physiology

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◉ Sheet ○ Slides

Number

8

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Quick revision about action potential

➞ Nerve signals are transmitted by action potentials, which are rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane.

➞ Action potential can be summarized as depolarization and repolarization of the membrane of the excitable cells.

➞ During **resting membrane** potential both voltage gated Na+ and k+ are closed.

➞ When a stimulus reaches the membrane, the membrane suddenly becomes permeable to sodium ions, allowing tremendous numbers of positively charged sodium ions to diffuse to the interior of the axon (opening some of Na+ gated channels).

➞ If the stimulus reaches the threshold, **all** Na+ gated channels will be opened causing faster **depolarization**, at the same time K+ channels are starting opening.

➞ Causing that inner membrane becomes positive with regard to outer membrane.

➞ **Repolarization Stage,** the sodium channels begin to close and the potassium channels open to a greater degree than normal re-establishes the normal negative resting membrane potential back.

Remember Na+ gated channels are faster than K+ gated channels

★ Last time we talk about excitable cells, cells that can generate action and we talk about that reaching threshold activates all Na+ gated channels causing very fast reflection of membrane potential (Na+ influx).

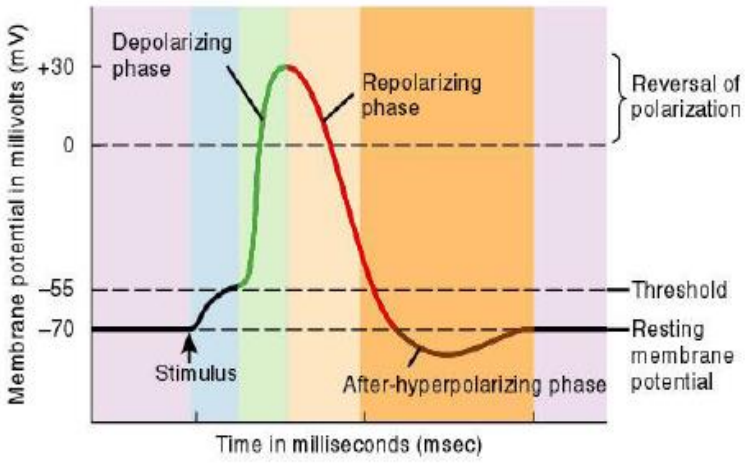
When reaching threshold both Na+ and K+ open with different velocities.

Firing level: fast refection of membrane potential.

Overshoot: when outside is negative to inside.

Undershoot: after-hyperpolarizing phase (caused by slowly closing voltage gated K+).

Permeability = conductance



"REFRACTORY PERIOD"

Once you reach threshold and getting the firing level, what happen if you stimulate the membrane at that time?

Are you getting action potential?

A new action potential cannot occur in an excitable fiber as long as the membrane is still depolarized from the preceding action potential. The reason for this restriction is that shortly after the action potential is initiated, the sodium channels (or calcium channels, or both) become inactivated and no amount of excitatory signal applied to these channels at this point will open the inactivation gates. The only condition that will allow them to reopen is for the membrane potential to return to or near the original resting membrane potential.

Refractory period divided into two periods:

1- Absolute refractory period **2- Relative refractory period**

These transitory changes make it harder for the axon to produce subsequent action potentials. Thus, the refractory period limits the number of action potentials that a given nerve cell can produce per unit time.

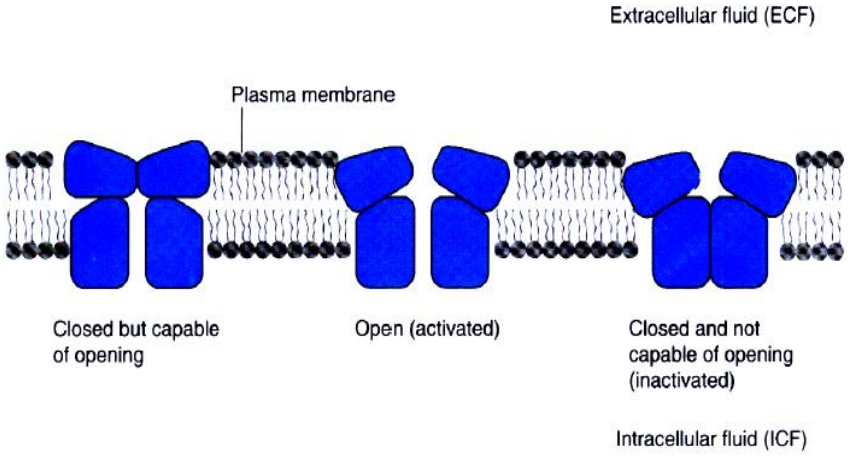
Absolute refractory period	Relative refractory period
This is the time during which another stimulus given to the neuron (no matter how strong) will not lead to a second action potential.	The period during which a stronger than normal stimulus is needed in order to initiate another action potential. After the absolute refractory period, Na^+ channels begin to recover from inactivation and if strong enough stimuli are given to the neuron, it may respond again by generating action potentials.
Na^+ channels are open	Na^+ channels are closed and not capable of opening

Subthreshold (weak stimulus): refers to a **stimulus** that is too small in magnitude to produce an action potential in excitable cells. In general, a **subthreshold stimulus** leads to the depolarization of the membrane, but the magnitude of the depolarization is not large enough to reach the threshold voltage.

Suprathreshold (strong stimulus): refers to a **stimulus** that is large enough in magnitude to produce an action potential in excitable cells

Recall that N+ gated channel has two gates

One outer and the second is inner



Absolute refractory period:

begins from the threshold and ends when all Na+ voltage gated channels getting closed, Precisely at the end of the first third of the falling phase.

It contains the following events:

1- voltage-gated Na+ channel activation gates are open

2- voltage- gated K+ channels are open AND Na+ voltage-gated channels are closed (inactivated).

⟶ During **Absolute refractory period**, it is never ever can be stimulated even if the stimulus was strong.

Relative refractory period:

From the beginning of the second phase until the resting membrane potential is achieved.

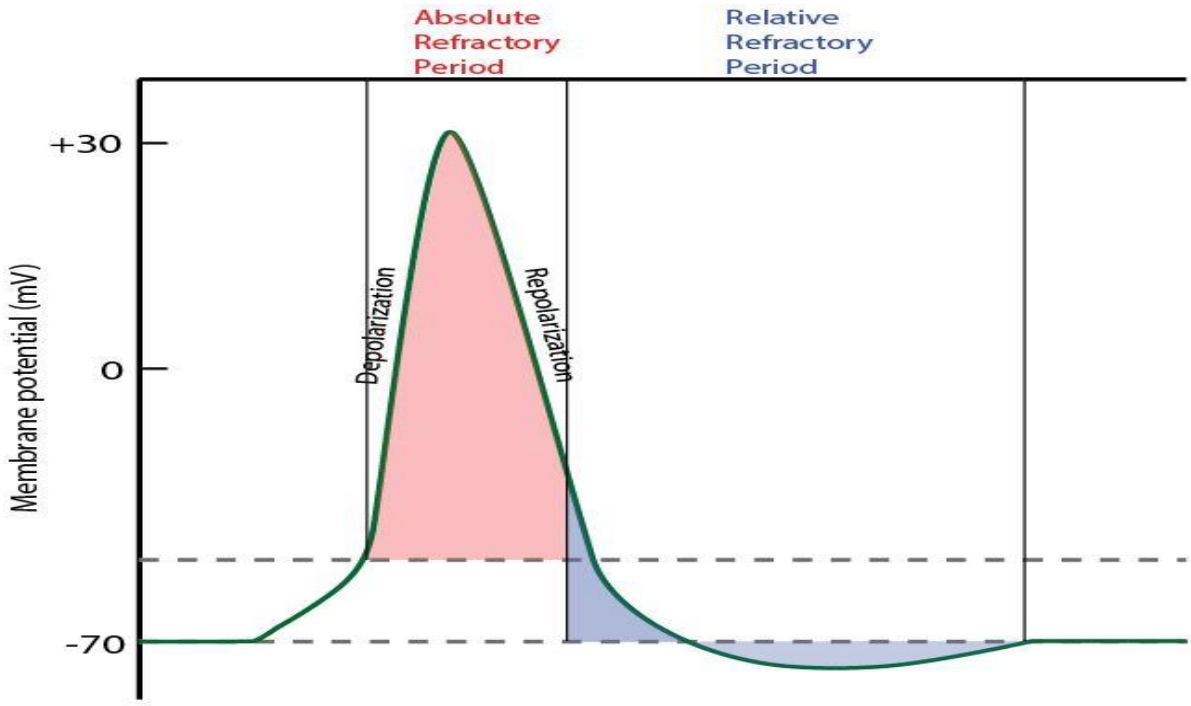
it contains the following event:

★ Voltage-gated K+ channels are still opening AND Na+ voltage-gated channels are closed (inactivated).

The cell cannot respond the usual stimulus, but a stronger stimulus (Suprathreshold) can change the membrane potential.

When Na+ gated channels are closed and not capable for open, Suprathreshold can open them and causes action potential but subthreshold can't open them.

At resting membrane potential Na+ are closed and capable to open.



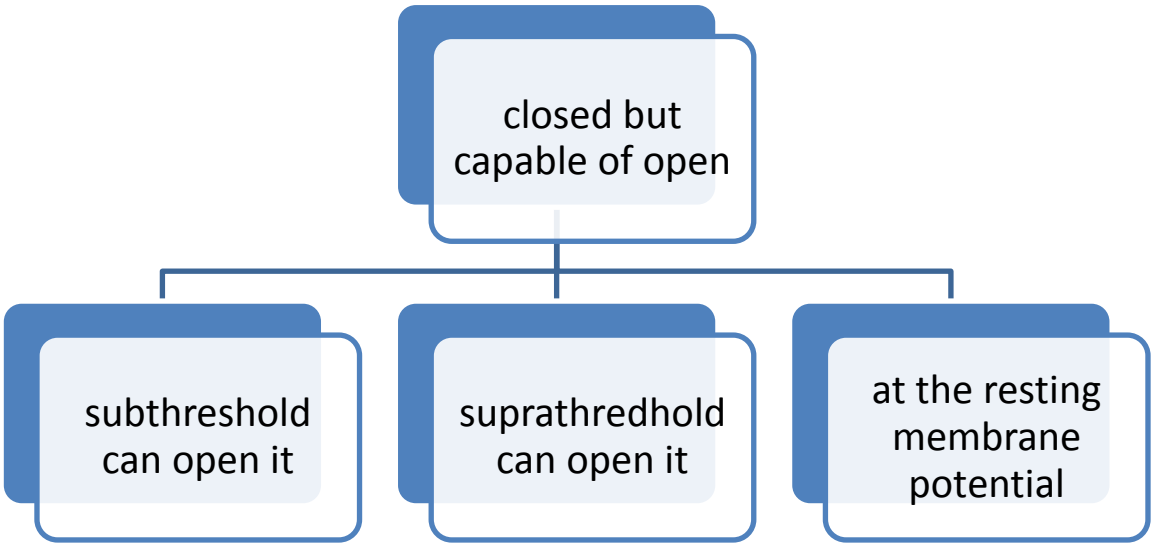
If the stimulus affected the membrane during the refractory period is another action potential is established?

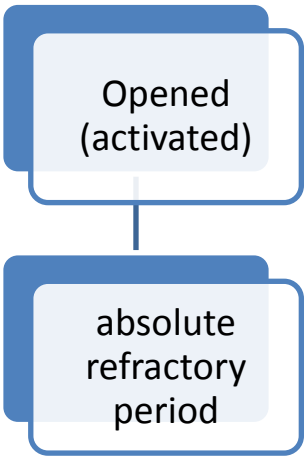
Actually, the answer is YES or NO it depends on two factors:

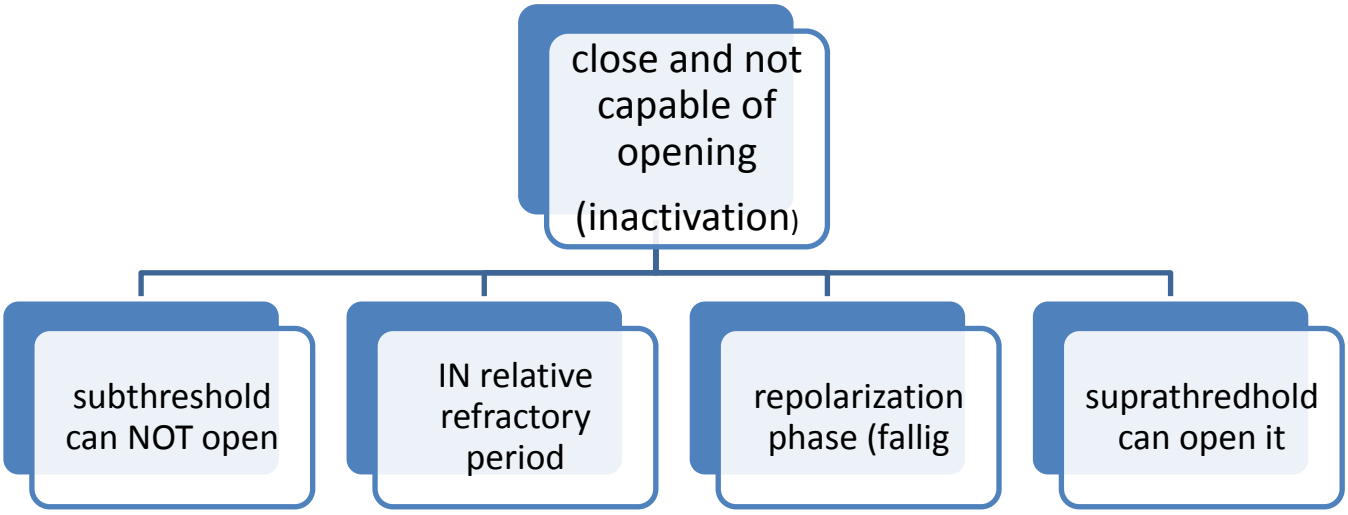
1. Thy type of refractory period that occurs during affecting of the stimulus

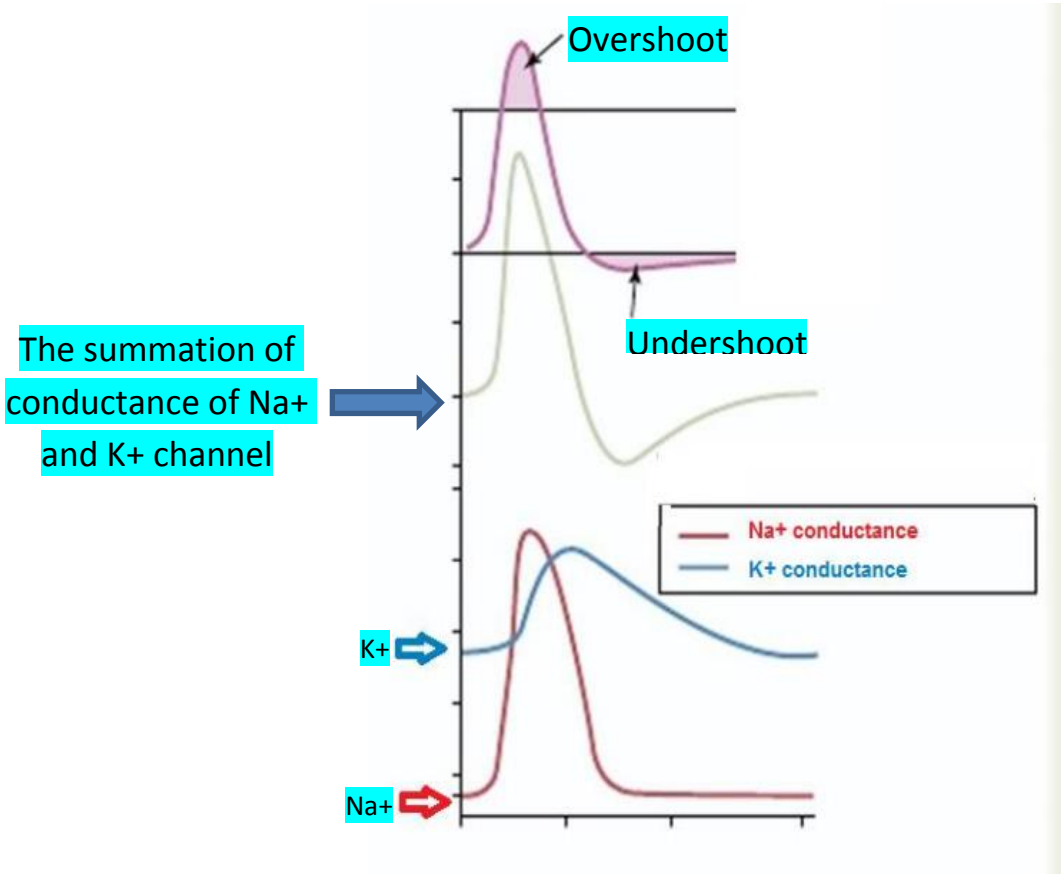
2. the strong of stimulus

➡ These charts illustrate the **states** of Na+ channels:









★ Na+ - K+ pump and action potential:

This pump has NO role in the electrical activity that are taking place during action potential. But it plays an important role in restoring ionic composition that has been altered during action potential. This role is important in maintaining the ionic composition of the intra-and the extracellular fluids.

NOTE:

The more negative a resting membrane potential is the more concentration of Na+ channels which are closed and capable of opening (the number of these channels in an area unit) are present. So, the membrane becomes more sensitive to any stimulus; thus we reach the Threshold faster. (more excitable)

The threshold also depends on the number of K+ voltage gated channels per unit area.

more negative membrane potential (at rest state) means more number of the Na+ channels which it is closed and capable for opening

Neurons (the most negative potential) are considered the most excitable cells, because they have high concentration of Na+ channels also high concentration of these channels are closed and capable for opening much easier to bring them to threshold.

Up until now, we have been studying the action potential affected by K+ and Na+ ions. Now, we will talk about the involvement of other ions in action potential.

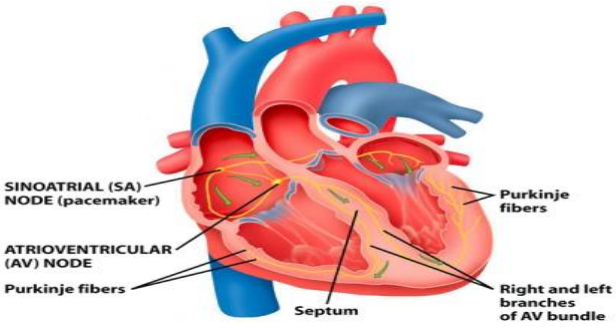
In cardiac and smooth muscles, we have another ion which is Ca++.

Actually in the heart two types of excitable tissue:

1-Cardiac muscles cell.

2-Conductive tissue of the heart (yellow in the figure below, small amount of this cells).

Here we have a higher leakage of Na+ channels, which it means a little bit higher permeability of Na+ ions.



Conductive tissue:

In this tissue, we can generate other configurations of action potentials than the previously-mentioned action potential.

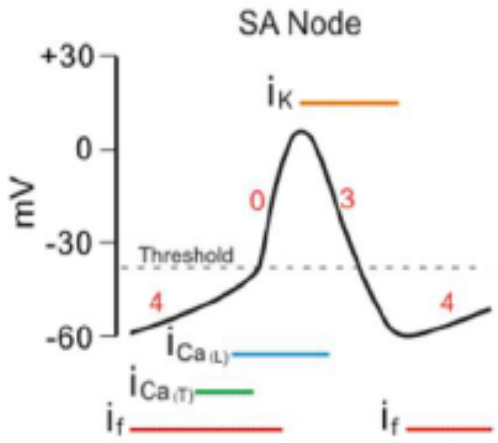
Now, Cardiac conductive cells have a property of "Na+ leakage", Na+ moves from outside to inside and this property causes **automatic** (spontaneous) Depolarization (can generate action potential without stimulus from outside).

Types of Ca++ channels;

Ca(T): Transient ⟹ T-type activated, firstly opened, lead to more depolarization, can activate at -50 (mv).

Ca(L): Long-lasting ⟹ L-type activated, secondary opened, lead to faster depolarization, can activate at -40 (mv).

This figure blew is very important:



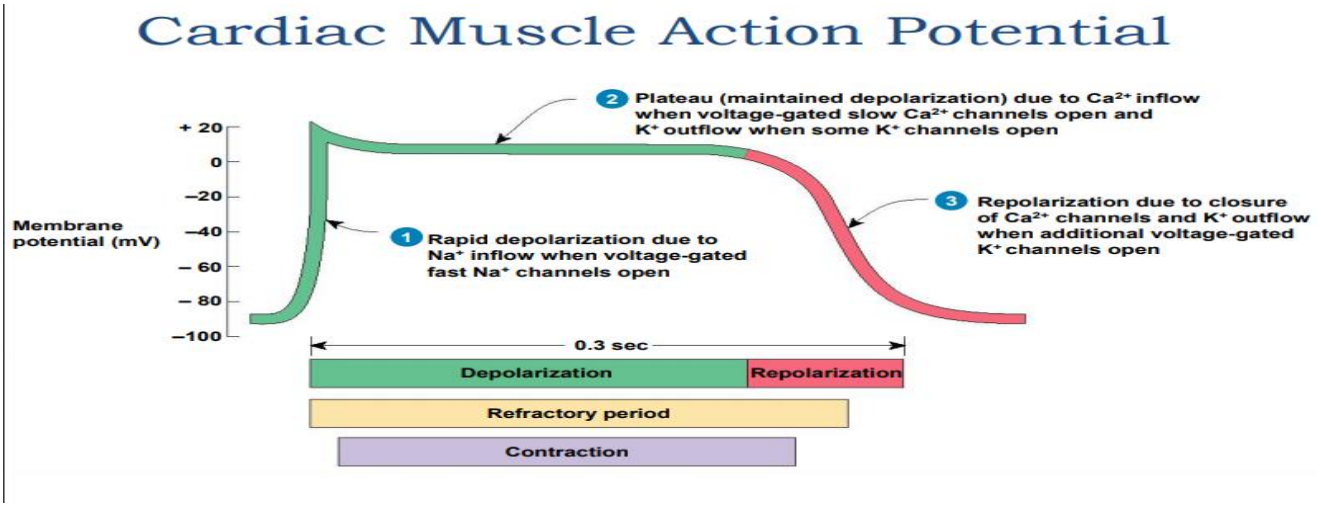
I(f): Funny current (Na+ current)

The effect of Na+ leakage channels is in the all of the time but appears in the depolarization phase and after repolarization ends.

Na+ current is called funny current, it is not common.

What happens after action potential ends another "slowly and spontaneous" depolarization phase occurs again.

➟ we have the resting potential at -60 mV (which is not enough negative voltage to keep the sodium channels totally closed) and that causes the slow depolarization (Na+ leakage). By that we reach -50 mV, at this potential we activate the 1st type of Ca++ channels which is the T-type. By activating it Ca++ is moving from outside to inside which means more Depolarization. Then we reach another point where we activate the L-type channels, the activation of the 2nd type helps reaching the Threshold, which results in having Depolarization.
At the tip, L-Ca++ channels get inactivated and the conductance of K+ increases which causes K+ current Repolarization, returning to the resting membrane.

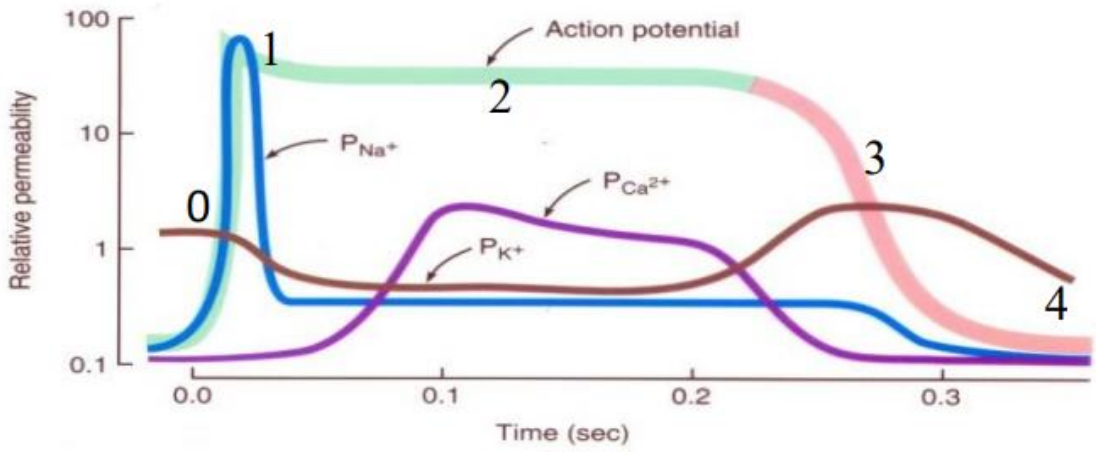


1 phase: spontaneous depolarization

2 phase: high activity of Ca++ (plateau; 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**)

3 phase: high activity of K+

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



(b) Membrane permeability (P) changes

SHORT QUIZ:

1- Which of the following is NOT true about the refractory period?

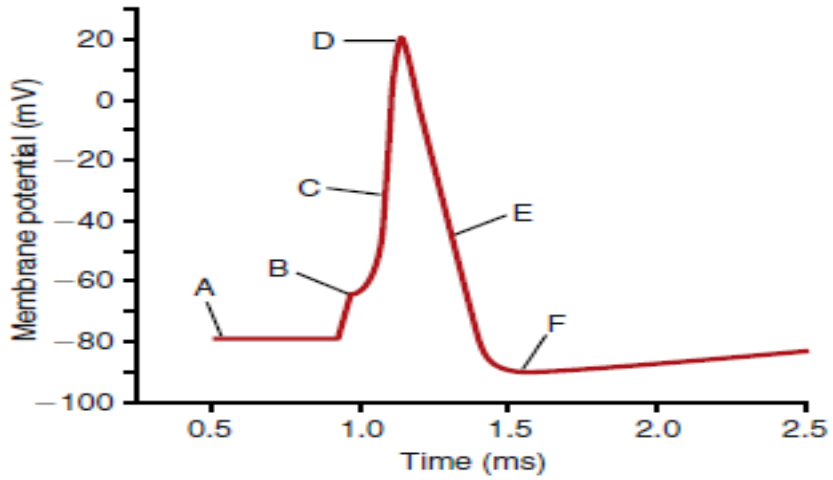
(A) It is thought that the refractory period is caused by the hyperpolarization phase of the action potential.

(B) The refractory period is important in preventing the overlap of succeeding action potential.

(C) The absolute refractory period refers to that time during which a stronger stimulus will lead to the generation of a new action potential.

(D) The relative refractory period refers to that time during which a stronger stimulus will lead to the generation of a new action potential.

(E) The relative refractory period coincides with the hyperpolarization phase of the action potential



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The above figure shows the change in membrane potential during an action potential in a giant squid axon. Refer to it when answering Questions 2 and 3.

2-Which of the following is primarily responsible for the change in membrane potential between points D and E?

A) Inhibition of the Na+, K+-ATPase

B) Movement of K+ into the cell

C) Movement of K+ out of the cell

D) Movement of Na+ into the cell

E) Movement of Na+ out of the cell

3-Which of the following is primarily responsible for the change in membrane potential between points B and D?

A) Inhibition of the Na+, K+-ATPase

B) Movement of K+ into the cell

C) Movement of K+ out of the cell

D) Movement of Na+ into the cell

E) Movement of Na+ out of the cell

4- Regarding the absolute refractory period, all are correct except:

A- It coincides with ascending limb of the spike potential
B- Excitability of nerve=0
C- It begins with activation of all voltage gated Na+ channels
D- A stronger stimulus is needed to excite the nerve

E- All of the above are correct

5- In a typical vertebrate axon, the absolute refractory period is 1.0 ms and the relative refractory period is 4.0 ms. Thus, the axon is refractory for a total of 5.0 ms. If the axon is continuously stimulated with stimuli only large enough in amplitude to ensure excitation when the neuron is at rest, what is the highest frequency of action potentials that can be generated?

(A) 50 Hz

(B) 100 Hz

(C) 200 Hz

(D) 500 Hz

(E) 1000 Hz

ملاحظات مهمة جدا :

١- في فكرة حكاها الدكتور انه حدود absolute or relative refractory period تعتمد على مصدر الدراسة وهي تختلف باختلاف المراجع .
٢- والله يا اخوان أنا وأسامة ما كذبنا بأشي هاض الي صار .
٣- بالنسبة للقلب وما يتعلق به احنا كتبنا كل اشي حكاه الدكتور ولكن في تفاصيل كثيرة بهالموضوع والدكتور انهى المحاضرة بعبارة انه في تفاصيل اكثر راح توخذوها مع الدكتور ينال, هو هيك حكى والله بس بالانجليزي .
٤- يخوان اذا قرأتو كل الشيت وما فهمتو اشي بالله لا تدعو علينا.
٥- كمان يخوان اذا ما عرفتو تحلو الامتحان كمان لا تدعو علينا .
٦- اذا قرأتو الشيت وما فهمتوه ولا عرفتو تحلو الامتحان لا هيك كثير ادعو براحتكم .
٧- الامتحان يتكون من 5 اسألة 1 و2 سهلات و 3,4 متوسط والسؤال الخامس يعد صعب جدا "بلغة اخرى اذا ما عرفت تحله اتركه ولا تضيع وقتك عليه ".
٨- الاجوبة ادناه:

ANSWERS: 1-C, 2-C, 3-D, 4-D, 5-C