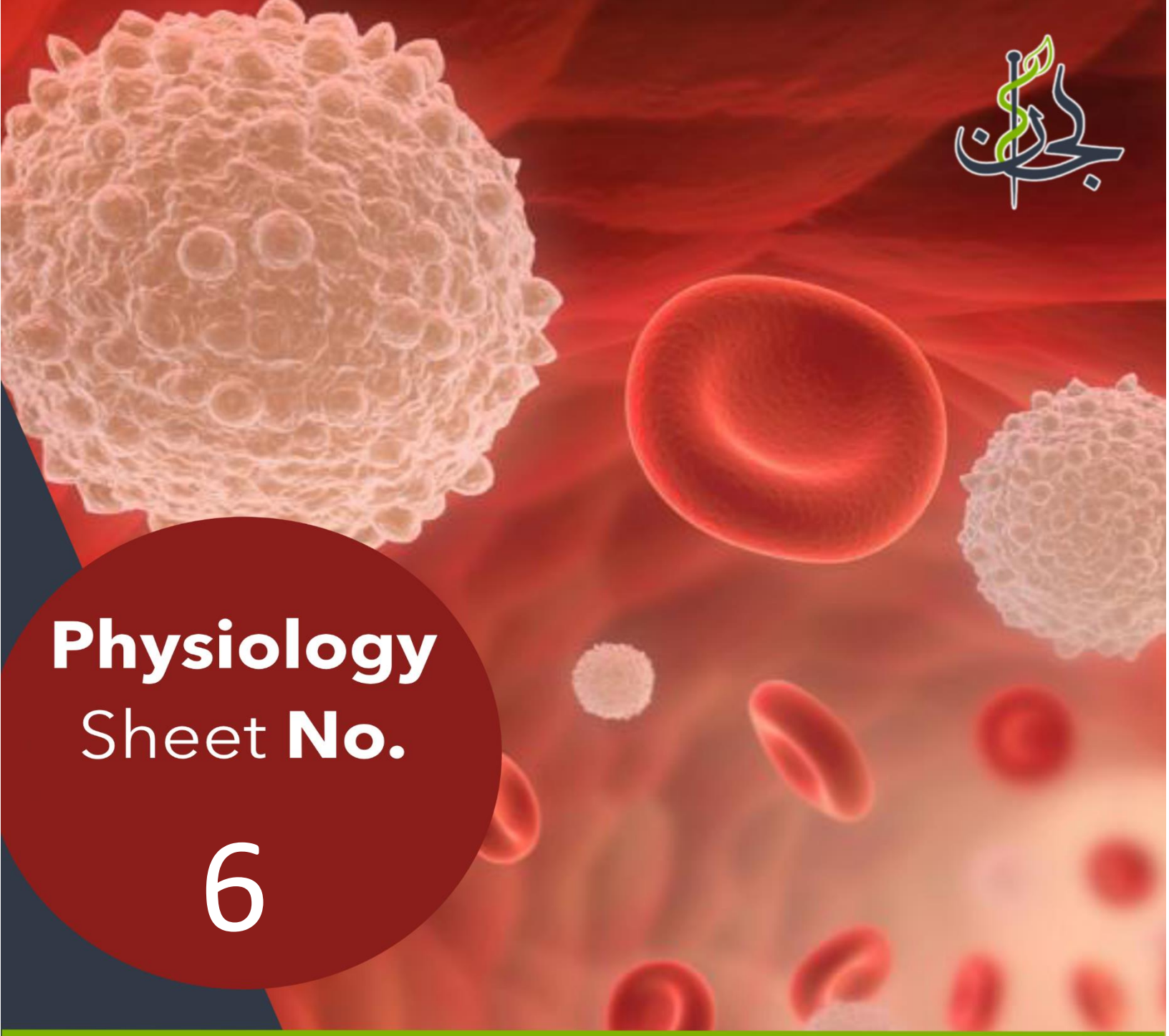

Physiology
Sheet No. 6

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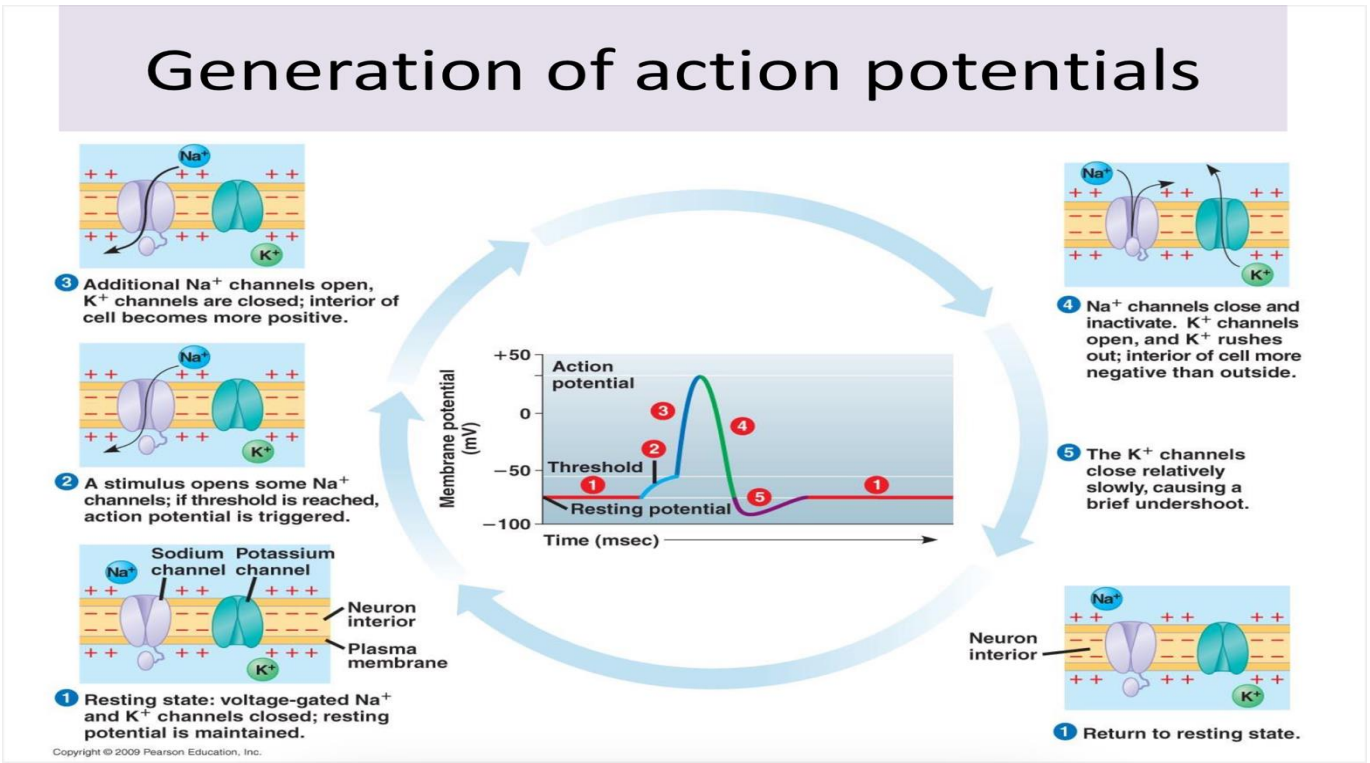


1.Resting membrane potential the membrane is polarized (negative inside and positive outside)

2. a stimulus opens some sodium channels

3. depolarization :once you have depolarized that membrane you have reached threshold by reaching threshold you are activating almost all voltage gated sodium channels so at threshold we are getting fast activation of Na channels (this stage is also called firing stage).

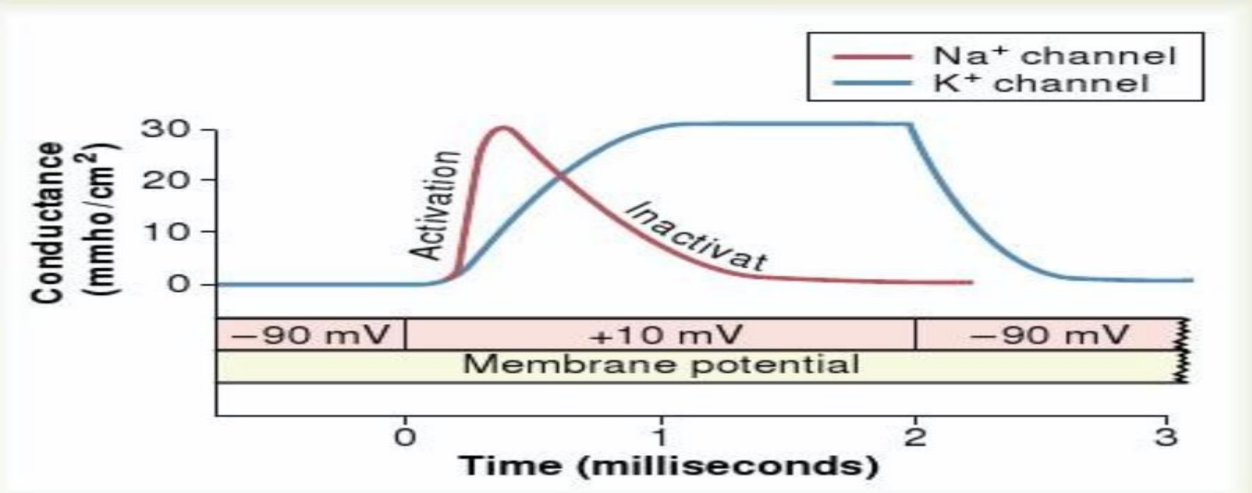
4.Repolarization:Once we have reached the tip reversed the potential we are getting fast inactivation of sodium channels ,by having fast inactivation of sodium channels and having higher activity for potassium channels we are getting the membrane potential turning back toward the resting state and we are getting what we are seeing here in phase 4 according to action potential. it called repolarization because the cells which are generating resting membrane potential (negative inside and positive outside) are called polarized cells so simply repolarization we are returning back to the polarized state .(also known as the falling phase)

5.Hyperpolarization: the potassium channels sre closing but they have broduced more negative potential than the resting membrane potential (also called positive after potential or after hyperpolarization phase or undershoot)

- The questions is why we are calling it positive after potential and it is more negative actually than the action potential that we are having? why we are calling it after hyperpolarization and we have no hyperpolarization before?

The first action potential was recorded as changes outside with regard to inside but now we are recording it as changes inside with regard to outside how it's look when we are recording the changes outside with regard to inside simply it like a mirror so you are getting from the resting potential you are get depolarization down then you are getting phase 4 then you are returning back toward the resting membrane potential then you are getting that wave as more positive than the resting potential so imagine that you're having the recording in a mirror image upside down so we are getting decrease (outside) with regard to inside then you are reaching the tip then you are returning toward the resting potential and you're getting a positive wave after potential and because of that it was called positive after potential so it has kept the old name that it had in addition to that we have here (3) the fast reflection so we have exceeding the zero voltage to record positive wave we called it over shot (positive inside with regard to outside we have a reversal aspect during that phase of a polarized membrane.

Voltage gated potassium channels change their behavior at specific voltage starting from the threshold (start to be activated) and the maximum activity of these channels is during phase 4 in the action potential while we are getting fast activation of Na-channels in the threshold potential (phase 2) which result in fast reflection of action potential toward zero maybe becoming even more positive inside with regard to outside toward the tip of that action potential which is called phase 3.



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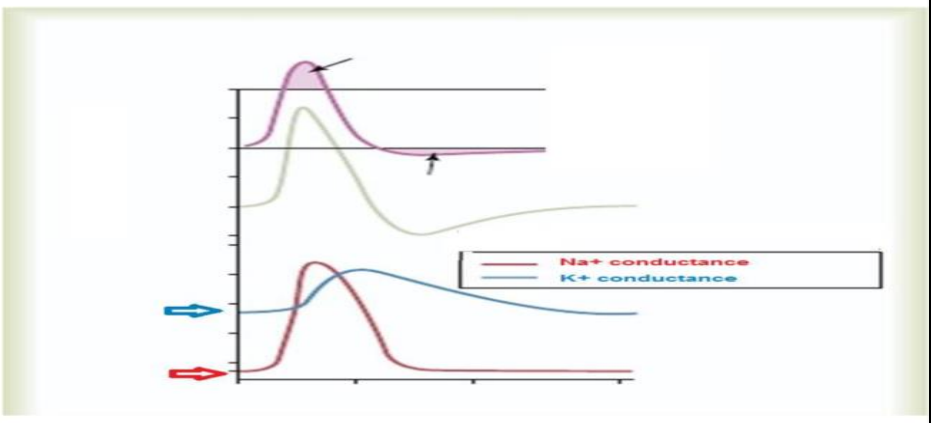
At threshold we are activating both types of these voltage gated channels we have fast activation for the sodium channels which results in that fast increase in the conductance for sodium as you see in the figure and we also start with slower activation of potassium channels which results in slow increase in the conductance for potassium .

once you have reached the maximum point at the tip of action potential the activity of sodium channels decreases so the conductance for sodium will also decrease very fast but we still activating the potassium channels and the conductance for potassium is still increasing so the highest activity or the highest conductance for potassium is during that phase of the action potential which is called phase (4).

Resting potential where you have very low conductance for sodium much higher conductance for potassium but once you have reached the threshold you are

- Na+ and K+ conductance at resting potentials



getting fast depolarization or fast change in the conductance force for sodium and the slower changes in the conductance for potassium .

What you are seeing that line in light green is the sum of the conductance of sodium and potassium both of conductances are positively charged particles but sodium is moving from outside to inside while potassium is moving from inside to outside so at the start we have very high conductance for sodium and lower conductance for potassium and because of that the sum of the two conductances favoring the high reflection up here toward +61 millivolts.

OVERSHOOT is when the Inside potential becomes larger than zero, but it NEVER reaches +61mV (the equilibrium potential of Na+)

Sodium channels have three states:

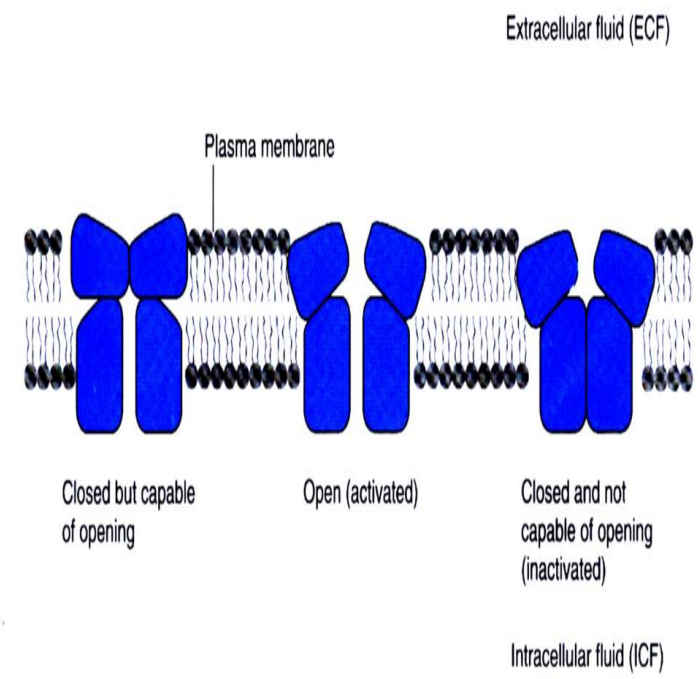
1.closed and capable of opening

During resting potential

2.open

When stimulated during the raising phase (firing) almost all Na+ channels are opened

3.Closed not capable of opening (when stimulated): when voltage dependent Na+ channels become closed after the membrane potential has reached positive values . During all the falling phase of an action potential. They can pass to the first state (closed and capable for opening) when the membrane potential returns to its normal level or to a more negative potential than resting potential.



Refractory periods

1.Abslute refractory period

During action potential the cell is not able to respond to another stimulus. From the firing stage to the end of first third of falling phase the cell will not respond at all even by a stronger stimulus.

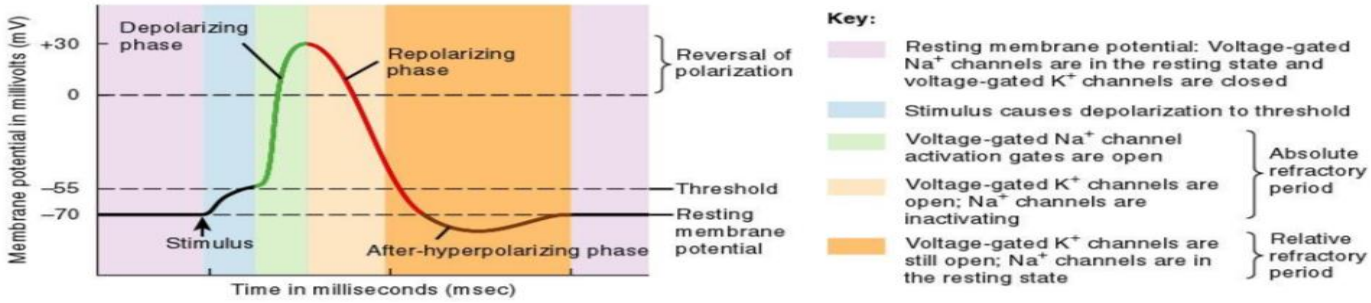
- no new action potential can be generated because the sodium channels are already in the opened state in this period, so a stimulus would NOT change anything.

2. Relative refractory period

From the beginning of the second phase until the resting membrane potential is achieved the cell cannot respond the usual stimulus, but a stronger stimulus can change the membrane potential.

a stronger (suprathreshold) stimulus may activate the closed channels that are not capable for opening by normal stimulation.

During absolute refractory period most sodium channels are in state of activate or opened during relative refractory period they are in the state of closed but not capable of opening if you are out of relative refractory period it closed but capable for opening



Some notes:

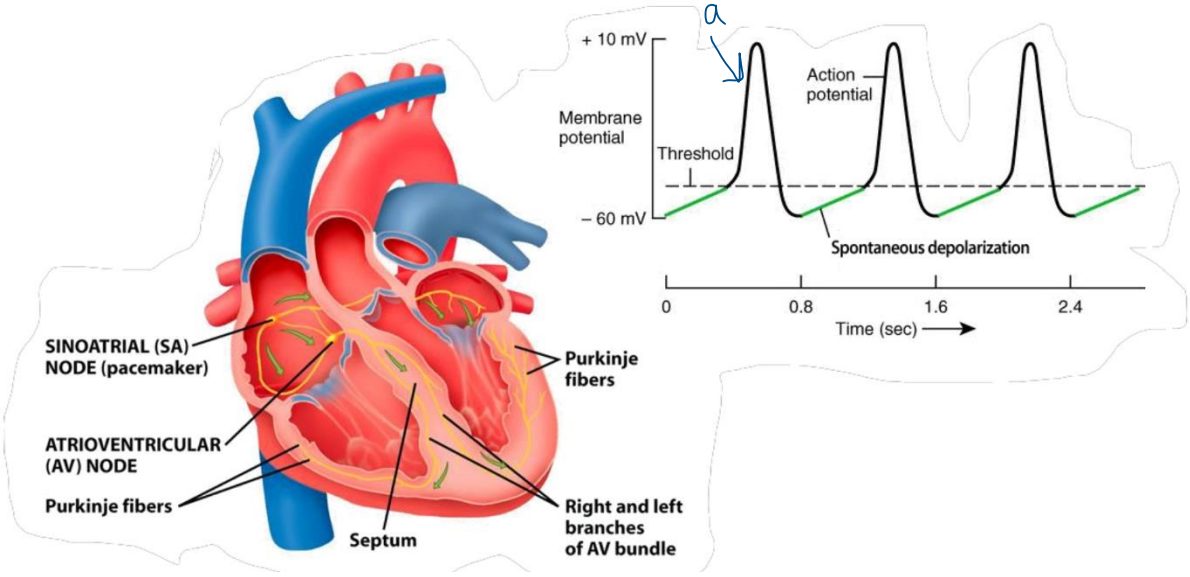
- From resting potential you have Depolarized to reach thresholdPotential that small change in potential some they are called it graded potential
- We are not getting sharp opening and sharp closing for the sodium channels once you have activated them we are getting very fast increase because you have activated almost all of them and activating more and more at the tip now you're starting inactivation of these sodium channels but you're not getting fast or sharp closing so you are needing a period of time to get more sodium channels become closed and not capable of opening and because of that we are considering we have some parts of the repolarization phase included in the absolute refractory period
- We are having after hyperpolarization phase because we are not getting sharp closing of potassium channels so still you have some potassium channels more active which results in a more negative potential than the resting potential until getting closing of all voltage potassium channels that have been active before we are then returning back to the resting membrane potential we are getting inactivation of potassium channels once you have reached resting potential

Involvement of other ions in action

➡ We can find others ions involved in the generation of action potentials we will take the details of them later on with dr.Faisal when he's talking about cardiac muscle and the cardiac conductive tissue.

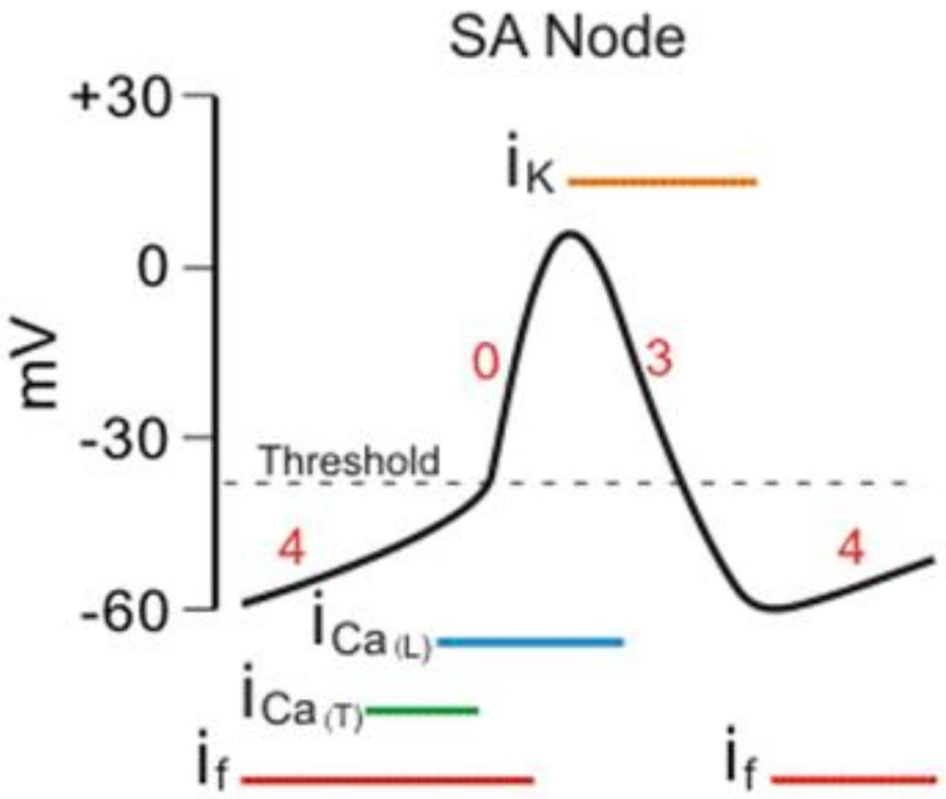
The heart it's a muscle but we have another type of tissue (what are you seeing in yellow) which is called conductive tissue of the heart it's not nervous tissue it's a type of excitable tissue which is having one property it can generate action potential in automatic way How?

Cardiac Conduction



the resting potential here is (-60) because the membrane of these cells which are forming these tissues are having a little bit higher permeability for sodium at any time you have higher permeability for sodium you will get depolarization (the green line) after depolarization you will reach a threshold where we are activating calcium channels and by this activation you are getting faster depolarization as you see in (a) then at the tip you have inactivated these calcium channels and having higher activity of potassium channels then you will returning back toward the resting potential (falling phase) once you have reached (-60)mv you are getting inactivation of this potassium channels and starting to see the effect by having a little bit higher permeability for sodium which is called leakage for sodium so you are starting a phase here which is slow depolarization reaching threshold getting a new action potential so on automatic way these types of tissues are generating action potentials .

Generation of action potential every 0.8 seconds ,or 75 action potentials per minute at the SA node (pacemaker of the heart)

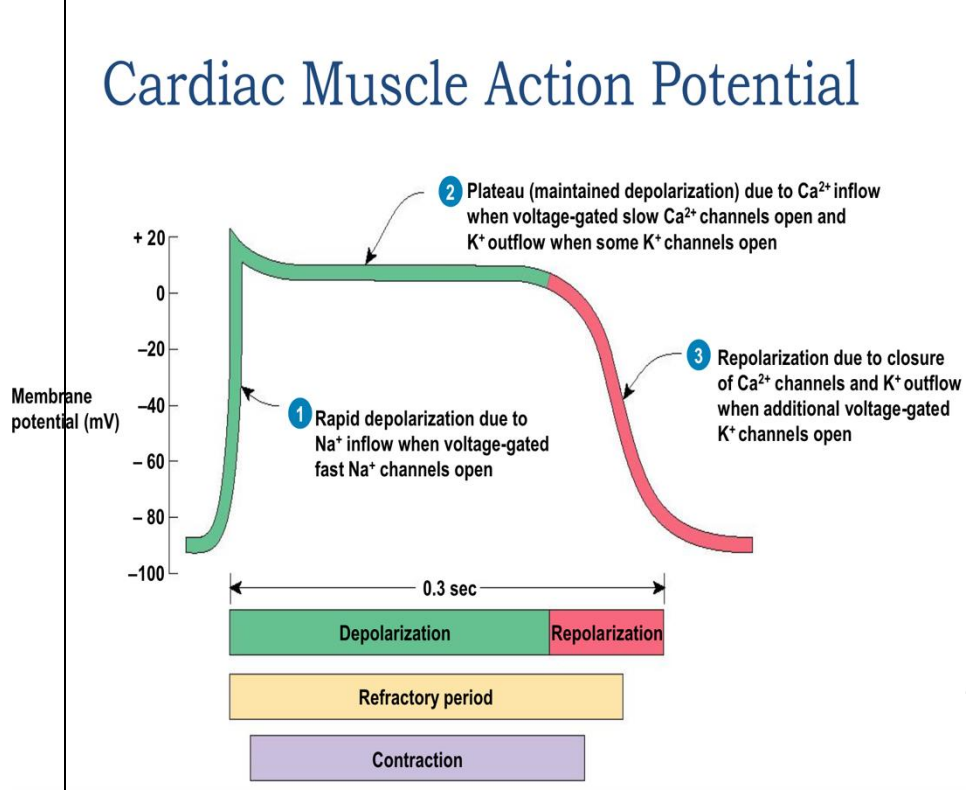


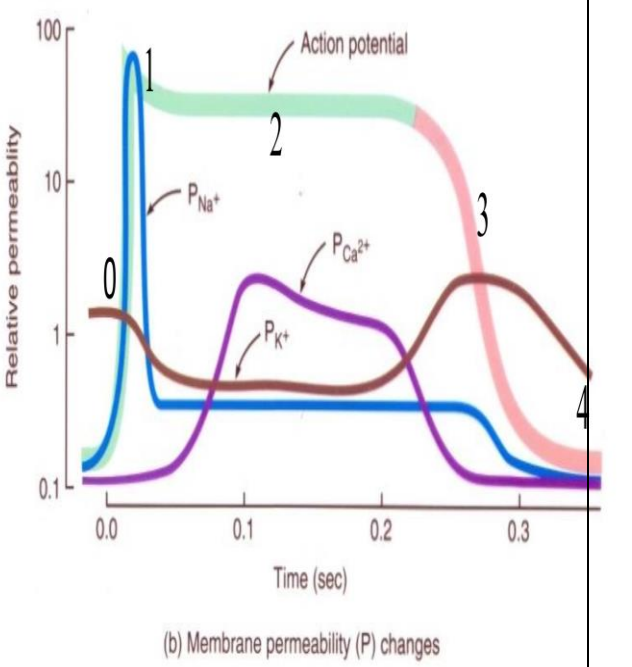
- From the resting potential we have slow depolarization by sodium current we have two steps actually for activation of calcium channels we have two types of calcium channels both of them they are voltage gated channels but the first type which is called the transient type activated for example at (-50) millivolts so once you have shifted the potential from (-60) to (-50) you have activated the first type of calcium channels which are the transient type .

- The activation of transient type causing more depolarization which can cause activation of the second type of calcium channels which are called L-type (long lasting type) by activation of them you are getting the fast depolarization reaching the tip you are starting inactivating these channels but starting also activating potassium channels and by activation of more potassium channels you're getting phase 3 during that period of time you have K channels active once you have returned back toward the resting potential K-channels will be inactivated

(potassium current will decrease) by that we are starting to see again the current created by sodium (the leakage that we have by sodium).

f current (if) is for sodium we called it funny current because it's unusual to have leakage of a membrane for sodium . And by these funny current which are sodium ions moving from outside to inside causing this slow depolarization then you are activating the first type of calcium channels then the second type then you are activating the potassium channels to get that phase which is phase 3 .





Now the cardiac muscle we have another configuration of this action potential .

1. we have very fast depolarization
2. reaching tip started to get repolarization but that repolarization is stopped for a while and getting longer period of action potential until the point where the color is changed.
3. and after that we are getting repolarization again

Figure b indicates the activities of channels that we are having.

0 stage: we have much higher permeability for sodium in the first of that stage

phase 1:reaching the tip slight repolarization why we have slight repolarization because we have very fast inactivation of the sodium channels then we are starting activating calcium channels by having higher activity of calcium channels you are keeping the potential for much longer time once you have inactivated these calcium channels and having higher activity for potassium channels you are getting phase three and returning back to the resting potential .

- Phase 2 called plateau and the whole action potential is called action potential in plateau
- The cardiac muscle is displaying a different configuration of the action potential and we have the involvement of calcium ion in generate it's potential
- The configuration of conductance tissue is messing phase 1 and 2

Action potential and Ca++:

As discussed before, the raising phase of an action potential results by fast activation of Na+ channels. These are called fast channels. In some excitable cells, like cardiac muscle and uterine muscle, cells are equipped with another type of channels known as slow Na+ – Ca++ channels. These channels are activated at slower rate than Na+ channels. The slow and prolonged opening of slow channels will cause mainly Ca++ to enter the cell and prevents the rapid fall induced by activation of K+ channels, and the membrane potential is maintained for a while then the potential falls to its resting level. This is known as plateau in action potential. The presence of plateau in this type of cells is important in prolonging the time of an action potential, giving more time for the cell to be able to respond to another stimulus, because the cell remains longer time in refractory period.