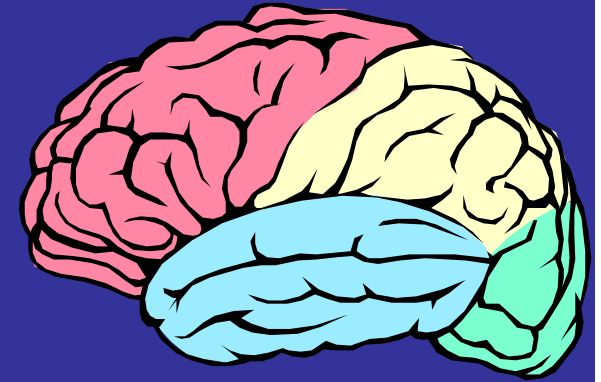


The Nervous System



- A network of billions of nerve cells linked together in a highly organized fashion to form the rapid control center of the body.
- Functions include:
 - Integrating center for homeostasis, movement, and almost all other body functions.
 - The mysterious source of those traits that we think of as setting humans apart from animals

Basic Functions of the Nervous System

1. Sensation

- Monitors changes/events occurring in and outside the body. Such changes are known as *stimuli* and the cells that monitor them are *receptors*.

2. Integration

- The parallel processing and interpretation of sensory information to determine the appropriate response

3. Reaction

- Motor output.
 - The activation of muscles or glands (typically via the release of *neurotransmitters* (NTs))

Nervous vs. Endocrine System

- **Similarities:**

- They both monitor stimuli and react so as to maintain homeostasis.

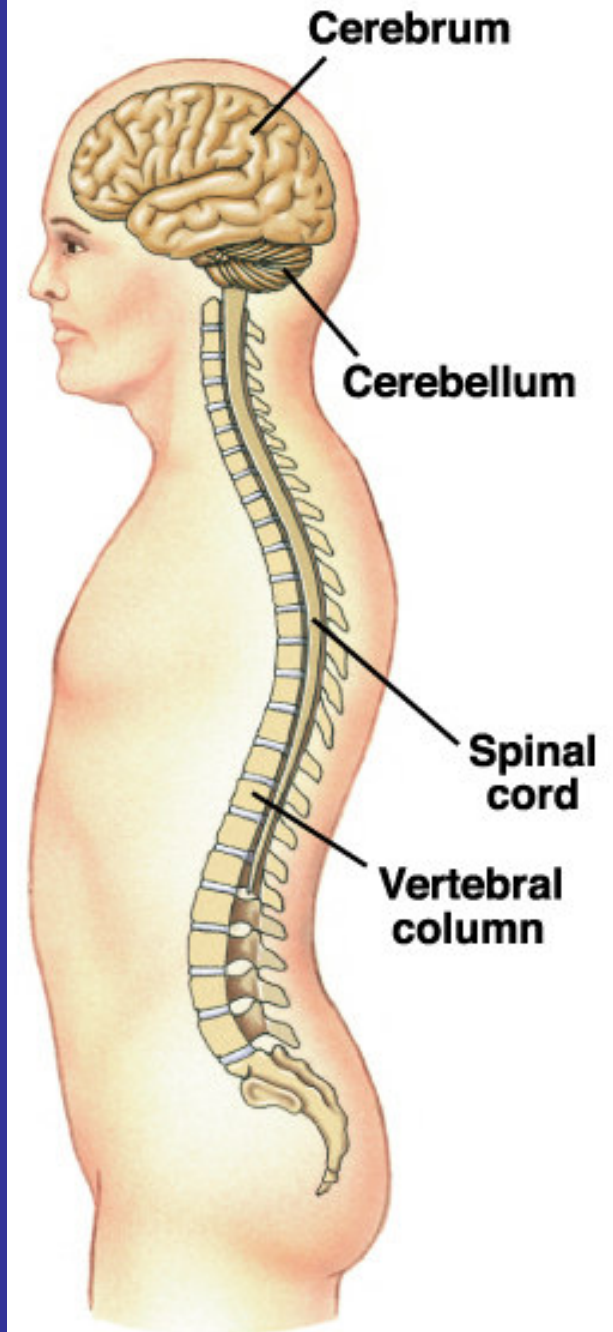
- **Differences:**

- The NS is a rapid, fast-acting system whose effects do not always persevere.

- The ES acts slower (via blood-borne chemical signals called H _____) and its actions are usually much longer lasting.

Organization of the Nervous System

- 2 big initial divisions:
 1. **Central Nervous System** →
 - The brain + the spinal cord
 - The center of integration and control
 2. **Peripheral Nervous System**
 - The nervous system outside of the brain and spinal cord
 - Consists of:
 - 31 Spinal nerves
 - » Carry info to and from the spinal cord
 - 12 Cranial nerves
 - » Carry info to and from the brain



Peripheral Nervous System

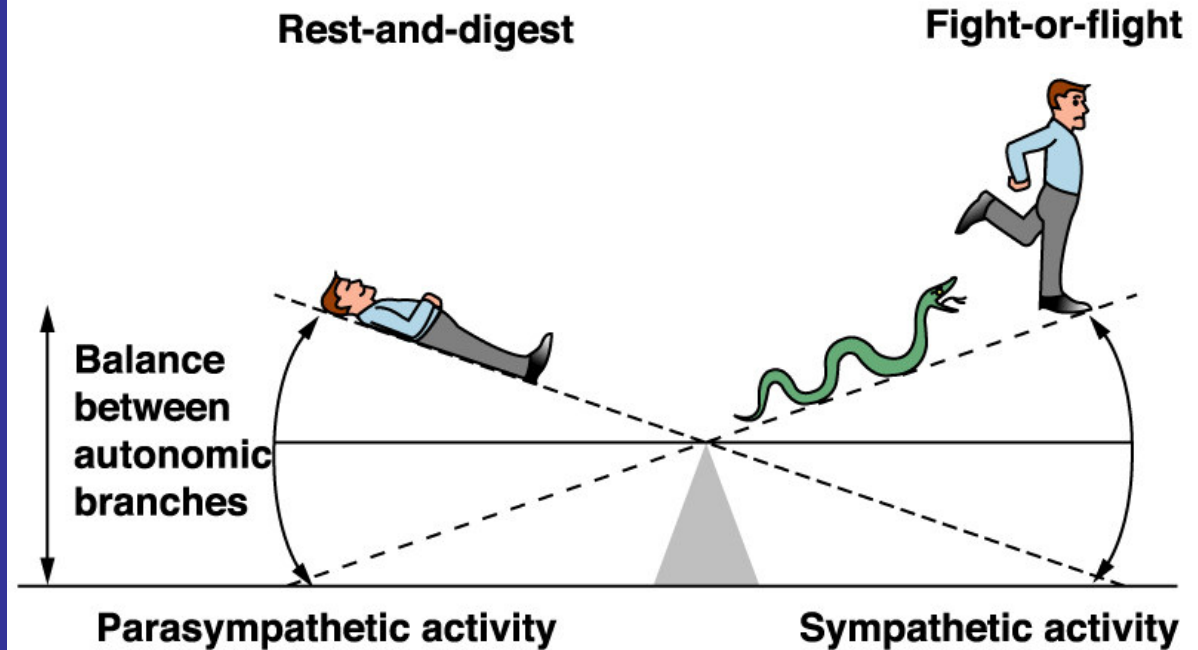
- Responsible for communication btwn the CNS and the rest of the body.
- Can be divided into:
 - **Sensory Division**
 - **Afferent division**
 - Conducts impulses from receptors to the CNS
 - Informs the CNS of the state of the body interior and exterior
 - Sensory nerve fibers can be **somatic** (from skin, skeletal muscles or joints) or **visceral** (from organs w/i the ventral body cavity)
 - **Motor Division**
 - **Efferent division**
 - Conducts impulses from CNS to effectors (muscles/glands)
 - Motor nerve fibers

Motor Efferent Division

- Can be divided further:
 - **Somatic nervous system**
 - VOLUNTARY (generally)
 - Somatic nerve fibers that conduct impulses from the CNS to skeletal muscles
 - **Autonomic nervous system**
 - INVOLUNTARY (generally)
 - Conducts impulses from the CNS to smooth muscle, cardiac muscle, and glands.

Autonomic Nervous System

- Can be divided into:
 - Sympathetic Nervous System
 - “Fight or Flight”
 - Parasympathetic Nervous System
 - “Rest and Digest”



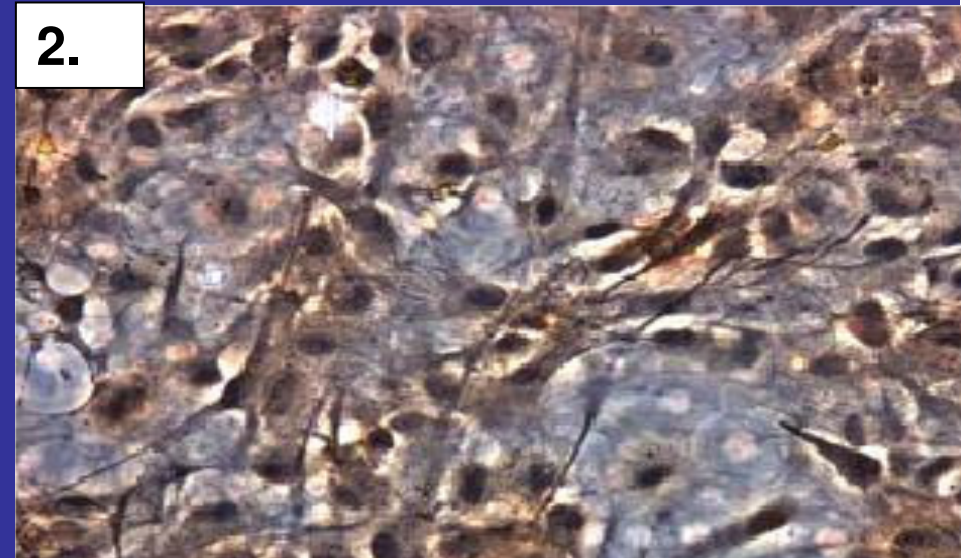
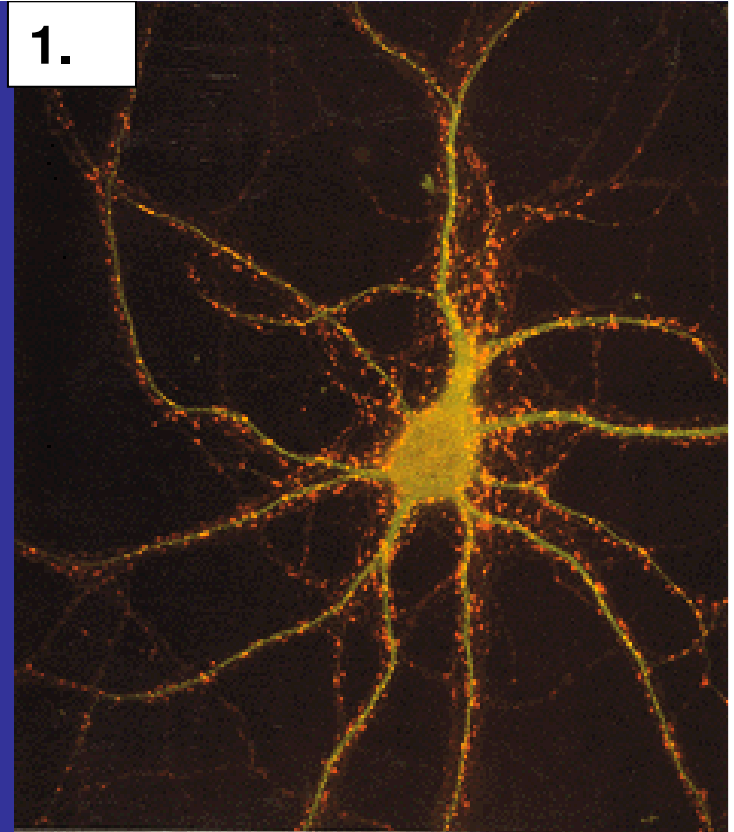
These 2 systems are antagonistic.

Typically, we balance these 2 to keep ourselves in a state of dynamic balance.

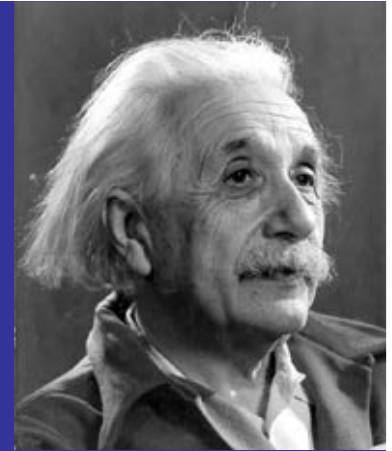
We'll go further into the difference btwn these 2 later!

Nervous Tissue

- Highly cellular
 - How does this compare to the other 3 tissue types?
- 2 cell types
 1. **Neurons**
 - Functional, signal conducting cells
 2. **Neuroglia**
 - Supporting cells



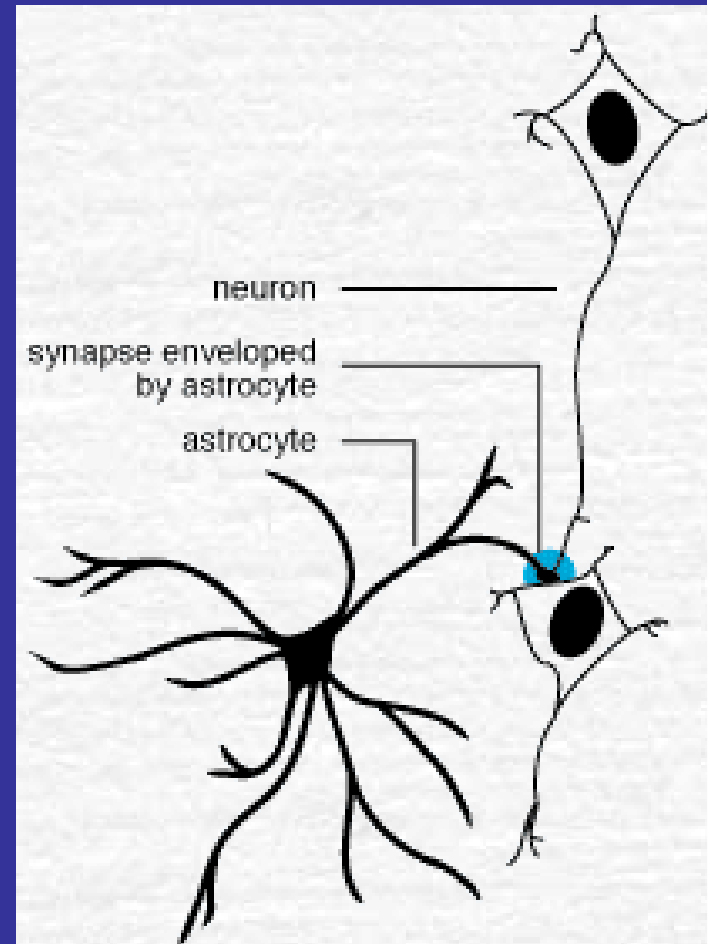
Neuroglia



- Outnumber neurons by about 10 to 1 (the guy on the right had an inordinate amount of them).
- 6 types of supporting cells
 - 4 are found in the CNS:

1. Astrocytes

- Star-shaped, abundant, and versatile
- Guide the migration of developing neurons
- Act as K^+ and NT buffers
- Involved in the formation of the blood brain barrier
- Function in nutrient transfer



Neuroglia

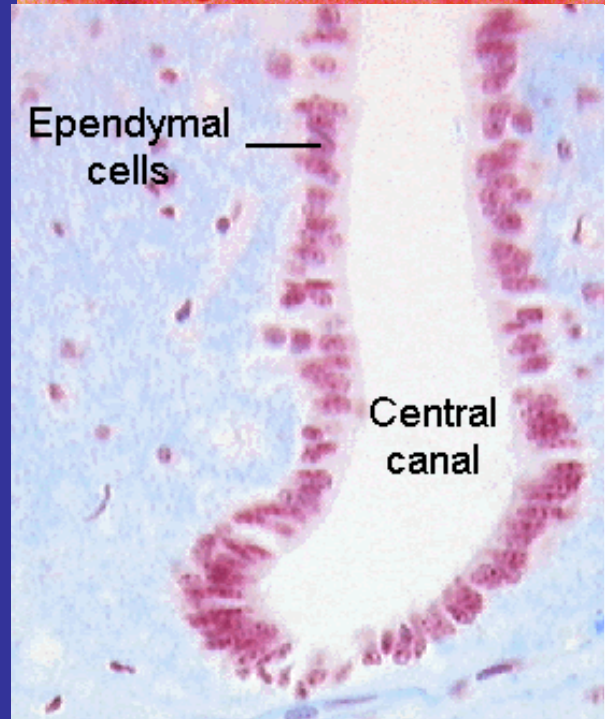
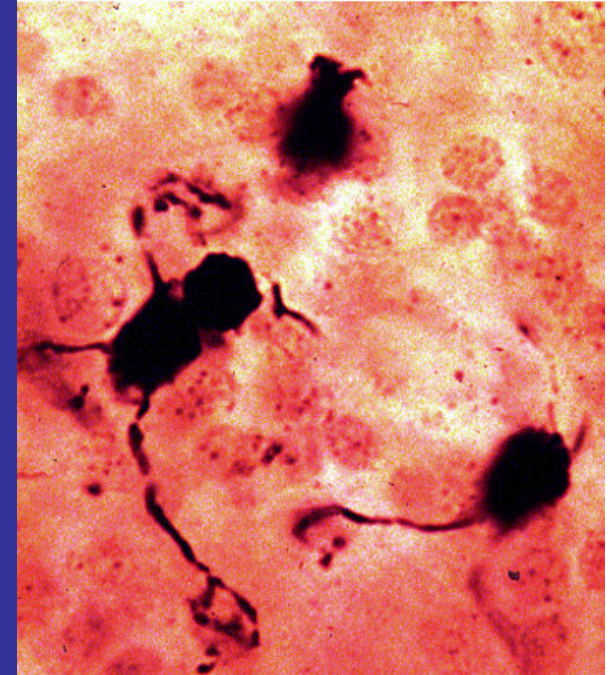
2. Microglia

- Specialized immune cells that act as the macrophages of the CNS
- Why is it important for the CNS to have its own army of immune cells?

3. Ependymal Cells

- Low columnar epithelial-esque cells that line the ventricles of the brain and the central canal of the spinal cord
- Some are ciliated which facilitates the movement of cerebrospinal fluid

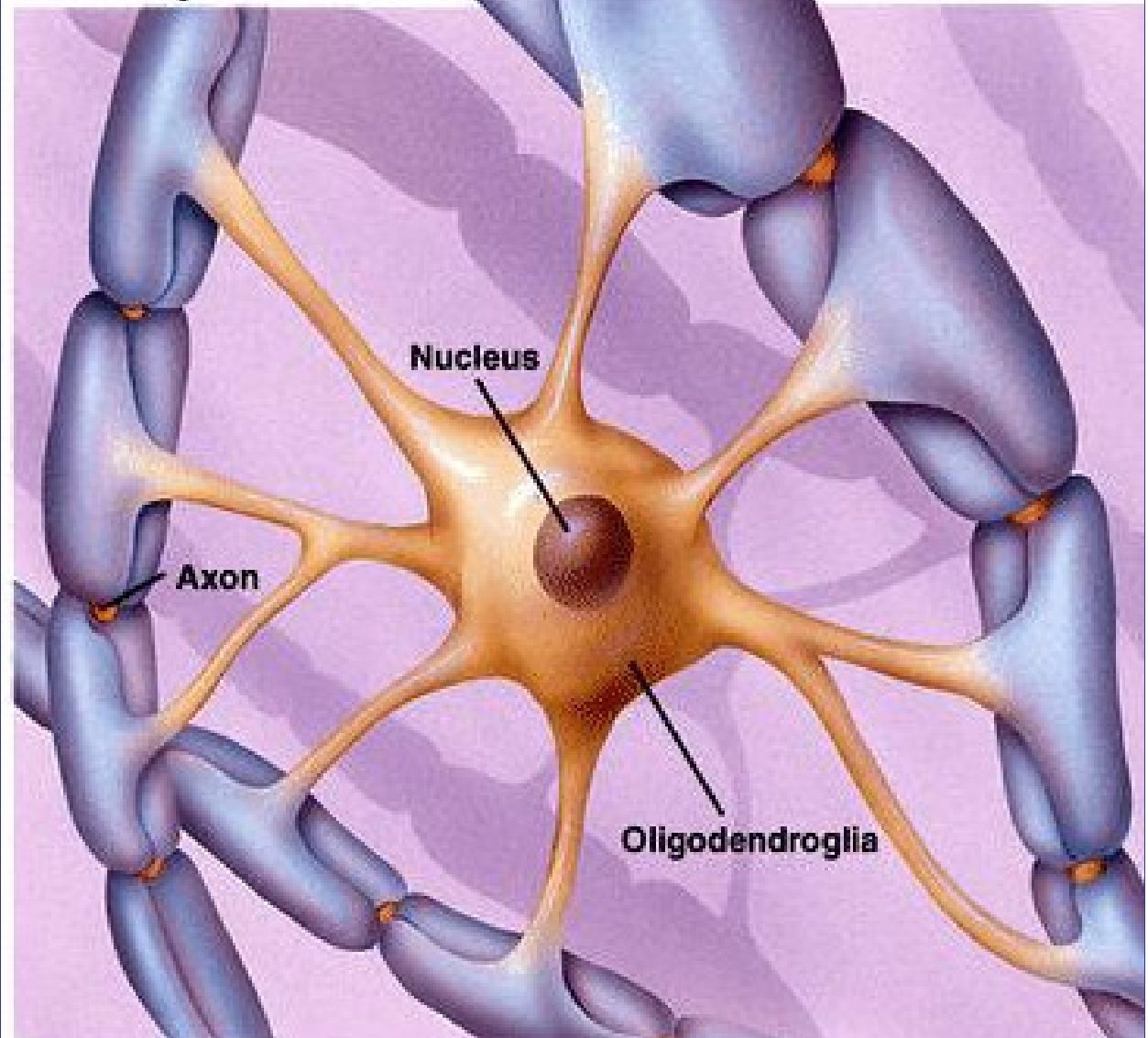
MICROGLIA CELL - GOLGI STAIN



Neuroglia

4. Oligodendrocytes
 - Produce the **myelin sheath** which provides the electrical insulation for certain neurons in the CNS

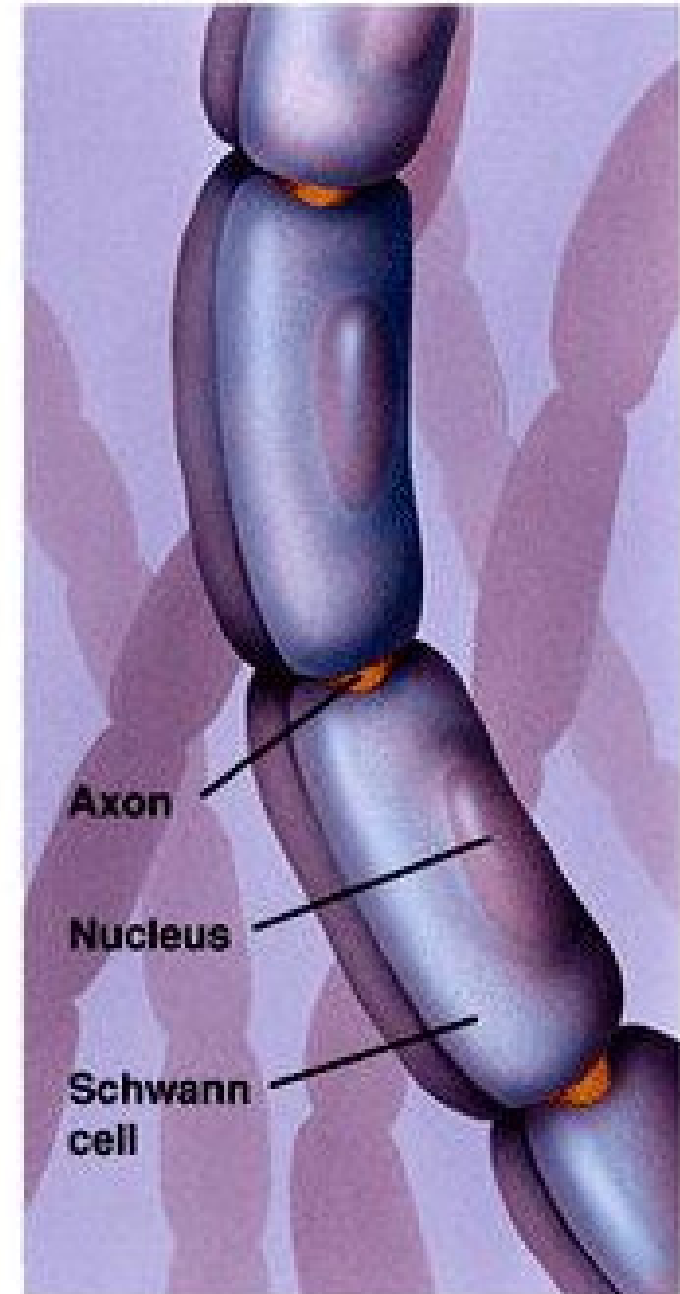
Myelination in the Central Nervous System



Neuroglia

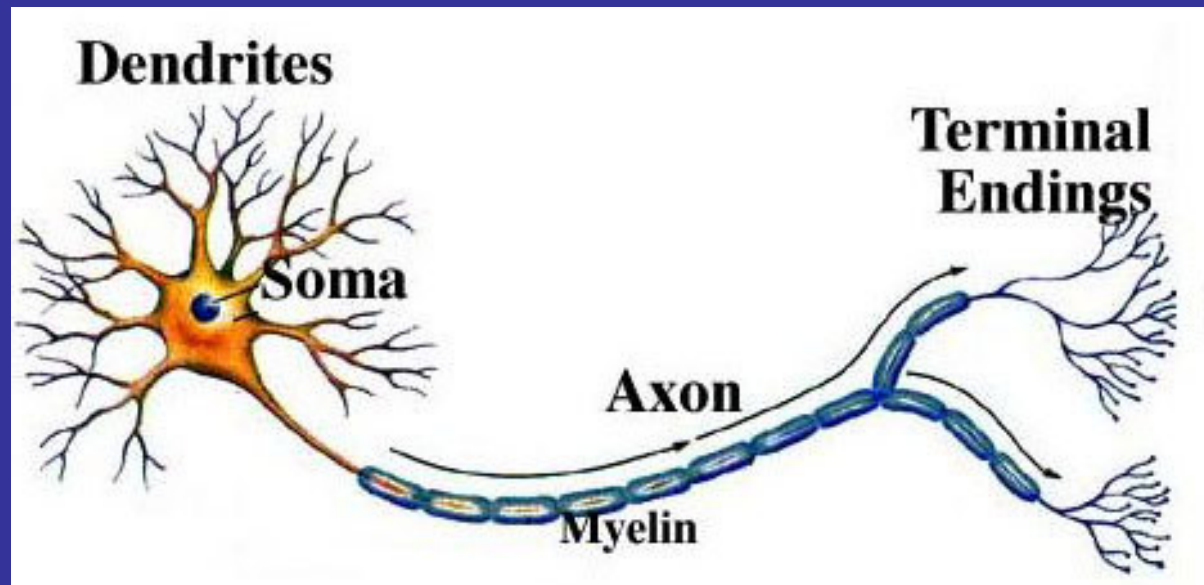
- 2 types of glia in the PNS
 1. **Satellite cells**
 - Surround clusters of neuronal cell bodies in the PNS
 - Unknown function
 2. **Schwann cells**
 - Form myelin sheaths around the larger nerve fibers in the PNS.
 - Vital to neuronal regeneration

Myelination in the Peripheral Nervous System



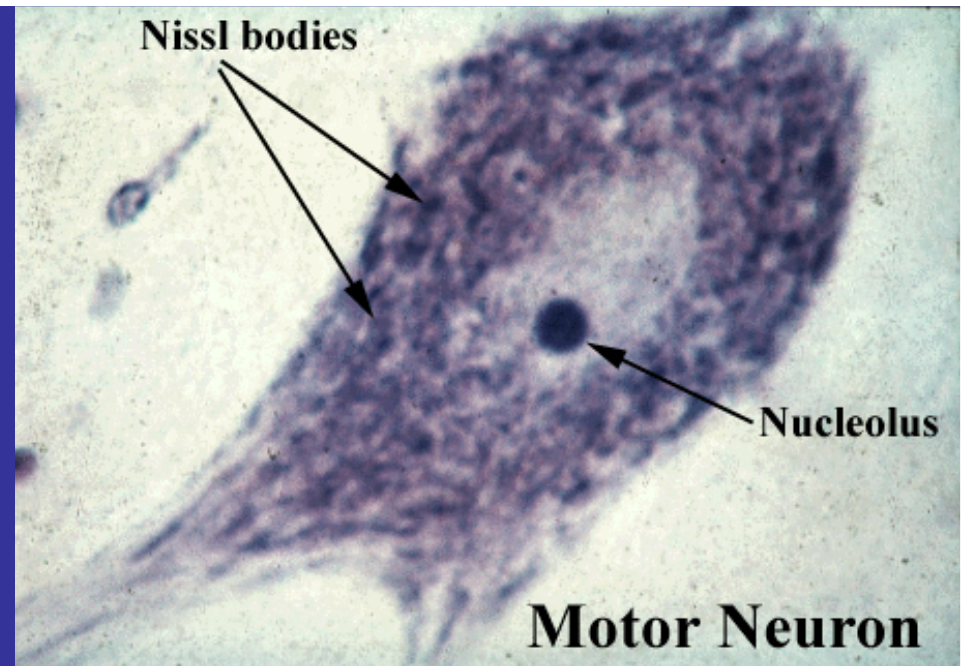
Neurons

- The functional and structural unit of the nervous system
- Specialized to conduct information from one part of the body to another
- There are many, many different types of neurons but most have certain structural and functional characteristics in common:
 - Cell body (**soma**)
 - One or more specialized, slender processes (**axons/dendrites**)
 - An input region (**dendrites/soma**)
 - A conducting component (**axon**)
 - A secretory (output) region (**axon terminal**)



Soma

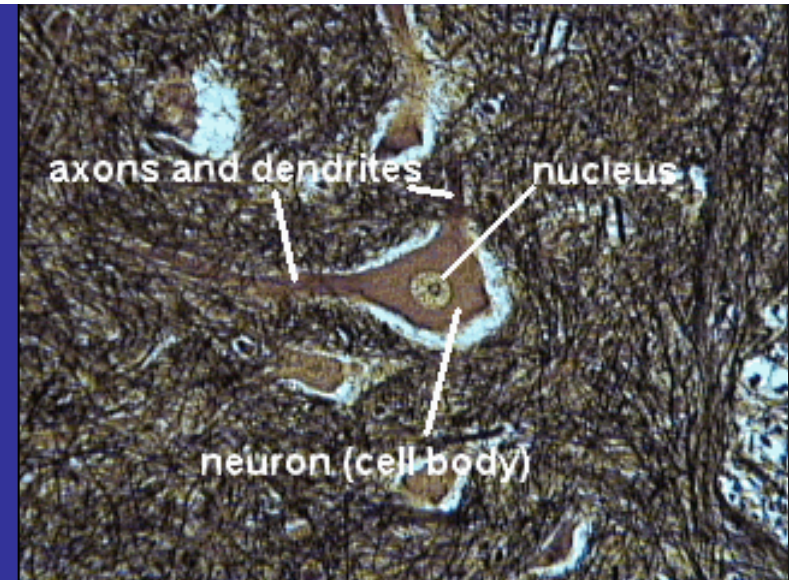
- Contains nucleus plus most normal organelles.
- Biosynthetic center of the neuron.
- Contains a very active and developed rough endoplasmic reticulum which is responsible for the synthesis of _____.
 - The neuronal rough ER is referred to as the **Nissl body**.
- Contains many bundles of protein filaments (**neurofibrils**) which help maintain the shape, structure, and integrity of the cell.



In the soma above, notice the small black circle. It is the **nucleolus**, the site of ribosome synthesis. The light circular area around it is the nucleus. The mottled dark areas found throughout the cytoplasm are the Nissl substance.

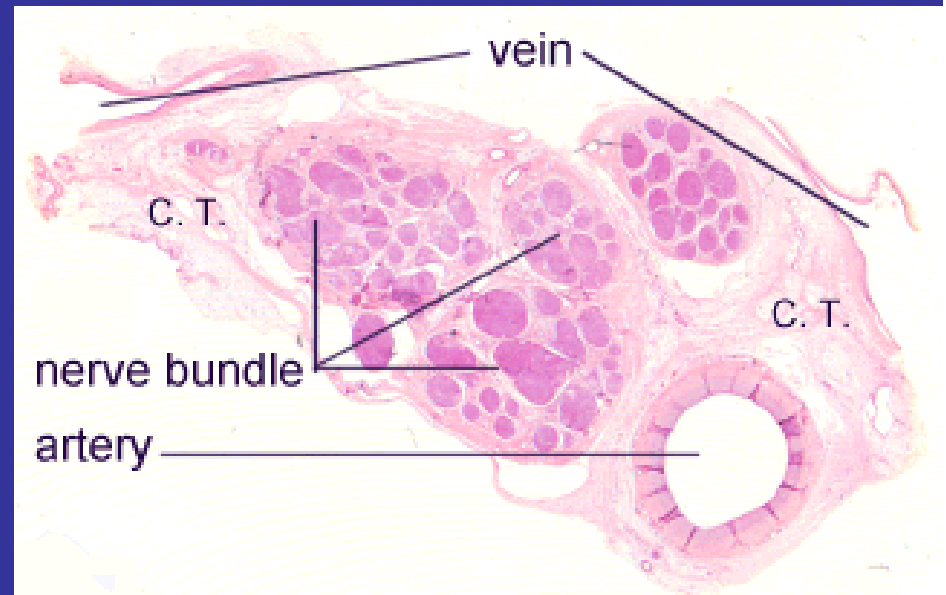
Somata

- Contain multiple mitochondria. *Why?*
- Acts as a receptive service for interaction with other neurons.
- Most somata are found in the bony environs of the CNS. *Why?*
- Clusters of somata in the CNS are known as **nuclei**. Clusters of somata in the PNS are known as **ganglia**.



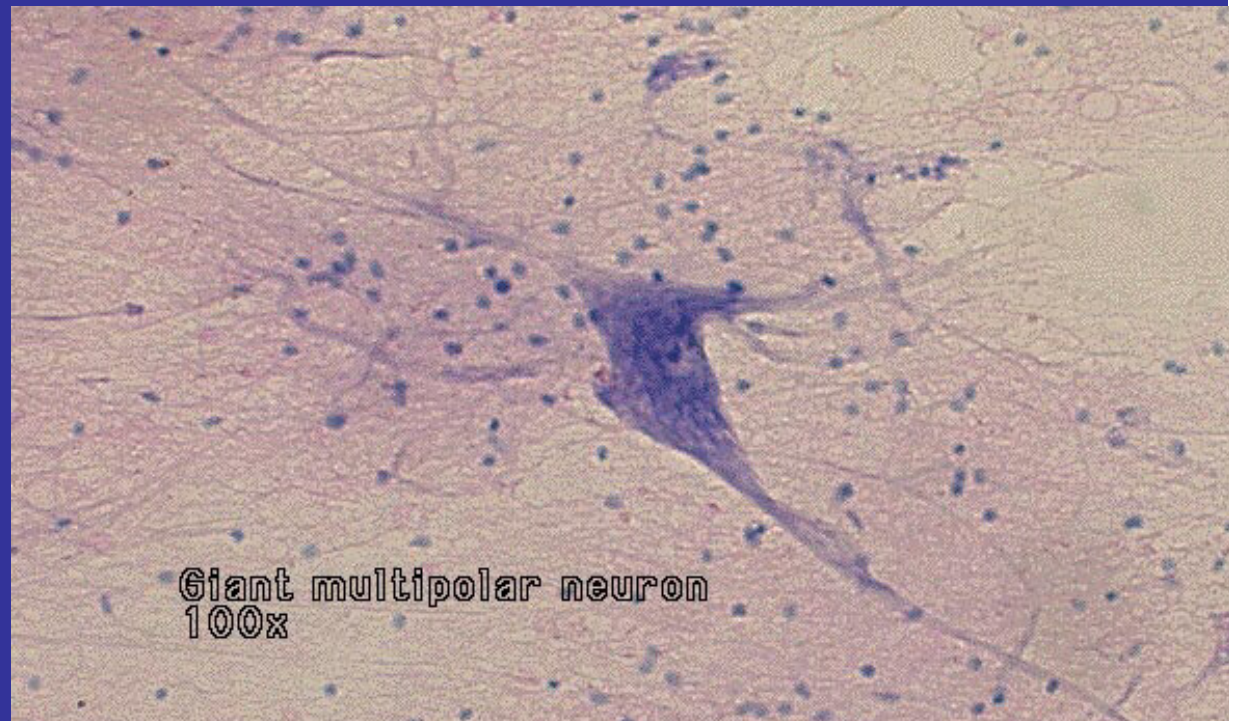
Neuronal Processes

- Armlike extensions emanating from every neuron.
- The CNS consists of both somata and processes whereas the bulk of the PNS consists of processes.
- **Tracts** = Bundles of processes in the CNS (**red arrow**)
- **Nerves** = Bundles of processes in the PNS
- 2 types of processes that differ in structure and function:
 - **Dendrites and Axons**

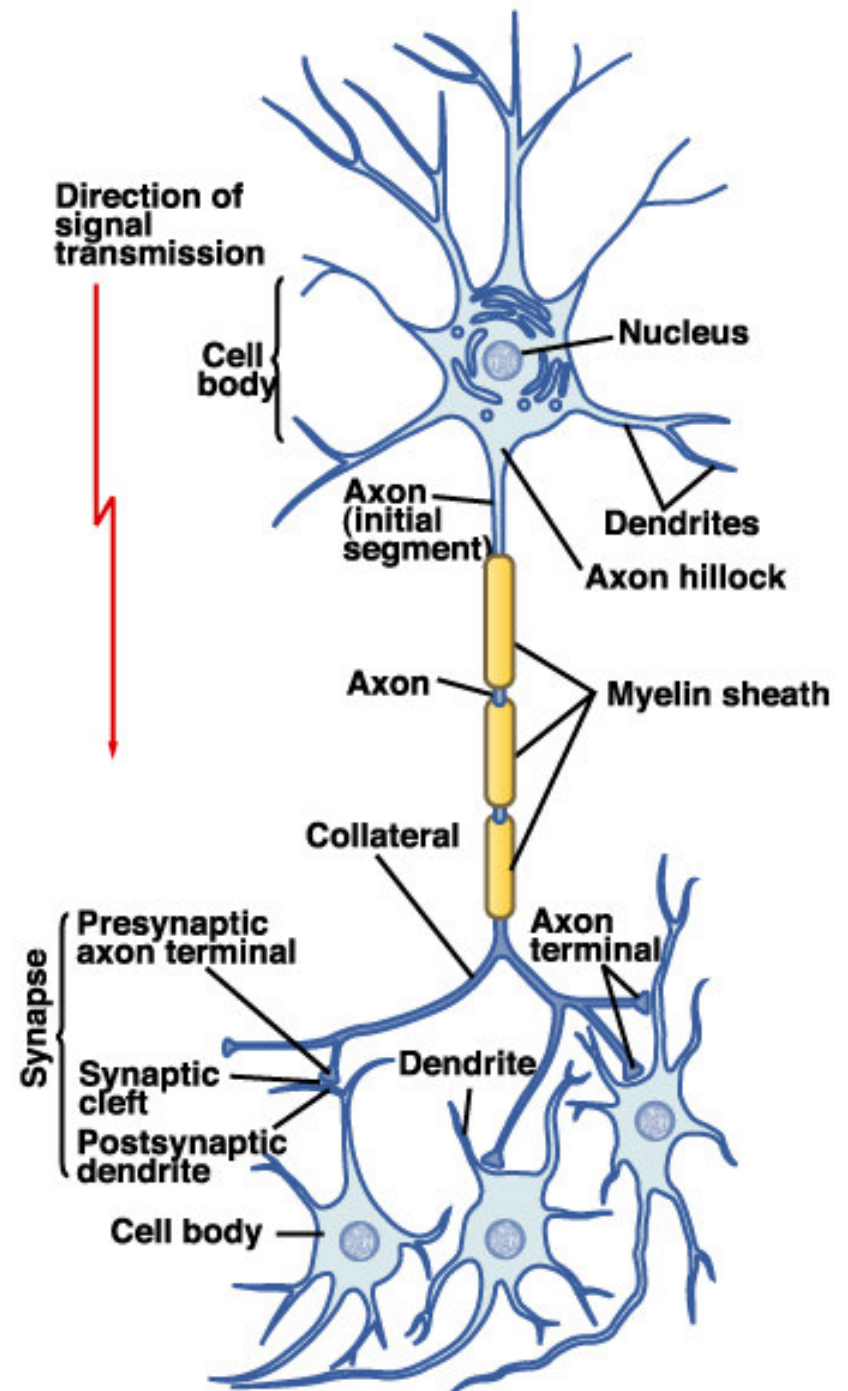


- Dendrites are thin, branched processes whose main function is to receive incoming signals.
- They effectively increase the surface area of a neuron to increase its ability to communicate with other neurons.
 - Small, mushroom-shaped **dendritic spines** further increase the SA
- Convey info towards the soma thru the use of **graded potentials** – which are somewhat similar to action potentials.

Notice the multiple processes extending from the neuron on the right. Also notice the multiple dark circular dots in the slide. They're not neurons, so they must be...

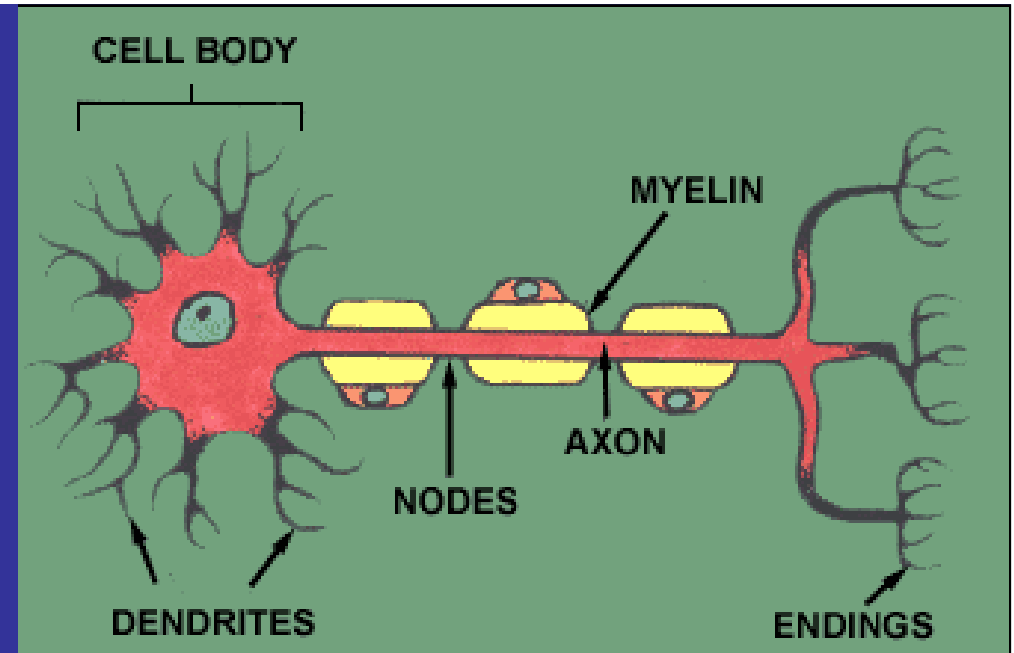


- Most neurons have a single axon – a long (up to 1m) process designed to convey info away from the cell body.
- Originates from a special region of the cell body called the **axon hillock**.
- Transmit APs from the soma toward the end of the axon where they cause NT release.
- Often branch sparsely, forming **collaterals**.
- Each collateral may split into **telodendria** which end in a **synaptic knob**, which contains **synaptic vesicles** – membranous bags of NTs.

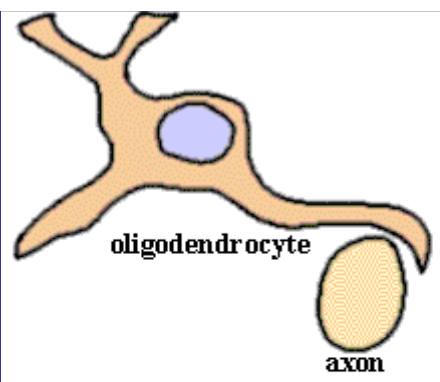


Axons

- **Axolemma** = axon plasma membrane.
- Surrounded by a **myelin sheath**, a wrapping of lipid which:
 - Protects the axon and electrically isolates it
 - Increases the rate of AP transmission
- The myelin sheath is made by _____ in the CNS and by _____ in the PNS.
- This wrapping is never complete. Interspersed along the axon are gaps where there is no myelin – these are **nodes of Ranvier**.
- In the PNS, the exterior of the Schwann cell surrounding an axon is the **neurilemma**

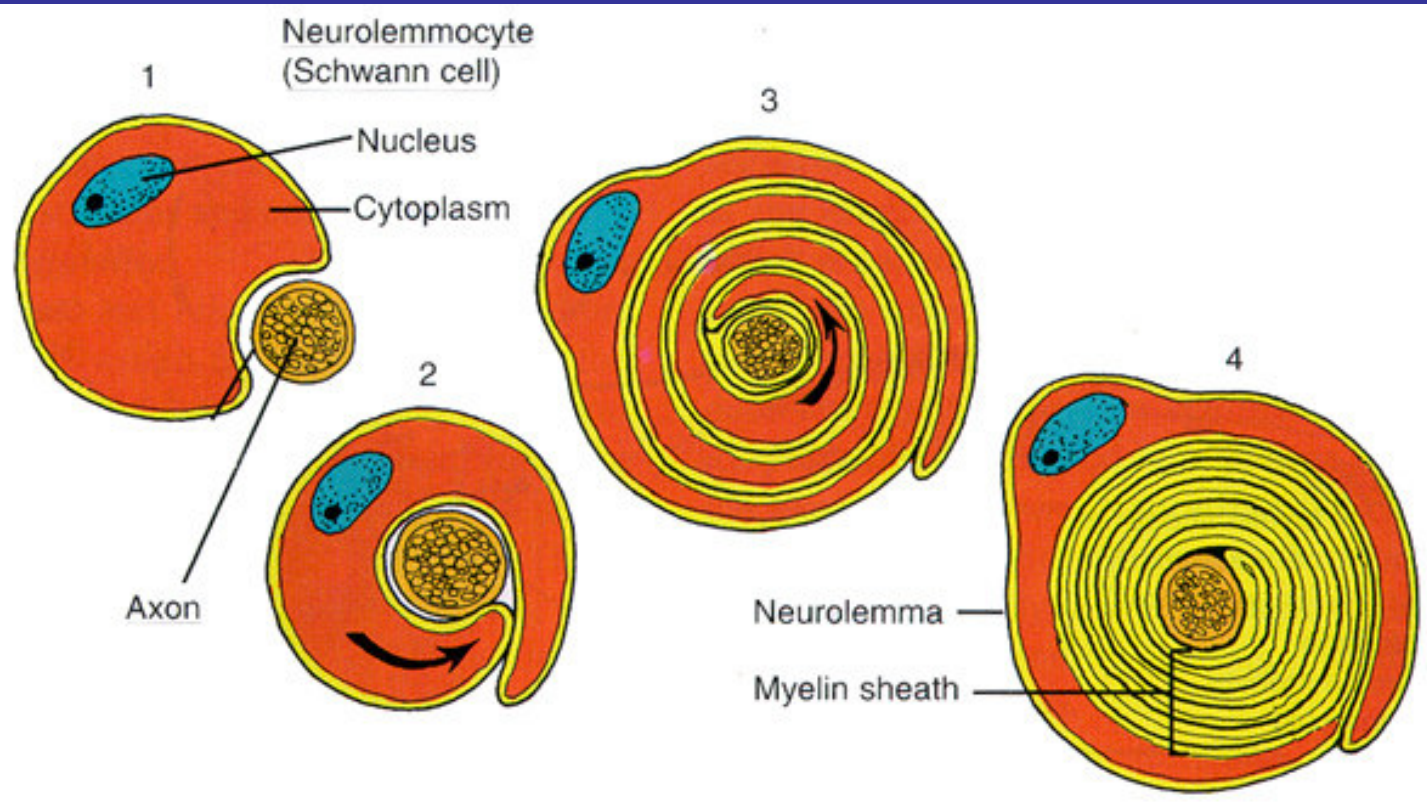


Myelination in the CNS



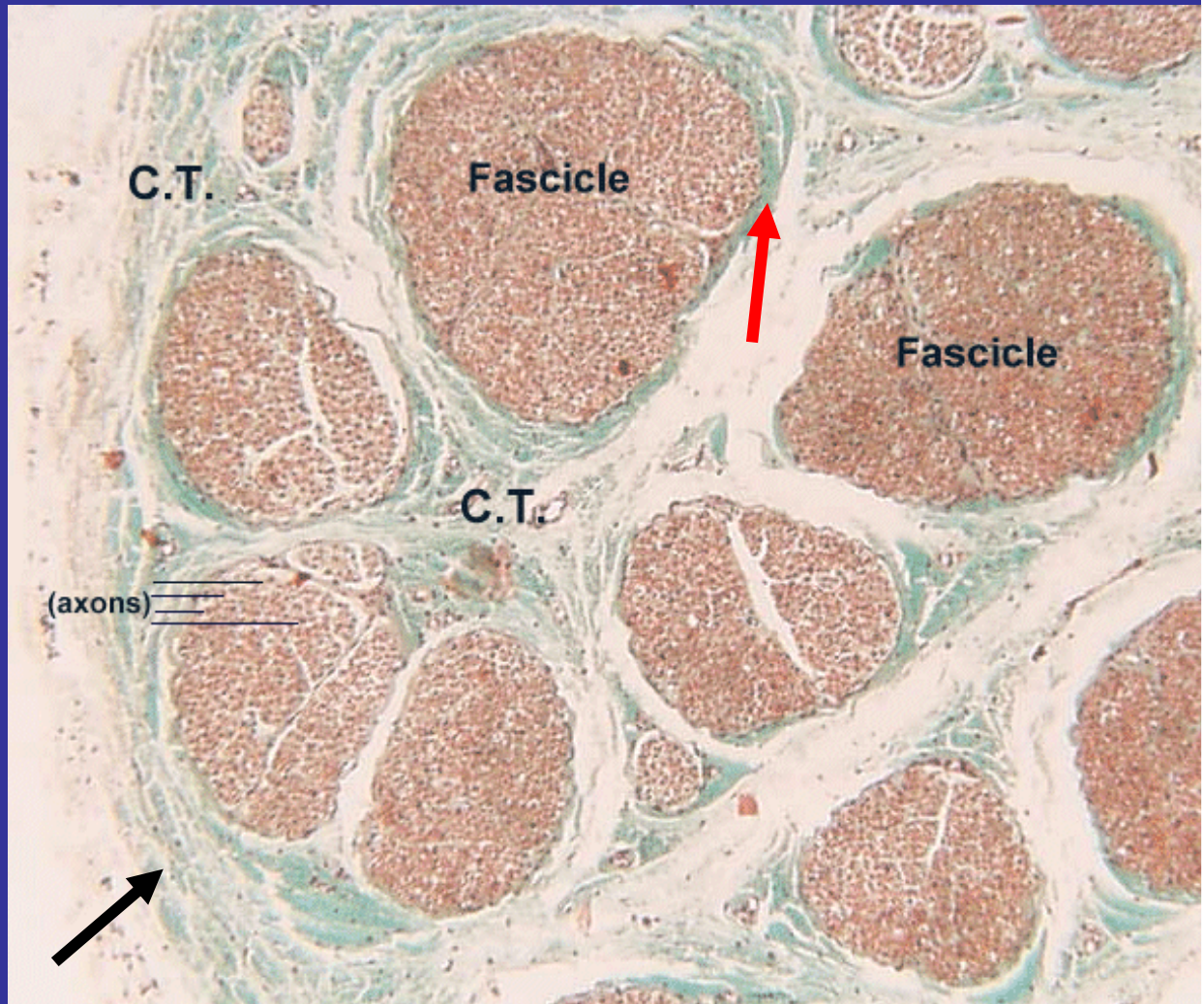
The Process of Myelination

Myelination in the PNS



- A bundle of processes in the PNS is a **nerve**.
- Within a nerve, each axon is surrounded by an **endoneurium** (*too small to see on the photomicrograph*) – a layer of loose CT.

- Groups of fibers are bound together into bundles (**fascicles**) by a **perineurium** (red arrow).
- All the fascicles of a nerve are enclosed by a **epineurium** (black arrow).



Communication

- Begins with the stimulation of a neuron.
 - One neuron may be stimulated by another, by a *receptor* cell, or even by some physical event such as pressure.
- Once stimulated, a neuron will communicate information about the causative event.
 - Such neurons are **sensory neurons** and they provide info about both the internal and external environments.
 - Sensory neurons (a.k.a. **afferent neurons**) will send info to neurons in the brain and spinal cord. There, **association neurons** (a.k.a. **interneurons**) will integrate the information and then perhaps send commands to **motor neurons** (**efferent neurons**) which synapse with muscles or glands.

Communication

- Thus, neurons need to be able to conduct information in 2 ways:
 1. From one end of a neuron to the other end.
 2. Across the minute space separating one neuron from another. (What is this called?)
 - *The 1st is accomplished electrically via APs.*
 - *The 2nd is accomplished chemically via neurotransmitters.*

Resting Potential

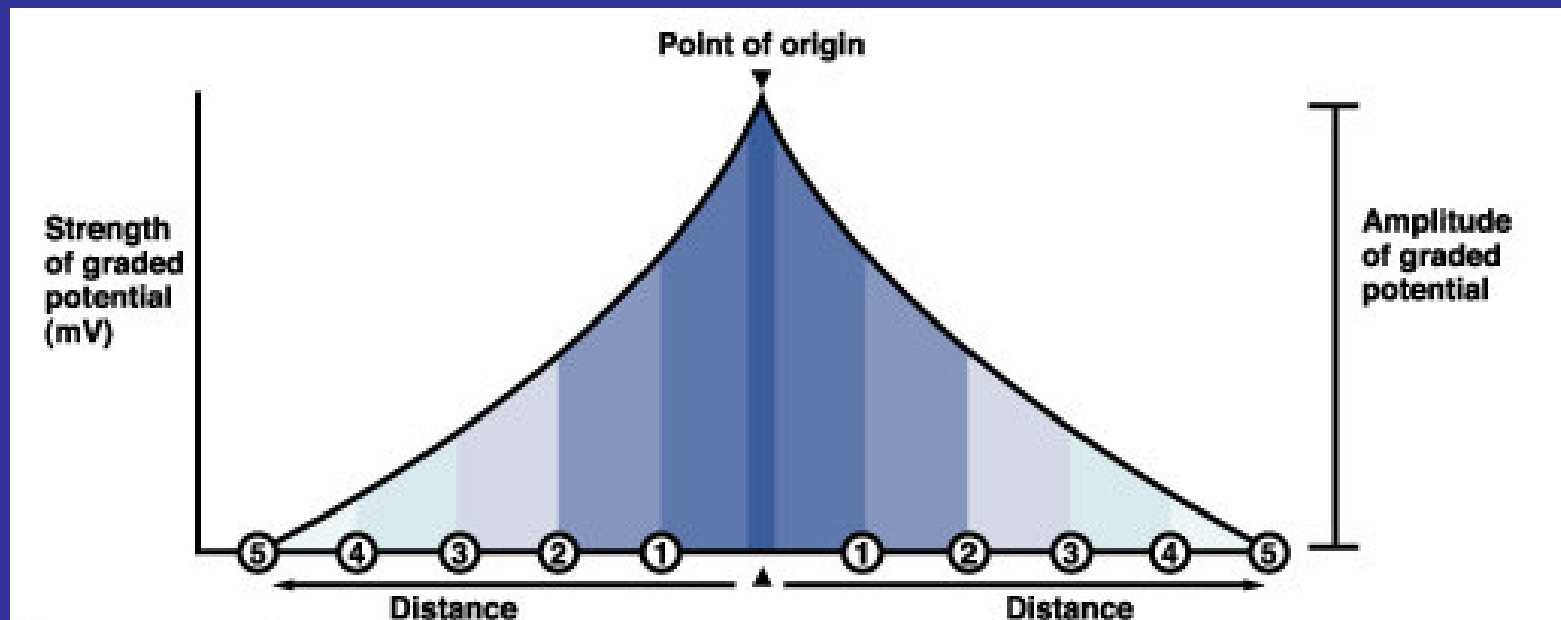
- Recall the definition of V_M from the muscle lectures.
 - Neurons are also highly polarized (w/ a V_M of about -70mV) due to:
 - » Differential membrane permeability to K^+ and Na^+
 - » The electrogenic nature of the Na^+/K^+ pump
 - » The presence of intracellular impermeable anions
- Changes in V_M allow for the generation of action potentials and thus informative intercellular communication.

Graded Potentials

- Let's consider a stimulus at the dendrite of a neuron.
- The stimulus could cause Na^+ channels to open and this would lead to depolarization. *Why?*
- However, dendrites and somata typically lack voltage-gated channels, which are found in abundance on the axon hillock and axolemma.
 - So what cannot occur on dendrites and somata?
- Thus, the question we must answer is, “what does this depolarization do?”

Graded Potentials

- The positive charge carried by the Na^+ spreads as a wave of depolarization through the cytoplasm (much like the ripples created by a stone tossed into a pond).
- As the Na^+ drifts, some of it will leak back out of the membrane.
 - What this means is that the degree of depolarization caused by the graded potential decreases with distance from the origin.

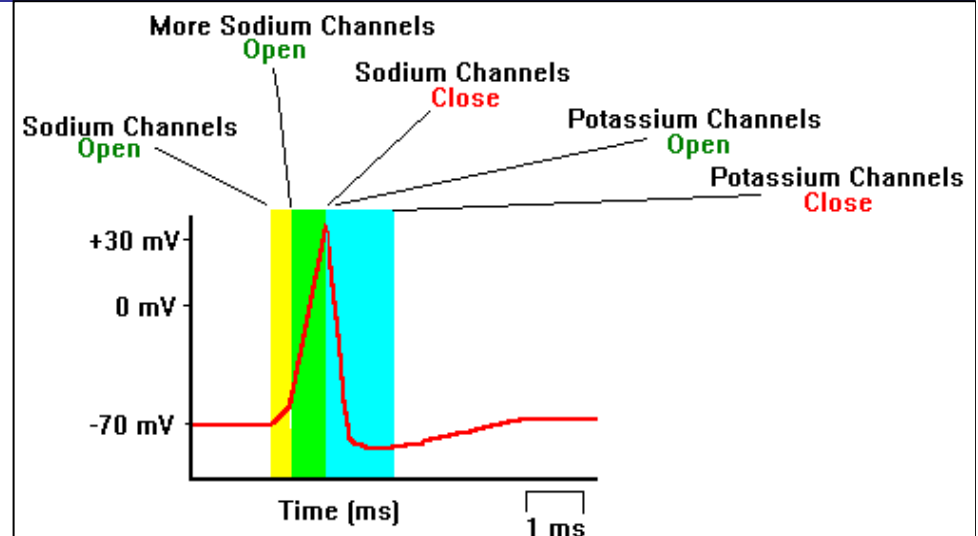
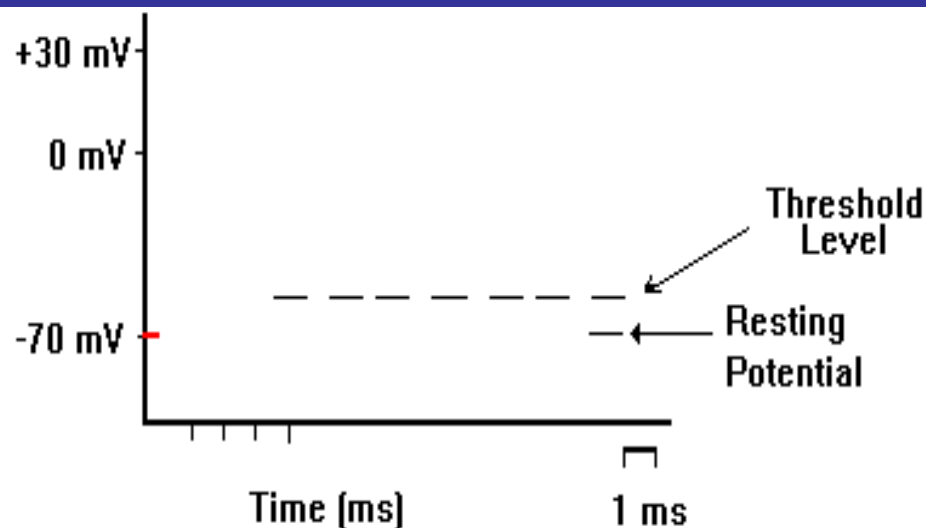


Graded Potentials

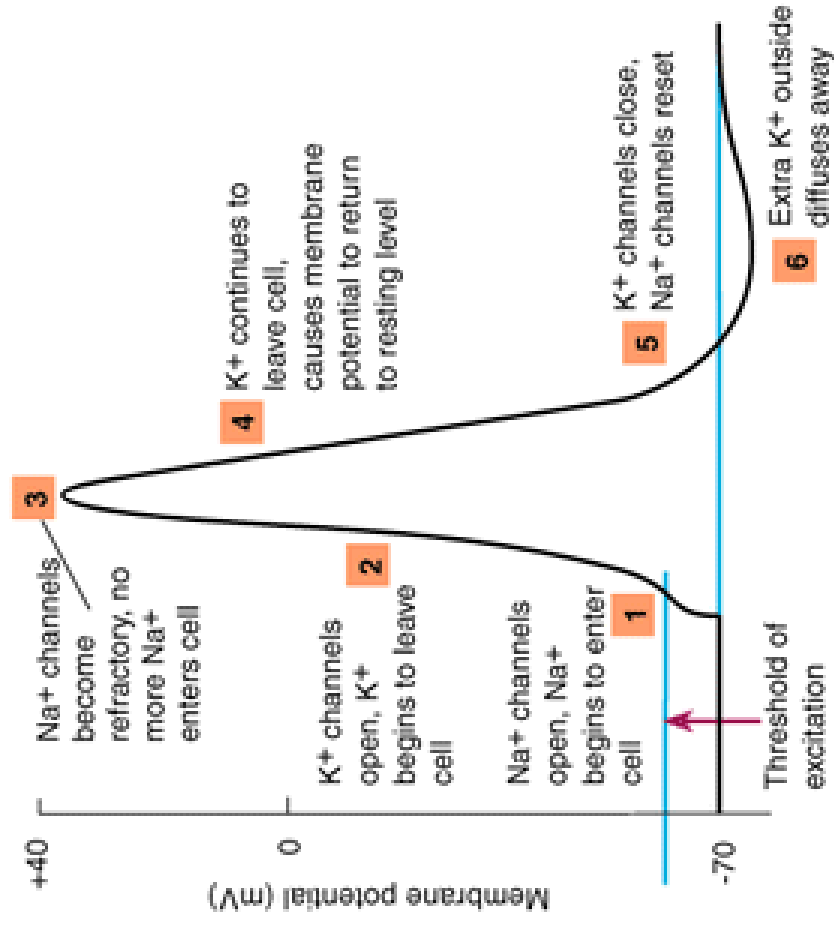
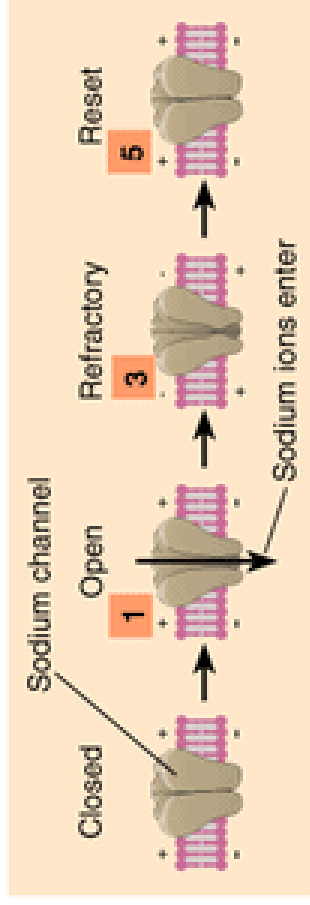
- Their initial amplitude may be of almost any size – it simply depends on how much Na^+ originally entered the cell.
- If the initial amplitude of the GP is sufficient, it will spread all the way to the axon hillock where V-gated channels reside.
- If the arriving potential change is suprathreshold, an AP will be initiated in the axon hillock and it will travel down the axon to the synaptic knob where it will cause NT exocytosis. If the potential change is subthreshold, then no AP will ensue and nothing will happen.

Action Potentials

- If V_M reaches threshold, Na^+ channels open and Na^+ influx ensues, depolarizing the cell and causing the V_M to increase. This is the rising phase of an AP.
- Eventually, the Na^+ channel will have inactivated and the K^+ channels will be open. Now, K^+ effluxes and repolarization occurs. This is the falling phase.
 - K^+ channels are slow to open and slow to close. This causes the V_M to take a brief dip below resting V_M . This dip is the **undershoot** and is an example of **hyperpolarization**.



► The Movements of Ions During the Action Potential

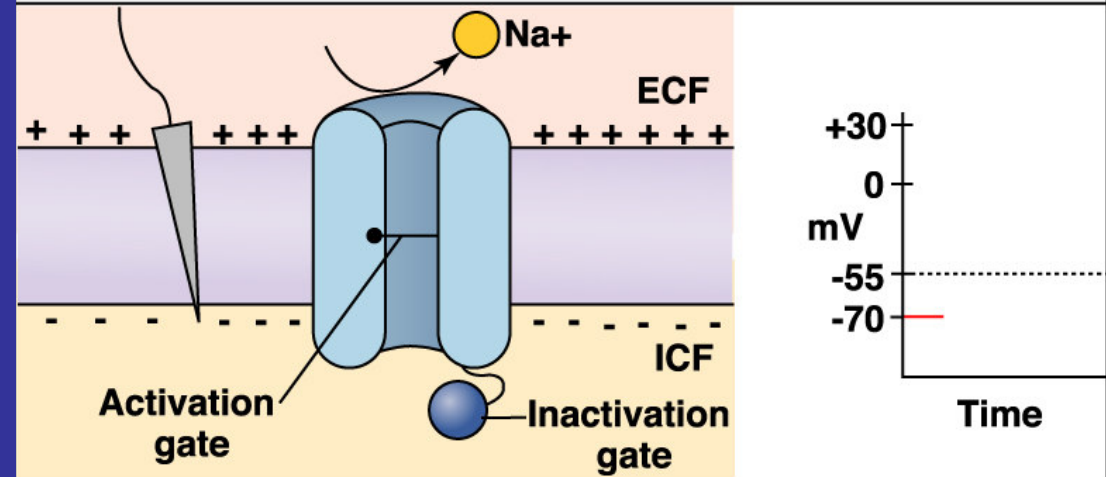


Na⁺ Channels

- They have 2 gates.
 - At rest, one is closed (the **activation gate**) and the other is open (the **inactivation gate**).
 - Suprathreshold depolarization affects both of them.

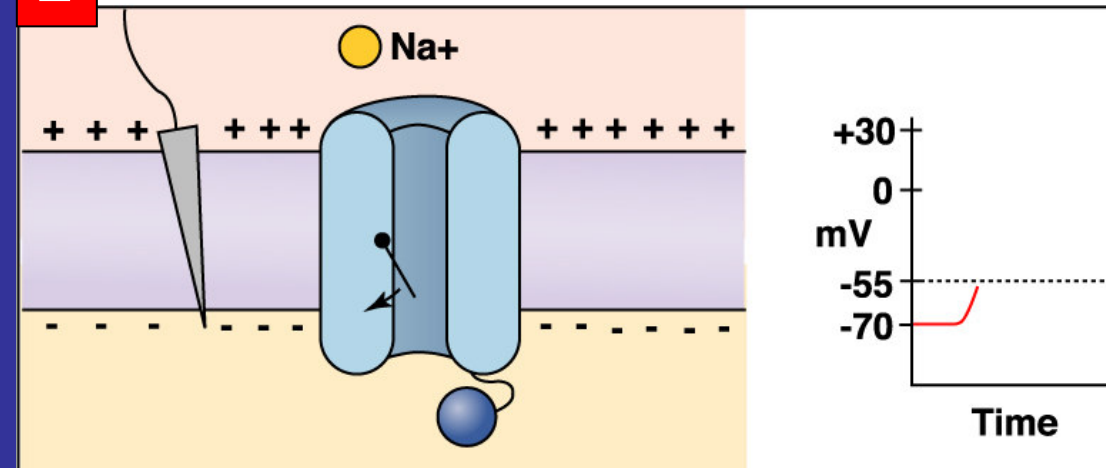
1

At the resting membrane potential, the activation gate closes the channel.

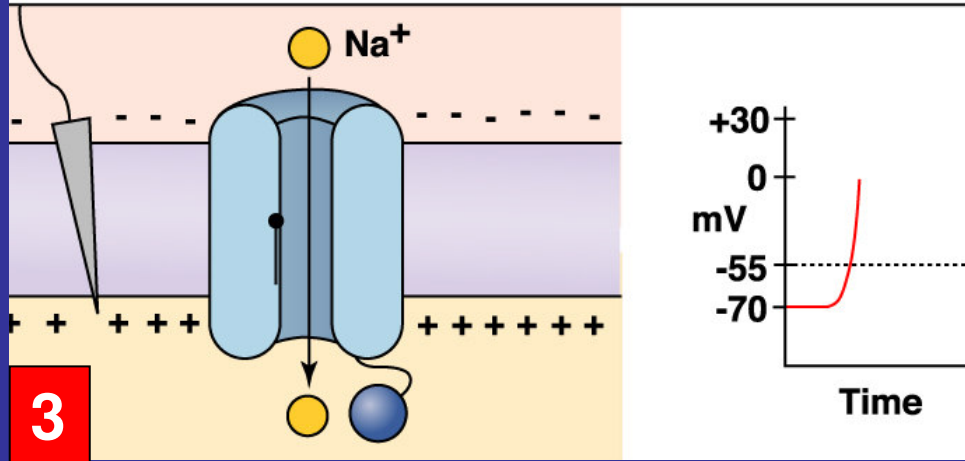


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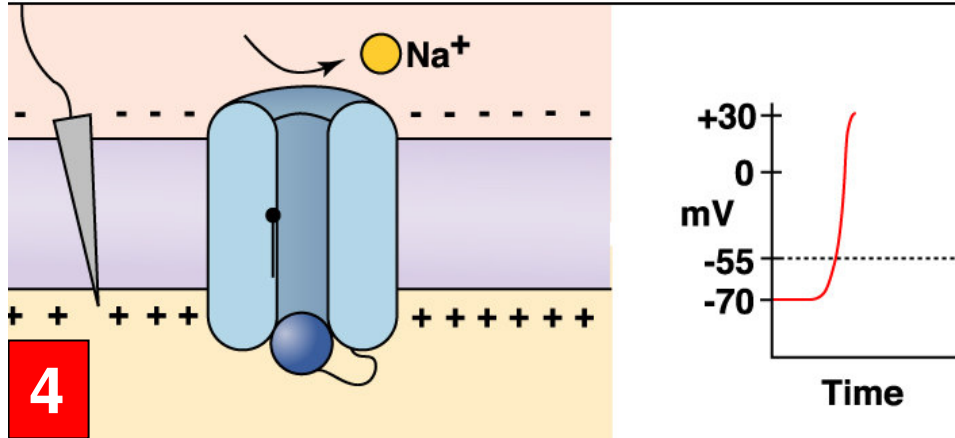
Depolarizing stimulus arrives at the channel.



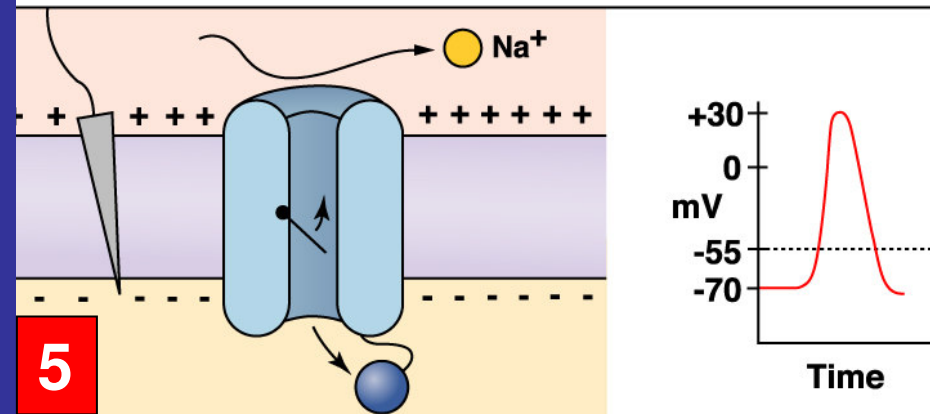
With activation gate open, Na^+ enters the cell.



Inactivation gate closes and Na^+ entry stops.



During repolarization caused by K^+ leaving the cell, the two gates reset to their original positions.



Absolute Refractory Period

- During the time interval between the opening of the Na^+ channel activation gate and the opening of the inactivation gate, a Na^+ channel CANNOT be stimulated.
 - This is the **ABSOLUTE REFRACTORY PERIOD**.
 - A Na^+ channel cannot be involved in another AP until the inactivation gate has been reset.
 - This being said, can you determine why an AP is said to be unidirectional.
 - What are the advantages of such a scenario?

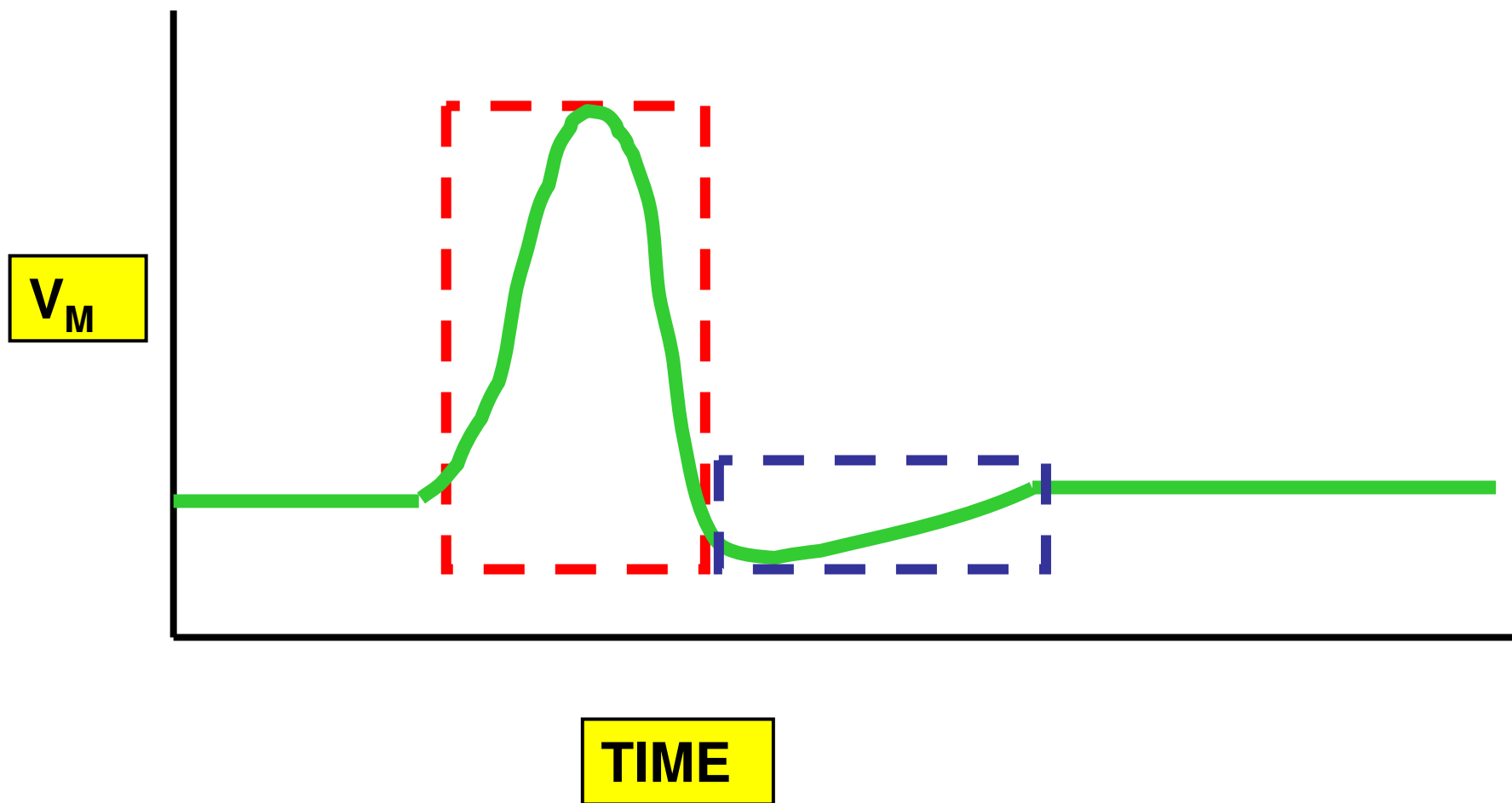
Relative Refractory Period

- Could an AP be generated during the undershoot?
 - Yes! But it would take an initial stimulus that is much, much stronger than usual.
 - *WHY?*
 - This situation is known as the **relative refractory period**.

Imagine, if you will, a toilet.

When you pull the handle, water floods the bowl. This event takes a couple of seconds and you cannot stop it in the middle. Once the bowl empties, the flush is complete. Now the upper tank is empty. If you try pulling the handle at this point, nothing happens (**absolute refractory**). Wait for the upper tank to begin refilling. You can now flush again, but the intensity of the flushes increases as the upper tank refills (**relative refractory**)

In this figure, what do the red and blue box represent?



Some Action Potential Questions

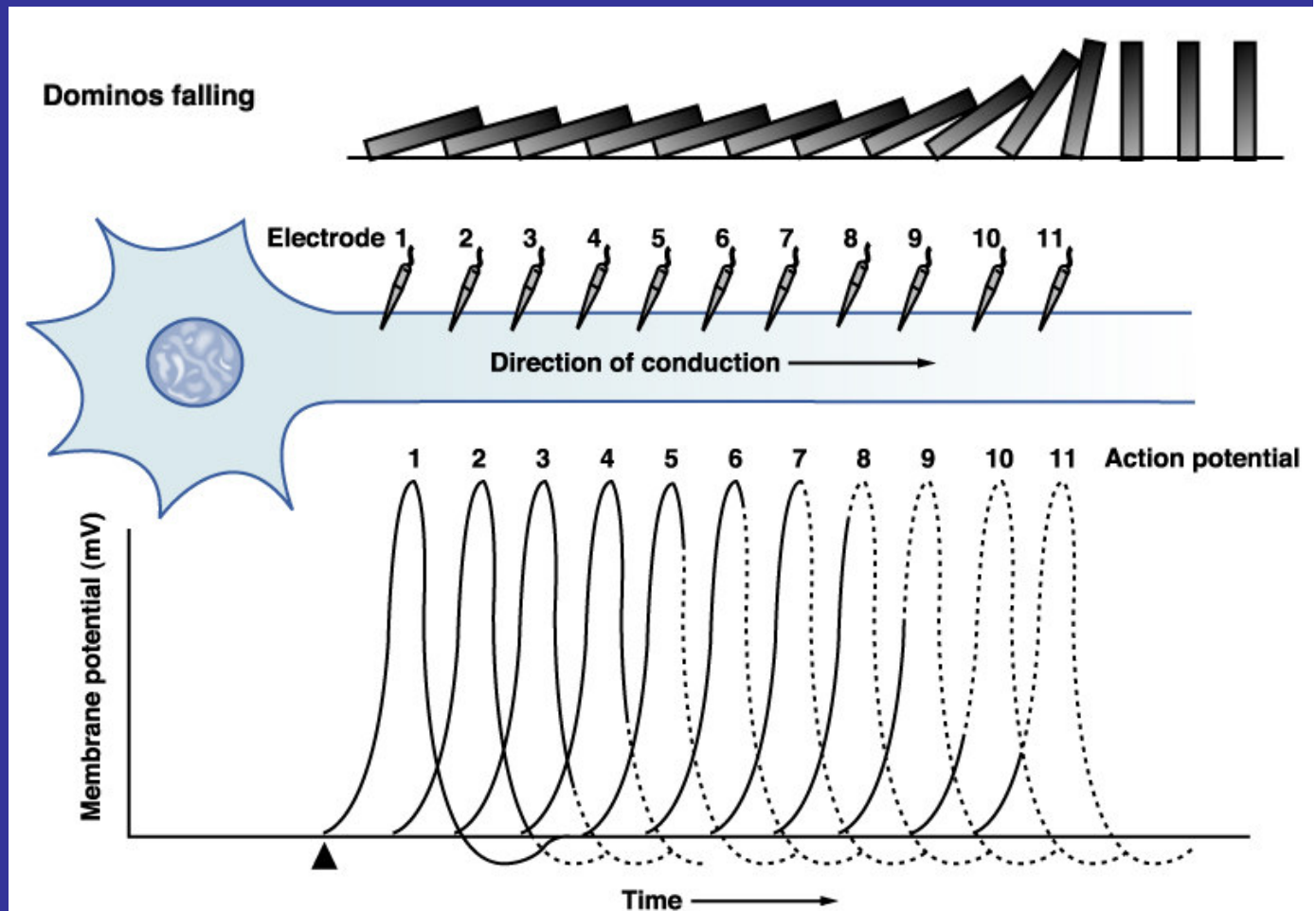
- *What does it mean when we say an AP is “all or none?”*
 - *Can you ever have $\frac{1}{2}$ an AP?*
- *How does the concept of threshold relate to the “all or none” notion?*
- *Will one AP ever be bigger than another?*
 - *Why or why not?*

Action Potential Conduction

- If an AP is generated at the axon hillock, it will travel all the way down to the synaptic knob.
- The manner in which it travels depends on whether the neuron is myelinated or unmyelinated.
- Unmyelinated neurons undergo the *continuous conduction* of an AP whereas myelinated neurons undergo *saltatory conduction* of an AP.

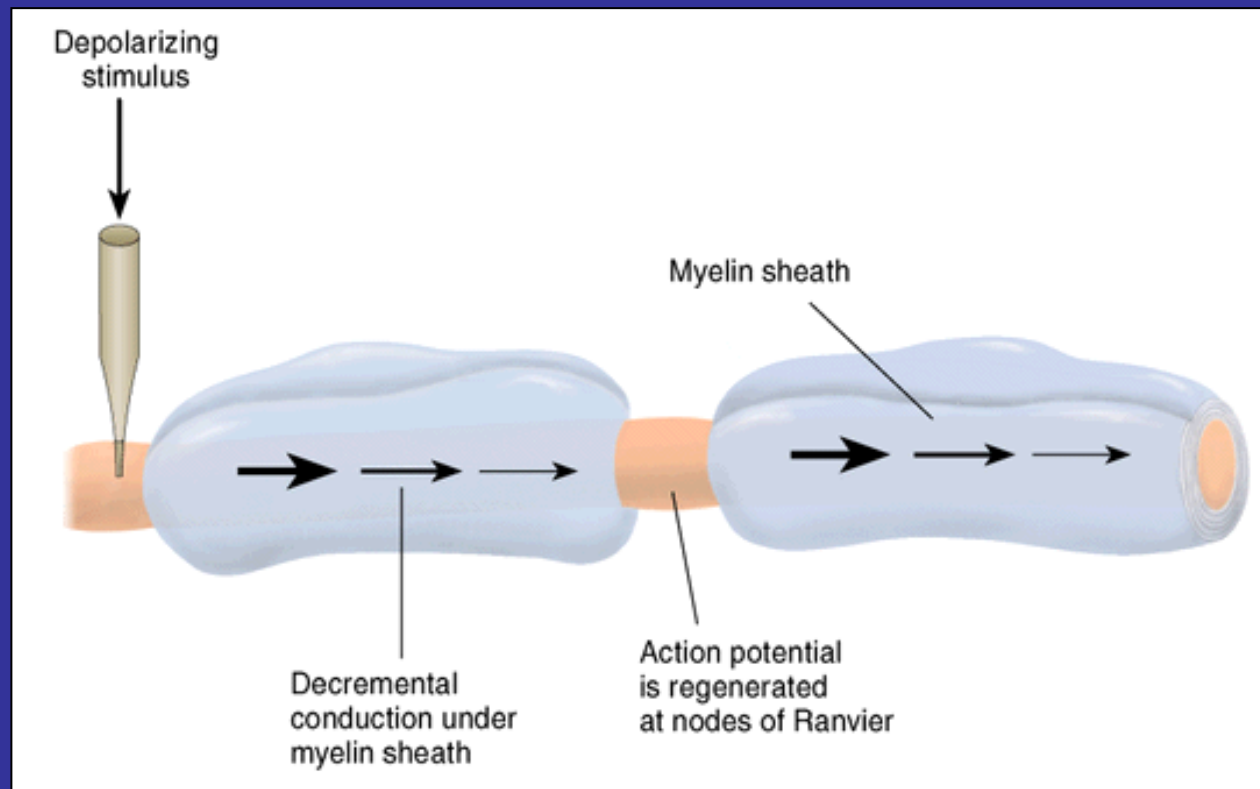
Continuous Conduction

- Occurs in unmyelinated axons.
- In this situation, the wave of de- and repolarization simply travels from one patch of membrane to the next adjacent patch.
- APs moved in this fashion along the sarcolemma of a muscle fiber as well.
- Analogous to dominoes falling.

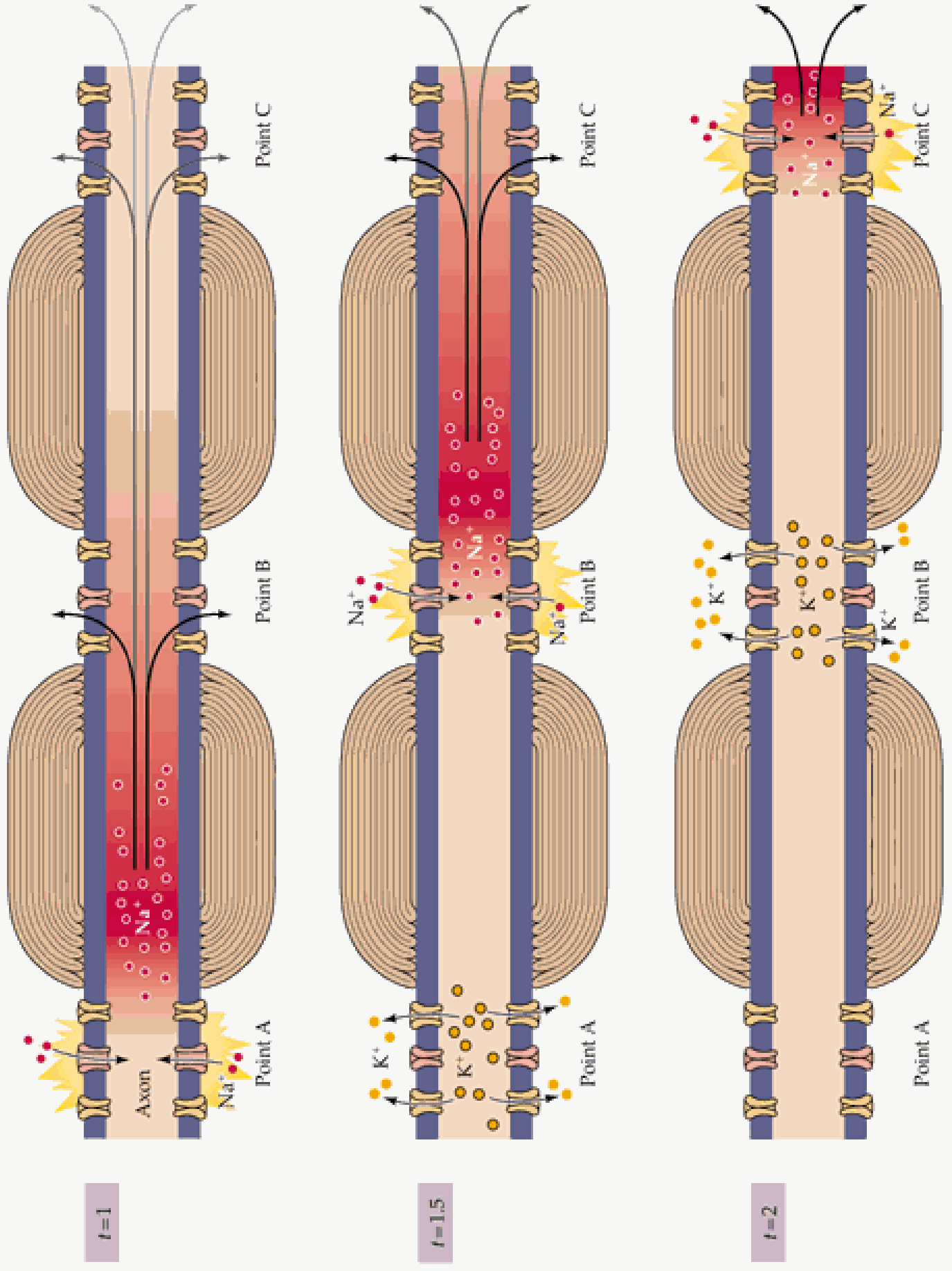


Saltatory Conduction

- Occurs in myelinated axons.
- *Saltare* is a Latin word meaning “to leap.”
- Recall that the myelin sheath is not completed. There exist myelin free regions along the axon, the nodes of Ranvier.



(B) Action potential propagation



Rates of AP Conduction

1. Which do you think has a faster rate of AP conduction – myelinated or unmyelinated axons?
2. Which do you think would conduct an AP faster – an axon with a large diameter or an axon with a small diameter?

The answer to #1 is a myelinated axon. If you can't see why, then answer this question: could you move 100ft faster if you walked heel to toe or if you bounded in a way that there were 3ft in between your feet with each step?

The answer to #2 is an axon with a large diameter. If you can't see why, then answer this question: could you move faster if you walked through a hallway that was 6ft wide or if you walked through a hallway that was 1ft wide?

Types of Nerve Fibers

1. Group A

- Axons of the somatic sensory neurons and motor neurons serving the skin, skeletal muscles, and joints.
- Large diameters and thick myelin sheaths.
 - How does this influence their AP conduction?

2. Group B

- Type B are lightly myelinated and of intermediate diameter.

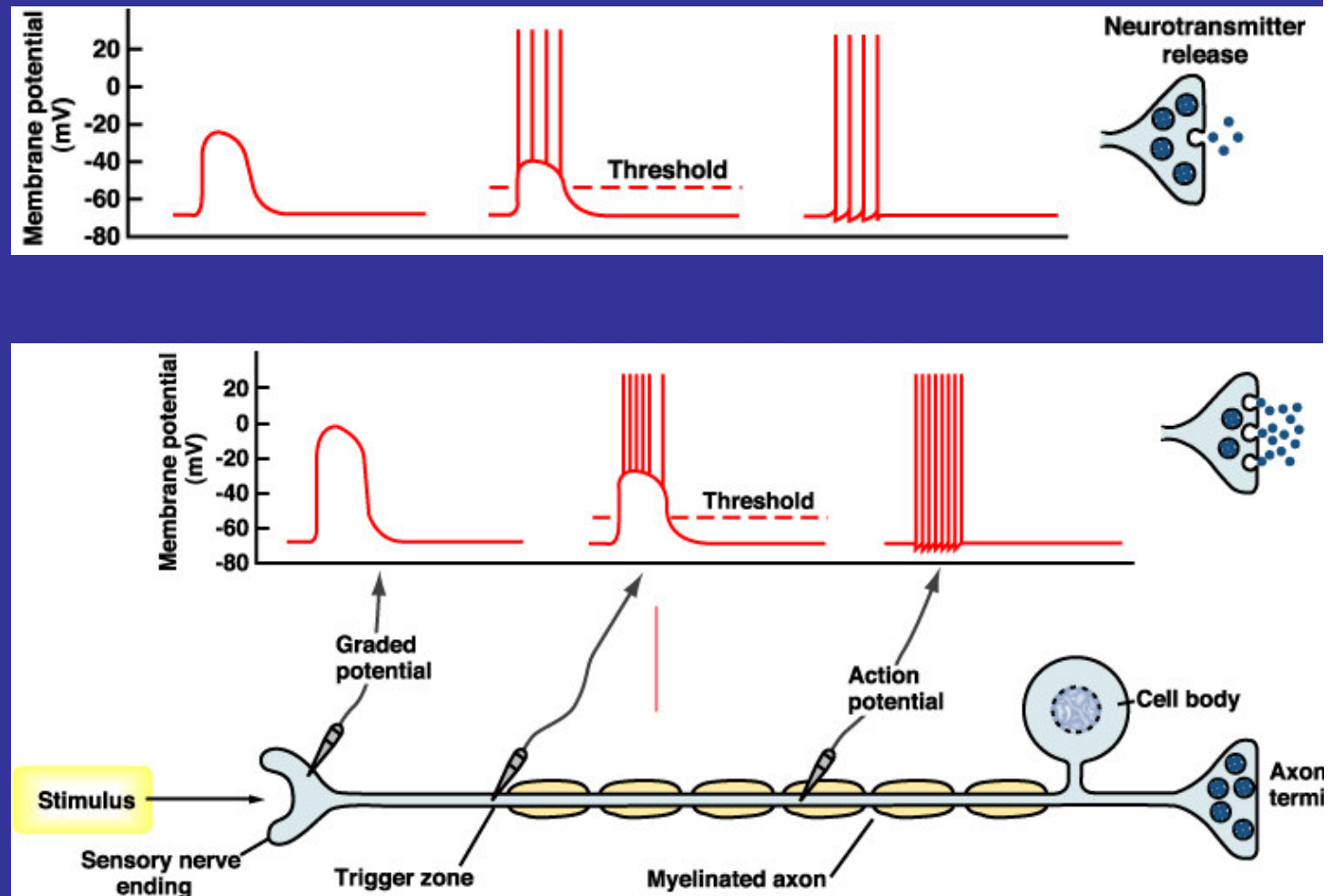
3. Group C

- Type C are unmyelinated and have the smallest diameter.
- Autonomic nervous system fibers serving the visceral organs, visceral sensory fibers, and small somatic sensory fibers are Type B and Type C fibers.

Now we know how signals get from one end of an axon to the other, but how exactly do APs send information?

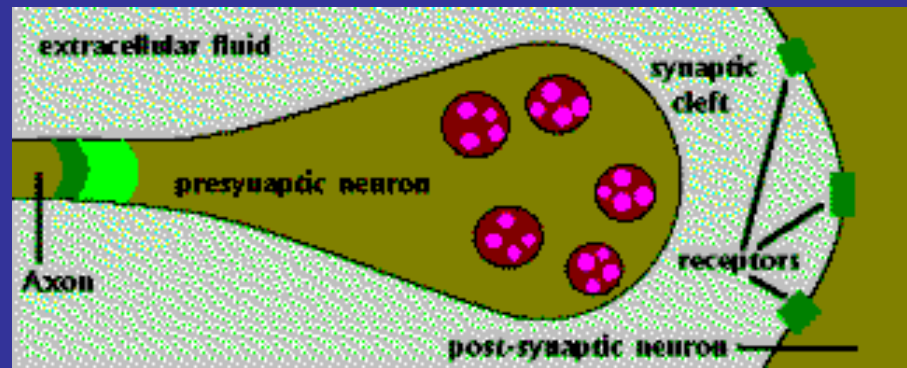
- Info can't be encoded in AP size, since they're "all or none."

In the diagram on the right, notice the effect that the size of the graded potential has on the frequency of AP's and on the quantity of NT released. The weak stimulus resulted in a small amt of NT release compared to the strong stimulus.



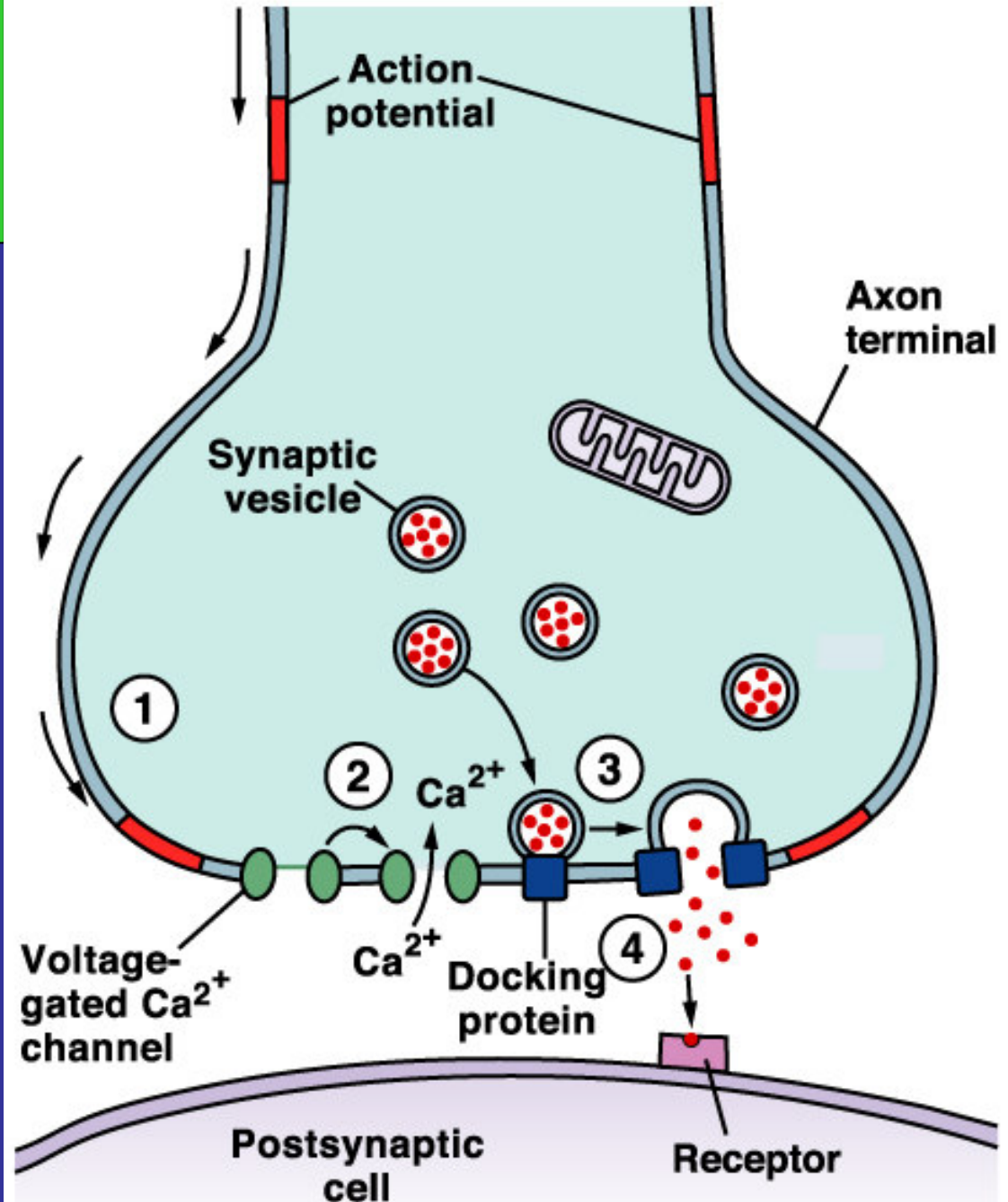
Chemical Signals

- One neuron will transmit info to another neuron or to a muscle or gland cell by releasing chemicals called neurotransmitters.
- The site of this chemical interplay is known as the **synapse**.
 - An axon terminal (**synaptic knob**) will abut another cell, a neuron, muscle fiber, or gland cell.
 - This is the site of **transduction** – the conversion of an electrical signal into a chemical signal.



Synaptic Transmission

- An AP reaches the axon terminal of the presynaptic cell and causes V-gated Ca^{2+} channels to open.
- Ca^{2+} rushes in, binds to regulatory proteins & initiates NT exocytosis.
- NTs diffuse across the synaptic cleft and then bind to receptors on the postsynaptic membrane and initiate some sort of response on the postsynaptic cell.

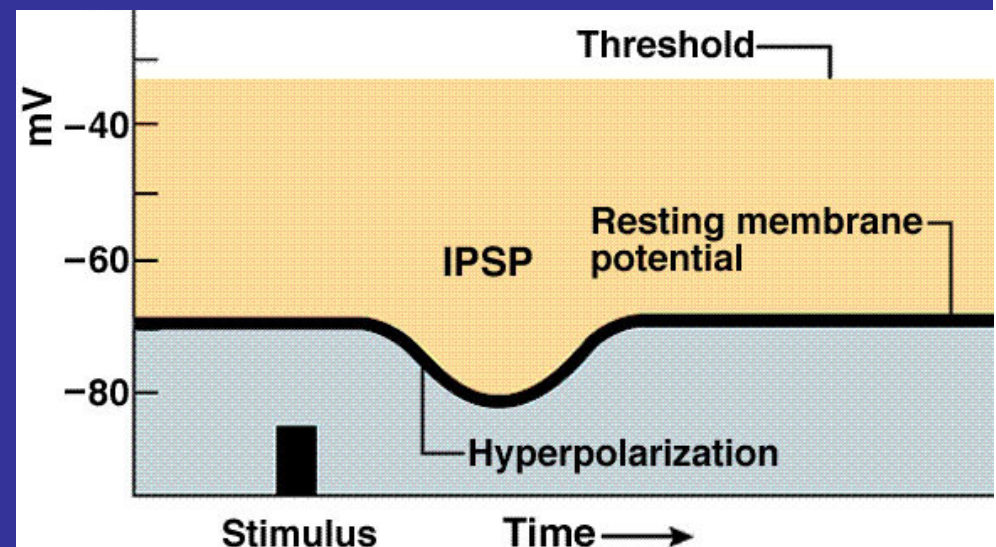
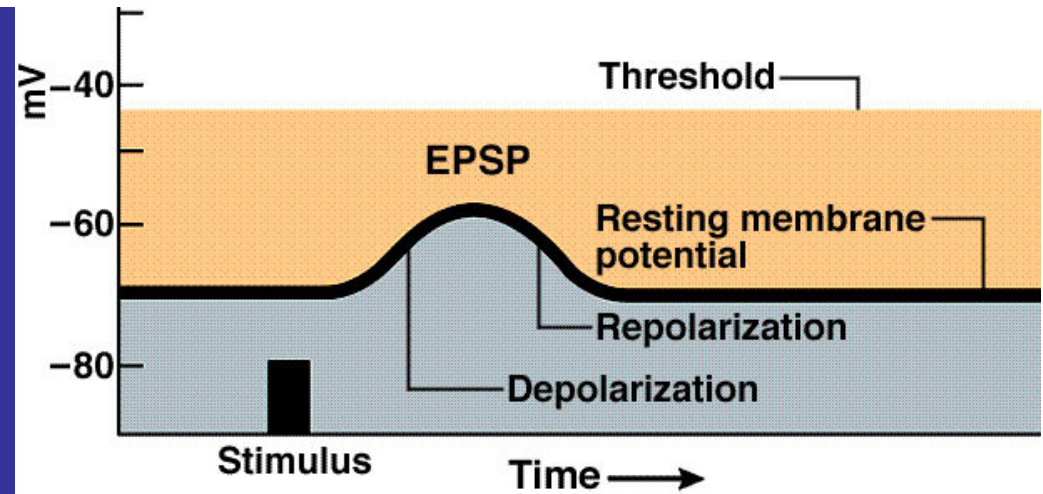


Effects of the Neurotransmitter

- Different neurons can contain different NTs.
- Different postsynaptic cells may contain different receptors.
 - Thus, the effects of an NT can vary.
- Some NTs cause cation channels to open, which results in a graded depolarization.
- Some NTs cause anion channels to open, which results in a graded hyperpolarization.

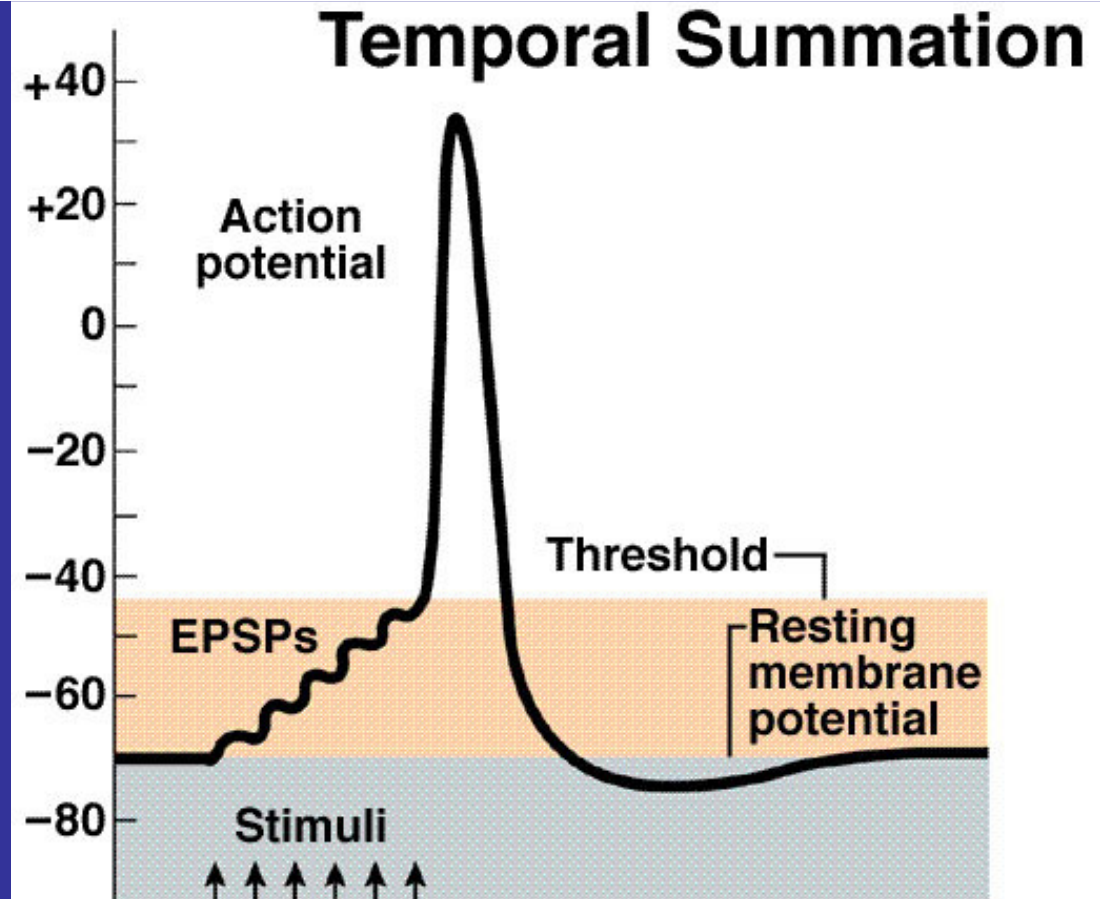
EPSPs & IPSPs

- Typically, a single synaptic interaction will not create a graded depolarization strong enough to migrate to the axon hillock and induce the firing of an AP.
 - However, a graded depolarization will bring the neuronal V_M closer to threshold. Thus, it's often referred to as an **excitatory postsynaptic potential or EPSP**.
 - Graded hyperpolarizations bring the neuronal V_M farther away from threshold and thus are referred to as **inhibitory postsynaptic potentials or IPSPs**.



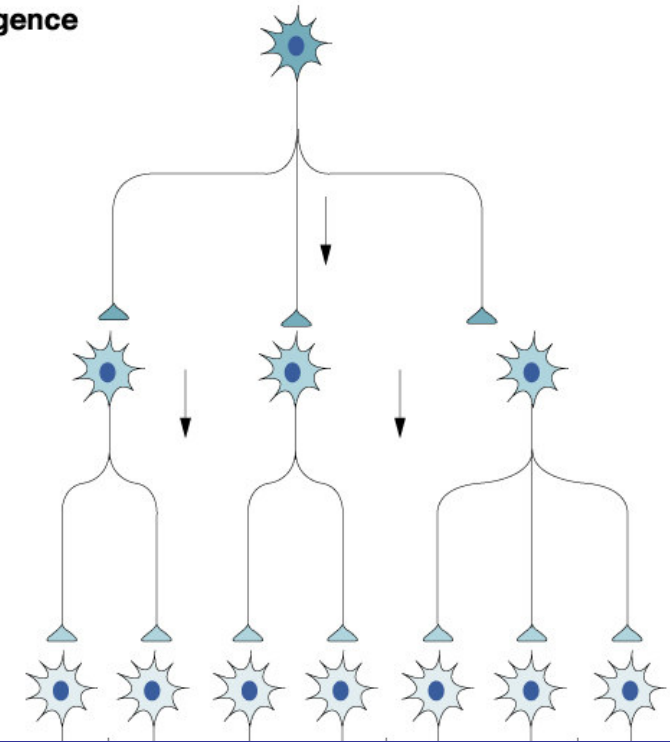
Summation

- One EPSP is usually not strong enough to cause an AP.
- However, EPSPs may be summed.
- **Temporal summation**
 - The same presynaptic neuron stimulates the postsynaptic neuron multiple times in a brief period. The depolarization resulting from the combination of all the EPSPs may be able to cause an AP.
- **Spatial summation**
 - Multiple neurons all stimulate a postsynaptic neuron resulting in a combination of EPSPs which may yield an AP

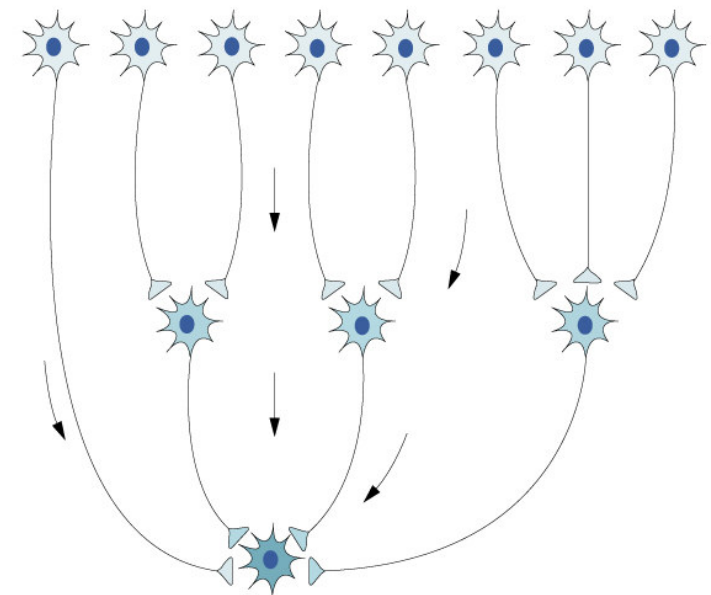


- Communication btwn neurons is not typically a one-to-one event.
 - Sometimes a single neuron branches and its collaterals synapse on multiple target neurons. This is known as **divergence**.
 - A single postsynaptic neuron may have synapses with as many as 10,000 presynaptic neurons. This is **convergence**.
 - *Can you think of an advantage to having convergent and divergent circuits?*

Divergence



Convergence



- Neurons may also form reverberating circuits.
 - A chain of neurons where many give off collaterals that go back and synapse on previous neurons.
 - What might be a benefit of this arrangement?



Neurotransmitter Removal

- Why did we want to remove ACh from the neuromuscular junction?
- How was ACh removed from the NMJ?
- NTs are removed from the synaptic cleft via:
 - Enzymatic degradation
 - Diffusion
 - Reuptake

