Physiology 439

MED439
KING SAUD UNIVERSITY

2

Action Potential

Editing file

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Red: Important
Black: In Male & Female slides
Blue: In male slides
Pink: In female slides
Gray: Notes & extra information

Objectives

01 Explain why some members are excitable

02 Describe the electrochemical basis of RMP

03 Describe the mechanism of generation and propagation of AP

04 Describe conduction along nerve fibers role of myelination and how nerve fibers are classified

The Action Potential

افهموا المحاضرة زين لأن جزء كبير من الطب خاصة*
الجهاز العصبي يعتمد على ال
polarization and depolarization

Nerve signals are transmitted by action potentials, which are rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane to produce physiological effects such as:

01 Transmission of impulse along nerve fibers

02 Release of neurotransmitters

03 Muscle contraction

04 Activation or inhibition of glandular secretion

Each action potential begins with a sudden change from the normal resting negative membrane potential to a positive potential and ends with an almost equally rapid change back to the negative potential i.e. inside of the cell is negatively charged at rest until a stimulus triggers then:

1- ICF becomes positive

2- ECF becomes negative

then equilibrium occurs and the charges go back to their normal state (negative inside, positive outside)

helpful video

Stages of the Action Potential

01

Resting Stage

It is the resting membrane potential before the action potential begins. The membrane is“polarized”.

02

Depolarization stage

The membrane suddenly becomes permeable to Na+ ions, allowing tremendous numbers of positively charged Na+ to diffuse to the interior of the axon (Upstroke.) (دخول طوفان من الصوديوم)

03

Repolarization Stage

Na+ channels begin to close and the K+ channels open. Rapid diffusion of K+ ions to the exterior re-establishes the normal negative resting membrane potential. (Downstroke)

04

Hyperpolarization Stage (do not necessarily occur)

For a brief period following repolarization, the K+conductance is higher than at rest.

Na +-K + ATPase pump now starts to move Na+ out & K+ in against their concentration gradient.

Efflux = Exit the cell
Influx = Enters the cell

Stages of active potential Overview

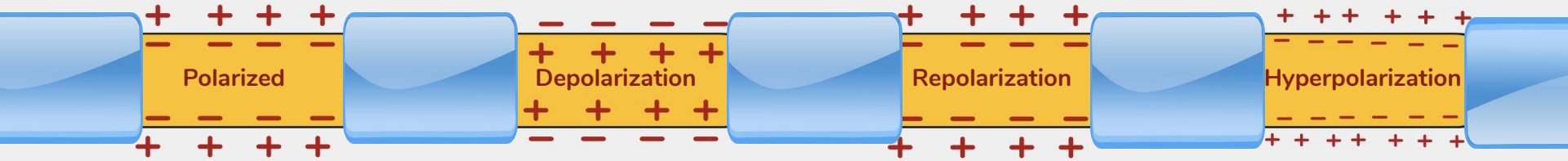
1- Polarized
It is passive transport

Resting membrane potential (RMP) (-70 m to -90 mV)

- No action
- Negative charge inside
- Positive charge outside
  (Clarified previously)

2- Depolarization
It is passive transport

- ➔ Voltage gated Na+ channels are opened
- ➔ Na+ goes inside the cell
  i.e influx of Na+
- ➔ Positive charge inside, negative outside
- occurs after threshold stimulus



3-Repolarization

- ➔ Closure of voltage gated Na+ channels
- ➔ Opening of voltage gated K+ channels
- ➔ K+ Goes rapidly outside the cell
  i.e efflux of K+ • Since Potassium is positive, efflux of potassium means less positive charge inside, this means that the cell will become negative again 'repolarization'

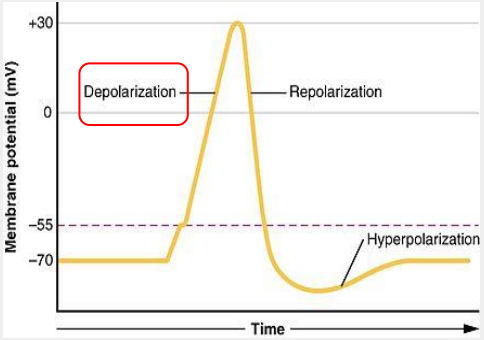
4-Hyperpolarization

- ➔ K+ tries to reestablish polarization
- ➔ K+ thus goes outside the cell rapidly
- ➔ Cell will become extremely polarized (-94mV)
- ➔ (range is -70 to -90)
- ➔ Na+, K+ pump will make equilibrium and repolarization occurs again
  It's Active transport

The change that occurred in the cell voltage due to an stimulus lead to the opening of these " Voltage gated channels "

Depolarization

stimulus comes from the brains highest center



That's why it becomes negative on the outside and positive in the inside

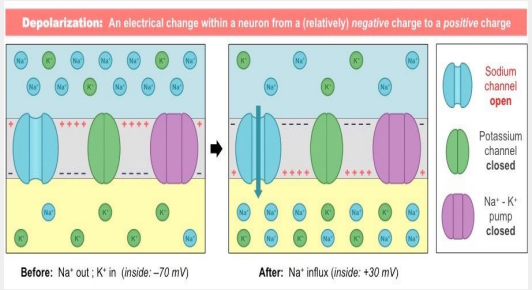
Lots of Na+ goes inside the cell (more positivity inside, less positivity outside)

Happens when the curve surpasses the threshold stimulus

The threshold stimulus is the weakest stimulus that could generate an action potential in a neuron (Will be discussed in a bit)

Occurs within milliseconds

in curve, it represents the upward shift



Animated explanation, click here!

Repolarization

هو فكرة الاسم أنه بالبداية يكون قطبيته سالبة (سالب ٧٠ إلى سالب ٩٠) بعدين تبدأ تزيد (الشحنة الموجبة خلال جزء من الثانية ويتكمل تزيد ويتصير موجبة (+٥٠ مثلا وبعدين بترجع سالبة زي ماكانت قبل ونرجع نسميها repolarization

Voltage gated Na+ channels are closed & Voltage gated K+ Channels are opened

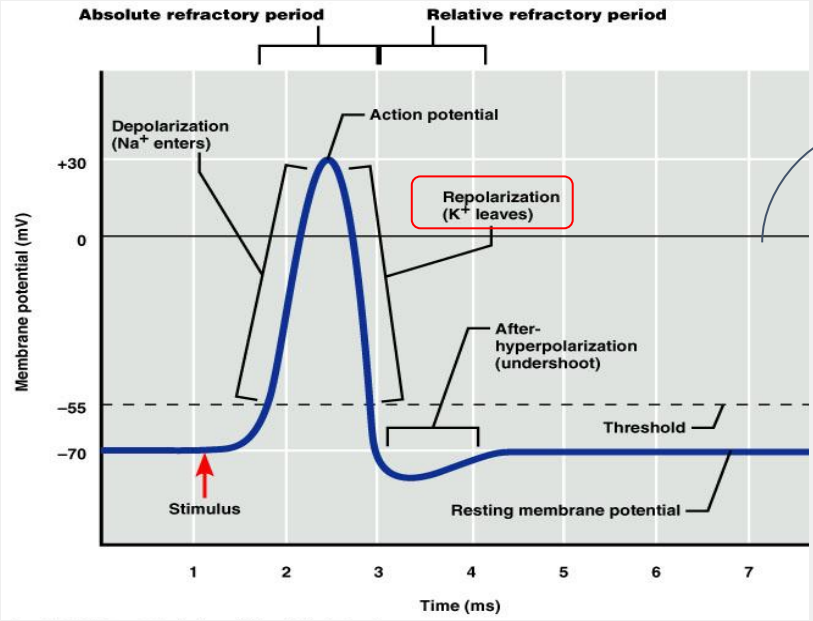
Rapid efflux of K+

Repolarization established

Hyperpolarization may or may not happen (Extreme amount K+ outside)

If happened

Na+ , K+ pump will achieve equilibrium by pumping 3 sodium ions out and 2 potassium ions in



Extra

Animation

Notice that the **upstroke** indicates depolarization, that's when influx of Na+ takes place. **Downstroke** indicates repolarization where the Na+ channels are closed and K+ gates are open for an efflux (because when you reduce positive charge. you gain more net negative charge) and that's the way it should be in a resting membrane

Repolarization is the downward shift in the curve

Since K+ is positive, Efflux of K+ means K+ will carry its positive charge all the way to the extracellular fluid, leaving the intracellular fluid negative

Hyperpolarization is when K+ is abundant outside the cell which causes the cell to become negative, yes. but not in the desired range (-70 to -90) hyperpolarization means its potential surpassed -90 mV (Will be discussed in a bit though)

Effects of stimuli

Quiz yourself on threshold stimulus here (2 questions)

Threshold Stimulus= (-55)

- The membrane potential at which occurrence of the action potential is inevitable.
- The minimum amount of stimulus that can produce excitation .
- نقطة اللاعودة

All or Nothing Principle:

- Once threshold value for excitation is reached a full action potential is produced

Ex : it has a dominos effect : (once the first domino falls (reaching the threshold) the rest of the line will automatically fall too (full action potential produced)

- action potential intensity CAN NOT be increased by increasing stimulus intensity

Acute Subthreshold Potential:

- Stimulus that results only in local depolarization when stimulus is below the threshold (acute local potentials) .

(Very weak stimulus to produce an excitation)

To be more familiar with threshold, take this for an example

- ➔ Imagine a cat sleeping in the middle of a street. there aren't any surrounding voices that could make the cat show signs of fear, right? that's where the membrane will be on rest.
- ➔ the cat heard a voice 50m away and he started to feel disturbed. that's where it hits the **sub**threshold potential (may or may not show signs of fear)
- ➔ Suddenly, a car showed up in the street and it was fast, very fast to the point where the cat did hit the threshold stimulus and started to fear and that's when there is no going back. The cat would immediately go away from the street as a response to the stimuli (the threshold stimuli)

Types of transport channels through the nerve membrane

1-Voltage gated Na+ channels

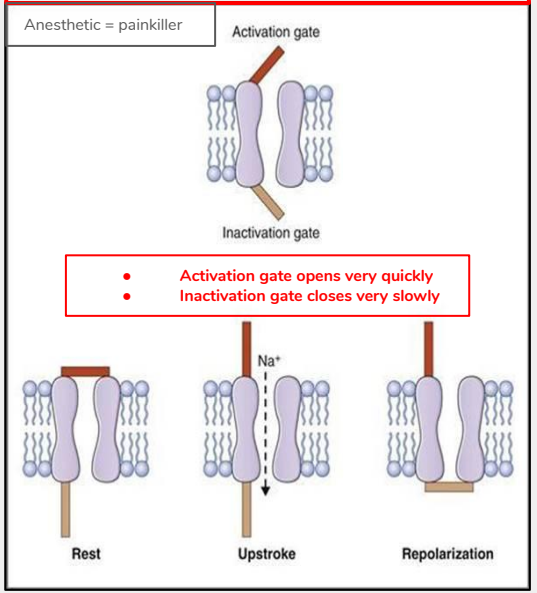
- At rest, the activation gate is closed and the inactivation gate is open.
- During the upstroke (depolarization) of the action potential, both gates are open and Na+ flows into the cell down its electrochemical potential gradient.
- During repolarization ,the activation gate remains open but the inactivation gate is closed.

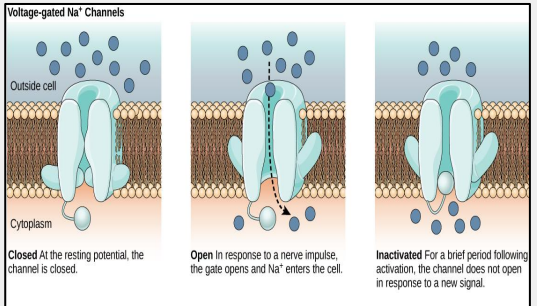
During Rest → Once there is an action potential → To achieve repolarization → Voltage gated K+ Channels takes place

- activation (outside) gate will be closed and Sodium cannot cross the membrane
- activation gates will open, more and more sodium will enter and more net positive charge will be present inside the cell, right?
- Potassium must go out of the cell but before that, inactivation gate of Na+ must close in order to prevent more Na+ to go inside
- discussed in next slide

local anesthetic **Lidocaine** blocks this channel

Anesthetic = painkiller

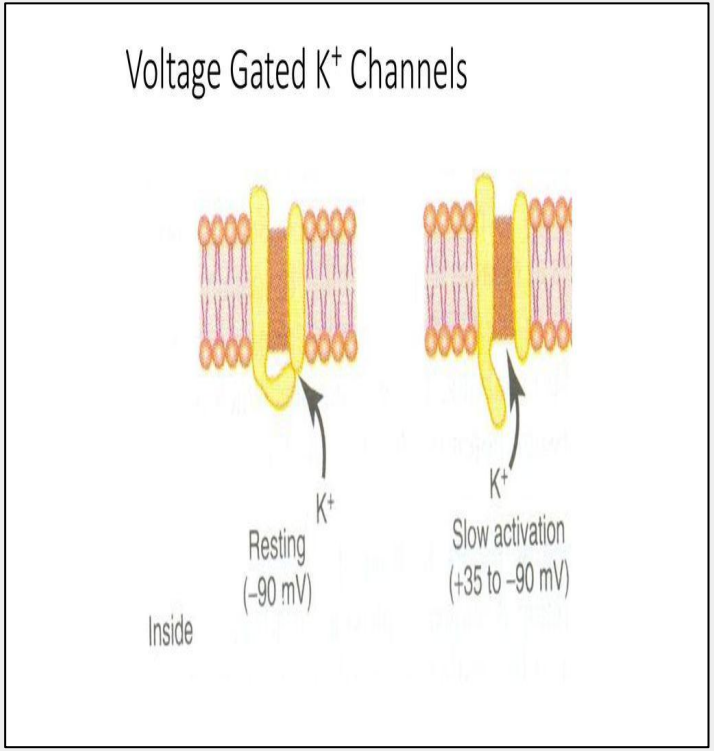




Types of transport channels through the nerve membrane

2-Voltage gated K+ channels

- Has one gate only
- at rest, the gate of the potassium channel is closed and potassium ions are prevented from passing through this channel to the exterior.
- Shortly after depolarization,when the sodium channel begins to be inactivated, the potassium channel opens.
- K+ exits (Efflux) i.e. Repolarization



1. Now as I said in the previous slide, sodium inactivation gate will be closed because if not, there will be no point in the efflux of K+ (positive charges go in, positive charges go out) what we want is positive charges staying inside and positive charges going outside to reduce the net positive charge.

2. Keep in mind that voltage gated K+ channels have only one channel (intracellular gate) because its only goal is to reduce the positive charge by pumping out potassium

3. This stage occurs when the membrane potential hits a specific voltage (for example it increases from -70 to +55)

Tetraethylammonium (TEA) blocks this channel

Refractory Periods

Absolute refractory period

The period during which a second action potential cannot be elicited, even with a strong stimulus (after threshold).

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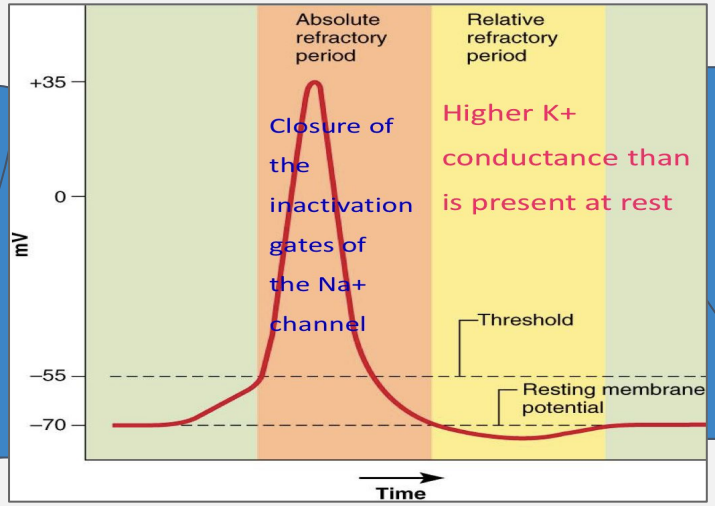


Relative refractory period

Can trigger new action potential if stimulus is very strong(higher than the threshold).(at hyperpolarization)

هنا في هذه المرحلة نسبي معناها يعتمد على قوة التحفيز إذا كان قوي وكافي يستجيب

Propagation of the action potential

Propagation of the action potential (one of the most important features of the AP)

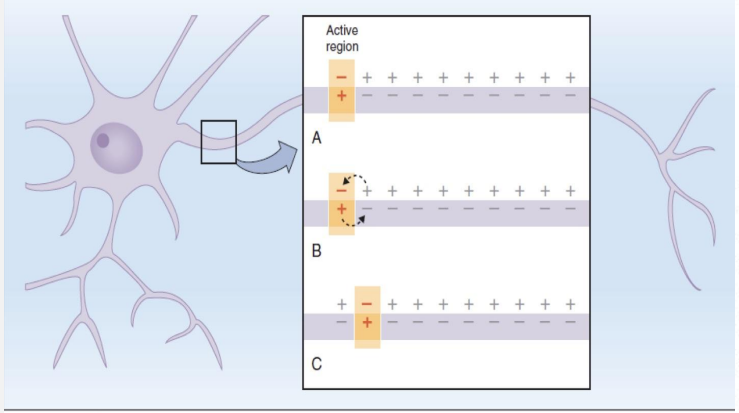
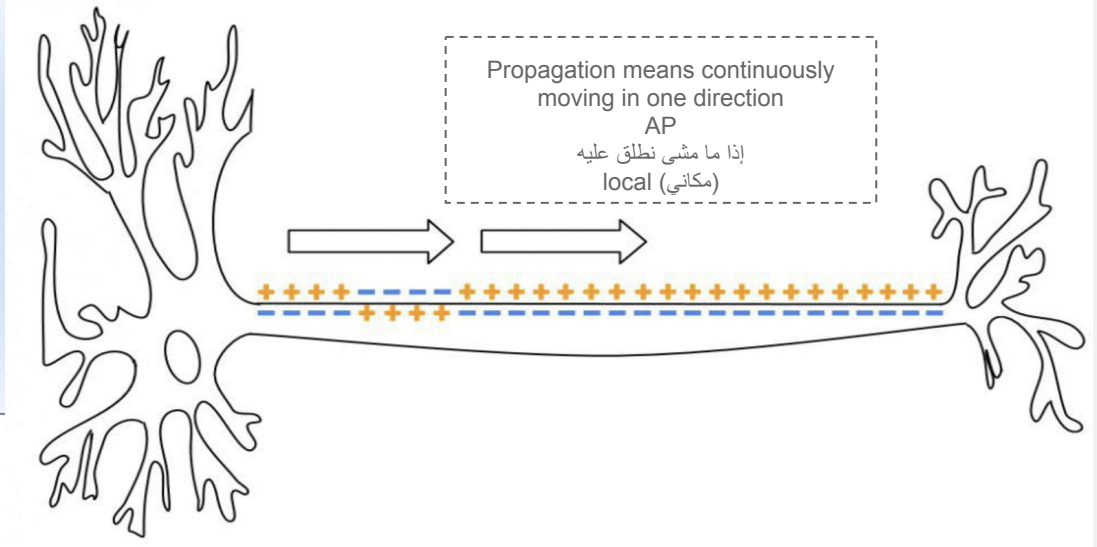


Figure 1–15 Spread of depolarization down a nerve fiber by local currents. **A**, The initial segment of the axon has fired an action potential, and the potential difference across the cell membrane has reversed to become inside positive. The adjacent area is inactive and remains at the resting membrane potential, inside negative. **B**, At the active site, positive charges inside the nerve flow to the adjacent inactive area. **C**, Local current flow causes the adjacent area to be depolarized to threshold and to fire action potentials; the original active region has repolarized back to the resting membrane potential.



Conduction Velocity

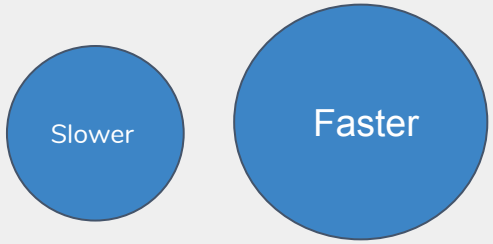
It is the speed at which action potentials are conducted (propagated) along a nerve or muscle fiber.

Mechanisms that increase conduction velocity along a nerve:

Nerve diameter

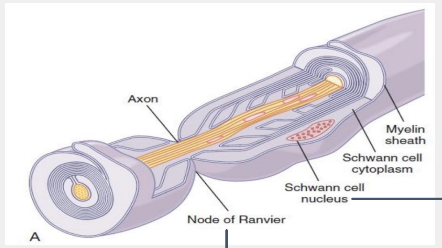
The larger the diameter, the faster the transmission,
Because:
-Large fiber offers Less resistance to local current flow & more ions will flow.

القطر الأكبر يمرر سيال وشحنات أكثر كذلك ما يصير عندي اصطدام و احتكاك بين الشحنات فممكن تلغي بعض نفس ما يحدث بالقطر الضيق



Myelination:

Myelin is an insulator that makes it more difficult for charges to flow between intracellular and extracellular fluids.



The layers of Schwann cell membrane contain the lipid substance **sphingomyelin** which is excellent electrical insulator that decreases ion flow through the membrane.
(مسؤولة عن تكوين قطع الميلانين)

small uninsulated area where ions can flow with ease.

Myelination

Test your knowledge on action potential here!

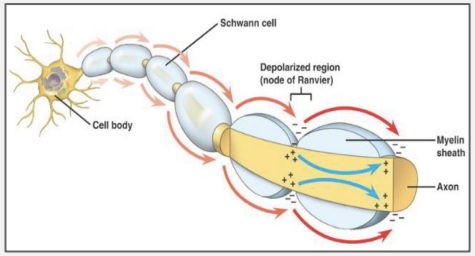
Saltatory Conduction (jumping)

It is the jumping of action potentials from one node of ranvier to the next as they propagate along a myelinated fiber.

- **Value:**

1- Increases conduction velocity.

2- Conserves energy for axon because only nodes depolarize.



What happens if myelination is lost?

1- **Multiple sclerosis** (Usually young adults)

–Autoimmune disease (Immune system attacks the myelin sheaths surrounding axons as well as the axons themselves).

– Blindness, problems

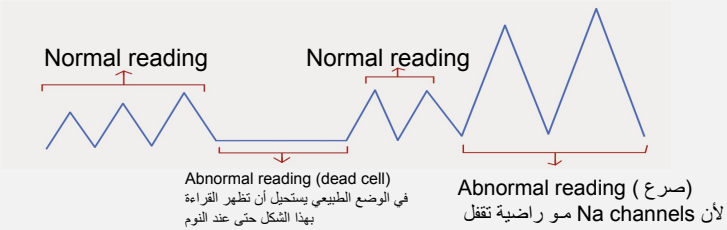
– controlling muscles

2- **Ultimately paralysis**

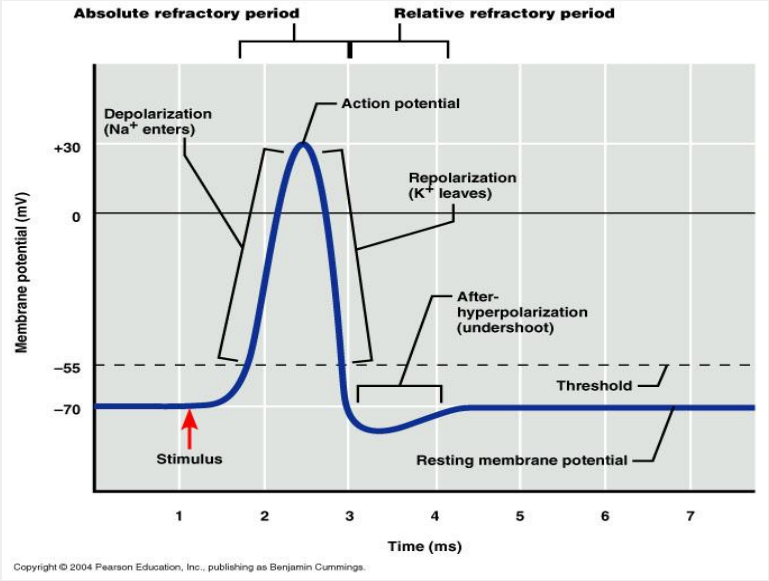
3- **Scar tissues (scleroses) replaces some damaged cells.**

- **Affects the respiratory tracts muscles and can cause death**

Clinical application:
electroencephalogram test **(EEG)**: is a test used to find problems related to electrical activity of the brain



SUMMARY



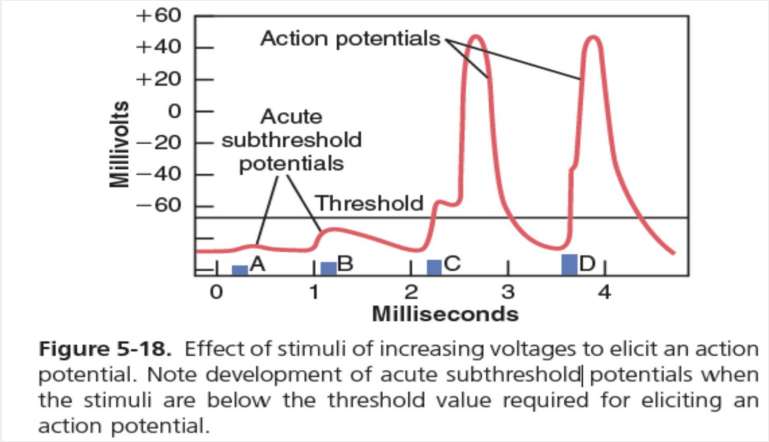


Figure 5-18. Effect of stimuli of increasing voltages to elicit an action potential. Note development of acute subthreshold potentials when the stimuli are below the threshold value required for eliciting an action potential.

1- Polarized

Resting membrane potential (RMP) (-70 mV to -90 mV)

- No action
- Negative charge inside
- Positive charge outside
  (Clarified previously)

2- Depolarization

- ➔ Voltage gated Na+ channels are opened
- ➔ Na+ goes inside the cell
  i.e influx of Na+
- ➔ Positive charge inside, negative outside
- occurs after threshold stimulus

3-Repolarization

- ➔ Closure of voltage gated Na+ channels
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- ➔ K+ Goes rapidly outside the cell
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4-Hyperpolarization

- ➔ K+ tries to reestablish polarization
- ➔ K+ thus goes outside the cell rapidly
- ➔ Cell will become extremely polarized (-94mV)
- ➔ (range is -70 to -90)
- ➔ Na+, K+ pump will make equilibrium and repolarization occurs again

QUIZ!

MCQs

Q1: Relative refractory period can trigger new action potential if stimulus is .....?			
A) Equal to the threshold	B) Lower than the threshold	C) after threshold	D) higher than the threshold
Q2 : The layers of Schwann cell membrane contain which lipid substance?			
A) Phospholipids	B) steroids	C) sphingomyelin	D) glycolipids
Q3 : A term used when there is a stimulus which is not sufficient enough to produce an action potential response (local effect)			
A) Threshold	B) Subthreshold	C) All or Nothing	D) A and B
Q4 : Which of the following effluxes in respond to repolarization stage			
A) Calcium	B) Potassium	C) Sodium	D) B and C
Q5 : When talking about action potential, which one of these stages is not a necessarily occuring stage?			
A) Depolarization	B) Repolarization	C) Hyperpolarization	D) Polarization
Q6 :which nerve has the highest velocity ?			
A) unmyelinated nerve with small diameter	B) unmyelinated nerve with large length	C) myelinated nerve	D) unmyelinated nerve with small length

SAQ

Q1: Name two benefits of the Saltatory Conduction?

Q2: Speaking of the activation and inactivation gates of voltage gated Na+ channels, which gate opens quickly and which one does closes slowly?

MCQs key answer :

1) D
2) C
3) B
4) B
5) C
6) C

SAQ answer key :

1)1- Increases conduction velocity.
2- Conserves energy for axon because only nodes depolarize.
2) Activation gate opens quickly, inactivation gate closes slowly

Physiology 439

THANK YOU

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Question bank