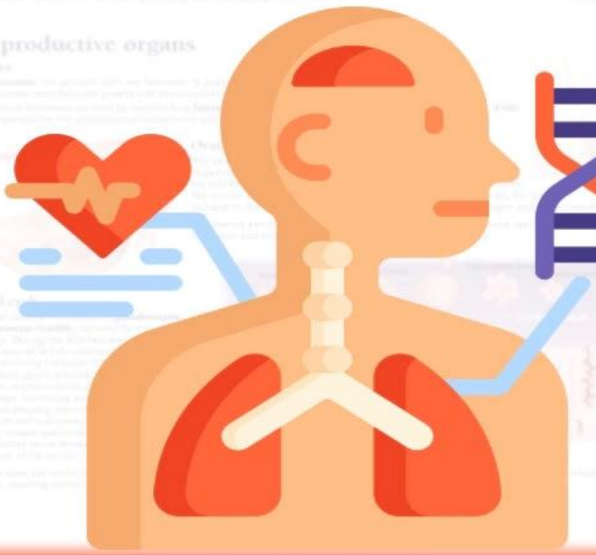
Doctor 022

Physiology

Sheet no.



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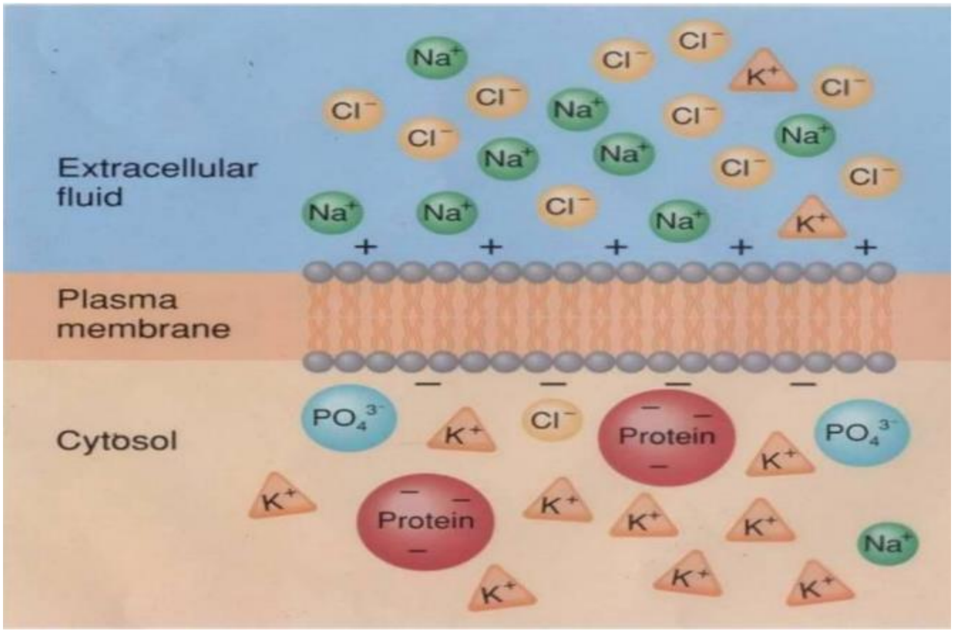
-Introduction

-In previous lectures, we have talked about transporting particles generally. In this lecture, we will talk about transporting again, specifically about what happens when charged particles such as K^+, Na^+, Cl^-, Ca^{+2} and so on , are transported across the plasma membrane.

-We know that the plasma membrane separates two compartments:

1-The Extracellular Matrix (ECM) outside the cells. (High concentration of Na^+)

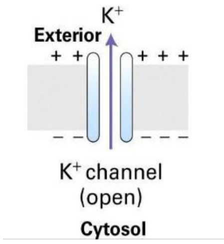
2- The Cytoplasm inside the cells. (High concentration of K^+)



-Based on the concentration gradient, the Na^+ ions have a high tendency to move from the outside to the inside, while K^+ ions have a high tendency to move from the inside to the outside.

-Assuming a membrane that is permeable only for K^+ ions and nothing else, the K^+ ions will move from the inside to the outside of the cell, creating an electrical potential across the membrane (negative inside, positive outside) and will reach *equilibrium*.

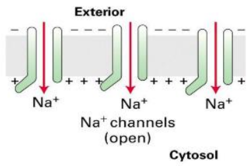
-What type of equilibrium?



Is it chemical equilibrium (concentration gradient)? The answer is no. The equilibrium that we are talking about is the **electrochemical equilibrium**. (Electro: from the potential, Chemical: from the concentration gradient)

-The electrical potential that is created by the movement of the ions will oppose the chemical potential (the positive outside will prevent more K^+ from moving to the ECF), and all of this will create large negative charge inside.

-Another Assumption: what will happen if the membrane is only permeable for Na^+?



The Na^+ ions will move from the outside to the inside of the cell, creating a potential across the membrane (positive inside, negative outside), also reaching equilibrium.

-For Cl^- ions: movement will be from outside to inside

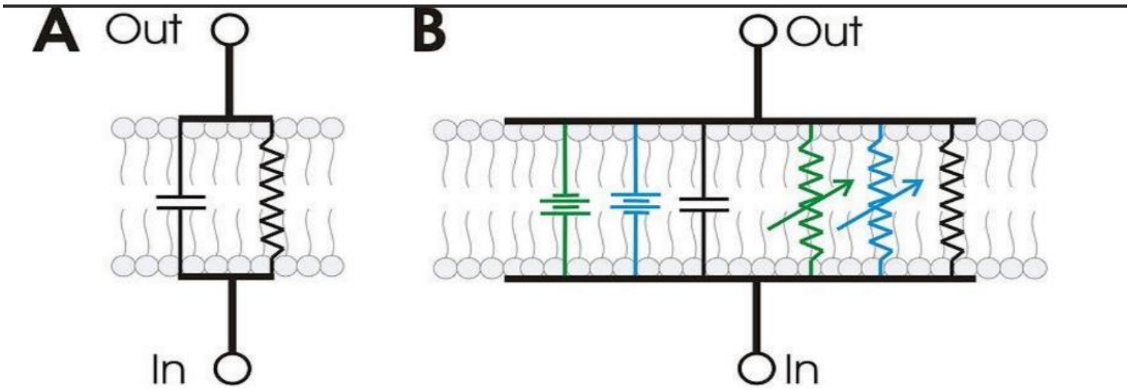
potential (negative inside, positive outside)

-For Ca^{+2} ions: movement will be from outside to inside

potential (positive inside, negative outside)

-As we are talking about charges, and a lipid bilayer (membrane separating them), we can think about this membrane as an electrical circuit, how is that?

-**Note:** the doctor did not talk about this point in detail, but it is in the slides



- **Part A:** A basic en:RC circuit, superimposed on an image of a membrane bilayer to show the relationship between the two. **Part B:** A more elaborate en:RC circuit, superimposed on an image of a membrane bilayer. This RC circuit represents the electrical characteristics of a minimal patch of membrane containing at least one Na and two K channels. Elements shown are the transmembrane voltages produced by concentration gradients in potassium (green) and sodium (blue), The voltage-dependent ion channels that cross the membrane (variable resistors;K=green, Na=blue), the non-voltage-dependent K channel (black), and the membrane capacitance.

Nernest Equation

-This is an equation that can be used to calculate the electrical potential across the membrane if the membrane is permeable for only one ion.

Nernest equation

$$E = \frac{RT}{ZF} \ln \frac{[C]out}{[C]in}$$

R (Gas Constant) = 8.314472 (J/K·mol)
T (Absolute Temperature) = t °C + 273.15 (°K)
Z (Valence)
F (Faraday's Constant) = 9.6485309×10^4 (C/mol)
[C]out (Outside Concentration, mM)
[C]in (Inside Concentration, mM)

Electrochemical Equilibrium

$\Delta G_{conc} + \Delta G_{volt} = 0$

ΔG_{conc}: The difference in energy generated by the concentration gradient.

ΔG_{volt}: The difference in energy generated by the voltage across the membrane.

Electro-chemical Equilibrium

$$\Delta G_{conc} + \Delta G_{volt} = 0$$

$$zFV - RT \ln \frac{C_o}{C_i} = 0$$

$$V = \frac{RT}{zF} \ln \frac{C_o}{C_i} = 2.3 \frac{RT}{zF} \log_{10} \frac{C_o}{C_i}$$

R, T and **F** are **constants**, replacing them with their values and when z=1 for K^+:

$$E_{K+} = 61.54 \log([K^+]_{out}/[K^+]_{in})$$

$$E_{K+} = 61.54 \log(4.5/160)$$

$$E_{K+} = -95 \text{ mV}$$

R, **T** and **F** are **constants**, replacing them with their values and when z=1 for Cl^-:

$$E_{Cl-} = 61.54 \log([Cl^-]in/[Cl-]out)$$

$$E_{Cl-} = 61.54 \log(5/100)$$

$$E_{Cl-} = -80 \text{ mV}$$

R, **T** and **F** are **constants**, replacing them with their values and when z=1 for Na^{+}:

$$E_{Na+}=61.54\log([Na^{+}]out/Na^{+}]in)$$

$$E_{Na+}=61.54\log(145/15)$$

$$E_{Na+}= 60\ mV$$

R, **T** and **F** are **constants**, replacing them with their values and when z=2 for Ca^{+2}:

$$E_{Ca+2}=(61.54/2)\log([Ca^{+2}]out/[Ca^{+2}]in)$$

$$E_{Ca+2}=(61.54/2)\log(1.8/10^{-4})$$

$$E_{Ca+2}=130\ mV$$

Concentration of Ions

Ion	Extracellular (mM)	Intracellular (mM)	Nernst Potential (mV)
Na^{+}	145	15	60
Cl^{-}	100	5	−80
K^{+}	4.5	160	−95
Ca^{2+}	1.8	10^{-4}	130

+ → positive inside in comparison to the outside.

- → negative inside in comparison to the outside.

-What if the membrane is permeable for many ions? (the normal state)

As we mentioned, **Nernest Equation** can calculate the potential for a membrane that is permeable for only one ion, but our cells' membranes are permeable for multiple ions, so we need another equation.

Goldman Hodgkin Katz equation

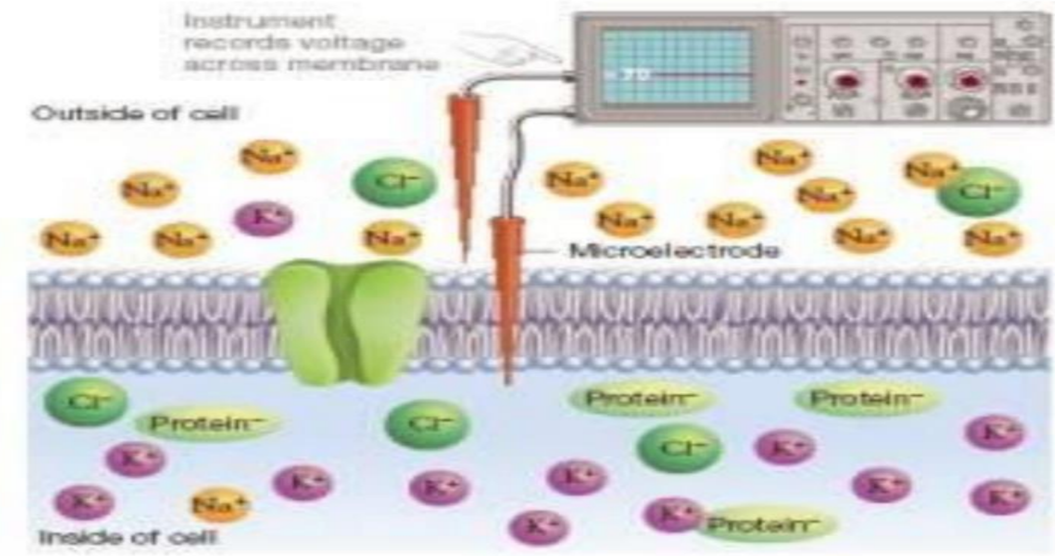
$$E_m = \frac{RT}{F} \ln \left(\frac{P_{Na^+}[Na^+]_o + P_{K^+}[K^+]_o + P_{Cl^-}[Cl^-]_i}{P_{Na^+}[Na^+]_i + P_{K^+}[K^+]_i + P_{Cl^-}[Cl^-]_o} \right)$$

i = Conc. inside
O = Conc. outside
P = permeability of the membrane to that ion.

-The movement of the chloride ion from outside to inside effect is a reversal of the movement of sodium ion from outside to inside effect, it also has the same effect of potassium ion that is moving from inside to outside.

-You should know that, if a membrane is pearmeable for only one ion, you will get back to Nernest Equation.

-We can measure the potential across the membrane using the voltmeter as shown in the picture in the next page, we must place the electrodes just at the inside (not deep) and just at the outside (not far) of the membrane.



-Our excitable cells have a very high permeability for K^+ ions and very low permeability for Na^+ ions, which results in creating potential, which is negative inside and positive outside, closer to the equilibrium potential for K+ ions(-86 mV for example), but it will never reach it, because we have some permeability for Na+ ions.

-The Na^+/K^+ pump is also responsible for establishing **the resting membrane potential**. By activating the pump, the membrane potential will get more negative inside (-4 mV):

-86+-4=-90 mV and that is the resting membrane potential

-The 3 factors that determine the resting membrane potential are:

1. High permeability for K^+
2. Low permeability for Na^+
3. The Na^+/K^+ pump

-Note: The high concentration of proteins inside is not a reason for the resting membrane potential.