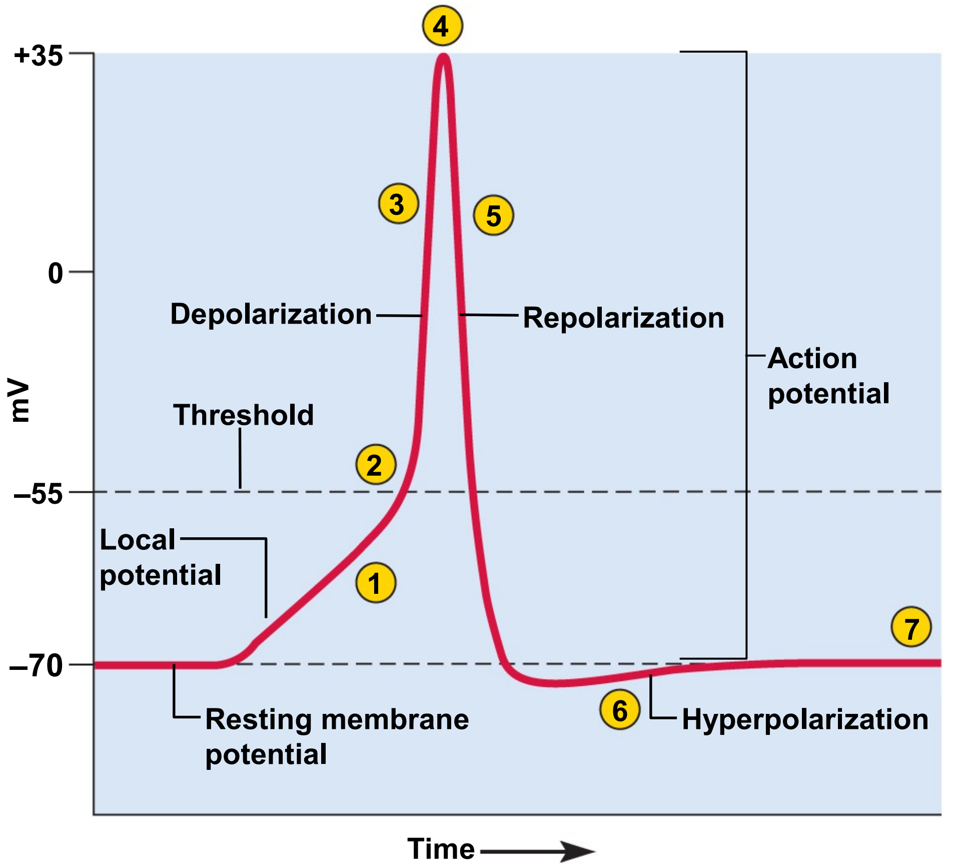
Chapter 12

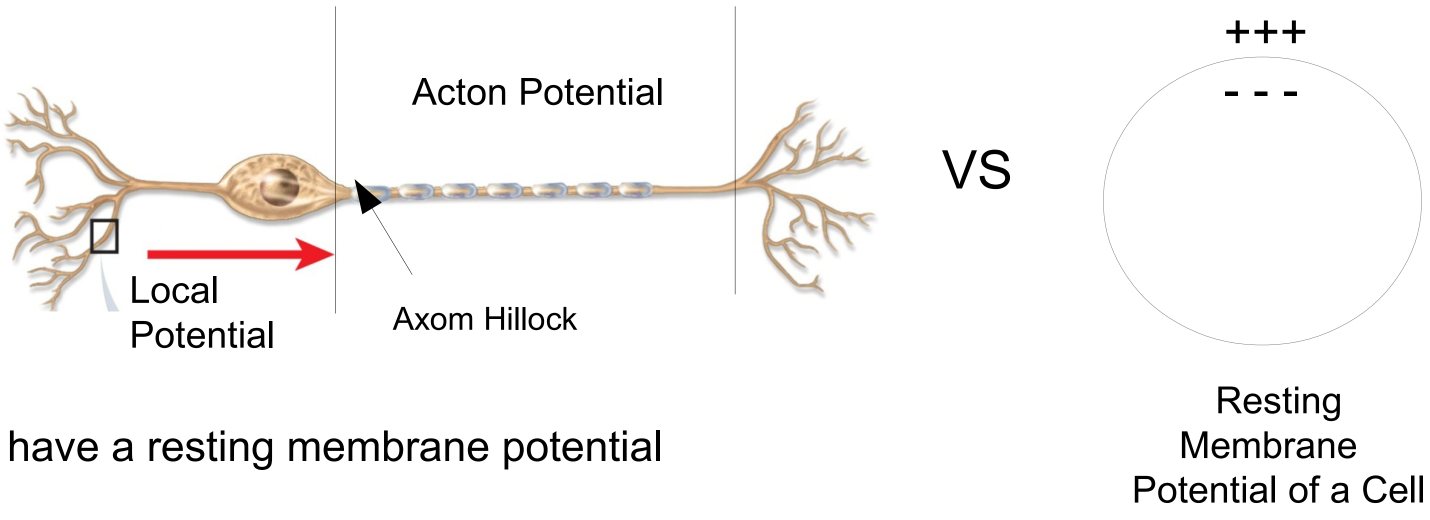
Electrical Potentials



Different Types of Electrical Potentials

- Resting Membrane Potential
- Local Potential
- Action Potential
- Receptor Potential
- End Plate Potential

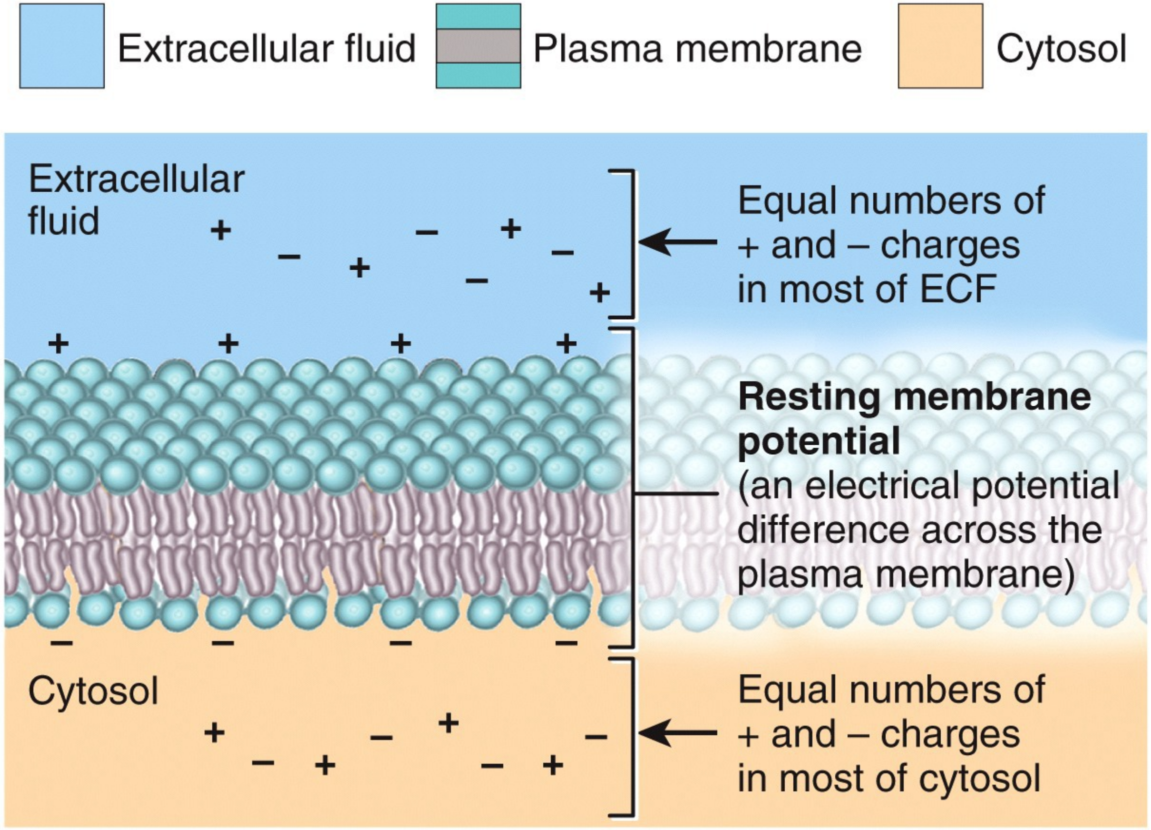
Local Potential VS Action Potential VS Resting Potential



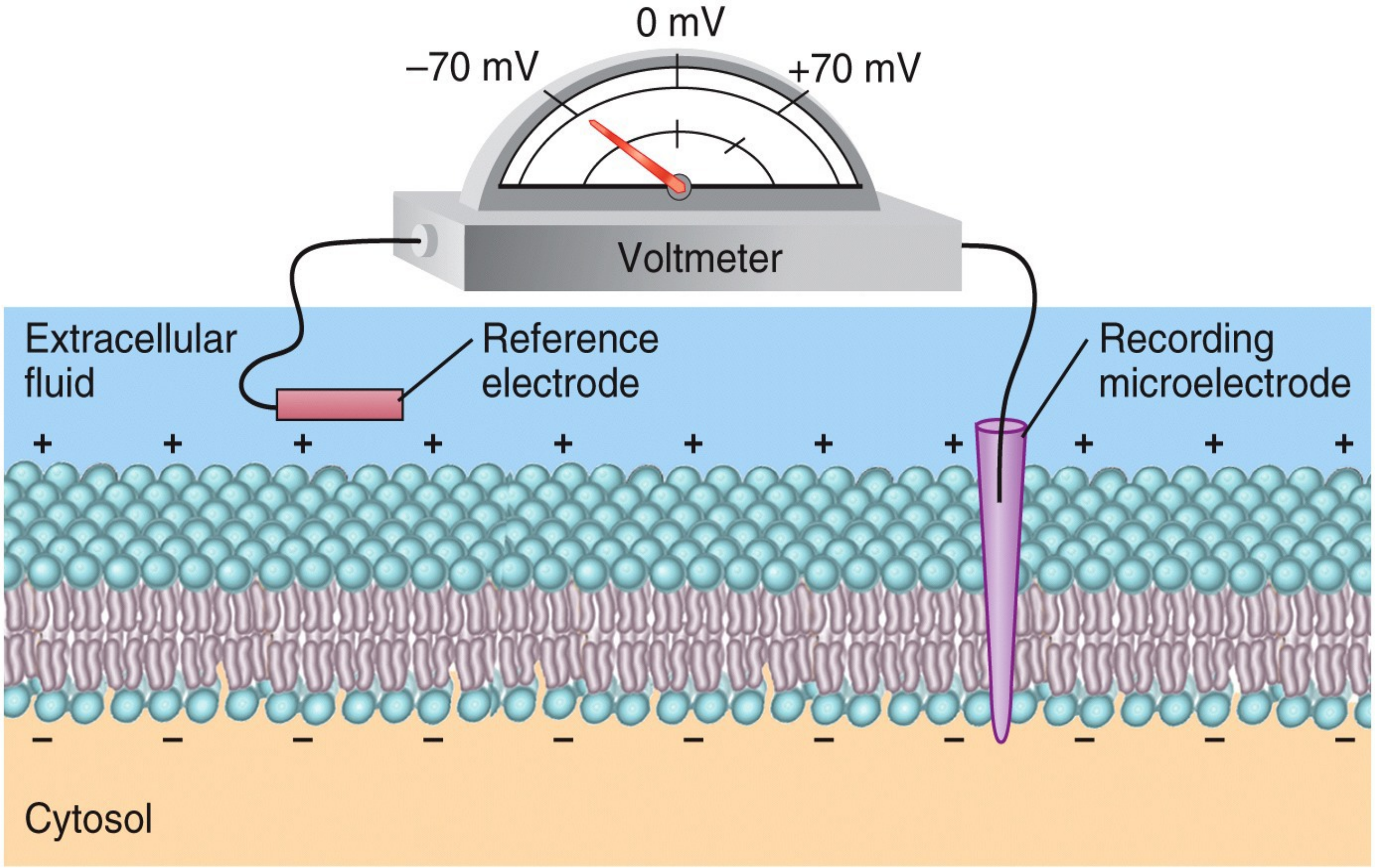
- All cells have a resting membrane potential
- Nerves have a resting potential when they are not stimulated
- Dendrites exhibit local potentials (similar to receptor potentials). If the stimulus is great enough then the local potential may become an action potential.
- Local potentials are graded, decremental, reversible, and may either advance or inhibit the formation of an action potential
- If stimulus is strong enough, local potential spreads to the trigger zone (axon hillock)
- If LP stimulus reaches trigger zone then it initiates an action potential that travels down axon (all or none and uni-directional)

Electrical Potentials

- Electrical potential = a difference in the concentration of charged particles separated by a barrier (the unit membrane)



(a) Distribution of charges that produce the resting membrane potential of a neuron



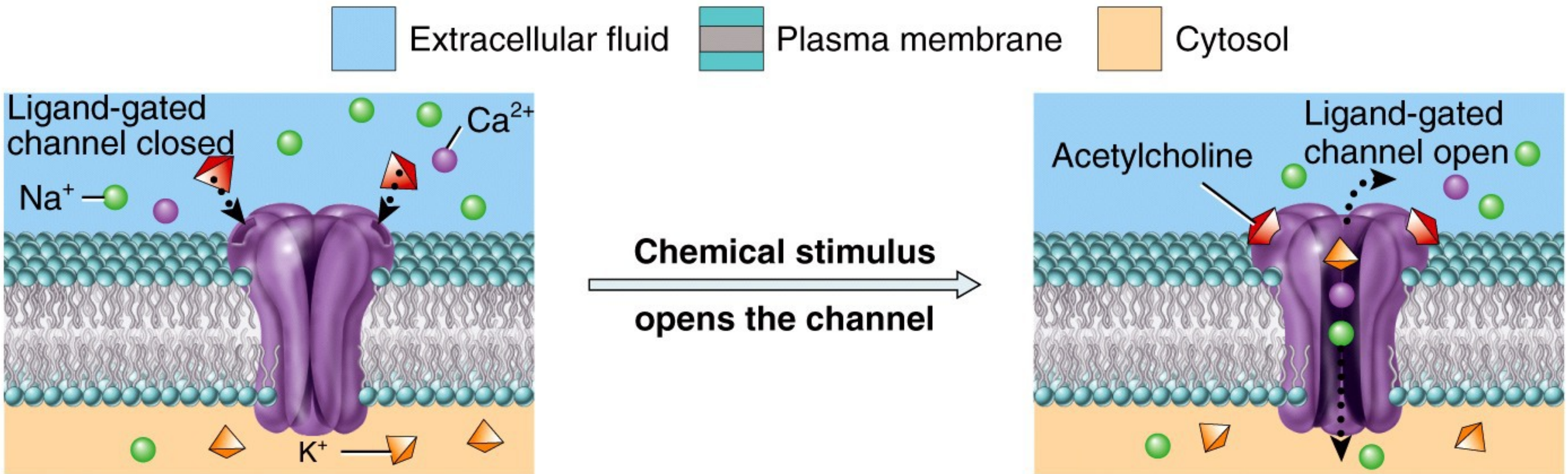
(b) Measurement of the resting membrane potential of a neuron

Notes:

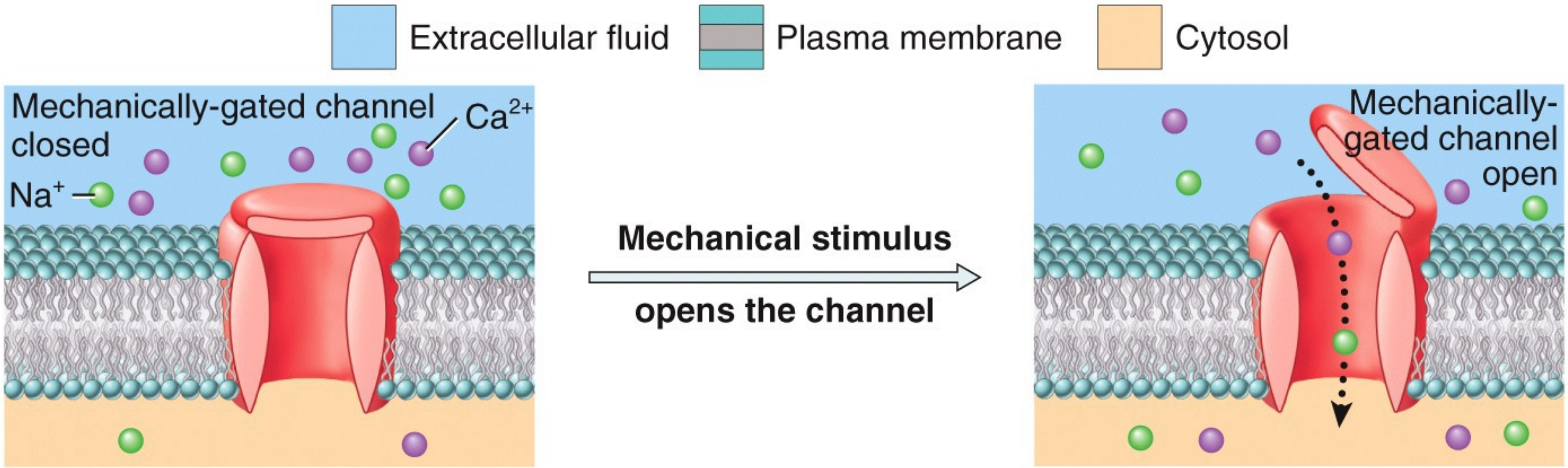
- Voltage values may vary depending on tissue type
- What is the difference between voltage and current?

Voltage and Current

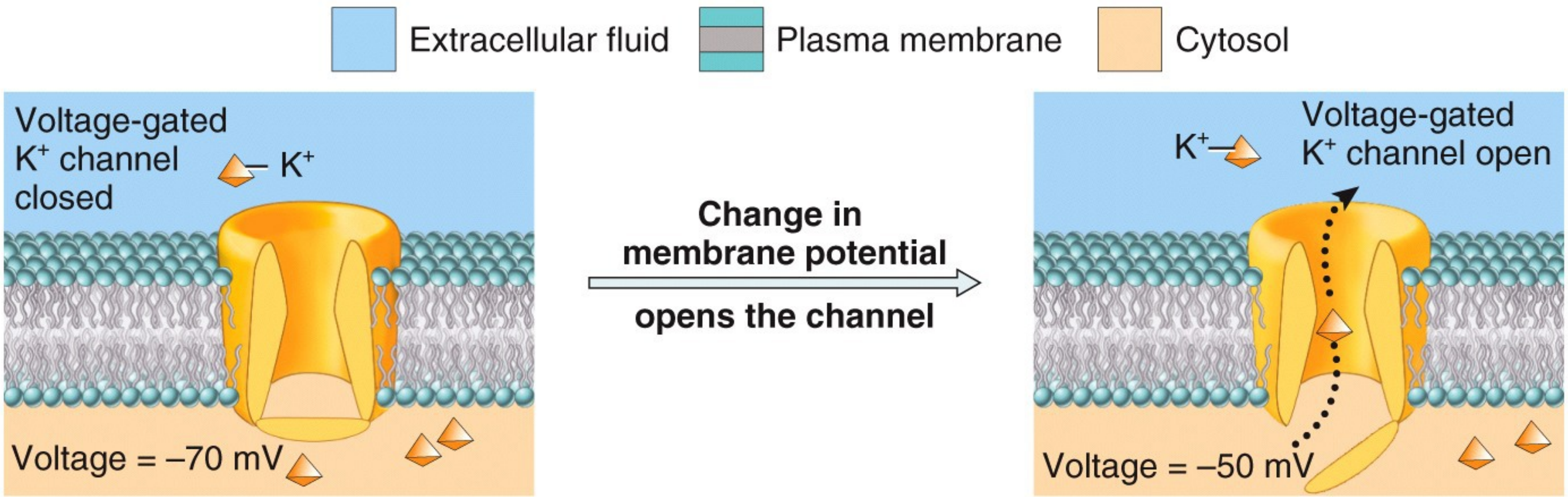
- Voltage = separation of ions
- Electrical current = the flow of ions
  - in the body, currents created by movement of ions (e.g. Na^+ or K^+) through gated channels in the plasma membrane
  - gated channels are opened or closed by various stimuli (voltage / ligand / mechanical)
  - some transmembrane protein channels are not regulated but simply “leak ions” (we will overlook this factor in our discussion of action potentials)
  - *Key idea: regulated gates enables cell to allow ions to flow /// results in electrical currents /// creates mechanism that can be used to regulate cellular events*



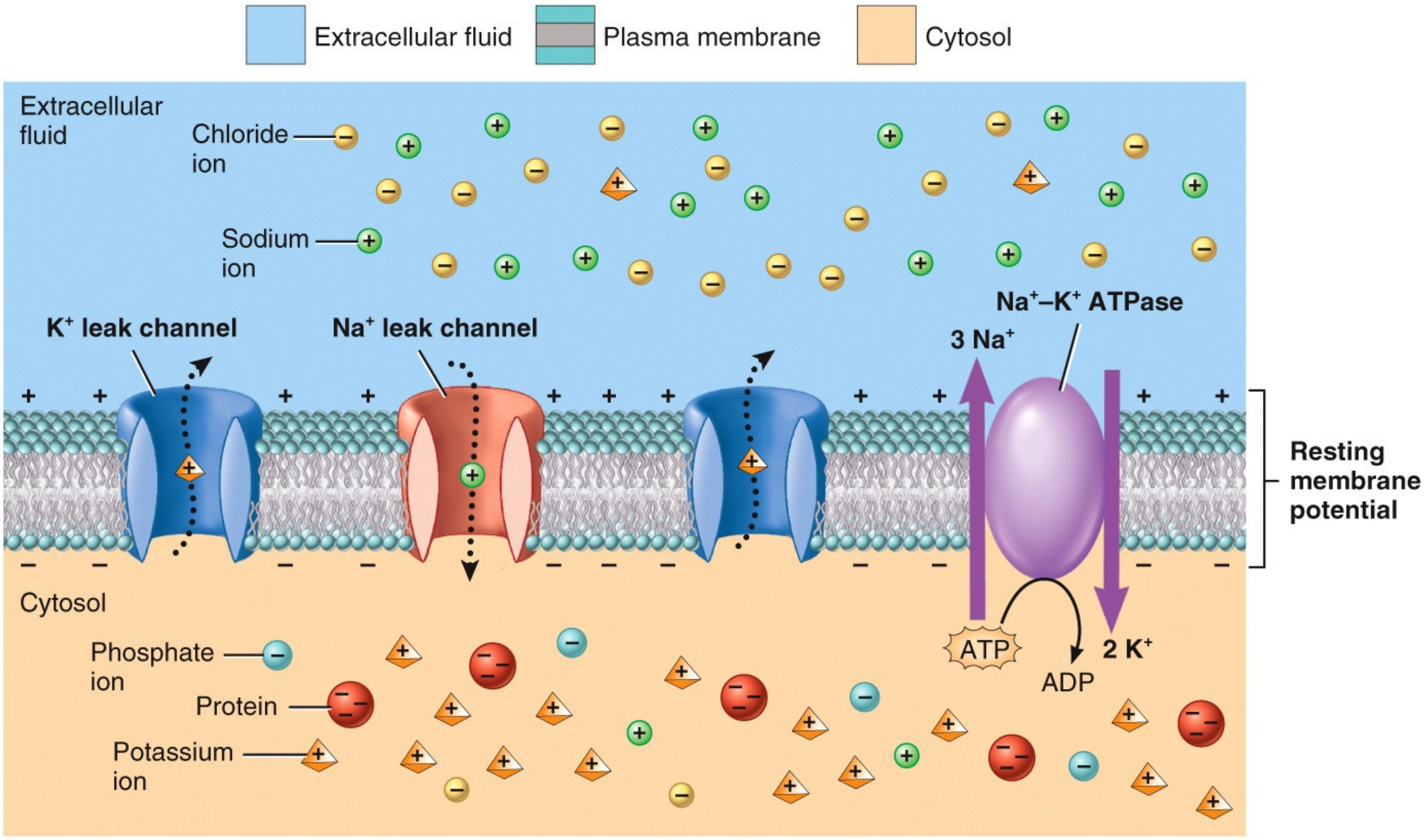
(b) Ligand-gated channel



(c) Mechanically-gated channel



(d) Voltage-gated channel



Note: proteins are mostly negatively charges // therefore anions of the proteins are “trapped” inside the cell // major factor in determining negative charge on inner face of plasma membrane

Resting Membrane Potential

- All living cells are polarized // called the resting membrane potential (RMP)
  - charge difference across the plasma membrane
  - -70 mV RMP
  - negative value means there are more negatively charged particles on the inside face of the membrane than on the outside face (like a little battery)
  - nervous and muscle tissue may alter their resting membrane potential // sequentially opening and closing different gates to first reverse then restore the charge across the membrane // these are excitable tissue

Resting Membrane Potential

- RMP exists because of unequal electrolyte distribution across membrane
  - between extracellular fluid (ECF) and intracellular fluid (ICF)
- RMP results from the combined effect of three factors:
  - ions diffuse down their concentration gradient through membrane channels
  - plasma membrane channels are selectively permeable and allows some ions to pass easier than others
  - electrical attraction of cations and anions to each other

Factors Contributing to the Creation of the Resting Membrane Potential

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- Large cytoplasmic anions (e.g. proteins) can not escape
  - due to size or charge (phosphates, sulfates, small organic acids, proteins, ATP, and RNA)
  - these all carry negative charges
- Potassium ions (K^+) have the 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 and net diffusion of K^+ stops
  - K^+ is about 40 times as concentrated in the ICF as in the ECF

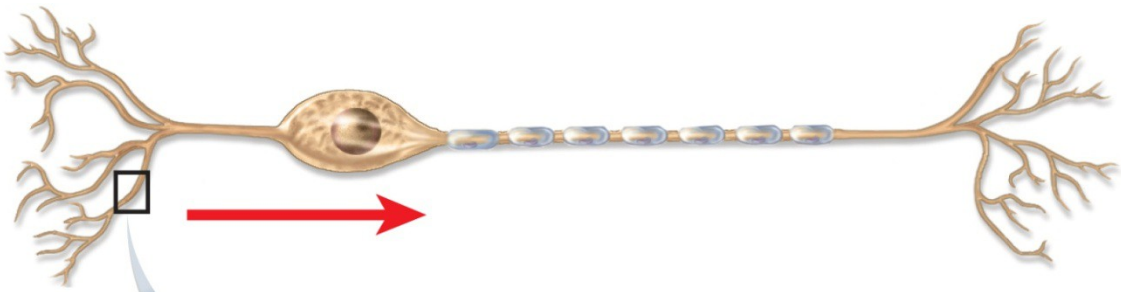
Factors Contributing to the Creation of Resting Membrane Potential

- Membrane much less permeable to high concentration of sodium (Na^+) found outside the cell
  - some sodium leak and diffuse into the cell // move down concentration gradient
  - Na^+ is about 12 times as concentrated in the ECF as in the ICF
  - resting membrane is much less permeable to Na^+ than K^+

Factor Contributing to the Creation and Maintenance of Resting Membrane Potential

- Na^+/K^+ ATPase pump // Transmembrane protein channel // moves out 3 Na^+ and moves in 2 K^+ for each ATP consumed
  - works continuously to compensate for Na+ and K+ leakage
  - requires great deal of ATP // A single cortical neuron utilizes approximately 4.7 billion ATPs per second in a resting human brain.
  - Tracing oxygen consumption, the brain accounts for about 20% of the body's energy consumption, despite only representing 2 percent of its weight. That's around 0.3 kilowatt hours (kWh) per day for an average adult, more than 100 times what the typical smartphone requires daily.Apr 27, 2023
  - necessitates glucose and oxygen be supplied to nerve tissue (energy needed to create the resting potential)
  - pump contributes about -3 mV to the cell's resting membrane potential of -70 mV

Local Potentials



- Sodium ions move into neuron at dendrites and/or somas when a neuron is stimulated
- Local potential response is initiated at the dendrite then spreads across the soma to trigger zone
- If stimulus great enough then local potential reaches the trigger zone /// achieves "threshold" and an action potential results
- *Other names for local potentials are end plate potential or receptor potential*

Local Potentials

- Occurs when a **neuron is stimulated** by chemicals, light, heat or mechanical disturbance
  - Stimulus opens the Na^+ gates and allows Na^+ to rush in to the cell
  - Na^+ inflow neutralizes some of the internal negative charge
  - Voltage measured across the membrane drifts toward zero
  - This is known as depolarization

Local Potentials

- Occurs when membrane voltage shifts to a less negative value
- Na^+ diffuses across plasma membrane producing a current
- This depolarizing event moves across neuron's membrane towards the cell's trigger zone // located at proximal end of the axon
- Current movement across dendrite and soma is the **local potential**
- If stimulus causing local potential strong enough so it reaches trigger zone then an action potential occurs in the axon

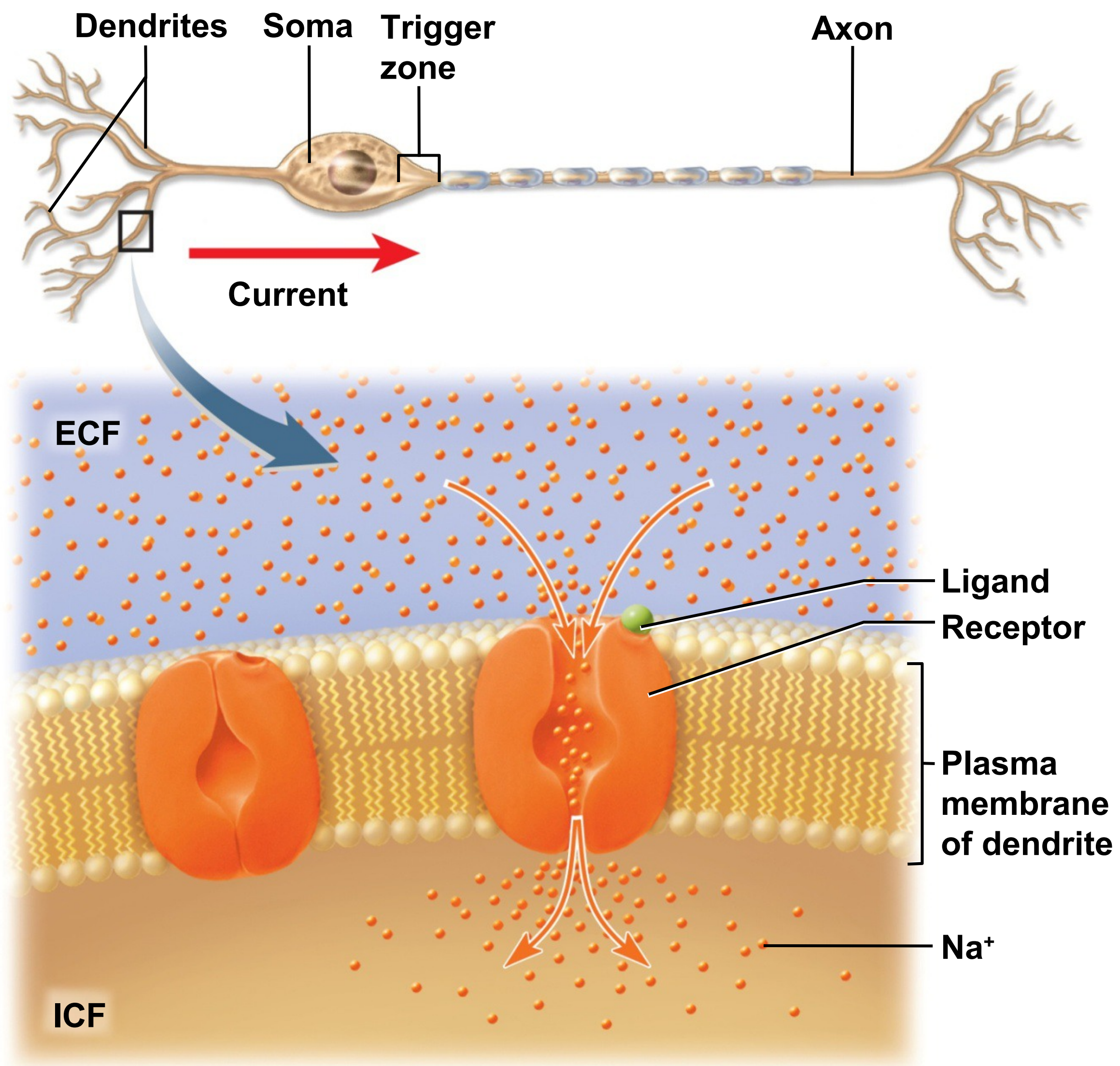
Four Characteristics of a Local Potentials

- Local potentials behave differently than 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 rapidly with distance

Four Characteristics of a Local Potentials

- Local potentials behave differently than action potentials:
  - **Reversible**
    - when stimulation ceases flow of Na stops
    - then K^+ diffusion out of cell // returns the cell to its normal resting potential
  - **Either excitatory** or **inhibitory**
    - E.g. / the neurotransmitter glycine make the membrane potential more negative
    - hyperpolarize membrane // less likely to produce an action potential // inhibitory

Excitation of a Neuron by a Chemical Stimulus



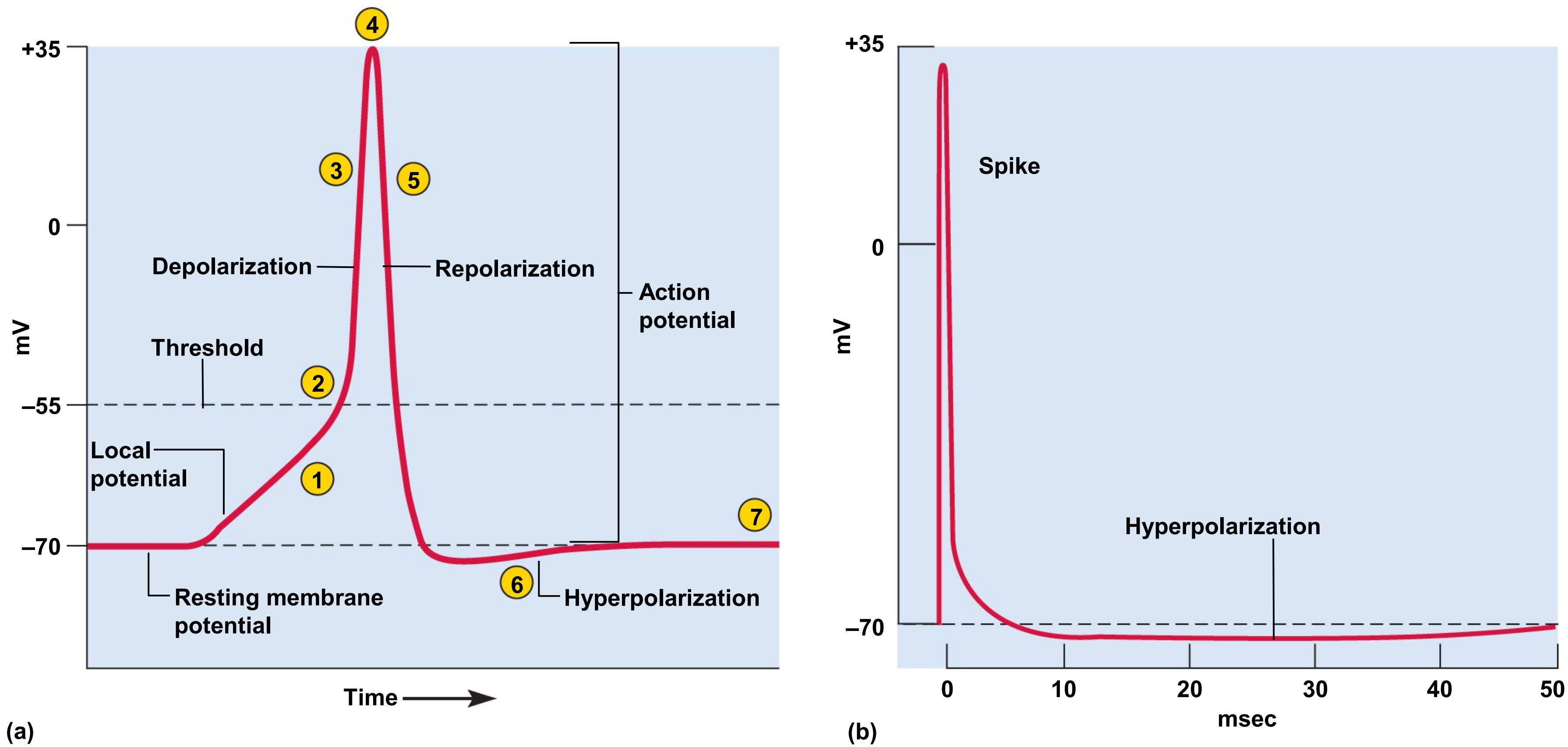
Action Potentials

- AP is a more dramatic change than local potential // AP is a positive feedback mechanism
- Produced by voltage-regulated ion gates in the plasma membrane at axon hillock
  - only occur where there is a high enough density of voltage-regulated gates (axon hillock = trigger zone)
  - **soma** (50 -75 gates per μm^2) - cannot generate an action potential
  - **trigger zone** (350 – 500 gates per μm^2) – where action potential is generated
  - if local potential spreads all the way to the trigger zone // will open gates at axon hillock to generate an action potential

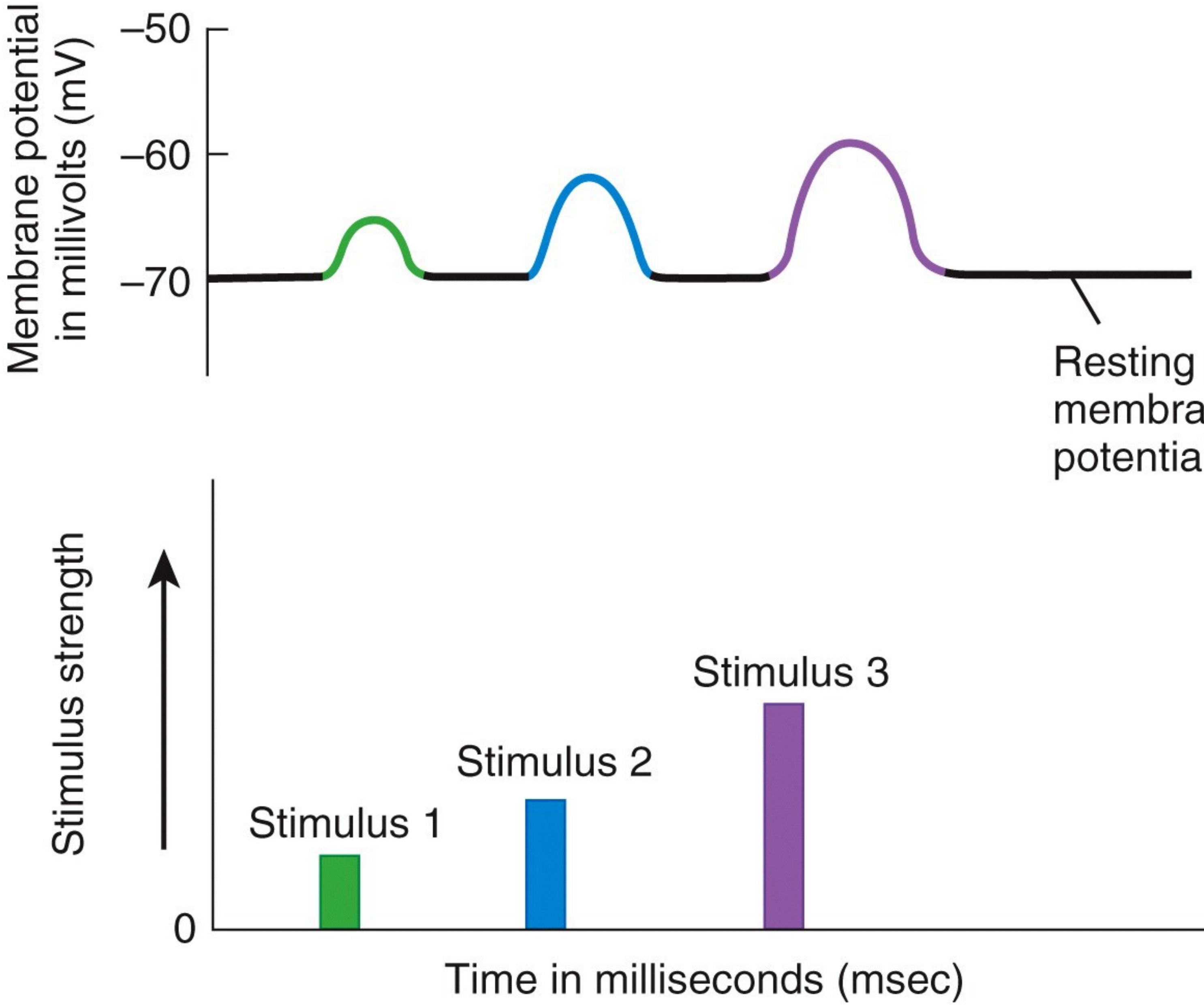
Action Potentials

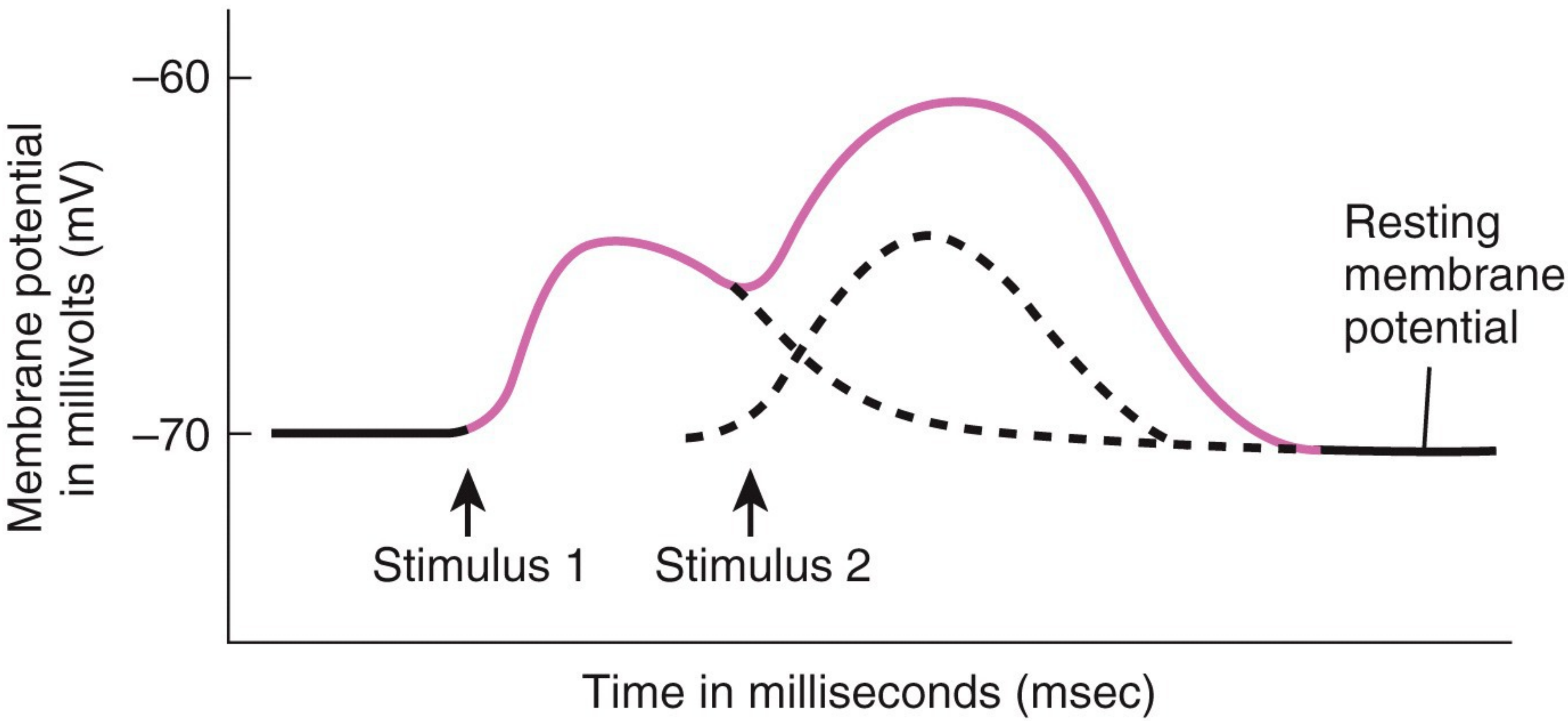
- An action potential is a rapid up-and-down shift in the membrane voltage
  - **threshold** – critical voltage which local potentials must reach in order to open the voltage-regulated gates at axon hillock
  - negative 55mV is threshold value in neurons

Action Potential

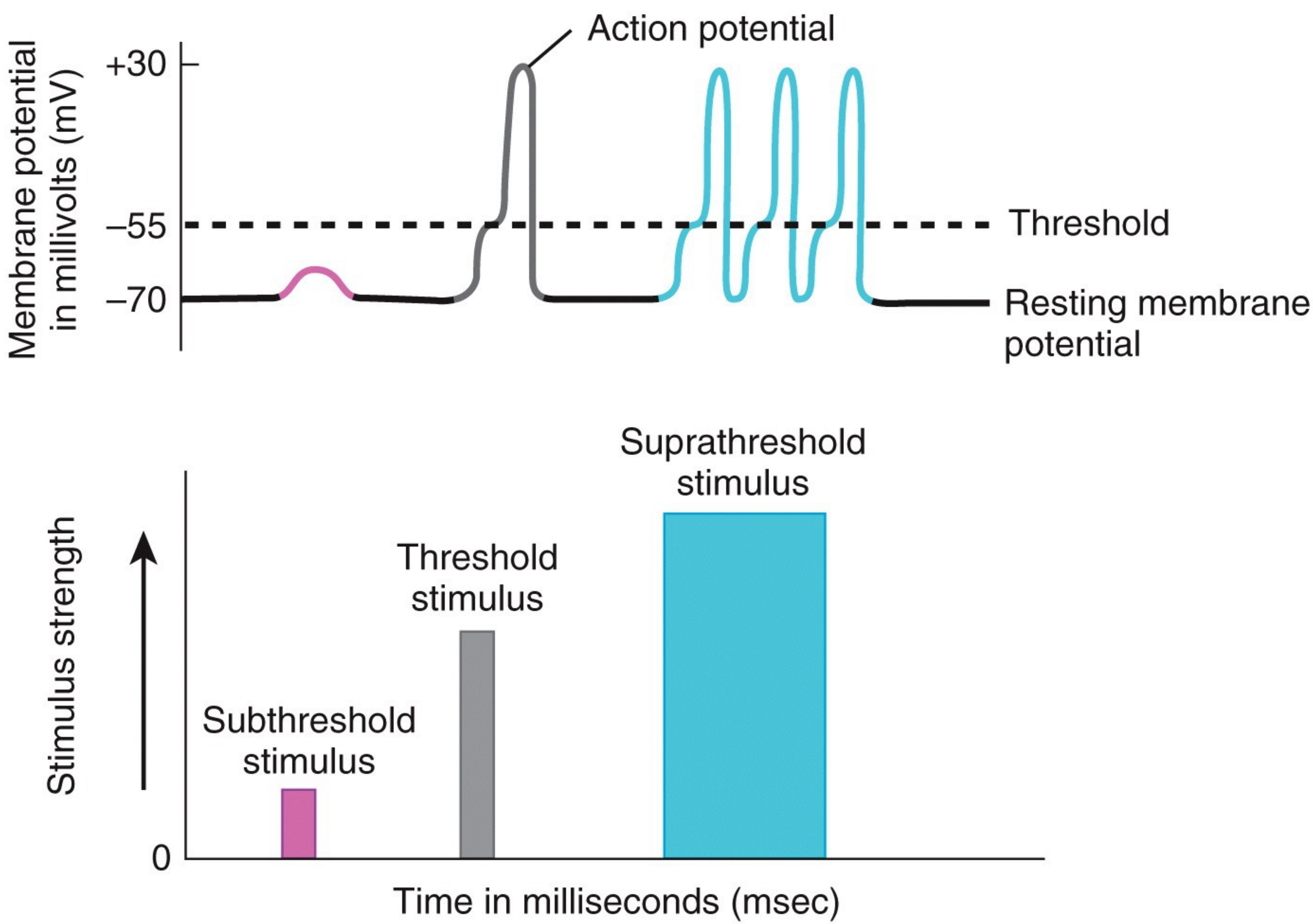


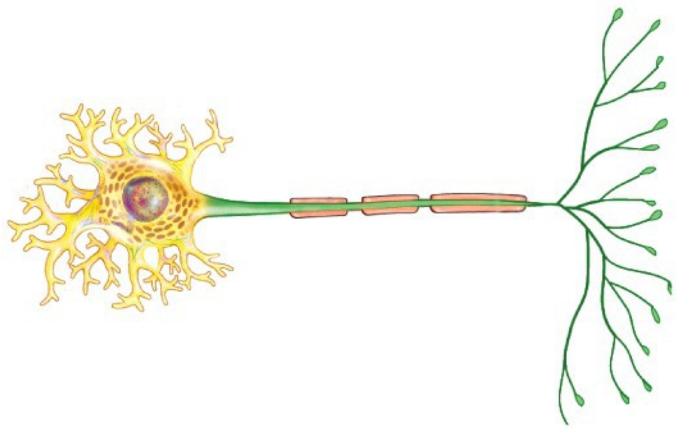
Action potential occurs so fast it is often referred to as a “spike”

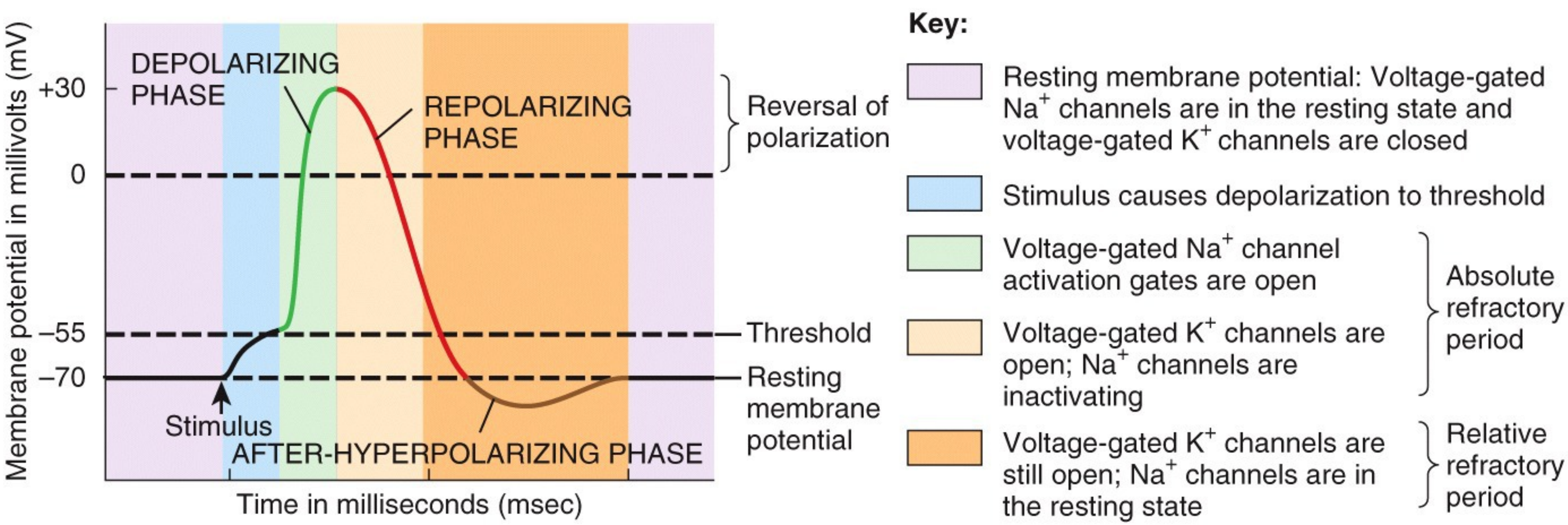

Membrane potential in millivolts (mV)
−50
−60
−70
Resting membrane potential
Stimulus strength
Stimulus 3
Stimulus 2
Stimulus 1
0
Time in milliseconds (msec)



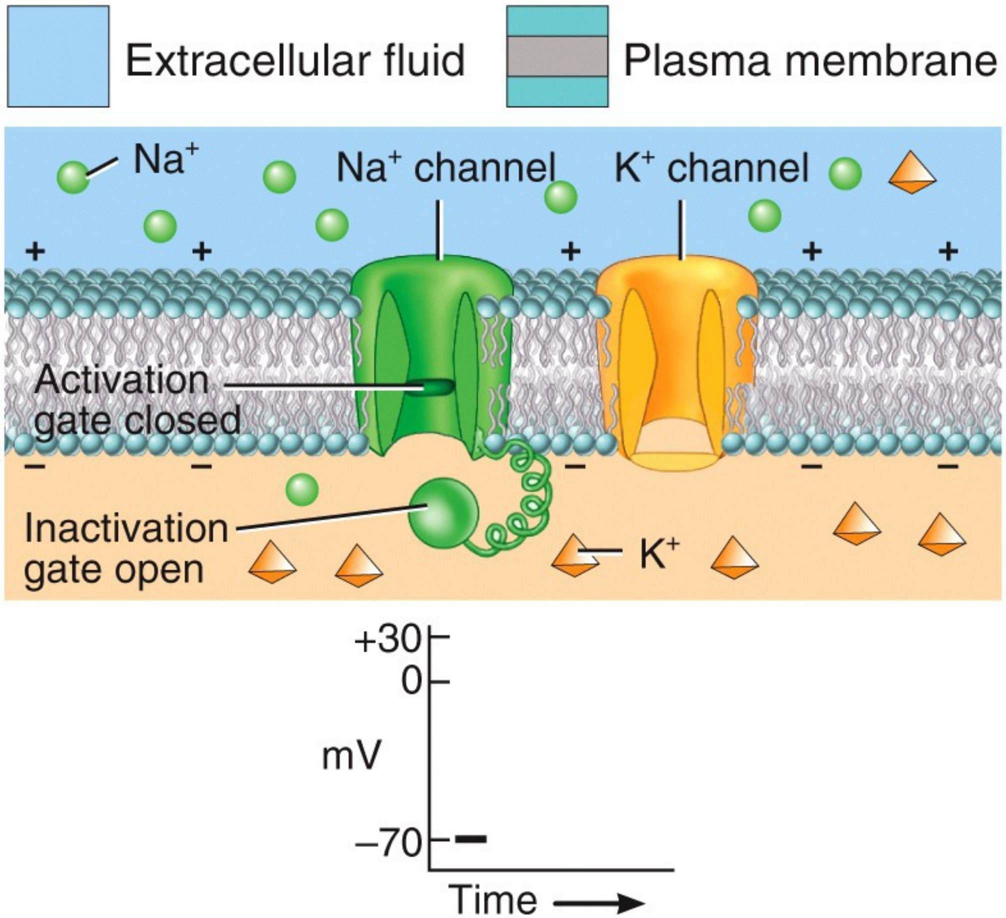
–60
–70
Membrane potential in millivolts (mV)
Resting membrane potential
Stimulus 1
Stimulus 2
Time in milliseconds (msec)


Action potential
Membrane potential in millivolts (mV)
+30
–55
–70
Threshold
Resting membrane potential
Stimulus strength
0
Subthreshold stimulus
Threshold stimulus
Suprathreshold stimulus
Time in milliseconds (msec)



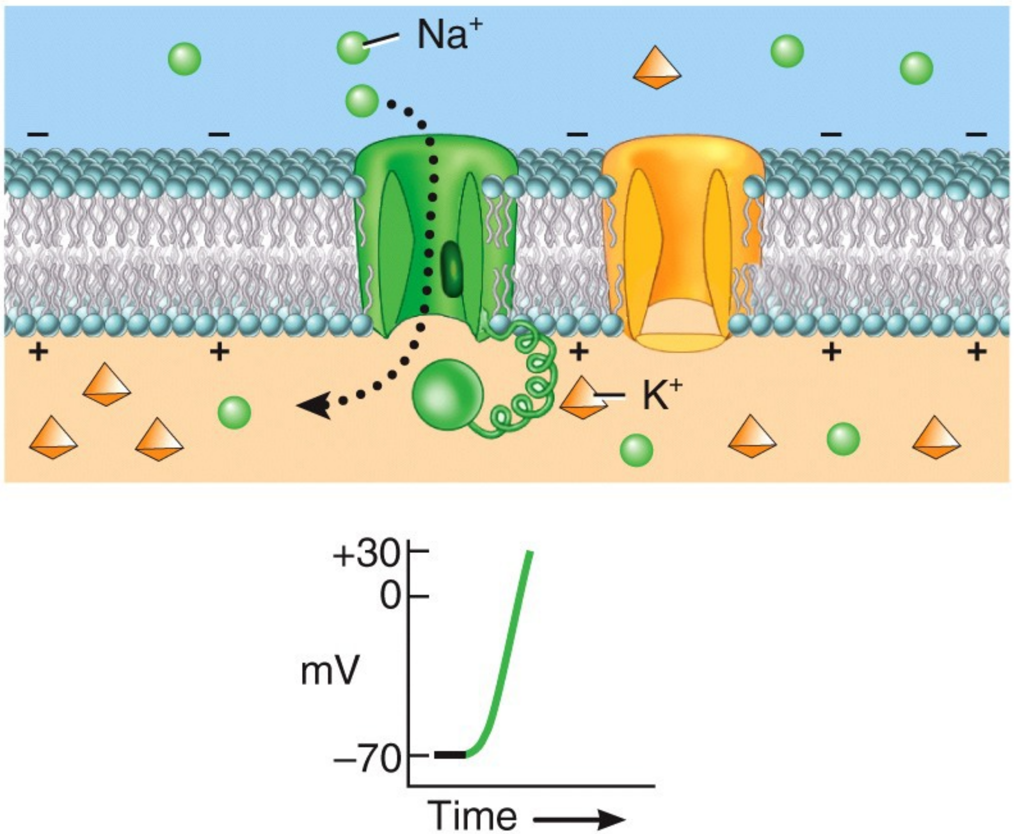


Four Phases: Resting – Depolarization – Repolarization - Hyperpolarizing

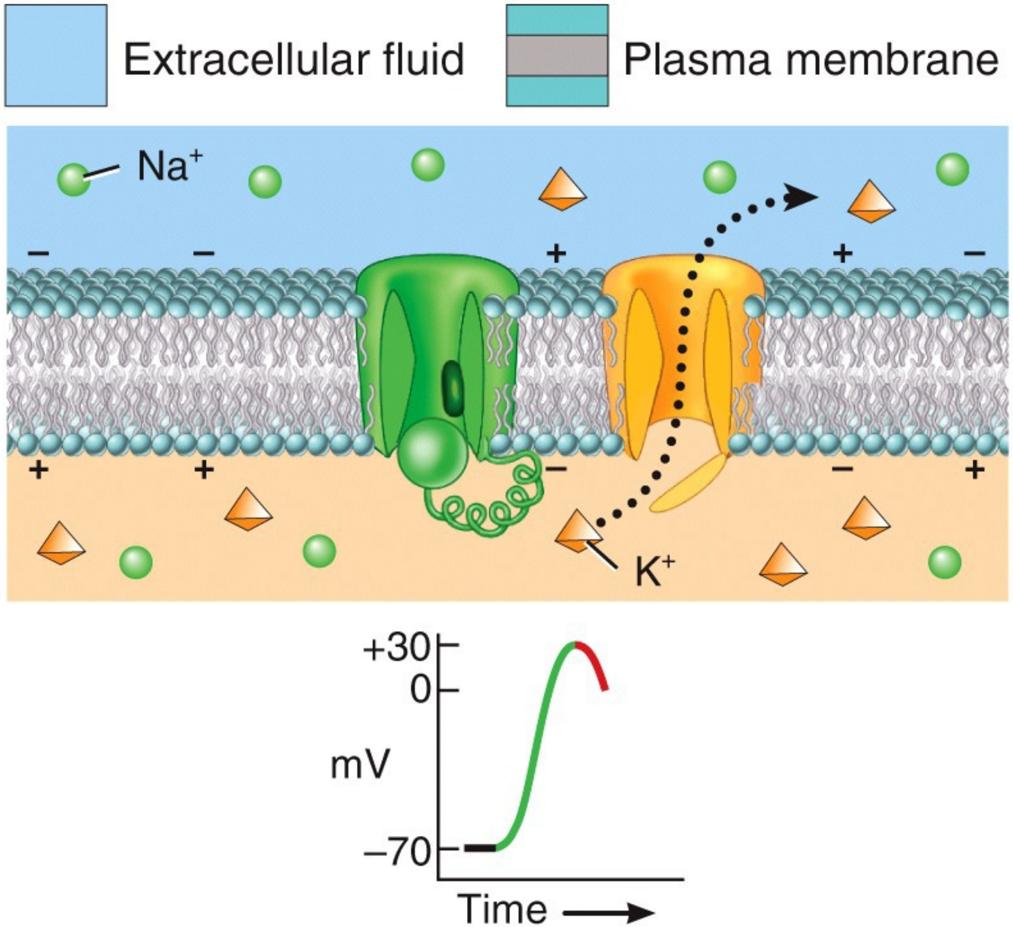


1. Resting state:

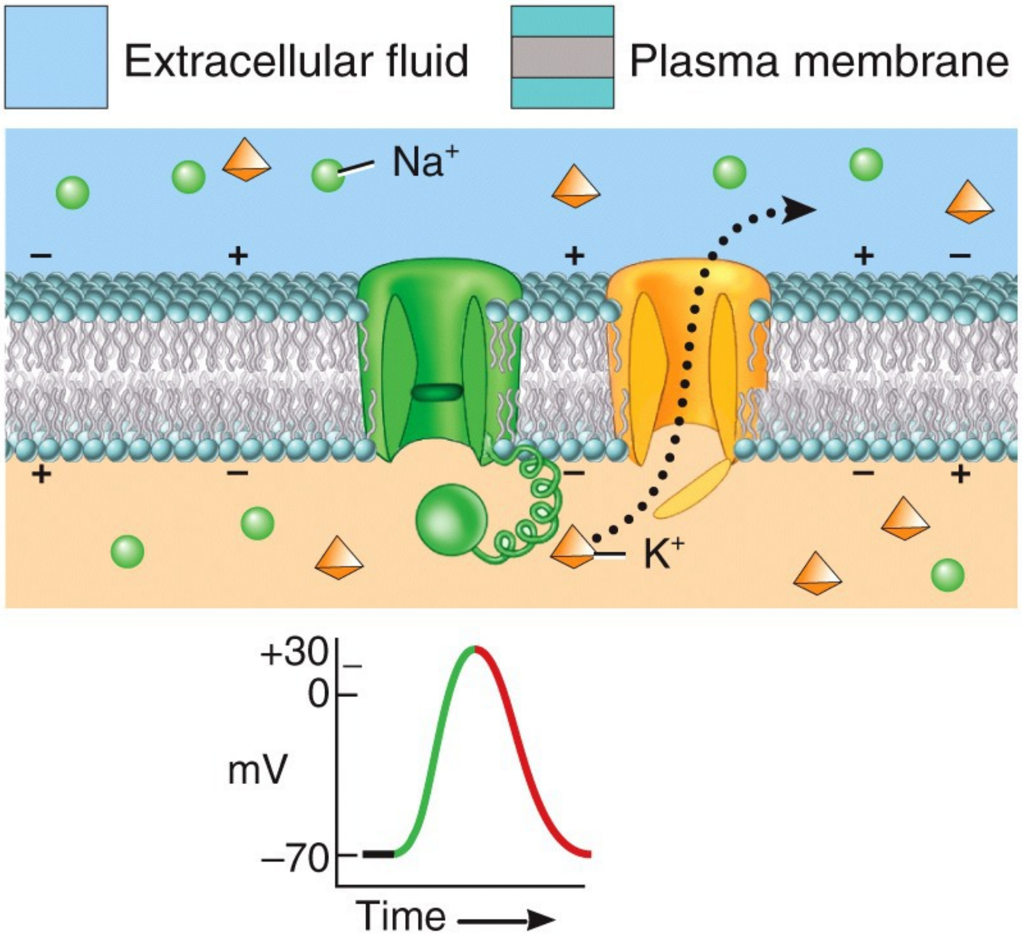
All voltage-gated Na^+ and K^+ channels are closed. The axon plasma membrane is at resting membrane potential: small buildup of negative charges along inside surface of membrane and an equal buildup of positive charges along outside surface of membrane.



2. Depolarizing phase: When membrane potential of axon reaches threshold, the Na^+ channel activation gates open. As Na^+ ions move through these channels into the neuron, a buildup of positive charges forms along inside surface of membrane and the membrane becomes depolarized.

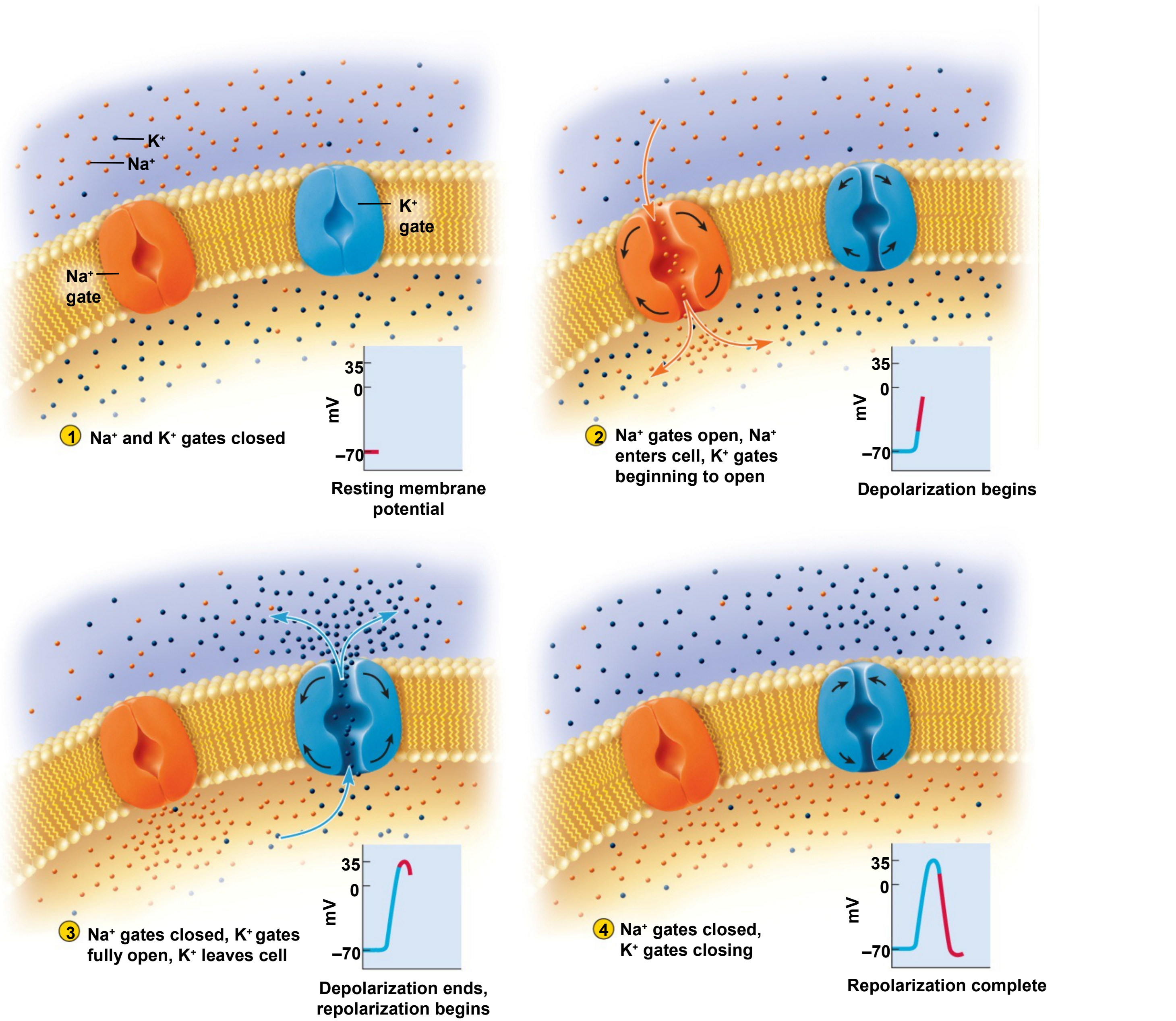


3. Repolarizing phase begins: Na^+ channel inactivation gates close and K^+ channels open. The membrane starts to become repolarized as some K^+ ions leave the neuron and a few negative charges begin to build up along the inside surface of the membrane.



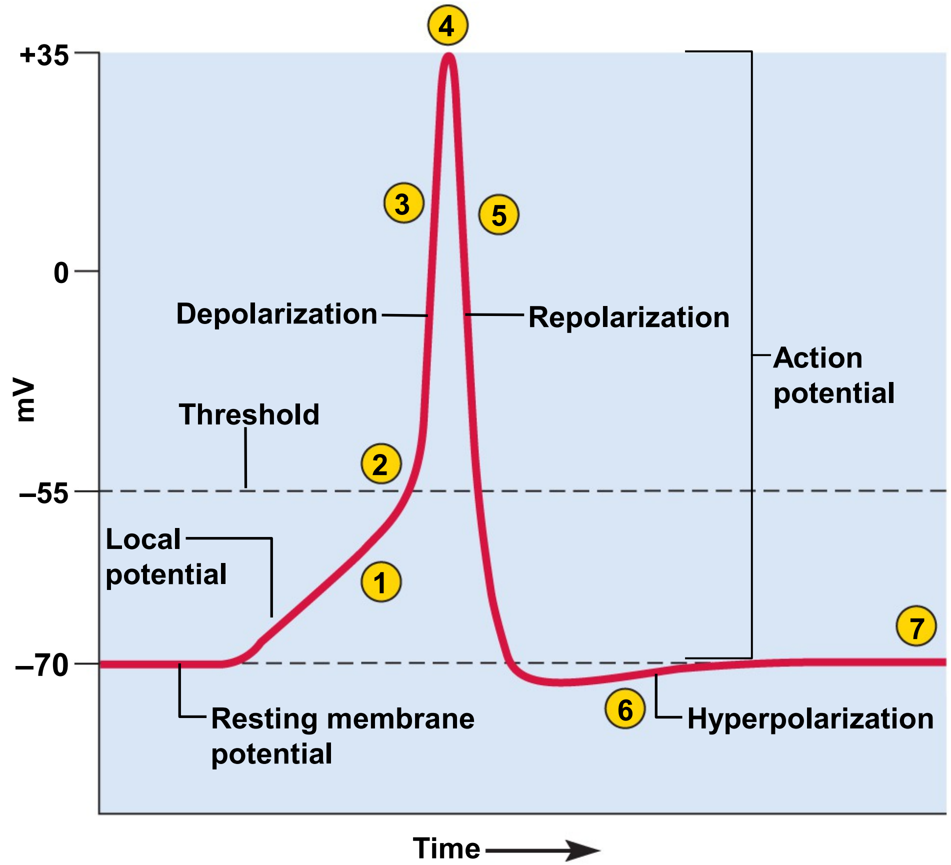
4. Repolarization phase continues:
K^+ outflow continues. As more K^+ ions leave the neuron, more negative charges build up along inside surface of membrane. K^+ outflow eventually restores resting membrane potential. Na^+ channel activation gates close and inactivation gates open. Return to resting state when K^+ gates close.

Sodium and Potassium Gates Function During Action Potential



Action Potentials

- only a thin layer of the cytoplasm next to the cell membrane is affected /// very few ions are involved
- action potential is often called a **spike**
- called spike because AP happens so fast



Action Potential Characteristics ★★

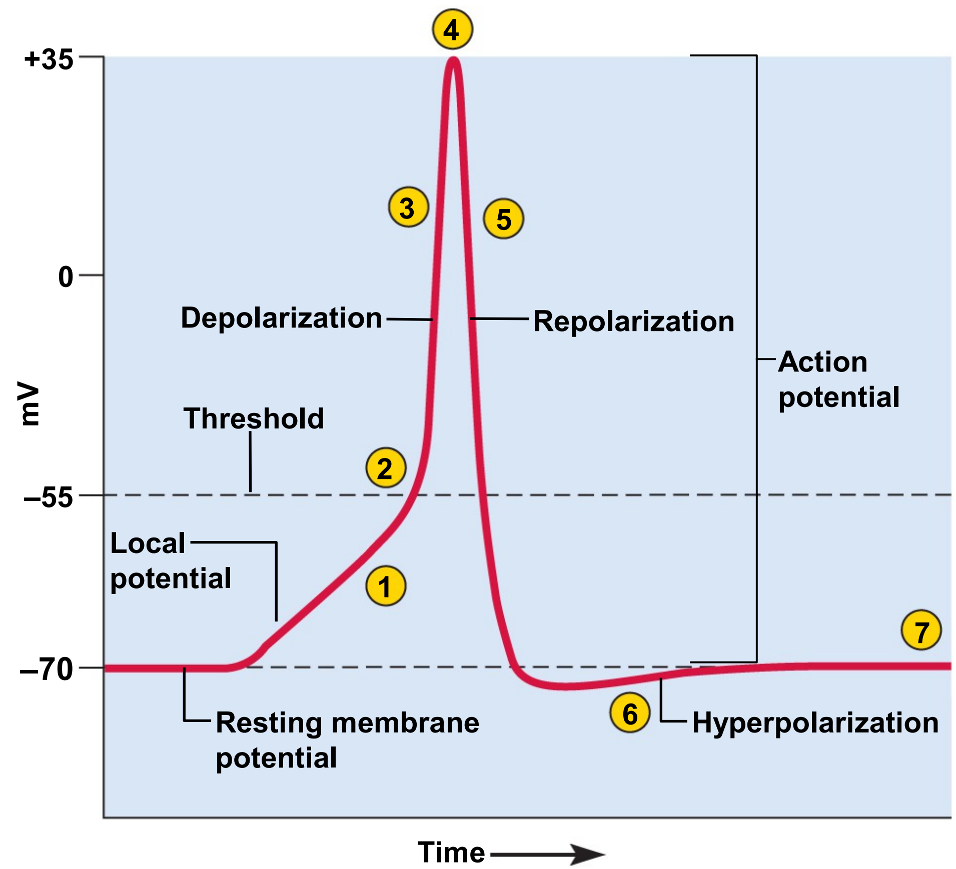
characteristics of action potential (event in axon) versus a local potential (event in dendrite/soma)

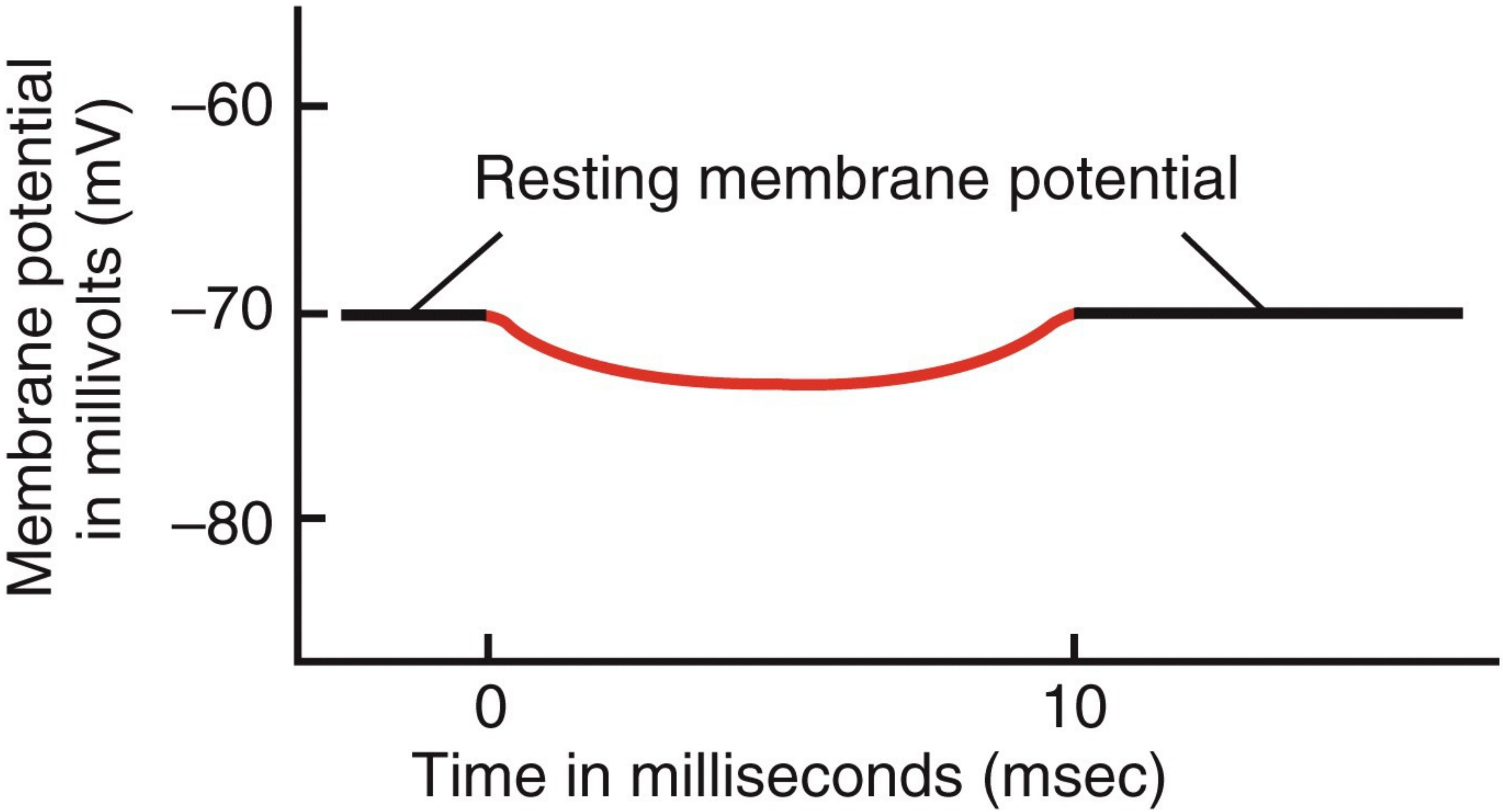
all-or-none law // if threshold is reached, neuron fires at its maximum voltage

if threshold is not reached it does not fire

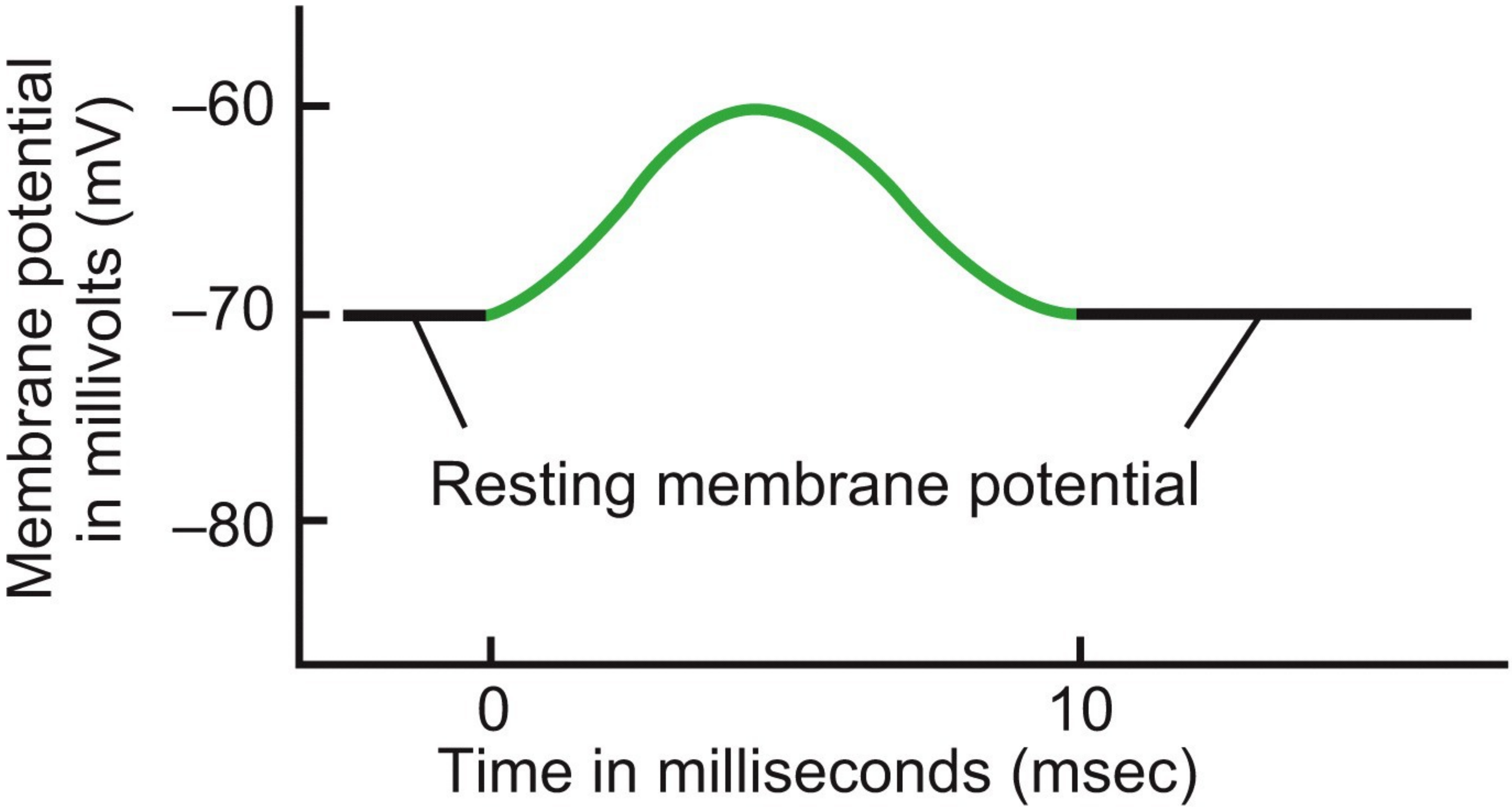
non-decremental - does not become weaker with distance

irreversible - once started goes to completion and can not be stopped



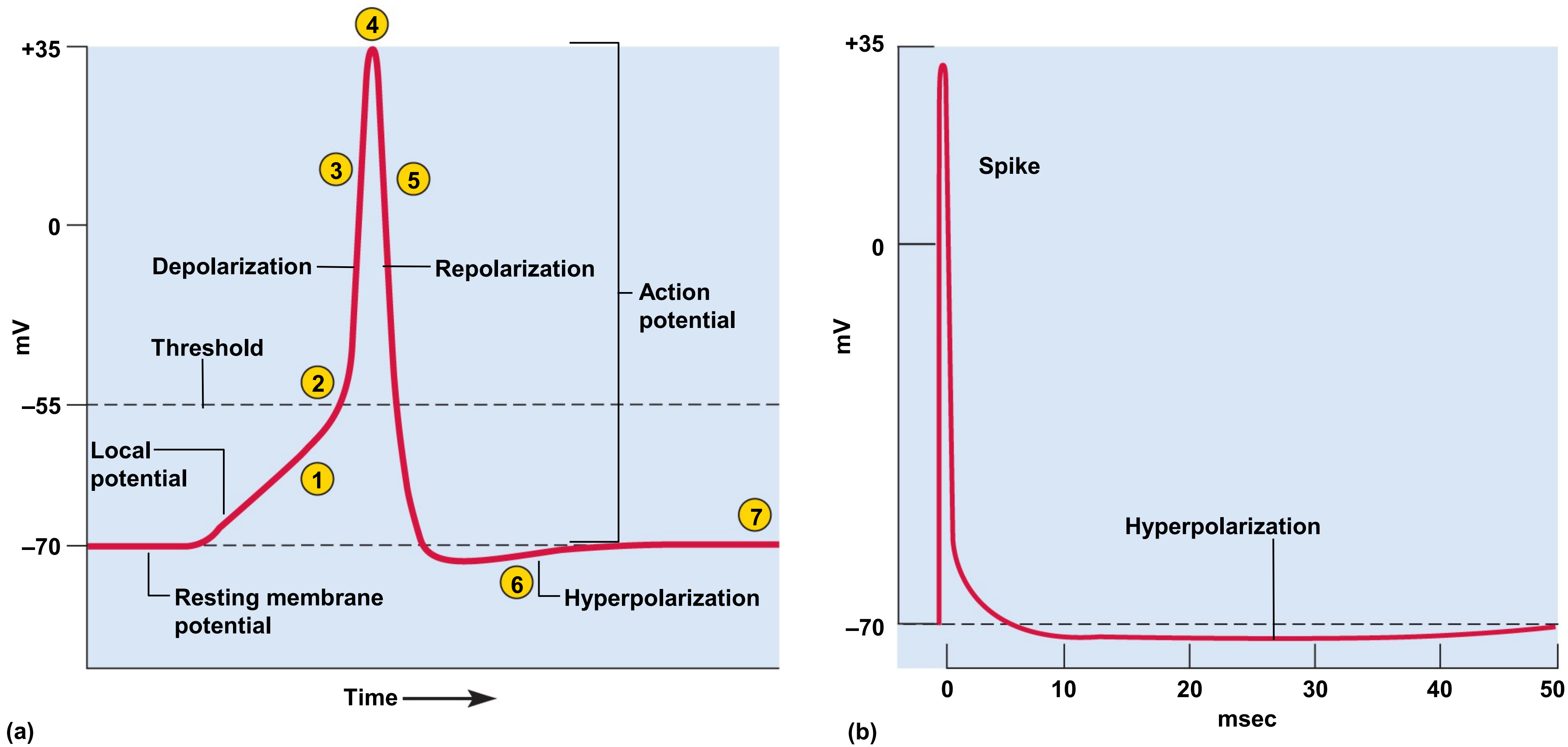


(a) Hyperpolarizing graded potential



(b) Depolarizing graded potential

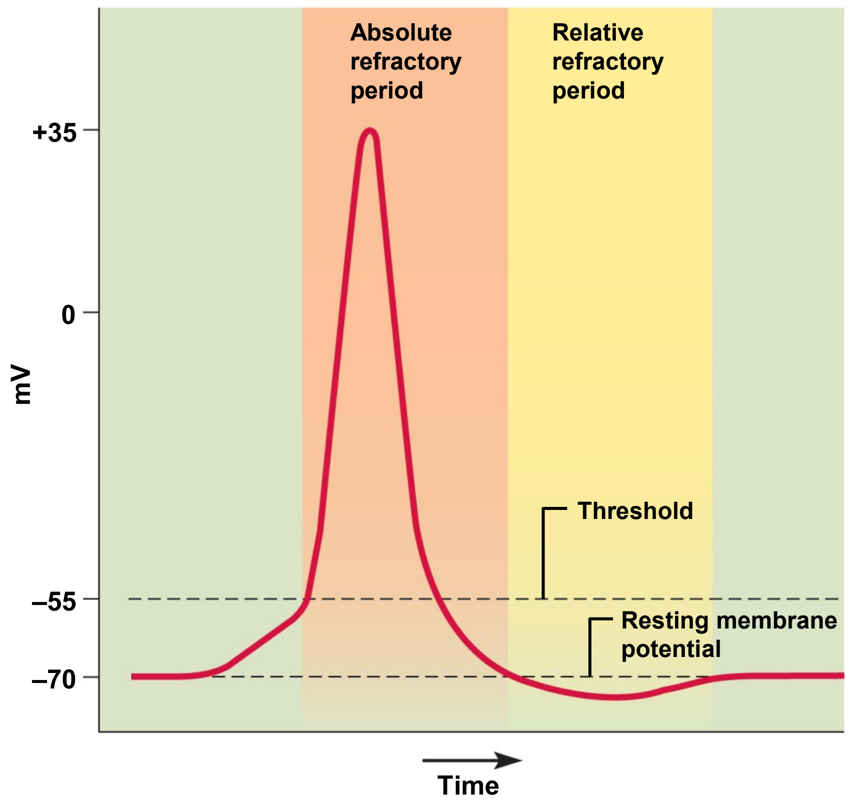
Action Potential



Action potential occurs so fast it is often referred to as a “spike”

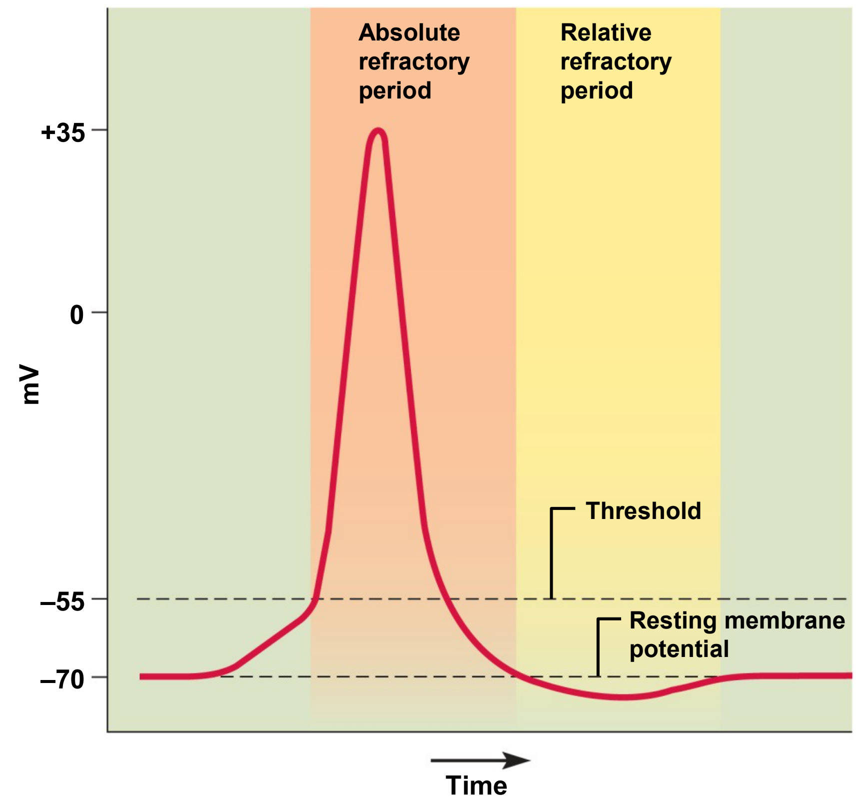
The Refractory Period

- **refractory period** – the period of resistance to stimulation
  - 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.
- two phases of the refractory period
  - **absolute refractory period**
    - no stimulus of any strength will trigger AP
    - as long as Na^+ gates are open
    - from action potential to RMP



The Refractory Period

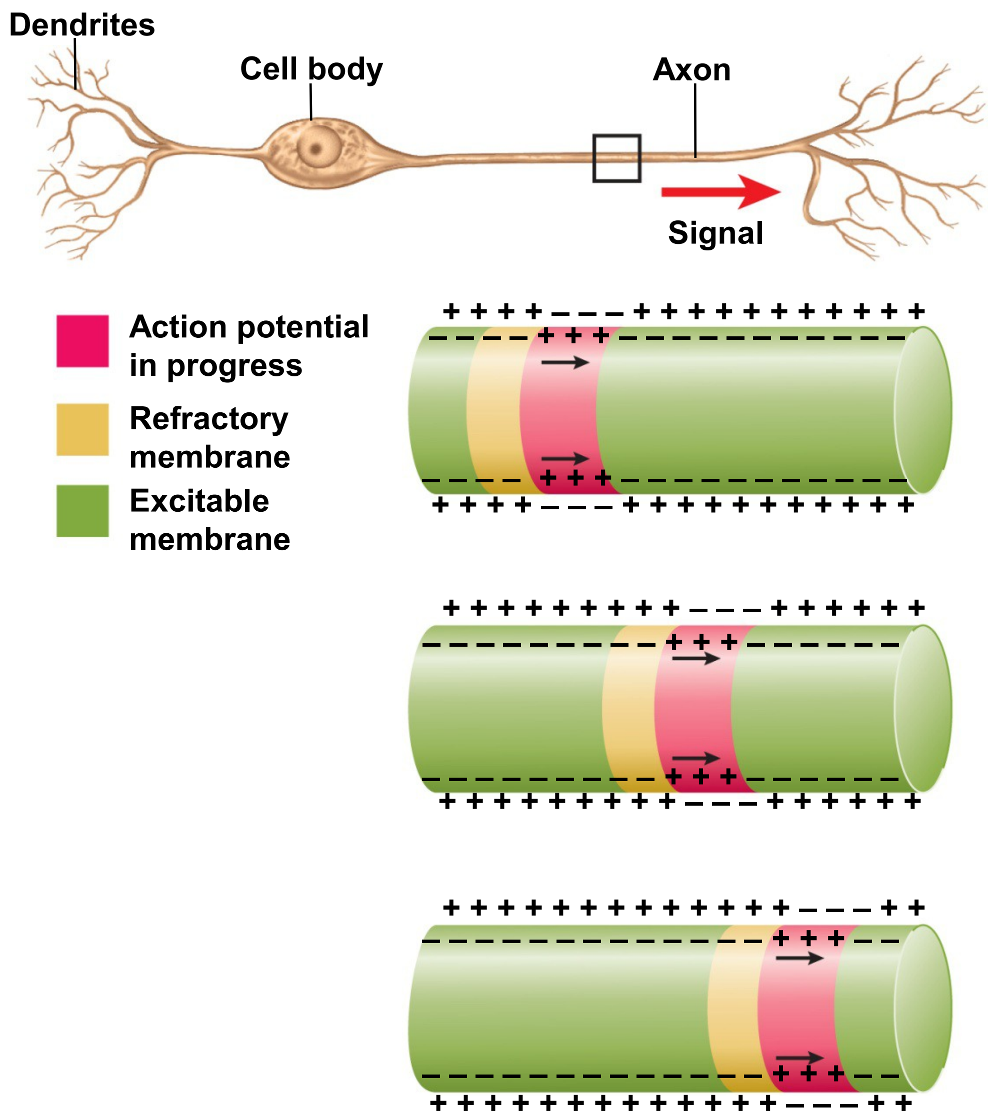
- two phases of the refractory period
  - **relative refractory period**
    - only especially strong stimulus will trigger new AP
    - K^+ gates are still open and any affect of incoming Na^+ is opposed by the outgoing K^+
- refractory period is occurring only at a small patch of the neuron's membrane at one time
- other parts of the neuron can be stimulated while the small part is in refractory period



Signal Conduction in Un-myelinated Fibers

- for AP conduction to occur, the nerve signal must travel to the end of the axon (reach synaptic knobs)
- unmyelinated fiber have voltage-regulated ion gates along its entire length
- action potential from the trigger zone causes Na^+ to enter the axon and diffuse into adjacent regions beneath the membrane
- the depolarization excites voltage-regulated gates immediately distal to the action potential.
- Na^+ and K^+ gates open and close producing a new action potential
- by repetition the membrane distal to that is excited
- chain reaction continues to the end of the axon
- unidirectional

Nerve Signal Conduction Unmyelinated Fibers

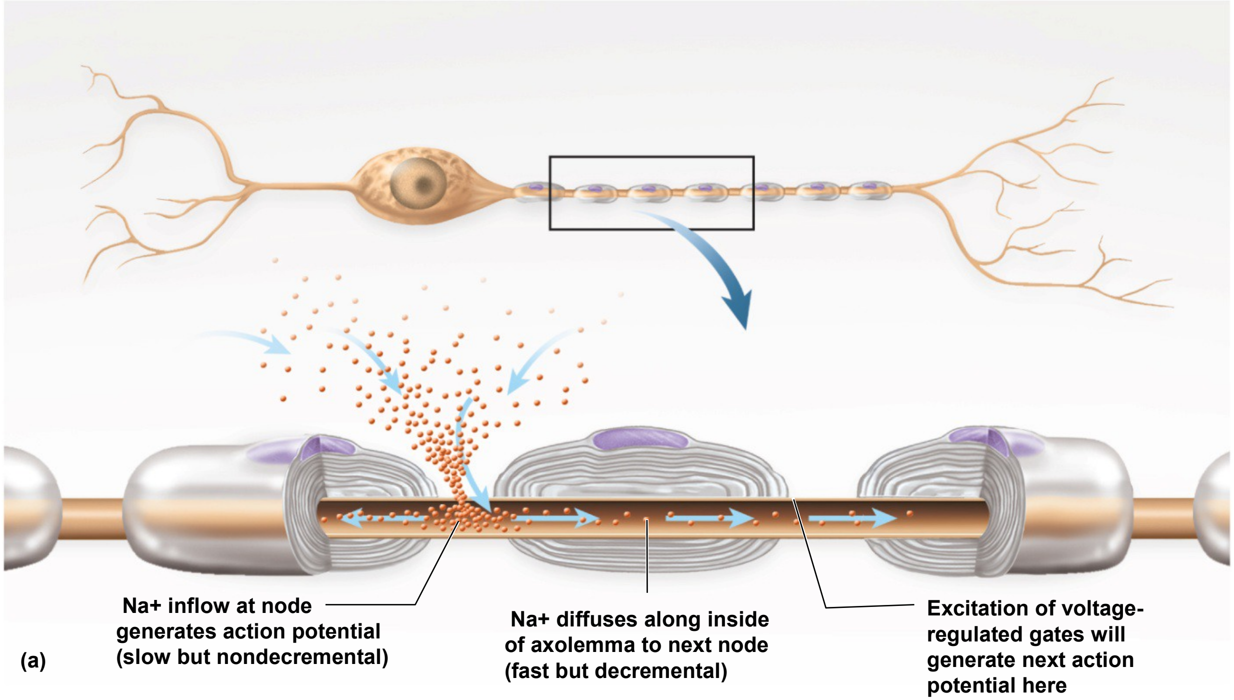


Saltatory Conduction in Myelinated Axons

- voltage-gated channels needed for AP
  - fewer than 25 per μm^2 in myelin-covered regions (internodes)
  - up to 12,000 per μm^2 in nodes of Ranvier

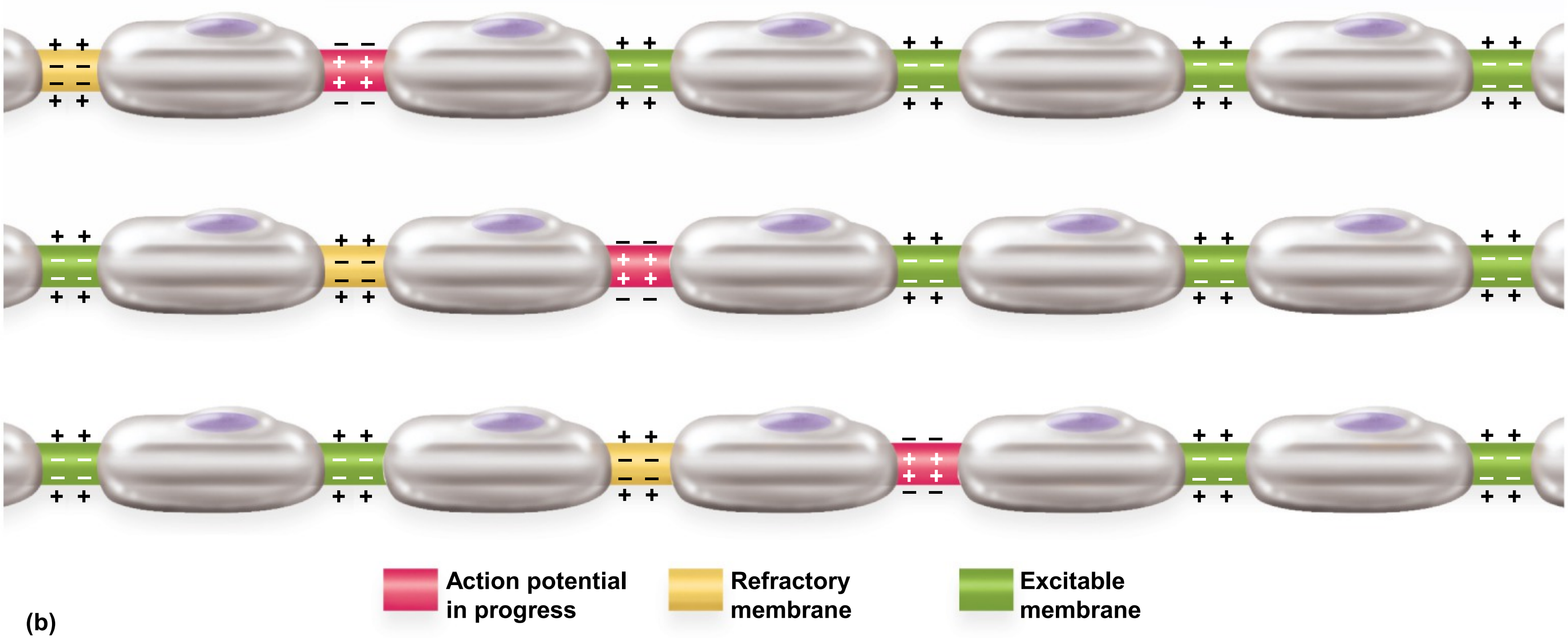
- fast Na^+ diffusion occurs between nodes /// signal weakens under myelin sheath, but still strong enough to stimulate an action potential at next node

- saltatory conduction – the nerve signal seems to jump from node to node // faster than in unmyelinated axons

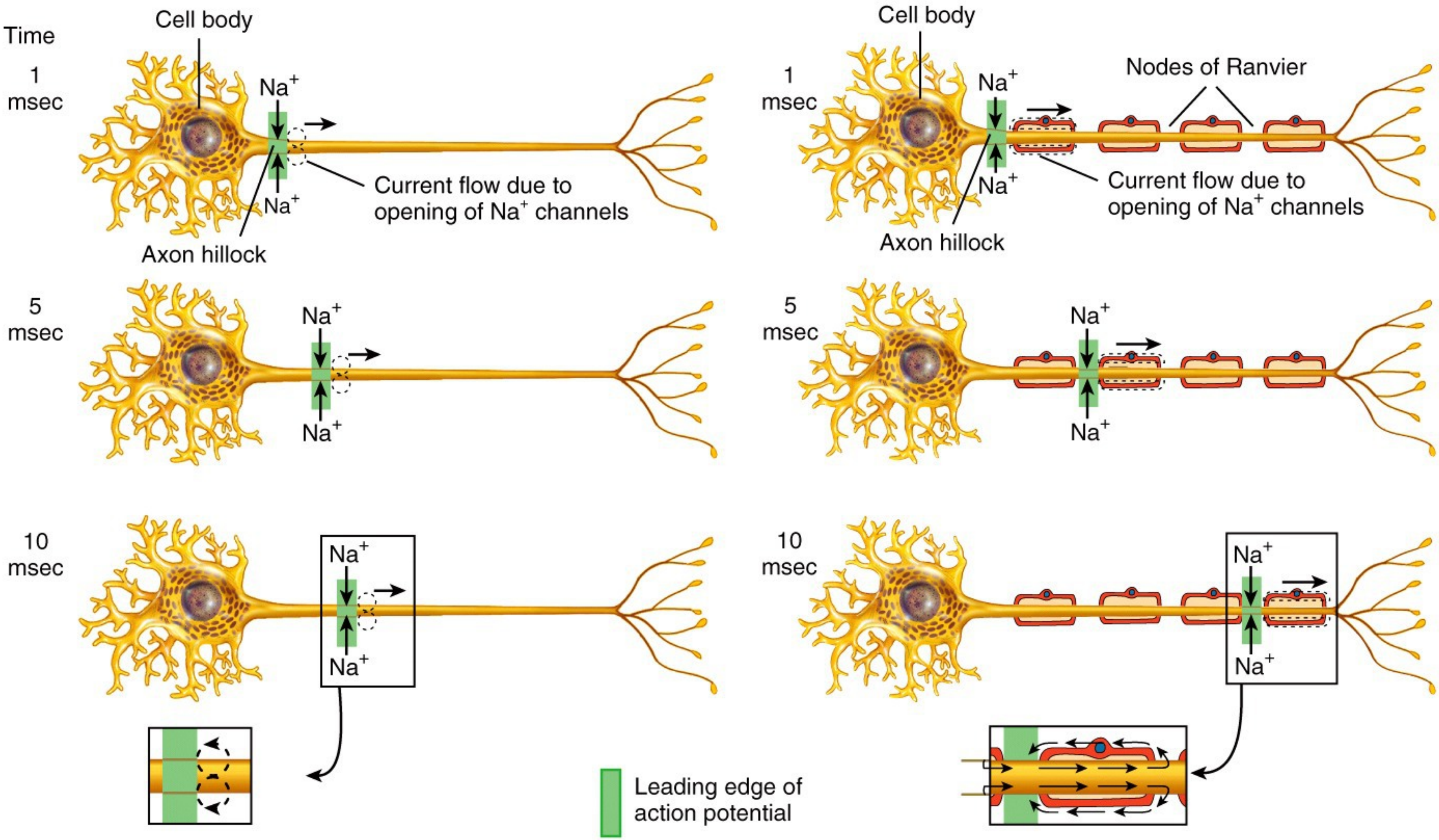


(a)

Saltatory Conduction

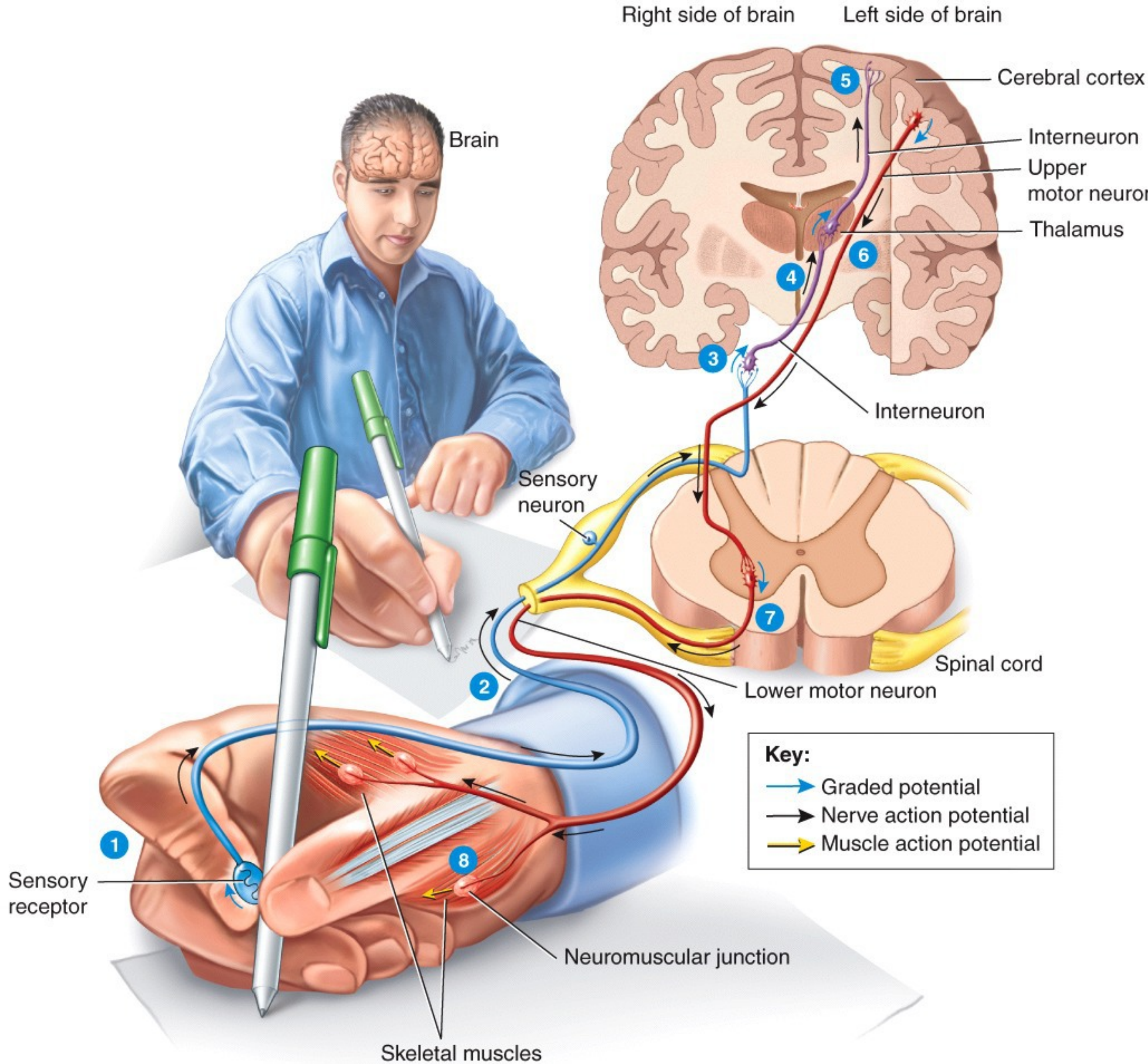


- faster than conduction speed in an unmyelinated axons

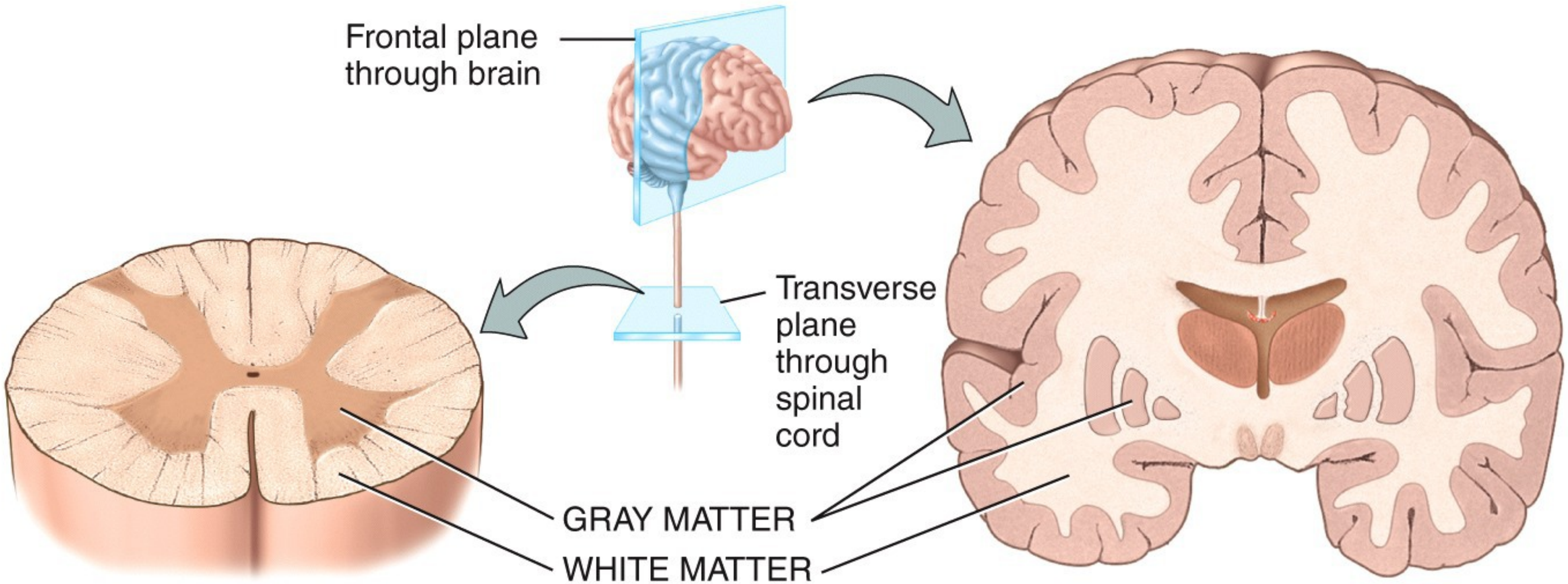


(a) Continuous conduction

(b) Saltatory conduction

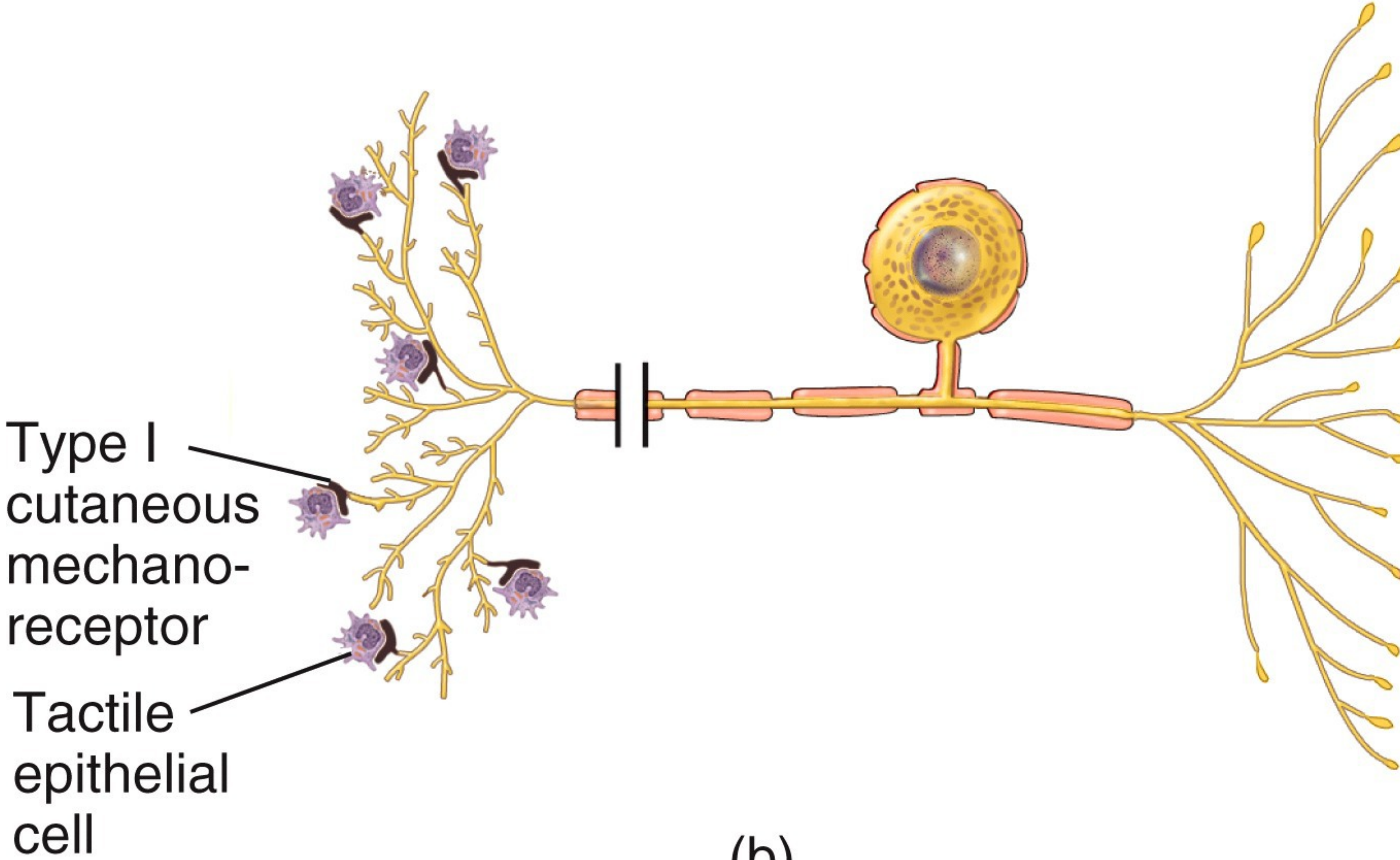


Right side of brain
Left side of brain
Cerebral cortex
Interneuron
Upper
motor neuron
Thalamus
Brain
1
2
3
4
5
6
7
8
Interneuron
Sensory
neuron
Spinal cord
Lower motor neuron
Sensory
receptor
Neuromuscular junction
Skeletal muscles
Key:
Graded potential
Nerve action potential
Muscle action potential

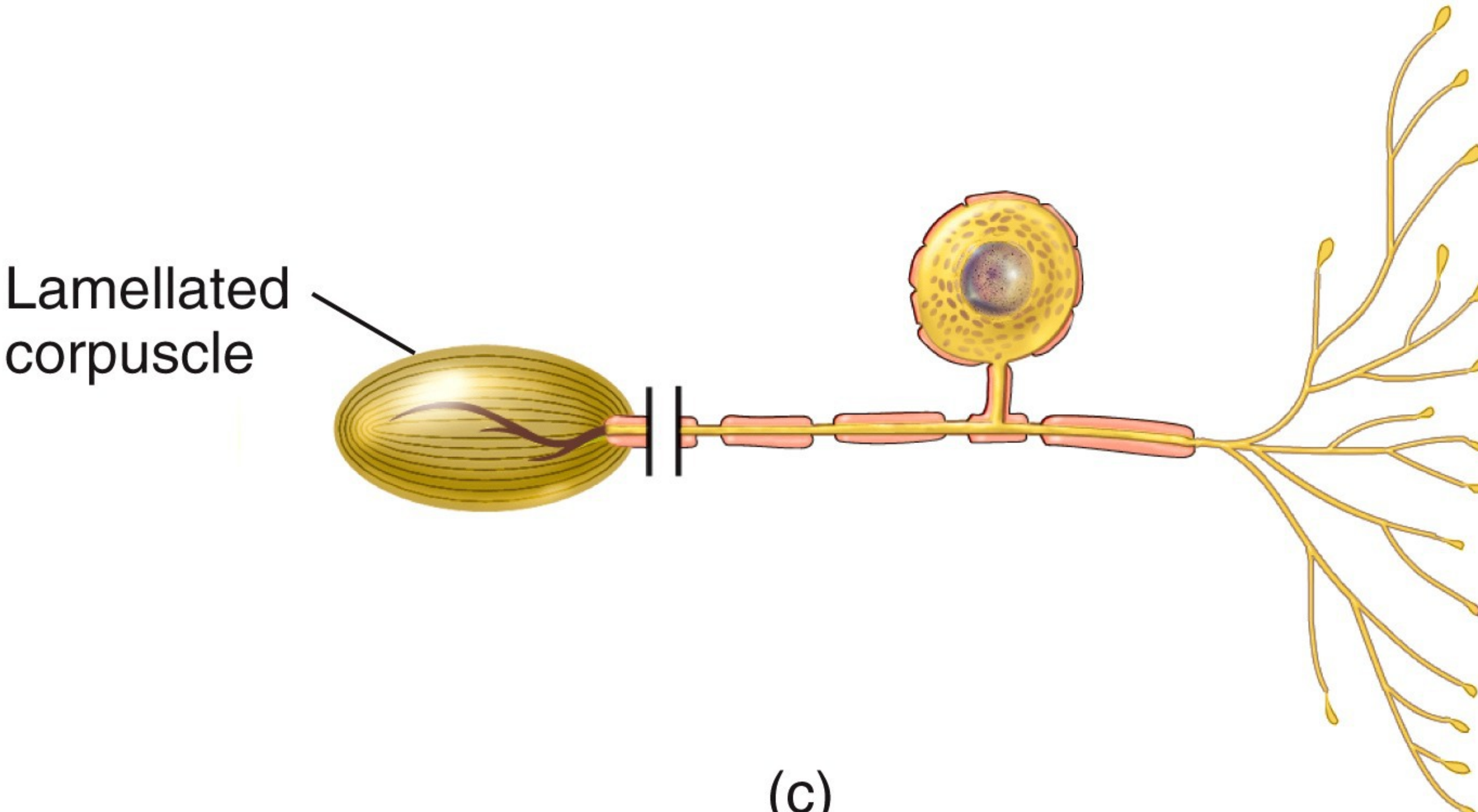


(a) Transverse section of spinal cord

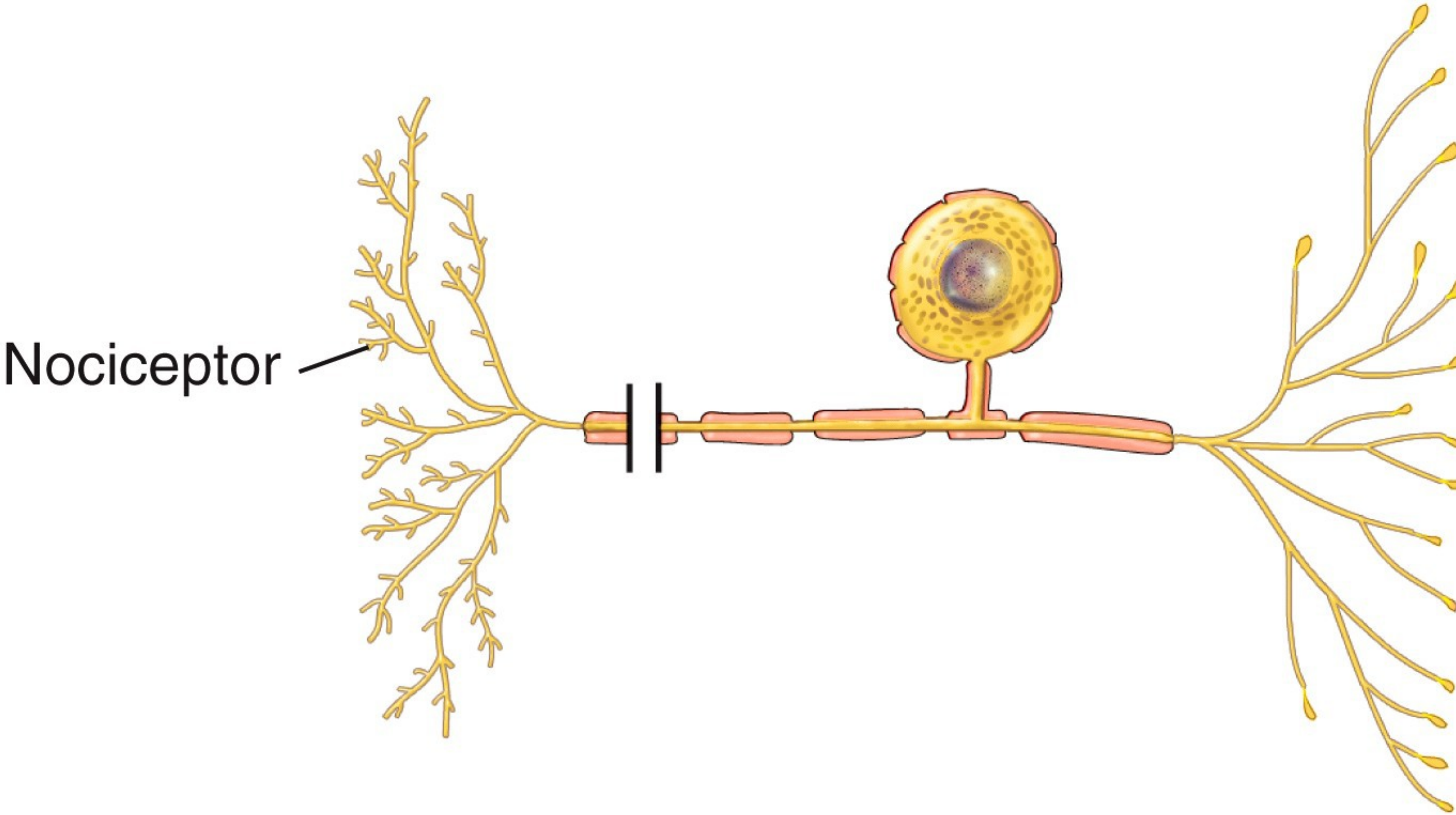
(b) Frontal section of brain


Type I
cutaneous
mechano-
receptor
Tactile
epithelial
cell

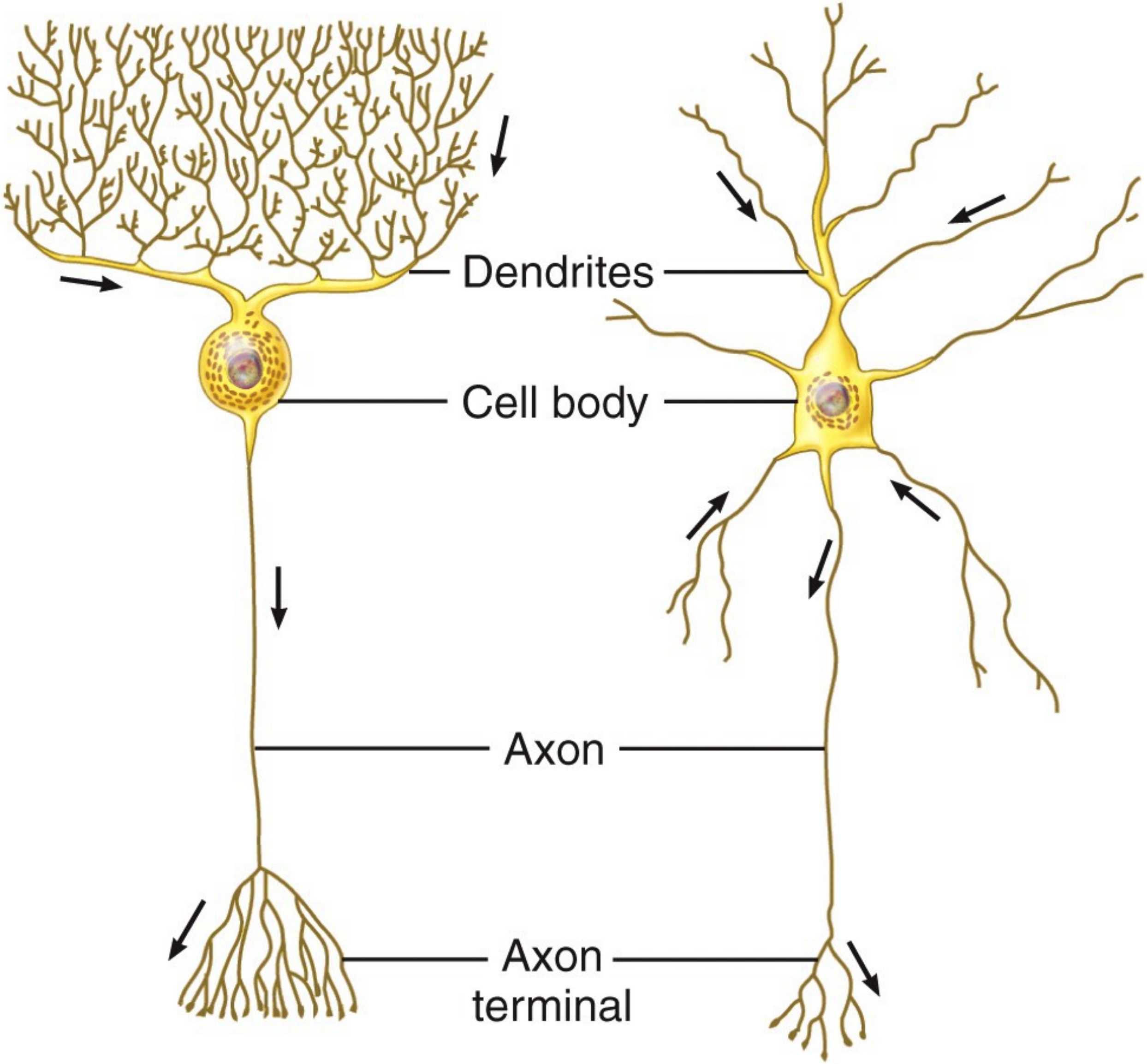
(b)



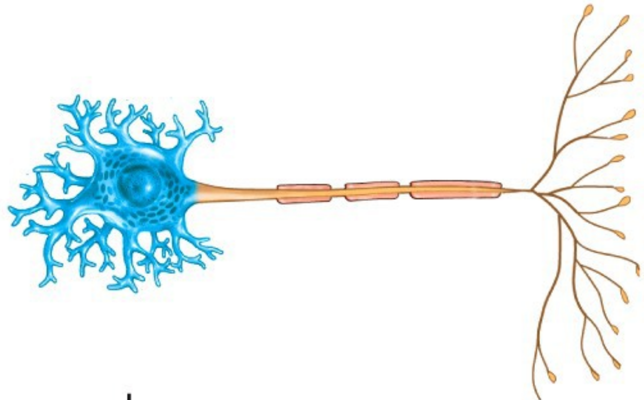
(c)

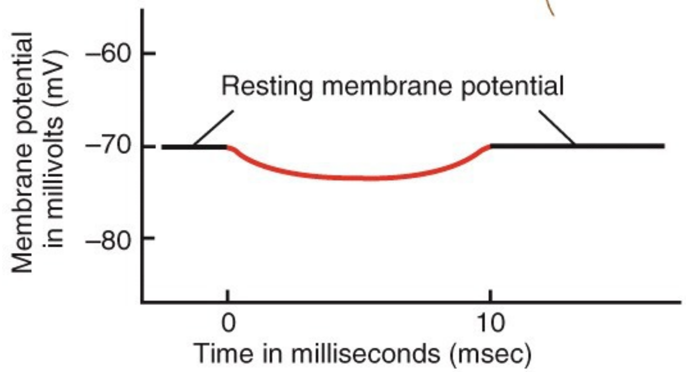


(d)

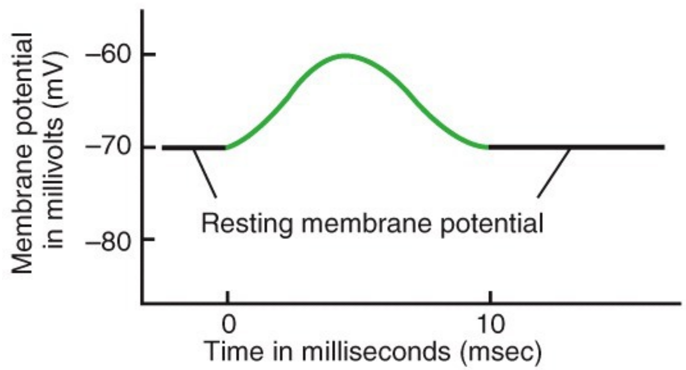


(a) Purkinje cell (b) Pyramidal cell

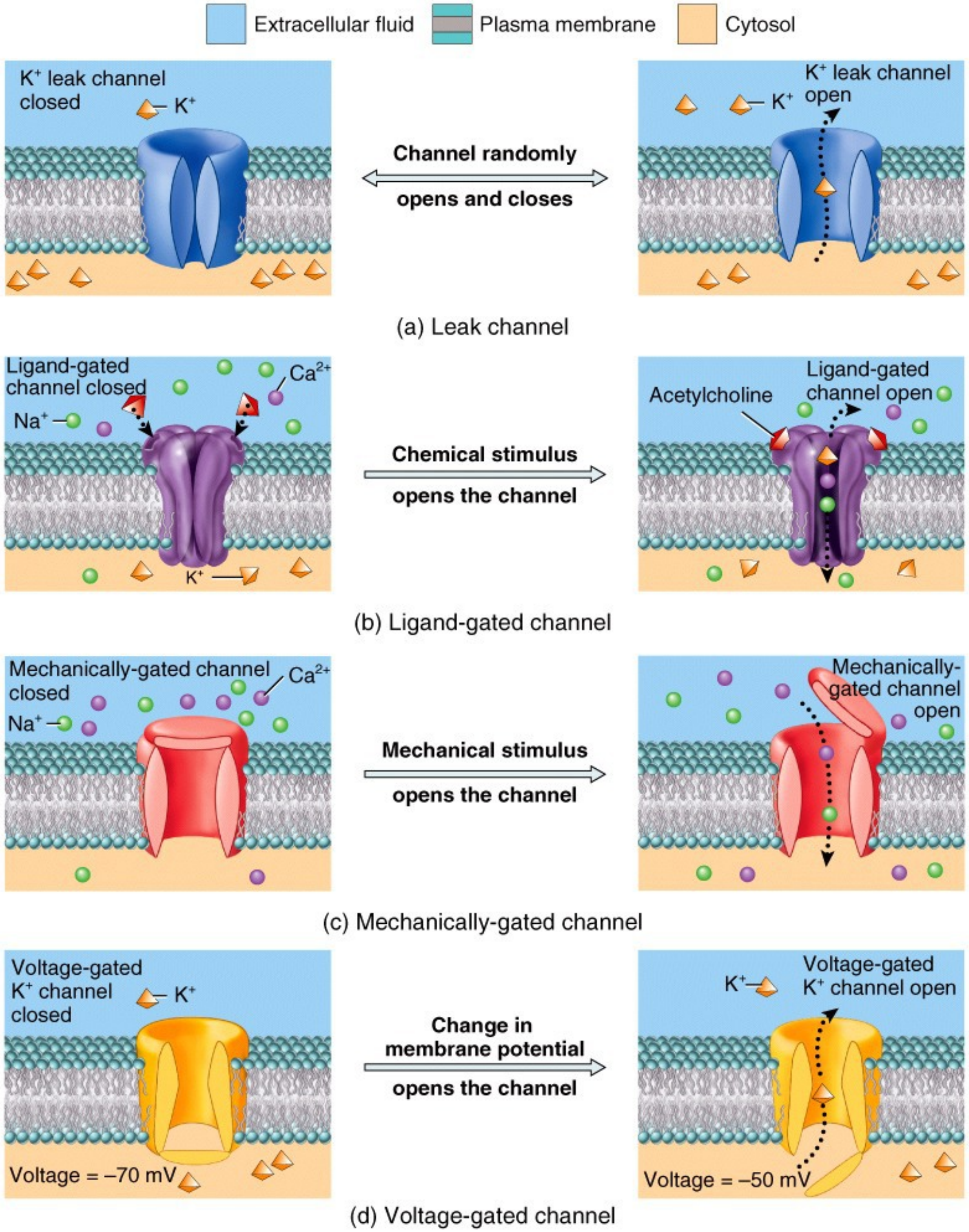


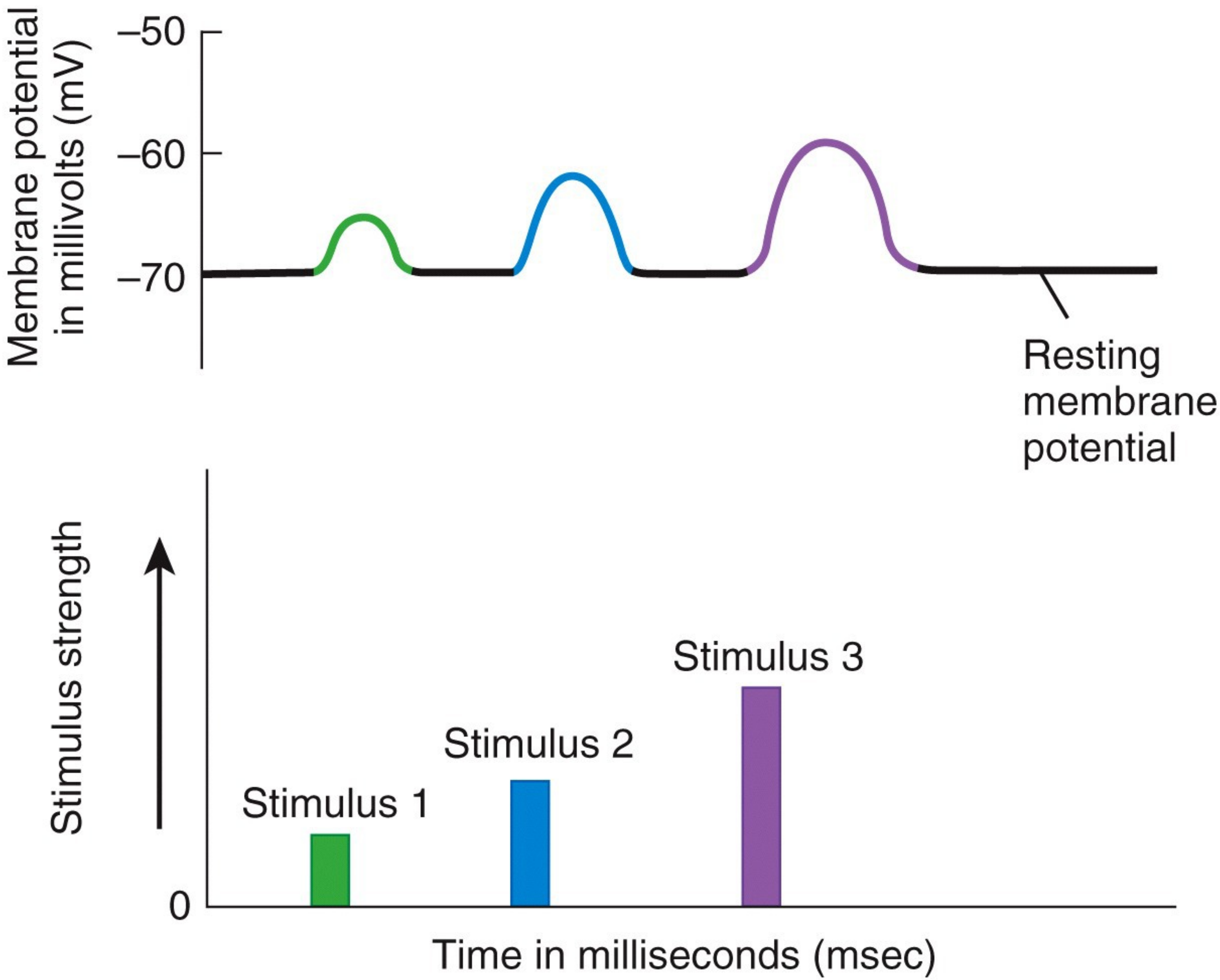


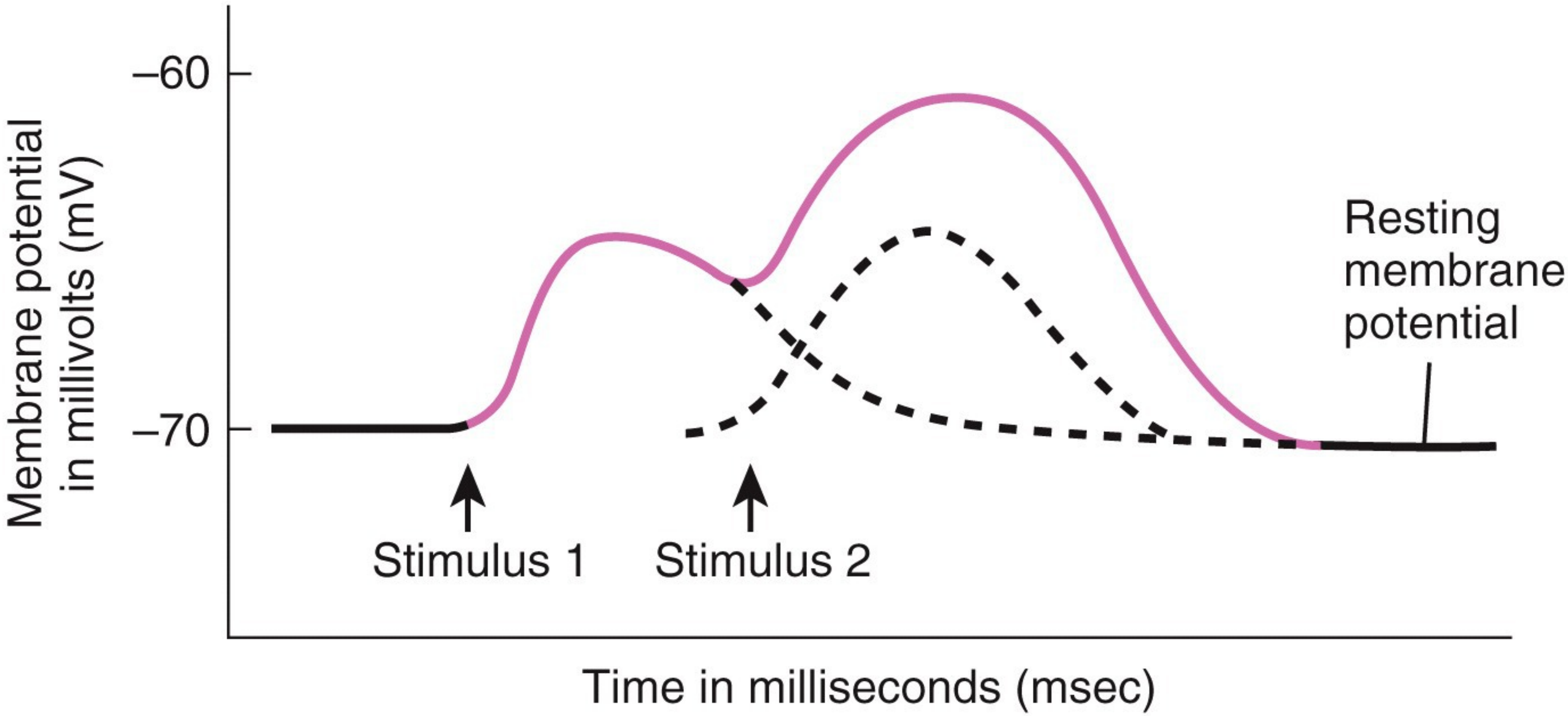
(a) Hyperpolarizing graded potential



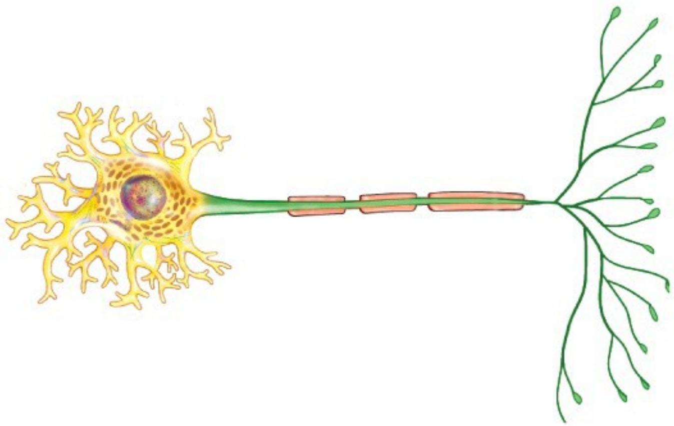
(b) Depolarizing graded potential

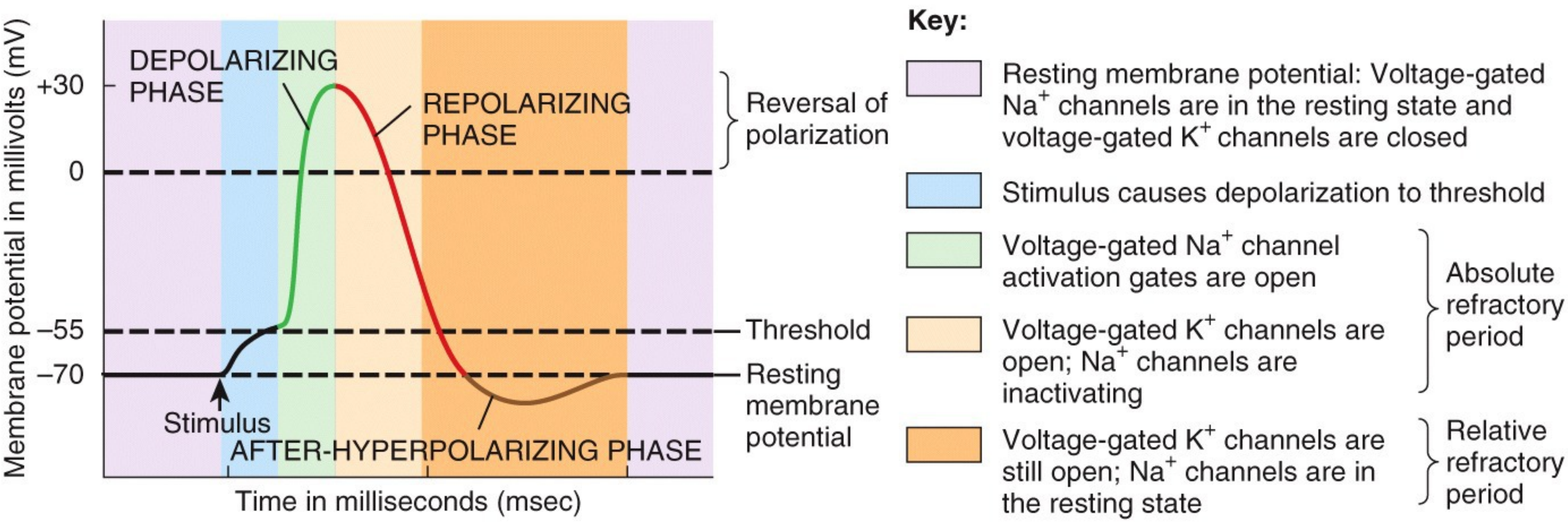

Extracellular fluid
Plasma membrane
Cytosol
K^+ leak channel closed
K^+
Channel randomly opens and closes
K^+ leak channel open
K^+
(a) Leak channel
Ligand-gated channel closed
Ca^{2+}
Na^+
K^+
Chemical stimulus opens the channel
Acetylcholine
Ligand-gated channel open
(b) Ligand-gated channel
Mechanically-gated channel closed
Ca^{2+}
Na^+
Mechanical stimulus opens the channel
Mechanically-gated channel open
(c) Mechanically-gated channel
Voltage-gated K^+ channel closed
K^+
Voltage = –70 mV
Change in membrane potential opens the channel
Voltage-gated K^+ channel open
K^+
Voltage = –50 mV
(d) Voltage-gated channel

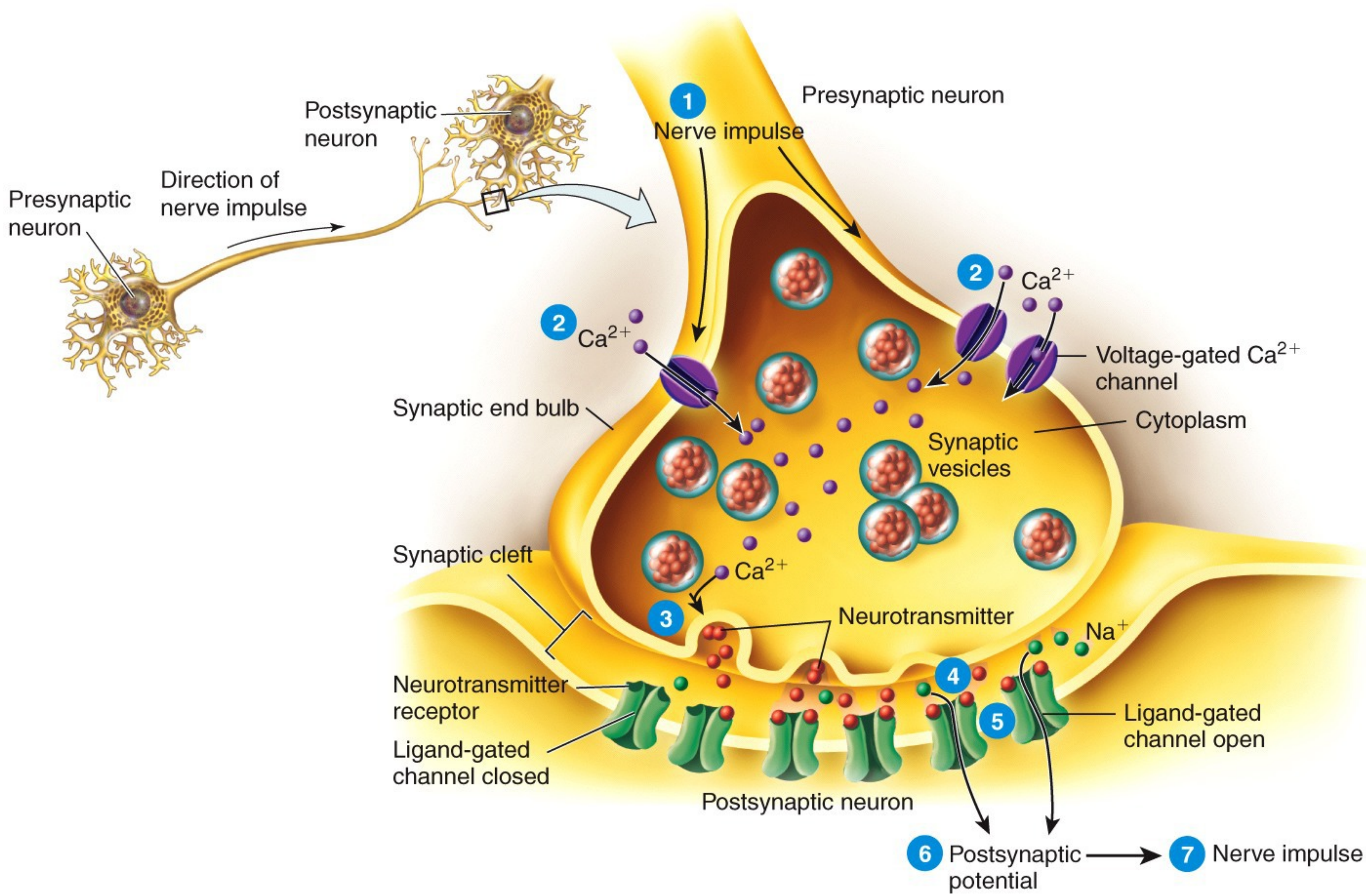

Membrane potential in millivolts (mV)
−50
−60
−70
Resting membrane potential
Stimulus strength
0
Stimulus 1
Stimulus 2
Stimulus 3
Time in milliseconds (msec)

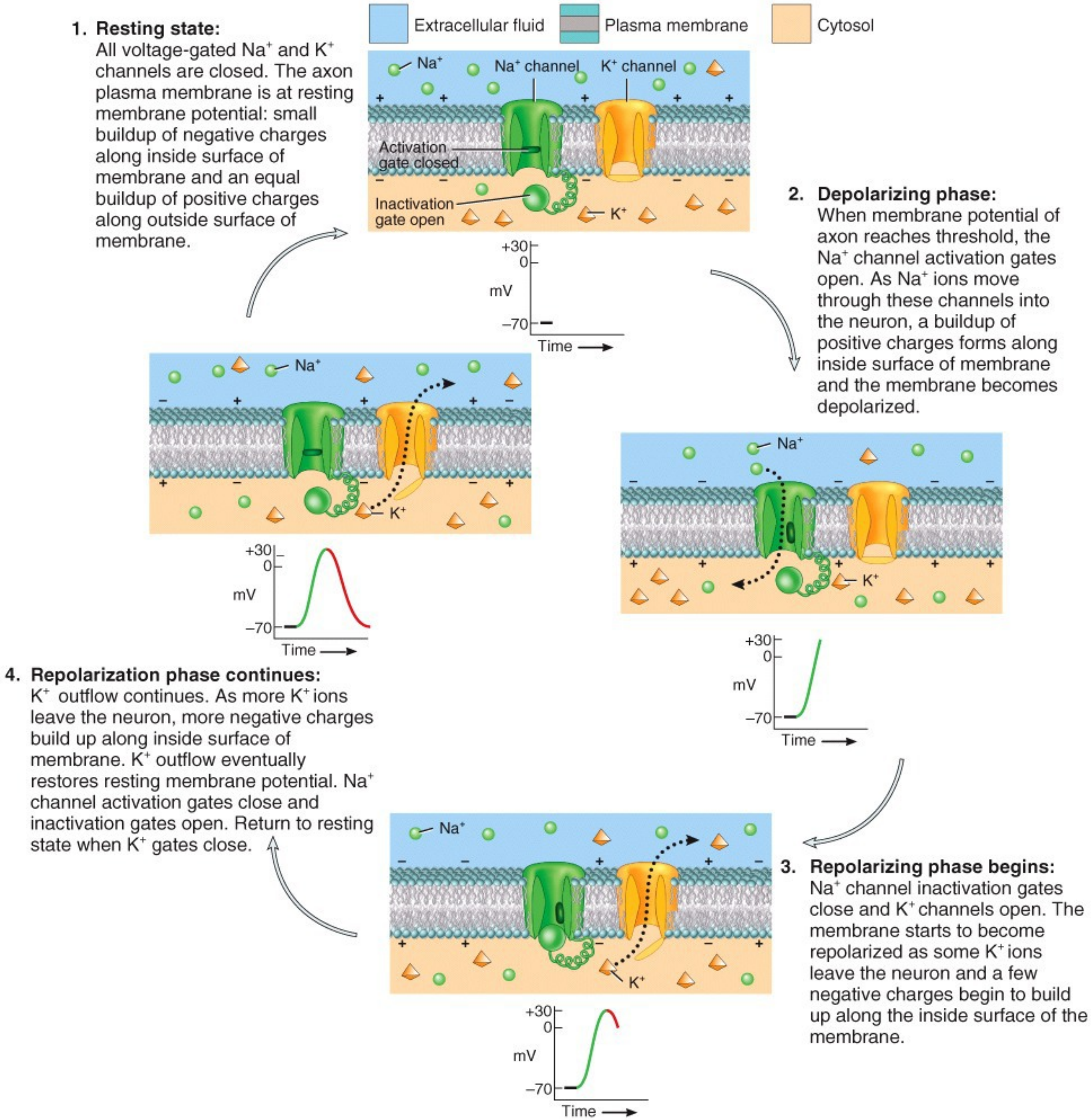


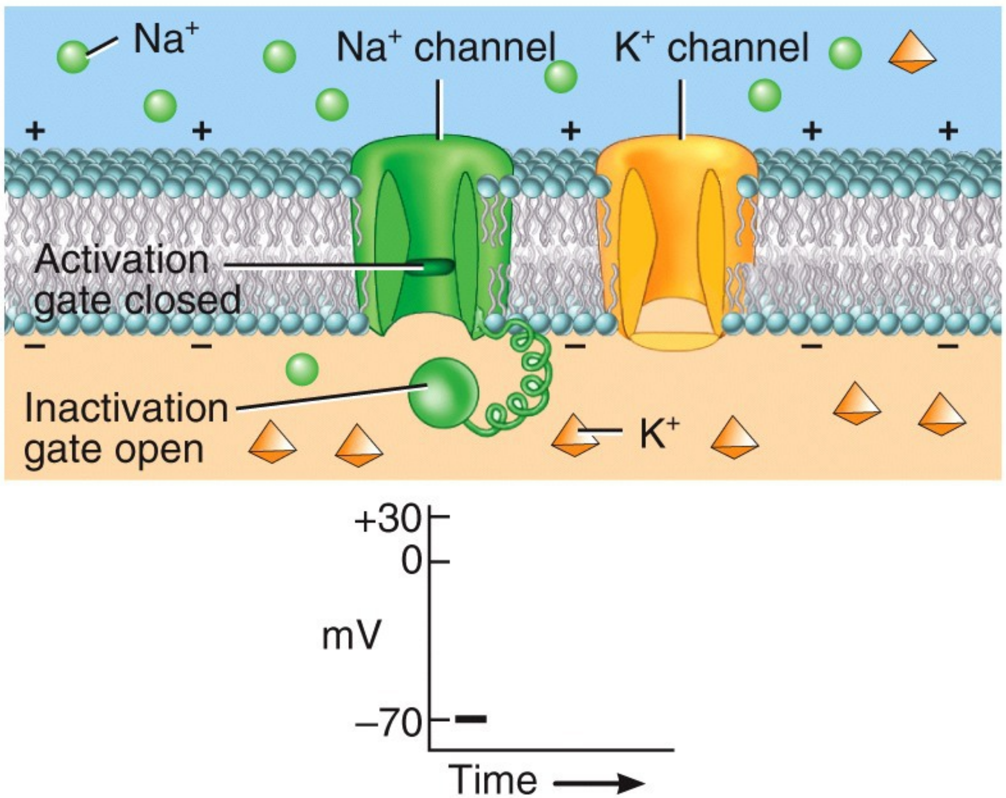
Membrane potential in millivolts (mV)
–60
–70
Resting membrane potential
Stimulus 1
Stimulus 2
Time in milliseconds (msec)



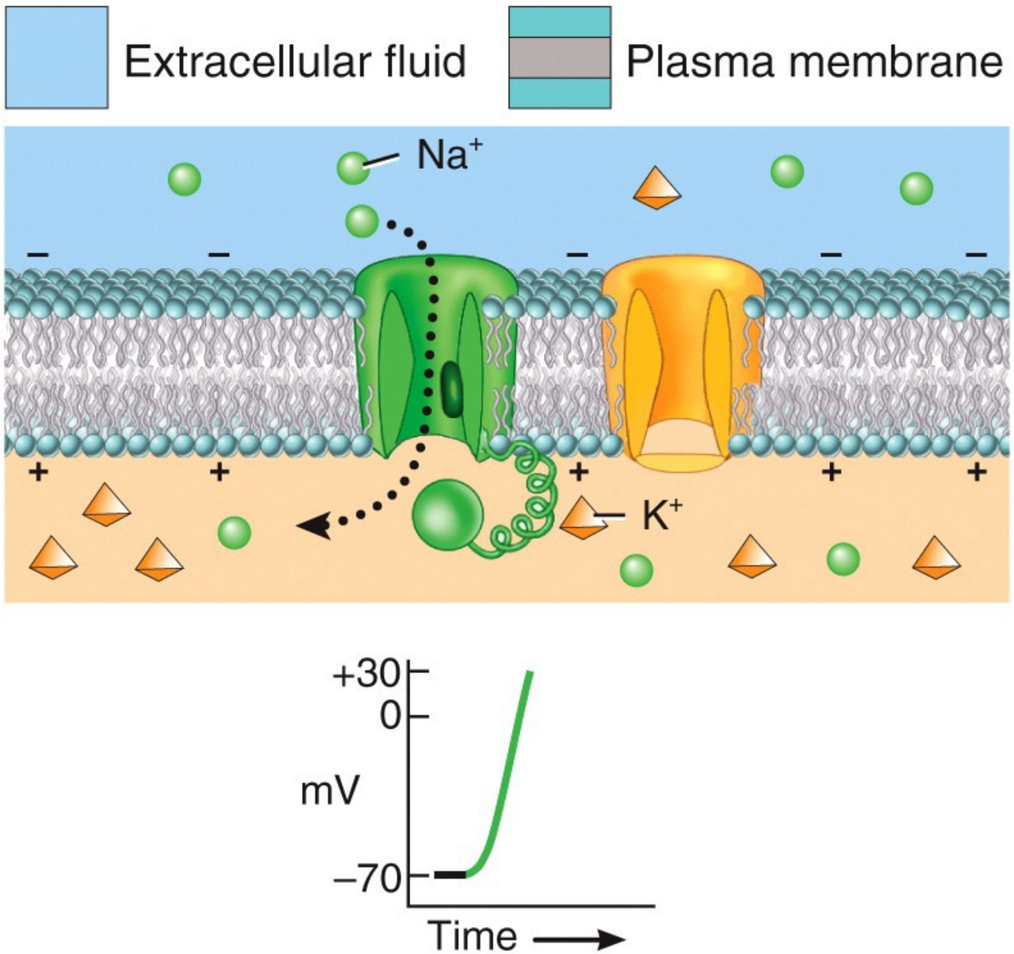

Membrane potential in millivolts (mV)
+30
0
–55
–70
DEPOLARIZING PHASE
REPOLARIZING PHASE
Reversal of polarization
Threshold
Resting membrane potential
Stimulus
AFTER-HYPERPOLARIZING PHASE
Time in milliseconds (msec)
Key:
Resting membrane potential: Voltage-gated Na+ channels are in the resting state and voltage-gated K+ channels are closed
Stimulus causes depolarization to threshold
Voltage-gated Na+ channel activation gates are open
Voltage-gated K+ channels are open; Na+ channels are inactivating
Absolute refractory period
Voltage-gated K+ channels are still open; Na+ channels are in the resting state
Relative refractory period


Postsynaptic neuron
Presynaptic neuron
Direction of nerve impulse
1 Nerve impulse
Presynaptic neuron
2 Ca2+
2 Ca2+
Voltage-gated Ca2+ channel
Synaptic end bulb
Cytoplasm
Synaptic vesicles
Synaptic cleft
Ca2+
3
Neurotransmitter
Na+
4
Neurotransmitter receptor
5
Ligand-gated channel open
Ligand-gated channel closed
Postsynaptic neuron
6 Postsynaptic potential
7 Nerve impulse

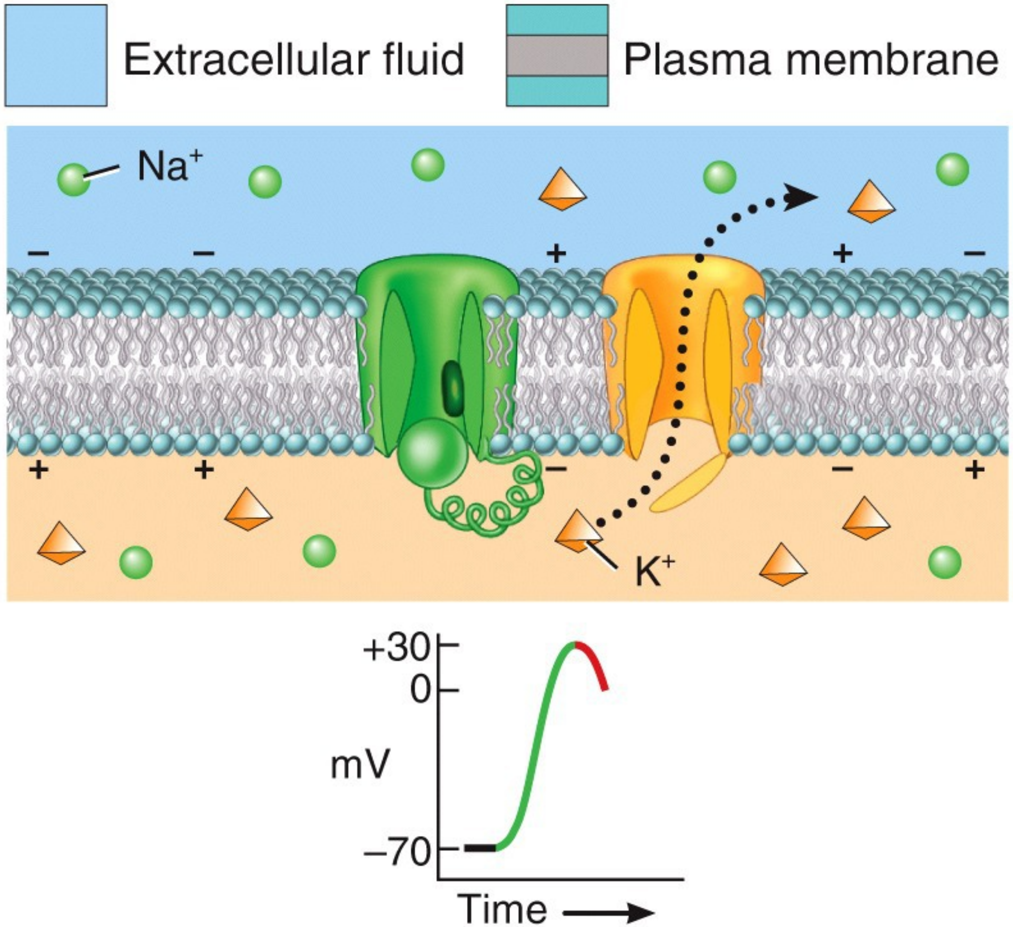

Extracellular fluid
Plasma membrane
Cytosol
1. Resting state:
All voltage-gated Na⁺ and K⁺ channels are closed. The axon plasma membrane is at resting membrane potential: small buildup of negative charges along inside surface of membrane and an equal buildup of positive charges along outside surface of membrane.
Na⁺
Na⁺ channel
K⁺ channel
Activation gate closed
Inactivation gate open
K⁺
+30
0
mV
–70
Time
2. Depolarizing phase:
When membrane potential of axon reaches threshold, the Na⁺ channel activation gates open. As Na⁺ ions move through these channels into the neuron, a buildup of positive charges forms along inside surface of membrane and the membrane becomes depolarized.
Na⁺
K⁺
+30
0
mV
–70
Time
3. Repolarizing phase begins:
Na⁺ channel inactivation gates close and K⁺ channels open. The membrane starts to become repolarized as some K⁺ ions leave the neuron and a few negative charges begin to build up along the inside surface of the membrane.
Na⁺
K⁺
+30
0
mV
–70
Time
4. Repolarization phase continues:
K⁺ outflow continues. As more K⁺ ions leave the neuron, more negative charges build up along inside surface of membrane. K⁺ outflow eventually restores resting membrane potential. Na⁺ channel activation gates close and inactivation gates open. Return to resting state when K⁺ gates close.
Na⁺
K⁺
+30
0
mV
–70
Time



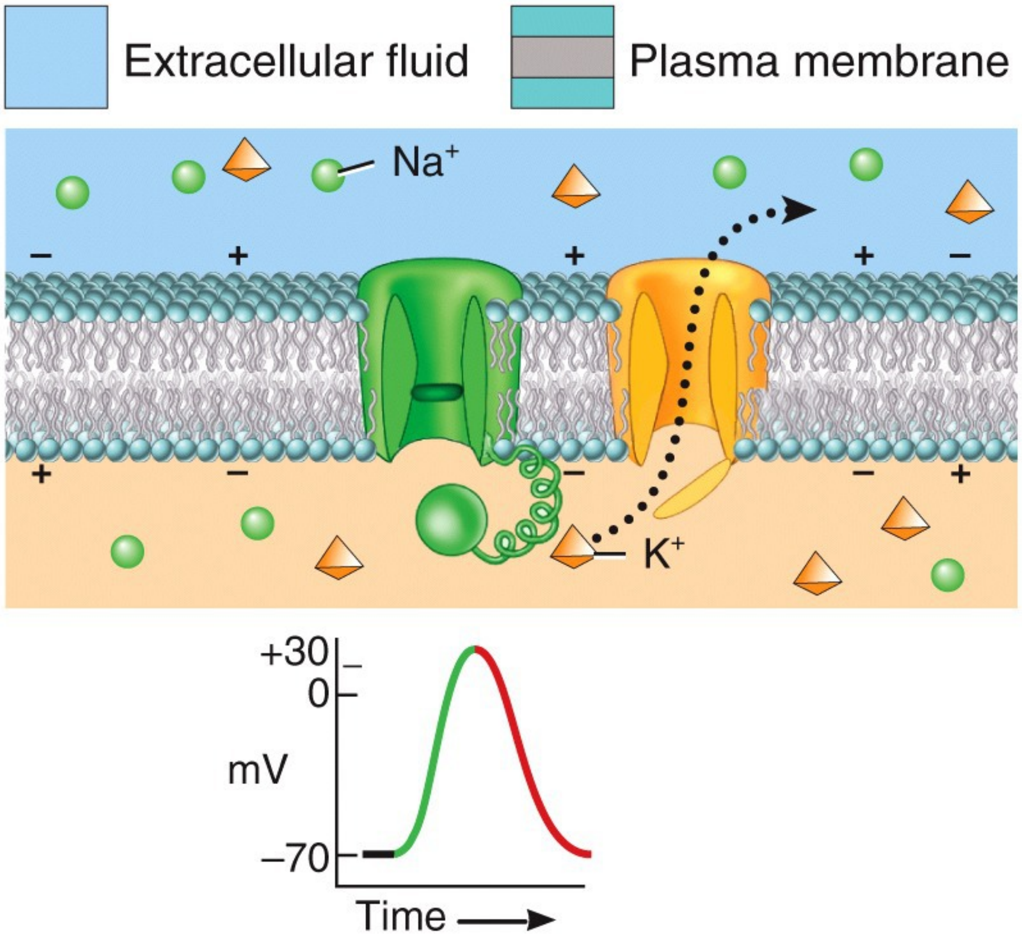
1. Resting state:
All voltage-gated Na^+ and K^+ channels are closed. The axon plasma membrane is at resting membrane potential: small buildup of negative charges along inside surface of membrane and an equal buildup of positive charges along outside surface of membrane.



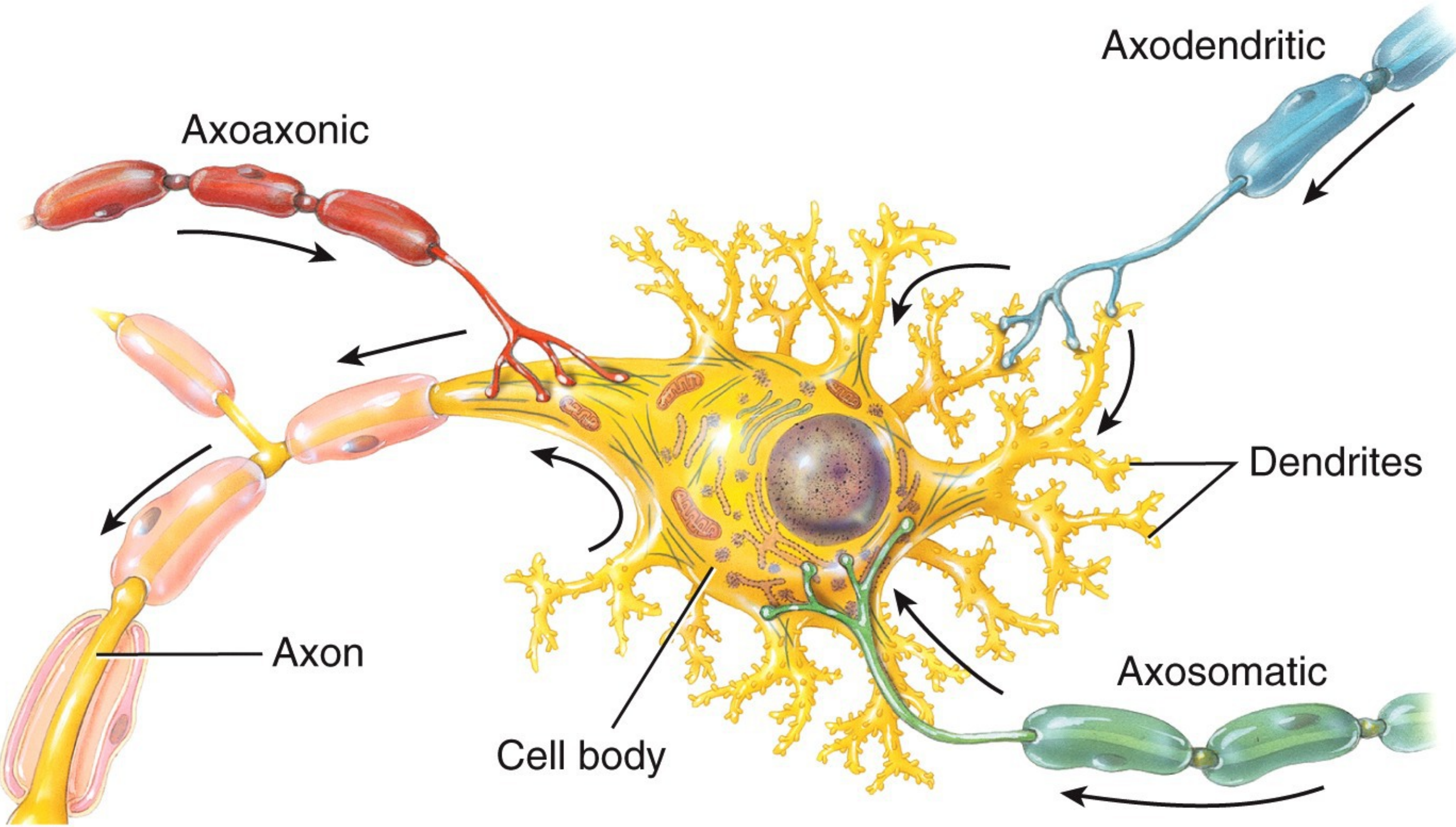
2. Depolarizing phase: When membrane potential of axon reaches threshold, the Na^+ channel activation gates open. As Na^+ ions move through these channels into the neuron, a buildup of positive charges forms along inside surface of membrane and the membrane becomes depolarized.

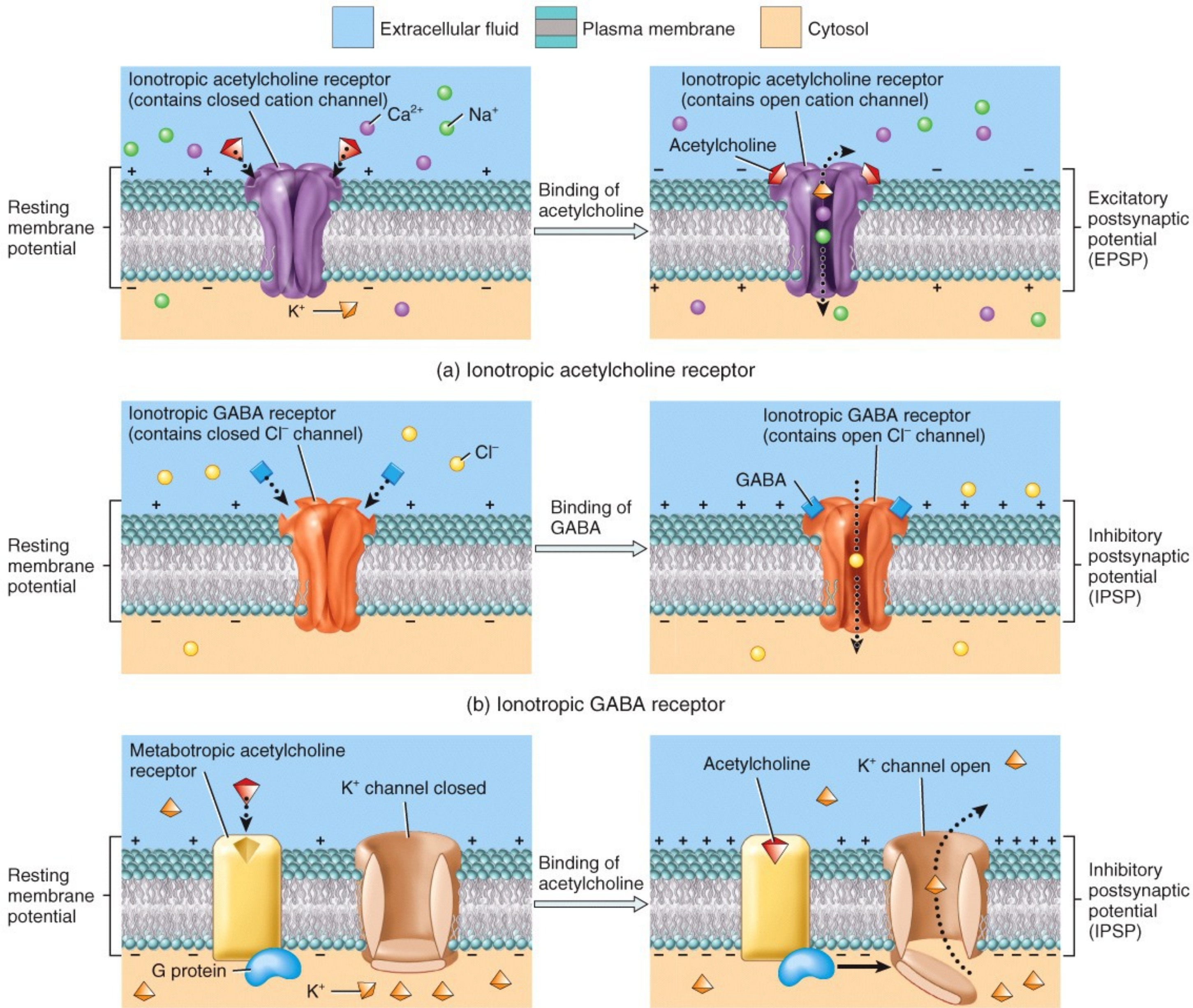


3. Repolarizing phase begins: Na^+ channel inactivation gates close and K^+ channels open. The membrane starts to become repolarized as some K^+ ions leave the neuron and a few negative charges begin to build up along the inside surface of the membrane.



4. Repolarization phase continues:
K^+ outflow continues. As more K^+ ions leave the neuron, more negative charges build up along inside surface of membrane. K^+ outflow eventually restores resting membrane potential. Na^+ channel activation gates close and inactivation gates open. Return to resting state when K^+ gates close.

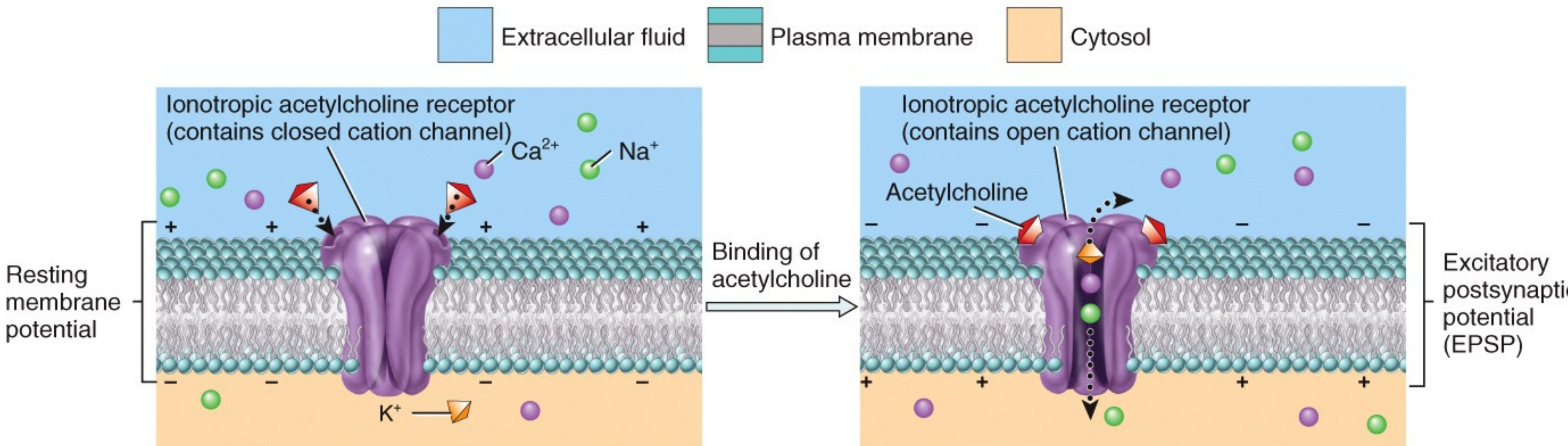

Axodendritic
Axoaxonic
Dendrites
Axon
Axosomatic
Cell body



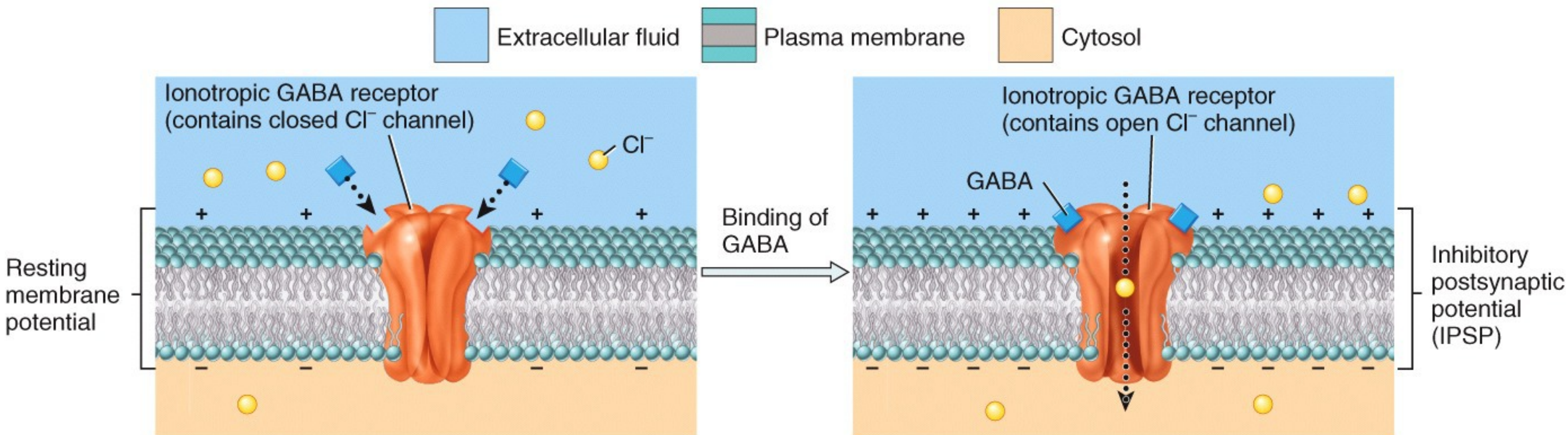
(a) Ionotropic acetylcholine receptor

(b) Ionotropic GABA receptor

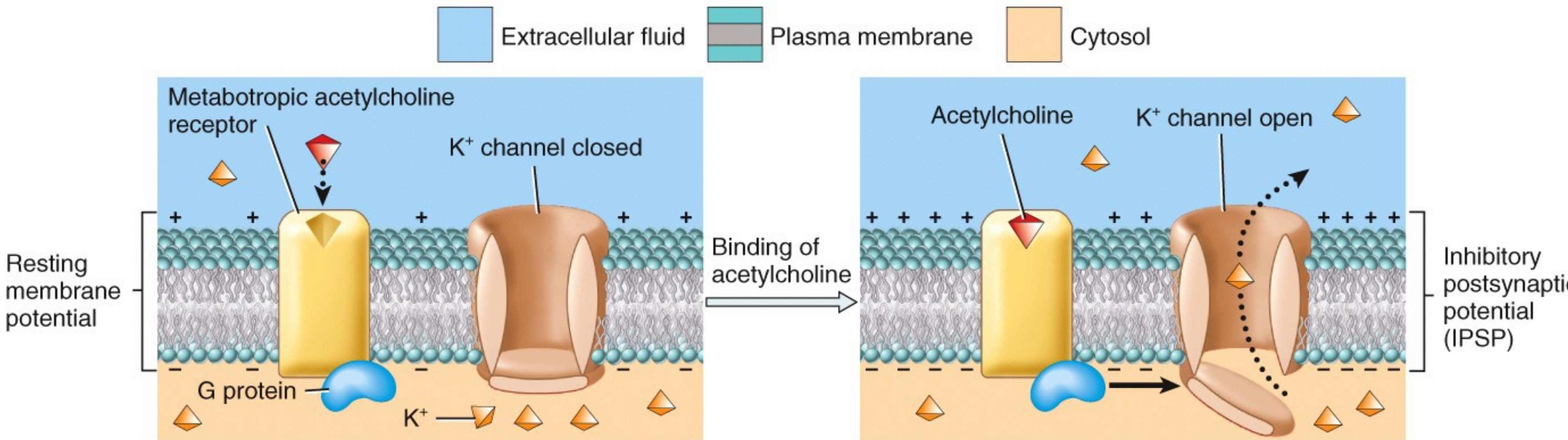
(c) Metabotropic acetylcholine receptor



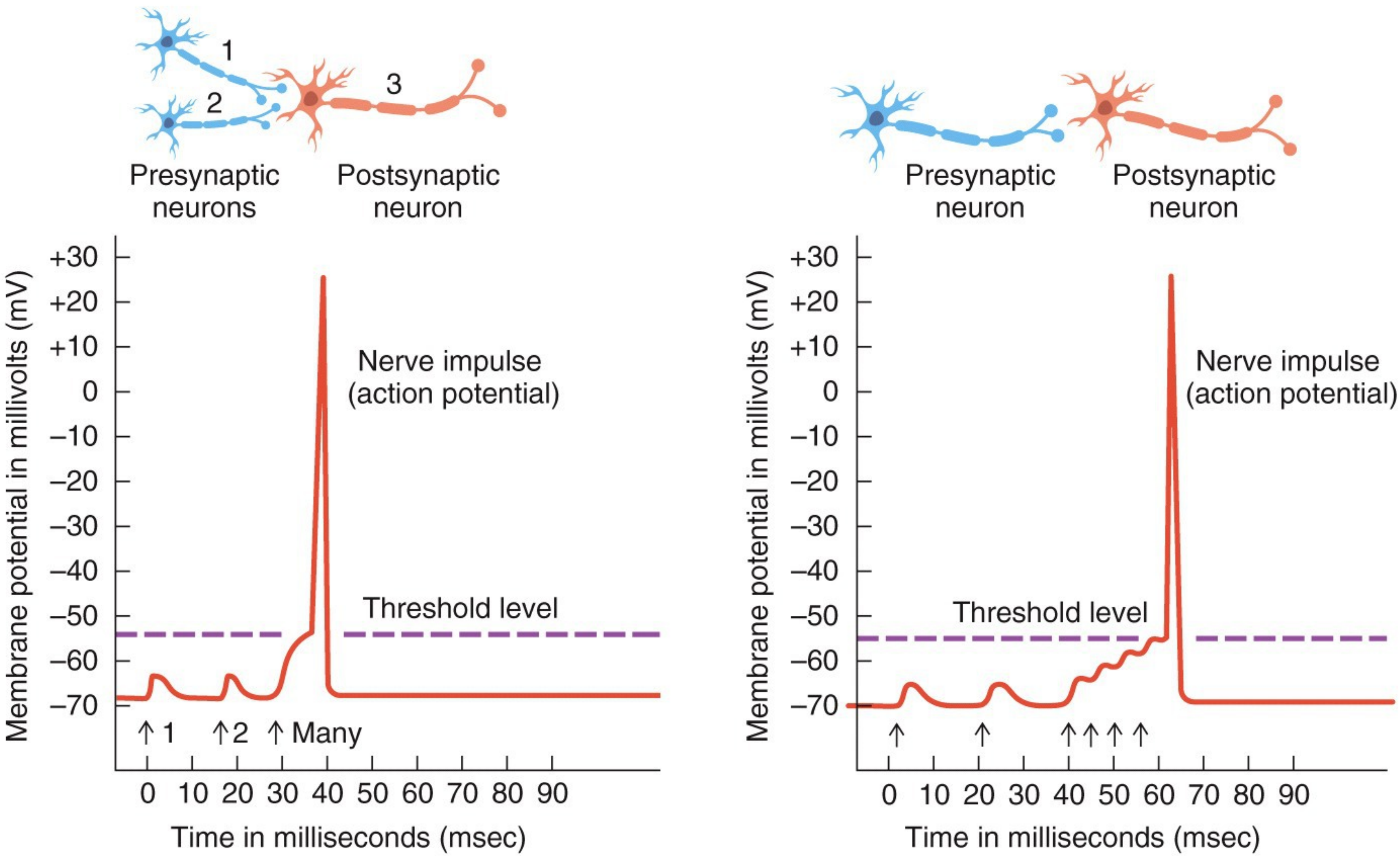
(a) Ionotropic acetylcholine receptor



(b) Ionotropic GABA receptor

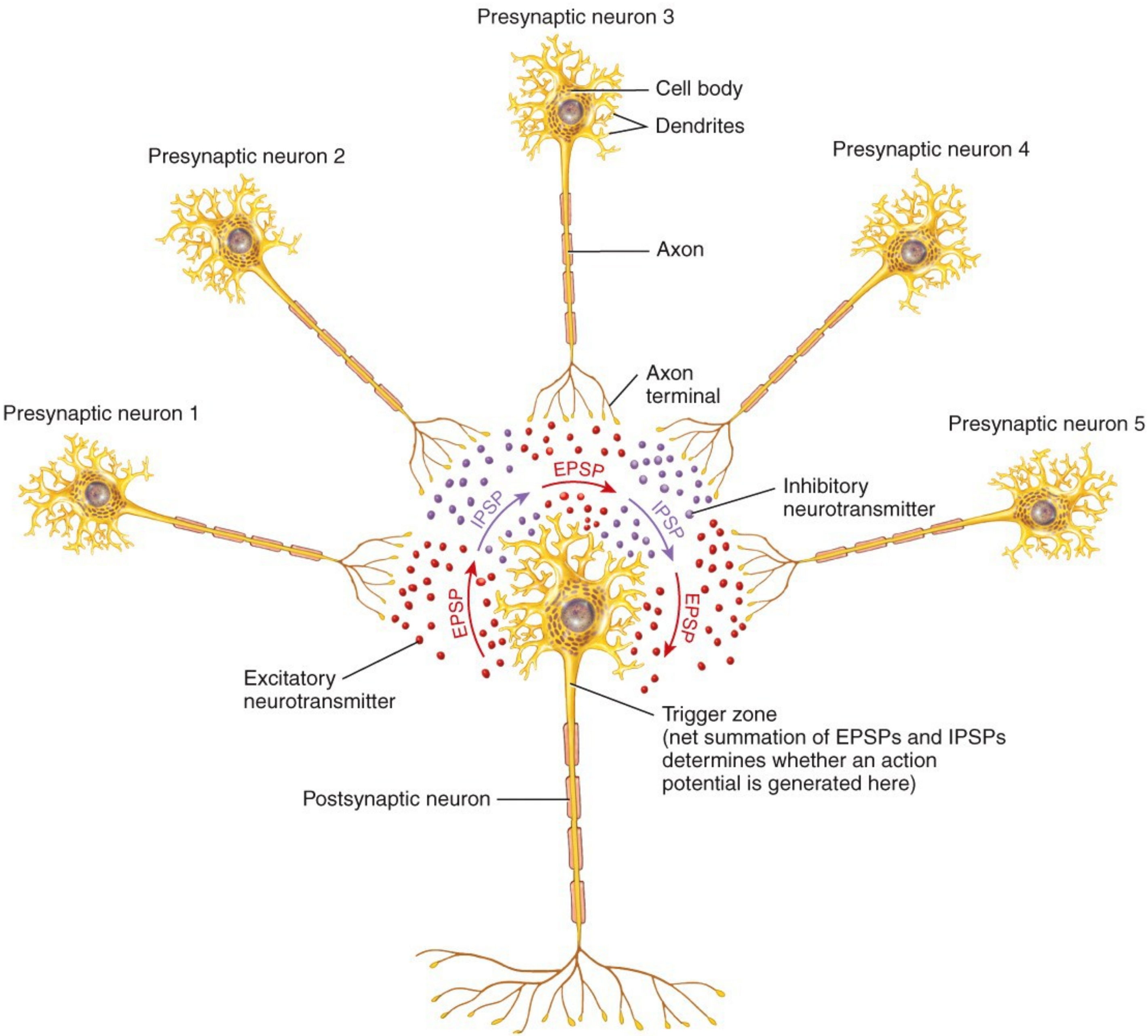


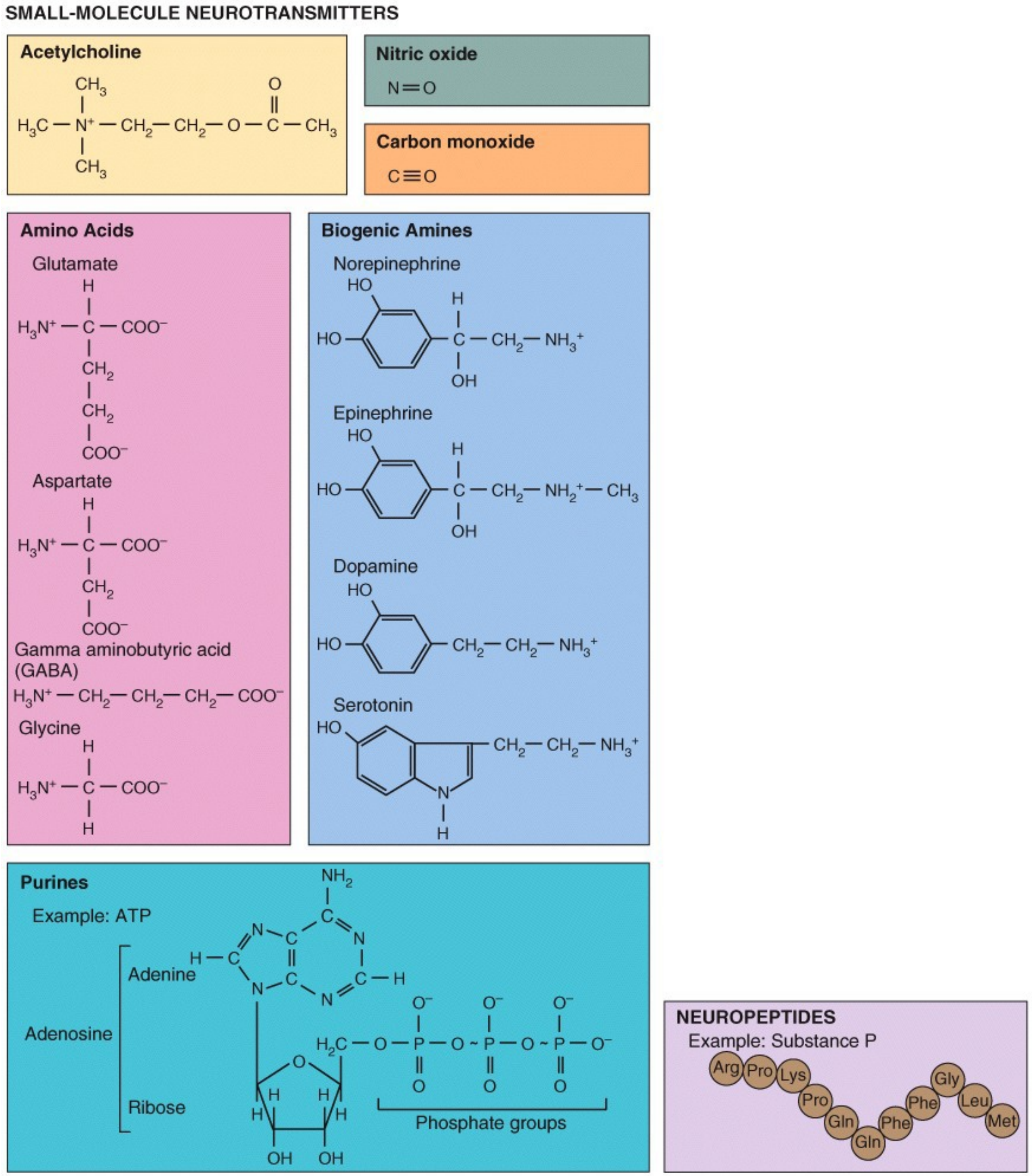
(c) Metabotropic acetylcholine receptor



(a) Spatial summation

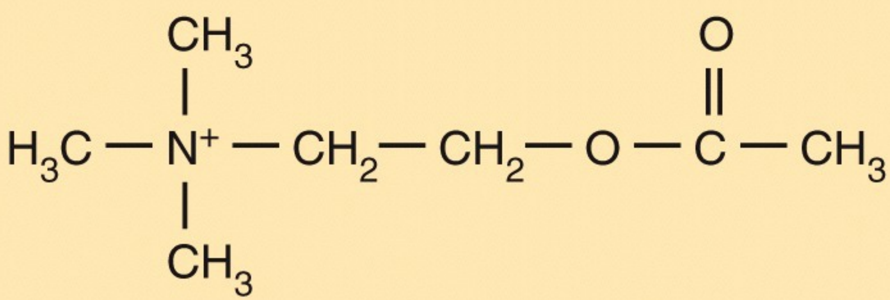
(b) Temporal summation


Presynaptic neuron 3
Cell body
Dendrites
Presynaptic neuron 2
Presynaptic neuron 4
Axon
Axon terminal
Presynaptic neuron 1
Presynaptic neuron 5
EPSP
IPSP
IPSP
Inhibitory neurotransmitter
EPSP
EPSP
Excitatory neurotransmitter
Trigger zone
(net summation of EPSPs and IPSPs determines whether an action potential is generated here)
Postsynaptic neuron


SMALL-MOLECULE NEUROTRANSMITTERS
Acetylcholine
Nitric oxide
N═O
Carbon monoxide
C≡O
Amino Acids
Glutamate
Aspartate
Gamma aminobutyric acid (GABA)
Glycine
Biogenic Amines
Norepinephrine
Epinephrine
Dopamine
Serotonin
Purines
Example: ATP
Adenine
Adenosine
Ribose
Phosphate groups
NEUROPEPTIDES
Example: Substance P
Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu Met

SMALL-MOLECULE NEUROTRANSMITTERS

Acetylcholine



Nitric oxide

$N=O$

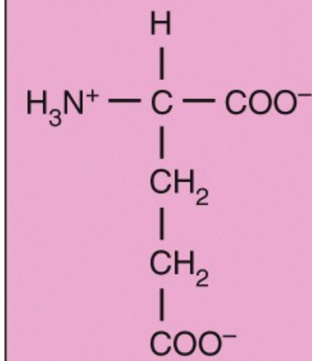
Carbon monoxide

$C\equiv O$

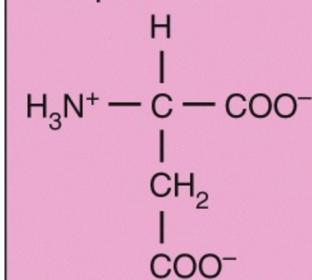
SMALL-MOLECULE NEUROTRANSMITTERS

Amino Acids

Glutamate



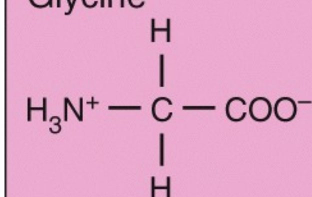
Aspartate



Gamma aminobutyric acid (GABA)

$$H_3N^+ — CH_2 — CH_2 — CH_2 — COO^-$$

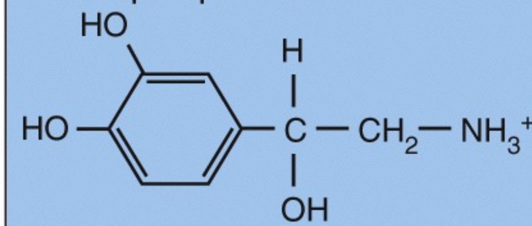
Glycine



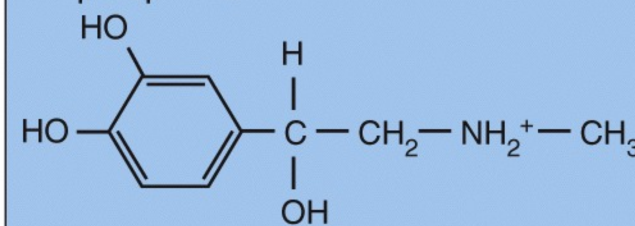
SMALL-MOLECULE NEUROTRANSMITTERS

Biogenic Amines

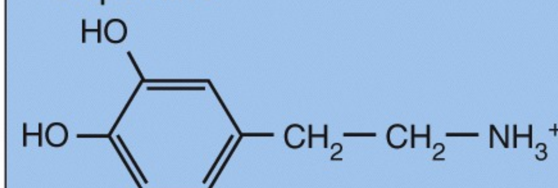
Norepinephrine



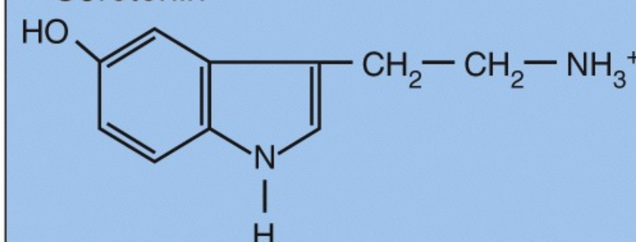
Epinephrine



Dopamine



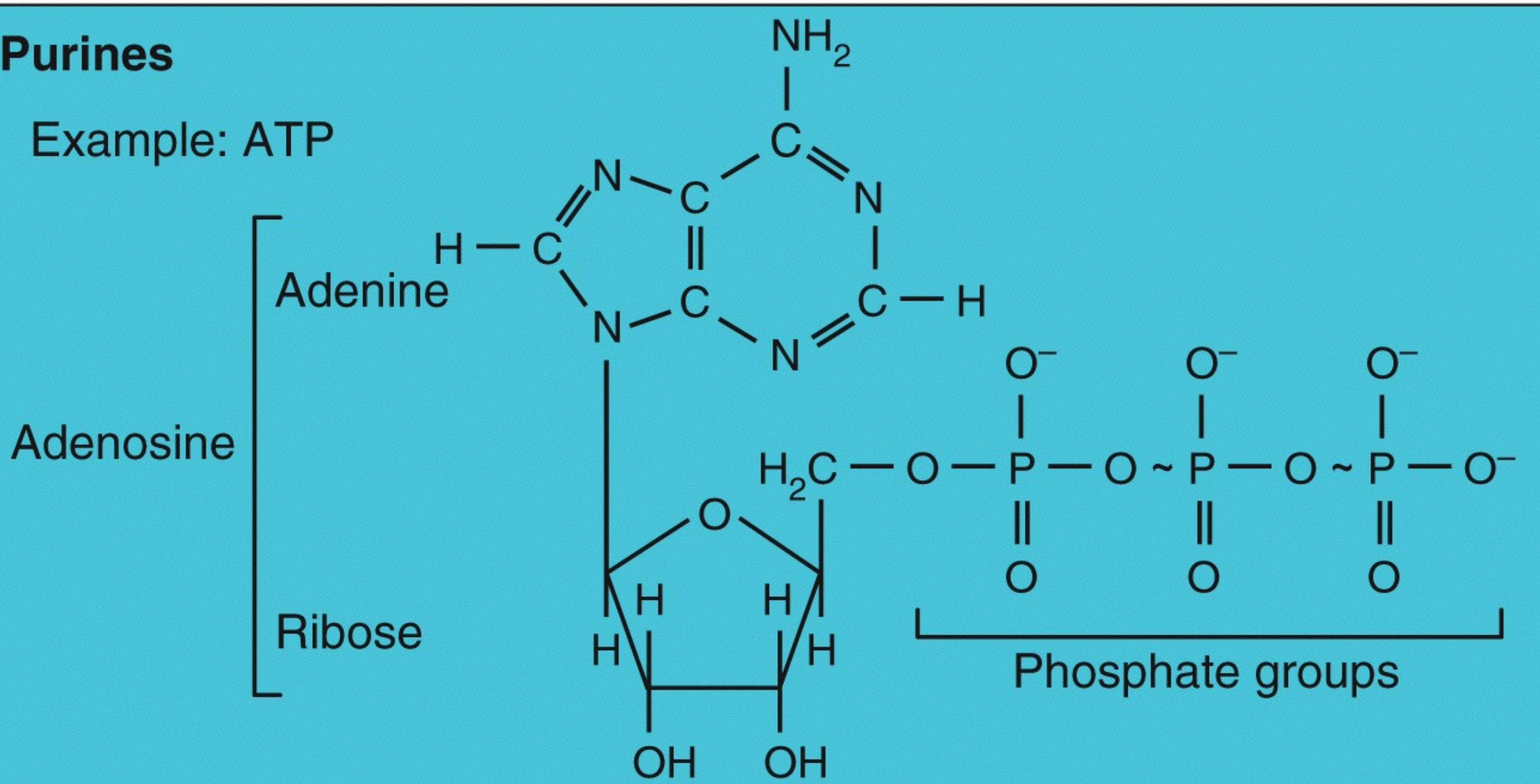
Serotonin



SMALL-MOLECULE NEUROTRANSMITTERS

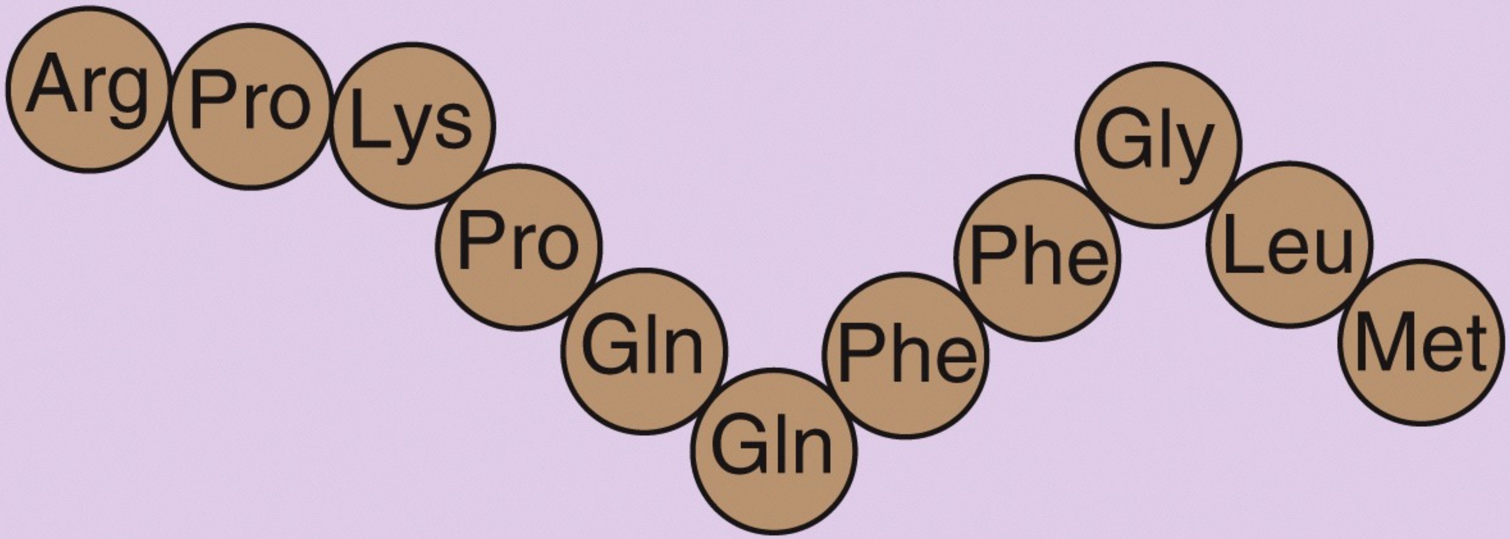
Purines

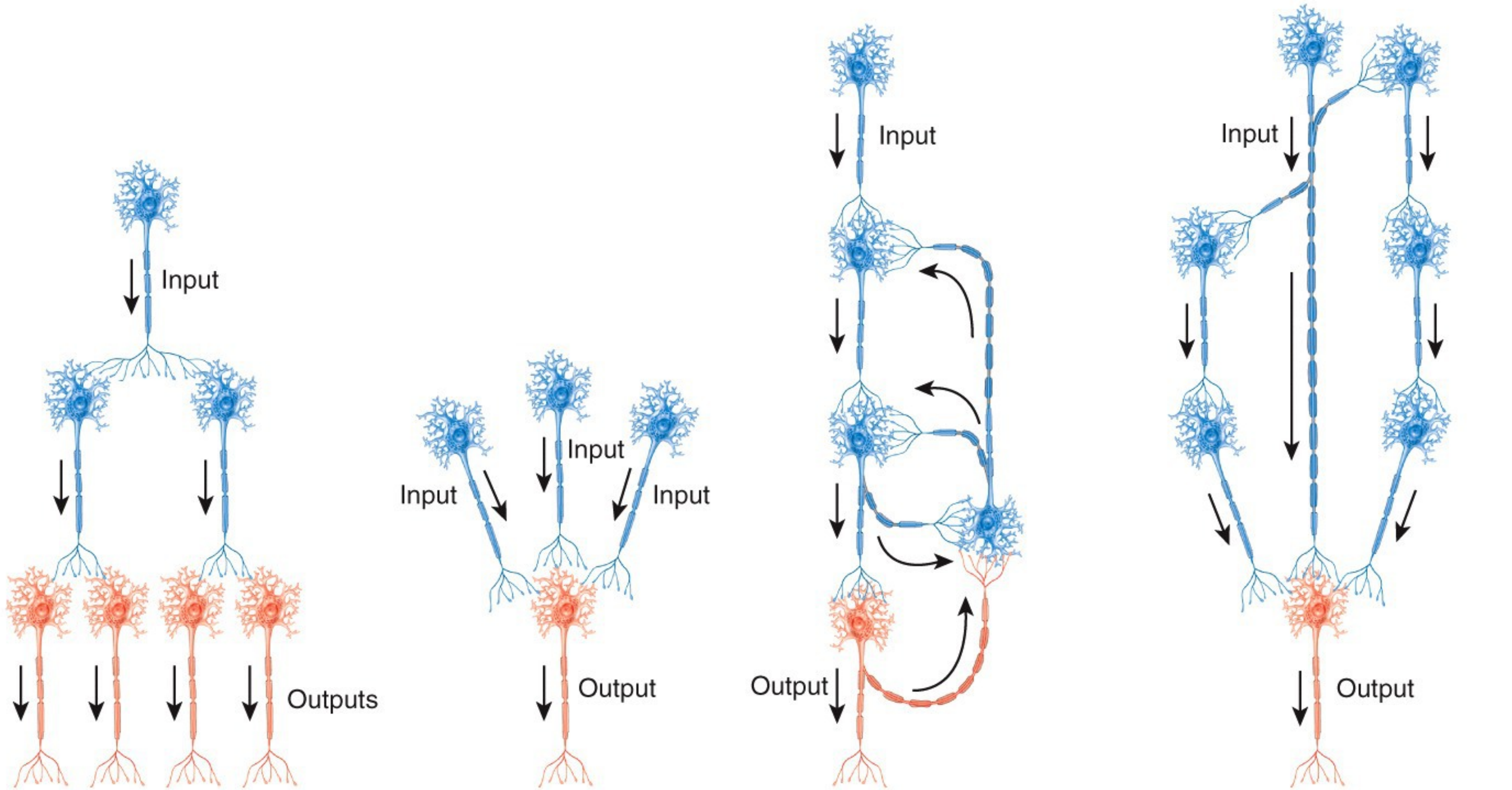
Example: ATP



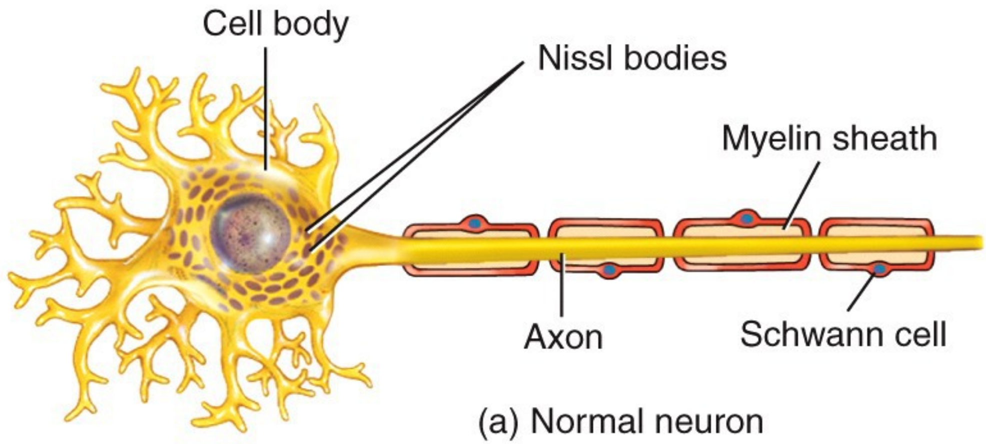
NEUROPEPTIDES

Example: Substance P

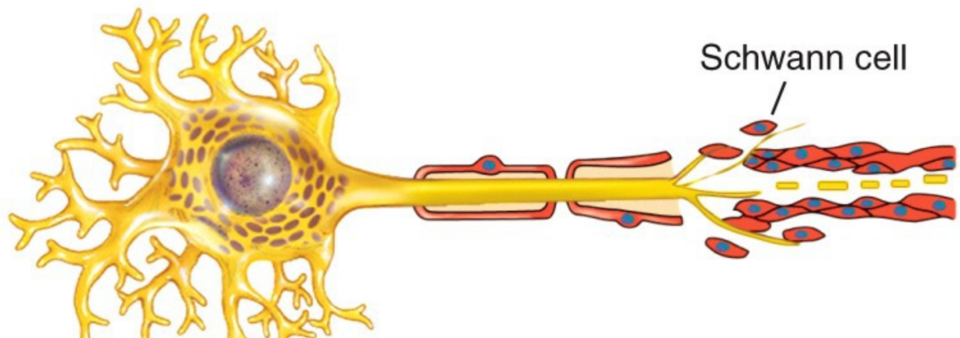




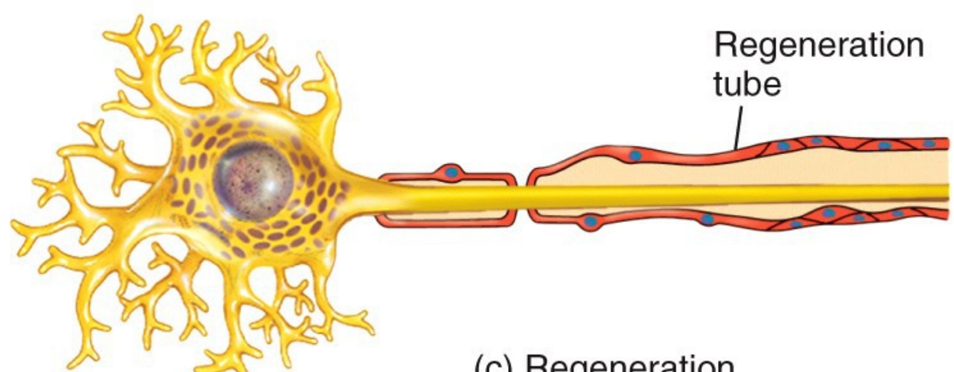
(a) Diverging circuit (b) Converging circuit (c) Reverberating circuit (d) Parallel after-discharge circuit



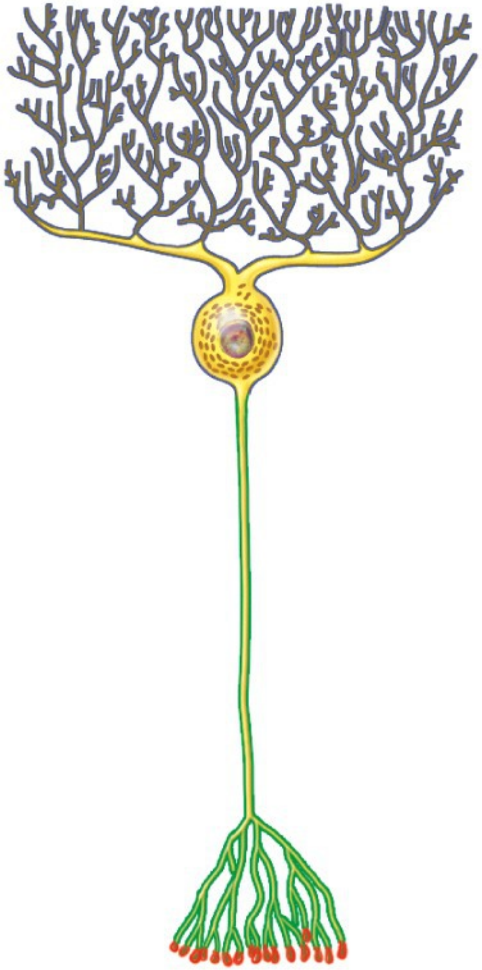
(a) Normal neuron



(b) Chromatolysis and Wallerian degeneration

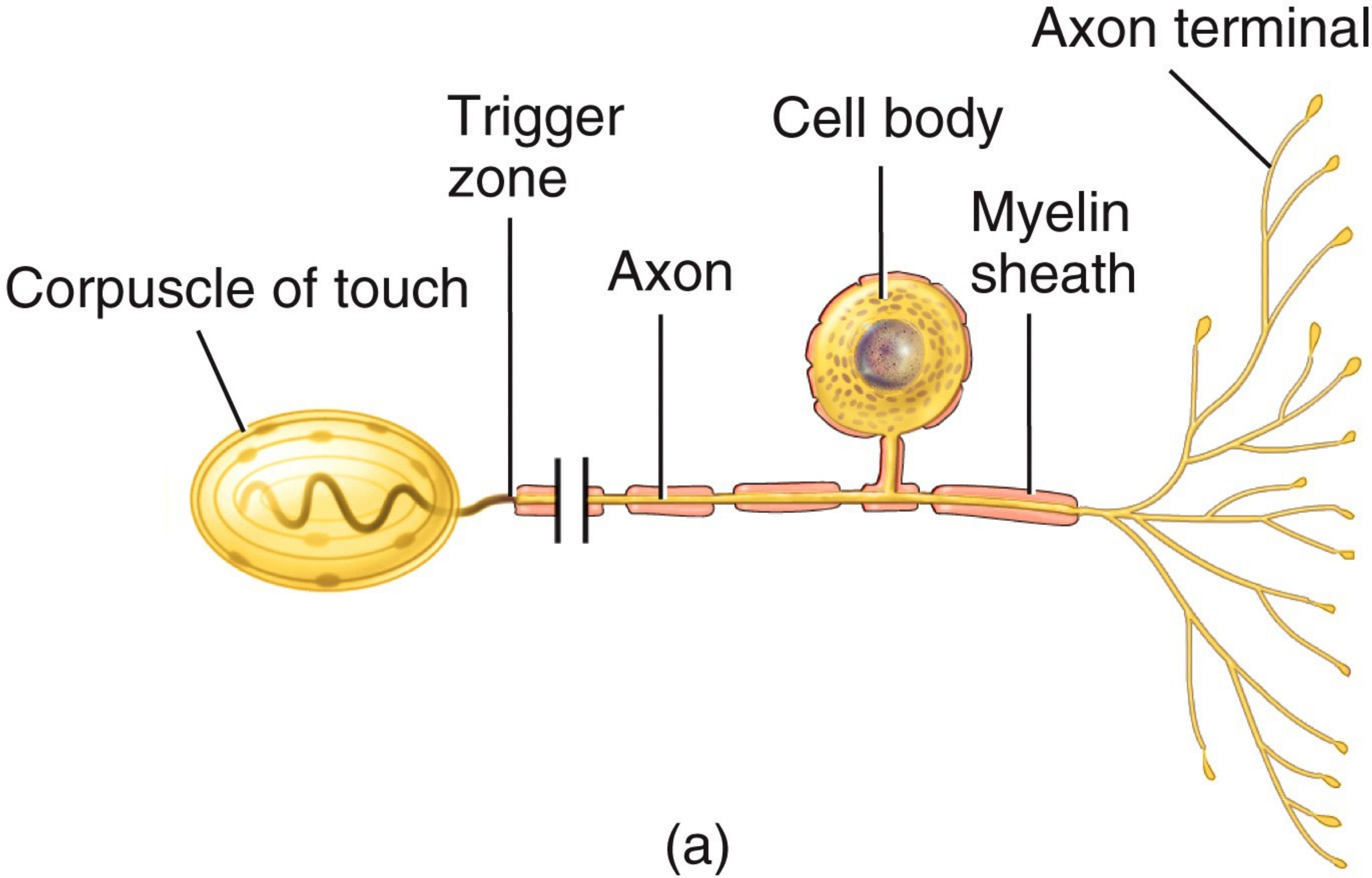


(c) Regeneration



Key:

- Blue: Plasma membrane includes chemically gated channels
- Green: Plasma membrane includes voltage-gated Na^+ and K^+ channels
- Red: Plasma membrane includes voltage-gated Ca^{2+} channels


Axon terminal
Trigger
zone
Cell body
Myelin
sheath
Axon
Corpuscle of touch

(a)