Faculty of Medicine 2012

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Physiology

Sheet

Medical Committee
The University of Jordan

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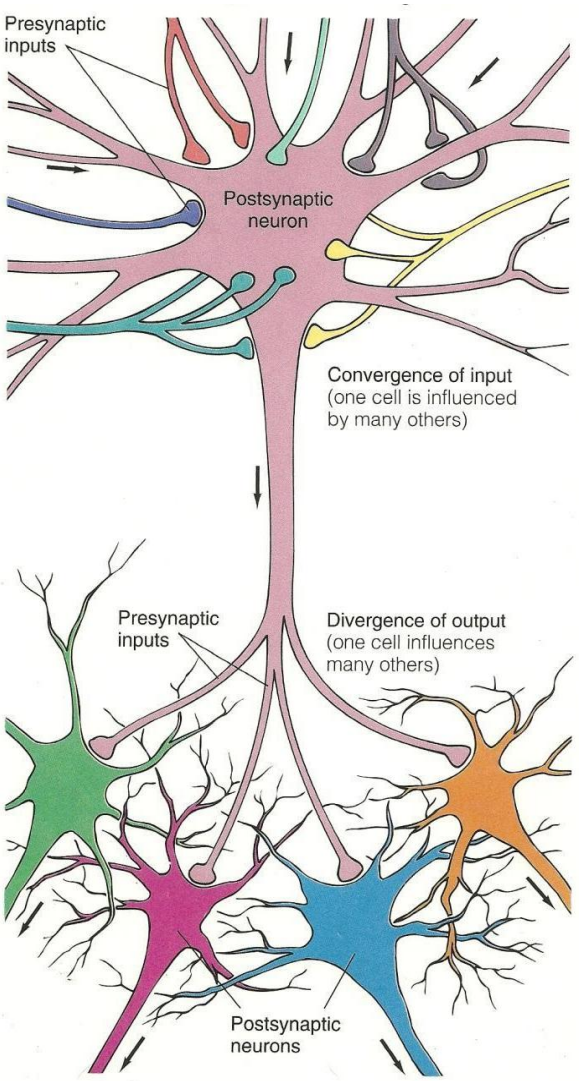
Physiology

Lecture 4 – Dr.Eman Al-Khateeb.



Arrows indicate direction in which information is being conveyed.

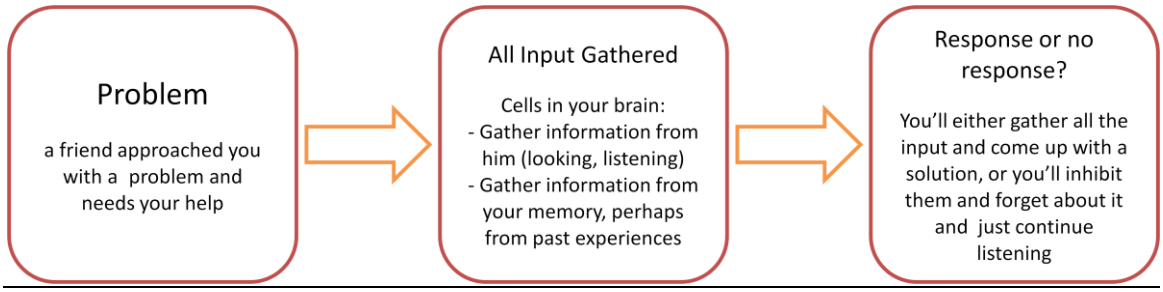
❖ Convergence and Divergence

This diagram represents a small piece of what is happening inside our brain regarding the neurons and their connections. As you can see, for each neuron to function it must have many connections from different sources, but the most important connections in our brain are those that give us the ability to think, store things and retrieve them from our memory, write..Etc

- ❖ This characteristic is called **Convergence**: when all the inputs come together (converge) on one neuron.
- ❖ This same neuron will have an axon that will bifurcate (branch) to give to many other neurons, this is called **Divergence**. There could more than 200000 connections.

A neuron cannot respond to each stimulus (input) on its own; it must first *gather all the information* and inputs and *then decide* if it should fire (respond) or not. This is why we need a second language (electrical activity) that will enable the neuron to understand the situation fully prior to responding.

- **An example of convergence:**



The same applies to solving a math problem, or coming across a tough question in an exam.

❖ Graded Potential

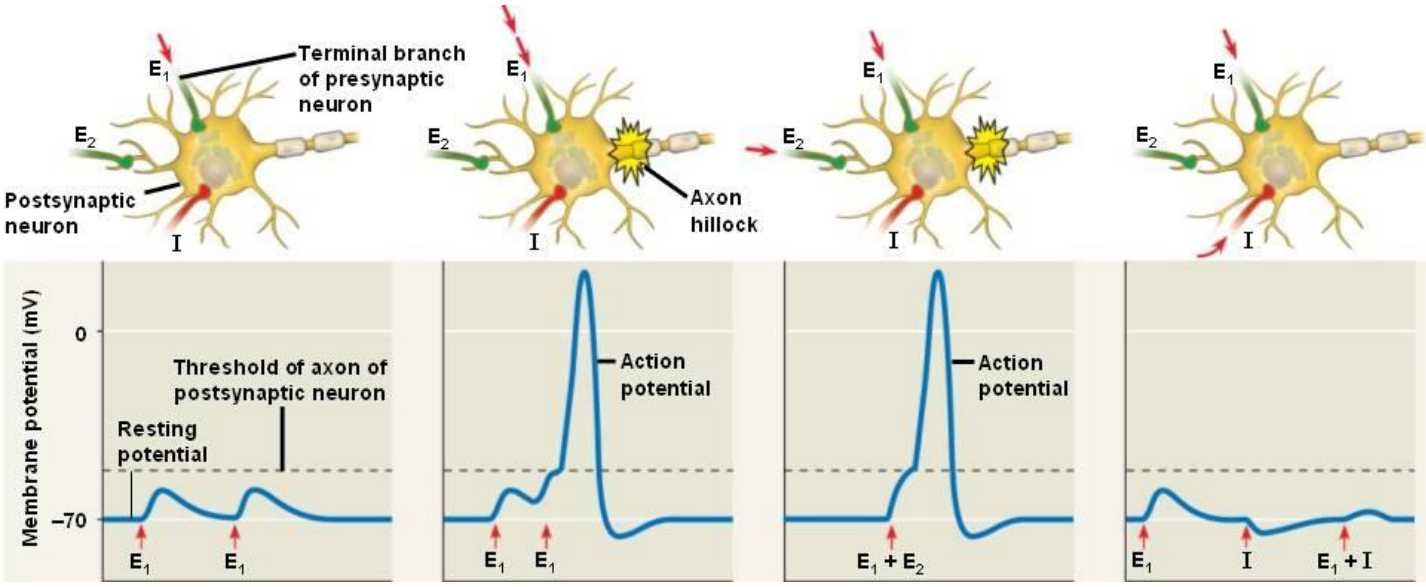
We are now going to address the second language (electrical activity) our brain uses other than Action Potential.

Graded Potential is important since:

- **Action Potential** → Each stimulus must have a response.
- **Graded Potential** → We gather all the information *then* decide if there should be a response or not.

One of the most important properties of graded potential is **Summation** since we need to gather information.

This figure shows a neuron that has received 3 connections (only for simplicity, usually there's much more). E1 and E2 are Excitatory, I is Inhibitory.



Threshold is not reached when:

- Only E1 is excited, it produces a small graded potential and it is not summated, therefore it decays and the membrane potential returns to normal. If E1 is excited again after a long period of time, there will be no change in the cell (returns to resting membrane potential) and there will be no response.

- If both E1 stimulates the neuron and then after a long period of time E2 stimulates it, there is no summation so the graded potential of E1 decays, cell returns to membrane potential, E2 stimulates the neuron, threshold is not reached, there is no action potential and hence there will be no response.

Threshold could be reached by <u>Summation</u>; there are *two types* of Summation:

1. **<u>Temporal Summation</u>**

*It depends on **<u>time</u>**. When the two graded potentials were on top of each other they were able to summate and fire an action potential.*

- E1 graded potential immediately followed by a 2nd and a 3rd → Summation → Threshold is reached → Cell fires an Action Potential → Response

(input from E1 was strong enough so cell decided to respond)

2. **<u>Spatial Summation</u>**

*It depends on **<u>space</u>**. Graded potentials from different sources are summated together at the same moment, and fire an action potential.*

- If E1 + E2 stimulate the neuron at the same time (fire at the same moment) → Summation → Threshold is reached → Cell fires an Action Potential → Response

When an Inhibitory and an Excitatory are stimulated at the same time:

- If for example E1 gives a voltage +0.5MV and I gives -0.5MV the algebraic sum is 0 → Mutual cancellation → Nothing happens → Membrane potential goes back to the resting potential

You should know:
- Each input (stimulus) can't change the resting membrane potential more than 0.5MV, and to reach the threshold we have to change the membrane potential by 15MV, therefore we need a minimum of 30 to work at the same time, or one to give 30 impulses one on top of the other for an action potential to be set up. (this is very simplified, in real life what happens in the brain is much more complicated where 100s and 1000s fire simultaneously).
-Temporal and spatial summations could occur at the same time.

<u>Whether or not a neuron reaches the threshold and fires depends on the algebraic sum of all the excitatory and all the inhibitory stimulations that are firing at the same moment or repetitively.</u>

❖ What determines if the effect on the cell is inhibitory or excitatory?

- **Excitatory:**

  Sodium channels open → Sodium influx → Depolarization → Intracellular positive charge increases

- **Inhibitory:**

  - Potassium channels open → Potassium efflux → Hyperpolarization → Intracellular negative charge increases
  - Chloride Channels open. There's a greater concentration of chloride outside the cell membrane (remember Chloride always follows Sodium) → Chloride influx → Brings in negative charges along with it to inside the cell

Neurotransmitters determine which of these channels open.

- The *major inhibitory neurotransmitter* in the brain is called: GABA (Gamma-Aminobutyric Acid)
  - Used in many drugs, helps reduce anxiety and stress in people that are nervous (if someone is graduating, saying a public speech, getting engaged...etc)
  - Increases the inhibition in the brain so it slows down and the person is calmer.
  - Valium, alcohol and anti anxiety medications use it (decreases excitation, increases inhibition)

We will discuss the importance of neurotransmitters later on and their roles in determining your mood, behavior and personality.

Note:
- Summation happens in all ganglia outside the brain.
- Groups of nerve cells in the brain are referred to as: Nuclei
- Outside the brain: Ganglia
- Graded potential also occurs in receptors.

❖ The other cells of the Brain:

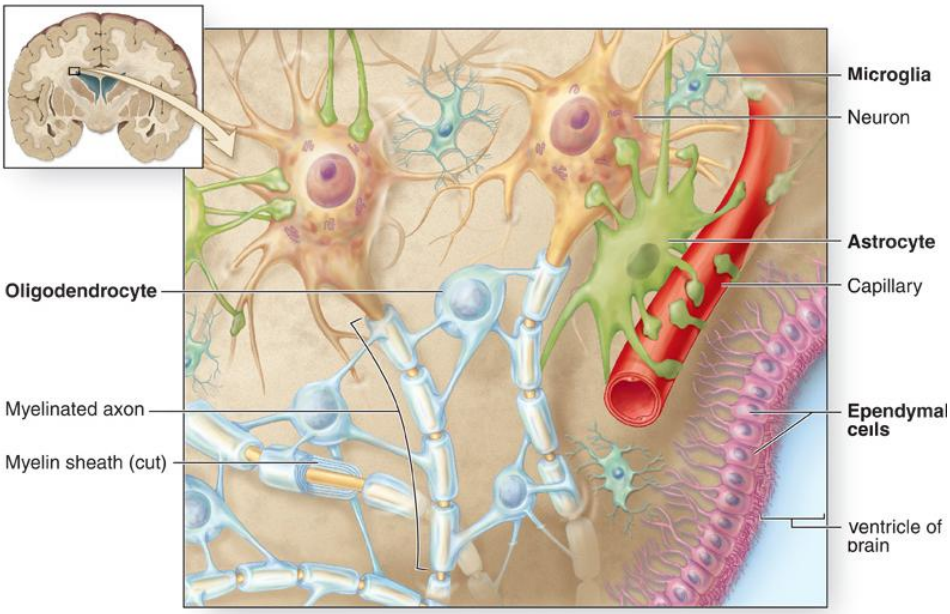
We have many supportive cells in the CNS which cannot initiate a Graded Potential or an Action Potential but give **nutrition** and **immunity** to the neurons.

1) Astrocytes

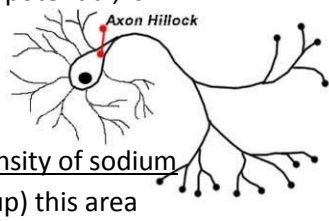
2) Oligodendrocytes

3) Microglia

4) Ependymal cells



❖ **Another characteristic of graded potential**, which is completely different than action potential, is that it *Decays with distance*.



- The best site of firing an Action Potential is the axon hillock because there's a high density of sodium voltage gated channels there. So for the neuron to fire (an action potential to be set up) this area must reach the threshold.

- The distance of the stimulus from the axon hillock is really important (*the further away the inputs are, the more the decay of electrical activity*). This is because the neuron is large compared to the nerve and contains fluid; and since we know that depolarization is an ionic change, when Sodium enters in little quantities it is distributed in the fluid inside the cell, so there wouldn't be any difference in the ionic composition.

- The further away the inputs are, the more excitatory input needed for the axon hillock (trigger zone) to reach the threshold and fire an action potential. When they are closer they are more powerful and more effective.

Figure (a):

If all the stimuli are excitatory

- They will summate
- If they reach the threshold
- An action potential will be set up → Response

Figure (b):

All excitatory except 1/3rd Inhibitory

- By the time the graded potential arrives to the trigger zone it won't be able to reach the threshold (since it is decremental) → No Action Potential set up → No Response

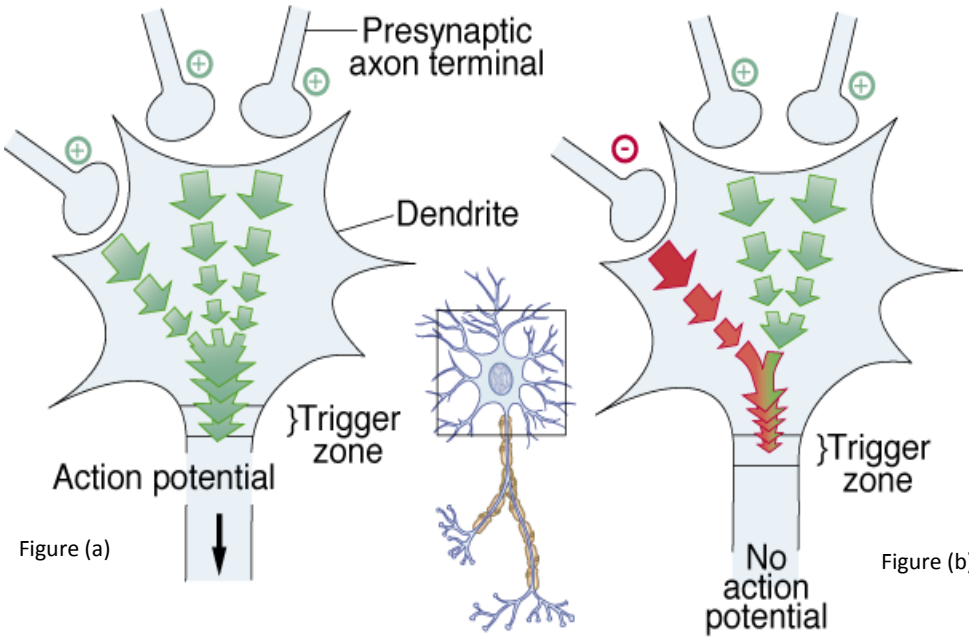


Figure (a)

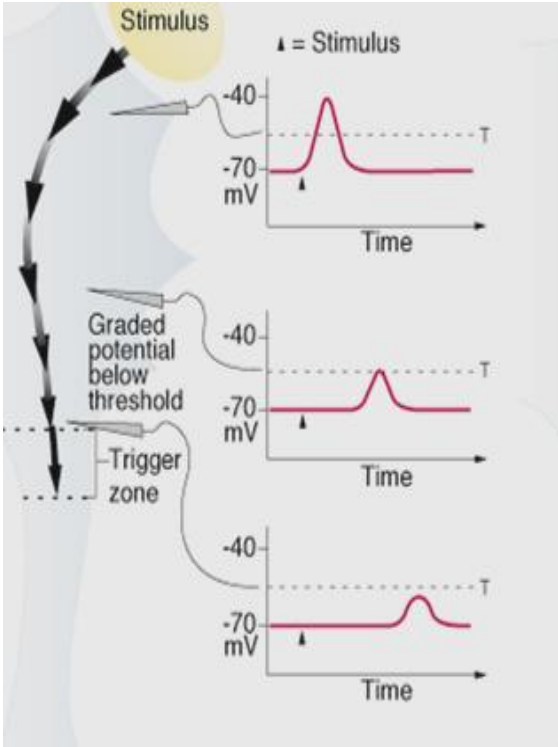
Figure (b)

We measure this by microelectrodes (Intracellular Recording)

(Glass pipettes, made in the lab) KCl is used as an electrolyte.

- As we measure the impulses at locations closer to the trigger zone (further from the point of stimulus) we notice that the electrical activity decreases, if it stays above the threshold then an action potential will be set up, but if doesn't → no action potential.

  Graded potentials travel through the neuron until they reach the trigger zone. If they depolarize the membrane above threshold voltage, an action potential is triggered and it travels down the axon.



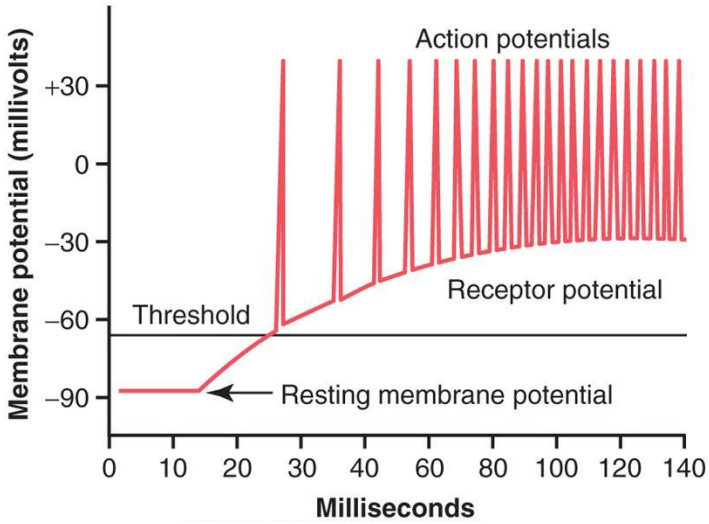
❖ **The amplitude for the Graded potential is lower than that of the Action Potential**

- Graded Potential has a subthreshold
- Graded Potential threshold = 50MV (maximum) where as the Action Potential threshold is >100MV.

- When the graded potential is just above the threshold → frequency of AP is low
- When the graded potential is very high (above the threshold) → frequency of AP is high

This is how we determine if the touch sensation/pain is mild, moderate or severe. This depends on the amplitude of the receptor potential which is graded (and consequently the frequency of the action potential).

Example: Strong stimulus → opens many Na channels → depolarization → voltage goes up to +50 → frequency of Action Potentials (AP) increases.



❖ Graded Potential Includes:

- Receptor potential
- End plate potential
- Excitatory Post Synaptic Potential - EPSP (Na influx)
- Inhibitory Post Synaptic Potential - IPSP (Cl influx, K efflux)

A Summary of the differences between AP and GP:

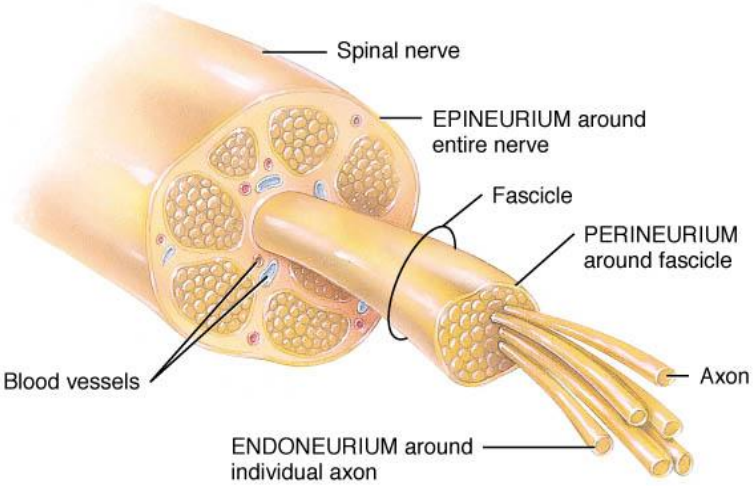
Action Potential	Graded Potential
Propagates at axon	Usually arises from the dendrites and the soma
Involves voltage gates channels	Involves ligand gated and mechanically gated channels
Information faithfully unchanged	Decremental
Propagates	Non-propagating (localized)
Amplitude always constant, Greater than GP (>100MV)	Amplitude depends on stimulus strength (0.5-50MV), Longer duration than AP
Regenerative, All or none	Either hyperpolarizing or depolarizing (depends on NT)
Has a refractory period	No refractory period (so it would summate)
No Summation	Summates

Major benefits of Graded Potential:

- Higher cortical functions (thinking, retrieval, memory, problem solving) all controlled be GP
- The retina (inner layer of the eye, behaves like brain neurons) has two vision receptors: Rods and Cones. Three different cones sense 3 different colors (Red, Green, Blue), if we have Action Potentials only we would only see those 3 colors; but because of the summation of Graded Potentials we can see different shades of colors (mixed percentages of different colors).

We need both languages (AP & GP) to perform higher and simple brain functions.

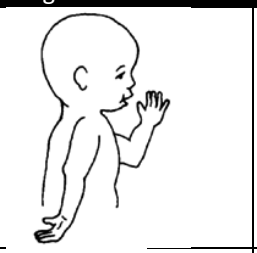
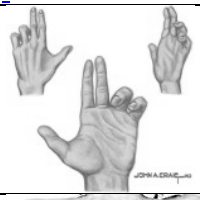
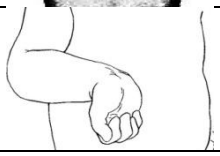
❖ **Nerves & Common Injuries:**



- *We are not like squids.* You won't find a single nerve fiber passing alone in your body even in branches.
- Each nerve contains a bunch of nerve fibers, nerves pass in groups of hundreds in the whole arm or leg.

The job of electro-physiologists in the lab is to do an EMG (electromyography) for a patient who for example has Spinal Disc Herniation, which led to pressure being exerted on a nerve, in order for us to see what damage has occurred. Then the surgeon operates and removes the disc, and after the surgery we do another EMG to check on the patient's status.

The same goes for any other patient with nerve injuries; these are some injuries in nerves related to the Brachial Plexus:

Condition	Nerve Involved	Image	Further Notes
Erb–Duchenne Palsy	C5-C6 Nerves		- Also called: Waiter's tip - When a baby is born head first (cephalic presentation) and the baby is pulled strongly from the neck and the upper brachial nerves are damaged.
Wrist Drop	Radial Nerve		- Also called: Saturday Night Syndrome - Radial nerve damaged → no extension → wrist drops
Median Nerve Palsy	Median Nerve		- Carpal Tunnel Syndrome → Median Nerve is damaged
Ulnar Nerve Palsy	Ulnar Nerve		-
Winging of Scapula	Nerves C5-C7, Long Thoracic Nerve		-
Klumke Paralysis	C8-T1		- When a baby is born feet first (breech presentation) and head last, sometimes it is pulled strongly from the neck so the lower brachial nerves are damaged.

❖ **If I suspect one of those injuries, how do I investigate them?**

By: **Electrophysiology.** We stimulate from one place and record from another place to check if the electrical signals are normal.

Electromyography:

- There are two wires (the stimulating electrodes)
  - Cathode
  - Anode
- There is another electrode used for recording.

We need a very high understanding of anatomy for us to know electrodes and wires.

- The electrical signals are displayed on the screen.

*This setting needs **earthing** in between the stimulating and recording electrodes so no electric shock would occur to either the patient or the examiner since we deal with relatively high voltages (20-30).*

EMG Machine

The recording electrode has a weak signal, it is hence amplified by a loud speaker (displays sound and image) and it will displayed on the screen so we can confirm that it's an actual signal and not due to the noise from the surrounding electricity.

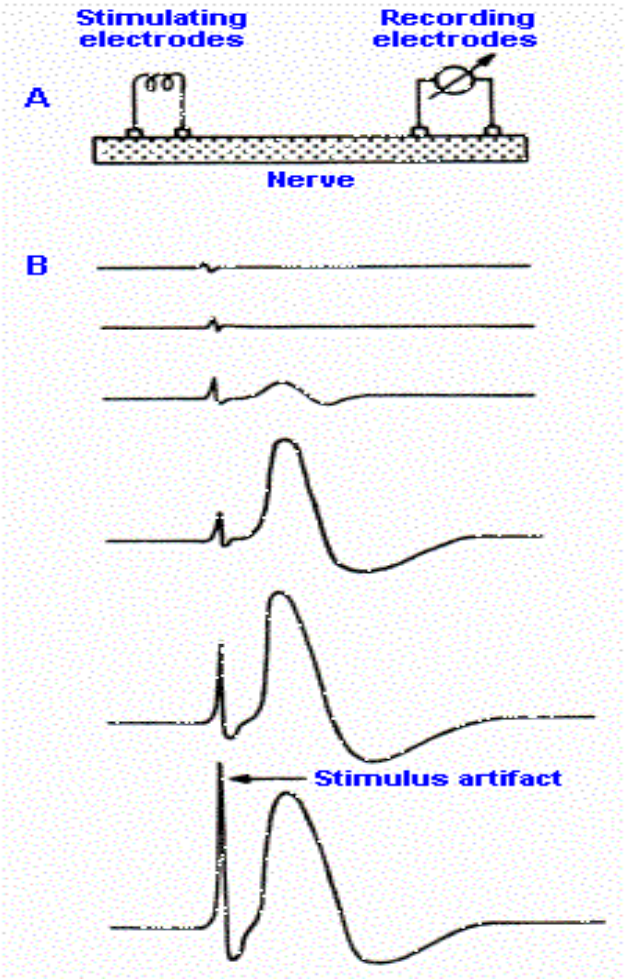
We might give the patient an EMG slip which is basically a document for what we have recorded.

❖ **<u>When a bundle of nerve fibers is being stimulated; for example if the electrodes are on the radial nerve and we are recording from it, what are we going to record? Graded potential or action potential? Why?</u>**

We will record a **<u>Compound Action Potential</u>:** a *<u>graded</u>* signal that represents the *<u>summation</u>* of many *<u>action potentials</u>* that have been generated in the hundreds of axons. Each action potential represents a nerve fiber.

- If we start stimulating minimally (0.1MV) we will record nothing
- When we start increasing the voltage to 1V we will get small electrical activity (amplitude)
- As we increase stimulus strength amplitude will increase as well
- This happens until a *<u>maximum amplitude</u>* is reached (at 5MV for example), after which there will be *<u>no further increase in the amplitude</u>* even if we increase the voltage to 50MV,

This indicates that the Action Potential has a fixed amplitude, but the thing that led to those varying amplitudes is the number of Action Potentials **<u>summated by the machine</u>**.
When we stimulate slightly only the nerve fibers near the skin generate an Action Potential until an adequate stimulus is reached, then there will be a maximum summation of all Action Potentials after which the amplitude will remain the same regardless of the strength of the stimuli. This indicates that Action Potential has an "All or none" response, but **<u>Compound Action Potential</u>** became graded because it's a property of the machine, it gathers an action potential on top of another action potential.



Best of Luck!