Physiology Team

MEDICAL COLLAGE 433

Action potential & properties of nerves

Color Index

Red = important

Purple = Addition

Orange = Explanation

@PhysiologyTeam

Pht433@gmail.com

Contact us: pht433@gmail.com

Objectives

At the end of this lecture the student should be able to :

- Describe the voltage-gated sodium and potassium membrane channels and their states .
- Explain the resting membrane potential (RMP), Threshold Potential, Reversal Potential , Local Response and Action Potential .
- Describe components of a neuron dendrites , soma , axon . axon hillock and their physiological significance
- Describe the electrical changes in membrane potential during the action potential , their chemical bases and excitability changes .
- Describe conduction along nerve fibers , role of myelination and how nerve fibers are classified .

Abbreviations

- **EPSP :** Excitatory Postsynaptic Potential
- **IPSP :** Inhibitory Postsynaptic Potential
- **AP :** Action Potential
- **MP :** membrane potential

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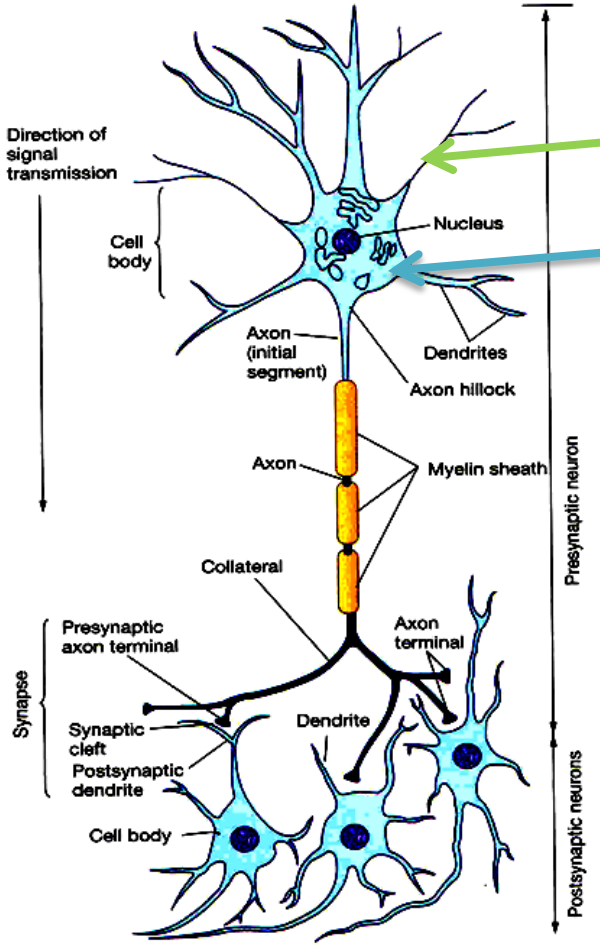
The Neuron consists of



Dendrites

Soma (cell-body) : جسم الخلية

Membrane potential (MP) :

the Voltage (Potential) : الفولتاج(أي فرق الجهد الكهربائي) بين داخل و خارج جدار الخلية

Resting Membrane Potential (RMP): فولتاج الخلية المرتاحة

Local Response Response : إستجابة محلية

Action potential (AP) : فولتاج الخلية النشطة أو النبضة الكهربائية

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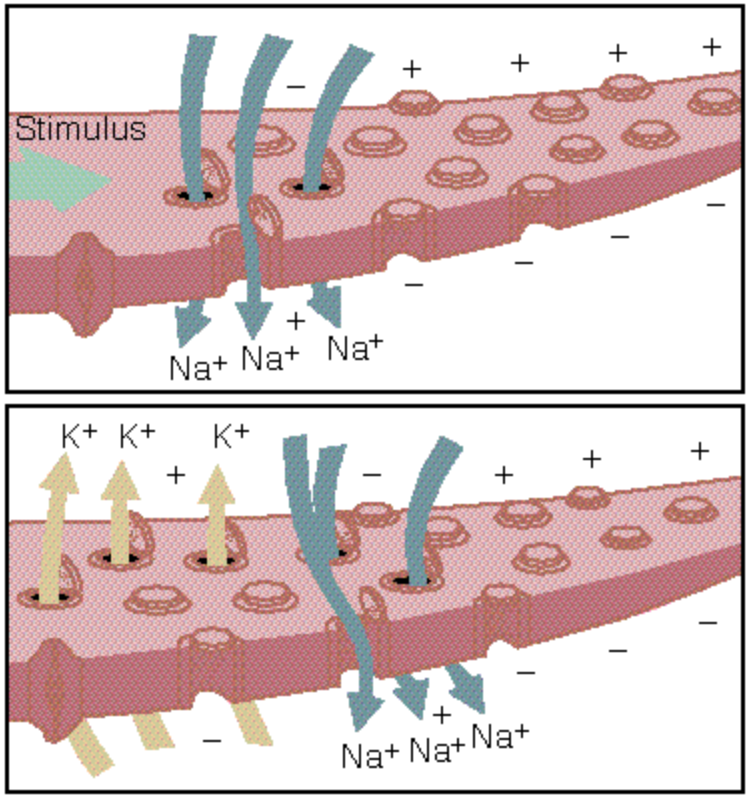
Nerve physiology: Action potential



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The Action Potential (AP)

We need to describe 3 types of event :

(1) Electrical changes in the cell-membrane (hyperpolarization)

(2) Chemical events (Na+ influx and and K+ efflux across the membrane ionic changes in membrane channels → leading to the a/m electrical events)

(3) Excitability changes & **refractory states** (when will be the cell ready to respond to stimulation & produce a second AP after a previous/preceding one)

Three aspects of AP to be discussed:

1/ Electrical Changes (Changes in the MP)

التحولات أو التغيرات الكهربائية التي نرصدها علي الخليّة في مختلف مراحل ال AP

2/ Their Chemical Basis

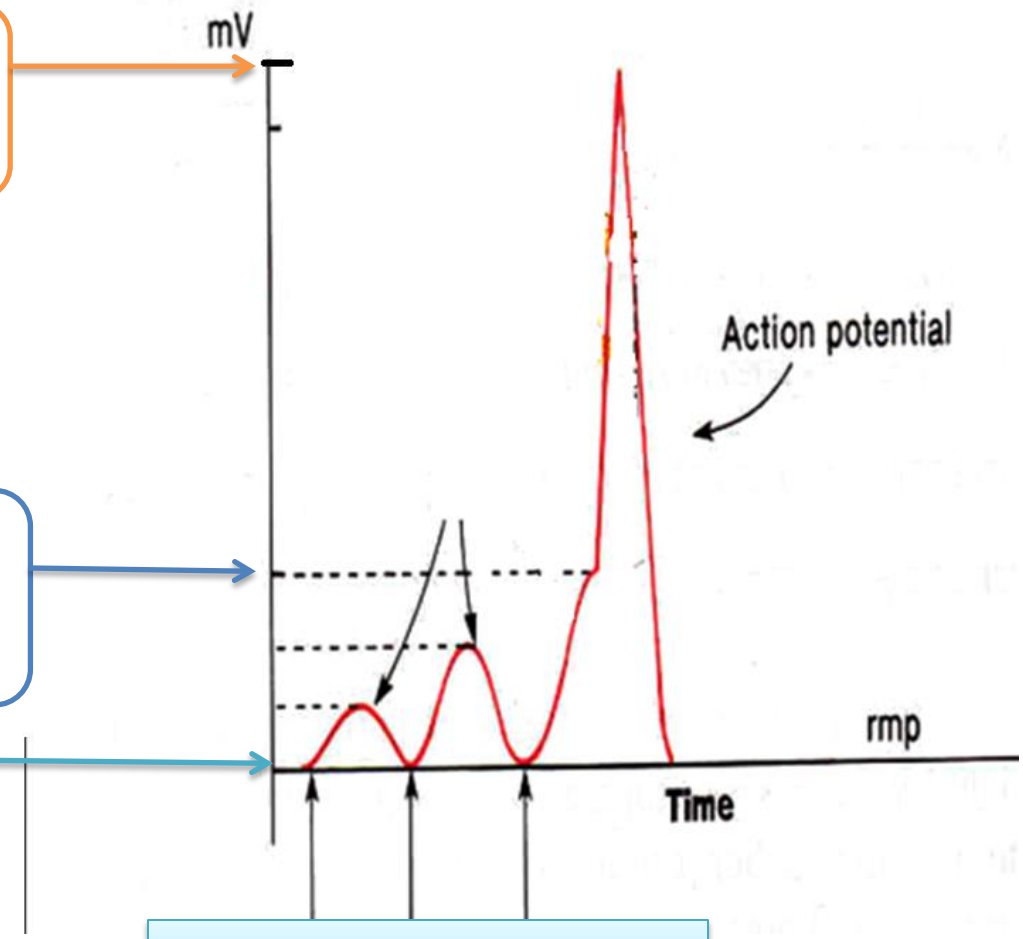
دور الصوديوم و البوتاسيوم في هذه التغيرات أو التحولات الكهربائية

3/ Excitability Changes in the cell

متي يمكن تحفيزالخلية لتنتج AP جديد ثاني بعد الأول

لو حفزناها مرة ثانية مباشرة بعد التحفيز الأول

Reversal Potential
= + 35 mV



Threshold
Potential (Firing Level)
= -50 to -65 mV

RMP= -90 mV

Increasing Stimulation

Q : What opens the voltage-gated channels ?

Opened by a stimulus strong enough to depolarize them to threshold

We need to start from the Baseline

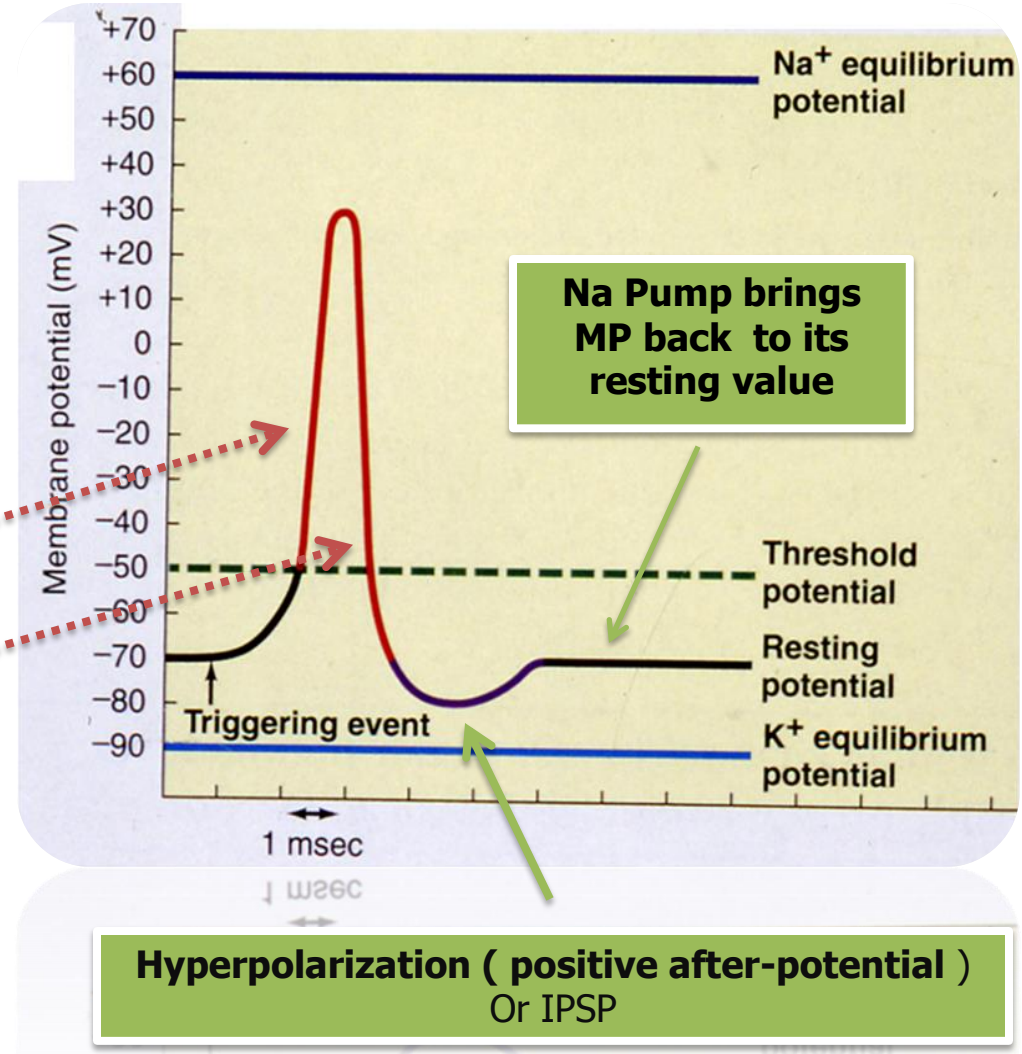
i.e., Resting State of the cell (at the RMP)

A threshold Stimulus will lead to →

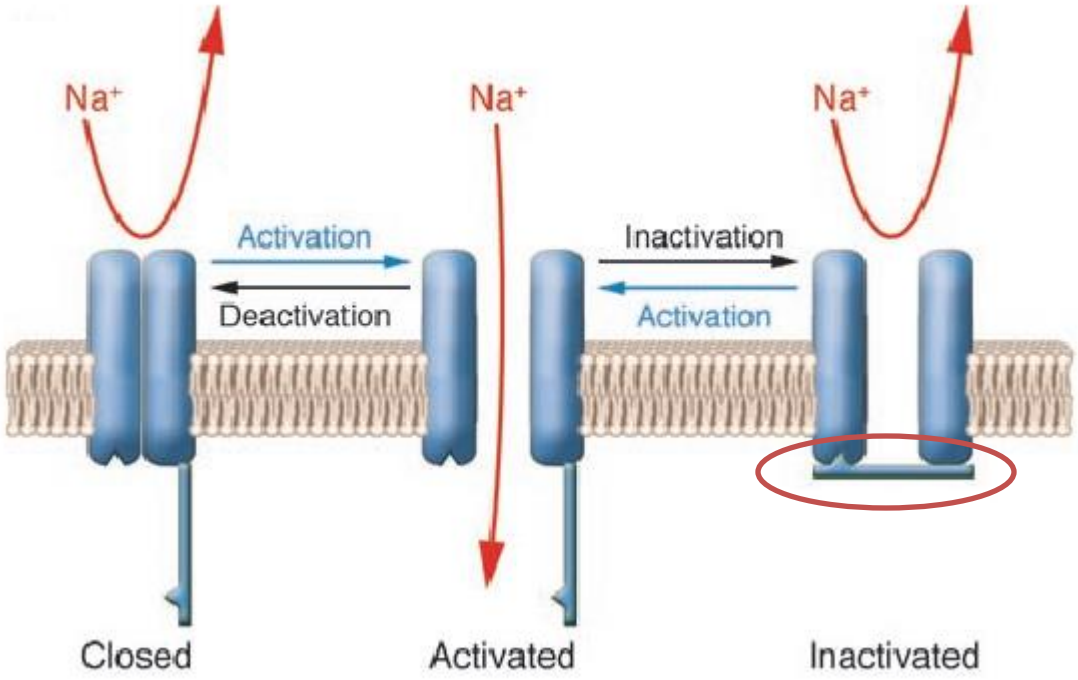
(1) Depolarization (EPSP)

(2) Repolarization.

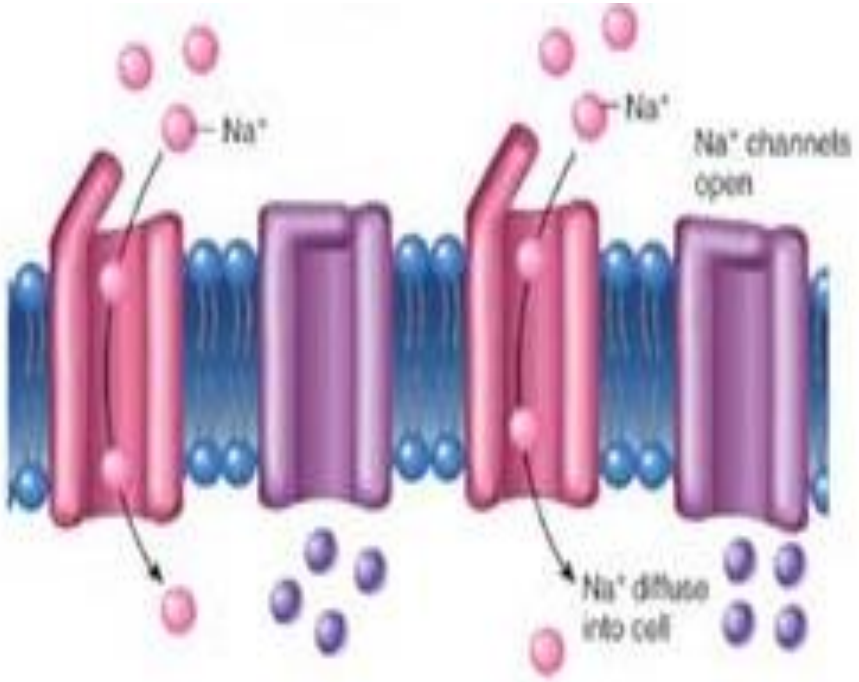
(3) In some neurons there is a 3rd phase called **Hyperpolarization (IPSP)**

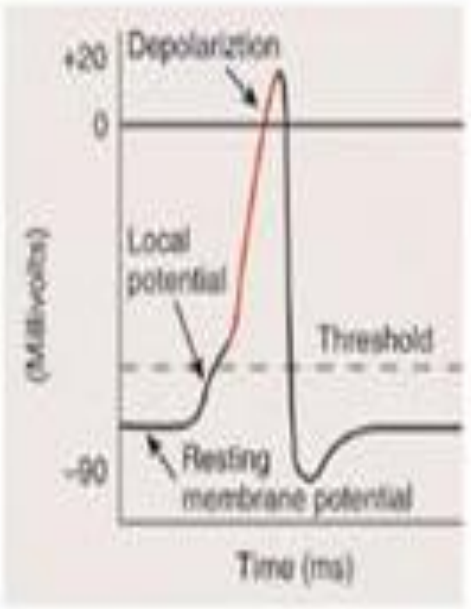


Activation-Inactivation-Deactivation



Depolarization





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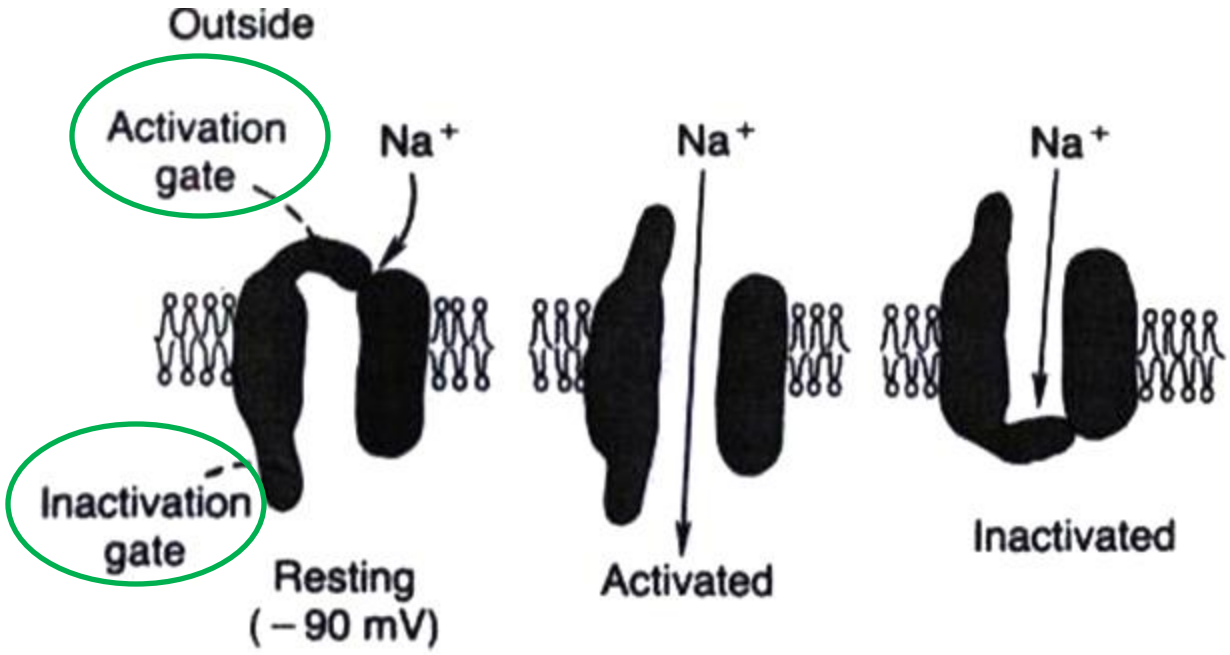
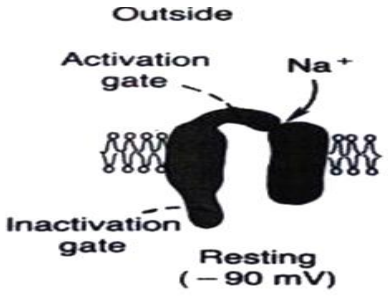
The Na+ Voltage-Gated Channel



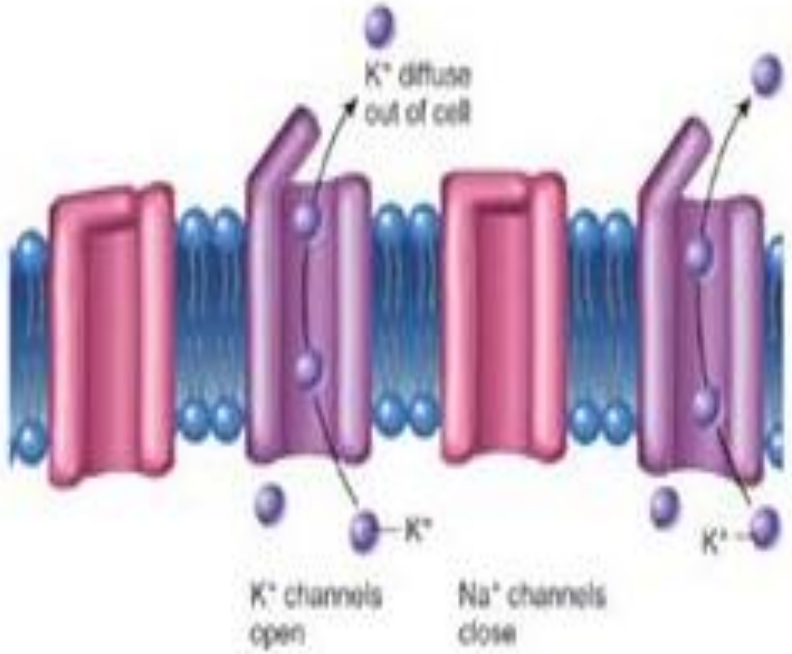
Has 2 gates :

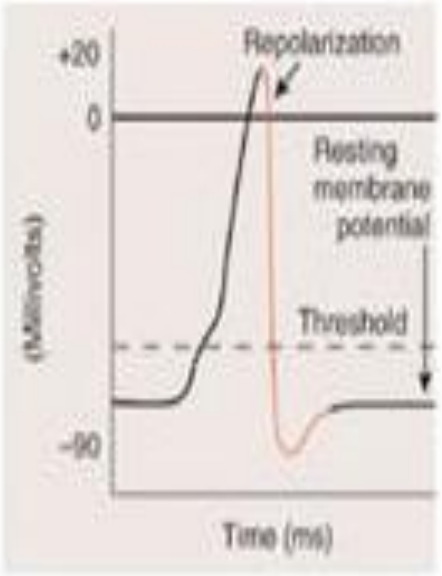
- ❖ one on the outer side of the membrane and is called the activation gate ,
- ❖ and another one on the inner side of membrane called the inactivation gate .

This channel has 3 states

1) Resting state :	2) Activated State	3)Inactivated 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.	• **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 • (NB in this case BOTH the 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 , depolarizing it more & more , until there is **reversal of MP** . • After the AP , the inactivation gate will not open by a second stimulus → & the cell becomes Refractory (ممانعة) to another stimulation . • This goes on until the MP has gone back to its resting (RMP) level (-70 to -90mV).	**A few milliseconds after the activation gate opens , the channel becomes inactivated** → in this case , while the activation gate is still open ,the inactivation gate is closed.
		

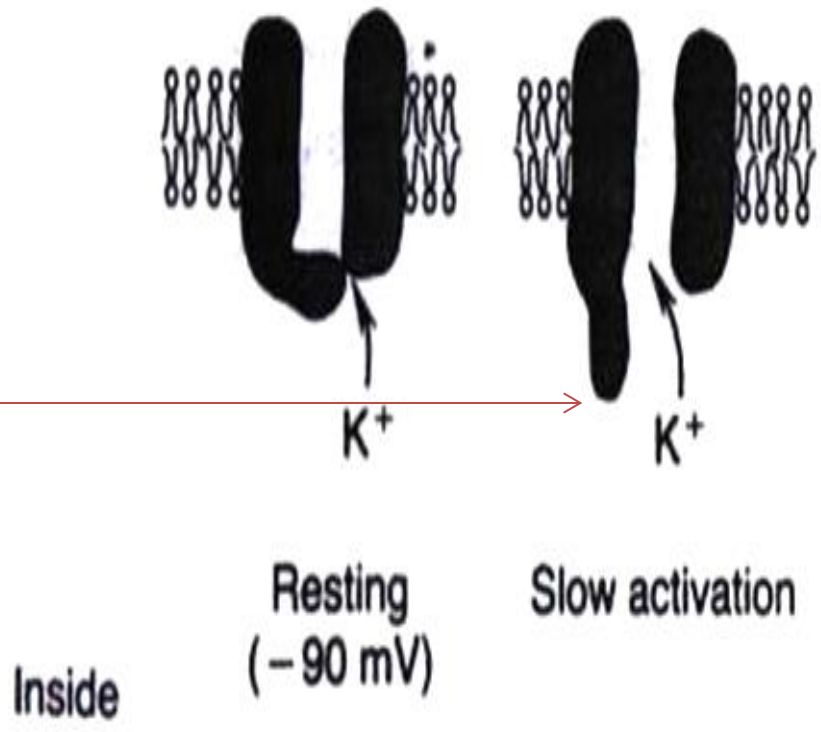
Repolarization





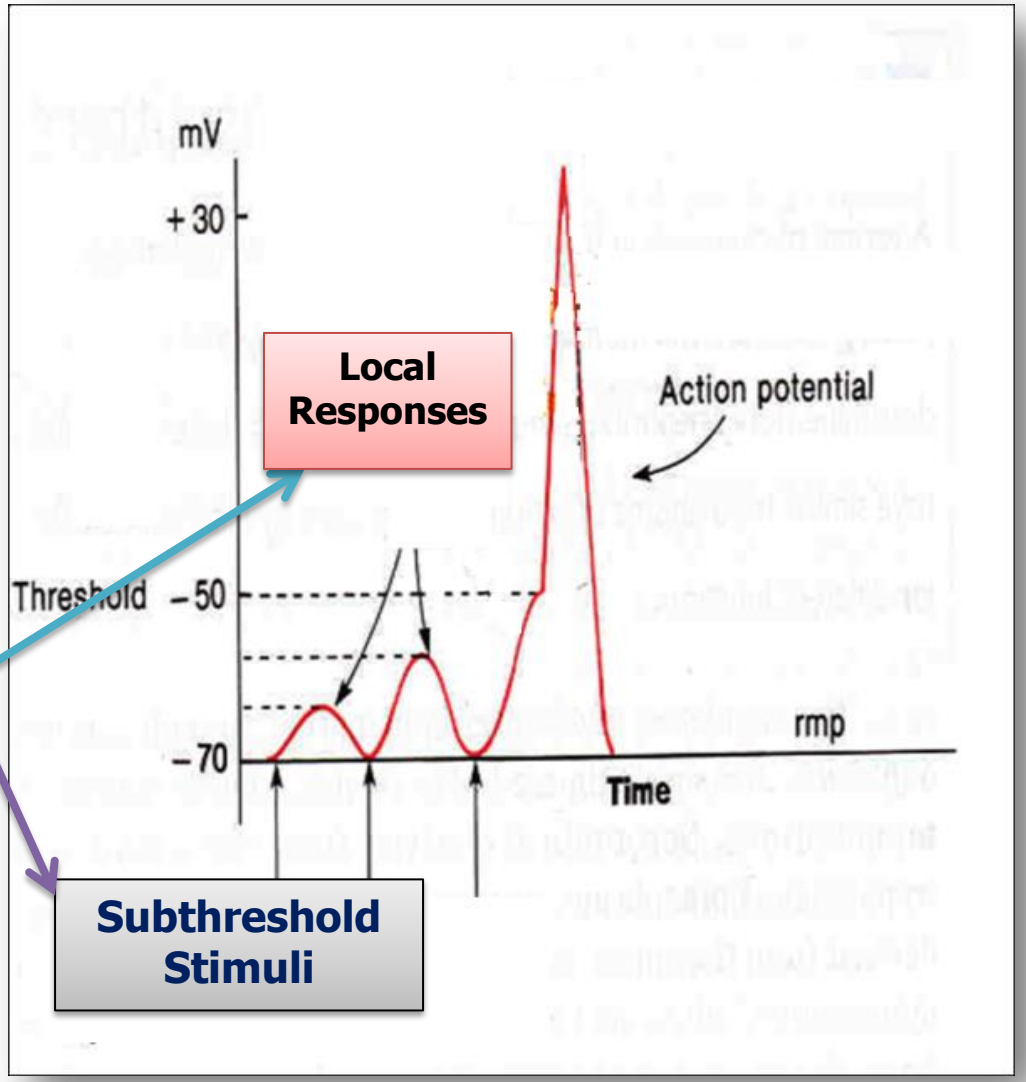
The Potassium Voltage-Gated Channel

- Has one gate only .
- During the resting state , the gate of the potassium channel is closed , and K+ cannot enter through it .
- Shortly after depolarization , when the sodium channel begins to be inactivated , the potassium channel opens .
- → K+ exits (called K+ Efflux)
  خروج البوتاسيوم
- → Repolarization

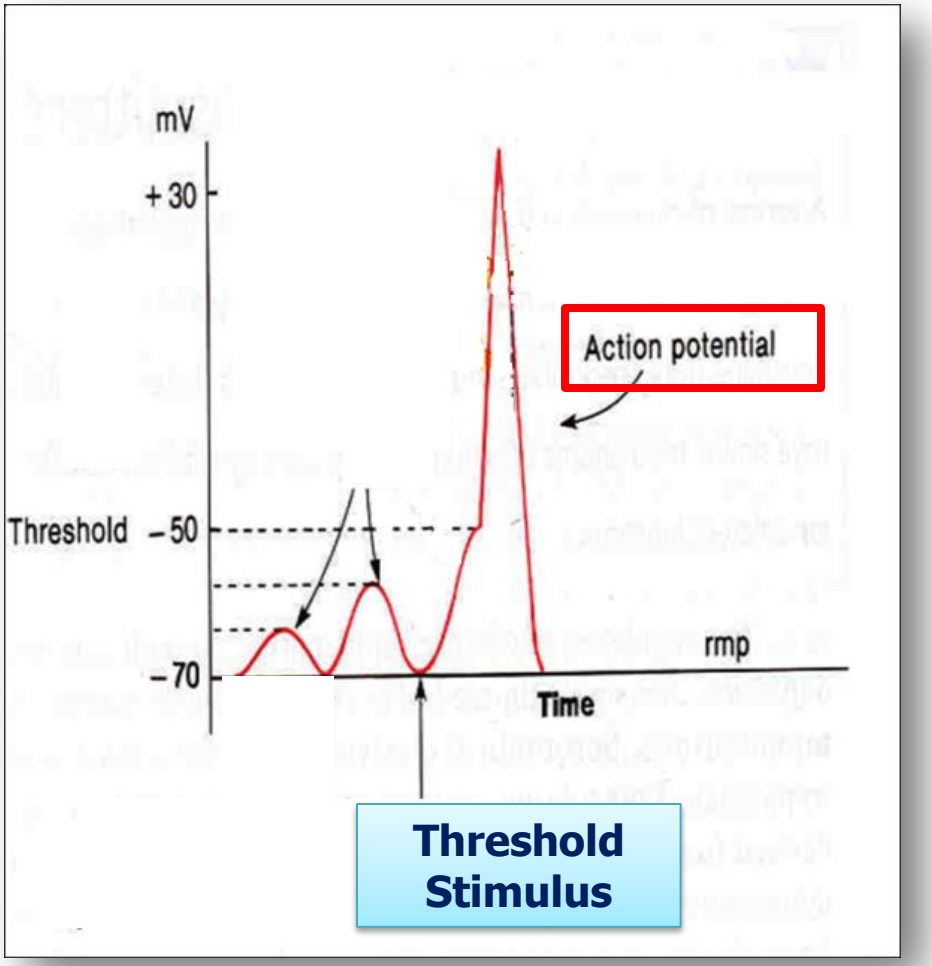


- **Q : What is a Subthreshold Stimulus ?**
- A : it is a **weak stimulus**, not strong enough to carry the MP to the Threshold Level

- i.e., it may depolarize the membrane to less than threshold level → **fails to produce AP , and can produce only Local Response**



- Q : What is a Threshold Stimulus ?
- A : it is a stimulus strong enough to depolarize the membrane & move the MP to Membrane Threshold Level =
- -50 to -65 mV
- Which is the ***firing level*** at which the Action Potential is triggered.



- **The minimal stimulus which produces an AP:**

أقل كمية من التحفيز يمكن أن تسبب نبضة كهربائية

- **THRESHOLD STIMULUS:**

تحفيز الثير شولد والذي يستطيع توليد آكشن بوتينشل

- **SUBTHRESHOLD STIMULUS:**

تحفيزأقل من الثرشهولد لا يستطيع توليد آكشن بوتنشيال ولكنه قادر على إستجابة محلية

- **SUPRATHREHOLD STIMULUS:**

تحفيزأكثر من الثرشهولد لا يستطيع زيدة الآكشن بوتنشيال طولا أو عرضا و لكنه يسبب زيادة سرعة ترديد (تكرار) الآكشن بوتنشيال

- **THRESHOLD LEVEL OF THE MP:**

The value of the MP at which a stimulus can produce an AP

قيمة الجهد الكهربائي لغشاء الخلية التي يمكن منها إستهلال النبضة الكهربائية

Graded Potential (Local Response)

Stimulation of the neuron by a weak subthreshold stimulus produces a local, non-propagated potential which is measurable only in the immediate vicinity of stimulated point , but not farther than that .

It does not obey All-or-None Law

Action potential (AP)

AP is the MP value in case of a cell that is generating a propagated electrical potential

It can be measured anywhere along the nerve

It obeys All-or-None Law

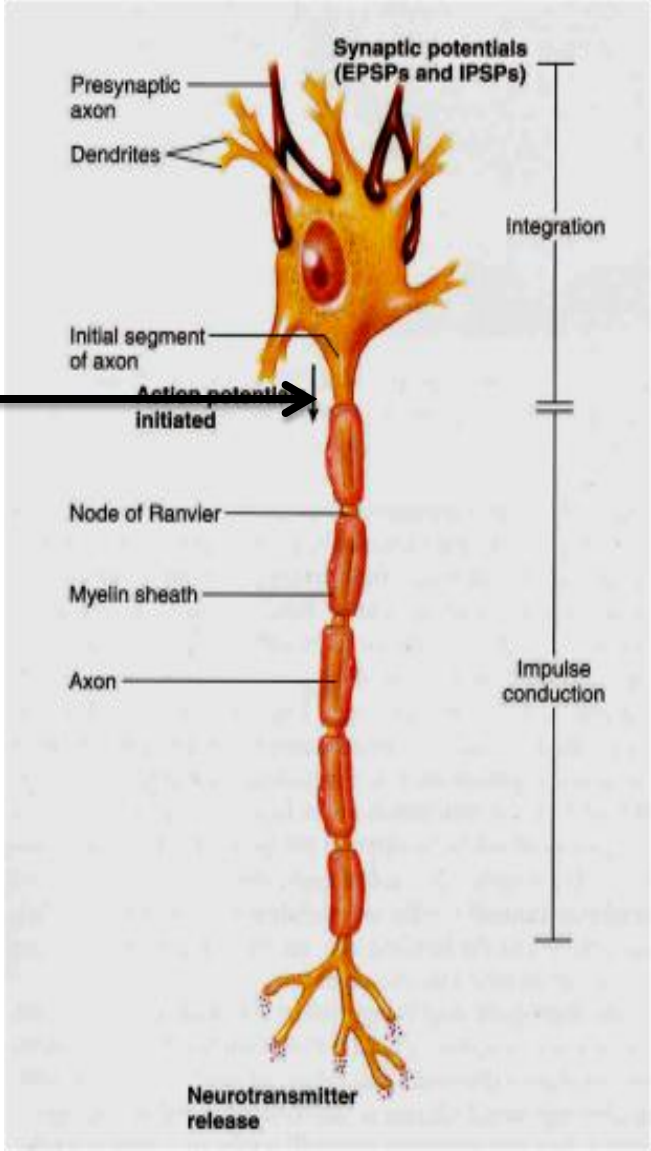
At the peak of the AP , the value of the MP reaches +35 to +40 mV

AP obeys all-or-none law BUT Local response does NOT obey all-or-none law

In all above cases the -ve or +ve sign refers to the inside of the membrane .

In nerves , the AP is generated at the initial segment of the axon , which is called **Axon hillock**

but , by contrast , a local responses can be generated at any membrane area if the stimulation is sufficient



Summary 1

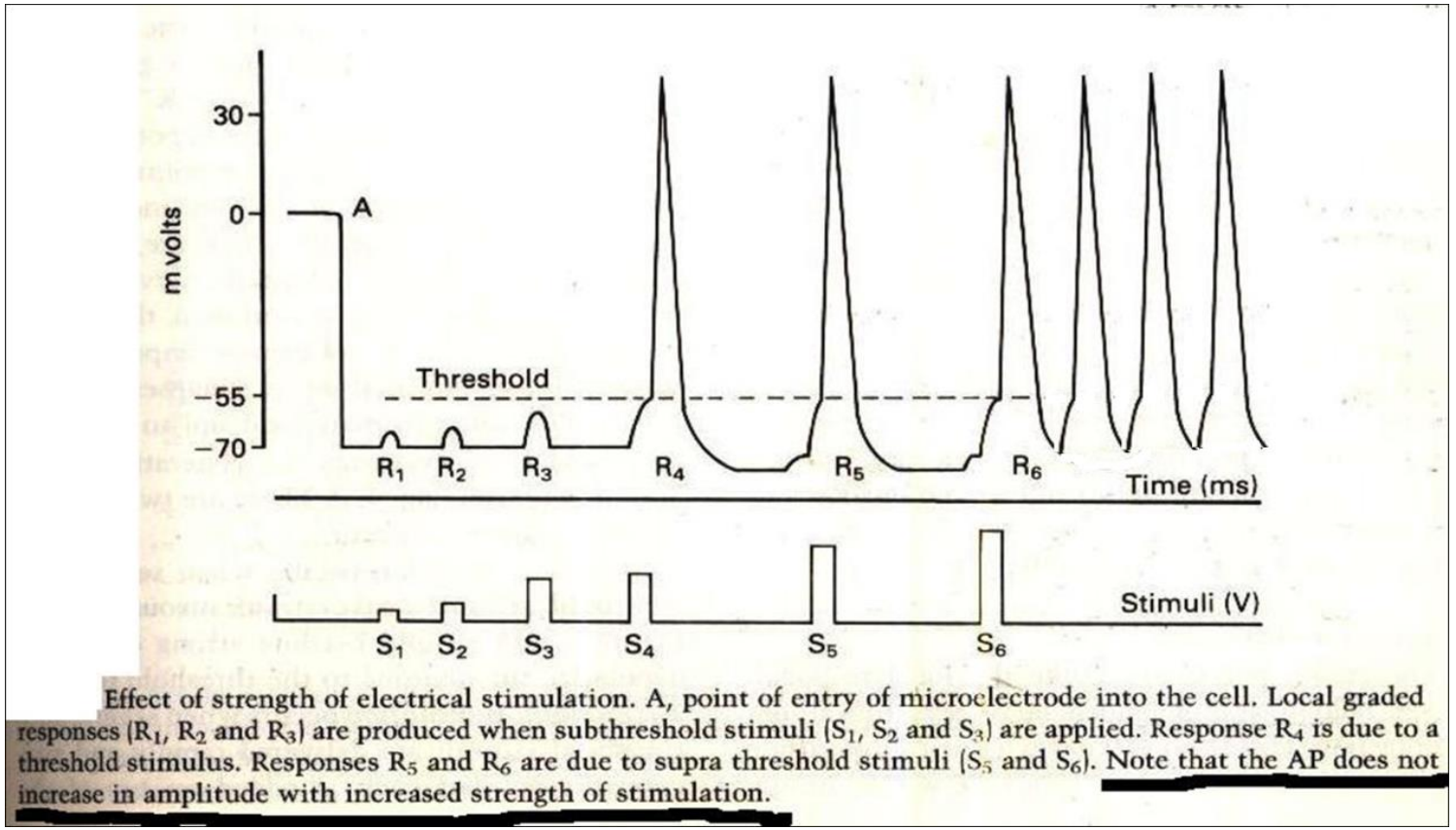
- A/ When the cell is inactive (resting) → we call the MP : Resting Membrane Potential (RMP) .
- B/ When the cell is stimulated weakly by subthreshold stimulus → a small number of voltage-gated channels open → we get only a Local Response (which is graded and does not propagated).
- C/ However , if the stimulus is Threshold Stimulus i.e., strong enough to carry the MP to its Threshold Level → it opens many voltage-gated sodium channels open → and action potential (AP) is generated .
- The AP differs from local response in that it is (1) not graded obeys All-or None Law) , and (2) propagated (conducted for long distances) .

Please Note that:

- (1) If we stimulate a sensory receptor (e.g., pain nerve-ending in skin) with a **Subthreshold stimulus** → this will cause depolarization of the receptor cell membrane to **below** threshold level → will result only in a **Local Response**.

- (2) If we stimulate it with a **threshold stimulus** → i.e., a stimulus that carries the MP to **the Firing Level** (Threshold Level **= -65 mV**) → we get AP

- (3) If we stimulate with a **Suprathreshold** (above threshold) stimulus → AP will not increase in size or duration , but will **increase in frequency** سرعة تردد

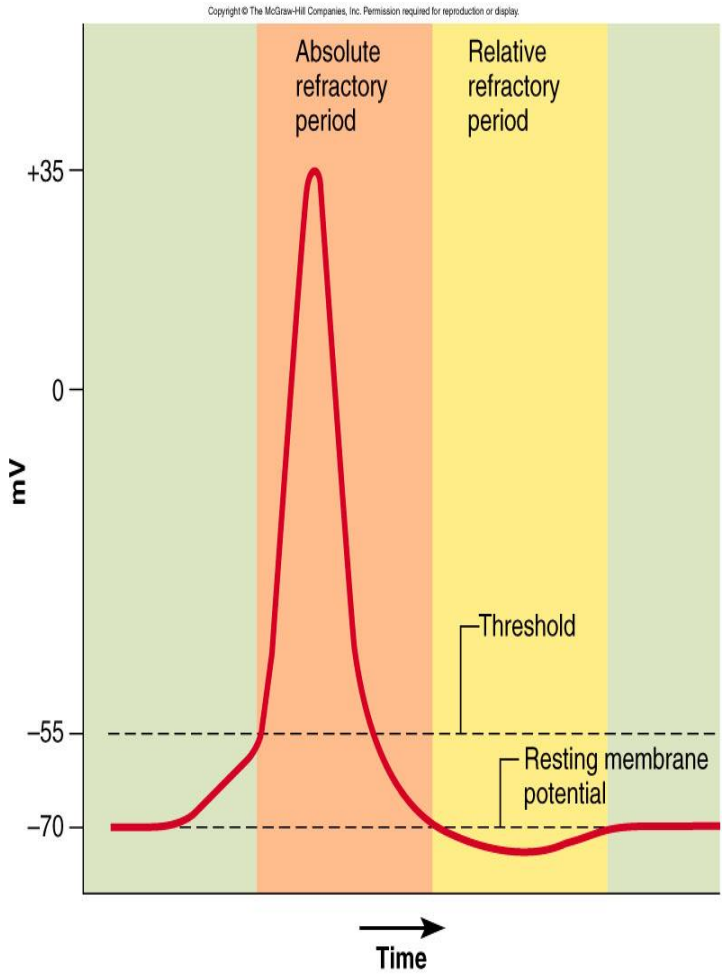


Effect of strength of electrical stimulation. A, point of entry of microelectrode into the cell. Local graded responses (R_1, R_2 and R_3) are produced when subthreshold stimuli (S_1, S_2 and S_3) are applied. Response R_4 is due to a threshold stimulus. Responses R_5 and R_6 are due to supra threshold stimuli (S_5 and S_6). Note that the AP does not increase in amplitude with increased strength of stimulation.

Increasing stimulation will NOT increase the amplitude (height) or duration (width) of AP , but will increase frequency of AP

What happens after an action potential?

- **Refractory period: few millisecs**
  - Time during which can't stimulate neuron a second time
  - Happens until recovery of resting potential
- **Two stages**
  - **Absolute refractory period**
    - No new action potential possible
  - **Relative refractory period**
    - Can trigger new action potential if stimulus is very strong



- **Meaning : when can the cell respond to a second stimulus (after the first stimulus which produced the first AP)**

متى تكون الخلية مستعدة للأستجابة لمحفز تاني بعد المحفز الأول الذي سبب الآكشن بوتنشيال الأول الأصلي؟

1- Absolute Refractory Period (period during depolarization & early repolarization)**: where no stimulus , however strong , can produce a second AP . It is due to inactivation of Na+ channels .**

- **Note:** During it the nerve cannot excited by a a second stimulus & a second spike action potential cannot be elicited whatever strength of the stimulus (even suprathreshold= above the threshold)

Why??

(Because all Na channels are already opened & Na influx occurred & a new stimulus cannot open further Na channels)

2- Relative Refractory Period

- **a stimulus higher than threshold is needed to produce an AP . Due to continued outflow of K+ .**

Types of Nerve Fibers

- **Nerve fibers can be classified in 2 ways :**

A/ Classification According to Myelination

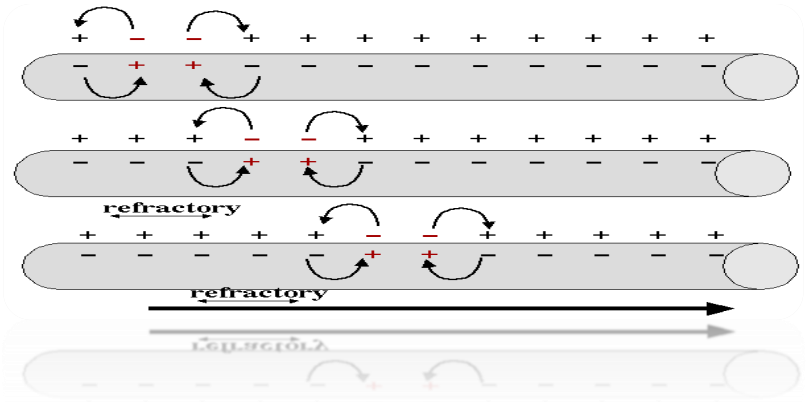
B/ Classification According to Diameter : A, B & C fibers

According to Myelination	**Myelinated Fibers :** Myelin sheath covers the axis cylinder , separated by Nodes of Ranvier (naked , uncovered parts) at 2-3 Micron intervals	**Un-Myelinated :** without myelin sheath
According to Diameter	A and B (Myelinated) Because conduction velocity depends upon diameter , A are **fastest**	C (Unmyelinated) The **slowest** in conduction

Propagation (Conduction) of Action Potential

- In both myelinated and Unmyelinated nerve fibers impulses are propagated (conducted) by :

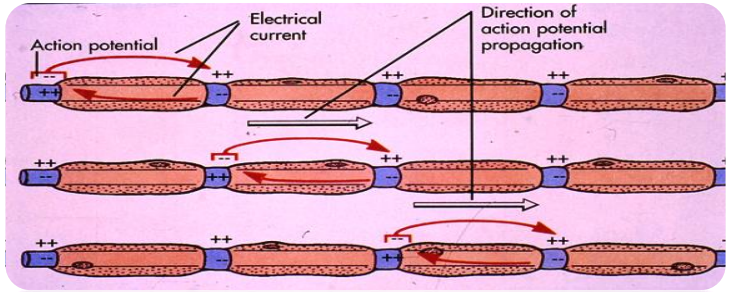
Sodium Ionic Current Flows تيارات أيونية /كهربائية



- In unmyelinated fibers , they are contiguous متلاصقة ، متلامسة

occurring at almost each adjacent متجاورة point on the membrane .This is called Continuous (Contiguous)conduction of nerve impulses

- And in myelinated nerves there **Saltatory Conduction** , where ionic currents travel by jumping from one Node of Ranvier to the next .

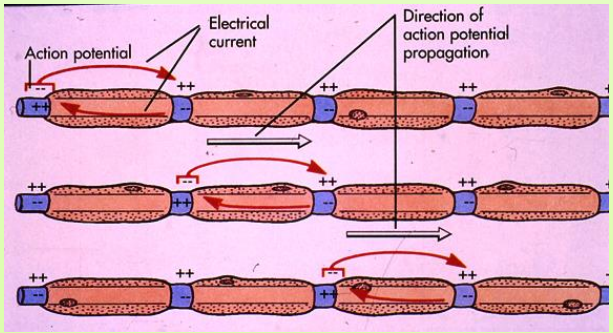


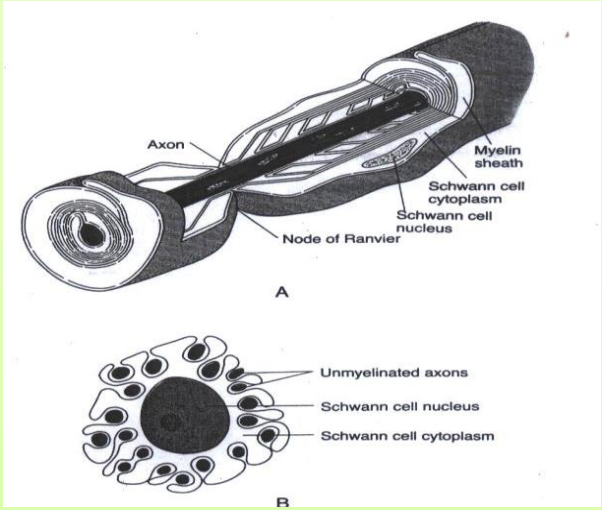
Saltatory Conduction (propagation) of APs in myelinated nerves :

- **Myelin is an excellent insulator : it prevents leakage تسرب و فقدان (& hence loss) of ions from inside the cell through membrane .**
- **Ions are allowed to pass only at Nodes of Ranvier**
- **Myelin sheath makes conduction in myelinated nerves →**

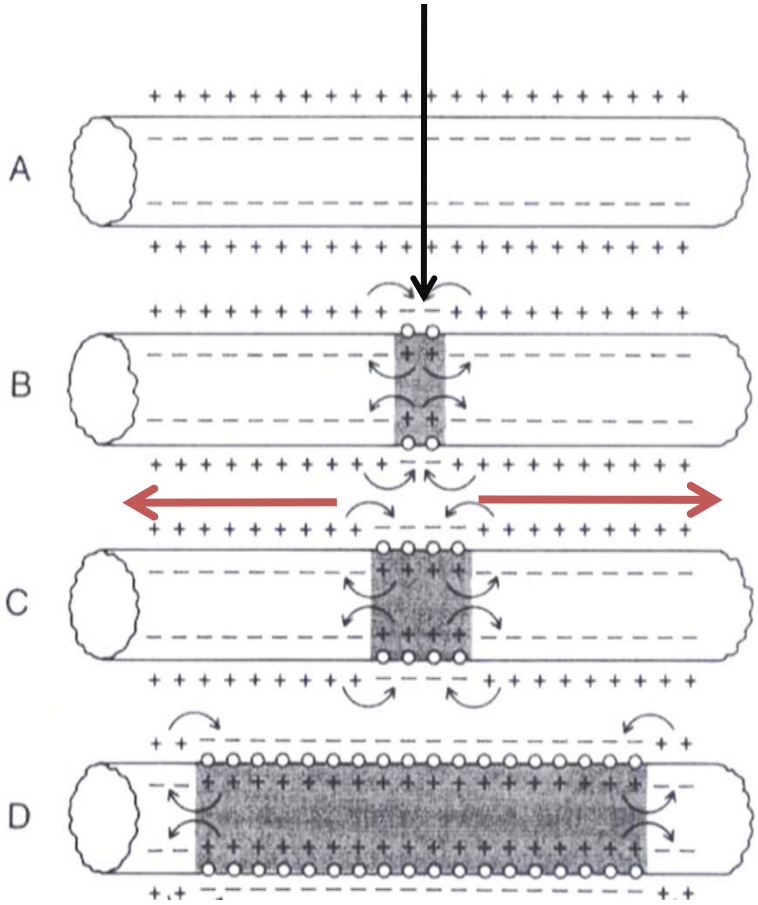
❖ **(1) more economical (because it prevents leakage of ions + because N+-K+ pump only works at Nodes of Ranvier , unlike unmyelinated nerves where it works at every point in the membrane) , and**

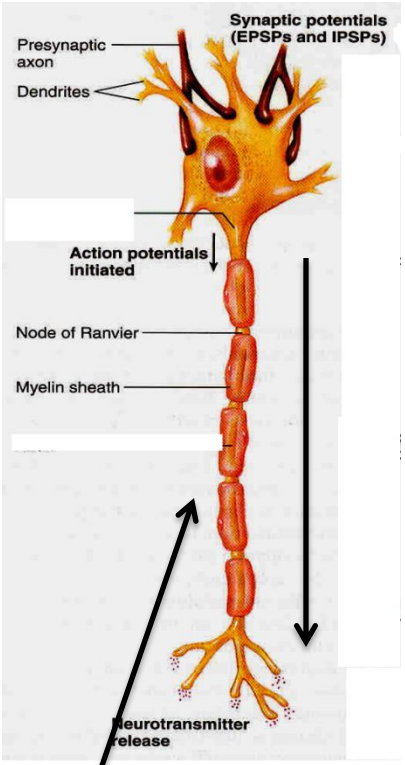
❖ **(2) faster-conducting**





Artificial Electrical Stimulation





Under Artificial condition of electrical stimulation in the laboratory , the AP propagates in both directions .
But normally AP starts in axon hillock & propagates distally in one directions.

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Summary 2

- The voltage gated sodium channel has two gates (activation and inactivation gates)and three states (rest, activated ,inactivated)states.
- The main components of a neuron : dendrites , soma , axon . axon hillock.
- the electrical changes in membrane potential during the action potential: 1) depolarization 2) repolarization 3) hyperpolarization.
- conduction of impulse is faster in myelinated fibers .
- the conduction in unmyelinated fiber is called Continuous
- (Contiguous) conduction of nerve impulses.
- the conduction in mylinated fibers is called Saltatory Conduction.

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Neuron action potential mechanism

http://www.youtube.com/watch?v=MZz4OUOyFvg

Action Potentials

http://www.youtube.com/watch?v=ifD1YG07fB8

Multiple Choice Questions

True or false:

1- when stimulating the nerve Under Artificial condition the AP propagates in both directions
( ) .

True or false:

2- during Absolute Refractory Period the nerve can be excited by second stimulus
( ).

3- In both myelinated and Unmyelinated nerve fibers impulses are propagated by:

A) Saltatory Conduction
B) Sodium Ionic Current Flows
C) Continuous (Contiguous) conduction
D) All of above

4- Subthreshold Stimulus:

A) Can produce a local response .
B) the minimal stimulus which produces an AP
C) Is a stimulus stronger than the threshold.
D) None of above

5- Suprathreshold Will lead to:

A) Decrease the duration of AP
B) Increase the amplitude of AP
C) Increase the frequency of AP
D) Increase the duration of AP

6- What is the location of Action Potential?

A) Axon terminal
B) Axon hillock
C) Synaptic vesicles
D) Soma (cell body)

7- Which of the following myelinated nerve fiber?

A) A type
B) B type
C) C type
D) Both A and B

8- where ionic currents travel by jumping from one Node of Ranvier to the next called?

A) Saltatory Conduction
B) Sodium Ionic Current Flows C) Discontinuous conduction
D) Continuous conduction

9-the AP propagates in both directions in ?

A) Normal conditions
B) Artificial conditions
C) Resting conditions
D) All of above

1-T 2-F 3-B 4-A 5-C 6-B 7-D 8-A 9-B

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