Physiology Team 432

4th & 5th Lecture: The AP and Properties of Nerve Fibers

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Lecture Objectives

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

- Define and draw giving membrane potential in mv and time course in msec and label all components such as threshold level (firing level), depolarization , spike overshoot, repolarization and positive after potential.

-Identify different types of voltage –gated channels.

-Correlate the conductance changes with opening (activation) or closing (inactivation) of relevant gates.

- Distinguish between a local potential and an action potential.

-Define absolute and relative refractory period on basis of excitability changes.

- Classify neurons by using letters or numbers on basis of diameters and velocity.

- Define myelin sheath, myelinated and unmyelinated nerve fibers.

- Describe differences in the propagation of action potential in myelinated and unmyelinated nerve fibers.

- Define all and none law.

- Differentiate monophasic, biphasic and compound action potential.

Types of Nerve Fibers

Classification According to Myelination:

Myelinated		*Un-Myelinated*
Diameter more than 1um		Diameter less than 1um
Type A	**Type B**	**Type C**
Somatic (motor) nerves to skeletal muscles.	**Preganglionic** autonomic nerves.	**Postganglionic** autonomic & **pain** fibers.

Classification According to Diameter:

- Diameter: **A**> B > C
  Because conduction velocity depends upon diameter, ***A are fastest and C are slowest.***

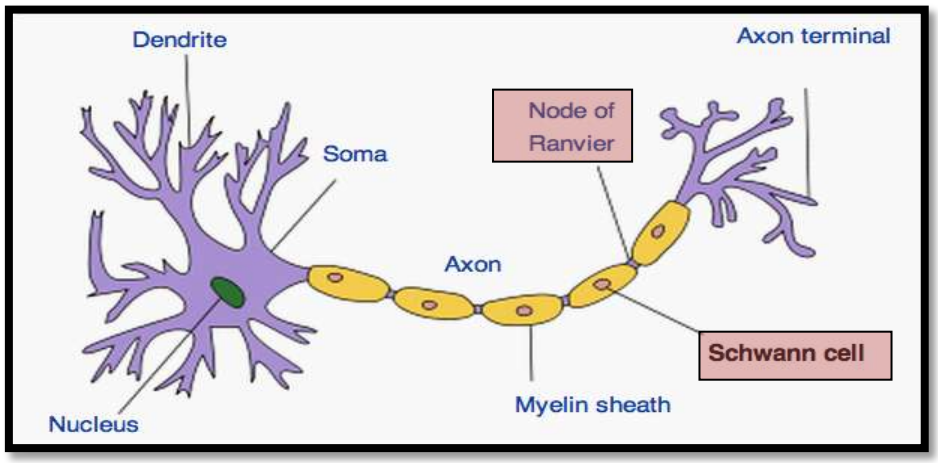
There are 4 types of A nerve:
1) A (alpha) : to muscle
2) A (beta) : touch and pressure
3) A (Gama) : going to receptor on the muscle
4) A (delta) : pain

Myelin sheath:

Formed by **schwann cell** which deposit lipid substance called **sphingomyelin** around the nerve fiber.

The schwann cells are *not continuous*! They're interrupted at **nodes of Ranvier** (2-3 micron) at the junction between 2 cells.

** Nodes of Ranvier have NO schwann cells **



Functions of Myelin sheath:

1. **Insulator عازلة:** makes ion flow across the membrane much more harder & decrease ion flow through the membrane.
   "يمنع خروج الآيونات"
2. **Increase conduction velocity:** (Because ionic currents need to "jump "(from one node of Ranvier To the next)
   كلما زادت المايلينيتيد كلما زادت سرعة السيالات العصبية
3. **Protection.**
4. **Conserve energy:** المايلنيتد نيرف يستخدم طاقة أقل أثناء مرور السيالات العصبية

Changes that occur in the nerve after stimulation by an effective stimulus are:

1. **Electrical changes**
2. **Excitability changes**
3. Thermal changes
4. Chemical changes

** If it was ***sub effective stimulus*** there won't be any changes! **

1. Electrical changes:

The nerve action potential:

It is potential difference along nerve membrane after stimulation by (**Threshold = effective**) stimulus.
فعّال محفّز بـ عليه التأثير بعد للعصب تحصل التي التغيرات.
- Nerve signals (impulses) are transmitted as nerve action potentials conducted along the nerve fiber as a wave of depolarization to its end.

The channels necessary for nerve action potential are: Voltage gated Na+ & k+ channels.

- During action potential we use **oscilloscope** to measure ***rapid changes*** in membrane potential.

Summary of stages of action potential are:

1-RMP:

"Resting Membrane Potential" At the resting state (no stimulation) the membrane is polarized (***-ve inside*** = -90 mv)

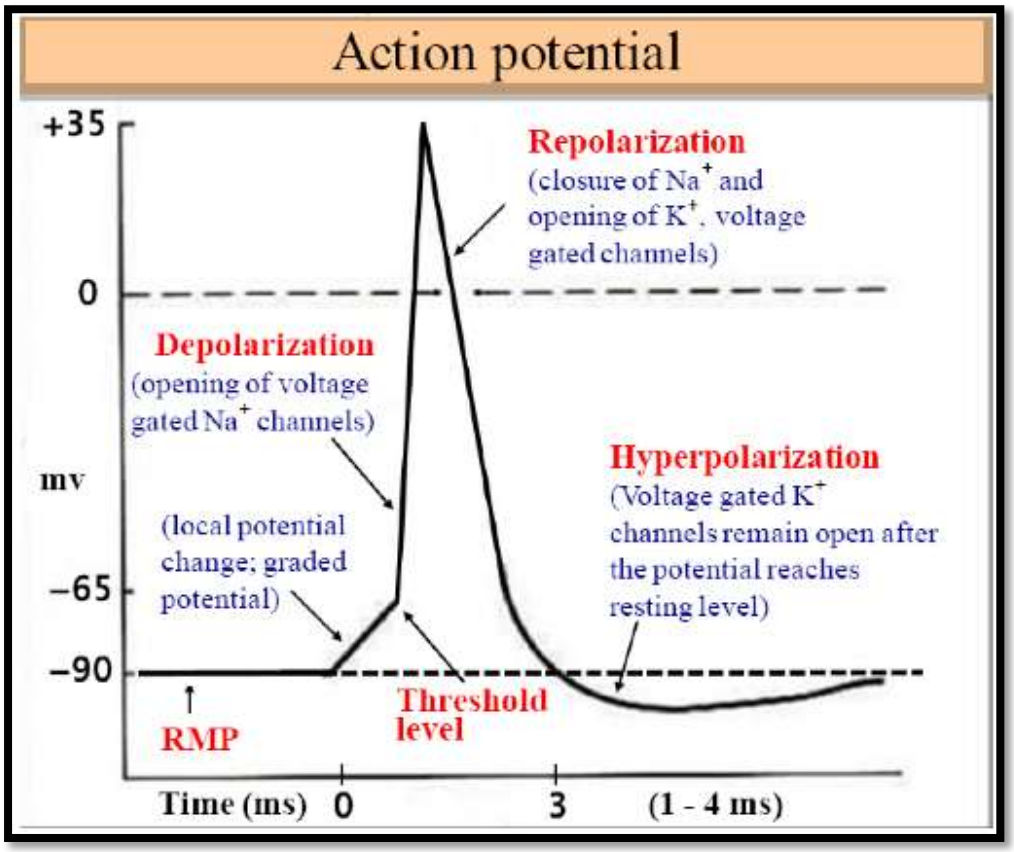
2-Depolarization: "التأين إزالة"

Sudden Na inflow (influx)→ polarized state is lost & potential rises to positive values (reach zero & overshoot to + ve values).

3-Repolarization: "التأين استعادة"

Na channels close & K channels open & K outflow (outflux) to outside → restoration of the normal –ve RMP.

Nerve action potential "spike potential":



Summary of events that causes AP (spike potential):

1-Initiation of Action Potential (AP) & +ve feedback

Vicious circle that opens Na channels CAUSING DEPOLARIZATION STAGE.

Positive Feedback: when Na channels open, Na ions enter the cell, the entry of Na cause more Na Channels to open, more Na ions to enter, this is the meaning of Positive feedback.

Vicious circle: continuous events that reinforce itself through a Positive feedback (when Na enters the cell, cause more Na channels to open, more Na to Enter and so on)

2-Gradual depolarization stage:

- **Threshold stimulus** (An effective stimulus strong enough) → to cause voltage gated Na channels to open & **Na influx** to inside nerve membrane → rises resting potential from-90 **towards zero.**

- **Rise of membrane potential** → open more Na channels & more Na influx (+ve feedback vicious circle) until all voltage gated Na channels open.

- The increase in membrane potential **from -90 to -65** mv cause **explosive opening** of all Na channels & Na conductance is 5000 times great → massive Na+ influx.

So -65mv is called firing level

During Depolarization stage, and as the negativity inside is lost gradually -90 >> -65 >> 0, Na voltage channels opens gradually (Not all of them), but when depolarization reaches the -65, All Na channels open, allow MASSIVE Na influx inside.

3-Depolarization stage:

- **Sharp & rapid depolarization** occurs & membrane potential reach **zero** value & then **overshoot** to reach +35 mv (reversal of polarity) occurs & the inside of the cell becomes +ve
- **The peak** of AP is reached at (+35 to +40 mV).
- At this value all Na+ channels become refractory (begin to **close** suddenly & no more Na+ entry)

& Depolarization ends.

4-Repolarization (return to polarized state):

Cause:

Due to high K conductance (flow) to outside of nerve membrane by **opening of all K channels** → (K outflux carrying **positivity to outside** & **raising negativity inside**)

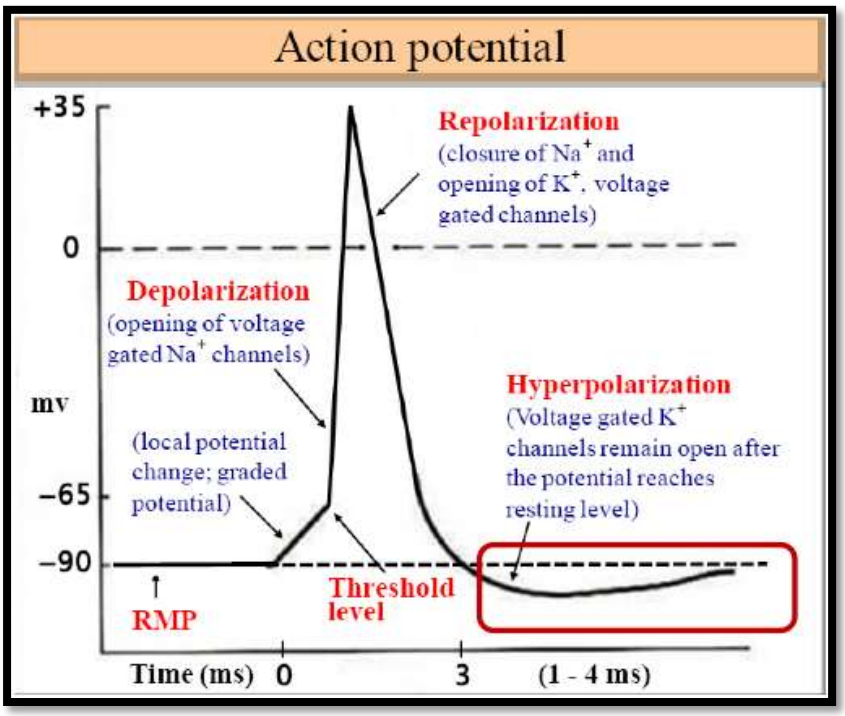
(Also **zero flow of Na** to inside as all Na channels close) → causes negativity inside.

- Membrane **returns** to resting potential (**drop from +35mv towards zero** then to negative resting potential **-90 mv**)

5-Positive after potential (In some nerves):

Membrane potential becomes more negative than resting level.
(Because many K channels remain open & K out flux continue → causing more –ve inside = **hyperpolarized state**)

-(*Positive after potential is wrong terminology it is historical one*)



6-Re-establishment of Na & K ionic gradients & return to resting membrane potential:

A- Na that had inflexed in & K that had oufluxed out returned to **original state** by Na-K pump (active process -need ATP & ATPase)

B- Closure of some K channels so keep some K+ inside (raise positivity inside)

- Gain of these two processes is:

K remain inside causing some positivity to raise potential towards -90 mv

- Duration of nerve action potential is 1-1.5 ms

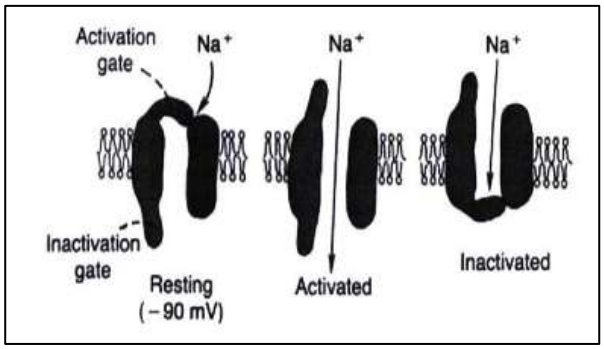
If the nerve takes more than 1-5 ms to produce an AP the nerve here is weak.

The factors necessary for depolarization & repolarization are:

1- Na voltage –gated channels important for both depolarization & repolarization.
2- K voltage –gated channels important for repolarization.

A- Voltage –gated Na channels:

Outer activation gates & inner inactivation gates.

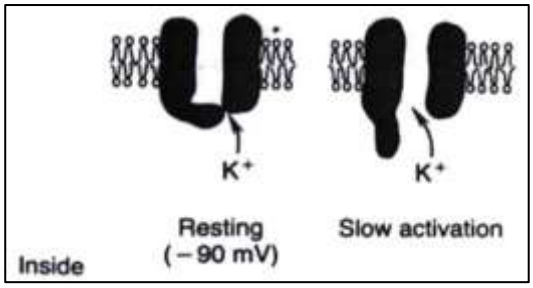


1-Resting state: at RMP -90 mv activation gates close & inactivation gates open → No Na entry.

2- Activated state: after stimulation, the membrane potential rises at a voltage between - 90 to -65mv, **conformational change** occur & activation gates open (now both gates are open) & Na influx causing depolarization.

3- Inactivation state: inactivation gates close slowly while the activation gate is still open & they close completely at **+35 mv** & stops Na influx & repolarization begins.

B- Voltage –gated K channels:



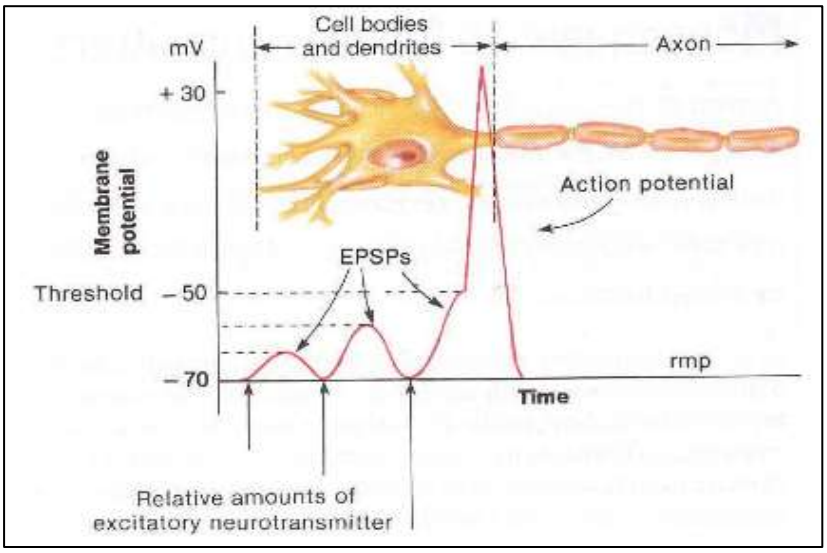
- Only one gate

A- **At RMP** (resting state) the gate of K is closed & no K passes to out.

B- **After stimulation & between -90 to zero mv**, the potassium channel opens slowly & K outflux begins slowly.

- **They open completely only when Na gates close** & when Na influx stop, causing rapid repolarization.

-Acute local potential (acute local response):



A very weak stimulus **(not threshold)** can cause local change in membrane potential.
e.g. from -90 to -85 mv which is not sufficient for generation of AP, this is acute subthreshold potential
(Which is graded متدرج and does not propagate).
It should **increase** to threshold level to **produce AP.**

-The AP differs from local response in that AP is:

(1) Not graded
(2) Obeys All-or None Law
(2) Propagated (conducted for long distances).

Local response	AP
Graded.	**Not graded.**
Does not obey All-or-None Law	Obeys All-or None Law.
Not propagated.	**Propagated** (conducted for long distances).

All or nothing principle:

- The nerve respond to a threshold stimulus maximally or does not respond at all (there are **no half** solutions)

- Once threshold stimulus applied, it gives AP spread all over the nerve fiber.

- Its intensity (peak amplitude) **can not increase** by increasing stimulus intensity (or by suprathreshold).

- **Sub**threshold stimulus cannot elicit action potential (but produce a local response which does not obey this law).

Direction of propagation of AP:

- In one direction from axon hillock to nerve terminal.

- (**Experimentally**) if nerve stimulated at its **importation**, AP passes in **both directions**, Under Artificial condition of electrical stimulation in the laboratory (**only**).

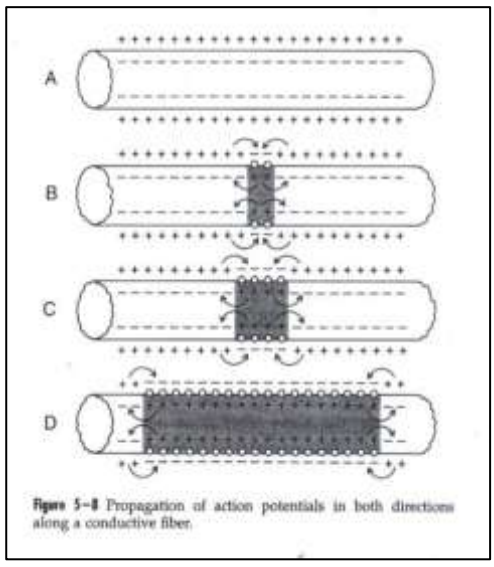


Figure 5–8 Propagation of action potentials in both directions along a conductive fiber.

Na & K conductance (flow) during action potential:

1-At resting state, before AP:

K conductance through K leak channels is 50-100 times as Na.

2-At onset of action potential:

Voltage gated Na channels activated & Na conductance is 5000 folds, at the same time voltage gated K channels begin to **open slowly**.

3-During depolarization:

Na conductance / K conductance > **1000 fold.**

4-At peak of AP:

Na channels close & voltage gated K channels **open** & K conductance **increase.**

5-At repolarization:

The ratio Na conductance/ K conductance **decreases**.

6-At end of AP:

Return to –ve potential, **close** voltage gated K channels & no K+ conductance.

2-Excitability changes

The ability to respond to a second stimulus

1- Latent period. لا يحصل شيء خلالها

2- Absolute refractory (period during depolarization & early repolarization).
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)

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

3- Relative refractory period:-

It is during the late third of repolarization (½ to ¼ absolute refractory periods in its duration)

It is the period during which a second action potential of low amplitude can be elicited by stimulus stronger than normal suprathreshold

Why suprathreshol stimulus?

Because:

1- Na channels still inactive so need stronger stim to open

2- Rapid flow of K to outside during repolarization oppose any Stimulation to occur (so need stronger stim to cause a new AP.)

Propagation of action potential

Transmission of depolarization process along a nerve= spread of nerve impulse:

1- In myelinated nerve fibers by:-

Salutatory conduction (jumping)

AP occurs at nods of Ranvier & directed from node to node, through axoplasm inside & ECF outside. By jumping.

APs can develop only at the Nodes of Ranvier Where

(1) Ions can relatively easily flow in & out

(2) There are voltage-gated channels

Value:-

1- ↑velocity of conduction (100 m/sec in large myelinated nerve fibers in comparison to 0.25 m/sec in small unmyelinated nerve fibers).

2- Conserve energy for axon because only nodes depolarize (need little energy for reestablishment of Na &K ions). 3-Insulation by myelin sheath allow repolarization to occur rapidly (with many K channels have not open)

2- Nonmyelinated nerves by:-

local circuits=Continuous Conduction =point to point

-depolarization pass by local circuits.

-depolarization in an area, + ve charge carried inward by Na ions flow for several 1-3 mm in the axon core & increases the voltage inside the nerve to threshold value to cause depolarization in a new area & Na channels open & depolarization spread to new areas.

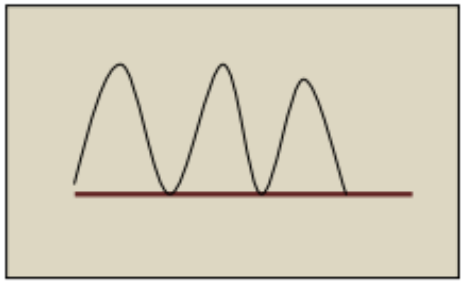
Recording of AP: -

By cathode ray oscilloscope:

1-Monophasic AP:

One microelectrode outside & one inserted into nerve fiber

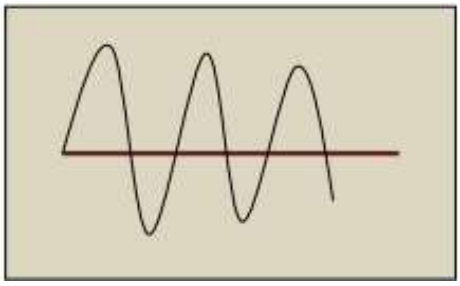
AP↑



2-Biphasic AP:

Tow microelectodes placed on outside of nerve fibers (biphasic means one in one direction then second in second direction.

AP↓



Nerve conduct in one direction

Arthodormic:

اتجاه الاكشن بوتينشال يكون من ناحية وحدة مثال:
السينسوري نيرف الي باليد لو صارله ستيميوليشن بينقل من اليد الى المخ

Antidormic :

لا يمكن تصير بجسم الانسان :
ياخذون نيرف ويسوون عليه التجربة بحيث اذا صارله ستيميوليشن بنقطه معينة ينقلها بالاتجاهين.

Questions

True or False

Q1: if you stimulate any nerve at any place or point, the AP will go in both directions. (True)

Q2: if you stimulate normal nerve from its origin to terminal, the AP will go also in both directions. (False)
AP will go in one direction

Stimulation of nerve cells will increase frequency of signals not duration or length

GOOD LUCK