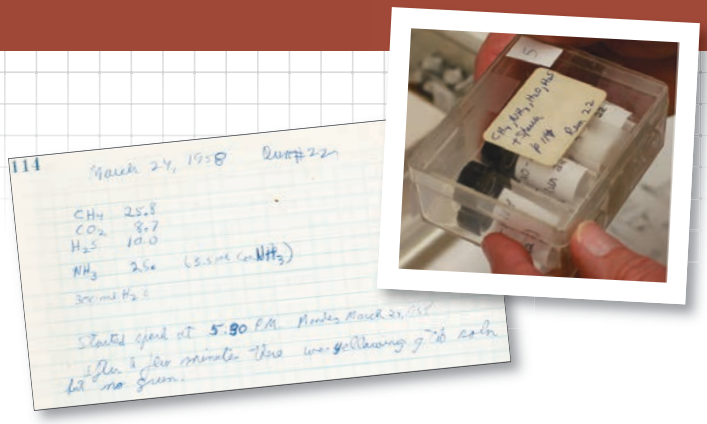
Data from the Experiment The table below shows 4 of the 23 amino acids detected in the 2011 analysis of the samples from Miller's 1958 H_2S experiment.

Product Compound	Molecular Formula	Molar Ratio (Relative to Glycine)
Glycine	$C_2H_5NO_2$	1.0
Serine	$C_3H_7NO_3$	3.0×10^{-2}
Methionine	$C_5H_{11}NO_2S$	1.8×10^{-3}
Alanine	$C_3H_7NO_2$	1.1

Data from E. T. Parker et al., Primordial synthesis of amines and amino acids in a 1958 Miller H_2S-rich spark discharge experiment, *Proceedings of the National Academy of Sciences USA* 108:5526-5531 (2011). www.pnas.org/cgi/doi/10.1073/pnas.1019191108.

INTERPRET THE DATA

1. A *mole* is the number of particles of a substance with a mass equivalent to its molecular (or atomic) mass in daltons. There are 6.02×10^{23} molecules (or atoms) in 1.0 mole (Avogadro's number; see Concept 3.2). The data table shows the "molar ratios" of some of the products from the Miller H_2S experiment. In a molar ratio, each unitless value is expressed relative to a standard for that experiment. Here, the standard is the number of moles of the amino acid glycine, which is set to a value of 1.0. For instance, serine has a molar ratio of 3.0×10^{-2}, meaning that for every mole of glycine, there is 3.0×10^{-2} mole of serine. (a) Give the molar ratio of methionine to glycine and explain what it means. (b) How many molecules of glycine are present in 1.0 mole? (c) For every 1.0 mole of glycine in the sample, how many molecules of methionine are present? (Recall that to multiply two numbers with exponents, you add their exponents; to divide them, you subtract the exponent in the denominator from that in the numerator.)
2. (a) Which amino acid is present in higher amounts than glycine? (b) How many more molecules of that amino acid are present than the number of molecules in 1.0 mole of glycine?
3. The synthesis of products is limited by the amount of reactants. (a) If one mole each of CH_4, NH_3, H_2S, and CO_2 is added to 1 liter of water (= 55.5 moles of H_2O) in a flask, how many moles of hydrogen, carbon, oxygen, nitrogen, and sulfur are in the flask? (b) Looking at the molecular formula in the table, how many moles of each element would be needed to make 1.0 mole of glycine? (c) What is the maximum number of moles of glycine that could be made in that flask, with the specified ingredients, if no other molecules were made? Explain. (d) If serine or methionine were made individually, which element(s) would be used up first for each? How much of each product could be made?
4. The earlier published experiment carried out by Miller did not include H_2S in the reactants (see Figure 4.2). Which of the compounds shown in the data table can be made in the H_2S experiment but could not be made in the earlier experiment?



▲ Some of Stanley Miller's notes from his 1958 hydrogen sulfide (H_2S) experiment along with his original vials.

Instructors: A version of this Scientific Skills Exercise can be assigned in MasteringBiology.

of living organisms we see on the planet (and in fossil remains) is made possible by the unique chemical versatility of the element carbon.

CONCEPT CHECK 4.1

1. Why was Wöhler astonished to find he had made urea?
2. **VISUAL SKILLS** ➤ See Figure 4.2. Miller carried out a control experiment without discharging sparks and found no organic compounds. What might explain this result?

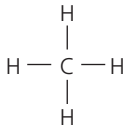
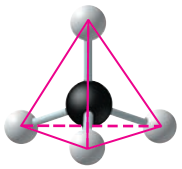
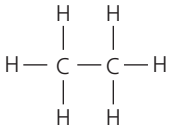
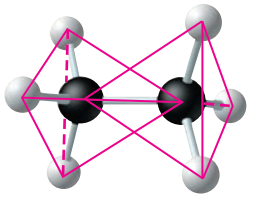
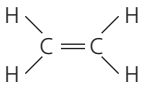
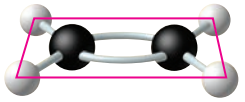
For suggested answers, see Appendix A.

CONCEPT 4.2

Carbon atoms can form diverse molecules by bonding to four other atoms

The key to an atom's chemical characteristics is its electron configuration. This configuration determines the kinds and number of bonds an atom will form with other atoms. Recall that it is the valence electrons, those in

Figure 4.3 The shapes of three simple organic molecules.

Molecule and Molecular Shape	Molecular Formula	Structural Formula	Ball-and-Stick Model (molecular shape in pink)	Space-Filling Model
(a) Methane. When a carbon atom has four single bonds to other atoms, the molecule is tetrahedral.	CH_4			
(b) Ethane. A molecule may have more than one tetrahedral group of single-bonded atoms. (Ethane consists of two such groups.)	C_2H_6			
(c) Ethene (ethylene). When two carbon atoms are joined by a double bond, all atoms attached to those carbons are in the same plane, and the molecule is flat.	C_2H_4			

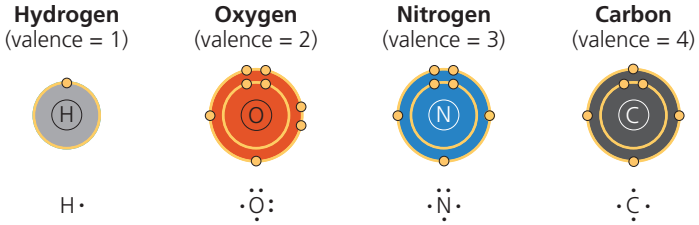
the outermost shell, that are available to form bonds with other atoms.

The Formation of Bonds with Carbon

Carbon has 6 electrons, with 2 in the first electron shell and 4 in the second shell; thus, it has 4 valence electrons in a shell that can hold up to 8 electrons. A carbon atom usually completes its valence shell by sharing its 4 electrons with other atoms so that 8 electrons are present. Each pair of shared electrons constitutes a covalent bond (see Figure 2.10d). In organic molecules, carbon usually forms single or double covalent bonds. Each carbon atom acts as an intersection point from which a molecule can branch off in as many as four directions. This enables carbon to form large, complex molecules.

When a carbon atom forms four single covalent bonds, the arrangement of its four hybrid orbitals causes the bonds to angle toward the corners of an imaginary tetrahedron. The bond angles in methane (CH_4) are 109.5° **(Figure 4.3a)**, and they are roughly the same in any group of atoms where carbon has four single bonds. For example, ethane (C_2H_6) is shaped like two overlapping tetrahedrons **(Figure 4.3b)**. In molecules with more carbons, every grouping of a carbon bonded to four other atoms has a tetrahedral shape. But when two carbon atoms are joined by a double bond, as in ethene (C_2H_4), the bonds from both carbons are all in the same plane, so the atoms joined to those carbons are in the same plane as well **(Figure 4.3c)**. We find it convenient to write molecules as structural formulas, as if the molecules being represented are two-dimensional,

Figure 4.4 Valences of the major elements of organic molecules. Valence, the number of covalent bonds an atom can form, is generally equal to the number of electrons required to complete the valence shell. All electrons are shown in the electron distribution diagrams (top), but only valence shell electrons are shown in the Lewis dot structures (bottom). Note that carbon can form four bonds.



MAKE CONNECTIONS ➤ *Draw the Lewis dot structures for sodium, phosphorus, sulfur, and chlorine. (Refer to Figure 2.7.)*

but keep in mind that molecules are three-dimensional and that the shape of a molecule is central to its function.

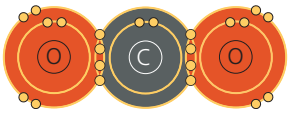
The number of unpaired electrons in the valence shell of an atom is generally equal to the atom's **valence**, the number of covalent bonds it can form. **Figure 4.4** shows the valences of carbon and its most frequent bonding partners—hydrogen, oxygen, and nitrogen. These are the four main atoms in organic molecules.

The electron configuration of carbon gives it covalent compatibility with many different elements. Let's consider how valence and the rules of covalent bonding apply to carbon atoms with partners other than hydrogen. We'll look at two examples, the simple molecules carbon dioxide and urea.

In the carbon dioxide molecule (CO_2), a single carbon atom is joined to two atoms of oxygen by double covalent bonds. The structural formula for CO_2 is shown here:

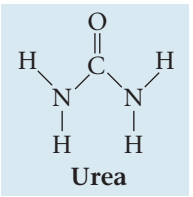
$$O{=}C{=}O$$

Each line in a structural formula represents a pair of shared electrons. Thus, the two double bonds in CO_2 have the same number of shared electrons as four single bonds. The arrangement completes the valence shells of all atoms in the molecule:



Because CO_2 is a very simple molecule and lacks hydrogen, it is often considered inorganic, even though it contains carbon. Whether we call CO_2 organic or inorganic, however, it is clearly important to the living world as the source of carbon, via photosynthetic organisms, for all organic molecules in organisms (see Concept 2.4).

Urea, $CO(NH_2)_2$, is the organic compound found in urine that Wöhler synthesized in the early 1800s. Again, each atom has the required number of covalent bonds. In this case, one carbon atom participates in both single and double bonds.



Urea

Urea and carbon dioxide are molecules with only one carbon atom. But as Figure 4.3 shows, a carbon atom can also use one or more valence electrons to form covalent bonds to other carbon atoms, each of which can also form four bonds. Thus, the atoms can be linked into chains of seemingly infinite variety.

Molecular Diversity Arising from Variation in Carbon Skeletons

Carbon chains form the skeletons of most organic molecules. The skeletons vary in length and may be straight, branched, or arranged in closed rings **(Figure 4.5)**. Some carbon skeletons have double bonds, which vary in number and location. Such variation in carbon skeletons is one important source of the molecular complexity and diversity that characterize living matter. In addition, atoms of other elements can be bonded to the skeletons at available sites.

Hydrocarbons

All of the molecules that are shown in Figures 4.3 and 4.5 are **hydrocarbons**, organic molecules consisting of only carbon and hydrogen. Atoms of hydrogen are attached to the carbon skeleton wherever electrons are available for covalent bonding. Hydrocarbons are the major components of petroleum, which is called a fossil fuel because it consists of the partially decomposed remains of organisms that lived millions of years ago.

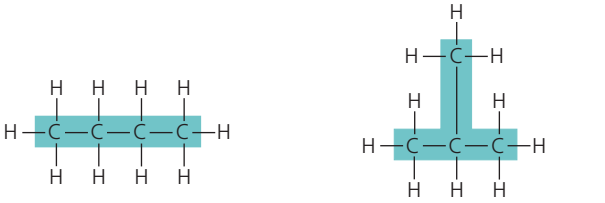
Figure 4.5 Four ways that carbon skeletons can vary.

(a) Length


Ethane Propane

Carbon skeletons vary in length.

(b) Branching


Butane 2-Methylpropane (commonly called isobutane)

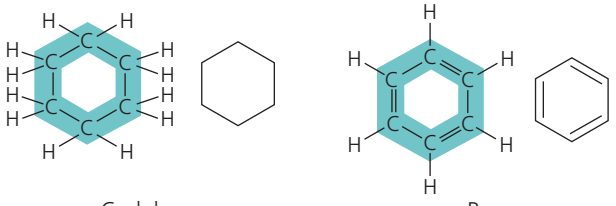
Skeletons may be unbranched or branched.

(c) Double bond position


1-Butene 2-Butene

The skeleton may have double bonds, which can vary in location.

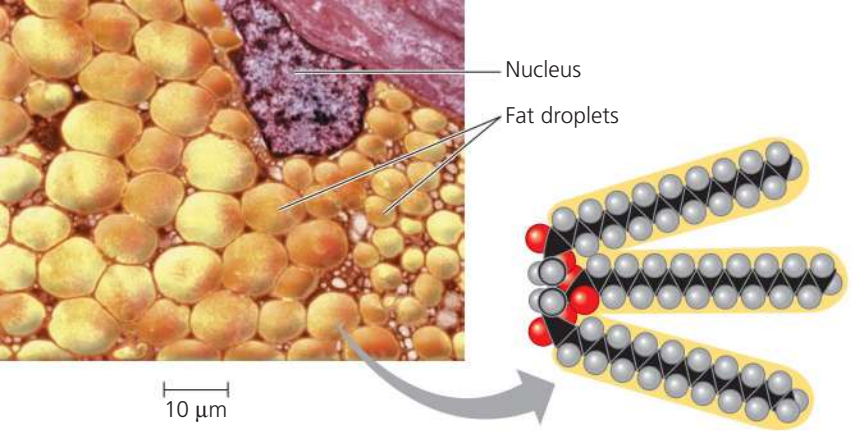
(d) Presence of rings


Cyclohexane Benzene

Some carbon skeletons are arranged in rings. In the abbreviated structural formula for each compound (to its right), each corner represents a carbon and its attached hydrogens.

Animation: Diversity of Carbon-Based Molecules

Although hydrocarbons are not prevalent in most living organisms, many of a cell's organic molecules have regions consisting of only carbon and hydrogen. For example, the molecules known as fats have long hydrocarbon tails attached to a nonhydrocarbon component **(Figure 4.6)**. Neither petroleum nor fat dissolves in water; both are hydrophobic compounds because the great majority of their bonds are relatively nonpolar carbon-to-hydrogen linkages. Another characteristic of hydrocarbons is that they can undergo reactions that release a relatively large amount of energy. The gasoline that fuels a car consists of hydrocarbons, and the hydrocarbon tails of fats serve as stored fuel for plant embryos (seeds) and animals.



(a) Part of a human adipose cell **(b) A fat molecule**

Figure 4.6 The role of hydrocarbons in fats.
(a) Mammalian adipose cells stockpile fat molecules as a fuel reserve. This colorized micrograph shows part of a human adipose cell with many fat droplets, each containing a large number of fat molecules. **(b)** A fat molecule consists of a small, nonhydrocarbon component joined to three hydrocarbon tails that account for the hydrophobic behavior of fats. The tails can be broken down to provide energy. (Black = carbon; gray = hydrogen; red = oxygen.)

MAKE CONNECTIONS ➤ *How do the tails account for the hydrophobic nature of fats? (See Concept 3.2.)*

Isomers

Variation in the architecture of organic molecules can be seen in **isomers**, compounds that have the same numbers of atoms of the same elements but different structures and hence different properties. We will examine three types of isomers: structural isomers, *cis-trans* isomers, and enantiomers.

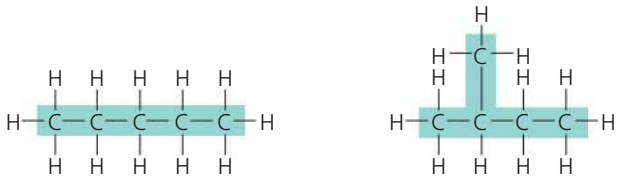
Structural isomers differ in the covalent arrangements of their atoms. Compare, for example, the two five-carbon compounds in **Figure 4.7a**. Both have the molecular formula C_5H_{12}, but they differ in the covalent arrangement of their carbon skeletons. The skeleton is straight in one compound but branched in the other. The number of possible isomers increases tremendously as carbon skeletons increase in size. There are only three forms of C_5H_{12} (two of which are shown in Figure 4.7a), but there are 18 variants of C_8H_{18} and 366,319 possible structural isomers of $C_{20}H_{42}$. Structural isomers may also differ in the location of double bonds.

In ***cis-trans* isomers**, carbons have covalent bonds to the same atoms, but these atoms differ in their spatial arrangements due to the inflexibility of double bonds. Single bonds allow the atoms they join to rotate freely about the bond axis without changing the compound. In contrast, double bonds do not permit such rotation. If a double bond joins two carbon atoms, and each C also has two different atoms (or groups of atoms) attached to it, then two distinct *cis-trans* isomers are possible. Consider a simple molecule with two double-bonded carbons, each of which has an H and an X attached to it **(Figure 4.7b)**. The arrangement with both Xs on the same side of the double bond is called a *cis isomer*, and that with the Xs on opposite sides is called a *trans isomer*. The subtle difference in shape between such isomers can have a dramatic effect on the biological activities of organic molecules. For example, the biochemistry of vision involves a light-induced change of retinal, a chemical compound in the eye, from the *cis* isomer to the *trans* isomer (see Figure 50.17). Another example involves *trans* fats, harmful fats formed during food processing that are discussed in Concept 5.3.

Enantiomers are isomers that are mirror images of each other and that differ in shape due to the presence of an *asymmetric carbon*, one that is attached to four different atoms or groups of atoms. (See the middle carbon in the ball-and-stick models shown in **Figure 4.7c**.) The four groups can

Figure 4.7 Three types of isomers. Isomers are compounds that have the same molecular formula but different structures.

(a) Structural isomers



Structural isomers differ in covalent partners, as shown in this example of two isomers of C_5H_{12}.

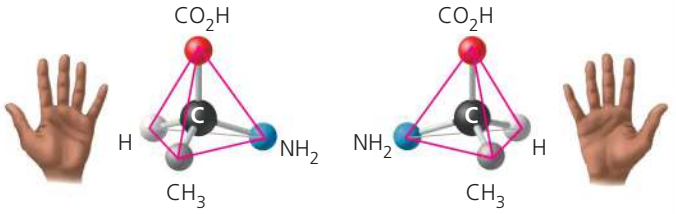
(b) *Cis-trans* isomers

cis isomer: The two Xs are on the same side.

trans isomer: The two Xs are on opposite sides.

Cis-trans isomers differ in arrangement about a double bond. In these diagrams, X represents an atom or group of atoms attached to a double-bonded carbon.

(c) Enantiomers

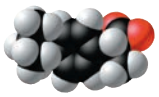
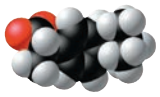
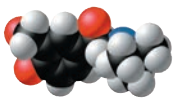
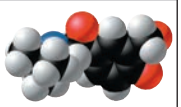


Enantiomers differ in spatial arrangement around an asymmetric carbon, resulting in molecules that are mirror images, like left and right hands. The two isomers here are designated the L and D isomers from the Latin for "left" and "right" (*levo* and *dextro*). Enantiomers cannot be superimposed on each other.

DRAW IT ➤ *There are three structural isomers of C_5H_{12}; draw the one not shown in (a).*

Animation: Isomers

Figure 4.8 The pharmacological importance of enantiomers. Ibuprofen and albuterol are drugs whose enantiomers have different effects. (*S* and *R* are used here to distinguish between enantiomers.) Ibuprofen is commonly sold as a mixture of the two enantiomers; the *S* enantiomer is 100 times more effective than the *R* form. Albuterol is synthesized and sold only as the *R* form of that particular drug; the *S* form counteracts the active *R* form.

Drug	Effects	Effective Enantiomer	Ineffective Enantiomer
Ibuprofen	Reduces inflammation and pain	 *S*-Ibuprofen	 *R*-Ibuprofen
Albuterol	Relaxes bronchial (airway) muscles, improving airflow in asthma patients	 *R*-Albuterol	 *S*-Albuterol

be arranged in space around the asymmetric carbon in two different ways that are mirror images. Enantiomers are, in a way, left-handed and right-handed versions of the molecule. Just as your right hand won't fit into a left-handed glove, a "right-handed" molecule won't fit into the same space as the "left-handed" version. Usually, only one isomer is biologically active because only that form can bind to specific molecules in an organism.

The concept of enantiomers is important in the pharmaceutical industry because the two enantiomers of a drug may not be equally effective, as is the case for both ibuprofen and the asthma medication albuterol **(Figure 4.8)**. Methamphetamine also occurs in two enantiomers that have very different effects. One enantiomer is the highly addictive stimulant drug known as "crank," sold illegally in the street drug trade. The other has a much weaker effect and is the active ingredient in an over-the-counter vapor inhaler for treatment of nasal congestion. The differing effects of enantiomers in the body demonstrate that organisms are sensitive to even the subtlest variations in molecular architecture. Once again, we see that molecules have emergent properties that depend on the specific arrangement of their atoms.

CONCEPT CHECK 4.2

1. **DRAW IT** ➤ (a) Draw a structural formula for C_2H_4. (b) Draw the *trans* isomer of $C_2H_2Cl_2$.
2. **VISUAL SKILLS** ➤ Which two pairs of molecules in Figure 4.5 are isomers? For each pair, identify the type of isomer.
3. How are gasoline and fat chemically similar?
4. **VISUAL SKILLS** ➤ See Figures 4.5a and 4.7. Can propane (C_3H_8) form isomers? Explain.

For suggested answers, see Appendix A.

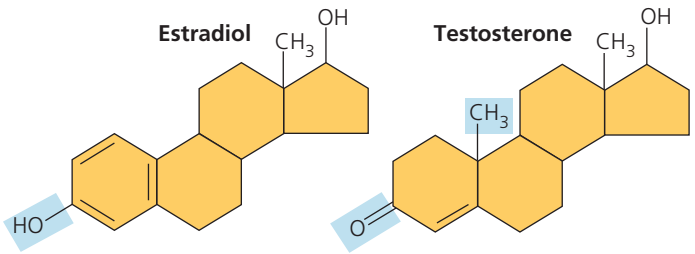
CONCEPT 4.3

A few chemical groups are key to molecular function

The properties of an organic molecule depend not only on the arrangement of its carbon skeleton but also on the various chemical groups attached to that skeleton. We can think of hydrocarbons, the simplest organic molecules, as the underlying framework for more complex organic molecules. A number of chemical groups can replace one or more hydrogens of the hydrocarbon. These groups may participate in chemical reactions or may contribute to function indirectly by their effects on molecular shape; they help give each molecule its unique properties.

The Chemical Groups Most Important in the Processes of Life

Consider the differences between estradiol (a type of estrogen) and testosterone. These compounds are female and male sex hormones, respectively, in humans and other vertebrates. Both are steroids, organic molecules with a common carbon skeleton in the form of four fused rings. They differ only in the chemical groups attached to the rings (shown here in abbreviated form); the distinctions in molecular architecture are shaded in blue:

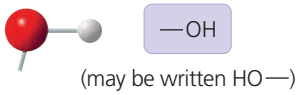
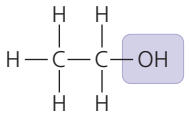
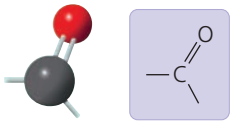
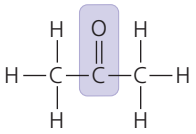
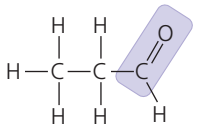
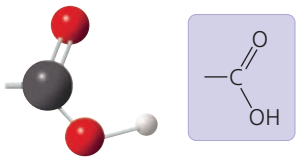
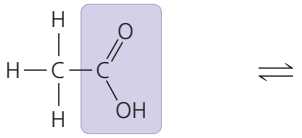
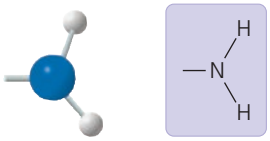
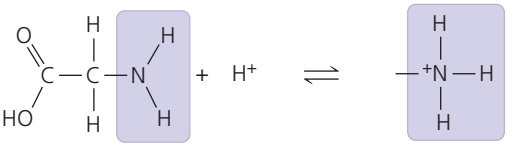
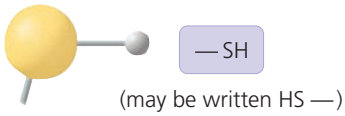
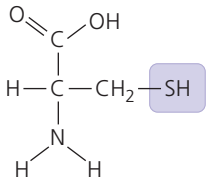
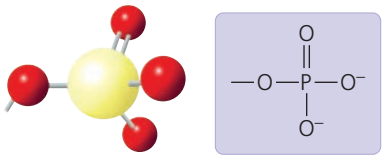
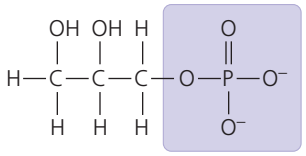
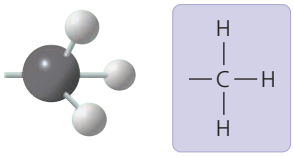
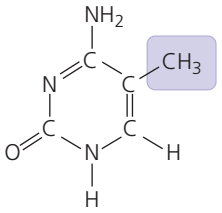


The different actions of these two molecules on many targets throughout the body are the basis of gender, producing the contrasting features of male and female vertebrates. In this case, the chemical groups are important because they affect molecular shape, contributing to function.

In other cases, chemical groups are directly involved in chemical reactions; such groups are known as **functional groups**. Each has certain properties, such as shape and charge, that cause it to participate in chemical reactions in a characteristic way.

The seven chemical groups most important in biological processes are the hydroxyl, carbonyl, carboxyl, amino, sulfhydryl, phosphate, and methyl groups. The first six groups can be chemically reactive; of these six, all except the sulfhydryl group are also hydrophilic and thus increase the solubility of organic compounds in water. The methyl group is not reactive, but instead often serves as a recognizable tag on biological molecules. Study **Figure 4.9** to become familiar with these biologically important chemical groups.

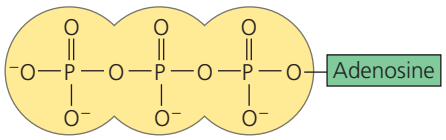
Figure 4.9 Some biologically important chemical groups.

Chemical Group	Group Properties and Compound Name	Examples
Hydroxyl group (—OH)  (may be written HO—)	Is polar due to electronegative oxygen. Forms hydrogen bonds with water, helping dissolve compounds such as sugars. Compound name: **Alcohol** (specific name usually ends in *-ol*)	 **Ethanol**, the alcohol present in alcoholic beverages
Carbonyl group (>C=O) 	Sugars with ketone groups are called ketoses; those with aldehydes are called aldoses. Compound name: **Ketone** (carbonyl group is within a carbon skeleton) or **aldehyde** (carbonyl group is at the end of a carbon skeleton)	 **Acetone**, the simplest ketone  **Propanal**, an aldehyde
Carboxyl group (—COOH) 	Acts as an acid (can donate H^+) because the covalent bond between oxygen and hydrogen is so polar. Compound name: **Carboxylic acid**, or **organic acid**	 **Acetic acid**, which gives vinegar its sour taste Ionized form of —COOH (carboxylate ion), found in cells
Amino group (—NH_2) 	Acts as a base; can pick up an H^+ from the surrounding solution (water, in living organisms). Compound name: **Amine**	 **Glycine**, an amino acid (note its carboxyl group) Ionized form of —NH_2, found in cells
Sulfhydryl group (—SH)  (may be written HS —)	Two —SH groups can react, forming a "cross-link" that helps stabilize protein structure. Hair protein cross-links maintain the straightness or curliness of hair; in hair salons, permanent treatments break cross-links, then re-form them while the hair is in the desired shape. Compound name: **Thiol**	 **Cysteine**, a sulfur-containing amino acid
Phosphate group (—OPO_3^{2-}) 	Contributes negative charge (1– when positioned inside a chain of phosphates; 2– when at the end). When attached, confers on a molecule the ability to react with water, releasing energy. Compound name: **Organic phosphate**	 **Glycerol phosphate**, which takes part in many important chemical reactions in cells
Methyl group (—CH_3) 	Affects the expression of genes when on DNA or on proteins bound to DNA. Affects the shape and function of male and female sex hormones. Compound name: **Methylated compound**	 **5-Methylcytosine**, a component of DNA that has been modified by addition of a methyl group

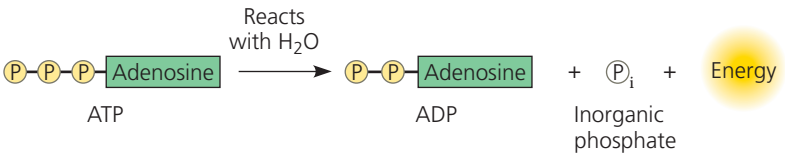
Animation: Functional Groups

ATP: An Important Source of Energy for Cellular Processes

The "Phosphate group" row in Figure 4.9 shows a simple example of an organic phosphate molecule. A more complicated organic phosphate, **adenosine triphosphate,** or **ATP**, is worth mentioning here because its function in the cell is so important. ATP consists of an organic molecule called adenosine attached to a string of three phosphate groups:



Where three phosphates are present in series, as in ATP, one phosphate may be split off as a result of a reaction with water. This inorganic phosphate ion, $HOPO_3^{2-}$, is often abbreviated $\textcircled{P}_i$ in this book, and a phosphate group in an organic molecule is often written as $\textcircled{P}$. Having lost one phosphate, ATP becomes adenosine *di*phosphate, or ADP. Although ATP is sometimes said to store energy, it is more accurate to think of it as storing the potential to react with water. This reaction releases energy that can be used by the cell. You will learn about this in more detail in Concept 8.3.



The Chemical Elements of Life: *A Review*

Living matter, as you have learned, consists mainly of carbon, oxygen, hydrogen, and nitrogen, with smaller amounts of sulfur and phosphorus. These elements all form strong covalent bonds, an essential characteristic in the architecture of complex organic molecules. Of all these elements, carbon is the virtuoso of the covalent bond. The versatility of carbon makes possible the great diversity of organic molecules, each with particular properties that emerge from the unique arrangement of its carbon skeleton and the chemical groups appended to that skeleton. This variation at the molecular level provides the foundation for the rich biological diversity found on our planet.

CONCEPT CHECK 4.3

1. **VISUAL SKILLS ➤** What does the term *amino acid* signify about the structure of such a molecule? See Figure 4.9.
2. What chemical change occurs to ATP when it reacts with water and releases energy?
3. **DRAW IT ➤** Suppose you had an organic molecule such as cysteine (see Figure 4.9, sulfhydryl group example), and you chemically removed the $—NH_2$ group and replaced it with —COOH. Draw this structure. How would this change the chemical properties of the molecule? Is the central carbon asymmetric before the change? After?

For suggested answers, see Appendix A.

4 Chapter Review

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SUMMARY OF KEY CONCEPTS

CONCEPT 4.1

Organic chemistry is the study of carbon compounds *(pp. 57–58)*

VOCAB SELF-QUIZ goo.gl/6u55ks

- **Organic** compounds, once thought to arise only within living organisms, were finally synthesized in the laboratory.
- Living matter is made mostly of carbon, oxygen, hydrogen, and nitrogen. Biological diversity results from carbon's ability to form a huge number of molecules with particular shapes and properties.

? *How did Stanley Miller's experiments support the idea that, even at life's origins, physical and chemical laws govern the processes of life?*

CONCEPT 4.2

Carbon atoms can form diverse molecules by bonding to four other atoms *(pp. 58–62)*

- Carbon, with a valence of 4, can bond to various other atoms, including O, H, and N. Carbon can also bond to other carbon atoms, forming the carbon skeletons of organic compounds. These skeletons vary in length and shape and have bonding sites for atoms of other elements.
- **Hydrocarbons** consist of carbon and hydrogen.
- **Isomers** are compounds that have the same molecular formula but different structures and therefore different properties. Three types of isomers are **structural isomers, *cis-trans* isomers**, and **enantiomers**.

VISUAL SKILLS ➤ *Refer back to Figure 4.9. What type of isomers are acetone and propanal? How many asymmetric carbons are present in acetic acid, glycine, and glycerol phosphate? Can these three molecules exist as forms that are enantiomers?*

CONCEPT 4.3

A few chemical groups are key to molecular function *(pp. 62–64)*

- Chemical groups attached to the carbon skeletons of organic molecules participate in chemical reactions (**functional groups**) or contribute to function by affecting molecular shape (see Figure 4.9).
- **ATP (adenosine triphosphate)** consists of adenosine attached to three phosphate groups. ATP can react with water, forming

The Structure and Function of Large Biological Molecules

5

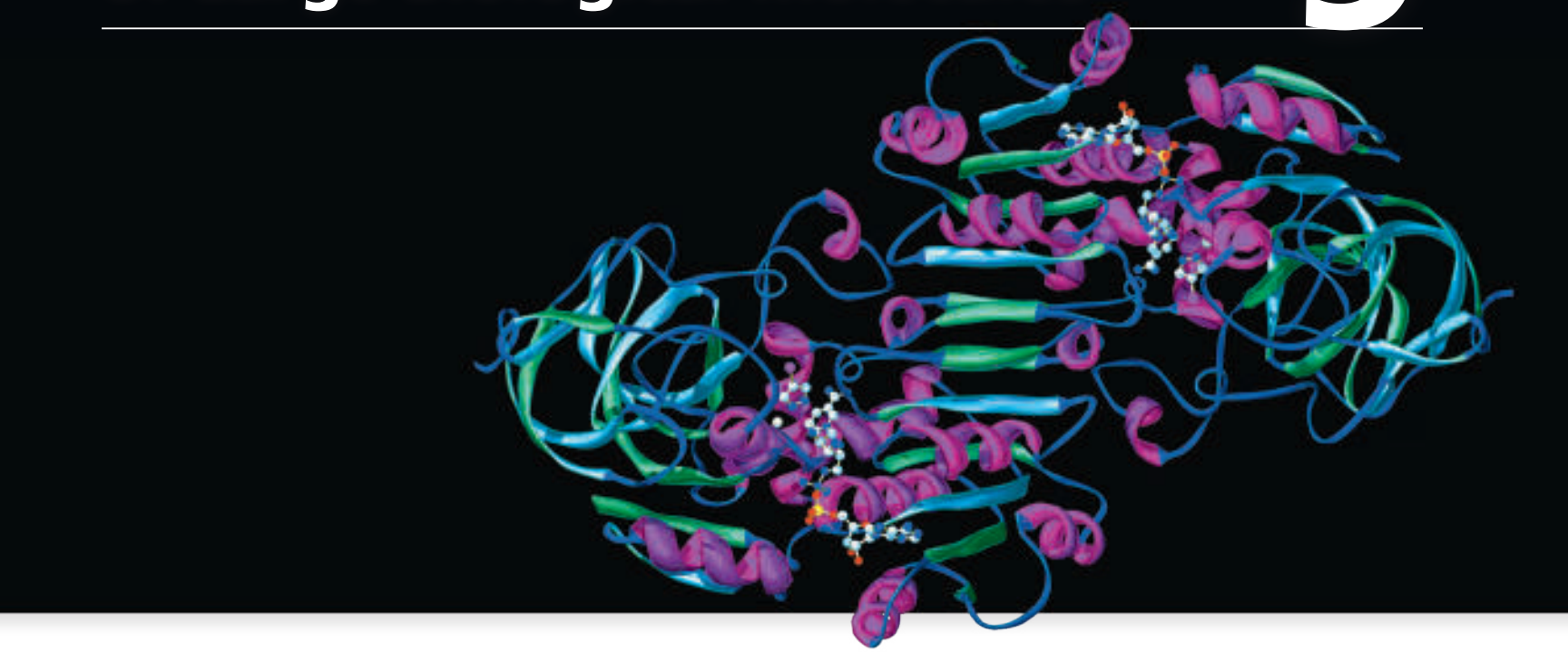


Figure 5.1 **Why is the structure of a protein important for its function?**

KEY CONCEPTS

The Molecules of Life

Given the rich complexity of life on Earth, it might surprise you that the most important large molecules found in all living things—from bacteria to elephants—can be sorted into just four main classes: carbohydrates, lipids, proteins, and nucleic acids. On the molecular scale, members of three of these classes—carbohydrates, proteins, and nucleic acids—are huge and are therefore called **macromolecules**. For example, a protein may consist of thousands of atoms that form a molecular colossus with a mass well over 100,000 daltons. Considering the size and complexity of macromolecules, it is noteworthy that biochemists have determined the detailed structure of so many of them. The image in **Figure 5.1** is a molecular model of a protein called alcohol dehydrogenase, which breaks down alcohol in the body.

The architecture of a large biological molecule plays an essential role in its function. Like water and simple organic molecules, large biological molecules exhibit unique emergent properties arising from the orderly arrangement of their atoms. In this chapter, we'll first consider how macromolecules are built. Then we'll examine the structure and function of all four classes of large biological molecules: carbohydrates, lipids, proteins, and nucleic acids.

The scientist in the foreground is using 3-D glasses to help her visualize the structure of the protein displayed on her screen.

When you see this blue icon, log in to **MasteringBiology** and go to the Study Area for digital resources.

Get Ready for This Chapter

CONCEPT 5.1

Macromolecules are polymers, built from monomers

Large carbohydrates, proteins, and nucleic acids are chain-like molecules called polymers (from the Greek *polys*, many, and *meros*, part). A **polymer** is a long molecule consisting of many similar or identical building blocks linked by covalent bonds, much as a train consists of a chain of cars. The repeating units that serve as the building blocks of a polymer are smaller molecules called **monomers** (from the Greek *monos*, single). In addition to forming polymers, some monomers have functions of their own.

The Synthesis and Breakdown of Polymers

Although each class of polymer is made up of a different type of monomer, the chemical mechanisms by which cells make and break down polymers are basically the same in all cases. In cells, these processes are facilitated by **enzymes**, specialized macromolecules that speed up chemical reactions. The reaction connecting monomers is a good example of a **dehydration reaction**, a reaction in which two molecules are covalently bonded to each other with the loss of a water molecule **(Figure 5.2a)**. When a bond forms between two monomers, each monomer contributes part of the water molecule that is released during the reaction: One monomer provides a hydroxyl group (—OH), while the other provides a hydrogen (—H). This reaction is repeated as monomers are added to the chain one by one, making a polymer (also called polymerization).

Polymers are disassembled to monomers by **hydrolysis**, a process that is essentially the reverse of the dehydration reaction **(Figure 5.2b)**. Hydrolysis means water breakage (from the Greek *hydro*, water, and *lysis*, break). The bond between monomers is broken by the addition of a water molecule, with a hydrogen from water attaching to one monomer and the hydroxyl group attaching to the other. An example of hydrolysis within our bodies is the process of digestion. The bulk of the organic material in our food is in the form of polymers that are much too large to enter our cells. Within the digestive tract, various enzymes attack the polymers, speeding up hydrolysis. Released monomers are then absorbed into the bloodstream for distribution to all body cells. Those cells can then use dehydration reactions to assemble the monomers into new, different polymers that can perform specific functions required by the cell. (Dehydration reactions and hydrolysis can also be involved in the formation and breakdown of molecules that are not polymers, such as some lipids.)

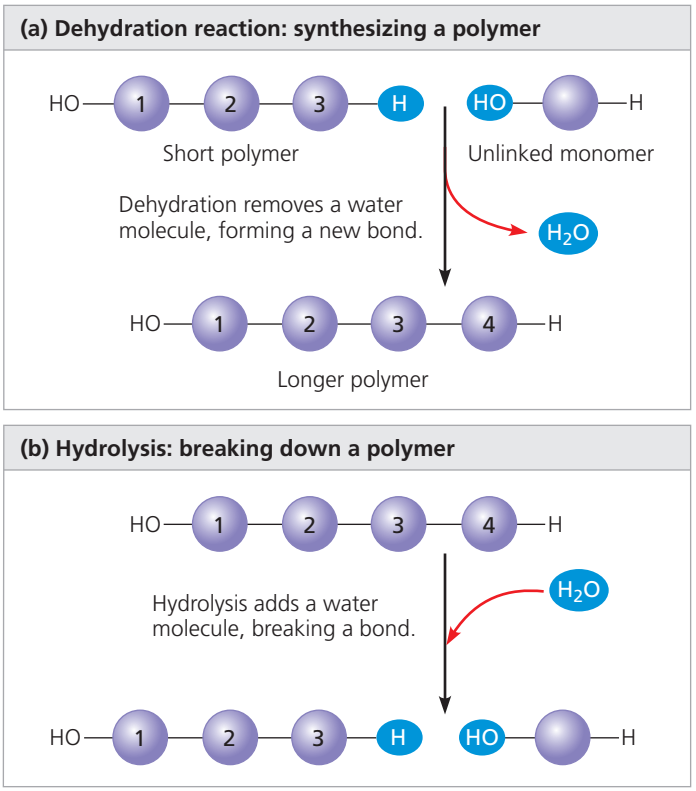
The Diversity of Polymers

A cell has thousands of different macromolecules; the collection varies from one type of cell to another. The inherited differences between close relatives, such as human siblings, reflect small variations in polymers, particularly DNA and proteins. Molecular differences between unrelated individuals are more extensive, and those between species greater still. The diversity of macromolecules in the living world is vast, and the possible variety is effectively limitless.

What is the basis for such diversity in life's polymers? These molecules are constructed from only 40 to 50 common monomers and some others that occur rarely. Building a huge variety of polymers from such a limited number of monomers is analogous to constructing hundreds of thousands of words from only 26 letters of the alphabet. The key is arrangement—the particular linear sequence that the units follow. However, this analogy falls far short of describing the great diversity of macromolecules because most biological polymers have many more monomers than the number of letters in even the longest word. Proteins, for example, are built from 20 kinds of amino acids arranged in chains that are typically hundreds of amino acids long. The molecular logic of life is simple but elegant: Small molecules common to all organisms act as building blocks that are ordered into unique macromolecules.

Despite this immense diversity, molecular structure and function can still be grouped roughly by class. Let's examine each of the four major classes of large biological molecules. For each class, the large molecules have emergent properties not found in their individual components.

Figure 5.2 The synthesis and breakdown of polymers.



Animation: Making and Breaking Polymers

CONCEPT CHECK 5.1

1. What are the four main classes of large biological molecules? Which class does not consist of polymers?
2. How many molecules of water are needed to completely hydrolyze a polymer that is ten monomers long?
3. **WHAT IF? ➤** If you eat a piece of fish, what reactions must occur for the amino acid monomers in the protein of the fish to be converted to new proteins in your body?

For suggested answers, see Appendix A.

CONCEPT 5.2

Carbohydrates serve as fuel and building material

Carbohydrates include sugars and polymers of sugars. The simplest carbohydrates are the monosaccharides, or simple sugars; these are the monomers from which more complex carbohydrates are built. Disaccharides are double sugars, consisting of two monosaccharides joined by a covalent bond. Carbohydrate macromolecules are polymers called polysaccharides, composed of many sugar building blocks.

Animation: Carbohydrates

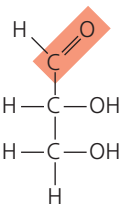
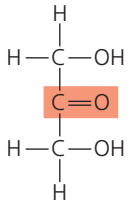
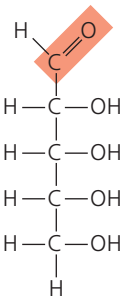
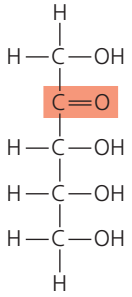
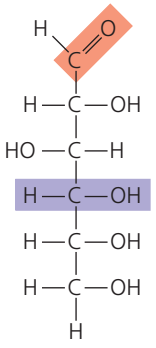
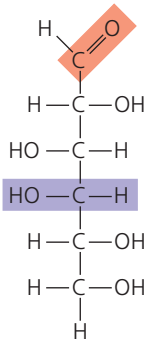
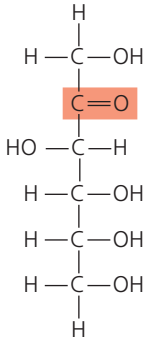
Sugars

Monosaccharides (from the Greek *monos*, single, and *sacchar*, sugar) generally have molecular formulas that are some multiple of the unit CH_2O. Glucose ($C_6H_{12}O_6$), the most common monosaccharide, is of central importance in the chemistry of life. In the structure of glucose, we can see the trademarks of a sugar: The molecule has a carbonyl group, $\diagdown C{=}O$, and multiple hydroxyl groups, —OH **(Figure 5.3)**. Depending on the location of the carbonyl group, a sugar is either an aldose (aldehyde sugar) or a ketose (ketone sugar). Glucose, for example, is an aldose; fructose, an isomer of glucose, is a ketose. (Most names for sugars end in *-ose*.) Another criterion for classifying sugars is the size of the carbon skeleton, which ranges from three to seven carbons long. Glucose, fructose, and other sugars that have six carbons are called hexoses. Trioses (three-carbon sugars) and pentoses (five-carbon sugars) are also common.

Still another source of diversity for simple sugars is in the way their parts are arranged spatially around asymmetric carbons. (Recall that an asymmetric carbon is a carbon attached to four different atoms or groups of atoms.) Glucose and galactose, for example, differ only in the placement of parts around one asymmetric carbon (see the purple boxes in Figure 5.3). What seems like a small difference is significant enough to give the two sugars distinctive shapes and binding activities, thus different behaviors.

Although it is convenient to draw glucose with a linear carbon skeleton, this representation is not completely accurate. In aqueous solutions, glucose molecules, as well as most other

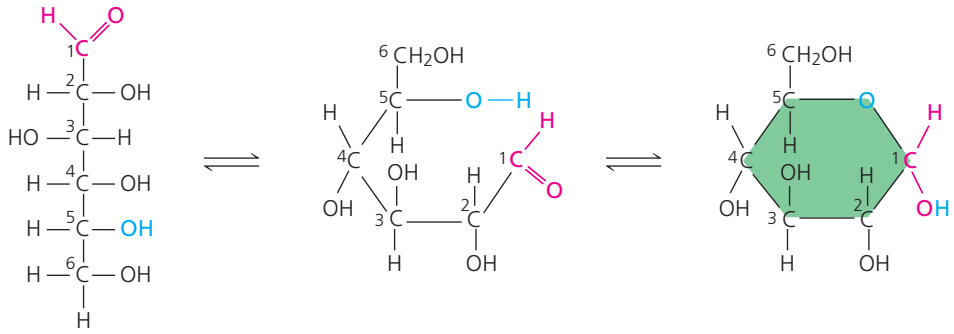
Figure 5.3 The structure and classification of some monosaccharides. Sugars vary in the location of their carbonyl groups (orange), the length of their carbon skeletons, and the way their parts are arranged spatially around asymmetric carbons (compare, for example, the purple portions of glucose and galactose).

Aldoses (Aldehyde Sugars) Carbonyl group at end of carbon skeleton	**Ketoses (Ketone Sugars)** Carbonyl group within carbon skeleton
Trioses: three-carbon sugars ($C_3H_6O_3$)	
 **Glyceraldehyde** An initial breakdown product of glucose	 **Dihydroxyacetone** An initial breakdown product of glucose
Pentoses: five-carbon sugars ($C_5H_{10}O_5$)	
 **Ribose** A component of RNA	 **Ribulose** An intermediate in photosynthesis
Hexoses: six-carbon sugars ($C_6H_{12}O_6$)	
 **Glucose**  **Galactose** Energy sources for organisms	 **Fructose** An energy source for organisms

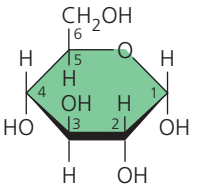
MAKE CONNECTIONS ➤ *In the 1970s, a process was developed that converts the glucose in corn syrup to its sweeter-tasting isomer, fructose. High-fructose corn syrup, a common ingredient in soft drinks and processed food, is a mixture of glucose and fructose. What type of isomers are glucose and fructose? (See Figure 4.7.)*

Animation: Monosaccharides

Figure 5.4 Linear and ring forms of glucose.



(a) Linear and ring forms. Chemical equilibrium between the linear and ring structures greatly favors the formation of rings. The carbons of the sugar are numbered 1 to 6, as shown. To form the glucose ring, carbon 1 (magenta) bonds to the oxygen (blue) attached to carbon 5.



(b) Abbreviated ring structure. Each unlabeled corner represents a carbon. The ring's thicker edge indicates that you are looking at the ring edge-on; the components attached to the ring lie above or below the plane of the ring.

DRAW IT ➤ *Start with the linear form of fructose (see Figure 5.3) and draw the formation of the fructose ring in two steps, as shown in (a). First, number the carbons starting at the top of the linear structure. Then draw the molecule in a ringlike orientation, attaching carbon 5 via its oxygen to carbon 2. Compare the number of carbons in the fructose and glucose rings.*

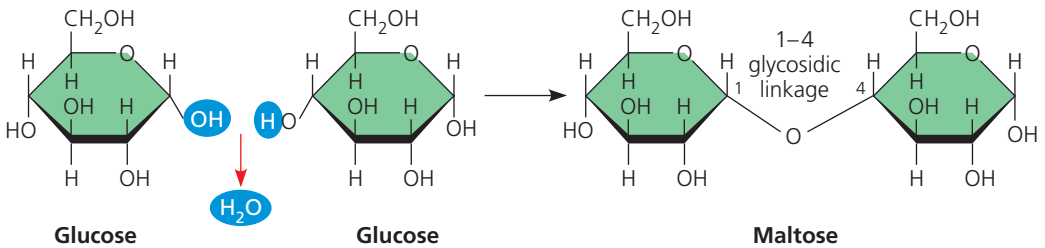
five- and six-carbon sugars, form rings, because they are the most stable form of these sugars under physiological conditions **(Figure 5.4)**.

Monosaccharides, particularly glucose, are major nutrients for cells. In the process known as cellular respiration, cells extract energy from glucose molecules by breaking them down in a series of reactions. Not only are simple-sugar molecules a major fuel for cellular work, but their carbon skeletons also serve as raw material for the synthesis of other types of small organic molecules, such as amino acids and fatty acids. Sugar molecules that are not immediately used in these ways are generally incorporated as monomers into disaccharides or polysaccharides, discussed next.

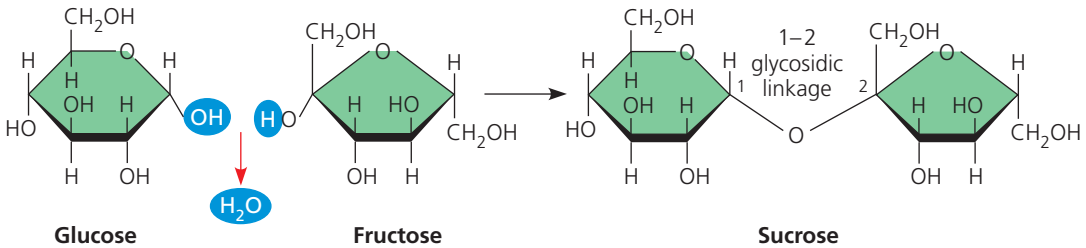
A **disaccharide** consists of two monosaccharides joined by a **glycosidic linkage**, a covalent bond formed between two monosaccharides by a dehydration reaction (*glyco* refers to carbohydrate). For example, maltose is a disaccharide formed by the linking of two molecules of glucose **(Figure 5.5a)**. Also known as malt sugar, maltose is an ingredient used in brewing beer. The most prevalent disaccharide is sucrose, or table sugar. Its two monomers are glucose and fructose **(Figure 5.5b)**. Plants generally transport carbohydrates from leaves to roots

Figure 5.5 Examples of disaccharide synthesis.

(a) Dehydration reaction in the synthesis of maltose. The bonding of two glucose units forms maltose. The 1–4 glycosidic linkage joins the number 1 carbon of one glucose to the number 4 carbon of the second glucose. Joining the glucose monomers in a different way would result in a different disaccharide.



(b) Dehydration reaction in the synthesis of sucrose. Sucrose is a disaccharide formed from glucose and fructose. Notice that fructose forms a five-sided ring, though it is a hexose like glucose.



DRAW IT ➤ *Referring to Figures 5.3 and 5.4, number the carbons in each sugar in this figure. How does the name of each linkage relate to the numbers?*

Animation: Synthesis of Sucrose

and other nonphotosynthetic organs in the form of sucrose. Lactose, the sugar present in milk, is another disaccharide, in this case a glucose molecule joined to a galactose molecule. Disaccharides must be broken down into monosaccharides to be used for energy by organisms. Lactose intolerance is a common condition in humans who lack lactase, the enzyme that breaks down lactose. The sugar is instead broken down by intestinal bacteria, causing formation of gas and subsequent cramping. The problem may be avoided by taking the enzyme lactase when eating or drinking dairy products or consuming dairy products that have already been treated with lactase to break down the lactose.

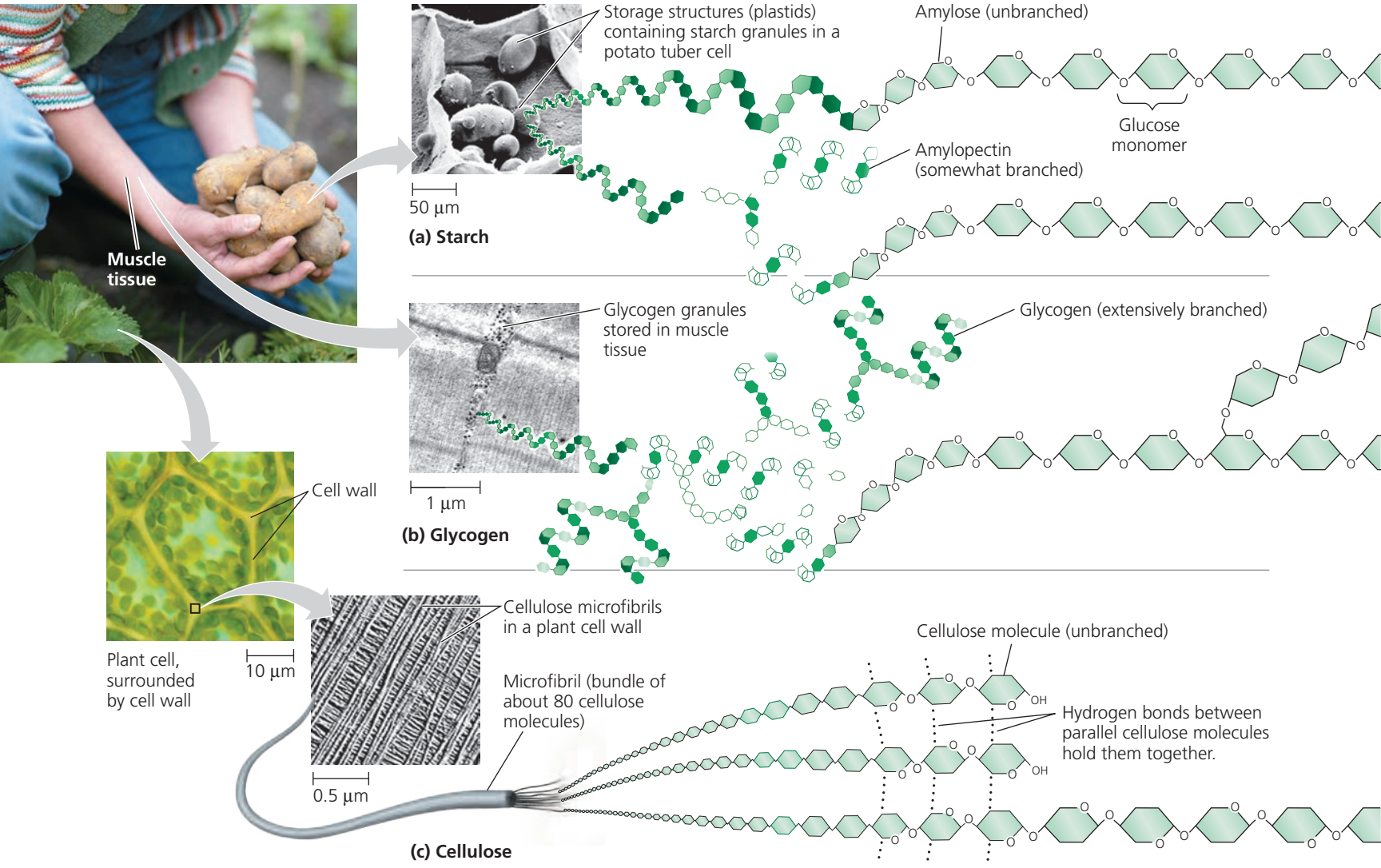
Polysaccharides

Polysaccharides are macromolecules, polymers with a few hundred to a few thousand monosaccharides joined by glycosidic linkages. Some polysaccharides serve as storage material, hydrolyzed as needed to provide sugar for cells. Other polysaccharides serve as building material for structures that protect the cell or the whole organism. The architecture and function of a polysaccharide are determined by its sugar monomers and by the positions of its glycosidic linkages.

Storage Polysaccharides

Both plants and animals store sugars for later use in the form of storage polysaccharides **(Figure 5.6)**. Plants store **starch**, a polymer of glucose monomers, as granules within cellular structures known as plastids. (Plastids include chloroplasts.) Synthesizing starch enables the plant to stockpile surplus glucose. Because glucose is a major cellular fuel, starch represents stored energy. The sugar can later be withdrawn by the plant from this carbohydrate "bank" by hydrolysis, which breaks the

Figure 5.6 Polysaccharides of plants and animals. (a) Starch stored in plant cells, **(b)** glycogen stored in muscle cells, and **(c)** structural cellulose fibers in plant cell walls are all polysaccharides composed entirely of glucose monomers (green hexagons). In starch and glycogen, the polymer chains tend to form helices in unbranched regions because of the angle of the linkages between glucose molecules. There are two kinds of starch: amylose and amylopectin. Cellulose, with a different kind of glucose linkage, is always unbranched.



bonds between the glucose monomers. Most animals, including humans, also have enzymes that can hydrolyze plant starch, making glucose available as a nutrient for cells. Potato tubers and grains—the fruits of wheat, maize (corn), rice, and other grasses—are the major sources of starch in the human diet.

Most of the glucose monomers in starch are joined by 1–4 linkages (number 1 carbon to number 4 carbon), like the glucose units in maltose (see Figure 5.5a). The simplest form of starch, amylose, is unbranched. Amylopectin, a more complex starch, is a branched polymer with 1–6 linkages at the branch points. Both of these starches are shown in **Figure 5.6a**.

Animals store a polysaccharide called **glycogen**, a polymer of glucose that is like amylopectin but more extensively branched **(Figure 5.6b)**. Vertebrates store glycogen mainly in liver and muscle cells. Hydrolysis of glycogen in these cells releases glucose when the demand for sugar increases. (The extensively branched structure of glycogen fits its function: More free ends are available for hydrolysis.) This stored fuel cannot sustain an animal for long, however. In humans, for example, glycogen stores are depleted in about a day unless they are replenished by eating. This is an issue of concern in low-carbohydrate diets, which can result in weakness and fatigue.

Structural Polysaccharides

Organisms build strong materials from structural polysaccharides. For example, the polysaccharide called **cellulose** is a major component of the tough walls that enclose plant cells **(Figure 5.6c)**. Globally, plants produce almost 10^{14} kg (100 billion tons) of cellulose per year; it is the most abundant organic compound on Earth.

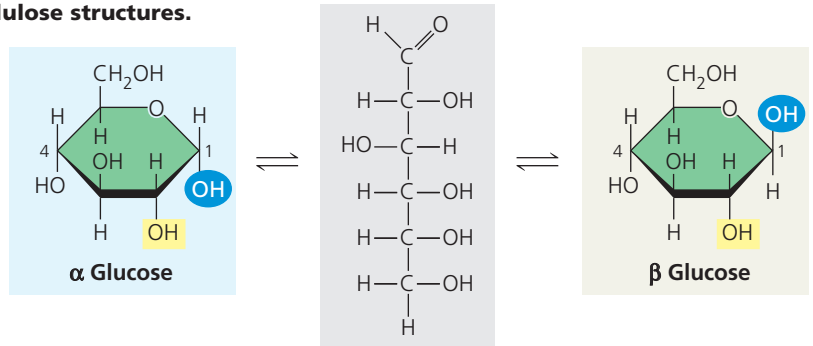
Like starch, cellulose is a polymer of glucose with 1–4 glycosidic linkages, but the linkages in these two polymers differ. The difference is based on the fact that there are actually two slightly different ring structures for glucose **(Figure 5.7a)**. When glucose forms a ring, the hydroxyl group attached to the number 1 carbon is positioned either below or above the plane of the ring. These two ring forms for glucose are called alpha (α) and beta (β), respectively. (Greek letters are often used as a "numbering" system for different versions of biological structures, much as we use the letters a, b, c, and so on for the parts of a question or a figure.) In starch, all the glucose monomers are in the α configuration **(Figure 5.7b)**, the arrangement we saw in Figures 5.4 and 5.5. In contrast, the glucose monomers of cellulose are all in the β configuration, making every glucose monomer "upside down" with respect to its neighbors (**Figure 5.7c**; see also Figure 5.6c).

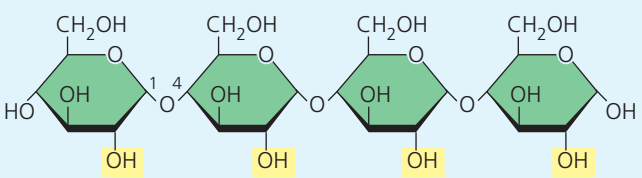
The differing glycosidic linkages in starch and cellulose give the two molecules distinct three-dimensional shapes. Certain starch molecules are largely helical, fitting their function of efficiently storing glucose units. Conversely, a cellulose molecule is straight. Cellulose is never branched, and some hydroxyl groups on its glucose monomers are free to hydrogen-bond with the hydroxyls of other cellulose molecules lying parallel to it. In plant cell walls, parallel cellulose molecules held together in this way are grouped into units called microfibrils (see Figure 5.6c). These cable-like microfibrils are a strong building material for plants and an important substance for humans because cellulose is the major constituent of paper and the only component of cotton. The unbranched structure of cellulose thus fits its function: imparting strength to parts of the plant.

Enzymes that digest starch by hydrolyzing its α linkages are unable to hydrolyze the β linkages of cellulose due to the different shapes of these two molecules. In fact,

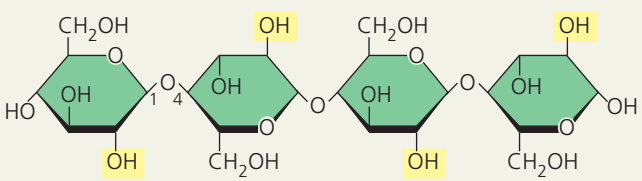
Figure 5.7 Starch and cellulose structures.

(a) α and β glucose ring structures. These two interconvertible forms of glucose differ in the placement of the hydroxyl group (highlighted in blue) attached to the number 1 carbon.





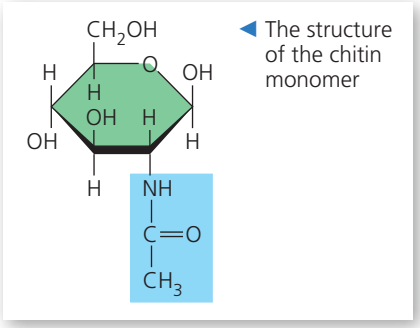
(b) Starch: 1–4 linkage of α glucose monomers. All monomers are in the same orientation. Compare the positions of the —OH groups highlighted in yellow with those in cellulose (c).



(c) Cellulose: 1–4 linkage of β glucose monomers. In cellulose, every β glucose monomer is upside down with respect to its neighbors. (See the highlighted —OH groups.)

Animation: Starch, Cellulose, and Glycogen Structures

Figure 5.8 Chitin, a structural polysaccharide.



The structure of the chitin monomer

Chitin, embedded in proteins, forms the exoskeleton of arthropods. This emperor dragonfly (*Anax imperator*) is molting—shedding its old exoskeleton (brown) and emerging upside down in adult form.

few organisms possess enzymes that can digest cellulose. Almost all animals, including humans, do not; the cellulose in our food passes through the digestive tract and is eliminated with the feces. Along the way, the cellulose abrades the wall of the digestive tract and stimulates the lining to secrete mucus, which aids in the smooth passage of food through the tract. Thus, although cellulose is not a nutrient for humans, it is an important part of a healthful diet. Most fruits, vegetables, and whole grains are rich in cellulose. On food packages, "insoluble fiber" refers mainly to cellulose.

Some microorganisms can digest cellulose, breaking it down into glucose monomers. A cow harbors cellulose-digesting prokaryotes and protists in its gut. These microbes hydrolyze the cellulose of hay and grass and convert the glucose to other compounds that nourish the cow. Similarly, a termite, which is unable to digest cellulose by itself, has prokaryotes or protists living in its gut that can make a meal of wood. Some fungi can also digest cellulose in soil and elsewhere, thereby helping recycle chemical elements within Earth's ecosystems.

Another important structural polysaccharide is **chitin**, the carbohydrate used by arthropods (insects, spiders, crustaceans, and related animals) to build their exoskeletons **(Figure 5.8)**. An exoskeleton is a hard case that surrounds the soft parts of an animal. Made up of chitin embedded in a layer of proteins, the case is leathery and flexible at first, but becomes hardened when the proteins are chemically linked to each other (as in insects) or encrusted with calcium carbonate (as in crabs). Chitin is also found in fungi, which use this polysaccharide rather than cellulose as the building material for their cell walls. Chitin is similar to cellulose, with β linkages, except that the glucose monomer of chitin has a nitrogen-containing attachment (see Figure 5.8).

CONCEPT CHECK 5.2

1. Write the formula for a monosaccharide that has three carbons.
2. A dehydration reaction joins two glucose molecules to form maltose. The formula for glucose is $C_6H_{12}O_6$. What is the formula for maltose?
3. **WHAT IF?** ➤ After a cow is given antibiotics to treat an infection, a vet gives the animal a drink of "gut culture" containing various prokaryotes. Why is this necessary?

For suggested answers, see Appendix A.

CONCEPT 5.3

Lipids are a diverse group of hydrophobic molecules

Lipids are the one class of large biological molecules that does not include true polymers, and they are generally not big enough to be considered macromolecules. The compounds called **lipids** are grouped with each other because they share one important trait: They mix poorly, if at all, with water. The hydrophobic behavior of lipids is based on their molecular structure. Although they may have some polar bonds associated with oxygen, lipids consist mostly of hydrocarbon regions. Lipids are varied in form and function. They include waxes and certain pigments, but we will focus on the types of lipids that are most important biologically: fats, phospholipids, and steroids.

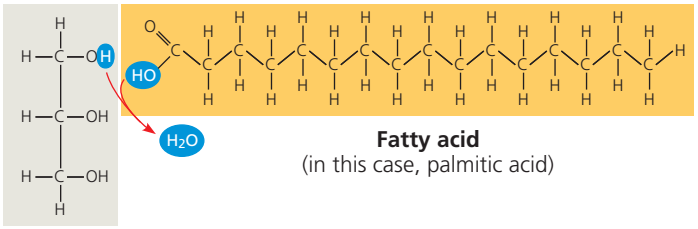
Animation: Lipids

Fats

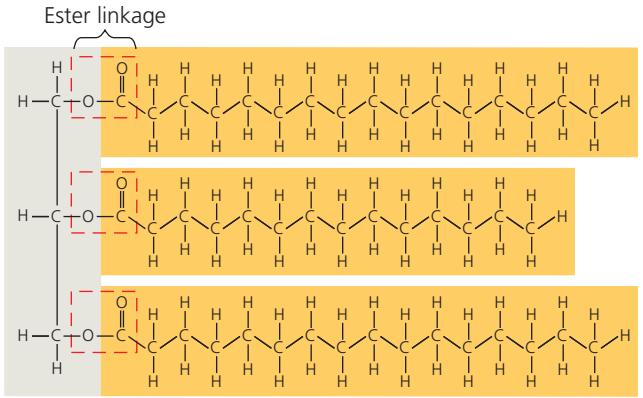
Although fats are not polymers, they are large molecules assembled from smaller molecules by dehydration reactions, like the dehydration reaction described for the polymerization of monomers in Figure 5.2a. A **fat** is constructed from two kinds of smaller molecules: glycerol and fatty acids **(Figure 5.9a)**. Glycerol is an alcohol; each of its three carbons bears a hydroxyl group. A **fatty acid** has a long carbon skeleton, usually 16 or 18 carbon atoms in length. The carbon at one end of the skeleton is part of a carboxyl group, the functional group that gives these molecules the name fatty *acid*. The rest of the skeleton consists of a hydrocarbon chain. The relatively nonpolar C—H bonds in the hydrocarbon chains of fatty acids are the reason fats are hydrophobic. Fats separate from water because the water molecules hydrogen-bond to one another and exclude the fats. This is why vegetable oil (a liquid fat) separates from the aqueous vinegar solution in a bottle of salad dressing.

In making a fat, three fatty acid molecules are each joined to glycerol by an ester linkage, a bond formed by a dehydration reaction between a hydroxyl group and a carboxyl group. The resulting fat, also called a **triacylglycerol**, thus consists of three fatty acids linked to one glycerol molecule. (Still another name for a fat is *triglyceride*, a word often found

Figure 5.9 The synthesis and structure of a fat, or triacylglycerol. The molecular building blocks of a fat are one molecule of glycerol and three molecules of fatty acids. **(a)** One water molecule is removed for each fatty acid joined to the glycerol. **(b)** A fat molecule with three fatty acid units, two of them identical. The carbons of the fatty acids are arranged zigzag to suggest the actual orientations of the four single bonds extending from each carbon (see Figures 4.3a and 4.6b).



(a) One of three dehydration reactions in the synthesis of a fat



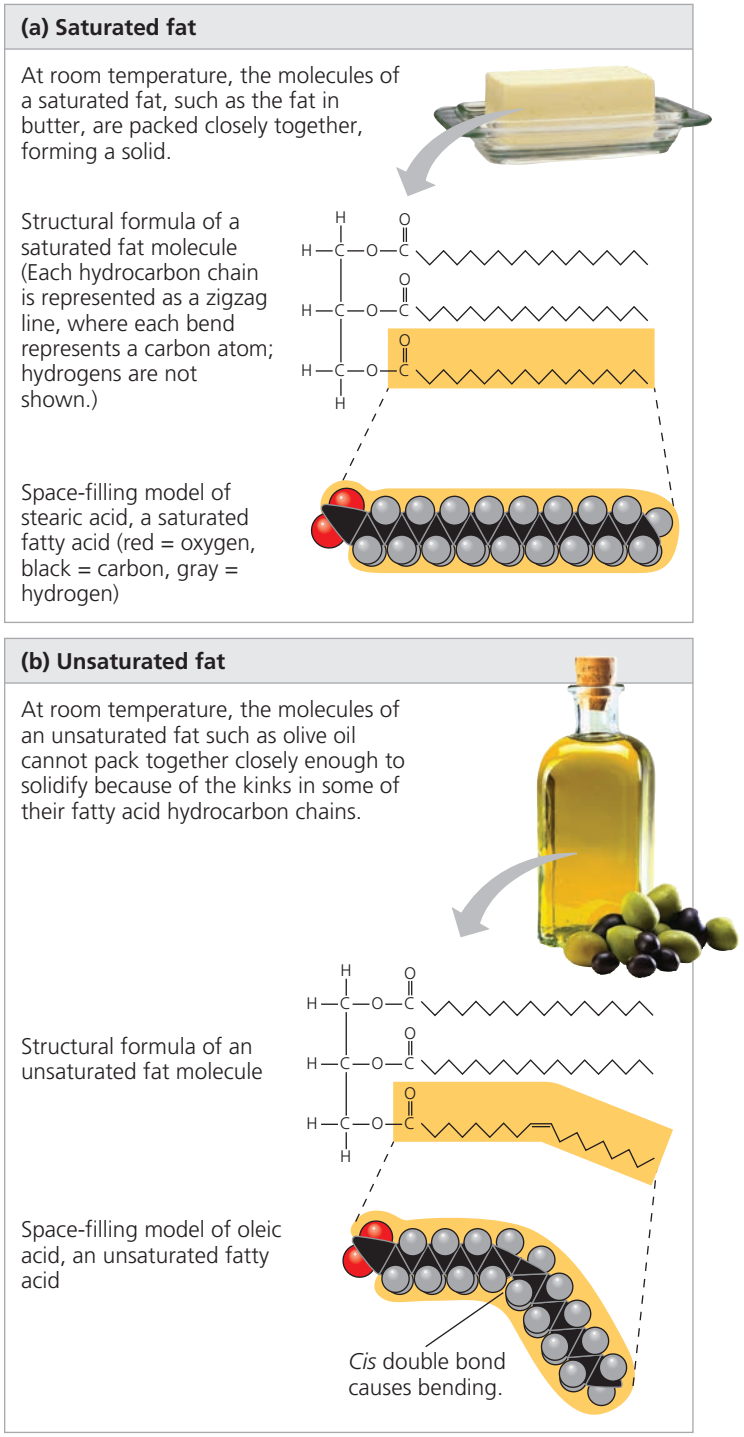
(b) Fat molecule (triacylglycerol)

in the list of ingredients on packaged foods.) The fatty acids in a fat can all be the same, or they can be of two or three different kinds, as in **Figure 5.9b**.

The terms *saturated* fats and *unsaturated* fats are commonly used in the context of nutrition **(Figure 5.10)**. These terms refer to the structure of the hydrocarbon chains of the fatty acids. If there are no double bonds between carbon atoms composing a chain, then as many hydrogen atoms as possible are bonded to the carbon skeleton. Such a structure is said to be *saturated* with hydrogen, and the resulting fatty acid is therefore called a **saturated fatty acid (Figure 5.10a)**. An **unsaturated fatty acid** has one or more double bonds, with one fewer hydrogen atom on each double-bonded carbon. Nearly every double bond in naturally occurring fatty acids is a *cis* double bond, which creates a kink in the hydrocarbon chain wherever it occurs **(Figure 5.10b)**. (See Figure 4.7b to remind yourself about *cis* and *trans* double bonds.)

A fat made from saturated fatty acids is called a saturated fat. Most animal fats are saturated: The hydrocarbon chains of their fatty acids—the "tails" of the fat molecules—lack double bonds, and their flexibility allows the fat molecules to pack together tightly. Saturated animal fats—such as lard

Figure 5.10 Saturated and unsaturated fats and fatty acids.



and butter—are solid at room temperature. In contrast, the fats of plants and fishes are generally unsaturated, meaning that they are built of one or more types of unsaturated fatty acids. Usually liquid at room temperature, plant and fish fats are referred to as oils—olive oil and cod liver oil are examples. The kinks where the *cis* double bonds are located prevent the molecules from packing together closely enough to solidify at room temperature. The phrase "hydrogenated vegetable oils"

on food labels means that unsaturated fats have been synthetically converted to saturated fats by adding hydrogen, allowing them to solidify. Peanut butter, margarine, and many other products are hydrogenated to prevent lipids from separating out in liquid (oil) form.

A diet rich in saturated fats is one of several factors that may contribute to the cardiovascular disease known as atherosclerosis. In this condition, deposits called plaques develop within the walls of blood vessels, causing inward bulges that impede blood flow and reduce the resilience of the vessels. The process of hydrogenating vegetable oils produces not only saturated fats but also unsaturated fats with *trans* double bonds. It appears that ***trans* fats** can contribute to coronary heart disease (see Concept 42.4). Because *trans* fats are especially common in baked goods and processed foods, the U.S. Food and Drug Administration (FDA) requires nutritional labels to include information on *trans* fat content. In addition, the FDA has ordered *trans* fats to be removed from the U.S. food supply by 2018. Some countries, such as Denmark and Switzerland, have already banned *trans* fats in foods.

The major function of fats is energy storage. The hydrocarbon chains of fats are similar to gasoline molecules and just as rich in energy. A gram of fat stores more than twice as much energy as a gram of a polysaccharide, such as starch. Because plants are relatively immobile, they can function with bulky energy storage in the form of starch. (Vegetable oils are generally obtained from seeds, where more compact storage is an asset to the plant.) Animals, however, must carry their energy stores with them, so there is an advantage to having a more compact reservoir of fuel—fat. Humans and other mammals stock their long-term food reserves in adipose cells (see Figure 4.6a), which swell and shrink as fat is deposited and withdrawn from storage. In addition to storing energy, adipose tissue also cushions such vital organs as the kidneys, and a layer of fat beneath the skin insulates the body. This subcutaneous layer is especially thick in whales, seals, and most other marine mammals, insulating their bodies in cold ocean water.

Phospholipids

Cells as we know them could not exist without another type of lipid—phospholipids. Phospholipids are essential for cells because they are major constituents of cell membranes. Their structure provides a classic example of how form fits function at the molecular level. As shown in **Figure 5.11**, a **phospholipid** is similar to a fat molecule but has only two fatty acids attached to glycerol rather than three. The third hydroxyl group of glycerol is joined to a phosphate group, which has a negative electrical charge in the cell. Typically, an additional small charged or polar molecule is also linked to the phosphate group. Choline is one such molecule (see Figure 5.11), but there are many others as well, allowing formation of a variety of phospholipids that differ from each other.

The two ends of phospholipids show different behaviors with respect to water. The hydrocarbon tails are hydrophobic and are excluded from water. However, the phosphate group and its attachments form a hydrophilic head that has an affinity for water. When phospholipids are added to water, they self-assemble into a double-layered sheet called a "bilayer"

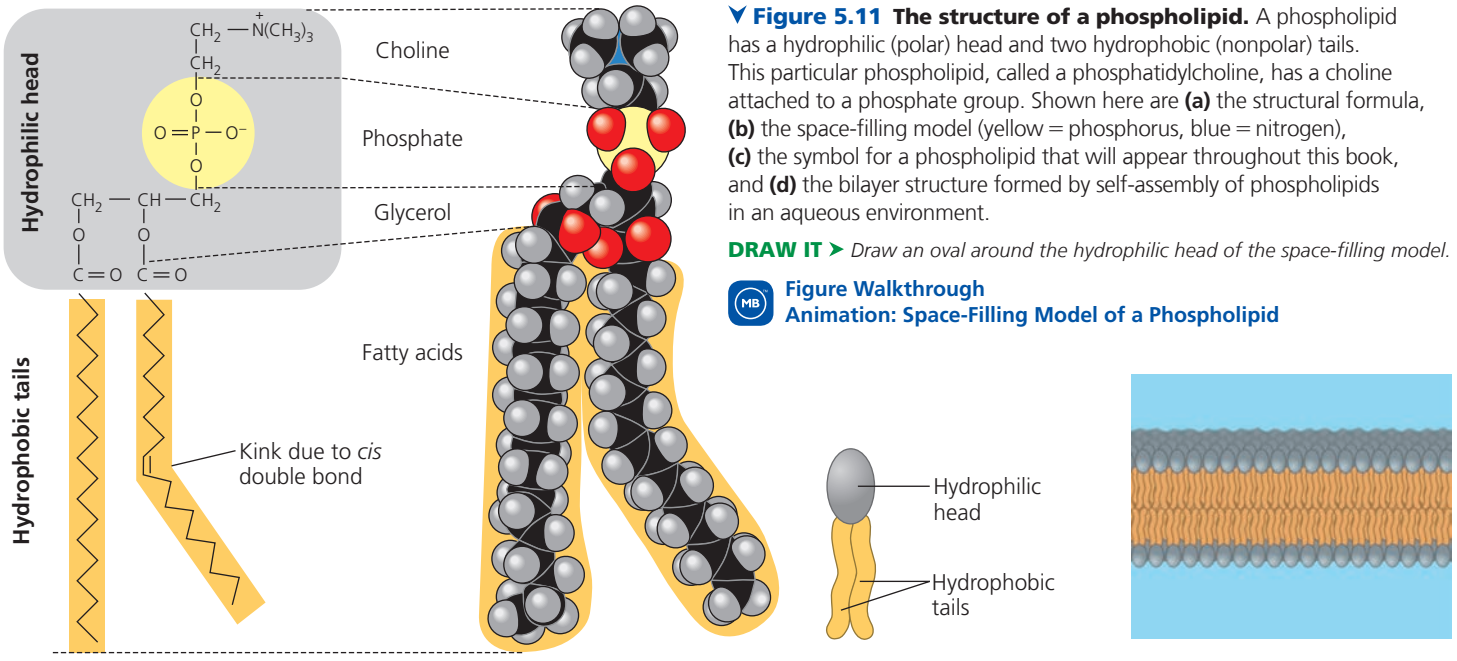


Figure 5.11 The structure of a phospholipid. A phospholipid has a hydrophilic (polar) head and two hydrophobic (nonpolar) tails. This particular phospholipid, called a phosphatidylcholine, has a choline attached to a phosphate group. Shown here are **(a)** the structural formula, **(b)** the space-filling model (yellow = phosphorus, blue = nitrogen), **(c)** the symbol for a phospholipid that will appear throughout this book, and **(d)** the bilayer structure formed by self-assembly of phospholipids in an aqueous environment.

DRAW IT ➤ *Draw an oval around the hydrophilic head of the space-filling model.*

Figure Walkthrough
Animation: Space-Filling Model of a Phospholipid

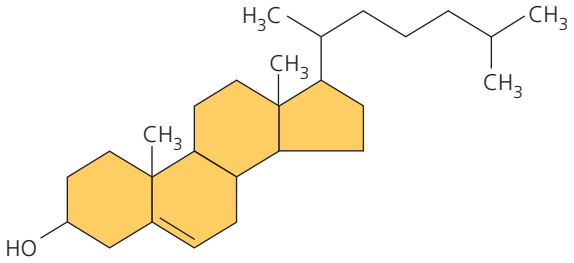
that shields their hydrophobic fatty acid tails from water (Figure 5.11d).

At the surface of a cell, phospholipids are arranged in a similar bilayer. The hydrophilic heads of the molecules are on the outside of the bilayer, in contact with the aqueous solutions inside and outside of the cell. The hydrophobic tails point toward the interior of the bilayer, away from the water. The phospholipid bilayer forms a boundary between the cell and its external environment and establishes separate compartments within eukaryotic cells; in fact, the existence of cells depends on the properties of phospholipids.

Steroids

Steroids are lipids characterized by a carbon skeleton consisting of four fused rings. Different steroids are distinguished by the particular chemical groups attached to this ensemble of rings. **Cholesterol**, a type of steroid, is a crucial molecule in animals **(Figure 5.12)**. It is a common component of animal cell membranes and is also the precursor from which other steroids, such as the vertebrate sex hormones, are synthesized. In vertebrates, cholesterol is synthesized in the liver and is also obtained from the diet. A high level of cholesterol in the blood may contribute to atherosclerosis, although some researchers are questioning the roles of cholesterol and saturated fats in the development of this condition.

Figure 5.12 Cholesterol, a steroid. Cholesterol is the molecule from which other steroids, including the sex hormones, are synthesized. Steroids vary in the chemical groups attached to their four interconnected rings (shown in gold).



MAKE CONNECTIONS ➤ *Compare cholesterol with the sex hormones shown in the figure at the beginning of Concept 4.3. Circle the chemical groups that cholesterol has in common with estradiol; put a square around the chemical groups that cholesterol has in common with testosterone.*

Interview with Lovell Jones: Investigating the effects of sex hormones on cancer (see the interview before Chapter 2)

CONCEPT CHECK 5.3

1. Compare the structure of a fat (triglyceride) with that of a phospholipid.
2. Why are human sex hormones considered lipids?
3. **WHAT IF? ➤** Suppose a membrane surrounded an oil droplet, as it does in the cells of plant seeds and in some animal cells. Describe and explain the form it might take.

For suggested answers, see Appendix A.

CONCEPT 5.4

Proteins include a diversity of structures, resulting in a wide range of functions

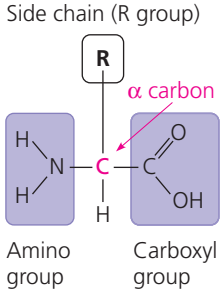
Nearly every dynamic function of a living being depends on proteins. In fact, the importance of proteins is underscored by their name, which comes from the Greek word *proteios*, meaning "first," or "primary." Proteins account for more than 50% of the dry mass of most cells, and they are instrumental in almost everything organisms do. Some proteins speed up chemical reactions, while others play a role in defense, storage, transport, cellular communication, movement, or structural support. **Figure 5.13** shows examples of proteins with these functions, which you'll learn more about in later chapters.

Life would not be possible without enzymes, most of which are proteins. Enzymatic proteins regulate metabolism by acting as **catalysts**, chemical agents that selectively speed up chemical reactions without being consumed in the reaction. Because an enzyme can perform its function over and over again, these molecules can be thought of as workhorses that keep cells running by carrying out the processes of life.

A human has tens of thousands of different proteins, each with a specific structure and function; proteins, in fact, are the most structurally sophisticated molecules known. Consistent with their diverse functions, they vary extensively in structure, each type of protein having a unique three-dimensional shape.

Proteins are all constructed from the same set of 20 amino acids, linked in unbranched polymers. The bond between amino acids is called a *peptide bond*, so a polymer of amino acids is called a **polypeptide**. A **protein** is a biologically functional molecule made up of one or more polypeptides, each folded and coiled into a specific three-dimensional structure.

Amino Acid Monomers



All amino acids share a common structure. An **amino acid** is an organic molecule with both an amino group and a carboxyl group (see Figure 4.9); the small figure shows the general formula for an amino acid. At the center of the amino acid is an asymmetric carbon atom called the *alpha* (α) *carbon*. Its four different partners are an amino group, a carboxyl group, a hydrogen atom, and a variable group symbolized by R. The R group, also called the side chain, differs with each amino acid.

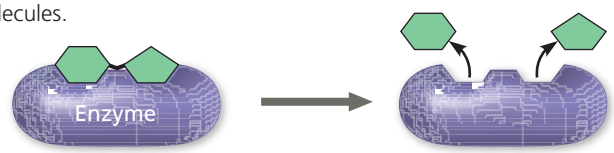
Figure 5.13 An overview of protein functions.

Animation: Protein Functions

Enzymatic proteins

Function: Selective acceleration of chemical reactions

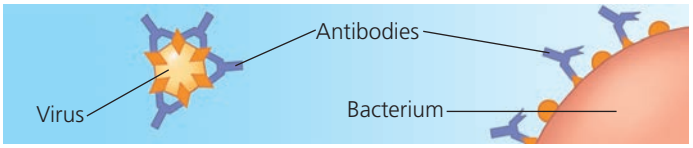
Example: Digestive enzymes catalyze the hydrolysis of bonds in food molecules.



Defensive proteins

Function: Protection against disease

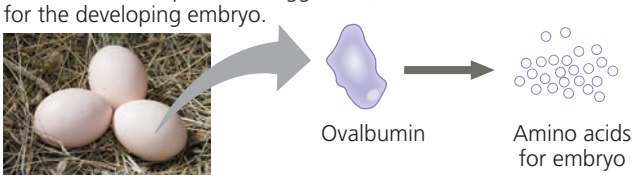
Example: Antibodies inactivate and help destroy viruses and bacteria.



Storage proteins

Function: Storage of amino acids

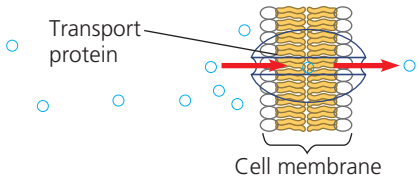
Examples: Casein, the protein of milk, is the major source of amino acids for baby mammals. Plants have storage proteins in their seeds. Ovalbumin is the protein of egg white, used as an amino acid source for the developing embryo.



Transport proteins

Function: Transport of substances

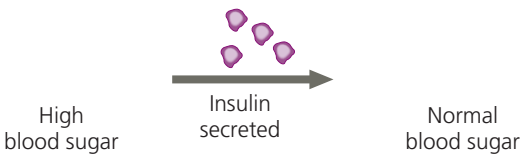
Examples: Hemoglobin, the iron-containing protein of vertebrate blood, transports oxygen from the lungs to other parts of the body. Other proteins transport molecules across membranes, as shown here.



Hormonal proteins

Function: Coordination of an organism's activities

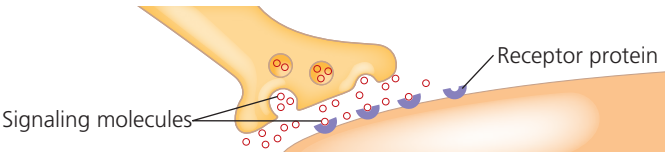
Example: Insulin, a hormone secreted by the pancreas, causes other tissues to take up glucose, thus regulating blood sugar concentration.



Receptor proteins

Function: Response of cell to chemical stimuli

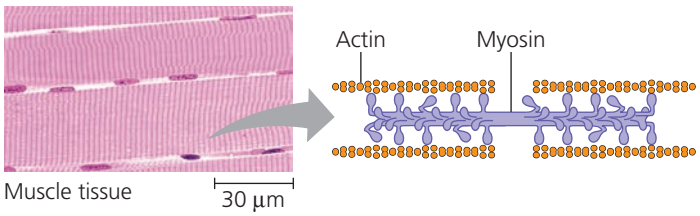
Example: Receptors built into the membrane of a nerve cell detect signaling molecules released by other nerve cells.



Contractile and motor proteins

Function: Movement

Examples: Motor proteins are responsible for the undulations of cilia and flagella. Actin and myosin proteins are responsible for the contraction of muscles.



Structural proteins

Function: Support

Examples: Keratin is the protein of hair, horns, feathers, and other skin appendages. Insects and spiders use silk fibers to make their cocoons and webs, respectively. Collagen and elastin proteins provide a fibrous framework in animal connective tissues.

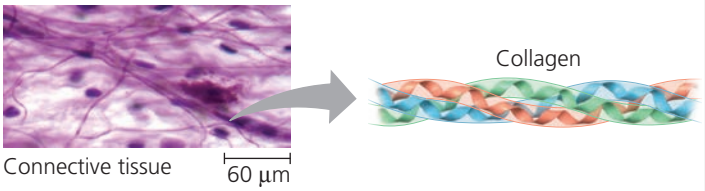
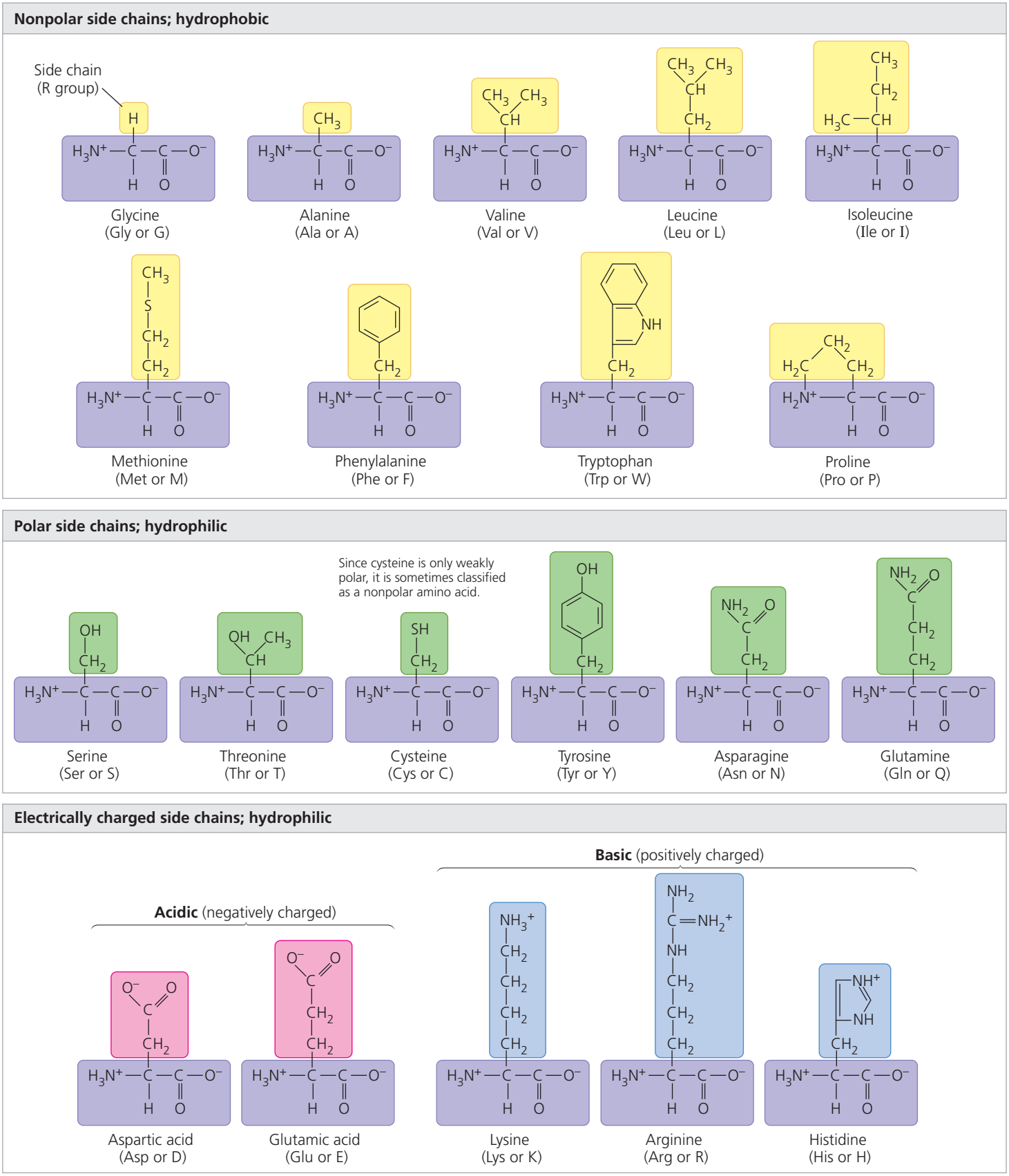


Figure 5.14 shows the 20 amino acids that cells use to build their thousands of proteins. Here the amino groups and carboxyl groups are all depicted in ionized form, the way they usually exist at the pH found in a cell. The side chain (R group) may be as simple as a hydrogen atom, as in the amino acid glycine, or it may be a carbon skeleton with various functional groups attached, as in glutamine.

The physical and chemical properties of the side chain determine the unique characteristics of a particular amino acid, thus affecting its functional role in a polypeptide. In Figure 5.14, the amino acids are grouped according to the properties of their side chains. One group consists of amino acids with nonpolar side chains, which are hydrophobic. Another group consists of amino acids with polar side chains, which are hydrophilic. Acidic amino acids have side chains that are generally negative in charge due to the presence of a carboxyl group, which is usually dissociated (ionized) at cellular pH. Basic amino acids have amino groups in their side chains that are generally positive in charge. (Notice that *all* amino acids have carboxyl groups and amino groups; the terms *acidic* and *basic* in this context refer only to groups in the side chains.) Because they are charged, acidic and basic side chains are also hydrophilic.

Figure 5.14 The 20 amino acids of proteins. The amino acids are grouped here according to the properties of their side chains (R groups) and shown in their prevailing ionic forms at pH 7.2, the pH within a cell. The three-letter and one-letter abbreviations for the amino acids are in parentheses. All of the amino acids used in proteins are L enantiomers (see Figure 4.7c).

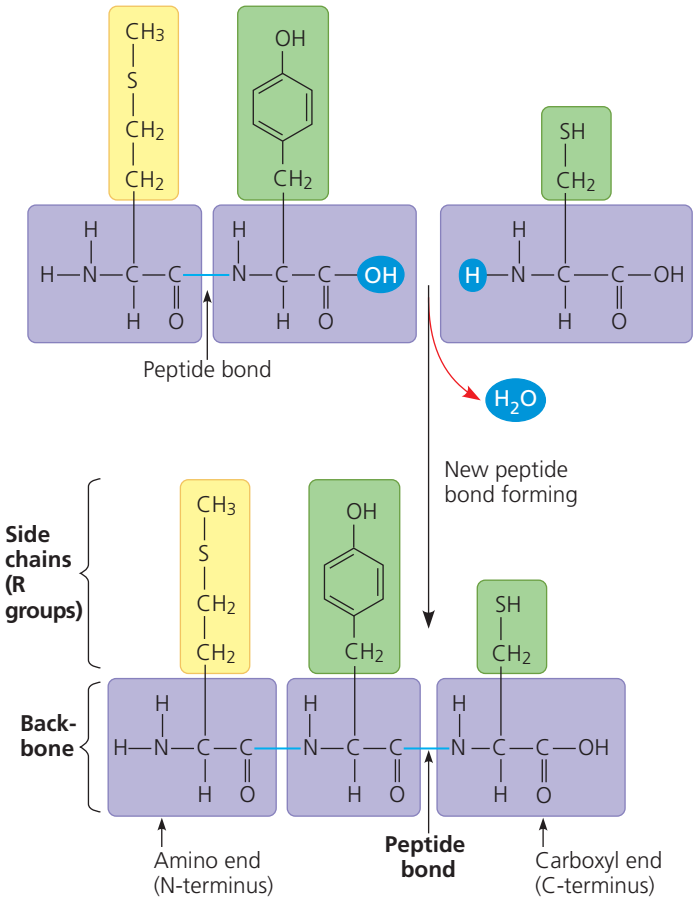


Polypeptides (Amino Acid Polymers)

Now that we have examined amino acids, let's see how they are linked to form polymers **(Figure 5.15)**. When two amino acids are positioned so that the carboxyl group of one is adjacent to the amino group of the other, they can become joined by a dehydration reaction, with the removal of a water molecule. The resulting covalent bond is called a **peptide bond**. Repeated over and over, this process yields a polypeptide, a polymer of many amino acids linked by peptide bonds. You'll learn more about how cells synthesize polypeptides in Concept 17.4.

The repeating sequence of atoms highlighted in purple in Figure 5.15 is called the *polypeptide backbone*. Extending from this backbone are the different side chains (R groups) of the amino acids. Polypeptides range in length from a few amino acids to 1,000 or more. Each specific polypeptide has a unique linear sequence of amino acids. Note that one end of the polypeptide chain has a free amino group (the N-terminus of the polypeptide), while the opposite end has a free carboxyl group (the C-terminus). The chemical nature of the molecule as a whole is determined by the kind and sequence of the side chains, which determine how a polypeptide folds and thus its final shape and chemical characteristics. The immense variety of polypeptides in nature illustrates an important concept introduced earlier—that cells can make many different polymers by linking a limited set of monomers into diverse sequences.

Figure 5.15 Making a polypeptide chain. Peptide bonds are formed by dehydration reactions, which link the carboxyl group of one amino acid to the amino group of the next. The peptide bonds are formed one at a time, starting with the amino acid at the amino end (N-terminus). The polypeptide has a repetitive backbone (purple) to which the amino acid side chains (yellow and green) are attached.



DRAW IT ➤ *Label the three amino acids in the upper part of the figure using three-letter and one-letter codes. Circle and label the carboxyl and amino groups that will form the new peptide bond.*

Protein Structure and Function

The specific activities of proteins result from their intricate three-dimensional architecture, the simplest level of which is the sequence of their amino acids. What can the amino acid sequence of a polypeptide tell us about the three-dimensional structure (commonly referred to simply as the "structure") of the protein and its function? The term *polypeptide* is not synonymous with the term *protein*. Even for a protein consisting of a single polypeptide, the relationship is somewhat analogous to that between a long strand of yarn and a sweater of particular size and shape that can be knitted from the yarn. A functional protein is not *just* a polypeptide chain, but one or more polypeptides precisely twisted, folded, and coiled into a molecule of unique shape, which can be shown in several different types of models **(Figure 5.16)**. And it is the amino acid sequence of each polypeptide that determines what three-dimensional structure the protein will have under normal cellular conditions.

When a cell synthesizes a polypeptide, the chain may fold spontaneously, assuming the functional structure for that protein. This folding is driven and reinforced by the formation of various bonds between parts of the chain, which in turn depends on the sequence of amino acids. Many proteins are roughly spherical (*globular proteins*), while others are shaped like long fibers (*fibrous proteins*). Even within these broad categories, countless variations exist.

A protein's specific structure determines how it works. In almost every case, the function of a protein depends on its ability to recognize and bind to some other molecule. In an especially striking example of the marriage of form and function, **Figure 5.17** shows the exact match of shape between an antibody (a protein in the body) and the particular foreign substance on a flu virus that the antibody binds to and marks for destruction. Also, you may recall another example of molecules with matching shapes from Concept 2.3: endorphin molecules (produced by the body) and morphine molecules (a manufactured drug), both of which fit into receptor proteins on the surface of brain cells in humans, producing euphoria and relieving pain. Morphine, heroin, and other opiate drugs are able to mimic endorphins because they all have a shape similar to that of endorphins and can thus fit into and bind to endorphin receptors in the brain. This fit is very specific, something like a lock and key (see Figure 2.16). The endorphin receptor, like other receptor molecules, is a protein. The function of a protein—for instance, the ability of a receptor protein to bind to a particular pain-relieving signaling molecule—is an emergent property resulting from exquisite molecular order.

Figure 5.16 Visualizing Proteins

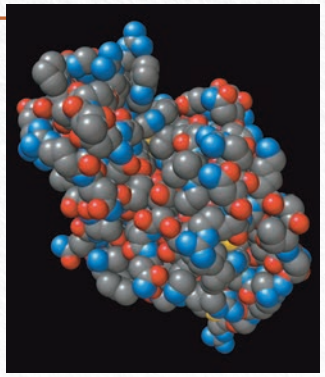
Proteins can be represented in different ways, depending on the goal of the illustration.

Structural Models

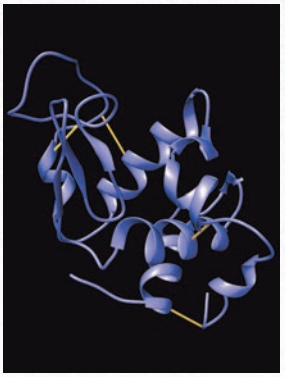
Using data from structural studies of proteins, computers can generate various types of models. Each model emphasizes a different aspect of the protein's structure, but no model can show what a protein actually looks like. These three models depict lysozyme, a protein in tears and saliva that helps prevent infection by binding to target molecules on bacteria.

1 *In which model is it easiest to follow the polypeptide backbone?*

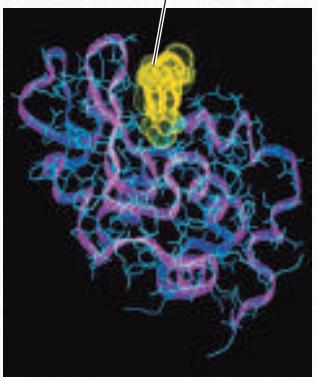
MB **Instructors:** The tutorial "Molecular Model: Lysozyme," in which students rotate 3-D models of lysozyme, can be assigned in MasteringBiology.



Space-filling model: Shows all the atoms of the protein (except hydrogen), emphasizing the overall globular shape. The atoms are color-coded: gray = carbon, red = oxygen, blue = nitrogen, and yellow = sulfur.



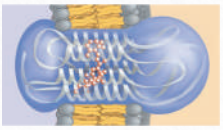
Ribbon model: Shows only the backbone of the polypeptide, emphasizing how it folds and coils to form a 3-D shape, in this case stabilized by disulfide bridges (yellow lines).



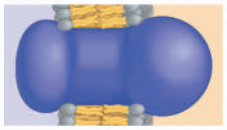
Wireframe model (blue): Shows the backbone of the polypeptide chain with side chains (R groups) extending from it (see Figure 5.15). A ribbon model (purple) is superimposed on the wireframe model.

Simplified Diagrams

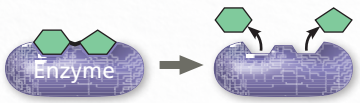
It isn't always necessary to use a detailed computer model; simplified diagrams are useful when the focus of the figure is on the function of the protein, not the structure.



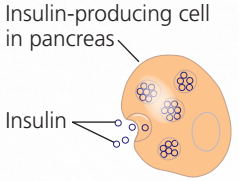
In this diagram of the protein rhodopsin, a simple transparent shape is drawn around the contours of a ribbon model, showing the overall shape of the molecule as well as some internal details.



When structural details are not needed, a solid shape can be used to represent a protein.



A simple shape is used here to represent a generic enzyme because the diagram focuses on enzyme action in general.



Sometimes a protein is represented simply as a dot, as shown here for insulin.

2 *Draw a simple version of lysozyme that shows its overall shape, based on the molecular models in the top section of the figure.*

3 *Why is it unnecessary to show the actual shape of insulin here?*

Figure 5.17 Complementarity of shape between two protein surfaces. A technique called X-ray crystallography was used to generate a computer model of an antibody protein (blue and orange, left) bound to a flu virus protein (yellow and green, right). This is a wireframe model modified by adding an "electron density map" in the region where the two proteins meet. Computer software was then used to back the images away from each other slightly.

VISUAL SKILLS *What do these computer models allow you to see about the two proteins?*

Four Levels of Protein Structure

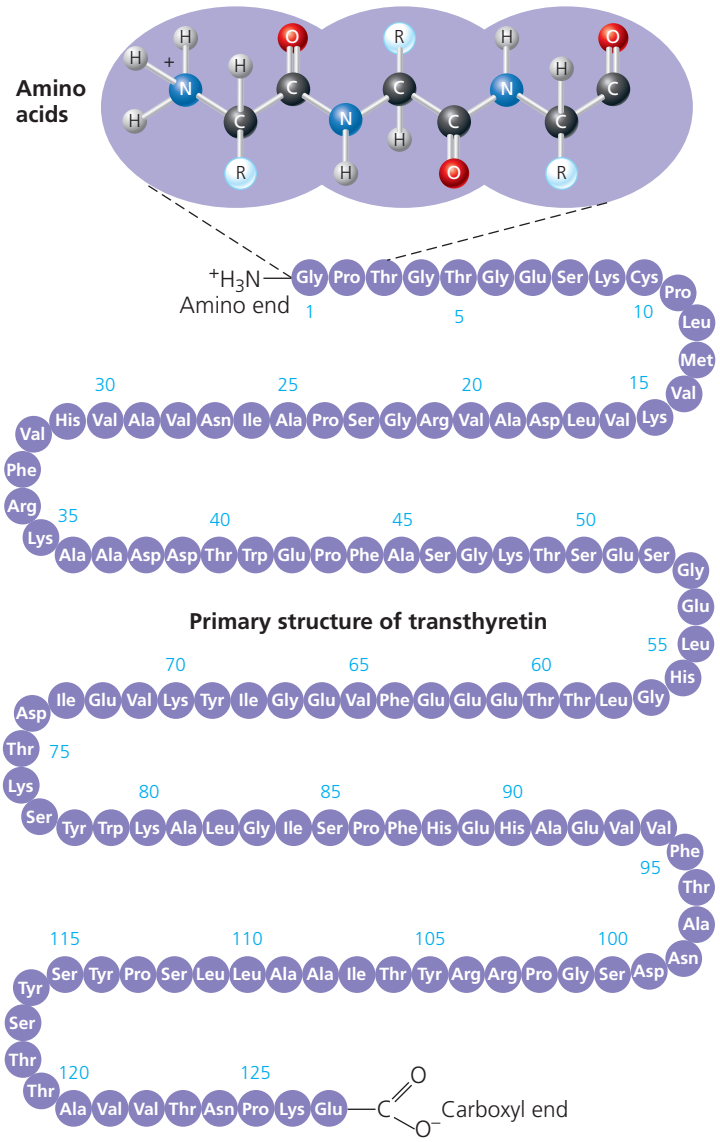
In spite of their great diversity, proteins share three superimposed levels of structure, known as primary, secondary, and tertiary structure. A fourth level, quaternary structure, arises when a protein consists of two or more polypeptide chains. **Figure 5.18** describes these four levels of protein structure. Be sure to study this figure thoroughly before going on to the next section.

MB **Animation: Protein Structure**

Figure 5.18 Exploring Levels of Protein Structure

Primary Structure

Linear chain of amino acids

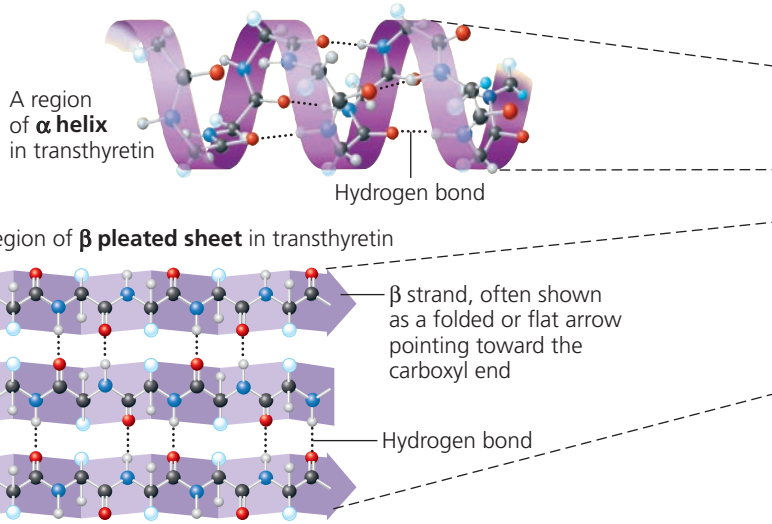


The **primary structure** of a protein is its sequence of amino acids. As an example, let's consider transthyretin, a globular blood protein that transports vitamin A and one of the thyroid hormones throughout the body. Transthyretin is made up of four identical polypeptide chains, each composed of 127 amino acids. Shown here is one of these chains unraveled for a closer look at its primary structure. Each of the 127 positions along the chain is occupied by one of the 20 amino acids, indicated here by its three-letter abbreviation.

The primary structure is like the order of letters in a very long word. If left to chance, there would be 20^{127} different ways of making a polypeptide chain 127 amino acids long. However, the precise primary structure of a protein is determined not by the random linking of amino acids, but by inherited genetic information. The primary structure in turn dictates secondary and tertiary structure, due to the chemical nature of the backbone and the side chains (R groups) of the amino acids along the polypeptide.

Secondary Structure

Regions stabilized by hydrogen bonds between atoms of the polypeptide backbone



Most proteins have segments of their polypeptide chains repeatedly coiled or folded in patterns that contribute to the protein's overall shape. These coils and folds, collectively referred to as **secondary structure**, are the result of hydrogen bonds between the repeating constituents of the polypeptide backbone (not the amino acid side chains). Within the backbone, the oxygen atoms have a partial negative charge, and the hydrogen atoms attached to the nitrogens have a partial positive charge (see Figure 2.14); therefore, hydrogen bonds can form between these atoms. Individually, these hydrogen bonds are weak, but because they are repeated many times over a relatively long region of the polypeptide chain, they can support a particular shape for that part of the protein.

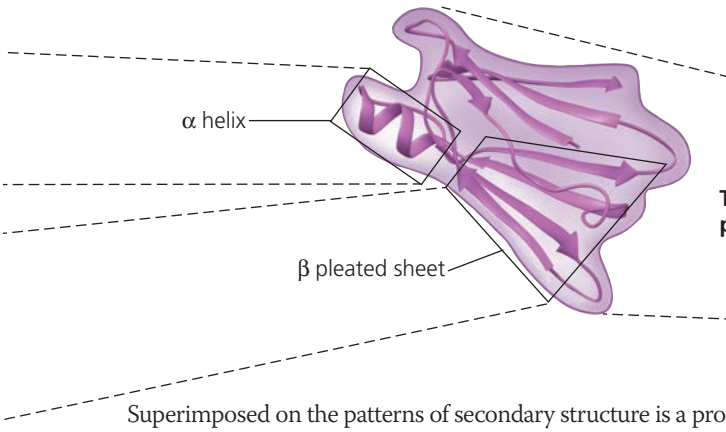
One such secondary structure is the **α helix**, a delicate coil held together by hydrogen bonding between every fourth amino acid, as shown above. Although each transthyretin polypeptide has only one α helix region (see the Tertiary Structure section), other globular proteins have multiple stretches of α helix separated by nonhelical regions (see hemoglobin in the Quaternary Structure section). Some fibrous proteins, such as α-keratin, the structural protein of hair, have the α helix formation over most of their length.

The other main type of secondary structure is the **β pleated sheet**. As shown above, in this structure two or more segments of the polypeptide chain lying side by side (called β strands) are connected by hydrogen bonds between parts of the two parallel segments of polypeptide backbone. β pleated sheets make up the core of many globular proteins, as is the case for transthyretin (see Tertiary Structure), and dominate some fibrous proteins, including the silk protein of a spider's web. The teamwork of so many hydrogen bonds makes each spider silk fiber stronger than a steel strand of the same weight.

▶ Spiders secrete silk fibers made of a structural protein containing β pleated sheets, which allow the spider web to stretch and recoil.

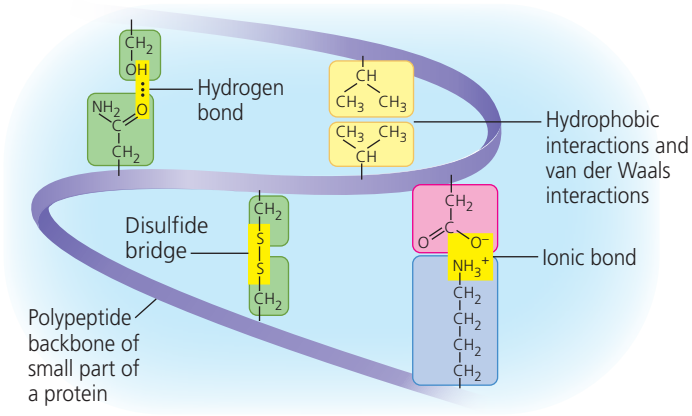
Tertiary Structure

Three-dimensional shape stabilized by interactions between side chains



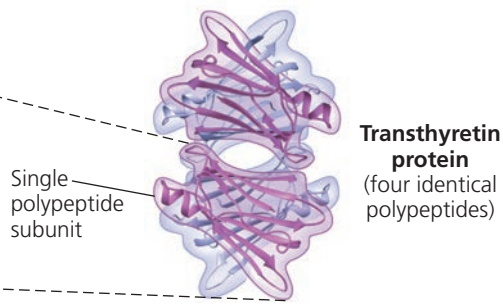
Superimposed on the patterns of secondary structure is a protein's tertiary structure, shown here in a ribbon model of the transthyretin polypeptide. While secondary structure involves interactions between backbone constituents, **tertiary structure** is the overall shape of a polypeptide resulting from interactions between the side chains (R groups) of the various amino acids. One type of interaction that contributes to tertiary structure is called—somewhat misleadingly—a **hydrophobic interaction**. As a polypeptide folds into its functional shape, amino acids with hydrophobic (nonpolar) side chains usually end up in clusters at the core of the protein, out of contact with water. Thus, a "hydrophobic interaction" is actually caused by the exclusion of nonpolar substances by water molecules. Once nonpolar amino acid side chains are close together, van der Waals interactions help hold them together. Meanwhile, hydrogen bonds between polar side chains and ionic bonds between positively and negatively charged side chains also help stabilize tertiary structure. These are all weak interactions in the aqueous cellular environment, but their cumulative effect helps give the protein a unique shape.

Covalent bonds called **disulfide bridges** may further reinforce the shape of a protein. Disulfide bridges form where two cysteine monomers, which have sulfhydryl groups (—SH) on their side chains (see Figure 4.9), are brought close together by the folding of the protein. The sulfur of one cysteine bonds to the sulfur of the second, and the disulfide bridge (—S—S—) rivets parts of the protein together (see yellow lines in Figure 5.16 ribbon model). All of these different kinds of interactions can contribute to the tertiary structure of a protein, as shown here in a small part of a hypothetical protein:



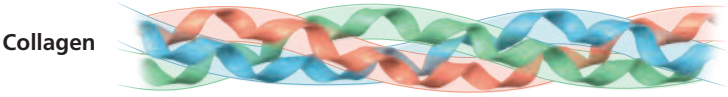
Quaternary Structure

Association of two or more polypeptides (some proteins only)

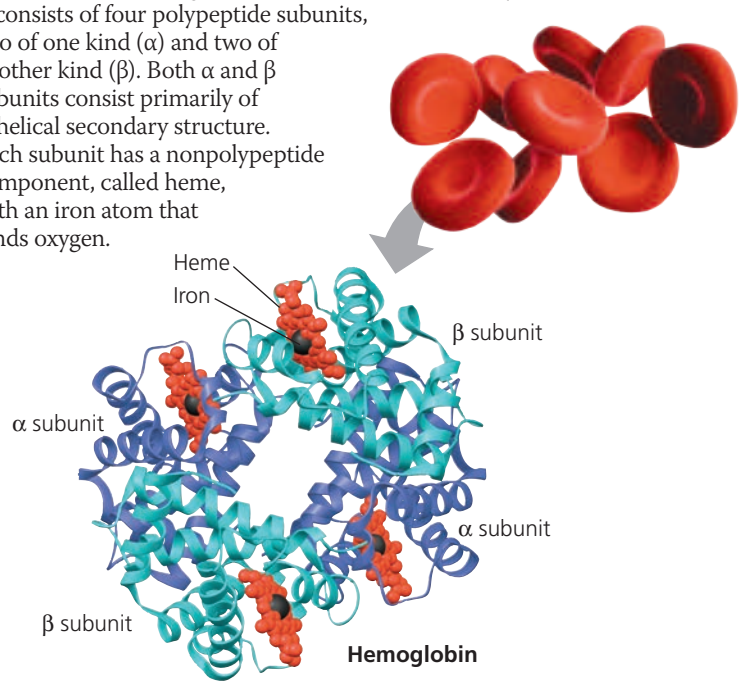


Some proteins consist of two or more polypeptide chains aggregated into one functional macromolecule. **Quaternary structure** is the overall protein structure that results from the aggregation of these polypeptide subunits. For example, shown above is the complete globular transthyretin protein, made up of its four polypeptides.

Another example is collagen, which is a fibrous protein that has three identical helical polypeptides intertwined into a larger triple helix, giving the long fibers great strength. This suits collagen fibers to their function as the girders of connective tissue in skin, bone, tendons, ligaments, and other body parts. (Collagen accounts for 40% of the protein in a human body.)

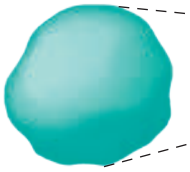
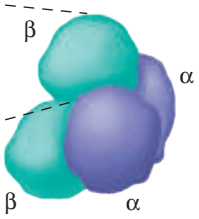
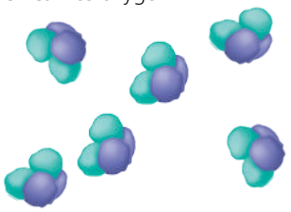
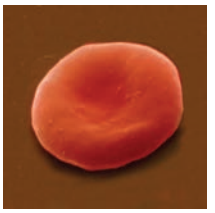
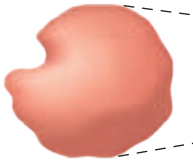
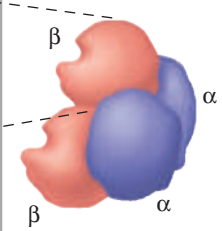
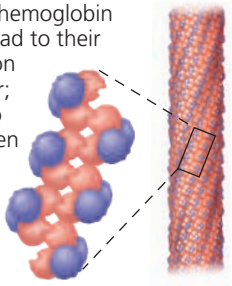
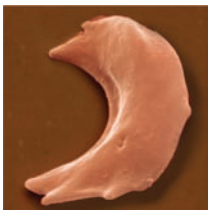


Hemoglobin, the oxygen-binding protein of red blood cells, is another example of a globular protein with quaternary structure. It consists of four polypeptide subunits, two of one kind (α) and two of another kind (β). Both α and β subunits consist primarily of α-helical secondary structure. Each subunit has a nonpolypeptide component, called heme, with an iron atom that binds oxygen.



Animation: Proteins
MP3 Tutor: Protein Structure and Function

Figure 5.19 A single amino acid substitution in a protein causes sickle-cell disease.

	Primary Structure	Secondary and Tertiary Structures	Quaternary Structure	Function	Red Blood Cell Shape
Normal hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Glu 7 Glu	Normal β subunit 	Normal hemoglobin 	Normal hemoglobin proteins do not associate with one another; each carries oxygen. 	Normal red blood cells are full of individual hemoglobin proteins. 
Sickle-cell hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Val 7 Glu	Sickle-cell β subunit 	Sickle-cell hemoglobin 	Hydrophobic interactions between sickle-cell hemoglobin proteins lead to their aggregation into a fiber; capacity to carry oxygen is greatly reduced. 	Fibers of abnormal hemoglobin deform red blood cell into sickle shape. 

MAKE CONNECTIONS ➤ *Considering the chemical characteristics of the amino acids valine and glutamic acid (see Figure 5.14), propose a possible explanation for the dramatic effect on protein function that occurs when valine is substituted for glutamic acid.*

MB **HHMI Animation: Sickle-Cell Disease** hhmi BioInteractive

Sickle-Cell Disease: A Change in Primary Structure

Even a slight change in primary structure can affect a protein's shape and ability to function. For instance, **sickle-cell disease**, an inherited blood disorder, is caused by the substitution of one amino acid (valine) for the normal one (glutamic acid) at the position of the sixth amino acid in the primary structure of hemoglobin, the protein that carries oxygen in red blood cells. Normal red blood cells are disk-shaped, but in sickle-cell disease, the abnormal hemoglobin molecules tend to aggregate into chains, deforming some of the cells into a sickle shape **(Figure 5.19)**. A person with the disease has periodic "sickle-cell crises" when the angular cells clog tiny blood vessels, impeding blood flow. The toll taken on such patients is a dramatic example of how a simple change in protein structure can have devastating effects on protein function.

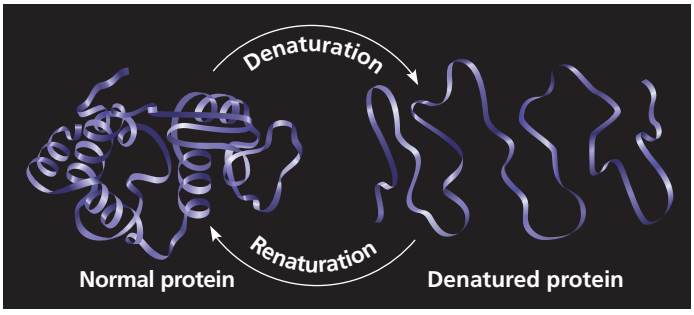
MB **Interview with Linus Pauling: Winner of the Nobel Prize in Chemistry and the Nobel Peace Prize**

What Determines Protein Structure?

You've learned that a unique shape endows each protein with a specific function. But what are the key factors determining protein structure? You already know most of the answer: A polypeptide chain of a given amino acid sequence can be arranged into a three-dimensional shape determined by the interactions responsible for secondary and tertiary structure. This folding normally occurs as the protein is being synthesized in the crowded environment within a cell, aided by other proteins. However, protein structure also depends on the physical and chemical conditions of the protein's environment. If the pH, salt concentration, temperature, or other aspects of its environment are altered, the weak chemical bonds and interactions within a protein may be destroyed, causing the protein to unravel and lose its native shape, a change called **denaturation (Figure 5.20)**. Because it is misshapen, the denatured protein is biologically inactive.

Most proteins become denatured if they are transferred from an aqueous environment to a nonpolar solvent, such as ether or chloroform; the polypeptide chain refolds so that

Figure 5.20 Denaturation and renaturation of a protein. High temperatures or various chemical treatments will denature a protein, causing it to lose its shape and hence its ability to function. If the denatured protein remains dissolved, it may renature when the chemical and physical aspects of its environment are restored to normal.



its hydrophobic regions face outward toward the solvent. Other denaturation agents include chemicals that disrupt the hydrogen bonds, ionic bonds, and disulfide bridges that maintain a protein's shape. Denaturation can also result from excessive heat, which agitates the polypeptide chain enough to overpower the weak interactions that stabilize the structure. The white of an egg becomes opaque during cooking because the denatured proteins are insoluble and solidify. This also explains why excessively high fevers can be fatal: Proteins in the blood tend to denature at very high body temperatures.

When a protein in a test-tube solution has been denatured by heat or chemicals, it can sometimes return to its functional shape when the denaturing agent is removed. (Sometimes this is not possible: For example, a fried egg will not become liquefied when placed back into the refrigerator!) We can conclude that the information for building specific shape is intrinsic to the protein's primary structure; this is often the case for small proteins. The sequence of amino acids determines the protein's shape—where an α helix can form, where β pleated sheets can exist, where disulfide bridges are located, where ionic bonds can form, and so on. But how does protein folding occur in the cell?

Protein Folding in the Cell

Biochemists now know the amino acid sequence for about 65 million proteins, with roughly 1.5 million added each month, and the three-dimensional shape for almost 35,000. Researchers have tried to correlate the primary structure of many proteins with their three-dimensional structure to discover the rules of protein folding. Unfortunately, however, the protein-folding process is not that simple. Most proteins probably go through several intermediate structures on their way to a stable shape, and looking at the mature structure does not reveal the stages of folding required to achieve that form. However, biochemists have developed methods for tracking a protein through such stages and learning more about this important process.

Misfolding of polypeptides in cells is a serious problem that has come under increasing scrutiny by medical researchers. Many diseases—such as cystic fibrosis, Alzheimer's, Parkinson's, and mad cow disease—are associated with an accumulation of misfolded proteins. In fact, misfolded versions of the transthyretin protein featured in Figure 5.18 have been implicated in several diseases, including one form of senile dementia.

Even when scientists have a correctly folded protein in hand, determining its exact three-dimensional structure is not simple, for a single protein has thousands of atoms. The method most commonly used to determine the 3-D structure of a protein is **X-ray crystallography**, which depends on the diffraction of an X-ray beam by the atoms of a crystallized molecule. Using this technique, scientists can build a 3-D model that shows the exact position of every atom in a protein molecule **(Figure 5.21)**. Nuclear magnetic resonance (NMR) spectroscopy and bioinformatics (see Concept 5.6) are complementary approaches to understanding protein structure and function.

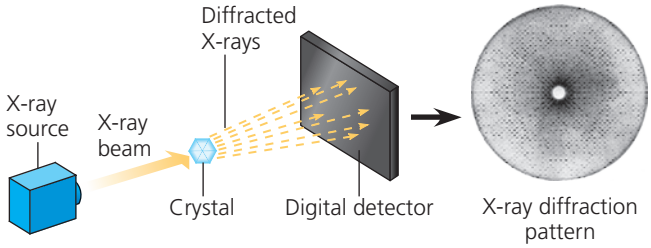
The structure of some proteins is difficult to determine for a simple reason: A growing body of biochemical research has revealed that a significant number of proteins, or regions of proteins, do not have a distinct 3-D structure until they interact with a target protein or other molecule. Their flexibility and indefinite structure are important for their function, which may require binding with different targets at different times. These proteins, which may account for 20–30% of mammalian proteins, are called *intrinsically disordered proteins* and are the focus of current research.

Figure 5.21

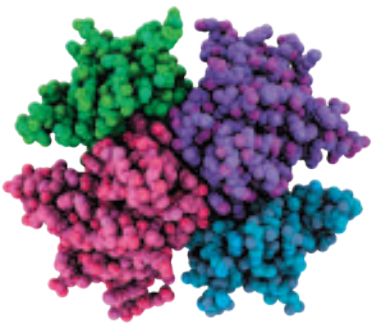
Research Method X-Ray Crystallography

Application Scientists use X-ray crystallography to determine the three-dimensional (3-D) structure of macromolecules such as nucleic acids and proteins.

Technique Researchers aim an X-ray beam through a crystallized protein or nucleic acid. The atoms of the crystal diffract (bend) the X-rays into an orderly array that a digital detector records as a pattern of spots called an X-ray diffraction pattern, an example of which is shown here.



Results Using data from X-ray diffraction patterns and the sequence of monomers determined by chemical methods, researchers can build a 3-D computer model of the macromolecule being studied, such as the four-subunit protein transthyretin (see Figure 5.18) shown here.



CONCEPT CHECK 5.4

1. What parts of a polypeptide participate in the bonds that hold together secondary structure? Tertiary structure?
2. Thus far in the chapter, the Greek letters α and β have been used to specify at least three different pairs of structures. Name and briefly describe them.
3. **WHAT IF?** ➤ Where would you expect a polypeptide region rich in the amino acids valine, leucine, and isoleucine to be located in a folded polypeptide? Explain.

For suggested answers, see Appendix A.

CONCEPT 5.5

Nucleic acids store, transmit, and help express hereditary information

If the primary structure of polypeptides determines a protein's shape, what determines primary structure? The amino acid sequence of a polypeptide is programmed by a discrete unit of inheritance known as a **gene**. Genes consist of DNA, which belongs to the class of compounds called nucleic acids. **Nucleic acids** are polymers made of monomers called nucleotides.

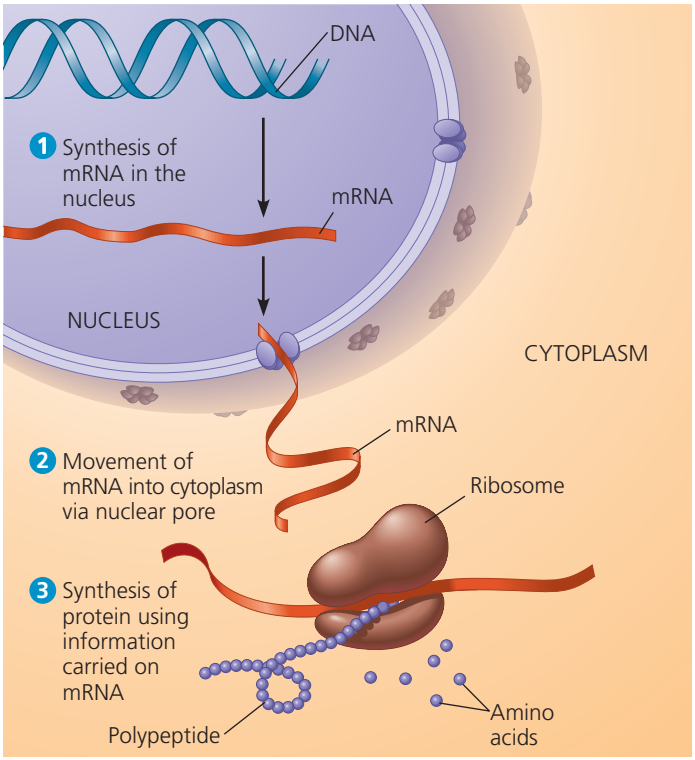
The Roles of Nucleic Acids

The two types of nucleic acids, **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**, enable living organisms to reproduce their complex components from one generation to the next. Unique among molecules, DNA provides directions for its own replication. DNA also directs RNA synthesis and, through RNA, controls protein synthesis; this entire process is called **gene expression** **(Figure 5.22)**.

DNA is the genetic material that organisms inherit from their parents. Each chromosome contains one long DNA molecule, usually carrying several hundred or more genes. When a cell reproduces itself by dividing, its DNA molecules are copied and passed along from one generation of cells to the next. The information that programs all the cell's activities is encoded in the structure of the DNA. The DNA, however, is not directly involved in running the operations of the cell, any more than computer software by itself can read the bar code on a box of cereal. Just as a scanner is needed to read a bar code, proteins are required to implement genetic programs. The molecular hardware of the cell—the tools that carry out biological functions—consists mostly of proteins. For example, the oxygen carrier in red blood cells is the protein hemoglobin that you saw earlier (see Figure 5.18), not the DNA that specifies its structure.

How does RNA, the other type of nucleic acid, fit into gene expression, the flow of genetic information from DNA to proteins? A given gene along a DNA molecule can direct synthesis of a type of RNA called *messenger RNA* (*mRNA*). The mRNA molecule interacts with the cell's protein-synthesizing machinery to direct production of a polypeptide, which folds into all or part of a protein. We can summarize the flow of genetic information as DNA → RNA → protein (see Figure 5.22). The sites of protein synthesis are cellular structures called ribosomes. In a eukaryotic cell, ribosomes are in the cytoplasm—the region between the nucleus and the plasma membrane, the cell's outer boundary—but DNA resides in the nucleus. Messenger RNA conveys genetic instructions for building proteins from the nucleus to the cytoplasm. Prokaryotic cells lack nuclei but still use mRNA to convey a message from the DNA to ribosomes and other cellular equipment that translate the coded information into amino acid sequences. Later in the book, you'll read about other functions of some recently discovered RNA molecules; the stretches of DNA that direct synthesis of these RNAs are also considered genes (see Concept 18.3).

Figure 5.22 Gene expression: DNA → RNA → protein. In a eukaryotic cell, DNA in the nucleus programs protein production in the cytoplasm by dictating synthesis of messenger RNA (mRNA).



BioFlix® Animation: Gene Expression

The Components of Nucleic Acids

Nucleic acids are macromolecules that exist as polymers called **polynucleotides** **(Figure 5.23a)**. As indicated by the name, each polynucleotide consists of monomers called **nucleotides**. A nucleotide, in general, is composed of three parts: a five-carbon sugar (a pentose), a nitrogen-containing (nitrogenous) base, and one to three phosphate groups **(Figure 5.23b)**. The beginning monomer used to build a polynucleotide has three phosphate groups, but two are lost during the polymerization process. The portion of a nucleotide without any phosphate groups is called a *nucleoside*.

To understand the structure of a single nucleotide, let's first consider the nitrogenous bases **(Figure 5.23c)**. Each nitrogenous base has one or two rings that include nitrogen atoms. (They are called nitrogenous *bases* because the nitrogen atoms tend to take up H^+ from solution, thus acting as bases.) There are two families of nitrogenous bases: pyrimidines and purines. A **pyrimidine** has one six-membered ring of carbon and nitrogen atoms. The members of the pyrimidine family are cytosine (C), thymine (T), and uracil (U). **Purines** are larger, with a six-membered ring fused to a

five-membered ring. The purines are adenine (A) and guanine (G). The specific pyrimidines and purines differ in the chemical groups attached to the rings. Adenine, guanine, and cytosine are found in both DNA and RNA; thymine is found only in DNA and uracil only in RNA.

Now let's add the sugar to which the nitrogenous base is attached. In DNA the sugar is **deoxyribose**; in RNA it is **ribose** (see Figure 5.23c). The only difference between these two sugars is that deoxyribose lacks an oxygen atom on the second carbon in the ring, hence the name *deoxy*ribose.

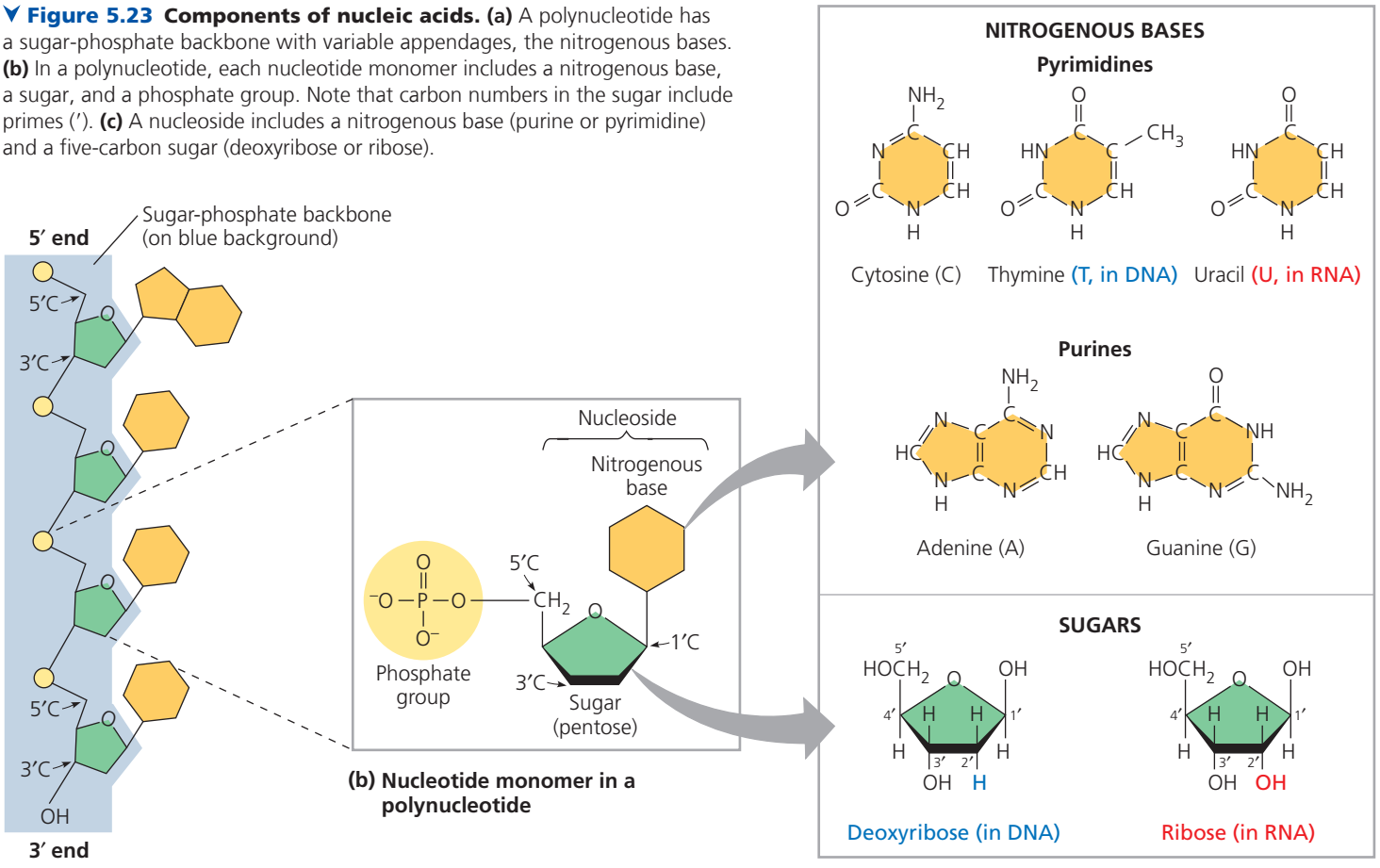
So far, we have built a nucleoside (base plus sugar). To complete the construction of a nucleotide, we attach one to three phosphate groups to the 5′ carbon of the sugar (the carbon numbers in the sugar include ′, the prime symbol; see Figure 5.23b). With one phosphate, this is a nucleoside monophosphate, more often called a nucleotide.

Nucleotide Polymers

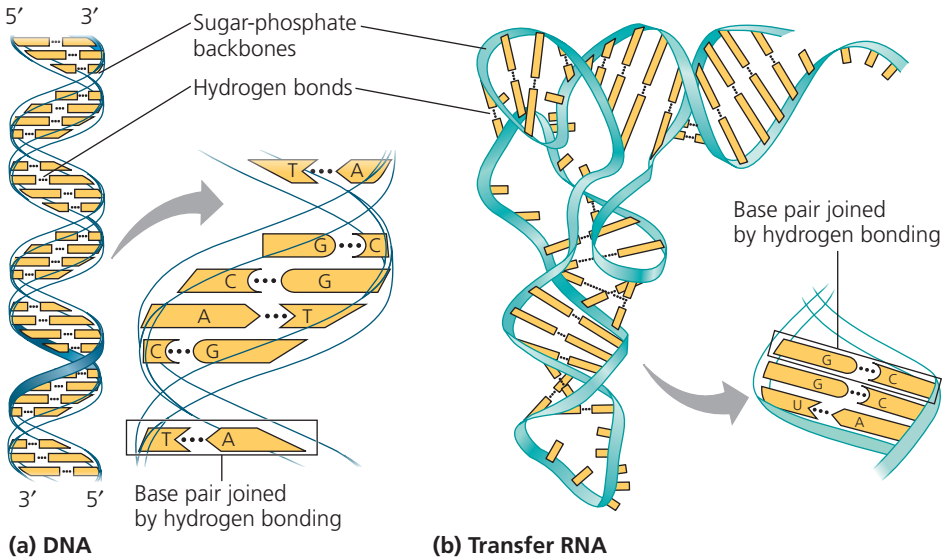
The linkage of nucleotides into a polynucleotide involves a dehydration reaction. (You will learn the details in Concept 16.2.) In the polynucleotide, adjacent nucleotides are joined by a phosphodiester linkage, which consists of a phosphate group that links the sugars of two nucleotides. This bonding results in a repeating pattern of sugar-phosphate units called the *sugar-phosphate backbone* (see Figure 5.23a). (Note that the nitrogenous bases are not part of the backbone.) The two free ends of the polymer are distinctly different from each other. One end has a phosphate attached to a 5′ carbon, and the other end has a hydroxyl group on a 3′ carbon; we refer to these as the *5′ end* and the *3′ end*, respectively. We can say that a polynucleotide has a built-in directionality along its sugar-phosphate backbone, from 5′ to 3′, somewhat like a one-way street. The bases are attached all along the sugar-phosphate backbone.

The sequence of bases along a DNA (or mRNA) polymer is unique for each gene and provides very specific information to the cell. Because genes are hundreds to thousands of nucleotides long, the number of possible base sequences is effectively limitless. The information carried by the gene is encoded in its specific sequence of the four DNA bases. For example, the sequence 5′-AGGTAACTT-3′ means one thing, whereas the sequence 5′-CGCTTTAAC-3′ has a different meaning. (Entire genes, of course, are much longer.) The linear order of bases in a gene specifies the amino acid sequence—the primary structure—of a protein, which in turn specifies that protein's 3-D structure, thus enabling its function in the cell.

Figure 5.23 Components of nucleic acids. (a) A polynucleotide has a sugar-phosphate backbone with variable appendages, the nitrogenous bases. **(b)** In a polynucleotide, each nucleotide monomer includes a nitrogenous base, a sugar, and a phosphate group. Note that carbon numbers in the sugar include primes (′). **(c)** A nucleoside includes a nitrogenous base (purine or pyrimidine) and a five-carbon sugar (deoxyribose or ribose).



HHMI Animation: The Chemical Structure of DNA



➤ Figure 5.24 The structures of DNA and tRNA molecules. (a) The DNA molecule is usually a double helix, with the sugar-phosphate backbones of the antiparallel polynucleotide strands (symbolized here by blue ribbons) on the outside of the helix. Hydrogen bonds between pairs of nitrogenous bases hold the two strands together. As illustrated here with symbolic shapes for the bases, adenine (A) can pair only with thymine (T), and guanine (G) can pair only with cytosine (C). Each DNA strand in this figure is the structural equivalent of the polynucleotide diagrammed in Figure 5.23a. **(b)** A tRNA molecule has a roughly L-shaped structure due to complementary base pairing of antiparallel stretches of RNA. In RNA, A pairs with U.

HHMI Animation: Paired DNA Strands

The Structures of DNA and RNA Molecules

DNA molecules have two polynucleotides, or "strands," that wind around an imaginary axis, forming a **double helix (Figure 5.24a)**. The two sugar-phosphate backbones run in opposite 5′ → 3′ directions from each other; this arrangement is referred to as **antiparallel**, somewhat like a divided highway. The sugar-phosphate backbones are on the outside of the helix, and the nitrogenous bases are paired in the interior of the helix. The two strands are held together by hydrogen bonds between the paired bases (see Figure 5.24a). Most DNA molecules are very long, with thousands or even millions of base pairs. The one long DNA double helix in a eukaryotic chromosome includes many genes, each one a particular segment of the molecule.

In base pairing, only certain bases in the double helix are compatible with each other. Adenine (A) in one strand always pairs with thymine (T) in the other, and guanine (G) always pairs with cytosine (C). Reading the sequence of bases along one strand of the double helix would tell us the sequence of bases along the other strand. If a stretch of one strand has the base sequence 5′-AGGTCCG-3′, then the base-pairing rules tell us that the same stretch of the other strand must have the sequence 3′-TCCAGGC-5′ The two strands of the double helix are *complementary*, each the predictable counterpart of the other. It is this feature of DNA that makes it possible to generate two identical copies of each DNA molecule in a cell that is preparing to divide. When the cell divides, the copies are distributed to the daughter cells, making them genetically identical to the parent cell. Thus, the structure of DNA accounts for its function of transmitting genetic information whenever a cell reproduces.

RNA molecules, by contrast, exist as single strands. Complementary base pairing can occur, however, between regions of two RNA molecules or even between two stretches of nucleotides in the *same* RNA molecule. In fact, base pairing within an RNA molecule allows it to take on the particular three-dimensional shape necessary for its function. Consider, for example, the type of RNA called *transfer RNA* (*tRNA*), which brings amino acids to the ribosome during the synthesis of a polypeptide. A tRNA molecule is about 80 nucleotides in length. Its functional shape results from base pairing between nucleotides where complementary stretches of the molecule can run antiparallel to each other **(Figure 5.24b)**.

Note that in RNA, adenine (A) pairs with uracil (U); thymine (T) is not present in RNA. Another difference between RNA and DNA is that DNA almost always exists as a double helix, whereas RNA molecules are more variable in shape. RNAs are versatile molecules, and many biologists believe RNA may have preceded DNA as the carrier of genetic information in early forms of life (see Concept 25.1).

Animation: Nucleic Acid Structure

CONCEPT CHECK 5.5

1. **DRAW IT ➤** Go to Figure 5.23a and, for the top three nucleotides, number all the carbons in the sugars, circle the nitrogenous bases, and star the phosphates.
2. **DRAW IT ➤** In a DNA double helix, a region along one DNA strand has this sequence of nitrogenous bases: 5′-TAGGCCT-3′. Copy this sequence, and write down its complementary strand, clearly indicating the 5′ and 3′ ends of the complementary strand.

For suggested answers, see Appendix A.

CONCEPT 5.6

Genomics and proteomics have transformed biological inquiry and applications

Experimental work in the first half of the 20th century established the role of DNA as the bearer of genetic information, passed from generation to generation, that

specified the functioning of living cells and organisms. Once the structure of the DNA molecule was described in 1953, and the linear sequence of nucleotide bases was understood to specify the amino acid sequence of proteins, biologists sought to "decode" genes by learning their nucleotide sequences (often called "base sequences").

The first chemical techniques for *DNA sequencing*, or determining the sequence of nucleotides along a DNA strand, one by one, were developed in the 1970s. Researchers began to study gene sequences, gene by gene, and the more they learned, the more questions they had: How was expression of genes regulated? Genes and their protein products clearly interacted with each other, but how? What was the function, if any, of the DNA that is not part of genes? To fully understand the genetic functioning of a living organism, the entire sequence of the full complement of DNA, the organism's *genome*, would be most enlightening. In spite of the apparent impracticality of this idea, in the late 1980s several prominent biologists put forth an audacious proposal to launch a project that would sequence the entire human genome—all 3 billion bases of it! This endeavor began in 1990 and was effectively completed in the early 2000s.

An unplanned but profound side benefit of this project—the Human Genome Project—was the rapid development of faster and less expensive methods of sequencing. This trend has continued: The cost for sequencing 1 million bases in 2001, well over $5,000, has decreased to less than $0.02 in 2016. And a human genome, the first of which took over 10 years to sequence, could be completed at today's pace in just a few days **(Figure 5.25)**. The number of genomes that have been fully sequenced has burgeoned, generating reams of data and prompting development of **bioinformatics**, the use of computer software and other computational tools that can handle and analyze these large data sets.

The reverberations of these developments have transformed the study of biology and related fields. Biologists often look at problems by analyzing large sets of genes or even comparing whole genomes of different species, an approach called **genomics**. A similar analysis of large sets of proteins, including their sequences, is called **proteomics**. (Protein sequences can be determined either by using biochemical techniques or by translating the DNA sequences that code for them.) These approaches permeate all fields of biology, some examples of which are shown in **Figure 5.26**.

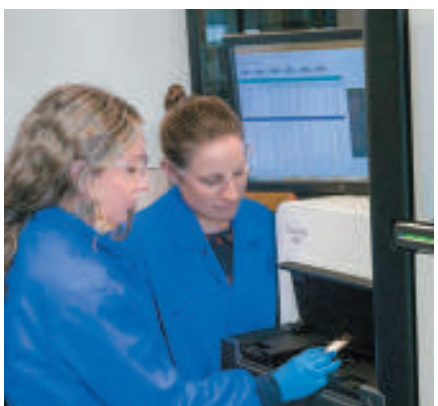


Figure 5.25
Automatic DNA sequencing machines and abundant computing power enable rapid sequencing of genes and genomes.

Perhaps the most significant impact of genomics and proteomics on the field of biology as a whole has been their contributions to our understanding of evolution. In addition to confirming evidence for evolution from the study of fossils and characteristics of currently existing species, genomics has helped us tease out relationships among different groups of organisms that had not been resolved by previous types of evidence, and thus infer evolutionary history.

DNA and Proteins as Tape Measures of Evolution

EVOLUTION We are accustomed to thinking of shared traits, such as hair and milk production in mammals, as evidence of shared ancestry. Because DNA carries heritable information in the form of genes, sequences of genes and their protein products document the hereditary background of an organism. The linear sequences of nucleotides in DNA molecules are passed from parents to offspring; these sequences determine the amino acid sequences of proteins. As a result, siblings have greater similarity in their DNA and proteins than do unrelated individuals of the same species.

Given our evolutionary view of life, we can extend this concept of "molecular genealogy" to relationships between species: We would expect two species that appear to be closely related based on anatomical evidence (and possibly fossil evidence) to also share a greater proportion of their DNA and protein sequences than do less closely related species. In fact, that is the case. An example is the comparison of the β polypeptide chain of human hemoglobin with the corresponding hemoglobin polypeptide in other vertebrates. In this chain of 146 amino acids, humans and gorillas differ in just 1 amino acid, while humans and frogs, more distantly related, differ in 67 amino acids. In the **Scientific Skills Exercise**, you can apply this sort of reasoning to additional species. And this conclusion holds true as well when comparing whole genomes: The human genome is 95–98% identical to that of the chimpanzee, but only roughly 85% identical to that of the mouse, a more distant evolutionary relative. Molecular biology has added a new tape measure to the toolkit biologists use to assess evolutionary kinship.

Comparing genomic sequences has practical applications as well. In the **Problem-Solving Exercise**, you can see how this type of genomic analysis can help you detect consumer fraud.

CONCEPT CHECK 5.6

1. How would sequencing the entire genome of an organism help scientists to understand how that organism functioned?
2. Given the function of DNA, why would you expect two species with very similar traits to also have very similar genomes?

For suggested answers, see Appendix A.

Figure 5.26 **MAKE CONNECTIONS**

Contributions of Genomics and Proteomics to Biology

Nucleotide sequencing and the analysis of large sets of genes and proteins can be done rapidly and inexpensively due to advances in technology and information processing. Taken together, genomics and proteomics have advanced our understanding of biology across many different fields.

Paleontology

New DNA sequencing techniques have allowed decoding of minute quantities of DNA found in ancient tissues from our extinct relatives, the Neanderthals (*Homo neanderthalensis*). Sequencing the Neanderthal genome has informed our understanding of their physical appearance (as in this reconstruction), as well as their relationship with modern humans. (See Figures 34.51 and 34.52.)

Medical Science

Identifying the genetic basis for human diseases like cancer helps researchers focus their search for potential future treatments. Currently, sequencing the sets of genes expressed in an individual's tumor can allow a more targeted approach to treating the cancer, a type of "personalized medicine." (See Figures 12.20 and 18.27.)

Evolution

A major aim of evolutionary biology is to understand the relationships among species, both living and extinct. For example, genome sequence comparisons have identified the hippopotamus as the land mammal sharing the most recent common ancestor with whales. (See Figure 22.20.)

Hippopotamus

Short-finned pilot whale

Species Interactions

Most plant species exist in a mutually beneficial partnership with fungi (right) and bacteria associated with the plants' roots; these interactions improve plant growth. Genome sequencing and analysis of gene expression have allowed characterization of plant-associated communities. Such studies will help advance our understanding of such interactions and may improve agricultural practices. (See the Chapter 31 Scientific Skills Exercise and Figure 37.11.)

Conservation Biology

The tools of molecular genetics and genomics are increasingly used by forensic ecologists to identify which species of animals and plants are killed illegally. In one case, genomic sequences of DNA from illegal shipments of elephant tusks were used to track down poachers and pinpoint the territory where they were operating. (See Figure 56.9.)

MAKE CONNECTIONS ➤ *Considering the examples provided here, describe how the approaches of genomics and proteomics help us to address a variety of biological questions.*

HHMI Video: The Making of the Fittest: The Birth and Death of Genes (Icefish)

SCIENTIFIC SKILLS EXERCISE

Analyzing Polypeptide Sequence Data

Are Rhesus Monkeys or Gibbons More Closely Related to Humans? In this exercise, you will look at amino acid sequence data for the β polypeptide chain of hemoglobin, often called β-globin. You will then interpret the data to hypothesize whether the monkey or the gibbon is more closely related to humans.

How Such Experiments Are Done Researchers can isolate the polypeptide of interest from an organism and then determine the amino acid sequence. More frequently, the DNA of the relevant gene is sequenced, and the amino acid sequence of the polypeptide is deduced from the DNA sequence of its gene.

Data from the Experiments In the data below, the letters give the sequence of the 146 amino acids in β-globin from humans, rhesus monkeys, and gibbons. Because a complete sequence would not fit on one line here, the sequences are broken into three segments. The sequences for the three different species are aligned so that you can compare them easily. For example, you can see that for all three species, the first amino acid is V (valine) and the 146th amino acid is H (histidine).

Species	Alignment of Amino Acid Sequences of β-globin
Human	1 VHLTPEEKSA VTALWGKVNV DEVGGEALGR LLVVYPWTQR FFESFGDLST
Monkey	1 VHLTPEEKNA VTTLWGKVNV DEVGGEALGR LLLVYPWTQR FFESFGDLSS
Gibbon	1 VHLTPEEKSA VTALWGKVNV DEVGGEALGR LLVVYPWTQR FFESFGDLST
Human	51 PDAVMGNPKV KAHGKKVLGA FSDGLAHLDN LKGTFATLSE LHCDKLHVDP
Monkey	51 PDAVMGNPKV KAHGKKVLGA FSDGLNHLDN LKGTFAQLSE LHCDKLHVDP
Gibbon	51 PDAVMGNPKV KAHGKKVLGA FSDGLAHLDN LKGTFAQLSE LHCDKLHVDP
Human	101 ENFRLLGNVL VCVLAHHFGK EFTPPVQAAY QKVVAGVANA LAHKYH
Monkey	101 ENFKLLGNVL VCVLAHHFGK EFTPQVQAAY QKVVAGVANA LAHKYH
Gibbon	101 ENFRLLGNVL VCVLAHHFGK EFTPQVQAAY QKVVAGVANA LAHKYH

INTERPRET THE DATA

1. Scan the monkey and gibbon sequences, letter by letter, circling any amino acids that do not match the human sequence. (a) How many amino acids differ between the monkey and the human sequences? (b) Between the gibbon and human?
2. For each nonhuman species, what percent of its amino acids are identical to the human sequence of β-globin?
3. Based on these data alone, state a hypothesis for which of these two species is more closely related to humans. What is your reasoning?
4. What other evidence could you use to support your hypothesis?

Data from Human: http://www.ncbi.nlm.nih.gov/protein/AAA21113.1; rhesus monkey: http://www.ncbi.nlm.nih.gov/protein/122634; gibbon: http://www.ncbi.nlm.nih.gov/protein/122616

Instructors: A version of this Scientific Skills Exercise can be assigned in MasteringBiology.

PROBLEM-SOLVING EXERCISE

Are you a victim of fish fraud?

When buying salmon, perhaps you prefer the more expensive wild-caught Pacific salmon (*Oncorhynchus* species) over farmed Atlantic salmon (*Salmo salar*). But studies reveal that about 40% of the time, you aren't getting the fish you paid for! Watch the video in the MasteringBiology Study Area for more information.

ABC News Video: Fake Fish in Stores and Restaurants

Instructors: A version of this Problem-Solving Exercise can be assigned in Chapter 5 of MasteringBiology. A more extensive investigation is in Chapter 26 of MasteringBiology.

In this exercise, you will investigate whether a piece of salmon has been fraudulently labeled.

Your Approach The principle guiding your investigation is that DNA sequences from within a species or from closely related species are more similar to each other than are sequences from more distantly related species.

Your Data You've been sold a piece of salmon labeled as coho salmon (*Oncorhynchus kisutch*). To see whether your fish was labeled correctly, you will compare a short DNA sequence from your sample to standard sequences from the same gene for three salmon species. The sequences are:

Sample labeled as *O. kisutch* (coho salmon)		5′–CGGCACCGCCCTAAGTCTCT–3′
Standard sequences	Sequence for *O. kisutch* (coho salmon)	5′–AGGCACCGCCCTAAGTCTAC–3′
	Sequence for *O. keta* (chum salmon)	5′–AGGCACCGCCCTGAGCCTAC–3′
	Sequence for *Salmo salar* (Atlantic salmon)	5′–CGGCACCGCCCTAAGTCTCT–3′

Your Analysis

1. Scan along the standard sequences (*O. kisutch, O. keta*, and *S. salar*), base by base, circling any bases that do not match the sequence from your fish sample.
2. How many bases differ between (a) *O. kisutch* and your fish sample? (b) *O. keta* and the sample? (c) *S. salar* and the sample?
3. For each standard, what percentage of its bases are identical to your sample?
4. Based on these data alone, state a hypothesis for the species identity of your sample. What is your reasoning?

5 Chapter Review

Go to **MasteringBiology**™ for Videos, Animations, Vocab Self-Quiz, Practice Tests, and more in the Study Area.

SUMMARY OF KEY CONCEPTS

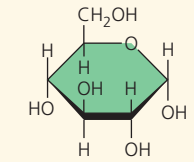
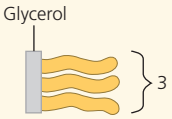
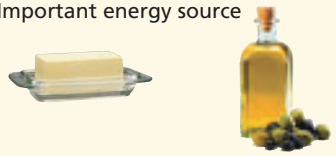
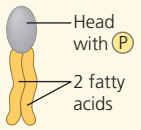
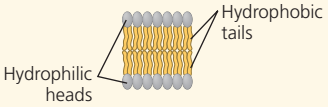
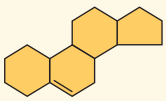
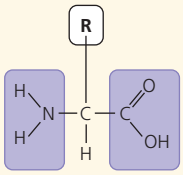
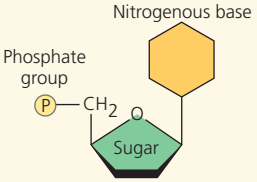
CONCEPT 5.1

Macromolecules are polymers, built from monomers *(pp. 67–68)*

VOCAB SELF-QUIZ goo.gl/6u55ks

- Large carbohydrates (polysaccharides), proteins, and nucleic acids are **polymers**, which are chains of **monomers**. The components of lipids vary. Monomers form larger molecules by **dehydration reactions**, in which water molecules are released. Polymers can disassemble by the reverse process, **hydrolysis**. An immense variety of polymers can be built from a small set of monomers.

? *What is the fundamental basis for the differences between large carbohydrates, proteins, and nucleic acids?*

Large Biological Molecules	Components	Examples	Functions
CONCEPT 5.2 **Carbohydrates serve as fuel and building material** *(pp. 68–72)* ? *Compare the composition, structure, and function of starch and cellulose. What role do starch and cellulose play in the human body?*	 Monosaccharide monomer	**Monosaccharides:** glucose, fructose	Fuel; carbon sources that can be converted to other molecules or combined into polymers
		Disaccharides: lactose, sucrose	
		Polysaccharides: ▪ Cellulose (plants) ▪ Starch (plants) ▪ Glycogen (animals) ▪ Chitin (animals and fungi)	▪ Strengthens plant cell walls ▪ Stores glucose for energy ▪ Stores glucose for energy ▪ Strengthens exoskeletons and fungal cell walls
CONCEPT 5.3 **Lipids are a diverse group of hydrophobic molecules** *(pp. 72–75)* ? *Why are lipids not considered to be polymers or macromolecules?*		**Triacylglycerols** (fats or oils): glycerol + three fatty acids	Important energy source 
		**Phospholipids:** glycerol + phosphate group + two fatty acids	Lipid bilayers of membranes 
	 Steroid backbone	**Steroids:** four fused rings with attached chemical groups	▪ Component of cell membranes (cholesterol) ▪ Signaling molecules that travel through the body (hormones)
CONCEPT 5.4 **Proteins include a diversity of structures, resulting in a wide range of functions** *(pp. 75–83)* ? *Explain the basis for the great diversity of proteins.*	 Amino acid monomer (20 types)	▪ Enzymes ▪ Defensive proteins ▪ Storage proteins ▪ Transport proteins ▪ Hormones ▪ Receptor proteins ▪ Motor proteins ▪ Structural proteins	▪ Catalyze chemical reactions ▪ Protect against disease ▪ Store amino acids ▪ Transport substances ▪ Coordinate organismal responses ▪ Receive signals from outside cell ▪ Function in cell movement ▪ Provide structural support
CONCEPT 5.5 **Nucleic acids store, transmit, and help express hereditary information** *(pp. 84–86)* ? *What role does complementary base pairing play in the functions of nucleic acids?*	 Nucleotide (monomer of a polynucleotide)	**DNA:**  ▪ Sugar = deoxyribose ▪ Nitrogenous bases = C, G, A, T ▪ Usually double-stranded	Stores hereditary information
		RNA:  ▪ Sugar = ribose ▪ Nitrogenous bases = C, G, A, U ▪ Usually single-stranded	Various functions in gene expression, including carrying instructions from DNA to ribosomes

CONCEPT 5.6

Genomics and proteomics have transformed biological inquiry and applications *(pp. 86–89)*

- Recent technological advances in DNA sequencing have given rise to **genomics**, an approach that analyzes large sets of genes or whole genomes, and **proteomics**, a similar approach for large sets of proteins. **Bioinformatics** is the use of computational tools and computer software to analyze these large data sets.
- The more closely two species are related evolutionarily, the more similar their DNA sequences are. DNA sequence data confirm models of evolution based on fossils and anatomical evidence.

? *Given the sequences of a particular gene in fruit flies, fish, mice, and humans, predict the relative similarity of the human sequence to that of each of the other species.*

TEST YOUR UNDERSTANDING

Level 1: Knowledge/Comprehension

PRACTICE TEST goo.gl/CUYGKD

1. Which of the following categories includes all others in the list?
   (A) disaccharide
   (B) polysaccharide
   (C) starch
   (D) carbohydrate
2. The enzyme amylase can break glycosidic linkages between glucose monomers only if the monomers are in the α form. Which of the following could amylase break down?
   (A) glycogen, starch, and amylopectin
   (B) glycogen and cellulose
   (C) cellulose and chitin
   (D) starch, chitin, and cellulose
3. Which of the following is true of *unsaturated* fats?
   (A) They are more common in animals than in plants.
   (B) They have double bonds in their fatty acid chains.
   (C) They generally solidify at room temperature.
   (D) They contain more hydrogen than do saturated fats having the same number of carbon atoms.
4. The structural level of a protein *least* affected by a disruption in hydrogen bonding is the
   (A) primary level.
   (B) secondary level.
   (C) tertiary level.
   (D) quaternary level.
5. Enzymes that break down DNA catalyze the hydrolysis of the covalent bonds that join nucleotides together. What would happen to DNA molecules treated with these enzymes?
   (A) The two strands of the double helix would separate.
   (B) The phosphodiester linkages of the polynucleotide backbone would be broken.
   (C) The pyrimidines would be separated from the deoxyribose sugars.
   (D) All bases would be separated from the deoxyribose sugars.

Level 2: Application/Analysis

6. The molecular formula for glucose is $C_6H_{12}O_6$. What would be the molecular formula for a polymer made by linking ten glucose molecules together by dehydration reactions?
   (A) $C_{60}H_{120}O_{60}$
   (B) $C_{60}H_{102}O_{51}$
   (C) $C_{60}H_{100}O_{50}$
   (D) $C_{60}H_{111}O_{51}$
7. Which of the following pairs of base sequences could form a short stretch of a normal double helix of DNA?
   (A) 5′-AGCT-3′ with 5′-TCGA-3′
   (B) 5′-GCGC-3′ with 5′-TATA-3′
   (C) 5′-ATGC-3′ with 5′-GCAT-3′
   (D) All of these pairs are correct.
8. Construct a table that organizes the following terms, and label the columns and rows.

Monosaccharides	Polypeptides	Phosphodiester linkages
Fatty acids	Triacylglycerols	Peptide bonds
Amino acids	Polynucleotides	Glycosidic linkages
Nucleotides	Polysaccharides	Ester linkages

9. **DRAW IT** Copy the polynucleotide strand in Figure 5.23a and label the bases G, T, C, and T, starting from the 5′ end. Assuming this is a DNA polynucleotide, now draw the complementary strand, using the same symbols for phosphates (circles), sugars (pentagons), and bases. Label the bases. Draw arrows showing the 5′ → 3′ direction of each strand. Use the arrows to make sure the second strand is antiparallel to the first. *Hint*: After you draw the first strand vertically, turn the paper upside down; it is easier to draw the second strand from the 5′ toward the 3′ direction as you go from top to bottom.

Level 3: Synthesis/Evaluation

10. **EVOLUTION CONNECTION** Comparisons of amino acid sequences can shed light on the evolutionary divergence of related species. If you were comparing two living species, would you expect all proteins to show the same degree of divergence? Why or why not? Justify your answer.
11. **SCIENTIFIC INQUIRY** Suppose you are a research assistant in a lab studying DNA-binding proteins. You have been given the amino acid sequences of all the proteins encoded by the genome of a certain species and have been asked to find candidate proteins that could bind DNA. What type of amino acids would you expect to see in the DNA-binding regions of such proteins? Explain your thinking.
12. **WRITE ABOUT A THEME: ORGANIZATION** Proteins, which have diverse functions in a cell, are all polymers of the same kinds of monomers—amino acids. Write a short essay (100–150 words) that discusses how the structure of amino acids allows this one type of polymer to perform so many functions.
13. **SYNTHESIZE YOUR KNOWLEDGE**

Given that the function of egg yolk is to nourish and support the developing chick, explain why egg yolks are so high in fat, protein, and cholesterol.

For selected answers, see Appendix A.

MB For additional practice questions, check out the **Dynamic Study Modules** in MasteringBiology. You can use them to study on your smartphone, tablet, or computer anytime, anywhere!

A Tour of the Cell

6

Figure 6.1 How do your cells help you learn about biology?

KEY CONCEPTS

6.1 Biologists use microscopes and biochemistry to study cells

6.2 Eukaryotic cells have internal membranes that compartmentalize their functions

6.3 The eukaryotic cell's genetic instructions are housed in the nucleus and carried out by the ribosomes

6.4 The endomembrane system regulates protein traffic and performs metabolic functions

6.5 Mitochondria and chloroplasts change energy from one form to another

6.6 The cytoskeleton is a network of fibers that organizes structures and activities in the cell

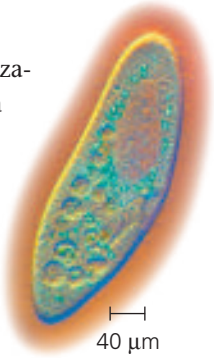
6.7 Extracellular components and connections between cells help coordinate cellular activities

6.8 A cell is greater than the sum of its parts

The Fundamental Units of Life

Cells are as fundamental to the living systems of biology as the atom is to chemistry. Many different types of cells are working for you right now. The contraction of muscle cells moves your eyes as you read this sentence. **Figure 6.1** shows extensions from a nerve cell (orange) making contact with muscle cells (red). The words on the page are translated into signals that nerve cells carry to your brain, where they are passed on to other nerve cells. As you study, your cells make connections between nerve cells that solidify memories and permit learning to occur.

All organisms are made of cells. In the hierarchy of biological organization, the cell is the simplest collection of matter that can be considered a living entity. Indeed, many forms of life exist as single-celled organisms, like the *Paramecium* shown here, a eukaryote that lives in pond water. Larger, more complex organisms, including plants and animals, are multicellular; their bodies are associations of many kinds of specialized cells that could not survive for long on their own. Even when cells are arranged into higher levels of organization, such as tissues and organs, the cell remains the organism's basic unit of structure and function.



All cells are related by their descent from earlier cells. During the long evolutionary history of life on Earth, cells have been modified in many different ways. But although cells can differ substantially from one another, they share common features. In this chapter, we'll first examine the tools and techniques that allow us to understand cells, then tour the cell and become acquainted with its components.

When you see this blue icon, log in to **MasteringBiology** and go to the Study Area for digital resources.

Get Ready for This Chapter

CONCEPT 6.1

Biologists use microscopes and biochemistry to study cells

How can cell biologists investigate the inner workings of a cell, usually too small to be seen by the unaided eye? Before we tour the cell, it will be helpful to learn how cells are studied.

Microscopy

The development of instruments that extend the human senses allowed the discovery and early study of cells. Microscopes were invented in 1590 and further refined during the 1600s. Cell walls were first seen by Robert Hooke in 1665 as he looked through a microscope at dead cells from the bark of an oak tree. But it took the wonderfully crafted lenses of Antoni van Leeuwenhoek to visualize living cells. Imagine Hooke's excitement when he visited van Leeuwenhoek in 1674 and the world of microorganisms—what his host called "very little animalcules"—was revealed to him.

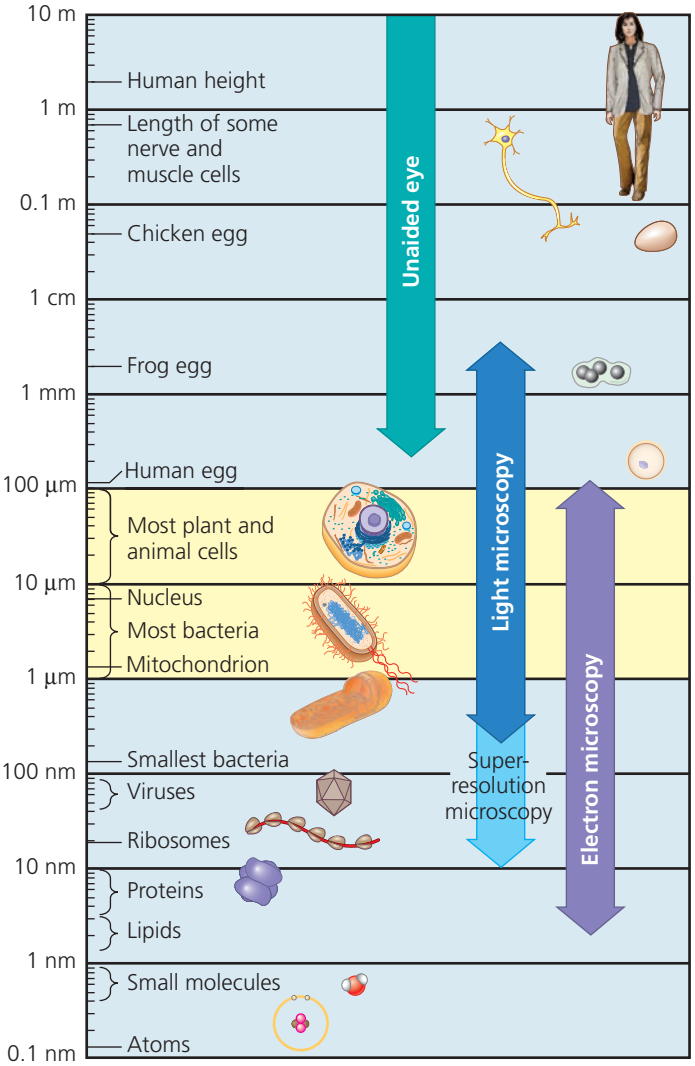
The microscopes first used by Renaissance scientists, as well as the microscopes you are likely to use in the laboratory, are all light microscopes. In a **light microscope (LM)**, visible light is passed through the specimen and then through glass lenses. The lenses refract (bend) the light in such a way that the image of the specimen is magnified as it is projected into the eye or into a camera (see Appendix D).

Three important parameters in microscopy are magnification, resolution, and contrast. *Magnification* is the ratio of an object's image size to its real size. Light microscopes can magnify effectively to about 1,000 times the actual size of the specimen; at greater magnifications, additional details cannot be seen clearly. *Resolution* is a measure of the clarity of the image; it is the minimum distance two points can be separated and still be distinguished as separate points. For example, what appears to the unaided eye as one star in the sky may be resolved as twin stars with a telescope, which has a higher resolving ability than the eye. Similarly, using standard techniques, the light microscope cannot resolve detail finer than about 0.2 micrometer (µm), or 200 nanometers (nm), regardless of the magnification **(Figure 6.2)**. The third parameter, *contrast*, is the difference in brightness between the light and dark areas of an image. Methods for enhancing contrast include staining or labeling cell components to stand out visually. **Figure 6.3** shows some different types of microscopy; study this figure as you read this section.

Until recently, the resolution barrier prevented cell biologists from using standard light microscopy when studying **organelles**, the membrane-enclosed structures within eukaryotic cells. To see these structures in any detail required the development of a new instrument. In the 1950s, the electron microscope was introduced to biology. Rather than focusing light, the **electron microscope (EM)** focuses a beam of electrons through the specimen or onto its surface (see Appendix D). Resolution is inversely related to the wavelength of the light (or electrons) a microscope uses for imaging, and electron beams have much shorter wavelengths than visible light. Modern electron microscopes can theoretically achieve a resolution of about 0.002 nm, though in practice they usually cannot resolve structures smaller than about 2 nm across. Still, this is a 100-fold improvement over the standard light microscope.

The **scanning electron microscope (SEM)** is especially useful for detailed study of the topography

Figure 6.2 The size range of cells. Most cells are between 1 and 100 µm in diameter (yellow region of chart) and their components are even smaller (see Figure 6.32), as are viruses. Notice that the scale along the left side is logarithmic, to accommodate the range of sizes shown. Starting at the top of the scale with 10 m and going down, each reference measurement marks a tenfold decrease in diameter or length. For a complete table of the metric system, see Appendix C.



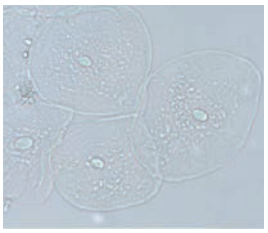
1 centimeter (cm) = 10^{-2} meter (m) = 0.4 inch
1 millimeter (mm) = 10^{-3} m
1 micrometer (µm) = 10^{-3} mm = 10^{-6} m
1 nanometer (nm) = 10^{-3} µm = 10^{-9} m

Animation: Metric System Review

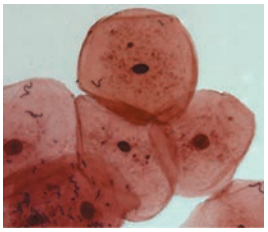
Figure 6.3 Exploring Microscopy

Light Microscopy (LM)

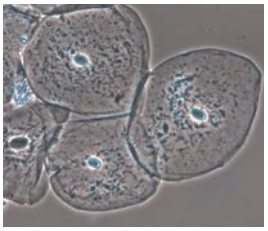
Brightfield (unstained specimen). Light passes directly through the specimen. Unless the cell is naturally pigmented or artificially stained, the image has little contrast. (The first four light micrographs show human cheek epithelial cells; the scale bar pertains to all four micrographs.)



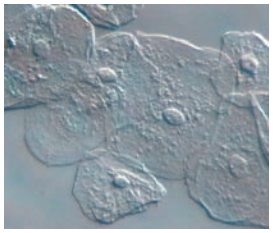
Brightfield (stained specimen). Staining with various dyes enhances contrast. Most staining procedures require that cells be fixed (preserved), thereby killing them.



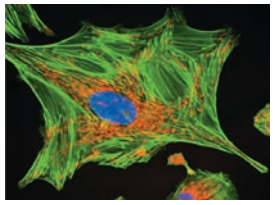
Phase-contrast. Variations in density within the specimen are amplified to enhance contrast in unstained cells; this is especially useful for examining living, unpigmented cells.



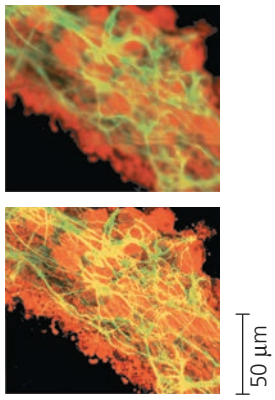
Differential interference contrast (Nomarski). As in phase-contrast microscopy, optical modifications are used to exaggerate differences in density; the image appears almost 3-D.



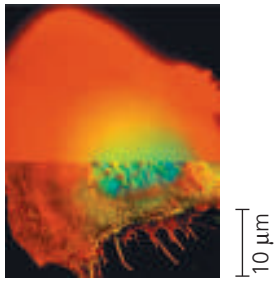
Fluorescence. The locations of specific molecules in the cell can be revealed by labeling the molecules with fluorescent dyes or antibodies; some cells have molecules that fluoresce on their own. Fluorescent substances absorb ultraviolet radiation and emit visible light. In this fluorescently labeled uterine cell, nuclear material is blue, organelles called mitochondria are orange, and the cell's "skeleton" is green.



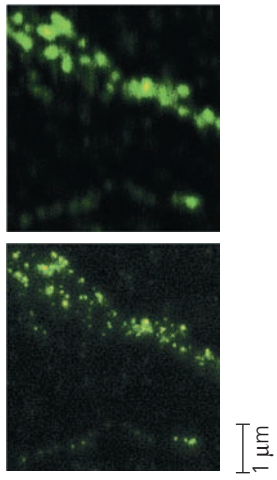
Confocal. The top image is a standard fluorescence micrograph of fluorescently labeled nervous tissue (nerve cells are green, support cells are orange, and regions of overlap are yellow); below it is a confocal image of the same tissue. Using a laser, this "optical sectioning" technique eliminates out-of-focus light from a thick sample, creating a single plane of fluorescence in the image. By capturing sharp images at many different planes, a 3-D reconstruction can be created. The standard image is blurry because out-of-focus light is not excluded.



Deconvolution. The top of this split image is a compilation of standard fluorescence micrographs through the depth of a white blood cell. Below is an image of the same cell reconstructed from many blurry images at different planes, each of which was processed using deconvolution software. This process digitally removes out-of-focus light and reassigns it to its source, creating a much sharper 3-D image.



Super-resolution. On the top is a confocal image of part of a nerve cell, using a fluorescent label that binds to a molecule clustered in small sacs in the cell (vesicles) that are 40 nm in diameter. The greenish-yellow spots are blurry because 40 nm is below the 200-nm limit of resolution for standard light microscopy. Below is an image of the same part of the cell, seen using a new super-resolution technique. Sophisticated equipment is used to light up individual fluorescent molecules and record their position. Combining information from many molecules in different places "breaks" the limit of resolution, resulting in the sharp greenish-yellow dots seen here. (Each dot is a 40-nm vesicle.)

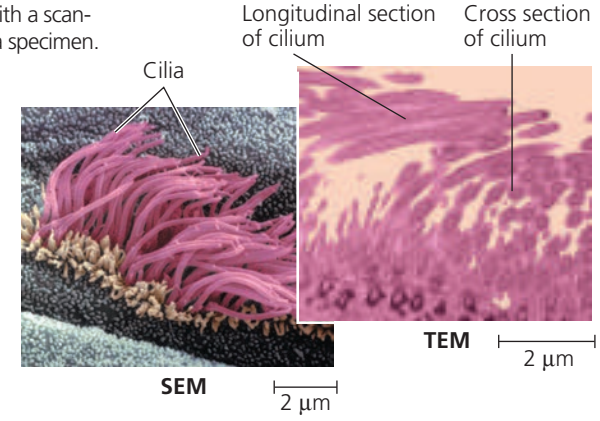


Electron Microscopy (EM)

Scanning electron microscopy (SEM). Micrographs taken with a scanning electron microscope show a 3-D image of the surface of a specimen. This SEM shows the surface of a cell from a trachea (windpipe) covered with cell projections called cilia. Electron micrographs are black and white but are often artificially colorized to highlight particular structures, as has been done with both electron micrographs shown here.

Abbreviations used in figure legends in this text:
LM = Light Micrograph
SEM = Scanning Electron Micrograph
TEM = Transmission Electron Micrograph

VISUAL SKILLS ➤ *When the tissue was sliced for the TEM, what was the orientation of the cilia in the upper left? On the right? Explain how the orientation determined the type of section we see.*



Transmission electron microscopy (TEM). A transmission electron microscope profiles a thin section of a specimen. This TEM shows a section through a tracheal cell, revealing its internal structure. In preparing the specimen, some cilia were cut along their lengths, creating longitudinal sections, while other cilia were cut straight across, creating cross sections.

of a specimen (see Figure 6.3). The electron beam scans the surface of the sample, usually coated with a thin film of gold. The beam excites electrons on the surface, and these secondary electrons are detected by a device that translates the pattern of electrons into an electronic signal sent to a video screen. The result is an image of the specimen's surface that appears three-dimensional.

The **transmission electron microscope (TEM)** is used to study the internal structure of cells (see Figure 6.3). The TEM aims an electron beam through a very thin section of the specimen, much as a light microscope aims light through a sample on a slide. For the TEM, the specimen has been stained with atoms of heavy metals, which attach to certain cellular structures, thus enhancing the electron density of some parts of the cell more than others. The electrons passing through the specimen are scattered more in the denser regions, so fewer are transmitted. The image displays the pattern of transmitted electrons. Instead of using glass lenses, both the SEM and TEM use electromagnets as lenses to bend the paths of the electrons, ultimately focusing the image onto a monitor for viewing.

Electron microscopes have revealed many subcellular structures that were impossible to resolve with the light microscope. But the light microscope offers advantages, especially in studying living cells. A disadvantage of electron microscopy is that the methods used to prepare the specimen kill the cells. Specimen preparation for any type of microscopy can introduce artifacts, structural features seen in micrographs that do not exist in the living cell.

In the past several decades, light microscopy has been revitalized by major technical advances (see Figure 6.3). Labeling individual cellular molecules or structures with fluorescent markers has made it possible to see such structures with increasing detail. In addition, both confocal and deconvolution microscopy have produced sharper images of three-dimensional tissues and cells. Finally, a group of new techniques and labeling molecules developed in recent years has allowed researchers to "break" the resolution barrier and distinguish subcellular structures even as small as 10–20 nm across. As this *super-resolution microscopy* becomes more widespread, the images we see of living cells are proving as exciting for us as van Leeuwenhoek's were for Robert Hooke 350 years ago.

Microscopes are the most important tools of *cytology*, the study of cell structure. Understanding the function of each structure, however, required the integration of cytology and *biochemistry*, the study of the chemical processes (metabolism) of cells.

Cell Fractionation

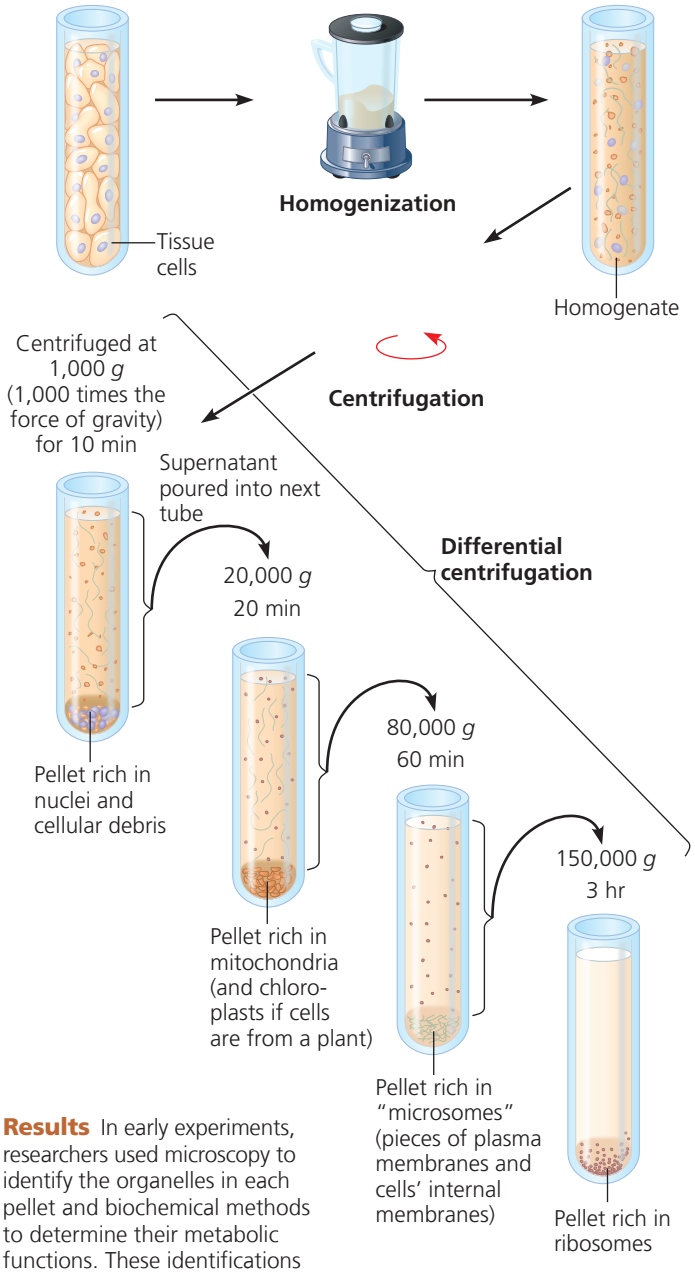
A useful technique for studying cell structure and function is **cell fractionation** **(Figure 6.4)**, which takes cells apart and separates major organelles and other subcellular

Figure 6.4

Research Method Cell Fractionation

Application Cell fractionation is used to separate (fractionate) cell components based on size and density.

Technique Cells are homogenized in a blender to break them up. The resulting mixture (homogenate) is centrifuged. The supernatant (the liquid above the pellet) is poured into another tube and centrifuged at a higher speed for a longer period. This process is repeated several times. This "differential centrifugation" results in a series of pellets, each containing different cell components.



Results In early experiments, researchers used microscopy to identify the organelles in each pellet and biochemical methods to determine their metabolic functions. These identifications established a baseline for this method, enabling today's researchers to know which cell fraction they should collect in order to isolate and study particular organelles.

MAKE CONNECTIONS ➤ *If you wanted to study the process of translation of proteins from mRNA, which part of which fraction would you use? (See Figure 5.22.)*

structures from one another. The piece of equipment that is used for this task is the centrifuge, which spins test tubes holding mixtures of disrupted cells at a series of increasing speeds. At each speed, the resulting force causes a subset of the cell components to settle to the bottom of the tube, forming a pellet. At lower speeds, the pellet consists of larger components, and higher speeds result in a pellet with smaller components.

Cell fractionation enables researchers to prepare specific cell components in bulk and identify their functions, a task not usually possible with intact cells. For example, on one of the cell fractions, biochemical tests showed the presence of enzymes involved in cellular respiration, while electron microscopy revealed large numbers of the organelles called mitochondria. Together, these data helped biologists determine that mitochondria are the sites of cellular respiration. Biochemistry and cytology thus complement each other in correlating cell function with structure.

CONCEPT CHECK 6.1

1. How do stains used for light microscopy compare with those used for electron microscopy?
2. **WHAT IF?** ➤ Which type of microscope would you use to study (a) the changes in shape of a living white blood cell and (b) the details of surface texture of a hair?

For suggested answers, see Appendix A.

CONCEPT 6.2

Eukaryotic cells have internal membranes that compartmentalize their functions

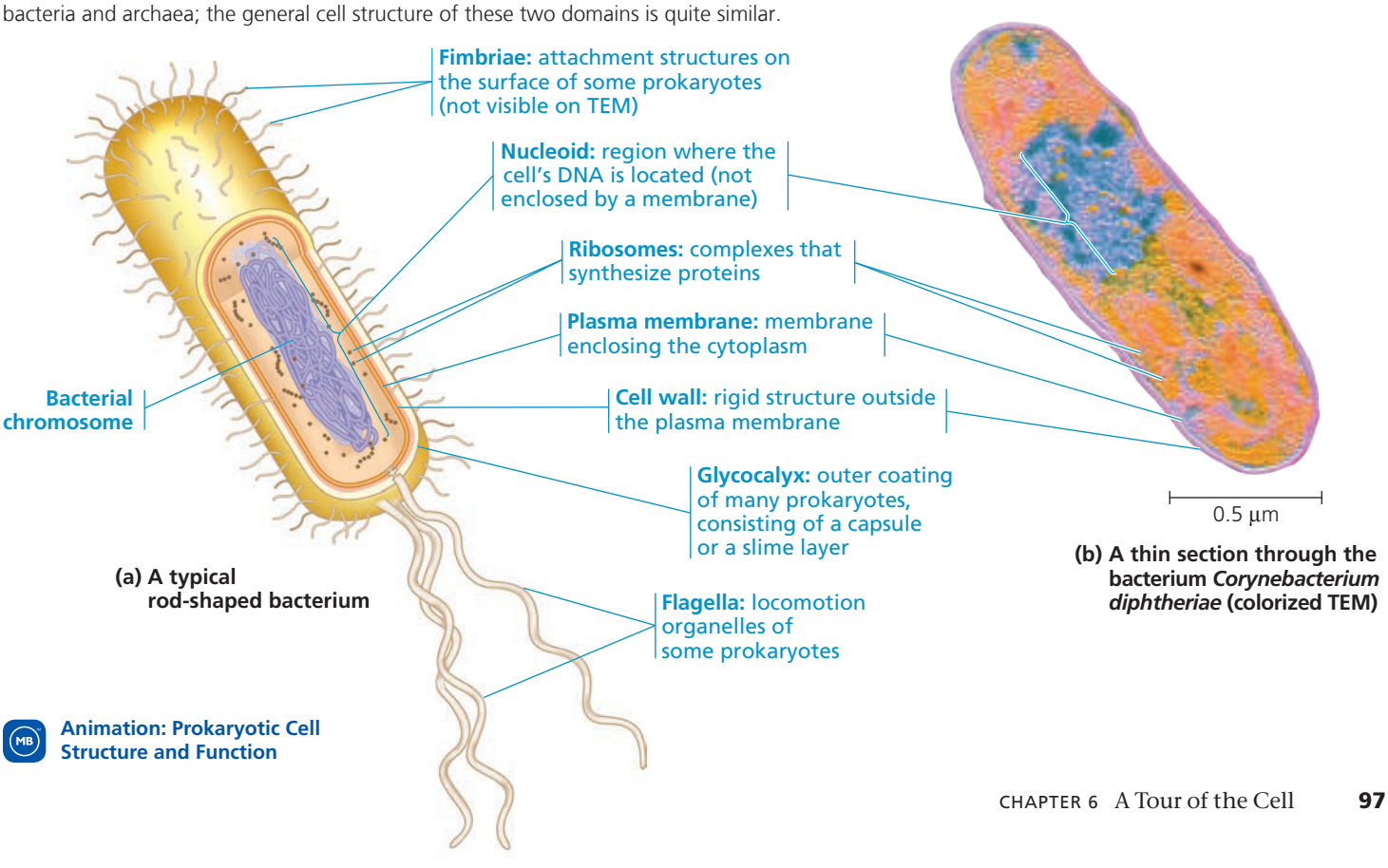
Cells—the basic structural and functional units of every organism—are of two distinct types: prokaryotic and eukaryotic. Organisms of the domains Bacteria and Archaea consist of prokaryotic cells. Protists, fungi, animals, and plants all consist of eukaryotic cells. ("Protist" is an informal term referring to a diverse group of mostly unicellular eukaryotes.)

Comparing Prokaryotic and Eukaryotic Cells

All cells share certain basic features: They are all bounded by a selective barrier, called the *plasma membrane* (also referred to as the cell membrane). Inside all cells is a semifluid, jellylike substance called **cytosol**, in which subcellular components are suspended. All cells contain *chromosomes*, which carry genes in the form of DNA. And all cells have *ribosomes*, tiny complexes that make proteins according to instructions from the genes.

A major difference between prokaryotic and eukaryotic cells is the location of their DNA. In a **eukaryotic cell**, most of the DNA is in an organelle called the *nucleus*, which is bounded by a double membrane (see Figure 6.8). In a **prokaryotic cell**, the DNA is concentrated in a region that is not membrane-enclosed, called the **nucleoid** (Figure 6.5).

Figure 6.5 A prokaryotic cell. Lacking a true nucleus and the other membrane-enclosed organelles of the eukaryotic cell, the prokaryotic cell appears much simpler in internal structure. Prokaryotes include bacteria and archaea; the general cell structure of these two domains is quite similar.



(a) A typical rod-shaped bacterium

(b) A thin section through the bacterium *Corynebacterium diphtheriae* (colorized TEM)

Animation: Prokaryotic Cell Structure and Function

Eukaryotic means "true nucleus" (from the Greek *eu*, true, and *karyon*, kernel, referring to the nucleus), and *prokaryotic* means "before nucleus" (from the Greek *pro*, before), reflecting the earlier evolution of prokaryotic cells.

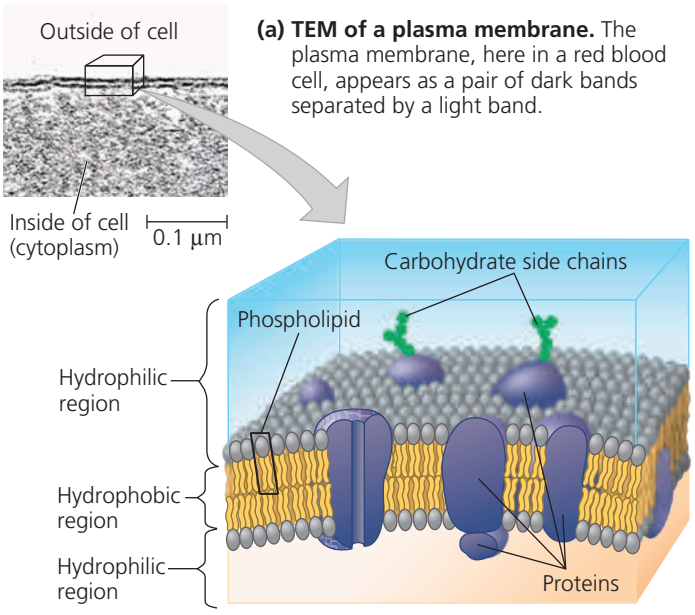
The interior of either type of cell is called the **cytoplasm**; in eukaryotic cells, this term refers only to the region between the nucleus and the plasma membrane. Within the cytoplasm of a eukaryotic cell, suspended in cytosol, are a variety of organelles of specialized form and function. These membrane-bounded structures are absent in almost all prokaryotic cells, another distinction between prokaryotic and eukaryotic cells. In spite of the absence of organelles, though, the prokaryotic cytoplasm is not a formless soup. For example, some prokaryotes contain regions surrounded by proteins (not membranes), within which specific reactions take place.

Eukaryotic cells are generally much larger than prokaryotic cells (see Figure 6.2). Size is a general feature of cell structure that relates to function. The logistics of carrying out cellular metabolism sets limits on cell size. At the lower limit, the smallest cells known are bacteria called mycoplasmas, which have diameters between 0.1 and 1.0 µm. These are perhaps the smallest packages with enough DNA to program metabolism and enough enzymes and other cellular equipment to carry out the activities necessary for a cell to sustain itself and reproduce. Typical bacteria are 1–5 µm in diameter, about ten times the size of mycoplasmas. Eukaryotic cells are typically 10–100 µm in diameter.

Metabolic requirements also impose theoretical upper limits on the size that is practical for a single cell. At the boundary of every cell, the **plasma membrane** functions as a selective barrier that allows passage of enough oxygen, nutrients, and wastes to service the entire cell **(Figure 6.6)**. For each square micrometer of membrane, only a limited amount of a particular substance can cross per second, so the ratio of surface area to volume is critical. As a cell (or any other object) increases in size, its surface area grows proportionately less than its volume. (Area is proportional to a linear dimension squared, whereas volume is proportional to the linear dimension cubed.) Thus, a smaller object has a greater ratio of surface area to volume **(Figure 6.7)**. The **Scientific Skills Exercise** gives you a chance to calculate the volumes and surface areas of two actual cells—a mature yeast cell and a cell budding from it. To see different ways organisms maximize the surface area of cells, see Make Connections Figure 33.9.

The need for a surface area large enough to accommodate the volume helps explain the microscopic size of most cells and the narrow, elongated shapes of others, such as nerve cells. Larger organisms do not generally have *larger* cells than smaller organisms—they simply have *more* cells (see Figure 6.7). A sufficiently high ratio of surface area to volume is especially important in cells that exchange a lot of material with their surroundings, such as intestinal cells. Such cells may have many long, thin projections from their surface called *microvilli*, which increase surface area without an appreciable increase in volume.

Figure 6.6 The plasma membrane. The plasma membrane and the membranes of organelles consist of a double layer (bilayer) of phospholipids with various proteins attached to or embedded in it. The hydrophobic parts of phospholipids and membrane proteins are found in the interior of the membrane, while the hydrophilic parts are in contact with aqueous solutions on either side. Carbohydrate side chains may be attached to proteins or lipids on the outer surface of the plasma membrane.



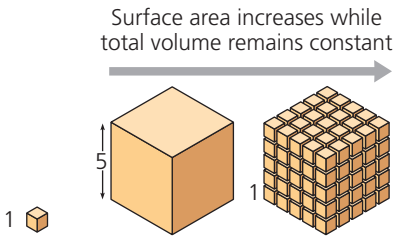
(a) TEM of a plasma membrane. The plasma membrane, here in a red blood cell, appears as a pair of dark bands separated by a light band.

(b) Structure of the plasma membrane

VISUAL SKILLS ➤ *What parts of the membrane diagram in (b) correspond to the dark bands, and which to the light band, in the TEM in (a)? (Review Figure 5.11.)*

MB **BioFlix® Animation: Membranes**

Figure 6.7 Geometric relationships between surface area and volume. In this diagram, cells are represented as boxes. Using arbitrary units of length, we can calculate the cell's surface area (in square units, or units^2), volume (in cubic units, or units^3), and ratio of surface area to volume. A high surface-to-volume ratio facilitates the exchange of materials between a cell and its environment.



Total surface area [sum of the surface areas (height × width) of all box sides × number of boxes]	6	150	750
Total volume [height × width × length × number of boxes]	1	125	125
Surface-to-volume (S-to-V) ratio [surface area ÷ volume]	6	1.2	6

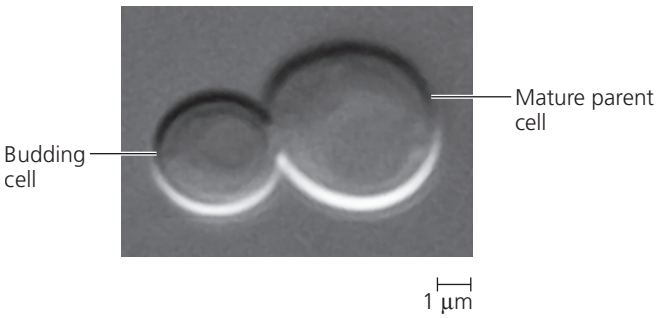
SCIENTIFIC SKILLS EXERCISE

Using a Scale Bar to Calculate Volume and Surface Area of a Cell

How Much New Cytoplasm and Plasma Membrane Are Made by a Growing Yeast Cell? The unicellular yeast *Saccharomyces cerevisiae* divides by budding off a small new cell that then grows to full size (see the yeast cells at the bottom of Figure 6.8). During its growth, the new cell synthesizes new cytoplasm, which increases its volume, and new plasma membrane, which increases its surface area. In this exercise, you will use a scale bar to determine the sizes of a mature parent yeast cell and a cell budding from it. You will then calculate the volume and surface area of each cell. You will use your calculations to determine how much cytoplasm and plasma membrane the new cell needs to synthesize to grow to full size.

How the Experiment Was Done Yeast cells were grown under conditions that promoted division by budding. The cells were then viewed with a differential interference contrast light microscope and photographed.

Data from the Experiment This light micrograph shows a budding yeast cell about to be released from the mature parent cell:

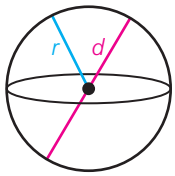


Micrograph from Kelly Tatchell, using yeast cells grown for experiments described in L. Kozubowski et al., Role of the septin ring in the asymmetric localization of proteins at the mother-bud neck in *Saccharomyces cerevisiae*, *Molecular Biology of the Cell* 16:3455–3466 (2005).

INTERPRET THE DATA

1. Examine the micrograph of the yeast cells. The scale bar under the photo is labeled 1 µm. The scale bar works in the same way as a scale on a map, where, for example, 1 inch equals 1 mile. In this case the bar represents one thousandth of a millimeter. Using the scale bar as a basic unit, determine the diameter of the mature parent cell and the new cell. Start by measuring the scale bar and the diameter of each cell. The units you use are irrelevant, but working in millimeters is convenient. Divide each diameter by the length of the scale bar and then multiply by the scale bar's length value to give you the diameter in micrometers.
2. The shape of a yeast cell can be approximated by a sphere. (a) Calculate the volume of each cell using the formula for the volume of a sphere:

$$V = \frac{4}{3}\pi r^3$$



Note that π (the Greek letter pi) is a constant with an approximate value of 3.14, d stands for diameter, and r stands for radius, which is half the diameter. (b) What volume of new cytoplasm will the new cell have to synthesize as it matures? To determine this, calculate the difference between the volume of the full-sized cell and the volume of the new cell.

3. As the new cell grows, its plasma membrane needs to expand to contain the increased volume of the cell. (a) Calculate the surface area of each cell using the formula for the surface area of a sphere: $A = 4\pi r^2$. (b) How much area of new plasma membrane will the new cell have to synthesize as it matures?
4. When the new cell matures, it will be approximately how many times greater in volume and how many times greater in surface area than its current size?

Instructors: A version of this Scientific Skills Exercise can be assigned in MasteringBiology.

The evolutionary relationships between prokaryotic and eukaryotic cells will be discussed later in this chapter, and prokaryotic cells will be described in detail elsewhere (see Chapter 27). Most of the discussion of cell structure that follows in this chapter applies to eukaryotic cells.

A Panoramic View of the Eukaryotic Cell

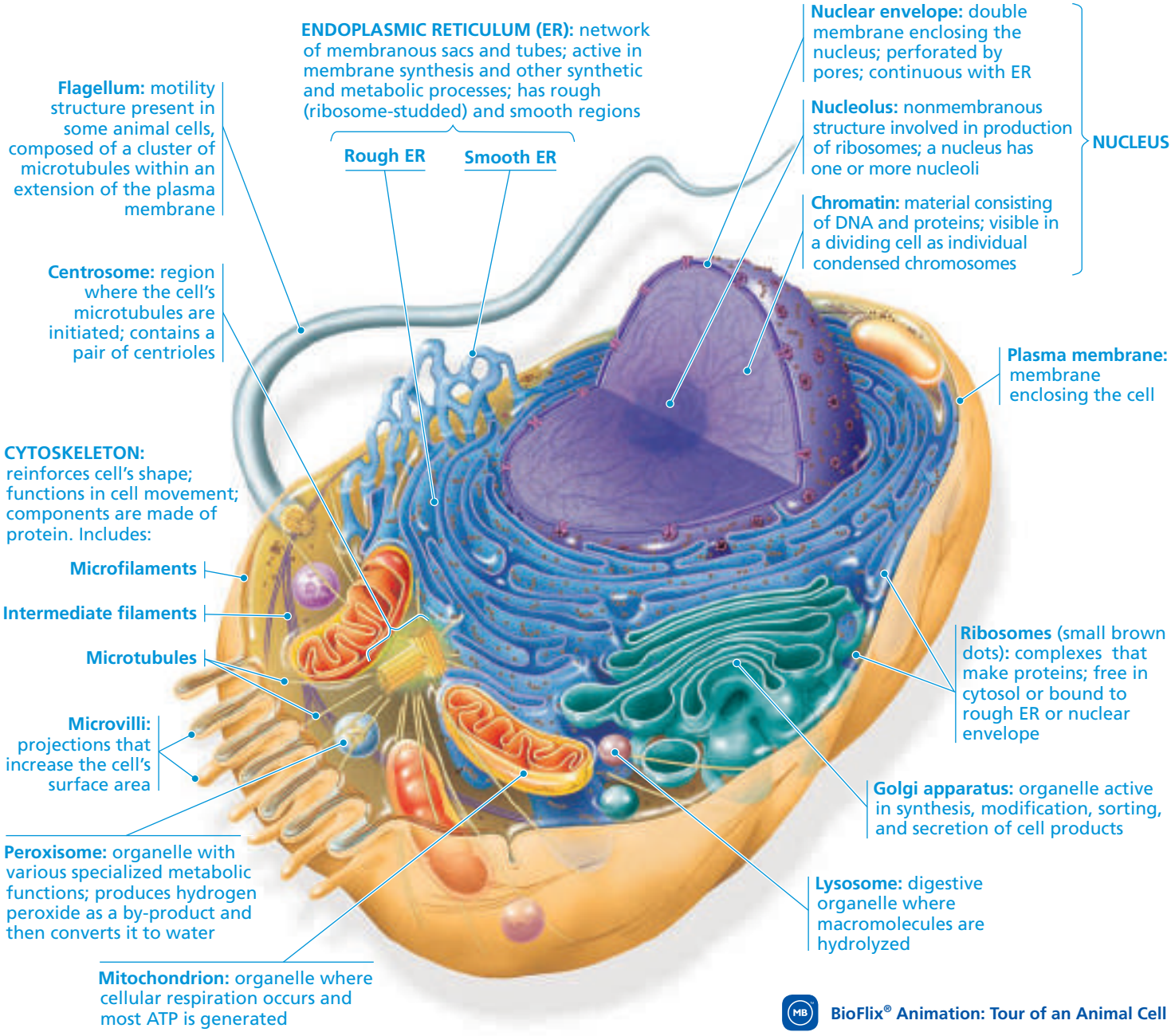
In addition to the plasma membrane at its outer surface, a eukaryotic cell has extensive, elaborately arranged internal membranes that divide the cell into compartments—the organelles mentioned earlier. The cell's compartments provide different local environments that support specific metabolic functions, so incompatible processes can occur simultaneously in a single cell. The plasma membrane and organelle membranes also participate directly in the cell's metabolism because many enzymes are built right into the membranes.

The basic fabric of most biological membranes is a double layer of phospholipids and other lipids. Embedded in this lipid bilayer or attached to its surfaces are diverse proteins (see Figure 6.6). However, each type of membrane has a unique composition of lipids and proteins suited to that membrane's specific functions. For example, enzymes embedded in the membranes of the organelles called mitochondria function in cellular respiration. Because membranes are so fundamental to the organization of the cell, Chapter 7 will discuss them in detail.

Before continuing with this chapter, examine the eukaryotic cells in **Figure 6.8**. The generalized diagrams of an animal cell and a plant cell introduce the various organelles and show the key differences between animal and plant cells. The micrographs at the bottom of the figure give you a glimpse of cells from different types of eukaryotic organisms.

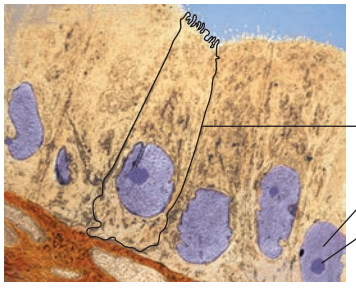
Figure 6.8 Exploring Eukaryotic Cells

Animal Cell (cutaway view of generalized cell)



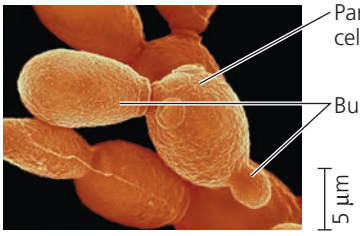
BioFlix® Animation: Tour of an Animal Cell

Animal Cells

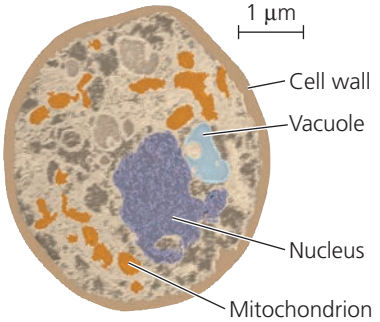


Human cells from lining of uterus (colorized TEM)

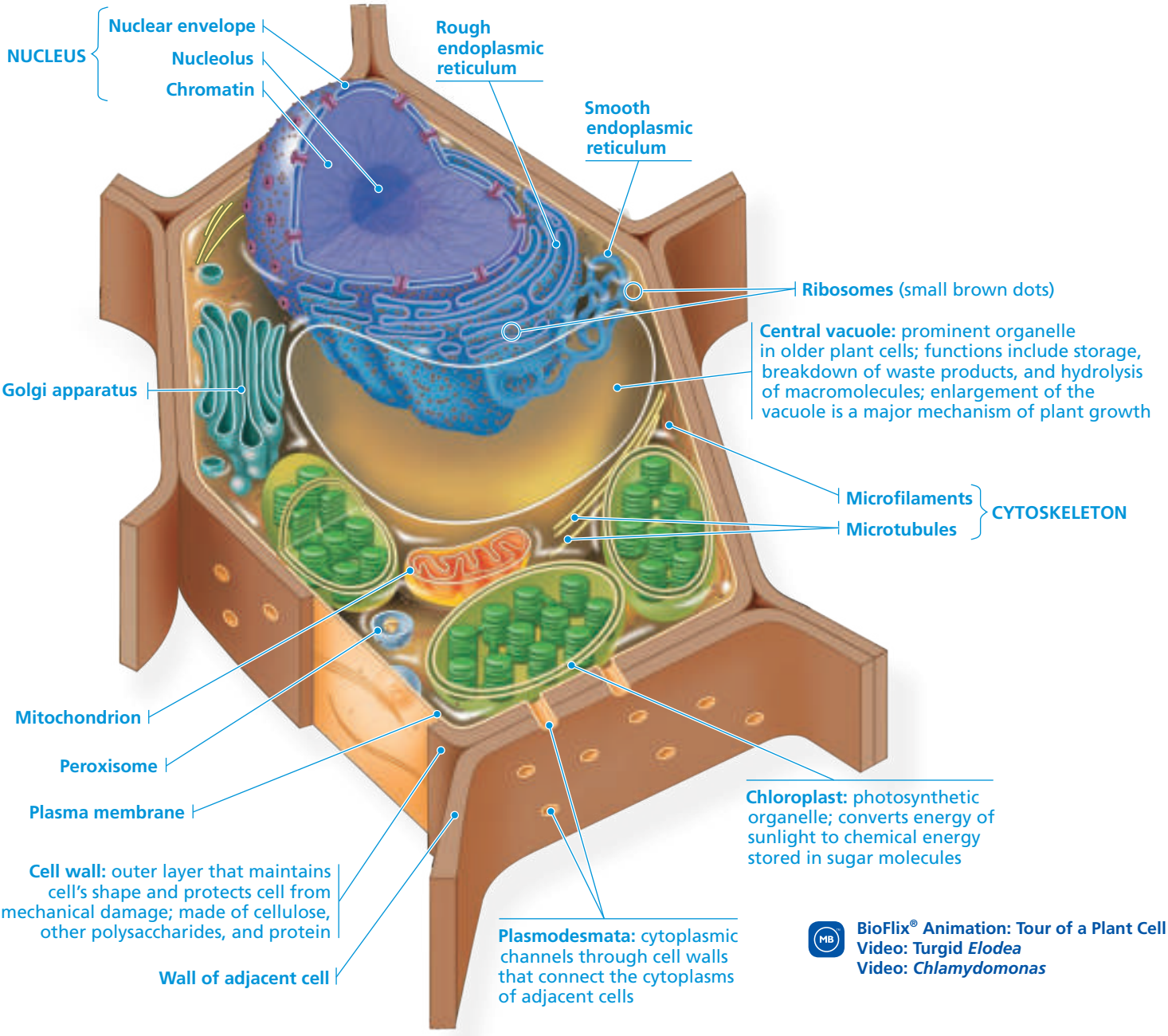
Fungal Cells



Yeast cells: reproducing by budding (above, colorized SEM) and a single cell (right, colorized TEM)

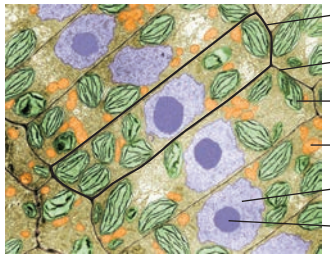


Plant Cell (cutaway view of generalized cell)



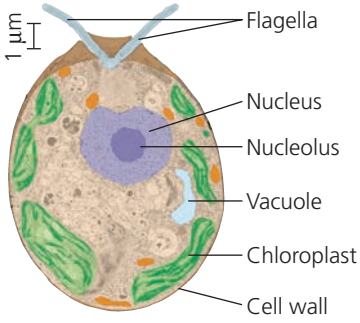
BioFlix® Animation: Tour of a Plant Cell
Video: Turgid *Elodea*
Video: *Chlamydomonas*

Plant Cells



Cells from duckweed (*Spirodela oligorrhiza*), a floating plant (colorized TEM)

Unicellular Eukaryotes



Unicellular green alga *Chlamydomonas* (above, colorized SEM; right, colorized TEM)

CONCEPT CHECK 6.2

1. Briefly describe the structure and function of the nucleus, the mitochondrion, the chloroplast, and the endoplasmic reticulum.
2. **DRAW IT** ➤ Draw a simplified elongated cell that measures 125 × 1 × 1 arbitrary units. A nerve cell would be roughly this shape. Predict how its surface-to-volume ratio would compare with those in Figure 6.7. Then calculate the ratio and check your prediction.

For suggested answers, see Appendix A.

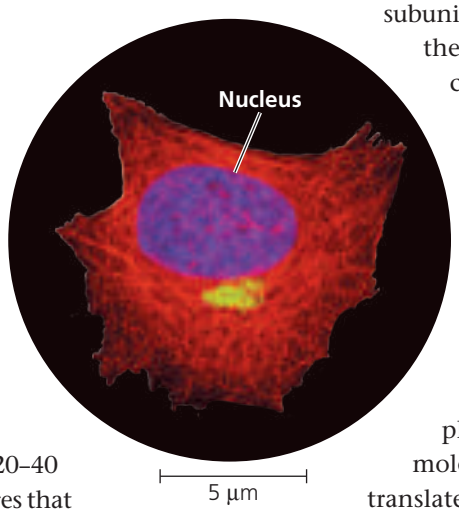
CONCEPT 6.3

The eukaryotic cell's genetic instructions are housed in the nucleus and carried out by the ribosomes

On the first stop of our detailed tour of the eukaryotic cell, let's look at two cellular components involved in the genetic control of the cell: the nucleus, which houses most of the cell's DNA, and the ribosomes, which use information from the DNA to make proteins.

The Nucleus: Information Central

The **nucleus** contains most of the genes in the eukaryotic cell. (Some genes are located in mitochondria and chloroplasts.) It is usually the most conspicuous organelle (see the purple structure in the fluorescence micrograph), averaging about 5 µm in diameter. The **nuclear envelope** encloses the nucleus **(Figure 6.9)**, separating its contents from the cytoplasm.



The nuclear envelope is a *double* membrane. The two membranes, each a lipid bilayer with associated proteins, are separated by a space of 20–40 nm. The envelope is perforated by pore structures that are about 100 nm in diameter. At the lip of each pore, the inner and outer membranes of the nuclear envelope are continuous. An intricate protein structure called a *pore complex* lines each pore and plays an important role in the cell by regulating the entry and exit of proteins and RNAs, as well as large complexes of macromolecules. Except at the pores, the nuclear side of the envelope is lined by the **nuclear lamina**, a netlike array of protein filaments (in animal cells, called *intermediate filaments*) that maintains the shape of the nucleus by mechanically supporting the nuclear envelope. There is also much evidence for a *nuclear matrix*, a framework of protein fibers extending throughout the nuclear interior. The nuclear lamina and matrix may help organize the genetic material so it functions efficiently.

Within the nucleus, the DNA is organized into discrete units called **chromosomes**, structures that carry the genetic information. Each chromosome contains one long DNA molecule associated with many proteins. Some of the proteins help coil the DNA molecule of each chromosome, reducing its length and allowing it to fit into the nucleus. The complex of DNA and proteins making up chromosomes is called **chromatin**. When a cell is not dividing, stained chromatin appears as a diffuse mass in micrographs, and the chromosomes cannot be distinguished from one another, even though discrete chromosomes are present. As a cell prepares to divide, however, the chromosomes coil (condense) further, becoming thick enough to be distinguished under a microscope as separate structures. Each eukaryotic species has a characteristic number of chromosomes. For example, a typical human cell has 46 chromosomes in its nucleus; the exceptions are the sex cells (eggs and sperm), which have only 23 chromosomes in humans. A fruit fly cell has 8 chromosomes in most cells and 4 in the sex cells.

A prominent structure within the nondividing nucleus is the **nucleolus** (plural, *nucleoli*), which appears through the electron microscope as a mass of densely stained granules and fibers adjoining part of the chromatin. Here a type of RNA called *ribosomal RNA* (rRNA) is synthesized from instructions in the DNA. Also in the nucleolus, proteins imported from the cytoplasm are assembled with rRNA into large and small subunits of ribosomes. These subunits then exit the nucleus through the nuclear pores to the cytoplasm, where a large and a small subunit can assemble into a ribosome. Sometimes there are two or more nucleoli; the number depends on the species and the stage in the cell's reproductive cycle.

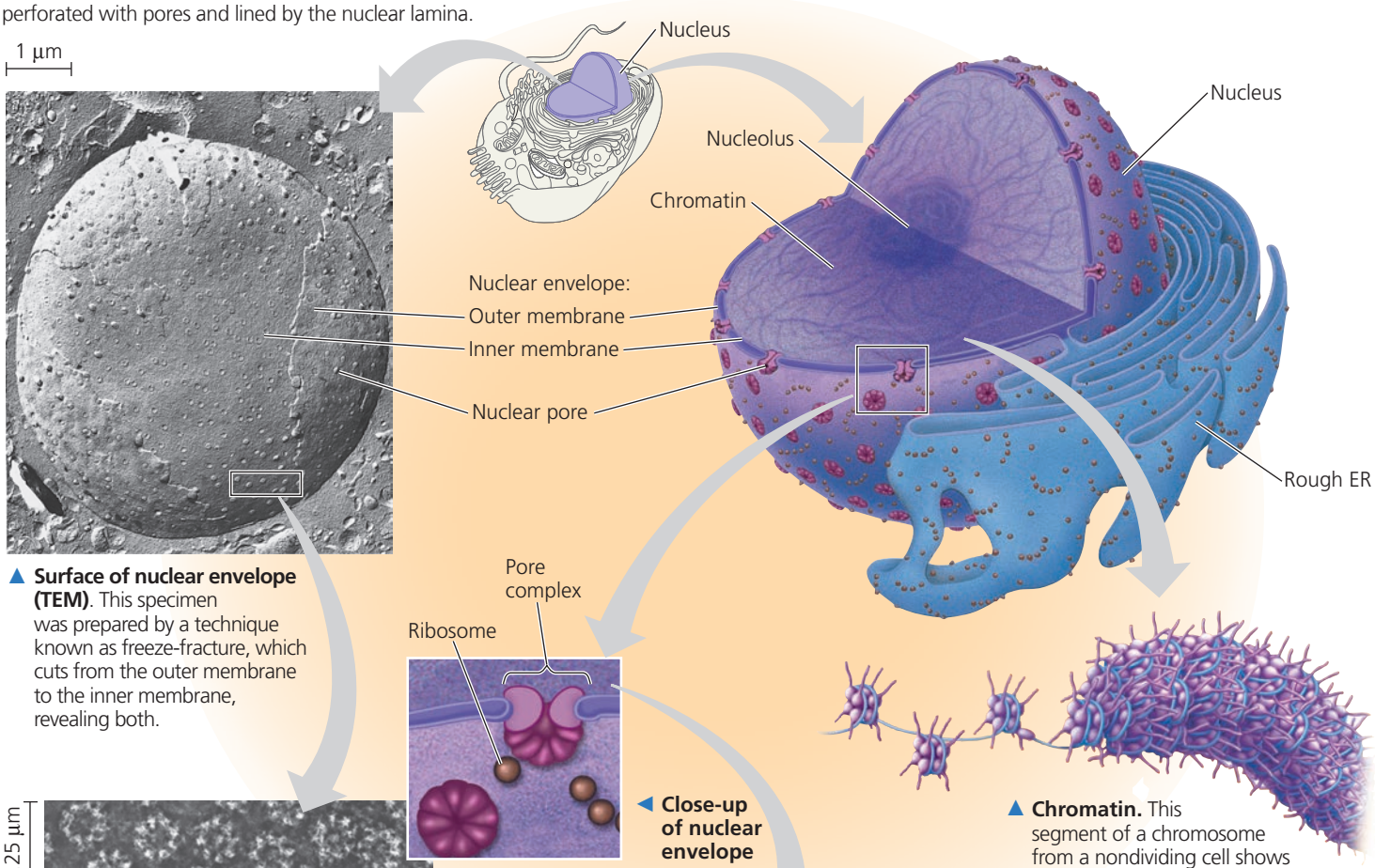
As we saw in Figure 5.22, the nucleus directs protein synthesis by synthesizing messenger RNA (mRNA) according to instructions provided by the DNA. The mRNA is then transported to the cytoplasm via the nuclear pores. Once an mRNA molecule reaches the cytoplasm, ribosomes translate the mRNA's genetic message into the primary structure of a specific polypeptide. (This process of transcribing and translating genetic information is described in detail in Chapter 17.)

BioFlix® Animation: Nucleus and Ribosomes

Ribosomes: Protein Factories

Ribosomes, which are complexes made of ribosomal RNAs and proteins, are the cellular components that carry out protein synthesis **(Figure 6.10)**. (Note that ribosomes are not membrane bounded and thus are not considered organelles.) Cells that have high rates of protein synthesis have particularly large numbers of ribosomes as well as prominent nucleoli, which makes sense, given the role of nucleoli in ribosome assembly. For example, a human pancreas cell, which makes many digestive enzymes, has a few million ribosomes.

Figure 6.9 The nucleus and its envelope. Within the nucleus are the chromosomes, which appear as a mass of chromatin (DNA and associated proteins) and one or more nucleoli (singular, *nucleolus*), which function in ribosome synthesis. The nuclear envelope, which consists of two membranes separated by a narrow space, is perforated with pores and lined by the nuclear lamina.



▲ **Surface of nuclear envelope (TEM).** This specimen was prepared by a technique known as freeze-fracture, which cuts from the outer membrane to the inner membrane, revealing both.

◀ **Close-up of nuclear envelope**

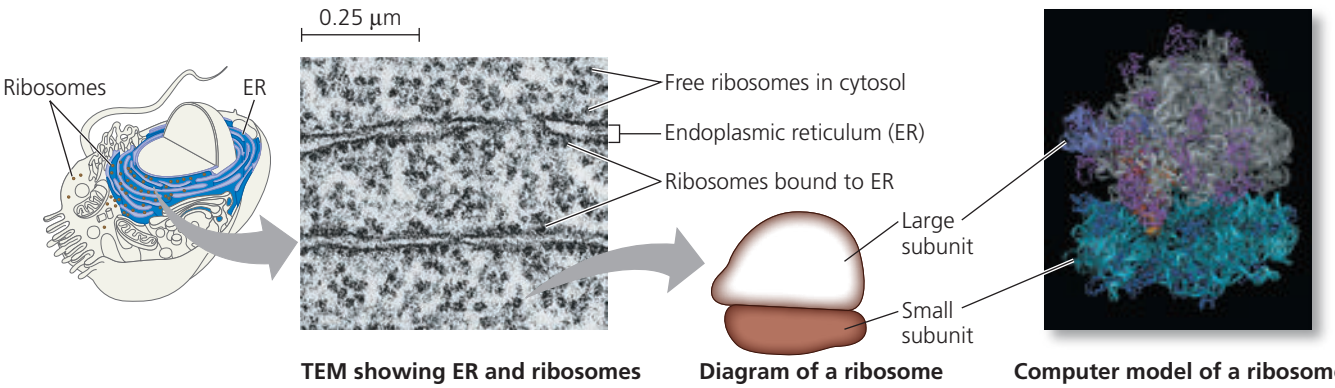
▲ **Chromatin.** This segment of a chromosome from a nondividing cell shows two states of coiling of the DNA (blue) and protein (purple) complex. The thicker form is sometimes also organized into long loops.

▲ **Pore complexes (TEM).** Each pore is ringed by protein particles.

▶ **Nuclear lamina (TEM).** The netlike lamina lines the inner surface of the nuclear envelope. (The light circular spots are nuclear pores.)

MAKE CONNECTIONS ➤ *Chromosomes contain the genetic material and reside in the nucleus; how does the rest of the cell get access to the information they carry? (See Figure 5.22.)*

Figure 6.10 Ribosomes. This electron micrograph of a pancreas cell shows both free and bound ribosomes. The simplified diagram and computer model show the two subunits of a ribosome.



TEM showing ER and ribosomes **Diagram of a ribosome** **Computer model of a ribosome**

DRAW IT ➤ *After you have read the section on ribosomes, circle a ribosome in the micrograph that might be making a protein that will be secreted.*

Interview with Venki Ramakrishnan: Studying ribosome structure

Ribosomes build proteins in two cytoplasmic locales. At any given time, *free ribosomes* are suspended in the cytosol, while *bound ribosomes* are attached to the outside of the endoplasmic reticulum or nuclear envelope (see Figure 6.10). Bound and free ribosomes are structurally identical, and ribosomes can play either role at different times. Most of the proteins made on free ribosomes function within the cytosol; examples are enzymes that catalyze the first steps of sugar breakdown. Bound ribosomes generally make proteins that are destined for insertion into membranes, for packaging within certain organelles such as lysosomes (see Figure 6.8), or for export from the cell (secretion). Cells that specialize in protein secretion—for instance, the cells of the pancreas that secrete digestive enzymes—frequently have a high proportion of bound ribosomes. (You will learn more about ribosome structure and function in Concept 17.4.)

CONCEPT CHECK 6.3

1. What role do ribosomes play in carrying out genetic instructions?
2. Describe the molecular composition of nucleoli and explain their function.
3. **WHAT IF?** ➤ As a cell begins the process of dividing, its chromosomes become shorter, thicker, and individually visible in an LM (light micrograph). Explain what is happening at the molecular level.

For suggested answers, see Appendix A.

CONCEPT 6.4

The endomembrane system regulates protein traffic and performs metabolic functions

Many of the different membrane-bounded organelles of the eukaryotic cell are part of the **endomembrane system**, which includes the nuclear envelope, the endoplasmic reticulum, the Golgi apparatus, lysosomes, various kinds of vesicles and vacuoles, and the plasma membrane. This system carries out a variety of tasks in the cell, including synthesis of proteins, transport of proteins into membranes and organelles or out of the cell, metabolism and movement of lipids, and detoxification of poisons. The membranes of this system are related either through direct physical continuity or by the transfer of membrane segments as tiny **vesicles** (sacs made of membrane). Despite these relationships, the various membranes are not identical in structure and function. Moreover, the thickness, molecular composition, and types of chemical reactions carried out in a given membrane are not fixed, but may be modified several times during the membrane's life. Having already discussed the nuclear envelope, we will now focus on the endoplasmic reticulum and the other endomembranes to which the endoplasmic reticulum gives rise.

The Endoplasmic Reticulum: Biosynthetic Factory

The **endoplasmic reticulum (ER)** is such an extensive network of membranes that it accounts for more than half the total membrane in many eukaryotic cells. (The word *endoplasmic* means "within the cytoplasm," and *reticulum* is Latin for "little net.") The ER consists of a network of membranous tubules and sacs called cisternae (from the Latin *cisterna*, a reservoir for a liquid). The ER membrane separates the internal compartment of the ER, called the *ER lumen* (cavity) or cisternal space, from the cytosol. And because the ER membrane is continuous with the nuclear envelope, the space between the two membranes of the envelope is continuous with the lumen of the ER **(Figure 6.11)**.

There are two distinct, though connected, regions of the ER that differ in structure and function: smooth ER and rough ER. **Smooth ER** is so named because its outer surface lacks ribosomes. **Rough ER** is studded with ribosomes on the outer surface of the membrane and thus appears rough through the electron microscope. As already mentioned, ribosomes are also attached to the cytoplasmic side of the nuclear envelope's outer membrane, which is continuous with rough ER.

Functions of Smooth ER

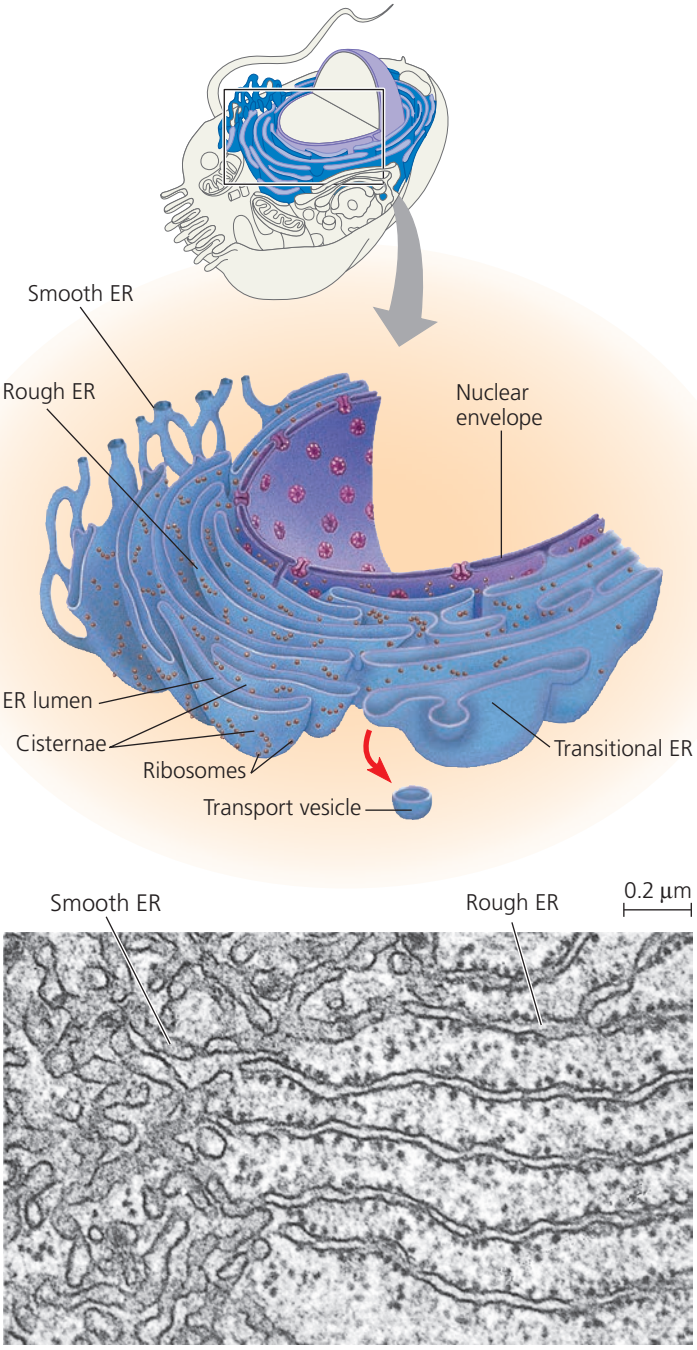
The smooth ER functions in diverse metabolic processes, which vary with cell type. These processes include synthesis of lipids, metabolism of carbohydrates, detoxification of drugs and poisons, and storage of calcium ions.

Enzymes of the smooth ER are important in the synthesis of lipids, including oils, steroids, and new membrane phospholipids. Among the steroids produced by the smooth ER in animal cells are the sex hormones of vertebrates and the various steroid hormones secreted by the adrenal glands. The cells that synthesize and secrete these hormones—in the testes and ovaries, for example—are rich in smooth ER, a structural feature that fits the function of these cells.

Other enzymes of the smooth ER help detoxify drugs and poisons, especially in liver cells. Detoxification usually involves adding hydroxyl groups to drug molecules, making them more soluble and easier to flush from the body. The sedative phenobarbital and other barbiturates are examples of drugs metabolized in this manner by smooth ER in liver cells. In fact, barbiturates, alcohol, and many other drugs induce the proliferation of smooth ER and its associated detoxification enzymes, thus increasing the rate of detoxification. This, in turn, increases tolerance to the drugs, meaning that higher doses are required to achieve a particular effect, such as sedation. Also, because some of the detoxification enzymes have relatively broad action,

the proliferation of smooth ER in response to one drug can increase the need for higher dosages of other drugs as well. Barbiturate abuse, for example, can decrease the effectiveness of certain antibiotics and other useful drugs.

Figure 6.11 Endoplasmic reticulum (ER). A membranous system of interconnected tubules and flattened sacs called cisternae, the ER is also continuous with the nuclear envelope, as shown in the cutaway diagram at the top. The membrane of the ER encloses a continuous compartment called the ER lumen (or cisternal space). Rough ER, which is studded on its outer surface with ribosomes, can be distinguished from smooth ER in the electron micrograph (TEM). Transport vesicles bud off from a region of the rough ER called transitional ER and travel to the Golgi apparatus and other destinations.



The smooth ER also stores calcium ions. In muscle cells, for example, the smooth ER membrane pumps calcium ions from the cytosol into the ER lumen. When a muscle cell is stimulated by a nerve impulse, calcium ions rush back across the ER membrane into the cytosol and trigger contraction of the muscle cell. In other cell types, release of calcium ions from the smooth ER triggers different responses, such as secretion of vesicles carrying newly synthesized proteins.

Functions of Rough ER

Many cells secrete proteins that are produced by ribosomes attached to rough ER. For example, certain pancreatic cells synthesize the protein insulin in the ER and secrete this hormone into the bloodstream. As a polypeptide chain grows from a bound ribosome, the chain is threaded into the ER lumen through a pore formed by a protein complex in the ER membrane. The new polypeptide folds into its functional shape as it enters the ER lumen. Most secretory proteins are **glycoproteins**, proteins with carbohydrates covalently bonded to them. The carbohydrates are attached to the proteins in the ER lumen by enzymes built into the ER membrane.

After secretory proteins are formed, the ER membrane keeps them separate from proteins in the cytosol, which are produced by free ribosomes. Secretory proteins depart from the ER wrapped in the membranes of vesicles that bud like bubbles from a specialized region called transitional ER (see Figure 6.11). Vesicles in transit from one part of the cell to another are called **transport vesicles**; we will discuss their fate shortly.

In addition to making secretory proteins, rough ER is a membrane factory for the cell; it grows in place by adding membrane proteins and phospholipids to its own membrane. As polypeptides destined to be membrane proteins grow from the ribosomes, they are inserted into the ER membrane itself and anchored there by their hydrophobic portions. Like the smooth ER, the rough ER also makes membrane phospholipids; enzymes built into the ER membrane assemble phospholipids from precursors in the cytosol. The ER membrane expands, and portions of it are transferred in the form of transport vesicles to other components of the endomembrane system.

The Golgi Apparatus: Shipping and Receiving Center

After leaving the ER, many transport vesicles travel to the **Golgi apparatus**. We can think of the Golgi as a warehouse for receiving, sorting, shipping, and even some manufacturing. Here, products of the ER, such as proteins, are modified and stored and then sent to other destinations. Not surprisingly, the Golgi apparatus is especially extensive in cells specialized for secretion.

The Golgi apparatus consists of a group of associated, flattened membranous sacs—cisternae—looking like a stack of pita bread **(Figure 6.12)**. A cell may have many, even hundreds, of these stacks. The membrane of each cisterna in a stack separates its internal space from the cytosol. Vesicles concentrated in the vicinity of the Golgi apparatus are engaged in the transfer of material between parts of the Golgi and other structures.

A Golgi stack has a distinct structural directionality, with the membranes of cisternae on opposite sides of the stack differing in thickness and molecular composition. The two sides of a Golgi stack are referred to as the *cis* face and the *trans* face; these act, respectively, as the receiving and shipping departments of the Golgi apparatus. The term *cis* means "on the same side," and the *cis* face is usually located near the ER. Transport vesicles move material from the ER to the Golgi apparatus. A vesicle that buds from the ER can add its membrane and the contents of its lumen to the *cis* face by fusing with a Golgi membrane on that side. The *trans* face ("on the opposite side") gives rise to vesicles that pinch off and travel to other sites.

Products of the endoplasmic reticulum are usually modified during their transit from the *cis* region to the *trans* region of the Golgi apparatus. For example, glycoproteins formed in the ER have their carbohydrates modified, first in the ER itself, and then as they pass through the Golgi. The Golgi removes some sugar monomers and substitutes others, producing a large variety of carbohydrates. Membrane phospholipids may also be altered in the Golgi.

In addition to its finishing work, the Golgi apparatus also manufactures some macromolecules. Many polysaccharides secreted by cells are Golgi products. For example, pectins and certain other noncellulose polysaccharides are made in the Golgi of plant cells and then incorporated along with cellulose into their cell walls. Like secretory proteins, nonprotein Golgi products that will be secreted depart from the *trans* face of the Golgi inside transport vesicles that eventually fuse with the plasma membrane.

The Golgi manufactures and refines its products in stages, with different cisternae containing unique teams of enzymes. Until recently, biologists viewed the Golgi as a static structure, with products in various stages of processing transferred from one cisterna to the next by vesicles. While this may occur, research from several labs has given rise to a new model of the Golgi as a more dynamic structure. According to the *cisternal maturation model*, the cisternae of the Golgi actually progress forward from the *cis* to the *trans* face, carrying and modifying their cargo as they move. Figure 6.12 shows the details of this model. The reality probably lies somewhere between the two models; recent research suggests the central regions of the cisternae may remain in place, while the outer ends are more dynamic.

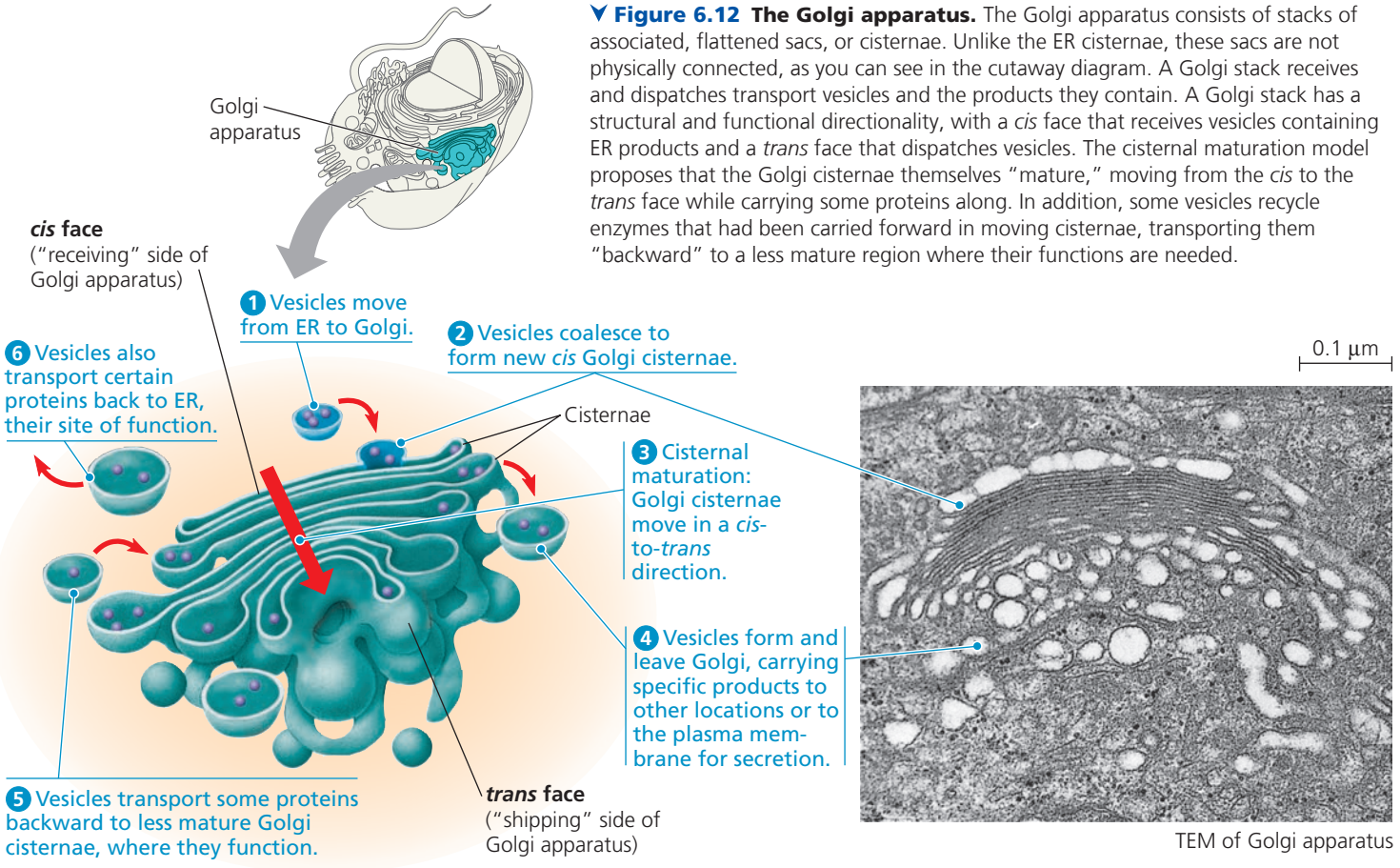


Figure 6.12 The Golgi apparatus. The Golgi apparatus consists of stacks of associated, flattened sacs, or cisternae. Unlike the ER cisternae, these sacs are not physically connected, as you can see in the cutaway diagram. A Golgi stack receives and dispatches transport vesicles and the products they contain. A Golgi stack has a structural and functional directionality, with a *cis* face that receives vesicles containing ER products and a *trans* face that dispatches vesicles. The cisternal maturation model proposes that the Golgi cisternae themselves "mature," moving from the *cis* to the *trans* face while carrying some proteins along. In addition, some vesicles recycle enzymes that had been carried forward in moving cisternae, transporting them "backward" to a less mature region where their functions are needed.

Before a Golgi stack dispatches its products by budding vesicles from the *trans* face, it sorts these products and targets them for various parts of the cell. Molecular identification tags, such as phosphate groups added to the Golgi products, aid in sorting by acting like zip codes on mailing labels. Finally, transport vesicles budded from the Golgi may have external molecules on their membranes that recognize "docking sites" on the surface of specific organelles or on the plasma membrane, thus targeting the vesicles appropriately.

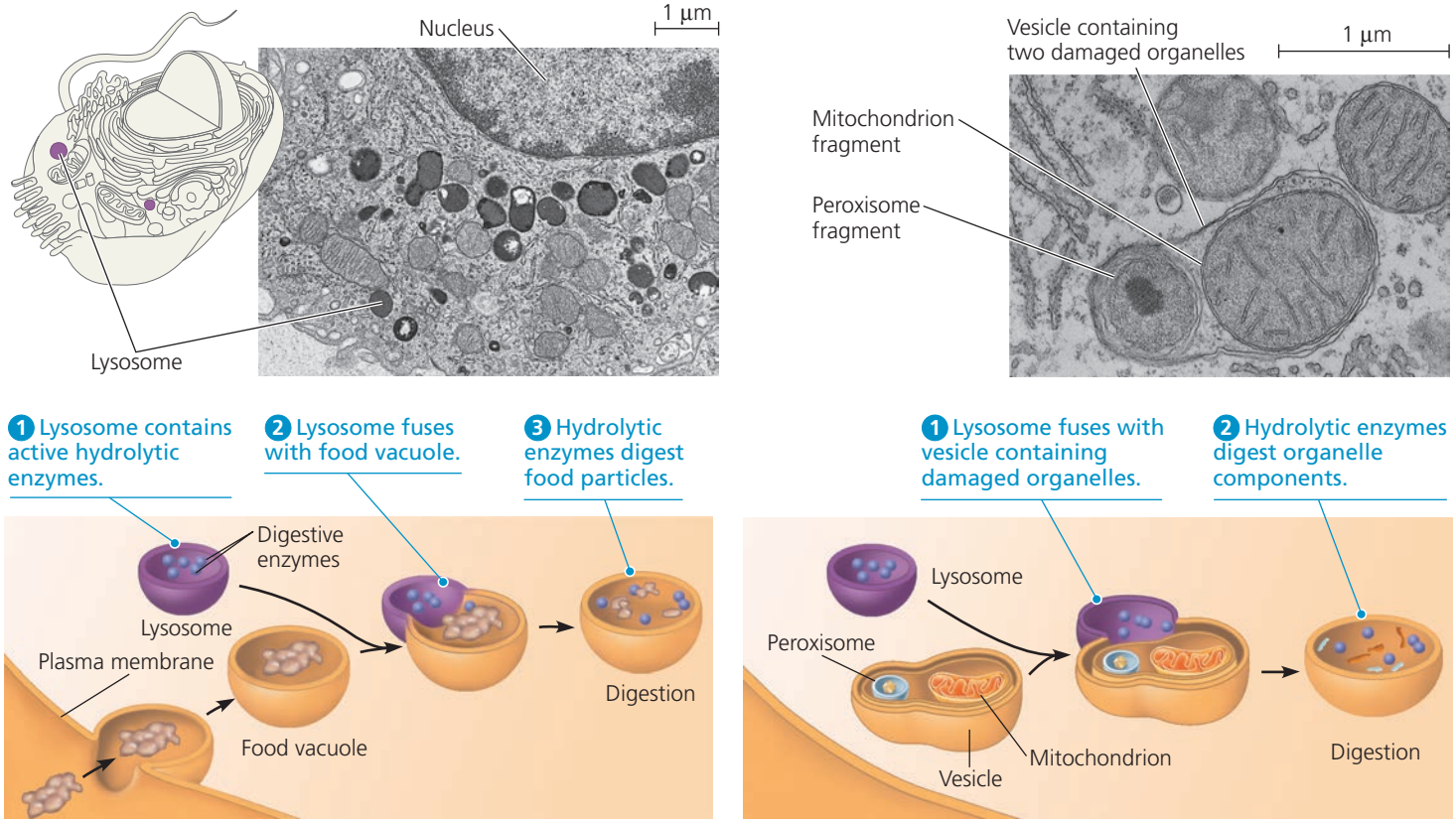
Lysosomes: Digestive Compartments

A **lysosome** is a membranous sac of hydrolytic enzymes that many eukaryotic cells use to digest (hydrolyze) macromolecules. Lysosomal enzymes work best in the acidic environment found in lysosomes. If a lysosome breaks open or leaks its contents, the released enzymes are not very active because the cytosol has a near-neutral pH. However, excessive leakage from a large number of lysosomes can destroy a cell by self-digestion.

Hydrolytic enzymes and lysosomal membrane are made by rough ER and then transferred to the Golgi apparatus for further processing. At least some lysosomes probably arise by budding from the *trans* face of the Golgi apparatus (see Figure 6.12). How are the proteins of the inner surface of the lysosomal membrane and the digestive enzymes themselves spared from destruction? Apparently, the three-dimensional shapes of these proteins protect vulnerable bonds from enzymatic attack.

Lysosomes carry out intracellular digestion in a variety of circumstances. Amoebas and many other unicellular eukaryotes eat by engulfing smaller organisms or food particles, a process called **phagocytosis** (from the Greek *phagein*, to eat, and *kytos*, vessel, referring here to the cell). The *food vacuole* formed in this way then fuses with a lysosome, whose enzymes digest the food **(Figure 6.13a**, bottom). Digestion products, including simple sugars, amino acids, and other monomers, pass into the cytosol and become nutrients for the cell. Some human cells also carry out phagocytosis. Among them are macrophages, a type of white blood cell that helps defend the body by engulfing and destroying bacteria and other invaders (see Figure 6.13a, top, and Figure 6.31).

Figure 6.13 Lysosomes.



(a) Phagocytosis. In phagocytosis, lysosomes digest (hydrolyze) materials taken into the cell. *Top:* In this macrophage (a type of white blood cell) from a rat, the lysosomes are very dark because of a stain that reacts with one of the products of digestion inside the lysosome (TEM). Macrophages ingest bacteria and viruses and destroy them using lysosomes. *Bottom:* This diagram shows a lysosome fusing with a food vacuole during the process of phagocytosis by a unicellular eukaryote.

(b) Autophagy. In autophagy, lysosomes recycle intracellular materials. *Top:* In the cytoplasm of this rat liver cell is a vesicle containing two disabled organelles (TEM). The vesicle will fuse with a lysosome in the process of autophagy, which recycles intracellular materials. *Bottom:* This diagram shows fusion of such a vesicle with a lysosome. This type of vesicle has a double membrane of unknown origin. The outer membrane fuses with the lysosome, and the inner membrane is degraded along with the damaged organelles.

Lysosomes also use their hydrolytic enzymes to recycle the cell's own organic material, a process called *autophagy*. During autophagy, a damaged organelle or small amount of cytosol becomes surrounded by a double membrane (of unknown origin), and a lysosome fuses with the outer membrane of this vesicle **(Figure 6.13b)**. The lysosomal enzymes dismantle the inner membrane with the enclosed material, and the resulting small organic compounds are released to the cytosol for reuse. With the help of lysosomes, the cell continually renews itself. A human liver cell, for example, recycles half of its macromolecules each week.

The cells of people with inherited lysosomal storage diseases lack a functioning hydrolytic enzyme normally present in lysosomes. The lysosomes become engorged with indigestible material, which begins to interfere with other cellular activities. In Tay-Sachs disease, for example, a lipid-digesting enzyme is missing or inactive, and the brain becomes impaired by an accumulation of lipids in the cells. Fortunately, lysosomal storage diseases are rare in the general population.

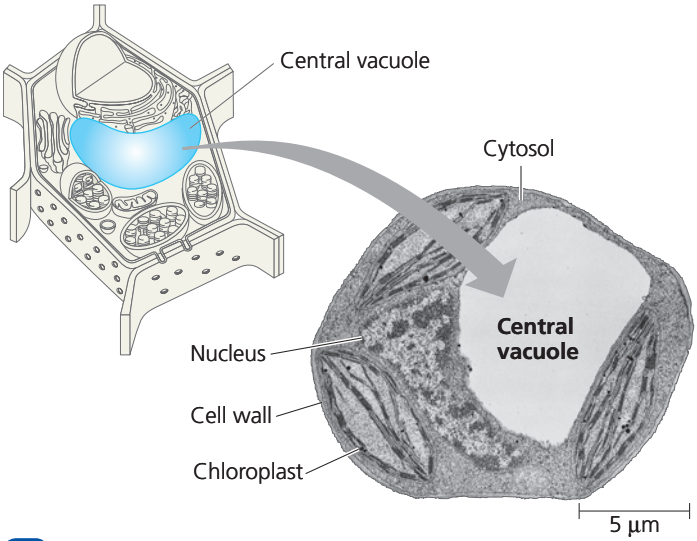
Vacuoles: Diverse Maintenance Compartments

Vacuoles are large vesicles derived from the endoplasmic reticulum and Golgi apparatus. Thus, vacuoles are an integral part of a cell's endomembrane system. Like all cellular membranes, the vacuolar membrane is selective in transporting solutes; as a result, the solution inside a vacuole differs in composition from the cytosol.

Vacuoles perform a variety of functions in different kinds of cells. **Food vacuoles**, formed by phagocytosis, have already been mentioned (see Figure 6.13a). Many unicellular eukaryotes living in fresh water have **contractile vacuoles** that pump excess water out of the cell, thereby maintaining a suitable concentration of ions and molecules inside the cell (see Figure 7.13). In plants and fungi, certain vacuoles carry out enzymatic hydrolysis, a function shared by lysosomes in animal cells. (In fact, some biologists consider these hydrolytic vacuoles to be a type of lysosome.) In plants, small vacuoles can hold reserves of important organic compounds, such as the proteins stockpiled in the storage cells in seeds. Vacuoles may also help protect the plant against herbivores by storing compounds that are poisonous or unpalatable to animals. Some plant vacuoles contain pigments, such as the red and blue pigments of petals that help attract pollinating insects to flowers.

Mature plant cells generally contain a large **central vacuole (Figure 6.14)**, which develops by the coalescence of smaller vacuoles. The solution inside the central vacuole, called cell sap, is the plant cell's main repository of inorganic ions, including potassium and chloride. The central vacuole plays a major role in the growth of plant cells, which enlarge as the vacuole absorbs water, enabling the cell to become larger with a minimal investment in new cytoplasm. The cytosol often occupies only a thin layer between the central vacuole and the plasma membrane, so the ratio of plasma membrane surface to cytosolic volume is sufficient, even for a large plant cell.

Figure 6.14 The plant cell vacuole. The central vacuole is usually the largest compartment in a plant cell; the rest of the cytoplasm is often confined to a narrow zone between the vacuolar membrane and the plasma membrane (TEM).



BioFlix® Animation: Central Vacuole

The Endomembrane System: *A Review*

Figure 6.15 reviews the endomembrane system, showing the flow of membrane lipids and proteins through the various organelles. As the membrane moves from the ER to the Golgi and then elsewhere, its molecular composition and metabolic functions are modified, along with those of its contents. The endomembrane system is a complex and dynamic player in the cell's compartmental organization.

We'll continue our tour of the cell with some organelles that are not closely related to the endomembrane system but play crucial roles in the energy transformations carried out by cells.

CONCEPT CHECK 6.4

1. Describe the structural and functional distinctions between rough and smooth ER.
2. Describe how transport vesicles integrate the endomembrane system.
3. **WHAT IF?** ➤ Imagine a protein that functions in the ER but requires modification in the Golgi apparatus before it can achieve that function. Describe the protein's path through the cell, starting with the mRNA molecule that specifies the protein.

For suggested answers, see Appendix A.

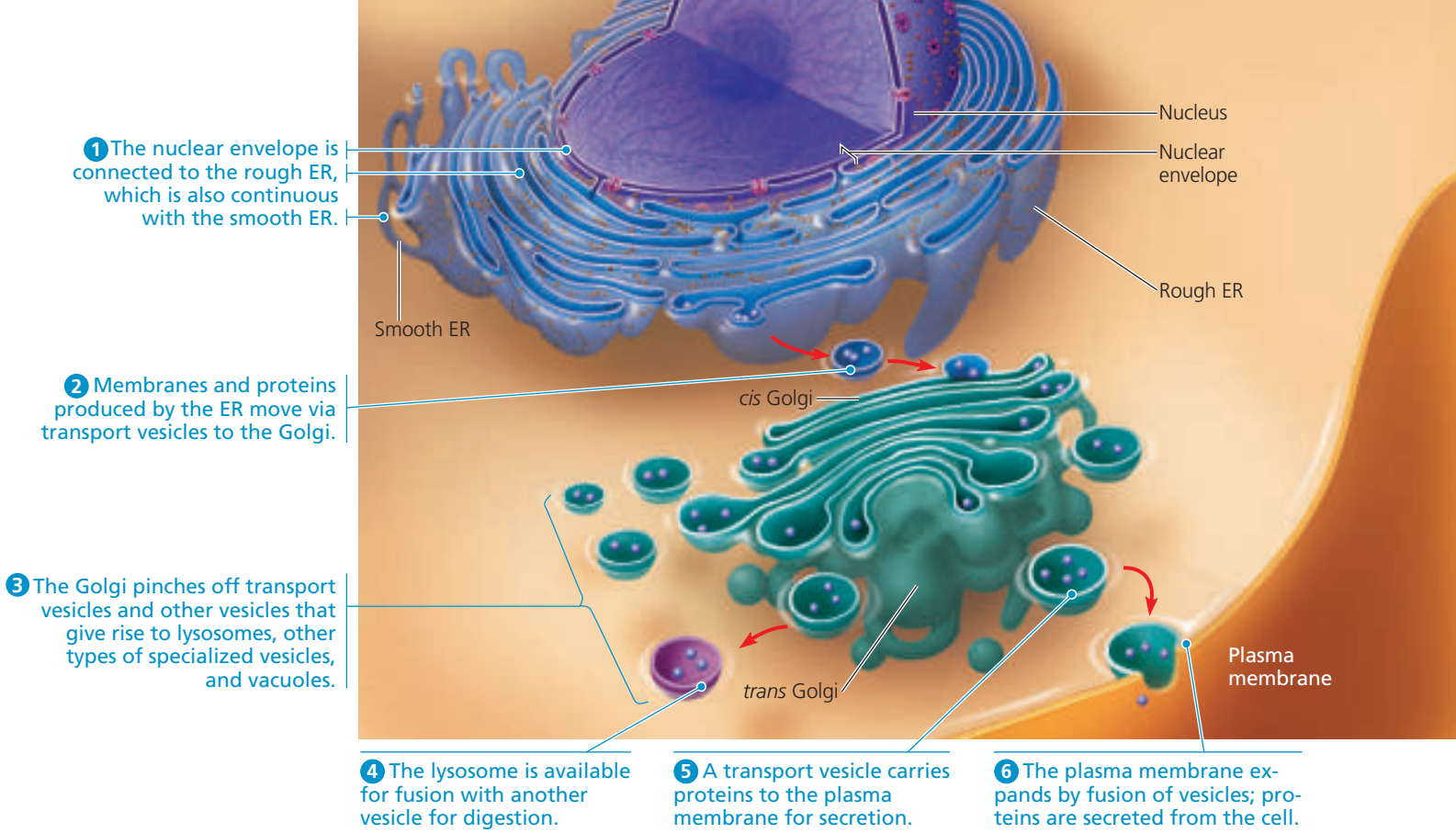


Figure 6.15 Review: relationships among organelles of the endomembrane system. The red arrows show some of the migration pathways for membranes and the materials they enclose.

BioFlix® Animation: Endomembrane System

CONCEPT 6.5

Mitochondria and chloroplasts change energy from one form to another

Organisms transform the energy they acquire from their surroundings. In eukaryotic cells, mitochondria and chloroplasts are the organelles that convert energy to forms that cells can use for work. **Mitochondria** (singular, *mitochondrion*) are the sites of cellular respiration, the metabolic process that uses oxygen to drive the generation of ATP by extracting energy from sugars, fats, and other fuels. **Chloroplasts**, found in plants and algae, are the sites of photosynthesis. This process in chloroplasts converts solar energy to chemical energy by absorbing sunlight and using it to drive the synthesis of organic compounds such as sugars from carbon dioxide and water.

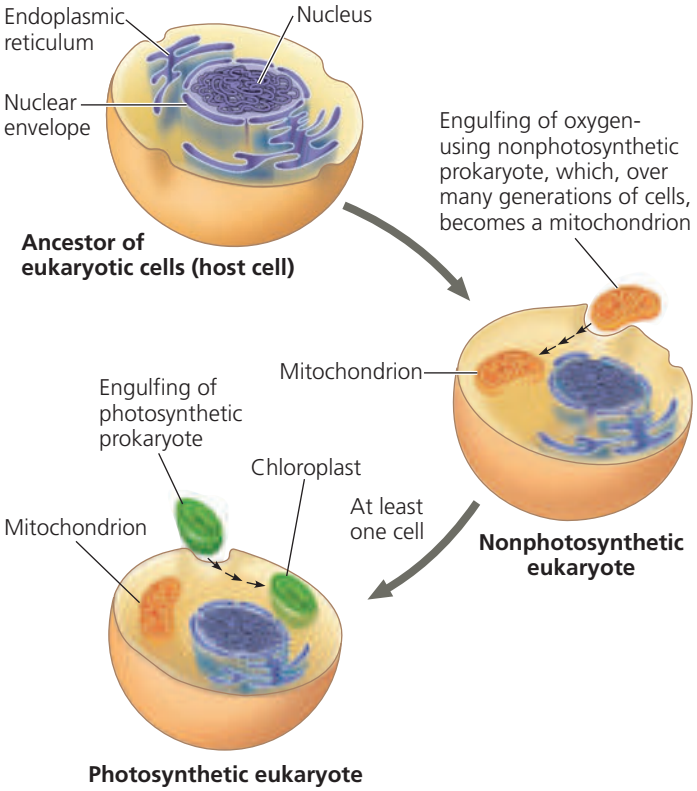
In addition to having related functions, mitochondria and chloroplasts share similar evolutionary origins, which we'll discuss briefly before describing their structures. In this section, we will also consider the peroxisome, an oxidative organelle. The evolutionary origin of the peroxisome, as well as its relation to other organelles, is still a matter of some debate.

The Evolutionary Origins of Mitochondria and Chloroplasts

EVOLUTION Mitochondria and chloroplasts display similarities with bacteria that led to the **endosymbiont theory**, illustrated in **Figure 6.16**. This theory states that an early ancestor of eukaryotic cells engulfed an oxygen-using nonphotosynthetic prokaryotic cell. Eventually, the engulfed cell formed a relationship with the host cell in which it was enclosed, becoming an *endosymbiont* (a cell living within another cell). Indeed, over the course of evolution, the host cell and its endosymbiont merged into a single organism, a eukaryotic cell with a mitochondrion. At least one of these cells may have then taken up a photosynthetic prokaryote, becoming the ancestor of eukaryotic cells that contain chloroplasts.

This is a widely accepted theory, which we will discuss in more detail in Concept 25.3. This theory is consistent with many structural features of mitochondria and chloroplasts. First, rather than being bounded by a single membrane like organelles of the endomembrane system, mitochondria and typical chloroplasts have two membranes surrounding them. (Chloroplasts also have an internal system of membranous sacs.) There is evidence that the ancestral engulfed

Figure 6.16 The endosymbiont theory of the origins of mitochondria and chloroplasts in eukaryotic cells. According to this theory, the proposed ancestors of mitochondria were oxygen-using nonphotosynthetic prokaryotes, while the proposed ancestors of chloroplasts were photosynthetic prokaryotes. The large arrows represent change over evolutionary time; the small arrows inside the cells show the process of the endosymbiont becoming an organelle, also over long periods of time.



prokaryotes had two outer membranes, which became the double membranes of mitochondria and chloroplasts. Second, like prokaryotes, mitochondria and chloroplasts contain ribosomes, as well as circular DNA molecules—like bacterial chromosomes—associated with their inner membranes. The DNA in these organelles programs the synthesis of some organelle proteins on ribosomes that have been synthesized and assembled there as well. Third, also consistent with their probable evolutionary origins as cells, mitochondria and chloroplasts are autonomous (somewhat independent) organelles that grow and reproduce within the cell.

Next, we focus on the structures of mitochondria and chloroplasts, while providing an overview of their structures and functions. (In Chapters 9 and 10, we will examine their roles as energy transformers.)

Mitochondria: Chemical Energy Conversion

Mitochondria are found in nearly all eukaryotic cells, including those of plants, animals, fungi, and most unicellular eukaryotes. Some cells have a single large mitochondrion, but more often a cell has hundreds or even thousands of mitochondria; the number correlates with the cell's level of metabolic activity. For example, cells that move or contract have proportionally more mitochondria per volume than less active cells.

Each of the two membranes enclosing the mitochondrion is a phospholipid bilayer with a unique collection of embedded proteins **(Figure 6.17)**. The outer membrane is smooth, but the inner membrane is convoluted, with infoldings called **cristae**. The inner membrane divides the mitochondrion into two internal compartments. The first is the intermembrane space, the narrow region between the inner and outer membranes. The second compartment, the **mitochondrial matrix**, is enclosed by the inner membrane. The matrix contains many different enzymes as well as the mitochondrial DNA and ribosomes. Enzymes in the matrix catalyze some of the steps of cellular respiration. Other proteins that function in respiration, including the enzyme that makes ATP, are built into the inner membrane. As highly folded surfaces, the cristae give the inner mitochondrial membrane a large surface area, thus enhancing the productivity of cellular respiration. This is another example of structure fitting function.

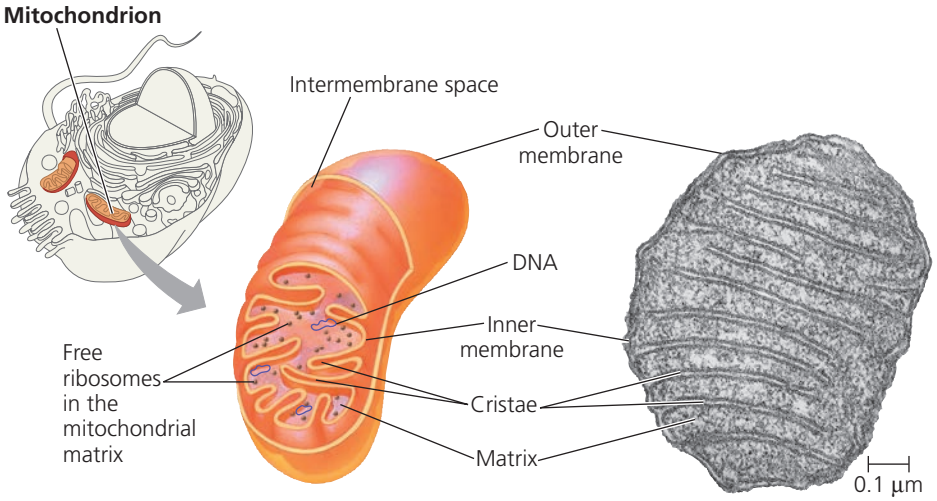
Mitochondria are generally in the range of 1–10 μm long. Time-lapse films of living cells reveal mitochondria moving around, changing their shapes, and fusing or dividing in two, unlike the static structures seen in electron micrographs of dead cells. These studies helped cell biologists understand that mitochondria in a living cell form a branched tubular network, seen in a whole cell in Figure 6.17b, that is in a dynamic state of flux.

Chloroplasts: Capture of Light Energy

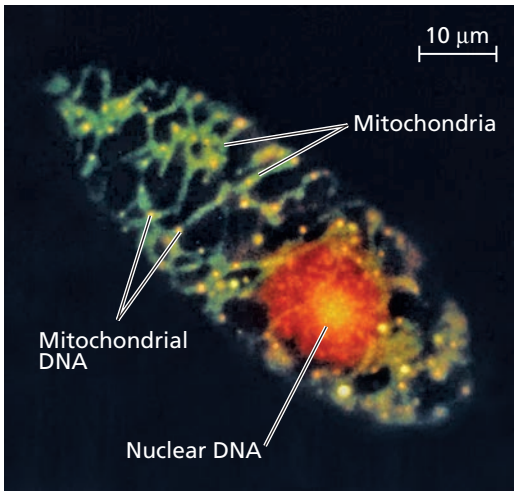
Chloroplasts contain the green pigment chlorophyll, along with enzymes and other molecules that function in the photosynthetic production of sugar. These lens-shaped organelles, about 3–6 μm in length, are found in leaves and other green organs of plants and in algae **(Figure 6.18**; see also Figure 6.26c).

The contents of a chloroplast are partitioned from the cytosol by an envelope consisting of two membranes separated by a very narrow intermembrane space. Inside the chloroplast is another membranous system in the form of flattened, interconnected sacs called **thylakoids**. In some regions, thylakoids are stacked like poker chips; each stack is called a **granum** (plural, *grana*). The fluid outside the thylakoids is the **stroma**, which contains the chloroplast DNA and ribosomes as well as many enzymes. The membranes of the chloroplast divide the chloroplast space into three compartments: the intermembrane space, the stroma, and the thylakoid space. This compartmental organization enables the chloroplast to convert light energy to chemical energy

Figure 6.17 The mitochondrion, site of cellular respiration. (a) The inner and outer membranes of the mitochondrion are evident in the drawing and electron micrograph (TEM). The cristae are infoldings of the inner membrane, which increase its surface area. The cutaway drawing shows the two compartments bounded by the membranes: the intermembrane space and the mitochondrial matrix. Many respiratory enzymes are found in the inner membrane and the matrix. Free ribosomes are also present in the matrix. The circular DNA molecules are associated with the inner mitochondrial membrane. **(b)** The light micrograph shows an entire unicellular eukaryote (*Euglena gracilis*) at a much lower magnification than the TEM. The mitochondrial matrix has been stained green. The mitochondria form a branched tubular network. The nuclear DNA is stained red; molecules of mitochondrial DNA appear as bright yellow spots.



(a) Diagram and TEM of mitochondrion



(b) Network of mitochondria in *Euglena* (LM)

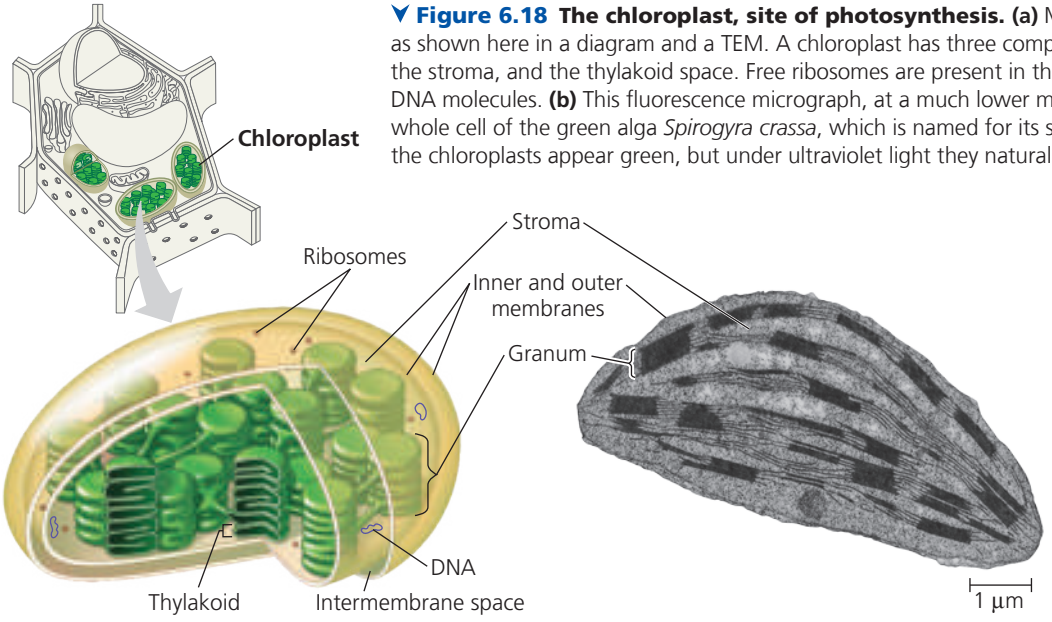
BioFlix® Animation: Mitochondria

during photosynthesis. (You will learn more about photosynthesis in Chapter 10.)

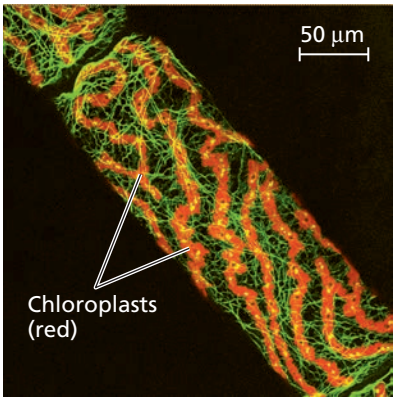
As with mitochondria, the static and rigid appearance of chloroplasts in micrographs or schematic diagrams cannot accurately depict their dynamic behavior in the living cell. Their shape is changeable, and they grow and occasionally pinch in two, reproducing themselves. They are mobile and, with mitochondria and other organelles, move around the cell along tracks of the cytoskeleton, a structural network we will consider in Concept 6.6.

The chloroplast is a specialized member of a family of closely related plant organelles called **plastids**. One type of plastid, the *amyloplast*, is a colorless organelle that stores starch (amylose), particularly in roots and tubers. Another is the *chromoplast*, which has pigments that give fruits and flowers their orange and yellow hues.

Figure 6.18 The chloroplast, site of photosynthesis. (a) Many plants have lens-shaped chloroplasts, as shown here in a diagram and a TEM. A chloroplast has three compartments: the intermembrane space, the stroma, and the thylakoid space. Free ribosomes are present in the stroma, as are copies of chloroplast DNA molecules. **(b)** This fluorescence micrograph, at a much lower magnification than the TEM, shows a whole cell of the green alga *Spirogyra crassa*, which is named for its spiral chloroplasts. Under natural light the chloroplasts appear green, but under ultraviolet light they naturally fluoresce red, as shown here.



(a) Diagram and TEM of chloroplast



(b) Chloroplasts in an algal cell

BioFlix® Animation: Chloroplasts and Mitochondria

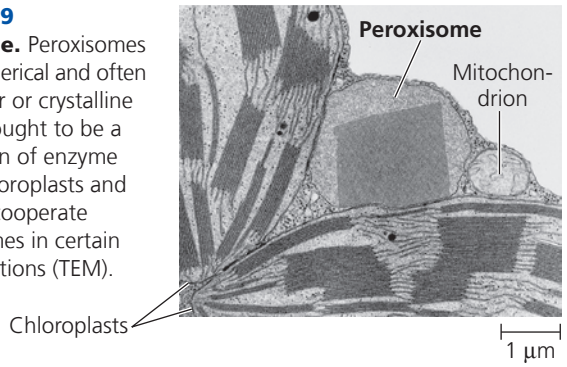


Figure 6.19 **A peroxisome.** Peroxisomes are roughly spherical and often have a granular or crystalline core that is thought to be a dense collection of enzyme molecules. Chloroplasts and mitochondria cooperate with peroxisomes in certain metabolic functions (TEM).

Peroxisomes: Oxidation

The **peroxisome** is a specialized metabolic compartment bounded by a single membrane **(Figure 6.19)**. Peroxisomes contain enzymes that remove hydrogen atoms from various substrates and transfer them to oxygen (O_2), producing hydrogen peroxide (H_2O_2) as a by-product (from which the organelle derives its name). These reactions have many different functions. Some peroxisomes use oxygen to break fatty acids down into smaller molecules that are transported to mitochondria and used as fuel for cellular respiration. Peroxisomes in the liver detoxify alcohol and other harmful compounds by transferring hydrogen from the poisonous compounds to oxygen. The H_2O_2 formed by peroxisomes is itself toxic, but the organelle also contains an enzyme that converts H_2O_2 to water. This is an excellent example of how the cell's compartmental structure is crucial to its functions: The enzymes that produce H_2O_2 and those that dispose of this toxic compound are sequestered away from other cellular components that could be damaged.

Specialized peroxisomes called *glyoxysomes* are found in the fat-storing tissues of plant seeds. These organelles contain enzymes that initiate the conversion of fatty acids to sugar, which the emerging seedling uses as a source of energy and carbon until it can produce its own sugar by photosynthesis.

How peroxisomes are related to other organelles is still an open question. They grow larger by incorporating proteins made in the cytosol and ER, as well as lipids made in the ER and within the peroxisome itself. Peroxisomes may increase in number by splitting in two when they reach a certain size, sparking the suggestion of an endosymbiotic evolutionary origin, but others argue against this scenario. Discussion of this issue is ongoing.

CONCEPT CHECK 6.5

1. Describe two characteristics shared by chloroplasts and mitochondria. Consider both function and membrane structure.
2. Do plant cells have mitochondria? Explain.
3. **WHAT IF?** A classmate proposes that mitochondria and chloroplasts should be classified in the endomembrane system. Argue against the proposal.

For suggested answers, see Appendix A.

CONCEPT 6.6

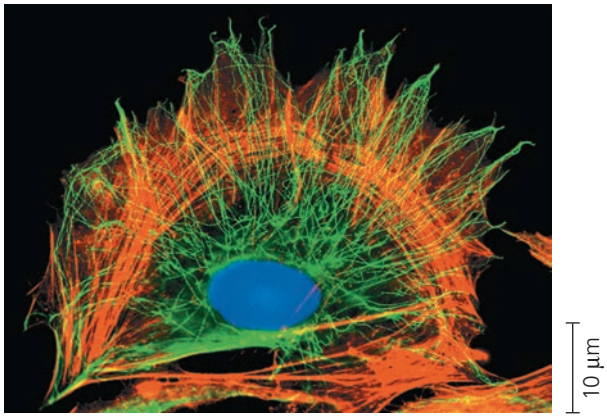
The cytoskeleton is a network of fibers that organizes structures and activities in the cell

In the early days of electron microscopy, biologists thought that the organelles of a eukaryotic cell floated freely in the cytosol. But improvements in both light microscopy and electron microscopy have revealed the **cytoskeleton**, a network of fibers extending throughout the cytoplasm **(Figure 6.20)**. Bacterial cells also have fibers that form a type of cytoskeleton, constructed of proteins similar to eukaryotic ones, but here we will concentrate on eukaryotes. The eukaryotic cytoskeleton, which plays a major role in organizing the structures and activities of the cell, is composed of three types of molecular structures: microtubules, microfilaments, and intermediate filaments.

Roles of the Cytoskeleton: Support and Motility

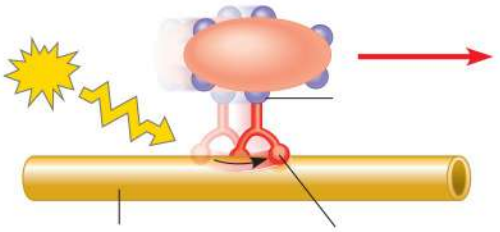
The most obvious function of the cytoskeleton is to give mechanical support to the cell and maintain its shape. This is especially important for animal cells, which lack walls. The remarkable strength and resilience of the cytoskeleton as a whole are based on its architecture. Like a dome tent, the cytoskeleton is stabilized by a balance between opposing forces exerted by its elements. And just as the skeleton of an animal helps fix the positions of other body parts, the cytoskeleton provides anchorage for many organelles and even cytosolic enzyme molecules. The cytoskeleton is more dynamic than an animal skeleton, however. It can be quickly dismantled in one part of the cell and reassembled in a new location, changing the shape of the cell.

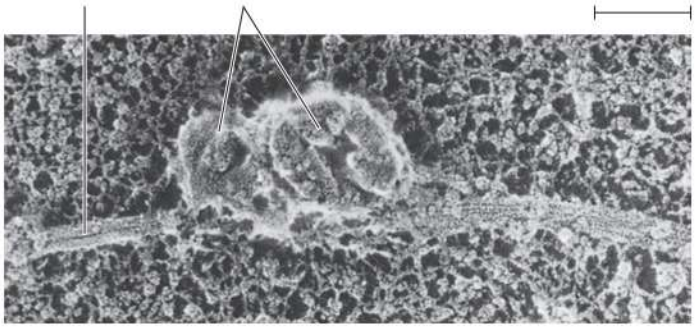
Figure 6.20 **The cytoskeleton.** As shown in this fluorescence micrograph, the cytoskeleton extends throughout the cell. The cytoskeletal elements have been tagged with different fluorescent molecules: green for microtubules and reddish-orange for microfilaments. A third component of the cytoskeleton, intermediate filaments, is not evident here. (The blue color tags the DNA in the nucleus.)

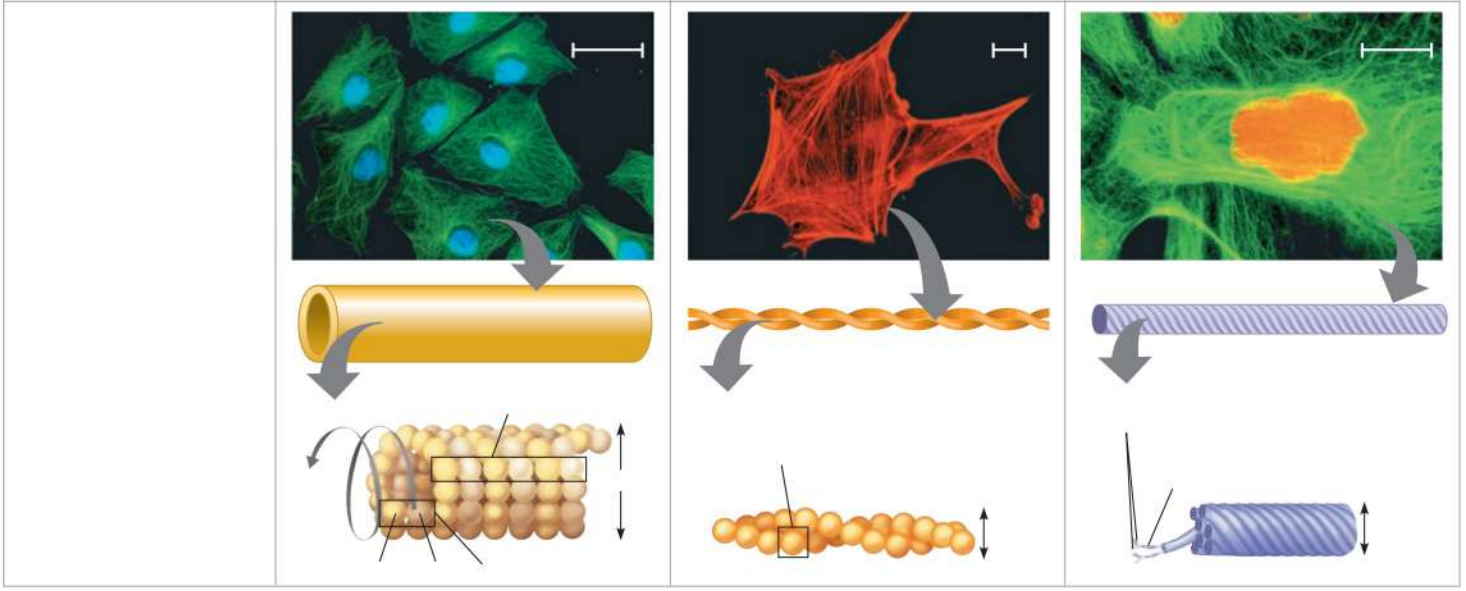


BioFlix® Animation: Cytoskeleton

Some types of cell motility (movement) also involve the cytoskeleton. The term *cell motility* includes both changes in cell location and movements of cell parts. Cell motility generally requires interaction of the cytoskeleton with **motor proteins**. There are many such examples: Cytoskeletal elements and motor proteins work together with plasma membrane molecules to allow whole cells to move along fibers outside the cell. Inside the cell, vesicles and other organelles often use motor protein "feet" to "walk" to their destinations along a track provided by the cytoskeleton. For example, this is how vesicles containing neurotransmitter molecules migrate to the tips of axons, the long extensions of nerve cells that release these molecules as chemical signals to adjacent nerve cells **(Figure 6.21)**. The cytoskeleton also manipulates the plasma membrane, bending it inward to form food vacuoles or other phagocytic vesicles.







Microtubules

All eukaryotic cells have **microtubules**, hollow rods constructed from globular proteins called tubulins. Each tubulin protein is a *dimer*, a molecule made up of two subunits. A tubulin dimer consists of two slightly different polypeptides, α-tubulin and β-tubulin. Microtubules grow in length by adding tubulin dimers; they can also be disassembled and their tubulins used to build microtubules elsewhere in the cell. Because of the orientation of tubulin dimers, the two ends of a microtubule are slightly different. One end can accumulate or release tubulin dimers at a much higher rate than the other, thus growing and shrinking significantly during cellular activities. (This is called the "plus end," not because it can only add tubulin proteins but because it's the end where both "on" and "off" rates are much higher.)

Microtubules shape and support the cell and also serve as tracks along which organelles equipped with motor proteins can move. In addition to the example in Figure 6.21, microtubules guide vesicles from the ER to the Golgi apparatus and from the Golgi to the plasma membrane. Microtubules are also involved in the separation of chromosomes during cell division, as shown in Figure 12.7.

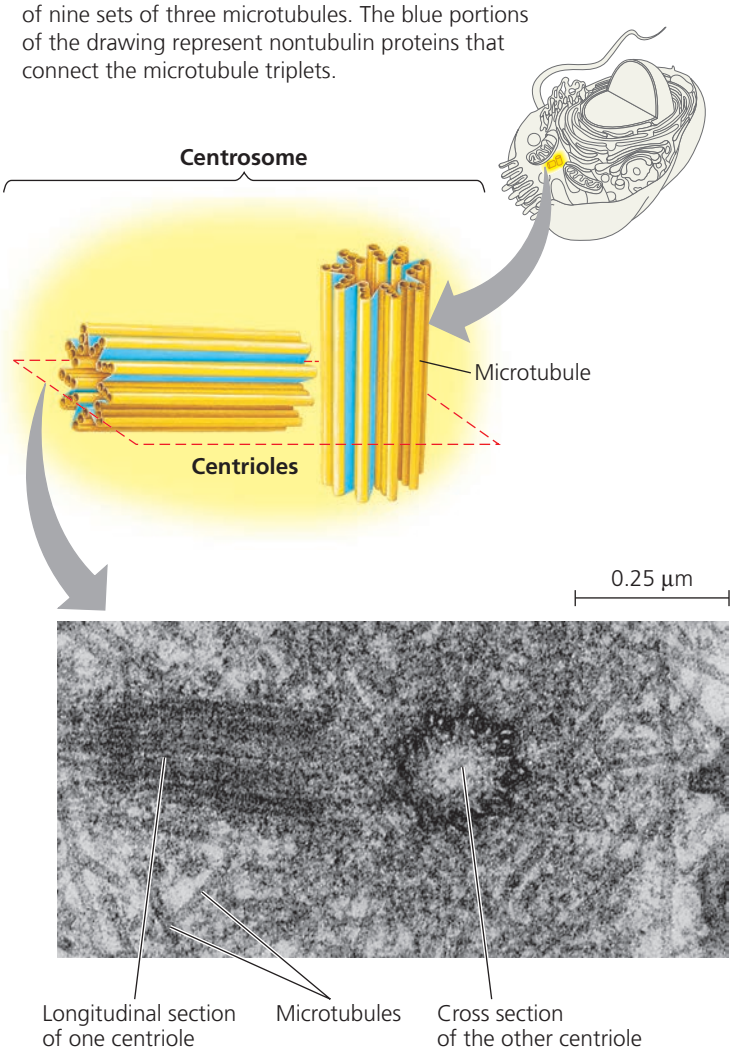
Centrosomes and Centrioles In animal cells, microtubules grow out from a **centrosome**, a region that is often located near the nucleus. These microtubules function as compression-resisting girders of the cytoskeleton. Within the centrosome is a pair of **centrioles**, each composed of nine sets of triplet microtubules arranged in a ring **(Figure 6.22)**. Although centrosomes with centrioles may help organize microtubule assembly in animal cells, many other eukaryotic cells lack centrosomes with centrioles and instead organize microtubules by other means.

Cilia and Flagella In eukaryotes, a specialized arrangement of microtubules is responsible for the beating of **flagella** (singular, *flagellum*) and **cilia** (singular, *cilium*), microtubule-containing extensions that project from some cells. (The bacterial flagellum, shown in Figure 6.5, has a completely different structure.) Many unicellular eukaryotes are propelled through water by cilia or flagella that act as locomotor appendages, and the sperm of animals, algae, and some plants have flagella. When cilia or flagella extend from cells that are held in place as part of a tissue layer, they can move fluid over the surface of the tissue. For example, the ciliated lining of the trachea (windpipe) sweeps mucus containing trapped debris out of the lungs (see the EMs in Figure 6.3). In a woman's reproductive tract, the cilia lining the oviducts help move an egg toward the uterus.

Motile cilia usually occur in large numbers on the cell surface. Flagella are usually limited to just one or a few per cell, and they are longer than cilia. Flagella and cilia differ in their beating patterns. A flagellum has an undulating motion like the tail of a fish. In contrast, cilia have alternating power and recovery strokes, much like the oars of a racing crew boat **(Figure 6.23)**.

A cilium may also act as a signal-receiving "antenna" for the cell. Cilia that have this function are generally nonmotile, and there is only one per cell. (In fact, in vertebrate animals, it appears that almost all cells have such a cilium, which is called a *primary cilium*.) Membrane proteins on this kind of cilium transmit molecular signals from the cell's environment to its interior, triggering signaling pathways that may lead to changes in the cell's activities. Cilium-based signaling appears to be crucial to brain function and to embryonic development.

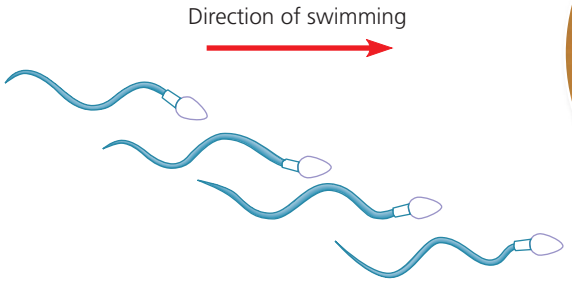
Figure 6.22 Centrosome containing a pair of centrioles. Most animal cells have a centrosome, a region near the nucleus where the cell's microtubules are initiated. Within the centrosome is a pair of centrioles, each about 250 nm (0.25 μm) in diameter. The two centrioles are at right angles to each other, and each is made up of nine sets of three microtubules. The blue portions of the drawing represent nontubulin proteins that connect the microtubule triplets.



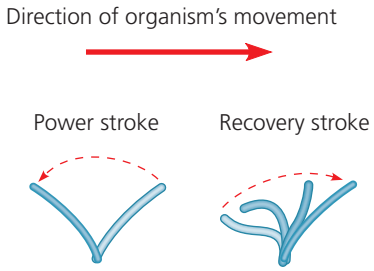
VISUAL SKILLS ➤ *How many microtubules are in a centrosome? In the drawing, circle and label one microtubule and describe its structure. Circle and label a triplet.*

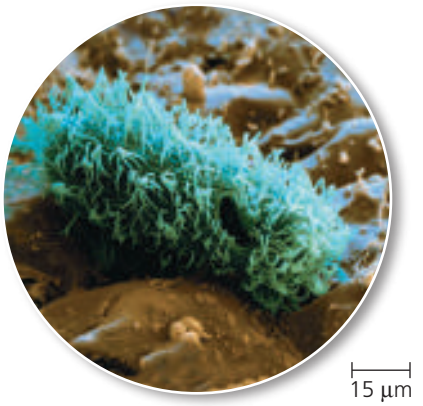
Figure 6.23 A comparison of the beating of flagella and motile cilia.

(a) Motion of flagella. A flagellum usually undulates, its snakelike motion driving a cell in the same direction as the axis of the flagellum. Propulsion of a human sperm cell is an example of flagellate locomotion (LM).



(b) Motion of cilia. Cilia have a back-and-forth motion. The rapid power stroke moves the cell in a direction perpendicular to the axis of the cilium. Then, during the slower recovery stroke,the cilium bends and sweeps sideways, closer to the cell surface. A dense nap of cilia, beating at a rate of about 40 to 60 strokes a second, covers this *Colpidium*, a freshwater protist (colorized SEM).





Video: Flagellum Movement in Swimming Sperm
Video: Flagellum Beating with ATP
Video: *Paramecium* Cilia

Though different in length, number per cell, and beating pattern, motile cilia and flagella share a common structure. Each motile cilium or flagellum has a group of microtubules sheathed in an extension of the plasma membrane **(Figure 6.24a)**. Nine doublets of microtubules are arranged in a ring with two single microtubules in its center **(Figure 6.24b)**. This arrangement, referred to as the "9 + 2" pattern, is found in nearly all eukaryotic flagella and motile cilia. (Nonmotile primary cilia have a "9 + 0" pattern, lacking the central pair of microtubules.) The microtubule assembly of a cilium or flagellum is anchored in the cell by a **basal body**, which is structurally very similar to a centriole, with microtubule triplets in a "9 + 0" pattern **(Figure 6.24c)**. In fact, in many animals (including humans), the basal body of the fertilizing sperm's flagellum enters the egg and becomes a centriole.

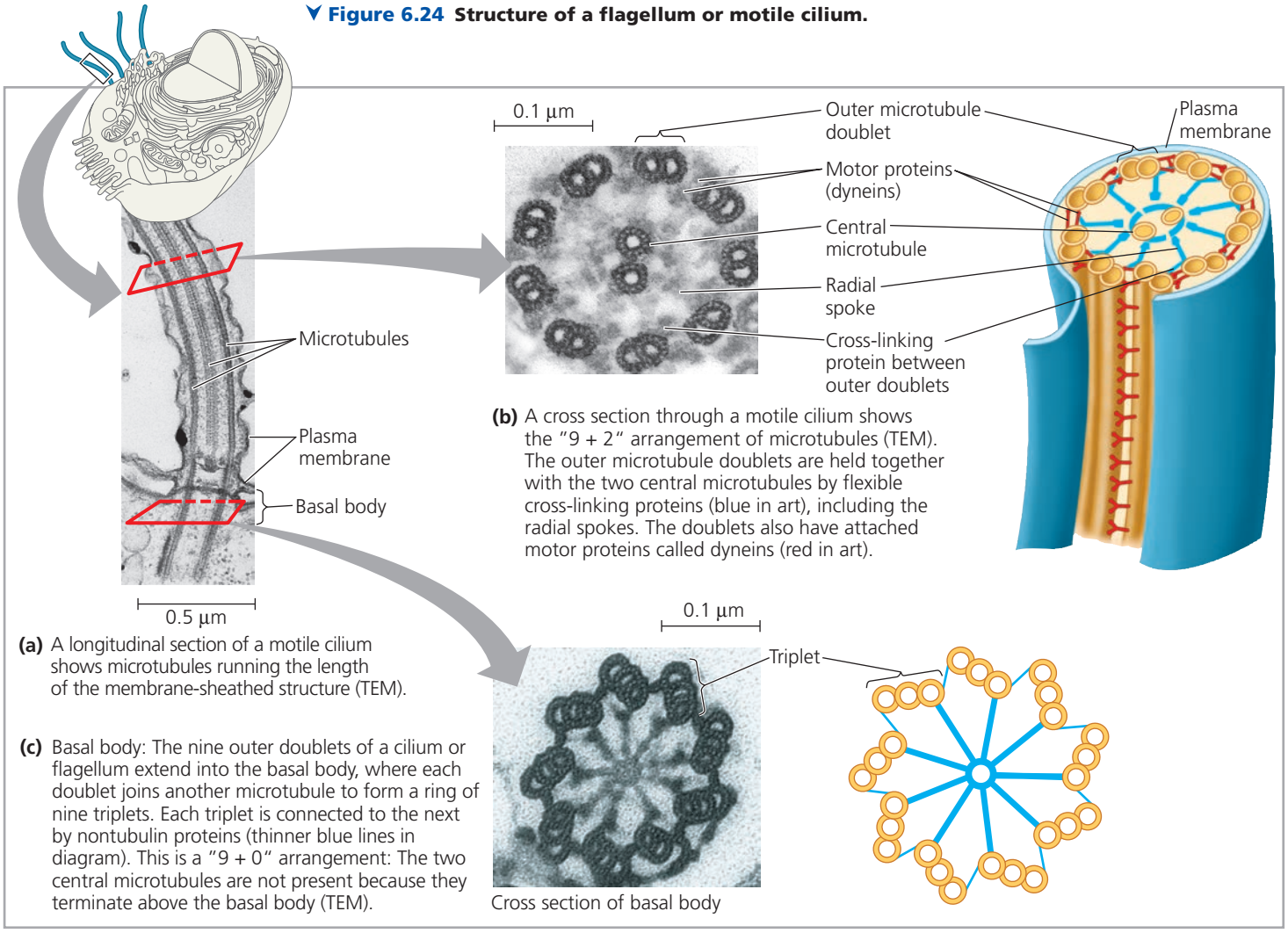
How does the microtubule assembly produce the bending movements of flagella and motile cilia? Bending involves large motor proteins called **dyneins** (red in the diagram in Figure 6.24) that are attached along each outer microtubule doublet. A typical dynein protein has two "feet" that "walk" along the microtubule of the adjacent doublet, using ATP for energy. One foot maintains contact, while the other releases and reattaches one step farther along the microtubule (see Figure 6.21). The outer doublets and two central microtubules are held together by flexible cross-linking proteins (blue in the diagram in Figure 6.24), and the walking movement is coordinated so that it happens on one side of the circle at a time. If the doublets were not held in place, the walking action would make them slide past each other. Instead, the movements of the dynein feet cause the microtubules—and the organelle as a whole—to bend.

Microfilaments (Actin Filaments)

Microfilaments are thin solid rods. They are also called actin filaments because they are built from molecules of **actin**, a globular protein. A microfilament is a twisted double chain of actin subunits (see Table 6.1). Besides occurring as linear filaments, microfilaments can form structural networks when certain proteins bind along the side of such a filament and allow a new filament to extend as a branch. Like microtubules, microfilaments seem to be present in all eukaryotic cells.

In contrast to the compression-resisting role of microtubules, the structural role of microfilaments in the cytoskeleton is to bear tension (pulling forces). A three-dimensional

Figure 6.24 Structure of a flagellum or motile cilium.



(a) A longitudinal section of a motile cilium shows microtubules running the length of the membrane-sheathed structure (TEM).

(b) A cross section through a motile cilium shows the "9 + 2" arrangement of microtubules (TEM). The outer microtubule doublets are held together with the two central microtubules by flexible cross-linking proteins (blue in art), including the radial spokes. The doublets also have attached motor proteins called dyneins (red in art).

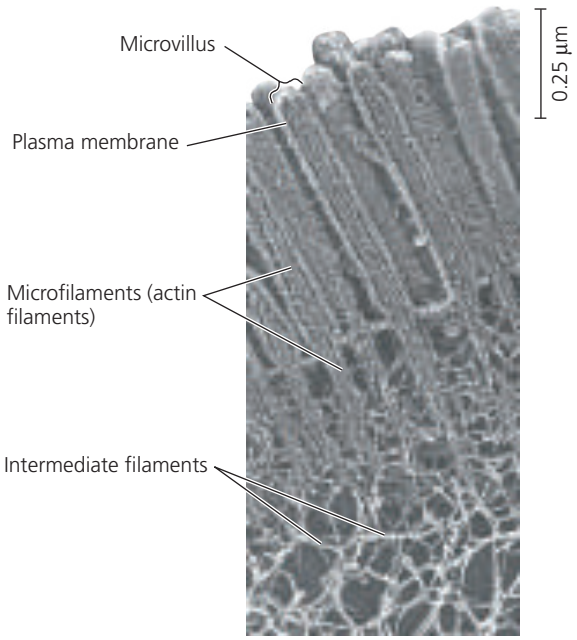
(c) Basal body: The nine outer doublets of a cilium or flagellum extend into the basal body, where each doublet joins another microtubule to form a ring of nine triplets. Each triplet is connected to the next by nontubulin proteins (thinner blue lines in diagram). This is a "9 + 0" arrangement: The two central microtubules are not present because they terminate above the basal body (TEM).

DRAW IT ➤ *In (a) and (b), circle and label the central pair of microtubules. In (a), show where they terminate, and explain why they aren't seen in the cross section of the basal body in (c).*

Animation: Cilia and Flagella

network formed by microfilaments just inside the plasma membrane (*cortical microfilaments*) helps support the cell's shape (see Figure 6.8). This network gives the outer cytoplasmic layer of a cell, called the **cortex**, the semisolid consistency of a gel, in contrast with the more fluid state of the interior cytoplasm. In some kinds of animal cells, such as nutrient-absorbing intestinal cells, bundles of microfilaments make up the core of microvilli, delicate projections that increase the cell's surface area **(Figure 6.25)**.

Microfilaments are well known for their role in cell motility. Thousands of actin filaments and thicker filaments



➤ **Figure 6.25 A structural role of microfilaments.** The surface area of this nutrient-absorbing intestinal cell is increased by its many microvilli (singular, *microvillus*), cellular extensions reinforced by bundles of microfilaments. These actin filaments are anchored to a network of intermediate filaments (TEM).

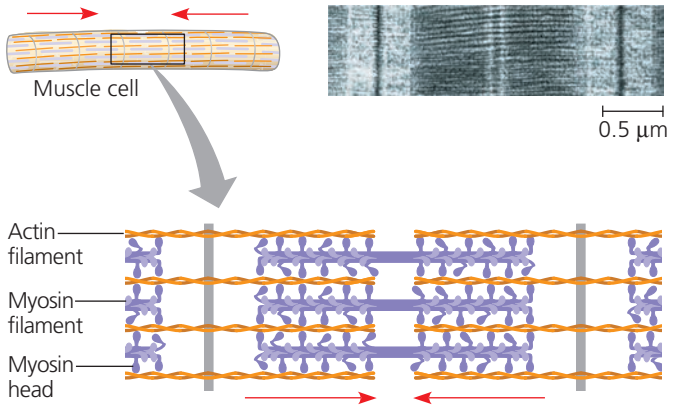
made of a protein called **myosin** interact to cause contraction of muscle cells **(Figure 6.26a)**; muscle contraction is described in detail in Concept 50.5. In the unicellular eukaryote *Amoeba* and some of our white blood cells, localized contractions brought about by actin and myosin are involved in the amoeboid (crawling) movement of the cells. The cell crawls along a surface by extending cellular extensions called **pseudopodia** (from the Greek *pseudes*, false, and *pod*, foot) and moving toward them **(Figure 6.26b)**. In plant cells, actin-protein interactions contribute to **cytoplasmic streaming**, a circular flow of cytoplasm within cells **(Figure 6.26c)**. This movement, which is especially common in large plant cells, speeds the movement of organelles and the distribution of materials within the cell.

Intermediate Filaments

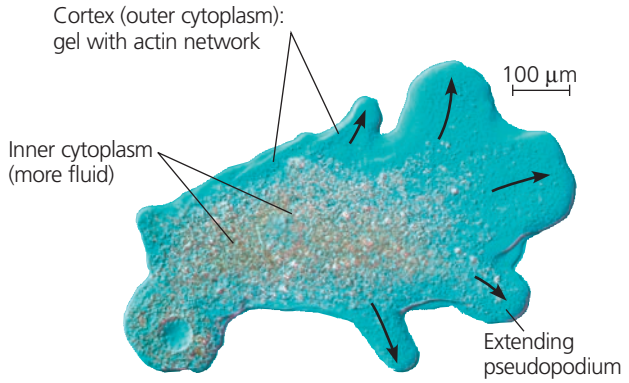
Intermediate filaments are named for their diameter, which is larger than the diameter of microfilaments but smaller than that of microtubules (see Table 6.1). While microtubules and microfilaments are found in all eukaryotic cells, intermediate filaments are only found in the cells of some animals, including vertebrates. Specialized for bearing tension (like microfilaments), intermediate filaments are a diverse class of cytoskeletal elements. Each type is constructed from a particular molecular subunit belonging to a family of proteins whose members include the keratins. Microtubules and microfilaments, in contrast, are consistent in diameter and composition in all eukaryotic cells.

Intermediate filaments are more permanent fixtures of cells than are microfilaments and microtubules, which are often disassembled and reassembled in various parts of a cell. Even after cells die, intermediate filament networks often persist; for example, the outer layer of our skin consists of dead skin cells full of keratin filaments. Chemical treatments that remove microfilaments and microtubules from the cytoplasm of living cells leave a web of intermediate filaments that retains its original shape. Such experiments suggest that intermediate filaments are especially sturdy and that they play an important role in reinforcing the shape of a cell and fixing the position of certain organelles. For instance, the nucleus typically sits within a cage made of intermediate filaments, fixed in location by branches of the filaments that extend into the cytoplasm. Other intermediate filaments make up the nuclear lamina, which lines the interior of the nuclear envelope (see Figure 6.9). By supporting a cell's shape, intermediate filaments help the cell carry out its specific function. For example, the network of intermediate filaments shown in Figure 6.25 anchors the microfilaments supporting the intestinal microvilli. Thus, the various kinds of intermediate filaments may function together as the permanent framework of the entire cell.

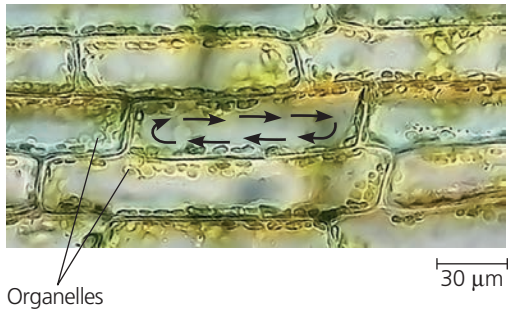
Figure 6.26 Microfilaments and motility. In these three examples, interactions between actin filaments and motor proteins bring about cell movement.



(a) Myosin motors in muscle cell contraction. The "walking" of myosin projections (the so-called heads) drives the parallel myosin and actin filaments past each other so that the actin filaments approach each other in the middle (red arrows). This shortens the muscle cell. Muscle contraction involves the shortening of many muscle cells at the same time (TEM).



(b) Amoeboid movement. Interaction of actin filaments with myosin causes contraction of the cell, pulling the cell's trailing end (at left) forward (to the right) (LM).



(c) Cytoplasmic streaming in plant cells. A layer of cytoplasm cycles around the cell, moving over tracks of actin filaments. Myosin motors attached to some organelles drive the streaming by interacting with the actin (LM).

MB **BioFlix® Animation: Actin and Myosin in Muscle Contraction**
Video: *Amoeba* Pseudopodia
Video: Cytoplasmic Streaming

CONCEPT CHECK 6.6

1. Describe how cilia and flagella bend.
2. **WHAT IF?** ➤ Males afflicted with Kartagener's syndrome are sterile because of immotile sperm, and they tend to suffer from lung infections. This disorder has a genetic basis. Suggest what the underlying defect might be.

For suggested answers, see Appendix A.

CONCEPT 6.7

Extracellular components and connections between cells help coordinate cellular activities

Having crisscrossed the cell to explore its interior components, we complete our tour of the cell by returning to the surface of this microscopic world, where there are additional structures with important functions. The plasma membrane is usually regarded as the boundary of the living cell, but most cells synthesize and secrete materials extracellularly (to the outside of the cell). Although these materials and the structures they form are outside the cell, their study is important to cell biology because they are involved in a great many essential cellular functions.

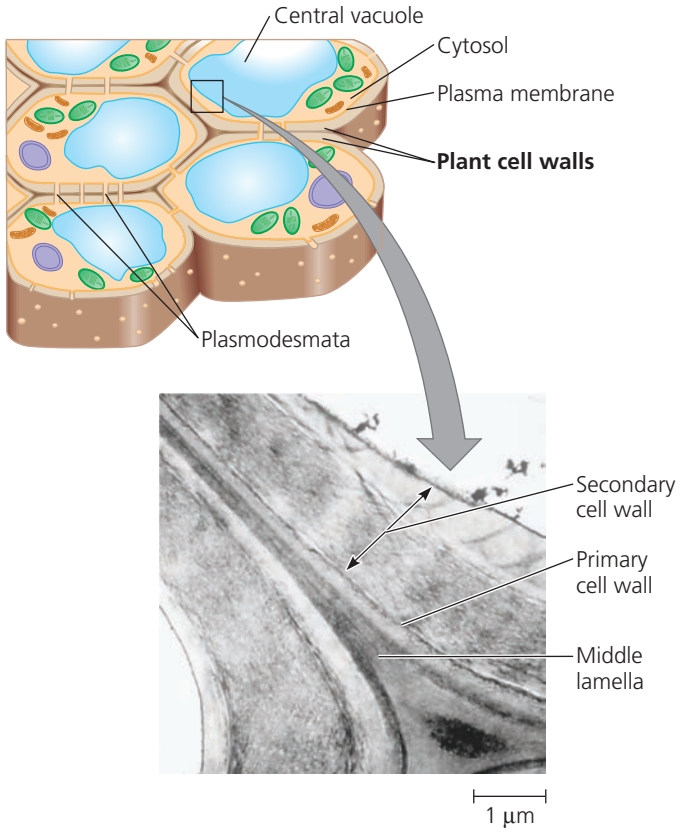
Cell Walls of Plants

The **cell wall** is an extracellular structure of plant cells **(Figure 6.27)**. This is one of the features that distinguishes plant cells from animal cells. The wall protects the plant cell, maintains its shape, and prevents excessive uptake of water. On the level of the whole plant, the strong walls of specialized cells hold the plant up against the force of gravity. Prokaryotes, fungi, and some unicellular eukaryotes also have cell walls, as you saw in Figures 6.5 and 6.8, but we will postpone discussion of them until Unit Five.

Plant cell walls are much thicker than the plasma membrane, ranging from 0.1 µm to several micrometers. The exact chemical composition of the wall varies from species to species and even from one cell type to another in the same plant, but the basic design of the wall is consistent. Microfibrils made of the polysaccharide cellulose (see Figure 5.6) are synthesized by an enzyme called cellulose synthase and secreted to the extracellular space, where they become embedded in a matrix of other polysaccharides and proteins. This combination of materials, strong fibers in a "ground substance" (matrix), is the same basic architectural design found in steel-reinforced concrete and in fiberglass.

A young plant cell first secretes a relatively thin and flexible wall called the **primary cell wall** (see the micrograph in Figure 6.27). Between primary walls of adjacent cells is the **middle lamella**, a thin layer rich in sticky polysaccharides called pectins. The middle lamella glues adjacent cells together. (Pectin is used in cooking as a thickening agent in jams and jellies.) When the cell matures and stops growing, it strengthens its wall. Some plant cells do this simply by secreting hardening substances into the primary wall. Other cells add a **secondary cell wall** between the plasma membrane and the primary wall. The secondary wall, often deposited in several laminated layers, has a strong and durable matrix that affords the cell protection and support. Wood, for example, consists mainly of secondary walls. Plant cell walls are usually perforated by channels between adjacent cells called plasmodesmata, which will be discussed shortly.

Figure 6.27 Plant cell walls. The drawing shows several cells, each with a cell wall, large vacuole, a nucleus, and several chloroplasts and mitochondria. The TEM shows the cell walls where two cells come together. The multilayered partition between plant cells consists of adjoining walls individually secreted by the cells.



The Extracellular Matrix (ECM) of Animal Cells

Although animal cells lack walls akin to those of plant cells, they do have an elaborate **extracellular matrix (ECM)**. The main ingredients of the ECM are glycoproteins and other carbohydrate-containing molecules secreted by the cells. (Recall that glycoproteins are proteins with covalently bonded carbohydrates, usually short chains of sugars.) The most abundant glycoprotein in the ECM of most animal cells is **collagen**, which forms strong fibers outside the cells (see Figure 5.18). In fact, collagen accounts for about 40% of the total protein in the human body. The collagen fibers are embedded in a network woven out of **proteoglycans**

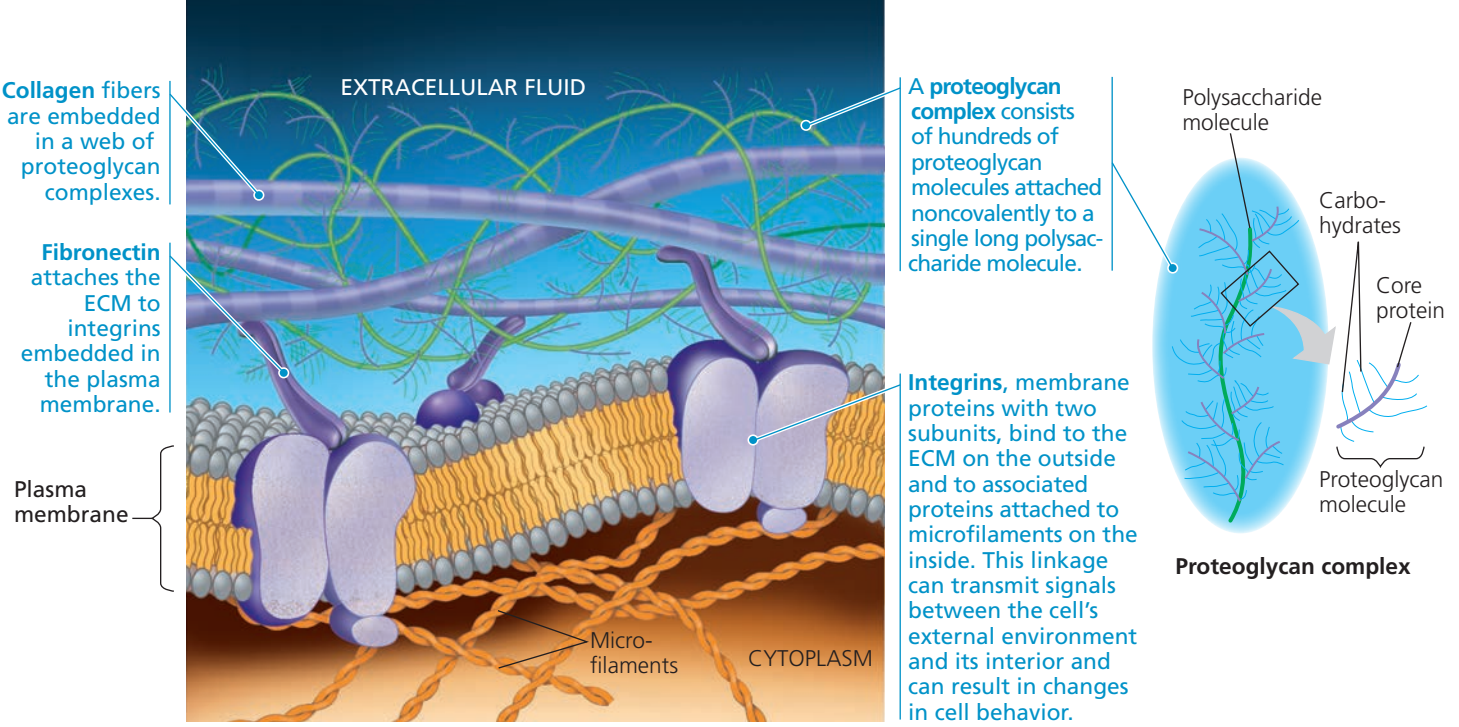


Figure 6.28 Extracellular matrix (ECM) of an animal cell. The molecular composition and structure of the ECM vary from one cell type to another. In this example, three different types of ECM molecules are present: collagen, fibronectin, and proteoglycans.

secreted by cells **(Figure 6.28)**. A proteoglycan molecule consists of a small core protein with many carbohydrate chains covalently attached, so that it may be up to 95% carbohydrate. Large proteoglycan complexes can form when hundreds of proteoglycan molecules become noncovalently attached to a single long polysaccharide molecule, as shown in Figure 6.28. Some cells are attached to the ECM by ECM glycoproteins such as **fibronectin**. Fibronectin and other ECM proteins bind to cell-surface receptor proteins called **integrins** that are built into the plasma membrane. Integrins span the membrane and bind on their cytoplasmic side to associated proteins attached to microfilaments of the cytoskeleton. The name *integrin* is based on the word *integrate*: Integrins are in a position to transmit signals between the ECM and the cytoskeleton and thus to integrate changes occurring outside and inside the cell.

Current research on fibronectin, other ECM molecules, and integrins reveals the influential role of the ECM in the lives of cells. By communicating with a cell through integrins, the ECM can regulate a cell's behavior. For example, some cells in a developing embryo migrate along specific pathways by matching the orientation of their microfilaments to the "grain" of fibers in the extracellular matrix. Researchers have also learned that the extracellular matrix around a cell can influence the activity of genes in the nucleus. Information about the ECM probably reaches the nucleus by a combination of mechanical and chemical signaling pathways. Mechanical signaling involves fibronectin, integrins, and microfilaments of the cytoskeleton. Changes in the cytoskeleton may in turn trigger signaling pathways inside the cell, leading to changes in the set of proteins being made by the cell and therefore changes in the cell's function. In this way, the extracellular matrix of a particular tissue may help coordinate the behavior of all the cells of that tissue. Direct connections between cells also function in this coordination, as we discuss next.

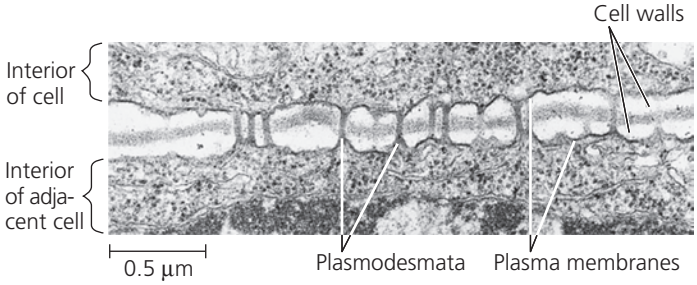
Cell Junctions

Cells in an animal or plant are organized into tissues, organs, and organ systems. Neighboring cells often adhere, interact, and communicate via sites of direct physical contact.

Plasmodesmata in Plant Cells

It might seem that the nonliving cell walls of plants would isolate plant cells from one another. But in fact, as shown in **Figure 6.29**, cell walls are perforated with **plasmodesmata** (singular, *plasmodesma*; from the Greek *desma*, bond), channels that connect cells. Cytosol passing through the

Figure 6.29 Plasmodesmata between plant cells. The cytoplasm of one plant cell is continuous with the cytoplasm of its neighbors via plasmodesmata, cytoplasmic channels through the cell walls (TEM).

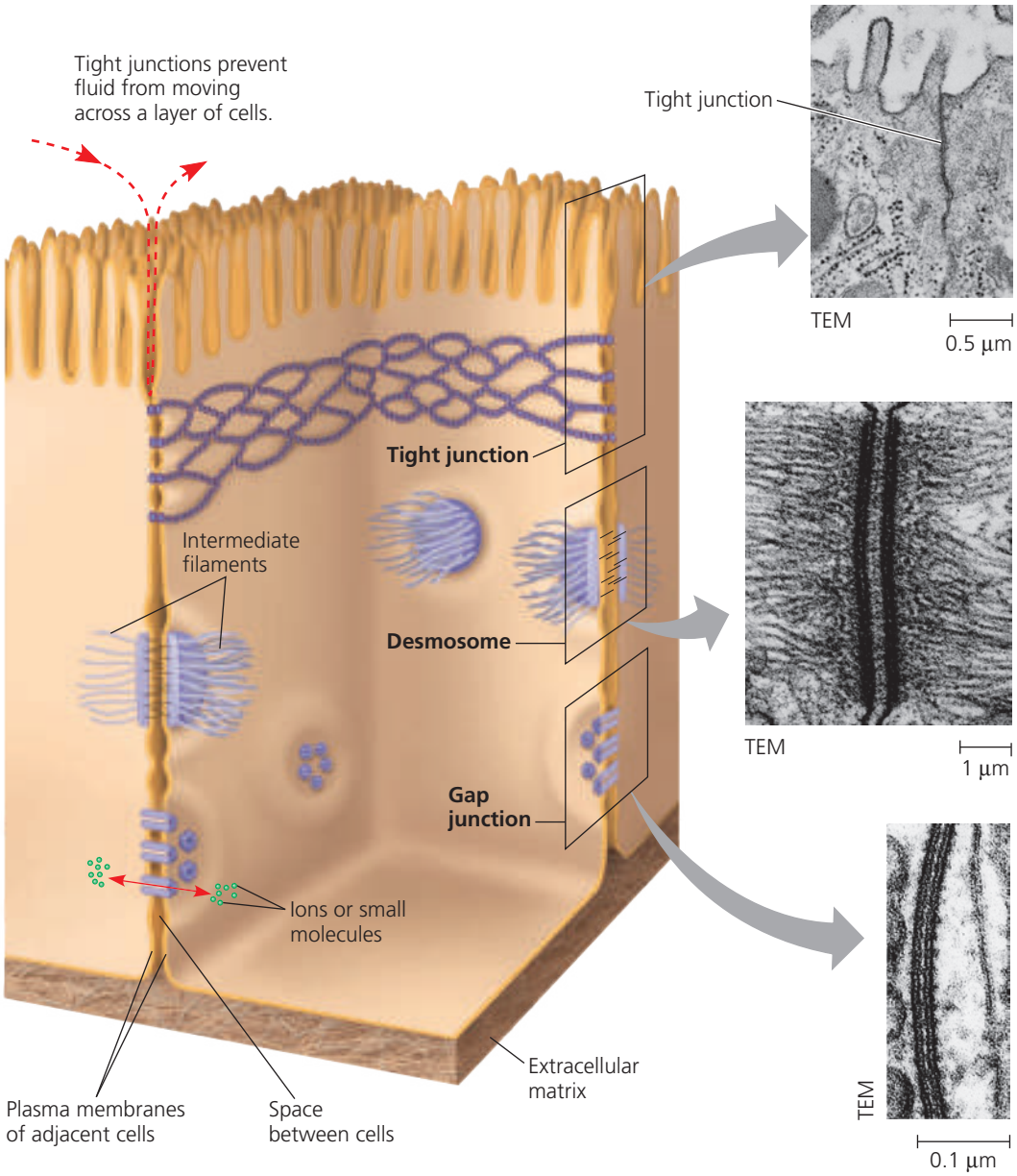


plasmodesmata joins the internal chemical environments of adjacent cells. These connections unify most of the plant into one living continuum. The plasma membranes of adjacent cells line the channel of each plasmodesma and thus are continuous. Water and small solutes can pass freely from cell to cell, and several experiments have shown that in some circumstances, certain proteins and RNA molecules can do this as well (see Concept 36.6). The macromolecules transported to neighboring cells appear to reach the plasmodesmata by moving along fibers of the cytoskeleton.

Tight Junctions, Desmosomes, and Gap Junctions in Animal Cells

In animals, there are three main types of cell junctions: *tight junctions, desmosomes*, and *gap junctions*. (Gap junctions are most like the plasmodesmata of plants, although gap junction pores are not lined with membrane.) All three types of cell junctions are especially common in epithelial tissue, which lines the external and internal surfaces of the body. **Figure 6.30** uses epithelial cells of the intestinal lining to illustrate these junctions.

Figure 6.30 Exploring Cell Junctions in Animal Tissues



Tight Junctions

At **tight junctions**, the plasma membranes of neighboring cells are very tightly pressed against each other, bound together by specific proteins. Forming continuous seals around the cells, tight junctions establish a barrier that prevents leakage of extracellular fluid across a layer of epithelial cells (see red dashed arrow). For example, tight junctions between skin cells make us watertight.

Desmosomes

Desmosomes (one type of *anchoring junction*) function like rivets, fastening cells together into strong sheets. Intermediate filaments made of sturdy keratin proteins anchor desmosomes in the cytoplasm. Desmosomes attach muscle cells to each other in a muscle. Some "muscle tears" involve the rupture of desmosomes.

Gap Junctions

Gap junctions (also called *communicating junctions*) provide cytoplasmic channels from one cell to an adjacent cell and in this way are similar in their function to the plasmodesmata in plants. Gap junctions consist of membrane proteins that surround a pore through which ions, sugars, amino acids, and other small molecules may pass. Gap junctions are necessary for communication between cells in many types of tissues, such as heart muscle, and in animal embryos.

Animation: Cell Junctions

CONCEPT CHECK 6.7

1. In what way are the cells of plants and animals structurally different from single-celled eukaryotes?
2. **WHAT IF? ➤** If the plant cell wall or the animal extracellular matrix were impermeable, what effect would this have on cell function?
3. **MAKE CONNECTIONS ➤** The polypeptide chain that makes up a tight junction weaves back and forth through the membrane four times, with two extracellular loops, and one loop plus short C-terminal and N-terminal tails in the cytoplasm. Looking at Figure 5.14, what would you predict about the amino acid sequence of the tight junction protein?

For suggested answers, see Appendix A.

CONCEPT 6.8

A cell is greater than the sum of its parts

From our panoramic view of the cell's compartmental organization to our close-up inspection of each organelle's architecture, this tour of the cell has provided many opportunities to correlate structure with function. (This would be a good time to review cell structure by returning to Figure 6.8.)

BioFlix® Animation: Tour of an Animal Cell
BioFlix® Animation: Tour of a Plant Cell

Even as we dissect the cell, remember that none of its components works alone. As an example of cellular integration, consider the microscopic scene in **Figure 6.31**. The large cell is a macrophage (see Figure 6.13a). It helps defend the mammalian body against infections by ingesting bacteria (the smaller cells) into phagocytic vesicles. The macrophage crawls along a surface and reaches out to the bacteria with thin pseudopodia (specifically, filopodia). Actin filaments interact with other elements of the cytoskeleton in these movements. After the macrophage engulfs the bacteria, they are destroyed by lysosomes produced by the elaborate endomembrane system. The digestive enzymes of the lysosomes and the proteins of the cytoskeleton are all made by ribosomes. And the synthesis of these proteins is programmed by genetic messages dispatched from the DNA in the nucleus. All these processes require energy, which mitochondria supply in the form of ATP.

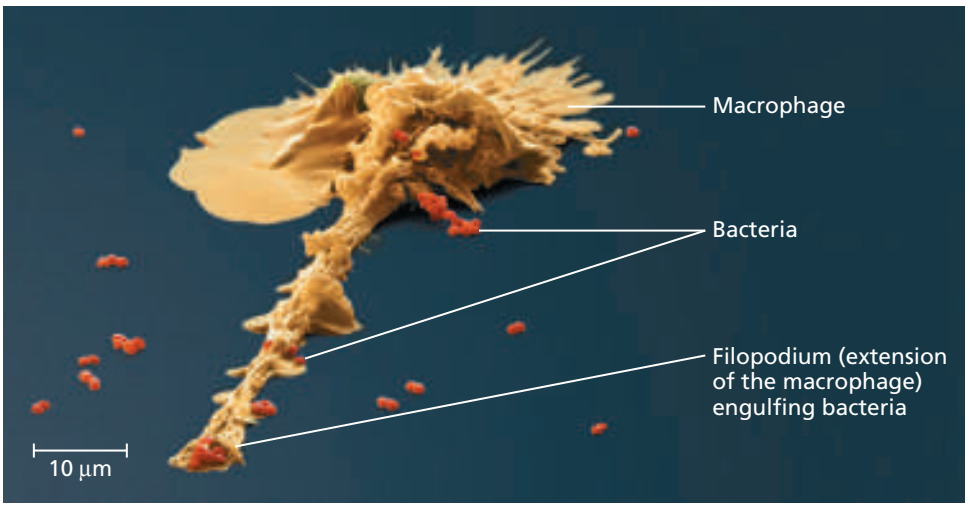
Cellular functions arise from cellular order: The cell is a living unit greater than the sum of its parts. The cell in Figure 6.31 is a good example of integration of cellular processes, seen from the outside. But what about the internal organization of a cell? As you proceed in your study of biology to consider different cellular processes, it will be helpful to try to visualize the architecture and furnishings inside a cell. **Figure 6.32** is designed to help you get a sense of the relative sizes and organization of important biological molecules and macromolecules, along with cellular structures and organelles. As you study this figure, see if you can shrink yourself down to the size of a protein and contemplate your surroundings.

CONCEPT CHECK 6.8

1. *Colpidium colpoda* is a unicellular eukaryote that lives in freshwater, eats bacteria, and moves by cilia (see Figure 6.23b). Describe how the parts of this cell work together in the functioning of *C. colpoda*, including as many organelles and other cell structures as you can.

For suggested answers, see Appendix A.

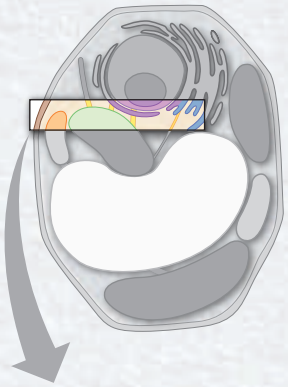
Figure 6.31 The emergence of cellular functions. The ability of this macrophage (brown) to recognize, apprehend, and destroy *Staphylococcus* bacteria (orange) is a coordinated activity of the whole cell. Its cytoskeleton, lysosomes, and plasma membrane are among the components that function in phagocytosis (colorized SEM).

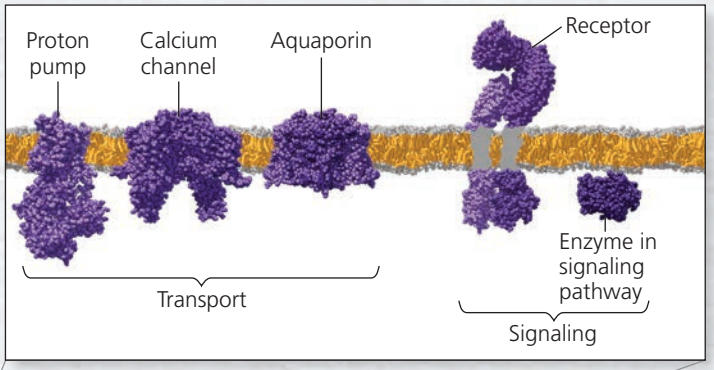


Animation: Review of Animal Cell Structure and Function

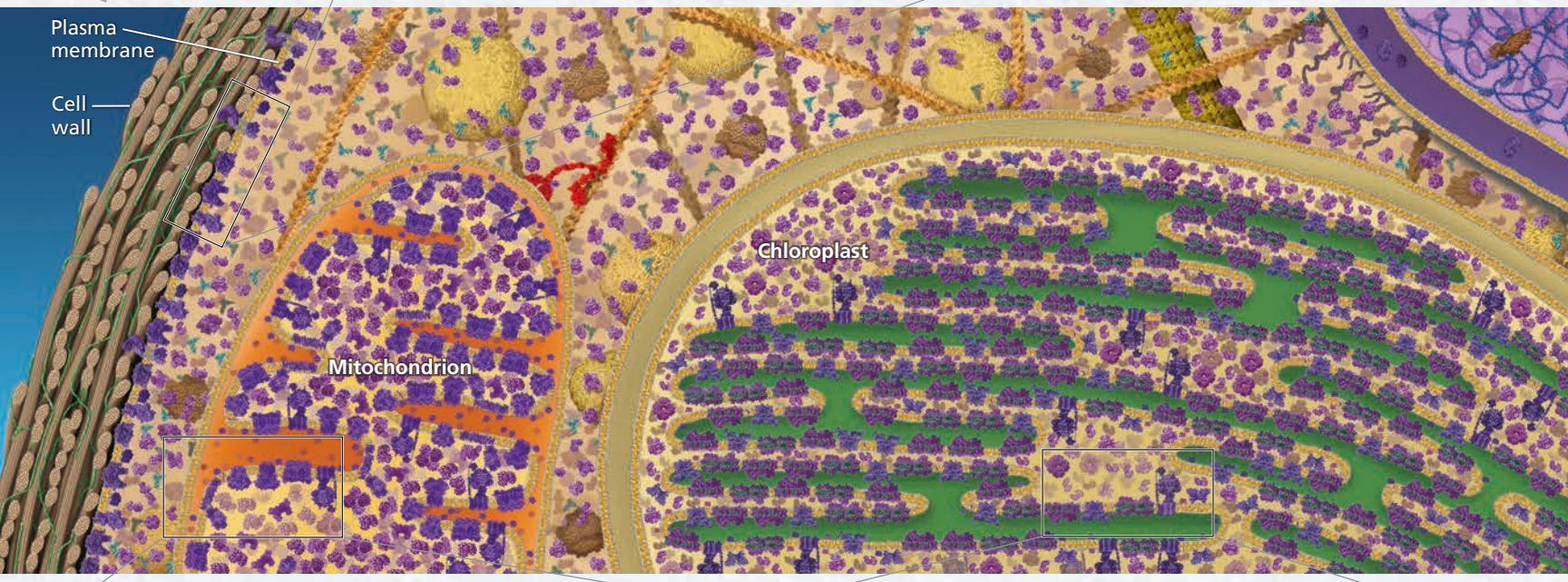
Figure 6.32 Visualizing the Scale of the Molecular Machinery in a Cell

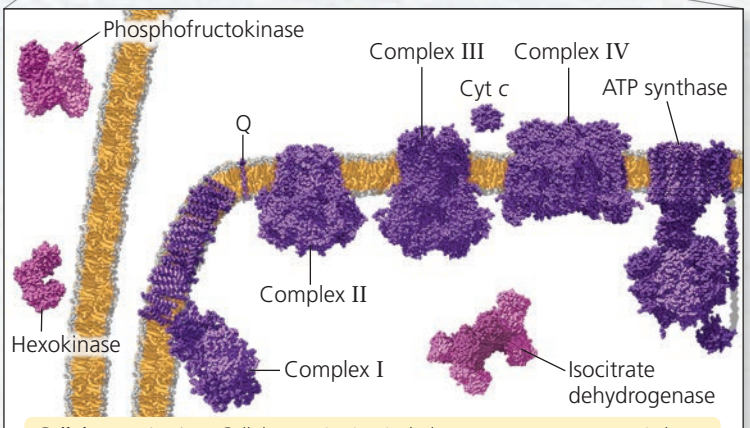
A slice of a plant cell's interior is illustrated in the center panel, with all structures and molecules drawn to scale. Selected molecules and structures are shown above and below, all enlarged by the same factor so you can compare their sizes. All protein and nucleic acid structures are based on data from the Protein Data Bank; regions whose structure has not yet been determined are shown in gray.



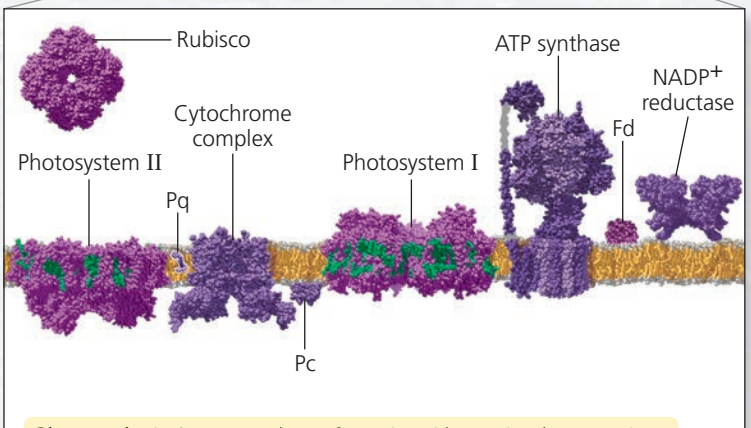


Membrane proteins: Proteins embedded in the plasma membrane or other cellular membranes help transport substances across membranes, conduct signals from one side of the membrane to the other, and participate in other crucial cellular functions. Many proteins are able to move within the membrane.



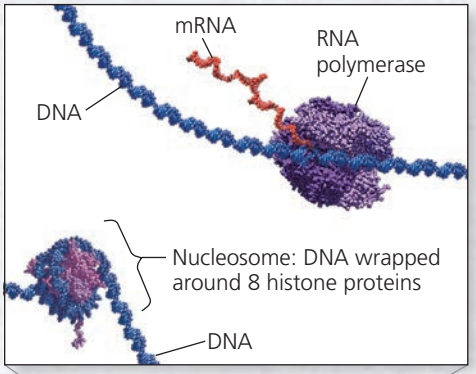


Cellular respiration: Cellular respiration includes many steps, some carried out by individual proteins or protein complexes in the cytoplasm and the mitochondrial matrix. Other proteins and protein complexes, involved in generating ATP from food molecules, form a "chain" in the inner mitochondrial membrane.



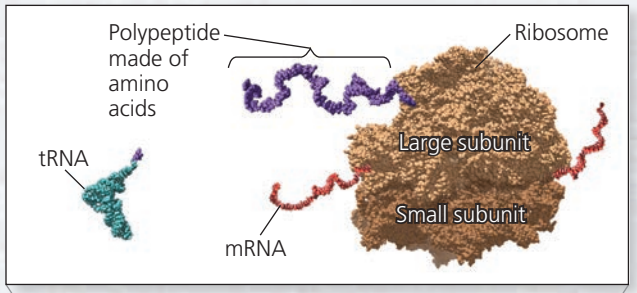
Photosynthesis: Large complexes of proteins with associated nonprotein molecules are embedded in chloroplast membranes. Together, they can trap light energy in molecules that are later used by other proteins inside the chloroplast to make sugars. This is the basis for all life on the planet.

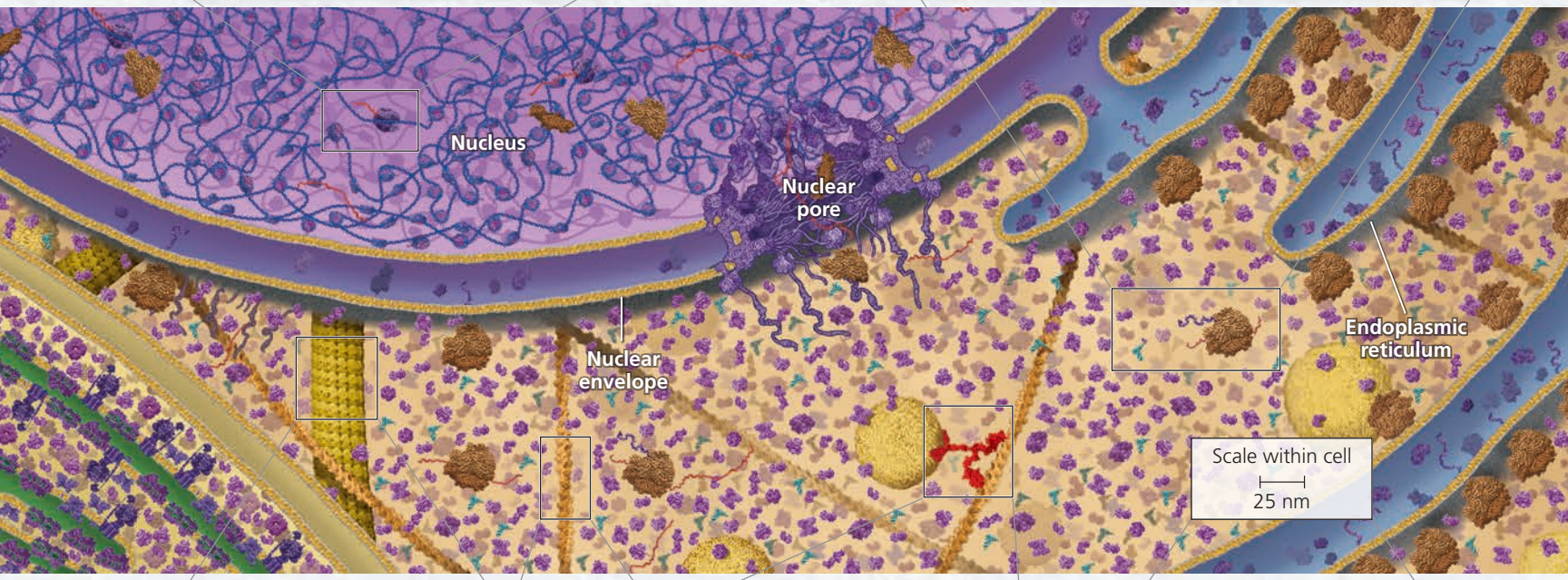
Transcription: In the nucleus, the information contained in a DNA sequence is transferred to messenger RNA (mRNA) by an enzyme called RNA polymerase. After their synthesis, mRNA molecules leave the nucleus via nuclear pores.

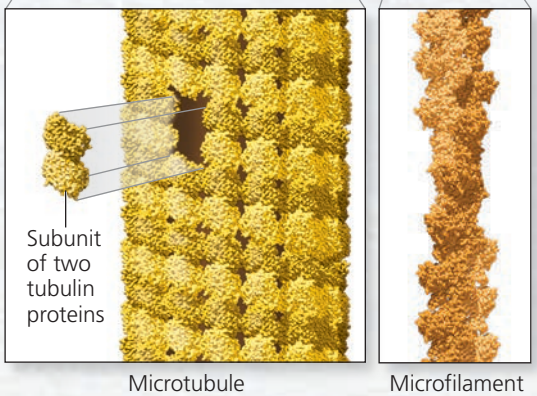


Nuclear pore: The nuclear pore complex regulates molecular traffic in and out of the nucleus, which is bounded by a double membrane. Among the largest structures that pass through the pore are the ribosomal subunits, which are built in the nucleus.

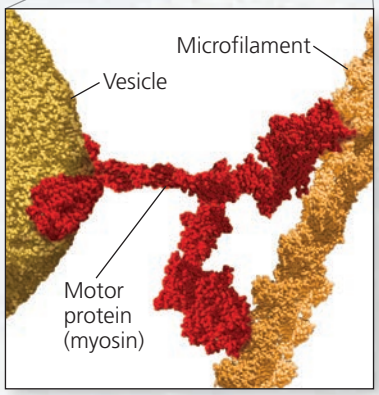
Translation: In the cytoplasm, the information in mRNA is used to assemble a polypeptide with a specific sequence of amino acids. Both transfer RNA (tRNA) molecules and a ribosome play a role. The eukaryotic ribosome, which includes a large subunit and a small subunit, is a colossal complex composed of four large ribosomal RNA (rRNA) molecules and more than 80 proteins. Through transcription and translation, the nucleotide sequence of DNA determines the amino acid sequence of a polypeptide, via the intermediary mRNA.



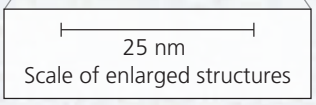




Cytoskeleton: Cytoskeletal structures are polymers of protein subunits. Microtubules are hollow structural rods made of tubulin protein subunits, while microfilaments are cables that have two chains of actin proteins wound around each other.



Motor proteins: Responsible for transport of vesicles and movement of organelles within the cell. This requires energy, often provided by ATP hydrolysis.



1. *List the following structures from largest to smallest: proton pump, nuclear pore, Cyt c, ribosome.*
2. *Considering the structures of a nucleosome and of RNA polymerase, speculate about what must happen before RNA polymerase can transcribe the DNA wrapped around the histone proteins of a nucleosome.*
3. *Find another myosin motor protein walking on a microfilament in this figure. What organelle is being moved by that myosin protein?*

Instructors: Additional questions related to this Visualizing Figure can be assigned in MasteringBiology.

6 Chapter Review

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SUMMARY OF KEY CONCEPTS

CONCEPT 6.1

Biologists use microscopes and biochemistry to study cells *(pp. 94–97)*

VOCAB SELF-QUIZ goo.gl/6u55ks

- Improvements in microscopy that affect the parameters of magnification, resolution, and contrast have catalyzed progress in the study of cell structure. **Light microscopy** (LM) and **electron microscopy** (EM), as well as other types, remain important tools.
- Cell biologists can obtain pellets enriched in particular cellular components by centrifuging disrupted cells at sequential speeds, a process known as **cell fractionation**.

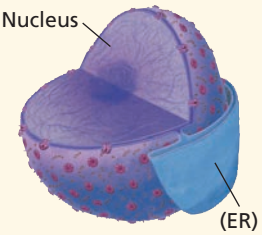
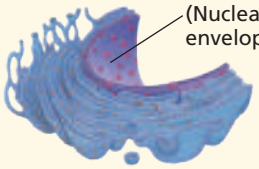
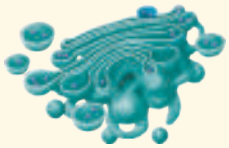
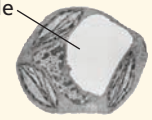
? *How do microscopy and biochemistry complement each other to reveal cell structure and function?*

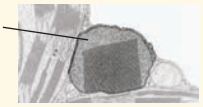
CONCEPT 6.2

Eukaryotic cells have internal membranes that compartmentalize their functions *(pp. 97–102)*

- All cells are bounded by a **plasma membrane**.
- **Prokaryotic cells** lack nuclei and other membrane-enclosed **organelles**, while **eukaryotic cells** have internal membranes that compartmentalize cellular functions.
- The surface-to-volume ratio is an important parameter affecting cell size and shape.
- Plant and animal cells have most of the same organelles: a nucleus, endoplasmic reticulum, Golgi apparatus, and mitochondria. Chloroplasts are present only in cells of photosynthetic eukaryotes.

? *Explain how the compartmental organization of a eukaryotic cell contributes to its biochemical functioning.*

	Cell Component	Structure	Function
CONCEPT 6.3 **The eukaryotic cell's genetic instructions are housed in the nucleus and carried out by the ribosomes** *(pp. 102–104)* ? *Describe the relationship between the nucleus and ribosomes.*	Nucleus 	Surrounded by nuclear envelope (double membrane) perforated by nuclear pores; nuclear envelope continuous with endoplasmic reticulum (ER)	Houses chromosomes, which are made of chromatin (DNA and proteins); contains nucleoli, where ribosomal subunits are made; pores regulate entry and exit of materials
	Ribosome 	Two subunits made of ribosomal RNAs and proteins; can be free in cytosol or bound to ER	Protein synthesis
CONCEPT 6.4 **The endomembrane system regulates protein traffic and performs metabolic functions** *(pp. 104–109)* ? *Describe the key role played by transport vesicles in the endomembrane system.*	Endoplasmic reticulum (ER) 	Extensive network of membrane-bounded tubules and sacs; membrane separates lumen from cytosol; continuous with nuclear envelope	Smooth ER: synthesis of lipids, metabolism of carbohydrates, Ca^{2+} storage, detoxification of drugs and poisons Rough ER: aids in synthesis of secretory and other proteins on bound ribosomes; adds carbohydrates to proteins to make glycoproteins; produces new membrane
	Golgi apparatus 	Stacks of flattened membranous sacs; has polarity (*cis* and *trans* faces)	Modification of proteins, carbohydrates on proteins, and phospholipids; synthesis of many polysaccharides; sorting of Golgi products, which are then released in vesicles
	Lysosome 	Membranous sac of hydrolytic enzymes (in animal cells)	Breakdown of ingested substances, cell macromolecules, and damaged organelles for recycling
	Vacuole 	Large membrane-bounded vesicle	Digestion, storage, waste disposal, water balance, cell growth, and protection

	Cell Component	Structure	Function
CONCEPT 6.5 **Mitochondria and chloroplasts change energy from one form to another** *(pp. 109–112)* ? *What does the endosymbiont theory propose as the origin for mitochondria and chloroplasts? Explain.*	Mitochondrion 	Bounded by double membrane; inner membrane has infoldings	Cellular respiration
	Chloroplast 	Typically two membranes around fluid stroma, which contains thylakoids stacked into grana	Photosynthesis (chloroplasts are in cells of photosynthetic eukaryotes, including plants)
	Peroxisome 	Specialized metabolic compartment bounded by a single membrane	Contains enzymes that transfer H atoms from substrates to oxygen, producing H_2O_2 (hydrogen peroxide), which is converted to H_2O.

CONCEPT 6.6

The cytoskeleton is a network of fibers that organizes structures and activities in the cell *(pp. 112–118)*

- The **cytoskeleton** functions in structural support for the cell and in motility and signal transmission.
- **Microtubules** shape the cell, guide organelle movement, and separate chromosomes in dividing cells. **Cilia** and **flagella** are motile appendages containing microtubules. Primary cilia also play sensory and signaling roles. **Microfilaments** are thin rods that function in muscle contraction, amoeboid movement, **cytoplasmic streaming**, and support of microvilli. **Intermediate filaments** support cell shape and fix organelles in place.

? *Describe the role of motor proteins inside the eukaryotic cell and in whole-cell movement.*

CONCEPT 6.7

Extracellular components and connections between cells help coordinate cellular activities *(pp. 118–121)*

- Plant **cell walls** are made of cellulose fibers embedded in other polysaccharides and proteins.
- Animal cells secrete glycoproteins and proteoglycans that form the **extracellular matrix (ECM)**, which functions in support, adhesion, movement, and regulation.
- Cell junctions connect neighboring cells. Plants have **plasmodesmata** that pass through adjoining cell walls. Animal cells have **tight junctions, desmosomes**, and **gap junctions**.

? *Compare the structure and functions of a plant cell wall and the extracellular matrix of an animal cell.*

CONCEPT 6.8

A cell is greater than the sum of its parts *(pp. 121–123)*

- Many components work together in a functioning cell.

? *When a cell ingests a bacterium, what role does the nucleus play?*

TEST YOUR UNDERSTANDING

PRACTICE TEST
goo.gl/CUYGKD

Level 1: Knowledge/Comprehension

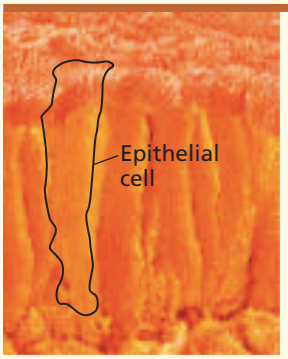
1. Which structure is *not* part of the endomembrane system?
   (A) nuclear envelope (C) Golgi apparatus
   (B) chloroplast (D) plasma membrane
2. Which structure is common to plant *and* animal cells?
   (A) chloroplast (C) mitochondrion
   (B) central vacuole (D) centriole
3. Which of the following is present in a prokaryotic cell?
   (A) mitochondrion (C) nuclear envelope
   (B) ribosome (D) chloroplast

Level 2: Application/Analysis

4. Cyanide binds to at least one molecule involved in producing ATP. If a cell is exposed to cyanide, most of the cyanide will be found within the
   (A) mitochondria. (C) peroxisomes.
   (B) ribosomes. (D) lysosomes.
5. Which cell would be best for studying lysosomes?
   (A) muscle cell (C) bacterial cell
   (B) nerve cell (D) phagocytic white blood cell
6. **DRAW IT** From memory, draw two eukaryotic cells. Label the structures listed here and show any physical connections between the internal structures of each cell: nucleus, rough ER, smooth ER, mitochondrion, centrosome, chloroplast, vacuole, lysosome, microtubule, cell wall, ECM, microfilament, Golgi apparatus, intermediate filament, plasma membrane, peroxisome, ribosome, nucleolus, nuclear pore, vesicle, flagellum, microvilli, plasmodesma.

Level 3: Synthesis/Evaluation

7. **EVOLUTION CONNECTION** (a) What cell structures best reveal evolutionary unity? (b) Provide an example of diversity related to specialized cellular modifications.
8. **SCIENTIFIC INQUIRY** Imagine protein X, destined to span the plasma membrane. Assume that the mRNA carrying the genetic message for protein X has already been translated by ribosomes in a cell culture. If you fractionate the cells (see Figure 6.4), in which fraction would you find protein X? Explain by describing its transit through the cell.
9. **WRITE ABOUT A THEME: ORGANIZATION** Considering some of the characteristics that define life and drawing on your knowledge of cellular structures and functions, write a short essay (100–150 words) that discusses this statement: Life is an emergent property that appears at the level of the cell. (See Concept 1.1.)
10. **SYNTHESIZE YOUR KNOWLEDGE**



The cells in this SEM are epithelial cells from the small intestine. Discuss how aspects of their structure contribute to their specialized functions of nutrient absorption and as a barrier between the intestinal contents and the blood supply on the other side of the sheet of epithelial cells.

For selected answers, see Appendix A.

MB For additional practice questions, check out the **Dynamic Study Modules** in MasteringBiology. You can use them to study on your smartphone, tablet, or computer anytime, anywhere!

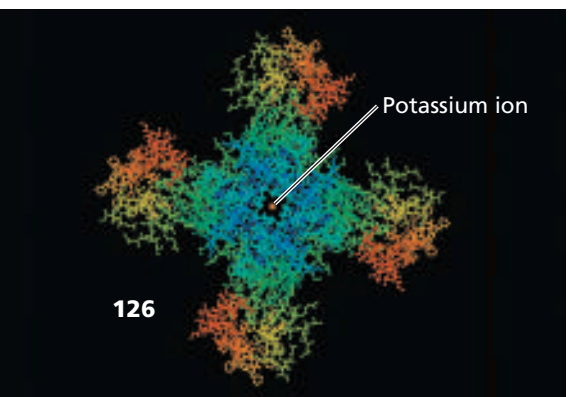
Membrane Structure and Function

7

Figure 7.1 How do cell membrane proteins like this aquaporin (blue ribbons) help regulate chemical traffic?

KEY CONCEPTS

Potassium ion channel protein



Life at the Edge

The plasma membrane that surrounds the cell can be considered the edge of life, the boundary that separates a living cell from its surroundings and controls all inbound and outbound traffic. Like all biological membranes, the plasma membrane exhibits **selective permeability**; that is, it allows some substances to cross it more easily than others. The ability of the cell to discriminate in its chemical exchanges is fundamental to life, and it is the plasma membrane and its component molecules that make this selectivity possible.

In this chapter, you will learn how cellular membranes control the passage of substances, often with transport proteins. For example, the image in **Figure 7.1** shows a computer model of a short section of the phospholipid bilayer of a membrane (hydrophilic heads are yellow, and hydrophobic tails are green). The blue ribbons within the lipid bilayer represent helical regions of a membrane transport channel protein called an aquaporin. One molecule of this protein enables billions of water molecules (red and gray) to pass through the membrane every second, many more than could cross on their own. Another type of transport protein is the ion channel shown here; it allows potassium ions to pass through the membrane. To understand how the plasma membrane and its proteins enable cells to survive and function, we begin by examining membrane structure, then explore how plasma membranes control transport into and out of cells.

When you see this blue icon, log in to **MasteringBiology** and go to the Study Area for digital resources.

Get Ready for This Chapter

Animation: Membrane in Motion
Interview with Peter Agre: Discovering aquaporins

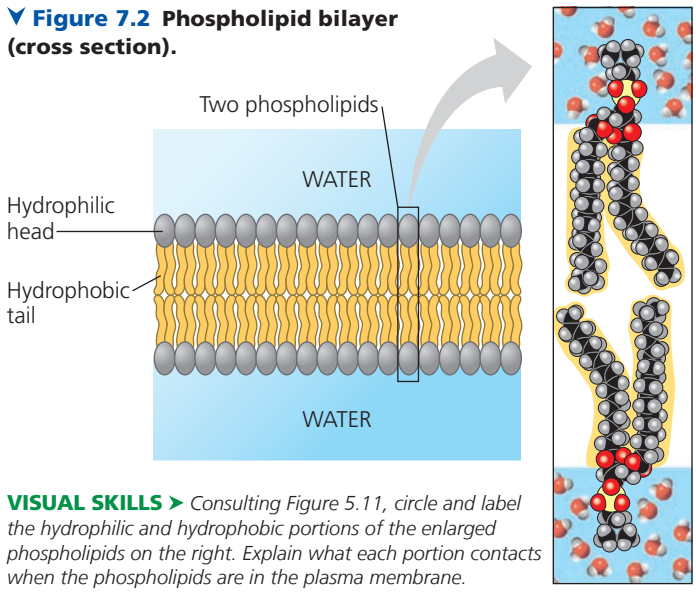
CONCEPT 7.1

Cellular membranes are fluid mosaics of lipids and proteins

Lipids and proteins are the staple ingredients of membranes, although carbohydrates are also important. The most abundant lipids in most membranes are phospholipids. The ability of phospholipids to form membranes is inherent in their molecular structure. A phospholipid is an **amphipathic** molecule, meaning it has both a hydrophilic ("water-loving") region and a hydrophobic ("water-fearing") region (see Figure 5.11). Other types of membrane lipids are also amphipathic. A phospholipid bilayer can exist as a stable boundary between two aqueous compartments because the molecular arrangement shelters the hydrophobic tails of the phospholipids from water while exposing the hydrophilic heads to water **(Figure 7.2)**.

Like membrane lipids, most membrane proteins are amphipathic. Such proteins can reside in the phospholipid bilayer with their hydrophilic regions protruding. This molecular orientation maximizes contact of hydrophilic regions of proteins with water in the cytosol and extracellular fluid, while providing their hydrophobic parts with a nonaqueous environment. **Figure 7.3** shows the currently accepted model of the arrangement of molecules in the plasma membrane. In this **fluid mosaic model**, the membrane is a mosaic of protein molecules bobbing in a fluid bilayer of phospholipids.

Figure 7.2 Phospholipid bilayer (cross section).



VISUAL SKILLS *Consulting Figure 5.11, circle and label the hydrophilic and hydrophobic portions of the enlarged phospholipids on the right. Explain what each portion contacts when the phospholipids are in the plasma membrane.*

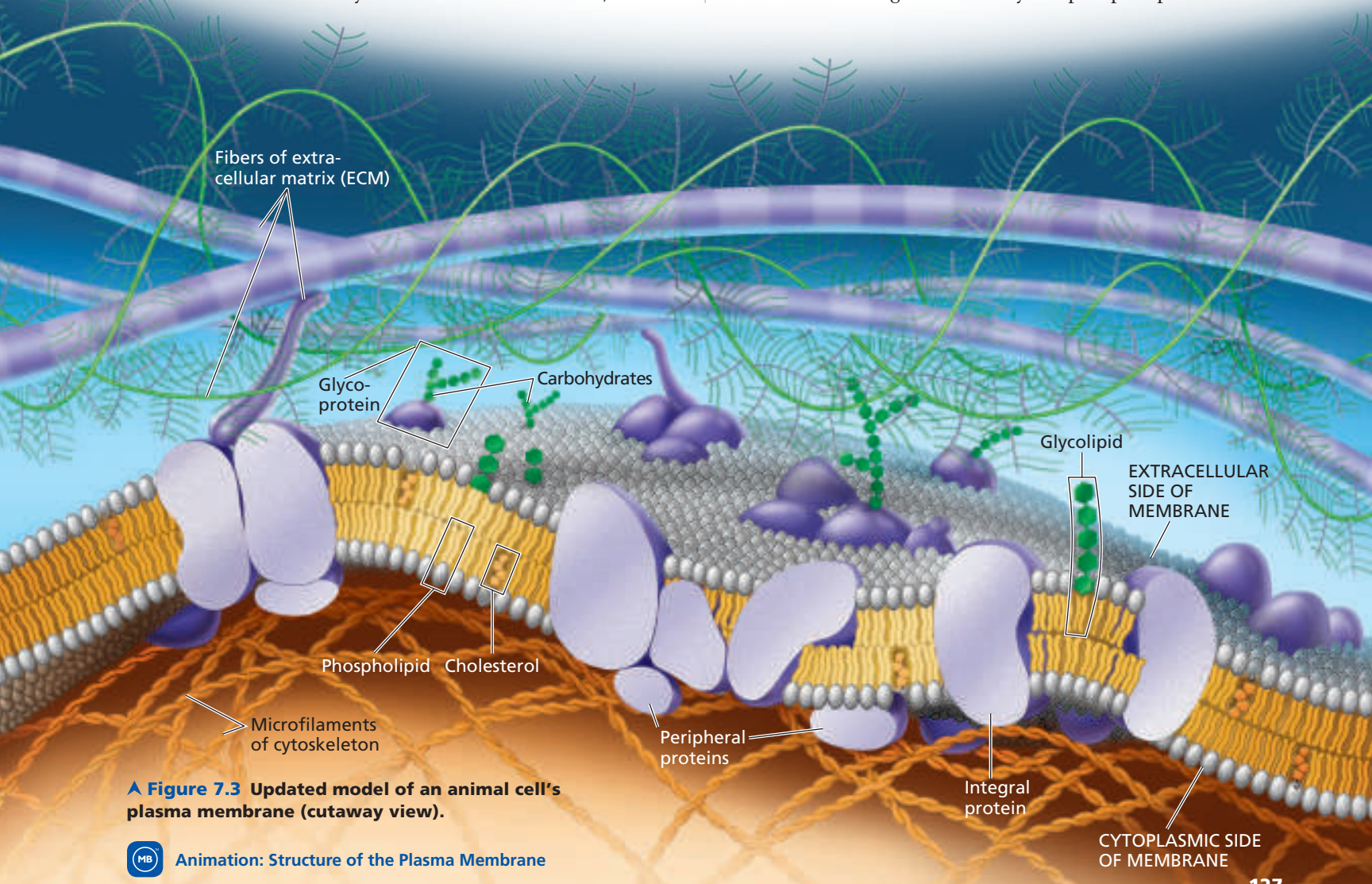


Figure 7.3 Updated model of an animal cell's plasma membrane (cutaway view).

Animation: Structure of the Plasma Membrane

The proteins are not randomly distributed in the membrane, however. Groups of proteins are often associated in long-lasting, specialized patches, where they carry out common functions. Researchers have found specific lipids in these patches as well and have proposed naming them *lipid rafts*, but there is ongoing controversy about whether such structures exist in living cells or are an artifact of biochemical techniques. Like all models, the fluid mosaic model is continually being refined as new research reveals more about membrane structure.

The Fluidity of Membranes

Membranes are not static sheets of molecules locked rigidly in place. A membrane is held together mainly by hydrophobic interactions, which are much weaker than covalent bonds (see Figure 5.18). Most of the lipids and some proteins can shift about sideways—that is, in the plane of the membrane, like partygoers elbowing their way through a crowded room. Very rarely, also, a lipid may flip-flop across the membrane, switching from one phospholipid layer to the other.

The sideways movement of phospholipids within the membrane is rapid. Adjacent phospholipids switch positions about 10^7 times per second, which means that a phospholipid can travel about 2 µm—the length of many bacterial cells—in 1 second. Proteins are much larger than lipids and move more slowly, but some membrane proteins do drift, as shown in a classic experiment described in **Figure 7.4**. Some membrane proteins seem to move in a highly directed manner, perhaps driven along cytoskeletal fibers in the cell by motor proteins connected to the membrane proteins' cytoplasmic regions. However, many other membrane proteins seem to be held immobile by their attachment to the cytoskeleton or to the extracellular matrix (see Figure 7.3).

A membrane remains fluid as temperature decreases until the phospholipids settle into a closely packed arrangement and the membrane solidifies, much as bacon grease forms lard when it cools. The temperature at which a membrane solidifies depends on the types of lipids it is made of. As the temperature decreases, the membrane remains fluid to a lower temperature if it is rich in phospholipids with unsaturated hydrocarbon tails (see Figures 5.10 and 5.11). Because of kinks in the tails where double bonds are located, unsaturated hydrocarbon tails cannot pack together as closely as saturated hydrocarbon tails, making the membrane more fluid **(Figure 7.5a)**.

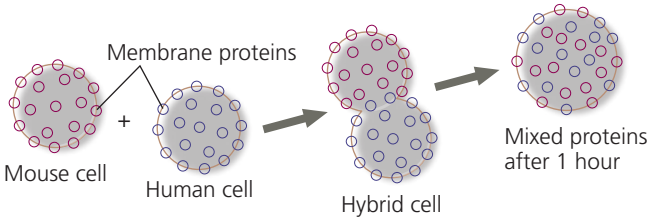
The steroid cholesterol, which is wedged between phospholipid molecules in the plasma membranes of animal cells, has different effects on membrane fluidity at different temperatures **(Figure 7.5b)**. At relatively high temperatures—at 37°C, the body temperature of humans, for example—cholesterol makes the membrane less fluid by restraining phospholipid movement. However, because cholesterol also hinders the close packing of phospholipids, it lowers the temperature required for the membrane to solidify. Thus, cholesterol can be thought of as a "fluidity buffer" for the membrane, resisting changes in membrane fluidity that can be caused by changes in temperature. Compared to animals, plants have very low levels of cholesterol; rather, related steroid lipids buffer membrane fluidity in plant cells.

Figure 7.4

Inquiry Do membrane proteins move?

Experiment Larry Frye and Michael Edidin, at Johns Hopkins University, labeled the plasma membrane proteins of a mouse cell and a human cell with two different markers and fused the cells. Using a microscope, they observed the markers on the hybrid cell.

Results



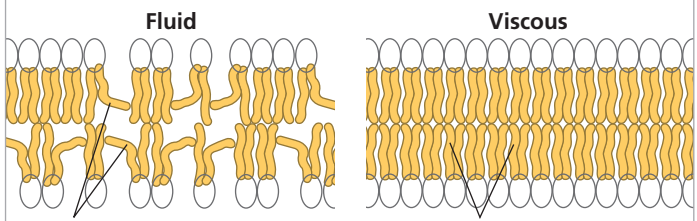
Conclusion The mixing of the mouse and human membrane proteins indicates that at least some membrane proteins move sideways within the plane of the plasma membrane.

Data from L. D. Frye and M. Edidin, The rapid intermixing of cell surface antigens after formation of mouse-human heterokaryons, *Journal of Cell Science* 7:319 (1970).

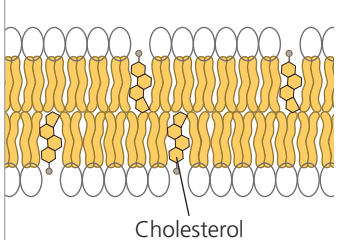
WHAT IF? ➤ *Suppose the proteins did not mix in the hybrid cell, even many hours after fusion. Would you be able to conclude that proteins don't move within the membrane? What other explanation could there be?*

Figure 7.5 Factors that affect membrane fluidity.

(a) Unsaturated versus saturated hydrocarbon tails.



(b) Cholesterol within the animal cell membrane.



Cholesterol reduces membrane fluidity at moderate temperatures by reducing phospholipid movement, but at low temperatures it hinders solidification by disrupting the regular packing of phospholipids.

Membranes must be fluid to work properly; the fluidity of a membrane affects both its permeability and the ability of membrane proteins to move to where their function is needed. Usually, membranes are about as fluid as salad oil. When a membrane solidifies, its permeability changes, and enzymatic proteins in the membrane may become inactive if their activity requires movement within the membrane. However, membranes that are too fluid cannot support protein function either. Therefore, extreme environments pose a challenge for life, resulting in evolutionary adaptations that include differences in membrane lipid composition.

Evolution of Differences in Membrane Lipid Composition

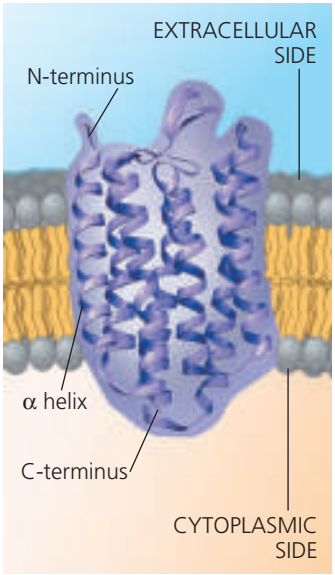
EVOLUTION Variations in the cell membrane lipid compositions of many species appear to be evolutionary adaptations that maintain the appropriate membrane fluidity under specific environmental conditions. For instance, fishes that live in extreme cold have membranes with a high proportion of unsaturated hydrocarbon tails, enabling their membranes to remain fluid (see Figure 7.5a). At the other extreme, some bacteria and archaea thrive at temperatures greater than 90°C (194°F) in thermal hot springs and geysers. Their membranes include unusual lipids that may prevent excessive fluidity at such high temperatures.

The ability to change the lipid composition of cell membranes in response to changing temperatures has evolved in organisms that live where temperatures vary. In many plants that tolerate extreme cold, such as winter wheat, the percentage of unsaturated phospholipids increases in autumn, an adjustment that keeps the membranes from solidifying during winter. Certain bacteria and archaea can also change the proportion of unsaturated phospholipids in their cell membranes, depending on the temperature at which they are growing. Overall, natural selection has apparently favored organisms whose mix of membrane lipids ensures an appropriate level of membrane fluidity for their environment.

Membrane Proteins and Their Functions

Now we come to the *mosaic* aspect of the fluid mosaic model. Somewhat like a tile mosaic (shown here), a membrane is a collage of different proteins, often clustered together in groups, embedded in the fluid matrix of the lipid bilayer (see Figure 7.3). In the plasma membrane of red blood cells alone, for example, more than 50 kinds of proteins have been found so far. Phospholipids form the main fabric of the membrane, but proteins determine most of the membrane's functions. Different types of cells contain different sets of membrane proteins, and the various membranes within a cell each have a unique collection of proteins.

➤ Figure 7.6 The structure of a transmembrane protein. Bacteriorhodopsin (a bacterial transport protein) has a distinct orientation in the membrane, with its N-terminus outside the cell and its C-terminus inside. This ribbon model highlights the secondary structure of the hydrophobic parts, including seven transmembrane α helices, which lie mostly within the hydrophobic interior of the membrane. The nonhelical hydrophilic segments are in contact with the aqueous solutions on the extracellular and cytoplasmic sides of the membrane.



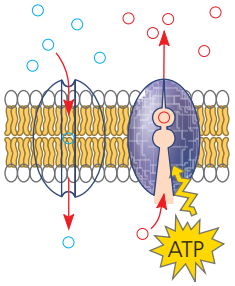
Notice in Figure 7.3 that there are two major populations of membrane proteins: integral proteins and peripheral proteins. **Integral proteins** penetrate the hydrophobic interior of the lipid bilayer. The majority are *transmembrane proteins*, which span the membrane; other integral proteins extend only partway into the hydrophobic interior. The hydrophobic regions of an integral protein consist of one or more stretches of nonpolar amino acids (see Figure 5.14), typically 20–30 amino acids in length, usually coiled into α helices **(Figure 7.6)**. The hydrophilic parts of the molecule are exposed to the aqueous solutions on either side of the membrane. Some proteins also have one or more hydrophilic channels that allow passage through the membrane of hydrophilic substances (even of water itself; see Figure 7.1). **Peripheral proteins** are not embedded in the lipid bilayer at all; they are loosely bound to the surface of the membrane, often to exposed parts of integral proteins (see Figure 7.3).

On the cytoplasmic side of the plasma membrane, some membrane proteins are held in place by attachment to the cytoskeleton. And on the extracellular side, certain membrane proteins may attach to materials outside the cell. For example, in animal cells, membrane proteins may be attached to fibers of the extracellular matrix (see Figure 6.28; *integrins* are one type of integral, transmembrane protein). These attachments combine to give animal cells a stronger framework than the plasma membrane alone could provide.

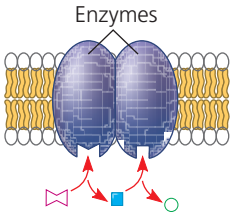
A single cell may have cell-surface membrane proteins that carry out several different functions, such as transport through the cell membrane, enzymatic activity, or attaching a cell to either a neighboring cell or the extracellular matrix. Furthermore, a single membrane protein may itself carry out multiple functions. Thus, the membrane is not only a structural mosaic, with many proteins embedded in the membrane, but also a functional mosaic, carrying out a range

Figure 7.7 Some functions of membrane proteins. In many cases, a single protein performs multiple tasks.

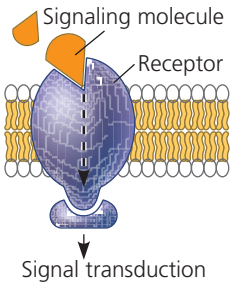
(a) Transport. *Left:* A protein that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute. *Right:* Other transport proteins shuttle a substance from one side to the other by changing shape (see Figure 7.14b). Some of these proteins hydrolyze ATP as an energy source to actively pump substances across the membrane.



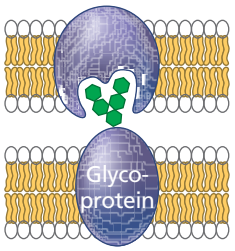
(b) Enzymatic activity. A protein built into the membrane may be an enzyme with its active site (where the reactant binds) exposed to substances in the adjacent solution. In some cases, several enzymes in a membrane are organized as a team that carries out sequential steps of a metabolic pathway.



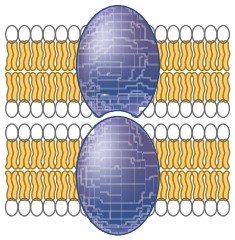
(c) Signal transduction. A membrane protein (receptor) may have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external messenger (signaling molecule) may cause the protein to change shape, allowing it to relay the message to the inside of the cell, usually by binding to a cytoplasmic protein (see Figure 11.6).



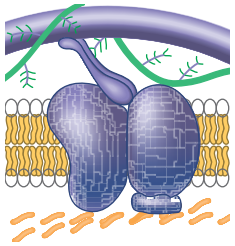
(d) Cell-cell recognition. Some glycoproteins serve as identification tags that are specifically recognized by membrane proteins of other cells. This type of cell-cell binding is usually short-lived compared to that shown in (e).



(e) Intercellular joining. Membrane proteins of adjacent cells may hook together in various kinds of junctions, such as gap junctions or tight junctions (see Figure 6.30). This type of binding is more long-lasting than that shown in (d).



(f) Attachment to the cytoskeleton and extracellular matrix (ECM). Microfilaments or other elements of the cytoskeleton may be noncovalently bound to membrane proteins, a function that helps maintain cell shape and stabilizes the location of certain membrane proteins. Proteins that can bind to ECM molecules can coordinate extracellular and intracellular changes (see Figure 6.28).



VISUAL SKILLS ➤ *Some transmembrane proteins can bind to a particular ECM molecule and, when bound, transmit a signal into the cell. Use the proteins shown in (c) and (f) to explain how this might occur.*

of functions. **Figure 7.7** illustrates six major functions performed by proteins of the plasma membrane.

Animation: Functions of the Plasma Membrane

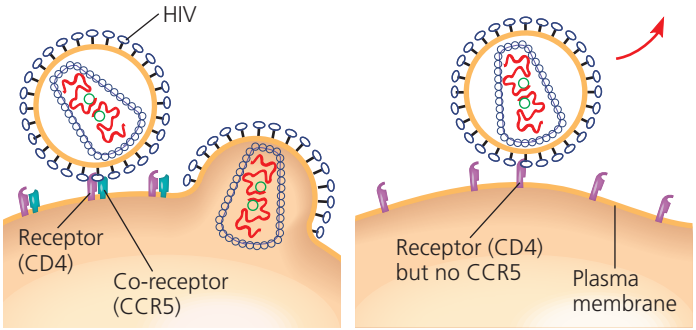
Proteins on a cell's surface are important in the medical field. For example, a protein called CD4 on the surface of immune cells helps the human immunodeficiency virus (HIV) infect these cells, leading to acquired immune deficiency syndrome (AIDS). Despite multiple exposures to HIV, however, a small number of people do not develop AIDS and show no evidence of HIV-infected cells. Comparing their genes with the genes of infected individuals, researchers learned that resistant people have an unusual form of a gene that codes for an immune cell-surface protein called CCR5. Further work showed that although CD4 is the main HIV receptor, HIV must also bind to CCR5 as a "co-receptor" to infect most cells **(Figure 7.8a)**. An absence of CCR5 on the cells of resistant individuals, due to the gene alteration, prevents the virus from entering the cells **(Figure 7.8b)**.

This information has been key to developing a treatment for HIV infection. Interfering with CD4 causes dangerous side effects because of its many important functions in cells. Discovery of the CCR5 co-receptor provided a safer target for development of drugs that mask this protein and block HIV entry. One such drug, maraviroc (brand name Selzentry), was approved for treatment of HIV in 2007 and is now being tested to determine whether this drug might also work to prevent HIV infection in uninfected, at-risk patients.

The Role of Membrane Carbohydrates in Cell-Cell Recognition

Cell-cell recognition, a cell's ability to distinguish one type of neighboring cell from another, is crucial to the functioning of an organism. It is important, for example, in the sorting of cells into tissues and organs in an animal embryo. It is also

Figure 7.8 The genetic basis for HIV resistance.



(a) HIV can infect a cell with CCR5 on its surface, as in most people.

(b) HIV cannot infect a cell lacking CCR5 on its surface, as in resistant individuals.

MAKE CONNECTIONS ➤ *Study Figures 2.16 and 5.17; each shows pairs of molecules binding to each other. What would you predict about CCR5 that would allow HIV to bind to it? How could a drug molecule interfere with this binding?*

the basis for the rejection of foreign cells by the immune system, an important line of defense in vertebrate animals (see Concept 43.1). Cells recognize other cells by binding to molecules, often containing carbohydrates, on the extracellular surface of the plasma membrane (see Figure 7.7d).

Membrane carbohydrates are usually short, branched chains of fewer than 15 sugar units. Some are covalently bonded to lipids, forming molecules called **glycolipids**. (Recall that *glyco* refers to carbohydrate.) However, most are covalently bonded to proteins, which are thereby **glycoproteins** (see Figure 7.3).

The carbohydrates on the extracellular side of the plasma membrane vary from species to species, among individuals of the same species, and even from one cell type to another in a single individual. The diversity of the molecules and their location on the cell's surface enable membrane carbohydrates to function as markers that distinguish one cell from another. For example, the four human blood types designated A, B, AB, and O reflect variation in the carbohydrate part of glycoproteins on the surface of red blood cells.

Synthesis and Sidedness of Membranes

Membranes have distinct inside and outside faces. The two lipid layers may differ in lipid composition, and each protein has directional orientation in the membrane (see Figure 7.6). **Figure 7.9** shows how membrane sidedness arises: The asymmetrical arrangement of proteins, lipids, and their associated carbohydrates in the plasma membrane is determined as the membrane is being built by the endoplasmic reticulum (ER) and Golgi apparatus, components of the endomembrane system (see Figure 6.15).

CONCEPT CHECK 7.1

1. **VISUAL SKILLS ➤** Carbohydrates are attached to plasma membrane proteins in the ER (see Figure 7.9). On which side of the vesicle membrane are the carbohydrates during transport to the cell surface?
2. **WHAT IF? ➤** How would the membrane lipid composition of a native grass found in very warm soil around hot springs compare with that of a native grass found in cooler soil? Explain.

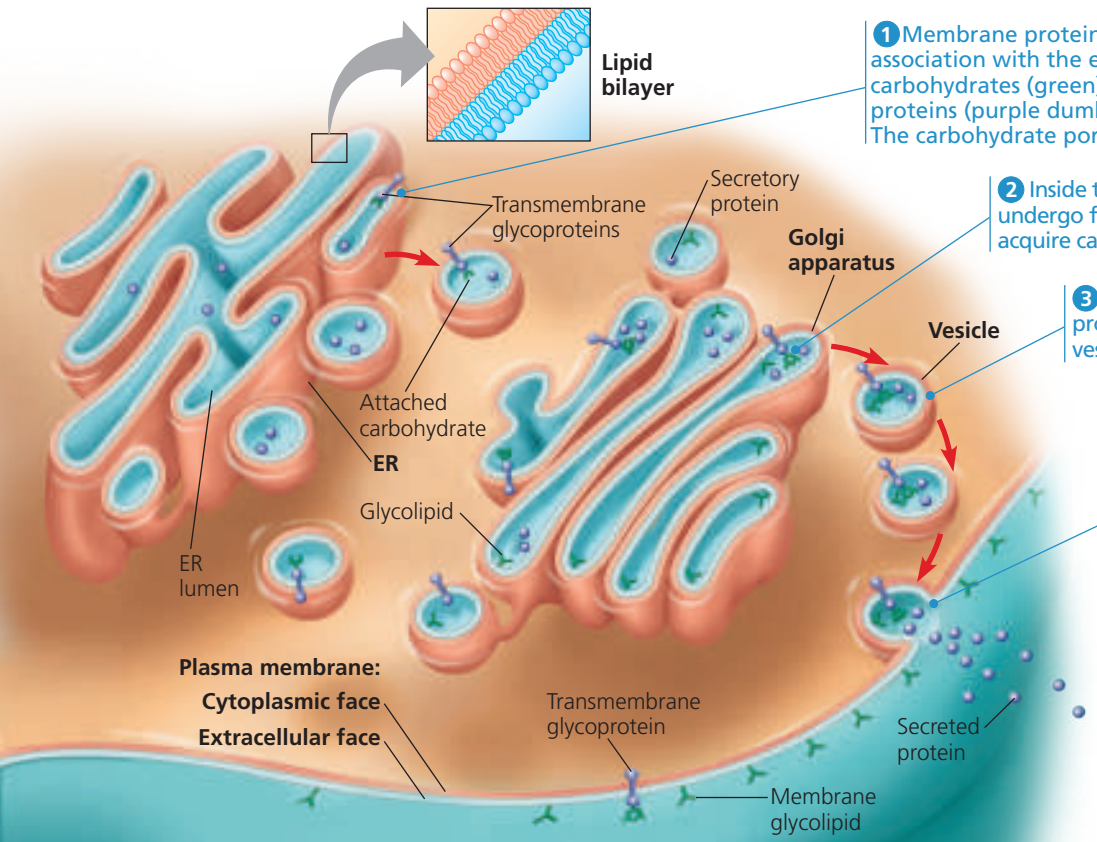
For suggested answers, see Appendix A.

CONCEPT 7.2

Membrane structure results in selective permeability

The biological membrane is an exquisite example of a supramolecular structure—many molecules ordered into a higher level of organization—with emergent properties beyond those of the individual molecules. The remainder of this chapter focuses on one of those properties: the ability to regulate transport across cellular boundaries, a function essential to the cell's existence. We will see once again that form fits

Figure 7.9 Synthesis of membrane components and their orientation in the membrane. The cytoplasmic (orange) face of the plasma membrane differs from the extracellular (aqua) face. The latter arises from the inside face of ER, Golgi, and vesicle membranes.



DRAW IT ➤ *Draw an integral membrane protein extending from partway through the ER membrane into the ER lumen. Next, draw the protein where it would be located in a series of numbered steps ending at the plasma membrane. Would the protein contact the cytoplasm or the extracellular fluid? Explain.*

function: The fluid mosaic model helps explain how membranes regulate the cell's molecular traffic.

A steady traffic of small molecules and ions moves across the plasma membrane in both directions. Consider the chemical exchanges between a muscle cell and the extracellular fluid that bathes it. Sugars, amino acids, and other nutrients enter the cell, and metabolic waste products leave it. The cell takes in O_2 for use in cellular respiration and expels CO_2. Also, the cell regulates its concentrations of inorganic ions, such as Na^+, K^+, Ca^{2+}, and Cl^-, by shuttling them one way or the other across the plasma membrane. Although the heavy traffic through them may seem to suggest otherwise, cell membranes are selectively permeable, and substances do not cross the barrier indiscriminately. The cell is able to take up some small molecules and ions and exclude others.

The Permeability of the Lipid Bilayer

Nonpolar molecules, such as hydrocarbons, CO_2, and O_2, are hydrophobic, as are lipids. They can all therefore dissolve in the lipid bilayer of the membrane and cross it easily, without the aid of membrane proteins. However, the hydrophobic interior of the membrane impedes direct passage through the membrane of ions and polar molecules, which are hydrophilic. Polar molecules such as glucose and other sugars pass only slowly through a lipid bilayer, and even water, a very small polar molecule, does not cross rapidly relative to nonpolar molecules. A charged atom or molecule and its surrounding shell of water (see Figure 3.8) are even less likely to penetrate the hydrophobic interior of the membrane. Furthermore, the lipid bilayer is only one aspect of the gatekeeper system responsible for a cell's selective permeability. Proteins built into the membrane play key roles in regulating transport.

Transport Proteins

Specific ions and a variety of polar molecules can't move through cell membranes on their own. However, these hydrophilic substances can avoid contact with the lipid bilayer by passing through **transport proteins** that span the membrane.

Some transport proteins, called *channel proteins*, function by having a hydrophilic channel that certain molecules or atomic ions use as a tunnel through the membrane (see Figure 7.7a, left). For example, the passage of water molecules through the membrane in certain cells is greatly facilitated by channel proteins known as **aquaporins** (see Figure 7.1). Each aquaporin allows entry of up to *3 billion* (3×10^9) water molecules per second, passing single file through its central channel, which fits ten at a time. Without aquaporins, only a tiny fraction of these water molecules would pass through the same area of the cell membrane in a second, so the channel protein brings about a tremendous increase in rate. Other transport proteins, called *carrier proteins*, hold onto their passengers and change shape in a way that shuttles them across the membrane (see Figure 7.7a, right).

A transport protein is specific for the substance it translocates (moves), allowing only a certain substance (or a small group of related substances) to cross the membrane. For example, a specific carrier protein in the plasma membrane of red blood cells transports glucose across the membrane 50,000 times faster than glucose can pass through on its own. This "glucose transporter" is so selective that it even rejects fructose, a structural isomer of glucose. Thus, the selective permeability of a membrane depends on both the discriminating barrier of the lipid bilayer and the specific transport proteins built into the membrane.

Animation: Selective Permeability of Membranes

What establishes the *direction* of traffic across a membrane? And what mechanisms drive molecules across membranes? We will address these questions next as we explore two modes of membrane traffic: passive transport and active transport.

CONCEPT CHECK 7.2

1. What property allows O_2 and CO_2 to cross a lipid bilayer without the aid of membrane proteins?
2. **VISUAL SKILLS ➤** Examine Figure 7.2. Why is a transport protein needed to move many water molecules rapidly across a membrane?
3. **MAKE CONNECTIONS ➤** Aquaporins exclude passage of hydronium ions (H_3O^+), but some aquaporins allow passage of glycerol, a three-carbon alcohol (see Figure 5.9), as well as H_2O. Since H_3O^+ is closer in size to water than glycerol is, yet cannot pass through, what might be the basis of this selectivity?

For suggested answers, see Appendix A.

CONCEPT 7.3

Passive transport is diffusion of a substance across a membrane with no energy investment

Molecules have a type of energy called thermal energy, due to their constant motion (see Concept 3.2). One result of this motion is **diffusion**, the movement of particles of any substance so that they spread out into the available space. Each molecule moves randomly, yet diffusion of a *population* of molecules may be directional. To understand this process, let's imagine a synthetic membrane separating pure water from a solution of a dye in water. Study **Figure 7.10a** carefully to appreciate how diffusion would result in both solutions having equal concentrations of the dye molecules. Once that point is reached, there will be a dynamic equilibrium, with roughly as many dye molecules crossing the membrane each second in one direction as in the other.

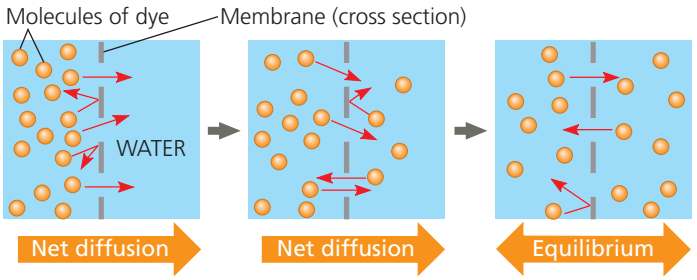
We can now state a simple rule of diffusion: In the absence of other forces, a substance will diffuse from where it is more concentrated to where it is less concentrated. Put another way, any substance will diffuse down its **concentration gradient**,

the region along which the density of a chemical substance increases or decreases (in this case, decreases). No work must be done to make this happen; diffusion is a spontaneous process, needing no input of energy. Note that each substance diffuses down its *own* concentration gradient, unaffected by the concentration gradients of other substances **(Figure 7.10b)**.

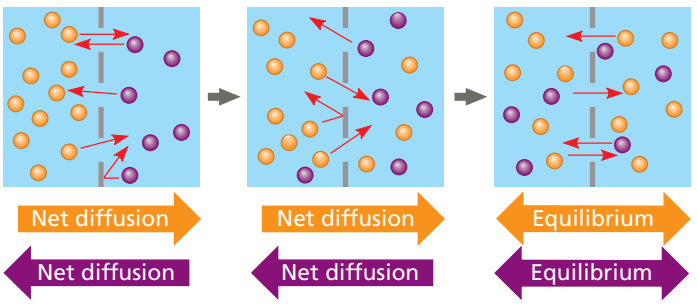
Much of the traffic across cell membranes occurs by diffusion. When a substance is more concentrated on one side of a membrane than on the other, there is a tendency for the substance to diffuse across the membrane down its concentration gradient (assuming that the membrane is permeable to that substance). One important example is the uptake of oxygen by a cell performing cellular respiration. Dissolved oxygen diffuses into the cell across the plasma membrane. As long as cellular respiration consumes the O_2 as it enters, diffusion into the cell will continue because the concentration gradient favors movement in that direction.

The diffusion of a substance across a biological membrane is called **passive transport** because the cell does not have to expend energy to make it happen. The concentration gradient itself represents potential energy (see Concept 2.2 and Figure 8.5b) and drives diffusion. Remember, however, that membranes are selectively permeable and therefore have different effects on the rates of diffusion of various molecules. In the case of water, the presence of aquaporin proteins allows water to diffuse very rapidly across the membranes of certain cells compared with diffusion in the absence of aquaporins. As we'll see next, the movement of water across the plasma membrane has important consequences for cells.

Figure 7.10 The diffusion of solutes across a synthetic membrane. Each of the large arrows under the diagrams shows the net diffusion of the dye molecules of that color.



(a) Diffusion of one solute. The membrane has pores large enough for molecules of dye to pass through. Random movement of dye molecules will cause some to pass through the pores; this will happen more often on the side with more dye molecules. The dye diffuses from where it is more concentrated to where it is less concentrated (called diffusing down a concentration gradient). This leads to a dynamic equilibrium: The solute molecules continue to cross the membrane, but at roughly equal rates in both directions.



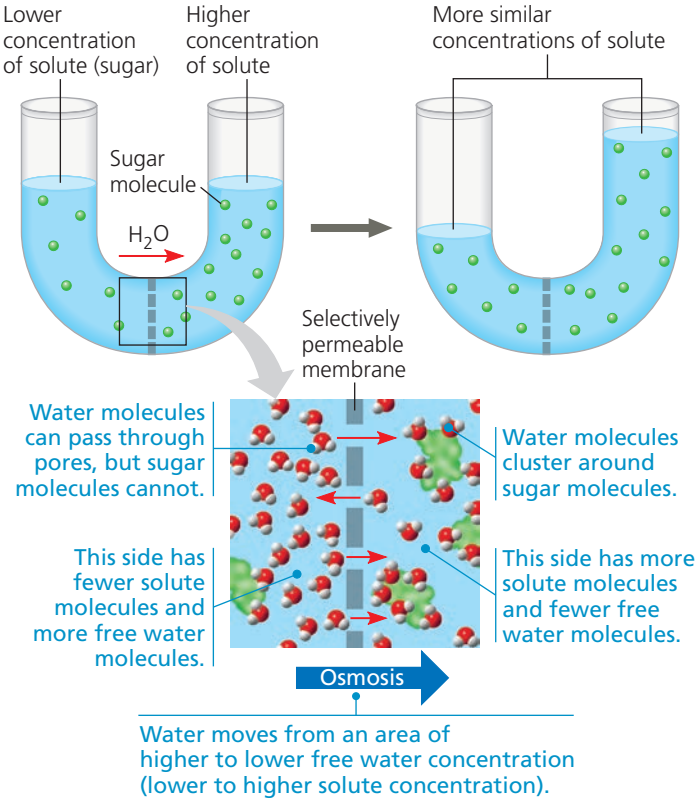
(b) Diffusion of two solutes. Solutions of two different dyes are separated by a membrane that is permeable to both. Each dye diffuses down its own concentration gradient. There will be a net diffusion of the purple dye toward the left, even though the *total* solute concentration was initially greater on the left side.

Animation: Diffusion

Effects of Osmosis on Water Balance

To see how two solutions with different solute concentrations interact, picture a U-shaped glass tube with a selectively permeable artificial membrane separating two sugar solutions **(Figure 7.11)**. Pores in this synthetic membrane are too small

Figure 7.11 Osmosis. Two sugar solutions of different concentrations are separated by a membrane that the solvent (water) can pass through but the solute (sugar) cannot. Water molecules move randomly and may cross in either direction, but overall, water diffuses from the solution with less concentrated solute to that with more concentrated solute. This passive transport of water, or osmosis, makes the sugar concentrations on both sides more nearly equal. (The concentrations are prevented from being exactly equal due to the effect of water pressure on the higher side, which is not discussed here, for simplicity.)



VISUAL SKILLS ➤ *If an orange dye capable of passing through the membrane was added to the left side of the tube above, how would it be distributed at the end of the experiment? (See Figure 7.10.) Would the final solution levels in the tube be affected?*

Figure Walkthrough

for sugar molecules to pass through but large enough for water molecules. However, tight clustering of water molecules around the hydrophilic solute molecules makes some of the water unavailable to cross the membrane. As a result, the solution with a higher solute concentration has a lower *free* water concentration. Water diffuses across the membrane from the region of higher free water concentration (lower solute concentration) to that of lower free water concentration (higher solute concentration) until the solute concentrations on both sides of the membrane are more nearly equal. The diffusion of free water across a selectively permeable membrane, whether artificial or cellular, is called **osmosis**. The movement of water across cell membranes and the balance of water between the cell and its environment are crucial to organisms. Let's now apply what we've learned about osmosis in this system to living cells.

Water Balance of Cells Without Cell Walls

To explain the behavior of a cell in a solution, we must consider both solute concentration and membrane permeability. Both factors are taken into account in the concept of **tonicity**, the ability of a surrounding solution to cause a cell to gain or lose water. The tonicity of a solution depends in part on its concentration of solutes that cannot cross the membrane (nonpenetrating solutes) relative to that inside the cell. If there is a higher concentration of nonpenetrating solutes in the surrounding solution, water will tend to leave the cell, and vice versa.

If a cell without a cell wall, such as an animal cell, is immersed in an environment that is **isotonic** to the cell (*iso* means "same"), there will be no *net* movement of water across the plasma membrane. Water diffuses across the membrane, but at the same rate in both directions. In an isotonic environment, the volume of an animal cell is stable **(Figure 7.12a)**.

Let's transfer the cell to a solution that is **hypertonic** to the cell (*hyper* means "more," in this case referring to nonpenetrating solutes). The cell will lose water, shrivel, and probably die. This is why an increase in the salinity (saltiness) of a lake can kill the animals there; if the lake water becomes hypertonic to the animals' cells, they might shrivel and die. However, taking up too much water can be just as hazardous as losing water. If we place the cell in a solution that is **hypotonic** to the cell (*hypo* means "less"), water will enter the cell faster than it leaves, and the cell will swell and lyse (burst) like an overfilled water balloon.

A cell without rigid cell walls can tolerate neither excessive uptake nor excessive loss of water. This problem of water balance is automatically solved if such a cell lives in isotonic surroundings. Seawater is isotonic to many marine invertebrates. The cells of most terrestrial (land-dwelling) animals are bathed in an extracellular fluid that is isotonic to the cells. In hypertonic or hypotonic environments, however, organisms that lack rigid cell walls must have other adaptations for **osmoregulation**, the control of solute concentrations and water balance. For example, the unicellular eukaryote *Paramecium* lives in pond water, which is hypotonic to the cell. *Paramecium* has a plasma membrane that is much less permeable to water than the membranes of most other cells, but this only slows the uptake of water, which continually enters the cell. The *Paramecium* cell doesn't burst because it is also equipped with a contractile vacuole, an organelle that functions as a bilge pump to force water out of the cell as fast as it enters by osmosis **(Figure 7.13)**. In contrast, the bacteria and archaea that live in hypersaline (excessively salty) environments (see Figure 27.1) have cellular mechanisms that balance the internal and external solute concentrations to ensure that water does not move out of the cell. We will examine other evolutionary adaptations for osmoregulation by animals in Concept 44.1.

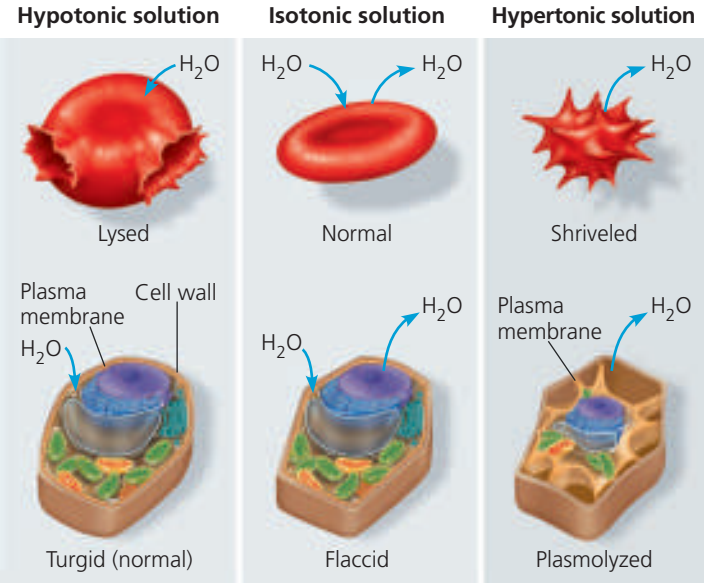
Water Balance of Cells with Cell Walls

The cells of plants, prokaryotes, fungi, and some unicellular eukaryotes are surrounded by cell walls (see Figure 6.27). When such a cell is immersed in a hypotonic solution—bathed in rainwater, for example—the cell wall helps maintain the cell's

Figure 7.12 The water balance of living cells. How living cells react to changes in the solute concentration of their environment depends on whether or not they have cell walls. **(a)** Animal cells, such as this red blood cell, do not have cell walls. **(b)** Plant cells do have cell walls. (Arrows indicate net water movement after the cells were first placed in these solutions.)

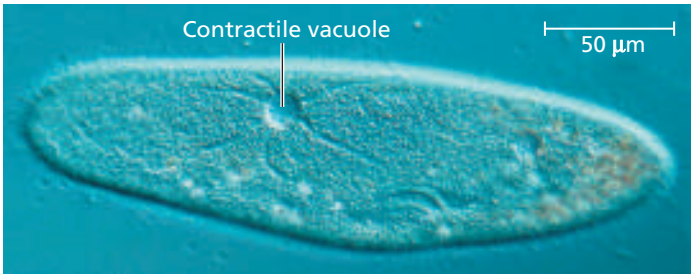
(a) Animal cell. An animal cell fares best in an isotonic environment unless it has special adaptations that offset the osmotic uptake or loss of water.

(b) Plant cell. Plant cells are turgid (firm) and generally healthiest in a hypotonic environment, where the uptake of water is eventually balanced by the wall pushing back on the cell.



Animation: Osmosis and Water Balance in Cells
Video: Turgid *Elodea*
Video: Plasmolysis in *Elodea*

Figure 7.13 The contractile vacuole of *Paramecium*. The vacuole collects fluid from canals in the cytoplasm. When full, the vacuole and canals contract, expelling fluid from the cell (LM).



Video: *Paramecium* Vacuole

water balance. Consider a plant cell. Like an animal cell, the plant cell swells as water enters by osmosis **(Figure 7.12b)**. However, the relatively inelastic cell wall will expand only so much before it exerts a back pressure on the cell, called *turgor pressure*, that opposes further water uptake. At this point, the cell is **turgid** (very firm), the healthy state for most plant cells. Plants that are not woody, such as most houseplants, depend for mechanical support on cells kept turgid by a surrounding hypotonic solution. If a plant's cells and surroundings are isotonic, there is no net tendency for water to enter and the cells become **flaccid** (limp); the plant wilts.

However, a cell wall is of no advantage if the cell is immersed in a hypertonic environment. In this case, a plant cell, like an animal cell, will lose water to its surroundings and shrink. As the plant cell shrivels, its plasma membrane pulls away from the cell wall at multiple places. This phenomenon, called **plasmolysis**, causes the plant to wilt and can lead to plant death. The walled cells of bacteria and fungi also plasmolyze in hypertonic environments.

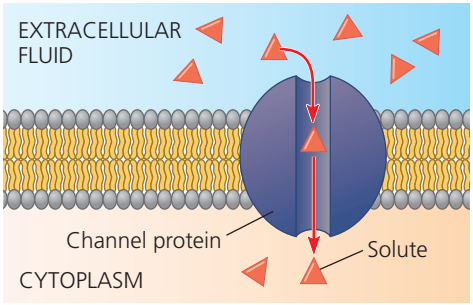
Facilitated Diffusion: Passive Transport Aided by Proteins

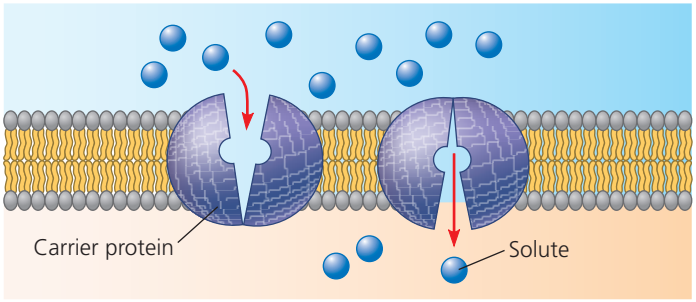
Let's look more closely at how water and certain hydrophilic solutes cross a membrane. As mentioned earlier, many polar molecules and ions impeded by the lipid bilayer of the membrane diffuse passively with the help of transport proteins that span the membrane. This phenomenon is called **facilitated diffusion**. Cell biologists are still trying to learn exactly how various transport proteins facilitate diffusion. Most transport proteins are very specific: They transport some substances but not others.

As mentioned earlier, the two types of transport proteins are channel proteins and carrier proteins. Channel proteins simply provide corridors that allow specific molecules or ions to cross the membrane **(Figure 7.14a)**. The hydrophilic passageways provided by these proteins can allow water molecules or small ions to diffuse very quickly from one side of the membrane to the other. Aquaporins, the water channel proteins, facilitate the massive levels of diffusion of water (osmosis) that occur in plant cells and in animal cells such as

Figure 7.14 Two types of transport proteins that carry out facilitated diffusion. In both cases, the protein can transport the solute in either direction, but the net movement is down the concentration gradient of the solute.

(a) A channel protein has a channel through which water molecules or a specific solute can pass.





(b) A carrier protein alternates between two shapes, moving a solute across the membrane during the shape change.

Animation: Facilitated Diffusion

red blood cells (see Figure 7.12). Certain kidney cells also have a high number of aquaporins, allowing them to reclaim water from urine before it is excreted. If the kidneys did not perform this function, you would excrete about 180 L of urine per day—and have to drink an equal volume of water!

Channel proteins that transport ions are called **ion channels**. Many ion channels function as **gated channels**, which open or close in response to a stimulus. For some gated channels, the stimulus is electrical. In a nerve cell, for example, an ion channel opens in response to an electrical stimulus, allowing a stream of potassium ions to leave the cell. (See the potassium ion channel at the beginning of this chapter.) This restores the cell's ability to fire again. Other gated channels open or close when a specific substance other than the one to be transported binds to the channel. These gated channels are also important in the functioning of the nervous system, as you'll learn in Concepts 48.2 and 48.3.

Interview with Elba Serrano: Investigating how ion channels enable you to hear (see the interview before Chapter 6)

Carrier proteins, such as the glucose transporter mentioned earlier, seem to undergo a subtle change in shape that somehow translocates the solute-binding site across the membrane **(Figure 7.14b)**. Such a change in shape may be triggered by the binding and release of the transported molecule. Like ion channels, carrier proteins involved in facilitated diffusion result in the net movement of a substance down its concentration gradient.