

Graded potential

We agreed that we have only 2 languages for the brain to execute all the hundred of thousands of functions that execute on the daily bases.

We talked about action potential and I assume today everybody knows exactly what is the major carrier of the action potential and what is the major function of action potential.

Today we will talk about second language that actually complete and help the action potential to execute the other functions : it is the graded potential or electrtonic potential.

When we start thinking and when we start keeping our memory and when we start creating things (higher cortical functions) it is difficult to execute them by action potential , we need another language that can integrate from different sources to give the intelligence that you are enjoying to give you the memory , the way that you are capable to solve problems.

Taking in consideration that each neuron receives hugely .

- **How many inputs to neuron do you expect in an average ? 10 ? 100? 1000 ??**

the average starts from 200 into 200000 , the more connections this cell having, the more intelligent you are , the more capable of thinking . The more this cell (neurons) are bald the more you are in the low IQ.

The intelligence depends on the number of connections, it depends on synapses not on the size of the brain , the more your neurons are sophisticated (having a lot of connections), the more you are intelligent and capable to create , to think and learn.

In an experiment that has been done on animals they have found that in the first few days of delivery (animal very young) if they cover one eye (and this experiment also applicable to human being) if a baby is just borned and you cover one eye for a month he will be blind for this eye for the rest of his life . why that? Because all of the connection are gone .

The brain will realize that there is no light coming from this eye , so this eye is no more functioning , and the brain will use the are for other things .

- **That what we called plasticity of brain.**

This what we call it the more you work on your brain , the more you increase the connections , and the more you are intelligent and capable and having a lot of tools to navigate in life .

What we are talking about is the most difficult >> graded potential.

Lets remember that the brain although composes to percent of the weight of the body yet utilize 20% of the energy in form of ATP to .70% of 20% goes only to maintain the $Na^+ - K^+$ pump . connections to each neuron are from 200 to 20000 in the electoral area and the area math and solving problems and the area of decision making (when you want to make decision) and there are some areas that have only 200 connections.

This connection between the terminals and neurons starts like that but by the time it arrives to the trigger zone it is still above the threshold.

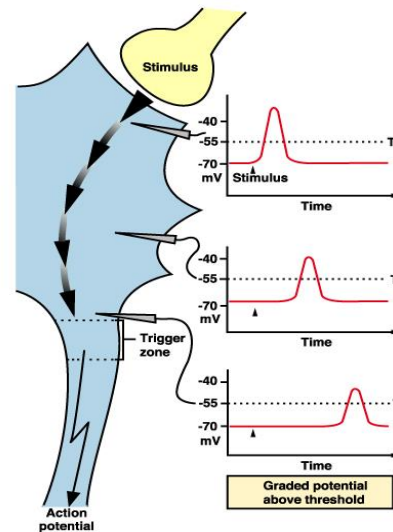
note : single synapses can not cause the action potential to reach above threshold .

- **What do you except: If it has many synapses, is this cell capable to fire an action potential or not?**

- **definitely yes , because the trigger zone which is called the axon hillock is full of Na^+ voltage gated channels , so any electrical activity that**

reaches here and causes this area to depolarize above threshold definitely action potential will propagate to the end of the nerve terminal .

- **How many do we need ? usually each one of these connections gives a change about 0.5 mV, in order to give 15 mV to reach the threshold we need 30 connections. So.. it decays with distance.**



When we have this electrical activity that upon arrival to the trigger zone it becomes subthreshold .Is this cell capable to fire an action potential ? No !

1# number one that you learn from graded potential that it decays by distance.

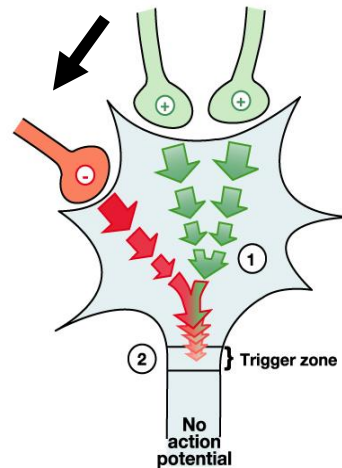
2# it has the capability to summate (بعكس ال action potential)

here we have the capability to summate the synapses , what does that mean?

if I have 3 excitatory and when I say excitatory postsynaptic potential which channel will be opened here? Na^+ and nothing else than Na^+ , but when I say it is inhibitory the channel which will be opened is K^+ or Cl^- .

- Any excitatory postsynaptic potential means opening of Na^+ channel causing depolarization (Na^+ will enter and increase positivity inside) and make excitation.
- Any substance that will lead to inhibitory postsynaptic potential has to make the cell in red color (where is the arrow) more negative , (Either we input Cl^- by opening channels or we open K^+ channel that will let K^+ to go out by concentration gradient and make the inside of the cell more negative (hyperpolarizing))

Note : Ca^{++} relates more to neuron transmitter release and heart. In our nervous system it is all about Na^+ and K^+ and sometimes Cl^- .



- ① Two excitatory potentials are diminished by summation with an inhibitory potential.
- ② The summed potentials are below threshold, so no action potential is generated.

- When we have multiple inputs to this cell and all of them are firing at same moment upon arriving to the trigger zone if they succeed in letting the trigger zone reach above the threshold , the cell will be excited .
- If we have 2 excitatory and one inhibitory here we will get the algebraic sum , by the time it arrives to trigger zone it is less than threshold so it won't be able to fire action potential .
- For example : suppose you have a friend of yours and he comes he has a problem and he starts telling you about what he went through and you are looking to him (visual information coming to the brain) you listen to him (hearing information gathering also) on a certain area of decision-making.

You might try to bring information from your memory whether you have gone through the same experience before or you have heard a previous experience similar to it. So that you will reach to a decision. Here the cell which is responsible for decision-making is gonna bring information from many sources to put them together up to you whether you keep quiet or you start solving his problem.

Another example: suppose you are a medical student and you came for an exam and you are looking to this question and you don't know if it A the correct answer is or B or C or D or even E.

So you try to think, how do you try to think? You try to remember things that that you have seen on the net, things that you have read before. You might gather information to reach to a conclusion, all of these have to be gathered, so that you come with an answer.

- Our brain is very sophisticated it can't response like by action potential (yes no yes no) there is an integration; there is gathering of information to make the idea. When you think about something when you want to take decision about your carrier, about your social life you need to gather a lot of information.
- Type of summation that usually we experience in our brain is in, 2 types one we call it temporal and the other one is called spatial summation.

If I have E1 (excitatory 1) In green color (IN SLIDES)

It is charging then it has a few seconds of rest then it is charging again

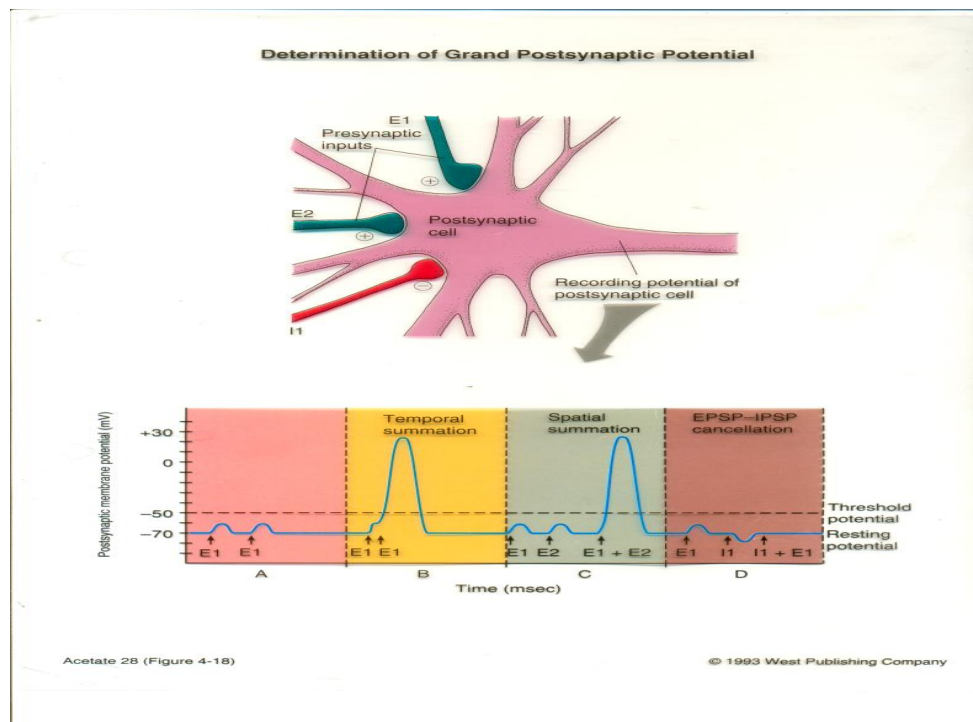
Resting membrane potential...Nothing will happen...Why?

Because there is time difference between the two depolarizing potential (here the timing is very important). If there is a delay between first and second nothing will happen, summation will not occur.

But if they come one after another this cell might reach the threshold and fire an action potential.

- Look here I have E1 and E2 when they fire by a separation (there is a time difference between them) nothing will happen. But when they fire together they might reach the threshold and fire an action potential

Look here when I told you about E1 for example and I1 (inhibitory) (nothing will happen because one of them is depolarizing and the another is hyperpolarizing and cell will never be excited because the axon hillock will never reach the threshold).



- Question: this is a neuron with a lot of connections which one of these do you think is the most effective on this neuron? Notice that each neuron has got a lot of dendrites

Huge dendritic arborization to make connections it is estimated like 80%-95 % of the connections are on the dendrites, we are left with a very little from 5 to 20 connections directly to the neuron.

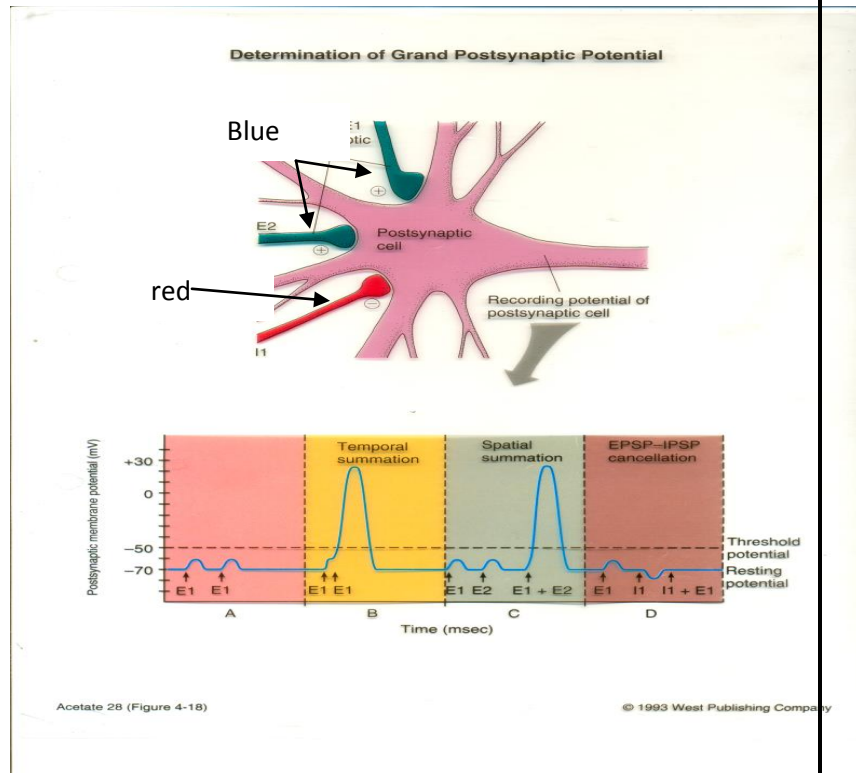
- In your opinion this excitatory in red and inhibitory in blue which one is the most effective in firing action potential or inhibiting the neuron ?
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Which one is more effective on the neuron?

The closest one is the most dangerous and most effective whether inhibitory or excitatory because they will immediately stop any excitation or start excitation (because it decays with distance then the one which is the closest to the axon hillock is the most effective and dangerous).

7 times the axon hillock has got a condensation of Na^+ voltage gated channels so anything that is excitatory it will excite this area more , anything which is inhibitory, this area will be immediately affected with it (this area is very sensitive histological)

- **These synaptic connections are very dangerous**



The effect of PH (Acidity and alkalinity of the blood on the synaptic connections)

*what is the pH ? the hydrogen concentration in a solution .

The PH of us = 7.35 to 7.45 is perfectly normal .

Anything less than 7.35 is acidity (acidosis) , anything more than 7.45 is alkalinity (alkalosis).

PH is very important, one of the most important things that we care about as physicians.

An example about acidosis is : diabetic patient

In a country like Jordan where 1/3 of the population are diabetic , I think that you as a future physicians should really master anything that is related to diabetes.

What is the abnormality in patient with diabetes ?

Glucose is the main energy source , diabetic patient and any person of us needs insulin to take the glucose and put it inside the cell , so that it will be used as a form of energy. The diabetic patient problem is that he doesn't have insulin on his cells , or his cells don't respond to insulin (it depends on the type of diabetes) .

He will not be able to use glucose (glucose full in the blood , he urinates a lot of glucose) and the first time when a diabetic was discovered was when a doctor was testing a urine of patient and the sample after two hours had a lot ants on it , so he concluded that there was a lot of sugar (glucose remains in the blood and our body gets rid of it by a urine , and the body does not benefit from it) , so diabetes patient use fat and break it as source of energy , breaking too much fat in our body will lead to acidosis (keton bodies which called diabetic ketoacidosis) .

If acidosis occurs (less than 7.35), the patient will go in a coma (diabetic coma) it affects the synaptic connections, it decreases excitability of brain and patient goes to coma.

In our nervous system if the excitability increases it will cause the epilepsy as in alkalosis and when it decreases it causes a coma as in acidosis.

alkalosis increases excitability and causes epilepsy. For example: hysterical hyperventilation حالة الهستيريا

(when a guy promises his family to do well in high school and when the result announced he was fail , they start to blaming him , he might cry , he might start (hysterical hyperventilation) because he cannot express his pain and feelings of shame.

He start (hysterical hyperventilation) and CO_2 will go out, hysterical hyperventilation will decreases the hydrogen ion in the body leading to a alkalosis and tetany happened.

Alkaloses >>is very simple to treat but if you don't treat it, it will go to epilepsy and that will hurt the brain.

HOW TO TREAT him ? one way is to slap him, the best treatment is to give him a paper bag (not plastic bag) and you ask him to put it in his mouth and nose and and keep breathing in it (CO_2 goes out then comes back) and he will come better . but if you don't treat him he will go in epilepsy which we try to avoid it as much as possible because it is dangerous. alkaloses increases the excitability of nervous tissue and synapses where the acidosis decreases it.

Drinking a cup of coffee increases the excitability of synapses. caffeine in coffee and Theophyllin in tea and thiobromine in coco all of these are stimuli , but they are natural they are not like acidosis and alkaloses they don't take you to the epilepsy but they really help in causing excitation.

In order to conclude all in graded potential these area major characters :

- Arises mainly from the dendrites and soma. (but in action potential it arises from axons).
- Ligand-gated(chemically gated channels) or Mechanically gated channels (some times in other areas like receptors or you press mechanically gated channel also exist , but it is never ever voltage gated).

- Decremental (non-propagating) conduction
- Amplitude depends on stimulus strength (1-50 mv) (amplitude is usually subthreshold when it summate it might reach the threshold (its amplitude is less than action potential)
- Duration is much longer than Action Potential (it rises rapidly and decays exponentially)
- Hyperpolarizing (inhibitory) or depolarizing (excitatory)
- No refractory period (because if it it has a refractory period it can't do summation)
- Temporal / Spatial Summation.

Function:

1. higher cortical functions; thinking, solving problems, retrieval...etc
2. Seeing all the mixed colors. In our eyes we have only three different cones that are responsible for seeing the colors: the red, the green and blue. So if we have only action potential we will be able to see Only these 3 colors and none other than this frame. I will be able to see green, red and blue. But in fact we see all mixed colors and we are enjoying spring colors that you are wearing today because of graded potential

It is this percentage of partial summation of the three of these cones gives me the capability to see all the mixed colors , I can see purple , gray , brown and everything, it is due to the graded potential. Graded potential is not only for electoral capability of brain but also to improve our vision.

Major electrical signals of brain are:

1. Action potential
2. Electrtonic, graded potential

- We want to apply to our patients, we want see for us as a neurologist what we gonna record, and how we diagnose diseases.

If I'm investigating a patient who suffers from a problem in nerves of upper limbs, we have major 3 nerves : ulnar, radial and median nerves

- Ulnar nerve when it is damaged that will cause the Claw hand. Where is the major site of the injury of ulnar nerve ? The medial epicondyle of humerus , near the elbow joint when the fracture happens, it causes injury .
- Median nerve major injury is in the carpal tunnel, median nerve passes under the flexor retinaculum , and anyone who gains weight , anyone who has a fracture in joint (small bones), anyone who has edema due to the the increase in body liquids, that will cause a pressure on the median nerve and that is called carpal tunnel in fingers (index , thumb, half of middle) not as ulnar (little and ring) .
- The common site of injury of median nerve is near the wrist.

- Radial nerve when it is damaged wrist drop will happen and the common site of injury is in the spiral groove of humerus .
- Also patient who walks on crutches causes pressure on axilla on the site of radial nerve .
Also prisoners in Iraq who were held by their hands are an example .

Crutches , fracture in the groove, person who stays holding his whole body by his hands (overstretching of radial nerve) that will cause the radial injury and causes wrist drop. (the reasons of radial injury in our countries)

- In USA and Europe the wrist drop is called the Saturday night syndrome , it is same to wrist drop , but in developed countries they work hard in the week days when they come to the weekends they go parting and they drink alcohol by the end of the day either he let his girlfriend sleeps on the humerus or he sleeps on the bar a way overstretching the radial nerve , so he will have a wrist drop at morning .

- **Erb's Palsy & Klumpke's Palsy , what is the difference between them?**

Upper brachial plexus when it is damaged (c5,c6) the patient or baby who is born is the waiter step, because in UK usually , waiters when you tip them they usually put their hand in this way so that you tip them because they are not beggar, they are serving you , so they call it waiter step hand or Erb's palsy and we can see this in the babies who are born cephalically (يسحب)
(الطفل من رأسه الذي يكون للأسفل)

But when the baby is coming on his buds (lower limb) first then we pull the body , then we pull the arms , the brachial plexuses will be hurted in the lower part and that will cause **Klumpke's dejerine** like ulnar nerve (c8,T1) . **breach presentation**

Lower part comes out first and his hand is like claw hand but there is more symptoms in the upper limb and that why we call it: klumpke-dejerine paralysis (partial damage to C8,T1 which is lower thoracic).

Question: if I am examining my patient and I put electrodes on the medial nerve what will I record? action potential or graded potential?

GOOD LUCK ☺

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