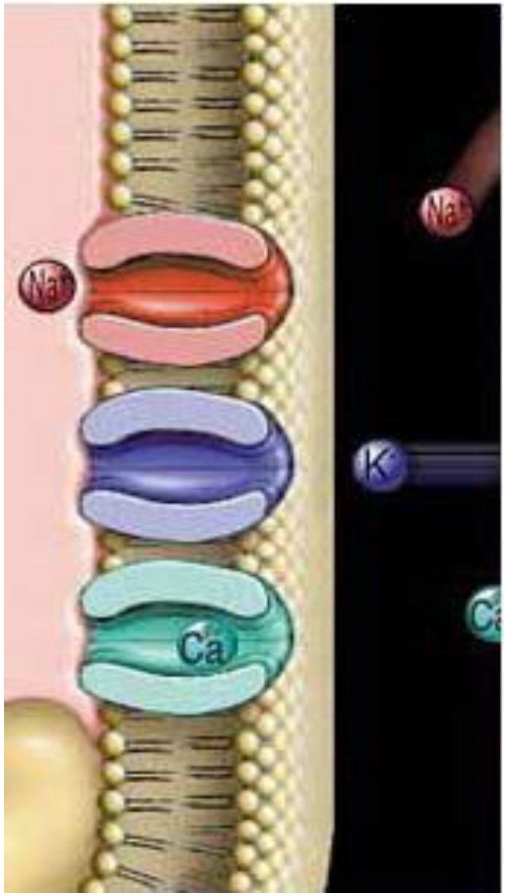
Resting Membrane Potential (Voltage)

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 11TH EDITION

UNIT II CHAPTER 5



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RESTING MEMBRANE POTENTIAL OBJECTIVES

By the end of this lecture, the student should be able to:

- Identify and describe different potentials & types of membrane ionic channels & equal or unequal distribution of ions across the membrane
- Identify cell membrane creating concentration and electrical gradients.
- Identify and describe diffusion and equilibrium potential
- Apply Nernst equation to calculate equilibrium potential.
- Identify resting membrane potential (RMP)
- describe genesis of resting membrane potential (RMP) and appreciate the effect of changes in ionic composition and/or permeability on genesis of RMP and the role of ions channels, and Na+ - K+ pump
- Identify voltmeter to measure very small membrane potential difference between inside & outside as resting membrane potential.

Q **: What are Excitable tissues ? سريع الانفعال**

A: They are nerve and muscle

Q: What property do excitable tissues have that makes them different from other body tissues ?

A: Their membrane acts as an electric capacitor مكثف storing opposite charges on the opposite sides of the membrane. This will create:

- Resting membrane potential(**RMP) of high value (-70 to -90 mV) compared to other body cells (in RBC , for example MP= -5 mV) .**

This high RMP makes the nerve or muscle membrane function as a capacitor , that can “discharge” , يفرغ producing large voltage changes (action potentials).

Q : What is the membrane potential (MP) الجهد الغشائي ?

It is the difference in potential (voltage) between the inner side & outer side of the membrane (nerve or muscle membranes)

Q : What are the states of MP ?

(1) Resting Membrane Potential (RMP) : value of MP in a " resting " state (unstimulated excitable membrane). It ranges between -70 and -90 mV in different excitable tissue cells, in large myelinated nerves = -90 mV

(2) Graded Potential (Local Response) : MP in a stimulated cell that is producing a local , non-propagated potential غير منتشر (an electrical change which is measurable only in the immediate vicinity منطقة مجاوره of the cell but not far from it) .

(3) Action potential (AP) : MP in case of a nerve that is generating a propagated منتشر electrical potential after stimulation by effective stimulus (an electrical potential which can be measured even at long distances far from the cell-body of the nerve)

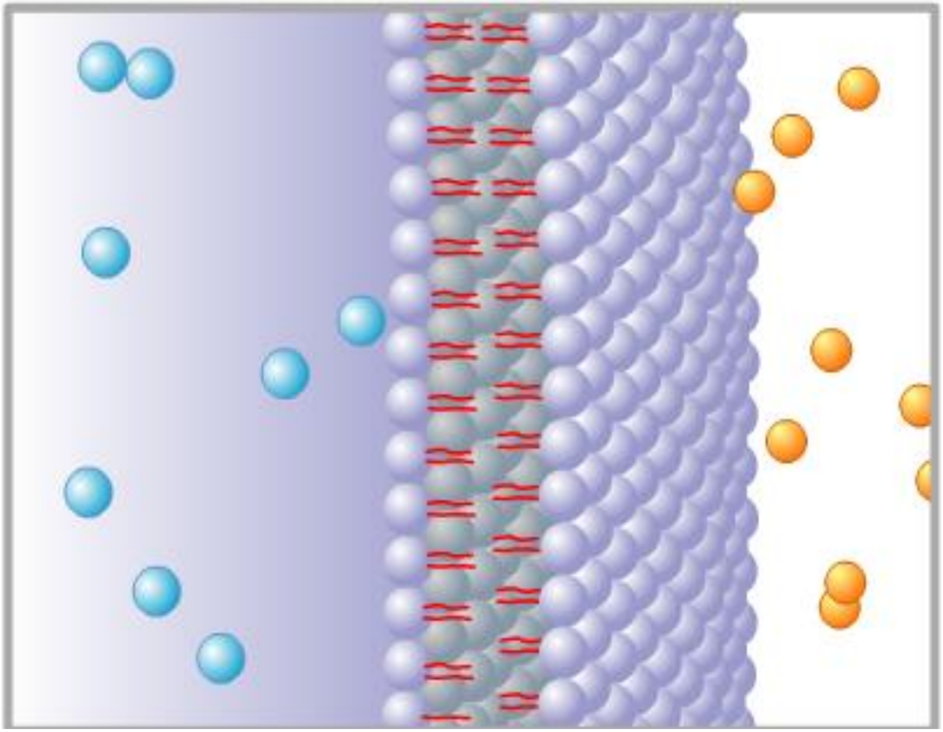
Q: What are the types of membrane ionic channels ?

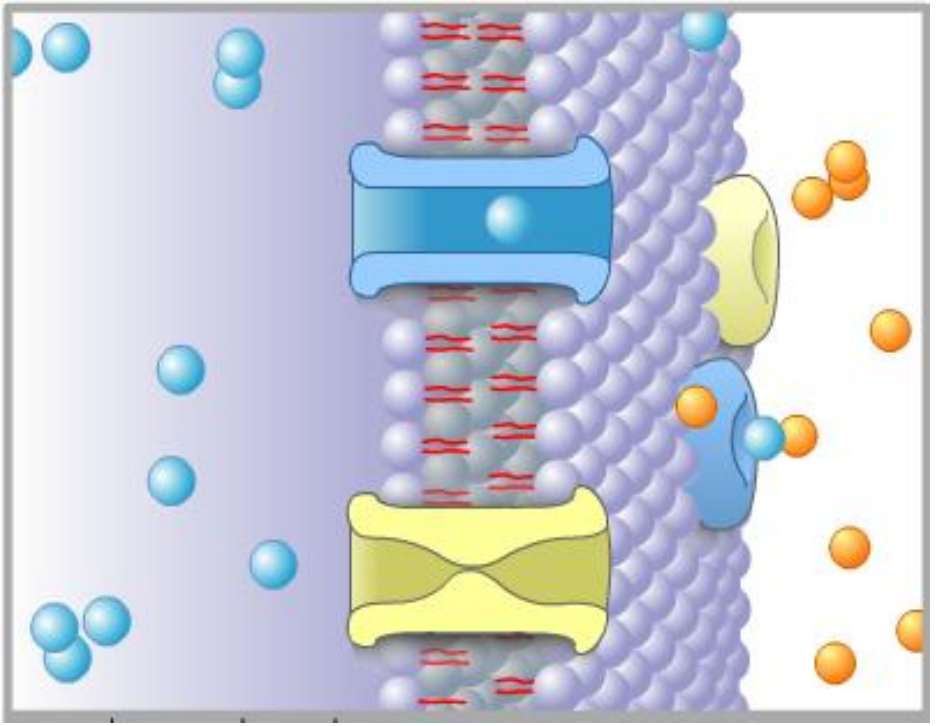
(1) Leak (تسرب Diffusion , Passive) channels : - Pores in the cell-membrane which are open all the time , therefore ions diffuse through them according to the ion Concentration Gradient .

(2) Voltage-gated channels : قنوات ذات بوابا ت تعمل بالجهد الكهربى
open when the cell-membrane is electrically activated .

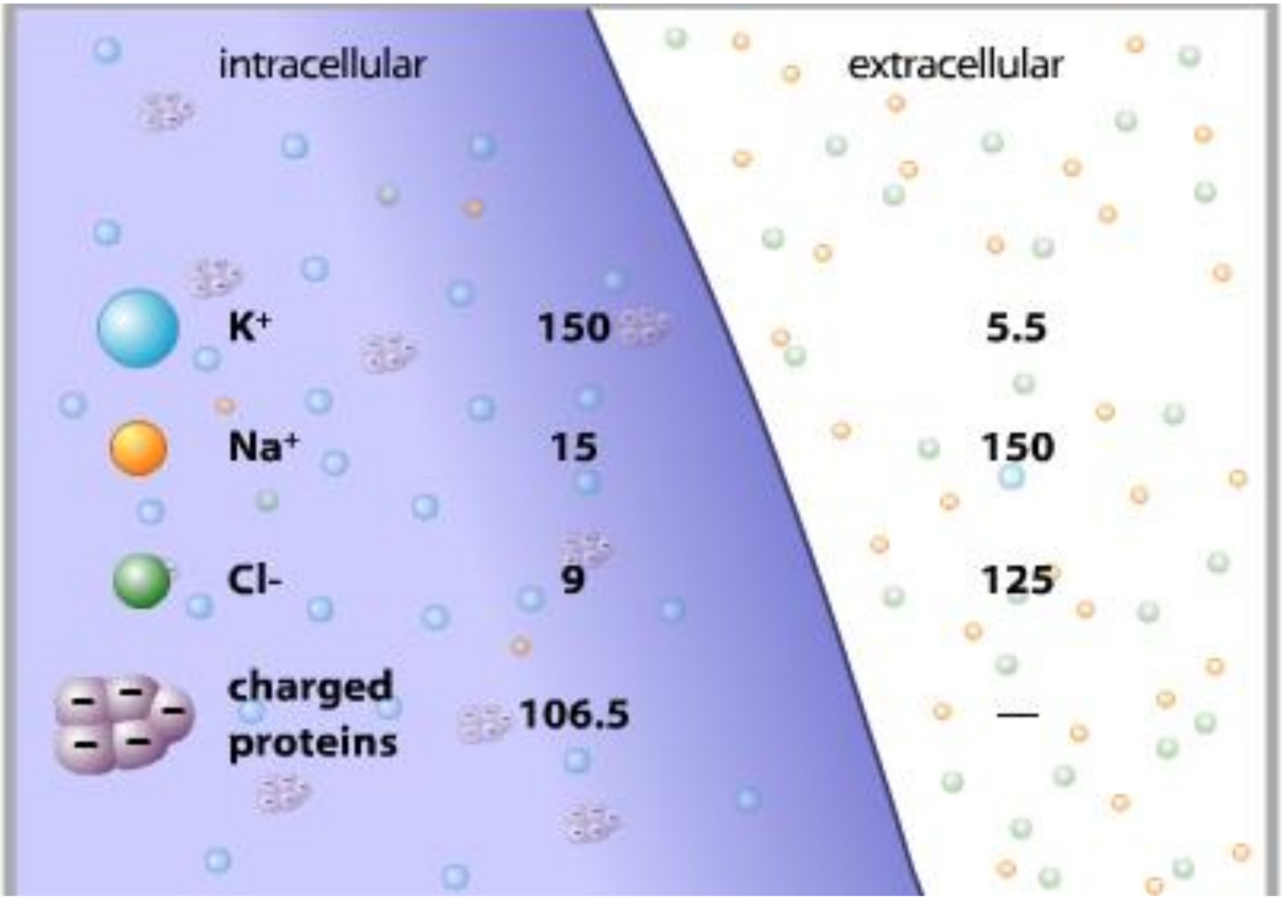
(3) Chemically-gated (ligand-gated) channels : open by chemical neurotransmitters at neuromuscular junctions & synapses)connections b/w neurons).

Cell Membrane





Ion Concentration



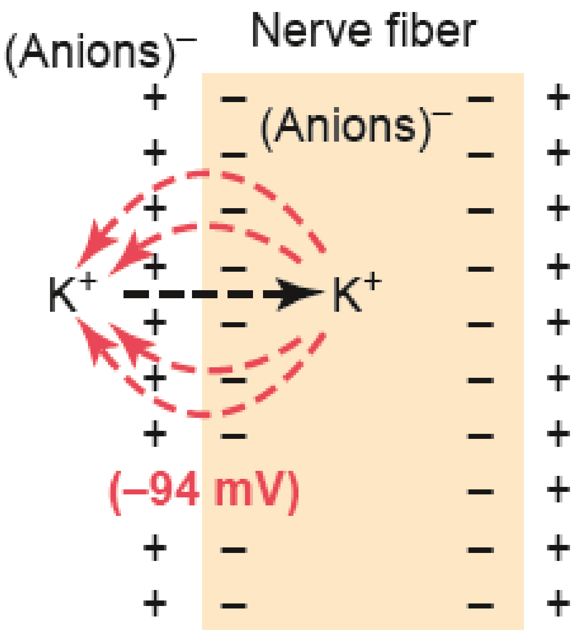
Basic physics of membrane potential

Diffusion (Concentration) Potential

-**Nerve has semi-permeable membrane separating the ECF from the ICF .**

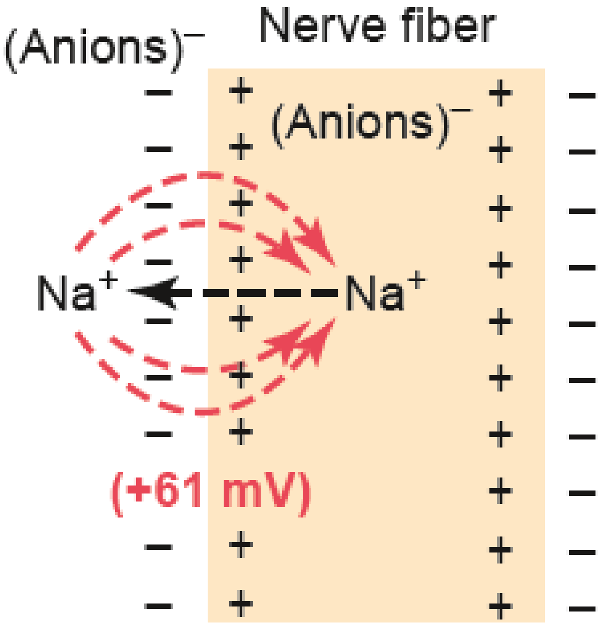
- **K+ is high inside the nerve membrane & low outside → therefore potassium continuously diffuses through the K+ leak channels from inside the cell to outside .**

-So diffusion of K+ ions through membrane occurs from high conc inside to outside carrying +ve charge with it → build up of electropositivity outside & electronegativity inside

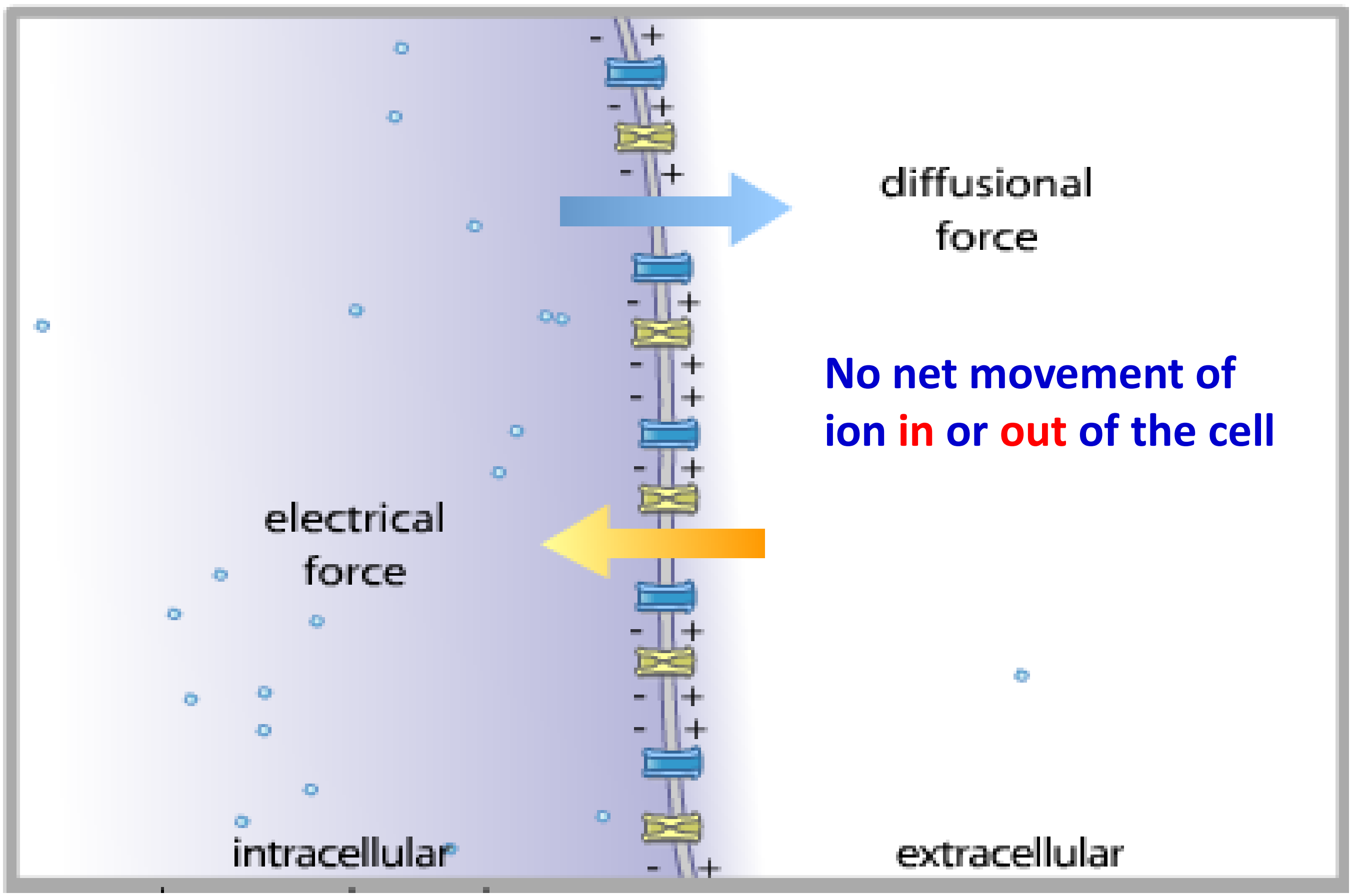


Diffusion (Concentration) Potential

- Na+ is high outside membrane & very low inside membrane, so the direction of the Na+ chemical (concentration gradient) gradient is inward → and sodium continuously diffuses through the Na+ leak channels from outside (the extracellular fluid , ECF) to inside the cell (the intracellular fluid , ICF). → build up of electronegativity outside & electropositivity inside.



Opposing Forces Acting on Ions



No net movement of ion in or out of the cell

NERNST EQUATION

-The Potassium Nernst (Equilibrium) Potential

•- Nernst calculated the level of concentration potential of ions across the membrane that prevent net diffusion of ions to inside or outside

Nernst made a hypothesis which said that if we suppose that

(1)the ECF and ICF contained ONLY potassium ion ,

(2)and that the cell-membrane was freely permeable to K+

→ then K+ will diffuse down its concentration (chemical) gradient (via the K+ leak channels) from inside the cell to outside , carrying with it +ve charges to the outside ,

-This progressively increasing the negativity on the inner side of the membrane because we are losing +ve charges from inside).

•At this goes on and on , negative charges build inside, an opposing negative electrical potential , tending to prevent the exit of the +ve potassium ions (force tends to keep K+ inside) .

This negative electrical potential will grow INSIDE until it becomes strong enough to balance and counteract مضادة وتبطل the concentration gradient which tends to push K+ OUTSIDE

*When this electrical gradient (electrical force) , which tends to keep K+ inside equals (=), the concentration gradient (which tends to push K+ outside) → there will be no net K+ movement across the membrane .

The membrane potential (MP) in that case is called:-
Nernst Potential for K+ (or K+ Equilibrium or Diffusion Potential)
It equals = -94 mV (The -ve charge always refers to the inside of the cell relative to the outside)
(This value was calculated by Nernst equation)

$$E.M.F\ (mV) = +61 \log \frac{K^+\ \text{Conc. Inside}}{\text{Conc outside}} = -94\ mV\ K^+$$

The SODIUM Nernst (Equilibrium) Potential

Nernst made a hypothesis which said that if we suppose that:-
(1) the ECF and ICF contained ONLY sodium ions ,
(2) and that the nerve-membrane was freely permeable to Na+

→ then Na+ will diffuse down its concentration gradient to the Inside of the cell, carrying with it +ve charges , and progressively decreasing the negativity on the inner side of the membrane .
-As this goes on and on , and as the positive charges build inside , an opposing Electrical Potential begins to develop , tending to prevent the +ve Na+ ions from entering.

This electrical potential will grow until it becomes strong enough to balance and counteract يبطل the concentration gradient which tends to push Na+ inside .

When this electrical gradient (force) , which tends to drive (PUSH) Na+ outside equals = the concentration gradient (which tends to push Na+ in) → there will be no Na+ movement across the membrane .

The MP potential in that case is called:-

Nernst Potential for Na+ (or Na+ Equilibrium or Diffusion Potential) = +61 mV . (The charge always refers to the inside of the cell)

What determines the magnitude (value) of the Equilibrium (Nernst) Potential ?

- The ratio of the ion concentration on the two sides of the membrane (inside&outside).

- The value of this potential & EMF can be determined by :

Nernst potential = electromotive force (EMF)

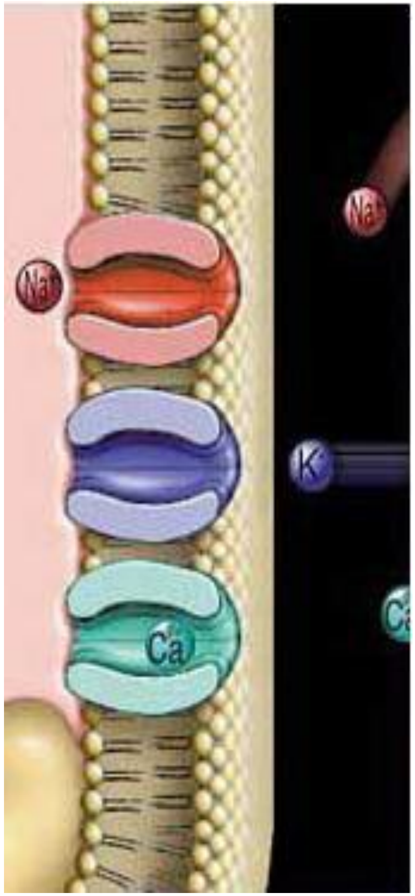
$$\textbf{EMF (mV)} = \pm 61 \times \log \frac{\text{Ion conc. Inside}}{\text{Ion conc. outside}}$$

-The greater the ratio (it means ion conc. inside is higher than outside) the greater the force for ions to diffuse in one direction (from inside to outside)

- **For K = - 94 mv & for Na = + 61 mv**

((it is –ve for K & + ve for Na (K diffuses out so ↓ the ratio & Na diffuses inside so ↑ the ratio))

THE RESTING MEMBRANE POTENTIAL OF NERVES



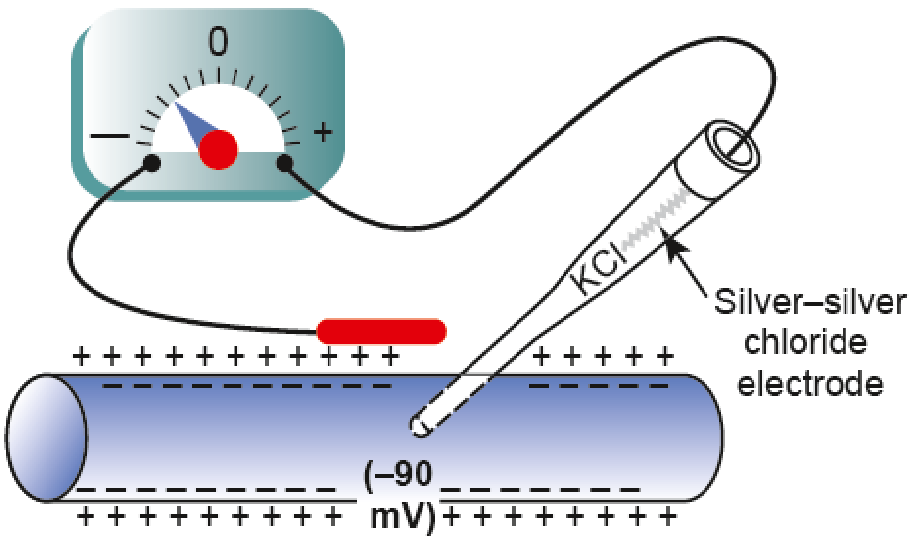
Measuring membrane potential

- **VOLTMETER**

To measure very small membrane potential difference between inside & outside as resting membrane potential .

How?

- **-A small filled pipette containing electrolyte solution is inserted inside the nerve fiber & another electrode is placed in the outside & membrane potential difference between inside & outside is measured using the voltmeter.**



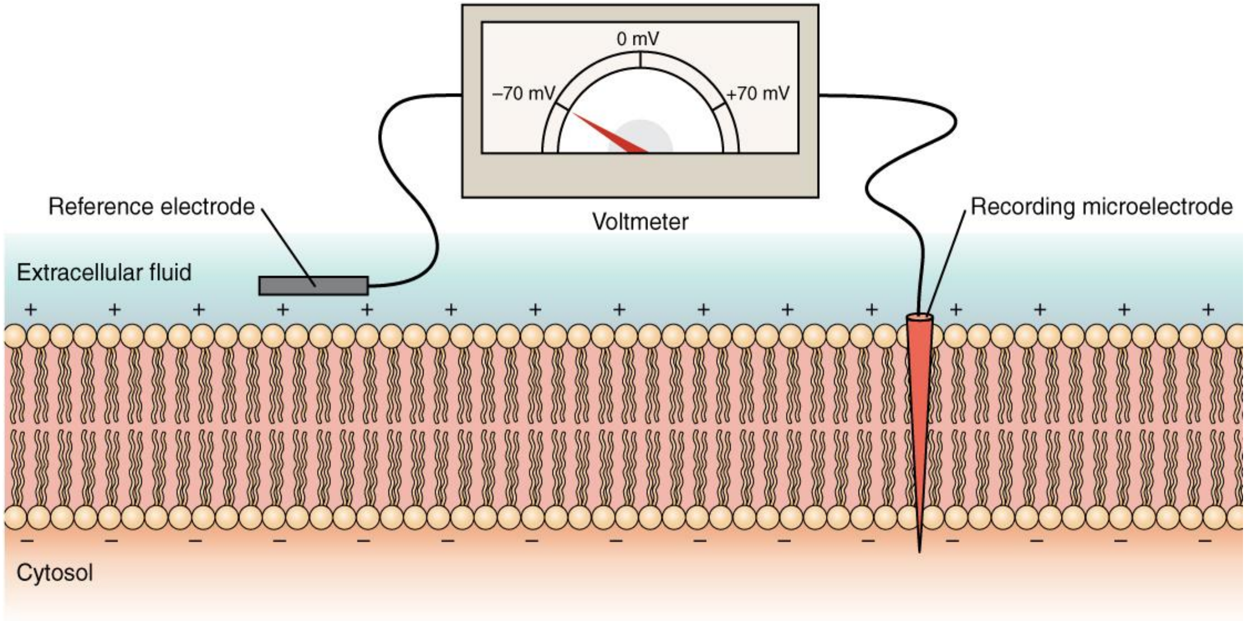
RESTING MEMBRANE POTENTIAL

الجهد الكهربائى الغشائى فى حالة عدم النشاط

Def:- It is a potential difference across cell membrane during rest (without stimulation)

Value:- -90 mV in large nerve fibers (-ve inside) (ranges between -70 mV TO -90 mV) (the -ve or +ve sign referes to the inside of the membrane)

-The membrane is <u>polarized</u>



• Q1: What are the factors that make the inside of the cell negative ?

Depend mainly on transport properties of resting membrane, the factors that make the inside of the cell negative:

1- Contribution of K & Na diffusion potential through Na & K leak channels of nerve membrane

2- Active transport of Na & K ions (Na/K pump)

3- Negative ions inside membrane as proteins & phosphate sulphate

Origin of RMP:

1- Contribution of K diffusion potential:-

N.B/ K diffusion contributes far more to membrane potential than Na diffusion .

- **At rest , K inside is 35 times higher than outside**

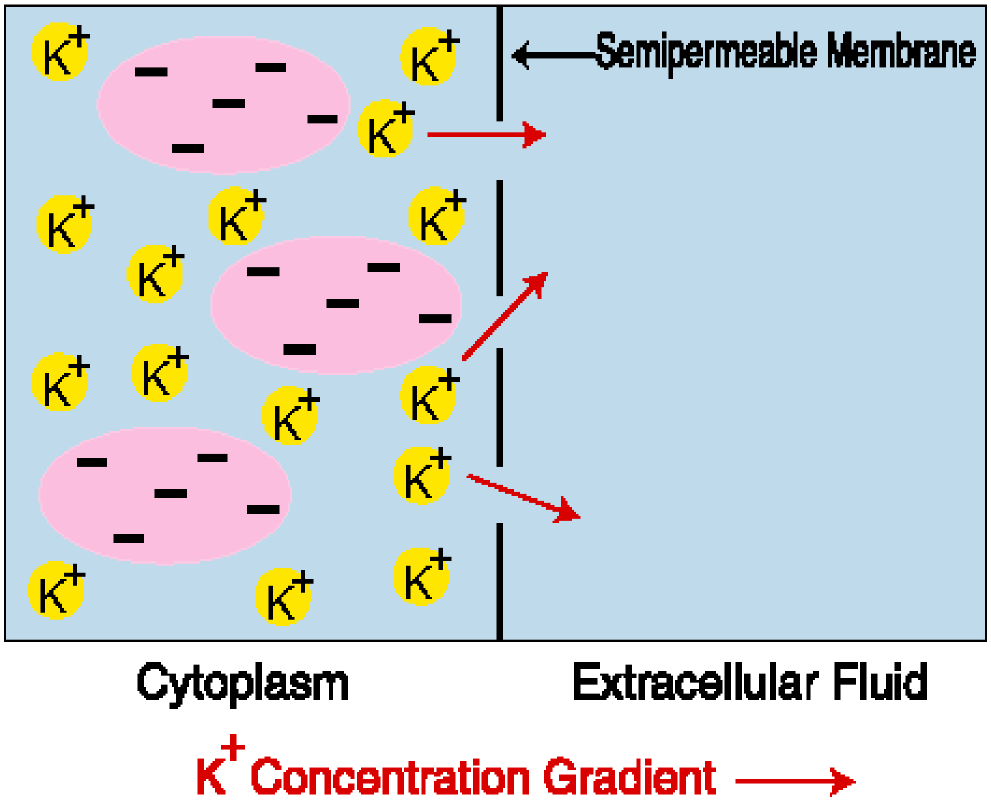
K+ leak channels → more K+ diffuses to outside than Na+ to inside , because **K leak channels are far more permeable to K than Na about 50-100 time due to small size of K molecules → more potassium lost than sodium gained → net loss of +ve ions from inside the cell → more negative inside** (net **K OUTFLUX TO OUTSIDE causing –ve inside)**

- **Applying Nernst Equation:-**

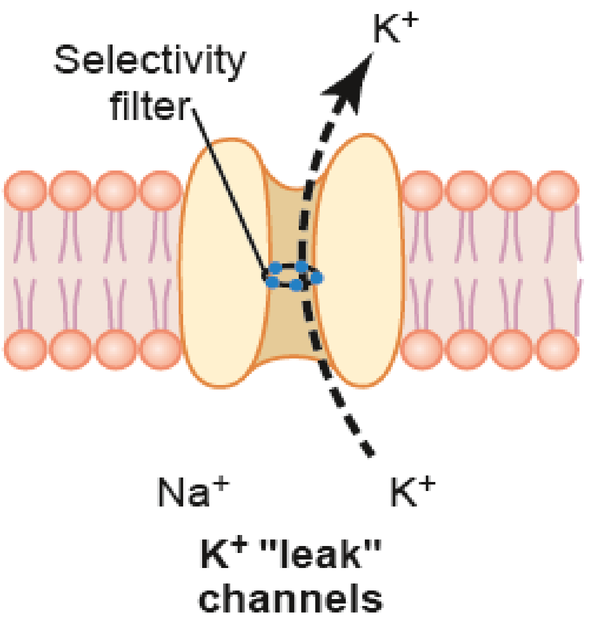
-K inside is 35 times higher than outside (35/1)

- Nernst potential = - 61 x log 35/1 (1.54) = -94 mV,

(if K is the only ion act on membrane →RMP = -94 mv with negativity inside the nerve)


Semipermeable Membrane
Cytoplasm
Extracellular Fluid
K+ Concentration Gradient

Outside


Selectivity filter
K+
Na+
K+
K+ "leak" channels

2- Contribution of Na diffusion potential:-

- **Na leak channels:-** have Slight permeability to Na ions from outside to inside.

- \- Nernst potential = + 61 x log (Na inside/ Na outside = 0.1) =

+ 61 x log 0.1= + 61 mV

-Nernst potential for Na inside membrane = + 61mV

(if Na is the only ion acting on the membrane → RMP = + 61mV

with positivity inside the nerve

- Na diffusion potential = + 61mv & that of K = - 94 mv

-using this values in Goldman equation

(To calculate diffusion potential when membrane permeable for several ions)

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

** Net value of the internal membrane potential of about -86 mV

N.B/ almost all of this determined by K diffusion

(because membrane is 100 times permeable to K than to Na)

- i.e. Potassium potential has the upper hand .

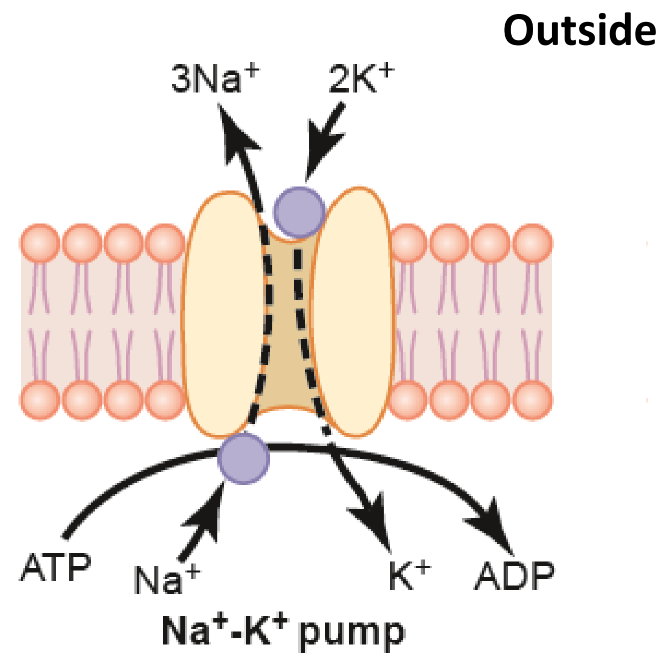
3- Contribution of Na/K PUMP:-

- This is a powerful ***electrogenic pump*** on the cell membrane.

- It Pump 3 Na to outside & 2 K to inside, causing → net loss of +ve ions ,loss of + ve charge from inside , create negativity about - 4mV inside

The Na/K pump also causes large concentration gradients for sodium and potassium across the resting nerve membrane. These gradients are:

Na + (outside): 142 mEq/L
Na + (inside): 14 mEq/L
K + (outside): 4 mEq/L
K + (inside): 140 mEq/L



-So **<u>NET MEMBRANE POTENTIAL</u>** **will be :-**

Diffusion potential (caused by K & Na diffusion) + *Electrogenic* Na/K pump

<u>(-86 mV) + (- 4mV) = -90 mV</u>

4- Effect of Large intracellular anions(negative ions)

(proteins , sulphates & phosphates), very low effect.