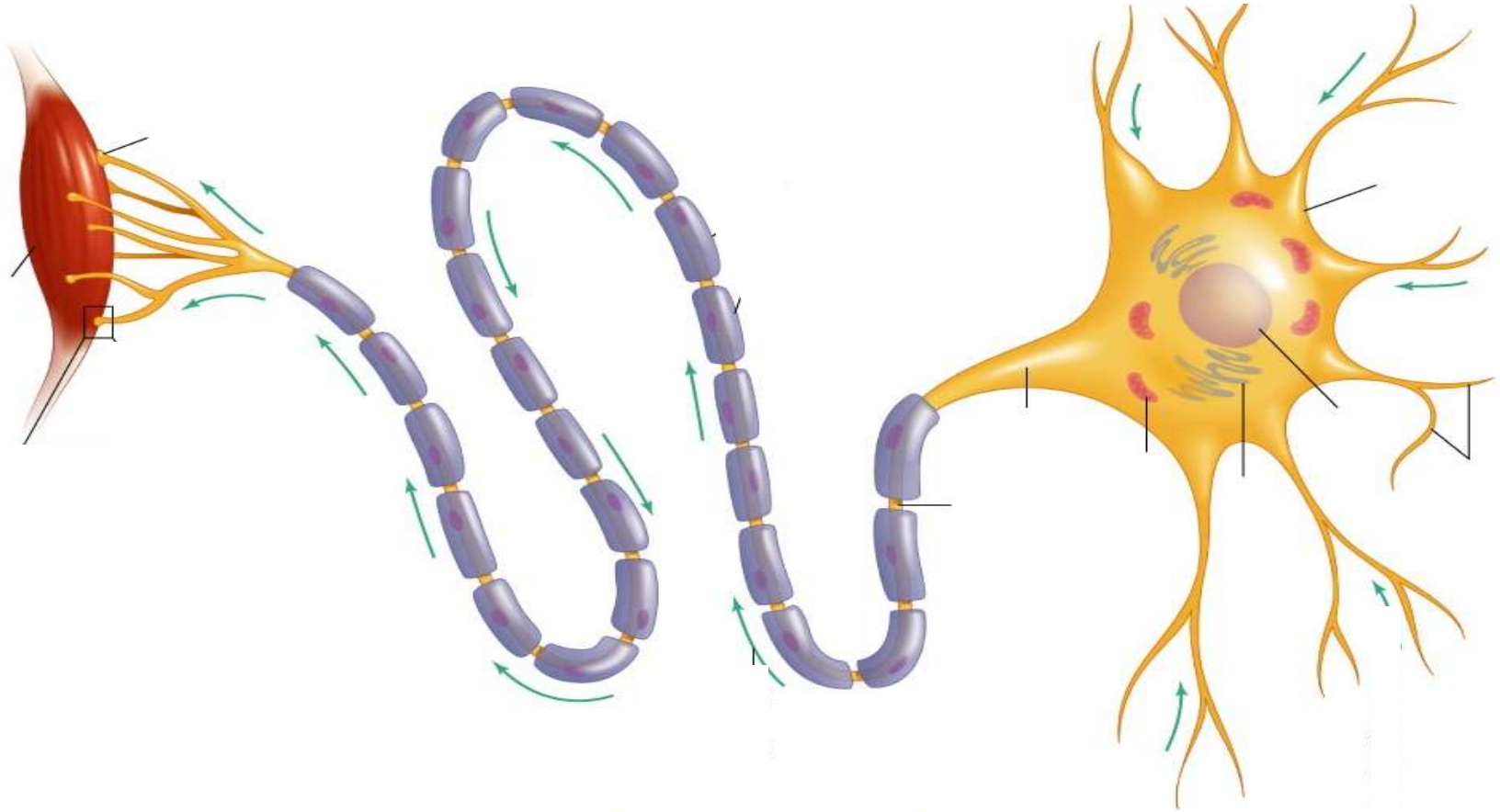
Nervous Systems:

Neuron Structure and Function



Integration

- An animal needs to function like a coherent organism, not like a loose collection of cells.

- **Integration** = refers to processes such as summation and coordination that produce coherency and result in harmonious function.

Integration

- **Cellular integration** = processes within cells

- **Whole-animal integration** = selective combination and processing of sensory, endocrine, and central nervous system (CNS) information in ways that promote harmonious functioning of the whole organism within its environment.
  - This includes its all its cells, tissues, and organs

Integration

- Nerve cells are specialized for control and coordination.

- Integration ensures that an animal's responses are smooth and coordinated rather than clashing or disjointed.

Excitable Cells

- **Neurons** are a type of *excitable cell*
  - Specially adapted to generate an electrical signal

- Can rapidly alter their membrane potential in response to an incoming signal.

- Vary in structure and function but use the same basic mechanism to send signals.

Neuron Function – Main Points

- Specialized for processing and conveying information.
- Information is coded into changes in electrical potential across cell membranes.
- Neurons use action potentials to transmit these signals across long distances.
- Neurons allow animals to sense and respond to their environment.

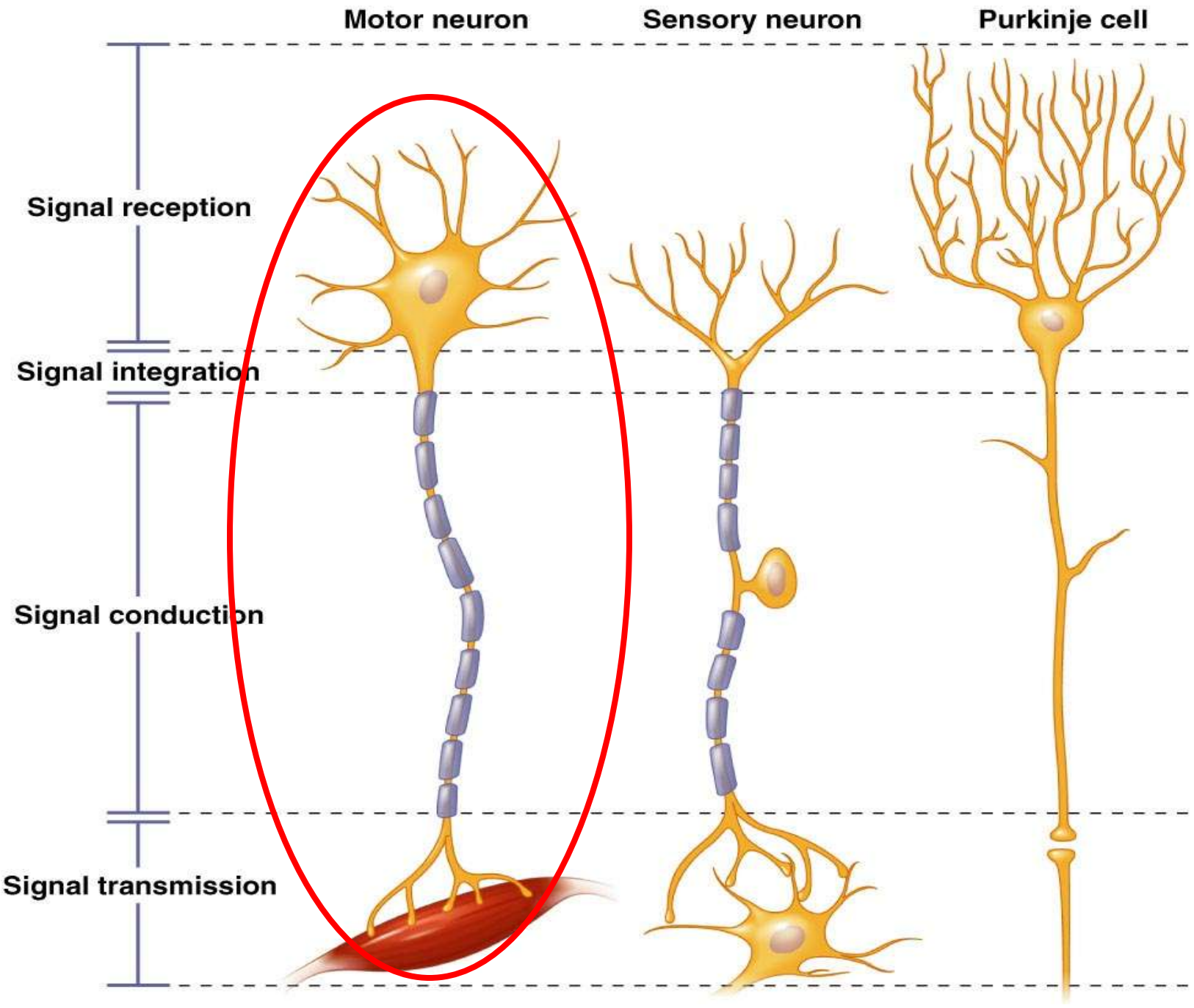
Benefits of Neurons

- Plants (no neurons):

  Action potentials travel @ 1-3 cm/sec

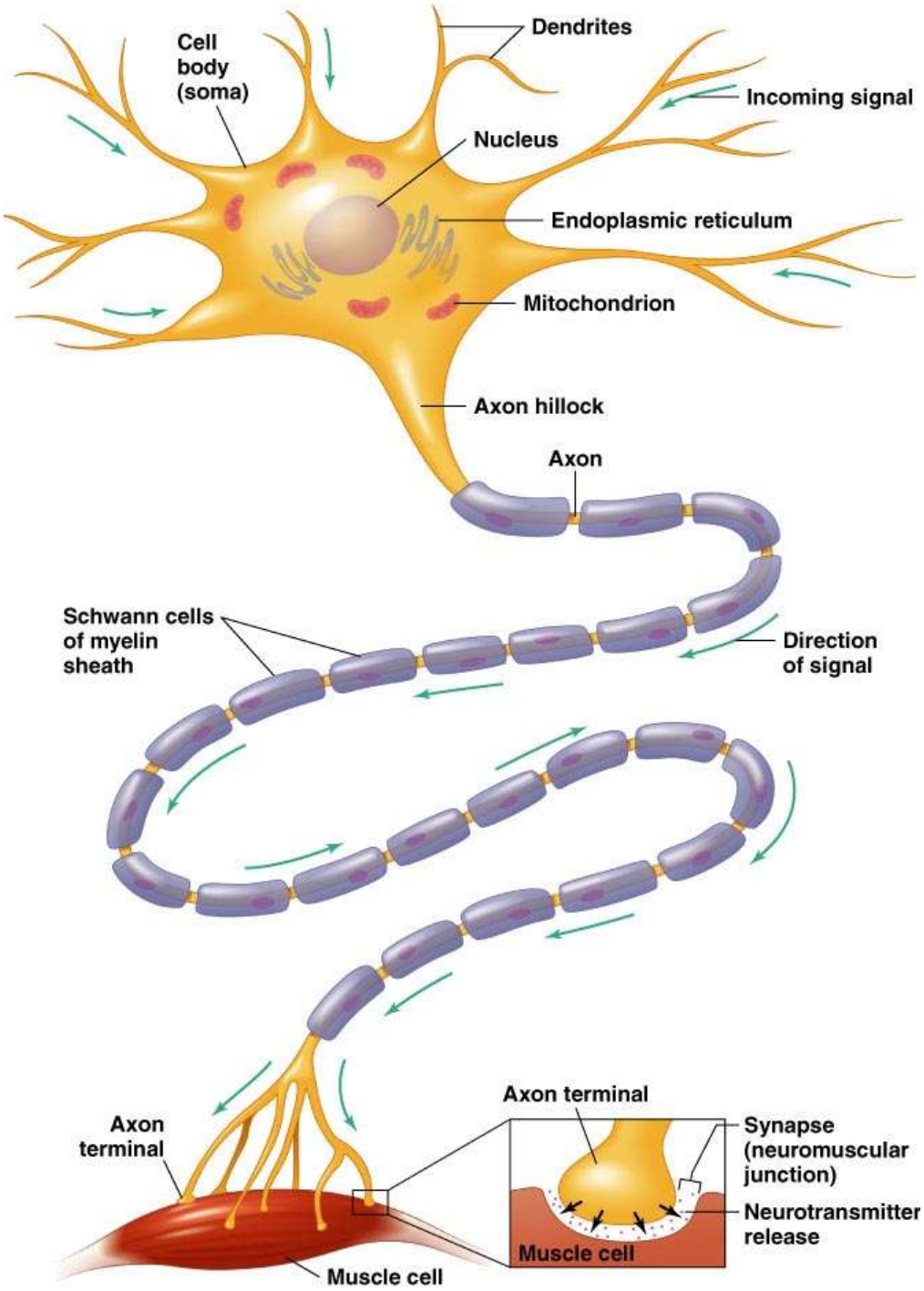
- Animals (neurons):

  Action potentials travel @ 100m/sec
  or 10,000cm/sec


Motor neuron
Sensory neuron
Purkinje cell
Signal reception
Signal integration
Signal conduction
Signal transmission

CNS to Muscles

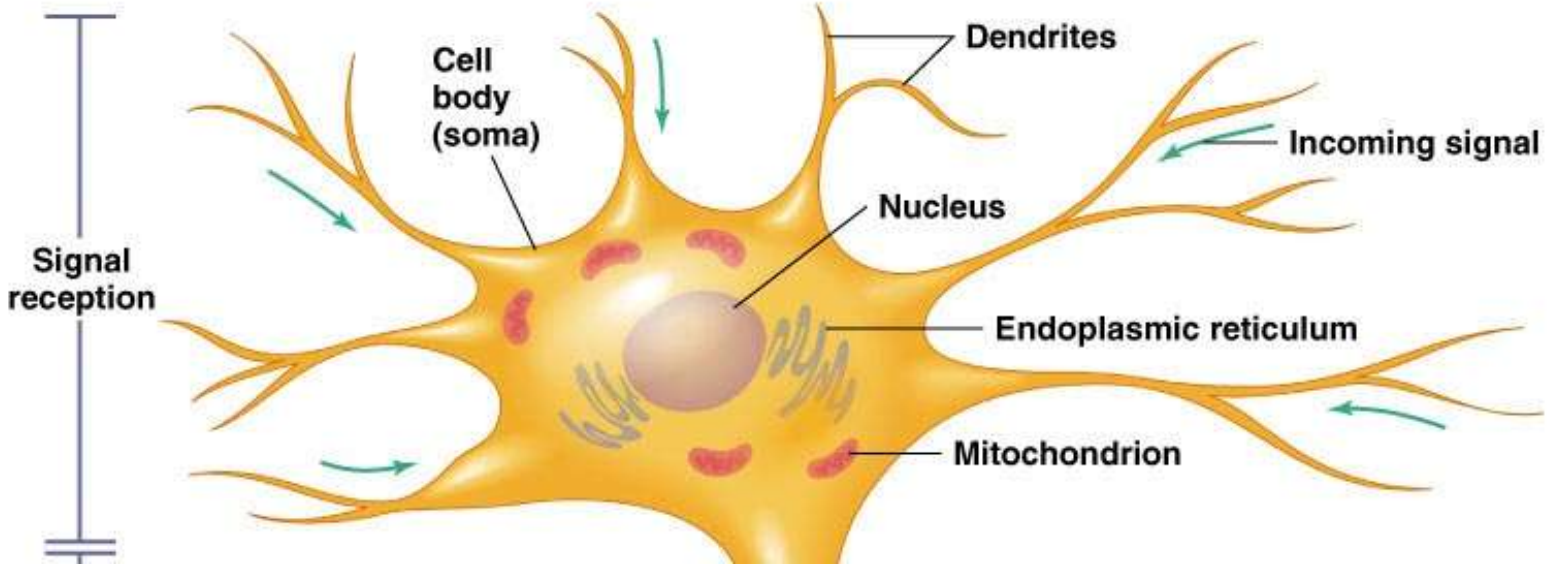
- Signal Reception
- Signal Integration
- Signal Conduction
- Signal Transmission
- Dendrites & Cell Body
- Axon Hillock
- Axon
- Axon Terminals


Dendrites
Cell body (soma)
Incoming signal
Nucleus
Endoplasmic reticulum
Mitochondrion
Axon hillock
Axon
Schwann cells of myelin sheath
Direction of signal
Axon terminal
Axon terminal
Synapse (neuromuscular junction)
Neurotransmitter release
Muscle cell
Muscle cell

Signal Reception

- **Dendrites** sense and convert incoming signals into electrical signals by changing membrane potential.

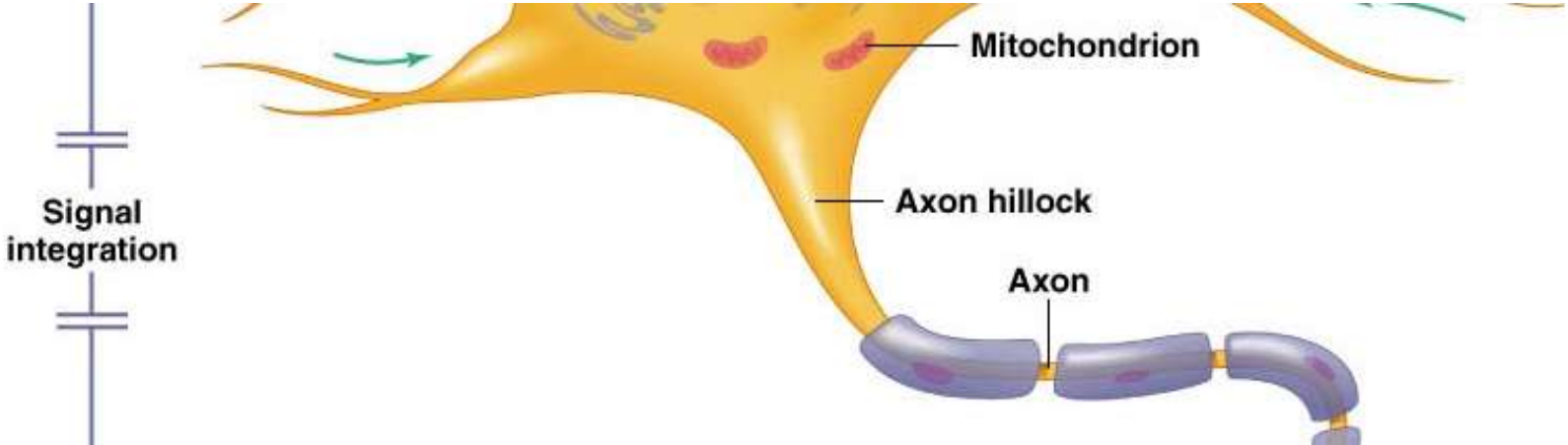
- Cell Body = routine metabolic functions



Signal Integration

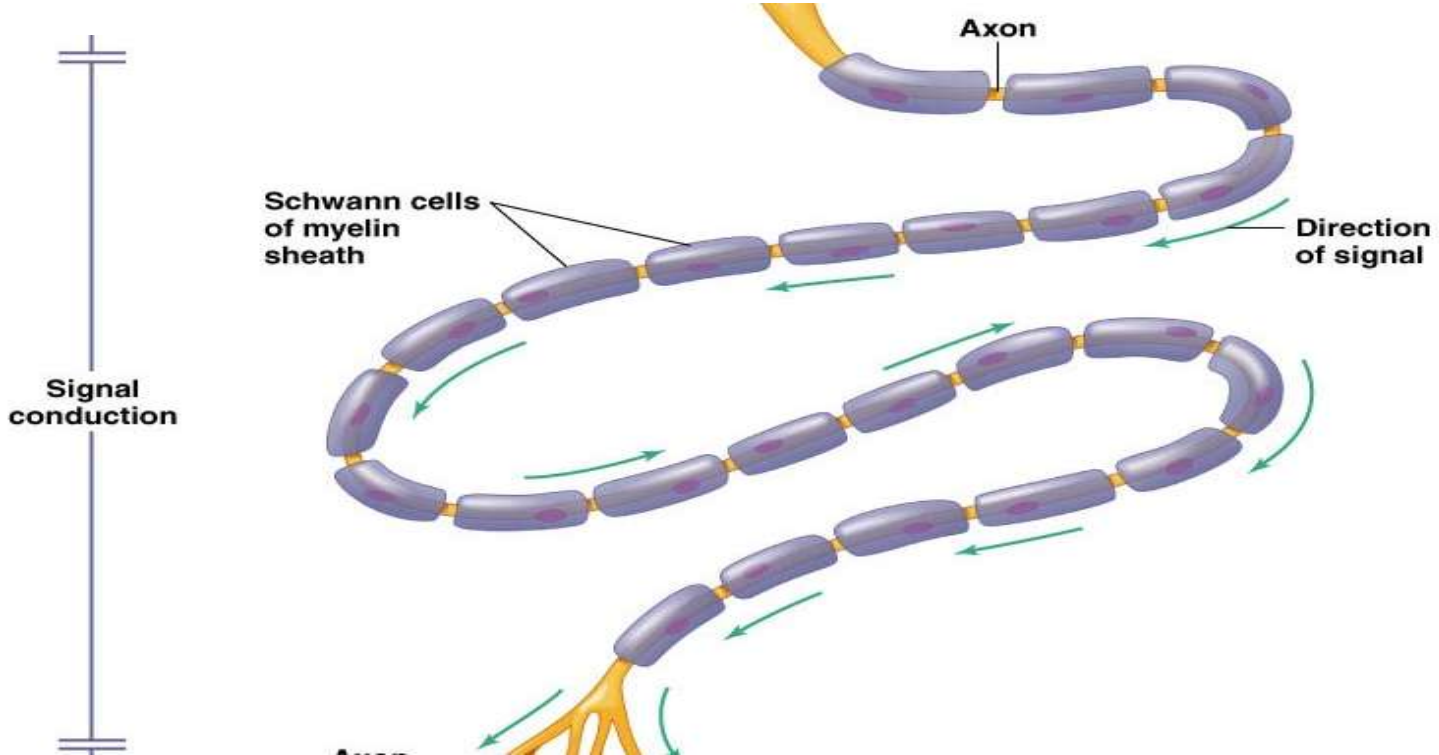
- Incoming signals are conducted to the **axon hillock**

- If signal is sufficiently large an electrical signal, or *action potential*, is initiated.



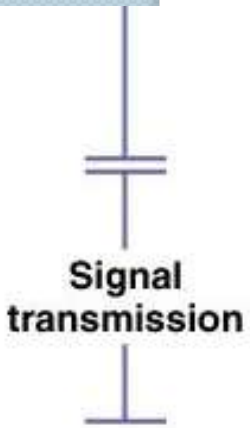
Signal Conduction

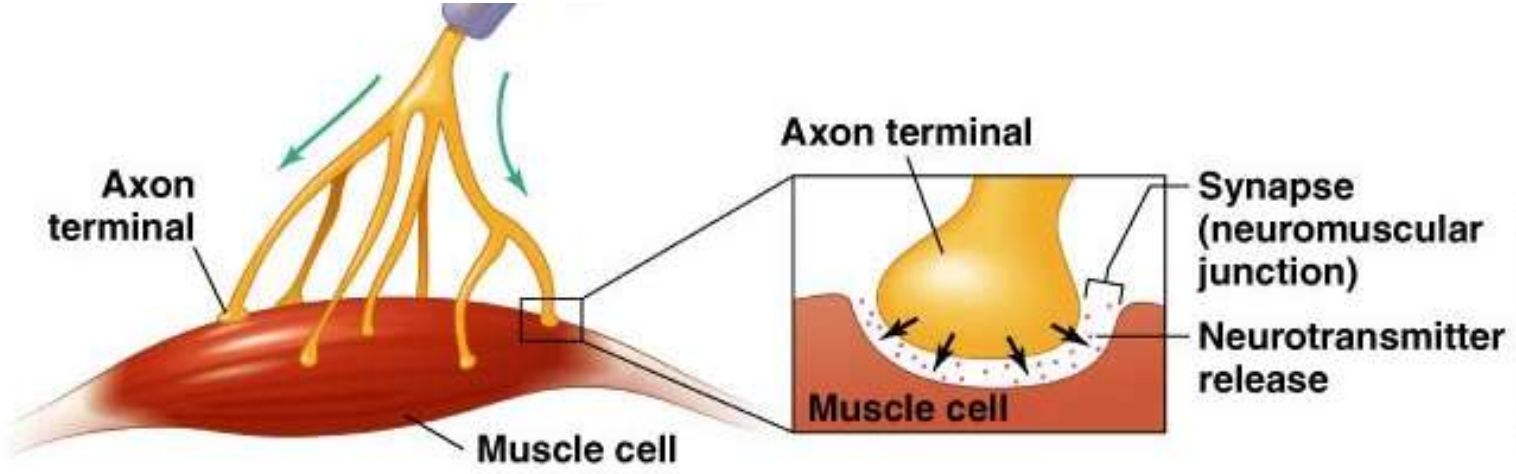
- **Axon**: One per neuron. Vary in length.
- Wrapped in myelin sheath that aids in the conduction of nerve impulses.



Signal Transmission

- **Axon terminals** form synapses with target skeletal muscle cells.





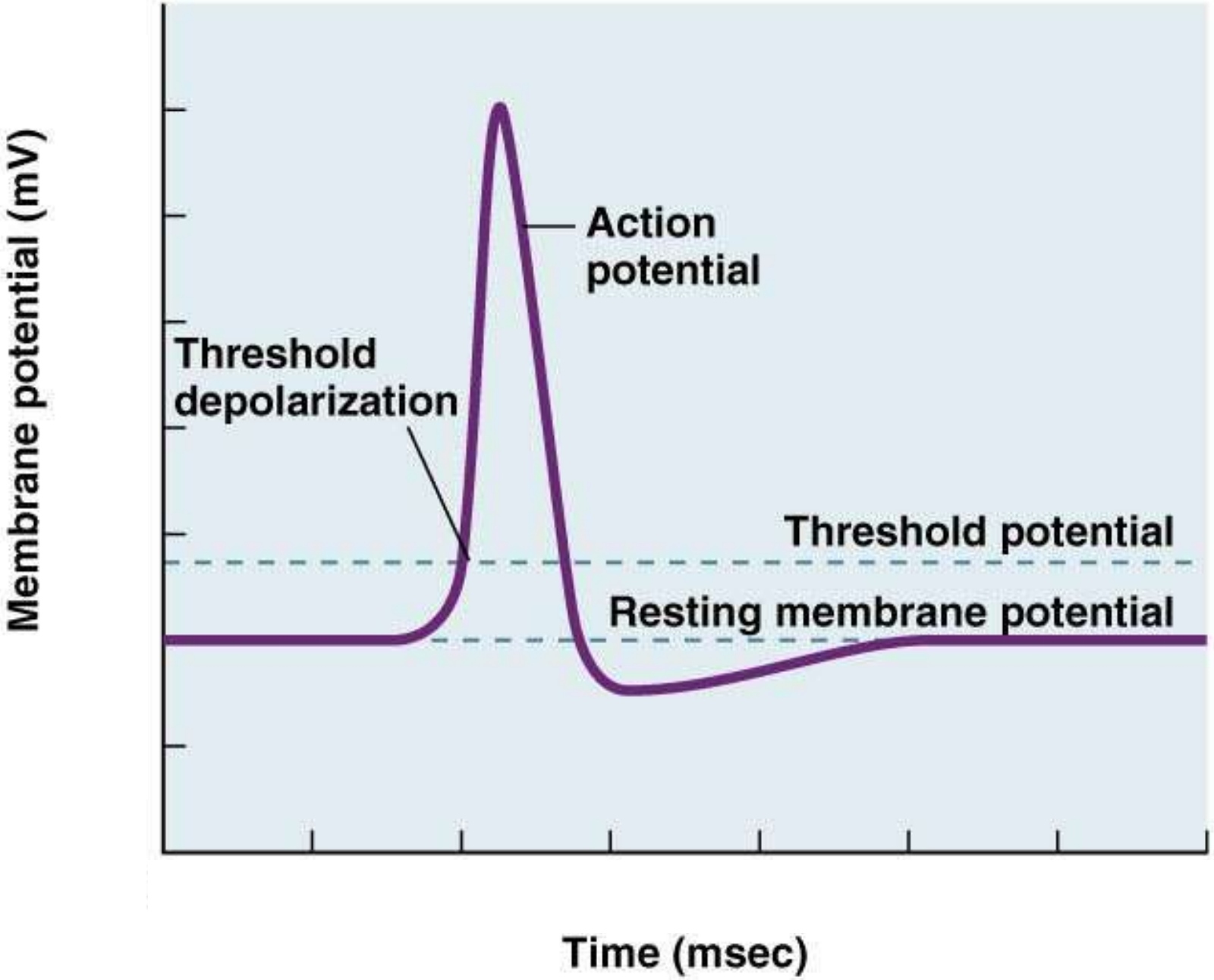
- Electrical signal results in the release of chemical neurotransmitters.

Motor Neuron Overall Process

1. Receive incoming signal
2. Convert to change in membrane potential
3. Trigger action potentials that conduct signals across long distances
4. Transmit signals to target cells in the form of a neurotransmitter

Electrical Signals in Neurons

- Average resting membrane potential is approximately -70mV.
- **Depolarization** = the charge *difference* between the inside & outside of the cell membrane decreases.
- **Hyper-polarization** = membrane potential becomes more negative.
- **Repolarization** = cell membrane potential goes back to resting levels.


Membrane potential (mV)
Action potential
Threshold depolarization
Threshold potential
Resting membrane potential
Time (msec)

Membrane Potential

- 3 factors contribute to membrane potential:
  - Distribution of ions across the membrane
  - Permeability of the membrane to these ions
  - The charge of the ions

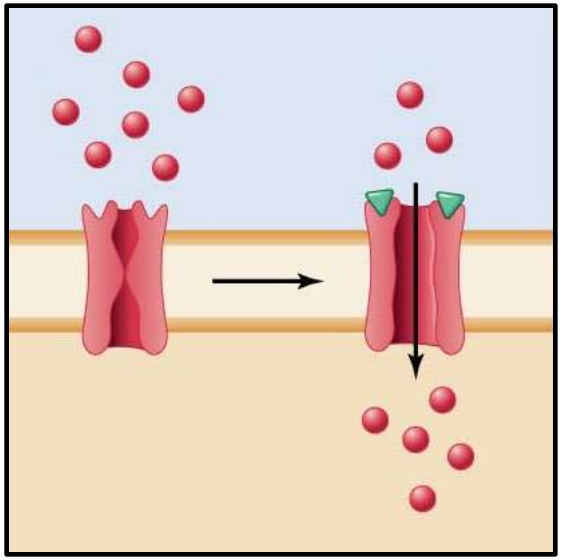
Membrane Potential

- Neurons selectively alter permeability of their membranes to ions (ex. Na^+ & K^+).

- Opening and close gated ion channels.
  - **Na^+ influx**
  - **K^+ efflux**

Ligand Gated Ion Channels

- Open and close in response to a stimulus, such as the binding of a neurotransmitter.

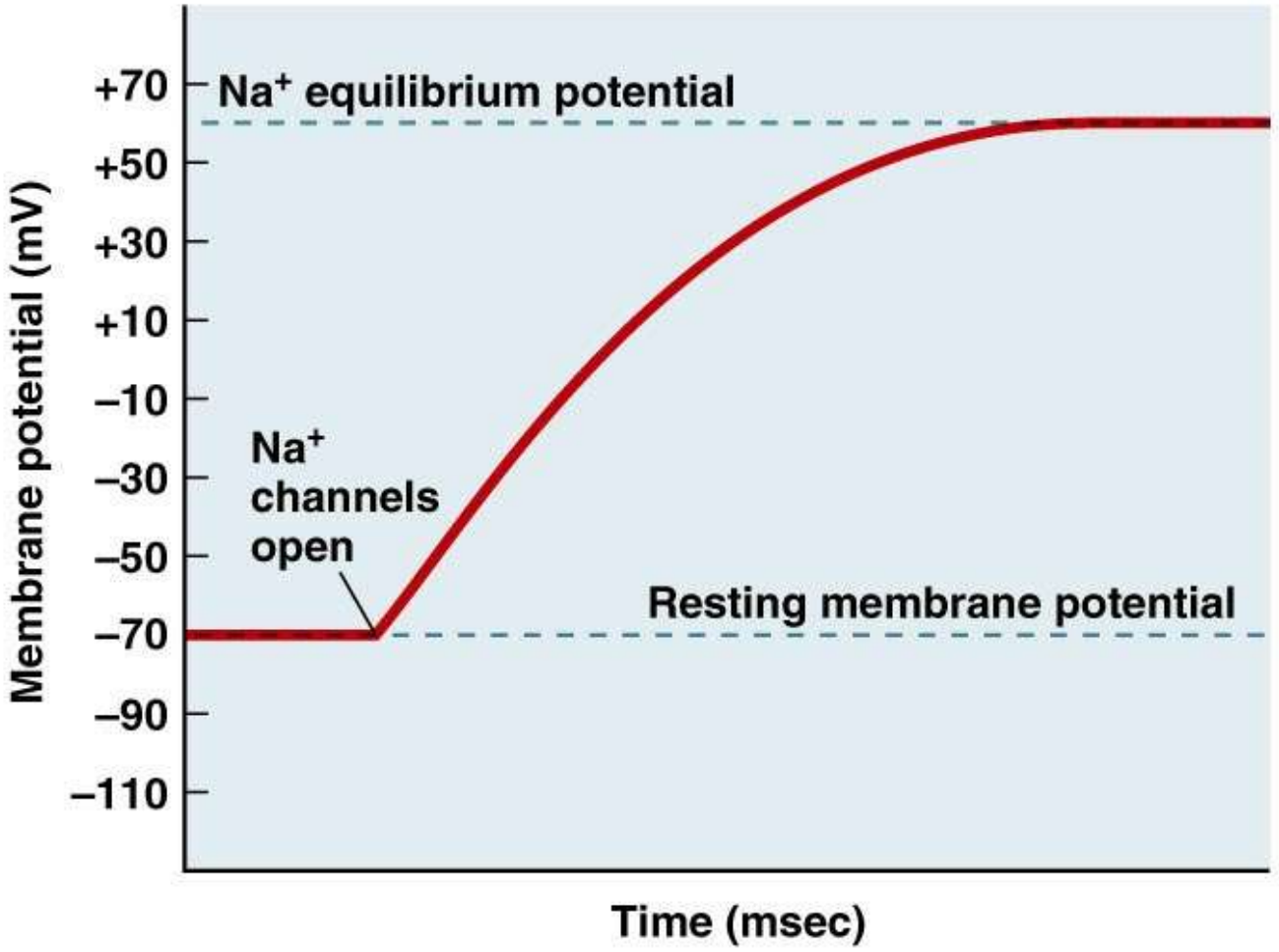


LIGAND GATED ION CHANNEL

Membrane Potential

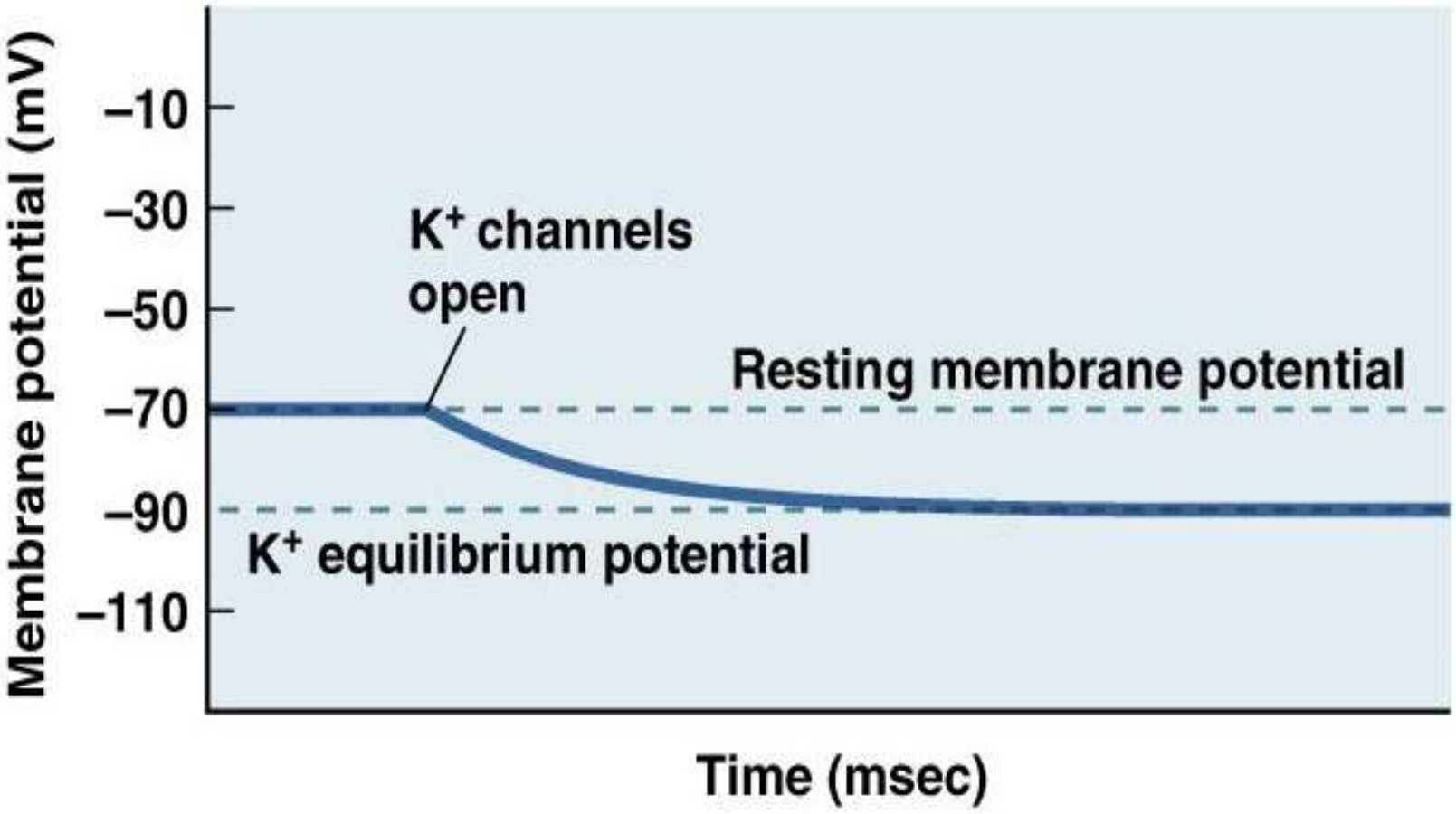
- Changes in permeability alters membrane potential and generates electrical signals.
- Opening Na^+ channels results in depolarization
- Opening K^+ channels results in hyperpolarization

Electrochemical Driving Force



(a) Opening of Na^+ channels depolarizes the membrane

Electrochemical Driving Force



(b) Opening of K^+ channels hyperpolarizes the membrane

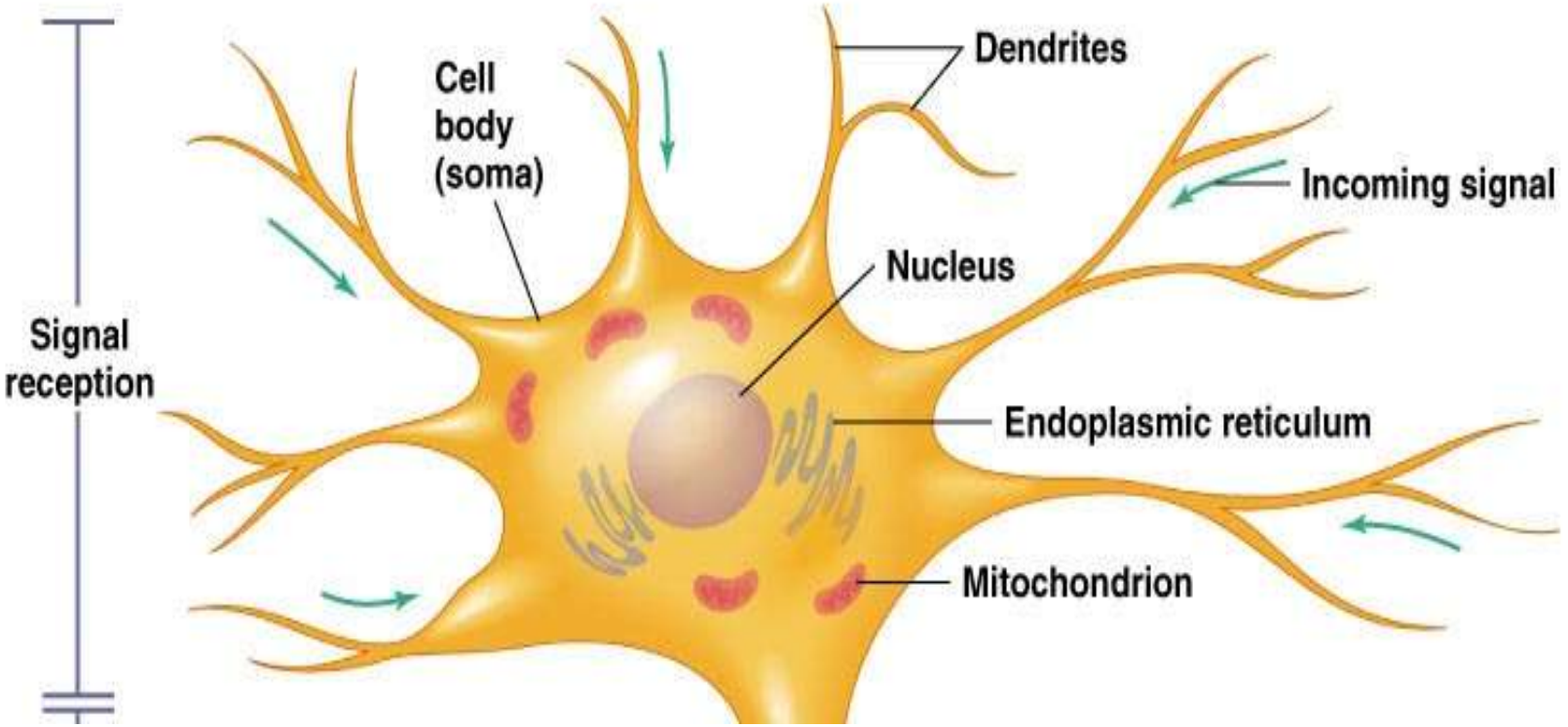
Electrochemical Driving Force

- **Equilibrium point** = membrane potential at which electrical and chemical gradients favoring movement of an ion exactly balance each other.

- no NET movement across membrane.

- Therefore, at equilibrium, there is no electrochemical driving force.

Signals in Dendrites & Cell Body



Signals in Dendrites & Cell Body

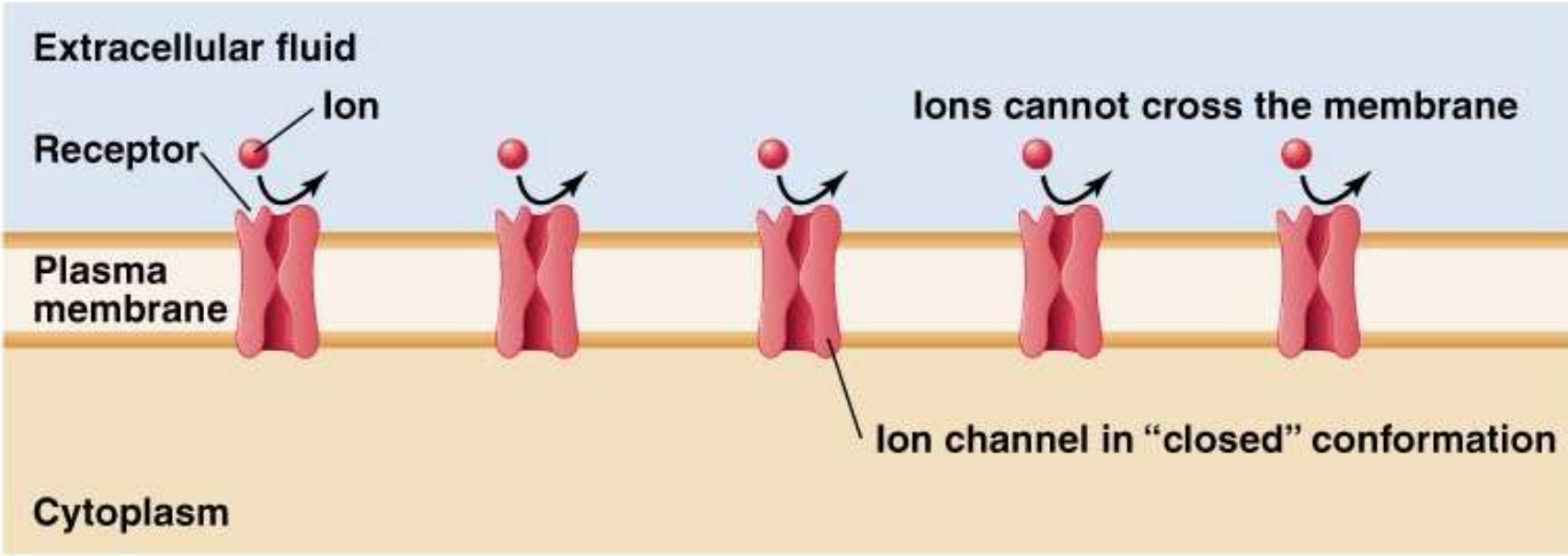
- Incoming Signal = Neurotransmitter
- Binds to membrane bound receptor = Ligand Gated Ion Channel
- Changes in permeability alter membrane potential.

Signals in Dendrites & Cell Body

- In the dendrites and cell bodies of neurons electrical signals are called graded potentials

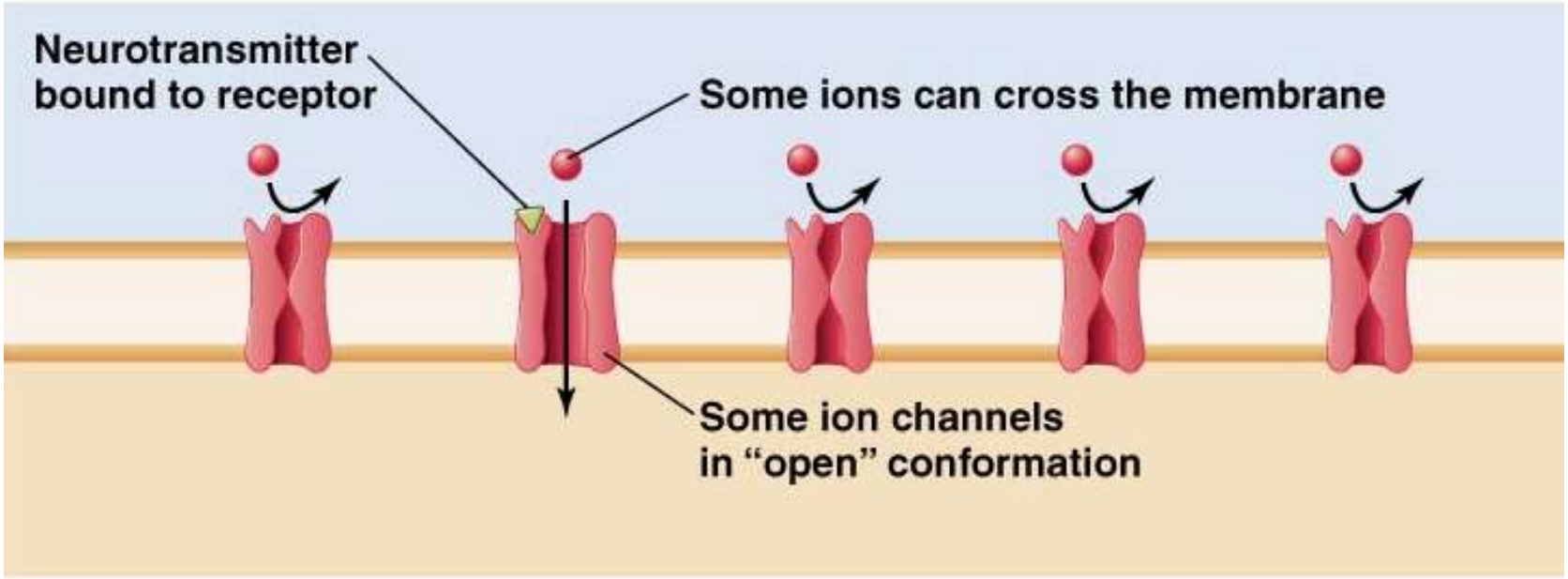
- **Graded potentials** vary in magnitude depending on the strength of the stimulus

No Neurotransmitter



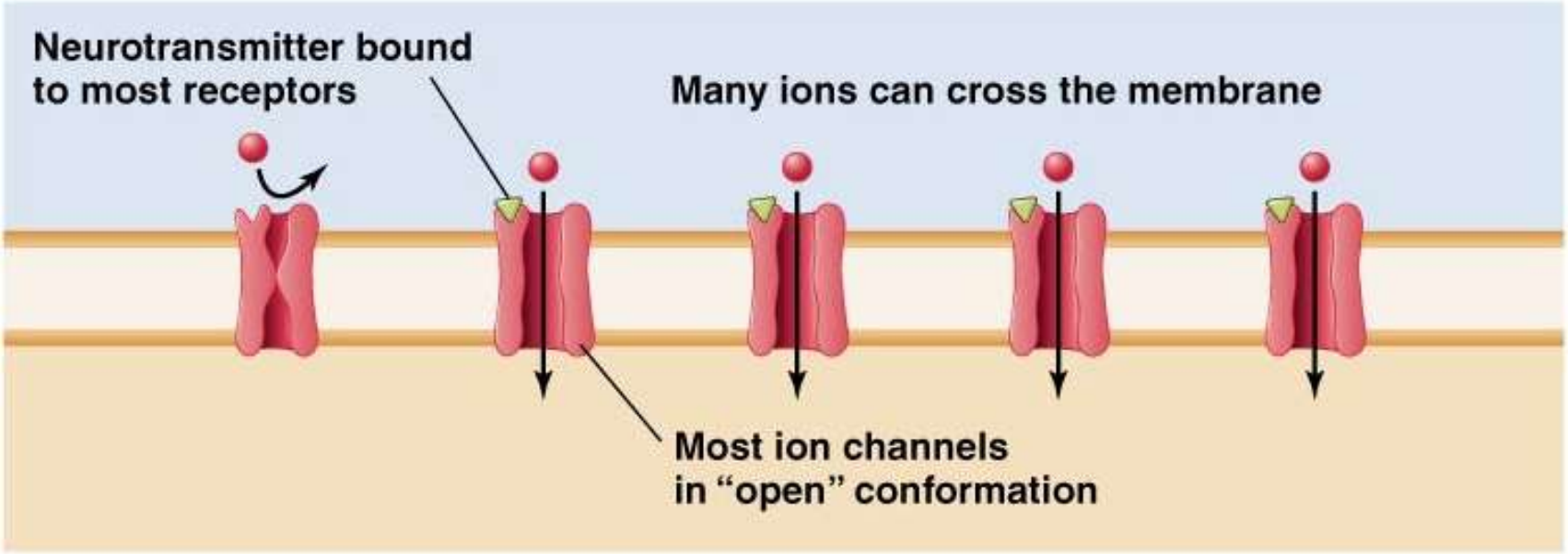
(a) No neurotransmitter

Low [Neurotransmitter]



(b) Low concentration of neurotransmitter

High [Neurotransmitter]

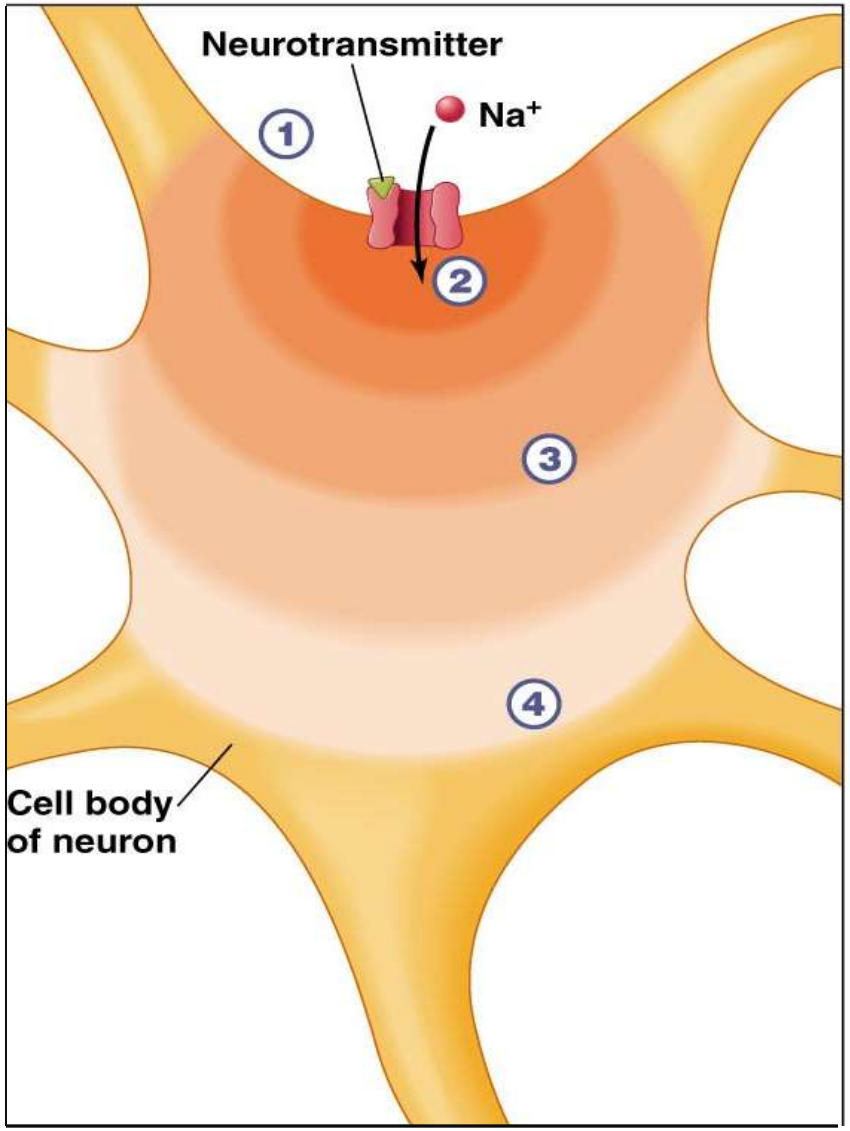


(c) High concentration of neurotransmitter

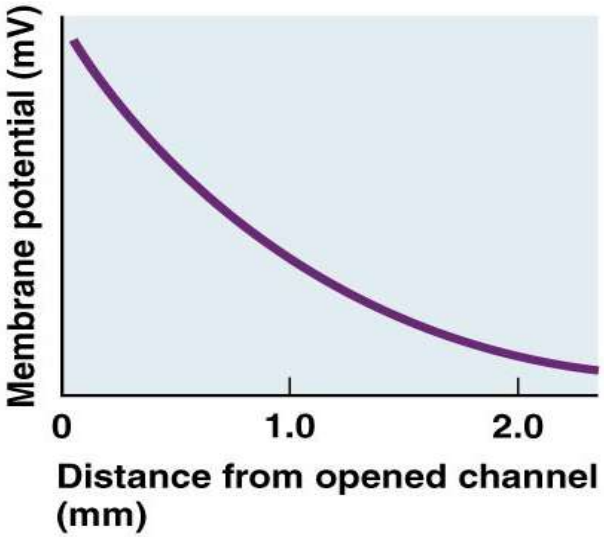
Depolarization v. Hyperpolarization

- Most important ion channels in the dendrites and cell body of a neuron are:
  - Na^+, K^+, Cl^-, and Ca^{2+}
- Open Na^+ or Ca^{2+} = depolarization
- Open K^+ or Cl^- = hyperpolarization

Graded Potential



1. Neurotransmitter binds to a ligand-gated Na^+ channel.
2. Na^+ enters cell through the open channel.
3. Current spreads through the cell.
4. The strength of the signal decreases with distance.

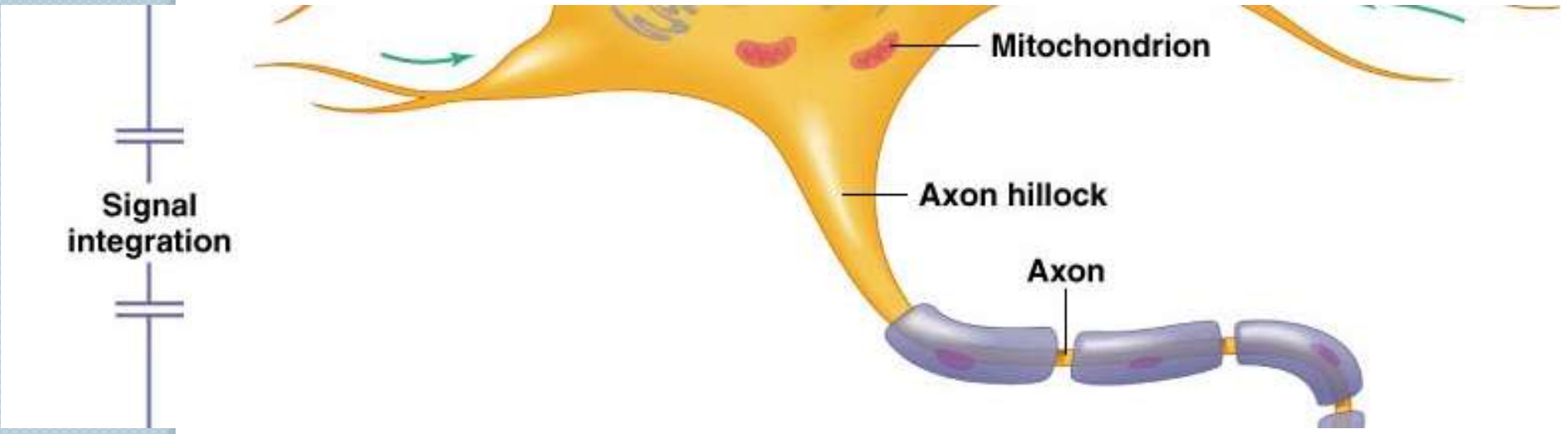


Graded Potentials

- Short distance signals due to:
  - leakage of charged ions
  - electrical resistance of the cytoplasm
- Cannot travel long distances without dying away.

Signals at the Axon Hillock

- "Trigger Zone"



Signals at the Axon Hillock

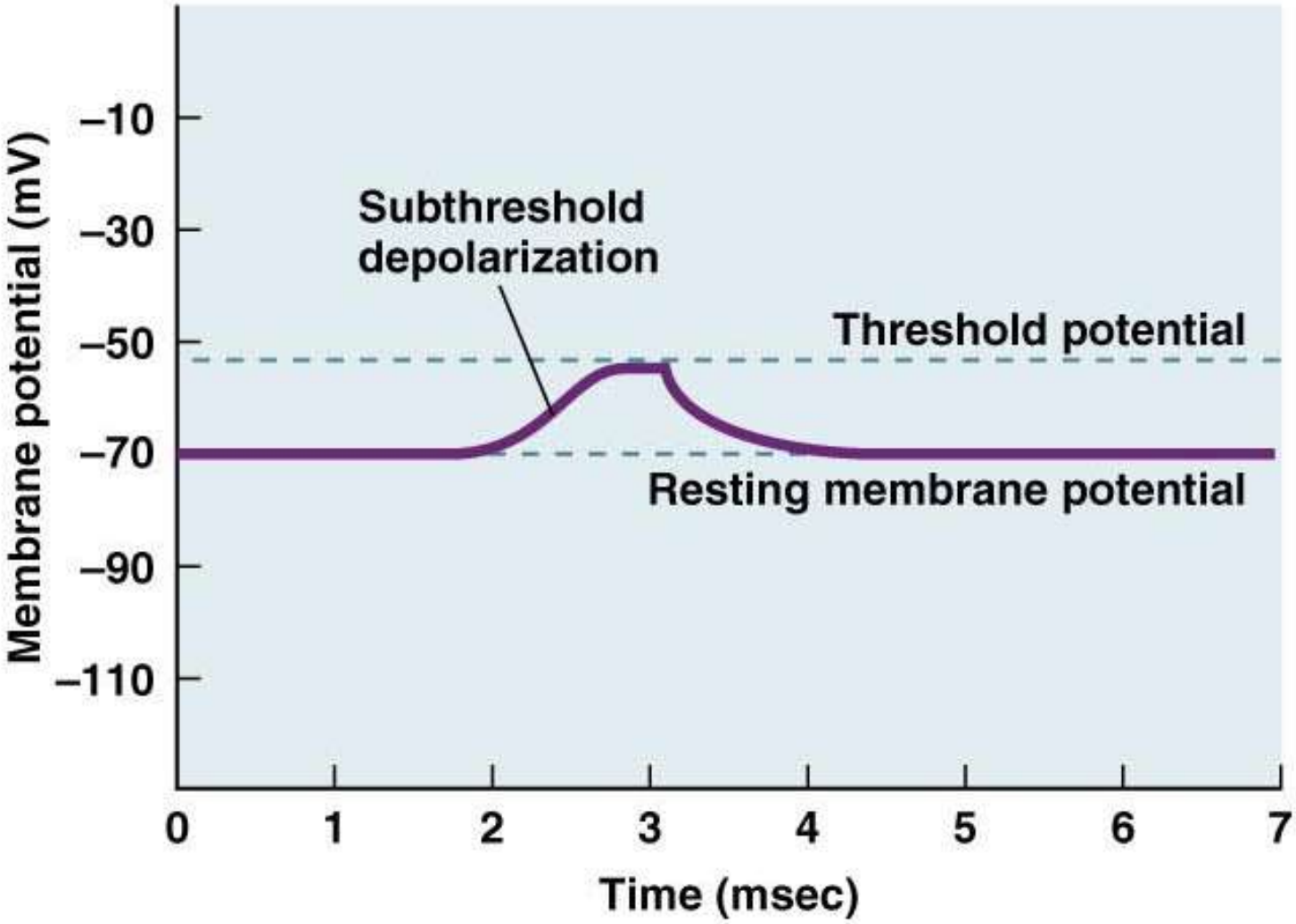
- Action potentials are *triggered* by the **NET** graded potential at the membrane of the axon hillock.

- Action potentials are "fired" when the net graded potential is beyond the **threshold potential**.

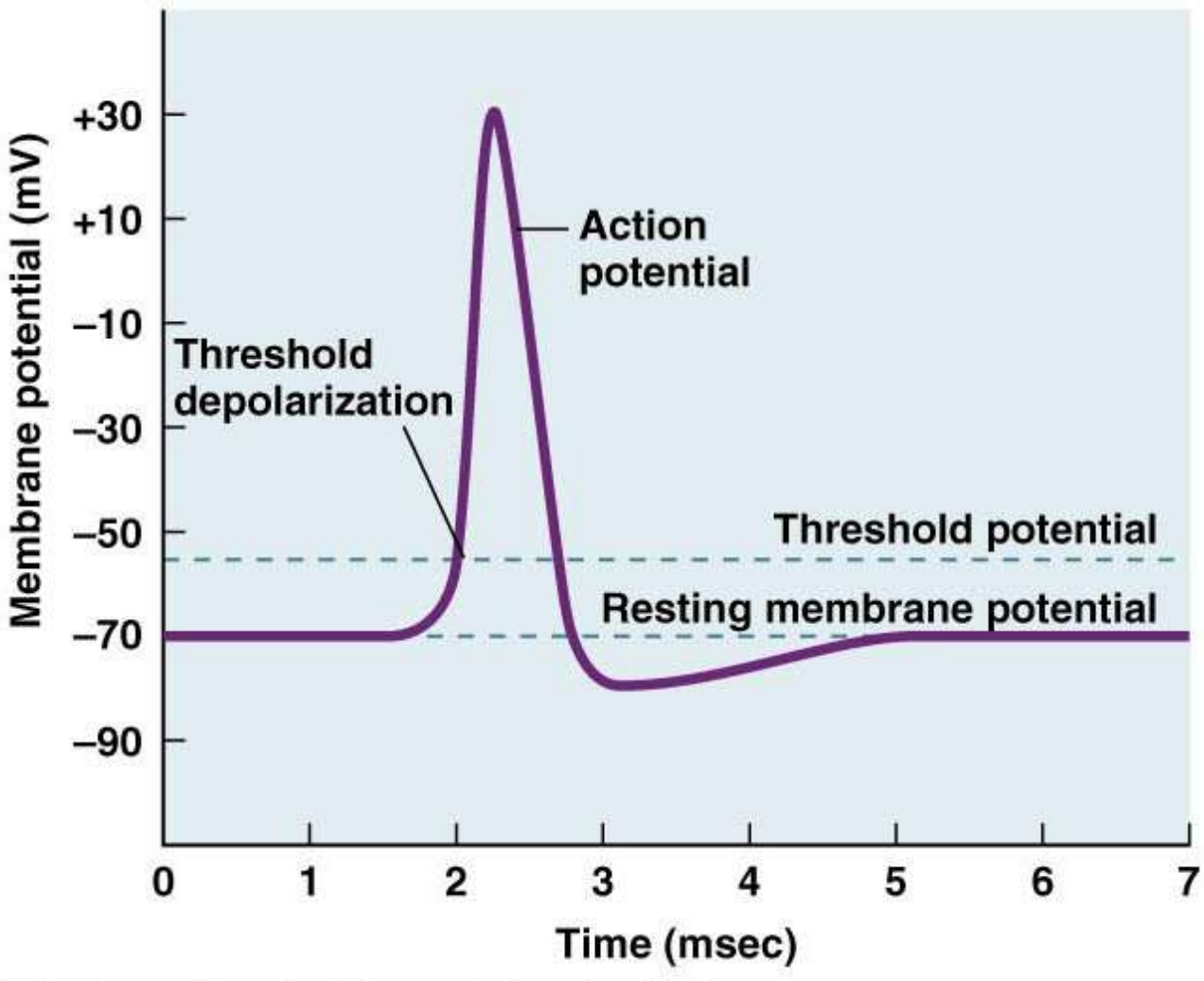
Signals at the Axon Hillock

- The net graded potential at the axon hillock membrane can be a:
  - Subthreshold Potential
  - Suprathreshold Potential

Subthreshold Potential

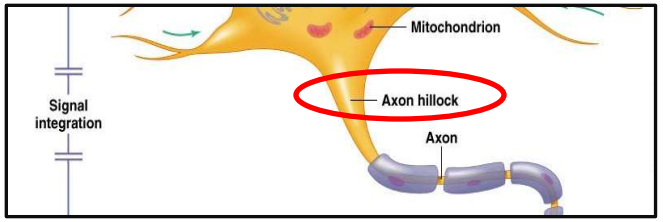


Suprathreshold Potential



Signals at the Axon Hillock

- Excitatory potential =
  - Depolarizing graded potential
  - Brings the membrane potential closer to threshold potential



- Inhibitory potential =
  - Hyperpolarizing graded potential
  - Moves membrane potential farther away from threshold potential.

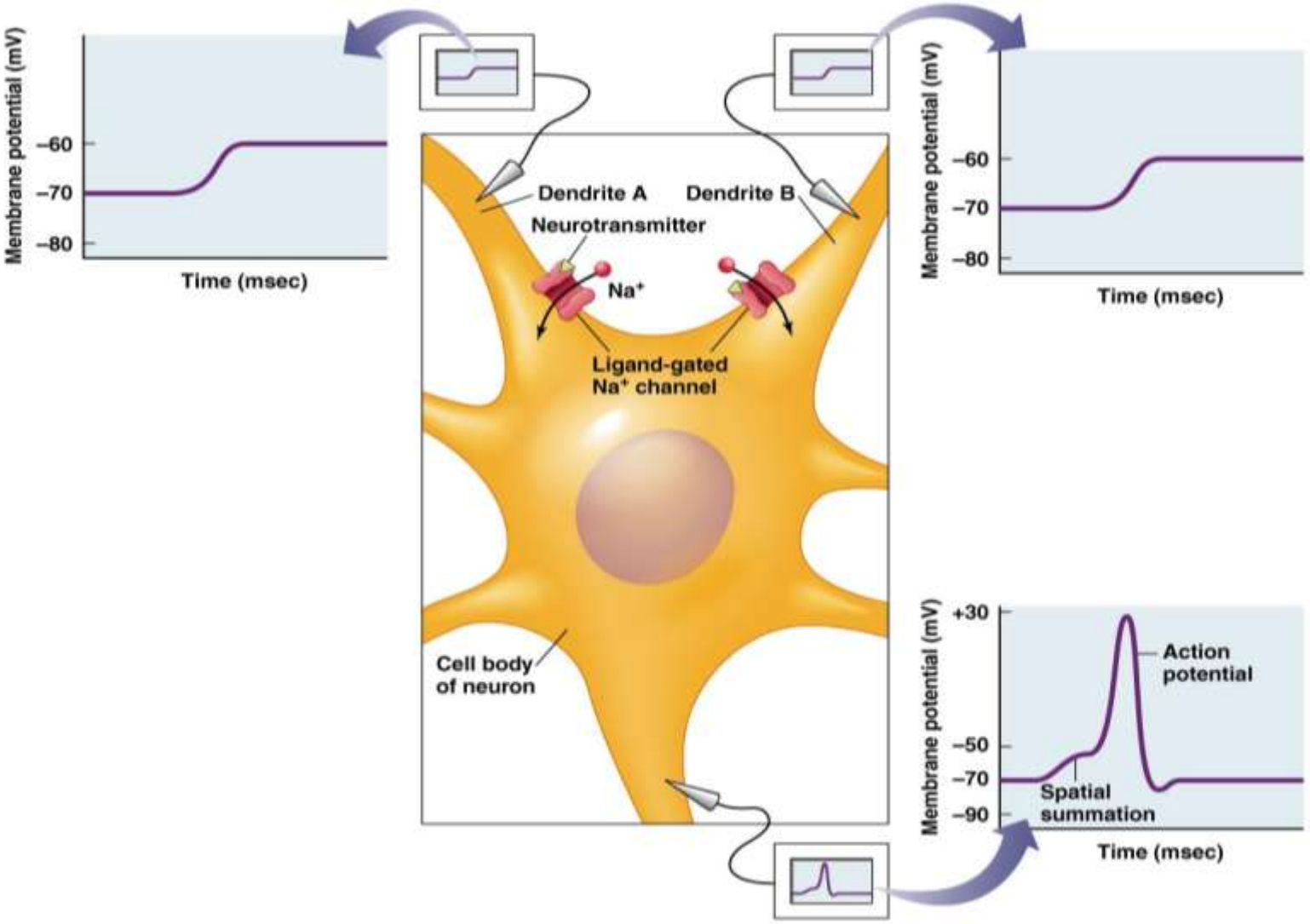
Multiple Graded Potentials

- Neurons can generate many graded potentials at once

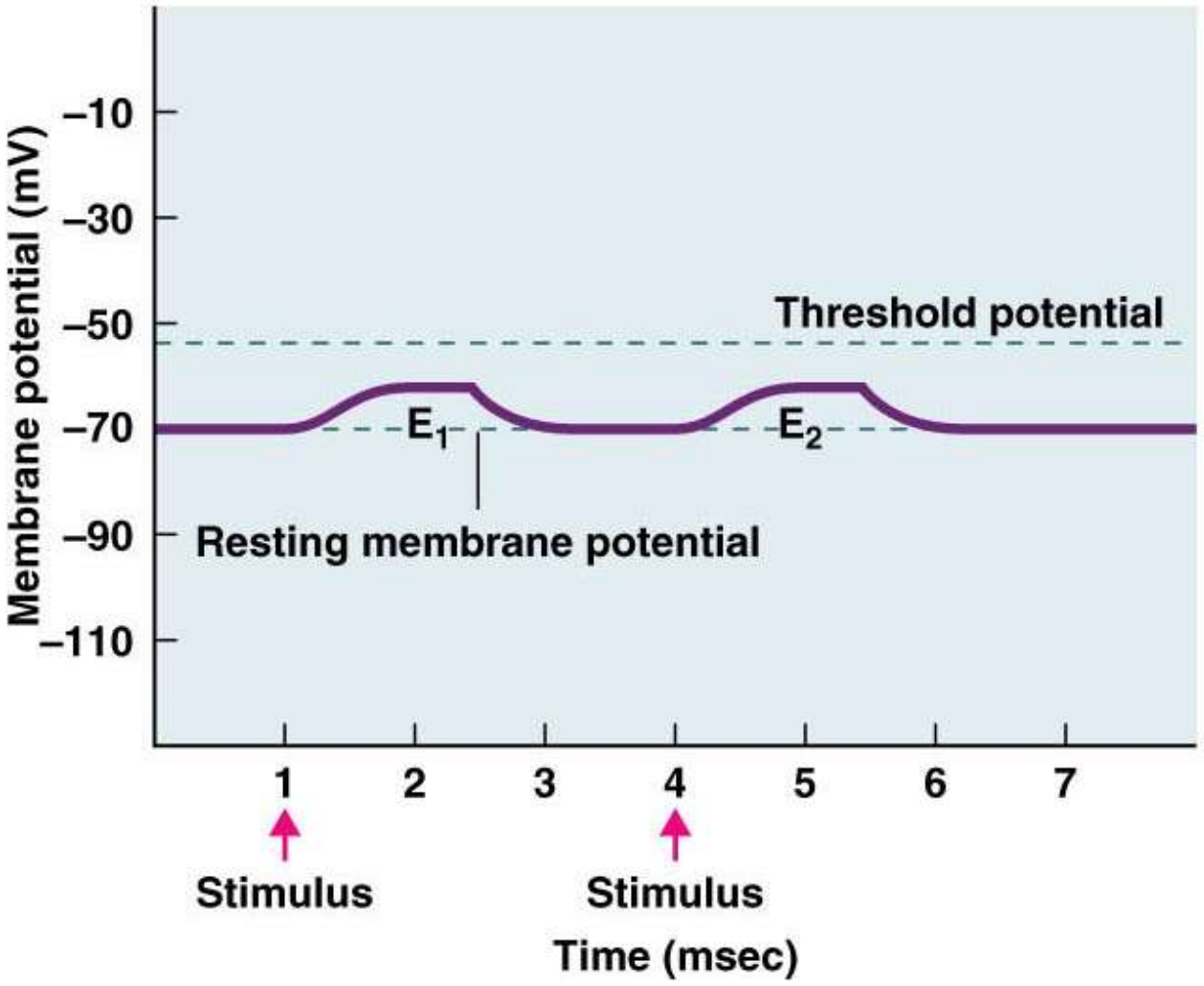
- **Spatial summation:**
  Sum of multiple potentials

- **Temporal summation:**
  Potentials may build on each other as long as they are not too far apart in time.

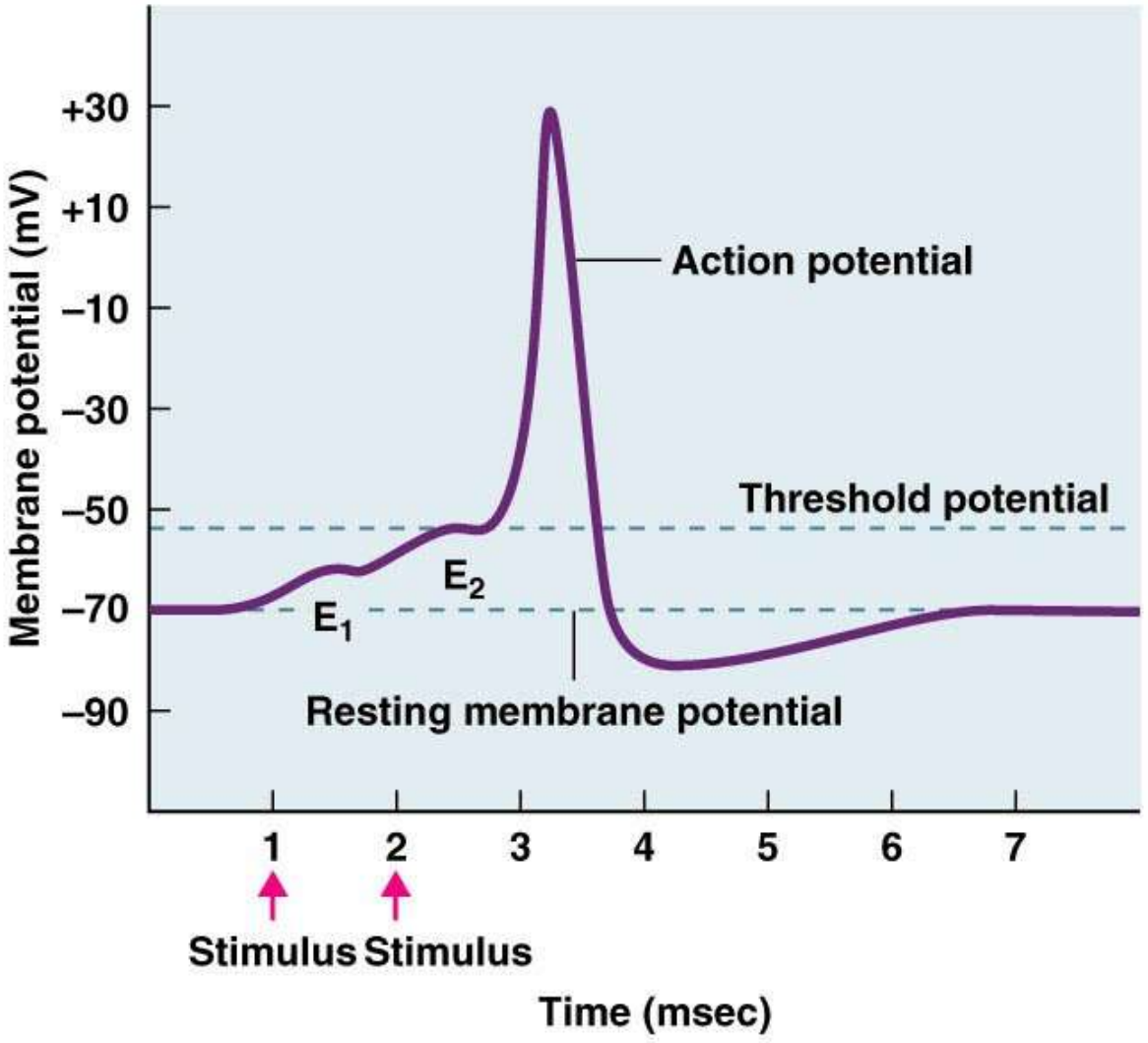
Spatial Summation



Temporal Summation



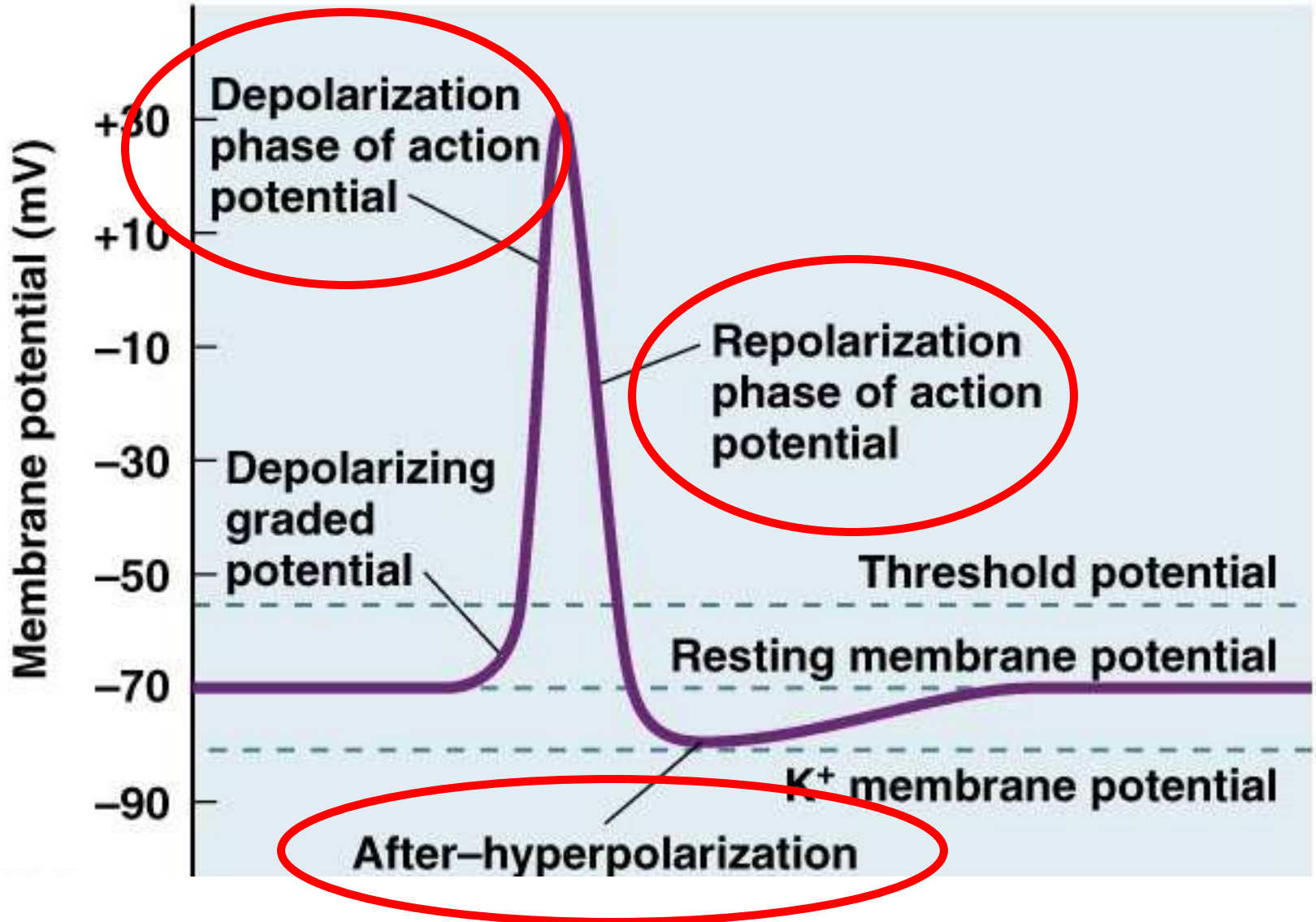
Temporal Summation



Signals in the Axon

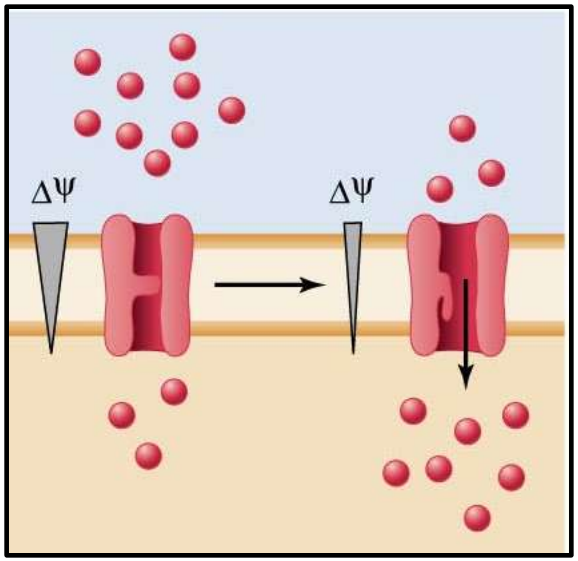
- AP is triggered when membrane potential at the axon hillock reaches its threshold.
- Action Potentials have 3 phases:
  - Depolarization – reaches +30 mV
  - Repolarization – returns to -70mV
  - After-hyperpolarization – overshoots

3 Main Phases of Action Potentials



Voltage Gated Ion Channels

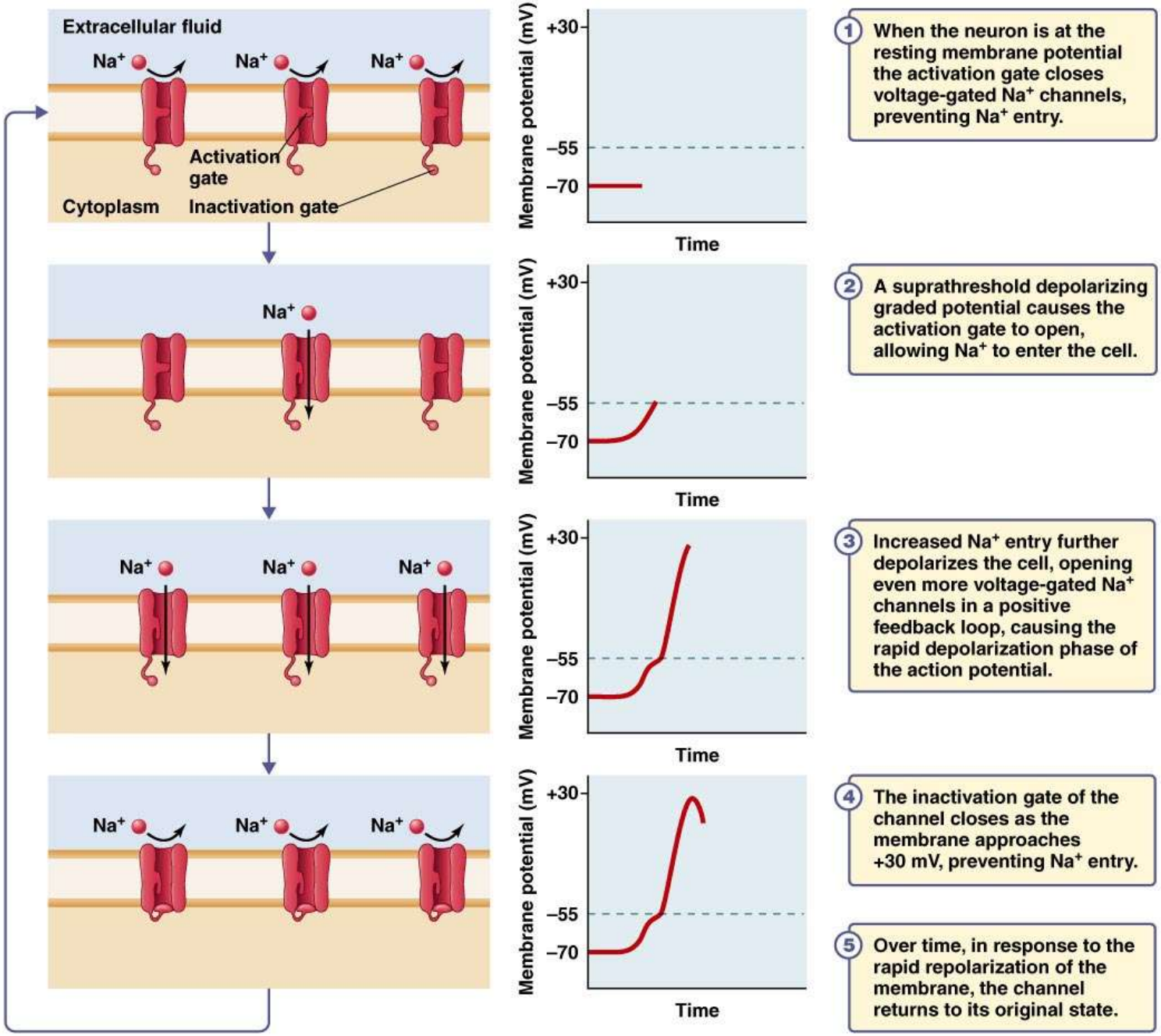
- Changes in membrane potential cause structural changes in voltage gated channels, resulting in changes in permeability.



VOLTAGE GATED ION CHANNEL

Voltage Gated Na^+ Channels

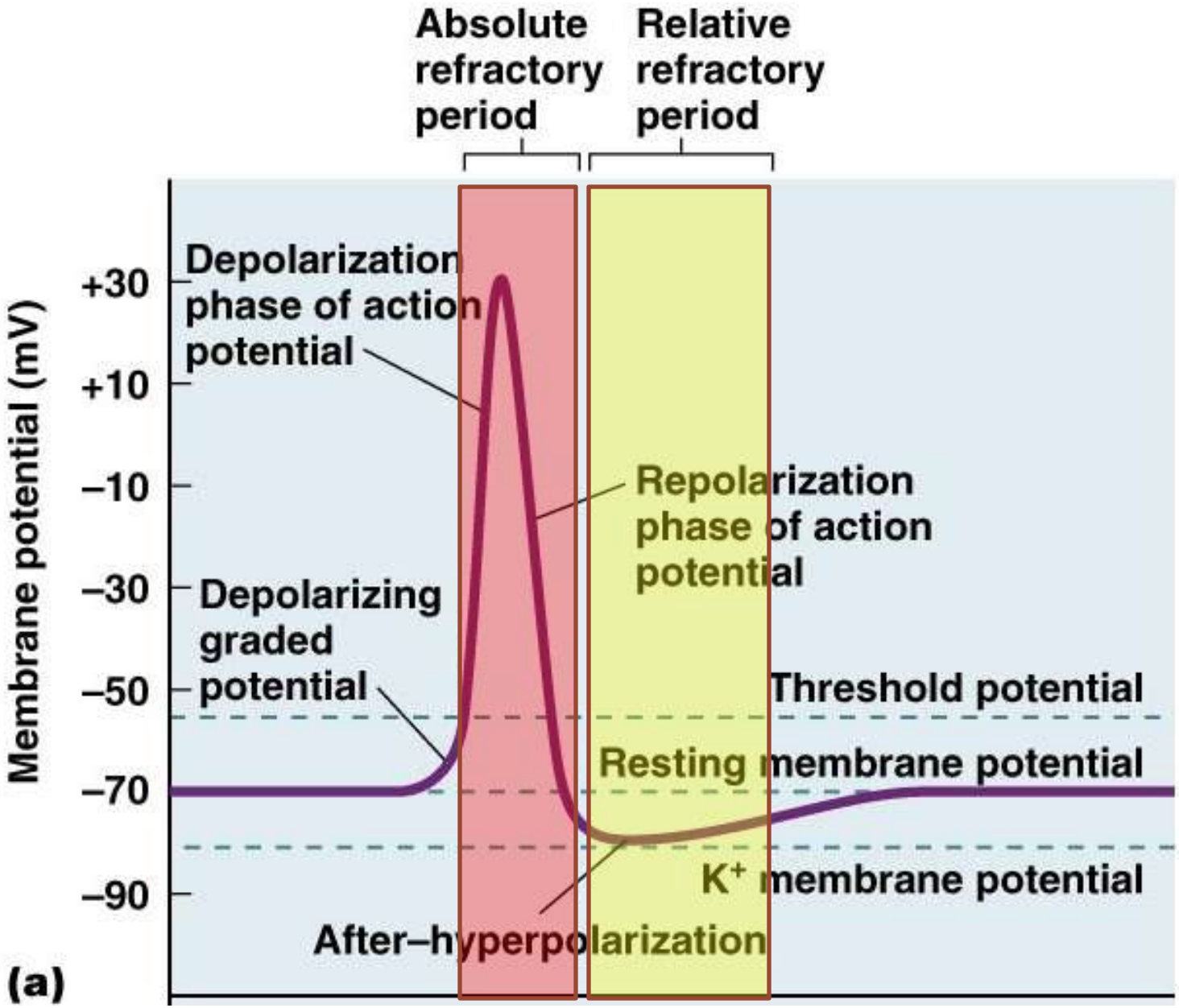
- Voltage Gated Na^+ Channels have 2 gates:
  - Activation gate
  - Inactivation gate



Refractory Periods

- **Absolute refractory period =**
  - axon is incapable of regenerating a new action potential no matter how strong the stimulus

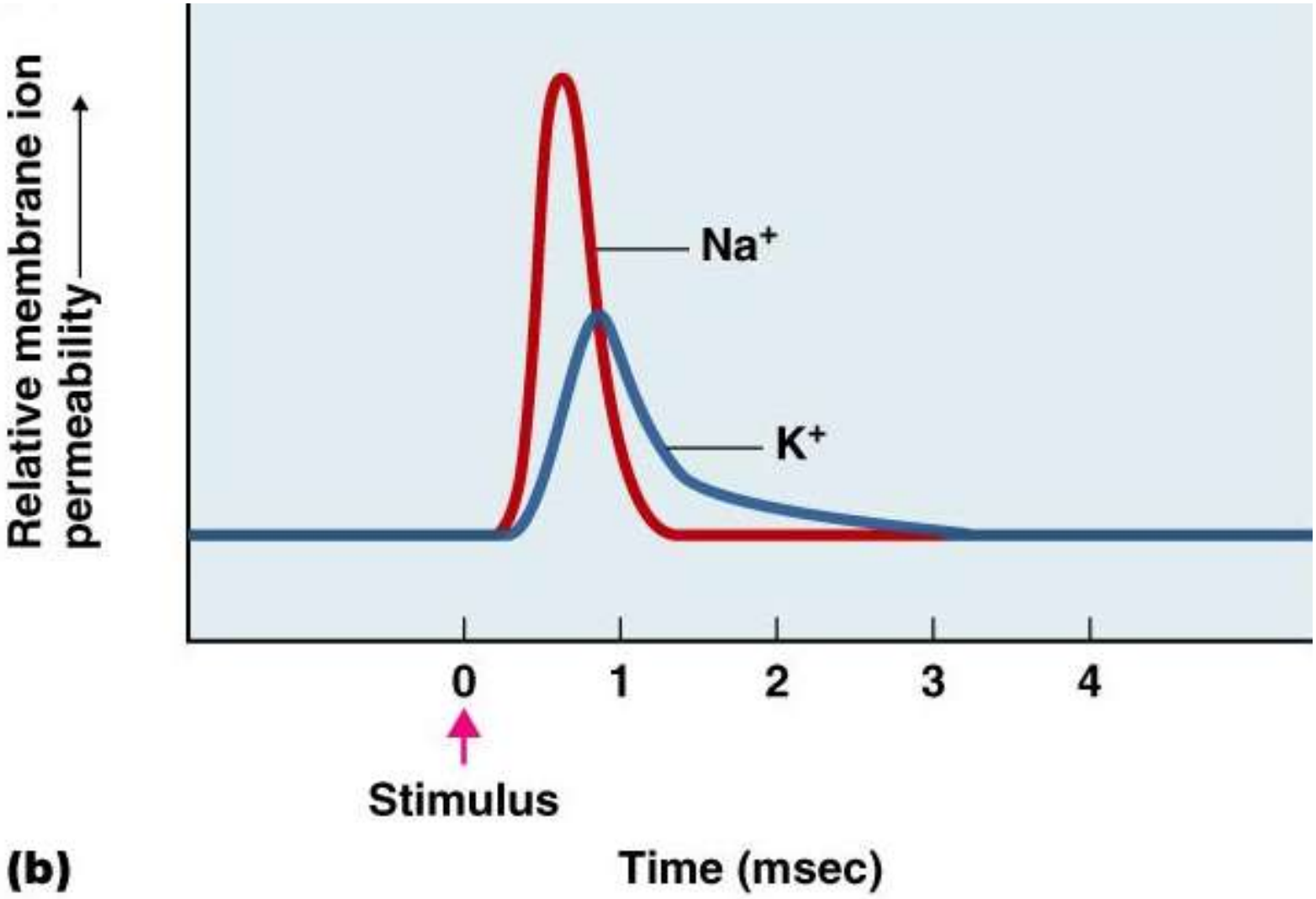
- **Relative refractory period =**
  - new action potential can be generated, but only by a very large stimulus


Absolute refractory period
Relative refractory period
Depolarization phase of action potential
Repolarization phase of action potential
Depolarizing graded potential
Threshold potential
Resting membrane potential
K+ membrane potential
After–hyperpolarization
Membrane potential (mV)
+30
+10
–10
–30
–50
–70
–90
(a)

Refractory Periods

- Due to the opening and closing of voltage gated ion channels
- Opening Na^+ channels = depolarization
- Opening K^+ channels = repolarization

Refractory Periods



Refractory Periods

- Opening Na^+ Channels
  - Positive feedback loop of Na^+ entry results in extremely rapid changes in Na^+ permeability
  - Before reaching Na^+ equilibrium (+60mV), Na^+ channels close, terminating depolarization

Refractory Periods

- Opening K^+ channels:
  - open more slowly
  - only open in substantial numbers just before Na^+ channels close.
  - K^+ moves out of the cell, cell becomes more negative, and causes repolarization.
  - K^+ channels close slow, explaining why there is the after-hyperpolarization phase.

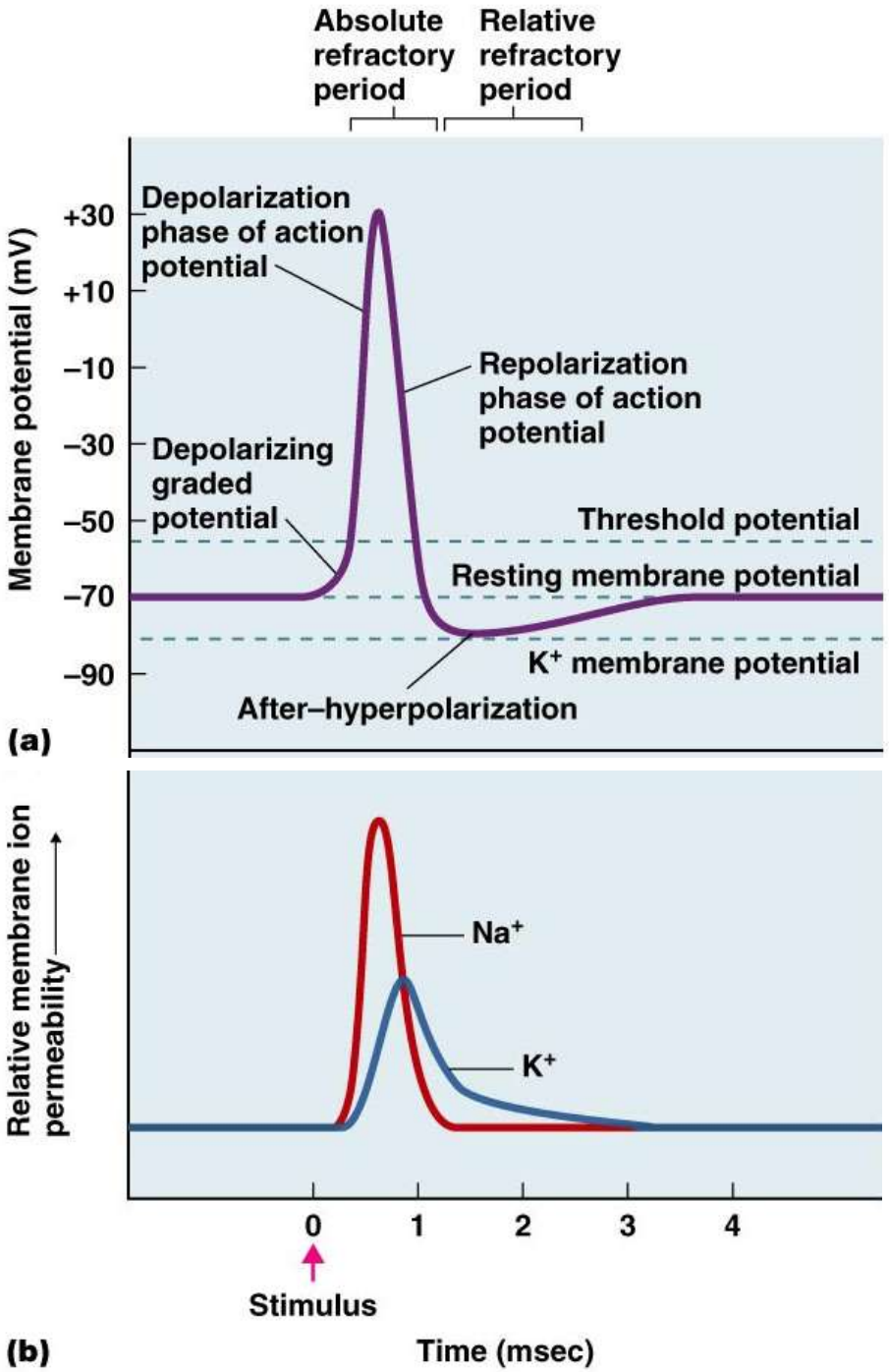
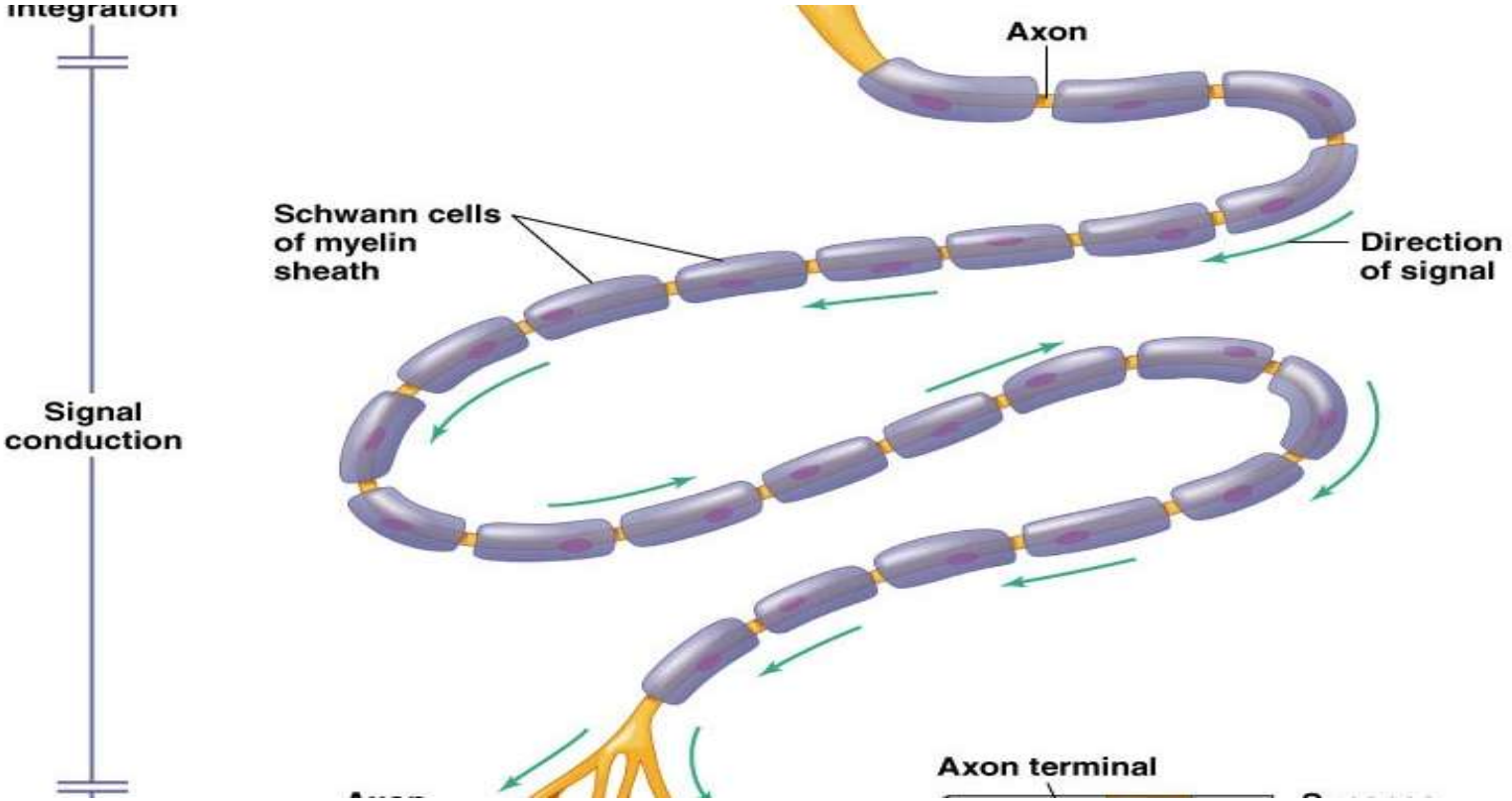

Absolute refractory period
Relative refractory period
Depolarization phase of action potential
Repolarization phase of action potential
Depolarizing graded potential
Threshold potential
Resting membrane potential
K+ membrane potential
After–hyperpolarization
Membrane potential (mV)
+30
+10
–10
–30
–50
–70
–90
(a)
Relative membrane ion permeability
Na+
K+
0
1
2
3
4
Stimulus
(b)
Time (msec)

Table 4.1 Differences between graded potentials and action potentials.

Graded potentials	Action potentials
Vary in magnitude	Always the same magnitude (in a given cell type)
Vary in duration	Always the same duration (in a given cell type)
Decay with distance	Can be transmitted across long distances
Occur in dendrites and cell body	Occur in axons
Caused by opening and closing of many kinds of ion channels	Caused by opening and closing of voltage-gated ion channels

“Traveling” Along the Axon



"All-or-None"

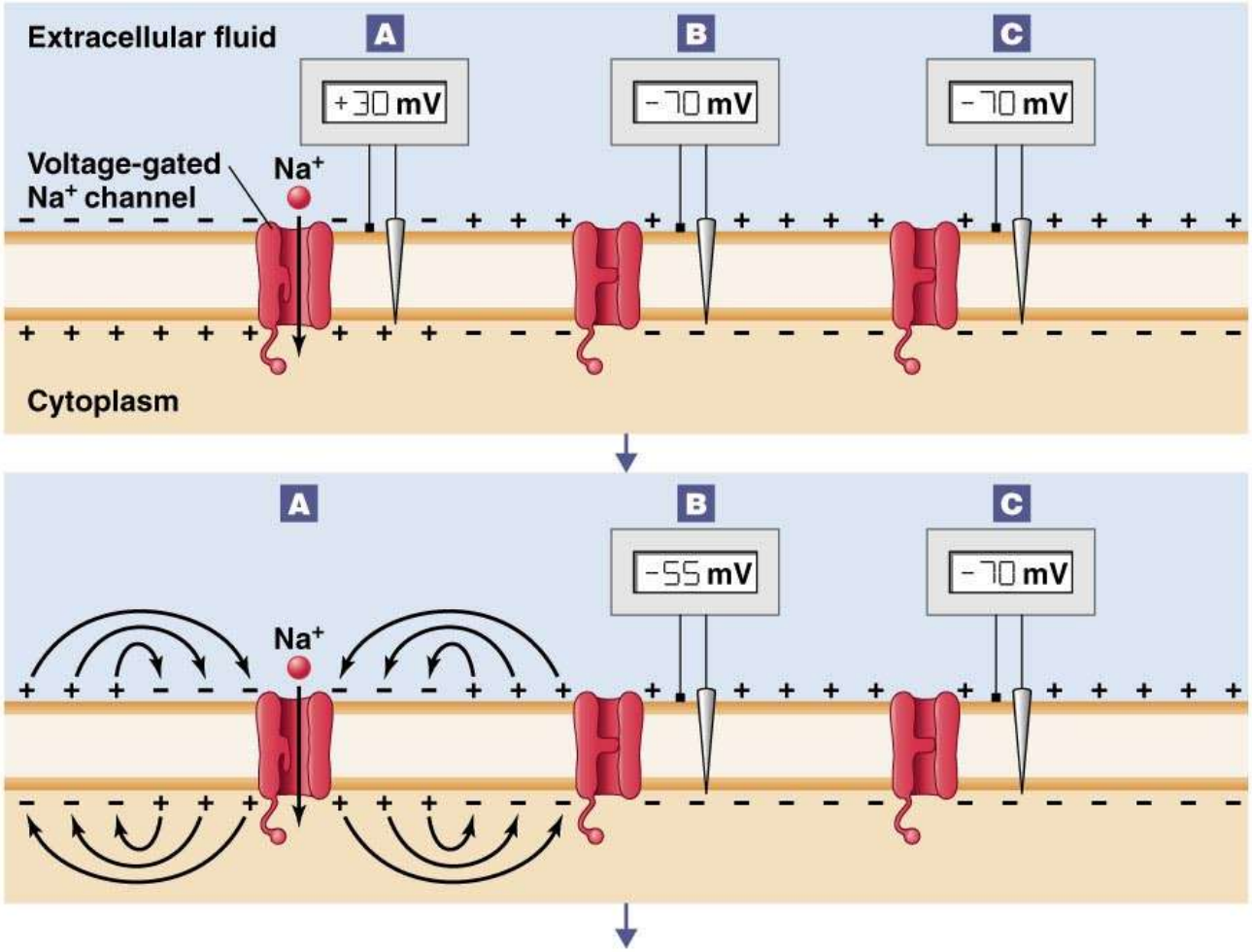
- Axons conduct action potentials **unidirectionally.**

- Travel along axon in an "All-or-None" fashion.
  - Reach threshold potential and fire, or don't.

"Traveling" Along the Axon

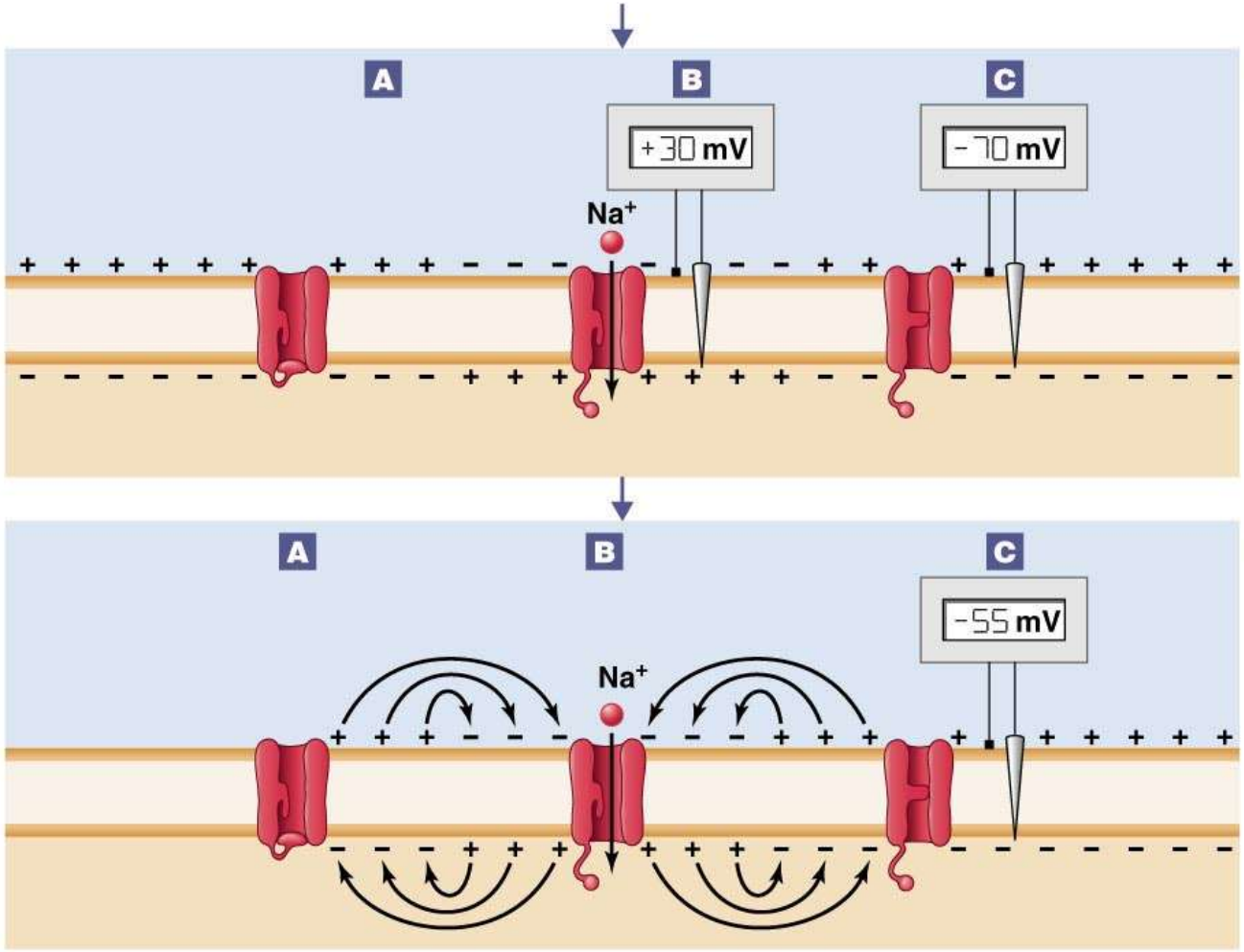
- Action potentials in one part of the axon trigger action potentials in adjacent areas of axonal membrane.
  - Dominoes.

- Therefore, action potentials are conducted across long distances without decaying.



1. When an action potential occurs at A on the membrane, Na^+ enters the axon through opened voltage-gated Na^+ channels. This action potential depolarizes the membrane at A to +30 mV.

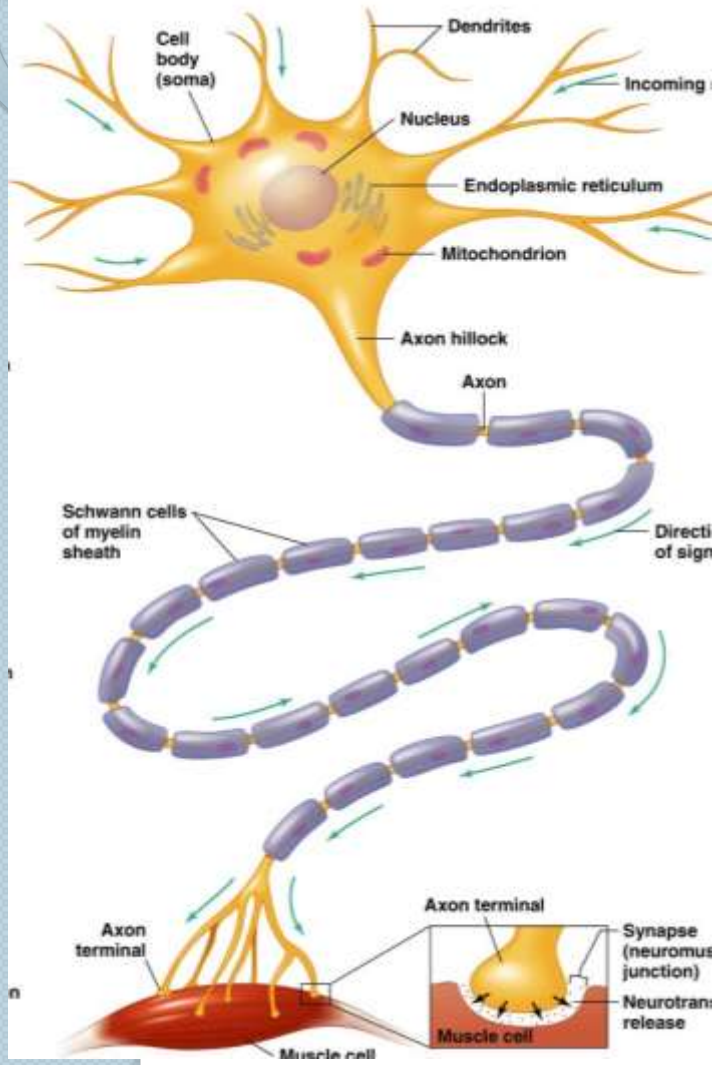
2. The depolarization due to the action potential at A spreads electrotonically by local current flow through the axon, depolarizing adjacent areas of the membrane toward threshold (–55 mV).



3 When the depolarization at B reaches threshold, voltage-gated Na^+ channels at B open, initiating an action potential that depolarizes B to +30 mV.

4 The depolarization due to the action potential at B spreads electrotonically by local current flow through the axon, depolarizing adjacent areas of the membrane toward threshold (–55 mV), triggering an action potential at C. Voltage-gated Na^+ channels at A are inactivated (and thus refractory), so a new action potential is not initiated at A.

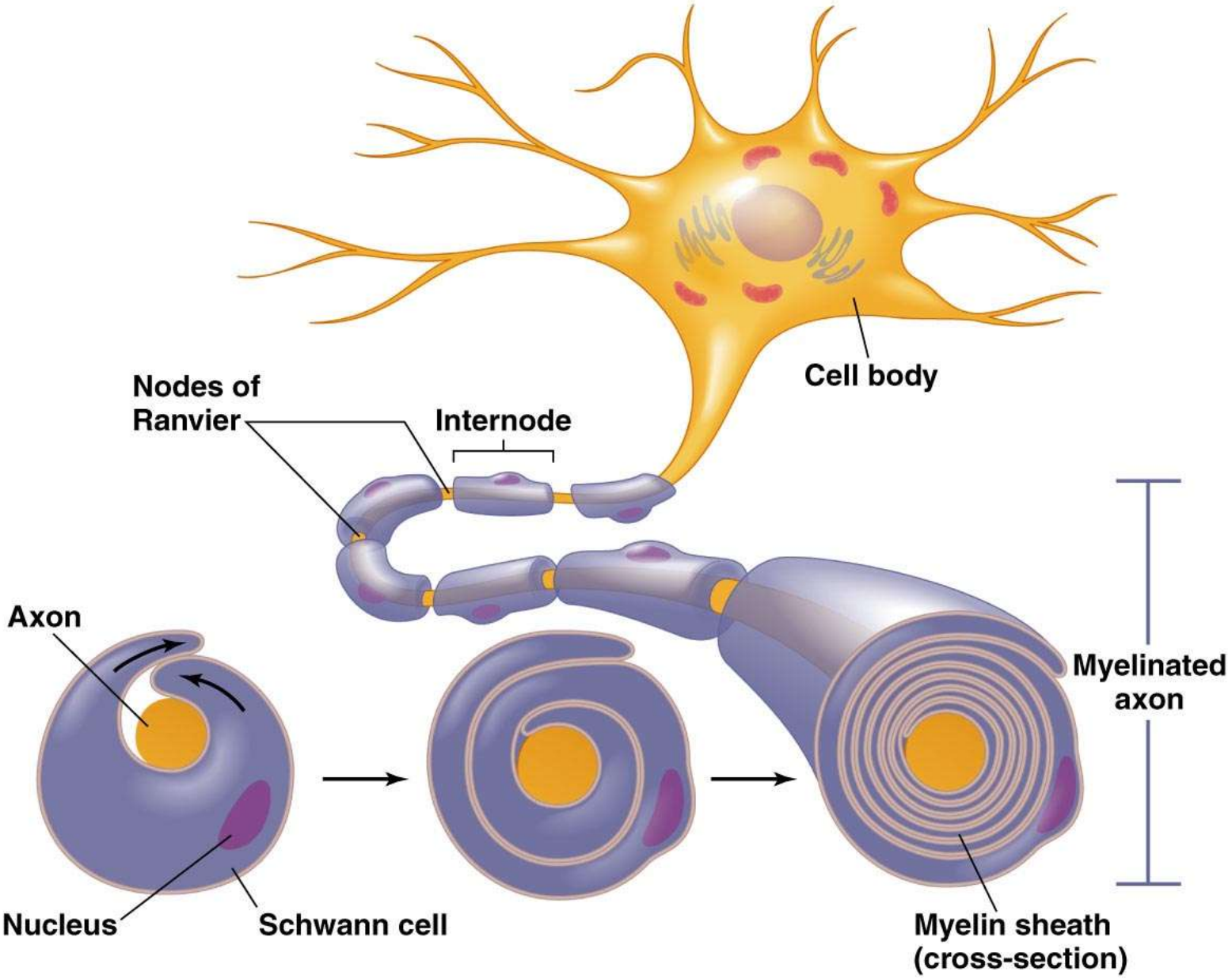
Myelinated Axons



- Vertebrate motor nerves are **myelinated**:
  - Wrapped in an insulating layer of myelin
- **Schwann cells** = specialized lipid-rich cells that form a myelin sheath by wrapping in a spiral pattern around a single axon.

Myelinated Axons

- Several Schwann cells may wrap long axons.
- Myelinated regions = **internodes**.
- **Nodes of Ranvier** = exposed sections of axonal membrane in between internodes.
  - contain high densities of voltage-gated ion channels.



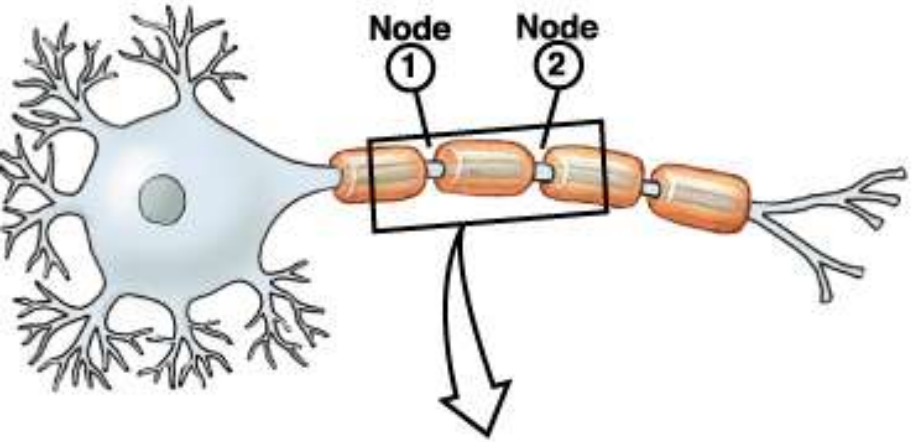
Saltatory Conduction

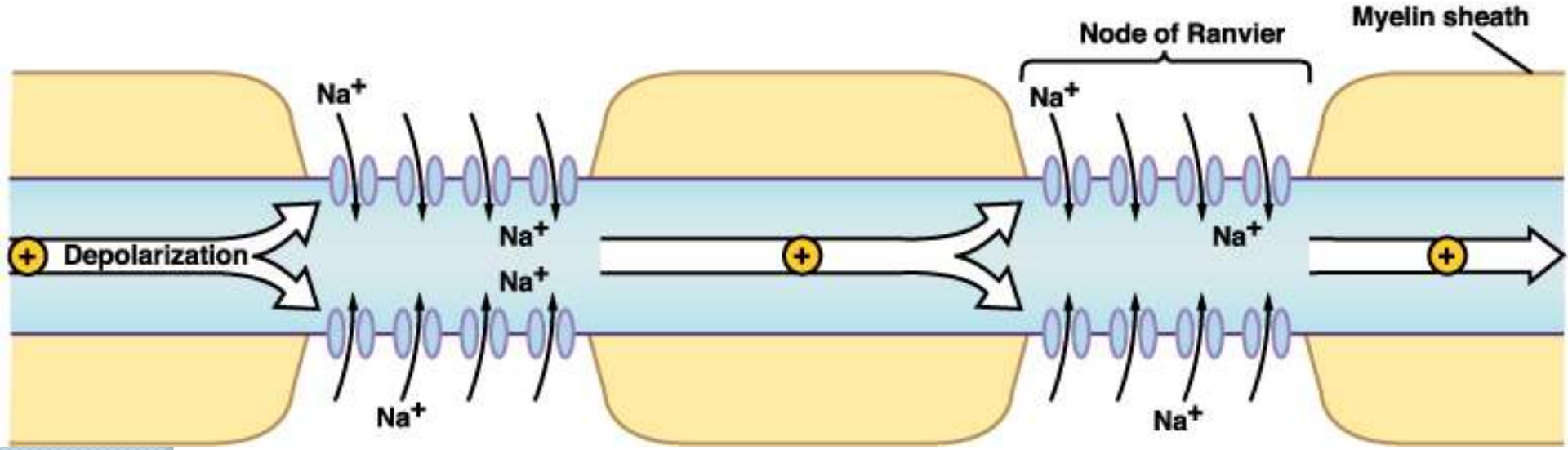
- Action potentials only occur in nodes of Ranvier.
- Current spreads electrically through internodes

Saltatory Conduction

- Action potentials appear to "jump" from one node to another along the axon.
- Conduction occurs faster and with less degradation along myelinated axons than along unmyelinated axons.

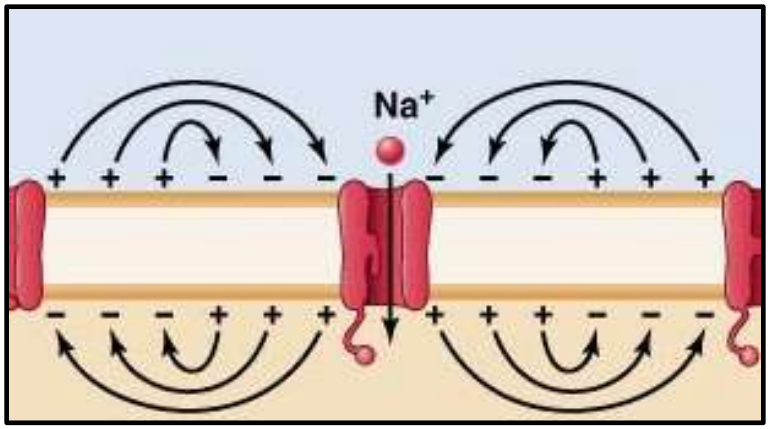
Saltatory Conduction





Unidirectional Conduction

- If you electrically stimulate an axon halfway along it's length, APs will be generated in both directions.

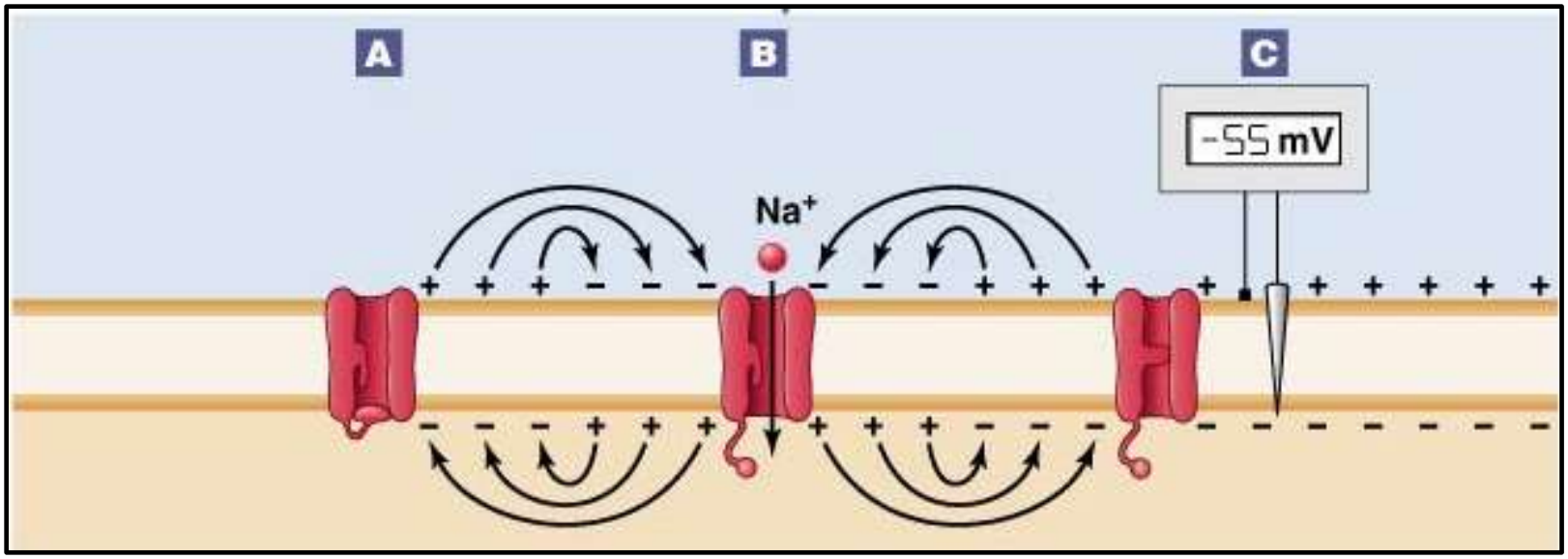


- Why do action potentials only occur in the downstream direction?

Unidirectional Conduction

- In a natural action potential, the stimulus is initiated at the axon hillock.
- As the action potential travels along the axon, the region just upstream has just produced an action potential.
- Voltage gated Na^+ channels there are in a conformation unable to open in response to changes in membrane potential.

Unidirectional Conduction



- Voltage gated channel (A): corresponds to the absolute refractory period.

Unidirectional Conduction

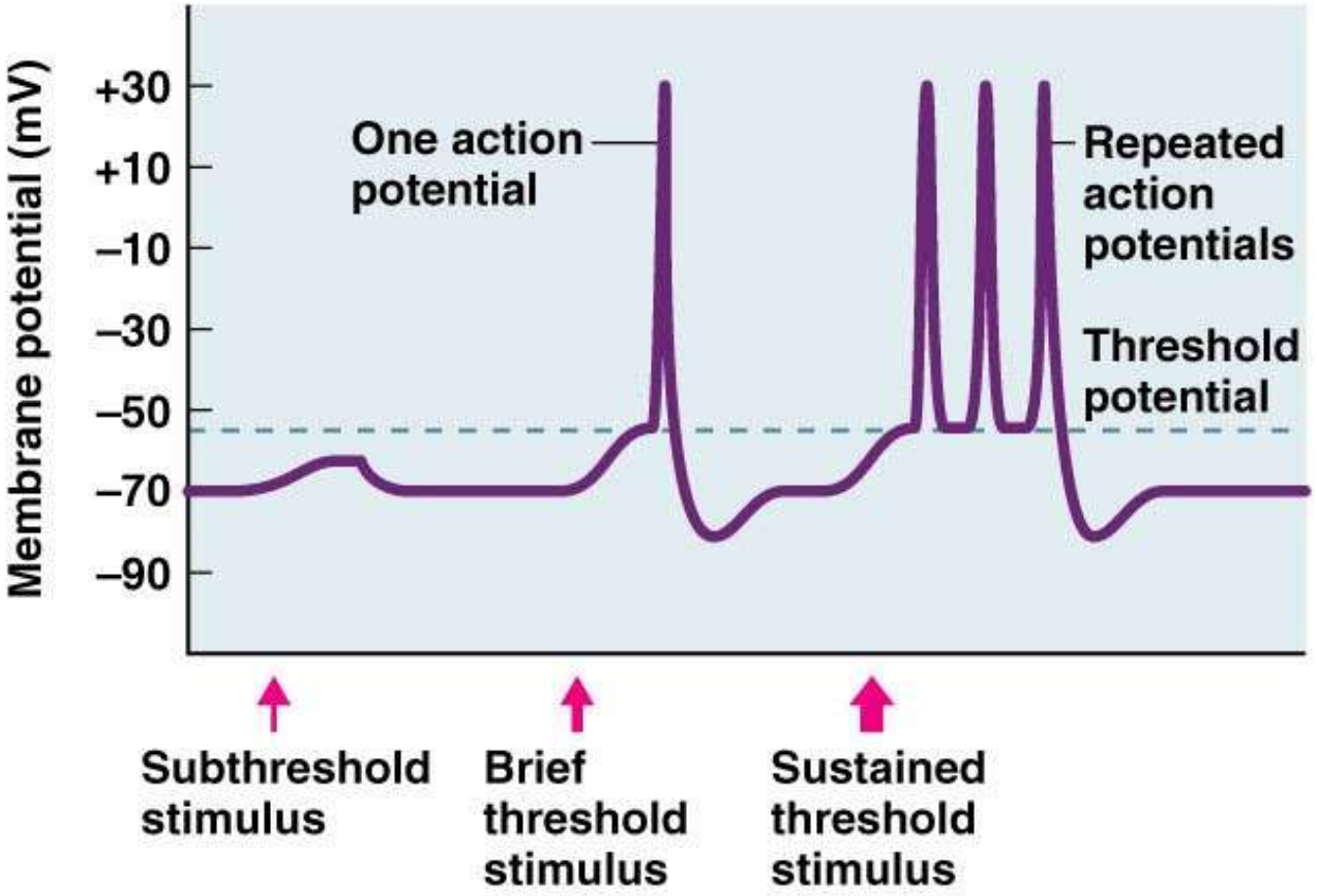
- Together, absolute refractory periods and relative refractory periods prevent **retrograde** (backwards) transmission of action potentials.

Action Potential Frequency

- Action potentials carry information about the strength of a graded potential by changing *frequency* rather than *amplitude*.

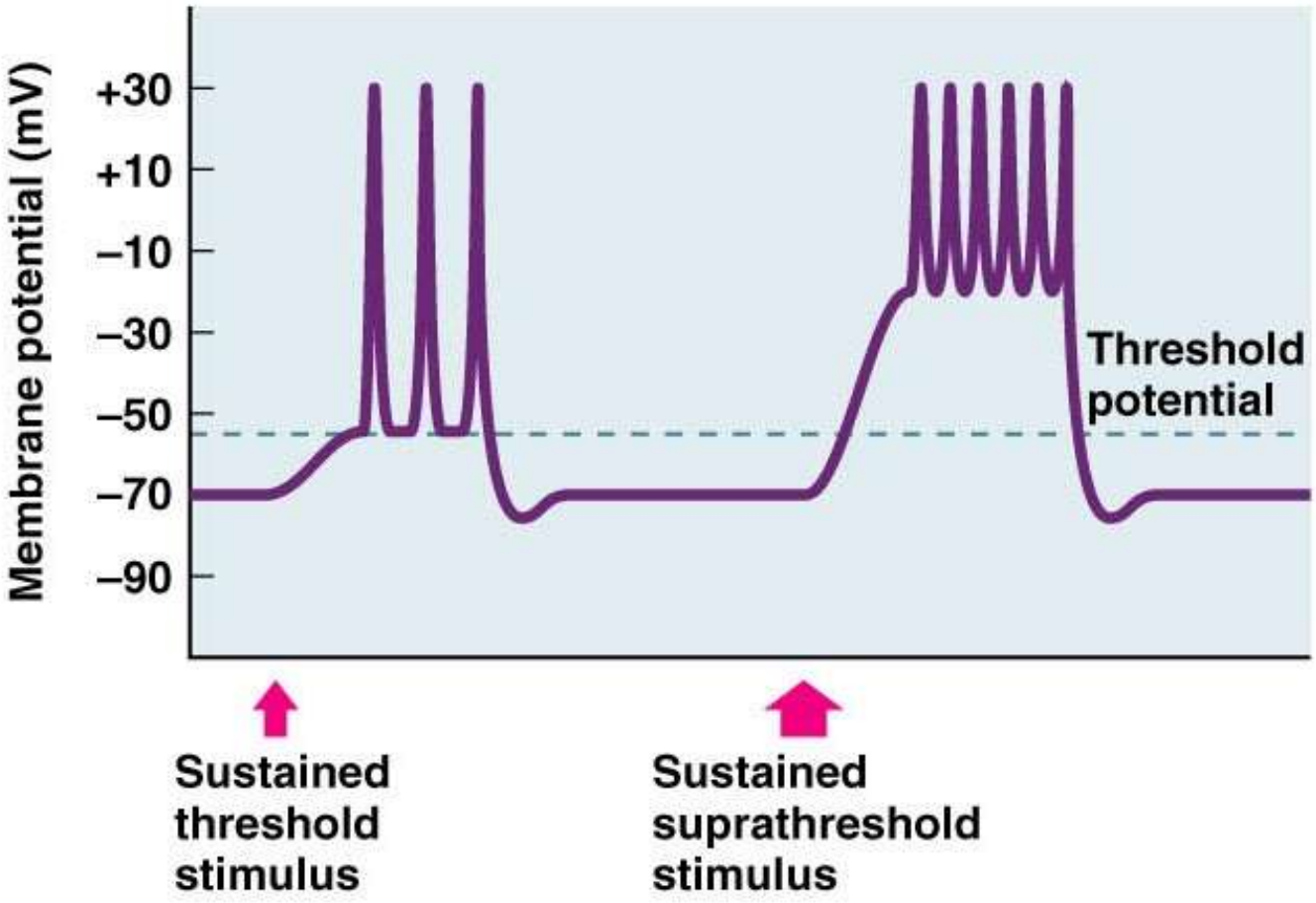
- Remember "all-or-none"

Action Potential Frequency



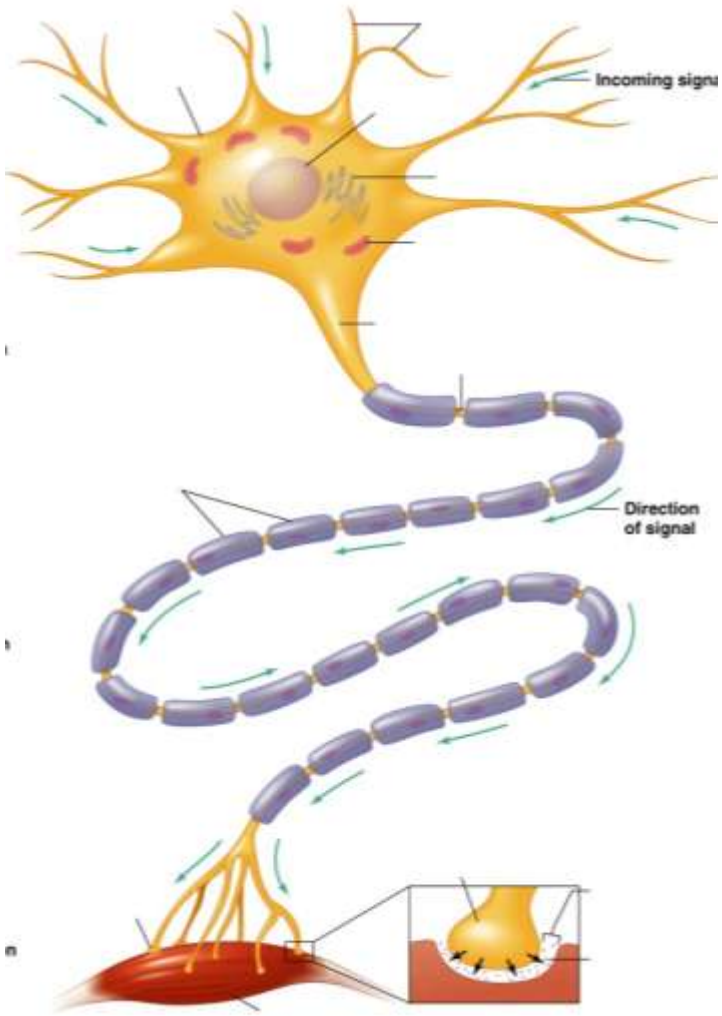
(a) A weak stimulus triggers a low frequency of action potentials

Action Potential Frequency



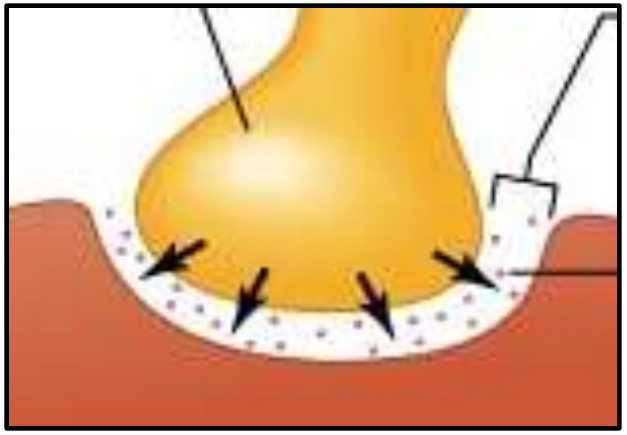
(b) A suprathreshold stimulus triggers a high frequency of action potentials

Signals Across the Synapse



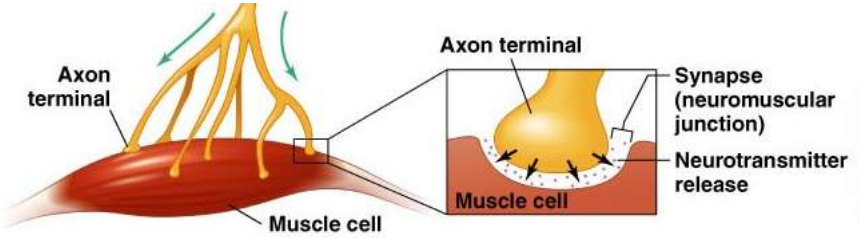
Signals Across the Synapse

- Synapse is made up of 3 parts:
  - Presynaptic cell – cell that transmits the signal
  - Postsynaptic cell – cell that receives the signal
  - Synaptic cleft – space in between



Types of Synapses

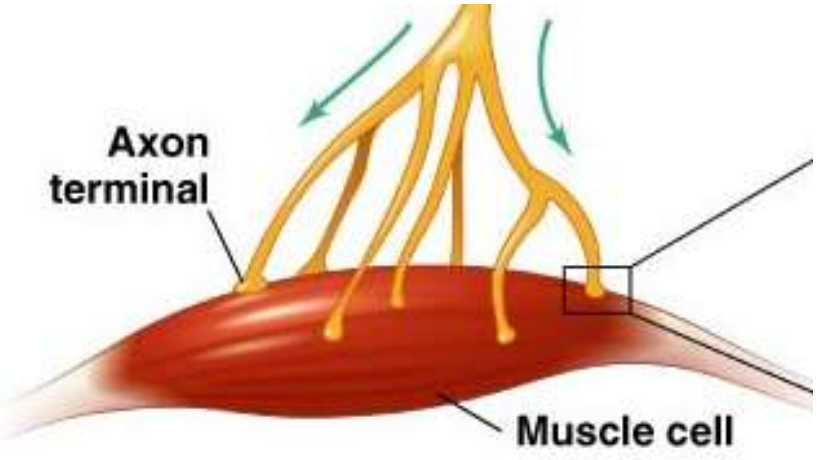
- Neurons can form synapses with many types of cells including:
  - Neurons
  - Muscles
  - Endocrine cells



- **Neuromuscular junction** =

  Synapse between a motor neuron and a skeletal muscle cell.

Neuromuscular Junction



- Neurotransmitter release is regulated by intracellular Ca^{2+} levels.

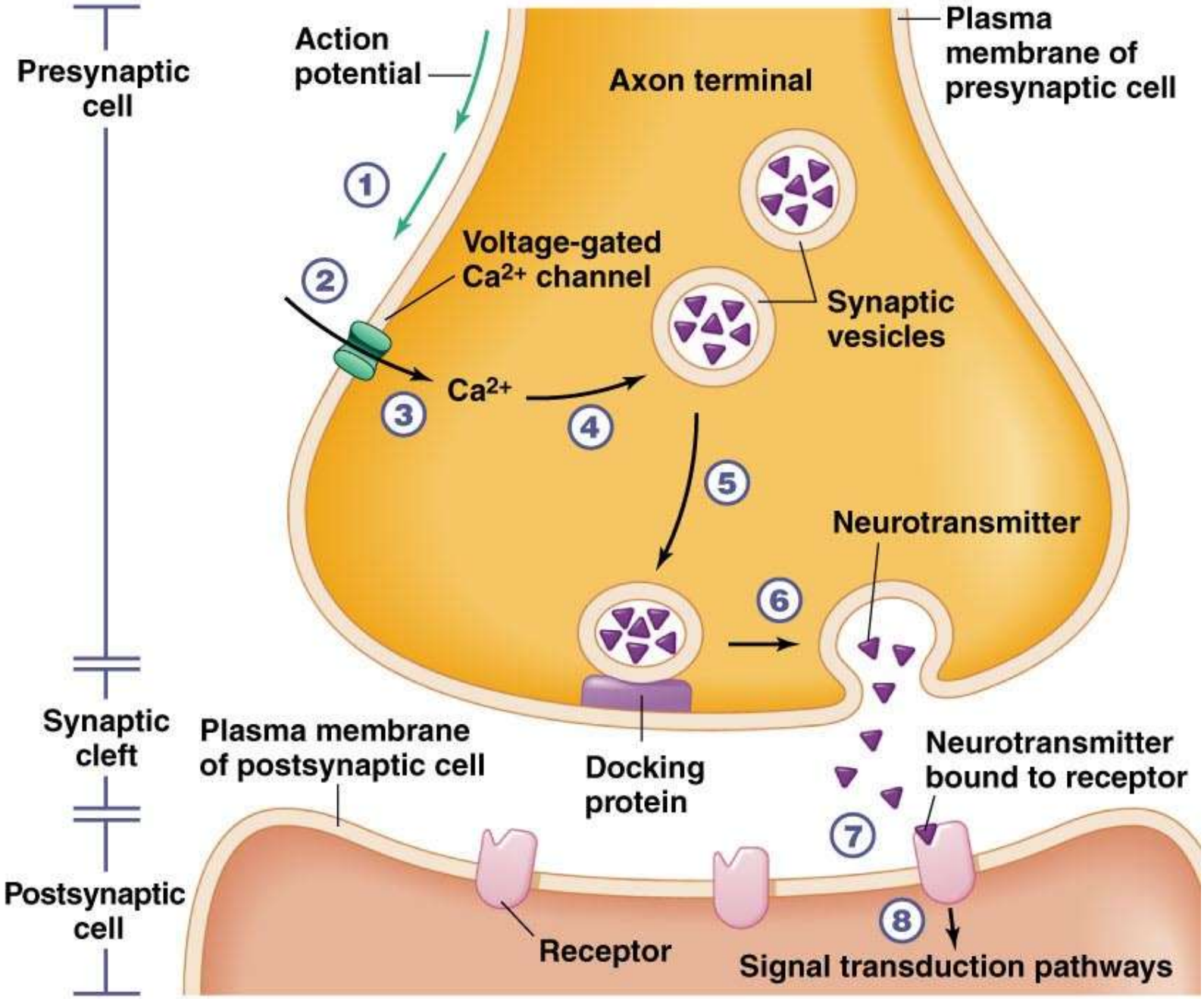

Presynaptic cell
Action potential
Axon terminal
Plasma membrane of presynaptic cell
1
Voltage-gated Ca2+ channel
2
Synaptic vesicles
Ca2+
3
4
5
Neurotransmitter
6
Synaptic cleft
Plasma membrane of postsynaptic cell
Docking protein
Neurotransmitter bound to receptor
7
Postsynaptic cell
Receptor
8
Signal transduction pathways

FIGURE 4.16

Synaptic Vesicles

- 2 pools of **synaptic vesicles**:
  - Ready Releasable Pool
    - Located at active zone of synapse
    - Bound to docking proteins
    - Ready to release contents by exocytosis
  - Storage Pool
    - Bound to cytoskeleton
    - Not docked to membrane

Synaptic Vesicles

- Increases in Ca^{2+} concentration in the axon terminal act as a signal to neurotransmitting synaptic vesicles:
  - Vesicles from readily releasable pool fuse with plasma membrane and release contents by exocytosis
  - Vesicles from storage pool move to active zone and bind to docking proteins.

Vesicles & Neurotransmitters

- Many neurotransmitters in one vesicle
- The number of neurotransmitters per vesicle is similar for all vesicles.
- Increasing action potentials increases the number of vesicles moving to the membrane and releasing their contents.

Vesicles & Neurotransmitters

- When action potentials arrive at high frequencies, cellular removal of Ca^{2+} cannot keep up with the influx of Ca^{2+} through activation channels.

- Resulting in:
  - ↑ intracellular [Ca^{2+}]
  - Results in a stronger signal for exocytosis.

Vesicles & Neurotransmitters:
"Take Home Process"

↑ Frequency Action Potentials

↑ Intracellular [Ca^{2+}]

↑ Signal Intensity

↑ Neurotransmitter Release

Acetylcholine (ACh)

- Primary neurotransmitter at the vertebrate neuromuscular junction.
- ACh is packaged into synaptic vesicles and released into the synapse by exocytosis

Acetylcholinesterase (AChE)

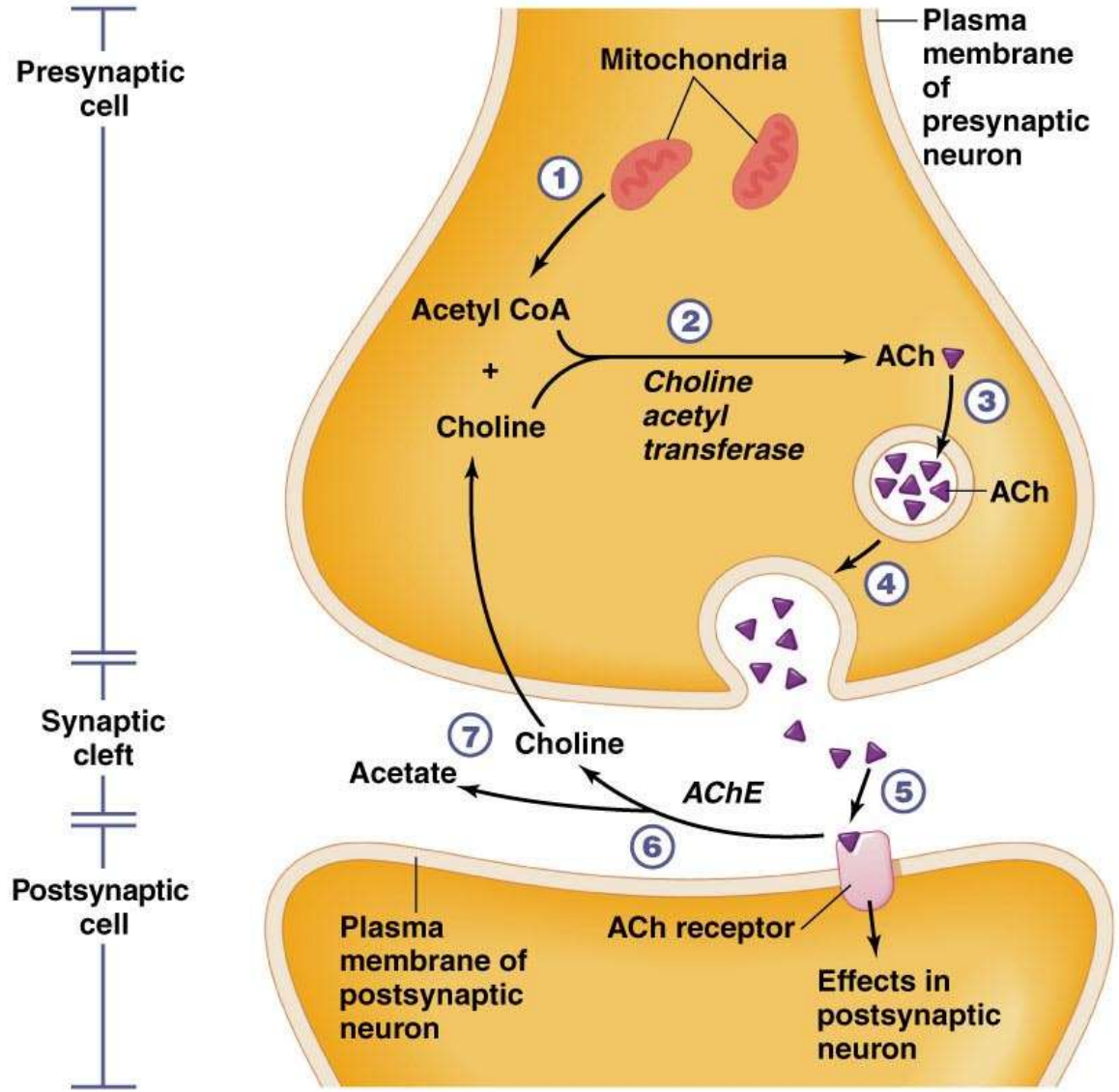
- Signalling between a ligand, such as a neruotransmitter, and its receptor must be terminated in order to be effective.

- AChE = specific enzyme in synapse that removes Ach from it's receptor.
  - Breaks Ach down

Acetylcholinesterase (AChE)

- Important role in regulating the strength of the signal to the post synaptic cell by regulating the concentration of neurotransmitter in the synapse.

Recycling of Acetylcholine (ACh)

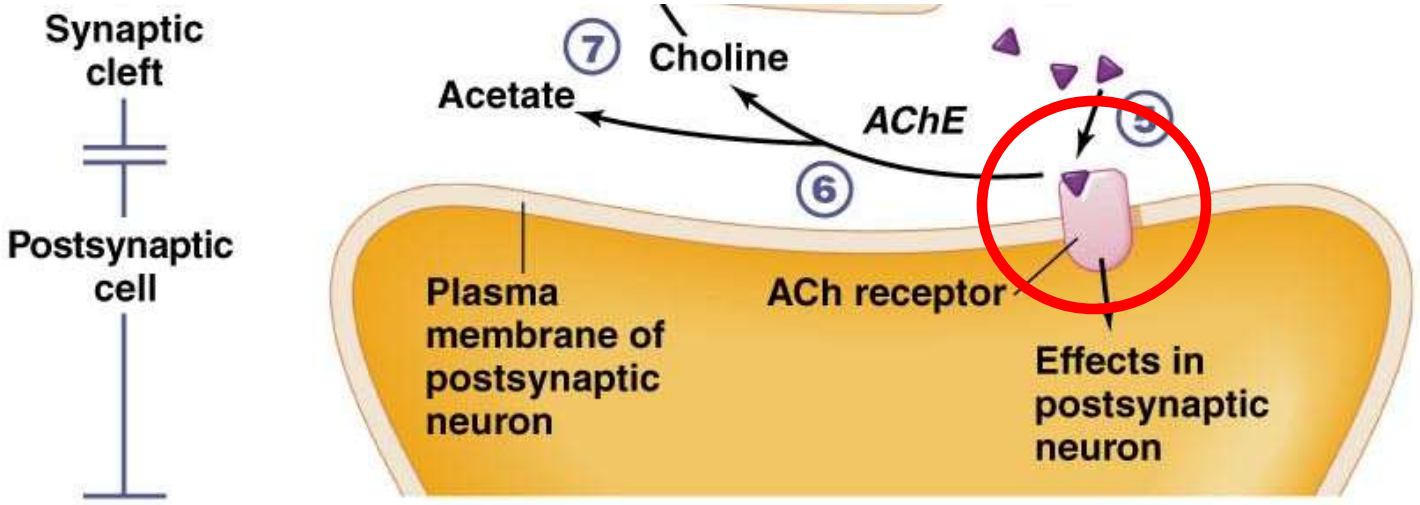


1. Acetyl CoA is synthesized in the mitochondria.
2. Choline acetyl transferase catalyzes the conversion of choline and acetyl CoA to acetylcholine (ACh).
3. The ACh is packaged into synaptic vesicles.
4. ACh is released into the synapse.
5. ACh binds to its receptor on the postsynaptic cell.
6. Acetylcholinesterase (AChE) breaks down ACh into choline and acetate, terminating the signal in the postsynaptic cell.
7. The presynaptic cell takes up and recycles the choline, and the acetate diffuses out of the synapse.

Postsynaptic Reception

- Postsynaptic cells detect neurotransmitters using specific cell-surface receptors.

- **Nicotinic Ach receptors** = ligand gated ion channels in muscle cells.



Postsynaptic Reception

- Nicotinic ACh receptors contain a relatively non-selective channel.
  - Permeable to Na^+, K^+,

    and to a lesser extent Ca^{2+}

- Resulting graded potential in post-synaptic cells is dominated by Na^+ ions.

Postsynaptic Reception

- ACh binding to nicotinic receptors on skeletal muscle **always** results in a rapid excitatory postsynaptic potential because of the resulting influx of Na^+ →

  →depolarization of the muscle cell.

Postsynaptic Reception

- The amount of neurotransmitter and the number of receptors on the post synaptic cell influence the strength of signal in the target cell.

Postsynaptic Reception

[Neurotransmitter] in the synapse =
balance of release (presynaptic)
and removal (postsynaptic)

Removal can depend on :
(1) diffusion
(2) surrounding cells
(3) enzymes present in the synapse
(ex. Acetylcholinesterase)

Outline of Postsynaptic Reception

1. Neurotransmitter (Ach) binds to receptor (Nicotinic receptors).

2. Receptor changes shape, acting as a signal in the target cell.

3. A pore opens in the middle of the receptor allowing ions to cross the membrane.

4. Rapid influx Na^+ influx depolarizes the postsynaptic muscle cell. (contraction)