Propagation of the Nerve Impulse

10

Learning Objectives

- Describe the ionic basis for the propagation of a nerve impulse.
- State the all-or-nothing principle in relation to propagation of a nerve impulse.
- Describe how nerves are classified.
- Describe the ionic basis of saltatory conduction in myelinated fibers.

Glossary of Terms

Nerve impulse Transmission of an action potential along a nerve.

Orthodromic conduction Conduction of a nerve impulse in the normal direction, e.g., from a receptor for a sensory nerve.

Antidromic conduction Conduction of a nerve impulse in a direction opposite to its normal direction, e.g., towards a receptor for a sensory nerve.

All-or-nothing principle Once an action potential is elicited on a nerve fiber, it travels the entire length of the fiber.

Saltatory conduction The "jumping" of the nerve impulse from one node of Ranvier to another in a myelinated nerve fiber.

In the preceding chapter, we discussed the action potential as it occurs at one spot on the membrane. However, an action potential elicited at any one point on an excitable membrane usually excites adjacent portions of the membrane, resulting in propagation of the action potential along the membrane. This mechanism is demonstrated in Figure 10-1. Figure 10-1*A* shows a normal resting nerve fiber, and Figure 10-1*B* shows a nerve fiber that has been excited in its midportion—that is, the midportion suddenly develops increased permeability to sodium. The arrows show a "local circuit" of current flow from the depolarized areas of the membrane to the adjacent resting membrane areas. That is, positive electrical charges are carried by the inward-diffusing sodium ions through the depolarized membrane and then for several millimeters in both directions along the core of the axon. These positive charges increase the voltage for a distance of 1 to 3 millimeters inside the large myelinated fiber to above the threshold voltage value for initiating an action potential. Therefore, the sodium channels in these new areas immediately open, as shown in Figure 10-1*C* and *D*, and the explosive action potential spreads. These newly depolarized areas produce still more local circuits of current flow farther along the membrane causing progressively more and more depolarization. Thus, the depolarization process travels along the entire length of the fiber. This transmission of the depolarization process along a nerve or muscle fiber is called a *nerve* or *muscle impulse.*

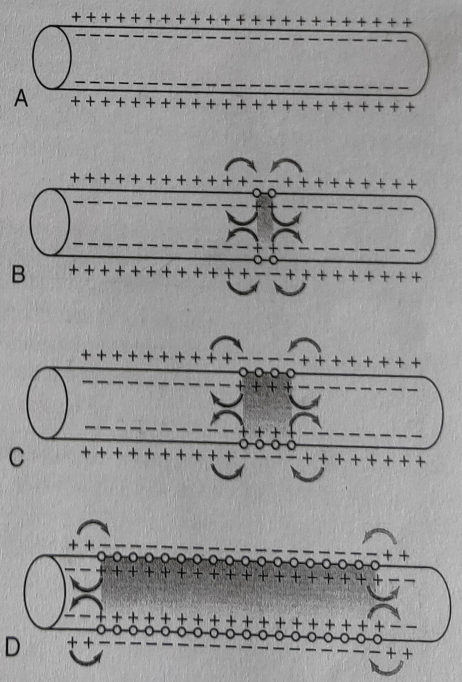

Figure 10-1 Propagation of action potentials in both directions along a conductive fiber.

Direction of Propagation

As demonstrated in Figure 10-1, an excitable membrane has no single direction of propagation but the action

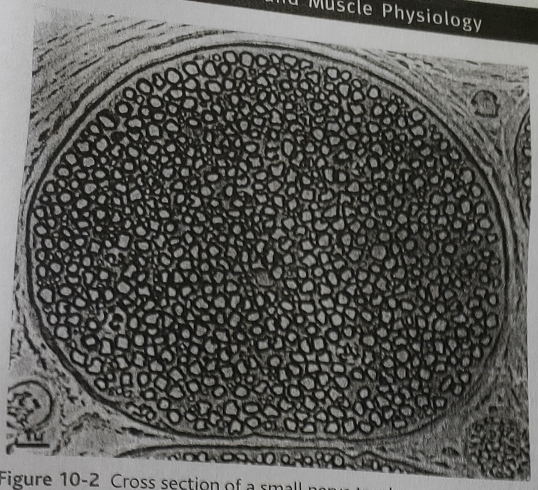

Figure 10-2 Cross section of a small nerve trunk containing both myelinated and unmyelinated fibers.

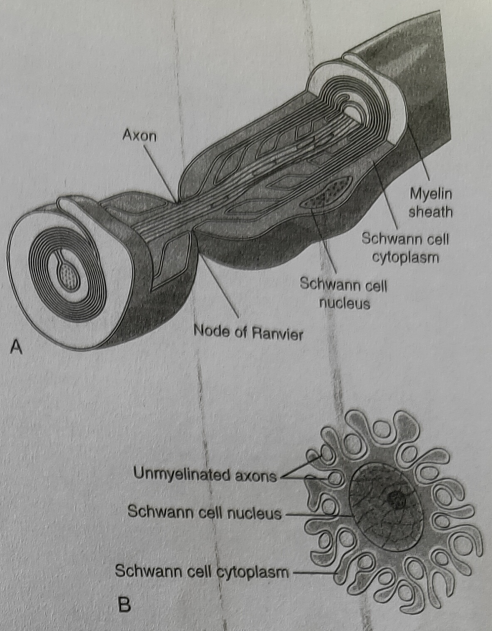

Figure 10-3 Function of the Schwann cell to insulate nerve fibers. A, Wrapping of a Schwann cell membrane around a large axon to form the myelin sheath of the myelinated nerve fiber. B, Partial wrapping of the membrane and cytoplasm of a Schwann cell around multiple unmyelinated nerve fibers (shown in cross section). (A, Modified from Leeson TS, Leeson R: *Histology*. Philadelphia: WB Saunders, 1979.)

potential travels in all directions away from the stimulus—even along all branches of a nerve fiber—until the entire membrane has become depolarized. Thus when a nerve impulse is propagated in the normal direction it is referred to as *orthodromic* conduction while if the impulse is conducted in the opposite direction it is referred to as *antidromic* conduction.

All-or-Nothing Principle

Once an action potential has been elicited at any point on the membrane of a normal fiber, the depolarization process travels over the entire membrane if conditions are right, or it does not travel at all if conditions are not right. This is called the *all-or-nothing principle*, and it applies to all normal excitable tissues. Occasionally, the action potential reaches a point on the membrane at which it does not generate sufficient voltage to stimulate the next area of the membrane. When this occurs, the spread of depolarization stops. Therefore, for continued propagation of an impulse to occur, the ratio of action potential to threshold for excitation must be at all times greater than 1. This "greater than 1" requirement is called the *safety factor* for propagation.

Special Characteristics of Signal Transmission in Nerve Trunks

Myelinated and Unmyelinated Nerve Fibers

Figure 10-2 shows a cross section of a typical small nerve revealing many large nerve fibers that constitute most of the cross-sectional area. However, a more careful look reveals many more small fibers lying between the large ones. The large fibers are *myelinated* and the small ones

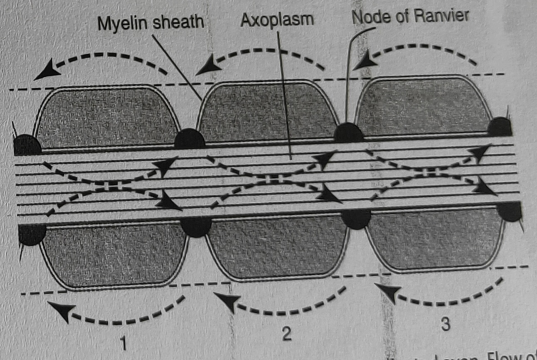

Figure 10-4 Saltatory conduction along a myelinated axon. Flow of electrical current from node to node is illustrated by the arrows 1,2,3.

are *unmyelinated*. The average nerve trunk contains about twice as many unmyelinated fibers as myelinated fibers.

Figure 10-3 shows a typical myelinated fiber. The central core of the fiber is the *axon*, and the membrane of the axon is the membrane that actually conducts the action potential. The axon is filled in its center with *axoplasm*, which is

Table 10-1 Classification of Nerves Based on Their Diameter and Myelination, and the Conduction Velocity

Fiber Type	Fiber Diameter (μm)	Myelination	Conduction Velocity (m/sec)	Type of Fiber / Receptor Supplied
Aα	16	Yes	100	Golgi tendon organ, muscle spindles, extrafusal muscle fibers
Aβ	8	Yes	50	Muscle spindles, skin mechanoreceptors
Aγ	5	Yes	25	Intrafusal muscle fibers
Aδ	4	Yes, but thin	15	Skin receptors
B	3	Yes	8	Preganglionic autonomic fibers
C	1	No	1	Postganglionic autonomic, skin receptors

A, B, and C fibers differ in their susceptibility to drugs and injury. For instance:

- C fibers are most susceptible to local anesthetics.
- A fibers are most susceptible to pressure.
- B fibers are most susceptible to hypoxia.

a viscid intracellular fluid. Surrounding the axon is a *myelin sheath* that is often much thicker than the axon itself. About once every 1 to 3 millimeters along the length of the myelin sheath is a *node of Ranvier.*

The myelin sheath is deposited around the axon by Schwann cells in the following manner: The membrane of a Schwann cell first envelops the axon. Then the Schwann cell rotates around the axon many times, laying down multiple layers of Schwann cell membrane containing the lipid substance *sphingomyelin.* This substance is an excellent electrical insulator that decreases ion flow through the membrane about 5000-fold. At the juncture between each two successive Schwann cells along the axon, a small uninsulated area only 2 to 3 *micro*meters in length remains where ions still can flow with ease through the axon membrane between the extracellular fluid and the intracellular fluid inside the axon. This area is called the *node of Ranvier.*

"Saltatory" Conduction in Myelinated Fibers from Node to Node

Even though almost no ions can flow through the thick myelin sheaths of myelinated nerves, they can flow with ease through the nodes of Ranvier. Therefore, action potentials occur *only at the nodes.* Yet the action potentials are conducted from node to node, as shown in Figure 10-4; this is called *saltatory conduction.* That is, electrical current flows through the surrounding extracellular fluid outside the myelin sheath, as well as through the axoplasm inside the axon from node to node, exciting successive nodes one after another. Thus, the nerve impulse jumps along the fiber, which is the origin of the term "saltatory."

Saltatory conduction is of value for two reasons. First, by causing the depolarization process to jump long intervals along the axis of the nerve fiber, this mechanism increases the velocity of nerve transmission in myelinated fibers as much as 5- to 50-fold. Second, saltatory conduction conserves energy for the axon because only the nodes depolarize, allowing perhaps 100 times less loss of ions than would otherwise be necessary, and therefore requiring little metabolism for re-establishing the sodium and potassium concentration differences across the membrane after a series of nerve impulses.

Still another feature of saltatory conduction in large myelinated fibers is the following: The excellent insulation afforded by the myelin membrane and the 50-fold decrease in membrane capacitance allow repolarization to occur with little transfer of ions.

Erlanger and Gasser won the Nobel Prize in 1944 for their study of the characteristics of peripheral nerves and of conduction velocity. They classified nerves based on their diameter and myelination and the conduction velocity and a modification of this is depicted in Table 10-1. Thus the velocity of action potential conduction in nerve fibers varies from as little as 0.25 m/sec in small unmyelinated fibers to as great as 100 m/sec (the length of a football field in 1 second) in large myelinated fibers.

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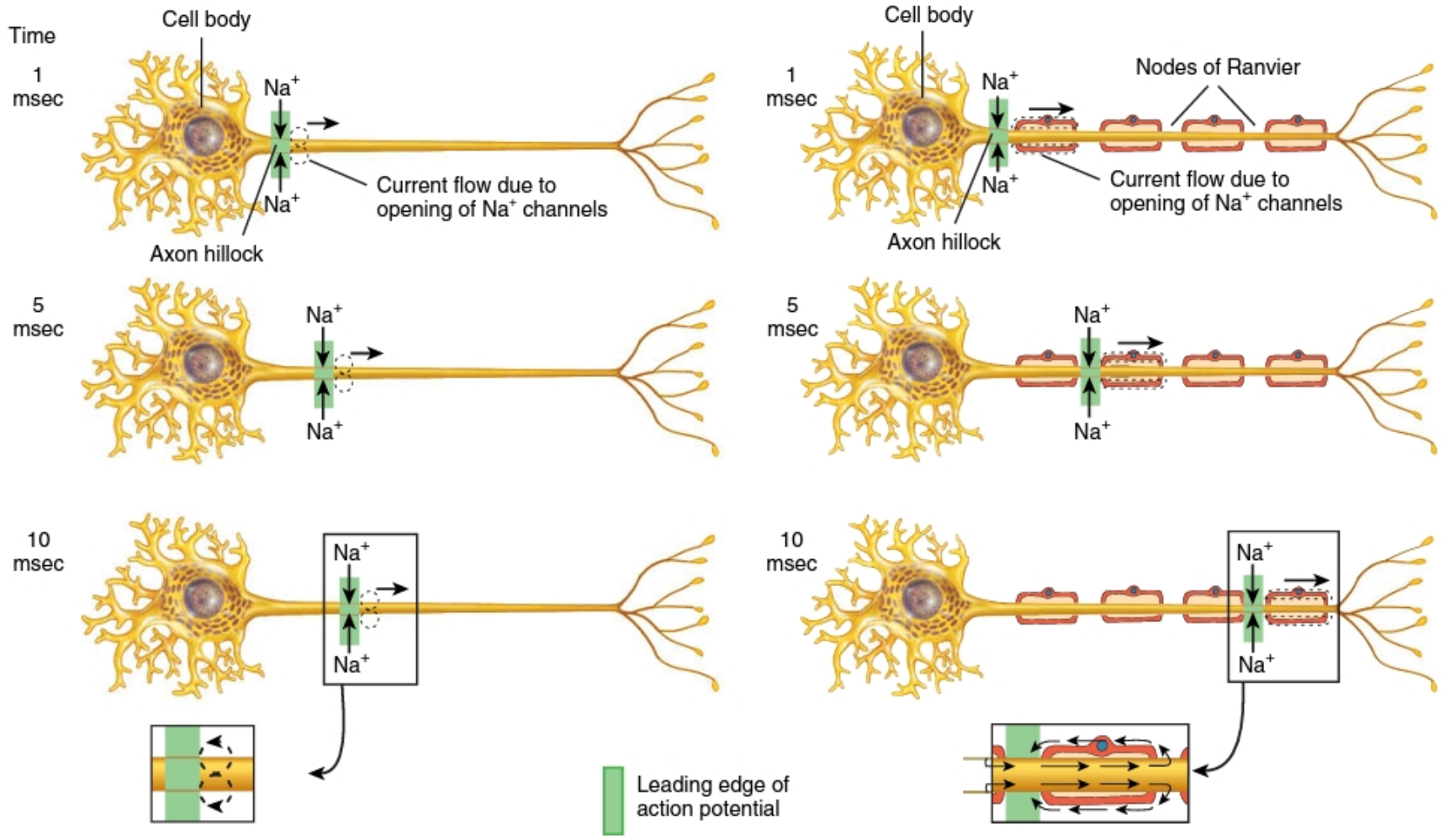
Kandel ER, Schwartz JH, Jessell TM: *Principles of Neural Science*, ed 4, New York, 2000, McGraw-Hill.

Poliak S, Peles E: The local differentiation of myelinated axons at nodes of Ranvier, *Nat Rev Neurosci* 12:968, 2003.

FIGURE 12.21 Propagation of an action potential in a neuron after it arises at the trigger zone. Dotted lines indicate ionic current flow. The insets show the path of current flow. (a) In continuous conduction along an unmyelinated axon, ionic currents flow across each adjacent segment of the membrane. (b) In saltatory conduction along a myelinated axon, the action potential (nerve impulse) at the first node generates ionic currents in the cytosol and interstitial fluid that open voltage-gated Na^+ channels at the second node, and so on at each subsequent node.

Unmyelinated axons exhibit continuous conduction; myelinated axons exhibit saltatory conduction.



(a) Continuous conduction

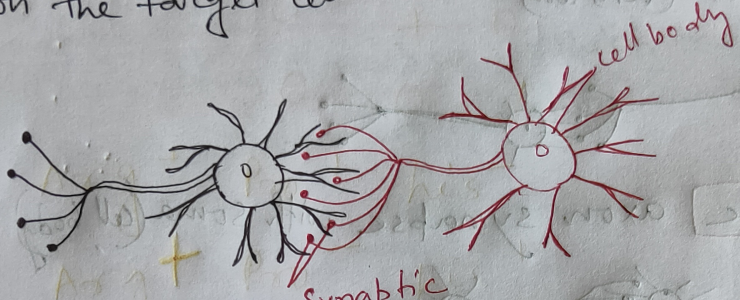
(b) Saltatory conduction

Q What factors determine the speed of propagation of an action potential?

Synapse

A specialized junction at which neurone communicate with a target cell (another nurone/ muscle/ gland etc).

At a synapse, a neurone releases chemical trasmitter that activates special sites called receptors on the target cell.

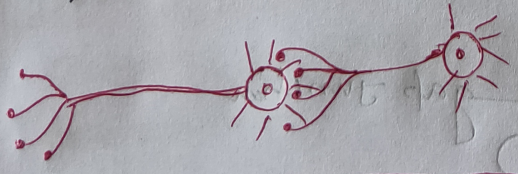


Types

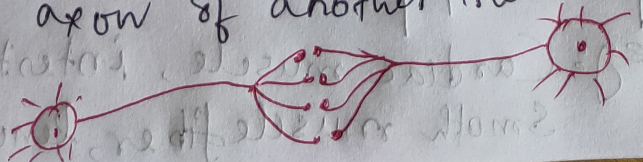
(A) Anatomical classification.
(B) Functional classification.
(C) Based on functions.

Anatomical classification

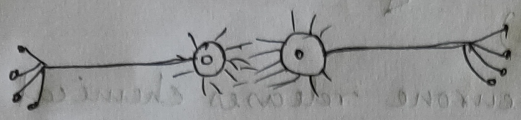
(1) **Axodendrite synapse**: axon of one nurone synapse with dendrites of another neuron.



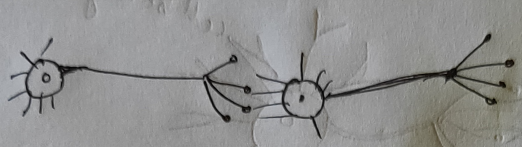
(2) **Axoaxonic synapse**: axon of one nurone synapse with axon of another neurons.



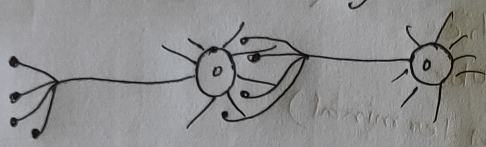
(3) Dendro-dendritic : synapse between dendrites & dendrites



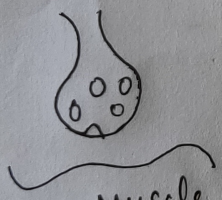
(4) Dendro-axonic : a dendrite communicates with axon (very low)



(5) Axosomatic axon synapse with soma (cell body)

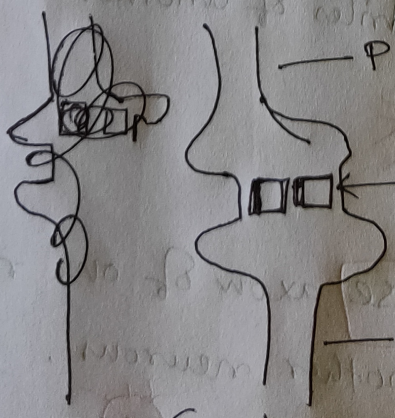


(6) Neuromuscular junction axon ends on muscle fiber.



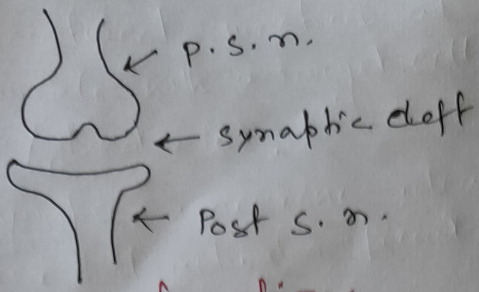
Functional classification

Electrical synapse



eg: Cardiac muscle, intestine Smoth muscle fiber, Rence of

Chemical synapse



Based on function

① Excitatory synapse – which transmit the impulses (excitatory function)

eg – Ach.

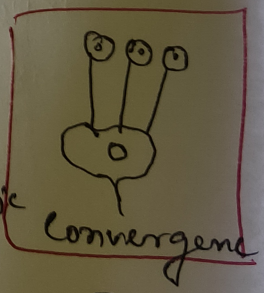
② Inhibitory synapse : which inhibit the transmission of impulses (Inhibitory function)

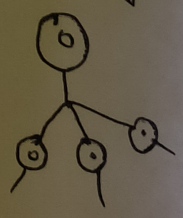
eg: GABA, Dopamin, Glycine

Gama amino butaric acid.

* **Convergence** : Many presynaptic neurons terminates on single post synaptic neurons.

* **Divergence**: one presynaptic neuron terminate on many postsynaptic neurons.





Divergens.

Electrical Synapses

At an **electrical synapse**, action potentials (impulses) conduct directly between the plasma membranes of adjacent neurons through structures called **gap junctions**. Each gap junction contains a hundred or so tubular *connexons*, which act like tunnels to connect the cytosol of the two cells directly (see **Figure 4.2e**). As ions flow from one cell to the next through the connexons, the action potential spreads from cell to cell. Gap junctions are common in visceral smooth muscle, cardiac muscle, and the developing embryo. They also occur in the brain.

Electrical synapses have two main advantages:

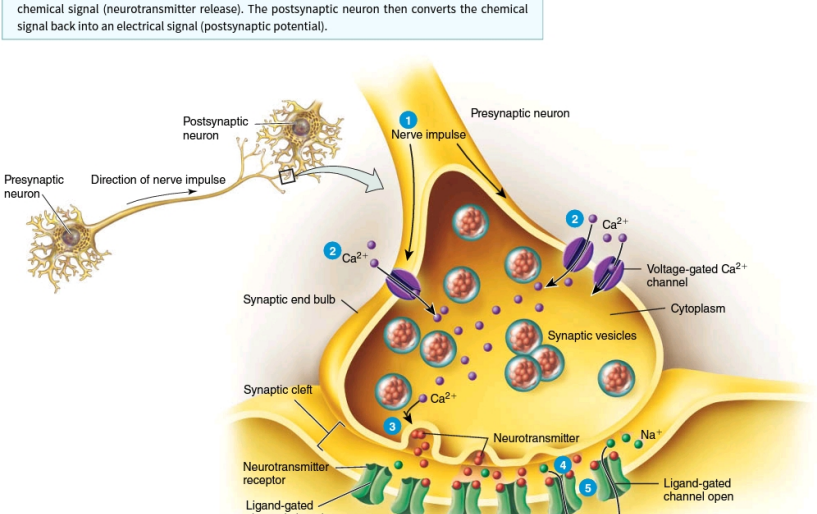
1. ***Faster communication.*** Because action potentials conduct directly through gap junctions, electrical synapses are faster than chemical synapses. At an electrical synapse, the action potential passes directly from the presynaptic cell to the postsynaptic cell. The events that occur at a chemical synapse take some time and delay communication slightly.
2. ***Synchronization.*** Electrical synapses can synchronize (coordinate) the activity of a group of neurons or muscle fibers. In other words,

Although the plasma membranes of presynaptic and postsynapt neurons in a **chemical synapse** are close, they do not touch. They a separated by the **synaptic cleft**, a space of 20–50 nm* that is fille with interstitial fluid. Nerve impulses cannot conduct across the sy aptic cleft, so an alternative, indirect form of communication occur In response to a nerve impulse, the presynaptic neuron releases neurotransmitter that diffuses through the fluid in the synaptic cle and binds to receptors in the plasma membrane of the postsynapt neuron. The postsynaptic neuron receives the chemical signal and turn produces a **postsynaptic potential**, a type of graded potentia Thus, the presynaptic neuron converts an electrical signal (nerv impulse) into a chemical signal (released neurotransmitter). The pos synaptic neuron receives the chemical signal and in turn generates a electrical signal (postsynaptic potential). The time required for thes processes at a chemical synapse, a **synaptic delay** of about 0.5 mse is the reason that chemical synapses relay signals more slowly tha electrical synapses.

*1 nanometer (nm) = 10^{-9} (0.000000001) meter.

FIGURE 12.23 Signal transmission at a chemical synapse. Through exocytosis of synaptic vesicles, a presynaptic neuron releases neurotransmitter molecules. After diffusing across the synaptic cleft, the neurotransmitter binds to receptors in the plasma membrane of the postsynaptic neuron and produces a postsynaptic potential.

At a chemical synapse, a presynaptic neuron converts an electrical signal (nerve impulse) into a chemical signal (neurotransmitter release). The postsynaptic neuron then converts the chemical signal back into an electrical signal (postsynaptic potential).



Q Why may electrical synapses work in two directions, but chemical synapses can transmit a signal in only one direction?

A typical chemical synapse transmits a signal as follows (**Figure 12.23**):

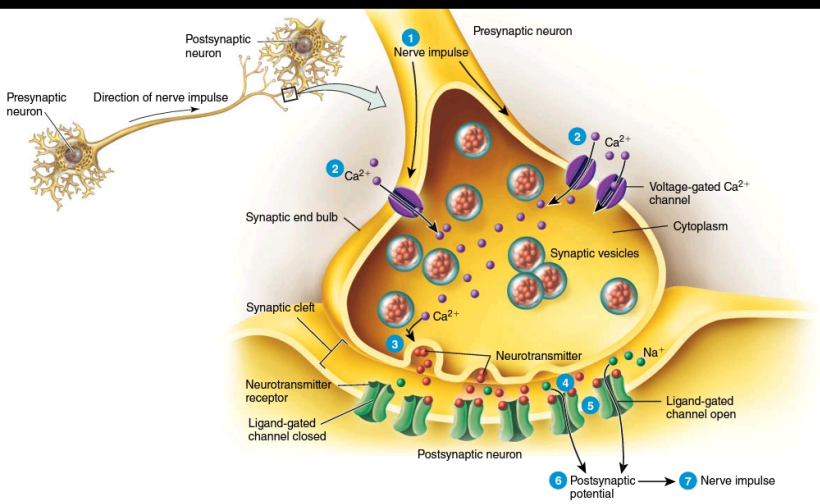
1. A nerve impulse arrives at a synaptic end bulb (or at a varicosity) of a presynaptic axon.
2. The depolarizing phase of the nerve impulse opens **voltage-gated Ca^{2+} channels**, which are present in the membrane of synaptic end bulbs. Because calcium ions are more concentrated in the extracellular fluid, Ca^{2+} flows inward through the opened channels.
3. An increase in the concentration of Ca^{2+} inside the presynaptic neuron serves as a signal that triggers exocytosis of the synaptic vesicles. As vesicle membranes merge with the plasma membrane, neurotransmitter molecules within the vesicles are released into the synaptic cleft. Each synaptic vesicle contains several thousand molecules of neurotransmitter.
4. The neurotransmitter molecules diffuse across the synaptic cleft and bind to **neurotransmitter receptors** in the postsynaptic neuron's plasma membrane. The receptor shown in **Figure 12.23** is part of a ligand-gated channel (see **Figure 12.11b**); you will soon learn that this type of neurotransmitter receptor is called an *ionotropic receptor*. Not all neurotransmitters bind to ionotropic receptors; some bind to *metabotropic receptors* (described shortly).
5. Binding of neurotransmitter molecules to their receptors on ligand-gated channels opens the channels and allows particular ions to flow across the membrane.

6. As ions flow through the opened channels, the voltage across the membrane changes. This change in membrane voltage is a **postsynaptic potential**. Depending on which ions the channels admit, the postsynaptic potential may be a depolarization (excitation) or a hyperpolarization (inhibition). For example, opening of Na^+ channels allows inflow of Na^+, which causes depolarization. However, opening of Cl^- or K^+ channels causes hyperpolarization. Opening Cl^- channels permits Cl^- to move into the cell, while opening the K^+ channels allows K^+ to move out—in either event, the inside of the cell becomes more negative.
7. When a depolarizing postsynaptic potential reaches threshold, it triggers an action potential in the axon of the postsynaptic neuron.

based on whether the neurotransmitter binding site and the ion cha nel are components of the same protein or are components of diffe ent proteins.

Ionotropic Receptors

An **ionotropic receptor** (I-on-o TROP-ik) is a type of neurotransmitter receptor that contains neurotransmitter binding site and an ion channel. In other words, th neurotransmitter binding site and the ion channel are componen of the *same* protein. An ionotropic receptor is a type of ligand-gate channel (see **Figure 12.11b**). In the absence of neurotransmitte (the ligand), the ion channel component of the ionotropic recepto is closed. When the correct neurotransmitter binds to the ionotrop



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7. When a depolarizing postsynaptic potential reaches threshold, it triggers an action potential in the axon of the postsynaptic neuron.

At most chemical synapses, only *one-way information transfer* can occur—from a presynaptic neuron to a postsynaptic neuron or an effector, such as a muscle fiber or a gland cell. For example, synaptic transmission at a neuromuscular junction (NMJ) proceeds from a somatic motor neuron to a skeletal muscle fiber (but not in the opposite direction). Only synaptic end bulbs of presynaptic neurons can release neurotransmitter, and only the postsynaptic neuron's membrane has the receptor proteins that can recognize and bind that neurotransmitter. As a result, action potentials move in one direction.

Excitatory and Inhibitory Postsynaptic Potentials

A neurotransmitter causes either an excitatory or an inhibitory graded potential. A neurotransmitter that causes *depolarization* of the postsynaptic membrane is excitatory because it brings the membrane closer to threshold (see **Figure 12.14b**). A depolarizing postsynaptic potential is called an **excitatory postsynaptic potential (EPSP)**. Although a single EPSP normally does not initiate a nerve impulse, the postsynaptic cell does become more excitable. Because it is partially depolarized, it is more likely to reach threshold when the next EPSP occurs.

A neurotransmitter that causes *hyperpolarization* of the postsynaptic membrane (see **Figure 12.14a**) is inhibitory. During hyperpolarization, generation of an action potential is more difficult than usual because the membrane potential becomes inside more negative and thus even farther from threshold than in its resting state. A hyperpolarizing postsynaptic potential is termed an **inhibitory postsynaptic potential (IPSP)**.

Structure of Neurotransmitter Receptors

As you have already learned, neurotransmitters released from a presynaptic neuron bind to **neurotransmitter receptors** in the plasma based on whether the neurotransmitter binding site and the ion channel are components of the same protein or are components of different proteins.

Ionotropic Receptors

An **ionotropic receptor** (I-on-ō-TROP-ik) is a type of neurotransmitter receptor that contains a neurotransmitter binding site and an ion channel. In other words, the neurotransmitter binding site and the ion channel are components of the *same* protein. An ionotropic receptor is a type of ligand-gated channel (see **Figure 12.11b**). In the absence of neurotransmitter (the ligand), the ion channel component of the ionotropic receptor is closed. When the correct neurotransmitter binds to the ionotropic receptor, the ion channel opens, and an EPSP or IPSP occurs in the postsynaptic cell.

Many excitatory neurotransmitters bind to ionotropic receptors that contain cation channels (**Figure 12.24a**). EPSPs result from opening these cation channels. When cation channels open, they allow passage of the three most plentiful cations (Na^+, K^+, and Ca^{2+}) through the postsynaptic cell membrane, but Na^+ inflow is greater than either Ca^{2+} inflow or K^+ outflow, and the inside of the postsynaptic cell becomes less negative (depolarized).

Many inhibitory neurotransmitters bind to ionotropic receptors that contain chloride channels (**Figure 12.24b**). IPSPs result from opening these Cl^- channels. When Cl^- channels open, a larger number of chloride ions diffuse inward. The inward flow of Cl^- ions causes the inside of the postsynaptic cell to become more negative (hyperpolarized).

Metabotropic Receptors

A **metabotropic receptor** (meh-tab′-ō-TRO-pik) is a type of neurotransmitter receptor that contains a neurotransmitter binding site but lacks an ion channel as part of its structure. However, a metabotropic receptor is coupled to a separate ion channel by a type of membrane protein called a *G protein*. When a neurotransmitter binds to a metabotropic receptor, the G protein either directly opens (or closes) the ion channel or it may act indirectly by activating another molecule, a "second messenger," in the cytosol, which in turn opens (or closes) the ion channel (see Section 18.4 for a detailed discussion of G proteins). Thus, a metabotropic receptor differs from an ionotropic receptor in that the neurotransmitter binding site and the ion channel are components of *different* proteins.

Some inhibitory neurotransmitters bind to metabotropic receptors that are linked to K^+ channels (**Figure 12.24c**). IPSPs result from the opening of these K^+ channels. When K^+ channels open, a larger number of potassium ions diffuses outward. The outward flow of K^+ ions causes the inside of the postsynaptic cell to become more negative (hyperpolarized).

Different Postsynaptic Effects for the Same