Human Physiology

Lecture 6 – Monday 29/2/2016

“Resting Membrane Potential” with Dr. Esraa’ Kiwan

(Slides are on e-learning)

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PSU

Reminder: Similar charges repel each other, and opposite charges attract each other. Separation of opposite charges requires work or potential. (إبعاد الشحنات المتضادة عن بعضها البعض يحتاج للجهد أو الطاقة)

Membrane potential (الجهد الغشائي):

- Definition: separation of opposite charges across the plasma membrane.
- When the cell is in **resting state**, it has **resting membrane potential**.
- The unit for potential is volts, but since the magnitude of membrane potential is very small we use **millivolts (mV).**
- "Separation" means that there is a difference of cations and anions inside & and outside the cell.
- Note: If there is
  - Inside the cell: 50 cations & 50 anions
  - Outside the cell: 50 cations & 50 anions

    then there is <u>no</u> membrane potential as there is no difference in cation/anion number.
- Most of the ions inside and outside the cell are electrically neutral (كل شحنة موجبة تقابلها شجنة سالبة).
- The charges that are electrically NOT neutral are arranged in a thin layer along the inner/outer surface of the membrane.
- As the degree of separation increases, the membrane potential increases as membrane potential depends on separation of ions.
- All cells have resting membrane potential but the magnitude is different for some:
  - **Nerve cells: -70 mV**
  - **Skeletal & Cardiac muscles: -80 to -90 mV**
  - **Smooth muscle: -60 mV**
- Notice how the resting membrane potential is negative. The reason for the negative sign is to represent the polarity (تقاطب) inside the cell. A negative charge means that

the inside of the cell membrane is more negative than the outside.

Note: So if we get a question in the exam with "+30 mV", it means the inside of the cell is more positive than the outside.

- All cells in our body have resting membrane potential, but only the nerve & muscle (or the "excitable cells") are able to change the potential.

Ions responsible for membrane potential:

- The main 3 ions that are responsible for membrane potential are
    - Na^+
    - K^+
    - A^- (negatively charged intracellular proteins)
- Reminder: The main cation of ECF (extracellular fluid) is Na^+, and the main cation of ICF (intracellular fluid) is K^+.
- A^- represents the proteins inside the cell, and these proteins cannot penetrate the cell membrane so they will always remain inside. (البروتينات لا تستطيع إختراق غشاء الخلية، لذلك الشحنة السالبة الناتجة منهم ثابتة)

TABLE 3-3

Concentration and Permeability of Ions Responsible for Membrane Potential in a Resting Nerve Cell

ION	CONCENTRATION (millimoles/liter) Extracellular	Intracellular	RELATIVE PERMEABILITY
Na^+	150	15	1
K^+	5	150	50–75
A^-	0	65	0

- As we can see, K^+ is 50-75 times more permeable than Na^+. (نفاذية البوتاسيوم أعلى)
- It is also notable that the permeability of A^- is 0 -> meaning that these proteins cannot leave the cell at all.

- Concentration gradient: when the ions move down their concentration; from an area of high concentration to area of low concentration.
    - According to concentration gradient, Na^+ should tend to move inside (Na^+ is higher outside) & K^+ should tend to move outside (K^+ is higher inside). However, at resting state, K^+ is 50-75 times more permeable than Na^+. This means that more K^+ moves.
- Since the permeability of K^+ is 50-75 times higher than that of Na^+, that means you will find more channel proteins that transport K^+.
- 80% of why the inside is more negative //OR// **80% of the resting membrane potential** is caused by **passive diffusion**: <u>(NOTE: Dr. Esraa said this is going to be a question in the first exam).</u>
    - Unequal distribution of K^+ ions.
    - K^+ is frequently leaving the cell (so the outside becomes more positive) as it is 50-75 times more permeable than Na^+. // A^- is negative and is always inside the cell.

If 80% of resting membrane potential is caused by passive diffusion, what about the remaining 20%?

- The remaining 20% is controlled by the **Na-K (Sodium-Potassium) pump.**
- Reminder: passive diffusion occurs when ions move down (higher to lower) the concentration gradient. It is called "passive" because it does not require energy.
- The Na-K pump however – moves Na^+ & K^+ from lower to higher concentration. Doing this requires energy, so it is called **active transport**.
- The Na-K pump moves **3 Na^+ out, and 2K^+ in**, and this maintains the concentration gradient of Na & K.
- Pumping 3 positive charges out & 2 positive charges in causes the outside to be more positive

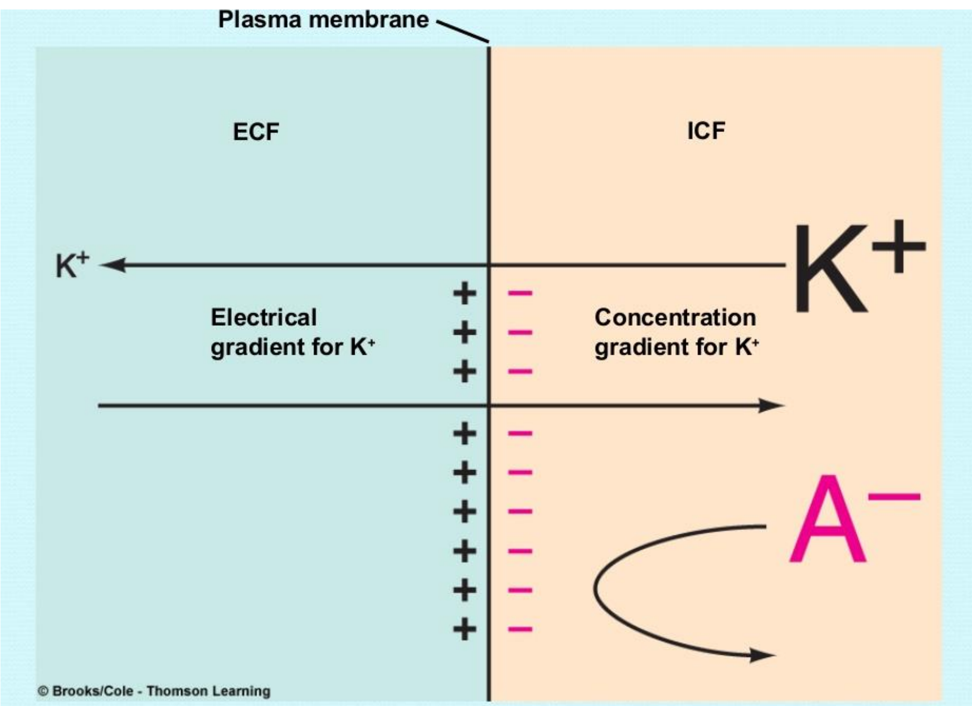
What happens as a result of concentration & electrical gradients?

- Concentration gradient: Ions move from higher to lower concentration. So Na^+ moves inside, and K^+ moves outside.
- **Electrical gradient**: at resting state the cell has a negative membrane potential. Na^+ is a positive ion, and since positive is attracted to negative charge Na^+ will move inside. K^+ is also a positive ion so it will also want to move inside. So electrical gradient is movement of a charged ion to an oppositely charged membrane.

	Concentration gradient	Electrical Gradient
K+	K+ moves outside	K+ moves inside
Na+	Na+ moves inside	Na+ moves inside

Let us imagine a hypothetical situation. (سندرس حالة إفتراضية، لا تحصل في الواقع)

Let us imagine a membrane with no Na^+, and K^+ & A^- inside the cell.

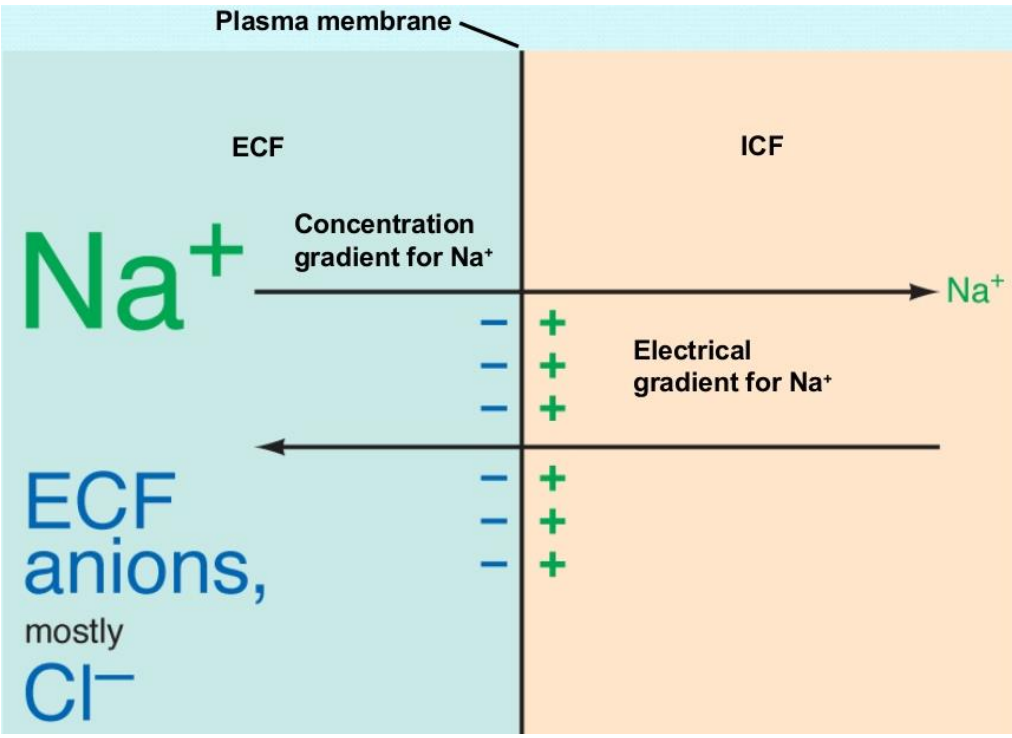


(1): There is a higher concentration of K^+ inside than outside. We know that A^- cannot move outside, and K^+ will tend to move down the concentration gradient -> K^+ tends to move outside

(2): This creates an electrical gradient (K^+ is positive and wants to move towards the negative ICF)

(3): The process of K^+ moving inside and outside is continuous, and will only stop when concentration gradient = electrical gradient. At this point, there is no net movement of K^+. This point is called K^+ equilibrium potential.
Research found the equilibrium of K^+ to be at -90mV. (Reminder: -90mV means the inside is more negative).

Let's try the same thing but with Na^+:



We have Na^+ outside the cell, and we also included ECF & its anions (mostly Cl-).

(1): Since Na^+ is higher outside, it will move down its concentration gradient into the cell.

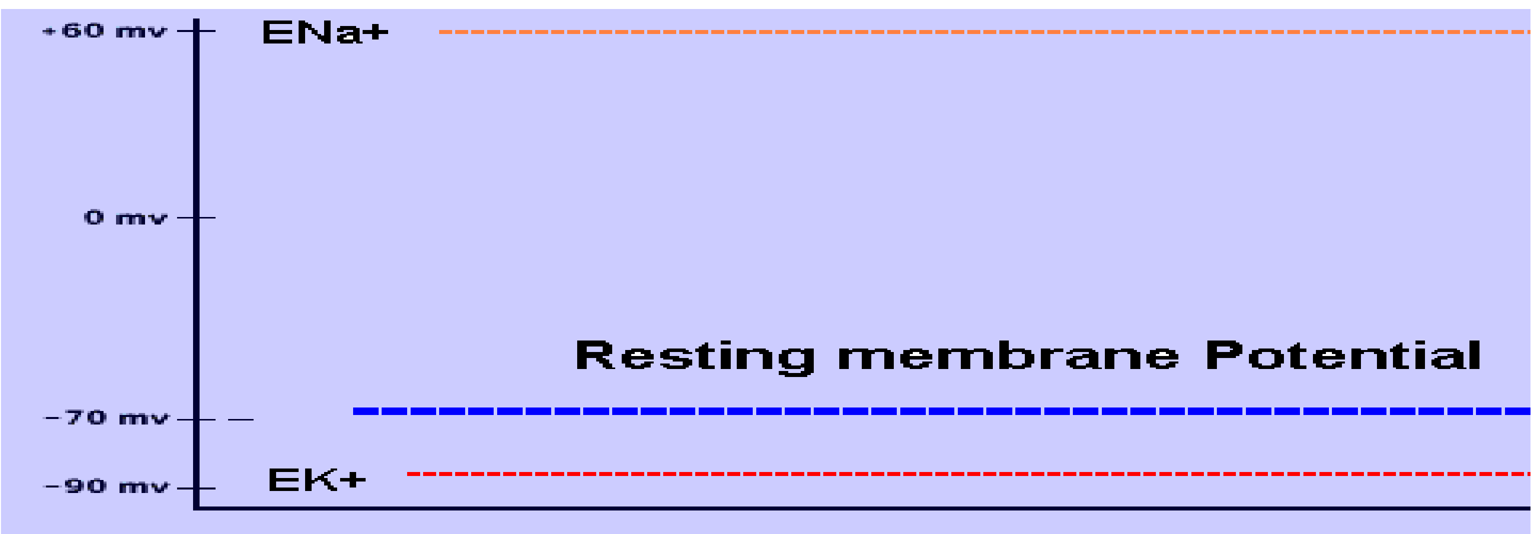
(2): This makes the inside more positive, and makes the outside more negative. However, since there are anions like Cl^- outside, this creates an electrical gradient that will cause Na^+ to move outside.
(3): Just like K^+; This process of Na^+ moving inside and outside is continuous up until the concentration gradient = electrical gradient. This point is called Na^+ equilibrium potential, and researchers found it to be +60mV (+60 as the inside is more positive).

Summary:

a) K+ equilibrium:
   1) K+ moves outside by concentration gradient
   2) K+ moving outside creates negative charge inside
   3) K+ starts to move inside by electrical gradient
   4) At -90mV, concentration gradient = electrical gradient
b) Na+ equilibrium:
   1) Na+ moves inside by concentration gradient
   2) Na+ moving inside creates negative charge outside
   3) Na+ starts to move outside by electrical gradient
   4) At +60mV, concentration gradient = electrical gradient.

Which ion has a greater effect on resting membrane potential?

- **E_{K+} = -90mV & E_{Na+} = +60mV.**



- Resting membrane potential is close to E_{K+} & away from E_{Na+} as K^+ is 50-75 more permeable.
- This means that K^+ has the more dominant effect on membrane potential.