PHYSIOLOGY

Lec: 11+12 أول جزئين

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((قوة الانتشار))

Down it's gradient

General physiology
Spring 2024
Lecture 10
Diffusion Potential and Equilibrium Potential

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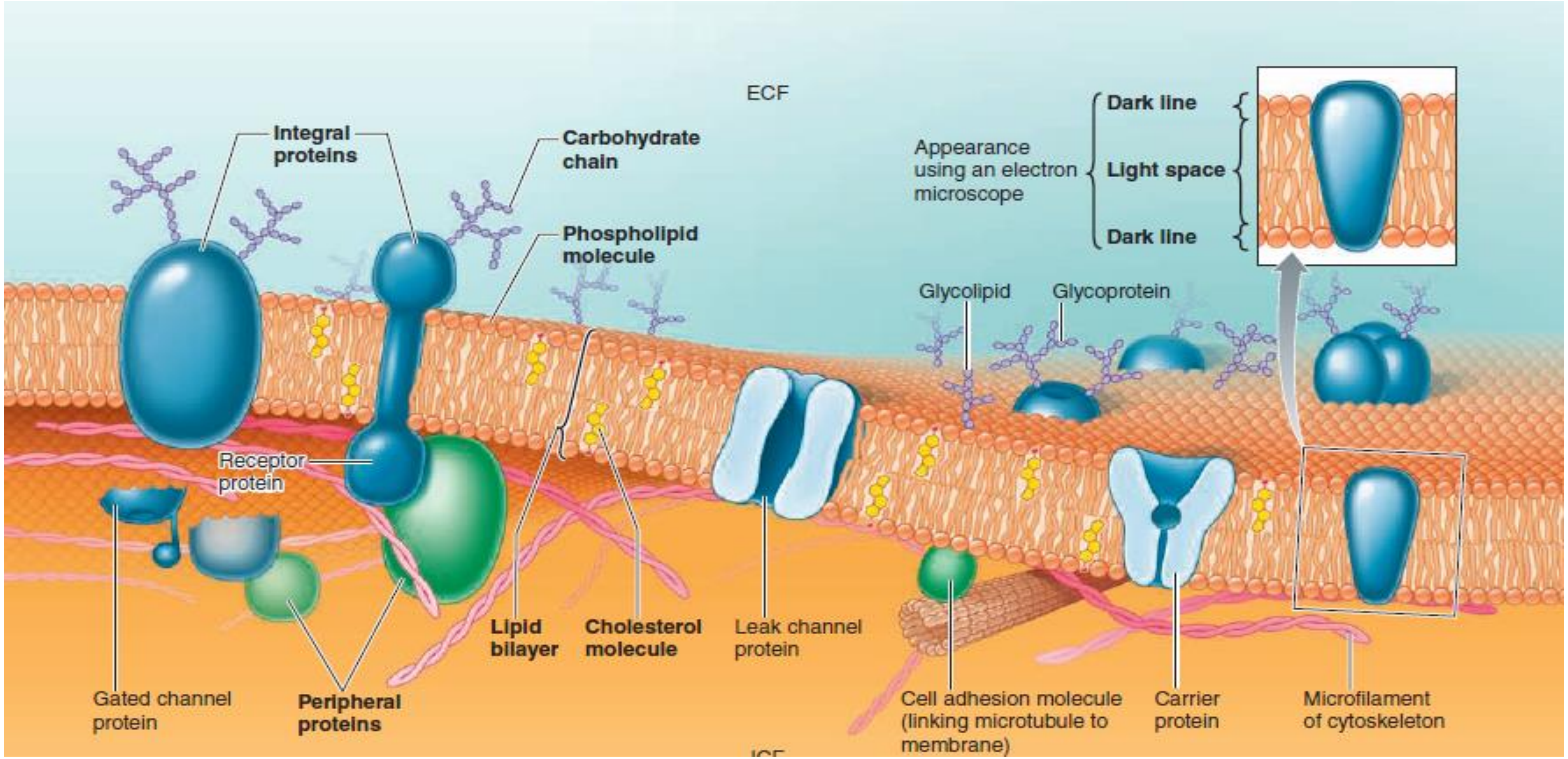
Lecture Objectives

- Describe the ionic concentration of major ions in the ECF and ICF (Review)
- Describe the ionic channels in the cell membrane (Review)
- Understand the function of the Na-K ATPase pup (Review)
- Understand and define the concept of diffusion potentials and equilibrium potential
- Understand the Nerst equation and its application to in calculating the equilibrium potentials of different ions and resting membrane potential
- Understand the GHK equation and its use in estimating the resting membrane potential

Cell membrane channels



Ion Channels In The Cell Membrane

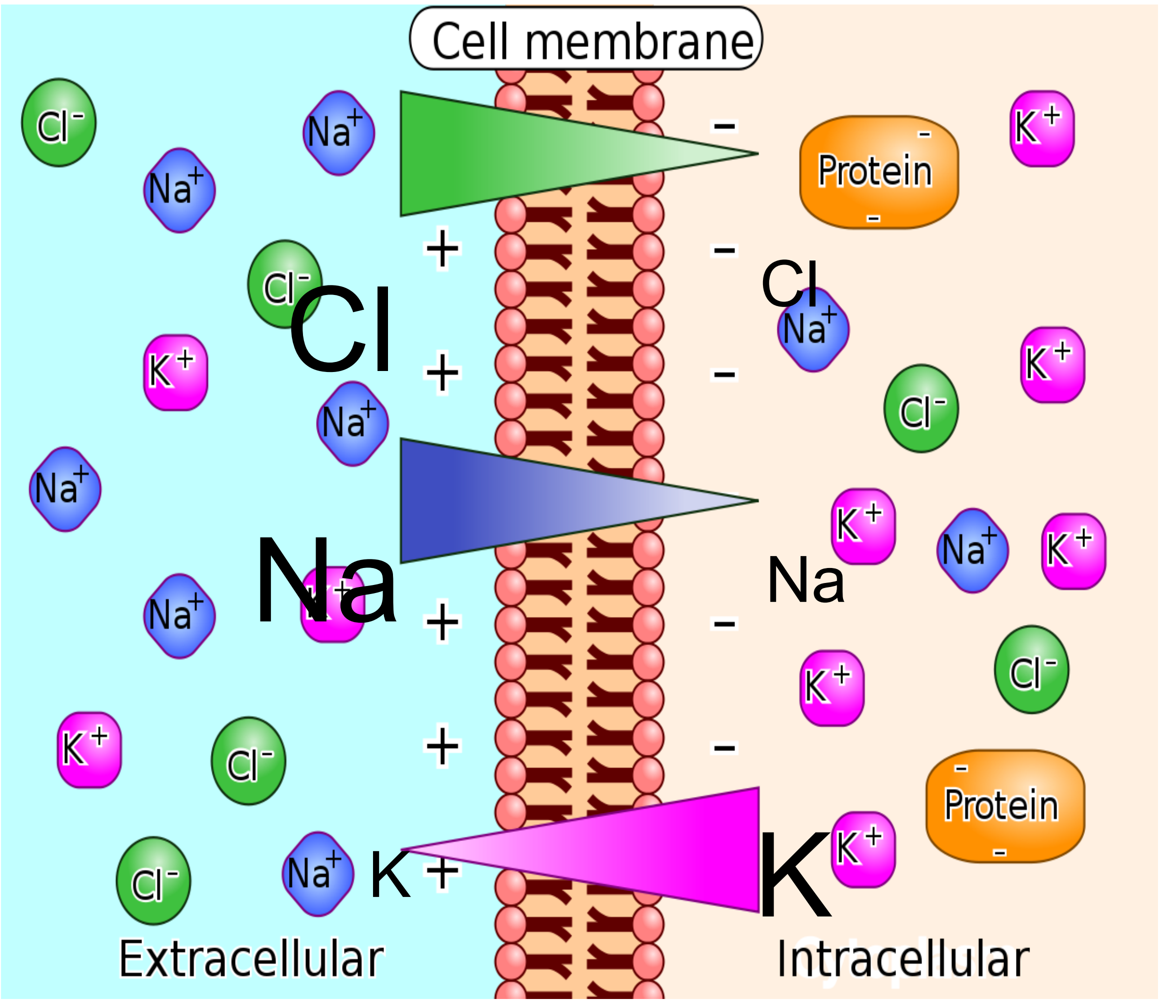
- Leak ionic channels always permit the movements of selected ions across the cell membrane. Example K and Na channels
- Voltage-gated channels have gates that are controlled by changes in membrane potential. For example, the activation gate on the nerve Na+ channel is opened by depolarization of the nerve cell membrane; opening of this channel is responsible for the upstroke of the action potential.
- Ligand-gated channels have gates that are controlled by hormones and neurotransmitters like acetylcholine

Ionic composition and distribution across the cell membrane

Na+/K+

K^+ جوا ↑

Na^+ برا ↑



Na^+(outside): 142 mEq/L

Na^+(inside): 14 mEq/L

K^+(outside): 4 mEq/L

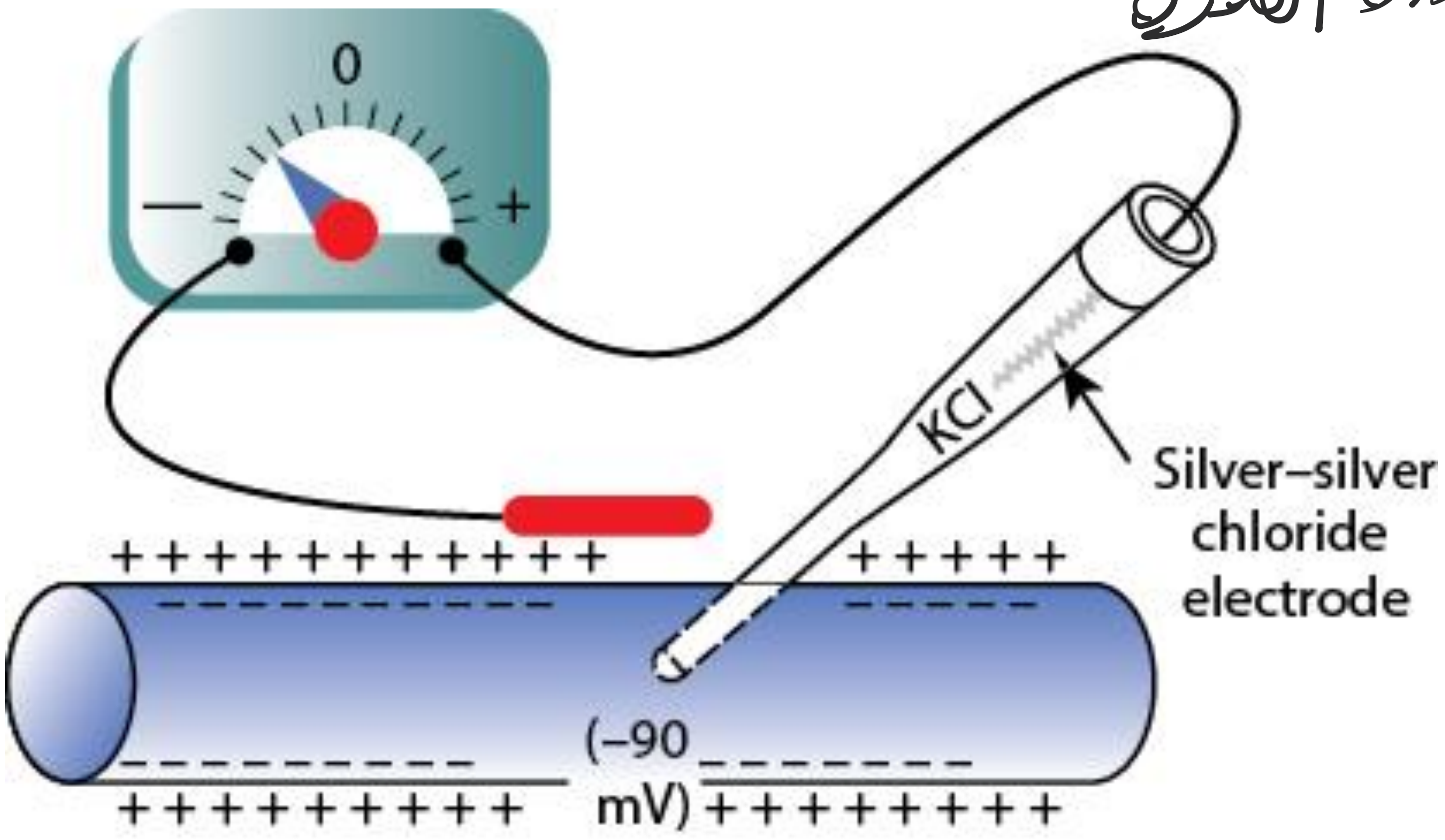
K^+(inside): 140 mEq/L

$$Na^+_{inside} / Na^+_{outside} = 0.1$$

$$K^+_{inside} / K^+_{outside} = 35.0$$

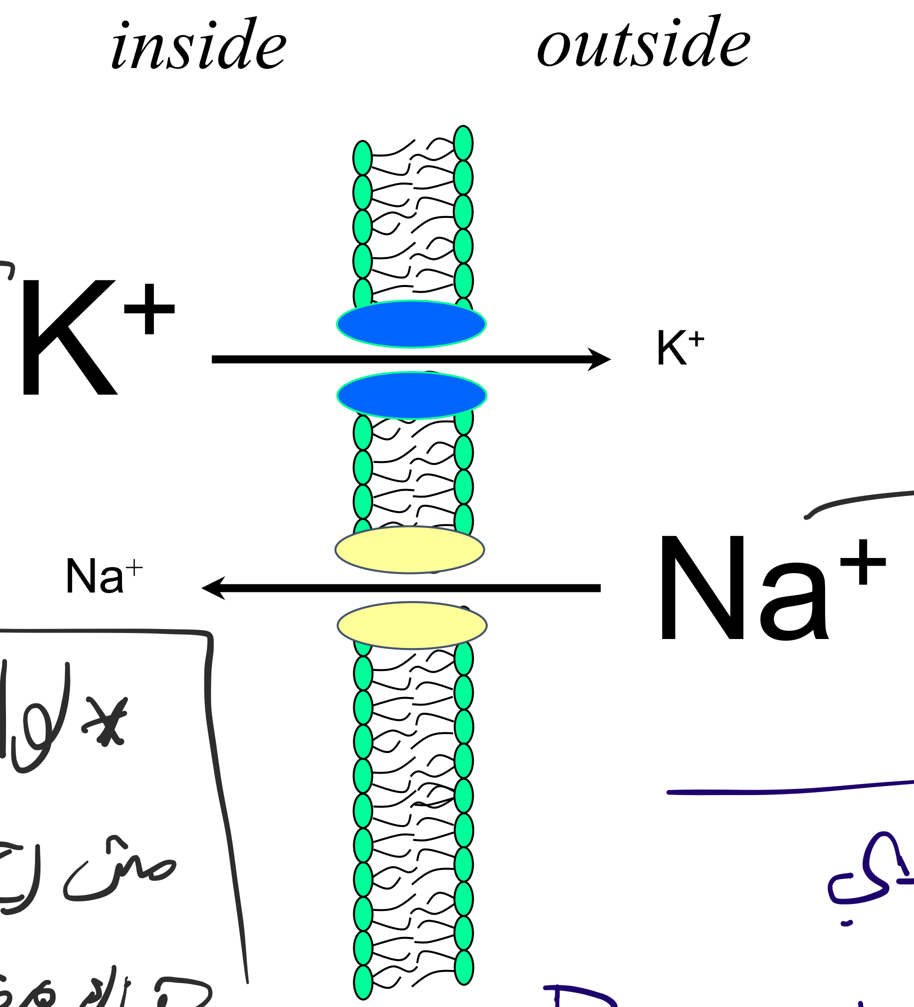
Measurement of resting membrane potential

يلي بتثبت
عنده القدرة



Simple Diffusion of Na^+ and K^+

through leak channels



Passive

لازم تنزل تراكيزها كالي تدخل
down

تركيزها بال
كالي تتحمل Down

* لو اكتفينا بال Passive الخلية
مش راح تشتغل لأنه مش راح يكون
هناك فرق تركيز لأنه بوجد
Active حتى يحافظ

نحتاج ال Active حتى نخلي
ال K^+ وال Na^+ out of their equilibrium

Active Transport of Na^+ and K^+

Upward

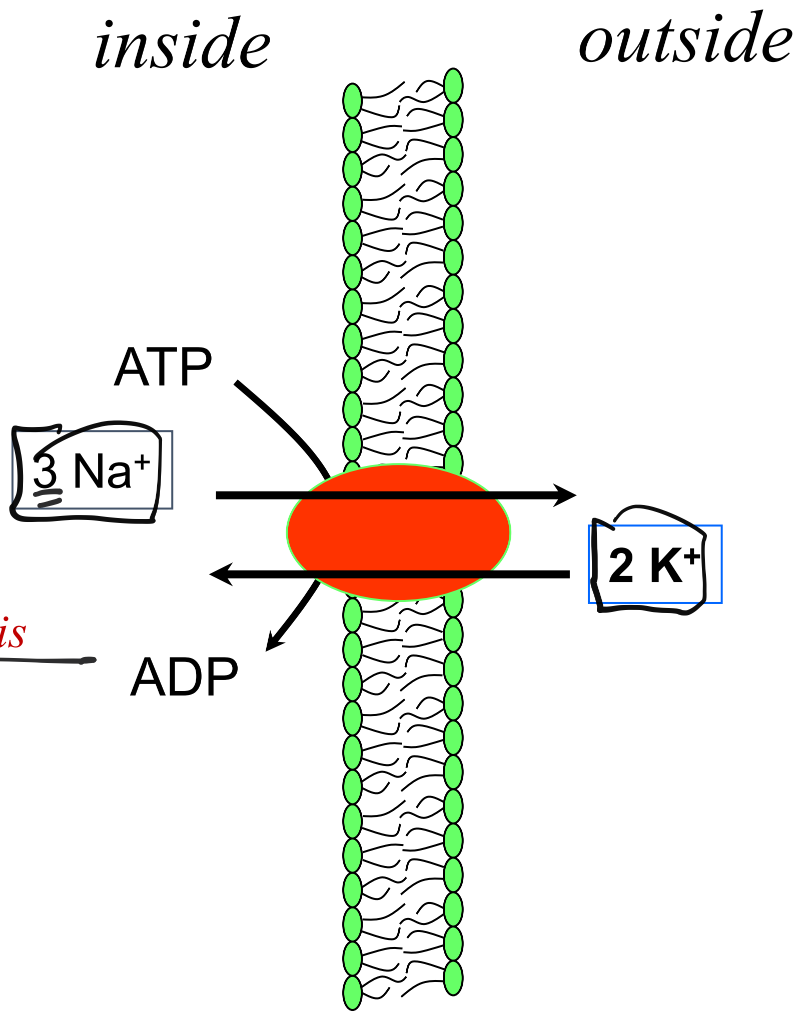
Active

K^+

Na+

Na^+

K+



Na K ATPase pump

Moves ions against concentration gradients

Sodium is pumped out of the cell, potassium is pumped in

The ATPase Na , K pump maintains concentration gradients

Coupling ratio is 3Na : 2K

3 : 2

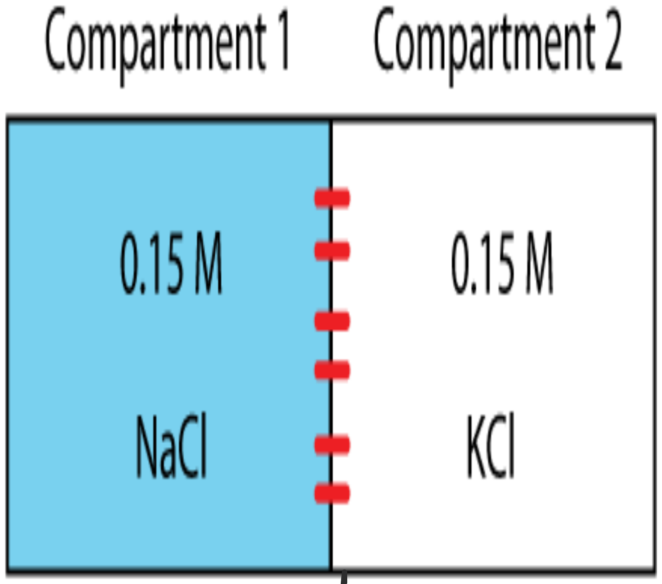
Concentration gradient

Diffusion Potential

- A diffusion potential is the potential difference generated across a membrane when a charged solute (an ion like K or Na) diffuses down its concentration gradient. (is caused by diffusion of ions)
- The magnitude of a diffusion potential, measured in millivolts (mV),and it depends on the magnitude of the concentration gradient, where the concentration gradient is the driving force.
- The sign of the diffusion potential depends on the charge of the diffusing ion and the direction of movement
- Finally, diffusion potentials are created by the movement of only a few ions, and they do not cause changes in the concentration of ions in bulk solution.

Diffusion potentials

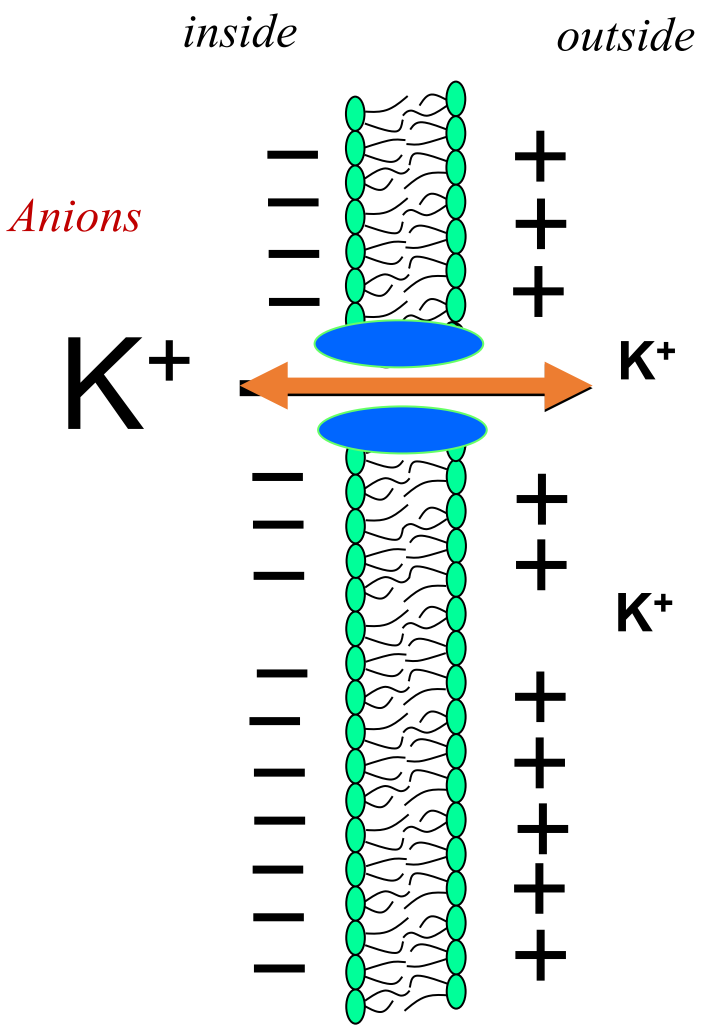
- No channels
- So no diffusion across the membrane despite concentration gradients
- No separation of charge
- Membrane potential = 0



Diffusion potential across cell membrane when the membrane is only permeable to K ions

If a membrane were permeable to only K^+ then…

K^+ would diffuse down its **concentration gradient** *creating positivity outside the membrane and electronegativity inside because of negative anions that remain behind and do not diffuse outward with the potassium* until the **electrical potential** across the membrane countered diffusion.
At equilibrium potential no net movement of K ions across cell membrane occurs



فرق الجهد

Potential

The electrical potential that counters net diffusion of K^+ is called the K^+ equilibrium potential (E_K)/ K^+ Nernst Potential

لما عندما ينتقل ال K^+ من ال inside لل outside وطبعاً هو اتجاهه

يصبح الايونات الموجبة بالخارج كثير ويسمى بال Gradient Positive charge

والداخل يزيد فيه نسبة الايونات السالبة فيصبح هناك electrical potential

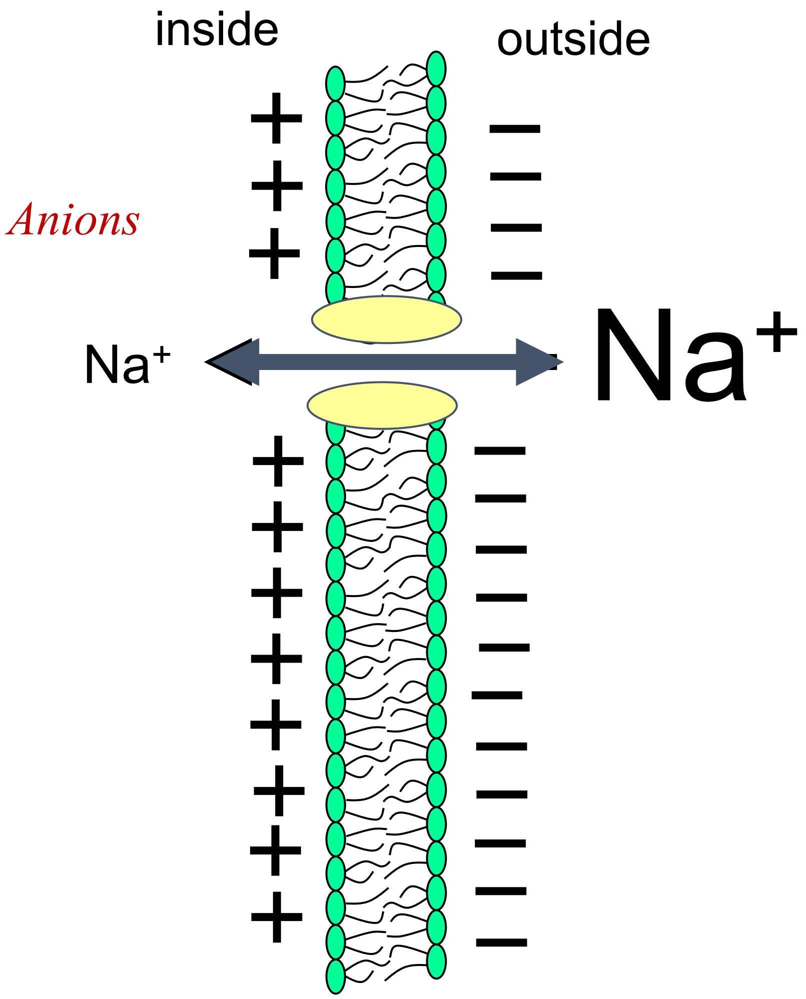
وفي حالة ال equilibrium لا يكون هناك انتقال لل K^+ يجب التعادل.

والعكس لل Na^+ الذي ينتقل من الخارج للداخل

Diffusion potential when the membrane is permeable to Na ions

If a membrane were permeable to only Na^+ then…

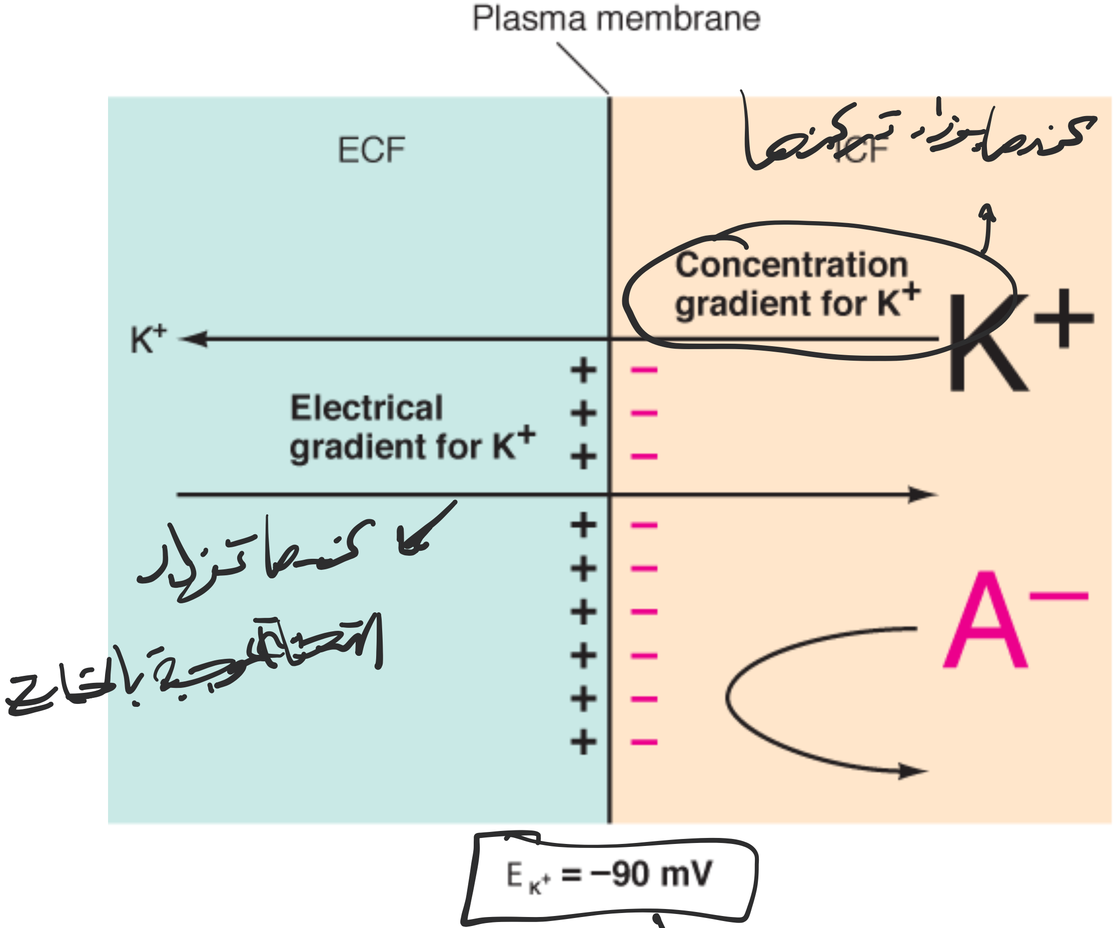
Na^+ would diffuse down its concentration gradient→negativity outside and positivity inside until potential across the membrane countered diffusion.



> ***The electrical potential that counters net diffusion of Na^+ is called the Na^+ equilibrium potential (E_{Na}).***

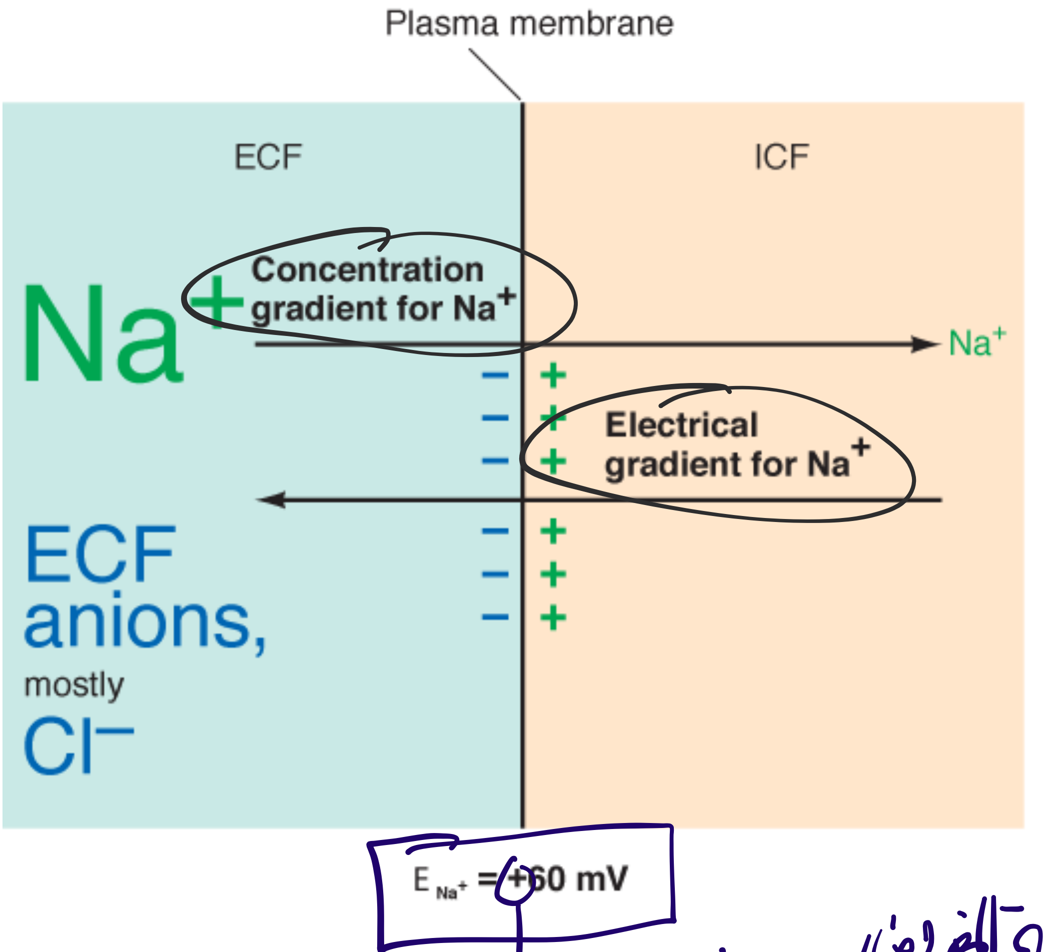
أيكم انتقال Na^+
حتى طار في equilibrium

Diffusion potential and equilibrium potential for K ions



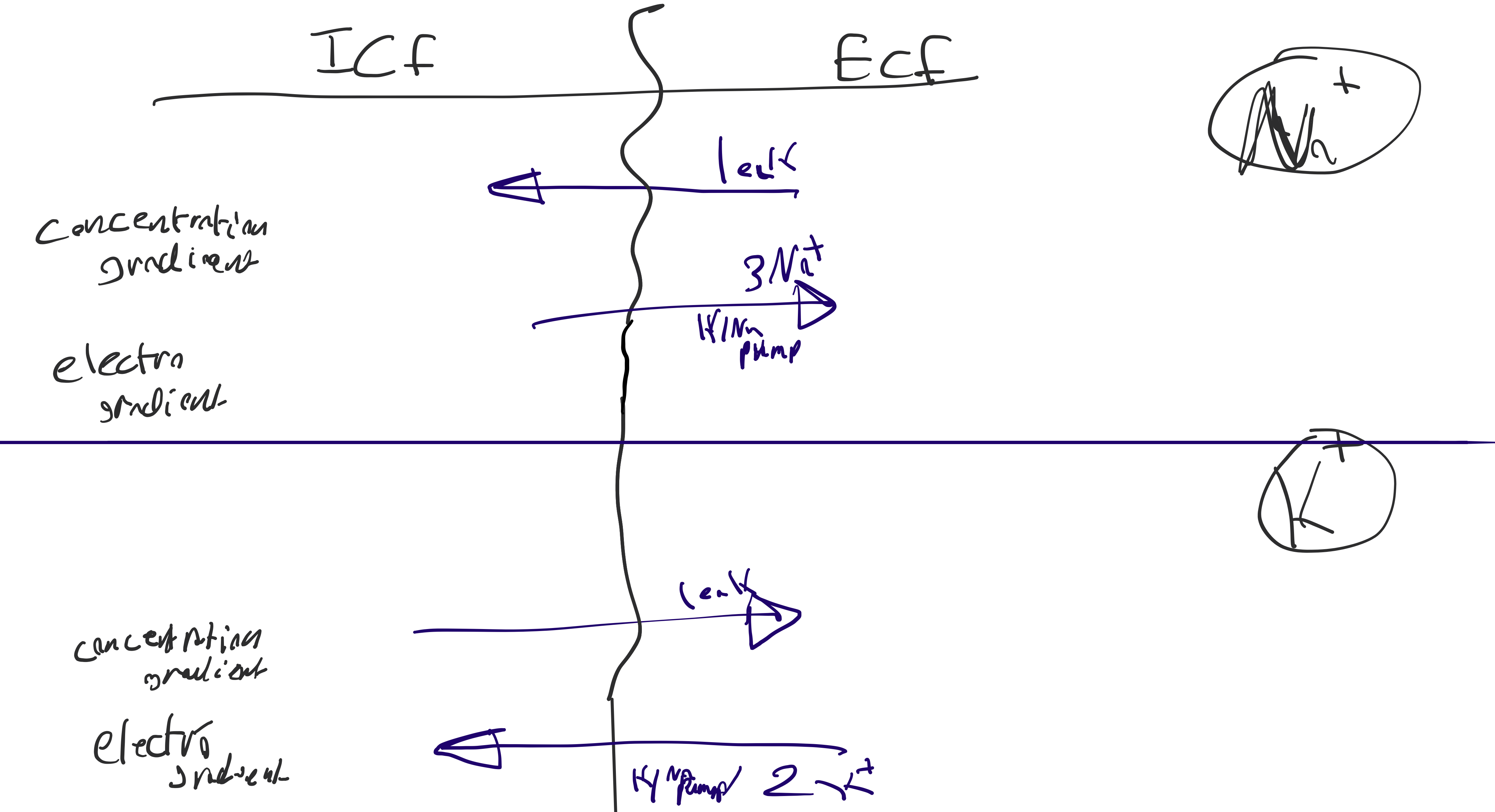
1. The concentration gradient for K^+ tends to push this ion out of the cell.
2. The outside of the cell becomes more + as the positively charged K^+ ions move to the outside down their concentration gradient.
3. The membrane is impermeable to the large intracellular protein anion (A^-). The inside of the cell becomes more – as the positively charged K^+ ions move out, leaving behind the negatively charged A^-.
4. The resulting electrical gradient tends to move K^+ into the cell.
5. No further net movement of K^+ occurs when the inward electrical gradient exactly counterbalances the outward concentration gradient. The membrane potential at this equilibrium point is the equilibrium potential for K^+ (E_{K^+}) at –90mV.

Diffusion potential and equilibrium potential for Na ions



because it's into the cell

1. The concentration gradient for Na^+ tends to push this ion into the cell.
2. The inside of the cell becomes more + as the positively charged Na^+ ions move to the inside down their concentration gradient.
3. The outside becomes more – as the positively charged Na^+ ions move in, leaving behind in the ECF unbalanced negatively charged ions, mostly Cl^-.
4. The resulting electrical gradient tends to move Na^+ out of the cell.
5. No further net movement of Na^+ occurs when the outward electrical gradient exactly counterbalances the inward concentration gradient. The membrane potential at this equilibrium point is the equilibrium potential for Na^+ (E_{Na^+}) at +60 mV.



ICF
ECF
Na+
leak
concentration gradient
3Na+
K/Na pump
electro gradient
K+
leak
concentration gradient
electro gradient
K/Na pump
2 K+

بعد ما عرفنا كيف ينتقل ال Na, K الآن بدنا نستكشف شو ممكن تكون العمليات يلي بتصير عليهم

like action potential in stimulated cell

Equilibrium potential (Nerst potential)

(It is the voltage required to maintain the concentration gradient

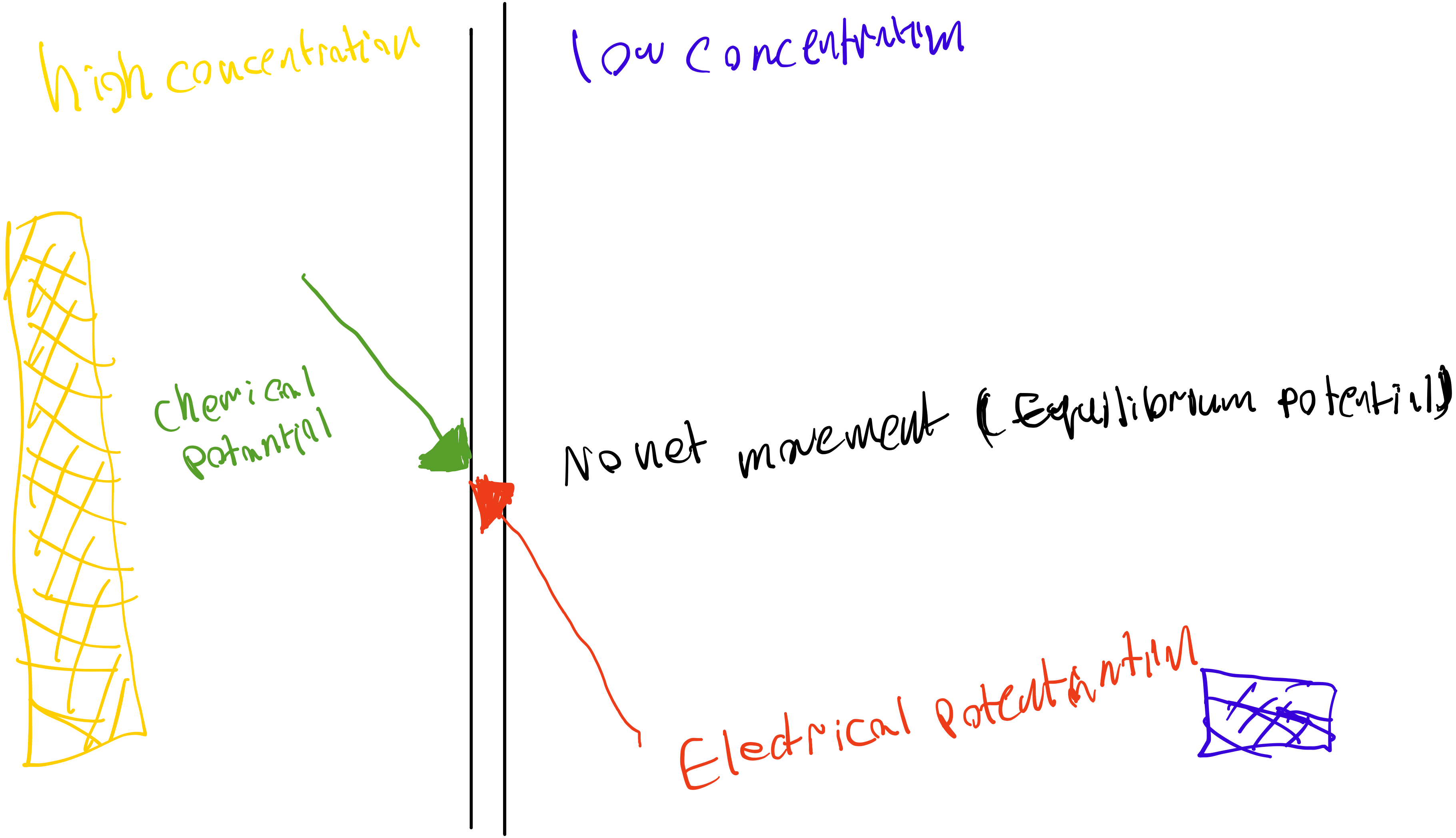
- The concept of is simply an extension of the concept of diffusion potential. If there is a concentration difference for an ion across a membrane and the membrane is permeable to that ion, a potential difference (the diffusion potential) is created. Eventually, net diffusion of the ion slows and then stops because of that potential difference
- **Equilibrium potential** is the diffusion potential that exactly balances (*opposes*) the tendency for diffusion caused by a concentration difference. At electrochemical equilibrium, the chemical and electrical driving forces that act on an ion are equal and opposite; therefore, no net diffusion of the ions occur.
- **Nerst Potential** The potential across the cell membrane that exactly opposes net diffusion of a particular ion through the membrane= the membrane potential at which there is no net (overall) flow of that particular ion from one side of the membrane to the other
- At electrochemical equilibrium (Equilibrium Potential) , the chemical and electrical driving forces acting on an ion are equal and opposite, and no further net diffusion occurs
- Nernst Equation is used to calculate the equilibrium potential for an ion at a given concentration difference across a membrane, assuming that the membrane is permeable to that ion

* لما يصير اختلاف بالتركيز ع جانبي الغشاء بصير انتقال للأيونات وبصير فيه فرق

بالجهد ثم يتباطأ الانتقال حتى يقف والجهد يلي وقفنا عليه هو ال

equilibrium potential (الجهد اللي يقف (أو التعادل بين الشحنة والتركيز ⟹ Electrochemical equilibrium

Nernst Equation → تستخدم لحساب equi potential لكل أيون ويكون التراكيز معطاة وطبعًا مع الافتراض أن الغشاء منفذ لهذا الأيون .


high concentration
low concentration
chemical potential
No net movement (Equilibrium potential)
Electrical potential

Nernst equation and calculations of the equilibrium potential (Nerst potential)

- Electromotive force (mv)

= (RT/ZF) log (C_i /C_o)

. EMF (mV) = ±61 x log $\frac{\text{Ion conc. Inside}}{\text{Ion conc. outside}}$

- C is concentration of the ion [X^+]
- ***C_o = [X+] outside cell***
- ***C_i = [X+] inside cell***

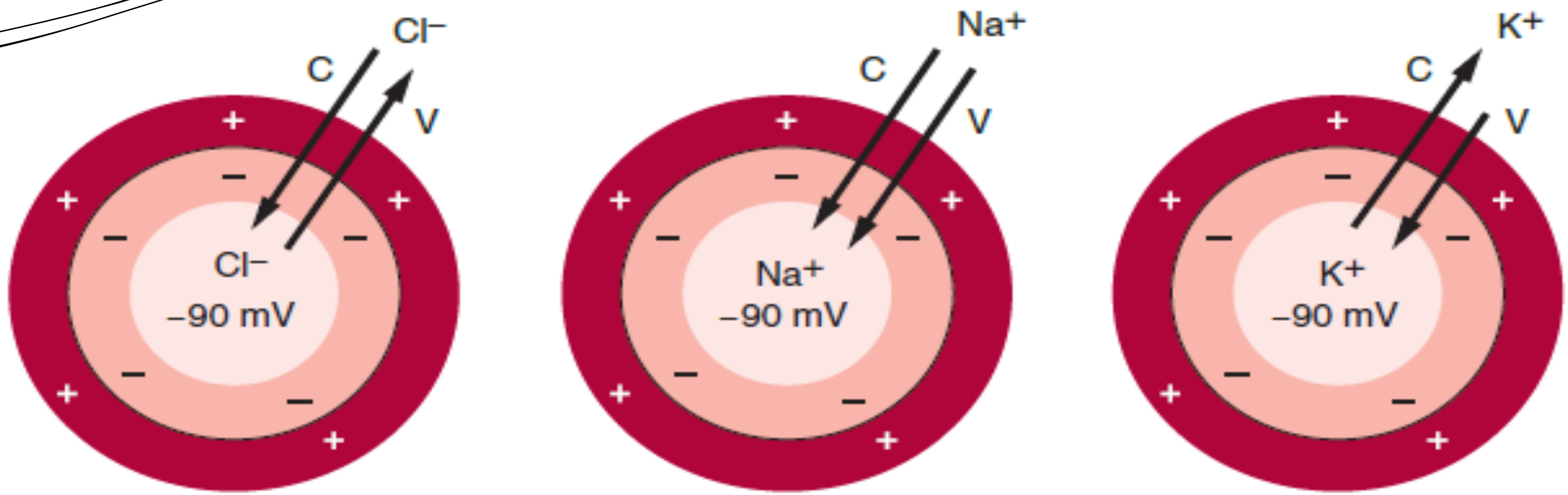
- R = gas constant 8.31 J/Kmol
- T = Temp. ° Kelvin 25C° / 298K
- Z = charge on ion
  - -1 for Cl^-, +2 for Ca^{2+}, K^+ Na^+ (+1)
- F = Faraday's number
  - charge per mol of ion
- ln means log to base e

$$E_x = \frac{R \cdot T}{Z \cdot F} \log \frac{X_{in}}{X_{out}}$$

= ±61 x log $\frac{X_{in}}{X_{out}}$

The driving force on ions crossing through the membrane, voltage gradients (V), and concentration gradients (C) for the three most common ions in the solutions in the intracellular and extracellular fluids

أمثلة واقعية



$$E_{Cl} = \frac{60\ mV}{-1} \log\frac{132}{4}$$

$$E_{Cl} = -90\ mV$$

$$E_{Na} = \frac{60\ mV}{+1} \log\frac{12}{145}$$

$$E_{Na} = +65\ mV$$

$$E_K = \frac{60\ mV}{+1} \log\frac{158}{4}$$

$$E_K = -95\ mV$$

The Potassium Nernst Potential

…also called the equilibrium potential

$$E_K = -61 \times \log \frac{K_i}{K_o}$$

Example: If K_o = 4 mM and K_i = 140 mM

E_K = -61 log(140/4)
E_K = -61 log(35)
E_K = -94 mV

So, if the membrane were permeable only to K+, the membrane potential (Vm) would be -94 mV

The Sodium Nernst Potential

$$E_{Na} = -61 \times \log \frac{Na_i}{Na_o}$$

Example: If Na_o = 142 mM and Na_i = 14 mM

E_{Na} = -61 log(14/142)

E_{Na} = -61 log(0.1)

E_{Na} = +61 mV

So, if the membrane were permeable only to Na^+, the membrane potential (Vm) would be +61 mV

The Goldman-Hodgkin-Katz Equation

(also called the Goldman Equation)

Calculates V_m when more than one ion is involved.

$$\text{EMF (millivolts)} = -61 \times \log \frac{C_{Na_i^+}P_{Na^+} + C_{K_i^+}P_{K^+} + C_{Cl_o^-}P_{Cl^-}}{C_{Na_o^+}P_{Na^+} + C_{K_o^+}P_{K^+} + C_{Cl_i^-}P_{Cl^-}}$$

Na, K & Cl are the most important ions involved in development of membrane potentials in nerve and muscle fibers & neuronal cells

the diffusion potential depends on:

(1) permeability of the membrane (P) to each ion

(2) concentrations (C) of the respective ions on the inside (i) and outside (o) of the membrane

The Goldman-Hodgkin-Katz Equation

(also called the Goldman Equation)

Calculates V_m when more than one ion is involved.

$$\text{EMF (millivolts)} = -61 \times \log \frac{C_{Na^+_i} P_{Na^+} + C_{K^+_i} P_{K^+} + C_{Cl^-_o} P_{Cl^-}}{C_{Na^+_o} P_{Na^+} + C_{K^+_o} P_{K^+} + C_{Cl^-_i} P_{Cl^-}}$$

the **quantitative importance** of each of the ions in determining the voltage is **proportional to the membrane permeability for that particular ion**.

The Goldman-Hodgkin-Katz Equation

Take home message…

The resting membrane potential is closest to the equilibrium potential for the ion with the highest permeability!

Question

اسئلة حسابية على ذلك

[Nai]=15 mM [Ki]=150 mM [Cli]=10 mM
[Nao]=145 mM [Ko]=4 mM [Clo]=24 mM

determine the resting membrane potential in a typical neuron. Assume that pK = 1, pNa = 0.05, and pCl = 0.5.

$$\text{EMF (millivolts)} = -61 \times \log \frac{C_{Na_i^+} P_{Na^+} + C_{K_i^+} P_{K^+} + C_{Cl_o^-} P_{Cl^-}}{C_{Na_o^+} P_{Na^+} + C_{K_o^+} P_{K^+} + C_{Cl_i^-} P_{Cl^-}}$$

$$= -61 \text{ X } \log \frac{15\text{X}0.05 + 150\text{X}1 + 24\text{X}0.5}{145\text{X}0.05 + 4\text{X}1 + 10\text{X}0.5}$$

=-61 X log 10
=-61 mV

Question

[Nai]=15 mM [Ki]=150 mM [Cli]=10 mM
[Nao]=145 mM [Ko]=4 mM [Clo]=24 mM

Assume that in a neuron, the plasma membrane permeability values for potassium (K^+), sodium (Na^+), and Cl^- are the following: $p_K = 1$, $p_{Na} = 12$, and $p_{Cl} = 0.5$.
determine the membrane potential in this neuron.

$$\text{EMF (millivolts)} = -61 \times \log \frac{C_{Na^+_i} P_{Na^+} + C_{K^+_i} P_{K^+} + C_{Cl^-_o} P_{Cl^-}}{C_{Na^+_o} P_{Na^+} + C_{K^+_o} P_{K^+} + C_{Cl^-_i} P_{Cl^-}}$$

$$= -61 \text{ X } \log \frac{15\text{X}12 + 150\text{X}1 + 24\text{X}0.5}{145\text{X}12 + 4\text{X}1 + 10\text{X}0.5}$$

$= -61 \text{ X } \log 0.195$

$= -61 \text{ X } -0.71$
$= + 43$ mV