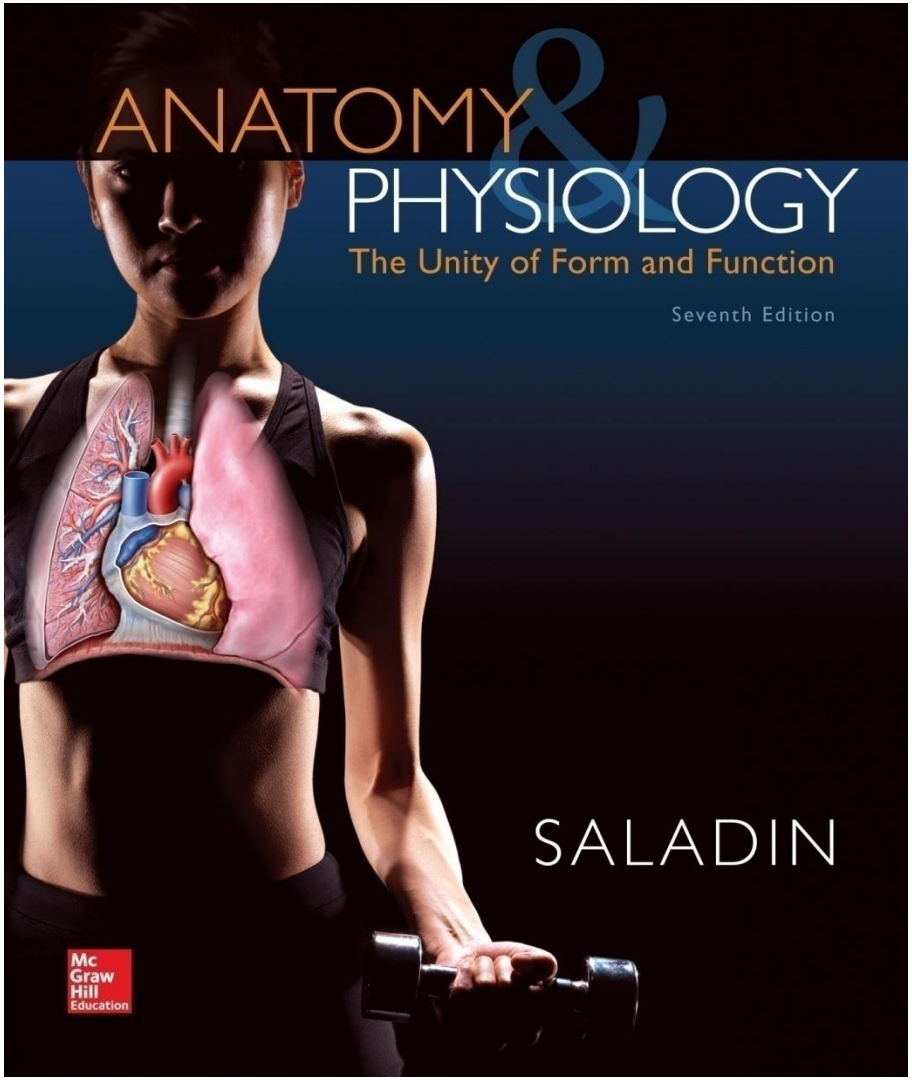
Chapter 12
Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.



Introduction

- **The nervous system is very complex**
- **Nervous system is the foundation of our conscious experience, personality, and behavior**
- **Neurobiology combines the behavioral and life sciences**

Overview of the Nervous System

- **Expected Learning Outcomes**
  - Describe the overall function of the nervous system.
  - Describe its major anatomical and functional subdivisions.

Overview of the Nervous System

- **Endocrine** and **nervous systems** 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

Overview of the Nervous System

- **Nervous system** carries out its task in **three basic steps**
  - Sense organs **receive information** about changes in the body and external environment, and **transmit coded messages** to the brain and spinal cord (CNS: central nervous system)
  - CNS **processes this information,** relates it to past experiences, and determines appropriate response
  - CNS **issues commands** to muscles and gland cells to carry out such a response

Overview of the Nervous System

- **Two major subdivisions of nervous system**
  - **Central nervous system (CNS)**
    - Brain and spinal cord 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

Overview of the Nervous System

- **Peripheral nervous system** contains sensory and motor divisions each with somatic and visceral subdivisions
  - **Sensory (afferent) division:** carries signals from receptors to CNS
    - **Somatic sensory division:** carries signals from receptors in the skin, muscles, bones, and joints
    - **Visceral sensory division:** carries signals from the viscera (heart, lungs, stomach, and urinary bladder)

Overview of the Nervous System

- **Motor (efferent) division**—carries signals from CNS to **effectors** (glands and muscles 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 and smooth muscle
    - Its involuntary responses are **visceral reflexes**

Overview of the Nervous System

- **Visceral motor division (autonomic nervous system)**
  - **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 the Nervous System

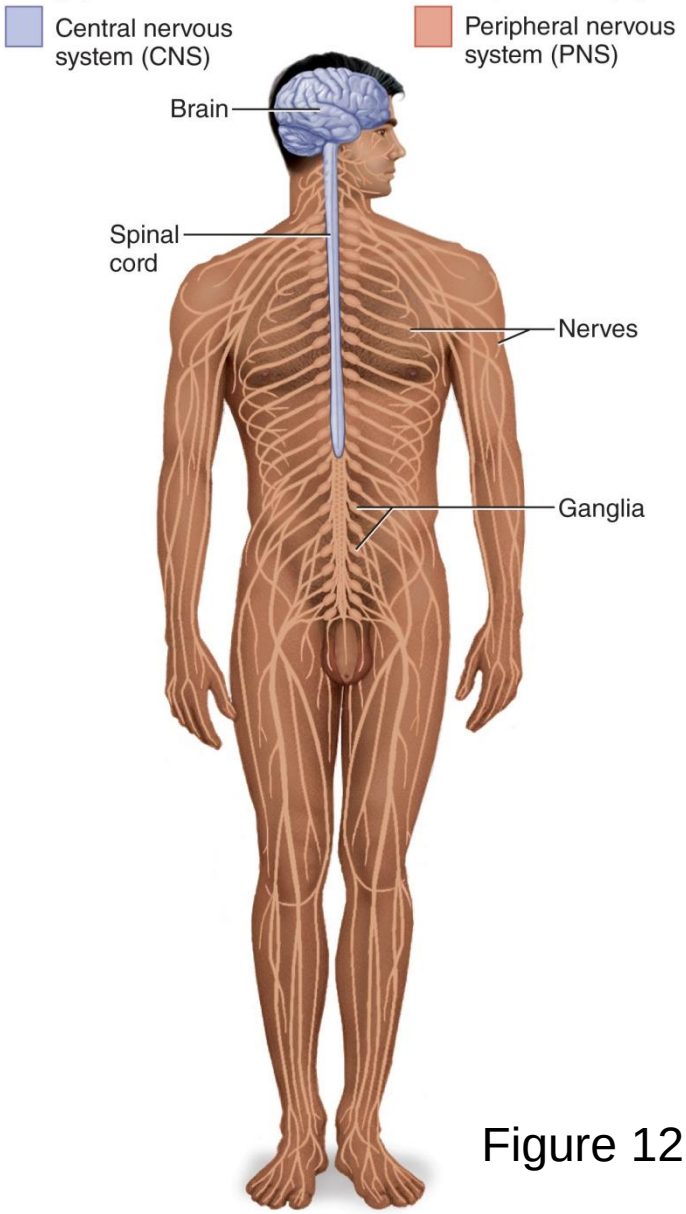


Figure 12.1

Subdivisions of the Nervous System

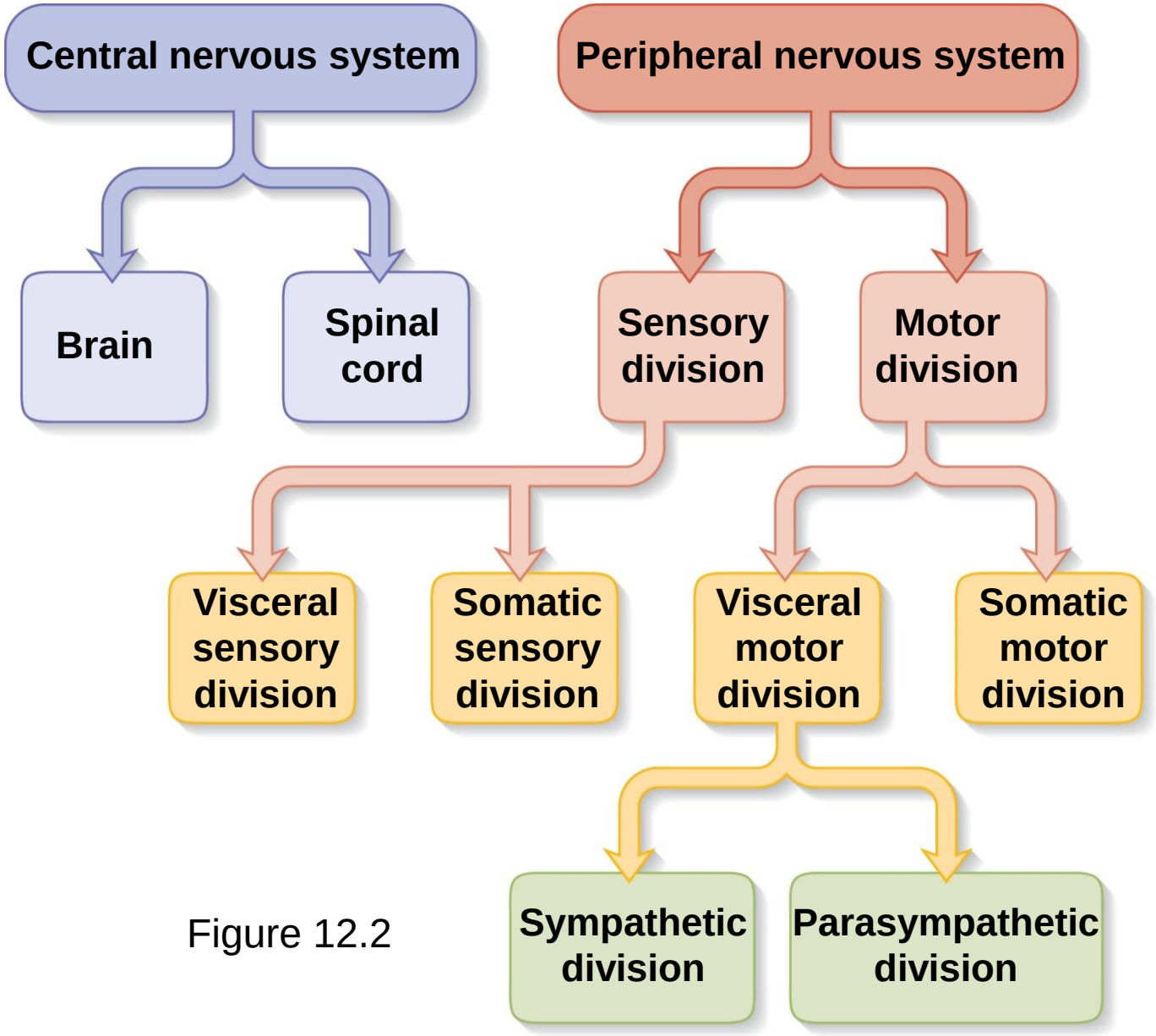


Figure 12.2

Properties of Neurons

- **Expected Learning Outcomes**
  - Describe three functional properties found in all neurons.
  - Define the three most basic functional categories of neurons.
  - Identify the parts of a neuron.
  - Explain how neurons transport materials between the cell body and tips of the axon.

Universal Properties of Neurons

- **Excitability (irritability)**
  - Respond to environmental changes called **stimuli**
- **Conductivity**
  - Respond to stimuli by producing electrical signals that are quickly conducted to other cells at distant locations
- **Secretion**
  - When an electrical signal reaches the end of nerve fiber, the cell secretes a chemical **neurotransmitter** that influences the next cell

Functional Classes of Neurons

- **Sensory (afferent) neurons**
  - Detect stimuli and transmit information about them toward the CNS
- **Interneurons (association neurons)**
  - Lie entirely within CNS connecting motor and sensory pathways (about 90% of all neurons)
  - Receive signals from many neurons and carry out **integrative functions** (make decisions on responses)
- **Motor (efferent) neuron**
  - Send signals out to muscles and gland cells (the **effectors**)

Classes of Neurons

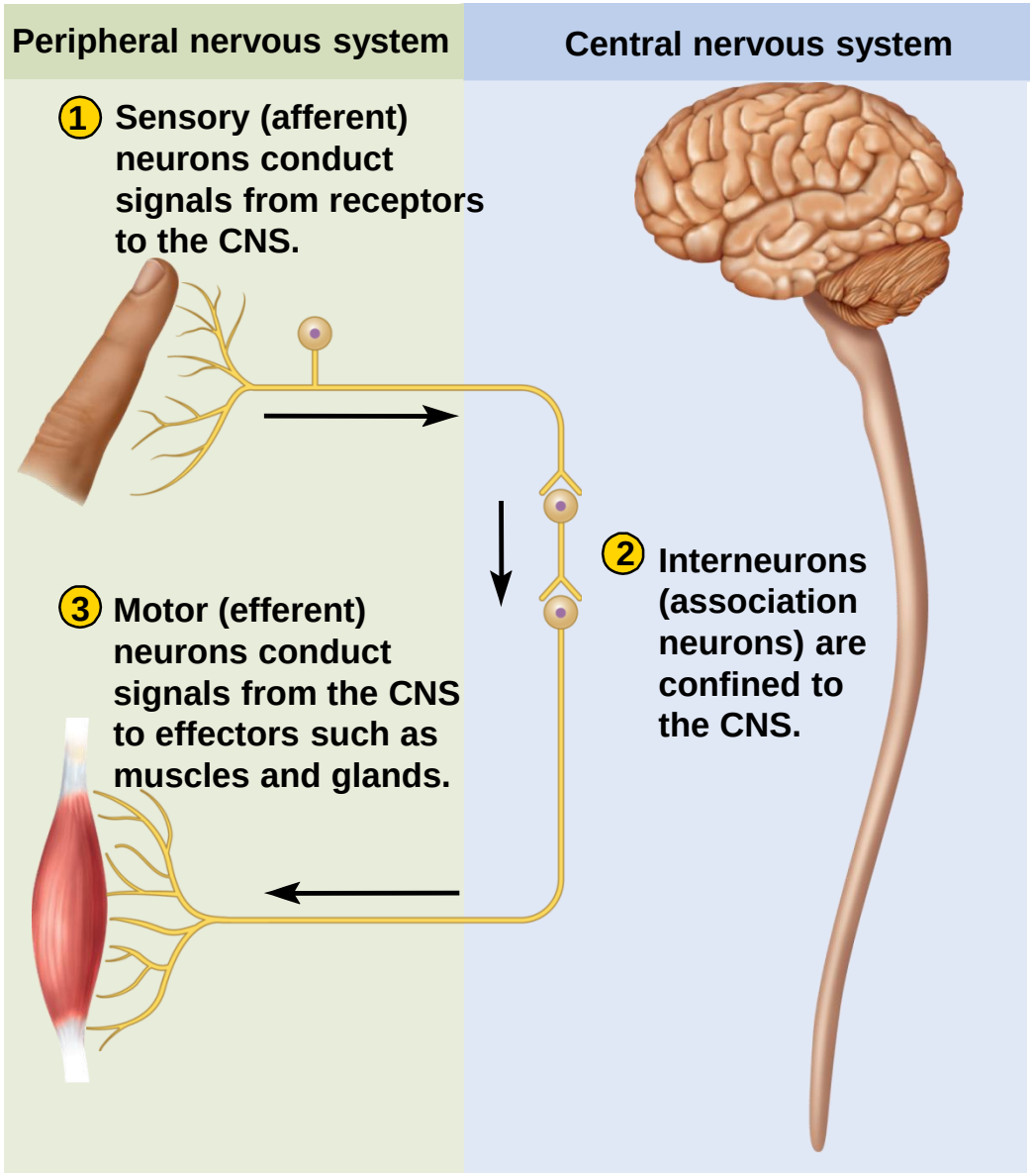


Figure 12.3

Structure of a Neuron

- **Soma**—control center of neuron
  - Also called **neurosoma or cell body**
  - Has a single, centrally located nucleus with large nucleolus
  - **Cytoplasm** contains mitochondria, lysosomes, Golgi complex, inclusions, extensive rough ER and cytoskeleton
    - Inclusions: glycogen, lipid droplets, melanin, and lipofuscin pigment (produced when lysosomes digest old organelles)
    - Cytoskeleton has dense mesh of microtubules and **neurofibrils** (bundles of actin filaments) that compartmentalizes rough ER into dark-staining **Nissl bodies**
    - No centrioles, no mitosis

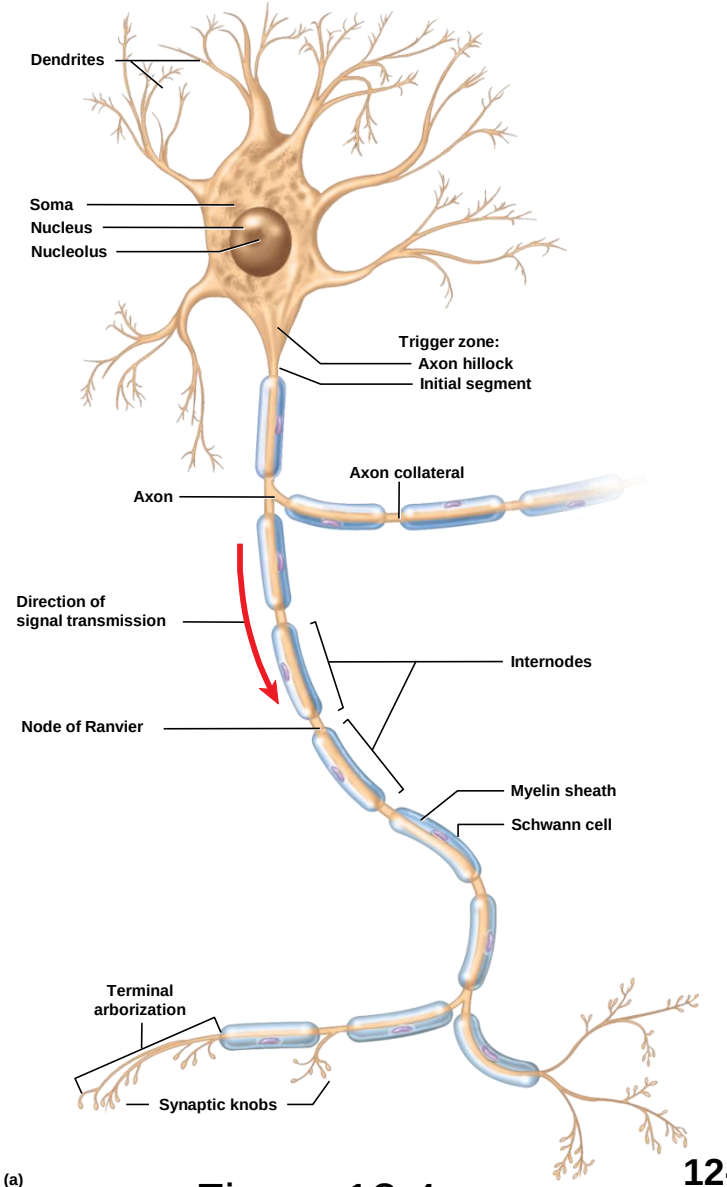


Figure 12.4a

Structure of a Neuron

- **Dendrites**—branches that come off the soma
  - Primary site for receiving signals from other neurons
  - The more dendrites the neuron has, the more information it can receive
  - Provide precise pathways for the reception and processing of information

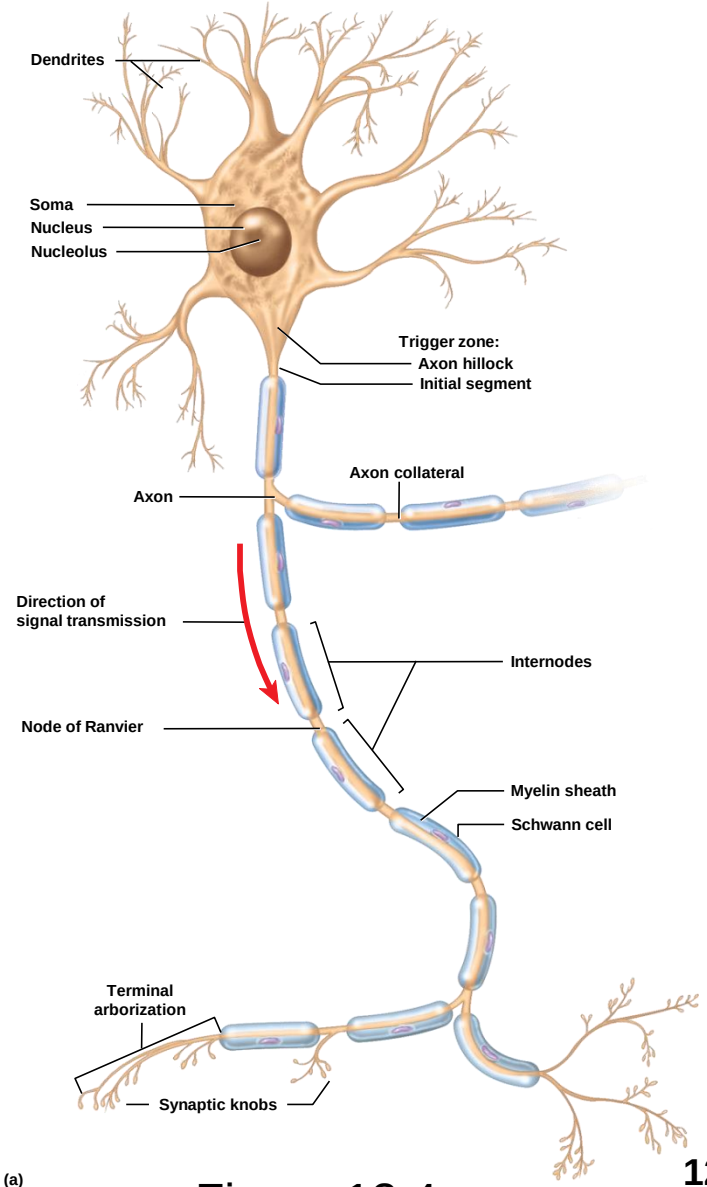


Figure 12.4a

Structure of a Neuron

- **Axon (nerve fiber)**—originates from a mound on the soma called the **axon hillock**
- **Axon is cylindrical, relatively unbranched for most of its length**
  - **Axon collaterals**—branches of axon
  - Branch extensively on distal end
  - Specialized for rapid conduction of signals to distant points
  - **Axoplasm:** cytoplasm of axon
  - **Axolemma:** plasma membrane of axon
  - Only **one axon per neuron** (some neurons have none)
  - **Myelin sheath** may enclose axon

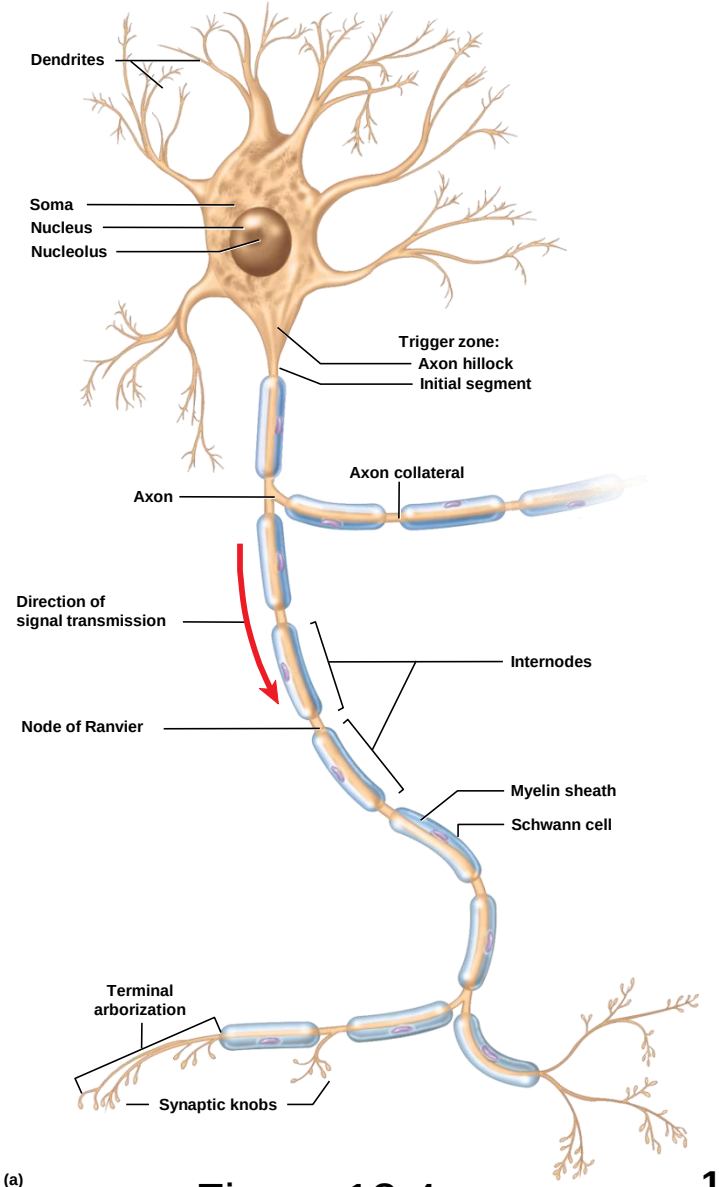


Figure 12.4a

Structure of a Neuron

- Distal end of 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

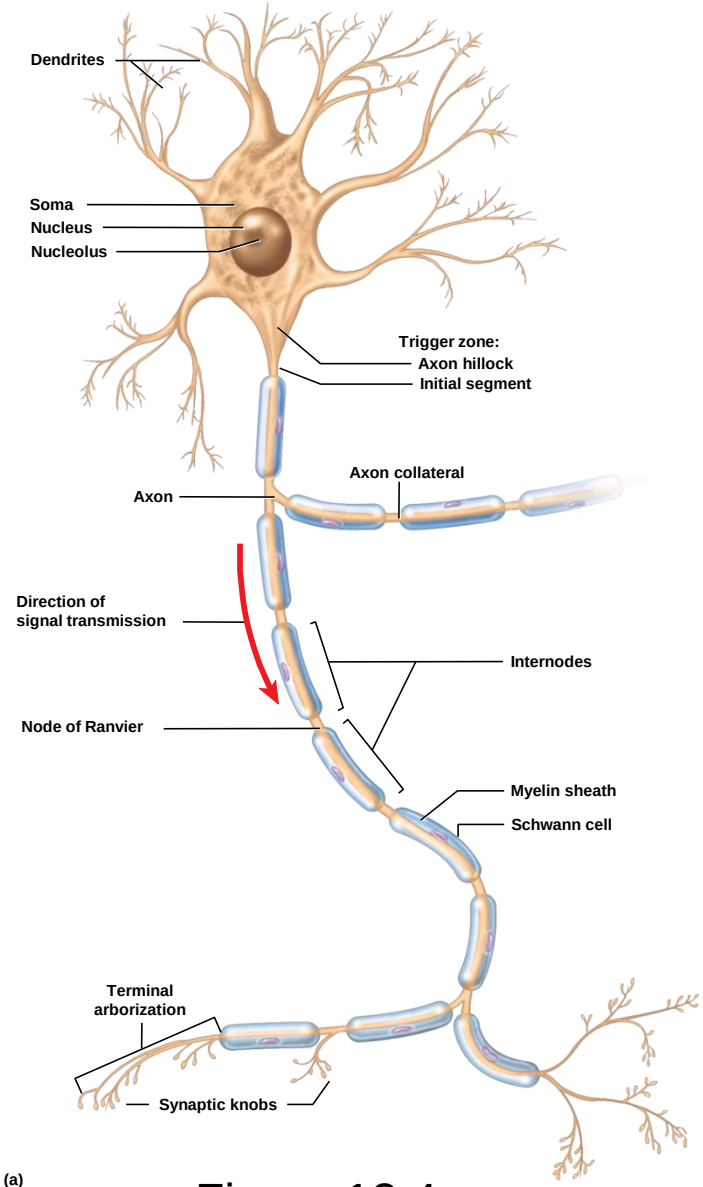


Figure 12.4a

Structure of a Neuron

- **Multipolar neuron**
  - One axon and multiple dendrites
  - Most common – most neurons in CNS
- **Bipolar neuron**
  - One axon and one dendrite
  - Olfactory cells, retina, inner ear
- **Unipolar neuron**
  - Single process leading away from soma
  - Sensory cells from skin and organs to spinal cord
- **Anaxonic neuron**
  - Many dendrites but no axon
  - Retina, brain, and adrenal gland

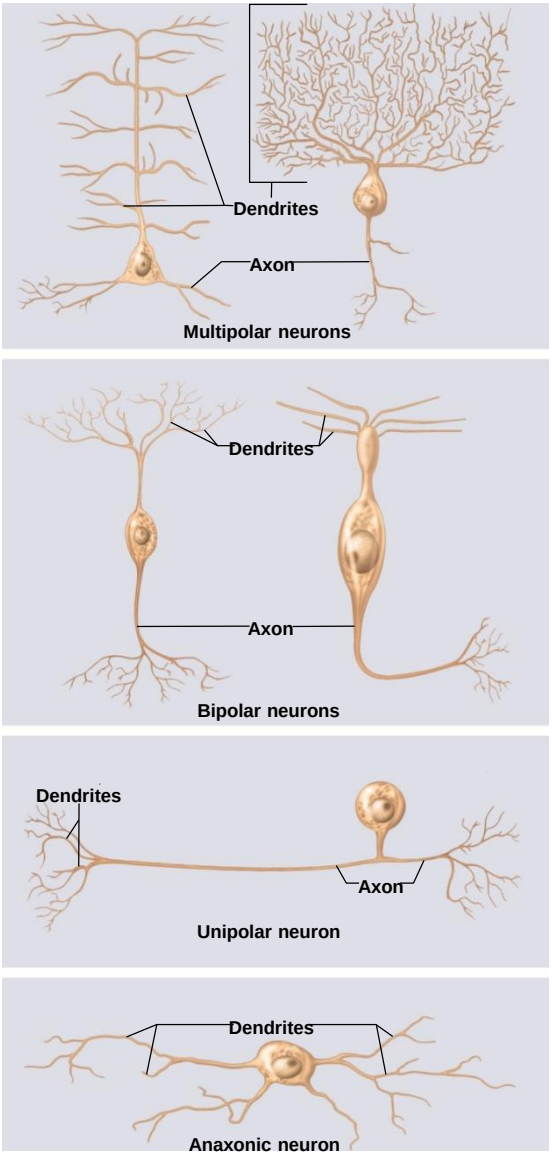


Figure 12.5

Axonal Transport

- **Many proteins made in soma must be transported to axon and axon terminal**
  - To repair axolemma, serve as gated ion channels, enzymes or neurotransmitters
- **Axonal transport—**two-way passage of proteins, organelles, and other material along an axon
  - **Anterograde transport:** movement down the axon away from soma
  - **Retrograde transport:** movement up the axon toward the soma
- **Microtubules** guide materials along axon
  - Motor proteins (kinesin and dynein) carry materials “on their backs” while they “crawl” along microtubules
    - **Kinesin—**motor proteins in anterograde transport
    - **Dynein—**motor proteins in retrograde transport

Axonal Transport

- **Fast axonal transport**—rate of 20 to 400 mm/day
  - **Fast anterograde transport**
    - Organelles, enzymes, synaptic vesicles, and small molecules
  - **Fast retrograde transport**
    - For recycled materials and pathogens—rabies, herpes simplex, tetanus, polio viruses
      - Delay between infection and symptoms is time needed for transport up the axon
- **Slow axonal transport**—0.5 to 10 mm/day
  - Always anterograde
  - Moves enzymes, cytoskeletal components, and new axoplasm down the axon during repair and regeneration of damaged axons
  - Damaged nerve fibers regenerate at a speed governed by slow axonal transport

Supportive Cells (Neuroglia)

- **Expected Learning Outcomes**
  - Name the six types of cells that aid neurons and state their respective functions.
  - Describe the myelin sheath that is found around certain nerve fibers and explain its importance.
  - Describe the relationship of unmyelinated nerve fibers to their supportive cells.
  - Explain how damaged nerve fibers regenerate.

Supportive Cells (Neuroglia)

- About **1 trillion neurons** in the nervous system
- **Neuroglia** outnumber neurons by at least **10 to 1**
- **Neuroglia** or **glial cells**
  - Protect neurons and help them function
  - 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, it is covered by glial cells
    - Prevents neurons from touching each other
    - Gives precision to conduction pathways

Types of Neuroglia

- **Four types of glia** occur **in CNS:** oligodendrocytes, ependymal cells, microglia, and astrocytes
  - **Oligodendrocytes**
    - Form myelin sheaths in CNS that speed signal conduction
      - Arm-like processes wrap around nerve fibers
  - **Ependymal cells**
    - Line internal cavities of the brain; secrete and circulate cerebrospinal fluid (CSF)
      - Cuboidal epithelium with cilia on apical surface
  - **Microglia**
    - Wander through CNS looking for debris and damage
      - Develop from white blood cells (monocytes) and become concentrated in areas of damage

Types of Neuroglia

- **Astrocytes**
  - Most abundant glial cell in CNS, covering brain surface and most nonsynaptic regions of neurons in the gray matter
  - Diverse functions:
    - Form supportive framework
    - Have extensions **(perivascular feet)** that contact blood capillaries and stimulate them to form a seal called the **blood–brain barrier**
    - Convert glucose to **lactate** and supply this to neurons
    - Secrete **nerve growth factors**
    - Communicate electrically with neurons
    - Regulate chemical composition of tissue fluid by absorbing excess neurotransmitters and ions
    - **Astrocytosis** or **sclerosis**—when neuron is damaged, astrocytes form hardened scar tissue and fill in space

Neuroglial Cells of CNS

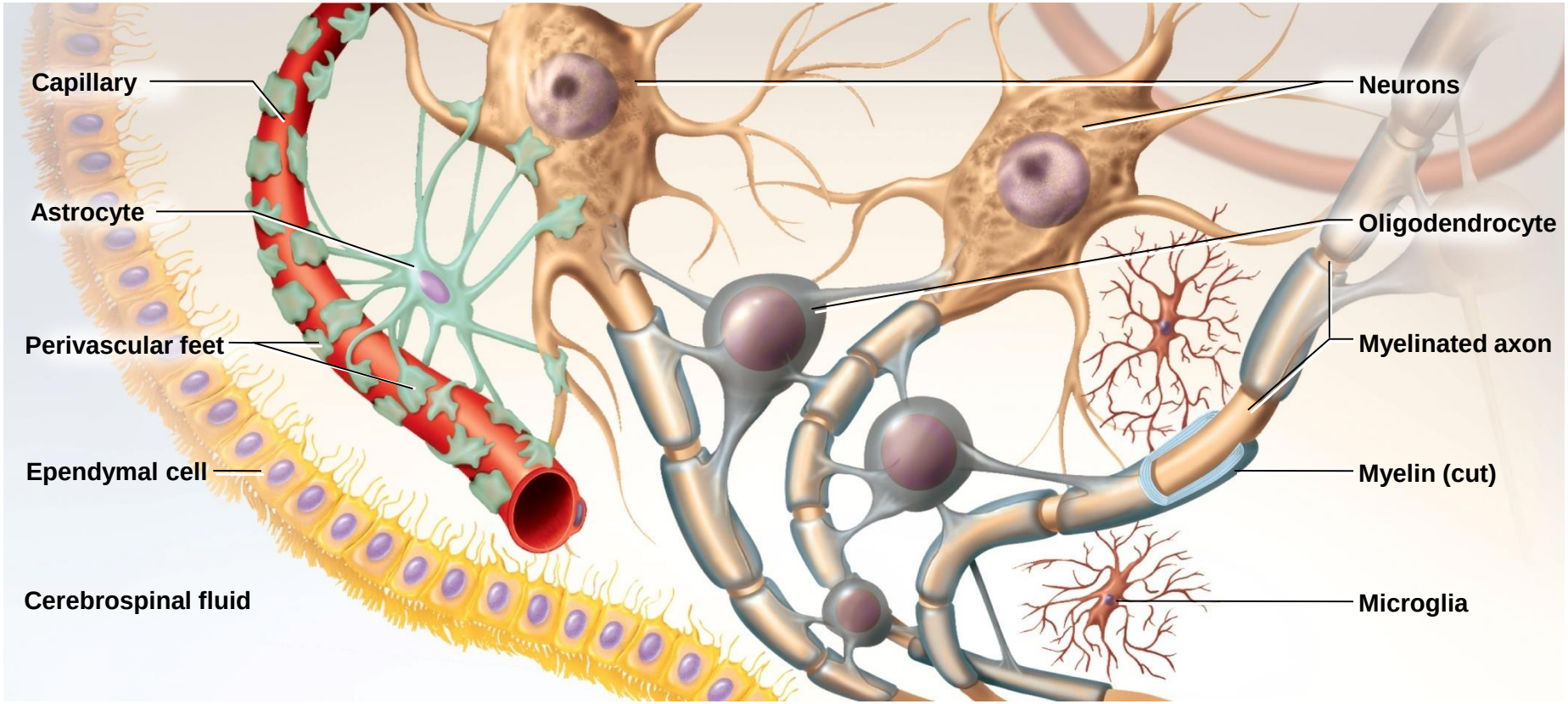


Figure 12.6

Types of Neuroglia

- **Two types occur only in PNS**
  - **Schwann cells**
    - Envelope nerve fibers in PNS
    - Wind repeatedly around a nerve fiber
    - Produce a **myelin sheath** similar to the ones produced by oligodendrocytes in CNS
    - Assist in 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

Myelin

- **Myelin sheath—**insulation 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 at week 14 of fetal development
  - Proceeds rapidly during infancy
  - Completed in late adolescence
  - Dietary fat is important to CNS development

Myelin

- In PNS, **Schwann cell** spirals repeatedly around a single nerve fiber
  - Lays down as many as one hundred layers of 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**

Myelin Sheath in PNS

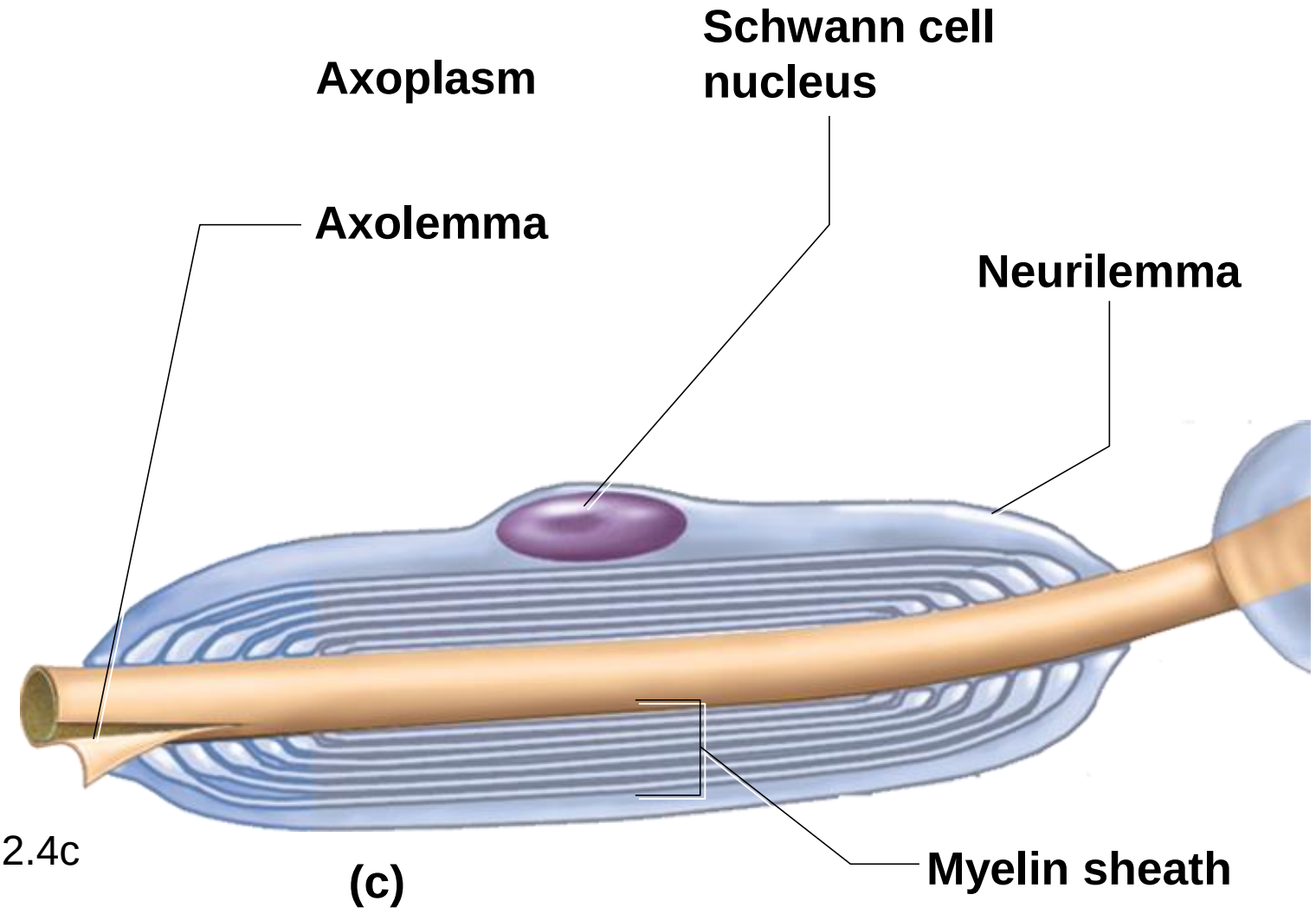


Figure 12.4c

(c)

Nodes of Ranvier and internodes

Myelination in PNS

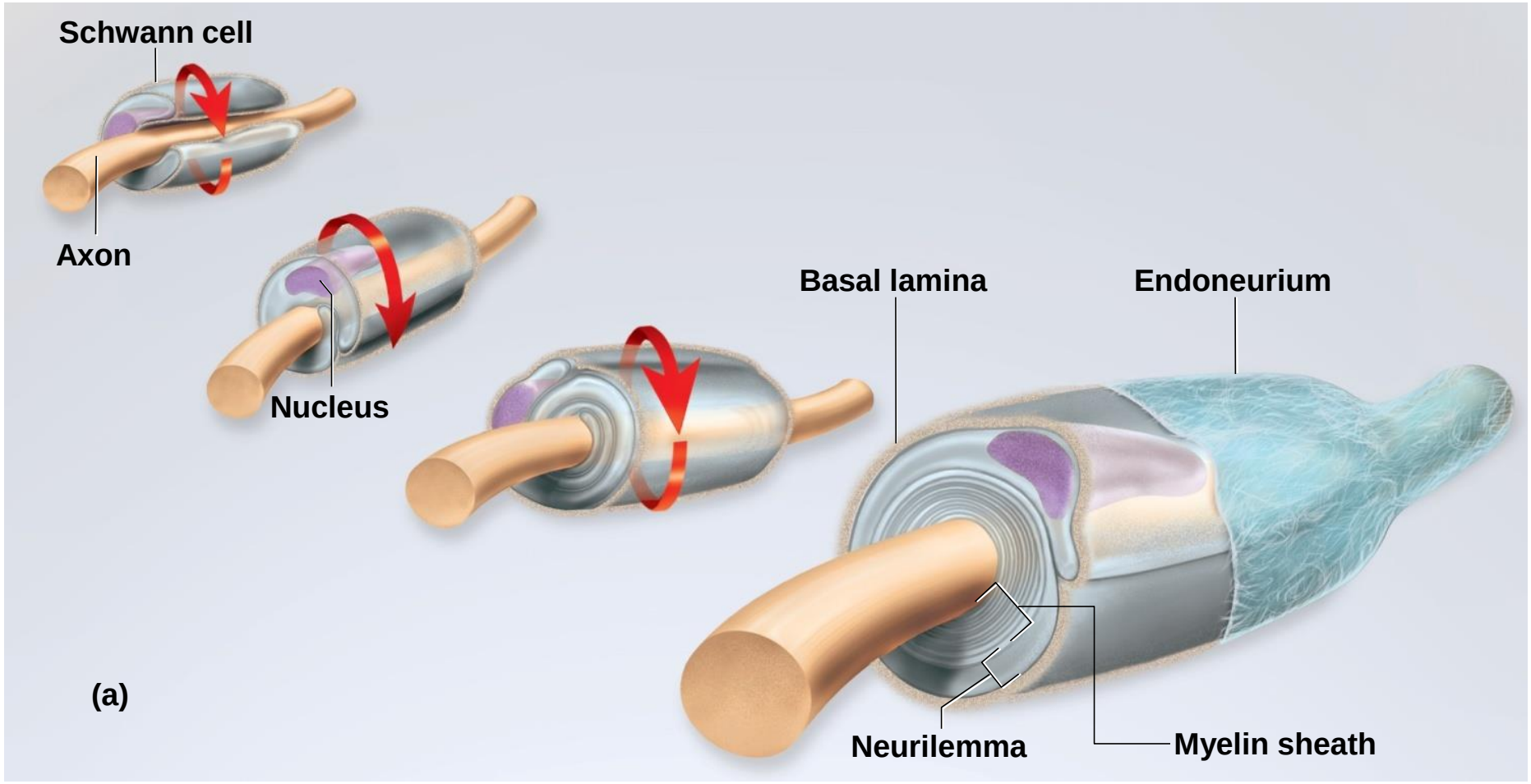


Figure 12.7a

Myelin

- In CNS—an **oligodendrocyte** myelinates 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

Myelination in CNS

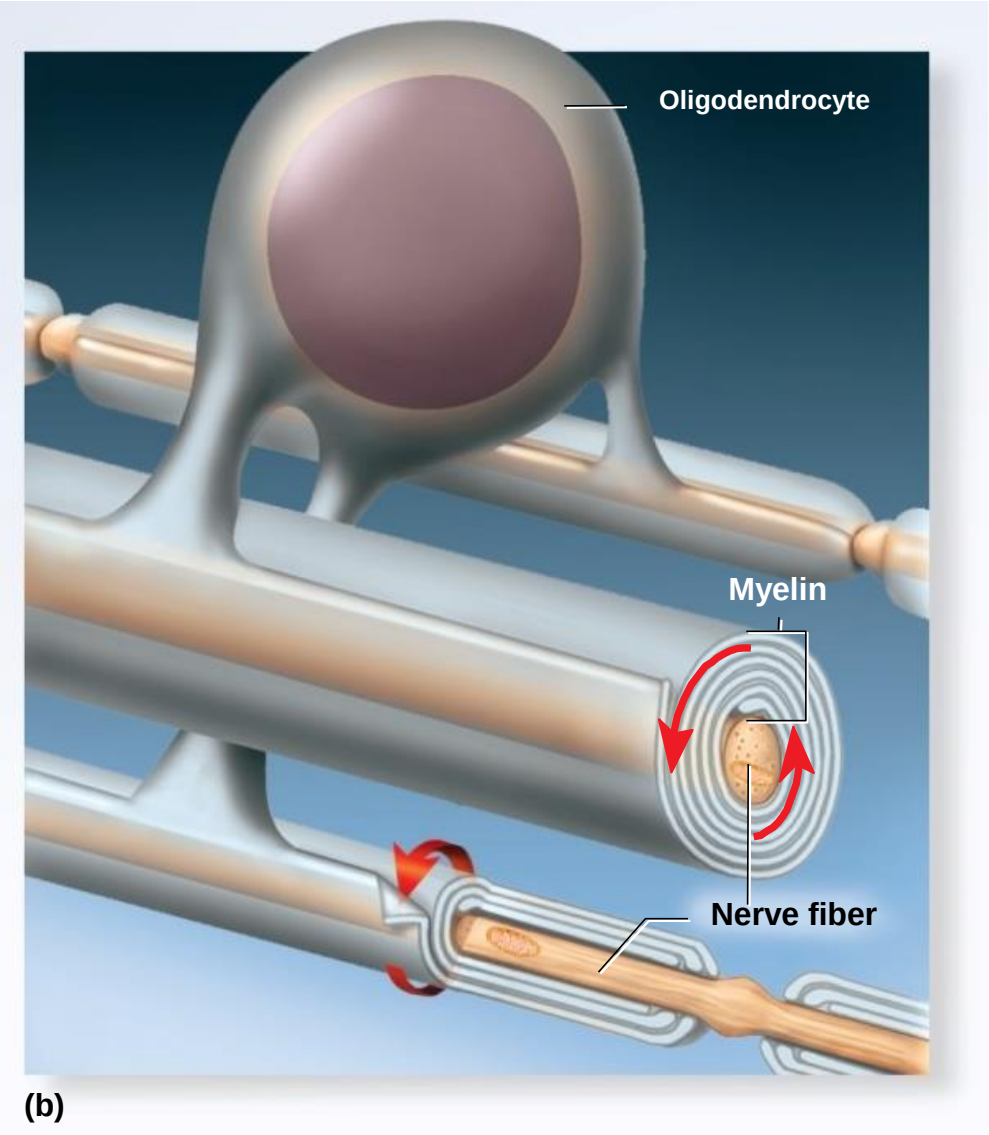


Figure 12.7b

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

Glial Cells and Brain Tumors

- **Tumors—**masses of rapidly dividing cells
  - Mature neurons have little or no capacity for mitosis and seldom form tumors
- **Brain tumors** arise from:
  - Meninges (protective membranes of CNS)
  - Metastasis from nonneuronal tumors in other organs
  - Often glial cells that are mitotically active throughout life
- **Gliomas** grow rapidly and are highly malignant
  - Blood–brain barrier decreases effectiveness of chemotherapy
  - Treatment consists of radiation or surgery

Diseases of the Myelin Sheath

- **Degenerative disorders of the myelin sheath**
  - **Multiple sclerosis**
    - Oligodendrocytes and myelin sheaths in the CNS deteriorate
    - Myelin replaced by hardened scar tissue
    - Nerve conduction disrupted (double vision, tremors, numbness, speech defects)
    - Onset between 20 and 40 and fatal from 25 to 30 years after diagnosis
    - Cause may be autoimmune triggered by virus

Diseases of the Myelin Sheath

(continued)

- **Degenerative disorders of the myelin sheath**
  - **Tay–Sachs disease:** a hereditary disorder of infants of Eastern European Jewish ancestry
    - Abnormal accumulation of glycolipid called **GM_2** in the myelin sheath
      - Normally decomposed by lysosomal enzyme
      - Enzyme missing in individuals homozygous for Tay–Sachs allele
      - Accumulation of **ganglioside** (GM_2) disrupts conduction of nerve signals
      - Blindness, loss of coordination, and dementia
    - Fatal before age 4

Unmyelinated Nerve Fibers

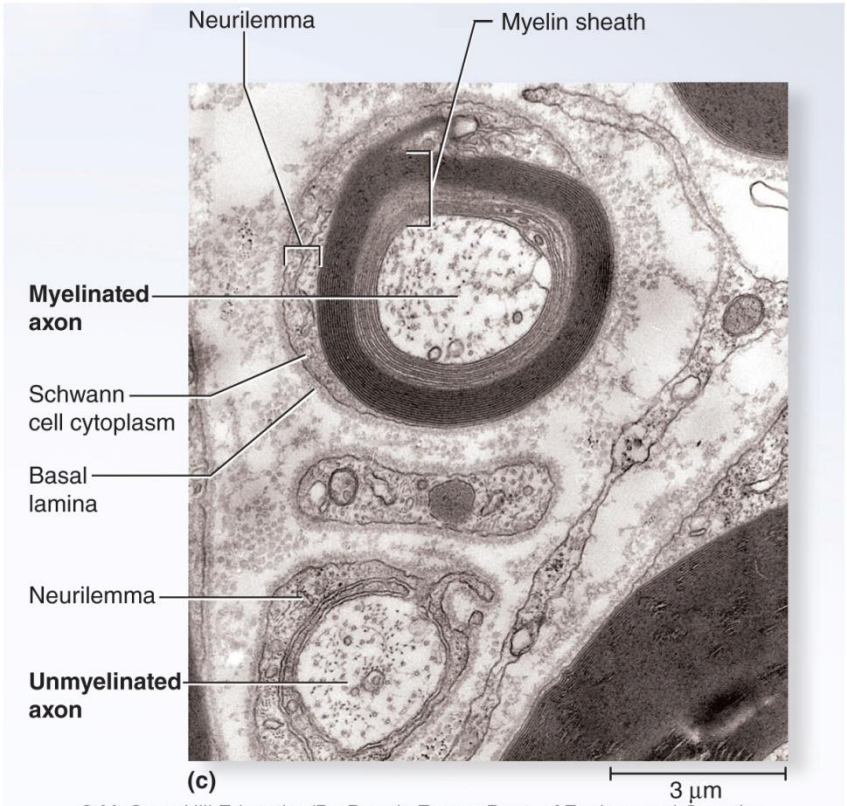


Figure 12.7c

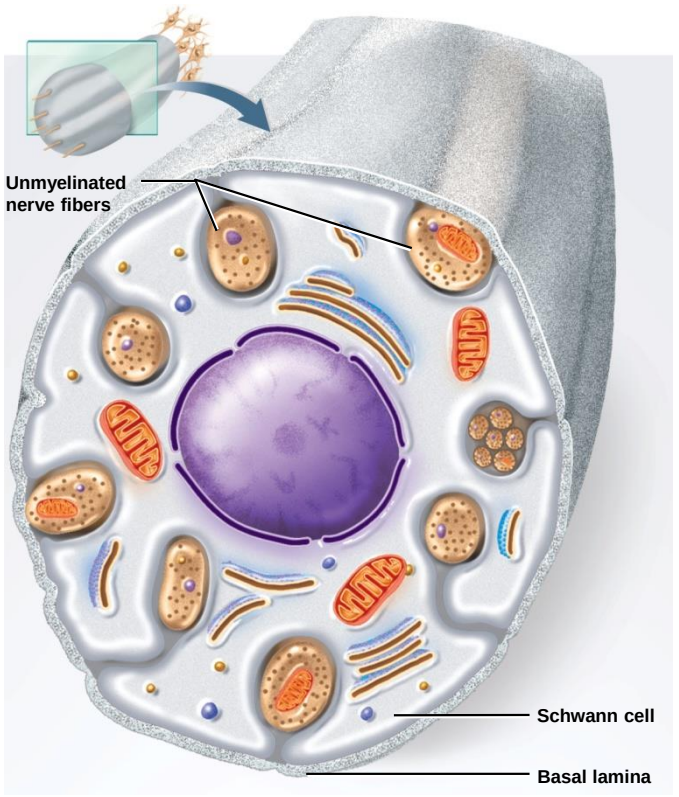


Figure 12.8

- Many CNS and PNS fibers are unmyelinated
- In PNS, Schwann cells hold 1 to 12 small nerve fibers in surface grooves
- Membrane folds once around each fiber

Conduction Speed of Nerve Fibers

- **Speed at which a nerve signal travels along surface of nerve fiber depends on two factors**
  - **Diameter of fiber**
    - Larger fibers have more surface area and conduct signals more rapidly
  - **Presence or absence of myelin**
    - Myelin further speeds signal conduction

Conduction Speed of Nerve Fibers

- **Conduction speed**
  - Small, unmyelinated fibers: 0.5 to 2.0 m/s
  - Small, myelinated fibers: 3 to 15.0 m/s
  - Large, myelinated fibers: up to 120 m/s
  - Slow signals sent to the gastrointestinal tract where speed is less of an issue
  - Fast signals sent to skeletal muscles where speed improves balance and coordinated body movement

Regeneration of Nerve Fibers

- **Regeneration of damaged peripheral nerve fiber can occur if:**
  - Its **soma is intact**
  - At least **some neurilemma remains**
- **Steps of regeneration:**
  - Fiber distal to the injury cannot survive and degenerates
    - Macrophages clean up tissue debris at point of injury and beyond
  - Soma swells, ER breaks up, and nucleus moves off center
    - Due to loss of nerve growth factors from neuron's target cell
  - Axon stump sprouts multiple growth processes as severed distal end continues to degenerate
  - Schwann cells, basal lamina and neurilemma form a regeneration tube
    - Enables neuron to regrow to original destination and reestablish synaptic contact

Regeneration of Nerve Fibers

- **Once contact is reestablished with original target, the soma shrinks and returns to its original appearance**
  - Nucleus returns to normal shape
  - Atrophied muscle fibers regrow
- **But regeneration is not fast, perfect, or always possible**
  - Slow regrowth means process may take 2 years
  - Some nerve fibers connect with the wrong muscle fibers; some die
  - Regeneration of damaged nerve fibers in the **CNS cannot occur at all**

Regeneration of Nerve Fiber

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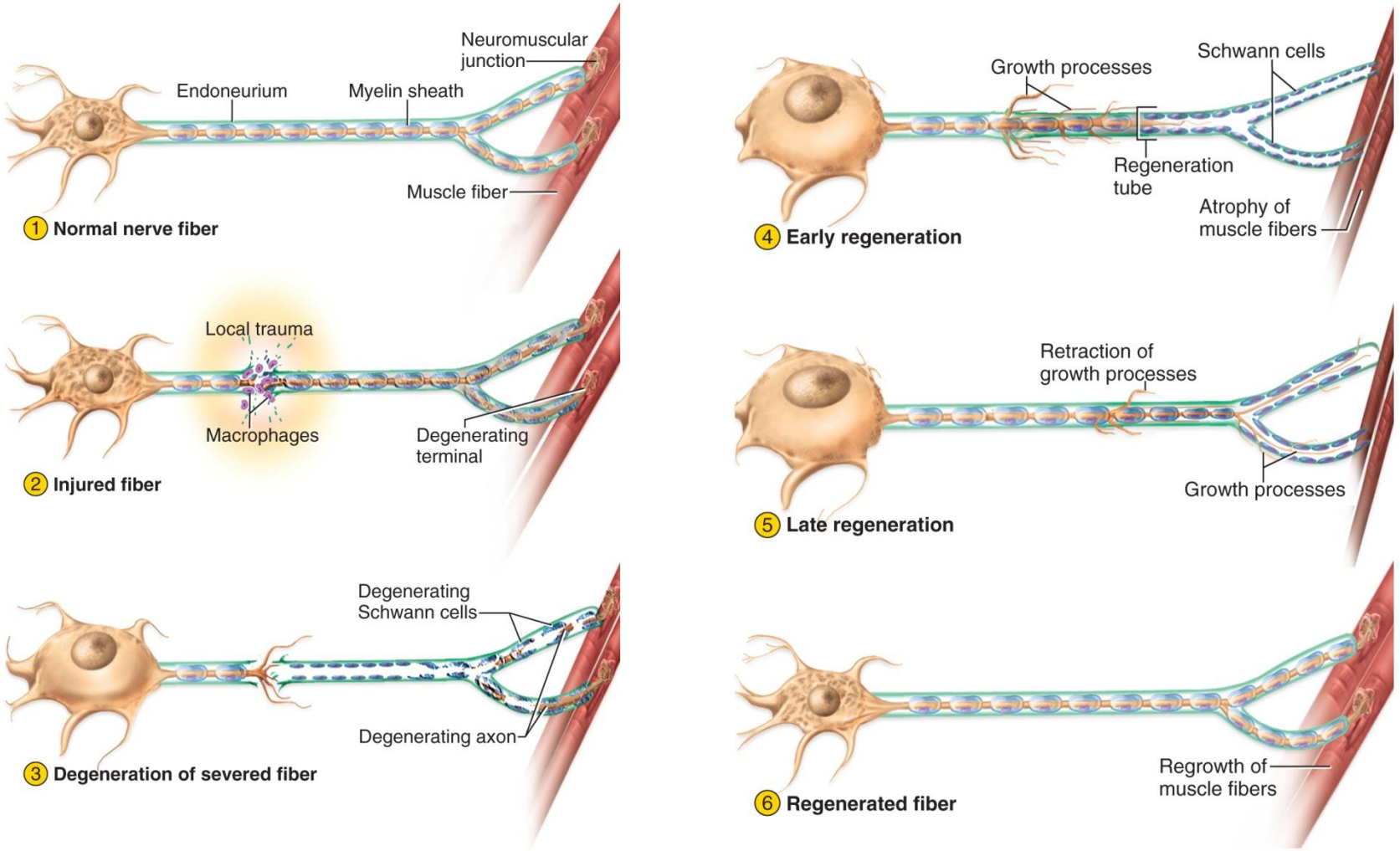


Figure 12.9

Nerve Growth Factor

- **Nerve growth factor (NGF)**—protein secreted by a gland, muscle, or glial cells and picked up by the axon terminals of neurons
  - Prevents **apoptosis** (programmed cell death) in growing neurons
  - Enables growing neurons to make contact with their targets
- **Isolated by Rita Levi-Montalcini in 1950s**
- **Won Nobel prize in 1986 with Stanley Cohen**
- **Use of growth factors is now a vibrant field of research**

Figure 12.10

Electrophysiology of Neurons

- **Expected Learning Outcomes**
  - Explain why a cell has an electrical charge difference (voltage) across its membrane.
  - Explain how stimulation of a neuron causes a local electrical response in its membrane.
  - Explain how local responses generate a nerve signal.
  - Explain how the nerve signal is conducted down an axon.

Electrophysiology of Neurons

- **Galen (Roman physician)** thought brain pumped a vapor called *psychic pneuma* through hollow nerves and into muscles to make them contract
- **René Descartes** in the 17th century supported Galen's theory
- **Luigi Galvani** discovered the role of electricity in muscle contraction in the 18th century
- **Camillo Golgi** developed an important method for staining neurons with silver in the 19th century
- **Santiago Ramón y Cajal** (1852-1934) used stains to trace neural pathways
  - He showed that pathways were made of distinct neurons (not continuous tubes)
  - He demonstrated how separate neurons were connected by synapses

Electrophysiology of Neurons

- **Cajal's theory brought up two key questions:**
  - How does a neuron generate an electrical signal?
  - How does it transmit a meaningful message to the next cell?

Electrical Potentials and Currents

- **Electrophysiology**—study of cellular mechanisms for producing electrical potentials and currents
  - Basis for neural communication and muscle contraction
- **Electrical potential**—a difference in concentration of charged particles between one point and another
  - Living cells are polarized and have a resting membrane potential
  - Cells have more negative particles on inside of membrane than outside
  - Neurons have about −70 mV resting membrane potential
- **Electrical current**—a flow of charged particles from one point to another
  - In the body, **currents** are movements of ions, such as Na^+ or K^+, through channels in the plasma membrane
  - Gated channels are opened or closed by various stimuli
  - Enables cell to turn electrical currents on and off

The Resting Membrane Potential

- **Resting membrane potential (RMP) exists because of unequal electrolyte distribution between extracellular fluid (ECF) and intracellular fluid (ICF)**
- **RMP results from the combined effect of three factors**
  - Ions diffuse down their concentration gradient through the membrane
  - Plasma membrane is selectively permeable and allows some ions to pass easier than others
  - Electrical attraction of cations and anions to each other

The Resting Membrane Potential

- **Potassium (K^+)** has greatest influence on RMP
  - Plasma membrane is more permeable to K^+ than any other ion
  - Leaks out until electrical charge of cytoplasmic anions attracts it back in and equilibrium is reached (no more net movement of K^+)
  - K^+ is about 40 times as concentrated in the ICF as in the ECF
- **Cytoplasmic anions** cannot escape due to size or charge (phosphates, sulfates, small organic acids, proteins, ATP, and RNA)

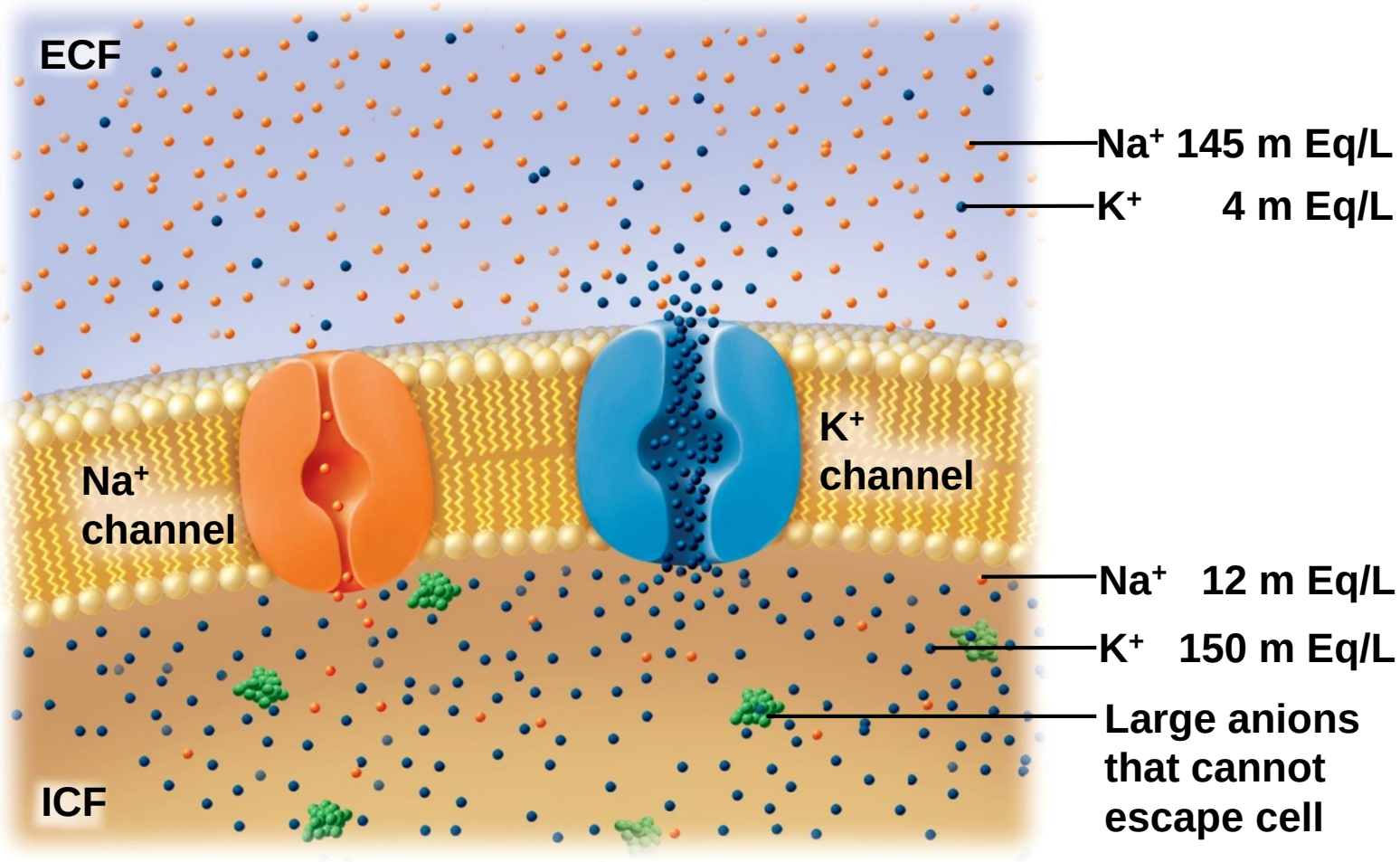
The Resting Membrane Potential

- Membrane is not very permeable to **sodium (Na^+)** but RMP is slightly influenced by it
  - Na^+ is about 12 times as concentrated in the ECF as in the ICF
  - Some Na^+ leaks into the cell, diffusing down its concentration and electrical gradients
  - This Na^+ leakage makes RMP slightly less negative than it would be if RMP were determined solely by K^+

The Resting Membrane Potential

- **Na^+/K^+ pump** moves 3 Na^+ out for every 2 K^+ it brings in
  - Works continuously to compensate for Na^+ and K^+ leakage, and requires great deal of ATP (1 ATP per exchange)
    - 70% of the energy requirement of the nervous system
  - Necessitates glucose and oxygen be supplied to nerve tissue (energy needed to create the resting potential)
  - The exchange of 3 positive charges for only 2 positive charges contributes about −3 mV to the cell's resting membrane potential of −70 mV

The Resting Membrane Potential



- Na^+ concentrated outside of cell (ECF)
- K^+ concentrated inside cell (ICF)

Figure 12.11

Local Potentials

- **Local potentials—**changes in membrane potential of a neuron occurring at and nearby the part of the cell that is stimulated
- **Different neurons can be stimulated by chemicals, light, heat, or mechanical disturbance**
- **A chemical stimulant binds to a receptor on the neuron**
  - Opens Na^+ gates and allows Na^+ to enter cell
  - Entry of a positive ion makes the cell less negative; this is a **depolarization:** a change in membrane potential toward zero mV
  - Na^+ entry results in a current that travels toward the cell's trigger zone; this short-range change in voltage is called a **local potential**

Local Potentials

- Properties of **local potentials** (unlike action potentials)
  - **Graded:** vary in magnitude with stimulus strength
    - Stronger stimuli open more Na^+ gates
  - **Decremental:** get weaker the farther they spread from the point of stimulation
    - Voltage shift caused by Na^+ inflow diminishes with distance
  - **Reversible:** if stimulation ceases, the cell quickly returns to its normal resting potential
  - **Either excitatory** or **inhibitory:** some neurotransmitters make the membrane potential more negative—hyperpolarize it—so it becomes less likely to produce an action potential

Local Potentials

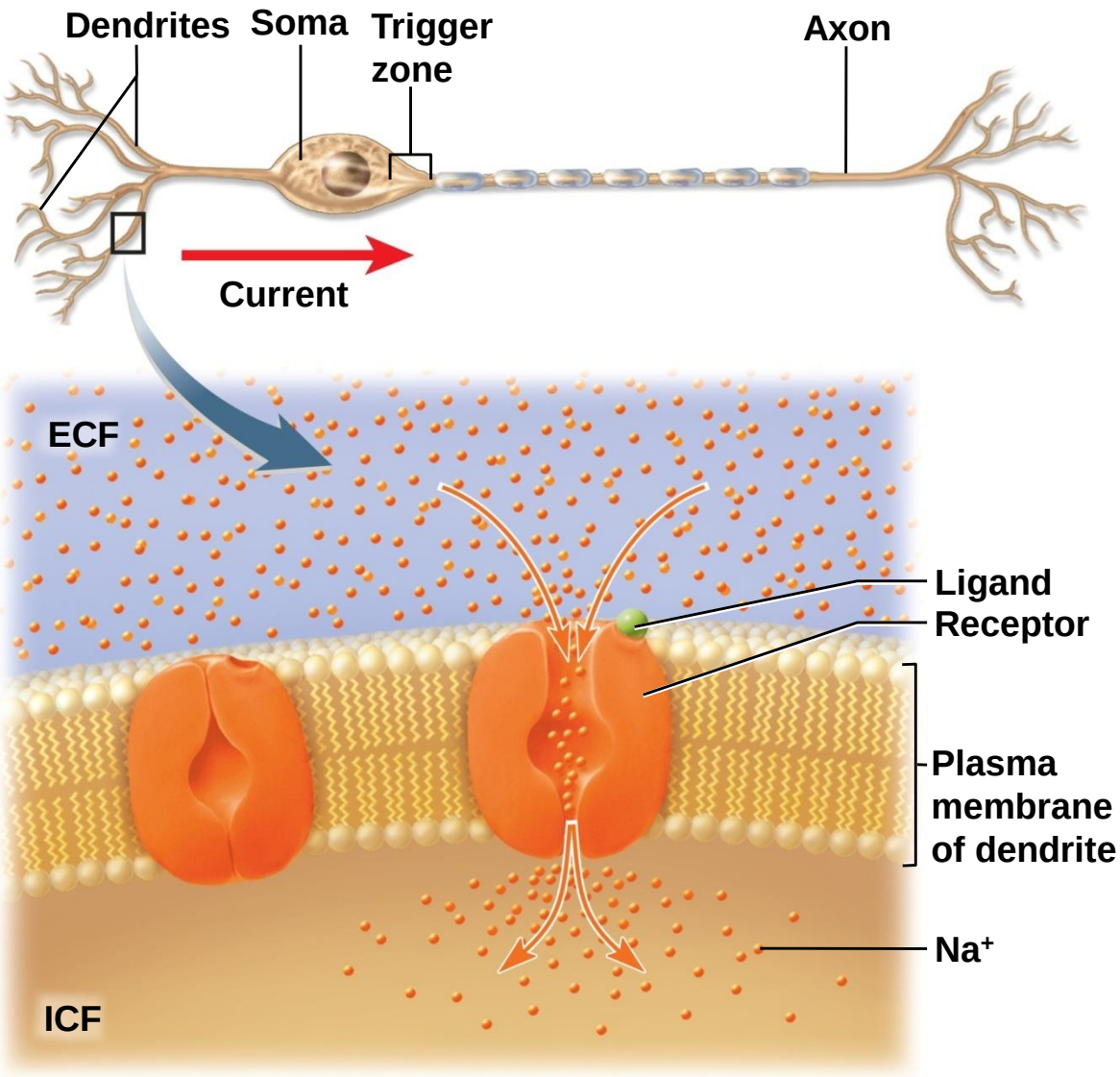


Figure 12.12

Action Potentials

- **Action potential—**dramatic change in membrane polarity produced by voltage-gated ion channels
  - Only occurs where there is a high enough density of voltage-regulated gates
  - **Soma** (50 to 75 gates per μm^2); cannot generate an action potential
  - **Trigger zone** (350 to 500 gates per μm^2); where action potential is generated
    - If excitatory local potential reaches trigger zone and is still strong enough, it can open these gates and generate an action potential

Action Potentials

- **Action potential is a rapid up-and-down shift in the membrane voltage involving a sequence of steps:**
  - Arrival of current at axon hillock depolarizes membrane
  - Depolarization must reach **threshold:** critical voltage (about -55 mV) required to open voltage-regulated gates
  - Voltage-gated Na^+ channels open, Na^+ enters and depolarizes cell, which opens more channels resulting in a rapid positive feedback cycle as voltage rises

Action Potentials

- **(Steps in action potential shift in membrane voltage, *Continued*)**
  - As membrane potential rises above 0 mV, Na^+ channels are inactivated and close; voltage peaks at about +35 mV
  - Slow K^+ channels open and outflow of K^+ repolarizes the cell
  - K^+ channels remain open for a time so that membrane is briefly hyperpolarized (more negative than RMP)
  - RMP is restored as Na^+ leaks in and extracellular K^+ is removed by astrocytes

Action Potentials

- **Only a thin layer of the cytoplasm next to the cell membrane is affected**
  - In reality, very few ions are involved
- Action potential is often called a **spike,** as it happens so fast

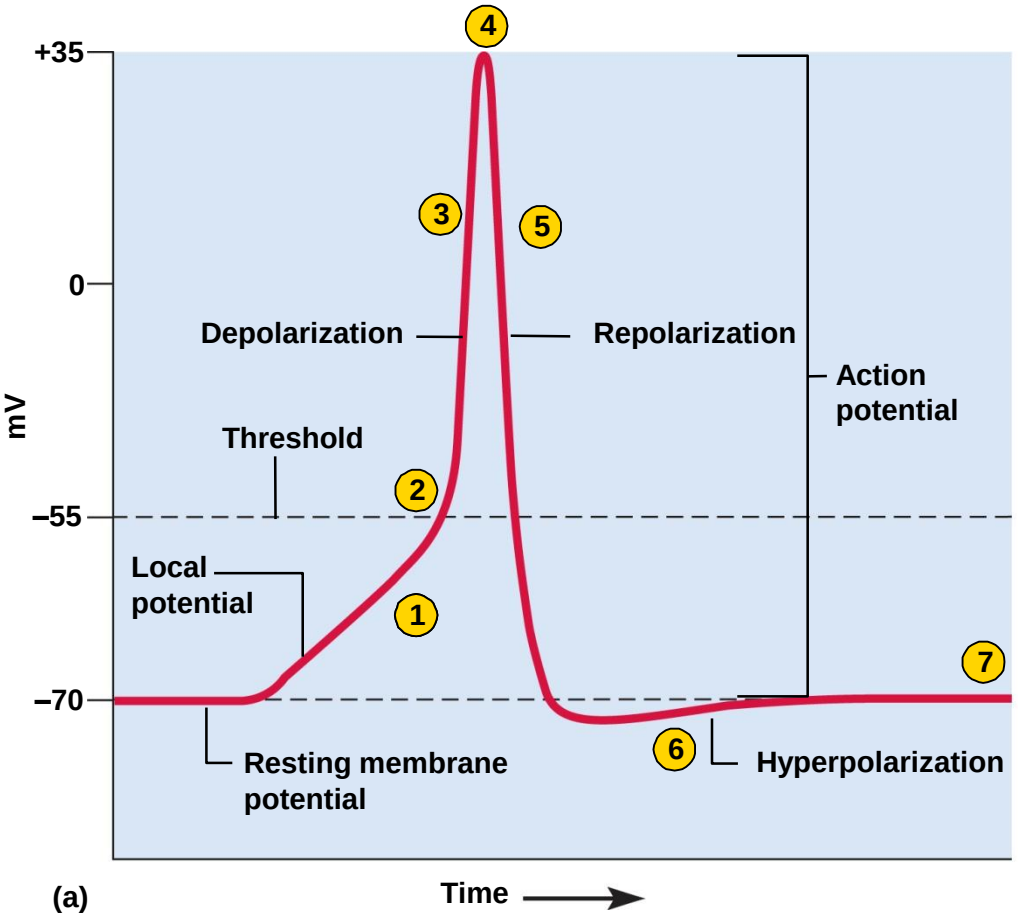


Figure 12.13a

Action Potentials

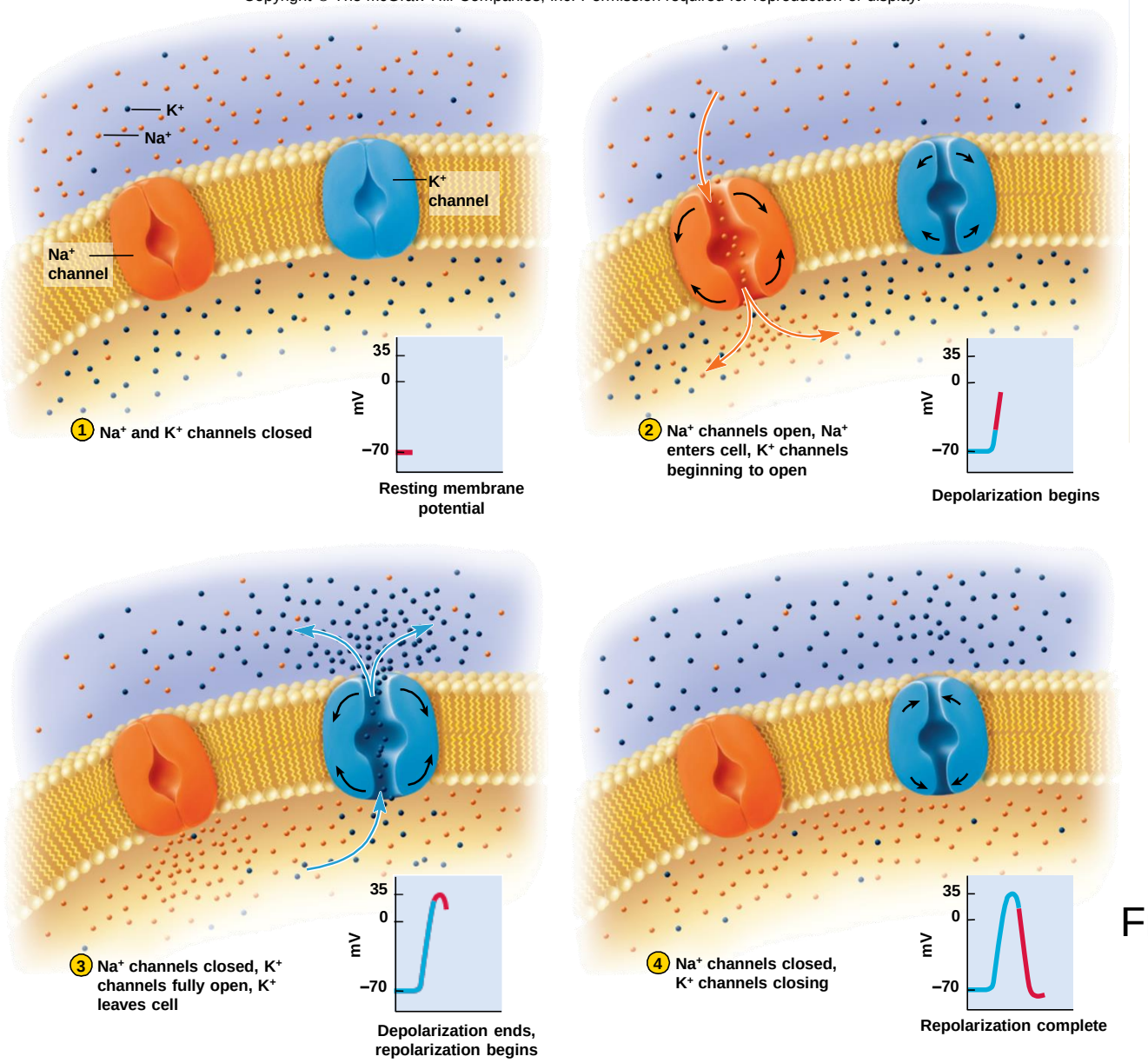


Figure 12.14

Action Potentials

- **Characteristics of action potential (unlike local potential)**
  - Follows an **all-or-none law**
    - If threshold is reached, neuron fires at its maximum voltage
    - If threshold is not reached, it does not fire
  - **Nondecremental:** do not get weaker with distance
  - **Irreversible:** once started, goes to completion and cannot be stopped

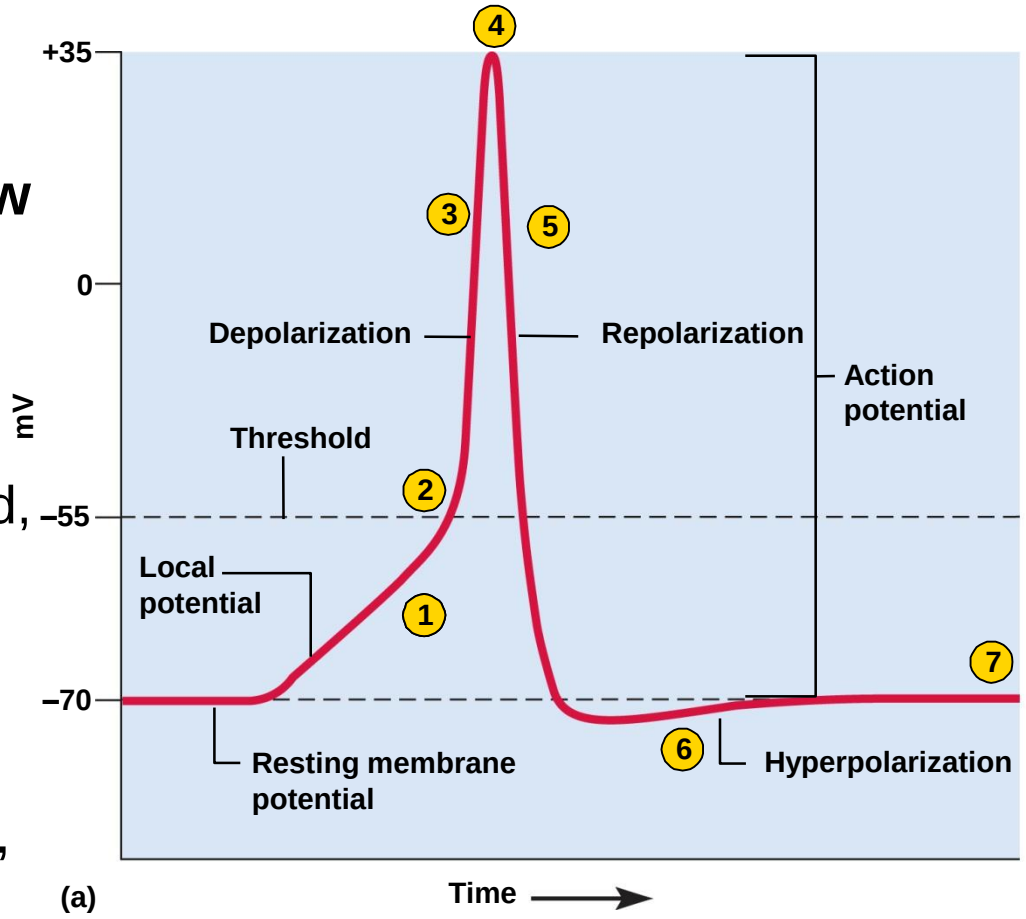


Figure 12.13a

Action Potential vs. Local Potential

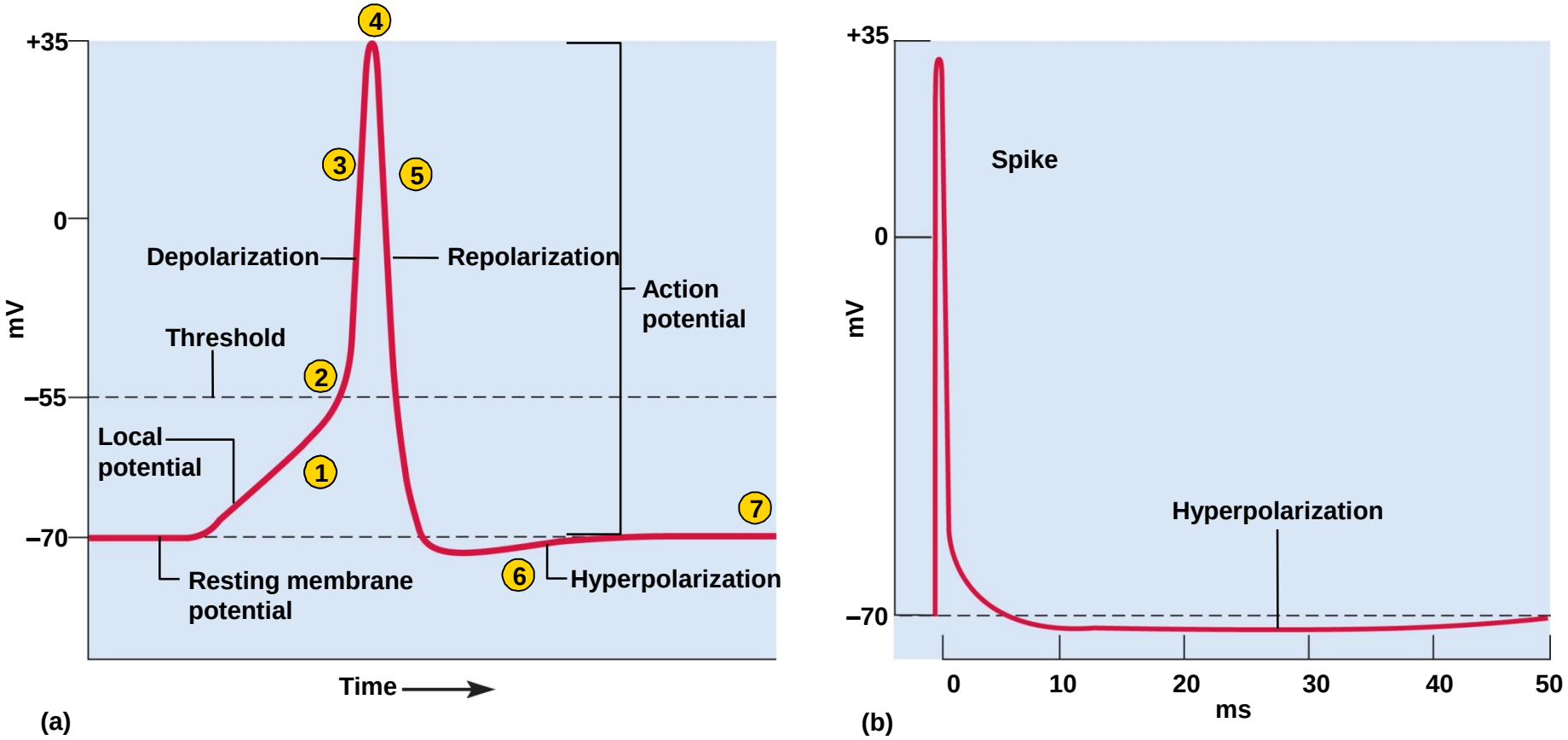


Figure 12.13a,b

Action Potential vs. Local Potential

TABLE 12.2 Comparison of Local Potentials and Action Potentials

Local Potential	Action Potential
Produced by gated channels on the dendrites and soma	Produced by voltage-gated channels on the trigger zone and axon
May be a positive (depolarizing) or negative (hyperpolarizing) voltage change	Always begins with depolarization
Graded; proportional to stimulus strength	All or none; either does not occur at all or exhibits the same peak voltage regardless of stimulus strength
Reversible; returns to RMP if stimulation ceases before threshold is reached	Irreversible; goes to completion once it begins
Local; has effects for only a short distance from point of origin	Self-propagating; has effects a great distance from point of origin
Decremental; signal grows weaker with distance	Nondecremental; signal maintains same strength regardless of distance

Table 12.2

The Refractory Period

- **During an action potential and for a few milliseconds after, it is difficult or impossible to stimulate that region of a neuron to fire again**

- **Refractory period**—the period of resistance to stimulation

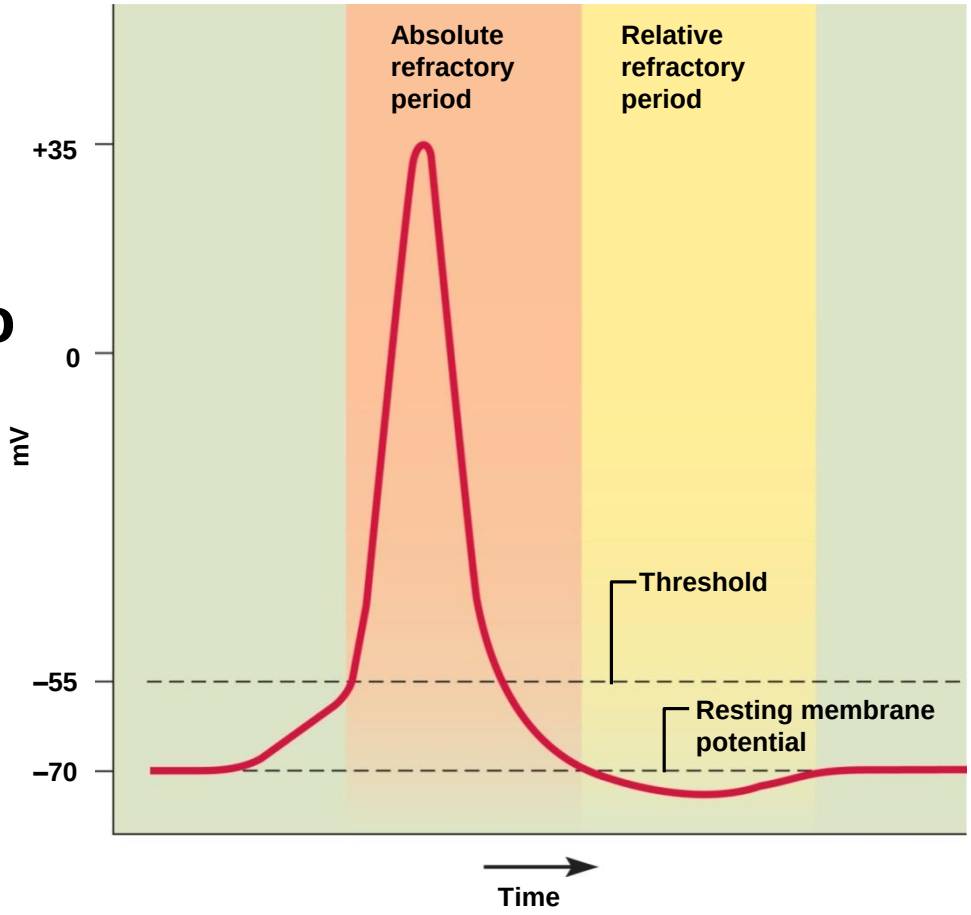


Figure 12.15

The Refractory Period

- **Two phases**
  - **Absolute refractory period**
    - No stimulus of any strength will trigger AP
    - Lasts as long as Na^+ gates are open, then inactivated
  - **Relative refractory period**
    - Only especially strong stimulus will trigger new AP
    - K^+ gates are still open and any effect of incoming Na^+ is opposed by the outgoing K^+
    - Generally lasts until hyperpolarization ends
- **Only a small patch of neuron's membrane is refractory at one time (other parts of the cell can be stimulated)**

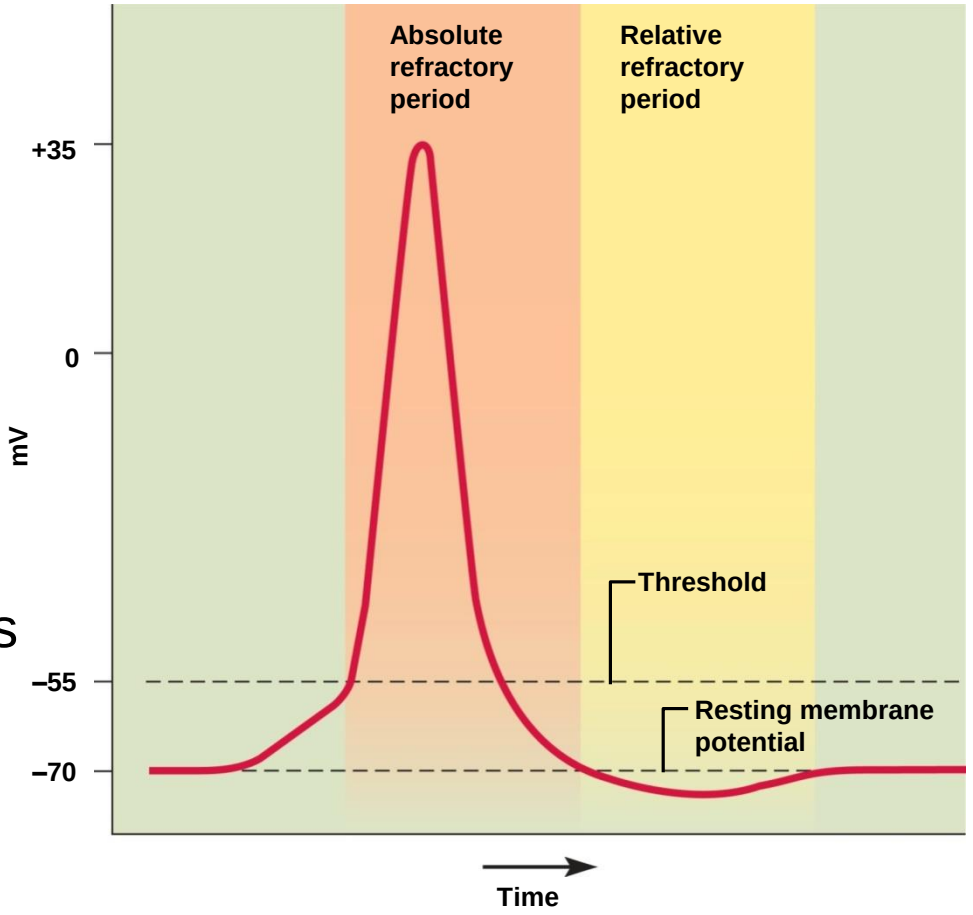
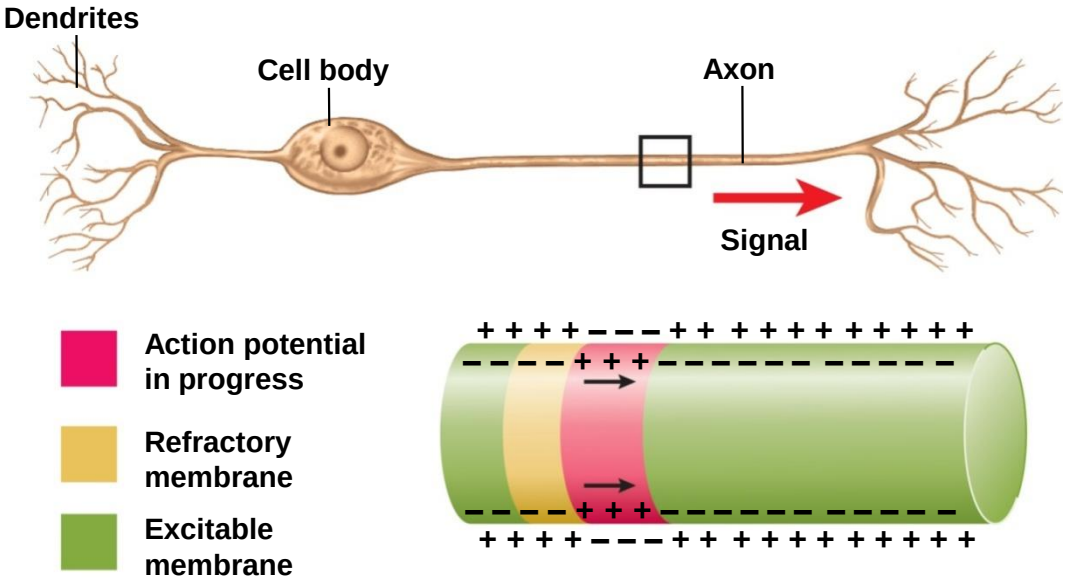


Figure 12.15

Signal Conduction in Nerve Fibers

- **Unmyelinated fibers** have voltage-gated channels along their entire length
- **Action potential at trigger zone causes Na^+ to enter the axon and diffuse into adjacent regions; this depolarization excites voltage-gated channels**
- **Opening of voltage-gated ion channels results in a new action potential which then allows Na^+ diffusion to excite the membrane immediately distal to that**
- **Chain reaction continues until the nerve signal reaches the end of the axon**
  - The nerve signal is like a wave of falling dominoes

Signal Conduction in Nerve Fibers



- **Refractory membrane ensures that action potential travels in one direction**

Figure 12.16

Signal Conduction in Nerve Fibers

- Myelinated fibers conduct signals with **saltatory conduction**—signal seems to jump from node to node
- **Nodes of Ranvier contain many voltage-gated ion channels, while myelin-covered internodes contain few**
- **When Na^+ enters the cell at a node, its electrical field repels positive ions inside the cell**
- **As these positive ions move away, their positive charge repels their positive neighbors, transferring energy down the axon rapidly (conducting the signal)**

Signal Conduction in Nerve Fibers

(***Continued***)

- **Myelin speeds up this conduction by minimizing leakage of Na^+ out of the cell and further separating the inner positive ions from attraction of negative ions outside cell**
  - But the signal strength does start to fade in the internode
- **When signal reaches the next node of Ranvier it is strong enough to open the voltage gated ion channels, and a new, full-strength action potential occurs**

Signal Conduction in Nerve Fibers

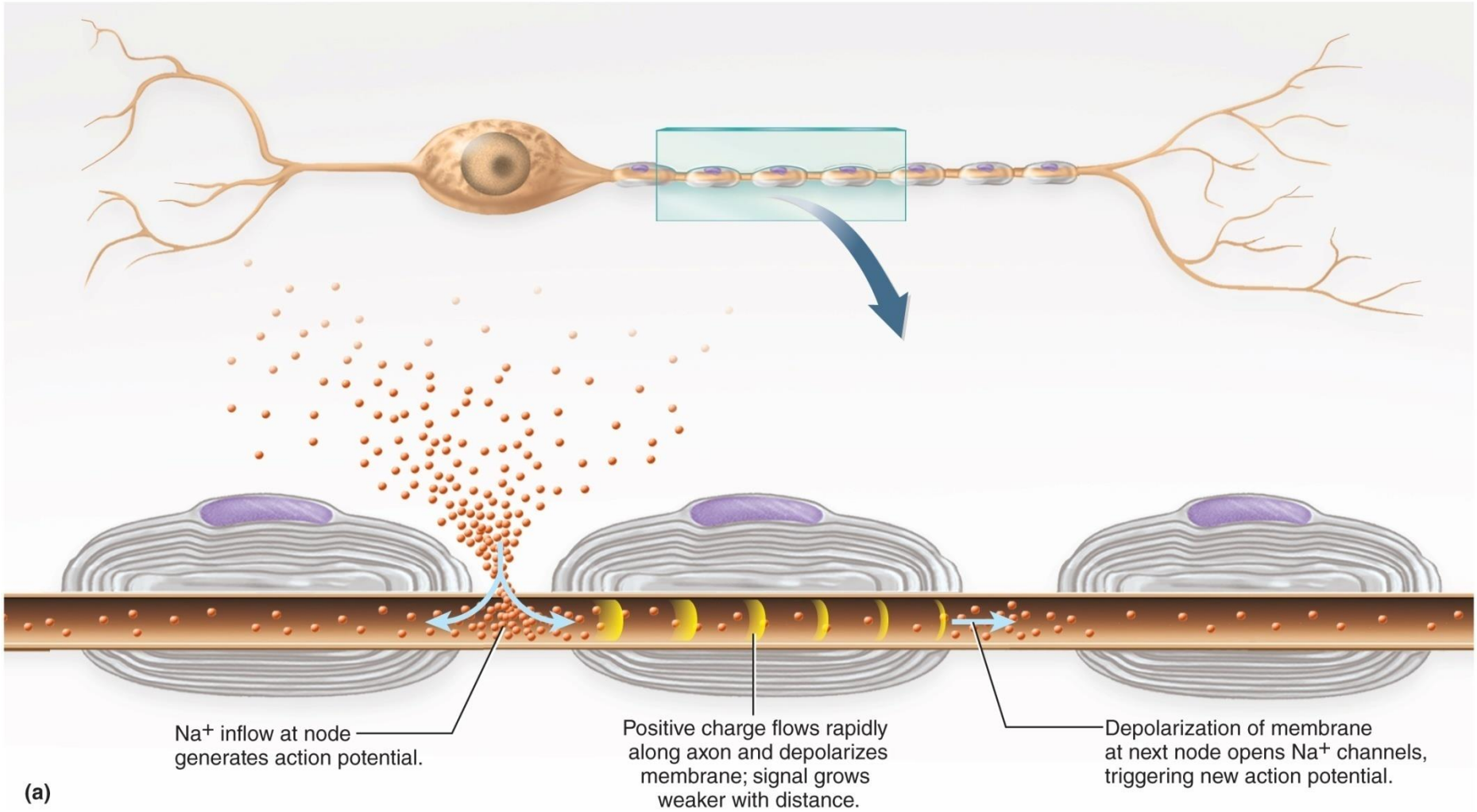


Figure 12.17a

Signal Conduction in Nerve Fibers

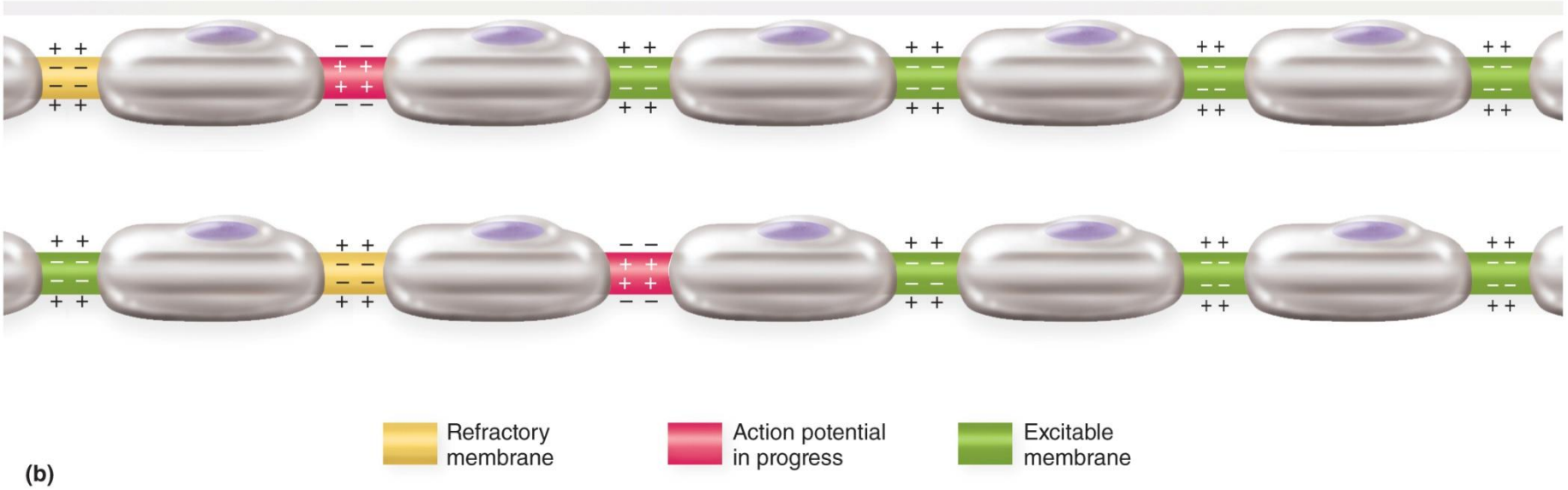


Figure 12.17b

- **Much faster than conduction in unmyelinated fibers**

Synapses

- **Expected Learning Outcomes**
  - Explain how messages are transmitted from one neuron to another.
  - Give examples of neurotransmitters and neuromodulators and describe their actions.
  - Explain how stimulation of a postsynaptic cell is stopped.

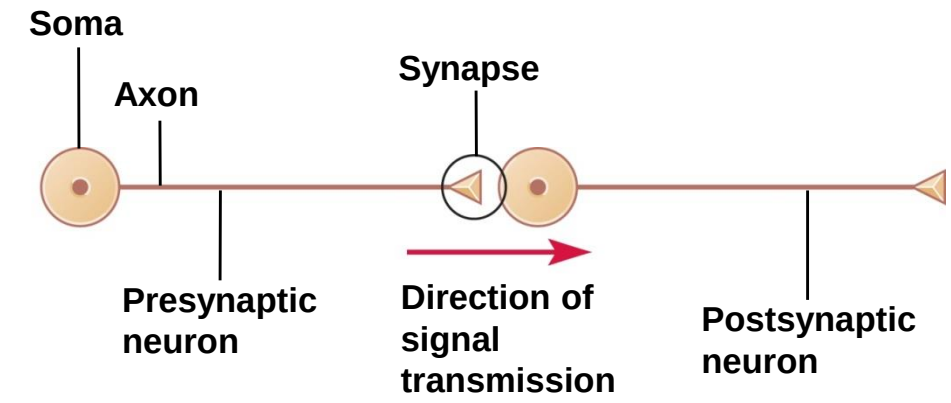
Synapses

- **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**
  - First neuron in the signal path is the **presynaptic neuron**
    - Releases neurotransmitter
  - Second neuron is **postsynaptic neuron**
    - Responds to neurotransmitter

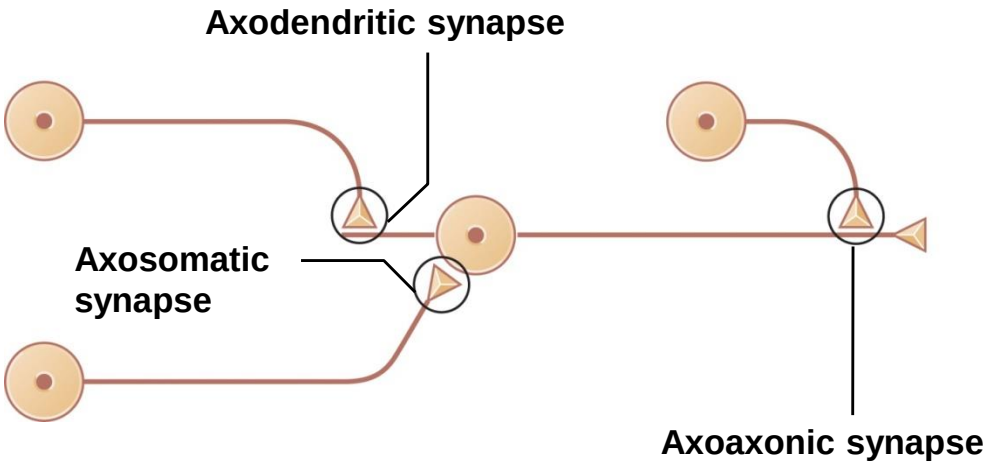
Synapses

- **Presynaptic neuron** may synapse with a dendrite, soma, or axon of postsynaptic neuron to form **axodendritic, axosomatic,** or **axoaxonic synapses**
- **A neuron can have an enormous number of synapses**
  - Spinal motor neuron covered by about 10,000 synaptic knobs from other neurons
    - 8,000 ending on its dendrites
    - 2,000 ending on its soma
- **In the cerebellum of brain, one neuron can have as many as 100,000 synapses**

Synapses



(a)



(b)

Figure 12.18

The Discovery of Neurotransmitters

- **Synaptic cleft**—gap between neurons was discovered by Ramón y Cajal through histological observations
- **Otto Loewi,** in 1921, demonstrated that neurons communicate by releasing chemicals—**chemical synapses**
  - He flooded exposed hearts of two frogs with saline
  - Stimulated vagus nerve of the first frog and the heart slowed
  - Removed saline from that frog and found it slowed heart of second frog
  - Named it **Vagusstoffe** (“vagus substance”)
    - Later renamed **acetylcholine,** the first known neurotransmitter

The Discovery of Neurotransmitters

- **Electrical synapses** do exist
  - Occur between some neurons, neuroglia, and cardiac and single-unit smooth muscle
  - **Gap junctions** join adjacent cells
    - Ions diffuse through the gap junctions from one cell to the next
  - **Advantage** of quick transmission
    - No delay for release and binding of neurotransmitter
  - **Disadvantage** that they cannot integrate information and make decisions
    - Ability reserved for **chemical synapses** in which neurons communicate with neurotransmitters

Structure of a Chemical Synapse

- **Synaptic knob** of **presynaptic neuron** contains **synaptic vesicles** containing **neurotransmitter**
  - Many vesicles are docked on release sites on plasma membrane ready to release neurotransmitter
  - A reserve pool of synaptic vesicles is located further away from membrane
- **Postsynaptic neuron** membrane contains **proteins** that function as **receptors** and **ligand-regulated ion gates**

Structure of a Chemical Synapse

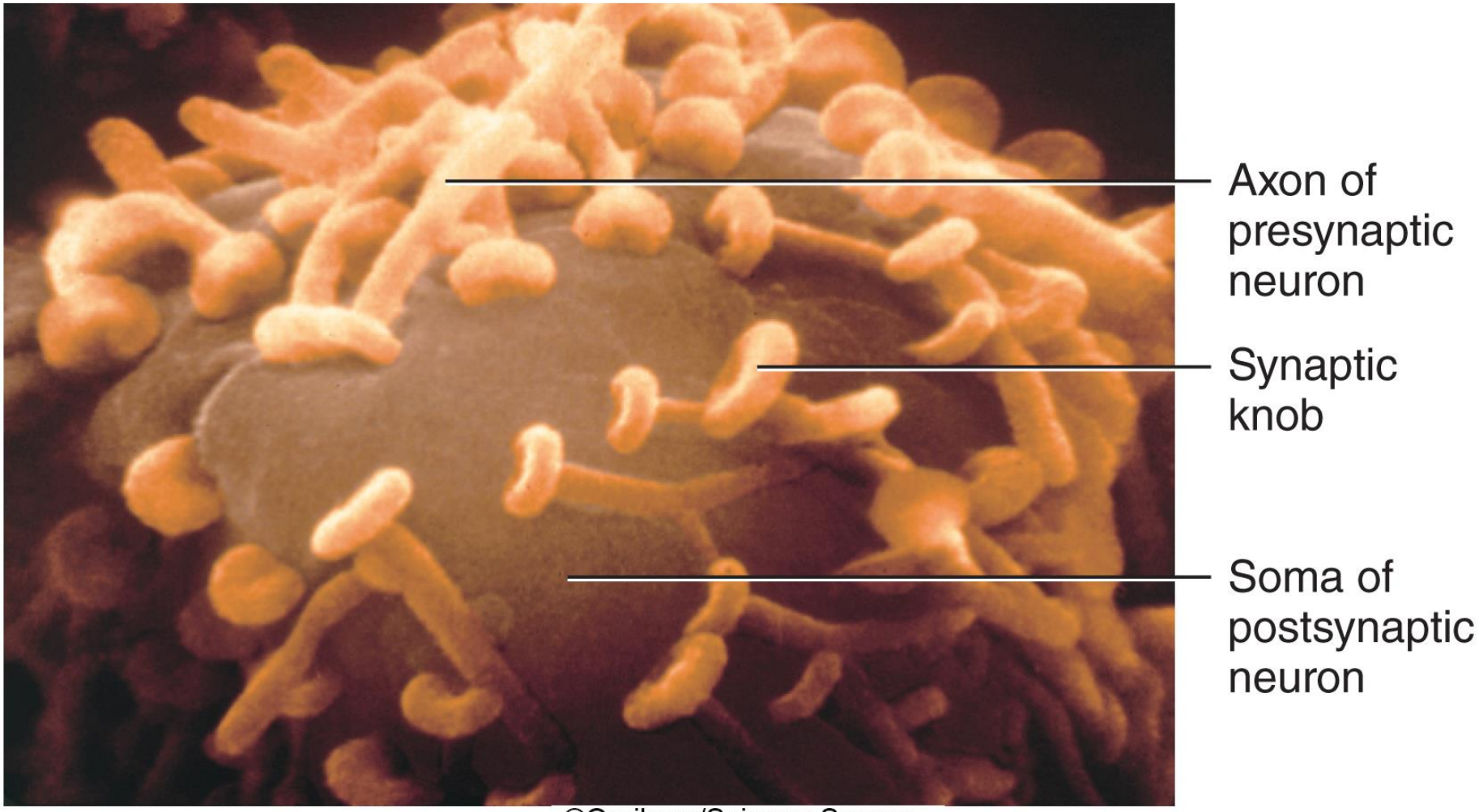


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Figure 12.19

Structure of a Chemical Synapse

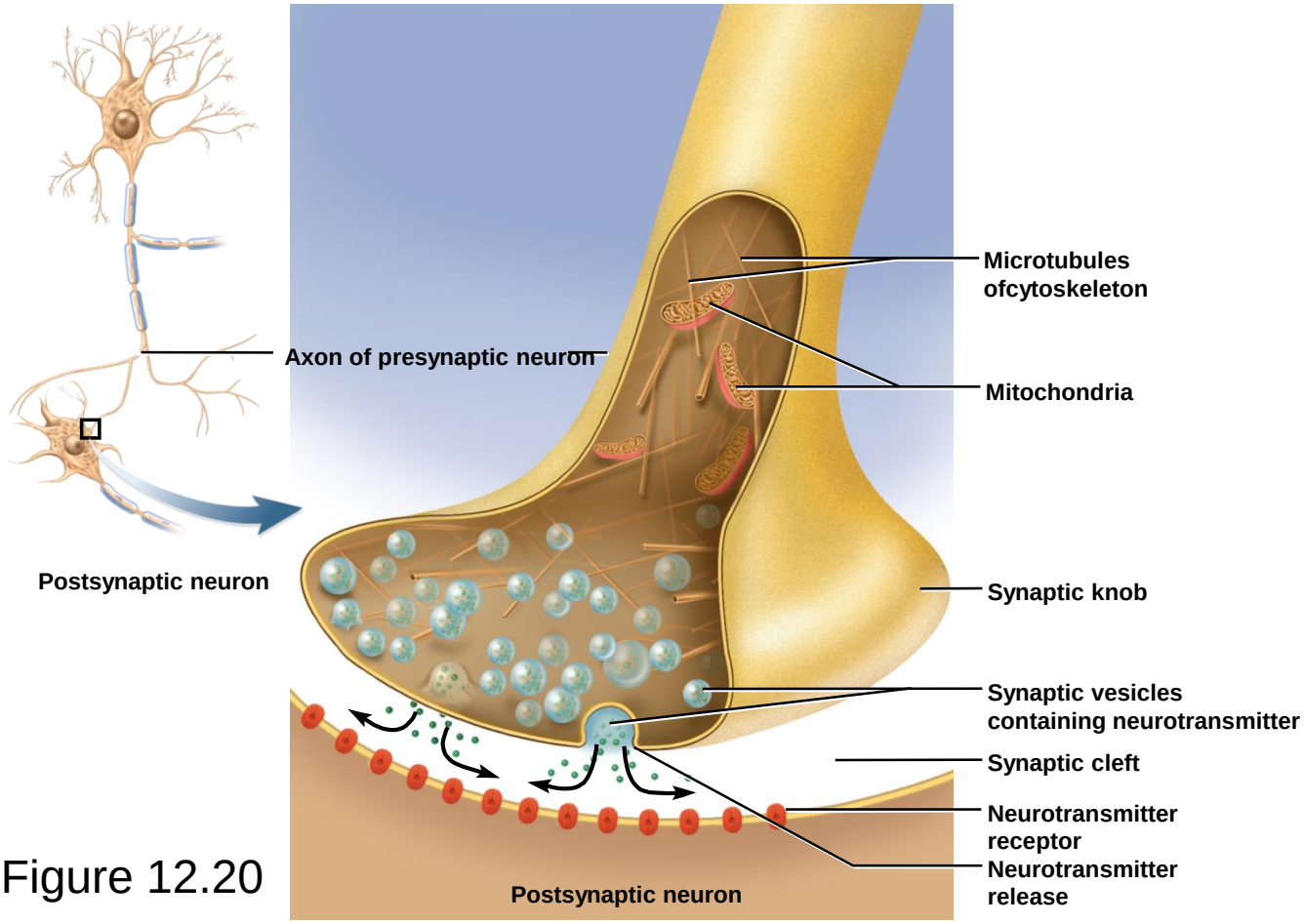


Figure 12.20

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

Neurotransmitters and Related Messengers

- **Neurotransmitters** are molecules that are released when a signal reaches a synaptic nob that binds to a receptor on another cell and alter that cell's physiology
- More than 100 neurotransmitters have been identified but most fall into four major chemical categories: **acetylcholine, amino acids, monoamines, and neuropeptides**
  - **Acetylcholine**
    - In a class by itself
    - Formed from acetic acid and choline
  - **Amino acid neurotransmitters**
    - Include glycine, glutamate, aspartate, and γ-aminobutyric acid (GABA)

Neurotransmitters and Related Messengers

(Continued)

- **Monoamines**
  - Synthesized from amino acids by removing the –COOH group while retaining the $–NH_2$ (amino) group
  - Include the **catecholamines:**
    - **Epinephrine**, **norepinephrine**, **dopamine**
  - Also include histamine, ATP, and serotonin
- **Neuropeptides**
  - Chains of 2 to 40 amino acids
  - Stored in secretory granules
  - Include: cholecystokinin and substance P

Neurotransmitters and Related Messengers

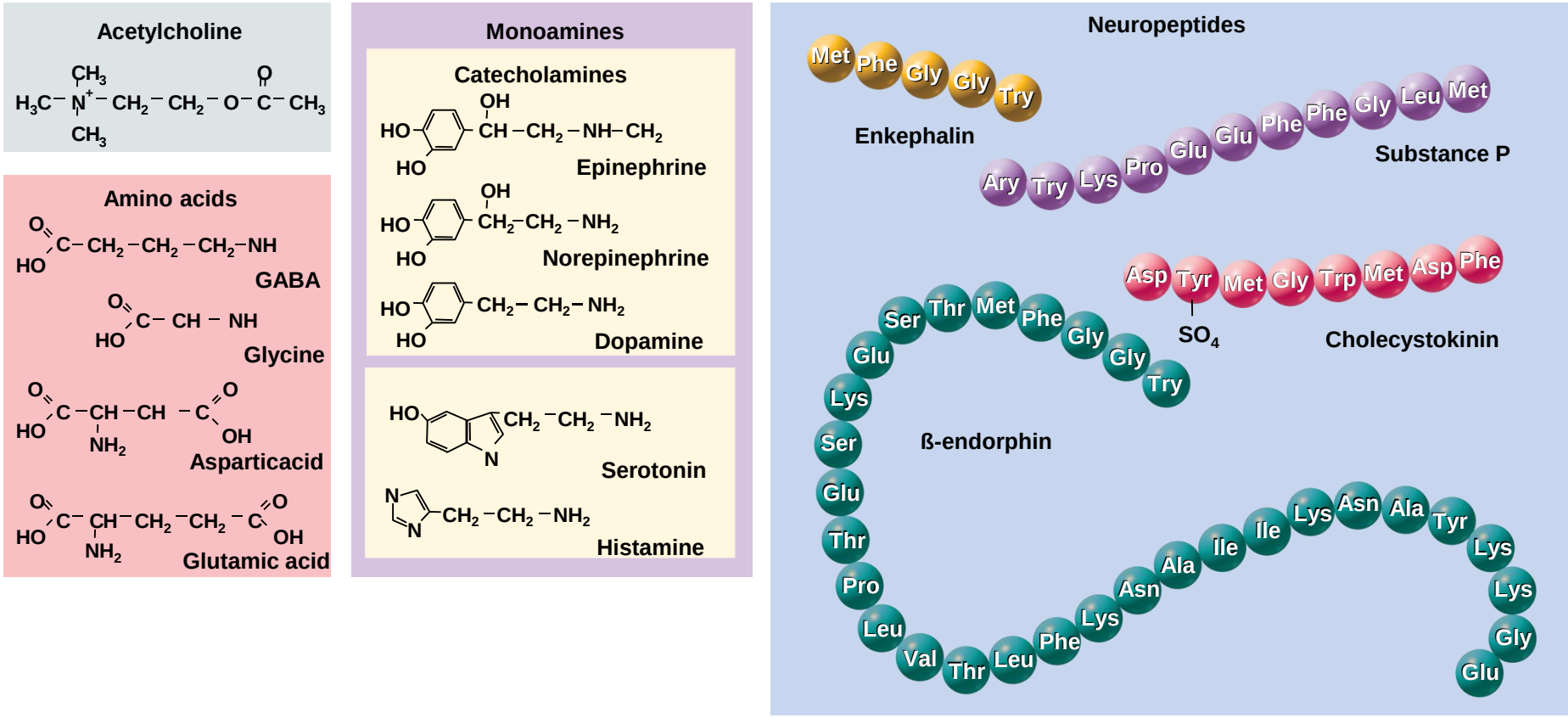


Figure 12.21

Neurotransmitters and Related Messengers

- **Neuropeptides are chains of 2 to 40 amino acids**
  - Beta-endorphin and substance P
- **Act at lower concentrations than other neurotransmitters**
- **Longer lasting effects**
- Stored in axon terminal as larger **secretory granules** (called dense-core vesicles)
- **Some function as hormones or neuromodulators**
- **Some also released from digestive tract**
  - Gut–brain peptides cause food cravings

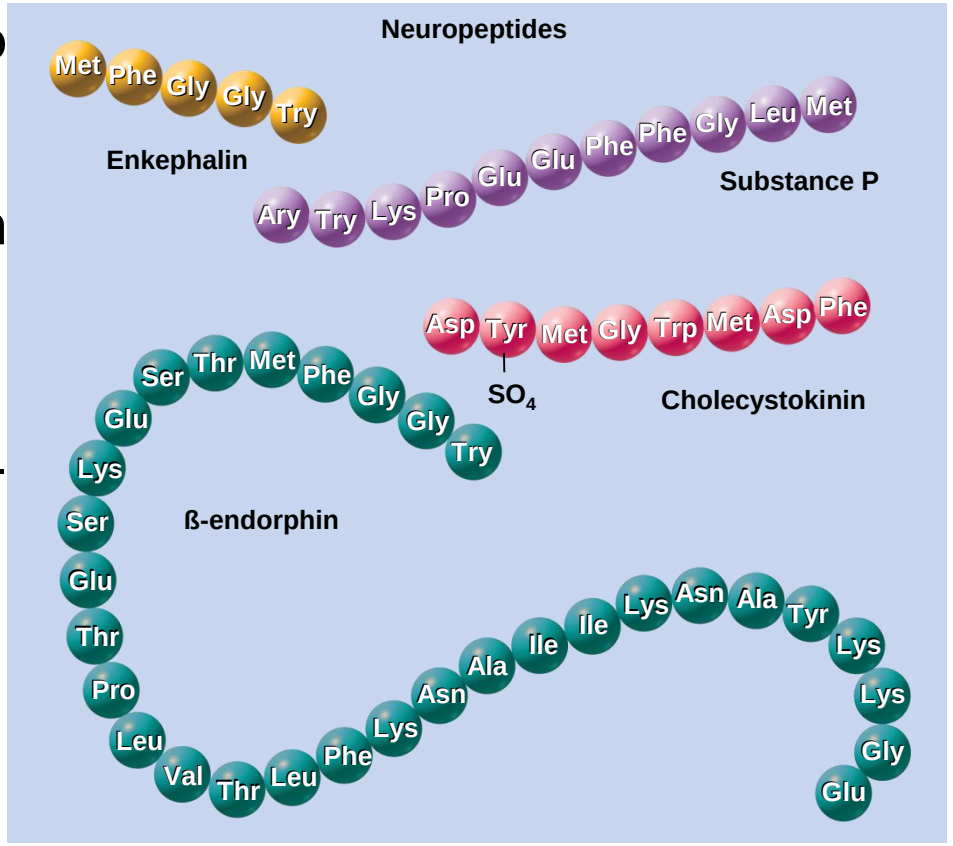


Figure 12.21

Synaptic Transmission

- **Synapses vary**
  - Some neurotransmitters are excitatory, others are inhibitory, and sometimes a transmitter's effect differs depending on the type of receptor on the postsynaptic cell
  - Some receptors are ligand-gated ion channels and others act through second messengers

- **Next we consider three kinds of synapses:**
  - **Excitatory cholinergic synapse**
  - **Inhibitory GABA-ergic synapse**
  - **Excitatory adrenergic synapse**

An Excitatory Cholinergic Synapse

- **Cholinergic synapse—**uses acetylcholine (ACh)
  - Nerve signal arrives at synaptic knob and opens voltage-gated Ca^{2+} channels
  - Ca^{2+} enters knob and triggers exocytosis of Ach
  - Ach diffuses across cleft and binds to postsynaptic receptors
  - The receptors are ion channels that open and allow Na^{+} and K^{+} to diffuse
  - Entry of Na^{+} causes a depolarizing postsynaptic potential
  - If depolarization is strong enough, it will cause an action potential at the trigger zone

An Excitatory Cholinergic Synapse

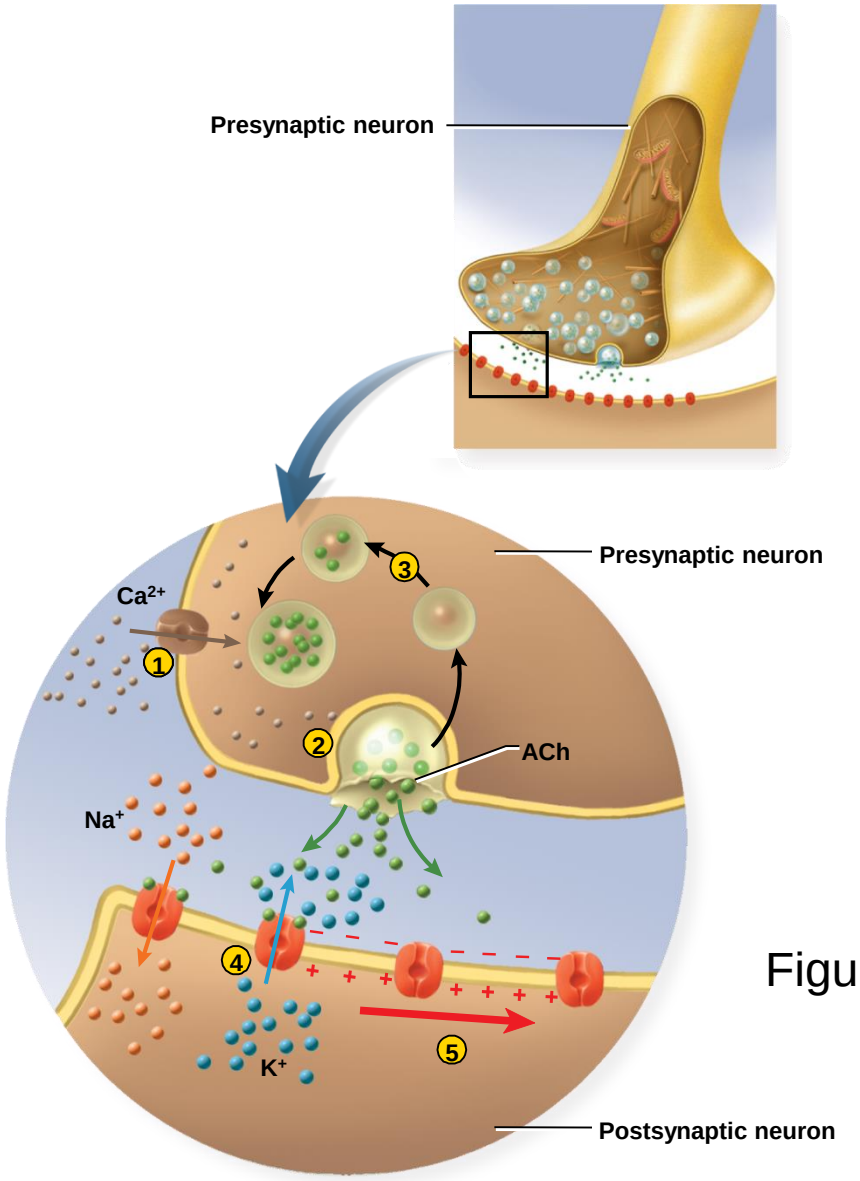


Figure 12.22

An Inhibitory GABA-ergic Synapse

- GABA-ergic synapse employs **γ-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**

An Excitatory Adrenergic Synapse

- **Adrenergic synapse** employs the neurotransmitter **norepinephrine (NE),** also called noradrenaline
- NE and other monoamines, and neuropeptides, act through **second-messenger systems** such as **cyclic AMP (cAMP)**
- **Receptor** is not an ion gate, but a **transmembrane protein associated with a G protein**
- **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

An Excitatory Adrenergic Synapse

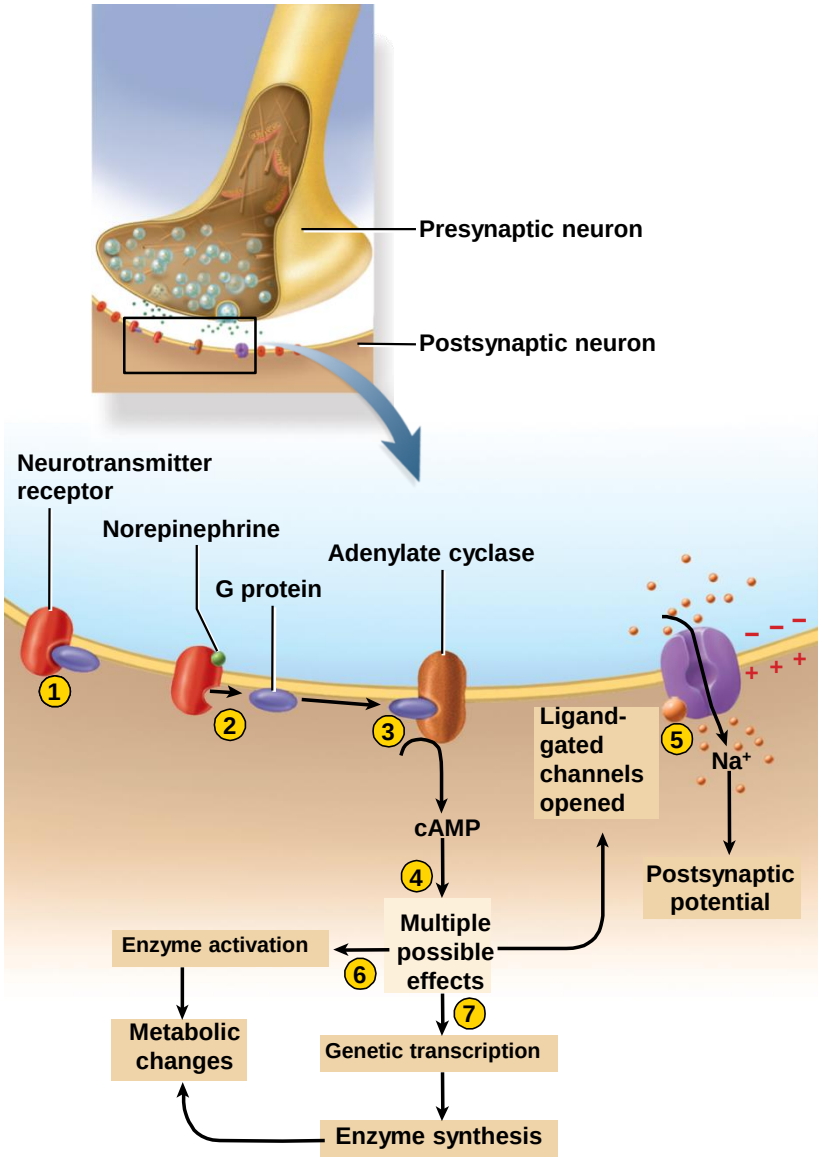


Figure 12.23

Cessation of the Signal

- Synapses must **turn off stimulation** to keep postsynaptic neuron from firing indefinitely
- **Presynaptic cell stops releasing neurotransmitter**
- **Neurotransmitter only stays bound to its receptor for about 1 ms and then is cleared**
  - Neurotransmitter **diffuses** into nearby ECF
    - Astrocytes in CNS absorb it and return it to neurons
  - Synaptic knob **reabsorbs** neurotransmitter by endocytosis
    - Monoamine transmitters are broken down after reabsorption by monoamine oxidase
  - Acetylcholine is **broken down** by acetylcholinesterase (AchE) in the synaptic cleft
    - After degradation, the presynaptic cell reabsorbs the fragments of the molecule for recycling

Neuromodulators

- **Neuromodulators—**chemicals secreted by neurons that have long term effects on groups of neurons
  - May alter the rate of neurotransmitter synthesis, release, reuptake, or breakdown
  - May adjust sensitivity of postsynaptic membrane
- **Nitric oxide (NO) is a simple neuromodulator**
  - It is a gas that enters postsynaptic cells and activates 2nd messenger pathways (example: relaxing smooth muscle)
- **Neuropeptides are chains of amino acids that can act as neuromodulators**
  - Enkephalins and endorphins are neuropeptides that inhibit pain signals in the CNS

Neural Integration

- **Expected Learning Outcomes**
  - Explain how a neuron “decides” whether or not to generate action potentials.
  - Explain how the nervous system translates complex information into a simple code.
  - Explain how neurons work together in groups to process information and produce effective output.
  - Describe how memory works at cellular and molecular levels.

Neural Integration

- **Neural integration—the ability to process, store, and recall information and use it to make decisions**
- **Chemical synapses allow for decision making**
  - Brain cells are incredibly well connected allowing for complex integration
    - Pyramidal cells of cerebral cortex have about 40,000 contacts with other neurons
  - Trade off: chemical transmission involves a synaptic delay that makes information travel slower than it would be if there was no synapse

Postsynaptic Potentials

- **Neural integration** is based on postsynaptic potentials occurring in a cell receiving chemical signals
- **For a cell to fire an action potential it must be excited to its threshold level (typically −55 mV)**
  - An **excitatory postsynaptic potential (EPSP)** is a voltage change from RMP toward threshold
  - EPSP usually results from Na^+ flowing into the cell
- **Some chemical messages inhibit the postsynaptic cell by hyperpolarizing it**
  - An **inhibitory postsynaptic potential (IPSP)** occurs when the cell's voltage becomes more negative than it is at rest (it is less likely to fire)
  - IPSP can result from Cl^- entry or K^+ exit from cell

Postsynaptic Potentials

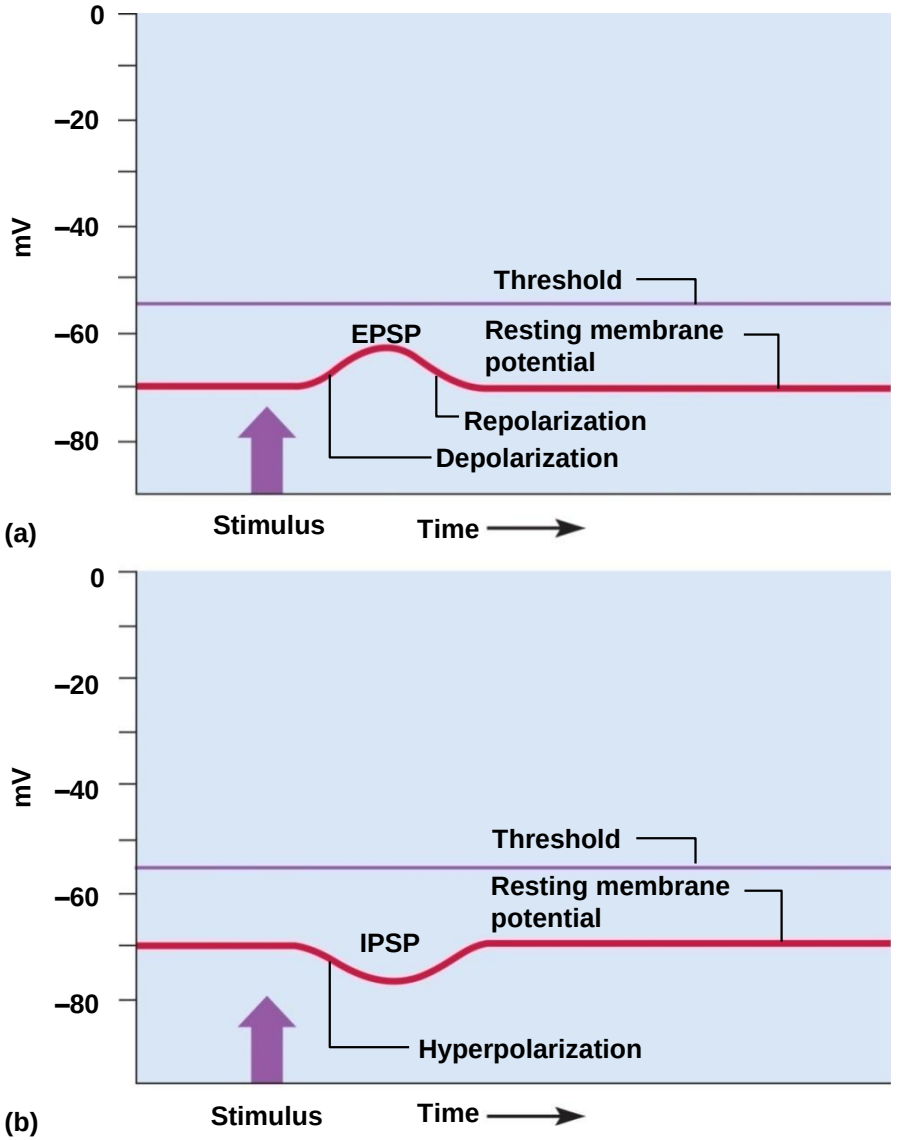


Figure 12.24

Postsynaptic Potentials

- **Different neurotransmitters cause different types of postsynaptic potentials in the cells they bind to**
  - Glutamate and aspartate produce EPSPs in brain cells
  - Glycine and GABA produce IPSPs
- **A neurotransmitter might excite some cells and inhibit others, depending on the type of receptors the postsynaptic cells have**
  - Acetylcholine (Ach) and norepinephrine work this way
  - Ach excites skeletal muscle but inhibits cardiac muscle because of different Ach receptors

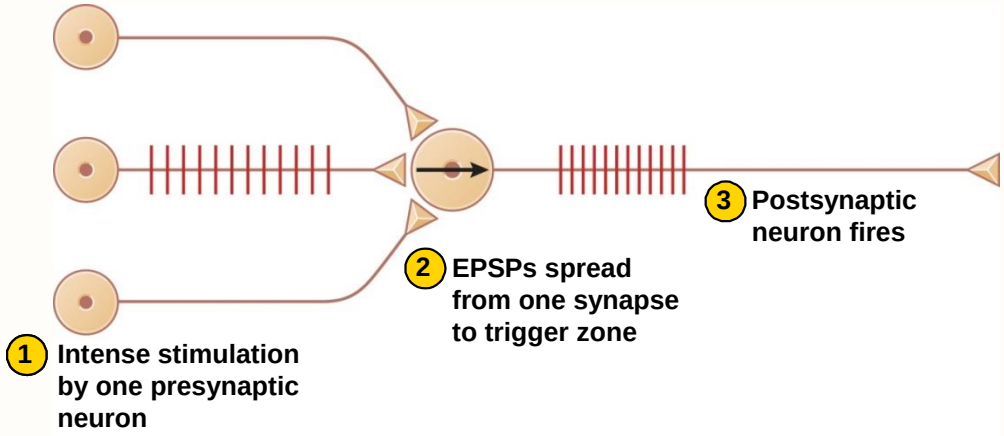
Summation, Facilitation, and Inhibition

- **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

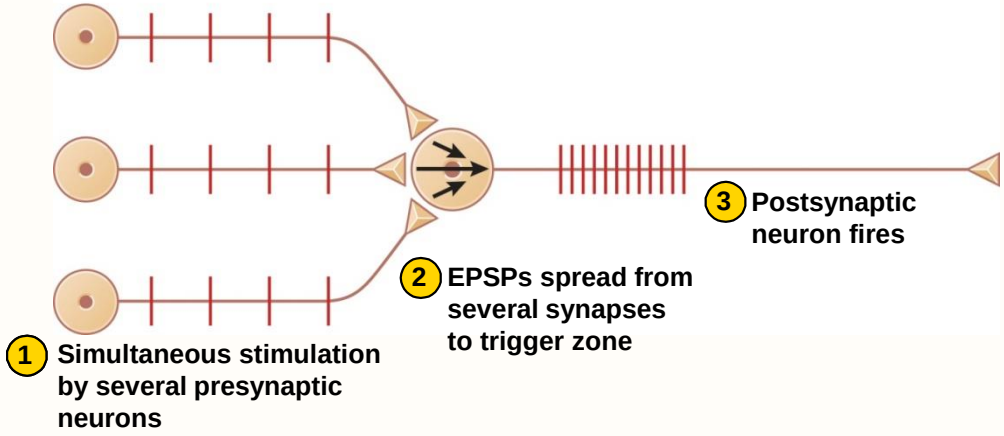
Summation, Facilitation, and Inhibition

- **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 collaborate to induce the postsynaptic neuron to fire
  - An example of **facilitation—**a process in which one neuron enhances the effect of another

Temporal and Spatial Summation



(a) Temporal summation



(b) Spatial summation

Figure 12.25

Summation of EPSPs

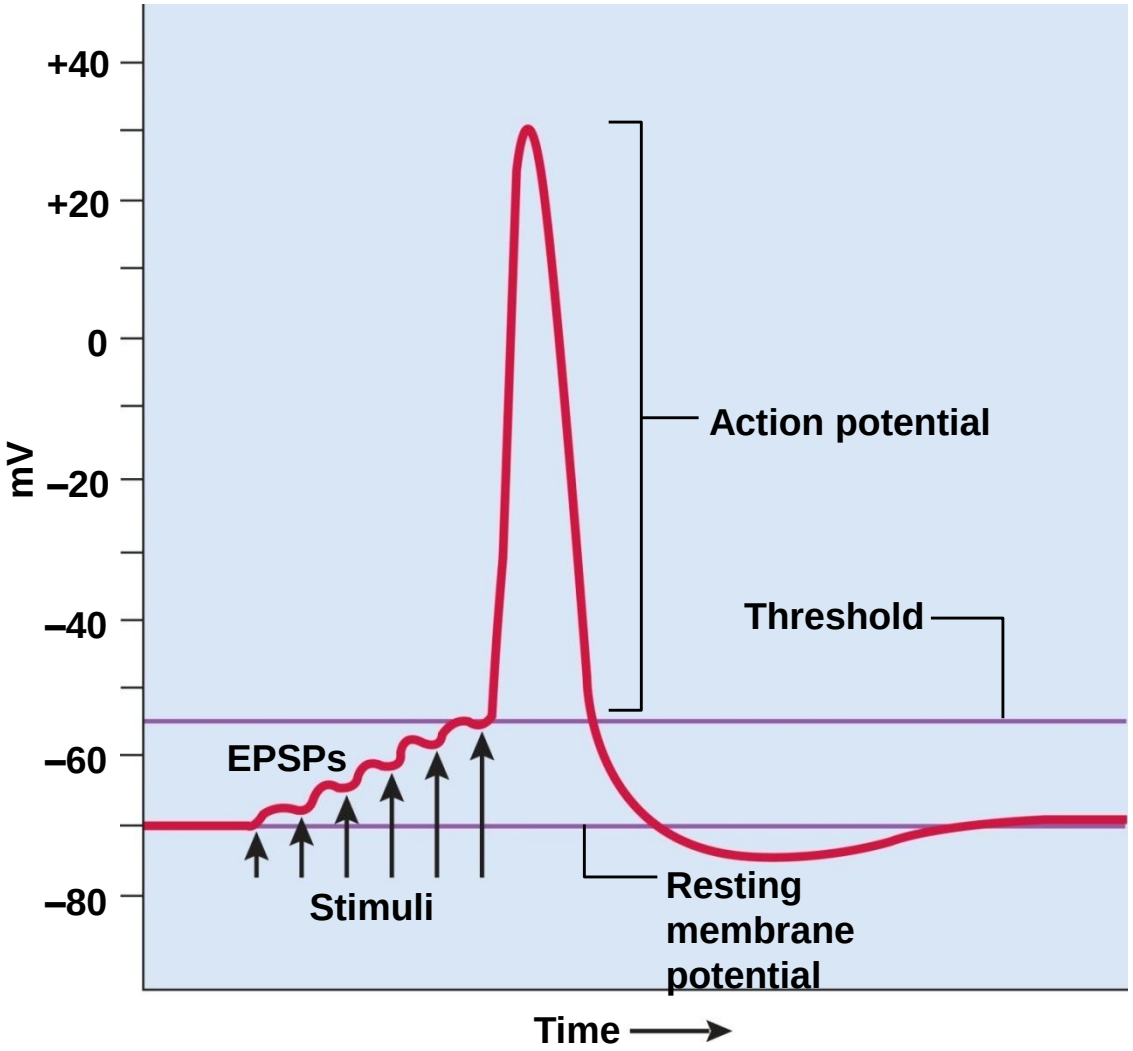


Figure 12.26

- Does this represent spatial or temporal summation?

Summation, Facilitation, and Inhibition

- **Presynaptic inhibition**—process in which one presynaptic neuron suppresses another one (opposite of facilitation)
  - Reduces or halts unwanted synaptic transmission
  - Inhibiting neuron (cell "I" in figure) releases GABA
    - Prevents voltage-gated calcium channels in synaptic knob ("S" in figure) from opening and so knob releases little or no neurotransmitter

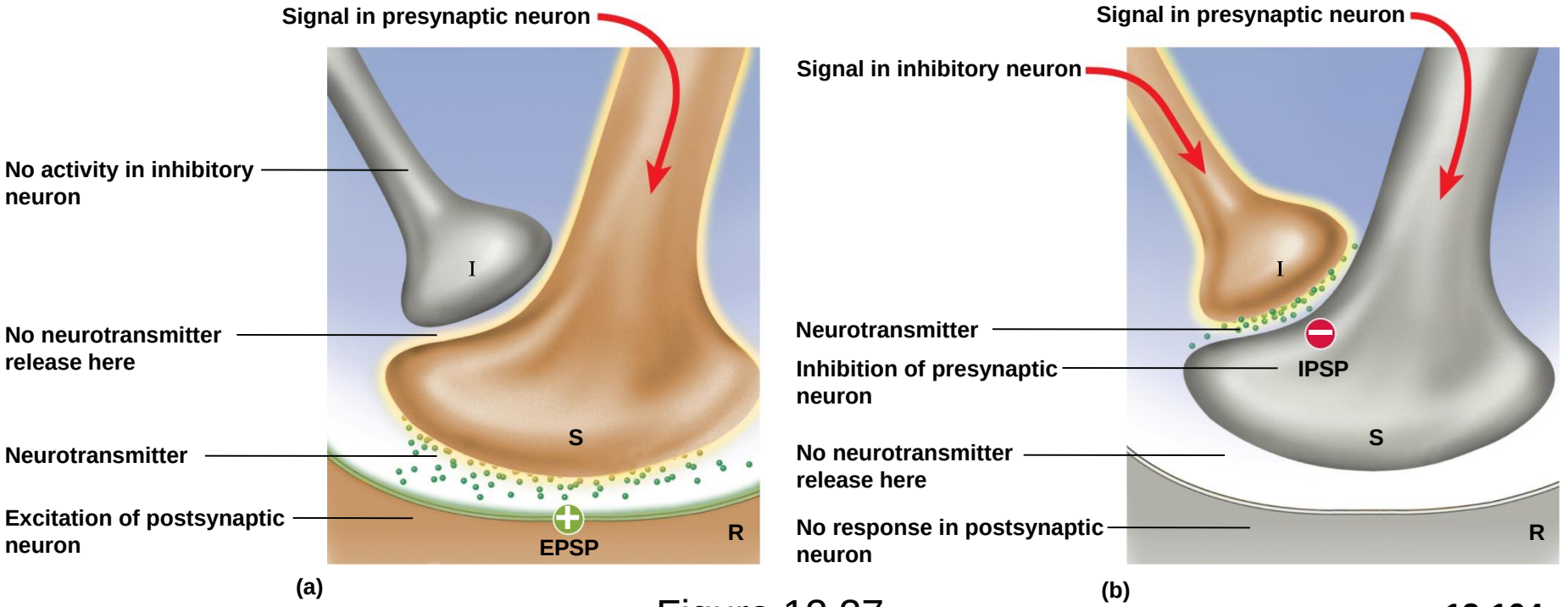


Figure 12.27

Neural Coding

- **Neural coding**—the way the nervous system converts information into a meaningful pattern of action potentials
- **Qualitative information** depends on which neurons fire
  - **Labeled line code:** each sensory nerve fiber to the brain leads from a receptor that recognizes a specific stimulus type (e.g., optic nerve labeled as “light”)
- **Quantitative information**—information about the intensity of a stimulus is encoded in two ways:
  - Weak stimuli excite only low threshold stimuli whereas strong stimuli also **recruit** higher threshold neurons
  - Weak stimuli cause neurons to fire at a slower rate whereas strong stimuli cause a higher firing frequency (more action potentials per second)

Neural Coding

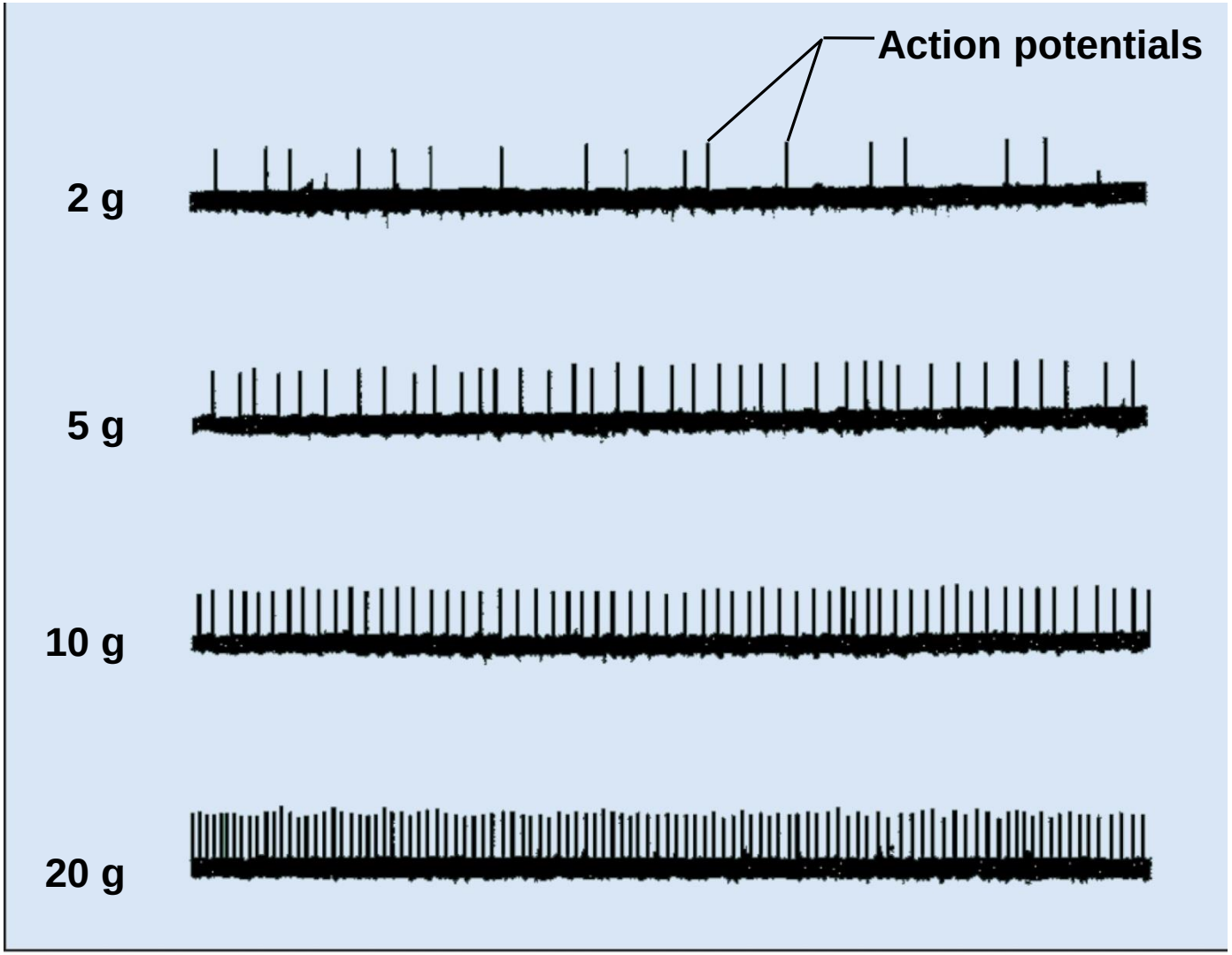


Figure 12.28

Neural Pools and Circuits

- **Neural pools**—neurons function in large groups, each of which consists of thousands of interneurons concerned with a particular body function
  - Control rhythm of breathing
  - Moving limbs rhythmically when walking

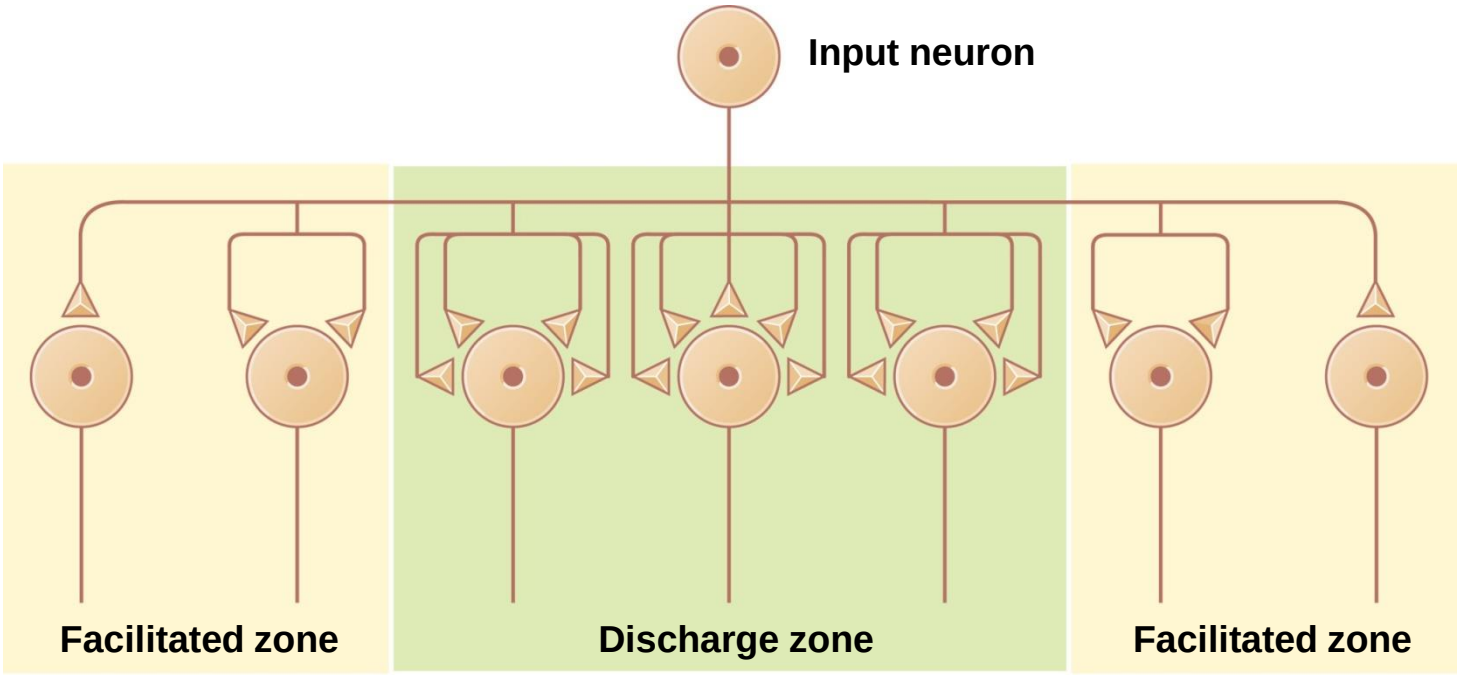


Figure 12.29

Neural Pools and Circuits

- **Information arrives at a neural pool through one or more input neurons**
  - Input neurons branch repeatedly to synapse with many targets
  - Some input neurons form multiple synapses with a single postsynaptic cell
    - Can simultaneously produce EPSPs at all those synapses and (through spatial summation) make it fire
  - Within input neuron's **discharge zone** it can act alone to make postsynaptic cells fire
  - In its broader **facilitated zone,** the input neuron makes fewer, less powerful synapses
    - Can only stimulate targets with the assistance of other input neurons

Neural Pools and Circuits

- **Diverging circuit**
  - One nerve fiber branches and synapses with several postsynaptic cells
  - One neuron may produce output through hundreds of neurons
- **Converging circuit**
  - Input from many different nerve fibers can be funneled to one neuron or neural pool
  - Opposite of diverging circuit

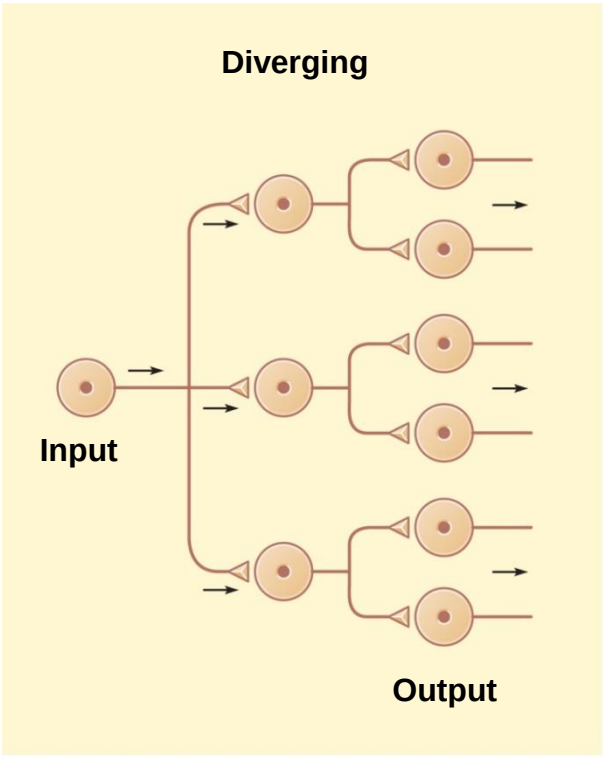
Neural Pools and Circuits

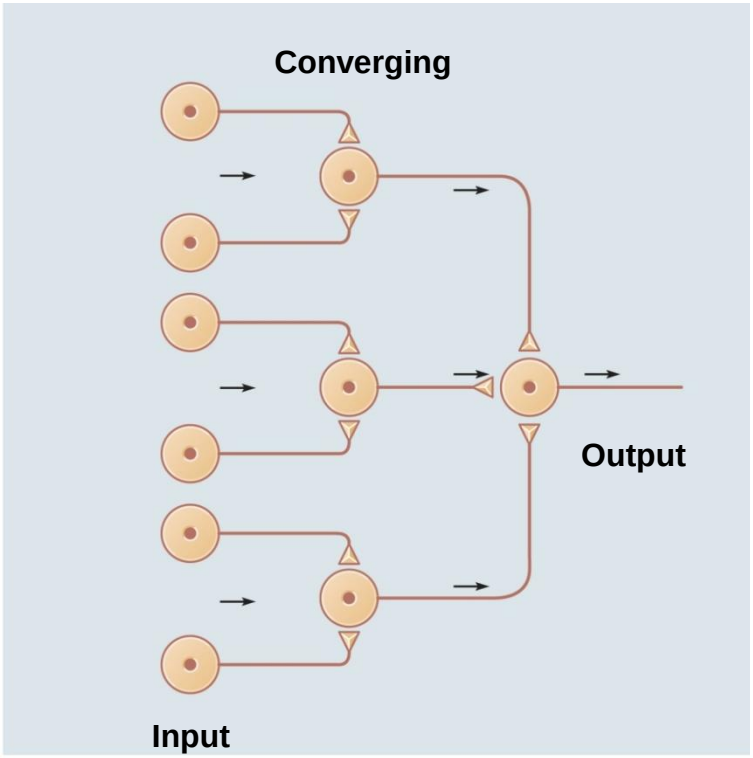
(Continued)

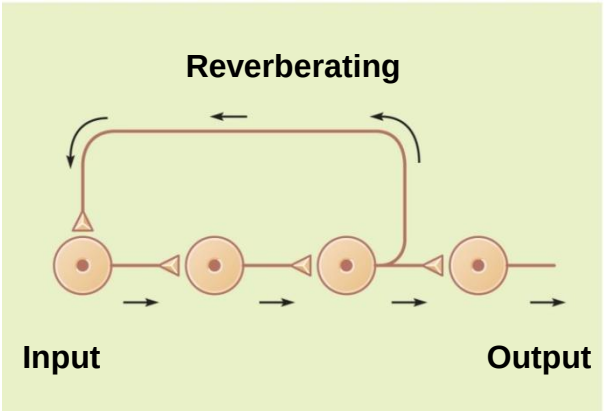
- **Reverberating circuits**
  - Neurons stimulate each other in linear sequence but one or more of the later cells restimulates the first cell to start the process all over
  - Diaphragm and intercostal muscles

- **Parallel after-discharge circuits**
  - Input neuron diverges to stimulate several chains of neurons
    - Each chain has a different number of synapses
    - Eventually they all reconverge on one or a few output neurons but with varying delays
    - After-discharge—continued firing after the stimulus stops

Neural Pools and Circuits







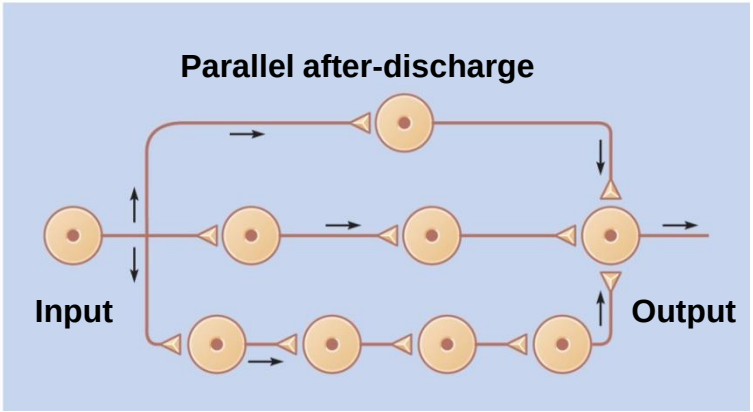


Figure 12.30

Memory and Synaptic Plasticity

- Physical basis of memory is a pathway through the brain called a **memory trace** or **engram**
  - Along this pathway, new synapses were created or existing synapses modified to make transmission easier
  - **Synaptic plasticity:** the ability of synapses to change
  - **Synaptic potentiation:** the process of making transmission easier
- **Kinds of memory**
  - **Immediate, short**- and **long-term** memory
  - Correlate with different modes of synaptic potentiation

Immediate Memory

- **Immediate memory—**ability to hold something in your thoughts for a few seconds
  - Essential for reading ability
- **Feel for the flow of events (sense of the present)**
- **Our memory of what just happened "echoes" in our minds for a few seconds**
  - May depend on reverberating circuits

Short-Term Memory

- **Short-term memory (STM)**—lasts from seconds to a few hours
  - Includes **working memory** for taking action
    - Example: calling a phone number you just looked up
- Storage appears to occur in circuits of **facilitated synapses**
  - **Tetanic stimulation:** rapid arrival of repetitive signals at a synapse may foster very brief memories
    - Causes Ca^{2+} accumulation and makes postsynaptic cell more likely to fire
  - **Posttetanic potentiation:** appears to be involved in jogging a memory from a few hours ago
    - Ca^{2+} level in synaptic knob stays elevated
    - Little stimulation needed to recover memory

Long-Term Memory

- **Long term memory (LTM) may last a lifetime and can hold more information than short term memory**
- **Types of long-term memory**
  - **Declarative:** retention of events you can put into words
  - **Procedural:** retention of motor skills
- **Some LTM involves remodeling of synapses or formation of new ones**
  - New branching of axons or dendrites
- Some LTM involves molecular changes such as **long-term potentiation**

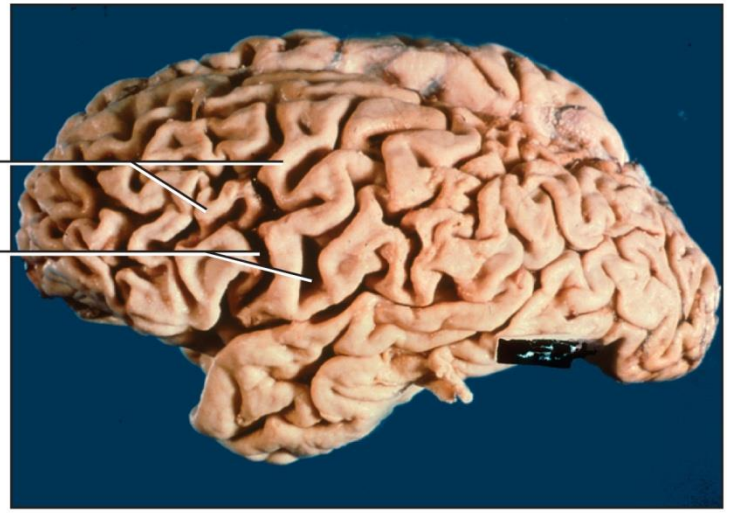
Long-Term Memory

- **Long-term potentiation** involves NMDA receptors on dendritic spines of pyramidal neurons
- **When NMDA receptors bind glutamate and receive tetanic stimuli, they allow Ca^{2+} to enter the cell**
- **Ca^{2+} acts as second messenger causing:**
  - More NMDA receptors to be produced
  - Synthesis of proteins involved in synapse remodeling
  - Releases of signals (maybe nitric oxide) that trigger more neurotransmitter release from presynaptic neuron

Alzheimer Disease

- **100,000 deaths/year**
  - Affects 11% of population over 65; 47% by age 85
- **Memory loss for recent events, moody, combative, lose ability to talk, walk, and eat**
- **Show deficiencies of acetylcholine and nerve growth factor (NGF)**
- **Diagnosis confirmed at autopsy**
  - Atrophy of gyri (folds) in cerebral cortex
  - Neurofibrillary tangles and senile plaques
  - Formation of β-amyloid protein from breakdown product of plasma membranes
- **Treatment**
  - Trying to find ways to clear β-amyloid or halt its production, but research halted due to serious side effects
  - Patients show modest results with NGF or cholinesterase inhibitors

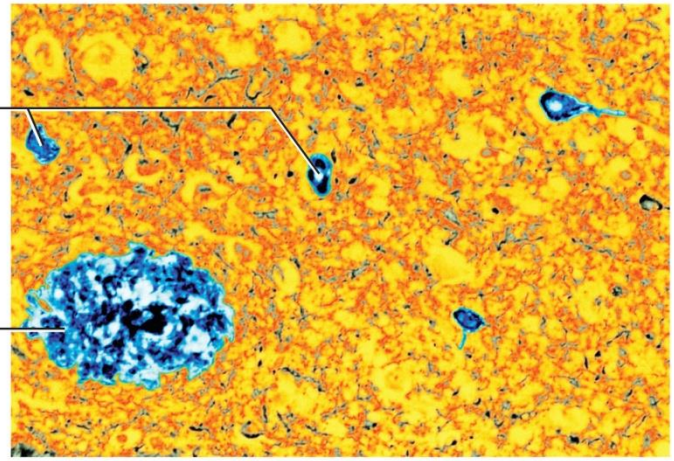
Alzheimer Disease



(a)

a: ©Custom Medical Stock Photo, Inc.

Figure 12.31a



(b)

b: ©Simon Fraser/Science Source

Figure 12.31b

Parkinson Disease

- **Progressive loss of motor function beginning in 50s or 60s— no recovery**
  - Degeneration of dopamine-releasing neurons
    - Dopamine normally prevents excessive activity in motor centers (basal nuclei)
    - Involuntary muscle contractions
      - Pill-rolling motion, facial rigidity, slurred speech
      - Illegible handwriting, slow gait
- **Treatment—drugs and physical therapy**
  - Dopamine precursor (L-dopa) crosses brain barrier; bad side effects on heart and liver
  - MAO inhibitor slows neural degeneration
  - Surgical technique to relieve tremors