Overview of Nervous System

- **endocrine** and **nervous system** maintain internal coordination
  - **endocrine system** - communicates by means of chemical messengers (**hormones**) secreted into to the blood
  - **nervous system** - employs electrical and chemical means to send messages from cell to cell
- **nervous system** carries out its task in **three basic steps**:
  - sense organs **receive information** about changes in the body and the external environment, and **transmits coded messages** to the spinal cord and the brain
  - brain and spinal cord **processes this information**, relates it to past experiences, and determine what response is appropriate to the circumstances
  - brain and spinal cord **issue commands** to muscles and gland cells to carry out such a response

Two Major Anatomical Subdivisions of Nervous System

- **central nervous system** (CNS)
  - brain and spinal cord enclosed in bony coverings
    - enclosed by cranium and vertebral column

- **peripheral nervous system** (PNS)
  - all the nervous system except the brain and spinal cord
  - composed of **nerves** and **ganglia**
    - **nerve** – a bundle of nerve fibers (axons) wrapped in fibrous connective tissue
    - **ganglion** – a knot-like swelling in a nerve where neuron cell bodies are concentrated

Subdivisions of Nervous System

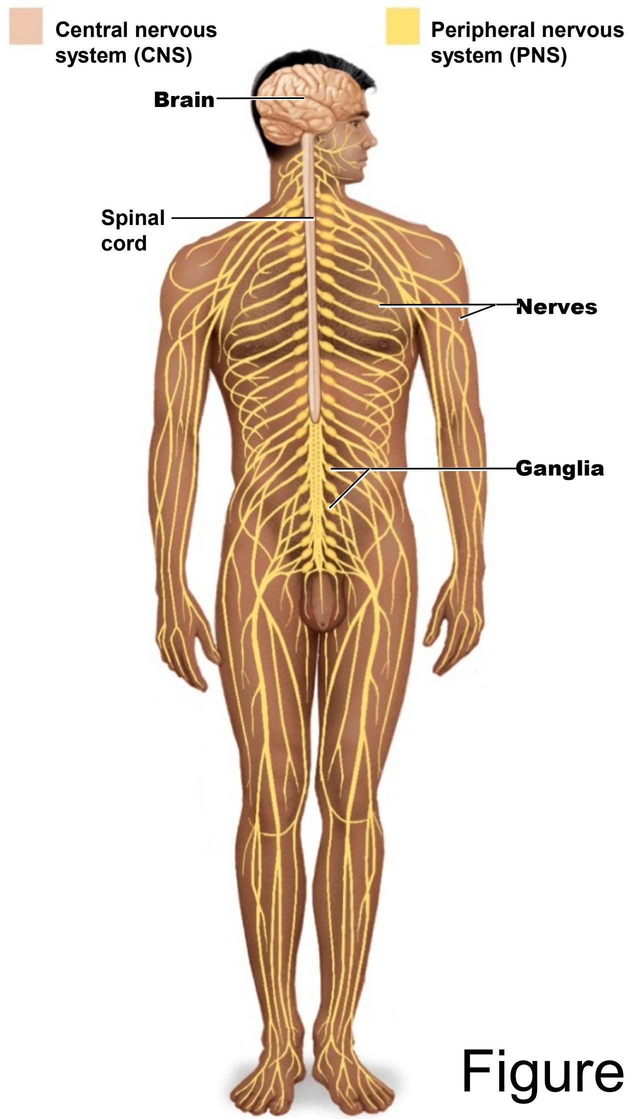


Figure 12.1

Sensory Divisions of PNS

- **sensory (afferent) division** – carries sensory signals from various receptors to the CNS
  - informs the CNS of stimuli within or around the body
  - **somatic sensory division** – carries signals from receptors in the skin, muscles, bones, and joints
  - **visceral sensory division** – carries signals from the viscera of the thoracic and abdominal cavities
    - heart, lungs, stomach, and urinary bladder

Motor Divisions of PNS

- **motor (efferent) division** – carries signals from the CNS to gland and muscle cells that carry out the body's response
  - **somatic motor division** – carries signals to skeletal muscles
    - output produces muscular contraction as well as **somatic reflexes** – involuntary muscle contractions
  - **visceral motor division** (**autonomic nervous system**) - carries signals to glands, cardiac muscle, and smooth muscle
    - involuntary, and responses of this system and its receptors are **visceral reflexes**
    - **sympathetic division**
      - tends to arouse body for action
      - accelerating heart beat and respiration, while inhibiting digestive and urinary systems
    - **parasympathetic division**
      - tends to have calming effect
      - slows heart rate and breathing
      - stimulates digestive and urinary systems

Subdivisions of Nervous System

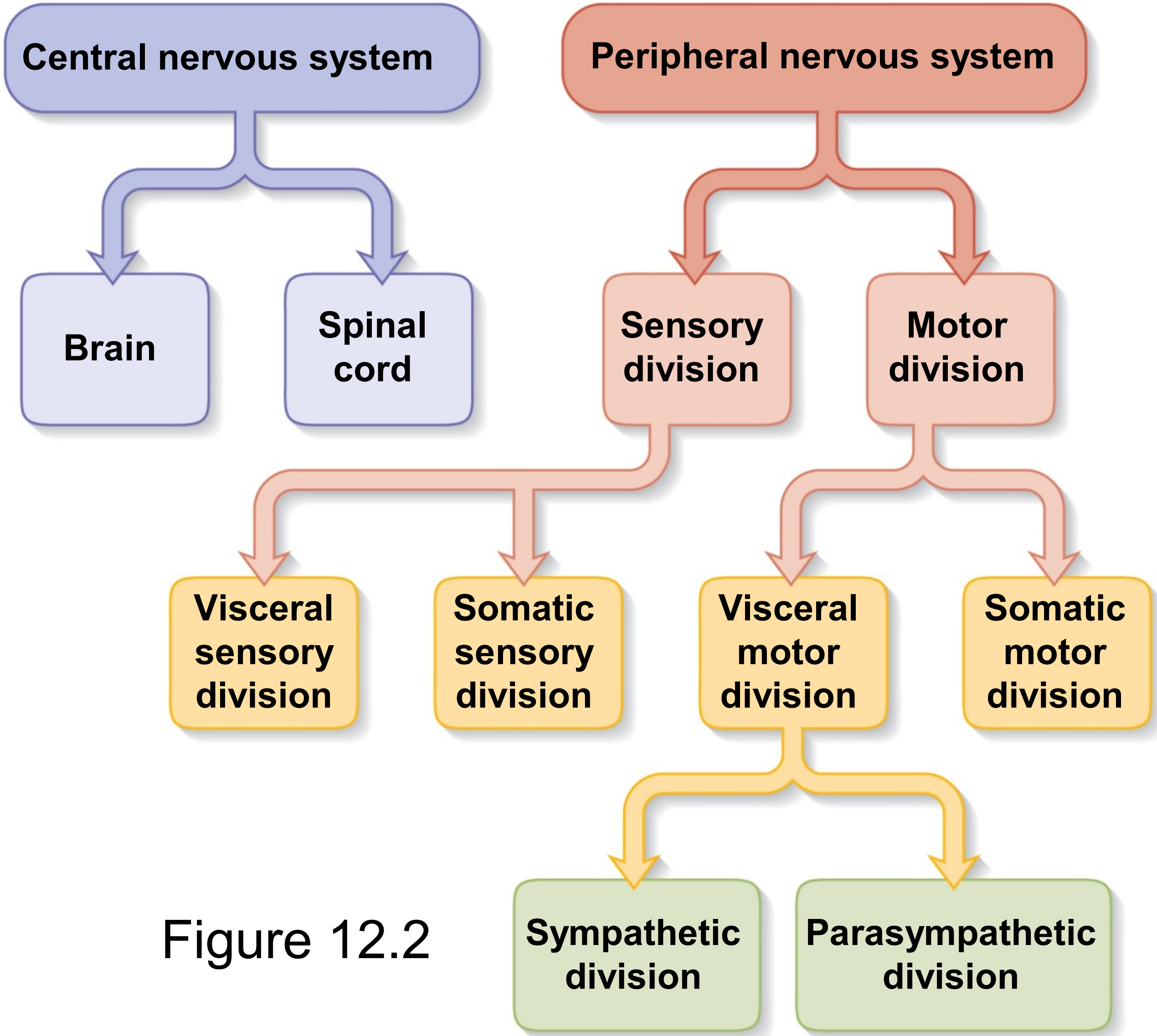


Figure 12.2

Universal Properties of Neurons

- **excitability** (**irritability**)
  - respond to environmental changes called **stimuli**
- **conductivity**
  - neurons respond to stimuli by producing electrical signals that are quickly conducted to other cells at distant locations
- **secretion**
  - when electrical signal reaches end of nerve fiber, a chemical **neurotransmitter** is secreted that crosses the gap and stimulates the next cell

Functional Types of Neurons

- **sensory** (**afferent**) **neurons**
  - specialized to detect stimuli
  - transmit information about them to the CNS
    - begin in almost every organ in the body and end in CNS
    - **afferent** – conducting signals toward CNS
- **interneurons** (**association**) **neurons**
  - lie entirely within the CNS
  - receive signals from many neurons and carry out the **integrative function**
    - process, store, and retrieve information and 'make decisions' that determine how the body will respond to stimuli
  - 90% of all neurons are **interneurons**
  - lie between, and interconnect the incoming sensory pathways, and the outgoing motor pathways of the CNS
- **motor** (**efferent**) **neuron**
  - send signals out to muscles and gland cells (the **effectors**)
    - **motor** because most of them lead to muscles
    - **efferent** neurons conduct signals away from the CNS

Functional Classes of Neurons

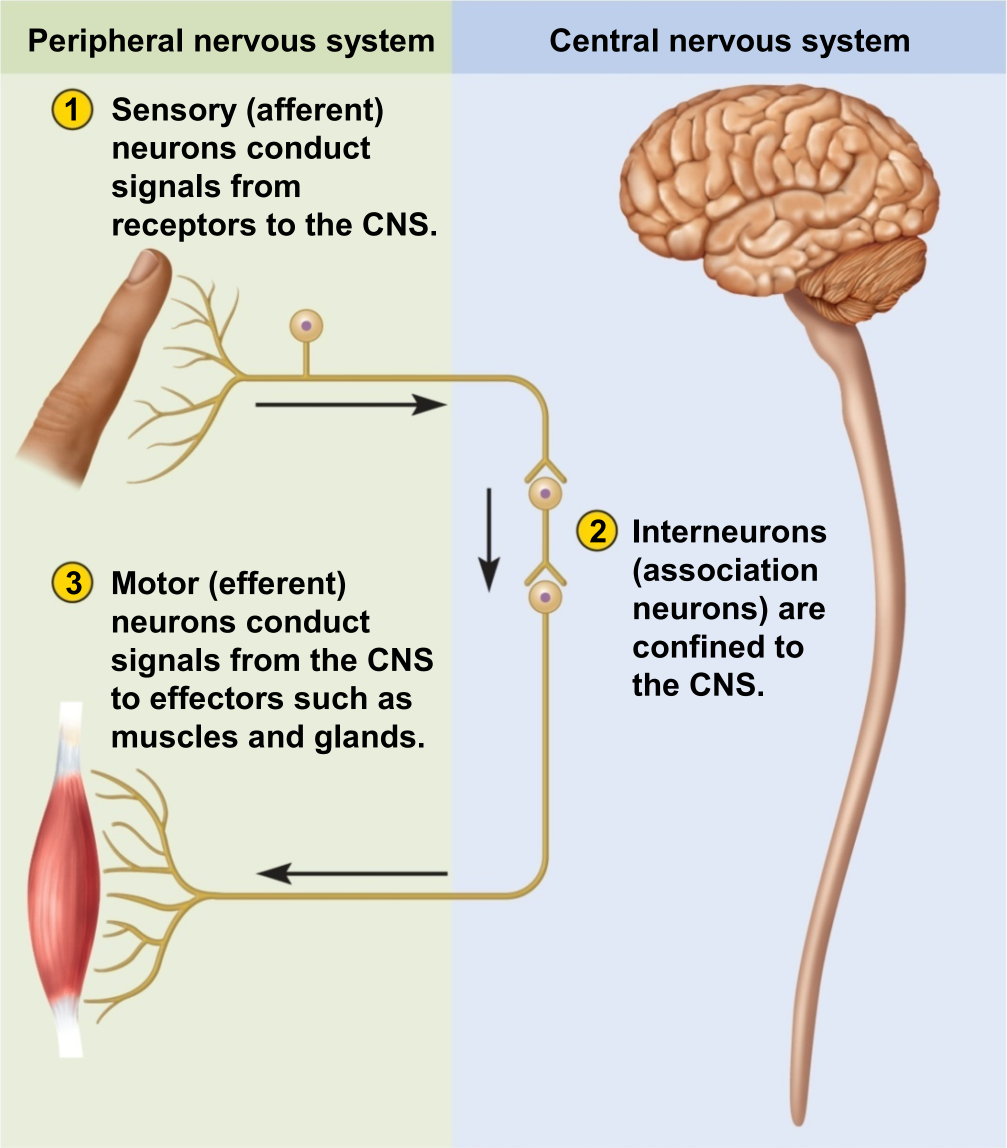
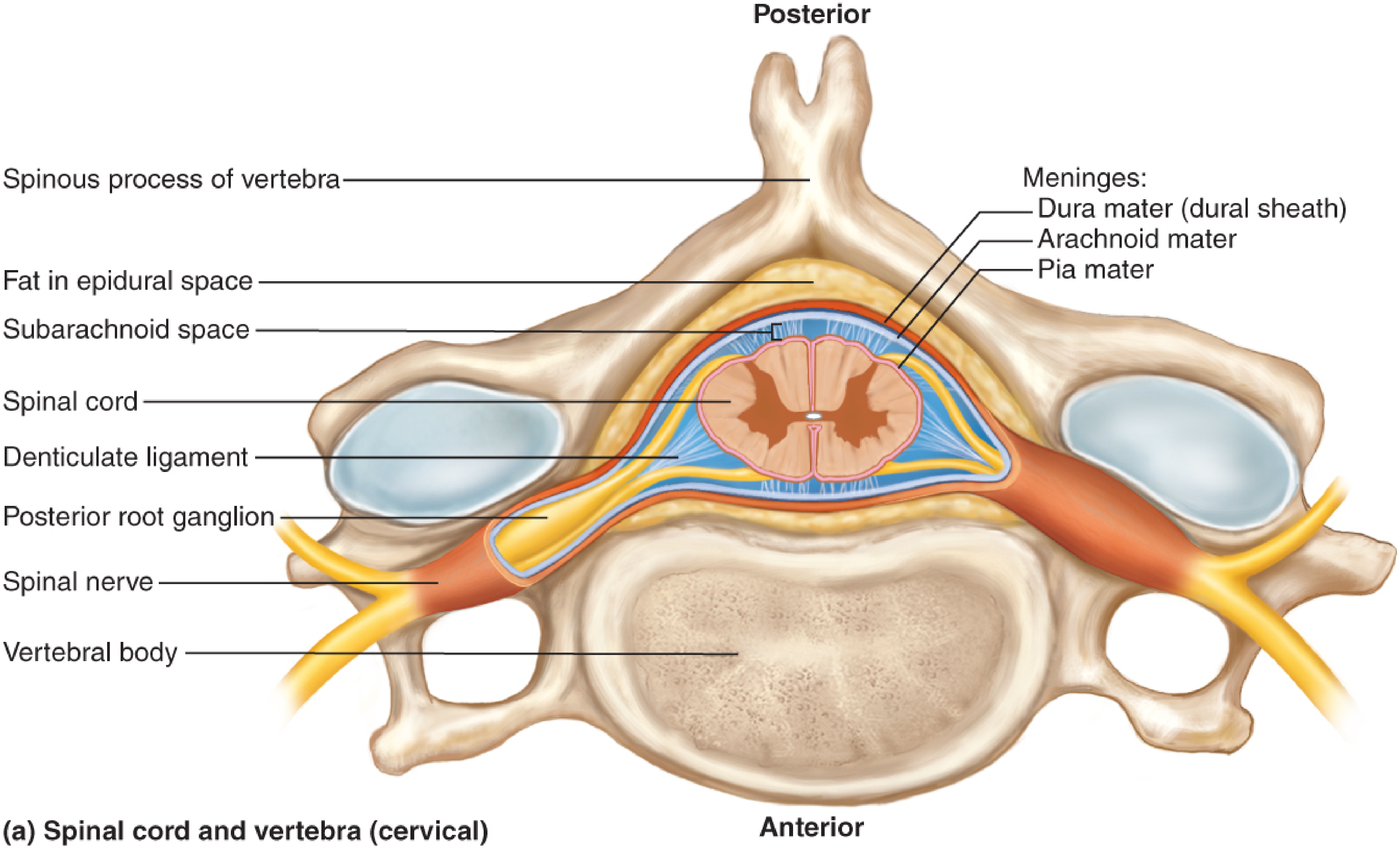
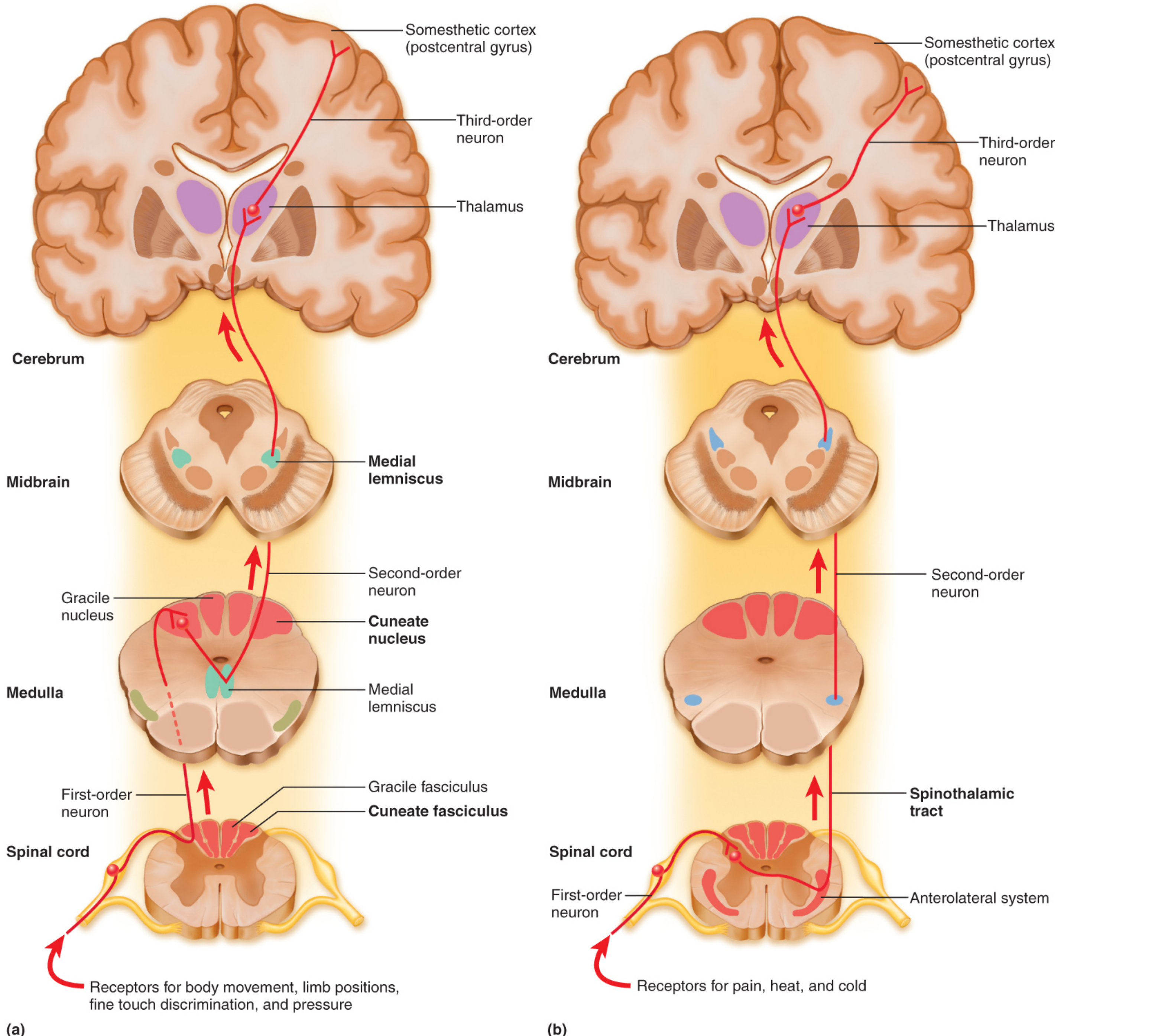
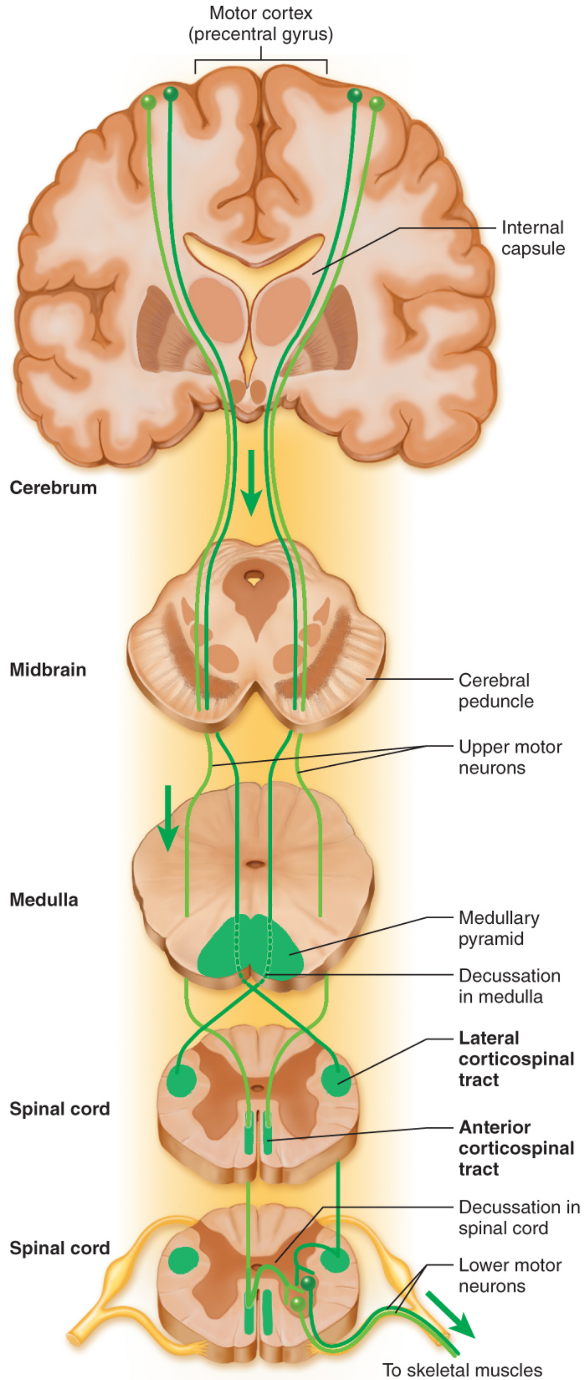


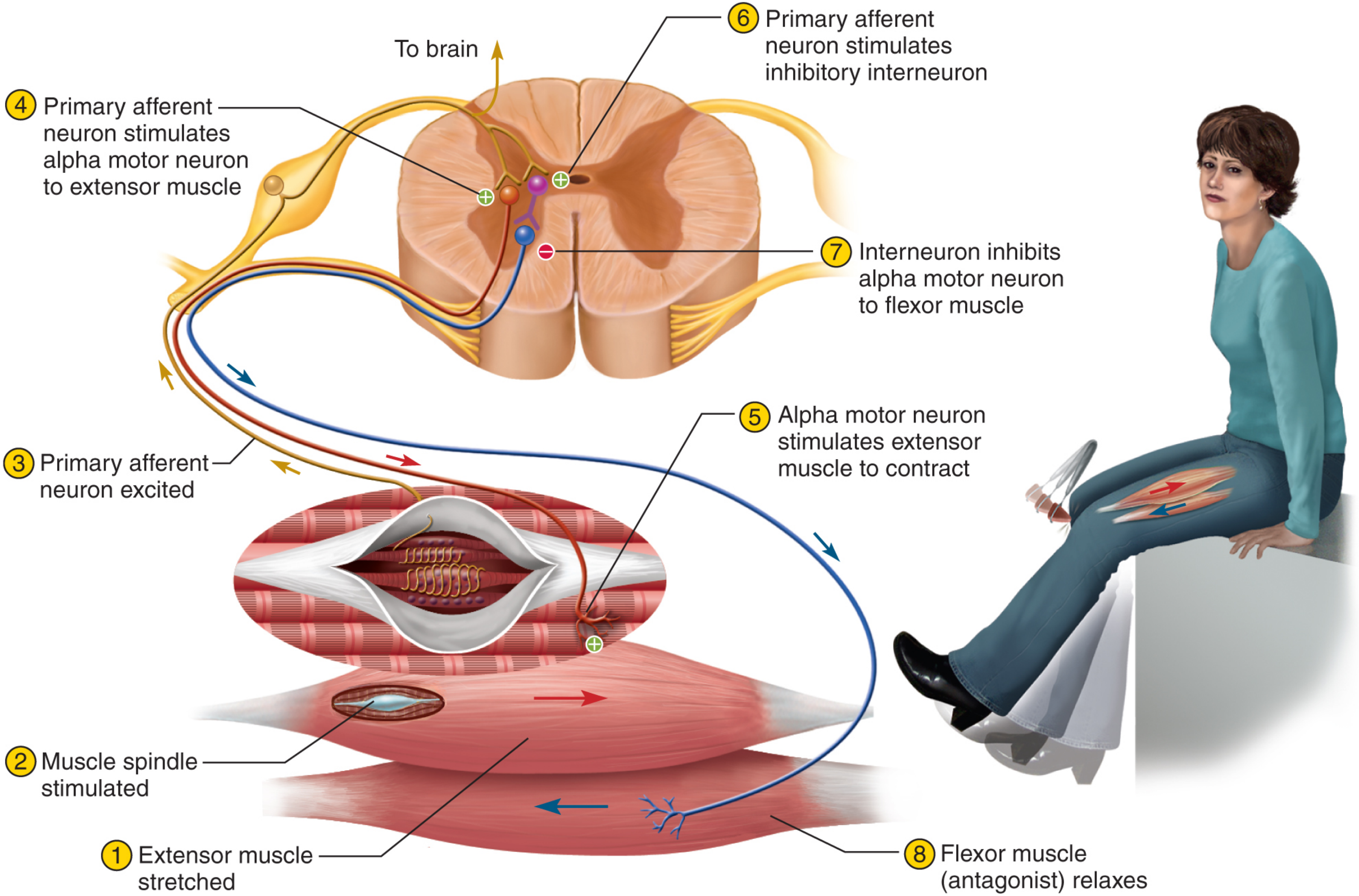
Figure 12.3

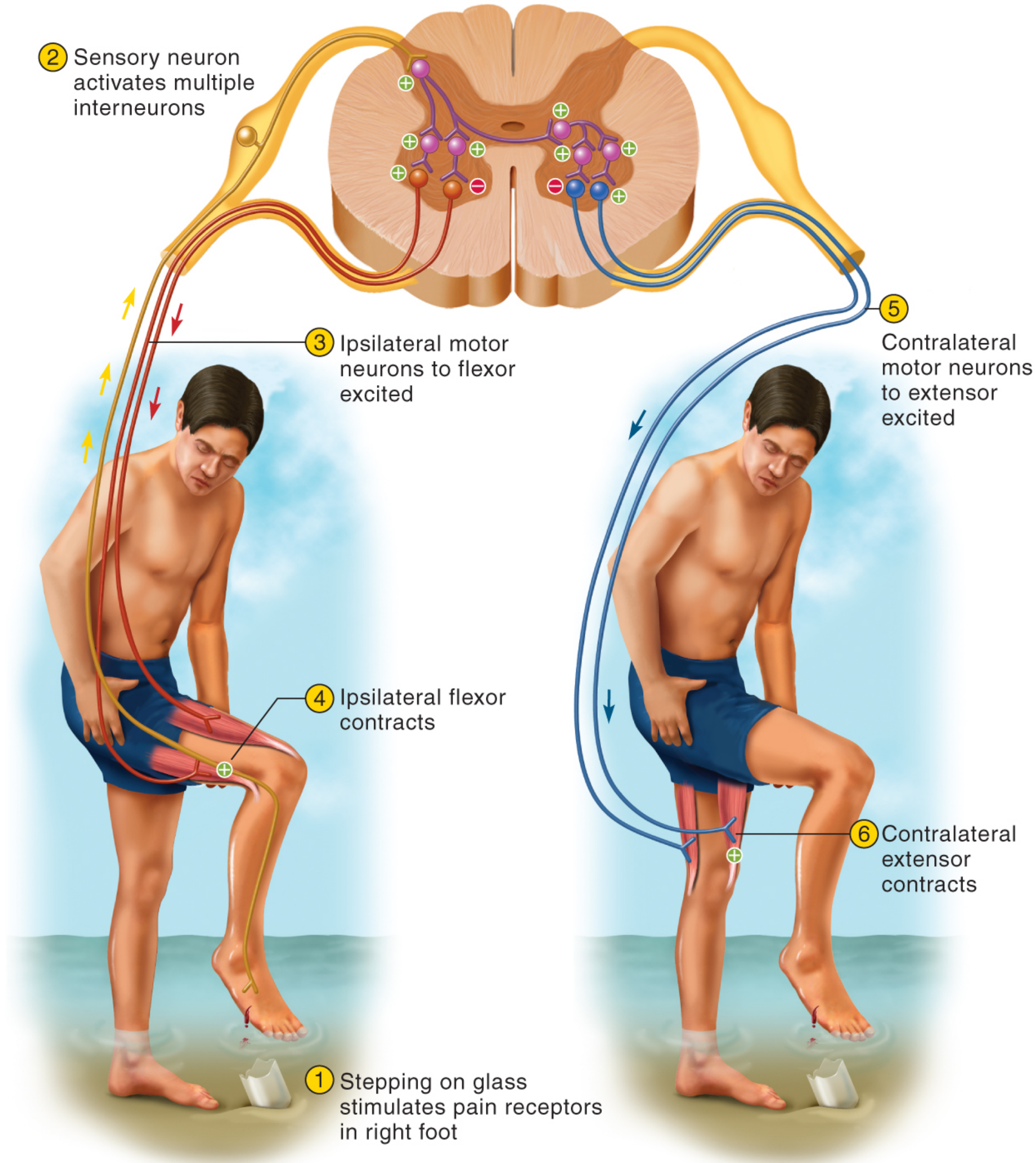


(a) Spinal cord and vertebra (cervical)


Somesthetic cortex
(postcentral gyrus)
Third-order
neuron
Thalamus
Cerebrum
Midbrain
Medial
lemniscus
Second-order
neuron
Gracile
nucleus
Cuneate
nucleus
Medulla
Medial
lemniscus
First-order
neuron
Gracile fasciculus
Cuneate fasciculus
Spinal cord
Receptors for body movement, limb positions,
fine touch discrimination, and pressure
(a)
Somesthetic cortex
(postcentral gyrus)
Third-order
neuron
Thalamus
Cerebrum
Midbrain
Second-order
neuron
Medulla
Spinothalamic
tract
Spinal cord
First-order
neuron
Anterolateral system
Receptors for pain, heat, and cold
(b)

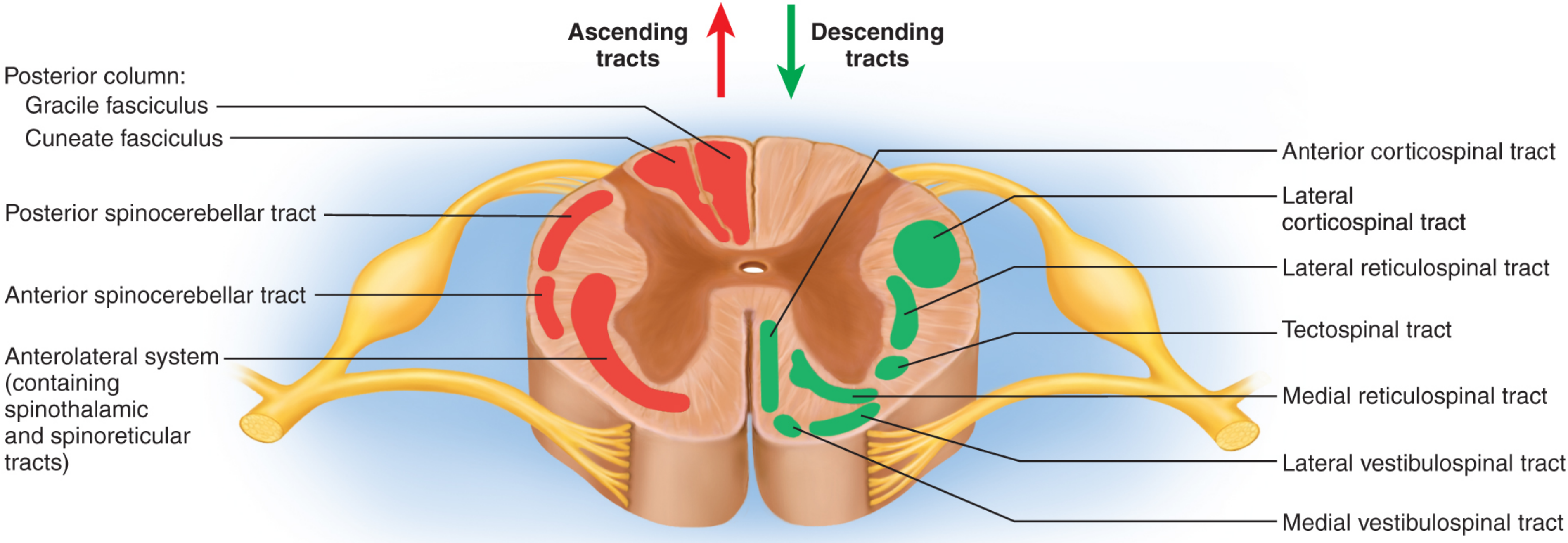

Motor cortex
(precentral gyrus)
Internal
capsule
Cerebrum
Midbrain
Cerebral
peduncle
Upper motor
neurons
Medulla
Medullary
pyramid
Decussation
in medulla
Lateral
corticospinal
tract
Spinal cord
Anterior
corticospinal
tract
Decussation in
spinal cord
Spinal cord
Lower motor
neurons
To skeletal muscles


To brain
6 Primary afferent neuron stimulates inhibitory interneuron
4 Primary afferent neuron stimulates alpha motor neuron to extensor muscle
7 Interneuron inhibits alpha motor neuron to flexor muscle
5 Alpha motor neuron stimulates extensor muscle to contract
3 Primary afferent neuron excited
2 Muscle spindle stimulated
1 Extensor muscle stretched
8 Flexor muscle (antagonist) relaxes



Withdrawal of right leg (flexor reflex)

Extension of left leg (crossed extension reflex)


Ascending tracts
Descending tracts
Posterior column:
Gracile fasciculus
Cuneate fasciculus
Posterior spinocerebellar tract
Anterior spinocerebellar tract
Anterolateral system (containing spinothalamic and spinoreticular tracts)
Anterior corticospinal tract
Lateral corticospinal tract
Lateral reticulospinal tract
Tectospinal tract
Medial reticulospinal tract
Lateral vestibulospinal tract
Medial vestibulospinal tract

Structure of a Neuron

- **cell body**
  - has a single, centrally located nucleus with large nucleolus
  - **cytoplasm** contains mitochondria, lysosomes, a Golgi complex, numerous inclusions, and extensive rough endoplasmic reticulum and cytoskeleton
  - no centrioles – no further cell division

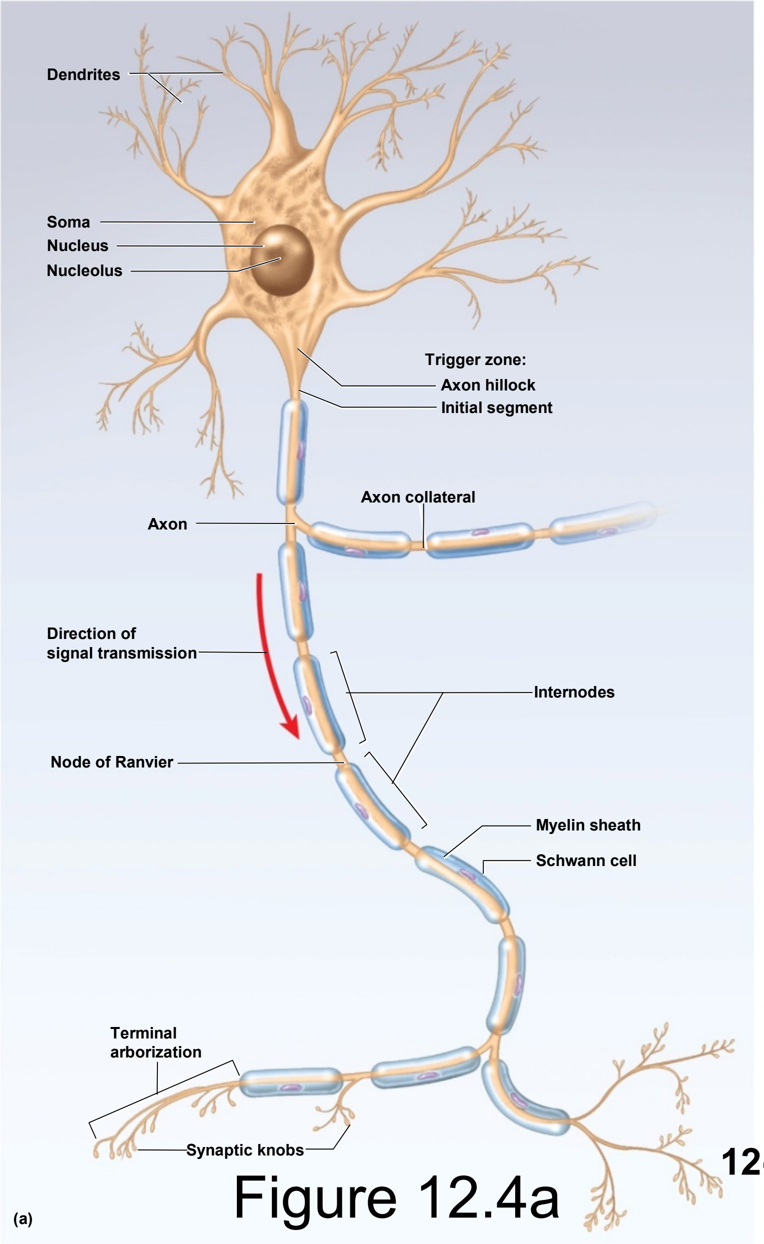


Figure 12.4a

Structure of a Neuron

- **dendrites** – vast number of branches coming from a few thick branches from the soma
  - primary site for receiving signals from other neurons
  - the more dendrites the neuron has, the more information it can receive and incorporate into decision making
  - provide precise pathway for the reception and processing of neural information

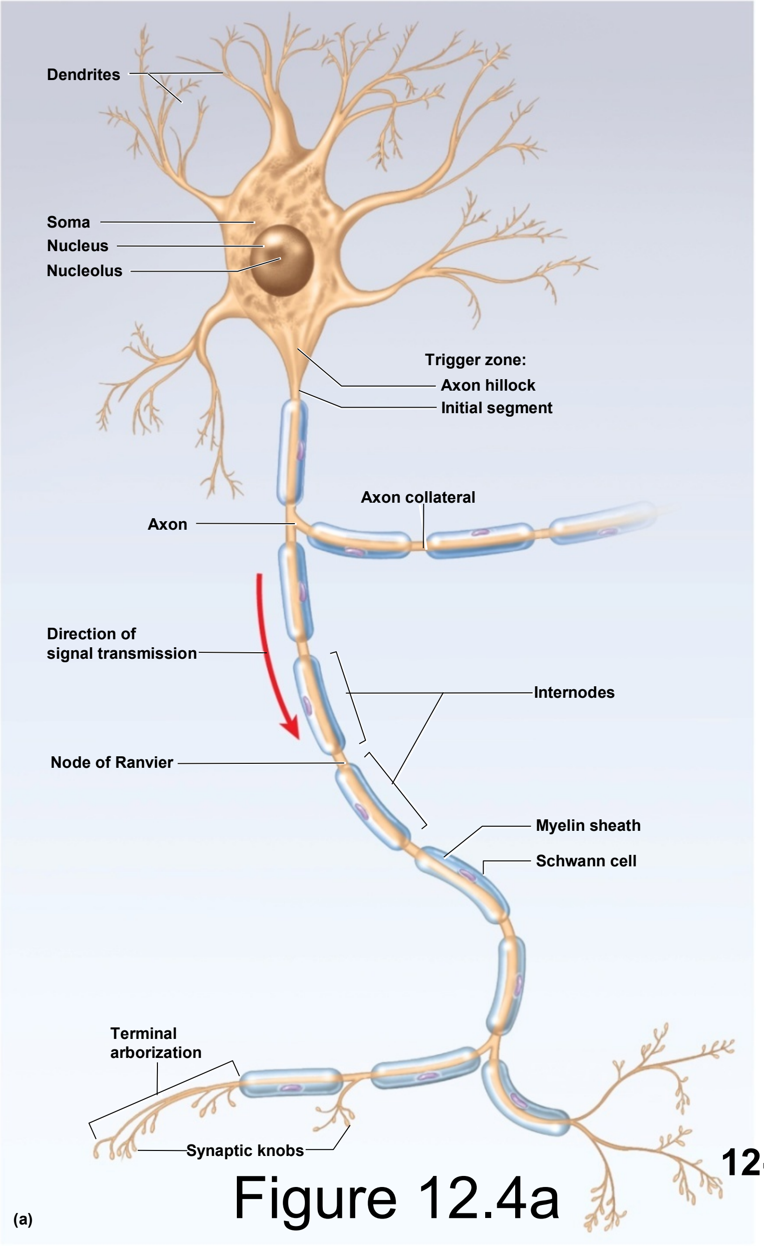


Figure 12.4a

Structure of a Neuron

- **axon** (**nerve fiber**) – originates from a mound on one side of the soma called the **axon hillock**
  - cylindrical, relatively unbranched for most of its length
    - **axon collaterals** – branches of axon
  - branch extensively on distal end
  - specialized for rapid conduction of nerve signals to points remote to the soma
  - **axoplasm** – cytoplasm of axon
  - **axolemma** – plasma membrane of axon
  - only **one axon per neuron**
  - **Schwann cells** and **myelin sheath** enclose axon
  - distal end, axon has **terminal arborization** – extensive complex of fine branches
    - **synaptic knob** (terminal button) – little swelling that forms a junction (synapse) with the next cell
    - contains **synaptic vesicles** full of neurotransmitter

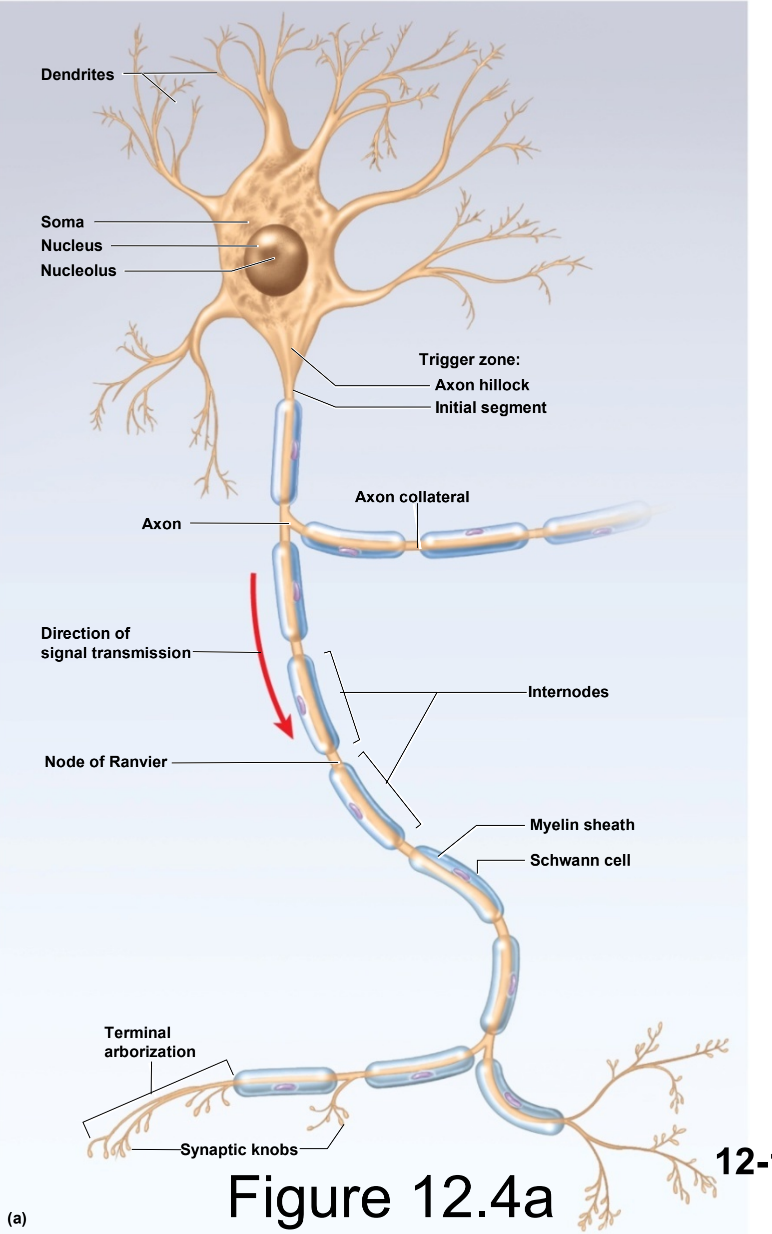


Figure 12.4a

Variation in Neuron Structure

- **multipolar neuron**
  - one axon and multiple dendrites
  - most common
  - most neurons in the brain and spinal cord
- **bipolar neuron**
  - one axon and one dendrite
  - olfactory cells, retina, inner ear
- **unipolar neuron**
  - single process leading away from the soma
  - sensory from skin and organs to spinal cord
- **anaxonic neuron**
  - many dendrites but no axon
  - help in visual processes

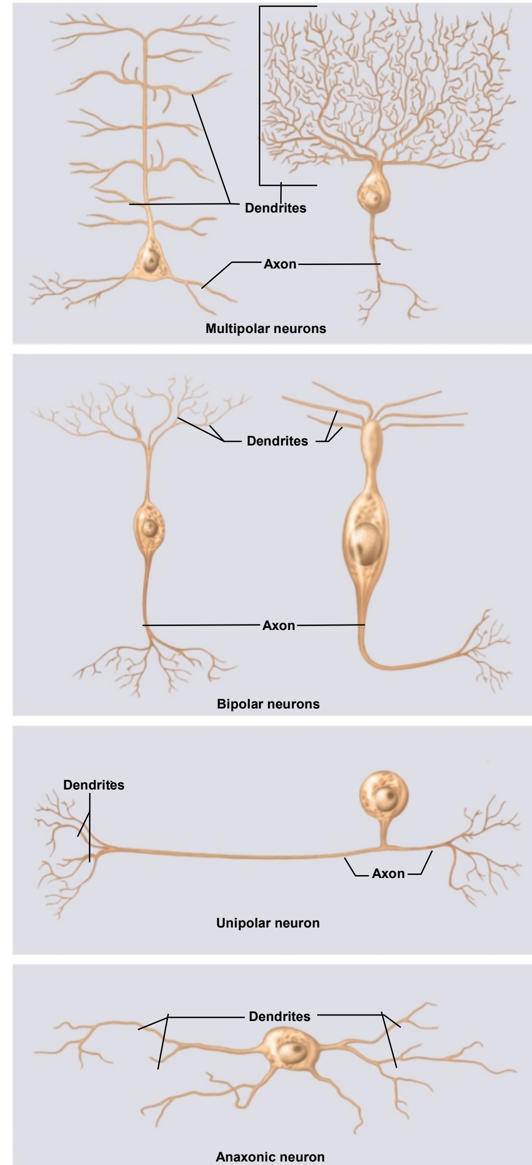


Figure 12.5

Neuroglial Cells

- about **a trillion** (10^{12}) **neurons** in the nervous system
- **neuroglia** outnumber the neurons by as much as **50 to 1**
- **neuroglia** or **glial cells**
  - support and protect the neurons
  - bind neurons together and form framework for nervous tissue
  - in fetus, guide migrating neurons to their destination
  - if mature neuron is not in synaptic contact with another neuron is covered by glial cells
    - prevents neurons from touching each other
    - gives precision to conduction pathways

Six Types of Neuroglial Cells

- four types occur only in CNS
  - **oligodendrocytes**
    - form myelin sheaths in CNS
    - each arm-like process wraps around a nerve fiber forming an insulating layer that speeds up signal conduction
  - **ependymal cells**
    - lines internal cavities of the brain
    - cuboidal epithelium with cilia on apical surface
    - secretes and circulates cerebrospinal fluid (CSF)
      - clear liquid that bathes the CNS
  - **microglia**
    - small, wandering macrophages formed white blood cell called **monocytes**
    - thought to perform a complete checkup on the brain tissue several times a day
    - wander in search of cellular debris to phagocytize

Six Types of Neuroglial Cells

- four types occur only in CNS
  - **astrocytes**
    - most abundant glial cell in CNS
    - cover entire brain surface and most nonsynaptic regions of the neurons in the gray matter of the CNS
    - diverse functions
      - Support, regulation, nutrition, growth

Six Types of Neuroglial Cells

- two types occur only in PNS
  - **Schwann cells**
    - envelope nerve fibers in PNS
    - wind repeatedly around a nerve fiber
    - produces a **myelin sheath** similar to the ones produced by oligodendrocytes in CNS
    - assist in the regeneration of damaged fibers
  - **satellite cells**
    - surround the neurosomas in ganglia of the PNS
    - provide electrical insulation around the soma
    - regulate the chemical environment of the neurons

Neuroglial Cells of CNS

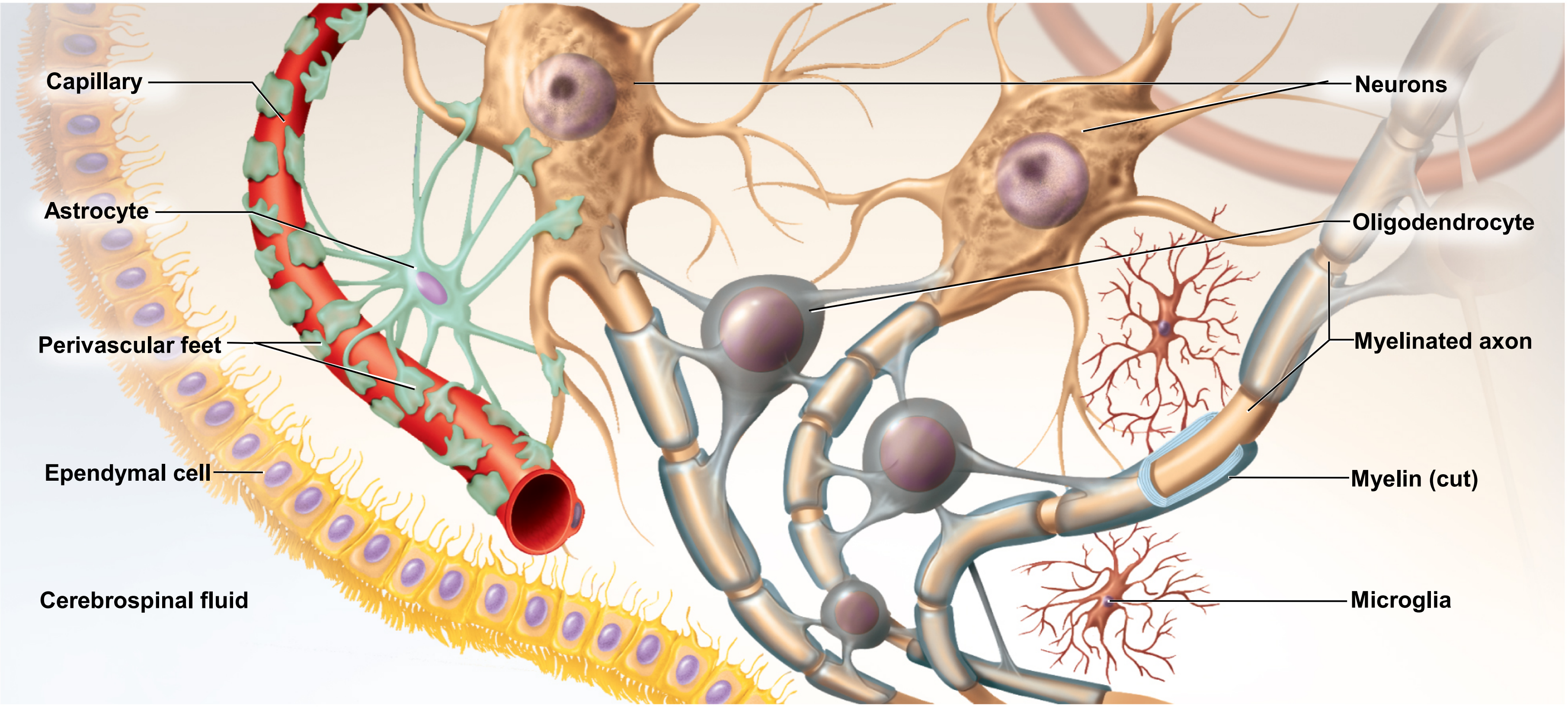


Figure 12.6

Myelin

- **myelin sheath** – an insulating layer around a nerve fiber
  - formed by **oligodendrocytes in CNS** and **Schwann cells in PNS**
  - consists of the plasma membrane of glial cells
    - 20% protein and 80 % lipid
- **myelination** – production of the myelin sheath
  - begins the 14^{th} week of fetal development
  - proceeds rapidly during infancy
  - completed in late adolescence
  - dietary fat is important to nervous system development

Myelin

- in PNS, **Schwann cell** spirals repeatedly around a single nerve fiber
  - lays down as many as a hundred layers of its own membrane
  - no cytoplasm between the membranes
  - **neurilemma** – thick outermost coil of myelin sheath
    - contains nucleus and most of its cytoplasm
    - external to neurilemma is basal lamina and a thin layer of fibrous connective tissue – **endoneurium**
- in CNS – **oligodendrocytes** reaches out to myelinate several nerve fibers in its immediate vicinity
  - anchored to multiple nerve fibers
  - cannot migrate around any one of them like Schwann cells
  - must push newer layers of myelin under the older ones
    - so myelination spirals inward toward nerve fiber
  - nerve fibers in CNS have no neurilemma or endoneurium

Myelin

- many Schwann cells or oligodendrocytes are needed to cover one nerve fiber
- **myelin sheath** is **segmented**
  - **nodes of Ranvier** – gap between segments
  - **internodes** – myelin covered segments from one gap to the next
  - **initial segment** – short section of nerve fiber between the axon hillock and the first glial cell
  - **trigger zone** – the axon hillock and the initial segment
    - play an important role in initiating a nerve signal

Myelin Sheath in PNS

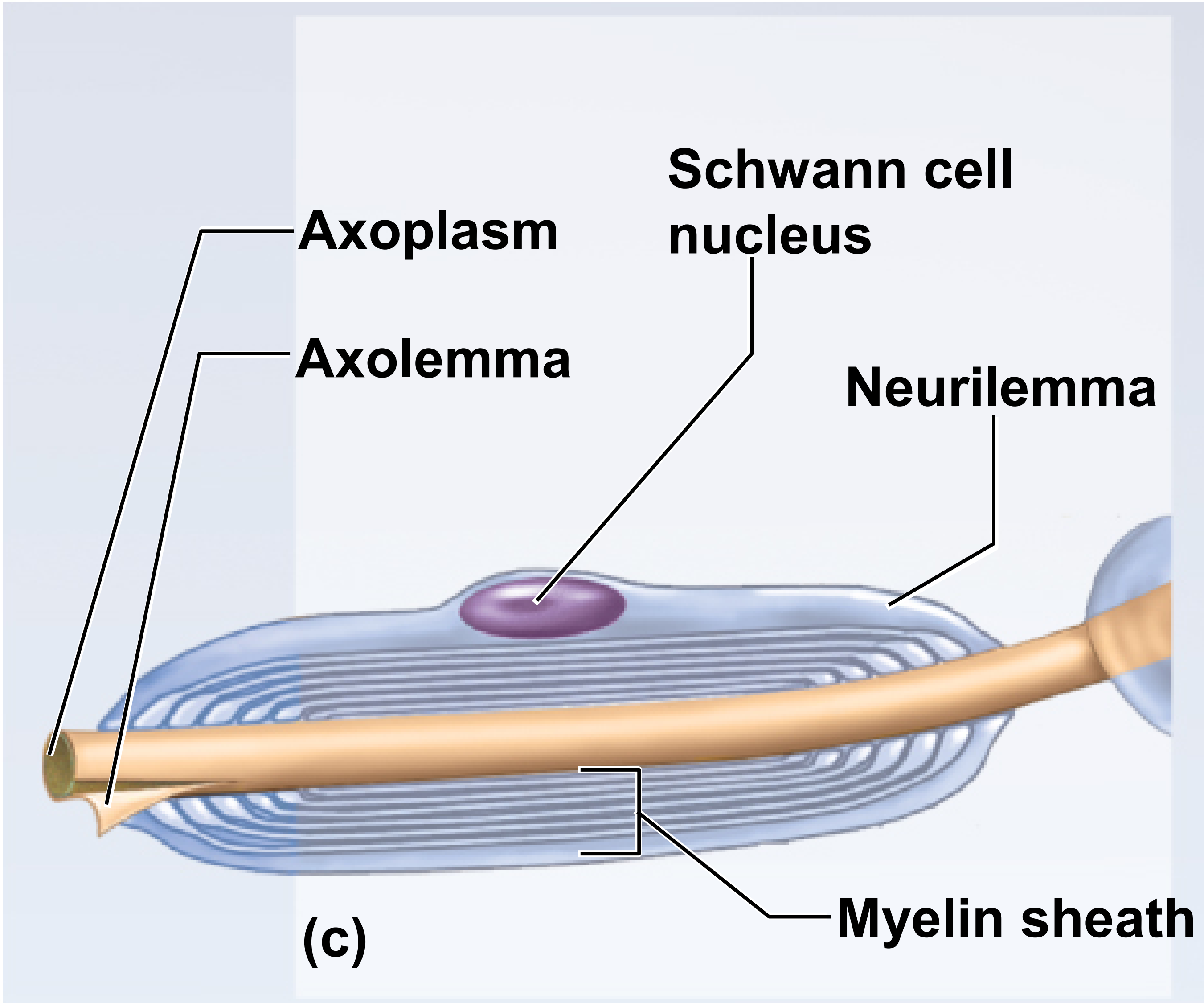
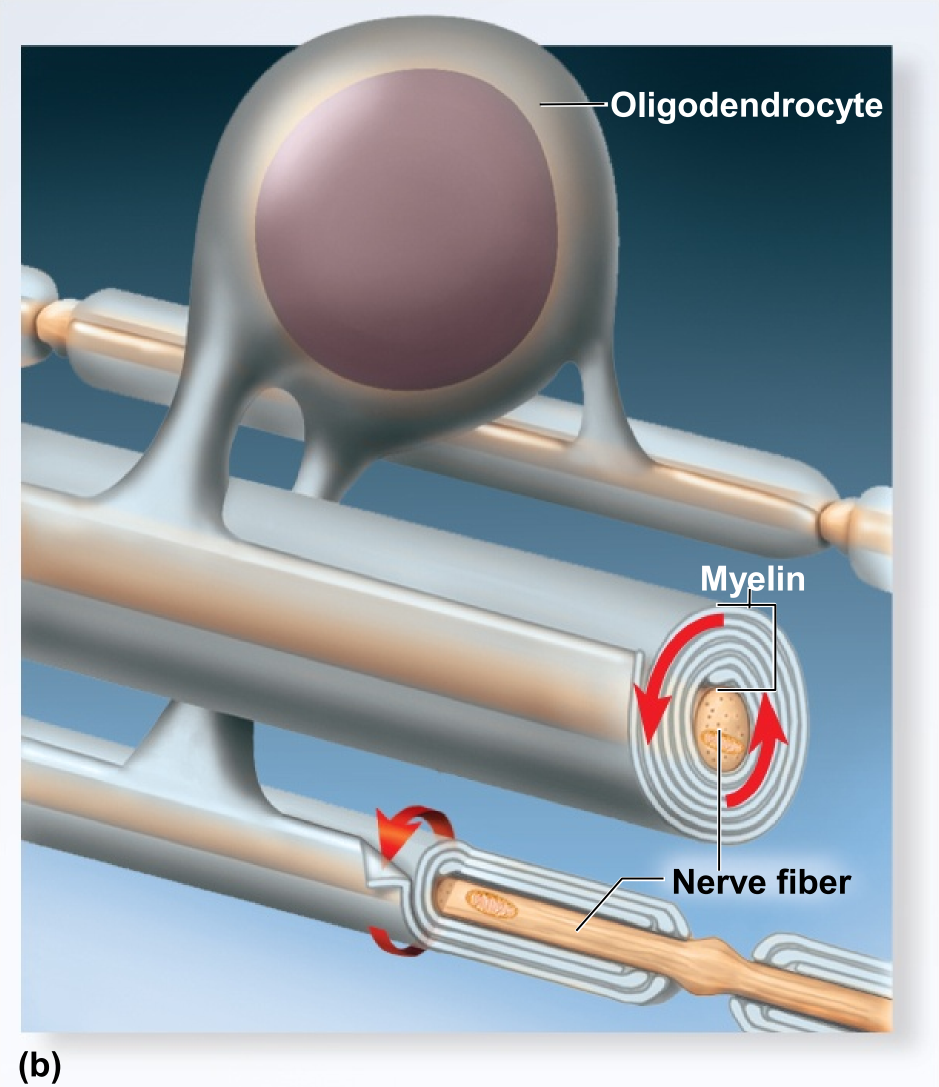


Figure 12.4c

nodes of Ranvier and internodes

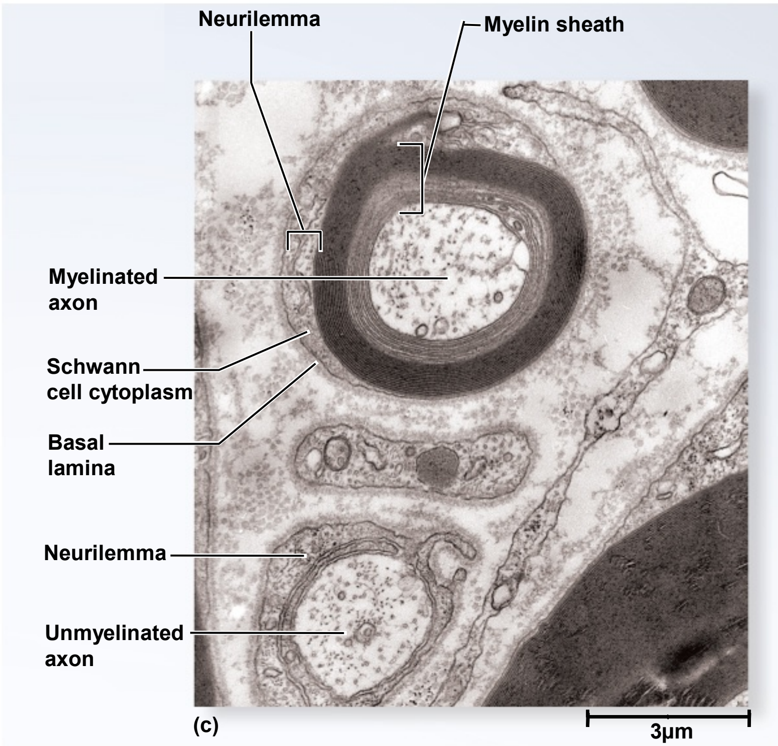
Myelination in CNS



(b)

Figure 12.7b

Unmyelinated Axons of PNS



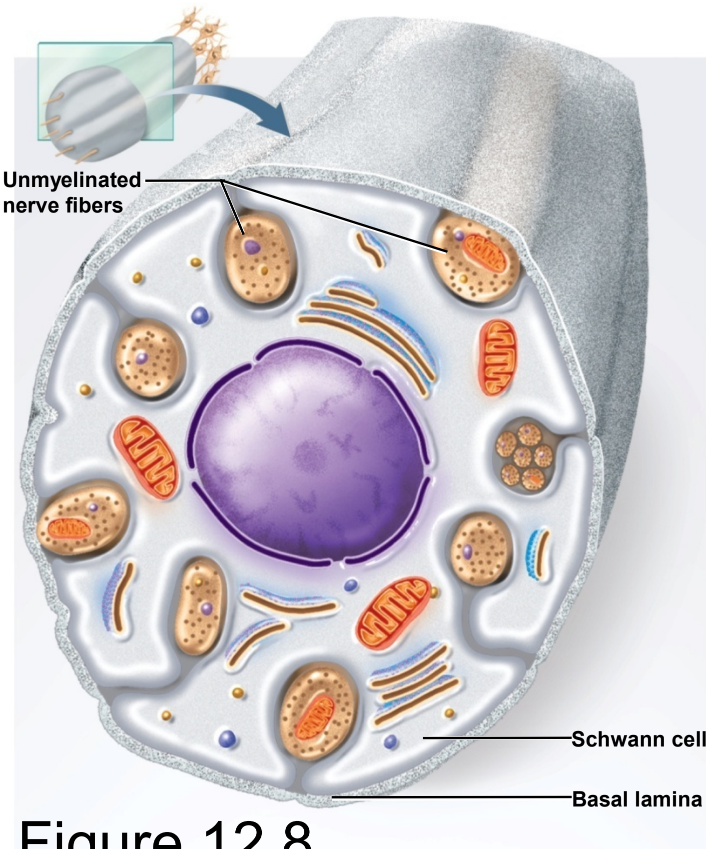


Figure 12.7c Figure 12.8

- Schwann cells hold 1 – 12 small nerve fibers in grooves on its surface
- membrane folds once around each fiber overlapping itself along the edges
- **mesaxon –** neurilemma wrapping of unmyelinated nerve fibers

Conduction Speed of Nerve Fibers

- speed at which a nerve signal travels along a nerve fiber depends on two factors
  - **diameter of fiber**
  - **presence or absence of myelin**
- signal conduction occurs along the surface of a fiber
  - larger fibers have more surface area and conduct signals more rapidly
  - myelin further speeds signal conduction

Nerve Signal Conduction Unmyelinated Fibers

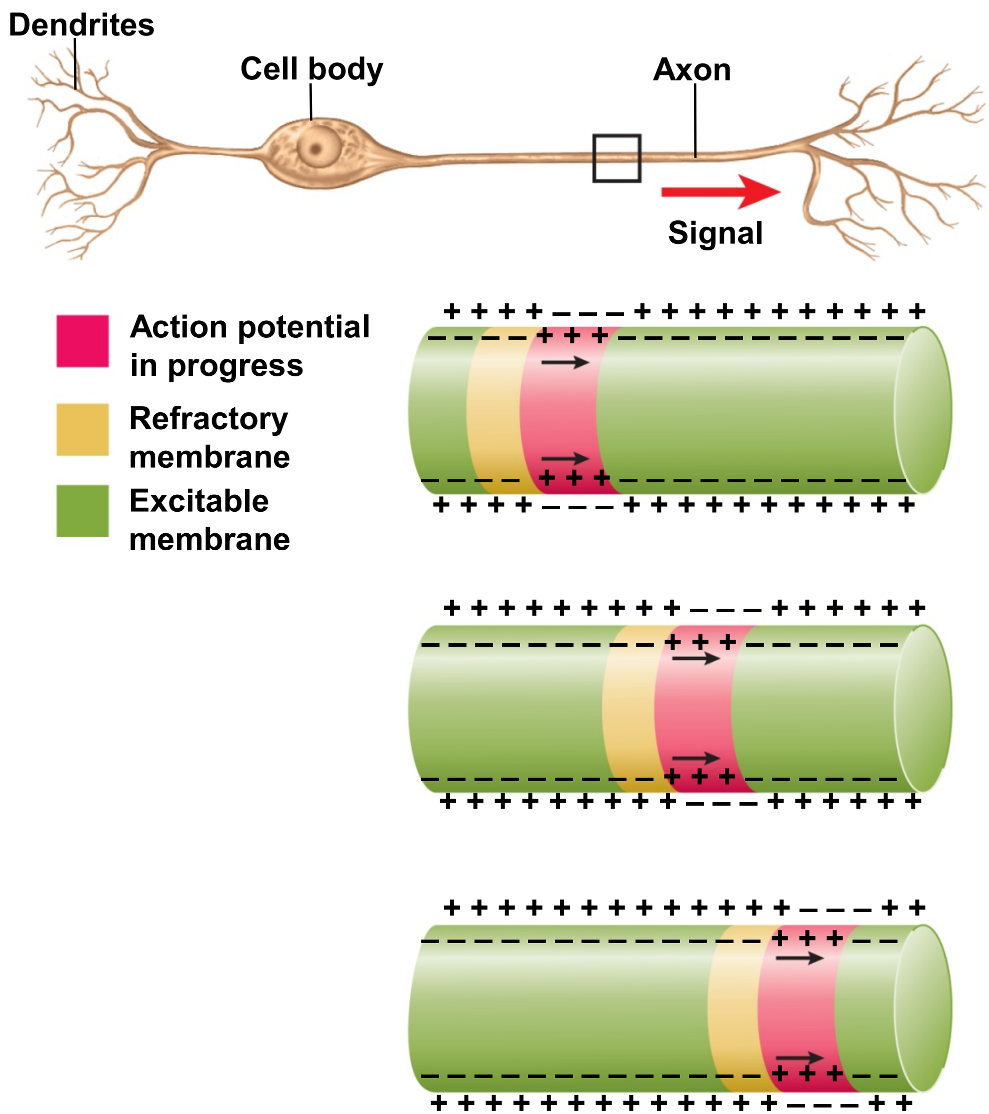


Figure 12.16

Saltatory Conduction Myelinated Fibers

- voltage-gated channels needed for APs
  - fewer than 25 per μm^2 in myelin-covered regions (internodes)
  - up to 12,000 per μm^2 in nodes of Ranvier
- fast Na^+ diffusion occurs between nodes
  - signal weakens under myelin sheath, but still strong enough to stimulate an action potential at next node
- **saltatory conduction** – the nerve signal seems to jump from node to node

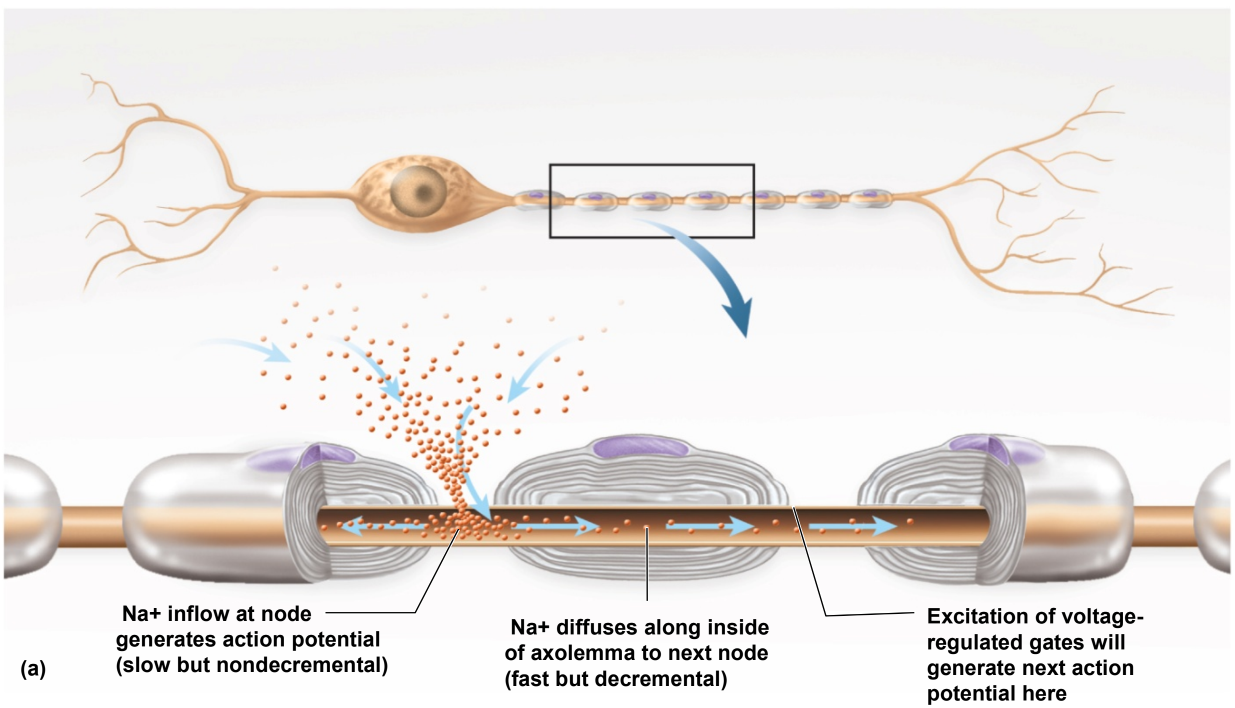


Figure 12.17a

Saltatory Conduction

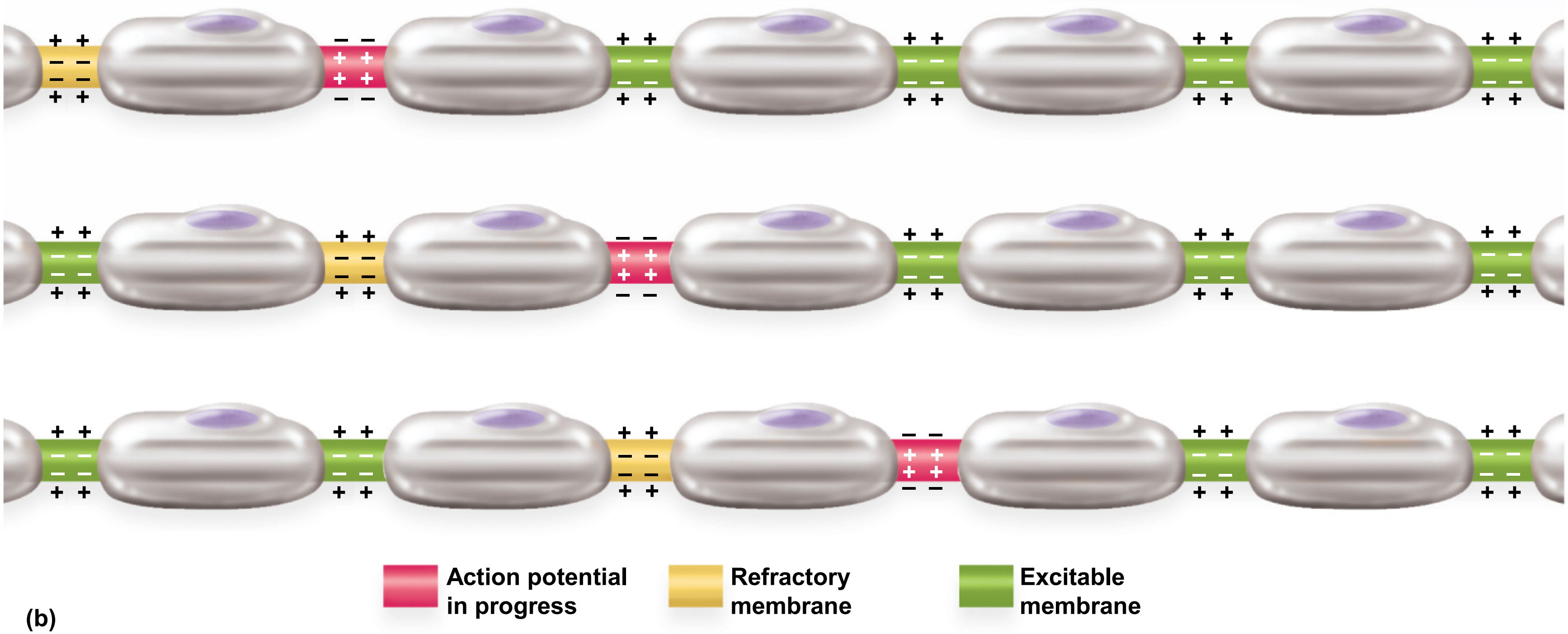


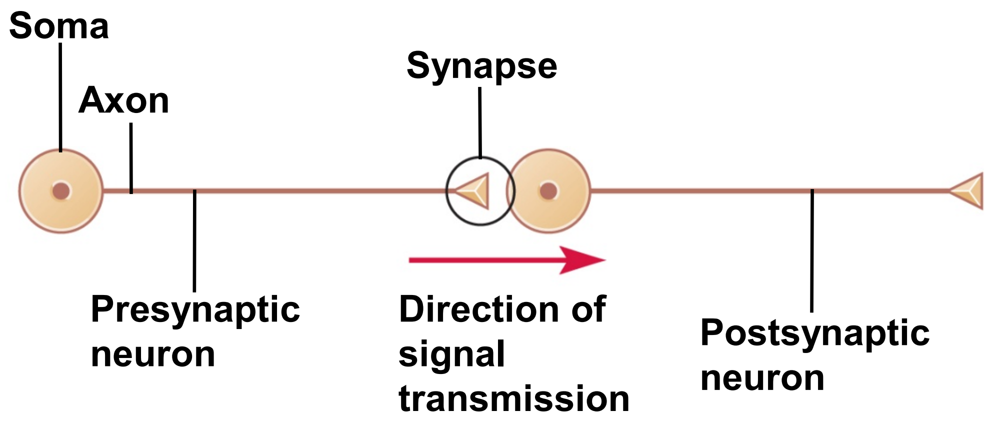
Figure 12.17b

- much faster than conduction in unmyelinated fibers

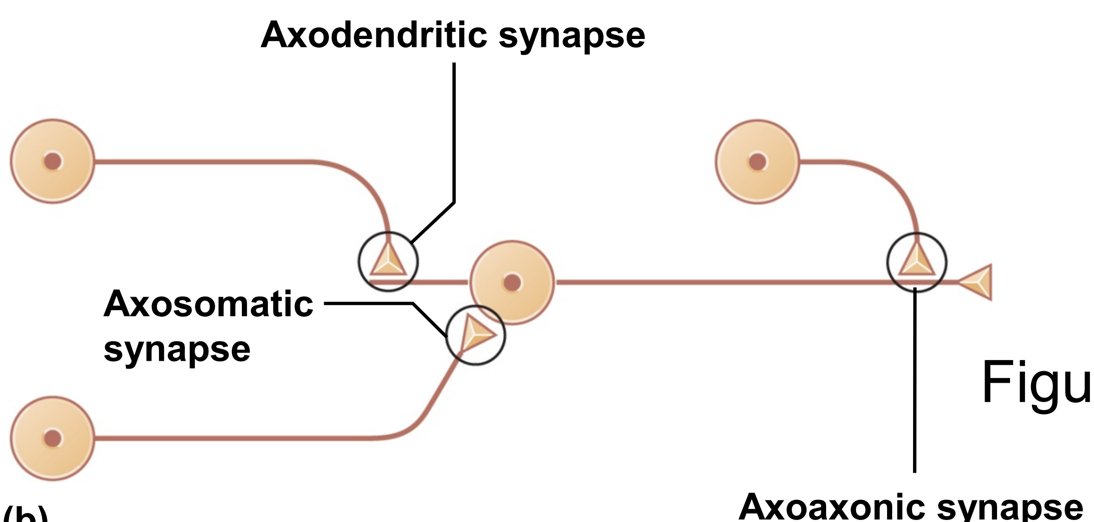
Synapses

- a nerve signal can go no further when it reaches the end of the axon
  - triggers the release of a neurotransmitter
  - stimulates a new wave of electrical activity in the next cell across the synapse
- synapse between two neurons
  - 1st neuron in the signal path is the **presynaptic neuron**
    - releases neurotransmitter
  - 2nd neuron is **postsynaptic neuron**
    - responds to neurotransmitter
- **presynaptic neuron** may synapse with a dendrite, soma, or axon of postsynaptic neuron to form **axodendritic**, **axosomatic** or **axoaxonic synapses**
- neuron can have an enormous number of synapses
  - spinal motor neuron covered by about 10,000 synaptic knobs from other neurons
    - 8000 ending on its dendrites
    - 2000 ending on its soma
- in cerebellum of brain, one neuron can have as many as 100,000 synapses

Synaptic Relationships Between Neurons



(a)



(b)

Figure 12.18

Synaptic Knobs

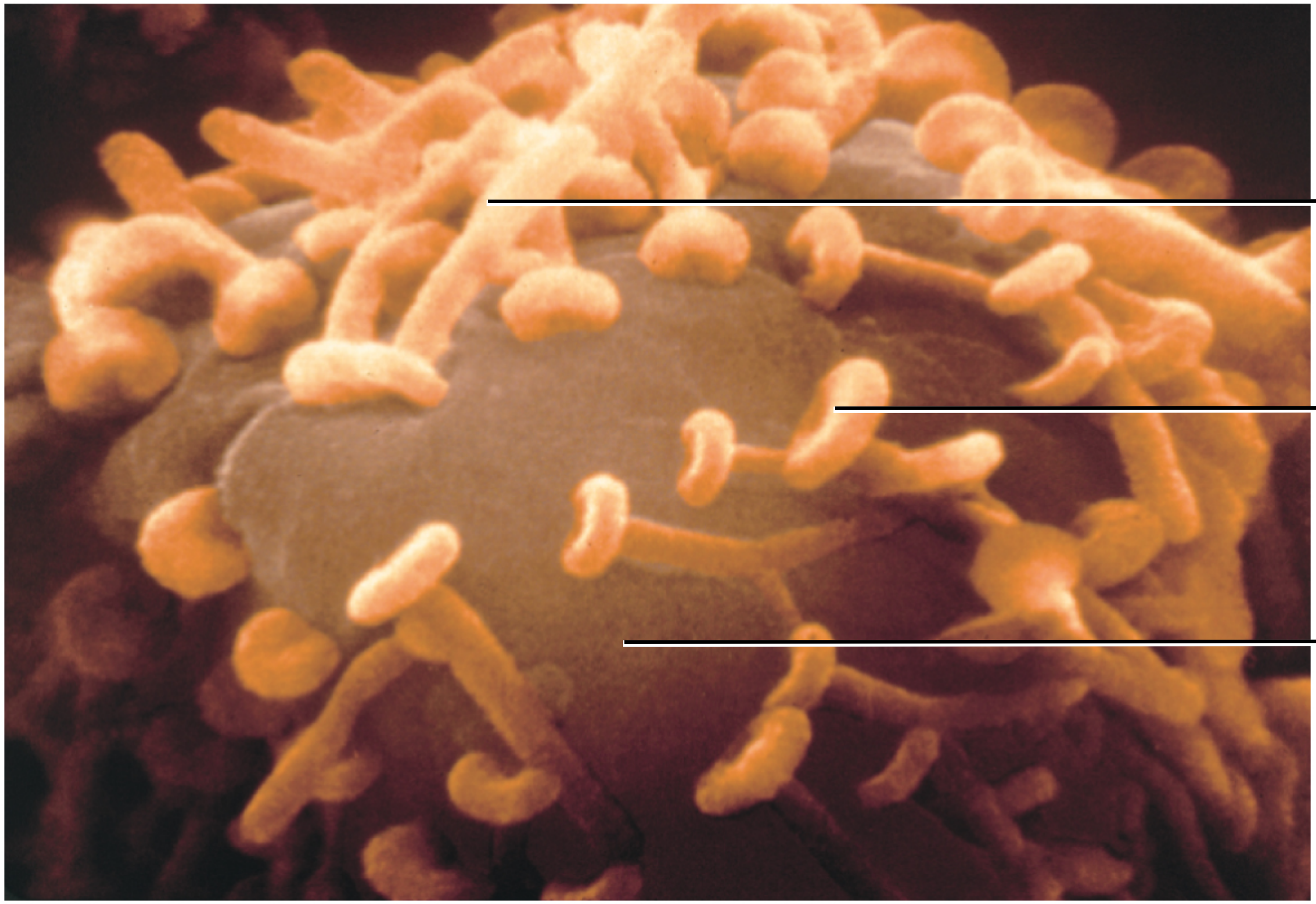


Figure 12.19

Structure of a Chemical Synapse

- **synaptic knob** of **presynaptic neuron** contains **synaptic vesicles** containing **neurotransmitter**
  - many docked on release sites on plasma membrane
    - ready to release neurotransmitter on demand
  - a reserve pool of synaptic vesicles located further away from membrane
- **postsynaptic neuron** membrane contains **proteins** that function as **receptors** and **ligand-regulated ion gates**

Structure of a Chemical Synapse

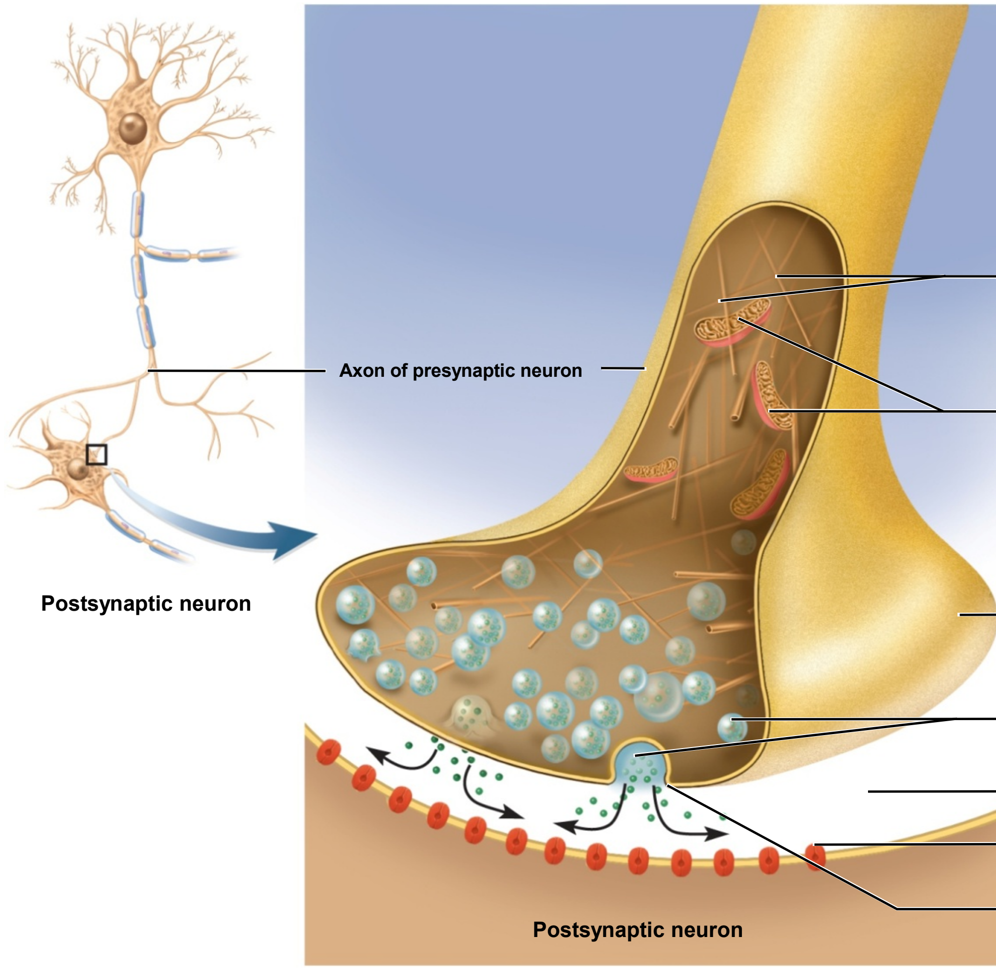


Figure 12.20

- presynaptic neurons have synaptic vesicles with neurotransmitter and postsynaptic have receptors and ligand-regulated ion channels

Neurotransmitters and Related Messengers

- more than 100 neurotransmitters have been identified
- fall into four major categories according to chemical composition
  - **acetylcholine**
    - in a class by itself
  - **amino acid neurotransmitters**
    - include glycine, glutamate, aspartate, and ■aminobutyric acid (GABA)
  - **monoamines**
    - synthesized from amino acids by removal of the –COOH group
    - retaining the $-NH_2$ (amino) group
    - major monoamines are:
      - **epinephrine**, **norepinephrine**, **dopamine (catecholamines)**
      - histamine and serotonin
  - **neuropeptides**

Categories of Neurotransmitters

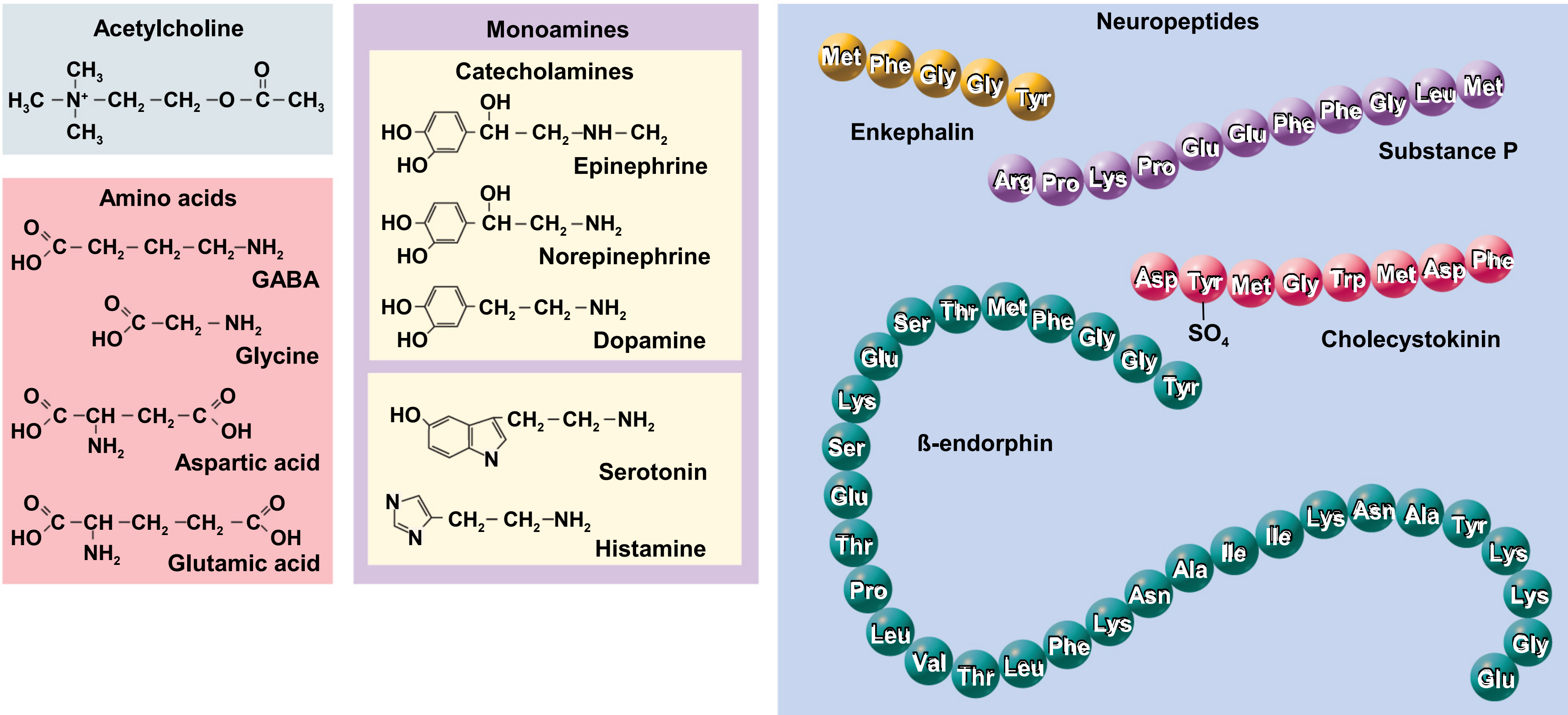


Figure 12.21

Neuropeptides

- chains of 2 to 40 amino acids
- act at lower concentrations than other neurotransmitters
- longer lasting effects
- some also released from digestive tract
  - gut-brain peptides cause food cravings

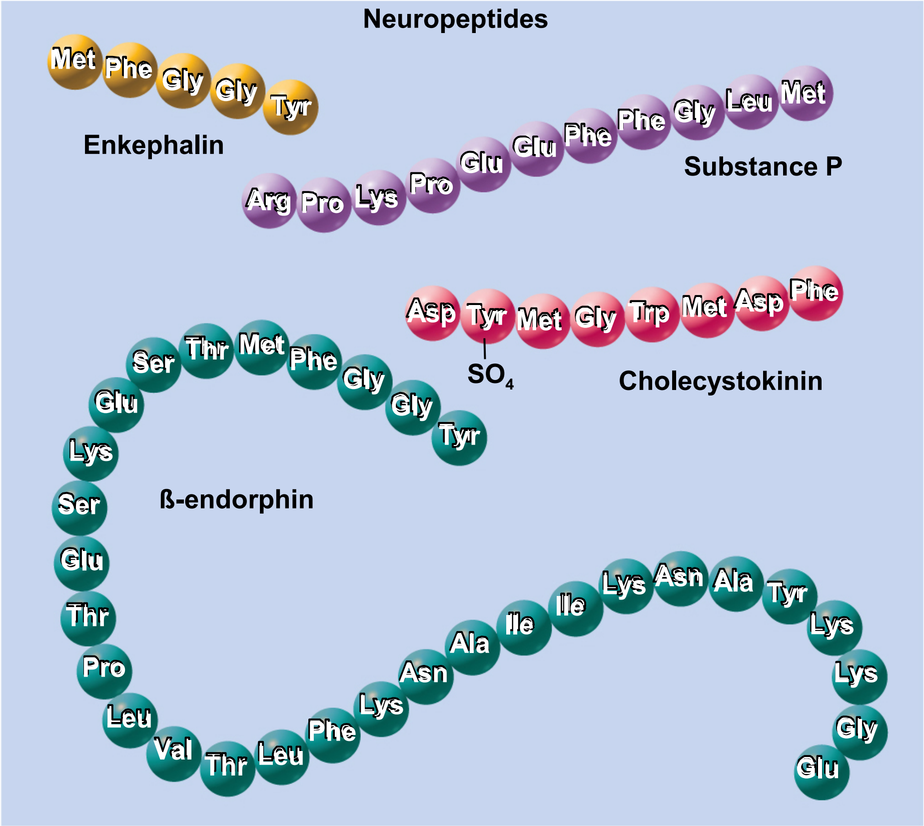


Figure 12.21

Function of Neurotransmitters at Synapse

- they are synthesized by the presynaptic neuron
- they are released in response to stimulation
- they bind to specific receptors on the postsynaptic cell
- they alter the physiology of that cell

Effects of Neurotransmitters

- a given neurotransmitter does not have the same effect everywhere in the body
- multiple receptor types exist for a particular neurotransmitter
  - 14 receptor types for serotonin
- receptor governs the effect the neurotransmitter has on the target cell

Synaptic Transmission

- **neurotransmitters** are diverse in their action
  - some excitatory
  - some inhibitory
  - some the effect depends on what kind of receptor the postsynaptic cell has
  - some open ligand-regulated ion gates
  - some act through second-messenger systems
- three kinds of synapses with different modes of action
  - **excitatory cholinergic synapse**
  - **inhibitory GABA-ergic synapse**
  - **excitatory adrenergic synapse**
- **synaptic delay** – time from the arrival of a signal at the axon terminal of a presynaptic cell to the beginning of an action potential in the postsynaptic cell
  - 0.5 msec for all the complex sequence of events to occur

Excitatory Cholinergic Synapse

- **cholinergic synapse** – employs acetylcholine (ACh) as its neurotransmitter
  - ACh excites some postsynaptic cells
    - skeletal muscle
  - inhibits others
- describing **excitatory action**
  - nerve signal approaching the synapse, opens the voltage-regulated calcium gates in synaptic knob
  - Ca^{2+} enters the knob
  - triggers exocytosis of synaptic vesicles releasing ACh
  - empty vesicles drop back into the cytoplasm to be refilled with ACh
  - reserve pool of synaptic vesicles move to the active sites and release their ACh
  - ACh diffuses across the synaptic cleft
  - binds to ligand-regulated gates on the postsynaptic neuron
  - gates open
  - allowing Na^{+} to enter cell and K^{+} to leave
    - pass in opposite directions through same gate
  - as Na^{+} enters the cell it spreads out along the inside of the plasma membrane and depolarizes it producing a local potential called the postsynaptic potential
  - if it is strong enough and persistent enough
  - it opens voltage-regulated ion gates in the trigger zone
  - causing the postsynaptic neuron to fire

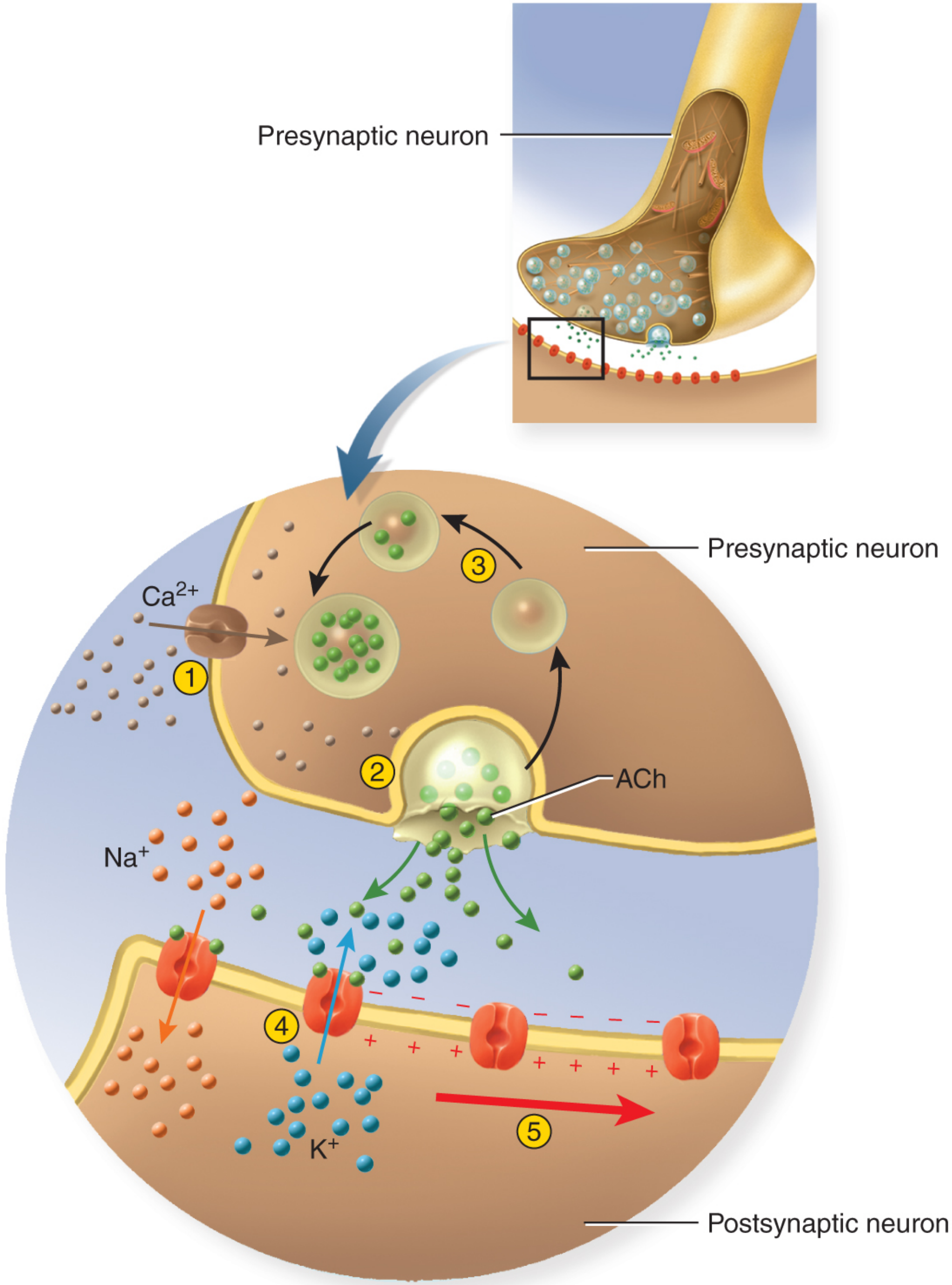
Inhibitory GABA-ergic Synapse

- GABA-ergic synapse employs ■**aminobutyric acid** as its neurotransmitter
- nerve signal triggers release of GABA into synaptic cleft
- GABA receptors are **chloride channels**
- **Cl^-** enters cell and makes the inside more negative than the resting membrane potential
- postsynaptic neuron is inhibited, and less likely to fire

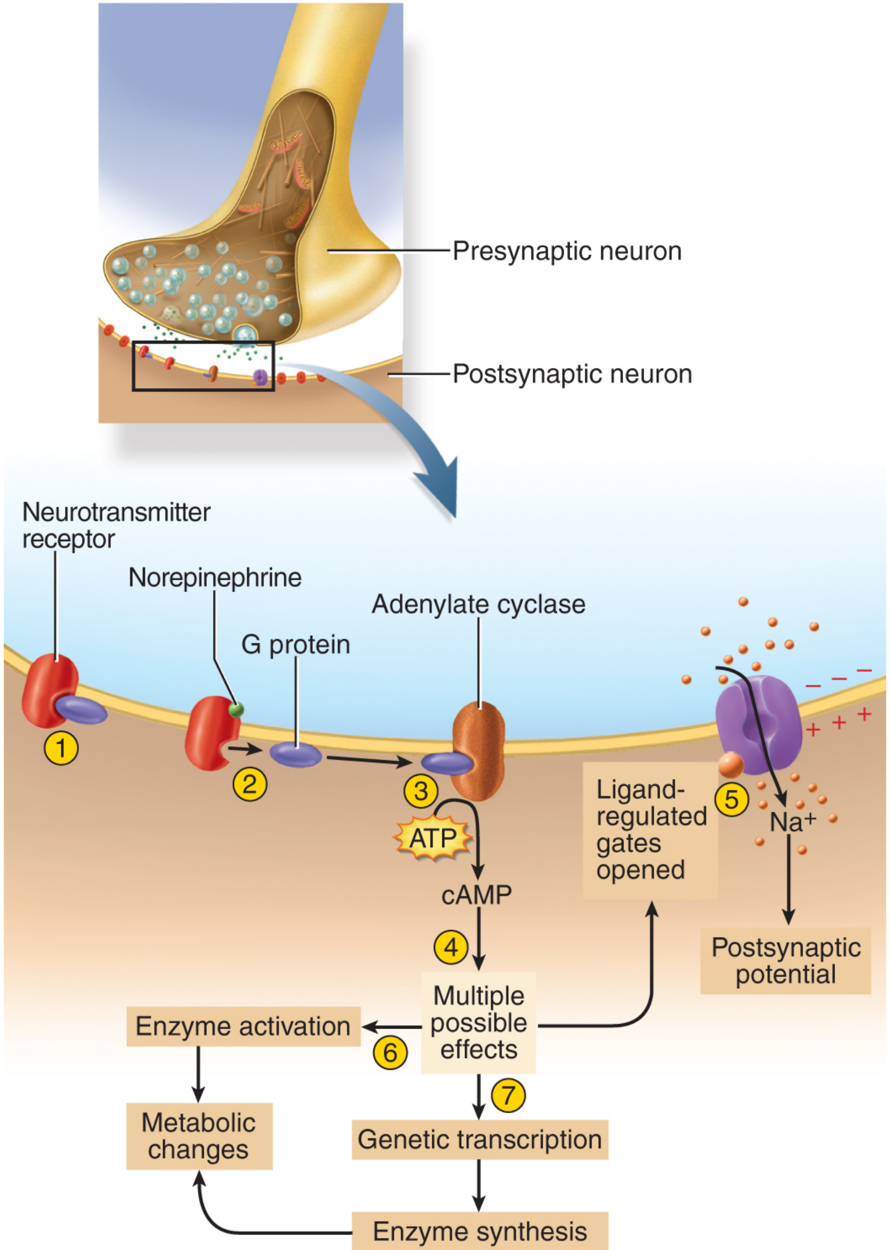
Excitatory Adrenergic Synapse

- **adrenergic synapse** employs the neurotransmitter **norepinephrine** (NE) also called noradrenaline
- NE and other monoamines, and neuropeptides acts through **second messenger systems** such as **cyclic AMP** (cAMP)
- **receptor** is not an ion gate, but a **transmembrane protein associated with a G protein**
  - unstimulated NE receptor is bound to a G protein
  - binding of NE to the receptor causes the G protein to dissociate from it
  - G protein binds to adenylate cyclase
    - activates this enzyme
  - induces the conversion of **ATP** to **cyclic AMP**
  - cyclic AMP can induce several alternative effects in the cell
    - causes the production of an internal chemical that binds to a ligand-regulated ion gate from inside of the membrane, opening the gate and **depolarizing the cell**
    - can activate preexisting **cytoplasmic enzymes** that lead do diverse metabolic changes
    - can induce **genetic transcription**, so that the cell produces new cytoplasmic enzymes that can lead to diverse metabolic effects
- slower to respond than cholinergic and GABA-ergic synapses
- has advantage of **enzyme amplification** – single molecule of NE can produce vast numbers of product molecules in the cell

Excitatory Cholinergic Synapse



Excitatory Adrenergic Synapse



Cessation of the Signal

- mechanisms to **turn off stimulation** to keep postsynaptic neuron from firing indefinitely
  - neurotransmitter molecule binds to its receptor for only 1 msec or so
    - then dissociates from it
  - if presynaptic cell continues to release neurotransmitter
    - one molecule is quickly replaced by another and the neuron is restimulated
- **stop adding neurotransmitter** and **get rid of that which is already there**
  - stop signals in the presynaptic nerve fiber
  - getting rid of neurotransmitter by:
    - **diffusion**
    - **reuptake**
    - **degradation in the synaptic cleft**

Neural Integration

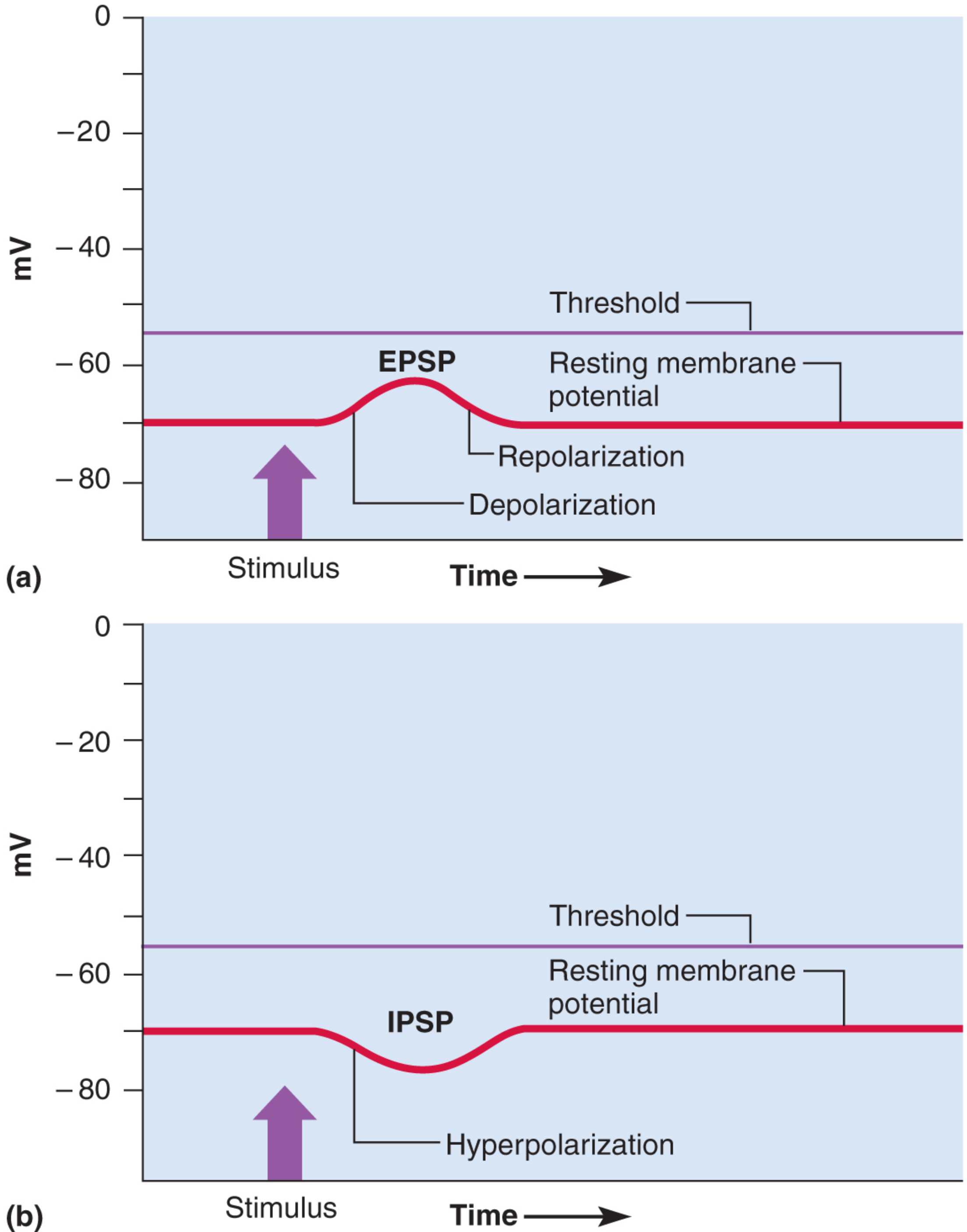
- synaptic delay slows the transmission of nerve signals
- more synapses in a neural pathway, the longer it takes for information to get from its origin to its destination
  - synapses are not due to limitation of nerve fiber length
  - gap junctions allow some cells to communicate more rapidly than chemical synapses
- then why do we have synapses?
  - to process information, store it, and make decisions
  - chemical synapses are the decision making devises of the nervous system
  - the more synapses a neuron has, the greater its information-processing capabilities.
  - **pyramidal cells** in cerebral cortex have about 40,000 synaptic contacts with other neurons
  - **cerebral cortex** (main information-processing tissue of your brain) has an estimated 100 trillion (10^{14}) synapses
- **neural integration** – the ability of your neurons to process information, store and recall it, and make decisions

Postsynaptic Potentials - EPSP

- **neural integration** is based on the postsynaptic potentials produced by neurotransmitters
- typical neuron has a resting membrane potential of -70 mV and threshold of about -55 mV
- **excitatory postsynaptic potentials (EPSP)**
  – any voltage change in the direction of threshold that makes a neuron more likely to fire
    - usually results from Na^+ flowing into the cell cancelling some of the negative charge on the inside of the membrane
  – **glutamate** and **aspartate** are excitatory brain neurotransmitters that produce EPSPs

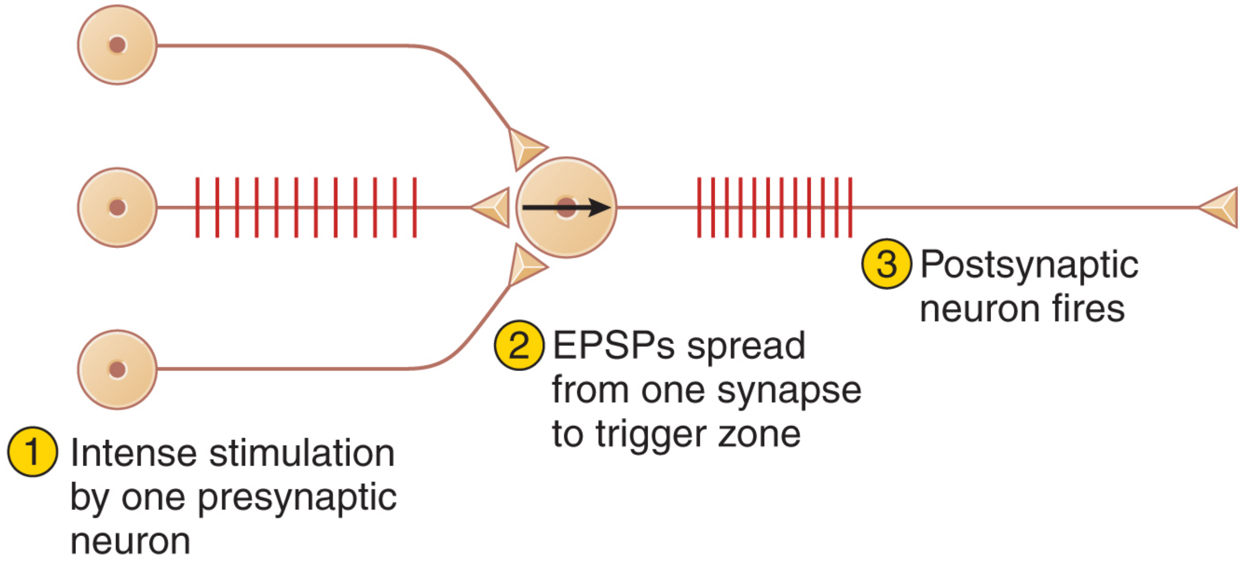
Postsynaptic Potentials - IPSP

- **inhibitory postsynaptic potentials (IPSP)**
  - any voltage change away from threshold that makes a neuron less likely to fire
    - neurotransmitter hyperpolarizes the postsynaptic cell and makes it more negative than the RMP making it less likely to fire
    - produced by neurotransmitters that open ligand-regulated chloride gates
      - causing inflow of Cl- making the cytosol more negative
  - **glycine** and **GABA** produce IPSPs and are **inhibitory**
  - **acetylcholine (ACh)** and **norepinephrine** are excitatory to some cells and inhibitory to others
    - depending on the type of receptors on the target cell
    - ACh excites skeletal muscle, but inhibits cardiac muscle due to the different type of receptors

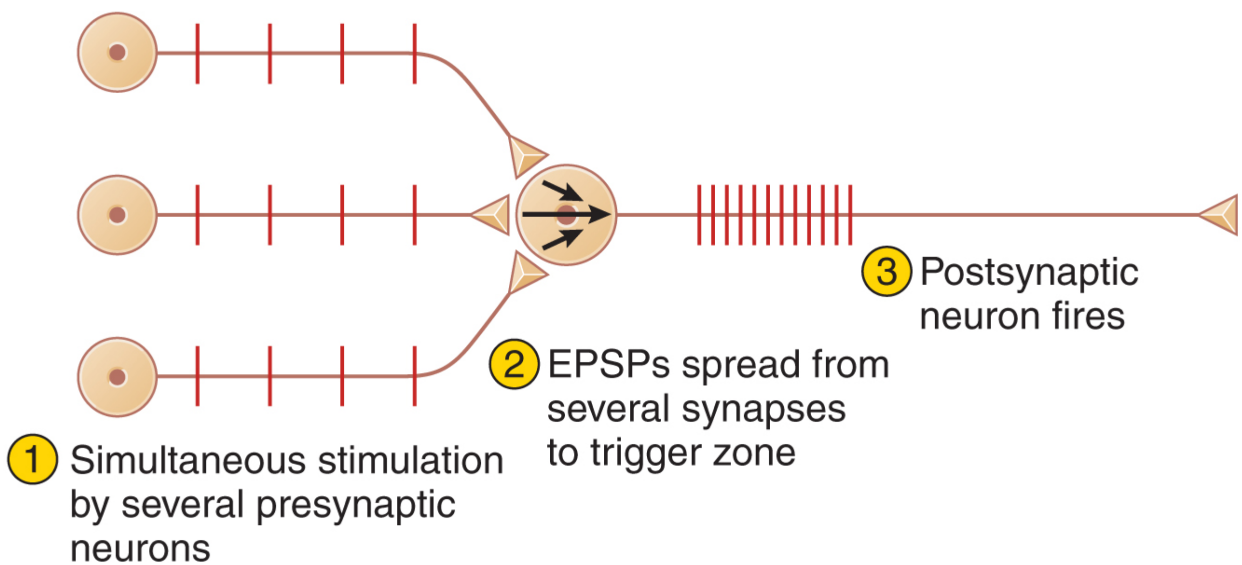

0
−20
−40
−60
−80
mV
Threshold
EPSP
Resting membrane potential
Repolarization
Depolarization
Stimulus
Time
(a)
0
−20
−40
−60
−80
mV
Threshold
Resting membrane potential
IPSP
Hyperpolarization
Stimulus
Time
(b)

Summation, Facilitation, and Inhibition

- one neuron can receive input from thousands of other neurons
- some incoming nerve fibers may produce EPSPs while others produce IPSPs
- neuron's response depends on whether the net input is excitatory or inhibitory
- **summation** – the process of adding up postsynaptic potentials and responding to their **net** effect
  - occurs in the trigger zone
- the balance between EPSPs and IPSPs enables the nervous system to make decisions
- **temporal summation** – occurs when a single synapse generates EPSPs so quickly that each is generated before the previous one fades
  - allows EPSPs to add up over time to a threshold voltage that triggers an action potential
- **spatial summation** – occurs when EPSPs from several different synapses add up to threshold at an axon hillock.
  - several synapses admit enough Na^+ to reach threshold
  - presynaptic neurons cooperate to induce the postsynaptic neuron to fire



(a) Temporal summation



(b) Spatial summation

Summation of EPSPs

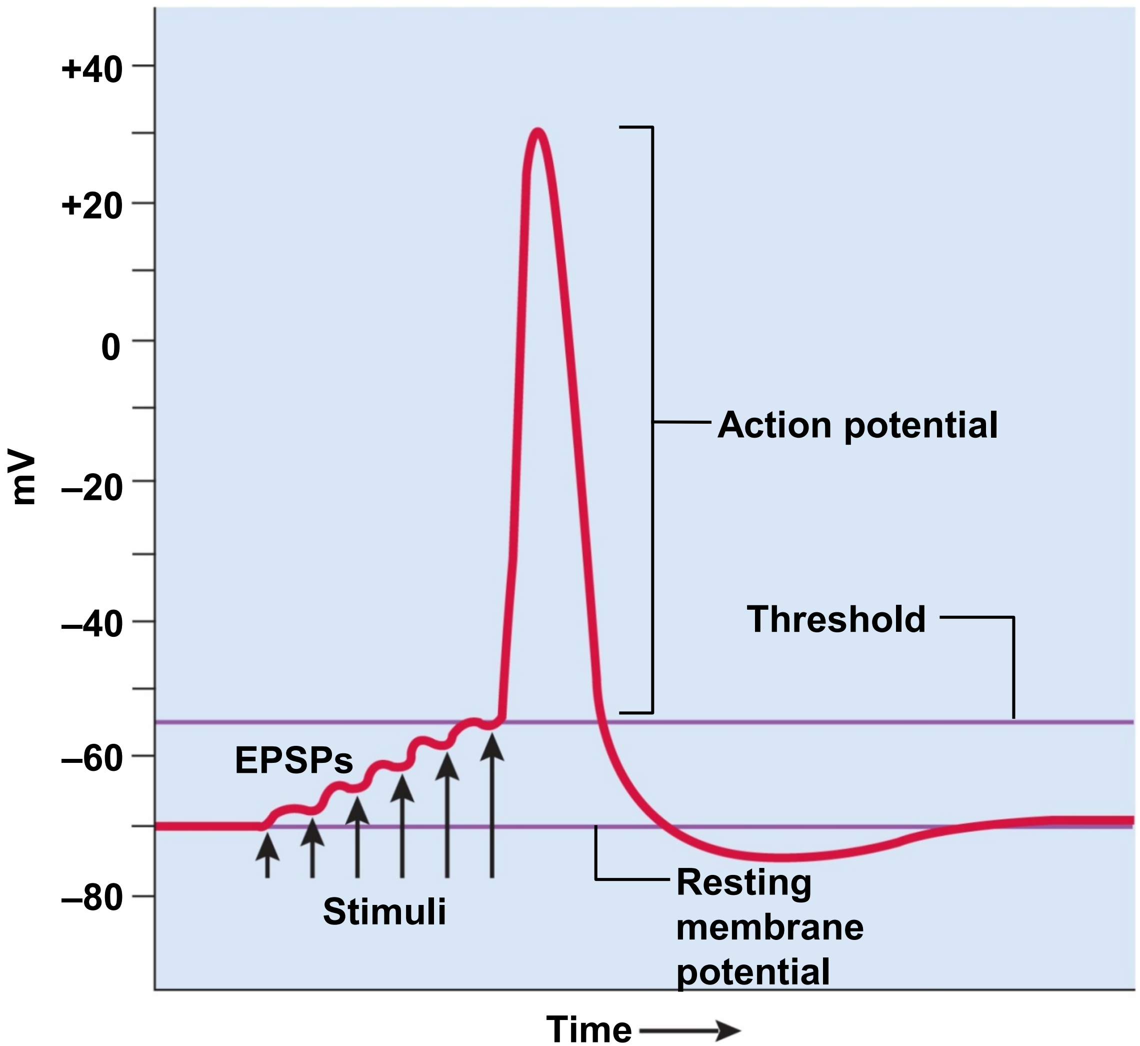
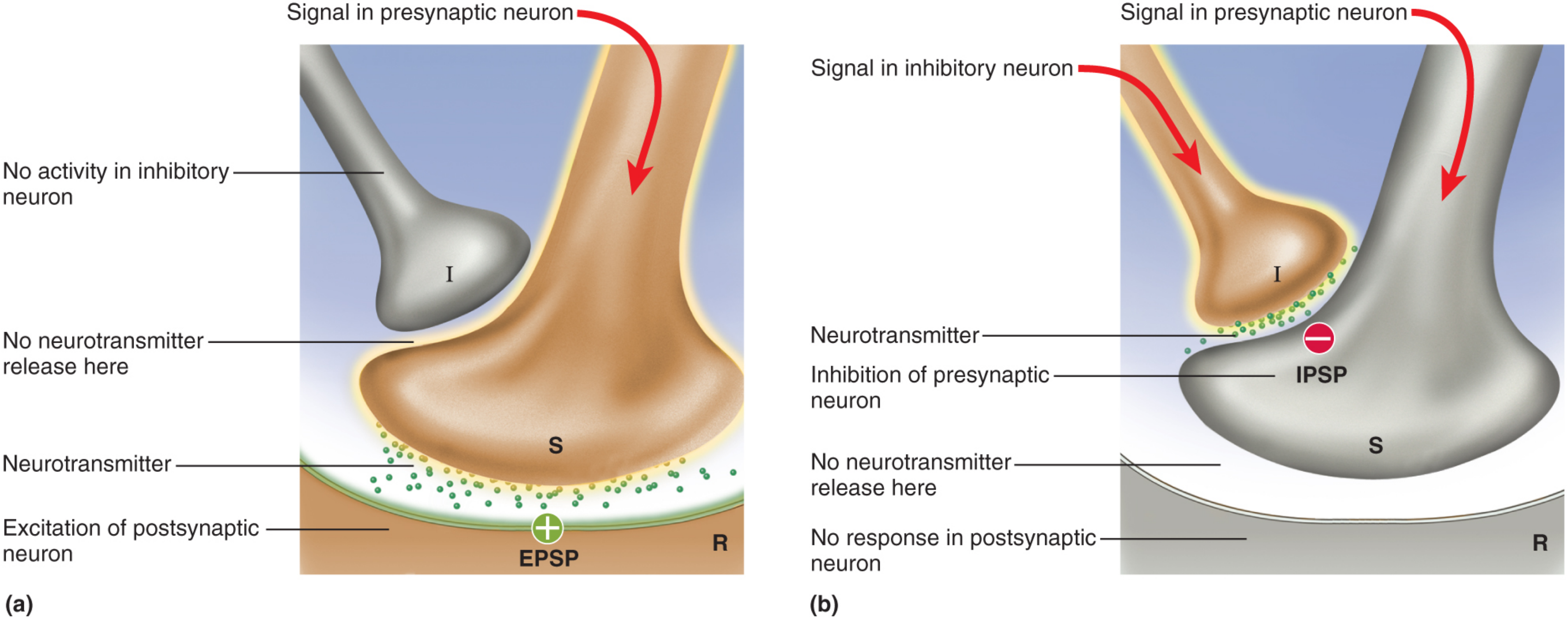


Figure 12.26

Summation, Facilitation, and Inhibition

- neurons routinely work in groups to modify each other's action
- **facilitation** – a process in which one neuron enhances the effect of another one
  - combined effort of several neurons facilitates firing of postsynaptic neuron
- **presynaptic inhibition** – process in which one presynaptic neuron suppresses another one
  - the opposite of facilitation
  - reduces or halts unwanted synaptic transmission
  - neuron I releases inhibitory GABA
    - prevents voltage-gated calcium channels from opening in synaptic knob and presynaptic neuron releases less or no neurotransmitter



Signal in presynaptic neuron
No activity in inhibitory neuron
I
No neurotransmitter release here
S
Neurotransmitter
Excitation of postsynaptic neuron
EPSP
R
(a)
Signal in presynaptic neuron
Signal in inhibitory neuron
I
Neurotransmitter
Inhibition of presynaptic neuron
IPSP
S
No neurotransmitter release here
No response in postsynaptic neuron
R
(b)