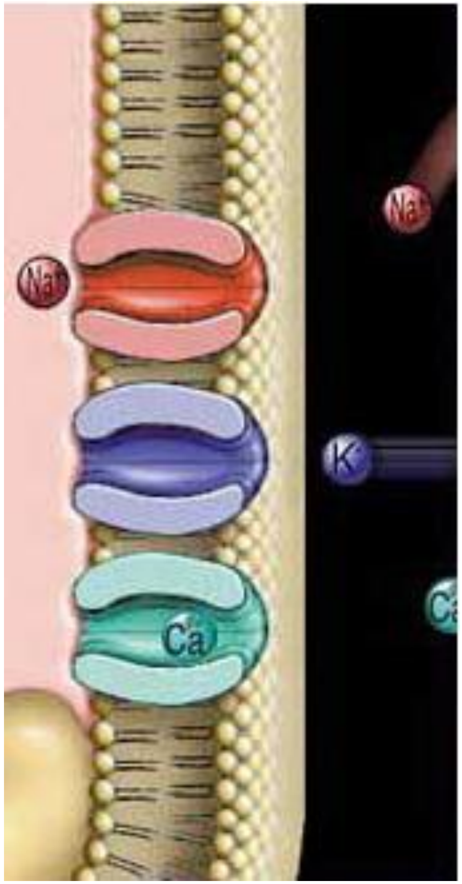

Musculoskeletal Physiology

Physiology of Excitable Tissues : Nerve andSkeletal Muscle

by

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Lecture 3

NEURON
& THE NERVE
RESTING MEMBRANE
POTENTIAL

الجهد الغشائي

Lecture 1: NEURON & NERVE RESTING MEMBRANE POTENTIAL

Objectives:-

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

-Identify and describe structural components of neurons and functions.

•Identify Excitable tissues

•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 diffusional 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

- Apply Nerst equation in calculating resting membrane potential

-Identify voltmeter to measure very small membrane potential difference between inside & outside as resting membrane potential.

Q : What are Excitable tissues سريع الانفعال?

A: <u>They are nerve and muscle</u>

<u>Q: what property do excitable tissues have that makes them different from other body tissues ?</u>

A: Their membrane acts as an electric capacitor مكثف, storing opposite charges on the opposite sides of the membrane this creates:

-Resting membrane potential(**<u>RMP)</u> 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).

Neuron:-

-DIF;-unit of function of the central nervous system, mostly anterior horn cell in the spinal cord supply skeletal muscle

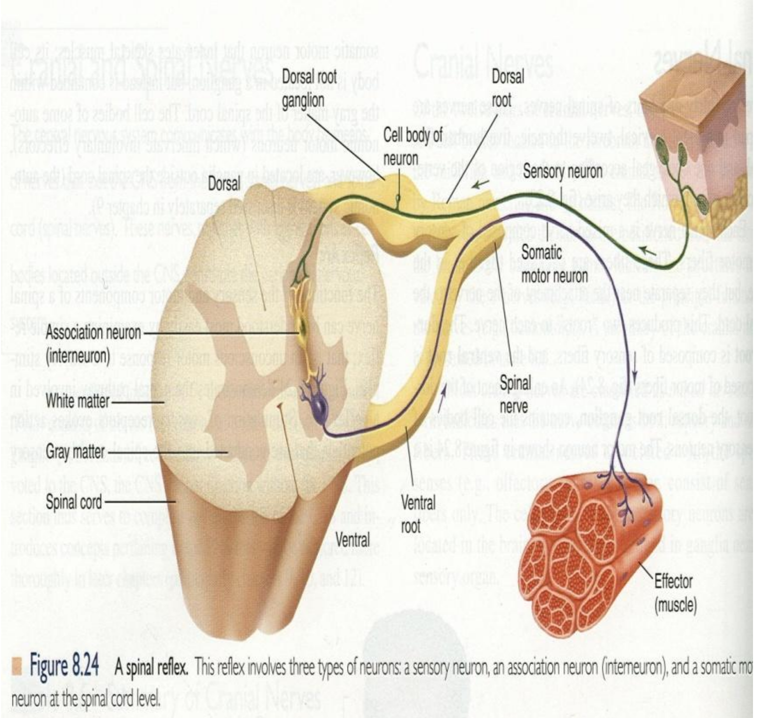
Parts of motor neuron & function of each part:

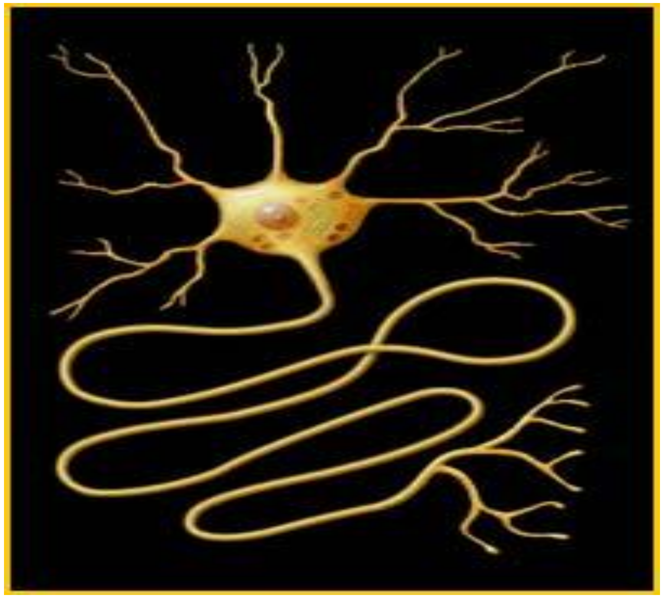
1- Soma (cell body)

2-Dendrites carry nerve impulses from surroundings to the soma

3 Axon hillock at which nerve impulses begin &pass in one direction from soma to the axon(nerve fiber) then to axon terminal.

4-Axon and axon terminal end on skeletal muscle





Q : What is the membrane potential (MP) ?
It is the difference in potential (voltage) between the inner side & outer side of the membrane (nerve membrane)
Q : What are the states of MP ?

(1) Resting Membrane Potential (RMP) : value of MP in a " resting " state (unstimulated excitable nerve 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 (nerve) 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).

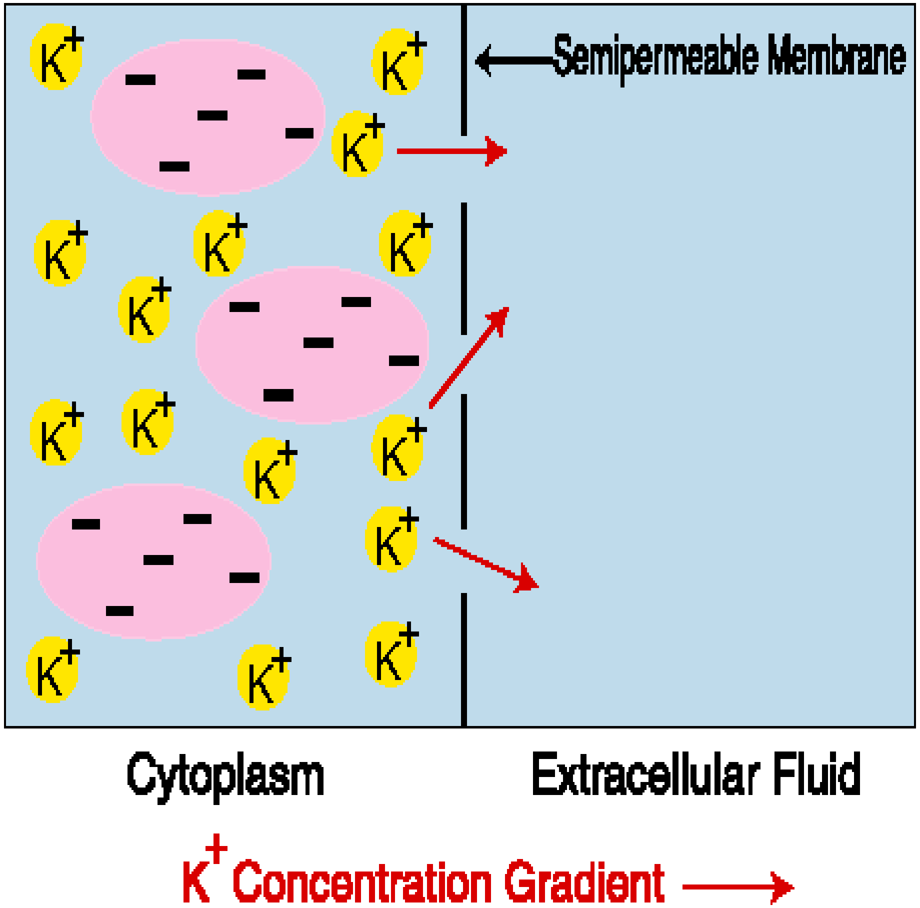
Basic physics of membrane potential

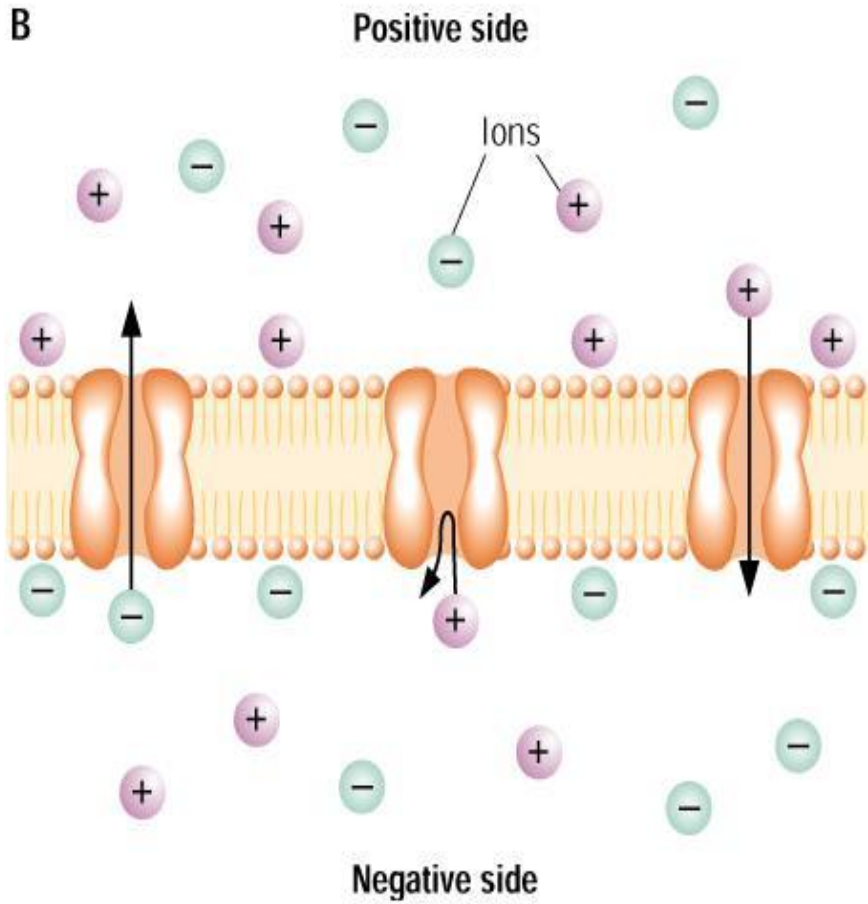
- Nerve has semipermeable membrane separating the ECF from the ICF .

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

-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

2- 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.


K+
Semipermeable Membrane
Cytoplasm
Extracellular Fluid
K+ Concentration Gradient


B
Positive side
Ions
Negative side

NERNST EQUATION

-The Potassium Nernst (Equilibrium) potential

- - Nerst calculate 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)

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

-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 :

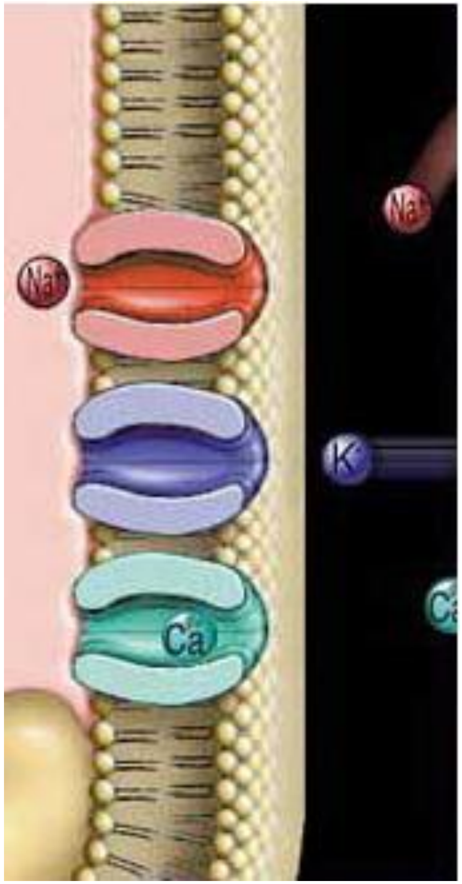
Nernst potential = electromotive force (EMF)

$$E.M.F\ (mV) = +61 \times \log \frac{\text{Ion conc. Inside}}{\text{Ion Conc outside}}$$

-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

RESTING MEMBRANE POTENTIAL
الجهد الكهربائى الغشائى فى حالة عدم النشاط

DIF:- **it is potential difference across nerve membrane during rest (without stimulation)**

Value:- **-90 mv in large nerve fibers (-ve inside) (range-70 mv TO -90 mv)**

(the -ve or +ve sign referes to the inside of the membrane)

-The membrane is polarized

- **Two questions should be asked :**
- Q1: What are the factors that make the inside of the cell negative ?
- Q2: and give the RMP of large myelinated nerves the value of - 90 mvolts(or -70 to -90 mV)?

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 phosphate sulphate & proteins**

Origin of RMP:

1- Contribution of K diffusion potential:-

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

(1) 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**

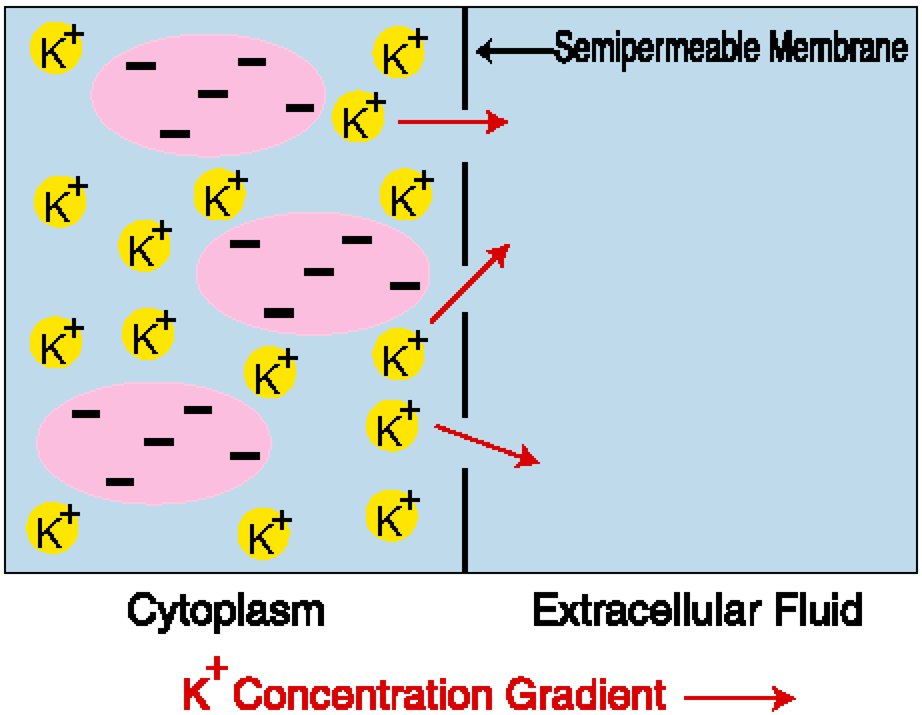
(net **K OUTFLUX TO OUTSIDE causing –ve inside)**

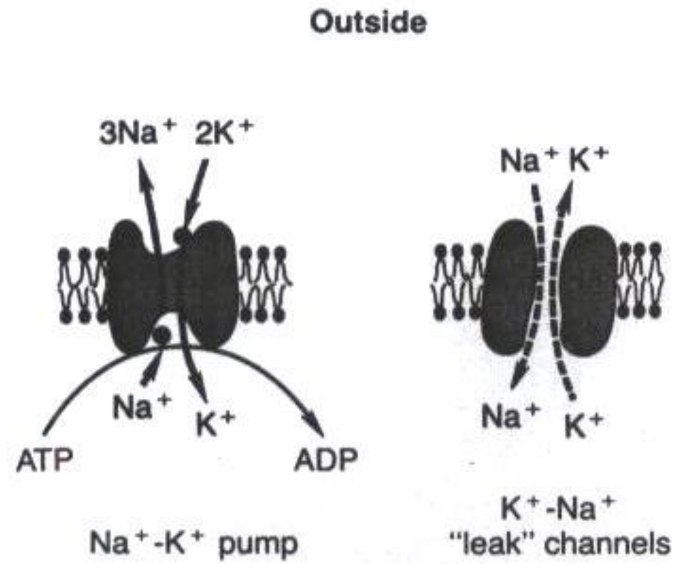
(1) Applying Nernst Equation:-

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

- Nernst potential = - 61mv 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
K^+
Cytoplasm
Extracellular Fluid
K^+ Concentration Gradient


Outside
$3Na^+$ $2K^+$
Na^+
K^+
ATP
ADP
Na^+-K^+ pump
Na^+ K^+
Na^+ K^+
K^+-Na^+
"leak" channels

- **2- Contribution of Na diffusion potential:-**

Na leak channels :- have Slight permeability to Na ions from outside to inside.(why slight?)

- 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 act on 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)

**** net value of the internal membrane potential of**

about -86 mv

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

(because membrane is 50- 100 times permeable to K than to Na)

- i.e potassium potential has the upper hand .

- **3- contribution of Na/K PUMP:-**

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

-so net membrane potential will be :-

(-86 mv) + (- 4mv) = -90 mv

4- Effect of Large intracellular anions(**negative ions)** (proteins , sulphates & phosphates) very low effect

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 put inside the nerve fiber & another electrode is placed in the outside & membrane potential difference between inside & outside measued**