physiology

premed 2018 - JU

◉ Sheet ○ Slides

Number

6

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Dear colleges, plz have a look on the notes I wrote at the end of this sheet ^^

In the previous lectures we have concluded that there's a higher concentration of K^+ inside nerve fibers, and a higher concentration of Na^+ outside.

We also compared the membrane to an electrical circuit; it works like a capacitor by separating charges across the plasma membrane.

The movement of any ion down its own electrochemical gradient will tend to move the membrane potential towards the equilibrium potential of that ion.

eg: If a membrane is permeable to Cl^- , electrical potential will be negative inside

If it's permeable to Ca^{2+} , electrical potential will be positive inside

The equilibrium potential that we calculate for ions is an electrochemical equilibrium since we are dealing with concentration parameters as well as parameters relating to electrical charges.

At equilibrium, energy created by concentration gradient (ΔG_{conc}) is equal to the energy created by electrical charges (ΔG_{volt})

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

Sometimes we might find **the Nernst equation** in this form:

$$E_{ion} = -61.5 \log \frac{C_{in}}{C_{out}}$$

Note that we added a negative sign since we switched the logarithms.

Now, for Na+ you know that the concentration inside is around (14 meqv/l) and outside 140 (meqv/l) and using the equation above we will find that the equilibrium potential for Na+ equals = +60 mV, repeating the same with K+ you will get -94 mV

-?-What do we mean by equivalent concentration?

It's referring to molar concentration of the ion that can react with or replace or react a molar concentration of hydrogen. (we don't look at the charge or valence) so if you take it for sodium for example you will find that it equals the molar concentration, but in calcium its going to be double the molar concentration as one mole of Ca+ can replace two moles of hydrogen

But be carefull, *we are not taking in consideration valence electrons*, always go back to to the definition we mentioned above, take Cl- as an example→ you will find that it has 7 valence electrons while it moves one mole of hydrogen ^^.

And what do we mean by **equilibrium potential** for a specific ion?

It means that when we reach this potential, there is no **net** movement for this ion across the membrane(eg. When we reach +60 mV there is no net movement for Na+)

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

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*The membrane potential is a result of the movement of **Na^+, K^+ and Cl^-** mainly. Since more than one ion channel is present in the plasma membrane, the membrane potential moves towards the "average" of the equilibrium potentials for the specific ions that can cross the membrane. The "average" depends on relative permeabilities for the different ions - the more permeable the membrane is for an ion, the more the equilibrium potential of that ion will influence the membrane potential. The membrane potential can be calculated using the Goldman-Hodgkin-Katz equation.

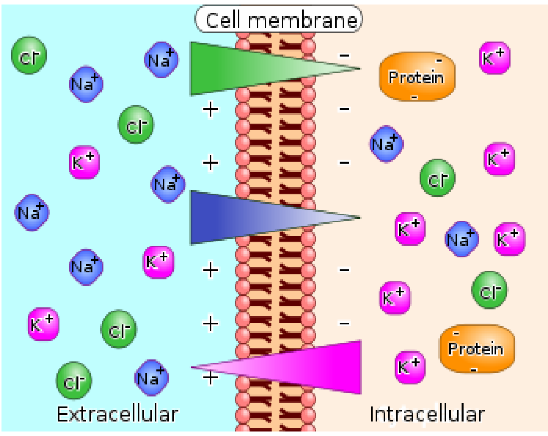
$$E_m = \frac{RT}{F} \ln \left(\frac{P_{Na^+}[Na^+]_o + P_{K^+}[K^+]_o + P_{Cl^-}[Cl^-]_i}{P_{Na^+}[Na^+]_i + P_{K^+}[K^+]_i + P_{Cl^-}[Cl^-]_o} \right)$$

Goldman-Hodgkin-Katz (GHK) equation:

where Em: membrane potential **R: gas constant (8.314)**
T: absolute temperature in Kelvin **F: Faraday's constant (96485)**

[ion]i: ion's concentration inside **[ion]o: ion's concentration outside Pion: permeability of membrane to ion**

* The effect of movement of Cl^- is **a reversal** of the movement of other positive ions like Na^+/K^+ since it has a valency of -1. This is why we reversed it in the equation (it becomes concentration inside ÷ concentration outside). This applies to all other negative ions.



Assume a membrane is highly permeable to K^+ and slightly permeable to Na^+ and is not permeable at all for Cl^-. In this case, the potential across it will be closer to the equilibrium potential for K^+ (E_{K+}) but not equal to it (around -80 mV) according to the GHK equation

* If the membrane has zero permeability for K^+ and Cl^- , its potential becomes equal to the equilibrium potential for Na^+ (E_{Na+}). If it had zero permeability for Na^+ and Cl^- , its potential equals the equilibrium potential for K^+ (E_{K+}) . Finally, if it had zero permeability for K^+ and Na^+, its potential equals the equilibrium potential for Cl^- (E_{Cl-}

.

In excitable cells the membrane potential isn't constant. When the cell is stimulated, the membrane potential changes. These changes in membrane potential are due to changes in permeability of plasma membrane to different ions. The permeability of one cell to a certain ion can vary at different positions across the plasma membrane of that same cell; this occurs due to the control of transport mechanism.

Resting Membrane Potential:

The resting membrane potential is the membrane potential for a cell under resting conditions; when no stimulus is introduced. **Also, it differs between different types of excitable cells.**

In **neurons**, resting membrane is equal to **-90 mV**. This represents the potential difference between the inside and outside when the neuron is not active. We usually ignore Cl^- . Resting membrane values are different in different cell types; for example in **cardiac muscle cells** it could be -60 mV, in smooth muscle cells -50, in **skeletal muscle cells** – 70(a little bit more permeability for sodium or less for potassium so we are moving the membrane to a less –ve potential), and in non-excitable cells it could be -10 or even +10 or +20mV

The question is why do we have different resting membranes? It is according to the permeability to Na^+, K^+ , and the presence of the Na^+ - K^+ pump.

**Factors affecting resting membrane potential:

1. Activity of K^+ channels

Using the Nernst equation, we calculate that it corresponds to an equilibrium potential of -94 mV.

2. Activity of Na^+ channels

The cell membrane of the nerve is slightly permeable to Na^+ resulting in an equilibrium potential of +61 mV.

***** Using the Goldman equation, we can calculate the potential inside the nerve cell as -86 mV. This potential is much closer to the equilibrium potential of K^+ (E_{K+}) since the membrane is much more permeable to K^+ than Na^+ (100 times more).

3. Na^+/K^+ pump (electrogenic pump)

If it is working alone it can establish a resting potential of -4 mV; means negative inside and positive outside. This is because for every 3 Na^+ pumped outside 2 K^+ are pumped inside, causing a continual loss of positive charges from inside the membrane, adding an extra 4 mV of negativity.

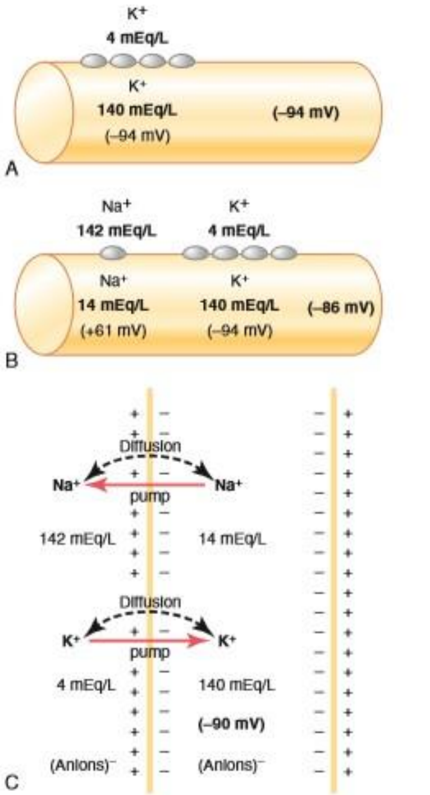


Figure 5-5. Establishment of resting membrane potentials in nerve fibers under three conditions: **A,** when the membrane potential is caused entirely by potassium diffusion alone; **B,** when the membrane potential is caused by diffusion of both sodium and potassium ions; and **C,** when the membrane potential is caused by diffusion of both sodium and potassium ions plus pumping of both these ions by the Na^+-K^+ pump.

***** Taking the effect of the Na^+/K^+ pump into account, the net membrane potential when all these factors are operative at the same time is about **-90 mV**

*** The establishment of the resting membrane potential:** is due to **high** permeability to K^+, some permeability (**low**) to Na^+ and the activity ofthe Na^+/K^+ pump

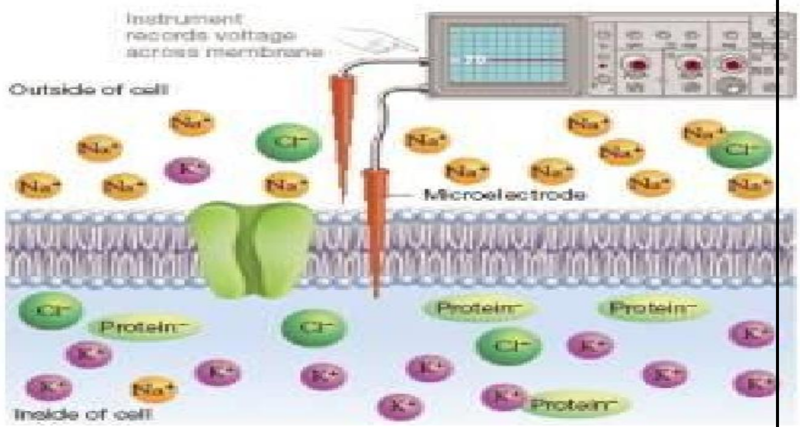
I.e. permeability for Na+ channels makes the potential LESS negative, while the permeability of K+ channel and sodium-potassuim pump makes the membrane potential MORE –ve.

→Do you remember what you take at school that amounts of proteins inside affect the membrane potential? Actually, it doesn't play a role here ☺

We measure the resting membrane potential just across the plasma membrane using a galvanometer i.e. we put an electrode just above the cell membrane and one just below the cell membrane- not far of the membrane or deep inside- to obtain the correct membrane potential. If we measure it far outside and far inside the cell, it would be electroneutral (no electrical difference). This is due to the **Donnan effect**; the negatively charged proteins in the cell are neutralized by cations (positive ions) so it's electroneutral both on the outside and the inside.

* Note*:The maximum resting membrane potential is -94 mV and occurs at maximum permeability to K^+. Even if the membrane has high permeability for Cl^-, we can't go below -94 mV.

As shown in the figure aside we can use a device to measure the membrane potential.



What does the negative sign implies?

this implies that inside the cell membrane is negative relative to outside of it

keep in mind that we have a driving force for sodium from outside to inside in which is the **electrochemical** gradient , but it cant move! Because there is limited number of active sodium channels (low permeability).

- ✓ Think about it that way, in each cell per surface area you have a certain concentration of channels, according to the activity of these channels, you will have high diffusion for specific ion and less diffusion for another.

Important: the question is if we have Cl- channels open over the resting membrane potential for Cl- , what is the effect on membrane potential?

When we reach the equilibrium potential for Cl- then channels open, and the net movement of Cl- is zero , so there is no affect. (it will affect in one case if we have change the membrane potential , the activity of Cl- channels will return it to the original .

Here are some notes:

-this sheet was written by doctors 2017 and edited according to our records 2018

- THE HANDOUT OF DR.KHATATBEH IS VERY VERY IMPORTANT AND YOU SHOULD STUDY IT WELL !

-many things are added here..notice them

Study well :P

(إنّ الضّرباتِ الّتي لا تقصِمُ ظهركَ، تُقوّيه)

-عُمر المختار.