potential. At electrical synapses, the synaptic delay—the time between the presynaptic spike and the postsynaptic potential—is remarkably short (Figure 11–2B).

Such a short latency is not possible with chemical transmission, which requires several biochemical steps: release of a transmitter from the presynaptic neuron, diffusion of transmitter molecules across the synaptic cleft to the postsynaptic cell, binding of transmitter to a specific receptor, and subsequent gating of ion channels (all described in this and the next chapter). Only current passing directly from one cell to another can produce the near-instantaneous transmission observed at the giant motor electrical synapse.

Another feature of electrical transmission is that the change in potential of the postsynaptic cell is directly related to the size and shape of the change in potential of the presynaptic cell. Even when a weak subthreshold depolarizing current is injected into the presynaptic neuron, some current enters the postsynaptic cell and depolarizes it (Figure 11–3). In contrast, at a chemical synapse, the current in the presynaptic cell must reach the threshold for an action potential before it can release transmitter and elicit a response in the postsynaptic cell.

Most electrical synapses can transmit both depolarizing and hyperpolarizing currents. A presynaptic action potential with a large hyperpolarizing afterpotential produces a biphasic (depolarizing-hyperpolarizing) change in potential in the postsynaptic cell. Signal transmission at electrical synapses is similar to the passive propagation of subthreshold electrical signals along axons (Chapter 9) and therefore is also referred to as *electrotonic transmission*. At some specialized gap junctions, the channels have voltage-dependent gates that permit them to conduct depolarizing current in only one direction, from the presynaptic cell to the postsynaptic cell. These junctions are called *rectifying synapses*. (The crayfish giant motor synapse is an example.)

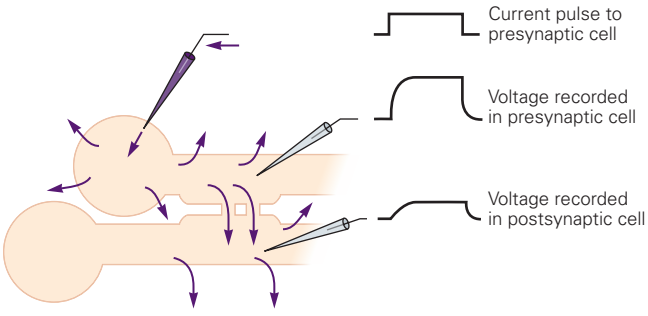

Figure 11–3 Electrical transmission is graded. It occurs even when the current in the presynaptic cell is below the threshold for an action potential. As demonstrated by single-cell recordings, a subthreshold depolarizing stimulus causes a passive depolarization in the presynaptic and postsynaptic cells. (Depolarizing or outward current is indicated by an upward deflection.)

Cells at an Electrical Synapse Are Connected by Gap-Junction Channels

At an electrical synapse, the pre- and postsynaptic components are apposed at the *gap junction*, where the separation between the two neurons (4 nm) is much less than the normal nonsynaptic space between neurons (20 nm). This narrow gap is bridged by *gap-junction channels*, specialized protein structures that conduct ionic current directly from the presynaptic to the postsynaptic cell.

A gap-junction channel consists of a pair of *hemichannels*, or *connexons*, one in the presynaptic and the other in the postsynaptic cell membrane. These hemichannels thus form a continuous bridge between the two cells (Figure 11–4). The pore of the channel has a large diameter of approximately 1.5 nm, much larger than the 0.3- to 0.5-nm diameter of ion-selective ligand-gated or voltage-gated channels. The large pore of gap-junction channels does not discriminate among inorganic ions and is even wide enough to permit small organic molecules and experimental markers such as fluorescent dyes to pass between the two cells.

Each connexon is composed of six identical subunits, called *connexins*. Connexins in different tissues are encoded by a large family of 21 separate but related genes. In mammals, the most common connexon in neurons is formed from the product of *connexin 36.* Connexin genes are named for their predicted molecular weight, in kilodaltons, based on their primary amino acid sequence. All connexin subunits have an intracellular N- and C-terminus with four interposed α-helixes that span the cell membrane (Figure 11–4C).

Many gap-junction channels in different cell types are formed by the products of different connexin genes and thus respond differently to modulatory factors that control their opening and closing. For example, although most gap-junction channels close in response to lowered cytoplasmic pH or elevated cytoplasmic Ca^{2+}, the sensitivity of different channel isoforms to these factors varies widely. The closing of gap-junction channels in response to pH and Ca^{2+} plays an important role in the decoupling of damaged cells from healthy cells, as damaged cells contain elevated Ca^{2+} levels and a high concentration of protons. Finally, neurotransmitters released from nearby chemical synapses can modulate the opening of gap-junction channels through intracellular metabolic reactions (Chapter 14).

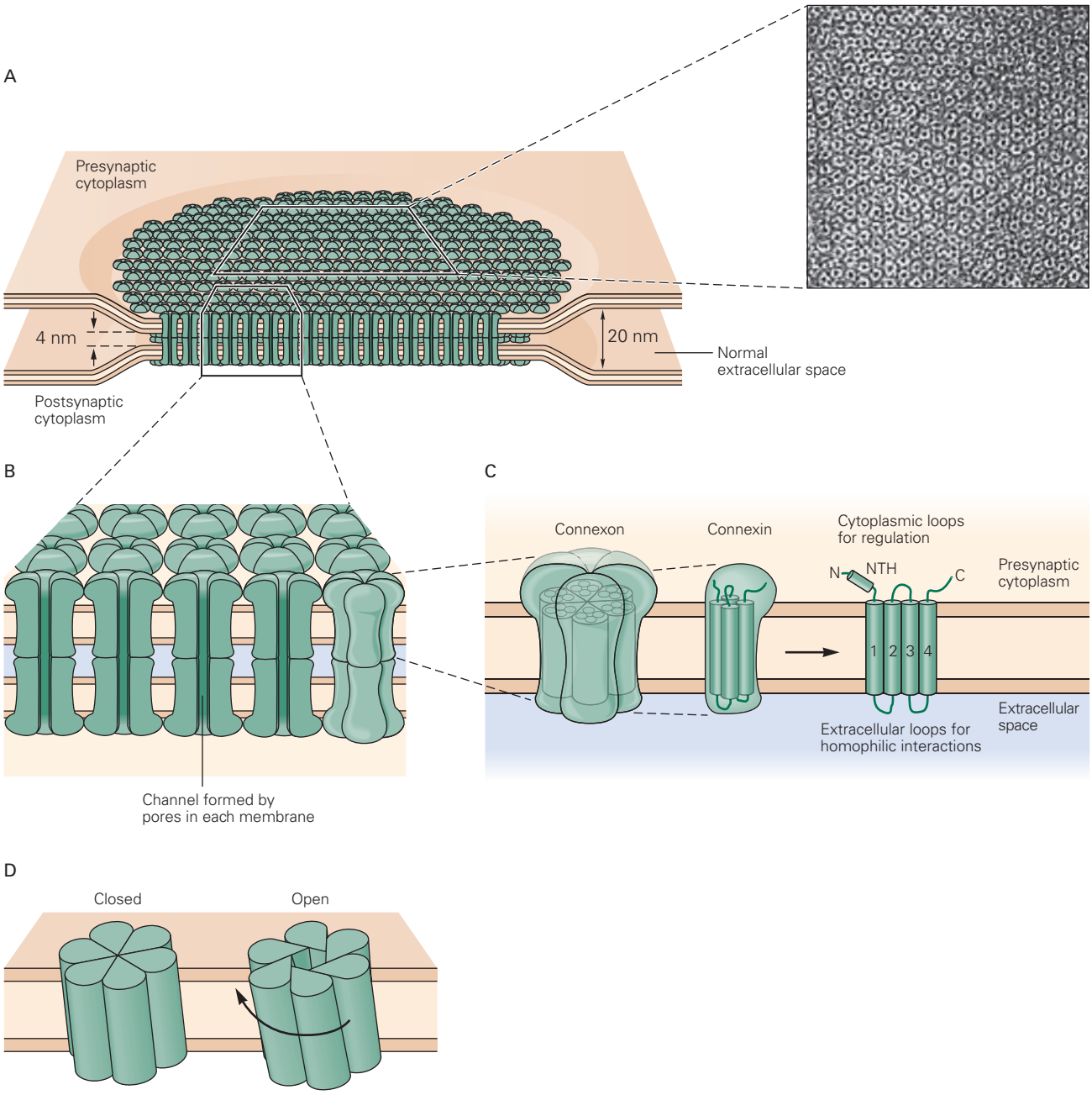

Figure 11–4 A three-dimensional model of the gap-junction channel, based on X-ray and electron diffraction studies.

A. The electrical synapse, or gap junction, is composed of numerous specialized channels that span the membranes of the pre- and postsynaptic neurons. These gap-junction channels allow current to pass directly from one cell to the other. The array of channels in the electron micrograph was isolated from the membrane of a rat liver cell that had been negatively stained, a technique that darkens the area around the channels and in the pores. Each channel appears hexagonal in outline. Magnification ×307,800. (Reproduced, with permission, from N. Gilula.)

B. A gap-junction channel is actually a pair of hemichannels, one in each apposite cell that connects the cytoplasm of the two cells. (Adapted from Makowski et al. 1977.)

C. Each hemichannel, or connexon, is made up of six identical subunits called connexins. Each connexin is approximately 7.5 nm long and spans the cell membrane. A single connexin has intracellular N- and C-terminals, including a short intracellular N-terminal α-helix (**NTH**), and four membrane-spanning α-helixes (**1–4**). The amino acid sequences of gap-junction proteins from many different kinds of tissue have regions of similarity that include the transmembrane helixes and the extracellular regions, which are involved in the homophilic matching of apposite hemichannels.

D. The connexins are arranged in such a way that a pore is formed in the center of the structure. The resulting connexon, with a pore diameter of approximately 1.5 to 2 nm, has a characteristic hexagonal outline, as shown in the photograph in part A. In some gap-junction channels, the pore is opened when the subunits rotate approximately 0.9 nm at the cytoplasmic base in a clockwise direction. (Reproduced, with permission, from Unwin and Zampighi 1980. Copyright © 1980 Springer Nature.)

The three-dimensional structure of a gap-junction channel formed by the human connexin 26 subunit has been determined by X-ray crystallography. This structure shows how the membrane-spanning α-helixes assemble to form the central pore of the channel and how the extracellular loops connecting the transmembrane helixes interdigitate to connect the two hemichannels (Figure 11–5). The pore is lined with polar residues that facilitate the movement of ions. An N-terminal α-helix may serve as the voltage gate of the connexin 26 channel, plugging the cytoplasmic mouth of the pore in the closed state. A separate gate

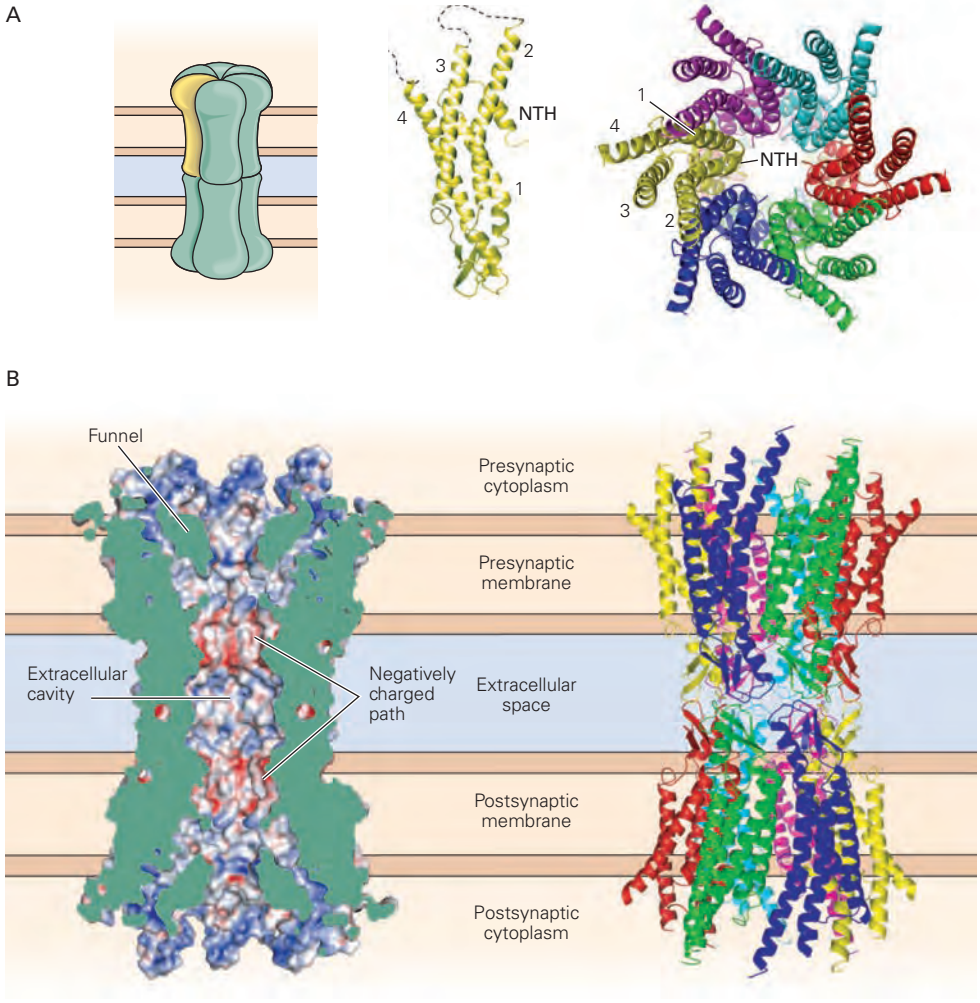

Figure 11–5 High-resolution three-dimensional structure of a gap-junction channel. All structures were determined by X-ray crystallography of gap-junction channels formed by the human connexin 26 subunit. (Reproduced, with permission, from Maeda et al. 2009. Copyright © 2009 Springer Nature.)

A. *Left:* Diagram of an intact gap-junction channel showing the pair of apposed hemichannels. *Middle:* This high-resolution structure of a single connexin subunit shows four transmembrane α-helixes (**1–4**) and a short N-terminal helix (**NTH**). The orientation of the subunit corresponds to that of the yellow subunit in the diagram to the right. *Right:* Bottom-up view looking into a hemichannel from the cytoplasm. Each of the six subunits has a different color. The helixes of the yellow subunit are numbered. The orientation corresponds to that of the yellow hemichannel in the diagram at left, following a 90-degree rotation toward the viewer.

B. Two side views of the gap-junction channel in the plane of the membrane show the two apposed hemichannels. The orientation is the same as in part A. *Left:* Cross section through the channel shows the internal surface of the channel pore. **Blue** indicates positively charged surfaces; **red** indicates negatively charged surfaces. The **green mass** inside the pore at the cytoplasmic entrance (funnel) is thought to represent the channel gate formed by the N-terminal helix. *Right:* A side view of the channel shows each of the six connexin subunits in the same color scheme as in part A. The entire gap-junction channel is approximately 9 nm wide by 15 nm tall.

at the extracellular side of the channel, formed by the extracellular loop connecting the first two membrane helixes, has been inferred from functional studies. This loop gate is thought to close isolated hemichannels that are not docked to a hemichannel partner in the apposing cell.

Electrical Transmission Allows Rapid and Synchronous Firing of Interconnected Cells

How are electrical synapses useful? As we have seen, electrical synaptic transmission is rapid because it results from the direct passage of current between cells. Speed is important for escape responses. For example, the tail-flip response of goldfish is mediated by a giant neuron in the brain stem (known as the Mauthner cell), which receives sensory input at electrical synapses. These electrical synapses rapidly depolarize the Mauthner cell, which in turn activates the motor neurons of the tail, allowing rapid escape from danger.

Electrical transmission is also useful for orchestrating the actions of groups of neurons. Because current crosses the membranes of all electrically coupled cells at the same time, several small cells can act together as one large cell. Moreover, because of the electrical coupling between the cells, the effective resistance of the network is smaller than the resistance of an individual cell. Thus, from Ohm's law, the synaptic current required to fire electrically coupled cells is larger than that necessary to fire an individual cell. That is, electrically coupled cells have a higher firing threshold. Once this high threshold is surpassed, however, electrically coupled cells fire synchronously because voltage-activated Na^+ currents generated in one cell are very rapidly conducted to other cells.

Thus, a behavior controlled by a group of electrically coupled cells has an important adaptive advantage: It is triggered explosively. For example, when seriously perturbed, the marine snail *Aplysia* releases massive clouds of purple ink that provide a protective screen. This stereotypic behavior is mediated by three electrically coupled motor cells that innervate the ink gland. Once the action potential threshold is exceeded in these cells, they fire synchronously (Figure 11–6). In certain fish, rapid eye movements (called saccades) are also mediated by electrically coupled motor neurons

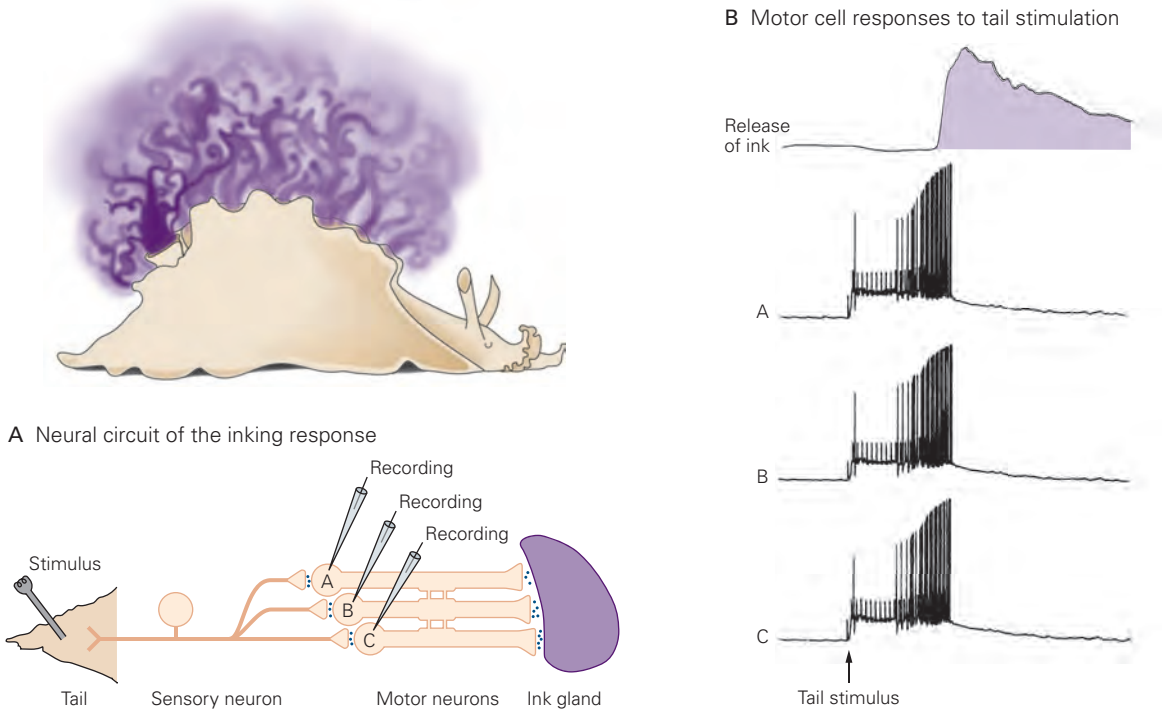

Figure 11–6 Electrically coupled motor neurons firing together can produce synchronous behaviors. (Adapted, with permission, from Carew and Kandel 1976.)

A. In the marine snail *Aplysia*, sensory neurons from the tail ganglion form synapses with three motor neurons that innervate the ink gland. The motor neurons are interconnected by electrical synapses.

B. A train of stimuli applied to the tail produces a synchronized discharge in all three motor neurons that results in the release of ink.

firing together. Gap junctions are also important in the mammalian brain, where the synchronous firing of electrically coupled inhibitory interneurons generates synchronous 40- to 100-Hz (gamma) oscillations in large populations of cells.

In addition to providing speed or synchrony in neuronal signaling, electrical synapses also can transmit metabolic signals between cells. Because of their large-diameter pore, gap-junction channels conduct a variety of inorganic cations and anions, including the second messenger Ca^{2+}, and even conduct moderate-sized organic compounds (<1 kDa molecular weight) such as the second messengers inositol 1,4,5-trisphosphate (IP_3), cyclic adenosine monophosphate (cAMP), and even small peptides.

Gap Junctions Have a Role in Glial Function and Disease

Gap junctions are formed between glial cells as well as between neurons. In glia, the gap junctions mediate both intercellular and intracellular signaling. In the brain, individual astrocytes are connected to each other through gap junctions forming a glial cell network. Electrical stimulation of neuronal pathways in brain slices can release neurotransmitters that trigger a rise in intracellular Ca^{2+} in certain astrocytes. This produces a wave of Ca^{2+} that propagates from astrocyte to astrocyte at a rate of approximately 1–20 μm/s, about a million-fold slower than the propagation of an action potential (10–100 m/s). Although the precise function of the waves is unknown, their existence suggests that glia may play an active role in intercellular signaling in the brain.

Gap-junction channels also enhance communication *within* certain glial cells, such as the Schwann cells that produce the myelin sheath of axons in the peripheral nervous system. Successive layers of myelin formed by a single Schwann cell are connected by gap junctions. These gap junctions may help to hold the layers of myelin together and promote the passage of small metabolites and ions across the many layers of myelin. The importance of the Schwann cell gap-junction channels is underscored by certain genetic diseases. For example, the X chromosome–linked form of Charcot-Marie-Tooth disease, a demyelinating disorder, is caused by single mutations that disrupt the function of *connexin 32*, the gene expressed in Schwann cells. Inherited mutations that prevent the function of a connexin in the cochlea (connexin 26), which normally forms gap-junction channels that are important for fluid secretion in the inner ear, underlie up to half of all instances of congenital deafness.

Chemical Synapses Can Amplify Signals

In contrast to electrical synapses, at chemical synapses, there is no structural continuity between presynaptic and postsynaptic neurons. In fact, the separation between the two cells at a chemical synapse, the synaptic cleft, is usually slightly wider (20–40 nm) than the nonsynaptic intercellular space (20 nm). Chemical synaptic transmission depends on a neurotransmitter, a chemical substance that diffuses across the synaptic cleft and binds to and activates receptors in the membrane of the target cell. At most chemical synapses, transmitter is released from specialized swellings of the presynaptic axon—synaptic boutons—that typically contain 100 to 200 synaptic vesicles, each of which is filled with several thousand molecules of neurotransmitter (Figure 11–7).

The synaptic vesicles are clustered at specialized regions of the synaptic bouton called *active zones.* During a presynaptic action potential, voltage-gated Ca^{2+} channels at the active zone open, allowing Ca^{2+} to enter the presynaptic terminal. The rise in intracellular Ca^{2+}concentration triggers a biochemical reaction that causes the vesicles to fuse with the presynaptic membrane and release neurotransmitter into the synaptic cleft, a process termed *exocytosis*. The transmitter molecules then diffuse across the synaptic cleft and bind

Figure 11–7 The fine structure of a presynaptic terminal. This electron micrograph shows an axon terminal in the cerebellum. The large dark structures are mitochondria. The many small round bodies are vesicles that contain neurotransmitter. The fuzzy dark thickenings along the presynaptic membrane (**arrows**) are the active zones, specialized areas that are thought to be docking and release sites for synaptic vesicles. The synaptic cleft is the space separating the pre- and postsynaptic cell membranes. (Reproduced, with permission, from Heuser and Reese 1977.)

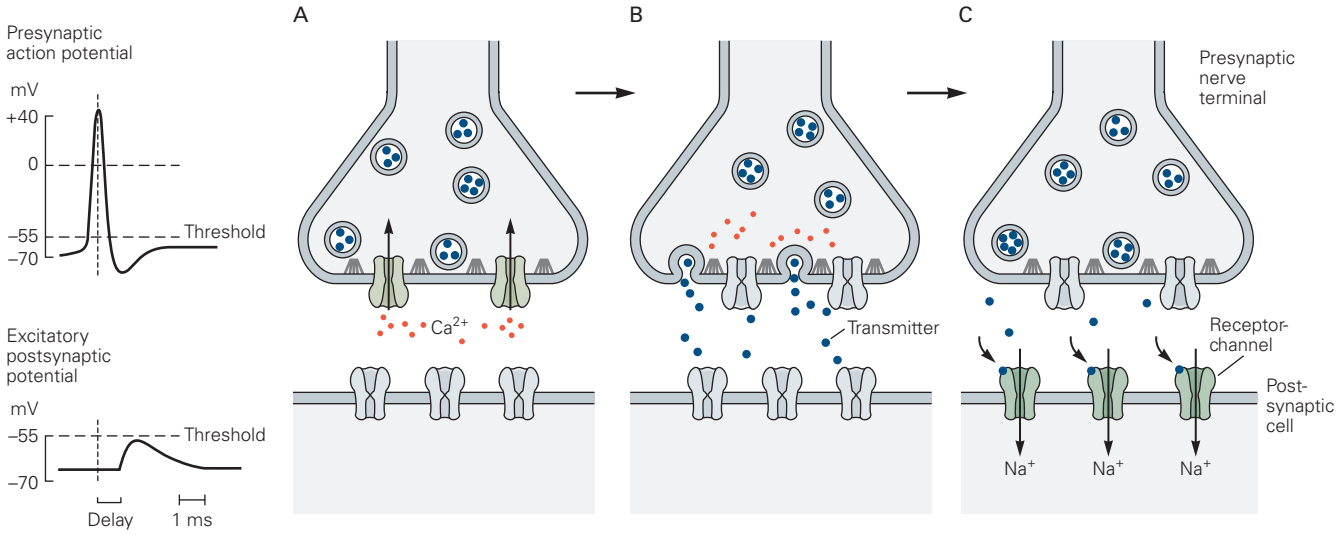

Figure 11–8 Synaptic transmission at chemical synapses involves several steps. The complex process of chemical synaptic transmission accounts for the delay between an action potential in the presynaptic cell and the synaptic potential in the postsynaptic cell, as compared with the virtually instantaneous transmission of signals at electrical synapses (see Figure 11–2B).

A. An action potential arriving at the terminal of a presynaptic axon causes voltage-gated Ca^{2+} channels at the active zone to open. The **gray filaments** represent the docking and release sites of the active zone.

B. The Ca^{2+} channel opening produces a high concentration of intracellular Ca^{2+} near the active zone, causing vesicles containing neurotransmitter to fuse with the presynaptic cell membrane and release their contents into the synaptic cleft (a process termed *exocytosis*).

C. The released neurotransmitter molecules then diffuse across the synaptic cleft and bind specific receptors on the postsynaptic membrane. These receptors cause ion channels to open (or close), thereby changing the membrane conductance and membrane potential of the postsynaptic cell.

to their receptors on the postsynaptic cell membrane. This in turn activates the receptors, leading to the opening or closing of ion channels. The resulting flux of ions alters the membrane conductance and potential of the postsynaptic cell (Figure 11–8).

These several steps account for the synaptic delay at chemical synapses. Despite its biochemical complexity, the release process is remarkably efficient—the synaptic delay is usually only 1 ms or less. Although chemical transmission lacks the immediacy of electrical synapses, it has the important property of *amplification*. Just one synaptic vesicle releases several thousand molecules of transmitter that together can open thousands of ion channels in the target cell. In this way, a small presynaptic nerve terminal, which generates only a weak electrical current, can depolarize a large postsynaptic cell.

The Action of a Neurotransmitter Depends on the Properties of the Postsynaptic Receptor

Chemical synaptic transmission can be divided into two steps: a transmitting step, in which the presynaptic cell releases a chemical messenger, and a receptive step, in which the transmitter binds to and activates the receptor molecules in the postsynaptic cell. The transmitting process in neurons resembles endocrine hormone release. Indeed, chemical synaptic transmission can be seen as a modified form of hormone secretion. Both endocrine glands and presynaptic terminals release a chemical agent with a signaling function, and both are examples of regulated secretion (Chapter 7). Similarly, both endocrine glands and neurons are usually some distance from their target cells.

There is one important difference, however, between endocrine and synaptic signaling. Whereas the hormone released by a gland travels through the blood stream until it interacts with all cells that contain an appropriate receptor, a neuron usually communicates only with the cells with which it forms synapses. Because the presynaptic action potential triggers the release of a chemical transmitter onto a target cell across a distance of only 20 nm, the chemical signal travels only a small distance to its target. Therefore, neuronal signaling has two special features: It is fast and it is precisely directed.

In most neurons, this directed or focused release is accomplished at the active zones of synaptic boutons.

In presynaptic neurons neurons without active zones, the distinction between neuronal and hormonal transmission becomes blurred. For example, the neurons in the autonomic nervous system that innervate smooth muscle reside at some distance from their postsynaptic cells and do not have specialized release sites in their terminals. Synaptic transmission between these cells is slower and relies on a more widespread diffusion of transmitter. Furthermore, the same transmitter substance can be released differently from different cells. A substance can be released from one cell as a conventional transmitter acting directly on neighboring cells. From other cells, it can be released in a less focused way as a modulator, producing a more diffuse action; and from still other cells, it can be released into the blood stream as a neurohormone.

Although a variety of chemicals serve as neurotransmitters, including both small molecules and peptides (Chapter 16), the action of a transmitter depends on the properties of the postsynaptic receptors that recognize and bind the transmitter, not the chemical properties of the transmitter. For example, ACh can excite some postsynaptic cells and inhibit others, and at still other cells, it can produce both excitation and inhibition. It is the receptor that determines the action of ACh, including whether a cholinergic synapse is excitatory or inhibitory.

Within a group of closely related animals, a transmitter substance binds conserved families of receptors and is often associated with specific physiological functions. In vertebrates, ACh acts on excitatory ACh receptors at all neuromuscular junctions to trigger contraction while also acting on inhibitory ACh receptors to slow the heart.

The distinction between the transmitting and receptive processes is not absolute; many presynaptic terminals contain transmitter receptors that can modify the release process. In some instances, these presynaptic receptors are activated by the transmitter released from the same presynaptic terminal. In other instances, the presynaptic terminal can be contacted by presynaptic terminals from other classes of neurons that release distinct neurotransmitters.

The notion of a receptor was introduced in the late 19th century by the German bacteriologist Paul Ehrlich to explain the selective action of toxins and other pharmacological agents and the great specificity of immunological reactions. In 1900, Ehrlich wrote: "Chemical substances are only able to exercise an action on the tissue elements with which they are able to establish an intimate chemical relationship … [This relationship] must be specific. The [chemical] groups must be adapted to one another … as lock and key."

In 1906, the English pharmacologist John Langley postulated that the sensitivity of skeletal muscle to curare and nicotine was caused by a "receptive molecule." A theory of receptor function was later developed by Langley's students (in particular, A.V. Hill and Henry Dale), a development that was based on concurrent studies of enzyme kinetics and cooperative interactions between small molecules and proteins. As we shall see in the next chapter, Langley's "receptive molecule" has been isolated and characterized as the ACh receptor of the neuromuscular junction.

All receptors for chemical transmitters have two biochemical features in common:

1. They are membrane-spanning proteins. The region exposed to the external environment of the cell recognizes and binds the transmitter from the presynaptic cell.
2. They carry out an effector function within the target cell. The receptors typically influence the opening or closing of ion channels.

Activation of Postsynaptic Receptors Gates Ion Channels Either Directly or Indirectly

Neurotransmitters control the opening of ion channels in the postsynaptic cell either directly or indirectly. These two classes of transmitter actions are mediated by receptor proteins derived from different gene families.

Receptors that gate ion channels directly, such as the ACh receptor at the neuromuscular junction, are composed of four or five subunits that form a single macromolecule. Such receptors contain both an extracellular domain that forms the binding site for the transmitter and a membrane-spanning domain that forms an ion-conducting pore (Figure 11–9A). This kind of receptor is often referred to as *ionotropic* because the receptor directly controls ion flux. Upon binding neurotransmitter, the receptor undergoes a conformational change that opens the ion channel. The actions of ionotropic receptors, also called *receptor-channels* or *ligand-gated channels*, are discussed in detail in Chapters 12 and 13.

Receptors that gate ion channels indirectly, like the several types of receptors for norepinephrine or dopamine in neurons of the cerebral cortex, are normally composed of one or at most two subunits that are distinct from the ion channels they regulate. These receptors, which commonly have seven membrane-spanning α-helixes, act by altering intracellular metabolic reactions and are often referred to as *metabotropic receptors*. Activation of these receptors often stimulates

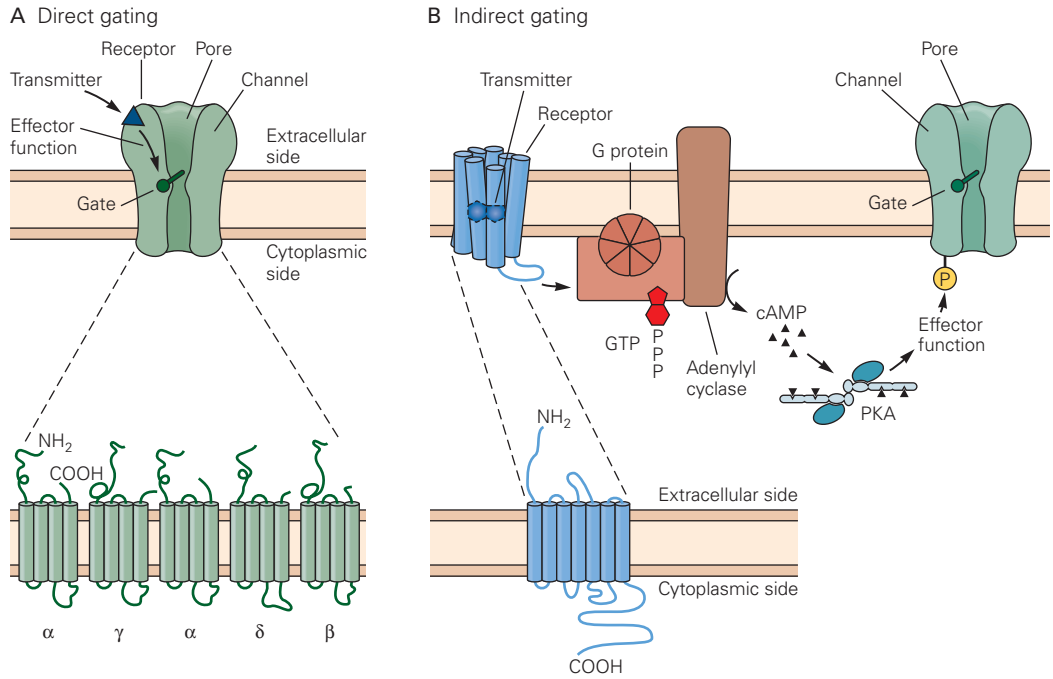

Figure 11–9 Neurotransmitters open postsynaptic ion channels either directly or indirectly.

A. A receptor that directly opens ion channels is an integral part of the macromolecule that also forms the channel. Many such ligand-gated channels are composed of five subunits, each of which is thought to contain four membrane-spanning α-helical regions.

B. A receptor that indirectly opens an ion channel is a distinct macromolecule separate from the channel it regulates. In one large family of such receptors, the receptors are composed of a single subunit with seven membrane-spanning α-helical regions that bind the ligand within the plane of the membrane. These receptors activate a guanosine triphosphate (**GTP**)–binding protein (**G protein**), which in turn activates a second-messenger cascade that modulates channel activity. In the cascade illustrated here, the G protein stimulates adenylyl cyclase, which converts adenosine triphosphate (**ATP**) to cyclic adenosine monophosphate (**cAMP**). The cAMP activates the cAMP-dependent protein kinase (**PKA**), which phosphorylates the channel (**P**), leading to a change in opening.

the production of second messengers, small freely diffusible intracellular metabolites such as cAMP or diacylglycerol. Many of these second messengers activate protein kinases, enzymes that phosphorylate different substrate proteins. In many instances, the protein kinases directly phosphorylate ion channels, including gap-junction channels and ionotropic receptors, modulating their opening or closing (Figure 11–9B). The actions of metabotropic receptors are examined in detail in Chapter 14.

Ionotropic and metabotropic receptors have different functions. The ionotropic receptors produce relatively fast synaptic actions lasting only milliseconds. These are commonly found at synapses in neural circuits that mediate rapid behaviors, such as the stretch receptor reflex. The metabotropic receptors produce slower synaptic actions, lasting hundreds of milliseconds to minutes. These slower actions can modulate a behavior by altering the excitability of neurons and the strength of the synaptic connections in the neural circuit that mediates the behavior. Such modulatory synaptic actions often act as crucial reinforcing pathways in the process of learning.

Electrical and Chemical Synapses Can Coexist and Interact

As we now realize, both Henry Dale and John Eccles were correct about the existence of chemical and electrical synapses, respectively. Furthermore, we now know that both forms of synaptic transmission can coexist in the same neuron and that electrical and chemical synapses can modify each other's efficacy. For example, during development, many neurons are initially connected by electrical synapses, whose presence helps in the formation of chemical synapses. As chemical

synapses begin to form, they often initiate the down-regulation of electrical transmission.

Both types of synapses also can coexist in neurons in the mature nervous system. The role of these two types of synapses is perhaps best understood in the circuitry of the retina. There, rod and cone photoreceptors release the neurotransmitter glutamate and form chemical synapses on a class of interneurons called bipolar cells. Each bipolar cell extends its dendrites horizontally, receiving chemical synaptic input from a number of overlying rods and cones that respond to light from a very small region of the visual field. The receptive field of a bipolar neuron, however, extends about twice as far as the receptive field of the photoreceptors from which it receives chemical synaptic input. This is a result of electrical synapses formed between neighboring bipolar cells and between bipolar cells and a second type of interneuron, the amacrine cell (Chapter 22).

Finally, the efficacy of gap junctions can be regulated by phosphorylation through different protein kinases, which generally enhances gap-junction coupling. For example, dopamine and other transmitters can increase or decrease gap-junction coupling by acting on metabotropic G protein–coupled receptors to regulate levels of cAMP and thereby enhance or decrease channel phosphorylation. Such complex signaling loops are a hallmark of many neural circuits and greatly expand their computational powers.

Highlights

1. Neurons communicate by two major mechanisms: electrical and chemical synaptic transmission.
2. Electrical synapses are formed at regions of tight apposition called gap junctions, which provide a direct pathway for charge to flow between the cytoplasm of communicating neurons. This results in very rapid synaptic transmission that is suited for synchronizing the activity of populations of neurons.
3. Neurons at electrical synapses are connected through gap-junction channels, which are formed from a pair of hemichannels, called connexons, one each contributed by the presynaptic and postsynaptic cells. Each connexon is a hexamer, composed of six subunits termed connexins.
4. At chemical synapses, a presynaptic action potential triggers the release of a chemical transmitter from the presynaptic cell through the process of exocytosis. Transmitter molecules then rapidly diffuse across the synaptic cleft to bind to and activate transmitter receptors in the postsynaptic cell.
5. Although slower than electrical synaptic transmission, chemical transmission allows for amplification of the presynaptic action potential through the release of tens of thousands of molecules of transmitter and the activation of hundreds to thousands of receptors in the postsynaptic cell.
6. There are two major classes of transmitter receptors. Ionotropic receptors are ligand-gated ion channels. Binding of transmitter to an extracellular binding site triggers a conformational change that opens the channel pore, generating an ionic current that excites (depolarizes) or inhibits (hyperpolarizes) the postsynaptic cell, depending on the receptor. Ionotropic receptors underlie fast chemical synaptic transmission that mediates rapid signaling in the nervous system.
7. Metabotropic receptors are responsible for the second major class of chemical synaptic actions. These receptors activate intracellular metabolic signaling pathways, often leading to the synthesis of second messengers, such as cAMP, that regulate levels of protein phosphorylation. Metabotropic receptors underlie slow, modulatory synaptic actions that contribute to changes in behavioral state and arousal.

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