Skeletal muscle physiology for medical students

Action potential and NMJ

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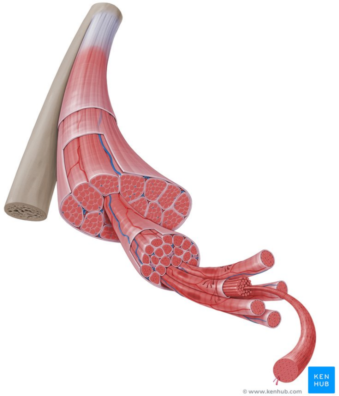


References

- **Guyton and Hall Textbook of Medical Physiology, 13th edition.**

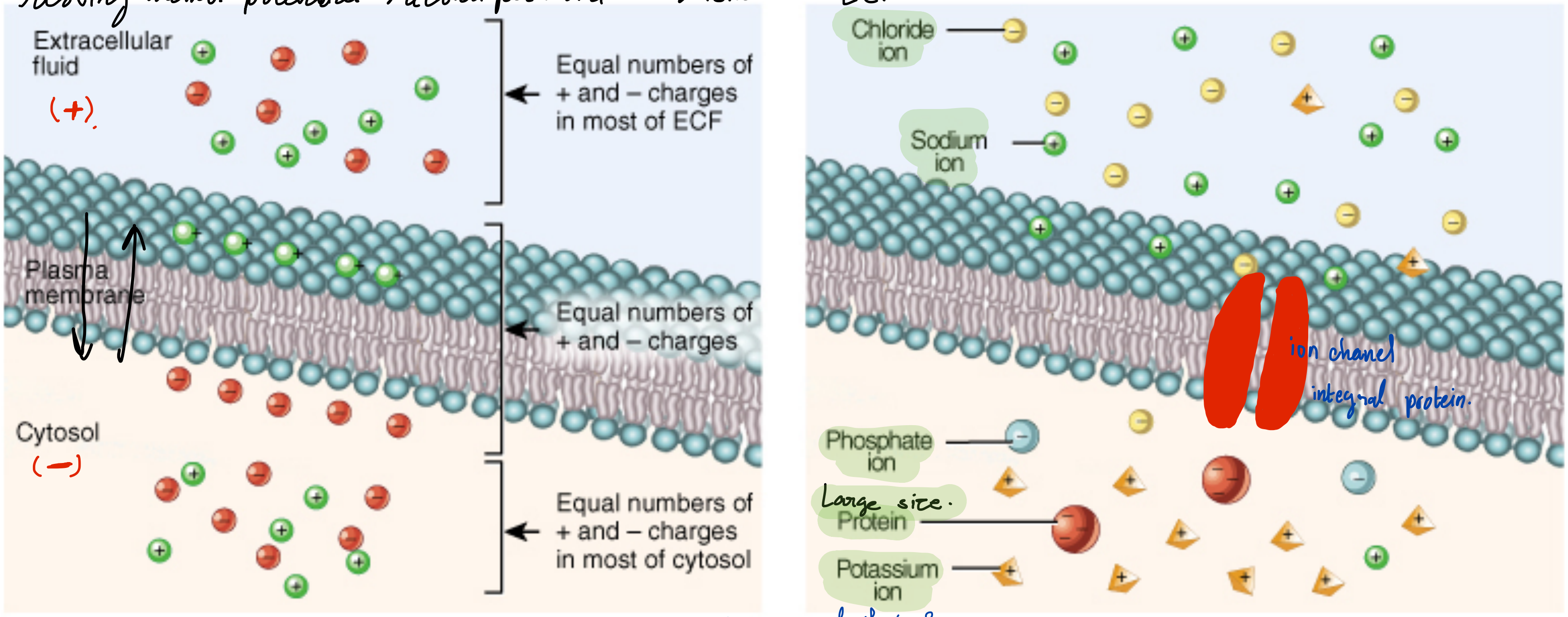
- Principles of Anatomy and Physiology Tortora and Derrickson 15th edition.

- Other references will be cited on individual slides.

Away from the membrane, the charges are equall & have no effect, but near the membrane there is a difference in charges that results in "Polarity"

resting memb. potential / action potential ·····> ions.

ECF



(a) Distribution of charges

(b) Distribution of ions

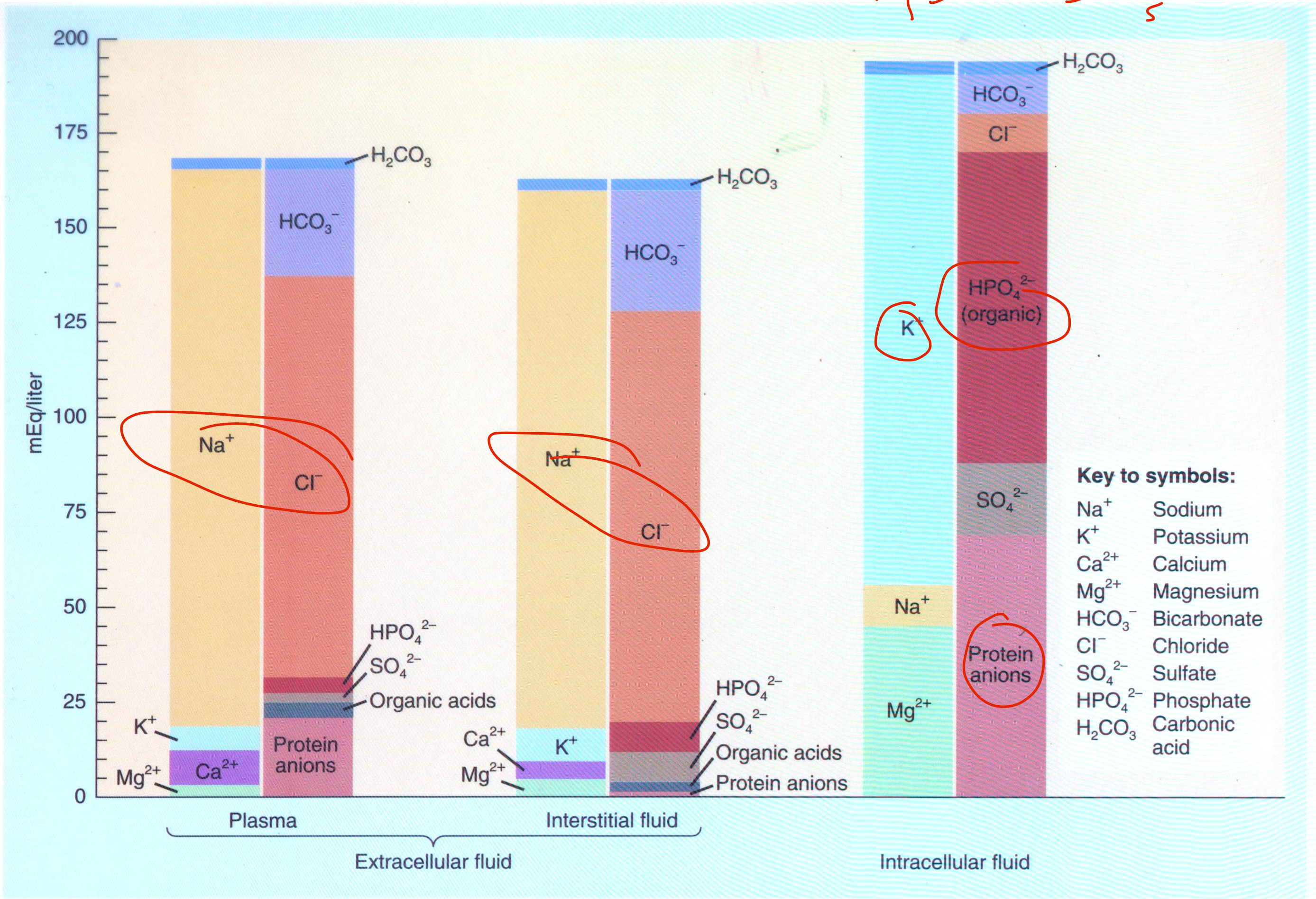
What determines the movement of ions?

* concentration gradient.
* charge.
* plasma membrane permeability.

Large size proteins that r intracellularly will never ever leave the cell.

إعادة للكلام.

there are other components, but they don't play a major role like K+, Cl-...



Comparison of Electrolyte and Protein Anion Concentrations in the Body Fluid Compartments,

Concentration and Permeability of Ions Responsible for Membrane Potential

Ion	Extracellular Concentration*	Intracellular Concentration*	Relative Permeability
Na^+	150 *	15	1
K^+	5	150 *	25–30
A^-	0	65	0 *

(10 : 1)

1 ← it's kind impermeable; it's actually permeable, but not as for k^+

25–30 ← more permeable.

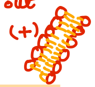
A^- → proteins ⊖ mainly present intracellularly, they stay there.

*Concentration expressed in millimoles per liter, mM

the plasma membrane is much more permeable for k^+ than any other ion.

it's 25-30 times more permeable for k^+ than Na^+

WHAT'S RESPONSIBLE OF RESTING MEMBRANE POTENTIAL ?



unequal distribution of ions → leaky channels, go to slide 9

→ large size negatively charged proteins stay inside → more (–) inside the cell.

→ Na^+/K^+ ATPase pump. (against concentration gradient ⇝ needs ATP)

Gradient across the membrane

- The selective permeability of the plasma membrane allows a living cell to maintain different concentrations of certain substances on either side of the plasma membrane.

- The plasma membrane also creates a difference in the distribution of positively and negatively charged ions between the two sides of the plasma membrane.

Gradient across the membrane

- Typically, the inner surface of the plasma membrane is more negatively charged and the outer surface is more positively charged.
- This charge difference is termed the **membrane potential**.

THE MOST IMP. ION RESPONSIBLE FOR
THE PRODUCTION OF RMP? K^+

Resting membrane potential

- A separation of positive and negative electrical charges is a form of potential energy, which is measured in volts or millivolts.

- The greater the difference in charge across the membrane, the larger the membrane potential (voltage).

- The buildup of charge occurs only very close to the membrane. The cytosol or extracellular fluid elsewhere in the cell contains equal numbers of positive and negative charges and is electrically neutral.

the ion channels that r responsible of production of RMP?

① leaky channels ; K^+ Na^+ leaky channels.

↳ according to : concentration gradient.

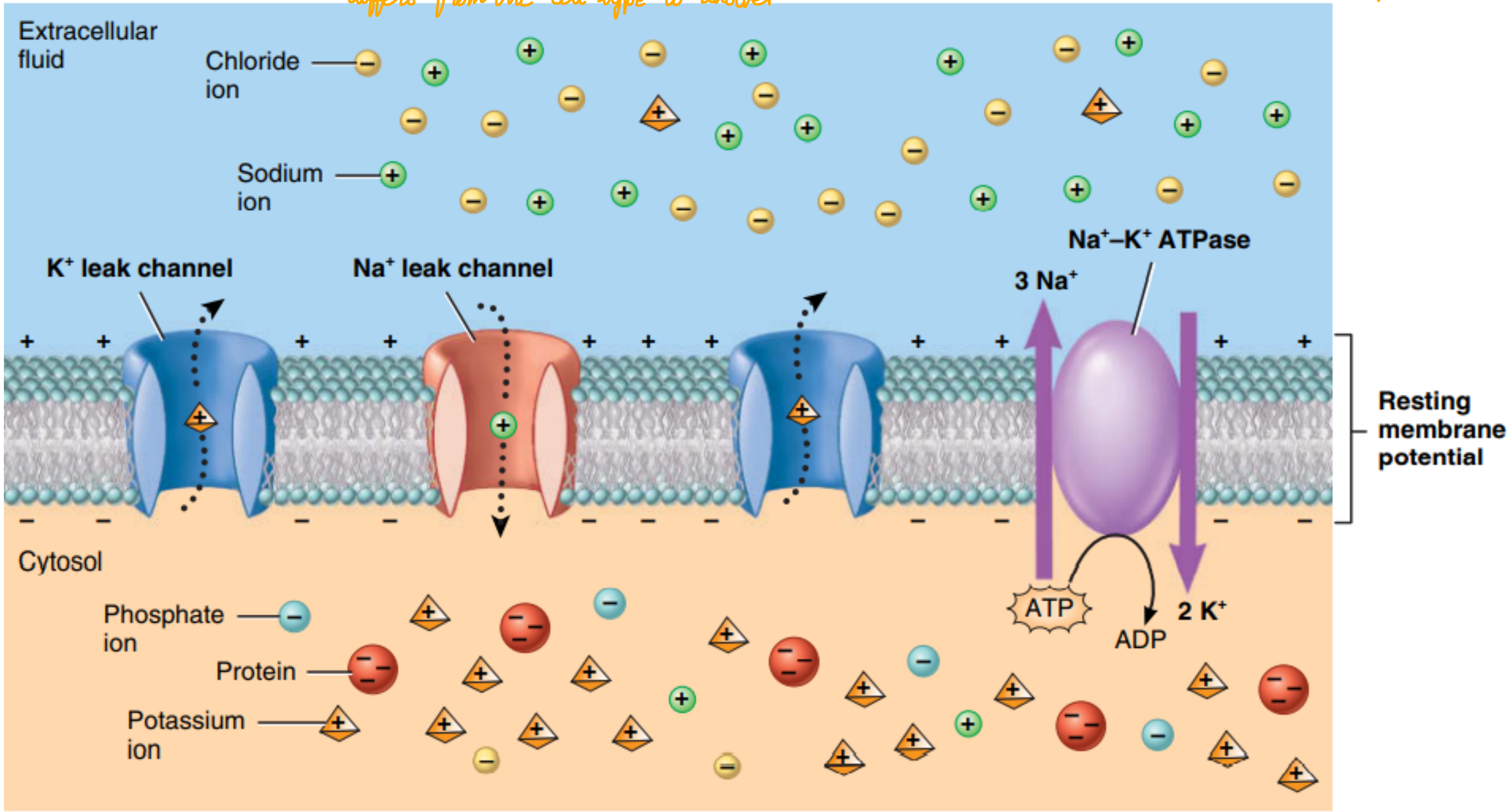
number of K^+ leaky channels is much more than that of Na^+

[ICF K^+ ⇉ ← Na^+ ECF]

Resting membrane potential (RMP)

I'll refer to it as: (RMP) اختصاراً

↳ differs from one cell type to another



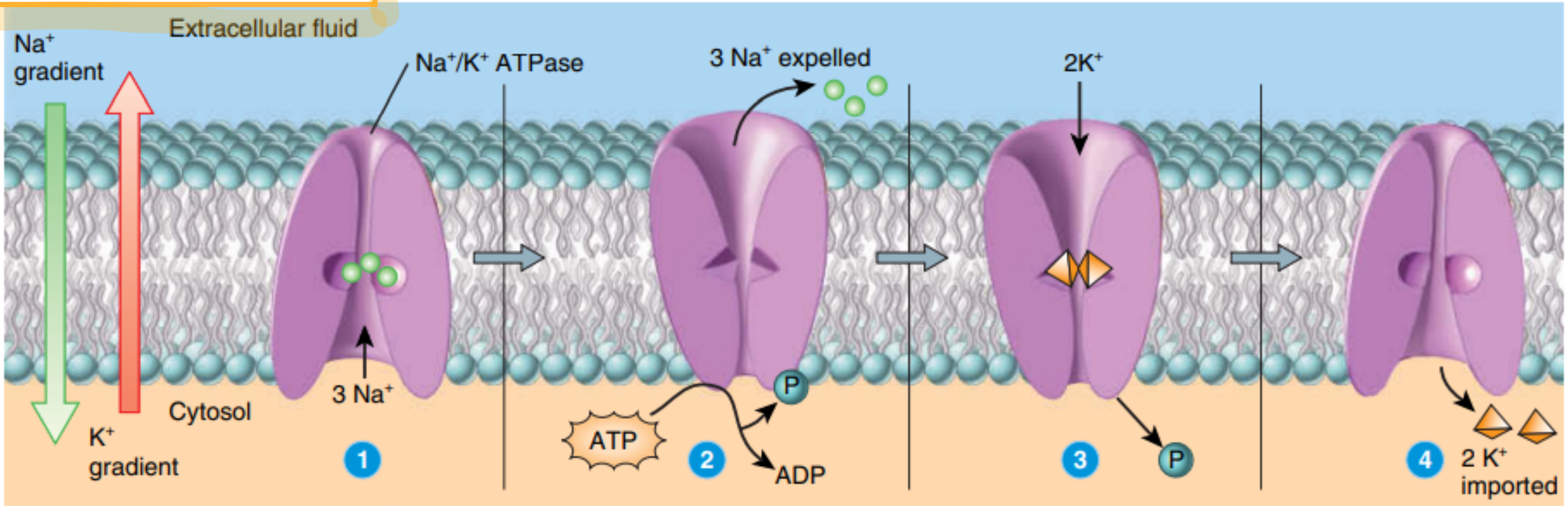
(K^+) in ⟶ out

↳ So negative in Nernst Equation.
and RMP mainly depends on K^+, which has negative charge in nernst equation, so when we calculate the net by Goldman Equation.

the RMP will be negative.

Na+/ K+ pump

Against conc. gradient.



in other words: Under resting conditions the membran is permeable to K^+, but it's permeability to Na^+ is very less, so under resting conditions. the potential is largely determined by the diffusion potential of K^+

That's why the RMP in most cells is about −70 mvolt, which is close to the equilibrium potential of K^+

Resting membrane potential

The resting membrane potential arises from three major factors:

- 1- **Unequal distribution of ions in the ECF and cytosol**. Extracellular fluid is rich in Na^+ and Cl^-. In cytosol, however, the main cation is K^+, and the two dominant anions are phosphates attached to molecules, such as ATP, and amino acids in proteins.

Resting membrane potential

- Because the plasma membrane typically has more K+ channels than Na+ channels, the number of K+ that diffuse down their concentration gradient out of the cell into the ECF is greater than the number of Na+ that diffuse down their concentration gradient from the ECF into the cell.

- As more and more positive K+ exit, the inside of the membrane becomes increasingly negative, and the outside of the membrane becomes increasingly positive.

Resting membrane potential

2- **Inability of most anions to leave the cell**.

(−)

Most anions inside the cell are not free to leave. They cannot follow the K+ out of the cell because they are attached to non-diffusible molecules such as ATP and large proteins.

Resting membrane potential

3- **Electrogenic nature of the Na+–K+ ATPases**.

Na+–K+ ATPases (sodium–potassium pumps) help maintain the resting membrane potential by pumping out Na+ as fast as it leaks in. At the same time, the Na+–K+ ATPases bring in K+. However, K+ eventually leak back out of the cell as they move down their concentration gradient.

Resting membrane potential

The Na^+–K^+ ATPases expel three Na^+ for each two K^+ imported. Since these pumps remove more positive charges from the cell than they bring into the cell, they are **electrogenic**, which means they contribute to the negativity of the resting membrane potential.

Excitable cells

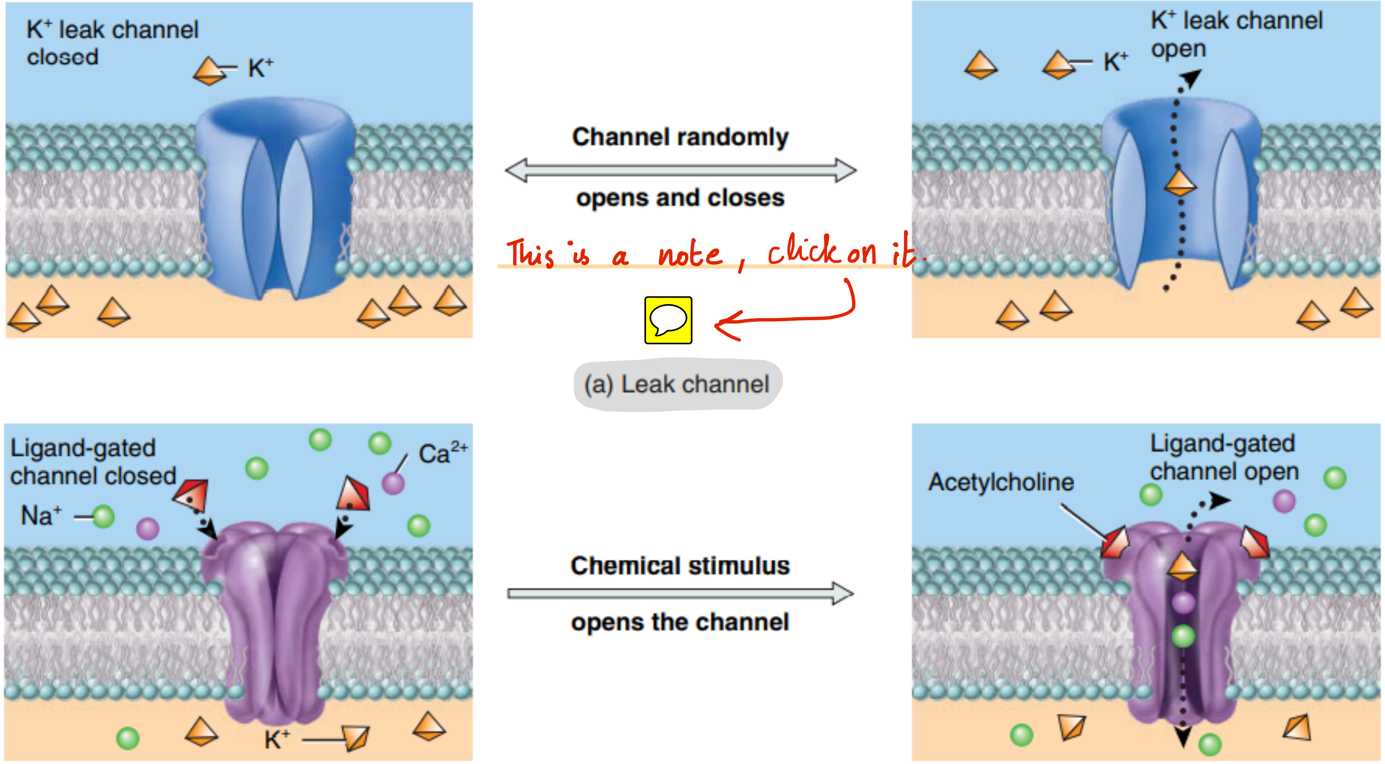
neurons
muscle fibers

- **Neurons and muscle fibers** are considered excitable cells because they exhibit electrical excitability, the ability to respond to certain stimuli by producing electrical signals (action potential).
- These cells generate rapidly changing electrochemical impulses at their membranes, and these impulses are used to transmit signals along their membranes.

Ion channels in excitable cells

- The electrical signals produced by neurons and muscle fibers rely on four types of ion channels: leak channels, ligand-gated channels, mechanically-gated channels, and voltage-gated channels:

Ion channels in excitable cells

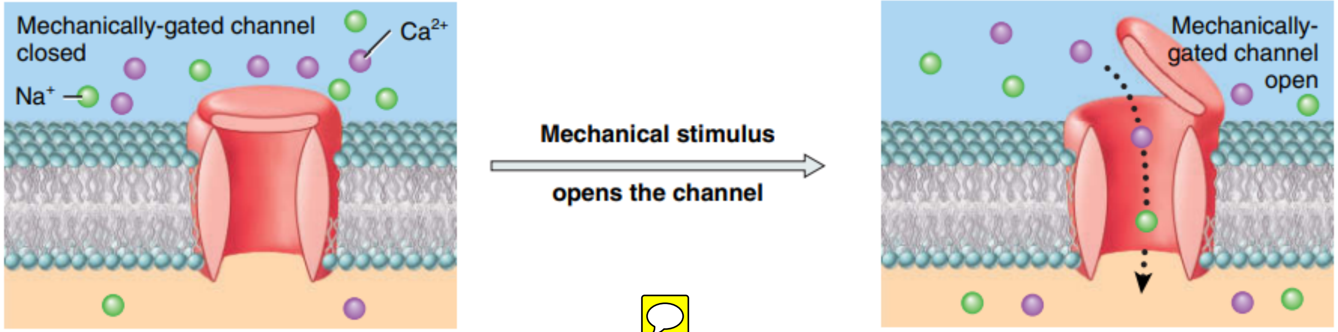


(b) Ligand-gated channel

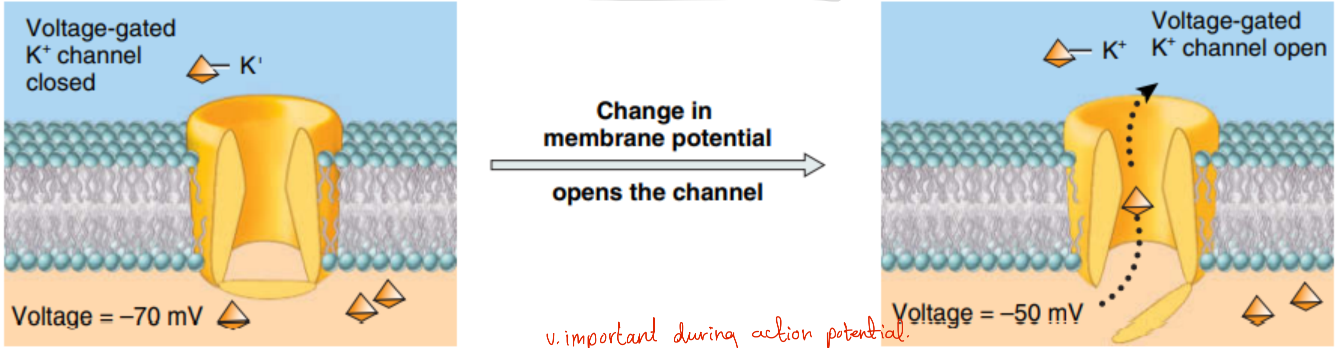
Ex:- Neurotransmitter

DOES NOT enter the cell.

Ion channels in excitable cells



(c) Mechanically-gated channel



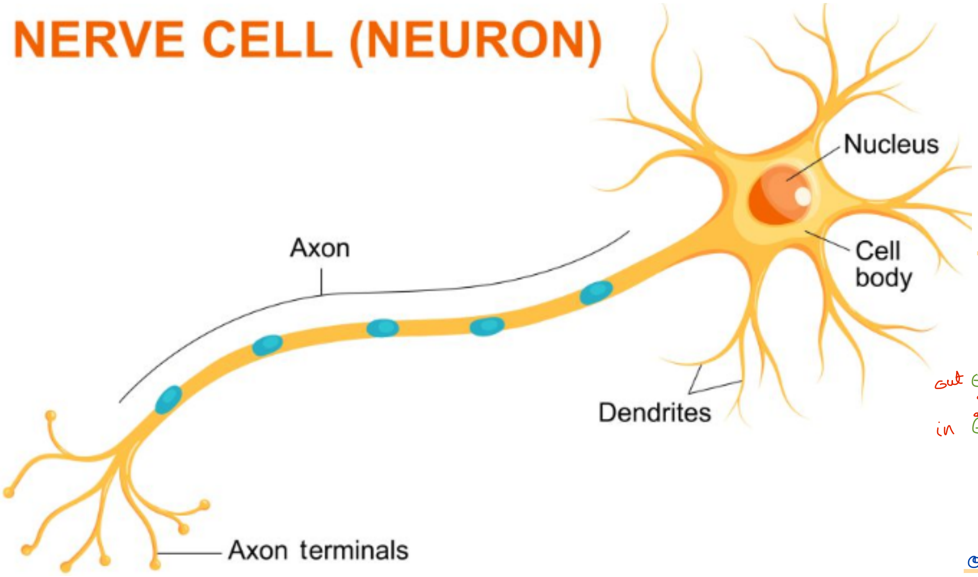
v. important during action potential.

(d) Voltage-gated channel

↳ activated when polarity differs.

⇒ Depends on plasma membrane polarity.

Excitable cells



They communicate with one another using two types of electrical signals:

the stimulus that reaches dendrites + cell body. Slight changes on membrane potential

- Graded potentials are used for short-distance communication only.

in the Axon.

- Action potentials allow communication over long distances within the body.

out ⊖

in ⊕

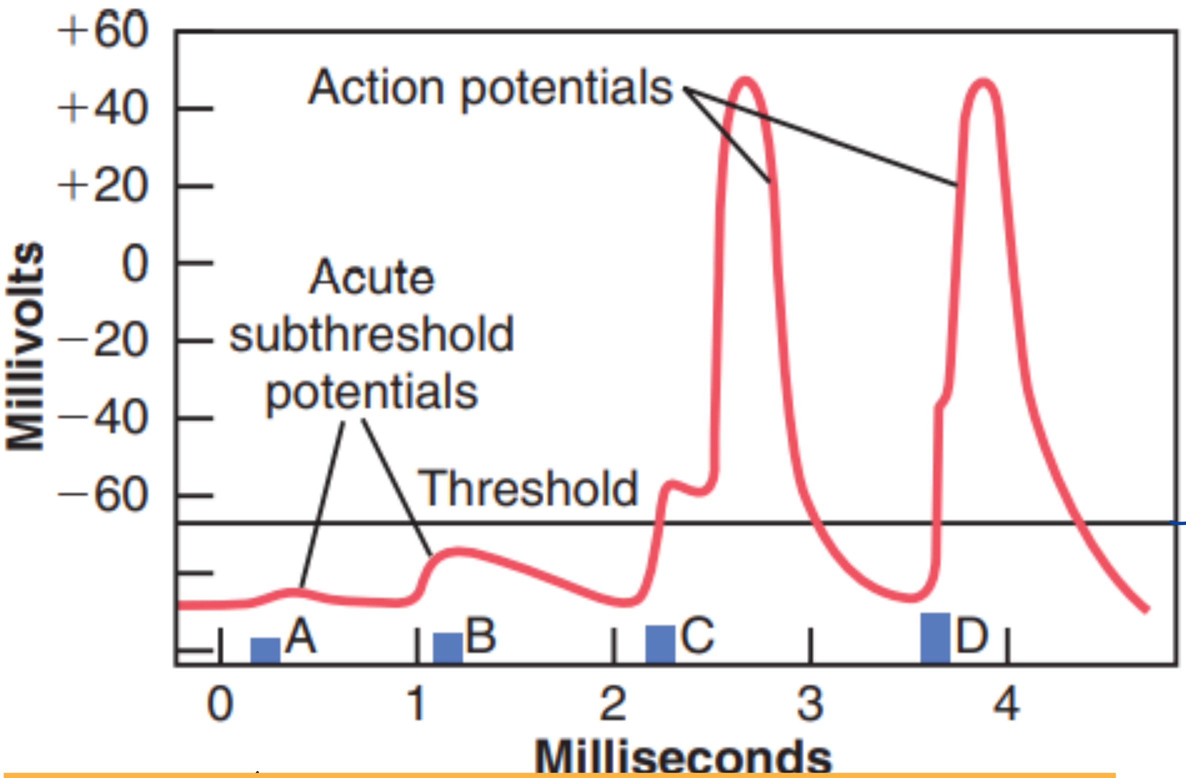
Once the graded potential exceeds the hillock (which connects the cell body to the Axon) the graded potential turns in to Action potential.

mainly mechanical / ligand channels

Voltage gated channels.

Why Graded pot. not AP? The channels differ in (dendrites + cell body) from that in the Axon.

Graded potential vs action potential



The threshold potential

the critical level to which a membrane potential must be depolarized to initiate an action potential.

up → depolarization

down → hyperpolarization. → Graded potential can be up or down, NOT TOGETHER.

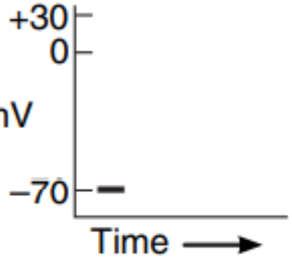
Graded potential vs Action potential

have the summation property

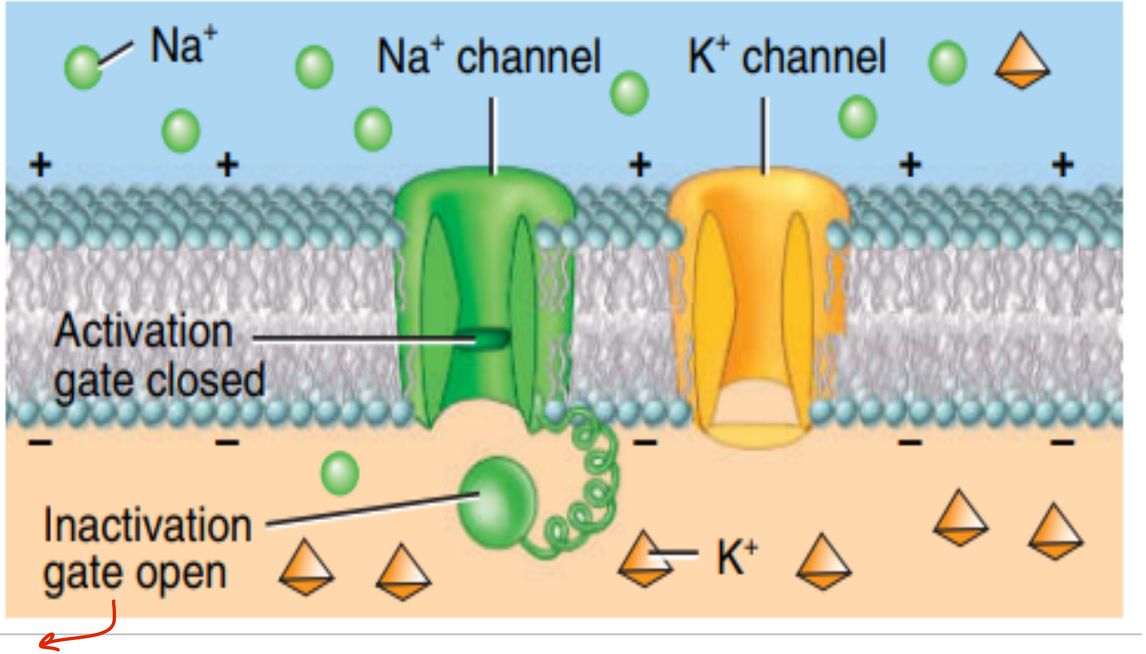
CHARACTERISTIC	GRADED POTENTIALS	ACTION POTENTIALS
Origin	Arise mainly in dendrites and cell body.	Arise at trigger zones and propagate along axon.
Types of channels	Ligand-gated or mechanically-gated ion channels.	Voltage-gated channels for Na^+ and K^+.
Conduction	Decremental (not propagated); permit communication over short distances.	Propagate and thus permit communication over longer distances.
Amplitude (size)	Depending on strength of stimulus, varies from less than 1 mV to more than 50 mV.	All or none; typically about 100 mV.
Duration	Typically longer, ranging from several milliseconds to several minutes.	Shorter, ranging from 0.5 to 2 msec.
Polarity	May be hyperpolarizing (inhibitory to generation of action potential) or depolarizing (excitatory to generation of action potential).	Always consist of depolarizing phase followed by repolarizing phase and return to resting membrane potential.
Refractory period	Not present; summation can occur.	Present; summation cannot occur.

- we won't dive into graded potential
- but AP ✓

Action potential

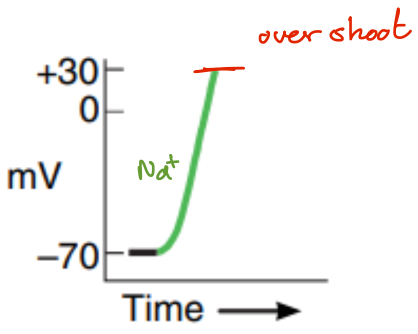


1. Resting state:
All voltage-gated Na^+ and K^+ channels are closed. The axon plasma membrane is at resting membrane potential: small buildup of negative charges along inside surface of membrane and an equal buildup of positive charges along outside surface of membrane.



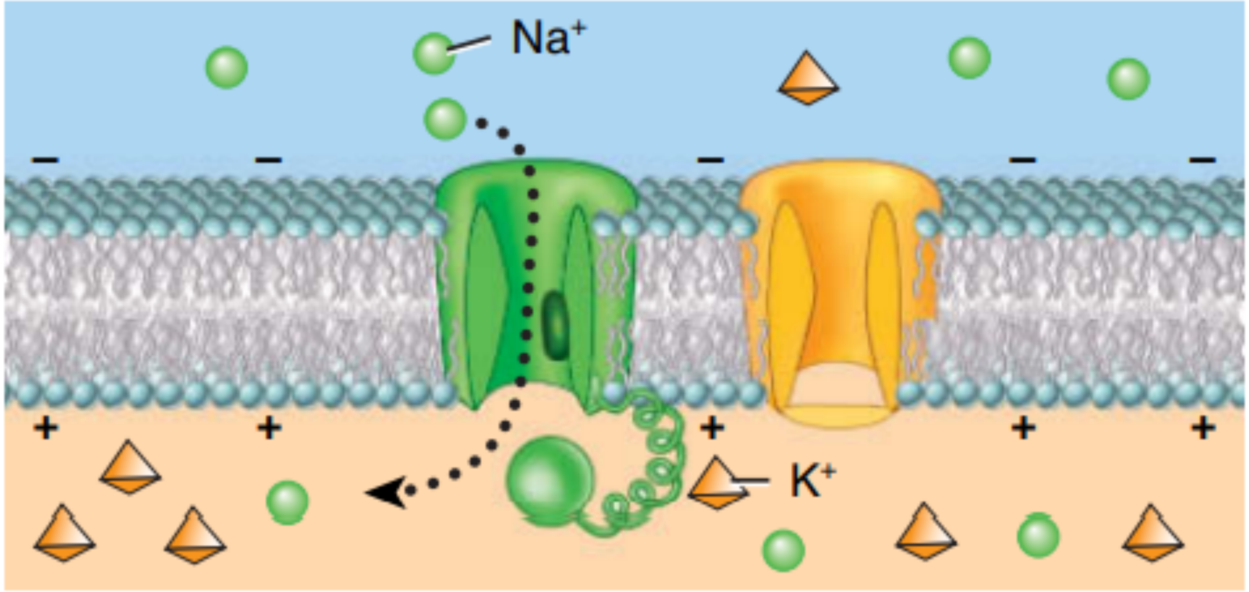
in resting inactivation → opened.

Action potential

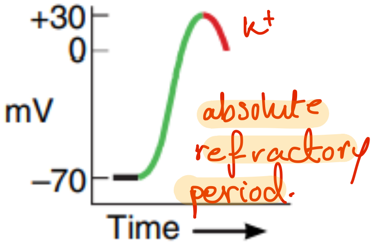


in this stage → positive feedback ; more Na+ channels open.

2. Depolarizing phase:
When membrane potential of axon reaches threshold, the Na^+ channel activation gates open. As Na^+ ions move through these channels into the neuron, a buildup of positive charges forms along inside surface of membrane and the membrane becomes depolarized.



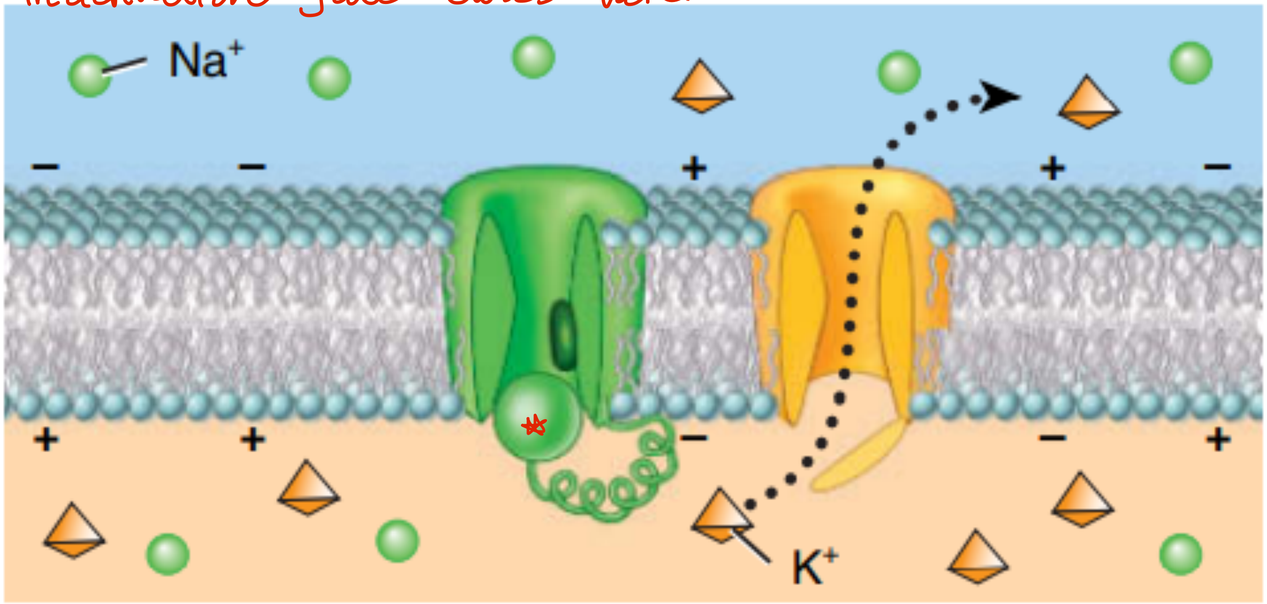
Action potential



Repolarizing phase begins:
Na+ channel inactivation gates close and K+ channels open.

The membrane starts to become repolarized as some K+ ions leave the neuron and a few negative charges begin to build up along the inside surface of the membrane.

* inactivation gate closes here.



Action potential

Repolarization phase continues:

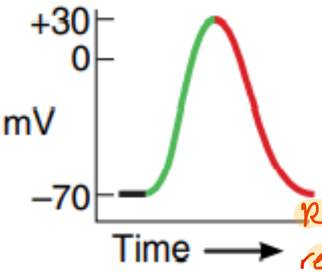
K+ outflow continues.
As more K+ ions leave the neuron, more negative charges build up along inside surface of membrane.

K+ outflow eventually restores resting membrane potential.

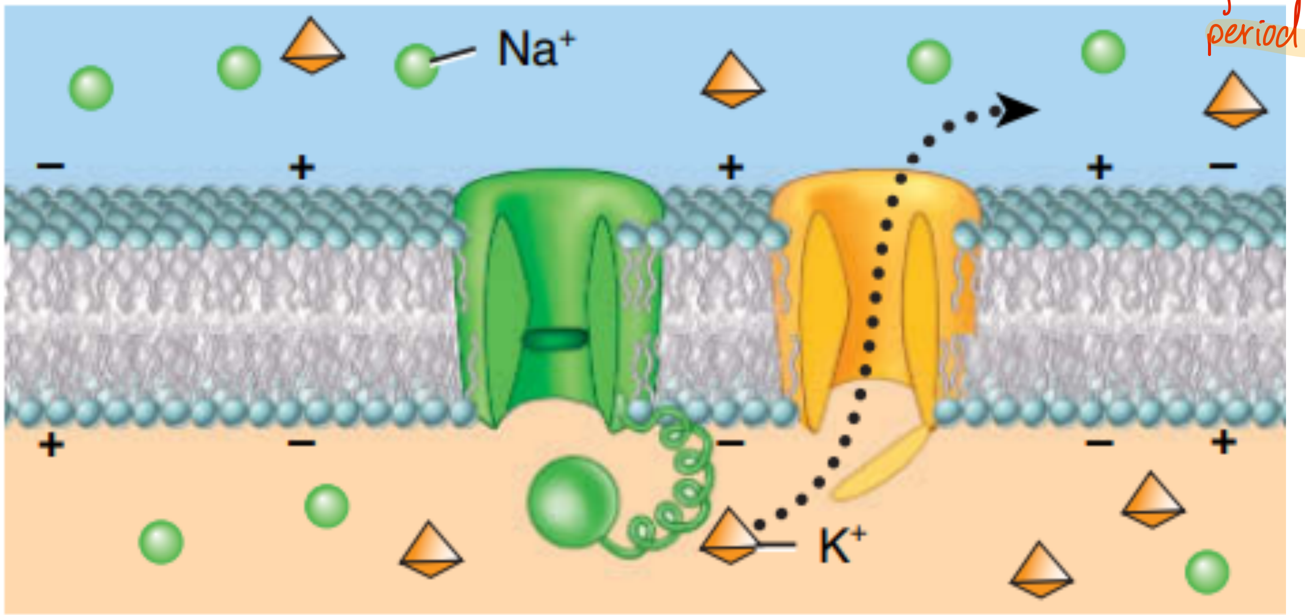
Na+ channel activation gates close and inactivation gates open.

Return to resting state when K+ gates close.

inactivation gate ⟶ resting status
activation gate ⟶ closed.



Relative refractory period



voltage gated K+ channels still opened (closes slowly)
at this stage I need a stronger stimulus   Relative refractory period.

Refractory period

- Shortly after the action potential is initiated, the sodium channels become inactivated and no amount of excitatory signal applied to these channels at this point will open the inactivation gates.

- The period during which a second action potential cannot be elicited, even with a strong stimulus, is called the absolute refractory period.

Refractory period

- The only condition that will allow them to reopen is for the membrane potential to return to or near the original resting membrane potential level. Then, within another small fraction of a second, the inactivation gates of the channels open and a new action potential can be initiated.

Re-establishing membrane potential

- Because **Na+ -K+ ATPase pump** requires energy for operation, this "recharging" of the nerve fiber is an active metabolic process.

- A special feature of this pump is that its degree of activity is strongly stimulated when excess sodium ions accumulate inside the cell membrane.

Action Potential

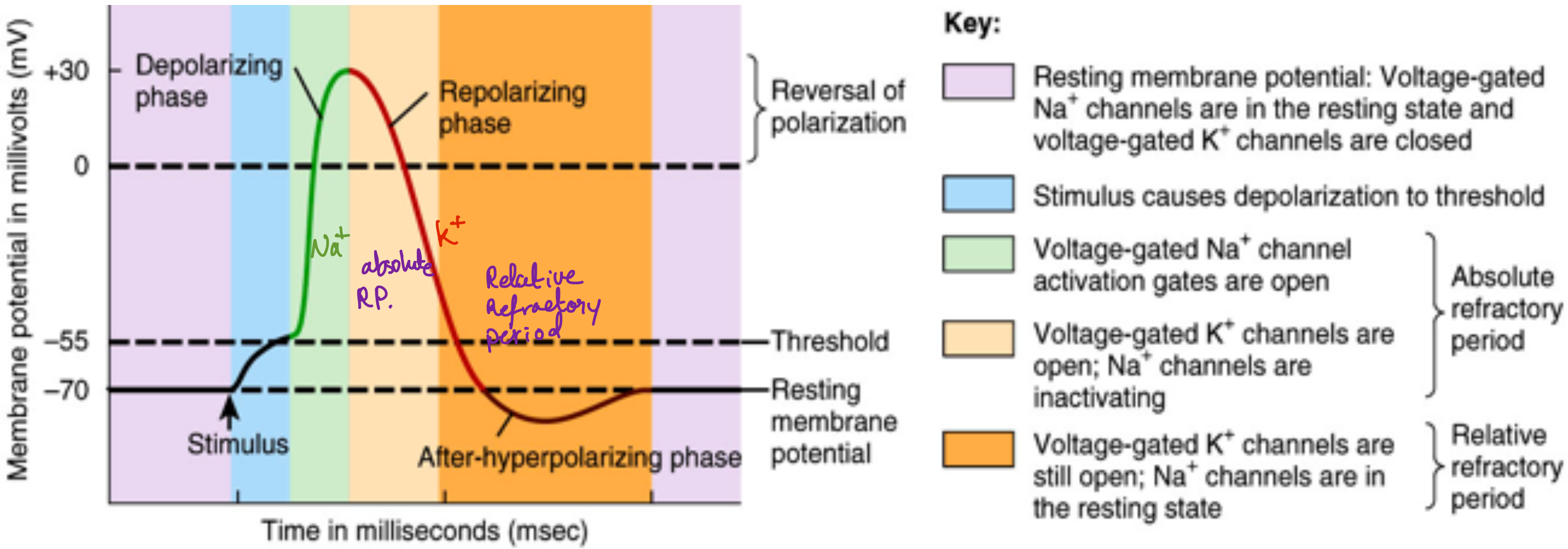


Figure 12.19 Tortora - PAP 12/e

* Action potential ---> All or none prencipal