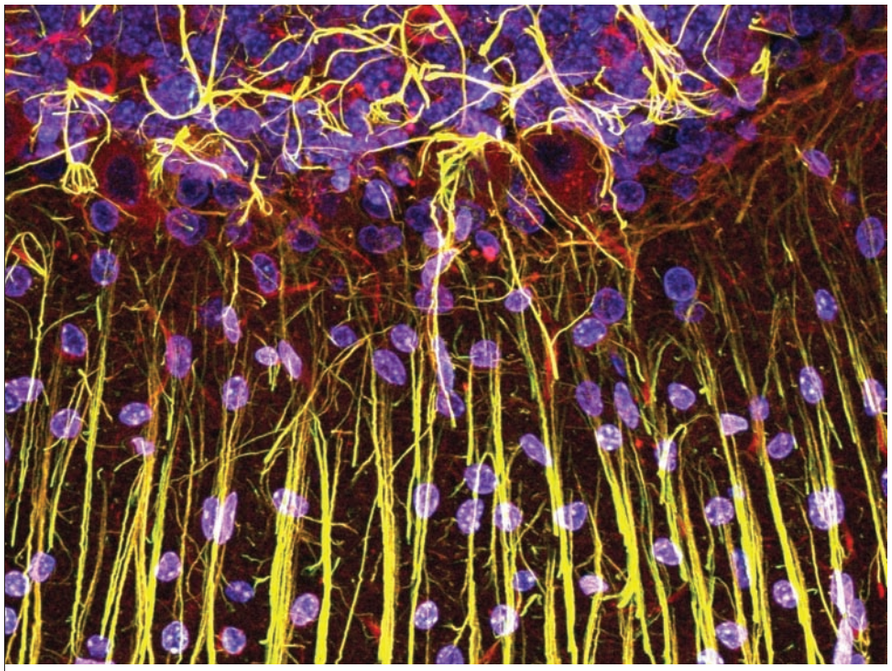


Section through the cerebellum, a part of the brain that integrates signals coming from particular regions of the body (confocal light micrograph). Neurons, the cells that send and receive signals, are red; glial cells, which provide structural and functional support for neurons, are yellow; and nuclei are purple.

Study Plan

37 Information Flow and the Neuron

Why It Matters

The dog stands alert, muscles tense, motionless except for a wagging tail. His eyes are turned toward his master, a boy poised to throw a Frisbee for him to catch. Even before the Frisbee is released, the dog has anticipated the direction of its flight from the eyes and stance of the boy.

With a snap of the wrist, the boy throws the Frisbee, and the dog springs into action. Legs churning, eyes following the Frisbee, the dog runs beneath its track, closing the distance as the Frisbee reaches the peak of its climb and begins to descend. All this time, parts of the dog's brain have been processing information received through various sensory inputs. The eyes report his travel over the ground and the speed and arc of the Frisbee. Sensors in the inner ears, muscles, and joints detect the position of the dog's body, and his brain sends out signals that keep his movements on track and in balance. Other parts of the brain register inputs from sensors monitoring body temperature and carbon dioxide levels in the blood, and send signals that adjust heart and breathing rate accordingly.

At just the right instant, a burst of signals from the dog's brain causes trunk and leg muscles to contract in a coordinated pattern, and

© Gary Gerovac/Masterfile

Figure 37.1
With perfect timing, a dog leaps to catch a Frisbee. The coordinated leap involves processing and integration of information by the dog's nervous system.

the dog leaps to intercept the Frisbee in midair with an assured snap of his jaws **(Figure 37.1).** Now the animal twists, turning his head and eyes toward the ground as his brain calculates the motions required to land on his feet and in balance. The dog makes a perfect landing and trots happily back to his master, ready to repeat the entire performance.

The functions of the dog's nervous system in the chase and capture are astounding in the amount and variety of sensory inputs, the rate and complexity of the brain's analysis and integration of incoming information, and the flurry of signals the brain sends to make compensating adjustments in body activities. Yet they are ordinary in the sense that the same activities take place countless times each day in the nervous system of all but the simplest animals.

All these activities, no matter how complex, depend on the functions of only two major cell types: *neurons* and *glial cells*. In most animals, these cells are organized into complex networks called *nervous systems*. This chapter describes neuron structure and tells how neurons send and receive signals with the aid and support of glial cells. The next chapter considers the neural networks of the brain and its associated structures. Chapter 39 discusses the sensory receptors that detect environmental changes and convert that information into signals for integration by the nervous system.

37.1 Neurons and Their Organization in Nervous Systems

An animal constantly receives stimuli from both internal and external sources. **Neural signaling,** communication by neurons, is the process by which an animal responds appropriately to a stimulus **(Figure 37.2).** In most animals, the four components of neural signaling are *reception, transmission, integration,* and *response*. **Reception,** the detection of a stimulus, is performed by **neurons,** the cellular components of nervous systems, and by specialized sensory receptors such as those in the eye and skin. **Transmission** is the sending of a message along a neuron, and then to another neuron or to a muscle or gland. **Integration** is the sorting and interpretation of neural messages and the determination of the appropriate response(s). **Response** is the "output" or action resulting from the integration of neural messages. For a dog catching a Frisbee, for instance, sensors in the eye receive light stimuli from the environment, and internal sensors receive stimuli from all the animal's organ systems. The neural messages generated are transmitted through the nervous system and integrated to determine the appropriate response, in this case stimulating the muscles so the dog jumps into the air and catches the Frisbee.

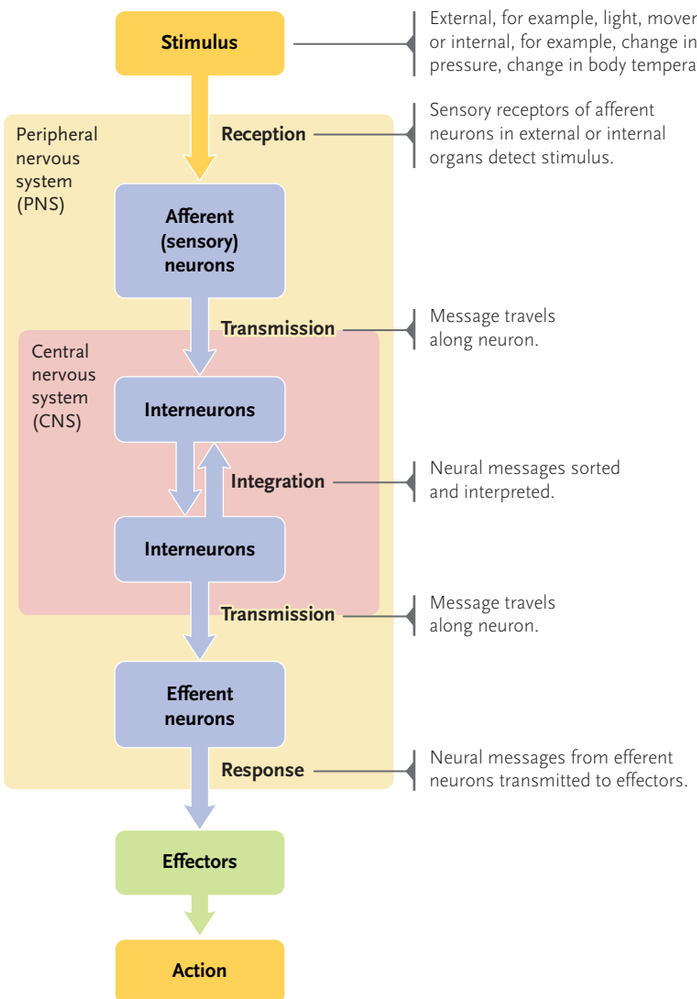


Figure 37.2
Neural signaling: the information-processing steps in the nervous system.

Neurons Are Cells Specialized for the Reception and Transmission of Informational Signals

Neural signaling involves three functional classes of neurons (the blue boxes in Figure 37.2). **Afferent neurons** (also called **sensory neurons**) transmit stimuli collected by their sensory receptors to **interneurons,** which integrate the information to formulate an appropriate response. In humans and some other primates, 99% of neurons are interneurons. **Efferent neurons** carry the signals indicating a response away from the interneuron networks to the **effectors,** the muscles and glands. Efferent neurons that carry signals to skeletal muscle are called **motor neurons.** The information-processing steps in the nervous system can be summarized, therefore, as: (1) sensory receptors on

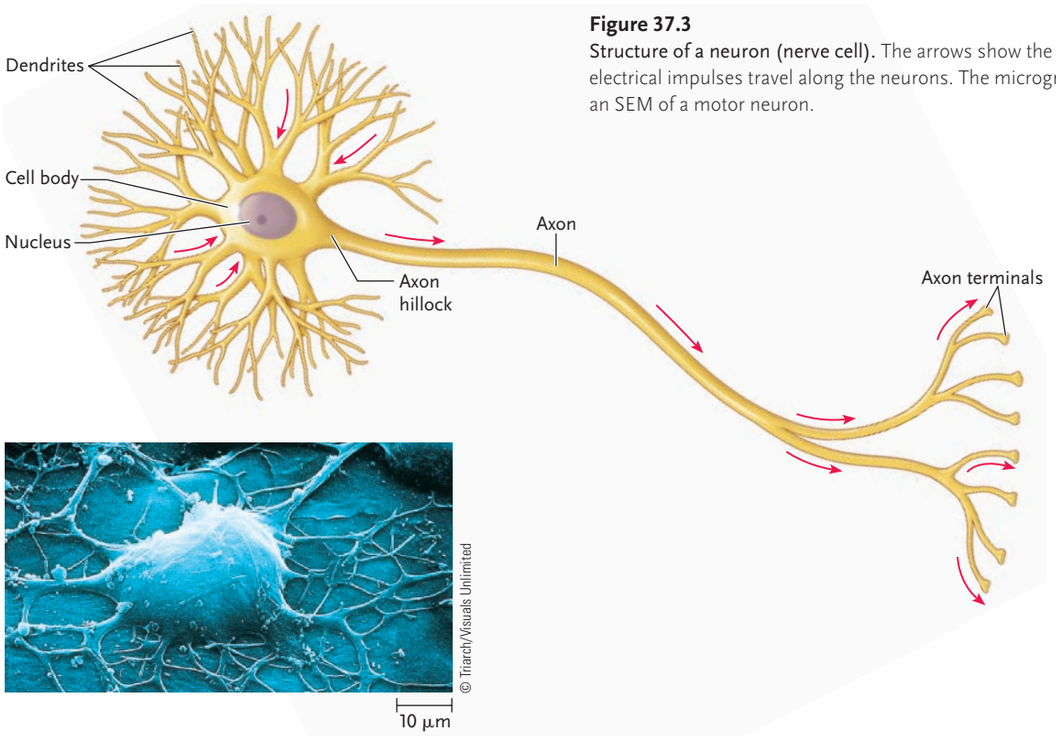


Figure 37.3
Structure of a neuron (nerve cell). The arrows show the direction electrical impulses travel along the neurons. The micrograph is an SEM of a motor neuron.

afferent neurons receive a stimulus; (2) afferent neurons transmit the information to interneurons; (3) interneurons integrate the neural messages; and (4) efferent neurons transmit the neural messages to effectors, which act in a way appropriate to the stimulus.

Neurons vary widely in shape and size. All have an enlarged cell body and two types of extensions or processes, called dendrites and axons **(Figure 37.3).** The **cell body,** which contains the nucleus and the majority of cell organelles, synthesizes most of the proteins, carbohydrates, and lipids of the neuron. Dendrites and axons conduct electrical signals, which are produced by ions flowing down concentration gradients through channels in the plasma membrane of the neuron. **Dendrites** receive the signals and transmit them toward the cell body. Dendrites are generally highly branched, forming a treelike outgrowth at one end of the neuron (*dendros* = tree). **Axons** conduct signals away from the cell body to another neuron or an effector. Neurons typically have a single axon, which arises from a junction with the cell body called an **axon hillock.** The axon has branches at its tip that end as small, buttonlike swellings called **axon terminals.** The more terminals contacting a neuron, the greater its capacity to integrate incoming information.

Connections between axon terminals of one neuron and the dendrites or cell body of a second neuron form **neuronal circuits.** A typical neuronal circuit contains an afferent (sensory) neuron, one or more interneurons, and an efferent neuron. The circuits combine into networks that interconnect the parts of the nervous system. In vertebrates, the afferent neurons and efferent neurons collectively form the *peripheral nervous system (PNS)*. The interneurons form the brain and spinal cord, called the *central nervous system (CNS)*. As depicted in Figure 37.2, afferent (*afferre* = carry toward) information is ultimately transmitted to the CNS where efferent (*efferre* = carry away) information is initiated. The nervous systems of most invertebrates are also divided into central and peripheral divisions.

Neurons Are Supported Structurally and Functionally by Glial Cells

Glial cells are nonneuronal cells that provide nutrition and support to neurons. One type, called **astrocytes** because they are star-shaped **(Figure 37.4),** occurs only in the vertebrate CNS, where they closely cover the surfaces of blood vessels. Astrocytes provide physical support to neurons and help maintain the concentrations of ions in the interstitial fluid surrounding them. Two other types of glial cells—**oligodendrocytes** in the CNS and **Schwann cells** in the PNS—wrap around axons in a jelly roll fashion to form myelin sheaths **(Figure 37.5).** Myelin sheaths have a high lipid content because of the

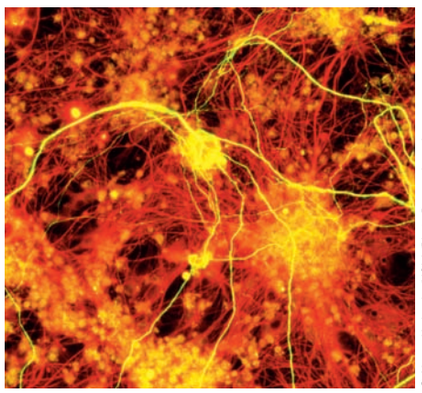


Figure 37.4
Astrocytes (orange), a type of glial cell, and a neuron (yellow) in brain tissue.

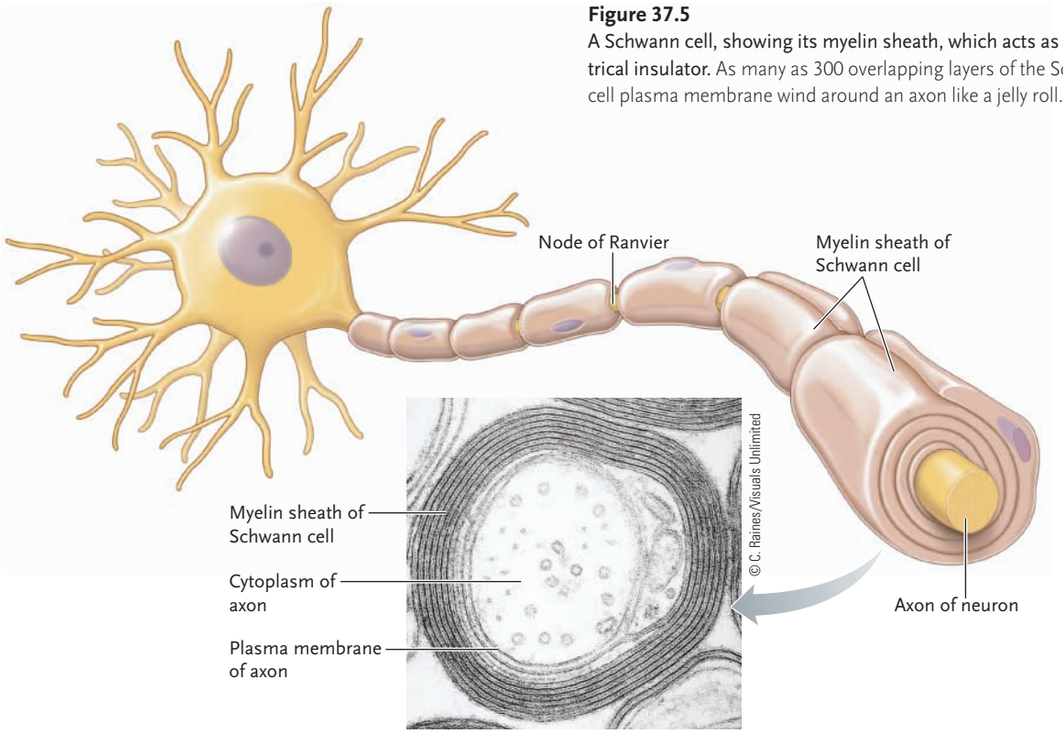


Figure 37.5
A Schwann cell, showing its myelin sheath, which acts as an electrical insulator. As many as 300 overlapping layers of the Schwann cell plasma membrane wind around an axon like a jelly roll.

many layers of plasma membranes of the myelin-forming cells. Because of their high lipid content, the myelin sheaths act as electical insulators. The gaps between Schwann cells, called **nodes of Ranvier,** expose the axon membrane directly to extracellular fluids. This structure speeds the rate at which electrical impulses move along the axons covered by glial cells.

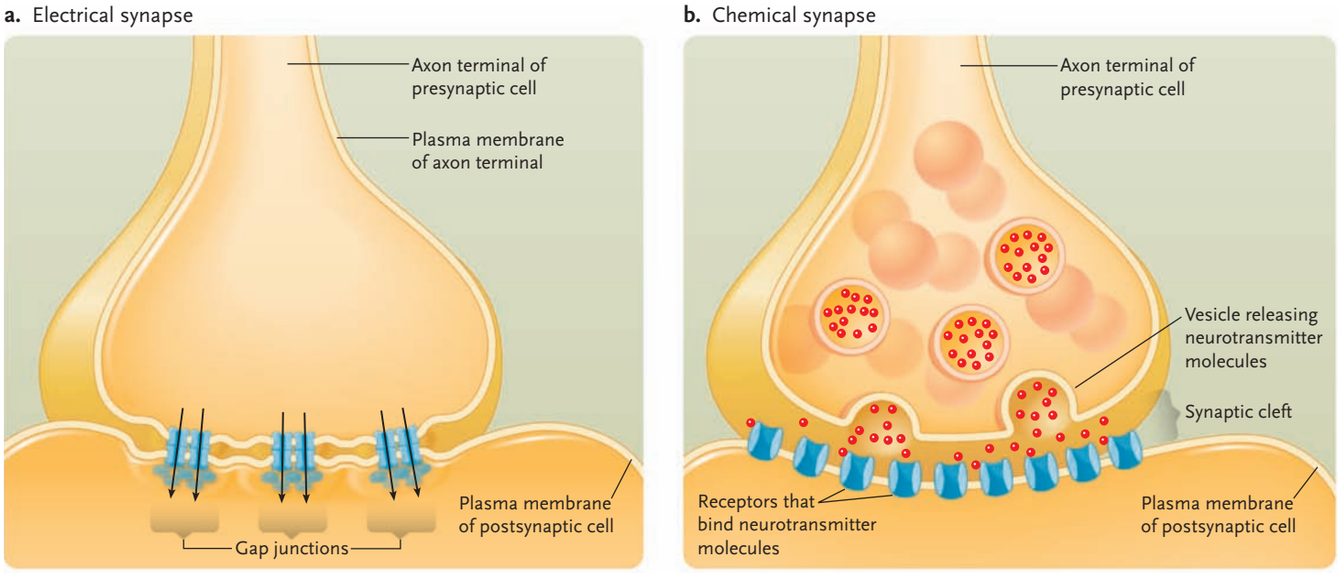
Unlike most neurons, glial cells retain the capacity to divide throughout the life of the animal. This capacity allows glial tissues to replace damaged or dead cells, but also makes them the source of almost all brain tumors, produced when regulation of glial cell division is lost.

Neurons Communicate via Synapses

A **synapse** (*synapsis* = juncture) is a site where a neuron makes a communicating connection with another neuron or with an effector such as a muscle fiber or gland. On one side of the synapse is an axon terminal of the **presynaptic cell,** the neuron that transmits the signal. On the other side is the cell body or a dendrite of the **postsynaptic cell,** the neuron or the surface of an effector that receives the signal. Communication across a synapse may occur by the direct flow of an electrical signal or by means of a **neurotransmitter,** a chemical released by an axon terminal at a synapse. The vast majority of vertebrate neurons communicate by means of neurotransmitters.

In **electrical synapses,** the plasma membranes of the presynaptic and postsynaptic cells are in direct contact **(Figure 37.6a).** When an electrical impulse arrives at the axon terminal, gap junctions (see Section 36.2) allow ions to flow directly between the two cells, leading to unbroken transmission of the electrical signal. Although electrical synapses allow the most rapid conduction of signals, this type of connection is essentially "on" or "off" and unregulated. In humans, electrical synapses occur in locations such as the pulp of a tooth, where they contribute to the almost instant and intense pain we feel if the pulp is disturbed.

In **chemical synapses,** the plasma membranes of the presynaptic and postsynaptic cells are separated by a narrow gap, about 25 nm wide, called the **synaptic cleft (Figure 37.6b).** When an electrical impulse arrives at an axon terminal, it causes the release of a neurotransmitter into the synaptic cleft. The neurotransmitter diffuses across the synaptic cleft and binds to a receptor in the plasma membrane of the postsynaptic cell. If enough neurotransmitter molecules bind to these receptors, the postsynaptic cell generates a new electrical impulse, which travels along its axon to reach a synapse with the next neuron or effector in the circuit. A chemical synapse is more than a simple on-off switch because many factors can influence the generation of a new electrical impulse in the postsynaptic cell, including neurotransmitters that inhibit that cell rather than stimulating it. The balance of stimulatory and inhibitory effects in chemical synapses contributes to the integration of incoming information in a receiving neuron.



In an electrical synapse, the plasma membranes of the presynaptic and postsynaptic cells make direct contact. Ions flow through gap junctions that connect the two membranes, allowing impulses to pass directly to the postsynaptic cell.

In a chemical synapse, the plasma membranes of the presynaptic and postsynaptic cells are separated by a narrow synaptic cleft. Neurotransmitter molecules diffuse across the cleft and bind to receptors in the plasma membrane of the postsynaptic cell. The binding opens channels to ion flow that may generate an impulse in the postsynaptic cell.

Figure 37.6
The two types of synapses by which neurons communicate with other neurons or effectors.

Study Break

1. Distinguish between a dendrite and an axon.
2. Distinguish between the functions and locations of afferent neurons, efferent neurons, and interneurons.
3. What is the difference between an electrical synapse and a chemical synapse?

37.2 Signal Conduction by Neurons

All cells of an animal have a **membrane potential**, a separation of positive and negative charges across the plasma membrane. Outside the cell the charge is positive, and inside the cell it is negative. This charge separation produces *voltage*—an electrical potential difference—across the plasma membrane.

The membrane potential is caused by the uneven distribution of Na^+ and K^+ inside and outside the cell. As you learned in Chapter 6, plasma membranes are *selectively* permeable in that they allow some ions but not others to move across the membrane through protein channels embedded in the phospholipid bilayer. Plasma membrane-embedded Na^+/K^+ active transport pumps use energy from ATP hydrolysis to pump simultaneously three Na^+ out of the cell for every two K^+ pumped in. This exchange generates a higher Na^+ concentration outside the cell than inside, and a higher K^+ concentration inside the cell than outside, explaining the positive charge outside the cell. The inside of the cell is negatively charged because the cell also contains many negatively charged molecules (anions) such as proteins, amino acids, and nucleic acids.

In most cells, the membrane potential does not change. However, neurons and muscle cells use the membrane potential in a specialized way. That is, in response to electrical, chemical, mechanical, and certain other types of stimuli, their membrane potential changes rapidly and transiently. Cells with this property are said to be *excitable cells*. Excitability, produced by a sudden flow across the plasma membrane, is the basis for nerve impulse generation.

Resting Potential Is the Unchanging Membrane Potential of an Unstimulated Neuron

The membrane of a neuron that is not being stimulated is not conducting an impulse—exhibits a steady negative membrane potential, called the **resting potential** because the neuron is at rest. The resting potential has been measured at between −50 and −60 millivolts (mV) for neurons in the body, and at about −70 mV in isolated neurons **(Figure 37.7).** A neuron exhibiting the resting potential is said to be *polarized*.

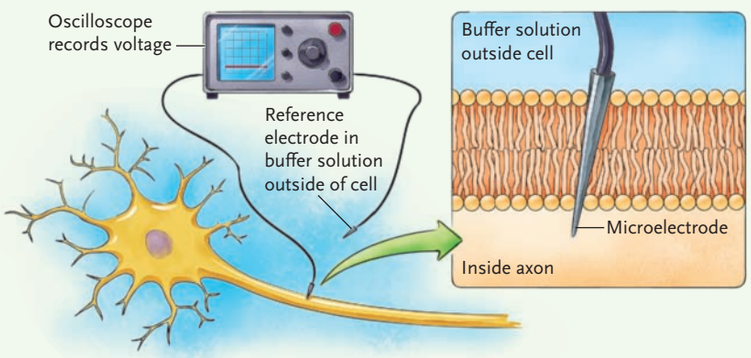
The distribution of ions inside and outside an axon that produces the resting potential is shown in **Figure 37.8.** As described earlier in this section, the Na^+/K^+ pump is responsible for creating the imbalance of Na^+ and K^+ inside and outside of the cell, and the concentration of negatively charged molecules within the cell results in the inside being negatively charged and the

Figure 37.7 Research Method

Measuring Membrane Potential

PURPOSE: To determine the membrane potentials of unstimulated and stimulated neurons and muscle cells.

PROTOCOL: Prepare a microelectrode by drawing out a glass capillary tube to a tip with a diameter much smaller than that of a cell and filling it with a salt solution that can conduct an electric current. Under a microscope, use a micromanipulator (mechanical positioning device) to insert the tip of the microelectrode into an axon. Place a reference electrode in the solution outside the cell. Use an oscilloscope or voltmeter to measure the voltage between the microelectrode tip in the axon and the reference electrode outside the cell.



INTERPRETING THE RESULTS: The oscilloscope or voltmeter indicates the membrane potential in volts. Changes in membrane potential caused by stimuli or chemical treatments can be measured and recorded. For an isolated, unstimulated neuron (shown above) the membrane potential is typically about −70 mV.

outside being positively charged. As we will see in the following description of the changes in a neuron that occur when it is stimulated, the *voltage-gated ion channels* for Na^+ and K^+ open and close when the membrane potential changes.

The Membrane Potential Changes from Negative to Positive during an Action Potential

When a neuron conducts an electrical impulse, an abrupt and transient change in membrane potential occurs; this is called the **action potential.** An action potential begins as a stimulus that causes positive charges from outside the neuron to flow inward, making the cytoplasmic side of the membrane less negative **(Figure 37.9).** As the membrane potential becomes less negative, the membrane (which was polarized at rest) becomes **depolarized.** Depolarization proceeds relatively slowly until it reaches a level known as the **threshold potential,** about −50 to −55 mV in isolated neurons. Once the threshold is reached, the action potential fires—and the membrane potential suddenly increases. In less than 1 msec (millisecond, one-thousandth of a second), it rises so high that the inside of the plasma membrane becomes positive due to an influx of positive ions across the cell membrane, momentarily reaching a value of +30 mV or more. The potential then falls again, in many cases dropping to about −80 mV before rising again to the resting potential. When the potential is below the resting value, the membrane is said to be **hyperpolarized.** The entire change, from initiation of the action potential to the return to the resting potential, takes less than 5 msec in the fastest neurons. Action potentials take the same basic form in neurons of all types, with differences in the values of the resting potential and the peak of the action potential, and in the time required to return to the resting potential.

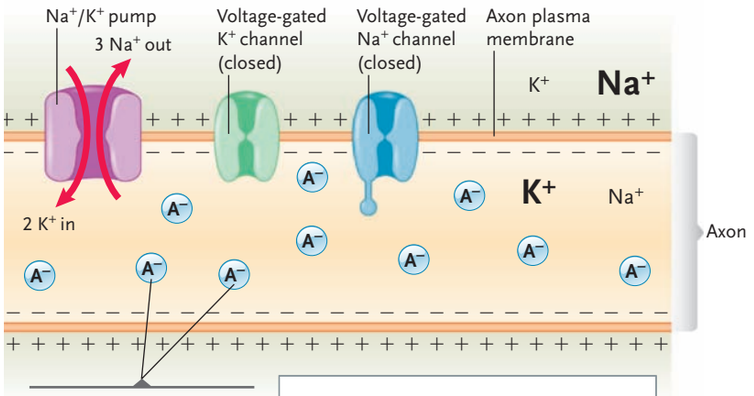
All stimuli cause depolarization of a neuron, but an action potential is produced only if the stimulus is strong enough to cause depolarization to reach the threshold. This is referred to as the **all-or-nothing principle;** once triggered, the changes in membrane potential take place independently of the strength of the stimulus.

Beginning at the peak of an action potential, the membrane enters a **refractory period** of a few milliseconds during which the threshold required for generation of an action potential is much higher than normal. The refractory period lasts until the membrane has stabilized at the resting potential. As we shall see, the refractory period keeps impulses traveling in a one-way direction in neurons.

The Action Potential Is Produced by Ion Movements through the Plasma Membrane

The action potential is produced by movements of Na^+ and K^+ through the plasma membrane. The movements are controlled by specific **voltage-gated ion channels,** membrane-embedded proteins that open and close as the membrane potential changes (see Figure 37.8). Voltage-gated Na^+ channels have two gates, an *activation gate* and an *inactivation gate,* whereas voltage-gated K^+ channels have one gate, an *activation gate.*

How the two voltage-gated ion channels operate to generate an action potential is shown in **Figure 37.10.** When the membrane is at the resting potential, the activation gates of both the Na^+ and K^+ channels are closed. As a depolarizing stimulus raises the membrane potential to the threshold, the activation gate of the Na^+ channels opens, allowing a burst of Na^+ ions to flow into the axon along their concentration gradient. Once above the threshold, more Na^+ channels open, causing a rapid inward flow of positive charges that raises the membrane potential to-



Charged Particle Concentrations (mM)		
	Inside	Outside
Na^+	15	150
K^+	150	5
A^-	100	0

Figure 37.8
The distribution of ions inside and outside an axon that produces the resting potential, −70 mV. The distribution of ions that do not directly affect the resting potential, such as Cl^-, is not shown. The voltage-gated ion channels open and close when the membrane potential changes.

ward the peak of the action potential. As the action potential peaks, the inactivation gate of the Na^+ channel closes (resembling putting a stopper in the sink), which stops the inward flow of Na^+. The refractory period now begins.

At the same time, the activation gates of the K^+ channels begin to open, allowing K^+ ions to flow rapidly outward in response to their concentration gradient. The K^+ ions contribute to the refractory period and compensate for the inward movement of Na^+ ions, returning the membrane to the resting potential. As the resting potential is reestablished, the activation gates of the K^+ channels close, as do those of the Na^+ channels, and the inactivation gates of the Na^+ channels open. These events end the refractory period and ready the membrane for another action potential.

In some neurons, closure of the gated K^+ channels lags, and K^+ continues to flow outward for a brief time after the membrane returns to the resting potential. This excess outward flow causes the hyperpolarization shown in Figure 37.9, in which the membrane potential dips briefly below the resting potential.

At the end of an action potential, the membrane potential has returned to its resting state, but the ion distribution has changed slightly. That is, some Na^+ ions have entered the cell, and some K^+ ions have left the cell—but not many, relative to the total number of ions, and the distribution is not altered enough to prevent other action potentials from occurring. In the long term, the Na^+/K^+ active transport pumps restore the Na^+ and K^+ to their original locations.

Some of what is known about how ion flow through channels can change membrane potential has come from experiments using the *patch-clamp* technique. In the patch part of the technique, a micropipette with a tip 1 to 3 μm in diameter is touched to the plasma membrane of a neuron (or other cell type). The contact seals the membrane to the micropipette and, when the micropipette is pulled away, a patch of membrane with one or a few ion channels comes with it. The clamp part of the technique refers to a voltage clamp, in which an electronic device holds the membrane potential of the patch at a steady value chosen by the investigator. The investigator can add a stimulus that is expected to open or close ion channels. The amount of current the clamping device needs to keep the voltage constant is directly related to the number and charge of the ions moving through the channels and, hence, measures channel activity.

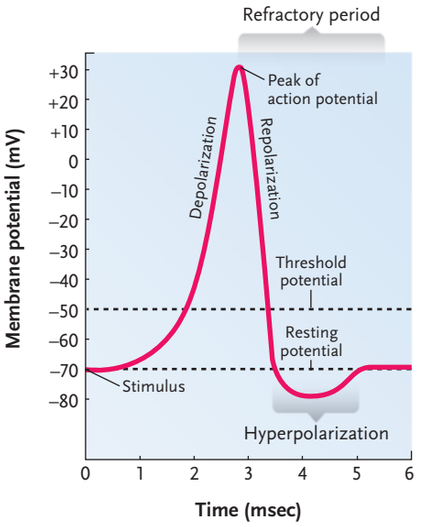
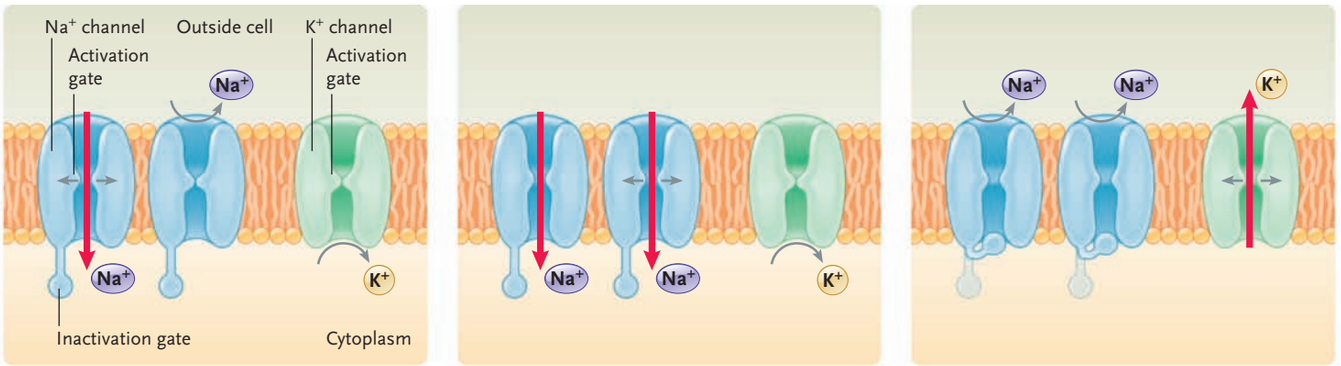
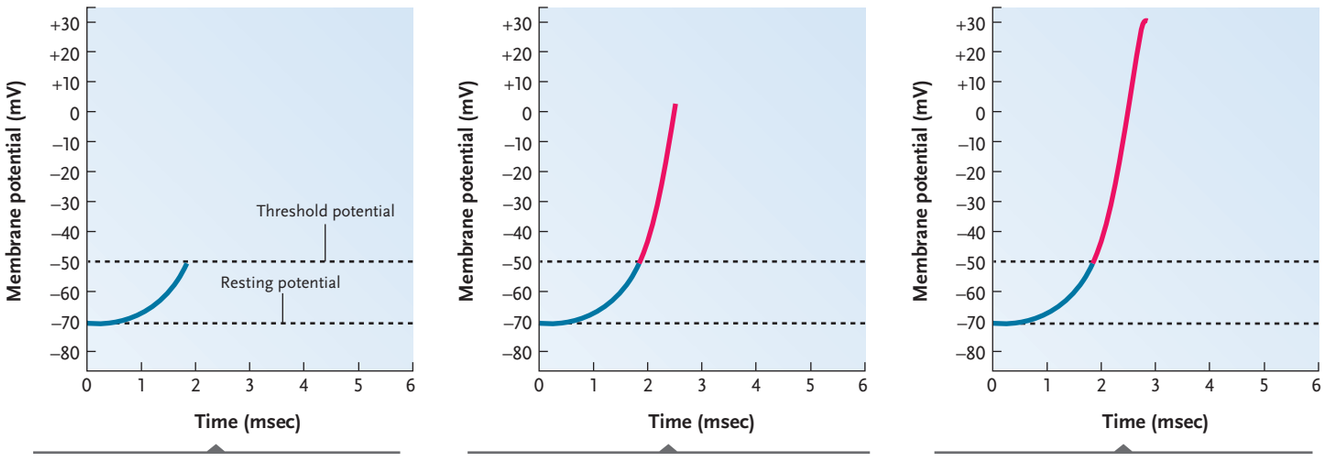


Figure 37.9
Changes in membrane potential during an action potential.





1 A stimulus raises the membrane potential to threshold. The activation gate of the Na^+ channel opens.

2 Above the threshold, more Na^+ channels open and Na^+ flows inward along its concentration gradient, raising the membrane potential toward the peak of the action potential.

3 As the action potential reaches its peak, the inactivation gate of the Na^+ channel closes and the K^+ channel activation gate opens, allowing K^+ ions to flow outward.

Figure 37.10
Changes in voltage-gated Na^+ and K^+ channels that produce the action potential.

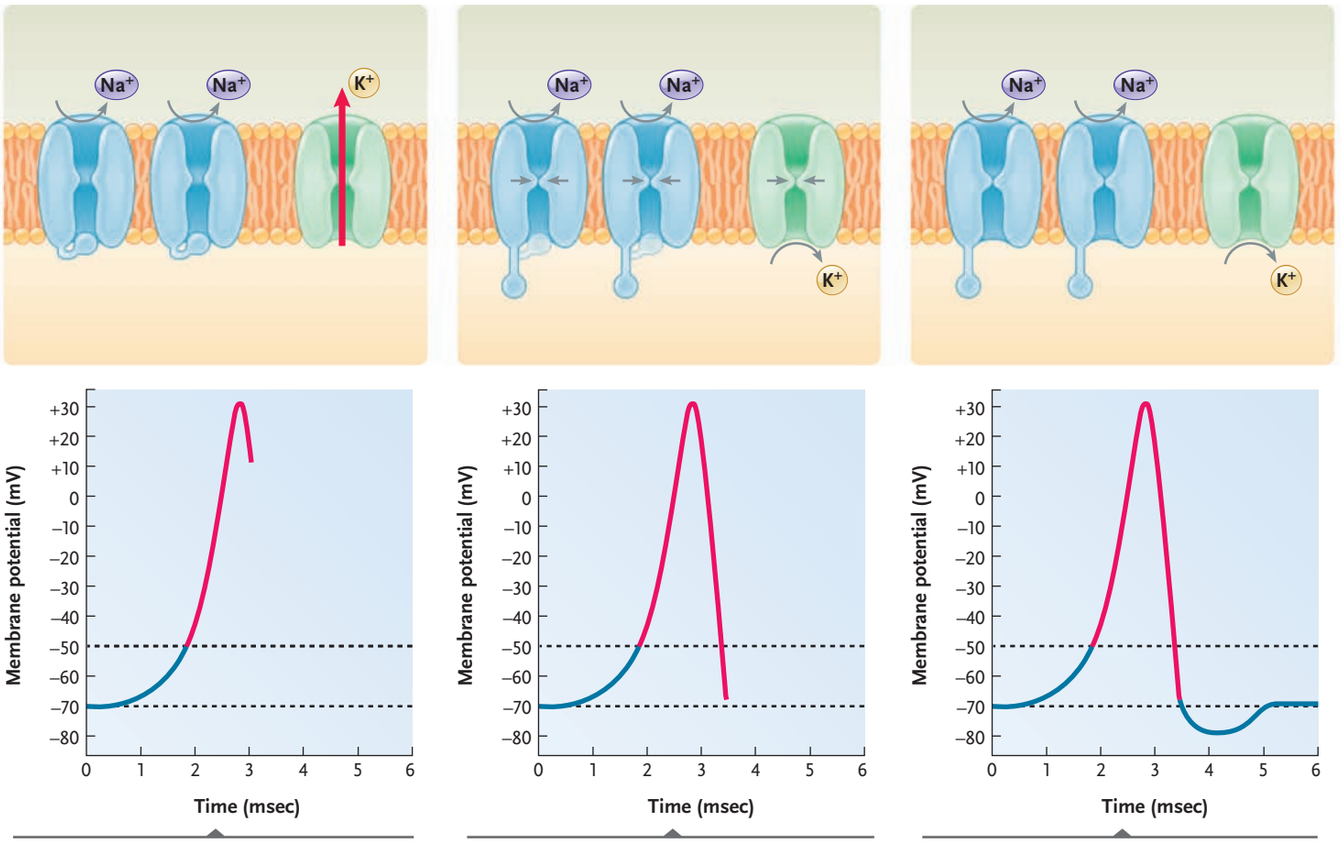
Neural Impulses Move by Propagation of Action Potentials

Once an action potential is initiated at the dendrite end of the neuron, it passes along the surface of a nerve or muscle cell as an automatic wave of depolarization traveling away from the stimulation point **(Figure 37.11).** The action potential does not need further trigger events in order for it to be propagated along the axon to the terminals. In a segment of an axon that is generating an action potential, the outside of the membrane becomes temporarily negative and the inside positive. Because opposites attract, as the region outside becomes negative, local current flow occurs between the area undergoing an action potential and the adjacent downstream inactive area both inside and outside the membrane (arrows, Figure 37.11). This current flow makes nearby regions the axon membrane less positive on the outside and more positive on the inside; in other words, they depolarize the membrane.

The depolarization is large enough to push the membrane potential past the threshold, opening the voltage-gated Na^+ and K^+ channels and starting an action potential in the downstream adjacent region. In this way, each segment of the axon stimulates the next segment to fire, and the action potential moves rapidly along the axon as a nerve impulse.

The refractory period keeps an action potential from reversing direction at any point along an axon; only the region in front of the action potential can fire. The refractory period results from the properties of the voltage-gated ion channels. Once they have been opened to their activated state, the upstream voltage-gated ion channels need time to reset to their original positions before they can open again. Therefore, only downstream voltage-gated ion channels are able to open, ensuring the one-way movement of the action potential along the axon toward the axon tips. By the time the refractory period ends in a membrane segment that has just fired an action potential, the action potential has moved too far away to cause a second action potential to develop in the same segment.

The magnitude of an action potential stays the same as it travels along an axon, even where the axon



4 The outward flow of K^+ along its concentration gradient causes the membrane potential to begin to fall.

5 As the membrane potential reaches the resting value, the activation gate of the Na^+ channel closes and the inactivation gate opens. The K^+ activation gate also closes.

6 Closure of the K^+ activation gate stabilizes the membrane potential at the resting value.

branches at its tips. Thus the propagation of an action potential resembles a burning fuse, which burns with the same intensity along its length, and along any branches, once it is lit at one end. Unlike a fuse, however, an axon can fire another action potential of the same intensity within a few milliseconds after an action potential passes through.

Due to the all-or-nothing principle of action potential generation, the intensity of a stimulus is reflected in the *frequency* of action potentials—the greater the stimulus, the more action potentials per second, up to a limit depending on the axon type—rather than by the change in membrane potential. For most neuron types, the limit lies between 10 and 100 action potentials per second.

Both natural and synthetic substances target specific parts of the mechanism generating action potentials. Local anesthetics, such as procaine and lidocaine, bind to voltage-gated Na^+ channels and block their ability to transport ions; thus, sensory nerves in the anesthetized region cannot transmit pain signals. The potent poison of the pufferfish, tetrodotoxin, also blocks voltage-gated Na^+ channels in neurons, potentially causing muscle paralysis and death. The pufferfish is highly prized as a delicacy in Japan, eaten after careful preparation to remove organs carrying the tetrodotoxin. A mistake can kill the diners, however, making pufferfish sashimi a kind of culinary Russian roulette.

Saltatory Conduction Increases Propagation Rate in Small-Diameter Axons

In the propagation pattern shown in Figure 37.11, an action potential spreads along every segment of the membrane along the length of the axon. For this type of action potential propagation, the rate of conduction increases with the diameter of the axon. Axons with a very large diameter have evolved in invertebrates such as lobsters, earthworms, and squids as well as a few marine fishes. Giant axons typically carry signals that produce an escape or withdrawal response, such as the sudden flexing of the tail (abdomen) in lobsters that propels the animal backward. The largest known axons, 1.7 mm in diameter, occur in fanworms *(Myxicola)*.

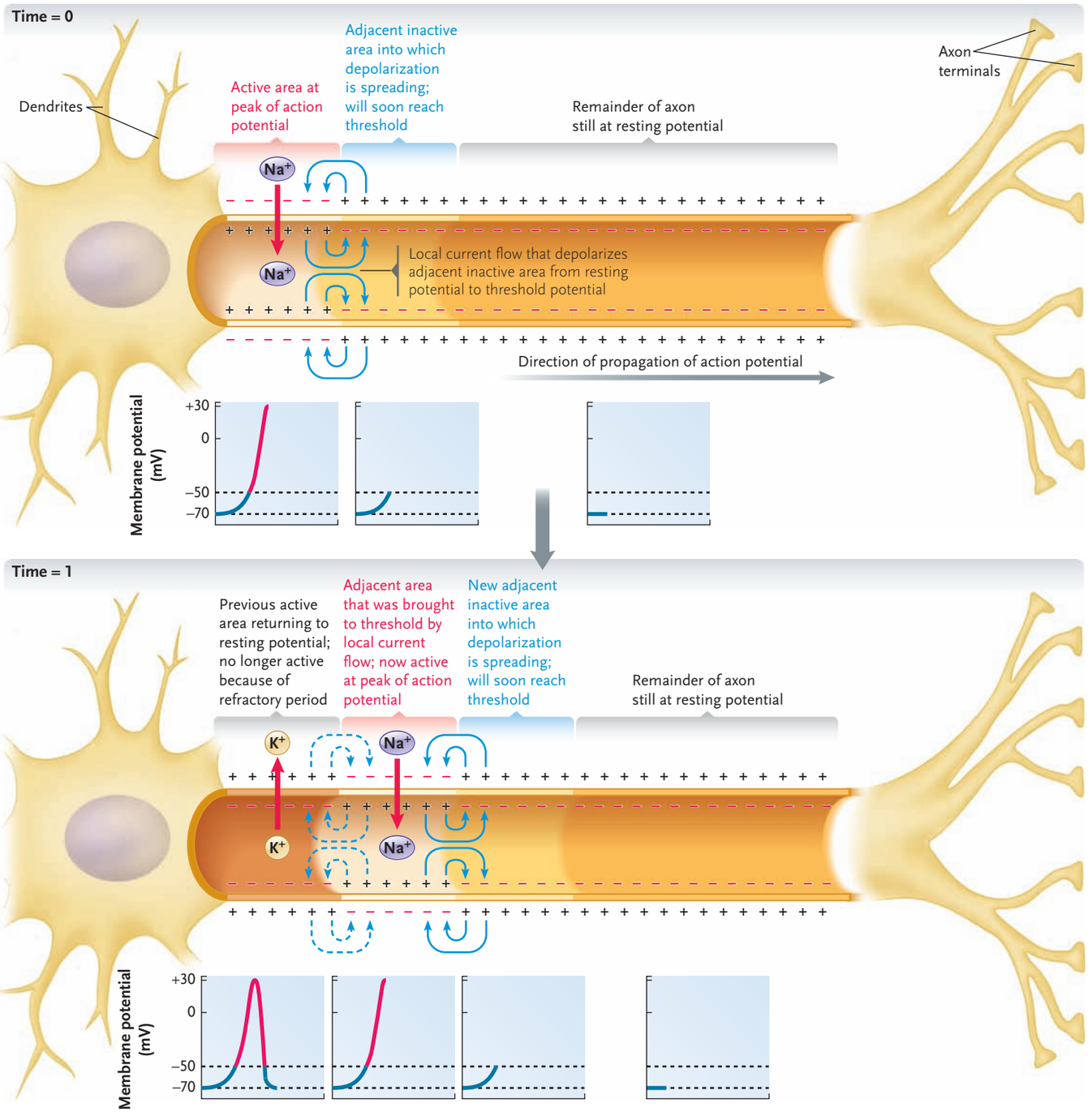


Figure 37.11
Propagation of an action potential along an unmyelinated axon by ion flows between a firing segment and an adjacent unfired region of the axon. Each firing segment induces the next to fire, causing the action potential to move along the axon.

The signals they carry contract a muscle that retracts the fanworm's body into a protective tube when the animal is threatened.

Although large-diameter axons can conduct impulses as rapidly as 25 m/sec (over twice the speed of the world record 100-meter dash), they take up a great deal of space. In complex vertebrates, natural selection has led to a mechanism that allows small-diameter axons to conduct impulses rapidly. The mechanism, called **saltatory conduction** (*saltere* = to leap), allows action potentials to "hop" rapidly along axons instead of burning smoothly like a fuse.

Saltatory conduction depends on the insulating myelin sheath that forms around some axons and in particular on the nodes of Ranvier exposing the axon membrane to extracellular fluids. Voltage-gated Na^+ and K^+ channels crowded into the nodes allow action potentials to develop at these positions **(Figure 37.12).** The inward movement of Na^+ ions produces depolarization, but the excess positive ions are unable to leave the axon through the membrane regions covered by the myelin sheath. Instead, they diffuse rapidly to the next node where they cause depolarization, inducing an action potential at that node. As this mechanism repeats, the action potential jumps rapidly along the axon from node to node. Saltatory conduction proceeds at rates up to 130 m/sec while an unmyelinated axon of the same diameter conducts action potentials at about 1 m/sec.

Saltatory conduction allows thousands to millions of fast-transmitting axons to be packed into a relatively small diameter. For example, in humans the optic nerve leading from the eye to the brain is only 3 mm in diameter but is packed with more than a million axons. If those axons were unmyelinated, each would have to be about 100 times thicker to conduct impulses at the same velocity, producing an optic nerve about 300 mm (12 inches) in diameter.

The disease *multiple sclerosis* (*sclero* = hard) underscores the importance of myelin sheaths to the operation of the vertebrate nervous system. In this disease, myelin is progressively lost from axons and replaced by hardened scar tissue. The changes block or slow the transmission of action potentials, producing numbness, muscular weakness, faulty coordination of movements, and paralysis that worsens as the disease progresses.

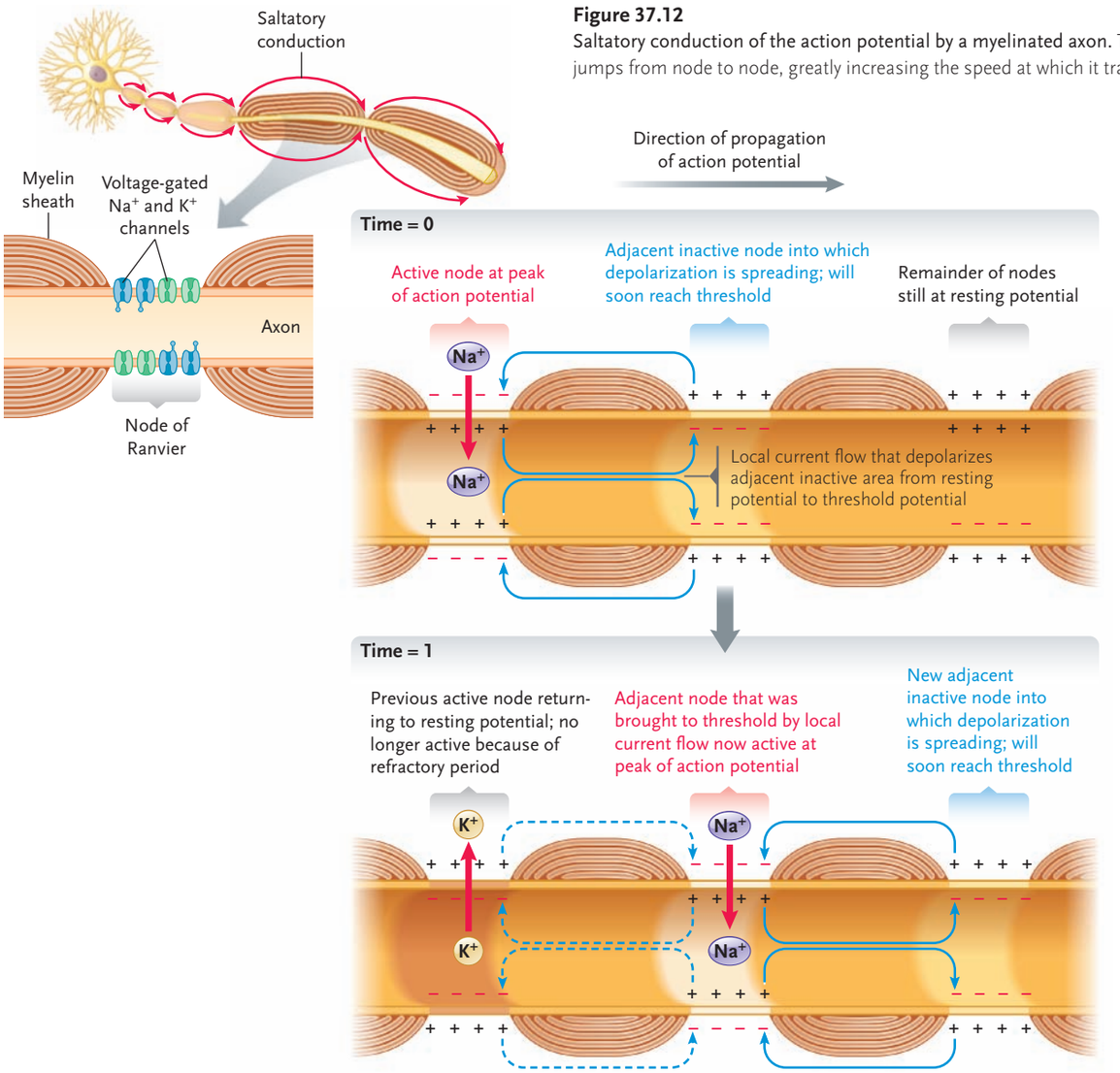


Figure 37.12
Saltatory conduction of the action potential by a myelinated axon. The action potential jumps from node to node, greatly increasing the speed at which it travels along the axon.

Study Break

1. What mechanism ensures that an electrical impulse in a neuron is conducted in only one direction down the axon?
2. How does having a myelin sheath affect the conduction of impulses in neurons?

37.3 Conduction across Chemical Synapses

Action potentials are transmitted directly across electrical synapses, but they cannot jump across the cleft in a chemical synapse. Instead, the arrival of an action potential causes neurotransmitter molecules—which are synthesized in the cell body of the neuron—to be released by the plasma membrane of the axon terminal, called the **presynaptic membrane (Figure 37.13).** The neurotransmitter diffuses across the cleft and alters ion conduction by activating *ligand-gated ion channels* in the **postsynaptic membrane**, the plasma membrane of the postsynaptic cell. **Ligand-gated ion channels** are channels that open or close when a specific chemical, such as a neurotransmitter, binds to the channel. Neurotransmitter communication from presynaptic to postsynaptic cells is a specialized case of cell-to-cell communication and signal transduction, which you learned about in Chapter 7. Neurobiologists study this phenomenon from the standpoint of understanding the function of neurons, but some of the details being learned are similar in many other types of cells.

Neurotransmitters work in one of two ways. **Direct neurotransmitters** bind directly to a ligand-gated ion channel in the postsynaptic membrane, which opens or closes the channel gate and alters the flow of a specific ion or ions in the postsynaptic cell. The time between arrival of an action potential at an axon terminal and alteration of the membrane potential in the postsynaptic cell may be as little as 0.2 msec.

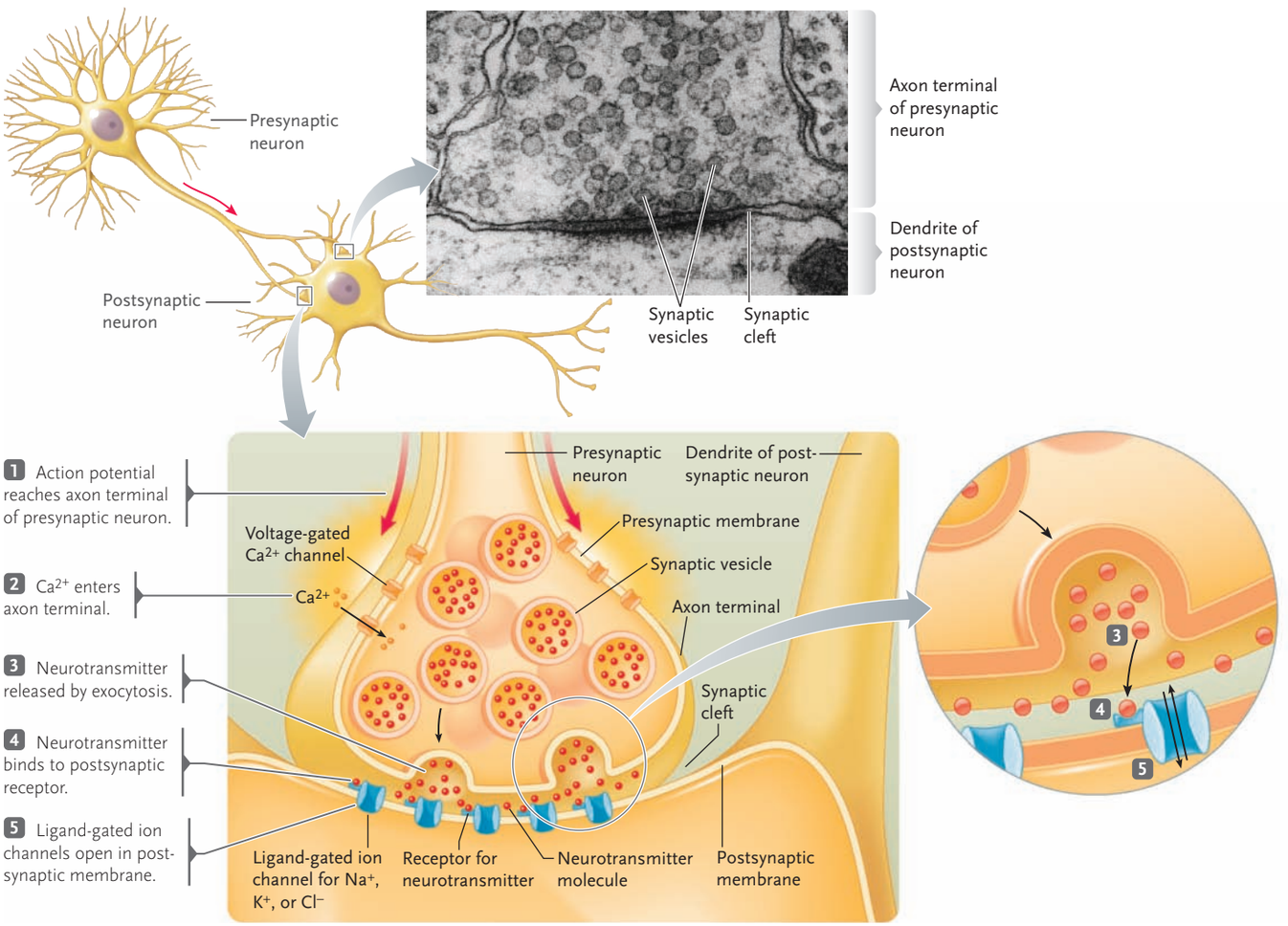


Figure 37.13
Structure and function of chemical synapses.
(Micrograph: © Dennis Kunkel/Visuals Unlimited.)

Indirect neurotransmitters work more slowly (on the order of hundreds of milliseconds). They act as *first messengers,* binding to G-protein-coupled receptors in the postsynaptic membrane, which activates the receptor and triggers generation of a *second messenger* such as cyclic AMP or other processes (see Section 7.4). The cascade of second messenger reactions opens or closes ion-conducting channels in the postsynaptic membrane. Indirect neurotransmitters typically have effects that may last for minutes or hours. Some substances can act as either direct or indirect neurotransmitters, depending on the types of receptors they bind in the receiving cell.

The time required for the release, diffusion, and binding of neurotransmitters across chemical synapses delays transmission as compared with the almost instantaneous transmission of impulses across electrical synapses. However, communication through chemical synapses allows neurons to receive inputs from hundreds to thousands of axon terminals at the same time. Some neurotransmitters have stimulatory effects, while others have inhibitory effects. All of the information received at a postsynaptic membrane is integrated to produce a response. Thus, by analogy, communication by electrical synapses resembles the effect of simply touching one wire to another; communication by direct and indirect neurotransmitters resembles the integration of multiple inputs by a computer chip.

Neurotransmitters Are Released by Exocytosis

Neurotransmitters are stored in secretory vesicles called **synaptic vesicles** in the cytoplasm of an axon terminal. The arrival of an action potential at the terminal releases the neurotransmitters by *exocytosis:* the vesicles fuse with the presynaptic membrane and release the neurotransmitter molecules into the synaptic cleft.

The release of synaptic vesicles depends on voltage-gated Ca^{2+} channels in the plasma membrane of an axon terminal (see Figure 37.13). Ca^{2+} ions are constantly pumped out of all animal cells by an active transport protein in the plasma membrane, keeping their concentration higher outside than inside. As an action potential arrives, the change in membrane potential opens the Ca^{2+} channel gates in the axon terminal, allowing Ca^{2+} to flow back into the cytoplasm. The rise in Ca^{2+} concentration triggers a protein in the membrane of the synaptic vesicle that allows the vesicle to fuse with the plasma membrane, releasing neurotransmitter molecules into the synaptic cleft.

Each action potential arriving at a synapse typically causes approximately the same number of synaptic vesicles to release their neurotransmitter molecules. For example, arrival of an action potential at one type of synapse causes about 300 synaptic vesicles to release a neurotransmitter called acetylcholine. Each vesicle contains about 10,000 molecules of the neurotransmitter, giving a total of some 3 million acetylcholine molecules released into the synaptic cleft by each arriving action potential.

When a stimulus is no longer present, action potentials are no longer generated and a response is no longer needed. In this case a series of events prevents continued transmission of the signal. When action potentials stop arriving at the axon terminal, the voltage-gated Ca^{2+} channels in the axon terminal close and the Ca^{2+} in the axon cytoplasm is quickly pumped to the outside. The drop in cytoplasmic Ca^{2+} stops vesicles from fusing with the presynaptic membrane, and no further neurotransmitter molecules are released. Any free neurotransmitter molecules remaining in the cleft quickly diffuse away, are broken down by enzymes in the cleft, or are pumped back into the axon terminals or into glial cells by active transport. Transmission of impulses across the synaptic cleft ceases within milliseconds after action potentials stop arriving at the axon terminal.

Most Neurotransmitters Alter Ion Flow through Na^+ or K^+ Channels

Neurotransmitters work by opening or closing membrane-embedded ligand-gated ion channels; most of these channels conduct Na^+ or K^+ across the postsynaptic membrane, although some regulate chloride ions (Cl^-). The altered ion flow in the postsynaptic cell that results from the opening or closing of the gates may stimulate or inhibit the generation of action potentials by that cell. For example, if Na^+ channels are opened, the inward Na^+ flow brings the membrane potential of the postsynaptic cell toward the threshold (the membrane becomes depolarized). If K^+ channels are opened, the outward flow of K^+ has the opposite effect (the membrane becomes hyperpolarized). The combined effects of the various stimulatory and inhibitory neurotransmitters at all the chemical synapses of a postsynaptic neuron or muscle cell determine whether the postsynaptic cell triggers an action potential. (*Insights from the Molecular Revolution* describes experiments that worked out the structure and function of an ion channel gated directly by a neurotransmitter.)

Many Different Molecules Act as Neurotransmitters

In all, nearly 100 different substances are now known or suspected to be neurotransmitters. Most of them are relatively small molecules that diffuse rapidly across the synaptic cleft. Some axon terminals release only one type of neurotransmitter while others release several types. Depending on the type of receptor to which it binds, the same neurotransmitter may stimulate or inhibit the generation of action potentials in the post-

Insights from the Molecular Revolution

Dissecting Neurotransmitter Receptor Functions

Many receptors for direct neurotransmitters are part of an ion channel that is opened or closed by the binding of a neurotransmitter molecule. Each of these receptors has two regions: a large, hydrophilic portion on the outside surface of the plasma membrane that binds the neurotransmitter and a hydrophobic transmembrane portion that anchors the receptor in the plasma membrane and forms the ion-conducting channel.

Jean-Luc Eiselé and his coworkers at the National Center of Scientific Research and the Central Medical University in Switzerland were interested in determining whether the two primary activities of these receptors—binding neurotransmitters and conducting ions—depend on parts of the protein that work independently or reflect an integration of the entire protein structure.

To find out, Eiselé and his colleagues constructed artificial receptors using regions of the receptors for two different neurotransmitters, acetylcholine and serotonin. These two receptors, although related in amino acid sequence and structure, bind different neurotransmitters and react differently to calcium ions. Ion conduction by the acetylcholine receptor is enhanced by Ca^{2+}, while Ca^{2+} ions block the channel of the serotonin receptor and stop ion conduction.

To create the artificial receptors, the investigators broke the genes encoding the acetylcholine and serotonin receptors into two parts. They then reassembled the parts so that in the protein encoded by the composite gene, the part of the acetylcholine receptor located on the membrane surface was joined to the transmembrane channel of the serotonin receptor. Five versions of the artificial gene, encoding proteins in which the two parts were joined at different positions in the amino acid sequence, were then cloned to increase their quantity and injected into oocytes of the clawed frog, *Xenopus laevis.* Once in the oocytes, the genes were translated into the artificial receptor proteins, which were inserted into the oocyte plasma membranes.

Of the five artificial receptors, all were able to bind acetylcholine, but only two were able to conduct ions in response to binding the neurotransmitter, as measured by an increase in the electrical current flowing across the plasma membrane of the oocytes. Agents that inhibit the normal acetylcholine receptor, such as curare, also inhibited the artificial receptors. Serotonin, in contrast, was not bound and did not open the receptor channels, and agents that inhibit the normal serotonin receptor had no effect on the artificial receptors. However, elevated Ca^{2+} concentrations blocked the channel, as in the normal serotonin receptor.

The remarkable research by Eiselé and his coworkers indicates that the parts of a receptor binding a neurotransmitter and conducting ions function independently. Their work also demonstrates the feasibility of constructing composite receptors as a means for dissecting the functions of subregions of the receptors.

synaptic cell. **Figure 37.14** depicts some examples of neurotransmitters.

Acetylcholine acts as a neurotransmitter in both invertebrates and vertebrates. In vertebrates, it acts as a direct neurotransmitter between neurons and muscle cells and as an indirect neurotransmitter between neurons carrying out higher brain functions such as memory, attention, perception, and learning. Acetylcholine-releasing neurons in the brain degenerate in people who develop Alzheimer disease, in which memory, speech, and perceptual abilities decline.

Acetylcholine is the target of many natural and artificial poisons. Curare, a plant extract used as an arrow poison by some indigenous peoples of South America, blocks muscle contraction and produces paralysis by competing directly with acetylcholine for binding sites in synapses that control muscle cells. Atropine, an ingredient of the drops an eye doctor uses to dilate your pupils, is also a plant extract; it relaxes the iris muscles by blocking their acetylcholine receptors. Nicotine also binds to acetylcholine receptors, but acts as a stimulant by turning the receptors on rather than off.

Several amino acids operate as direct neurotransmitters in the CNS of vertebrates and in nerve-muscle synapses of insects and crustaceans. *Glutamate* and *aspartate* stimulate action potentials in postsynaptic cells. They are directly involved in vital brain functions such as memory and learning. *Gamma aminobutyric acid (GABA),* a derivative of glutamate, acts as an inhibitor by opening Cl^- channels in postsynaptic membranes. *Glycine* is also an inhibitor.

Other substances can block the operation of these neurotransmitters. For example, tetanus toxin, released by the bacterium *Clostridium tetani,* blocks GABA release in synapses that control muscle contraction. The body muscles contract so forcibly that the body arches painfully and the teeth become tightly clenched, giving the condition its common name of lockjaw. Once the effects extend to respiratory muscles, the victim quickly dies.

The biogenic amines, which are derived from amino acids, act primarily as indirect neurotransmitters in the CNS. *Norepinephrine, epinephrine,* and *dopamine,* all derived from tyrosine, function as neurotransmitters between interneurons involved in such diverse brain and body functions as consciousness, memory, mood, sensory perception, muscle movements, maintenance of blood pressure, and sleep. Norepinephrine

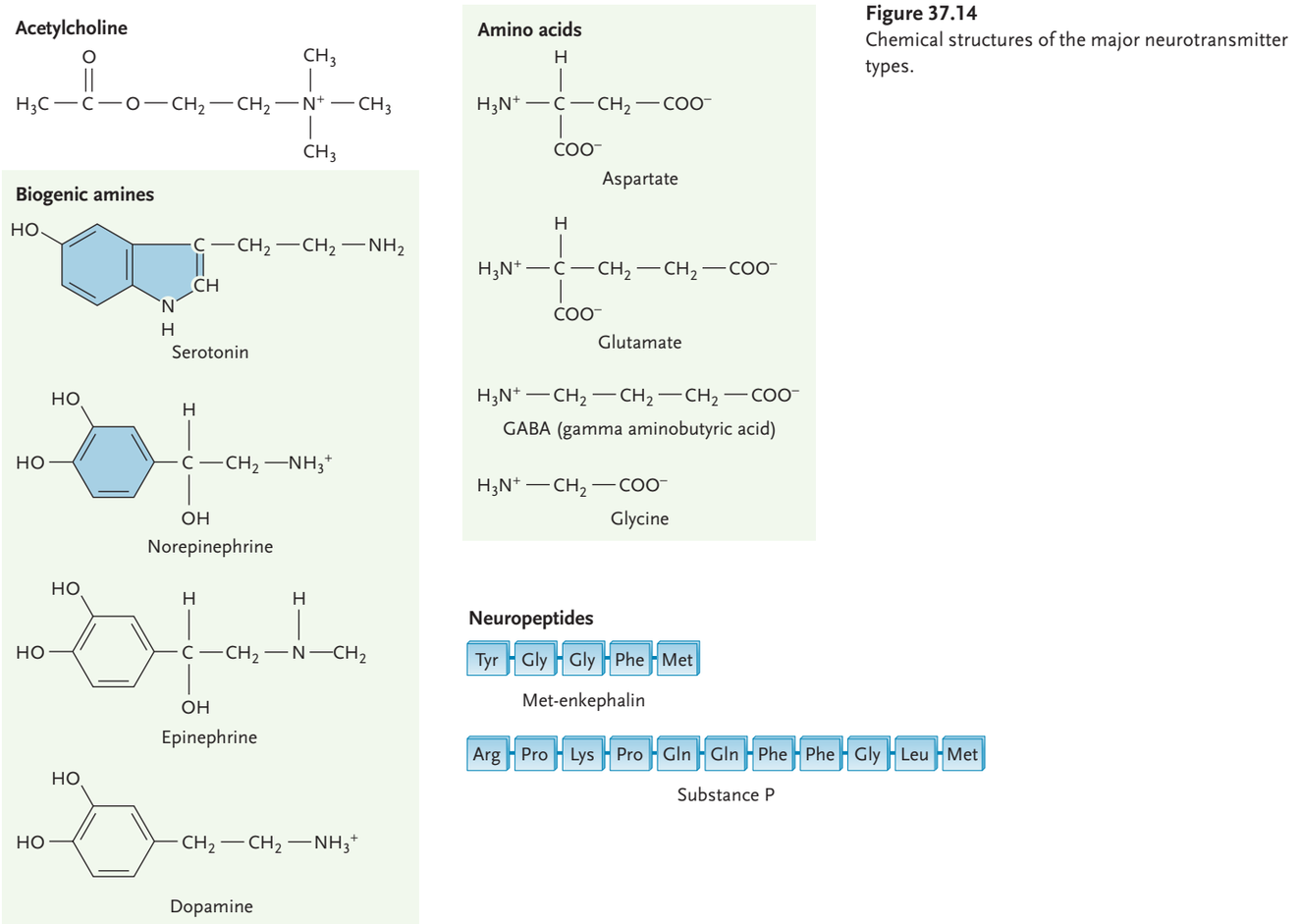


Figure 37.14
Chemical structures of the major neurotransmitter types.

and epinephrine are also released into the general body circulation as hormones. Parkinson disease, in which there is a progressive loss of muscle control, results from degeneration of dopamine-releasing neurons in regions of the brain that coordinate muscular movements. *Serotonin,* which is derived from tryptophan, is released by interneurons in the pathways regulating appetite, reproductive behavior, muscular movements, sleep, and emotional states such as anxiety.

Several drugs enhance or inhibit the action of biogenic amines. For example, cocaine binds to the transporters for active reuptake of certain neurotransmitters such as norepinephrine, dopamine, and serotonin from the synaptic cleft, thereby preventing them from being reabsorbed by the neurons that released them. As a result, the concentrations of the neurotransmitters increase in the synapses, leading to amplification of their natural effects. That is, the affected neurons produce symptoms characteristic of cocaine use, namely high energy from the norepinephrine, euphoria from the dopamine, and feelings of confidence from the serotonin.

Neuropeptides, which are short chains of two or more amino acids, act as indirect neurotransmitters in the central and peripheral nervous systems of both vertebrates and invertebrates. More than 50 neuropeptides are now known. Neuropeptides are also released into the general body circulation as peptide hormones.

Neuropeptides called *endorphins* ("endogenous morphines") are released during periods of pleasurable experience such as eating or sexual intercourse, or physical stress such as childbirth or extended physical exercise. These neurotransmitters have the opiatelike property of reducing pain and inducing euphoria, well known to exercise buffs as a pleasant by-product of their physical efforts. Most endorphins act on the PNS and effectors such as muscles, but *enkephalins,* a subclass of the endorphins, bind to particular receptors in the CNS. Morphine, a potent drug extracted from the opium poppy, blocks the sensation of pain and produces a sensation of well-being by binding to the same receptors in the brain.

Another neuropeptide associated with pain response is *substance P,* which is released by special neurons in the spinal cord. Its effect is to increase messages associated with intense, persistent, or severe pain. For example, suppose you put your hand on a hot barbecue grill. You will snatch your hand away immediately by reflex action, and you will feel the "ouch" of the pain a little later. Why do events occur in this order? The reflex

action is driven by rapid nerve impulse conduction along myelinated neurons. The neurons that release substance P are not myelinated, however, so their signal is conducted more slowly and the feeling of pain is delayed. The action of endorphins is antagonistic to substance P, reducing the perception of pain.

In mammals and probably other vertebrates, some neurons synthesize and release dissolved carbon monoxide and nitric oxide as neurotransmitters. For example, in the brain, carbon monoxide regulates the release of hormones from the hypothalamus. Nitric oxide contributes to many nervous system functions such as learning, sensory responses, and muscle movements. By relaxing smooth muscles in the walls of blood vessels, nitric oxide causes the vessels to dilate, increasing the flow of blood. For example, when a male is sexually aroused, neurons release nitric oxide into the erectile tissues in the penis. Relaxation of the muscles increases blood flow into the tissues, causing them to fill with blood and produce an erection. The impotency drug Viagra aids erection by inhibiting an enzyme that normally reduces nitric oxide concentration in the penis.

Study Break

1. What features characterize a substance as a neurotransmitter?
2. Describe how a direct neurotransmitter in a presynaptic neuron controls action potentials in a postsynaptic neuron.

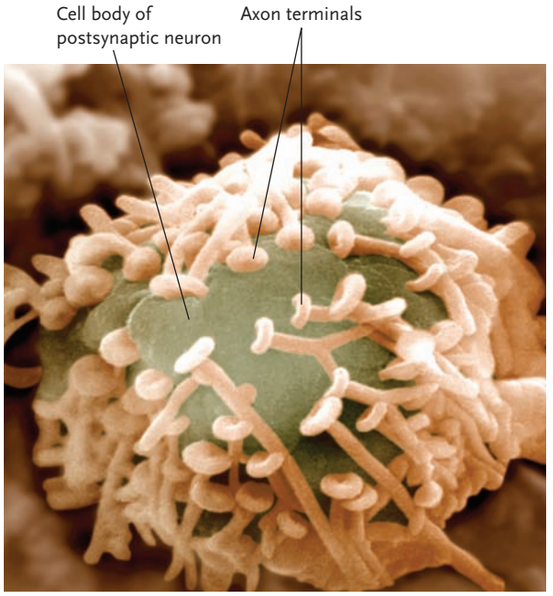
37.4 Integration of Incoming Signals by Neurons

Most neurons receive a multitude of stimulatory and inhibitory signals carried by both direct and indirect neurotransmitters. These signals are integrated by the postsynaptic neuron into a response that reflects their combined effects. The integration depends primarily on the patterns, number, types, and activity of the synapses the postsynaptic neuron makes with presynaptic neurons. Inputs from other sources, such as indirect neurotransmitters and other signal molecules, can modify the integration. The response of the postsynaptic neuron is elucidated by the frequency of action potentials it generates.

Integration at Chemical Synapses Occurs by Summation

As mentioned earlier, depending on the type of receptor to which it binds, a neurotransmitter may stimulate or inhibit the generation of action potentials in the postsynaptic neuron. If a neurotransmitter opens a ligand-gated Na^+ channel, Na^+ enters the cell, causing a depolarization. This change in membrane potential pushes the neuron closer to threshold; that is, it is excitatory and is called an **excitatory postsynaptic potential**, or **EPSP.** On the other hand, if a neurotransmitter opens a ligand-gated ion channel that allows Cl^- to flow into the cell and K^+ to flow out, hyperpolarization occurs. This change in membrane potential pushes the neuron farther from threshold; that is, it is inhibitory and is called an **inhibitory postsynaptic potential**, or **IPSP.** In contrast to the all-or-nothing operation of an action potential, EPSPs and IPSPs are **graded potentials**, in which the membrane potential increases or decreases without necessarily triggering an action potential. And there are no refractory periods for EPSPs and IPSPs.

A neuron typically has hundreds to thousands of chemical synapses formed by axon terminals of presynaptic neurons contacting its dendrites and cell body **(Figure 37.15).** The events that occur at a single synapse produce either an EPSP or an IPSP in that postsynaptic neuron. But how is an action potential produced if a single EPSP is not sufficient to push the postsynaptic neuron to threshold? The answer involves the summation of the inputs received through those many chemical synapses formed by presynaptic neurons. At any given time, some or many of the presynaptic neurons may be firing, producing EPSPs and/or IPSPs in the postsynaptic neuron. The sum of all the EPSPs and IPSPs at a given time determines the total potential in the postsynaptic neuron and, therefore, how that neu-



E. R. Lewis, T. E. Everhart, Y. Y. Zevi/Visuals Unlimited

Figure 37.15
The multiple chemical synapses relaying signals to a neuron. The drying process used to prepare the neuron for electron microscopy has toppled the axon terminals and pulled them away from the neuron's surface.

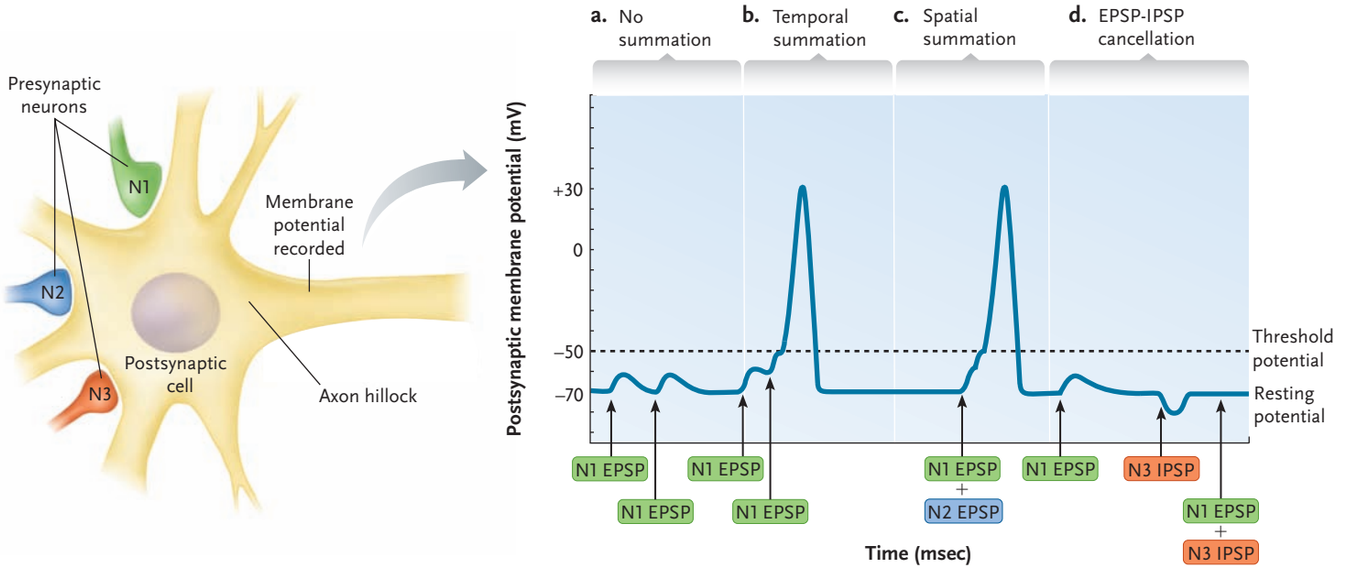


Figure 37.16
Summation of EPSPs and IPSPs by a postsynaptic neuron.

ron responds. **Figure 37.16** shows, in a greatly simplified way, the effects of EPSPs and IPSPs on membrane potential, and how summation of inputs brings a postsynaptic neuron to threshold.

The postsynaptic neuron in the figure has three neurons, N1–N3, forming synapses with it. Suppose that the axon of N1 releases a neurotransmitter, which produces an EPSP in the postsynaptic cell (see Figure 37.16a). The membrane depolarizes, but not enough to reach threshold. If N1 input causes a new EPSP after the first EPSP has died down, it will be of the same magnitude as the first EPSP and no progression toward threshold has taken place—no summation has occurred. If instead, N1 input causes a new EPSP before the first EPSP has died down, the second EPSP will sum with the first and a greater depolarization will have taken place (see Figure 37.16b). This summation of two (or more) EPSPs produced by successive firing of a single presynaptic neuron over a short period of time is called **temporal summation.** If the total depolarization achieved in this way reaches threshold, an action potential will be produced in the postsynaptic neuron. The postsynaptic cell may also be brought to threshold by **spatial summation**, the summation of EPSPs produced by the firing of different presynaptic neurons, such as N1 and N2 (see Figure 37.16c). Lastly, EPSPs and IPSPs can cancel each other out. In the example shown in Figure 37.16d, firing of N1 alone produces an EPSP, firing of N3 alone produces an IPSP, while firing of N1 and N3 simultaneously produces no change in the membrane potential.

The summation point for EPSPs and IPSPs is the axon hillock of the postsynaptic neuron. The greatest density of voltage-gated Na^+ channels occurs in that region, resulting in the lowest threshold potential in the neuron.

The Patterns of Synaptic Connections Contribute to Integration

The total number of connections made by a neuron may be very large—some single interneurons in the human brain, for example, form as many as 100,000 synapses with other neurons. The synapses are not absolutely fixed; they can change through modification, addition, or removal of synaptic connections—or even entire neurons—as animals mature and experience changes in their environments. The combined activities of all the neurons in the nervous system, constantly integrating information from sensory receptors and triggering responses by effectors, control the internal activities of animals and regulate their behavior. This behavior ranges from the simple reflexes of a flatworm to the complex behavior of mammals, including consciousness, emotions, reasoning, and creativity in humans.

Although researchers do not yet understand how processes such as ion flow, synaptic connections, and neural networks produce complex mental activities, they continue to find correspondences between them and the types of neuronal communication described in this chapter. In the next chapter we learn about how nervous systems of animals are organized, and how higher functions such as memory, learning, and consciousness are produced.

Study Break

How does a postsynaptic neuron integrate signals carried by direct and indirect neurotransmitters?

Unanswered Questions

What is the basic wiring diagram of the brain?

In this chapter, you've learned that neurons communicate with each other through synaptic actions that can directly or indirectly cause a change in the membrane potential of a postsynaptic neuron. In order to understand how the brain processes information, it is important first to understand the wiring that handles this information and what forms that communication can take. There are about 100,000,000,000 neurons in the human brain. This is a daunting number, but it can be managed by grouping the neurons into classes or categories. It has been estimated that there are fewer than 10,000 different neuronal classes in the entire brain. Still, each neuron makes and receives synaptic contacts with about 1,000 other neurons on average, making the wiring diagram quite complex. We do not have an adequate means to represent this complexity, nor do we have a means of understanding how information flows through such a complex network. Just as modern sequencing technology allowed a revolution in the field of genomics (the categorization of all of the genes in an organism); similar breakthroughs will need to occur in the field of neuromics (the categorization of all of the neurons and their interactions). These breakthroughs will have to be in data management, computational simulations, and multisite recording techniques.

In our lab, we are working on a way to represent our knowledge of the brain's wiring with an online knowledge base called NeuronBank. To test NeuronBank, we are using the simple nervous systems of sea slugs, especially *Tritonia diomedea*. A sea slug brain has only 10,000 neurons total, many of which are individually identifiable from animal to animal. Eventually, different branches of NeuronBank will represent our knowledge about the basic wiring of the nervous systems of different animals, allowing the neurons and their connections to be compared across species. Having ready access to this information will allow researchers to better design drugs that target specific neurons. This may aid in treatments for neurological conditions ranging from Parkinson's disease to some forms of blindness.

The way information is conveyed between neurons is not yet understood fully. Much of neuroscience has focused on classical neurotransmission. However, the brain uses many other signaling devices. In our lab, we are also using sea slugs to study neuromodulatory signaling by neurons that release the neurotransmitter serotonin, which regulates appetite, reproductive behavior, muscular movements, sleep, and emotional states such as anxiety. We have found that these neurons can change the strength of connections made by other neurons, and that the effects of a serotonin-releasing neuron depend upon the state of the neuron that it is modulating. So, signaling in the nervous system is not a simple matter of summating excitatory and inhibitory inputs; it involves complex, state-dependent actions. Understanding the complexities of neuronal signaling will allow researchers to understand better how the brain processes information. Another unanswered question is simply, "What are all of the different ways that neurons use for communicating information?"

The ultimate question is "How does all of this processing in the brain lead to self-awareness or consciousness?" We do not have an answer for this question as yet. We know that blocking the activity in parts of the brain, through injury, disease, or drugs, can decrease or alter consciousness. But we do not understand how this activity gives rise to the sensation of "being." That is the ultimate question about how the brain works.

Paul Katz is a professor of biology and the director of the Center for Neuromics at Georgia State University. His research interests include neuromics, neuromodulation, and the evolution of neuronal circuits. Learn more about his work at http://www2.gsu.edu/~biopsk.

Review

Go to ThomsonNOW™ at www.thomsonedu.com/login to access quizzing, animations, exercises, articles, and personalized homework help.

37.1 Neurons and Their Organization in Nervous Systems: An Overview

- The nervous system of an animal (1) receives information about conditions in the internal and external environment, (2) transmits the message along neurons, (3) integrates the information to formulate an appropriate response, and (4) sends out signals to muscles or glands that accomplish the response (Figure 37.2).
- Neurons have dendrites, which receive information and conduct signals toward the cell body, and axons, which conduct signals away from the cell body to another neuron or an effector (Figure 37.3).
- Afferent neurons conduct information from sensory receptors to interneurons, which integrate the information into a response. The response signals are passed to efferent neurons, which activate the effectors carrying out the response (Figure 37.2).
- The combination of an afferent neuron, an interneuron, and an efferent neuron makes up a basic neuronal circuit. The circuits combine into networks that interconnect the peripheral and central nervous systems.
- Glial cells help maintain the balance of ions surrounding neurons and form insulating layers around the axons (Figure 37.5).
- Neurons make connections by two types of synapses. In an electrical synapse, impulses pass directly from the sending to the receiving cell. In a chemical synapse, neurotransmitter molecules released by the presynaptic cell diffuse across a narrow synaptic cleft and bind to receptors in the plasma membrane of the postsynaptic cell (Figure 37.6).

Animation: Neuron structure and function

Animation: Nerve structure

Animation: Impulse travelling through a nerve

37.2 Signal Conduction by Neurons

- The membrane potential of a cell depends on the unequal distribution of positive and negative charges on either side of the membrane, which establishes a potential difference across the membrane.
- Three primary conditions contribute to the resting potential of neurons: (1) an Na^+/K^+ active transport pump that sets up concentration gradients of Na^+ ions (higher outside) and K^+ ions (higher inside); (2) an open channel that allows K^+ to flow out

freely; and (3) negatively charged proteins and other molecules inside the cell that cannot pass through the membrane (Figure 37.8).

- An action potential is generated when a stimulus pushes the resting potential to the threshold value at which voltage-gated Na^+ and K^+ channels open in the plasma membrane. The inward flow of Na^+ changes membrane potential abruptly from negative to a positive peak. The potential falls to the resting value again as the gated K^+ channels allow this ion to flow out (Figure 37.10).
- Action potentials move along an axon as the ion flows generated in one segment depolarize the potential in the next segment (Figure 37.11).
- Action potentials are prevented from reversing direction by a brief refractory period, during which a segment of membrane that has just generated an action potential cannot be stimulated to produce another for a few milliseconds.
- In myelinated axons, ions can flow across the plasma membrane only at nodes where the myelin sheath is interrupted. As a result, action potentials skip rapidly from node to node by saltatory conduction (Figure 37.12).

Animation: Ion concentrations

Animation: Ion flow in myelinated axons

Animation: Action potential propagation

Animation: Measuring membrane potential

Animation: Stretch reflex

37.3 Conduction across Chemical Synapses

- Neurotransmitters released into the synaptic cleft bind to receptors in the plasma membrane of the postsynaptic cell, altering the flow of ions across the plasma membrane of the postsynaptic cell and pushing its membrane potential toward or away from the threshold potential (Figure 37.13).
- A direct neurotransmitter binds to a receptor associated with a ligand-gated ion channel in the postsynaptic membrane; the binding opens or closes the channel.
- An indirect neurotransmitter binds to a receptor in the postsynaptic membrane and triggers generation of a second messenger, which leads to the opening or closing of a gated channel.
- Neurotransmitters are released from synaptic vesicles into the synaptic cleft by exocytosis, which is triggered by entry of Ca^{2+} ions into the cytoplasm of the axon terminal through voltage-gated Ca^{2+} channels opened by the arrival of an action potential.
- Neurotransmitter release stops when action potentials cease arriving at the axon terminal. Neurotransmitters remaining in the synaptic cleft are broken down by enzymes or taken up by the axon terminal or glial cells.
- Types of neurotransmitters include acetylcholine, amino acids, biogenic amines, neuropeptides, and gases such as NO and CO (Figure 37.14). Many of the biogenic amines and neuropeptides are also released into the general body circulation as hormones.

Animation: Chemical synapse

37.4 Integration of Incoming Signals by Neurons

- Neurons carry out integration by summing excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs); the summation may push the membrane potential of the postsynaptic cell toward or away from the threshold for an action potential (Figure 37.16).
- The combined effects of summation in all the neurons in the nervous system control behavior in animals and underlie complex mental processes in mammals.

Animation: Synaptic integration

Questions

Self-Test Questions

1. Nerve signals travel in the following manner:
   a. A dendrite of a sensory neuron receives the signal; its cell body transmits the signal to a motor neuron's axon, and the signal is sent to the target.
   b. An axon of a motor neuron receives the signal; its cell body transmits the signal to a sensory neuron's dendrite, and the signal is sent to the target.
   c. Efferent neurons conduct nerve impulses toward the cell body of sensory neurons, which send them on to interneurons and ultimately to afferent motor neurons.
   d. A dendrite of a sensory neuron receives a signal; the cell's axon transmits the signal to an interneuron; the signal is then transmitted to dendrites of a motor neuron and sent forth on its axon to the target.
   e. The axons of oligodendrocytes transmit nerve impulses to the dendrites of astrocytes.
2. Glial cells:
   a. are unable to divide after an animal is born.
   b. in the PNS called Schwann cells form the insulating myelin sheath around axons.
   c. called astrocytes form the nodes of Ranvier in the brain.
   d. called oligodendrocytes are star-shaped cells in the PNS.
   e. are neuronal cells that connect to interneurons.
3. An example of a synapse could be the site where:
   a. neurotransmitters released by an axon travel across a gap and are picked up by receptors on a muscle cell.
   b. an electrical impulse arrives at the end of a dendrite causing ions to flow onto axons of presynaptic neurons.
   c. postsynaptic neurons transmit a signal across a cleft to a presynaptic neuron.
   d. oligodendrocytes contact the dendrites of an afferent neuron directly.
   e. an on-off switch stimulates an electrical impulse in a presynaptic cell to stimulate, not inhibit, other presynaptic cells.
4. The resting potential in neurons requires:
   a. membrane transport channels to be constantly open for Na^+ and K^+ flow.
   b. the inside of neurons to be positive relative to the outside.
   c. a slow movement of K^+ outward with a charge difference in the neural membrane set up by this movement of K^+.
   d. an active Na^+/K^+ pump, which pumps Na^+ and K^+ into the neuron.
   e. three Na^+ ions to be pumped through three Na^+ gates and two K^+ ions to be pumped through two K^+ gates.
5. The major role of the sodium potassium pump is to:
   a. cause a rapid firing of the action potential so the inside of the membrane becomes momentarily positive.
   b. decrease the resting potential to zero.
   c. hyperpolarize the membrane above resting value.
   d. increase a high action potential to enter a refractory period.
   e. maintain the resting potential at a constant negative value.

6. In the propagation of a nerve impulse:
   a. the refractory period begins as the K^+ channel opens, allowing K^+ ions to flow outward with their concentration gradient.
   b. Na^+ ions rush with their concentration gradient out of the axon.
   c. positive charges lower the membrane potential to its lowest action potential.
   d. gated K^+ channels open at the same time as the activation gate of Na^+ channels closes.
   e. the depolarizing stimulus lowers the membrane potential to open the Na^+ gates.
7. Which of the following does not contribute to propagation of action potentials?
   a. As the area outside the membrane becomes negative, it attracts ions from adjacent regions; as the inside of the membrane becomes positive, it attracts negative ions from nearby in the cytoplasm. These events depolarize nearby regions of the axon membrane.
   b. The refractory period allows the impulse to travel in only one direction.
   c. Each segment of the axon prevents the adjacent segments from firing.
   d. The magnitude of the action potential stays the same as it travels down the axon.
   e. Increasing the intensity of the stimulus increases the number of action potentials up to a limit.
8. Which of the following statements best describes saltatory conduction?
   a. It inhibits direct neurotransmitter release.
   b. It transmits the action potential at the nodes of Ranvier and thus speeds up impulses on myelinated axons.
   c. It increases neurotransmitter release at the presynaptic membrane.
   d. It decreases neurotransmitter uptake at chemically gated postsynaptic channels.
   e. It removes neurotransmitters from the synaptic cleft.
9. Transmission of a nerve impulse to its target cell requires:
   a. endocytosis of neurotransmitters by the excitatory presynaptic vesicles.
   b. thousands of molecules of neurotransmitter that had been stored in the postsynaptic cell to be released into the synaptic cleft.
   c. Ca^{2+} ions to diffuse through voltage-gated Ca^{2+} channels.
   d. the fall in Ca^{2+} to trigger a protein that causes the presynaptic vesicle to fuse with the plasma membrane.
   e. an action potential to open the Ca^{2+} gates so that Ca^{2+} ions, in higher concentration outside the axon, can flow back into the cytoplasm of the neuron.
10. Autopsy reports reveal that above a certain threshold, brain size is not related to intelligence. A possible explanation is that the brains of:
   a. gifted people have a much vaster network of neural synapses than do the brains of people with normal intelligence.
   b. people with normal intelligence release far more NO and CO neurotransmitters than do those of the gifted.
   c. people with normal intelligence contain more glutamate and aspartate than do those of the gifted.
   d. gifted people have excessive quantities of gamma aminobutyric acid.
   e. people with normal intelligence contain more glycine than do those of the gifted.

Questions for Discussion

1. In some cases of ADHD (attention deficit hyperactivity disorder) the impulsive, erratic behavior typical of affected people can be calmed with drugs that *stimulate* certain brain neurons. Based on what you have learned about neurotransmitter activity in this chapter, can you suggest a neural basis for this effect?
2. Most sensory neurons form synapses either on interneurons in the spinal cord or on motor neurons. However, in many vertebrates, certain sensory neurons in the nasal epithelium synapse directly on brain neurons that activate behavioral responses to odors. Suggest at least one reason why natural selection might favor such an arrangement.
3. How did evolution of chemical synapses make higher brain functions possible?
4. Use an Internet search engine with the term "Pediatric Neurotransmitter Disease" and, for one such disease, explain how the symptoms relate to neurotransmitter function.

Experimental Analysis

Design an experiment to test whether neurons are connected via electrical or chemical synapses.

Evolution Link

A biologist hypothesized that the mechanism for the propagation of action potentials down a neuron evolved only once. What evidence would you collect from animals living today to support or refute that hypothesis?