no.

Physiology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

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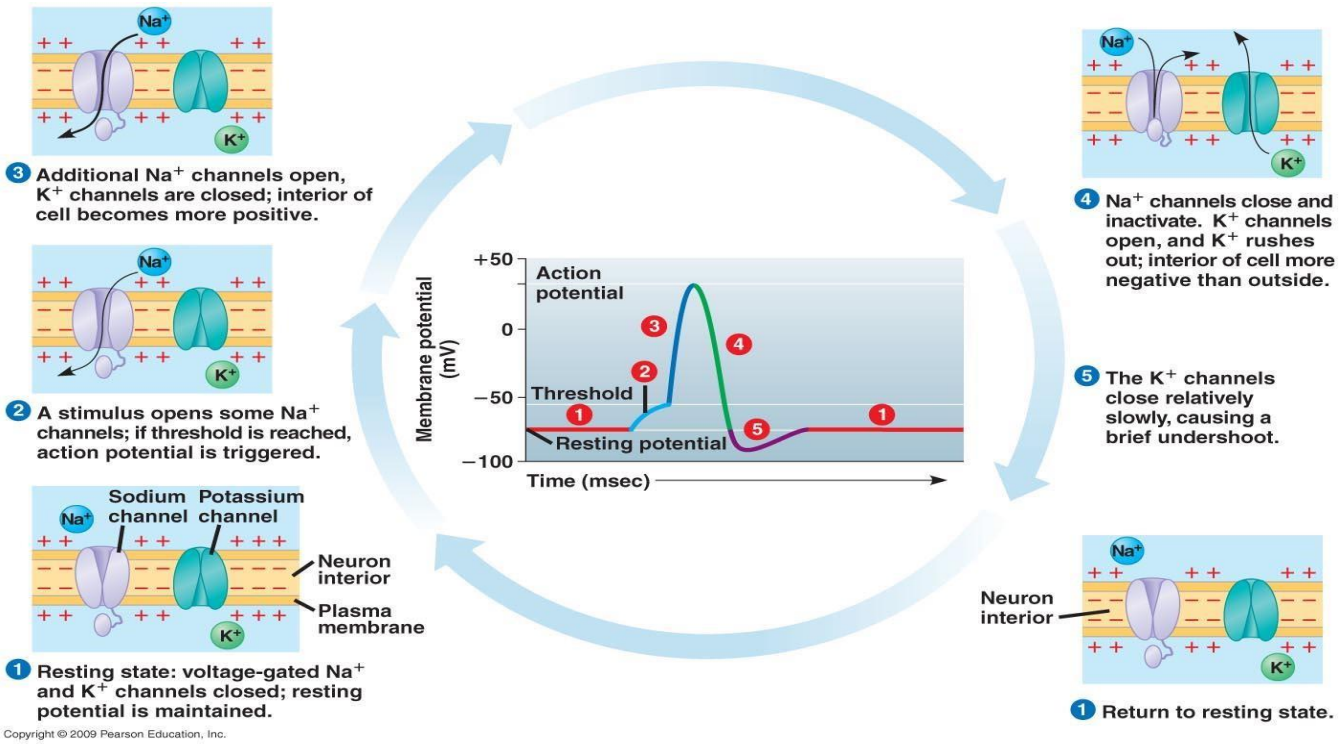
Action Potential



Description of the action potential stages

1. **Resting membrane potential:** The membrane is polarized (it can separate opposite charges), and the inside is negative.
2. Activation of some sodium channels leads to influx of sodium ions until the threshold (the potential at which the action potential is inevitable to happen) is reached
3. **Depolarization**: ALL sodium channels are activated quickly after reaching the **threshold** which leads to an increase of positive potential inside (this stage is also called **Firing stage**)
   - potassium channels also start to open when the threshold is reached but at a slower rate than sodium channels.

> *OVERSHOOT* is when the Inside potential becomes larger than zero, but it NEVER reaches +61mV (the equilibrium potential of Na+)
> - happens in large nerve fibers but not in smaller fibers and many central nervous system neurons

4. **Repolarization:** activation of potassium channels and closing of inactivation gates of sodium channels which leads to efflux of potassium and restores the resting potential. (also known as the **falling phase**)

5. **Hyperpolarization:** the potassium channels are closing, yet they produce a more negative potential than resting potential (also called *undershoot* or *positive after potential* or *after hyperpolarization*).

These changes in membrane potential can be recorded by placing one electrode inside the cell and the other outside the cell. By recording of whole action potential in this way, we will obtain a **Monophasic Action Potential.**

A stimulus must be applied to change the activity of sodium and potassium channels at the membrane.

- Activation of Na+ channels leads to influx of sodium decreasing the potential (becomes less negative) and causes depolarization.

- Activation of K+ channels will lead to efflux of potassium ions which increases the potential (becomes more negative) and causes repolarization.

Action potential and the role of Na+ channels

There are three types of Na channels on the membrane:

a. **Chemical gated channels**: activated by a chemical stimulus (a ligand).
b. **Voltage gated channels**: activated by an electrical stimulus (a change in the membrane potential).
c. **Channels activated by a mechanical stimulus**.

The binding of a ligand to its receptor will induce activation of chemical gated Na+ channels. Once activated, the membrane potential will decrease (becomes less negative) and the membrane depolarizes. (for example, synapses are chemical stimuli)

This voltage change in the membrane will lead to the activation of voltage gated Na+ channels and this will cause more depolarization.

As more and more depolarization occurs by a positive feedback mechanism…. most voltage gated Na+ channels will be activated and there would be a sudden increase in Na+ permeability…….this will lead to **Overshoot**→ the membrane would become positive inside and negative outside.

NOTE: Overshoot happens because Na+ is trying to approach its equilibrium potential (E_{Na}) but it NEVER reaches it.

NONE or ALL Principle

Induction of an action potential in an excitable cell follows this principle

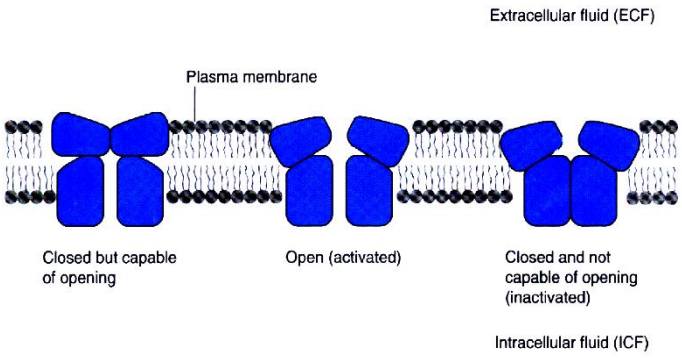
When a stimulus causes depolarization of a membrane and the sodium channels open there are 2 possibilities:

1. If the potential reaches the threshold then the firing stage will happen, and an action potential will be generated.
2. If the potential doesn't reach the threshold the membrane will NOT enter the firing stage and no action potential would be generated.

Action potential and the role of K+ channels

- There is some leakage of k+ ions at the resting state which maintains the potential close to k+ equilibrium potential.
- Depolarization causes activation of voltage gated K+ channels but at a **slower rate** than sodium channels
- Delayed and slower opening of k+ channels with the inactivation of Na+ channels would lead to the ***Falling phase*** (repolarization)
- The membrane potential might keep getting more negative because of excess efflux of k+ ions and this is called **Positive after potential.**

Sodium channels have three states:



1. **Closed and capable of opening**
   During resting potential.
2. **Open**
   Nearly all sodium channels are open during firing stage
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 a large electrical stimulus).

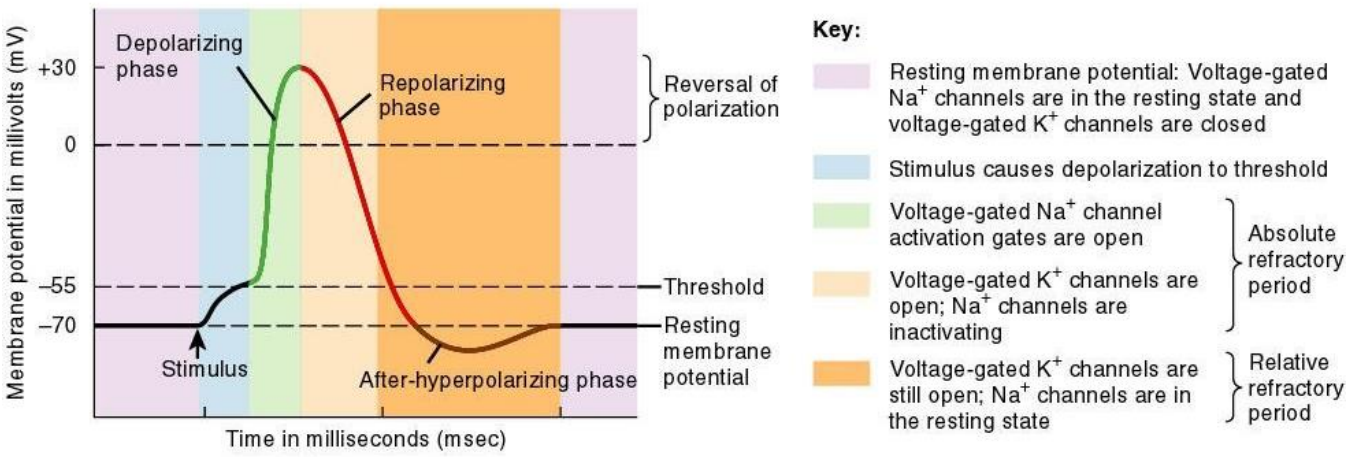
Refractory Periods

Absolute refractory period

- A period of time at which a membrane cannot generate a new action potential even when there is a large or a small stimulus.
- This period starts after the threshold to the end of first third of falling(repolarization) phase.
- 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.

Relative refractory period

- A period of time at which a membrane cannot generate a new action potential when there is a small stimulus
  BUT If there is a large stimulus(suprathreshold), a new action potential would be generated.
- This period starts after the Absolute refractory period and ends when the resting membrane potential is achieved.
- The sodium channels are in the closed and incapable of opening stage but a strong stimulus(suprathreshold) may activate these channels.

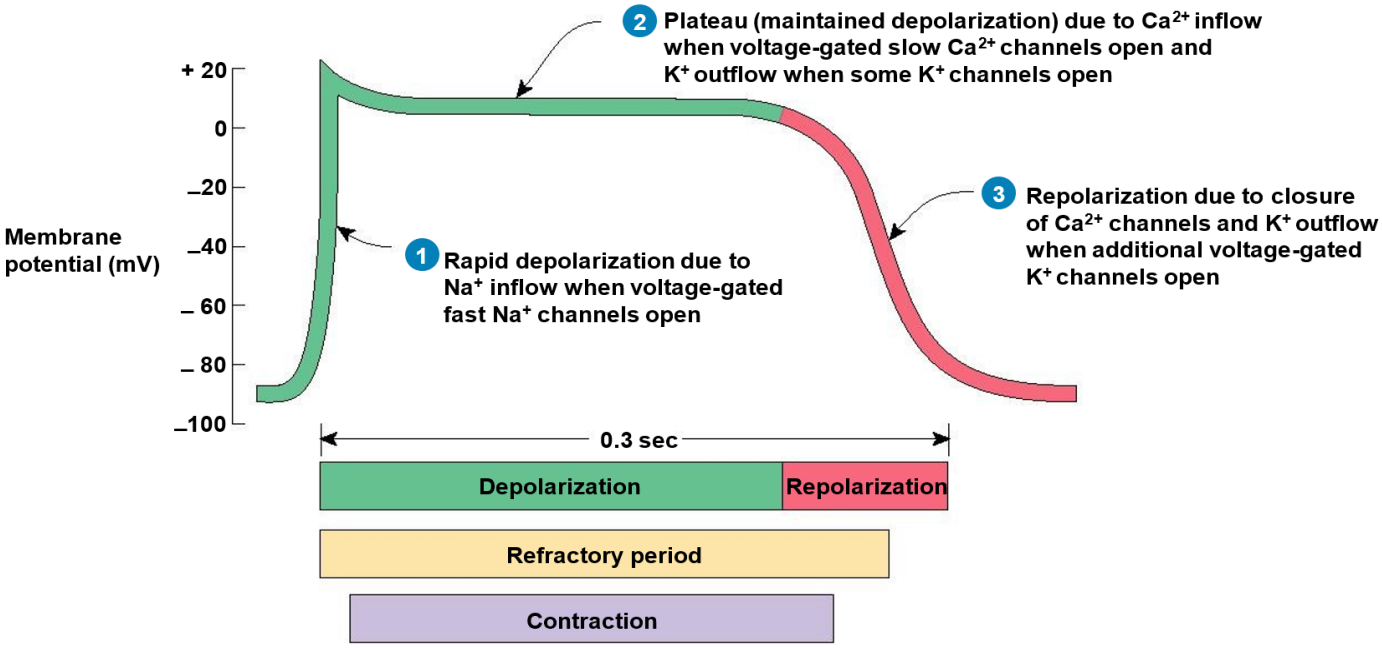


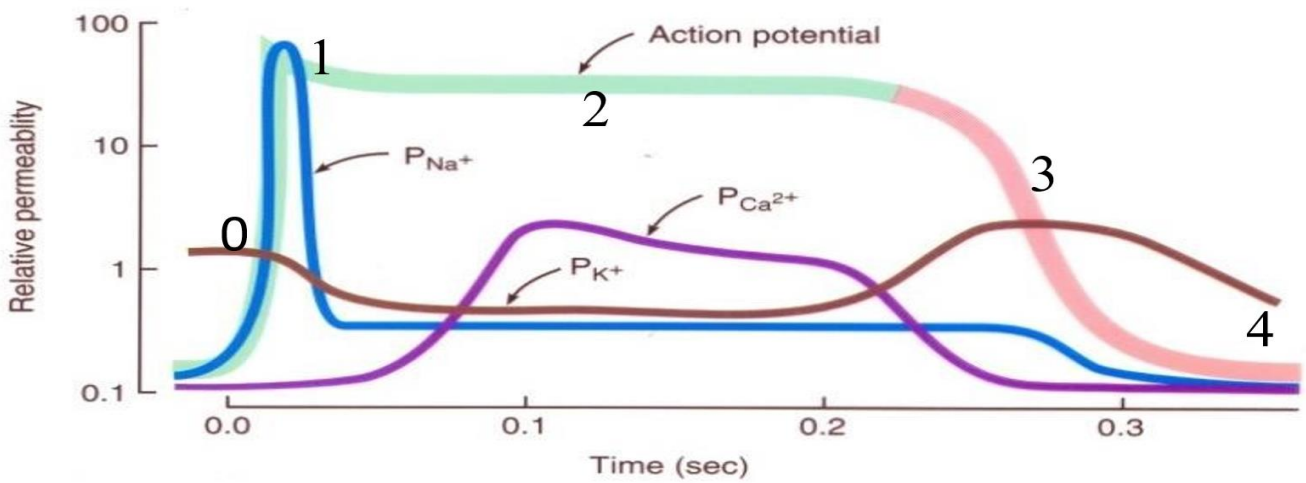
Involvement of other ions in action potential

- 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 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.

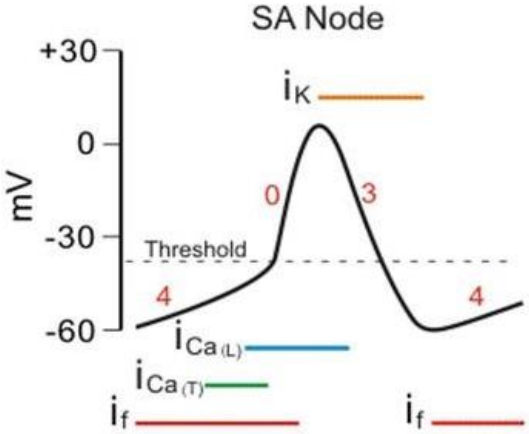




(b) Membrane permeability (P) changes

The SA node

- A small amount of tissue of the heart called **sinoatrial node** (the pacemaker of the heart)
- This tissue has an important ability called **automatic regeneration of action potential.**
- All structures in the heart can generate an action potential but at a lower rate that this structure because it has a <u>much higher leakage of sodium ions</u> which means faster depolarization, and this leads to a fast rhythm.



Fast depolarization of sodium ions leads to the activation of two calcium channels: One is called **<u>transient</u>** type and one is the **<u>long-lasting</u>** type (which is activated after the transient type → at a less negative potential)

IMPORTANT NOTES

Both K+ and Na+ channels activate at the same time, but the rest of the Na channels activate faster

Positive after potential is called this way because when membrane potentials were first recorded they were recorded from the OUTSIDE relative to the INSIDE (the exact opposite happens now)

The exact time when the membrane goes from the absolute refractory period to the relative refractory period is not known yet.

Arrogance destroys the footholds of victory.

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