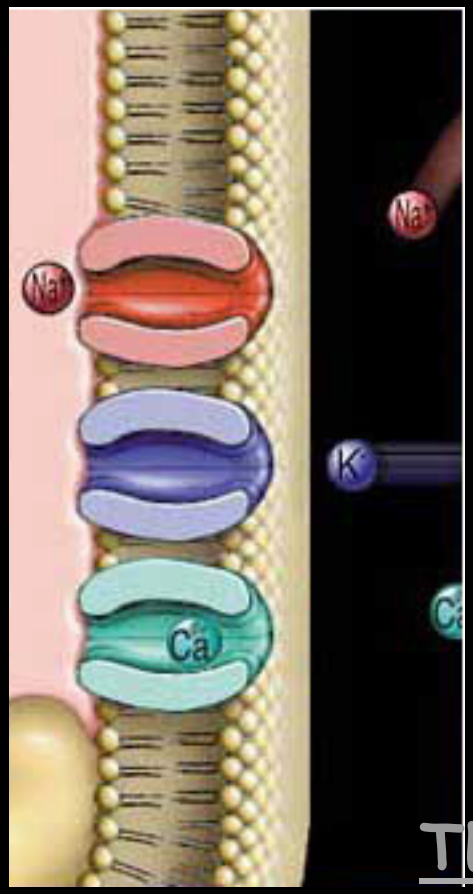


The excitable tissues (Nerve+ Muscle)

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 13TH EDITION

UNIT II CHAPTER 5

Objectives

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

- Discuss the resting membrane potential and its genesis.
- Know the ionic channels involved in resting membrane potential.
- Describe the function Na+-K+ pump and the stages of action potential.
- Explain the threshold Potential, local Response and action Potentials.
- 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.

The nerve

Neuron:-

DIF: unit of function of the central nervous system

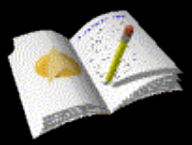
Parts of motor neuron & function of each part:

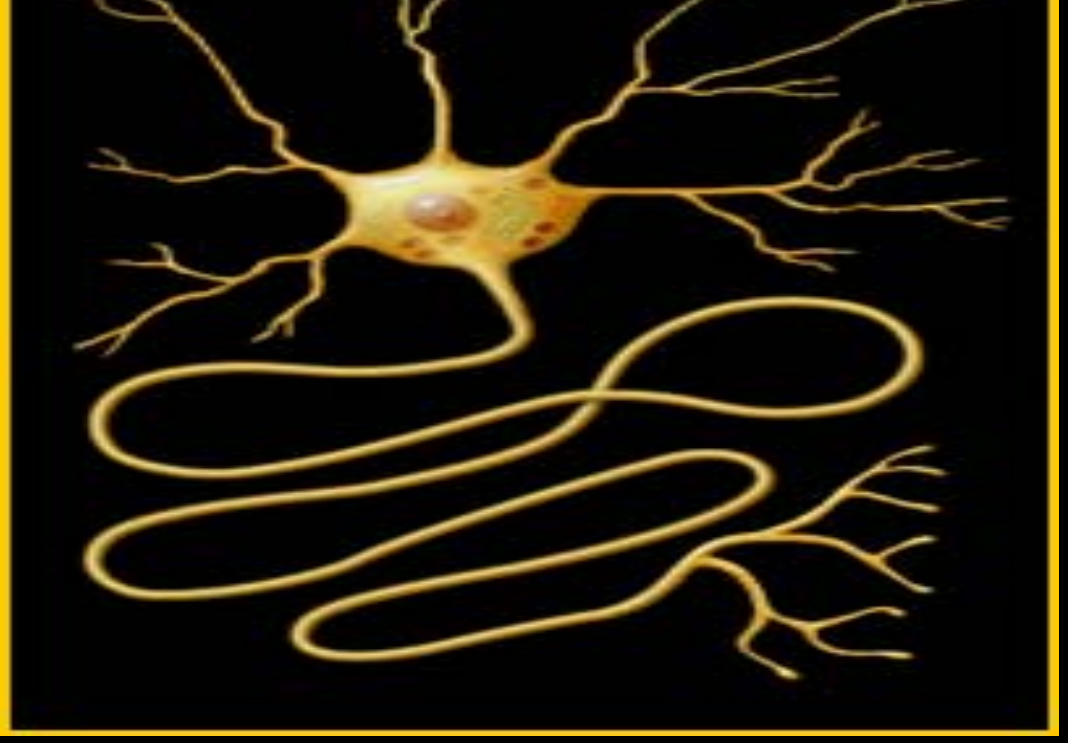
1- Soma (cell body)

2-Dendrites carry nerve impulses from surroundings to the soma

3 Axon hillock

4-Axon & axon terminal





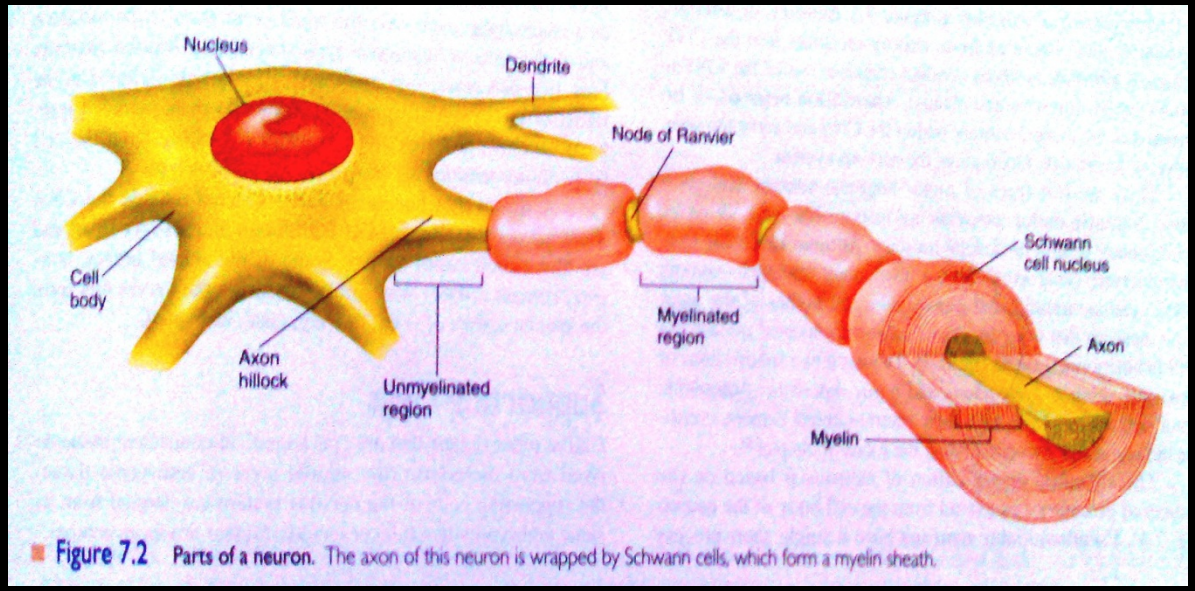
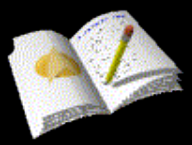


Figure 7.2 **Parts of a neuron.** The axon of this neuron is wrapped by Schwann cells, which form a myelin sheath.

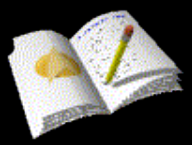


-Histological classification of axons:-

1- myelinated : have myelin sheath (diameter more than 1um)

2- unmyelinated (diameter less than1um)

-type C :postganglionic autonomic &pain fibers

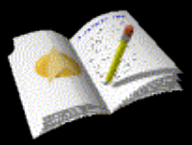


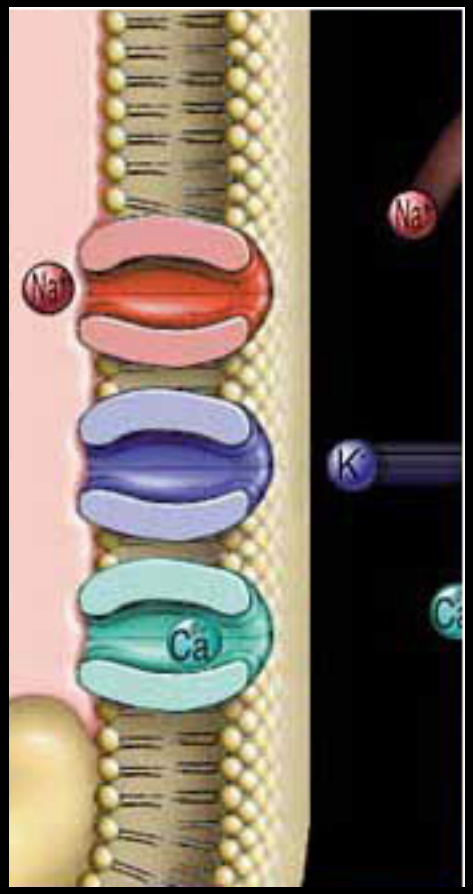
- -Myelin sheath is formed by schwann cell which deposit sphingomyelin

Functions of myelin sheath

1-insulator

3- increase conduction velocity





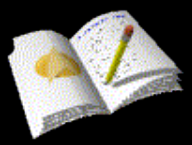
The resting membrane potential of nerves

RESTING MEMBRANE POTENTIAL

DIF: it is potential difference across membrane during rest (without stimulation)

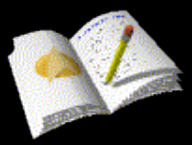
Value:- -70 to-90 mv in large nerve fibers (-ve inside)

-The membrane is polarized



Causes of RMP:

- 1. RMP is 100 times more permeable to K+ than Na+. K+ tends to leak out of the cell down its conc gradient, carrying +ve charge with it. (through K leak channels).
- 2. non-diffusible anions (proteins, sulphate and phosphate ions) cannot leave the cell.
- 3. very small amount of Na+ diffuses into the cell down its conc gradient. The mb only slightly permeable to Na+. (through Na+ leak channels).
- 4. Na+-K+ pump maintain conc gradients of K+, and Na+ between the two sides of the mb.

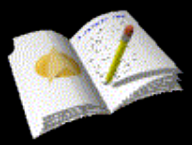


Origin of RMP:

1- Contribution of K diffusion potential:-

N.B/ K diffusion contributes far more to membrane potential .

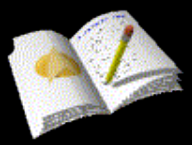
-K leak channels:- K OUTFLUX TO OUTSIDE causing –ve inside (from high conc inside to outside carrying +ve charge with it→ electropositivity outside& electronegativity inside

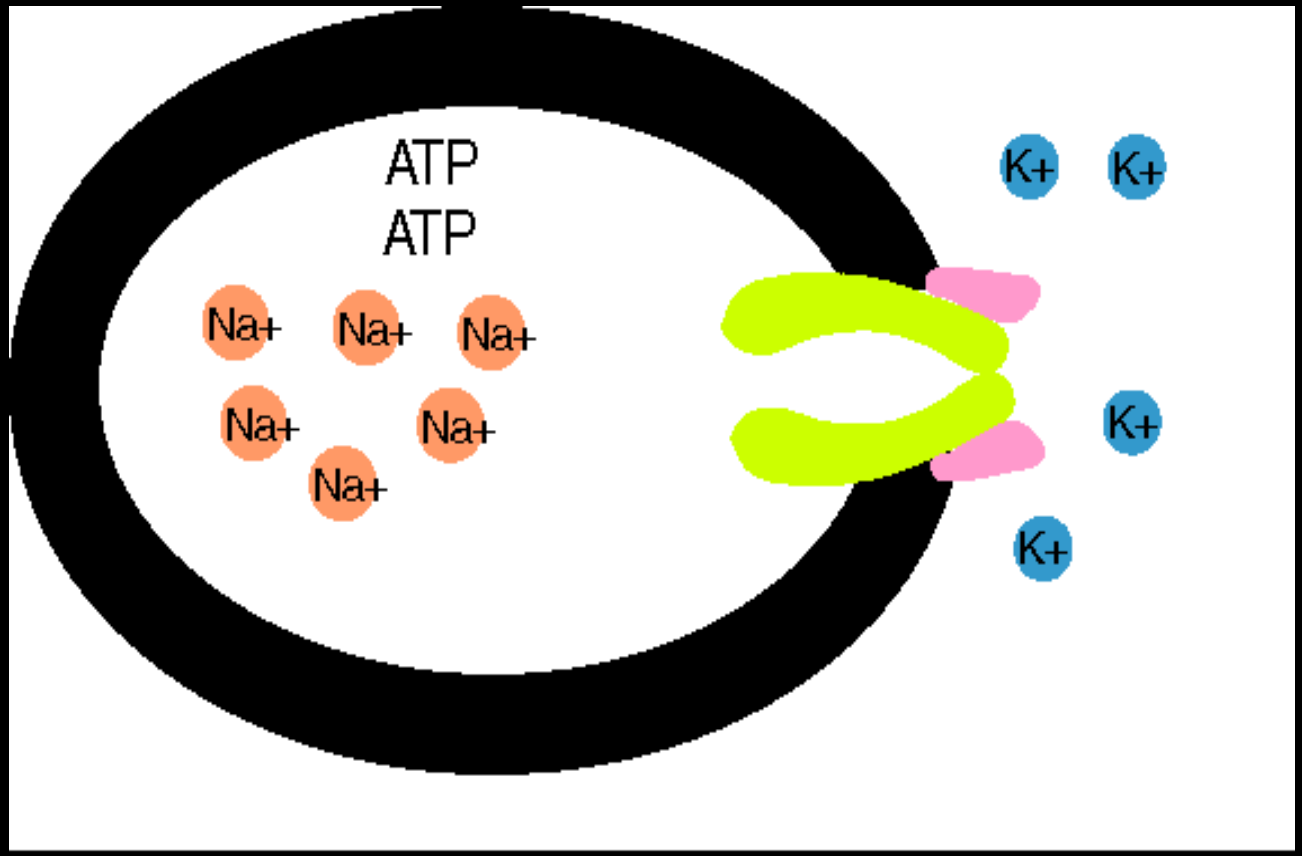


- **2- Contribution of Na diffusion potential:-**

  Na leak channels :- Slight membrane permeability to Na ions in leak channels from outside to inside.(why slight?)

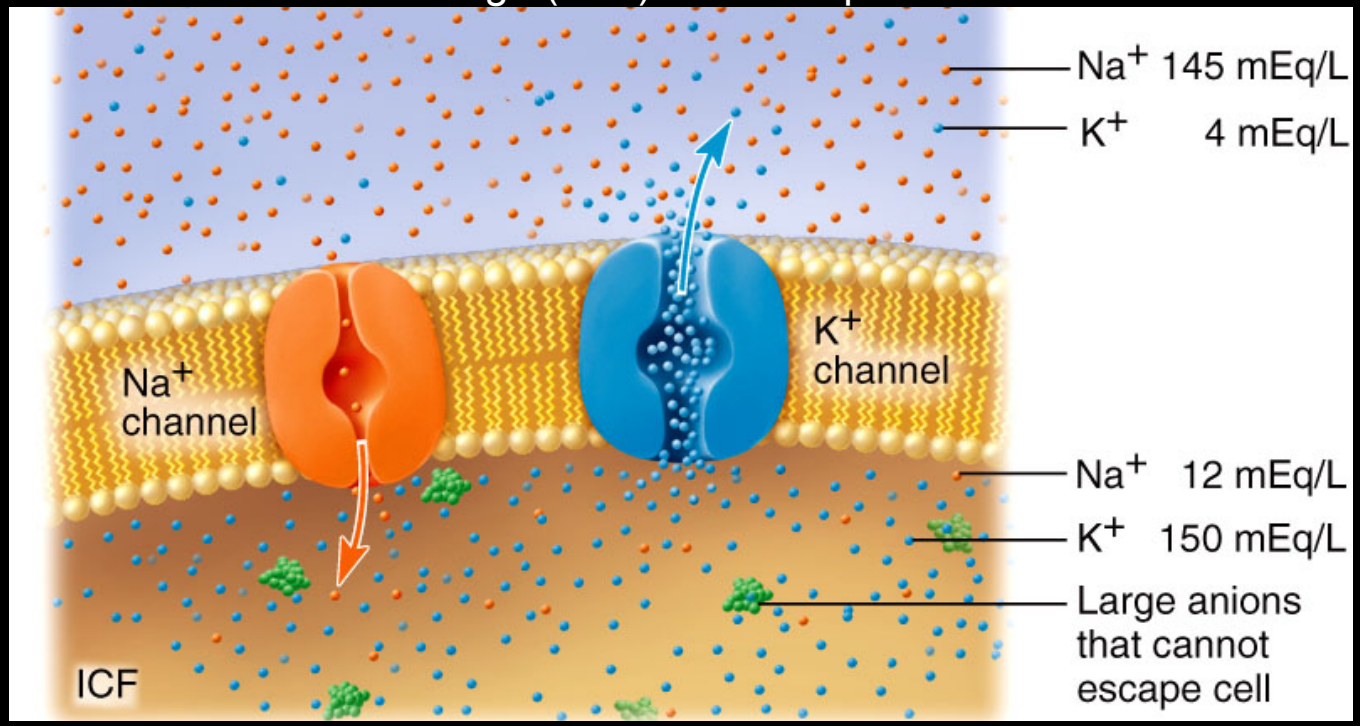
3. **Na+-K+ pump** maintain conc gradients of K+, and Na+ between the two sides of the mb.




ATP
ATP
Na+
Na+
Na+
Na+
Na+
Na+
K+
K+
K+
K+

What does it mean when a neuron “fires”?

- Firing = excitability = action potential = nerve impulse
- Recall resting potential of all cells
  - High K+ in; high Na+ out
  - Cell is polarized
  - Cell overall neg. charge 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



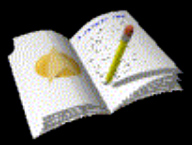
Changes that occure through the nerve after stimulation by threshold (effective) stimulus:-

1- Electrical changes (nerve action potential)

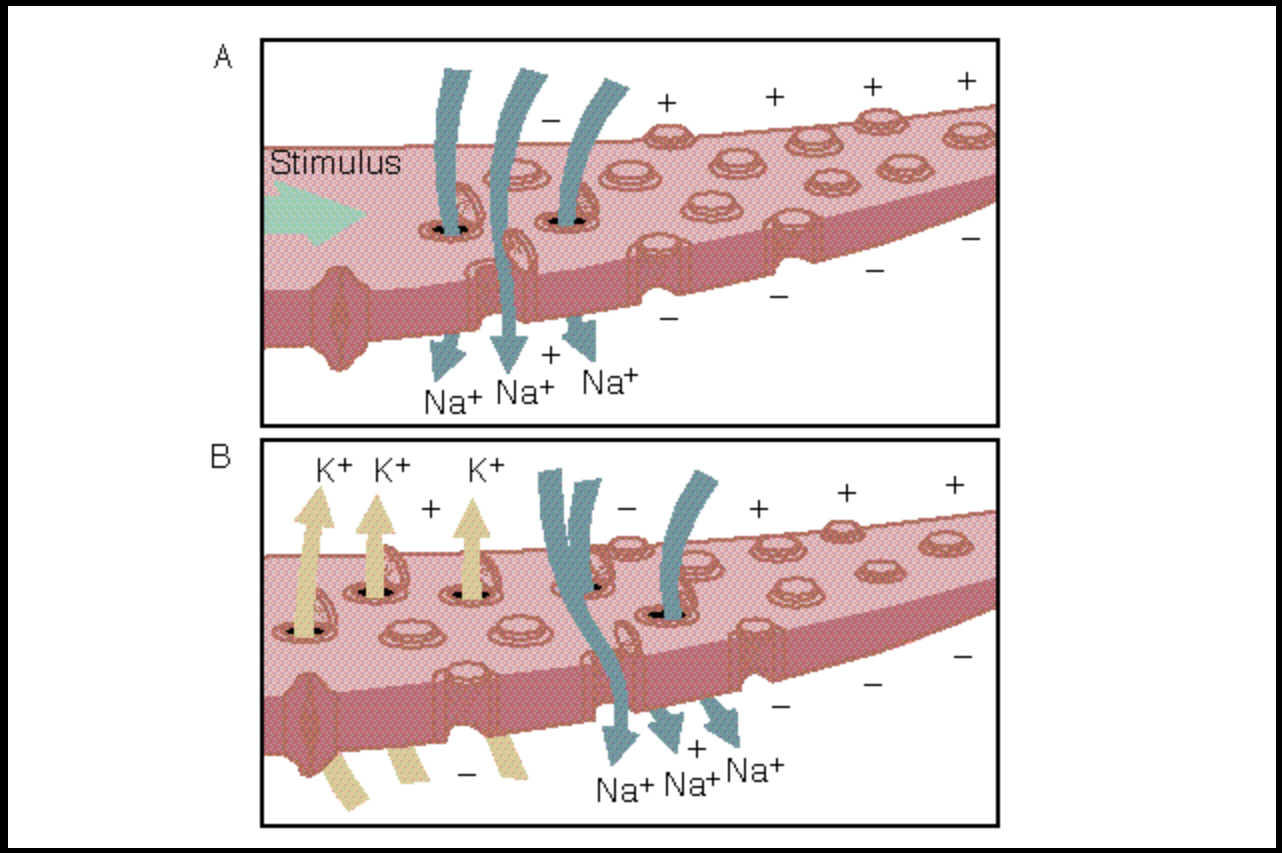
2- Excitability changes

3-Thermal changes

4-Chemical changes

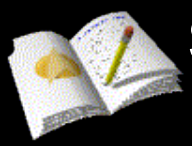


Nerve physiology: Action potentials



The 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



1- Electrical changes

The nerve action potential

-It is potential difference along nerve membrane after stimulation

by threshold (effective)stimulus

- oscilloscope to measure rapid changes in membrane potential

-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 voltage gated Na &

Voltage gated k channels

Threshold stimulus

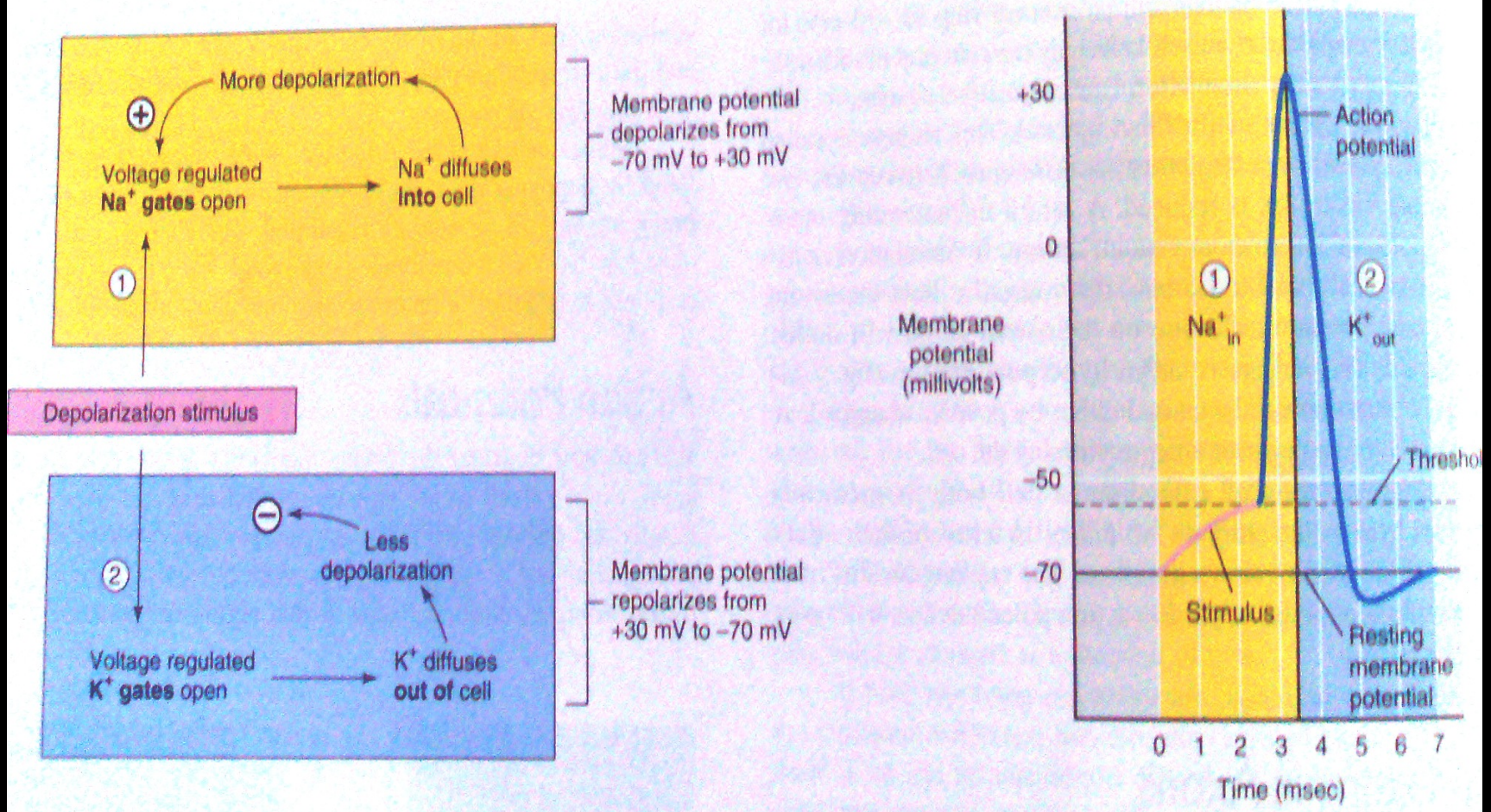


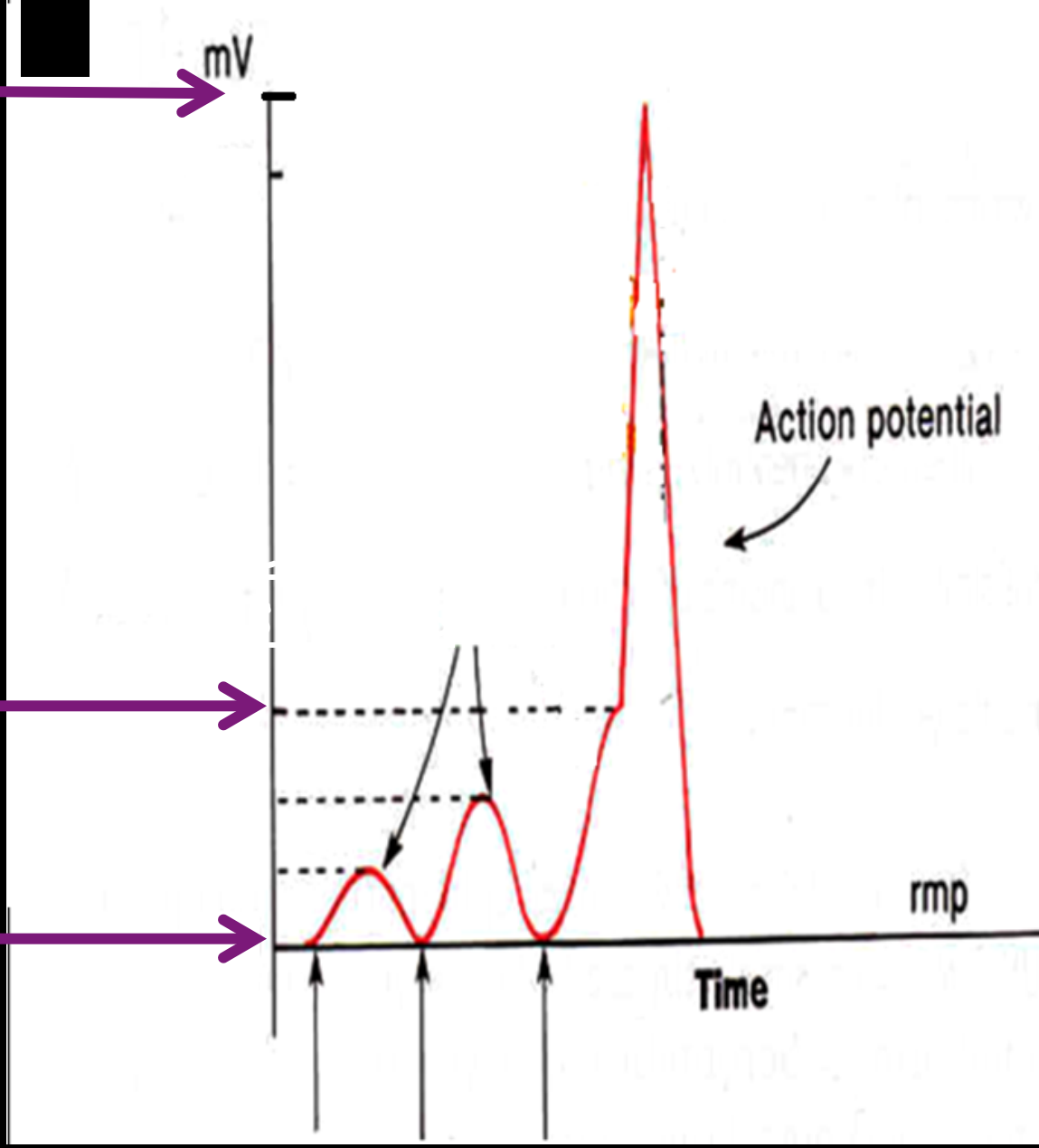
Figure 7.13 Depolarization of an axon affects Na^+ and K^+ diffusion in sequence. *(1)* Na^+ gates open and Na^+ diffuses into the cell. *(2)* After a brief

Reversal Potential = + 35 mV

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

RMP= -90 mV

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



Increasing Stimulation

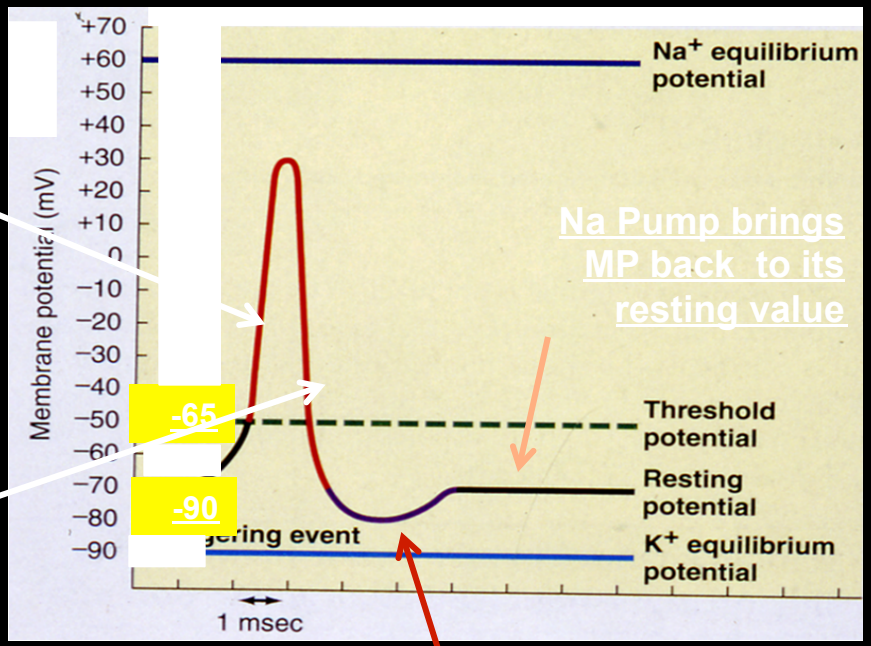
We need to start from the baseline i.e., Resting State of the cell i.e, at the RMP

✓ A threshold Stimulus will lead to →

✓ (1) Depolarization

(2) Repolarization phase .

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

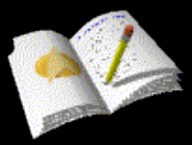


Hyperpolarization (positive after-potential)

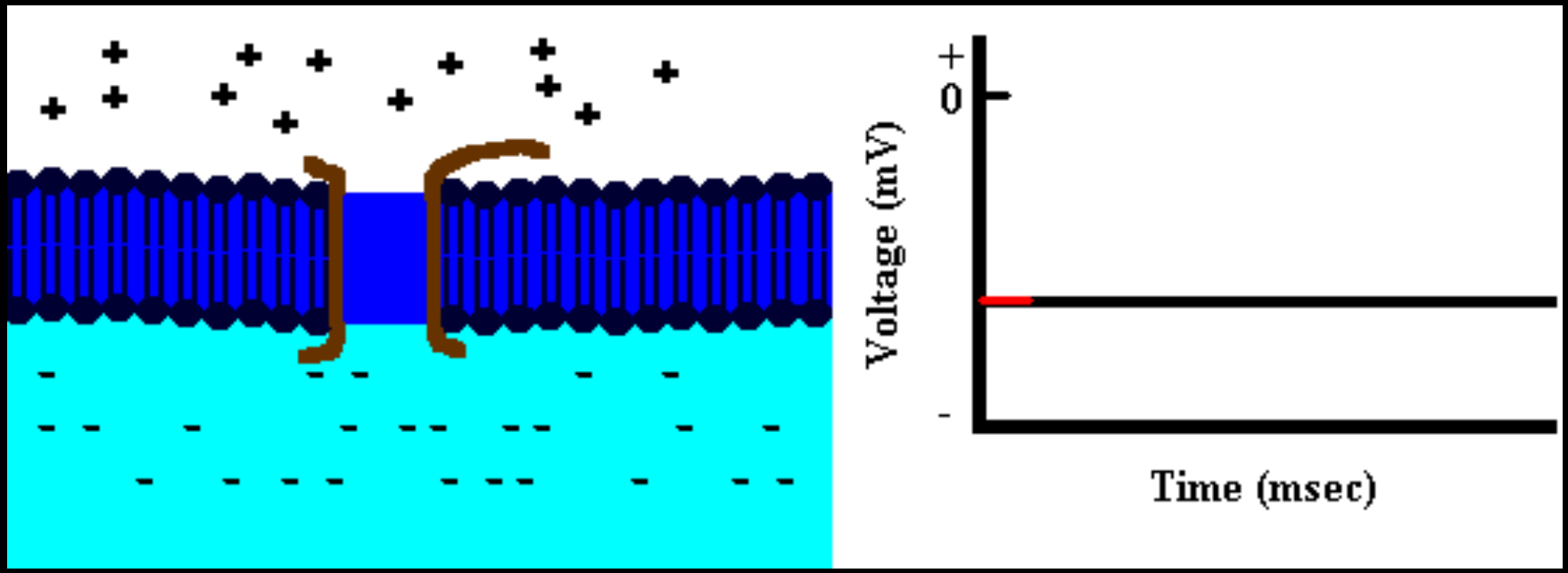
Summary of events that causes AP:-

1-Initiation of Action Potential (AP)

- -70 to-90 mv is the resting potential
- Threshold stimulus open voltage gated Na channels & 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.

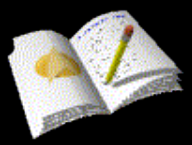


Depolarization

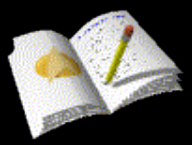


2-Depolarization occurs & membrane potential reach zero value to reach + 35 mv,

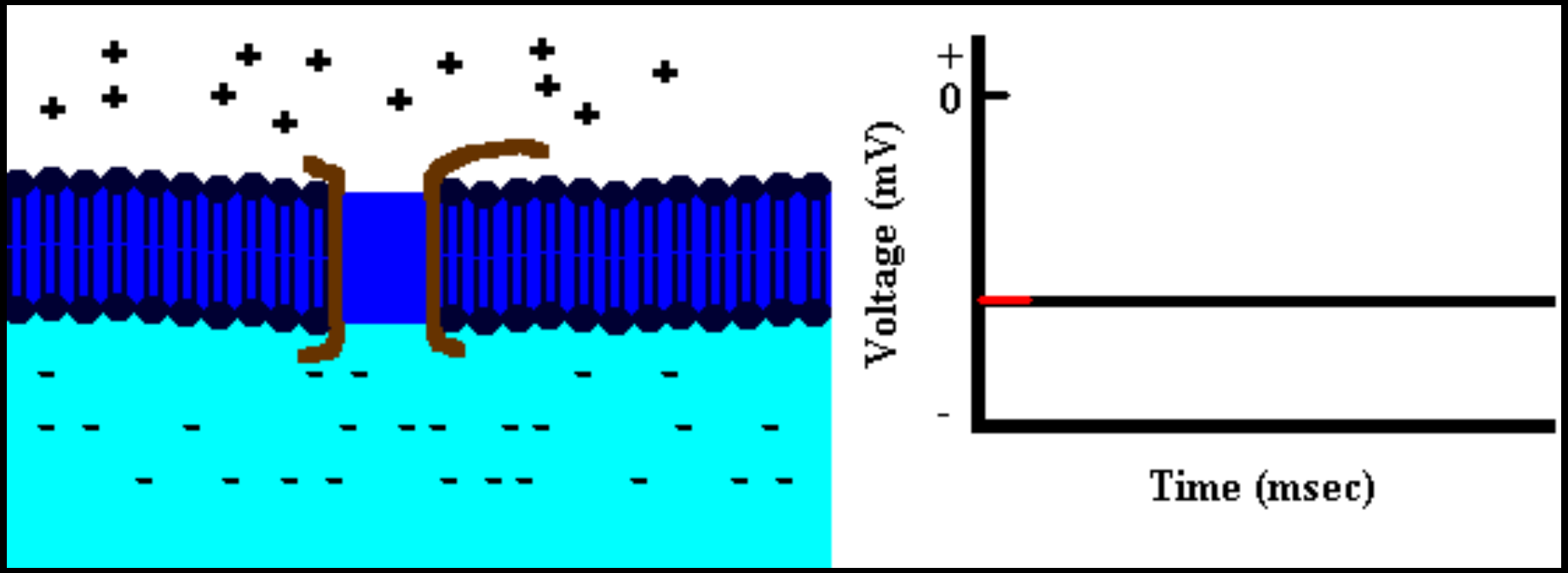
-at + 35 mv all Na channels begin to close suddenly(Depolarization ends)



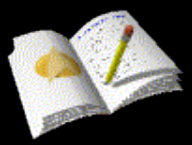
c-Repolarization :- due to high K conductance(flow) to outside (K outflux) by openning of all voltage gated K channels (causes negativity inside)



Repolarization



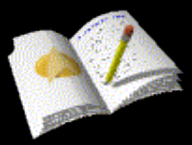
- Hyperpolarization: Why?
- Na-K pump now start to move Na out & K in against their concentration gradient, so the RMP is resumed and the membrane is ready for another stimulus



The action potential (cont.)***

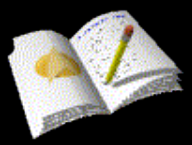
Threshold stimulus:

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 **AP**



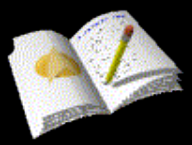
Subthreshold stimulus:

Stimulus that result only in local depolarisation



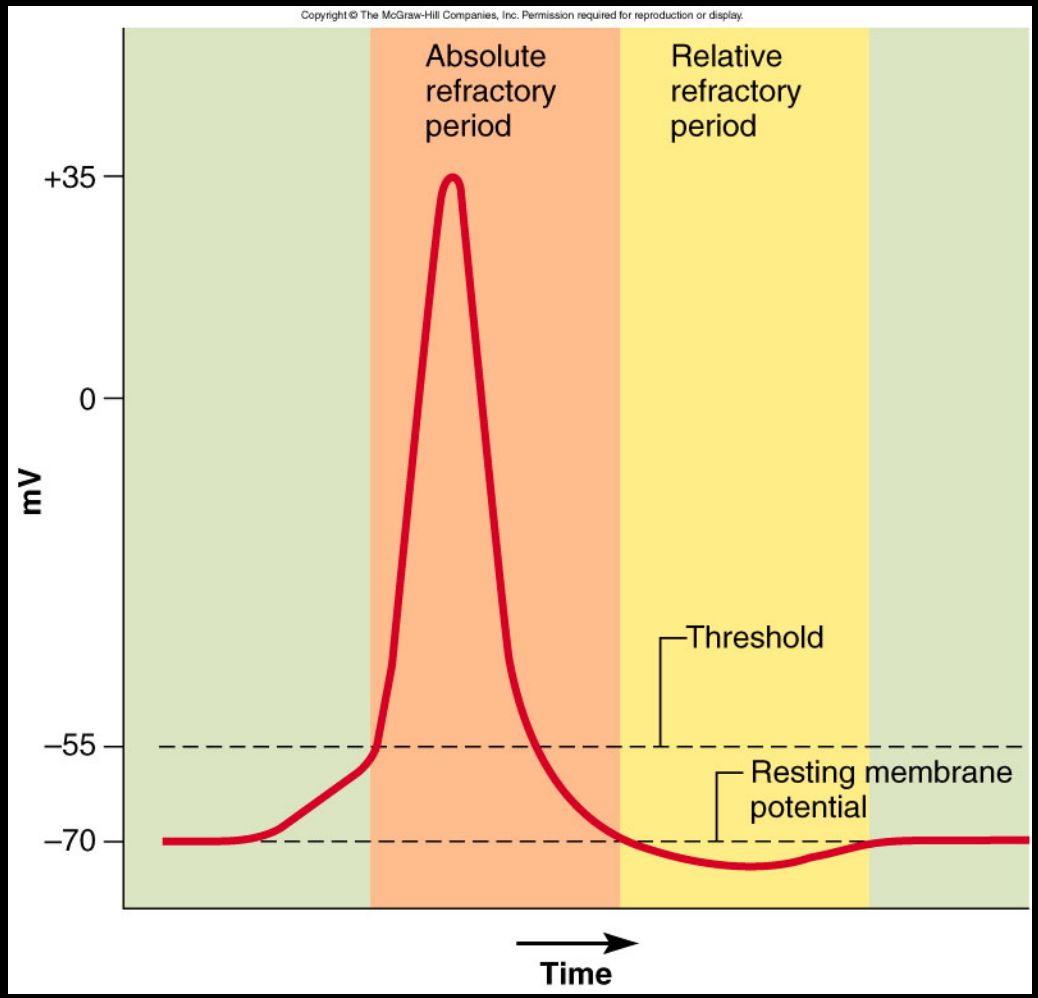
All or nothing principle:-

- Once threshold value for excitation is reached a full AP produced ,its intensity can not increased by increasing stimulus intensity (suprathreshold)

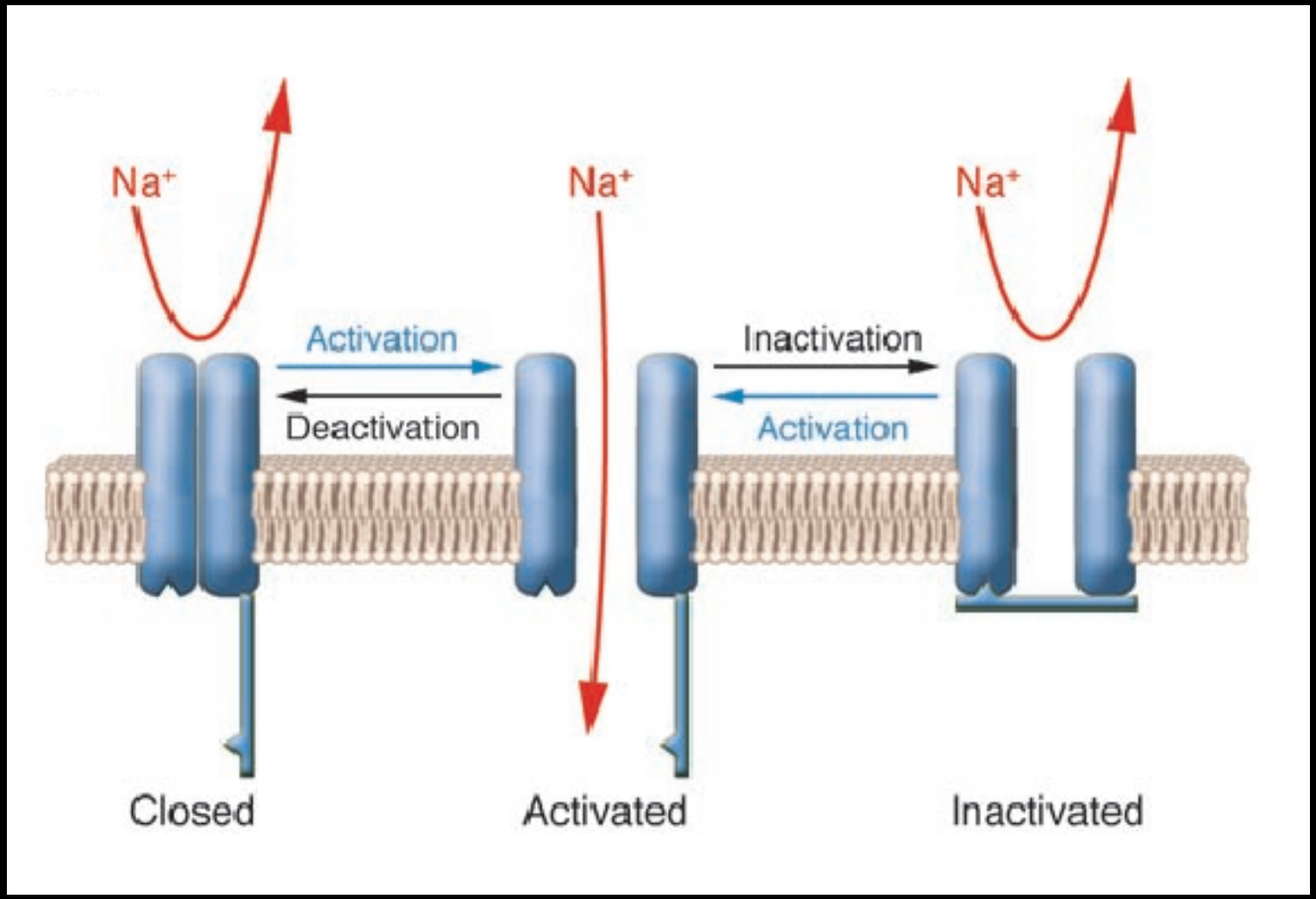


What happens after an action potential?

- 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

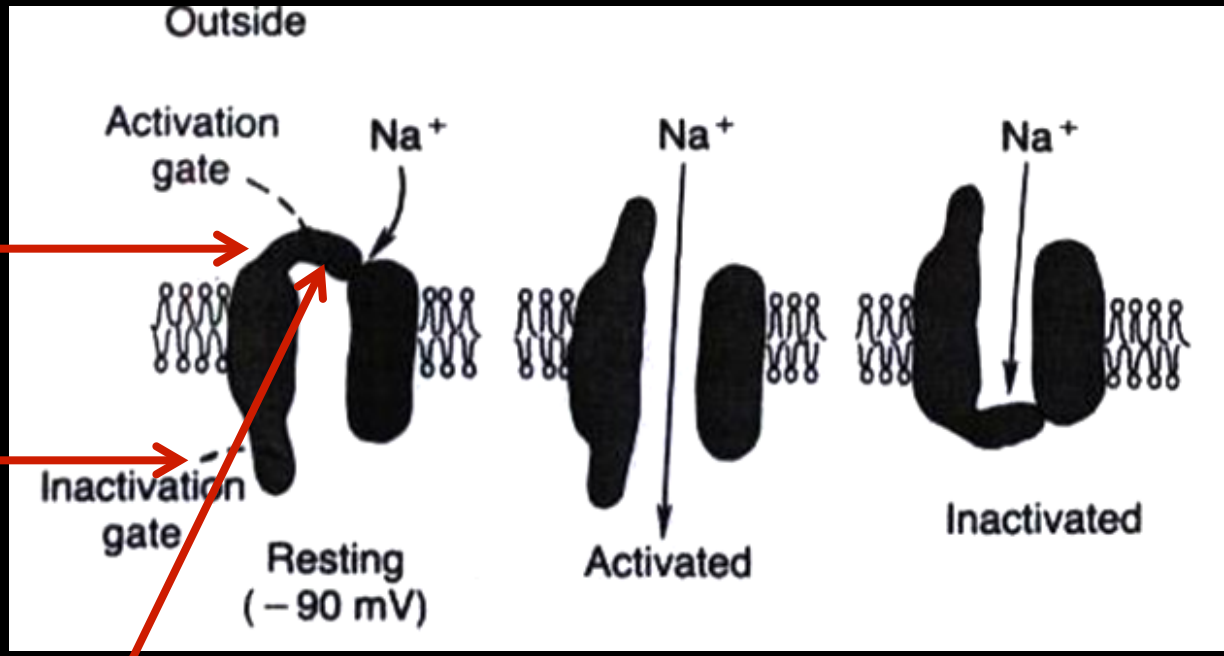


Activation-Inactivation-Deactivation



The Na+ Voltage-Gated Channel (1)

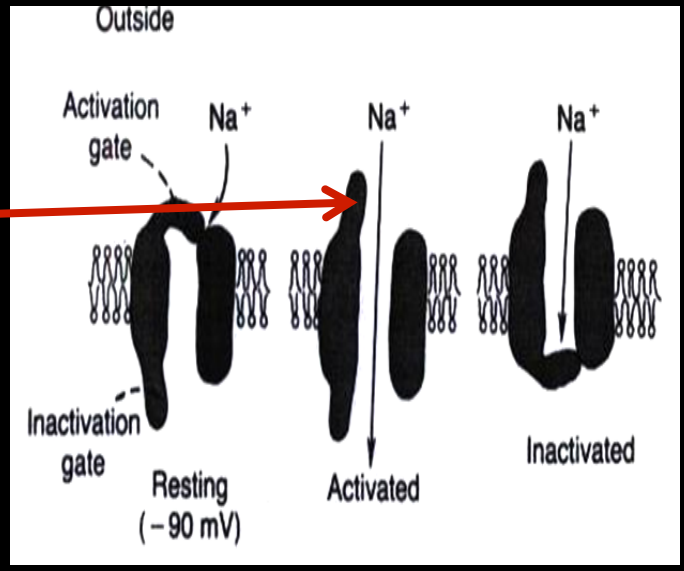
- Has 2 gates : one on the outer side of the membrane and is called the activation gate ,
- and another one on the inner side of membrane called the inactivation gate .
- And this channel has 3 states :



- (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.

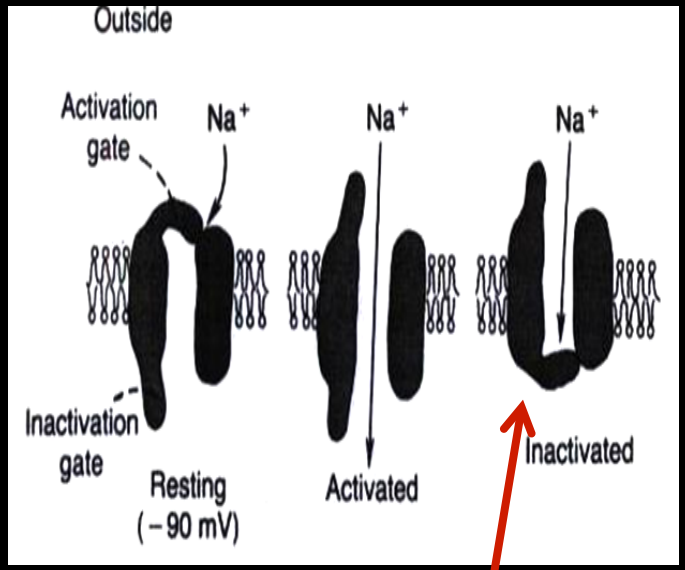
Activated State of Sodium Channel

- (2) <u>Activated state :</u> 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 <u>open)</u> →
- permeability to Na+ becomes increased 500 to 5000 times → Na+ influx
- Na+ flows into the cell in large amounts ,



Inactivated State of Sodium Channel

- (3) Inactivated state : A few milliseconds after the activation gate opens , the channel becomes inactivated :



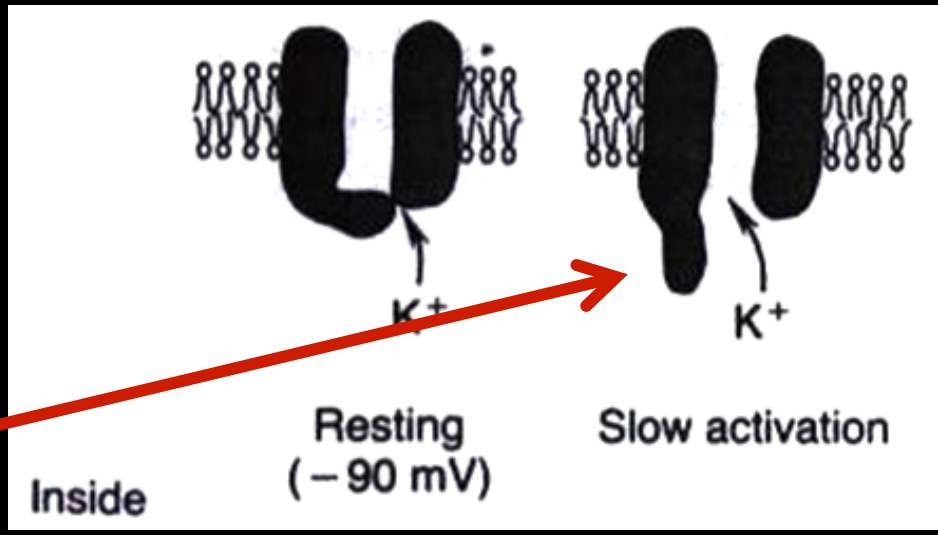
At the peak of AP the inactivation gate will close

- **the inactivation gate will not open by a second stimulus → & 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).**

- → in this case , while the activation gate is still open , the inactivation gate is closed .

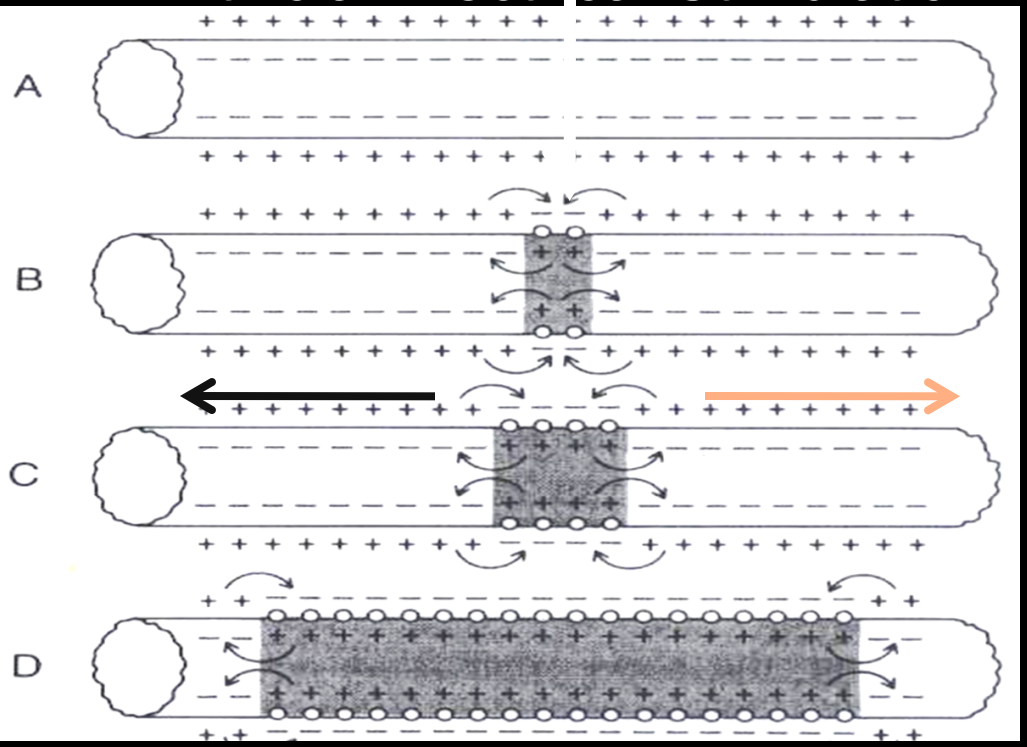
The Potassium Voltage-Gated Channel

- Has one gate only .
- During the resting state , the gate of the potassium channel is closed , and K+ can not 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



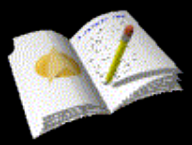
Direction of AP Propagation (Conduction)

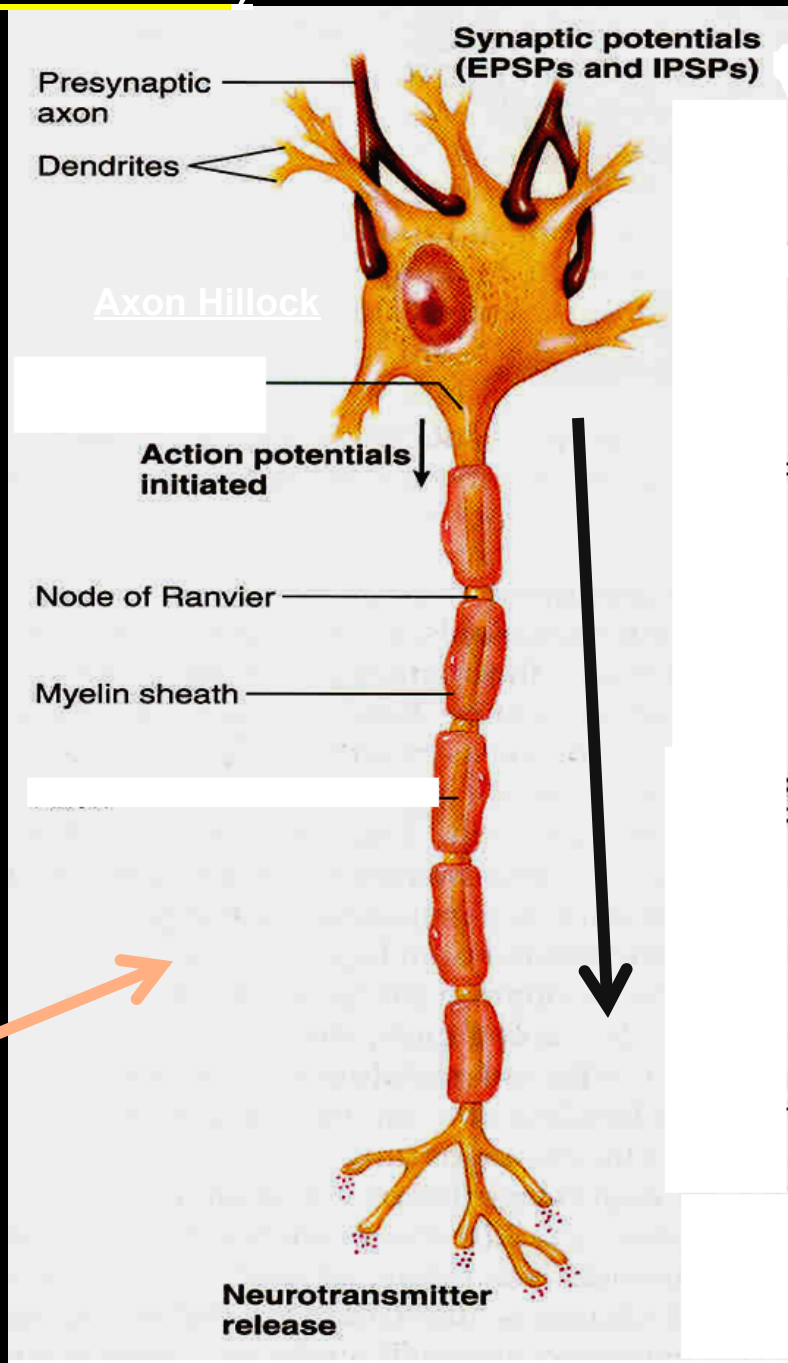
Artificial Electrical Stimulation



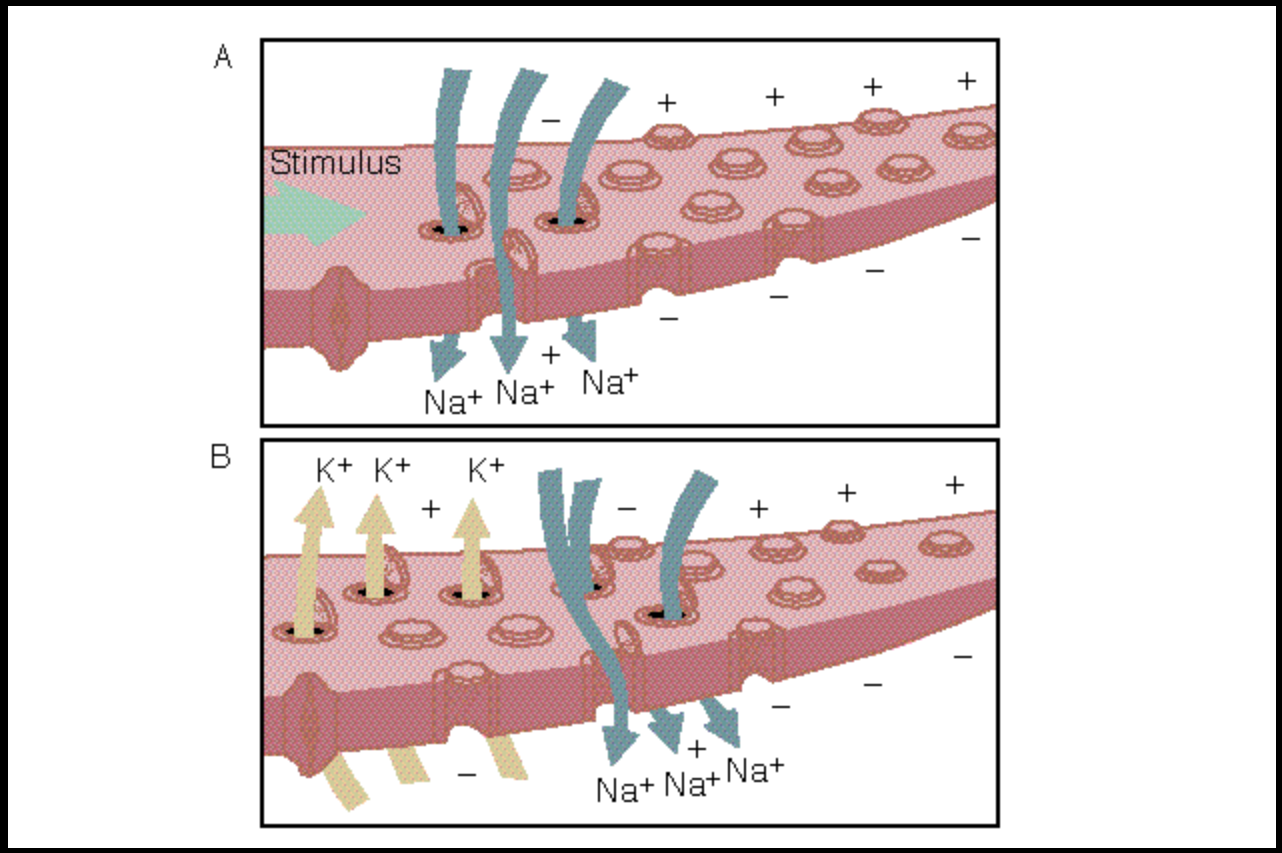
✓Under Artificial condition of electrical stimulation in the laboratory , the AP propagates in both directiions .

✓But normally AP starts in axon hillock & propagates distally in one directions





Nerve physiology: Action potentials



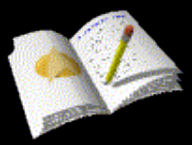
Propagation of action potential

1- in myelinated nerve fibers:-
Saltatory conduction (jumping)

Value:-

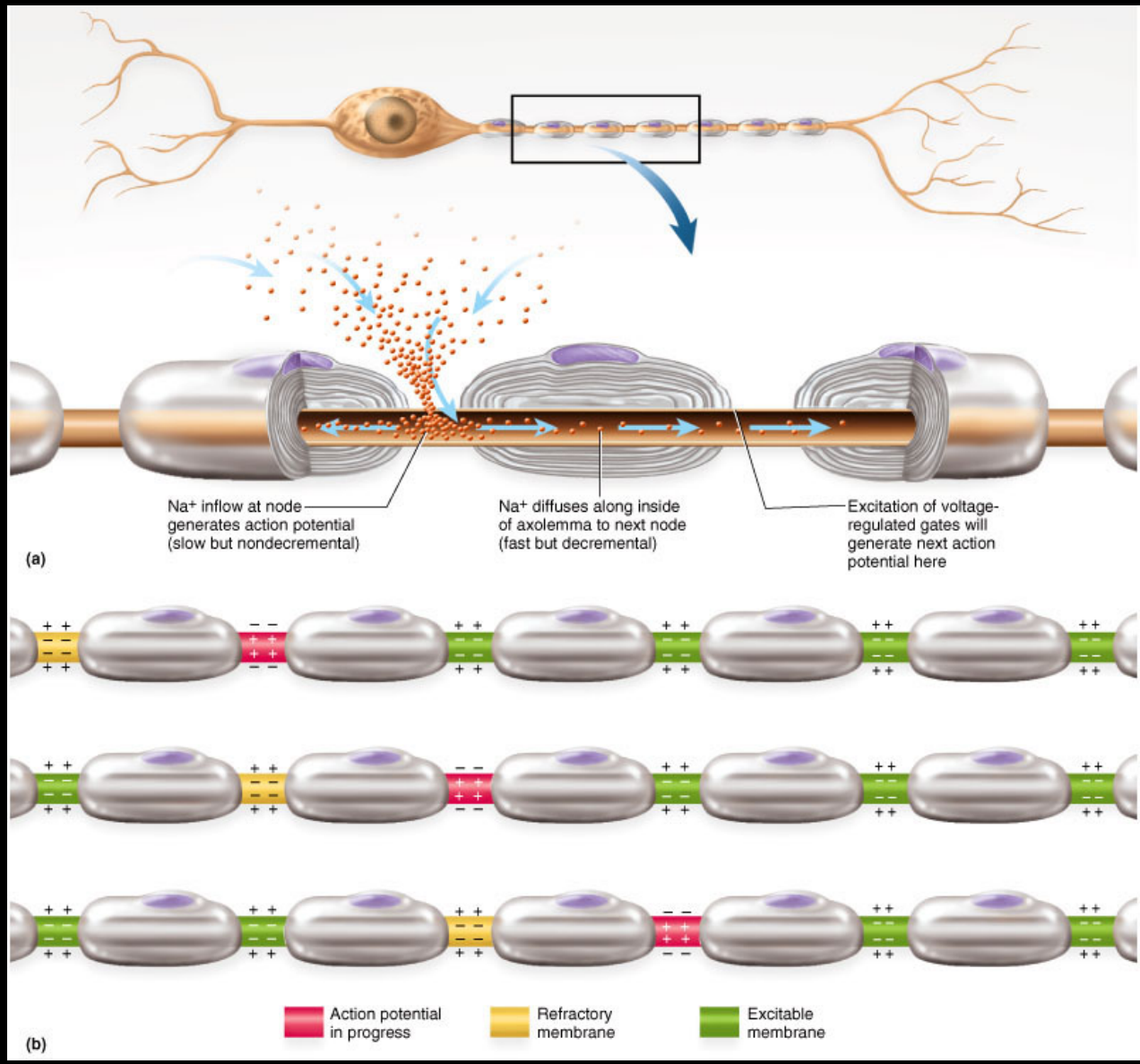
1-↑ velocity of conduction of nerve impulses

2-Conserve energy for axon because only nodes depolarize



How do action potentials travel down the axon?

- Myelinated sheaths
  - Many times faster transmission
  - Action potential skips from one node of Ranvier to the next
    - Called saltatory conduction
    - http://www.blackwellpublishing.com/matthews/actionp.html



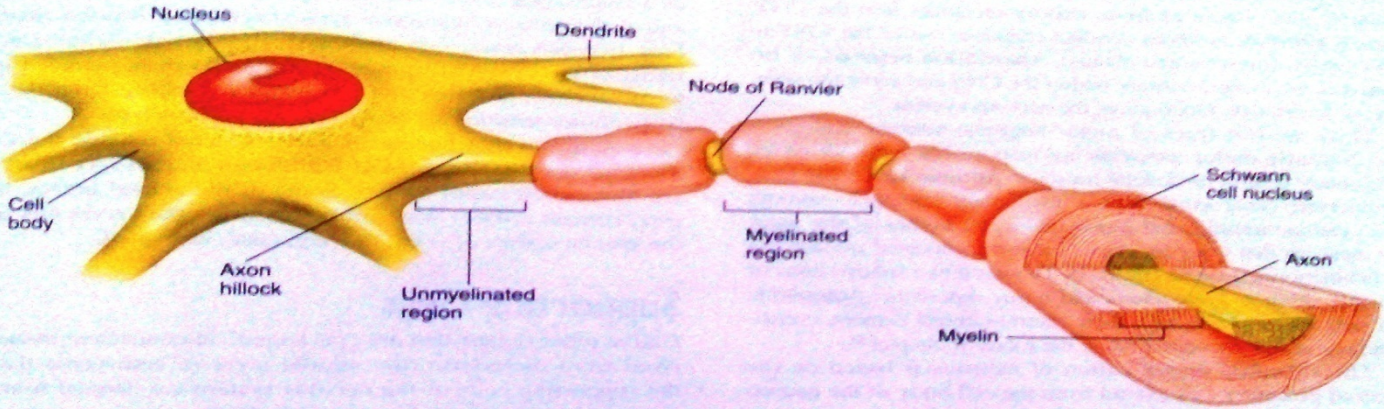
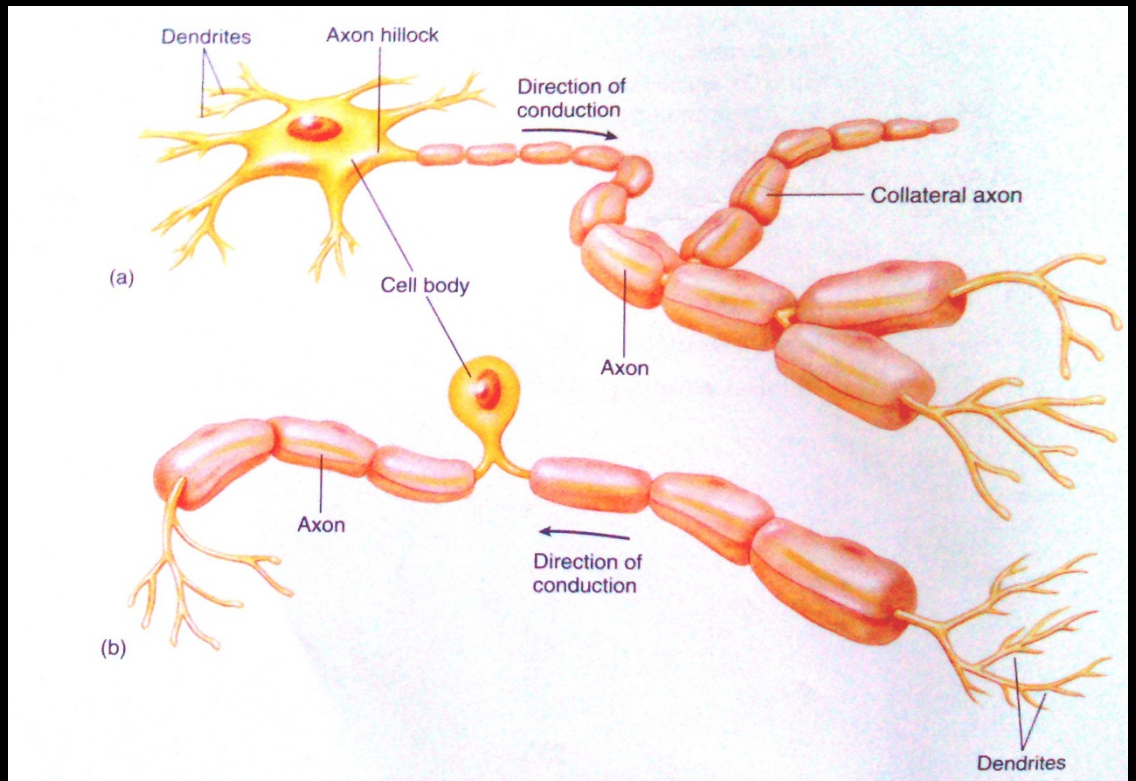


Figure 7.2 **Parts of a neuron.** The axon of this neuron is wrapped by Schwann cells, which form a myelin sheath.

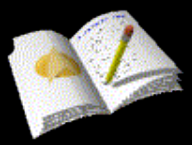


The structure of two kinds of neurons. *(a)* A motor neuron and *(b)* a sensory neuron are depicted here.

2- Non- myelinated nerves:-

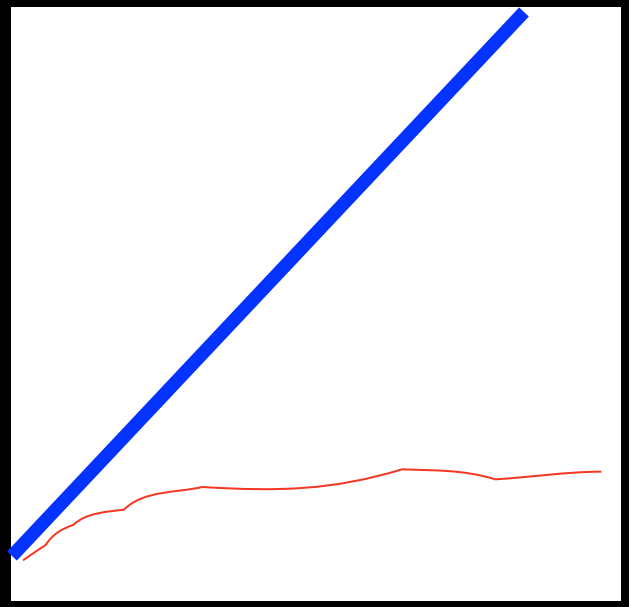
(local circuits)=point to point

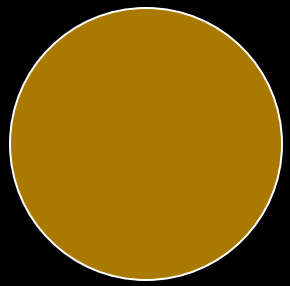
-depolarization pass by local circuits. -

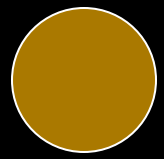


What else influences speed of action potential?

- Axon diameter
  - -The larger the diameter, the faster the speed of transmission
  - -Less resistance to current flow with larger diameter

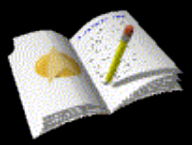






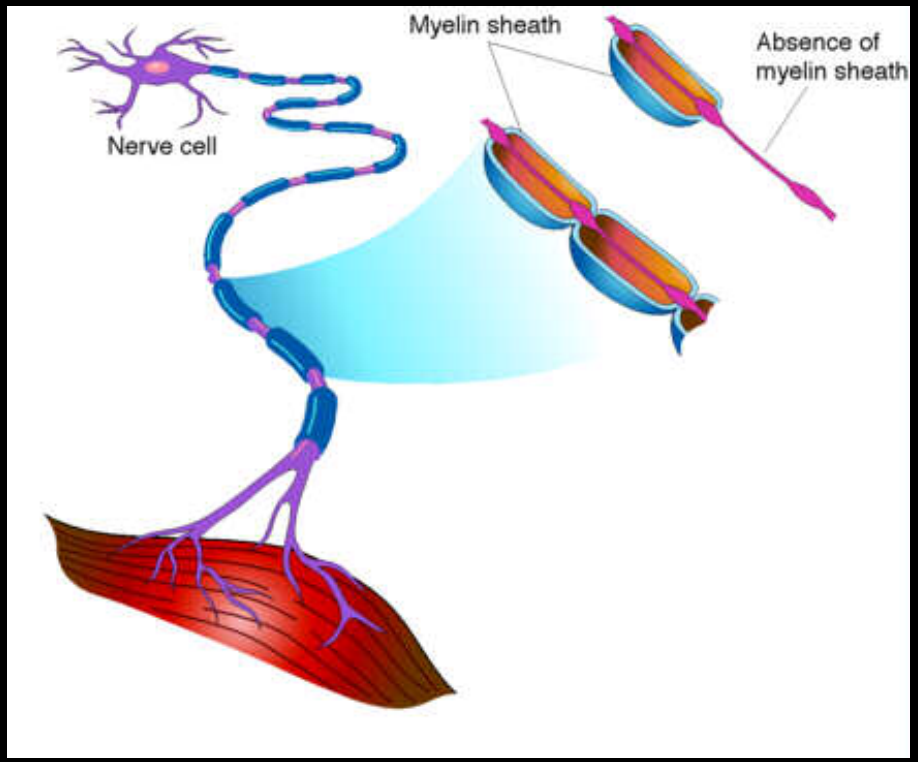
Faster transduction

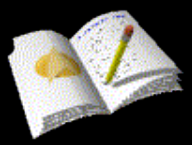
Slower transduction



What happens if myelination is lost?

- Multiple sclerosis
  - Autoimmune disease
  - Usually young adults
  - Blindness, problems controlling muscles
    - Ultimately paralysis
  - Immune system attacks myelin sheaths and nerve fibers
    - Scar tissue (scleroses) replaces some damaged cells
    - Other now unmyelinated axons sprout Na+ channels
      - Accounts for sporadic nature of disease?





- Thank You