Nerve Signaling

Membrane Potential

Action potential

Synapse

Neurotransmitter

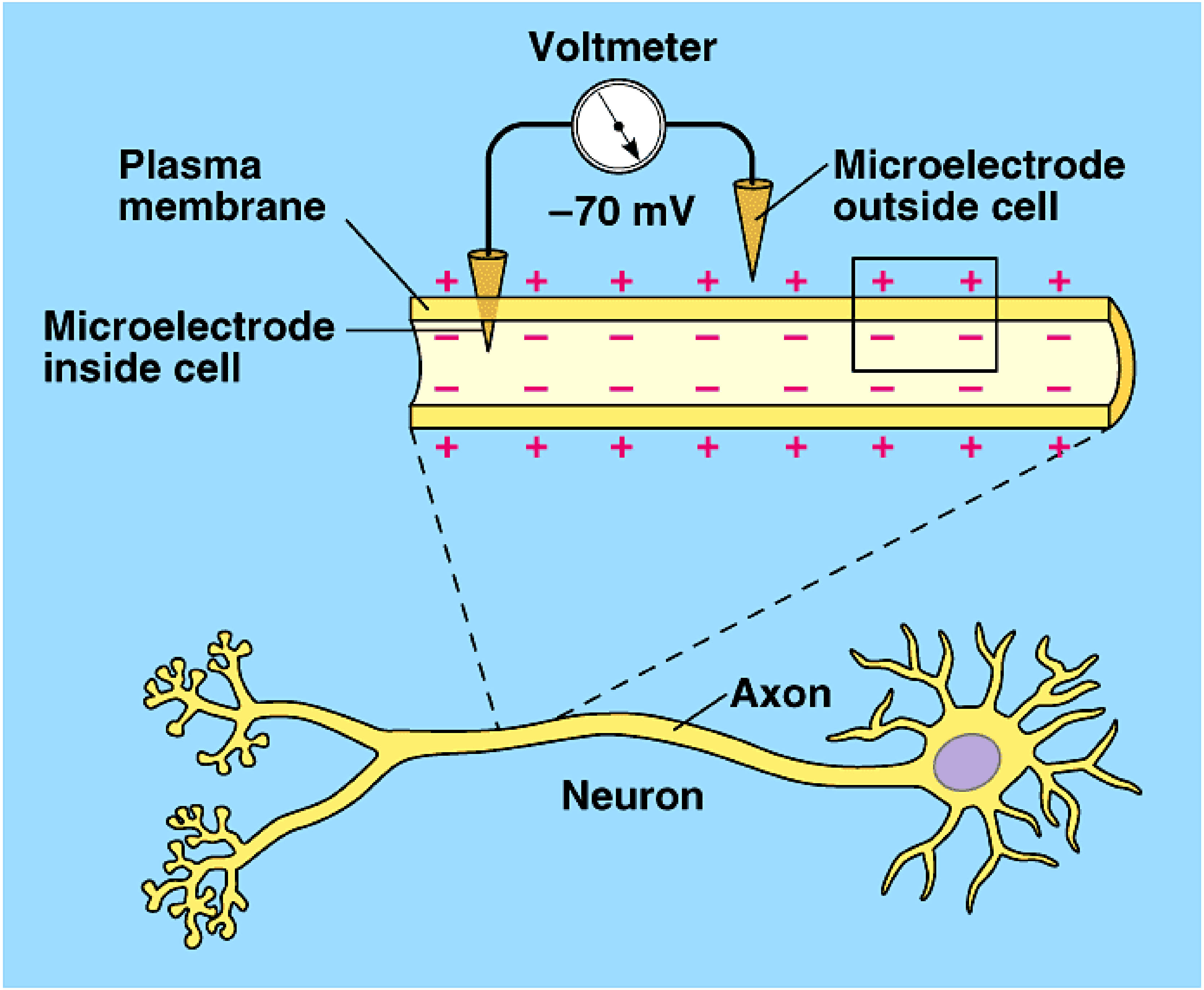
Chapter 48 page 1026-1038

Membrane Potential

- Voltage (V)
  - difference in electrical potential (charge separation)
  - difference in the amount of energy in charged ions between two points
- Membrane potential (V_m): voltage across a membrane
  - Outside of nerve cell: excess of cations (+)
  - Inside of nerve cell: excess anions (-)

Measuring membrane potential

- Voltmeter
- $V_m = V_{in} – V_{out}$
  - V_m: membrane potential
  - V_{in}: potential on inside of cell
  - V_{out}: potential on outside of cell
- By convention, V_{out} is defined as zero
- **Resting potential** (V_R): membrane potential of a neuron at rest (**–70mV**)


Voltmeter
Plasma membrane
–70 mV
Microelectrode outside cell
Microelectrode inside cell
Axon
Neuron

Membrane Potential

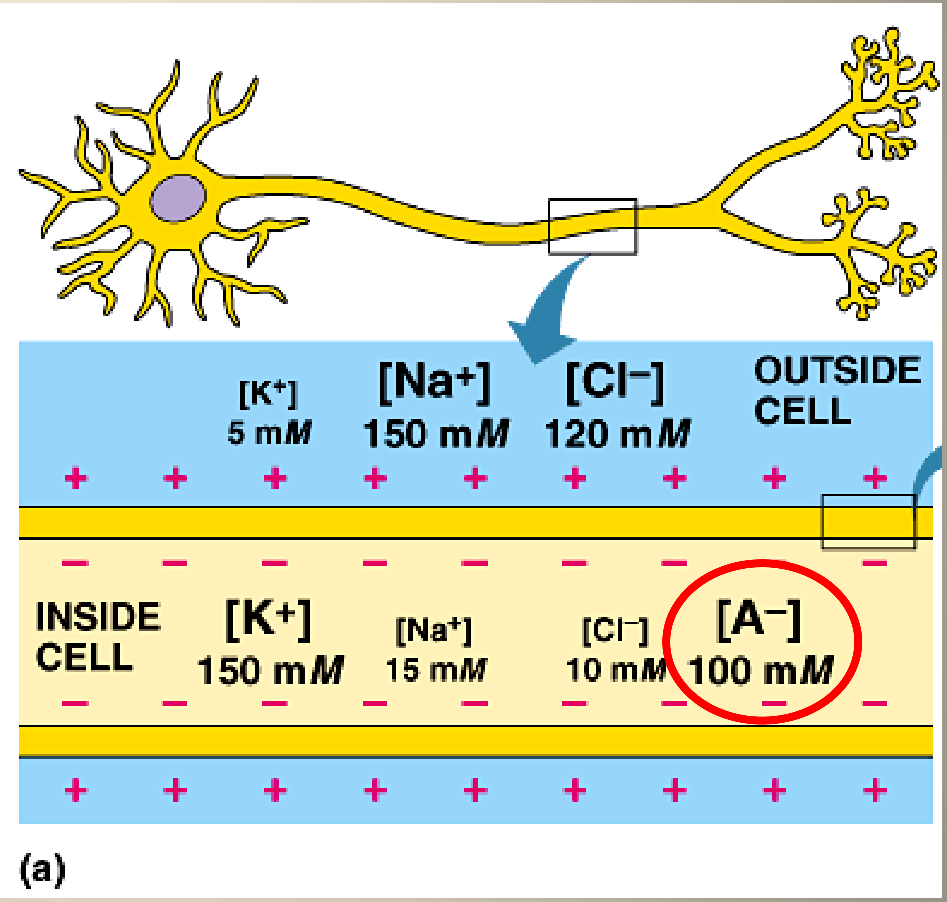
- All cells have a membrane potential
- Only a few cells can generate a large enough change in membrane potential
  - Neurons
  - Muscle cells

Maintenance of Resting Potential of Neurons

1. Ion distribution:
   - large pool of negatively charged molecules (e.g. proteins) inside the neuron
2. Membrane permeability:
   - Na+ and K+ leak channels
   - more permeable to K+ (efflux) than Na+ (influx)
3. Na+/K+ pump
   - moves 3 Na+ out for every 2 K+ in

1. Ion Distribution

- Large internal pool of negatively charged molecules: **proteins**, amino acids, sulfate, phosphate etc.
- large molecules that cannot cross membrane



2. Membrane Permeability

- Charged ions cannot directly diffuse across cell membrane (lipid, nonpolar)
- Transmembrane proteins (leak channels) regulate movement of ions
  - Facilitated diffusion (passive transport)
  - Does not determine direction or rate of flow
  - More K+ leak channels than Na+ leak channels

Equilibrium potential (E_x)

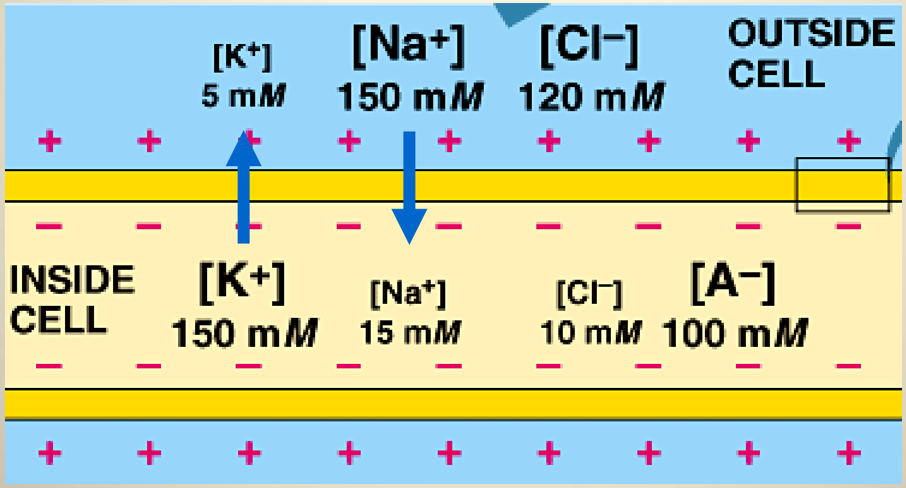
- Potential at which there is no net movement of an ion (at equilibrium)
- Due to passive movement of ions
- Dependent on electrochemical gradient

Electrochemical Gradient

- Chemical gradient:
  - Concentration gradient
  - Chemical force
  - movement from high to low ion concentration
- Electrical gradient:
  - Ion gradient (relative electrical charge)
  - electrical force
  - movement of positive ion to area of negative ion concentration and vice versa

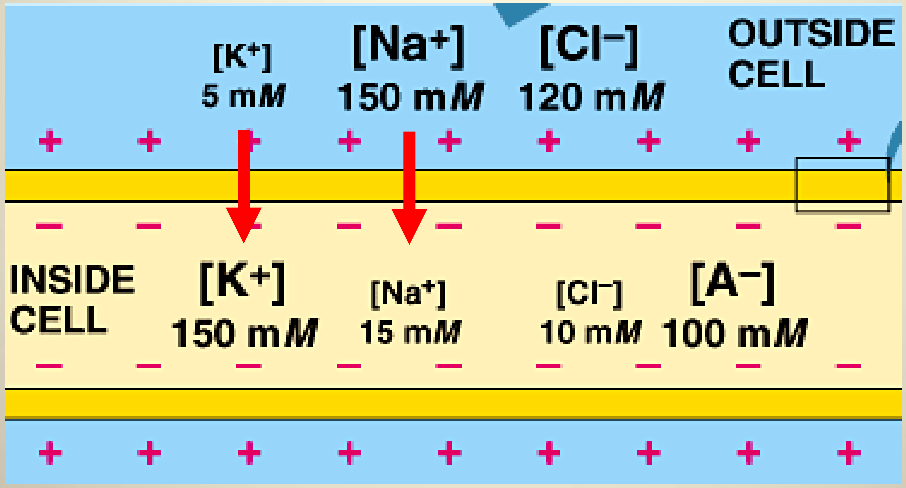
Chemical Gradient

- K+ channels: passive movement out of cell
- Na+ channels: passive movement into cell



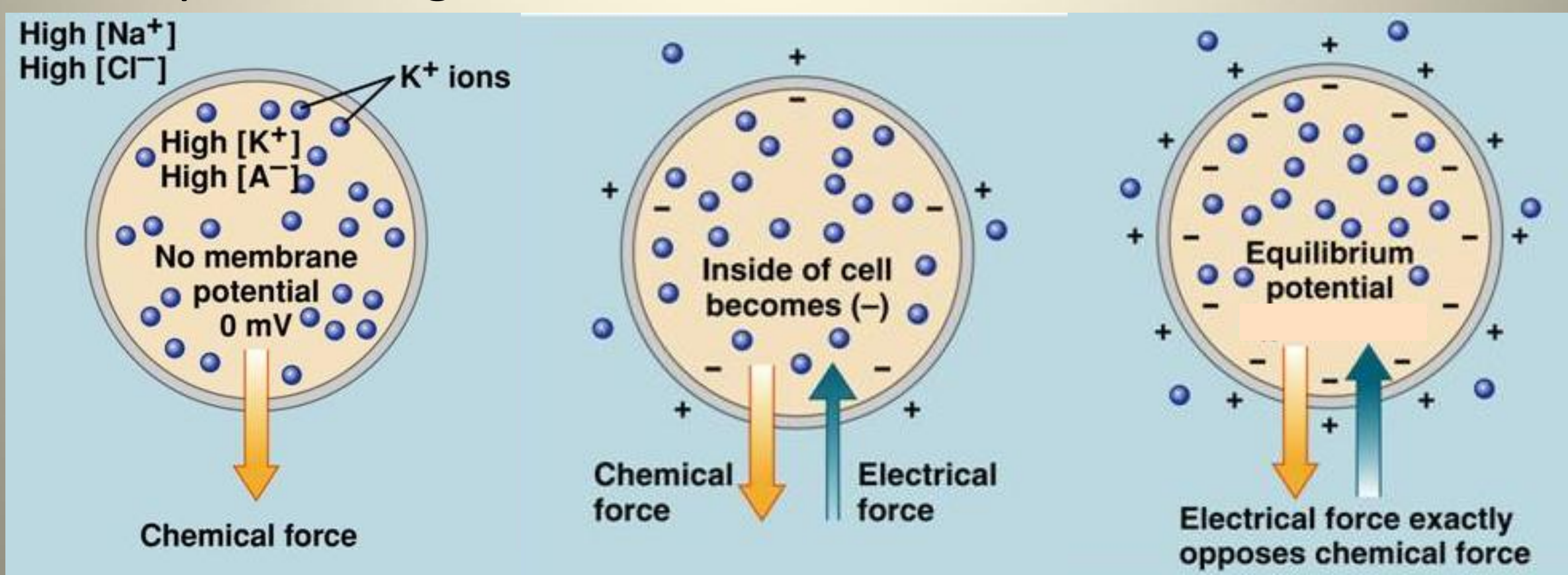
Electrical Gradient

- K+ channels: passive movement into cell
- Na+ channels: passive movement into cell



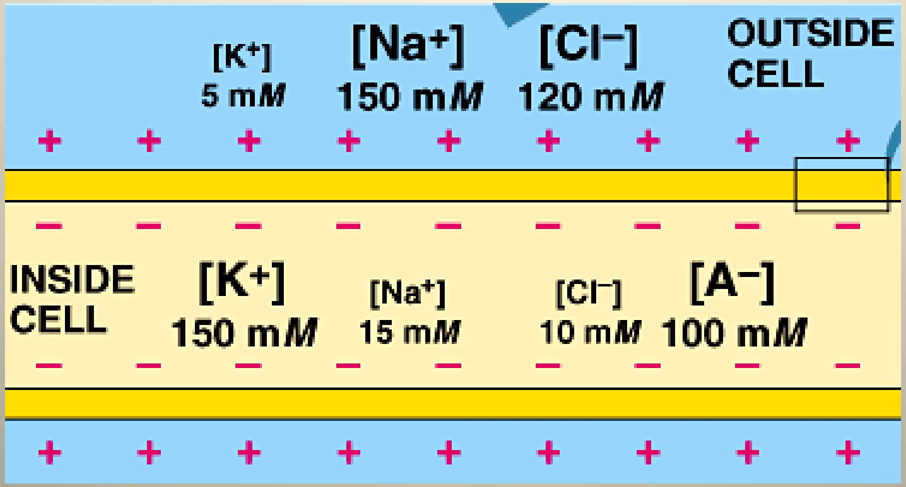
Establishing Equilibrium with K+

- Chemical force: K+ diffusion out of cell
- Inside cell becomes more negative
- Electrical force "pull" K+ back into cell
- Equilibrium when chemical and electrical forces are:
  - in opposite directions
  - equal in magnitude



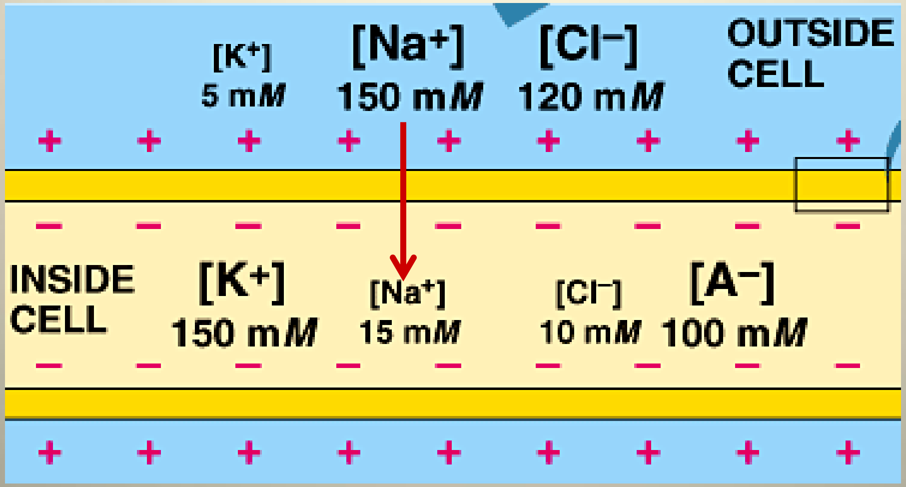
Establishing Equilibrium with K+

- If only permeable to K+:
  - EK = –85 mV
  - more negative than resting potential of –70mV
- Thus, must involve movement of some cations into the cell



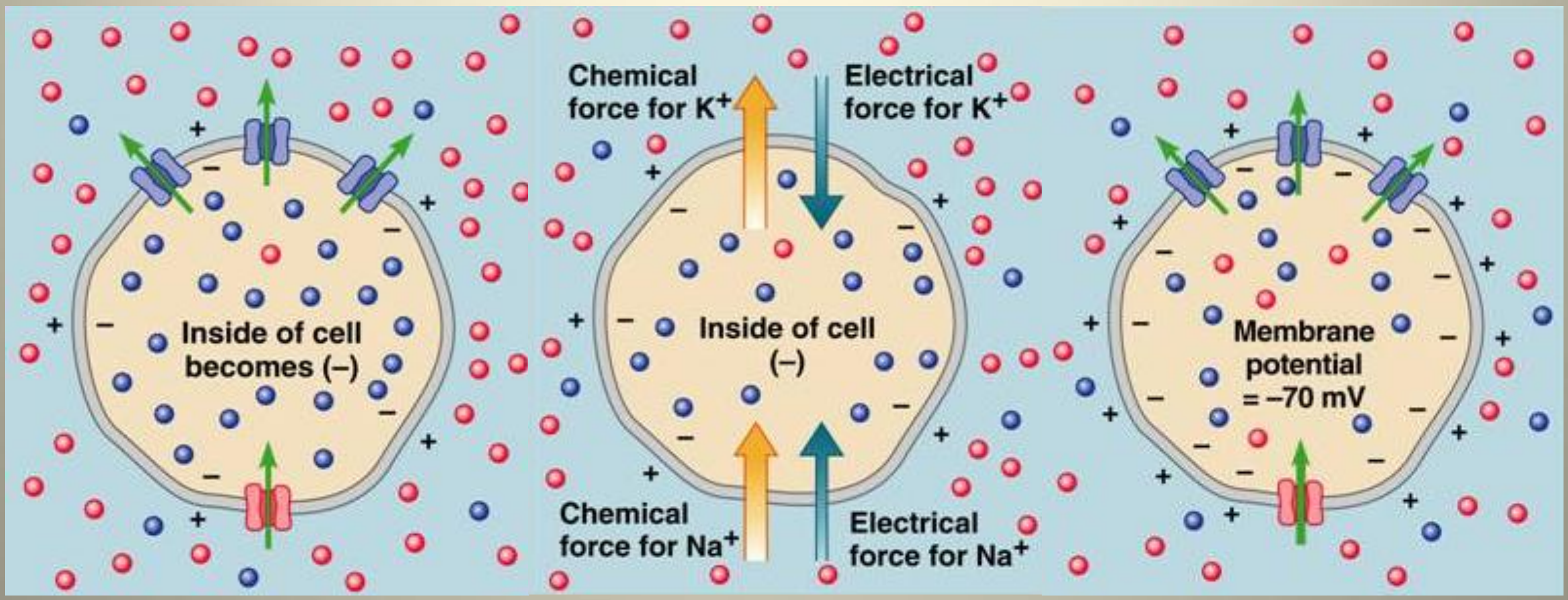
Establishing Equilibrium with Na+

- Na+ permeability
  - Na+ chemical force: influx
  - Na+ electrical force: influx



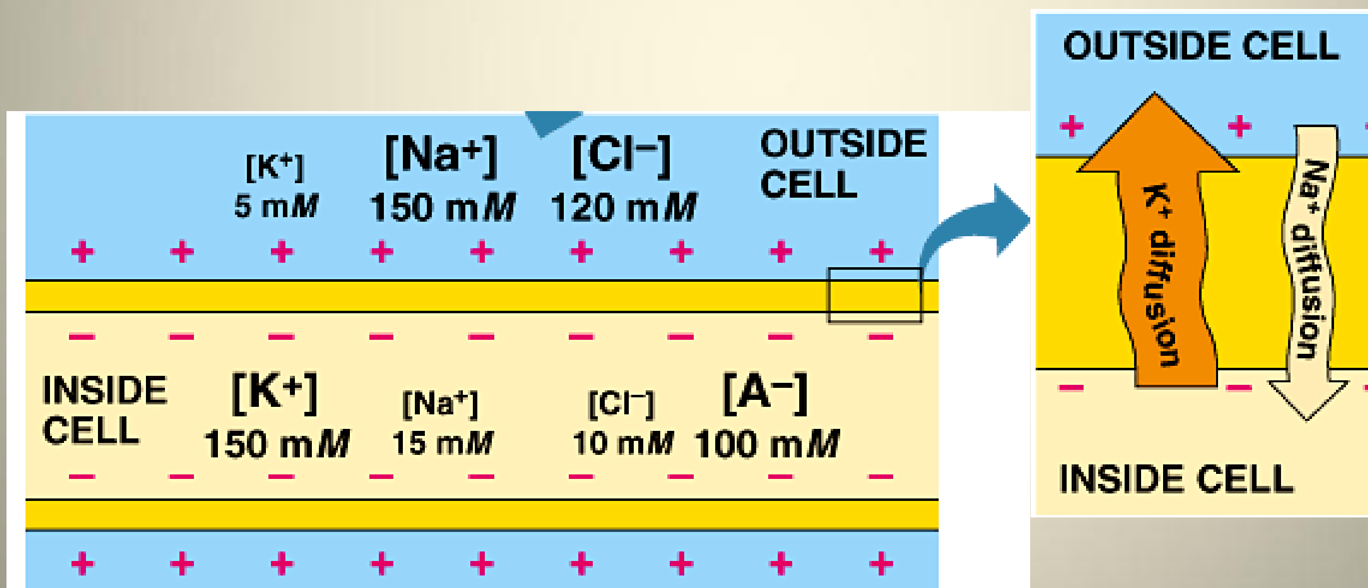
Establishing Equilibrium with K+ and Na+

- Resting potential maintained with movement of both K+ and Na+
- But to maintain –70mV, neuron has more K+ efflux than Na+ influx



Establishing Equilibrium with K+ and Na+

- Neuron is more permeable to K+ than Na+
- More opened K+ channels than Na+ channels

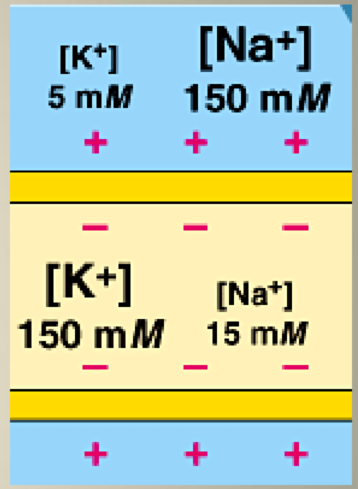


Animation: Resting Membrane Potential

- http://www.sumanasinc.com/webcontent/animations/content/electricalsignaling.html

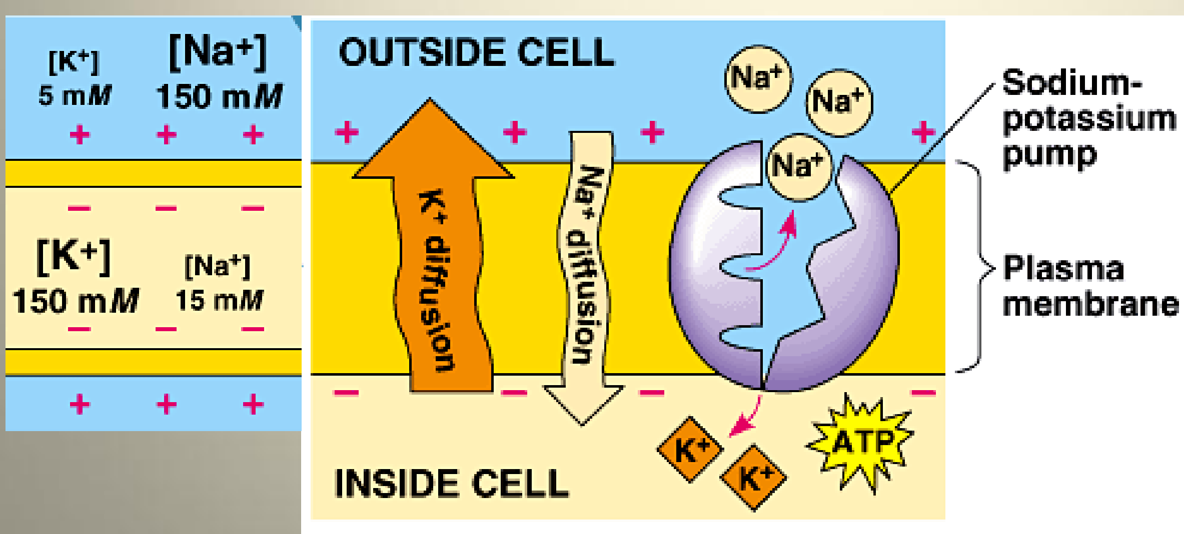
Establishing Steady State

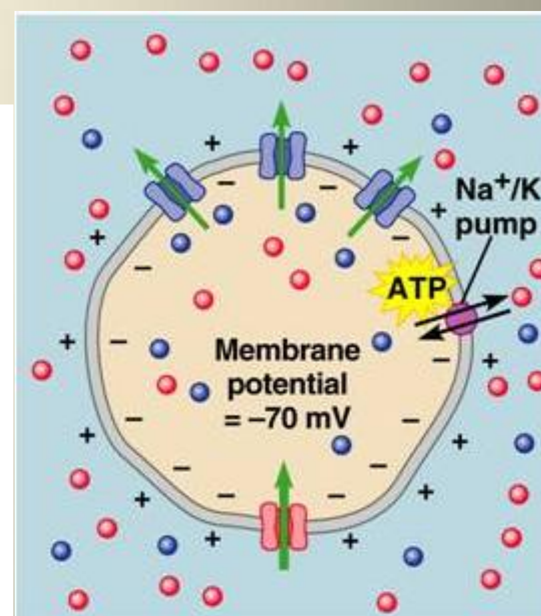
- Overtime if cell left unchecked:
  - influx of Na+ makes cell less negative
  - Drives steady efflux of K+
  - Concentration gradient dissipates
- This doesn’t happen. If it does, you’re dead.
  - Want to keep the gradient and avoid equilibrium

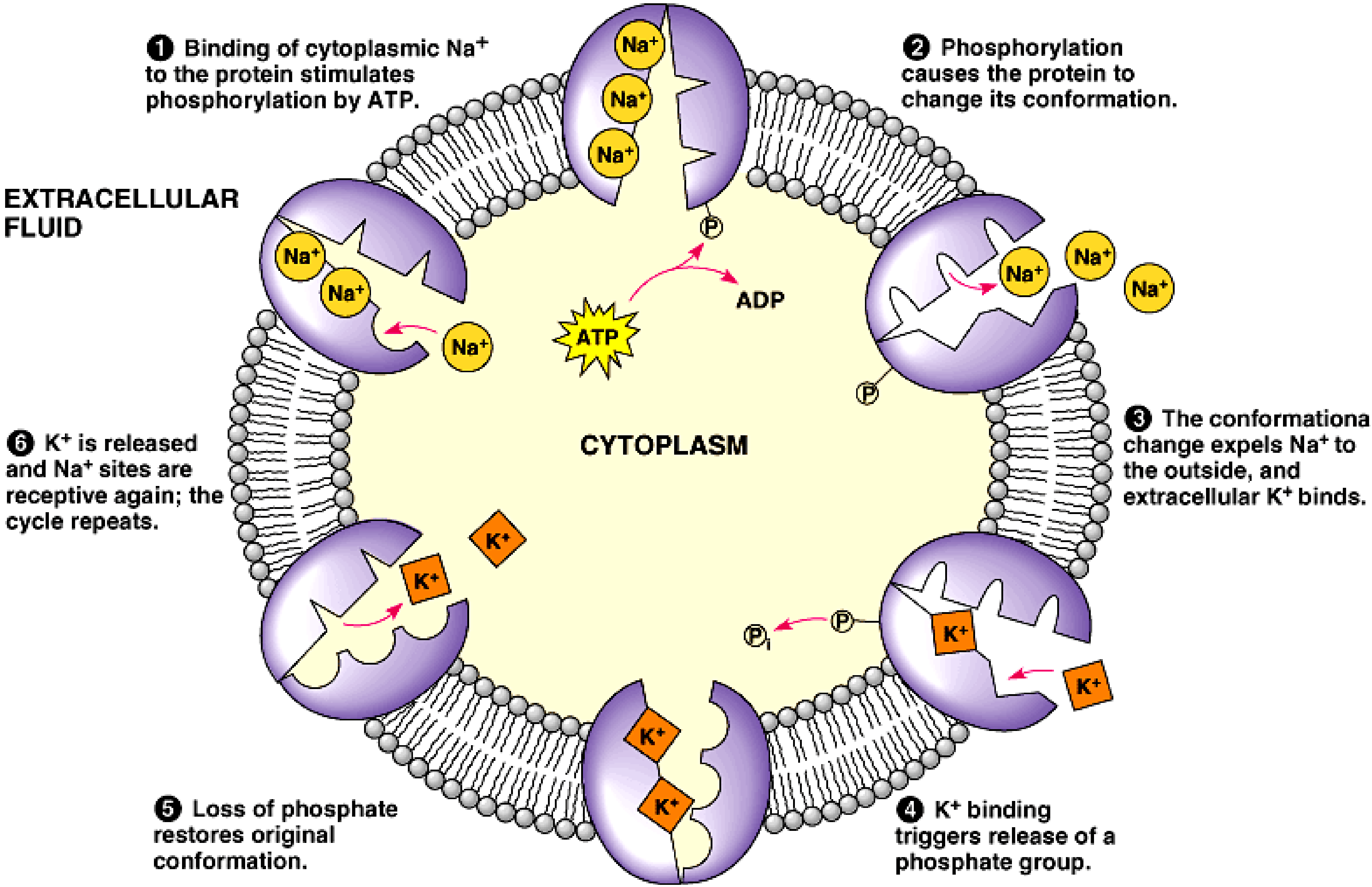


3. Na^+/K^+ pump

- use ATP to drive active transport
- 3 Na+ out of cell, 2 K+ into cell
- maintain ionic gradients



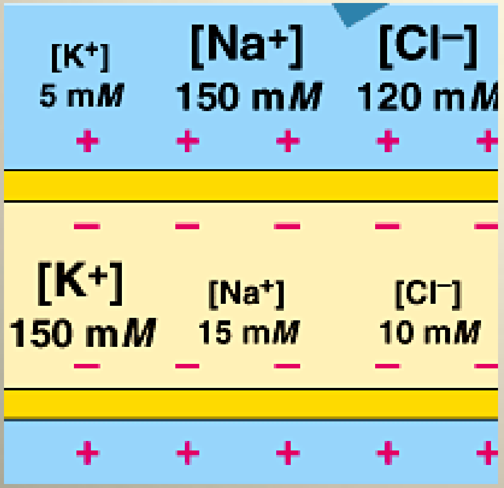


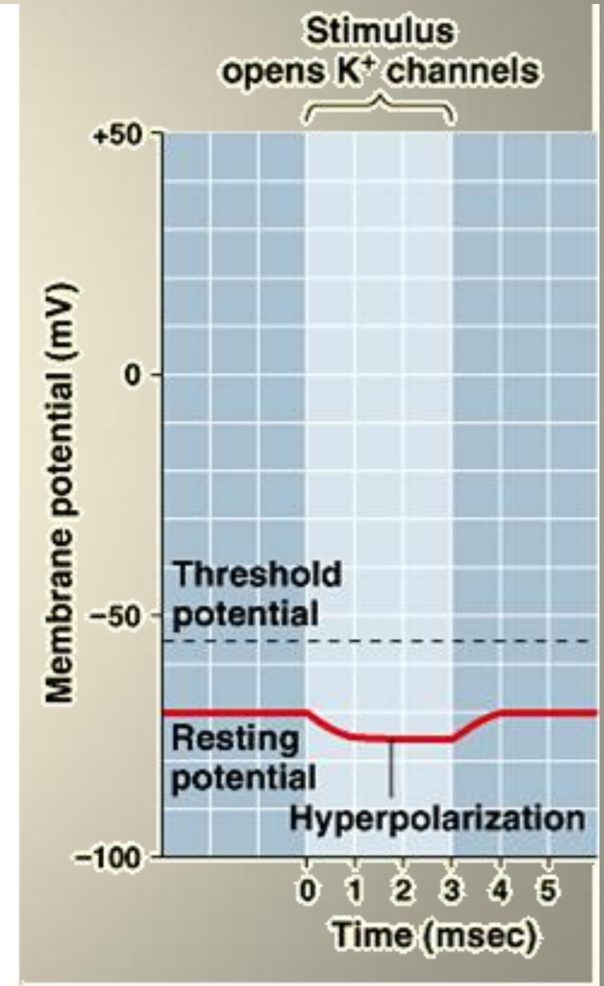


Animation: http://highered.mcgraw-hill.com/olc/dl/120107/bio_a.swf

Polarization

- **Hyperpolarization**: an increase in voltage across the membrane
  - More negative
  - E.g. K+ outflow, Cl- inflow

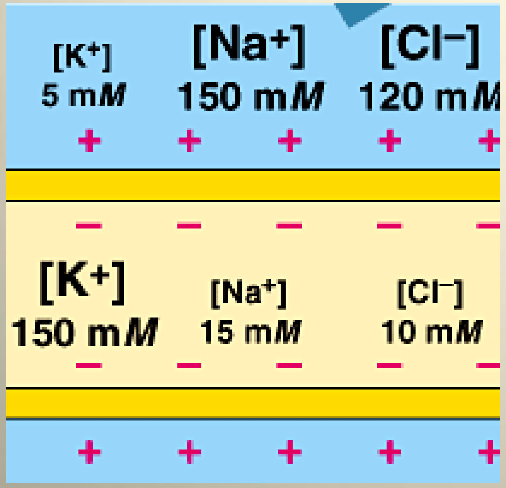


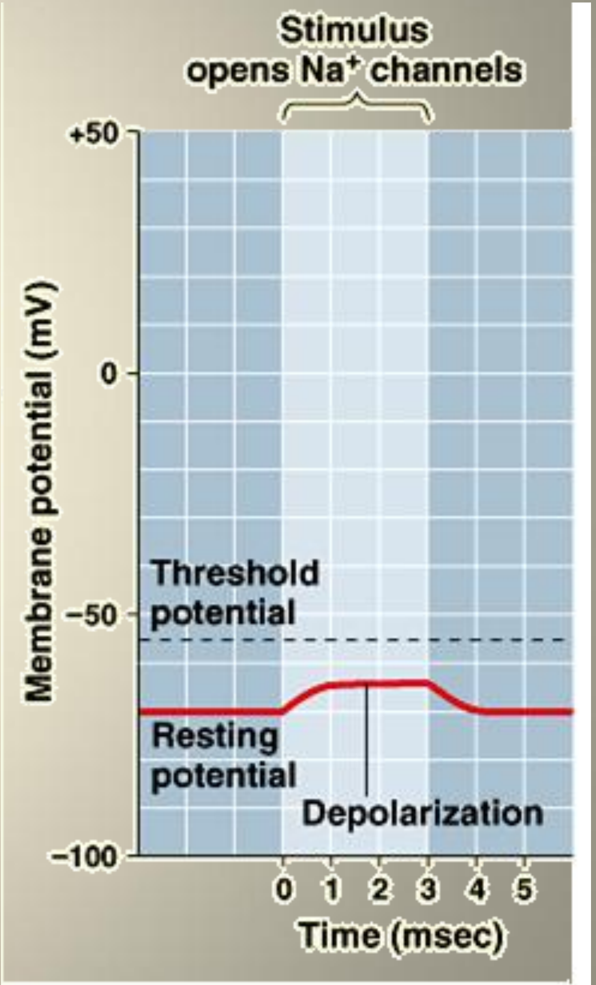


(a) Graded potential: hyperpolarization

Polarization

- **Depolarization**: reduction in voltage across the membrane
  - Less negative, more positive
  - E.g. increased Na+ inflow

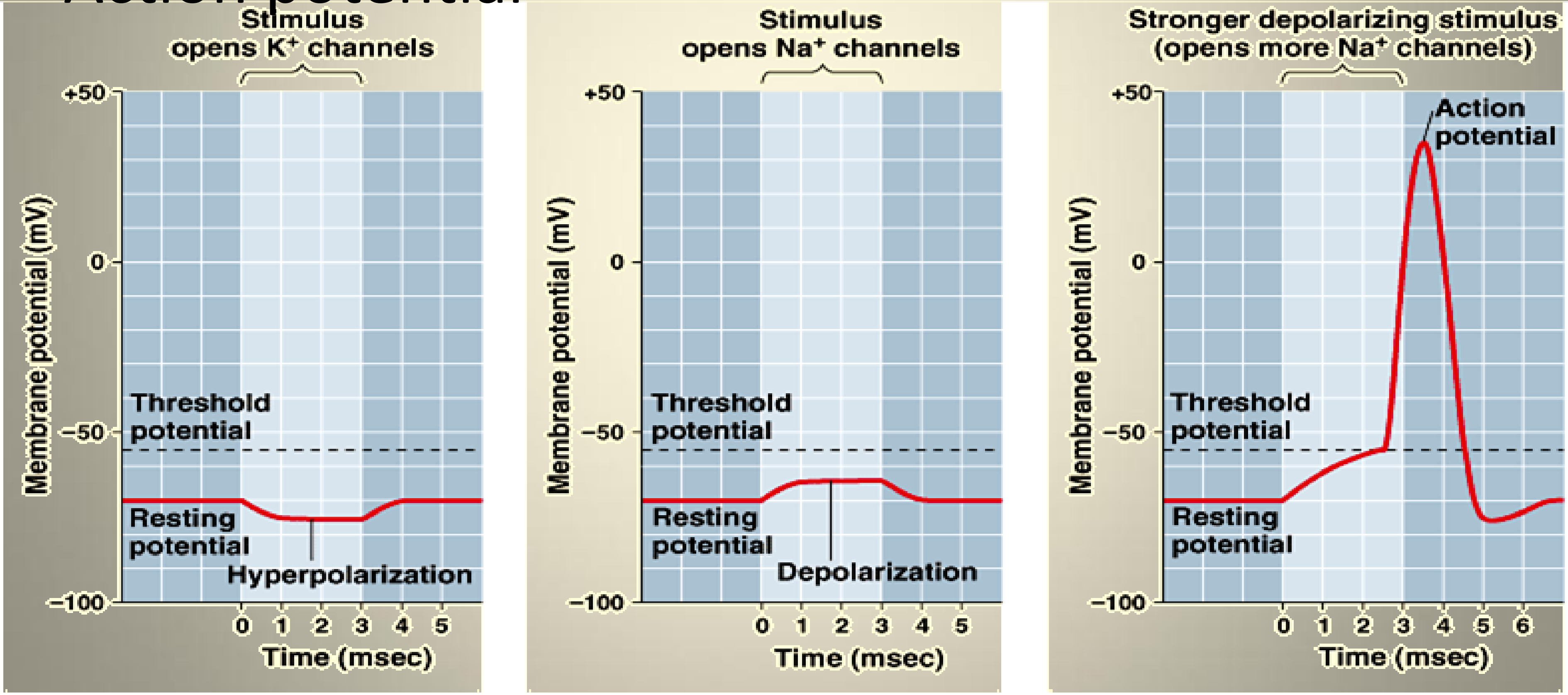




(b) Graded potential: depolarization

Types of Potentials

- Graded potential
- Threshold potential
- Action potential



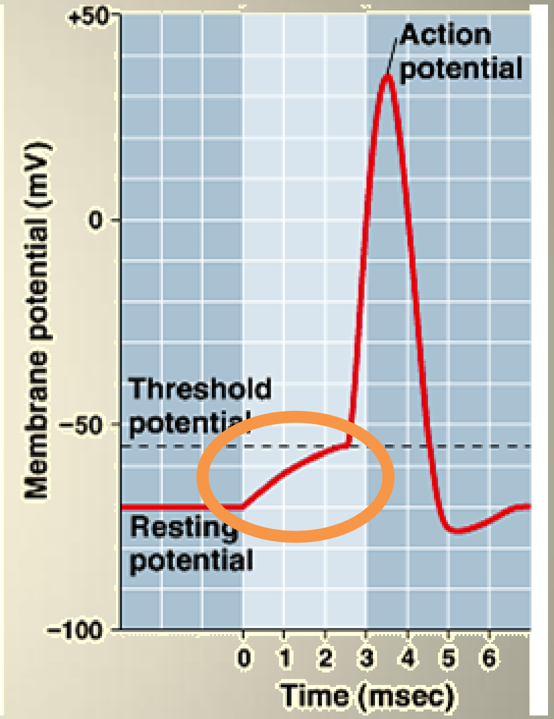
(a) Graded potential: hyperpolarization

(b) Graded potential: depolarization

(c) Action potential

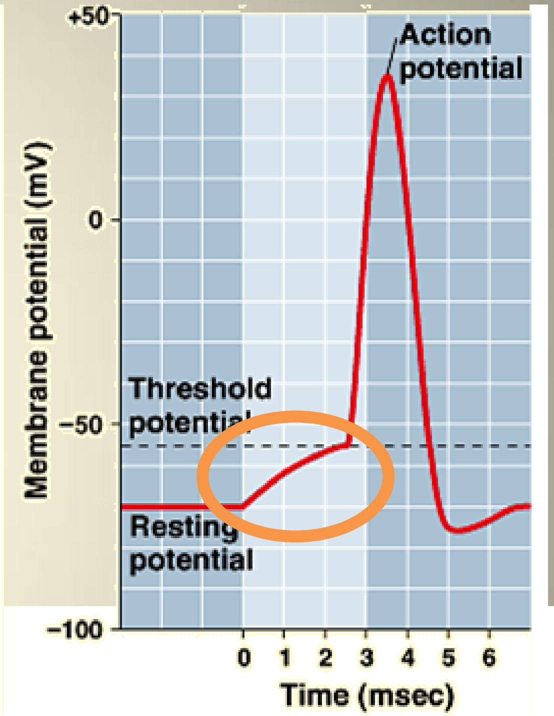
Graded Potential

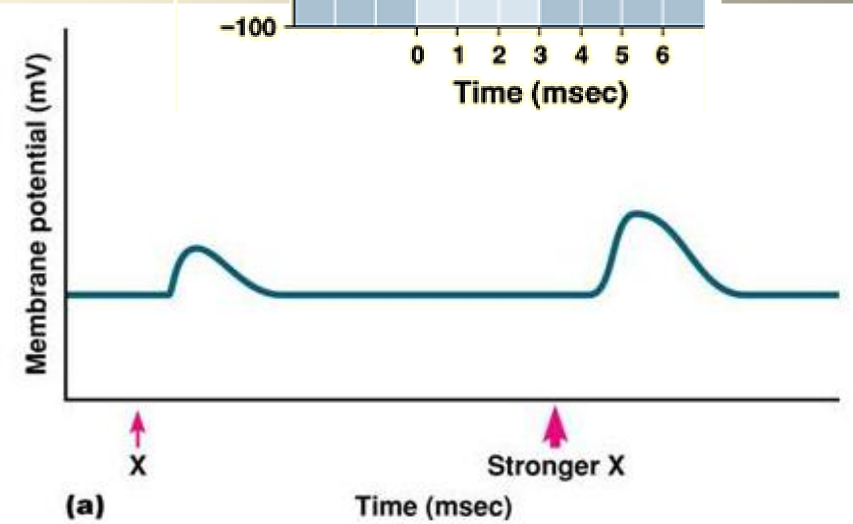
- All membrane potentials that is below threshold
- Magnitude of membrane potential affected by:
  - Strength of stimulus
  - Distance that stimulus travels



Graded Potential: Stimulus Strength

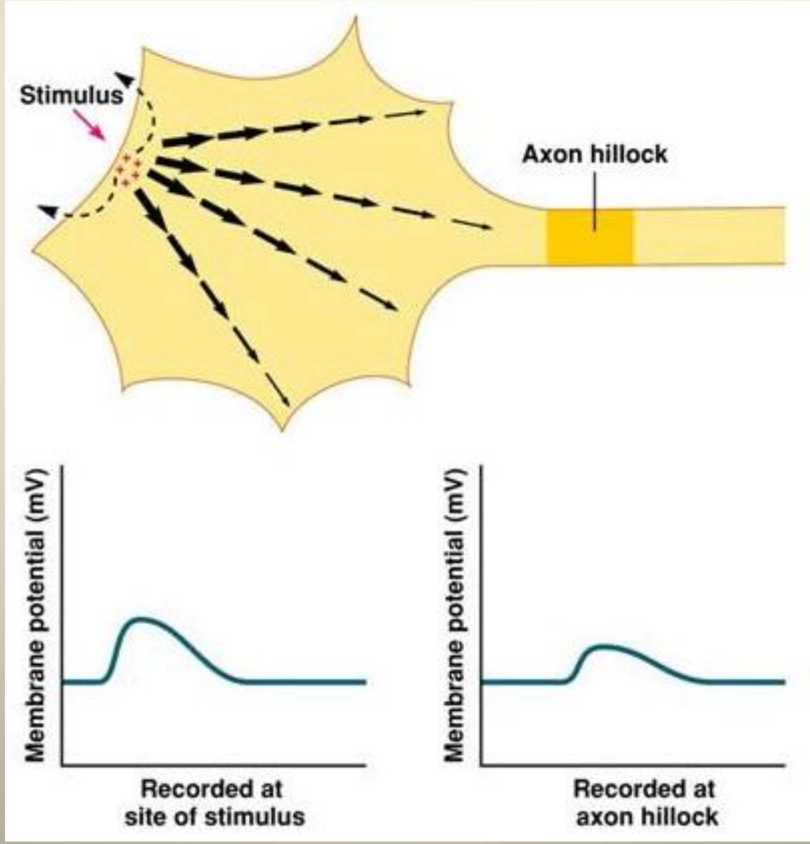
- **Magnitude** of polarization depends on the **strength of the stimulus**
- Example:
  - larger stimulus opens more channels
  - increases cells permeability for that to the ion
  - producing a larger change in membrane potential





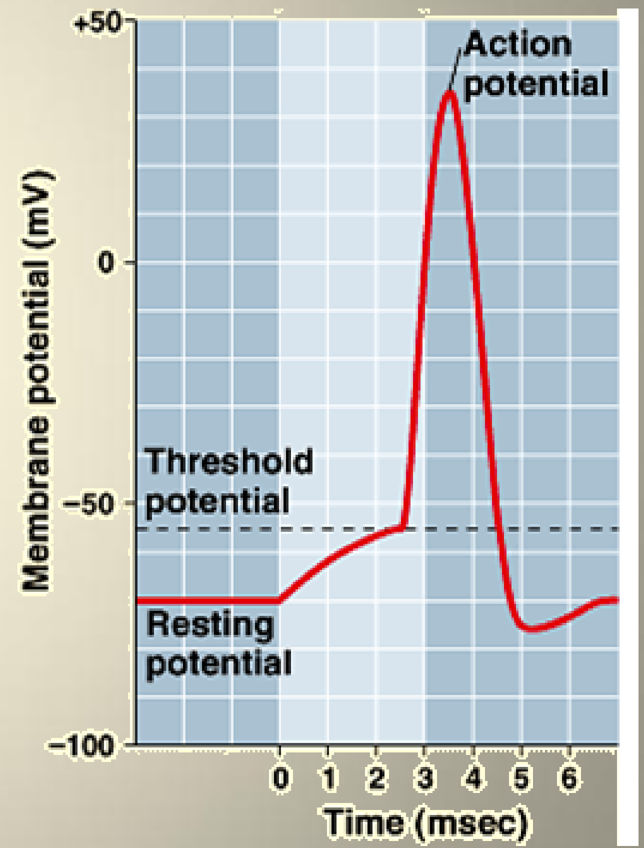
Graded Potential: Stimulus Distance

- **Decremental**: magnitude decays/degenerates as it spreads



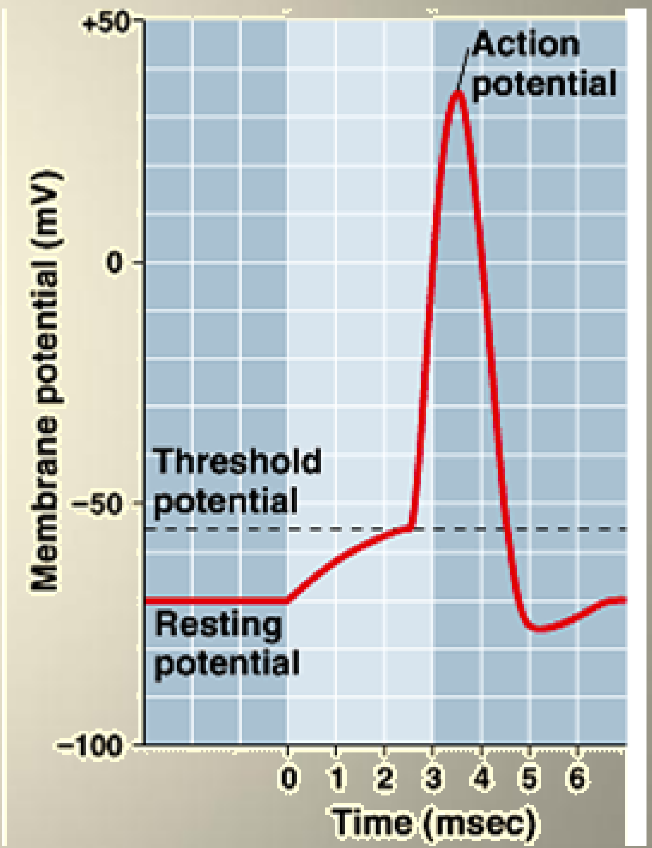
Threshold Potential

- The potential at which an action potential occurs
- Around –50 to –55 mV
- After threshold is reached:
  - Stimulus intensity plays no role in the magnitude
  - No longer graded potential but an action potential

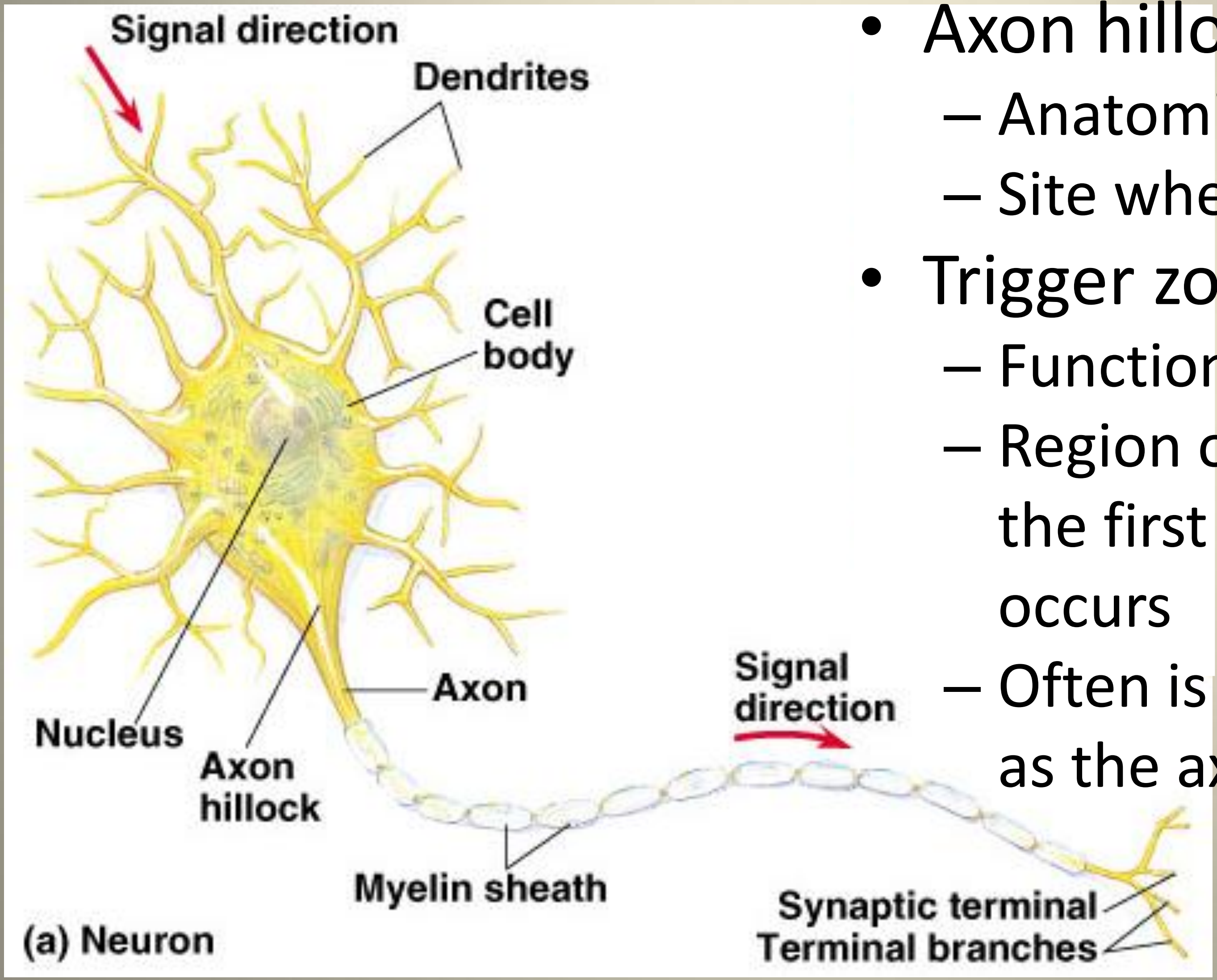


Action Potential

- A large depolarization followed by repolarizing back to resting
- Reaches the same magnitude each time (+35 mV)
- Only generated in the axon

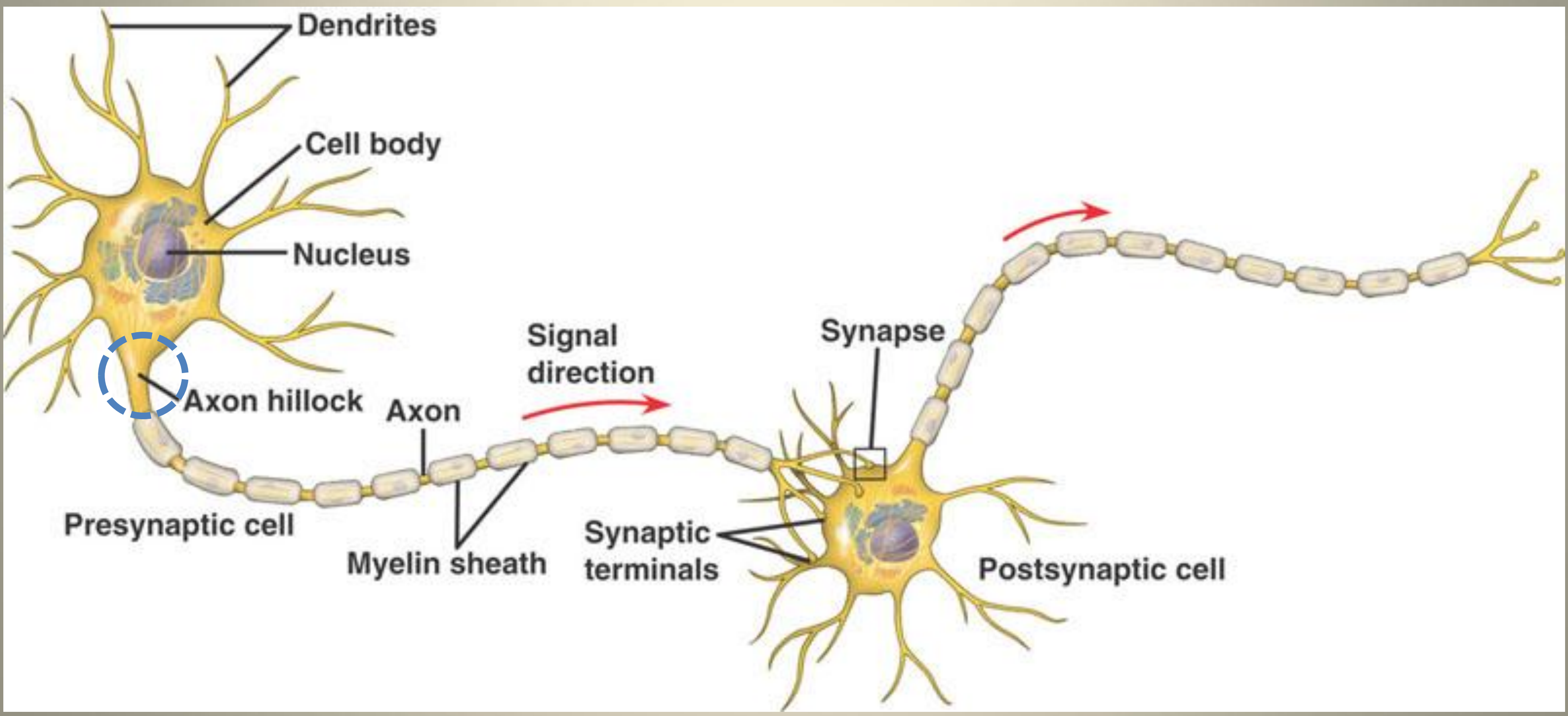


Action Potential



- Axon hillock:
  - Anatomical description
  - Site where axon begins
- Trigger zone:
  - Functional description
  - Region on axon in which the first action potential occurs
  - Often is the same place as the axon hillock

Nerve Signaling



Types of Channels

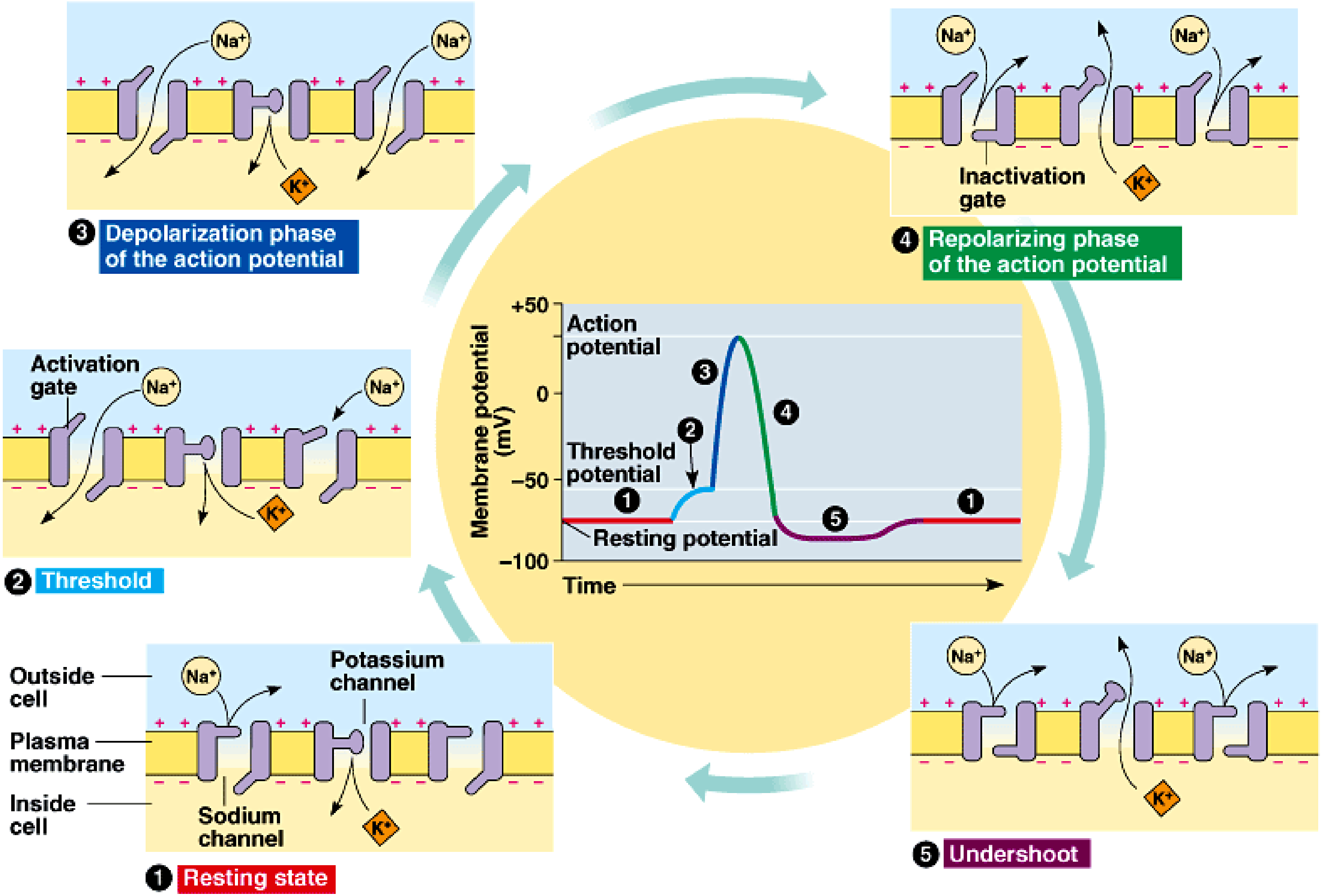
Channels	Description	Example
Ungated, Leak	open at all times	Na+ and K+ channels involved maintaining resting potential
Voltage-gated	open or close in response to changes in membrane potential	Na+ and K+ channels involved in an action potential along axons
Chemically-gated	open or close in response to chemicals	Receptors on dendrites open when neurotransmitters bind

Voltage-Gated Channels in Action Potential

Channel	Gate	Resting position	Depolarization stimulus	Speed
K+	K+	Closed	Opens	Slow
Na+	activation	Closed	Opens	Rapid
Na+	inactivation	Open	Closes	Slow

Phases of action potential

- Rapid depolarization
- Rapid repolarization
- Undershoot
- Return to resting



Depolarization phase of the action potential
Repolarizing phase of the action potential
Inactivation gate
Activation gate
Threshold
Undershoot
Resting state
Outside cell
Plasma membrane
Inside cell
Potassium channel
Sodium channel
Na+
K+
Membrane potential (mV)
+50
0
−50
−100
Action potential
Threshold potential
Resting potential
Time

Step 1: Resting State

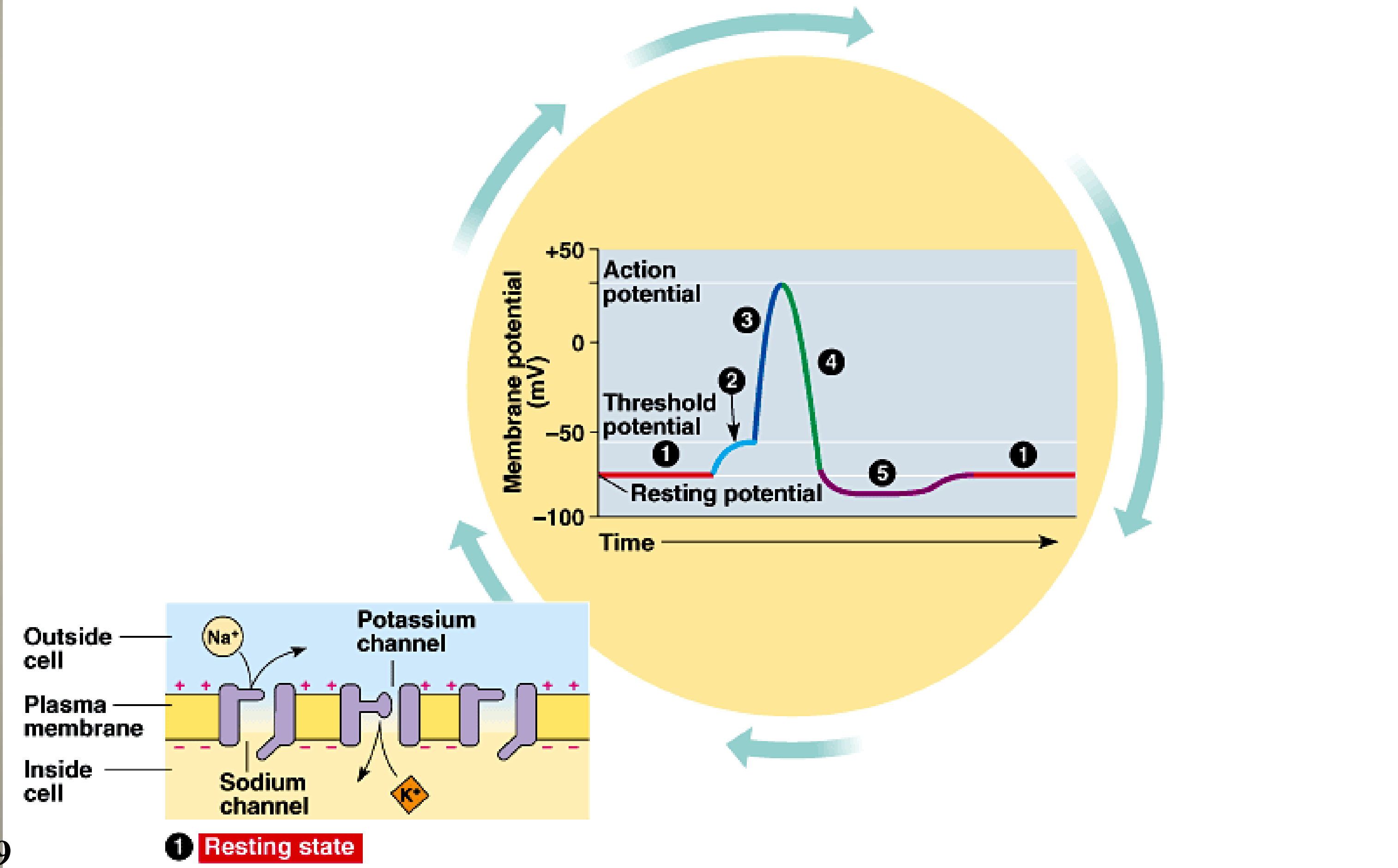


Fig. 48.9

Step 2: Threshold

- Depolarization stimulus opens some Na gates
- Results in a graded potential that reaches threshold

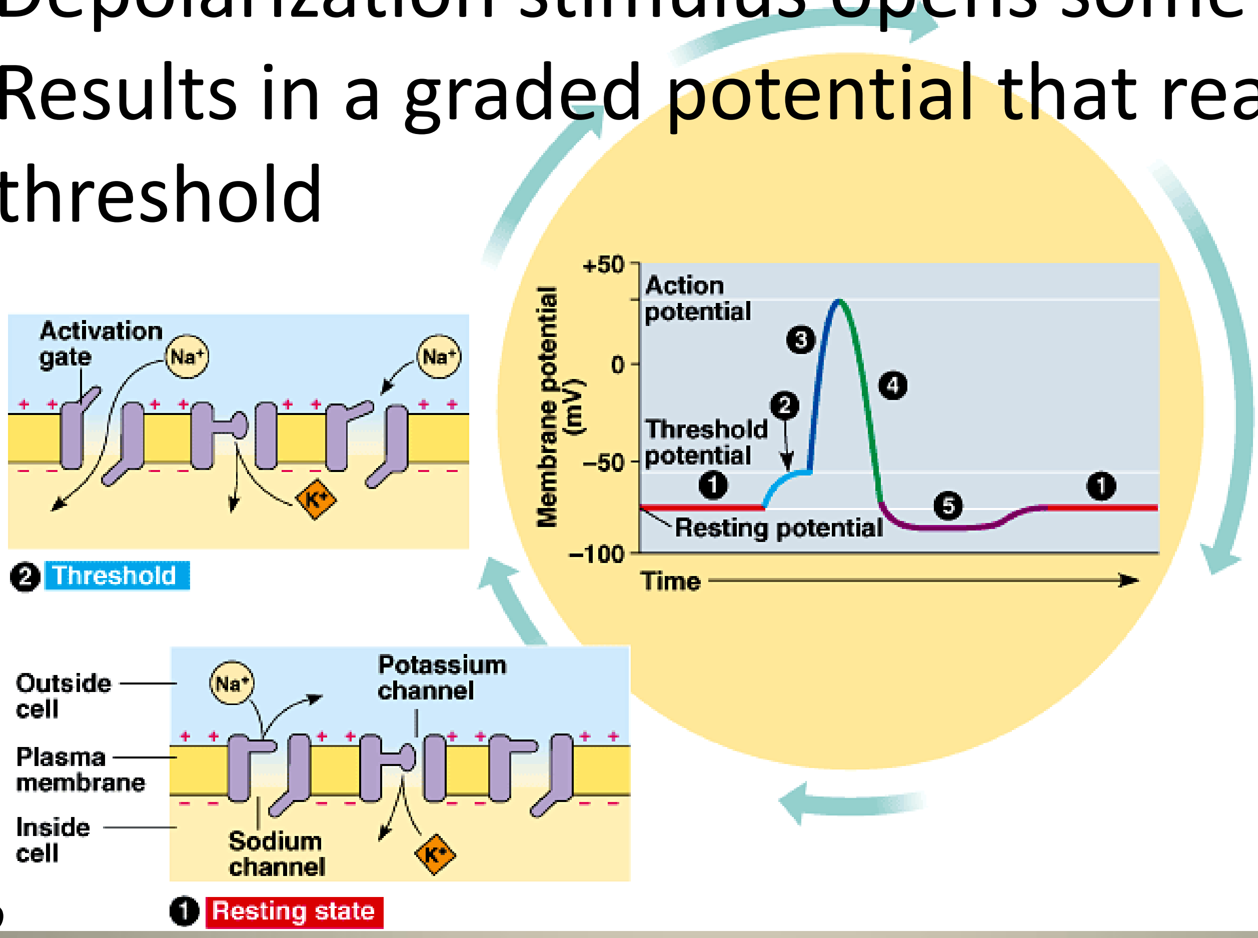
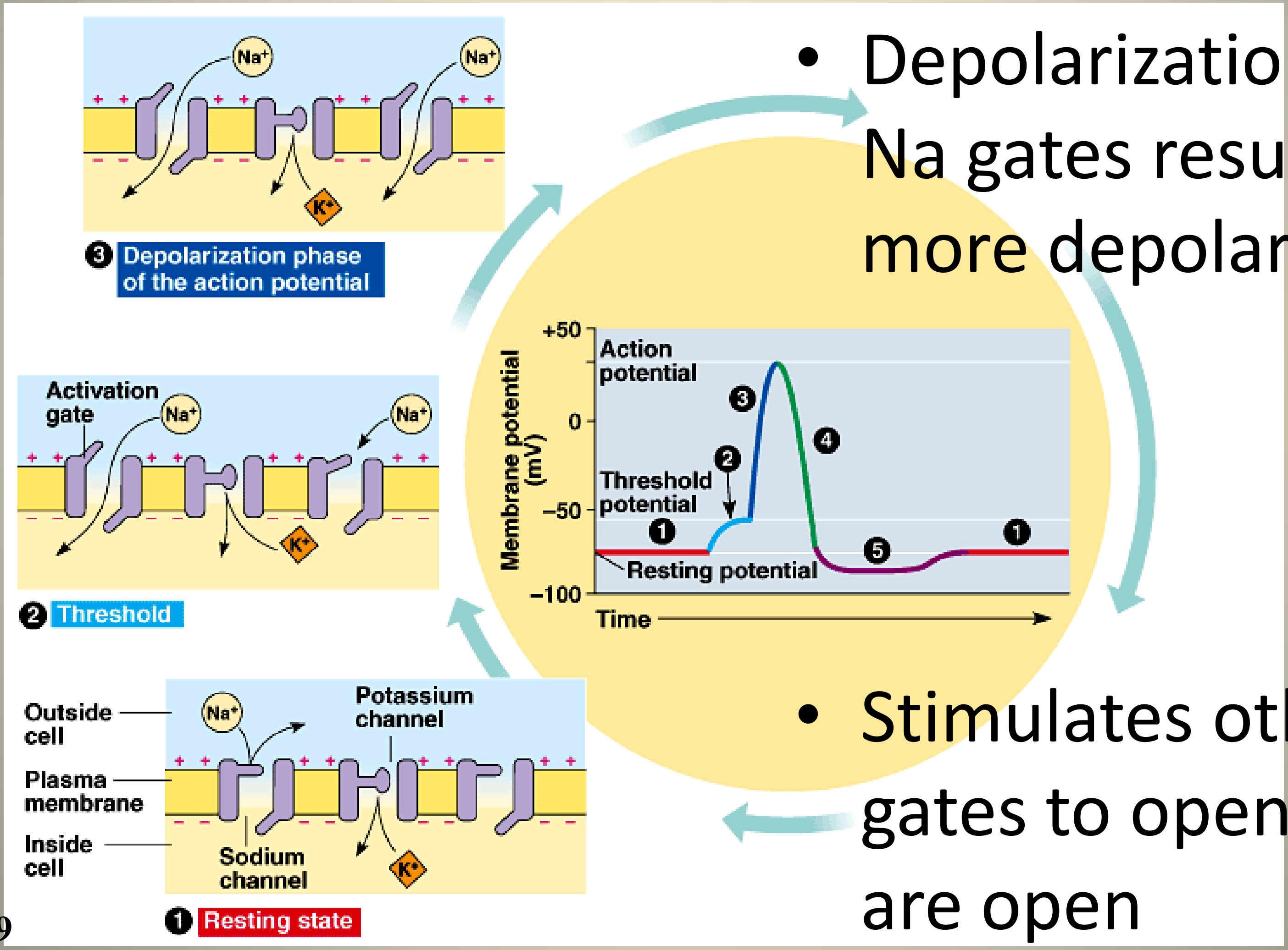


Fig. 48.9

Step 3. Depolarization Phase



- Depolarization opens Na gates resulting in more depolarization
- Stimulates other Na gates to open until all are open

Fig. 48.9

Step 3. Depolarization Phase

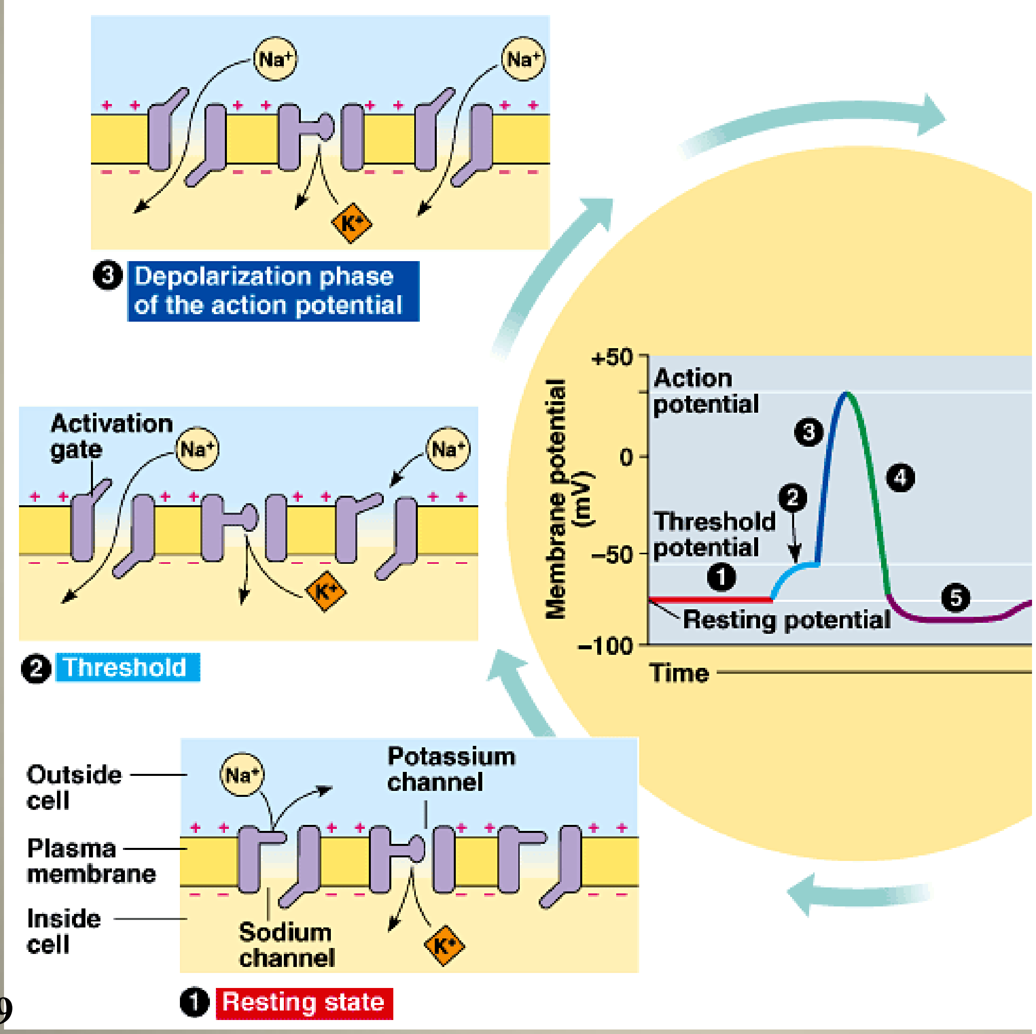


Fig. 48.9

- An example of positive feedback
- Depolarization to threshold potential triggers a larger depolarization to action potential

Step 4. Repolarizing Phase

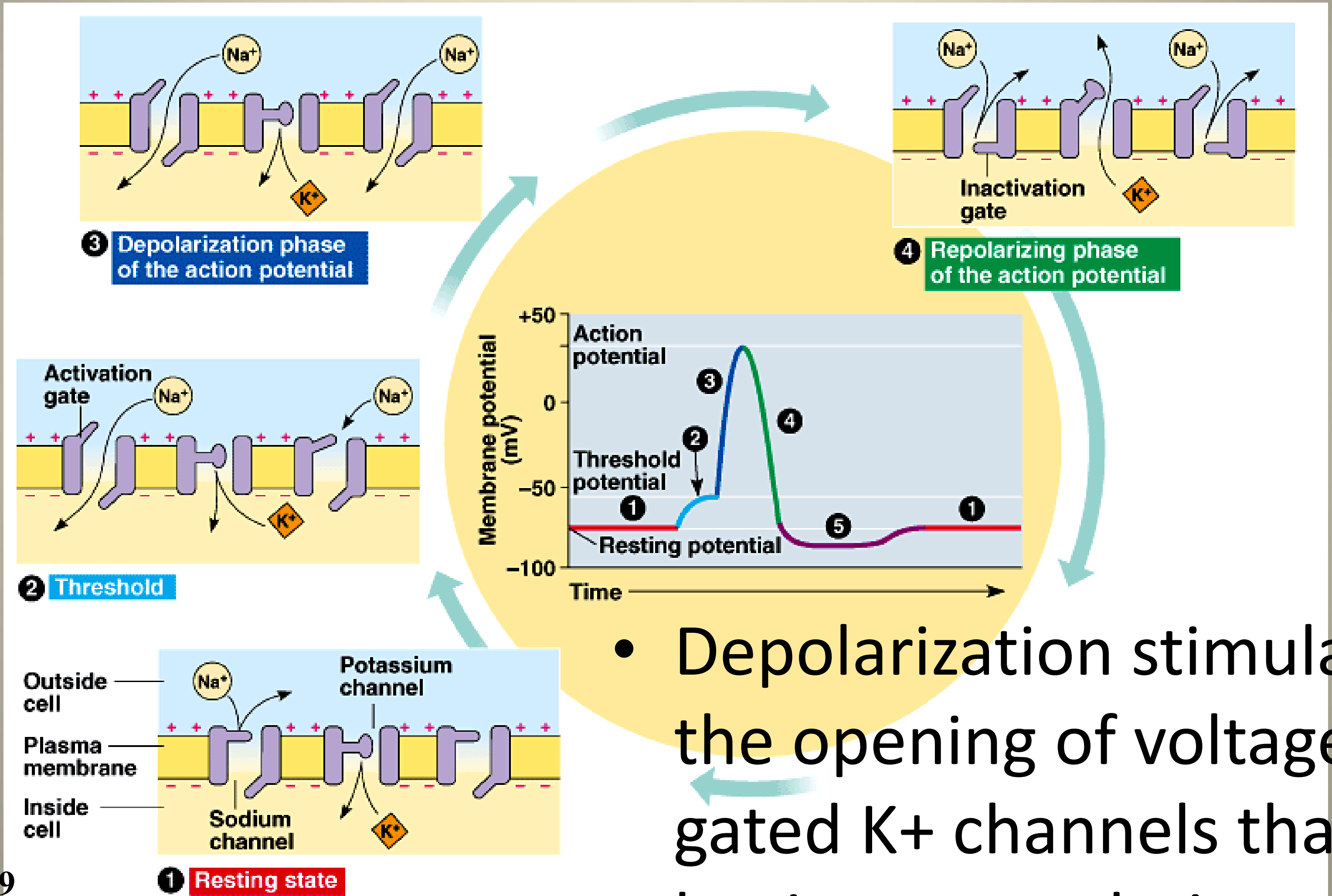


Fig. 48.9

- Depolarization stimulates the opening of voltage-gated K+ channels that begins to repolarize cell

Step 5. Undershoot

- Slow closing K+ gates allows too many K+ out of cell resulting in hyperpolarization
- Re-establish resting potential with the Na+ and K+ leak channels

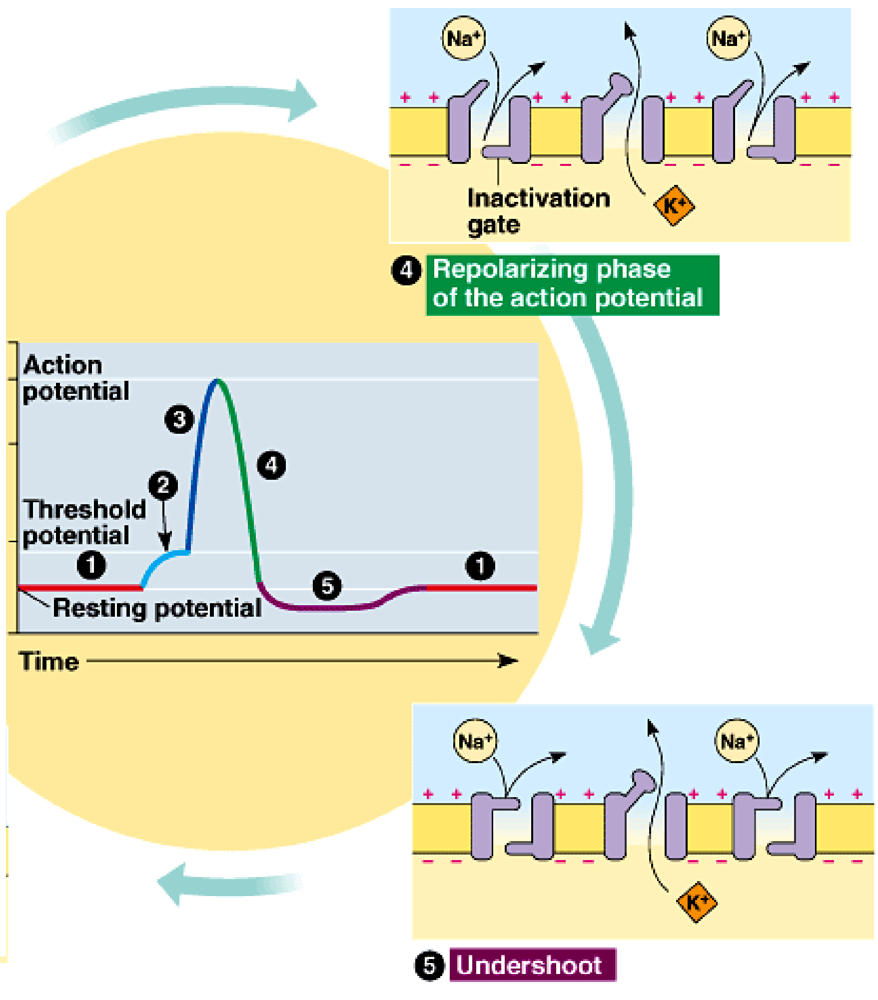
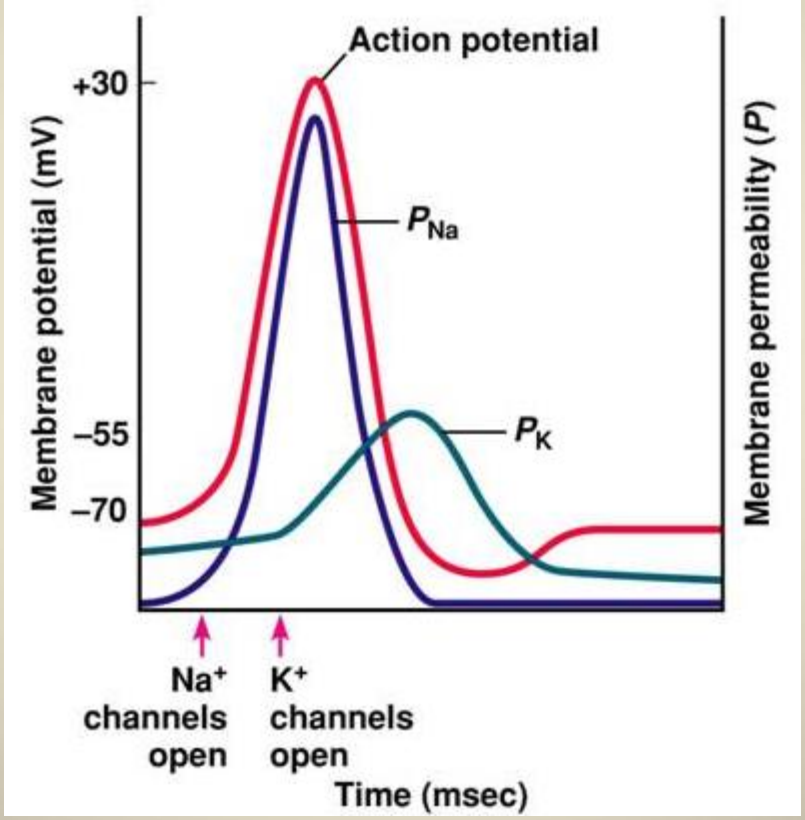


Fig. 48.9

Permeability of ions during an action potential



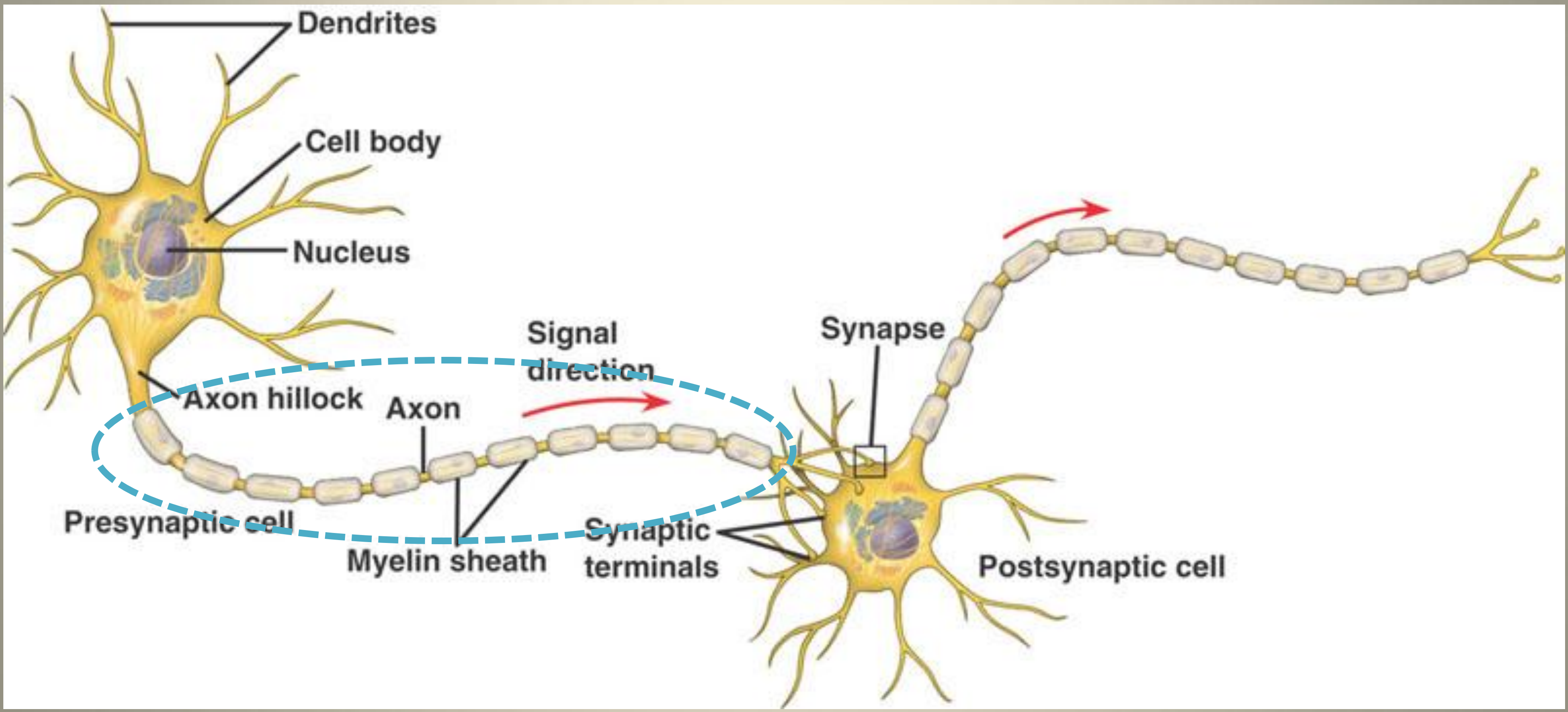
Mechanism of action potential

Phases	K+ gate (slow)	Na+ activation Gate (fast)	Na+ inactivation Gate (slow)	Membrane potential
Resting	Closed	Closed	Open	-70 mV
Threshold	Closed	Some open	Open	-50 to –55 mV
Depolarization	Opening slowly	All open	Closing slowly	+35 mV
Repolarization	All open	Open	All Closed	-70 mV
Undershoot	Closing slowly	Closed	Closed	-75 mV

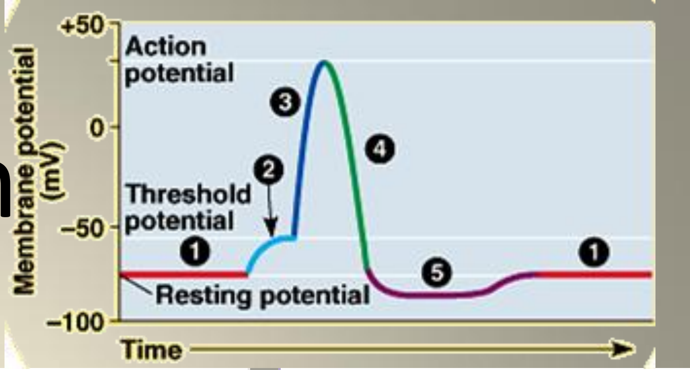
Animation: Action Potential

- http://highered.mcgraw-hill.com/olc/dl/120107/anim0013.swf
- http://bcs.whfreeman.com/thelifewire/content/chp44/4402s.swf
- http://www.psych.ualberta.ca/~ITL/ap/ap.swf
- http://outreach.mcb.harvard.edu/animations/actionpotential.swf
- http://www.sumanasinc.com/webcontent/animations/content/actionpotential.html
- http://www.sumanasinc.com/webcontent/animations/content/action_potential.html
- http://highered.mcgraw-hill.com/olc/dl/120107/bio_d.swf (unmyelinated axon)

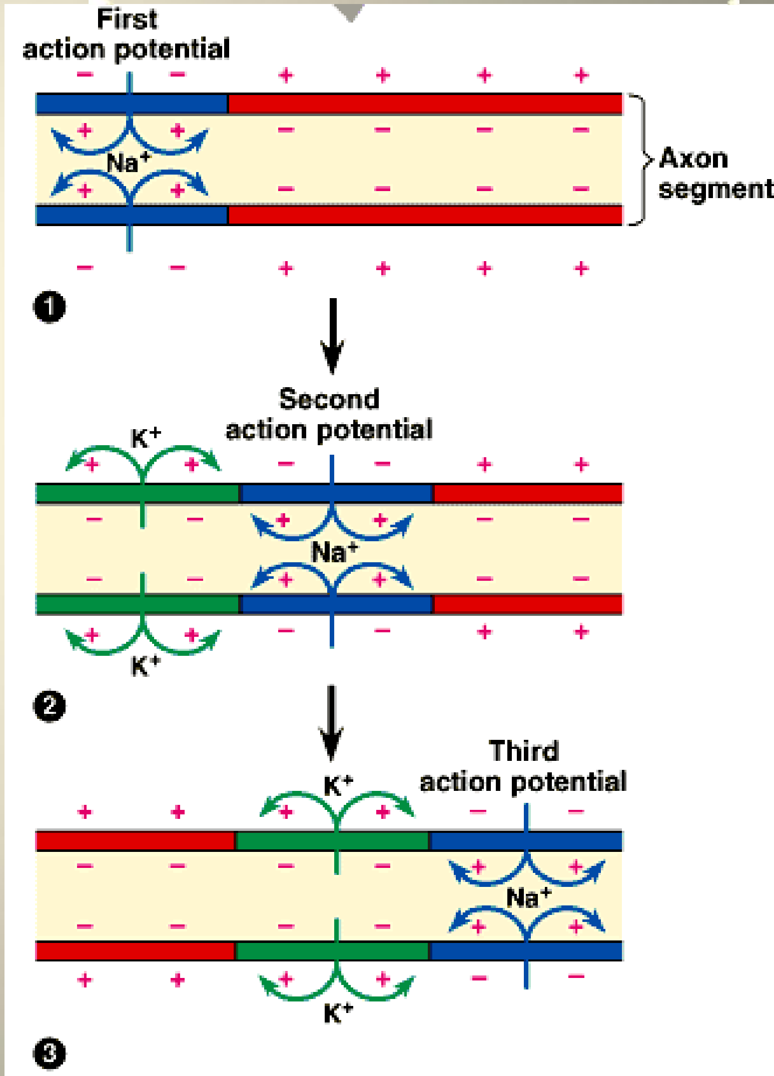
Nerve Signaling



Propagation

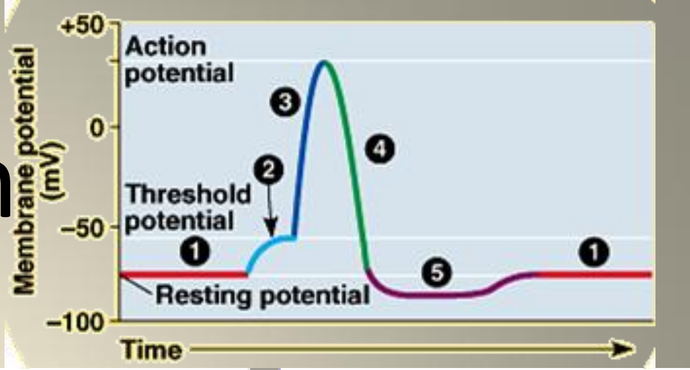


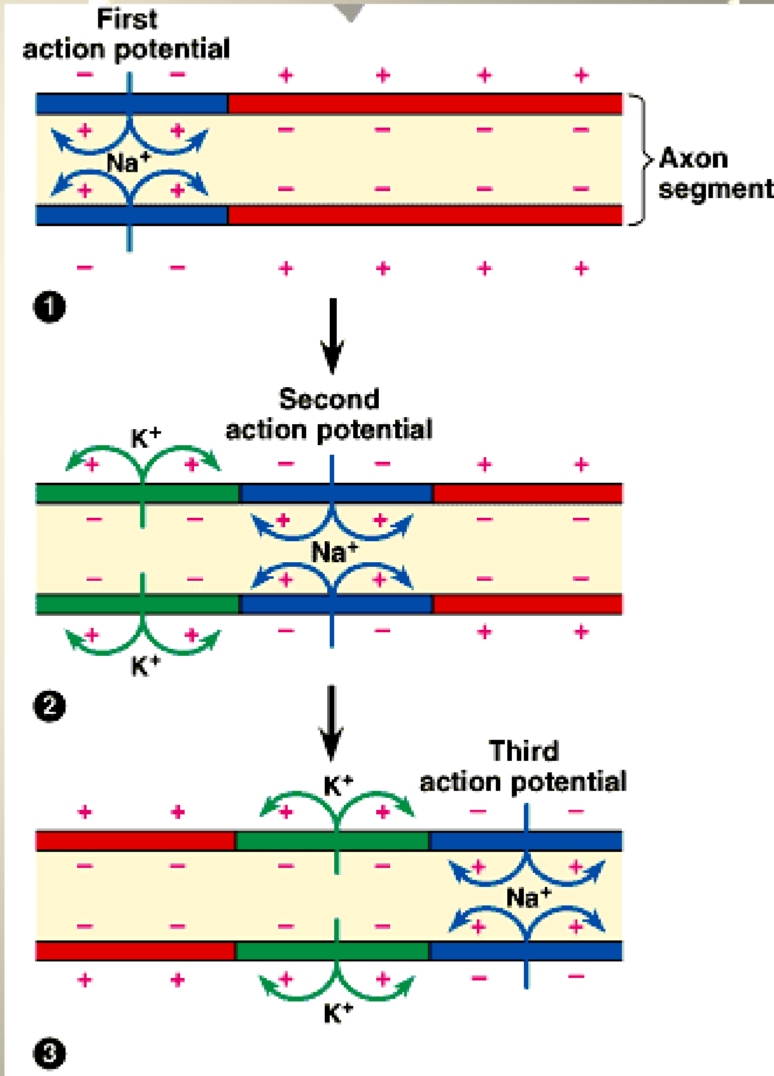
- Action potential "travels" by repeated regeneration along axon
- Depolarization by influx of Na depolarizes neighboring region above threshold
- Unidirectional



Propagation

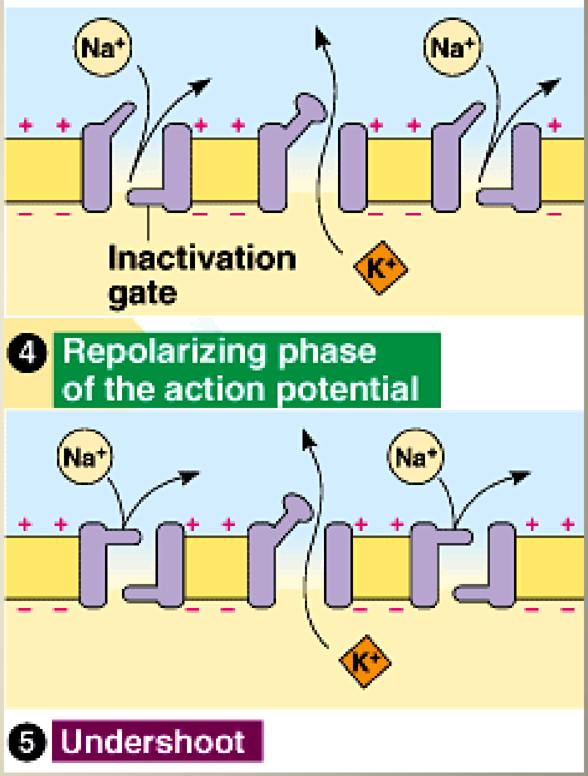
- Why can't the action potential be propagated backwards (bidirectional)?
- Recall:
  - Na inactivation gate





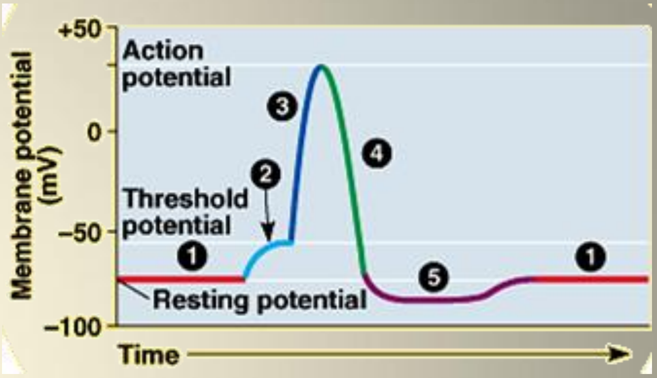
Refractory Period

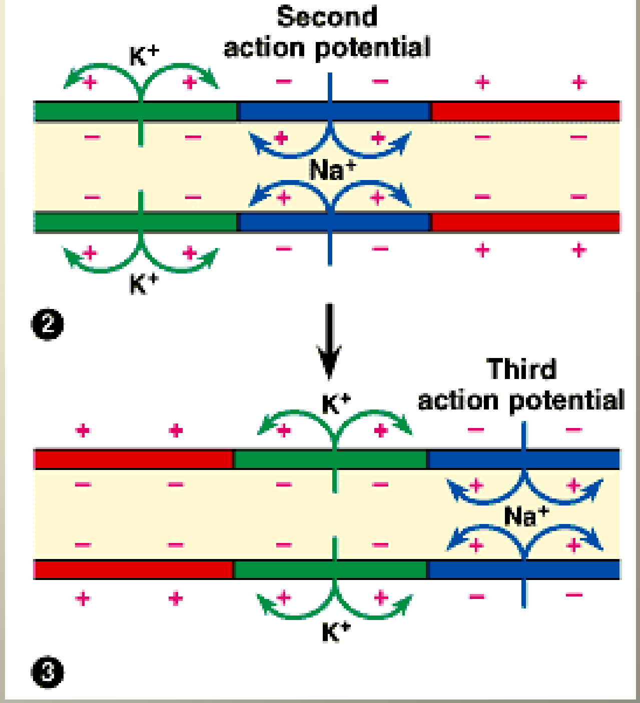
- Period when neuron is insensitive to depolarization
- Caused by a closed Na inactivation gate
- Occurs during repolarization and undershoot phases
- Depolarization closes Na inactivation gates
- Can only respond to another stimulus when Na inactivation gates are reopened



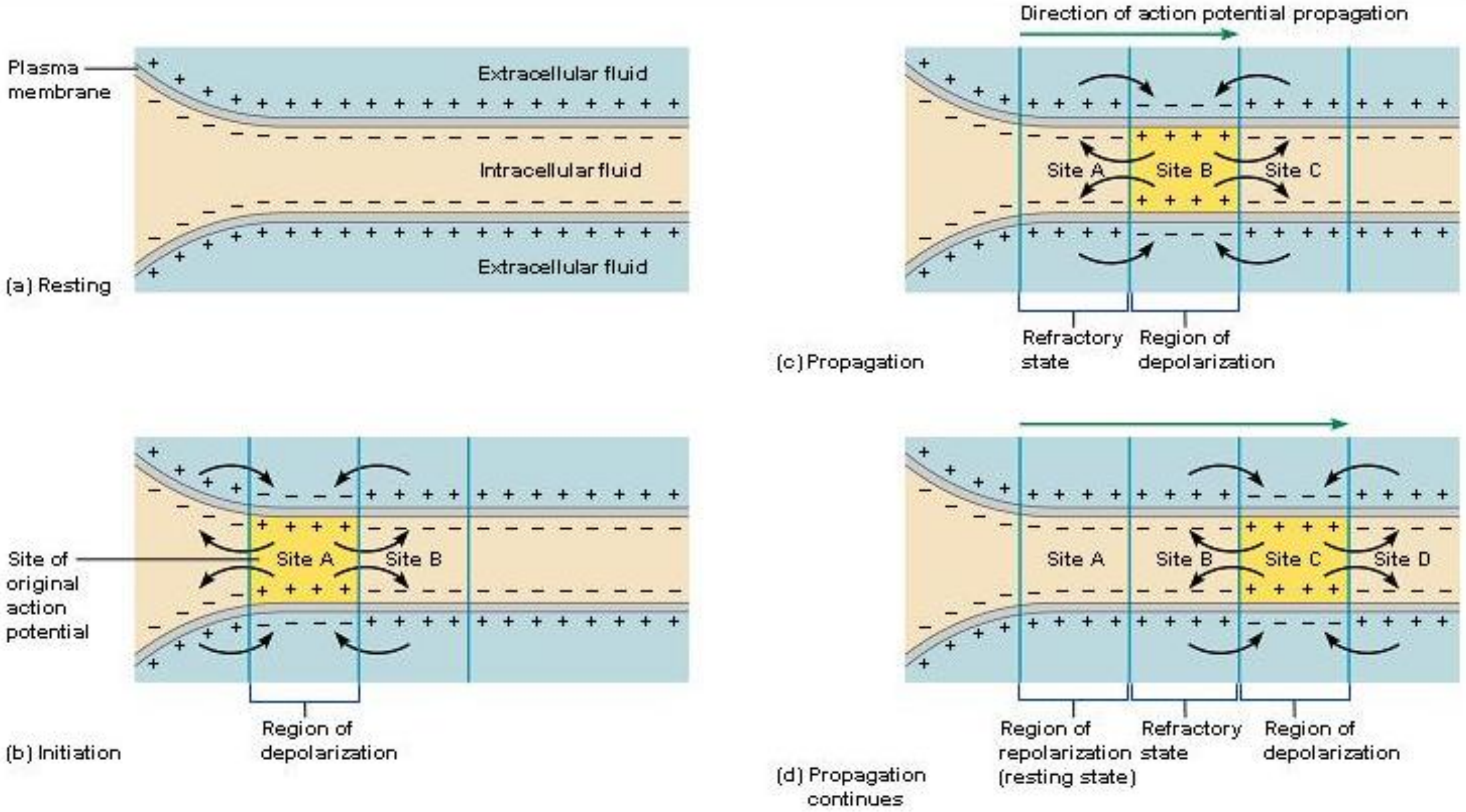
Refractory Period

- Purpose: prevents action potential from moving backwards
- Limits maximum frequency with which action potential can be generated





Unmyelinated (Continuous) Conduction

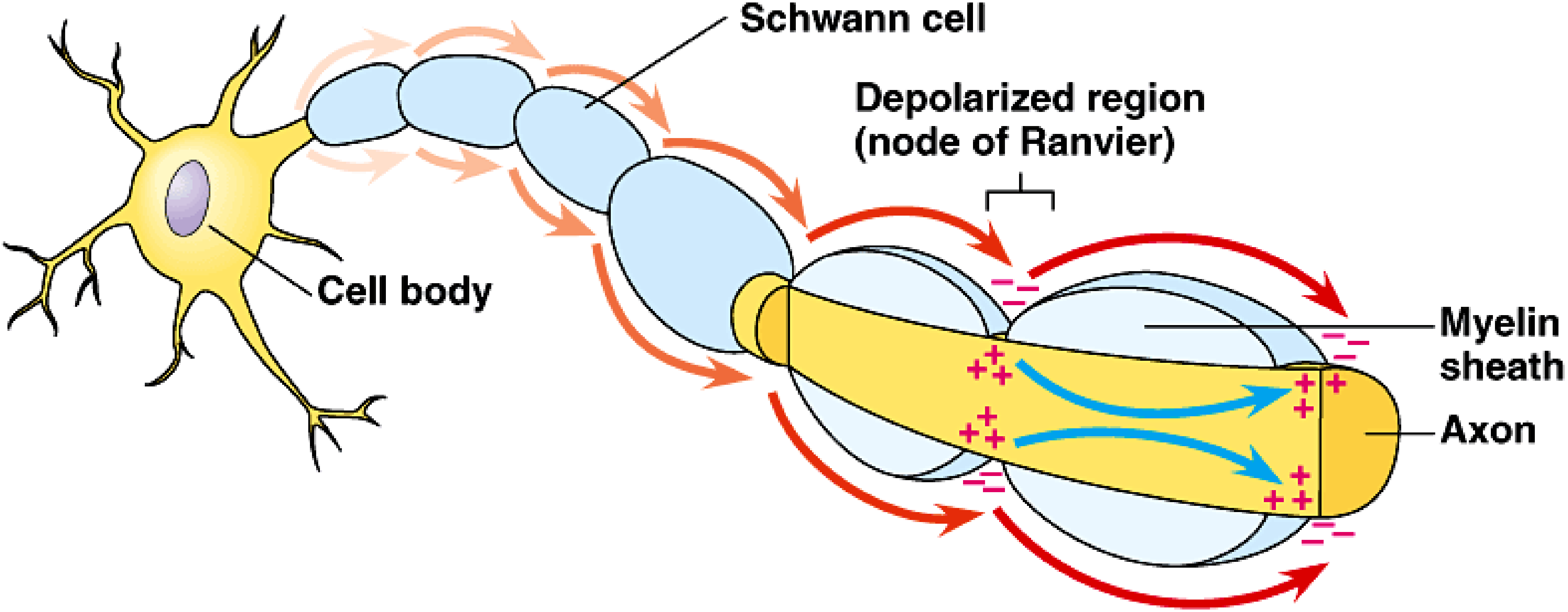


Factors affecting speed of conduction

- Axon diameter
  - Larger → faster
  - Due to less resistance
- Myelination
  - Voltage-gated ion channels only in nodes of Ranvier (unmyelinated region)
  - Axon only exposed to ions in ECF at nodes
  - No action potential in regions between nodes

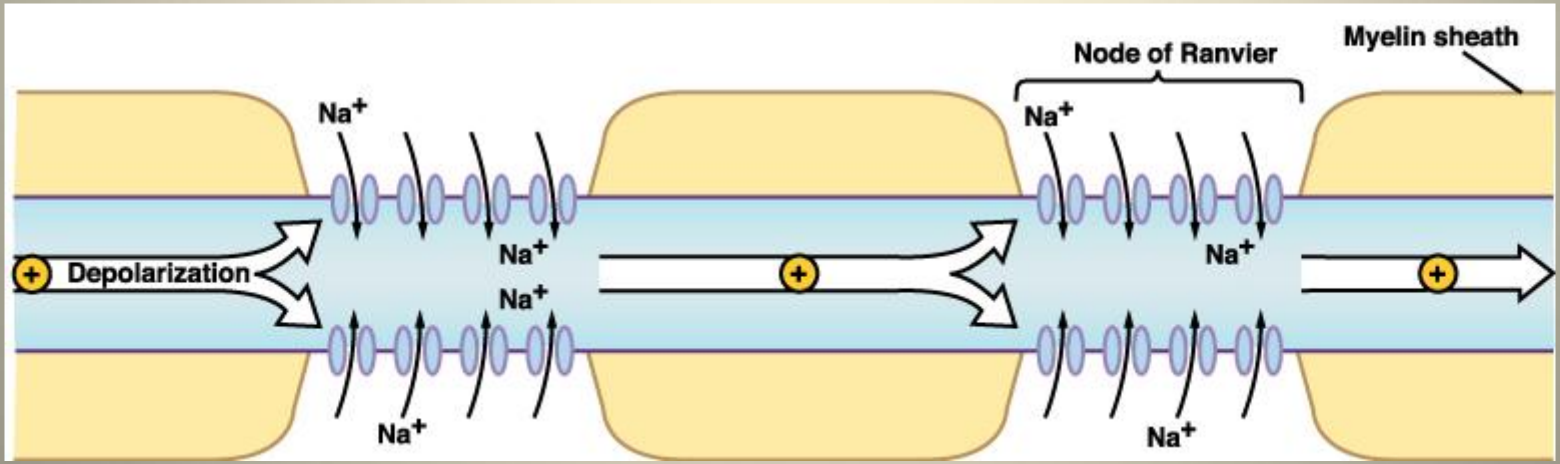
Saltatory Conduction

- Current generated by action potential at a node "leaps" to next node to stimulate new action potential

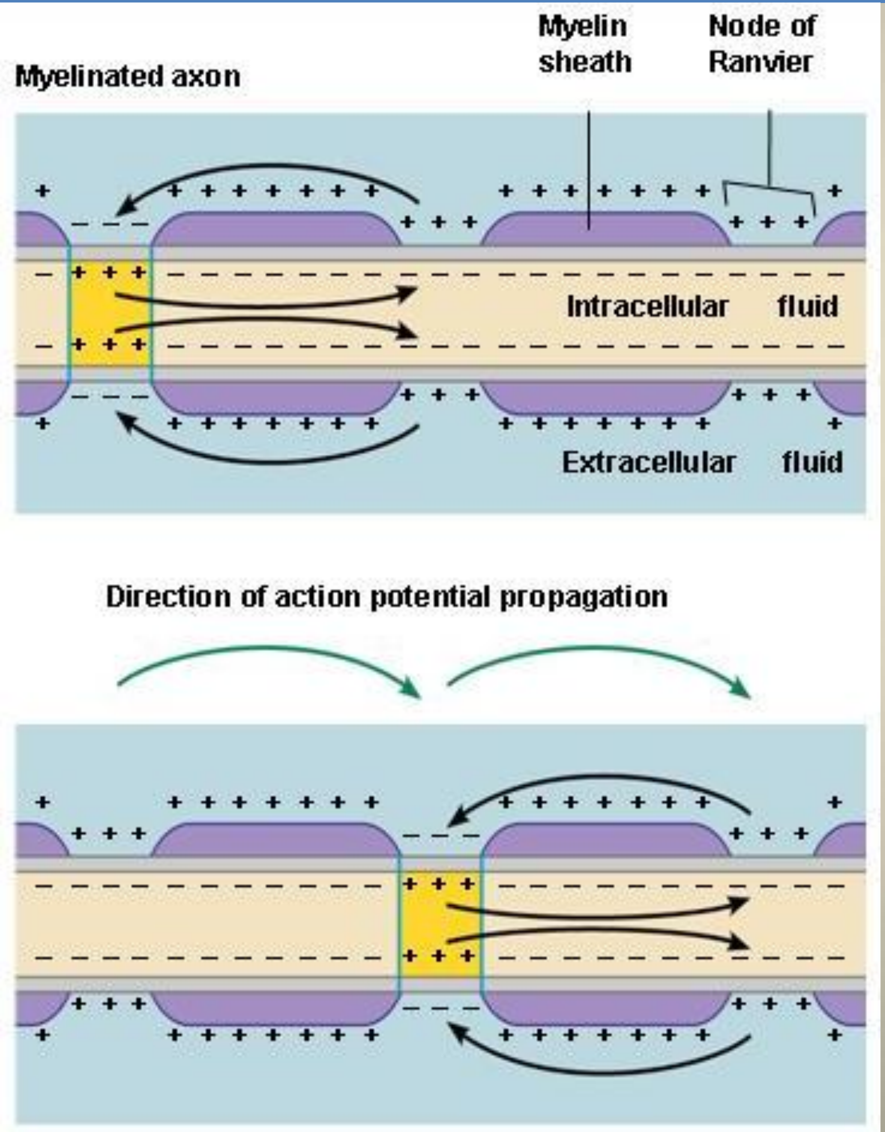


Saltatory Conduction

- Na+ and K+ exchange can only occur where the axons are exposed to the extracellular fluid.
- allows for faster signal conduction along the axon



Myelinated Conduction

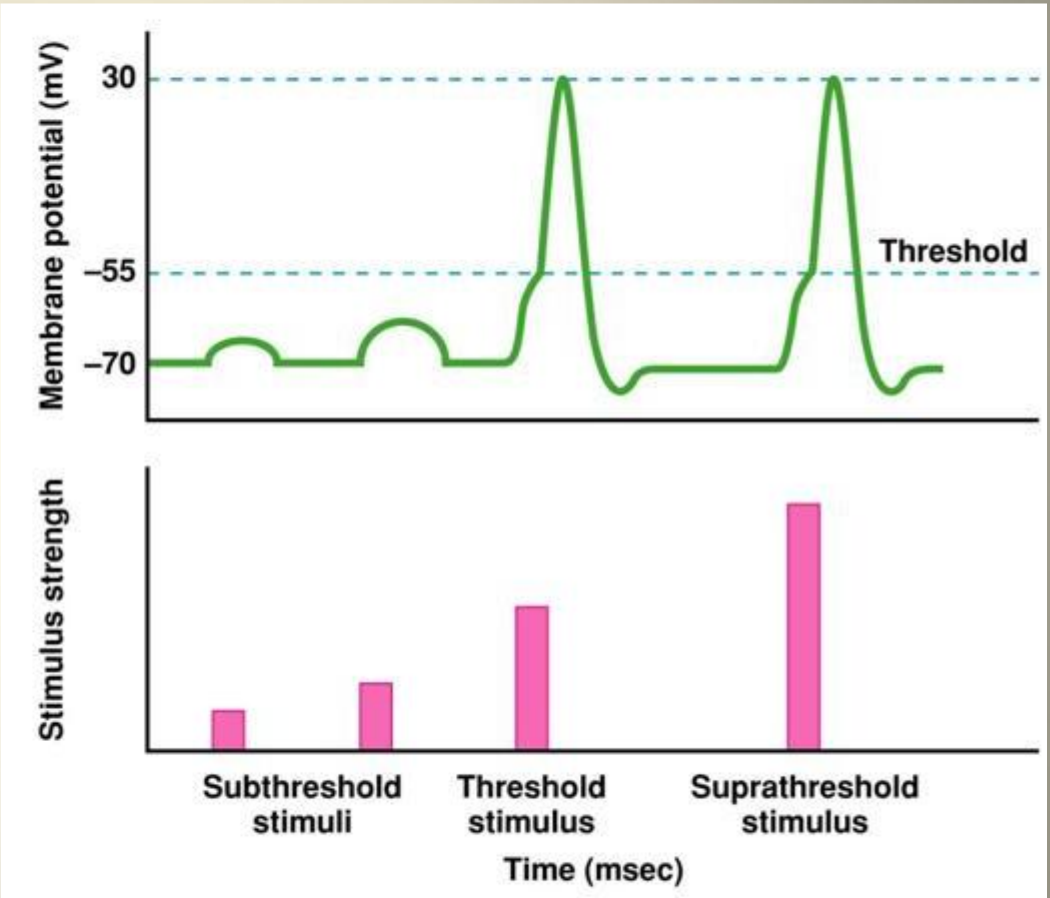


Animation: Conduction

- http://www.blackwellpublishing.com/matthews/actionp.html

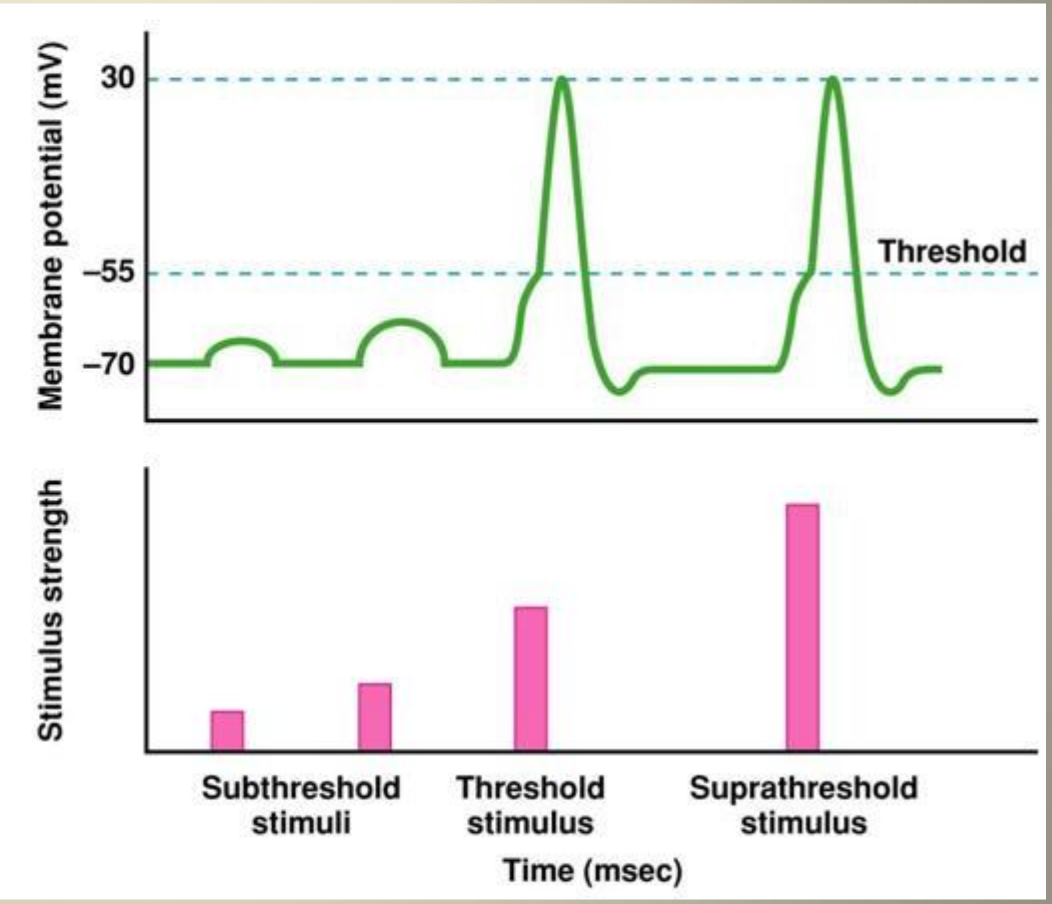
Action Potential: All-or-nothing

- Non-graded, all-or-none event
- **Magnitude** of action potential is **independent of stimulus strength** once threshold is reached
- **Amplitude** (magnitude) of all action potentials is **constant**



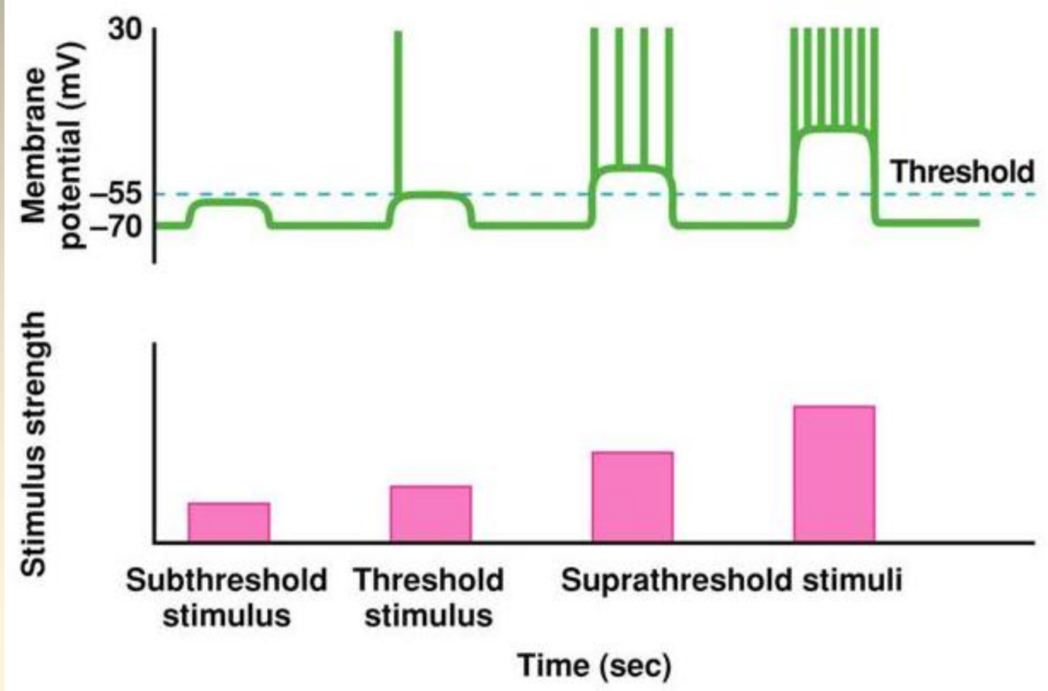
Action Potential: All-or-nothing

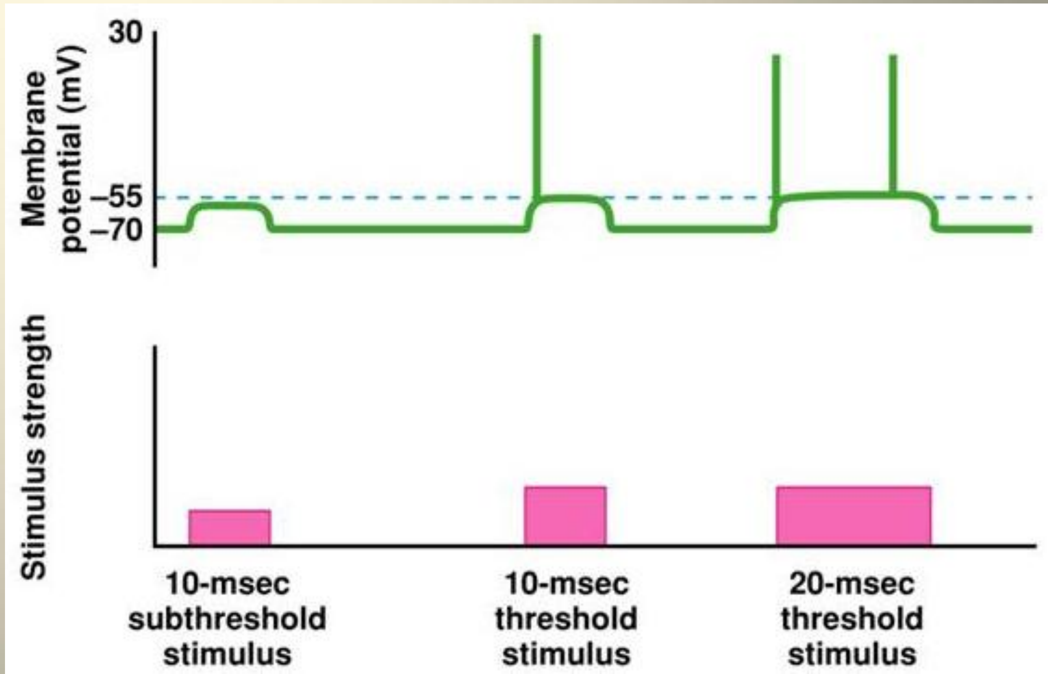
- Question: So how is stimulus strength translated into an action potential if the stimulus strength can't change the magnitude?



Frequency Coding

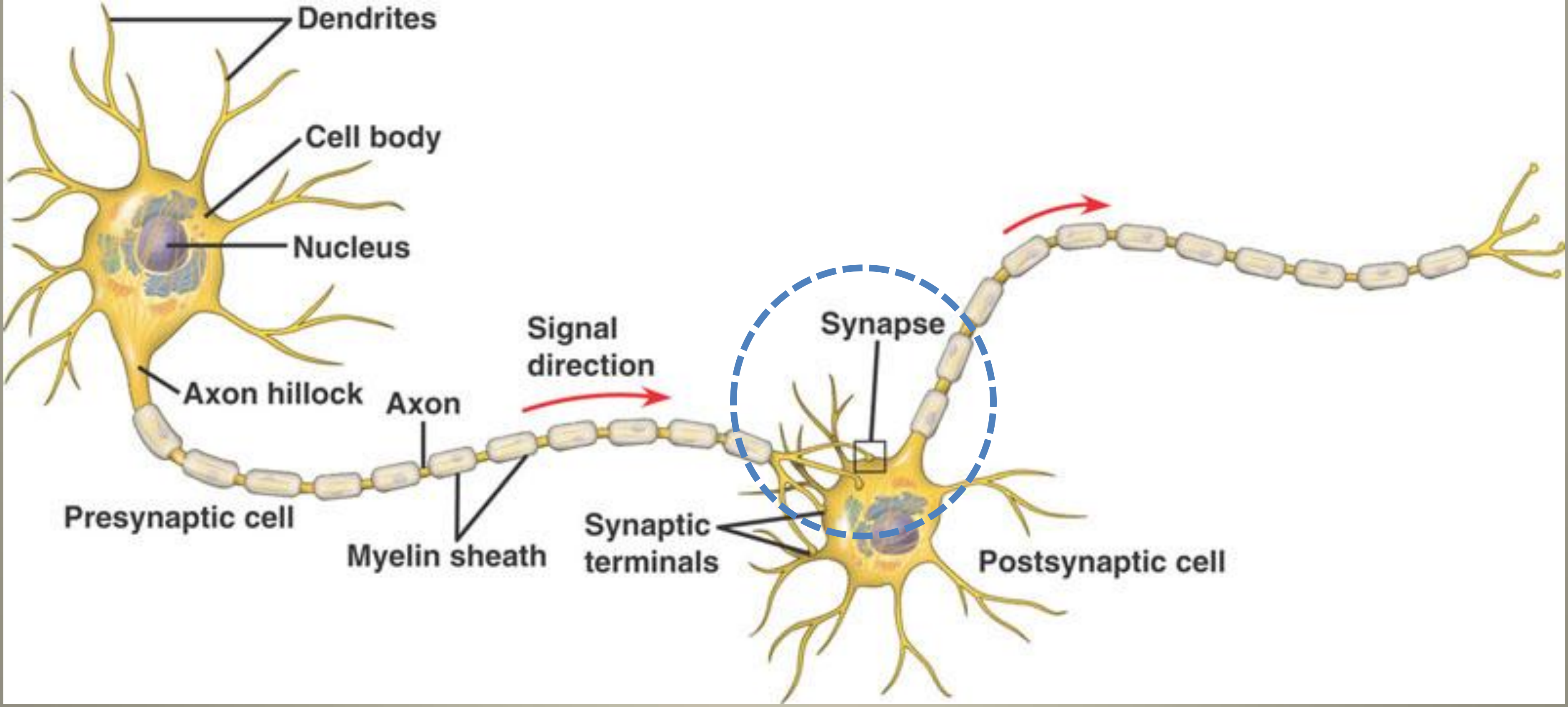
- **Stimulus strength & duration correlates to frequency** of action potential





Synapse

- A cell junction that controls communication between a neuron and another cell

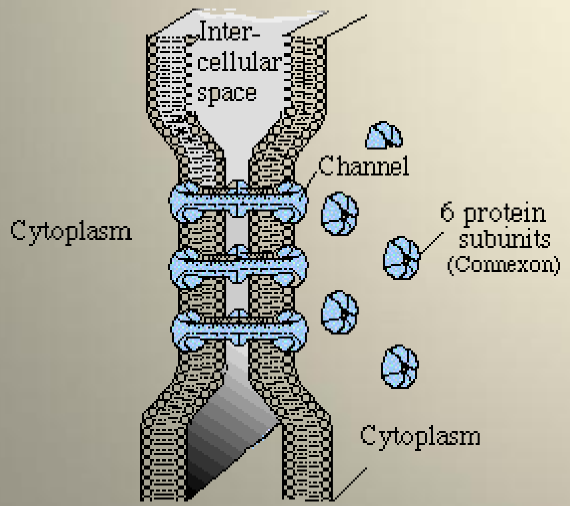


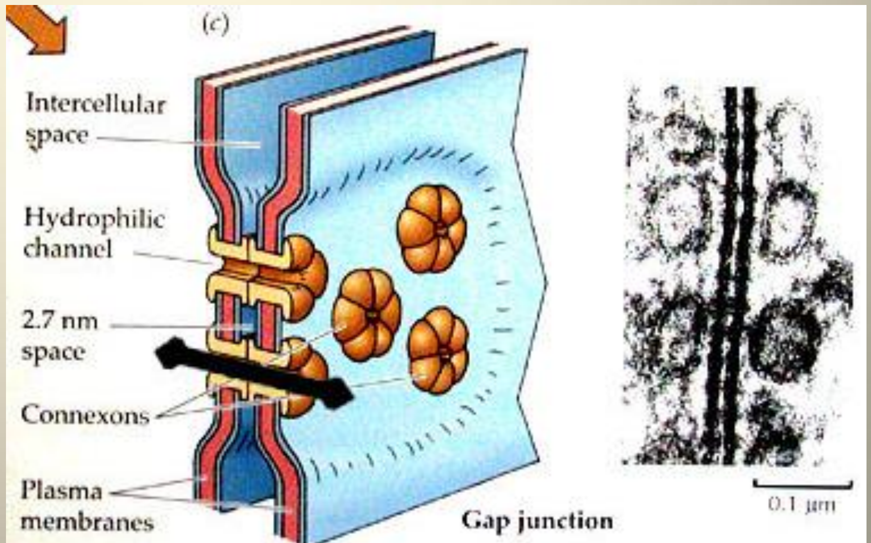
Synapse Locations

Pathway	Pre-synaptic Cell	Post-synaptic Cell
Sensory input (afferent)	Sensory receptor	Sensory neuron
Integration	Sensory Neuron Interneuron	Interneuron Motor neuron
Motor output (efferent)	Motor neuron	Muscle cells Glands

Electrical Synapse

- Current from presynaptic cell flows directly to the postsynaptic cell through gap junctions
- **Gap junctions**: pores, channels between adjacent cells, through which ions and other small molecules can pass
- Direct communication through **physical connection**

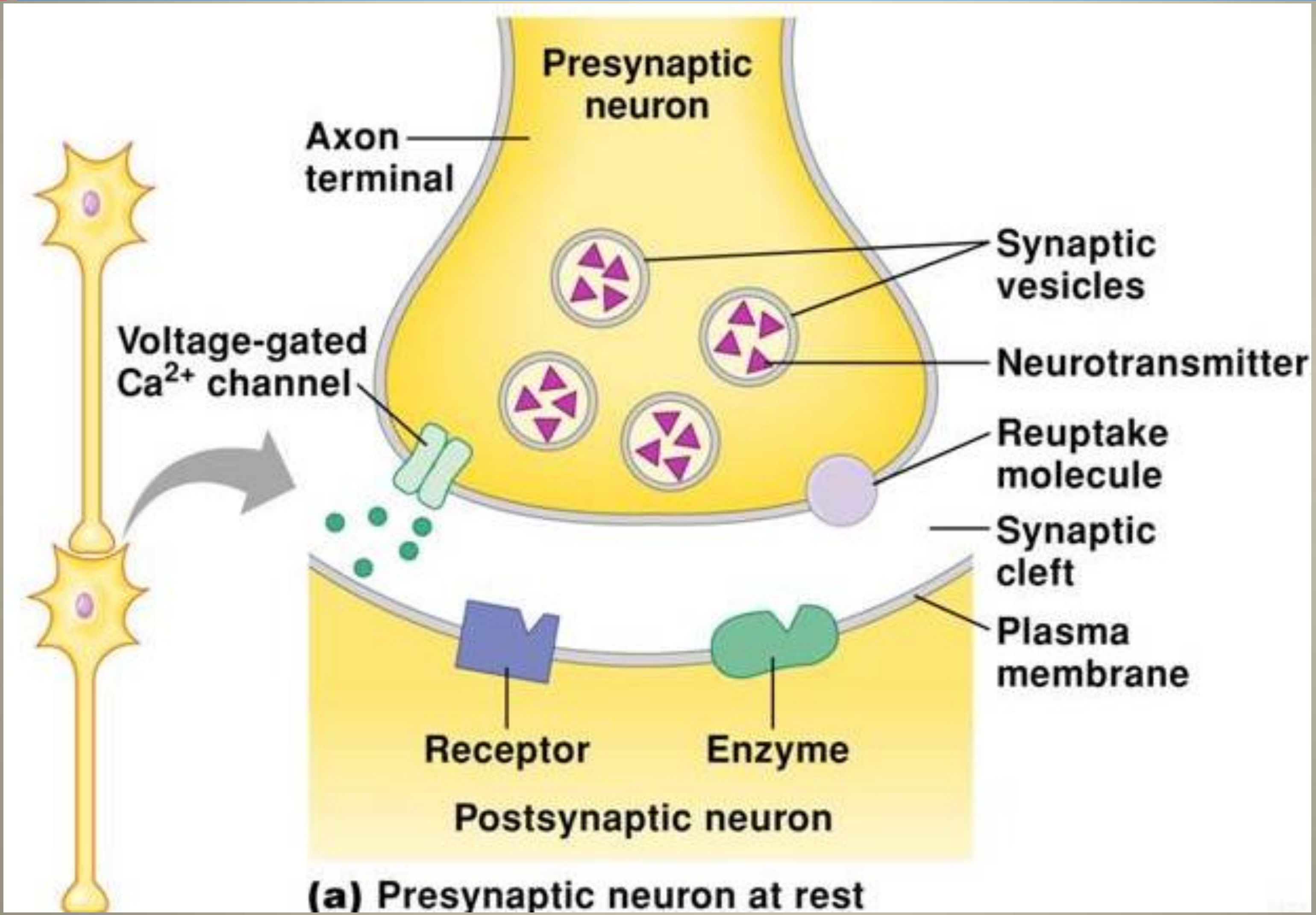




Electrical Synapse

- Found in giant axons in crustaceans
- Not common in vertebrates
- Advantage: rapid transmission of action potential from cell to cell
- Disadvantage: more difficult to regulate

Anatomy of a chemical synapse

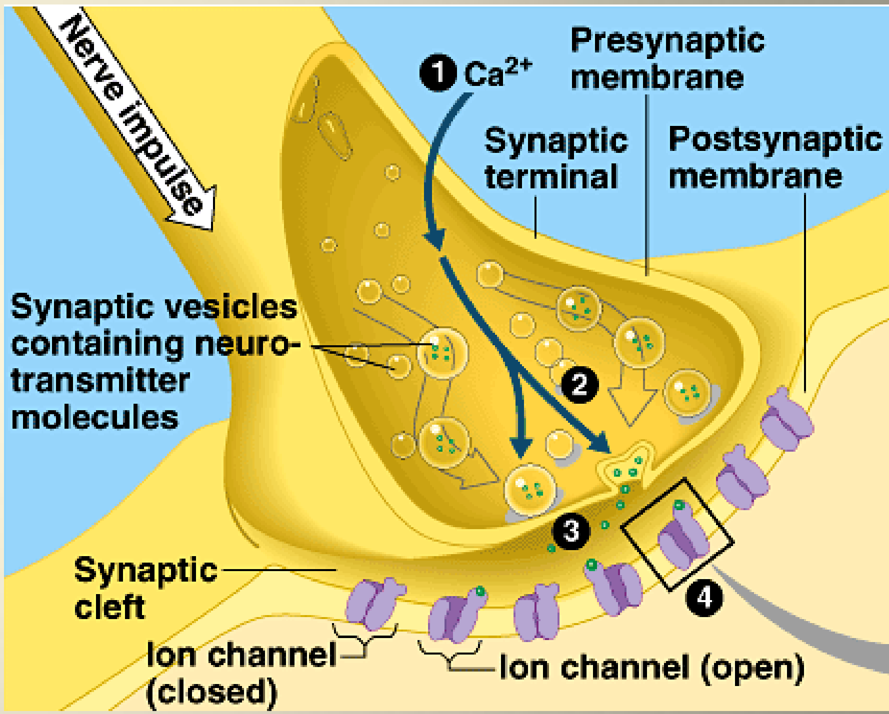


Synaptic cleft

- **narrow gap** separating pre- and postsynaptic cell
- Thus, cells are not electrically coupled
- Signal conversion:
electrical → chemical → electrical

Chemical Synapse

a. Presynaptic membrane depolarized by action potential
b. **Voltage-gated** Ca^{2+} channels open
c. Ca^{2+} enters cell
d. Stimulates exocytosis of synaptic vesicles



Synaptic Vesicles

- Sacs at the synaptic terminal that contains neurotransmitters
- **Neurotransmitter**: substance released by presynaptic cell as an intercellular messenger into synaptic cleft
- Each neuron usually secretes only one type of neurotransmitter

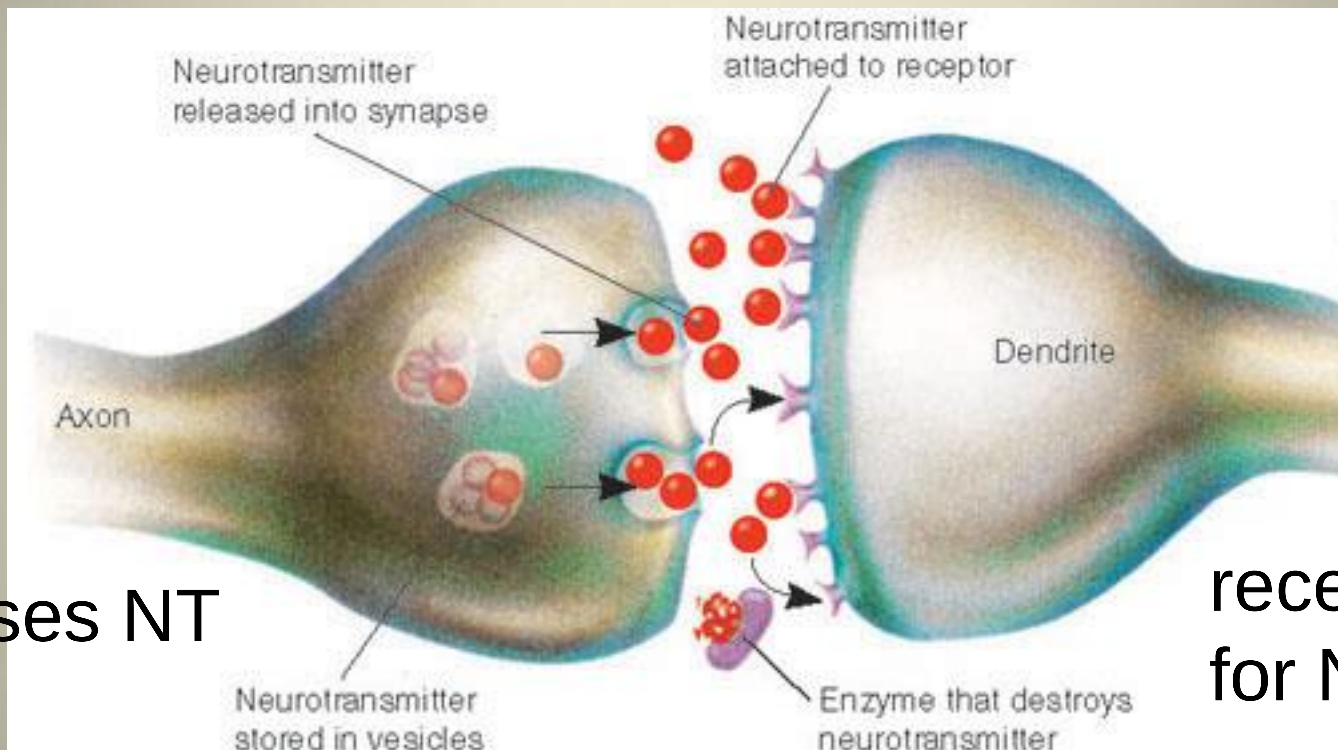
Examples of Neurotransmitters

NT Type	Description	Examples
Acetylcholine (Ach)	Most common	Acts on motor neurons and skeletal muscles
Amino acids	Affects mainly the CNS	Glutamate (+ in CNS), GABA (- in brain), glycine (- in spinal cord)
Neuropeptides	Short chain of amino acids	Endorphins (- pain), Substance P (+ pain)
Biogenic amines	Derived from amino acids	Catecholamines (tyr), serotonin (trp), dopamine (phe/tyr)
Gaseous signals	Not stored in synaptic vesicles, made as needed	Nitric oxide

Effect of changing Ca Levels

- Voltage-gated Ca^{2+} channels close soon after opening
- Ca^{2+} actively transported out of axon terminal bringing it back to resting level
- But if another action potential arrives soon after previous, then Ca^{2+} levels continue to increase
- Frequency of AP → [Ca] → [NT]

Chemical Synapse



releases NT

receptors for NT

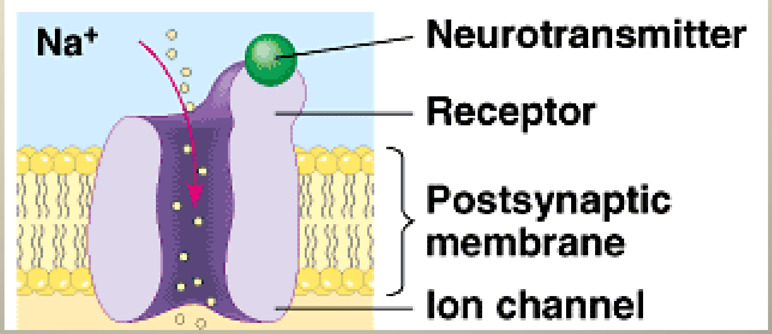
Presynaptic neuron (axon)

Postsynaptic neuron (dendrite)

http://www.txtwriter.com/Backgrounders/Drugaddiction/synapse.jpg

NT binds to receptor

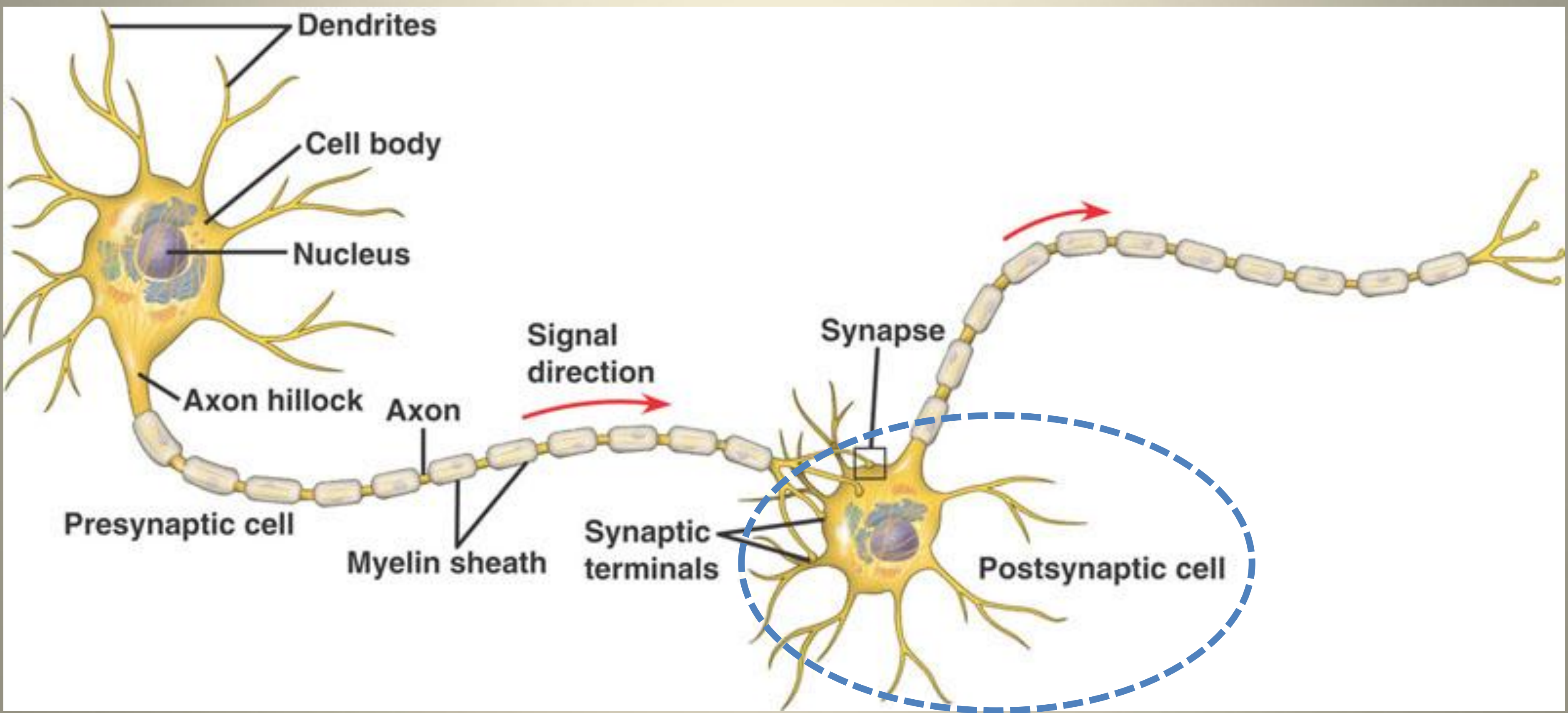
- Each type of receptor on the post-synaptic membrane specifically recognize one neurotransmitter
- Receptors are part of a gated ion channel
- When NT binds, gates open allowing in a specific ion (i.e. Na, K, Cl)
- Thus these channels are **chemically gated**



Postsynaptic Potentials (PSP)

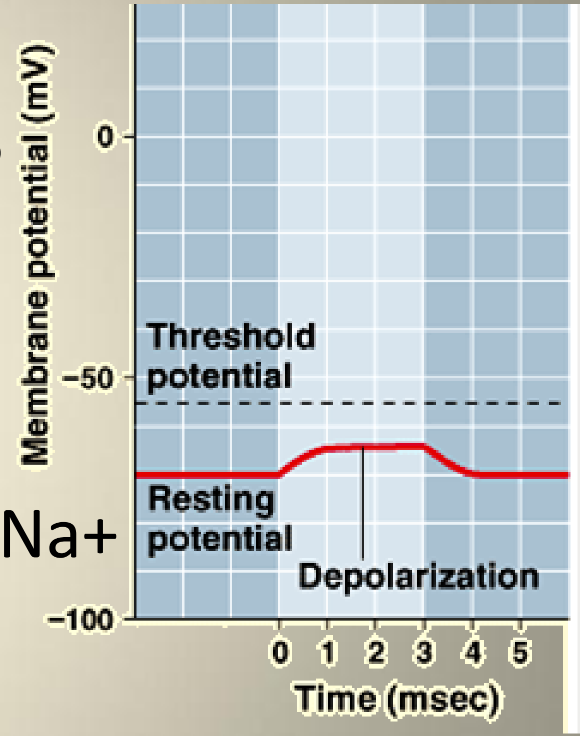
- Start at the dendrites and progress to the axon hillock on the post-synaptic neuron
- Are graded potentials
  - vary in magnitude with NT
  - Decremental (degenerates with distance)
- 2 types:
  - Excitatory (EPSP)
  - Inhibitory (IPSP)

Nerve Signaling



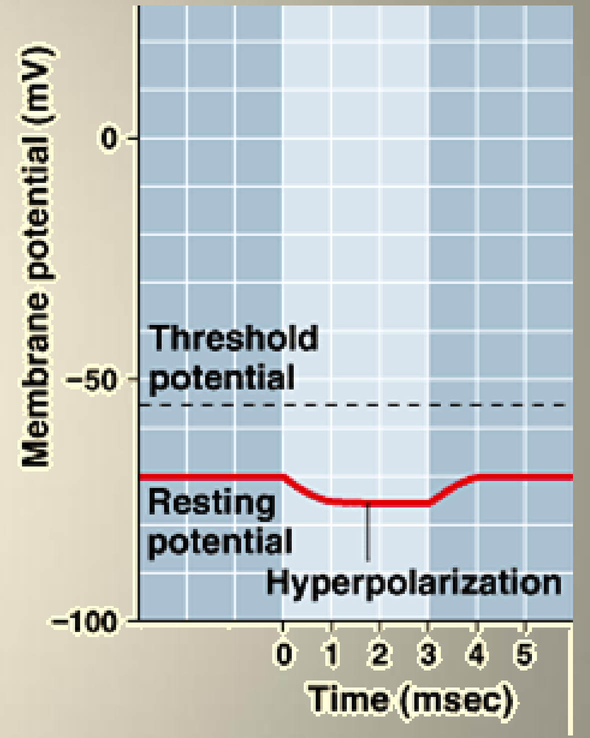
Excitatory postsynaptic potential (EPSP)

- Excitatory synapse:
  - Increase chance of generating an AP
  - Depolarization
  - Net flow of positive charge into cell
- Example:
  - NT binding to receptor opens gated Na+ channels
  - Na+ enters
- For an AP to occur, the EPSP must be strong enough to reach and depolarize to threshold potential at the axon hillock



Inhibitory Postsynaptic Potential (IPSP)

- Inhibitory synapse:
  - Decrease chance of generating an AP
  - Hyperpolarization
  - Net flow of negative charge into cell
- Example:
  - NT binding to receptor opens gated K+ and Cl- channels
  - Diffusion down electrochemical gradients: K+ leaves, Cl- enters



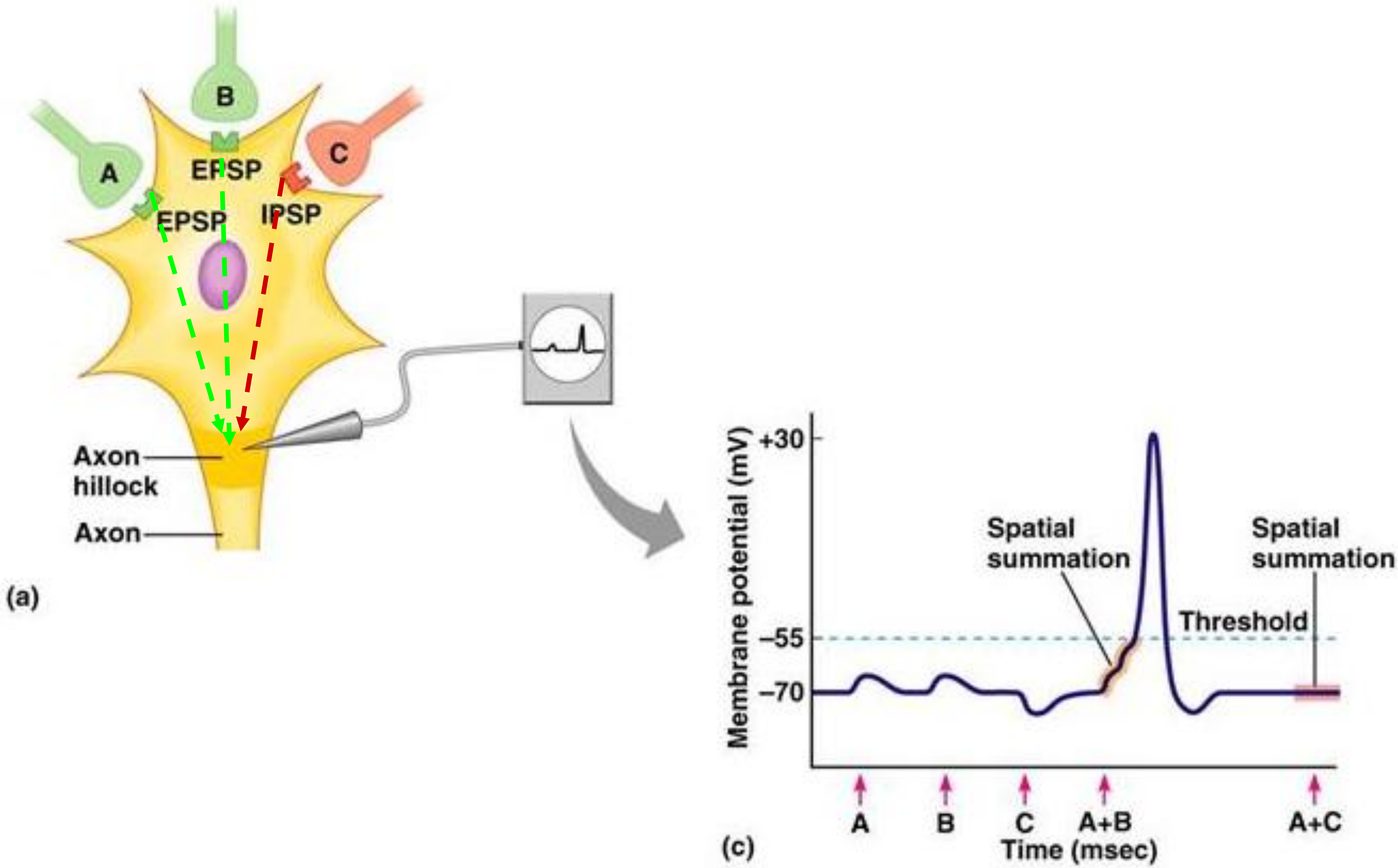
Summation

- Additive effects of PSP
  - Single EPSP usually not strong enough to trigger an AP (same application to IPSP)
  - Several EPSP working simultaneously on the same postsynaptic cell can have cumulative impact
  - IPSP and EPSP can counter each other's effects
- Can result in stimulatory (EPSP) or inhibitory (IPSP) effects
- Occurs at the axon hillock (neuron's integrating center)

Types of Summation

- Spatial Summation
  - Several PSP from different sources
- Temporal Summation
  - Several PSP from the same location but in close sequence

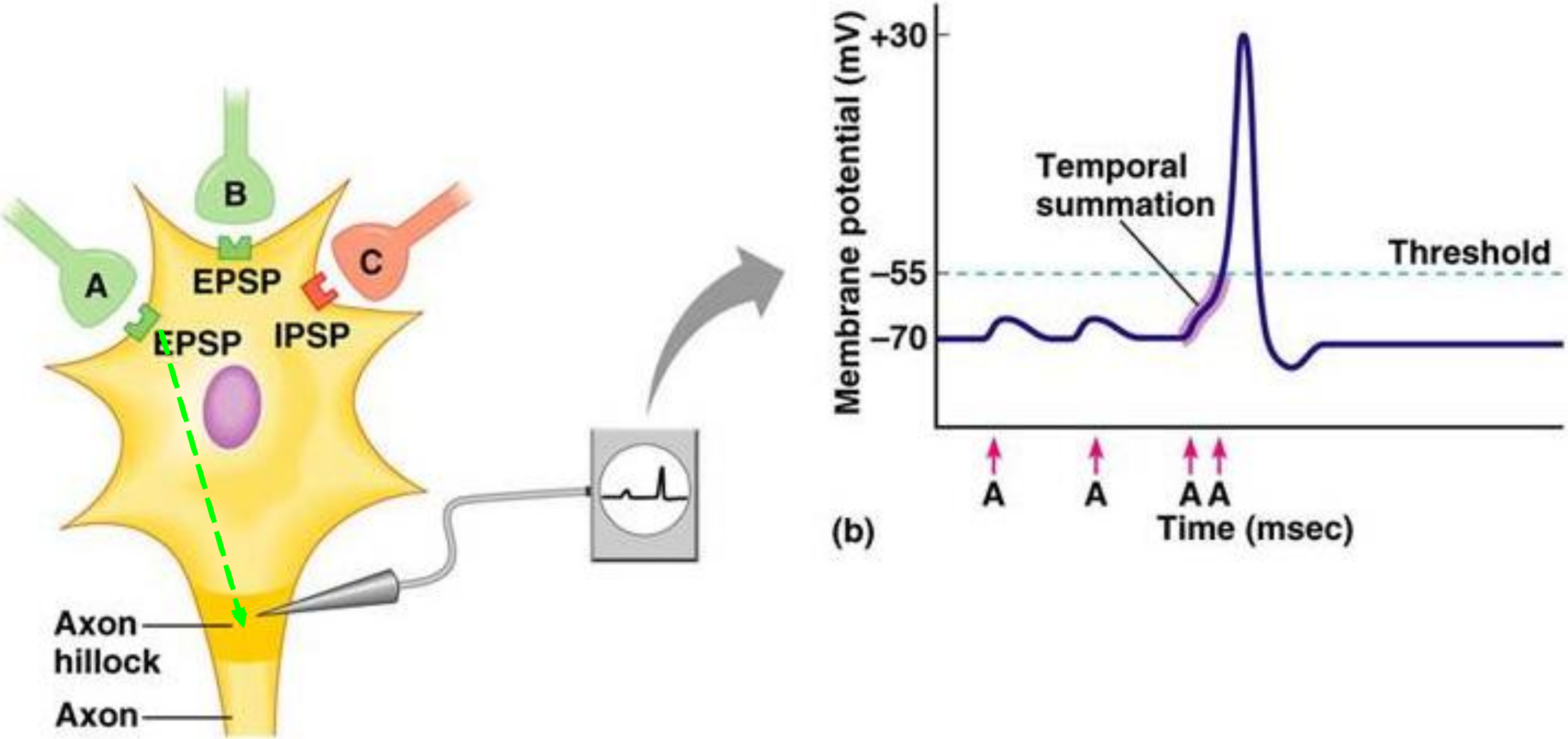
Spatial Summation



Spatial Summation

- Several **different synaptic terminals** (usually from different presynaptic cells) stimulating the same postsynaptic cell at the **same time**

Temporal Summation

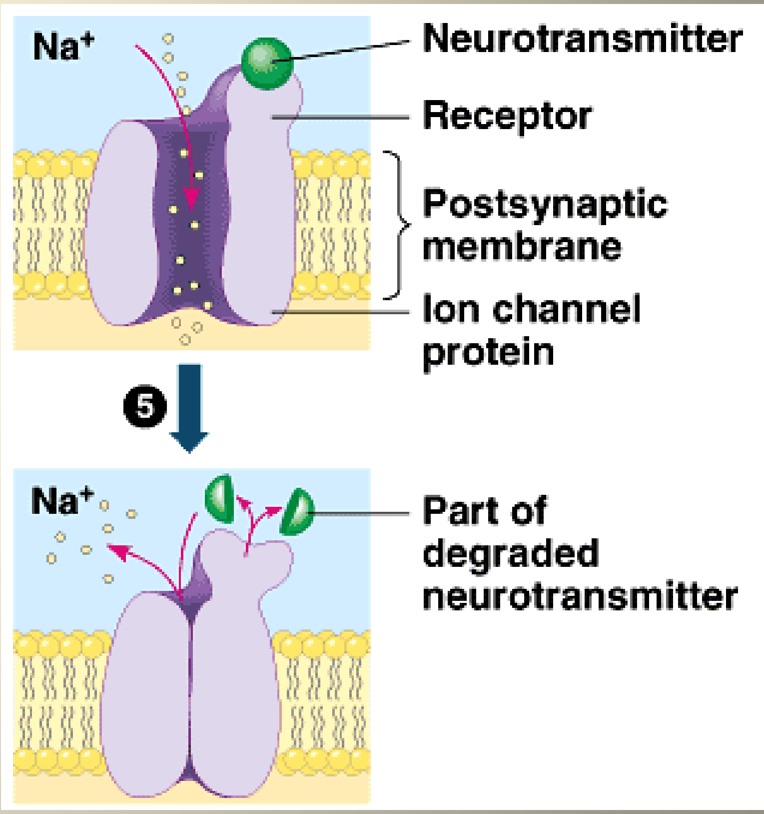


Temporal Summation

- Chemical transmission from one or more synaptic terminal occurring **close together in time** affecting membrane on postsynaptic membrane before the voltage can return to resting potential

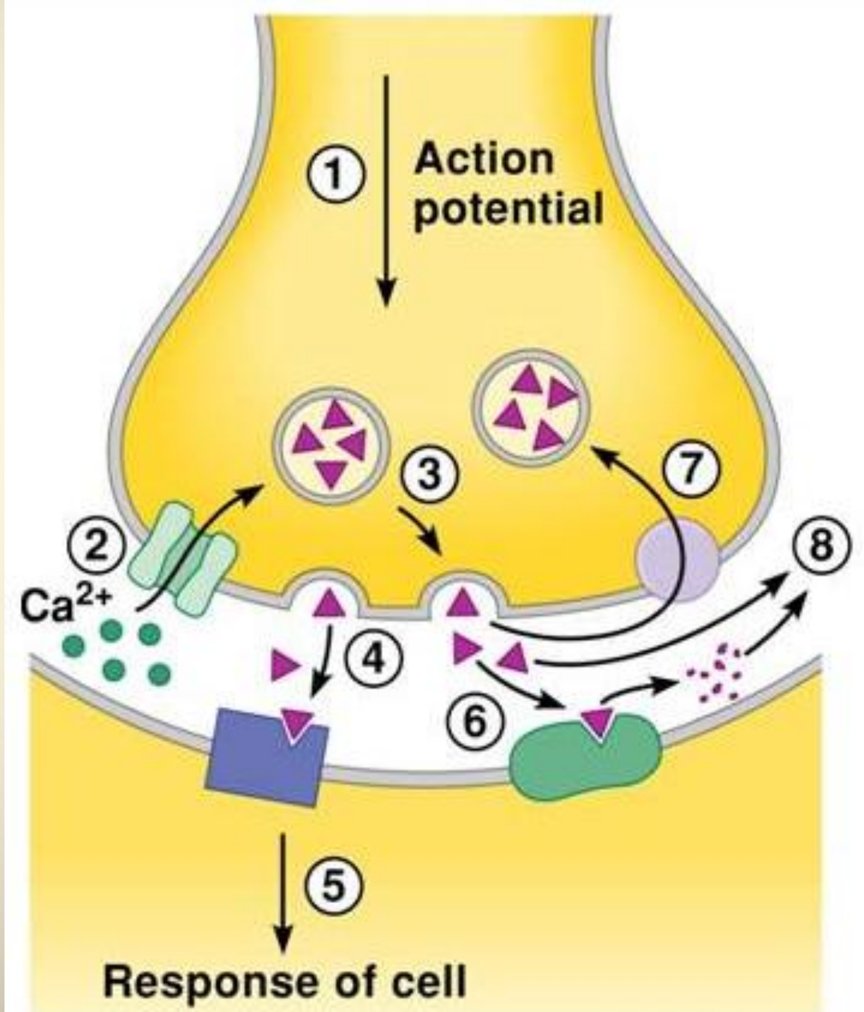
Neurotransmitter Removal

- Process:
  - enzymatic degradation
  - reuptake into presynaptic cell
  - diffusion out of the cleft
- Consequence:
  - ensures effect of NT is brief and precise
  - allows transmission of the next action potential



Communication across a synapse

1. Action potential
2. Calcium channels open
3. Calcium enters cell and triggers release of NT by exocytosis
4. NT diffuse across synaptic cleft
5. Binds to receptor on postsynaptic cell causing a response by postsynaptic cell
6. Removal by enzymatic degradation
7. Removal by reuptake by presynaptic cell
8. Removal by diffusion away from synaptic cleft



(b) Active presynaptic neuron

Nerve Signaling Cycle of Events

- Receptors on dendrites receive neurotransmitters
- Chemically-gated channels open
- Summation of signal at axon hillock
- AP generated and conducted down axon
- Release of neurotransmitters into synaptic cleft