

What Are the Units of Brain Function?

The Cells of the Nervous System

Neurons
Glial Cells
Focus on Disorders: Brain Tumors
Focus on Disorders: Multiple Sclerosis

The Internal Structure of a Cell

Elements and Atoms
Molecules
The Parts of a Cell

Genes, Cells, and Behavior

Chromosomes and Genes
Genotype and Phenotype
Dominant and Recessive Genes
Genetic Mutations
Mendel's Principles Apply to Genetic Disorders
Chromosome Abnormalities
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Genetic Engineering

In the search for how a nervous system produces behaviors, robots may help provide answers. Robots, after all, engage in goal-oriented actions, just as animals do. A computer must guide and coordinate those actions, doing much the same work as a nervous system does. Barbara Webb's little robot, shown in Figure 3-1, illustrates this interesting use of electronic technology. Although far more cumbersome than nature's model, this robot is designed to mimic a female cricket that listens for and travels to the source of a male's chirping song. These behaviors are not as simple as they may seem. In approaching a male, a female cricket must avoid open, well-lit places where a predator could easily detect her. In addition, a female cricket must often choose between competing males, sometimes preferring the male that makes the longest chirps. All these behaviors must be "wired into" a successful cricket robot, making sure that one behavior does not interfere with another. In simulating cricket behavior in a

robot, Webb is duplicating the rules of a cricket's nervous system.

Do not be surprised that we begin this chapter by comparing a cricket's nervous system to a robot's computer-driven parts. In their attempts to explain behavior, scientists, like philosophers, frequently search for analogies among the things they know. In earlier times, the nervous system was compared to simpler mechanical devices, such as a water pump or a clock. Today's comparison to computerized robots is just a modern version. But this analogy is one that may also help us to learn more. Researchers such as Webb switch back and forth between studying the nervous system and the behaviors that it enables and writing computer programs designed to simulate those behaviors. When the animal under study and the computerized robot respond in exactly the same way, the researchers can be fairly sure that they understand how part of the nervous system works.

This chapter explores how the nervous system works by investigating the units from which it is built. These units are cells, the basic building blocks of life. Our bodies are composed of many kinds of cells, but the ones of interest to us in this book are the neurons and glia that make up the nervous system. These nervous system cells allow us to respond to stimuli in the environment, process that information, and act. There are different types of neurons and glia, each distinctive in its structure and function. Just as we can explore the function of a robot by examining its overall structure, so we can investigate the overall structure of a cell as a source of insight into its work.

This chapter also investigates the internal structures of cells, the so-called organelles inside cells that perform various tasks.

If you think of a cell as nature's microscopic robot, the organelles become the miniaturized components that allow the cell to do its job. Learning about these components is essential to understanding not only how a single cell works but also how the brain produces behavior.

Robert P. Carr / Bruce Coleman Inc. (animal); Barbara Webb (model)

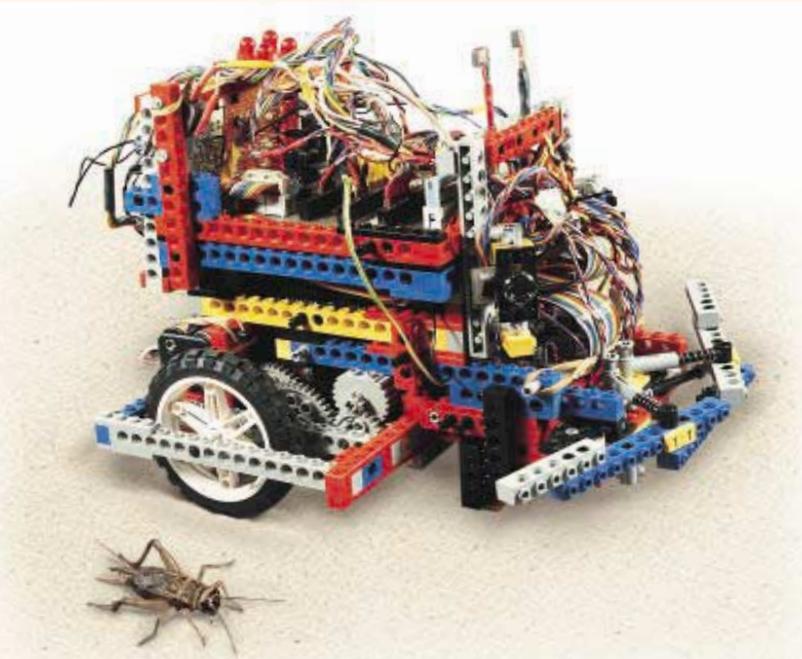


Figure 3-1

Robotic and real crickets differ in many physical attributes. The rules obtained from the study of crickets can be programmed into robots to be tested. This robot, which is constructed from Lego blocks, wires, and a motor, follows the rules used by a female cricket to travel to the source of a chirping sound made by a male cricket.

From "A Cricket Robot," by B. Webb, 1996, *Scientific American*, 214(12), p. 99.

Genes intimately participate in the production of behavior. Genes located in the chromosomes of each cell determine the proteins that a particular cell will make and consequently the functions that the cell will serve. Ultimately, the genes of female and male crickets determine their behavior. Think of the challenge of programming into a robot all the instructions needed to carry out its every task. Yet a cell, nature's tiny robot, contains all the instruc-

tions that it requires packed away in its chromosomes. At the end of this chapter, you will learn a little about how genes function and how their workings can go awry, sometimes with devastating consequences for behavior. Many of the neurological disorders described in this book are caused by errors that occur as genetic information is passed from parent to child, which is why we explore the process of genetic transmission in this chapter.

◉ Link to articles about robotics at the Web site at www.worthpublishers.com/kolb/chapter3.

◉ Visit the CD to learn about different ways to look at the brain. In the module on Research Methods, you'll find a section on histology which includes samples of six common stains for brain sections.

THE CELLS OF THE NERVOUS SYSTEM

If Barbara Webb's little robot mysteriously arrived in a box on your doorstep, you might examine its structure carefully to guess what it is designed to do. The robot's wheels imply that it is meant to move, and the gears next to the wheels suggest that it can vary its speed or perhaps change directions by varying the speed of one wheel relative to the other. The robot's many exposed wires show that it is not intended to go into water. And, because this robot has no lights or cameras, you can infer that it is not meant to see. The structure of the robot suggests its function. So it is with cells.

But there is a problem in examining the cells of the nervous system for insights into their function. Nervous system cells are very small, are packed tightly together, and have the consistency of jelly. To see a brain cell, you must first isolate it from surrounding cells, stain it to make it visible, and then magnify it by using a microscope. Anatomists have developed ways of removing most of the water from the brain by soaking it in formaldehyde, after which the brain can be cut into thin slices to be stained with various dyes that either color its cells completely or color some of the cells' components. Now the cells can be placed under a microscope for viewing.

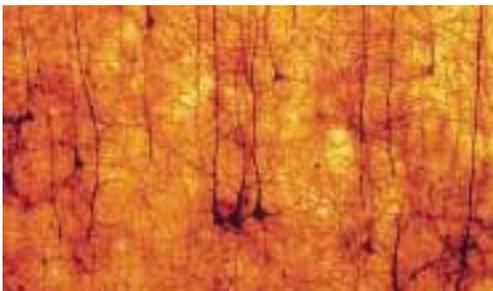
There is still, however, the problem of making sense of what you see. Different brain samples can yield different images, and different people can interpret those images in different ways. So began a controversy over how the brain is structured between two great scientists of the late nineteenth and early twentieth centuries. One was the Italian Camillo Golgi and the other the Spaniard Santiago Ramón y Cajal. Both men were awarded the Nobel Prize for medicine in 1906.

Imagine that you are Camillo Golgi hard at work in your laboratory staining and examining cells of the nervous system. You immerse a thin slice of brain tissue in a solution containing silver nitrate and other chemicals, a technique used at the time to produce black-and-white photographic prints, producing a microscopic image that looks something like the one in Figure 3-2. The image is beautiful and intriguing, but what do you make of it? To Golgi, this structure suggested that the nervous system is composed of a network of interconnected fibers. He thought that information, like water running through pipes, somehow flowed around this nerve net and produced behavior. His theory was not implausible, given what he saw.

But Santiago Ramón y Cajal came to a different conclusion. He studied the brain tissue of chick embryos because he assumed that their nervous systems would be simpler and easier to understand. Figure 3-3 shows one of the images that he obtained from an embryo. Cajal concluded that the nervous system is made up of discrete cells that begin life with a rather simple structure, which becomes more complex with age. In adulthood, these cells consist of a main body with extensions projecting from it. The structure looks something like a radish, with branches coming out of the top and roots coming out of the bottom.

Figure 3-2

These human pyramidal cells are stained by using the Golgi technique.



Cajal's belief that these complexly shaped cells are the functional units of the nervous system is now universally accepted. Today, we refer to these nervous system cells as *neurons*, a name that comes from the Greek word for "nerve." The idea proposed by Cajal, that neurons are the units of brain function, is called the **neuron hypothesis**.

Figure 3-3 shows the three basic parts of a neuron. The neuron's core region is called the **cell body**. Most of a neuron's branching extensions are called **dendrites** (Latin for "branch"), but the main "root" is called the **axon** (Greek for "axle"). A neuron has only one axon, but most neurons have many dendrites. Some small neurons have so many dendrites that they look like a garden hedge.

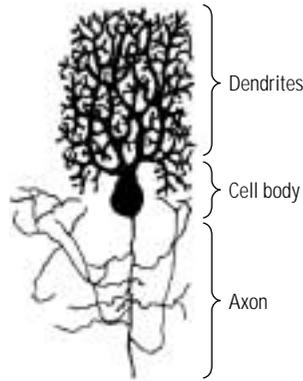


Figure 3-3

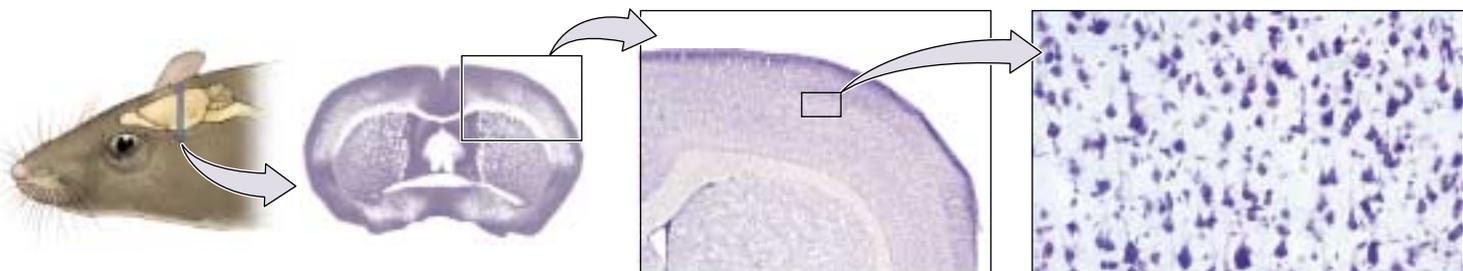
A neuron consists of three parts: dendrites, cell body, and axon. The dendrites gather information from other neurons, the cell body integrates the information, and the axon sends the information to other neurons. Note that, although there is only one axon, it may have branches called collaterals.

Adapted from *Histologie du système nerveux de l'homme et des vertèbres*, by S. Ramón y Cajal, 1909–1911, Paris: Maloine.

As stated earlier, the nervous system is composed not only of neurons, but also of cells called glia (the name comes from the Greek word for "glue"). The neurons are the functional units that enable us to receive information, process it, and produce actions. The glia help the neurons out, tying them together (some *do* act as glue) and providing support. In the human nervous system, there are about 100 billion neurons and perhaps 10 times as many glial cells. No, no one has counted them all. Scientists have estimated the total number by counting the cells in a small sample of brain tissue and then multiplying by the brain's volume (Figure 3-4).

Explaining how 100 billion cells cooperate, make connections, and produce behavior is not an easy matter. But, fortunately, the examination of how one cell works can be a source of insight that can be generalized to other cells. Brain cells really are like robots built to a common plan, depending on their particular type. In this section, you will learn to recognize some of the different types of neurons and glial cells in your body. You will also see how their specialized structures contribute to their functions.

🔗 Click on the Web site to read more about the history of the neuron hypothesis at www.worthpublishers.com/kolb/chapter3.



Neurons

As the information-processing units of the brain, neurons must do many things. They must acquire information from sensory receptors, pass that information on to other neurons, and make muscles move to produce behaviors. They must also hold the instructions for how we behave—that is, they must encode memories—and they have to produce our thoughts and emotions as well. At the same time, they must regulate all the many body processes to which we seldom give a thought, such as breathing, heartbeat, body temperature, and the sleep–wake cycle. This is a tall order but apparently easily accomplished by things as small as neurons.

Some scientists think that a specific function is sometimes assigned to a single neuron. For example, Fernando Nottebohm and his colleagues (1994) studied how birds produce songs and believe that a single neuron may be responsible for each note sung. Most scientists, however, think that neurons work together in groups of many hundreds to many thousands to produce some aspect of behavior. According to this view, the loss of a neuron or two would be no more noticeable than the loss of one or

Figure 3-4

How are cells counted? We first obtain a thin slice of brain tissue from a rat. Then we select a region of the cortex for cell counting. By counting the number of cells in this part of the tissue and multiplying that number by the volume of the cortex, we can estimate the number of cells in the cortex. The cells in this example are stained with Cresyl violet, which adheres to protein molecules in the cell body and gives the cell body a blue color.

Neuron hypothesis. The idea that the neuron is the basic unit of behavior.

Visit the Web site to watch a movie on a neuron in action at www.worthpublishers.com/kolb/chapter3.

two voices from a cheering crowd of people. It is the crowd that produces the overall action, not each individual person. In much the same way, although we say that neurons are the information-processing units of the brain, we really mean that large teams of neurons serve this function.

It is also somewhat inaccurate to speak of *the* structure of a particular neuron, as if that structure never changed. If fresh brain tissue were kept alive in a dish of salty water and viewed occasionally through a microscope, the neurons would reveal themselves to be surprisingly active in both producing new dendrite branches and losing old ones. In fact, if you could watch neurons over a long period of time — say, years — they would appear, like living plants, to be continuously growing and shrinking and changing their shape. The neurons in our brains are similarly changing from day to day and from year to year. For some neurons, these physical changes result from coding and storing our experiences and memories. Neural changes of all kinds are possible because of a special property that neurons possess. Even in a mature, fully grown neuron, the cell's genetic blueprints can be “reopened,” allowing the neuron to alter its structure, produce new chemicals, or modify its activities in other ways.

Another important property of neurons is their longevity. Most neurons in our bodies are never replaced; rather, they survive with us throughout our lives. This survival is fortunate because neurons have much less ability than other cells to replace themselves when seriously injured. For example, if the brain or spinal cord is damaged, most lost neurons are not replaced. For most of the twentieth century, the idea that the human brain cannot gain new neurons after birth was dogma. Recently, a lot of exceptions to this dogma have been reported. It is now correct to say that most of your neurons are with you for life and, if you lose some through injury, it is not yet possible to replace them all.

BASIC NEURON STRUCTURE AND FUNCTION

Figure 3-5 displays the external features of neurons in more detail. The surface area of the cell body is increased immensely by extensions of the cell membrane into dendrites. The dendritic area is further increased by many small protrusions called **dendritic spines**. A neuron may have from 1 to 20 dendrites, each of which may have from one to many branches, and the spines on the branches may number in the many thousands. Because dendrites collect information from other cells, their surface area indicates how much information the neuron can gather. Each neuron also has a single axon. It begins at an expansion of the cell body known as the **axon hillock** (hillock means “little hill”). The axon may have branches called **axon collaterals**, which usually emerge from it at right angles. Toward its end, the axon may divide into a number of smaller branches called **teleodendria** (end branches). At the end of each teleodendrion is a knob called an **end foot** or **terminal button**. The end foot is very close to a dendritic spine of another neuron, although it does not touch it (see Figure 3-5C). This “almost connection,” which includes the surfaces of the end foot and the neighboring dendritic spine as well as the space between them, is called a **synapse**.

Chapter 4 describes how a neuron works in some detail, but here we will simply draw some generalizations about its function by examining its shape. A neuron has a cell wall within which are enclosed its contents. The dendrites and axon are fluid-filled extensions of the cell body. Imagine looking at a river system from an airplane. You see many small streams merging to make creeks, which join to form tributaries, which join to form the main river channel. As the river reaches its delta, it breaks up into a number of smaller channels again before discharging its contents into the sea. The shape of a neuron is somewhat similar to such a river system, and the neuron works in a broadly similar way. It collects information from many different sources on its dendrites, channels that information onto its axon, and then sends the information

Plug in the CD to see more about synapses in the module on Neural Communication in the section on the structure of a neuron.

Turn on the CD to view an animation of neural integration in the module on Neural Communication.

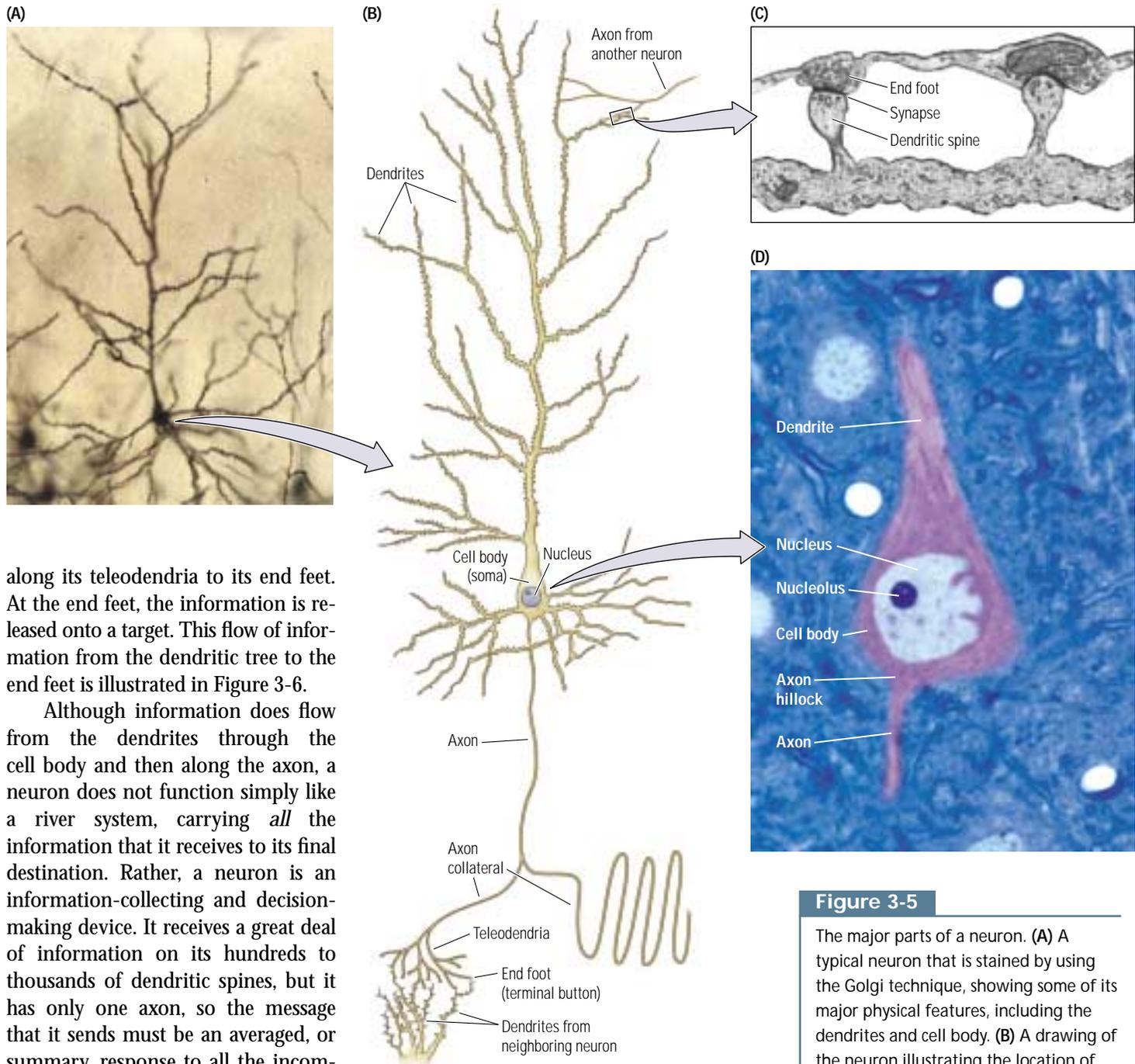


Figure 3-5

The major parts of a neuron. (A) A typical neuron that is stained by using the Golgi technique, showing some of its major physical features, including the dendrites and cell body. (B) A drawing of the neuron illustrating the location of some of its dendrites, the cell body, and the axon. (C) An electron micrographic image of the contacts between an axon from another neuron and a dendrite, illustrating the synapse formed by the opposition of the end foot of the axon and the dendritic spine of the dendrite. (D) A high-power light-microscopic view of the cell body, illustrating the nucleus and the nucleolus. Note that the different stains highlight different aspects of the neuron.

along its teleodendria to its end feet. At the end feet, the information is released onto a target. This flow of information from the dendritic tree to the end feet is illustrated in Figure 3-6.

Although information does flow from the dendrites through the cell body and then along the axon, a neuron does not function simply like a river system, carrying *all* the information that it receives to its final destination. Rather, a neuron is an information-collecting and decision-making device. It receives a great deal of information on its hundreds to thousands of dendritic spines, but it has only one axon, so the message that it sends must be an averaged, or summary, response to all the incoming information. Because it produces a summary response, a neuron is also a computational device. It is like an instructor who listens to comments from all of the students in her class about a recently administered examination and then decides to make the next examination a little different. It is also like a river system blocked by dams that can be opened to allow more water flow at some times and less at others. Chapter 4 will describe in detail how these decision-making processes take place.

TYPES OF NEURONS

The nervous system contains an array of neurons of different shapes and sizes, some of which appear quite simple and others very complex. With a little practice in looking into a microscope, you can quickly learn to recognize some neuron types by their

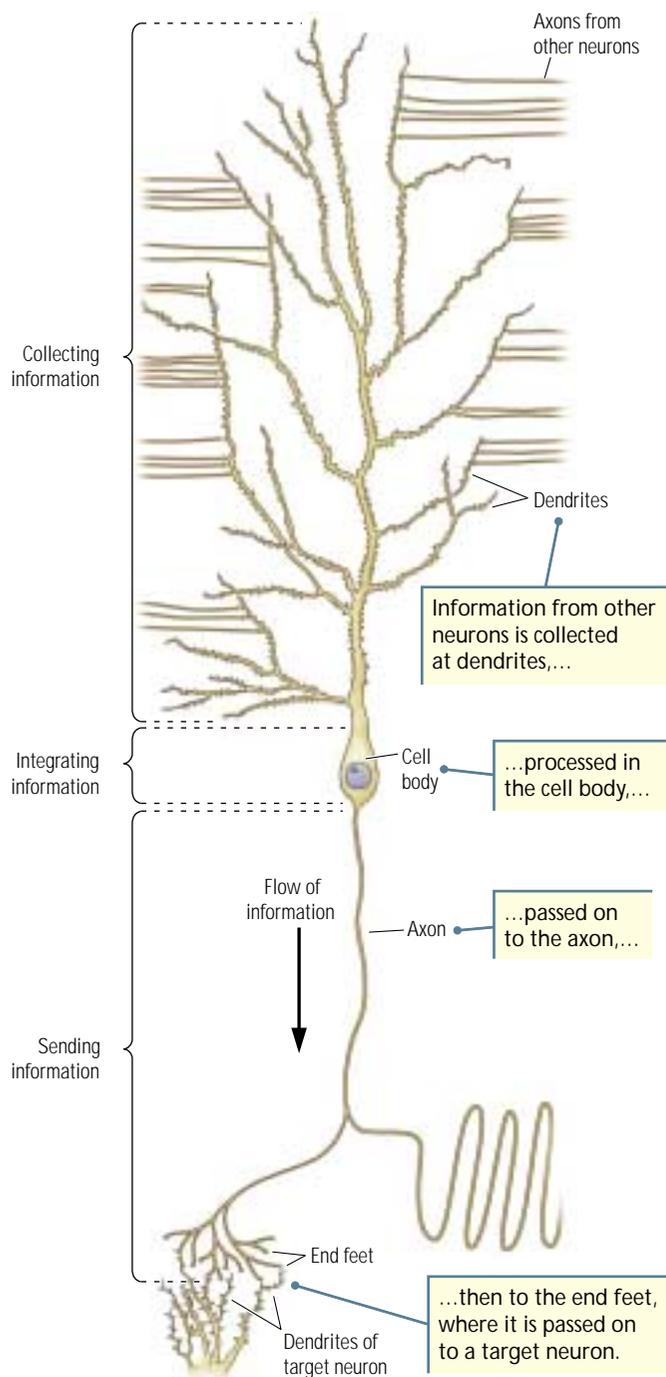


Figure 3-6

In this schematic representation of information flow in a neuron, information from other neurons is collected on dendrites, processed at the cell body, and then sent through the axon to the dendrites of other neurons.

features. Figure 3-7 shows the relative sizes and shapes of some representative kinds of neurons. The simplest is called a **bipolar neuron**. It has a single short dendrite on one side of its cell body and a single short axon on the other side. A more complicated neuron is a **sensory neuron**. It has its dendrite connected directly to its axon, so its cell body sits to one side of this long pathway. **Interneurons** include association cells, pyramidal cells, and Purkinje cells. An association cell, also called a **stellate cell** (meaning a cell that is star shaped), is characteristically small, with many dendrites extending from the cell body. Its axon is difficult to see among the maze of dendrites. A **pyramidal cell** has a long axon, a pyramidal-shaped cell body, and two sets of dendrites, one of which projects from the apex of the cell body and the other from the cell body's side. A **Purkinje cell** (named for its discoverer) is a distinctive kind of pyramidal cell with extremely branched dendrites that form a fan shape. Finally, a **motor neuron** has an extensive network of dendrites, a large cell body, and a long axon that goes to a muscle.

You may wonder if there is any sense to all the many different kinds of neurons that are packed into the nervous system. There is. Neurons are “workers” in an information-processing “factory,” and the appearance of each neuron tells us something about the job that it must do. For instance, one of the most obvious differences in neurons is size, particularly the size of the cell body. In general, neurons with large cell bodies have extensions that are very long, whereas neurons with small cell bodies have short extensions. The long extensions carry information to distant parts of the nervous system, whereas the short extensions are engaged in local processing. The size of the cell body therefore is in accord with the work that it must do in providing nutrients and other supplies for its axons and dendrites.

Neurons are also structured differently because of their specialized tasks. Some neurons are designed to bring information into the brain from sensory receptors, others to process it within the brain, and still others to carry it out of the brain to the body's various muscles. On the basis of these three major functions, neurons are categorized into three major groups: *sensory neurons*, *interneurons* (also called association cells because they associate sensory and motor activity), and *motor neurons*. A major difference between animals with small brains and animals with large brains is that large-brained animals have more interneurons.

By looking at different kinds of neurons with these three major functions in mind, you can see how they are structured to perform their various roles. Sensory neurons are designed to be efficient relay cells. A bipolar cell, for example, is a type of sensory neuron. Bipolar cells are found in the eye's light-receptor region, called the retina. The dendrites of bipolar cells collect information from the retina's photoreceptors and pass it along their axons to other neurons that carry it to the brain. The very simple structure of a bipolar cell is all that is needed to serve the relay function in this location. In other parts of the nervous system, other sensory neurons have much longer dendrites and axons. For instance, a sensory neuron carrying information from the body surface has its single long dendrite connected to a similarly long axon. This long, joined fiber efficiently serves as an information “highway” across large distances. For example, the

tips of the dendrites of some sensory neurons are located in your big toe, whereas the target of their axons is at the base of your brain. These sensory neurons send information over a distance as large as 2 meters.

Interneurons, a group that comprises all the neurons between sensory and motor neurons, have a wide range of structures that conform to their functions. For example, the interneurons called stellate cells receive incoming sensory information in a number of brain structures. Their bushy dendrites suggest that they collect information from many sources, which they must pass on to nearby neurons, because the axon on a stellate cell is not very long (the axon seems “lost” among the dendrites). Pyramidal cells are the most distinctive of the interneurons found in the neocortex. From the neocortex, they send information to other nervous system structures. For example, some of your neocortex’s pyramidal cells have axons that descend to your spinal cord, a distance as large as a meter, depending on your height. Purkinje cells are the most distinctive interneurons found in the brain’s cerebellum. The Purkinje cell’s bushy dendrites suggest that it collects information from a wide variety of other neurons, and its large cell body indicates that it sends the information to a distant target. Purkinje cells are, in fact, the output neurons for the cerebellum.

The basic function of motor neurons can be seen in their structure, too. As the nervous system’s final pathway to enabling movement, motor neurons have cell bodies that are located in the spinal cord. Their long axons extend to muscles, which they stimulate to contract. The bushy dendritic trees of motor neurons collect information from many other cells.

COMMUNICATING ACROSS SYNAPSES

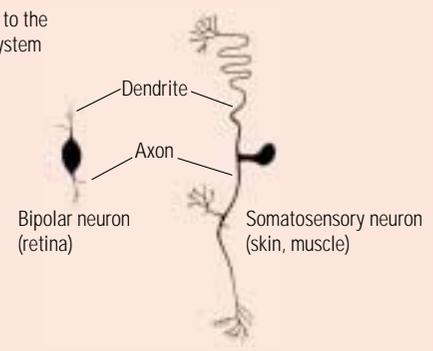
Subsequent chapters will present a detailed account of how neurons communicate, but a brief summary of communication between neurons will be useful here. Neurons must communicate with each other to pass along information, but, as you know, a tiny gap separates an axon’s end foot from another neuron’s dendritic spine. Until the 1950s, scientists were not aware that these gaps existed. They thought that end feet and dendritic spines were directly connected. Two discoveries changed this view. First, when synapses were examined with an electron microscope, it was clear that end feet come close to, but do not contact, dendritic spines. Second, neurons were also found to contain chemicals in their end feet, which suggested that they use chemical messages to communicate.

The large number of dendritic spines on neurons suggests that each neuron has many synaptic connections with other neurons. The number of connections may be from hundreds to a hundred thousand, depending on the particular neuron. And this transfer of information is not just one-way communication. Most neurons send axon collaterals back to the neurons from which they receive signals. A close look at the neuron in Figure 3-3 on page 79 reveals many axon collaterals coming off the main axon. These collaterals target the cells from which the neuron receives connections. The process of sending information back to a source is called *feedback*, and feedback allows a neuron to say, “Yes, I got the message,” or perhaps, “Say that again.”

Most connections made between neurons are with immediate neighbors. The information processing takes place in a local area. Within this area, some cells also send or receive information to or from more distant locations. The majority of cells, however, communicate locally. Chapter 5 deals with communication between neurons in greater detail.

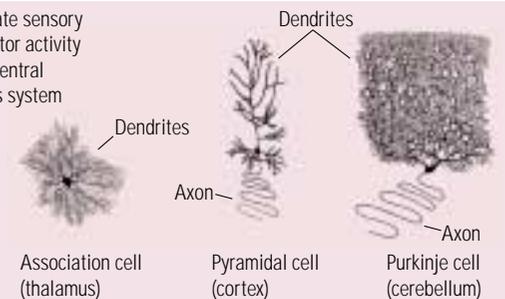
(A) Sensory neurons

Bring information to the central nervous system



(B) Interneurons

Associate sensory and motor activity in the central nervous system



(C) Motor neurons

Send signals from the brain and spinal cord to muscles

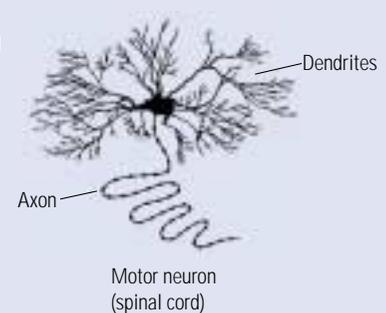


Figure 3-7

Examples of some nervous system cells (not to scale): **(A)** sensory neurons, **(B)** interneurons, and **(C)** motor neurons. Note that the appearance of the different kinds of neurons is distinctive; the appearance of each kind of neuron is due to its function. A sensory neuron collects information from a source and passes it on to an interneuron. The many branches of interneurons suggest that they collect information from many sources. Motor neurons are distinctively large and collect information from many sources; they pass this information on to command muscles to move.

THE LANGUAGE OF NEURONS: EXCITATION AND INHIBITION

Neurons are in constant communication with each other, but what is the nature of the messages they send? The biochemical explanation will be presented in Chapter 4. Here, an introduction to the basic language of neurons will suffice. Neurons either *excite* other neurons (turn them on) or *inhibit* other neurons (turn them off). In other words, neurons send “yes” or “no” signals to each other; the “yes” signals are the excitatory signals, and the “no” signals are the inhibitory signals. Each neuron receives thousands of these excitatory and inhibitory signals every second.

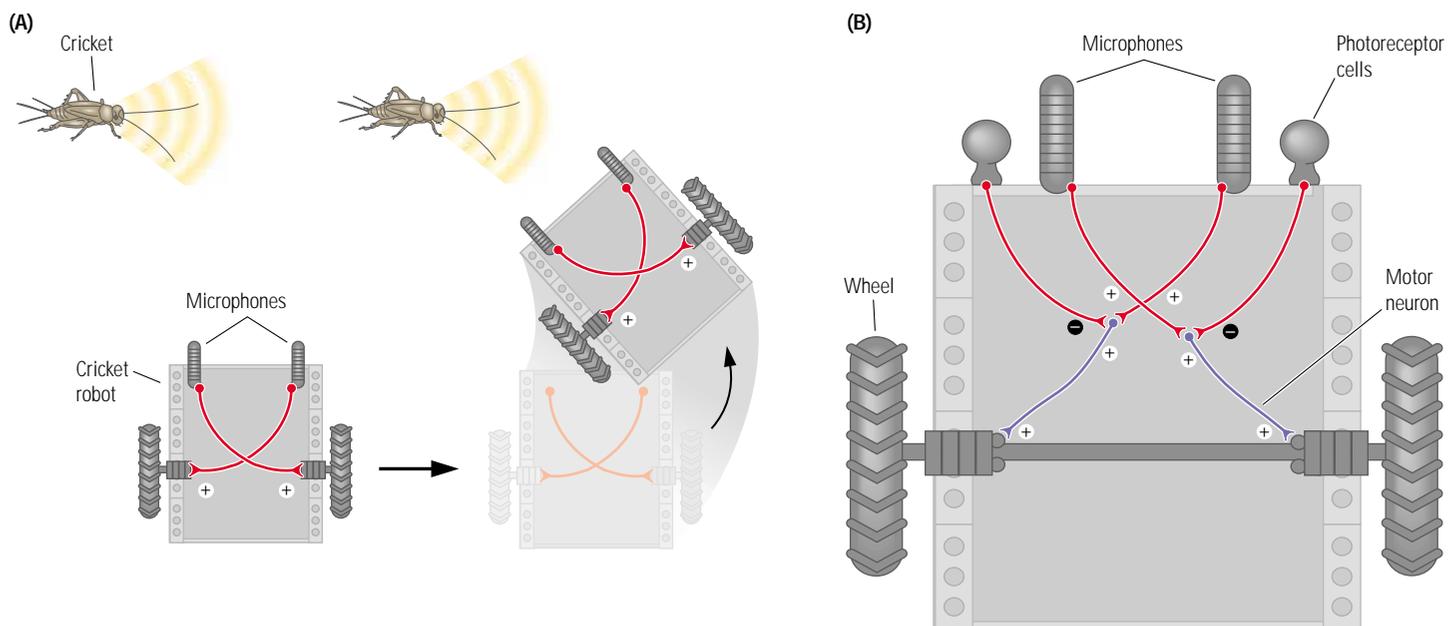
What does a neuron do with the thousands of “yes” or “no” signals that it receives? Its response to all those inputs is democratic. It *sums* the inputs. A neuron is spurred into action only if its excitatory inputs exceed its inhibitory inputs. If the reverse is true and inhibitory inputs exceed excitatory inputs, the neuron does not act.

We can apply this simple principle of neuron action to the workings of a robot, such as the little cricket robot described at the beginning of this chapter. Suppose we could insert a neuron between the microphone for sound detection on each side of this robot and the motor on the *opposite* side. Figure 3-8A shows how the two neurons would be connected. It would take only two rules to make the robot seek out a chirping male cricket. Rule 1 is that, each time a microphone detects a male cricket’s song, an excitatory message is sent to the opposite wheel’s motor, activating it. This rule ensures that the robot turns toward the cricket each time it hears a chirp. Rule 2 ensures that the robot travels in the right direction. It says that the message sent should be proportional to the intensity of the sound. This rule means that, if the chirp is coming from the robot’s left side, it will be detected as being louder by the microphone on the left, which will make the right wheel turn a little faster, swinging the robot to the left. The opposite would happen if the sound came from the right. If the sound comes from straight ahead, both microphones will detect it equally, and the robot will move directly forward.

To make the robot act more like a real cricket requires more neurons. Figure 3-8B shows how we could mimic the idea of sensory and motor neurons. The robot now has two sound-detecting sensory neurons receiving input from its microphones. When activated, each of these sensory neurons excites a motor neuron that turns on

Figure 3-8

(A) Excitatory inputs from the chirping of a male cricket are heard by the cricket robot through its microphones, and the sounds turn the robot’s wheels. The robot will orient to the cricket because the microphone that hears the loudest chirp (the closest microphone) will turn its wheel, located on the opposite side, more quickly than the wheel attached to the other microphone can be turned.
(B) In a slightly more complex cricket robot that will not travel in the light, the sensory neurons from the speaker excite motor neurons, but inhibitory input also comes from photoreceptors that, when illuminated, turn the motor neurons off.



one of the two wheel motors. But there are also sensory neurons coming from photoreceptors that detect light. These light-detecting sensory neurons, when activated, inhibit the motor neurons leading to the wheels and so prevent the robot from moving toward a male until it is dark and “safe.” This arrangement might give the robot some interesting properties. For example, at dusk there might be a conflict between excitatory signals from sound and weak inhibitory signals from the dim light. The robot might make small “intention” movements that orient it to the male while not actually searching for it. A researcher might want to examine the behavior of a real female cricket to see if it acts in the same way under these conditions.

If this arrangement sounds relatively complex, bear in mind that it contains only six neurons and each has only one connection with another neuron. We have not even placed interneurons in the robot. Imagine how infinitely more complex a human nervous system is with its hundred billion neurons, most of which are interneurons, each with its thousands of connections. Still, this simple example serves a valuable purpose. It shows the great versatility of function possible from using neurons along with the dual principles of excitation and inhibition. From the simple yes-or-no language of neurons emerges enormous possibilities for behavior.

Glial Cells

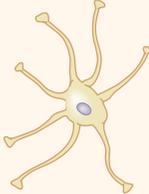
Imagine how much more efficient you could make a small robot if you had components dedicated to supporting your simulated neurons. Some of these components could attach the “neurons” to the appropriate parts of the robot, whereas others could insulate the “neurons” to prevent them from short-circuiting each other. These insulating components might also increase the speed with which messages traveled along the robot’s wired pathways. Still other auxiliary components could lubricate moving parts, whereas others could function to eliminate debris, keeping your robot clean and shiny. Do auxiliary components that could do all this sound too good to be true? Not really. All these functions are served by glial cells in your nervous system.

Glial cells are often described as the support cells of the nervous system. Although they do not transmit information themselves, they help neurons carry out this task. Unlike neurons, which form only in the first few years of life, glial cells are constantly replacing themselves. (Uncontrolled growth of glial cells can result in brain tumors; see “Brain Tumors” on page 86). Table 3-1 lists the five major classes of glial cells. Each has a characteristic structure and function. We begin by exploring ependymal cells.

EPENDYMAL CELLS

On the walls of the ventricles, or cavities, inside your brain are **ependymal cells**, one of the glial-cell classes. Ependymal cells produce and secrete the cerebrospinal fluid that fills the ventricles. This fluid, which is constantly being formed, flows through the ventricles toward the base of the brain, where it is absorbed into the blood vessels. Cerebrospinal fluid serves several purposes. It acts as a shock absorber when the brain is jarred; it provides a medium through which waste products are eliminated; it may play a role in brain cooling; and it may be a source of nutrients for certain parts of the brain located adjacent to the ventricles.

Table 3-1 Types of Glial Cells

Type	Appearance	Features and function
Ependymal cell		Small, ovoid; secretes cerebrospinal fluid (CSF)
Astrocyte		Star-shaped, symmetrical; nutritive and support function
Microglial cell		Small, mesodermally derived; defensive function
Oligodendroglial cell		Asymmetrical; forms myelin around axons in brain and spinal cord
Schwann cell		Asymmetrical; wraps around peripheral nerves to form myelin

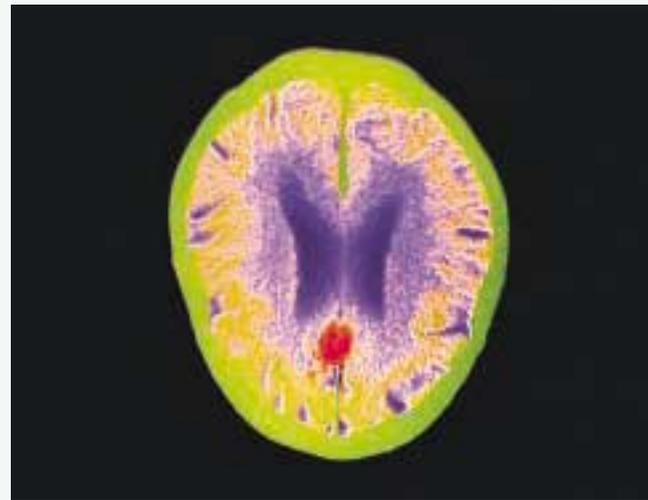
Brain Tumors

R. J. was a 19-year-old college sophomore. One day while she was watching a movie in a neuropsychology class, she collapsed on the floor and began twitching, displaying symptoms of a brain seizure. The instructor helped her to the university clinic, where she recovered, except for a severe headache. She reported that she had suffered from severe headaches on a number of previous occasions. A computer tomographic (CT) scan of her brain a few days later showed that she had a tumor over her left frontal lobe. She underwent surgery to have the tumor removed and returned to classes after an uneventful recovery. She successfully completed her studies, finished law school, and has been practicing law for more than 15 years without any further symptoms.

A *tumor* is a mass of new tissue that persists and grows independently of surrounding structures. No region of the body is immune to tumors, but the brain is a common site of them. Brain tumors do not grow from neurons; instead, they grow from glia or other supporting cells. The rate of growth depends on the type of cell undergoing uncontrolled growth. Some tumors are benign and not likely to recur after removal (such as R. J.'s tumor), whereas other tumors are malignant, likely to progress, and apt to recur after removal. Both kinds of tumors can pose a risk to life if they develop in sites from which they are difficult to remove.

The first symptoms of a brain tumor are usually due to increased pressure on surrounding brain structures. These symptoms can include headaches, vomiting, mental dullness, and changes in sensory and motor abilities. They can also include seizures like R. J.'s. Many symptoms depend on the precise location of the tumor.

There are three major types of brain tumors based on how they originate. *Gliomas* are tumors that arise from glial cells. They constitute roughly half of all brain tumors. Gliomas that arise from astrocytes are usually slow growing, not very malignant, and relatively easy to treat. In contrast, gliomas that arise from blast or germinal cells (precursor cells that grow into glial cells) are much more malignant, grow more quickly, and often recur after treatment. *Menin-*



The red area in this colored CT scan is a meningioma, a noncancerous tumor arising from the arachnoid membrane covering the brain. A meningioma may grow large enough to compress the brain but usually does not invade brain tissue.

gliomas are a second type of brain tumor, the type that R. J. had. They attach to the meninges, or covering of the brain, and so grow entirely outside the brain, as shown in the accompanying photograph. These tumors are usually well encapsulated, and, if they are located in places that are accessible, recovery after surgery is good. A third type of brain tumor is the *metastatic tumor*, which becomes established by a transfer of tumor cells from one region of the body to another (this transfer of disease from one organ to another is what the term *metastatic* means). Typically, metastatic tumors are present in multiple locations, making treatment difficult. Symptoms of the condition often first appear when the tumor cells reach the brain.

Treatment for a brain tumor is usually surgery, which also is one of the main means of diagnosing the type of tumor. If possible, the entire tumor is removed. Radiotherapy (treatment with X rays) is useful for destroying developing tumor cells. Chemotherapy, although common for treating tumors in other parts of the body, is less successful in the treatment of brain tumors because it is difficult to get the chemicals across the blood–brain barrier.

As cerebrospinal fluid flows through the ventricles, it passes through some narrow passages, especially the fourth ventricle, which runs through the brainstem. If the fourth ventricle is fully or partly blocked, the flow of cerebrospinal fluid is restricted. Because the fluid is continuously being produced, this blockage causes a buildup of pressure that begins to expand the ventricles, which in turn push on the surrounding brain. If such a blockage occurs in a newborn infant, before the skull bones are fused, the pressure on the brain is conveyed to the skull and the baby's head consequently swells. This condition, called **hydrocephalus** (literally, water brain), can cause severe mental retardation and even death. To treat it, doctors insert one end of a tube, called a shunt, into the blocked ventricle and the other end into a vein. The shunt allows the cerebrospinal fluid to drain into the bloodstream.

ASTROGLIA

Astrocytes (star-shaped glia), also called *astroglia*, provide structural support within the central nervous system. Their extensions attach to blood vessels and to the brain's lining, thus creating scaffolding that holds neurons in place. These same extensions provide pathways for the movement of certain nutrients between blood vessels and neurons. Astroglia also secrete chemicals that keep neurons healthy and help them heal if injured. At the same time, astroglia play an important role in forming a protective barrier between blood vessels and the brain, called the **blood–brain barrier**.

As shown in Figure 3-9, the end feet of astrocytes attach to the cells of blood vessels, causing the blood-vessel cells to bind tightly together. This tight binding prevents an array of substances, including many toxic ones, from entering the brain through the blood-vessel walls. The molecules (smallest units) of these substances are too large to pass between the blood-vessel cells unless the blood–brain barrier is somehow injured. But the downside to the blood–brain barrier is that many kinds of useful drugs, including antibacterial drugs such as penicillin, cannot pass through to the brain either. As a result, brain infections are very difficult to treat.

Yet another important function of astroglia is to enable increased brain activity. When you engage a part of your brain for some behavior, the brain cells of that area require more oxygen and glucose. In response, the blood vessels of the area dilate, allowing greater oxygen- and glucose-carrying blood flow. But what triggers the blood vessels to dilate? This is where the astrocytes come in. They convey signals from the neurons to the blood vessels, stimulating them to expand and so provide more oxygen.

Astroglia also contribute to the process of healing damaged brain tissue. If the brain is injured by a blow to the head or by some sharp object, astroglia form a scar to seal off the damaged area. Although the scar tissue is beneficial in healing the injury, it can unfortunately act as a barrier to the regrowth of the damaged neurons. Some experimental approaches to repairing brain tissue seek to get the axons and dendrites of central nervous system neurons to grow around or through a glial scar.

MICROGLIA

Microglia are small glial cells scattered throughout normal brain tissue. Unlike other glial cells, which originate in the brain, microglia originate in the blood and migrate into the brain. Microglia monitor the health of brain tissue. When brain cells are damaged, microglia invade the area to provide growth factors that aid in

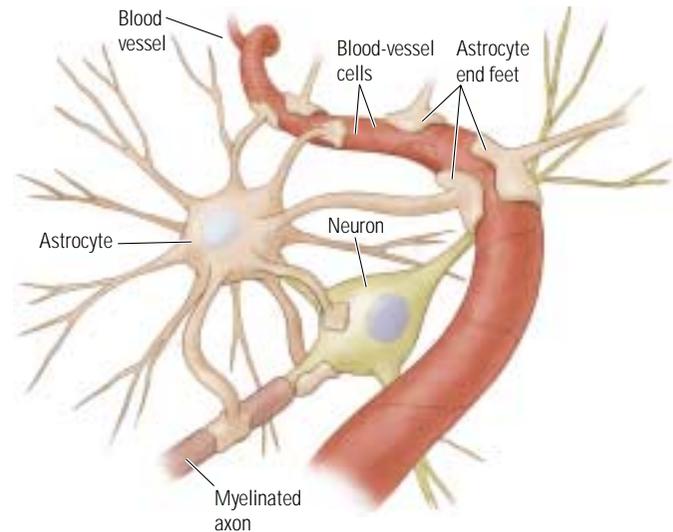


Figure 3-9

Astrocytes have processes that can attach both to neurons and to blood vessels. They provide support between different structures in the brain, they stimulate the cells on blood vessels to form tight junctions and so form the blood–brain barrier, and they transport chemicals excreted by neurons to blood vessels.

Hydrocephalus. A condition in which the flow of ventricular fluid is blocked, causing a buildup of pressure in the brain and swelling of the head that can result in retardation.

Blood–brain barrier. A barrier formed by tight junctions of capillaries, preventing the passage of most substances from the blood into the brain.

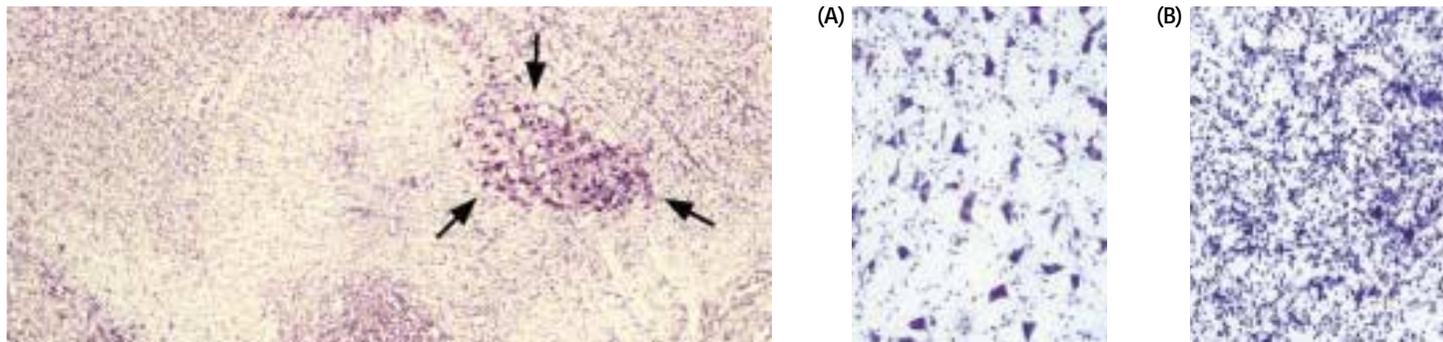


Figure 3-10

The arrows in the micrograph at left indicate a brain area called the red nucleus in a rat. **(A)** Cresyl violet–stained neurons in the red nucleus. **(B)** Appearance of the tissue after the cells have been killed with a neurotoxin, leaving only microglia.

repair. If tissue is dead, microglia engulf cell debris to remove it, a process called **phagocytosis**. Damage to the brain can be detected in a postmortem examination because, as illustrated in Figure 3-10, microglia will be left where neurons were once located.

OLIGODENDROGLIA AND SCHWANN CELLS

Two kinds of glial cells provide **myelin**, or “insulation,” to the axons of neurons: oligodendroglia and Schwann cells. Like the rubber insulation on electrical wires, myelin prevents adjacent neurons from short-circuiting each other’s activity. The **oligodendroglia**, or glia with few branches (the prefix *oligo* means “few,” referring to the fact that these glia have few branches in comparison with astroglia, which have many branches), provide myelin to axons in the brain and spinal cord. Oligodendroglia send out large flat branches that enclose and separate adjacent axons. **Schwann cells** provide myelin to axons in the peripheral nervous system. Each Schwann cell wraps itself repeatedly around a part of an axon, forming a structure somewhat like a bead on a string. Between two oligodendroglia or two Schwann cells is a small exposed segment of the axon called a **node of Ranvier**. Thus, the myelin produces a banded pattern of exposed and insulated axon. In addition to the myelination that Schwann cells and oligodendroglia provide to axons, they contribute to a neuron’s nutrition and function. They absorb chemicals that the neuron releases and release chemicals that the neuron absorbs.

The functions of myelin and the nodes of Ranvier will be discussed in detail later. For the present, it is sufficient to know that myelin plays an important role in speeding up the flow of information along a neuron. Neurons that are heavily myelinated are able to send information much faster than neurons having little or no myelin. Most neurons that must send messages over long distances, including sensory and motor neurons, are heavily myelinated. If myelin is damaged, a neuron may be unable to send any messages over its axons. In **multiple sclerosis**, myelin is damaged and the functions of the neurons whose axons it encases are disrupted. “Multiple Sclerosis,” on page 89, describes the symptoms of the disease.

GLIAL CELLS AND NEURON REPAIR

When you receive a deep cut on your body, such as on your arm or leg, the axons connecting your spinal cord to muscles and sensory receptors may be cut as well. Severed motor-neuron axons will render you unable to move the affected part of your body, whereas severed sensory fibers will result in loss of sensation from that body part. When both movement and sensation are gone, the condition is called **paralysis**. Over a period of weeks to months after motor and sensory axons were severed, movement and sensation return. The human body can repair this kind of nerve damage, and so the paralysis is not permanent.

Myelin. The glial coating that surrounds axons in the central and peripheral nervous system.

Paralysis. The loss of sensation and movement due to nervous system injury.

Multiple Sclerosis

One day J. O., an accountant, noticed a slight cloudiness in her right eye that did not go away when she wiped the eye. The area of cloudiness grew over the next few days. Her optometrist suggested that she see a neurologist, who diagnosed optic neuritis, a symptom that could be a flag for multiple sclerosis (MS). The eye cleared over the next few months, and J. O. had no further symptoms until after the birth of her first child 3 years later. She felt a tingling in her right hand that spread up her arm, until gradually she lost movement in the arm. Movement was restored 5 months later. Then 2½ years later, after her second child was born, she felt a tingling in her left big toe that spread along the sole of her foot and then up to her leg, eventually leading again to loss of movement. J. O. received corticosteroid treatment, which helped, but the condition rebounded when she stopped treatment. Then it subsided and eventually disappeared.

Since then, J. O. has had no major outbreaks of motor impairment, but she still feels occasional tingling in her trunk, some weakness in her left leg, and brief periods of tingling and numbness in different body parts that last a couple of weeks before clearing. The feeling is very similar to the numbness in the face after a dentist gives a local anesthetic. Although she suffers no depression, J. O. reports enormous fatigue, takes daily long naps, and is ready for bed early in the evening. Her sister and a female cousin have experienced similar symptoms. One of J. O.'s grandmothers was confined to a wheelchair, although the source of her problem was not known. J. O. occasionally wears a brace to support her left knee and sometimes wears a collar to support her neck. She makes every effort to reduce stress to a mini-

mum, but otherwise she lives a normal life that includes exercise and even vigorous sports such as water skiing.

J. O.'s extremely strange symptoms, which are often difficult to diagnose, are typical of multiple sclerosis. The first symptoms usually appear in adulthood, and their onset is quite sudden and swift. These initial symptoms may be loss of sensation in the face, limbs, or body or loss of control over movements or loss of both sensation and control. Motor symptoms usually appear first in the hands or feet. Often there is remission of early symptoms, after which they may not appear again for years. In some of its forms, however, the disease may progress rapidly over a period of just a few years until the person is reduced to bed care. In cases in which the disease is fatal, the average age of death is between 65 and 84.

Although we do not yet understand what causes multiple sclerosis, we do know that it is characterized by a loss of myelin, both on pathways bringing sensory information to the brain and on pathways taking commands to muscles. This loss of myelin occurs in patches, and scarring is frequently left in the affected areas. Computer tomographic scans on both J. O. and her sister revealed scarring in the spinal cord, a condition that helped confirm an MS diagnosis for them. Eventually, a hard plaque may form in the affected areas, which is why the disease is called sclerosis (from the Greek word meaning "hardness"). Associated with the loss of myelin is impairment in neuron function, causing patients to have the symptoms of sensory loss and difficulty in moving. Fatigue, pain, and depression are common related symptoms. Bladder dysfunction, constipation, and sexual dysfunction all complicate the condition. MS greatly affects a person's emotional, social, and vocational functioning. As yet, it has no cure.

Both microglia and Schwann cells play a part in repairing damage to the peripheral nervous system. When a peripheral nervous system axon is cut, the portion still attached to the cell body dies. Microglia remove all the debris left by the dying axon. Meanwhile, the Schwann cells that provided its myelin first shrink and then divide, forming numerous smaller glial cells along the path that the axon formerly took. The neuron then sends out axon sprouts that search for and follow the path made by the Schwann cells. Eventually, one sprout reaches the intended target, and this sprout becomes the new axon, whereas all other sprouts retract. The Schwann cells envelop

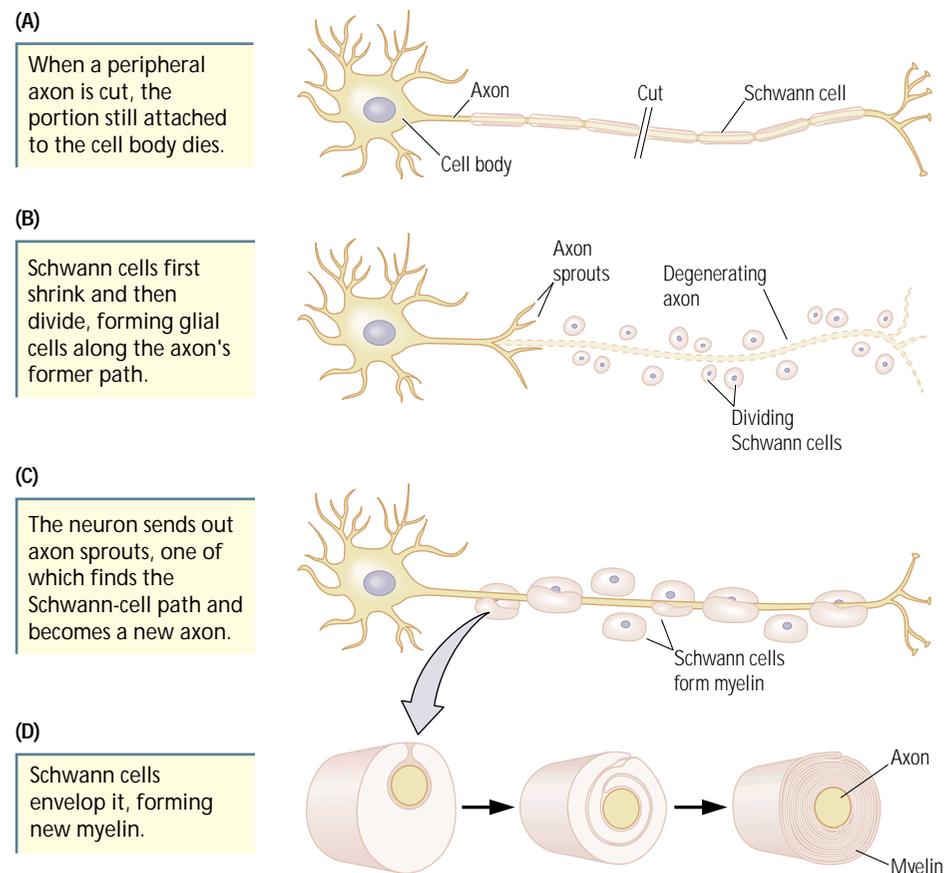
the new axon, forming new myelin and restoring normal function, as shown in Figure 3-11. In the peripheral nervous system, then, Schwann cells serve as signposts to guide axons to their appropriate end points. Axons can get lost, however, as sometimes happens after surgeons reattach a severed limb. If axons destined to innervate one finger end up innervating another finger instead, the wrong finger will move when a message is sent along that neuron.

Unfortunately, glial cells are not able to help neurons in the central nervous system regrow. When the central nervous system is damaged, as happens, for example, when the spinal cord is cut, function does not return, even though the distance that damaged fibers must bridge is short. That recovery should take place in the peripheral nervous system but not in the central nervous system is both a puzzle and a challenge in attempts to help people with brain and spinal-cord injury. The absence of recovery after spinal-cord injury is especially frustrating, because the spinal cord contains many axon pathways, just like those found in the peripheral nervous system. So why do axons regrow in the peripheral nervous system but not in the spinal cord and brain?

A number of factors appear to be implicated. First, as already stated, astroglia form a scar to seal off a damaged area of the central nervous system, but, in doing so, they create a barrier to regrowing axons. Second, the oligodendroglia of the central nervous system do not appear to divide and provide the same signposts for regrowing axons as do Schwann cells in the peripheral nervous system. In fact, the oligodendroglia that provide the myelin of any remaining neurons may actively repel regrowing axons with an antigrowth agent called NOGO. This repellent is probably useful under normal circumstances because it prevents the random regrowth of axons; however, in injury, it acts as a deterrent to repair.

Figure 3-11

Schwann cells aid the regrowth of axons in the peripheral nervous system. **(A)** A peripheral nerve, such as that projecting from the spinal cord to a muscle, is wrapped in myelin by Schwann cells. **(B)** After a cut, the axon dies from the cut back to the cell body, and the Schwann cells divide and produce new cells. **(C)** Sprouts form from the cell body and, when one sprout finds the Schwann cells, it follows the path that they make to the original target. **(D)** Schwann cells then wrap around the axon to form new myelin on the axon.



Researchers investigating how to encourage the regrowth of central nervous system neurons have focused on all these factors. For instance, in attempts to circumvent glial barriers, they have placed tubes across an injured area, trying to get axons to regrow through them. They have also inserted immature glial cells into injured areas to facilitate axon regrowth, and they have used chemicals to block NOGO. Some success has been obtained with each of these techniques, but none is as yet sufficiently successful to be used as a treatment for people with spinal-cord injury.

In Review

There are two types of nervous system cells: neurons and glia. The three types of neurons are sensory neurons, interneurons, and motor neurons. They are the information-conducting units of the nervous system and either excite or inhibit each other through their connecting synapses. The five types of glial cells are ependymal cells, astroglia, microglia, oligodendroglia, and Schwann cells. Their function is to nourish, insulate, support, and repair neurons.

THE INTERNAL STRUCTURE OF A CELL

What is it about the structure of neurons that gives them their remarkable ability to receive, process, store, and send a seemingly limitless amount of information? To answer this question, we must look inside a neuron to see what its components are. Fortunately, the internal features of a neuron can be colored with stains and examined under a light microscope or, if they are very small, under an electron microscope. Just as we can take apart a robot to see how its pieces work, we can take apart a cell to understand how its pieces function.

Because a cell is so small, it is sometimes hard to imagine that it, too, has components. Yet packed inside a cell is a whole system of interrelated parts that do the cell's work. This feature is as true of neurons as it is of any other cell type. A cell is a miniature "factory" of work centers, which manufacture and transport the proteins that are the cell's products. To a large extent, the characteristics of cells are determined by their proteins. Time and again, when we ask how a cell performs a certain function, the answer lies in the structure of a certain protein.

The smallest unit of a protein, or any other chemical substance, is known as a molecule. Molecules, and the even smaller atoms of which they are made up, are the basic units of a cell factory's inputs and outputs. Our journey into the interior of a cell will therefore begin with a look at these basic components. You may be familiar with basic chemistry; so, if you understand the structure of water and you know what a salt is and what ions are, this section will serve as a brief review.

Elements and Atoms

Of the earth's 92 natural **elements**, substances that cannot be broken down into other substances, 10 account for most of a cell's composition. These 10 elements are listed in Table 3-2. Three of them—oxygen, carbon, and hydrogen—account for 96 percent of the cell, with the other 7 elements constituting most of the remaining 4 percent. Cells also contain many other elements, but these elements, although important, are present in extremely small quantities.

Scientists represent each element with a symbol, many of which are simply the first one or two letters of the element's English name. Examples are the symbols O for

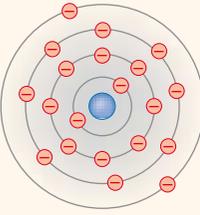
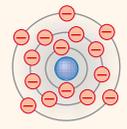
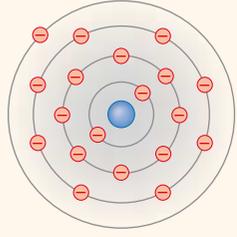
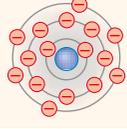
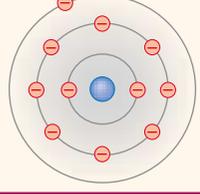
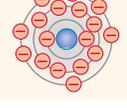
oxygen, C for carbon, and H for hydrogen. Other symbols, however, come from the element's Latin name: K, for instance, is the symbol for potassium, called *kalium* in Latin, and Na is the symbol for sodium, in Latin called *natrium*.

An **atom** is the smallest quantity of an element that retains the properties of that element. An atom has a nucleus that contains **neutrons** and **protons**. The neutrons are

neutral in charge, but the protons carry a positive charge (+). Atoms are surrounded by orbiting particles called **electrons**, each of which carries a negative charge (-). The basic structures of a cell's most common atoms are shown in the right-hand column of Table 3-2.

Ordinarily an atom has an equal number of positive and negative charges, but elements that are chemically reactive can lose or gain one or more electrons. When an atom gives up an electron, it becomes positively charged; when it takes on an electron, it becomes negatively charged. In either case, it is now called an **ion**. An ion that is formed by losing one electron is represented by the element's symbol and a plus sign. For example, K^+ represents a potassium ion, and Na^+ represents a sodium ion. An ion formed by losing two electrons is represented by the element's symbol followed by two positive charges (Ca^{2+} for a calcium ion). Some of the other ions that are important for cell function have gained electrons rather than lost them. Such an ion is represented by the element's symbol followed by a negative sign (for example, Cl^- representing an ion of chlorine, called a chloride ion).

Table 3-2 Chemical Composition of the Brain

Name of element	Symbol	% weight	Nucleus and electrons
Hydrogen	H	9.5	
Carbon	C	18.5	
Oxygen	O	65	
Nitrogen	N	3.5	
Calcium	Ca	1.5	
Phosphorus	P	1.0	
Potassium	K	0.4	
Sulfur	S	0.2	
Sodium	Na	0.2	
Chlorine	Cl	0.2	

Molecules

When atoms become bound together, they form a molecule of a substance. A **molecule** is the smallest unit of a substance that contains all that substance's properties. For example, a water molecule is the smallest unit of water that still retains the properties of water. Breaking down water any further would divide it into its two component gases—hydrogen and oxygen.

A substance can be represented by atomic symbols that specify the substance's formula. For example, H_2O , the formula for water, indicates that a water molecule is a union of two hydrogen atoms and one oxygen atom. Similarly, $NaCl$, the formula for table salt, shows that this substance consists of one sodium atom and one chlorine atom, whereas KCl , the formula for potassium chloride, another kind of salt, says that this substance is composed of one potassium atom and one chlorine atom.

Atoms join together in different ways to form different kinds of substances. Salts are substances that break into their constituent ions in water. When salts such as $NaCl$ and KCl are formed, the sodium or potassium atom gives up an electron to the chlorine atom. Therefore these salts are actually composed of negatively and positively charged ions tightly held together by their electrical attraction. In contrast, the atoms that constitute a water molecule are held together by *shared* electrons.

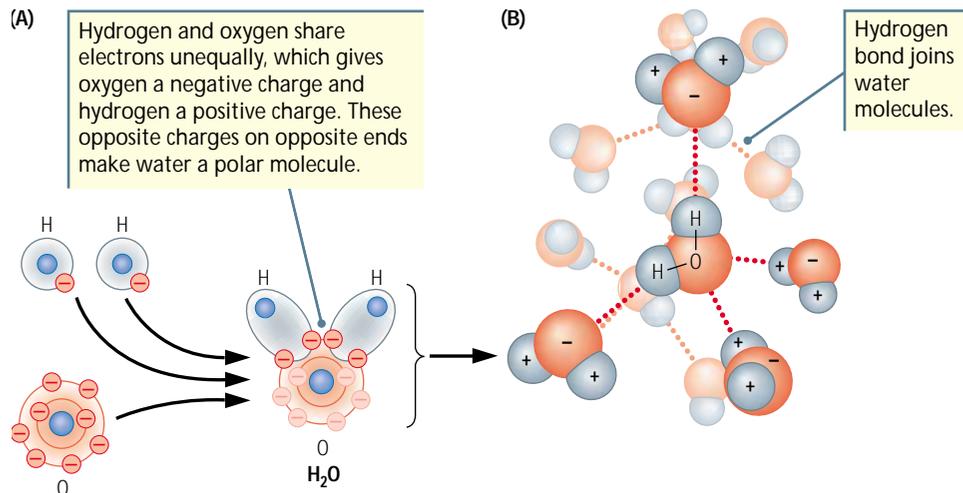


Figure 3-12

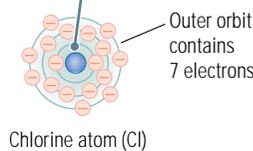
(A) In bonding to oxygen (O), two hydrogen atoms (H) share electrons with one oxygen atom. The resulting molecule is polar. Each hydrogen carries a positive charge (+) because it shares an electron with oxygen. Oxygen is negatively charged, having gained a share of the electrons. (B) The charged regions of a polar water molecule are attracted to oppositely charged parts of neighboring molecules. Each water molecule can hydrogen-bond to a maximum of four partners.

As you can see in Figure 3-12, the electrons provided by the H atoms spend some of their time orbiting the O atom. In this particular case, the electron sharing is not equal. The shared electrons spend more time orbiting the O than they do the H. This gives the oxygen region of the molecule a slight negative charge and leaves the hydrogen regions with a slight positive charge. Water, therefore, is a **polar molecule**, meaning that it has opposite charges on opposite ends (just as the earth does at the North and South Poles).

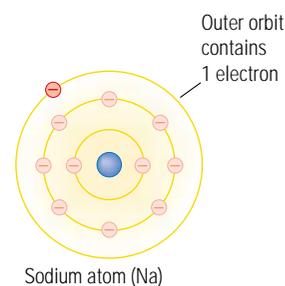
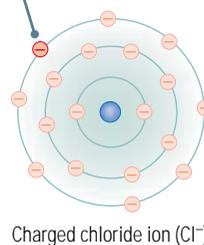
Because water molecules are polar, they are electrically attracted to each other. A slightly positively charged hydrogen of one molecule is attracted to the slightly negatively charged oxygen of a nearby molecule. This attracting force is called a **hydrogen bond**. Each water molecule can form hydrogen bonds with a maximum of four neighbors. Hydrogen bonding gives water some interesting properties, such as high surface tension (small insects can walk across water), strong cohesion (water runs down window panes in relatively large droplets), and a high boiling point (the temperature at which water's hydrogen bonds are finally broken). The attraction of water molecules for each other is also described by the term **hydrophilic**, or water loving (from Greek *hydro*, meaning "water," and *philic*, meaning "love"). Other polar molecules also are hydrophilic—that is, they, too, are attracted to water molecules.

Salts are a completely different matter. As noted earlier, salts are compounds that come apart in water. An example is sodium chloride, or table salt. As already stated, NaCl is formed when sodium atoms give up electrons to chlorine atoms and the resulting positively and negatively charged ions (Na^+ and Cl^-) join together to form a crystal because of their electrical attraction. Salt cannot retain its crystal shape

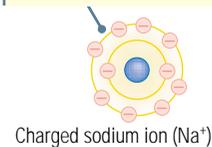
The nucleus contains neutrons and protons.



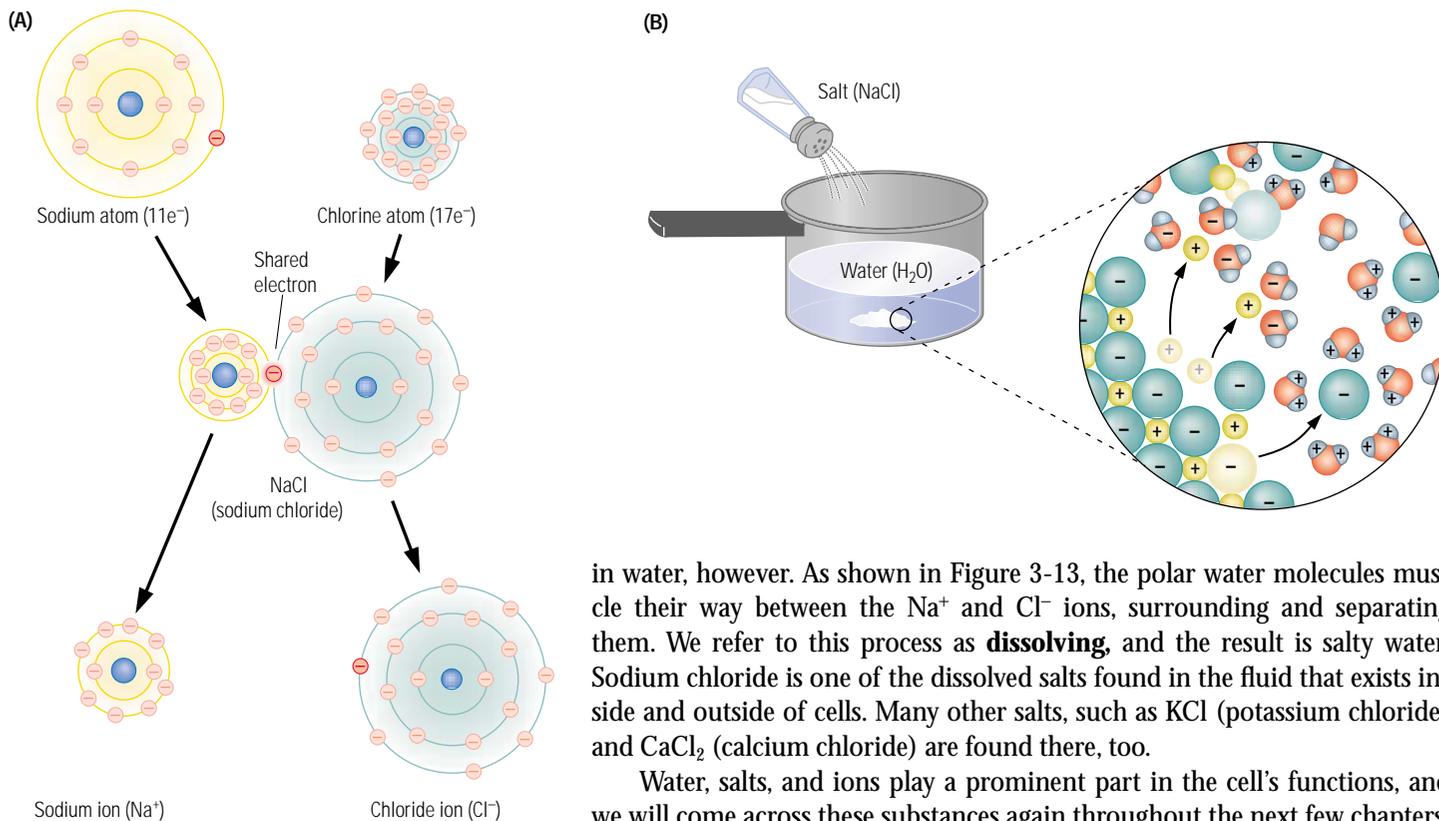
The outer orbit gains an electron.



The outer orbit disappears because it lost its only electron.



Hydrophilic. Refers to a substance that binds weakly to polar water molecules.



in water, however. As shown in Figure 3-13, the polar water molecules muscle their way between the Na^+ and Cl^- ions, surrounding and separating them. We refer to this process as **dissolving**, and the result is salty water. Sodium chloride is one of the dissolved salts found in the fluid that exists inside and outside of cells. Many other salts, such as KCl (potassium chloride) and CaCl_2 (calcium chloride) are found there, too.

Water, salts, and ions play a prominent part in the cell's functions, and we will come across these substances again throughout the next few chapters.

Figure 3-13

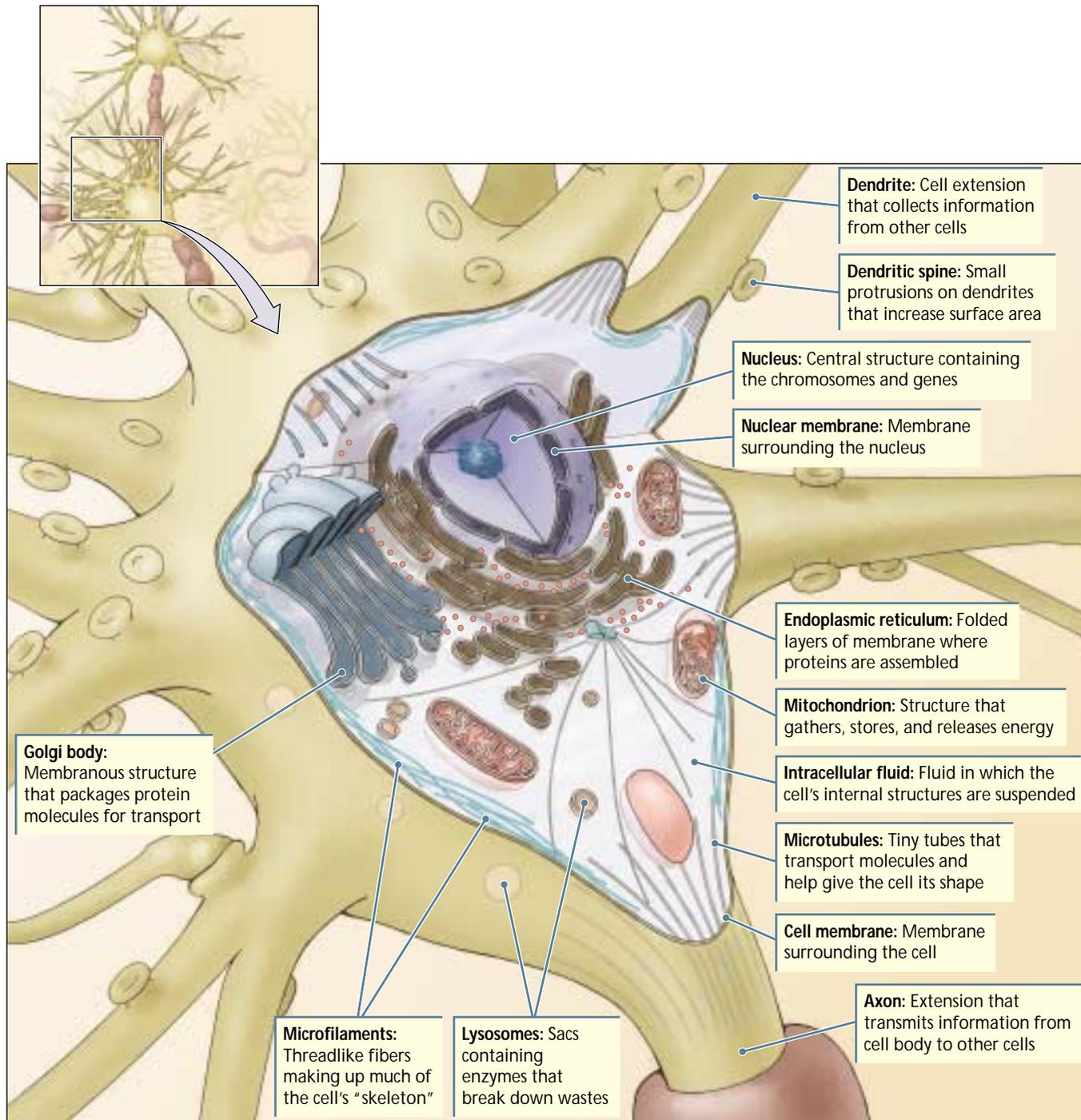
(A) Table salt is formed by the joining of sodium and chlorine, which share an electron. If they are separated, the sodium ion is short one electron and so carries a positive charge (Na^+), whereas the chloride gains an electron and so has a negative charge (Cl^-). (B) Because water molecules are weakly bonded, they can surround Na^+ ions and Cl^- ions, thus dissolving the salt. The positive part of the water molecule is attracted to the negative Cl^- ion, and the negative part of the water molecule is attracted to the positive Na^+ ion.

The Parts of a Cell

Earlier, we compared a cell to a miniature factory, with work centers that cooperate to make and ship the cell's products, proteins. We can now carry this analogy even further as we start to investigate the internal parts of a cell and how they function. Figure 3-14 illustrates many of the parts of a cell. Just as a factory has an outer wall that separates it from the rest of the world and gives it some security from unwanted intruders, a cell has an outer **cell membrane** that separates it from its surroundings and allows it to regulate what enters and leaves its domain. The cell membrane surrounds the cell body of a neuron, the dendrites and their spines, and the axon and its terminals and so forms a boundary around a continuous intracellular compartment. Very few substances can enter or leave a cell because the cell membrane serves as an almost impenetrable barrier. For substances to cross the cell membrane, the cell has to make proteins, which, when embedded in the cell membrane, can facilitate the transport of substances across the cell membrane. The proteins serve as the factory's gates. Furthermore, one of the main functions of the cell factory is making its own proteins.

Within the cell are other membranes that divide the cell into compartments, similar to the work areas that the inner walls of a factory create. In each of these compartments, the cell concentrates chemicals that are needed, while keeping out unneeded ones. Prominent among the membranes inside a cell is the **nuclear membrane**, which surrounds the cell's **nucleus**. The nucleus is like the executive office of a factory. It is here that the blueprints for the cell's proteins are stored, copied, and sent to the factory floor. The factory floor is analogous to a part of the cell called the **endoplasmic reticulum** (ER). The ER is an extension of the nuclear membrane and is where the cell's protein products are assembled in accord with the nucleus's "blueprint" instructions. When those products are finished, they have to be packed and sent

Cell membrane. Two layers of phospholipid molecules that surround the cell, separating its contents from the extracellular fluid; membranes that surround components inside the cell also are bilayer.

**Figure 3-14**

A typical cell consists of a nucleus, a number of membranes that enclose organelles in the cell (including the nucleus, lysosomes, and the endoplasmic reticulum), and Golgi bodies. It has an internal tubule system to provide motility, support, and material transport. Mitochondria provide energy. Many of the structures and organelles are found in the dendrites and axon of a neuron.

to their future users. Parts of the cell called the **Golgi bodies** provide the packaging rooms where the proteins are wrapped, addressed, and shipped. Other cell components are called **tubules**, of which there are a number of kinds. Some tubules provide structure to the cell, others are contractile and aid in the cell's movements, and still others create the transportation network that carries the cell's products to their destinations, much as a factory's interior system of trucks and forklifts delivers its goods. Two other important parts of the cell factory are the **mitochondria** and **lysosomes**. The mitochondria are the cell's power plants that supply its energy needs, whereas the lysosomes are sacklike vesicles that are the transportation vehicles for

incoming supplies and for the movement and storage of wastes. Interestingly, more lysosomes are found in old cells than in young ones. Cells apparently have trouble disposing of their garbage, just as we do.

THE CELL MEMBRANE: BARRIER AND GATEKEEPER

With this overview of the cell's internal structure in mind, we can look at its parts in more detail, beginning with the cell membrane. Although the neurons and glia of the brain appear to be tightly packed together, they, like all cells, are separated by **extracellular fluid**. This fluid is composed mainly of water with dissolved salts and many other chemical substances. Fluid is found inside a cell as well. It, too, is made up mainly of water with dissolved salts and other chemicals. The important point is that the concentrations of substances inside and outside the cell are different. The inner fluid of a cell is known as the **intracellular fluid**.

The cell membrane that encases a cell separates the intracellular from the extracellular fluid and so allows the cell to function as an independent unit. The structure of the membrane that allows it to separate two fluid environments is shown in Figure 3-15. In addition to being a barrier, the cell membrane also regulates the movement of substances into and out of the cell. One of these substances is water. If too much water entered a cell, the cell could burst, and if too much water left a cell, the cell could shrivel. The cell membrane helps ensure that neither will happen. The cell membrane also regulates the concentration of salts and other chemicals on its inner and outer sides. This regulation is important because, if the concentrations of chemicals within a cell become unbalanced, the cell will not function normally.

Look at the CD for more details on the internal structure of a neuron in the module on Neural Communication.

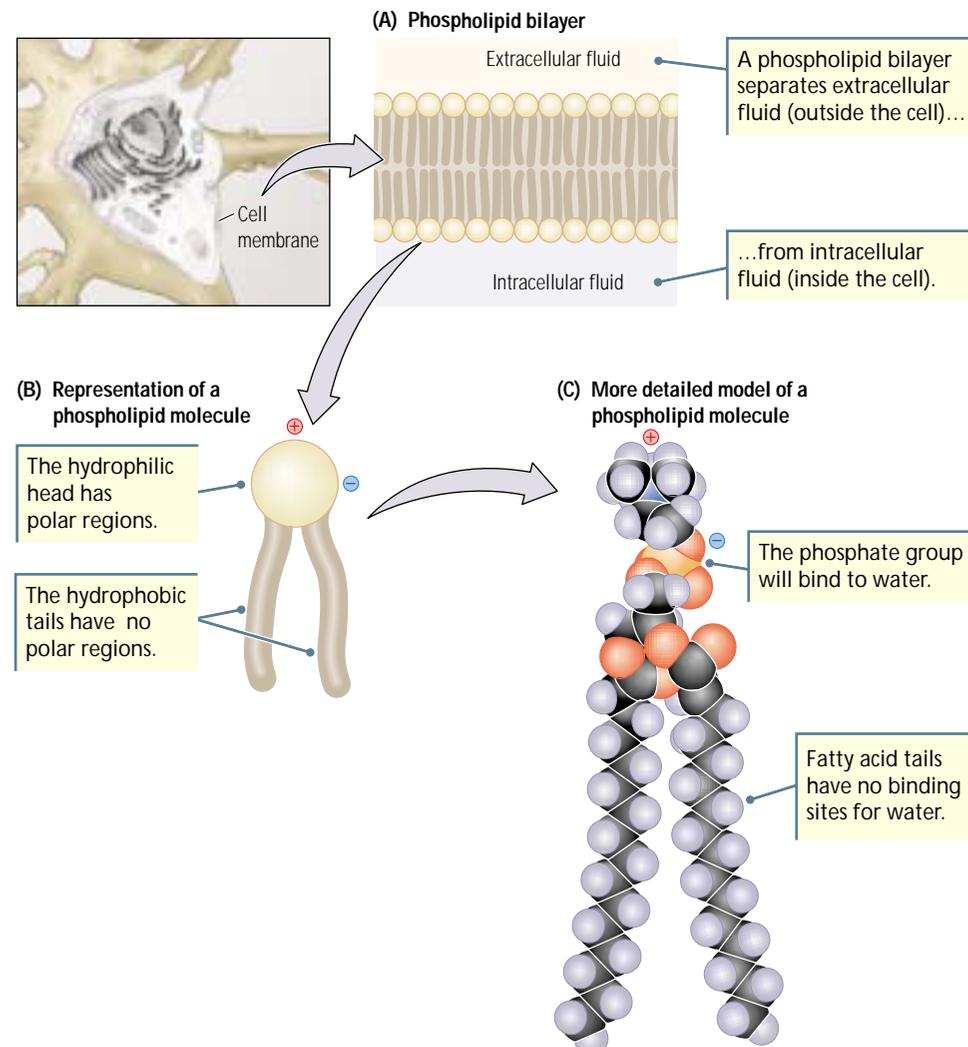


Figure 3-15

The cell membrane separates the fluid outside a cell from the fluid within the cell. **(A)** The membrane is composed of a bilayer (two layers) of phospholipid cells in which the tails of the phospholipids face inward and the heads face outward. **(B)** This conventional representation of a phospholipid molecule illustrates its head and tail regions. **(C)** This space-filling model of a phospholipid molecule shows that the head has polar regions (positive and negative poles) and so is hydrophilic and that the tail has no polar regions and so is hydrophobic.

What properties of a cell membrane allow it to regulate water and salt concentrations within the cell? One is the fact that a cell membrane is composed of a special kind of molecule called a **phospholipid**. This name comes from the molecule's structure. The molecule has a "head" that contains the element phosphorus (P) bound to some other atoms, and it has two "tails" that are lipids, or fats. The head is polar, with a slight positive charge in one location and a slight negative charge in another. The tails consist of hydrogen and carbon atoms that are tightly bound to each other in such a way that there are no polar regions. Figure 3-15C shows a model of this molecule.

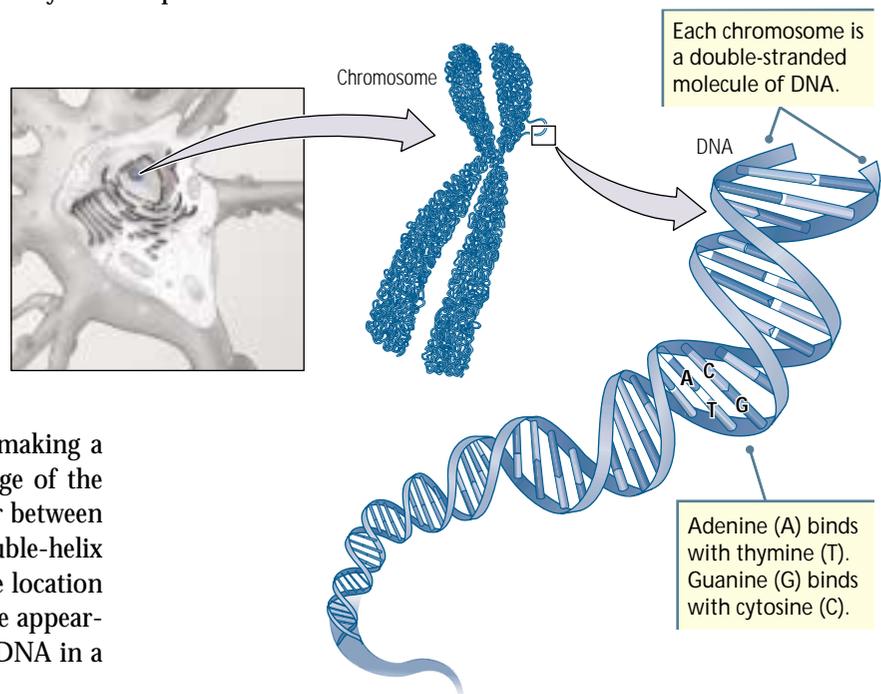
The polar head and the nonpolar tails of a phospholipid molecule are the underlying reasons that it can form membranes. The head is hydrophilic and so is attracted to polar water molecules. The nonpolar tails have no such attraction for water. They are **hydrophobic**, or water hating (the suffix *phobic* comes from the Greek word *phobia*, meaning "fear"). Quite literally, then, the head of a phospholipid loves water and the tails hate it. If phospholipid molecules are poured onto the surface of water, they stand on their heads with their tails in the air. You can confirm the behavior of fat molecules by pouring olive oil into water. The oil forms a bilayer (two-layer) bubble, with molecules of the oil having their heads on the outside and inside of the bubble pointing toward the water and their tails pointing inward toward each other. This arrangement puts the heads in contact with water both on the inside and on the outside of the bubble, while the tails stay dry, an arrangement that is much like that of a cell.

The cell membrane is flexible while still forming a remarkable barrier to a wide variety of substances. It is impenetrable to intracellular and extracellular water because polar water molecules cannot pass through the hydrophobic tails of the membrane. Ions in the extracellular and intracellular fluid also cannot penetrate this membrane, because they carry charges and thus cannot pass the phospholipid heads. In fact, only a few small molecules, such as oxygen (O₂), can pass through a phospholipid bilayer.

If cell membranes are such effective barriers to substances, there must be some mechanisms to carry needed materials into and out of cells. The cell factory, in other words, must have doors of some kind to receive its supplies, dispose of its wastes, and ship its products. Proteins that are embedded in the cell membrane serve as the gates and transportation systems that allow substances to cross the cell membrane. These mechanisms for crossing the cell membrane will be described a little later. First, we will consider how proteins are manufactured by the cell and how they are transported within the cell.

THE NUCLEUS: SITE OF GENE TRANSCRIPTION

In our factory analogy, the nucleus is described as the cell's executive office where the blueprints for making proteins are stored, copied, and sent to the factory floor. These blueprints are called **genes**, and they are encoded in the chemical structure of the nucleus's **chromosomes**. (The name *chromosome* means "colored bodies," referring to the fact that chromosomes can be readily stained with certain dyes.) The chromosomes are like a book of blueprints for making a complex building, whereas a gene is like one page of the book containing the plan for a door or a corridor between rooms. Each chromosome is a body with a double-helix structure and containing thousands of genes. The location of the chromosomes in the nucleus of the cell, the appearance of a chromosome, and the structure of the DNA in a chromosome are shown in Figure 3-16.



Hydrophobic. Refers to a substance containing no polar regions that will not bind with polar water molecules.

Gene. A segment of DNA that encodes a protein.

Chromosome. A double-helix structure containing the DNA of an organism's genes.

🔗 For animations of the membrane potential, look in the module on Neural Communication on your CD.

Figure 3-16

The cell nucleus contains chromosomes, each of which contains many genes. A chromosome is made up of two strands of DNA bound to each other by their nucleotide bases. The nucleotide base adenine (A) binds with thymine (T), and the nucleotide base guanine (G) binds with cytosine (C).

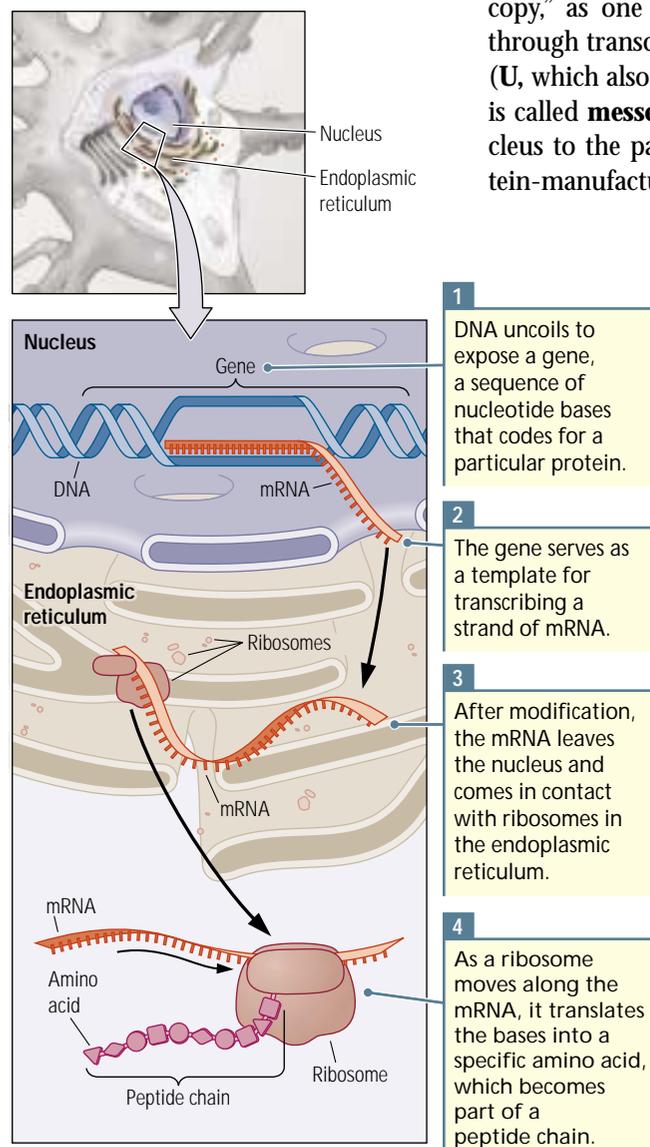
Transcription. The transfer of information from a DNA molecule to an RNA molecule.

Messenger RNA (mRNA). A type of RNA synthesized from DNA; attaches to ribosomes to specify the sequences of amino acids that form proteins.

Translation. The transfer of information from an RNA molecule into a polypeptide, in which the “language” of nucleic acids is translated into that of amino acids.

Figure 3-17

The flow of information in a cell is from DNA to mRNA to protein (peptide chain).



A human somatic cell has 23 pairs of chromosomes, or 46 in all (in contrast, a reproductive cell does not have paired chromosomes). Each chromosome is a double-stranded molecule of **deoxyribonucleic acid (DNA)**. The two strands of a DNA molecule coil around each other, as shown in Figure 3-16. Each strand possesses a variable sequence of four **nucleotide bases: adenine (A), thymine (T), guanine (G), and cytosine (C)**. Adenine on one strand always pairs with thymine on the other, whereas guanine on one strand always pairs with cytosine on the other. The two strands of the DNA helix are bonded together by the attraction that these paired bases have for one another.

Now you are ready to understand exactly what a gene is. A gene is simply a segment of a DNA strand that encodes the synthesis of a particular protein molecule. The code is contained in the sequence of the nucleotide bases, much as a sequence of letters spells out a word. The sequence of bases “spells out” the particular order in which amino acids, the building blocks of proteins, should be assembled to construct a certain kind of protein.

To initiate the process of producing a protein, the appropriate gene segment of the DNA strands first unwinds. The exposed sequence of nucleotide bases on one of the DNA strands then serves as a template on which a complementary strand of **ribonucleic acid (RNA)** is constructed from free-floating nucleotides. This process, called **transcription**, is shown at the top of Figure 3-17. (To transcribe means “to copy,” as one would copy in writing a piece of typed text.) The RNA produced through transcription is much like a single strand of DNA except that the base **uracil (U)**, which also is attracted to adenine) takes the place of thymine. The strand of RNA is called **messenger RNA (mRNA)** because it carries the genetic code out of the nucleus to the part of the cellular factory where proteins are manufactured. This protein-manufacturing center is the endoplasmic reticulum.

THE ENDOPLASMIC RETICULUM: SITE OF PROTEIN SYNTHESIS

Figure 3-17 shows that the endoplasmic reticulum consists of membranous sheets that are folded to form numerous channels. A distinguishing feature of the ER is that it may be studded with **ribosomes**, structures that play a vital role in the building of proteins. When an mRNA molecule reaches the ER, it passes through a ribosome, where its genetic code is “read.” In this process, called **translation**, a particular sequence of nucleotide bases in the mRNA is translated into a particular sequence of **amino acids**. (To translate means to convert one language into another, in contrast with transcription, in which the language remains the same.) **Transfer RNA (tRNA)** assists in translation. **Proteins** are just long chains of amino acids, folded up to form specific shapes.

The flow of the information contained in the genetic code is conceptually quite simple: a DNA strand is transcribed into an mRNA strand, and the mRNA strand is translated into a **polypeptide**. As shown in Figure 3-18, each group of three consecutive nucleotide bases along an mRNA molecule encodes one particular amino acid. These sequences of three bases are called **codons**. For example, the base sequence uracil, guanine, guanine (UGG) encodes the amino acid tryptophan (Trp), whereas the base sequence uracil, uracil, uracil (UUU) encodes the amino acid phenylalanine (Phe).

Humans require 20 different amino acids for the synthesis of proteins. All 20 of them are structurally similar, as illustrated in Figure 3-19. Each consists of a central carbon atom (C) bound to a hydrogen atom (H), an **amino group** (NH_3^+), a **carboxyl group** (COO^-), and

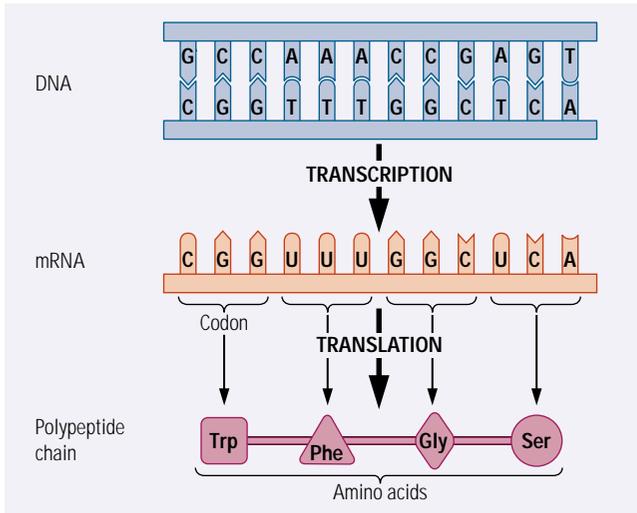
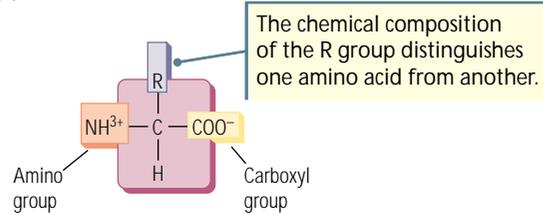


Figure 3-18

In the synthesis of a protein (see Figure 3-17), a strand of DNA is transcribed into mRNA. Each sequence of three bases in the mRNA encodes one amino acid and is translated to form the amino acid. The amino acids are linked together to form a polypeptide chain. The amino acids in this illustration are tryptophan (Trp), phenylalanine (Phe), glycine (Gly), and serine (Ser).

(A) Amino acid structure



(B) Polypeptide chain

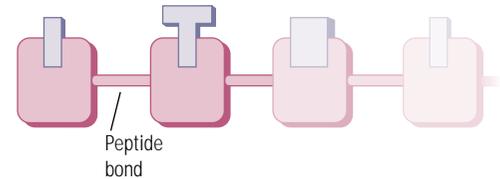


Figure 3-19

(A) Each amino acid consists of a central carbon atom (C) attached to an amine group (NH³⁺), a carboxyl group (COO⁻), and a side chain (R). **(B)** The amino acids are linked by peptide bonds to form a polypeptide chain.

a *side chain* (represented by the letter R). The side chain, which varies in chemical composition from one amino acid to another, is what helps to give different protein molecules their distinctive biochemical properties. Amino acids are linked together by a special bond called a *peptide bond*. A chain of amino acids is called a *polypeptide chain* (meaning “many peptides”). Just as a remarkable number of words can be made from the 26 letters of our alphabet, a remarkable number of peptide chains can be made from the 20 different amino acids. These amino acids can form 400 (20 × 20) different dipeptides (two-peptide combinations), 8000 (20 × 20 × 20) different tripeptides (three-peptide combinations), and an almost countless number of polypeptides.

A polypeptide chain and a protein are related, but they are not the same thing. The relation is somewhat analogous to that between a ribbon and a bow of a particular size and shape that can be made from the ribbon. As Figure 3-20 shows, a protein

Protein. An organic molecule whose folded and twisted shape is determined by its sequence of amino acids. A protein can comprise several polypeptides.

Polypeptide. A molecule in which a number of amino acids are connected by peptide bonds.

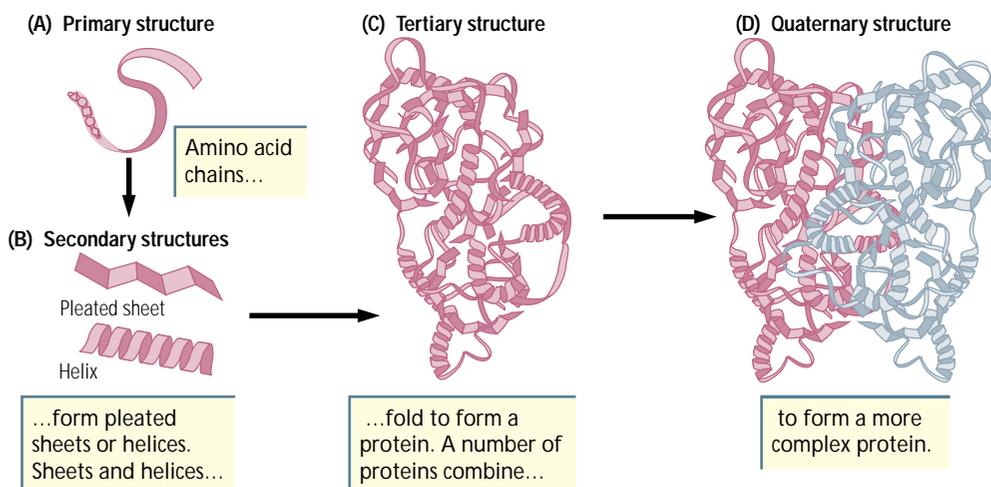


Figure 3-20

A protein can have as many as four levels of structure. **(A)** The primary structure consists of the chain of amino acids (that is, the polypeptide chain). **(B)** The secondary structure is a helix or pleated sheet formed by the primary chain. **(C)** The tertiary structure emerges when pleated sheets or helices or both fold to form a three-dimensional shape. **(D)** The quaternary structure also is three-dimensional and consists of two or more polypeptides. Whether a polypeptide chain forms a pleated sheet or a helix and what three-dimensional shape is ultimately formed are determined by the sequence of amino acids in the primary structure.

is formed when polypeptide chains form a particular shape. Long polypeptide chains have a strong tendency to twist into a helix (a spiral) or to form pleated sheets, which, in turn, have a strong tendency to fold together to form more complex shapes. A folded-up polypeptide chain constitutes a protein. In addition, two or more polypeptide chains may combine to form a single protein. Many proteins are globular (round) in shape and others are fibrous, but, within these broad categories, countless variations are possible.

GOLGI BODIES AND MICROTUBULES: PROTEIN PACKAGING AND SHIPMENT

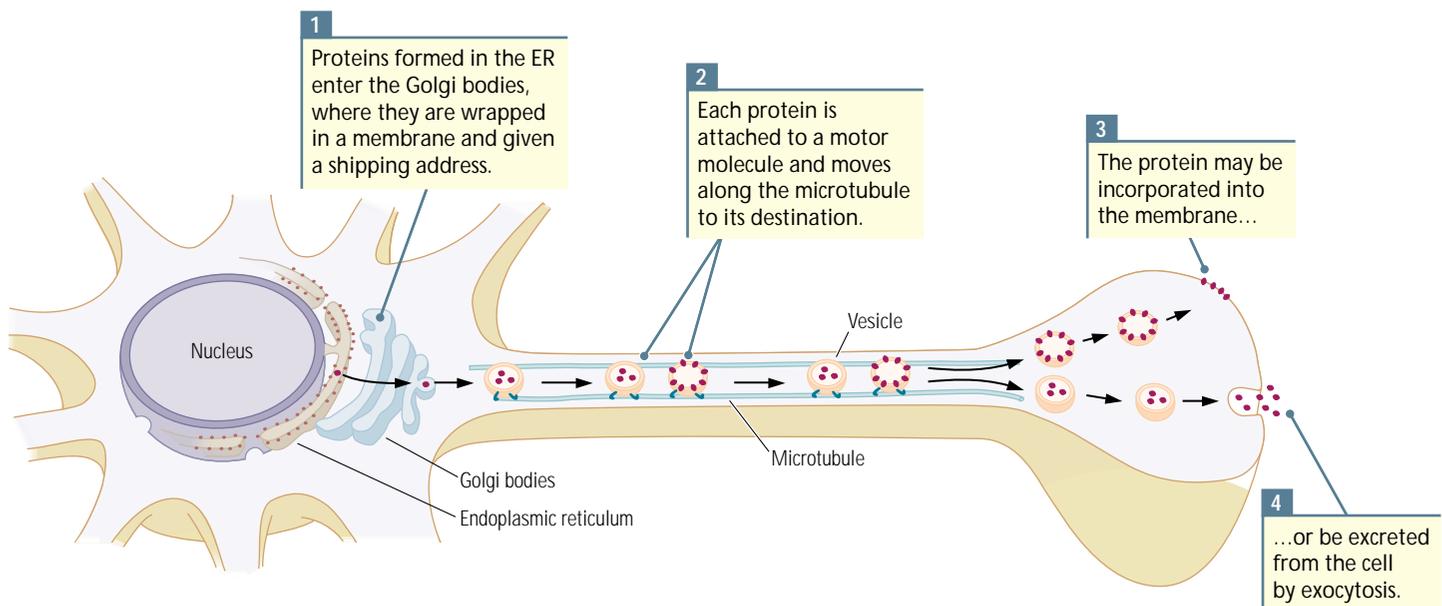
Within any one neuron, there may be as many as 10,000 protein molecules, all of which the cell has manufactured. Some of these proteins are destined to be incorporated into the structure of the cell. They become part of the cell membrane, the nucleus, the ER, and so forth. Other proteins remain in the intracellular fluid, where they act as enzymes, facilitating many of the cell's chemical reactions. Still other proteins are excreted by the cell as hormones or messenger molecules. How does the cell manage to get all these different proteins to the right destinations? The answer lies in cell components that package, label, and ship proteins. These components operate much like a postal service.

To reach their appropriate destinations, the protein molecules that have been synthesized in the cell must first be wrapped in membranes and given labels that indicate where they are to go. This wrapping and labeling takes place in organelles called *Golgi bodies*. The work of the Golgi bodies is illustrated in Figure 3-21. The packaged proteins are then loaded onto motor molecules that “walk” along one of the many tubules radiating through the cell, thus carrying the protein to its destination.

If a protein is destined to remain within the cell, it is unloaded into the intracellular fluid. If it is intended to be incorporated into the cell membrane, it is carried to the membrane, where it inserts itself. Suppose that a particular protein is destined to be excreted at the cell membrane. In this process, called **exocytosis**, the membrane in which the protein is wrapped first fuses with the membrane of the cell. Now the protein inside the “wrapper membrane” can be expelled into the extracellular fluid. Many excreted proteins travel to other cells to induce chemical reactions and so serve as messenger molecules.

Figure 3-21

The steps in exporting a protein consist of packaging, transport, and function at destination.



THE CELL MEMBRANE REVISITED: CHANNELS, GATES, AND PUMPS

Knowing something about the structure of proteins will help you to understand other ways that substances can travel across what would otherwise be an impermeable cell membrane. As already mentioned, some of the proteins that cells manufacture are carried to the cell membrane, where they become embedded. These membrane proteins play a number of important roles, one of which is transporting substances across the membrane. We will consider how three such membrane proteins work. In each case, notice how the function of the particular protein is an emergent property of its shape.

An important feature of protein molecules is that they can *change* shape. This changing of shape is done in a number of ways. For instance, some protein molecules change shape when other chemicals bind to them. The protein molecule is analogous to the lock in a door. When a key of the appropriate size and shape is inserted into the lock and turned, the locking device changes shape and becomes activated. An example of a shape-changing protein is the enzyme hexokinase, illustrated in Figure 3-22. The surface of this protein molecule has a groove, called a **receptor**, which is analogous to a keyhole. When another molecule—in this case, glucose—enters the receptor area, it induces a slight change in the shape of the protein, causing the hexokinase to embrace the glucose. Either small molecules or other proteins can bind to the receptors of proteins and cause the proteins to change their shapes. The changes in shape may then allow the proteins to serve some new functions.

Other types of changes in a protein's shape enable substances to cross the cell membrane. Some membrane proteins become shaped in such a way that they create **channels** through which substances can pass. Different-sized channels in different proteins allow different substances to pass. Figure 3-23A illustrates a protein with a particular shape forming a small channel in the cell membrane that is large enough for potassium (K^+) ions to pass through it. Other protein molecules allow sodium ions or chloride ions to pass through the cell membrane.

Other membrane proteins regulate the passage of substances across the cell membrane by changing their shapes in response to some trigger, as the protein hexokinase does. Figure 3-23B shows a protein molecule that acts as a **gate** in this way. The protein allows the passage of substances when its shape leaves the gate open and prevents the passage of substances when its shape leaves the gate closed.

Channel. An opening in a protein that is embedded in the cell membrane and allows the passage of ions through the cell membrane.

Gate. A protein that is embedded in a neural or glial membrane and allows substances to pass through the membrane on some occasions but not on others.

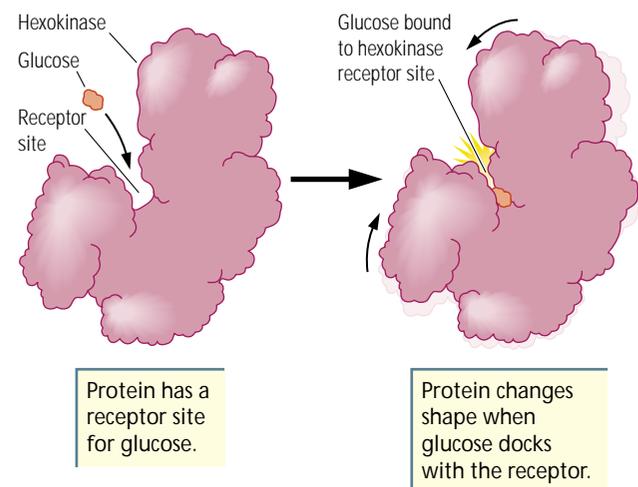


Figure 3-22

Hexokinase (purple) changes shape when a glucose molecule (orange) binds to its receptor.

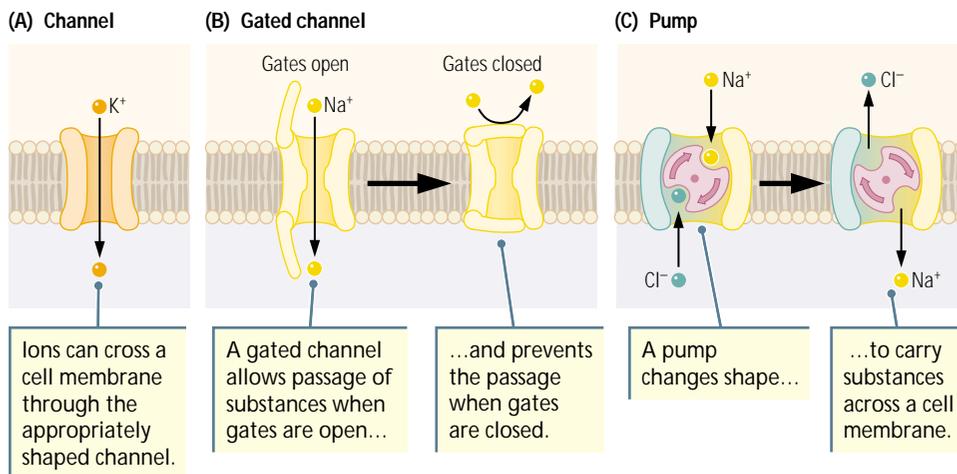


Figure 3-23

Transmembrane proteins form channels that allow substances to enter and exit the cell: (A) a channel that allows passage of potassium ions; (B) a gated channel that, in one conformation, allows the passage of sodium ions, whereas, in another conformation, it blocks their passage; (C) a pump that, when it changes shape, carries an ion across the membrane.

Pump. A protein, in the cell membrane, that actively transports a substance across the membrane.

the passage of substances when its shape leaves the gate closed. Changes in the shape of a protein can also allow it to act as a **pump**. Figure 3-23C shows a protein that changes its shape to carry (“pump”) substances across the membrane.

Channels, gates, and pumps all play an important role in allowing substances to enter and leave a cell. This passage of substances is critical to explaining how neurons send messages. Chapter 4 explores the topic of neuron communication in detail.

In Review

Cells contain elements that combine to form molecules that are in turn organized together to make up the constituent parts of the cell, including the cell membrane, the nucleus, the endoplasmic reticulum, Golgi bodies, tubules, and vesicles. Important products of the cell are proteins, which serve many functions including acting as channels, gates, and pumps to allow substances to cross the cell membrane. Simply put, the sequence of events in building a protein is: DNA makes mRNA and mRNA makes protein. When formed, the protein molecules are wrapped by the Golgi bodies and are transported to their designated sites of use by microtubules.

GENES, CELLS, AND BEHAVIOR

Genes are the blueprints for proteins, proteins are essential to the function of cells, and cells produce behavior. That sequence of connections sounds simple enough. But exactly how one connection leads to another is one of the big challenges for future research; so, if you choose a career in neuroscience, you will most likely be working out this relation. As already mentioned, genes are chromosome segments that encode proteins, and proteins serve as enzymes, channels, gates, and pumps. This knowledge does not tell you much about the ultimate structure and function of a cell, because so many genes and proteins take part. The eventual function of a cell is an emergent property of all its many constituent parts. Similarly, knowing that behaviors result from the actions of neurons does not tell you much about the ultimate form that behaviors will take, because so many neurons participate in them. Your behavior is a property of the action of all your billions of neurons. The challenge for future research is to be able to explain how genes, proteins, cells, and behavior are related.

Understanding the contributions of genes alone is a tremendous challenge. Humans have an estimated 100,000 genes, about half of which contribute to building the brain. If we knew what proteins all of these genes encode and what functions those proteins have, our understanding of how the brain is constructed and produces behavior would be greatly advanced. This understanding is a long-term goal of genetic research. Those working on the Human Genome Project have the human genome (all the genes in our species) catalogued, but identifying the function of every gene will take a long time.

Still, even though we cannot yet explain human behavior in relation to genes and neurons, we know the severe behavioral consequences of genetic abnormalities that affect the nervous system. About 2000 genetic abnormalities result in abnormalities in the brain and in behavior. For example, an error in a gene could produce a protein that should be a K^+ channel but will not allow K^+ to pass, it could produce a pump that will not pump, or it could produce a protein that the transportation system of the cell refuses to transport. If there are about 10,000 different proteins in a cell, a genetic mutation that results in an abnormality of any one protein could have a

🕒 For the latest update on the Human Genome Project, look at the current news feature at www.worthpublishers.com/kolb/chapter3.

beneficial effect, it could have little noticeable effect, or it could have severe consequences. Studying genetic abnormalities is one source of insight into how genes, neurons, and behaviors are linked. Such studies may also help us to reduce the negative effects of these abnormalities, perhaps someday even eliminating them completely. For example, just as the replacement of a malfunctioning part of a robot restores the function of the robot, the identification and replacement of an abnormal gene could provide a cure for the brain and the behavioral abnormalities that it produces. Genetic research, then, promises to have a revolutionary effect not only on the study of the brain and behavior, but also on the search for new ways to treat genetic disorders. For these reasons, we will focus on human genetics in the rest of this chapter.

Chromosomes and Genes

As stated earlier, the nucleus of each human somatic cell contains 23 pairs of chromosomes, or 46 in all. One set of 23 chromosomes comes from the mother, and the other set comes from the father. The chromosomes are numbered from 1 to 23, with chromosome 1 being the largest and chromosome 22 being almost the smallest (chromosome 21 is the smallest; Figure 3-24). The chromosomes numbered from 1 to 22 are called **autosomes**, and they contain the genes that contribute to most of our physical appearance and behavioral functions. The 23rd pair of chromosomes comprises the **sex chromosomes**, which eventually produce our physical and behavioral sexual characteristics. There are two types of sex chromosomes, referred to as X and Y because of their appearance. Female mammals have two X chromosomes, whereas males have an X and a Y.

Because your chromosomes are “matched” pairs, a cell contains two copies of every gene, one inherited from your mother, the other from your father. These two matching copies of a gene are called **alleles**. The term “matching” here does not necessarily mean identical. The nucleotide sequences in a pair of alleles may be either identical or different. If they are identical, the two alleles are called **homozygous** (*homo* means “the same”). If they are different, the two alleles are called **heterozygous** (*hetero* means “different”). The nucleotide sequence that is most common in a population is called the **wild-type** allele, whereas a less frequently occurring sequence is called a **mutation**. Mutant genes often determine genetic disorders.

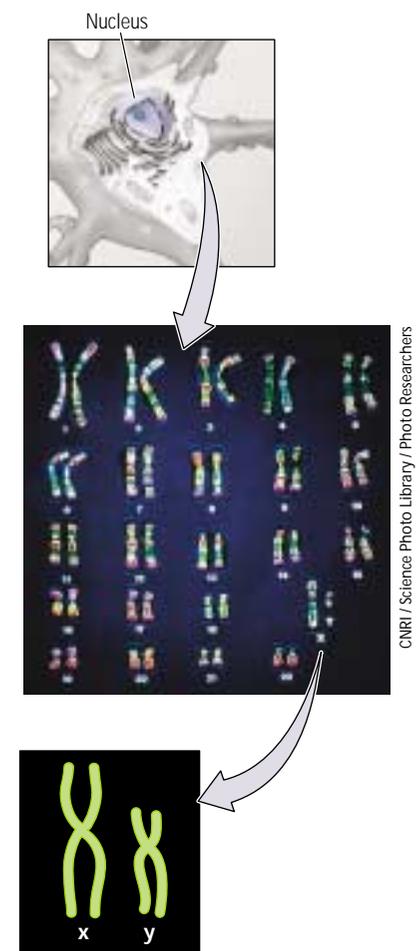
Genotype and Phenotype

The actions of genes give rise to what we call physical or behavioral *traits*, but these actions are not always straightforward. For a variety of reasons, some genes are not expressed as traits or they may be expressed only incompletely. For instance, the actions of a protein manufactured by one gene may be suppressed or modified by other genes. The proteins and genes that contribute to human skin color provide a good example. The color expressed depends on the precise complement of a number of different genes. In addition, environmental factors may modify gene expression. In regard to skin color, exposure to sunlight is often a factor modifying genetic influences.

Because genes and expressed traits can be so different, scientists distinguish between genotype and phenotype (the prefix *pheno* comes from the Greek word meaning “show”). **Genotype** refers to the full set of all the genes that an organism possesses, whereas **phenotype** refers to the appearance of an organism that results from the interaction of genes with one another and with the environment.

The extent of phenotypic variation, given the same genotype, can be dramatic. For example, in some strains of genetically identical mice, certain mice develop a brain with no corpus callosum, the large band of fibers that connects the two hemispheres

🕒 To learn more about genetics, you'll find links and tutorials on the Web site at www.worthpublishers.com/kolb/chapter3.



CNRI / Science Photo Library / Photo Researchers

Figure 3-24

The human nucleus contains 46 chromosomes, 23 derived from the father and 23 derived from the mother. A person's sex is determined by the sex chromosomes.

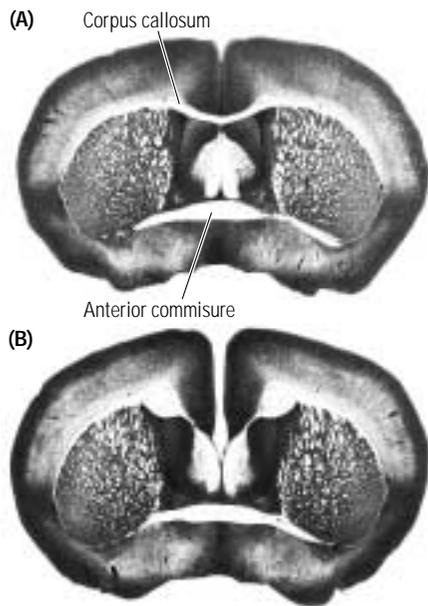


Figure 3-25

Both of these coronal sections through the brains of two genetically identical mice are in the same relative position in the brain, as shown by the presence of the anterior commissure, one of a number of large fiber pathways connecting the two hemispheres. The mouse in part A has a corpus callosum, whereas the mouse in part B does not. Despite their genetic identity, other factors determine each mouse's phenotype.

Adapted from "Defects of the Fetal Forebrain in Acallosal Mice," by D. Wahlsten and H. W. Ozaki, in *Callosal Agenesis* (p. 126), edited by M. Lassonde and M. A. Jeeves, 1994, New York: Plenum Press.

(Figure 3-25). The absence of a corpus callosum has a genetic cause, but something happens in the development of the brain that determines whether the trait is expressed in a particular mouse's phenotype. Although the precise causal factors are not known, they affect the embryo at about the time at which the corpus callosum should form. This example illustrates the importance of distinguishing between genotype and phenotype. Having identical genes does not mean that those genes will be identically expressed. By the same token, even if we knew everything about the structure and function of our own genes, it would be impossible to predict how much of our behavior is due to our genotype, because so much of our behavior is phenotypic.

Dominant and Recessive Genes

If both alleles in a pair of genes are the same (homozygous), the two encode the same protein, but if the two alleles in a pair are different (heterozygous), they encode two different proteins. There are three possible outcomes of the heterozygous condition when the proteins express a physical or behavioral trait: only the allele from the mother may be expressed; only the allele from the father may be expressed; or both alleles may be expressed simultaneously. A member of a gene pair that is expressed as a trait is called a **dominant** allele; an unexpressed allele is called a **recessive** allele. Alleles can vary considerably in their dominance, however. Some exhibit complete dominance, in which only their own trait is expressed in the phenotype. Others exhibit incomplete dominance, in which the expression of their own trait is only partial. And still others exhibit codominance, in which both their own trait and that of the other allele in the pair are expressed completely.

The concept of dominant and recessive alleles was first introduced by Gregor Mendel, a nineteenth-century monk who studied pea plants in his monastery garden, as mentioned in Chapter 1. Mendel showed that organisms possess discrete units of heredity, which we now call genes. Each gene makes an independent contribution to what the offspring of two parents inherit, even though that contribution may not always be visible in the offspring's phenotype. When paired with a dominant allele, a recessive allele often is not expressed. Still, it can be passed on to future generations and influence their phenotypes when not masked by the influence of some dominant trait.

Genetic Mutations

The mechanism for reproducing genes and passing them on to offspring is not infallible. Errors can arise in the nucleotide sequence when reproductive cells make gene copies. The new versions of the genes are mutations. The number of potential genetic mutations is enormous. A mutation may consist of something as small as a change in a single nucleotide base. Because the average gene has more than 1200 nucleotide bases, an enormous number of mutations can potentially occur on a single gene. For example, the *BRCA1* gene, found on chromosome 17, predisposes women to breast cancer, and more than 100 different mutations have already been found on this gene.

A change in a nucleotide or the addition of a nucleotide in a gene sequence can be either beneficial or disruptive. An example of a mutation that is both causes sickle-cell anemia, a condition in which blood cells have an abnormal shape. The sickle-shaped blood cells offer some protection against malaria, but they also have poor oxygen-carrying capacity, thus weakening the person who possesses them. Other genetic mutations are more purely beneficial in their results, and still others are seemingly neutral to the functioning of the organism that carries them. Most mutations, however, have a negative effect. If not lethal, they produce in their carriers debilitating physical and behavioral abnormalities.

A mutation may have a specific effect on one particular trait or it can have widespread effects. The ability of a gene to affect an organism in many ways is called **pleiotropy** (from the Greek word *pleion*, meaning “more”). Most mutant genes responsible for hereditary disorders in humans cause multiple symptoms. The abnormal protein produced by the gene takes part in many different chemical reactions, and so the affected person may have an abnormal appearance as well as abnormal function.

Mendel’s Principles Apply to Genetic Disorders

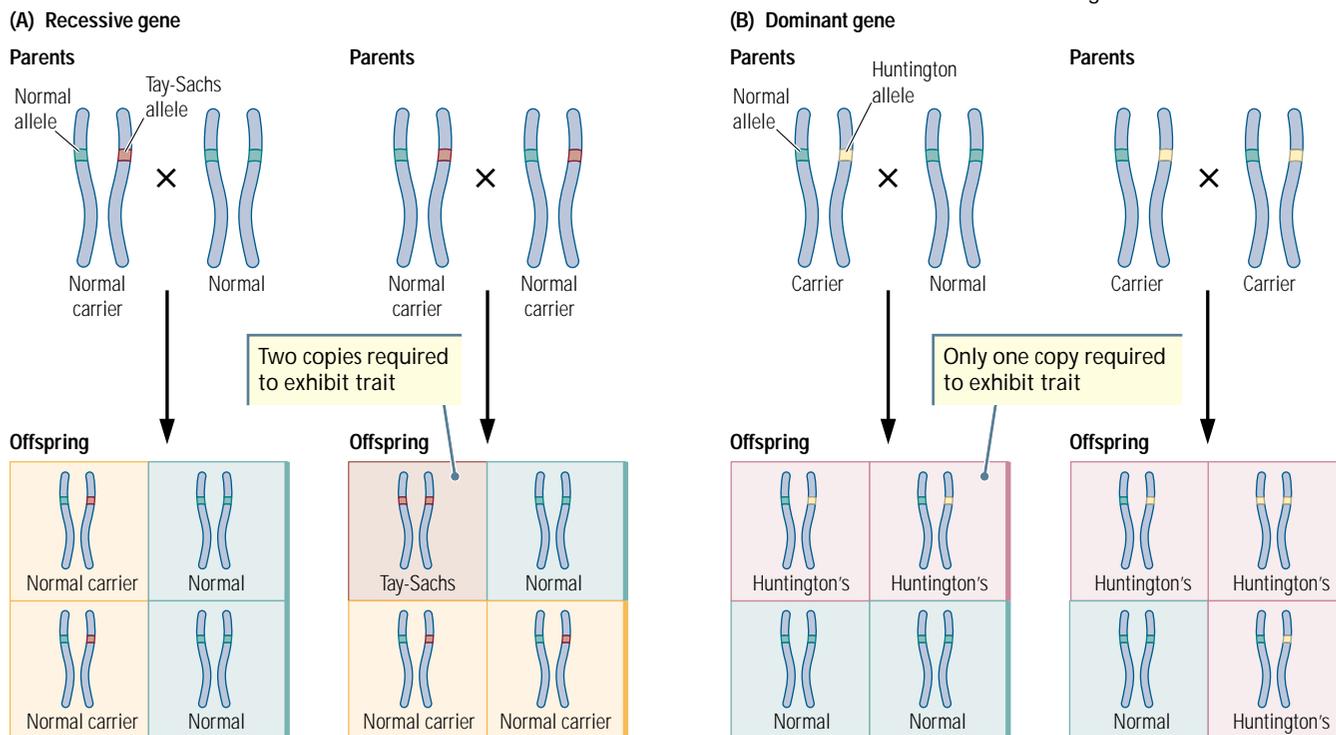
Some disorders caused by mutant genes clearly illustrate Mendel’s principles of dominant and recessive alleles. One of them, called **Tay-Sachs disease**, is caused by a dysfunctional protein that acts as an enzyme known as HexA (hexosaminidase A), which fails to break down a class of lipids (fats) in the brain. Symptoms usually appear a few months after birth. The baby begins to suffer seizures, blindness, and degenerating motor and mental abilities. Inevitably, the child dies within a few years. The Tay-Sachs mutation appears in high frequency among certain ethnic groups, such as Jews of European origin and French Canadians.

Figure 3-26A shows that the dysfunctional Tay-Sachs enzyme is caused by a recessive allele, which means that two copies of the allele (one from both the mother *and* the father) are needed for the disorder to develop. Distinctive inheritance patterns result from a recessive allele. A baby can inherit Tay-Sachs disease only when both parents carry the recessive Tay-Sachs allele. Because both parents have survived to adulthood, they must also both possess a corresponding normal allele for that particular gene pair. The egg and sperm cells produced by this man and woman will therefore contain a copy of one or the other of these two alleles. Which allele is passed on is determined completely by chance.

This situation gives rise to three different potential gene combinations in any child produced by two Tay-Sachs carriers. The child may have two normal alleles, in which case he or she will be spared the disorder. The child may have one normal and

Figure 3-26

(A) The gene for Tay-Sachs disease is recessive. Each parent has two copies of a gene that encodes the production of an enzyme. If one parent has a mutant allele, that parent does not show symptoms of the disease but is called a carrier. Mating (×) with a normal partner, whose chromosomes are randomly assorted to the offspring, produces a 50 percent chance that the offspring will be normal and a 50 percent chance that they will be carriers. If two parents are carriers, the offspring have a 25 percent chance of developing Tay-Sachs disease, a 50 percent chance of being carriers, and a 25 percent chance of being normal noncarriers. (B) The gene for Huntington’s disease is dominant. A person with the Huntington allele will develop the disease. If this person mates with a normal partner, offspring have a 50 percent chance of developing Huntington’s disease and a 50 percent chance of being normal. If both parents are carriers, both will develop the disease. Their offspring have a 75 percent chance of developing the disease and a 25 percent chance of being normal.



one Tay-Sachs allele, in which case he or she, like the parents, will be a carrier of the disorder. Or the child may have two Tay-Sachs alleles, in which case he or she will have Tay-Sachs disease. Figure 3-26 shows that the chance of a child of two carriers being normal is 25 percent, the chance of being a carrier is 50 percent, and the chance of having Tay-Sachs disease is 25 percent as well. If only one of the parents is a Tay-Sachs carrier and the other is normal, then any of their children has a 50-50 chance of being either normal or a carrier. Such a couple has no chance of conceiving a baby with Tay-Sachs disease.

Fortunately, there is a way of determining whether a person is a carrier of the recessive Tay-Sachs allele. This allele operates independently of the dominant allele, just as Mendel described. As a result, it still produces the defective HexA enzyme, so the person who carries it has a higher-than-normal lipid accumulation in the brain. Because this person also has a normal allele that produces a functional enzyme, the abnormal lipid accumulation is not enough to cause Tay-Sachs disease. The condition can, however, be detected with a blood test. People found to be carriers can then make informed decisions about conceiving children. If they avoid having children with another Tay-Sachs carrier, none of their children will have the disorder, although some will probably be carriers.

The one normal allele that a carrier of Tay-Sachs possesses produces enough functional enzyme to enable the brain to operate in a satisfactory way. This would *not* be the case if the normal allele were recessive, however, as happens with a genetic disorder called **Huntington's chorea**. In Huntington's chorea, a protein known as huntingtin builds up in nervous system cells. This protein causes the death of brain cells, especially cells in the basal ganglia and the cortex, as discussed further in "Huntington's Chorea." Symptoms can begin anytime from infancy to old age, but they most often start in midlife. These symptoms include abnormal involuntary movements, which is why the disorder is called chorea (Greek *chorea*, meaning "dance"). Other symptoms are memory loss and eventually a complete deterioration of behavior, followed by death. The Huntington allele is dominant to a normal allele, so only one defective allele is needed to cause the disorder.

Figure 3-26B illustrates the inheritance patterns associated with a dominant allele that produces a disorder, such as Huntington's chorea. If one of a child's parents has the defective allele, that child will have a 50 percent chance of inheriting the disorder, too. If both parents have the defective allele, the chance of inheriting it increases to 75 percent. Because the Huntington allele is usually not expressed until midlife, after the people who possess it have already had children, it can be passed from generation to generation even though it is lethal.

As with the Tay-Sachs allele, there is now a test for determining if a person possesses the allele that causes Huntington's chorea. If a person is found to have the allele, he or she can elect not to produce children. A decision not to have children in this case will reduce the incidence of the Huntington allele in the human gene pool.

Chromosome Abnormalities

Genetic disorders are not caused only by single defective alleles. Some disorders are caused by aberrations in a part of a chromosome or even an entire chromosome. One such condition is **Down's syndrome**, which affects approximately 1 of every 700 children. Down's syndrome is usually the result of an extra copy of chromosome 21. One of the parents (usually the mother) passes on two of these chromosomes to the child, rather than the normal single chromosome. Combining these two chromosomes with one from the other parent yields three chromosomes, an abnormal number called a trisomy.

Huntington's Chorea

Woody Guthrie was born in Oklahoma on July 14, 1912, and grew up to be a great songwriter and entertainer. (His best-known song is "This Land Is Your Land.") After marrying and having three children, he was caught up in the great midwestern drought of the 1930s and moved to California with thousands of other farmers. There his protest songs made him a spokesman for farm workers. Along with other entertainers, including Pete Seeger, Lee Hayes, and Leadbelly, he became one of the founders of American folk music. Bob Dylan, who gave his first concert wearing Woody Guthrie's suit, was instrumental in reviving Woody's popularity in the 1960s.

Woody was described as always being a little odd, but in the 1950s his odd behavior began to disrupt his life. He started having trouble playing his guitar and remembering his songs, and he was in and out of hospitals. He died in 1967 after struggling with the symptoms of what was eventually diagnosed as Huntington's chorea. His mother died of a similar condition, although her illness had never been diagnosed. Two of Guthrie's five children, produced in two marriages, developed the same disease. His second wife, Marjorie, became active in promoting the study of Huntington's chorea. Arlo Guthrie, his son, has become a singer and songwriter in his own right.

Huntington's chorea is a devastating disorder. It is characterized by memory impairments, abnormal uncontrollable movements, and marked changes in personality, eventually leading to virtually total loss of normal behavioral and emotional and intellectual functioning. Fortunately, it is a relatively rare disease, with an incidence of only 5 to 10 victims in 100,000 people. It is most common in people of European origin.

The symptoms of Huntington's chorea result from the degeneration of neurons in the basal ganglia and cortex. Those symptoms can appear at any age but usually start in midlife. In 1983, the gene responsible for Huntington's chorea was located on chromosome 4, and 10 years later its abnormality was identified as an expanded region character-



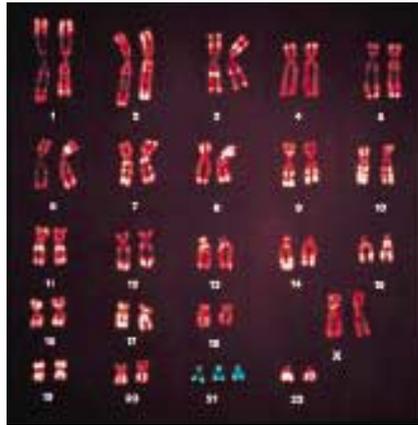
Photofest

Woody Guthrie.

ized by many repeats of the codon CAG. (Normal people have fewer than 30 CAG repeats.) The CAG nucleotide sequence encodes the amino acid glutamine. As a result, the protein produced by the defective Huntington gene contains many repeats of glutamine in its polypeptide chain. As the number of repeats increases beyond 30, the onset of the disease comes earlier and earlier. Thus the disease can begin from very early to very late in life, depending on the number of repeats. The area of CAG repeats is also prone to expansion in transmission from the father, when it can double or even triple in size. In inheritance from the mother, the area of repeats remains stable. Typically, non-Europeans have fewer CAG repeats than do Europeans, which accounts for their decreased susceptibility to Huntington's chorea.

Despite our current insights into the causes of Huntington's chorea, there are still many unanswered questions about it. One such question is why symptoms take so long to develop even with many CAG repeats. Another is why the abnormal Huntington protein causes cell death only in certain regions of the brain. As yet, we also know little about how the progress of the disease might be stopped.

Dr. Dennis Kunkel / Phototake



Ron Batzdorf / Everett Collection

**Figure 3-27**

(Top) Down's syndrome is also known as trisomy 21, to indicate that it is caused by an extra copy (a trisomy, or abnormal number) of chromosome 21. (Bottom) Chris Burke, who has Down's syndrome, played a leading role on the television series *Life Goes On* in the 1990s.

Genetic engineering. An application of genetics directed toward changing physical or behavioral traits by changing genes.

Cloning. The creation of an identical twin from the DNA of a donor animal.

Although chromosome 21 is the smallest human chromosome, its trisomy severely alters a person's phenotype. As illustrated in Figure 3-27, people with Down's syndrome have characteristic facial features and short stature. They also have heart defects, susceptibility to respiratory infections, and mental retardation. They are prone to developing leukemia and Alzheimer's disease. Although people with Down's syndrome usually have a much shorter-than-normal life span, some live to middle age or beyond. Improved education for children with Down's syndrome shows that they can learn to compensate greatly for their mental handicap.

Genetic Engineering

Enormous advances have been made in understanding the structure and function of genes. Still, there remains a huge gap between understanding genes and understanding how genes produce behavior. Despite this gap, geneticists have invented a number of methods to influence the traits that genes express. The most recent of these methods is called **genetic engineering**, but other methods have preceded it.

Probably the oldest means of influencing genetic traits is selective breeding. Beginning with the domestication of wolves more than 12,000 years ago, about 20 species of animals have been domesticated by selectively breeding males and females that display particular traits. For instance, the selective breeding of dogs has produced breeds that can run fast, haul heavy loads, retrieve prey, dig for burrowing animals, climb rocky cliffs in search of sea birds, herd sheep and cattle, or sit on an owner's lap and cuddle. Although selective breeding is an effective way to alter gene expression, at present little is known about the basis of the genetic alterations that are obtained in this way.

Maintaining spontaneous mutations is another method of affecting genetic traits. By using this method, researchers create whole populations of animals possessing some unusual trait that originally arose as an unexpected mutation in only one or a few individual animals. In laboratory colonies of mice, for example, large numbers of spontaneous mutations have been discovered and maintained. There are strains of mice that have abnormal movements, such as reeling, staggering, and jumping. Some have diseases of the immune system; others have sensory deficits and are blind or cannot hear. Many of these genetic abnormalities can also be found in humans. As a result, the neural and genetic bases of the altered behavior in the mice can be studied systematically to develop treatments for human disorders.

More direct approaches to manipulating the expression of genetic traits are to alter early embryonic development. One of these approaches is **cloning**, or producing genetically identical organisms. To clone an animal, scientists allow a fertilized egg to replicate a number of times and then implant the identical cells into the uterus of a female. Because all of the individual animals that develop from these cells are genetically the same, such clones can be used to study the relative influences of heredity and environment. Dolly, a female sheep and the first mammal to be cloned (Figure 3-28), opened up a new technology in which identical animals can be produced. If such animals are genetically engineered to produce medicines in their milk, those medicines can be easily extracted from the milk to treat human diseases (Coleman, 1999). It is also possible to produce **chimeric animals**, which have genes from two different species. A cell from one species is introduced into the early embryonic stage of a different species. The resulting animal has cells with genes from both parent species and behaviors that are a product of those gene combinations. Psychologists interested in behavior can find that a chimeric animal displays an interesting mix of the behaviors of the parent species. For example, chickens that have received Japanese quail cells in early embryogenesis display some aspects of quail crowing behavior rather than

chicken crowing behavior, thus providing evidence for the genetic basis of some bird vocalization (Balaban et al., 1988). The chimeric preparation provides an investigative tool for studying the neural basis of crowing because quail neurons can be distinguished from chicken neurons when examined under a microscope.

Genetic engineering, derived from DNA research, is the most direct avenue for the study of gene expression. In its simplest form, genetic engineering entails either removing a gene from a genome or adding a gene to it. In so-called **transgenic animals**, usually mice, a gene added to the genome is passed along and expressed in subsequent generations. One application of genetic engineering is in the study and treatment of human genetic disorders. For instance, researchers have introduced into a line of mice the human gene that causes Huntington's chorea (Lione et al., 1999). The mice express the Huntington gene and display symptoms similar to those of human Huntington's chorea. This mouse line is being used to study potential therapies for this disorder in humans. So-called **knockout technology** can be used to inactivate a gene so that a line of mice fails to express it (Mayford & Kandel, 1999). That line of mice can then be used to study possible therapies for human disorders caused by the loss of a single protein due to a mutant gene. Remarkably interesting knockout animals can be produced. For example, a knockout mouse may be prepared that will grow up with a superior memory or with no memory or a mouse may be allowed to grow up quite normally and the gene is then knocked out in adulthood. It is potentially possible to knock out genes that are related to certain kinds of memory, such as emotional memory, social memory, or spatial memory. Such technology provides a useful way of investigating the neural basis of memory. So genetic research is directed not only toward finding cures for genetic abnormalities in brain and behavior, but also toward studying normal brain function.



AP Photo / John Chadwick

Figure 3-28

Dolly (at right) was the first mammal to be artificially cloned from an adult somatic cell. In 1996, a team of researchers in Scotland implanted a nucleus from a mammary-gland cell of an adult sheep into another ewe's unfertilized egg, from which the nucleus had been removed. Once the nucleus had been induced to begin dividing, the embryo was implanted into a third sheep's uterus. Dolly, a clone of the donor of the original mammary cell, subsequently produced a lamb (at left) from an egg fertilized in the traditional manner.

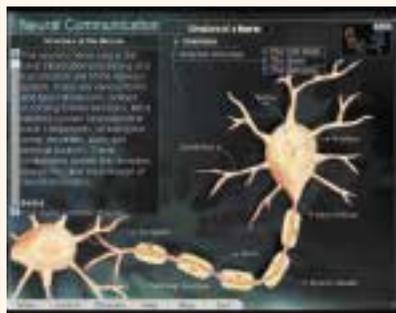
In Review

Our 46 chromosomes each contain thousands of genes, and each gene contains the code for one protein. The genes that we receive from our mothers and fathers may include slightly different versions (alleles) of particular genes, which will be expressed in slightly different proteins. The proteins are the building blocks of cells, forming the cells' various organelles as well as the channels, pumps, neurotransmitters, and receptors that are central to the cells' functions. Abnormalities in a gene, caused by mutations, can result in an abnormally formed protein that, in turn, results in the abnormal function of cells. The abnormal function of cells can result in neurological disorders such as Tay-Sachs disease and Huntington's chorea. Genetic engineering is a new science in which the genome of an animal is altered. Cloned animals have the identical genetic composition of a parent or sibling; transgenic animals contain new or altered genes; and knockouts have genomes from which a gene has been deleted. The study of alterations in the nervous systems or in the behavior of animals produced by these manipulations can be a source of insight into how genes produce proteins and how proteins contribute to the structure and function of the nervous system.

Transgenic animal. An animal that has artificially received a new gene.

Knockout technology. A method in genetics in which a gene is deleted from a chromosome or its expression is blocked.

neuroscience interactive



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■ www.worthpublishers.com/kolb/chapter3

Try some self-tests to reinforce your mastery of the material. Look at some of the news updates reflecting current research on the brain. You'll also be able to link to other sites which will reinforce what you've learned.

■ <http://neurowww.neur.cwru.edu/teach/movies.htm>

Link to a video of neurons in action from the National Institutes of Health.

■ <http://vector.cshl.org/dnaftb/>

Review genetics at this Web site from the Cold Spring Harbor Laboratory.

On your CD-ROM you'll be able to quiz yourself on your comprehension of the chapter. You'll also be able to begin learning about the cells of the nervous system in the module on Neural Communication. This module includes animations and detailed drawings of the neuron. In addition, the Research Methods module includes a video clip of neurons and glia as well as a detailed overview of various histological techniques.

SUMMARY

1. *What kinds of cells are found in the nervous system?* The nervous system is composed of two kinds of cells: neurons, which transmit information, and glia, which are support cells. The three types of neurons are sensory neurons (which send information from the body's sensory receptors), motor neurons (which send commands enabling muscles to move), and interneurons (which link sensory and motor activities). Glial cells also can be grouped by their structure and function. Ependymal cells produce cerebrospinal fluid; astroglia structurally support neurons, help to form the blood–brain barrier, and seal off damaged brain tissue; microglia aid in the repair of brain cells; and oligodendroglia and Schwann cells provide myelin to axons in the central and peripheral nervous systems, respectively.
2. *What is the basic external structure of a neuron?* A neuron is composed of three basic parts: a cell body, or soma; branching extensions called dendrites designed to receive information; and a single axon that passes information along to other cells. A dendrite's area is greatly increased by numerous dendritic spines; an axon may have branches called axon collaterals, which are further divided into telodendria, each ending at a terminal button. The “almost connection” between a terminal button and the dendritic spine of another neuron is known as a synapse.
3. *How is a cell internally structured?* A cell is surrounded by a cell membrane that protects the cell and regulates what enters and leaves it. Within the cell are a number of compartments, also enclosed in membranes. These compartments include the nucleus (which contains the cell's chromosomes and genes), the endoplasmic reticulum (where proteins are manufactured), the mitochondria (where energy is gathered and stored), the Golgi bodies (where protein molecules are packaged for transport), and lysosomes (which break down wastes). A cell also contains a system of tubules that aid cell movements, provide structural support, and act as highways for transporting substances.
4. *Why are proteins important to cells?* The nucleus of a cell contains chromosomes, which are long chains of genes, each of which carries the code for manufacturing a certain protein that is necessary for the cell's structure and function. Proteins perform many different tasks by virtue of their many different shapes. Some act as enzymes to facilitate chemical reactions; others serve as membrane channels, gates, and pumps; and still others are exported from the cell that made them for use in other parts of the body. To a large extent, the work of cells is carried out by proteins.
5. *How do genes work?* A gene is a segment of a DNA molecule and is made up of a sequence of nucleotide bases. Through a process called transcription, a copy of a gene is produced in a strand of mRNA. The mRNA then travels to the endoplasmic reticulum, where it passes through a ribosome and is translated into a sequence of amino acids. The resulting chain of amino acids is called a polypeptide. Polypeptides fold and combine to form protein molecules with distinctive shapes that are used for specific purposes in the body.
6. *What do we inherit genetically from our parents?* From each parent, we inherit one of each of the chromosomes in our 23 chromosome pairs. Because chromosomes are “matched” pairs, a cell contains two copies (alleles) of every gene, one from the mother and one from the father. Sometimes alleles are homozygous (the same), and sometimes they are heterozygous (different). An allele may be dominant and expressed as a trait, recessive and not expressed, or codominant, in which case both it and the other allele in the pair are expressed. One allele of each gene is designated the wild type, or most common one in a population, whereas the other alleles of that gene are called mutations. A person might inherit any of these alleles from a parent, depending on that parent's genotype.

7. *What is the relation between genes, cells, and behavior?* Comprehending the links between genes, cells, and behavior is the ultimate goal of future research, but as yet these links are only poorly understood. The structure and function of a cell are properties of all its many genes and proteins, just as behavior is a property of the actions of billions of nerve cells. It will take years to learn how such a complex system works. In the meantime, the study of genetic abnormalities is a potential source of insight into the relation among gene, neurons, and behavior.
8. *What causes genetic abnormalities?* Genes can potentially undergo many mutations, in which their codes are altered by one or more changes in the nucleotide sequence. Most mutations are harmful and may produce abnormalities in nervous system structure and behavioral function. Examples are Tay-Sachs disease and Huntington's chorea. Genetic research seeks to prevent the expression of such abnormalities and to find cures for those that are expressed.

KEY TERMS

blood-brain barrier, p. 87	hydrocephalus, p. 87	neuron hypothesis, p. 79
cell membrane, p. 94	hydrophilic, p. 93	paralysis, p. 88
channel, p. 101	hydrophobic, p. 97	polypeptide, p. 99
chromosome, p. 97	knockout technology,	protein, p. 99
cloning, p. 108	p. 109	pump, p. 102
gate, p. 101	messenger RNA (mRNA),	transcription, p. 98
gene, p. 97	p. 98	transgenic animal, p. 109
genetic engineering, p. 108	myelin, p. 88	translation, p. 98

REVIEW QUESTIONS

1. Describe five kinds of neurons and five kinds of glia and their functions.
2. Describe the functions of the different parts of a cell.
3. Why can so many nervous system diseases be due to faulty genes?

FOR FURTHER THOUGHT

People often compare the “machine of the day” to the nervous system. Why can we never understand our nervous system by comparing it to a computer and how it works?

RECOMMENDED READING

- Alberts, B., Bray, D., Lewis, J., Raff, M., Roberts, K., & Watson, J.D. (1983). *Molecular biology of the cell* (3rd ed.). New York: Garland. This standard text provides a comprehensive description of the cells and cell function in living organisms.
- Levitan, I. B., & Kaczmarek, L. K. (1997). *The neuron: Cell and molecular biology* (2nd ed.). Oxford: Oxford University Press. An extremely readable text describing the function of the neuron. Although the coverage is comprehensive, the text is enjoyable to read and is accompanied by numerous illustrations that assist in explanation.