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Nerve Cells, Neural Circuitry, and Behavior

The remarkable range of human behavior depends on a sophisticated array of sensory receptors connected to the brain, a highly flexible neural organ that selects from among the stream of sensory signals those events in the environment and in the internal milieu of the body that are important for the individual. The brain actively organizes sensory information for perception, action, decision-making, aesthetic appreciation, and future reference—that is to say, memory. It also ignores and discards information judiciously, one hopes, and reports to other brains about some of these operations and their psychological manifestations. All this is accomplished by interconnected nerve cells.

Individual nerve cells, or neurons, are the basic signaling units of the brain. The human brain contains a huge number of these cells, on the order of 86 billion neurons, that can be classified into at least a thousand different types. Yet this great variety of neurons is less of a factor in the complexity of human behavior than is their organization into anatomical circuits with precise functions. Indeed, one key organizational principle of the brain is that nerve cells with *similar* properties can produce different actions because of the way they are interconnected.

Because relatively few principles of organization of the nervous system give rise to considerable functional complexity, it is possible to learn a great deal about how the nervous system produces behavior by focusing on five basic features of the nervous system:

1. The structural components of individual nerve cells;
2. The mechanisms by which neurons produce signals within themselves and between each other;
3. The patterns of connection between nerve cells and between nerve cells and their targets (muscle and gland effectors);
4. The relationship of different patterns of interconnection to different types of behavior; and
5. How neurons and their connections are modified by experience.

The parts of this book are organized around these five major topics. In this chapter, we introduce these topics in turn in an overview of the neural control of behavior. We first consider the structure and function of neurons and the glial cells that surround and support them. We then examine how individual cells organize and transmit signals and how signaling between a few interconnected nerve cells produces a simple behavior, the knee-jerk reflex. We then extend these ideas to more complex behaviors, mediated by more complex and malleable circuits.

The Nervous System Has Two Classes of Cells

There are two main classes of cells in the nervous system: nerve cells, or neurons, and glial cells, or glia.

Nerve Cells Are the Signaling Units of the Nervous System

A typical neuron has four morphologically defined regions: (1) the cell body, (2) dendrites, (3) an axon, and (4) presynaptic terminals (Figure 3–1). As we shall see, each region has a distinct role in generating signals and communicating with other nerve cells.

The cell body or *soma* is the metabolic center of the cell. It includes the nucleus, which contains the genes of the cell, and the endoplasmic reticulum, an extension of the nucleus where the cell's proteins are synthesized. The cell body usually gives rise to two kinds of processes: several short *dendrites* and one long, tubular *axon*. Dendrites branch out in tree-like fashion and are the main apparatus for receiving incoming signals

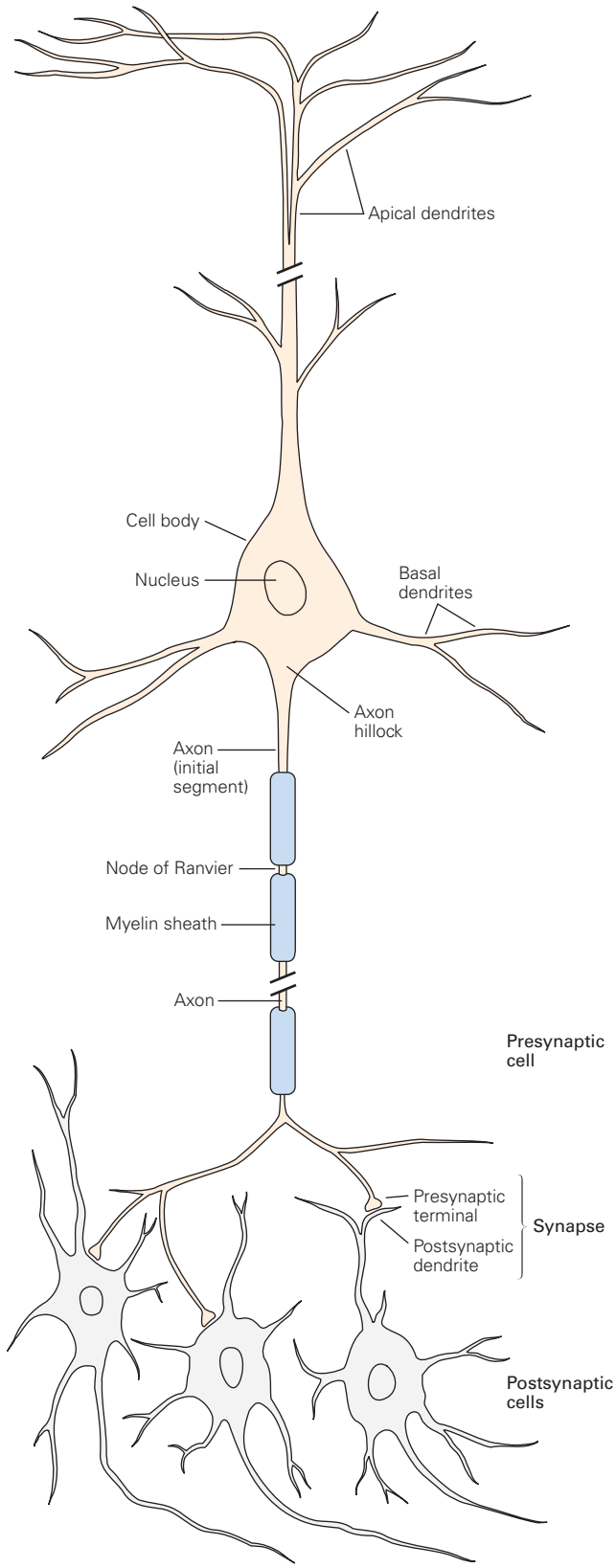

Figure 3–1 (Right) The structure of a neuron. Most neurons in the vertebrate nervous system have several main features in common. The cell body contains the nucleus, the storehouse of genetic information, and gives rise to two types of cell processes: axons and dendrites. Axons are the transmitting element of neurons; they vary greatly in length, some extending more than 1 m within the body. Most axons in the central nervous system are very thin (between 0.2 µm and 20 µm in diameter) compared with the diameter of the cell body (50 µm or more). Many axons are insulated by a sheath of fatty myelin that is regularly interrupted at gaps called the nodes of Ranvier. The action potential, the cell's conducting signal, is initiated at the initial segment of the axon and propagates to the synapse, the site at which signals flow from one neuron to another. Branches of the axon of the presynaptic neuron transmit signals to the postsynaptic cell. The branches of a single axon may form synapses with as many as 1,000 postsynaptic neurons. The apical and basal dendrites together with the cell body are the input elements of the neuron, receiving signals from other neurons.

from other nerve cells. The axon typically extends some distance from the cell body before it branches, allowing it to carry signals to many target neurons. An axon can convey electrical signals over distances ranging from 0.1 mm to 1 m. These electrical signals, or *action potentials*, are initiated at a specialized trigger region near the origin of the axon called the *initial segment* from which the action potentials propagate down the axon without failure or distortion at speeds of 1 to 100 m/s. The amplitude of an action potential traveling down the axon remains constant at 100 mV because the action potential is an all-or-none impulse that is regenerated at regular intervals along the axon (Figure 3–2).

Action potentials are the signals by which the brain receives, analyzes, and conveys information. These signals are highly stereotyped throughout the nervous system, even though they are initiated by a great variety of events in the environment that impinge on our bodies—from light to mechanical contact, from odorants to pressure waves. The physiological signals that convey information about vision are identical to those that carry information about odors. Here we see a key principle of brain function: the type of information conveyed by an action potential is determined not by the form of the signal but by the pathway the signal travels in the brain. The brain thus analyzes and interprets patterns of incoming electrical signals carried over specific pathways, and in turn creates our sensations of sight, touch, taste, smell, and sound.

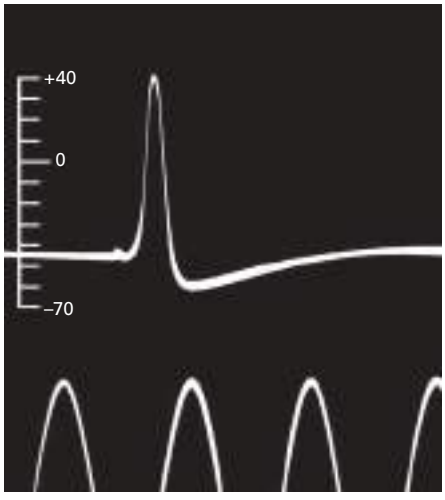

Figure 3–2 This historic tracing is the first published intracellular recording of an action potential. It was recorded in 1939 by Alan Hodgkin and Andrew Huxley from a squid giant axon, using glass capillary electrodes filled with sea water. The timing pulses (bottom) are separated by 2 ms. The vertical scale indicates the potential of the internal electrode in millivolts, the sea water outside being taken as zero potential. (Reproduced, with permission, from Hodgkin and Huxley 1939.)

To increase the speed by which action potentials are conducted, large axons are wrapped in an insulating sheath of a lipid substance, myelin. The sheath is interrupted at regular intervals by the nodes of Ranvier, uninsulated spots on the axon where the action potential is regenerated. (Myelination is discussed in detail in Chapters 7 and 8 and action potentials in Chapter 10.)

Near its end, the axon divides into fine branches that contact other neurons at specialized zones of communication known as *synapses*. The nerve cell transmitting a signal is called the *presynaptic cell*; the cell receiving the signal is the *postsynaptic cell*. The presynaptic cell transmits signals from specialized enlarged regions of its axon's branches, called *presynaptic terminals* or *nerve terminals*. The presynaptic and postsynaptic cells are separated by a very narrow space, the *synaptic cleft*. Most presynaptic terminals end on the postsynaptic neuron's dendrites, but some also terminate on the cell body or, less often, at the beginning or end of the axon of the postsynaptic cell (see Figure 3–1). Some presynaptic neurons excite their postsynaptic target cells; other presynaptic neurons inhibit their target cells.

The neuron doctrine (Chapter 1) holds that each neuron is a discrete cell with distinctive processes arising from its cell body and that neurons are the signaling units of the nervous system. In retrospect, it is hard to appreciate how difficult it was for scientists to accept this elementary idea when first proposed. Unlike other tissues, whose cells have simple shapes and fit into a single field of the light microscope, nerve cells have complex shapes. The elaborate patterns of dendrites and the seemingly endless course of some axons made it extremely difficult to establish a relationship between these elements. Even after the anatomists Jacob Schleiden and Theodor Schwann put forward the cell theory in the early 1830s—and the idea that cells are the structural units of all living matter became a central dogma of biology—most anatomists did not accept that the cell theory applied to the brain, which they thought of as a continuous, web-like reticulum of very thin processes.

The coherent structure of the neuron did not become clear until late in the 19th century, when Ramón y Cajal began to use the silver-staining method introduced by Golgi. Still used today, this method has two advantages. First, in a random manner that is not understood, the silver solution stains only about 1% of the cells in any particular brain region, making it possible to examine a single neuron in isolation from

its neighbors. Second, the neurons that do take up the stain are delineated in their entirety, including the cell body, axon, and full dendritic tree. The stain reveals that there is no cytoplasmic continuity between neurons, and Cajal concluded, prophetically and correctly, that there is no continuity even at synapses between two cells.

Ramón y Cajal applied Golgi's method to the embryonic nervous systems of many animals as well as humans. By examining the structure of neurons in almost every region of the nervous system, he could describe classes of nerve cells and map the precise connections between many of them. In this way, Ramón y Cajal deduced, in addition to the neuron doctrine, two other principles of neural organization that would prove particularly valuable in studying communication in the nervous system.

The first of these, the *principle of dynamic polarization*, states that electrical signals within a nerve cell flow in only one direction: from the postsynaptic sites of the neuron, usually the dendrites and cell body, to the trigger region at the axon. From there, the action potential is propagated along the entire length of the axon to its terminals. In most neurons studied to date, electrical signals in fact travel along the axon in one direction.

The second principle advanced by Ramón y Cajal, *connectional specificity*, states that nerve cells do not connect randomly with one another in the formation of networks but make specific connections—at particular contact points—with certain postsynaptic target cells and not with others. The principles of dynamic polarization and connectional specificity are the basis of the modern cellular-connectionist approach to studying the brain.

Ramón y Cajal was also among the first to realize that the feature that most distinguishes one type of neuron from another is form, specifically the number of the processes arising from the cell body. Neurons are thus classified into three large groups: unipolar, bipolar, and multipolar.

Unipolar neurons are the simplest because they have a single primary process, which usually gives rise to many branches. One branch serves as the axon; other branches function as receiving structures (Figure 3–3A). These cells predominate in the nervous systems of invertebrates; in vertebrates, they occur in the autonomic nervous system.

Bipolar neurons have an oval soma that gives rise to two distinct processes: a dendritic structure that receives signals from other neurons and an axon that carries information toward the central nervous system (Figure 3–3B). Many sensory cells are bipolar, including those in the retina and olfactory epithelium of the nose. The receptor neurons that convey touch, pressure, and pain signals to the spinal cord develop initially as bipolar cells, but the two cell processes fuse into a single continuous structure that emerges from a single point in the cell body, and the dendrite is endowed with the specializations that render it an axon. In these so-called pseudo-unipolar cells, one axon transmits information from the sensory receptors in the skin, joints, and muscle toward the cell body, while the other carries this sensory information to the spinal cord (Figure 3–3C).

Multipolar neurons predominate in the nervous system of vertebrates. They typically have a single axon and many dendritic structures emerging from various points around the cell body (Figure 3–3D). Multipolar cells vary greatly in shape, especially in the length of their axons and in the extent, dimensions, and intricacy of their dendritic branching. Usually the extent of branching correlates with the number of synaptic contacts that other neurons make onto them. A spinal motor neuron with a relatively modest number of dendrites receives about 10,000 contacts—1,000 on the cell body and 9,000 on dendrites. In Purkinje cells in the cerebellum, the dendritic tree is much larger and bushier, receiving as many as a million contacts!

Nerve cells are also classified into three major functional categories: sensory neurons, motor neurons, and interneurons. *Sensory neurons* carry information from the body's peripheral sensors into the nervous system for the purpose of both perception and motor coordination. Some primary sensory neurons are called *afferent neurons*, and the two terms are used interchangeably. The term *afferent* (carried toward the central nervous system) applies to all information reaching the central nervous system from the periphery, whether or not this information leads to sensation. The term *sensory* designates those afferent neurons that convey information to the central nervous system from the sensory epithelia, from joint sensory receptors, or from muscle, but the concept has been expanded to include neurons in primary and secondary cortical areas that respond to changes in a sensory feature, such as displacement of an object in space, a shift in sound frequency, or the angular rotation of the head (via vestibular organs in the ear) or even something as complex as a face.

The term *efferent* applies to all information carried from the central nervous system toward the motor organs, whether or not this information leads to action. *Motor neurons* carry commands from the brain or spinal cord to muscles and glands (efferent information). The traditional definition of a *motor neuron* (or motoneuron) is a neuron that excites a muscle, but the designation of motor neuron now includes other

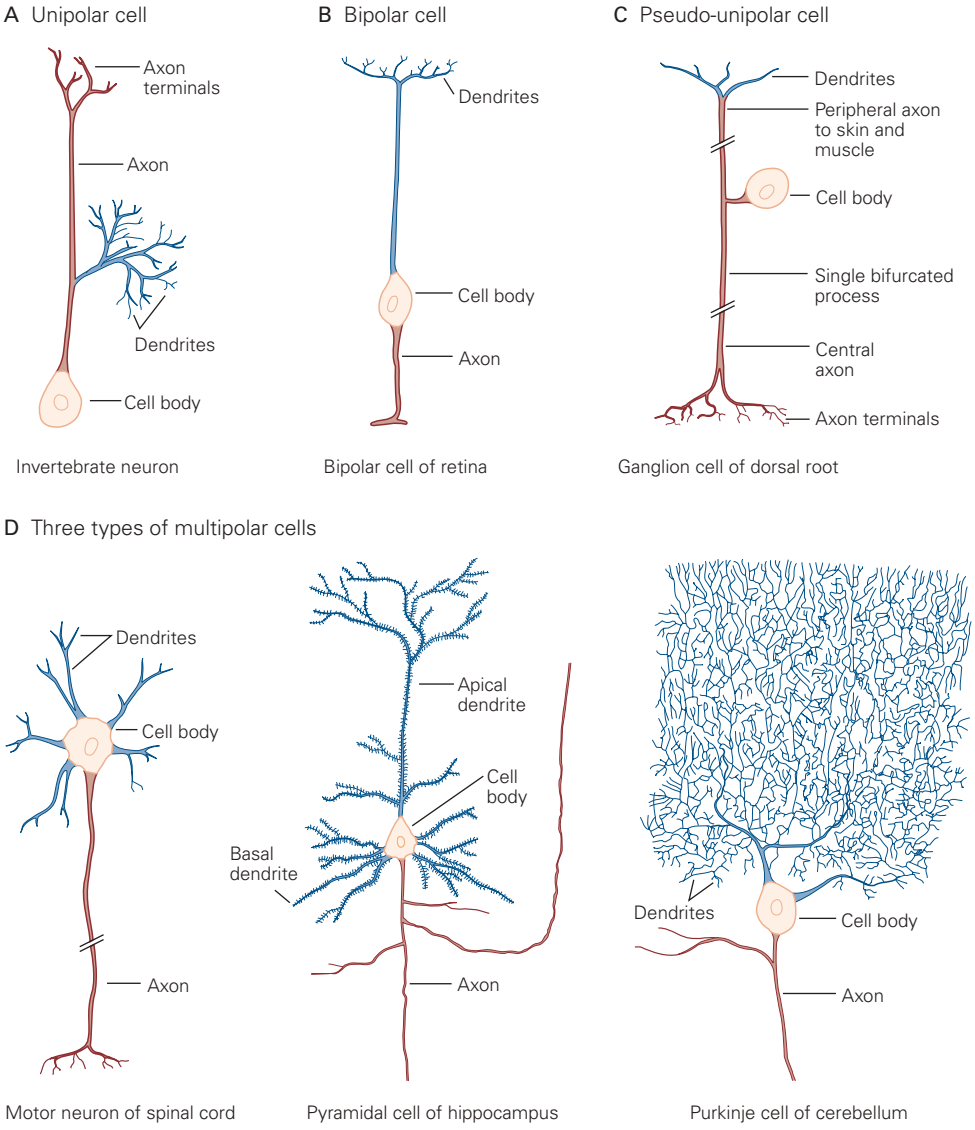

Figure 3–3 Neurons are classified as unipolar, bipolar, or multipolar according to the number of processes that originate from the cell body.

A. Unipolar cells have a single process emanating from the cell. Different segments serve as receptive surfaces or releasing terminals. Unipolar cells are characteristic of the invertebrate nervous system.

B. Bipolar cells have two types of processes that are functionally specialized. The dendrite receives electrical signals and the axon transmits signals to other cells.

C. Pseudo-unipolar cells, which are variants of bipolar cells, carry somatosensory information to the spinal cord. During development, the two processes of the embryonic bipolar cell fuse and emerge from the cell body as a single process that has two functionally distinct segments. Both segments function as axons; one extends to peripheral skin or muscle, the other to the central spinal cord. (Adapted, with permission, from Ramón y Cajal 1933.)

D. Multipolar cells have a single axon and many dendrites. They are the most common type of neuron in the mammalian nervous system. Three examples illustrate the large diversity of these cells. Spinal motor neurons innervate skeletal muscle fibers. Pyramidal cells have a roughly triangular cell body; dendrites emerge from both the apex (the apical dendrite) and the base (the basal dendrites). Pyramidal cells are found in the hippocampus and throughout the cerebral cortex. Purkinje cells of the cerebellum are characterized by a rich and extensive dendritic tree that accommodates an enormous number of synaptic inputs. (Adapted, with permission, from Ramón y Cajal 1933.)

neurons that do not innervate muscle directly but that command action indirectly. A useful characterization of motor and sensory neurons alike is their temporal fidelity to matters outside the nervous system. Their activity keeps up with changes in external stimuli and dynamical forces exerted by the body musculature. Sensory neurons supply the brain with data, whereas motor neurons convert ideation into praxis. Together they compose our interface with the world.

Interneurons comprise the most numerous functional category and are subdivided into two classes: relay and local. Relay or projection interneurons have long axons and convey signals over considerable distances, from one brain region to another. Local interneurons have short axons because they form connections with nearby neurons in local circuits. Since almost every neuron can be regarded as an interneuron, the term is often used to distinguish between neurons that project to another neuron within a local circuit as opposed to neurons that project to a separate neural structure. The term is also sometimes used as shorthand for an inhibitory neuron, especially in studies of cortical circuits, but for clarity, the term *inhibitory interneuron* should be used when appropriate.

Each functional classification can be subdivided further. Sensory system interneurons can be classified according to the type of sensory stimuli to which they respond; these initial classifications can be broken down still further, according to location, density, and size as well as patterns of gene expression. Indeed, our view of neuronal complexity is rapidly evolving due to advances in mRNA sequence analysis that have enabled the molecular profiling of individual neurons. Such analyses have recently revealed a much greater heterogeneity of neuronal types than previously thought (Figure 3–4).

Glial Cells Support Nerve Cells

Glial cells greatly outnumber neurons—there are 2 to 10 times more glia than neurons in the vertebrate central nervous system. Although the name for these cells derives from the Greek for glue, glia do not commonly hold nerve cells together. Rather they surround the cell bodies, axons, and dendrites of neurons. Glia differ from neurons morphologically; they do not form dendrites and axons.

Glia also differ functionally. Although they arise from the same embryonic precursor cells, they do not have the same membrane properties as neurons and thus are not electrically excitable. Hence, they are not directly involved in electrical signaling, which is the function of nerve cells. Yet they play a role in allowing electrical signals to move quickly along the axons

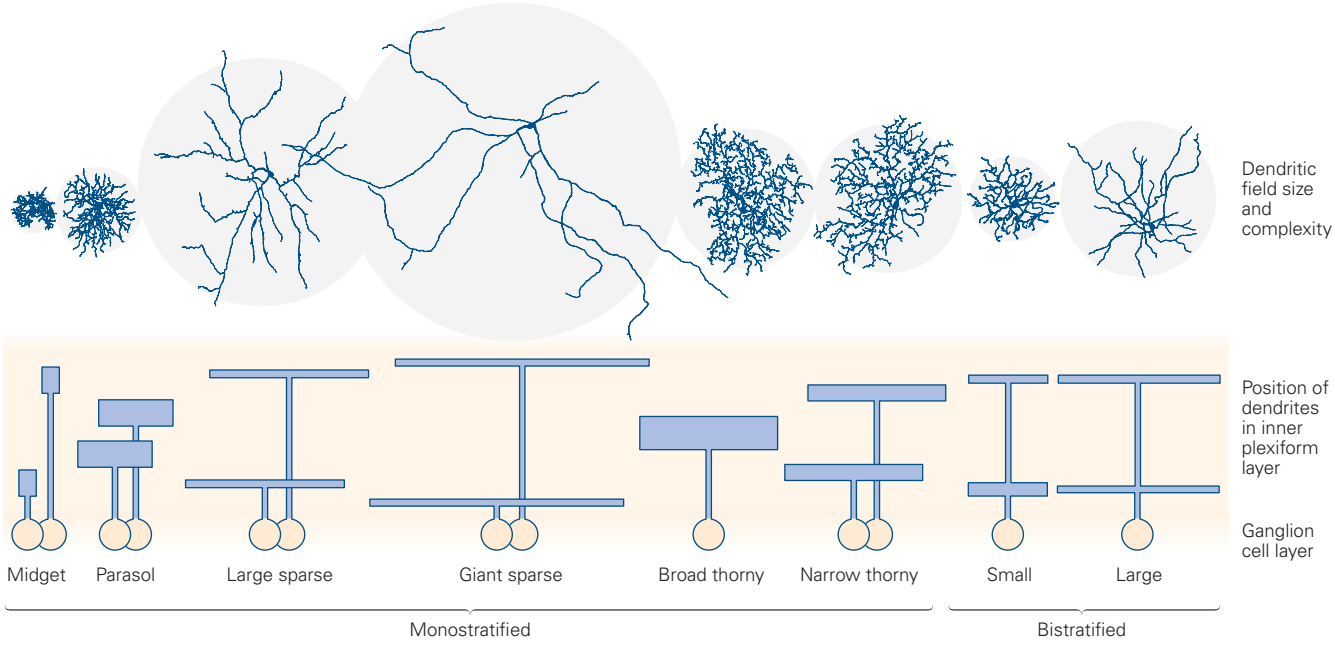

Figure 3–4 Sensory neurons can be subdivided into functionally distinct groups. For example, at least 13 types of retinal ganglion cells are distinguished based on the size and shape of their dendrites combined with the depth within the retina at which they receive their inputs. The inner plexiform layer contains the connections between interneurons of the retina (bipolar and amacrine cells) and the ganglion cells. (Reproduced, with permission, from Dacey et al. 2003. Copyright © 2003 Elsevier.)

of neurons, and they appear to play an important role in guiding connectivity during early development and stabilizing new or altered connections between neurons that occur through learning. Over the past decade, interest in the diverse functions of glia has accelerated, and their characterization has changed from support cells to functional partners of neurons (Chapter 7).

Each Nerve Cell Is Part of a Circuit That Mediates Specific Behaviors

Every behavior is mediated by specific sets of interconnected neurons, and every neuron's behavioral function is determined by its connections with other neurons. A simple behavior, the knee-jerk reflex, will illustrate this. The reflex is initiated when a transient imbalance of the body stretches the quadriceps extensor muscles of the leg. This stretching elicits sensory information that is conveyed to motor neurons, which in turn send commands to the extensor muscles to contract so that balance is restored.

This reflex is used clinically to test the integrity of the nerves as well as the cerebrospinal control of the reflex amplitude (or gain). The underlying mechanism is important because it maintains normal tone in the quadriceps and prevents our knees from buckling when we stand or walk. The tendon of the quadriceps femoris, an extensor muscle that moves the lower leg, is attached to the tibia through the tendon of the patella (kneecap). Tapping this tendon just below the patella stretches the quadriceps femoris. This stretch initiates reflex contraction of the quadriceps muscle to produce the familiar knee jerk. By increasing the tension of a select group of muscles, the stretch reflex changes the position of the leg, suddenly extending it outward (Figure 3–5).

The cell bodies of the sensory neurons involved in the knee-jerk reflex are clustered near the spinal cord in the dorsal root ganglia. They are pseudo-unipolar cells; one branch of each cell's axon runs to the quadriceps muscle at the periphery, while the other runs centrally into the spinal cord. The branch that innervates the quadriceps makes contact with stretch-sensitive receptors (muscle spindles) and is excited when the muscle is stretched. The branch reaching the spinal cord forms excitatory connections with the motor neurons that innervate the quadriceps and control its contraction. This branch also contacts local interneurons that *inhibit* the motor neurons controlling the opposing flexor muscles (Figure 3–5). Although these local interneurons are not involved in producing the stretch reflex itself, they increase the stability of the reflex by coordinating the actions of opposing muscle groups.

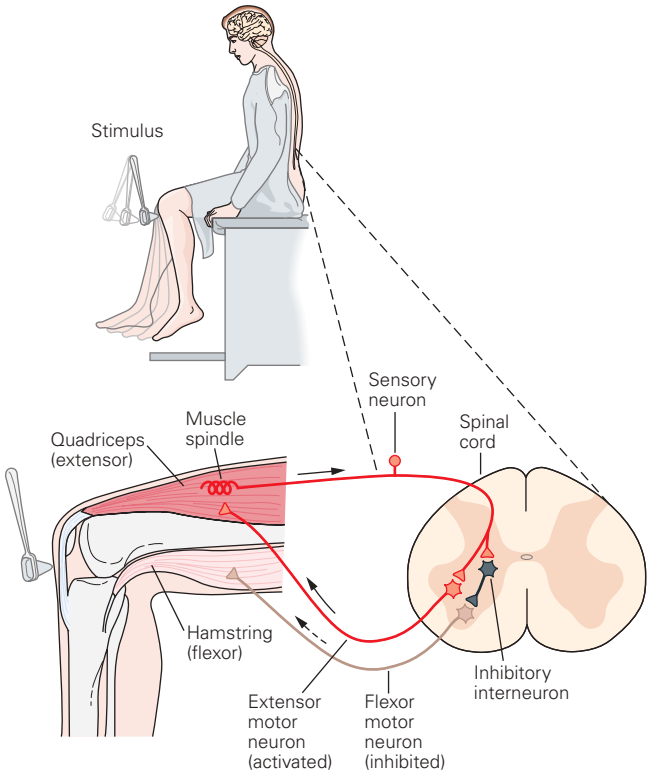

Figure 3–5 The knee-jerk reflex is controlled by a simple circuit of sensory and motor neurons. Tapping the kneecap with a reflex hammer pulls on the tendon of the quadriceps femoris, a muscle that extends the lower leg. When the muscle stretches in response to the pull of the tendon, information regarding this change in the muscle is conveyed to the central nervous system by sensory neurons. In the spinal cord, the sensory neurons form excitatory synapses with extensor motor neurons that contract the quadriceps, the muscle that was stretched. The sensory neurons act indirectly, through interneurons, to inhibit flexor motor neurons that would otherwise contract the opposing hamstring muscles. These actions combine to produce the reflex behavior. In the drawing, each extensor and flexor motor neuron represents a population of many cells.

Thus, the electrical signals that produce the stretch reflex carry four kinds of information:

1. Sensory information is conveyed to the central nervous system (the spinal cord) from muscle.
2. Motor commands from the central nervous system are issued to the muscles that carry out the knee jerk.
3. Inhibitory commands are issued to motor neurons that innervate opposing muscles.
4. Information about local neuronal activity related to the knee jerk is sent to higher centers of the central nervous system, permitting the brain to coordinate different behaviors simultaneously or in series.

In addition, the brain asserts context-dependent control of the reflex to adjust its gain. For example, when we run, the hamstring muscles flex the knee, thereby stretching the quadriceps. The brain and spinal cord suppress the stretch reflex to allow the quadriceps to relax. When these descending pathways are disrupted, as in some strokes, the reflex is exaggerated and the joint has stiffness.

The stretching of just one muscle, the quadriceps, activates several hundred sensory neurons, each of which makes direct contact with 45 to 50 motor neurons. This pattern of connection, in which one neuron activates many target cells, is called *divergence* (Figure 3–6A). It is especially common in the input stages of the nervous system; by distributing its signals to many target cells, a single neuron can exert wide and diverse influence. Conversely, a single motor cell in the knee-jerk circuit receives 200 to 450 input contacts from approximately 130 sensory cells. This pattern of connection is called *convergence* (Figure 3–6B). It is common at the output stages of the nervous system; a target motor cell that receives information from many sensory neurons is able to integrate information from many sources. Each sensory neuron input produces relatively weak excitation, so convergence also ensures that a motor neuron is activated only when a sufficient number of sensory neurons are activated together.

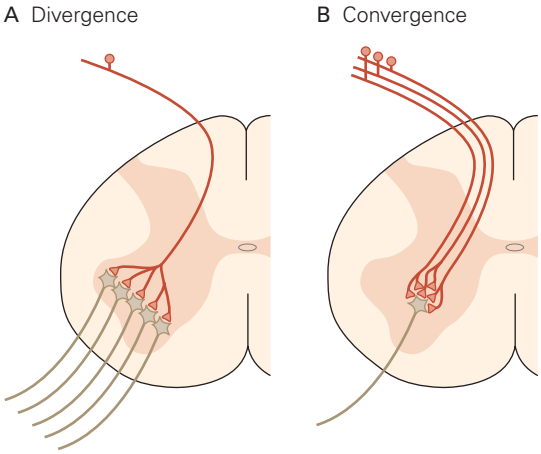

Figure 3–6 Diverging and converging neuronal connections are a key organizational feature of the brain.

A. In the sensory systems, each receptor neuron usually contacts several neurons that represent the second stage of processing. At subsequent processing stages, the incoming connections diverge even more. This allows sensory information from a single site to be distributed more widely in the spinal cord and brain.

B. By contrast, motor neurons are the targets of progressively converging connections. With this arrangement, input from many presynaptic cells is required to activate the motor neuron.

A stretch reflex such as the knee-jerk reflex is a simple behavior produced by two classes of neurons connecting at excitatory synapses. But not all important signals in the brain are excitatory. Many neurons produce inhibitory signals that reduce the likelihood of firing. Even in the simple knee-jerk reflex, the sensory neurons make both excitatory and inhibitory connections. Excitatory connections in the leg's extensor muscles cause these muscles to contract, whereas connections with inhibitory interneurons prevent the antagonist flexor muscles from contracting. This feature of the circuit is an example of *feedforward inhibition* (Figure 3–7A). In the knee-jerk reflex, feedforward

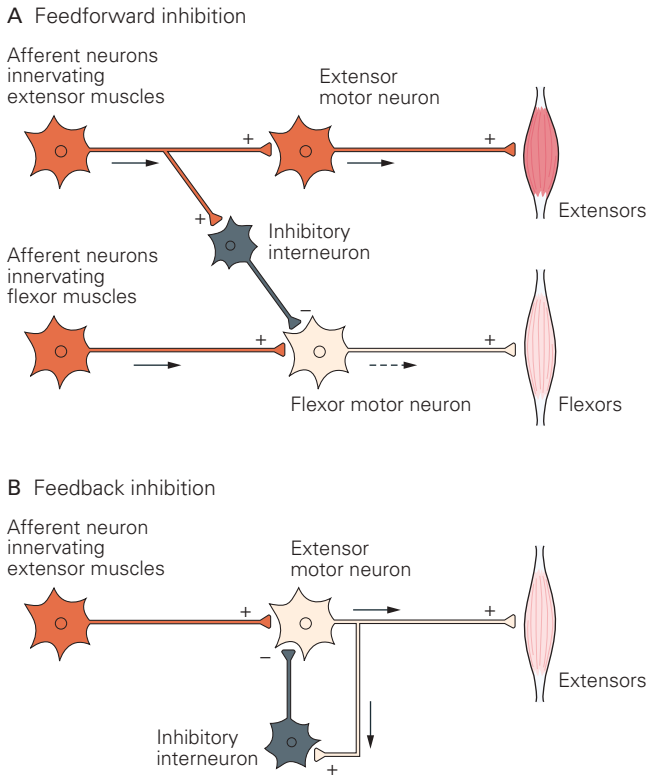

Figure 3–7 Inhibitory interneurons can produce either feedforward or feedback inhibition.

A. Feedforward inhibition enhances the effect of the active pathway by suppressing the activity of pathways mediating opposing actions. Feedforward inhibition is common in monosynaptic reflex systems. For example, in the knee-jerk reflex circuit (**Figure 3–5**) afferent neurons from extensor muscles excite not only the extensor motor neurons but also inhibitory interneurons that prevent the firing of the motor cells innervating the opposing flexor muscles.

B. Feedback inhibition is a self-regulating mechanism. Here extensor motor neurons act on inhibitory interneurons that in turn act on the extensor motor neurons themselves and thus reduce their probability of firing. The effect is to dampen activity within the stimulated pathway and prevent it from exceeding a certain critical level.

inhibition is *reciprocal*, ensuring that the flexor and extensor pathways always inhibit each other so that only muscles appropriate for the movement and not those opposed to it are recruited.

Some circuits provide *feedback inhibition*. For example, a motor neuron may have excitatory connections with both a muscle and an inhibitory interneuron that itself forms a connection with the motor neuron. When the inhibitory interneuron is excited by the motor neuron, the interneuron is able to limit the ability of the motor neuron to excite the muscle (Figure 3–7B). We will encounter many examples of feedforward and feedback inhibition when we examine more complex behaviors in later chapters.

Signaling Is Organized in the Same Way in All Nerve Cells

To produce a behavior, a stretch reflex for example, each participating sensory and motor nerve cell must generate four different signals in sequence, each at a different site within the cell. Despite variations in cell size and shape, transmitter biochemistry, or behavioral function, almost all neurons can be described by a model neuron that has four functional components that generate the four types of signals: a receptive component for producing graded input signals, a summing or integrative component that produces a trigger signal, a conducting long-range signaling component that produces all-or-none conducting signals, and a synaptic component that produces output signals to the next neuron in line or to muscle or gland cells (Figure 3–8).

The different types of signals generated in a neuron are determined in part by the electrical properties of the cell membrane. Every cell, including a neuron, maintains a certain difference in the electrical potential on either side of the plasma membrane when the cell is at rest. This is called the *resting membrane potential*. In a typical resting neuron, the voltage of the inside of the cell is about 65 mV more negative than the voltage outside the cell. Because the voltage outside the membrane is defined as zero, we say the resting membrane potential is –65 mV. The resting potential in different nerve cells ranges from –40 to –80 mV; in muscle cells, it is greater still, about –90 mV. As described in detail in Chapter 9, the resting membrane potential results from two factors: the unequal distribution of electrically charged ions, in particular the positively charged Na^+ and K^+ ions, and the selective permeability of the membrane.

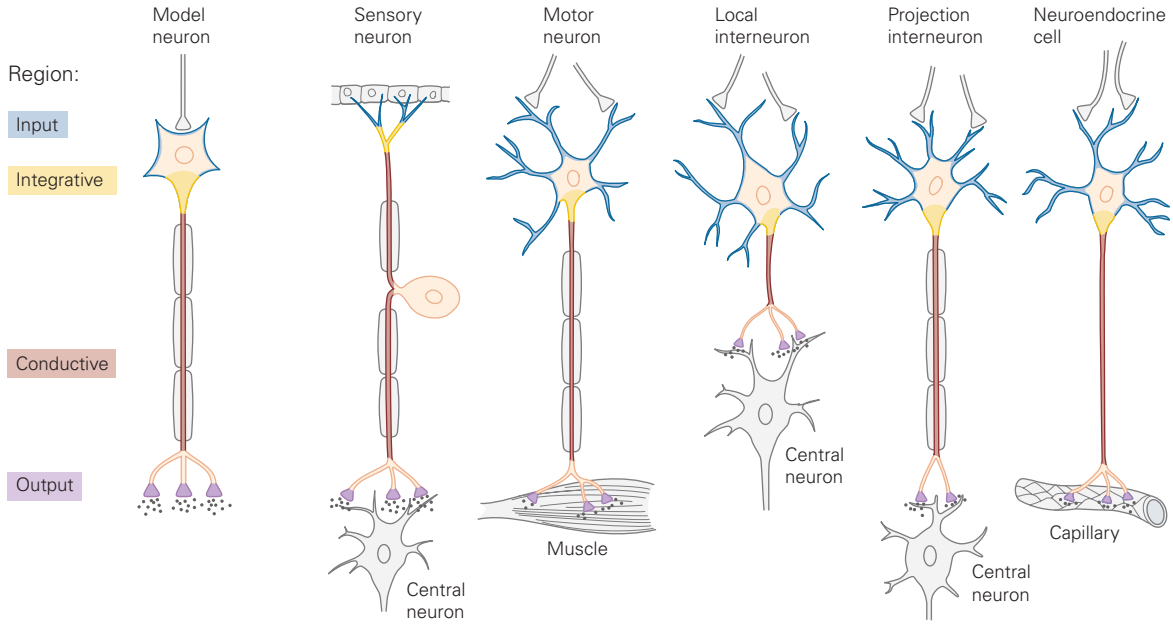

Figure 3–8 **Most neurons have four functional regions in which different types of signals are generated.** Thus, the functional organization of most neurons, regardless of type, can be represented schematically by a model neuron. This model neuron is the physiological expression of Ramón y Cajal's principle of dynamic polarization. The input, integrative, and conductive signals are all electrical and integral to the cell, whereas the output signal is a chemical substance ejected by the cell into the synaptic cleft. Not all neurons share all of these features; for example, some local interneurons lack a conductive component.

The unequal distribution of positively charged ions on either side of the cell membrane is maintained by two main mechanisms. Intracellular Na^+ and K^+ concentrations are largely controlled by a membrane protein that actively pumps Na^+ out of the cell and K^+ back into it. This *Na^+-K^+ pump*, about which we shall learn more in Chapter 9, keeps the Na^+ concentration in the cell low (about one-tenth the concentration outside the cell) and the K^+ concentration high (about 20 times the concentration outside). The extracellular concentrations of Na^+ and K^+ are maintained by the kidneys and the astroglial cells, also known as astrocytes.

The otherwise impermeable cell membrane contains proteins that form pores called *ion channels*. The channels that are active when the cell is at rest are highly permeable to K^+ but considerably less permeable to Na^+. The K^+ ions tend to leak out of these open channels, down the ion's concentration gradient. As K^+ ions exit the cell, they leave behind a cloud of unneutralized negative charge on the inner surface of the membrane, so that the net charge inside the membrane is more negative than that outside. With this state of affairs, the membrane potential is typically maintained at around –65 mV relative to outside of the neuron, and the neuron is said to be at rest.

The resting state is perturbed when the cell begins to take up Na^+ (or Ca^{2+}), which are at a higher concentration outside the cell. The inward movement of these positively charged ions (*inward current*) partially neutralizes the negative voltage inside the cell. We will say more about these events below. What happens next, however, holds the key to understanding what it is about neurons that makes signaling suitable for conveying information.

A cell, such as nerve and muscle, is said to be excitable when its membrane potential can be quickly and significantly altered. In many neurons, a 10-mV change in membrane potential (from –65 to –55 mV) makes the membrane much more permeable to Na^+ than to K^+. The resultant influx of Na^+ further neutralizes the negative charge inside the cell, leading to even more permeability to Na^+. The result is a brief and explosive change in membrane potential to +40 mV, the *action potential*. This potential is actively conducted down the cell's axon to the axon's terminal, where it initiates an elaborate chemical interaction with postsynaptic neurons or muscle cells. Since the action potential is actively propagated, its amplitude does not diminish by the time it reaches the axon terminal. An action potential typically lasts approximately 1 ms, after which the membrane returns to its resting state, with its normal separation of charges and higher permeability to K^+ than to Na^+.

The mechanisms underlying the resting potential and action potential are discussed in detail in Chapters 9 and 10. In addition to the long-distance signals represented by the action potential, nerve cells also produce local signals—receptor potentials and synaptic potentials—that are not actively propagated and that typically decay within just a few millimeters (see next section).

Changes in membrane potential that generate long-range and local signals can be either a decrease or an increase from the resting potential. That is, the resting membrane potential is the baseline from which all signaling occurs. A reduction in membrane potential, called *depolarization*, enhances a cell's ability to generate an action potential and is thus excitatory. In contrast, an increase in membrane potential, called *hyperpolarization*, makes a cell less likely to generate an action potential and is therefore inhibitory.

The Input Component Produces Graded Local Signals

In most neurons at rest, no current flows from one part of the cell to another, so the resting potential is the same throughout. In sensory neurons, current flow is typically initiated by a physical stimulus, which activates specialized receptor proteins at the neuron's receptive surface. In our example of the knee-jerk reflex, stretching of the muscle activates specific ion channels that open in response to stretch of the sensory neuron membrane, as we shall learn in Chapter 18. The opening of these channels when the cell is stretched permits the rapid influx of Na^+ ions into the sensory cell. This ionic current changes the membrane potential, producing a local signal called the *receptor potential*.

The amplitude and duration of a receptor potential depend on the intensity of the muscle stretch: The larger or longer-lasting the stretch, the larger or longer-lasting is the resulting receptor potential (Figure 3–9A). That is, receptor potentials are graded, unlike the all-or-none action potential. Most receptor potentials are depolarizing (excitatory); hyperpolarizing (inhibitory) receptor potentials are found in the retina.

The receptor potential is the first representation of stretch to be coded in the nervous system. However, because this depolarization spreads passively from the stretch receptor, it does not travel far. The distance is longer if the diameter of the axon is bigger, shorter if the diameter is smaller. Also, the distance is shorter if current can pass easily through the membrane, and longer if the membrane is insulated by myelin. The receptor potential from the stretch receptor therefore travels only 1 to 2 mm. In fact, just 1 mm away, the

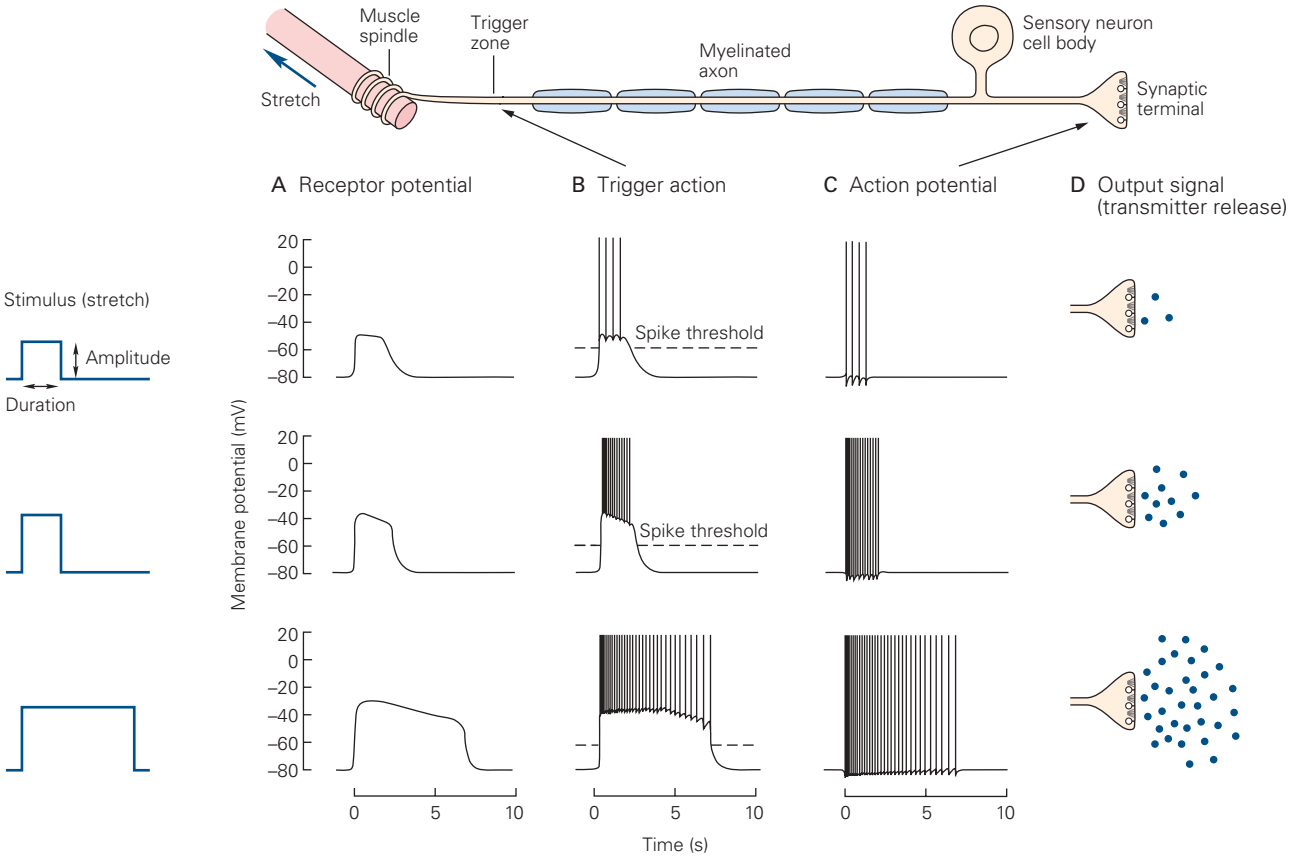

Figure 3–9 Each of the neuron's four signaling components produces a characteristic signal. The figure shows a sensory neuron activated by stretching of a muscle, which the neuron senses through a specialized receptor, the muscle spindle.

A. The input signal, called a receptor potential, is graded in amplitude and duration, proportional to the amplitude and duration of the stimulus.

B. The trigger zone sums the depolarization generated by the receptor potential. An action potential is generated only if the receptor potential exceeds a certain voltage threshold. Once this threshold is surpassed, any further increase in amplitude of the receptor potential can only increase the frequency with which the action potentials are generated, because action potentials have a constant amplitude. The duration of the receptor potential determines the duration of the train of action potentials. Thus, the graded amplitude and duration of the receptor potential are translated into a frequency code in the action potentials generated at the trigger zone. All action potentials produced are propagated faithfully along the axon.

C. Action potentials are all-or-none. Because all action potentials have a similar amplitude and duration, the frequency and duration of firing encodes the information carried by the signal.

D. When the action potential reaches the synaptic terminal, it initiates the release of a neurotransmitter, the chemical substance that serves as the output signal. The frequency of action potentials in the presynaptic cell determines how much neurotransmitter is released by the cell.

amplitude of the signal is only about one-third what it was at the site of generation. To be carried successfully to the spinal cord, the local signal must be amplified—it must generate an action potential. In the knee-jerk reflex, if the receptor potential in the sensory neuron reaches the first node of Ranvier in the axon and is large enough, it will trigger an action potential (Figure 3–9B), which then propagates without failure to the axon terminals in the spinal cord (Figure 3–9C). At the synapse between the sensory neuron and a motor neuron, the action potential produces a chain of events that results in an input signal to the motor neuron.

In the knee-jerk reflex, the action potential in the presynaptic terminal of the sensory neuron initiates the release of a chemical substance, or neurotransmitter, into the synaptic cleft (Figure 3–9D). After diffusing across the cleft, the transmitter binds to receptor proteins in the postsynaptic membrane of the motor neuron, thereby directly or indirectly opening ion channels. The ensuing flow of current briefly alters the membrane potential of the motor cell, a change called the *synaptic potential*.

Like the receptor potential, the synaptic potential is graded; its amplitude depends on how much transmitter is released. In the same cell, the synaptic