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MODULE 11.1 OVERVIEW OF THE NERVOUS SYSTEM

OVERVIEW OF THE NERVOUS SYSTEM

- **Nervous system** – controls our *perception* and *experience* of world
  - Directs *voluntary movement*
  - Seat of *consciousness, personality, learning*, and *memory*
  - Regulates many aspects of *homeostasis* along with endocrine system, including:
    - respiratory rate
    - blood pressure
    - body temperature
    - sleep/wake cycle
    - blood pH

ANATOMICAL DIVISIONS OF THE NERVOUS SYSTEM

- Divided anatomically into **central nervous system** (**CNS**) and **peripheral nervous system** (**PNS**) (**Figure 11.1**):
  - **CNS** – includes **brain** and **spinal cord**
    - **Brain** – made up of billions of nerve cells or **neurons**; protected by bones of skull
    - **Spinal cord** begins at foramen magnum and continues through vertebral foramina of first cervical to first or second lumbar vertebra
      - Made up of millions of neurons; much fewer than brain
      - Enables brain to *communicate* with most of body below head and neck

ANATOMICAL DIVISIONS OF THE NERVOUS SYSTEM

- **PNS** – consists of all **nerves** in body outside protection of skull and vertebral column
  - **Nerves** consist of **axons** of neurons bundled together with *blood vessels* and *connective tissue*; carry signals to and from CNS; classified based on *origin* or *destination*
    - 12 pairs of nerves traveling back to or from *brain*; called **cranial nerves**
    - 31 pairs of nerves traveling back to or from *spinal cord*; called **spinal nerves**

ANATOMICAL DIVISIONS OF THE NERVOUS SYSTEM

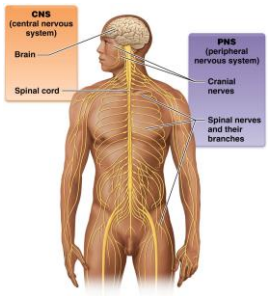


Figure 11.1 Structure of the nervous system.

Functional Divisions of the Nervous System

- Nervous system performs millions of tasks *simultaneously* every *second*; fall into three *functional categories*: sensory, integrative, or motor:
  - **Sensory functions** – gather information about internal and external environments of body; input is gathered by **sensory or afferent division** of PNS**;** further divided into **somatic** and **visceral** divisions; Sensory input from both divisions is carried from sensory receptors to spinal cord and/or brain by spinal and cranial nerves
    - **Somatic sensory division** – consists of neurons that carry signals from skeletal muscles, bones, joints, and skin; also transmits signals from organs of vision, hearing, taste, smell, and balance; sometimes called **special sensory division**
    - **Visceral sensory division** – consists of neurons that transmit signals from **viscera** (organs) such as heart, lungs, stomach, kidneys, and urinary bladder

Functional Divisions of the Nervous System

- **Integrative functions** – *analyze* and *interpret* incoming sensory information and determine an *appropriate response*
  - 99% of integrated sensory information is *subconsciously disregarded* as unimportant
  - Remaining sensory stimuli that CNS does respond to generally leads to a *motor response*

Functional Divisions of the Nervous System

- **Motor functions** – actions performed in response to integration; performed by **motor** or **efferent division** of PNS; can be further subdivided into **somatic** and **autonomic** divisions, based on *organs* that neurons contact
  - **Motor/efferent division –** consists of **motor neurons** that carry out *motor functions*; travel from brain and spinal cord via cranial and spinal nerves; organs that *carry out effects* of nervous system are commonly called **effectors** (Subdivisions are on next slide…)

Functional Divisions of the Nervous System

- **Motor division** (continued):
  - **Somatic motor division** consists of neurons that transmit signals to *skeletal muscle*; under *voluntary* control (aka **voluntary motor division**)
  - **Autonomic nervous system** (**ANS**) or **visceral motor division**
    - » Consists of neurons that carry signals to *thoracic* and *abdominal viscera*; critical for maintaining homeostasis of body's internal environment
    - » Regulates secretion of certain *glands*, contraction of *smooth muscle*, and contraction of *cardiac muscle* in heart; *involuntary* (aka **involuntary motor division**)

Functional Divisions of the Nervous System

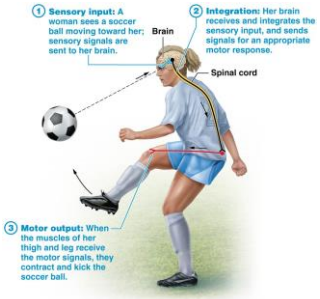


Figure 11.2 Functions of the nervous system.

Functional Divisions of the Nervous System

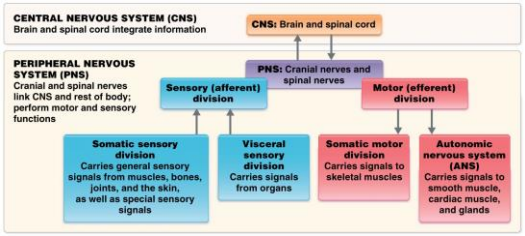


Figure 11.3 Summary of the structural and functional divisions of the nervous system

MODULE 11.2 NERVOUS TISSUE

NEURONS

Neurons – *excitable* cell type responsible for sending and receiving signals in form of **action potentials**; most consist of three parts (**Figures 11.4, 11.5**):

- **Cell body** (**soma**) – most *metabolically active* region of neuron; manufactures all proteins needed for whole neuron; the following organelles support this high level of biosynthetic activity
  - Both free ribosomes and rough endoplasmic reticulum for *protein synthesis*; **Nissl bodies** are RER that can be seen with microscope
  - Golgi apparatus (*vesicular transport*) and large or multiple nucleoli (*ribosomal RNA*)
  - Mitochondria supply *energy* required for high metabolic activity

NEURONS

- **Cytoskeleton** – contains microtubules; provide *structural support* and a means for *chemical transportation* between cell body and axon
- **Neurofibrils** – composed of intermediate filaments of cytoskeleton; provide *structural support* that extends into neuron processes
- **Processes** – cytoplasmic extensions that originate at cell body and include dendrites and axons; allow neurons to *communicate* with other cells

- **Dendrites** – short, branched processes; *receive input* from other neurons, which they transmit to toward cell body in form of electrical impulses; each neuron may have multiple dendrites

NEURONS

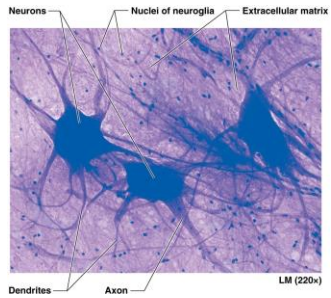


Figure 11.4 Nervous tissue.

NEURONS

- Each neuron has only one **axon** or **nerve fiber** that can *generate* and *conduct* action potentials; axon may have following distinct regions
  - **Axon hillock** – region where axon *originates* from cell body
  - **Axon collaterals** – *branches* that extend from main axon
  - **Telodendria** – *small branches* that arise from axon and axon collaterals near where these extensions end
  - **Axon terminals** or **synaptic bulbs** – arise from telodendria; components that *communicate* with a target cell

NEURONS

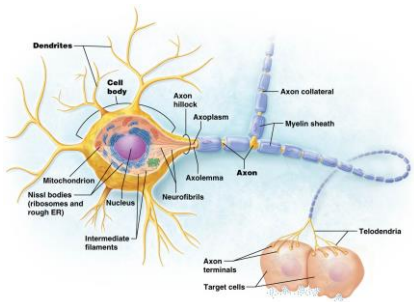


Figure 11.5 Neuron structure.

NEURONS

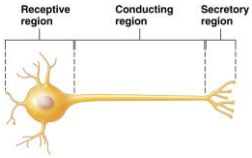
- **Axolemma** – plasma membrane that surrounds axon and its cytoplasm or **axoplasm**
- Substances may *travel through axoplasm* using one of two types of transport, which are together termed **axonal transport** or **flow**
  - **Slow axonal transport –** transports substances like cytoskeleton proteins from cell body through axon at a rate of 1–3 mm/day
  - **Fast axonal transport –** requires *motor proteins* and *consumes ATP;* vesicles and membrane-bound organelles travel more quickly back toward (**retrograde transport**) or away from (**anterograde transport**) cell body at a maximum rate of 200 mm/day and 400 mm/day respectively

POLIOVIRUS AND RETROGRADE AXONAL TRANSPORT

- **Poliomyelitis** – caused by *poliovirus*; infection that impacts CNS and especially spinal cord; can result in *deformity* and *paralysis*
- No cure exists, but polio can be easily prevented by *vaccination*
- Virus accesses CNS by first entering muscle cells; then passes into motor neurons at neuromuscular junction; travels length of axon by **retrograde axonal transport** until reaching spinal cord
- Other viruses (**herpes simplex, rabies**) and toxins (**tetanus**) also have ability to invade via this method

NEURONS

- Neurons have three main *functional regions*:
  - **Receptive region –** includes *dendrites* and *cell body*
  - **Conducting region** – includes *axon*
  - **Secretory region –** includes *axon terminal*



NEURONS

- Neurons can be classified according to *structural features* into 3 groups (**Table 11.1**):
  - **Multipolar neurons** – with a single *axon* and multiple *dendrites,* make up over 99% of all neurons
  - **Bipolar neurons –** with *one* axon and one dendrite and a cell body between them; found in eye and olfactory epithelium in nasal cavity
  - **Pseudounipolar neurons –** have only one *fused axon* that extends from cell body and *divides into two processes*: one process carries sensory information from sensory receptors to cell body; other process carries sensory information from cell body to spinal cord; sensory neurons that carry information related to *pain, touch, and pressure*

NEURONS

- Neurons can also be classified into three *functional groups* (**Table 11.1**):
  - **Sensory** or **afferent neurons** – carry information toward CNS; neuron cell bodies in PNS receive information from sensory receptors and relay information via axons to brain or spinal cord; usually *pseudounipolar* or *bipolar*
  - **Interneurons** or **association neurons** – relay information within CNS between sensory and motor neurons; make up most of neurons in body; *multipolar*, communicating with many other neurons
  - **Motor** or **efferent neurons** – carry information away from cell body in CNS to *muscles* and glands; mostly *multipolar*

NEURONS

TABLE 11.1 NEURON CLASSIFICATION

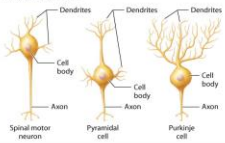
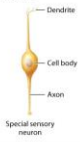
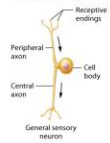
Structural Class	Multipolar Neurons	Bipolar Neurons	Pseudounipolar Neurons
Structural Features	One axon with two or more dendrites; typically have highly branched dendritic tree	One axon and one dendrite	Single short process that splits into two axons (no dendrites)
			
	Spinal motor neuron; Pyramidal cell; Purkinje cell	Special sensory neuron	General sensory neuron
Typical Functional Class	Motor (efferent) neurons, interneurons	Sensory (afferent) neurons	Sensory (afferent) neurons
Location	Most neurons in the CNS; motor neurons in the PNS	Special sense organs in the PNS, such as the retina and olfactory epithelium	Sensory neurons in the PNS associated with touch, pain, and vibration sensations

Table 11.1 Neuron Classification.

NEURONS

- Specific neuron components group together:
  - **CNS**:
    - **Nuclei** – clusters of neuron cell bodies
    - **Tracts** – bundles of axons
  - **PNS**:
    - **Ganglia –** clusters of neuron cell bodies
    - **Nerves –** bundles of axons

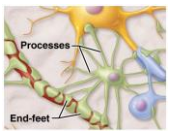
NEUROGLIA

- **Neuroglia** or **neuroglial cells** not only provide *structural support* and protection for neurons but also maintain their *environment* (**Figures 11.6, 11.7**)
  - Able to *divide* and *fill in space* left behind when a neuron dies; form of each type of neuroglial cell is *specialized for its function*, another example of the **Structure-Function Core Principle**

NEUROGLIA

- **Neuroglia** or **neuroglial cells** (continued)
  - 4 types reside in CNS:
    - **Astrocytes**
    - **Oligodendrocytes**
    - **Microglia**
    - **Ependymal cells**
  - 2 types reside in PNS:
    - **Schwann cells**
    - **Satellite cells**

NEUROGLIA



- **Neuroglia** or **neuroglial cells**
  - **Astrocytes** – large *star-shaped* cells whose many processes terminate in structures called **end-feet**; function to:
    - *Anchor* neurons and blood vessels in place; help define and maintain *three-dimensional structure* of brain
    - Facilitate *transport* of nutrients and gases between blood vessels and neurons; regulate *extracellular environment* of brain
    - Assist in formation of **blood-brain barrier**; protective structure that surrounds capillary endothelial cells and makes them *impenetrable* to most polar compounds and proteins
    - *Repair* damaged brain tissue by rapid cell division

Figure 11.6 Neuroglial cells of the CNS.

NEUROGLIA

- **Neuroglia** or **neuroglial cells** (continued)
  - **Oligodendrocytes** – also found in CNS; have radiating processes with *flattened sacs* that wrap around axons of nearby neurons to form **myelin**

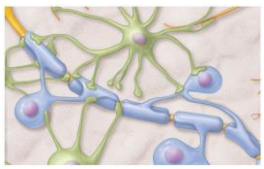


Figure 11.6 Neuroglial cells of the CNS.

NEUROGLIA

- **Neuroglia** or **neuroglial cells** (continued)
  - **Microglia –** small and scarce cells; *activated by injury* into wandering *phagocytic cells* within CNS; ingest disease-causing microorganisms, dead neurons, and cellular debris

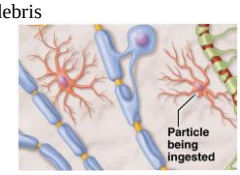


Figure 11.6 Neuroglial cells of the CNS.

NEUROGLIA

- **Neuroglia** or **neuroglial cells** (continued)
  - **Ependymal cells –** *ciliated cells* that line hollow spaces found within CNS (brain and spinal cord); function to *manufacture* and *circulate* **cerebrospinal fluid**

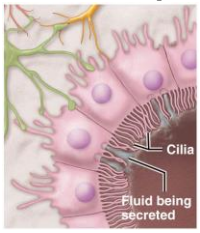
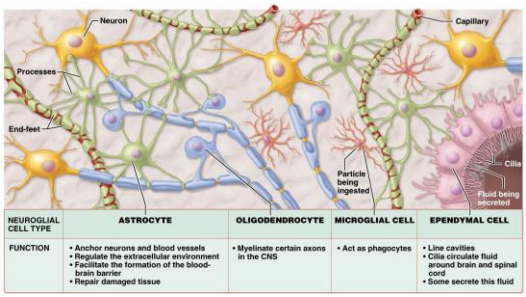


Figure 11.6 Neuroglial cells of the CNS.

NEUROGLIA



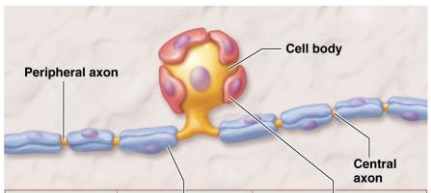
NEUROGLIAL CELL TYPE	ASTROCYTE	OLIGODENDROCYTE	MICROGLIAL CELL	EPENDYMAL CELL
FUNCTION	• Anchor neurons and blood vessels • Regulate the extracellular environment • Facilitate the formation of the blood-brain barrier • Repair damaged tissue	• Myelinate certain axons in the CNS	• Act as phagocytes	• Line cavities • Cilia circulate fluid around brain and spinal cord • Some secrete this fluid

Figure 11.6 Neuroglial cells of the CNS.

NEUROGLIA

- **Neuroglia** or **neuroglial cells** (continued)
  - **Schwann cells** – encircle axons found in PNS to provide them with **myelination** (**Figure 11.7**)
  - **Satellite cells** – found *surrounding cell bodies* of neurons in PNS to provide *supportive functions* (still not well defined)

NEUROGLIA



NEUROGLIAL CELL TYPE	SCHWANN CELL	SATELLITE CELL
FUNCTION	• Myelinate certain axons in the PNS	• Surround and support cell bodies

Figure 11.7 Neuroglial cells of the PNS.

THE MYELIN SHEATH

Myelin Sheath – composed of repeating layers of **plasma membrane** of Schwann cell or oligodendrocyte in PNS and CNS respectively (**Figures 11.8, 11.9**):

- **Myelination** – process that forms myelin sheath from plasma membranes of neuroglial cells; wrap themselves around axon forming multiple layers of membrane (myelin)
  - Electric current – generated by movement of ions in body fluids
  - Lipid content of myelin sheath **insulates** axon (prevents ion movements) like rubber around copper wire; increases speed of action potential conduction
  - Myelinated axons conduct action potentials about 15–20 times faster than unmyelinated axons

THE MYELIN SHEATH

- Following differences are noted between myelination in PNS (Schwann cells) and the CNS (oligodendrocytes):
  - **Neurolemma** – found on outer surface of a myelinated axon in PNS; composed of *Schwann cell nucleus, organelles, and cytoplasm*; not present in CNS (**Figure 11.8a, b**)
  - **Number of axons myelinated** – oligodendrocytes have *multiple processes* that can provide myelination for multiple axons in CNS while a Schwann cell only provides myelination for one axon in PNS
  - **Timing of myelination** – myelination begins early in fetal development in PNS and much later in the CNS; very little myelin present in brain of newborn

THE MYELIN SHEATH

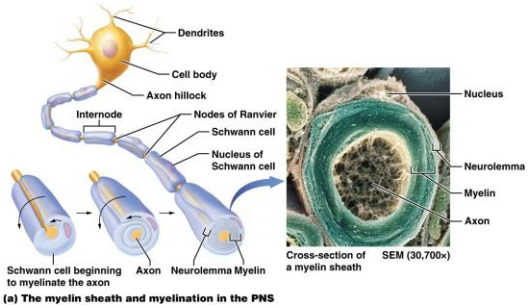


Figure 11.8a The myelin sheath in the PNS and CNS.

THE MYELIN SHEATH

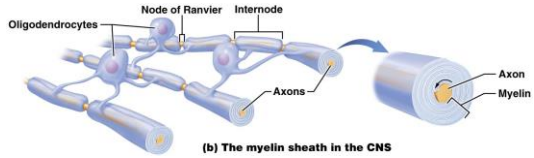


Figure 11.8b The myelin sheath in the PNS and CNS.

THE MYELIN SHEATH

- Axons in both CNS and PNS are generally longer than neuroglial cells so multiple cells must provide a *complete myelin sheath*
  - **Internodes** – segments of axon that are *covered by neuroglia*
  - **Node of Ranvier** – gap between adjacent neuroglia**;** where myelin sheath is absent

THE MYELIN SHEATH

- *Small axons* in CNS and PNS are usually *unmyelinated*
- **White matter** – composed of *myelinated axons* that appear white
- **Gray matter** – composed of *neuron cell bodies*, *unmyelinated dendrites* and *axons* that appear gray

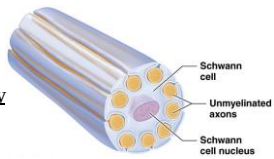


Figure 11.9 Unmyelinated peripheral axons and Schwann cells.

REGENERATION OF NERVOUS TISSUE

- **Regeneration** or replacement of damaged tissue is nearly *nonexistent* in CNS and is limited in PNS; neural tissue can regenerate only if *cell body remains intact*

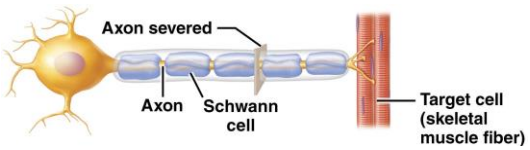


Figure 11.10 Repair of axon damage in the PNS.

REGENERATION OF NERVOUS TISSUE

- **Regeneration** steps (**Figure 11.10**):
  - Axon and myelin sheath *degenerate* distal to injury, a process facilitated by phagocytes; called **Wallerian degeneration**
  - **Growth processes** form from proximal end of axon
  - Schwann cells and basal lamina form a **regeneration tube**
  - Single growth process grows into regeneration tube; *directs new axon* toward its target cell
  - New axon is *reconnected* to its target cell

Regeneration of Nervous Tissue

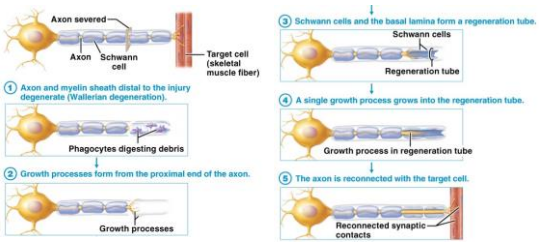
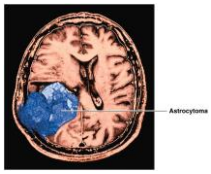


Figure 11.10 Repair of axon damage in the PNS.

Gliomas and Astrocytomas



- **Primary brain tumors** – originate in brain; most are **gliomas** (caused by abnormally high rate of division of glial cells)
- **Predisposing conditions** – exposure to ionizing *radiation* and certain diseases
- Most commonly affected cell is **astrocyte**; resulting tumor is called **astrocytoma**
  - Range in severity from mild with good prognosis to highly aggressive with a very poor prognosis
  - **Treatment** – varies with tumor type, age, and health of patient; generally involves *surgical removal* of mass with *chemotherapy* and perhaps *radiation* therapy

Module 11.3
Electrophysiology of Neurons

Introduction to Electrophysiology of Neurons

- All neurons are *excitable* or responsive in presence of various *stimuli*: chemical signals, local electrical signals, and mechanical deformation
- Stimuli generate *electrical changes* across neuron plasma membrane; rapidly *conducted* (**conductivity**) along entire length of membrane
- Two forms of electrical changes occur in neurons:
  - **Local potentials** – travel short distances
  - **Action potentials** – travel entire length of axon

Principles of Electrophysiology

Electrical changes across neuron plasma membranes rely on *ion channels* and a *resting membrane potential:*

- **Ion channels** – ions cannot diffuse through lipid component of plasma membrane; must rely on *specific protein channels*:
  - **Leak channels** – always open; continuously allow ions to flow down concentration gradients between cytosol and ECF
  - **Gated channels** – closed at rest and open in response to *specific stimulus*

Principles of Electrophysiology

- **Ion channels** (continued):
  - **Ligand-gated channels** – open in response to binding of *specific chemical or* **ligand** to a specific receptor
  - **Voltage-gated channels** – open in response to changes in *voltage* across membrane
  - **Mechanically-gated channels** – open or close in response to *mechanical stimulation* (pressure, stretch, or vibration)

PRINCIPLES OF ELECTROPHYSIOLOGY

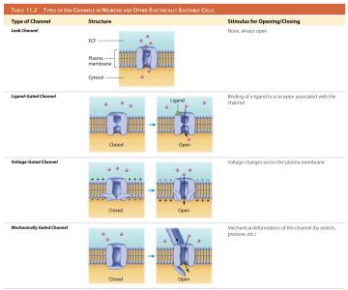


Table 11.2 Types of ion channels in neurons and other electrically excitable cells.

PRINCIPLES OF ELECTROPHYSIOLOGY

- **Resting membrane potential** – voltage present when a cell is at *rest* **(Figure 11.11)**
  - **Voltage** – *electrical gradient* established by separation of charges between two locations, in this case across plasma membrane
  - **Membrane potential** – electrical potential across cell membrane; source of *potential energy* for cell
  - Cell is **polarized** when *voltage difference* across plasma membrane does not equal 0 mV; typical neuron has a *resting membrane potential* of **–70 mV**

PRINCIPLES OF ELECTROPHYSIOLOGY

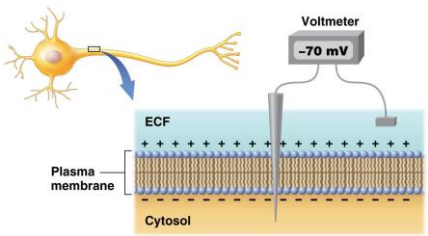


Figure 11.11 Measurement of the voltage across a plasma membrane.

PRINCIPLES OF ELECTROPHYSIOLOGY

- Generation of resting membrane potential (**Figure 11.12**) relies on:
  - *Ion concentration gradients* favor diffusion of potassium ions out of cell and sodium ions into cell; potassium ions diffuse through leak channels more *easily* than sodium ions
  - Cytosol *loses* more *positive charges* than it *gains*; membrane potential becomes more *negative* until it reaches resting membrane potential

PRINCIPLES OF ELECTROPHYSIOLOGY

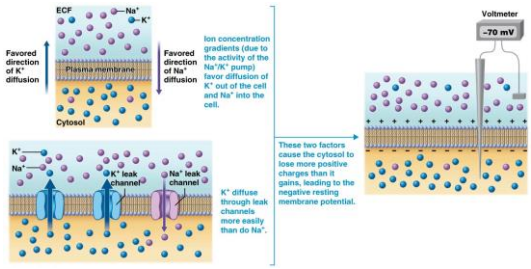


Figure 11.12 Generation of the resting membrane potential.

PRINCIPLES OF ELECTROPHYSIOLOGY

- Diffusion of an ion across plasma membrane is determined by both its *concentration* and *electrical gradients* collectively called **electrochemical gradient**; an example of **Gradients Core Principle**

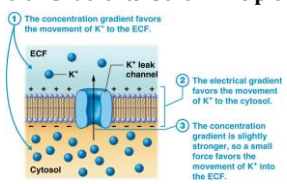
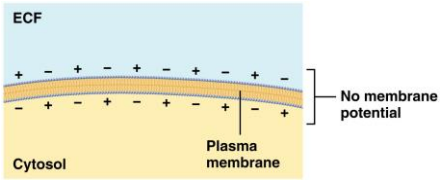


Figure 11.13 The electrochemical gradient for potassium ions.

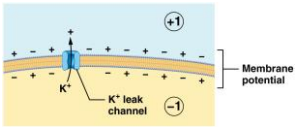
How Do Positive Ions Create a Negative Resting Membrane Potential

- Let's start with a neuron that has *no membrane potential*; charges are distributed equally across plasma membrane



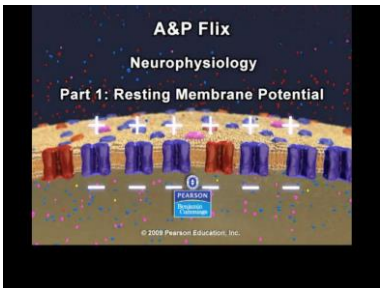
- Now, imagine that a potassium ion *diffuses out of cytosol* down concentration gradient through a leak channel…

How Do Positive Ions Create a Negative Resting Membrane Potential



- Six positive charges are now outside membrane and four positive charges inside; makes overall charge inside **cytosol –1** and in **extracellular fluid +1**—a *membrane potential* has been created
- Imagine that *many thousands* of potassium ions exit through leak channels; causes membrane potential to become progressively *more negative*

A&P Flix: Resting Membrane Potential



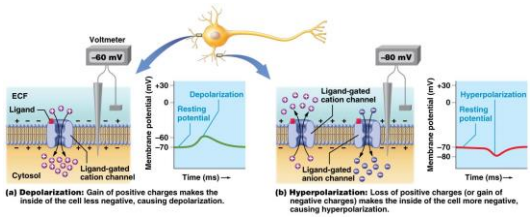
Principles of Electrophysiology

- **Changes in Resting Membrane Potential: Ion Movements** (**Figure 11.14**):
  - Resting membrane potential
    - Generated by unequal *distribution* of ions and their differing abilities for *crossing plasma membrane*
    - Opening a gated channel in plasma membrane alters membrane potential as it changes ability of ions to *move across plasma membrane*

Principles of Electrophysiology

- **Changes in Resting Membrane Potential: Ion Movements** (continued):
  - **Depolarization** – sodium channels open, allowing positively charged sodium ions to flow into cell; membrane potential becomes more *positive* (**Figure 11.14a**)
  - **Repolarization** – potassium ion channels open; allows positively charged potassium ions to flow out of cell; cell becomes *more negative*, returning to resting membrane potential
  - **Hyperpolarization** – cell becomes *more negative* than its normal resting membrane potential due to loss of potassium ions (cations) plus loss of anions such as chloride (**Figure 11.14b**)

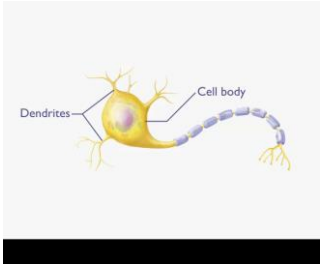
Principles of Electrophysiology



The changes shown here are **local potentials**.

Figure 11.14 Ion movements leading to changes in membrane potential.

BIG PICTURE ANIMATION: LOCAL POTENTIALS



REVIEW

Which of the following is NOT related to the opening of sodium ion channels?

a. Sodium rushes into the neuron
b. Cell becomes less polarized
c. Cell depolarizes
d. Interior of cell becomes more negative

REVIEW

Which of the following is NOT related to the opening of sodium ion channels?

a. Sodium rushes into the neuron
b. Cell becomes less polarized
c. Cell depolarizes
d. Interior of cell becomes more negative

REVIEW

Which of the following is NOT related to the opening of potassium ion channels?

a. Potassium rushes into the neuron
b. Cell becomes more polarized
c. Cell repolarizes
d. Interior of cell becomes more negative

REVIEW

Which of the following is NOT related to the opening of potassium ion channels?

a. Potassium rushes into the neuron
b. Cell becomes more polarized
c. Cell repolarizes
d. Interior of cell becomes more negative

REVIEW

Which of the following is TRUE regarding membrane hyperpolarization?

a. Potassium rushes into the neuron
b. Cell becomes less polarized than at rest
c. May result from chloride ion influx
d. Interior of cell becomes more positive

REVIEW

Which of the following is TRUE regarding membrane hyperpolarization?

a. Potassium rushes into the neuron

b. Cell becomes less polarized than at rest

c. May result from chloride ion influx

d. Interior of cell becomes more positive

LOCAL POTENTIALS

Local potentials – *small local changes* in potential of a neuron's plasma membrane; serve as vital triggers for *long-distance* action potentials

- May cause one of two effects (as in **Figure 11.14**):
  - **Depolarization** – *positive charges* enter cytosol and make membrane potential less *negative* (a change from –70 to –60 mV)
  - **Hyperpolarization** – either *positive charges* exit or *negative charges* enter cytosol; makes membrane potential more *negative* (a change from –70 to –80 mV)
- Sometimes called **graded potentials** because *vary greatly in size*

ACTION POTENTIALS

- **Action potential** – uniform, rapid depolarization and repolarization of membrane potential; only generated in *trigger zones* (include axolemma, axon hillock, and initial segment of axon) (**Figures 11.15, 11.16**)
- **States of voltage** – gated channels allow ions to move and change membrane potential of neuron; movement of potassium ions are responsible for *repolarization*:
  - *Voltage-gated potassium channels* have two possible states: resting (closed) and activated (open) (**Figure 11.15a**)
    - **Resting state** – channels are *closed*; no potassium ions are able to cross plasma membrane
    - **Activated state** – channels are *open*; potassium ions are able to flow down concentration gradients

ACTION POTENTIALS

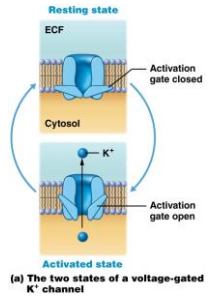


Figure 11.15a States of voltage-gated channels.

ACTION POTENTIALS

- Voltage-gated sodium channels have two gates, an **activation gate** and an **inactivation gate**, with three states (**Figure 15.15b**):
  - **Resting state** – **inactivation gate** is open and **activation** is closed; no sodium ions are able to move
  - **Activated state** – both activation and inactivation gates are open when an action potential is initiated; *voltage change* opens activation gate
  - **Inactivated state** – **inactivation gate** is closed and **activation** gate is open; channel no longer allows sodium ions to move through; once action potential is over, channel *returns to resting state*

ACTION POTENTIALS

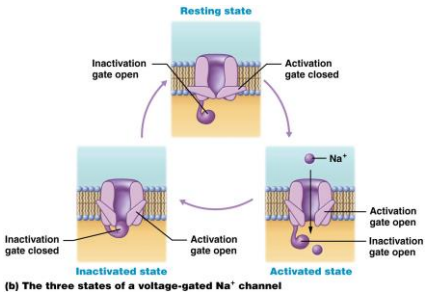


Figure 11.15b States of voltage-gated channels.

Action Potentials

- Neuronal action potential has three *general phases* and lasts only a few milliseconds:
  - **Depolarization phase** – membrane potential rises toward zero and then becomes *positive* briefly
  - **Repolarization phase** – membrane potential returns to a *negative* value
  - **Hyperpolarization phase** – membrane potential temporarily becomes more *negative* than resting membrane potential

Action Potentials

- Action potential proceeds through three phases because of opening and closing of specific ion channels; can be broken down into following steps (**Figure 11.16**):
  1. *Local potential* must be able to *depolarize axon* strongly enough to reach a level called **threshold** (usually –55 mV)
  2. Once threshold reached, voltage-gated sodium channels *activate* and sodium ions flow into axon causing **depolarization**
     - **Positive Feedback loop**—initial input (activation of sodium ion channels and depolarization) amplifies output (more sodium ion channels are activated and axolemma depolarizes further)
     - Example of **Feedback Loops Core Principle**

Action Potentials

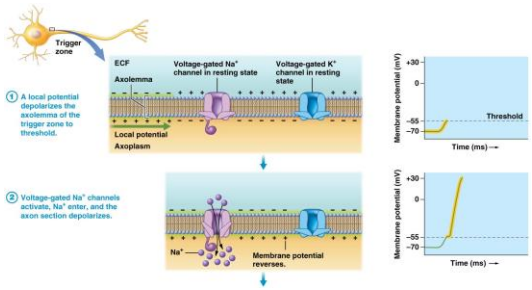


Figure 11.16 Events of an action potential.

Action Potentials

- Action potential steps (continued):
  3. Sodium ion channels *inactivate* and voltage-gated potassium ion channels *activate*: sodium ions stop flowing into axon and potassium begins exiting axon as *repolarization* begins
  4. Sodium ion channels return to *resting state* and repolarization continues
  5. Axolemma may *hyperpolarize* before potassium ion channels return to resting state; then axolemma returns to resting membrane potential

Action Potentials

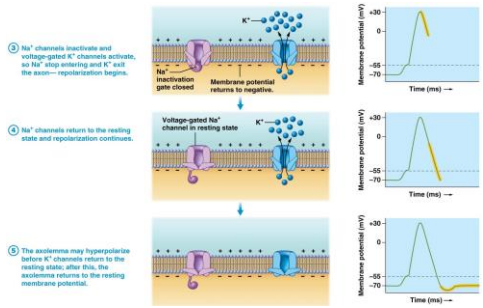
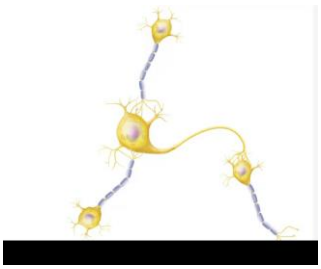


Figure 11.16 Events of an action potential.

Big Picture Animation: Action Potentials



REVIEW

Which of the following is NOT a general phase of the action potential?

a. Repolarization
b. Hypopolarization
c. Depolarization
d. Hyperpolarization

REVIEW

Which of the following is NOT a general phase of the action potential?

a. Repolarization
b. Hypopolarization
c. Depolarization
d. Hyperpolarization

REVIEW

Which of the following is the correct sequence for phases of the action potential?

a. Repolarization, depolarization, hyperpolarization
b. Depolarization, hyperpolarization, repolarization
c. Depolarization, repolarization, hyperpolarization
d. Hyperpolarization, depolarization, repolarization

REVIEW

Which of the following is the correct sequence for phases of the action potential?

a. Repolarization, depolarization, hyperpolarization
b. Depolarization, hyperpolarization, repolarization
c. Depolarization, repolarization, hyperpolarization
d. Hyperpolarization, depolarization, repolarization

REVIEW

An action potential is a good example of which core principle?

a. Gradients
b. Cell to cell communication
c. Structure vs function
d. Feedback loops

REVIEW

An action potential is a good example of which core principle?

a. Gradients
b. Cell to cell communication
c. Structure vs function
d. Feedback loops

REVIEW

The threshold value for neurons is typically

a. –90 mV
b. –70 mV
c. –55 mV
d. +30 mV

REVIEW

The threshold value for neurons is typically

a. –90 mV
b. –70 mV
c. –55 mV
d. +30 mV

REVIEW

The membrane potential at which sodium ion channels CLOSE and potassium channels OPEN during an action potential is

a. –90 mV
b. –70 mV
c. –55 mV
d. +30 mV

REVIEW

The membrane potential at which sodium ion channels CLOSE and potassium channels OPEN during an action potential is

a. –90 mV
b. –70 mV
c. –55 mV
d. +30 mV

LOCAL ANESTHETIC DRUGS

- **Local anesthetics** – (like **lidocaine**) commonly administered agents for *surgical* or *dental* procedures; produce *temporary numbness* in specific area
- Block *voltage-gated sodium channels* of neurons in treated area; prohibits *depolarization* and therefore action potentials relaying pain are not *transmitted to CNS*
- *Nonselective*; also affect sodium channels in muscles of area; causes *temporary paralysis*; reason for crooked smiles and drooling following dental work

REFRACTORY PERIOD

- **Refractory period** – period of time, after neuron has generated an action potential, when neuron cannot *be stimulated* to generate another action potential; can be divided into two phases (**Figure 11.17**):
- **Absolute refractory period** – when *no additional stimulus* (no matter how strong) is able to produce an additional action potential
  - Coincides with voltage-gated sodium channels being *activated* and *inactivated*
  - Sodium channels may not be activated until they *return to their resting states* with activation gates closed and inactivation gates open

Refractory Period

- **Relative refractory period** – follows immediately after absolute refractory period; only a *strong stimulus* can produce an action potential
  - Voltage-gated sodium channels have gone back to resting state and are *able to open again*
  - Potassium channels are activated and membrane is repolarizing or hyperpolarizing; takes a *much larger stimulus* to trigger an action potential

Refractory Period

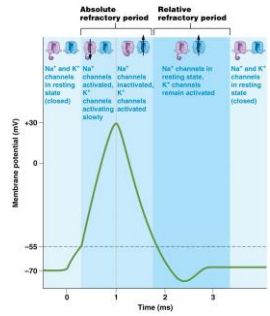


Figure 11.17 Refractory periods of an action potential.

Local and Action Potentials Compared

Graded local potentials produce *variable changes* in membrane potentials while actions potentials cause a *maximum depolarization to +30 mV*

- **All-or-none principle** refers to an event (action potential) that either *happens completely* or does not *occur at all*
  - If a neuron does not depolarize to threshold then *no action potential will occur*
  - Action potentials are not *dependent on strength, frequency, or length of stimulus* like local potentials

Local and Action Potentials Compared

- Local potentials are **reversible**; when stimulus ends neuron returns to resting membrane potential; action potentials are **irreversible**; once threshold is reached it cannot be stopped and will *proceed to completion* (**all-or-none**)
- *Signal distance* is greater for action potentials versus "local" potentials:
  - Local potentials are **decremental** or *decrease in strength* over a short distance
  - Action potentials are **nondecremental**; signal strength does not *decrease* despite traveling long distances

Propagation of Action Potentials

Action potentials must be **conducted** or **propagated** along entire length of axon to serve as a *long-distance signaling service* (**Figures 11.18, 11.19**):

- Action potentials – self-propagating and travel in only *one direction*:
  - Each action potential triggers another in *next section* of axon, usually starting at trigger zone and ending at axon terminals (like *dominoes*)
  - Action potentials travel in *one direction* as sodium ion channels of each successive section of axon go into a *refractory period* as next section depolarizes
  - *Action potential propagation* down an axon is termed a **nerve impulse**

Propagation of Action Potentials

- **Events of Propagation** – action potential is propagated down axon in following sequence of events:

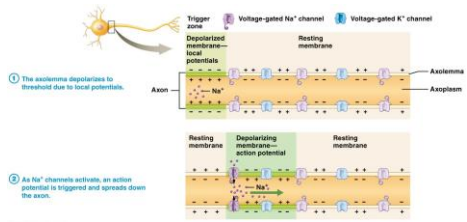


Figure 11.18 Propagation of an action potential.

Propagation of Action Potentials

- **Events of Propagation** (continued):

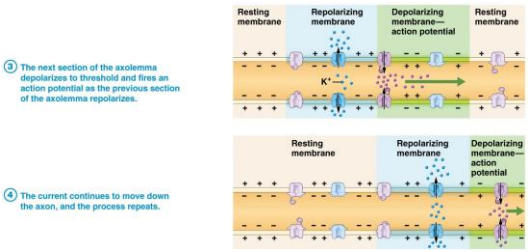
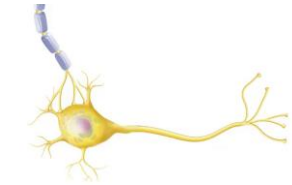


Figure 11.18 Propagation of an action potential.

Big Picture Animation: Propagation of Action Potentials



Review

Action potentials

a. Are short distance signals
b. Spread down dendrites
c. Can be bidirectional
d. Begin at the trigger zone

Review

Action potentials

a. Are short distance signals
b. Spread down dendrites
c. Can be bidirectional
d. Begin at the trigger zone

Review

The threshold potential is best defined as the potential at which

a. Voltage-gated potassium channels open
b. Chemically gated sodium channels open
c. Voltage-gated sodium channels open
d. Voltage-gated potassium channels close

Review

The threshold potential is best defined as the potential at which

a. Voltage-gated potassium channels open
b. Chemically gated sodium channels open
c. Voltage-gated sodium channels open
d. Voltage-gated potassium channels close

REVIEW

Action potentials propagate

a. Down axon from axon terminus to cell body
b. Across multiple synapses between neurons
c. Across entire surface of neuron cell body
d. Down axon from trigger zone to axon terminus

REVIEW

Action potentials propagate

a. Down axon from axon terminus to cell body
b. Across multiple synapses between neurons
c. Across entire surface of neuron cell body
d. Down axon from trigger zone to axon terminus

REVIEW

Action potentials self-propagate because

a. Each action potential triggers another in the next section of axon
b. ATP is always available to drive the action potential
c. Neurotransmitter is released constantly
d. They are a form of negative feedback

REVIEW

Action potentials self-propagate because

a. Each action potential triggers another in the next section of axon
b. ATP is always available to drive the action potential
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REVIEW

The refractory period of an action potential

a. Allows bidirectional flow of the action potential
b. Prevents flow of action potential toward cell body
c. Has no effect on direction of action potential propagation
d. Is not a component of every action potential

REVIEW

The refractory period of an action potential

a. Allows bidirectional flow of the action potential
b. Prevents flow of action potential toward cell body
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d. Is not a component of every action potential

Propagation of Action Potentials

- **Conduction speed** – *rate of propagation*; influenced by both *axon diameter* and presence or absence of *myelination*; conduction speed determines how rapidly signaling can occur within nervous system
  - Axons with larger *diameter* have faster *conduction speeds* because larger axons have a lower *resistance* to conduction (current flows through them *more easily*)
  - Good example of **Structure-Function Core Principle**
  - *Presence* of *absence* of myelination gives rise to two types of conduction: **saltatory** and **continuous conduction** (next)

Propagation of Action Potentials

- **Saltatory conduction** – in **myelinated axons** where insulating properties of myelin sheath increase *efficiency* and *speed* of signal conduction; action potentials only depolarize *nodes of Ranvier* and "jump over" *internodes*

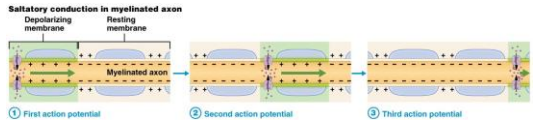


Figure 11.19 Comparison of saltatory and continuous conduction.

Propagation of Action Potentials

- **Continuous conduction** – in **unmyelinated axons** where every section of axolemma from trigger zone to axon terminal must *propagate action potential*; slows conduction speed as each successive section of axon must depolarize

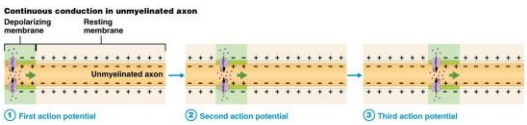


Figure 11.19 Comparison of saltatory and continuous conduction.

Propagation of Action Potentials

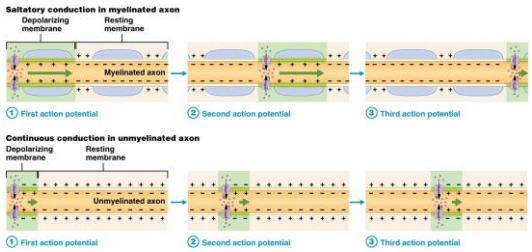
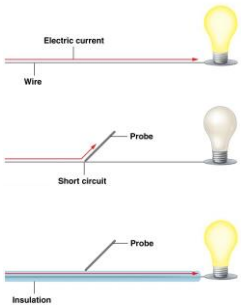


Figure 11.19 Comparison of saltatory and continuous conduction.

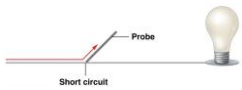
How Does Myelination Insulate an Axon and Increase Its Speed of Propagation?

- Ideally, current flows directly down wire and illuminates light bulb
- Touch wire with a metal probe; most current might instead flow down probe; known as a **short circuit**:
- If wire is encased in material that is a poor conductor of electricity, current is unable to move from copper wire to probe; prevents a short circuit



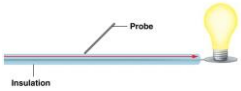
How Does Myelination Insulate an Axon and Increase Its Speed of Propagation?

- **Unmyelinated axon**
  - Most closely resembles wire in *middle illustration*; axolemma is very *leaky* with respect to current, so current flows easily from axoplasm to extracellular fluid, just as current flowed easily from copper wire to metal probe
  - Current *dissipates* over a short distance, which could cause action potential to fail; therefore must constantly be *regenerated* along length of axolemma; requires opening of voltage-gated ion channels, which takes time, so propagation is slow



How Does Myelination Insulate an Axon and Increase Its Speed of Propagation?

- **Myelinated axon**



  - More closely resembles wire in *final illustration* myelin is a very good insulator (poor conductor of electricity); prevents current from *leaking out* through axolemma
  - Signal strength decreases very little as it travels through an internode; does not have to be *regenerated*
  - At unmyelinated node of Ranvier current starts to *dissipate* and action potential must be *regenerated*
  - Action potentials appear to "leap" from node to node *through axoplasm*; much *faster* than continuous conduction

Propagation of Action Potentials

- **Classification of Axons by Conduction Speed**:
  - **Type A fibers –** *fastest* conduction speeds (120 m/sec or 250 mi/h); *largest* diameter (5–20 µm) and *myelinated*; found in sensory and motor axons associated with skeletal muscle and joints
  - **Type B fibers –** *slower* conduction speeds (15 m/sec or 32 mi/hr); mostly *myelinated* with *intermediate* diameter axons (2–3 µm); found in efferent fibers of autonomic nervous system (ANS) and some sensory axons
  - **Type C fibers –** *slowest* conduction speeds (0.5–2 m/sec or 1–5 mi/hr); smallest diameter fibers (0.5–1.5 µm); unmyelinated axons include efferent fibers of the ANS and sensory axons; transmit pain, temperature, and certain pressure sensations

Putting It All Together: The Big Picture of Action Potentials

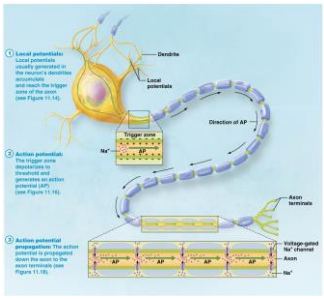


Figure 11.20 The Big Picture of Action Potentials.

Multiple Sclerosis

- **Multiple sclerosis (MS)** – certain cells of immune system *attack myelin sheaths* within CNS; type of **autoimmune disorder** (patient's own immune system attacks part of body)
- Causes *progressive loss of myelin sheath*; in turn causes *loss of current* from neurons
- **Symptoms** – result from *progressive slowing of action potential propagation*; exact symptoms depend on region of CNS affected; most exhibit changes in *sensation* (e.g., numbness), alterations in *behavior* and *cognitive abilities*, and *motor dysfunction*, including *paralysis*

Module 11.4 Neuronal Synapses

Overview of Neuronal Synapses

- Neurons must *communicate with other cells*, including other neurons, in order to carry out their functions—example of **Cell-Cell Communication Core Principle**
- **Synapse** – where a neuron meets its target cell **(**in this case another neuron) called a **neuronal synapse**; can be either *electrical* or *chemical* (**Figure 11.21**):
- Neuronal synapses can occur between an *axon* of one neuron and *another part* of another neuron (next slide)

Overview of Neuronal Synapses

- **Axodendritic synapse** – synapse between *axon* of one neuron and *dendrite* of another neuron
- **Axosomatic synapse** – synapse between *axon* of one neuron and *cell body* of another neuron
- **Axoaxonic synapse** – synapse between *axon* of one neuron and *axon* of another neuron

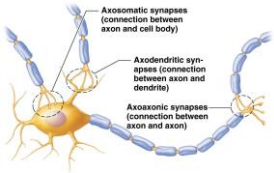


Figure 11.21 Structural types of synapses.

Overview of Neuronal Synapses

- Following terms are used to describe which neuron is *sending* and which is *receiving* message, regardless of type of synapse:
  - **Presynaptic neuron** – neuron *sending* message from its axon terminals
  - **Postsynaptic neuron** – neuron *receiving* message from presynaptic neuron at its cell body, axon, or dendrites

Overview of Neuronal Synapses

- **Synaptic transmission** – transfer of *chemical* or *electrical signals* between neurons at a synapse; *fundamental process* for most functions of nervous system
  - Allows for voluntary movement, cognition, sensation, and emotions to name a few
  - An average presynaptic neuron forms synapses with about 1000 postsynaptic neurons
  - A postsynaptic neuron can have as many as 10,000 synaptic connections with different presynaptic neurons

Electrical Synapses

- An **electrical synapse** occurs between cells that are *electrically coupled* via **gap junctions** (**Figure 11.22a**):
  - Axolemmas of each cell in synapse are nearly *touching*; gap junctions align channels that form *pores* that ions or other small substances can *flow through*
  - Found in areas of *brain* responsible for *programmed, automatic behaviors* such as breathing
  - Outside brain, found in *cardiac* and *visceral smooth muscle* to allow for *coordinated* muscle activity

Electrical Synapses

- Electrical current can flow directly from *axoplasm of one neuron to next*; creates two *unique features* of electrical synapses:
  - **Transmission is bidirectional** – either neuron can be *pre or postsynaptic* depending on which direction current is flowing between them
  - **Transmission is nearly instantaneous** – only delay is time it takes presynaptic neuron to depolarize (less than 0.1 milliseconds); much *faster* than chemical synapses (1 or more milliseconds)

Electrical Synapses

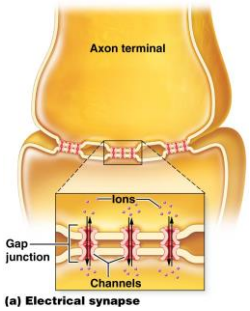


Figure 11.22a The structures of electrical and chemical synapses.

CHEMICAL SYNAPSES

- **Chemical Synapses** (**Figures 11.22, 11.23, 11.24, 11.25**):
  - Make up majority of synapses in nervous system
  - More *efficient* than electrical synapses because they convert electrical signals into chemical signals so *no signal strength is lost* (as is case at electrical synapses)

CHEMICAL SYNAPSES

- **Electrical and Chemical Synapses Compared** – three *structural differences* between chemical and electrical synapses are noteworthy (**Figure 11.22b**):
  - **Synaptic vesicles** filled with *chemical messengers* (**neurotransmitters**) that transmit signals from presynaptic to postsynaptic neurons are found at chemical synapses
  - **Synaptic cleft** – small *ECF-filled space*; separates presynaptic and postsynaptic neurons; found in chemical synapses; *gap junctions* connect neurons in electrical synapses

CHEMICAL SYNAPSES

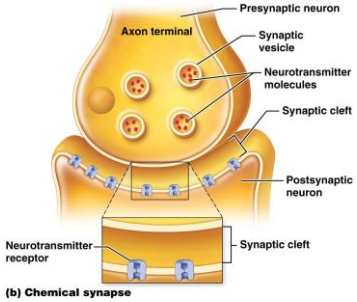


Figure 11.22b The structures of electrical and chemical synapses.

CHEMICAL SYNAPSES

- **Electrical and Chemical Synapses Compared** (continued):
  - Postsynaptic neuron has **neurotransmitter receptors;** bind to neurotransmitter secreted from presynaptic neuron that has diffused across synaptic cleft
  - **Synaptic delay** – *time gap* between *arrival* of action potential at axon terminal and *effect* on postsynaptic membrane
  - Chemical synapses are *unidirectional*, unlike electrical synapses, but allow for variable *signal intensities*
  - More neurotransmitter *released* from presynaptic neuron leads to stronger *response* at postsynaptic neuron

CHEMICAL SYNAPSES

- **Events at a Chemical Synapse.** Neuronal synapses are more complicated than neuromuscular junctions; there are multiple neurons secreting many different *types* of *excitatory* or *inhibitory* neurotransmitters (**Figure 11.23**):
  1. An action potential in presynaptic neuron triggers **voltage-gated calcium ion channels** in axon terminal to open
  2. *Influx of calcium ions* causes synaptic vesicles to *release neurotransmitter* into synaptic cleft
  3. Neurotransmitters *bind to receptors* on postsynaptic neuron
  4. Ion channels open, leading to a *local potential* and possibly an *action potential* if threshold is reached

CHEMICAL SYNAPSES

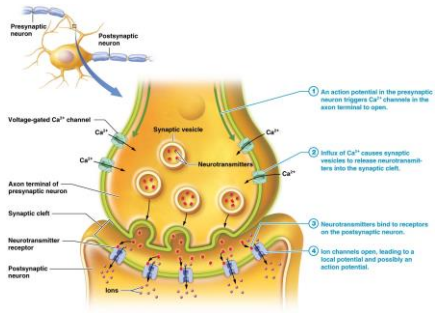
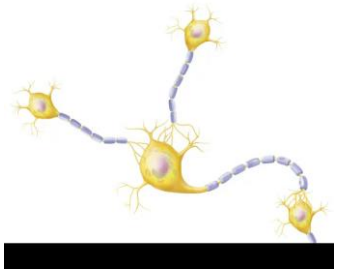


Figure 11.23 Events at a chemical synapse.

BIG PICTURE ANIMATION: SYNAPTIC TRANSMISSION



REVIEW

The correct order for events at a chemical synapse is

a. Neurotransmitter is released, action potential arrives at axon terminus, neurotransmitter binds to receptors, local potential occurs in postsynaptic cell

b. Local potential occurs in postsynaptic cell, neurotransmitter binds to receptors, neurotransmitter is released, action potential arrives at axon terminus

c. Action potential arrives at axon terminus, neurotransmitter is released, neurotransmitter binds to receptors, local potential occurs in postsynaptic cell

d. Neurotransmitter binds to receptors, action potential arrives at axon terminus, local potential occurs in postsynaptic cell, neurotransmitter is released

REVIEW

The correct order for events at a chemical synapse is

a. Neurotransmitter is released, action potential arrives at axon terminus, neurotransmitter binds to receptors, local potential occurs in postsynaptic cell

b. Local potential occurs in postsynaptic cell, neurotransmitter binds to receptors, neurotransmitter is released, action potential arrives at axon terminus

c. Action potential arrives at axon terminus, neurotransmitter is released, neurotransmitter binds to receptors, local potential occurs in postsynaptic cell

d. Neurotransmitter binds to receptors, action potential arrives at axon terminus, local potential occurs in postsynaptic cell, neurotransmitter is released

REVIEW

Action potential arrival at the synaptic terminus causes

a. Opening of voltage-gated calcium channels

b. Opening of voltage-gated sodium channels

c. Opening of voltage-gated potassium channels

d. Opening of voltage-gated chloride channels

REVIEW

Action potential arrival at the synaptic terminus causes

a. Opening of voltage-gated calcium channels

b. Opening of voltage-gated sodium channels

c. Opening of voltage-gated potassium channels

d. Opening of voltage-gated chloride channels

REVIEW

Neurotransmitter release from vesicles of the synaptic terminus results from

a. Influx of calcium into synaptic terminus

b. Efflux of calcium out of synaptic terminus

c. Influx of sodium into synaptic terminus

d. Efflux of sodium into synaptic terminus

REVIEW

Neurotransmitter release from vesicles of the synaptic terminus results from

a. Influx of calcium into synaptic terminus

b. Efflux of calcium out of synaptic terminus

c. Influx of sodium into synaptic terminus

d. Efflux of sodium into synaptic terminus

REVIEW

Neurotransmitter binding to receptors on the postsynaptic membrane

a. Opens or closes ligand-gated calcium channels

b. Opens or closes voltage-gated sodium channels

c. Opens or closes ligand-gated sodium channels

d. Opens or closes voltage-gated potassium channels

REVIEW

Neurotransmitter binding to receptors on the postsynaptic membrane

a. Opens or closes ligand-gated calcium channels

b. Opens or closes voltage-gated sodium channels

c. Opens or closes ligand-gated sodium channels

d. Opens or closes voltage-gated potassium channels

CHEMICAL SYNAPSES

- **Postsynaptic potentials** – *local potentials* found in membranes of *postsynaptic neuron* (**Figure 11.24**):
  - Membrane potential of postsynaptic neuron moves *closer to threshold*; caused by a small local *depolarization* (sodium or calcium channels open) called an **excitatory postsynaptic potential** (**EPSP**)

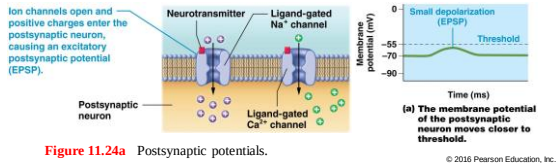


Figure 11.24a Postsynaptic potentials.

CHEMICAL SYNAPSES

- **Postsynaptic Potentials** (continued):
  - Membrane potential of postsynaptic neuron moves *farther away from threshold*; caused by a small local *hyperpolarization* (potassium or chloride ion channels open) called an **inhibitory postsynaptic potential** (**IPSP**)

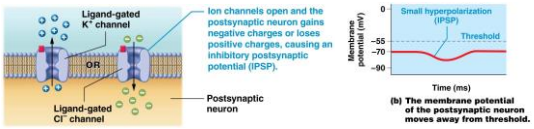


Figure 11.24b Postsynaptic potentials.

CHEMICAL SYNAPSES

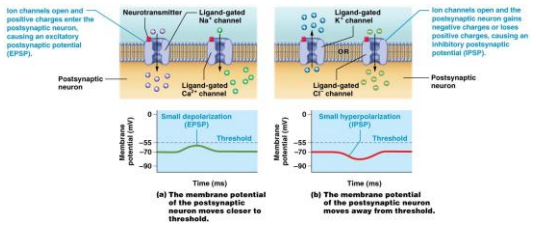
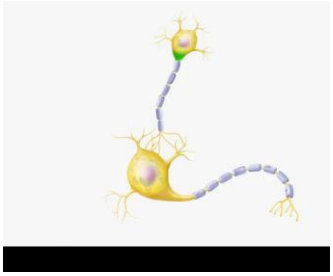


Figure 11.24 Postsynaptic potentials.

BIG PICTURE ANIMATION: POSTSYNAPTIC POTENTIALS



REVIEW

Postsynaptic potentials

a. Are always inhibitory
b. Always move the postsynaptic membrane toward threshold
c. Depend on which membrane channels open
d. Only involve sodium channel opening and closing

REVIEW

Postsynaptic potentials

a. Are always inhibitory
b. Always move the postsynaptic membrane toward threshold
c. **Depend on which membrane channels open**
d. Only involve sodium channel opening and closing

REVIEW

EPSPs

a. Are inhibitory
b. Move the postsynaptic membrane toward threshold
c. Result from potassium channels opening
d. Are usually large local potentials

REVIEW

EPSPs

a. Are inhibitory
b. **Move the postsynaptic membrane toward threshold**
c. Result from potassium channels opening
d. Are usually large local potentials

REVIEW

IPSPs

a. Are inhibitory
b. Move the postsynaptic membrane toward threshold
c. Result from sodium channels opening
d. Are usually large local potentials

REVIEW

IPSPs

a. **Are inhibitory**

b. Move the postsynaptic membrane toward threshold

c. Result from sodium channels opening

d. Are usually large local potentials

CHEMICAL SYNAPSES

- **Synaptic transmission** may be *terminated* by ending effects of neurotransmitter in one of three methods (**Figure 11.25**):
  - Some neurotransmitters *diffuse away* from synaptic cleft in ECF; can be *reabsorbed* into a neuron or an astrocyte
  - Neurotransmitter can be *broken down* in synaptic cleft by *enzymes*; by-products of reaction can be *reabsorbed* by presynaptic membrane for reassembly of original neurotransmitter
  - Some neurotransmitters are *reabsorbed* into presynaptic neuron by a process called **reuptake**

CHEMICAL SYNAPSES

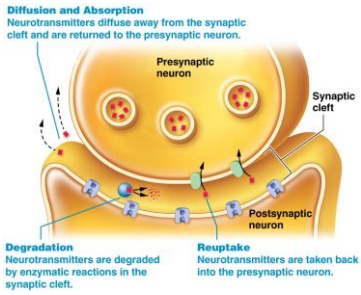
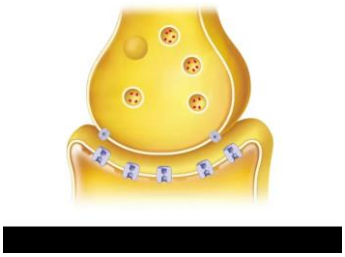


Figure 11.25 Methods of termination of synaptic transmission.

BIG PICTURE ANIMATION: TERMINATION OF SYNAPTIC TRANSMISSION



REVIEW

Termination of synaptic transmission is necessary because

a. Presynaptic neurons will run out of neurotransmitter

b. Receptor fatigue will occur

c. Effect of neurotransmitter is no longer needed

d. Postsynaptic response cannot be reinitiated until first response is terminated

REVIEW

Termination of synaptic transmission is necessary because

a. Presynaptic neurons will run out of neurotransmitter

b. Receptor fatigue will occur

c. Effect of neurotransmitter is no longer needed

d. **Postsynaptic response cannot be reinitiated until first response is terminated**

REVIEW

Which of the following is NOT a method for termination of synaptic transmission?

a. Diffusion and absorption

b. Receptor fatigue

c. Reuptake into presynaptic neuron

d. Degradation in synaptic cleft

REVIEW

Which of the following is NOT a method for termination of synaptic transmission?

a. Diffusion and absorption

b. Receptor fatigue

c. Reuptake into presynaptic neuron

d. Degradation in synaptic cleft

REVIEW

Which of the following is the correct sequence of major events during chemical synaptic transmission?

a. Postsynaptic potentials, synaptic transmission, action potential, synaptic transmission termination

b. Synaptic transmission termination, postsynaptic potentials, action potential, synaptic transmission

c. Action potential, synaptic transmission, postsynaptic potentials, synaptic transmission termination

d. Synaptic transmission, postsynaptic potentials, synaptic transmission termination, action potential

REVIEW

Which of the following is the correct sequence of major events during chemical synaptic transmission?

a. Postsynaptic potentials, synaptic transmission, action potential, synaptic transmission termination

b. Synaptic transmission termination, postsynaptic potentials, action potential, synaptic transmission

c. Action potential, synaptic transmission, postsynaptic potentials, synaptic transmission termination

d. Synaptic transmission, postsynaptic potentials, synaptic transmission termination, action potential

ARTHROPOD VENOM

- **Venomous arthropods** (in United States) include **spiders** and **scorpions**; many of their venoms affect neuronal synapses; termed **neurotoxins**
  - **Female black widow** (*Latrodectus mactans*) – toxin causes massive *release of neurotransmitter* leading to repetitive stimulation of postsynaptic neuron
  - **Bark scorpion** – most lethal of 40 species in United States; venom *prevents postsynaptic sodium channels from closing*; membrane remains polarized and continues to fire action potentials
- Mechanisms are different but *result* is similar; both lead to *overstimulation of postsynaptic neuron*;
- **Common symptoms** – muscle hyperexcitability, sweating, nausea and vomiting, and difficulty breathing
- **Treatment and prognosis** – depends on amount of venom received and availability of medical care; severe cases usually require **antivenin** to block effects of toxin

PUTTING IT ALL TOGETHER: THE BIG PICTURE OF CHEMICAL SYNAPTIC TRANSMISSION

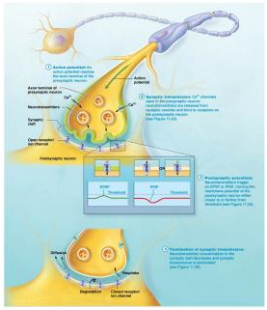


Figure 11.26 The Big Picture of Chemical Synaptic Transmission.

NEURAL INTEGRATION

- Neurons receive input, both *inhibitory* and *excitatory*, from multiple neurons, each of which influences whether an *action potential is generated*
- **Neural integration** – process in which postsynaptic neuron *integrates* all *incoming information* into a single *effect*

NEURAL INTEGRATION

- **Summation** – phenomenon whereby all input from several postsynaptic potentials are *added together* (EPSPs + IPSPs) to affect membrane potential at trigger zone
  - An action potential will only be generated if *threshold is reached*; means that *sum of EPSPs* must be enough to overcome *sum of IPSPs*
  - If sum of IPSPs is greater than EPSPs then membrane will *hyperpolarize*; threshold will not be reached and an action potential will not be generated

CONCEPT BOOST: HOW SUMMATION CONNECTS LOCAL POTENTIALS AND ACTION POTENTIALS

Link between local potentials and action potentials is **summation**—as excitatory local potentials summate, they depolarize trigger zone to threshold and initiate an action potential

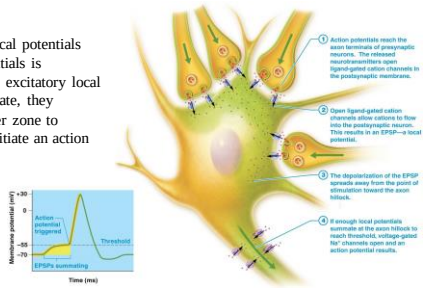


Figure 11.27 Local potentials summating and leading to an action potential

NEURAL INTEGRATION

- Two types of summation differ in timing of neurotransmitter release and number of presynaptic neurons present:
  - **Temporal summation** – neurotransmitter is released *repeatedly* from axon terminal of a single presynaptic neuron; each local potential (EPSP) is short-lived so they must be generated quickly to reach threshold and create action potential (**Figure 11.28a**)
  - **Spatial summation** involves *simultaneous* release of neurotransmitters from axon terminals of many presynaptic neurons (**Figure 11.28b**)
- IPSPs are also subject to both temporal and spatial summation but have *inhibitory effects;* make it less *likely* to reach threshold with subsequent action potential generation

NEURAL INTEGRATION

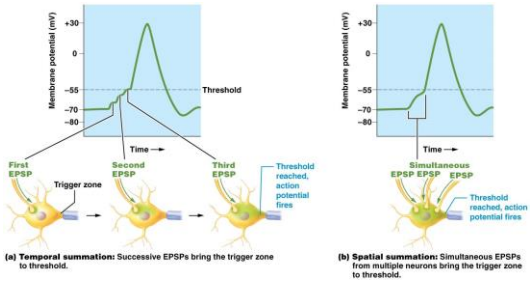


Figure 11.28 Temporal and spatial summation of EPSPs.

MODULE 11.5 NEUROTRANSMITTERS

NEUROTRANSMITTERS

- Nearly all neurotransmitters undergo a similar pattern of use despite fact that there are over 100 known substances; share *similar features*:
  - Made in cell body or axon terminal and packaged into *synaptic vesicles*
  - Released from axon terminals of presynaptic neurons; cross synaptic cleft; *bind to specific receptors* on postsynaptic membrane
  - Effects are often *rapidly terminated* through removal and/or degradation

NEUROTRANSMITTER RECEPTOR

- *Type of receptor* a neurotransmitter binds to on postsynaptic membrane *determines response*; two types:
  - **Ionotropic receptors** – receptors found as *components* of a **ligand-gated ion channels**; directly control *movement of ions* into or out of neuron when they bind to neurotransmitter (**Figure 11.29a**)
  - **Metabotropic receptors** – found within plasma membrane associated with a separate ion channel; directly connected to *metabolic processes* that are initiated when neurotransmitter binds (**Figure 11.29b**)

NEUROTRANSMITTER RECEPTOR

- **Metabotropic receptors** (continued):
  - **G-proteins** – group of intracellular enzymes associated with many metabotropic receptors; activate a cascade of *enzyme-catalyzed reactions*; ultimately form intracellular chemical messenger molecules called **second messengers (**neurotransmitter is "**first messenger**")
  - **Second messengers** can *open or close ion channels* in postsynaptic membrane
  - **Cyclic adenosine monophosphate** (**cAMP**) – common second messenger derived from ATP with *multiple functions* in neurons
  - **cAMP** can bind to a group of enzymes that can *add phosphate groups to ion channels*; either triggers channel to open or close

NEUROTRANSMITTER RECEPTOR

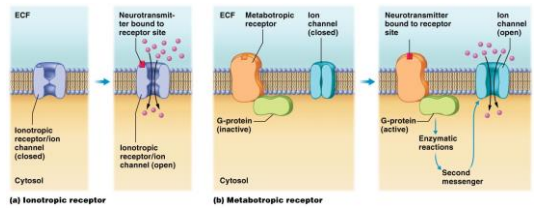


Figure 11.29 Types of neurotransmitter receptors.

MAJOR NEUROTRANSMITTERS

- Binding of neurotransmitter to receptor leads to either an EPSP (with **excitatory** effects) or an IPSP (with **inhibitory** effects)
- Most neurotransmitters can have both effects depending on which postsynaptic neuron receptors they bind; single neurotransmitter may have several *receptor types*
- Major neurotransmitters are classified into four groups based on *chemical structure* (**Table 11.3**)

MAJOR NEUROTRANSMITTERS

TABLE 11.3 MAJOR NEUROTRANSMITTERS

Neurotransmitter	Precursor Molecule(s)	Predominant Postsynaptic Effect	Location(s)	Type of Receptor(s)
Acetylcholine	Acetyl-CoA and choline	Excitatory	CNS: brain and spinal cord PNS: neuromuscular junction and ANS	Ionotropic and metabotropic
Biogenic Amines				
Catecholamines (norepinephrine, epinephrine, dopamine)	Tyrosine	Excitatory	CNS: brain and spinal cord PNS: ANS (sympathetic division)	Metabotropic
Serotonin	Tryptophan	Excitatory	CNS: brain	Metabotropic
Histamine	Histidine	Excitatory	CNS: brain	Metabotropic
Amino Acids				
Glutamate	Glutamine	Excitatory	CNS: brain (major neurotransmitter of the brain)	Ionotropic and metabotropic
GABA (γ-aminobutyric acid)	Glutamate	Inhibitory	CNS: brain and spinal cord	Ionotropic and metabotropic
Glycine	Serine	Inhibitory	CNS: brain and spinal cord (most common inhibitory neurotransmitter in the spinal cord)	Ionotropic
Neuropeptides				
Substance P	Amino acids	Excitatory and inhibitory	CNS: brain and spinal cord (major neurotransmitter for pain perception) PNS: enteric nervous system (neurons in the digestive tract)	Metabotropic
Opioids (enkephalin, α-endorphin, dynorphin-A)	Amino acids	Excitatory and inhibitory	CNS: brain and spinal cord (major neurotransmitters for pain control)	Metabotropic
Neuropeptide Y	—	Excitatory and inhibitory	CNS: brain PNS: ANS	Metabotropic

MAJOR NEUROTRANSMITTERS

- **Acetylcholine** (**ACh**) – small molecule neurotransmitter widely used by nervous system
  - **Cholinergic synapses** bind to ACh; found in neuromuscular junction, within brain and spinal cord and within autonomic nervous system
  - Largely *excitatory* but it does exhibit some inhibitory effects in PNS
  - *Synthesized* from **choline** and **acetyl-CoA** and packed into synaptic vesicles
  - Quickly *degraded* by **acetylcholinesterase** (**AChE**) an enzyme in synaptic cleft; by-products of reaction are taken back into presynaptic neuron for recycling and reuse

MAJOR NEUROTRANSMITTERS

- **Biogenic amines** (monoamines); class of five neurotransmitters *synthesized from amino acids*; used throughout CNS and PNS for many functions such as regulation of homeostasis and cognition; first three form **catecholamine** subgroup, all of which are made from amino acid **tyrosine**; mostly *excitatory*:
  - **Norepinephrine** (*catecholamine*, also known as **noradrenalin**) – found mainly in ANS where it influences heart rate, blood pressure, and digestion; in CNS it regulates sleep/wake cycle, attention, and feeding behaviors
  - **Epinephrine** (*catecholamine*, also known as **adrenalin**) – also used in ANS; has similar functions as norepinephrine; more widely used as a **hormone** by endocrine system.

MAJOR NEUROTRANSMITTERS

- **Biogenic amines** (continued):
  - **Dopamine** (catecholamine) – used extensively by CNS; helps to coordinate movement; involved in emotion and motivation
  - **Serotonin** – synthesized from amino acid **tryptophan**; most serotonin-secreting neurons are found in brainstem; axons project into multiple areas of brain; functions include mood regulation, emotions, attention, feeding behaviors, and daily rhythms
  - **Histamine** – synthesized from amino acid **histidine**; involved in regulation of arousal and attention

MAJOR NEUROTRANSMITTERS

- Three main **amino acid neurotransmitters**:
  - **Glutamate** – most important *excitatory* neurotransmitter in CNS; binds to its *ionotropic postsynaptic receptors* and opens channels that allow for flow of both sodium and calcium ions; generate EPSPs in postsynaptic neuron
  - **Glycine** and **GABA** – both major *inhibitory* neurotransmitters; induce IPSPs on postsynaptic neurons by opening chloride ion channels; hyperpolarize axolemma

MAJOR NEUROTRANSMITTERS

- **Neuropeptides** – group of neurotransmitters that have a wide variety of functions within nervous system; must be synthesized in cell body and transported to axon
  - **Substance P** – released from *type C sensory afferents* that carry information about pain and temperature; also released by other neurons in brain, spinal cord, and gut
  - **Opioids** – make up a group of more than *20 neuropeptides* that include **endorphins**, **enkephalins**, and **dynorphins**, all of which elicit pain relief and are nervous system depressants
  - **Neuropeptide Y** – neuropeptide involved in feeding behaviors and may mediate hunger or feeling full

PSYCHIATRIC DISORDERS AND TREATMENTS

- **Psychiatric disorders** affect thought processes; generally treated by *modifying synaptic transmission* to change how neurons communicate with each other
- **Psychopharmacology** (study of drugs that affect higher brain functions) targets either action potential generation or some aspect of neurotransmitter physiology:
  - **Schizophrenia** – characterized by repetitive **psychotic episodes** (periods during which patient is unable to appropriately test beliefs and perceptions against reality); thought to result from *excessive release of dopamine*; management involves blocking *postsynaptic dopamine receptors*

Psychiatric Disorders and Treatments (continued)

- **Depressive disorders** – marked by *disturbances in mood*; thought to result from deficiency in synaptic transmission of serotonin, norepinephrine, and/or dopamine; most widely used antidepressants are **selective serotonin reuptake inhibitors** (**SSRIs**); *block serotonin transporter* (only), preventing reuptake by presynaptic neuron
- **Anxiety disorders** – characterized by *exaggerated and inappropriate fear responses*; believed to stem from abnormalities in norepinephrine, serotonin, and GABA transmission; drugs for treatment include antidepressants, GABA activity enhancers, and others that modulate norepinephrine transmission
- **Bipolar disorders** – characterized by episodes of *abnormal elevated mood (mania) followed by depression;* treatments involve decreasing ease of action potential generation; generally block sodium channels in axolemma

Module 11.6 Functional Groups of Neurons

Neuronal Pools

- **Neuronal pools** – groups of *interneurons* within CNS (**Figure 11.30**):
  - Composed of neuroglial cells, dendrites, and axons in one location and cell bodies in another location
  - Type of information processed by a pool is defined by *synaptic connections* of pool
  - Connections between pools allow for *complex mental activity* such as planned movement, cognition, and personality
  - Input neurons initiate series of signals that starts activity of a pool

Neuronal Pools

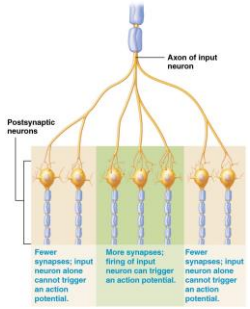


Figure 11.30 A neuronal pool.

Neuronal Circuits

- **Neural circuits** – *patterns of synaptic connection* between neural pools; two basic types of neural circuits (**Figure 11.31**):
  - **Diverging circuits** begin with a single input neuron axon that *branches out* to make contact with multiple postsynaptic neurons that follow same pattern (**Figure 11.31a**)
    - Critical because they allow a *single neuron* to communicate with *multiple parts of brain and/or body*
    - Characteristic of those transmitting *incoming sensory information* sent from spinal cord to different neuronal pools in brain for processing

Neuronal Circuits

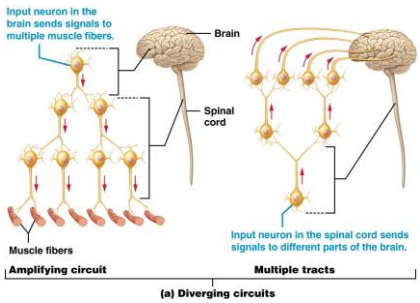


Figure 11.31a Types of neural circuits.

NEURONAL CIRCUITS

- **Neural Circuits** (continued)
  - **Converging circuits** – basically *opposite configuration* of diverging circuits; axon terminals from multiple input neurons converge on onto a single postsynaptic neuron (**Figure 11.31b**)
    - Critical for control of *skeletal muscle movement*
    - Allow nervous system to *respond to sensory information* that it collects and processes

NEURONAL CIRCUITS

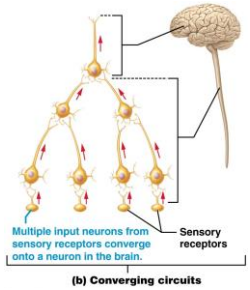


Figure 11.31b Types of neural circuits.

NEURONAL CIRCUITS

- CNS has two mechanisms that *stabilize neural circuits* to prevent electrical activity from becoming chaotic:
  - **First mechanism** – *inhibitory circuits* provide a *negative feedback mechanism* to control activity of other neural circuits
  - **Second mechanism** – **synaptic fatigue** by which synaptic transmission becomes *progressively weaker* with prolonged and intense excitation

EPILEPTIC SEIZURES

- **Epilepsy** – recurrent episodes of abnormal, disorganized electrical activity in brain (**seizures**)
- Seizures result from sudden bursts of excitatory electrical activity within a neuronal pool; may be triggered by *instability in membrane potential* of a single neuron
- Excess excitation *overwhelms inhibitory circuits* that normally prevent overexcitation
- Continuous wave of excitation spreads over part of brain (**partial seizure**) or entire brain (**generalized seizure**); no meaningful signals can be transmitted; ends due to *synaptic fatigue*
- **Symptoms** – mild sensory disturbances to loss of consciousness to characteristic jerking movements
- **Therapy** – medications aimed at preventing seizures and allowing inhibitory circuits to function properly