7.2 ELECTRICAL ACTIVITY IN AXONS

The permeability of the axon membrane to Na^+ and K^+ depends on gated channels that open in response to stimulation. Net diffusion of these ions occurs in two stages: first Na^+ moves into the axon, then K^+ moves out. This flow of ions, and the changes in the membrane potential that result, constitute an event called an action potential.

LEARNING OUTCOMES

After studying this section, you should be able to:

- ✔ Step-by-step, explain how an action potential is produced.
- ✔ Describe the characteristics of action potentials and explain how they are conducted by unmyelinated and myelinated axons.

All cells in the body maintain a potential difference (voltage) across the membrane, or **resting membrane potential (rmp),** in which the inside of the cell is negatively charged in comparison to the outside of the cell (for example, in neurons it is −70 mV). This potential difference is largely the result of the permeability properties of the plasma membrane (chapter 6, section 6.4). The membrane traps large, negatively charged organic molecules within the cell and permits only limited diffusion of positively charged inorganic ions. These properties result in an unequal distribution of these ions across the membrane. The action of the Na^+/K^+ pumps also helps to maintain a potential difference because they pump out 3 sodium ions (Na^+) for every 2 potassium ions (K^+) that they transport into the cell. Partly as a result of these pumps, Na^+ is more highly concentrated in the extracellular fluid than inside the cell, whereas K^+ is more highly concentrated within the cell.

Although all cells have a membrane potential, only a few types of cells have been shown to alter their membrane potential in response to stimulation. Such alterations in membrane potential are achieved by varying the membrane permeability to specific ions in response to stimulation. A central aspect of the physiology of neurons and muscle cells is their ability to produce and conduct these changes in membrane potential. Such an ability is termed *excitability* or *irritability.*

An increase in membrane permeability to a specific ion results in the diffusion of that ion down its *electrochemical gradient* (concentration and electrical gradients, considered together), either into or out of the cell. These *ion currents* occur only across limited patches of membrane where specific ion channels are located. Changes in the potential difference across the membrane at these points can be measured by the voltage developed between two microelectrodes (less than 1μm in diameter)—one placed inside the cell and the other placed outside the plasma membrane at the region being recorded. The voltage between these two recording electrodes can be visualized by connecting them to a computer or oscilloscope (fig. 7.11).

On a computer or oscilloscope screen, the voltage between the two recording electrodes over time is displayed as a line. This line deflects upward or downward in response to changes in the potential difference between the two electrodes. The display can be calibrated so that an upward deflection of the line indicates that the inside of the membrane has become less negative (or more positive) compared to the outside of the membrane. Conversely, a downward deflection of the line indicates that the inside of the cell has become more negative. The amplitude of the deflections (up or down) on the screen indicates the magnitude of the voltage changes.

If both recording electrodes are placed outside of the cell, the potential difference between the two will be zero (because there is no charge separation). When one of the two electrodes penetrates the plasma membrane, the computer

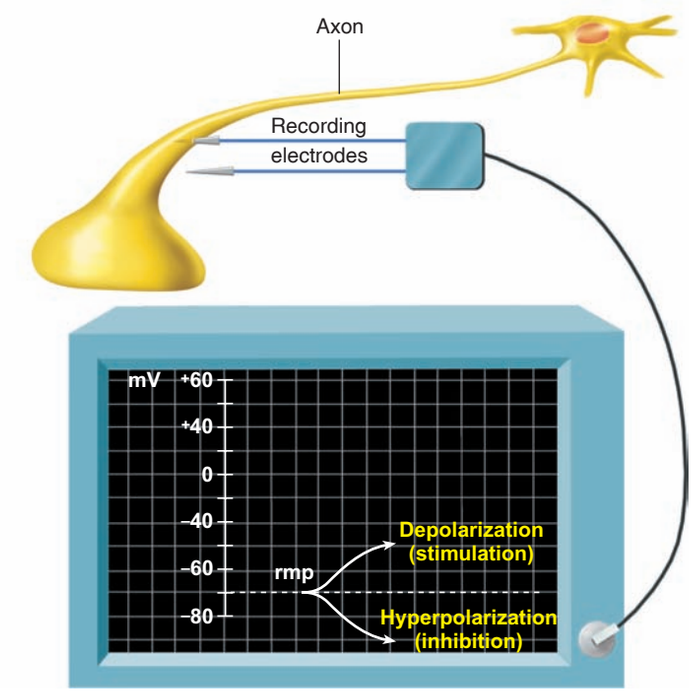

Figure 7.11 Observing depolarization and hyperpolarization. The difference in potential (in millivolts [mV]) between an intracellular and extracellular recording electrode is displayed on a computer or an oscilloscope screen. The resting membrane potential (rmp) of the axon may be reduced (depolarization) or increased (hyperpolarization). Depolarization is seen as a line deflecting upward from the rmp, and hyperpolarization by a line deflecting downward from the rmp.

will indicate that the intracellular electrode is electrically negative with respect to the extracellular electrode; a membrane potential is recorded. We will call this the *resting membrane potential (rmp)* to distinguish it from events described in later sections. All cells have a resting membrane potential, but its magnitude can be different in different types of cells. Neurons maintain an average rmp of −70 mV, for example, whereas heart muscle cells may have an rmp of −85 mV.

If appropriate stimulation causes positive charges to flow into the cell, the line will deflect upward. This change is called **depolarization** (or *hypopolarization*) because the potential difference between the two recording electrodes is reduced. A return to the resting membrane potential is known as **repolarization.** If stimulation causes the inside of the cell to become more negative than the resting membrane potential, the line on the oscilloscope will deflect downward. This change is called **hyperpolarization** (fig. 7.11). Hyperpolarization can be caused either by positive charges leaving the cell or by negative charges entering the cell.

Depolarization of a dendrite or cell body is *excitatory,* whereas hyperpolarization is *inhibitory,* in terms of their effects on the production of nerve impulses. The reasons for this relate to the nature of nerve impulses (action potentials), as will be explained shortly.

Ion Gating in Axons

The changes in membrane potential just described—depolarization, repolarization, and hyperpolarization—are caused by changes in the net flow of ions through ion channels in the membrane. Ions such as Na^+, K^+, and others pass through ion channels in the plasma membrane that are said to be *gated channels.* The "gates" are part of the proteins that compose the channels, and can open or close the ion channels in response to particular stimuli. When ion channels are closed, the plasma membrane is less permeable, and when the channels are open, the membrane is more permeable to an ion (fig. 7.12).

The ion channels for Na^+ and K^+ are specific for each ion. There are two types of channels for K^+. One type is gated, and the gates are closed at the resting membrane potential. The other type is not gated; these K^+ channels are thus always open and are often called *leakage channels.* Channels for Na^+, by contrast, are all gated and the gates are closed at the resting membrane potential. However, the gates of closed Na^+ channels appear to flicker open (and quickly close) occasionally, allowing some Na^+ to leak into the resting cell. As a result of these ion channel characteristics, the neuron at the resting membrane potential is much more permeable to K^+ than to Na^+, but some Na^+ does enter the cell. Because of the slight inward movement of Na^+, the resting membrane potential is a little less negative than the equilibrium potential for K^+.

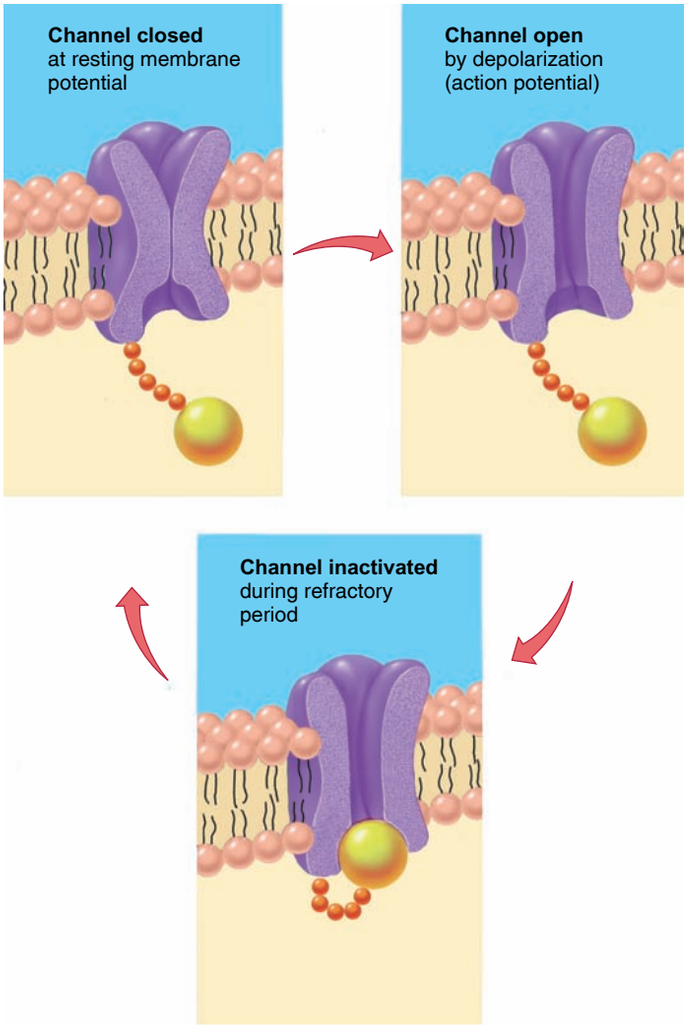

Figure 7.12 A model of a voltage-gated ion channel. The channel is closed at the resting membrane potential but opens in response to a threshold level of depolarization. This permits the diffusion of ions required for action potentials. After a brief period of time, the channel is inactivated by the "ball and chain" portion of a polypeptide chain (discussed later in the section on refractory periods).

Depolarization of a small region of an axon can be experimentally induced by a pair of stimulating electrodes that act as if they were injecting positive charges into the axon. If two recording electrodes are placed in the same region (one electrode within the axon and one outside), an upward deflection of the oscilloscope line will be observed as a result of this depolarization. If the depolarization is below a certain level, it will simply decay very shortly back to the resting membrane potential (see fig. 7.18). However, if a certain level of depolarization is achieved (from −70 mV to −55 mV, for example) by this artificial stimulation, a sudden and very rapid change in the membrane potential will be observed. This is because *depolarization to a threshold level causes the Na^+ channels to open.*

Now, for an instant, the plasma membrane is freely permeable to Na^+. Because the inside of the cell is negatively charged relative to the outside, and the concentration of Na^+ is lower inside of the cell, the **electrochemical gradient** (the combined electrical and concentration gradients) for Na^+ causes Na^+ to rush into the cell. This causes the membrane potential to move rapidly toward the sodium equilibrium potential (chapter 6, section 6.4). The number of Na^+ ions that actually rush in is relatively small compared to the total, so the extracellular Na^+ concentration is not measurably changed. However, the increased Na^+ within that tiny region of axon membrane greatly affects the membrane potential, as will be described shortly.

A fraction of a second after the Na^+ channels open, they close due to an inactivation process, as illustrated in figure 7.12. Just before they do, *the depolarization stimulus causes the gated K^+ channels to open.* This makes the membrane more permeable to K^+ than it is at rest, and K^+ diffuses down its electrochemical gradient out of the cell. This causes the membrane potential to move toward the potassium equilibrium potential (see fig. 7.14). The K^+ gates will then close and the permeability properties of the membrane will return to what they were at rest.

Because opening of the gated Na^+ and K^+ channels is stimulated by depolarization, these ion channels in the axon membrane are said to be **voltage-regulated,** or **voltage-gated, channels.** The channel gates are closed at the resting membrane potential of −70 mV and open in response to depolarization of the membrane to a threshold value.

Action Potentials

We will now consider the events that occur at one point in an axon, when a small region of axon membrane is stimulated artificially and responds with changes in ion permeabilities. The resulting changes in membrane potential at this point are detected by recording electrodes placed in this region of the axon. The nature of the stimulus *in vivo* (in the body), and the manner by which electrical events are conducted to different points along the axon, will be described in later sections.

When the axon membrane has been depolarized to a threshold level—in the previous example, by stimulating electrodes—the Na^+ gates open and the membrane becomes permeable to Na^+. This permits Na^+ to enter the axon by diffusion, which further depolarizes the membrane (makes the inside less negative, or more positive). The gates for the Na^+ channels of the axon membrane are voltage regulated, and so this additional depolarization opens more Na^+ channels and makes the membrane even more permeable to Na^+. As a result, more Na^+ can enter the cell and induce a depolarization that opens even more voltage-regulated Na^+ gates. A *positive feedback loop* (fig. 7.13) is thus created, causing the rate of Na^+ entry and depolarization to accelerate in an explosive fashion.

The explosive increase in Na^+ permeability results in a rapid reversal of the membrane potential in that region from −70 mV to +30 mV (fig. 7.13). At that point the channels for Na^+ close (they actually become inactivated,

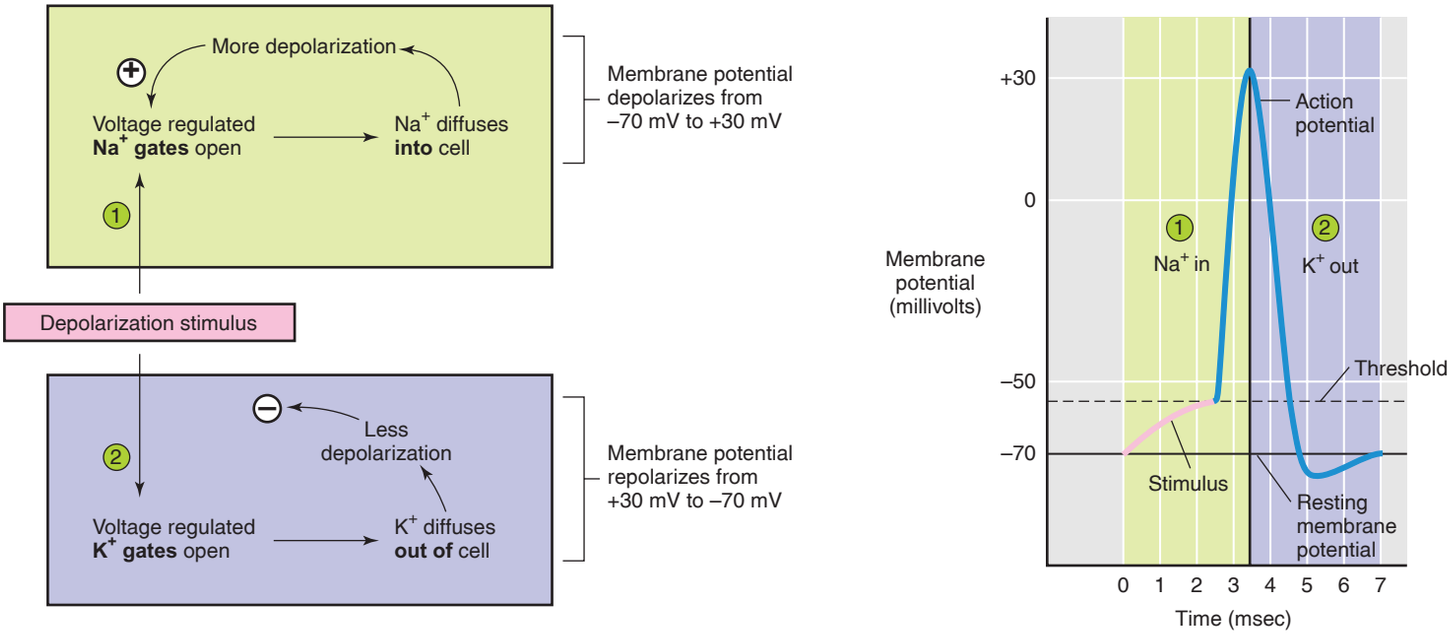

Figure 7.13 **Depolarization of an axon affects Na^+ and K^+ diffusion in sequence.** (*1*) Na^+ gates open and Na^+ diffuses into the cell. (*2*) After a brief period, K^+ gates open and K^+ diffuses out of the cell. An inward diffusion of Na^+ causes further depolarization, which in turn causes further opening of Na^+ gates in a positive feedback (+) fashion. The opening of K^+ gates and outward diffusion of K^+ makes the inside of the cell more negative, and thus has a negative feedback effect (–) on the initial depolarization.

CLINICAL APPLICATION

Local anesthetics block the conduction of action potentials in axons. They do this by reversibly binding to specific sites within the voltage-gated Na^+ channels, reducing the ability of membrane depolarization to produce action potentials. *Cocaine* was the first local anesthetic to be used, but because of its toxicity and potential for abuse, alternatives have been developed. The first synthetic analog of cocaine used for local anesthesia, *procaine,* was produced in 1905. Other local anesthetics of this type include *lidocaine* and *tetracaine.*

as illustrated in fig. 7.12), causing a rapid decrease in Na^+ permeability. This is why, at the top of the action potential, the voltage does not quite reach the +66 mV equilibrium potential for Na^+ (chapter 6, section 6.4). Also at this time, as a result of a time-delayed effect of the depolarization, voltage-gated K^+ channels open and K^+ diffuses rapidly out of the cell.

Because K^+ is positively charged, the diffusion of K^+ out of the cell makes the inside of the cell less positive, or more negative, and acts to restore the original resting membrane potential of −70 mV. This process is called **repolarization** and represents the completion of a *negative feedback loop* (fig. 7.13). These changes in Na^+ and K^+ diffusion and the resulting changes in the membrane potential they produce constitute an event called the **action potential,** or **nerve impulse.**

The correlation between ion movements and changes in membrane potential is shown in figure 7.14. The bottom portion of this figure illustrates the movement of Na^+ and K^+ through the axon membrane in response to a depolarization stimulus. Notice that the explosive increase in Na^+ diffusion causes rapid depolarization to 0 mV and then *overshoot* of the membrane potential so that the inside of the membrane actually becomes positively charged (almost +30 mV) compared to the outside (top portion of fig. 7.14). The greatly increased permeability to Na^+ thus drives the membrane potential toward the equilibrium potential for Na^+ (chapter 6, section 6.4). However, the peak action potential depolarization is less than the Na^+ equilibrium potential (+66 mV), due to inactivation of the Na^+ channels.

As the Na^+ channels are becoming inactivated, the gated K^+ channels open and the membrane potential moves toward the K^+ equilibrium potential. This outward diffusion of K^+ repolarizes the membrane. Actually, the membrane potential slightly overshoots the resting membrane potential, producing an *after-hyperpolarization* as a result of the continued outward movement of K^+ (fig. 7.14). However, the gated K^+ channels close before this after-hyperpolarization can reach the K^+ equilibrium potential (−90 mV). Then the after-hyperpolarization decays, and the resting membrane potential is reestablished.

The Na^+/K^+ pumps are constantly working in the plasma membrane. They pump out the Na^+ that entered the axon during an action potential and pump in the K^+ that had left.

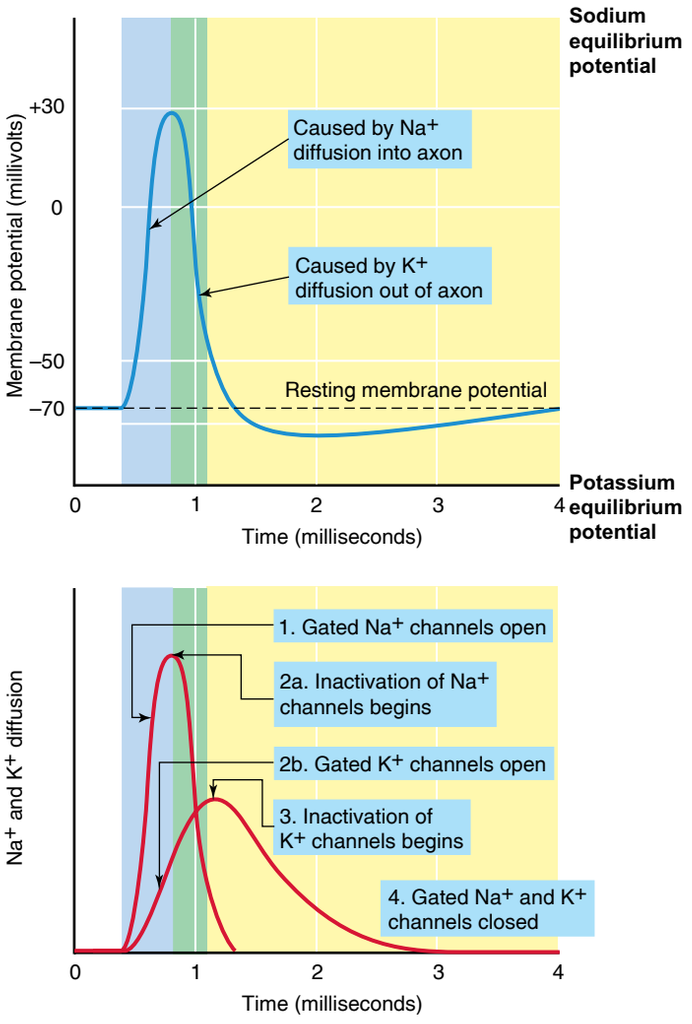

Figure 7.14 Membrane potential changes and ion movements during an action potential. The top graph depicts an action potential (blue line). The bottom graph (red lines) depicts the net diffusion of Na^+ and K^+ during the action potential. The *x*-axis for time is the same in both graphs, so that the depolarization, repolarization, and after-hyperpolarization in the top graph can be correlated with events in the Na^+ and K^+ channels and their effects on ion movements in the bottom graph. The inward movement of Na^+ drives the membrane potential toward the Na^+ equilibrium potential during the depolarization (rising) phase of the action potential, whereas the outward movement of K^+ drives the membrane potential toward the potassium equilibrium potential during the repolarization (falling) phase of the action potential.

Remember that only a relatively small amount of Na^+ and K^+ ions move into and out of the axon during an action potential. This movement is sufficient to cause changes in the membrane potential during an action potential but does not significantly affect the concentrations of these ions. Thus, active transport (by the Na^+/K^+ pumps) is still required to move Na^+ out of the axon and to move K^+ back into the axon after an action potential.

Notice that active transport processes are not directly involved in the production of an action potential; both depolarization and repolarization are produced by the diffusion of ions down their concentration gradients. A neuron poisoned with cyanide, so that it cannot produce ATP, can still produce action potentials for a period of time. After awhile, however, the lack of ATP for active transport by the Na^+/K^+ pumps will result in a decline in the concentration gradients, and therefore in the ability of the axon to produce action potentials. This shows that the Na^+/K^+ pumps are not directly involved; rather, they are required to maintain the concentration gradients needed for the diffusion of Na^+ and K^+ during action potentials.

All-or-None Law

Once a region of axon membrane has been depolarized to a threshold value, the positive feedback effect of depolarization on Na^+ permeability and of Na^+ permeability on depolarization causes the membrane potential to shoot toward about +30 mV. It does not normally become more positive than +30 mV because the Na^+ channels quickly close and the K^+ channels open. The length of time that the Na^+ and K^+ channels stay open is independent of the strength of the depolarization stimulus.

The amplitude (size) of action potentials is therefore **all or none.** When depolarization is below a threshold value, the voltage-regulated gates are closed; when depolarization reaches threshold, a maximum potential change (the action potential) is produced (fig. 7.15). Because the change from −70 mV to +30 mV and back to −70 mV lasts only about 3 msec, the image of an action potential on an oscilloscope screen looks like a spike. Action potentials are therefore sometimes called *spike potentials.*

The channels are open only for a fixed period of time because they are soon *inactivated,* a process different from simply closing the gates. Inactivation occurs automatically and lasts until the membrane has repolarized. Because of this automatic inactivation, all action potentials have about the same duration. Likewise, since the concentration gradient for Na^+ is relatively constant, the amplitudes of the action potentials are about equal in all axons at all times (from −70 mV to +30 mV, or about 100 mV in total amplitude).

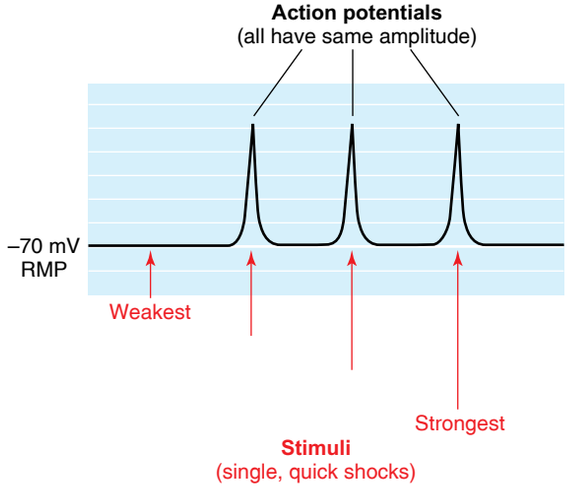

Figure 7.15 **The all-or-none law of action potentials.** A single, quick shock delivered to an axon can serve as a depolarizing stimulus. If the stimulus is below threshold, no action potential is produced by the axon. Once the stimulus has reached threshold, a full action potential is produced. Any greater stimulus does not produce greater action potentials. Thus, action potentials are not graded (varied); they are all-or-none.

Coding for Stimulus Intensity

Because action potentials are all-or-none events, a stronger stimulus cannot produce an action potential of greater amplitude. The code for stimulus strength in the nervous system is not amplitude modulated (AM). When a greater stimulus strength is applied to a neuron, identical action potentials are produced more frequently (more are produced per second). Therefore, the code for stimulus strength in the nervous system is frequency modulated (FM). This concept is illustrated in figure 7.16.

When an entire collection of axons (in a nerve) is stimulated, different axons will be stimulated at different stimulus intensities. A weak stimulus will activate only those few axons with low thresholds, whereas stronger stimuli can activate axons with higher thresholds. As the intensity of stimulation

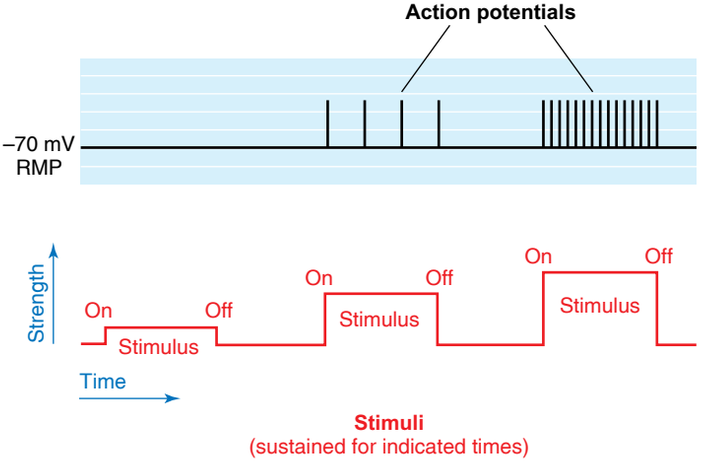

Figure 7.16 **The effect of stimulus strength on action-potential frequency.** Stimuli that are sustained for a period of time are given to an axon. In the first case, the stimulus is weaker than required to reach threshold, and no action potentials are produced. In the second case, a stronger stimulus is delivered, which causes the production of a few action potentials while the stimulus is sustained. In the last case, an even stronger stimulus produces a greater number of action potentials in the same time period. This demonstrates that stimulus strength is coded by the frequency (rather than the amplitude) of action potentials.

increases, more and more axons will become activated. This process, called **recruitment,** represents another mechanism by which the nervous system can code for stimulus strength.

Refractory Periods

If a stimulus of a given intensity is maintained at one point of an axon and depolarizes it to threshold, action potentials will be produced at that point at a given frequency (number per second). As the stimulus strength is increased, the frequency of action potentials produced at that point will increase accordingly. As action potentials are produced with increasing frequency, the time between successive action potentials will decrease—but only up to a minimum time interval. The interval between successive action potentials will never become so short as to allow a new action potential to be produced before the preceding one has finished.

During the time that a patch of axon membrane is producing an action potential, it is incapable of responding—is *refractory*—to further stimulation. If a second stimulus is applied during most of the time that an action potential is being produced, the second stimulus will have no effect on the axon membrane. The membrane is thus said to be in an **absolute refractory period;** it cannot respond to any subsequent stimulus.

The cause of the absolute refractory period is now understood at a molecular level. In addition to the voltage-regulated gates that open and close the channel, an ion channel may have a polypeptide that functions as a "ball and chain" apparatus dangling from its cytoplasmic side (see fig. 7.12). After a voltage-regulated channel is opened by depolarization for a set time, it enters an *inactive state.* The inactivated channel cannot be opened by depolarization. The reason for its inactivation depends on the type of voltage-gated channel. In the type of channel shown in figure 7.12, the channel becomes blocked by a molecular ball attached to a chain. In a different type of voltage-gated channel, the channel shape becomes altered through molecular rearrangements. The inactivation ends after a fixed period of time in both cases, either because the ball leaves the mouth of the channel, or because molecular rearrangements restore the resting form of the channel. In the resting state, unlike the inactivated state, the channel is closed but it can be opened in response to a depolarization stimulus of sufficient strength.

The transition of the gated Na^+ channels from the inactivated to the closed state doesn't occur in all channels at the same instant. When enough Na^+ channels are in the closed rather than inactivated state, it is theoretically possible to again stimulate the axon with a sufficiently strong stimulus. However, while the K^+ channels are still open and the membrane is still in the process of repolarizing, the effects of the outward movement of K^+ must be overcome, making it even more difficult to depolarize the axon to threshold. Only a very strong depolarization stimulus will be able to overcome these obstacles and produce a second action potential. Thus, during the time that the Na^+ channels are in the process of recovering from their inactivated state and the

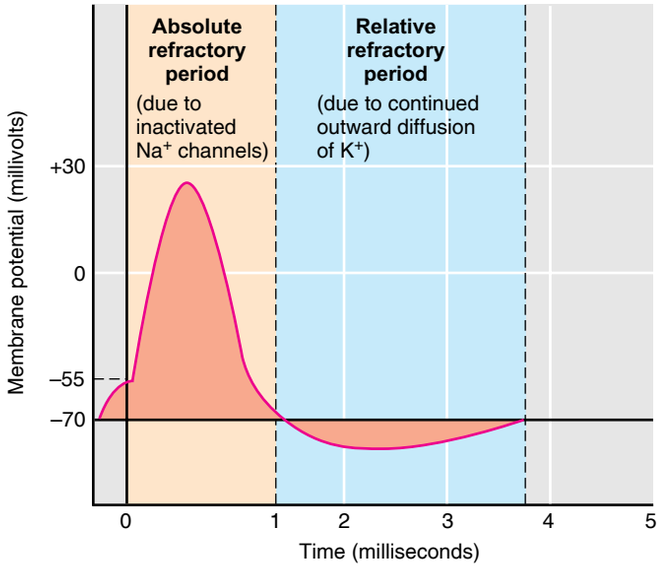

Figure 7.17 **Absolute and relative refractory periods.** While a segment of axon is producing an action potential, the membrane is absolutely or relatively resistant (refractory) to further stimulation.

K^+ channels are still open, the membrane is said to be in a **relative refractory period** (fig. 7.17).

Because the cell membrane is refractory when it is producing an action potential, each action potential remains a separate, all-or-none event. In this way, as a continuously applied stimulus increases in intensity, its strength can be coded strictly by the frequency of the action potentials it produces at each point of the axon membrane.

One might think that after a large number of action potentials have been produced, the relative concentrations of Na^+ and K^+ would be changed in the extracellular and intracellular compartments. This is not the case. In a typical mammalian axon, for example, only 1 intracellular K^+ in 3,000 would be exchanged for a Na^+ to produce an action potential. Since a typical neuron has about 1 million Na^+/K^+ pumps that can transport nearly 200 million ions per second, these small changes can be quickly corrected.

Cable Properties of Neurons

If a pair of stimulating electrodes produces a depolarization that is too weak to cause the opening of voltage-regulated Na^+ gates—that is, if the depolarization is below threshold (about −55 mV)—the change in membrane potential will be *localized* to within 1 to 2 mm of the point of stimulation (fig. 7.18). For example, if the stimulus causes depolarization from −70 mV to −60 mV at one point, and the recording electrodes are placed only 3 mm away from the stimulus, the membrane potential recorded will remain at −70 mV (the resting potential). The axon is thus a very poor conductor compared to a metal wire.

The **cable properties** of neurons are their abilities to conduct charges through their cytoplasm. These cable properties are quite poor because there is a high internal resistance to the

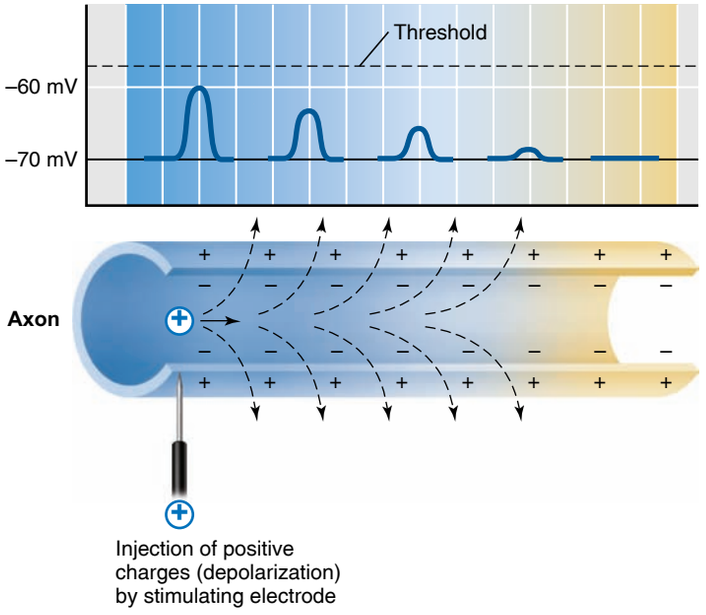

Figure 7.18 **Cable properties of an axon.** The cable properties of an axon are the properties that permit it to conduct potential changes over distances. If a stimulating electrode injects positive charges and produces a depolarization (*blue*) at one point in the axon, the depolarization will quickly dissipate if it doesn't trigger an action potential. The decreasing amplitude of the depolarization is due to leakage of charges through the axon membrane (*dashed arrows*). This results in a poor ability of the axon to conduct changes in potential over distances.

spread of charges and because many charges leak out of the axon through its membrane (fig. 7.18). If an axon had to conduct only through its cable properties, therefore, no axon could be more than a millimeter in length. The fact that some axons are a meter or more in length suggests that the conduction of nerve impulses does not rely on the cable properties of the axon.

Conduction of Nerve Impulses

When stimulating electrodes artificially depolarize one point of an axon membrane to a threshold level, voltage-regulated channels open and an action potential is produced at that small region of axon membrane containing those channels. For about the first millisecond of the action potential, when the membrane voltage changes from −70 mV to +30 mV, a current of Na^+ enters the cell by diffusion because of the opening of the Na^+ gates. Each action potential thus "injects" positive charges (sodium ions) into the axon (fig. 7.19).

These positively charged sodium ions are conducted, by the cable properties of the axon, to an adjacent region that still has a membrane potential of −70 mV. Within the limits of the cable properties of the axon (1 to 2 mm), this helps to depolarize the adjacent region of axon membrane. When this adjacent region of membrane reaches a threshold level of depolarization, it too produces the action potential as its voltage-regulated gates open.

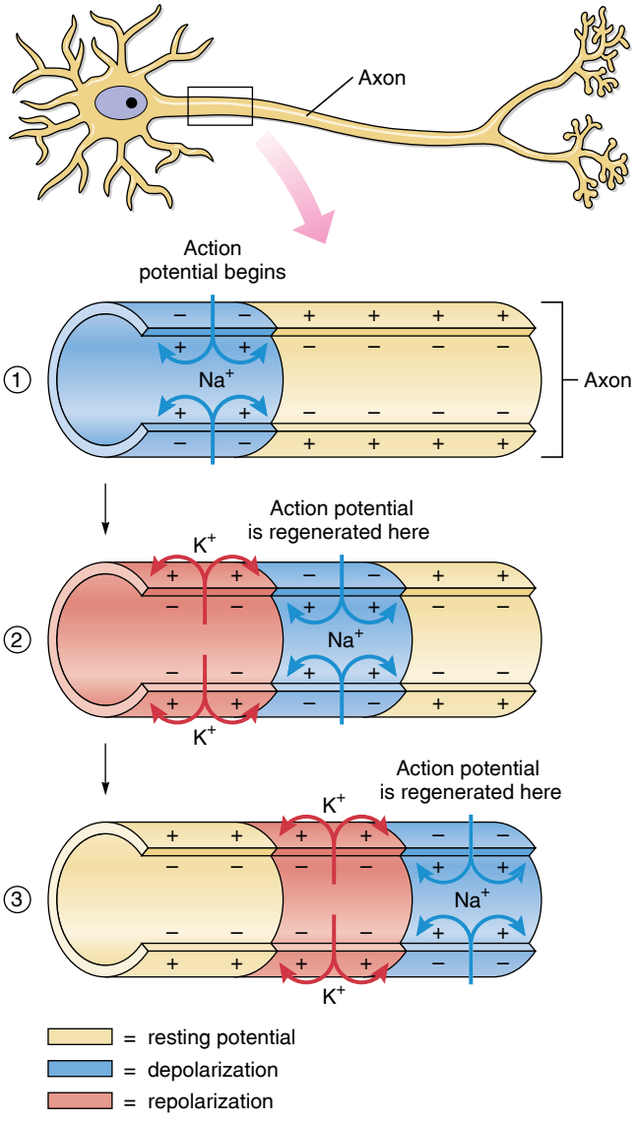

Figure 7.19 **The conduction of action potentials in an unmyelinated axon.** Each action potential "injects" positive charges that spread to adjacent regions. The region that has just produced an action potential is refractory. The next region, not having been stimulated previously, is partially depolarized. As a result, its voltage-regulated Na^+ gates open and the process is repeated. Successive segments of the axon thereby regenerate, or "conduct," the action potential.

The action potential produced at the first location in the axon membrane (usually at the axon hillock) thus serves as the depolarization stimulus for the next region of the axon membrane, which can then produce the action potential. The action potential in this second region, in turn, serves as a depolarization stimulus for the production of the action potential in a third region, and so on. This explains how the action potential is produced at all regions of the axon beyond the initial segment at the axon hillock. (The depolarization stimulus for the action potential at the initial segment of the axon results from synaptic transmission, discussed in section 7.3.)

Conduction in an Unmyelinated Axon

In an unmyelinated axon, every patch of membrane that contains Na^+ and K^+ channels can produce an action potential. Action potentials are thus produced along the entire length of the axon. The cablelike spread of depolarization induced by the influx of Na^+ during one action potential helps to depolarize the adjacent regions of membrane—a process that is also aided by movements of ions on the outer surface of the axon membrane (fig. 7.19). This process would depolarize the adjacent membranes on each side of the region to produce the action potential, but the area that had previously produced one cannot produce another at this time because it is still in its refractory period.

It is important to recognize that action potentials are not really "conducted," although it is convenient to use that word. Each action potential is a separate, complete event that is repeated, or *regenerated,* along the axon's length. This is analogous to the "wave" performed by spectators in a stadium. One person after another gets up (depolarization) and then sits down (repolarization). It is thus the "wave" that travels (the repeated action potential at different locations along the axon membrane), not the people.

The action potential produced at the end of the axon is thus a completely new event that was produced in response to depolarization from the previous region of the axon membrane. The action potential produced at the last region of the axon has the same amplitude as the action potential produced at the first region. Action potentials are thus said to be **conducted without decrement** (without decreasing in amplitude).

The spread of depolarization by the cable properties of an axon is fast compared to the time it takes to produce an action potential. Thus, the more action potentials along a given stretch of axon that have to be produced, the slower the conduction. Because action potentials must be produced at every fraction of a micrometer in an unmyelinated axon, the conduction rate is relatively slow. This conduction rate is somewhat faster if the unmyelinated axon is thicker, because thicker axons have less resistance to the flow of charges (so conduction of charges by cable properties is faster). The conduction rate is substantially faster if the axon is myelinated, because fewer action potentials are produced along a given length of myelinated axon.

Conduction in a Myelinated Axon

The myelin sheath provides insulation for the axon, preventing movements of Na^+ and K^+ through the membrane. If the myelin sheath were continuous, therefore, action potentials could not be produced. The myelin thus has interruptions—the *nodes of Ranvier,* as previously described.

Because the cable properties of axons can conduct depolarizations over only a very short distance (1 to 2 mm), the nodes of Ranvier cannot be separated by more than this distance. Studies have shown that Na^+ channels are highly concentrated at the nodes (estimated at 10,000 per square micrometer) and almost absent in the regions of axon membrane between the nodes. Action potentials, therefore, occur only at the nodes of Ranvier (fig. 7.20) and seem to "leap" from node to node—a process called **saltatory conduction** (from the Latin *saltario* = leap). The leaping is, of course, just a metaphor; the action potential at one node depolarizes the membrane at the next node to threshold, so that a new action potential is produced at the next node of Ranvier.

Myelinated axons conduct the action potential faster than unmyelinated axons. This is because myelinated axons have voltage-gated channels only at the nodes of Ranvier, which

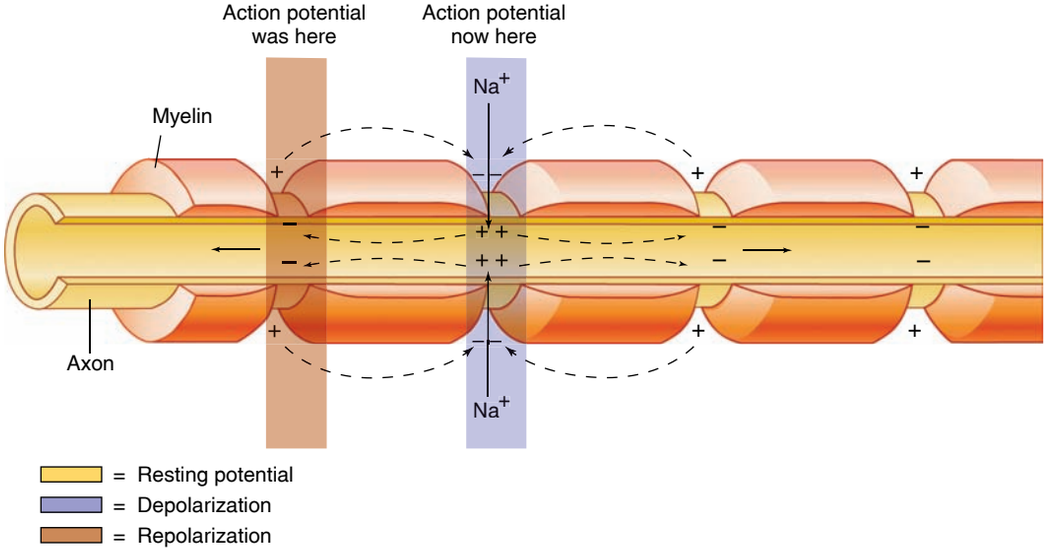

Figure 7.20 **The conduction of a nerve impulse in a myelinated axon.** Because the myelin sheath prevents inward Na^+ current, action potentials can be produced only at gaps in the myelin sheath called the nodes of Ranvier. This "leaping" of the action potential from node to node is known as saltatory conduction.

Table 7.3 | Conduction Velocities and Functions of Mammalian Nerves of Different Diameters

Diameter (μm)	Conduction Velocity (m/sec)	Examples of Functions Served
12–22	70–120	Sensory: muscle position
5–13	30–90	Somatic motor fibers
3–8	15–40	Sensory: touch, pressure
1–5	12–30	Sensory: pain, temperature
1–3	3–15	Autonomic fibers to ganglia
0.3–1.3	0.7–2.2	Autonomic fibers to smooth and cardiac muscles

are about 1 mm apart, whereas unmyelinated axons have these channels along their entire length. Because myelinated axons have more cablelike spread of depolarization (which is faster), and fewer sites at which the action potential is produced (which is slower) than unmyelinated axons, the conduction is faster in a myelinated axon. Conduction rates in the human nervous system vary from 1.0 m/sec—in thin, unmyelinated fibers that mediate slow, visceral responses—to faster than 100 m/sec (225 miles per hour)—in thick, myelinated fibers involved in quick stretch reflexes in skeletal muscles (table 7.3).

In summary, the speed of action potential conduction is increased by (1) increased diameter of the axon, because this reduces the resistance to the spread of charges by cable properties; and (2) myelination, because the myelin sheath results in saltatory conduction of action potentials. These methods of affecting conduction speed are generally combined in the nervous system: the thinnest axons tend to be unmyelinated and the thickest tend to be myelinated.

✔ | CHECKPOINT

6. Define the terms *depolarization* and *repolarization,* and illustrate these processes graphically.
7. Describe how the permeability of the axon membrane to Na^+ and K^+ is regulated and how changes in permeability to these ions affect the membrane potential.
8. Describe how gating of Na^+ and K^+ in the axon membrane results in the production of an action potential.
9. Explain the all-or-none law of action potentials, and describe the effect of increased stimulus strength on action potential production. How do the refractory periods affect the frequency of action potential production?
10. Describe how action potentials are conducted by unmyelinated nerve fibers. Why is saltatory conduction in myelinated fibers more rapid?

7.3 THE SYNAPSE

Axons end close to, or in some cases at the point of contact with, another cell. Once action potentials reach the end of an axon, they directly or indirectly stimulate (or inhibit) the other cell. In specialized cases, action potentials can directly pass from one cell to another. In most cases, however, the action potentials stop at the axon terminal, where they stimulate the release of a chemical neurotransmitter that affects the next cell.

LEARNING OUTCOMES

After studying this section, you should be able to:

- ✔ Describe the structure and function of electrical and chemical synapses.
- ✔ Identify the nature of excitatory and inhibitory postsynaptic potentials.

A **synapse** is the functional connection between a neuron and a second cell. In the CNS, this other cell is also a neuron. In the PNS, the other cell may be either a neuron or an *effector cell* within a muscle or gland. Although the physiology of neuron-neuron synapses and neuron-muscle synapses is similar, the latter synapses are often called **myoneural,** or **neuromuscular, junctions.**

Neuron-neuron synapses usually involve a connection between the axon of one neuron and the dendrites, cell body, or axon of a second neuron. These are called, respectively, *axodendritic, axosomatic,* and *axoaxonic synapses.* In almost all synapses, transmission is in one direction only—from the axon of the first (or **presynaptic**) neuron to the second (or **postsynaptic**) neuron. Most commonly, the synapse occurs between the axon of the presynaptic neuron and the dendrites or cell body of the postsynaptic neuron.

In the early part of the twentieth century, most physiologists believed that synaptic transmission was *electrical*—that is, that action potentials were conducted directly from one cell to the next. This was a logical assumption, given that nerve endings appeared to touch the postsynaptic cells and that the delay in synaptic conduction was extremely short (about 0.5 msec). Improved histological techniques, however, revealed tiny gaps in the synapses, and experiments demonstrated that the actions of autonomic nerves could be duplicated by certain chemicals. This led to the hypothesis that synaptic transmission might be *chemical*—that the presynaptic nerve endings might release chemicals called **neurotransmitters** that stimulated action potentials in the postsynaptic cells.

In 1921 a physiologist named Otto Loewi published the results of experiments suggesting that synaptic transmission was indeed chemical, at least at the junction between a branch of the vagus nerve (chapter 9; see fig. 9.6) and the