ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

The nervous system: anatomy and physiology

Part I: individuals cells

Cognition and Neuroscience
Academic year 2023/2024

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From individual cells to circuits to systems

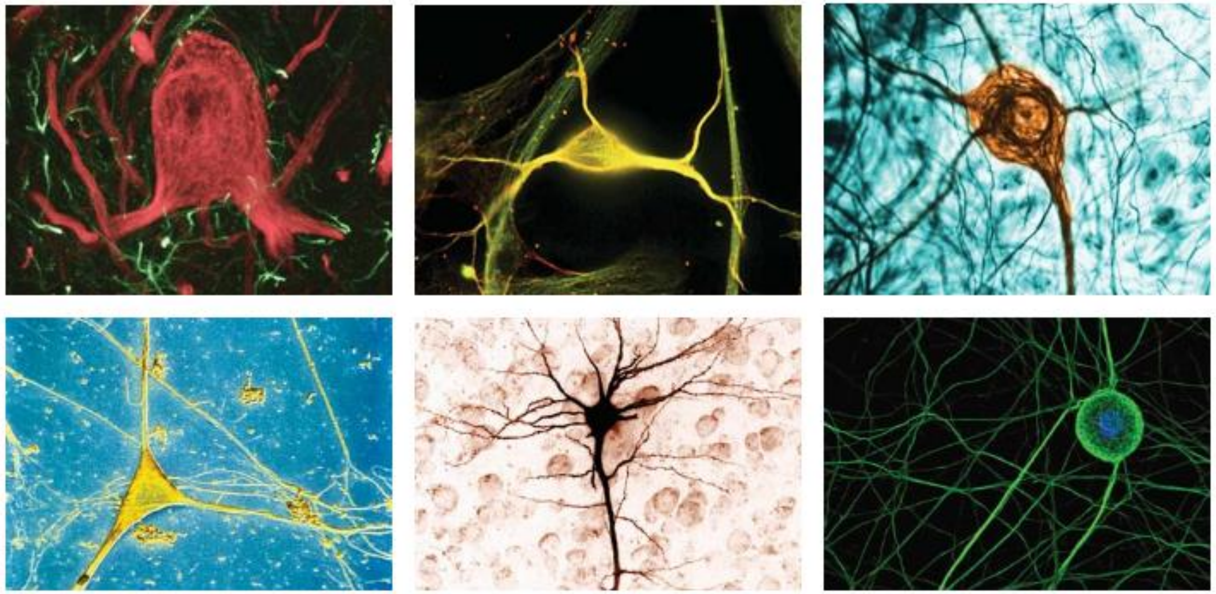

FIGURE 2.2 Mammalian neurons show enormous anatomical variety.

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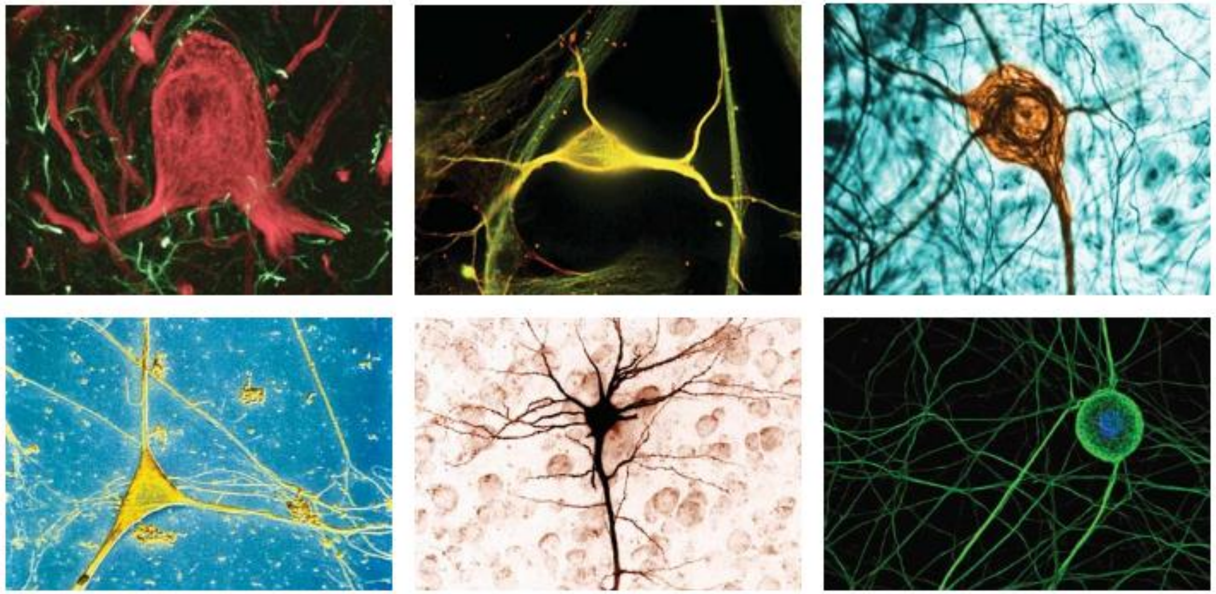

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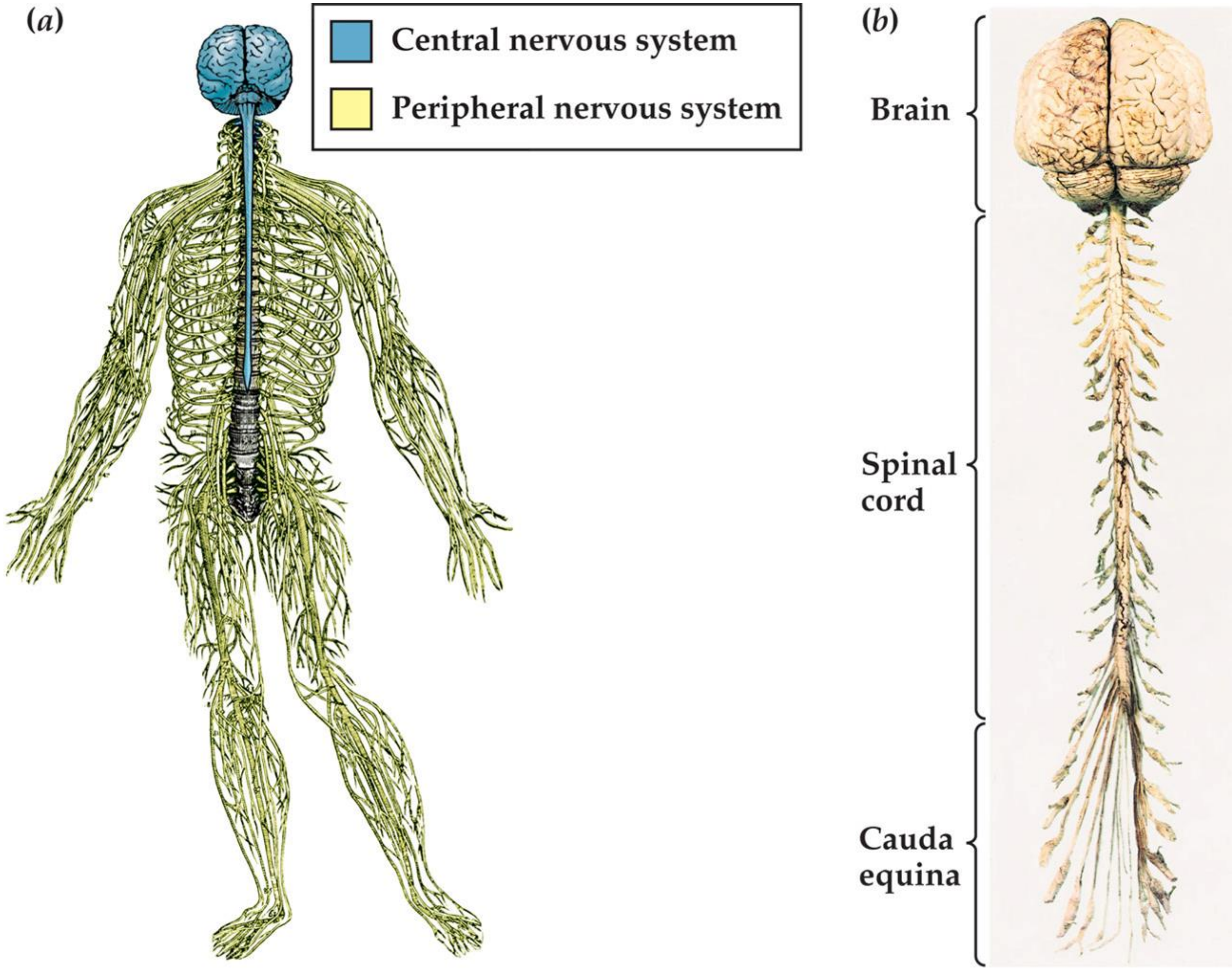
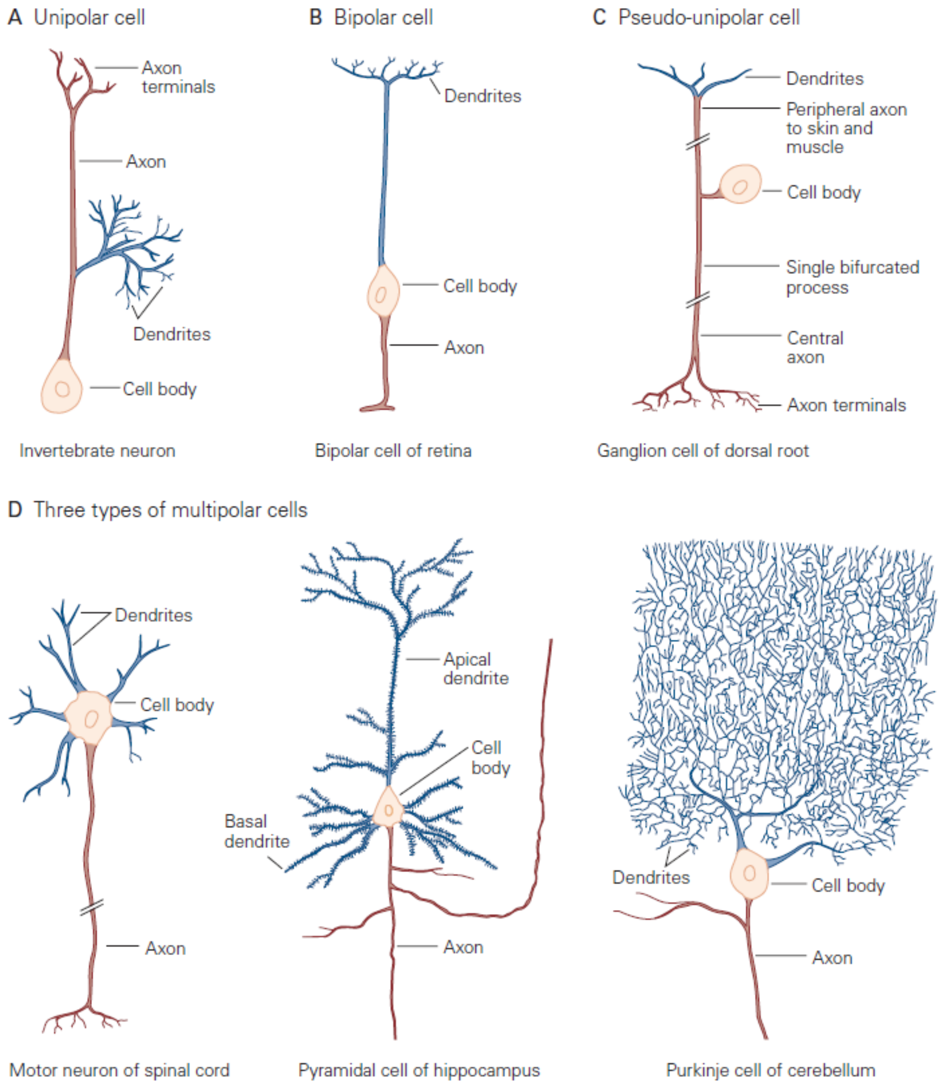


THE MIND'S MACHINE, Figure 2.6

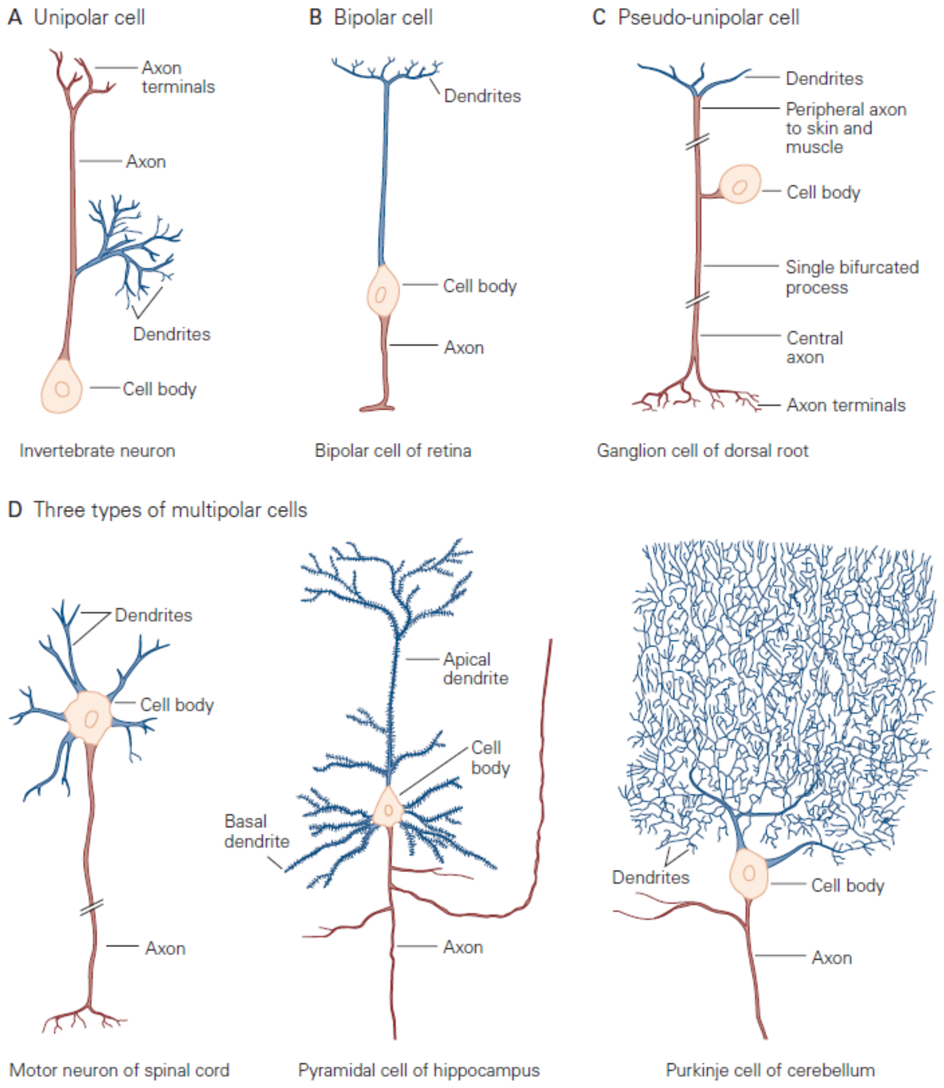
Individual cells

Nerve cells, or neurons



The Nervous System Has Two Classes of Cells

Nerve cells, or neurons



Glial cells, or neuroglia

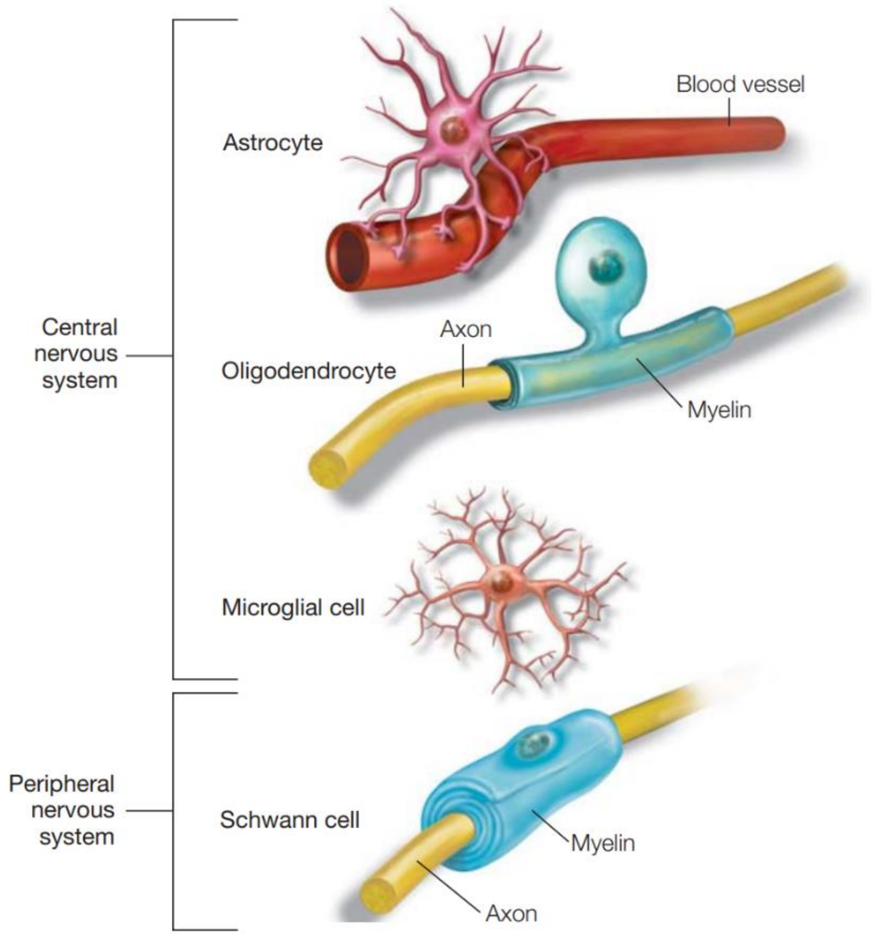


FIGURE 2.15 Various types of glial cells in the mammalian central and peripheral nervous systems.
An astrocyte is shown with end feet attached to a blood vessel. Oligodendrocytes and Schwann cells produce myelin around the axons of neurons—oligodendrocytes in the central nervous system, and Schwann cells in the peripheral nervous system. A microglial cell is also shown.

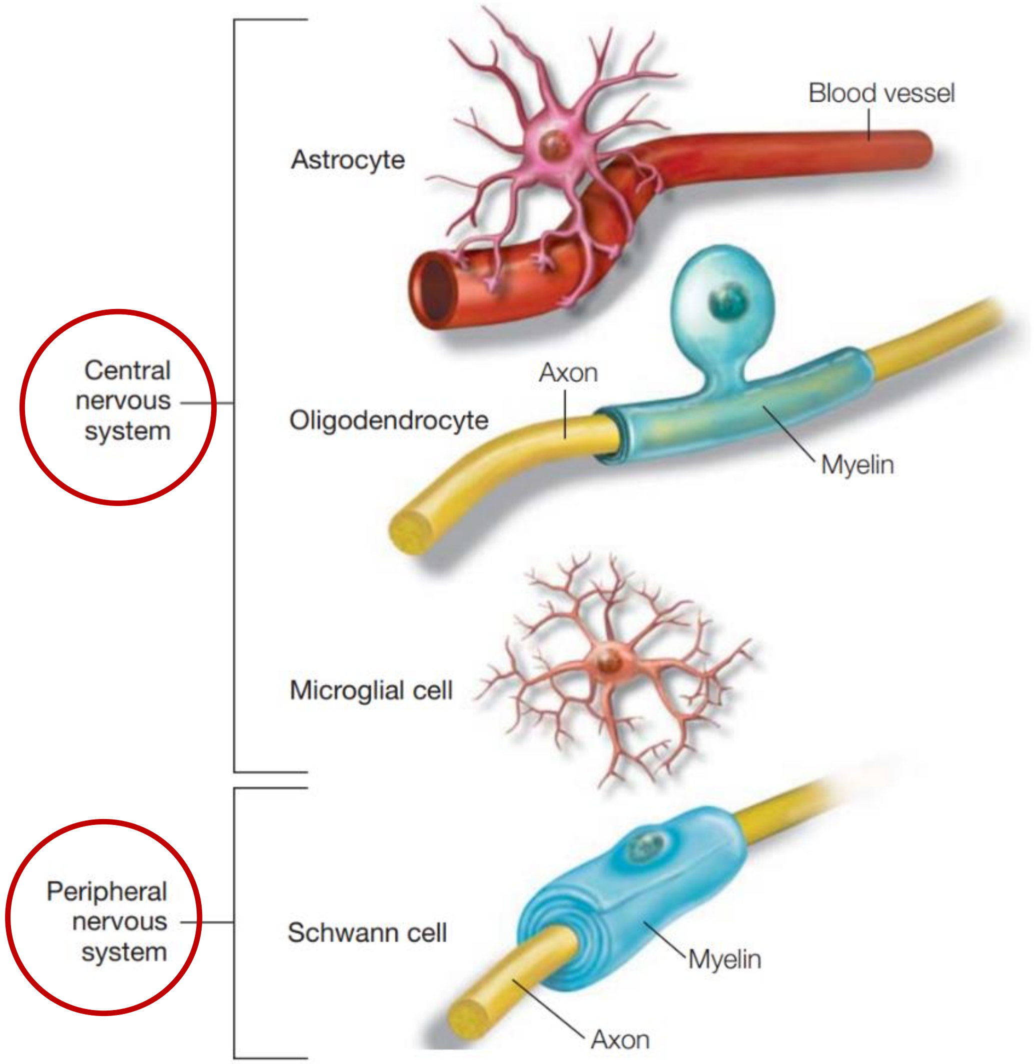
Neuroglia = "nerve glue"

Glial cells greatly outnumber neurons:

- there are 2 to 10 times more glia than neurons in the vertebrate central nervous system.

Glial Cells Support Nerve Cells:

- Structural
- Immune
- Nourishment
- Signaling



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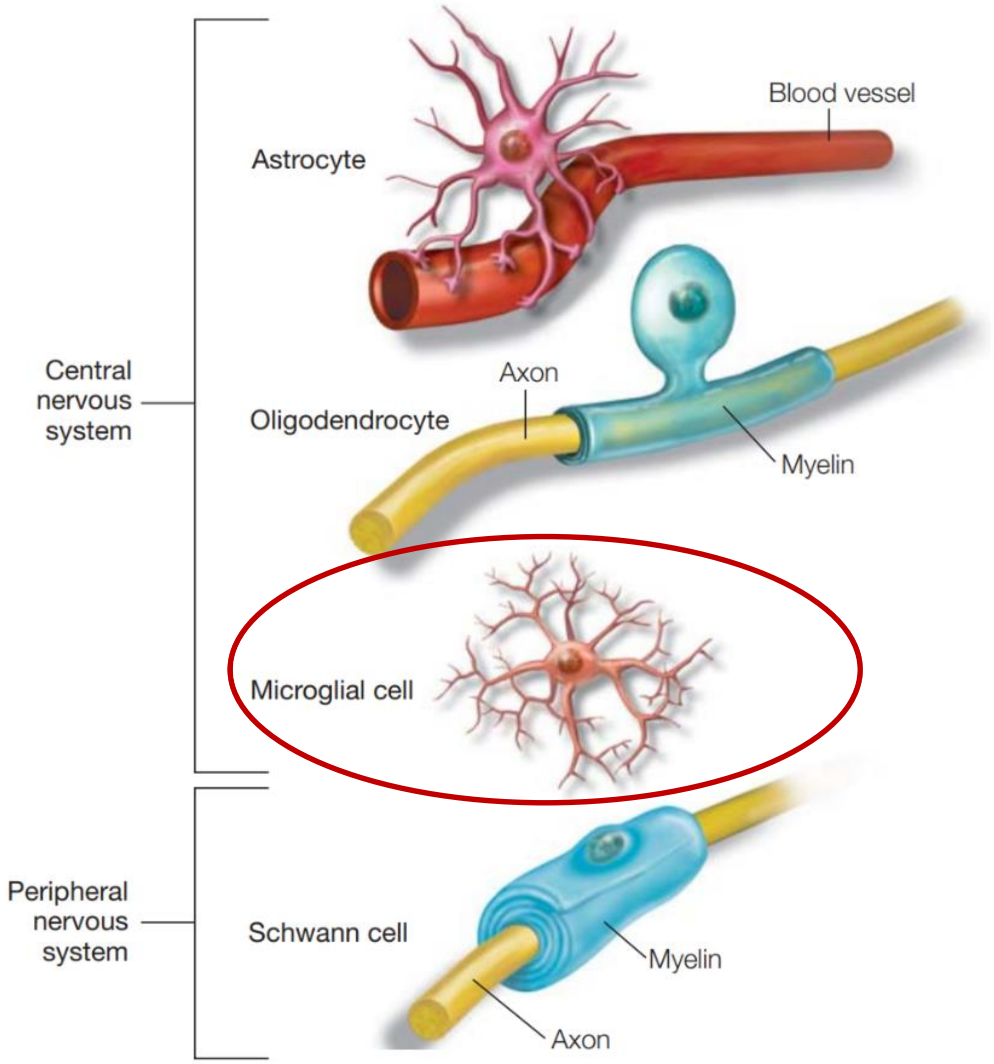
Immune support: microglia

Microglia are immune system cells

- brain's protectors: **identify when something has gone wrong and initiate a response that removes the toxic agent and/or clears away the dead cells**
- they are mobilized to present antigens and become phagocytes during injury, infection, or degenerative diseases



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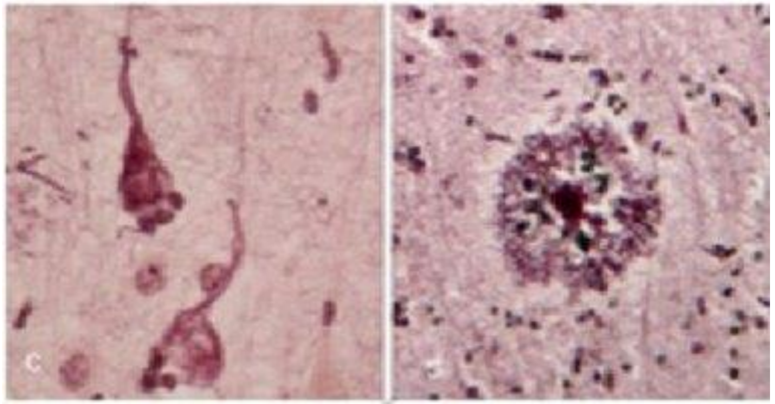
- In neurodegenerative disorders such as **Alzheimer's disease**, **microglia** may become **hyperactivated**, promoting neuroinflammation that can lead to the characteristic toxic protein deposits seen in Alzheimer's (amyloid plaques and neurofibrillary tangles)



amyloid plaques neurofibrillary tangles

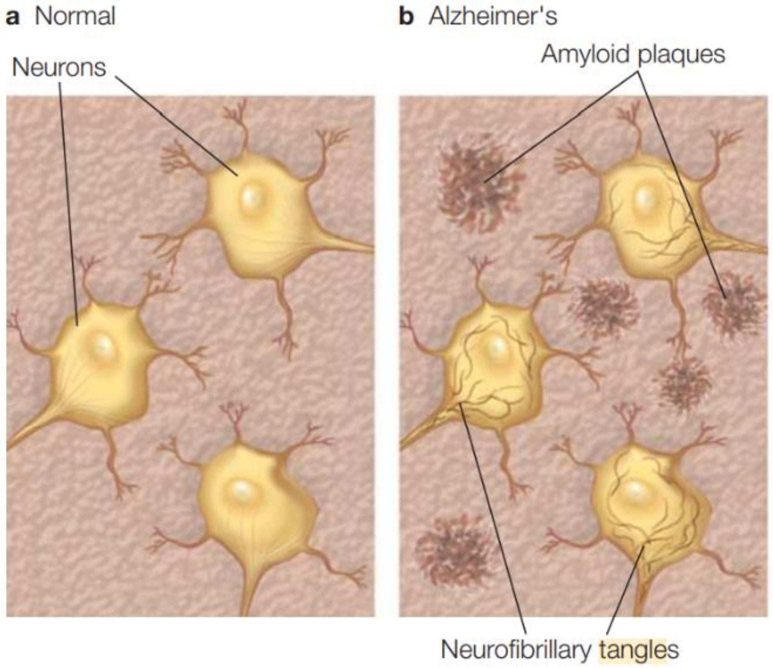


FIGURE 9.17 Comparison of cortex in Alzheimer's patients and normal participants.
These diagrams depict a normal section of cortex with cortical neurons **(a)** and a section of cortex in an Alzheimer's patient containing amyloid plaques between neurons and neurofibrillary tangles within neurons **(b)**.

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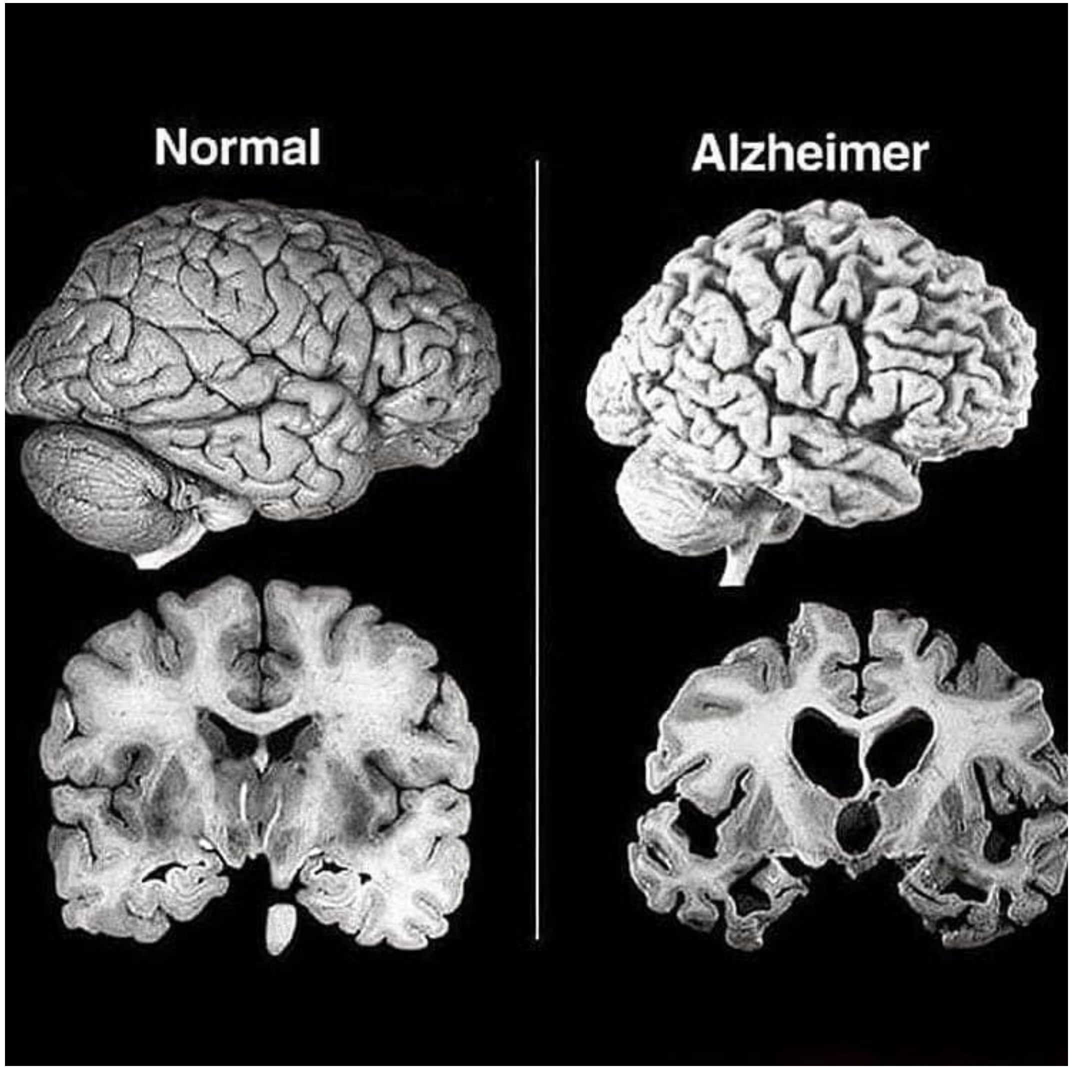
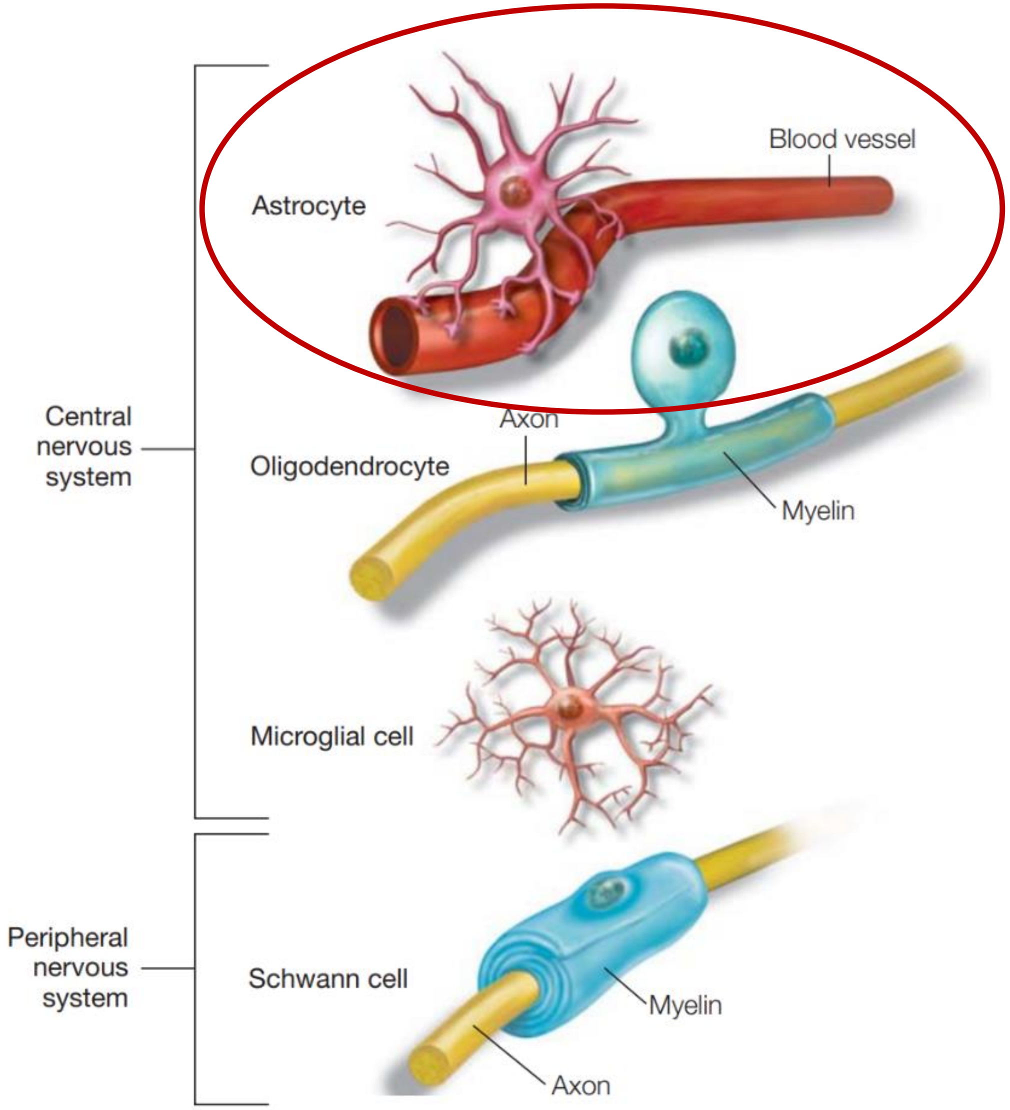


Nourishing support: astrocytes

- constitute nearly **half the number of brain cells**
- star-shaped, round form
- **surround neurons and are in close contact with the brain's vasculature** → important roles in **nourishing neurons and in regulating the concentrations of ions and neurotransmitters** in the extracellular space
- astrocytes and neurons communicate with each other to modulate synaptic signaling
- **maintain the blood-brain barrier**, between the tissues of the central nervous system and the blood



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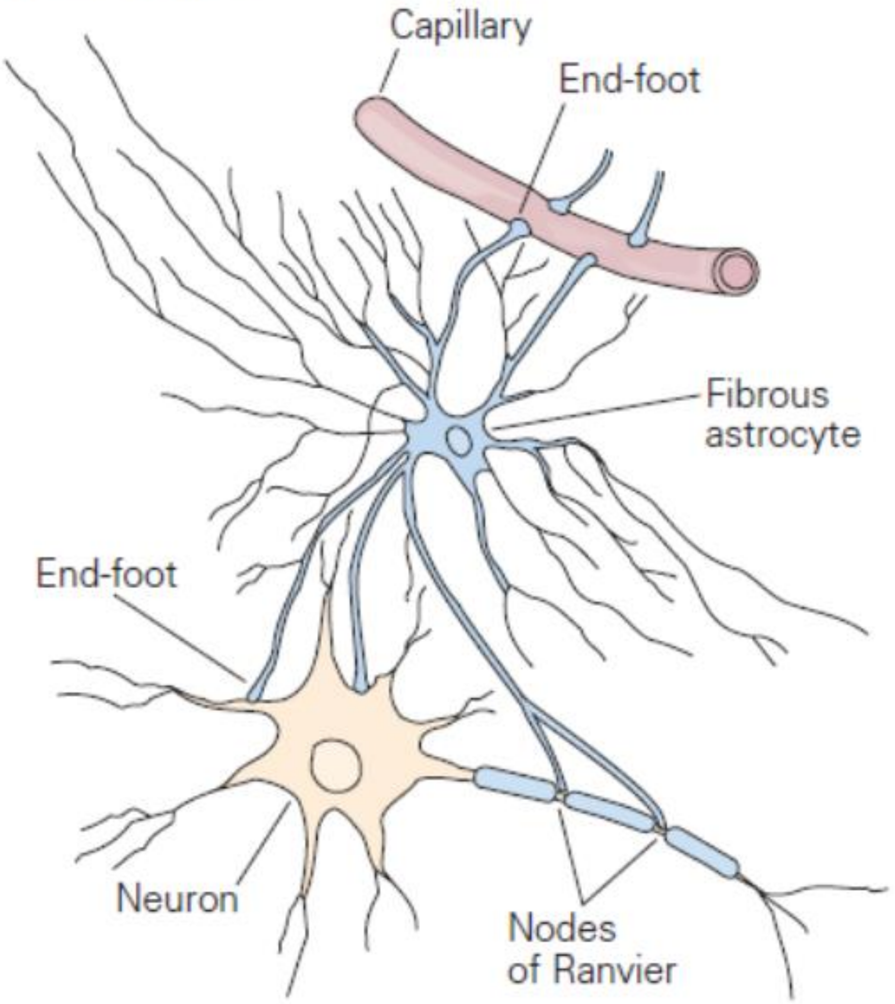
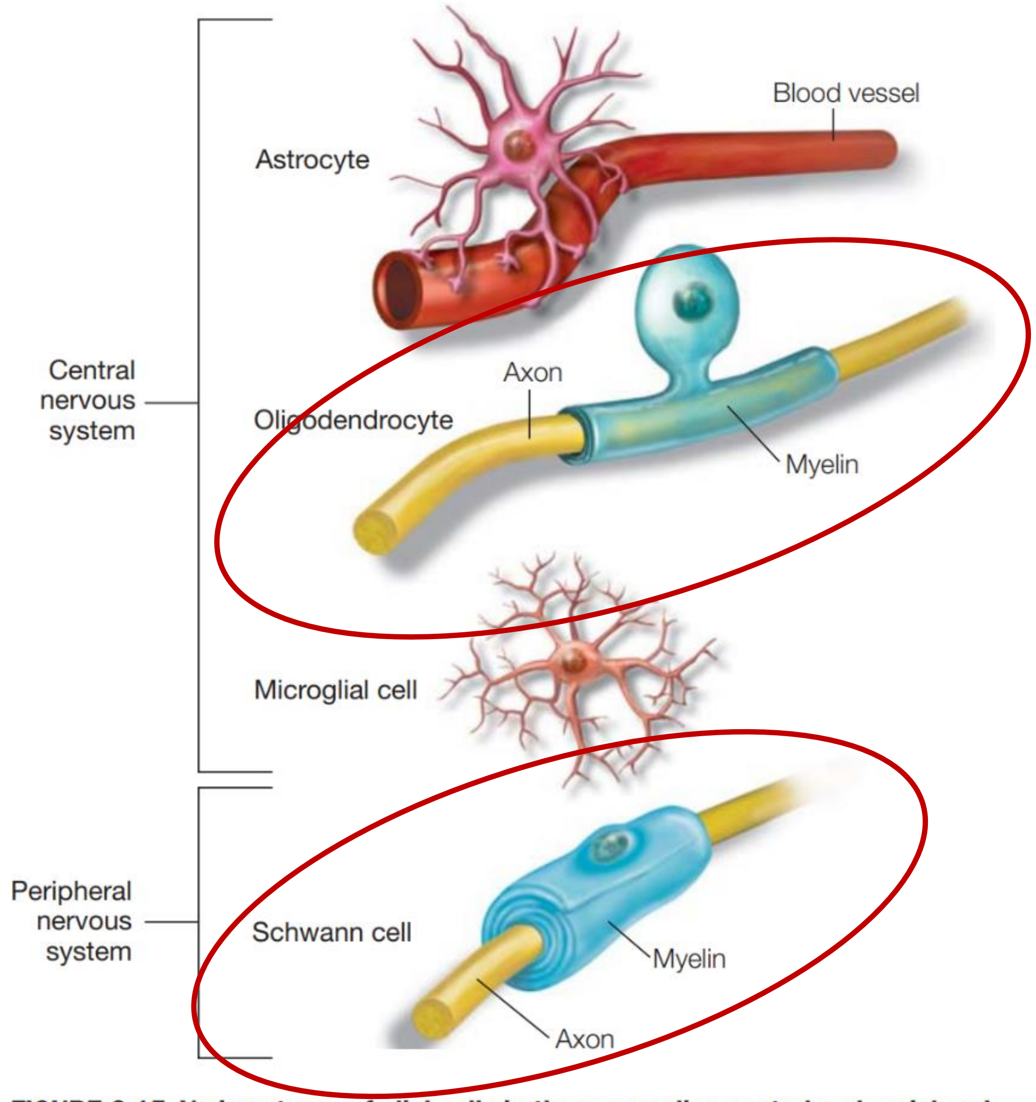
C Astrocyte



Signaling support: oligodendrocytes and Schwann cells

- Oligodendrocytes are in the central nervous system (CNS)
- Schwann cells are in the peripheral nervous system (PNS)

- **provide the insulating material along the axon**
- produce thin sheets of **myelin** that wrap concentrically, many times, around the axon of neurons to allow rapid conduction of electrical signals along the axon
- Myelin is white, giving "white matter" its name



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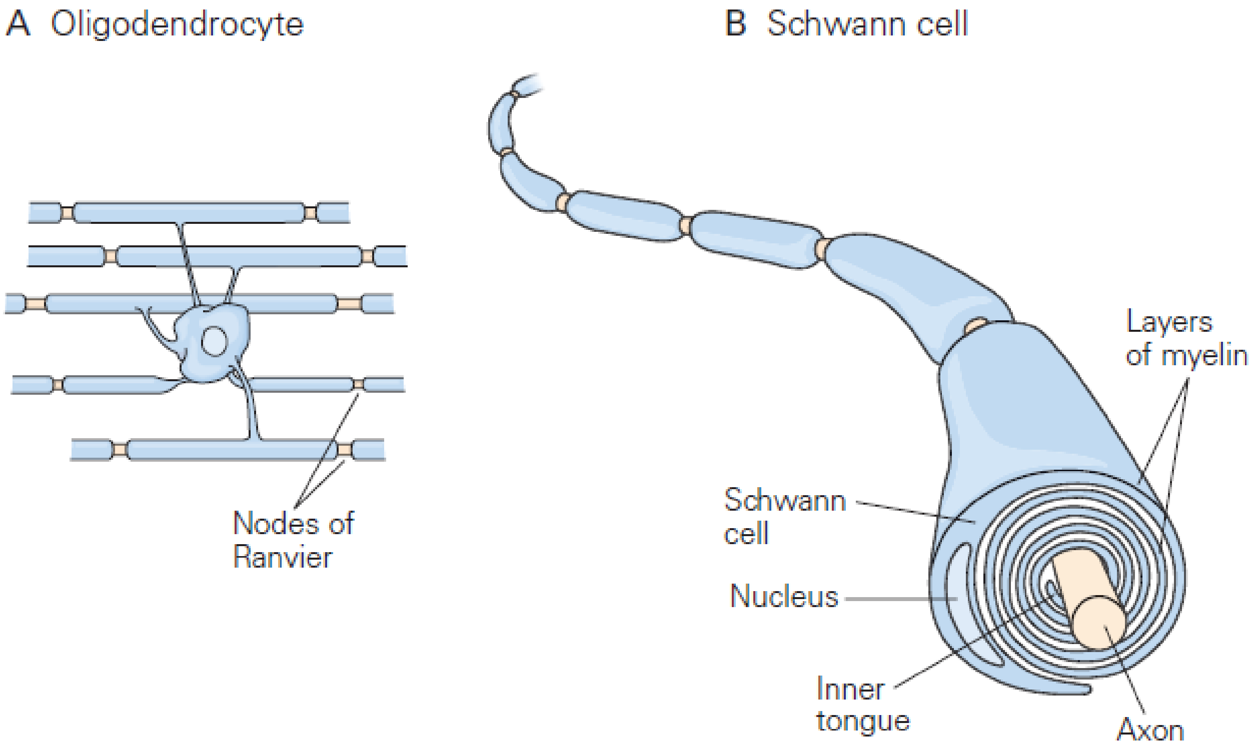
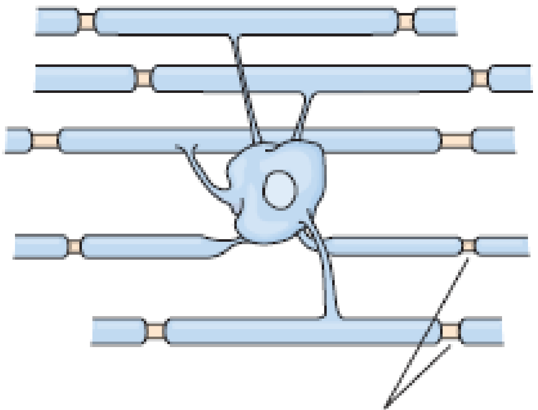
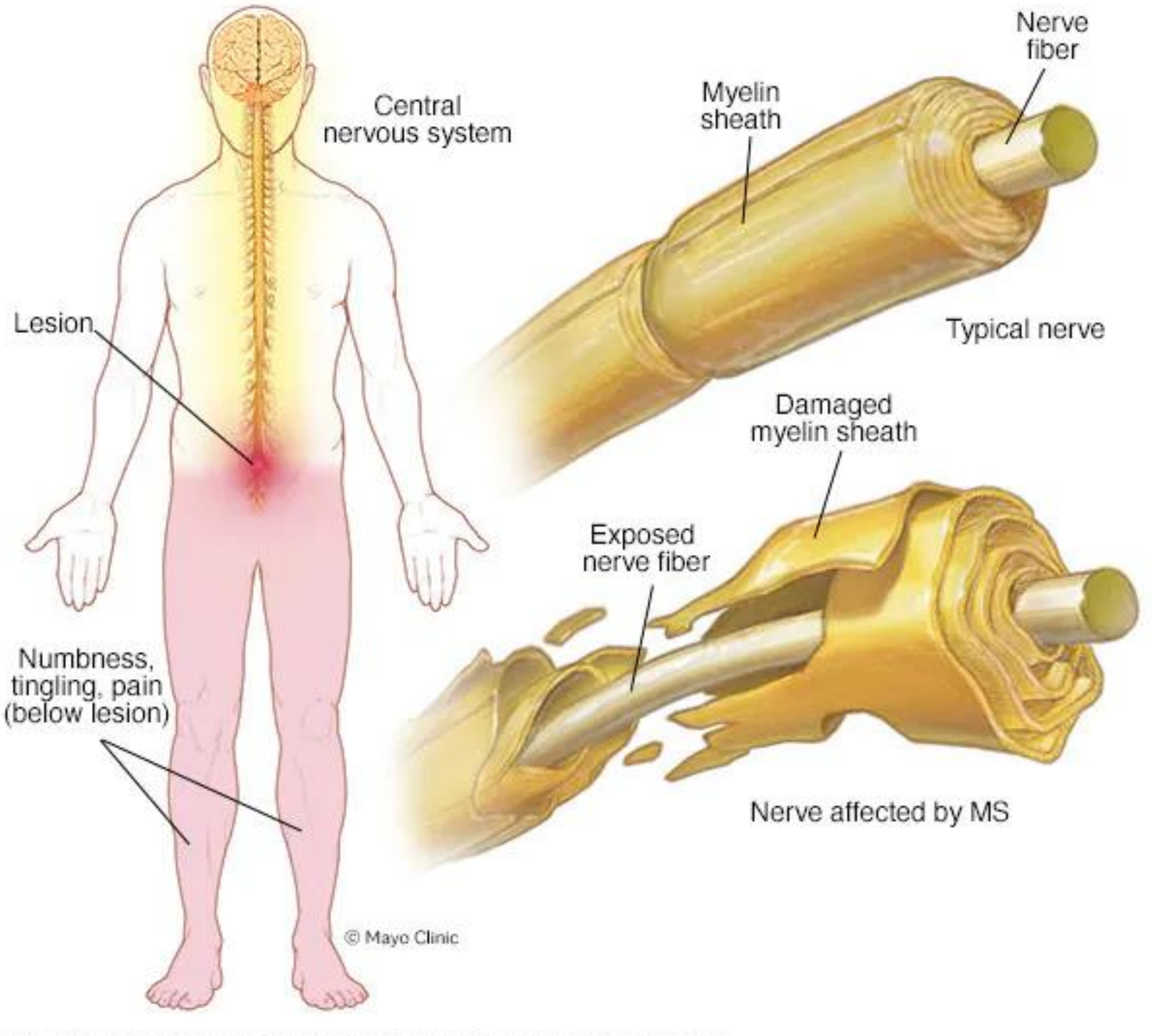


Signaling support: oligodendrocytes (in the CNS)

- In **Multiple Sclerosis the immune system mistakenly attacks the oligodendrocytes** (autoimmune disease)
- This damages and scars the myelin sheath in the CNS, meaning that messages travelling along the nerves become slowed or disrupted





Neurons are the signaling units of the nervous system

- 100 billion neurons in the nervous system
- 100 distinct types of neurons
    - Neurons vary in their form, location, and interconnectivity within the nervous system, and these variations in structure are closely related to their functions
- **Each neuron receives and gives rise to thousands of connections**
- Some of these connections are formed nearly a meter from the cell body of the neuron

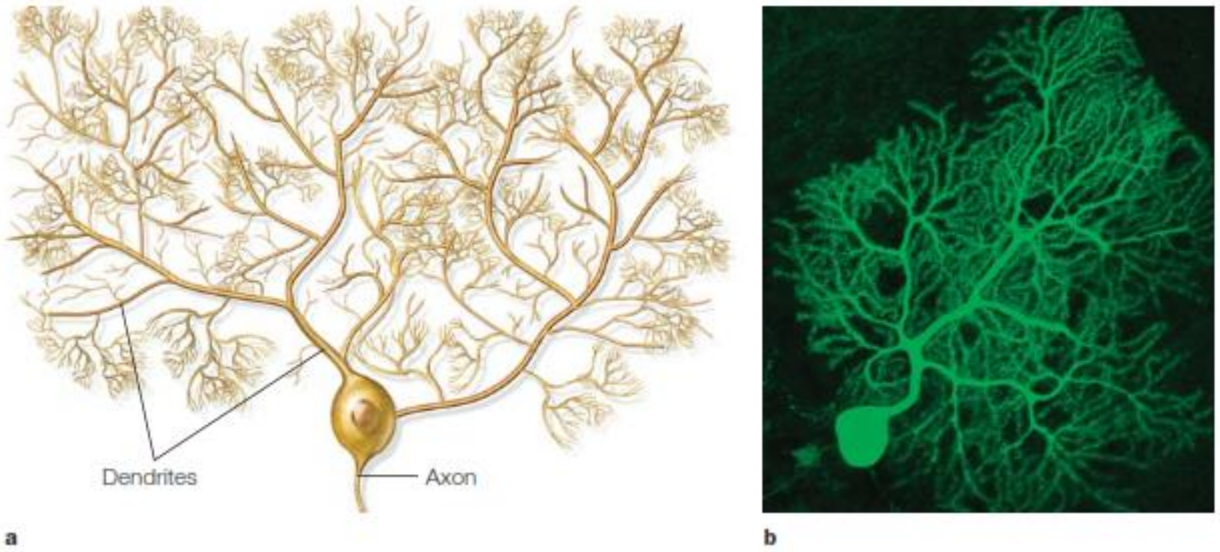


FIGURE 2.4 Soma and dendritic tree of a Purkinje cell from the cerebellum.

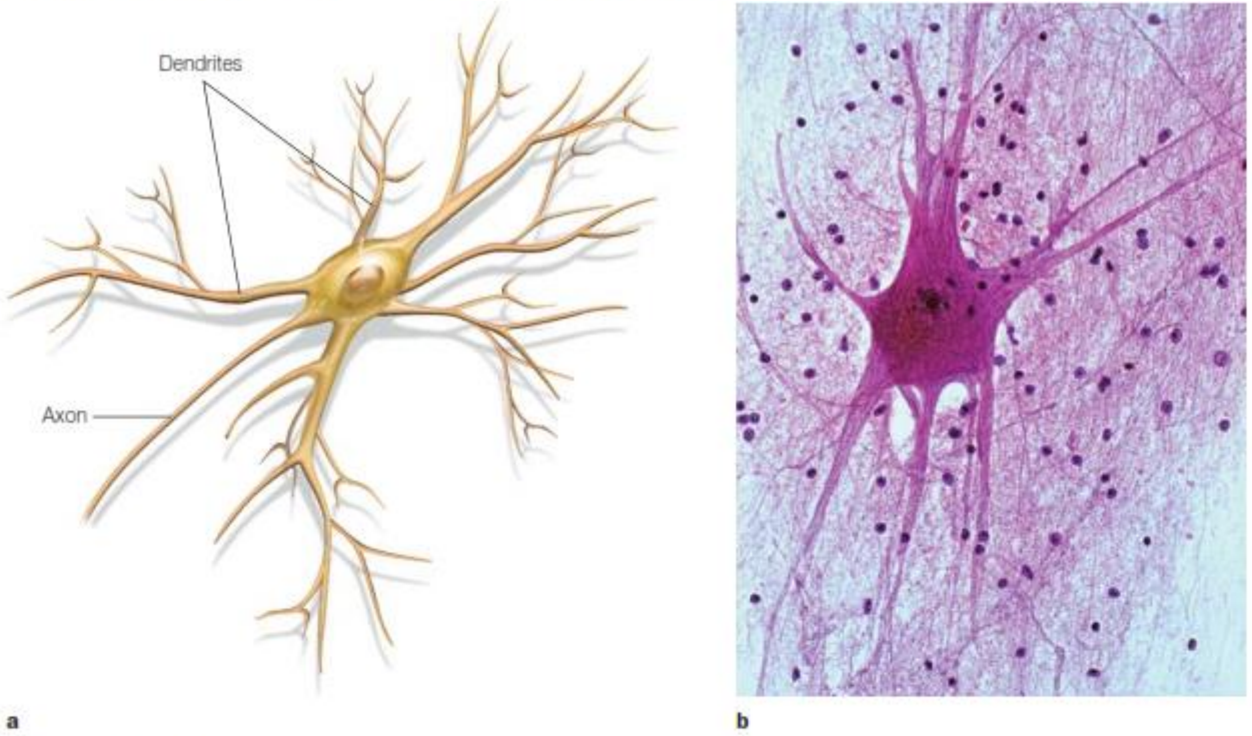
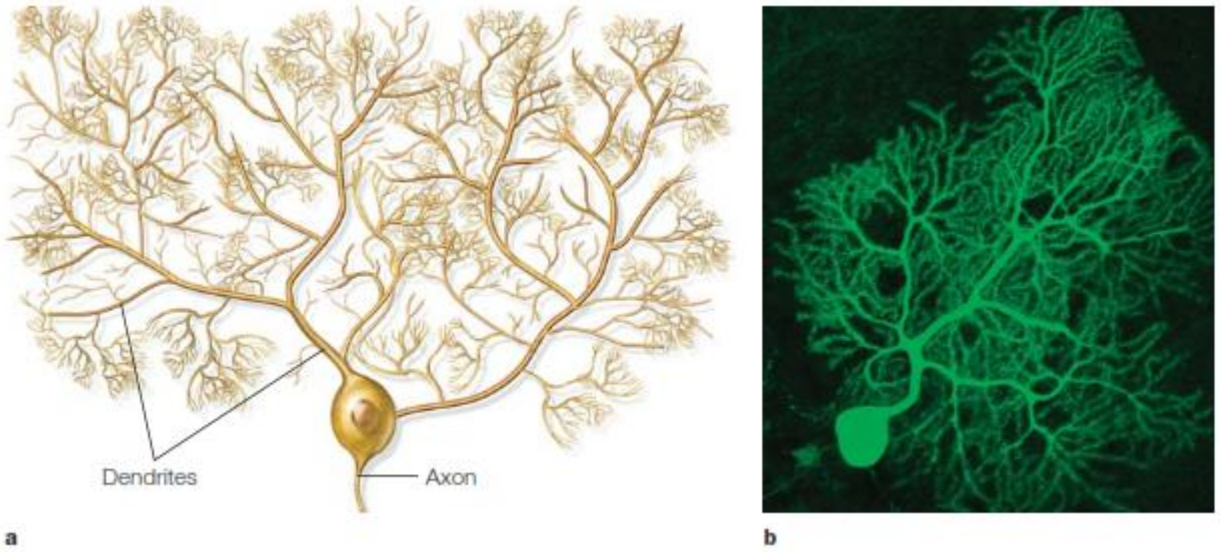


FIGURE 2.5 Spinal motor neuron.

Neurons are the signaling units of the nervous system

1. take in information
2. make a “ decision” about it, following some relatively simple rules
3. pass it along to other neurons, by changes in their activity levels



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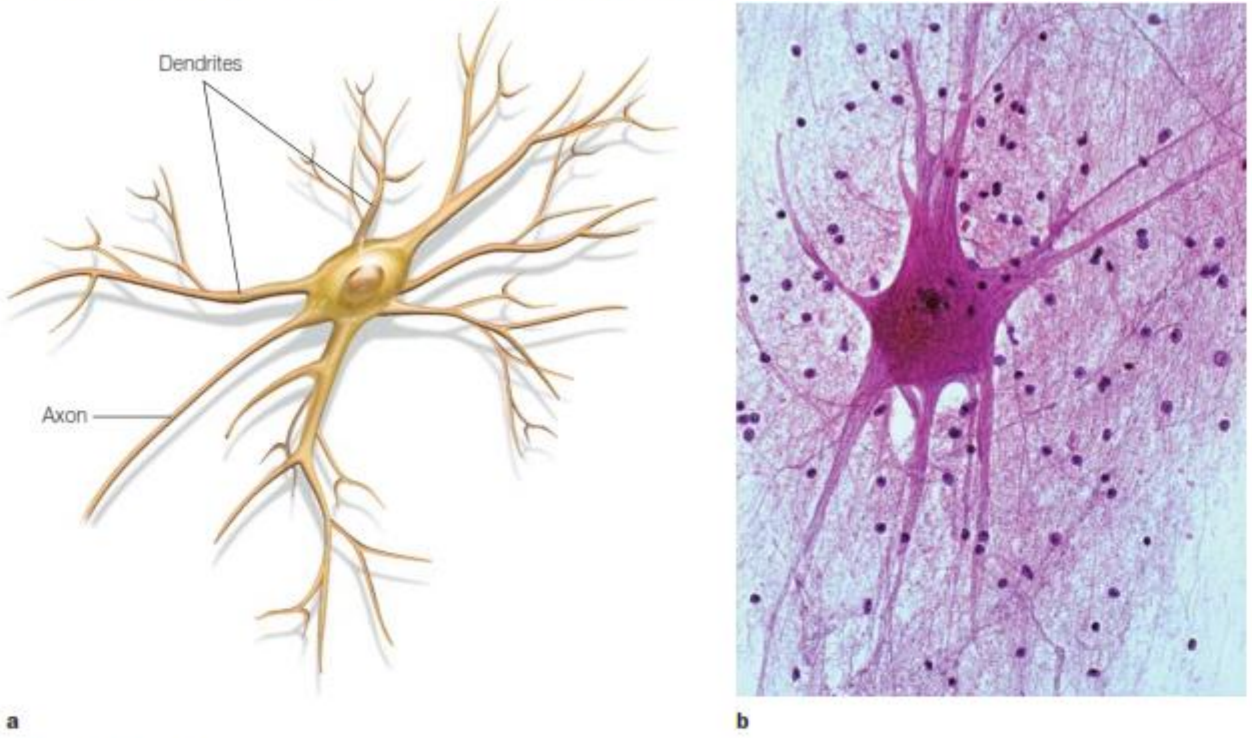
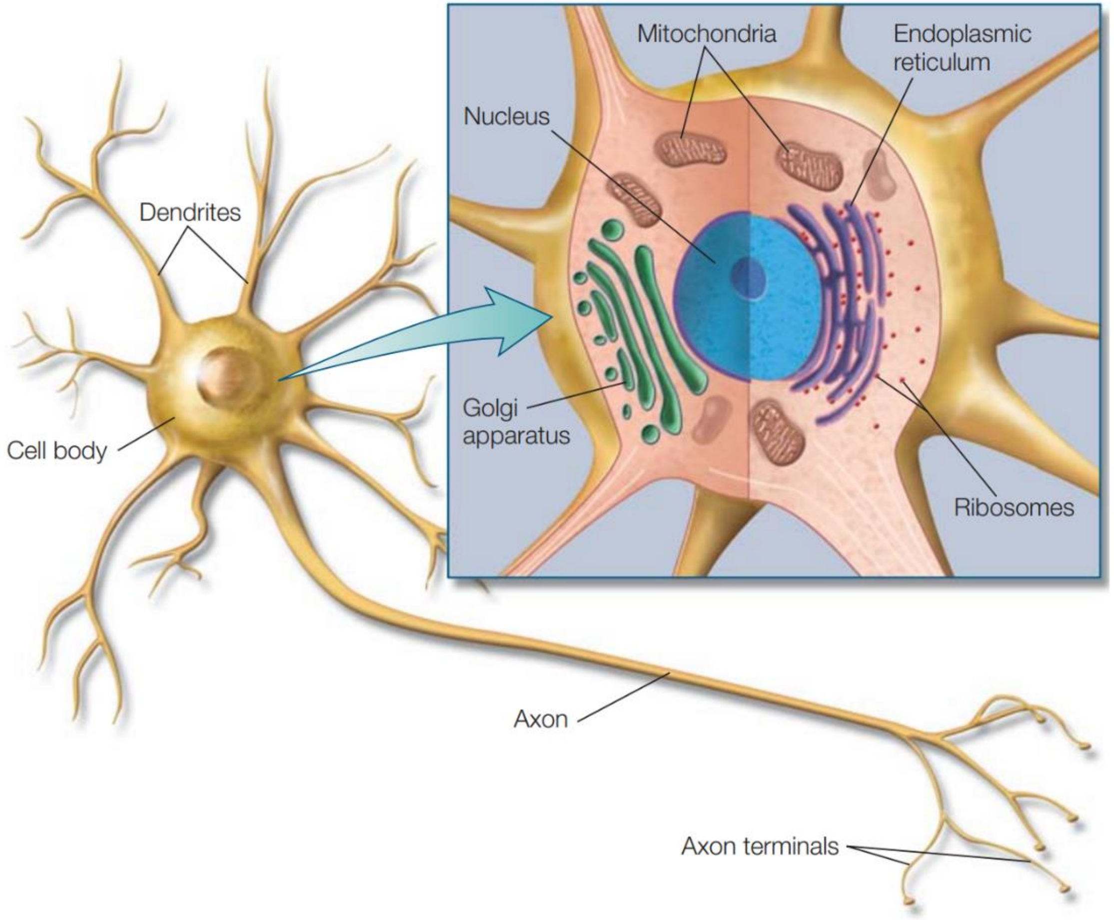


FIGURE 2.5 Spinal motor neuron.

The structure of neurons

Components found in almost all eukaryotic cells:

- **Cell membrane**: membrane that separates the intracellular and extracellular space
- **The cytoplasm**: intracellular fluid that is made up of a combination of ions, predominantly ions of potassium, sodium, chloride, and calcium, as well as molecules such as proteins.
- **The extracellular fluid**: a bath where the neurons sit, made up of a mixture of the same types of ions found in the intracellular fluid
- **Cell body or soma**: metabolic center of the cell. It contains the nucleus, which contains the genes of the cell, and the endoplasmic reticulum, where proteins are synthesized.

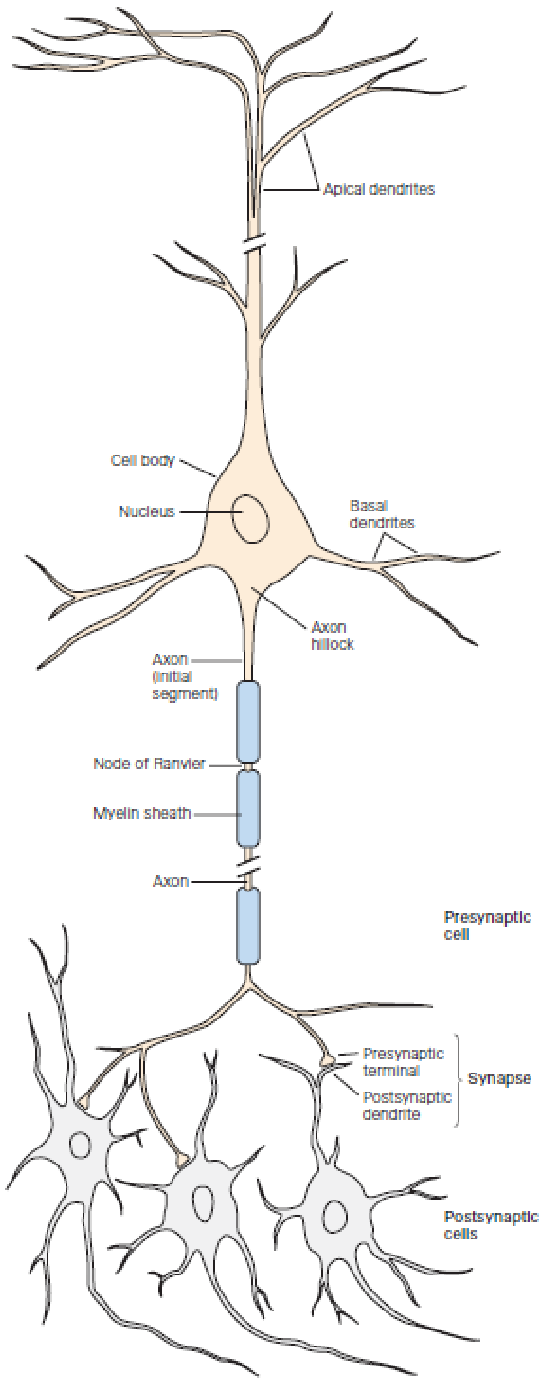


The structure of neurons

Components unique to neuronal cells:

1. Dendrites
2. Axon
3. Synapses

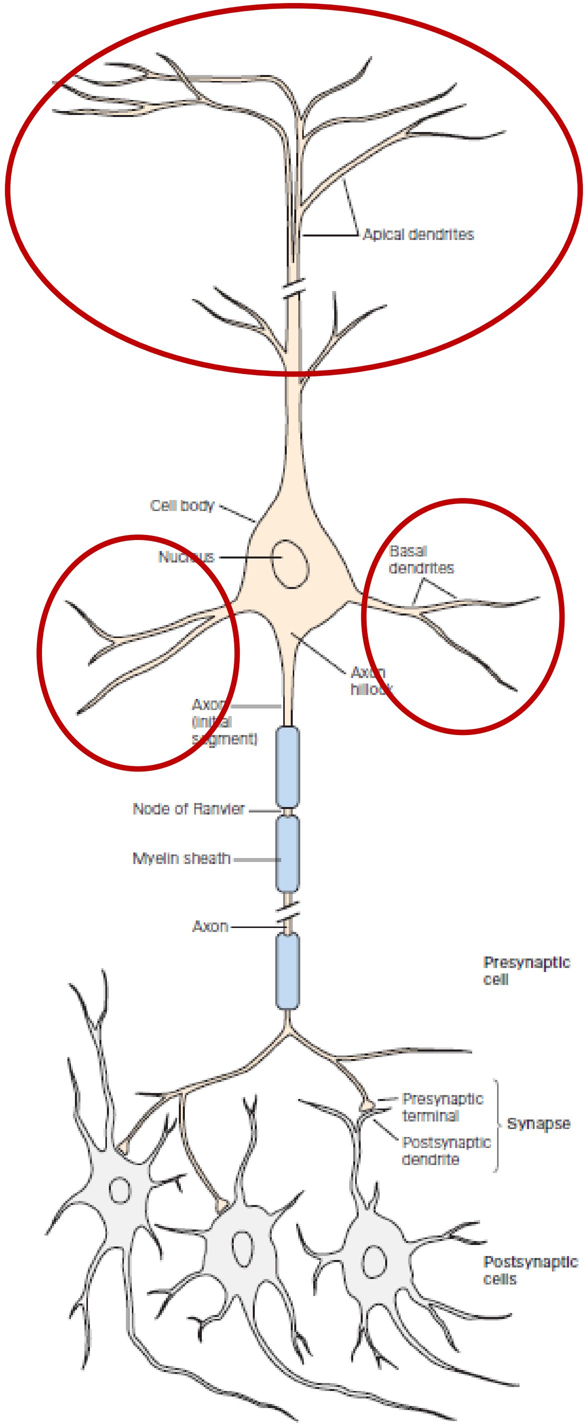
Each component has a distinct role in generating signals and communicating with other neurons.



The structure of neurons

1. **Dendrites**

- **multiple processes**
- represents the **receiving zone** of the neuron: receives inputs from other neurons
- the main apparatus for receiving incoming signals from other nerve cells
- Can take many varied and complex forms, depending on the type and location of the neuron



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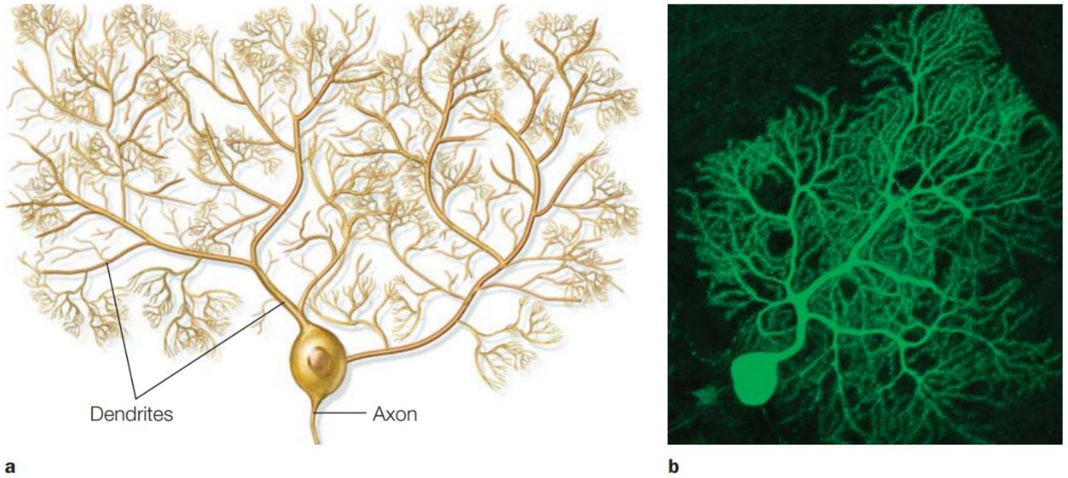

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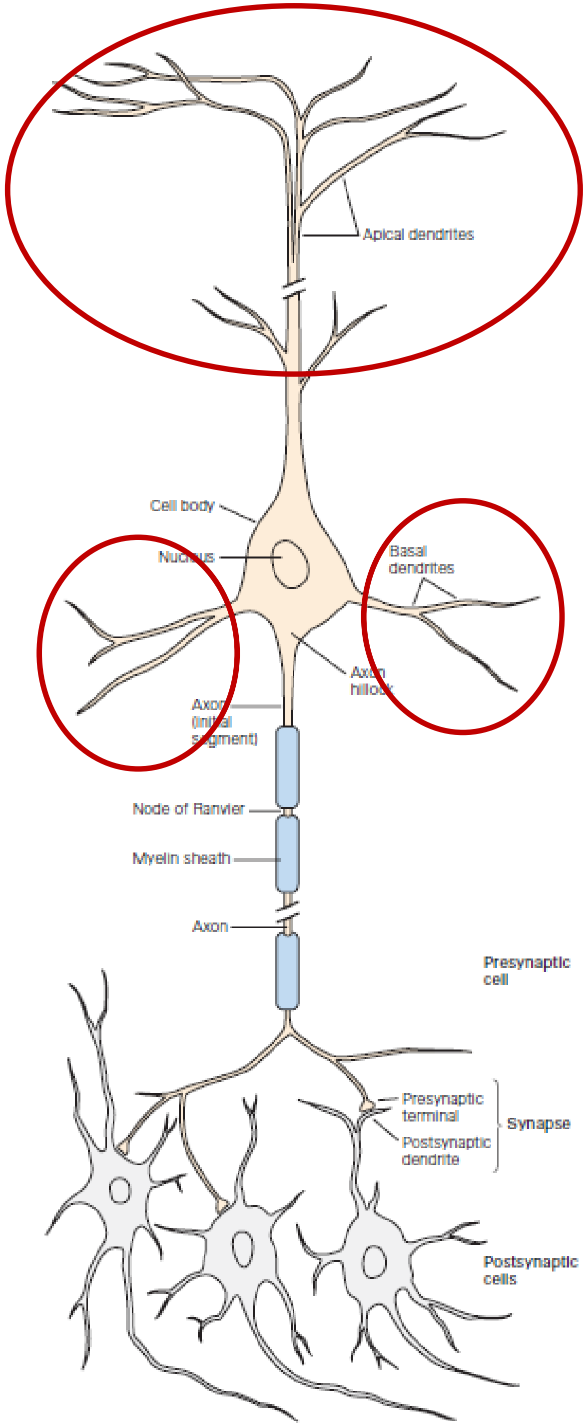
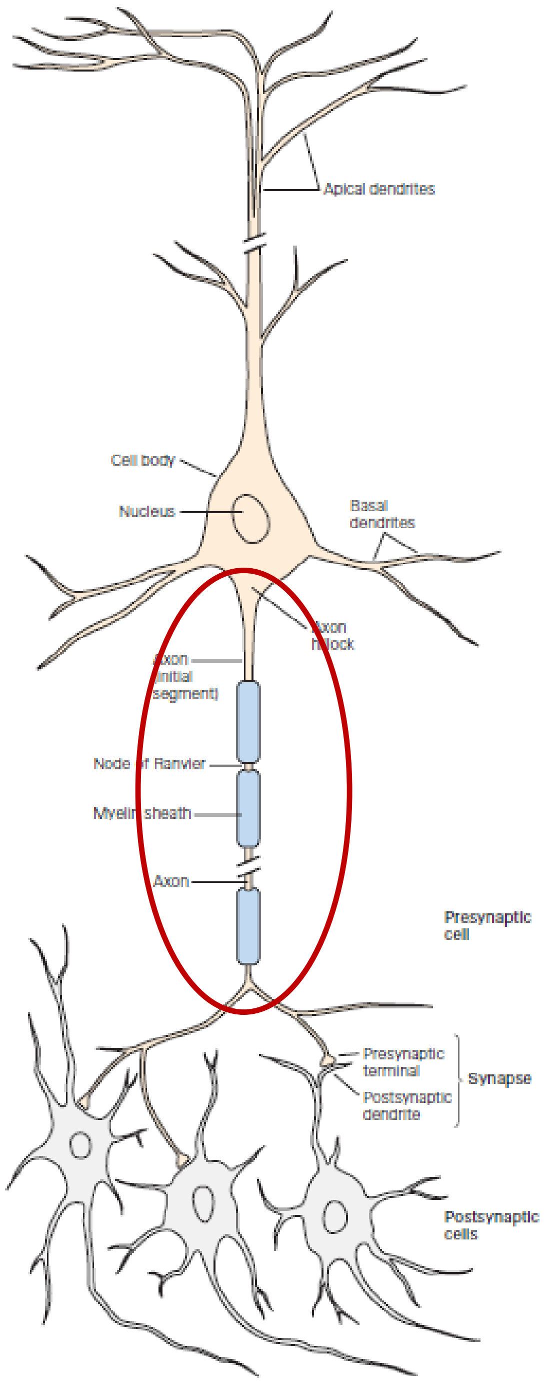


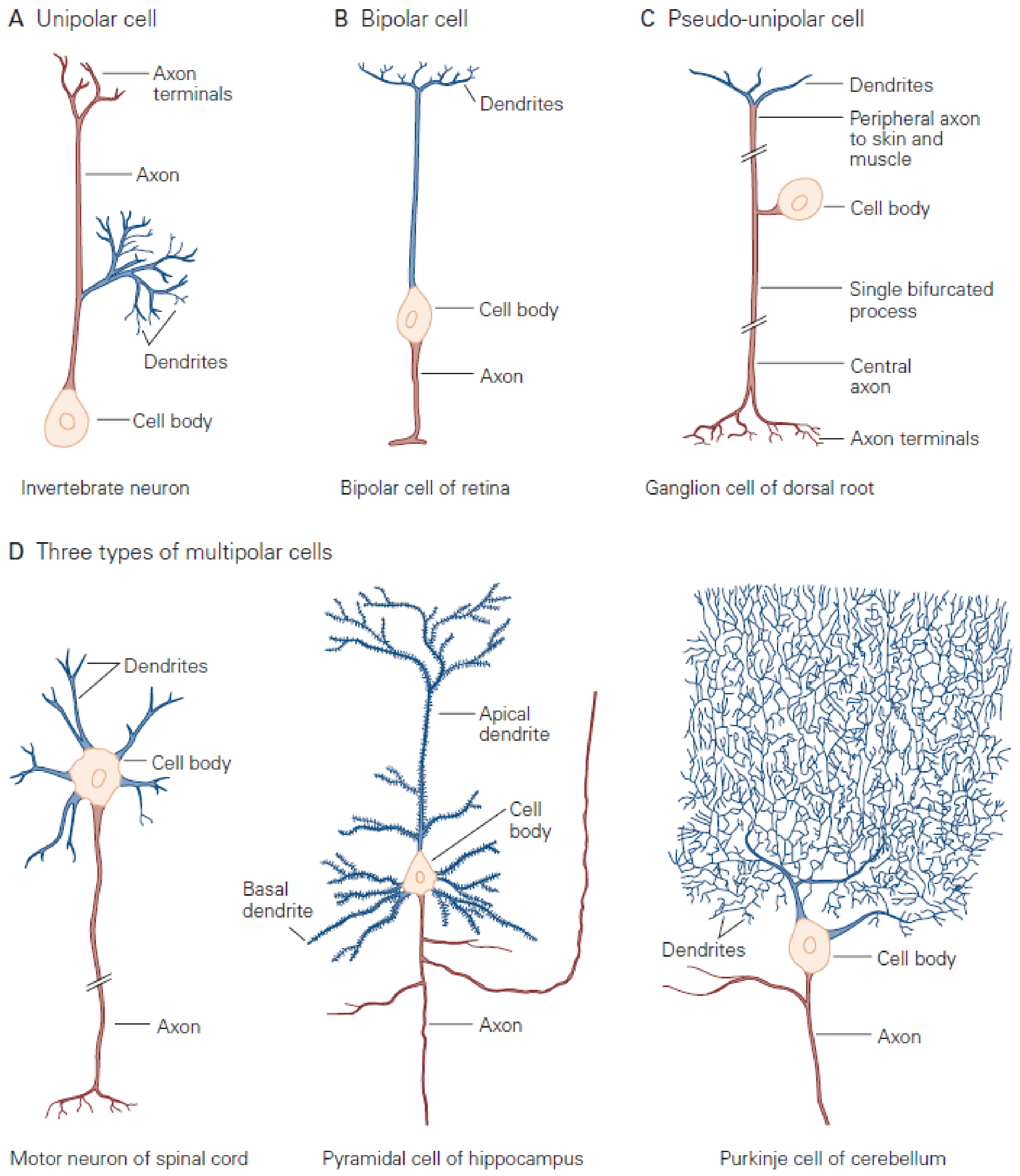
The structure of neurons

2. Axon:

- **single process**
- represents the **transmitting zone** of the neuron
- extends some distance from the cell body and carries signals from the input zone (dendrites) to the output zone (synapses)
- an axon can convey electrical signals over distances ranging from 0.1 mm to 2 m



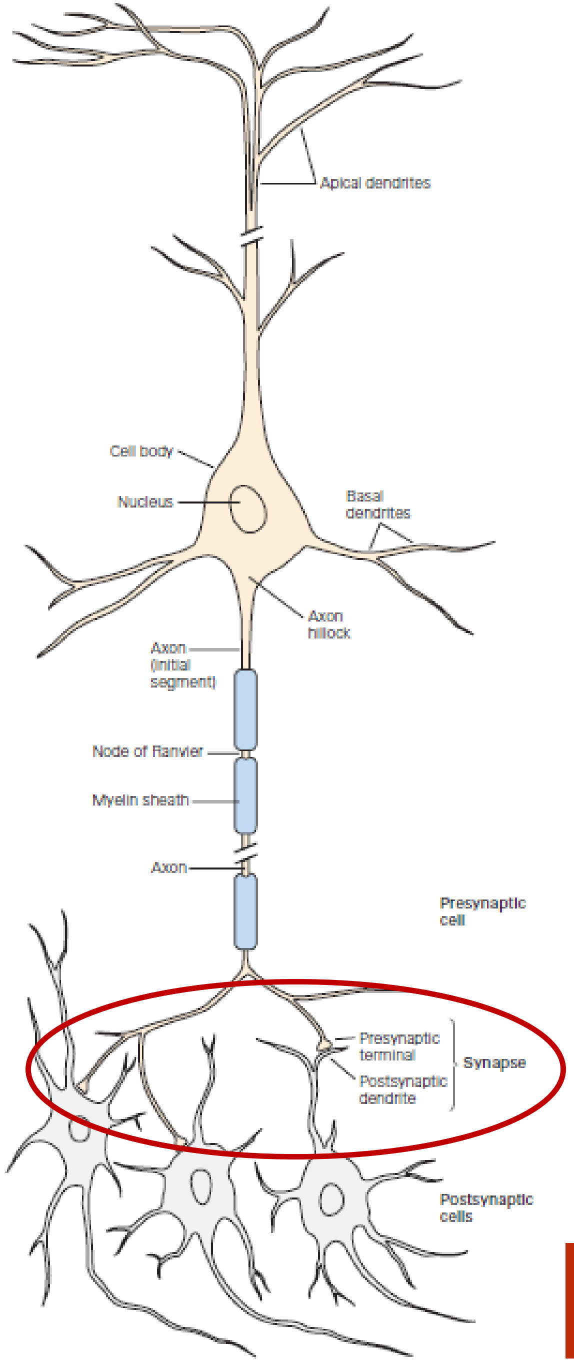
The structure of neurons



The structure of neurons

3. Synapse:

- **multiple processes**
- represents the **output zone** of the neuron
- specialized structure at the end of the axon, where two neurons come into close contact so that chemical or electrical **signals can be passed from one cell to the next**
- enable communication between neurons



Synapses enable communication between neurons

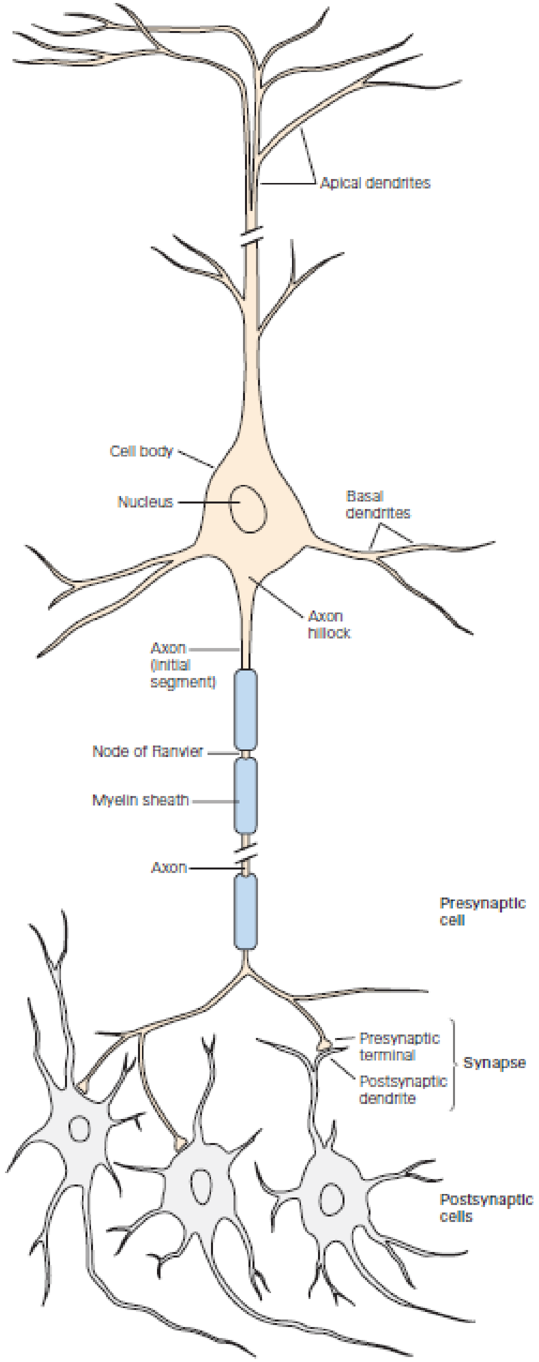
Presynaptic cell

- The nerve cell transmitting a signal
- From presynaptic terminals or nerve terminals, i.e. specialized enlarged regions of its axon's branches

Postsynaptic cell

- The cell receiving the signal

Synaptic cleft: the narrow space separating the presynaptic and postsynaptic cell



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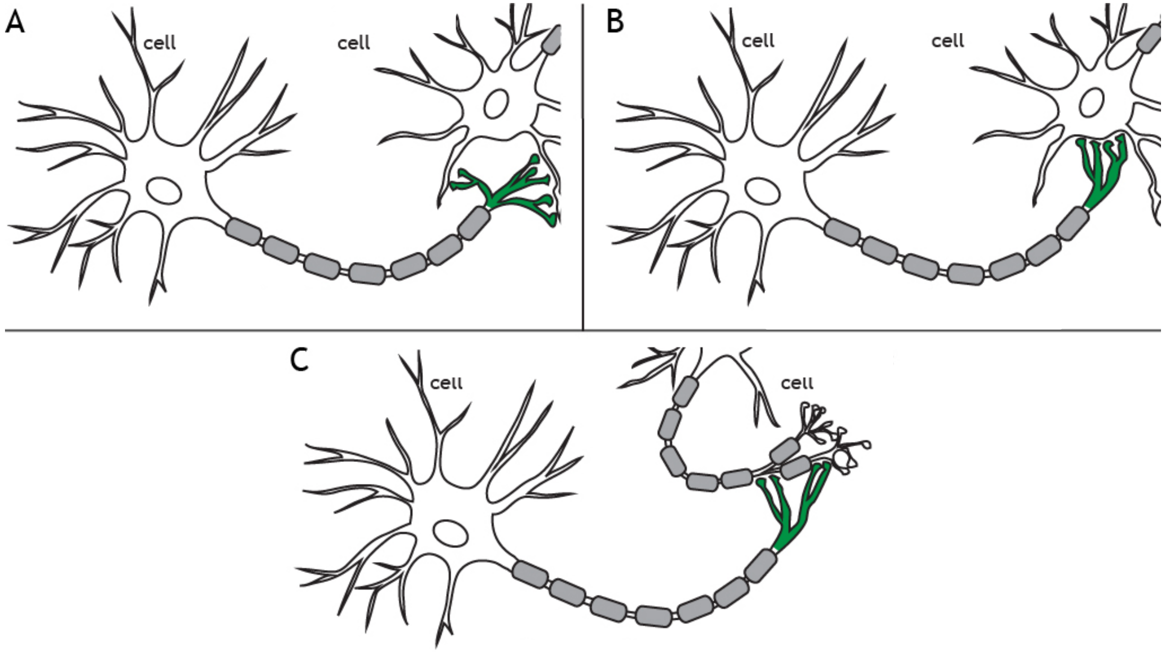
Which one is the pre-synaptic and which one the post-synaptic cell?



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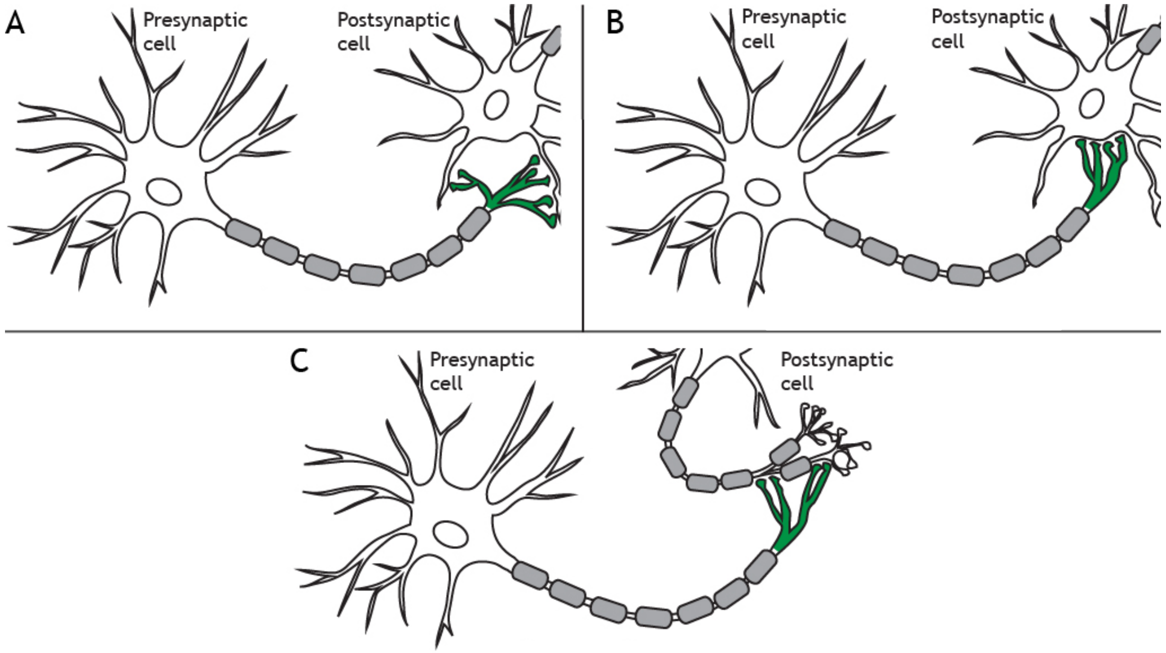
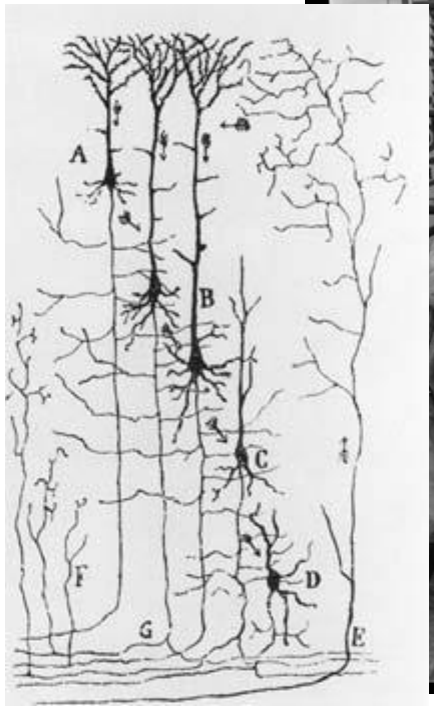
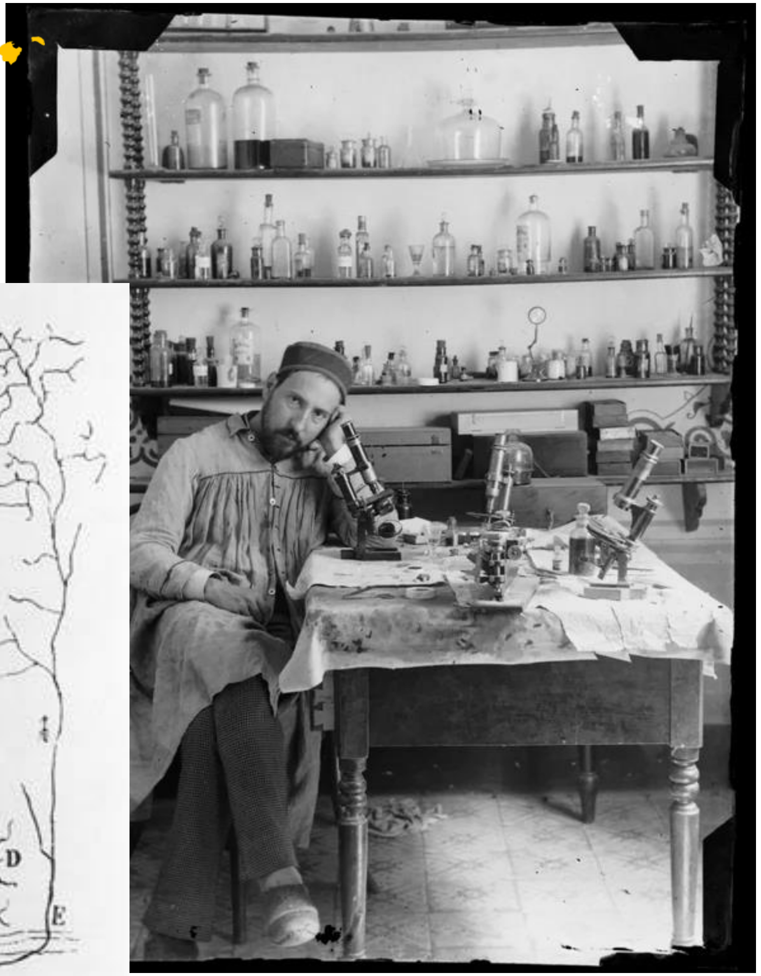


Principle of connectional specificity

Nerve cells do not connect randomly with one another in the formation of networks. Rather, each cell makes **specific connections - at particular contact points -** with certain postsynaptic target cells but not with others.



Ramón y Cajal's drawing of the afferent inflow to the mammalian cortex



Santiago Ramón y Cajal (1852–1934)

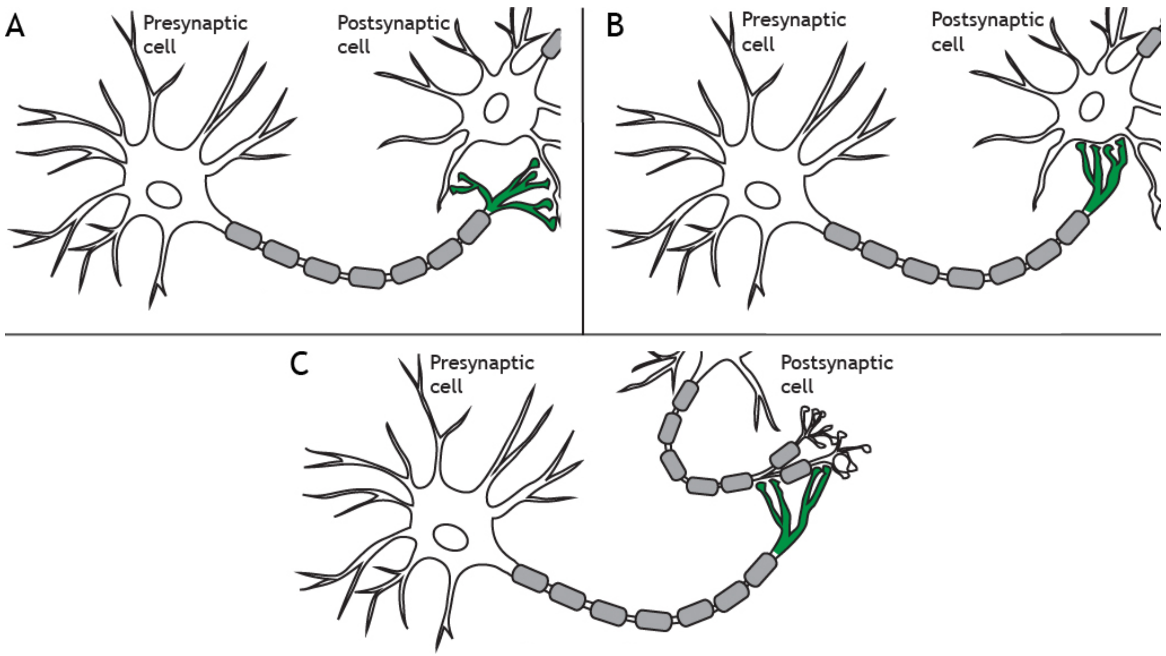
Three types of synapses

Axosomatic: synapses that are made onto the soma or cell body of a neuron.

Axodendritic: synapses that one neuron makes onto the dendrite of another neuron. The most common type.

Axoaxonic: synapses made by one neuron onto the synapse of another neuron. Axoaxonic synapses mediate presynaptic inhibition and presynaptic facilitation.

What kind of synapses are these?



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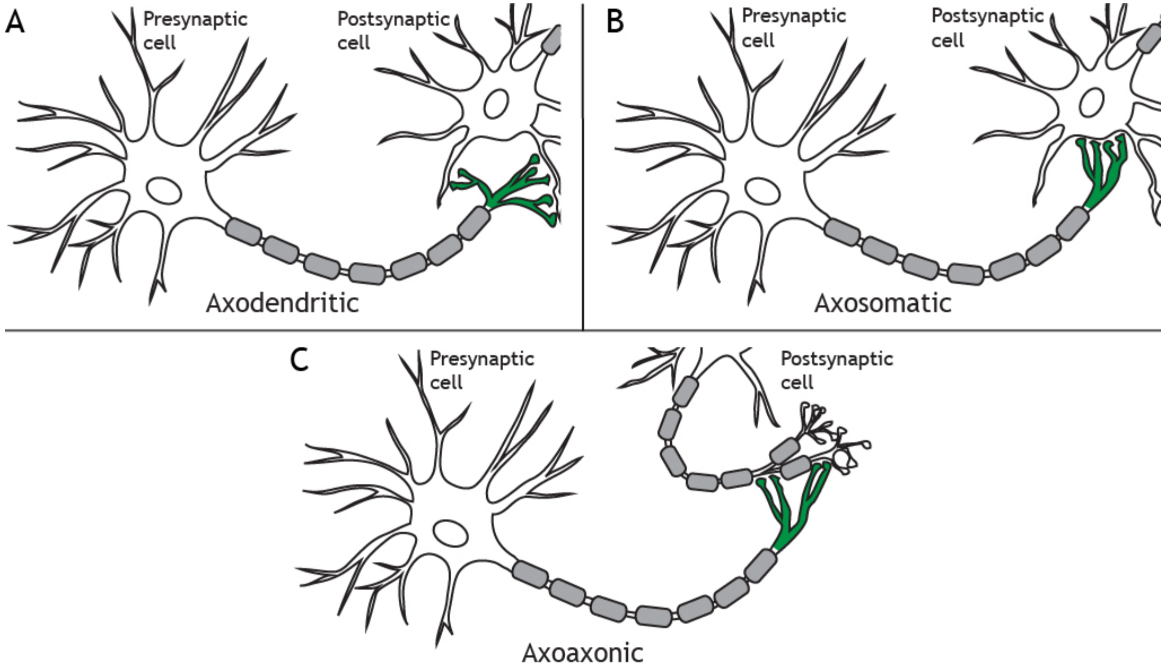
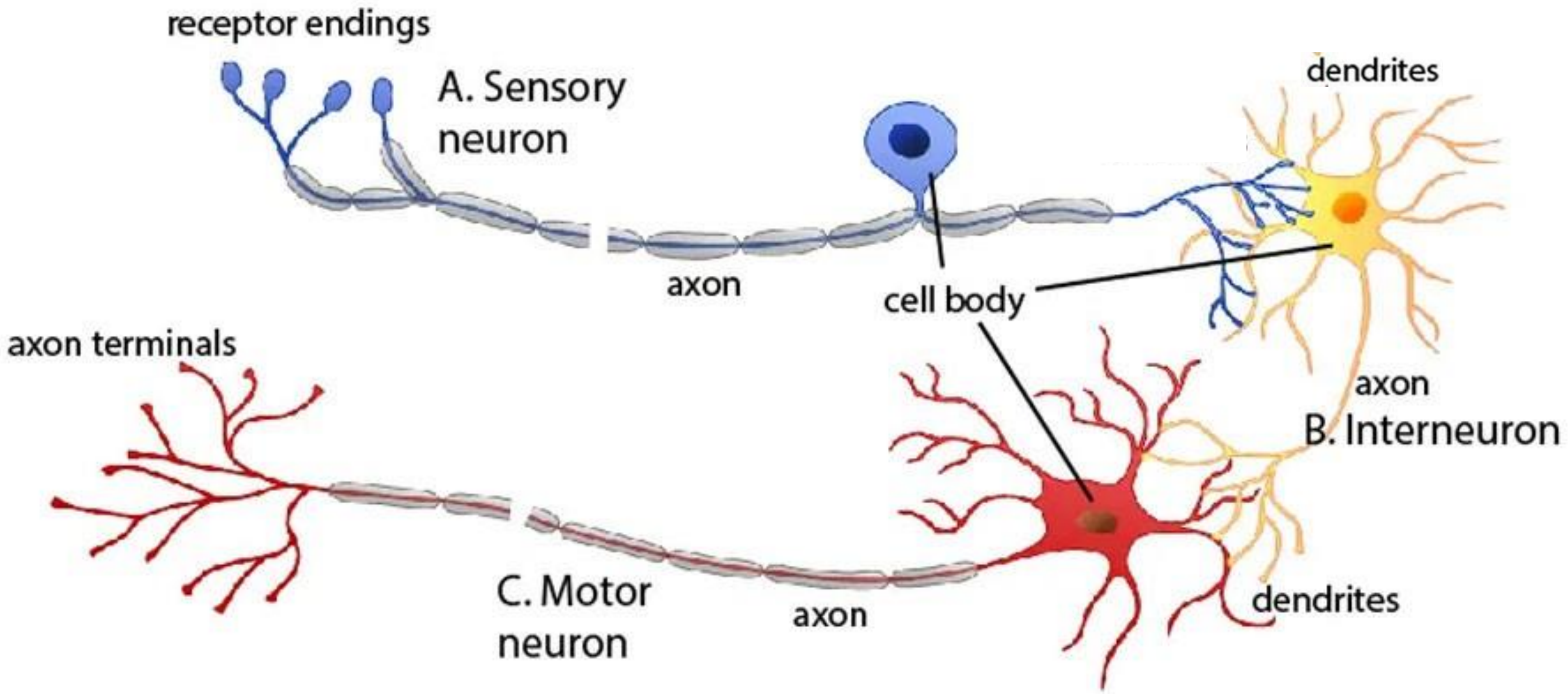


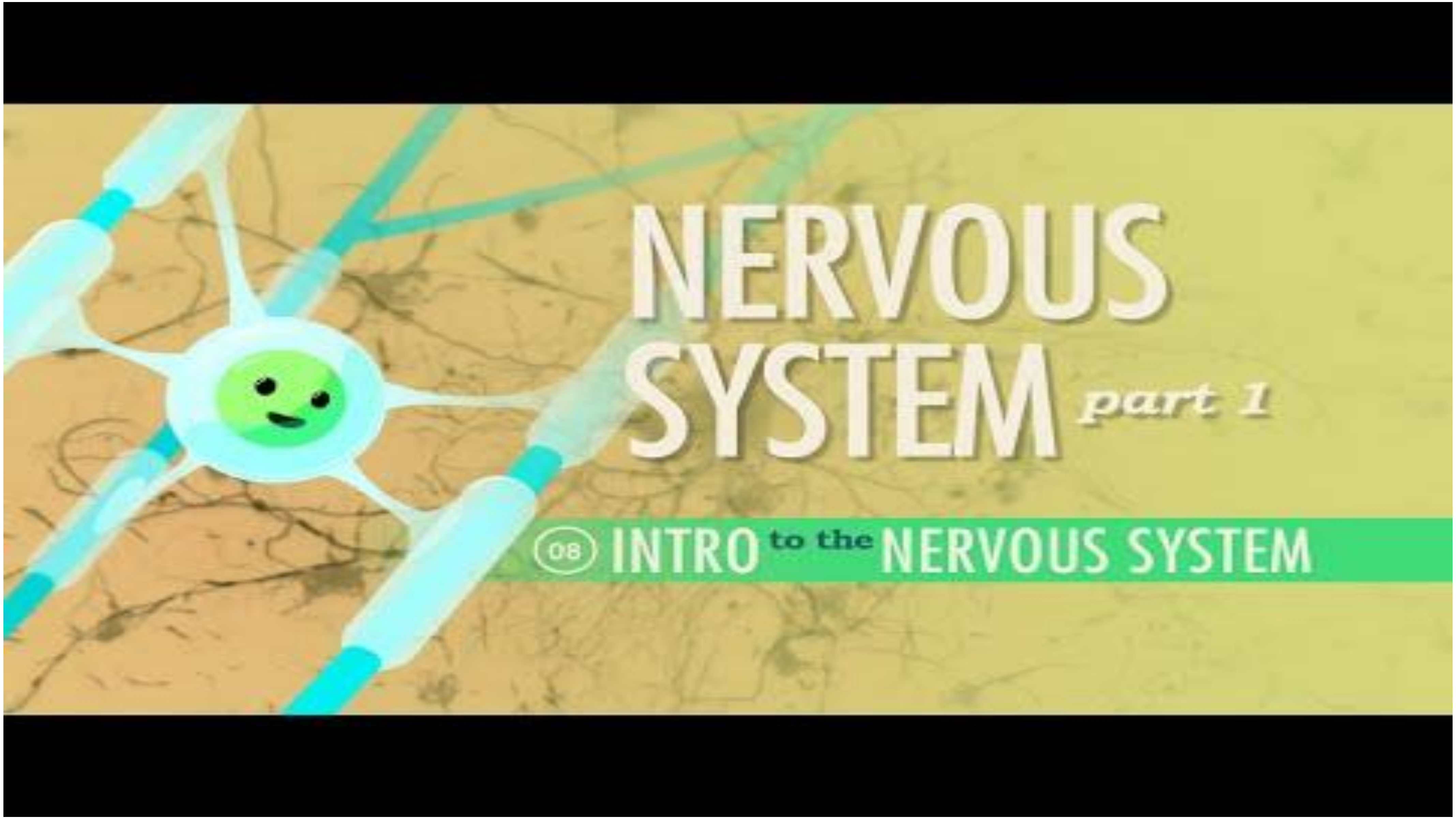
Neurons are also classified into three major functional categories

1. **Sensory neurons** carry information from the body's peripheral sensors into the nervous system for the purpose of both perception and motor coordination.
2. **Motor neurons** carry commands from the brain or spinal cord to muscles and glands.
3. **Interneurons** mediate impulses between sensory and motor neurons.



wooclap

Questions 1-3



https://youtu.be/qPix_X-9t7E

Information transfer within a single neuron

Neurons receive, evaluate, and transmit information

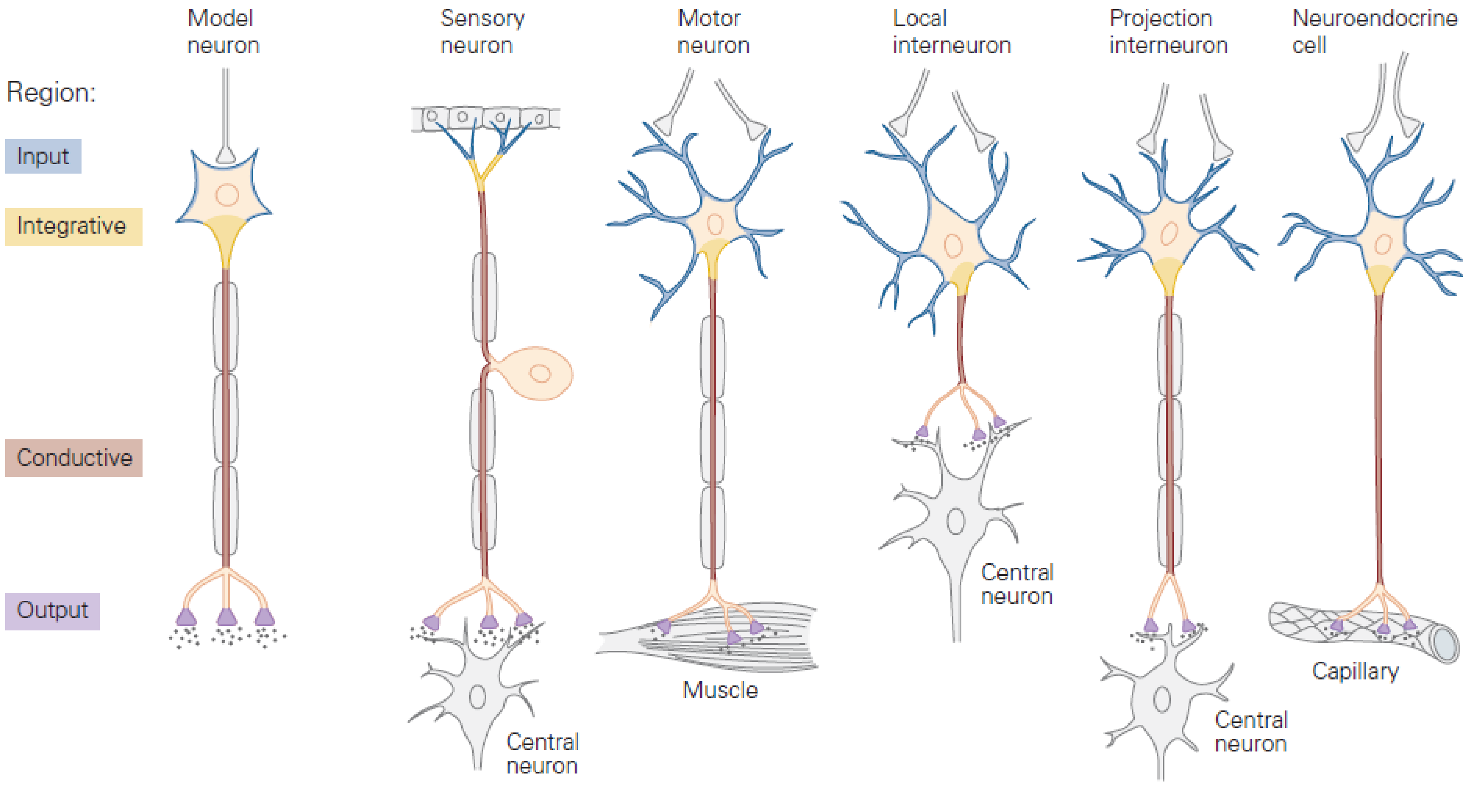
Information is transferred

1. **within a neuron**

- received at synapses on dendrites
- conducted within the neuron
- transmitted down the axon
- passed along at synapses on the axon terminals

2. **Between a neuron and**

- another neuron
- a non-neuronal cell:
e.g. muscles or glands

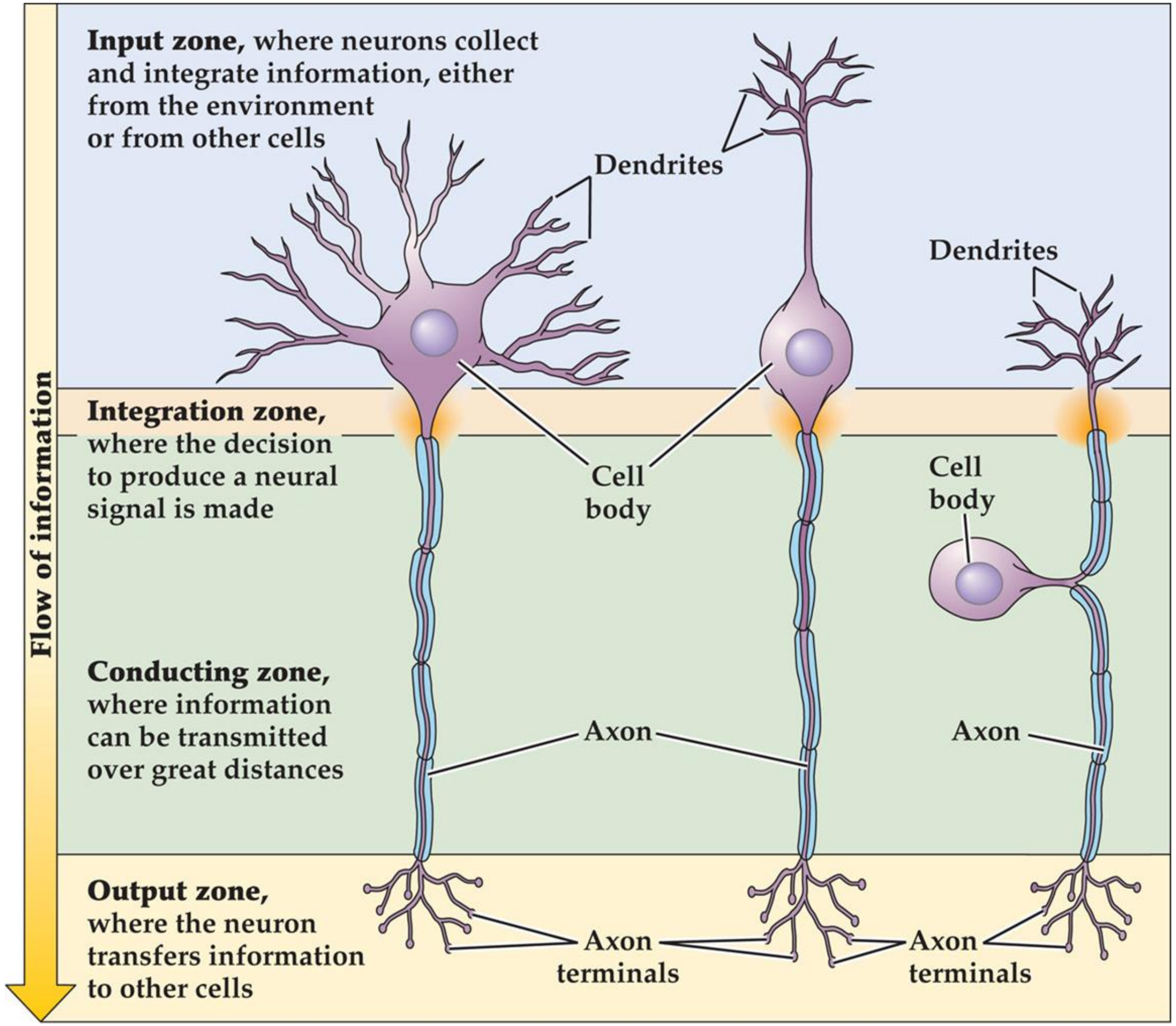


Signaling is organized in the same way in all nerve cells

4 regions that generate 4 types of signal:

1. Input signal: PSPs
2. Trigger signal: integration of all PSPs
3. Conductive signal: AP
4. Output signal: synaptic signal

Regardless of cell size and shape, transmitter biochemistry, or behavioral function



THE MIND'S MACHINE, Figure 2.3

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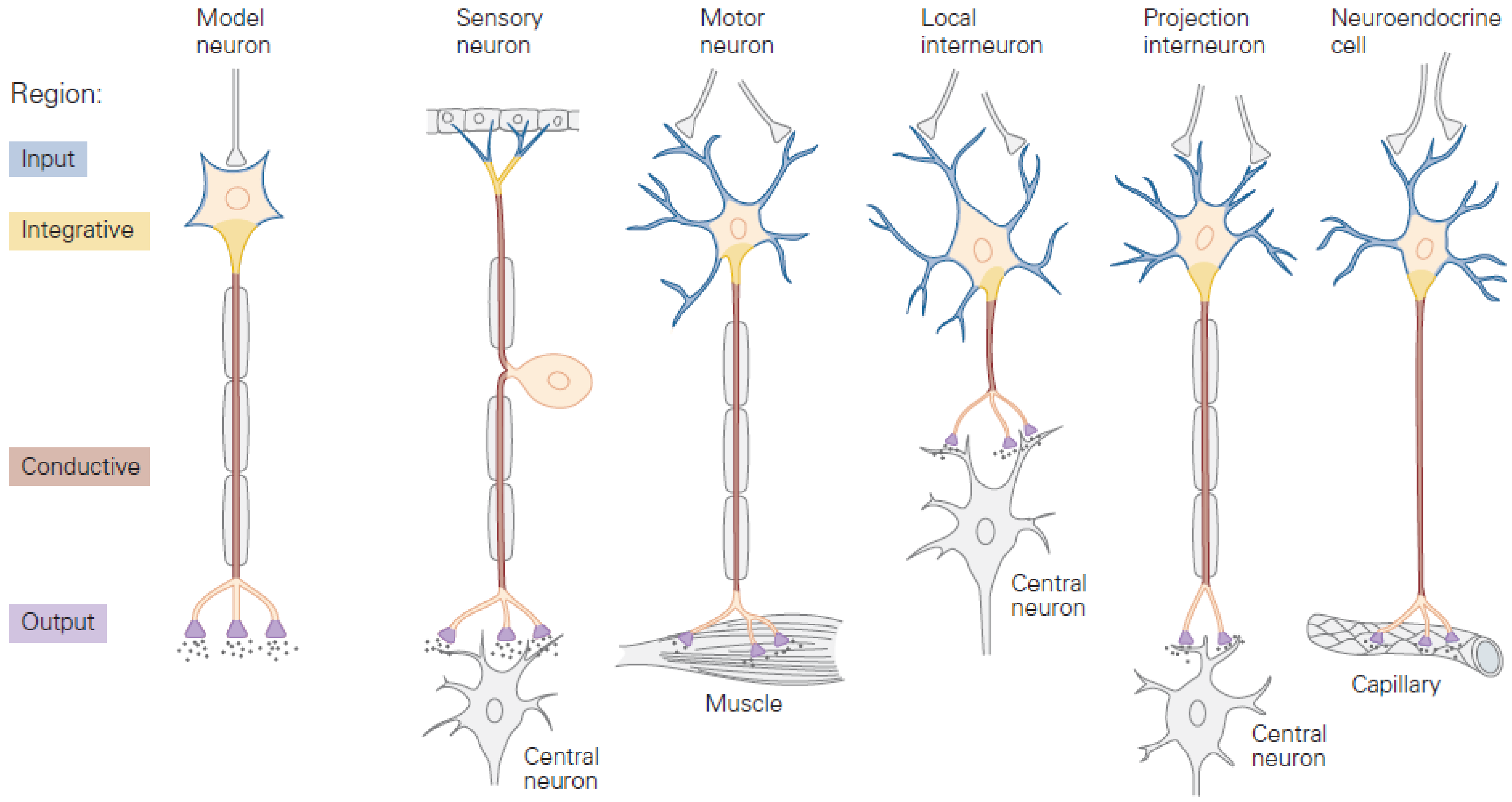
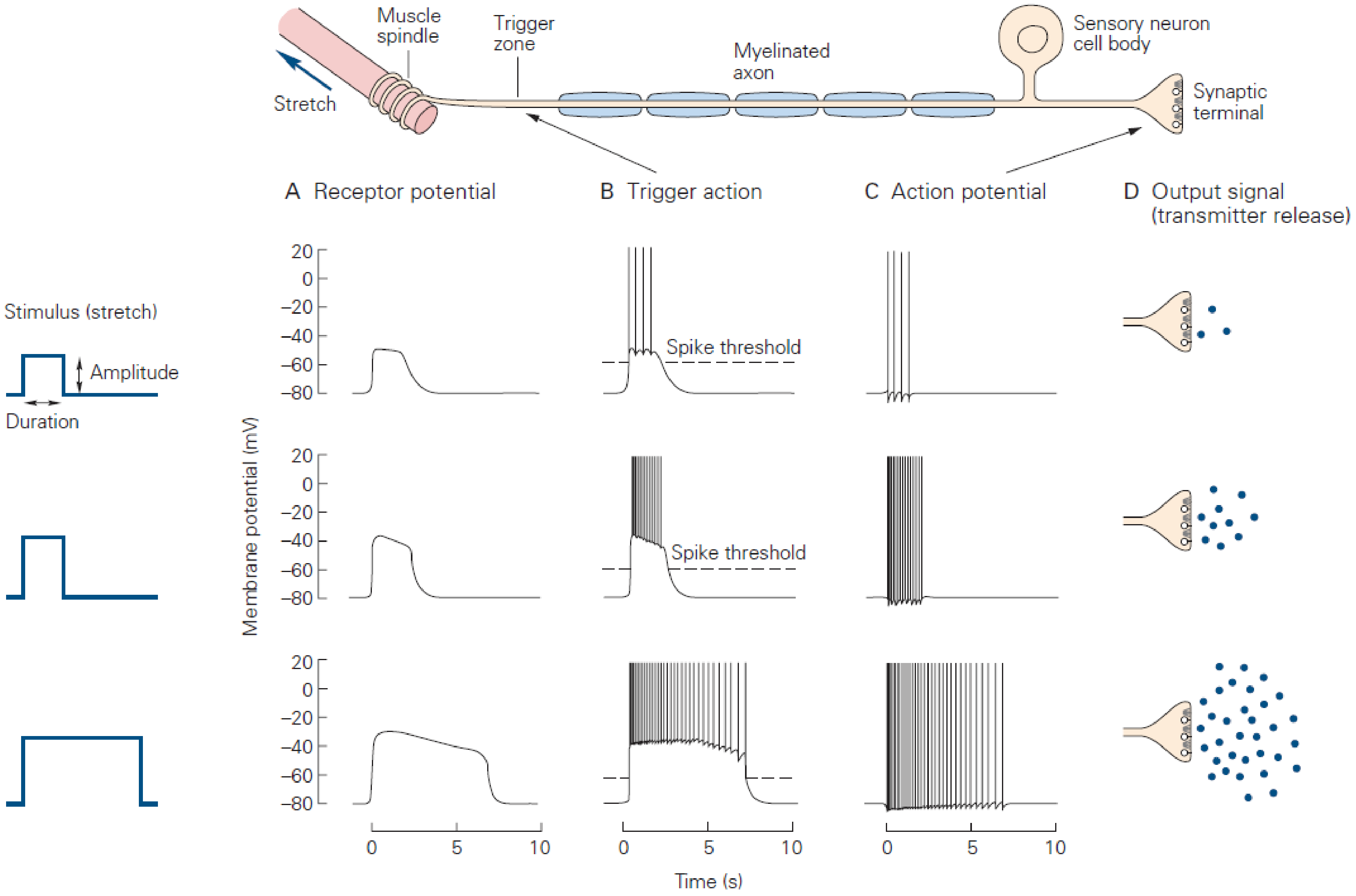


Each of the neuron's four signaling regions produces a characteristic signal

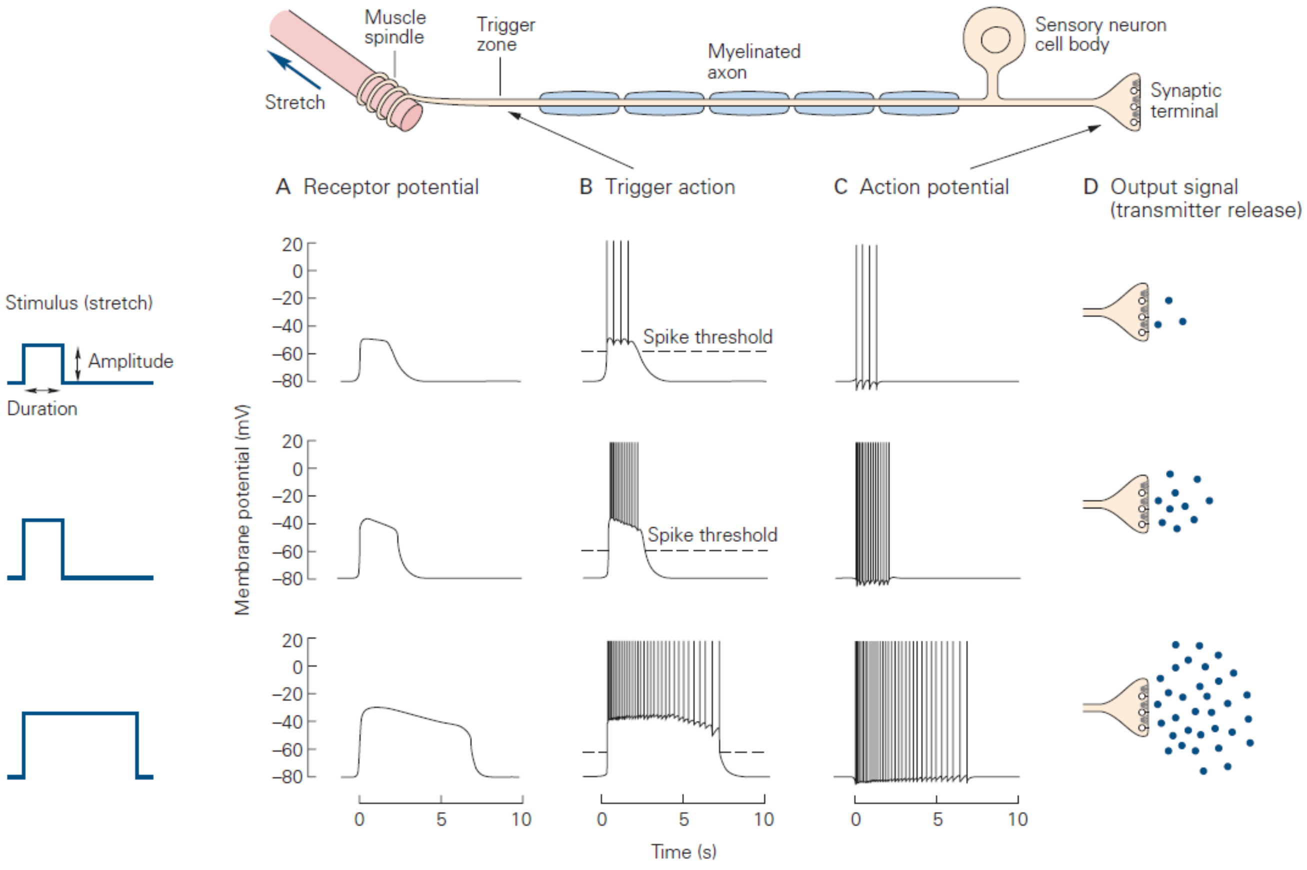


Each of the neuron's four signaling regions produces a characteristic signal

(A) At the input region, the input signal (PSP) is graded in:

- Amplitude
- Duration

Proportional to the amplitude and duration of the stimulus



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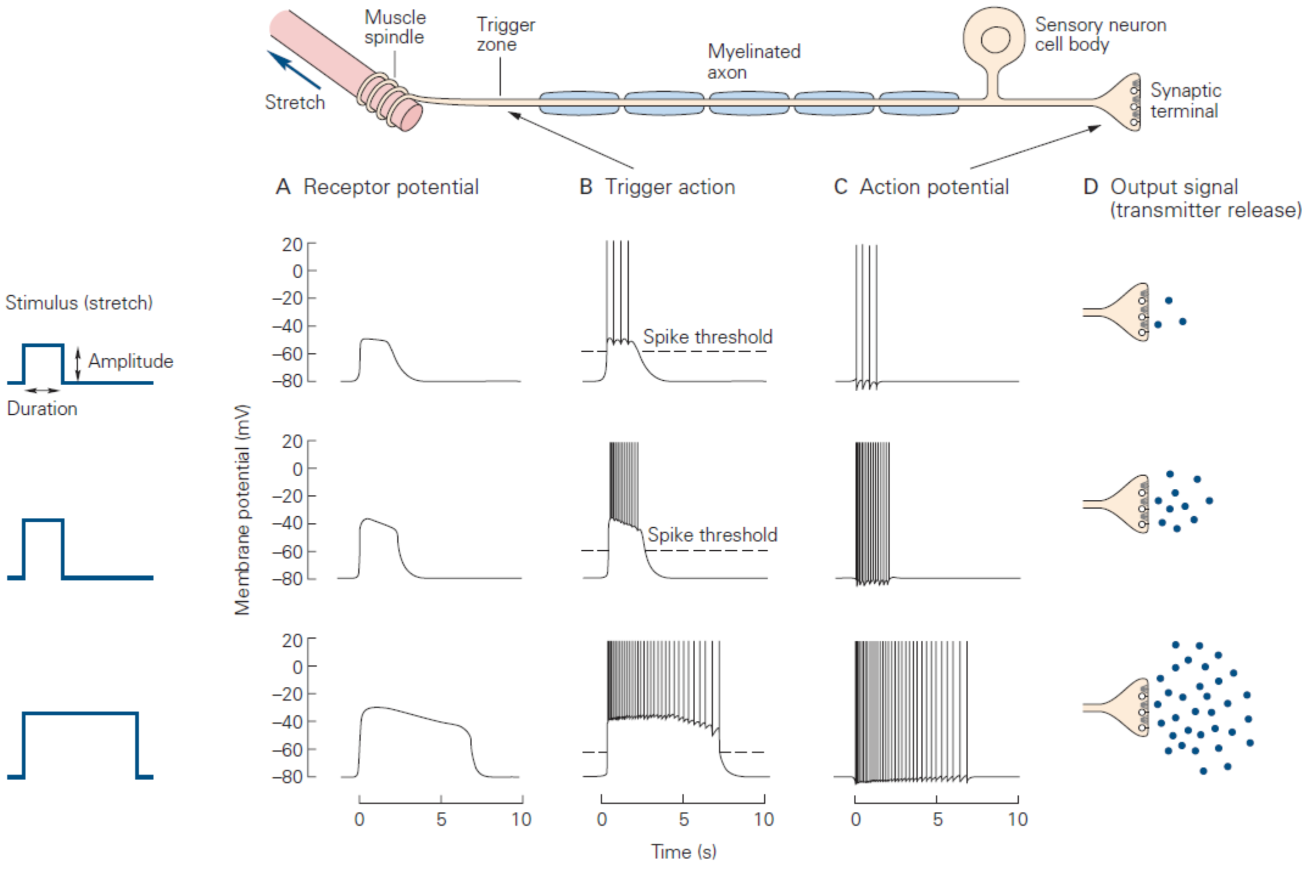
(B) The trigger zone sums the PSPs and "decides" whether to generate and AP

- An action potential is generated only if the input signal exceeds the voltage threshold for initiation (-55mV)
- Once the threshold is surpassed an action potential is generated
- Any further increase in amplitude of the input can only increase the **frequency of action potentials**
- The duration of the input determines the duration of the train of action potentials
- Thus, the graded amplitude and duration of PSPs is translated into a **frequency code** in the APs generated at the trigger zone. All APs produced are propagated along the axon.



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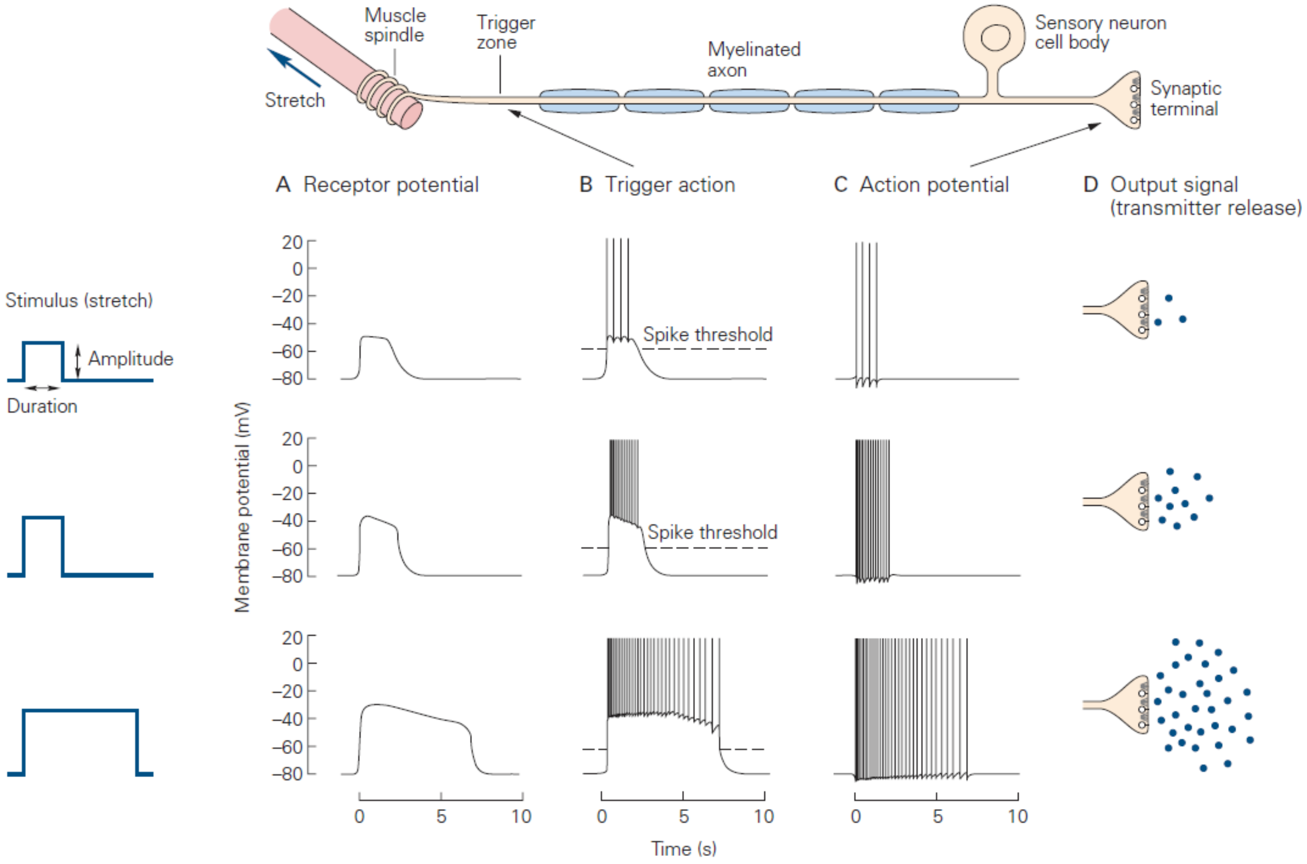
(C) Conductive region transmits action potentials

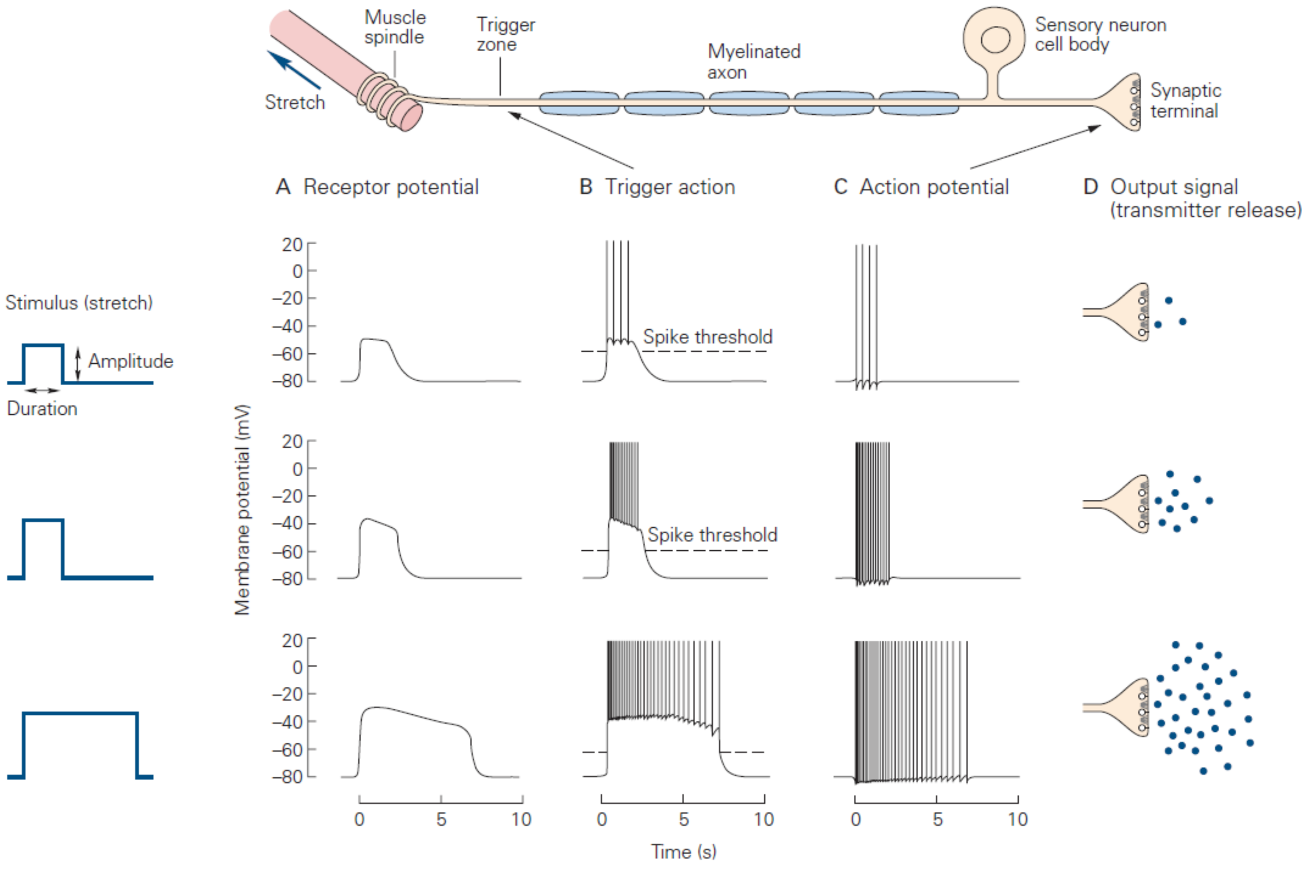
- Action potentials are all-or-none: they all have a similar amplitude and duration
- the frequency and duration of firing represents the information carried by the signal

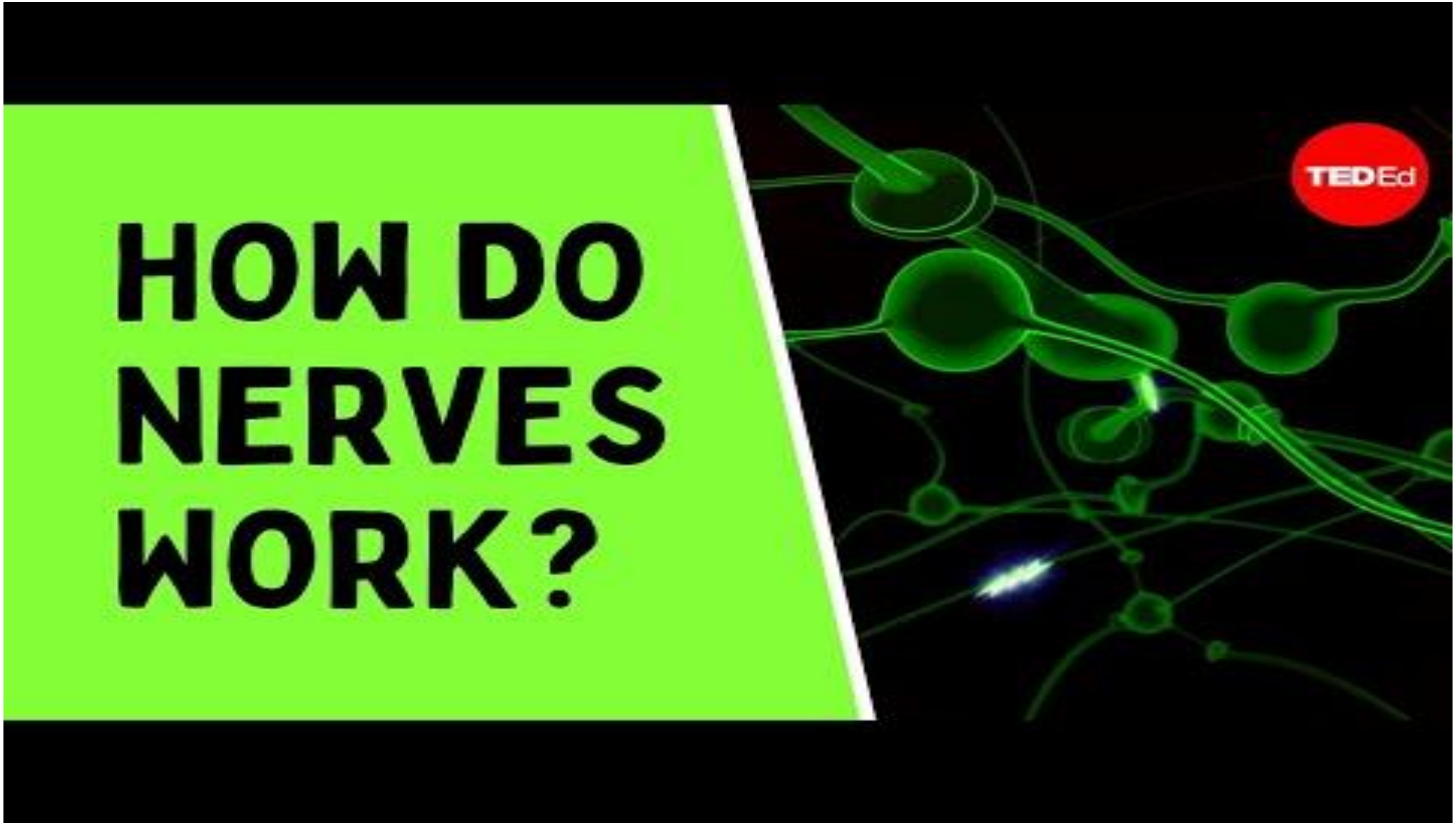


Each of the neuron's four signaling regions produces a characteristic signal

(D) Output region produces the output signal responsible for synaptic communication

- At chemical synapses, the frequency of action potentials determines exactly how much neurotransmitter is released by the cell
- At electrical synapses, the signal is directly transmitted to the postsynaptic neuron





https://youtu.be/uU_4uA6-zcE

Signaling within a neuron involves transient changes in the electrical state of the neuron

Produced by temporary changes in the electric current into and out of the cell

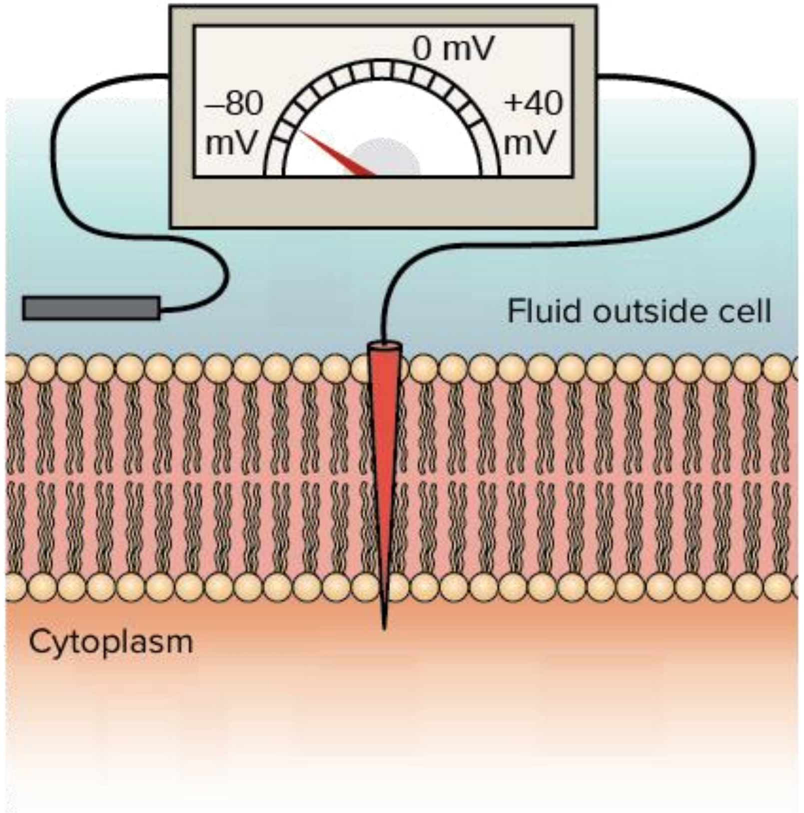
AND...

Signaling within a neuron involves transient changes in the electrical state of the neuron

Produced by temporary changes in the electric current into and out of the cell

AND…

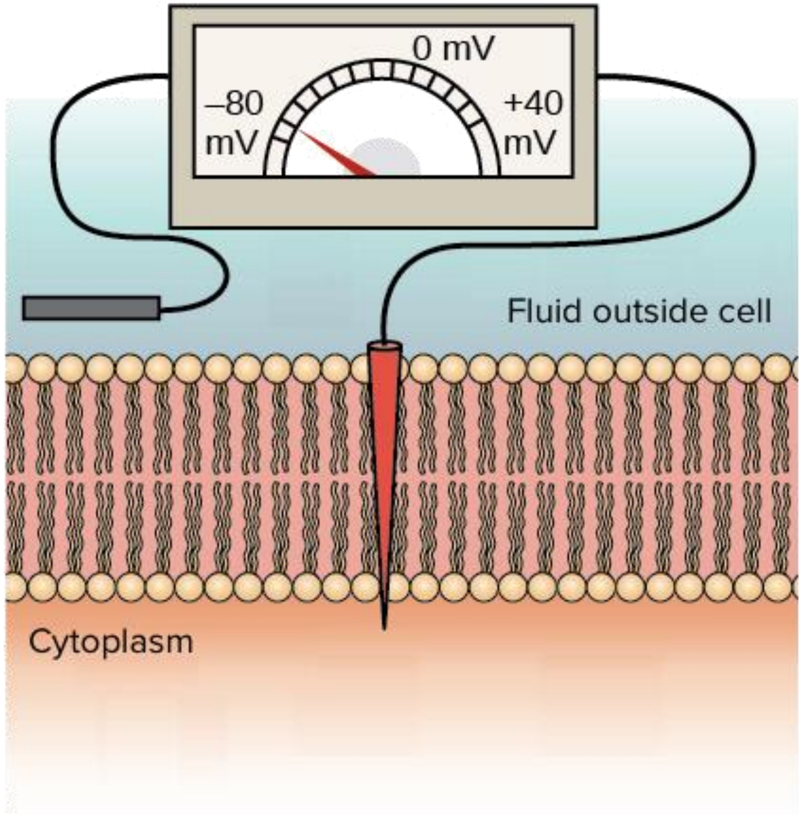
it all starts with the **resting membrane potential**



Resting membrane potential

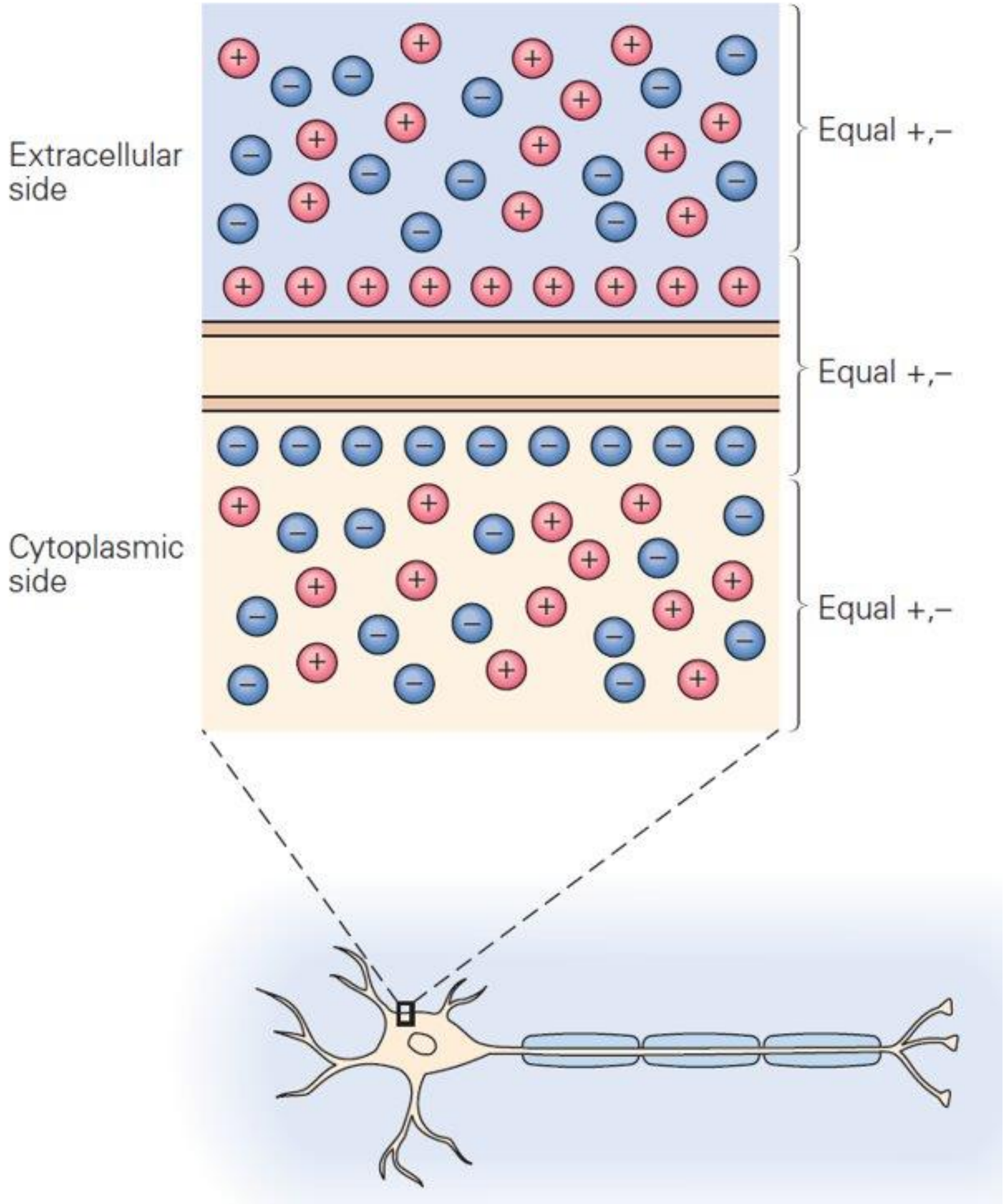
- In a resting neuron the voltage of the **inside** of the cell is about **70 mV more negative than** the voltage **outside** the cell

- This electrical potential difference means that the neuron has at its disposal a kind of battery
- like a battery, the stored energy can be used to do work, I.e. signaling work



Resting membrane potential

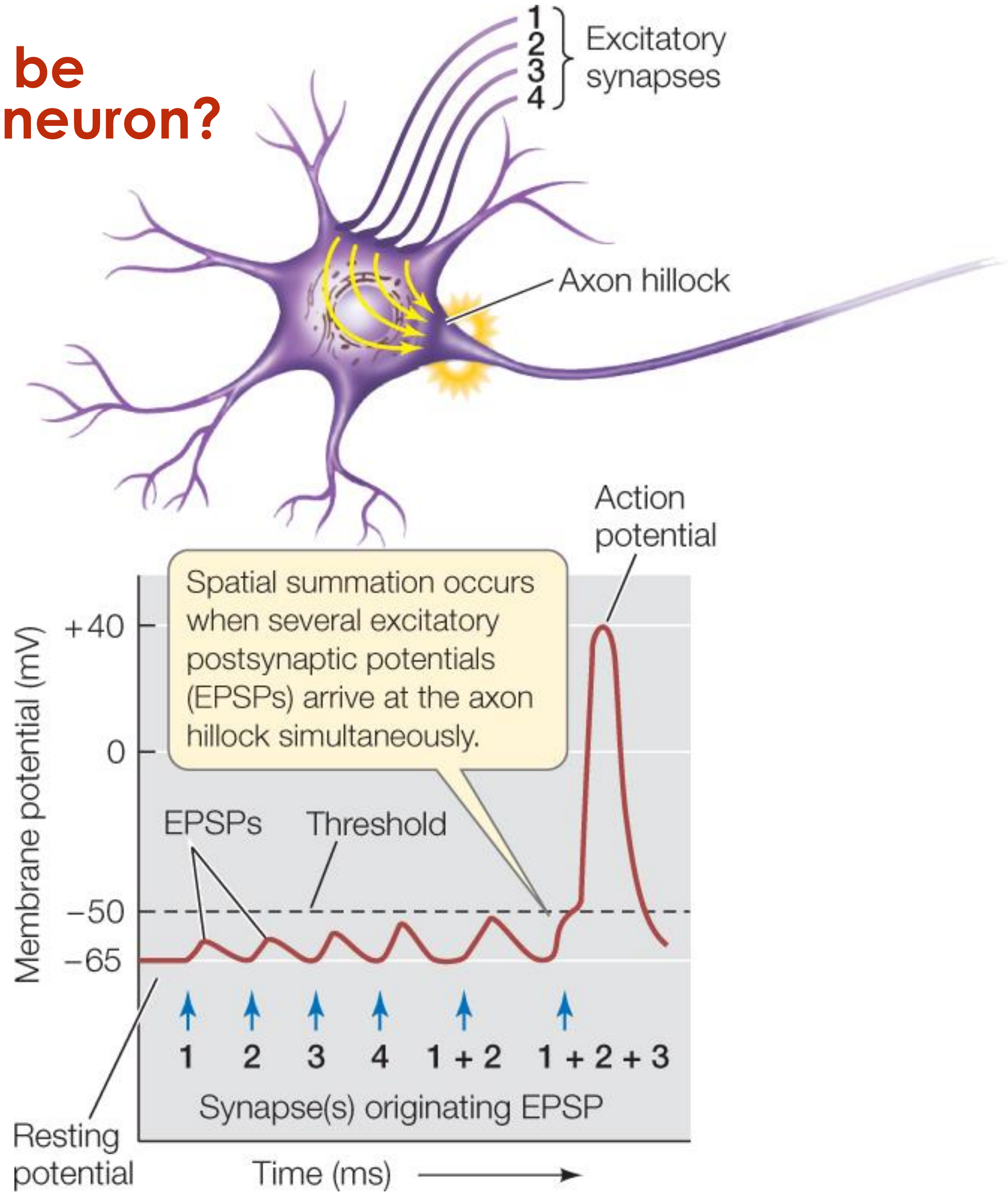
- It **arises from the asymmetric distribution of ions across the neuron's cell membrane:**
  - Electrochemical forces cause the inside of cell to have a more negative potential than the outside: **-70 mV**
- It is the baseline on which all signaling occurs
- It **can be quickly and significantly altered, serving as a signaling mechanism**



How can the resting membrane potential be exploited to transmit information within a neuron?

Postsynaptic potentials (PSPs) are

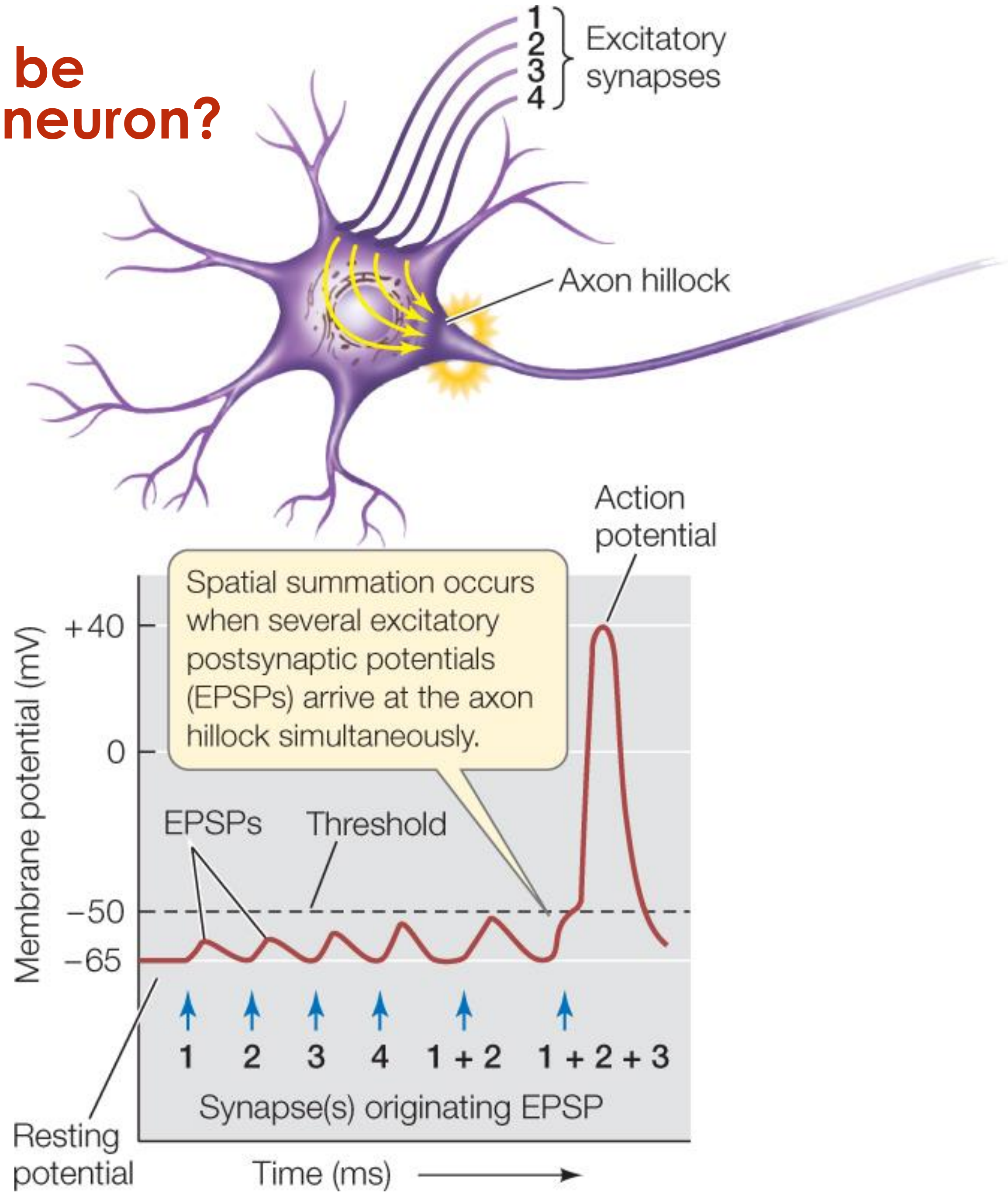
- **small changes in membrane potential** that move the cell away from its resting membrane potential
- **graded potentials**
  - The amount of change in the membrane potential is determined by the size of the stimulus that causes it
- **They have to cause a strong enough change in membrane potential** that surpasses a certain threshold, **to trigger an action potential**, which then passes the signal along the axon



How can the resting membrane potential be exploited to transmit information within a neuron?

Postsynaptic potentials (PSPs) can be

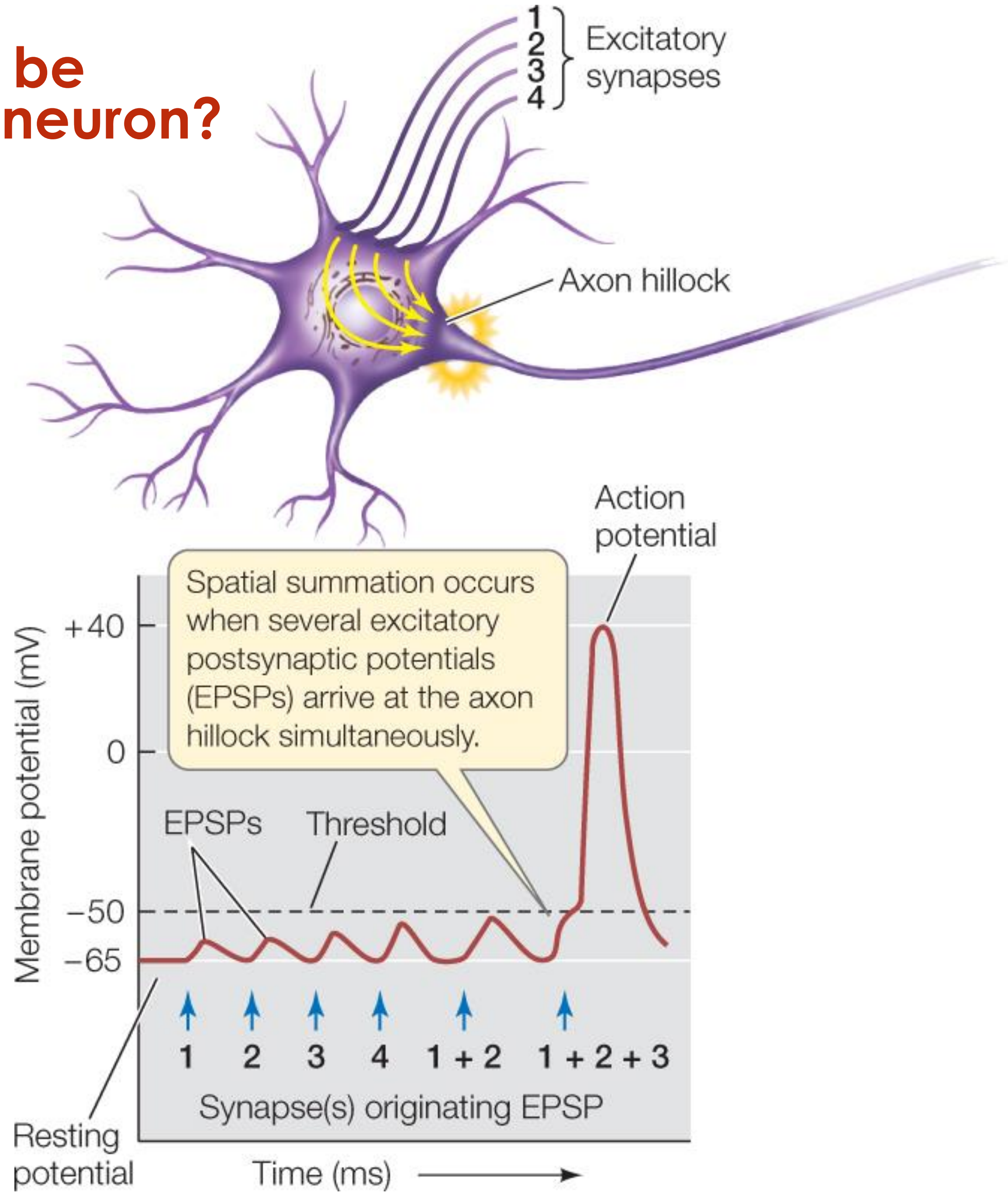
- **Depolarizing**
  - produce a **decrease in membrane potential**
  - Enhance the ability to generate action potential
  - **Excitatory** PSP



How can the resting membrane potential be exploited to transmit information within a neuron?

Postsynaptic potentials (PSPs) can be

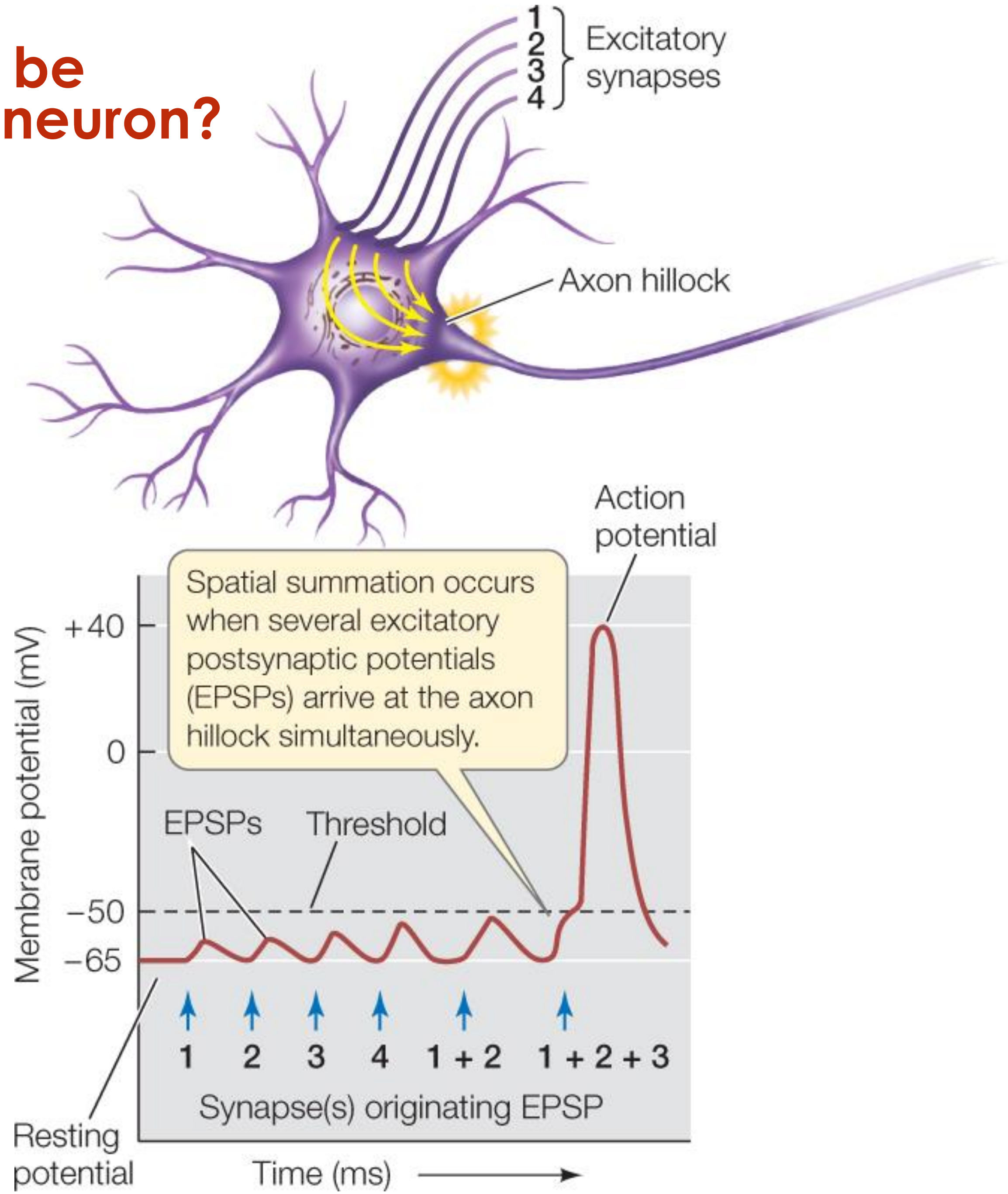
- **Depolarizing**
    - produce a **decrease in membrane potential**
    - Enhance the ability to generate action potential
    - **Excitatory** PSP
- **Hyperpolarizing**
    - produce an **increase in membrane potential**
    - Reduce the ability to generate action potential
    - **Inhibitory** PSP



How can the resting membrane potential be exploited to transmit information within a neuron?

Postsynaptic potentials (PSPs) are

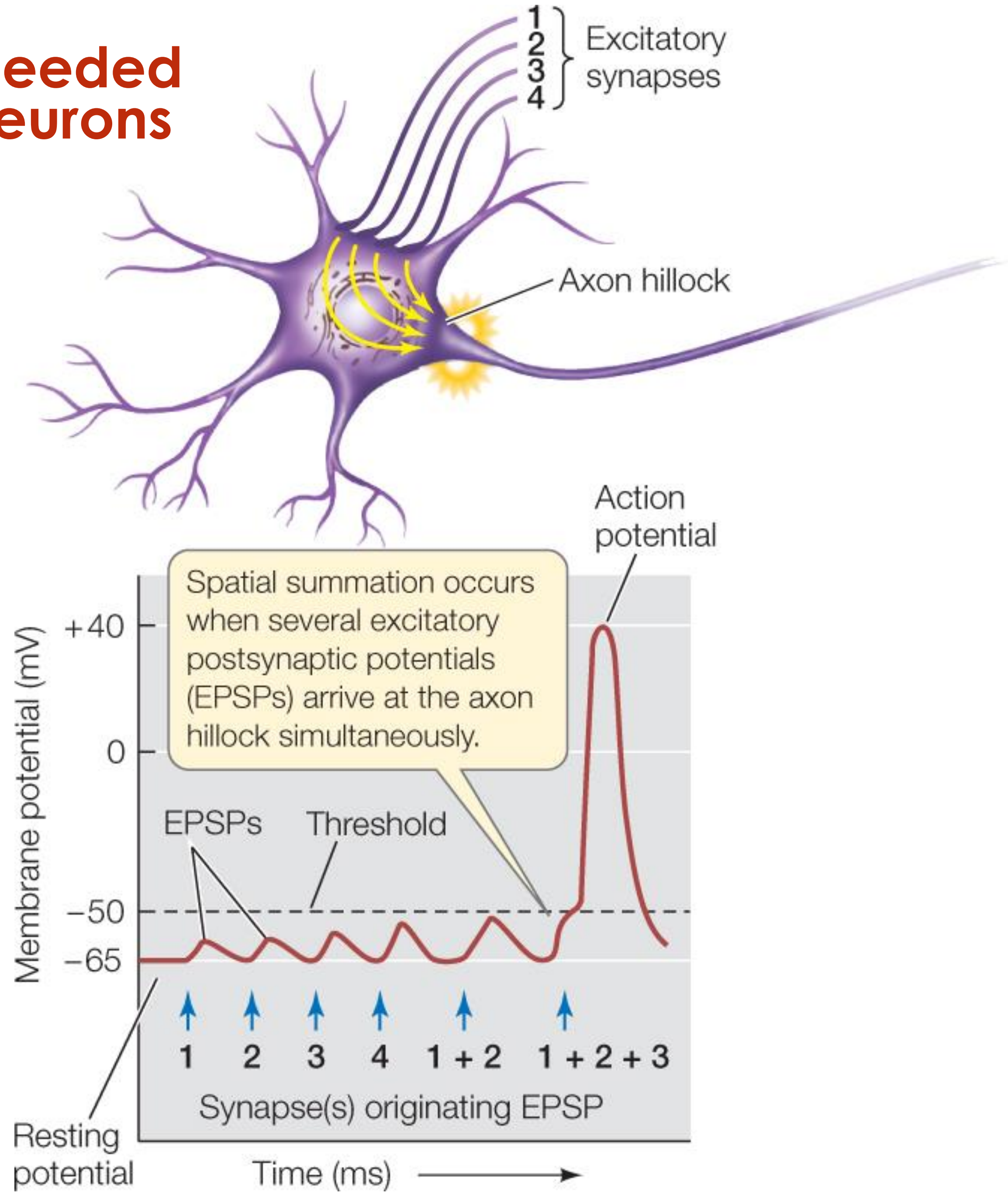
- **Small in amplitude**
- **passively conducted** through the cytoplasm of the dendrite and cell body
  - **decremental conduction**: it diminishes with distance from its origin (i.e. the synapse)
  - Will flow for maximum 1mm → too short to enable signal transmission down the entire the axon
  - **a single EPSP is not enough to trigger the firing of the neuron**



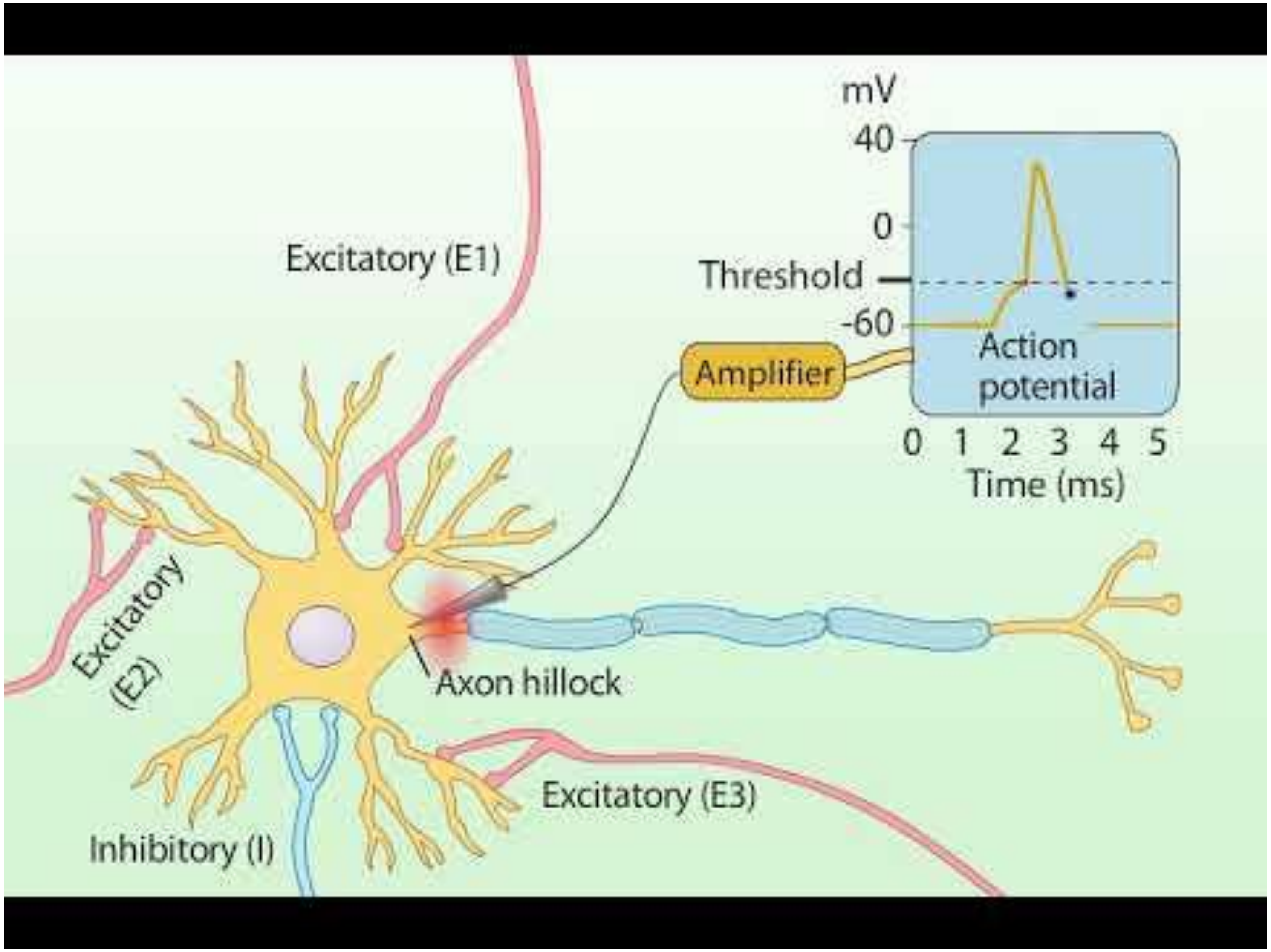
Input from many presynaptic neurons is needed to generate an action potential in most neurons

Because a single EPSP is not enough to trigger the firing of the neuron

- The passive electrical currents that are generated following EPSPs on multiple distant dendrites **sum together** at the **axon hillock** (integrative region)
  - **Spatial summation**
    - Summation of excitatory and inhibitory PSPs received at spatially separate synapses
  - **Temporal summation**
    - Summation of excitatory and inhibitory PSPs received at different time points



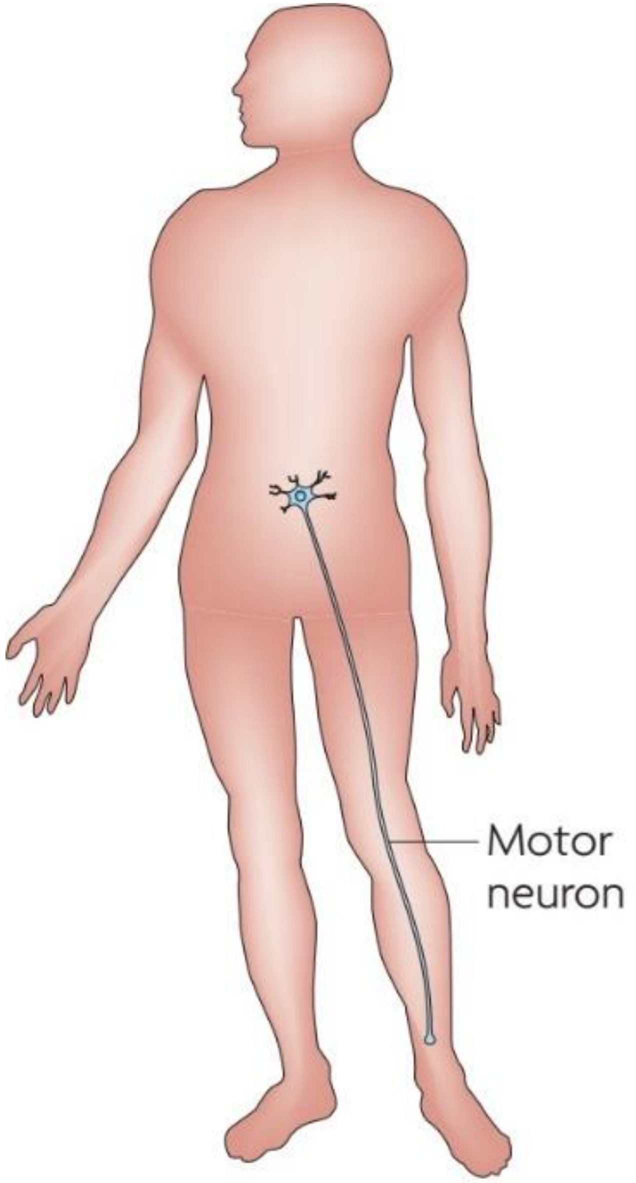
Postsynaptic potentials (PSPs)



https://www.youtube.com/watch?v=B92rsa1is_k

An evolutionary challenge...

- The maximum distance a passive current (e.g. EPSP) will flow is only about 1 millimeter.
- The longest axon of a human motor neuron can be over a meter long, reaching from the base of the spine to the toes. Sensory neurons can have axons that run from the toes to the posterior column of the spinal cord, over 1.5 meters in adults.
- To enable efficient communication, information must travel **far & fast**



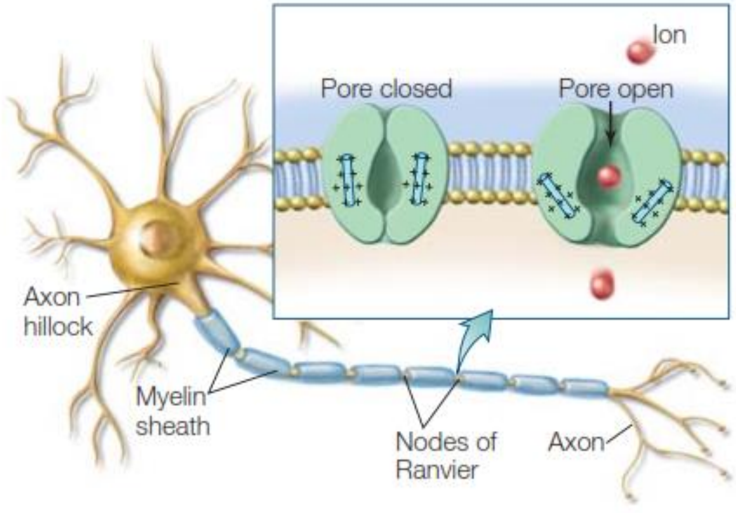
Neurons evolved a clever mechanisms to overcome this challenge

1. Travelling **far**: the **Action Potential (AP)**

- That is a **rapid depolarization and repolarization of a small region of the cell membrane** caused by the opening and closing of ion channels

2. Travelling **fast**: **Saltatory conduction**

- APs are generated only at specific locations along the axon (i.e. Nodes of Ranvier)
- The AP "jumps" down the axon



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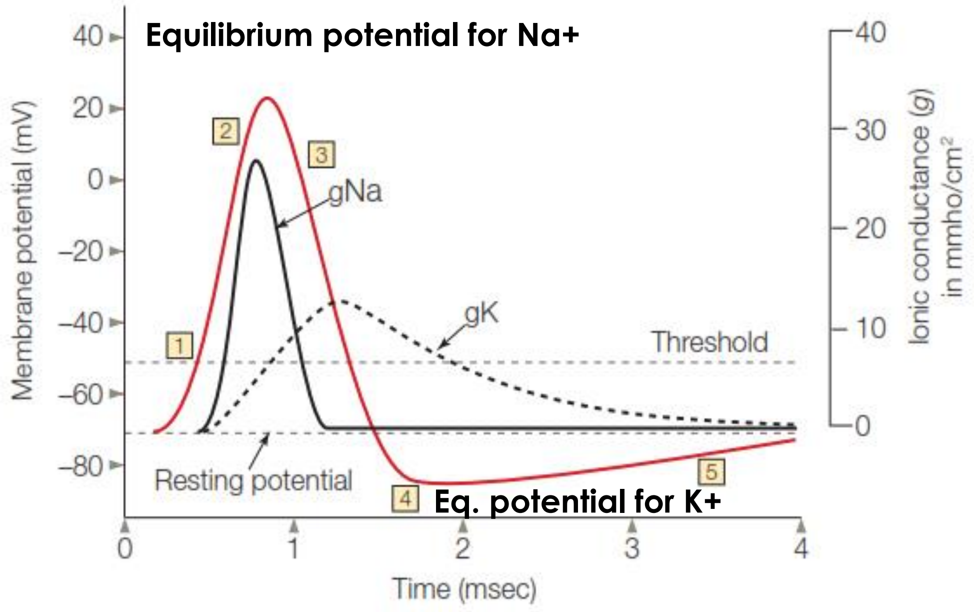
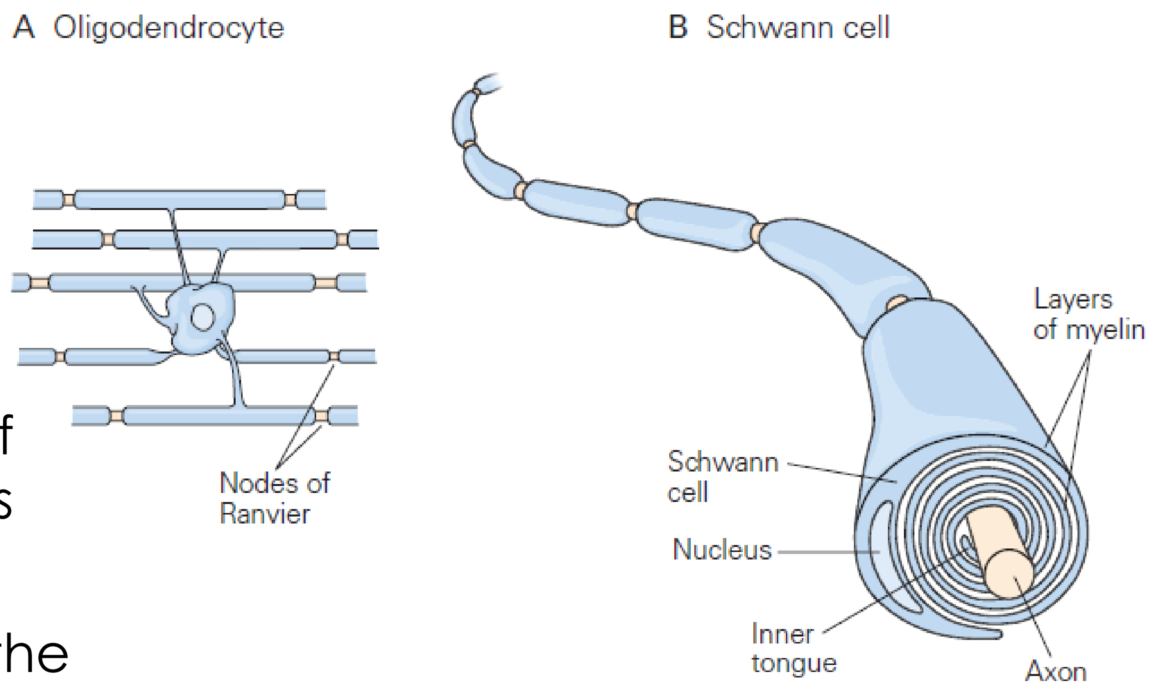
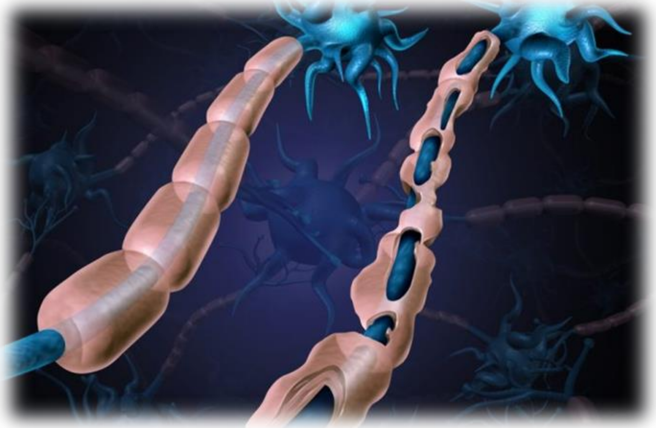


b

Travelling fast: Saltatory conduction

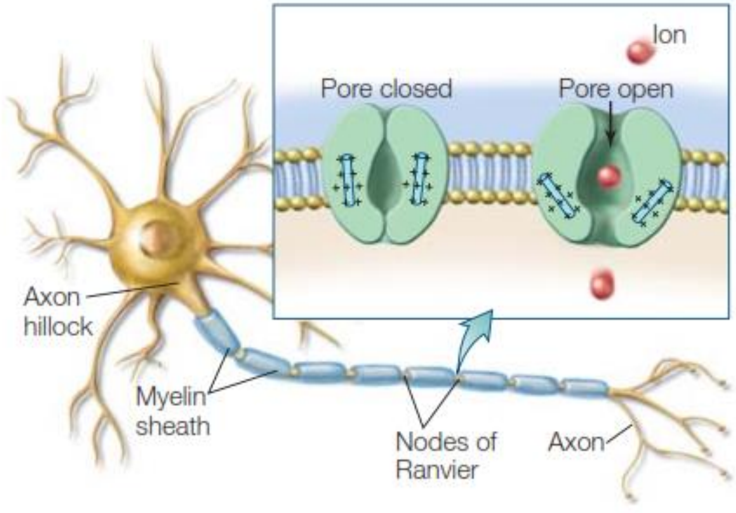
- Appearance that the AP "jumps" down the axon
- Oligodendrocytes (in CNS) and Schwann cells (in PNS) produce thin sheets of myelin that wrap around the axon of neurons
- Myelin
  - provides the insulating material along the axon → resistance to voltage loss
  - allows rapid conduction of APs along the axon
    - APs in myelinated axons can occur only at the Nodes of Ranvier, where myelination is interrupted and channels and pumps are actually located





Action potentials have four properties that enable efficient neuronal signaling

1. Threshold for initiation
2. Conducted without decrement
3. Refractory period
4. All-or-none nature



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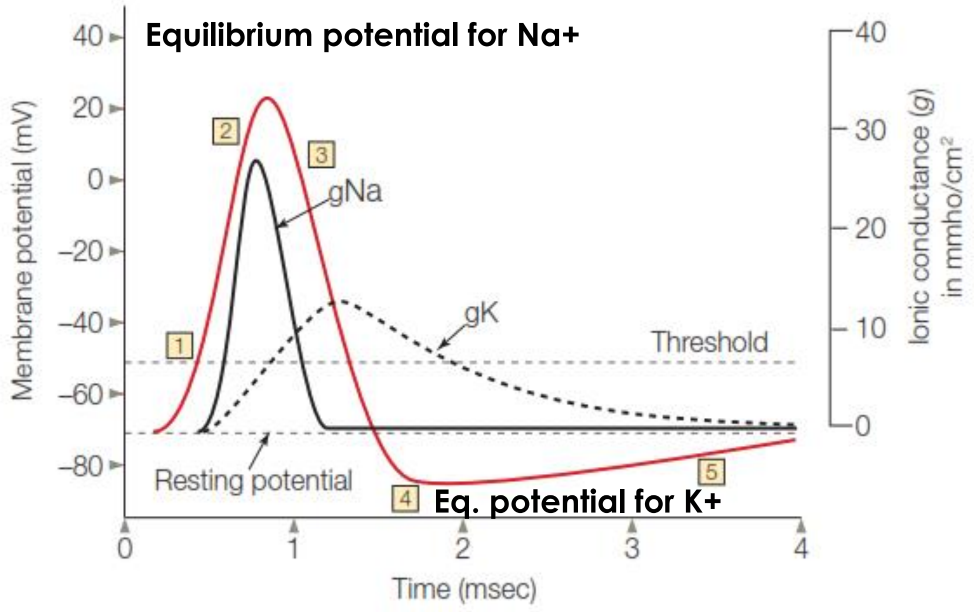

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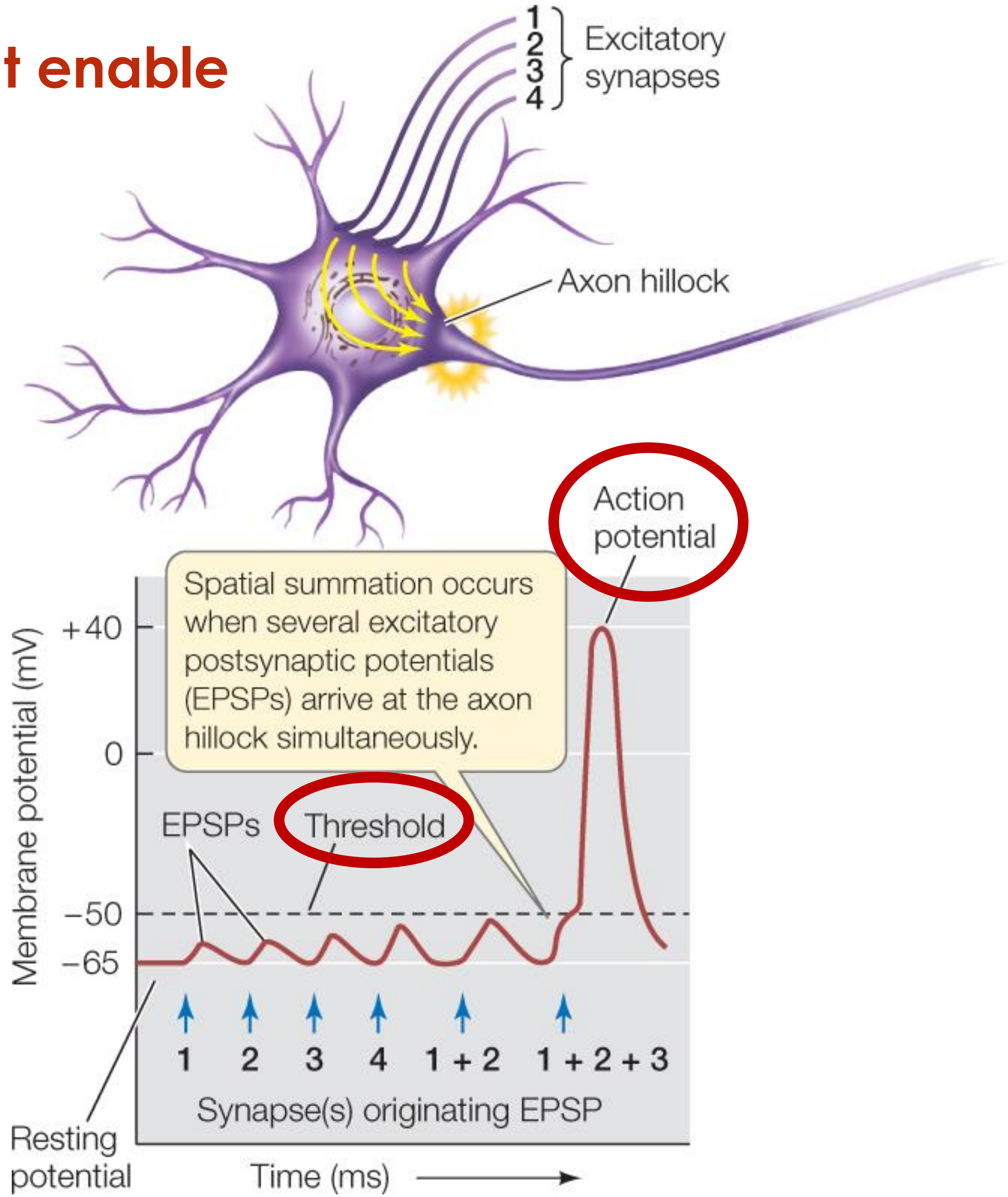
Action potentials have four properties that enable efficient neuronal signaling

1. Threshold for initiation

- The AP is triggered only if summation of EPSPs depolarizes the cell membrane to at least -55mV
- Implication:________________________



Action potentials have four properties that enable efficient neuronal signaling

1. Threshold for initiation

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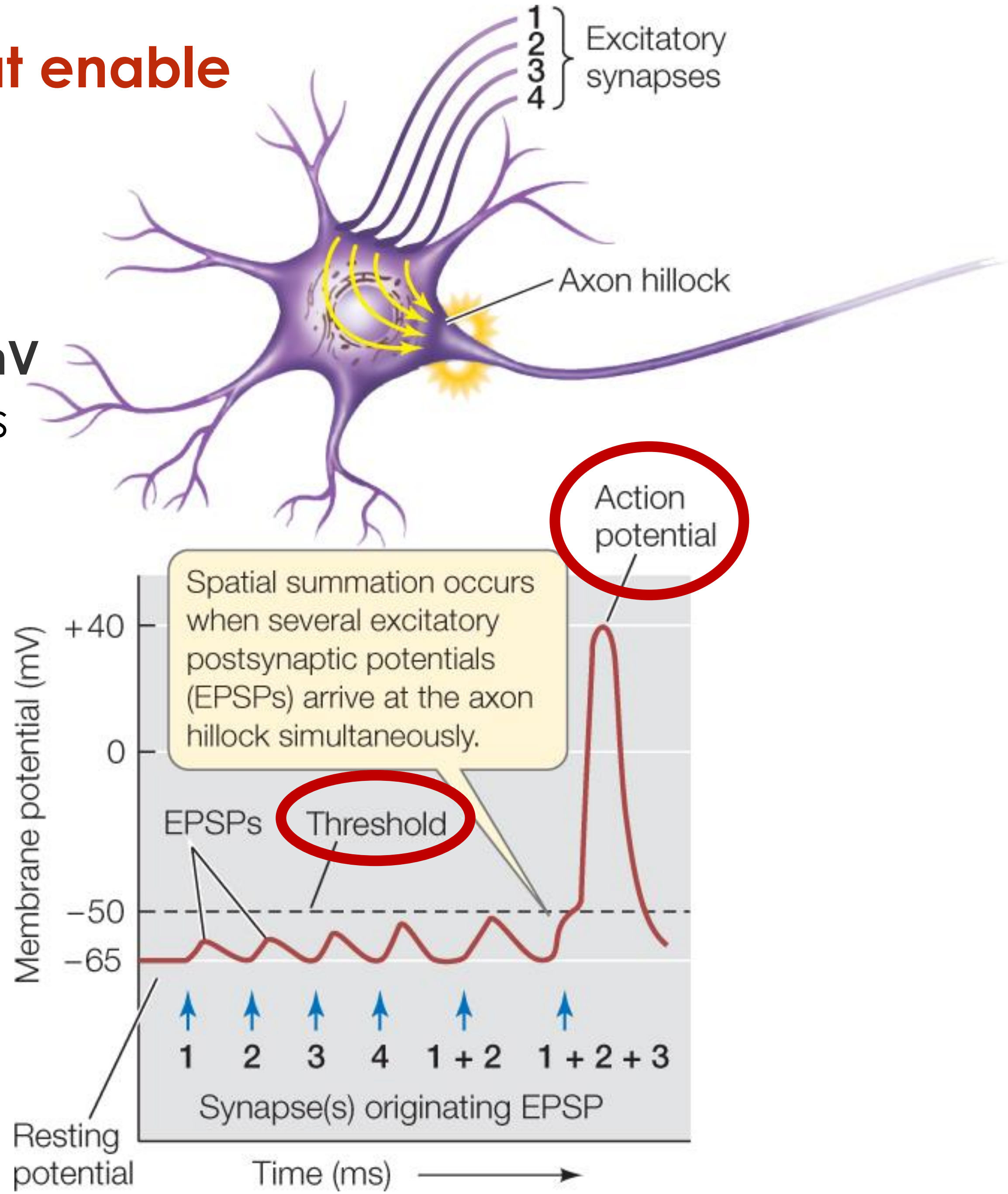
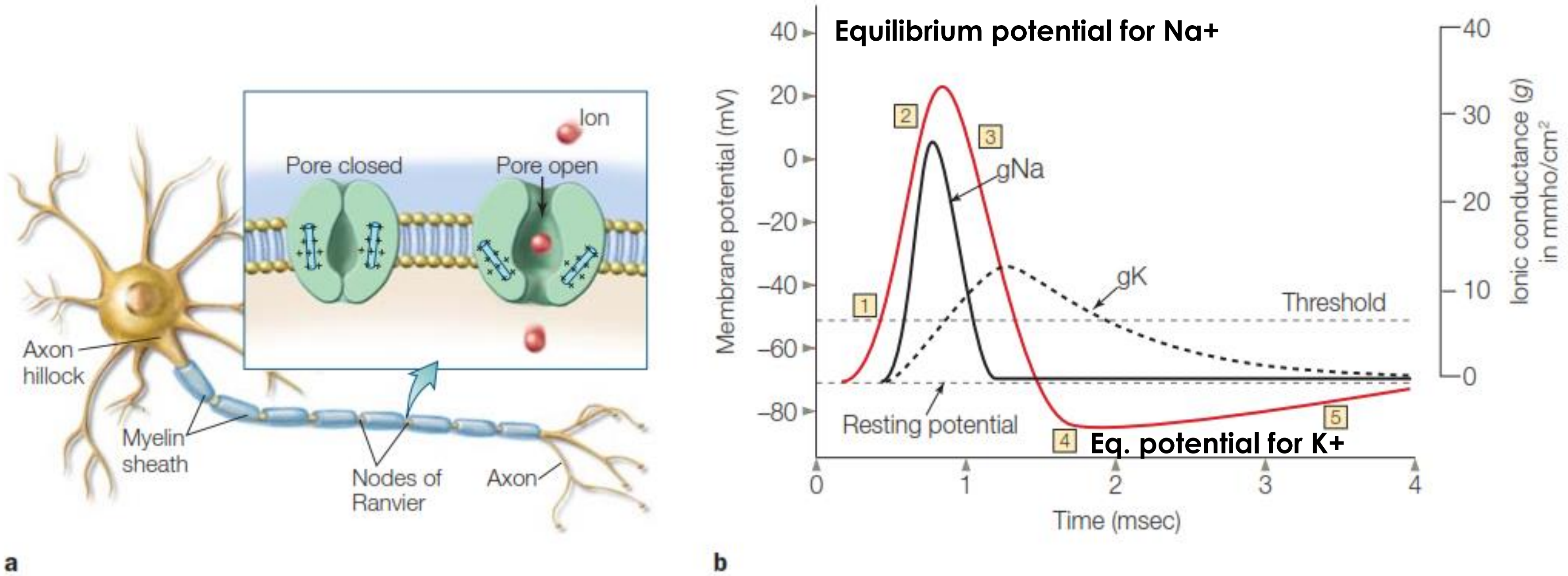


Action potentials have four properties that enable efficient neuronal signaling

1. Threshold for initiation

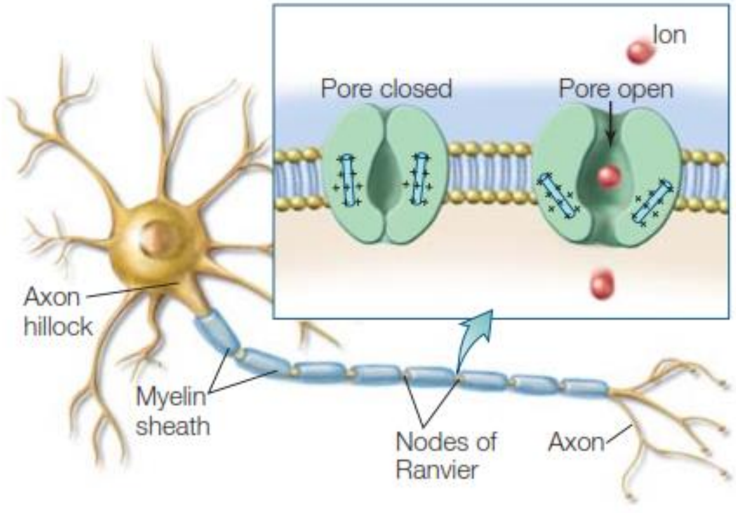
- The AP is triggered only if summation of EPSPs depolarizes the cell membrane to at least **-55mV** [1]
- Implication: only "meaningful" information leads to an AP



Action potentials have four properties that enable efficient neuronal signaling

2. Conducted without decrement

- The AP is actively propagated & **self-regenerative**
- Depolarization causes **voltage-gated Na+ channels** to open → Na+ flows into the neuron



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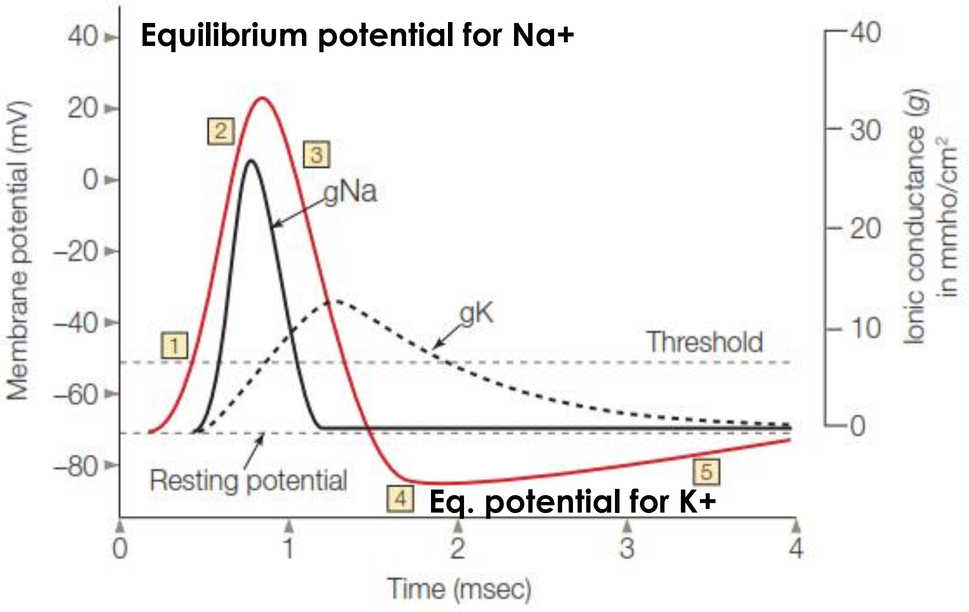

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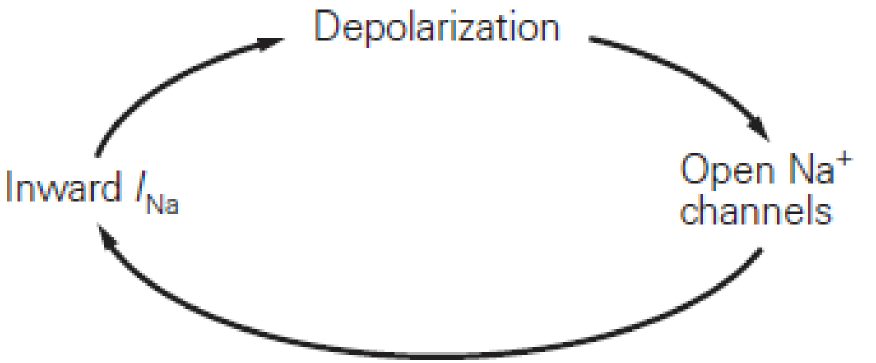
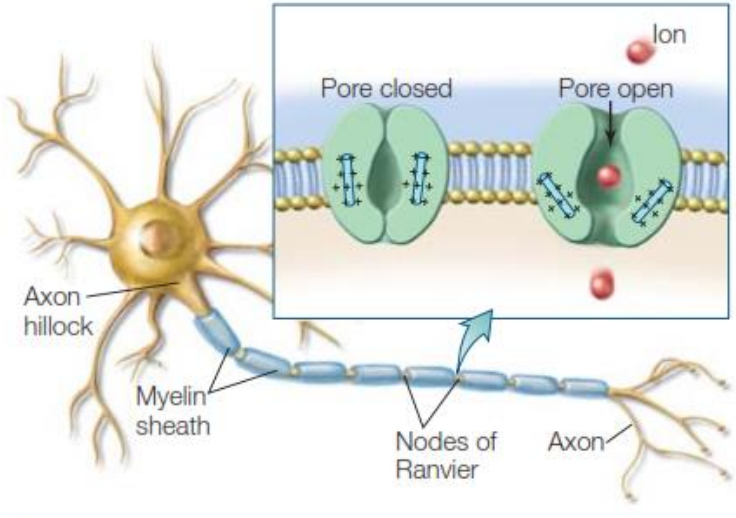
Action potentials have four properties that enable efficient neuronal signaling



2. Conducted without decrement

- The influx of positively charged Na+ neutralizes the negative charge inside the neuron
- This starts a cycle, causing more voltage-gated Na+ channels to open & further depolarizing the neuron
- The cycle continues until it reaches the equilibrium potential for Na+ [2]



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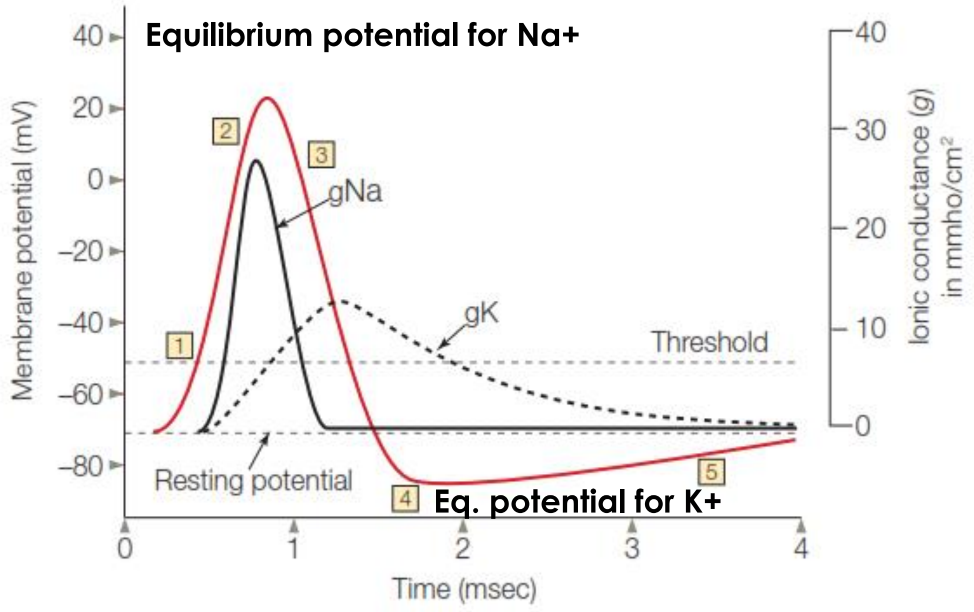
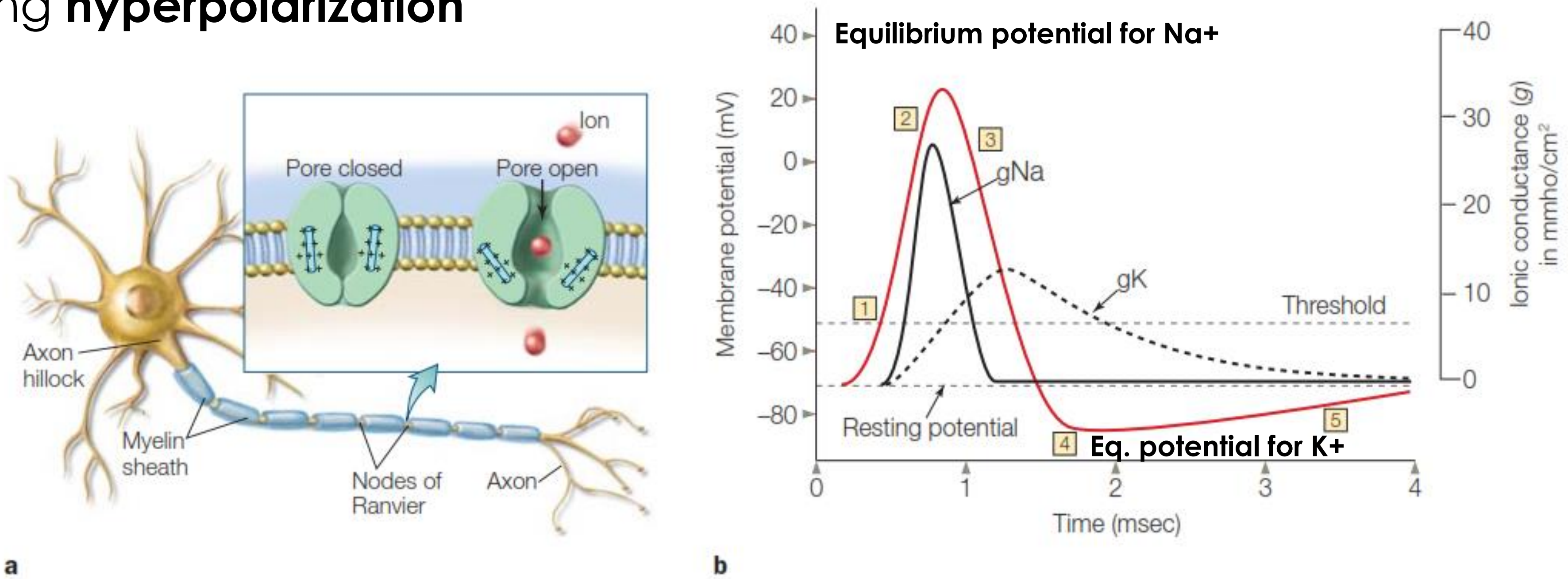


b

Action potentials have four properties that enable efficient neuronal signaling

2. Conducted without decrement

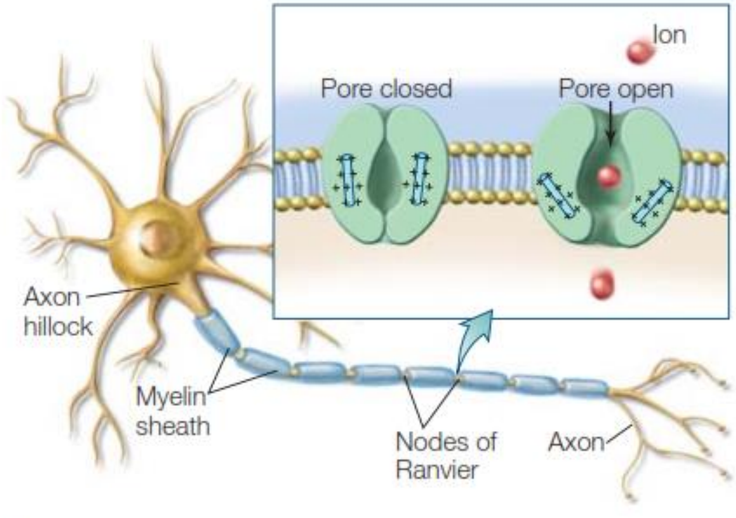
- Then, **voltage-gated K+ channels open**, allowing K+ to flow out of the neuron down its concentration gradient [3]
- This shifts the membrane potential back toward
    - its resting potential and even slightly below it
    - to the K+ equilibrium potential [4], which is more negative than the resting potential, causing **hyperpolarization**



Action potentials have four properties that enable efficient neuronal signaling

2. Conducted without decrement

- K+ channels then close
- The membrane potential can return to its resting state [5]



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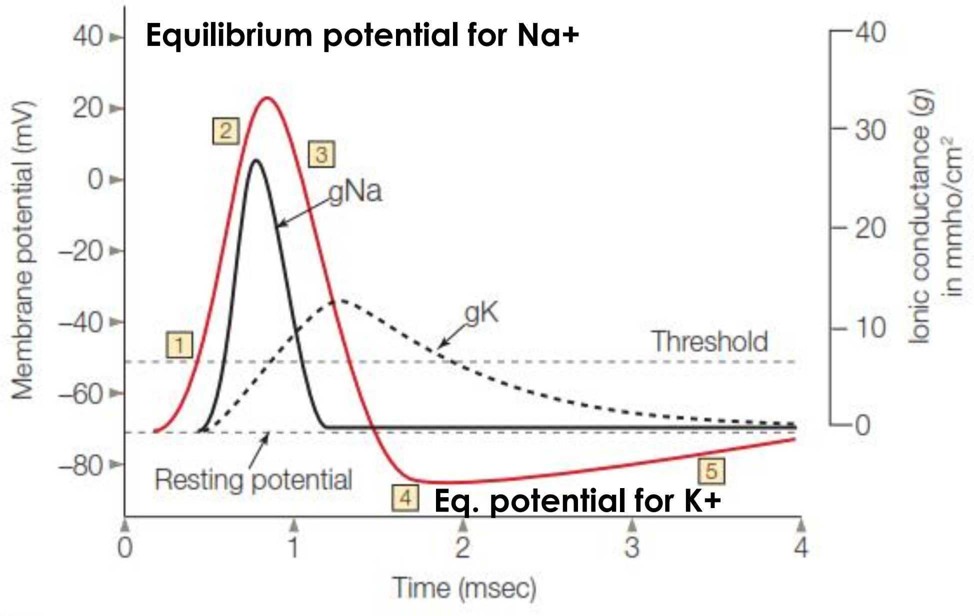

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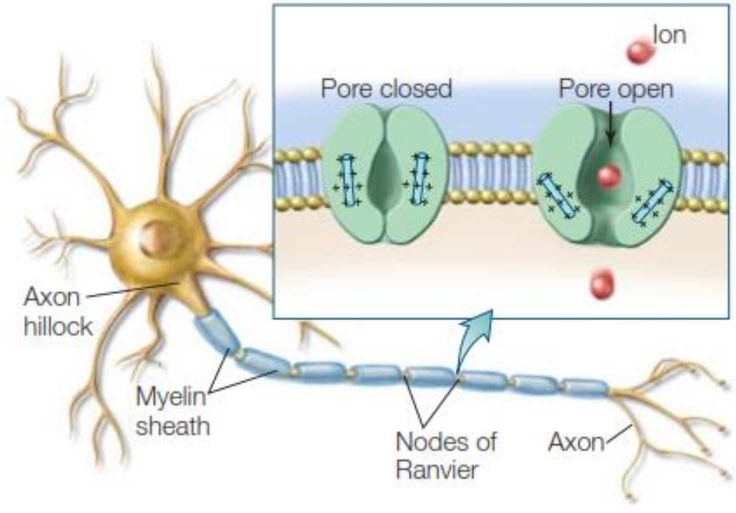
Action potentials have four properties that enable efficient neuronal signaling

2. Conducted without decrement

- Implication: ______________________________



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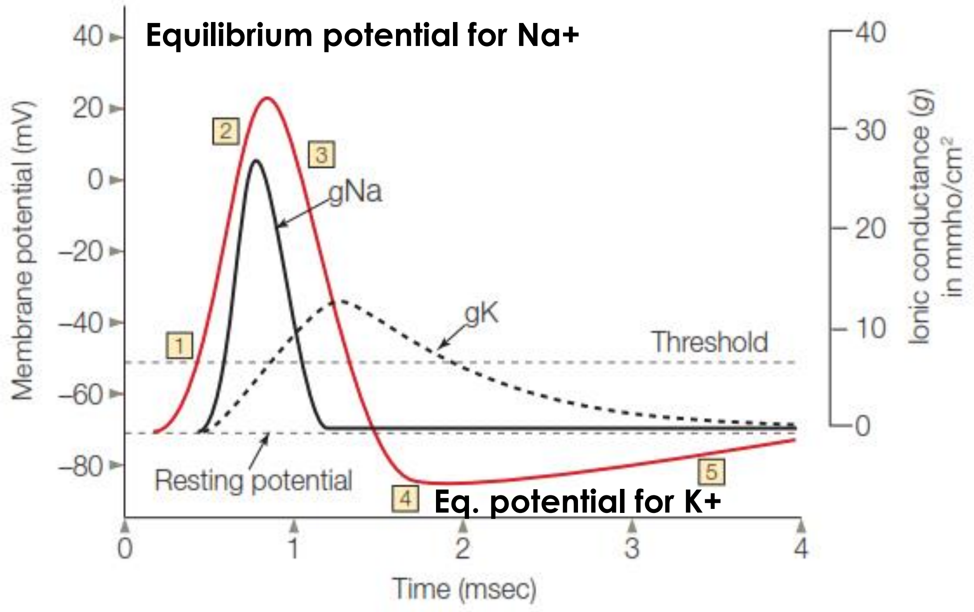

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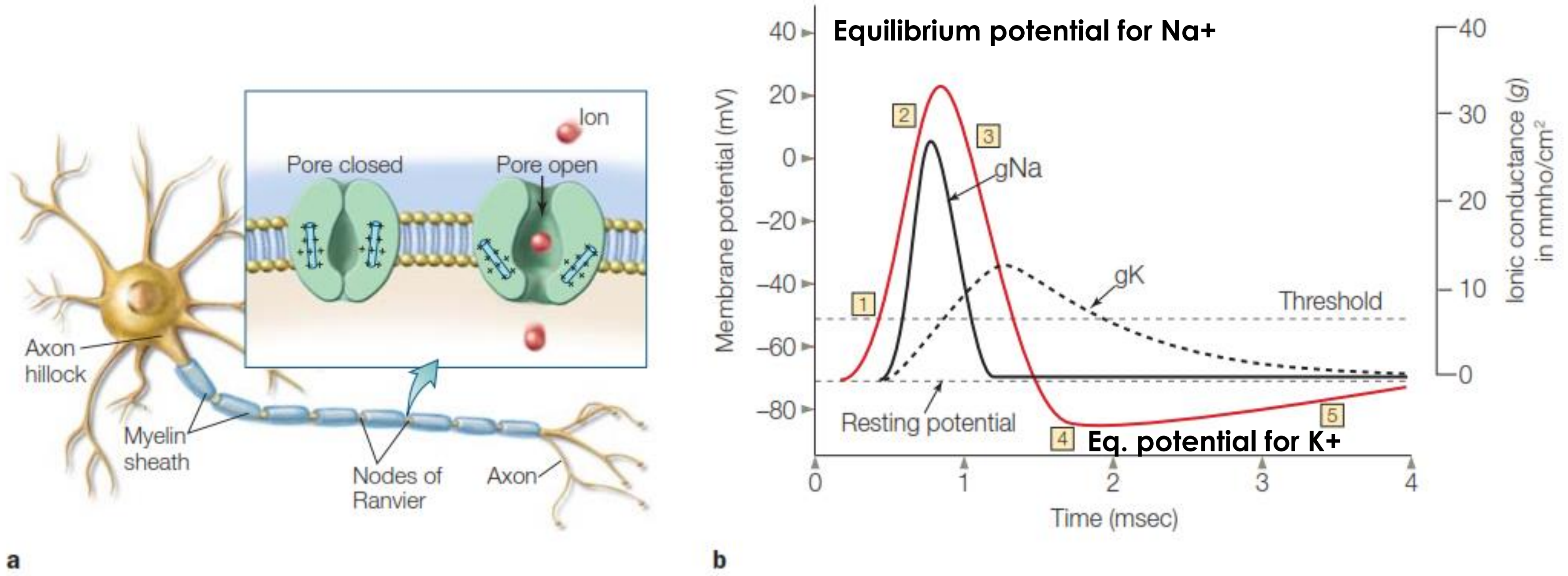
Action potentials have four properties that enable efficient neuronal signaling

2. Conducted without decrement

- Implication: the amplitude of the AP remains constant, even when it is conducted over great distances



Action potentials have four properties that enable efficient neuronal signaling

3. Refractory period

- During hyperpolarization the voltage-gated Na+ channels cannot open
- Implications:
    1. ____________________
    2. _____________________

Action potentials have four properties that enable efficient neuronal signaling

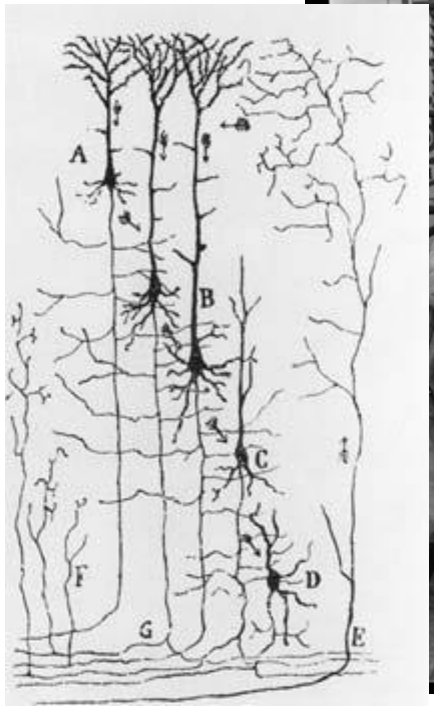
3. Refractory period

- During hyperpolarization the voltage-gated Na+ channels cannot open
- Implications:
    1. Limits the frequency of APs (i.e. # of APs that a neuron can generate in a given time)
    2. Unidirectional current flow: from the axon hillock toward the axon terminal.
        - The current cannot reopen the channels that generated it
        - It can depolarize the membrane a bit farther on, opening channels in the next portion of the membrane

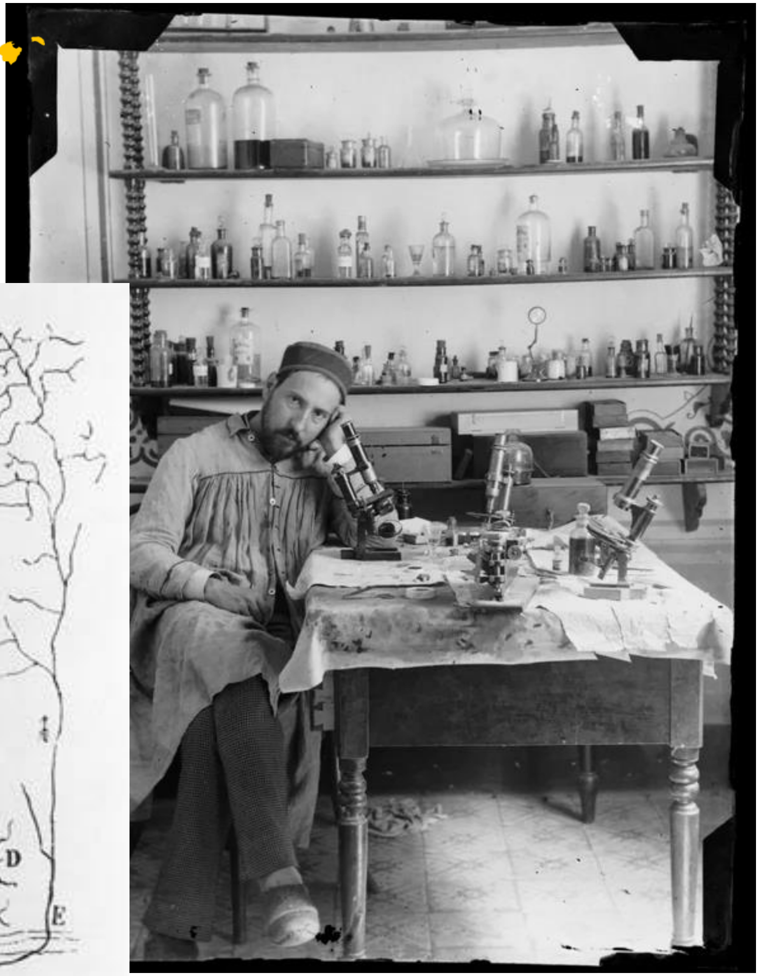
Principle of dynamic polarization

Electrical signals within a nerve cell flow **only in one direction**:

- received at synapses on dendrites
- Transmitted down the axon
- Passed along at synapses on the axon terminals



Ramón y Cajal's drawing of the afferent inflow to the mammalian cortex

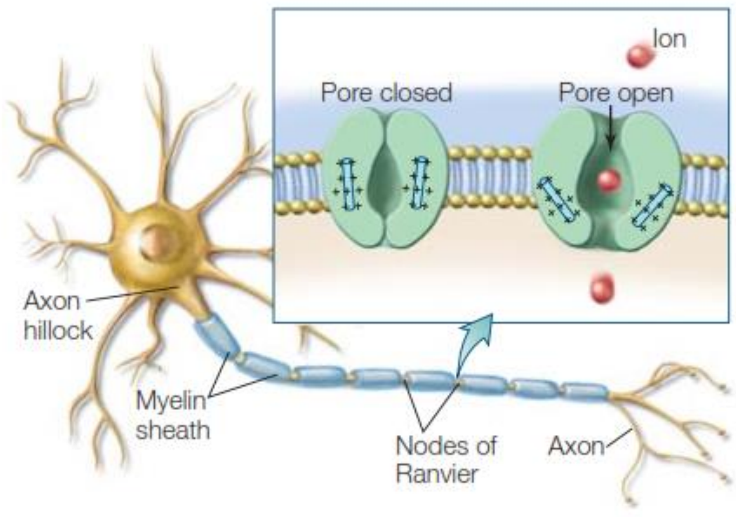


Santiago Ramón y Cajal (1852–1934)

Action potentials have four properties that enable efficient neuronal signaling

4. All-or-none nature

- APs have always similar amplitude and duration, regardless of the size of the PSP that generated it
- The size and shape of an AP initiated by a large PSP is the same as that of an AP evoked by a current that just surpasses the threshold
- APs are binary signals
- Implication: ____



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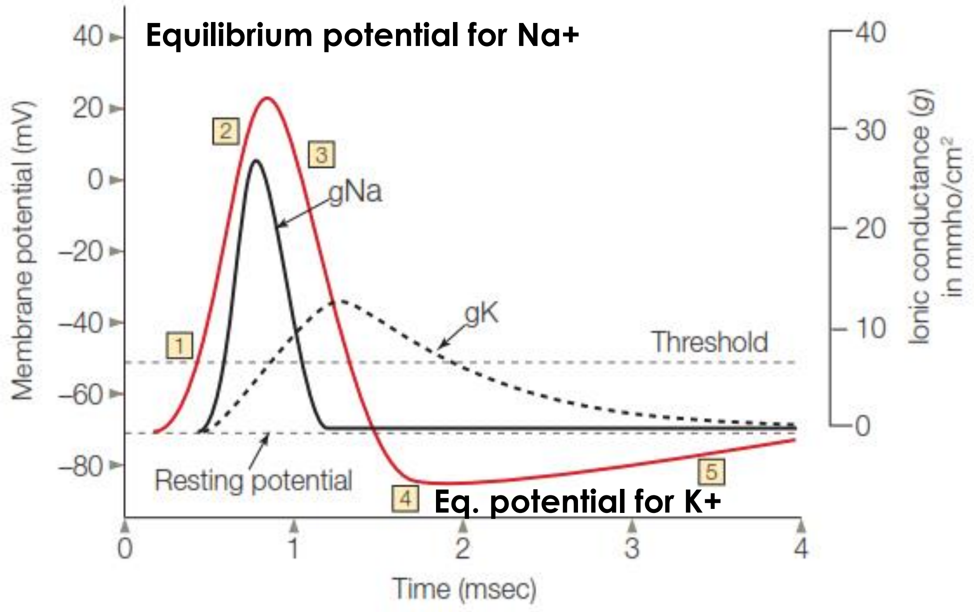

b

Action potentials have four properties that enable efficient neuronal signaling

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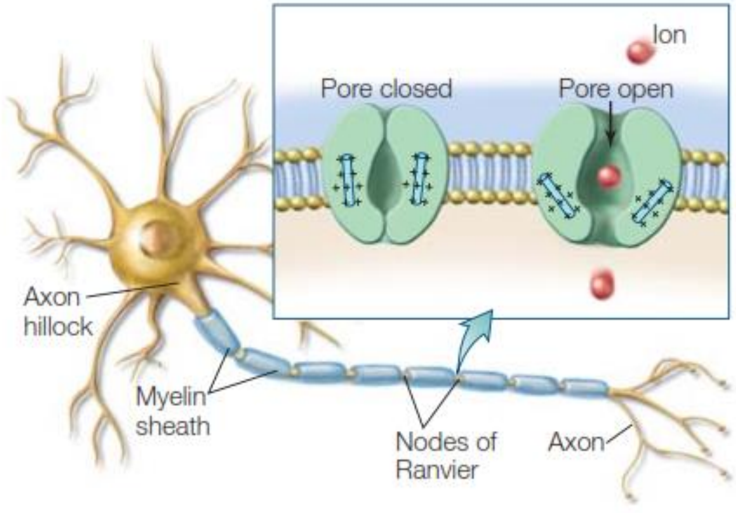
- APs have always similar amplitude and duration, regardless of the size of the PSP that generated it
- The size and shape of an AP initiated by a large PSP is the same as that of an AP evoked by a current that just surpasses the threshold
- APs are binary signals
- Implication: the strength of the AP does not communicate anything about the strength of the input stimulus



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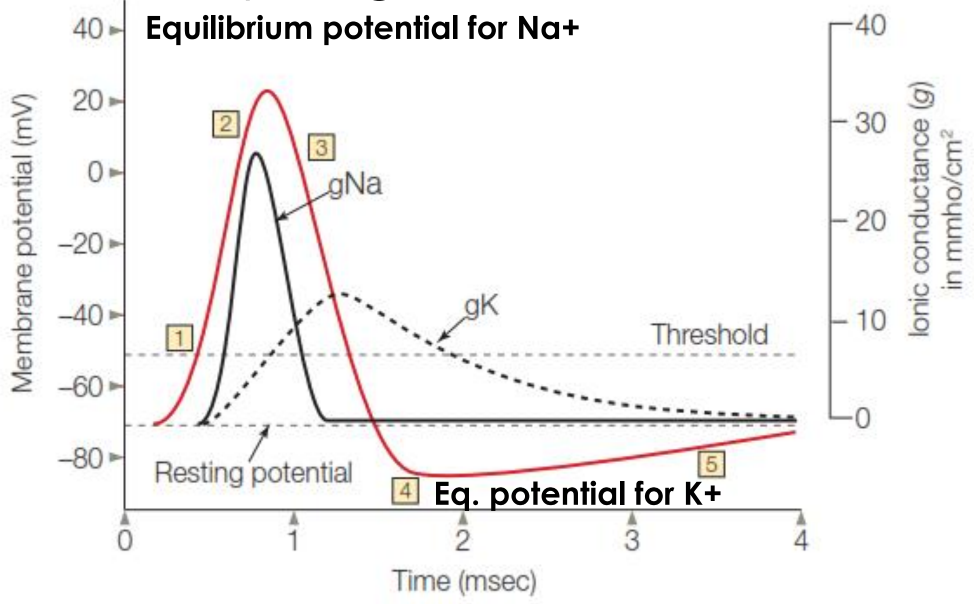

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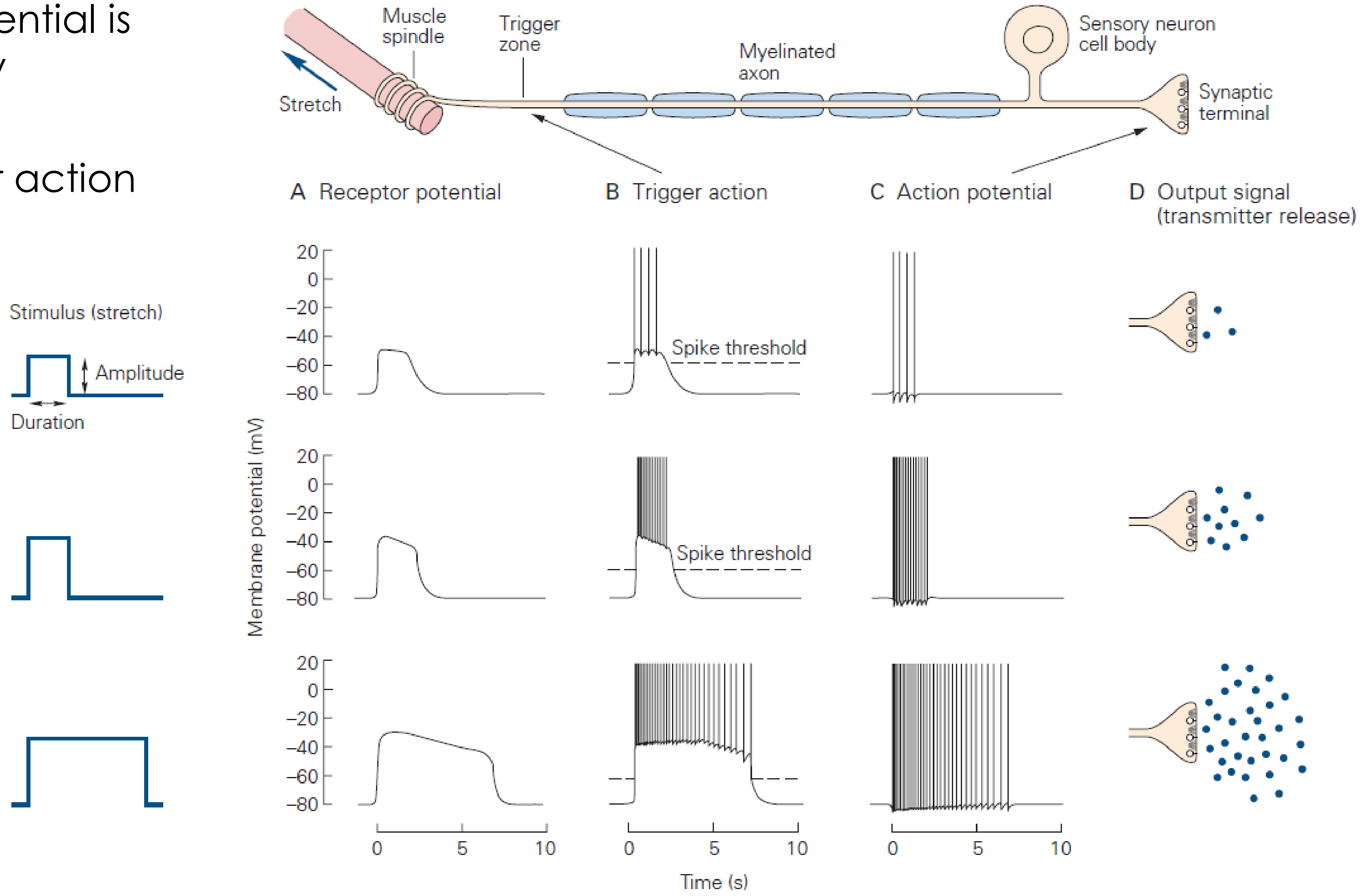
So how does the neuron communicate information about the strength of the input stimulus?

The firing rate of the action potential is proportional to stimulus intensity

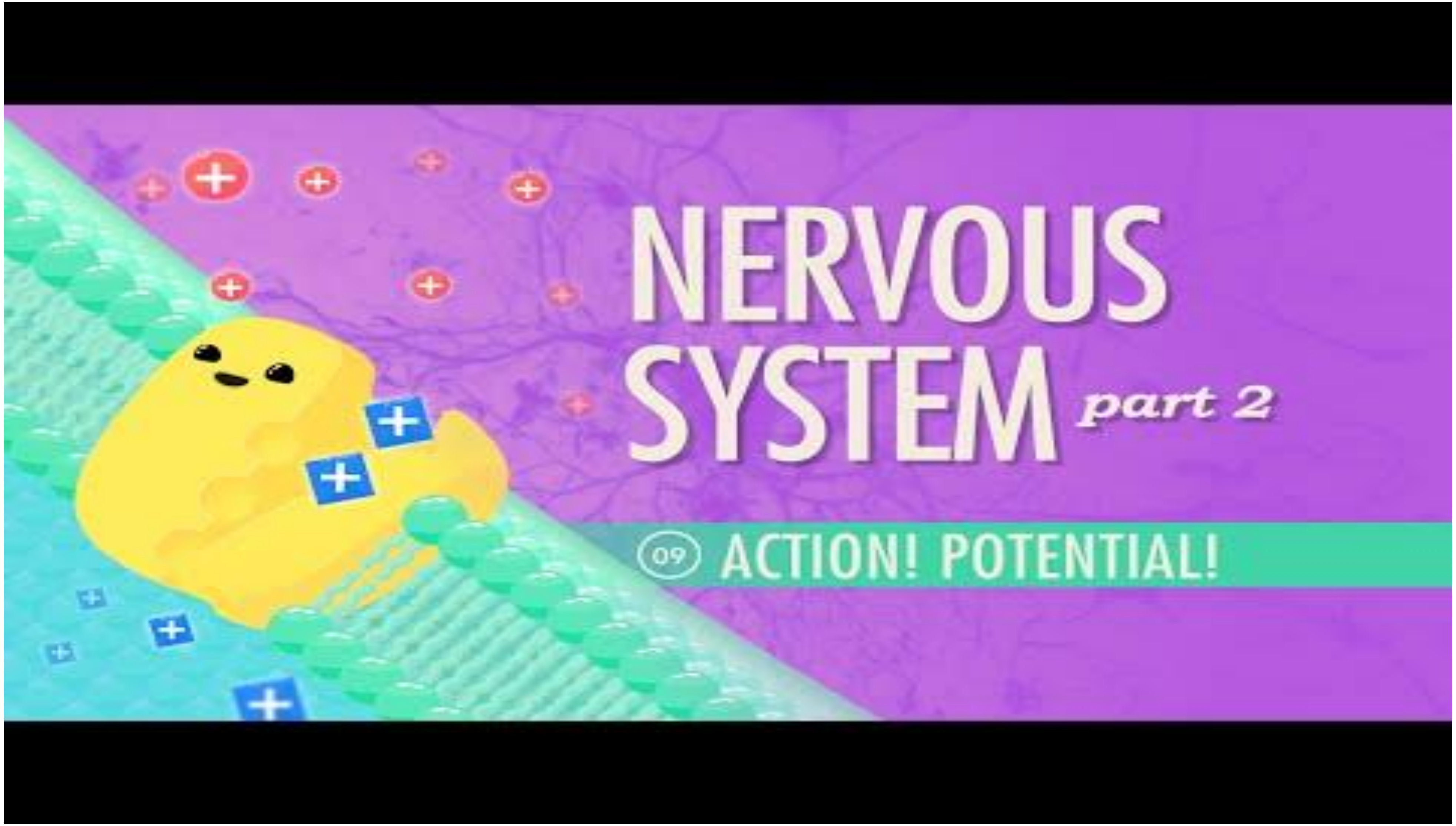
More intense stimuli elicit higher action potential firing rates.



wooclap

Questions 5-7

https://youtu.be/OZG8M_IdA1M?si=DX0OSVaYT9eJBNWe



https://youtu.be/OZG8M_IdA1M

Correct firing is crucial for correct functioning...

https://youtu.be/LcO9YU-Pdws

Correct firing is crucial for correct functioning...
Seizures: the misfiring of neurons

Recommended readings

- Gazzaniga, M. S., Ivry, R. B., & Mangun, G. R. (2014). Cognitive Neuroscience, The biology of the mind.
  - Chapter 2

- Kandel, E. R., Schwartz, J. H., Jessell, T. M., Siegelbaum, S., Hudspeth, A. J., & Mack, S. (Eds.). (2000). Principles of neural science. New York: McGraw-hill.
  - Chapter 2, 4, 6, 7, 8, 15