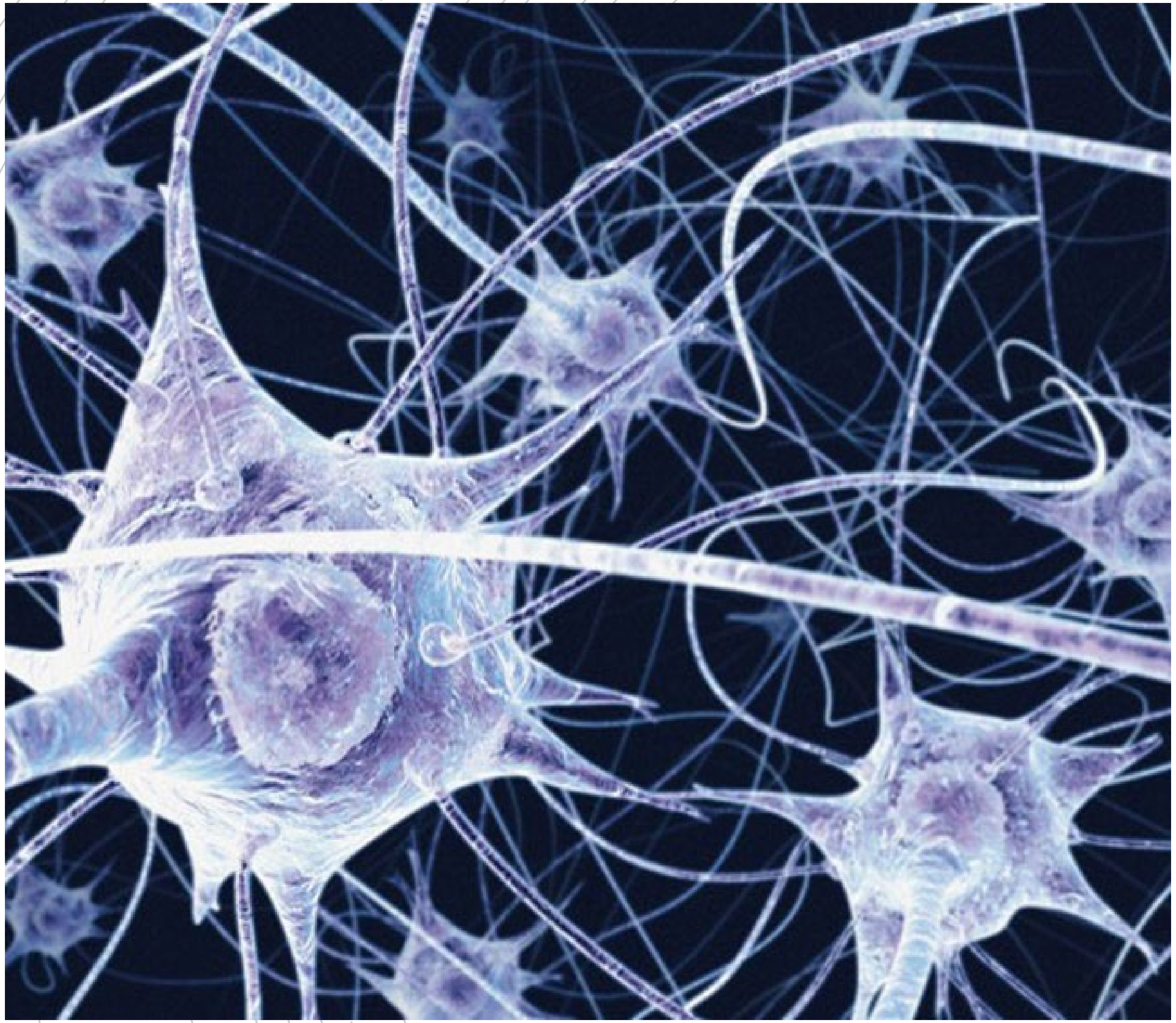
Nervous System

Doç Dr. Yasemin SALGIRLI DEMİRBAŞ
Resident ECAWBM

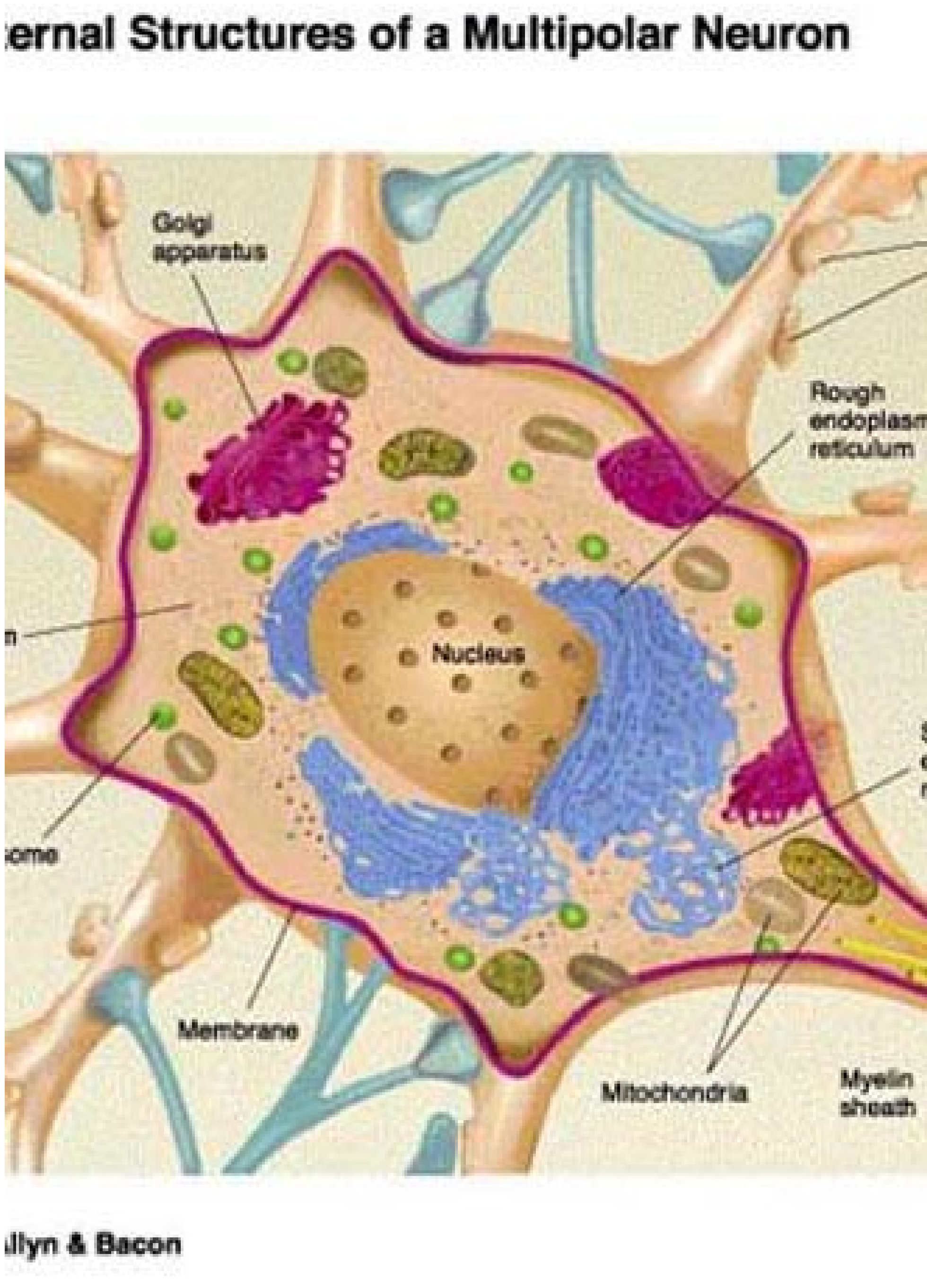


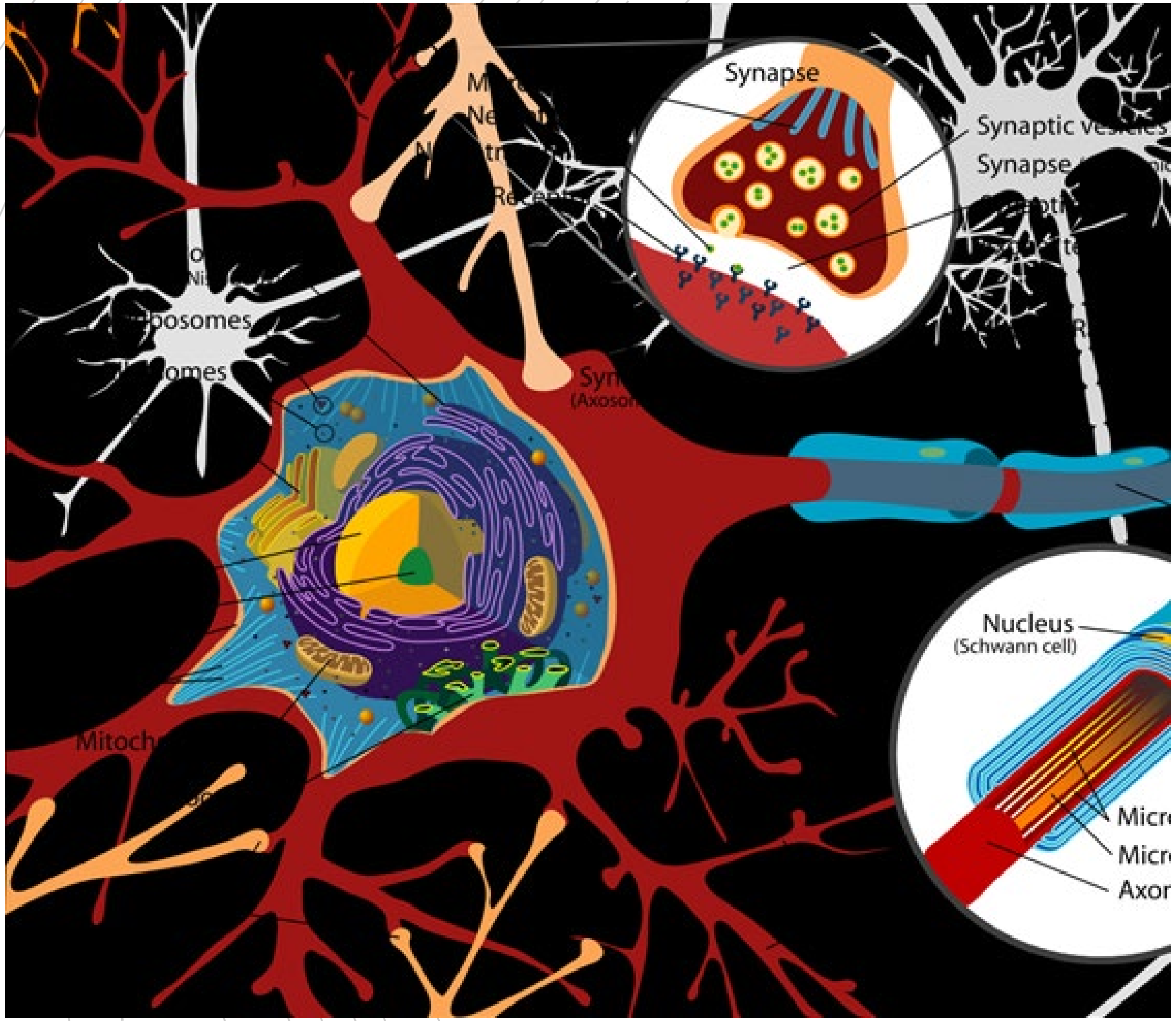
NEURONS

- The human body is made up of trillions of cells.
- Cells of the nervous system, called nerve cells or neurons, are specialized to carry "messages" through an electrochemical process.
- The human brain has about 100 billion neurons that carry out the nerve impulses through a process called **action potential**.

NEURAL TISSUE

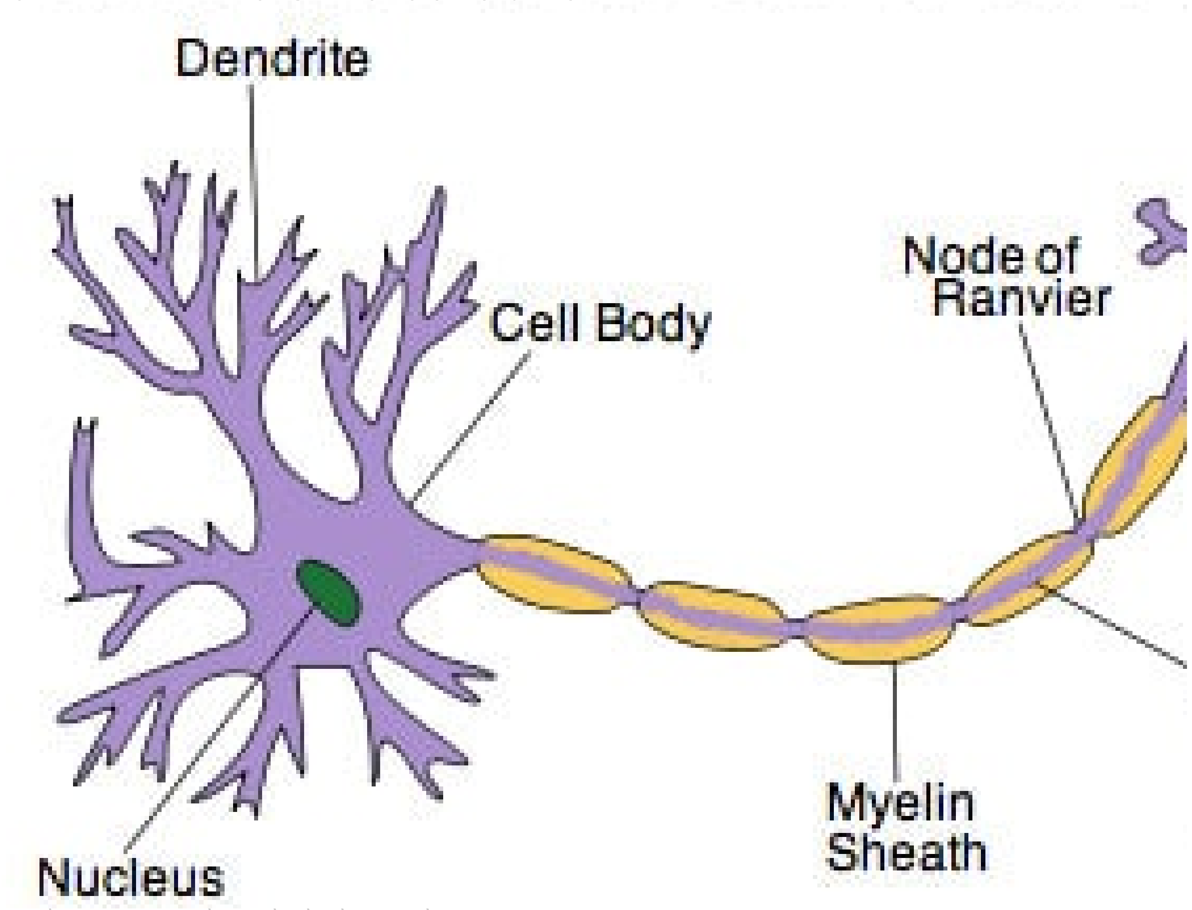
- The basic unit of the nervous system is the individual **nerve cell**, or **neuron**.
- Nerve cells operate by generating electric signals that pass from one part of the cell to another part of the same cell and by releasing chemical messengers—**neurotransmitters**—to communicate with other cells.
- **Nerves** are made up of bundles of nerve fibers.
- **Neuroglia** carry out a variety of functions to aid and protect components of the nervous system.





Similarities with other cells

1. Neurons are surrounded by a cell membrane.
2. Neurons have a nucleus that contains genes.
3. Neurons contain cytoplasm, mitochondria and other "organelles".
4. Neurons carry out basic cellular processes such as protein synthesis and energy production.



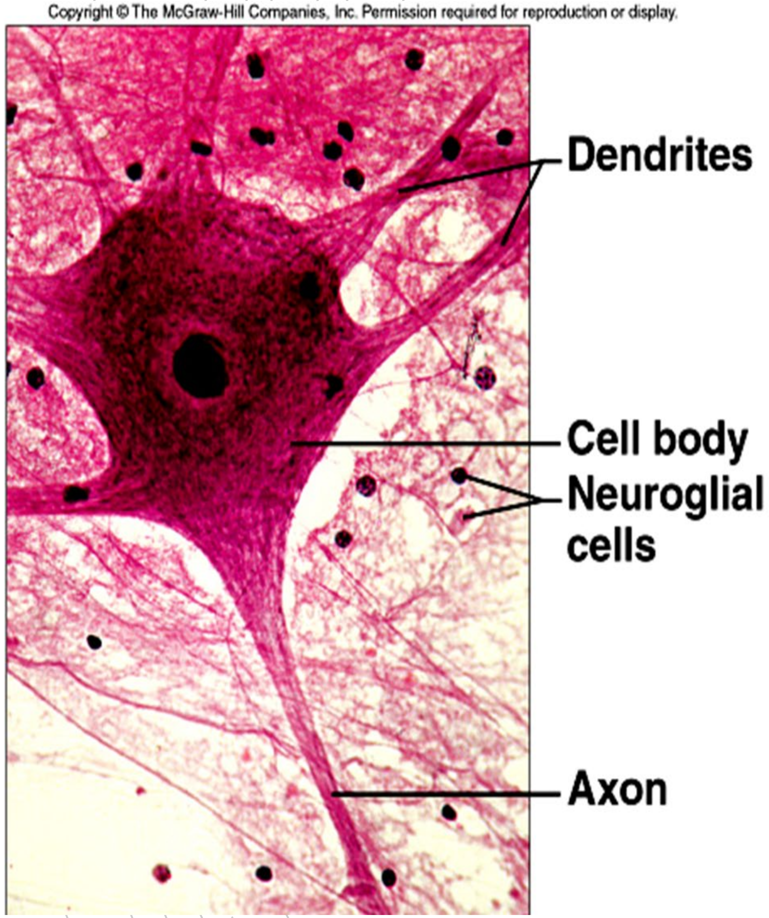
Differences from other cells:

1. Neurons have specialized extensions called dendrites and axons. Dendrites bring information to the cell body and axons take information away from the cell body.

2. Neurons communicate with each other through an electrochemical process.

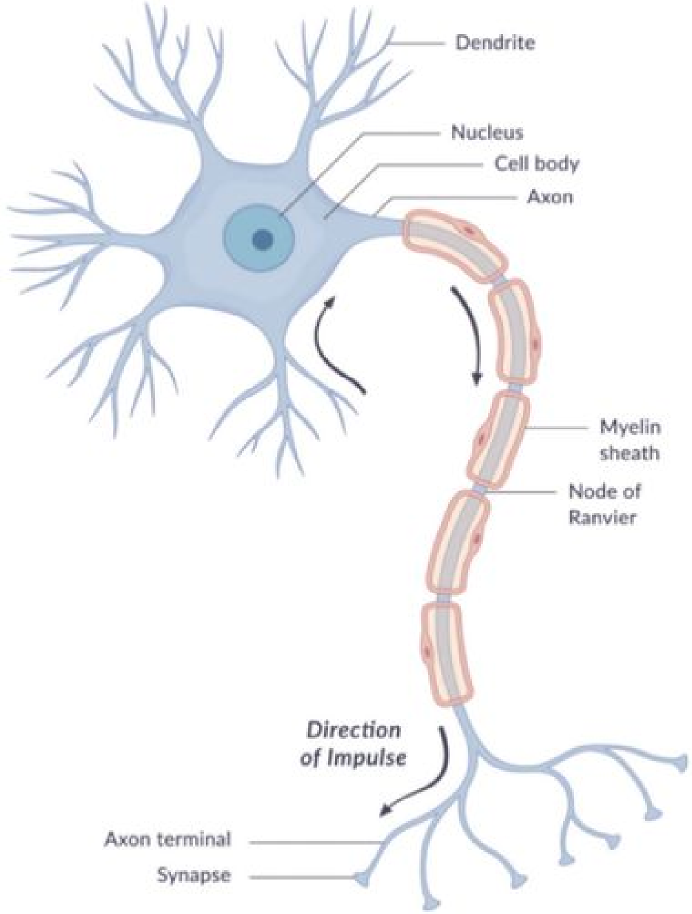
3. Neurons contain some specialized structures (for example, synapses) and chemicals (for example, neurotransmitters).

Structure of a neuron:



- A single neuron consist of:
  - **CELL BODY**: contains the nucleus and ribosomes and thus has the genetic information and machinery necessary for protein synthesis
  - **DENDRITES**: convey incoming messages to the cell body.
  - The branching dendrites (some neurons may have as many as 400,000!) increase the cell's receptive surface area - increase its capacity to receive signals from a myriad of other neurons.

Structure of a neuron:

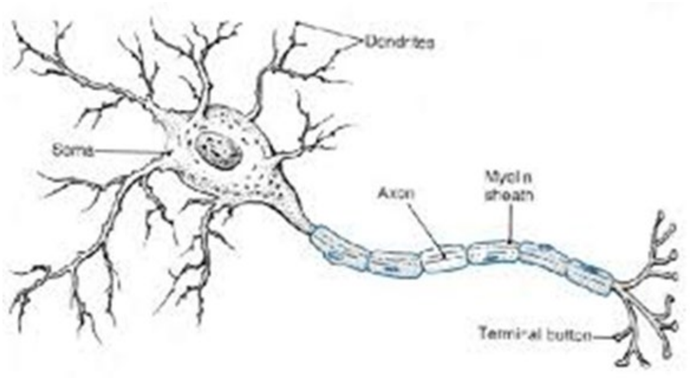


- **AXONS**: sometimes also called a nerve fiber, is a single long process that extends from the cell body to its target cells.
- In length, axons can be a few micrometers or a meter or more.
- The portion of the axon closest to the cell body plus the part of the cell body where the axon is joined are known as the **initial segment**, or **axon hillock**.
- **Presynaptic terminals:** The swollen, distal end of an axon; contains a neurotransmitter substance within synaptic vesicles. Also called synaptic ending or synaptic bouton.

Differences between axons and dendrites:

Axons

- Take information away from the cell body
- Smooth Surface
- Generally only 1 axon per cell
- No ribosomes
- Can have myelin
- Branch further from the cell body

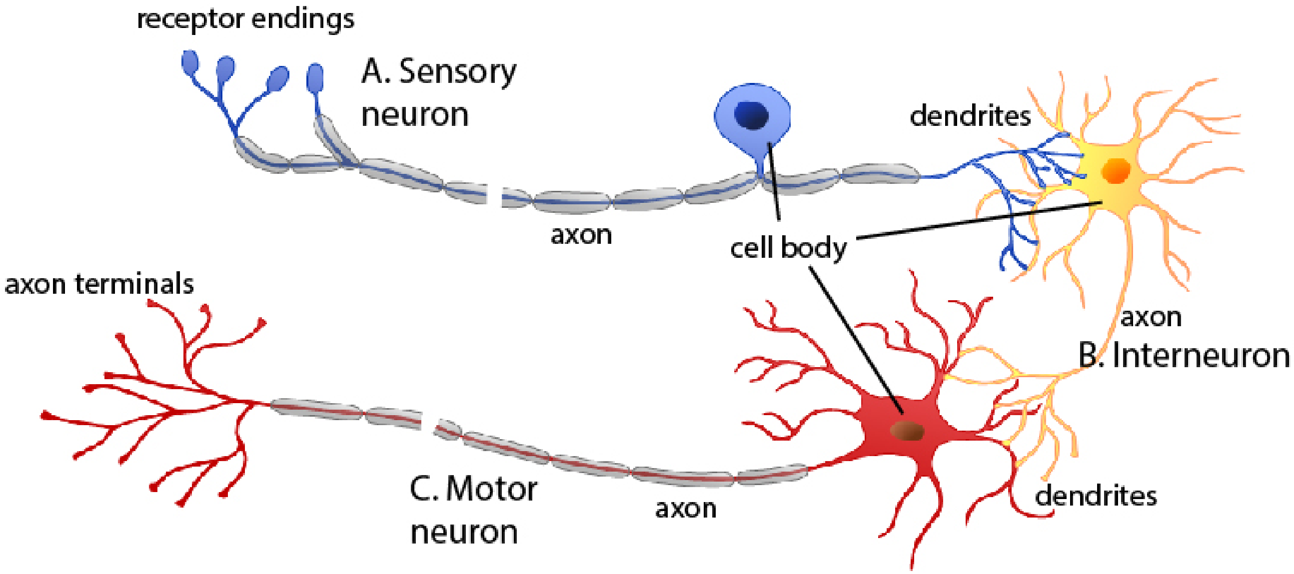


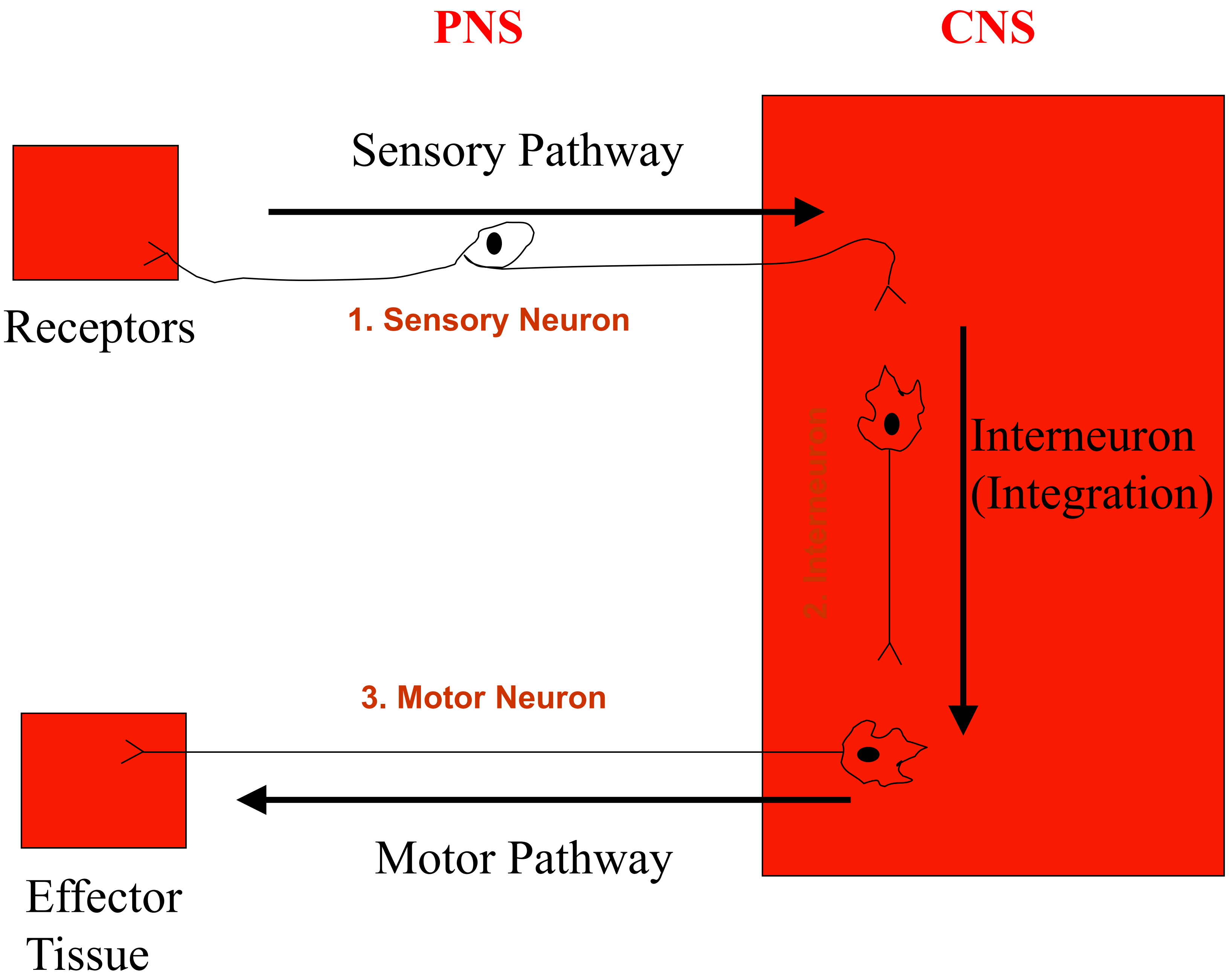
Dendrites

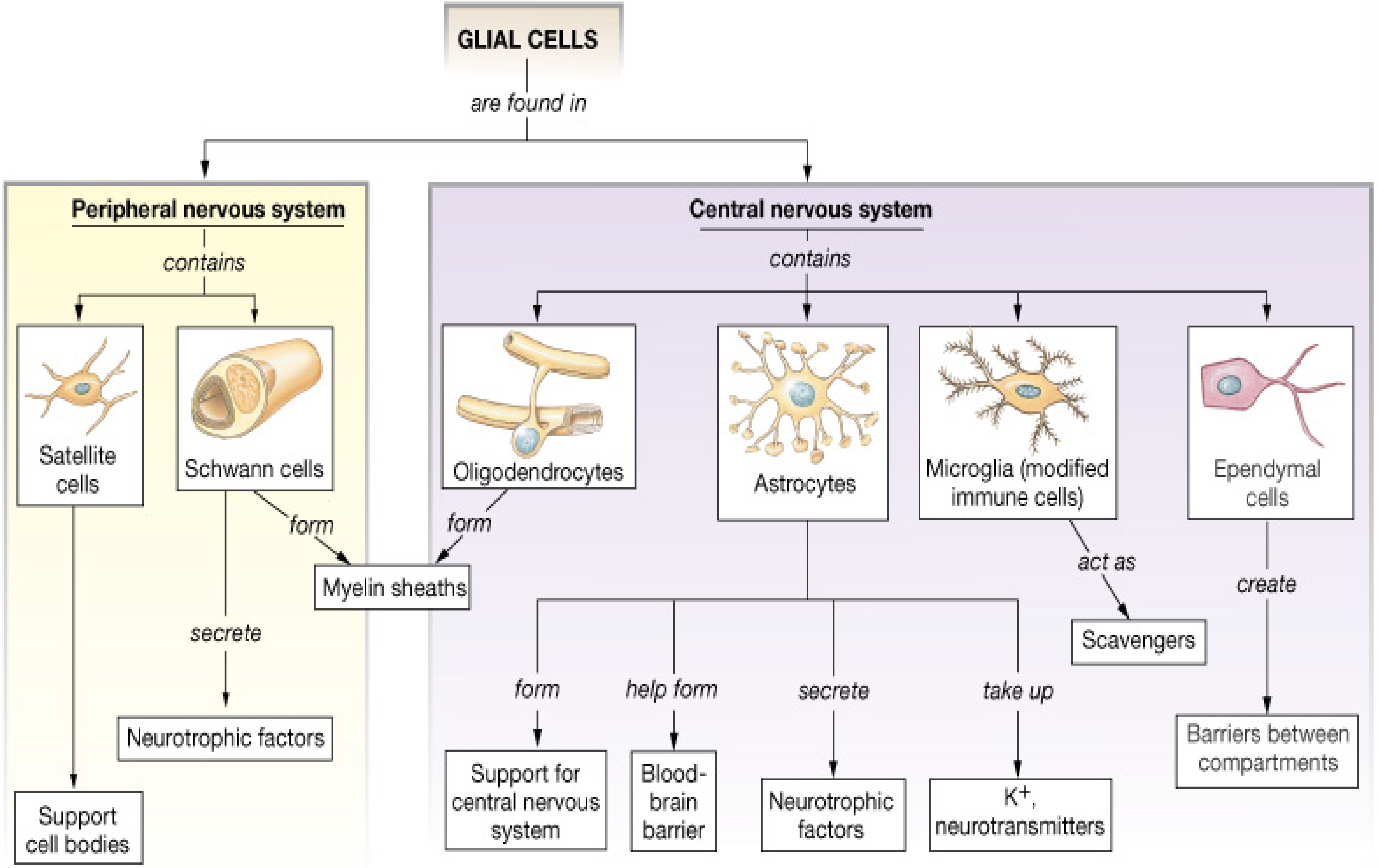
- Bring information to the cell body
- Rough Surface (dendritic spines)
- Usually many dendrites per cell
- Have ribosomes
- No myelin insulation
- Branch near the cell body

Functional Classes of Neurons

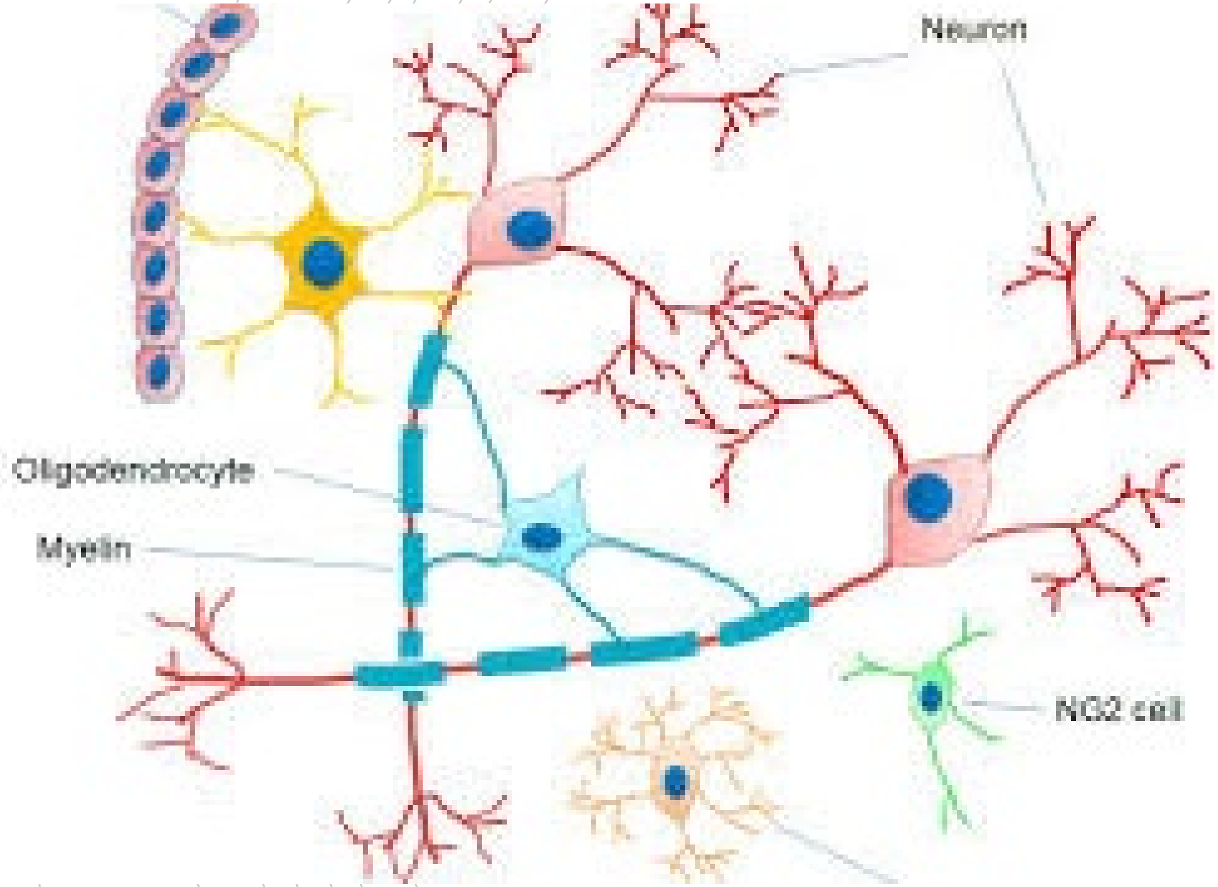
- At their peripheral ends (the ends farthest from the central nervous system), afferent neurons have **sensory receptors,** which respond to various physical or chemical changes in their environment by causing electric signals to be generated in the neuron.
- The receptor region may be a specialized portion of the plasma membrane or a separate cell closely associated with the neuron ending.




PNS
CNS
Sensory Pathway
Receptors
1. Sensory Neuron
2. Interneuron
Interneuron
(Integration)
3. Motor Neuron
Effector
Tissue
Motor Pathway

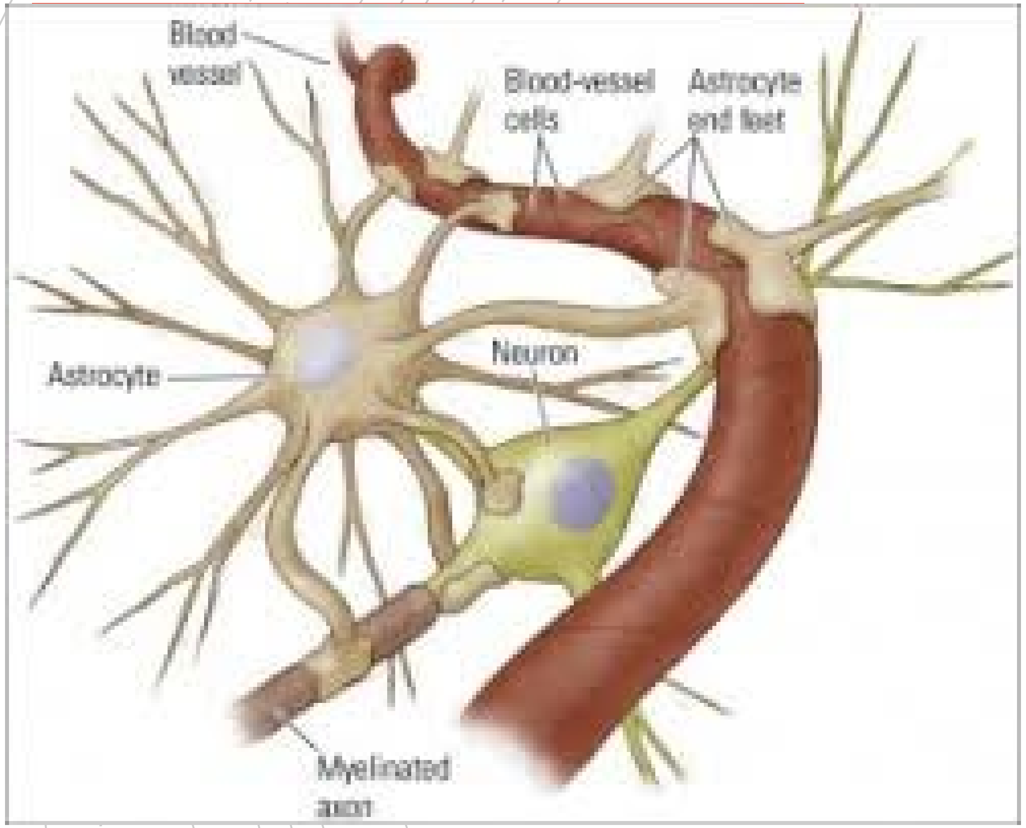

GLIAL CELLS
are found in
Peripheral nervous system
contains
Satellite cells
Schwann cells
Support cell bodies
secrete
Neurotrophic factors
form
Myelin sheaths
Central nervous system
contains
Oligodendrocytes
form
Astrocytes
Microglia (modified immune cells)
Ependymal cells
form
help form
secrete
take up
Support for central nervous system
Blood-brain barrier
Neurotrophic factors
K+, neurotransmitters
act as
Scavengers
create
Barriers between compartments

DONT UNDERESTIMATE GLIAL CELLS



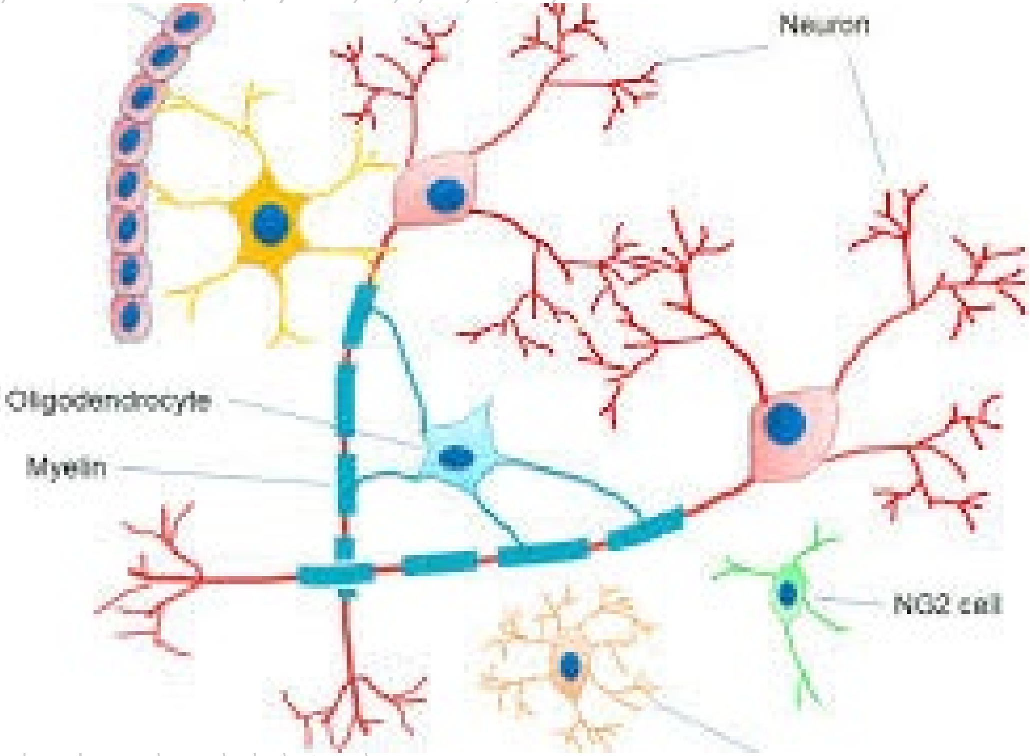
- Ten or twenty years ago, glial cells were considered minor players in the nervous system, even though they outnumber neurons 10-fold.
- Glia were thought to function as passive support cells, bringing nutrients to and removing wastes from the neurons, whereas the neurons carried out the critical nervous system functions of information processing, plasticity, learning, and memory.
- Recent studies are changing this view and demonstrating that glial cells play a key role in these essential brain functions.

NEUROGLIAL CELLS



- Neuroglial cells—usually referred to simply as **glial cells** or glia—are quite different from nerve cells.
- The major distinction is that glia do not participate directly in synaptic interactions and electrical signaling, although their supportive functions help define synaptic contacts and maintain the signaling abilities of neurons.
- Glia are more numerous than nerve cells in the brain, outnumbering them by a ratio of perhaps 3 to 1.
- Although glial cells also have complex processes extending from their cell bodies, they are generally smaller than neurons, and they lack axons and dendrites

NEUROGLIAL CELLS IN DISEASES

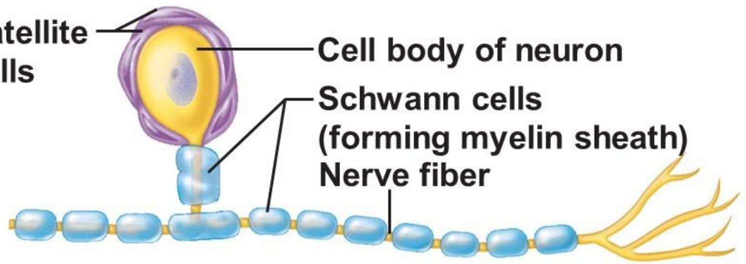


- Overwhelming evidence implicates glial cells in most neurological diseases.
- For example, in multiple sclerosis (MS) macrophages destroy myelin in grey and white matter.
- Cytological changes in oligodendrocytes – such as apoptosis, gross swelling with abnormal nuclei and deposition of activated complement – appear to precede or accompany the destruction of myelin by macrophages.
- In turn, macrophage activity in MS seems to represent a reaction to dead myelin following loss of oligodendrocytes.

2 Glial Cells of the PNS

1. Schwann cells – create the myelin sheath for axons in the PNS. Many Schwann cells help to myelinate axon.

2. Satellite cells - small cells that surround neurons ganglia in PNS. Act to protecting and repair ganglia.



(e) Satellite cells and Schwann cells (which form myelin) surround neurons in the PNS.

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Figure 11.3e

4 Glial Cells of the CNS

3. Oligodendrocytes - create the myelin sheaths of axons in CNS, providing insulation, allowing signals to propagate faster.

4. Astrocytes – help create the restrictive blood-brain barrier (BBB), to protect delicate nervous tissue.

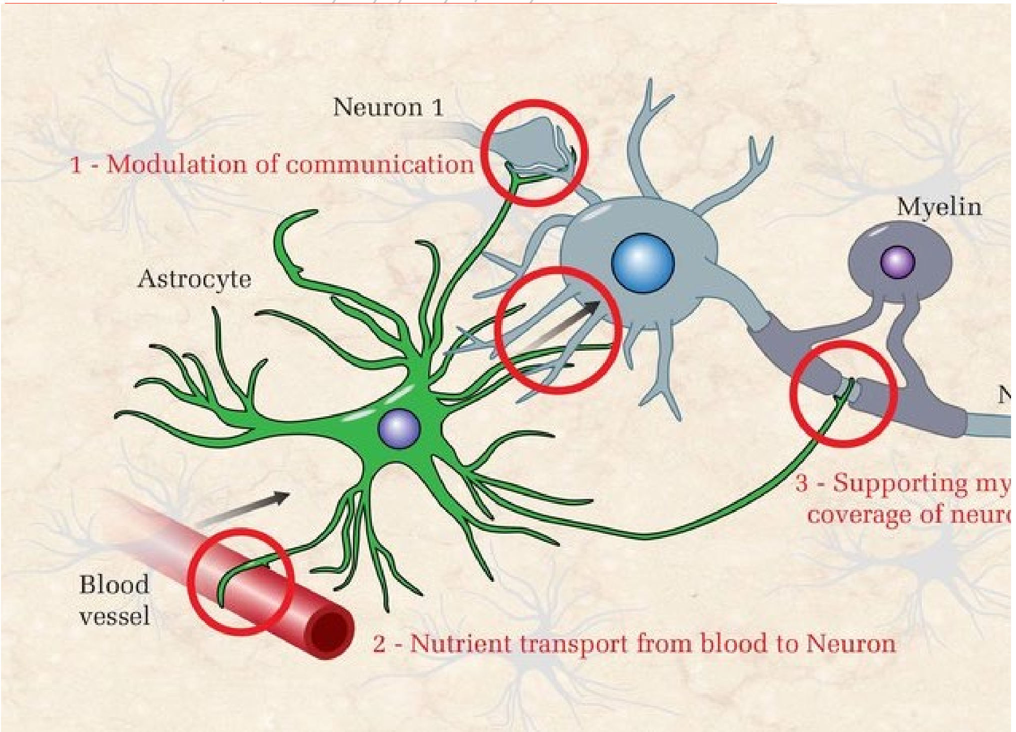
5. Microglia - phagocytic (like macrophages), acting as defense cells in CNS. Cells multiply if CNS is damaged or infected.

Microglia derive from monocytes and are central to the brain's immunity and defences.

Microglia also prune synapses and actively promote apoptosis, both of which are important in the CNS' development

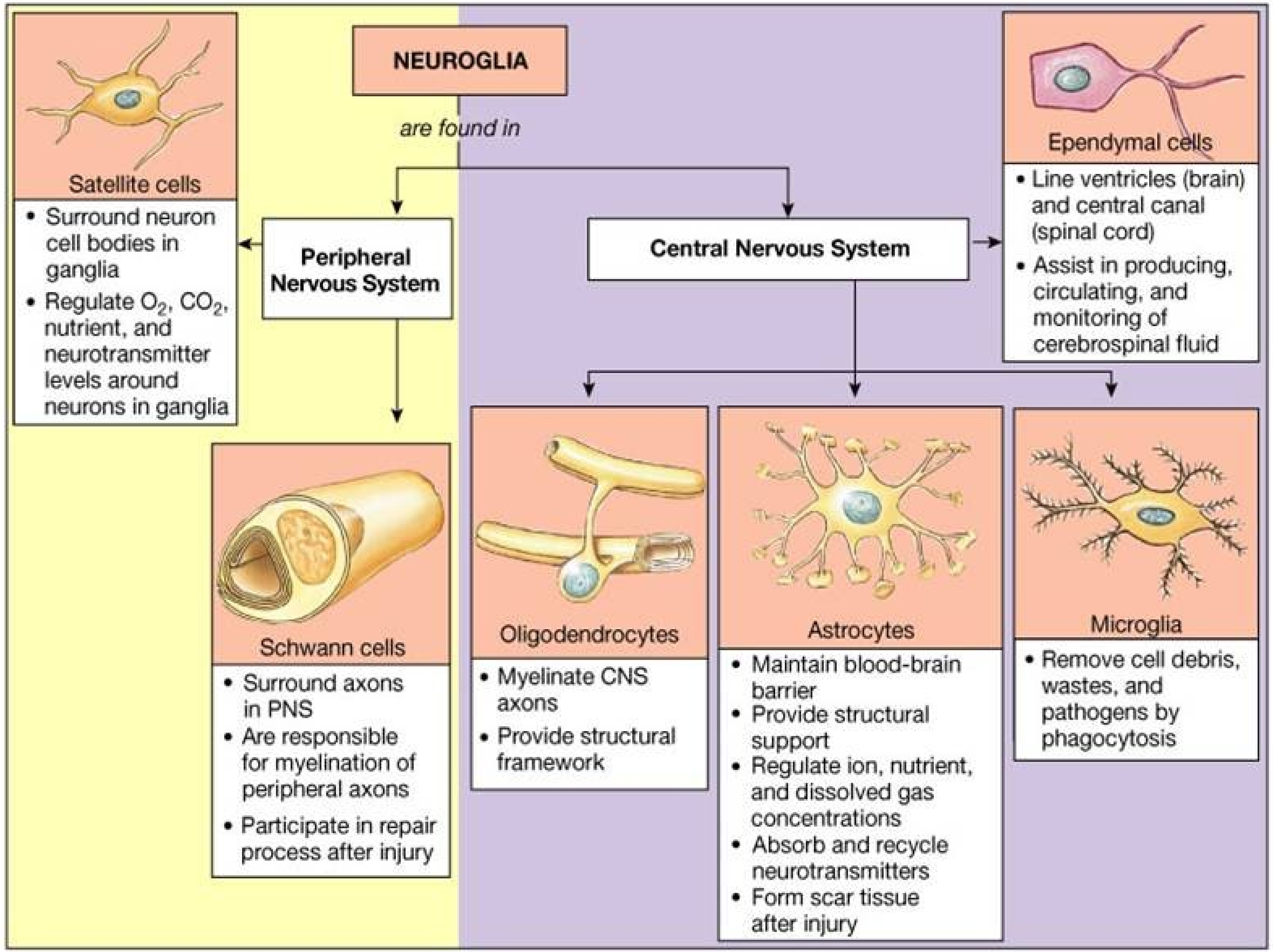
6. Ependymal cells - line fluid cavities of the CNS (e.g. ventricles and central canal). They help create and secrete cerebrospinal fluid (CSF).

ASTROCYTES



- Astrocytes also contribute to information processing in the CNS.
- Some processes form cuffs or veils around synapses.
- Signals between nerve terminals and these glial processes can modulate transmission.
- Astrocytes also release several transmitters including glutamate, ATP, GABA and D-serine.
- In other words, astrocytes **fine-tune** levels of **neurotransmitters** in the CNS

4 Glial Cells of the CNS



Graded Potentials

Localized change in membrane potential that varies in magnitude and is decremental.

Action Potentials

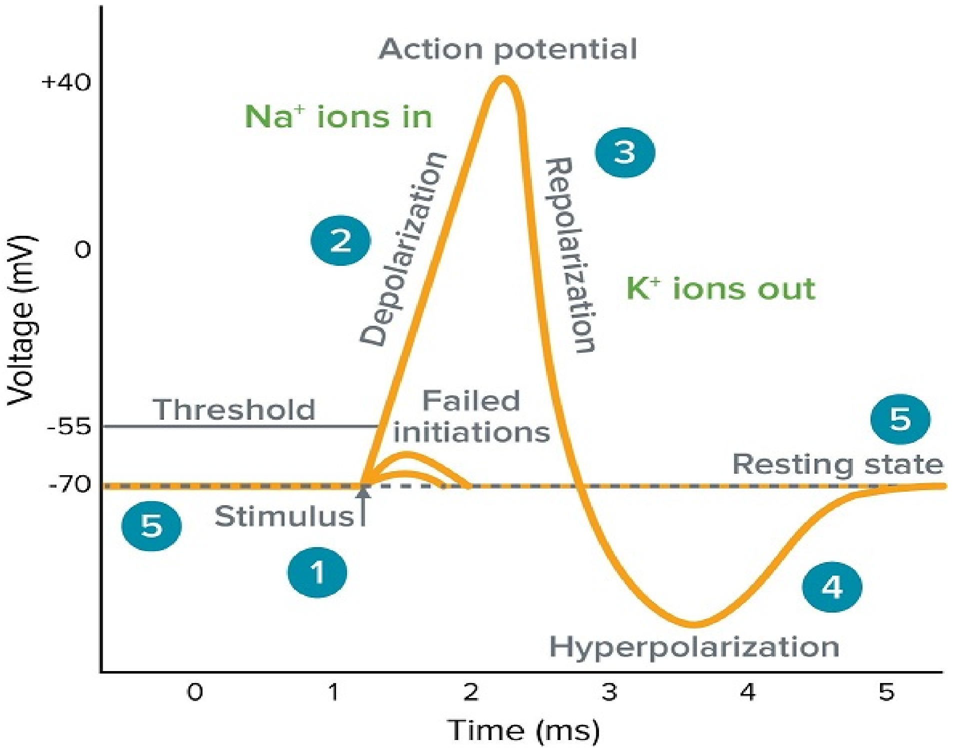
Rapid reversal in membrane potential (due to changes in ion permeability), with constant magnitude and is non-decremental.

ACTION POTENTIAL

- ➢ Are rapid, large alterations in the membrane potential during which time the membrane potential may change 100 mV, from -70 to +30 mV, and then repolarize to its resting membrane potential.

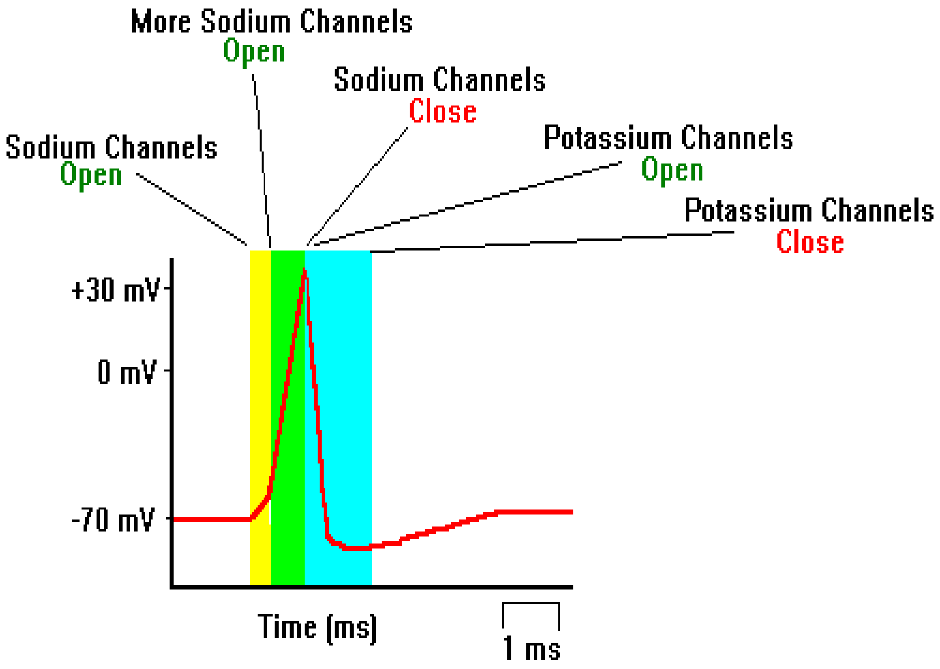
- ➢ Nerve and muscle cells as well as some endocrine, immune, and reproductive cells have plasma membranes capable of producing action potentials.

- ➢ These membranes are called excitable membranes, and their ability to generate action potentials is known as excitability



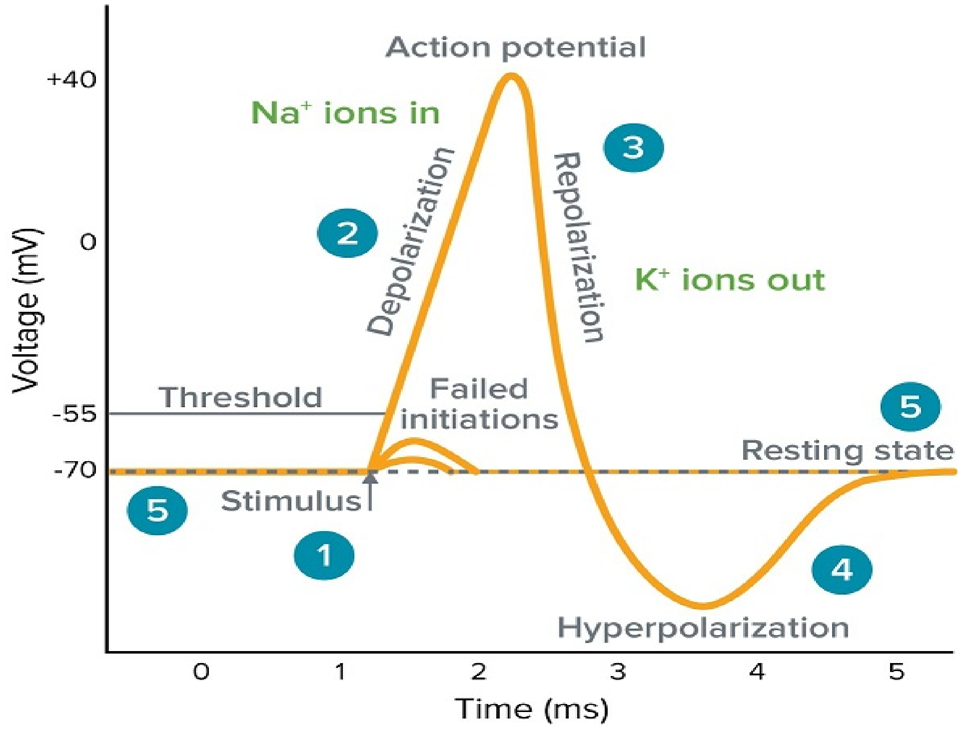
ACTION POTENTIAL

- The action potential results from a transient change in membrane ion permeability, which allows selected ions to move down their concentration gradients.
- In the resting state, the open channels in the plasma membrane are predominantly those that are permeable to potassium ions.
- Very few sodium-ion channels are open,
- the resting potential is close to the potassium equilibrium potential.



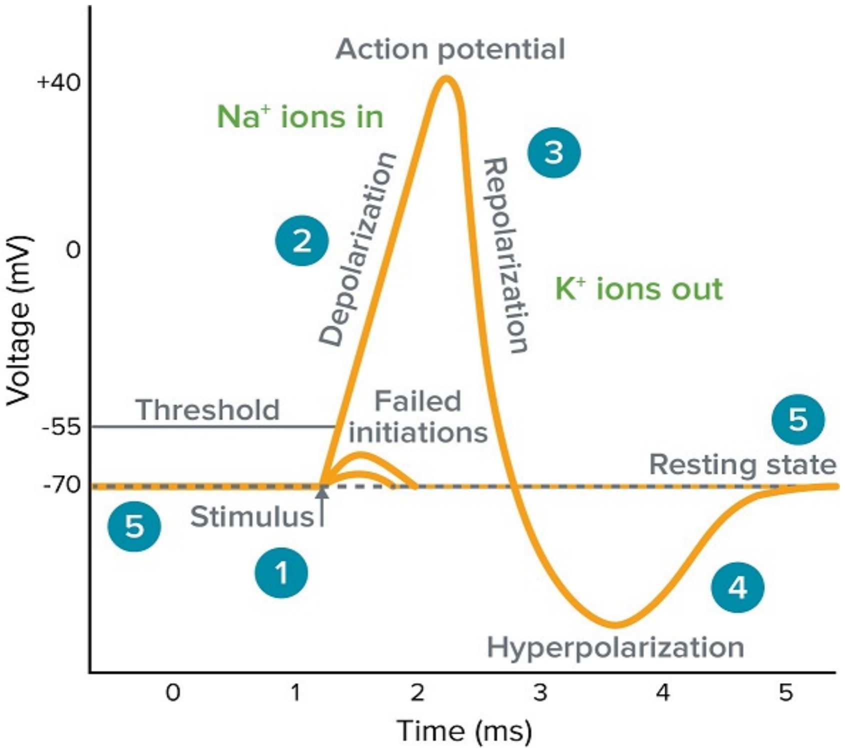
ACTION POTENTIAL

- During an action potential, the membrane permeabilities to sodium and potassium ions are markedly altered.
- The **depolarizing phase** of the action potential is due to the opening of voltage-gated sodium channels, which increases the membrane permeability to sodium ions several hundredfold.
- This allows more sodium ions to move into the cell.
- During this period more positive charge enters the cell in the form of sodium ions than leaves in the form of potassium ions, and the membrane depolarizes.
- It may even overshoot, becoming positive on the inside and negative on the outside of the membrane.
- In this phase, the membrane potential approaches but does not quite reach the sodium equilibrium potential (60 mV).



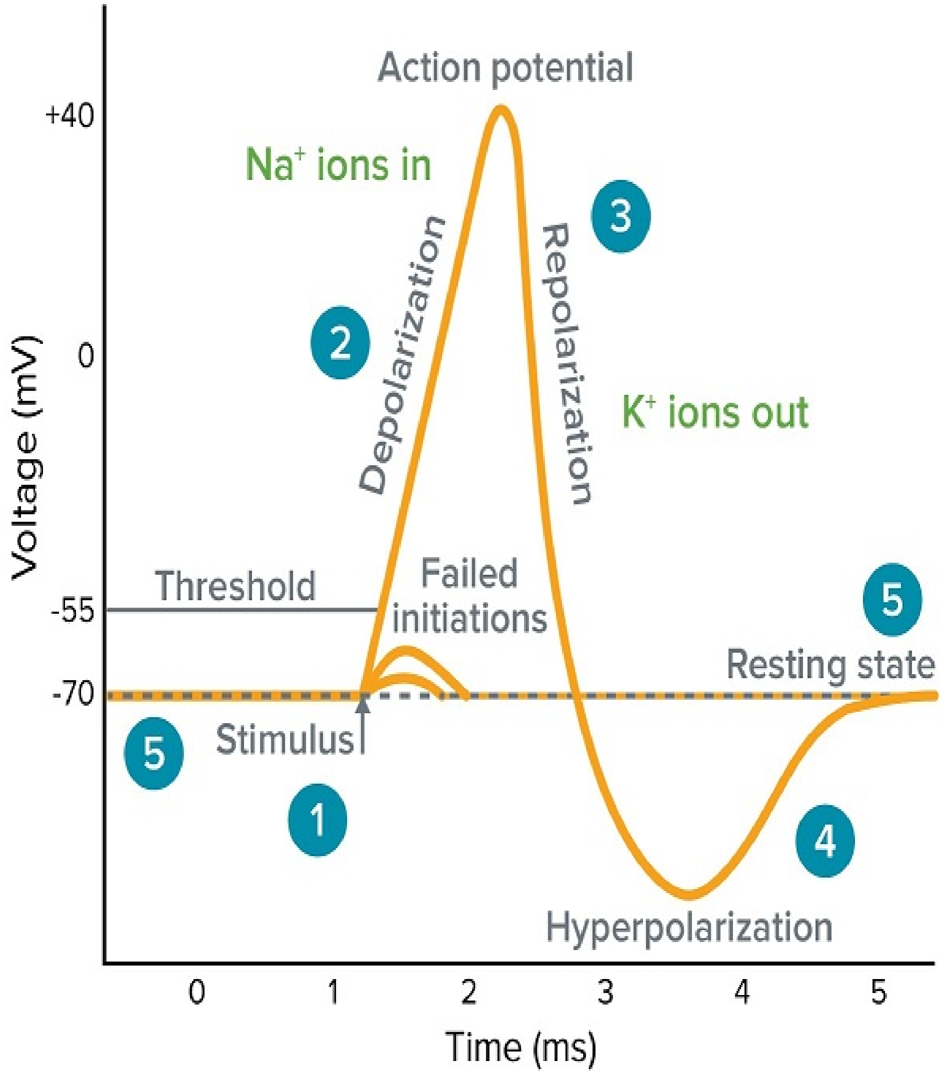
ACTION POTENTIAL

- Action potentials in **nerve cells** last only about 1 ms and typically show an overshoot.
- They may last much longer in certain types of **muscle cells**
- The membrane potential returns so rapidly to its resting level because:
- (1) the sodium channels that opened during the depolarization phase undergo inactivation near the peak of the action potential, which causes them to close; and
- (2) voltage-gated potassium channels which open more slowly than sodium channels, open in response to the depolarization.
- Closure of the sodium channels alone would restore the membrane potential to its resting level since potassium flux out would then exceed sodium flux in.



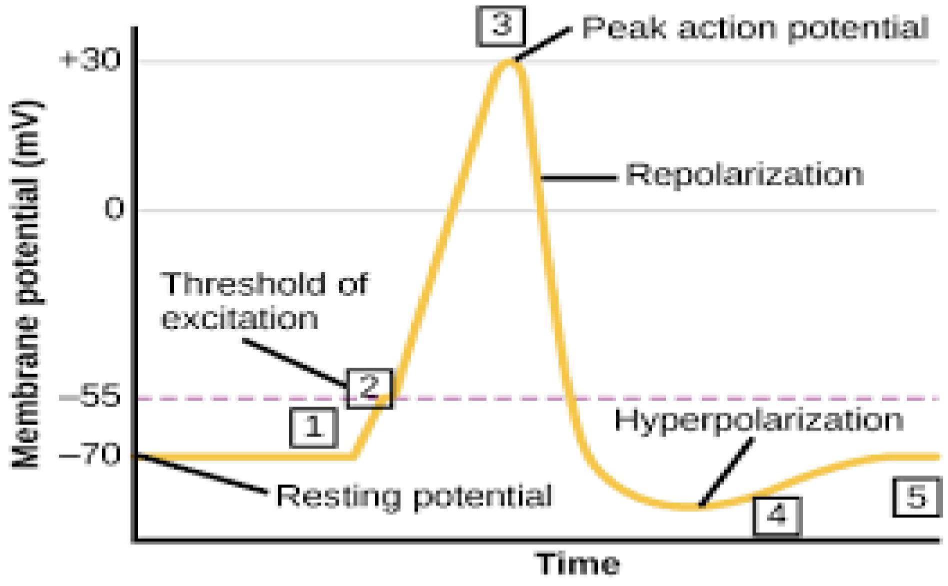
ACTION POTENTIAL

- The process is speeded up by the simultaneous increase in potassium permeability.
- Potassium diffusion out of the cell is then much greater than the sodium diffusion in, rapidly returning the membrane potential to its resting level.
- In fact, after the sodium channels have closed, some of the voltage-gated potassium channels are still open
- in nerve cells there is generally a small hyperpolarization of the membrane potential beyond the resting level
- cellular accumulation of sodium and loss of potassium are prevented by the continuous action of the membrane Na,K-ATPase pumps.



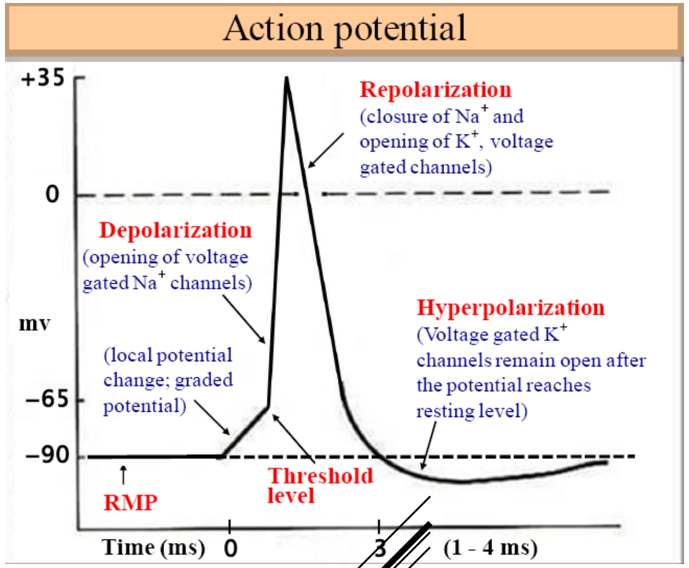
Mechanism of Ion-channel Changes

- The potassium channels that open during an action potential are also voltage-gated.
- In fact, their opening is triggered by the same depolarization that opens the sodium channels, but the potassium channel opening is slightly delayed.
- **What about the inactivation of the voltage-gated sodium channels that opened during the rising phase of the action potential?**
- This is the result of a voltage induced change in the conformation of the proteins that constitute the channel, which closes the channel after its brief opening.



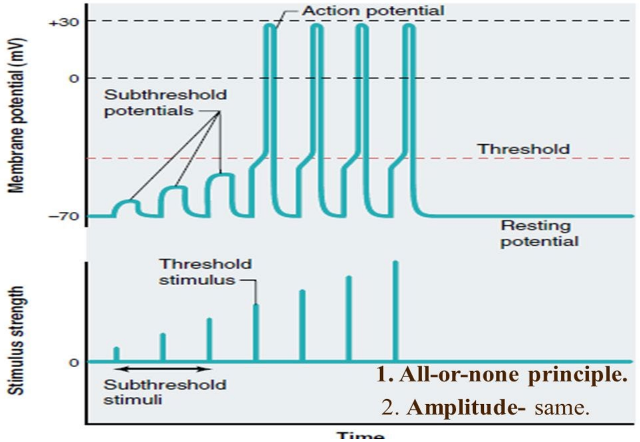
Threshold potential

- Action potentials occur only when the *net* movement of positive charge through ion channels is inward.
- The membrane potential at which this occurs is called the **threshold potential,**
- Stimuli that are just strong enough to depolarize the membrane to this level are **threshold stimuli**
- The threshold of most excitable membranes is about 15 mV less negative than the resting membrane potential.
- Thus, if the resting potential of a neuron is 70 mV, the threshold potential may be 55 mV.

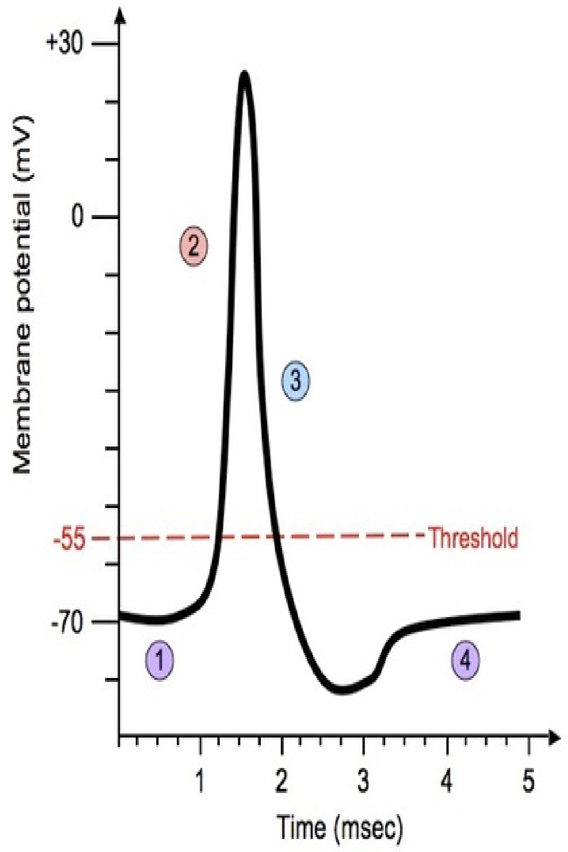


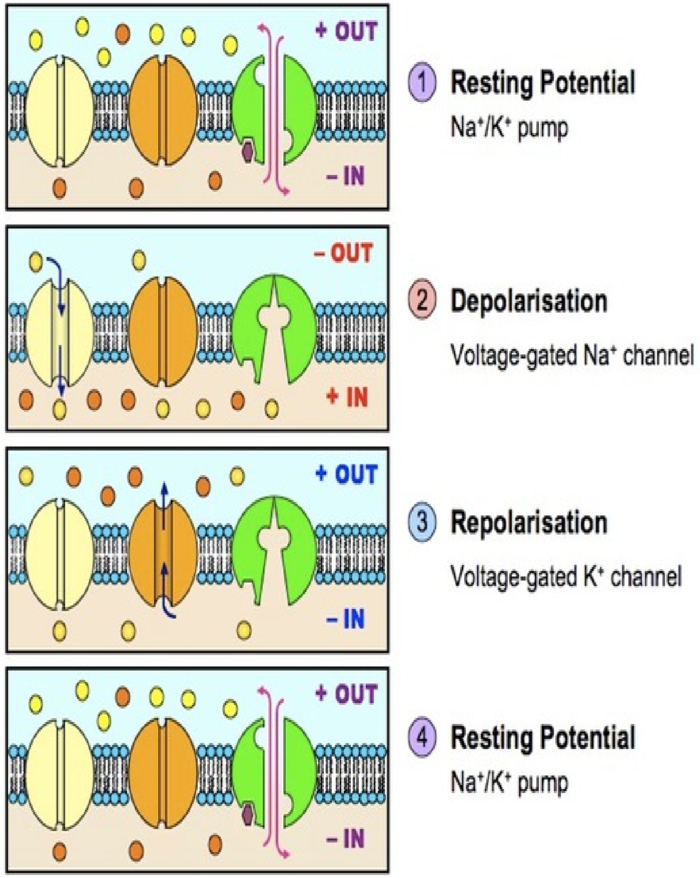
Threshold potential

- **At depolarizations less than threshold**, outward potassium movement still exceeds sodium entry, and the positive-feedback cycle cannot get started despite the increase in sodium entry.
- In such cases, the membrane will return to its resting level as soon as the stimulus is removed, and **no action potential is generated**.
- These weak depolarizations are **subthreshold potentials**, and the stimuli that cause them are **subthreshold stimuli**.



All – or-none





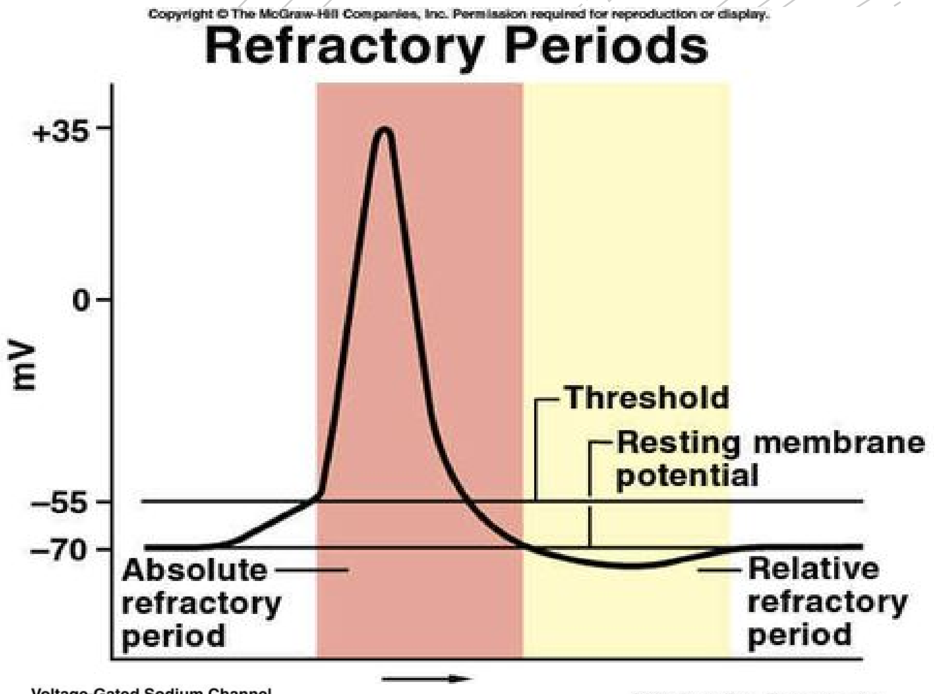
- Stimuli of more than threshold magnitude also elicit action potentials,
- The action potentials resulting from such stimuli have **exactly the same amplitud**e as those caused by threshold stimuli.
- **This is because once threshold is reached, membrane events are no longer dependent upon stimulus strength.**
- Rather, the depolarization generates an action potential because the positive-feedback cycle is operating.
- Action potentials either occur maximally or they do not occur at all.
- Another way of saying this is that action potentials are **all-or-none**.

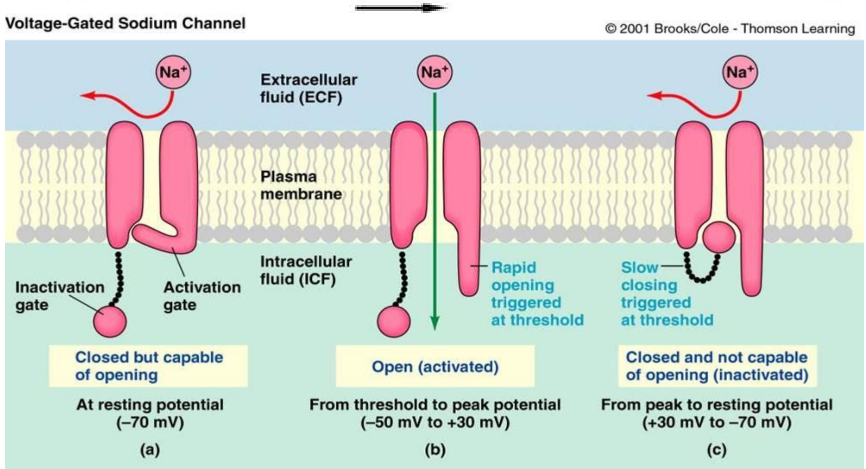
All – or-none

- The firing of a gun is a mechanical analogy that shows the principle of all-or-none behavior.
- The magnitude of the explosion and the velocity at which the bullet leaves the gun do not depend on how hard the trigger is squeezed.
- Either the trigger is pulled hard enough to fire the gun, or it is not; the gun cannot be fired halfway

- **How does one distinguish between a loud noise and a whisper, a light touch and a pinch?**

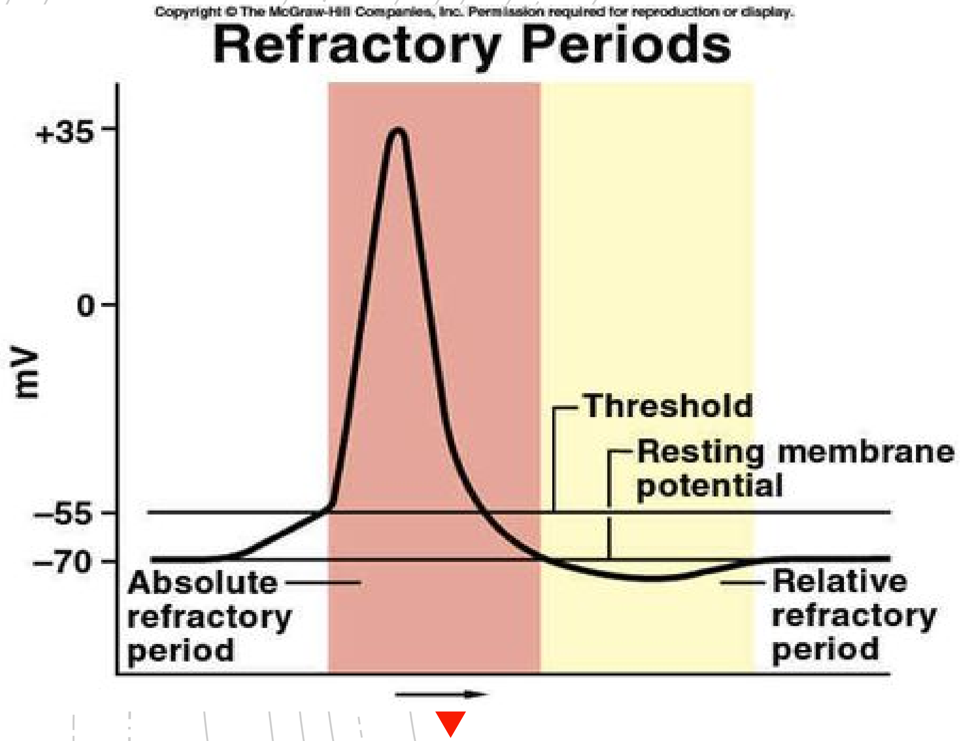
- This information depends upon the number and pattern of action potentials transmitted per unit of time and not upon their magnitude.





- During the action potential, the membrane is said to be in its **absolute refractory period.**
- A second stimulus, no matter how strong, will not produce a second action potential
- This occurs because the voltage-gated sodium channels enter a **closed, inactive state** at the peak of the action potential.
- The membrane must **repolarize** before the sodium channel proteins return to the state in which they can be opened again by depolarization.

ABSOLUTE Refractory PerIod

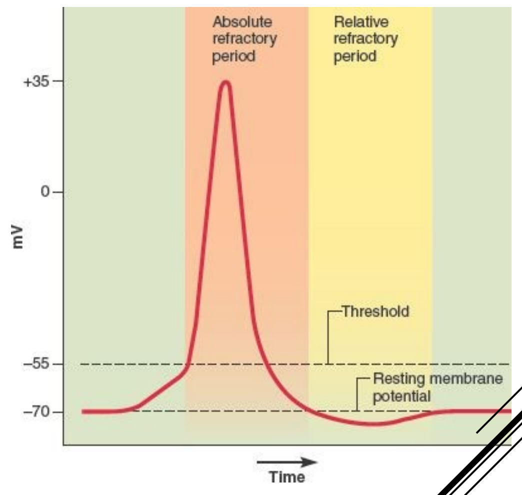


- Following the absolute refractory period, there is an interval during which a second action potential can be produced, but only if the stimulus strength is considerably greater than usual.
- This is the **relative refractory period,** which can last 10 to 15 ms or longer in neurons
- It coincides roughly with the period of after hyperpolarization.
- During the relative refractory period, there is lingering inactivation of the voltage-gated sodium channels, and an increased number of potassium channels are open.
- If a depolarization exceeds the increased threshold or outlasts the relative refractory period, additional action potentials will be fired.

RELATIVE Refractory PerIod

Functions of refractory period

- The refractory periods limit the number of action potentials that can be produced by an excitable membrane in a given period of time.
- They also increase the reliability of neural signaling because they help limit extra impulses.
- The refractory periods are key in determining the direction of action potential propagation.



Graded vs. Action Potentials

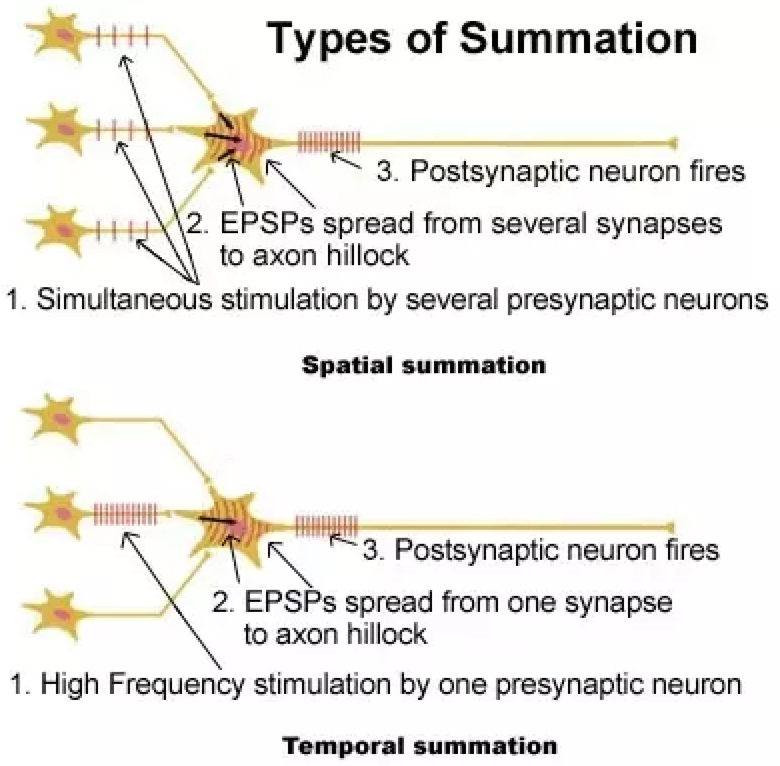
1. Magnitude varies
2. 2. Decremental (passive spread)
3. 3. No Refractory Periods

4. Summation is possible

5. Trigger: NT's, hormones
6. Occurs at cell body (direction can vary)

1. No variation - All or None
2. Non-decremental (self-regenerating)
3. Two Refractory periods: Absolute and Relative
4. No Summation possible
5. Trigger: Threshold
6. Occurs at axon hillock (one way direction)

Summation of Graded Potentials

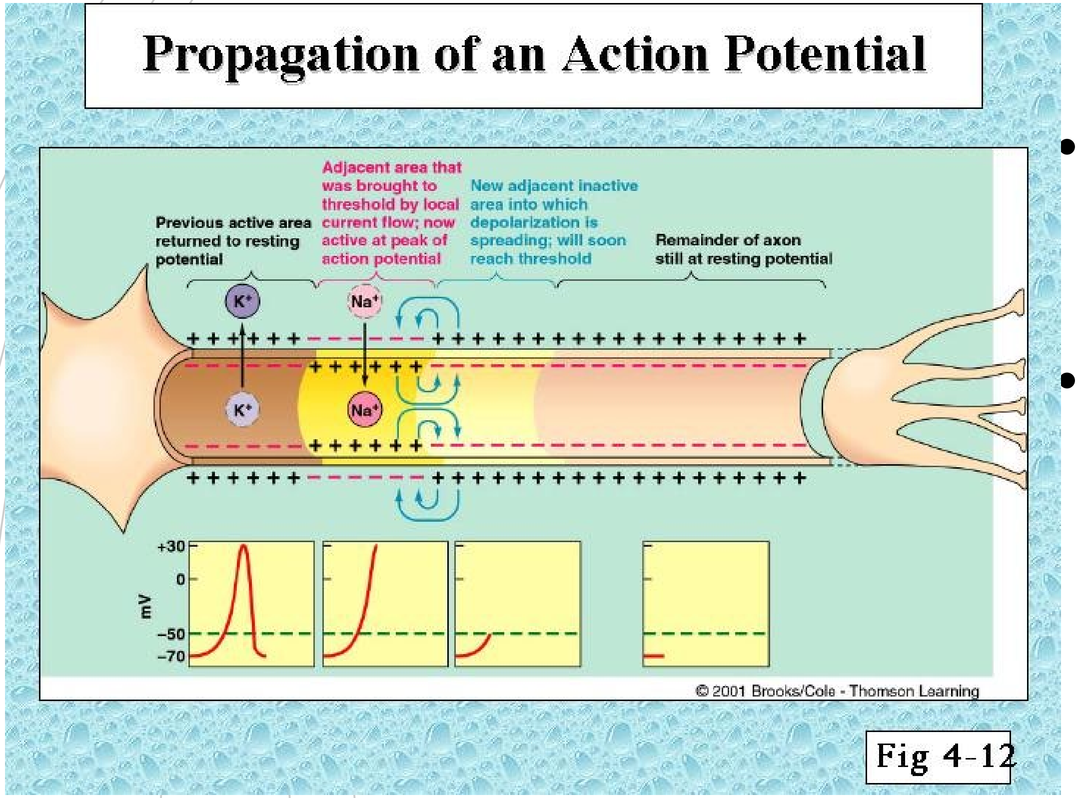


- Temporal Summation:

As the frequency of a single stimuli increases, the changes in membrane potential can be added and its magnitude can increase.

- Spatial Summation:

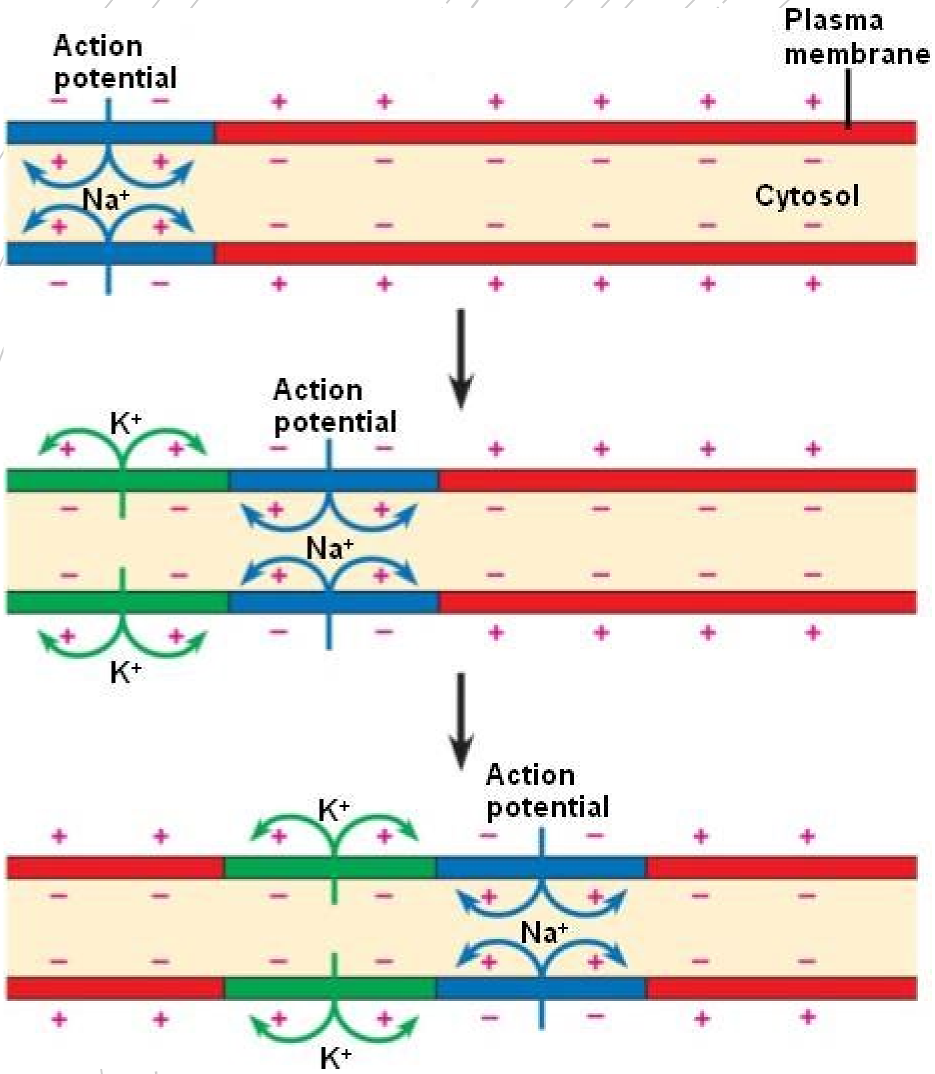
As multiple simultaneous stimuli occur at different places on the neuron, the changes in membrane potential can be added and its magnitude increased or decreased.



- There is a sequential opening and closing of sodium and potassium channels along the membrane.
- The action potential doesn't move but "sets off" a new action potential in the region of the axon just ahead of it.
- Because the membrane areas that have just undergone an action potential are refractory and cannot immediately undergo another, the only direction of action potential propagation is away from a region of membrane that has recently been active

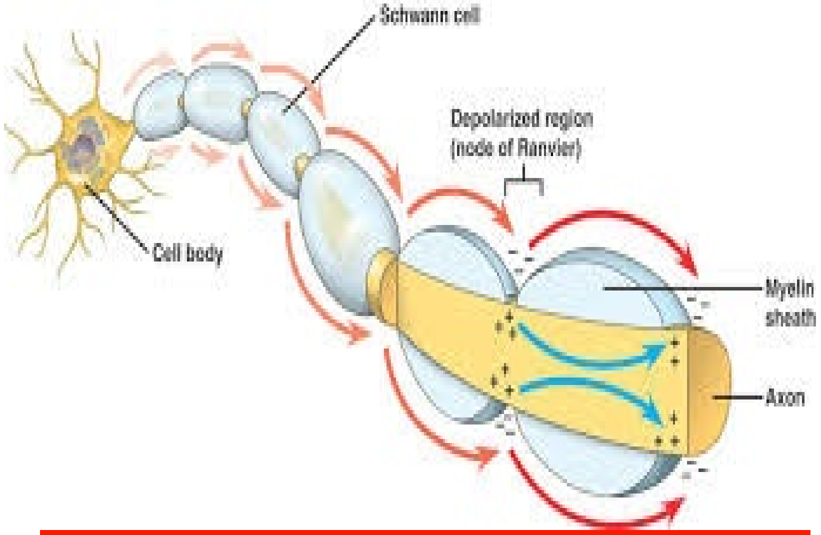
Action-Potentlal Propagatlon

Action-Potentlal Propagatlon



- The direction of propagation being determined by the stimulus location.
- For example, the action potentials in skeletal-muscle cells are initiated near the middle of these cylindrical cells and propagate toward the two ends.
- In most nerve cells, however, action potentials are initiated *physiologically* at one end of the cell (for reasons to be described in the next section) and propagate toward the other end

Actlon-Potentlal Propagatlon

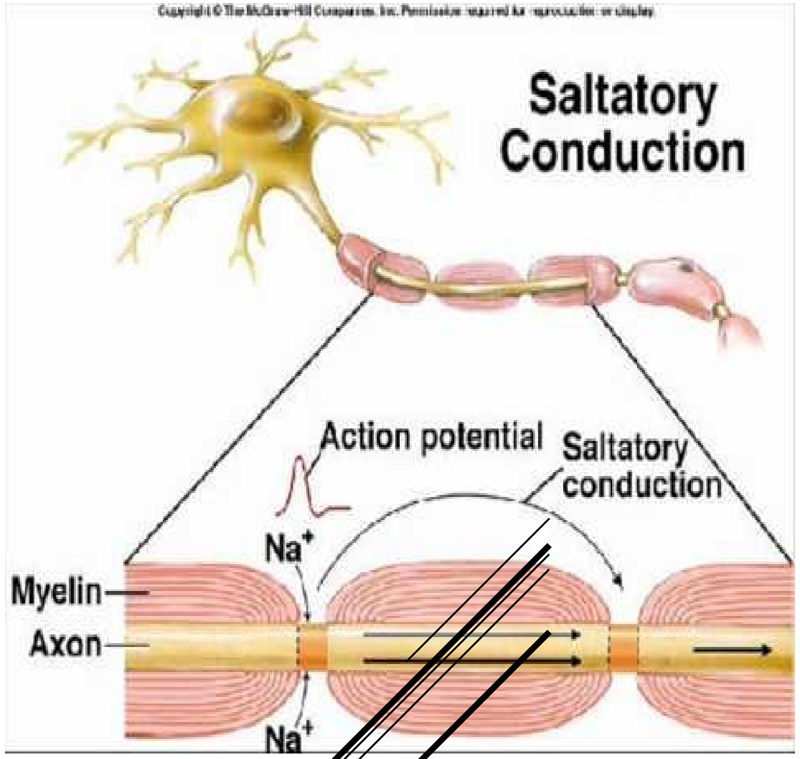


- The velocity with which an action potential propagates along a membrane depends upon fiber diameter and whether or not the fiber is myelinated.
- The larger the fiber diameter, the faster the action potential propagates.

- **WHY?**
- A large fiber offers less resistance to local current; more ions will flow in a given time, bringing adjacent regions of the membrane to threshold faster.

ActIon-PotentIal PropagatIon

- Myelin is an insulator that makes it more difficult for charge to flow between intracellular and extracellular fluid compartments.
- There is less “leakage” of charge across the myelin
- The concentration of voltage-gated sodium channels in the myelinated region of axons is low
- Therefore, action potentials occur only at the nodes of Ranvier where the myelin coating is interrupted and the concentration of voltage-gated sodium channels is high.
- Action potentials literally jump from one node to the next as they propagate along a myelinated fiber, and for this reason such propagation is called **saltatory conduction**



ANY QUESTION?