Physiology
Sheet No.
4

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Review

We can control the activity of ion channels; we have certain receptors which are linked to these channels and can change the permeability of the membrane.

Excitable cells can develop a potential across their membranes for example: (negative inside & positive outside).

Plasma membrane of excitable cells are analog with an electrical circuit, actually, they are analog to the capacitance (separators of charges) across that membrane (negative inside & positive outside).

We can generate a potential if we have that membrane permeable only for potassium (the rest membrane potential is so close to the potassium equilibrium potential), but if we have that membrane permeable only for sodium we have seen that the potential which could be created will be positive inside with regard to outside.

If we assume that a cellular membrane is permeable only to K+, which is found in a very high concentration inside the cell. K+ will diffuse to the extracellular fluid because of the concentration gradient. The diffusion of K+ will result in a movement of positive charges outside the cell and leaving behind negative charges inside the cell. This will create an electrical potential difference across membrane (positive outside and negative inside). Creation of this potential difference will oppose diffusion of K+ to the outside at a certain concentration difference. When you reach a point at which diffusion of K+ is completely opposed by the potential difference created across membrane and the net diffusion for K+ is zero even though you still have a concentration gradient, you have reached the equilibrium potential for K+ (EK). The equilibrium potential for any univalent ion at normal temperature can be calculated by Nernest equation:

$$E\ (mV) = -\ 61.\log\ (Ci/Co)$$

E = equilibrium potential for a univalent ion

Ci = concentration inside the cell.

Co = concentration outside the cell.

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

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)

You should know that only a small amount of ions is moving, once it is moving, it is creating a potential, once you have that potential, it is opposing more movement of that ion. We have reach the electrochemical equilibrium for that ion and that is calculated finally as equilibrium potential (in millivolts).

Electro-chemical Equilibrium

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

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

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

log = log base ten.

ln = the natural logarithm.

By multiplying all constants and replacing the natural logarithm by the log base ten, we get the equation of the final form: **E (mV) = - 61.log (Ci/Co)**

E_{k+}

$$E_{eq,K^+} = 61.54mV \log \frac{[K^+]_o}{[K^+]_i},$$

E (mV) = - 61.log (Ci/Co)

E = Equilibrium potential for a univalent ion

Ci = conc. inside the cell.

Co = conc. outside the cell.

Concentration of Ions

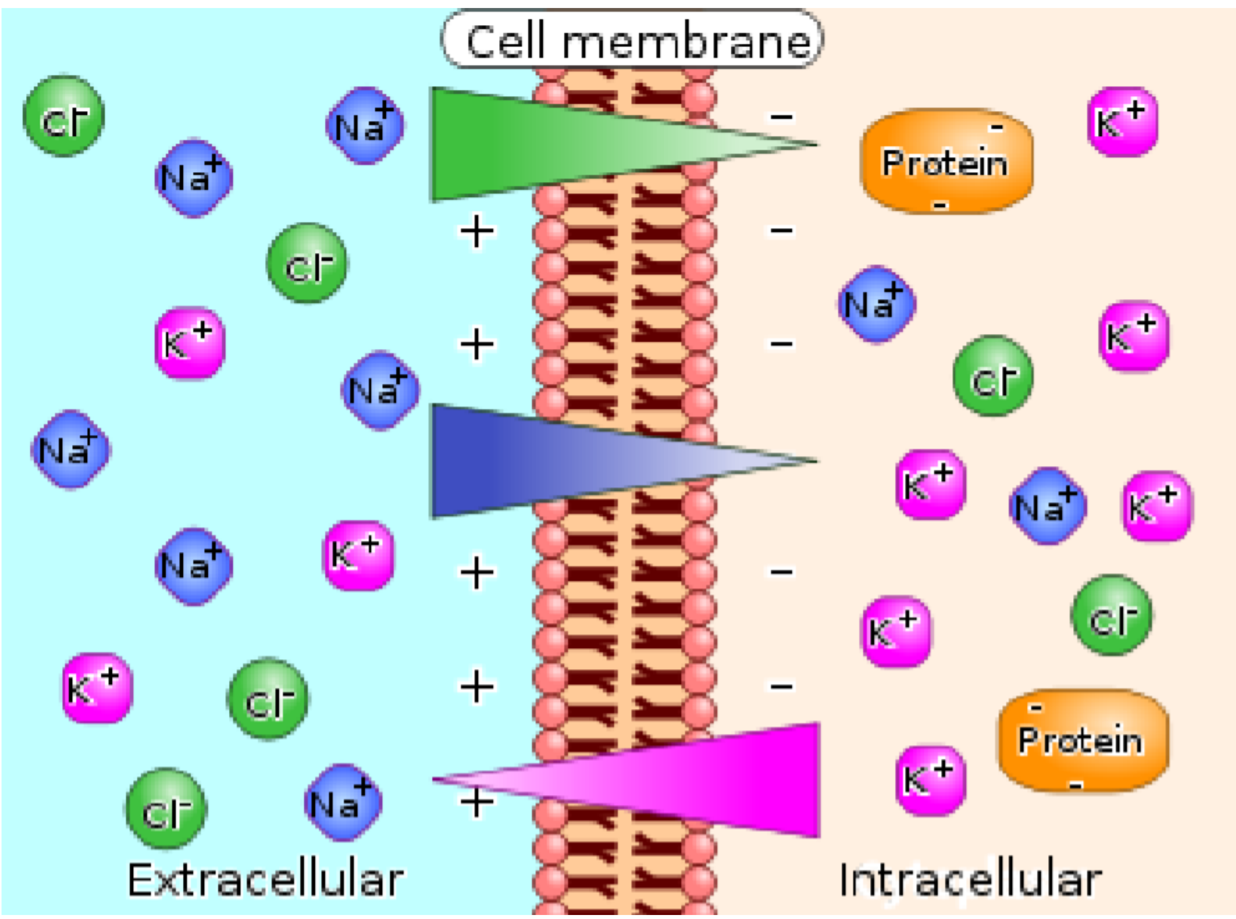
Ion	Extracellular (mM)	Intracellular (mM)	Nernst Potential (mV)
Na^+	145	15	60
Cl^-	100	5	-80
K^+	4.5	160	-95
Ca^{2+}	1.8	10^{-4}	130

Let's start our new lecture

Do we have a membrane permeable for only one ion? No

Do we have a membrane which has the same permeability for all ions? No

If we have a membrane with a high permeability for potassium and very low permeability of chloride and sodium, we are creating a potential which will be very close to the equilibrium potential for potassium.



When more ions are involved in creating the potential, we can calculate the potential according to **Goldman-Hodgkin-Katz 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.

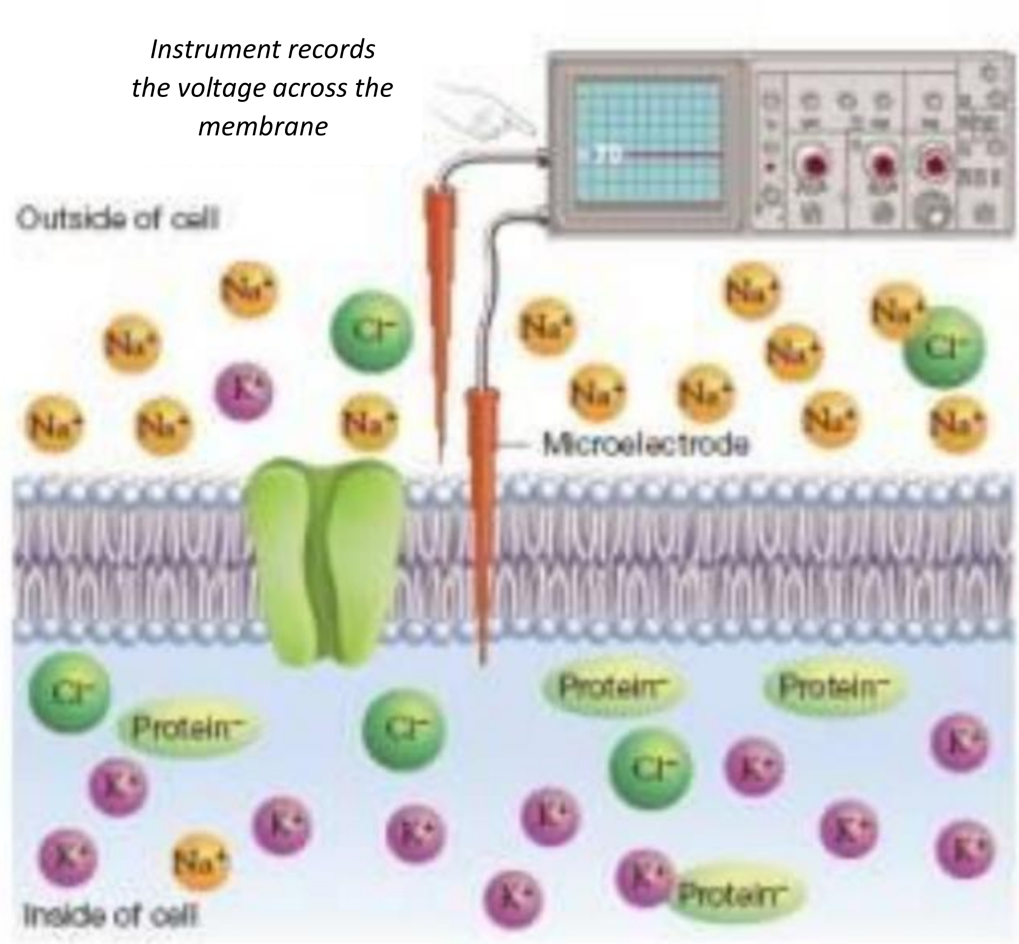
In this equation, Goldman and his colleagues considered that these ions are mostly involved in the development of membrane potential. According to this equation the permeability of the membrane to an ion is very important in determining the membrane potential. If the membrane is permeable only to K+ and not permeable to Cl- and Na+, the membrane potential will be equal to EK+.

Why we have the concentration of chloride ion inside the cell above the one outside? Because the valance of chloride = -1

We can place the concentration of chloride outside above the inside but we should multiply the equation by -1 BUT in this case we must place the concentration of Na+ and the concentration of K+ inside above the outside

If you have zero permeability of all ions except one, you will get Nernest equation.

We can easily measure the membrane potential by placing one electrode just inside the cell closely to the surface and not deeply in the cell and placing another electrode just out the cell and not far away from the surface.



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If we have a membrane which is permeable for more than one ion but it is more permeable for a certain ion, the membrane potential will be closer to the equilibrium potential for that ion.

DO ALL MEMBRANES HAVE THE SAME RESTING POTENTIAL? NO, SOME HAVE -90, -80, +10, 0 AND MAYBE -10.

The excitable cells have more negative resting membrane potential.

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What is determining the rest potential?

Generally, is the permeability.

The main factors which determine the rest potential are:

1. Activity of the k^+ channels

(Most influential) the k^+ ions move from the inside to the outside and cause a negative potential for the membrane.

Contribution of K+ diffusion:

As mentioned earlier, if the membrane is permeable only for K+

the calculated EK+ is about (-94mV).

$C_{o\,K}{}^+ = 4meq/l$ $C_{i\,K}{}^+ = 140meq/l$

$E_K{}^+ = -61. \log 140/4 =$ **-94mV**

Which is not far from the recorded membrane potential but not exactly.

2. Activity of the Na^+ channels

The membrane has less permeability for Na^+, so the rest potential will be closer to the equilibrium potential of k^+, but it will not equal it.

The contribution of Na+ diffusion:

Membrane is also permeable to Na+. The permeability of the plasma membrane for Na+ is much less than that of K+. If the membrane is permeable only to Na+, the calculated ENa+ = + 61mV.

($C_{o\,Na}{}^{+}$ = 142meq/l $C_{i\,Na}{}^{+}$ = 14meq/l)

These two kinds of channels produce both -86 mV

Because of the permeability of the membrane for the two ions, the E would be between (-94mV and +61mV). The calculated E for the two ions is –86 mV, which is not far from the EK+ because of the higher permeability of membrane for K+ than for Na^+ (100 times more).

So the Na+ contribution in resting potential is by bringing the membrane potential to a lower value than the calculated $E_K{}^+$.

3. Activity of Na^+/K^+ pump

(Electrogenic pump) $3Na^+$ outside $2K^+$ for inside, it can alone create a membrane potential.

Contribution of Na+ - K+ pump:

As mentioned earlier, this pump is electrogenic. It moves more positive charges outside the cell (3 for 2). This will induce loss of positive charges from the cell and bring the membrane potential to a higher negativity (about –4mV additional negativity).

It produces -4 mV

Therefore, all these factors, during rest, will give a net membrane potential of -90mV (called Resting Membrane Potential).

Some cells have lower permeability of K^+, so they have less negative potential.

Higher permeability for Na^+ means less negative (because the Na^+ moving reduces the negative potential).

Lower pump activity means less negative.

Lower Na^+ means more negative.

It is not the proteins content which affects the permeability.

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Resting membrane potential:

In excitable cells the membrane potential is not 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. For example, when neuron is stimulated, this will result in increased permeability to Na+. This will bring the membrane potential closely to E_{Na}. The recorded membrane potential for a cell under resting conditions when no stimulus is involved is known as resting membrane potential. For neurons the recorded resting membrane potential is about (– 90 mV). This represents a potential difference between the inside to the outside when neuron is not active.

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If you have -95 resting membrane potential (the activation of more K^+ channels will not affect the potential because this potential is equal to the equilibrium potential of k^+.

If you have a membrane with -80, the activation (the increasing of permeability) of Cl^- channels will not affect the membrane potential because it has the same value of the equilibrium potential of Cl^- ions even if you unlimited number of these channels.

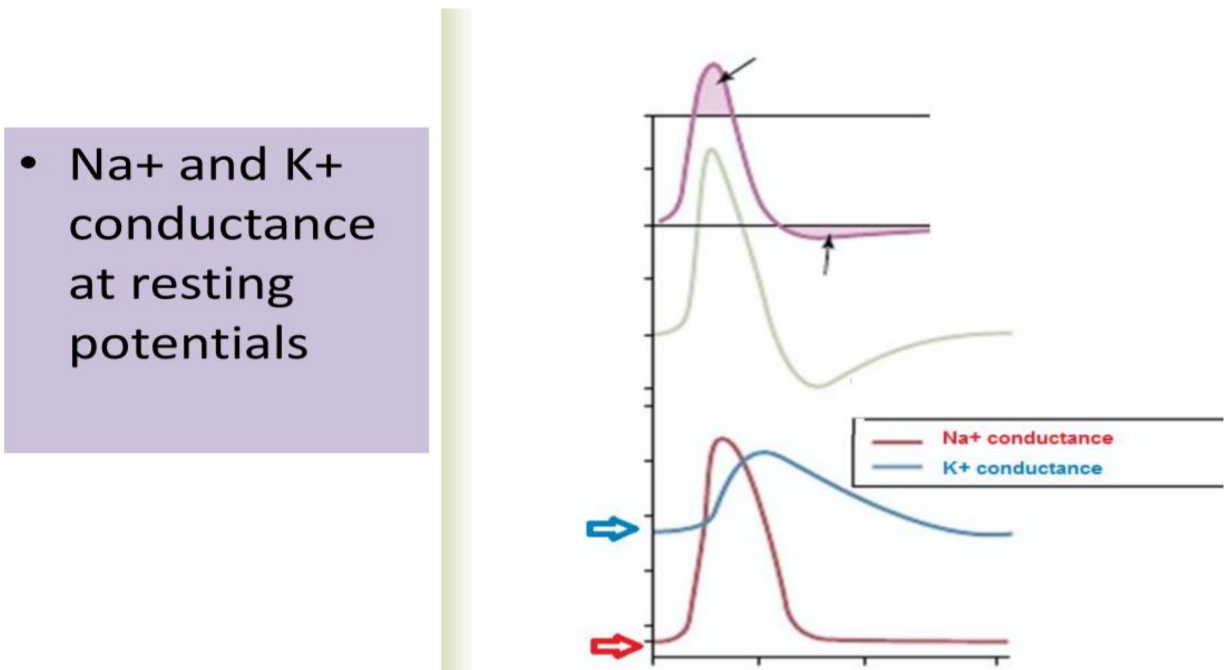
<u>The permeability of K^+ is about 100 times more than that in sodium.</u>

Conductance: the degree to which an object conducts electricity, calculated as the ratio of the current which flows to the potential difference present. This is the reciprocal of the resistance and is measured in siemens or mhos.

Conductance: how easy or how fast that ion is moving across the membrane which depends on the permeability (inversal with the resistance).

Rate of diffusion is the number of particles which are passing per time unite.

Low resistance means that more channels are opened (more current is produced)



The movement of ions (charges) produces a current.

We can calculate the current by Ohm's Law

Conductance of plasma membrane (Ohm's Law)

- $I = \Delta V/R$
- G (conductance)= $1/R$
- $I = G.\ \Delta V$

we can measure the potential of membrane by using the conductance.

Vm: Voltage of the membrane (potential)

The cord Conductance equation describes the contributions of permeant ions to the resting membrane potential

$$V_m = \frac{g_K}{g_{tot}} E_K + \frac{g_{Na}}{g_{tot}} E_{Na} + \frac{g_{Cl}}{g_{tot}} E_{Cl}$$

The membrane has a very low permeability for other ions like Ca^{+2}, so it can be neglected.

The major contribution is caused by potassium and sodium channels (especially from potassium).

Calculations

The single ion potential

Nernest Equation

The membrane potential caused by all ions

Goldman Hodgkin Katz equation

Current I = ΔV/R

G (conductance) = 1/R

I = G. ΔV

(Ohm's Law)

contributions of permeant ions to the resting membrane potential

The cord Conductance equation