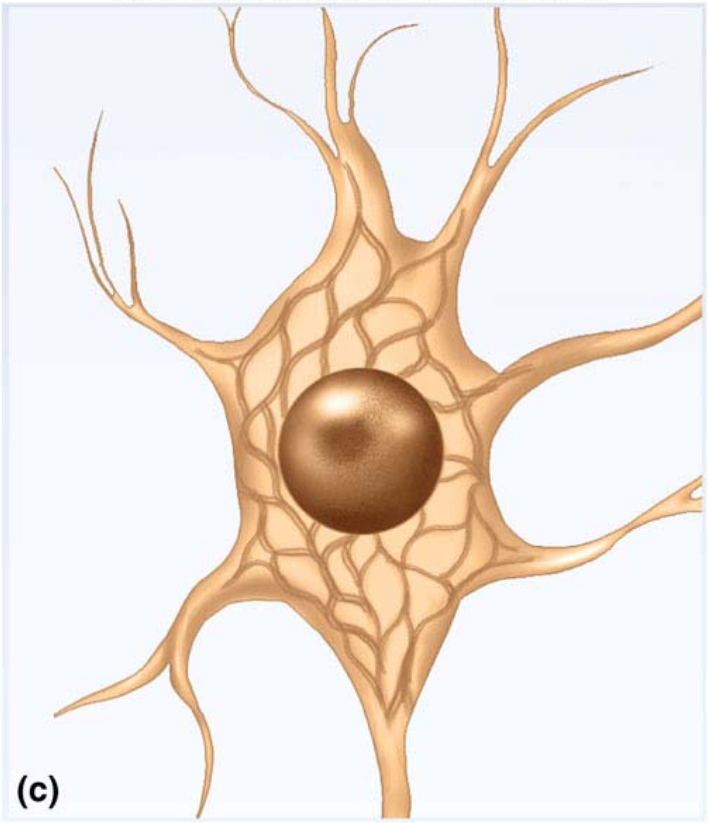
Nervous Tissue

- Overview of the nervous system
- Nerve cells (neurons)
- Supportive cells (neuroglia)
- Electrophysiology of neurons
- Synapses
- Neural integration



Overview of Nervous System

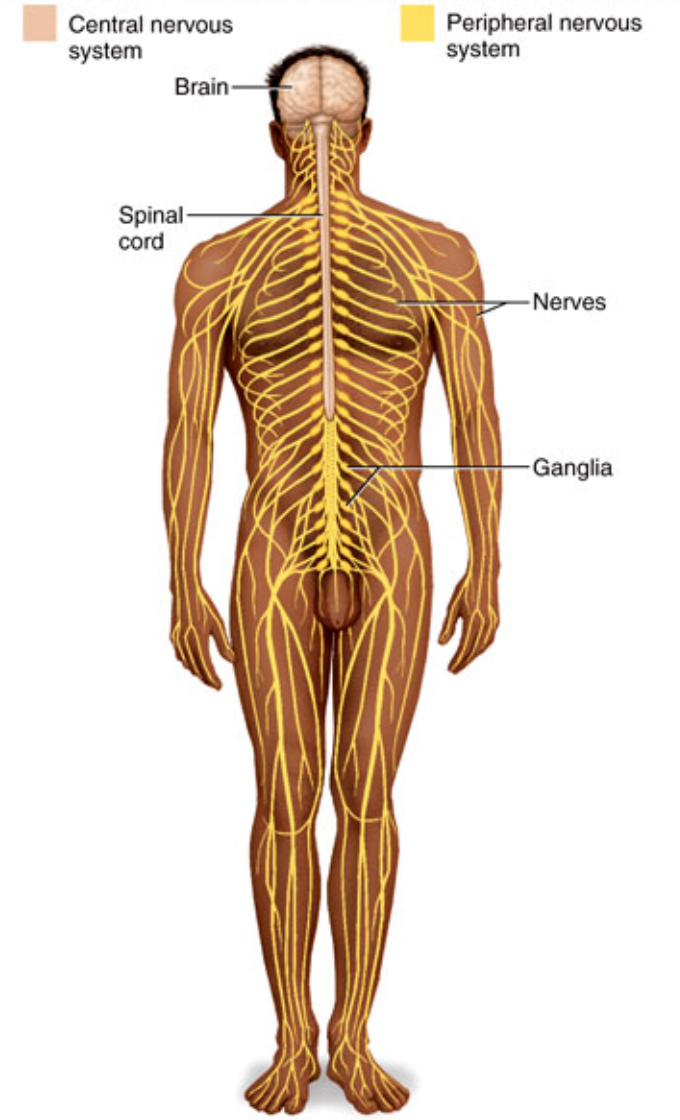
- **Endocrine and nervous system maintain internal coordination**
  - **endocrine = chemical messengers (hormones) delivered to the bloodstream**
  - **nervous = three basic steps**
    - **sense organs receive information**
    - **brain and spinal cord determine responses**
    - **brain and spinal cord issue commands to glands and muscles**

Subdivisions of Nervous System

Two major anatomical subdivisions

- **Central nervous system (CNS)**
  - **brain and spinal cord enclosed in bony coverings**
- **Peripheral nervous system (PNS)**
  - **nerve = bundle of axons in connective tissue**
  - **ganglion = swelling of cell bodies in a nerve**

Subdivisions of Nervous System



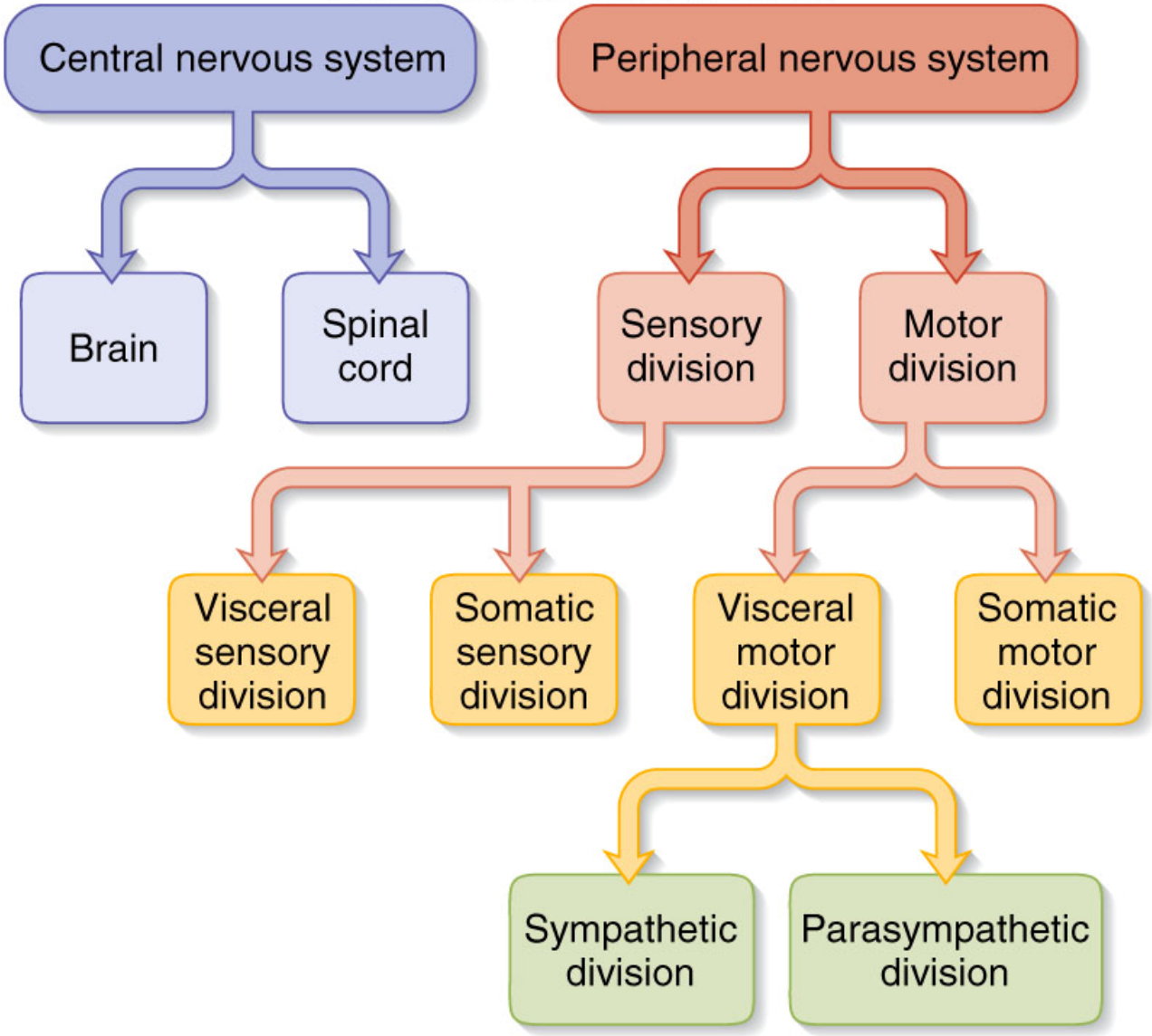
Functional Divisions of PNS

- **Sensory (afferent) divisions (receptors to CNS)**
  - **visceral sensory and somatic sensory division**
- **Motor (efferent) division (CNS to effectors)**
  - **visceral motor division (ANS)**

    effectors: cardiac, smooth muscle, glands
    - **sympathetic division (action)**
    - **parasympathetic division (digestion)**
  - **somatic motor division**

    effectors: skeletal muscle

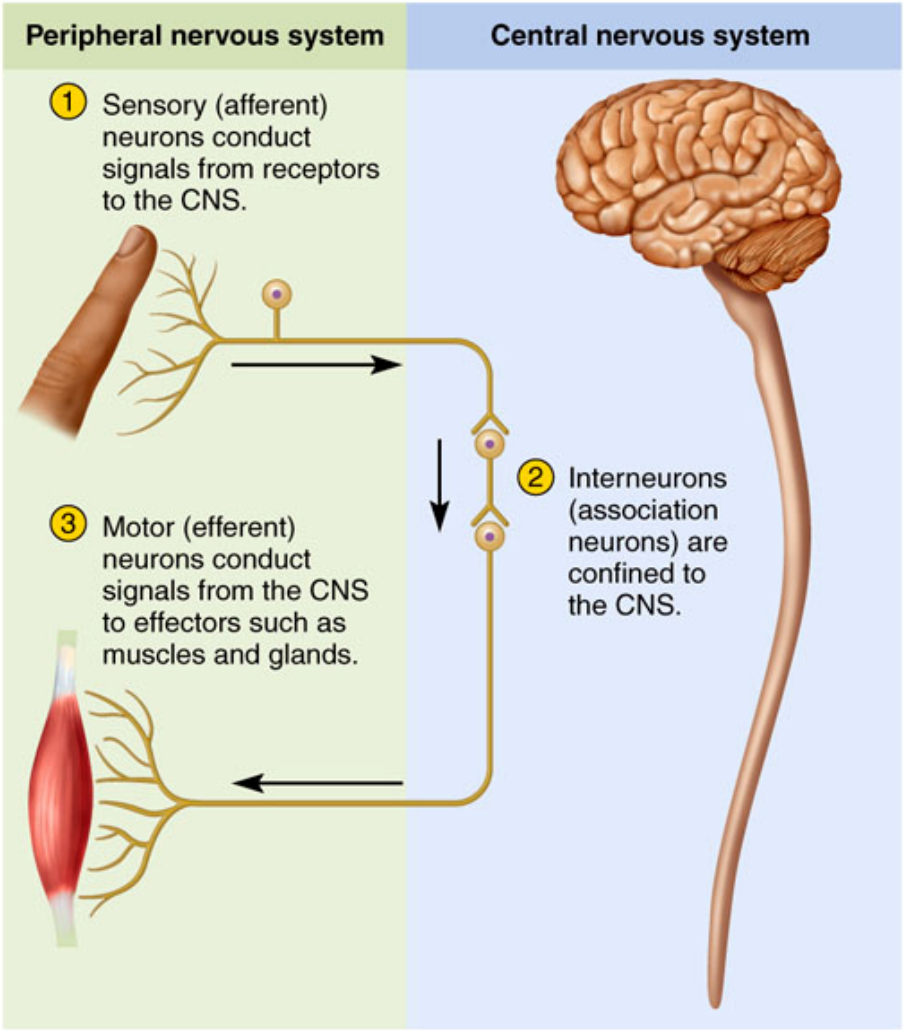
Subdivisions of Nervous System



Fundamental Types of Neurons

- **Sensory (afferent) neurons**
  - **detect changes in body and external environment**
  - **information transmitted into brain or spinal cord**
- **Interneurons (association neurons)**
  - **lie between sensory and motor pathways in CNS**
  - **90% of our neurons are interneurons**
  - **process, store and retrieve information**
- **Motor (efferent) neuron**
  - **send signals out to muscles and gland cells**
  - **organs that carry out responses called effectors**

Fundamental Types of Neurons

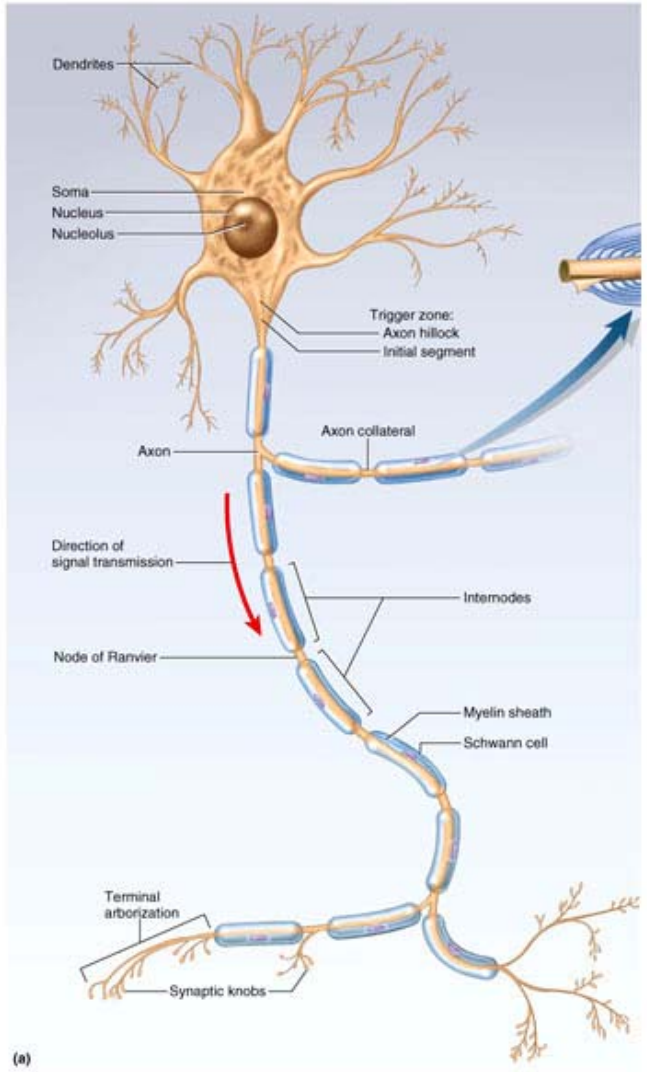


Properties of Neurons

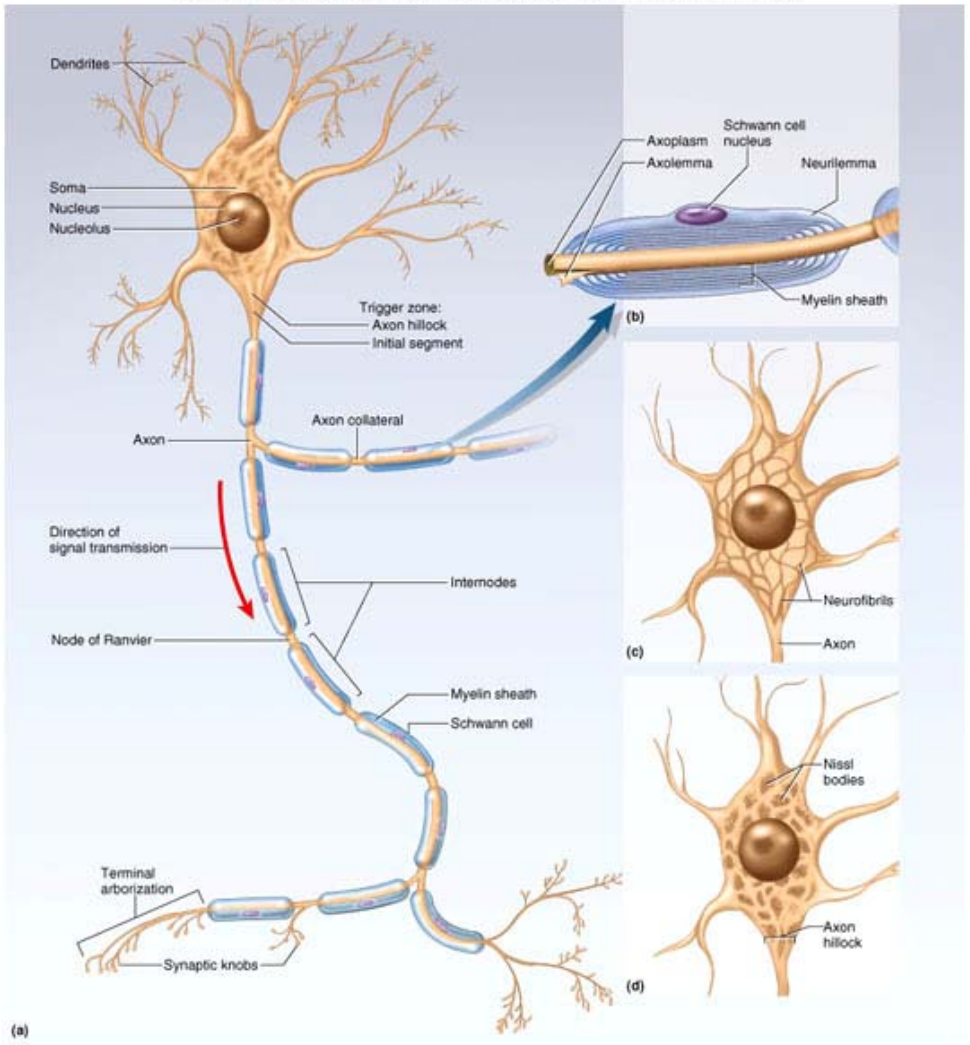
- **Excitability (irritability)**
  - **ability to respond to changes in the body and external environment called stimuli**
- **Conductivity**
  - **produce traveling electrical signals**
- **Secretion**
  - **when electrical signal reaches end of nerve fiber, a chemical neurotransmitter is secreted**

Structure of a Neuron

- **Cell body = perikaryon = soma**
  - **single, central nucleus with large nucleolus**
  - **cytoskeleton of microtubules and neurofibrils (bundles of actin filaments)**
    - **compartmentalizes RER into Nissl bodies**
  - **lipofuscin product of breakdown of worn-out organelles -- more with age**
- **Vast number of short dendrites**
  - **for receiving signals**
- **Singe axon (nerve fiber) arising from axon hillock for rapid conduction**
  - **axoplasm and axolemma and synaptic vesicles**

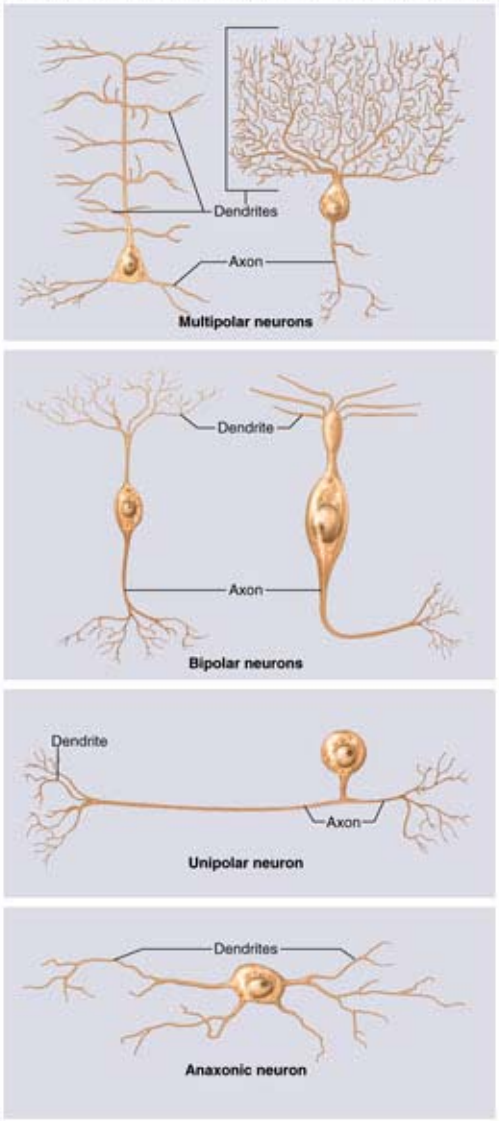


A Representative Neuron



Variation in Neural Structure

- **Multipolar neuron**
  - **most common**
  - **many dendrites/one axon**
- **Bipolar neuron**
  - **one dendrite/one axon**
  - **olfactory, retina, ear**
- **Unipolar neuron**
  - **sensory from skin and organs to spinal cord**
- **Anaxonic neuron**
  - **many dendrites/no axon**
  - **help in visual processes**



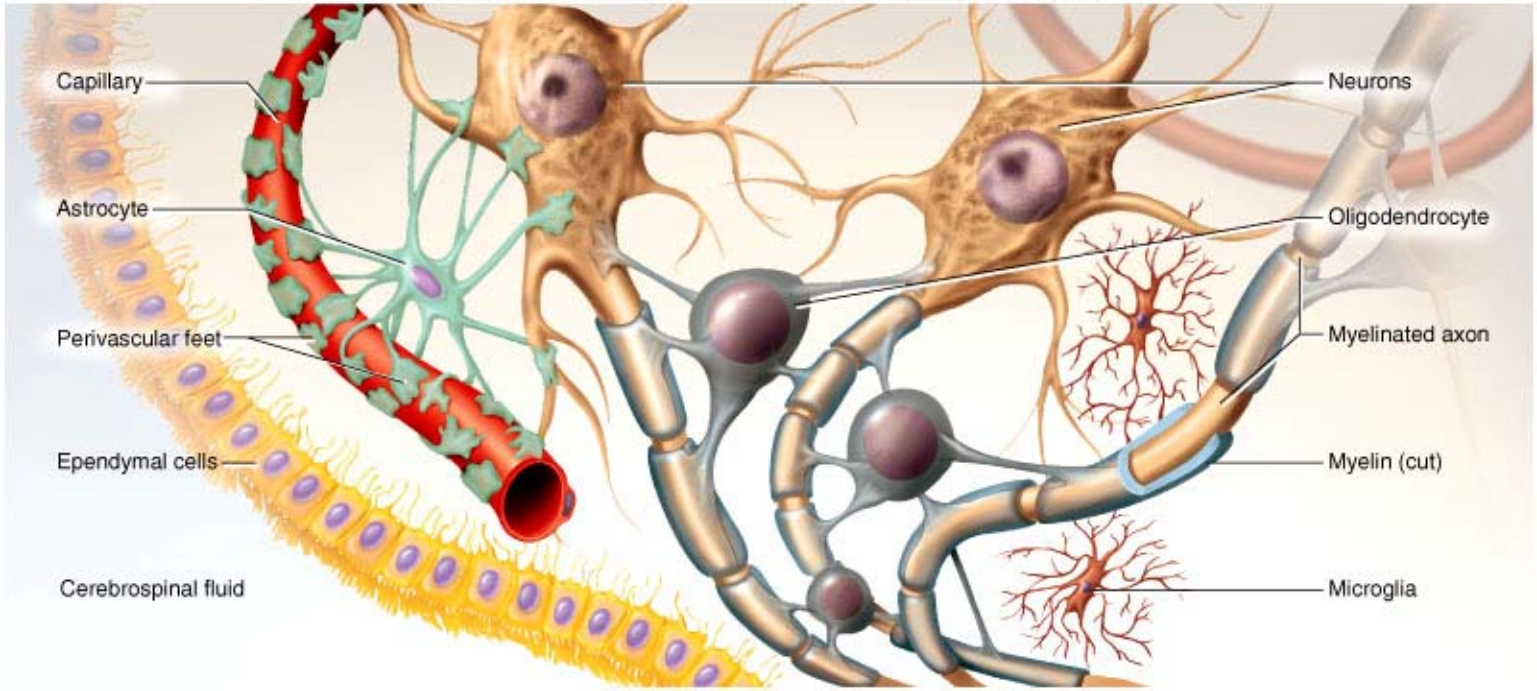
Types of Neuroglial Cells 1

- **Oligodendrocytes form myelin sheaths in CNS**
  - **each wraps around many nerve fibers**
- **Ependymal cells line cavities and produce CSF**
- **Microglia (macrophages) formed from monocytes**
  - **in areas of infection, trauma or stroke**

Types of Neuroglial Cells 2

- **Astrocytes**
  - **most abundant glial cells - form framework of CNS**
  - **contribute to BBB and regulate composition of brain tissue fluid**
  - **convert glucose to lactate to feed neurons**
  - **secrete nerve growth factor promoting synapse formation**
  - **electrical influence on synaptic signaling**
  - **sclerosis – damaged neurons replace by hardened mass of astrocytes**
- **Schwann cells myelinate fibers of PNS**
- **Satellite cells with uncertain function**

Neuroglial Cells of CNS



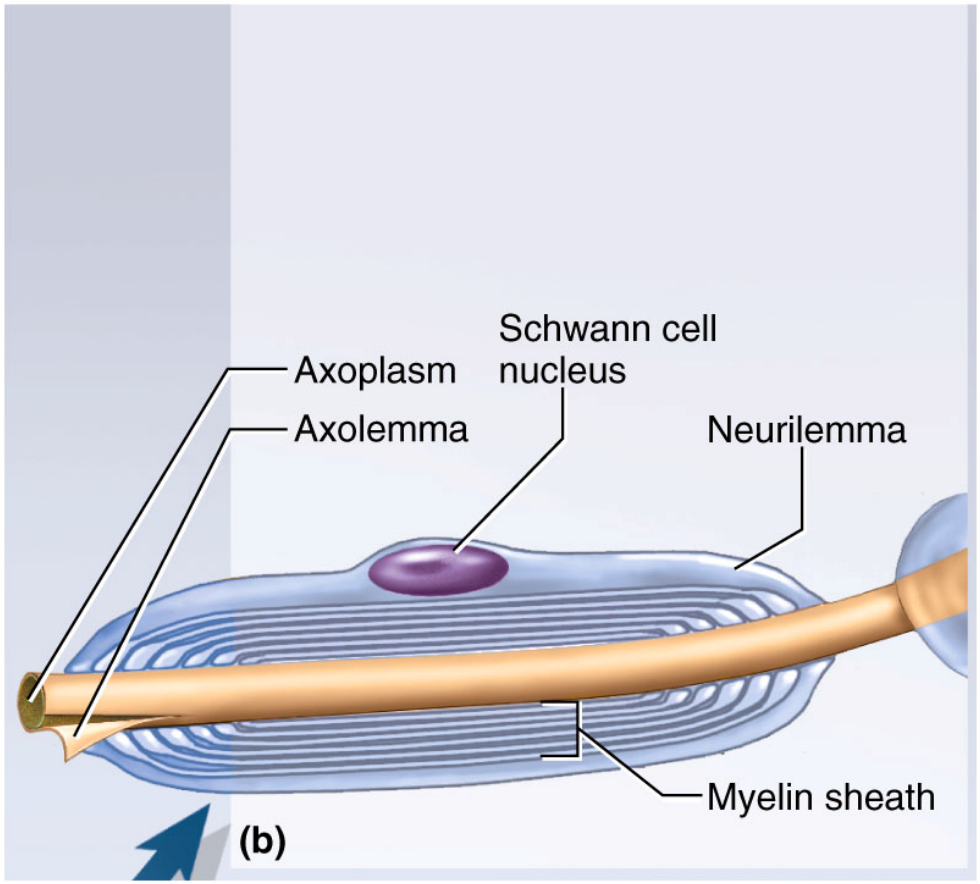
Myelin 1

- **Insulating layer around a nerve fiber**
  - **oligodendrocytes in CNS and schwann cells in PNS**
  - **formed from wrappings of plasma membrane**
    - **20% protein and 80 % lipid (looks white)**
  - **all myelination completed by late adolescence**
- **In PNS, hundreds of layers wrap axon**
  - **the outermost coil is schwann cell (neurilemma)**
  - **covered by basal lamina and endoneurium**

Myelin 2

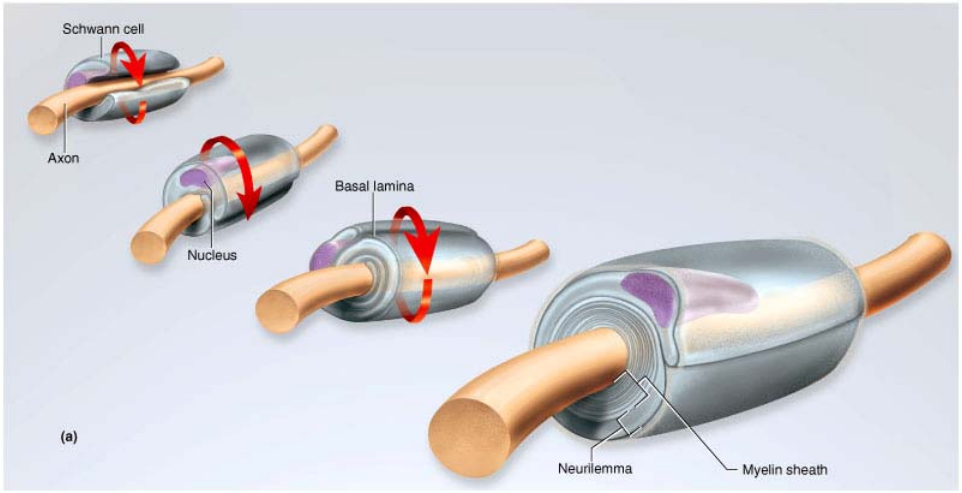
- In CNS - no neurilemma or endoneurium
- Oligodendrocytes myelinate several fibers
  - Myelination spirals inward with new layers pushed under the older ones
- Gaps between myelin segments = nodes of Ranvier
- Initial segment (area before 1st schwann cell) and axon hillock form trigger zone where signals begin

Myelin Sheath



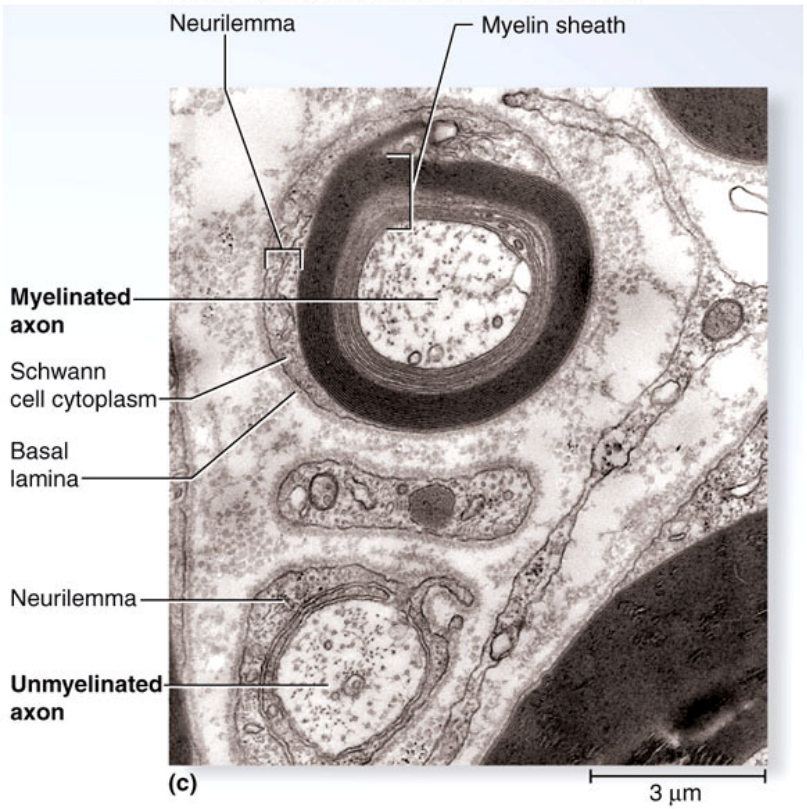
- **Note: Node of Ranvier between Schwann cells**

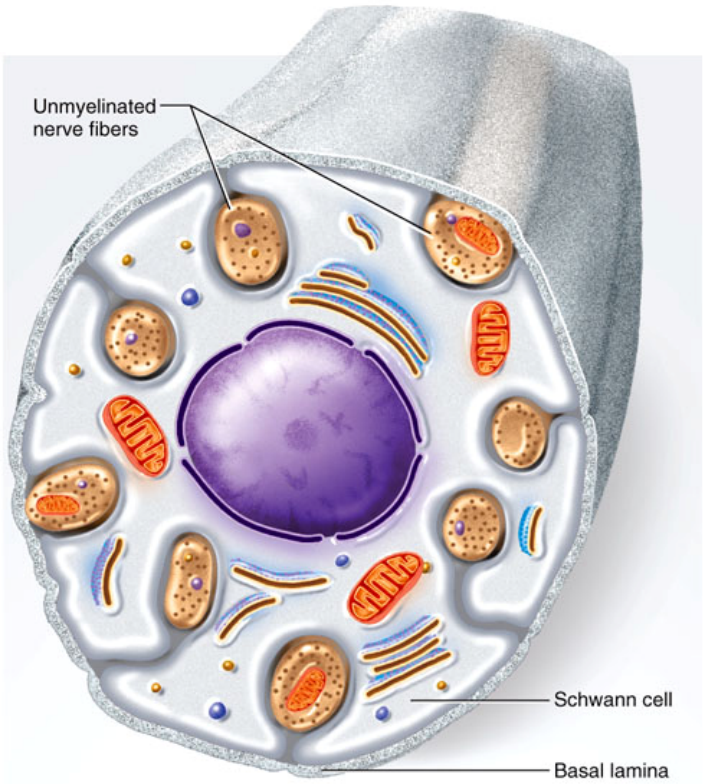
Myelination in PNS



- **Myelination begins during fetal development, but proceeds most rapidly in infancy.**

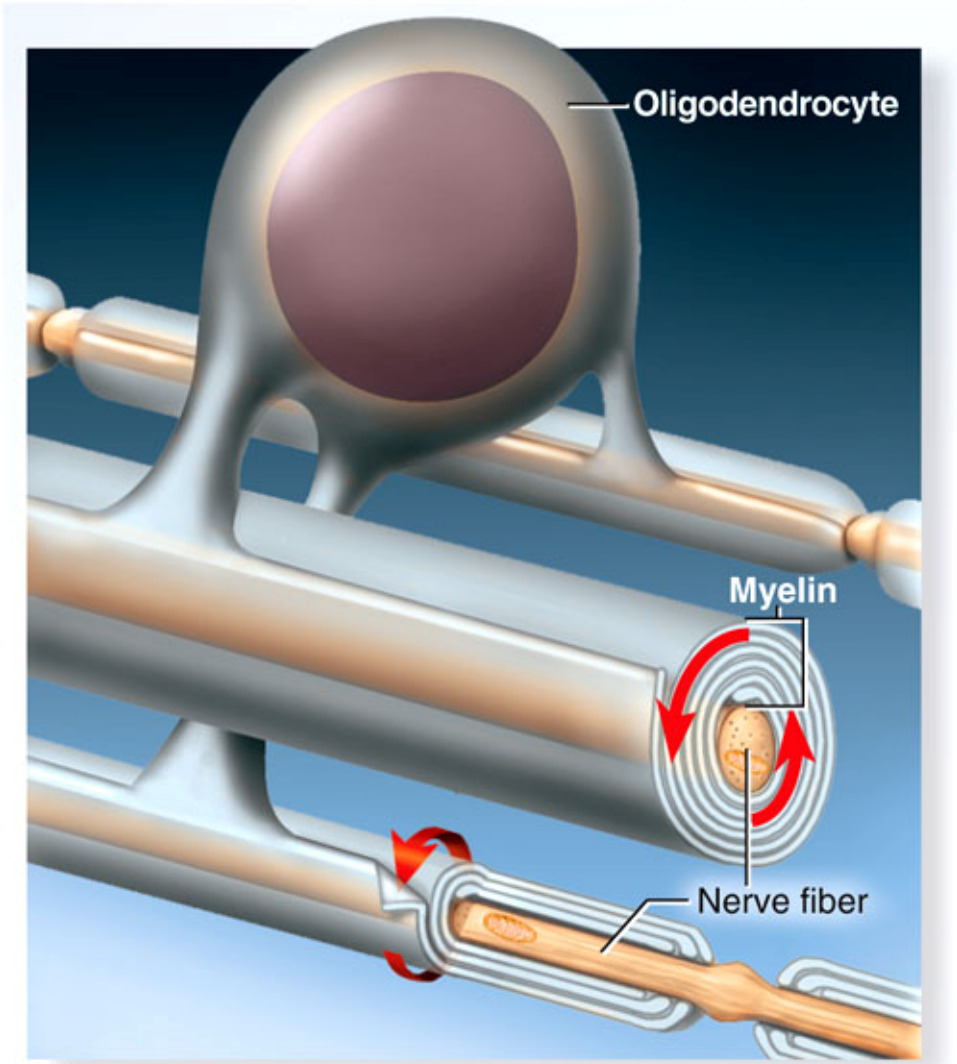
Unmyelinated Axons of PNS





- **Schwann cells hold small nerve fibers in grooves on their surface with only one membrane wrapping**

Myelination in CNS



(b)

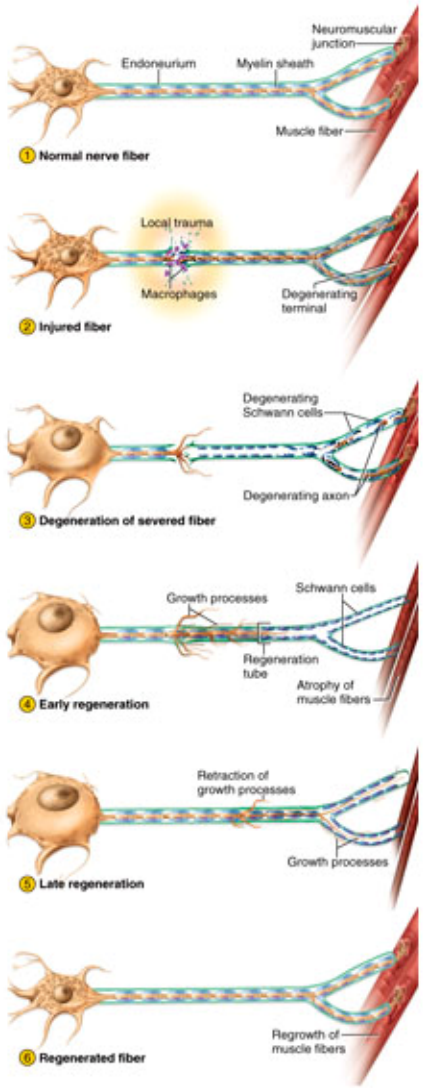
Speed of Nerve Signal

- **Diameter of fiber and presence of myelin**
  - **large fibers have more surface area for signals**
- **Speeds**
  - **small, unmyelinated fibers = 0.5 - 2.0 m/sec**
  - **small, myelinated fibers = 3 - 15.0 m/sec**
  - **large, myelinated fibers = up to 120 m/sec**
- **Functions**
  - **slow signals supply the stomach and dilate pupil**
  - **fast signals supply skeletal muscles and transport sensory signals for vision and balance**

Regeneration of Peripheral Nerves

- Occurs if soma and neurilemmal tube is intact
- Stranded end of axon and myelin sheath degenerate
  - cell soma swells, ER breaks up and some cells die
- Axon stump puts out several sprouts
- Regeneration tube guides lucky sprout back to its original destination
  - schwann cells produce nerve growth factors
- Soma returns to its normal appearance

Regeneration of Nerve Fiber



Electrical Potentials and Currents

- Nerve pathway is a series of separate cells
- neural communication = mechanisms for producing electrical potentials and currents
  - electrical potential - different concentrations of charged particles in different parts of the cell
  - electrical current - flow of charged particles from one point to another within the cell
- Living cells are polarized
  - resting membrane potential is -70 mV with a negative charge on the inside of membrane

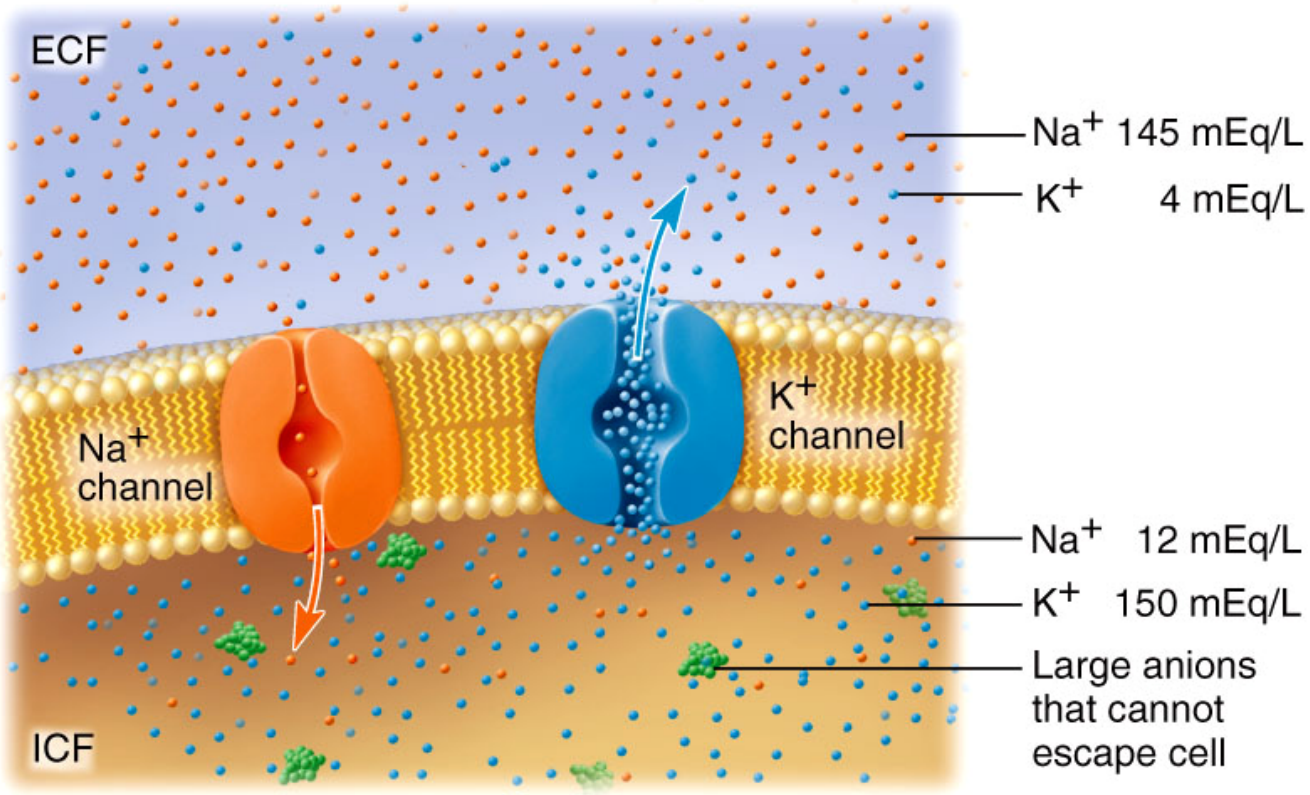
Resting Membrane Potential

- **Unequal electrolytes distribution between ECF/ICF**
- **Diffusion of ions down their concentration gradients**
- **Selective permeability of plasma membrane**
- **Electrical attraction of cations and anions**

Resting Membrane Potential 2

- Membrane very permeable to K^+
  - leaks out until electrical gradient created attracts it back in
- Cytoplasmic anions can not escape due to size or charge (PO_4^{2-}, SO_4^{2-}, organic acids, proteins)
- Membrane much less permeable to Na^+
- Na^+/K^+ pumps out 3 Na^+ for every 2 K^+ it brings in
  - works continuously and requires great deal of ATP
  - necessitates glucose and oxygen be supplied to nerve tissue

Ionic Basis of Resting Membrane Potential



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

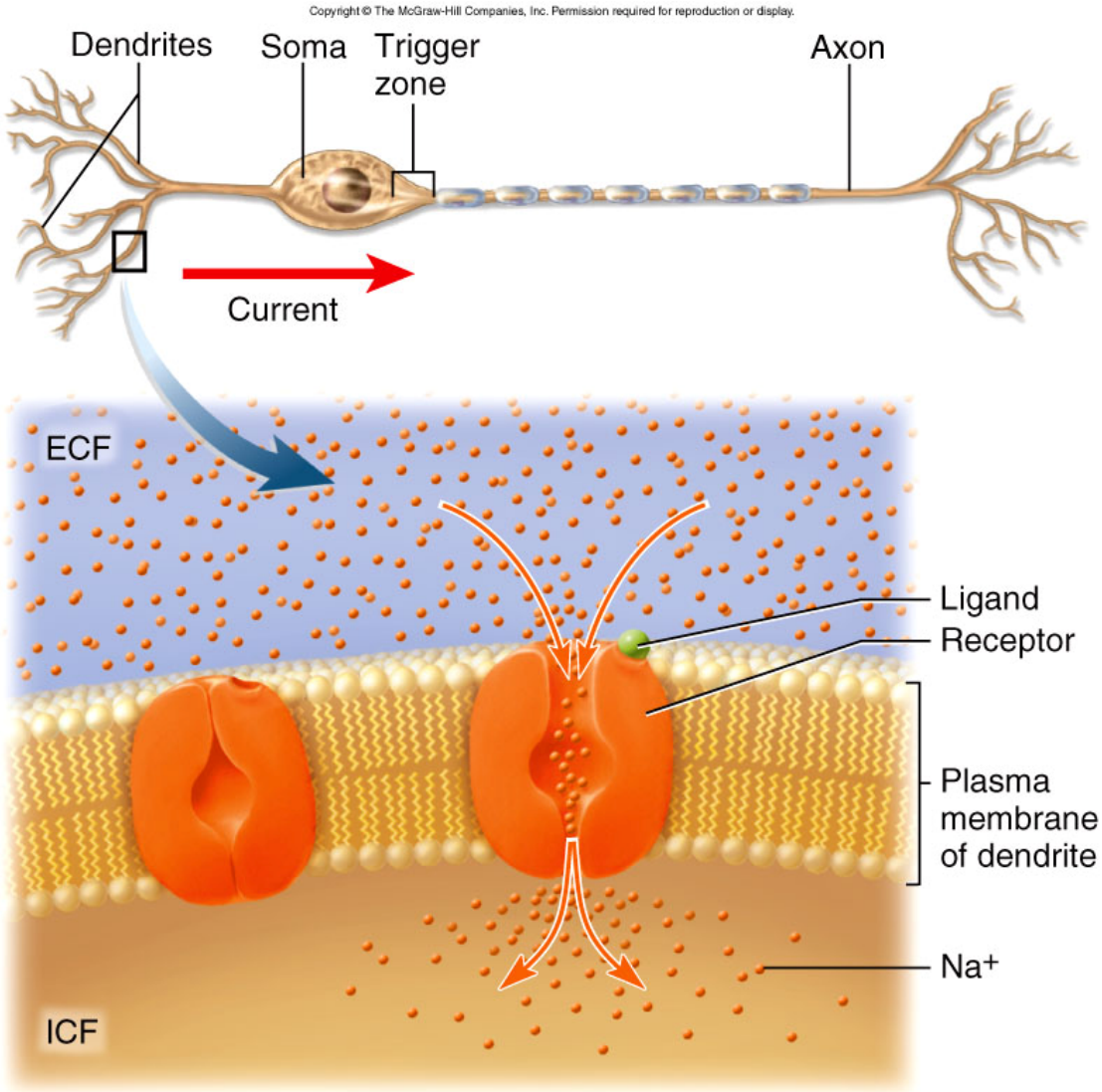
Local Potentials 1

- **Local disturbances in membrane potential**
  - **occur when neuron is stimulated by chemicals, light, heat or mechanical disturbance**
  - **depolarization decreases potential across cell membrane due to opening of gated Na^+ channels**
    - **Na^+ rushes in down concentration and electrical gradients**
    - **Na^+ diffuses for short distance inside membrane producing a change in voltage called a local potential**

Local Potentials 2

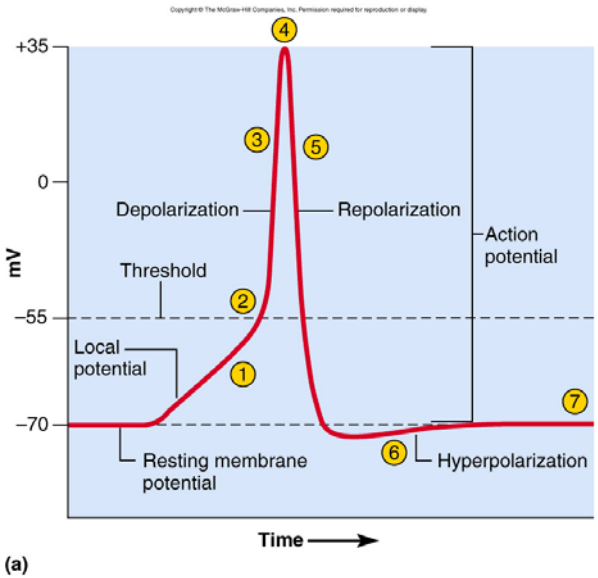
- **Differences from action potential**
  - **are graded (vary in magnitude with stimulus strength)**
  - **are decremental (get weaker the farther they spread)**
  - **are reversible as K^+ diffuses out of cell**
  - **can be either excitatory or inhibitory (hyperpolarize)**

Chemical Excitation



Action Potentials

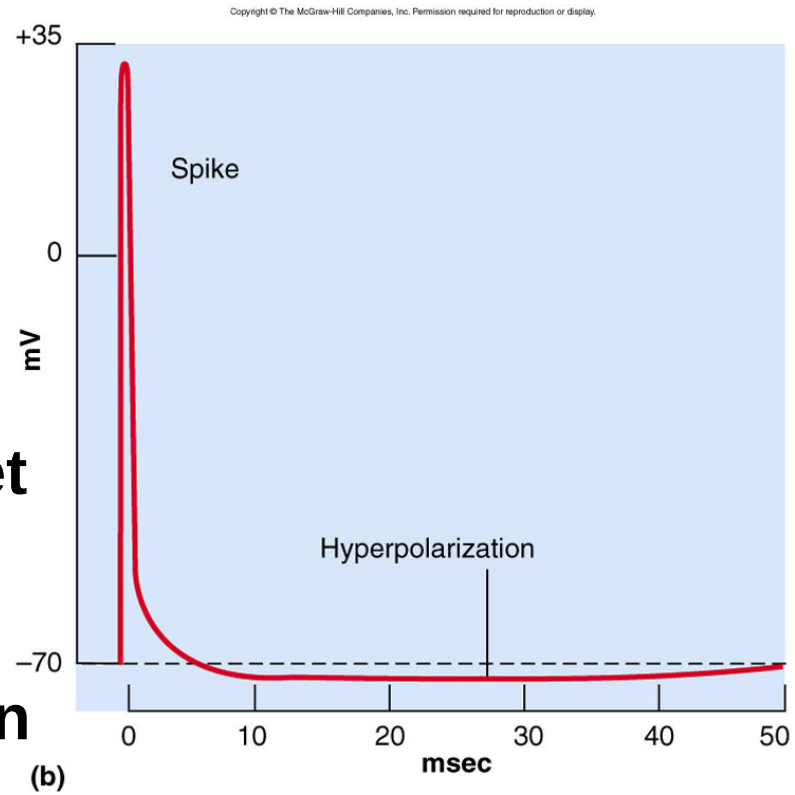
- More dramatic change in membrane produced where high density of voltage-gated channels occur
  - trigger zone up to 500 channels/μm^2 (normal is 75)
- If threshold potential (-55mV) is reached voltage-gated Na^+ channels open (Na^+ enters causing depolarization)
- Past 0 mV, Na^+ channels close = depolarization
- Slow K^+ gates fully open
- K^+ exits repolarizing the cell
- Negative overshoot produces hyperpolarization
  - excessive exiting of K^+



(a)

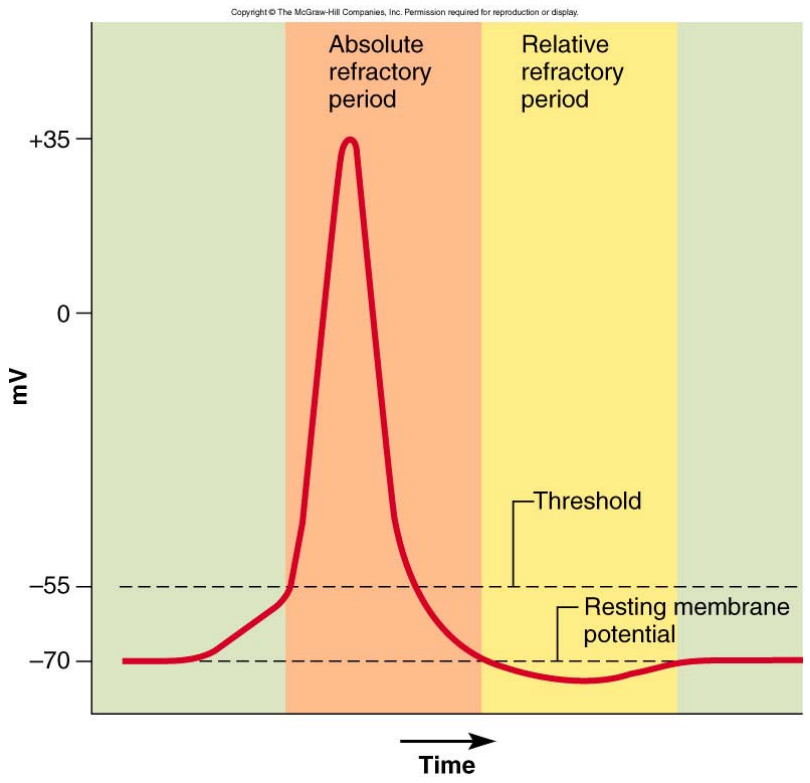
Action Potentials

- Called a spike
- Characteristics of AP
  - follows an all-or-none law
    - voltage gates either open or don't
  - nondecremental (do not get weaker with distance)
  - irreversible (once started goes to completion and can not be stopped)



The Refractory Period

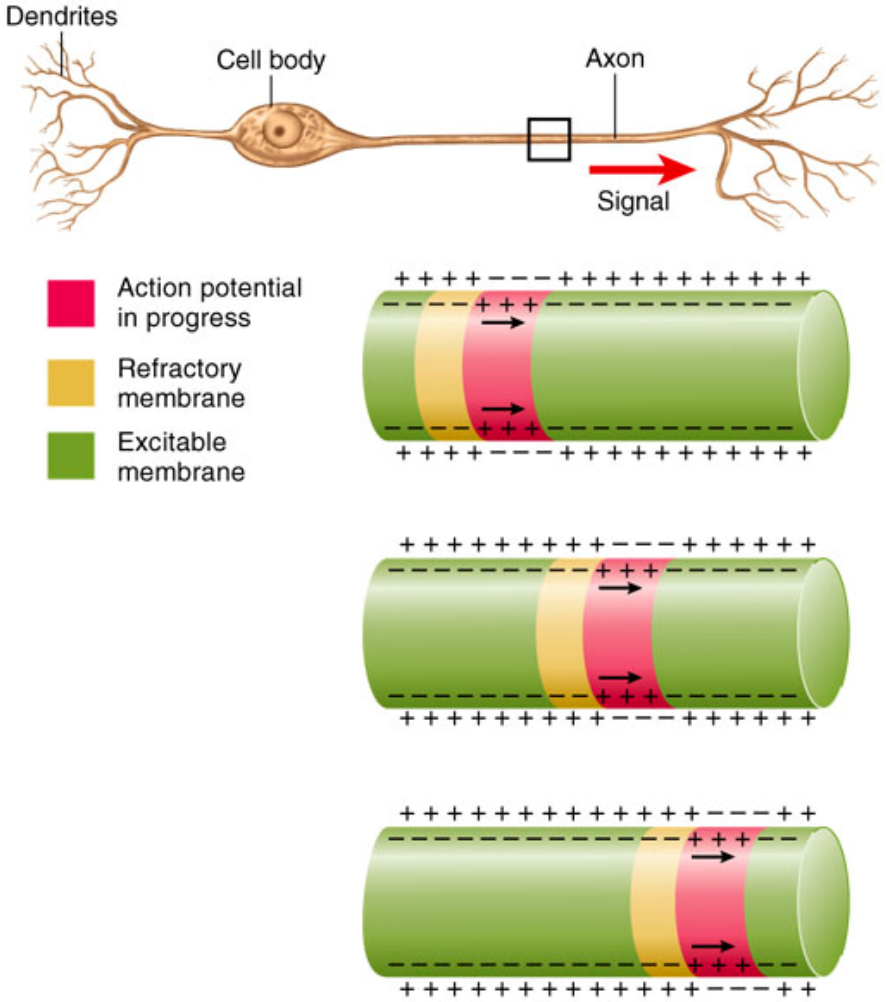
- Period of resistance to stimulation
- Absolute refractory period
  - as long as Na^+ gates are open
  - no stimulus will trigger AP
- Relative refractory period
  - as long as K^+ gates are open
  - only especially strong stimulus will trigger new AP
- Refractory period is occurring only to a small patch of membrane at one time (quickly recovers)



Impulse Conduction in Unmyelinated Fibers

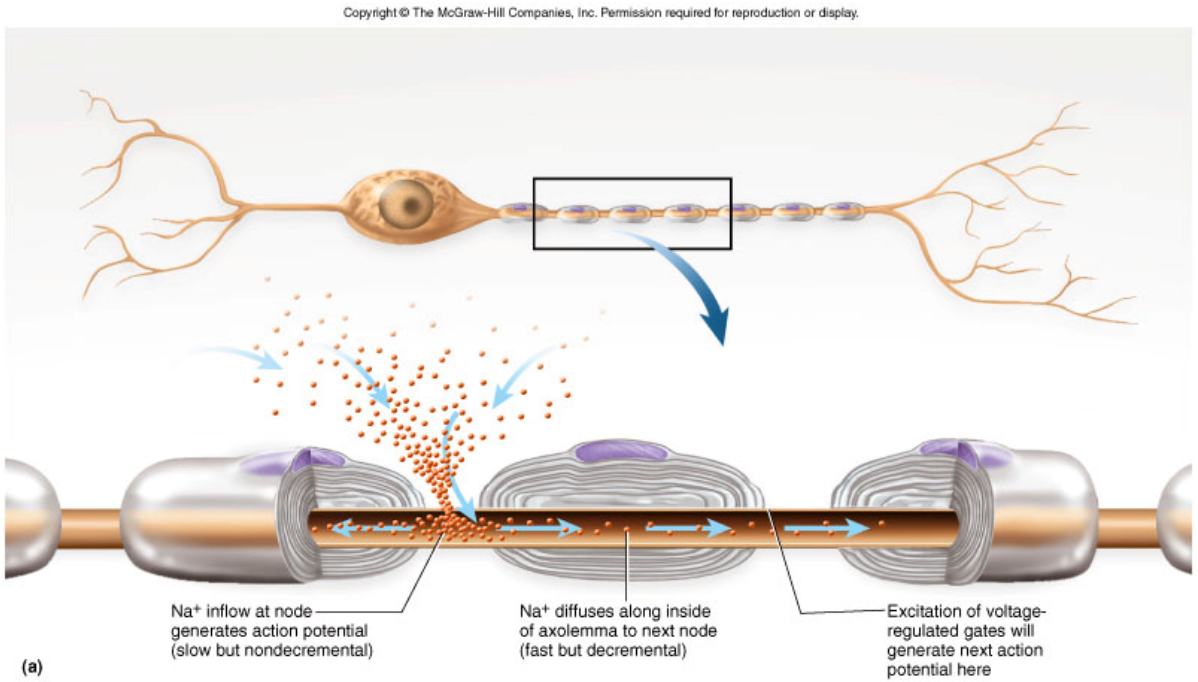
- **Threshold voltage in trigger zone begins impulse**
- **Nerve signal (impulse) - a chain reaction of sequential opening of voltage-gated Na^+ channels down entire length of axon**
- **Nerve signal (nondecremental) travels at 2m/sec**

Impulse Conduction - Unmyelinated Fibers

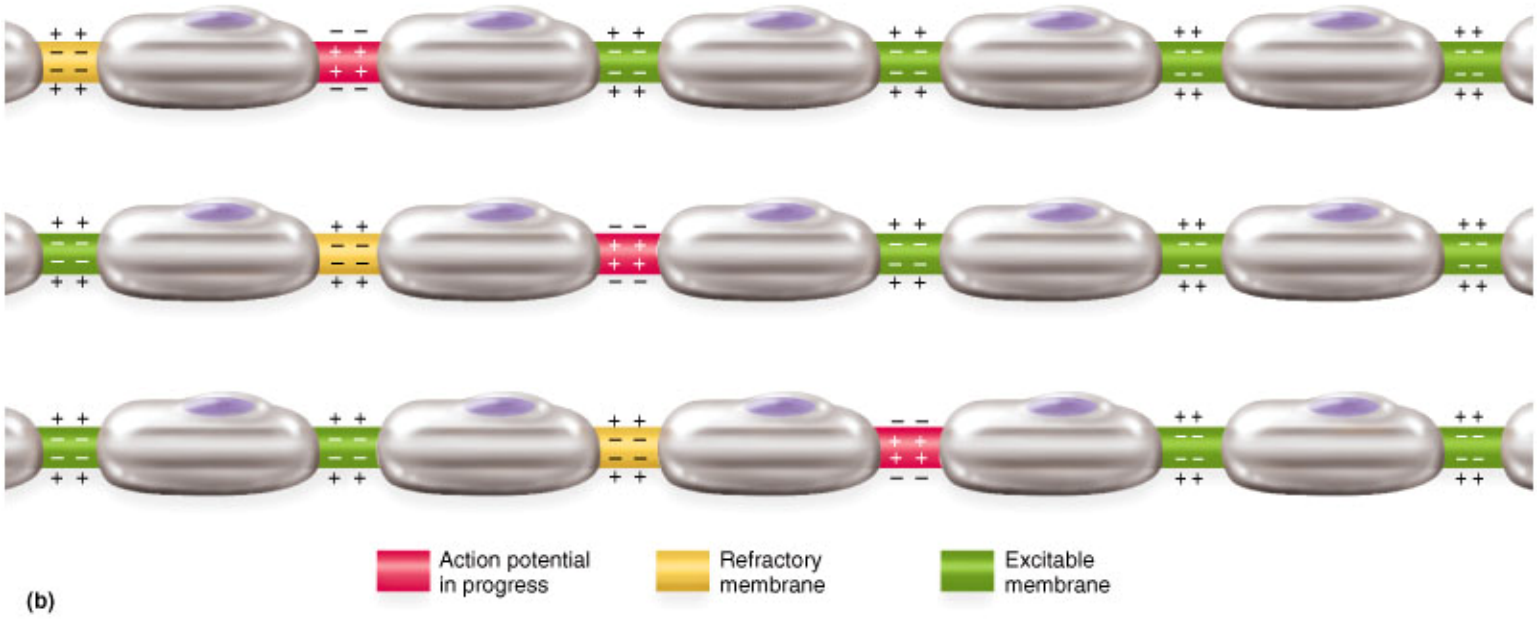


Saltatory Conduction - Myelinated Fibers

- **Voltage-gated channels needed for APs**
  - **fewer than 25 per μm^2 in myelin-covered regions**
  - **up to 12,000 per μm^2 in nodes of Ranvier**
- **Fast Na^+ diffusion occurs between nodes**



Saltatory Conduction

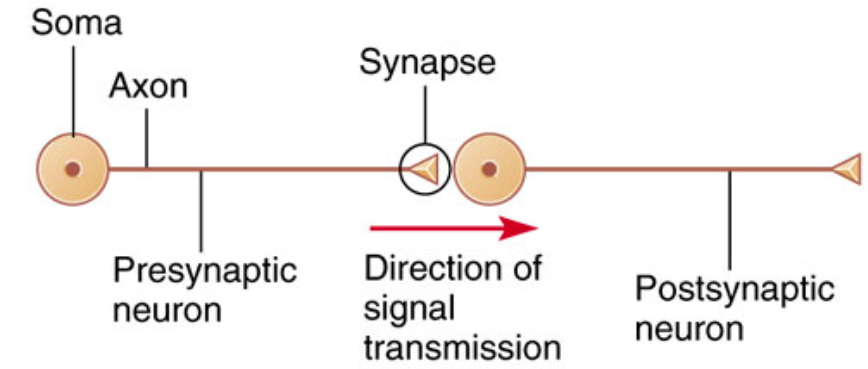


- **Notice how the action potentials jump from node of Ranvier to node of Ranvier.**

Synapses between Neurons

- First neuron releases neurotransmitter onto second neuron that responds to it
  - 1st neuron is presynaptic neuron
  - 2nd neuron is postsynaptic neuron
- Synapse may be axodendritic, axosomatic or axoaxonic
- Number of synapses on postsynaptic cell variable
  - 8000 on spinal motor neuron
  - 100,000 on neuron in cerebellum

Synaptic Relationships between Neurons



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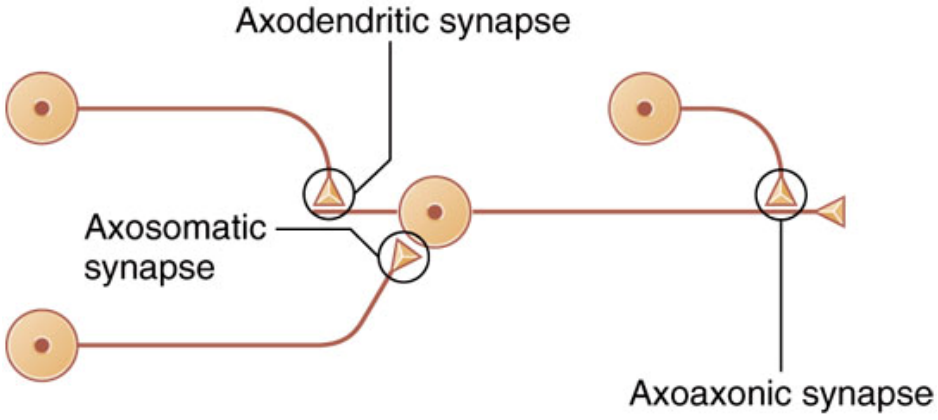
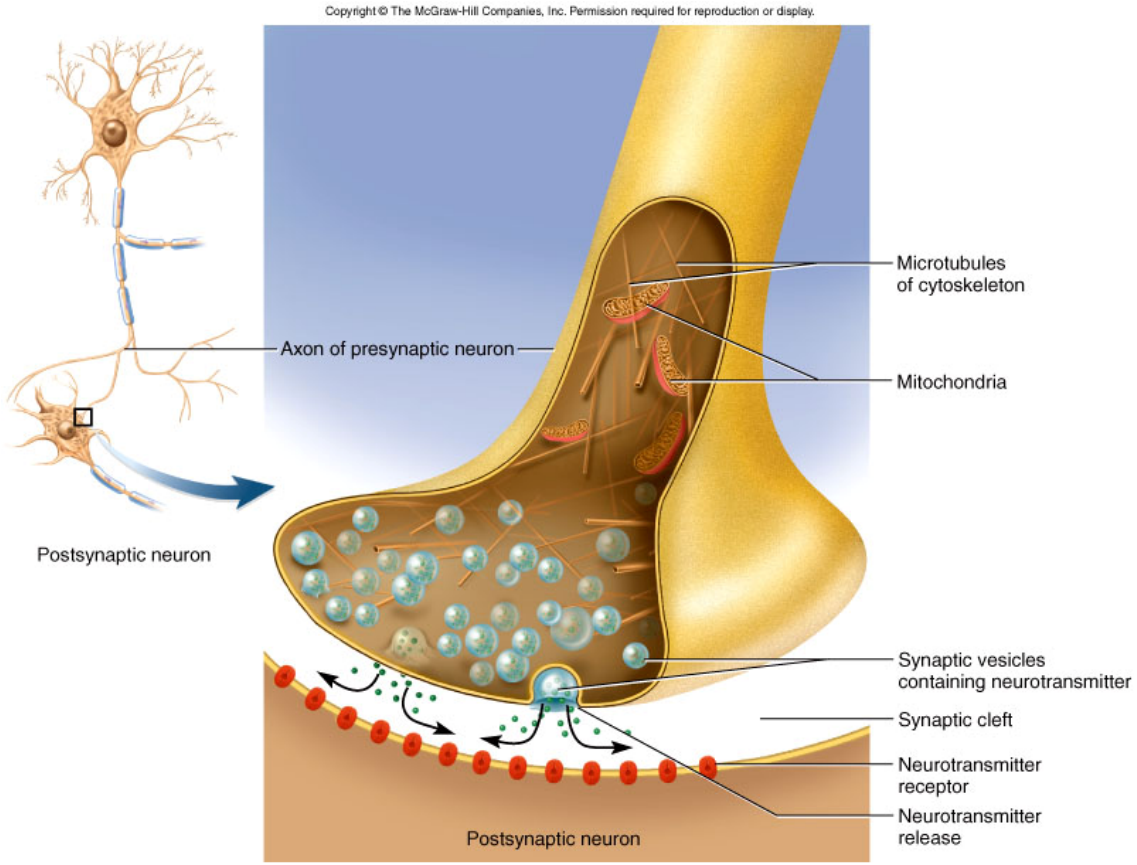


(b)

Discovery of Neurotransmitters

- **Histological observations revealed gap between neurons (synaptic cleft)**
- **Otto Loewi (1873-1961) demonstrate function of neurotransmitters**
  - **flooded exposed hearts of 2 frogs with saline**
  - **stimulated vagus nerve --- heart slowed**
  - **removed saline from that frog and found it slowed heart of 2nd frog --- "vagus substance"**
    - **later renamed acetylcholine**
- **Electrical synapses do = gap junctions**
  - **cardiac and smooth muscle and some neurons**

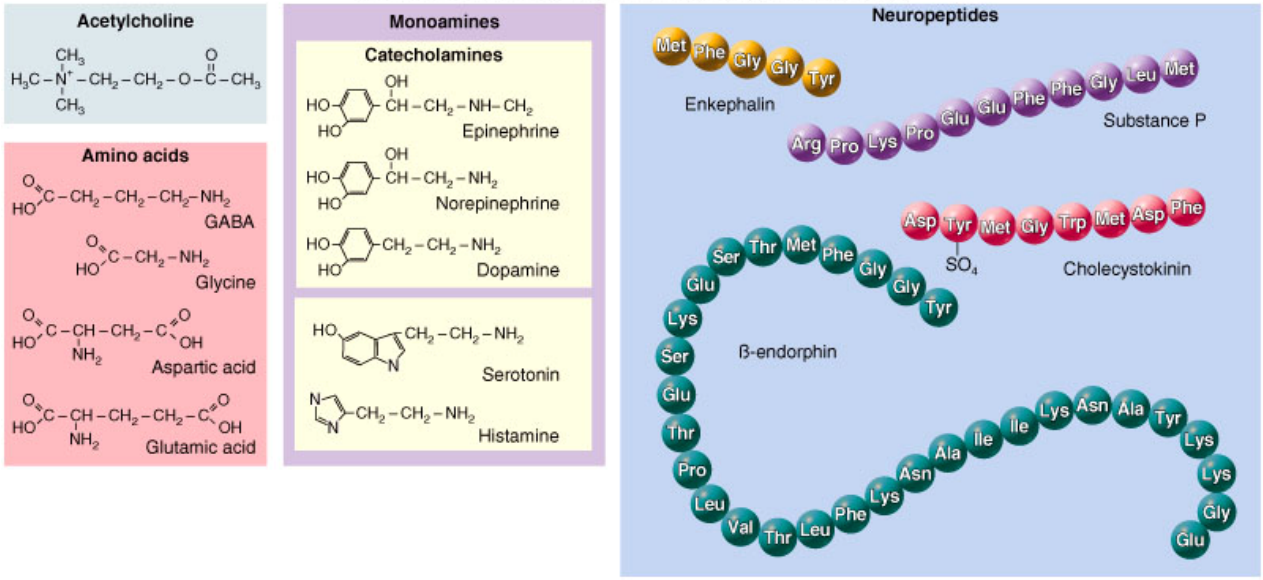
Chemical Synapse Structure



- **Presynaptic neurons have synaptic vesicles with neurotransmitter and postsynaptic have receptors**

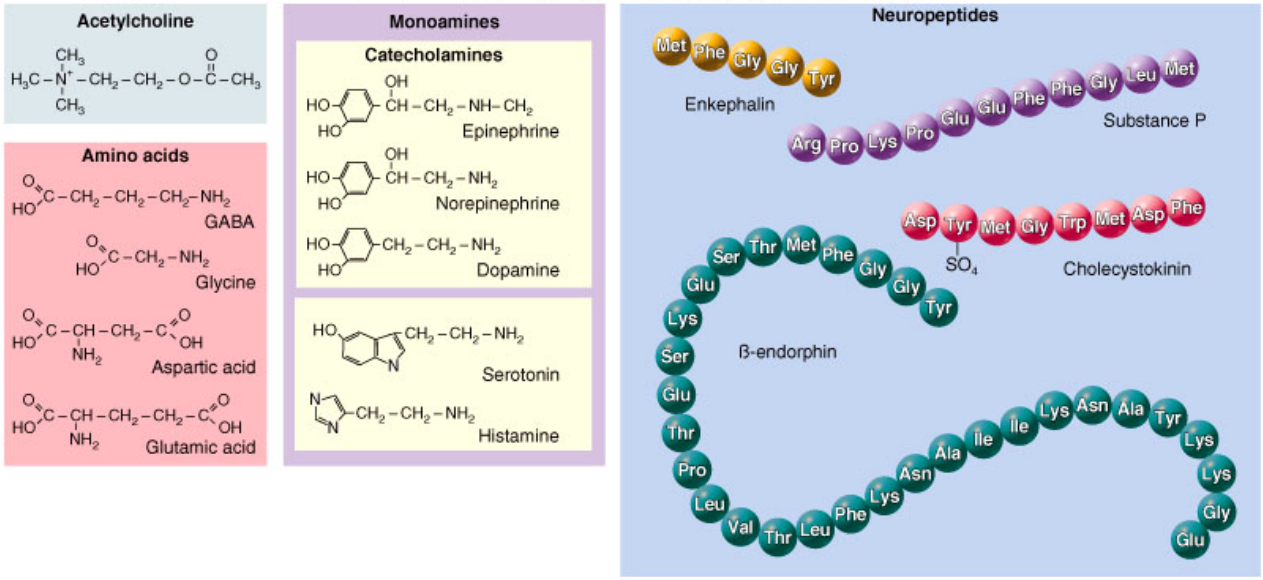
Types of Neurotransmitters

- Acetylcholine
  - formed from acetic acid and choline
- Amino acid neurotransmitters
- Monoamines
  - synthesized by replacing –COOH in amino acids with another functional group
  - catecholamines (epi, NE and dopamine)
  - indolamines (serotonin and histamine)
- Neuropeptides



Neuropeptides

- Chains of 2 to 40 amino acids
- Stored in axon terminal as larger secretory granules (called dense-core vesicles)
- Act at lower concentrations
- Longer lasting effects
- Some released from nonneural tissue
  - gut-brain peptides cause food cravings
- Some function as hormones
  - modify actions of neurotransmitters



Synaptic Transmission

3 kinds of synapses with different modes of action

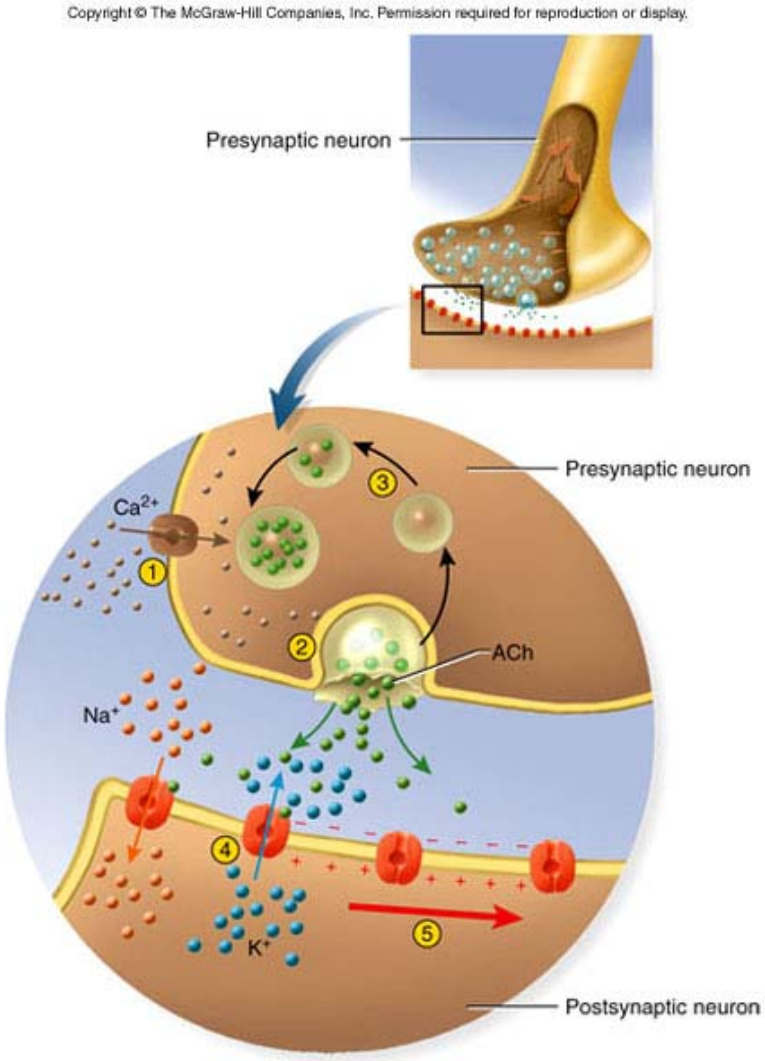
- **Excitatory cholinergic synapse = ACh**
- **Inhibitory GABA-ergic synapse = GABA**
- **Excitatory adrenergic synapse = NE**

Synaptic delay (.5 msec)

- **time from arrival of nerve signal at synapse to start of AP in postsynaptic cell**

Excitatory Cholinergic Synapse

- **Nerve signal opens voltage-gated calcium channels in synaptic knob**
- **Triggers release of ACh which crosses synapse**
- **ACh receptors trigger opening of Na^+ channels producing local potential (postsynaptic potential)**
- **When reaches -55mV, triggers AP in postsynaptic neuron**



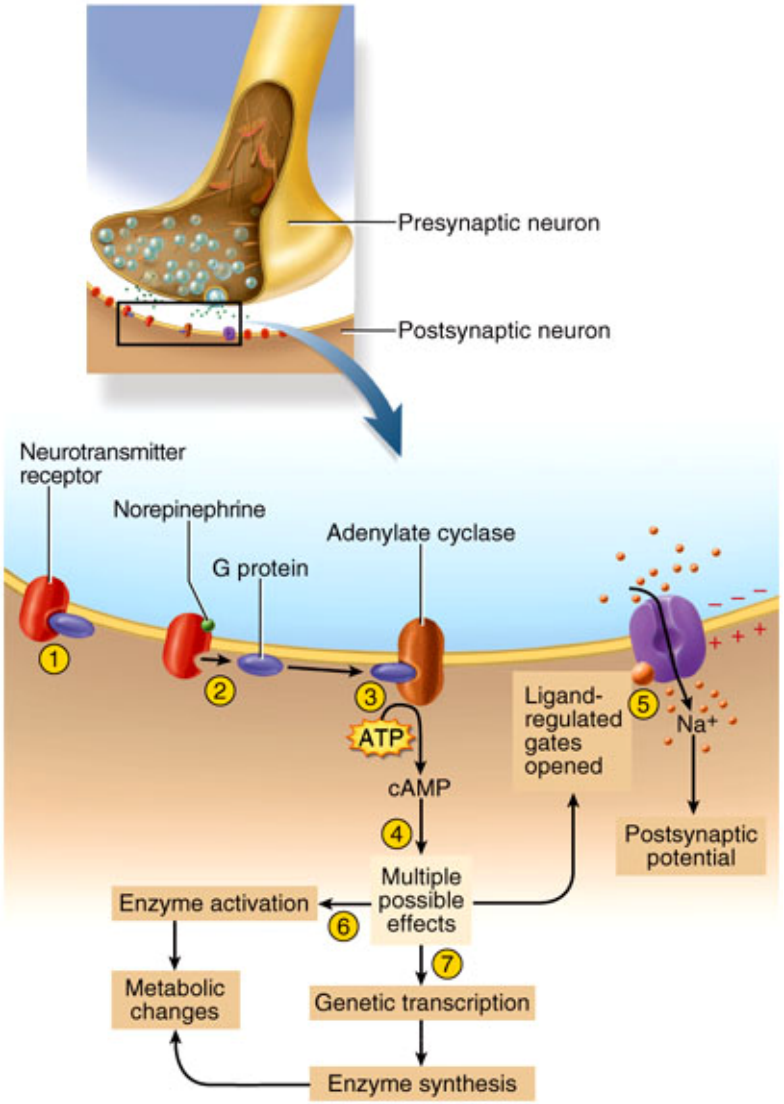
Inhibitory GABA-ergic Synapse

- **Nerve signal triggers release of GABA (γ-aminobutyric acid) which crosses synapse**
- **GABA receptors trigger opening of Cl^- channels producing hyperpolarization**
- **Postsynaptic neuron now less likely to reach threshold**

Excitatory Adrenergic Synapse

- **Neurotransmitter is NE (norepinephrine)**
- **Acts through 2nd messenger systems (cAMP)**
  - **receptor is an integral membrane protein associated with a G protein, which activates adenylate cyclase, which converts ATP to cAMP**
- **cAMP has multiple effects**
  - **binds to ion gate inside of membrane (depolarizing)**
  - **activates cytoplasmic enzymes**
  - **induces genetic transcription and production of new enzymes**
- **Its advantage is enzymatic amplification**

Excitatory Adrenergic Synapse



Cessation and Modification of Signal

- **Mechanisms to turn off stimulation**
  - **diffusion of neurotransmitter away into ECF**
    - **astrocytes return it to neurons**
  - **synaptic knob reabsorbs amino acids and monoamines by endocytosis**
  - **acetylcholinesterase degrades ACh**
    - **choline reabsorbed and recycled**
- **Neuromodulators modify transmission**
  - **raise or lower number of receptors**
  - **alter neurotransmitter release, synthesis or breakdown**

Neural Integration

- More synapses a neuron has the greater its information-processing capability
  - cells in cerebral cortex with 40,000 synapses
  - cerebral cortex estimated to contain 100 trillion synapses
- Chemical synapses are decision-making components of the nervous system
  - ability to process, store and recall information is due to neural integration
- Based on types of postsynaptic potentials produced by neurotransmitters

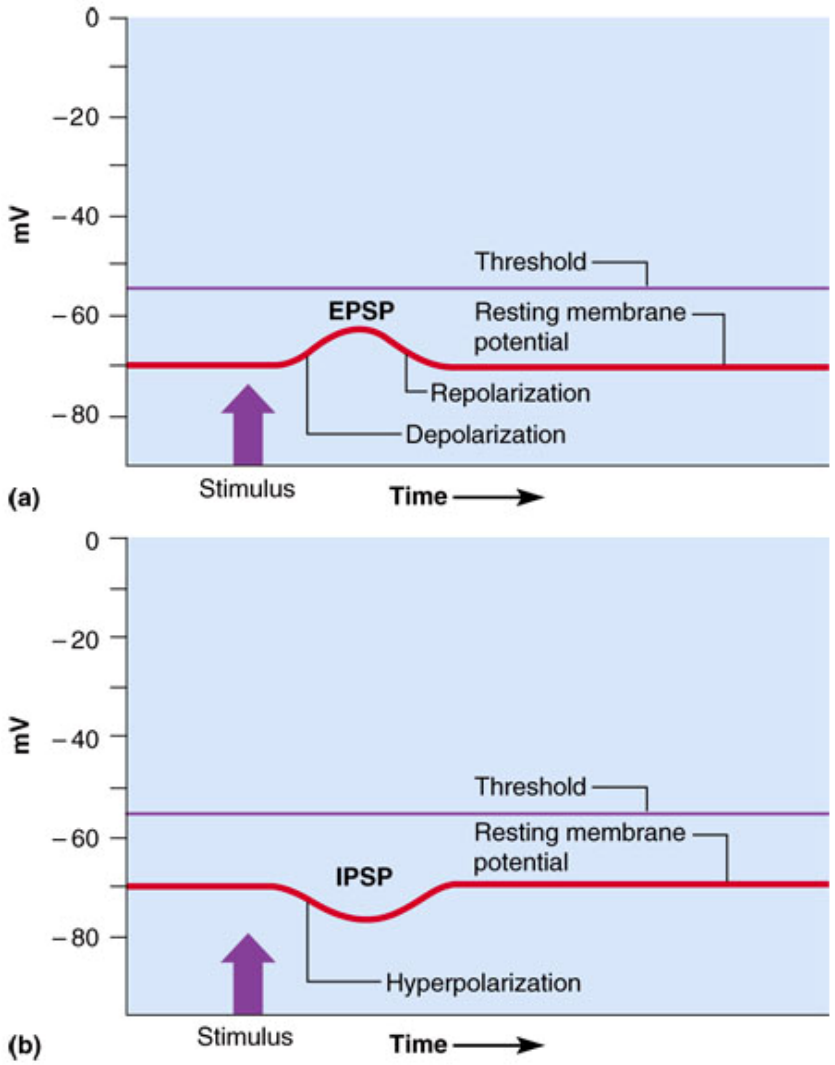
Postsynaptic Potentials- EPSP

- **Excitatory postsynaptic potentials (EPSP)**
  - **a positive voltage change causing postsynaptic cell to be more likely to fire**
    - **result from Na^+ flowing into the cell**
  - **glutamate and aspartate are excitatory neurotransmitters**
- **ACh and norepinephrine may excite or inhibit depending on cell**

Postsynaptic Potentials- IPSP

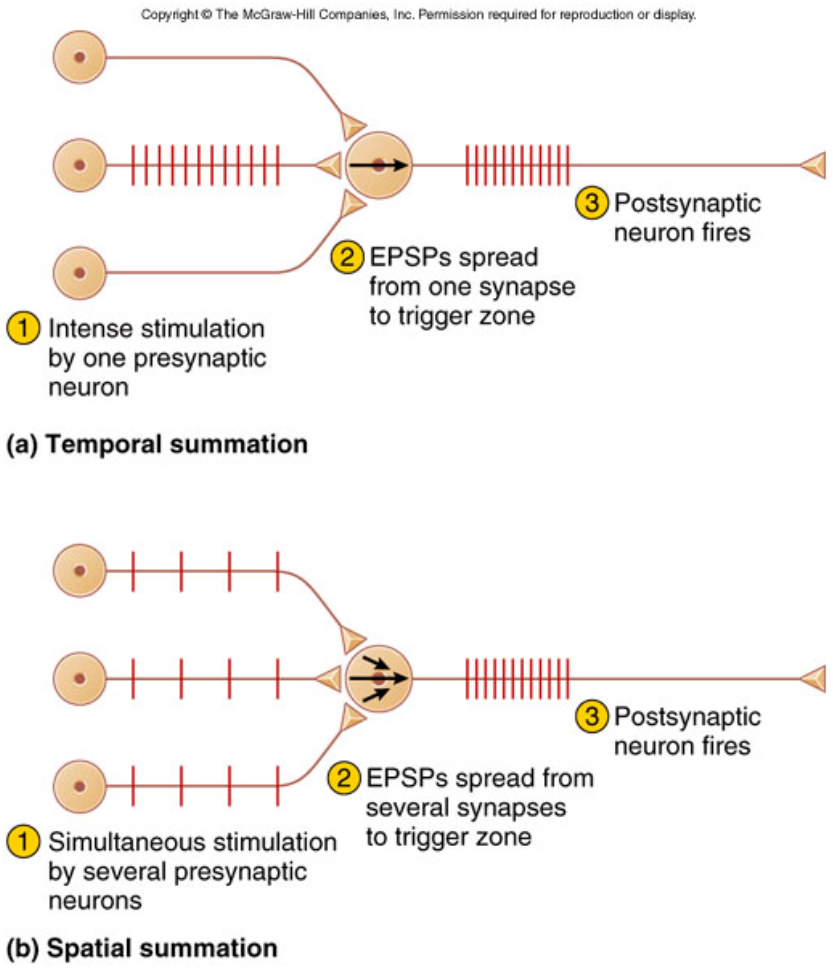
- **Inhibitory postsynaptic potentials (IPSP)**
  - **a negative voltage change causing postsynaptic cell to be less likely to fire (hyperpolarize)**
    - **result of Cl^- flowing into the cell or K^+ leaving the cell**
  - **glycine and GABA are inhibitory neurotransmitters**
- **ACh and norepinephrine may excite or inhibit depending upon cell**

Postsynaptic Potentials

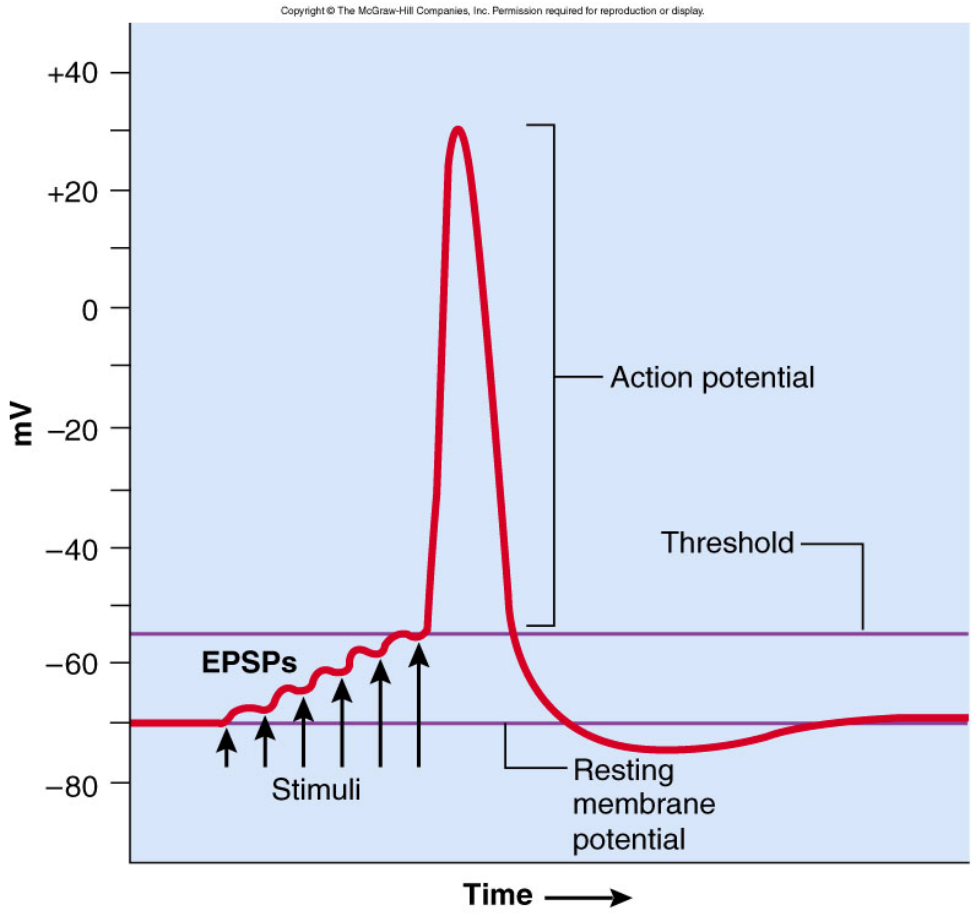


Summation - Postsynaptic Potentials

- **Net postsynaptic potentials in trigger zone**
  - **firing depends on net input of other cells**
    - **typical EPSP voltage = 0.5 mV and lasts 20 msec**
    - **30 EPSPs needed to reach threshold**
  - **temporal summation**
    - **single synapse receives many EPSPs in short time**
  - **spatial summation**
    - **single synapse receives many EPSPs from many cells**

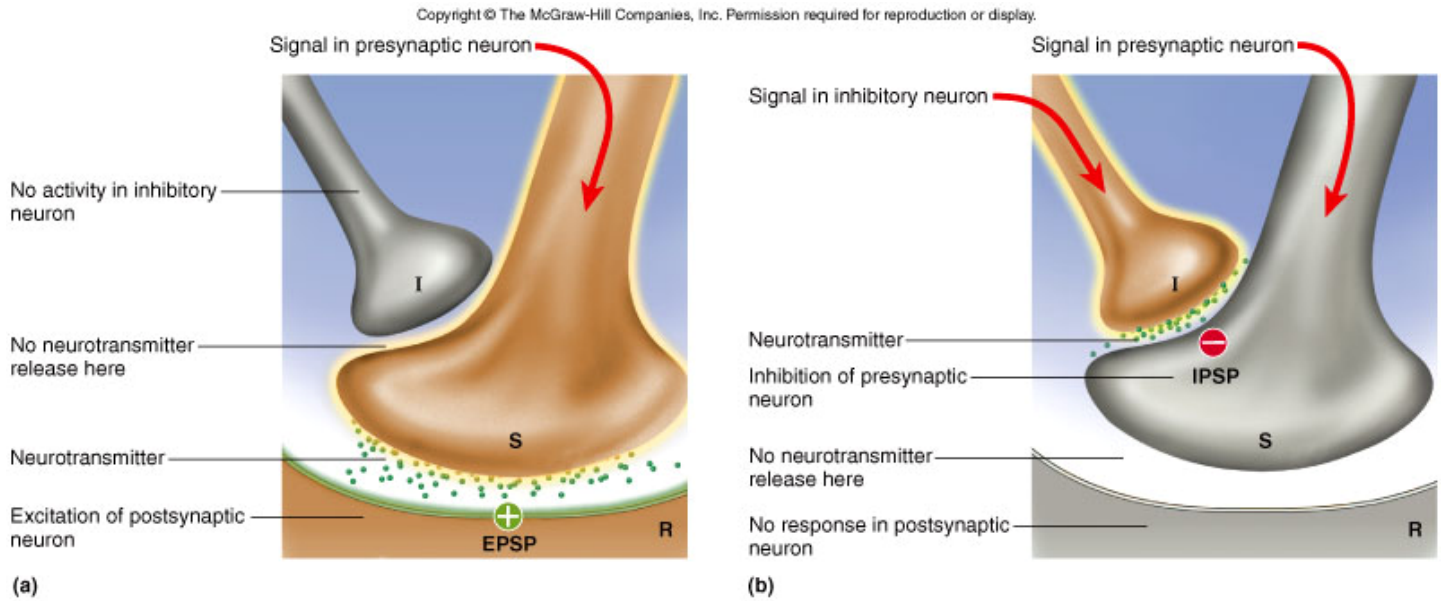


Summation of EPSP's



- **Does this represent spatial or temporal summation?**

Presynaptic Inhibition

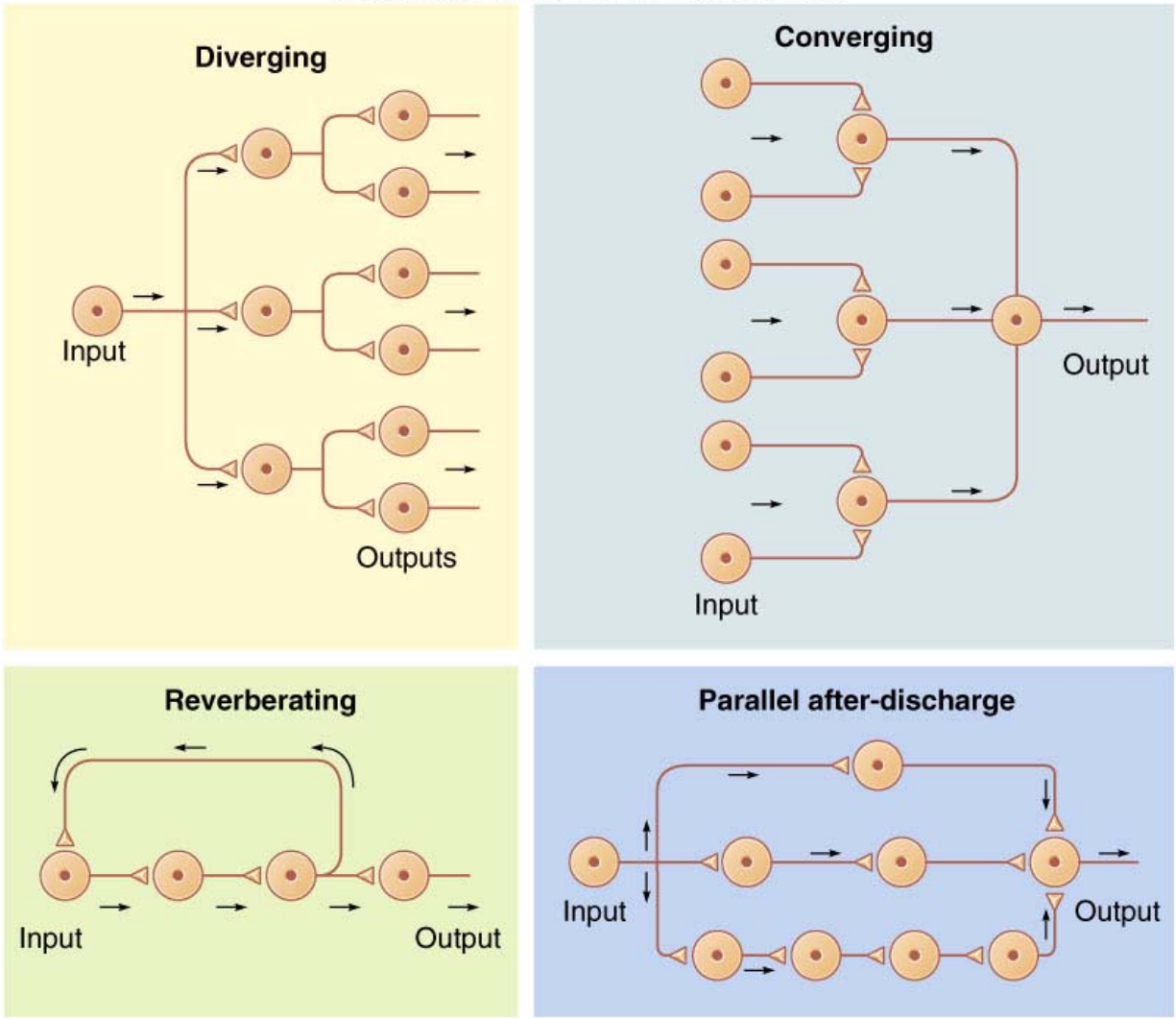


- **One presynaptic neuron suppresses another**
  - **neuron I releases inhibitory GABA**
    - **prevents voltage-gated calcium channels from opening -- it releases less or no neurotransmitter**

Neural Circuits

- **Diverging circuit -- one cell synapses on other that each synapse on others**
- **Converging circuit -- input from many fibers on one neuron (respiratory center)**
- **Reverberating circuits**
  - **neurons stimulate each other in linear sequence but one cell restimulates the first cell to start the process all over**
- **Parallel after-discharge circuits**
  - **input neuron stimulates several pathways which stimulate the output neuron to go on firing for longer time after input has truly stopped**

Neural Circuits Illustrated



Memory and Synaptic Plasticity

- **Physical basis of memory is a pathway**
  - **called a memory trace or engram**
  - **new synapses or existing synapses modified to make transmission easier (synaptic plasticity)**
- **Synaptic potentiation**
  - **transmission mechanisms correlate with different forms of memory**
    - **Immediate, short and long-term memory**

Immediate Memory

- **Ability to hold something in your thoughts for just 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**
  - **reverberating circuits**

Short-Term Memory

- Lasts from a few seconds to several hours
  - quickly forgotten if distracted
- Search for keys, dial the phone
  - reverberating circuits
- Facilitation causes memory to last longer
  - tetanic stimulation (rapid,repetitive signals) cause Ca^{2+} accumulation and cells more likely to fire
- Posttetanic potentiation (to jog a memory)
  - Ca^{2+} level in synaptic knob stays elevated
  - little stimulation needed to recover memory

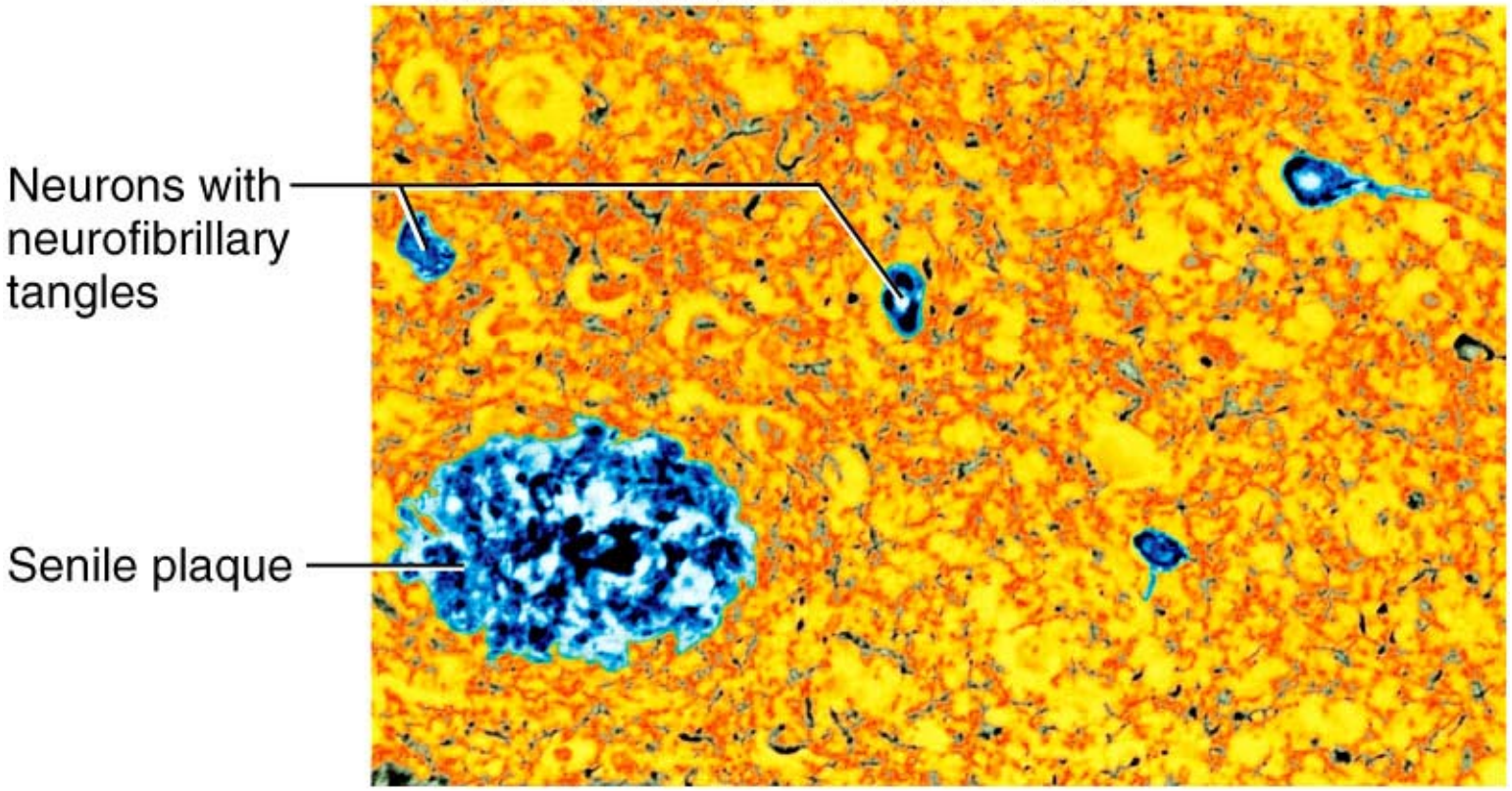
Long-Term Memory

- **Types of long-term memory**
  - **declarative = retention of facts as text**
  - **procedural = retention of motor skills**
- **Physical remodeling of synapses**
  - **new branching of axons or dendrites**
- **Molecular changes = long-term**
  - **tetanic stimulation causes ionic changes**
    - **neuron produces more neurotransmitter receptors**
    - **more protein synthesizes for synapse remodeling**
    - **releases nitric oxide, then presynaptic neuron releases more neurotransmitter**

Alzheimer Disease

- 100,000 deaths/year
  - 11% of population over 65; 47% by age 85
- Memory loss for recent events, moody, combative, lose ability to talk, walk, and eat
- Diagnosis confirmed at autopsy
  - atrophy of gyri (folds) in cerebral cortex
  - neurofibrillary tangles and senile plaques
- Degeneration of cholinergic neurons and deficiency of ACh and nerve growth factors
- Genetic connection confirmed

Alzheimer Disease Effects



(b)

Parkinson Disease

- **Progressive loss of motor function beginning in 50's or 60's -- no recovery**
  - **degeneration of dopamine-releasing neurons**
    - **prevents excessive activity in motor centers**
    - **involuntary muscle contractions**
      - **pill-rolling motion, facial rigidity, slurred speech,**
      - **illegible handwriting, slow gait**
- **Treatment = drugs and physical therapy**
  - **dopamine precursor crosses brain barrier**
  - **MAO inhibitor slows neural degeneration**
  - **surgical technique to relieve tremors**