

Figure 1 This is an artist's depiction of Galvani's laboratory, in which electrical conductivity was explored using the muscles of a dead frog.

Theories about the transmission of information through the nervous system date as far back as ancient Greece. The philosopher Alcmeon of Croton (540–500 BCE) discussed the presence of pores and channels in the brain and sensory organs. In 1781, Luigi Galvani, a doctor and physiologist at Italy's University of Bologna, discovered that the muscles of a dead frog would twitch when touched with different metals or an electric current (**Figure 1**). In his hypothesis of “animal electricity,” he proposed that electric forces generated in the muscles travelled from the nerves to the muscles and were responsible for muscle contractions and movements. While we now know that his hypothesis was only partially correct, his work sparked an increased interest in neurology.

Instruments to detect electrical transmission within nerves and muscles were introduced in 1848, with the work of Emil DuBois-Reymond at the University of Berlin. By 1906, Dutch physiologist Willem Einthoven had refined a machine that could detect electric impulses in the heart muscle, a methodology that is now the basis of the electrocardiogram (ECG). In 1929, Hans Berger, a German psychiatrist, measured electric currents during brain activity by placing electrodes on a patient's skull. One of Canada's first neurologists was Sir William Osler (1849–1919). He published almost 200 works about neurological disorders, often drawing details from autopsies he had performed. [CAREER LINK](#)

Continued research on the nervous system began to reveal differences between electrical and neural transmission. For example, scientists discovered that nerve impulses travel much more slowly than electric current. The cytosol in the cell body of a neuron provides significant resistance to the transmission of currents. Another notable difference was that nerve impulses do not undergo loss of strength during transmission, unlike electric currents, whose strength declines with the distance they travel. Scientists discovered that nerves use internal cellular energy to generate current, whereas electric current can arise only from an external energy source.

Around 1900, German physiologist Julius Bernstein proposed the idea that nerve impulses are the result of ions moving through the nerve cell membrane. Two researchers from Columbia University, K.S. Cole and H.J. Curtis, provided evidence for Bernstein's theory using an electrode applied to the large neuron of a squid. When the nerve became excited, the electrical potential across the membrane rose rapidly from about -70 mV at rest to about $+40$ mV.

The development of our knowledge of the nervous system, from early ideas to our current understanding, illustrates the progressive nature of science. Scientific knowledge builds on previous understanding, and it changes as new evidence becomes available. Our understanding of the nervous system will continue to grow with future research.

synapse a functional connection between neurons or between neurons and effectors

chemical synapse a synapse in which a neurotransmitter moves from a presynaptic cell to a postsynaptic cell through the synaptic cleft

neurotransmitter a chemical that is released from vesicles into synapses to facilitate nerve signal transmission

synaptic cleft the tiny gap between presynaptic and postsynaptic cells in a chemical synapse, across which the neurotransmitter diffuses

Neural Communication via Synapses

A **synapse** is a site where a neuron makes a connection with either another neuron or an effector, such as a muscle fibre or gland. On one side of the synapse is the axon terminal of a presynaptic cell, which is the neuron that transmits the signal. On the other side is either a dendrite or the cell body of a postsynaptic cell, which is the neuron or effector (such as a muscle cell) that receives the signal. Depending on the kind of neuron, communication across a synapse may occur either chemically or electrically.

In the more common **chemical synapse**, a chemical messenger called a **neurotransmitter** is released by an axon terminal at the synapse. The plasma membranes of the presynaptic and postsynaptic cells are separated by a narrow gap, about 25 nm wide, called the **synaptic cleft** (**Figure 2(a)**, next page).

In an **electrical synapse**, the plasma membranes of the presynaptic and postsynaptic cells are in direct contact, allowing the current to flow directly from one neuron to the next (**Figure 2(b)**). When an electric impulse arrives at the axon terminal, a gap junction allows ions to flow directly between the two cells, providing unbroken transmission of the electrical signal. Electrical synapses allow for very rapid transmission and synchronous activity in a group of neurons.

electrical synapse a synapse in which the presynaptic cell makes direct contact with the postsynaptic cell, allowing current to flow via gap junctions between the cells

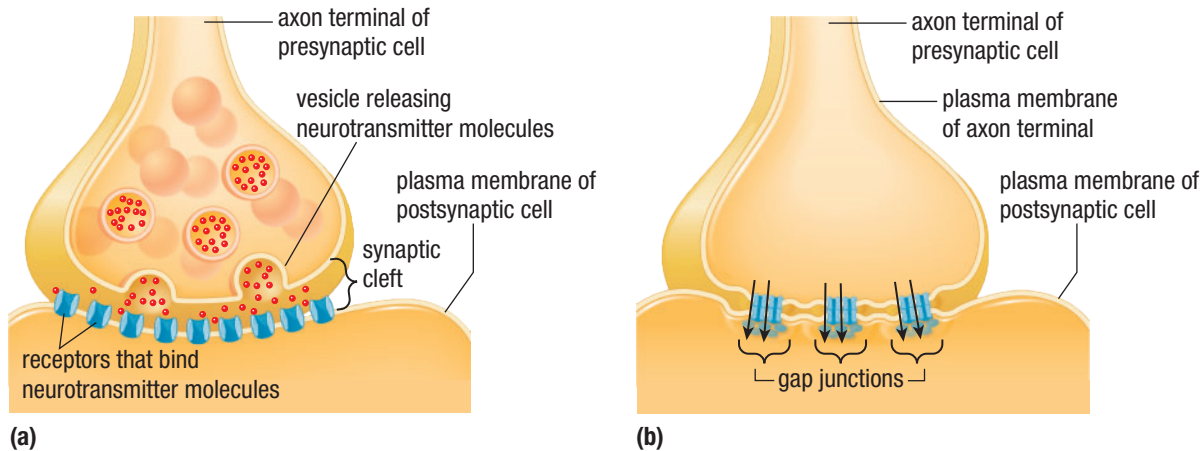


Figure 2 (a) In a chemical synapse, the neurotransmitter diffuses across the synaptic cleft and binds to a receptor in the plasma membrane of the postsynaptic cell. (b) Electrical signals transfer directly across gap junctions in an electrical synapse.

Conduction of Electrical Signals by Neurons

All animal cells have a separation of positive and negative charges across the plasma membrane. Outside the cell is positive, and inside the cell is negative. This charge separation, in part, produces a voltage, or electrical potential difference, across the plasma membrane. This potential difference is called the **membrane potential**. The membrane potential is caused by the uneven distribution of Na^+ and K^+ inside and outside the cell. Plasma membranes are selectively permeable—they allow some ions, but not others, to move across the membrane through embedded proteins called **ion channels**. Some ion channels are closed in their resting state, and they open only in response to a change in voltage. Other ion channels open upon the binding of a specific substance.

In most cells, the membrane potential remains stable. Neurons and muscle cells, however, respond to electrical, chemical, mechanical, and certain other stimuli, causing their membrane potential to change rapidly. Cells with this property are said to be excitable. Excitability, produced by a sudden flow of ions across the plasma membrane, is the basis for nerve impulse generation.

membrane potential the electrical potential of a membrane, which is caused by an imbalance of charges on either side of the membrane

ion channel a protein embedded in the plasma membrane that allows ions to pass through it

Resting Membrane Potential

A special ion channel, the Na^+/K^+ active transport pump, uses energy from ATP hydrolysis to pump three Na^+ out of the cell for every two K^+ pumped in, generating a higher Na^+ concentration outside the cell and a higher K^+ concentration inside the cell (**Figure 3**, next page). This explains the net positive charge outside the cell. The inside of the cell has additional negative charge because the cell also contains many anions (negatively charged ions).

The membrane of a typical neuron that is not conducting an impulse exhibits a steady negative membrane potential of about -70 mV. This is called the **resting potential**. A cell with a resting potential other than 0 V (that is, a cell with some separation of charge on either side of its membrane) is said to be polarized. The Na^+/K^+ pump creates the imbalance of Na^+ and K^+ inside and outside the cell. The concentration of anions within the cell results in the inside being negatively charged and the outside being positively charged.

resting potential the voltage difference across a nerve cell membrane of an unstimulated neuron; usually negative

Charged particle concentrations (mM)		
	Inside	Outside
Na ⁺	15	150
K ⁺	150	5
A ⁻	100	0

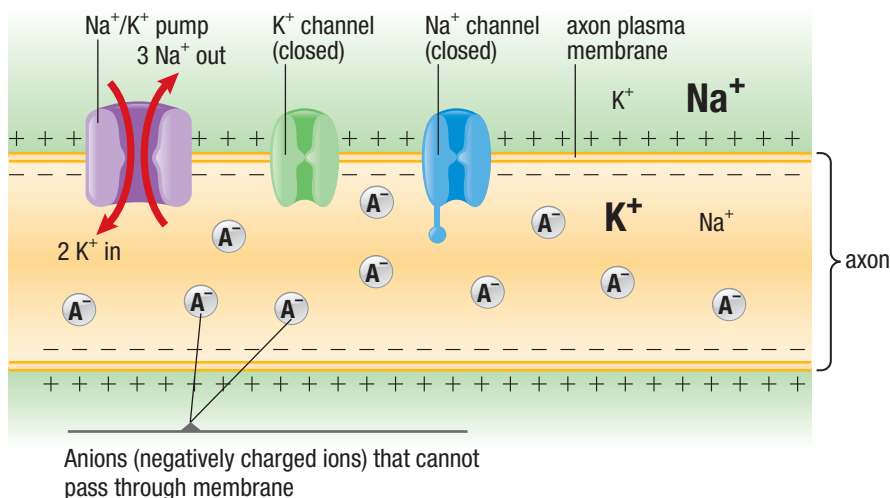


Figure 3 The distribution of ions inside and outside an axon produces the resting potential, -70 mV. Note that the Na⁺ and K⁺ ion channels are closed when the membrane is at the resting potential.

Action Potential

action potential the voltage difference across a nerve cell membrane when the nerve is excited

threshold potential the potential at which an action potential is generated by a neuron

When a neuron conducts an electric impulse, there is an abrupt and temporary change in membrane potential. This is called an **action potential**. An action potential begins as a stimulus that causes positive charges from outside the neuron to flow inward, making the interior side of the membrane less negative.

In phase 1 of an action potential (**Figure 4**), the incoming positive ions raise the membrane potential (which was polarized at rest) to a less negative value. This is called depolarization. If depolarization continues, when the membrane potential reaches a level called the **threshold potential** (about -50 to -55 mV in a typical neuron), Na⁺ channels open. In phase 2 (above threshold), Na⁺ channels continue to open and Na⁺ flows inward along its concentration gradient. The action potential then fires, causing the membrane potential to increase sharply. In less than 1 ms, the action potential rises so high that the inside of the plasma membrane becomes positive because of the influx of positive ions

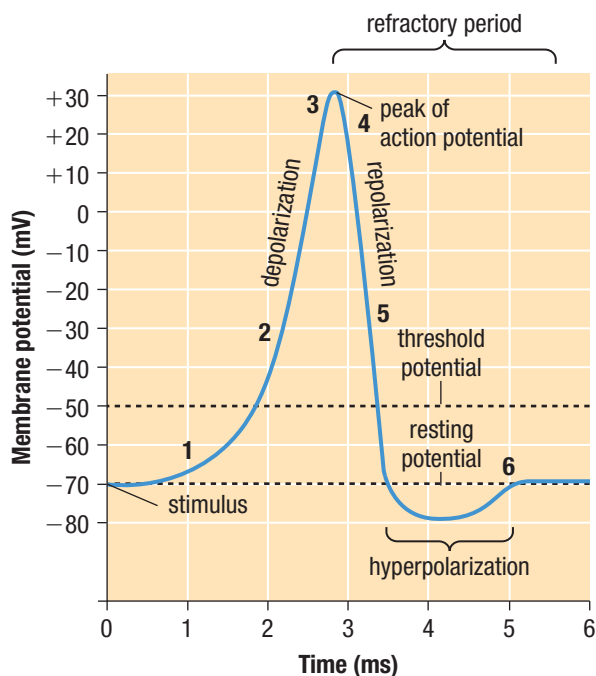


Figure 4 Changes in membrane potential during the six phases of the action potential

across the membrane. In phase 3, the action potential reaches its peak, momentarily reaching a value of +30 mV or more. The interior of the neuron is relatively positive. The Na^+ channels close and become inactive, and the K^+ channels open and allow K^+ to exit (phase 4). The outward flow of K^+ along its concentration gradient causes the membrane potential to fall rapidly during the process of repolarization. In phase 5, the voltage-gated K^+ channels begin to close slowly. The slow closure allows the membrane to undershoot its resting value briefly as it repolarizes. In phase 6, the final phase, the membrane potential stabilizes at the resting value and is ready for a new action potential.

When the potential is below the resting value, the membrane is said to be hyperpolarized. The entire change, from the initiation of the action potential to the return to the resting potential, takes less than 5 ms in the fastest neurons. An action potential takes the same basic form in all neurons. However, different types of neurons exhibit differences in the value of the resting potential and the peak of the action potential, and in the time required to return to the resting potential.

Many stimuli cause some degree of depolarization of a neuron, but an action potential is produced only if the stimulus is strong enough to cause the depolarization to reach the threshold. This is referred to as the all-or-nothing principle. Once triggered, the changes in membrane potential take place independently of the strength of the stimulus.

Once an action potential is initiated at the dendrite end of a neuron, it passes along the surface of a nerve or muscle cell as an automatic wave of depolarization. It travels away from the stimulation point, without requiring further triggering events. This is called propagation of the action potential.

Beginning at the peak of an action potential, the membrane enters a resting period, or **refractory period**, of a few milliseconds. During the refractory period, the threshold that is required for generation of an action potential is much higher than normal. The refractory period lasts until the membrane has stabilized at the resting potential. It keeps impulses travelling in a one-way direction in the neurons. This is because, once ion channels are opened to their activated state, they need time to reset to their original position before they can open again. Therefore, only downstream ion channels are able to open, ensuring the one-way movement of the action potential along the axon toward the axon terminals (**Figure 5**).

refractory period the period of time during which the threshold required for the generation of an action potential is much higher than normal

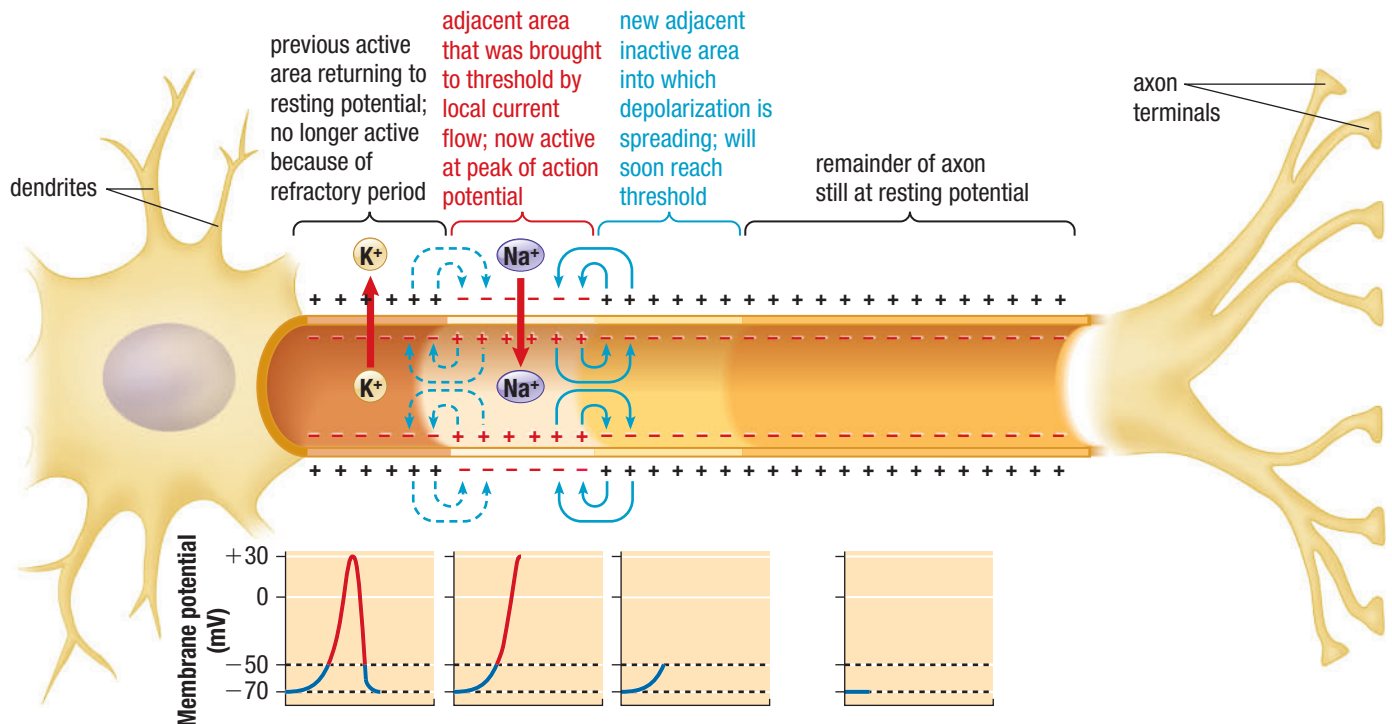


Figure 5 The action potential proceeds along the axon with a domino effect. Each rapid change in potential triggers a change in potential in the adjacent region, causing the action potential to move along the axon in a wave of depolarization.

The magnitude of an action potential stays the same as it travels along an axon, even where the axon branches at its tips. Thus, the propagation of an action potential resembles a fuse that burns with the same intensity along its length and along any branches once it is lit. Unlike a fuse, however, an axon is not spent. It can fire another action potential of the same intensity within a few milliseconds after the first has passed through.

The all-or-nothing characteristic of the action potential means that the intensity of a stimulus is reflected in the frequency of action potentials rather than in their magnitudes. (Within the same neuron, they are all the same magnitude.) The greater the stimulus, the faster the action potentials, up to a rate determined by the physical limitations of the neuron—usually between 10 and 100 per second! The rate of conduction increases with the diameter of the axon. While large axons can conduct impulses as rapidly as 25 m/s, they take up a large amount of space.

Conduction in Myelinated Axons

In jawed vertebrates, a specialized mechanism allows action potentials to hop rapidly along axons instead of burning smoothly like a fuse. Conduction by hopping relies on the gaps in the insulating myelin sheath that surrounds many axons. These gaps, known as nodes of Ranvier, expose the axon membrane to extracellular fluids. Na^+ and K^+ channels, which are crowded into the nodes, allow action potentials to develop at these positions, jumping rapidly from one node to the next. The inward movement of Na^+ ions produces depolarization, but the excess positive ions are unable to leave the axon through the membrane regions covered by the myelin sheath. Instead, they diffuse rapidly to the next node, where they cause depolarization, inducing an action potential at that node. As the mechanism repeats, the action potential jumps rapidly along the axon from node to node. This hopping form of conduction proceeds at rates of up to 130 m/s, which is much faster than the transmission rate of about 1 m/s in an unmyelinated axon of the same diameter.

Conduction by hopping allows thousands to millions of fast-transmitting axons to be packed into a relatively small diameter. For example, the optic nerve in humans, which leads from the eye to the brain, is only 3 mm in diameter but is packed with more than a million axons. If these axons were unmyelinated, each would have to be about 100 times as thick to conduct impulses at the same velocity. This would produce an optic nerve of about 300 mm in diameter!

The disease multiple sclerosis (from *sclero* meaning “hard”) underscores the importance of myelin sheaths in the operation of the vertebrate nervous system. In multiple sclerosis, myelin is attacked by the immune system and is progressively lost from axons and replaced by hardened scar tissue. The changes block or slow the transmission of action potentials, producing numbness, muscular weakness, faulty coordination of movements, and paralysis that worsens as the disease progresses. Although clear genetic factors are involved, research shows that environment may also play a role. For example, the incidence of the disease increases with the distance from the equator. The incidence in Canada, 2.4 people per 1000 population, is one of the highest in the world.

Conduction across Chemical Synapses

The vast majority of vertebrate neurons communicate by means of neurotransmitters. Action potentials are transmitted directly across electrical synapses, but they cannot jump across the synaptic cleft in a chemical synapse. The time required for the release, diffusion, and binding of neurotransmitters across a chemical synapse delays transmission, whereas the transmission of impulses across an electrical synapse is almost instantaneous. However, communication through chemical synapses allows neurons to receive input from hundreds to thousands of axon terminals at the same time.

Neurotransmitters are stored in synaptic vesicles in the cytosol of an axon terminal. Ca^{2+} ions are constantly pumped out of the cell by an active transport protein in the plasma membrane, keeping their concentration higher outside than inside.

As an action potential arrives, the Ca^{2+} channel gates in the axon terminal open, allowing Ca^{2+} to flow back into the cytosol. The rise in the Ca^{2+} concentration triggers a protein in the membrane of the synaptic vesicle. This protein allows the vesicle to fuse with the plasma membrane, releasing neurotransmitter molecules into the synaptic cleft by exocytosis (**Figure 6**).

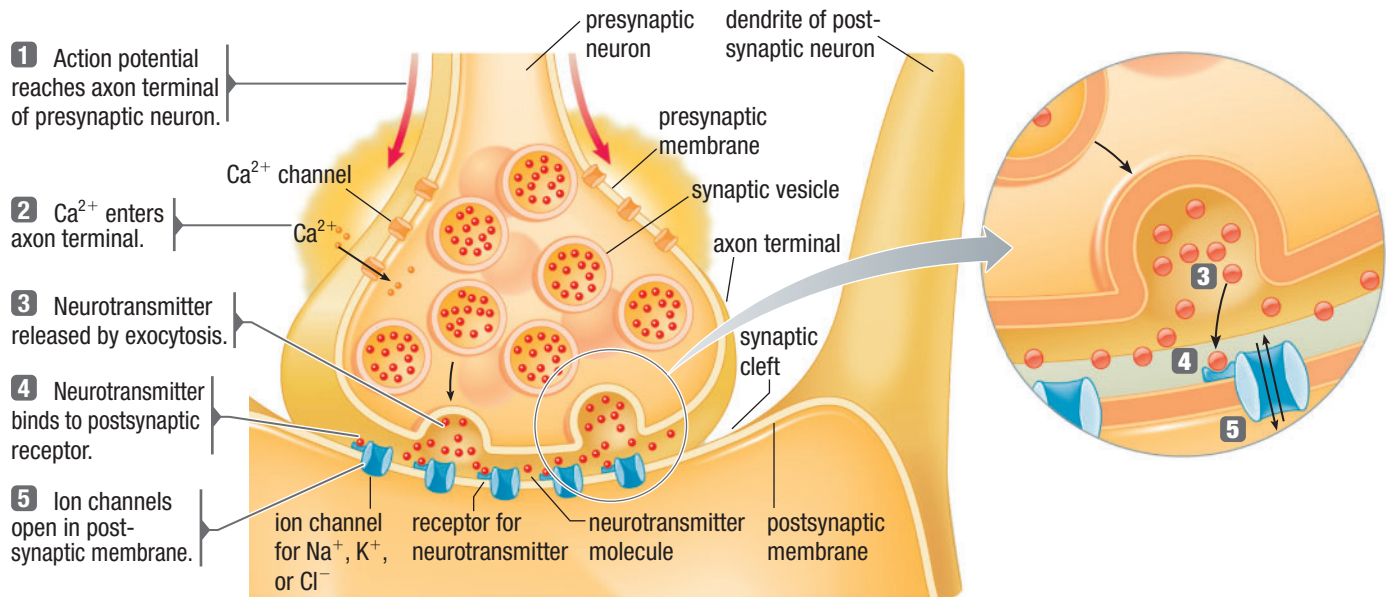


Figure 6 A chemical synapse, facilitated by a neurotransmitter

The neurotransmitter molecules diffuse across the cleft and bind to receptor molecules in the membrane of the postsynaptic cell. The binding of the neurotransmitter opens gated ion channels, allowing ions to flow into the dendrite or cell body of the postsynaptic neuron. Some neurotransmitters have stimulatory effects, whereas others have inhibitory effects. Most neurotransmitters work by opening or closing membrane-embedded ion channels that conduct Na^+ or K^+ across the postsynaptic membrane. Some regulate Cl^- (chloride ions).

If the postsynaptic neuron becomes depolarized to the point of threshold, it will generate a new action potential that travels along its axon to reach a synapse with the next neuron or effector in the circuit. A chemical synapse is more than a simple on/off switch. Many factors can influence the generation of a new electrical impulse in the postsynaptic cell, including neurotransmitters that inhibit that cell rather than stimulate it. The balance of stimulatory and inhibitory effects in chemical synapses contributes to the integration of incoming information in a receiving neuron.

Neurotransmitters

Nearly 100 different substances are known or suspected to be neurotransmitters. Most of them are relatively small molecules that diffuse rapidly across the synaptic cleft. Some axon terminals release only one type of neurotransmitter, whereas others release several types.

One of the best-known neurotransmitters is acetylcholine. In humans, it triggers muscle contraction, stimulates hormone secretion, and is involved in wakefulness, attentiveness, memory, learning, anger, aggression, and sexuality. Acetylcholine-releasing neurons in the brain degenerate in people who develop Alzheimer's disease, causing memory, speech, and perceptual abilities to decline. Acetylcholine is the target of many natural and artificial poisons. Curare, a plant extract that is used as an arrow poison by some Indigenous peoples of South America, blocks muscle contractions and produces paralysis by competing directly with acetylcholine for binding sites in the synapses that control muscle cells. Nicotine (the drug released from smoking tobacco) also binds to acetylcholine receptors, but it acts as a stimulant by turning the receptors on rather than off.

Investigation 11.2.1

Investigating the Nervous System of an Invertebrate (p. 555)

You have learned how nerve cells communicate. In this investigation, you will investigate how an organism senses and responds to its environment.

Other substances can block the operation of these neurotransmitters. For example, tetanus toxin, released by the bacterium *Clostridium tetani*, blocks the neurotransmitter in the synapses that control muscle contractions. The body muscles contract so forcibly that the body arches painfully and the teeth become tightly clenched, giving the condition its common name—lockjaw. Once the effects extend to the respiratory muscles, the victim quickly dies. The disease is entirely preventable, thanks to vaccination with inactivated tetanus toxin.

Neurotransmitters called endorphins are released during pleasurable experiences (such as eating or sexual intercourse) or physical stress (such as childbirth or extended physical exercise). These neurotransmitters have the opiate-like property of reducing pain and inducing euphoria, well known to exercise enthusiasts as a pleasant by-product of their physical efforts (Section 11.4.).

Octopamine is a neurotransmitter involved in insect-feeding activities. It has recently been linked to bee waggle-dance behaviour and is also associated with firefly flashing.

Research This

Neurological Disorders

Skills: Researching, Predicting, Planning, Analyzing, Evaluating, Communicating, Defending a Decision

SKILLS
HANDBOOK  A4.1

When neural signalling is hampered by drugs, injury, or disease, there can be profound implications for the functioning of the human body. In this activity, you will choose one of the following neurological diseases or disorders to research in detail: Parkinson's disease, Alzheimer's disease, Huntington disease, ALS (amyotrophic lateral sclerosis), NF2, Schwannomatosis, brain injury, or concussion.

1. Working with a partner, use the Internet and other sources to research one of the diseases or disorders listed above. Use the following points to guide your research:
 - the causes, symptoms, and treatments
 - the methods of diagnosis
 - recent research and advancements (preferably Canadian) in prevention and/or treatment
 - the impact of the disease/disorder on the individual, the family, the medical system, and society
2. As you do your research, keep detailed notes and record the reference information for each source.
 - A. With your partner, prepare a fictitious interview with an expert on the disease/disorder. The expert should be a person you have learned about through your research. Write five to seven questions you could ask this expert about the disease/disorder, and prepare detailed answers based on your research. **T/I C**
 - B. Prepare and present the interview in the form of a magazine article, a recorded audio interview, a video interview, or another format approved by your teacher. **T/I C**
 - C. Describe how you think the disease/disorder affects the everyday life of an individual who suffers from it. **T/I A**
 - D. Do you think the disease/disorder has implications for the medical system and society? Explain. **A**
 - E. Do you think it is better to focus future research on the prevention, treatment, or cure of the disease/disorder? Use information from your research to justify your opinion. **T/I C**










WEB LINK

11.2 Review

Summary

- Neurons make connections using two types of synapses: electrical and chemical.
- In an electrical synapse, impulses pass directly from the sending cell to the receiving cell by ion flow through gap junctions.
- The unequal distribution of positive and negative charges on either side of a neuron's cell membrane establishes a potential difference called the resting potential. It results from an active transport pump that sets up concentration gradients of Na^+ ions (higher outside) and K^+ ions (higher inside).
- An action potential is generated when a stimulus pushes the resting potential to the threshold value at which Na^+ channels open in the plasma membrane. The inward flow of Na^+ changes the membrane potential abruptly from a negative peak to a positive peak, opening the K^+ channels.
- Action potentials move along an axon as the ion flows generated in one location on the axon depolarize the potential in an adjacent location. Action potentials are prevented from reversing direction by a brief refractory period.
- In chemical synapses, neurotransmitters released from the presynaptic cell bind to the postsynaptic cell. This alters the flow of ions across the cell membrane and pushes the membrane potential toward or away from the threshold.

Questions

1. Why does neural signalling proceed in only one direction? 
2. Explain the movement of ions in a neuron that has each membrane potential. 
 - (a) -70 mV
 - (b) -51 mV
 - (c) -49 mV
 - (d) 0 mV
 - (e) $+30 \text{ mV}$
3. In multiple sclerosis, myelin is progressively lost from axons and replaced by hardened scar tissue. Given what you have learned about the function of myelin, explain how the degradation of myelin might affect the transmission of nerve impulses. 
4. Use the Internet and other sources to learn about active Canadian research on multiple sclerosis or another nervous system disorder that interests you. Explain your findings in a one-page summary.   
5.
 - (a) If an axon were severed, would the reception of a nerve impulse or the transmission of a nerve impulse be affected? Explain.
 - (b) How could you use this information to design a technology that could help a patient who has had nerves severed?
 - (c) What features would you have to include in your design to accommodate both the afferent and efferent signals? 



WEB LINK