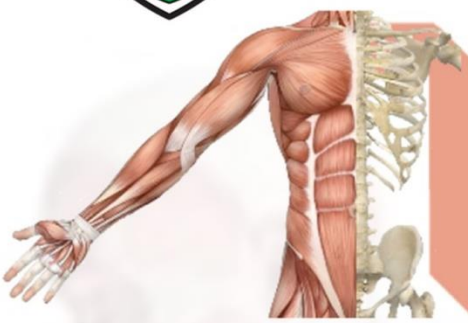

MSS

Musculoskeletal System

Doctor 2019 | Medicine | JU

NO.1

Physiology

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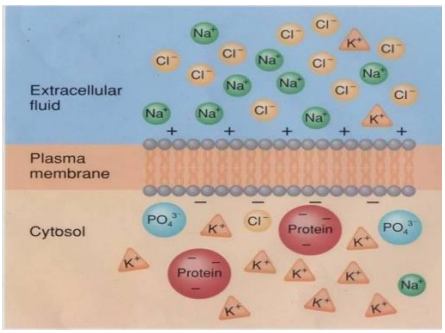
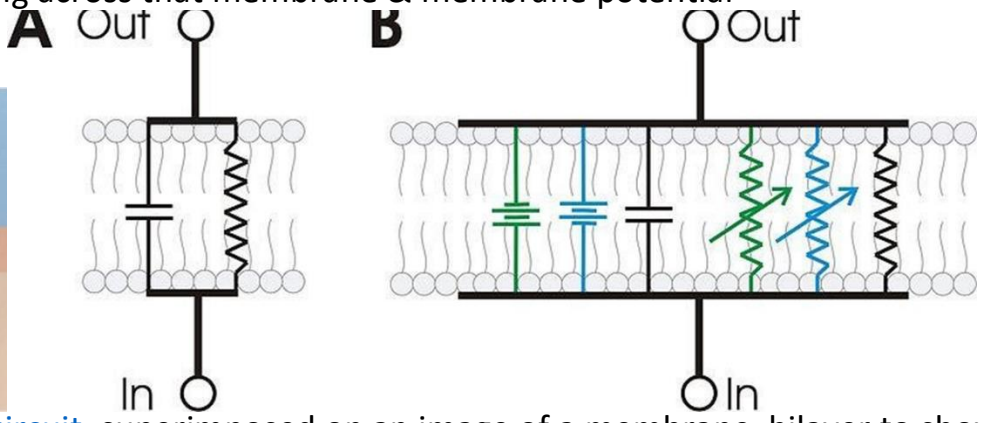
Grammatical correction:

Doctor: M.khatatbeh

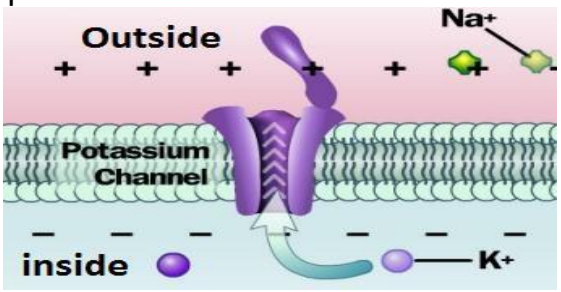
Plasma Membranes of Excitable Tissues (Review lecture):
00:00-11:39
plasma membrane of excitable tissues (review lecture)
electrical properties of the plasma membranes of excitable cells (the motor neurons & the muscles) :
those membranes separate two compartments with different composition (general property)
☞creating what we are calling across that membrane & membrane potential





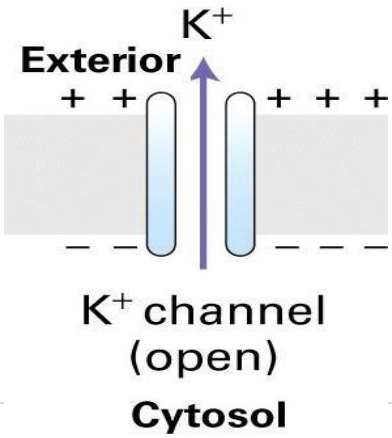
- **Part A:** A basic en:RC circuit, superimposed on an image of a membrane bilayer to show the relationship between the two. **Part B:** A more elaborate en:RC circuit, superimposed on an image of a membrane bilayer. This RC circuit represents the electrical characteristics of a minimal patch of membrane containing at least one Na and two K channels. Elements shown are the transmembrane voltages produced by concentration gradients in potassium (green) and sodium (blue), The voltage-dependent ion channels that cross the membrane (variable resistors;K=green, Na=blue), the non-voltage-dependent K channel (black), and the membrane capacitance.

we describe the plasma membrane as an electrical circuit : a capacitance switches as separator of charges.
-the membrane is negative inside & positive outside because we have different permeabilities for different ions which creates membrane potential

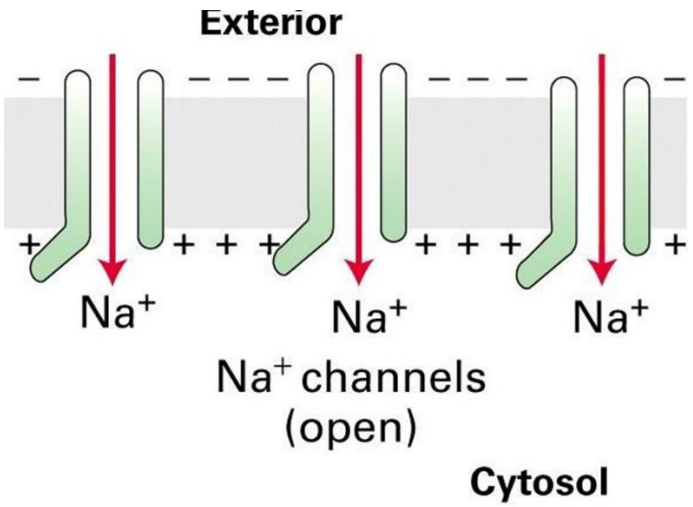


the membranes are equipped with channels (K, Na,..) that have different properties - once we have high activity for potassium chanels we are getting potassium leaving from the high concentration inside the cells toward the low concentration outside the cell

here we have the proper tune :active potassium channels
so we can develop a potential
(negative inside with regard to outside)



if we have sodium chanels open we can develop a potential (negative outside with regard to inside due to the movement of positive ions Na+ from outside to inside)



equations that are helpful for measuring or calculating the membrane potential :

Nernest equation : in case we assume that the membrane is only permeable for one ion

$$E = \frac{RT}{ZF} \ln \frac{[C]out}{[C]in}$$

R (Gas Constant) = 8.314472 (J/K·mol)
T (Absolute Temperature) = t °C + 273.15 (°K)
Z (Valence)
F (Faraday's Constant) = 9.6485309×10^4 (C/mol)
[C]out (Outside Concentration, mM)
[C]in (Inside Concentration, mM)

E : equilibrium potential for the permeable ion

Electro-chemical Equilibrium

the created potential by the electrochemical equilibrium is called the electrochemical potential
we have two forces that can move these ions : the concentration gradient for the ion & voltage gradient that can be created
at equilibrium the summation of the two forces = zero
this picture shows you how the Nernest equation is written

$$\Delta G_{conc} + \Delta G_{volt} = 0$$

$$zFV - RT \ln \frac{C_o}{C_i} = 0$$

$$V = \frac{RT}{zF} \ln \frac{C_o}{C_i} = 2.3 \frac{RT}{zF} \log_{10} \frac{C_o}{C_i}$$

simplified form of the equation (calculate the constants)

$$E_{eq,K+} = 61.54mV \log \frac{[K^+]_o}{[K^+]_i},$$

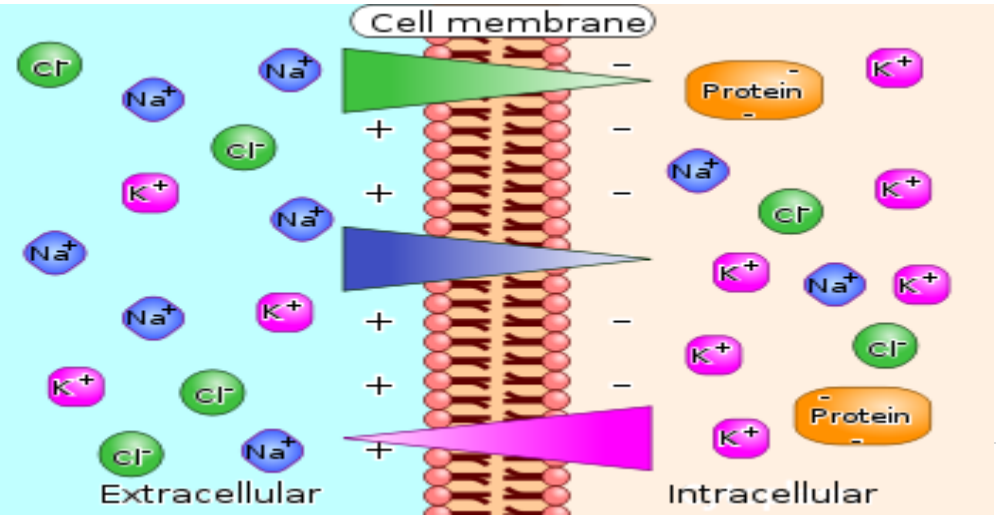
E (mV) = - 61.log (Ci/Co) E = Equilibrium potential for a univalent ion/ Ci = conc. inside the cell. /Co = conc. outside the cell.

Concentration of Ions :

Ion	Extracellular (mM)	Intracellular (mM)	Nernst Potential (mV)
Na^+	145	15	60
Cl^-	100	5	−80
K^+	4.5	160	−95
Ca^{2+}	1.8	10^{-4}	130

we have differences in the concentration for these different ions we can create potentials if assuming that the membrane is only permeable for one ion
for example :
-if assume that the membrane is only permeable for sodium we can create a potential across that membrane which is +60 milli volt (+: means it's positive inside with regard the outside).
-if assume that the membrane is only permeable for potassium we can create a potential = -95 mV (- : negative inside with regard to the outside)

Goldman Hodgkins Katz equation : assuming that the membrane is permeable for many ions



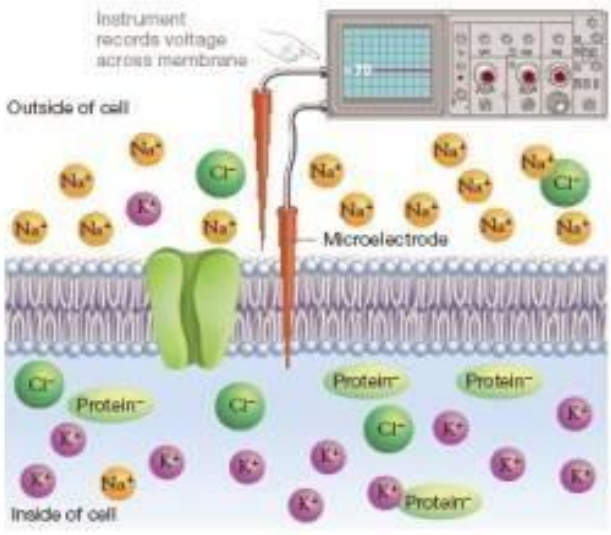
Goldman Hodgkins Katz equation :

the membranes can be permeable for many ions so we have another equation by which we can calculate the membrane potential- if we assume that we have permeability for many ions - according to the permeability and the concentrations we can calculate the membrane potential by using Goldman Hodgkin Katz equation.
(dr. said that :you can go back to the last year lectures to understand that equation & to figure out what would be the difference and how we can create that membrane potential).

$$E_m = \frac{RT}{F} \ln \left(\frac{P_{Na+}[Na^+]_o + P_{K+}[K^+]_o + P_{Cl-}[Cl^-]_i}{P_{Na+}[Na^+]_i + P_{K+}[K^+]_i + P_{Cl-}[Cl^-]_o} \right)$$

i = Conc. Inside /o = Conc. Outside / P = permeability of the membrane to that ion.

the potential can also be recorded but once you are recording you have to place the electrode just inside the membrane and the other electrode just outside the membrane to
measure the potential difference
across that membrane.



Resting membrane potential of the excitable cells depends on :
Activity K+ channels
Activity of Na+ channels
Na+/K+ pumps

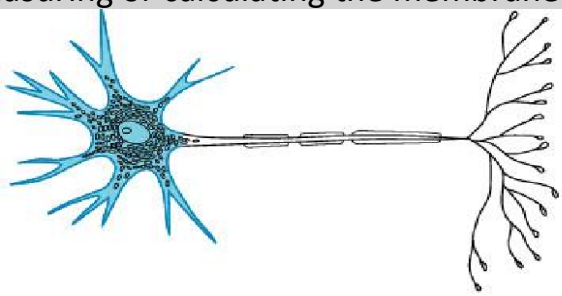
Conductance of plasma membrane (Ohm's Law) : the plasma membrane is also having conductance , once we have charged particles moving that means we have electrical current moving across that membrane, the the current
across that membrane can be calculated by ohm's low
I = ΔV/R
I : current / v : Voltage /R: resistance
G (conductance)= 1/R
the conductance : how many charged particles can move from one side to another
I = G. ΔV
cord conductance equation: equation describes the contributions of permeant ions to the resting membrane potential
another equation by which we can calculate the membrane potential according to the conductances for these ions

$$V_m = \frac{g_K}{g_{tot}} E_K + \frac{g_{Na}}{g_{tot}} E_{Na} + \frac{g_{Cl}}{g_{tot}} E_{Cl}$$

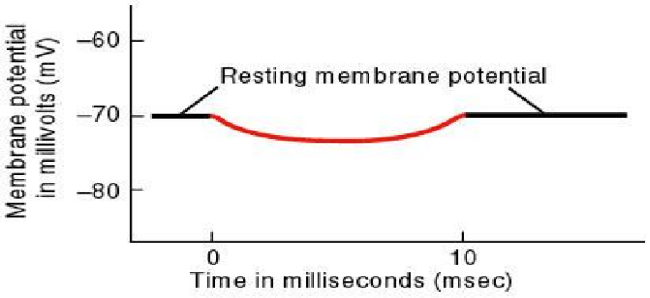
doctor said : "it isn't my intention to have you memorizing all the details, but only to remind) you about these equations that can be useful for measuring or calculating the membrane potentials "

11:39

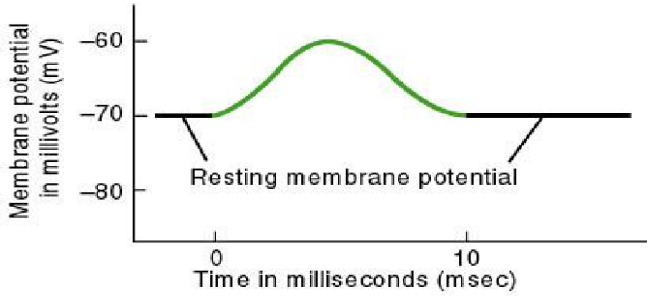
Changes in Resting membrane potential:



we have reached a point that we have what we ,are calling a resting membrane potential
but that membrane potential can change according to the changes in the permeabilities or changing in the conductances (the same meaning with different definitions between the permeabilities and the conductance, once we are talking about conductance : we are talking about currents, once we are talking about permeabilities we are talking about movement of (particles



(a) Hyperpolarizing graded potential

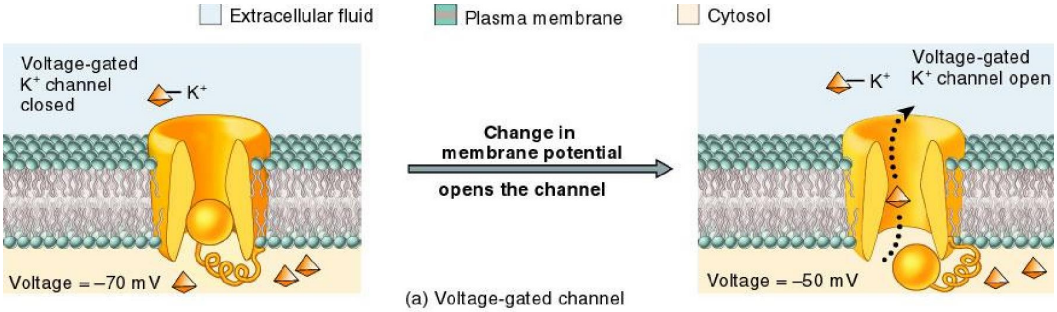


(b) Depolarizing graded potential

12.10

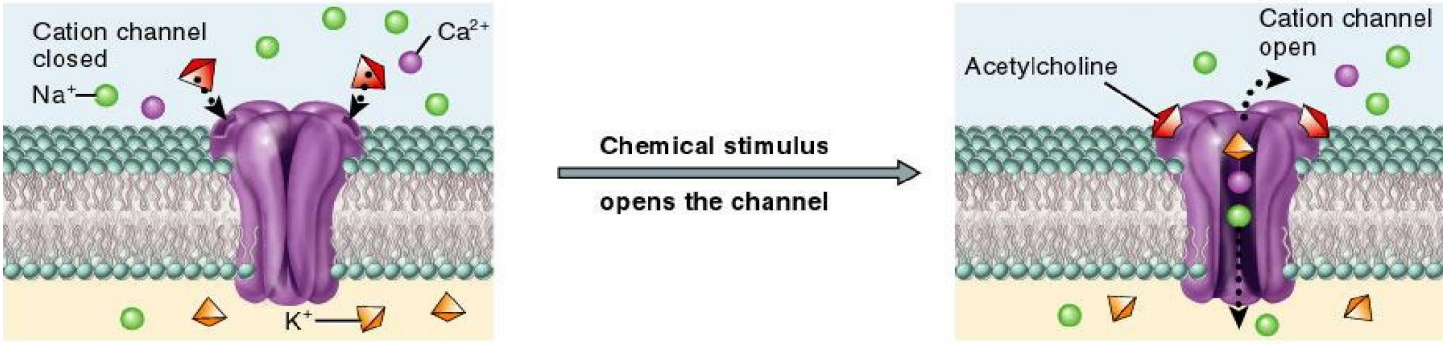
so what happens here in the first part of this picture (the red part)
if we have for example higher permeability (or higher conductance) for potassium we are getting more negative potential across that membrane can be created which is called hyperpolarization
the second part (in green) : if we have activated for example more sodium channels so we are getting less negative resting potential which is called depolarization
the membranes of excitable cells in addition that they can create a resting potential they also can depolarize or hyperpolarize and that happens by activation of channels that are found at thase plasma membranes

activating these channels: we have different modalities for the activation of these channels:



(a) Voltage-gated channel

voltage gated channels: we can activate these channels by changing voltages (by changing the membrane potential itself) so if you have depolarization for example you can activate some types of channels.

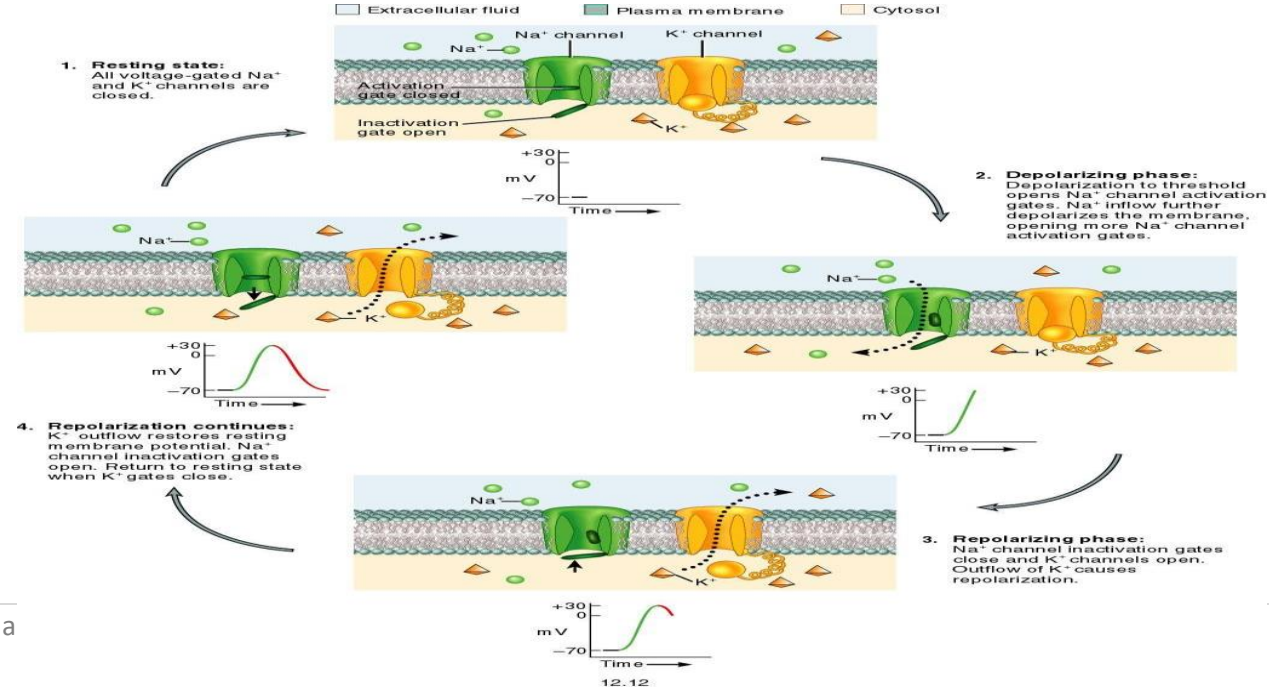


(b) Ligand-gated channel

12.08

chemical gated chanels : also we have another modality by which we can activate these channels is by chemical products or ligands which can bind to their receptors like acetylcholine binding to its receptor then causing activation of these channels

I think you remember the signal transduction mechanism by which we can get activation of " "some channels by having ligand binding to their receptor
this video may help you to remember https://youtu.be/-dbRterutHY-
so by this process the activation of these channels, the membrane of these excitable cells they can develop what we are calling action potentials
I think you remember the action potential so how that happens ?!
Changes in Channels activity results in action potential
from the resting potential the membrane is depolarizing causing activation of sodium chanels
(voltage gated channels) by activation of more voltage gated sodium channels the membrane potential is trying to reach the equilibrium potential of sodium which is about +60 mV, but at the tip of the development of this potential we can have inactivation of these
voltage gated channels and more activation of potassium channels which may result in repolarization phase of the action potential and then returning back to the resting potential
so this is the process we can have we are getting activation of voltage gated channels that can change the the membrane potential to get development of action potential



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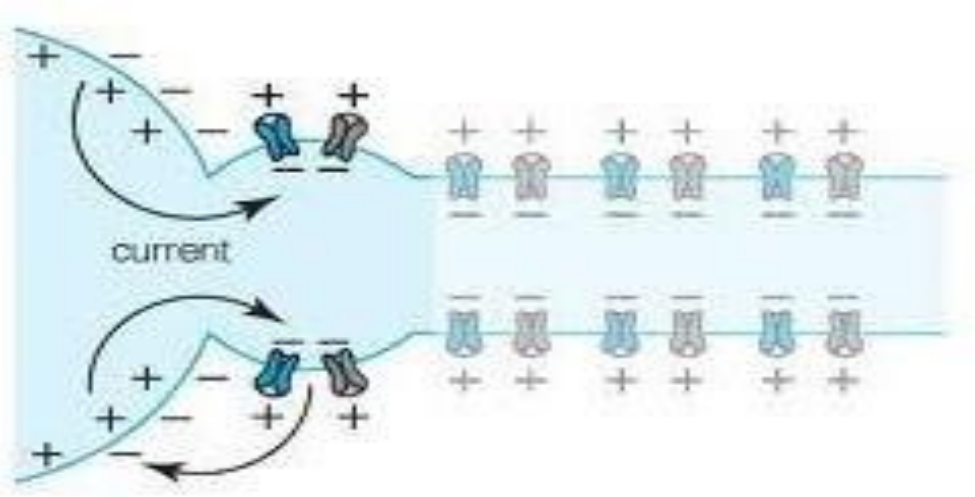
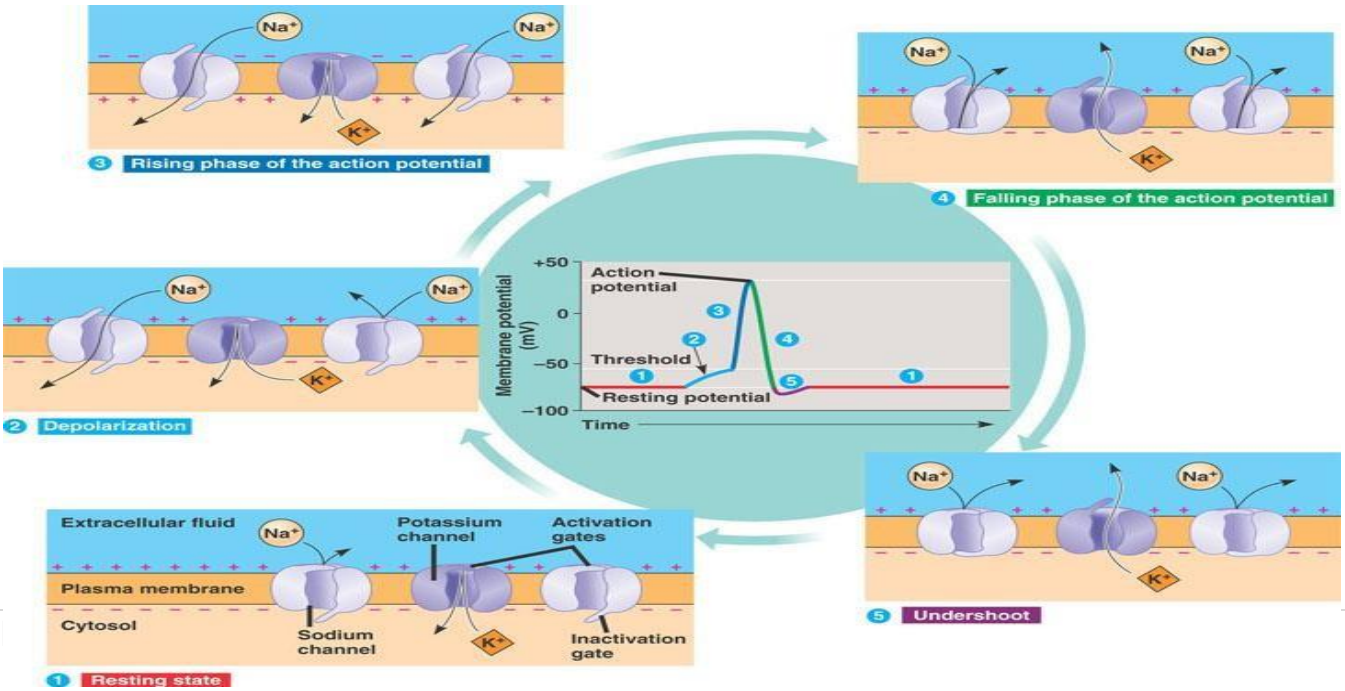


Ionic currents cause depolarization (follow the picture from left to the right)
how we activate this voltage gated channels simply by local currents, assuming here the cell body of neurons for example at this part of the cell body we are having action potential once you have action potential so we are creating positive potential inside and negative outside and the nearby channels at the resting potential so its negative inside with regard to the outside, by having that situation we are creating currents from the positive region towards the negative regions and by having these currents we are depolarizing the nearby part of the membrane to get activation of these channels and by the activation of the channels we are developing an action potential at this part and so on .

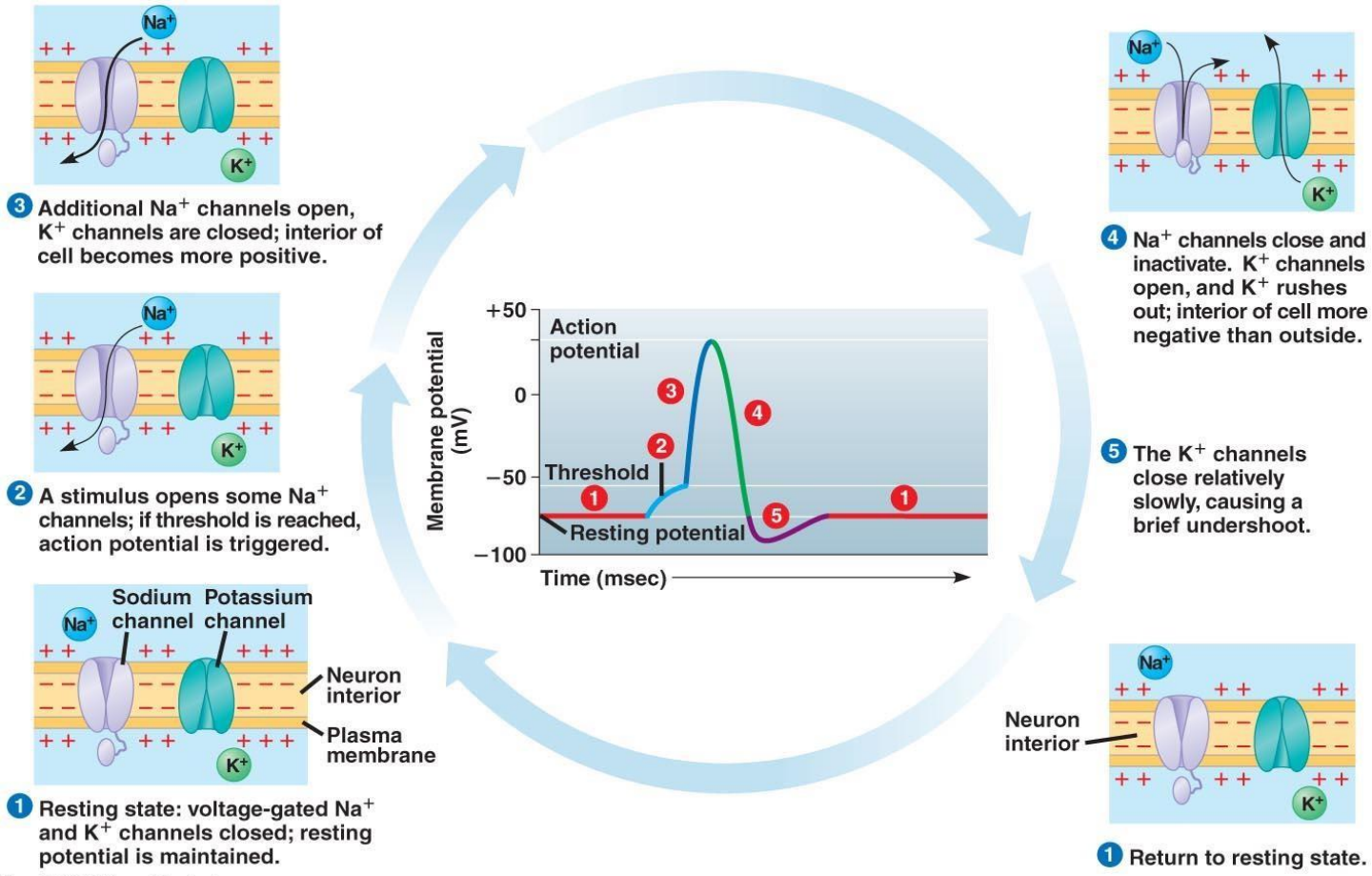
Resistance to Ionic currents and activation of channels

in addition of having currents moving at the surfaces but we have also high resistance of ionic currents across the membrane itself that resistance depends on the activity of channels, if you have more channels active you will have less resistance if you have less channels active you will have more resistance for currents across the membrane, also the resistance can be at the surface depends on the conditions that we are having, we will see some of these properties
-if you have more channels active that means the conductance is higher, if you have higher conductance that means the resistance is lower.



finally the membrane of excitable cells having a third property : they can develop what we .are calling action potential
and i think you remember from the last year how we are developing these action potentials recap:
so from the resting potential we have small depolarization reaching this point, which is called threshold, once you have reached it you are getting much faster depolarization which is called firing stage of action potential, reaching the tip here trying to reach the equilibrium potential for sodium and once you have reached the tip of the action potential you are getting inactivation of the sodium channels (voltage gated channels) and more activation of the potassium channels and then going back towards the resting potential
: so the picture is showing you the phases of the action potential at the excitable membranes starting from the resting state - depolarization - reaching threshold - activation of voltage gated sodium channels - inactivation of voltage gated sodium channels - more activation of potassium channels - getting repolarization - at stage 5 :we can record another wave which is after hyperpolarization (the positive after potential

20:39



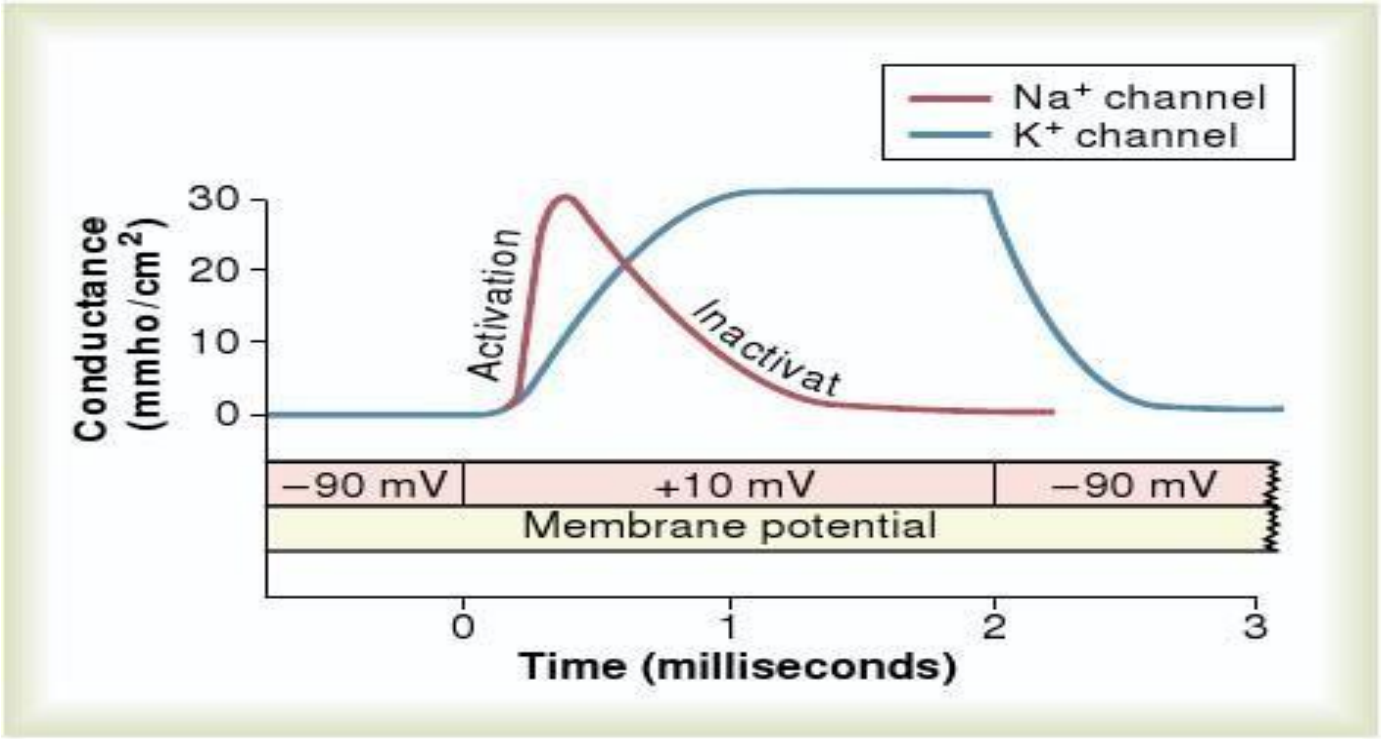


Figure 5–9

nowe we are going to discuss more details about the activity of each channel during each phase of action potential

- 90 mV: resting potential (see the picture)

we reach a point by depolarization to activate that resting potential we have low activity of sodium channels, some degrees we have active potassium channels which are establishing the resting membrane potential, what happens at threshold : fast activation of sodium channels, at the same time we are starting activation of potassium channels

blue : refers to the activity of potassium channels

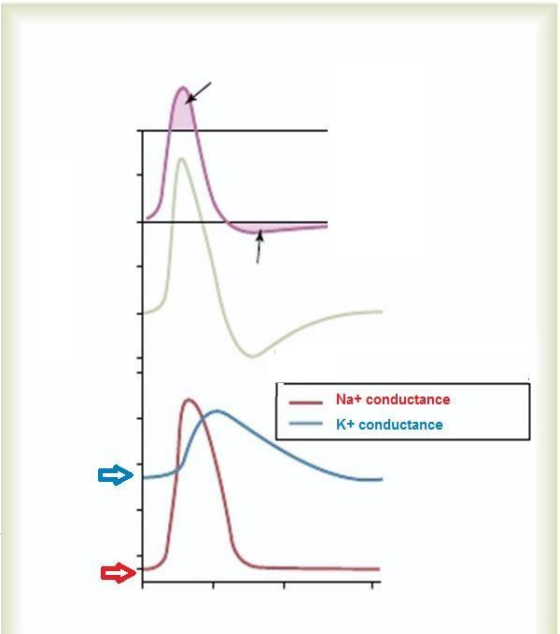
red : for sodium channels

once you reach the tip, 10 mV here : you are getting fast inactivation of sodium channels then starting repolarization getting more activity of potassium channels, once you return back to the resting potential which is about - 90 here you are getting inactivation of the voltage gated potassium channels

Na+ and K+ conductance at resting potentials

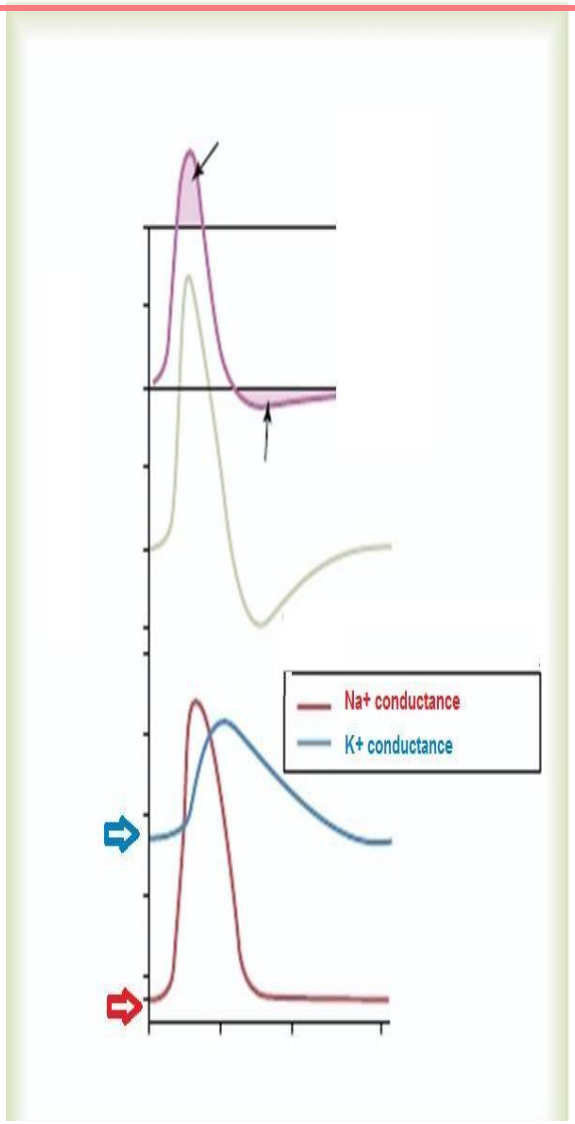
at the resting membrane : we have very low activity of sodium channels which means we have very low conductance for sodium, to some degree we have higher conductance for potassium which results in establishing the resting membrane potential of (-85~-90)which is .very close to the equilibrium potential for potassium

at threshold you are getting fast activation of sodium channels, you are also starting activation of potassium channels as the sum of these currents and conductances, you are getting a change in



the voltage which is the fast depolarization of the membrane which is
called the firing stage here you are reaching the tip of the action potential at the tip you are
starting inactivation of sodium channels but still activation the potassium channels, by
activation more potassium channels you are getting repolarization phase

in the middle is the sum of the conductances for the Na & K (both of them are positive but
moving at opposite directions so the sum of the conductance favoring Na first because we
have higher conductance for sodium while the sum of conductances during the falling phase
favoring the higher conductance for potassium which is moving from inside to outside in the
reverse direction for sodium movement
26:58



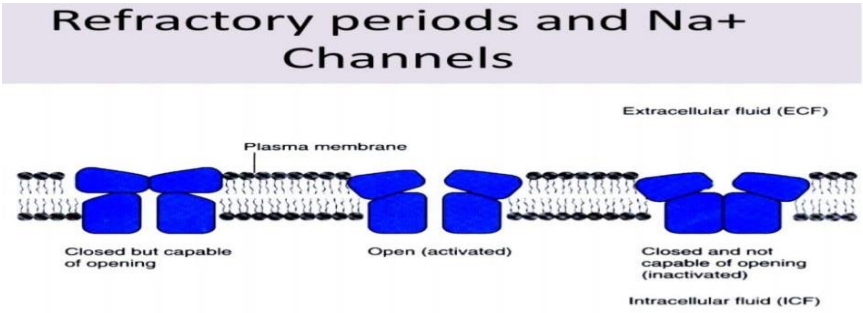
In neurons and skeletal muscle we have only the two ions which are involved in the development of action potential which are the sodium ions and the potassium ions.

➡ Remember: **Sodium channels have three states**:

1. **Closed but capable of opening** during the resting potential and depolarization until reaching the threshold. (once reaching threshold this channel becomes activated)

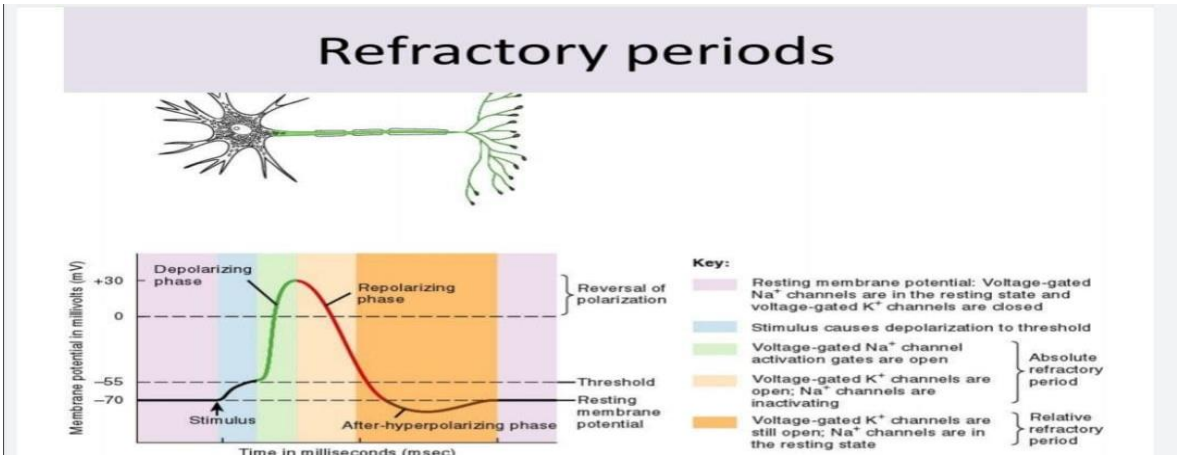
2**. Open** Nearly all sodium channels are open during firing stage. (once reaching the tip of action potential these channels become closed but incapable of opening)

3. **Closed but incapable of opening** this state occurs during the falling phase and the channels return to the first state when the resting membrane potential is reached (**NOTE**: The channels can be actually opened in this state but ONLY by large electrical stimulus



Refractory Periods

- **Absolute refractory period:** neither the usual currents nor higher currents can not open these channels (no new action potential can be generated because the sodium channels are already in the opened state in this period)
- **Relative refractory period:** is the interval immediately following the Absolute Refractory Period once channel transferred to closed but in capable of opening so initiation of a second action potential is INHIBITED, but not impossible. (needs stronger stimulus)

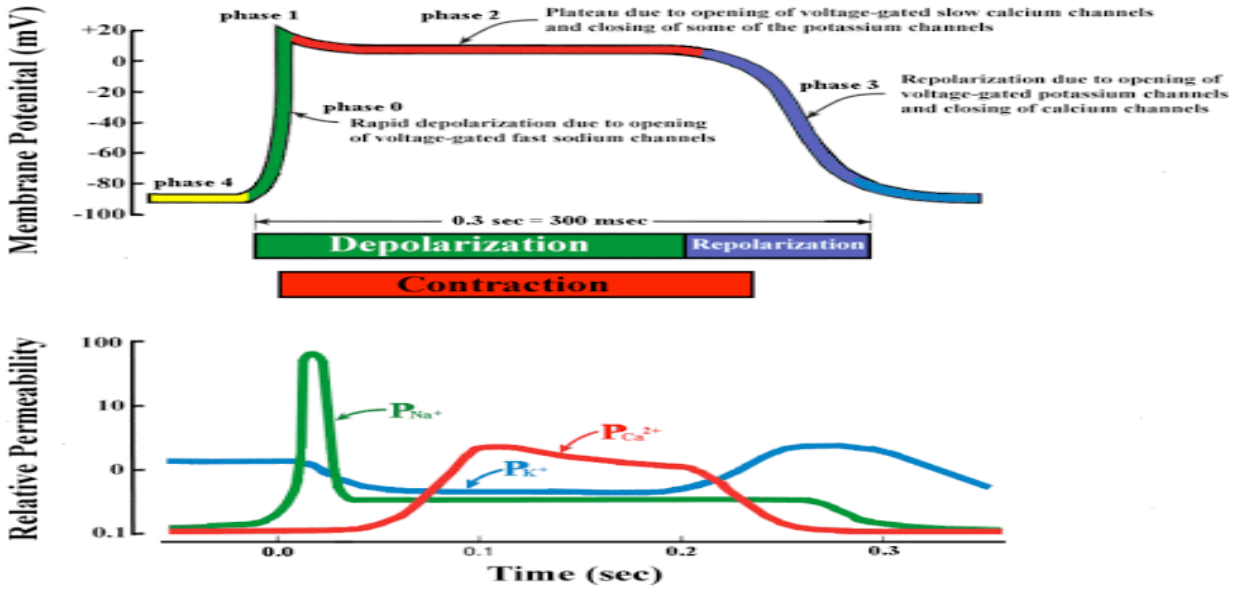


Involvement of other ions in action potential:

- In some excitable cells, like cardiac muscle , cells are equipped with another type of channels known as slow Na+ – Ca++ channels.

-These channels open at a much slower rate than Na+ channels and this will cause Ca+ to enter the cells and prevents the rapid fall induced by activation of k+ channels this is called Plateau.

This provides a longer refractory period giving more time for the cell to be able to respond to another stimulus. For example: the heart can contract and relax at the same time**.**



Nervous system cells are formed by: -Neurons - Supportive 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.

Neurons can be classified depending on the presence of myelinated nerve fibers to:

a- Myelinated nerve fibers:

➡Have Myelin sheath around the axons.

➡Nodes of Ranvier are exposed to extra cellular fluid so the action potential developed there is then transmitted from one node to another. This type of potential transmission called **Saltatory Conduction**.

➡current flow in Nodes of Ranvier so it is faster than in unmyelinated.

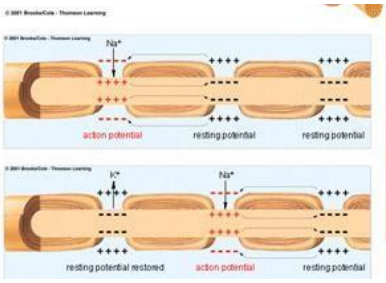
b- Unmyelinated nerve fibers:

➡These neurons have axons that are fully exposed to the extra cellular fluid so the potential developed along the axons and the current flow moves continuously from one area to the next. This type of potential transmission is called **Continuous Conduction**.

➡current flow along the axons.

NOTE: -The Neuron with the bigger diameter has faster current flow, due to the less resistance in its cross section area.

-The myelinated neuron also faster than unmyelinated, because we skip a big part of axon between Nodes of Ranvier.



Saltatory Conduction in Myelinated axons

In the saltatory conduction at any time you have action potential and local current in a node can cause depolarization of the next node and so on

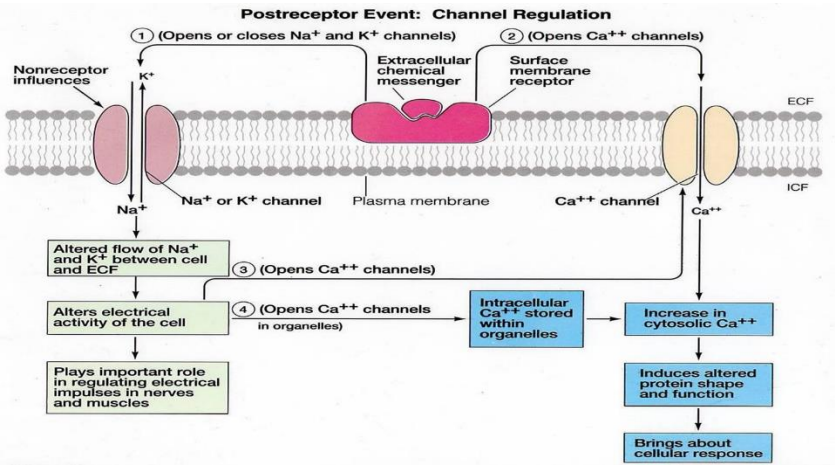
**- What happens at the synapse? ***the same transmission takes place on neuro muscular junction between motor neuron and muscle

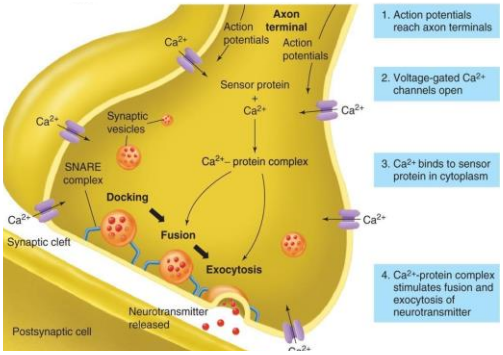
-* Once the impulse reaches the terminals of the presynaptic neuron, the activation of Ca++ channels occurs, allowing the influx of Ca++ into the synaptic knop that triggers the release of neurotransmitters into the synaptic cleft by exocytosis .

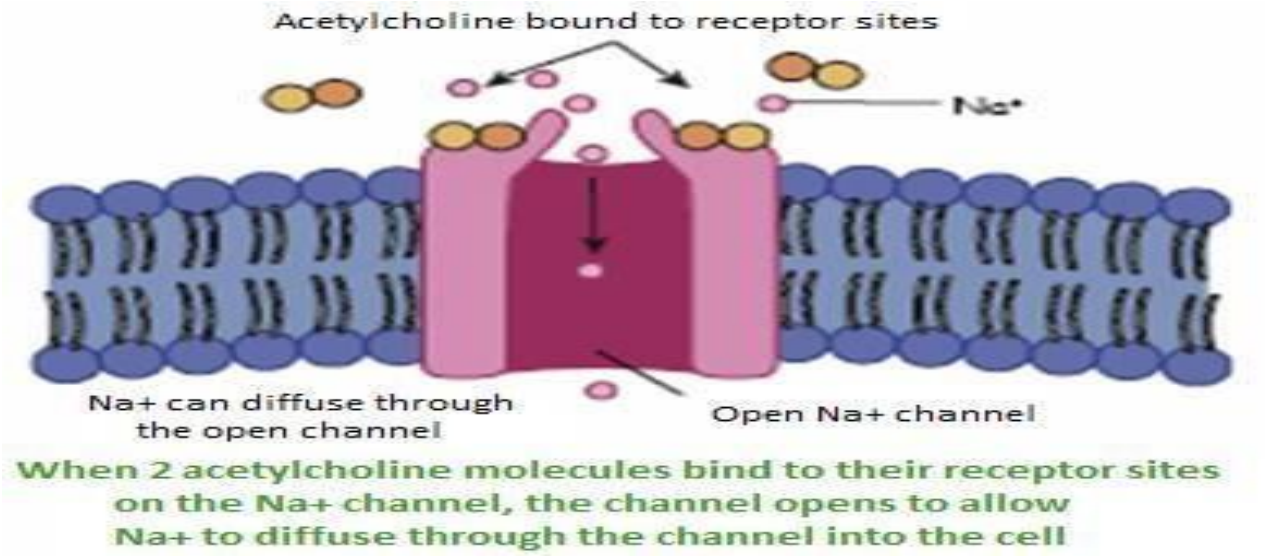
* These neurotransmitters bind to a specific receptors on the postsynaptic membrane (on skeletal muscles, the neurotransmitter is Ach that binds to nicotinic receptors). Depending on the type of these ligand gated channals , this will either trigger the activation of Na+ ligand gated channels which allows an influx of Na+ into the postsynaptic membrane that leads to depolarization , this is called **Excitatory Post Synaptic Potential (EPSP)**, these are not action potentials , but small depolarizations (post synaptic potential/subthreshold potentials). Or it might trigger the activation of K+ ligand gated channels,if present, which allows an efflux of K+ out of the postsynaptic membrane leading to hyperpolarization , this is called **Inhibitory Post Synaptic Potential (IPSP).**

NOW, Postsynaptic neurons generate either inhibitory post synaptic potentials (IPSP) or excitatory post synaptic potentials (EPSP), a process of summation of these potentials can occur. By these processes of summation an action potential can be or can't be triggered in the axon hillock by the post synaptic neurons.

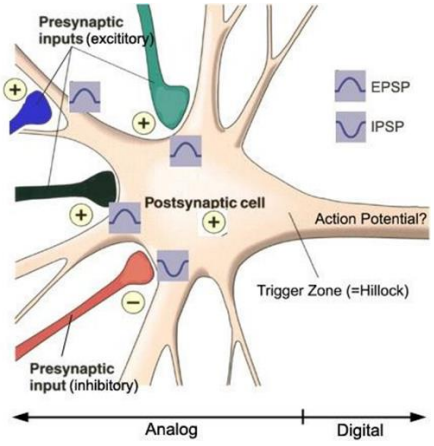
43: 00 At the neuromuscular junction we only have activation of sodium channels so we will develop at the muscle membrane like excitatory post synaptic potentials which are called motor endplate potentials we will discuss it more in the next lectures

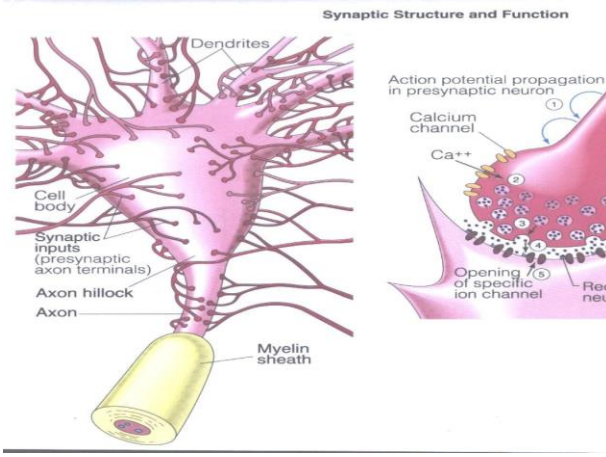


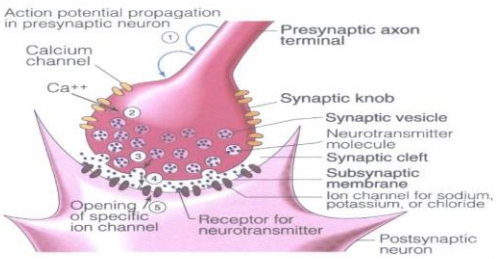




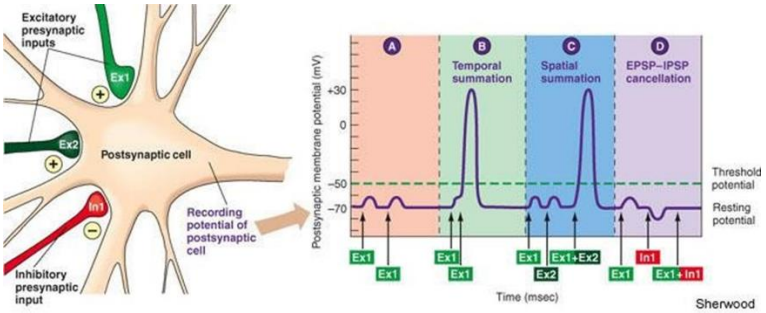
This what happens at the actually muscles, we have activated Na channels so we are getting depolarization, the neurotransmitter here is acetylcholine







the motor neuron is receiving many inputs, some of terminals that are synapsed with the cell body of motor neuron can cause excitatory potentials but you can have also some other terminals can cause inhibitory post synaptic membrane potential , what we are getting is integration of these potentials and by summation if have reached the threshold at the axon hillock we will get action potential



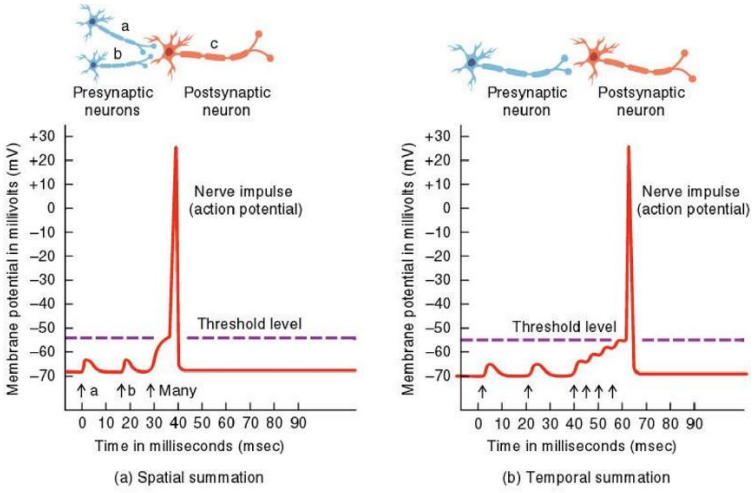
Summation

There are two types of summation:

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

Temporal summation : which appears when 2 or more potentials are generated from one presynaptic neuron at different times . These potentials are then summed together to induce more depolarization (frequency dependent).

<< So the chemicals (neurotransmitters) induce depolarizations that if they are subthreshold potentials can be summed to reach the threshold.



12.15

Synaptic organization:

1. **Converging circuit**: many presynaptic neurons synapsing with one neural
2. **Diverging circuit**: presynaptic neuron terminals synapsing with many post synaptic neurons.