11 Fundamentals of the Nervous System and Nervous Tissue

WHY THIS MATTERS

KEY CONCEPTS

You are driving down the freeway, and a horn blares to your right. You immediately swerve to your left. Charlie leaves a note on the kitchen table: "See you later. Have the stuff ready at 6." You know the "stuff" is chili with taco chips. You are dozing but you awaken instantly when your infant son cries softly.

What do these three events have in common? They are all everyday examples of the functioning of your nervous system, which has your body cells humming with activity nearly all the time.

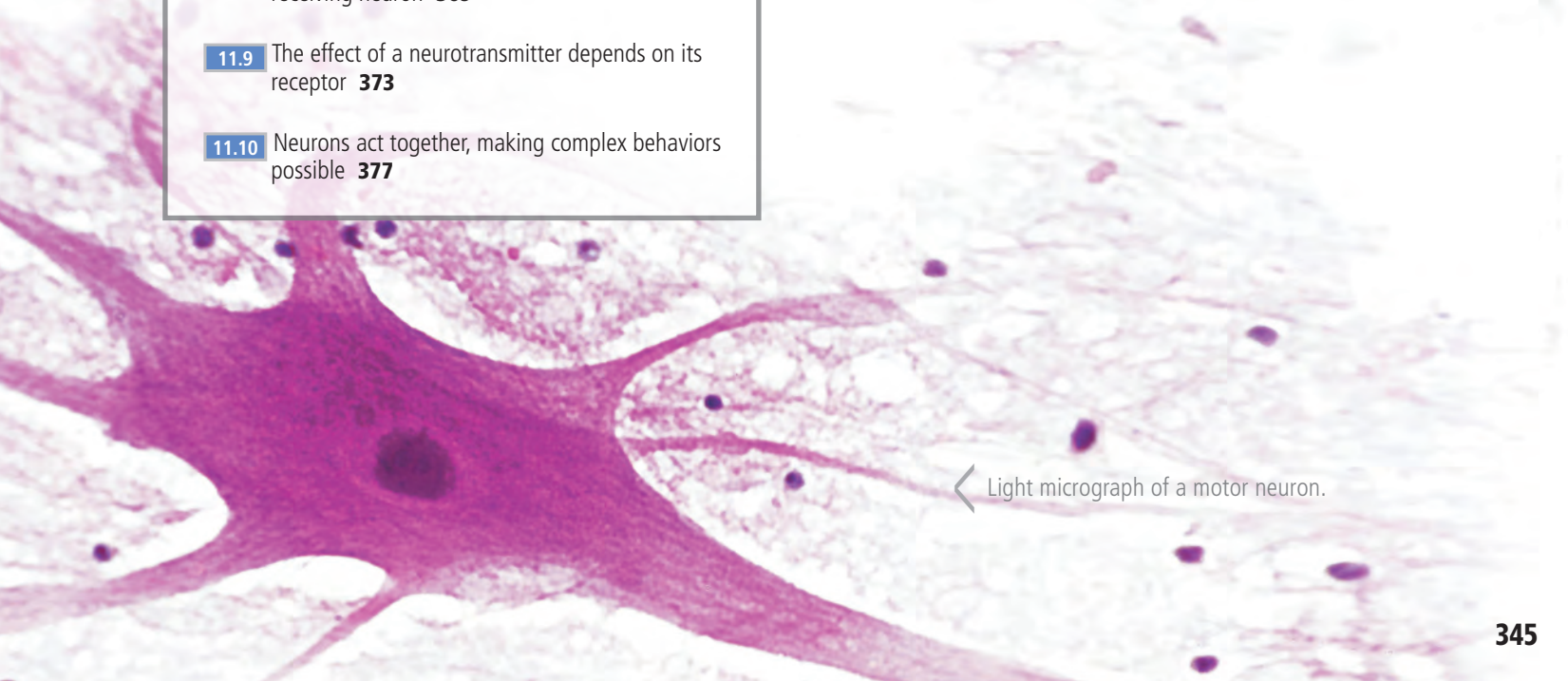
The **nervous system** is the master controlling and communicating system of the body. Every thought, action, and emotion reflects its activity. Its cells communicate by electrical and chemical signals, which are rapid and specific, and usually cause almost immediate responses.

We begin this chapter with a brief overview of the functions and organization of the nervous system. Then we focus on the functional anatomy of nervous tissue, especially the nerve cells, or *neurons*, which are the key to neural communication.

11.1 The nervous system receives, integrates, and responds to information

Learning Objectives

- **List the basic functions of the nervous system.**
- **Explain the structural and functional divisions of the nervous system.**



Light micrograph of a motor neuron.

The nervous system has three overlapping functions, illustrated by the example of a thirsty person seeing and then lifting a glass of water (**Figure 11.1**):

1. **Sensory input.** The nervous system uses its millions of sensory receptors to monitor changes occurring both inside and outside the body. The gathered information is called **sensory input**.
2. **Integration.** The nervous system processes and interprets sensory input and decides what should be done at each moment—a process called **integration**.
3. **Motor output.** The nervous system activates *effector organs*—the muscles and glands—to cause a *response*, called **motor output.**

Here's another example: You are driving and see a red light ahead (sensory input). Your nervous system integrates this information (red light means "stop"), and your foot hits the brake (motor output).

We have one highly integrated nervous system. For convenience, it is divided into two principal parts, *central* and *peripheral* (**Figure 11.2**).

The **central nervous system (CNS)** consists of the *brain* and *spinal cord*, which occupy the dorsal body cavity. The CNS is the integrating and control center of the nervous system. It interprets sensory input and dictates motor output based on reflexes, current conditions, and past experience.

The **peripheral nervous system (PNS)** is the part of the nervous system *outside* the CNS. The PNS consists mainly of nerves (bundles of axons) that extend from the brain and spinal cord, and *ganglia* (collections of neuron cell bodies). *Spinal nerves* carry impulses to and from the spinal cord, and *cranial nerves* carry impulses to and from the brain. These peripheral nerves serve as communication lines that link all parts of the body to the CNS.

The PNS has two functional subdivisions, as **Figure 11.3** shows. The **sensory**, or **afferent**, **division** (af′er-ent; "carrying toward") consists of nerve fibers (axons) that convey impulses *to* the central nervous system from sensory receptors located throughout the body.

- *Somatic sensory fibers* convey impulses from the skin, skeletal muscles, and joints (*soma* = body)
- *Visceral sensory fibers* transmit impulses from the visceral organs (organs within the ventral body cavity)

The sensory division keeps the CNS constantly informed of events going on both inside and outside the body.

The **motor**, or **efferent**, **division** (ef′er-ent; "carrying away") of the PNS transmits impulses *from* the CNS to effector organs, which are the muscles and glands. These impulses activate muscles to contract and glands to secrete. In other words, they *effect* (bring about) a motor response.

The motor division also has two main parts:

- The **somatic nervous system** is composed of somatic motor nerve fibers that conduct impulses from the CNS to skeletal muscles. It is often referred to as the **voluntary nervous system** because it allows us to consciously control our skeletal muscles.
- The **autonomic nervous system (ANS)** consists of visceral motor nerve fibers that regulate the activity of smooth muscles, cardiac muscles, and glands. *Autonomic* means "a law unto itself," and because we generally cannot control such activities as the pumping of our heart or the movement of

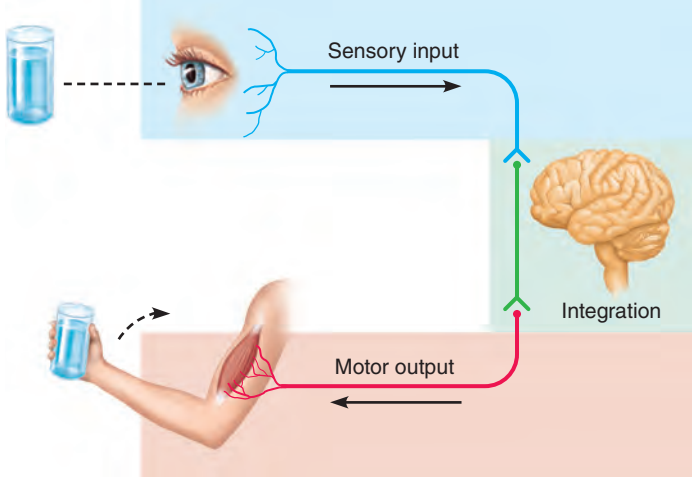


Figure 11.1 The nervous system's functions.

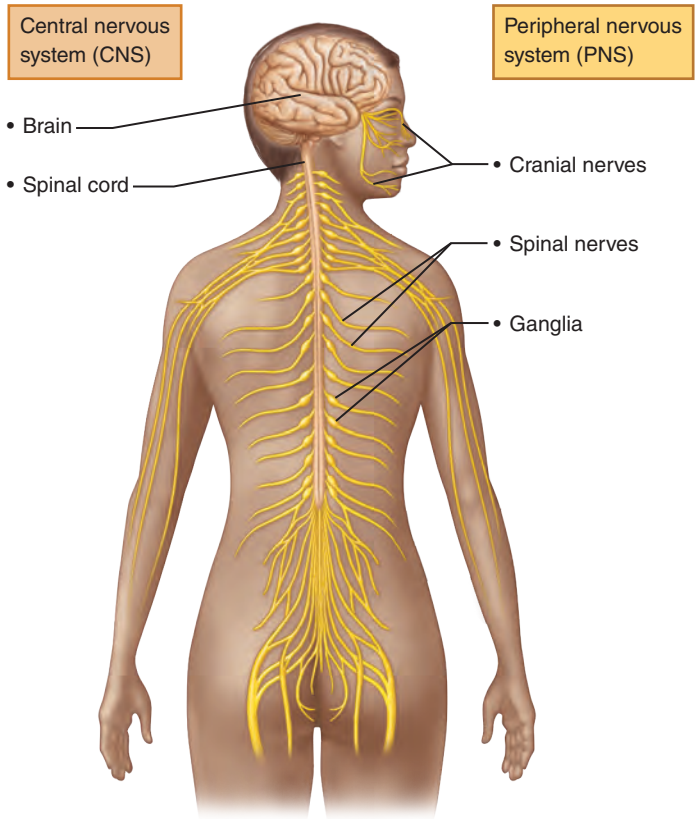


Figure 11.2 The nervous system. The brain and spinal cord (tan) make up the central nervous system. The peripheral nervous system (dark gold) mostly consists of pairs of cranial nerves, spinal nerves, and associated ganglia.

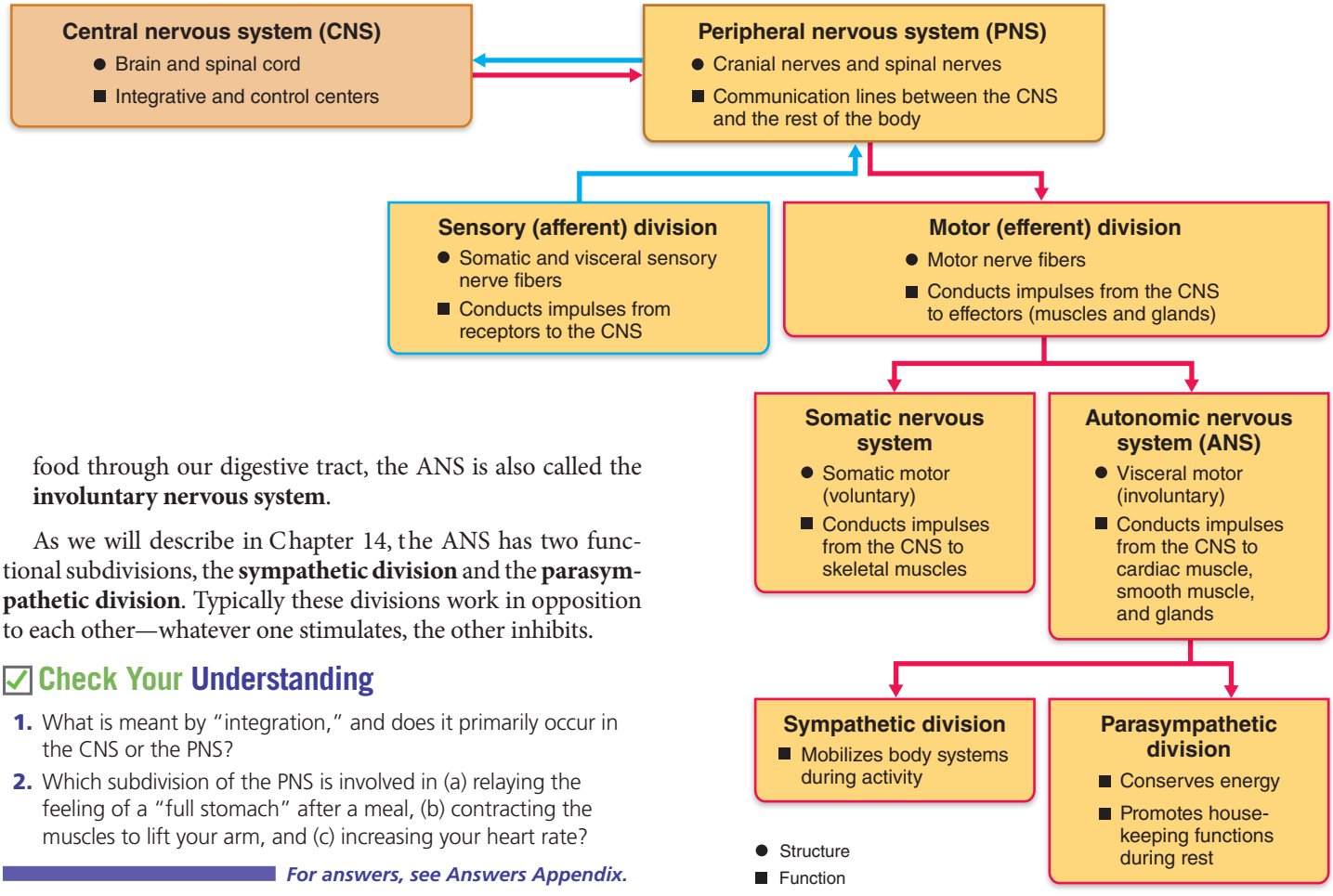


Figure 11.3 Organization of the nervous system. The human nervous system is organized into two major divisions, the central nervous system (CNS) and peripheral nervous system (PNS). Visceral organs (primarily located in the ventral body cavity) are served by visceral sensory fibers and by motor fibers of the autonomic nervous system. Motor fibers of the somatic nervous system and somatic sensory fibers serve the limbs and body wall (*soma* = body).

food through our digestive tract, the ANS is also called the **involuntary nervous system**.

As we will describe in Chapter 14, the ANS has two functional subdivisions, the **sympathetic division** and the **parasympathetic division**. Typically these divisions work in opposition to each other—whatever one stimulates, the other inhibits.

Check Your Understanding

1. What is meant by "integration," and does it primarily occur in the CNS or the PNS?
2. Which subdivision of the PNS is involved in (a) relaying the feeling of a "full stomach" after a meal, (b) contracting the muscles to lift your arm, and (c) increasing your heart rate?

For answers, see Answers Appendix.

The nervous system consists mostly of nervous tissue, which is highly cellular. For example, less than 20% of the CNS is extracellular space, which means that the cells are densely packed and tightly intertwined. Although it is very complex, nervous tissue is made up of just two principal types of cells:

- Supporting cells called *neuroglia*, small cells that surround and wrap the more delicate neurons
- *Neurons*, nerve cells that are excitable (responsive to stimuli) and transmit electrical signals

Figure 4.10 on p. 129 will refresh your memory about these two kinds of cells before we explore them further in the next two modules.

11.2 Neuroglia support and maintain neurons

Learning Objective

List the types of neuroglia and cite their functions.

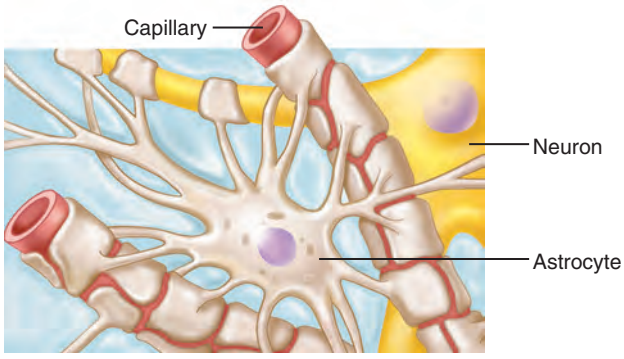
Neurons associate closely with much smaller cells called **neuroglia** (nu-rog′le-ah; "nerve glue") or **glial cells** (gle′al). There are six types of neuroglia—four in the CNS and two in the PNS (**Figure 11.4**). Once considered merely the "glue" or scaffolding that supports the neurons, neuroglia are now known to have many other important and unique functions.

Neuroglia in the CNS

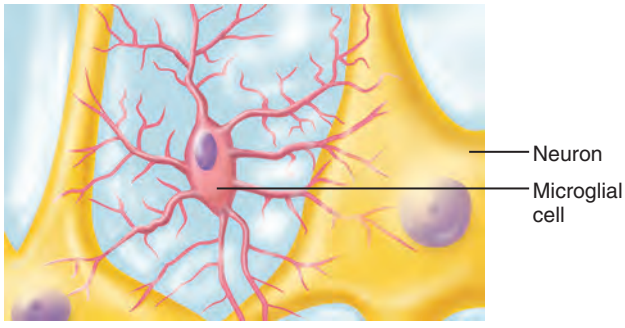
Neuroglia in the CNS include *astrocytes*, *microglial cells*, *ependymal cells*, and *oligodendrocytes* (Figure 11.4a–d). Like neurons, most neuroglia have branching processes (extensions) and a central cell body. They can be distinguished, however, by their much smaller size and their darker-staining nuclei. They outnumber neurons in the CNS by about 10 to 1, and make up about half the mass of the brain.

Astrocytes

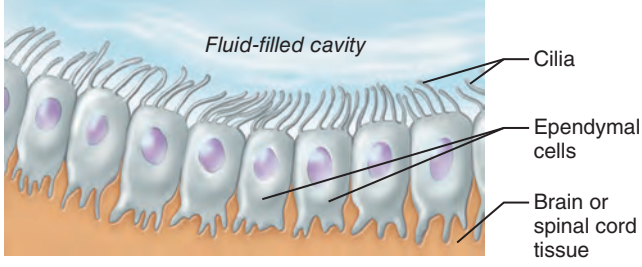
Shaped like delicate branching sea anemones, **astrocytes** (as′tro-sītz; "star cells") are the most abundant and versatile glial cells. Their numerous radiating processes cling to neurons and their synaptic endings, and cover nearby capillaries. They support and brace the neurons and anchor them to their nutrient supply lines (Figure 11.4a).



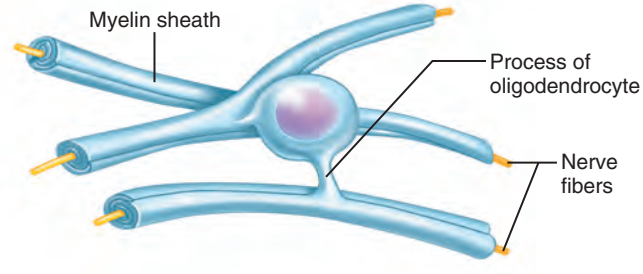
(a) Astrocytes are the most abundant CNS neuroglia.



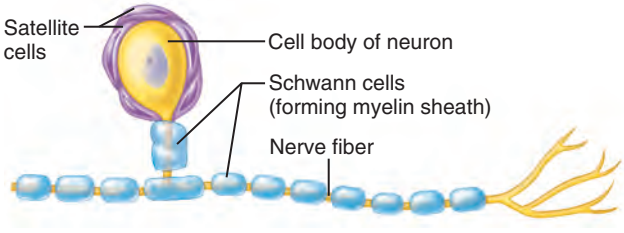
(b) Microglial cells are defensive cells in the CNS.



(c) Ependymal cells line cerebrospinal fluid–filled cavities.



(d) Oligodendrocytes have processes that form myelin sheaths around CNS nerve fibers.



(e) Satellite cells and Schwann cells (which form myelin) surround neurons in the PNS.

Figure 11.4 Neuroglia. (a–d) The four types of neuroglia of the CNS. **(e)** Neuroglia of the PNS.

Astrocytes play a role in making exchanges between capillaries and neurons, helping determine capillary permeability. They guide the migration of young neurons and formation of synapses (junctions) between neurons. Astrocytes also control the chemical environment around neurons, where their most important job is "mopping up" leaked potassium ions and recapturing and recycling released neurotransmitters. Furthermore, astrocytes have been shown to respond to nearby nerve impulses and released neurotransmitters.

Connected by gap junctions, astrocytes signal each other with slow-paced intracellular calcium pulses (calcium waves), and by releasing extracellular chemical messengers. Recent research shows they also influence neuronal functioning and therefore participate in information processing in the brain.

Microglial Cells

Microglial cells (mi-kro′gle-al) are small and ovoid with relatively long "thorny" processes (Figure 11.4b). Their processes touch nearby neurons, monitoring their health, and when they sense that certain neurons are injured or in other trouble, the microglial cells migrate toward them. Where invading microorganisms or dead neurons are present, the microglial cells transform into a special type of macrophage that phagocytizes the microorganisms or neuronal debris. This protective role is important because cells of the immune system have limited access to the CNS.

Ependymal Cells

Ependymal cells (ĕ-pen′dĭ-mul; "wrapping garment") range in shape from squamous to columnar, and many are ciliated (Figure 11.4c). They line the central cavities of the brain and the spinal cord, where they form a fairly permeable barrier between the cerebrospinal fluid that fills those cavities and the tissue fluid bathing the cells of the CNS. The beating of their cilia helps to circulate the cerebrospinal fluid that cushions the brain and spinal cord.

Oligodendrocytes

Though they also branch, the **oligodendrocytes** (ol″ĭ-go-den′dro-sīts) have fewer processes (*oligo* = few; *dendr* = branch) than astrocytes. Oligodendrocytes line up along the thicker nerve fibers in the CNS and wrap their processes tightly around the fibers, producing an insulating covering called a *myelin sheath* (Figure 11.4d).

Neuroglia in the PNS

The two kinds of PNS neuroglia—*satellite cells* and *Schwann cells*—differ mainly in location.

Satellite cells surround neuron cell bodies located in the peripheral nervous system (Figure 11.4e), and are thought to have many of the same functions in the PNS as astrocytes do in the CNS. Their name comes from a fancied resemblance to the moons (satellites) around a planet.

Schwann cells (also called *neurolemmocytes*) surround all nerve fibers in the PNS and form myelin sheaths around the thicker nerve fibers (Figure 11.4e and 11.5a). In this way, they are functionally similar to oligodendrocytes. (We describe the formation of myelin sheaths later in this chapter.) Schwann cells are vital to regeneration of damaged peripheral nerve fibers.

Check Your Understanding

3. Which type of neuroglia controls the extracellular fluid environment around neuron cell bodies in the CNS? In the PNS?
4. Which two types of neuroglia form insulating coverings called myelin sheaths?

For answers, see Answers Appendix.

11.3 Neurons are the structural units of the nervous system

Learning Objectives

- **Define neuron, describe its important structural components, and relate each to a functional role.**
- **Differentiate between (1) a nerve and a tract, and (2) a nucleus and a ganglion.**
- **Explain the importance of the myelin sheath and describe how it is formed in the central and peripheral nervous systems.**
- **Classify neurons by structure and by function.**

The billions of **neurons**, also called *nerve cells*, are the structural units of the nervous system. They are typically large, highly specialized cells that conduct messages in the form of nerve impulses from one part of the body to another. Besides their ability to conduct nerve impulses (excitability), they have three other special characteristics:

- Neurons have *extreme longevity*. Given good nutrition, they can function optimally for a lifetime.
- Neurons are *amitotic*. As neurons assume their roles as communicating links of the nervous system, they lose their ability to divide. We pay a high price for this feature because neurons cannot be replaced if destroyed. There *are* exceptions to this rule. For example, olfactory epithelium and some hippocampal regions of the brain contain stem cells that can produce new neurons throughout life.
- Neurons have an exceptionally *high metabolic rate* and require continuous and abundant supplies of oxygen and glucose. They cannot survive for more than a few minutes without oxygen.

Although neurons vary in structure, they all have a *cell body* and one or more slender *processes* (**Figure 11.5**).

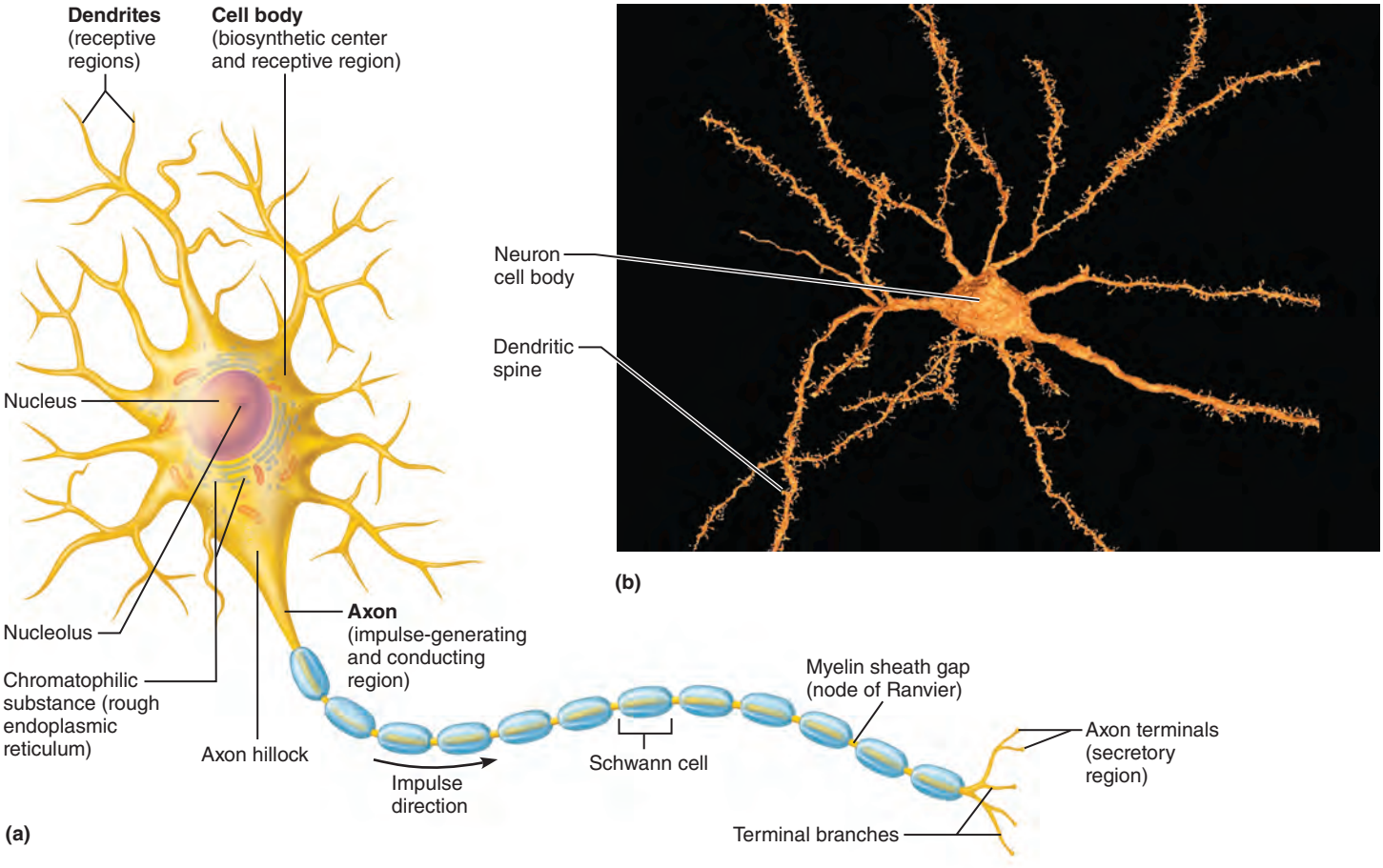


Figure 11.5 Structure of a motor neuron. (a) Diagrammatic view. **(b)** Digital reconstruction of a neuron showing the cell body and dendrites with obvious dendritic spines (1000×).

Neuron Cell Body

The **neuron cell body** consists of a spherical nucleus with a conspicuous nucleolus surrounded by cytoplasm. Also called the **perikaryon** (*peri* = around, *kary* = nucleus) or **soma**, the cell body ranges in diameter from 5 to 140 μm. The cell body is the major *biosynthetic center* of a neuron and so it contains the usual organelles needed to synthesize proteins and other chemicals.

The neuron cell body's protein- and membrane-making machinery, consisting of clustered free ribosomes and rough endoplasmic reticulum (ER), is probably the most active and best developed in the body. This rough ER, also called the **chromatophilic substance** (*chromatophilic* = color loving) or *Nissl bodies* (nis′l), stains darkly with basic dyes. The Golgi apparatus is also well developed and forms an arc or a complete circle around the nucleus.

Mitochondria are scattered among the other organelles. Microtubules and **neurofibrils**, which are bundles of intermediate filaments (*neurofilaments*), are important in maintaining cell shape and integrity. They form a network throughout the cell body.

The cell body of some neurons also contains pigment inclusions. For example, some contain a black melanin, a red iron-containing pigment, or a golden-brown pigment called *lipofuscin* (lip″o-fu′sin). Lipofuscin, a harmless by-product of lysosomal activity, is sometimes called the "aging pigment" because it accumulates in neurons of elderly individuals.

In most neurons, the plasma membrane of the cell body acts as *part of the receptive region* that receives information from other neurons.

Most neuron cell bodies are located in the CNS, where they are protected by the bones of the skull and vertebral column. Clusters of cell bodies in the CNS are called **nuclei**, whereas those that lie along the nerves in the PNS are called **ganglia** (gang′gle-ah; *ganglion* = "knot on a string," "swelling").

Neuron Processes

Armlike **processes** extend from the cell body of all neurons. The brain and spinal cord (CNS) contain both neuron cell bodies and their processes. The PNS consists chiefly of neuron processes. Bundles of neuron processes are called **tracts** in the CNS and **nerves** in the PNS.

The two types of neuron processes, *dendrites* and *axons* (ak′sonz), differ in the structure and function of their plasma membranes. The convention is to describe these processes using a motor neuron as an example. We shall follow this practice, but keep in mind that many sensory neurons and some tiny CNS neurons differ from the "typical" pattern we present here.

Dendrites

Dendrites of motor neurons are short, tapering, diffusely branching extensions. Typically, motor neurons have hundreds of twiglike dendrites clustering close to the cell body. Virtually all organelles present in the cell body also occur in dendrites.

Dendrites, the main **receptive** or **input regions**, provide an enormous surface area for receiving signals from other neurons. In many brain areas, the finer dendrites are highly specialized for collecting information. They bristle with *dendritic spines*—thorny appendages with bulbous or spiky ends—which represent points of close contact (synapses) with other neurons (Figure 11.5b).

Dendrites convey incoming messages *toward* the cell body. These electrical signals are usually *not* action potentials (nerve impulses) but are short-distance signals called *graded potentials*, as we will describe shortly.

The Axon: Structure

Each neuron has a single **axon** (*axo* = axis, axle). The initial region of the axon arises from a cone-shaped area of the cell body called the **axon hillock** ("little hill") and then narrows to form a slender process that is uniform in diameter for the rest of its length (Figure 11.5a). In some neurons, the axon is very short or absent, but in others it accounts for nearly the entire length of the neuron. For example, axons of the motor neurons controlling the skeletal muscles of your big toe extend a meter or more (3–4 feet) from the lumbar region of your spine to your foot, making them among the longest cells in the body. Any long axon is called a **nerve fiber**.

Each neuron has only one axon, but axons may have occasional branches along their length. These branches, called **axon collaterals**, extend from the axon at more or less right angles. An axon usually branches profusely at its end (terminus): 10,000 or more **terminal branches** (also called *terminal arborizations*) per neuron is not unusual. The knoblike distal endings of the terminal branches are called **axon terminals**.

The Axon: Functional Characteristics

The axon is the **conducting region** of the neuron (Figure 11.5). It *generates nerve impulses* and *transmits them*, typically away from the cell body, along the plasma membrane, or **axolemma** (ak″so-lem′ah). In motor neurons, the nerve impulse is generated at the junction of the axon hillock and axon (the *trigger zone*) and conducted along the axon to the axon terminals, which are the **secretory region** of the neuron.

When the impulse reaches the axon terminals, it causes *neurotransmitters*—signaling chemicals—to be released into the extracellular space. The neurotransmitters either excite or inhibit neurons (or effector cells) with which the axon is in close contact. Each neuron receives signals from and sends signals to scores of other neurons, carrying on "conversations" with many different neurons at the same time.

An axon contains the same organelles found in the dendrites and cell body with two important exceptions—it lacks rough endoplasmic reticulum and a Golgi apparatus, the structures involved with protein synthesis and packaging. Consequently, an axon depends (1) on its cell body to renew the necessary proteins and membrane components, and (2) on efficient transport mechanisms to distribute them. Axons quickly decay if cut or severely damaged.

Axonal Transport

Because axons are often very long, the task of moving molecules along their length might appear difficult. However, through the cooperative efforts of motor proteins and cytoskeletal elements (microtubules and actin filaments), substances travel continuously along the axon in both directions. Movement away from the cell body is *anterograde movement*, and that in the opposite direction is *retrograde movement*.

Substances moved in the anterograde direction include mitochondria, cytoskeletal elements, membrane components used to renew the axon plasma membrane, and enzymes needed to synthesize certain neurotransmitters. (Some neurotransmitters are synthesized in the cell body, packaged into vesicles, and then transported to the axon terminals.)

Substances transported through the axon in the retrograde direction are mostly organelles returning to the cell body to be degraded or recycled. Retrograde transport is also an important means of intracellular communication. This transport through the axon to the cell body allows the cell body to be advised of conditions at the axon terminals and delivers to the cell body vesicles containing signal molecules (such as nerve growth factor, which activates certain nuclear genes promoting growth).

One basic bidirectional transport mechanism appears to be responsible for axonal transport. It uses different ATP-dependent "motor" proteins (kinesin or dynein), depending on the direction of transport. These proteins propel cellular components along the microtubules like trains along tracks at speeds up to 40 cm (15 inches) per day.

HOMEOSTATIC IMBALANCE 11.1 CLINICAL

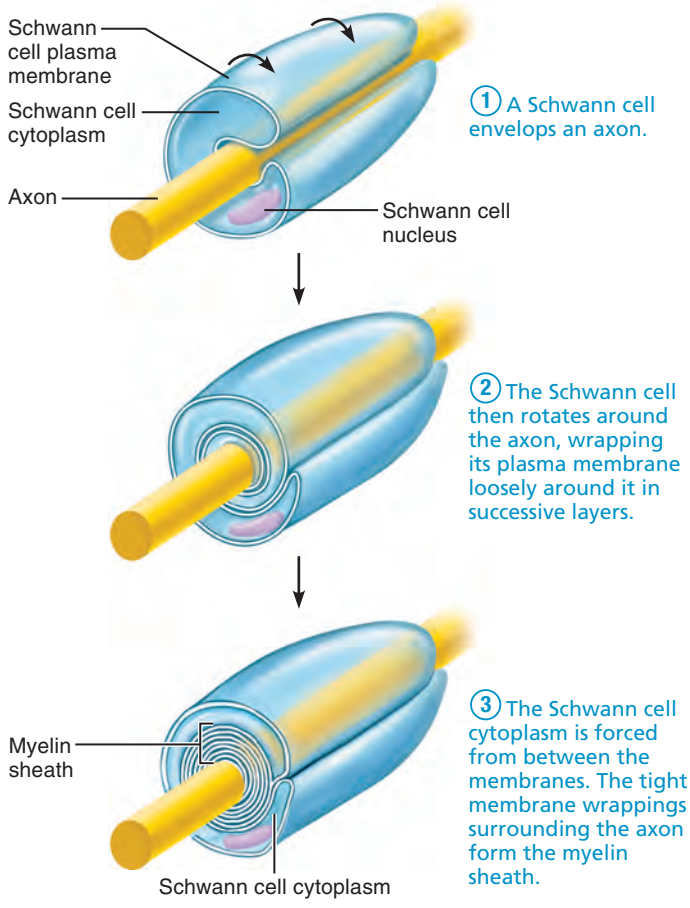
Certain viruses and bacterial toxins that damage neural tissues use retrograde axonal transport to reach the cell body. This transport mechanism has been demonstrated for polio, rabies, and herpes simplex viruses and for tetanus toxin. Researchers are investigating using retrograde transport to treat genetic diseases by introducing viruses containing "corrected" genes or microRNA to suppress defective genes. ✚

Myelin Sheath

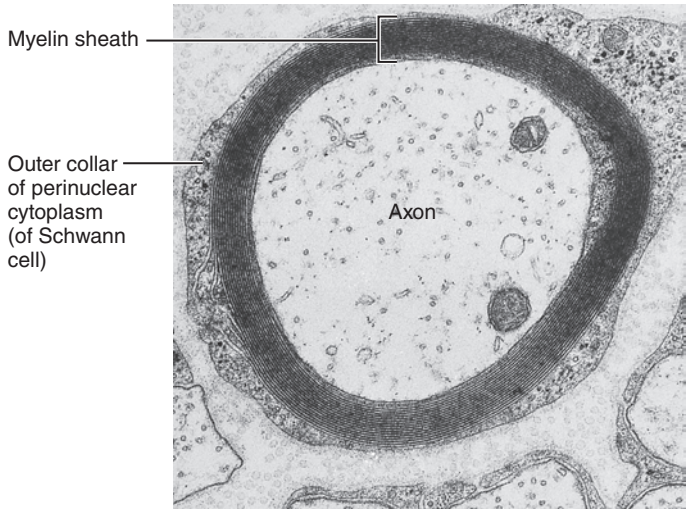
Many nerve fibers, particularly those that are long or large in diameter, are covered with a whitish, fatty (protein-lipoid), segmented **myelin sheath** (mi′ĕ-lin). Myelin protects and electrically insulates fibers, and it increases the transmission speed of nerve impulses. **Myelinated fibers** (axons bearing a myelin sheath) conduct nerve impulses rapidly, whereas **nonmyelinated fibers** conduct impulses more slowly. Note that myelin sheaths are associated only with axons. Dendrites are *always* nonmyelinated.

Myelination in the PNS

Myelin sheaths in the PNS are formed by Schwann cells, which indent to receive an axon and then wrap themselves around it in a jelly roll fashion (**Figure 11.6**). Initially the wrapping is loose, but the Schwann cell cytoplasm is gradually squeezed from between the membrane layers.



(a) Myelination of a nerve fiber (axon)



(b) Cross-sectional view of a myelinated axon (electron micrograph 24,000×)

Figure 11.6 PNS nerve fiber myelination.

When the wrapping process is complete, many concentric layers of Schwann cell plasma membrane enclose the axon, much like gauze wrapped around an injured finger. This tight coil of wrapped membranes is the myelin sheath, and its thickness depends on the number of spirals. The nucleus and most of

the cytoplasm of the Schwann cell end up as a bulge just external to the myelin sheath. This portion is called the *outer collar of perinuclear cytoplasm* (formerly known as the *neurilemma*) (Figure 11.6b).

Plasma membranes of myelinating cells contain much less protein than those of most body cells. Channel and carrier proteins are notably absent, making myelin sheaths exceptionally good electrical insulators. Another unique characteristic of these membranes is the presence of specific protein molecules that interlock to form a sort of molecular Velcro between adjacent myelin membranes.

Adjacent Schwann cells do not touch one another, so there are gaps in the sheath. These **myelin sheath gaps**, or **nodes of Ranvier** (ran′vē-ā″), occur at regular intervals (about 1 mm apart) along a myelinated axon. Axon collaterals can emerge at these gaps.

Sometimes Schwann cells surround peripheral nerve fibers but the coiling process does not occur. In such instances, a single Schwann cell can partially enclose 15 or more axons, each of which occupies a separate recess in the Schwann cell surface. Nerve fibers associated with Schwann cells in this manner are said to be *nonmyelinated* and are typically thin fibers.

Myelination in the CNS

The central nervous system contains both myelinated and nonmyelinated axons. However, in the CNS, it is the oligodendrocytes that form myelin sheaths (Figure 11.4d).

Unlike a Schwann cell, which forms only one segment of a myelin sheath, an oligodendrocyte has multiple flat processes that can coil around as many as 60 axons at the same time. As in the PNS, myelin sheath gaps separate adjacent sections of an axon's myelin sheath. However, CNS myelin sheaths lack an outer collar of perinuclear cytoplasm because cell extensions do the coiling and the squeezed-out cytoplasm is forced back toward the centrally located nucleus instead of peripherally.

As in the PNS, the smallest-diameter axons are nonmyelinated. These nonmyelinated axons are covered by the long extensions of adjacent glial cells.

Regions of the brain and spinal cord containing dense collections of myelinated fibers are referred to as **white matter** and are primarily fiber tracts. **Gray matter** contains mostly neuron cell bodies and nonmyelinated fibers.

Classification of Neurons

Neurons are classified both structurally and functionally. We describe both classifications here but use the functional classification in most discussions.

Structural Classification

Neurons are grouped structurally according to the number of processes extending from their cell body (**Table 11.1**).

- **Multipolar neurons** (*polar* = end, pole) have three or more processes—one axon and the rest dendrites. They are the most common neuron type in humans, with more than 99% of neurons in this class. Multipolar neurons are the major neuron type in the CNS.
- **Bipolar neurons** have two processes—an axon and a dendrite—that extend from opposite sides of the cell body. These rare neurons are found in some of the special sense organs such as in the retina of the eye and in the olfactory mucosa.
- **Unipolar neurons** have a single short process that emerges from the cell body and divides T-like into proximal and distal branches. The more distal **peripheral process** is often associated with a sensory receptor. The **central process** enters the CNS. Unipolar neurons are more accurately called **pseudounipolar neurons** (*pseudo* = false) because they originate as bipolar neurons. During early embryonic development, the two processes converge and partially fuse to form the short single process that issues from the cell body. Unipolar neurons are found chiefly in ganglia in the PNS, where they function as sensory neurons.

The fact that the fused peripheral and central processes of unipolar neurons are continuous and function as a single fiber might make you wonder whether they are axons or dendrites. The central process is definitely an axon because it conducts impulses away from the cell body (one definition of axon). However, the peripheral process is perplexing. Three facts favor classifying it as an axon: (1) It generates and conducts an impulse (functional definition of axon); (2) when large, it is heavily myelinated; and (3) it has a uniform diameter and is indistinguishable microscopically from an axon. But the older definition of a dendrite as a process that transmits impulses *toward* the cell body conflicts with that conclusion.

So which is it? We have chosen to emphasize the newer definition of an axon as generating and transmitting an impulse. For *unipolar neurons*, we will refer to the combined length of the peripheral and central process as an axon. In place of "dendrites," unipolar neurons have *receptive endings* (sensory terminals) at the end of the peripheral process.

Functional Classification

This scheme groups neurons according to the direction in which the nerve impulse travels relative to the central nervous system. Based on this criterion, there are sensory neurons, motor neurons, and interneurons (Table 11.1, last row).

Sensory, or **afferent**, **neurons** transmit impulses from sensory receptors in the skin or internal organs *toward* or *into* the central nervous system. Except for certain neurons found in some special sense organs, virtually all sensory neurons are unipolar, and their cell bodies are located in sensory ganglia *outside* the CNS. Only the most distal parts of these unipolar neurons act as impulse receptor sites, and the peripheral processes are often very long. For example, fibers carrying sensory impulses from the skin of your big toe travel for more than a meter before they reach their cell bodies in a ganglion close to the spinal cord.

The receptive endings of some sensory neurons are naked, in which case those terminals themselves function as sensory receptors, but many sensory neuron endings bear receptors that include other cell types. We describe the various types of general sensory receptor end organs, such as those of the skin, and the special sensory receptors of the ear, eye, and so on, in Chapter 13.

Table 11.1 Comparison of Structural Classes of Neurons

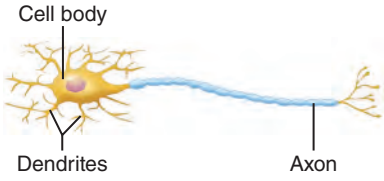
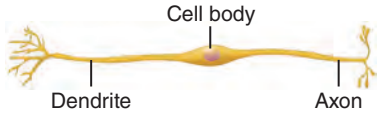
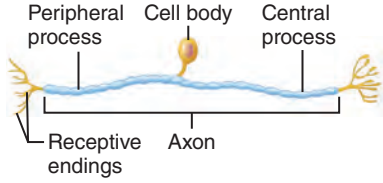
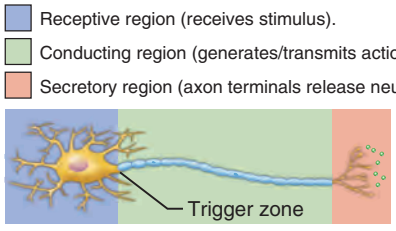
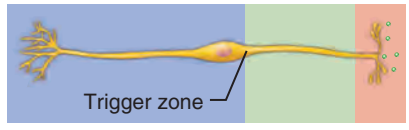
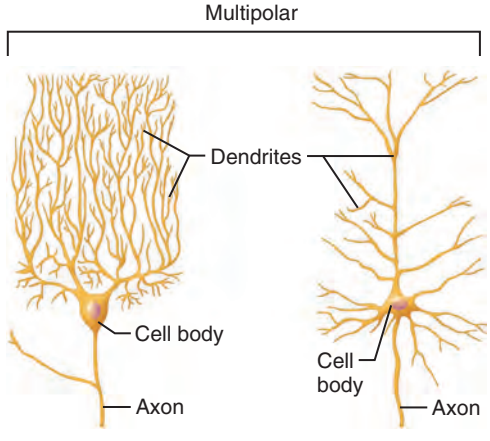
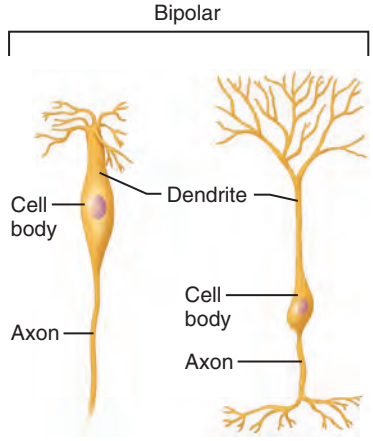
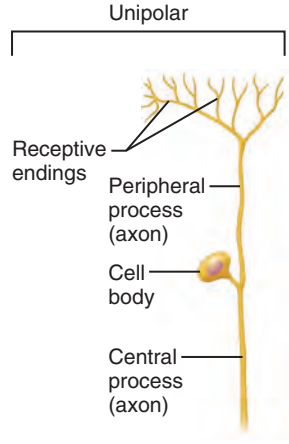
	NEURON TYPE	
MULTIPOLAR	**BIPOLAR**	**UNIPOLAR (PSEUDOUNIPOLAR)**
Structural Class: Neuron Type According to the Number of Processes Extending from the Cell Body		
Many processes extend from the cell body. All are dendrites except for a single axon.	Two processes extend from the cell body. One is a fused dendrite, the other is an axon.	One process extends from the cell body and forms central and peripheral processes, which together comprise an axon.
		
Relationship of Anatomy to the Three Functional Regions		
	 (Many bipolar neurons do not generate action potentials. In those that do, the location of the trigger zone is not universal.)	
Relative Abundance and Location in Human Body		
Most abundant in body. Major neuron type in the CNS.	Rare. Found in some special sensory organs (olfactory mucosa, eye, ear).	Found mainly in the PNS. Common only in dorsal root ganglia of the spinal cord and sensory ganglia of cranial nerves.
Structural Variations		
 Purkinje cell of cerebellum Pyramidal cell	 Olfactory cell Retinal cell	 Dorsal root ganglion cell

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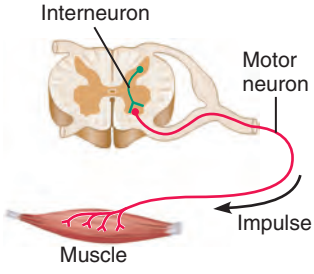
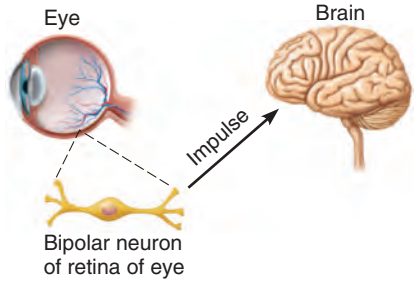
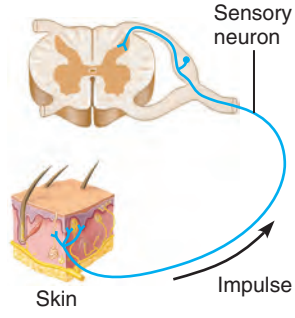
Table 11.1 Comparison of Structural Classes of Neurons *(continued)*

	NEURON TYPE	
MULTIPOLAR	**BIPOLAR**	**UNIPOLAR (PSEUDOUNIPOLAR)**
Functional Class: Neuron Type According to Direction of Impulse Conduction		
1. Most multipolar neurons are **interneurons** that conduct impulses within the CNS, integrating sensory input or motor output. May be one of a chain of CNS neurons, or a single neuron connecting sensory and motor neurons. 2. Some multipolar neurons are **motor neurons** that conduct impulses along the efferent pathways from the CNS to an effector (muscle/gland).	Essentially all bipolar neurons are **sensory neurons** that are located in some special sense organs. For example, bipolar cells of the retina are involved with transmitting visual inputs from the eye to the brain (via an intermediate chain of neurons).	Most unipolar neurons are **sensory neurons** that conduct impulses along afferent pathways to the CNS for interpretation. (These sensory neurons are called primary or first-order sensory neurons.)







Motor, or **efferent**, **neurons** carry impulses *away from* the CNS to the effector organs (muscles and glands) of the body. Motor neurons are multipolar. Except for some neurons of the autonomic nervous system, their cell bodies are located in the CNS.

Interneurons, or *association neurons*, lie between motor and sensory neurons in neural pathways and shuttle signals through CNS pathways where integration occurs. Most interneurons are confined within the CNS. They make up over 99% of the neurons of the body, including most of those in the CNS.

Almost all interneurons are multipolar, but there is considerable diversity in size and fiber-branching patterns. The Purkinje and pyramidal cells illustrated in Table 11.1 are just two examples of their variety.

Check Your Understanding

5. How does a nucleus within the brain differ from a nucleus within a neuron?
6. How is a myelin sheath formed in the CNS, and what is its function?
7. Which structural and functional type of neuron is activated first when you burn your finger? Which type is activated last to move your finger away from the source of heat?
8. MAKING connections Which part of the neuron is its fiber? How do nerve fibers differ from the fibers of connective tissue (see Chapter 4) and the fibers in muscle (see Chapter 9)?

For answers, see Answers Appendix.

11.4 The resting membrane potential depends on differences in ion concentration and permeability

Learning Objectives

- ☐ **Describe the relationship between current, voltage, and resistance.**
- ☐ **Identify different types of membrane ion channels.**
- ☐ **Define resting membrane potential and describe its electrochemical basis.**

Like all cells, neurons have a *resting membrane potential*. However, unlike most other cells, neurons can rapidly change their membrane potential. This ability underlies the function of neurons throughout the nervous system. In order to understand how neurons work, let's first explore some basic priciples of electricity and revisit the resting membrane potential.

Basic Principles of Electricity

The human body is electrically neutral—it has the same number of positive and negative charges. However, there are regions where one type of charge predominates, making those regions positively or negatively charged. Because opposite charges attract, energy must be used (work must be done) to separate them. On the other hand, the coming together of opposite charges liberates energy that can be used to do work. For this reason, situations in which there are separated electrical charges of opposite sign have potential energy.

Some Definitions: Voltage, Resistance, Current

Voltage, the measure of potential energy generated by separated electrical charges, is measured in either *volts* (V) or *millivolts* (1 mV = 0.001 V). Voltage is always measured between two points and is called the **potential difference** or simply the **potential** between the points. The greater the difference in charge between two points, the higher the voltage.

The flow of electrical charge from one point to another is a **current**, and it can be used to do work—for example, to power a flashlight. The amount of charge that moves between the two points depends on two factors: voltage and resistance. **Resistance** is the hindrance to charge flow provided by substances through which the current must pass. Substances with high electrical resistance are *insulators*, and those with low resistance are *conductors*.

Ohm's law gives the relationship between voltage, current, and resistance:

$$\text{Current } (I) = \frac{\text{voltage } (V)}{\text{resistance } (R)}$$

Ohm's law tells us three things:

- Current (I) is directly proportional to voltage: The greater the voltage (potential difference), the greater the current.
- There is no net current flow between points that have the same potential.
- Current is inversely related to resistance: The greater the resistance, the smaller the current.

In the body, electrical currents reflect the flow of ions across cellular membranes. (Unlike the electrons flowing along your house wiring, there are no free electrons "running around" in a living system.) Recall that there is a slight difference in the numbers of positive and negative ions on the two sides of cellular plasma membranes (a charge separation), so there is a potential across those membranes. The plasma membranes provide the resistance to current flow.

Role of Membrane Ion Channels

Recall that plasma membranes are peppered with a variety of membrane proteins that act as *ion channels*. Each of these channels is selective as to the type of ion (or ions) it allows to pass. For example, a potassium ion channel allows only potassium ions to pass.

Membrane channels are large proteins, often with several subunits. Some channels, **leakage** or **nongated channels**, are always open. Other channels are *gated*: Part of the protein forms a molecular "gate" that changes shape to open and close the channel in response to specific signals. There are three main types of gated channels:

- **Chemically gated channels**, also known as **ligand-gated channels**, open when the appropriate chemical (in this case a neurotransmitter) binds (**Figure 11.7a**).
- **Voltage-gated channels** open and close in response to changes in the membrane potential (Figure 11.7b).
- **Mechanically gated channels** open in response to physical deformation of the receptor (as in sensory receptors for touch and pressure).

When gated ion channels open, ions diffuse quickly across the membrane. Ions move along chemical *concentration gradients* when they diffuse passively from an area of their higher concentration to an area of lower concentration. They move

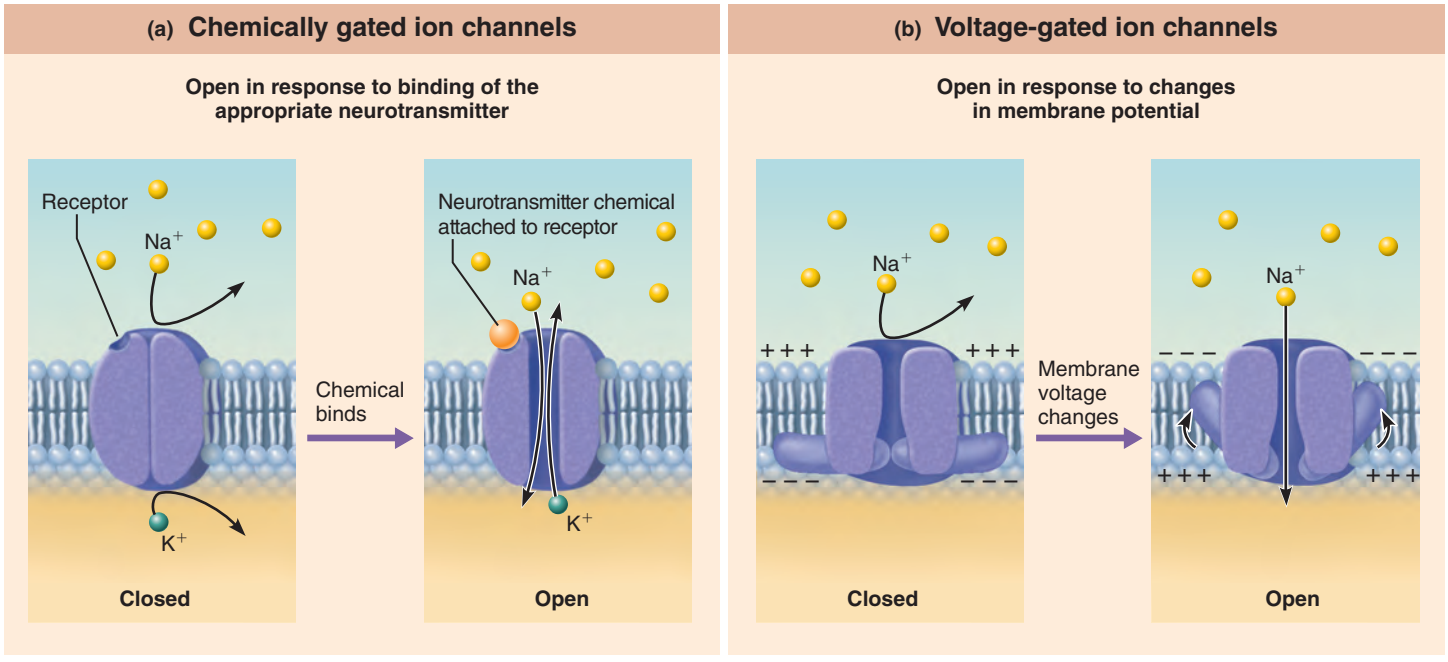


Figure 11.7 Operation of gated channels. (a) A chemically gated channel permeable to both Na^+ and K^+, and **(b)** a voltage-gated Na^+ channel.

Focus Figure 11.1 **Generating a resting membrane potential depends on (1) differences in K^+ and Na^+ concentrations inside and outside cells, and (2) differences in permeability of the plasma membrane to these ions.**

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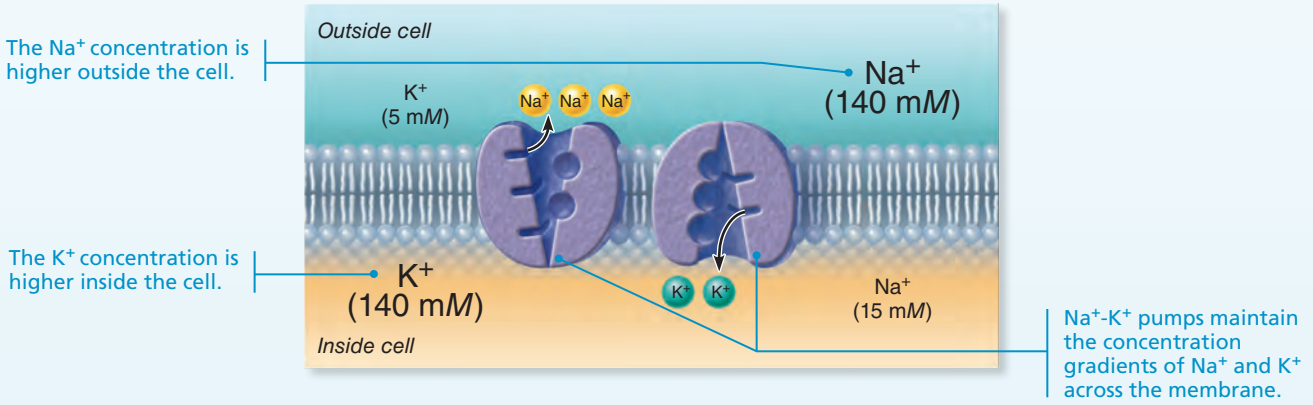
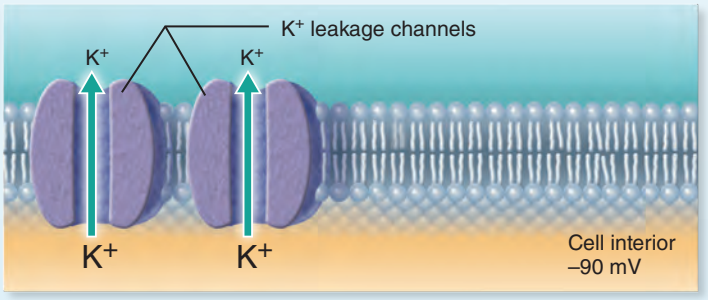
The concentrations of Na^+ and K^+ on each side of the membrane are different.



The permeabilities of Na^+ and K^+ across the membrane are different. In the next three panels, we will build the resting membrane potential step by step.

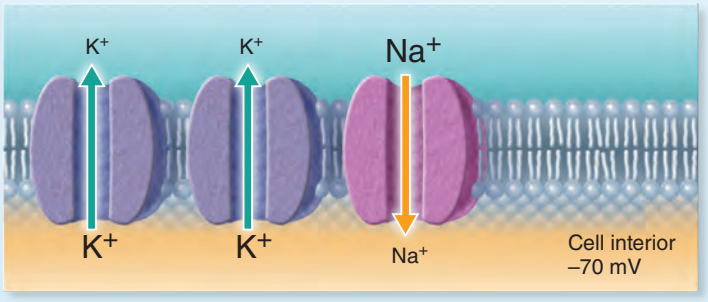
Suppose a cell has only K^+ channels...



K^+ loss through abundant leakage channels establishes a negative membrane potential.

- The membrane is highly permeable to K^+, so K^+ flows down its concentration gradient.
- As positive K^+ leaks out, a negative voltage (electrical gradient) develops on the membrane interior. This electrical gradient pulls K^+ back in.
- At –90 mV, the concentration and electrical gradients for K^+ are balanced.

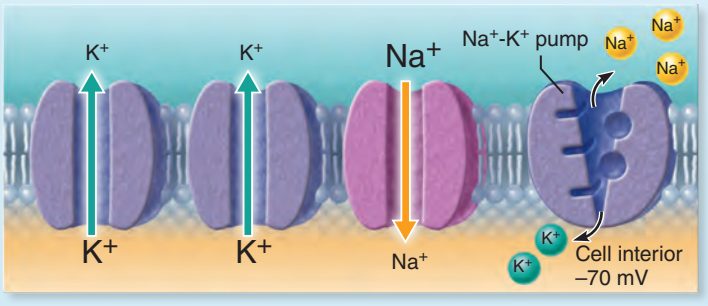
Now, let's add some Na^+ channels to our cell...



Na^+ entry through a few leakage channels reduces the negative membrane potential slightly.

- Adding Na^+ channels creates a small Na^+ permeability that brings the membrane potential to –70 mV.

Finally, let's add a pump to compensate for leaking ions.



Na^+-K^+ pumps maintain the concentration gradients, resulting in the resting membrane potential.

- A cell at rest is like a leaky boat: K^+ leaks out and Na^+ leaks in through open channels.
- The "bailing pump" for this boat is the **Na^+-K^+ pump**, which transports Na^+ out and K^+ in.

along *electrical gradients* when they move toward an area of opposite electrical charge. Together, electrical and concentration gradients constitute the **electrochemical gradient** that determines which way ions flow. Ions flowing along electrochemical gradients underlie all electrical events in neurons. Flowing ions create electrical currents and voltage changes across the membrane. These voltage changes are described by the rearranged Ohm's law equation:

$$\text{Voltage } (V) = \text{current } (I) \times \text{resistance } (R)$$

Generating the Resting Membrane Potential

A voltmeter is used to measure the potential difference between two points. When one microelectrode of the voltmeter is inserted into a neuron and the other is in the extracellular fluid, it records a voltage across the membrane of approximately −70 mV (**Figure 11.8**). The minus sign indicates that the cytoplasmic side (inside) of the membrane is negatively charged relative to the outside. This potential difference in a resting neuron (V_r) is called the **resting membrane potential**, and the membrane is said to be **polarized**. The value of the resting membrane potential varies (from −40 mV to −90 mV) in different types of neurons.

The resting potential exists only across the membrane; the bulk solutions inside and outside the cell are electrically neutral. Two factors generate the resting membrane potential: differences in the ionic composition of the intracellular and extracellular fluids, and differences in the permeability of the plasma membrane to those ions.

Differences in Ionic Composition

First, let's compare the ionic makeup of the intracellular and extracellular fluids, as shown in *Focus on Resting Membrane Potential* (**Focus Figure 11.1**). The cell cytosol contains a lower concentration of Na^+ and a higher concentration of K^+ than the extracellular fluid. Negatively charged (anionic) proteins (not shown) help to balance the positive charges of intracellular cations (primarily K^+). In the extracellular fluid, the positive charges of Na^+ and other cations are balanced chiefly by chloride ions (Cl^-). Although there are many other solutes (glucose, urea, and other ions) in both fluids, potassium (K^+) plays the most important role in generating the membrane potential.

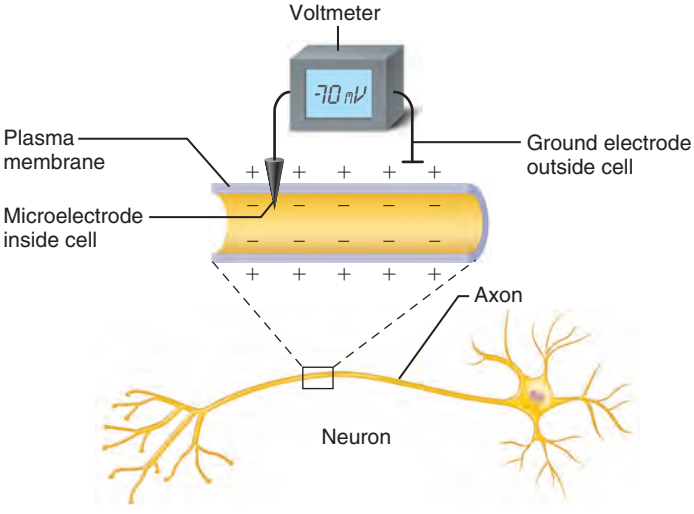


Figure 11.8 Measuring membrane potential in neurons. The potential difference between an electrode inside a neuron and the ground electrode in the extracellular fluid is approximately −70 mV (inside negative).

Differences in Plasma Membrane Permeability

Next, let's consider the differential permeability of the membrane to various ions (Focus Figure 11.1, bottom). At rest the membrane is impermeable to the large anionic cytoplasmic proteins, very slightly permeable to sodium, approximately 25 times more permeable to potassium than to sodium, and quite permeable to chloride ions. These resting permeabilities reflect the properties of the leakage ion channels in the membrane. Potassium ions diffuse out of the cell along their *concentration gradient* much more easily than sodium ions can enter the cell along theirs. K^+ flowing out of the cell causes the cell to become more negative inside. Na^+ trickling into the cell makes the cell just slightly more positive than it would be if only K^+ flowed. Therefore, at resting membrane potential, the negative interior of the cell is due to a much greater ability for K^+ to diffuse out of the cell than for Na^+ to diffuse into the cell.

Because some K^+ is always leaking out of the cell and some Na^+ is always leaking in, you might think that the concentration gradients would eventually "run down," resulting in equal concentrations of Na^+ and K^+ inside and outside the cell. This does not happen because the ATP-driven sodium-potassium pump first ejects three Na^+ from the cell and then transports two K^+ back into the cell. In other words, the **sodium-potassium pump (Na^+-K^+ ATPase)** stabilizes the resting membrane potential by maintaining the concentration gradients for sodium and potassium (Focus Figure 11.1, bottom).

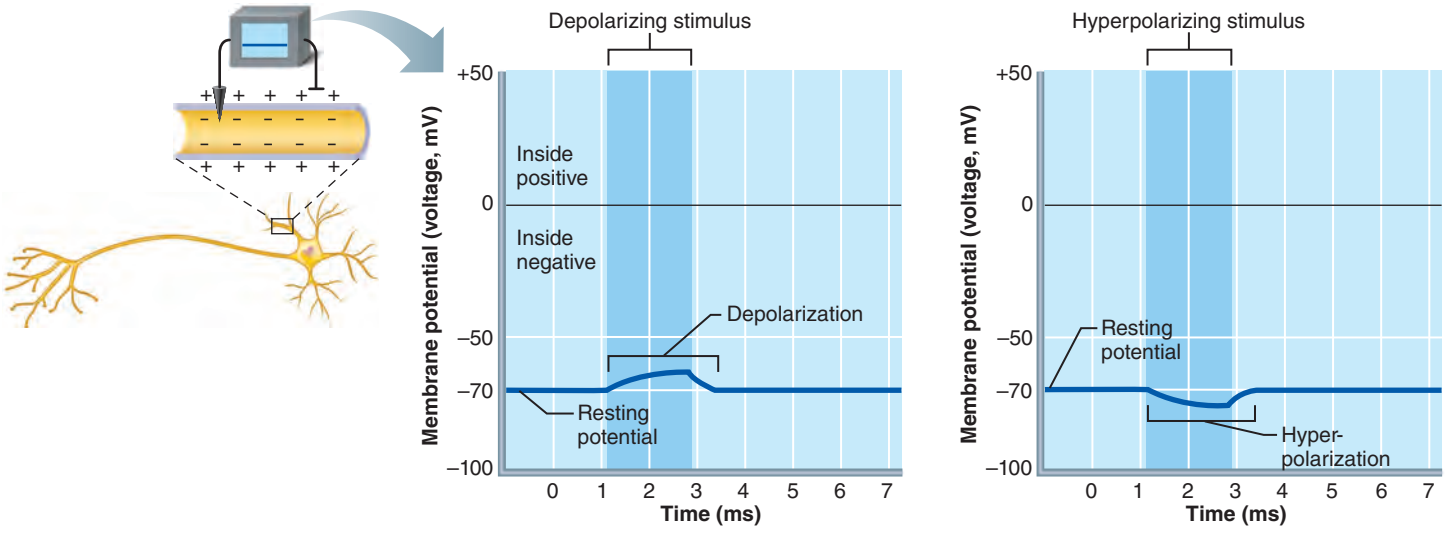
Changing the Resting Membrane Potential

Neurons use changes in their membrane potential as signals to receive, integrate, and send information. A change in membrane potential can be produced by (1) anything that alters ion concentrations on the two sides of the membrane, or (2) anything that changes membrane permeability to any ion. However, only permeability changes (changes in the number of open channels) are important for transferring information.

Changes in membrane potential can produce two types of signals:

- *Graded potentials*—usually incoming signals operating over short distances
- *Action potentials*—long-distance signals of axons

The terms *depolarization* and *hyperpolarization* describe changes in membrane potential *relative to resting membrane potential.*



(a) Depolarization: The membrane potential moves toward 0 mV, the inside becoming less negative (more positive).

(b) Hyperpolarization: The membrane potential increases, the inside becoming more negative.

Figure 11.9 Depolarization and hyperpolarization of the membrane. The resting membrane potential is approximately –70 mV (inside negative) in neurons.

Depolarization is a decrease in membrane potential: The inside of the membrane becomes *less negative* (moves closer to zero) than the resting potential. For instance, a change in resting potential from –70 mV to –65 mV is a depolarization (**Figure 11.9a**). Depolarization also includes events in which the membrane potential reverses and moves above zero to become positive.

Hyperpolarization is an increase in membrane potential: The inside of the membrane becomes *more negative* (moves further from zero) than the resting potential. For example, a change from –70 mV to –75 mV is hyperpolarization (Figure 11.9b). As we will describe shortly, depolarization increases the probability of producing nerve impulses, whereas hyperpolarization reduces this probability.

Check Your Understanding

9. For an open channel, what factors determine in which direction ions will move through that channel?

10. For which cation are there the largest number of leakage channels in the plasma membrane?

For answers, see Answers Appendix.

11.5 Graded potentials are brief, short-distance signals within a neuron

Learning Objective

Describe graded potentials and name several examples.

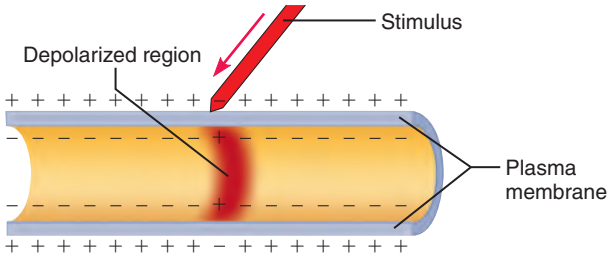
Graded potentials are short-lived, localized changes in membrane potential. They can be either depolarizations or hyperpolarizations. These changes cause current flows that decrease in magnitude with distance. Graded potentials are called "graded" because their magnitude varies directly with stimulus strength. The stronger the stimulus, the more the voltage changes and the farther the current flows.

Graded potentials are triggered by some change (a stimulus) in the neuron's environment that opens gated ion channels. Graded potentials are given different names, depending on where they occur and the functions they perform.

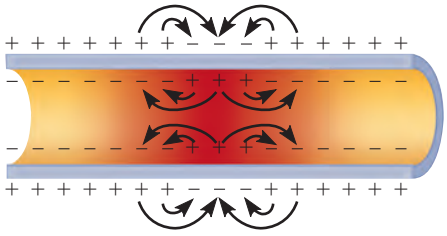
- When the receptor of a sensory neuron is excited by some form of energy (heat, light, or other), the resulting graded potential is called a *receptor potential* or *generator potential*. We will consider these types of graded potentials in Chapter 13.
- When the stimulus is a neurotransmitter released by another neuron, the graded potential is called a *postsynaptic potential* because the neurotransmitter is released into a fluid-filled gap called a synapse and influences the neuron beyond the synapse.

Fluids inside and outside cells are fairly good conductors, and current, carried by ions, flows through these fluids whenever voltage changes. Suppose a stimulus depolarizes a small area of a neuron's plasma membrane (**Figure 11.10a**). Current (ions) flows on both sides of the membrane between the depolarized (active) membrane area and the adjacent polarized (resting) areas. Positive ions migrate toward more negative areas (the direction of cation movement is the direction of current flow), and negative ions simultaneously move toward more positive areas (Figure 11.10b).

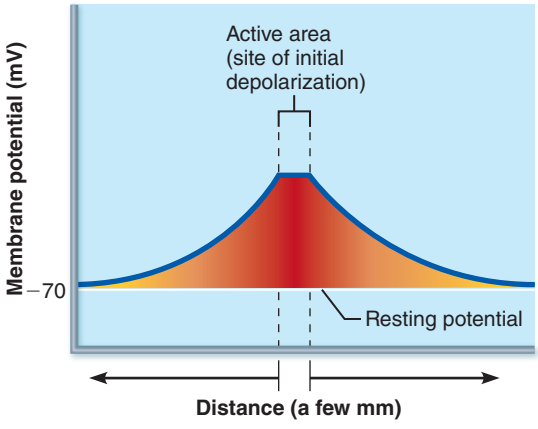
For our patch of plasma membrane, positive ions (mostly K^+) inside the cell move away from the depolarized area and accumulate on the neighboring membrane areas, where they neutralize negative ions. Meanwhile, positive ions on the outside of the membrane move toward the depolarized region,



(a) Depolarization: A small patch of the membrane (red area) depolarizes.



(b) Depolarization spreads: Opposite charges attract each other. This creates local currents (black arrows) that depolarize adjacent membrane areas, spreading the wave of depolarization.



(c) Membrane potential decays with distance: Because current is lost through the "leaky" plasma membrane, the voltage declines with distance from the stimulus (the voltage is *decremental*). Consequently, graded potentials are short-distance signals.

Figure 11.10 The spread and decay of a graded potential.

which is momentarily less positive. As these positive ions move, their "places" on the membrane become occupied by negative ions (such as Cl^- and HCO_3^-), sort of like ionic musical chairs. In this way, at regions next to the depolarized region, the inside becomes less negative and the outside becomes less positive. The depolarization spreads as the neighboring membrane patch is, in turn, depolarized.

As just explained, the flow of current to adjacent membrane areas changes the membrane potential there as well. However, the plasma membrane is permeable like a leaky garden hose, and most of the charge is quickly lost through leakage channels. Consequently, the current dies out within a few millimeters of its origin and is said to be *decremental* (Figure 11.10c).

Because the current dissipates quickly and decays (declines) with increasing distance from the site of initial depolarization, graded potentials can act as signals only over very short distances. Nonetheless, they are essential in initiating action potentials, the long-distance signals.

Check Your Understanding

11. What determines the size of a graded potential?

For answers, see Answers Appendix.

11.6 Action potentials are brief, long-distance signals within a neuron

Learning Objectives

- **Compare and contrast graded potentials and action potentials.**
- **Explain how action potentials are generated and propagated along neurons.**
- **Define absolute and relative refractory periods.**
- **Define saltatory conduction and explain how it differs from continuous conduction.**

The principal way neurons send signals over long distances is by generating and propagating (transmitting) action potentials. Only cells with *excitable membranes*—neurons and muscle cells—can generate action potentials.

An **action potential (AP)** is a brief reversal of membrane potential with a total amplitude (change in voltage) of about 100 mV (from −70 mV to +30 mV). Depolarization is followed by repolarization and often a short period of hyperpolarization. The whole event is over in a few milliseconds. Unlike graded potentials, action potentials do not decay with distance.

In a neuron, an AP is also called a **nerve impulse**, and is typically generated *only in axons*. A neuron generates a nerve impulse only when adequately stimulated. The stimulus changes the permeability of the neuron's membrane by opening specific voltage-gated channels on the axon.

These channels open and close in response to changes in the membrane potential. They are activated by local currents (graded potentials) that spread toward the axon along the dendritic and cell body membranes.

In many neurons, the transition from local graded potential to long-distance action potential takes place at the axon hillock. In sensory neurons, the action potential is generated by the peripheral (axonal) process just proximal to the receptor region. However, for simplicity, we will just use the term axon in our discussion. We'll look first at the generation of an action potential and then at its propagation.

Generating an Action Potential

Focus on an Action Potential (**Focus Figure 11.2**) on pp. 360–361 describes how an action potential is generated. Let's start with a neuron in the resting (polarized) state.

① **Resting state: All gated Na^+ and K^+ channels are closed.** Only the leakage channels are open, maintaining resting

Focus Figure 11.2 **The action potential (AP) is a brief change in membrane potential in a patch of membrane that is depolarized by local currents.**

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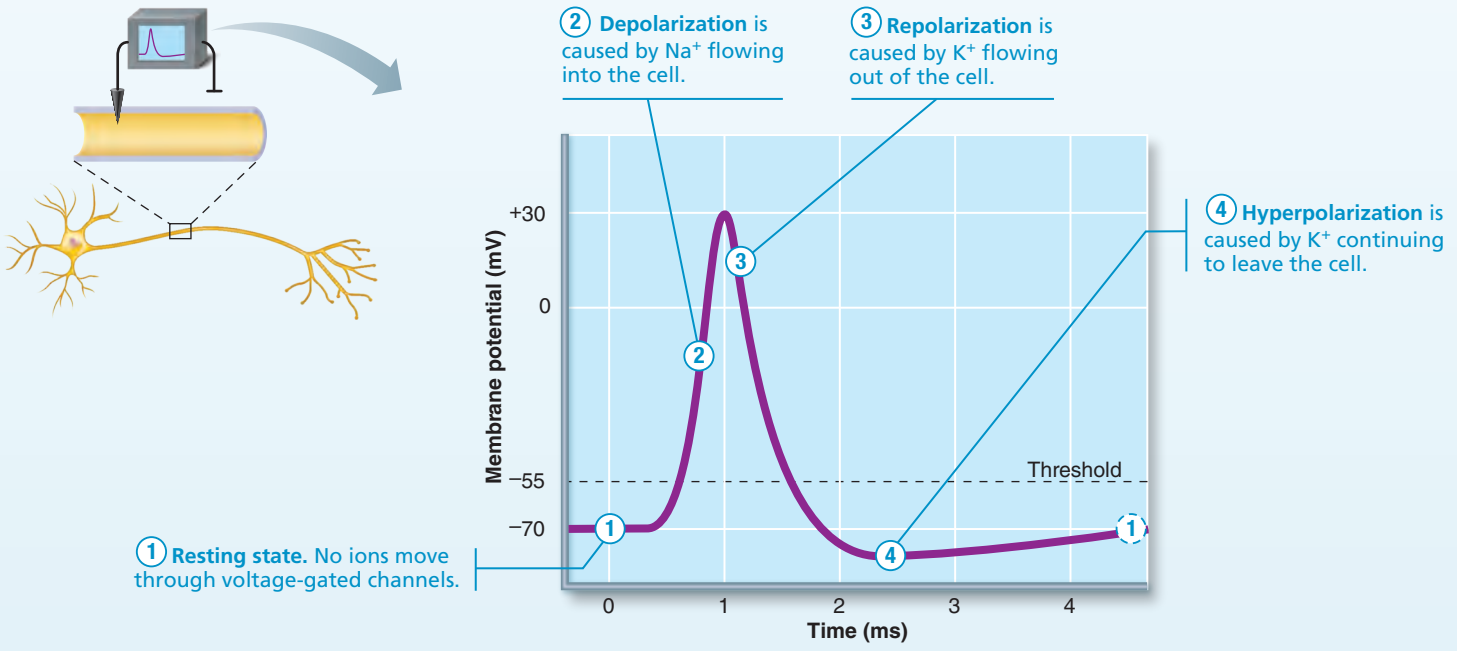
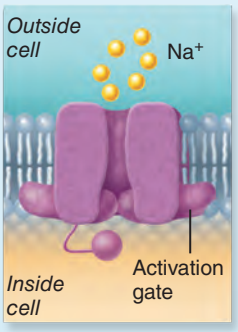
The big picture

What does this graph show? During the course of an action potential (below), voltage changes over time at a given point within the axon.

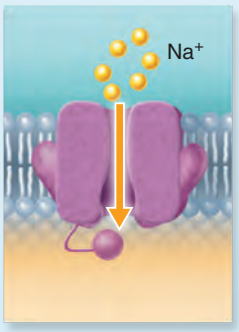


The key players

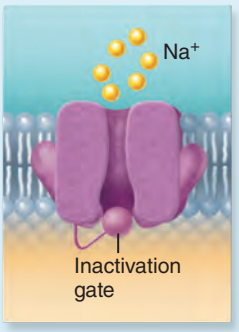
Voltage-gated Na^+ channels have two gates and alternate between three different states.



Closed at the resting state, so no Na^+ enters the cell through them

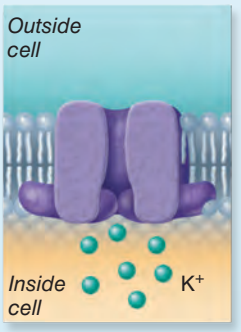


Opened by depolarization, allowing Na^+ to enter the cell

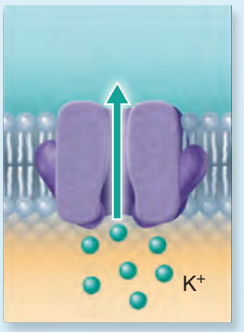


Inactivated— channels automatically blocked by inactivation gates soon after they open

Voltage-gated K^+ channels have one gate and two states.



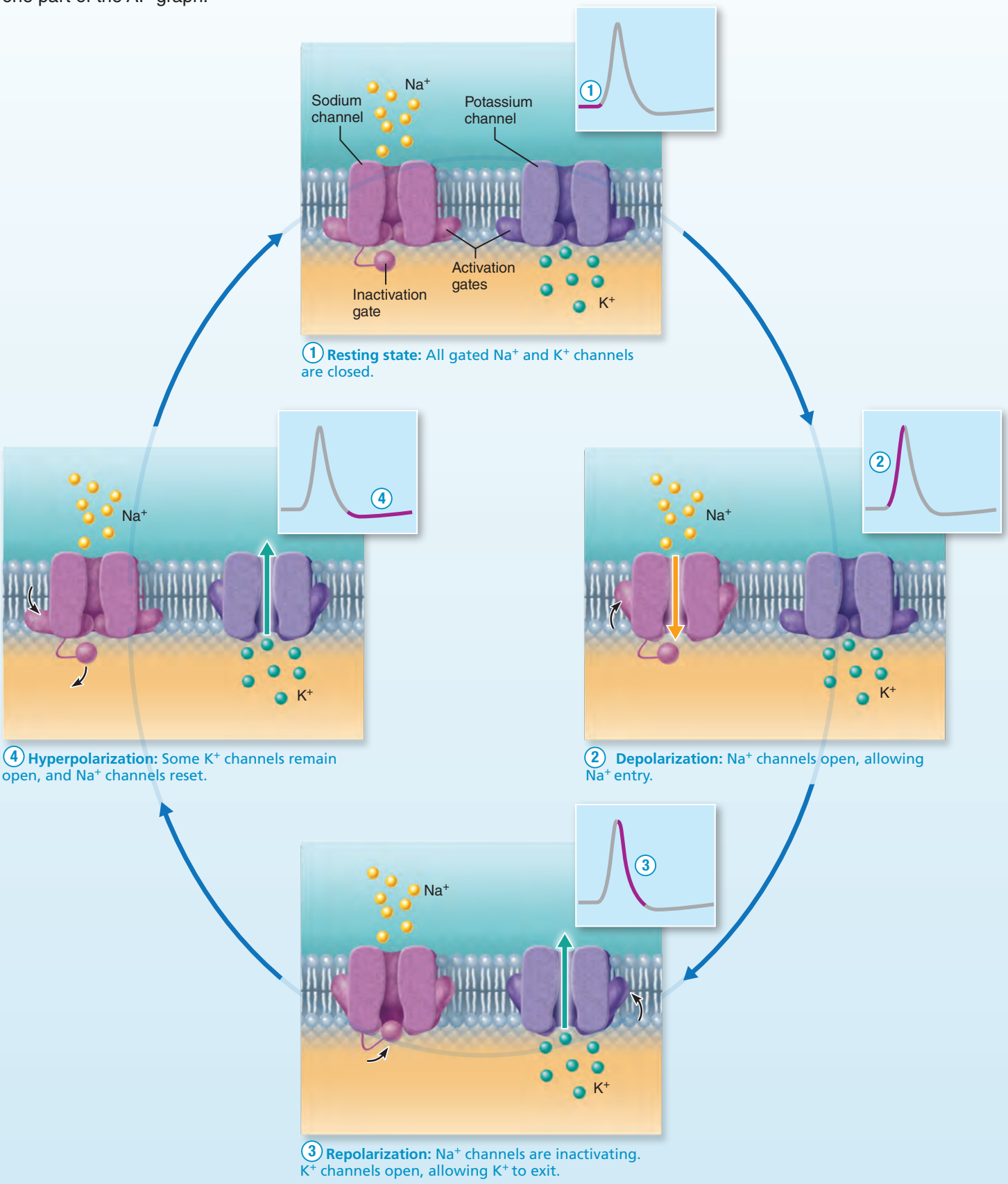
Closed at the resting state, so no K^+ exits the cell through them



Opened by depolarization, after a delay, allowing K^+ to exit the cell

The events

Each step corresponds to one part of the AP graph.



1 **Resting state:** All gated Na^+ and K^+ channels are closed.

2 **Depolarization:** Na^+ channels open, allowing Na^+ entry.

3 **Repolarization:** Na^+ channels are inactivating. K^+ channels open, allowing K^+ to exit.

4 **Hyperpolarization:** Some K^+ channels remain open, and Na^+ channels reset.

membrane potential. Each Na^+ channel has two gates: a voltage-sensitive *activation gate* that is closed at rest and responds to depolarization by opening, and an *inactivation gate* that blocks the channel once it is open. Thus, *depolarization opens and then inactivates sodium channels.*

Both gates must be open for Na^+ to enter, but the closing of *either* gate effectively closes the channel. In contrast, each active potassium channel has a single voltage-sensitive gate that is closed in the resting state and opens slowly in response to depolarization.

② **Depolarization: Na^+ channels open.** As local currents depolarize the axon membrane, the voltage-gated sodium channels open and Na^+ rushes into the cell. This influx of positive charge depolarizes that local patch of membrane further, opening more Na^+ channels so the cell interior becomes progressively less negative.

When depolarization reaches a critical level called **threshold** (often between −55 and −50 mV), depolarization becomes self-generating, urged on by positive feedback. As more Na^+ enters, the membrane depolarizes further and opens still more channels until all Na^+ channels are open. At this point, Na^+ permeability is about 1000 times greater than in a resting neuron. As a result, the membrane potential becomes less and less negative and then overshoots to about +30 mV as Na^+ rushes in along its electrochemical gradient. This rapid depolarization and polarity reversal produces the sharp upward *spike* of the action potential (Focus Figure 11.2).

Earlier, we stated that membrane potential depends on membrane permeability, but here we say that membrane permeability depends on membrane potential. Can both statements be true? Yes, because these two relationships establish a *positive feedback cycle*: Increasing Na^+ permeability due to increased channel openings leads to greater depolarization, which increases Na^+ permeability, and so on. This explosive positive feedback cycle is responsible for the rising (depolarizing) phase of an action potential—it puts the "action" in the action potential.

③ **Repolarization: Na^+ channels are inactivating, and K^+ channels open.** The explosively rising phase of the action potential persists for only about 1 ms. It is self-limiting because the inactivation gates of the Na^+ channels begin to close at this point. As a result, the membrane permeability to Na^+ declines to resting levels, and the net influx of Na^+ stops completely. Consequently, the AP spike stops rising.

As Na^+ entry declines, the slow voltage-gated K^+ channels open and K^+ rushes out of the cell, following its electrochemical gradient. This restores the internal negativity of the resting neuron, an event called **repolarization**. Both the abrupt decline in Na^+ permeability and the increased permeability to K^+ contribute to repolarization.

④ **Hyperpolarization: Some K^+ channels remain open, and Na^+ channels reset.** The period of increased K^+ permeability typically lasts longer than needed to restore the resting state. As a result of the excessive K^+ efflux before the potassium channels close, a hyperpolarization is seen on the AP curve as a slight dip following the spike. Also at this point, the Na^+ channels begin to reset to their original position by changing shape to reopen their inactivation gates and close their activation gates.

Repolarization restores resting electrical conditions, but it does *not* restore resting ionic conditions. After repolarization, the *sodium-potassium pump* redistributes the ions. While it might appear that tremendous numbers of Na^+ and K^+ ions change places during an action potential, this is not the case. Only small amounts of sodium and potassium cross the membrane. (The Na^+ influx required to reach threshold produces only a 0.012% c hange in in tracellular Na^+ concentration.) These small ionic changes are quickly corrected because an axon membrane has thousands of Na^+-K^+ pumps.

Threshold and the All-or-None Phenomenon

Not all local depolarization events produce APs. The depolarization must reach threshold values if an axon is to "fire." What determines the *threshold point*?

One explanation is that threshold is the membrane potential at which the outward current created by K^+ movement is exactly equal to the inward current created by Na^+ movement. Threshold is typically reached when the membrane has been depolarized by 15 to 20 mV from the resting value. This depolarization status represents an unstable equilibrium state. If one more Na^+ enters, further depolarization occurs, opening more Na^+ channels and allowing more Na^+ to enter. If, on the other hand, one more K^+ leaves, the membrane potential is driven away from threshold, Na^+ channels close, and K^+ continues to diffuse outward until the potential returns to its resting value.

Recall that local depolarizations are graded potentials and their magnitude increases when stimuli become more intense. Brief weak stimuli (*subthreshold stimuli*) produce subthreshold depolarizations that are not translated into nerve impulses. On the other hand, stronger *threshold stimuli* produce depolarizing currents that push the membrane potential toward and beyond the threshold voltage. As a result, Na^+ permeability rises to such an extent that entering sodium ions "swamp" (exceed) the outward movement of K^+, establishing the positive feedback cycle and generating an AP.

The critical factor here is the total amount of current that flows through the membrane during a stimulus (electrical charge × time). Strong stimuli depolarize the membrane to threshold quickly. Weaker stimuli must be applied for longer periods to provide the crucial amount of current flow. Very weak stimuli do not trigger an AP because the local current flows they produce are so slight that they dissipate long before threshold is reached.

An AP is an **all-or-none phenomenon**: It either happens completely or doesn't happen at all. We can compare the generation of an AP to lighting a match under a small dry twig. The changes occurring where the twig is heated are analogous to the change in membrane permeability that initially allows more Na^+ to enter the cell. When that part of the twig becomes hot enough (when enough Na^+ enters the cell), it reaches the flash point (threshold) and the flame consumes the entire twig, even if

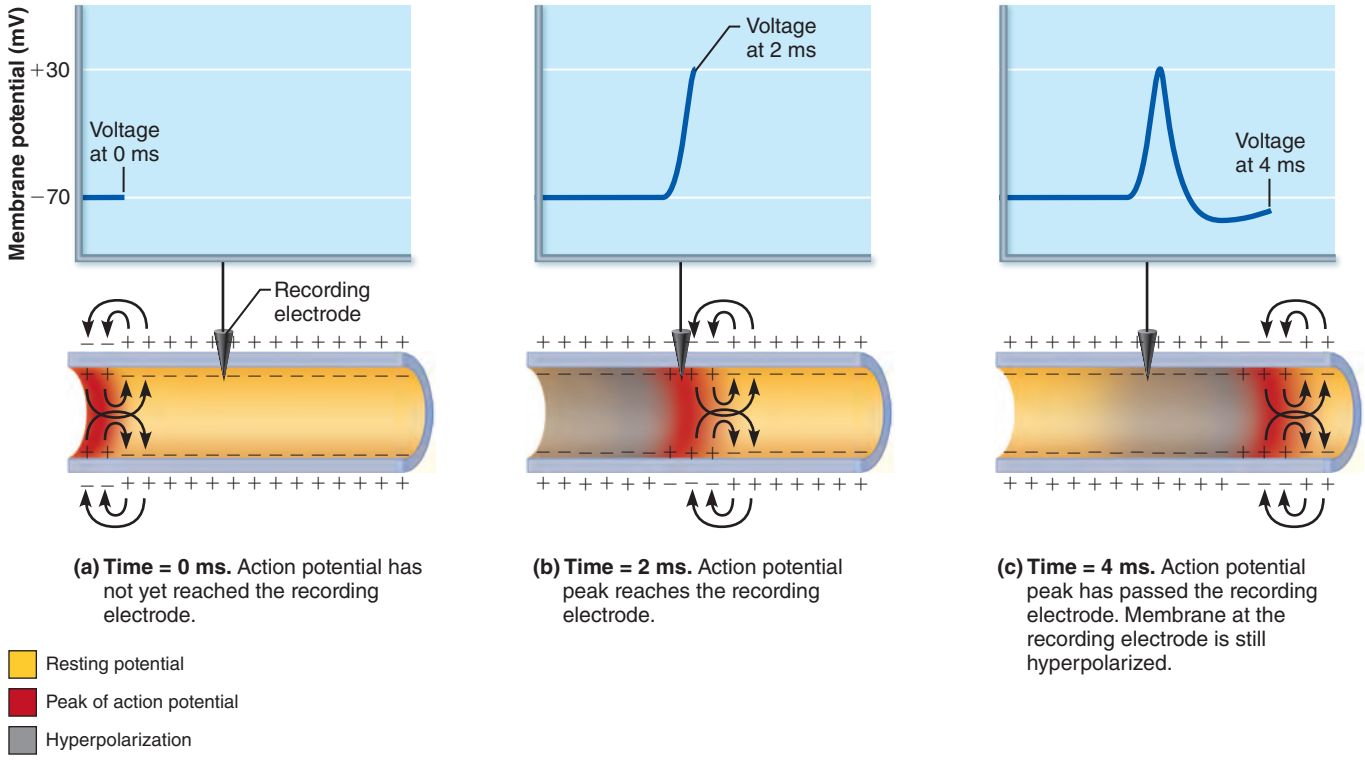


Figure 11.11 Propagation of an action potential (AP). Recordings at three successive times as an AP propagates along an axon (from left to right). The arrows show the direction of local current flow generated by the movement of positive ions. This current brings the resting membrane at the leading edge of the AP to threshold, propagating the AP forward.

you blow out the match. Similarly, the AP is generated and propagated whether or not the stimulus continues. But if you blow out the match before the twig reaches the threshold temperature, ignition will not take place. Likewise, if the number of Na^+ ions entering the cell is too low to achieve threshold, no AP will occur.

Propagation of an Action Potential

If it is to serve as the neuron's signaling device, an AP must be **propagated** along the axon's entire length. As we have seen, the AP is generated by the influx of Na^+ through a given area of the membrane. This influx establishes local currents that depolarize adjacent membrane areas in the forward direction (away from the origin of the nerve impulse), which opens voltage-gated channels and triggers an action potential there (**Figure 11.11**).

Because the area where the AP originated has just generated an AP, the sodium channels in that area are inactivated and no new AP is generated there. For this reason, the AP propagates away from its point of origin. (If an *isolated* axon is stimulated by an electrode, the nerve impulse will move away from the point of stimulus in both directions along the axon.) In the body, APs are initiated at one end of the axon and conducted away from that point toward the axon's terminals. Once initiated, an AP is *self-propagating* and continues along the axon at a constant velocity—something like a domino effect.

Following depolarization, each segment of axon membrane repolarizes, restoring the resting membrane potential in that region. Because these electrical changes also set up local currents, the repolarization wave chases the depolarization wave down the length of the axon.

The propagation process we have just described occurs on nonmyelinated axons. On p. 364, we will describe propagation along myelinated axons.

Although the phrase *conduction of a nerve impulse* is commonly used, nerve impulses are not really conducted in the same way that an insulated wire conducts current. In fact, neurons are fairly poor conductors, and as noted earlier, local current flows decline with distance because the charges leak through the membrane. The expression *propagation of a nerve impulse* is more accurate, because the AP is *regenerated anew* at each membrane patch, and every subsequent AP is identical to the one that was generated initially.

Coding for Stimulus Intensity

Once generated, all APs are independent of stimulus strength, and all APs are alike. So how can the CNS determine whether a particular stimulus is intense or weak—information it needs to initiate an appropriate response?

The answer is really quite simple: Strong stimuli generate nerve impulses more *often* in a given time interval than do weak stimuli. Stimulus intensity is coded for by the number of impulses per second—that is, by the *frequency of action potentials*—rather than by increases in the strength (amplitude) of the individual APs (**Figure 11.12**).

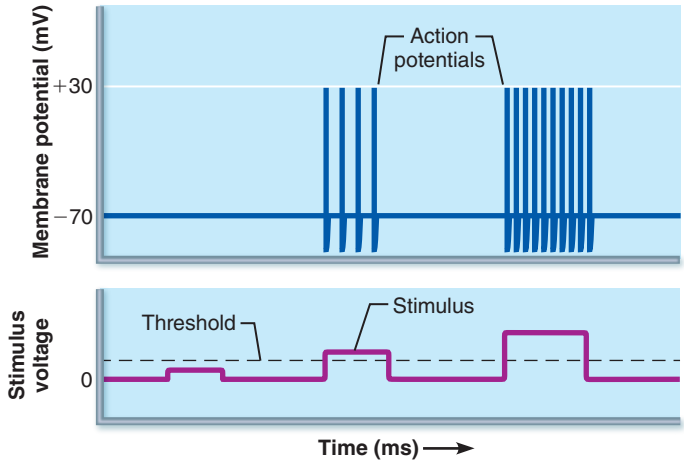


Figure 11.12 Relationship between stimulus strength and action potential frequency. APs are shown as vertical lines in the upper trace. The lower trace shows the intensity of the applied stimulus. A subthreshold stimulus does not generate an AP, but once threshold voltage is reached, the stronger the stimulus, the more frequently APs are generated.

Refractory Periods

When a patch of neuron membrane is generating an AP and its voltage-gated sodium channels are open, the neuron cannot respond to another stimulus, no matter how strong. This period, from the opening of the Na^+ channels until the Na^+ channels begin to reset to their original resting state, is called the **absolute refractory period** (**Figure 11.13**). It ensures that each AP is a separate, *all-or-none event* and enforces one-way transmission of the AP.

The **relative refractory period** follows the absolute refractory period. During the relative refractory period, most Na^+ channels have returned to their resting state, some K^+ channels are still open, and repolarization is occurring. The axon's threshold for AP generation is substantially elevated, so a stimulus that would normally generate an AP is no longer sufficient. An exceptionally strong stimulus can reopen the Na^+ channels that have already returned to their resting state and generate another AP. Strong stimuli trigger more frequent APs by intruding into the relative refractory period.

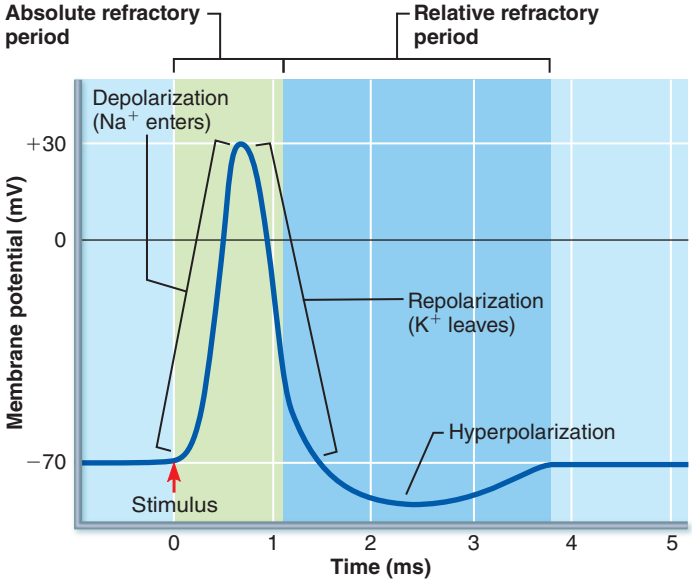


Figure 11.13 Absolute and relative refractory periods in an AP.

Conduction Velocity

How fast do APs travel? Conduction velocities of neurons vary widely. Nerve fibers that transmit impulses most rapidly (100 m/s or more) are found in neural pathways where speed is essential, such as those that mediate postural reflexes. Axons that conduct impulses more slowly typically serve internal organs (the gut, glands, blood vessels), where slower responses are not a handicap. The rate of impulse propagation depends largely on two factors:

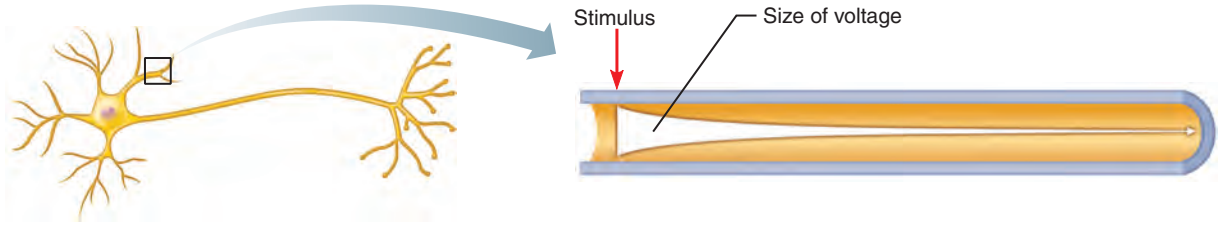
- **Axon diameter.** As a rule, the larger the axon's diameter, the faster it conducts impulses. Larger axons conduct more rapidly because they offer less resistance to the flow of local currents, bringing adjacent areas of the membrane to threshold more quickly.
- **Degree of myelination.** Action potentials propagate because they are regenerated by voltage-gated channels in the membrane (**Figure 11.14a**, **b**). In **continuous conduction**, AP propagation involving nonmyelinated axons, these channels are immediately adjacent to each other. Continuous conduction is relatively slow.

  The presence of a myelin sheath dramatically increases the rate of AP propagation. By acting as an insulator, myelin prevents almost all charge from leaking from the axon and allows the membrane voltage to change more rapidly. Current can pass through the membrane of a myelinated axon *only* at the myelin sheath gaps, where there is no myelin sheath and the axon is bare. Nearly all the voltage-gated Na^+ channels are concentrated in these gaps.

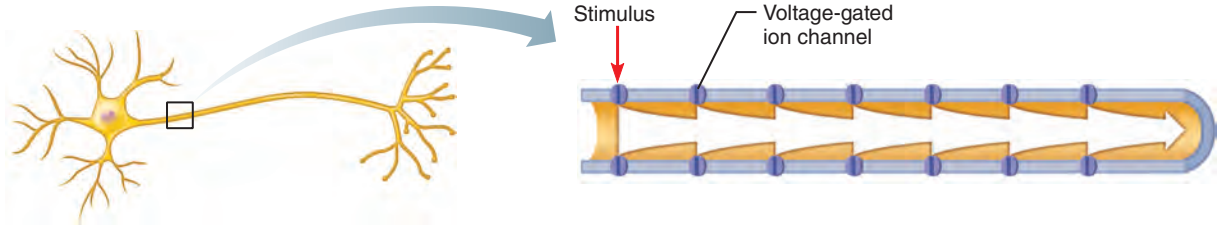
  When an AP is generated in a myelinated fiber, the local depolarizing current does not dissipate through the adjacent membrane regions, which are nonexcitable. Instead, the current is maintained and moves rapidly to the next myelin sheath gap, a distance of approximately 1 mm, where it triggers another AP. Consequently, APs are triggered only at the gaps, a type of conduction called **saltatory conduction** (*saltare* = to leap) because the electrical signal appears to jump from gap to gap along the axon (Figure 11.14c). Saltatory conduction is about 30 times faster than continuous conduction.

HOMEOSTATIC IMBALANCE 11.2 CLINICAL

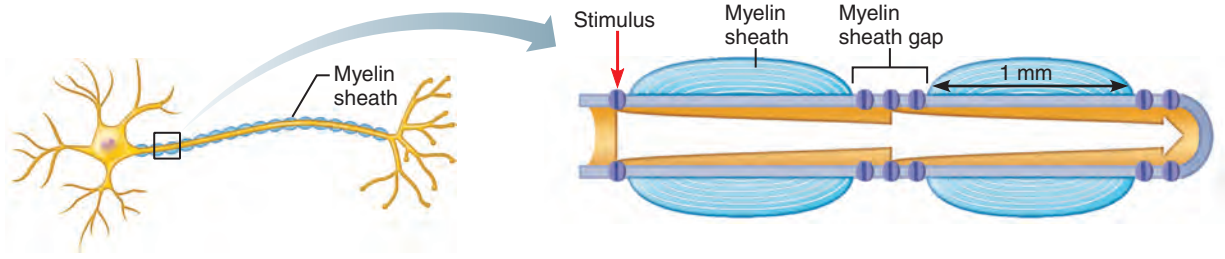
The importance of myelin to nerve transmission is painfully clear to people with demyelinating diseases such as **multiple sclerosis (MS)**. This autoimmune disease is a result of the



(a) In bare plasma membranes, voltage decays. Without voltage-gated channels, as on a dendrite, voltage decays because current leaks across the membrane.



(b) In nonmyelinated axons, conduction is slow (continuous conduction). Voltage-gated Na^+ and K^+ channels regenerate the action potential at each point along the axon, so voltage does not decay. Conduction is *slow* because it takes time for ions and for gates of channel proteins to move, and this must occur before voltage can be regenerated.



(c) In myelinated axons, conduction is fast (saltatory conduction). Myelin keeps current in axons (voltage doesn't decay much). APs are generated *only* in the myelin sheath gaps and appear to jump *rapidly* from gap to gap.

Figure 11.14 Action potential propagation in nonmyelinated and myelinated axons.

immune system's attack on myelin proteins and affects mostly young adults.

Multiple sclerosis gradually destroys myelin sheaths in the CNS, reducing them to nonfunctional hardened lesions called *scleroses*. The loss of myelin shunts and short-circuits the current so that successive gaps are excited more and more slowly, and eventually impulse conduction ceases. However, the axons themselves are not damaged and growing numbers of Na^+ channels appear spontaneously in the demyelinated fibers. This may account for the remarkably variable cycles of remission (symptom-free periods) and relapse typical of this disease. Common symptoms are visual disturbances (including blindness), problems controlling muscles (weakness, clumsiness, and ultimately paralysis), speech disturbances, and urinary incontinence.

The advent of drugs that modify the immune system's activity will continue to improve the lives of people with MS. These drugs seem to hold symptoms at bay, reducing complications and disability. Recent studies show that high blood levels of vitamin D reduce the risk of developing MS. ✚

Nerve fibers may be classified according to diameter, degree of myelination, and conduction speed.

- **Group A fibers** are mostly somatic sensory and motor fibers serving the skin, skeletal muscles, and joints. They have the largest diameter, thick myelin sheaths, and conduct impulses at speeds up to 150 m/s (over 300 miles per hour).
- **Group B fibers** are lightly myelinated fibers of intermediate diameter. They transmit impulses at an average rate of 15 m/s (about 30 mi/h).

- **Group C fibers** have the smallest diameter. They are nonmyelinated, so they are incapable of saltatory conduction and conduct impulses at a leisurely pace—1 m/s (2 mi/h) or less.

The B and C fiber groups include autonomic nervous system motor fibers serving the visceral organs; visceral sensory fibers; and the smaller somatic sensory fibers that transmit sensory impulses from the skin (such as pain and small touch fibers).

What happens when an action potential arrives at the end of a neuron's axon? That is the subject of the next section.

HOMEOSTATIC IMBALANCE 11.3 — CLINICAL

Impaired impulse propagation is caused by a number of chemical and physical factors. Local anesthetics like those used by your dentist act by blocking voltage-gated Na^+ channels. As we have seen, no Na^+ entry—no AP.

Cold and continuous pressure interrupt blood circulation, hindering the delivery of oxygen and nutrients to neuron processes and impairing their ability to conduct impulses. For example, your fingers get numb when you hold an ice cube for more than a few seconds, and your foot "goes to sleep" when you sit on it. When you remove the cold object or pressure, impulses are transmitted again, leading to an unpleasant prickly feeling. ✚

Check Your Understanding

12. Which is bigger, a graded potential or an action potential? Which travels further? Which initiates the other?

13. An action potential does not get smaller as it propagates along an axon. Why not?

14. Why does a myelinated axon conduct action potentials faster than a nonmyelinated axon?

15. If an axon receives two stimuli close together in time, only one AP occurs. Why?

For answers, see Answers Appendix.

11.7 Synapses transmit signals between neurons

Learning Objectives

- **Define synapse.**
- **Distinguish between electrical and chemical synapses by structure and by the way they transmit information.**

The operation of the nervous system depends on the flow of information through chains of neurons functionally connected by synapses (**Figure 11.15**). A **synapse** (sin′aps), from the Greek *syn*, "to clasp or join," is a junction that mediates information transfer from one neuron to the next or from a neuron to an effector cell—it's where the action is.

The neuron conducting impulses toward the synapse is the **presynaptic neuron**, and the neuron transmitting the electrical signal away from the synapse is the **postsynaptic neuron.** At a given synapse, the presynaptic neuron sends the information, and the postsynaptic neuron receives the information. As you might anticipate, most neurons function as both presynaptic and postsynaptic neurons. Neurons have anywhere from 1000 to 10,000 axon terminals making synapses and are stimulated by an equal number of other neurons. Outside the central nervous system, the postsynaptic cell may be either another neuron or an effector cell (a muscle cell or gland cell).

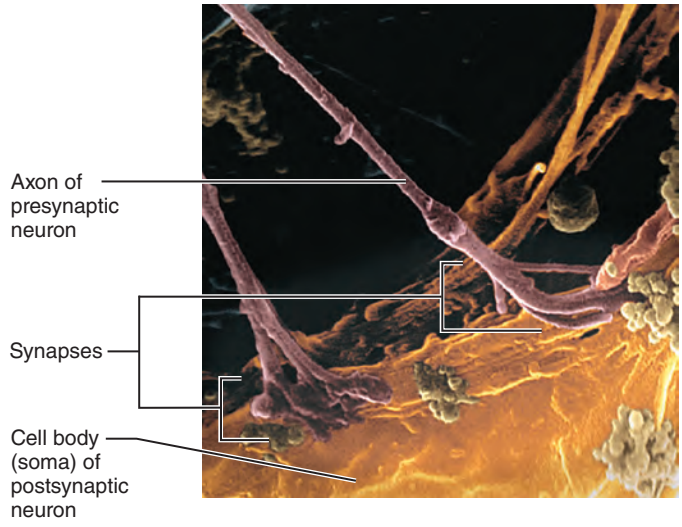


Figure 11.15 Synapses. Scanning electron micrograph (5300×).

Synapses between the axon endings of one neuron and the dendrites of other neurons are **axodendritic synapses**. Those between axon endings of one neuron and the cell body (soma) of another neuron are **axosomatic synapses** (**Figure 11.16**). Less common (and far less understood) are synapses between axons (*axoaxonal*), between dendrites (*dendrodendritic*), or between cell bodies and dendrites (*somatodendritic*).

There are two types of synapses: *chemical* and *electrical*.

Chemical Synapses

Chemical synapses are the most common type of synapse. They are specialized to allow the release and reception of chemical messengers known as *neurotransmitters*. A typical chemical synapse is made up of two parts:

- A knoblike *axon terminal* of the presynaptic neuron, which contains many tiny, membrane-bound sacs called **synaptic vesicles**, each containing thousands of neurotransmitter molecules
- A neurotransmitter *receptor region* on the postsynaptic neuron's membrane, usually located on a dendrite or the cell body

Although close to each other, presynaptic and postsynaptic membranes are separated by the **synaptic cleft**, a fluid-filled space approximately 30 to 50 nm (a bout one-millionth of an inch) wide.

Because the current from the presynaptic membrane dissipates in the fluid-filled cleft, chemical synapses prevent a nerve impulse from being *directly* transmitted from one neuron to another. Instead, an impulse is transmitted via a *chemical event* that depends on the release, diffusion, and receptor binding of

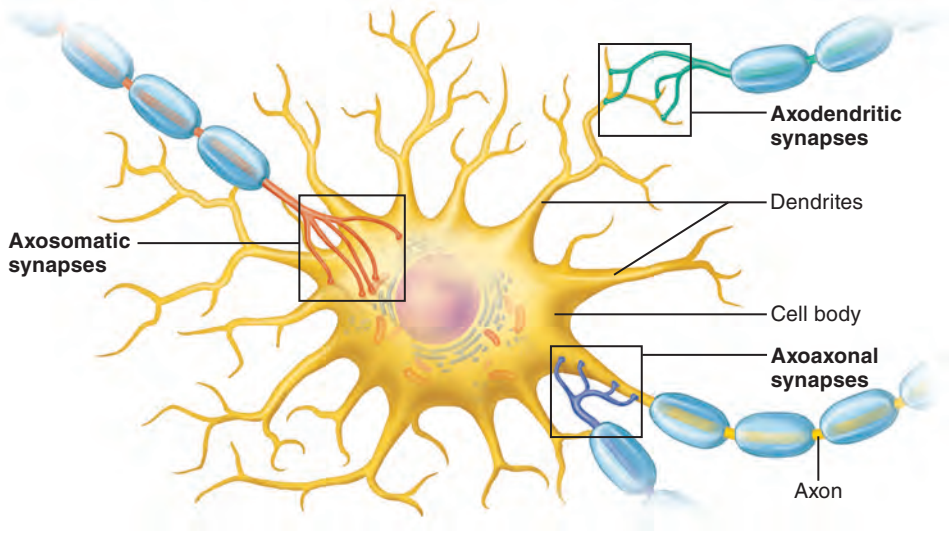


Figure 11.16 **Axodendritic, axosomatic, and axoaxonal synapses.**

neurotransmitter molecules and results in *unidirectional* communication between neurons.

In short, transmission of nerve impulses along an axon and across electrical synapses is a purely electrical event. However, chemical synapses convert the electrical signals to chemical signals (neurotransmitters) that travel across the synapse to the postsynaptic cells, where they are converted back into electrical signals.

Information Transfer across Chemical Synapses

In Chapter 9 we introduced a specialized chemical synapse called a neuromuscular junction (p. 255). The chain of events that occurs at the neuromuscular junction is simply one example of the general process that we will discuss next and show in *Focus on a Chemical Synapse* (**Focus Figure 11.3**):

1. **Action potential arrives at axon terminal.** Neurotransmission begins with the arrival of an AP at the presynaptic axon terminal.
2. **Voltage-gated Ca^{2+} channels open and Ca^{2+} enters the axon terminal.** Depolarization of the membrane by the action potential opens not only Na^+ channels but voltage-gated Ca^{2+} channels as well. During the brief time the Ca^{2+} channels are open, Ca^{2+} floods down its electrochemical gradient from the extracellular fluid into the terminal.
3. **Ca^{2+} entry causes synaptic vesicles to release neurotransmitter by exocytosis.** The surge of Ca^{2+} into the axon terminal acts as an intracellular messenger. A Ca^{2+}-sensing protein (*synaptotagmin*) binds Ca^{2+} and interacts with the SNARE proteins that control membrane fusion (see Figure 3.13 on p. 72). As a result, synaptic vesicles fuse with the axon membrane and empty their contents by exocytosis into the synaptic cleft. Ca^{2+} is then quickly removed from the terminal—either taken up into the mitochondria or ejected from the neuron by an active Ca^{2+} pump.

   For each nerve impulse reaching the presynaptic terminal, many vesicles (perhaps 300) empty into the synaptic cleft. The higher the impulse frequency (that is, the more intense the stimulus), the greater the number of synaptic vesicles that fuse and spill their contents, and the greater the effect on the postsynaptic cell.
4. **Neurotransmitter diffuses across the synaptic cleft and binds to specific receptors on the postsynaptic membrane.**
5. **Binding of neurotransmitter opens ion channels, creating graded potentials.** When a neurotransmitter binds to the receptor protein, this receptor changes its shape. This change in turn opens ion channels and creates graded potentials. Postsynaptic membranes often contain receptor proteins and ion channels packaged together as chemically gated ion channels. Depending on the receptor protein to which the neurotransmitter binds and the type of channel the receptor controls, the postsynaptic neuron may be either excited or inhibited.
6. **Neurotransmitter effects are terminated.** Binding of a neurotransmitter to its receptor is reversible. As long as it is bound to a postsynaptic receptor, a neurotransmitter continues to affect membrane permeability and block reception of additional signals from presynaptic neurons. For this reason, some means of "wiping the postsynaptic slate clean" is necessary. The effects of neurotransmitters generally last a few milliseconds before being terminated in one of three ways, depending on the particular neurotransmitter:
   - *Reuptake* by astrocytes or the presynaptic terminal, where the neurotransmitter is stored or destroyed by enzymes, as with norepinephrine
   - *Degradation* by enzymes associated with the postsynaptic membrane or present in the synaptic cleft, as with acetylcholine
   - *Diffusion* away from the synapse

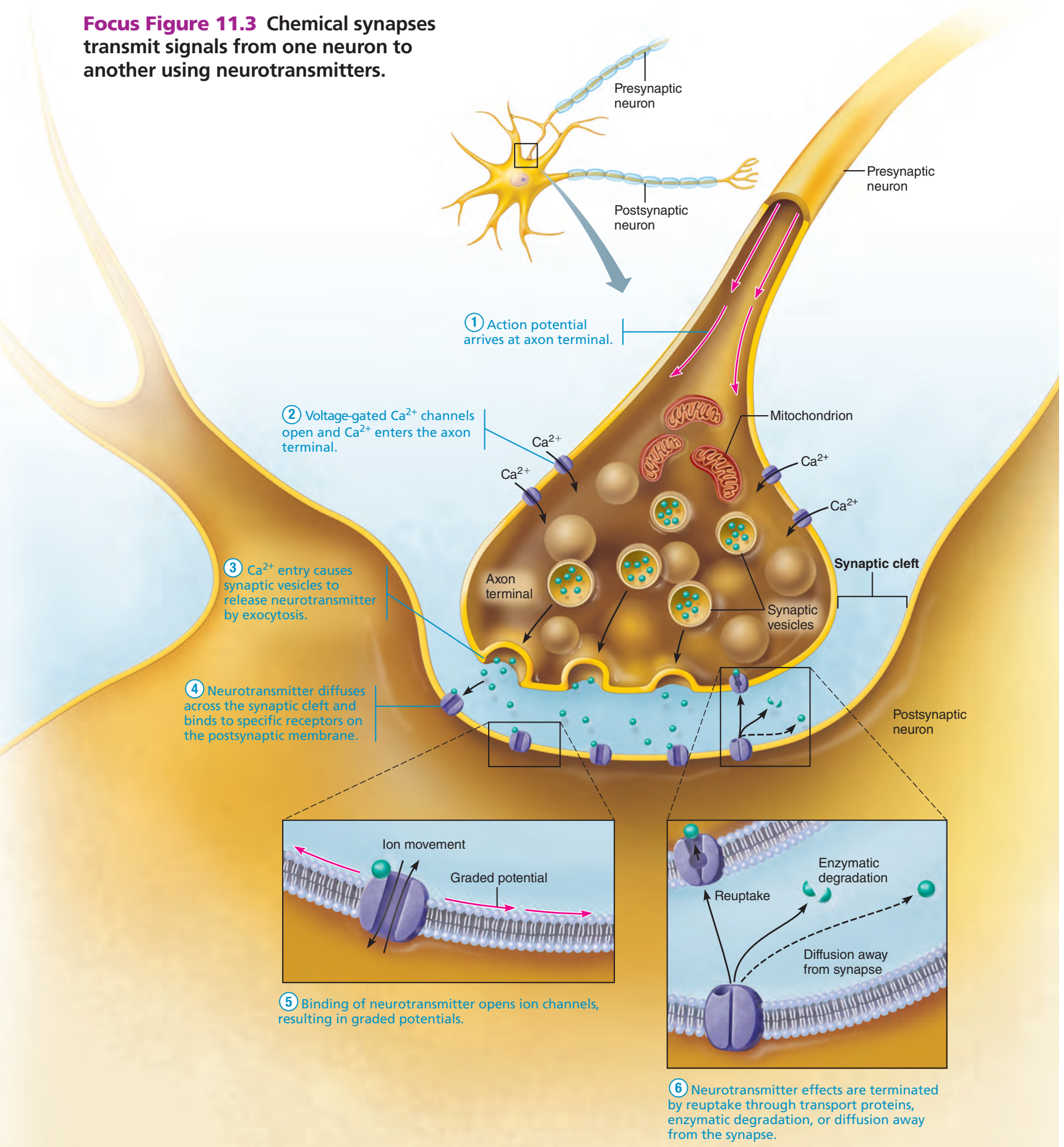
Synaptic Delay

An impulse may travel at speeds of up to 150 m/s (300 mi/h) down an axon, but neural transmission across a chemical synapse is comparatively slow. It reflects the time required for neurotransmitter to be released, diffuse across the synaptic cleft, and bind to receptors. Typically, this **synaptic delay** lasts 0.3–5.0 ms, making transmission across the chemical synapse the *rate-limiting* (slowest) step of neural transmission. Synaptic delay helps explain why transmission along neural pathways involving only two or three neurons occurs rapidly, but transmission along multisynaptic pathways typical of higher mental functioning occurs much more slowly. However, in practical terms these differences are not noticeable.

Electrical Synapses

Electrical synapses are much less common than chemical synapses. They consist of gap junctions like those found between certain other body cells. Their channel proteins (connexons)

Focus Figure 11.3 Chemical synapses transmit signals from one neuron to another using neurotransmitters.



connect the cytoplasm of adjacent neurons and allow ions and small molecules to flow directly from one neuron to the next. These neurons are *electrically coupled*, and transmission across these synapses is very rapid. Depending on the nature of the synapse, communication may be unidirectional or bidirectional.

Let's take a moment to compare the two methods of communication between neurons. The synaptic cleft of a chemical synapse is like a lake that the two neurons shout across. An electrical synapse, on the other hand, is like a doorway: Messages (ions) can move directly from one room (neuron) to another.

Electrical synapses between neurons provide a simple means of synchronizing the activity of all interconnected neurons. In adults, electrical synapses are found in regions of the brain responsible for certain stereotyped movements, such as the normal jerky movements of the eyes. They also occur in axoaxonal synapses in the hippocampus, a brain region involved in emotions and memory.

Electrical synapses are far more abundant in embryonic nervous tissue, where they permit exchange of guiding cues during early neuronal development so that neurons can connect properly with one another. As the nervous system develops, chemical synapses replace some electrical synapses and become the vast majority of all synapses. For this reason, we will focus on chemical synapses from now on.

Check Your Understanding

16. Events at a chemical synapse usually involve opening both voltage-gated ion channels and chemically gated ion channels. Where are these ion channels located and what causes each to open?

17. What structure joins two neurons at an electrical synapse?

For answers, see Answers Appendix.

11.8 Postsynaptic potentials excite or inhibit the receiving neuron

Learning Objectives

- **Distinguish between excitatory and inhibitory postsynaptic potentials.**
- **Describe how synaptic events are integrated and modified.**

Many receptors on postsynaptic membranes at chemical synapses are specialized to open ion channels, in this way converting chemical signals to electrical signals. Unlike the voltage-gated ion channels responsible for APs, these chemically gated channels are relatively insensitive to changes in membrane potential. Consequently, channel opening at postsynaptic membranes cannot become self-amplifying or self-generating. Instead, neurotransmitter receptors mediate graded potentials—local changes in membrane potential that are *graded* (vary in strength) based on the amount of neurotransmitter released and how long it remains in the area. **Table 11.2** compares graded potentials and action potentials.

Chemical synapses are either excitatory or inhibitory, depending on how they affect the membrane potential of the postsynaptic neuron.

Excitatory Synapses and EPSPs

At excitatory synapses, neurotransmitter binding depolarizes the postsynaptic membrane. In contrast to what happens on axon membranes, *chemically gated* ion channels open on postsynaptic membranes (those of dendrites and neuronal cell bodies). Each channel allows Na^+ and K^+ to diffuse *simultaneously* through the membrane but in opposite directions.

Although this two-way cation flow may appear to be self-defeating when depolarization is the goal, remember that the electrochemical gradient for sodium is much steeper than that for potassium. As a result, Na^+ influx is greater than K^+ efflux, and *net* depolarization occurs.

If enough neurotransmitter binds, depolarization of the postsynaptic membrane can reach 0 mV—well above an axon's threshold (about −50 mV) for firing an AP. However, unlike axons which have voltage-gated channels that make an AP possible, *postsynaptic membranes generally do not generate APs*. The dramatic polarity reversal seen in axons never occurs in membranes containing *only* chemically gated channels because the opposite movements of K^+ and Na^+ prevent excessive positive charge from accumulating inside the cell. For this reason, instead of APs, local graded depolarization events called **excitatory postsynaptic potentials (EPSPs)** occur at excitatory postsynaptic membranes (**Figure 11.17a**).

Each EPSP lasts a few milliseconds and then the membrane returns to its resting potential. The only function of EPSPs is to help trigger an AP distally at the axon hillock of the postsynaptic neuron. Although currents created by individual EPSPs decline with distance, they can and often do spread all the way to the axon hillock. If currents reaching the hillock are strong enough to depolarize the axon to threshold, axonal voltage-gated channels open and an AP is generated.

Inhibitory Synapses and IPSPs

Binding of neurotransmitters at inhibitory synapses *reduces* a postsynaptic neuron's ability to generate an AP. Most inhibitory neurotransmitters hyperpolarize the postsynaptic membrane by making the membrane more permeable to K^+ or Cl^-. Sodium ion permeability is not affected.

If K^+ channels open, K^+ moves out of the cell. If Cl^- channels open, Cl^- moves in. In either case, the charge on the inner face of the membrane becomes more negative. As the membrane potential increases and is driven farther from the axon's threshold, the postsynaptic neuron becomes *less and less likely* to "fire," and larger depolarizing currents are required to induce an AP. Hyperpolarizing changes in potential are called **inhibitory postsynaptic potentials (IPSPs)** (Figure 11.17b).

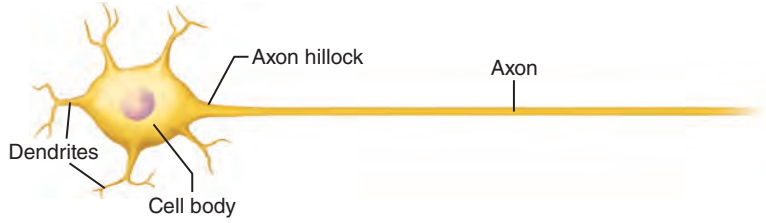
Integration and Modification of Synaptic Events

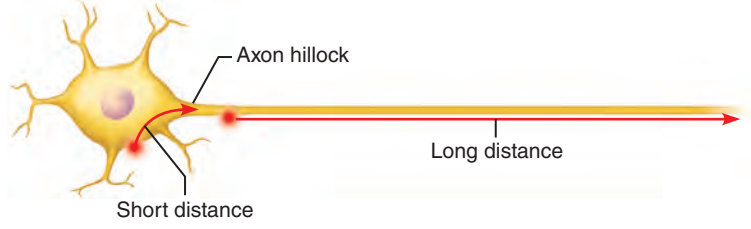
Summation by the Postsynaptic Neuron

A single EPSP cannot induce an AP in the postsynaptic neuron (**Figure 11.18a**, p. 372). But if thousands of excitatory axon terminals fire on the same postsynaptic membrane, or if a small number

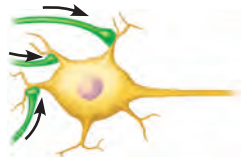
Table 11.2 Comparison of Graded Potentials and Action Potentials

	GRADED POTENTIAL (GP)	ACTION POTENTIAL (AP)
Location of event	Cell body and dendrites, typically	Axon hillock and axon
Distance traveled	Short distance—typically within cell body to axon hillock (0.1–1.0 mm)	Long distance—from trigger zone at axon hillock through entire length of axon (a few mm to over a meter)
Amplitude (size)	Various sizes (graded); decays with distance	Always the same size (all-or-none); does not decay with distance
Stimulus for opening ion channels	Chemical (neurotransmitter) or sensory stimulus (e.g., light, pressure, temperature)	Voltage (depolarization, triggered by GP reaching threshold)
Positive feedback cycle	Absent	Present
Repolarization	Voltage independent; occurs when stimulus is no longer present	Voltage regulated; occurs when Na^+ channels inactivate and K^+ channels open
Summation	Stimulus responses can summate to increase amplitude of graded potential	Does not occur; an all-or-none phenomenon





Temporal: increased frequency of stimuli



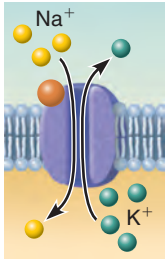
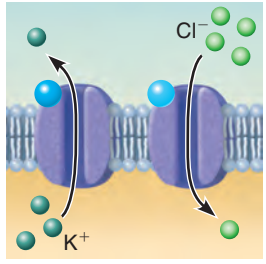
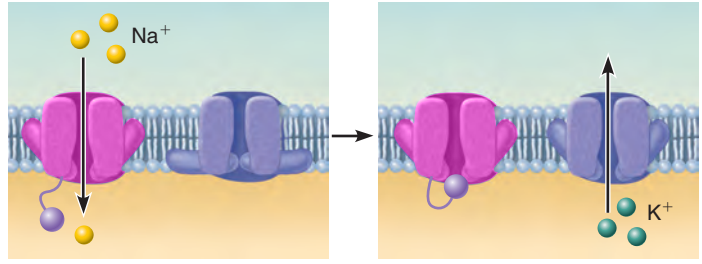
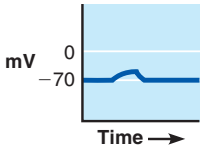
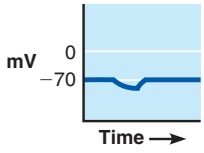
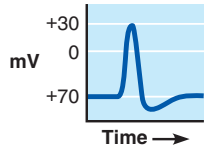
Spatial: stimuli from multiple sources

of terminals deliver impulses rapidly, the probability of reaching threshold soars. EPSPs can add together, or **summate**, to influence the activity of a postsynaptic neuron. Otherwise, nerve impulses would never result.

Two types of summation occur: temporal and spatial.

- **Temporal summation** (*temporal* = time) occurs when one or more presynaptic neurons transmit impulses in rapid-fire order and bursts of neurotransmitter are released in quick succession. The first impulse produces a small EPSP, and before it dissipates, successive impulses trigger more EPSPs. These summate, causing the postsynaptic membrane to depolarize much more than it would from a single EPSP (Figure 11.18b).
- **Spatial summation** occurs when the postsynaptic neuron is stimulated simultaneously by a large number of terminals from one or, more commonly, many presynaptic neurons. Huge numbers of its receptors bind neurotransmitter and simultaneously initiate EPSPs, which summate and dramatically enhance depolarization (Figure 11.18c).

Table 11.2 *(continued)*

	GRADED POTENTIAL (GP)		ACTION POTENTIAL (AP)
	POSTSYNAPTIC POTENTIAL (A TYPE OF GP)		
	EXCITATORY (EPSP)	INHIBITORY (IPSP)	
Function	Short-distance signaling; depolarization that spreads to axon hillock; moves membrane potential *toward* threshold for generating an AP	Short-distance signaling; hyperpolarization that spreads to axon hillock; moves membrane potential *away* from threshold for generating an AP	Long-distance signaling; constitutes the nerve impulse
Initial effect of stimulus	Opens chemically gated channels that allow simultaneous Na^+ and K^+ fluxes	Opens chemically gated K^+ or Cl^- channels	Opens voltage-gated channels; first opens Na^+ channels, then K^+ channels
			
Peak membrane potential	Depolarizes; moves toward 0 mV	Hyperpolarizes; moves toward –90 mV	+30 to +50 mV
			

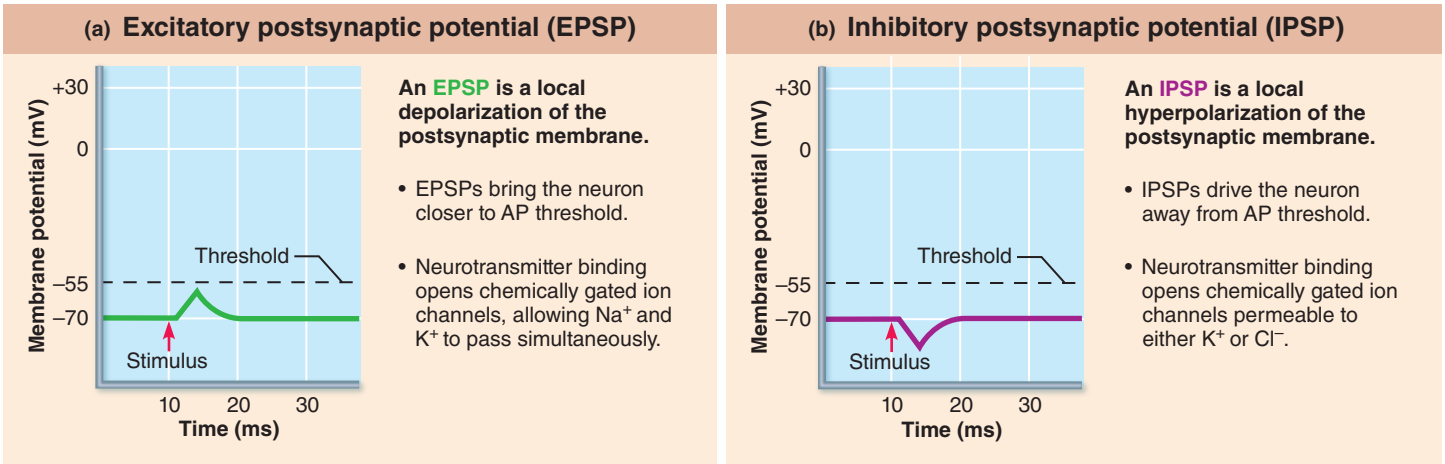


Figure 11.17 **Postsynaptic potentials can be excitatory or inhibitory.**

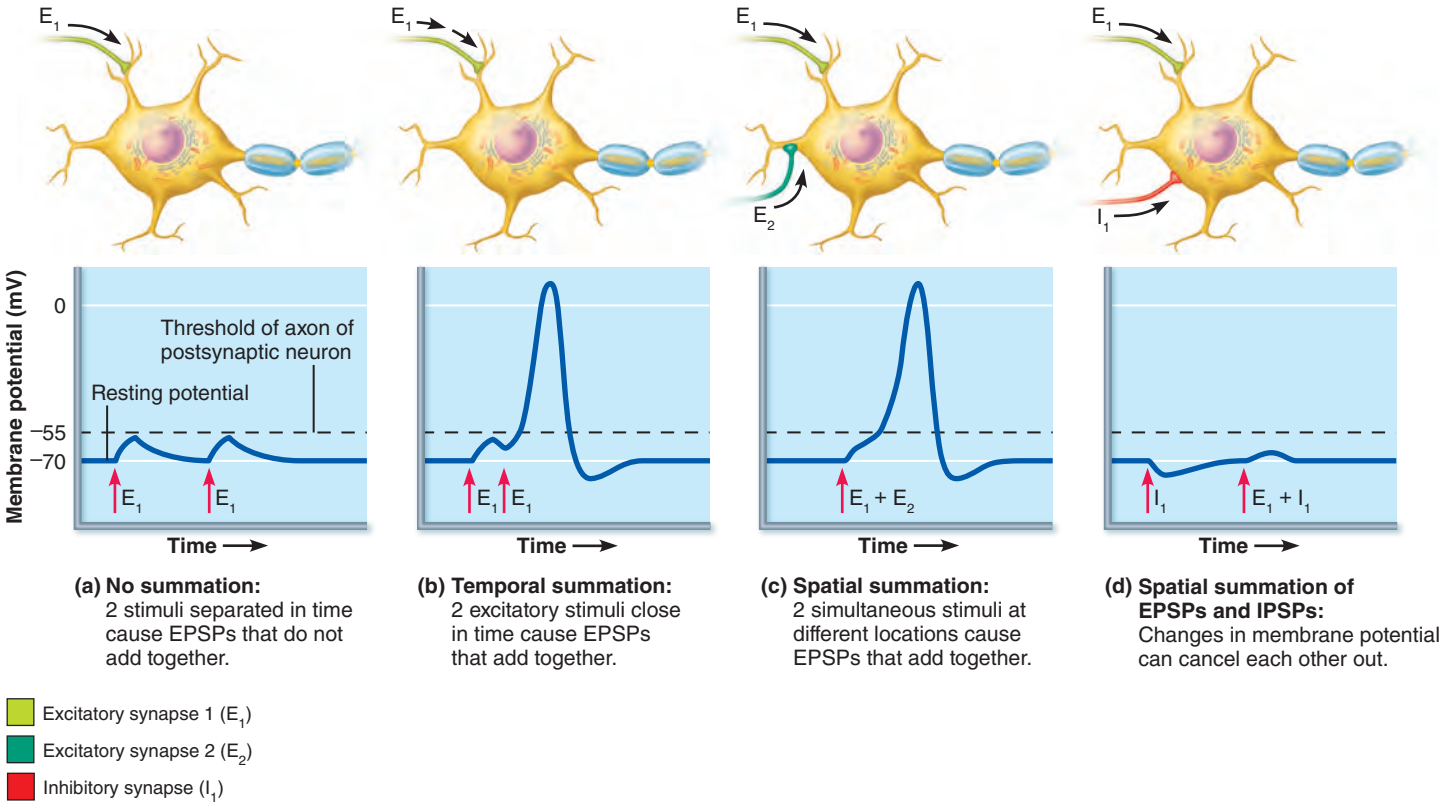


Figure 11.18 Neural integration of EPSPs and IPSPs.

11

Although we have focused on EPSPs, IPSPs also summate, both temporally and spatially. In this case, the postsynaptic neuron is inhibited to a greater degree.

Most neurons receive both excitatory and inhibitory inputs from thousands of other neurons. Additionally, the same axon may form different types of synapses (in terms of biochemical and electrical characteristics) with different types of target neurons. How is all this conflicting information sorted out?

Each neuron's axon hillock keeps a running account of all the signals it receives. Not only do EPSPs summate and IPSPs summate, but also EPSPs summate with IPSPs. If the stimulatory effects of EPSPs dominate the membrane potential enough to reach threshold, the neuron will fire. If summation yields only subthreshold depolarization or hyperpolarization, the neuron fails to generate an AP (Figure 11.18d).

However, partially depolarized neurons are **facilitated**—that is, more easily excited by successive depolarization events—because they are already near threshold. Thus, axon hillock membranes function as *neural integrators*, and their potential at any time reflects the sum of all incoming neural information.

Because EPSPs and IPSPs are graded potentials that decay the farther they spread, the most effective synapses are those closest to the axon hillock. Specifically, inhibitory synapses are most effective when located between the site of excitatory inputs and the site of action potential generation (the axon hillock). Accordingly, inhibitory synapses occur most often on the cell body and excitatory synapses occur most often on the dendrites (Figure 11.18d).

Synaptic Potentiation

Repeated or continuous use of a synapse (even for short periods) enhances the presynaptic neuron's ability to excite the postsynaptic neuron, producing larger-than-expected EPSPs. This phenomenon is **synaptic potentiation**. The presynaptic terminals at such synapses contain relatively high Ca^{2+} concentrations, a condition that triggers the release of more neurotransmitter, which in turn produces larger EPSPs.

Synaptic potentiation also brings about Ca^{2+} influx via dendritic spines into the postsynaptic neuron. As Ca^{2+} floods into the cell, it activates certain kinase enzymes that promote changes resulting in more effective responses to subsequent stimuli.

In some neurons, APs generated at the axon hillock propagate back up into the dendrites. This current flow may alter the effectiveness of synapses by opening voltage-gated Ca^{2+} channels, again allowing Ca^{2+} into the dendrites and promoting synaptic potentiation.

Synaptic potentiation can be viewed as a learning process that increases the efficiency of neurotransmission along a particular pathway. Indeed, the hippocampus of the brain, which plays a special role in memory and learning, exhibits an important type of synaptic plasticity called *long-term potentiation* (LTP).

Presynaptic Inhibition

Events at the presynaptic membrane can also influence postsynaptic activity. **Presynaptic inhibition** occurs when the release

of excitatory neurotransmitter by one neuron is inhibited by the activity of another neuron via an axoaxonal synapse. More than one mechanism is involved, but the end result is that less neurotransmitter is released and bound, forming smaller EPSPs.

In contrast to postsynaptic inhibition by IPSPs, which decreases the excitability of the postsynaptic neuron, presynaptic inhibition decreases the excitatory stimulation of the postsynaptic neuron. In this way, presynaptic inhibition is like a functional synaptic "pruning."

Check Your Understanding

18. Which ions flow through chemically gated channels to produce IPSPs? EPSPs?

19. What is the difference between temporal summation and spatial summation?

For answers, see Answers Appendix.

11.9 The effect of a neurotransmitter depends on its receptor

Learning Objectives

- **Define neurotransmitter and classify neurotransmitters by chemical structure and by function.**
- **Describe the action of neurotransmitters at channel-linked and G protein–linked receptors.**

Neurotransmitters, along with electrical signals, are the "language" of the nervous system—the means by which neurons communicate to process and send messages to the rest of the body. Sleep, thought, rage, hunger, memory, movement, and even your smile reflect the actions of these versatile molecules. Most factors that affect synaptic transmission do so by enhancing or inhibiting neurotransmitter release or destruction, or by blocking their binding to receptors. Just as speech defects may hinder interpersonal communication, anything that interferes with neurotransmitter activity may short-circuit the brain's "conversations" or internal talk.

More than 50 neurotransmitters or neurotransmitter candidates have been identified. Although some neurons produce and release only one kind of neurotransmitter, most make two or more and may release any one or all of them at a given time. It appears that in most cases, different neurotransmitters are released at different stimulation frequencies. This avoids producing a jumble of nonsense messages. However, co-release of two neurotransmitters from the same vesicles has been documented. The coexistence of more than one neurotransmitter in a single neuron makes it possible for that cell to exert several different influences.

Neurotransmitters are classified chemically and functionally. **Table 11.3** provides a detailed overview and key groups are discussed in the following sections.

Classification of Neurotransmitters by Chemical Structure

Neurotransmitters are grouped into several classes based on molecular structure.

Acetylcholine

Acetylcholine (ACh) (as″ĕ-til-ko′lēn), the first neurotransmitter identified, is still the best understood because it is released at neuromuscular junctions, which are much easier to study than synapses buried in the CNS.

ACh is synthesized from acetic acid (as acetyl CoA) and choline by the enzyme *choline acetyltransferase*, then transported into synaptic vesicles for later release. Once released by the presynaptic terminal, ACh binds briefly to the postsynaptic receptors. It is then released and degraded to acetic acid and choline by the enzyme **acetylcholinesterase (AChE)**, located in the synaptic cleft and on postsynaptic membranes. Presynaptic terminals recapture the released choline and reuse it to synthesize more ACh.

ACh is released by all neurons that stimulate skeletal muscles and by many neurons of the autonomic nervous system. ACh-releasing neurons are also found in the CNS.

Biogenic Amines

The **biogenic amines** (bi″o-jen′ik) include the **catecholamines** (kat″ĕ-kol′ah-mēnz), such as dopamine, norepinephrine (NE), and epinephrine, and the **indolamines**, which include sero-tonin and histamine. *Dopamine* and *NE* are synthesized from the amino acid tyrosine in a common pathway. The epinephrine-releasing cells of the brain and adrenal medulla use the same pathway. *Serotonin* is synthesized from the amino acid tryptophan. *Histamine* is synthesized from the amino acid histidine.

Biogenic amine neurotransmitters are broadly distributed in the brain, where they play a role in emotional behavior and help regulate the biological clock. Additionally, some motor neurons of the autonomic nervous system release catecholamines, particularly NE. Imbalances of these neurotransmitters are associated with mental illness. For example, overactive dopamine signaling occurs in schizophrenia. Additionally, certain psychoactive drugs (LSD and mescaline) can bind to biogenic amine receptors and induce hallucinations.

Amino Acids

It is difficult to prove a neurotransmitter role when the suspect is an amino acid, because amino acids occur in all cells of the body and are important in many biochemical reactions. The amino acids for which a neurotransmitter role is certain include **glutamate**, **aspartate**, **glycine**, and **gamma (γ)-aminobutyric acid (GABA)**, and there may be others.

Peptides

The **neuropeptides**, essentially strings of amino acids, include a broad spectrum of molecules with diverse effects. For example, a neuropeptide called **substance P** is an important mediator of pain signals. By contrast, **endorphins**, which include **beta endorphin**, **dynorphin**, and **enkephalins** (en-kef′ah-linz), act as natural opiates, reducing our perception of pain under stressful conditions. Enkephalin activity increases dramatically in pregnant women in labor. Endorphin release is enhanced when an athlete gets a so-called second wind and is probably responsible for the "runner's high." Additionally, some researchers claim that

(Text continues on p. 376.)

Table 11.3 Neurotransmitters and Neuromodulators

NEUROTRANSMITTER	FUNCTIONAL CLASSES	SITES WHERE SECRETED	COMMENTS
Acetylcholine (ACh)			
• At *nicotinic ACh receptors* (on skeletal muscles, autonomic ganglia, and in the CNS) • At *muscarinic ACh receptors* (on visceral effectors and in the CNS)	Excitatory Direct action Excitatory or inhibitory depending on subtype of muscarinic receptor Indirect action via second messengers	CNS: widespread throughout cerebral cortex, hippocampus, and brain stem PNS: all neuromuscular junctions with skeletal muscle; some autonomic motor endings (all preganglionic and parasympathetic postganglionic fibers)	Effects prolonged when AChE blocked by nerve gas or organophosphate insecticides (malathion), leading to tetanic muscle spasms. Release inhibited by botulinum toxin; binding to nicotinic ACh receptors inhibited by curare (a muscle paralytic agent) and to muscarinic ACh receptors by atropine. ACh levels decrease in certain brain areas in Alzheimer's disease; nicotinic ACh receptors destroyed in myasthenia gravis.
Biogenic Amines			
Norepinephrine (NE)	Excitatory or inhibitory depending on receptor type bound Indirect action via second messengers	CNS: brain stem, particularly in the locus coeruleus of the midbrain; limbic system; some areas of cerebral cortex PNS: main neurotransmitter of postganglionic neurons in the sympathetic nervous system	A "feel good" neurotransmitter. Release enhanced by amphetamines; removal from synapse blocked by tricyclic antidepressants and cocaine. Brain levels reduced by reserpine (an antihypertensive drug), leading to depression.
Dopamine	Excitatory or inhibitory depending on the receptor type bound Indirect action via second messengers	CNS: substantia nigra of midbrain; hypothalamus; the principal neurotransmitter of indirect motor pathways PNS: some sympathetic ganglia	A "feel good" neurotransmitter. Release enhanced by L-dopa and amphetamines; reuptake blocked by cocaine. Deficient in Parkinson's disease; dopamine neurotransmission increases in schizophrenia.
Serotonin (5-HT)	Mainly inhibitory Indirect action via second messengers; direct action at 5-HT_3 receptors	CNS: brain stem, especially midbrain; hypothalamus; limbic system; cerebellum; pineal gland; spinal cord	Plays a role in sleep, appetite, nausea, migraine headaches, and regulating mood. Drugs that block its uptake relieve anxiety and depression. Activity blocked by LSD and enhanced by ecstasy.
Histamine	Excitatory or inhibitory depending on receptor type bound Indirect action via second messengers	CNS: hypothalamus	Involved in wakefulness, appetite control, and learning and memory.
Amino Acids			
GABA (γ-aminobutyric acid)	Generally inhibitory Direct and indirect actions via second messengers	CNS: cerebral cortex, hypothalamus, Purkinje cells of cerebellum, spinal cord, granule cells of olfactory bulb, retina	Principal inhibitory neurotransmitter in the brain; important in presynaptic inhibition at axoaxonal synapses. Inhibitory effects augmented by alcohol, antianxiety drugs of the benzodiazepine class, and barbiturates. Substances that block its synthesis, release, or action induce convulsions.
Glutamate	Generally excitatory Direct action	CNS: spinal cord; widespread in brain where it represents the major excitatory neurotransmitter	Important in learning and memory. The "stroke neurotransmitter": excessive release produces excitotoxicity—neurons literally stimulated to death; most commonly caused by ischemia (oxygen deprivation, usually due to a blocked blood vessel).

Table 11.3 *(continued)*

NEUROTRANSMITTER	FUNCTIONAL CLASSES	SITES WHERE SECRETED	COMMENTS
Amino Acids, continued			
Glycine	Generally inhibitory Direct action	CNS: spinal cord and brain stem, retina	Principal inhibitory neurotransmitter of the spinal cord. Strychnine blocks glycine receptors, resulting in uncontrolled convulsions and respiratory arrest.
Peptides			
Endorphins, e.g., beta endorphin, dynorphin, enkephalins	Generally inhibitory Indirect action via second messengers	CNS: widely distributed in brain (hypothalamus; limbic system; pituitary) and spinal cord	Natural opiates; inhibit pain by inhibiting substance P. Effects mimicked by morphine, heroin, and methadone.
Tachykinins: substance P, neurokinin A (NKA)	Excitatory Indirect action via second messengers	CNS: basal nuclei, midbrain, hypothalamus, cerebral cortex PNS: certain sensory neurons of dorsal root ganglia (pain afferents), enteric neurons	Substance P mediates pain transmission in the PNS. In the CNS, tachykinins are involved in respiratory and cardiovascular controls and in mood.
Somatostatin	Generally inhibitory Indirect action via second messengers	CNS: widely distributed in brain (hypothalamus, basal nuclei, hippocampus, cerebral cortex) Pancreas	Often released with GABA. A gut-brain peptide. Inhibits growth hormone release.
Cholecystokinin (CCK)	Generally excitatory Indirect action via second messengers	Throughout CNS Small intestine	Involved in anxiety, pain, memory. A gut-brain peptide hormone. Inhibits appetite.
Purines			
ATP	Excitatory or inhibitory depending on receptor type bound Direct and indirect actions via second messengers	CNS: basal nuclei, induces Ca^{2+} wave propagation in astrocytes PNS: dorsal root ganglion neurons	ATP released by sensory neurons (as well as that released by injured cells) provokes pain sensation.
Adenosine	Generally inhibitory Indirect action via second messengers	Throughout CNS and PNS	Caffeine stimulates by blocking brain adenosine receptors. May be involved in sleep-wake cycle and terminating seizures. Dilates arterioles, increasing blood flow to heart and other tissues as needed.
Gases and Lipids			
Nitric oxide (NO)	Excitatory or inhibitory Indirect action via second messengers	CNS: brain, spinal cord PNS: adrenal gland; nerves to penis	Its release potentiates stroke damage. Some types of male impotence treated by enhancing NO action [e.g., with sildenafil (Viagra)].
Carbon monoxide (CO)	Excitatory or inhibitory Indirect action via second messengers	Brain and some neuromuscular and neuroglandular synapses	
Endocannabinoids, e.g., 2-arachidonoylglycerol, anandamide	Inhibitory Indirect action via second messengers	Throughout CNS	Involved in memory (as a retrograde messenger), appetite control, nausea and vomiting, neuronal development. Receptors activated by THC, the principal active ingredient of cannabis.

the placebo effect is due to endorphin release. These painkilling neurotransmitters remained undiscovered until investigators began to ask why morphine and other opiates reduce anxiety and pain. They found that these drugs attach to the same receptors that bind natural opiates, producing similar but stronger effects.

Some neuropeptides, known as **gut-brain peptides**, are also produced by nonneural body tissues and are widespread in the gastrointestinal tract. Examples include somatostatin and cholecystokinin (CCK).

Purines

Purines are nitrogen-containing chemicals (such as guanine and adenine) that are breakdown products of nucleic acids. **Adenosine triphosphate (ATP)**, the cell's universal form of energy, is now recognized as a major neurotransmitter (perhaps the most primitive one) in both the CNS and PNS. Like the receptors for glutamate and acetylcholine, certain receptors produce fast excitatory responses when ATP binds, while other ATP receptors trigger slow, second-messenger responses. Upon binding to receptors on astrocytes, ATP mediates Ca^{2+} influx.

In addition to the neurotransmitter action of extracellular ATP, **adenosine**, a part of ATP, also acts outside of cells on adenosine receptors. Adenosine is a potent inhibitor in the brain. Caffeine's well-known stimulatory effects result from blocking these adenosine receptors.

Gases and Lipids

Not so long ago, it would have been scientific suicide to suggest that small, short-lived, toxic gas molecules might be neurotransmitters. Nonetheless, the discovery of these unlikely messengers has opened up a new chapter in the story of neurotransmission.

Gasotransmitters These gases—the so-called "gasotransmitters" nitric oxide, carbon monoxide, and hydrogen sulfide—defy all the classical descriptions of neurotransmitters. Rather than being stored in vesicles and released by exocytosis, they are synthesized on demand and diffuse out of the cells that make them. Instead of attaching to surface receptors, they zoom through the plasma membrane of nearby cells to bind with intracellular receptors.

Both **nitric oxide (NO)** and **carbon monoxide (CO)** activate *guanylate cyclase*, the enzyme that makes the second messenger *cyclic GMP*. NO and CO are found in different brain regions and appear to act in different pathways, but their mode of action is similar. NO participates in a variety of processes in the brain, including the formation of new memories by increasing the strength of certain synapses.

Excessive release of NO is thought to contribute to the brain damage seen in stroke patients. In the PNS, NO causes blood vessels and intestinal smooth muscle to relax.

Less is known about **hydrogen sulfide (H_2S)**, the most recently discovered gasotransmitter. Unlike NO and CO, it appears to act directly on ion channels and other proteins to alter their function.

Endocannabinoids Just as there are natural opiate neurotransmitters in the brain, our brains make **endocannabinoids** (en″do-kă-nă′bĭ-noids) that act at the same receptors as tetrahydrocannabinol (THC), the active ingredient in marijuana. Their receptors, the *cannabinoid receptors*, are the most common G protein–linked receptors in the brain. Like the gasotransmitters, the endocannabinoids are lipid soluble and are synthesized on demand, rather than stored and released from vesicles. Like NO, they are thought to be involved in learning and memory. We are only beginning to understand the many other processes these neurotransmitters may be involved in, which include neuronal development, controlling appetite, and suppressing nausea.

Classification of Neurotransmitters by Function

In this text we can only sample the incredible diversity of functions that neurotransmitters mediate. We limit our discussion here to two broad ways of classifying neurotransmitters according to function, adding more details in subsequent chapters.

The important idea to keep in mind is this: The function of a neurotransmitter is determined by the receptor to which it binds.

Effects: Excitatory versus Inhibitory

Some neurotransmitters are excitatory (cause depolarization). Some are inhibitory (cause hyperpolarization). Others exert both effects, depending on the specific receptor types with which they interact.

For example, the amino acids GABA and glycine are usually inhibitory, whereas glutamate is typically excitatory (Table 11.3). On the other hand, ACh and NE each bind to at least two receptor types that cause opposite effects. For example, acetylcholine is excitatory at neuromuscular junctions in skeletal muscle and inhibitory in cardiac muscle.

Actions: Direct versus Indirect

Neurotransmitters that act *directly* are those that bind to and open ion channels. These neurotransmitters provoke rapid responses in postsynaptic cells by altering membrane potential. ACh and the amino acid neurotransmitters are typically direct-acting neurotransmitters.

Neurotransmitters that act *indirectly* promote broader, longer-lasting effects by acting through intracellular *second-messenger* molecules, typically via G protein pathways (see *Focus on G Proteins*, Focus Figure 3.2 on p. 76). In this way their action is similar to that of many hormones. The biogenic amines, neuropeptides, and dissolved gases are indirect neurotransmitters.

Neuromodulator is a term used to describe a chemical messenger released by a neuron that does not directly cause EPSPs or IPSPs but instead affects the strength of synaptic transmission. A neuromodulator may act presynaptically to influence the synthesis, release, degradation, or reuptake of neurotransmitter. Alternatively, it may act postsynaptically by altering the sensitivity of the postsynaptic membrane to neurotransmitter.

Receptors for neuromodulators are not necessarily found at a synapse. Instead, a neuromodulator may be released from one cell to act at many cells in its vicinity, similar to paracrines (chemical messengers that act locally and are quickly destroyed). The distinction between neurotransmitters and neuromodulators is fuzzy, but chemical messengers such as NO, adenosine, and a number of neuropeptides are often referred to as neuromodulators.

Neurotransmitter Receptors

In Chapter 3, we introduced the various receptors involved in cell signaling. Now we are ready to pick up that thread again as we examine the action of receptors that bind neurotransmitters. For the most part, neurotransmitter receptors are either channel-linked receptors, which mediate fast synaptic transmission, or G protein–linked receptors, which oversee slow synaptic responses.

Channel-Linked Receptors

Channel-linked receptors (*ionotropic receptors*) are ligand-gated ion channels that mediate direct neurotransmitter action. They are composed of several protein subunits in a "rosette" around a central pore. As the ligand binds to one (or more) receptor subunits, the proteins change shape. This event opens the central channel and allows ions to pass (**Figure 11.19**). As a result, the membrane potential of the target cell changes.

Channel-linked receptors are always located precisely opposite sites of neurotransmitter release, and their ion channels open instantly upon ligand binding and remain open 1 ms or less while the ligand is bound. At excitatory receptor sites (nicotinic ACh channels and receptors for glutamate, aspartate, and ATP), the channel-linked receptors are cation channels that allow small cations (Na^+, K^+, Ca^{2+}) to pass, but Na^+ entry contributes most to membrane depolarization. Channel-linked receptors that respond to GABA and glycine, and allow Cl^- to pass, mediate fast inhibition (hyperpolarization).

G Protein–Linked Receptors

Unlike responses to neurotransmitter binding at channel-linked receptors, which are immediate, simple, and brief, the activity mediated by **G protein–linked receptors** is indirect, complex, slow (hundreds of milliseconds or more), and often prolonged—ideal as a basis for some types of learning. Receptors in this class are transmembrane protein complexes. They include muscarinic ACh receptors and those that bind the biogenic amines and neuropeptides. Because their effects tend to bring about widespread metabolic changes, G protein–linked receptors are commonly called *metabotropic receptors*.

When a neurotransmitter binds to a G protein–linked receptor, the G protein is activated (**Figure 11.20**). (To orient yourself, refer back to the simpler G protein explanation in *Focus on G Proteins*, Focus Figure 3.2 on p. 76.) Activated G proteins typically work by controlling the production of second messengers such as **cyclic AMP**, **cyclic GMP**, **diacylglycerol**, or **Ca^{2+}**.

These second messengers, in turn, act as go-betweens to regulate the opening or closing of ion channels or activate kinase enzymes that initiate a cascade of reactions in the target cells. Some second messengers modify (activate or inactivate) other proteins, including channel proteins, by attaching phosphate groups to them. Others interact with nuclear proteins that activate genes and induce synthesis of new proteins in the target cell.

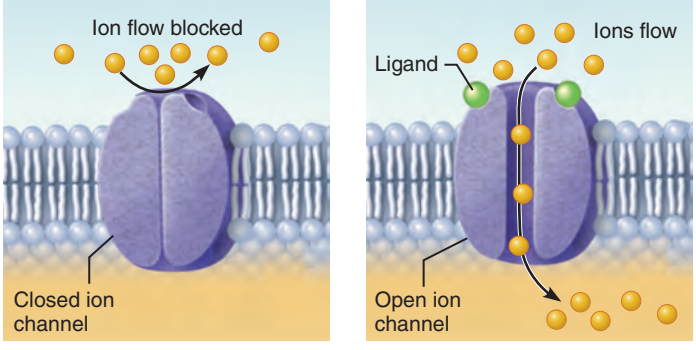


Figure 11.19 Channel-linked receptors cause rapid synaptic transmission. Ligand binding *directly* opens chemically gated ion channels.

Check Your Understanding

20. ACh excites skeletal muscle and yet it inhibits heart muscle. How can this be?

21. Why is cyclic AMP called a second messenger?

For answers, see Answers Appendix.

11.10 Neurons act together, making complex behaviors possible

Learning Objectives

- **Describe common patterns of neuronal organization and processing.**
- **Distinguish between serial and parallel processing.**

Until now, we have concentrated on the activities of individual neurons. However, neurons function in groups, and each group contributes to still broader neural functions. In this way, the organization of the nervous system is hierarchical.

Any time you have a large number of *anything*—people included—there must be *integration*. In other words, the parts must be fused into a smoothly operating whole.

In this module, we move to the first level of **neural integration**: *neuronal pools* and their patterns of communicating with other parts of the nervous system. In Chapter 12 we discuss the highest levels of neural integration—how we think and remember. With this understanding of the basics and of the larger picture, in Chapter 13 we examine how sensory inputs interface with motor activity.

Organization of Neurons: Neuronal Pools

The billions of neurons in the CNS are organized into **neuronal pools**. These functional groups of neurons integrate

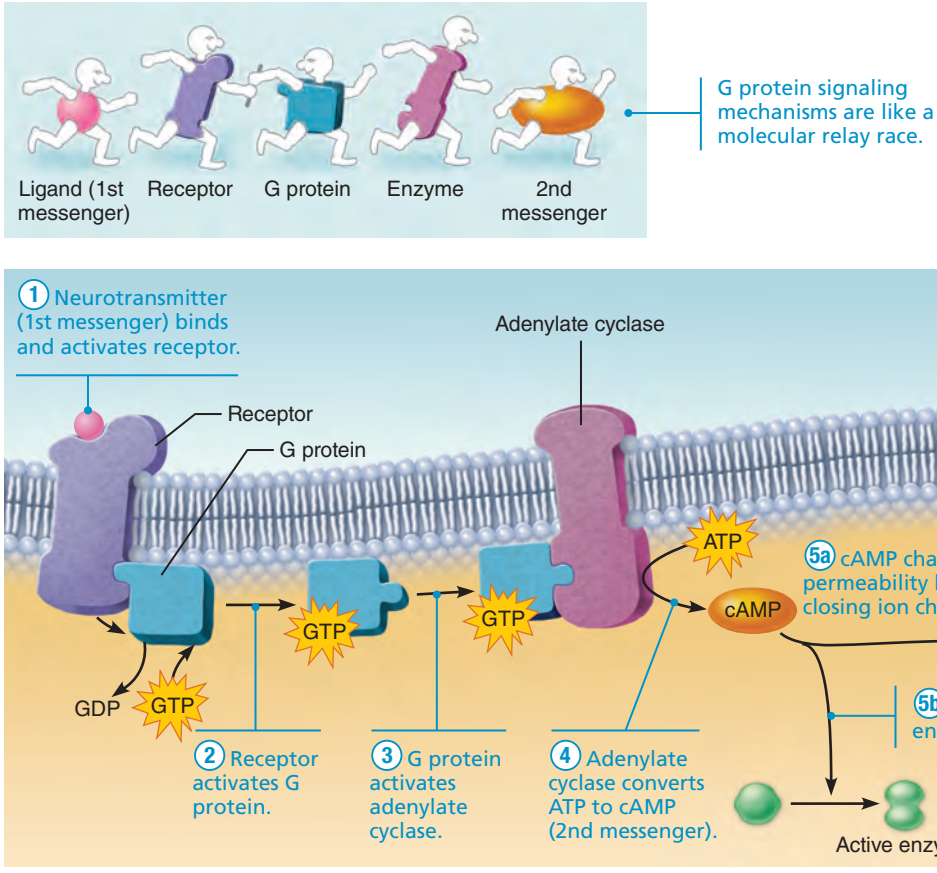


Figure 11.20 G protein–linked receptors cause the formation of intracellular second messengers. The neurotransmitter acts indirectly—via the second messenger cyclic AMP (cAMP) in this example—to bring about the cell's response. (For the basics of G protein signaling mechanisms, see Focus Figure 3.2 on p. 76.)

incoming information from receptors or different neuronal pools and then forward the processed information to other destinations.

In a simple type of neuronal pool (**Figure 11.21**), one incoming presynaptic fiber branches profusely as it enters the pool and then synapses with several different neurons in the pool. When the incoming fiber is excited, it will excite some postsynaptic neurons and facilitate others. Neurons most likely to generate impulses are those closely associated with the incoming fiber, because they receive the bulk of the synaptic contacts. Those neurons are in the *discharge zone* of the pool.

Neurons farther from the center are not usually excited to threshold, but they are facilitated and can easily be brought to threshold by stimuli from another source. For this reason, the periphery of the pool is the *facilitated zone*. Keep in mind, however, that our figure is a gross oversimplification. Most neuronal pools consist of thousands of neurons and include inhibitory as well as excitatory neurons.

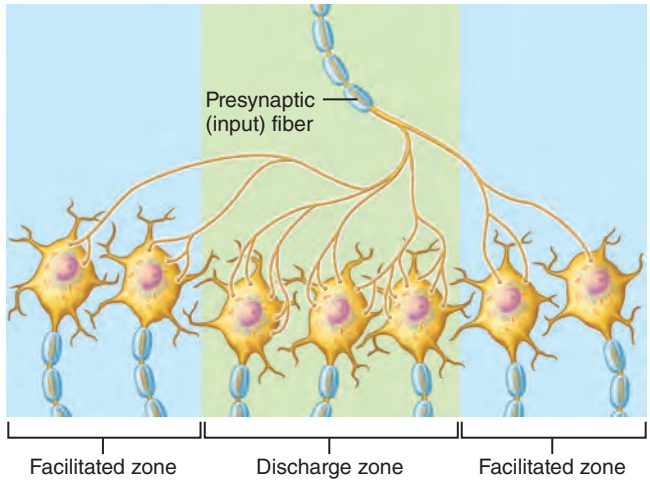


Figure 11.21 Simple neuronal pool. Postsynaptic neurons in the discharge zone receive more synapses and are more likely to discharge (generate APs). Postsynaptic neurons in the facilitated zone receive fewer synapses and are facilitated (brought closer to threshold).

Patterns of Neural Processing

Input processing is both *serial* and *parallel*. In serial processing, the input travels along one pathway to a specific destination. In parallel processing, the input travels along several different

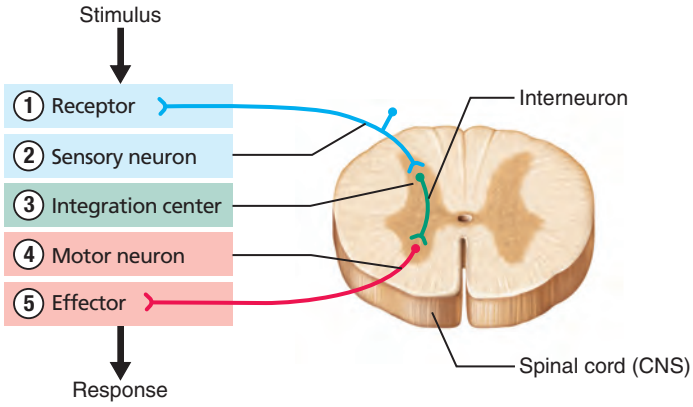


Figure 11.22 A simple reflex arc. Receptors detect a change in the internal or external environment that elicits a rapid stereotyped response. Effectors are muscles or glands.

pathways to be integrated in different CNS regions. Each mode has unique advantages, but as an information processor, the brain derives its power from its ability to process in parallel.

Serial Processing

In **serial processing**, the whole system works in a predictable all-or-nothing manner. One neuron stimulates the next, which stimulates the next, and so on, eventually causing a specific, anticipated response. The most clear-cut examples of serial processing are spinal reflexes. Straight-through sensory pathways from receptors to the brain are also examples. Because reflexes are the functional units of the nervous system, it is important that you understand them early on.

Reflexes are rapid, automatic responses to stimuli, in which a particular stimulus always causes the same response. Reflex activity, which produces the simplest behaviors, is stereotyped and dependable. For example, if you touch a hot object you jerk your hand away, and an object approaching your eye triggers a blink. Reflexes occur over neural pathways called **reflex arcs** that have five essential components—receptor, sensory neuron, CNS integration center, motor neuron, and effector (**Figure 11.22**).

Parallel Processing

In **parallel processing**, inputs are segregated into many pathways, and different parts of the neural circuitry deal simultaneously with the information delivered by each pathway. For example, smelling a pickle (the input) may cause you to remember picking cucumbers on a farm; or it may remind you that you don't like pickles or that you must buy some at the market; or perhaps it will call to mind *all* these thoughts. For each person, parallel processing triggers unique pathways. The same stimulus—pickle smell, in our example—promotes many responses beyond simple awareness of the smell. Parallel processing is not repetitious because the pathways do different things with the information. Each pathway or "channel" is decoded in relation to all the others to produce a total picture.

Think, for example, about what happens when you step on a sharp object while walking barefoot. The serially processed withdrawal reflex causes you to withdraw your foot immediately. At the same time, pain and pressure impulses are speeding up to your brain along parallel pathways that allow you to decide whether to simply rub the hurt spot or seek first aid.

Parallel processing is extremely important for higher-level mental functioning—for putting the parts together to understand the whole. For example, you can recognize a dollar bill in a split second. This task takes a serial-based computer a fairly long time, but your recognition is rapid because you use parallel processing. A single neuron sends information along several pathways instead of just one, so you process a large amount of information much more quickly.

Types of Circuits

Individual neurons in a neuronal pool both send and receive information, and synaptic contacts may cause either excitation or inhibition. The patterns of synaptic connections in neuronal pools, called **circuits**, determine the pool's functional capabilities. **Figure 11.23** illustrates four basic circuit patterns and their properties: diverging, converging, reverberating, and parallel after-discharge circuits.

☑ Check Your Understanding

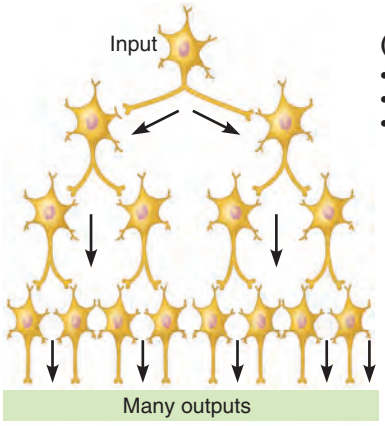
22. Which types of neural circuits would give a prolonged output after a single input?

23. What pattern of neural processing occurs when your finger accidentally touches a hot grill? What is this response called?

24. What pattern of neural processing occurs when we smell freshly baked apple pie and remember Thanksgiving at our grandparents' house, the odor of freshly cooked turkey, sitting by the fire, and other such memories?

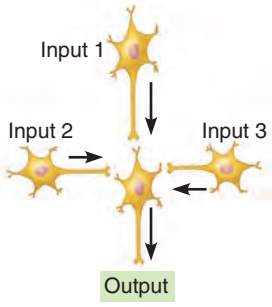
For answers, see Answers Appendix.

In this chapter, we have examined how the amazingly complex neurons, via electrical and chemical signals, serve the body in a variety of ways. Some serve as "lookouts," others process information for immediate use or for future reference, and still others stimulate the body's muscles and glands into activity. With this background, we are ready to study the most sophisticated mass of neural tissue in the entire body—the brain (and its continuation, the spinal cord), the focus of Chapter 12.



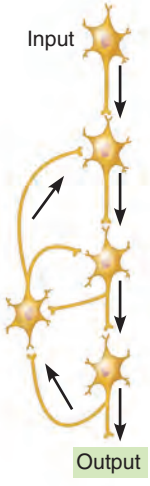
(a) Diverging circuit

- One input, many outputs
- An *amplifying* circuit
- **Example:** A single neuron in the brain can activate 100 or more motor neurons in the spinal cord and thousands of skeletal muscle fibers



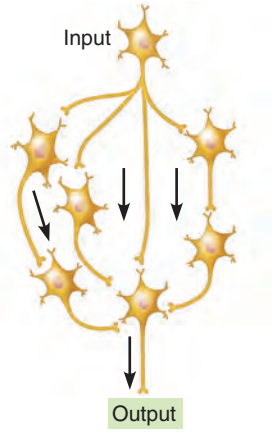
(b) Converging circuit

- Many inputs, one output
- A *concentrating* circuit
- **Example:** Different sensory stimuli can all elicit the same memory



(c) Reverberating circuit

- Signal travels through a chain of neurons, each feeding back to previous neurons
- An *oscillating* circuit
- Controls rhythmic activity
- **Example:** Involved in breathing, sleep-wake cycle, and repetitive motor activities such as walking



(d) Parallel after-discharge circuit

- Signal stimulates neurons arranged in parallel arrays that eventually converge on a single output cell
- Impulses reach output cell at different times, causing a burst of impulses called an *after-discharge*
- **Example:** May be involved in exacting mental processes such as mathematical calculations

Figure 11.23 **Types of circuits in neuronal pools.**

11

REVIEW QUESTIONS

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There you will find:

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Multiple Choice/Matching

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

1. Which of the following structures is not part of the central nervous system? **(a)** the brain, **(b)** a nerve, **(c)** the spinal cord, **(d)** a tract.
2. Match the names of the supporting cells found in column B with the appropriate descriptions in column A.

Column A	Column B
____ **(1)** myelinates nerve fibers in the CNS	**(a)** astrocyte
____ **(2)** lines brain cavities	**(b)** ependymal cell
____ **(3)** myelinates nerve fibers in the PNS	**(c)** microglial cell
____ **(4)** CNS phagocyte	**(d)** oligodendrocyte
____ **(5)** helps regulate the ionic composition of CNS extracellular fluid	**(e)** satellite cell
	(f) Schwann cell

3. What type of current flows through the axolemma during the steep phase of repolarization? **(a)** chiefly a sodium current, **(b)** chiefly a potassium current, **(c)** sodium and potassium currents of approximately the same magnitude.
4. Assume that an EPSP is being generated on the dendritic membrane. Which will occur? **(a)** specific Na^+ channels will open, **(b)** specific K^+ channels will open, **(c)** a single type of channel will open, permitting simultaneous flow of Na^+ and K^+, **(d)** Na^+ channels will open first and then close as K^+ channels open.
5. The velocity of nerve impulse conduction is greatest in **(a)** heavily myelinated, large-diameter fibers, **(b)** myelinated, small-diameter fibers, **(c)** nonmyelinated, small-diameter fibers, **(d)** nonmyelinated, large-diameter fibers.
6. Chemical synapses are characterized by all of the following except **(a)** the release of neurotransmitter by the presynaptic membranes, **(b)** postsynaptic membranes bearing receptors that bind neurotransmitter, **(c)** ions flowing through protein channels from the presynaptic to the postsynaptic neuron, **(d)** a fluid-filled gap separating the neurons.

7. Biogenic amine neurotransmitters include all but **(a)** norepinephrine, **(b)** acetylcholine, **(c)** dopamine, **(d)** serotonin.
8. The neuropeptides that act as natural opiates are **(a)** substance P, **(b)** somatostatin and cholecystokinin, **(c)** tachykinins, **(d)** enkephalins.
9. Inhibition of acetylcholinesterase by poisoning blocks neurotransmission at the neuromuscular junction because **(a)** ACh is no longer released by the presynaptic terminal, **(b)** ACh synthesis in the presynaptic terminal is blocked, **(c)** ACh is not degraded, hence prolonged depolarization is enforced on the postsynaptic cell, **(d)** ACh is blocked from attaching to the postsynaptic ACh receptors.
10. The anatomical region of a multipolar neuron where the AP is initiated is the **(a)** soma, **(b)** dendrites, **(c)** axon hillock, **(d)** distal axon.
11. An IPSP is inhibitory because **(a)** it hyperpolarizes the postsynaptic membrane, **(b)** it reduces the amount of neurotransmitter released by the presynaptic terminal, **(c)** it prevents calcium ion entry into the presynaptic terminal, **(d)** it changes the threshold of the neuron.
12. Identify the neuronal circuits described by choosing the correct response from the key.

    Key: **(a)** converging **(c)** parallel after-discharge
    (b) diverging **(d)** reverberating

    ____ **(1)** Impulses continue around and around the circuit until one neuron stops firing.
    ____ **(2)** One or a few inputs ultimately influence large numbers of neurons.
    ____ **(3)** Many neurons influence a few neurons.
    ____ **(4)** May be involved in exacting types of mental activity.

Short Answer Essay Questions

13. Explain both the anatomical and functional divisions of the nervous system. Include the subdivisions of each.
14. (a) Describe the composition and function of the cell body. (b) How are axons and dendrites alike? In what ways (structurally and functionally) do they differ?
15. (a) What is myelin? (b) How does the myelination process differ in the CNS and PNS?
16. (a) Contrast unipolar, bipolar, and multipolar neurons structurally. (b) Indicate where each is most likely to be found.
17. What is the polarized membrane state? How is it maintained? (Note the relative roles of both passive and active mechanisms.)
18. Describe the events that must occur to generate an AP. Relate the sequence of changes in permeability to changes in the ion channels, and explain why the AP is an all-or-none phenomenon.
19. Since all APs generated by a given nerve fiber have the same magnitude, how does the CNS "know" whether a stimulus is strong or weak?
20. (a) Explain the difference between an EPSP and an IPSP. (b) What specifically determines whether an EPSP or IPSP will be generated at the postsynaptic membrane?
21. Since at any moment a neuron is likely to have thousands of neurons releasing neurotransmitters at its surface, how is neuronal activity (to fire or not to fire) determined?
22. The effects of neurotransmitter binding are very brief. Explain.
23. During a neurobiology lecture, a professor repeatedly refers to group A and group B fibers, absolute refractory period, and myelin sheath gaps. Define these terms.
24. Distinguish between serial and parallel processing.

AT THE CLINIC

Clinical Case Study

Nervous System

Elaine Sawyer, 35, was on her way to the local elementary school with her three children when the accident on Route 91 occurred. As Mrs. Sawyer swerved to avoid the bus, the right rear corner of her minivan struck the side of the bus, causing the minivan to tip over and slide on its side. Her children were shaken but unhurt. Mrs. Sawyer, however, suffered a severe head injury that caused post-traumatic seizures.

The drugs initially prescribed for her treatment were insufficient to control these seizures. Her doctor additionally prescribed Valium (diazepam), but suggested that she use it only for a month because Valium induces tolerance (loses its effectiveness). After a month of Valium treatment, Mrs. Sawyer no longer had seizures and gradually reduced and eliminated her use of Valium. After being seizure-free for another year, restrictions on her driver's license were lifted.

1. Seizures reflect uncontrolled electrical activity of groups of neurons in the brain. Valium is described as a drug that can "quiet the nerves," which means that it inhibits the ability of neurons to generate electrical signals. What are these electrical signals called, and what is happening at the level of the cell when they are generated?
2. Valium enhances inhibitory postsynaptic potentials (IPSPs). What is an IPSP? How does it affect action potential generation?
3. Valium enhances the natural effects of the neurotransmitter GABA [gamma (γ)-aminobutyric acid]. What chemical class of neurotransmitters does GABA belong to? What are some of the other neurotransmitters that fall into this same class?
4. Theoretically, there are a number of possible ways that a drug such as Valium could act to enhance the action of GABA. What are three such possibilities?
5. Valium actually works postsynaptically to promote binding of GABA to its receptor, thereby enhancing the influx of Cl^- ions into the postsynaptic cell (the natural effect produced by GABA). Why would this effect reduce the likelihood that this cell would be able to produce an electrical signal?

For answers, see Answers Appendix.