PHYSIOLOGY

النادي الطبي

Lec: 12 الجزء الثاني من

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General physiology
Spring 2024
Lecture 12
Resting membrane potential

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Lecture objectives

- Define the resting membrane
- Review the different types of ionic channels in the cell membrane
- Understand ionic basis of resting potential by applying the concept of diffusion potential
- Describe the relation between the resting membrane potentials and K and Na equilibrium potentials
- Describe the contribution of Na-K ATPase pump to the resting potential
- Know the resting membrane of different cell types including neurons, muscle cells (Excitable Tissues)and other cell types of the body
- Describe the effects of hypokalemia, hyperkalemia and hypocalcemia on resting membrane potentails of excitable cells

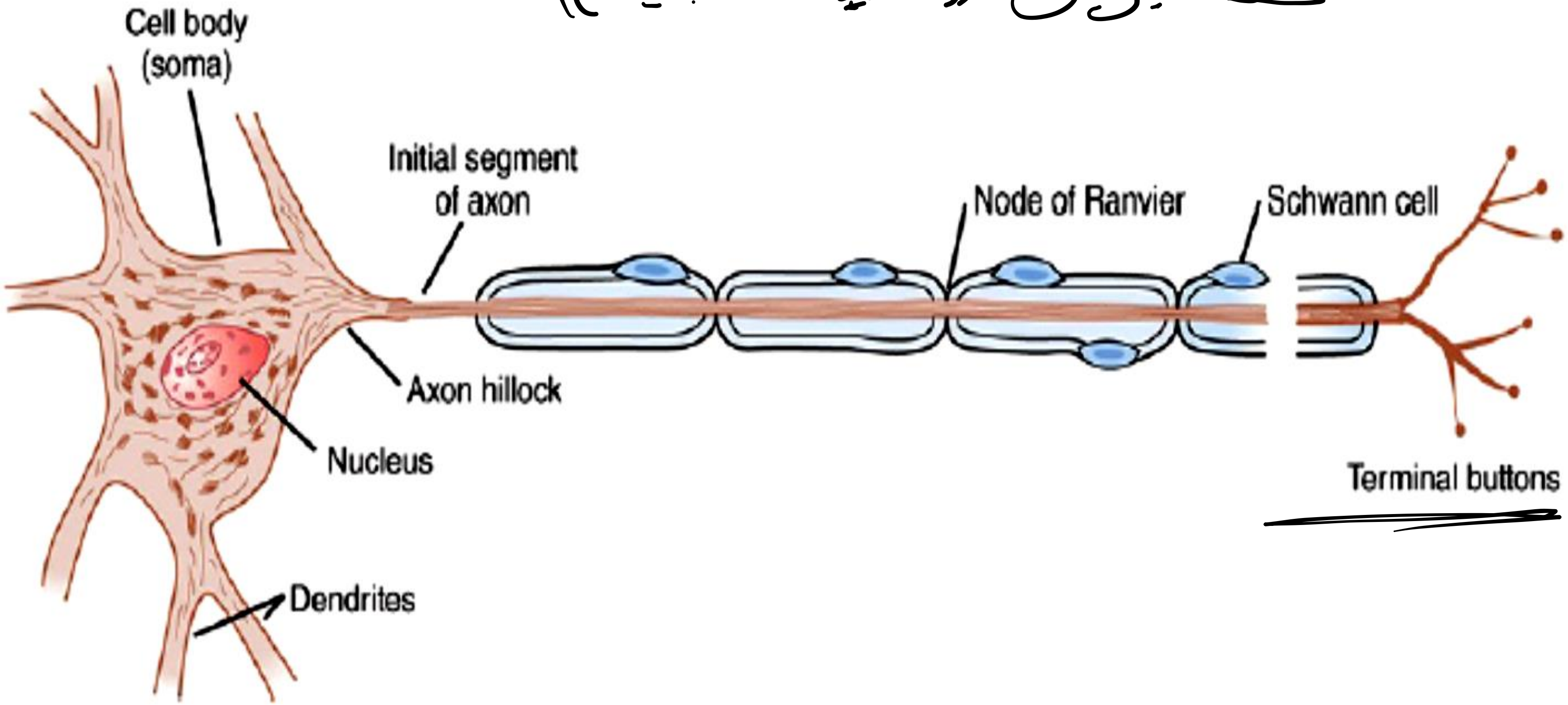
الخلايا النشطة والغير نشطة

Excitable tissues and none excitable tissue

- All cells have resting potential
- None excitable cells like RBC Epithelial cells in the kidney tubules in the gut have lower resring potential the excitable cells
- Excitable tissues include nerve cells and muscle cells . Usually have higher resting potential compared to none excitable cells . Excitable cells such as nerves and muscles have the ability to generate signals(action potential) that may be quickly transmitted to other nerve cells or muscle cells

Schematic diagram of a neurons

عصبون (خلية عصبية)



Measurement of Resting Membrane Potential (RMP)

باكارة تعريف لـ RMP

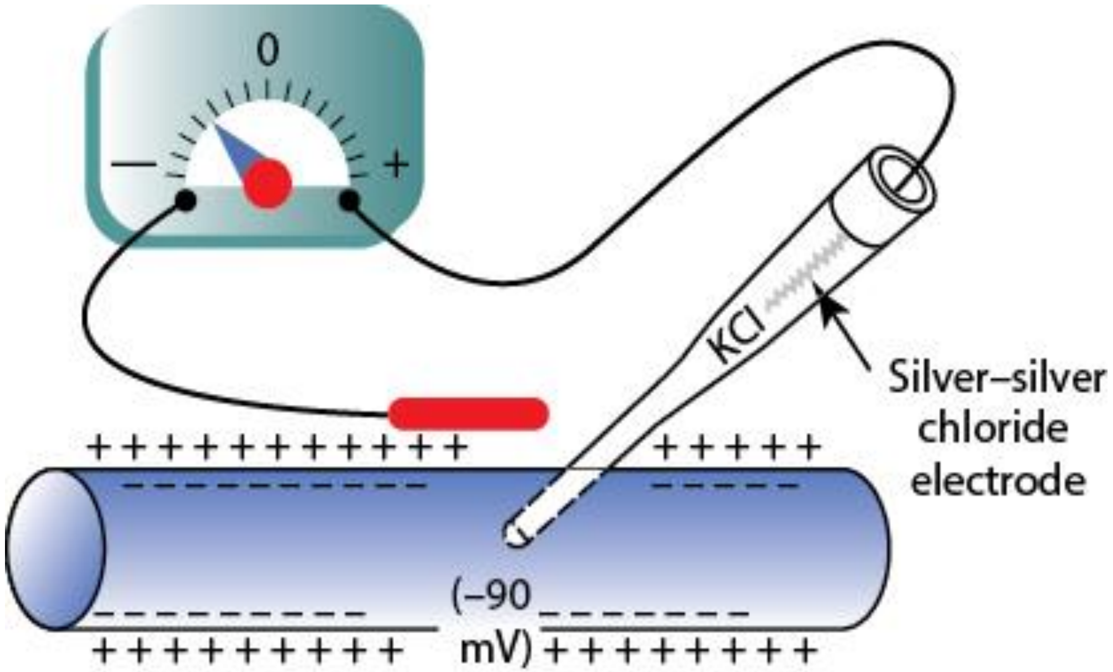
RMP is (a potential difference across biological membranes, and it reflects the separation of charges across the membrane.)

There are a few excess negative charges (about 1 pmol/cm2) on the inner surface and the same number of excess positive charges on the outer surface

* The resting membrane potential measured when the cell is at rest—that is, not active

Different cells have different resting potentials.

سبب تسميتها بال resting



Resting Membrane Potential of Different cell

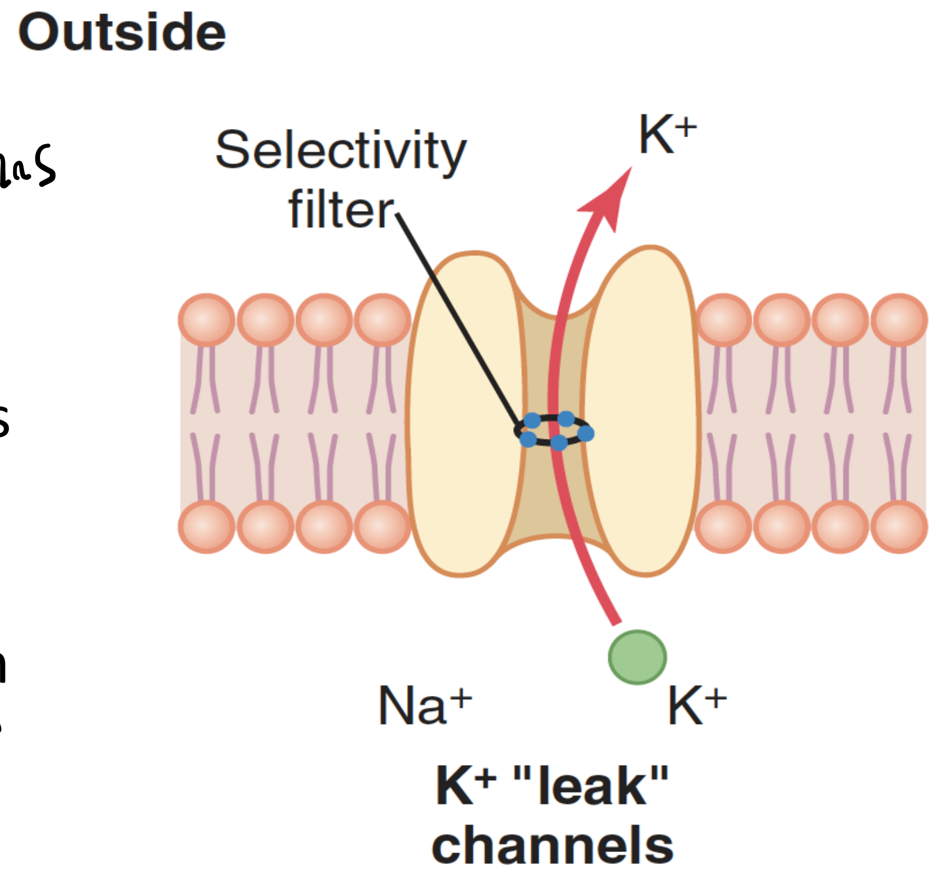
Cell types	Resting potential
Skeletal muscle fibers	-85 to 95 mV
Smooth muscle fibers	-50 to -60 mV
Astrocytes	-80 to -90 mV
Neurons	-60 to -70 mV
Erythrocytes	-8 to -12 mV
Photoreceptor cells	-40 mV (dark) to -70 mV (light)

Leaky Ionic channels in nerve cells

Leak Channels

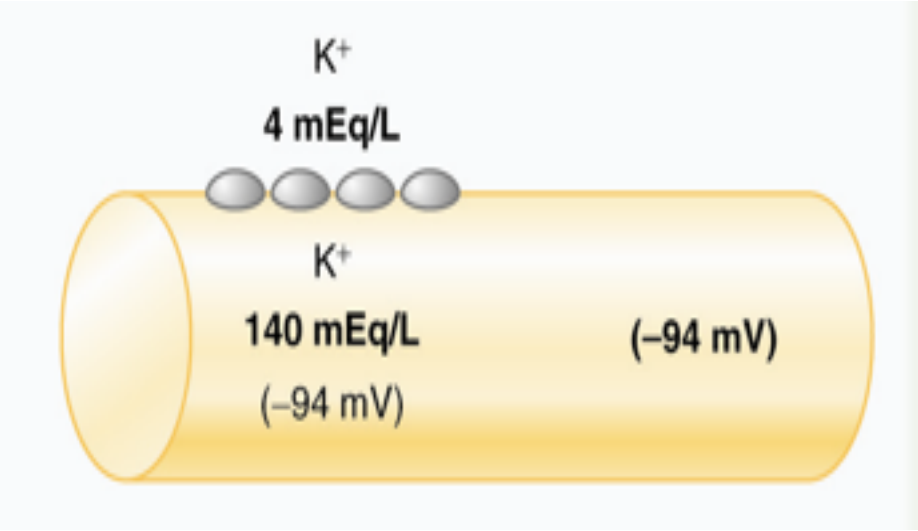
- Predominately for K Ions
- Some Na Leak channels
- cell membranes of Neurons and muscle cell in resting state are highly permeable to K ions than Na Ions ((100X))

3. Thus the resting membrane potential is mainly determined by the concentration gradients of K ion



Origin of Resting Membrane Potential of Neurons

$RMP = -90\ mV$



Contribution of K Diffusion Through the Nerve Membrane

Concentration difference 35 : 1 → K+ Nernst potential =-94 mV

If K+ ion concentration and permeability were the only factors causing RMP → RMP inside the fibber would be equal to −94 millivolts and will be equal to the Nerst potential of K ions

RMP بتطلع
بتساوي تقريبًا N EP تاع
ال $K^+ \approx -94\ mV$

Effects of disturbances of ionic concentration in the ECF on RMP

- Hyperkalemia : The cell membrane depolarize, (becomes less negative) and the resting potential moves closer to the threshold for eliciting an action potential and the neuron becomes more excitable
- When the K concentration reaches 7 mEq/L can lead to significant hemodynamic and neurologic consequences; levels exceeding 8.5 mEq/L can cause respiratory paralysis or disturbance in heart rhythm and cardiac arrest and can quickly be fata.

- Hyporkalemia If the extracellular level of K+ is decreased (hypokalemia), the membrane potential becomes is reduced (becomes more negative) and the neuron or muscles cells are hyperpolarized Changes in ECG are also expected during hypokalemia

Effects of hypocalcemia

- A decrease in extracellular Ca^{2+} concentration increases the excitability of nerve and muscle cells(membrane destabilization) and may lead to hypo calcemic tetany

Origin of Resting Membrane Potential of Neurons

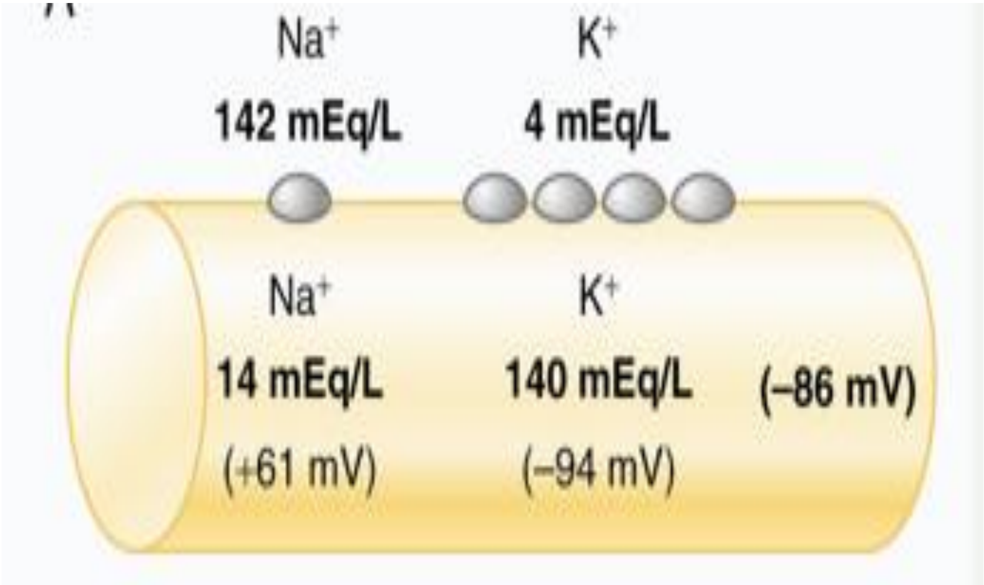
$RMP = -90\ mV$

Contribution of Na Diffusion Through the Nerve Membrane

Concentration difference 10 : 1 → Na+ Nernst potential =+61 mV

Slight permeability of the nerve membrane to Na+→ minute diffusion of Na Therefore , According to **Goldman equation** → RMP = −86 mV→ close to K potential but not equal to the equilibrium

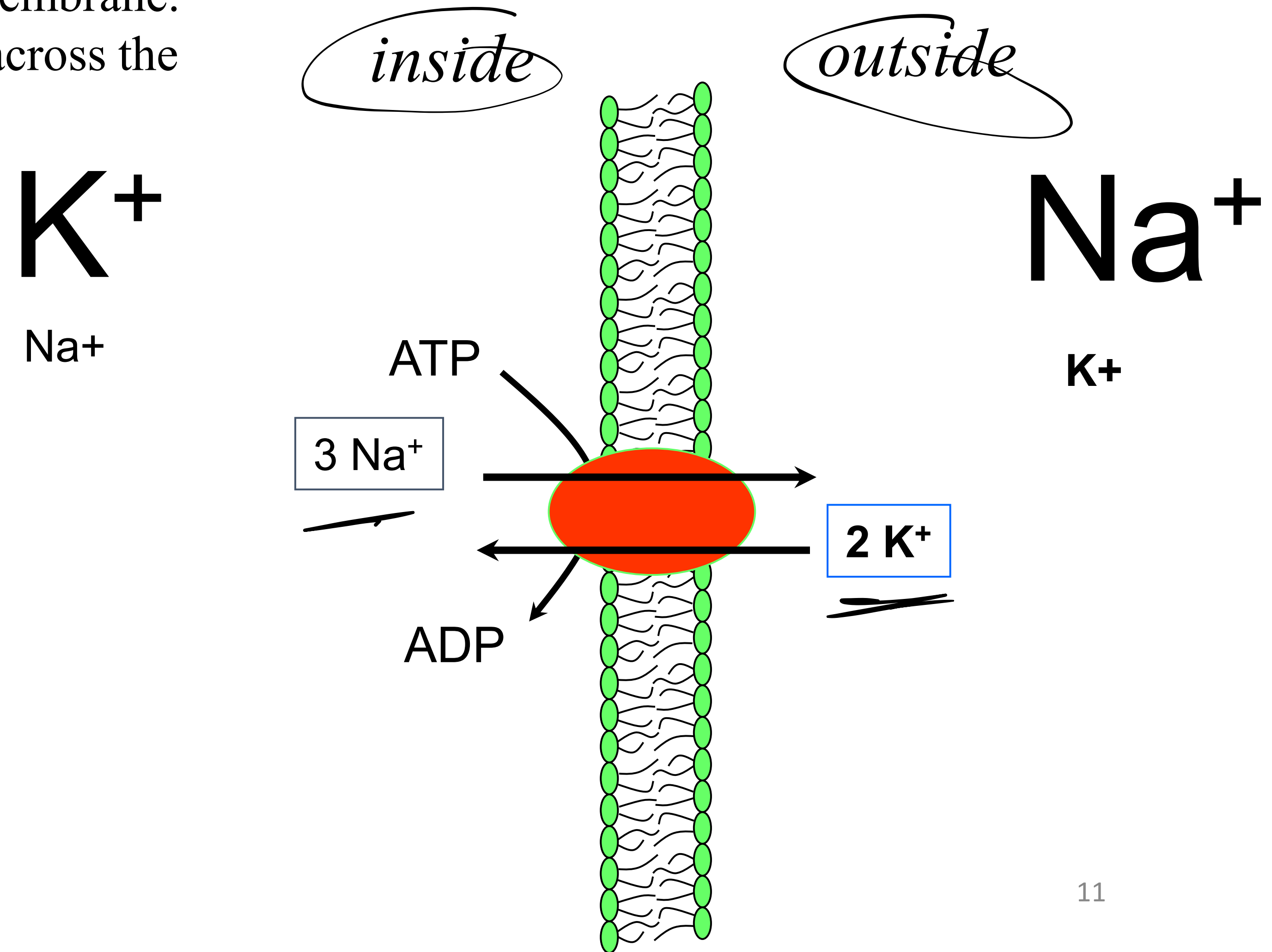
قليل



Active Transport of Na^+ and K^+

Electrogenic pump

More positive charges are pumped to the outside than to the inside→ causing **negative** potential inside the cell membrane. Causes **large concentration gradients** for Na & K across the resting nerve membrane.

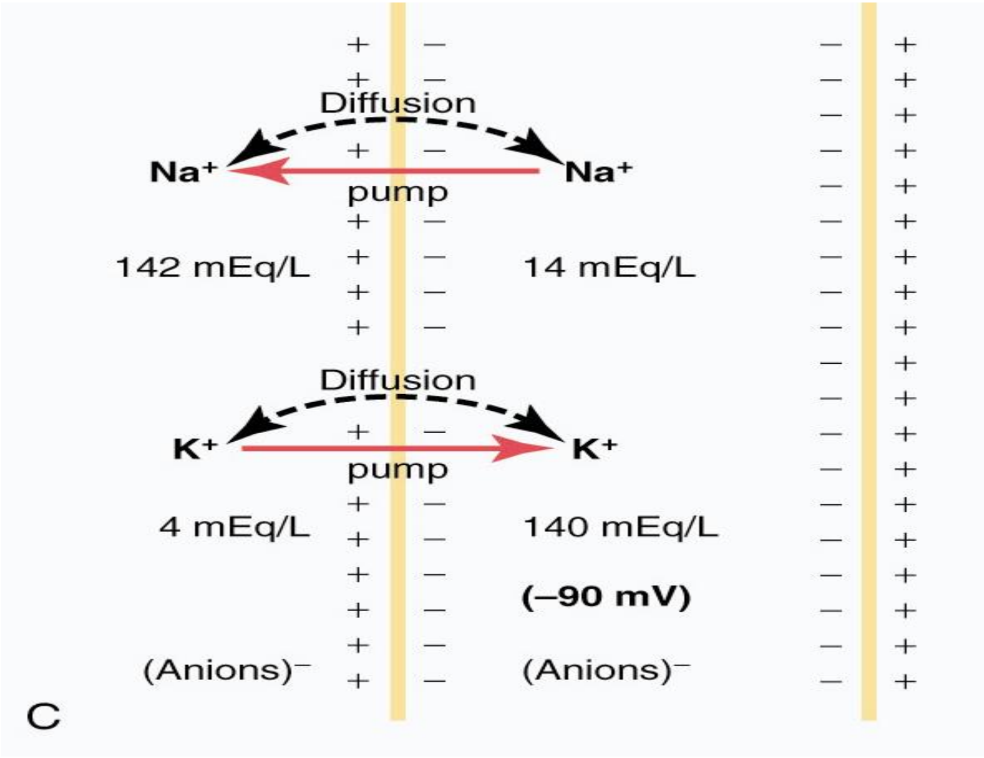


Origin of Resting Membrane Potential of Neurons

RMP $= -90\ mV$

Contribution of the Na+-K+ Pump

Creating additional degree of negativity (about −4 millivolts additional)→(-86+-4=-90 mV



The Resting Membrane Potential Summary

- Membrane potentials are generated mainly by diffusion of ions and are determined by
  - the ionic concentration differences across the membrane, and
  - the membrane's relative permeabilities to different ions.

Plasma-membrane Na,K-ATPase pumps maintain intracellular sodium concentration low and potassium high.

- In almost all resting cells, the plasma membrane is much more permeable to potassium than to sodium, so the membrane potential is close to the potassium equilibrium potential—that is, the inside is negative relative to the outside.
- The Na,K-ATPase pumps also contribute directly a small component of the potential because they are electrogenic.

Net Driving Force on Ions across the cell membrane

- When multiple ions contribute to membrane potential (Vm) of a cell→ membrane potential would **not** be at the equilibrium potential (Veq.) for any of the contributing ions. Thus, no ion would be at its equilibrium (i.e., Veq. ≠ Vm).

- i.e. chemical and electrical forces acting on K+, Na+, and Cl− are not equal→ electrochemical driving force (VDF) acts on the ion, causing the net movement of the ion across the membrane down its own electrochemical gradient.

v membrane

equilibrium (CF)

- VDF = Vm − Veq.

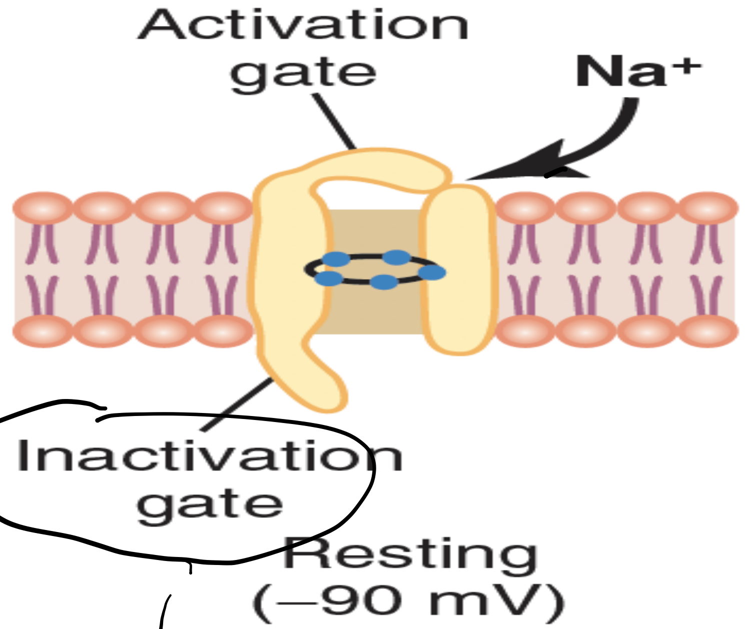
v driving force

Voltage-Gated Na Channel in neuronal cell membranes
Activation and Inactivation of the Voltage-Gated Na Channel

This channel has two gates:

1- activation gate → near the outside of the channel

2- inactivation gate → near the inside of the channel



* leaky channels → free flow of sub

* Voltage gated channels → it needs diff in the (V) (MP)

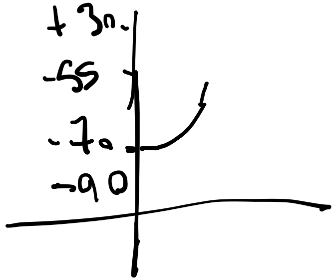
* شغال ل K^+ يقول انه يطلع لبرا عشان ال concentration gradient و يمشي الوقت

مابيقدر يطلع عشان ال <u>V</u>

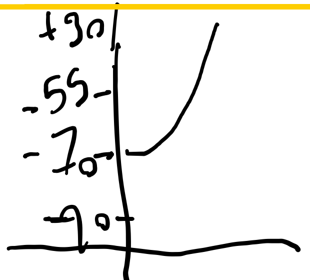
بحالة كانت الخلية مستريحة رح يكون في V-diffrence يسمى

بال zone- resting potential وفي حالة الاستجابة

العصبية Actionpotential بيدخل ال Na^+ الخلية العصبية عن طريق بروتينات تنقل



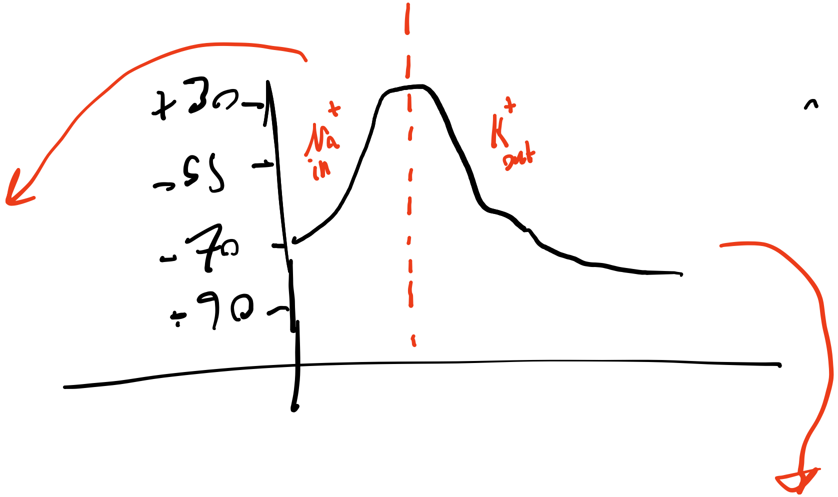
ويصبح داخل الخلية Na^+ كثير وهذا ما يسمى ال Potential



وهذا ما يفتح ال V-Gated Na^+ ويصبح يدخل Na^+ أكثر وأكثر ويرفع ال Potential

ويصبح داخل الخلية more ⊕ charge ووصل ل +30mv ح تفتح ال $V\text{-}Na^+$ Gated

وتفتح ال $V\text{-Gated } K^+$ حتى يصير في difference لتطلع الشحنات لبرا ليصير فيها drop



Depolarization

Potential ل

ليصل ل -90mv

Re Polarization

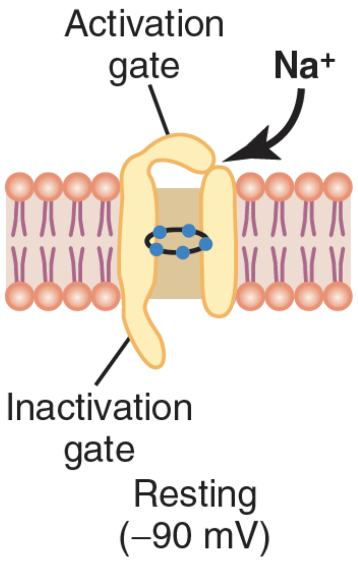
ال+ V-Gate تفتح

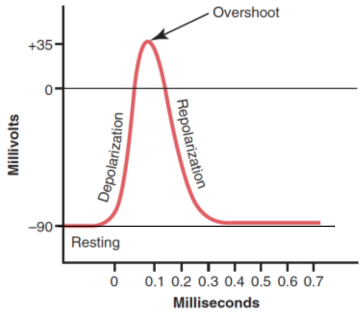
$3Na^+$ in / $2K^+$ out

Activation and Inactivation of the Voltage-Gated Na Channel

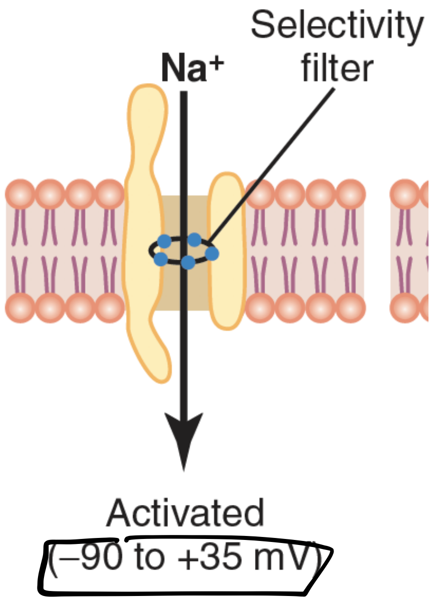
state of two gates in:

A- RMP=−90 mV.
activation gate is closed → prevents Na entry to the interior

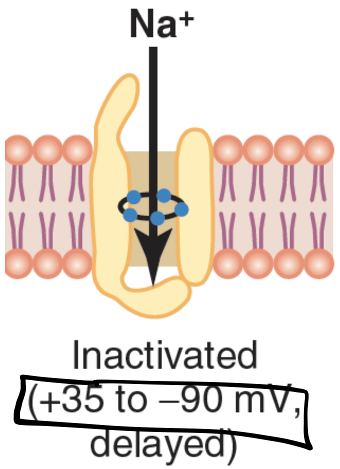




B- Activation of the Na Channel
activation gate → open position
inactivation gate → open→ Na pour inward, increasing Na permeability of membrane 500-5000X.



C-Inactivation of the Na Channel.
activation gate → open
Inactivation gate→ closed
No Na ions entry

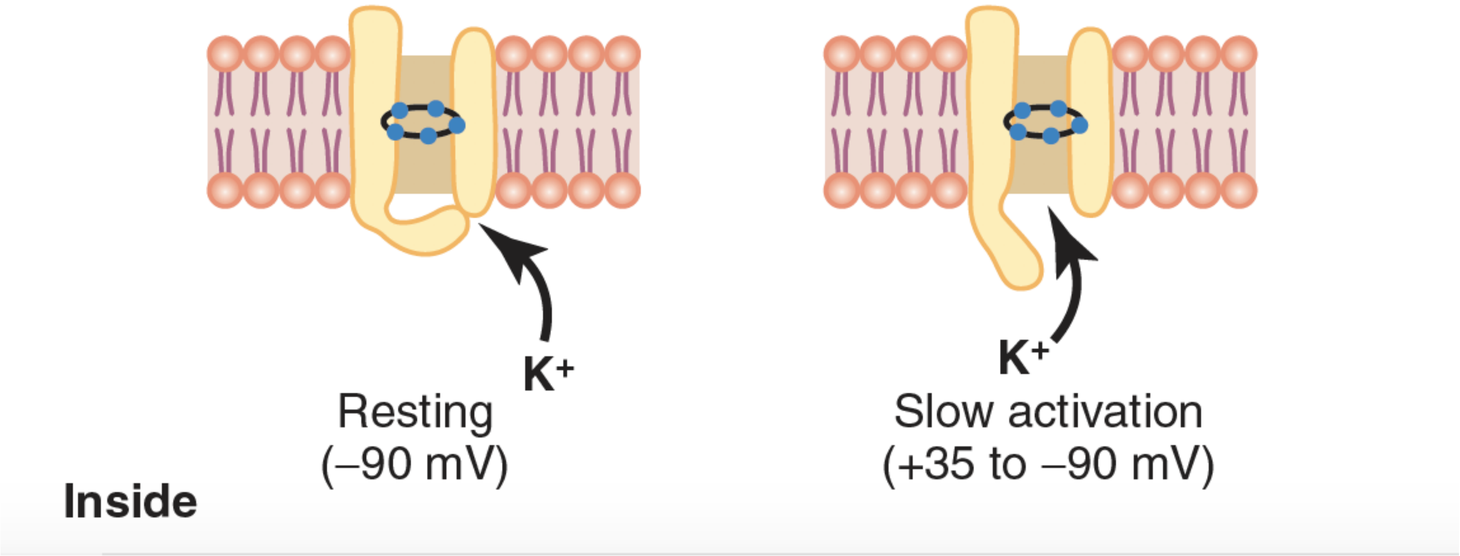


- Occurs a few 10,000ths of a second after **activation** gate opens.
- Conformational change that closes **inactivation** gate is a **slower** process than conformational change that opens the **activation** gate.
- The inactivation gate will not reopen until the membrane potential returns to or near the original RMP

Voltage-Gated K Channel and Its Activation

two states:
A- during the resting state→ Closed
B-Activation state → opened→ K diffusion **outward**

Opens just at the same time that the Na channels are beginning to **close** → ↓ Na entry & ↑ K exit→ recovery of RMP within another few 10,000ths of a second.



Thank you for your attention