Physiology Team

MEDICAL COLLAGE 433

Resting Membrane Potential (Voltage)

Color Index

Red = important

Purple = Addition

Orange = Explanation

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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.**

What are Excitable tissue and why they are excitable ?

Muscle + Nerve = Type of excitable tissues

Because they respond to stimuli, leading to change the voltage difference between the inside and outside of the cells.

Properties of excitable tissues

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 .

High RMP makes nerves or muscles membrane act as a capacitor that can discharge producing large voltage changes

لتوضيح النقطة السابقة:

ميزة الانسجة سريعة الانفعال هو وجود فرق جهد كهربائي عالي قيمته بين)-70الى -90(تجعل أغشية العضلات والاعصاب تعمل كمكثف يفرغ الشحنات مما ينتج عنه فرق جهد كهربائي يؤدي الى إمكانية حدوث الفعل.

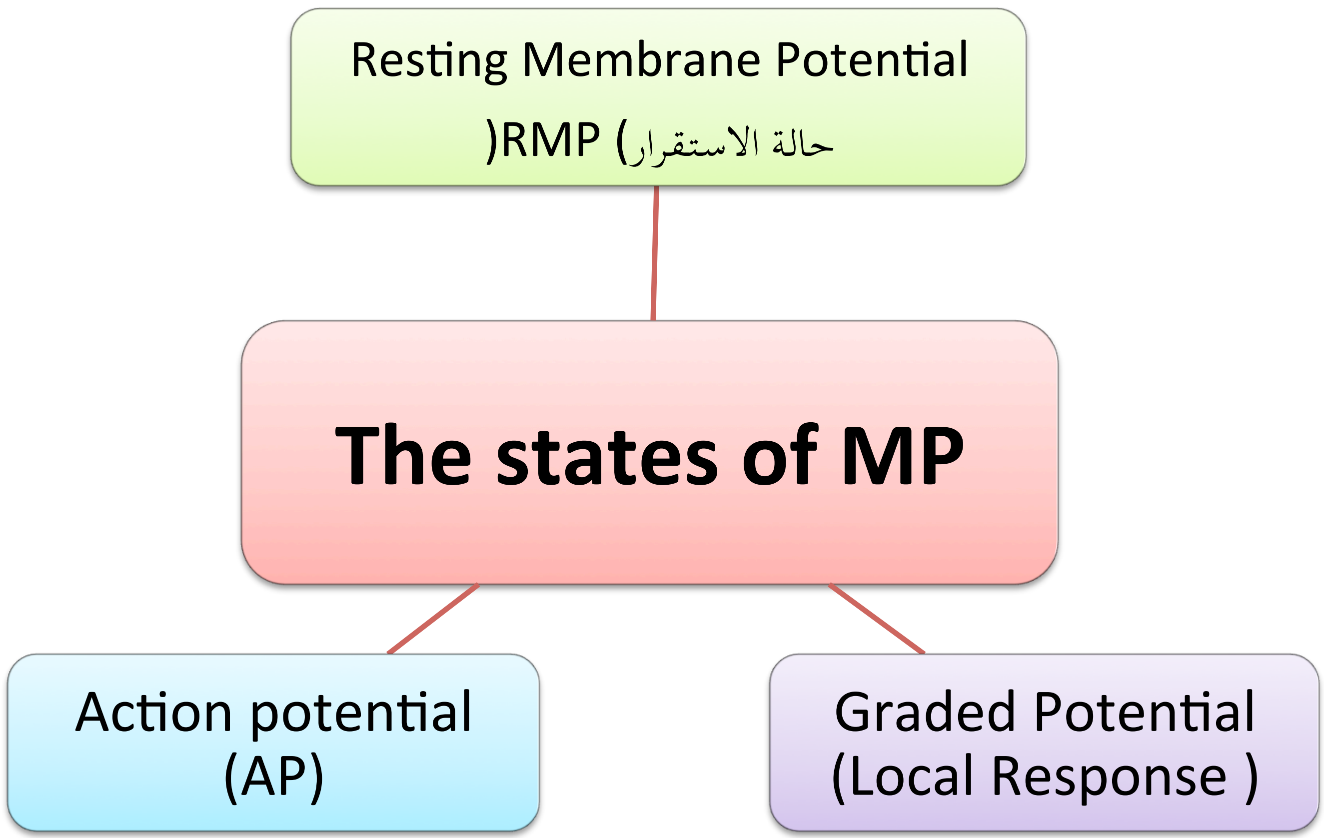
فعلى سبيل المثال نجد أن خلايا الدم الحمراء فرق جهدها -5 مما يدل على أن هذه الخلايا ذات نشاط محدود وهو حمل الاكسجين في حين ان الاعصاب والعضلات ذات فرق جهد عالي تكون ذات نشاط عالي يؤدي الى حدوث رد فعل واضح مثل الانقباض والانبساط

وعلى ذلك أي خلية ذات فرق جهد عالي ستكون نشطة .

جهاز قياس فرق الجهد يسمى بالفولتميتر وتكون نتيجة القياس بالسالب,لانه يقيس الشحنة اعتمادا على شحنة داخل الخلية

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).



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1- (RMP):value of MP in a " **resting** " state (unstimulated excitable membrane). It ranges between -70 and -90 mV in different excitable tissue cells.

(الخلية في هذة الحالة غير نشطة أي في حالة استقراروتختلف درجة استقرار كل غشاء بحسب نوع الخلية ففي أغشية الاعصاب المغطاة بالمايلين نجدها -90)

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).

(الخلية في هذه الحالة نشطة ولكن لم يصل نشاطها للحد الذي يجعلها تحدث رد فعل منتشر أي بمعنى انها تحدث رد فعل ولكن رد الفعل يكون محلي)

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)

(الخلية في هذه الحالة وصلت الى قيمة فرق جهد تجعلها قادرة على احداث فعل)

توضيح الحالات الثلاث السابقة:

هناك قاعدة في الفسيولوجي تنص على مايلي :

“ALL OR NON RESPONSE MECHANISM“

معناها اننا نحدث تحفيز ونحصل على رد فعل وهو ما يسمى ب **Action potential (AP)**

او تكون الخلية في حالة استقرارولانحصل على رد فعل وهو **“resting membrane potential”**

وما بين هاتين الحالتين هو اننا نحدث تحفيز ونحصل على رد فعل ولكن لا يتجاوز مكانه **“local response”**

مثلا :

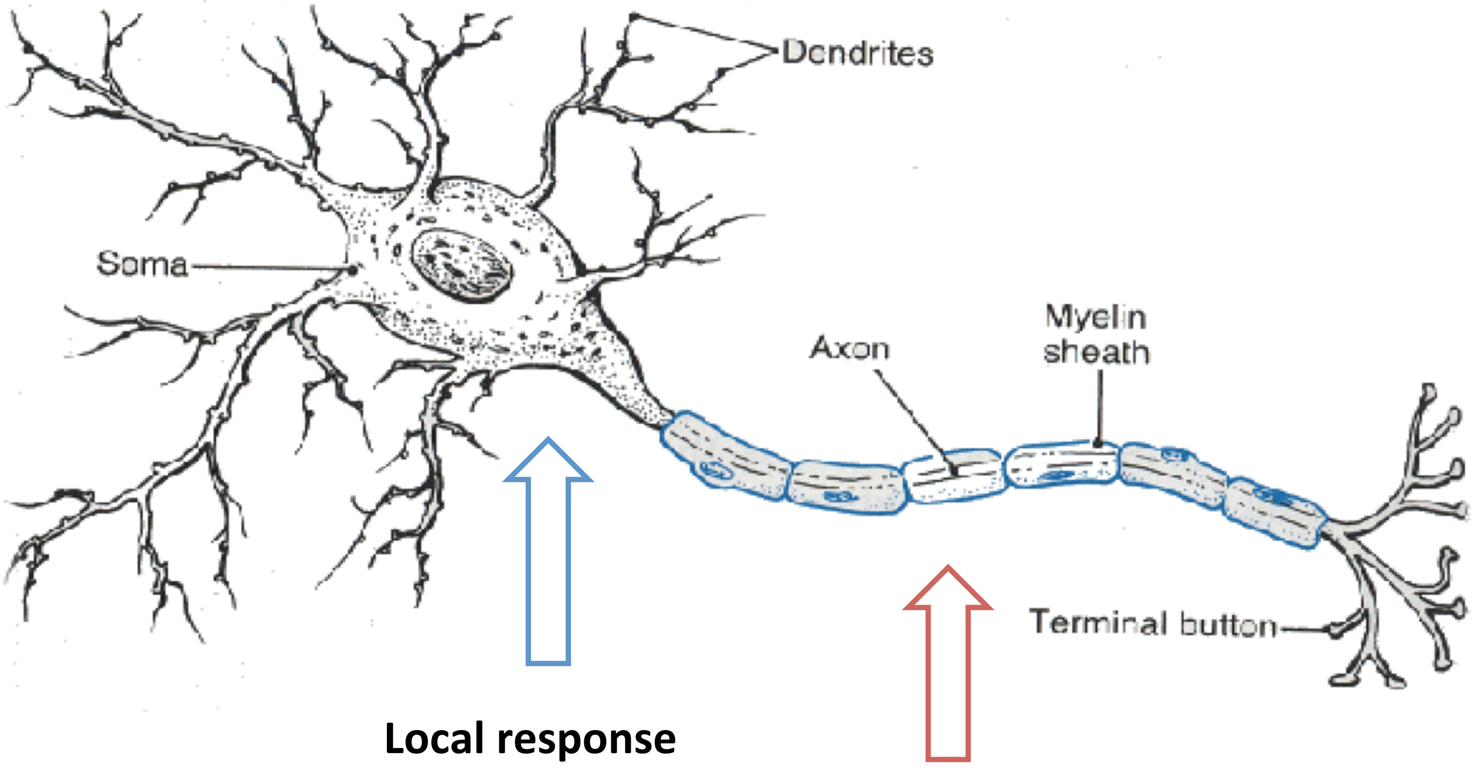
في الخلية العصبية عندما نقوم بتحفيزها قد يكون المحفز غير قوي بما فيه الكفاية ليحدث رد فعل منتشر,في هذه الحالة لا يعني انه لم يحدث رد فعل مطلقا ولكن رد الفعل الذي حدث قد يكون ادخل عدد معين من الايونات داخل جسم الخلية ولم ينتقل الى محور الخلية.وهذا يسمى **“ Sub threshold**.

وهذا فرق الجهد الذي يحدث رد فعل محلي اما فرق الجهد الذي يحدث رد فعل يسمى ب **“Threshold**

- **Any cell that formed excitable tissue has :**

1. **sub threshold**
2. **Threshold**

- **If we stimulate the cell by its sub threshold it will response locally and we can increase the stimulator till fire level where the action potential action.**
- **Action potential can not be stopped if it is happen. It will complete and give response .**



Local response

Action potential will propagate

Types of membrane ionic channels

lack (Diffusion , Passive channels)

مفتوحة دائما ولكن متخصصة

- It has **pores** in the cell membrane which are opened all the time
- The membrane is **semi permeability** therefore ions diffuse through it according to the ion Concentration Gradient .

Voltage-gated channels

قنوات تعمل بالجهد الكهربي

- open when the cell-membrane is **electrically activated**

Chemically-gated (ligand-gated) channels

- open by **chemical neurotransmitters** at neuromuscular junctions & synapses connections b/w (neurons).

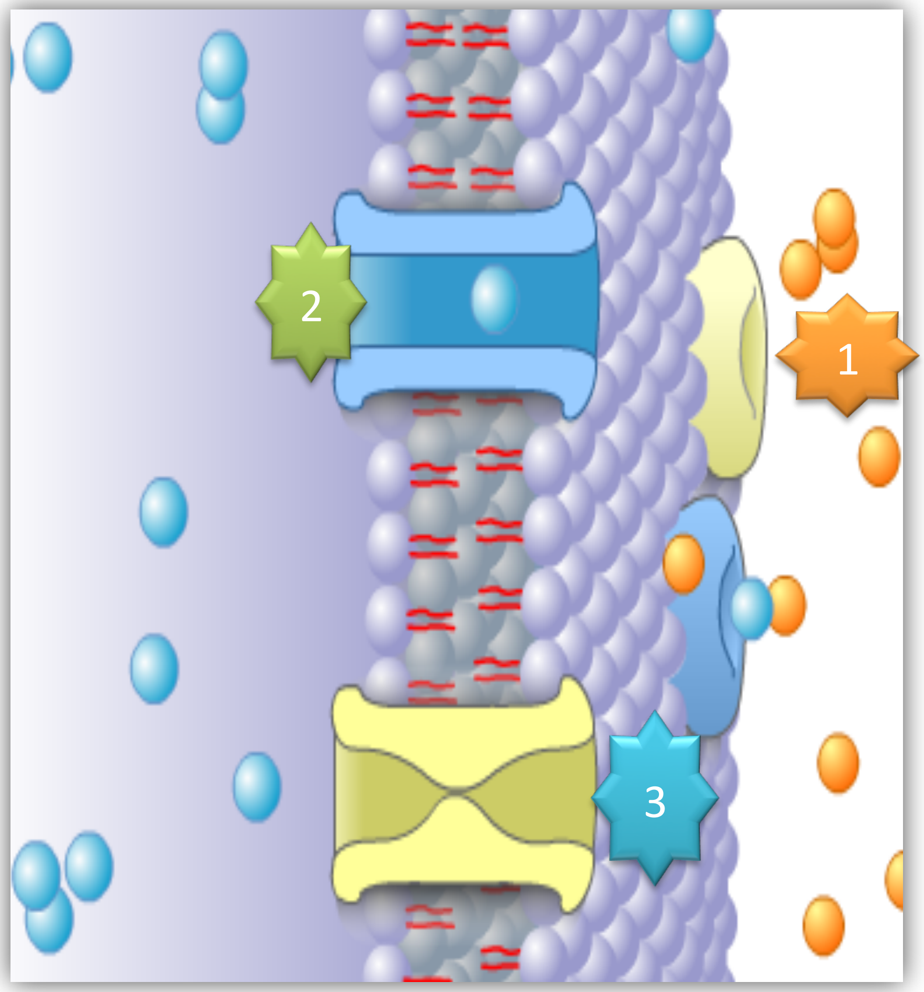
Ligand gates that are open by chemicals :
e.g. Epinephrine works on the entry of sodium ions that exceeded heartbeat.
acetylcholine works on potassium ions that reduces heartbeat.
Synapses: area between neurons & junctions: area between neurons and muscle

Type of Gates

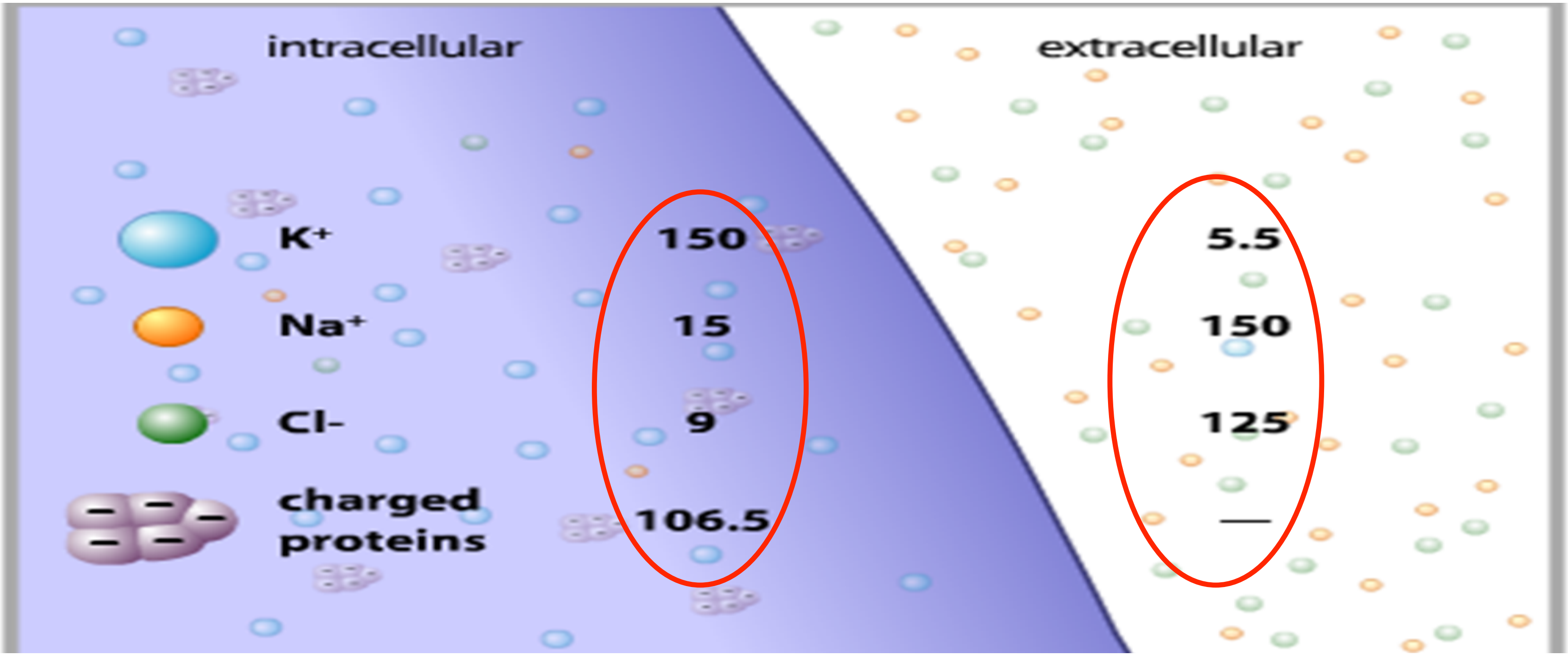
1-lecky gates.

2- voltage gate channel.

3- ligand channel.



Ion Concentration



In ICF: Potassium(k^+)is the chief cation
In ECF: Sodium(Na^+) is the chief cation

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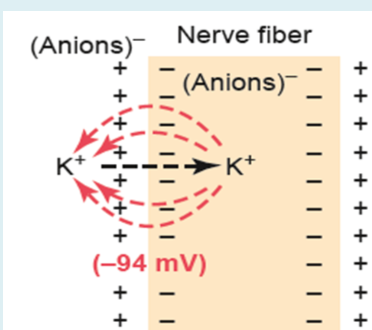
Basic physics of membrane potential

Diffusion (Concentration) Potential

K+

*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 .
*K+ ions diffused through membrane occurs from high conc inside to outside carrying +ve charge with it → build up of electro positivity outside & electronegativity inside.

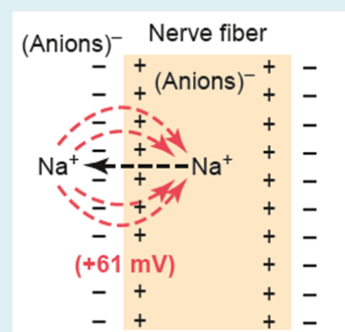


Na+

*Na+ is high outside membrane & very low inside membrane, so the direction of the Na + chemical (concentration .gradient) gradient is inward

*sodium continuously diffuses through the Na+ leak channels from outside to inside the cell

*So, it build up of electronegativity outside & electro positivity inside



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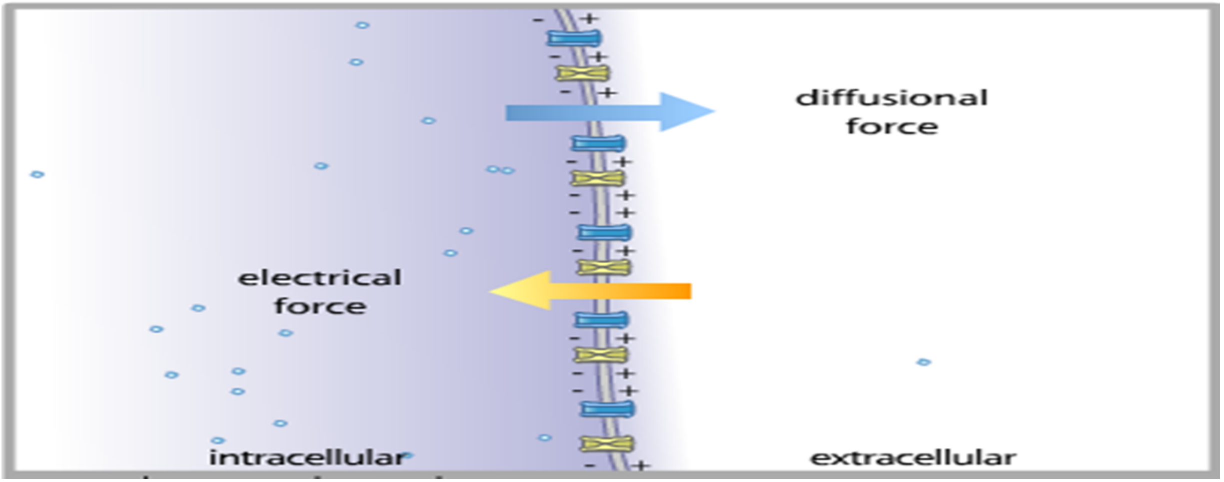
Diffusion (Concentration) Potential

- بالنسبة لانتقال الايونات فهي تنتقل اعتمادا على درجة التركيز حيث تنتقل من منطقة ذات تركيز مرتفع إلى منطقة ذات تركيز منخفض مثلا:البوتاسيوم تركيزها داخل الخلية اعلى فنجد انتقالها من الداخل إلى الخارج بينما الصوديوم ينتقل من الخارج إلى الداخل.
- كل ايون بوتاسيوم يخرج من داخل الخلية يترك شحنة سالبة خلفه داخل الخلية.
- هناك قوتين تتحكمان في دخول ايونات البوتاسيوم وخروجها وهما:

1-قوة فرق التركيز التي تجعل الايونات تخرج للخارج.

2-القوة السالبة التي كونها خروج البوتاسيوم والتي تحاول إعادته الى الداخل.

يقف مرور البوتاسيوم خارج الخلية اذا تساوت هاتين القوتين.



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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+

What will happen?

1

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 ,

2

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

3

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) .

4

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

5

*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 .

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What is the result ?

The membrane potential (MP) in that case is called:-

Nernst Potential for K+ (or K+ Equilibrium or Diffusion Potential))It equals = -94 mV)

وهي القيمة التي يتوقف عندها مرور البوتاسيوم

(The -ve charge always refers to the inside of the cell relative to the outside)

(This value was calculated by Nernst equation)

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

E.M.F = Electromotive Force

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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+

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What will happen?

1

Na+ will diffuse down its concentration gradient to the Inside of the cell, carrying with it +ve charges ,

2

and progressively decreasing the negativity on the inner side of the membrane

3

then -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.

4

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

5

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 .

What is the result ?

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)

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

(The charge always refers to the inside of the cell)
if Na → + 61
K → -61

The ratio of the ion concentration on the two sides of the membrane (inside & outside) determines (value) of the Equilibrium (Nernst) Potential.
لانها هي القيمة المتغيرة الوحيدة في المعادلة

- **Nernst Potential values**

For K = - 94 mv
for Na = + 61 mv
it is – ve for K & + ve for Na
K diffuses out so ↓ the ratio
And Na diffuses inside so ↑ the ratio.

- **The greater the ratio means**

→ ion conc. inside is higher than outside
→ the greater the force for ions to diffuse in one direction (from inside to outside).

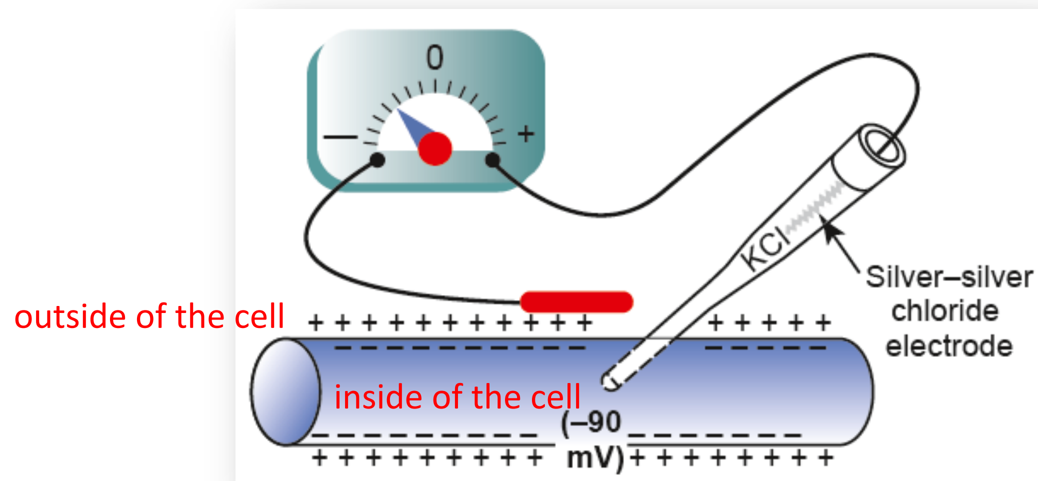
THE RESTING MEMBRANE POTENTIAL OF NERVES

(During resting condition the inside of the cell is negative with respect to the outside of the cell (positive))

We use the **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.



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RESTING MEMBRANE POTENTIAL

الجهد الكهربائى الغشائى فى حالة عدم النشاط

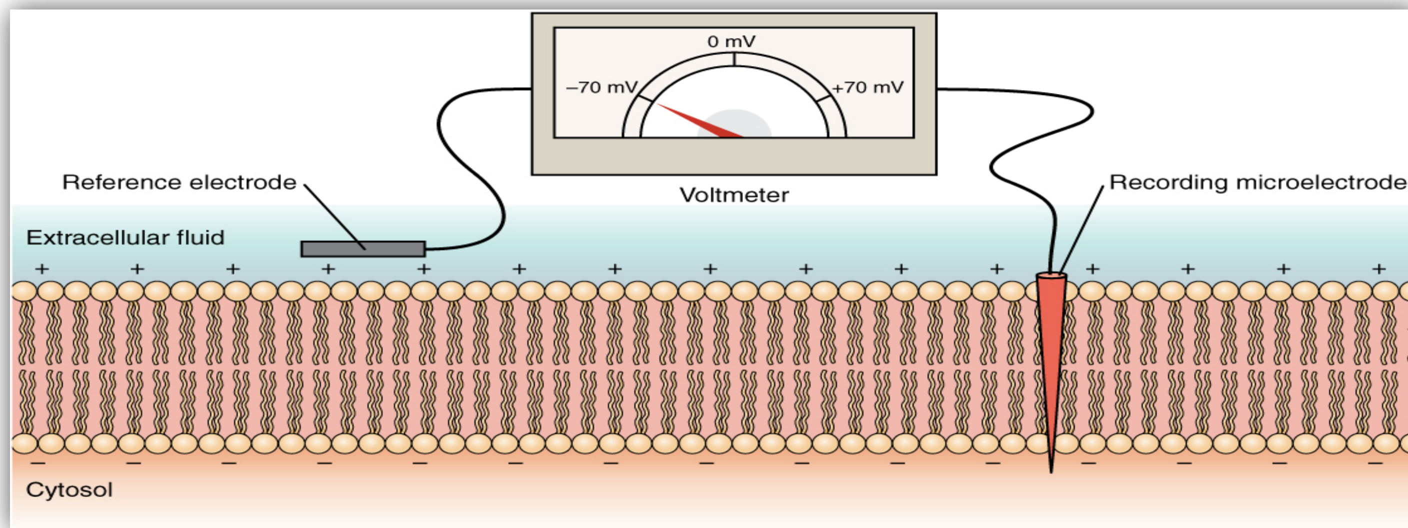
✓ **DIF:-** **It is a potential difference across cell membrane during rest (without stimulation)**

✓ **Value:-**

- **-90 mV in large nerve fibers (-ve inside)**
- **ranges between (-70 mV TO -90 mV) (Normal)**

  the -ve or +ve sign referes to the inside of the membrane
- **The membrane is polarized.**

If the membrane becomes in the resting state , it is called **polarized.**



❖ Factors that make the inside of the cell negative:

(Depend mainly on transport properties of resting membrane)

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 (RESTING MEMBRANE POTENTIAL) :

1- Contribution of K diffusion potential.

2- Contribution of Na diffusion potential.

3- Contribution of Na/K PUMP.

4- Effect of large intracellular anions (negative ions).

1- Contribution of K diffusion potential:

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

↓

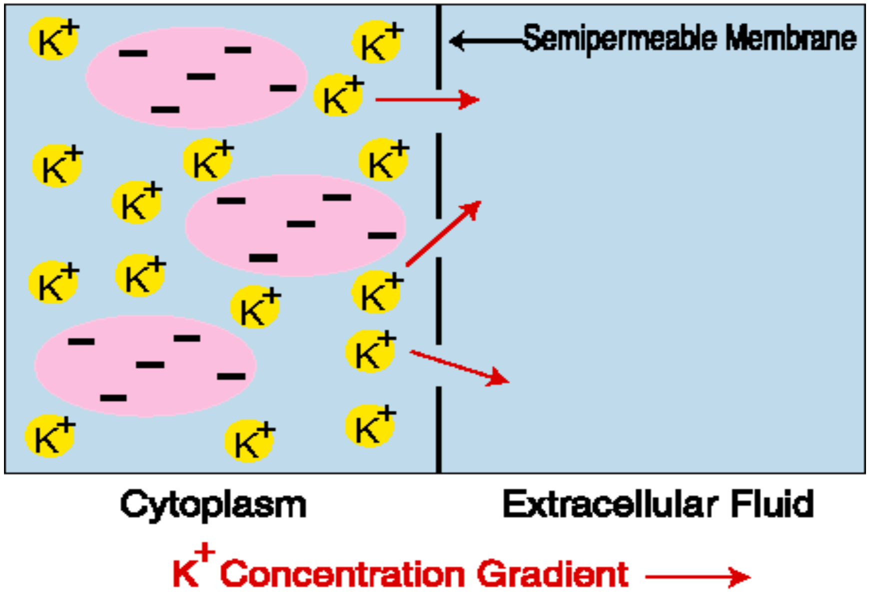
net loss of +ve ions from inside the cell → more negative inside
(net k outflux to outside causing –ve inside)

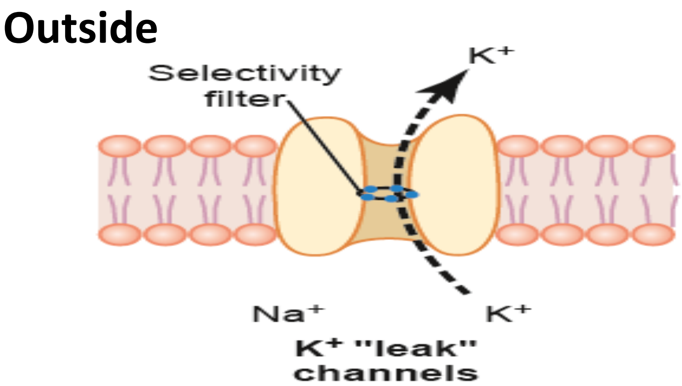
Applying Nernst Equation:-

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)





Contribution of K diffusion potential

2- Contribution of Na diffusion potential:

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

Applying Nernst Equation:-

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).

Goldman equation

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.**

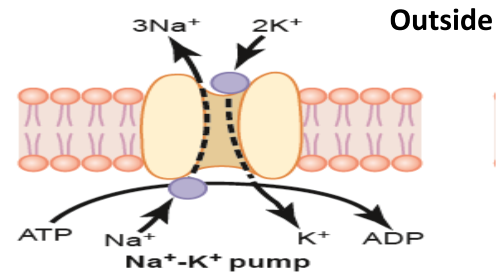
✓ **almost all of this determined by K diffusion.**

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

✓ **Potassium potential has the upper hand .**

Normal = -90 mv
النقص يعوض بـ Na/K pump أو charged proteins

3- Contribution of Na/K PUMP



- Restores the membrane to the resting level.

✓ 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, NET MEMBRANE POTENTIAL will be :-

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

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

4- Effect of Large intracellular anions(negative ions)

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

Summary

The cell membranes contain three types of routes for molecules to pass through it

1. Leak Channels; Always open and they function in diffusion
2. Voltage gated channels: opens when the the membrane is electrically altered
3. Chemical gated channels; open when ligand attaché to its receptors

There are more K+ channels : K+ ions move fast because of small molecular size
Less Na+ channels: Na+ moves slowly due to small molecular size

❖ K+ high inside, low outside. Diffusion will occur down the concentration gradient to outside
A relatively negative charge will increase inside because every K+ ion that goes out carries with it a positive charge. Na+ cant compensate يعوض this loss because of small number of channels and slow diffusion rate

❖ As Na+ moves inside, the positive charge increase but it will not eradicate تزيل the negative charge

This continuous state create a negative charge in the inner side of the membrane and a positive charge in the outer layer of the membrane
This creates the resting membrane potential that values between **-90 to -70 mV in nerve fibers**.

Nernest Equation

There are two forces

1. ***Diffusion force (chemical gradient):*** K+ potassium want to balance its concentration inside and outside
2. ***Electrical Force (Electrical gradient):*** Wants to balance the negative charge found inside and the positive charge outside

The membrane does not carry a potential, no charges on either side, they equal each other

- At first as a result of diffusion force, negative charge grows inside, then a week electrical force want to compensate the positive charge lost by bring back the K+ inside

- The amount of negative that needs to build inside for the electrical force to equal the diffusion force out side is calculated to be -94 mV

- The same thing for the Na+, Nernst found that a potential that equals +61 mV needs to be reached for chemical=electrical

Resting membrane potential

Depends upon:

- K+ and Na+ diffusion and the charges that they create, remember K+ diffuses faster than Na+. But there are other ions that also contribute like Cl-
    - **Ions other than K+ and Na+ also contribute, like Cl-. So Volkmann created an equation that will include cl- as well as K+ and Na+. The potential calculated was found to be -86 mV**

- K+/Na+ ATPase pump

As 3 Na+ are taken out and 2 K+ and brought in, the cell losses 3 positives and gains 2 positives

-3+2=-1

So every time the pump works the cell gains a negative charge, this charge will build up and it contributes a -4 mV potential

- Phosphate and negative proteins inside cell. They increase the negativity inside the cell.

Resting Membrane Potential
https://www.youtube.com/watch?v=v9THfG4ZoN4

Resting Membrane Potential (another tutorial)
https://www.youtube.com/watch?v=nWCTSWjVLzI

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Multiple Choice Questions

Q1: Which of the following is the action of the Na-K pump?

A) 3 sodium in & 2 Potassium out
B) 2 sodium in & 3 Potassium out
C) 3 sodium out & 2 Potassium in
D) 2 sodium out & 3 Potassium in

Q2: Which of the following is the Nernst potential for K +?

A) -94 mV
B) +94 mV
C) -61 mV
D) +61 mV

Q3: Which of the following is always inside cell and negative?

A) Potassium
B) Calcium
C) Sodium
D) Proteins

Q4: When the K+ level in the blood is lower than 5 this indicate that the patient is having

A) Hypokalemia
B) Hypotension
C) Hyperkalemia
D) Hypertension

Q5: The ratio of the ion concentration on the two sides of the membrane (inside & outside) determines (value) of the Equilibrium (Nernst) Potential

A) True
B) False

Q6: Which of the following has the upper hand (controlling) RMP?

A) Proteins
B) Potassium
C) Sodium
D) Both A & B

1-C 2-A 3-D 4-A 5-A 6-B

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