



Nervous System



Dr. Naim Kittana

**Department of Biomedical Sciences
Faculty of Medicine & Health Sciences
An-Najah National University**

Declaration

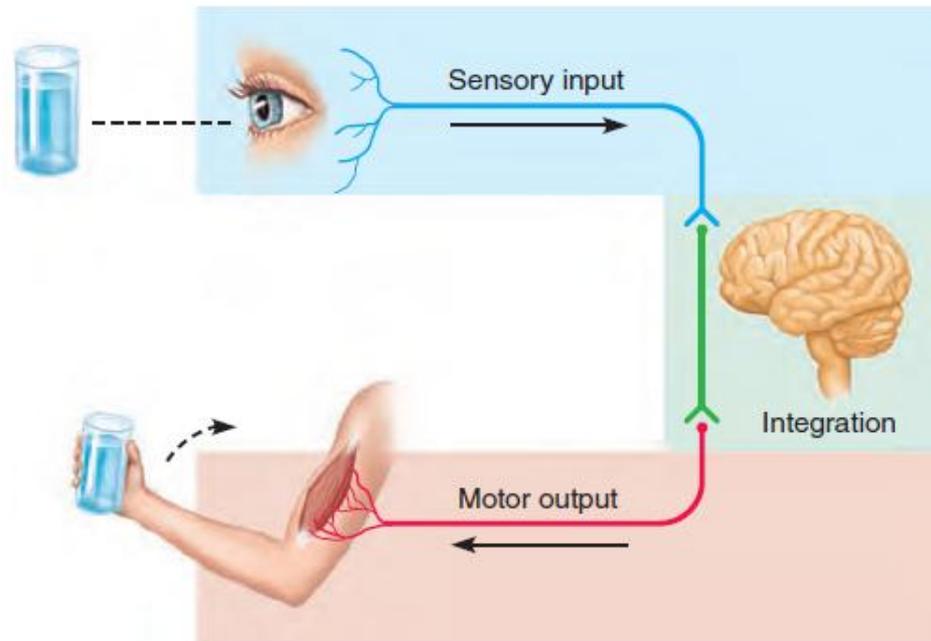
- The content and the figures of this seminar were directly adopted from the text book “Human Anatomy and Physiology / Ninth edition/ Eliane N. Marieb 2013”

Functions and Divisions of the Nervous System

- The nervous system is divided anatomically into the **central nervous system** (brain and spinal cord) and the **peripheral nervous system** (mainly cranial and spinal nerves).

The major functional divisions of the PNS are:

- The sensory (afferent) division, which conveys impulses to the CNS,
- The motor (efferent) division, which conveys impulses from the CNS.

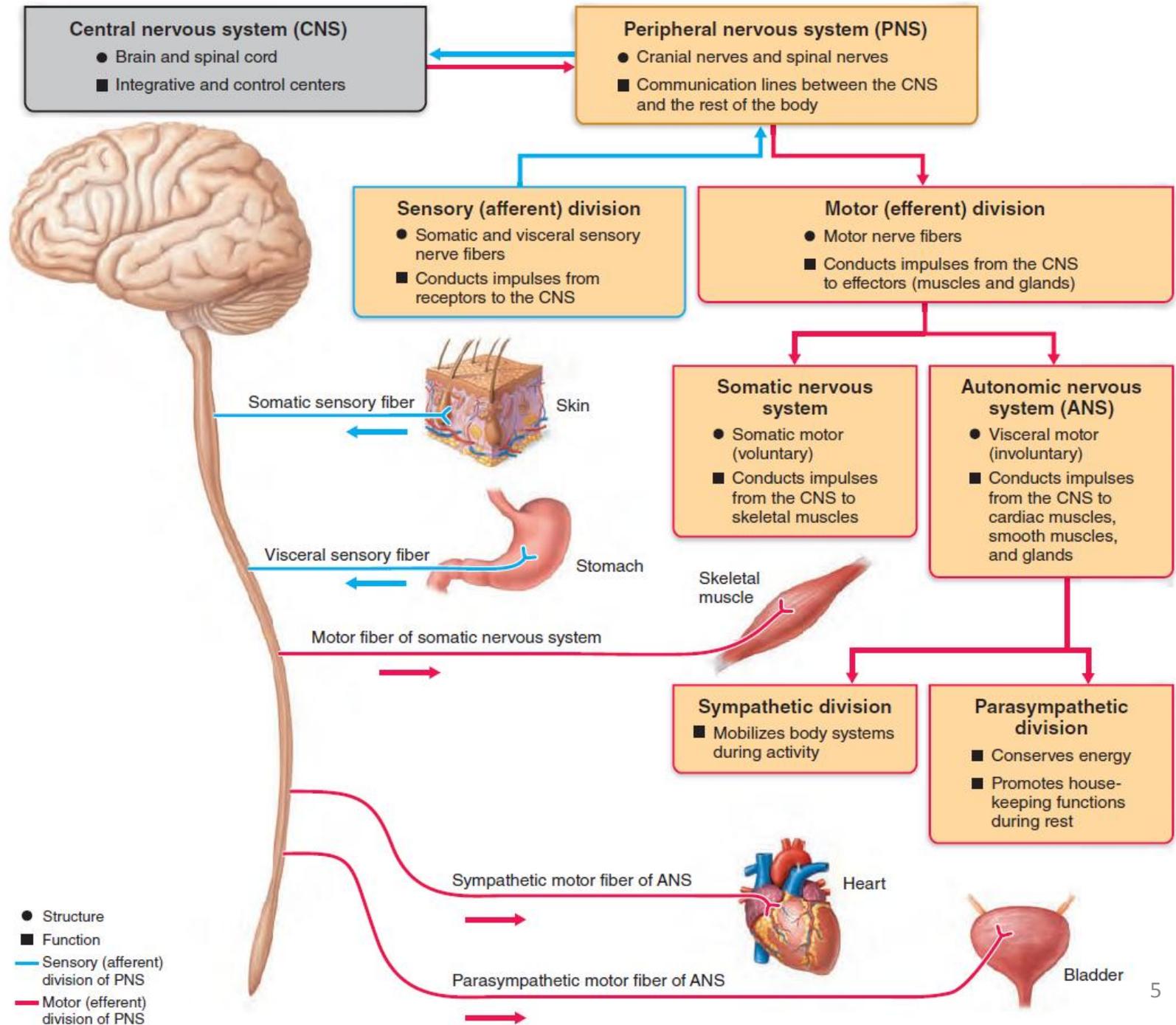


Functions and Divisions of the Nervous System

The efferent division includes :

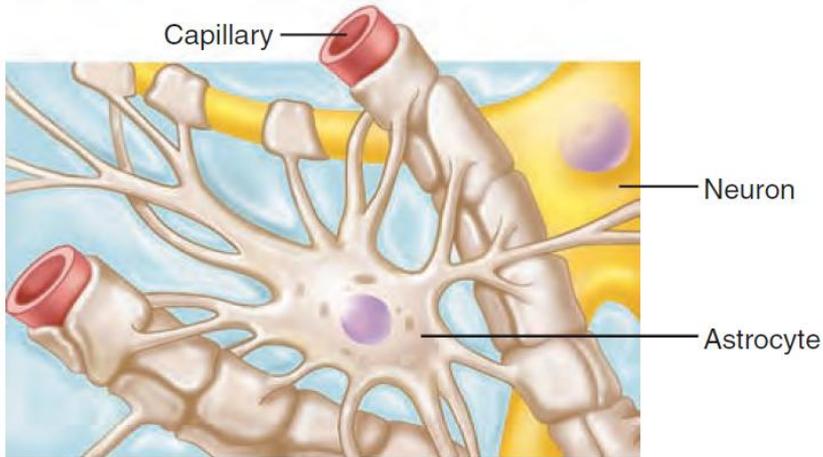
- The **somatic** (voluntary) system, which serves skeletal muscles
- The **autonomic** (involuntary) system, which innervates smooth and cardiac muscle and glands.
- The nervous system consists of two cell types: Neuroglia and Neurones

Levels of organization in the nervous system

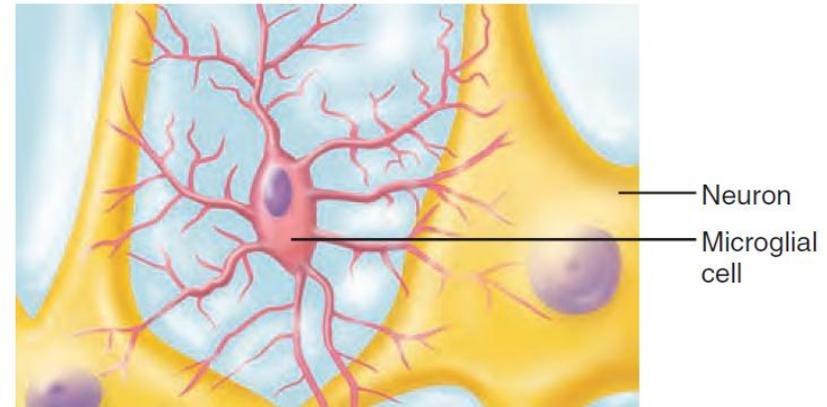


Neuroglia

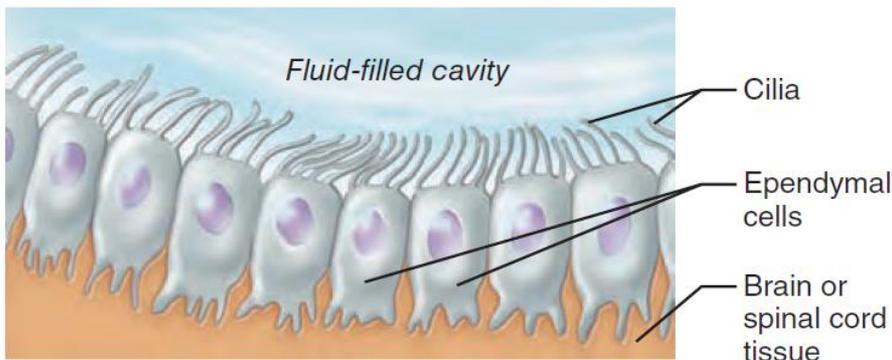
- Neuroglia (supporting cells) segregate and insulate neurons and assist neurons in various other ways.
- **CNS neuroglia include:** astrocytes, microglial cells, ependymal cells, and oligodendrocytes.



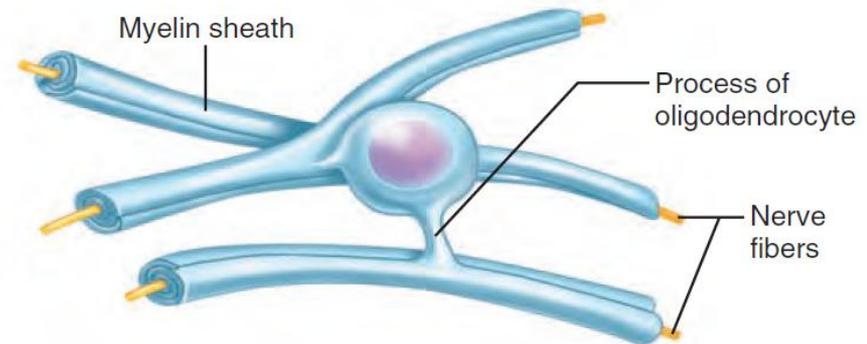
(a) Astrocytes are the most abundant CNS neuroglia.



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



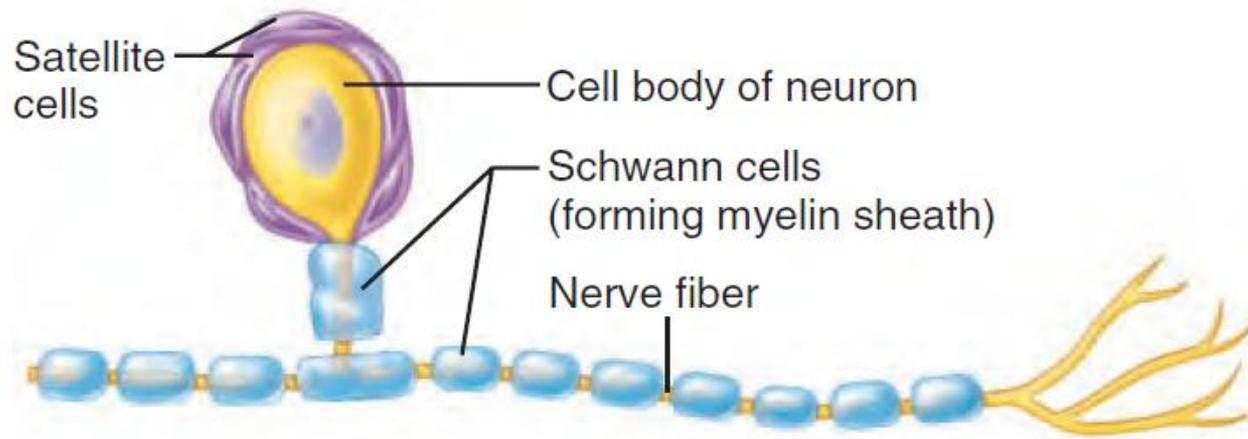
(c) Ependymal cells line cerebrospinal fluid-filled cavities.



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

Neuroglia

- **PNS neuroglia include:** Schwann cells and satellite cells.

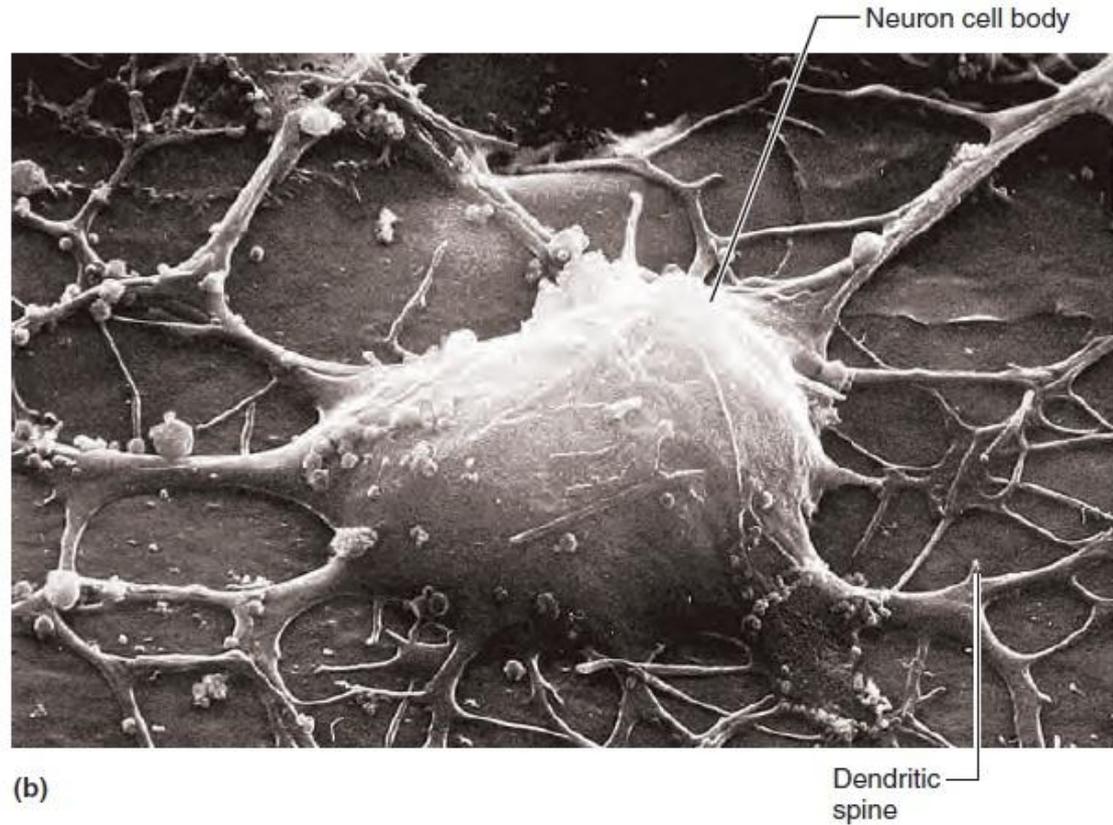
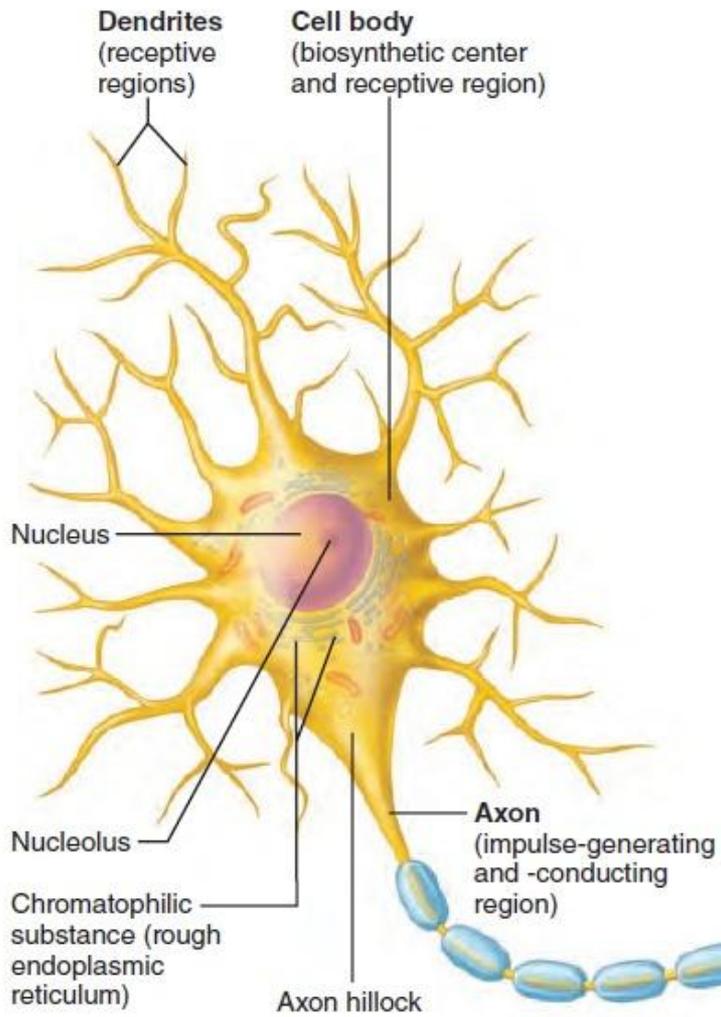


(e) Satellite cells and Schwann cells (which form myelin) surround neurons in the PNS.

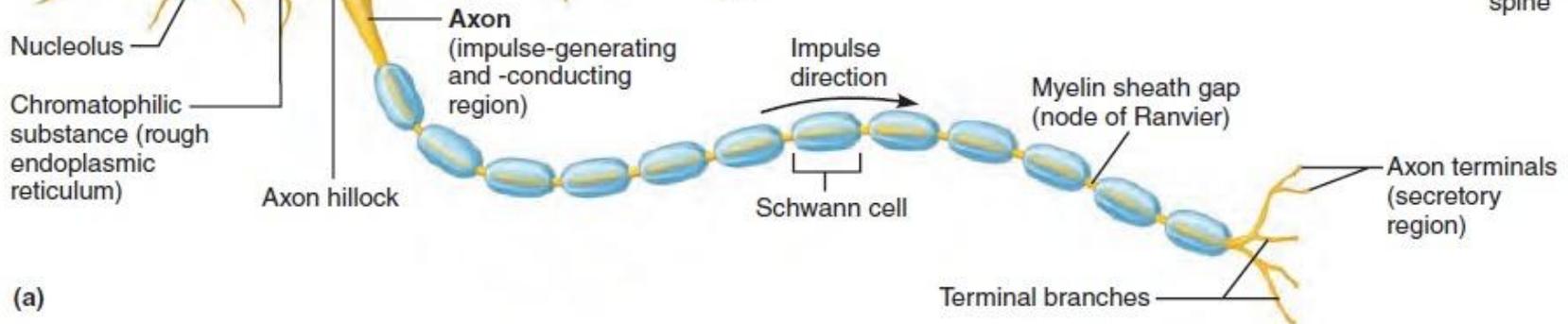
Neurons

- Neurons have a cell body and cytoplasmic processes called axons and dendrites.
- A bundle of nerve fibers is called a **tract** in the CNS and a **nerve** in the PNS.
- A collection of cell bodies is called a **nucleus** in the CNS and a **ganglion** in the PNS.
- The cell body is the biosynthetic (and receptive) center of the neuron.
- **Except for those found in ganglia**, cell bodies are found in the CNS.

Neurons



(b)



(a)

Neurons

- Most neurons have many dendrites, receptive processes that conduct signals from other neurons toward the nerve cell body.
- With few exceptions, all neurons have one axon, which generates and conducts nerve impulses away from the nerve cell body.
- Axon terminals release neurotransmitter.

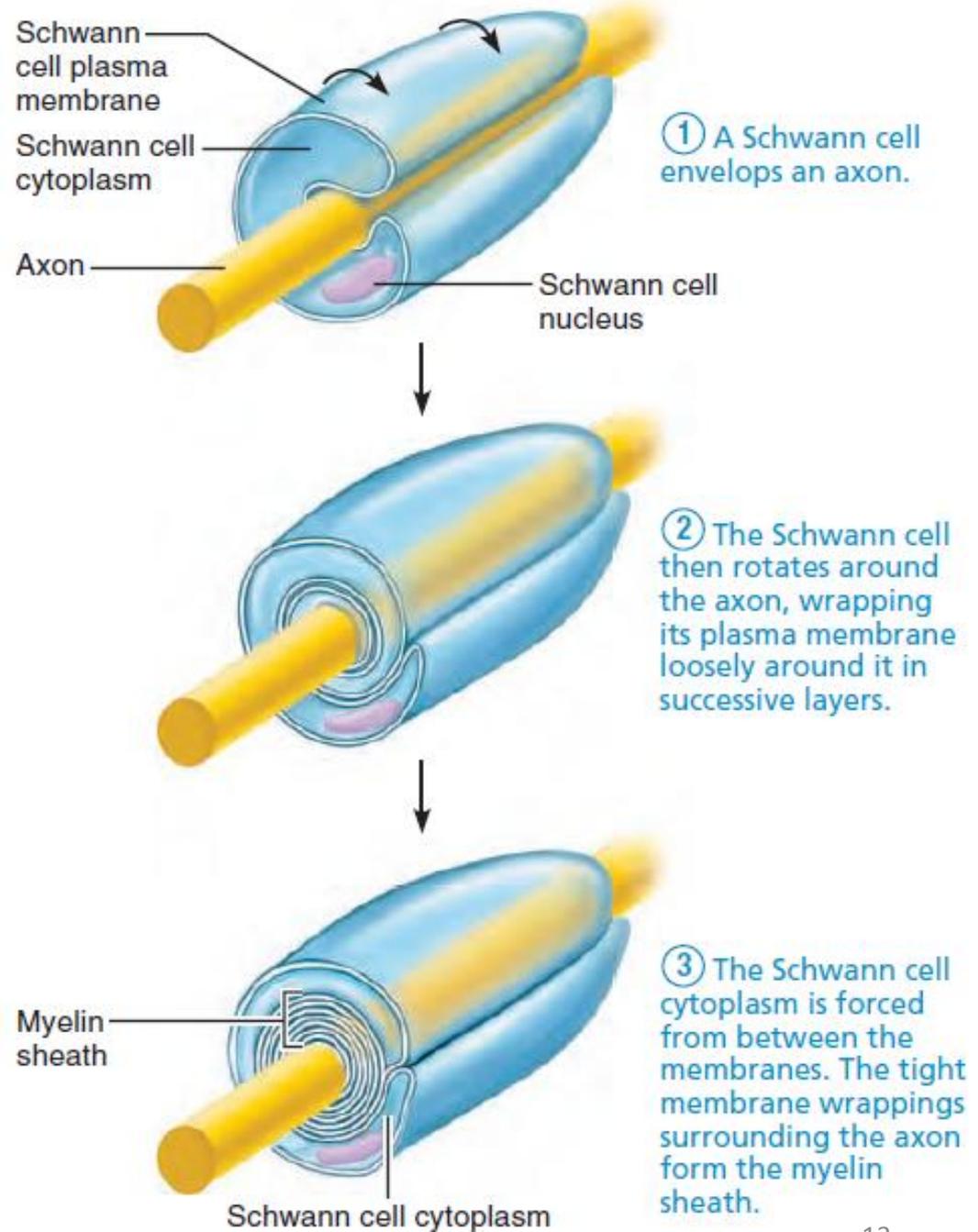
Neurons

- Bidirectional transport along axons uses ATP-dependent motor proteins “walking” along microtubule tracks.
- It moves vesicles, mitochondria, and cytosolic proteins toward the axon terminals and conducts substances destined for degradation back to the cell body.

Neurons

- Large nerve fibers (axons) are myelinated.
- The myelin sheath is formed in the PNS by Schwann cells and in the CNS by oligodendrocytes.
- The myelin sheath gaps are also called nodes of Ranvier.
- Nonmyelinated fibers are surrounded by supporting cells, but the membrane-wrapping process does not occur.
- Anatomically, neurons are classified according to the number of processes issuing from the cell body as multipolar, bipolar, or unipolar.

Neurons



(a) Myelination of a nerve fiber (axon)

Classification of neurons

Functionally, neurons are classified **according to the direction of nerve impulse** conduction:

- **Sensory** neurons conduct impulses toward the CNS
- **Motor** neurons conduct away from the CNS,
- **Interneurons** (association neurons) lie between sensory and motor neurons in the neural pathways.

Basic Principles of Electricity

- The measure of the potential energy of separated electrical charges is called voltage (V) or potential.
- Current (I) is the flow of electrical charge from one point to another.
- Resistance (R) is hindrance to current flow.
- Ohm's law gives the relationship among these: $I = V/R$.
- In the body, ions provide the electrical charges
- Cellular plasma membranes provide resistance to ion flow.
- The membranes contain leakage channels (nongated, always open) and gated channels.

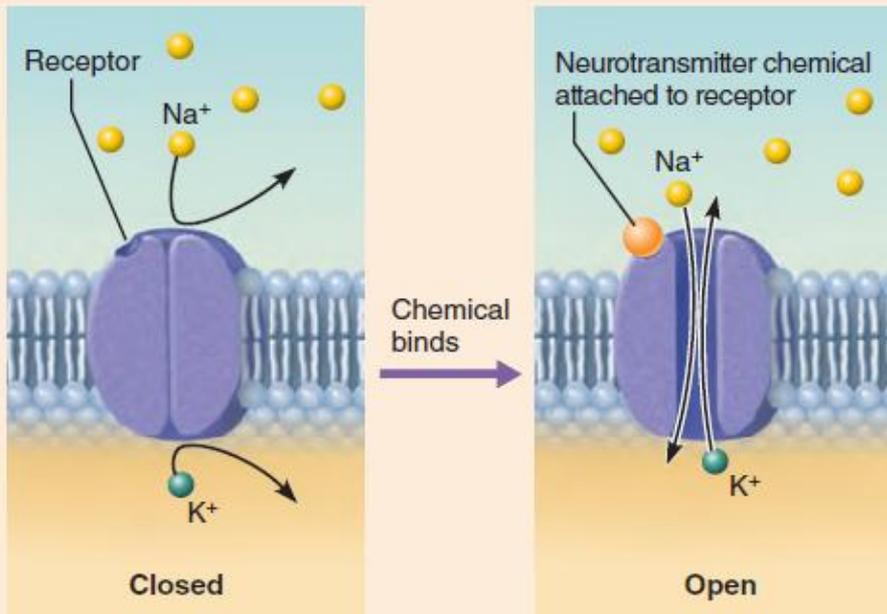
The Resting Membrane Potential

- A resting neuron exhibits a resting membrane potential, which is 270 mV (inside negative).
- It is due both to differences in sodium and potassium ion concentrations inside and outside the cell and to differences in permeability of the membrane to these ions.
- The ionic concentration differences result from the operation of the sodium-potassium pump, which **ejects 3 Na⁺ from the cell for each 2 K⁺ transported in.**

The Resting Membrane Potential

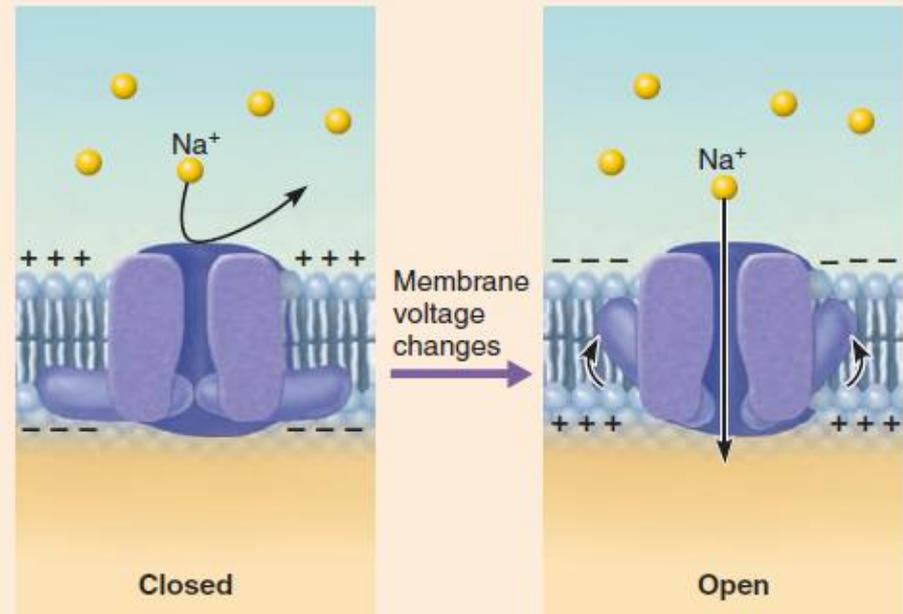
(a) Chemically gated ion channels

Open in response to binding of the appropriate neurotransmitter



(b) Voltage-gated ion channels

Open in response to changes in membrane potential

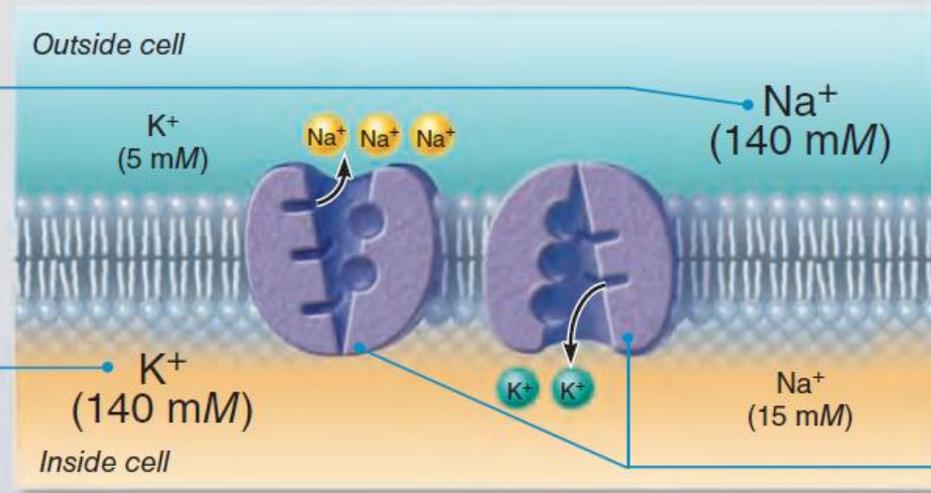


The Resting Membrane Potential

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

The Na^+ concentration is higher outside the cell.

The K^+ concentration is higher inside the cell.



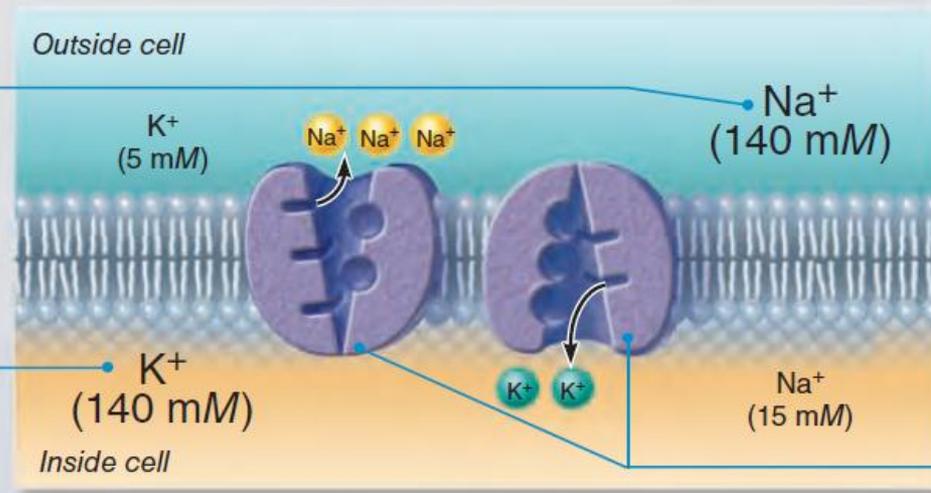
Na^+ - K^+ pumps maintain the concentration gradients of Na^+ and K^+ across the membrane.

The Resting Membrane Potential

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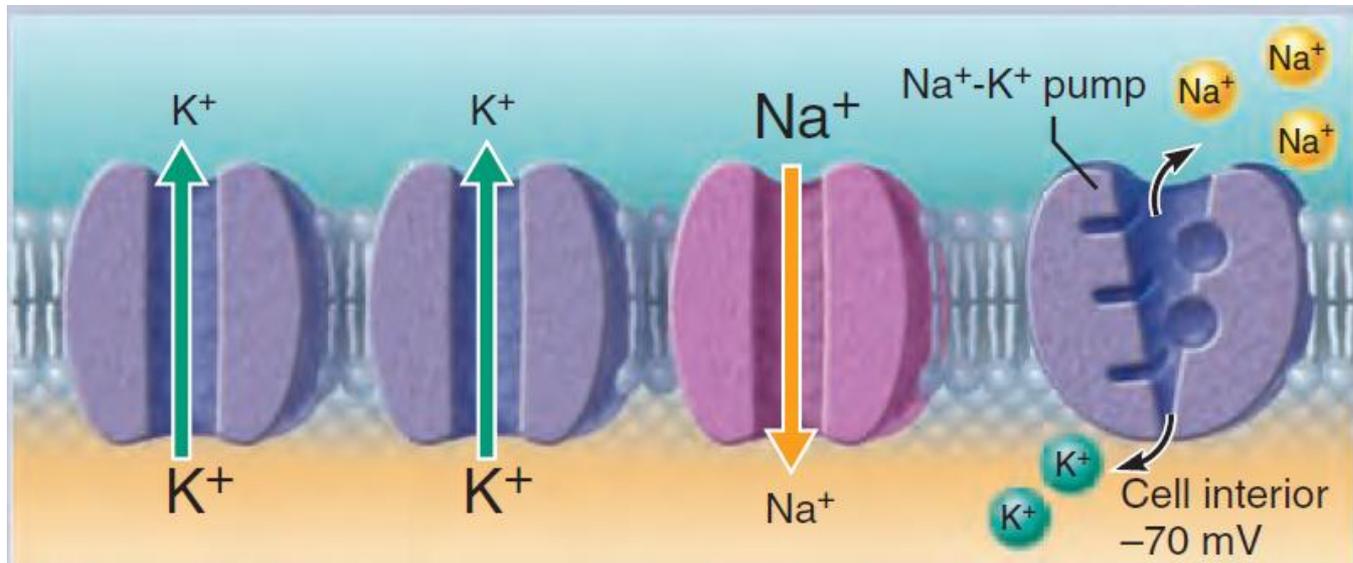
Membrane Potentials That Act as Signals

- Depolarization is a reduction in membrane potential (inside becomes less negative); hyperpolarization is an increase in membrane potential (inside becomes more negative).
- Graded potentials are small, brief, local changes in membrane potential that act as short-distance signals.
- The current produced dissipates with distance.
- An action potential (AP), or nerve impulse, is a large, but brief, depolarization signal (and polarity reversal) that underlies long-distance neural communication.
- AP it is an all-or-none phenomenon.

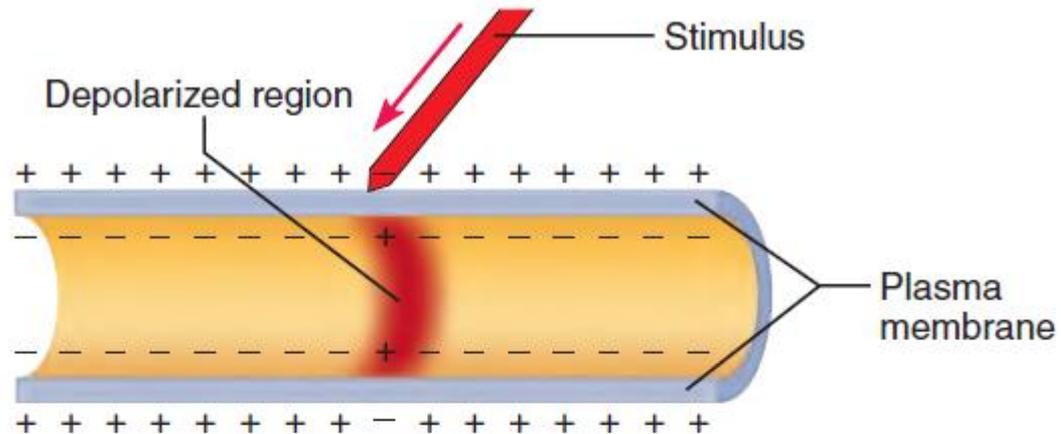
Membrane Potentials That Act as Signals

- In the AP graph, an AP begins and ends at resting membrane potential.
- Depolarization to approximately 130 mV (inside positive) is caused by Na⁺ influx.
- Depolarization ends when Na⁺ channels inactivate.
- Repolarization and hyperpolarization are caused by K⁺ efflux.
- If threshold is reached, an AP is generated. If not, depolarization remains local.

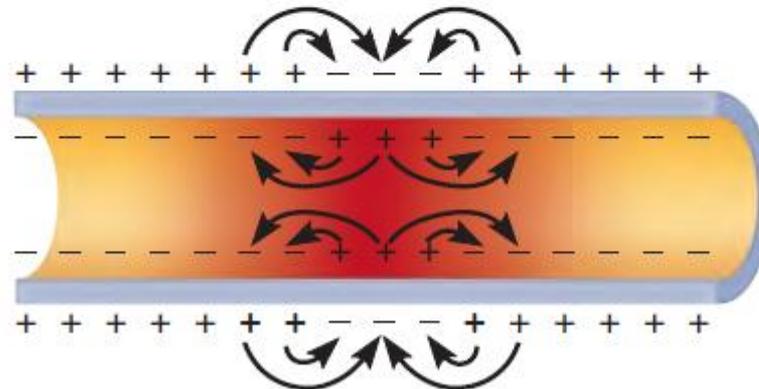
Membrane Potentials That Act as Signals



Membrane Potentials That Act as Signals



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



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

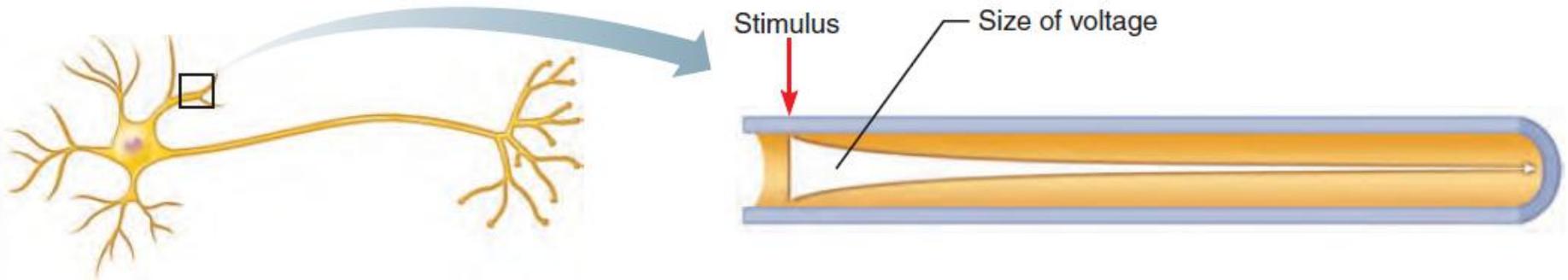
Membrane Potentials That Act as Signals

- In nerve impulse propagation, each AP provides the depolarizing stimulus for triggering an AP in the next membrane patch.
- Regions that have just generated APs are refractory; for this reason, the nerve impulse propagates in one direction only.
- APs are **independent of stimulus strength**: Strong stimuli cause APs to be generated more frequently **but not** with greater amplitude.

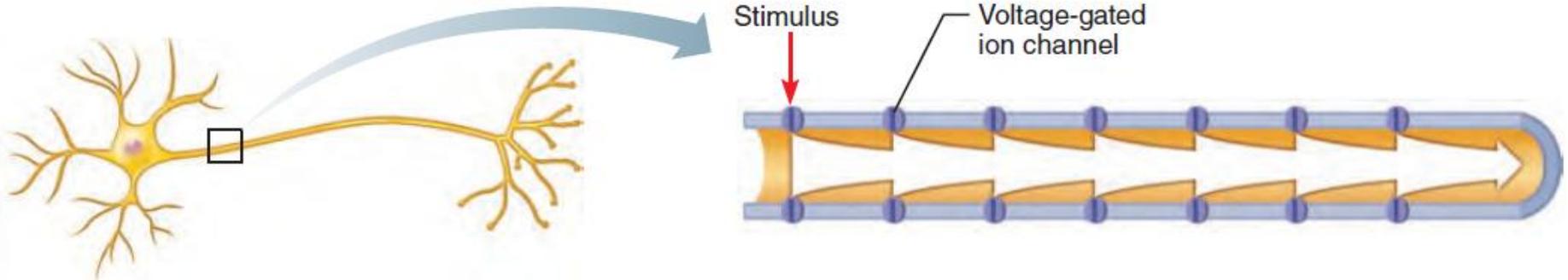
Membrane Potentials That Act as Signals

- During the absolute refractory period, a neuron cannot respond to another stimulus because it is already generating an AP.
- During the relative refractory period, the neuron's threshold is elevated because repolarization is ongoing.
- In nonmyelinated fibers, APs are produced in a wave all along the axon, that is, by continuous conduction.
- In myelinated fibers, APs are generated only at myelin sheath gaps and are propagated more rapidly by saltatory conduction.

Membrane Potentials That Act as Signals

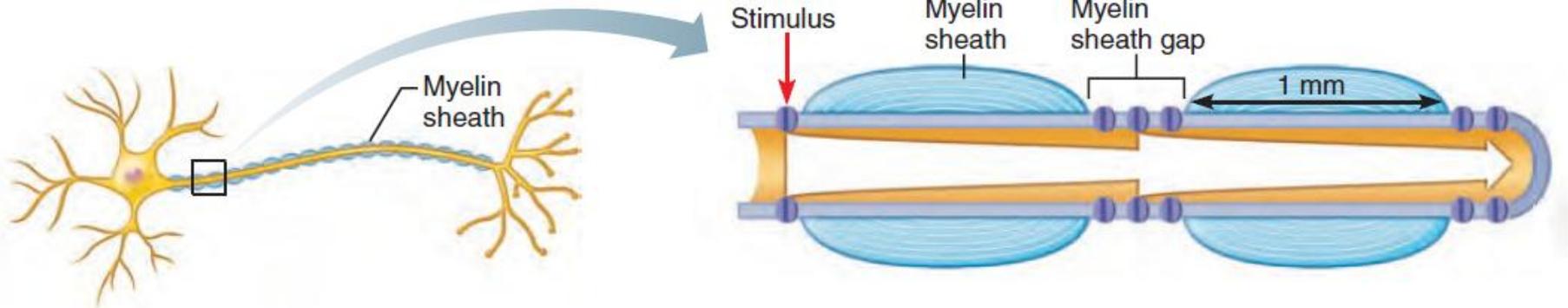


(a) In bare plasma membranes, voltage decays. Without voltage-gated channels, as on a dendrite, voltage decays because current leaks across the membrane.



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

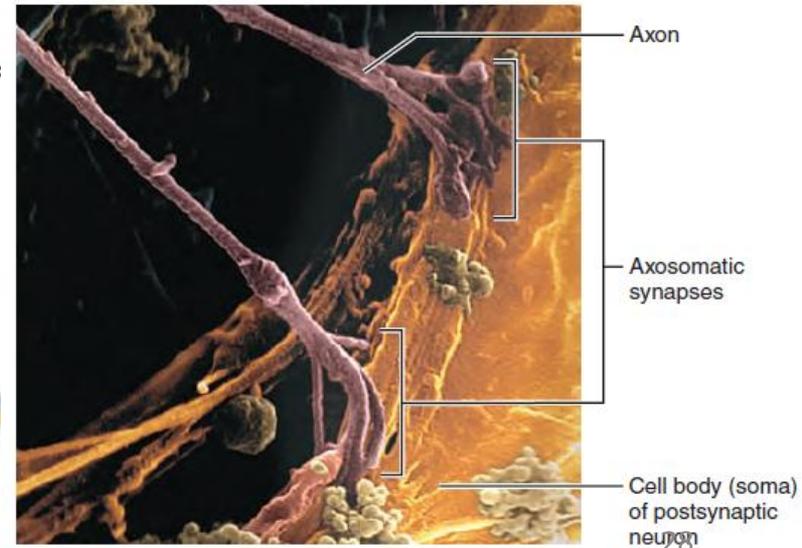
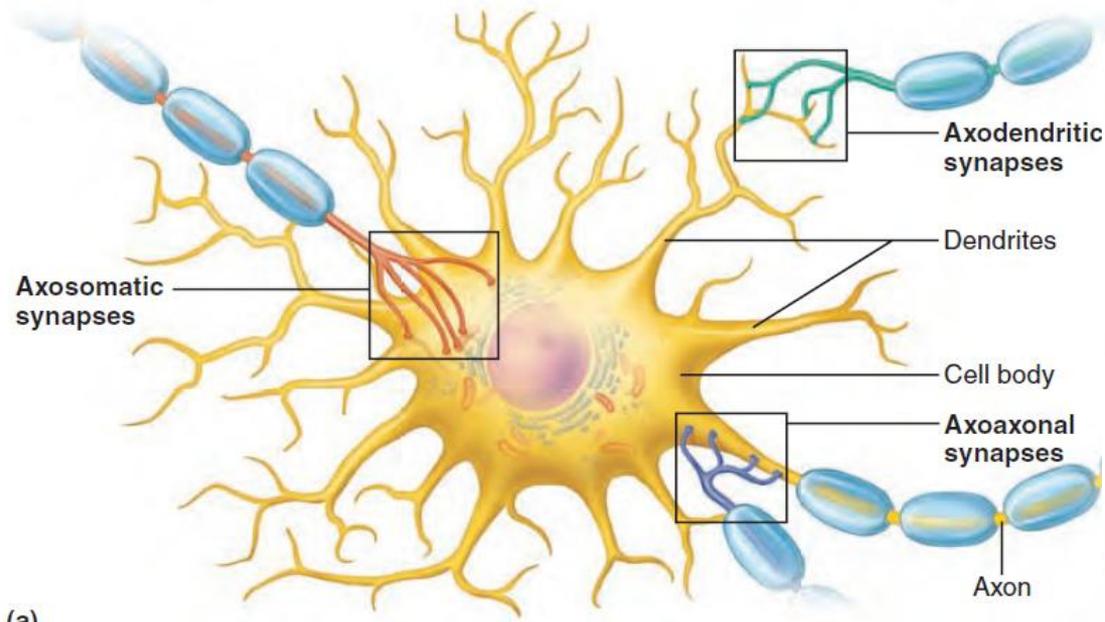
Membrane Potentials That Act as Signals



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

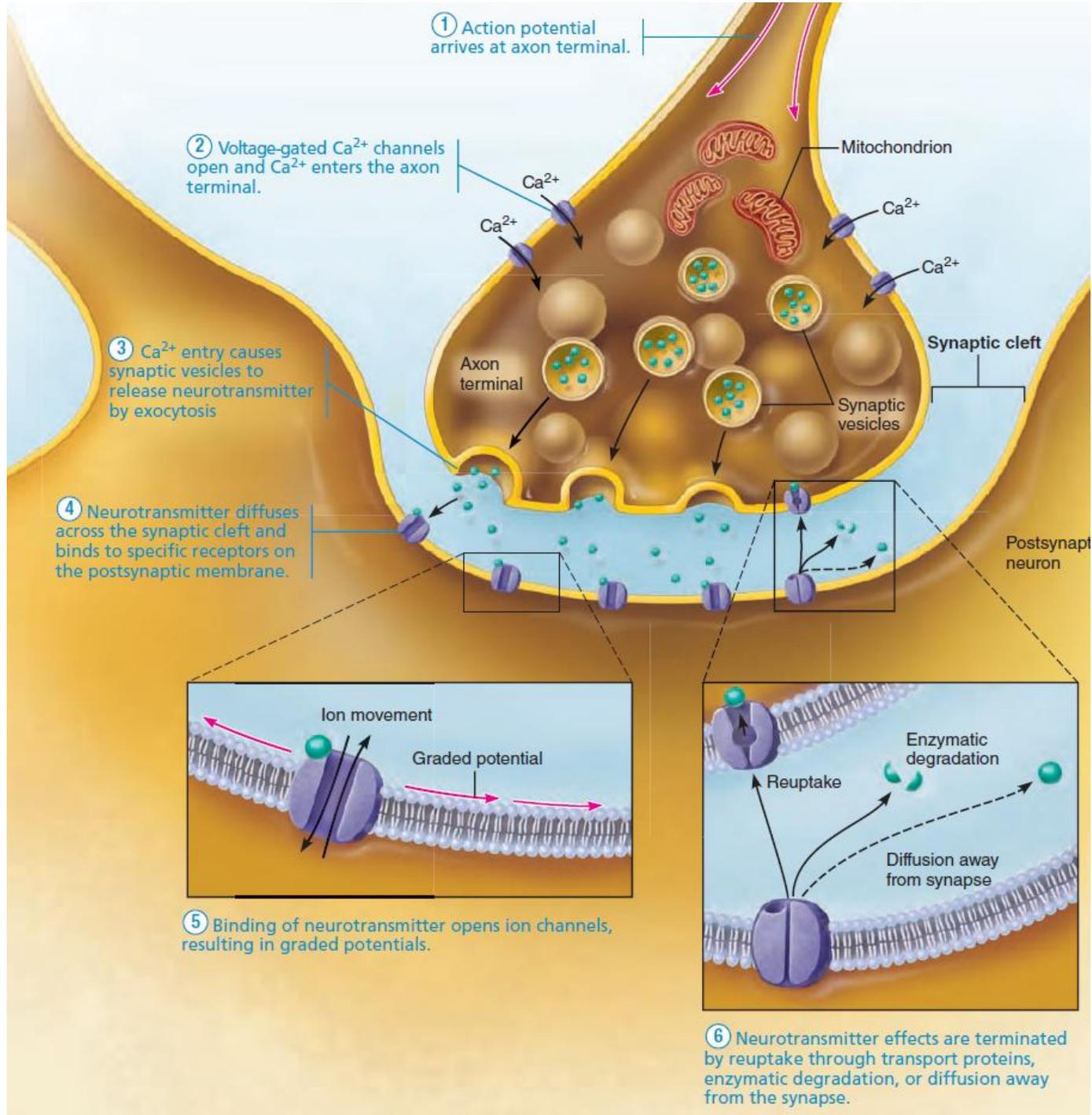
The Synapse

- A synapse is a functional junction between neurons.
- The information-transmitting neuron is the presynaptic neuron; the information-receiving neuron is the postsynaptic neuron.
- Electrical Synapses allow ions to flow directly from one neuron to another; the cells are electrically coupled.



Chemical Synapses

- Chemical synapses are sites of neurotransmitter release and binding.
- When the impulse reaches the presynaptic axon terminals, voltage-gated Ca^{2+} channels open, and Ca^{2+} enters the cell and mediates neurotransmitter release.
- Neurotransmitters diffuse across the synaptic cleft and attach to postsynaptic membrane receptors, opening ion channels.
- After binding, the neurotransmitters are removed from the synapse by diffusion, enzymatic breakdown, or reuptake into the presynaptic terminal or astrocytes.



Postsynaptic Potentials and Synaptic Integration

- Binding of neurotransmitter at excitatory chemical synapses results in local graded potentials called excitatory postsynaptic potential (EPSPs), caused by the opening of channels that allow simultaneous passage of Na^+ and K^+ .
- Neurotransmitter binding at inhibitory chemical synapses results in hyperpolarizations called inhibitory postsynaptic potential (IPSPs), caused by the opening of K^+ or Cl^- channels.
- IPSPs drive the membrane potential farther from threshold.

Postsynaptic Potentials and Synaptic Integration

- EPSPs and IPSPs summate temporally and spatially.
- The membrane of the axon hillock acts as a neuronal integrator.
- Synaptic potentiation, which enhances the postsynaptic neuron's response, is produced by intense repeated stimulation.
- Ionic calcium appears to mediate such effects, which may be the basis of learning.
- Presynaptic inhibition is mediated by axoaxonal synapses that reduce the amount of neurotransmitter released by the inhibited neuron

Classification of Neurotransmitters by Chemical Structure

- acetylcholine, biogenic amines, amino acids, peptides, purines, dissolved gases, and lipids.

Table 11.3 Neurotransmitters and Neuromodulators

NEUROTRANSMITTER	FUNCTIONAL CLASSES	SITES WHERE SECRETED	COMMENTS
Acetylcholine (ACh)			
<ul style="list-style-type: none"> At <i>nicotinic ACh receptors</i> (on skeletal muscles, autonomic ganglia, and in the CNS) At <i>muscarinic ACh receptors</i> (on visceral effectors and in the CNS) 	<p>Excitatory</p> <p>Direct action</p> <p>Excitatory or inhibitory depending on subtype of muscarinic receptor</p> <p>Indirect action via second messengers</p>	<p>CNS: widespread throughout cerebral cortex, hippocampus, and brain stem</p> <p>PNS: all neuromuscular junctions with skeletal muscle; some autonomic motor endings (all preganglionic and parasympathetic postganglionic fibers)</p>	<p>Effects prolonged when AChE blocked by nerve gas or organophosphate insecticides (malathion), leading to tetanic muscle spasms. Release inhibited by botulinum toxin; binding to nicotinic ACh receptors inhibited by curare (a muscle paralytic agent) and to muscarinic ACh receptors by atropine. ACh levels decrease in certain brain areas in Alzheimer's disease; nicotinic ACh receptors destroyed in myasthenia gravis. Binding of nicotine to nicotinic receptors in the brain enhances dopamine release, which may account for the behavioral effects of nicotine in smokers.</p>

Classification of Neurotransmitters by Chemical Structure

Biogenic Amines			
Norepinephrine (NE)	<p>Excitatory or inhibitory depending on receptor type bound</p> <p>Indirect action via second messengers</p>	<p>CNS: brain stem, particularly in the locus coeruleus of the midbrain; limbic system; some areas of cerebral cortex</p> <p>PNS: main neurotransmitter of postganglionic neurons in the sympathetic nervous system</p>	<p>A "feel good" neurotransmitter. Release enhanced by amphetamines; removal from synapse blocked by tricyclic antidepressants [amitriptyline (Elavil) and others] and cocaine. Brain levels reduced by reserpine (an antihypertensive drug), leading to depression.</p>
Dopamine	<p>Excitatory or inhibitory depending on the receptor type bound</p> <p>Indirect action via second messengers</p>	<p>CNS: substantia nigra of midbrain; hypothalamus; the principal neurotransmitter of indirect motor pathways</p> <p>PNS: some sympathetic ganglia</p>	<p>A "feel good" neurotransmitter. Release enhanced by L-dopa and amphetamines; reuptake blocked by cocaine. Deficient in Parkinson's disease; dopamine neurotransmission increases in schizophrenia.</p>
Serotonin (5-HT)	<p>Mainly inhibitory</p> <p>Indirect action via second messengers; direct action at 5-HT₃ receptors</p>	<p>CNS: brain stem, especially midbrain; hypothalamus; limbic system; cerebellum; pineal gland; spinal cord</p>	<p>Plays a role in sleep, appetite, nausea, migraine headaches, and regulating mood. Drugs that block its uptake [fluoxetine (Prozac)] relieve anxiety and depression. Activity blocked by LSD and enhanced by ecstasy (MDMA).</p>

Classification of Neurotransmitters by Chemical Structure

Histamine	<p>Excitatory or inhibitory depending on receptor type bound</p> <p>Indirect action via second messengers</p>	CNS: hypothalamus	<p>Involved in wakefulness, appetite control, and learning and memory. Also a paracrine (local signal) released from stomach (causes acid secretion) and connective tissue mast cells (mediates inflammation and vasodilation).</p>
Amino Acids			
GABA (γ -aminobutyric acid)	<p>Generally inhibitory</p> <p>Direct and indirect actions via second messengers</p>	<p>CNS: cerebral cortex, hypothalamus, Purkinje cells of cerebellum, spinal cord, granule cells of olfactory bulb, retina</p>	<p>Principal inhibitory neurotransmitter in the brain; important in presynaptic inhibition at axoaxonal synapses. Inhibitory effects augmented by alcohol, antianxiety drugs of the benzodiazepine class (e.g., Valium), and barbiturates, impairing motor coordination. Substances that block its synthesis, release, or action induce convulsions.</p>

Classification of Neurotransmitters by Chemical Structure

Amino Acids, continued			
Glutamate	Generally excitatory Direct action	CNS: spinal cord; widespread in brain where it represents the major excitatory neurotransmitter	Important in learning and memory. The “stroke neurotransmitter”: excessive release produces excitotoxicity—neurons literally stimulated to death; most commonly caused by ischemia (oxygen deprivation, usually due to a blocked blood vessel).
Glycine	Generally inhibitory Direct action	CNS: spinal cord and brain stem, retina	Principal inhibitory neurotransmitter of the spinal cord. Strychnine blocks glycine receptors, resulting in uncontrolled convulsions and respiratory arrest.

Classification of Neurotransmitters by Chemical Structure

Peptides			
Endorphins, e.g., beta endorphin, dynorphin, enkephalins	Generally inhibitory Indirect action via second messengers	CNS: widely distributed in brain; hypothalamus; limbic system; pituitary; spinal cord	Natural opiates; inhibit pain by inhibiting substance P. Effects mimicked by morphine, heroin, and methadone.
Tachykinins: substance P, neurokinin A (NKA)	Excitatory Indirect action via second messengers	CNS: basal nuclei, midbrain, hypothalamus, cerebral cortex PNS: certain sensory neurons of dorsal root ganglia (pain afferents), enteric neurons	Substance P mediates pain transmission in the PNS. In the CNS, tachykinins are involved in respiratory and cardiovascular controls and in mood.
Somatostatin	Generally inhibitory Indirect action via second messengers	CNS: hypothalamus, septum, basal nuclei, hippocampus, cerebral cortex Pancreas	Often released with GABA. A gut-brain peptide. Inhibits growth hormone release.
Cholecystokinin (CCK)	Generally excitatory Indirect action via second messengers	Throughout CNS Small intestine	Involved in anxiety, pain, memory. A gut-brain peptide hormone. Inhibits appetite.

Classification of Neurotransmitters by Chemical Structure

Purines			
ATP	<p>Excitatory or inhibitory depending on receptor type bound</p> <p>Direct and indirect actions via second messengers</p>	<p>CNS: basal nuclei, induces Ca^{2+} wave propagation in astrocytes</p> <p>PNS: dorsal root ganglion neurons</p>	ATP released by sensory neurons (as well as that released by injured cells) provokes pain sensation.
Adenosine	<p>Generally inhibitory</p> <p>Indirect action via second messengers</p>	Throughout CNS and PNS	Caffeine (coffee), theophylline (tea), and theobromine (chocolate) stimulate by blocking brain adenosine receptors. May be involved in sleep-wake cycle and terminating seizures. Dilates arterioles, increasing blood flow to heart and other tissues as needed.

Classification of Neurotransmitters by Chemical Structure

Gases and Lipids

Nitric oxide (NO)	Excitatory or inhibitory Indirect action via second messengers	CNS: brain, spinal cord PNS: adrenal gland; nerves to penis	Its release potentiates stroke damage. Some types of male impotence treated by enhancing NO action [e.g., with sildenafil (Viagra)].
Carbon monoxide (CO)	Excitatory or inhibitory Indirect action via second messengers	Brain and some neuromuscular and neuroglandular synapses	
Endocannabinoids, e.g., 2-arachidonoylglycerol, anandamide	Inhibitory Indirect action via second messengers	Throughout CNS	Involved in memory (as a retrograde messenger), appetite control, nausea and vomiting, neuronal development. Receptors activated by THC, the principal active ingredient of cannabis. Receptors also found on immune cells.

Classification of Neurotransmitters by Function

- (1) Inhibitory or excitatory (or both)

- (2) Direct or indirect action.
 - Direct acting neurotransmitters bind to and open ion channels.
 - Indirect acting neurotransmitters act through second messengers.
 - Neuro-modulators also act indirectly presynaptically or postsynaptically to change synaptic strength.

Neurotransmitter Receptors

Neurotransmitter receptors are either

- Channel-linked receptors that open ion channels, leading to fast changes in membrane potential, or
 - G protein–coupled receptors that oversee slow synaptic responses mediated by G proteins and intracellular second messengers.
- Second messengers most often activate kinases, which in turn act on ion channels or activate other proteins.

Channel-linked receptors

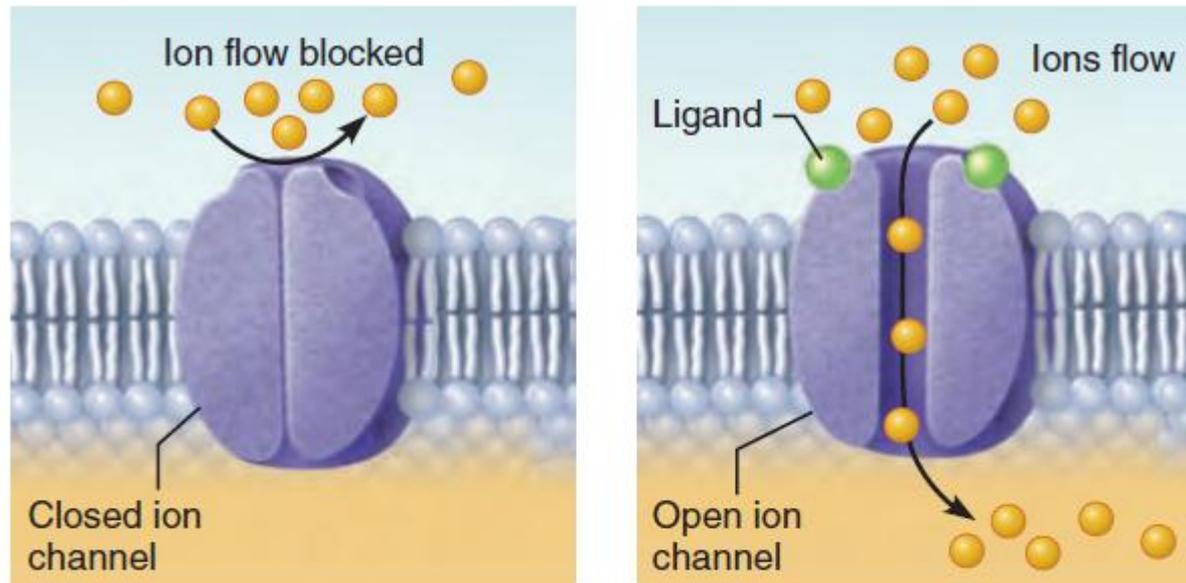
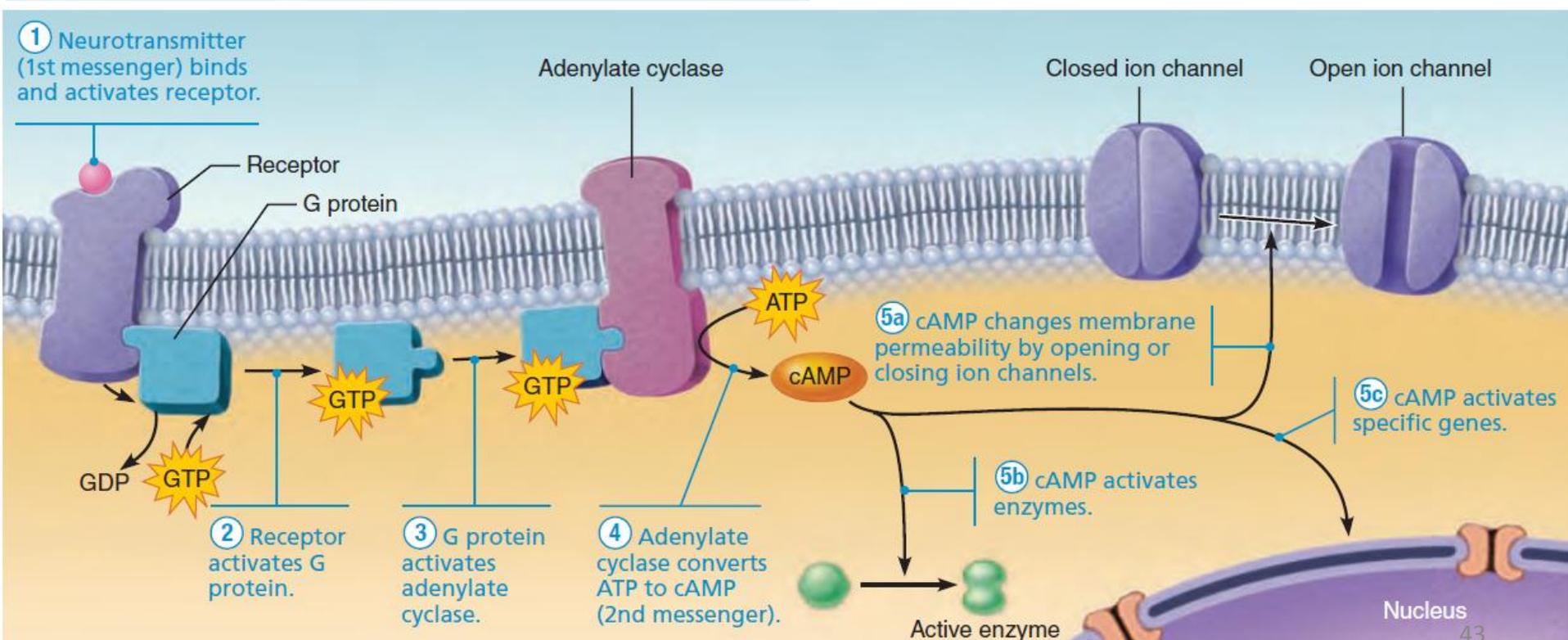
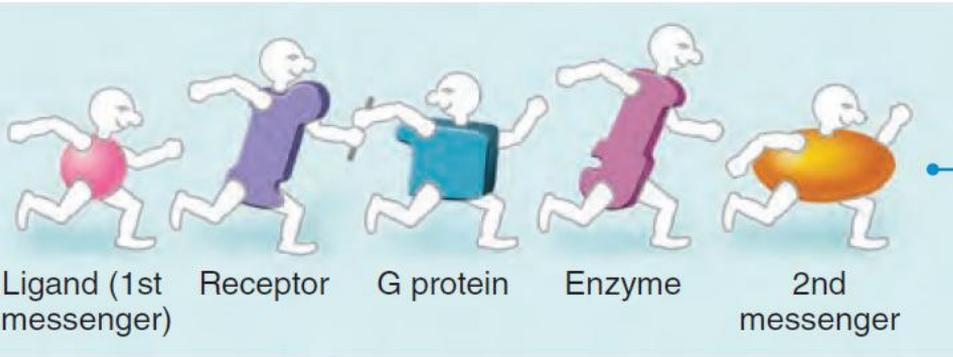


Figure 11.20 Direct neurotransmitter receptor mechanism: **Channel-linked receptors.** These chemically gated ion channels promote rapid synaptic transmission. In this case, ligand binding directly opens the channel.

G protein-coupled receptors



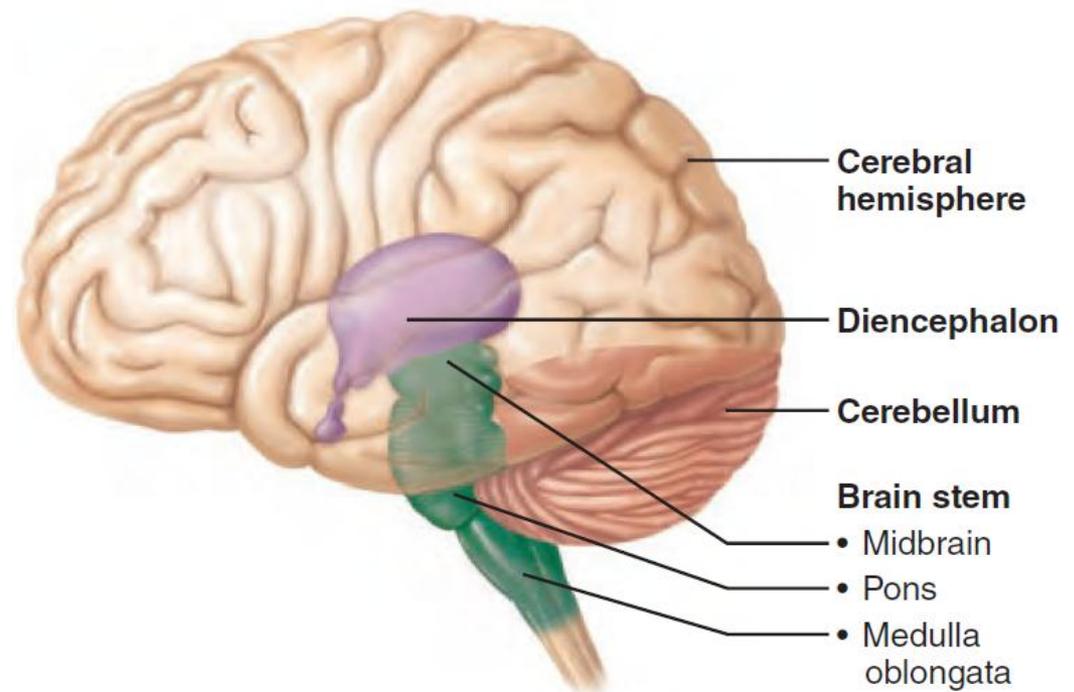
Patterns of Neural Processing

- In serial processing, one neuron stimulates the next in sequence, producing specific, predictable responses, as in spinal reflexes.
- A reflex is a rapid, involuntary motor response to a stimulus.
- Reflexes are mediated over neural pathways called reflex arcs.
- **The minimum number of elements in a reflex arc is five:** receptor, sensory neuron, integration center, motor neuron, and effector.

The Brain Regions and Organization

Adult brain is divided into

- The cerebral hemispheres
- Diencephalon (composed of the thalamus, the hypothalamus, and the pituitary gland)
- Brain stem
- Cerebellum



The Brain Regions and Organization

- The cerebral hemispheres and cerebellum have gray matter nuclei surrounded by white matter and an outer cortex of gray matter.
- The diencephalon and brain stem lack a cortex

The brain ventricles

- The brain contains four ventricles filled with cerebrospinal fluid.
- The lateral ventricles are in the cerebral hemispheres
- The third ventricle is in the diencephalon
- The fourth ventricle is between the brain stem and the cerebellum and connects with the central canal of the spinal cord.

The brain ventricles

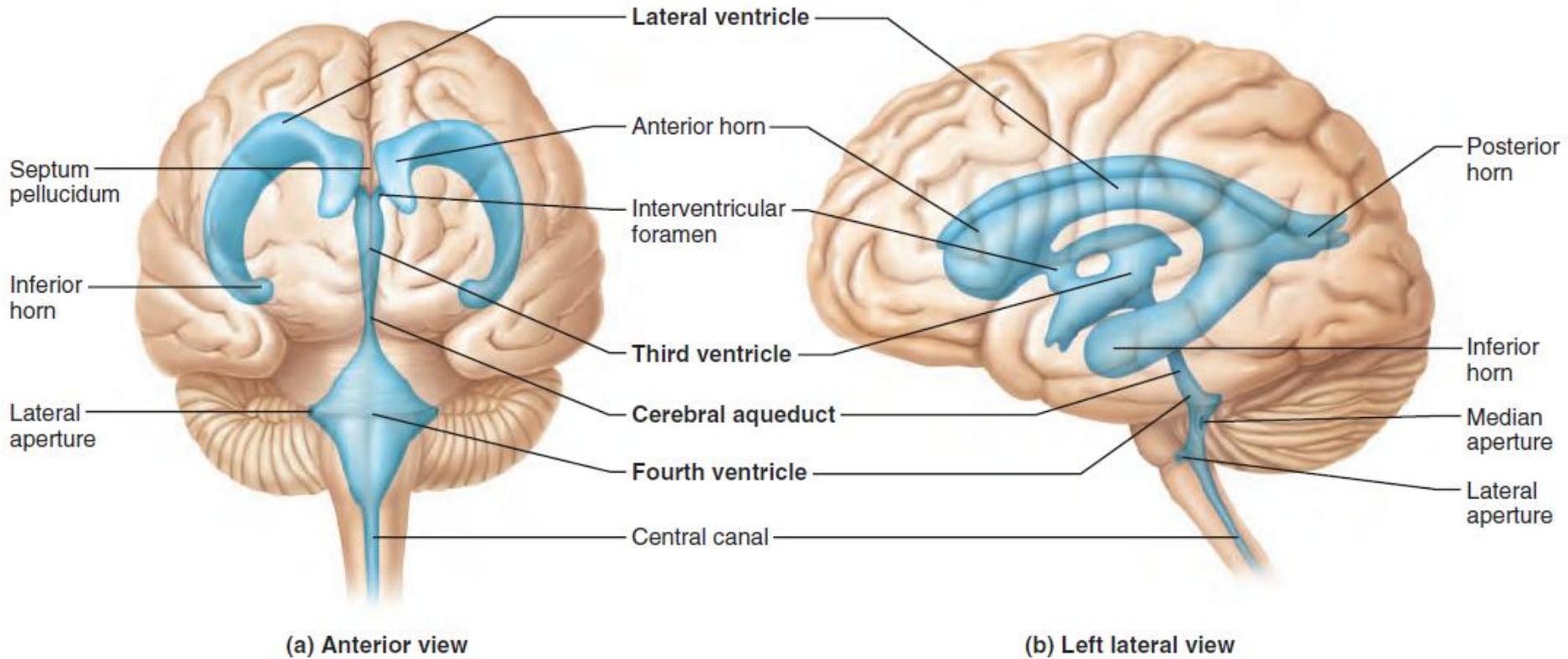


Figure 12.3 Ventricles of the brain. Different regions of the large lateral ventricles are labeled anterior horn, posterior horn, and inferior horn.

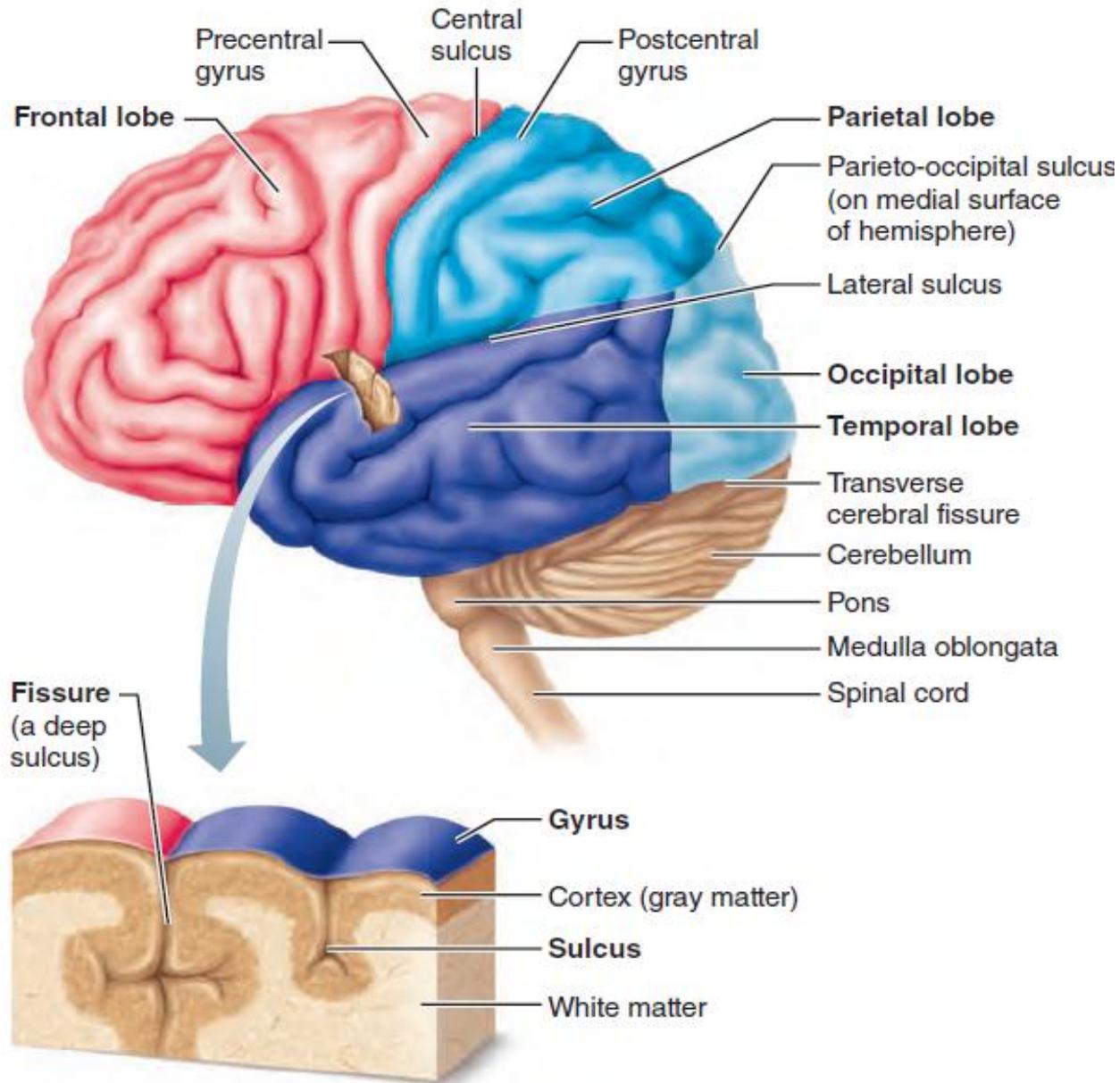
Cerebral Hemispheres

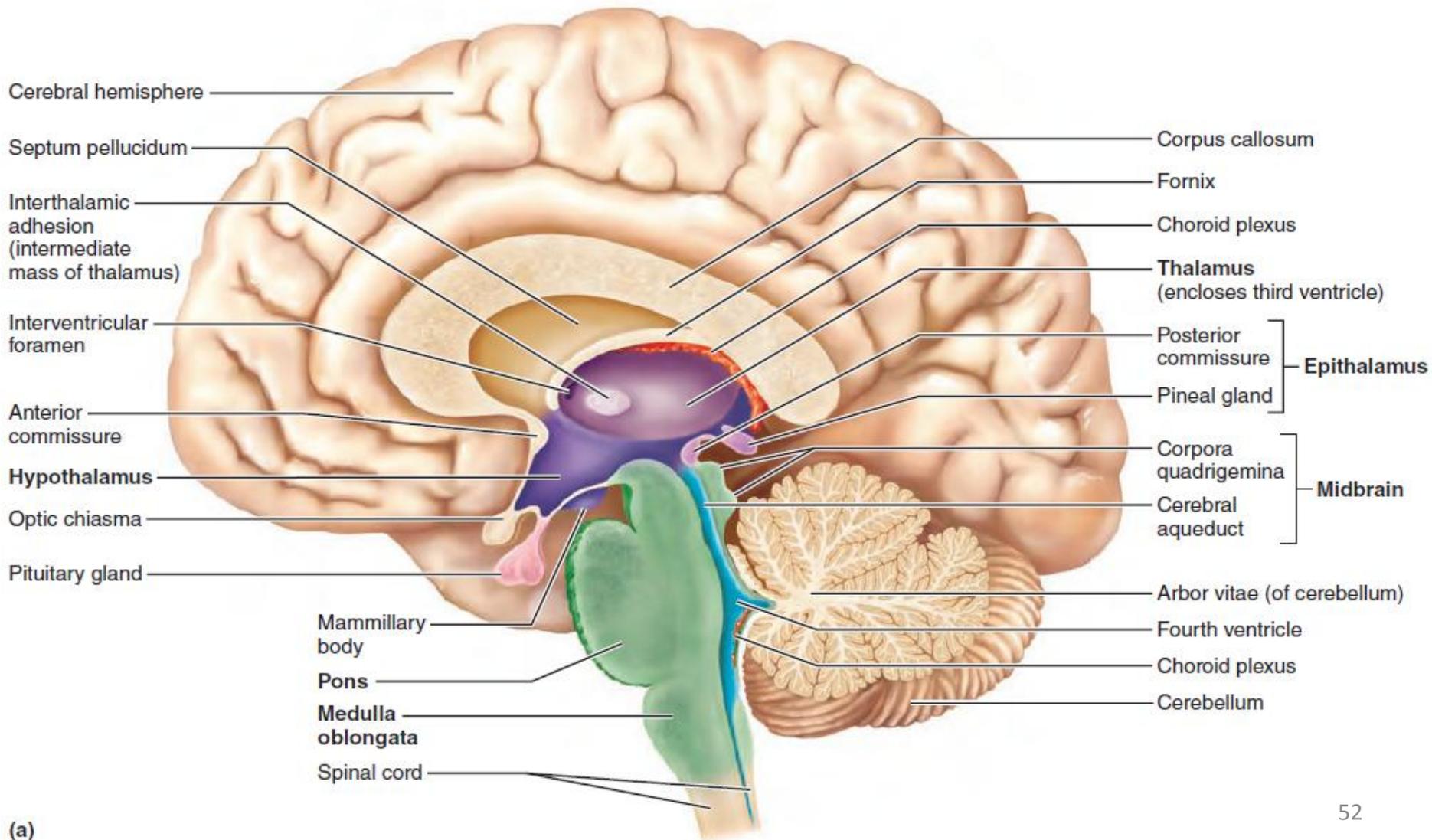
- The two cerebral hemispheres exhibit gyri, sulci, and fissures.
- The longitudinal fissure partially separates the hemispheres
- Other fissures or sulci subdivide each hemisphere into lobes.
- Each cerebral hemisphere consists of the cerebral cortex, the cerebral white matter, and basal nuclei (ganglia).

Cerebral Hemispheres

- Each cerebral hemisphere receives sensory impulses from, and dispatches motor impulses to, the opposite side of the body.
- The body is represented in an upside-down fashion in the sensory and motor cortices.

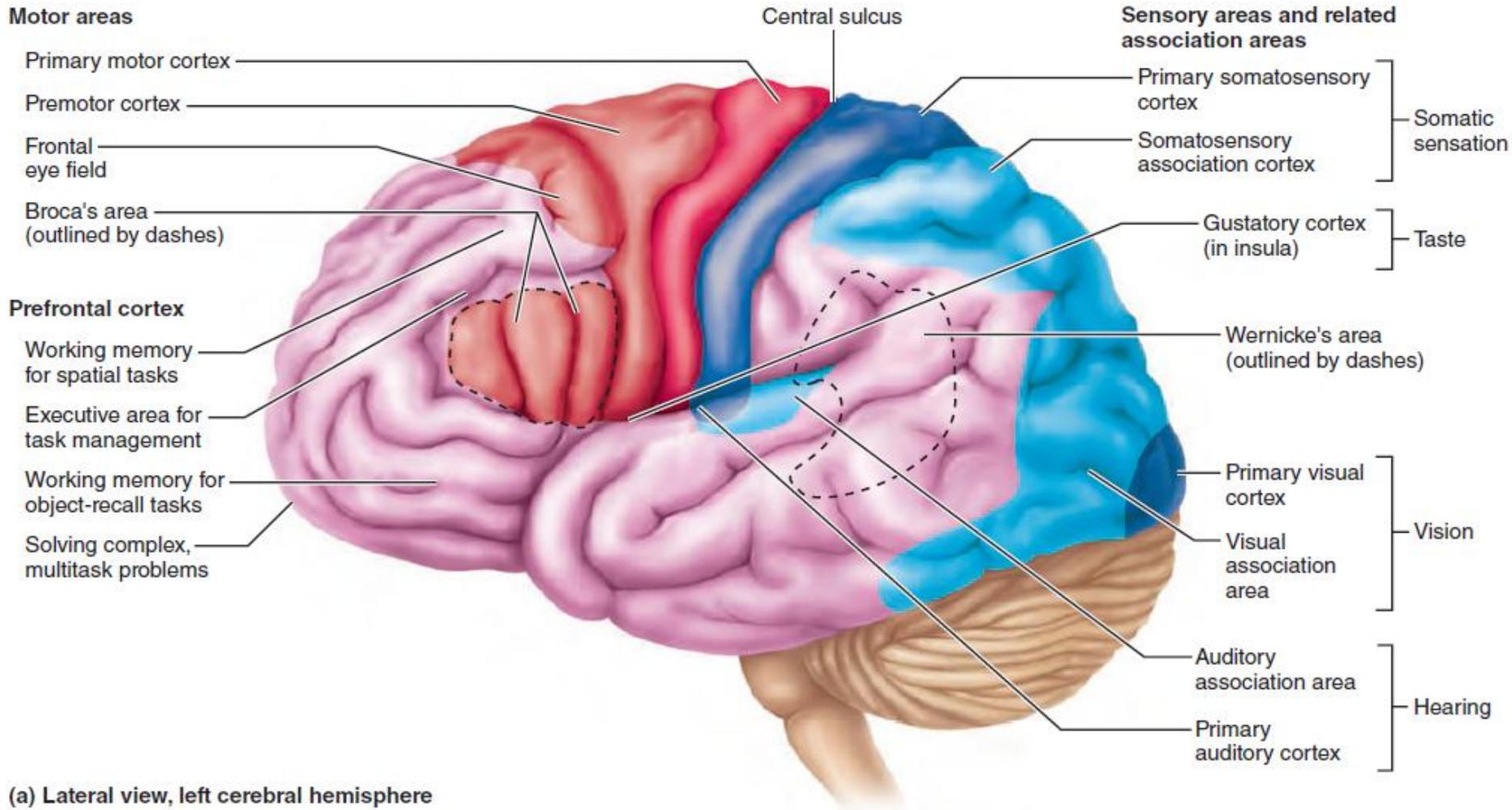
Functional areas of the cerebral cortex include





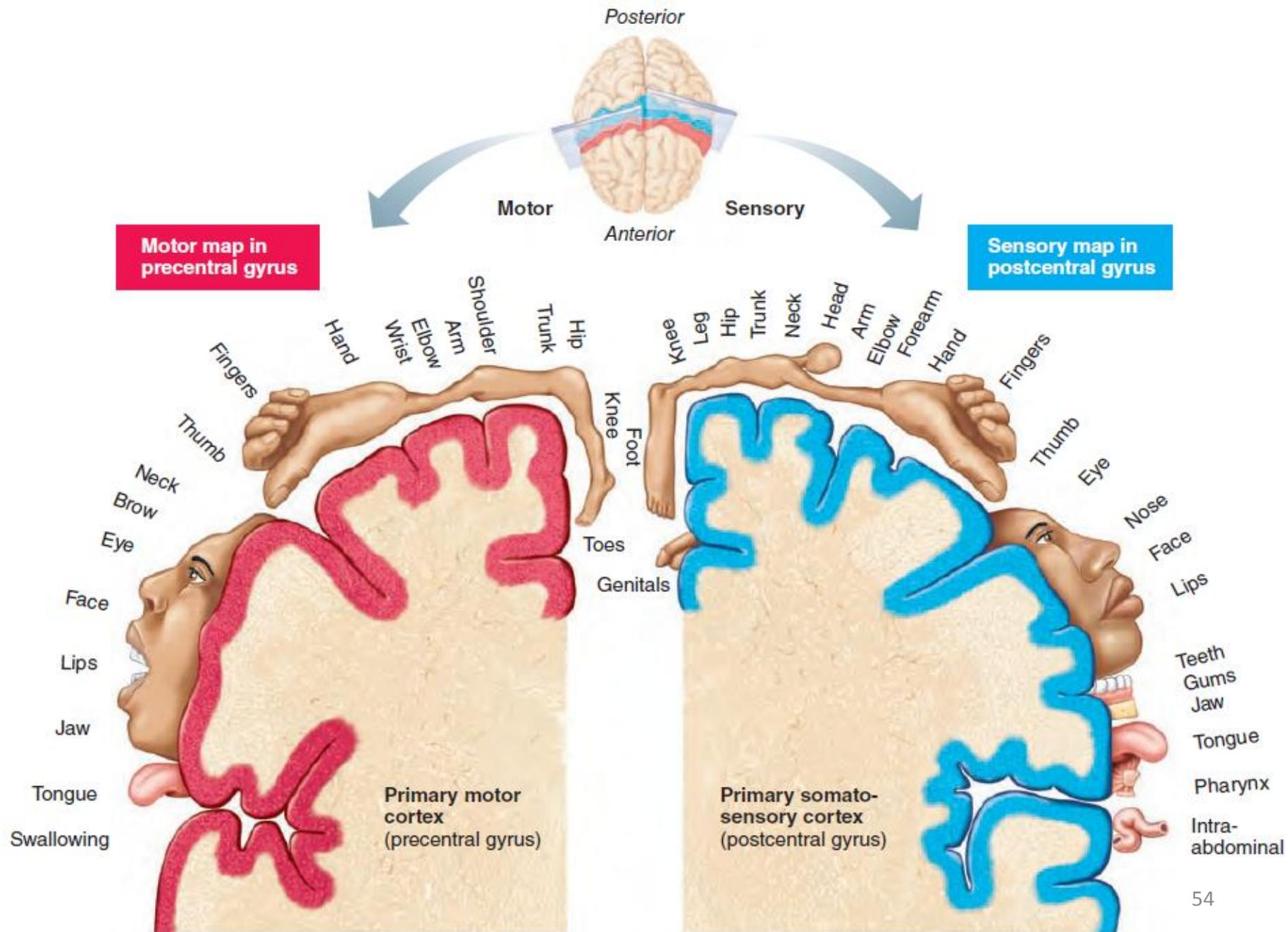
(a)

Functional areas of the cerebral cortex include



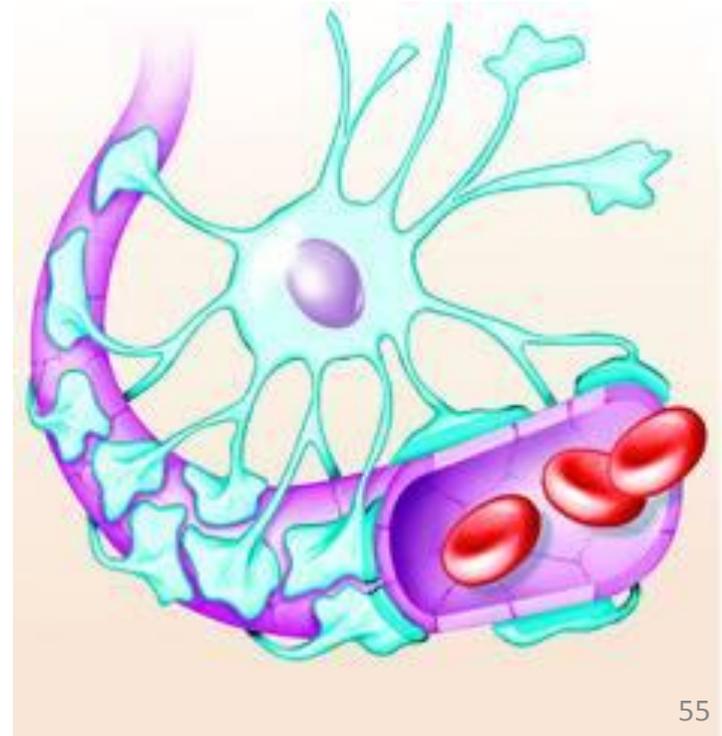
■ Primary motor cortex
 ■ Motor association cortex
 ■ Primary sensory cortex
 ■ Sensory association cortex
 ■ Multimodal association cortex

Body maps in the primary motor cortex and somatosensory cortex of the cerebrum



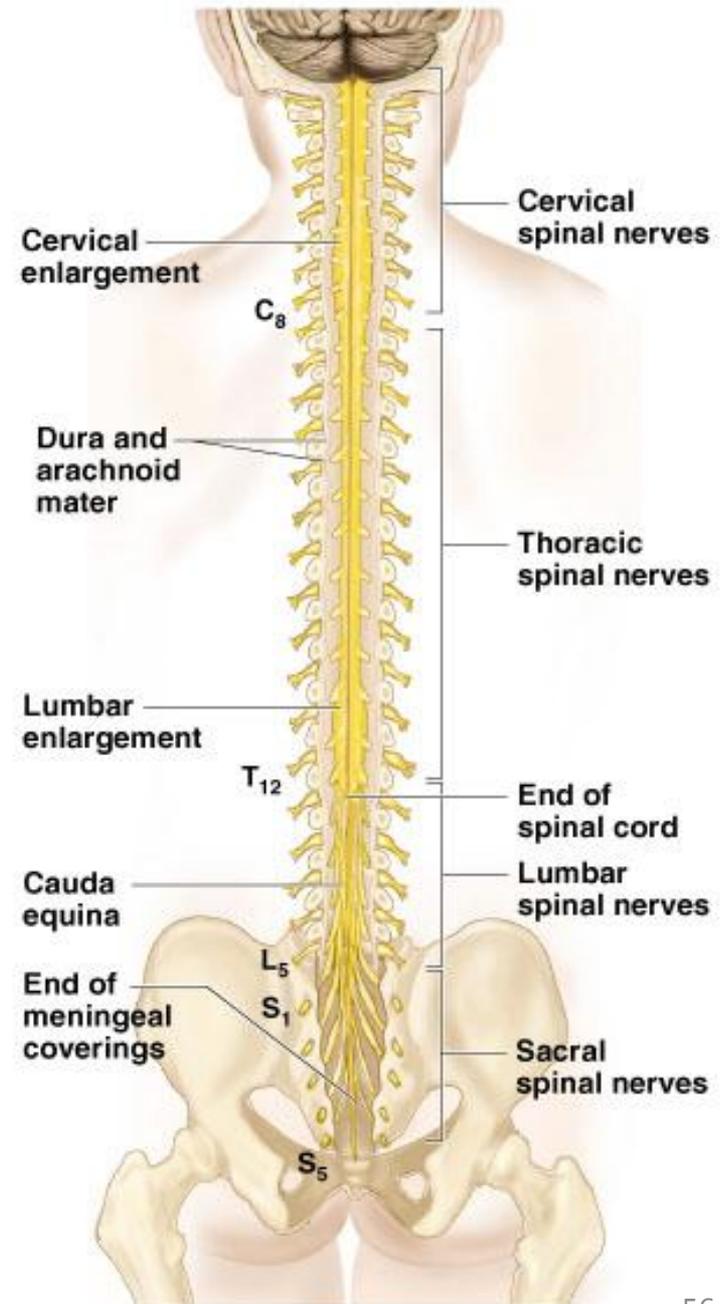
Blood Brain Barrier

- Includes the least permeable capillaries of the body
- Excludes many potentially harmful substances
- Useless against some substances:
 1. Fats and fat soluble molecules
 2. Respiratory gases
 3. Alcohol
 4. Nicotine
 5. Anesthesia

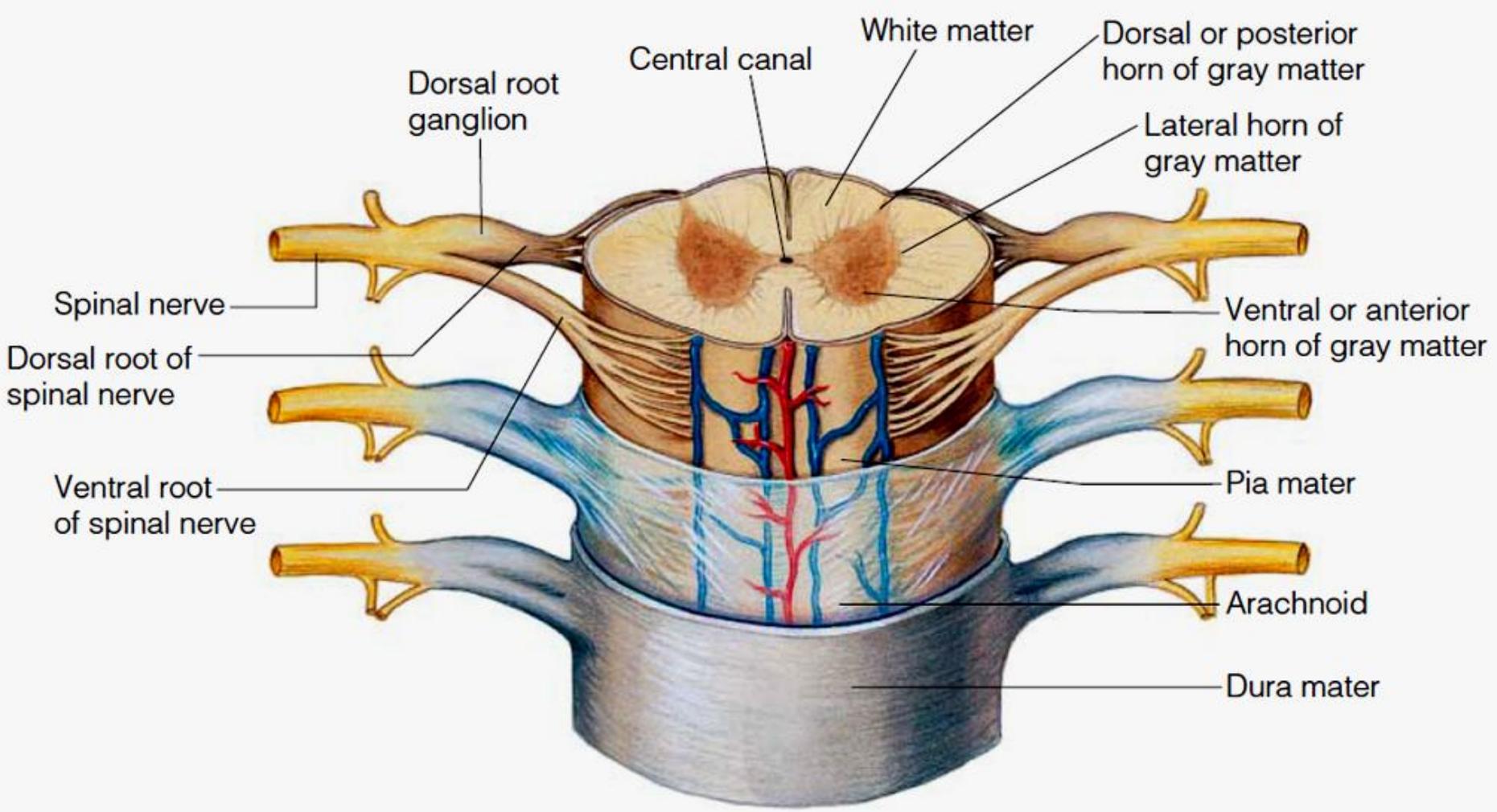


Spinal Cord

- Extends from the medulla oblongata to the region of T12
- Below T12 is the cauda equina (a collection of spinal nerves)
- Enlargements occur in the cervical and lumbar regions



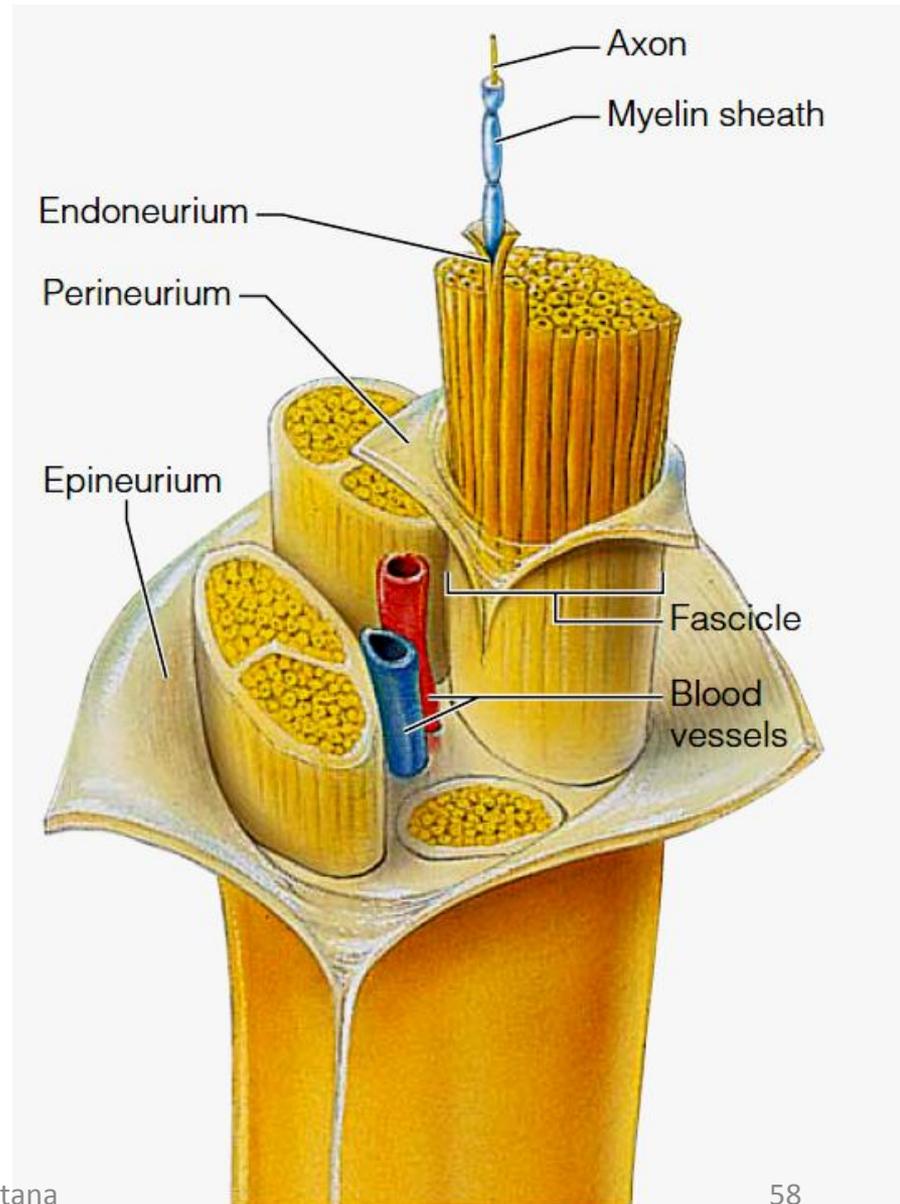
Spinal Cord Anatomy



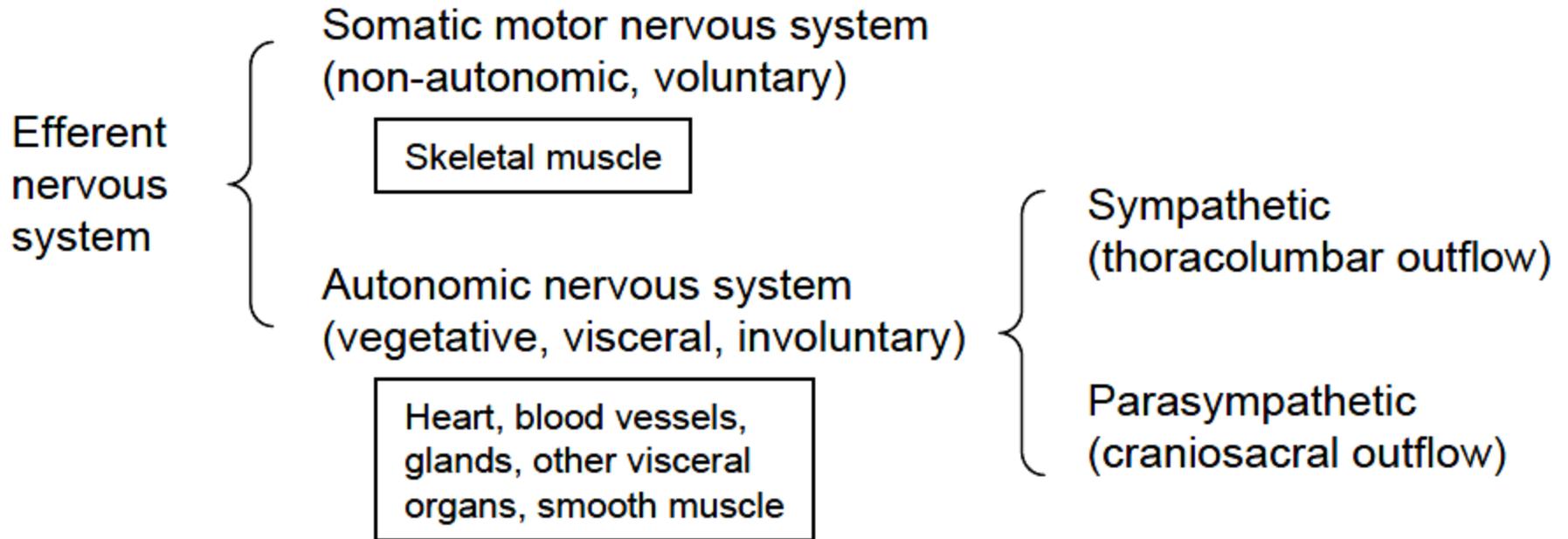
Peripheral Nervous System

Structure of a Nerve:

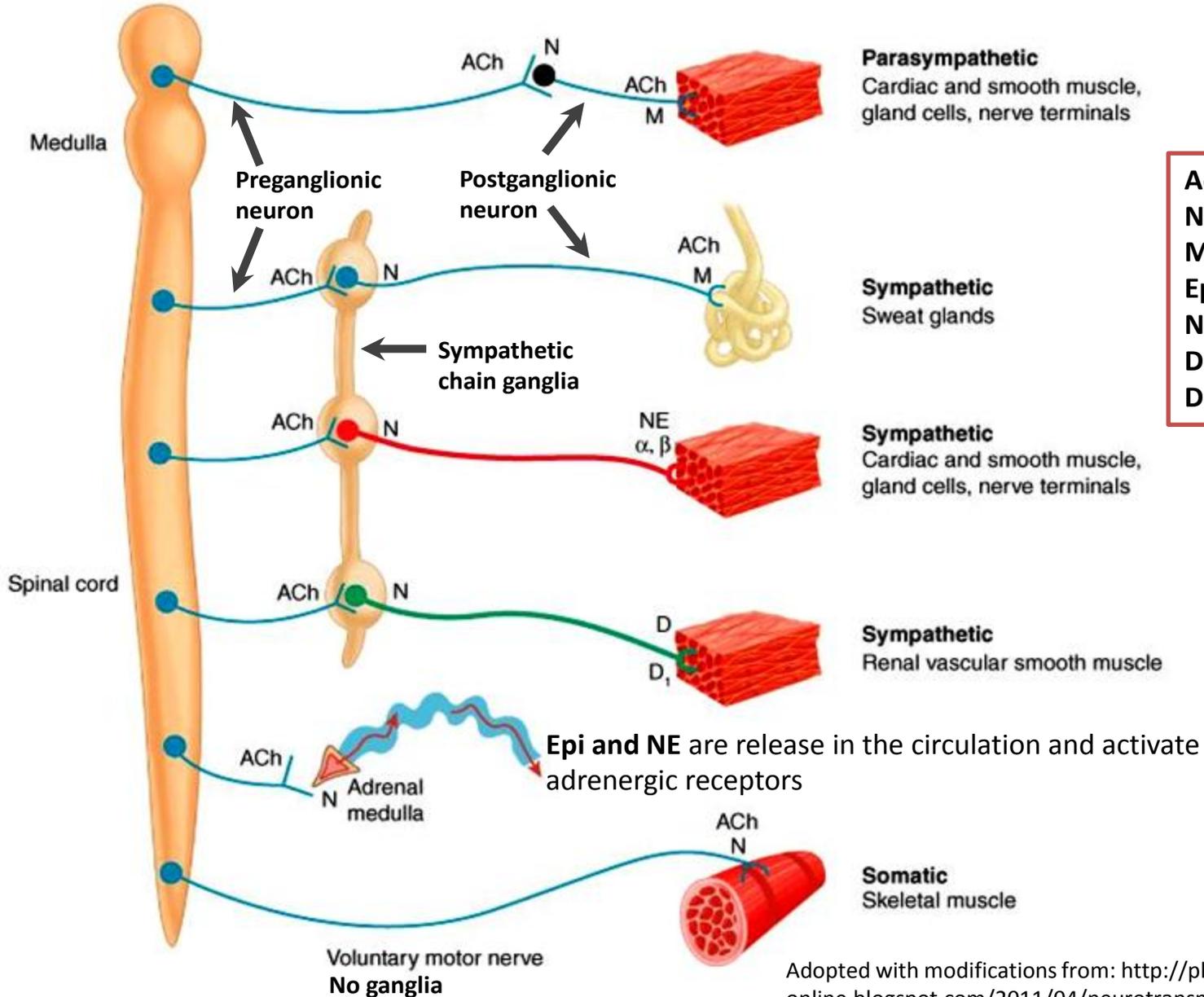
- Endoneurium surrounds each fiber
- Groups of fibers are bound into fascicles by perineurium
- Fascicles are bound together by epineurium



Peripheral Nervous system's branches



Comparison of efferent nervous system branches



Ach: acetylcholine
N: Nicotinic receptors
M: Muscarinic receptors
Epi: Epinephrine
NE: Norepinephrine
D: dopamine
D1: Type 1 D receptors

Central Nervous System

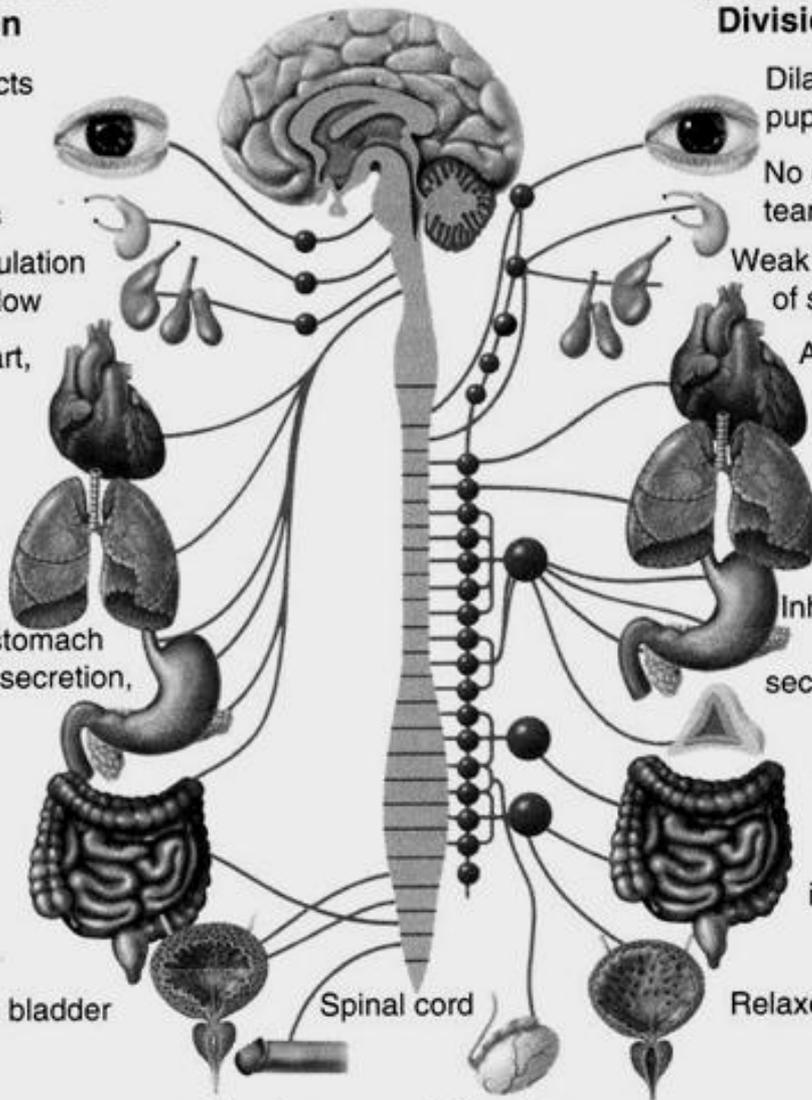
Brain

Parasympathetic Division

- Constricts pupil
- Stimulates tear glands
- Strong stimulation of salivary flow
- Inhibits heart, dilates arterioles
- Constricts bronchi
- Stimulates stomach motility and secretion, stimulates pancreas
- Stimulates intestinal motility
- Contracts bladder

Sympathetic Division

- Dilates pupil
- No effect on tear glands
- Weak stimulation of salivary flow
- Accelerates heart, constricts arterioles
- Dilates bronchi
- Inhibits stomach motility and secretion, inhibits pancreas and adrenals
- Inhibits intestinal motility
- Relaxes bladder



Stimulates erection

Stimulates ejaculation