3&4 Resting membrane potential and action potential

Very important

Extra information

Terms

Winners are not people who never fail
but people who never quit !

Objectives

1. Describe the voltage-gated sodium and potassium membrane channels and their states .
2. Explain the resting membrane potential (RMP) , Threshold Potential, Reversal Potential , Local Response and Action Potential .
3. Describe components of a neuron dendrites , soma , axon . axon hillock and their physiological significance
4. Describe the electrical changes in membrane potential during the action potential , their chemical bases and excitability changes .
5. Describe conduction along nerve fibers , role of myelination and how nerve fibers are classified.
6. Recognize the excitable tissues and their properties.
7. Recognize and describe the forces acting on ions.
8. Know how membrane potential is measured electrically.
9. Recognize and apply Nernst equation to calculate equilibrium potential.

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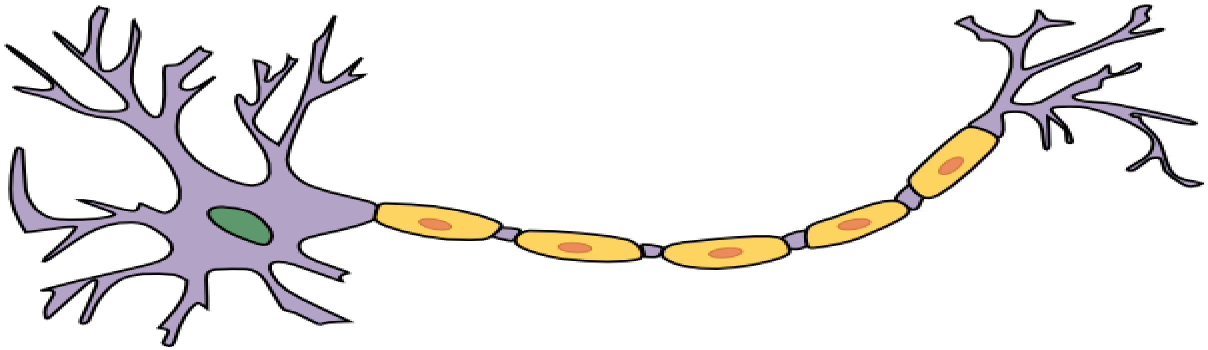
Nerve are composed of

Neurons

Neuron is the <u>functional unit</u> of the central nervous system

Axon	Cell body (soma)	Dendrites



The only tissues in our body that can be excitable (stimulate and respond) are nerves and muscles tissues.

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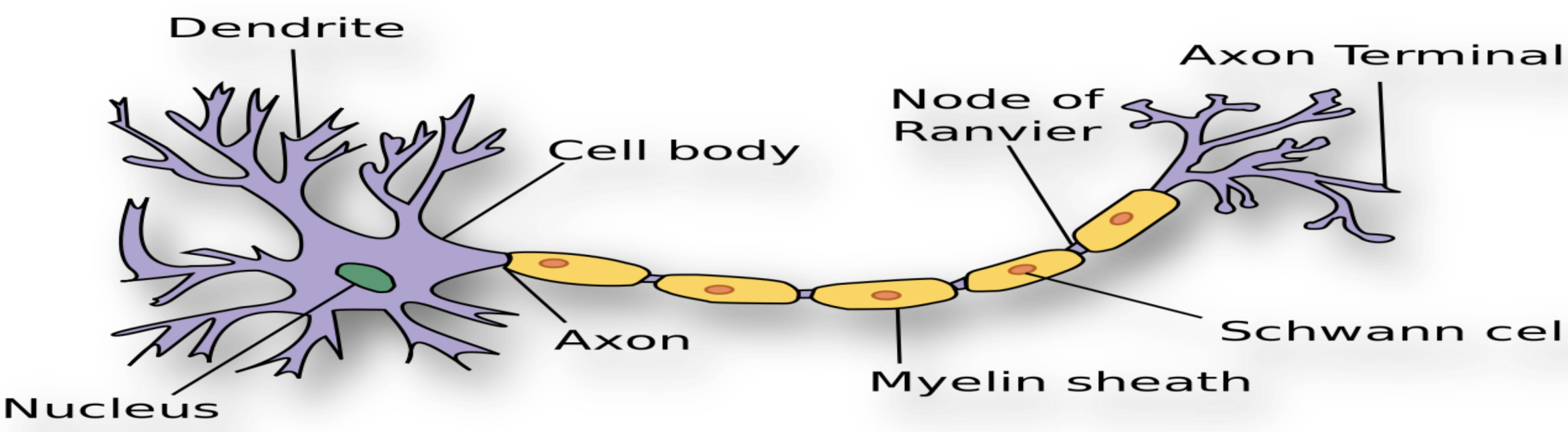
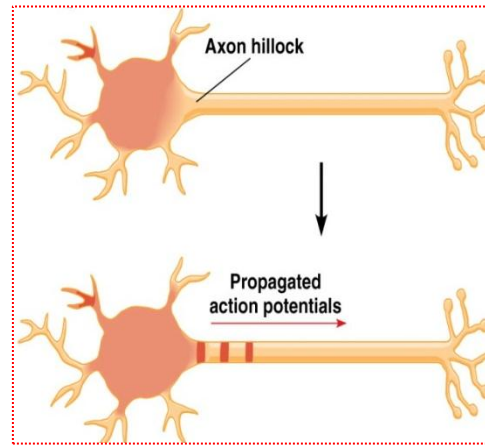


component	Function
Dendrites	**Carry nerve impulses from surrounding to the soma.**
Cell body	**contains organelles such as mitochondria , Golgi apparatus , endoplasmic rectum and nucleus like any other cell.**
Axon hillock	**It is the site where the axon is joined to the soma , it is the site of action potential initiation.**
Axon terminal	**transmit a neurotransmitter from one neuron to another**



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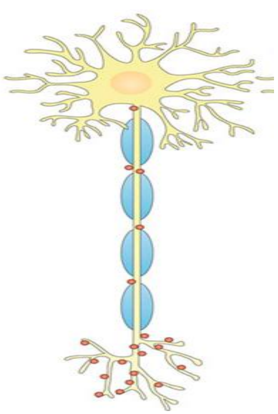
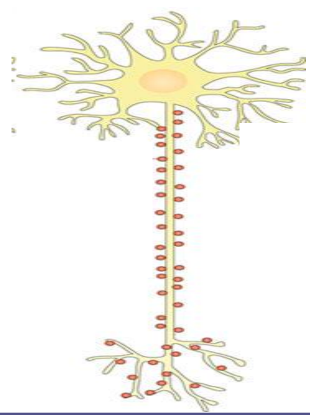
The axon

Histological classification	
Myelinated	**Unmyelinated**
• **Have myelin sheath.** • **Diameter More than 1 um.**	• **Type C Postganglionic autonomic** • **Pain fibers..** • **Diameter less than 1um.**
	

Do you remember the sympathetic & parasympathetic POST ganglionic neurons in ANS lecture ?
They were unmyelinated .
Type c refers to unmyelinated & slow neurons.

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Myelin sheath

Functions

Insulator

"عازل"

Increase conduction velocity

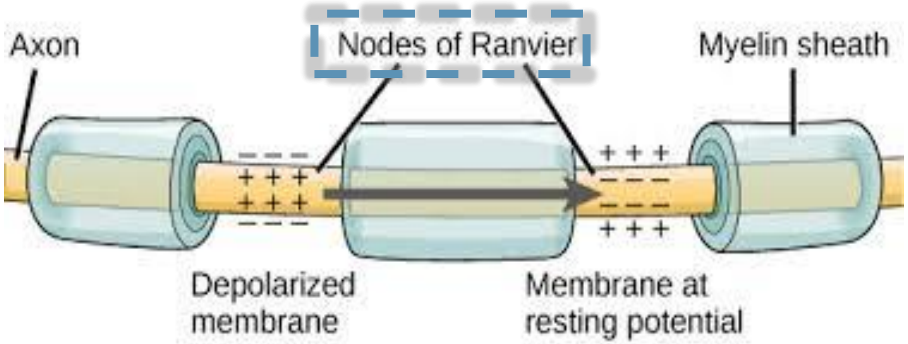
"faster transmission"

Conserve energy for axon

Definition

Myelin sheath :

Formed by Schwann cells which deposit sphingomyelin



[Video]

Node of Ranvier : the gaps between stretches of myelin sheath generated by neuron "unmyelinated / non-insulator"

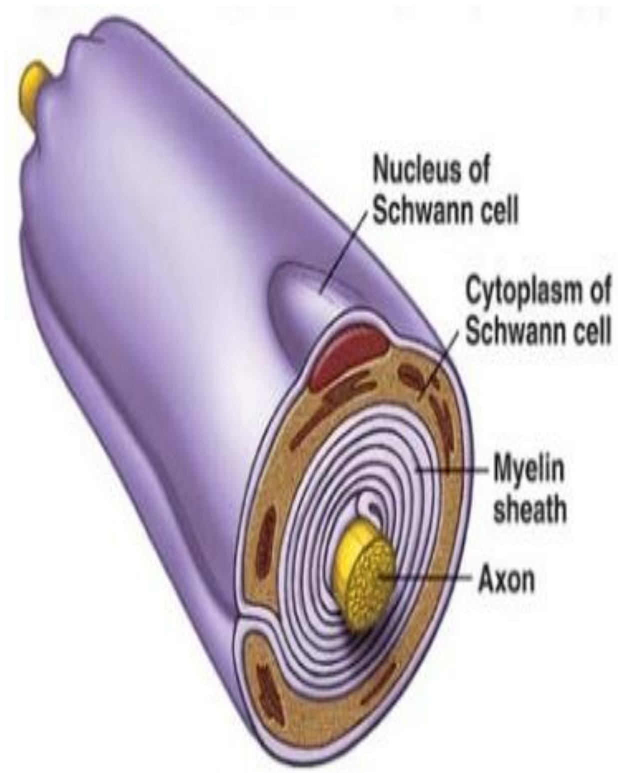
Extra

- How does myelin sheath become insulator ?

The myelin sheath is deposited around the axon by Schwann cells : the membrane of a Schwann cell first envelops the axon. Then the Schwann cell rotates around the axon many times, lying down multiple layers of Schwann cell membrane contain the lipid substance (Sphingomyelin). This substance is an excellent electrical insulator that decreases ion flow through the membrane.

مثال : سلك الكهرباء الغير مغلف بعازل عند لمسه مباشرة "يكهرب"
لكن إذا كان مغلف و معزول"ما يكهرب"

- Shwann cell can be found in myelinated and unmyelinated.



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RMP

- Resting membrane potential (RMP) :
  it is potential difference across membrane during rest (without stimulation)

- What are excitable tissues?
  1- nerves 2- muscles
  Both of them are negatively charged inside (AT RESTING)

- They are called excitable because :

1- produce response when stimulated.
2- their membranes act as electrical capacitor.
- and this will create a difference in charge between inside and outside the cell -

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Ions concentrations

Dr.Mohammed said that it is very important to memorize these numbers

	ICF	ECF
K+	140	4
Na+	14	142
Cl-	9	125
Charged proteins	106.5	-----

- If K+ is above 6 in ECF → Hyperkalemia
- Any type of protein inside the cell is negative and cannot cross cell membrane.

Types of ionic channels

1)Leak channels (diffusion) :

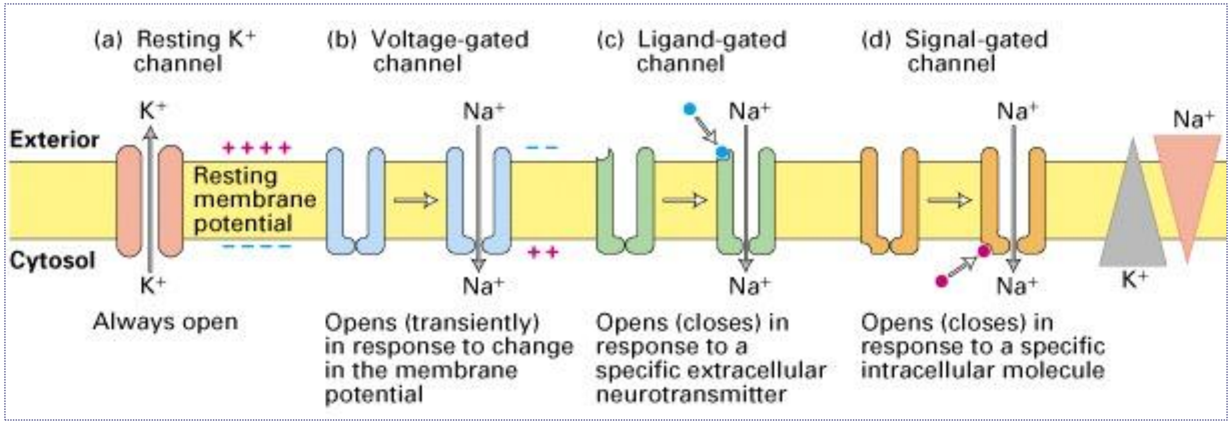
Open all the time "transports ions down their concentration gradient"

2)Voltage-gated channels :

Open when cell membrane is electrically activated "open and close is response to membrane potential"

3) Chemically-gated channels (Ligand-gated channels) :

Open is response to specific ligand "neurotransmitters"



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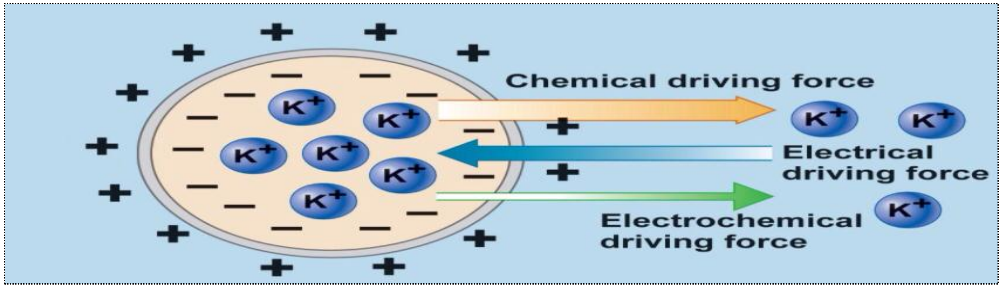
Diffusion potential

- IF we assumed that the membrane is permeable to K+ , and K+ is high inside and low outside the cell ⟶ therefore K+ will leak (diffuse) through K+ leak channels from inside to outside.
- And for every K+ ion diffuse through the membrane, it carry positive charge with it ⟶ build up of **electropositivity(+)** **outside** and **electronegativity(-)** **inside**.
- **We have 2 forces acting on ions:**

1)Diffusional force : push K+ outside the cell "concentration gradient"

2)Electrical force : pull back K+ inside the cell "electrical gradient"

- When these 2 forces are equals to each other ⟶ (**"Equilibrium Potential"**) No net movement of ions.



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Nernst equation

1- The potassium Nernst potential :

Nernst made hypothesis which said that if we suppose that:
- The ECF , ICF contain only K+
- Cell membrane is freely permeable to K+

What will happen?

1. K+ will diffuse down its conc. Gradient (via the K+ leak channels) from **high** to **low** carrying the +ve charge to **outside** the cell.
2. This progressively increasing the **inner negativity** of the membrane .
3. Opposing negative electric potential build up , tending to **prevent the exit of K+**
4. The –ve electrical potential will grow inside until it becomes balance with conc. gradient force
5. No net movement of K+

Nernst equation

- **What is the result ?**

The membrane potential in this case called Nernst potential for K+ it equals = - 94 mV

- **Calculated by the equation :-**

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

* EMF = Electromotive force

The magnitude of this Nernst potential is determined by the ratio of the conc. of that specific ion on the 2 sides of the membrane. The greater the ratio, the greater the tendency for the ion to diffuse in one direction. Therefore, the greater the Nernst potential required to prevent additional net diffusion. The equation written above called the Nernst equation.
The sign of the potential is ve+ if the ion diffusing from inside to outside is negative ion, and it is negative if the ion is positive.

Nernst equation

2- The Sodium Nernst potential :

Nernst made hypothesis which said that if we suppose that:

- the ECF , ICF contain only Na+

-Cell membrane is freely permeable to Na+

What will happen?

1. Na+ will diffuse down its conc. Gradient , from high to low , carrying the +ve charge to inside the cell
2. This progressively decreasing the **inner negativity** of the membrane .
3. Opposing negative electric potential build up , tending to **prevent the entire of Na+**
4. The –ve electrical potential will grow inside until it becomes balance with conc gradient force .
5. No net movement of Na+

Nernst equation

- **What is the result ?**

The membrane potential in this case called Nernst potential for Na+ it equals = +61 mV

- **Calculated by the equation :-**

$$\text{EMF (mV)} = +61 \log \text{Na+} \frac{\text{Conc. Inside}}{\text{Conc. outside}} = +61 \text{ mV}$$

- The Nernst Equation Describes the Relation of Diffusion Potential to the Ion Concentration Difference Across a Membrane.
- Nernst potential :

Is the diffusion potential level across a membrane that exactly opposes the net diffusion of a particular ion through the membrane.

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The resting membrane potential of nerves

Resting membrane potential (RMP)

Values:

-70 to -90 mv

(depends on the nerve if it is large -90, small -70)

The membrane is polarized

because we separate the positive charge from the negative charge by the cell membrane

Is potential difference across membrane during rest

(without stimulation)

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The resting membrane potential of nerves

The 3 factors that make the inside of the cell negative and give the RMP the value of -70 to -90 mV :

Causes of RMP

① K+ leak channels are more effective than Na+ leak channels :

RMP is 100 times more permeable to K+ than Na+.
K+ tends to leak out of the cell down its concentration gradient, carrying +ve charge with it.

(through K leak channels)

② very small amount of Na+ diffuses into the cell down its concentration gradient. The cell membrane only slightly permeable to Na+.

(through Na+ leak channels)

③ Large intracellular anions :

Non-diffusible anions (proteins, sulphate and phosphate ions) cannot leave the cell.

→ have much higher concentration inside the cell than outside it

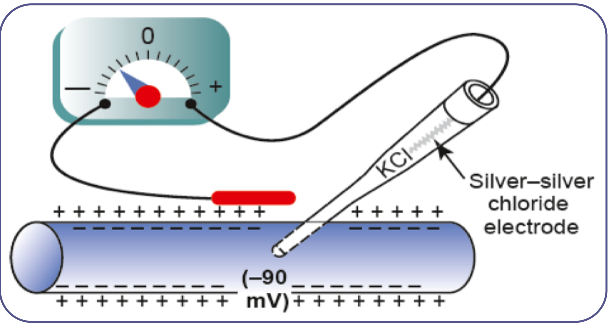
④ Active Transport :

Na+-K+ pump maintain concentration gradients of K+, and Na+ between the two sides of the cell membrane.

(3 Na+ pumped out in exchange for 2 K+ pumped in)

Measuring membrane potential

To Measuring membrane potential : by the (voltmeter)



A small filled pipette (microelectrode) containing electrolyte solution is inserted inside the nerve fibre & another electrode is placed in the outside

membrane potential difference between inside & outside is measured using the voltmeter

All excitable cells exhibit an electrical potential (voltage) called resting cell membrane potential (-70 to -90mV)

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The resting membrane potential of nerves

Origin of RMP

1) Contribution of K+ diffusion potential :

K+ diffusion contributes far more to membrane potential

leak channels:
K+ out flux to outside causing –ve inside (from high conc inside to outside carrying +ve charge with it :
Electropositivity outside
Electronegativity inside

2) Contribution of Na diffusion potential:-

Na+ leak channels Slight membrane permeability to Na+ ions in leak channels from outside to inside

3) Na+-K+ pump

maintain concentration gradients of K+ and Na+ between the two sides of the cell membrane.

Extra

في المختبر : أخذنا nerveمن ضفدع ثم وصلناه بـ Electrodes ثم وصلناها بـ Voltmeter :

the value of resting membrane potential is (-70) , why it is minus 70 ?

First we know that :

- The cell is contain a large amount of (K+) inside.
- K is a positively charged
- The cell also contain a little amount of protein and phosphate which are negatively charged .
- The cell membrane has a HIGH permeability for (K+)

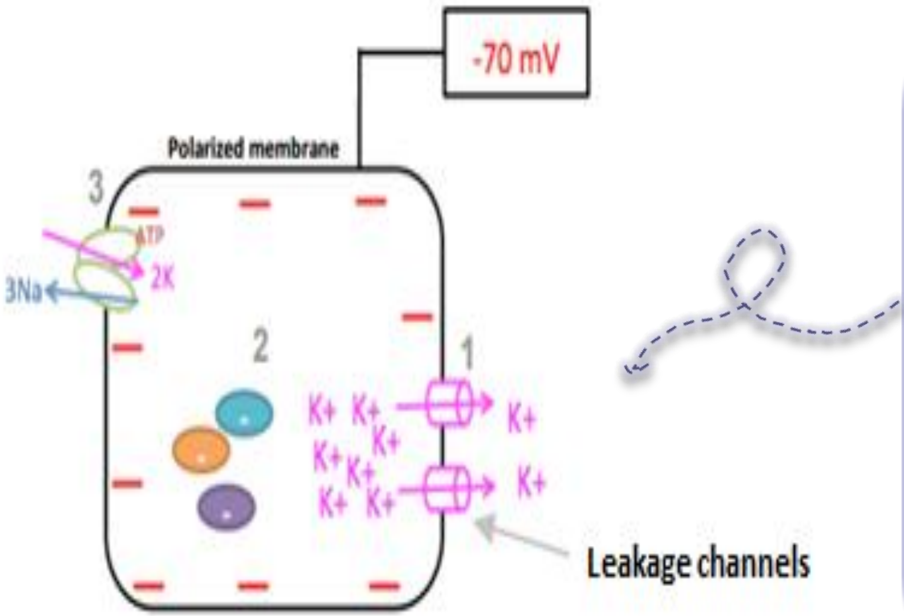
لديه نفاذية اختيارية عالية للبوتاسيوم ، بينما تكون نفاذيته قليلة جداً للصوديوم

(permeable to K+ 100 times more than Na+)

So what will happen ?

- The (K+) will outflux from the cell through a channel called :
  potassium leakage channel.
- protein & phosphate will stay inside the cell which will make it negatively charged.
- All cell membranes of the body have a powerful Na+/K+ pump that transports Na+ ions to the outside and K+ to the inside. More positive charges are pumped to the outside than to the inside (3 Na+ Vs. 2 K+) leaving a net deficit of positive ions on the inside which causes Negative potential inside the cell membrane.
  داخل الخلية سالب بالنسبة لخارجها نظراً لأن الخارج يزيد عن الداخل بأيون واحد موجب، وهذه جميع الأسباب التي تجعل الإشارة سالبة.

Extra



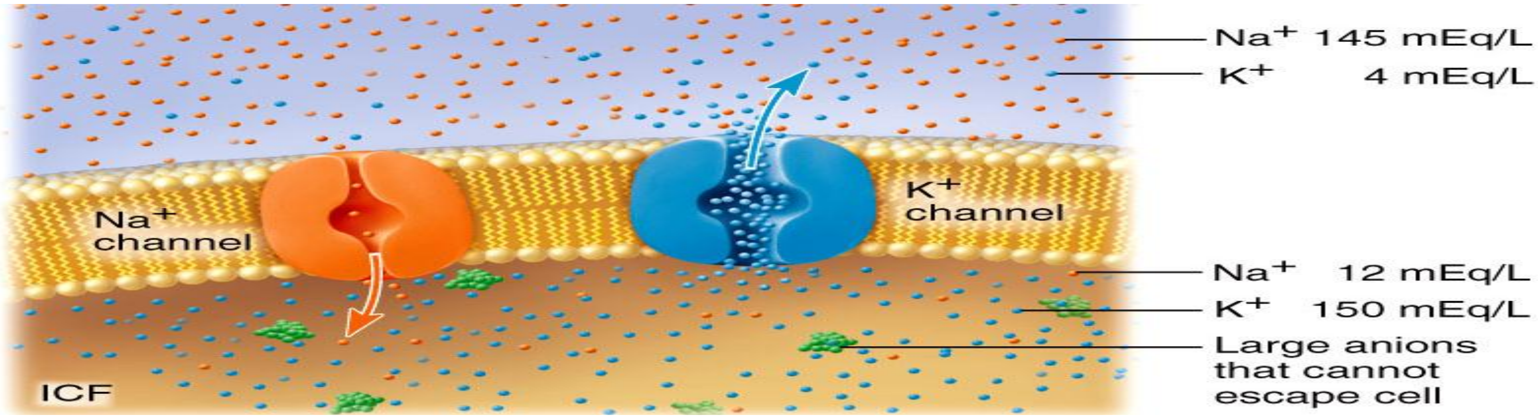
A nerve cell in resting state (without any stimulation) connect to a voltmeter that shows a negative charge (-70 mv), which means that the inside of the cell is negative comparing to the outside.

Charge measured in millivolts

1- Efflux of K+ (High leakage of potassium).
2- Large negatively charged molecules (such as protein, sulphate and phosphate).
3- Sodium-Potassium pump.

What does it mean when a neuron "fires"?

- **Recall resting potential of all cells :**
  - High K+ in; high Na+ out.
  - Cell is polarized
  - Cell overall negatively charged inside due to molecules like proteins (RNA, DNA).
  - Charge measured in millivolts
    - **Potential** = difference in charge across PM
    - **Current** = flow of charge (ions) from one point to another



Firing = excitability = action potential = nerve impulse

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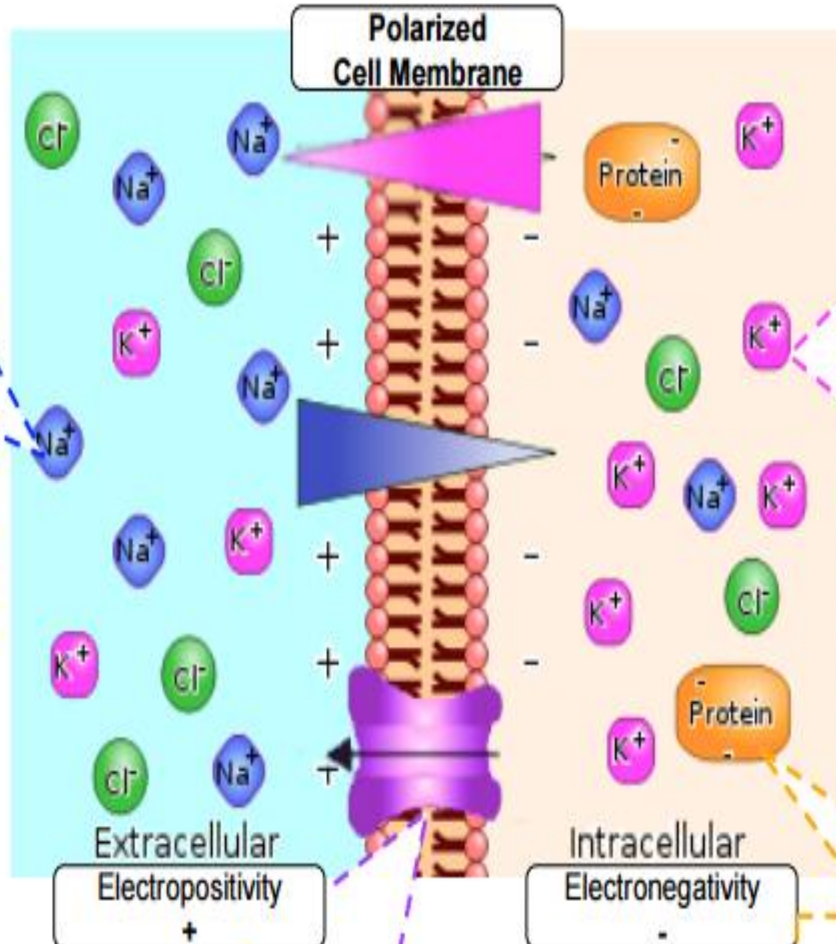
Low Na+ Permeability

-Small amount of *Na+* diffuse into cell (through *Na+ leak channels*)



High K+ Permeability

-RMP is 100 time more permeable to *K+* than *Na+*

-*K+* outflux outside cell carrying +ve charge (through *K+ leak channels*)

Na+/K+ Pump

-Maintain conc. gradients of *K+* and *Na+* between two sides of membrane

Non-Diffusible Anions

-*Proteins, Sulphate,* and *Phosphate ions* can't leave cell. (Large molecules)

Changes that occur through the nerve after stimulation by threshold (effective) stimulus

1- Electrical changes
(nerve action potential)

2- Excitability changes

3- Thermal changes

4- Chemical changes

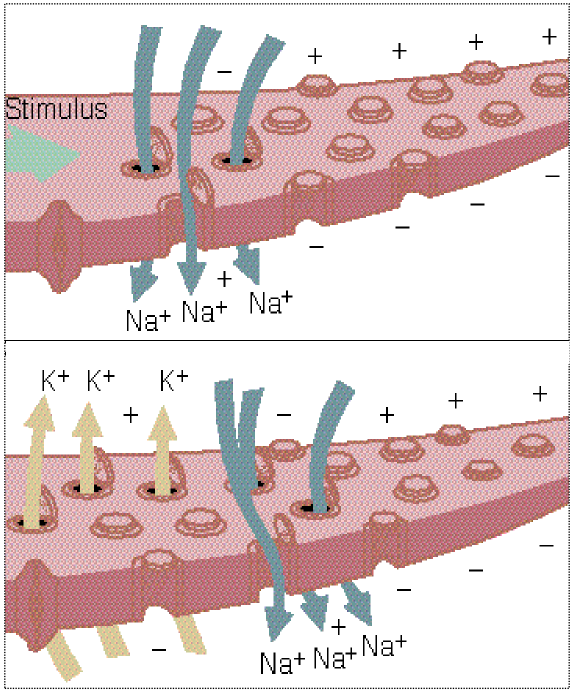
المقصود هنا هو ما يحدث عن استثارة العصب ، مثلاً حين ترى أسداً يحدث أولاً أن تصل السيالات العصبية للمركز العصبي (الدماغ والحبل الشوكي) لتخبره بوجود خطر ومن ثم يحدث استثارة للعصب وهو الإحساس بالخطر والهروب في هذا المثال ، يتبع ذلك ارتفاع في درجة حرارة الجسم يليه تغيرات كيميائية كإفراز كإفراز الـnoradrenaline.

Action potential

▪ Action potential :

It is sudden reversal of membrane polarity produced by a stimulus to produce a physiological effect such as:

- Transmission of impulse along nerve fibres.
- Release of neurotransmitters.
- Muscle contraction.
- Activation or inhibition of glandular secretion.



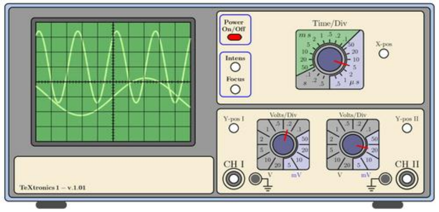
If the cell is equally charged (mean : the negative charged out side the cell equal to the positive charged inside the cell) mean : dead cell
إذا كانت الخلية متعادلة (متساوية الشحنات في الخارج والداخل) فهذا يعني أنها خلية ميتة
كون الخلية في حالة سكون لا يعني أنها متعادلة **(Resting ≠ equally charged)**

الغرض من استثارة الأعصاب هو إنتاج استجابة لغرضٍ ما ، كنقل الإشارات العصبية من خلال الأعصاب ، إفراز ناقلات عصبية مثل الأدرينالين والنور ادرينالين ، تثبيط أو تحفيز إفراز بعض الهرمونات ، أو انقباض العضلات.

Electrical changes
The nerve action potential

- **Electrical changes :** It is potential difference along nerve membrane after stimulation by threshold (effective) stimulus.

- **Oscilloscope :** Machine used to measure rapid changes in membrane potential. "Gives curve for impulses voltage"



- Nerve signals (impulses) are transmitted as nerve action potentials conducted along the nerve fiber as a wave of depolarization to its end.

The factors necessary for nerve action potential are :

1. **voltage gated K+ channels**
2. **voltage gated Na+ channels**
3. **Threshold stimulus.**

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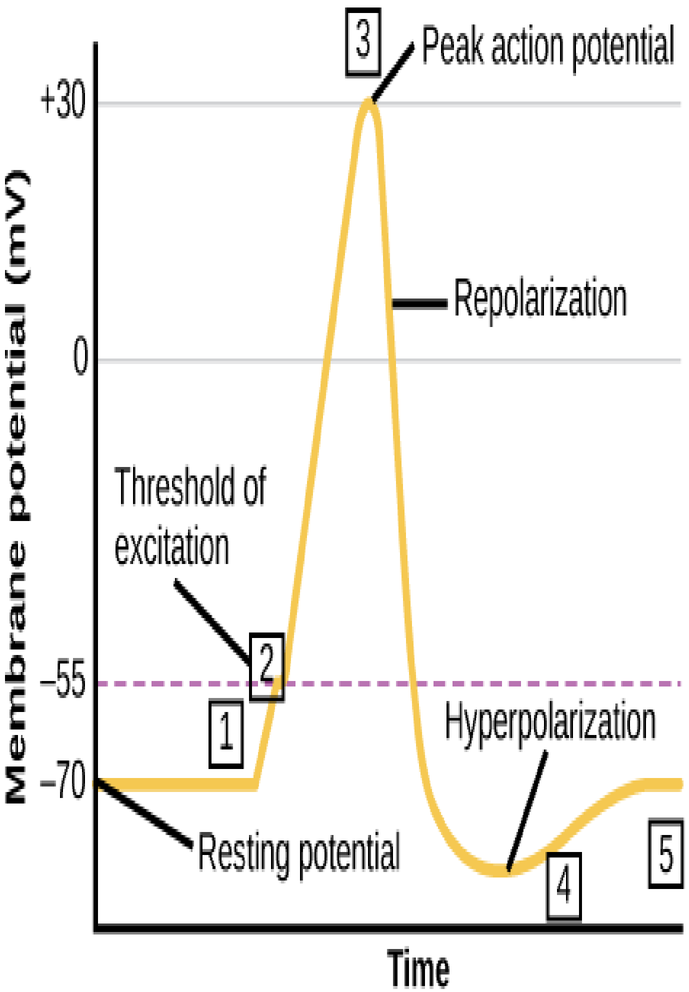
Action potential



كبداية مبسطة :

1- أولاً كانت الخلية في حالة سكون بدون أي استثارة resting membrane potential حيث يكون التيار مساوي لـ 70 mV- وتكون الخلية polarized

2-عند حدوث استثارة ستدخل الخلية في حالة تغير في التيار لإيصال السيالات العصبية ليعطي المخ استجابة لهذا المؤثر ، فيزيد التيار ليصبح 55- mV ويسمى threshold of excitation فتدخل الخلية في طور الـ Depolarization، حيث تبدأ تُفتح بوابات الصوديوم وتدخل أفواج من خلال voltage gated Na channels حتى تصل لـ reversal potential

3- عند نقطة الـ reversal potential تُقفل بوابات الصوديوم وتُفتح بوابات البوتاسيوم حيث تبدأ الخلية الدخول في طور الـ repolarization عند تيار قدره +35 mV

4- يبدأ ينخفض التيار مجدداً ليصل لمستوى مقارب أو أقل من حالة السكون ، ليصل تقريباً 90 mV- ويسمى في هذه الحالة hyperpolarization محاولاً العودة لحالة السكون من خلال Na & K pump

Video

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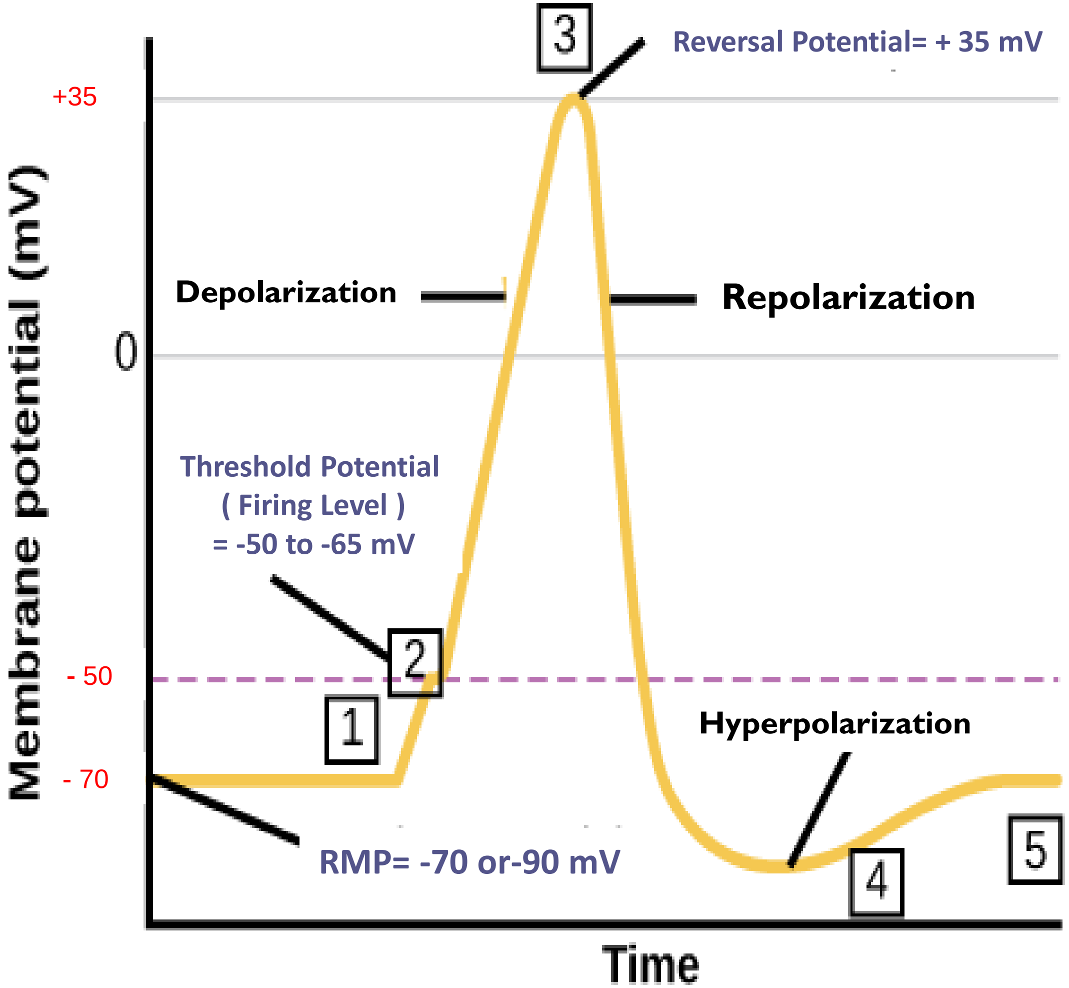
Action potential

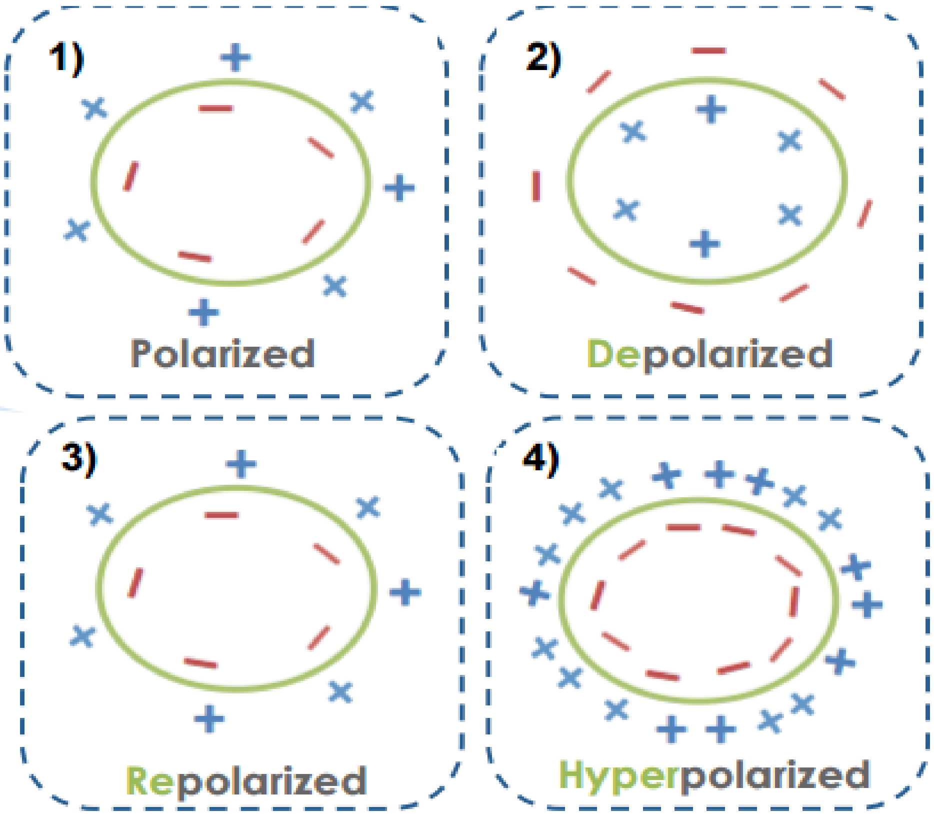


- We need to start from the baseline "Resting State of the cell" at the RMP.

A threshold Stimulus will lead to :

1) Depolarization.
2) Repolarization phase.
3) In <u>some</u> neurons there is a 3rd phase called : Hyperpolarization

Video



EXTRA

1) The cell membrane separates the ve+ & -ve charges , at rest state (RMP)

2) Now, there is an electrical stimulation +ve charges (IN) -ve charges (OUT).

3) The cell re-polarized it self : -ve charges (IN) +ve charges (OUT).

4) Increasing the number of charges inside and outside the cell, it may occur and may not.

فلنفترض أن هنالك شخص غاضب وكاتمٌ لغيظه " neuron at rest"
ويُظهر للناس أنه سعيد وإيجابي، ذات مرة استفزّه واستثاره كلام الناس عنه
مما أخرجه عن طوره فأخرج ما بجعبته من طاقة سلبية "Depolarization"
بعدها شعر بتأنيب الضمير وأدرك أنه تسرع لذلك قرر أن يعود إلى حالته السابقة
ويحتفظ بطاقته السلبية لنفسه"Repolarization"
وبسبب تأنيب الضمير المفرط ، زادت السالبية داخله وبدأ ينشر الإيجابية
ويتعامل مع الناس بود واحترام "Hyperpolarization"

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Summary of events that causes AP

1-Initiation of Action Potential (AP) :

- -70 to -90 mv is the resting potential.
- Threshold stimulus open voltage gated Na channels and Na influx rises resting potential from -90 towards zero (gradual depolarization).
- As membrane potential raises, open more Na channels & more Na influx (+ve feedback) until all voltage gated Na channels open.

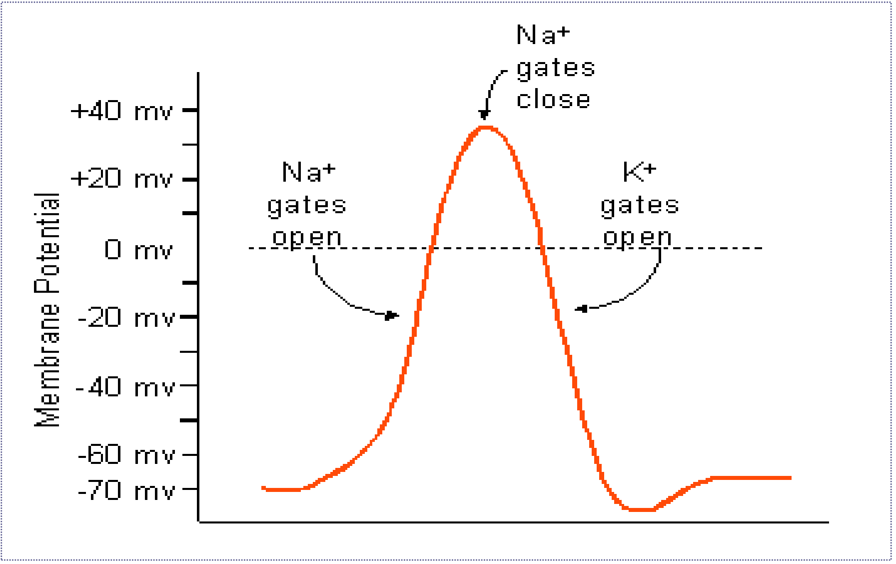
What opens the voltage gated channels ?
Opened by a stimulus strong enough to depolarize them to threshold.

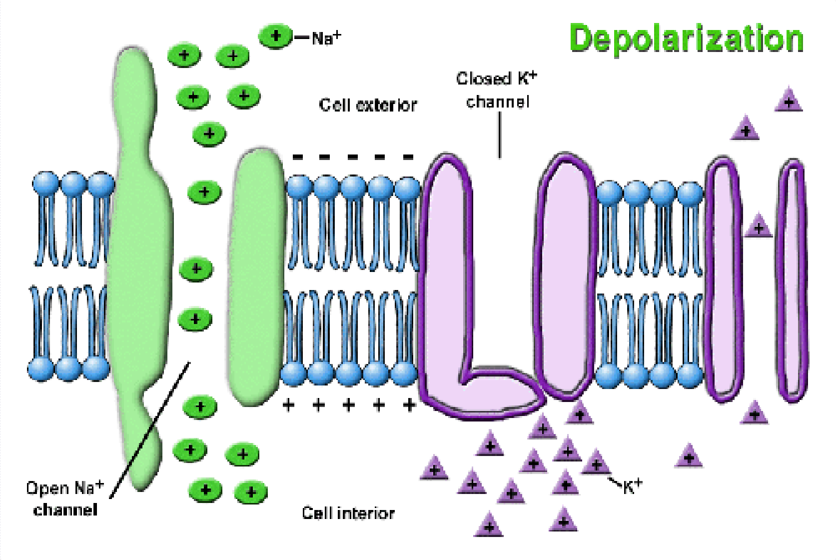
Resting state this is the resting membrane potential before the action potential begins. The membrane is said to be "polarized" during this state because of the -70 or -90 mv negative membrane potential that is present.

Summary of events that causes AP

2- Depolarization :

- Occurs when membrane potential reach zero value to reach + 35 mv.
- At + 35 mv all Na channels begin to close suddenly (Depolarization ends).





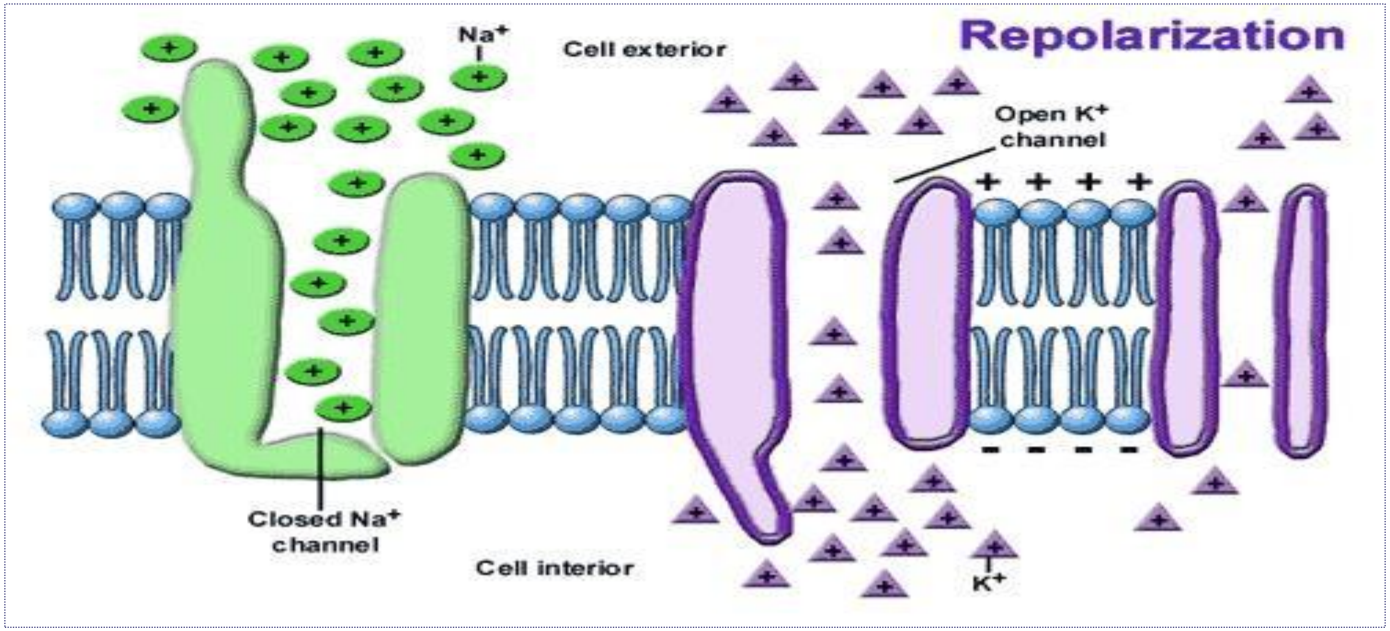
Depolarization state at this time, the membrane suddenly becomes permeable to sodium ions, allowing tremendous number of positively charged sodium ions to diffuse to the interior of the axon by the voltage gated sodium channel.

Video

Summary of events that causes AP

3- Repolarization :

Due to high K conductance(flow) to outside (K outflux) by opening of all voltage gated K channels (causes negativity inside).



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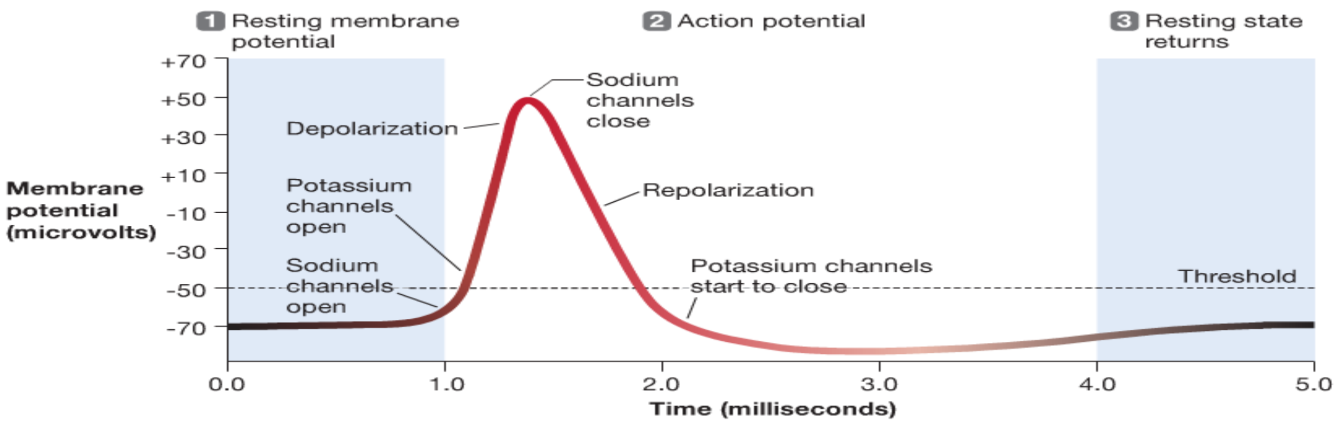
Summary of events that causes AP

4- Hyperpolarization. Why? Because K channel did not close. Video

5- Na-K pump now start to move Na out & K in against their concentration gradient, so the RMP is resumed and the membrane is ready for another stimulus.



Depolarized : المنحنى يتجه لأعلى
Repolarized : المنحنى يتجه لأسفل
Hyperpolarized : resting state المنحنى يكون تحت الـ

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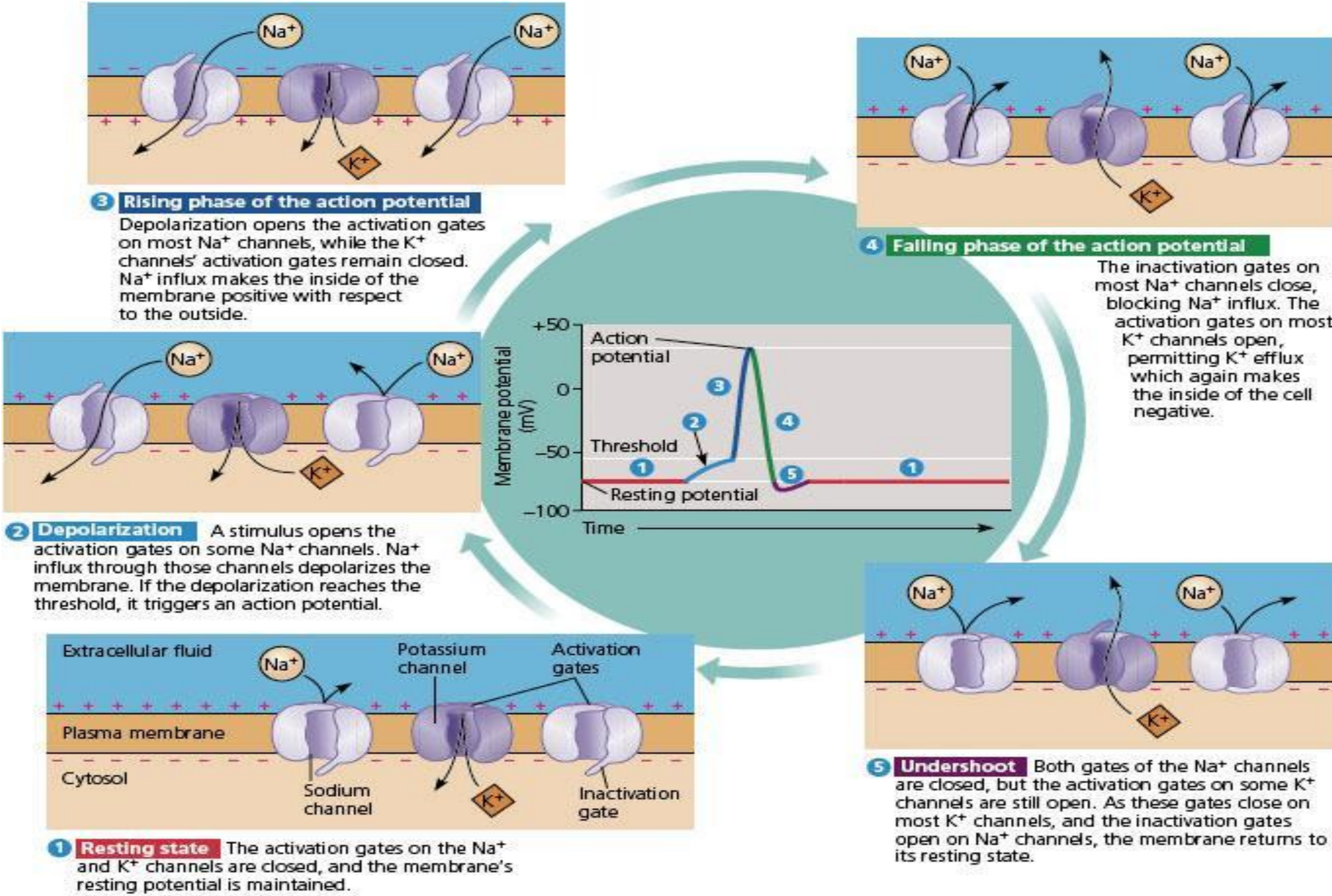
Na+
K+
3 Rising phase of the action potential
Depolarization opens the activation gates on most Na+ channels, while the K+ channels' activation gates remain closed. Na+ influx makes the inside of the membrane positive with respect to the outside.
4 Falling phase of the action potential
The inactivation gates on most Na+ channels close, blocking Na+ influx. The activation gates on most K+ channels open, permitting K+ efflux which again makes the inside of the cell negative.
Membrane potential (mV)
+50
0
−50
−100
Action potential
Threshold
Resting potential
Time
2 Depolarization
A stimulus opens the activation gates on some Na+ channels. Na+ influx through those channels depolarizes the membrane. If the depolarization reaches the threshold, it triggers an action potential.
Extracellular fluid
Plasma membrane
Cytosol
Potassium channel
Activation gates
Sodium channel
Inactivation gate
1 Resting state
The activation gates on the Na+ and K+ channels are closed, and the membrane's resting potential is maintained.
5 Undershoot
Both gates of the Na+ channels are closed, but the activation gates on some K+ channels are still open. As these gates close on most K+ channels, and the inactivation gates open on Na+ channels, the membrane returns to its resting state.

Threshold stimulus

Threshold stimulus could be :

- **Threshold stimulus** → If a stimulus is strong enough to move RMP from its resting value (-70mV) to the level of (-55mV) which leads to production of an action potential.
- **Subthreshold stimulus** → Stimulus that result only in local depolarization.
- **Suprathreshold stimulus** → greater than a threshold strength

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All or nothing

All or nothing principle

Once threshold value for excitation is reached a full action potential produced, its intensity can not increased by increasing stimulus intensity

* Explain :

if the threshold was (50) → then when you give 50 or more both will make the **same** action potential , but when you give less than 50 it will not make any action potential .. So :

- Suprathreshold → action potential
- Threshold → action potential
- Subthreshold → no action potential

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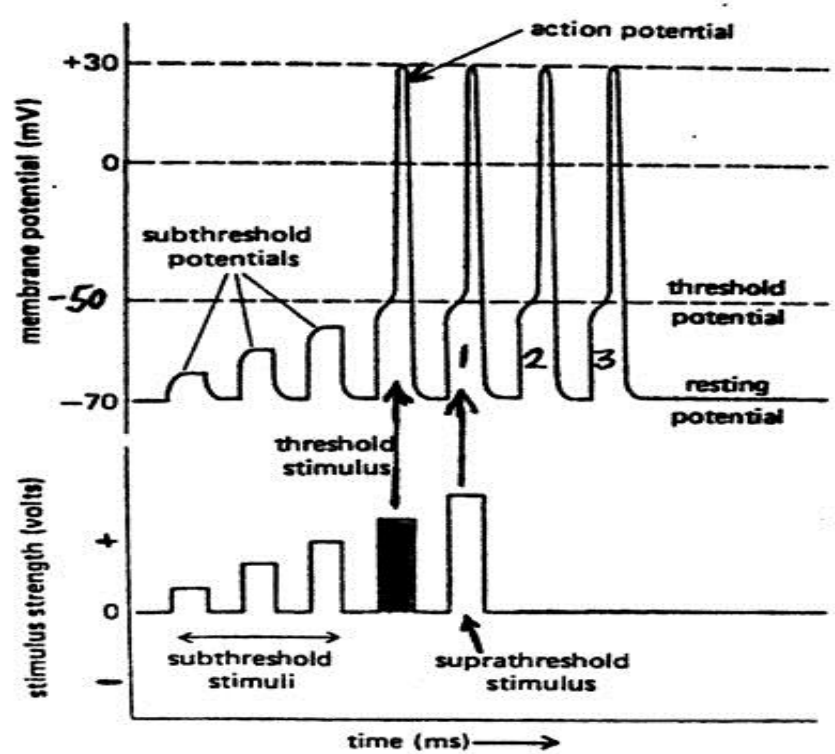
Extra

1. when we give a really weak stimulus (slowly going to a stronger one) we have this small little response labeled subthreshold potential. not an action potential it is **"local depolarization"**

2. If we keep giving it a stronger and stronger stimulus, strong enough to pass the threshold potential

3. Any stimulus greater than threshold give us a repeated action potential called **Suprathreshold** potential



In this we are shown a neuron and it shows how different intensities of stimuli affect the voltage changes.

Example

If something tickles your nose but it's not enough to make you sneeze, that's a subthreshold stimulus. If something tickles your nose just enough to make you sneeze once, that's a threshold stimulus. If something tickles your nose intensely and makes you sneeze three times in a row, that's a suprathreshold stimulus.

What will happen if another stimulus is given ?

- Refractory period:

  - few <u>milliseconds</u>
  - Time during which can't stimulate neuron a second time.
  - Happens until recovery of resting potential.
  - Has 2 stages :

Absolute refractory period

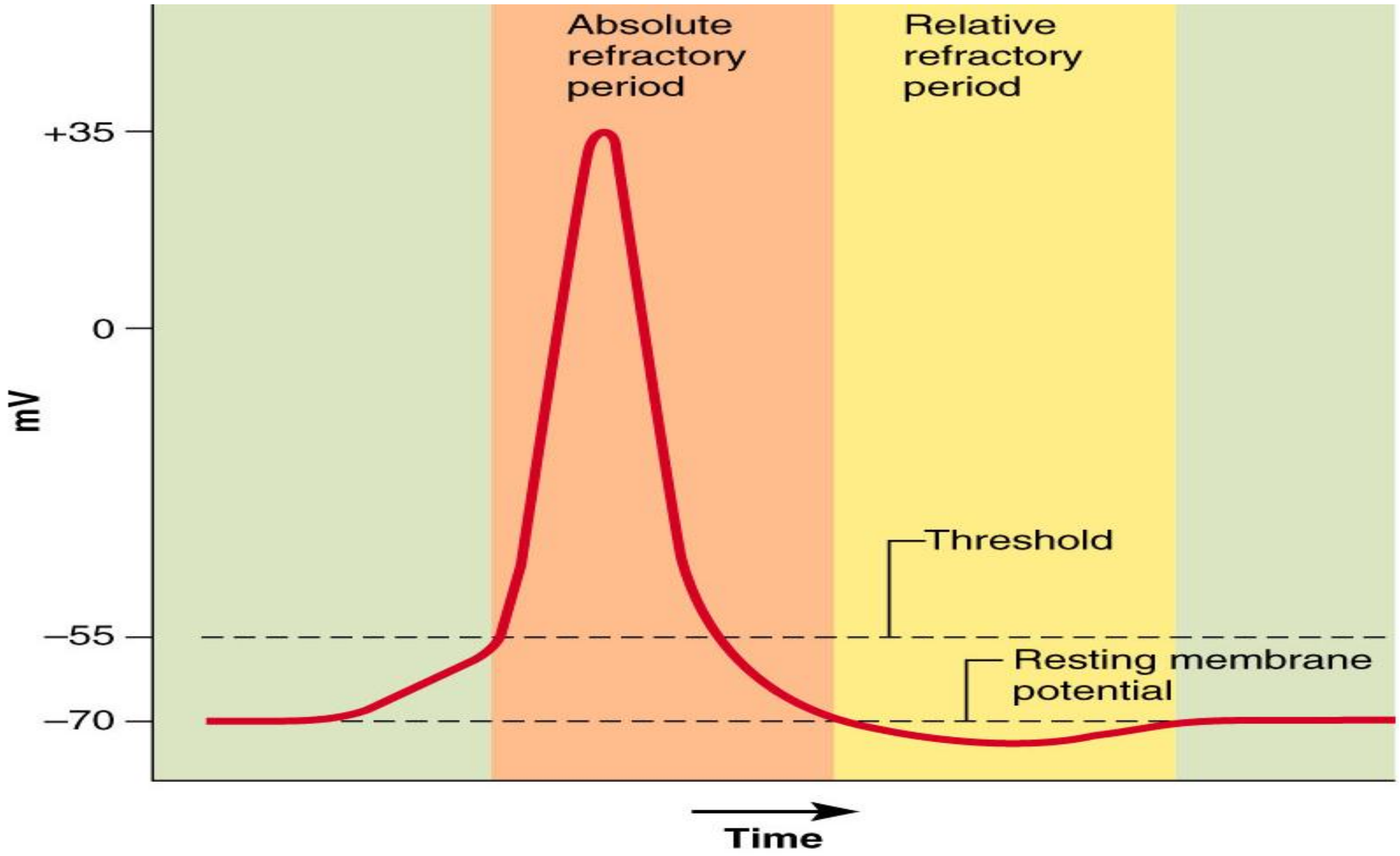
- **No new action potential possible**

Relative refractory period

- **Can trigger new action potential if stimulus is very strong**

Refractory period: This is the time during which another stimulus given to the neuron (no matter how strong) will not lead to a second action potential. Thus, because Na+ channels are inactivated during this time, additional depolarizing stimuli do not lead to new action potentials. The absolute refractory period takes about 1-2 ms.

Video



مثال :
عندما تُطلق امرأة ذات حسب وجمال للمرة الثالثة وجب عليها قضاء فترة العدة "Absolute refractory period" حيث أن جميع عروض الزواج "stimulus" في تلك الفترة لا يمكن قبولها (تكون في حالة الـ inactivate)
بعد قضاء عدتها "Relative refractory period" لا تقبل هذه المرأة إلا عرض زواج من رجل ذا جاه وسلطة ومال "strong stimulus" .

Voltage-Gated Sodium Channel

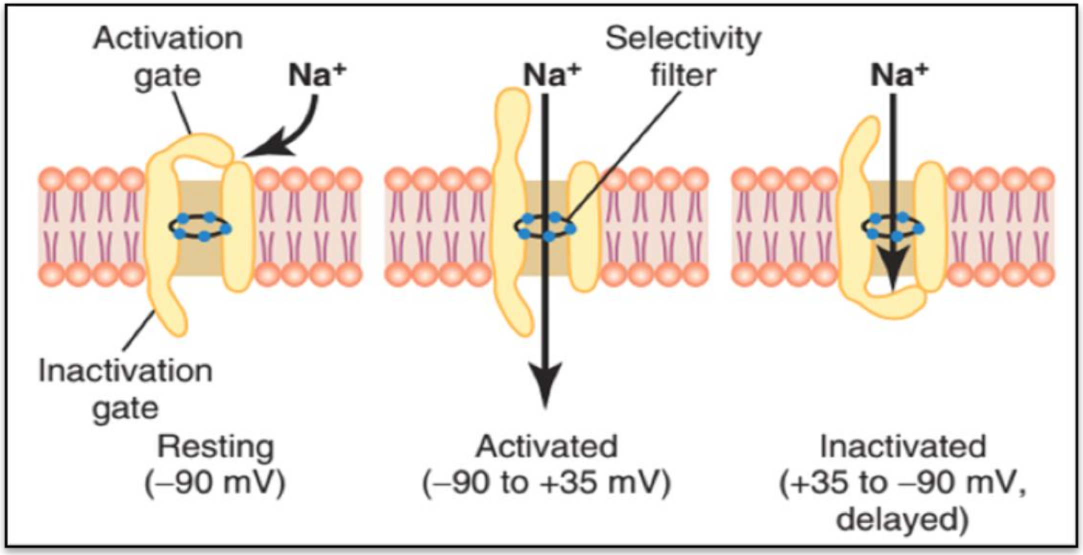
- This channel has two gates :

  1) one near the <u>outside</u> of the channel called **activation gate.**
  2) another one near the <u>inside</u> of the cell called **inactivation gate.**

Remember :
inside / inactivation

this channel has 3 states

- **Inactivated state**
- **Activated state**
- **Resting state**



This photo simply shows successive activation and inactivation of the sodium channel when the resting membrane potential changes from a negative to a positive value.

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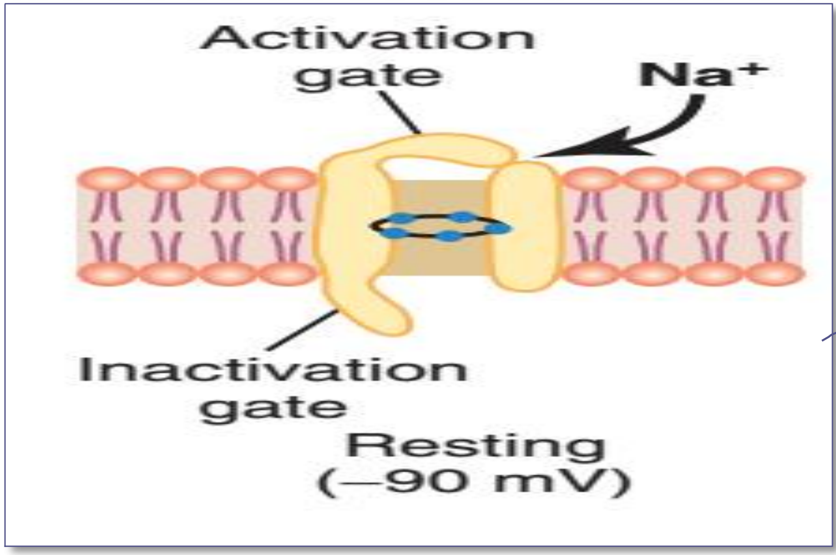
Video

Voltage-Gated Sodium Channel

1. Resting state :

(in the resting cell when the MP = RMP = -70 to -90 mV).

- The activation gate is closed
- This prevents entry of Na+ to the interior of the cell through this gate.



During rest the inactivation gate is open while the activation gate is closed.

Video

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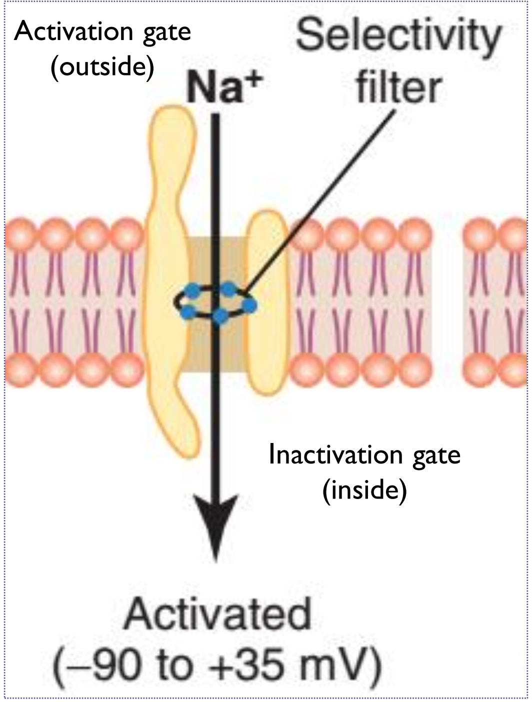
2. Activated state :

when a Threshold Depolarizing Stimulus moves the MP from its **resting value** (-90 mV) to its **Threshold value** (-65 to -55mV).

- This opens the activation gate , and now the Na+ channel is said to be in the **Activated State**.
- In this case **BOTH** activation gate & inactivation gate are open.
- permeability to Na+ becomes increased 500 to 5000 times → Na+ influx
- Na+ flows into the cell in large amounts.



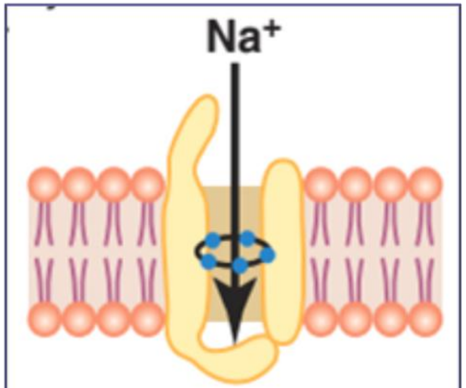
Activation of Sodium Channel:
When the membrane potential becomes less negative than during the resting state (rising from -90 to 0) at first it will reach a voltage usually between -70 and -50 millivolts and that will cause a sudden change in the activation gate, and finally opening it.
During this state, Sodium ions can pour inwards through the channel increasing the permeability of the membrane.

Voltage-Gated Sodium Channel

3. Inactivated state :

A few milliseconds after the activation gate opens , the channel becomes inactivated.

- At the peak of AP the **inactivation gate** will close.
- The **inactivation gate** will not open by a second stimulus and the cell becomes Refractory "ممانِعة" to another stimulation .
- This goes on until the MP has gone back to its resting (RMP) level (-70 to -90mV).
  - in this case , while the **activation gate** is still open
  - the **inactivation gate** is closed.



Inactivated (+35 to –90 mV, delayed)

Inactivation of Sodium Channel:
The same increase in voltage that opens the activation gate also closes the inactivation gate. However, the inactivation gate closes shortly after the activation gate is opened. Because the change that causes the inactivation gate to close is a slightly slower process than the one that opens the activation gate.
Thus, sodium ions can't flow in anymore. Which leads the membrane potential (MP) to recovery phase (which is the repolarization process) and then the resting membrane state (RMS).

* NOTE:
the inactivation gate won't reopen until MP returns to the original RMS level. So, its not usually possible for sodium channels to open again without repolarizing the nerve fiber.

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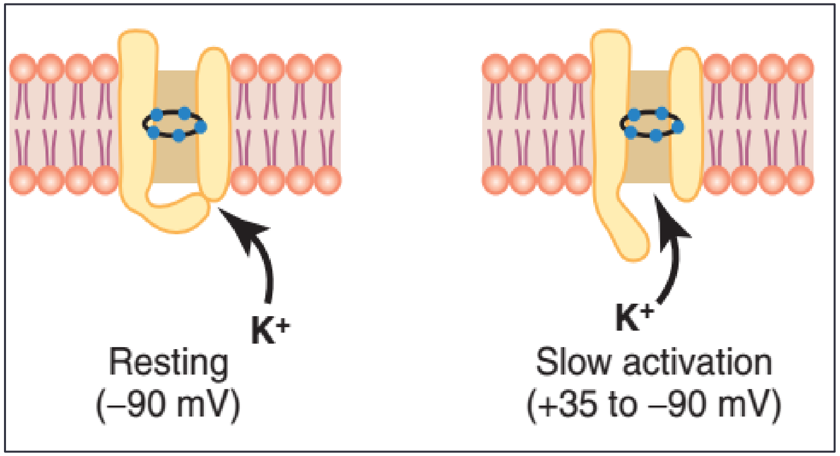
Video

Voltage-Gated Potassium Channel

❖ Has only one gate.

- **Two states of voltage gated potassium channel :**

During Activation state:
When membrane potential rises from -90 to 0, this voltage change will cause the gate to open allowing potassium ions to flow out.



During resting state:
The gate is closed and potassium ions cannot pass through the channel.

- Shortly **after depolarization** , when the Na+ channel begins to be **inactivated** the K+ channel opens → **K+ exits** (called K+ Efflux) → **Repolarization**

Because of the slight delay in opening the potassium channels, they open just as sodium channels begin to close due to inactivation. Thus, the decrease in sodium entry to the cell and the increase in potassium exit from the cell combine to speed up the repolarization process leading to full recovery of the resting membrane potential. Less sodium in + More potassium out = faster repolarization

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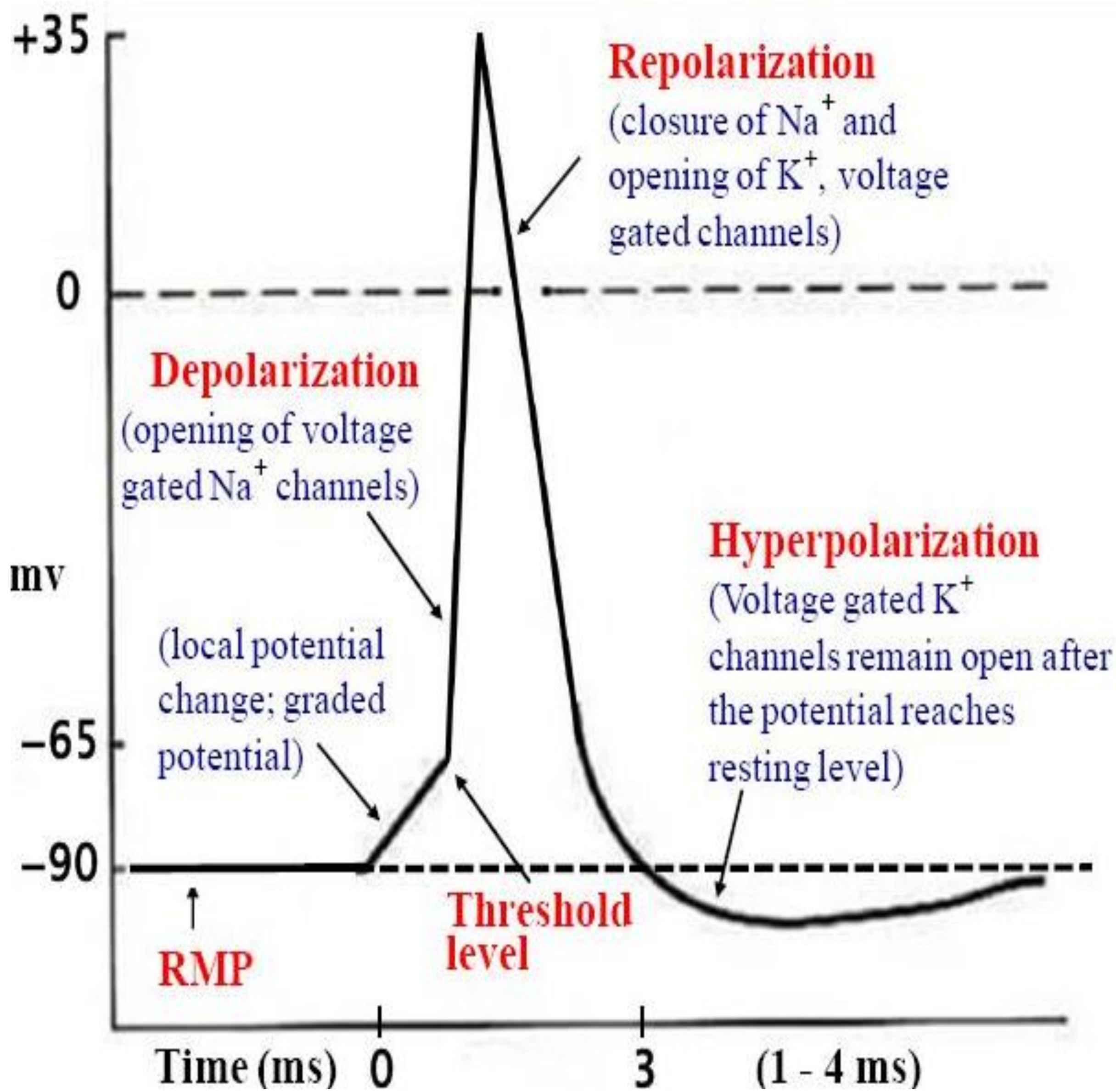
بوابات الصوديوم :
سريعة الفتح، سريعة الإغلاق
فبمجرد حدوث تغير في الفولت
تُفتح البوابة ويدخل فوج من
الصوديوم.

sodium voltage-gated channel opens and closes in only milliseconds. And if it reaches 35mV and doesn't close it may cause epilepsy (الصرع)

بوابات البوتاسيوم :
بطيئة الفتح ، بطيئة الإغلاق.
potassium voltage-gated channels open and close slowly and that's what cause hyperpolirization.



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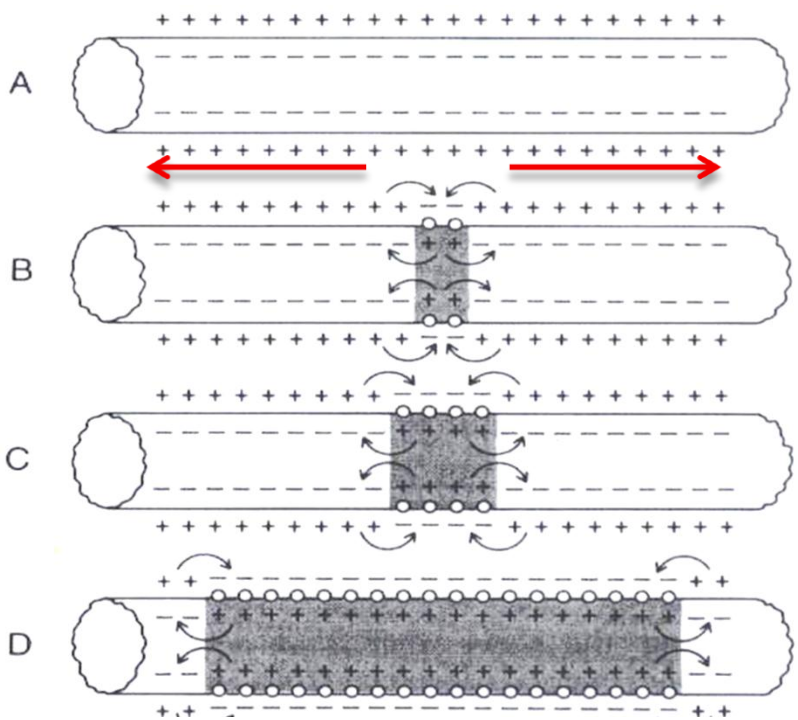
Direction of AP Propagation (Conduction)

- **Artificial condition :**

Electrical stimulation in the **laboratory** the action potential propagates in both directions .



- **Normally :**

Action potential starts in **axon hillock** and propagates distally in one direction

Why does the AP starts at axon hillock?
Because it is full of voltage gated Na channels

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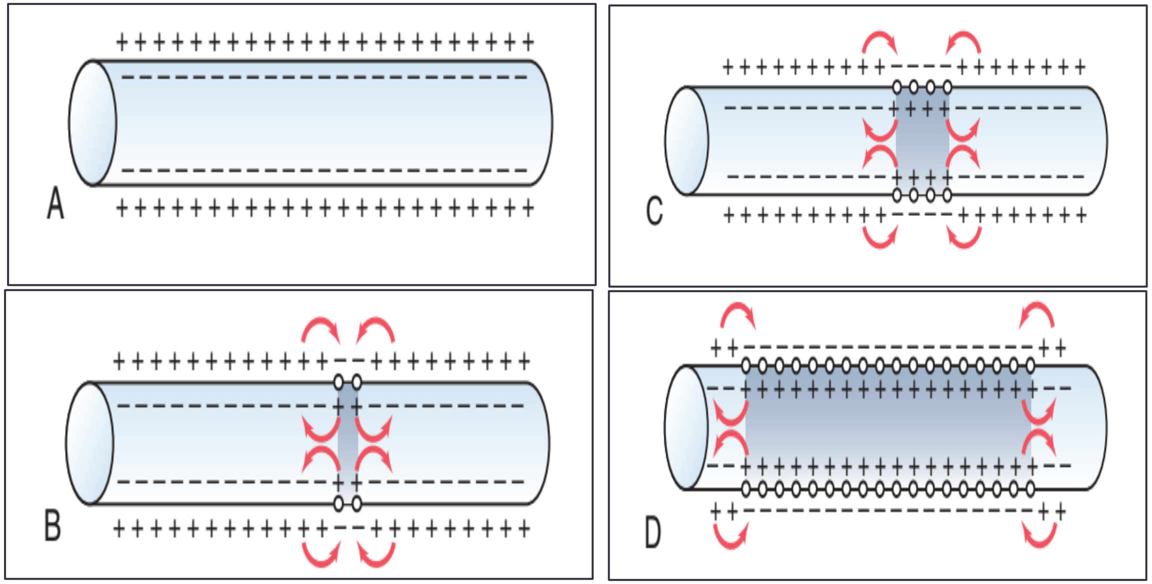
Video

Extra



Usually, an action potential elicited at any point on an excitable membrane will excite adjacent portions of
the membrane, which results in propagation of action potential along the membrane.

Direction of propagation:

- An excitable membrane has no single direction of propagation.
- The action potential moves away from the stimulus in all directions until the entire membrane becomes depolarized.

A. Normal resting nerve fiber

B. Nerve fiber is excited in its midportion meaning, it has developed permeability for Na.
The arrows show a local circuit of current flow from depolarized areas of the membrane (excited areas) tot he adjacent areas.
That is Positive electrical charges are carried by inward-diffusion sodium ions through the depolarized membrane.
These positive charges increase the voltage inside the large myelinated fiber until it becomes higher than the threshold voltage value (which initiates the action potential) Therefore, sodium channels in these areas immediately open as shown.
These newly depolarized areas produce more local circuits of current flow across the membrane causing more and more depolarization.
Thus, the depolarization process moves along the whole nerve fiber. And this transmission of depolarization process along a nerve or muscle fiber is called nerve or muscle impulses.

Further information

PHYSIOLOGY TEAM 435

Propagation of action potential

How do action potentials travel down the axon?

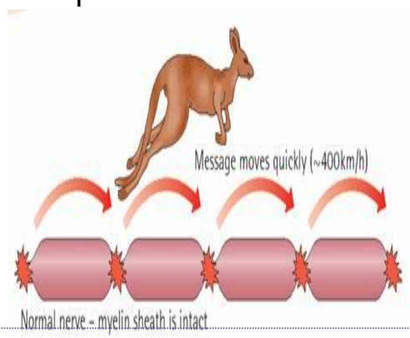
(Propagation)

Myelinated

Called: saltatory conduction (Jumping)

saltatory conduction
Action potential skips from one node of Ranvier to the next.

- increase velocity of conduction of nerve impulses.
- Conserve energy for axon because only nodes depolarize.



Non-myelinated

Called: local circuits (point to point)

local circuits
depolarization pass by local circuits

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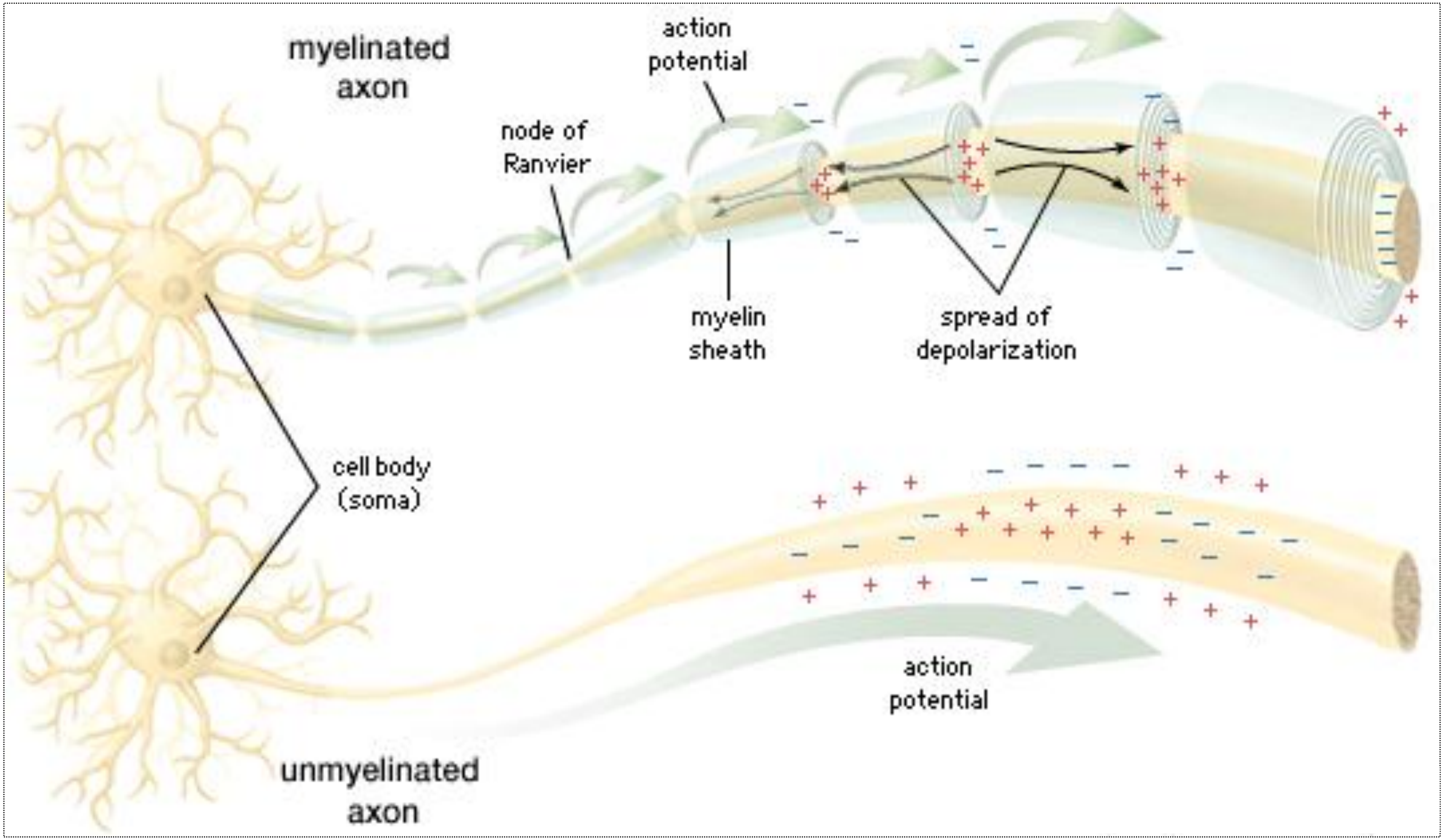

myelinated
axon
action
potential
node of
Ranvier
myelin
sheath
spread of
depolarization
cell body
(soma)
action
potential
unmyelinated
axon

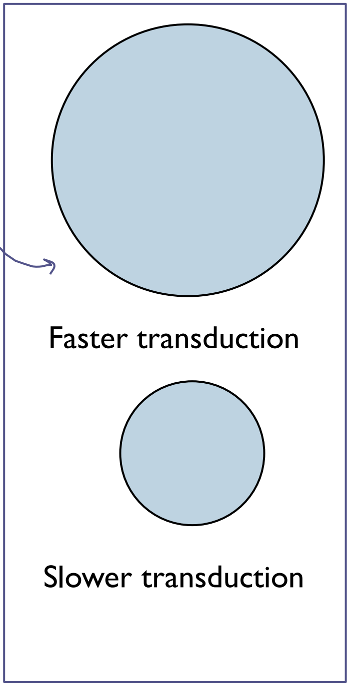
Factors influences speed of action potential

myelination

- Myelinated sheaths are many times faster transmission.

Axon diameter

- The larger the diameter the faster the speed of transmission
- Less resistance to current flow with large diameter.



The larger the diameter, the faster the speed
لو بنسوي إخلاء لـ ١٠٠ شخص : نفتح باب صغير ؟ أو نفتح باب كبير؟ أكيد الكبير لأنه يتسع لعدد أكبر من الأشخاص وكذلك فكرة تدفق الشحنات لها نفس المبدأ ، فكلما زادت سماكة العصب أو مساحته، كلما كان التوصيل أو التدفق أسرع.

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What happens if myelination is lost?

Multiple sclerosis

causes :

1-Blindness,

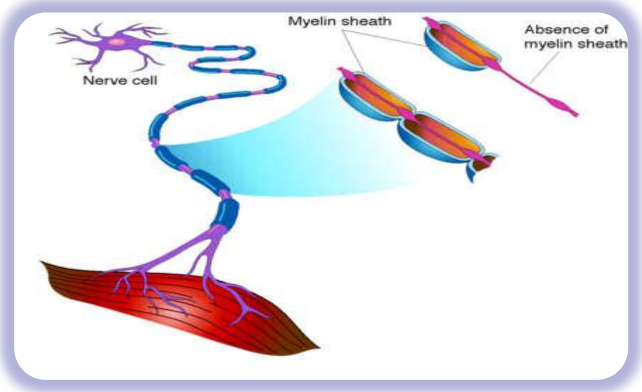
2-problems controlling muscles

Ultimately paralysis

Usually affects young adults

Immune system attacks myelin sheaths and nerve fibers

autoimmune disease



The myelin sheaths are lost → Scar tissue "fibrose tissue" (sclerosis) replaces damaged cells → Other now un myelinated axons sprout Na+ channels

Video

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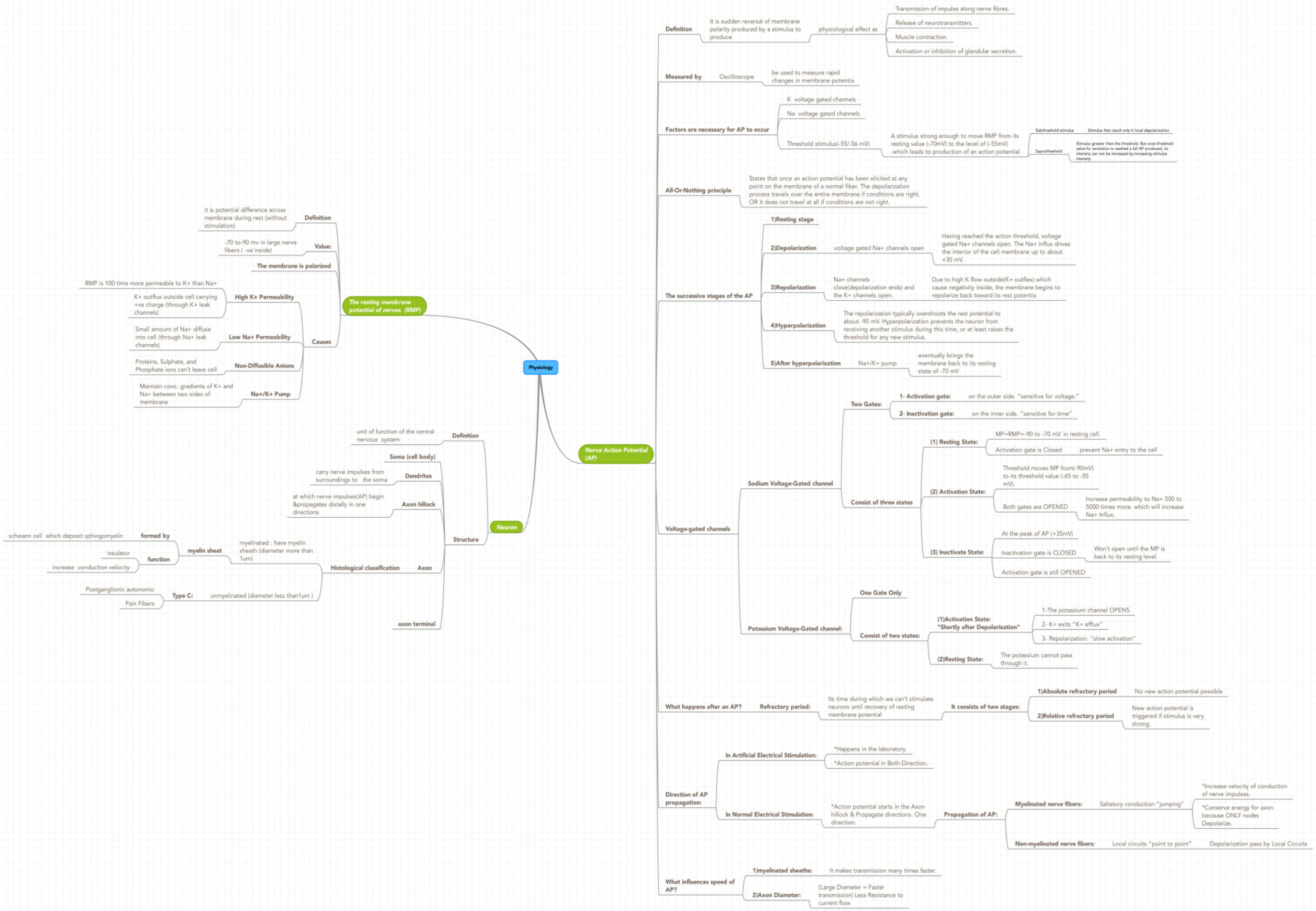
Physiology
The resting membrane potential of nerves (RMP)
Definition
it is potential difference across membrane during rest (without stimulation)
Value:
-70 to-90 mv in large nerve fibers (-ve inside)
The membrane is polarized
Causes
High K+ Permeability
RMP is 100 time more permeable to K+ than Na+
K+ outflux outside cell carrying +ve charge (through K+ leak channels)
Low Na+ Permeability
Small amount of Na+ diffuse into cell (through Na+ leak channels)
Non-Diffusible Anions
Proteins, Sulphate, and Phosphate ions can't leave cell
Na+/K+ Pump
Maintain conc. gradients of K+ and Na+ between two sides of membrane
Neuron
Definition
unit of function of the central nervous system
Structure
Soma (cell body)
Dendrites
carry nerve impulses from surroundings to the soma
Axon hillock
at which nerve impulses(AP) begin &propagates distally in one directions
Axon
Histological classification
myelinated : have myelin sheath (diameter more than 1um)
myelin sheat
formed by
schwann cell which deposit sphingomyelin
function
insulator
increase conduction velocity
unmyelinated (diameter less than1um)
Type C:
Postganglionic autonomic
Pain Fibers
axon terminal
Nerve Action Potential (AP)
Definition
It is sudden reversal of membrane polarity produced by a stimulus to produce
physiological effect as
Transmission of impulse along nerve fibres.
Release of neurotransmitters.
Muscle contraction.
Activation or inhibition of glandular secretion.
Measured by
Oscilloscope
be used to measure rapid changes in membrane potentia
Factors are necessary for AP to occur
K voltage gated channels
Na voltage gated channels
Threshold stimulus(-55/-56 mV)
A stimulus strong enough to move RMP from its resting value (-70mV) to the level of (-55mV) .which leads to production of an action potential
Subthreshold stimulus
Stimulus that result only in local depolarization
Suprathreshold
Stimulus greater than the threshold. But once threshold value for excitation is reached a full AP produced, its intensity can not be increased by increasing stimulus intensity
All-Or-Nothing principle
States that once an action potential has been elicited at any point on the membrane of a normal fiber. The depolarization process travels over the entire membrane if conditions are right. OR it does not travel at all if conditions are not right.
The successive stages of the AP
1)Resting stage
2)Depolarization
voltage gated Na+ channels open
Having reached the action threshold, voltage gated Na+ channels open. The Na+ influx drives the interior of the cell membrane up to about +30 mV.
3)Repolarization
Na+ channels close(depolarization ends) and the K+ channels open.
Due to high K flow outside(K+ outflex) which cause negativity inside, the membrane begins to repolarize back toward its rest potentia
4)Hyperpolarization
The repolarization typically overshoots the rest potential to about -90 mV. Hyperpolarization prevents the neuron from receiving another stimulus during this time, or at least raises the threshold for any new stimulus.
5)After hyperpolarization
Na+/K+ pump
eventually brings the membrane back to its resting state of -70 mV
Voltage-gated channels
Sodium Voltage-Gated channel
Two Gates:
1- Activation gate:
on the outer side. "sensitive for voltage."
2- Inactivation gate:
on the inner side. "sensitive for time"
Consist of three states
(1) Resting State:
MP=RMP=-90 to -70 mV. in resting cell.
Activation gate is Closed
prevent Na+ entry to the cell
(2) Activation State:
Threshold moves MP from(-90mV) to its threshold value (-65 to -55 mV).
Both gates are OPENED
Increase permeability to Na+ 500 to 5000 times more. which will increase Na+ Influx.
(3) Inactivate State:
At the peak of AP (+35mV)
Inactivation gate is CLOSED
Won't open until the MP is back to its resting level.
Activation gate is still OPENED
Potassium Voltage-Gated channel:
One Gate Only
Consist of two states:
(1)Activation State: "Shortly after Depolarization"
1-The potassium channel OPENS
2- K+ exits "K+ efflux"
3- Repolarization. "slow activation"
(2)Resting State:
The potassium cannot pass through it.
What happens after an AP?
Refractory period:
Its time during which we can't stimulate neurons until recovery of resting membrane potential
It consists of two stages:
1)Absolute refractory period
No new action potential possible
2)Relative refractory period
New action potential is triggered if stimulus is very strong.
Direction of AP propagation:
In Artificial Electrical Stimulation:
*Happens in the laboratory.
*Action potential in Both Direction.
In Normal Electrical Stimulation:
*Action potential starts in the Axon hillock & Propagate directions. One direction.
Propagation of AP:
Myelinated nerve fibers:
Saltatory conduction "jumping"
*Increase velocity of conduction of nerve impulses.
*Conserve energy for axon because ONLY nodes Depolarize.
Non-myelinated nerve fibers:
Local circuits "point to point"
Depolarization pass by Local Circuits
What influences speed of AP?
1)myelinated sheaths:
It makes transmission many times faster.
2)Axon Diameter:
(Large Diameter = Faster transmission) Less Resistance to current flow

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QUIZ 1
QUIZ 2

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