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Number

9

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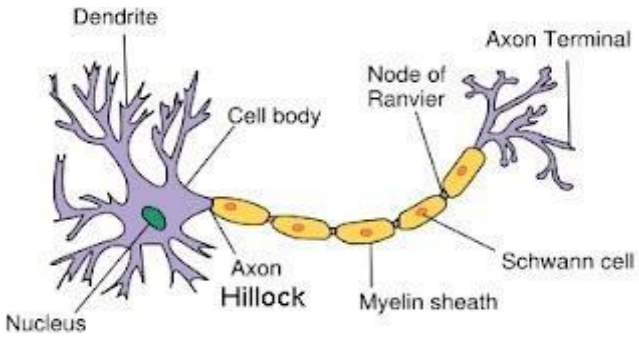
Nerve Cells (Neurons)

*Remember:

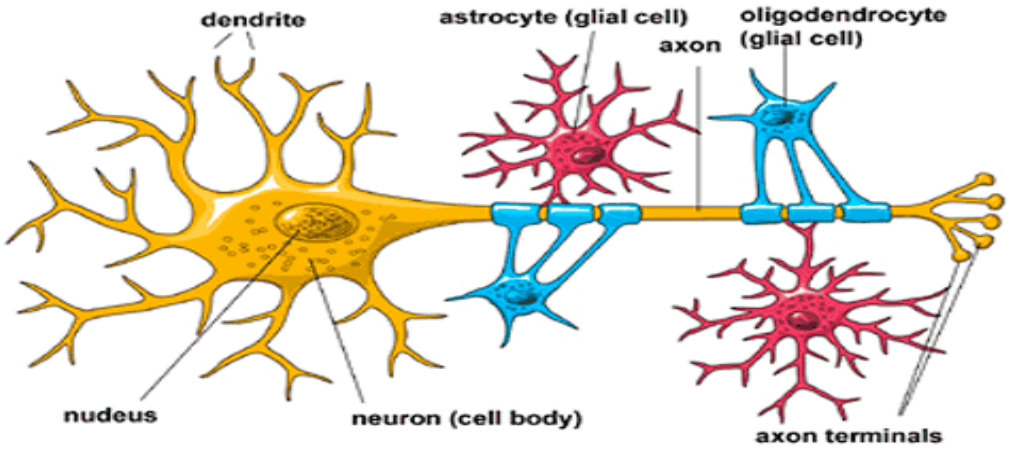
The neural cell consists of:
1-Cell body
2-Dendrites
3-Axon which ends as axon terminals.



The conduction of impulse through the neural cell:

The most general function of neural cells is to generate action potential. This action potential is generated at the axon hillock (the junction between the axon and the cell body) and then propagated towards the axon terminals.

Looking at the following figure, what can you notice?



In addition to neural cells, there are many types of **supportive cells** around the neurons that perform different functions such as:

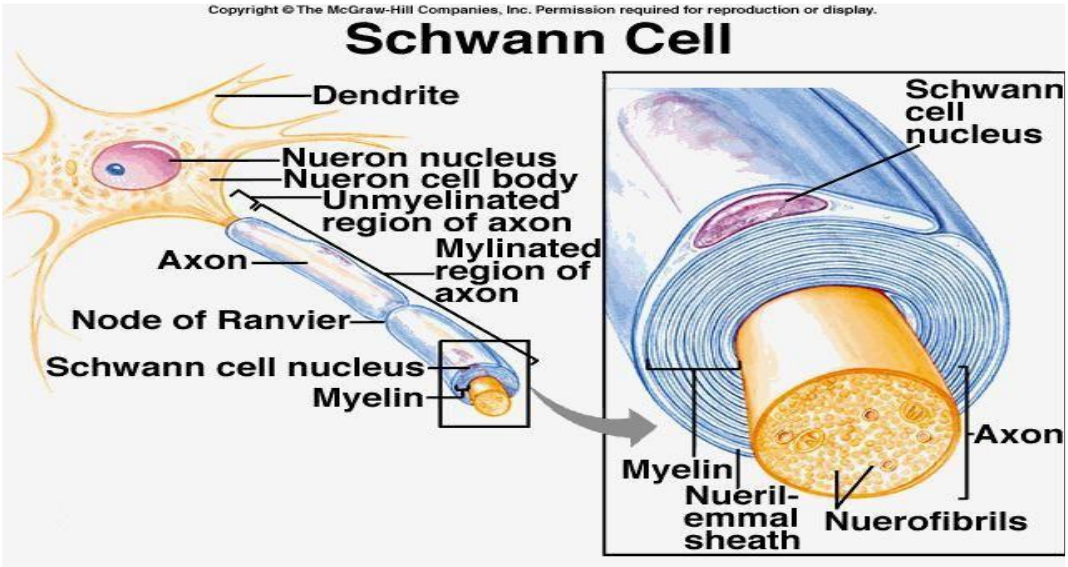
A. Cleaning the medium around the neuron: since neural cells are functioning all the time, potassium ions are released continuously, the neural cells return back some of these ions and these supportive cells help them.

→This is important for having a healthy medium and so a healthy function of the neurons (lowering K+ concentration leads to the highest negative resting potential and thus preventing the excitation by small stimuli).

B. Phagocytic activity: when a pathogen is trying to enter, a barrier called blood brain barrier prevents passage of any pathogen from the blood, but at any time we have some passage of these pathogens these supportive cells defeat them.

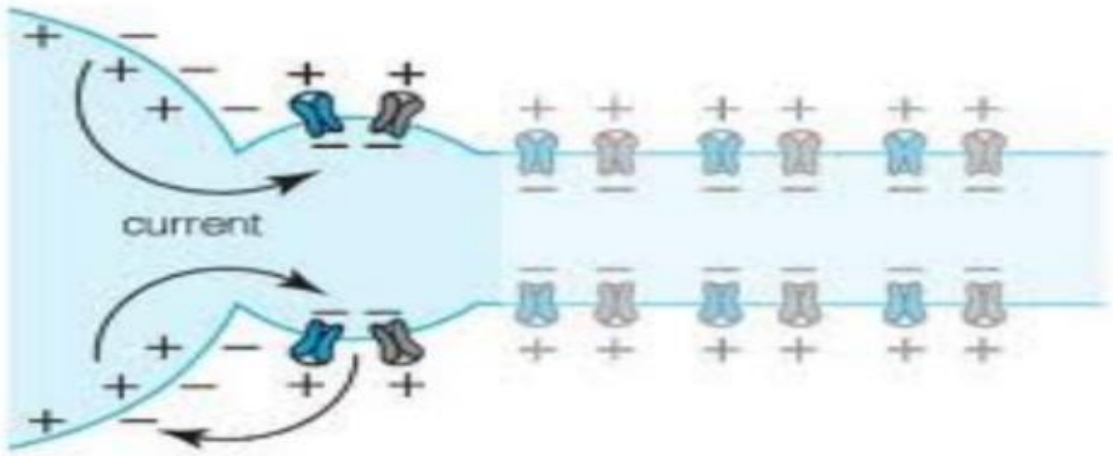
C. Releasing neurotrophic factors: since neural cells can't be replaced if they are destroyed (They do not divide by mitosis), neurotrophic factors are released to maintain the survival of these cells as long as possible.

D. **Myelination** (forming myelin sheath) of axons, by the help of specialized cells which are called **Schwann cells.** These cells wrap around the axon and secrete a lipid substance called **sphingomyelin** which is a great electrical insulator that decreases ion flow throughout the membrane. There are gaps/ uninsulated areas in the myelin sheath where ions can still flow with ease through the axon membrane and the intracellular fluid inside the axon. These gaps are called **Nodes of Ranvier** and are used for transmission of impulses along a myelinated nerve (generation of action potential).



How is an impulse travelling along the nerve fiber?

As an action potential is generated in one area, it becomes positive inside and negative outside while the nearer area is still polarized (negative inside and positive outside)
→This creates local ionic current as in the picture: current flow from the positively charged to the negatively charged (resting) regions at both sides of the membrane (but the internal current is more important) and this changes the membrane potential (becoming less negative inside and less positive outside in the neighbouring resting regions)
→so, the membrane is getting depolarized, reaching the threshold for action potential at that region.

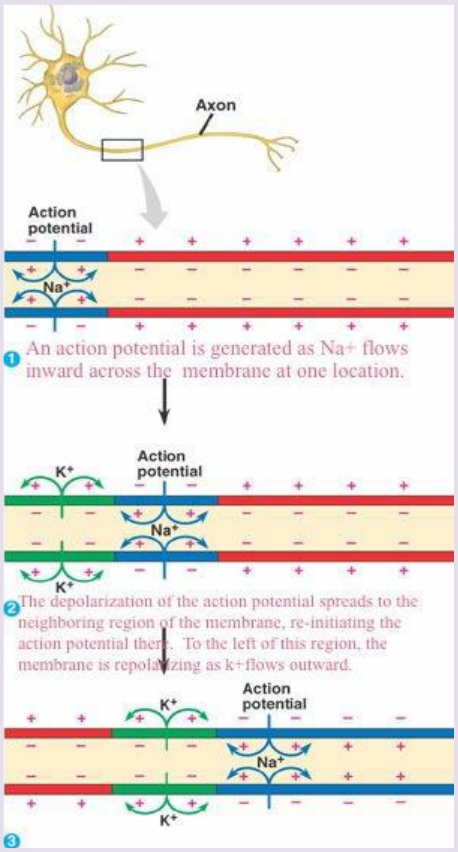
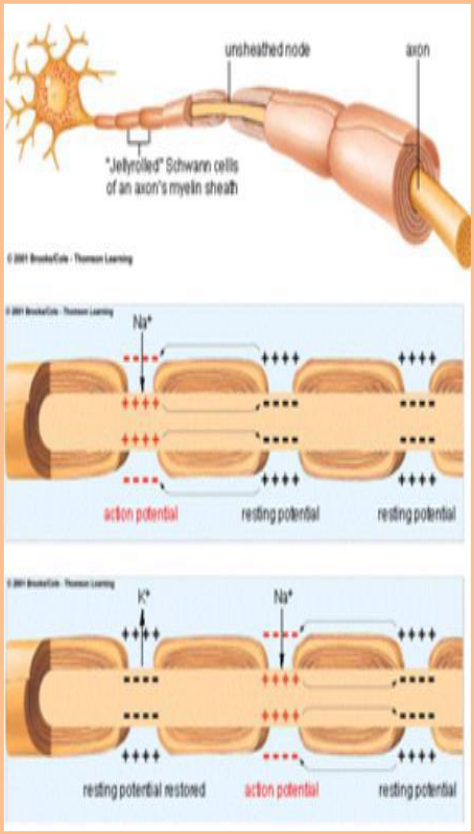


*Factors influencing the rate of conductance:

1- Myelination (If present, this increases the rate of conductance.)

2- Diameter of nerve fibers (Larger diameter, less resistance, higher current flow, faster depolarization, higher velocity of conductance.)

NOTE: By 'conductance' here we mean the movement or propagation of impulse (action potential) not the ion flow across the membrane.

Methods of action potential propagation		
1. Continuous conduction	Occurs in unmyelinated fibers. Local currents flow between the active area -which is at the peak of action potential- and inactive area, which is still in resting potential. This flow will cause activation of Na+ channels in inactive area and reduce the membrane potential to the threshold, which triggers an action potential in this area (that was previously inactive). This process is repeated all along the nerve fiber until the impulse has reached nerve terminals.	
2. Saltatory conduction	In myelinated fibers, the impulse skips the myelinated regions in the axon and jumps from one node of Ranvier to the adjacent node. This process ensures faster propagation of an action potential along the myelinated axons (50 times faster than in unmyelinated fibers of the same size). The conduction involves current flow between two adjacent nodes of Ranvier, which results in activation of Na+ channels in the adjacent node, which is still in resting potential. The process is repeated until the impulse activates the axon terminals.	

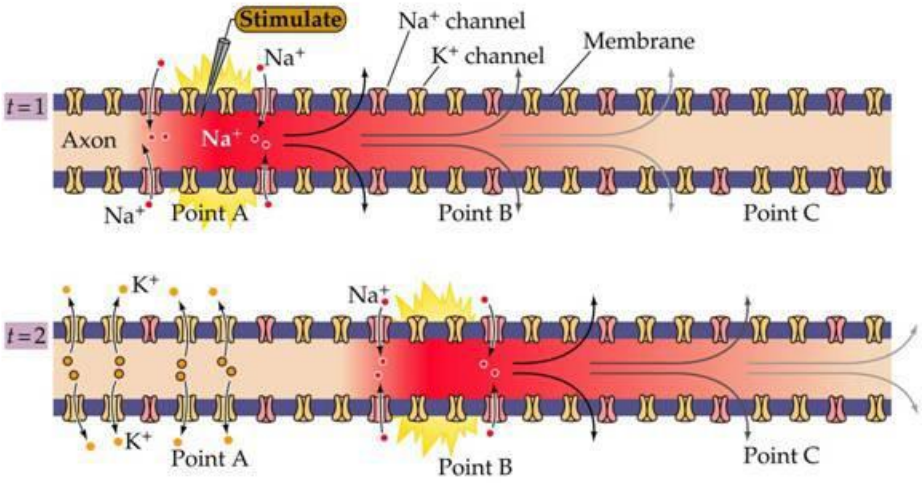
Now let's stop for a moment and have some brainstorming together…

What do you think is going to happen when the action potential reaches the axon terminal, can it go back in reverse direction?

No, it cannot. The preceding part is still in refractory period and our current flow is not strong enough to generate action potential there.

***Importance of Refractory Period:

Ensures that the propagation of action potential happens in one direction [Unidirectional, one-way]. For example, after action potential is propagated from point A to point B in the picture below, point A starts repolarizing, preventing any new action potential (relative refractory period). This assures the movement of the action potential in one direction, allows the neuron to adjust briefly for the propagation of the next stimulus, and limits the amount of action potentials sent per minute :)



NOTE: In motor neuron, direction of propagation is toward the cell body of another neuron. Meanwhile, in sensory neuron, it is toward the **CNS**(Central Nervous System).

{Extra Info}: **Sensory neurons** carry signals from the outer parts of your body (periphery) into the central nervous system. **Motor neurons** carry signals from the central nervous system to the outer parts (muscles, skin, glands) of your body.

Some Quick Definitions (not to be memorized ^_^):

Synapse: a junction of two neurons where the impulse is passed between them by diffusion of neurotransmitters.

Presynaptic membrane: The membrane of the first neuron (before synapse)

Postsynaptic membrane: It is where the neurotransmitters bind to receptors on the second neuron, thus allowing the action potential to proceed to the next neuron.

Synaptic cleft: A small space between the presynaptic and postsynaptic membranes, separating the axon terminal from the dendrites of the next cell.

What happens at the Synapse?

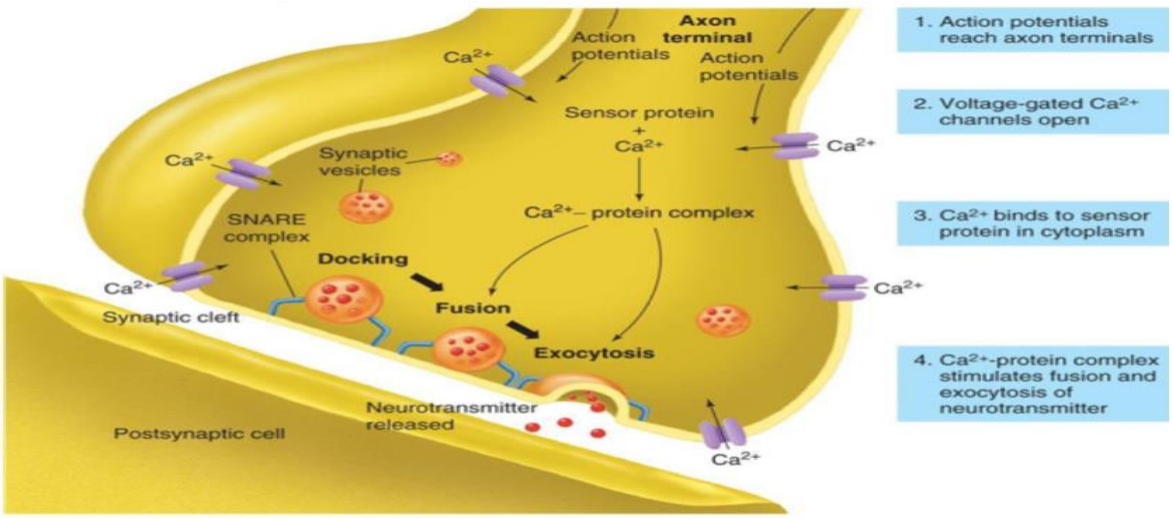
-Synapses operate in one direction. They allow the transmission of signals from one neuron to its neighbouring neuron.

1. Once the impulse reaches synaptic knob (a large bulge at the end of the presynaptic neuron), the activation of voltage gated Ca++ channels occurs (these channels are a part of the membrane of the presynaptic neuron.)

2. The concentration of Ca++ outside the axon terminal is much higher than the concentration of it inside the axon terminal. This creates a steep concentration gradient for Ca++, thus allowing an influx of Ca++ into the synaptic knob.

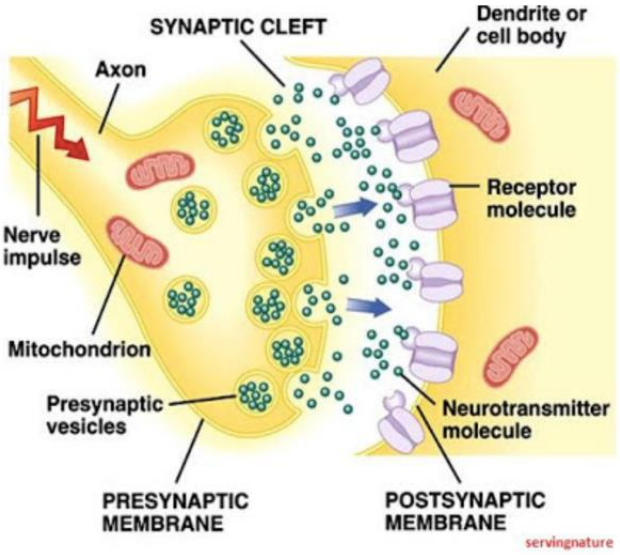
3. This increase in Ca++ concentration inside the axon terminal triggers the release of neurotransmitters into the synaptic cleft (by exocytosis).

Summary: Impulse→Open Ca++ voltage gated channels → Ca++ diffusion to inside → more positive inside → more vesicles docking → more neurotransmitters released.



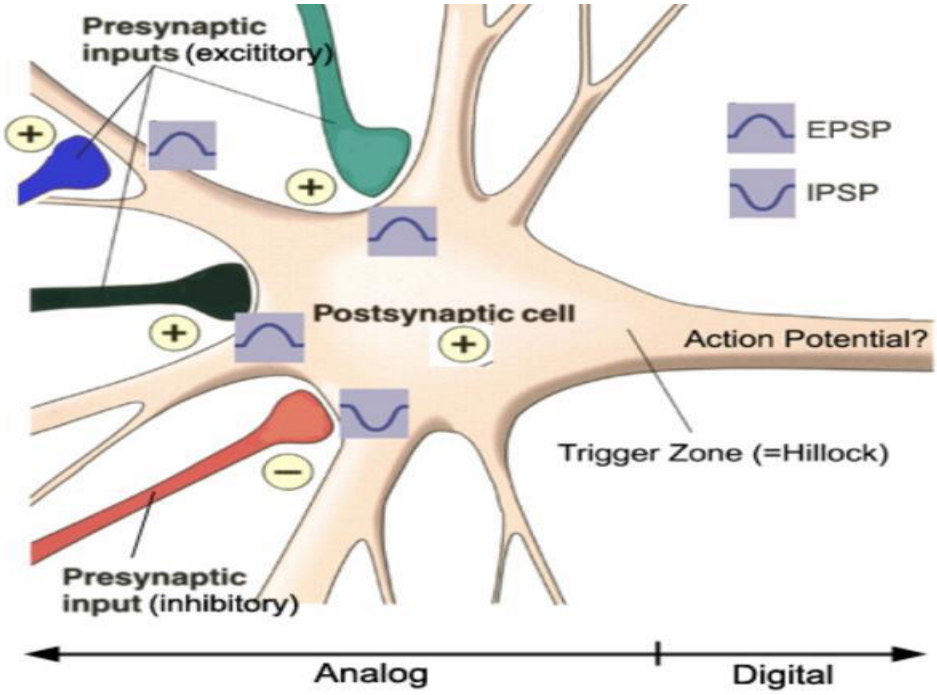
4. These neurotransmitters bind to the specific receptors on the postsynaptic membrane.

5. When the neurotransmitters bind onto the receptors, depending on the type of ligand gated channels present in the postsynaptic membrane, this will either trigger the activation of Na+ ligand gated channels which allows an influx of Na+ (into the postsynaptic neuron) and leads to depolarization. This is called **Excitatory Post Synaptic Potential** (EPSP). These are not action potentials, but small depolarizations (graded potentials).



6. Or, it might trigger the activation of K+ ligand gated channels, if present, which allows an efflux of K+ (out the postsynaptic membrane) and leads to hyperpolarization or decrease in membrane potential (more negative). This is called **Inhibitory Post Synaptic Potential** (IPSP). IPSPs, can also be induced by the activation of Cl- ligand gated channels which hold the membrane at the resting potential and prevent depolarization.

*Opening sodium channels is excitatory (towards the threshold)
*Opening Potassium/Chloride channels is inhibitory. (away from threshold)

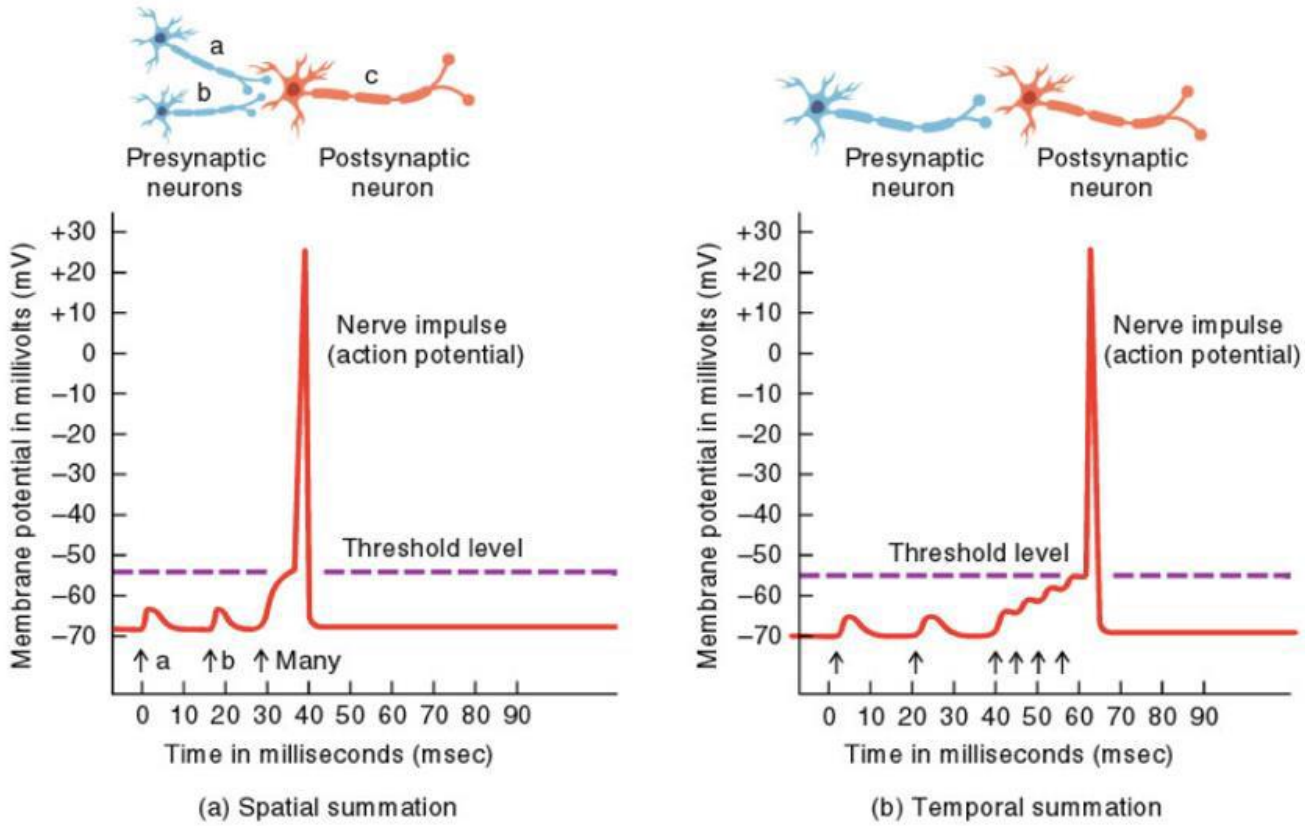


NOTE : Gap junction is an example of electrical synapses

Summation: Is the addition of post-synaptic potentials (sometimes called graded potentials), meaning for example, two depolarizations can sum to give a higher depolarization.
The two types of summation are:

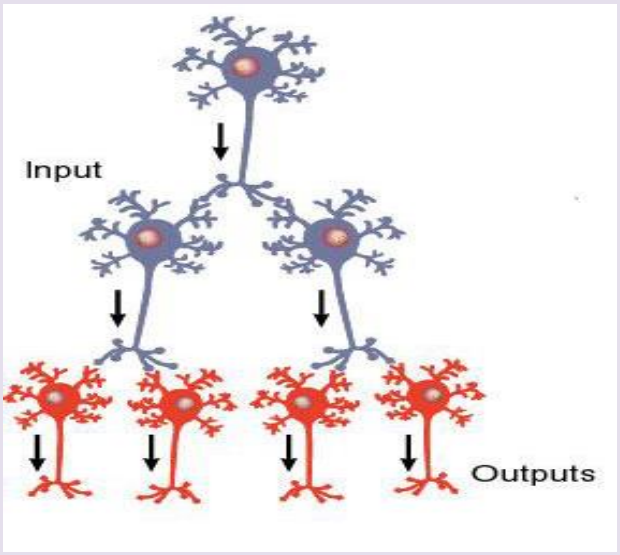
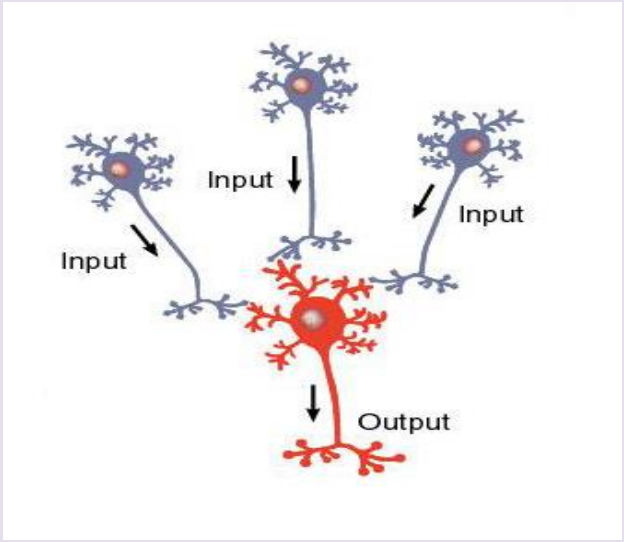
• **Spatial summation**: Which appears when 2 or more potentials (IPSP/EPSP) are generated from 2 or more different presynaptic neurons simultaneously at the same postsynaptic membrane. As a result, these two responses will be summed into a final response. May take a place between 2 EPSPs inducing more depolarization, or between 2 IPSPs triggering more hyperpolarization.

• **Temporal Summation**: Which appears when 2 or more potentials are generated from one presynaptic neuron at different times (short time gaps). These potentials are then summed together to induce more depolarization (frequency dependent).



NOTE : *We have a mix of the two types of summation in our body.
*Even if you got an infinite number of inhibitory potentials, you may never ever exceed the limit of -94 mV.

By observing the neural network structure, we can find two phenomena:

Divergence	Convergence
one presynaptic neuron (one axon) that has terminals synapsing with many postsynaptic neurons.	means signals from multiple inputs uniting to excite a single neuron.
	

Measuring action potential

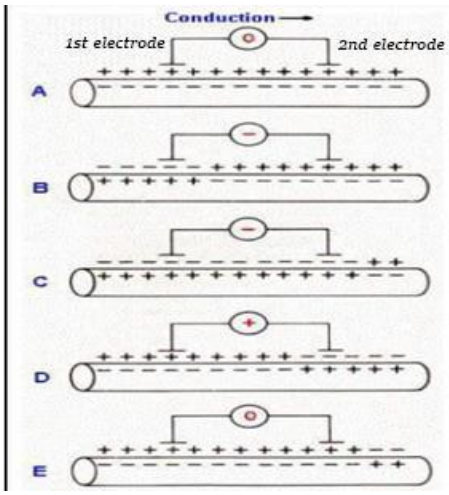
For **biphasic action potential** recording, both the recording electrodes can be placed either in extracellular fluid or intracellular fluid. (we can do this because this action potential has both positive and negative deflections)

a- In the Y axis when there is no stimulation of the nerve fiber, there is no potential difference between the two recording electrodes and hence the horizontal line is recorded (resting membrane potential)

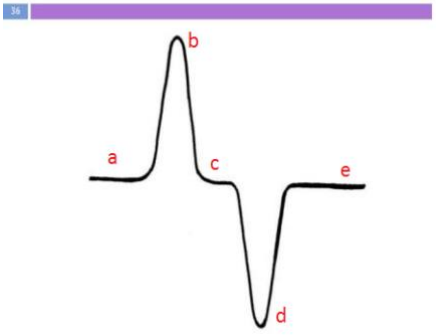
b- depolarization of the area around the 1st electrode causing the depolarization wave

c- depolarization of the area around the 2nd electrode: no potential difference between electrodes.

d- Repolarization of the area that depolarized first: repolarization wave (now we have different charges and in an opposite way of the one in b, so the wave is inverted downward)



Biphasic action potential

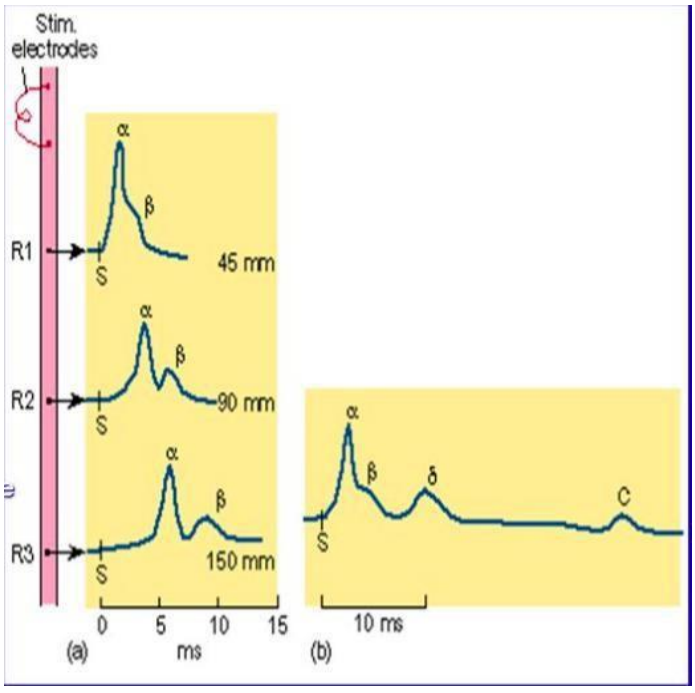


e- Repolarization of the adjacent area: no potential difference between electrodes.

For clinical use:

a similar but not the same method is used to record a compound action potential. In a mixed nerve, action potential appears with multiple peaks and is known as a **compound action potential**. This action potential results from the summation of action potentials of all fibers in the nerve. Its shape is due to the fact that a mixed nerve is made up of different fibers with varying speed of conduction (fibers with larger diameters have less resistance, thus showing greater velocities). Therefore, when all fibers are stimulated, the activity in fast conducting fibers arrives at the recording electrode sooner than the activity in slower fibers. The number and size of the peaks vary with the type of fibers in the particular nerve being studied.

{Extra Info}: When compound action potentials are recorded, one point on the nerve is stimulated. Then an electrode is placed on the skin near that point, the other electrode is connected to a high resistance (Because we are measuring the change according to the zero voltage). This allows us to get some information about the integrity and functionality of neurons and axons of the nerve fiber (to know if there is any problem in the nerve, fibers or in the conduction).



As we place the electrode further from the stimulation point, more waves will be recorded due to different velocities of conduction. When we placed it at R1 (not so far away), we got two peaks. Because we recorded over a small area, we could not find much differences. Recording over a greater portion of the nerve might lead to recording more waves (finding more differences among nerve fibers) The first wave represents the bigger nerve fibers because they have the highest velocity. The next wave represents slower fibers, and so on…

SHORT QUIZ

1-What's the type of Ca2+ channels that are found in the presynaptic area?

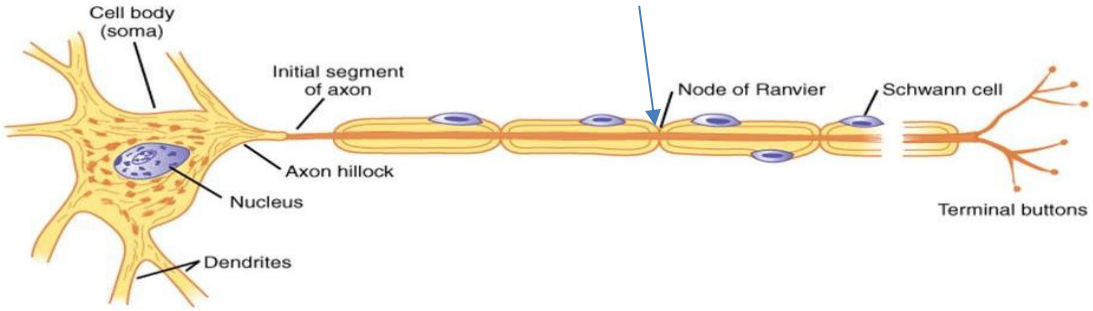
a-ligand gated channels
b-mechanical gated channels
c-voltage gated channels
d- symporters

2- Acetylcholine is an excitatory transmitter, what happens if we increase its concentration in the synaptic cleft?

a-more probability of binding with postsynaptic receptors causing an inhibitory potential
b-more probability of binding with postsynaptic receptors causing an excitatory potential
c- more probability of causing an action potential on the cell body of the postsynaptic neuron
d- both b and c

3- If we stimulate a neuron in the middle as shown in the picture, what happens?

(note: this doesn't happen in human body)



a- Propagation will occur in the right side (toward the axon terminals)

b- Propagation will occur in the left side (toward cell's body)

c- Propagation will occur in both directions

d- No action potential would be generated (must start with hillock)

4- We have one presynaptic terminal with one postsynaptic cell body in a synapse, what do we have to do to increase the probability of generating an action potential in the second neuron (Postsynaptic one)?

a-increase frequency of sub potentials
b-decrease number of receptors on postsynaptic region
c-increase concentration of neurotransmitters released in synaptic cleft
d-both a and c
e-all above

ANSWERS

1-c. Calcium channels in the presynaptic are voltage-gated channels.

2-b. Excitatory transmitters cause excitatory potential. No action potentials can be generated at the cell body. We must find the summation of all postsynaptic potentials then we can determine whether an action potential would be generated or not at the **axon hillock,** so **c** cannot be the right answer.

3-c. Why not? We know that one propagation will occur towards the axon terminals but another one going towards the cell body will occur as well because the part behind is in resting phase and not refractory period.

4-d. This is an example of temporal summation which is frequency-dependent.
Higher frequency = More potentials per time unit = Higher probability of action
We are talking about probability so obviously increasing the concentration of neurotransmitters will increase the probability of generating an action potential.

NOTES

*Please read the quiz as it contains important information that I thought would be better represented in the form of questions.

*Don't trouble yourself with extra details from other sources, as we are not required to know things other than ones said during lectures. ''*If we want to know everything about this topic, we are needing at least 6 months :)*''

*Refer to the book only if you have a specific point that you can't understand.

*GOD BLESS YOU ALL <3