MEMBRANE POTENTIAL AND SYNAPSES

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Objectives of the chapter

1-Membrane potential and mechanism of its generation.
2-How the activity of voltage - gated Na+ and K+ channels generates an action potential and the roles of those channels in each phase (depolarization, overshoot, repolarization, hyperpolarization) of the action potential.
3-The mechanisms of which an action potential is propagated along unmyelinated and myelinated axons.
4-Types of synapses

Types of cells in the nervous system:

(1) Nerve cells (neurons):

- these are the **structural units** of the nervous system.

(2) Neuroglial cells=nerve glue:

- neuroglial cells **support and protect** the neurons .

Structure of neurons

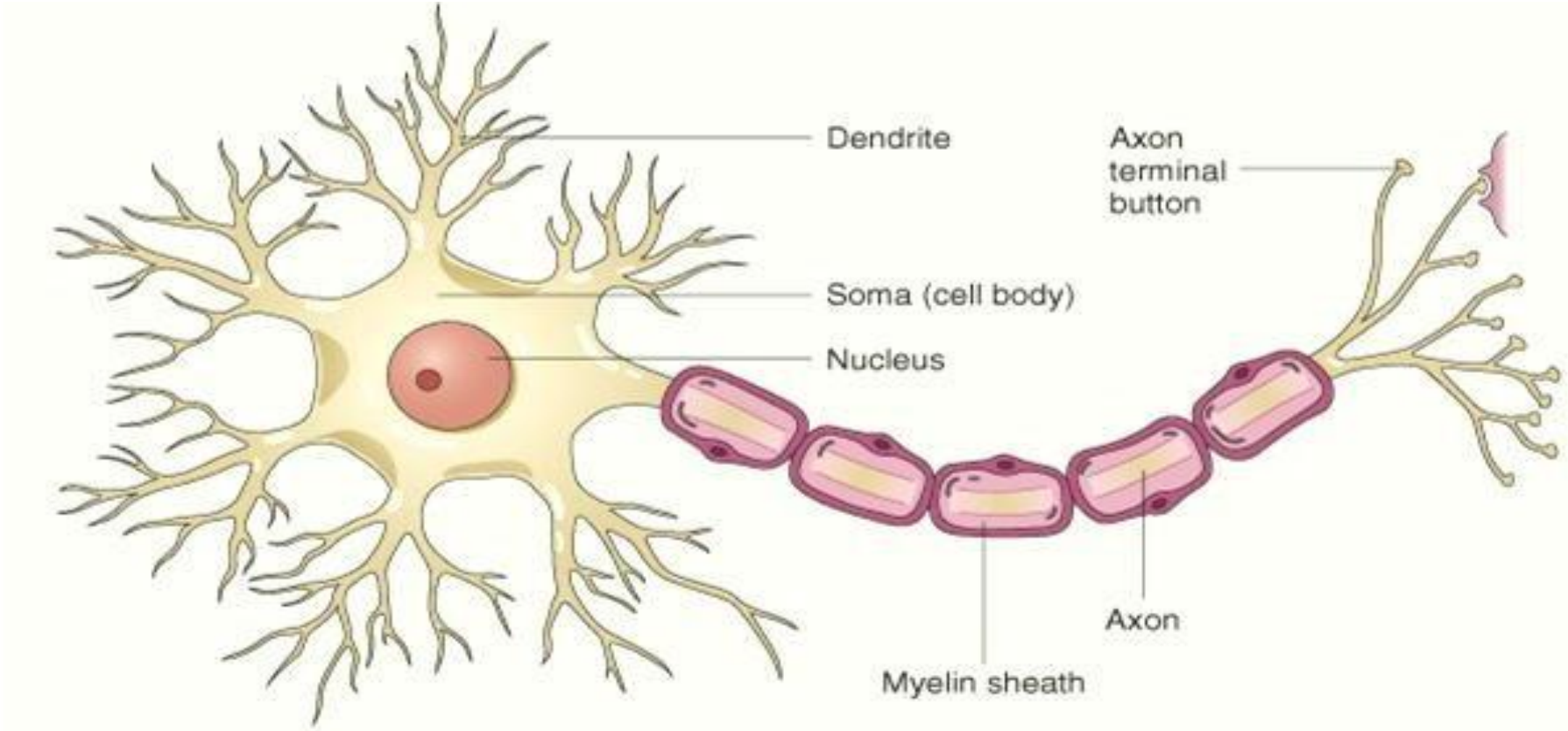
- Neurons vary considerably in size and shape according to **their sites & functions** in general they are formed **of the cell body and cell processes.**

A) Cell body (soma):

- The cell body is **the enlarged part of the neuron** which contains the nucleus, it **controls the metabolic processes** and provides nutrition for the whole neuron.
- The cell body contains:nucleus,neurofibrils,microtubules,microfilaments, **endoplasmic reticulum, Golgi apparatus, mitochondria and ribosomes**.

b) Cell processes:

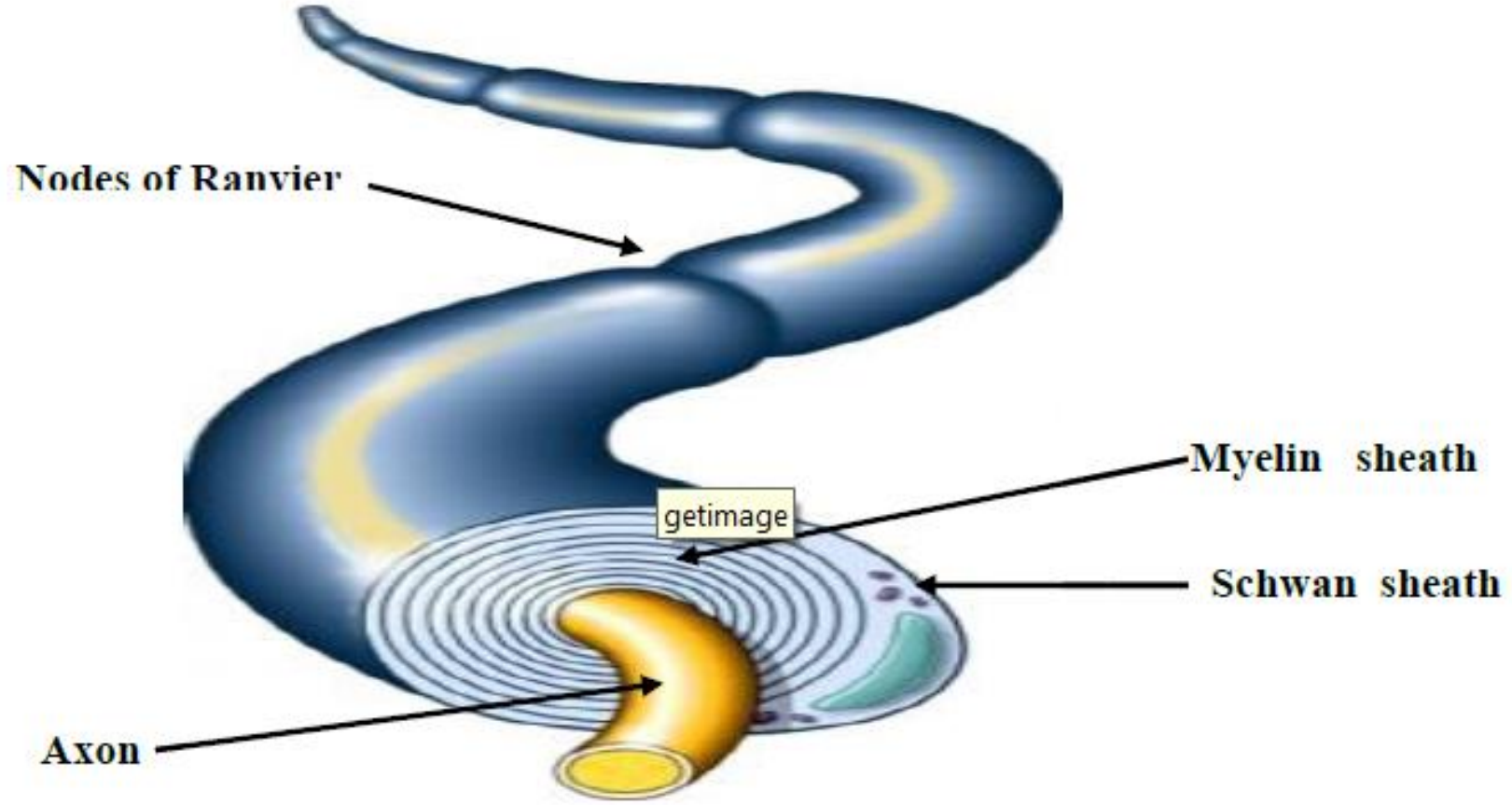
- The dendrites and the axon.


Dendrite
Axon terminal button
Soma (cell body)
Nucleus
Axon
Myelin sheath

Axons are covered by 2 sheaths:

1) Myelin (medullary) sheath:

Def:	**-myelin is white lipid rich substance which is responsible for the white color of the white matter of the brain and spinal cord.**
Synthesis	i-by **Schwann cell** in peripheral nervous system (PNS). ii-by **oligodendrocyte** (a type of neuroglia) in CNS *because Schwann cells are present only in the PNS.*
Function	**i- It protects neurons.** **ii- It acts as electric insulator.** **iii- It increases the speed of impulse transmission**.


Nodes of Ranvier
Myelin sheath
getimage
Schwan sheath
Axon

(2) Cellular sheath =Schwann sheath or neurilemma:

Def:	**a living sheath formed of called Schwann cells that surrounds neurns inthe peripheral nervous system (PNS) .**
Function	**i- Schwann cell forms myelin sheath** in PNS. **ii-Schwann cell** is essential for **regeneration of nerves in PNS (**no regeneration in CNS, why?).

Properties of nerves:

I) **Excitability.**

II) **Conductivity.**

I-Excitability (irritability)

- **Excitability** is a **bioelectric phenomenon** in which the nerve fibers respond to stimuli by **rapid changes** in **their resting membrane potential forming action potentials (impulses)**which are conducted along the nerve fibers to their terminals.

Resting membrane potential (RMP)

Introduction:

- During rest, **the nerve fibers spends** energy to **maintain it's state of polarization**.
- **In this state of polarization the inner surface of the nerve fiber is- vely** charged compared with outer surface which is +**vely** charged .

Definition of RMP:

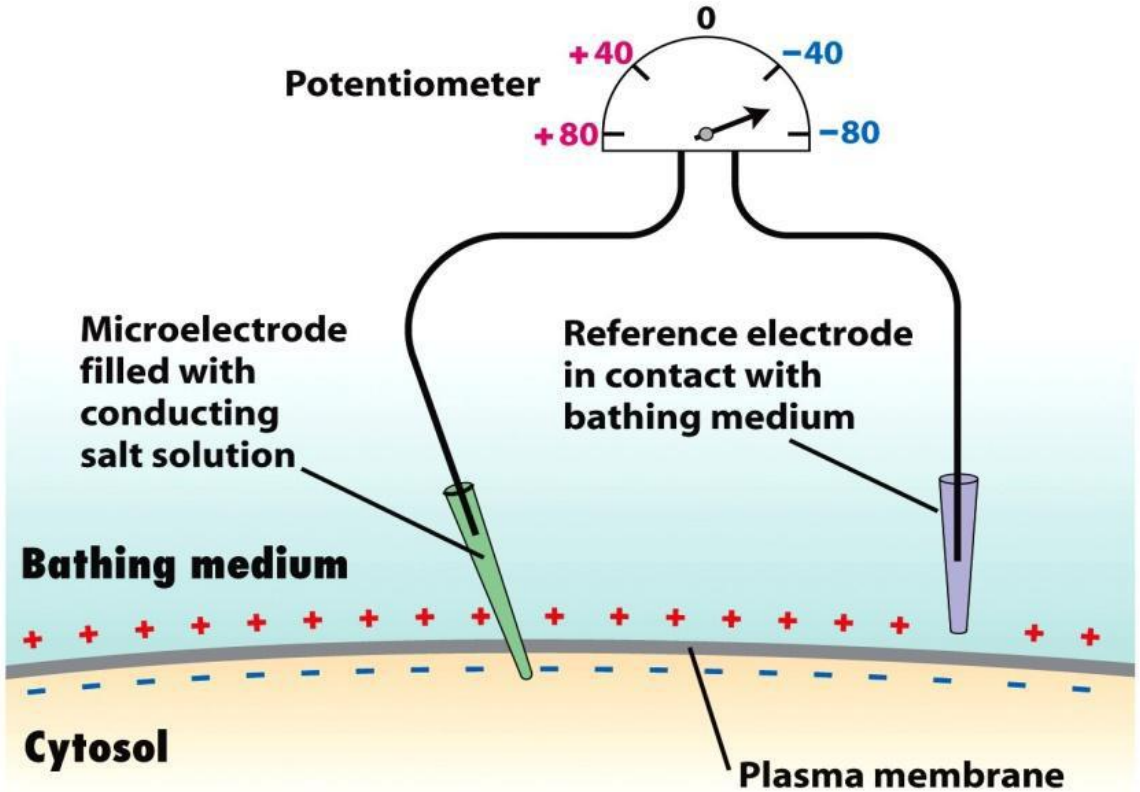
- RMP is the **potential difference between the inside and outside** of the **nervefiber in resting condition.**

Value of RMP:

70 m.v and is **expressed -70 m.v** because the inner surface of the plasma memb. is negatively charged **relative to the interstitial fluid.**

Measurement of RMP:

- **by micro voltmeter** when **one** electrode is introduced **inside** the nerve fibers and the **othe**r electrode is placed on the **outer surface** a potential **difference of -70 mv is recorded.**



Causes of RMP:

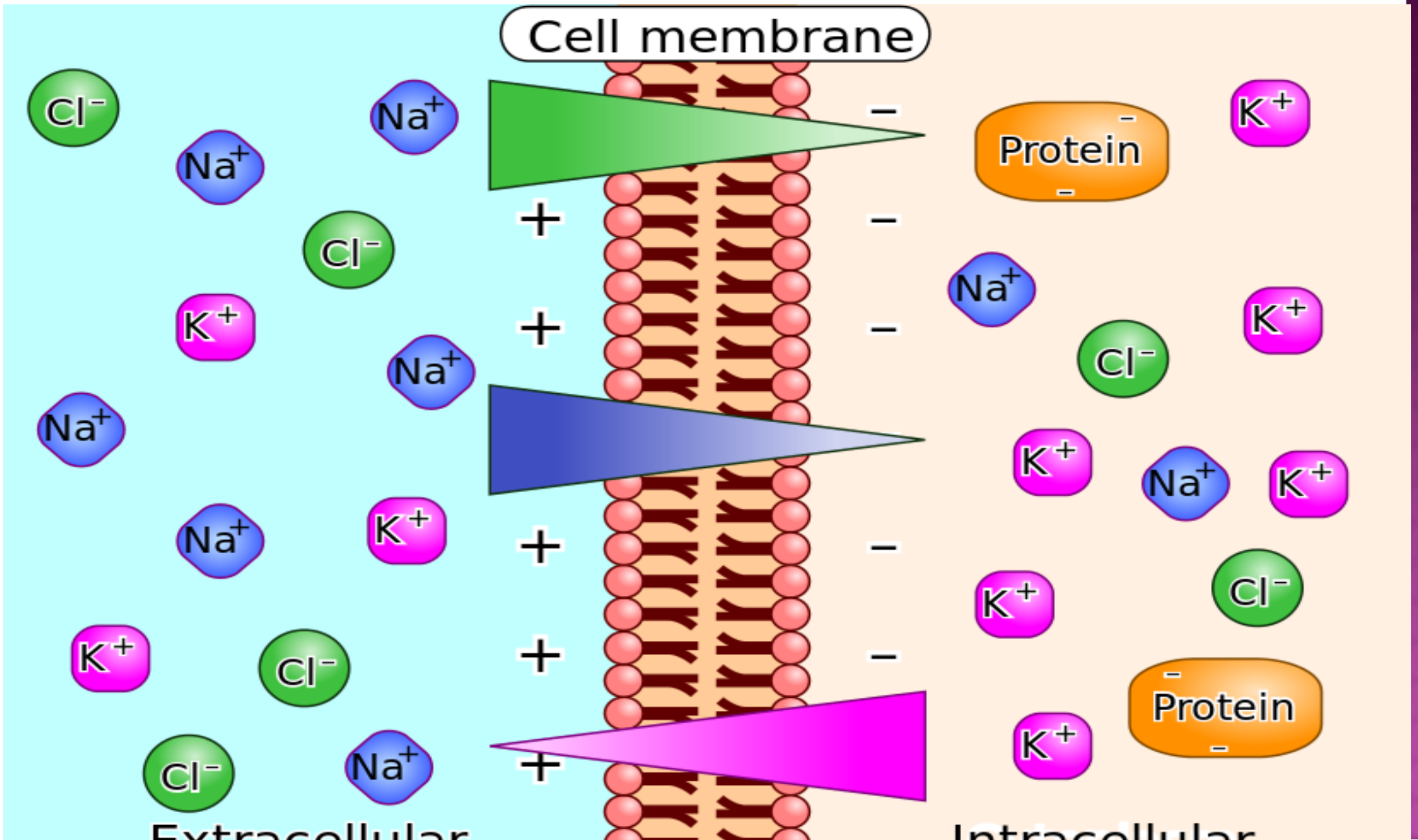
1-Selective permeability (main cause).

2-Sodium potassium pump.

3-Unequal distribution of ions (minor role):

1-Unequal distribution of ions (minor role):

	Inside nerve fiber	Outside nerve fiber
Cations		
K^+	140m.eq/l.	4 m.eq/l.
Na^+	14m.eq/l.	140m.eq/l
Anions		
$Proteins^-$	16 gm %.	2 gm %.
Cl^-	4m.eq/litre.	100m.eq/l


Cell membrane
Cl⁻
Na⁺
Na⁺
Cl⁻
K⁺
Na⁺
Na⁺
Na⁺
K⁺
Cl⁻
K⁺
Cl⁻
Na⁺
+
+
+
+
+
+
−
−
−
−
−
−
Protein
−
K⁺
Na⁺
K⁺
Cl⁻
K⁺
Na⁺
K⁺
K⁺
Cl⁻
Protein
−
K⁺
Extracellular
Intracellular

2) Selective permeability of the cell membrane:

- The cell memb. is formed of **double lipid** layer containing **specialized proteins containing pores** called **ion channels**.
- These ions channels **allow** only **specific ions** to pass &prevent **others because of their: 1)shape 2) charge 3) diameter**
- **K diffusion through passive channels is the main cause of RMP.**
- **K carry positive electrical charge to the outside ,thus creating electro positivity outside the membrane and electronegativity inside because of negative anions that don't diffuse with potassium .Such as protein ,phosphate and sulfate.**

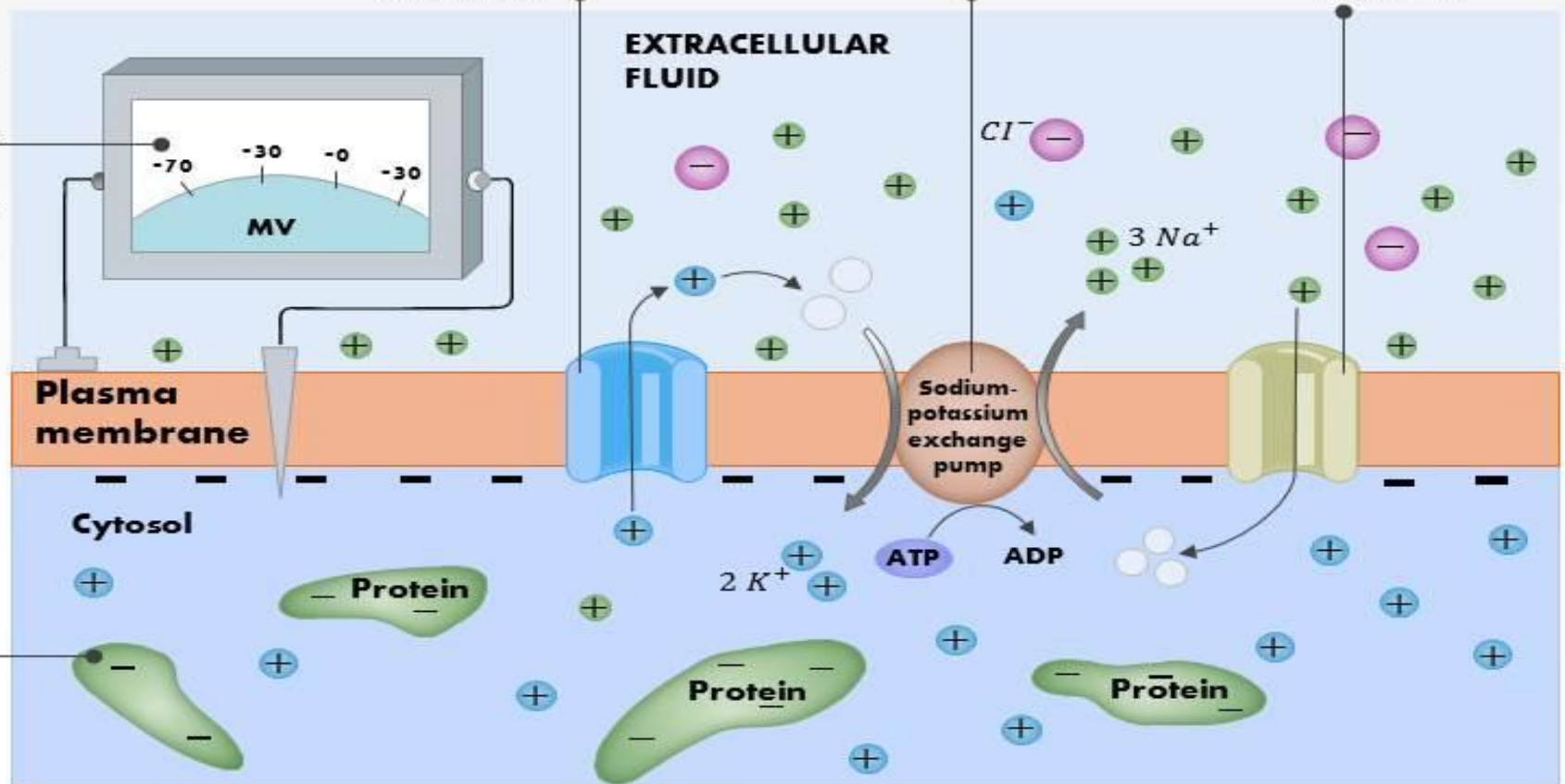
Passive & active maintain the membrane potential

The unite of measurement of potential difference is the volt (V), and the transmembrane potential of a neuron is usually near 0.07V. Such a value is usually expressed as -70 mV (or -70 millivolts-thousandths of a volt) with the minus sign indicating that the interior is negatively charged.

Potassium ions can diffuse out of the cell through potassium leak channels.

The sodium-potassium exchange pump ejects 3 Na+ for every 2 k+ recovered from the extracellular fluid. At a transmembrane potential of -70 mV, the rate of Na+ entry versus K+ loss is 3:2, and exchange pump maintains a stable resting potential.

Sodium ions can diffuse into the cell through sodium leak channels.



The cytosol contains an abundance of negatively charged proteins, whereas the extracellular fluid contains relatively few. These proteins cannot cross the plasma membrane.

- **There are three basic types of ion channels:**

  1) **Non gated channels = passive or leak ion channels.: they are the main cause of RMP.**

  2) **Gated channels:**

  a) **Chemical activated (or gated) channels.**

  b) **Voltage activated (or gated) channels.**

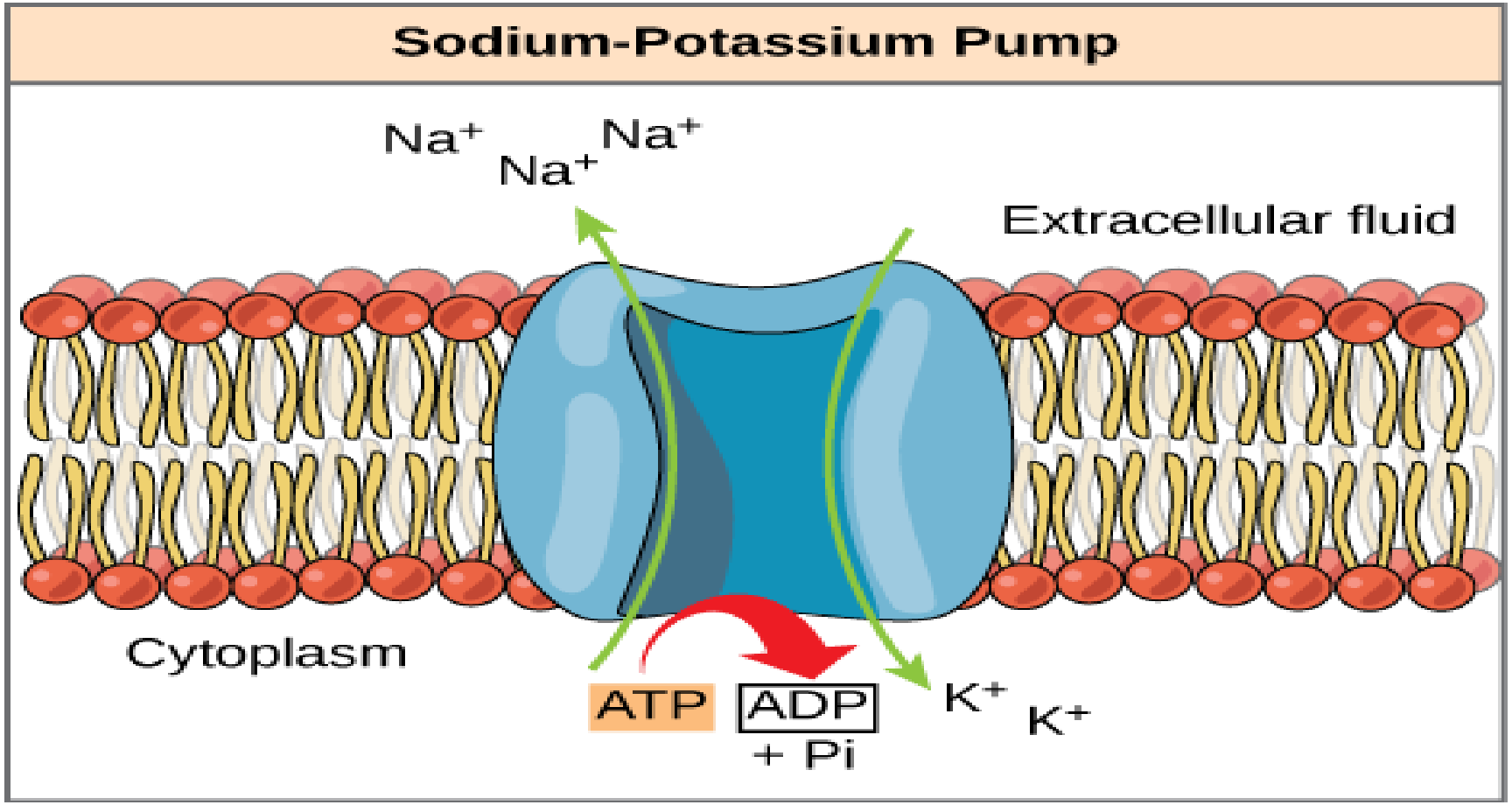
- **gated channels have no role in resting membrane potential but they are responsible for the action potential.**

II-Sodium and potassium pump (= Na^+ pump):

- **Na^+ - K^+ pump helps to maintain a high concentration of Na^+ ion outside and a high concentration of K^+ ion inside** the nerve cells **inspite of the continuous diffusion** of these ions across the membrane.
- **If Na-K pump is inhibited** by any condition (e.g. by cooling) **→↓ the metabolic activity of the cell →↓ ATP production so that:**

i) Na^+ ions will accumulate inside *the cell and* ***neutralize*** *the negative charges of* ***protein*** *ions leads to* ***loss of negativity inside..***

ii)K^+ ions which were held on the outer surface by the effect of protein will escape away → loss of positivity outside → loss of RMP →loss of excitability.


Sodium-Potassium Pump
Na+
Na+
Na+
Extracellular fluid
Cytoplasm
ATP
ADP
+ Pi
K+
K+

Action potential = nerve impulse

-Def: action potential is the **potential** changes which occur in RMP of the nerve due to stimulation by **effective stimulus**, these changes **propagate (self propagated)** along the nerve, then reach the effector organ to **produce action** (hence the name action potential).

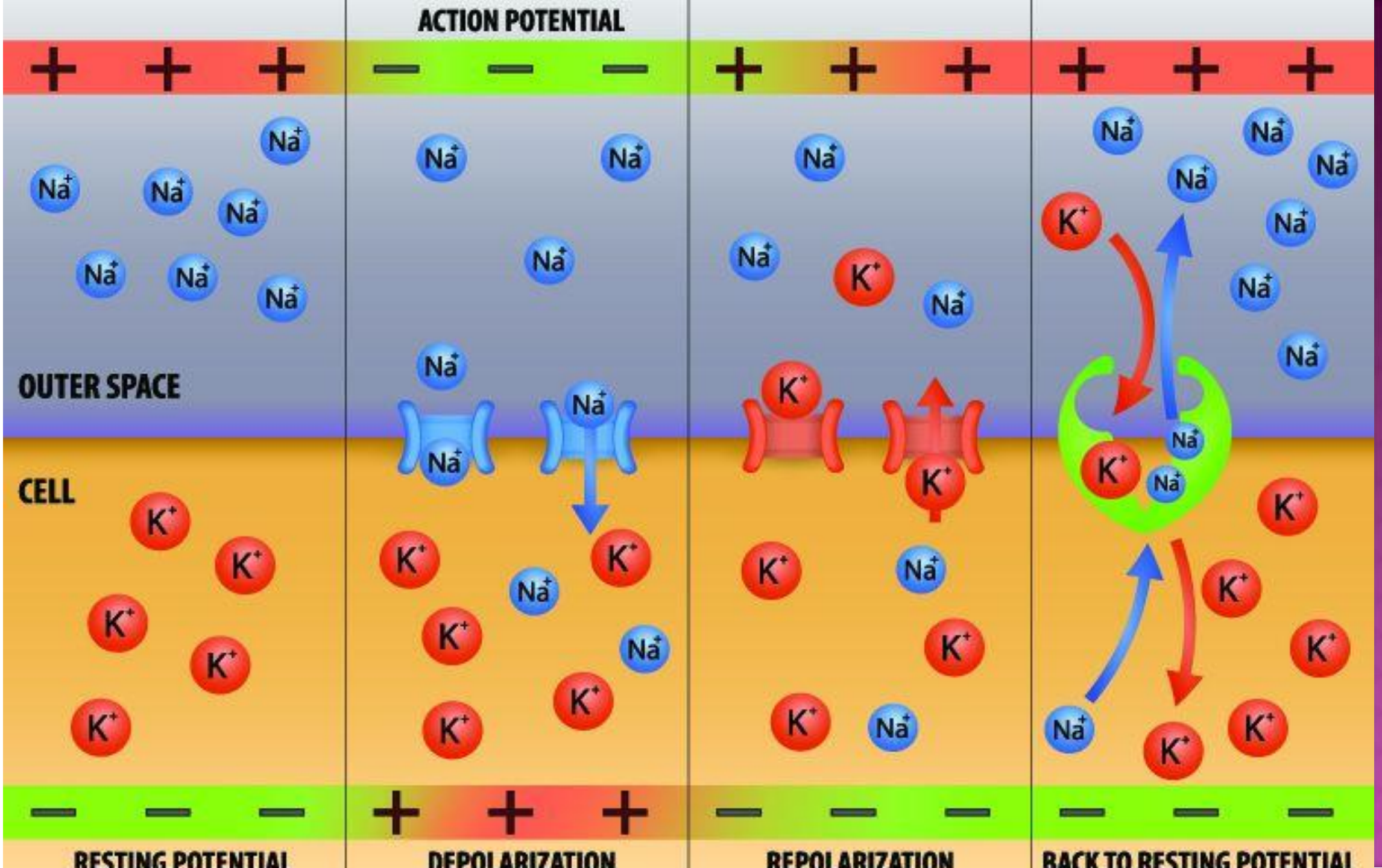
Ionic basis of action potential

Action potential is composed of 3 main processes:

A- Depolarization.

B- Repolarization.

C- Redistribution of ions.


ACTION POTENTIAL
OUTER SPACE
CELL
RESTING POTENTIAL
DEPOLARIZATION
REPOLARIZATION
BACK TO RESTING POTENTIAL

A) Depolarization:

Def:

-It is loss of normal polarized state of the membrane (potential difference between outer and inner surface of the membrane).

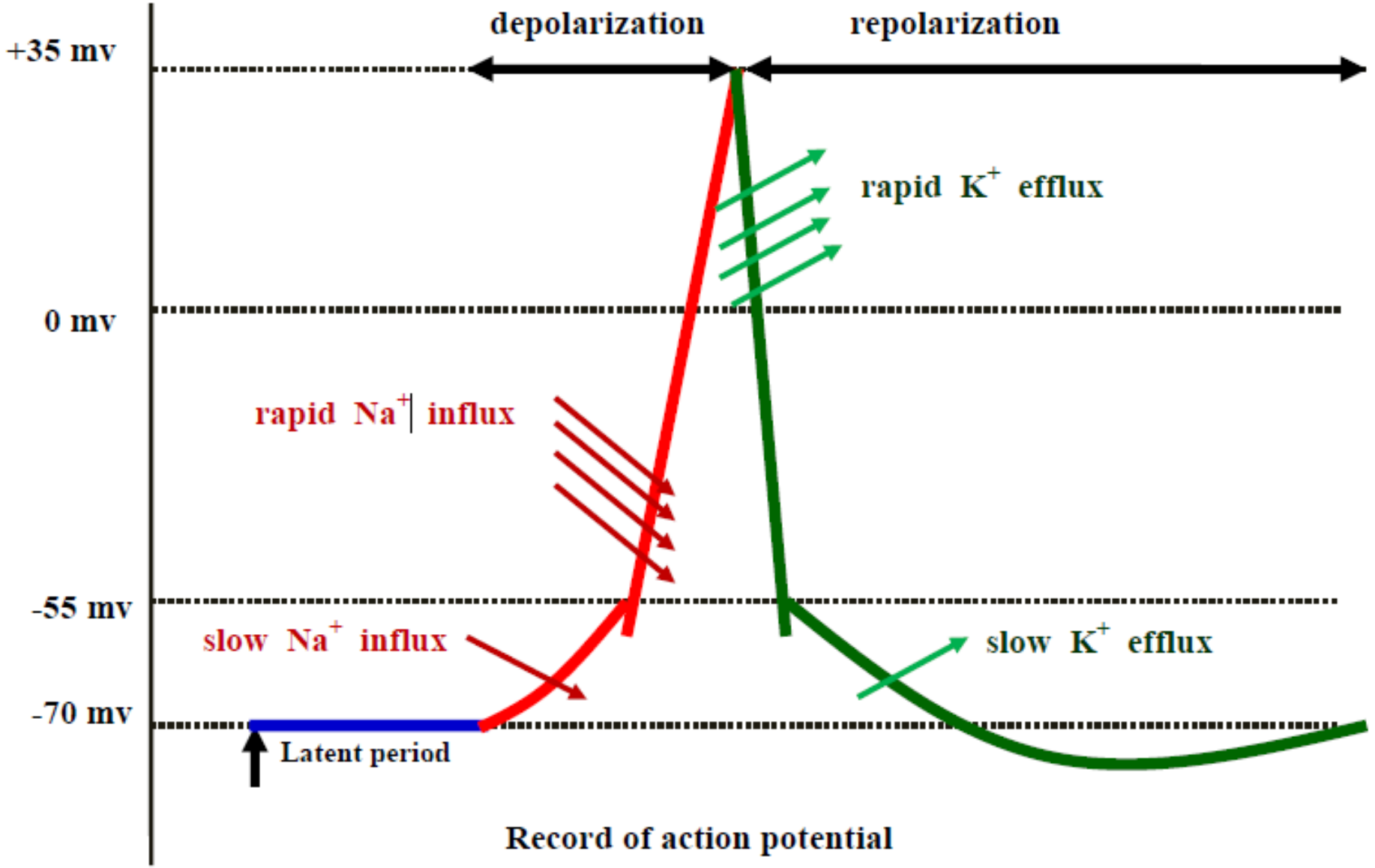
- the membrane potential changes from -70 mv to +35 mv.

Mechanism:

-The stimulus increases the permeability of the cell membrane to Na^+ ions, which diffuse inside causing gradual change in the membrane potential from the resting potential (-70m.v) to isoelectric line (zero) and exceed it to+35 mv (overshoot) by 2 steps separated by the firing level which equals – 55 mv.:

1-Slow depolarization: from -70 mv to -55 mv (firing level) due to opening of some Na^+ channels

2-Rapid depolarization: from -55 mv to +35 mv (overshot), due to opening of all Na^+ channels


depolarization
repolarization
+35 mv
0 mv
-55 mv
-70 mv
rapid K+ efflux
rapid Na+ influx
slow Na+ influx
slow K+ efflux
Latent period
Record of action potential

B) Repolarization:

Def:

- It is restoration of membrane potential i.e return to normal polarity

-The membrane returns from +35 mv to -70 mv.

Mechanism of repolarization:

1-stoppage of Na^+ influx.

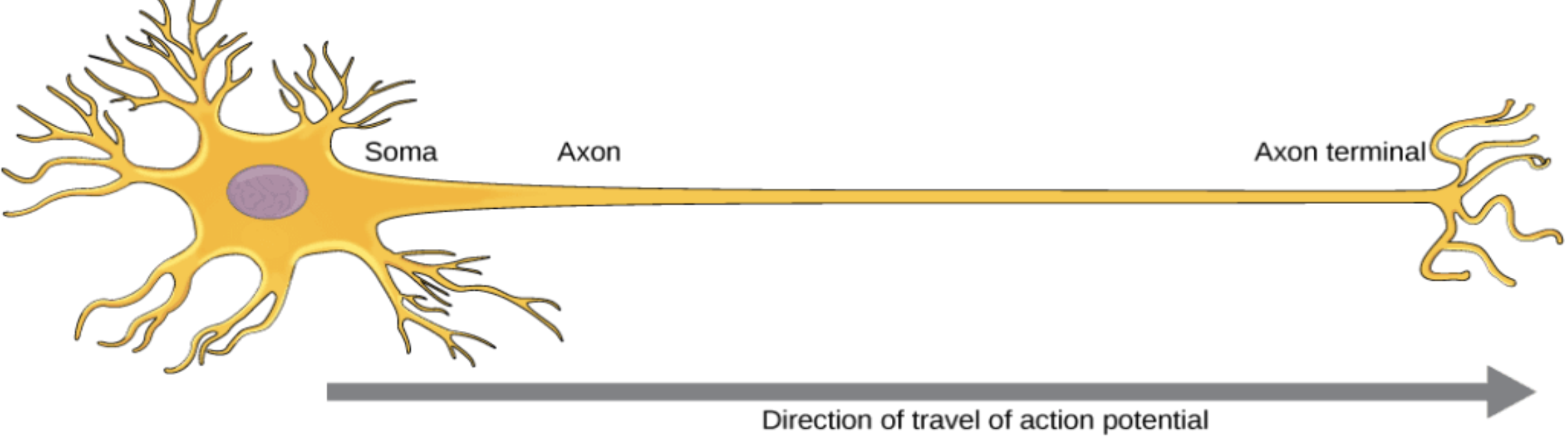
2-begining of K^+ efflux through opening of K^+ channels.

c) Redistribution of ions inside and outside:

-Redistribution of Na^+ and K^+ ions to the normal resting condition is **established by sodium potassium pump.**

II-Conductivity

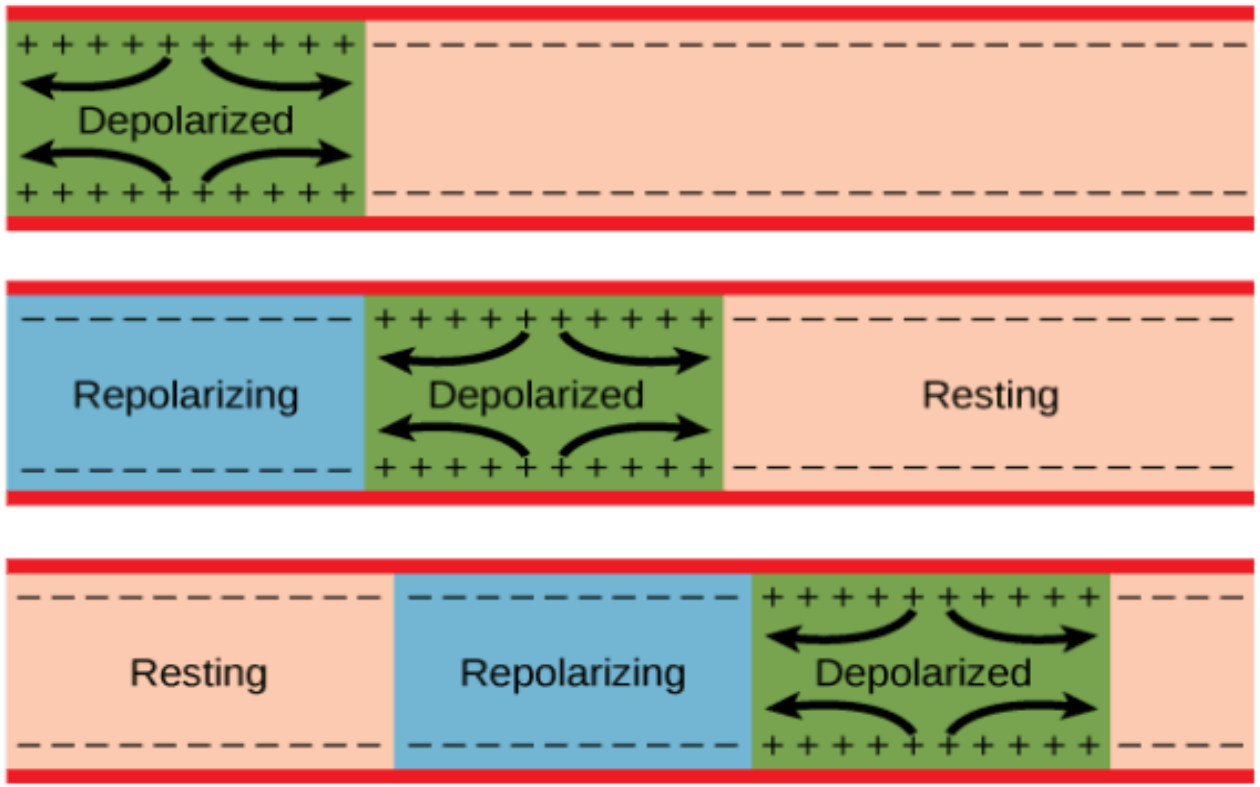
- **After action potential is initiated, it propagates along the axon .**
- The action potential must be **propagated in order to transfer information from one place in the nervous system to the other**.
- **Conduction is possible because the action potential** generated at one site on the axon**, acts as a stimulus for the production of another action potential in the adjacent sites of the axon.**

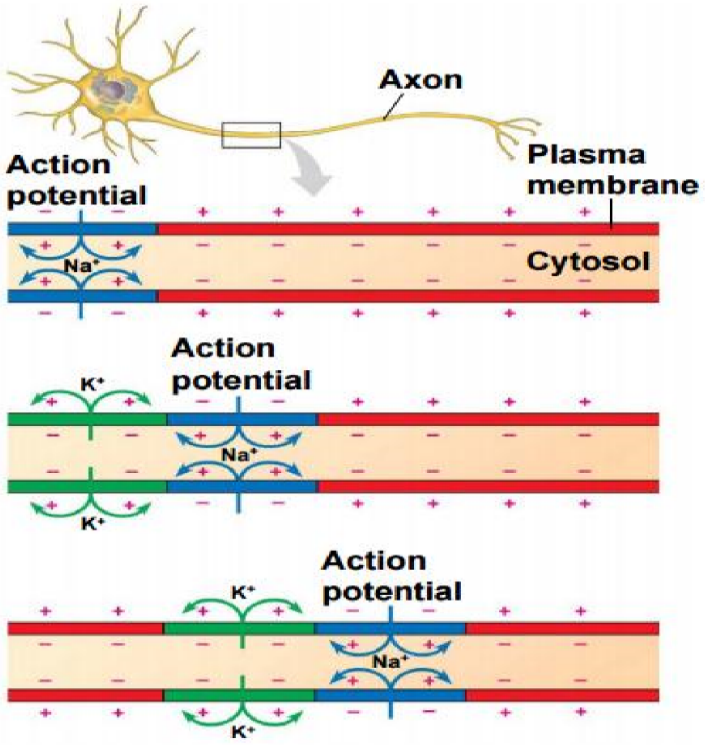
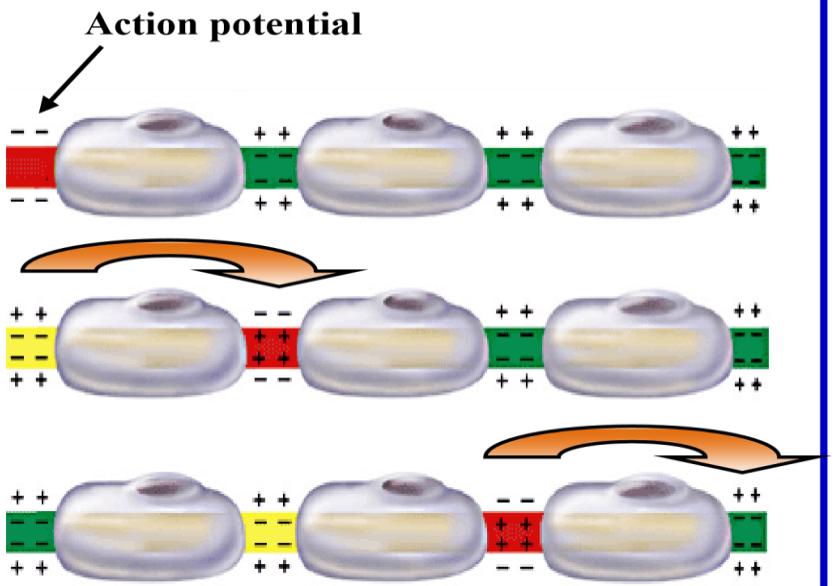


a. In response to a signal, the soma end of the axon becomes depolarized.

b. The depolarization spreads down the axon. Meanwhile, the first part of the membrane repolarizes. Because Na^+ channels are inactivated and additional K^+ channels have opened, the membrane cannot depolarize again.

c. The action potential continues to travel down the axon.



Continous conduction	Saltatory conduction
- It is propagation in **unmyelinated** nerve fibers.	- It is propagation in **myelinated** nerve fibers.
- action potential is conducted from one point to another by local electric ciruit. 	- charges jump from one node to another along the nerve causing spread of action potential along the nerve.. 
Velocity of conduction: **Slow (0.5-2.0** meter/sec)	**Velocity of conduction:** **Fast** (may reach up to **120** met/sec).

TYPES OF SYNAPSES

The human brain contains at **least 100 billion neurons**, each with the ability to influence many other cells. .

Such **communication is made possible by synapses**, the functional contacts between neurons.

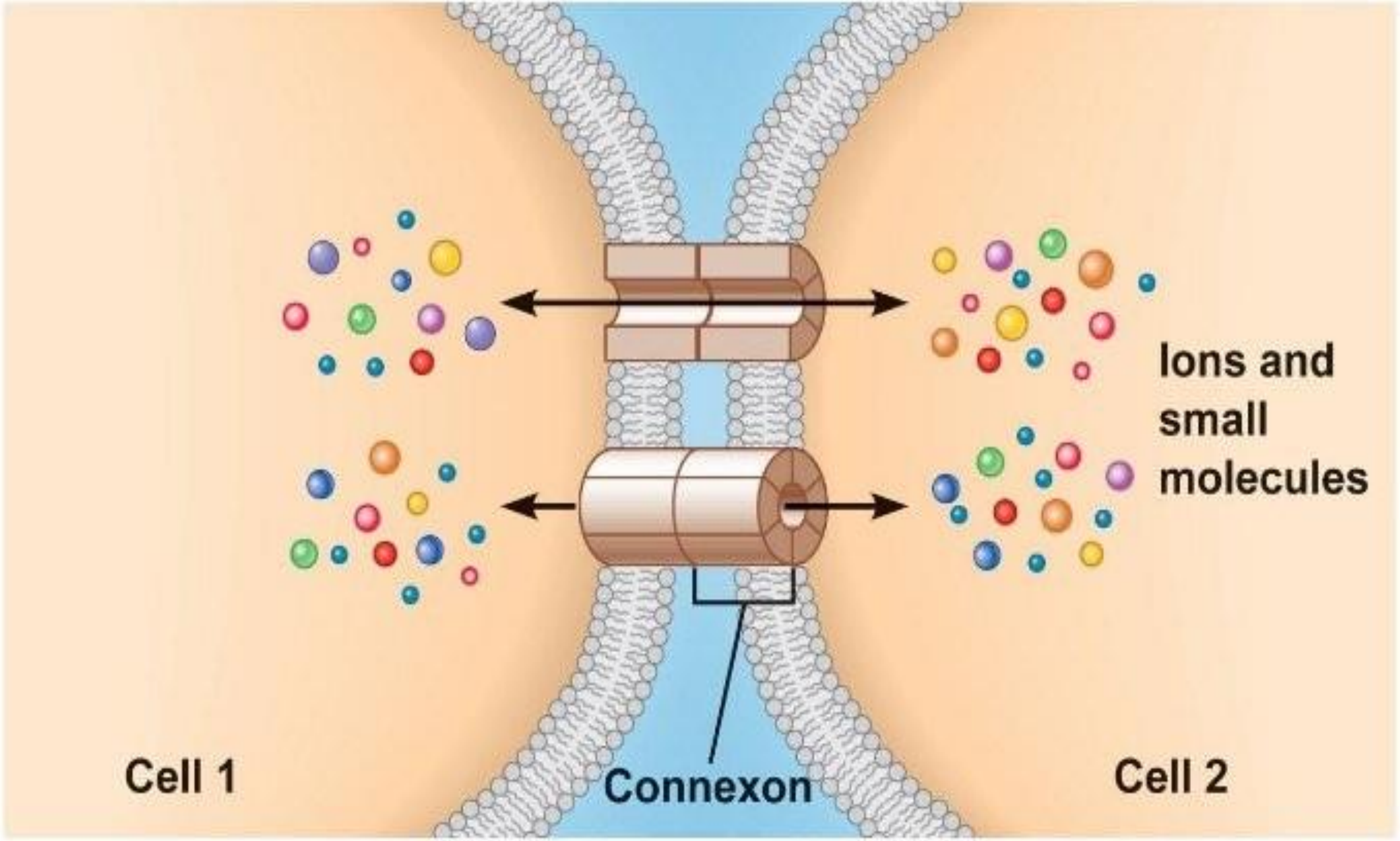
Although there are many kinds of synapses within the brain, they can be divided into two general classes: electrical synapses and chemical synapses.

SITES OF ELECTRICAL SYNAPSES

1-Electrical synapses are the neurophysiological product of gap junctional pores between neurons that **allow bidirectional flow of current between neurons. They are expressed throughout the mammalian nervous system, including cortex, hippocampus, thalamus, retina, cerebellum, and inferior olive.**

2- In cardiac muscle

3- in smooth muscles


Ions and
small
molecules
Cell 1
Connexon
Cell 2

TYPES OF SYNAPSES

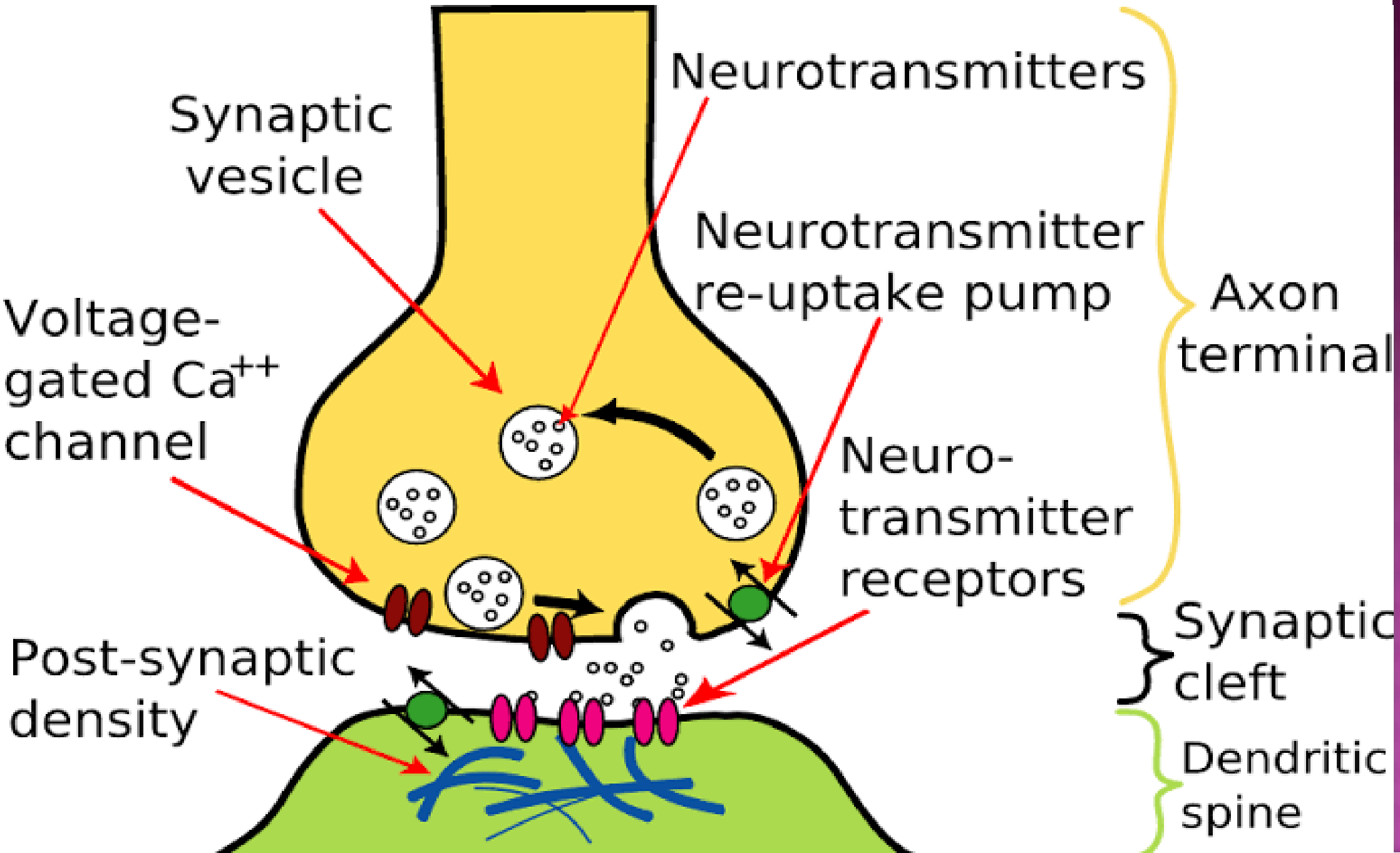
In contrast, chemical synapses **enable cell-to-cell communication** via the ⊙ secretion of neurotransmitters

; **the chemical agents released by the** presynaptic neurons produce secondary current flow in postsynaptic **neurons by activating**

specific receptor molecules

. The secretion of neurotransmitters is triggered by the influx of Ca^{2+} through voltage-gated channels, **which gives rise to a transient increase in Ca^{2+} concentration within the**

presynaptic terminal.


Synaptic vesicle
Neurotransmitters
Neurotransmitter re-uptake pump
Voltage-gated Ca++ channel
Neuro-transmitter receptors
Post-synaptic density
Axon terminal
Synaptic cleft
Dendritic spine

THE MECHANISM OF CHEMICAL SYNAPTIC TRANSMISSION

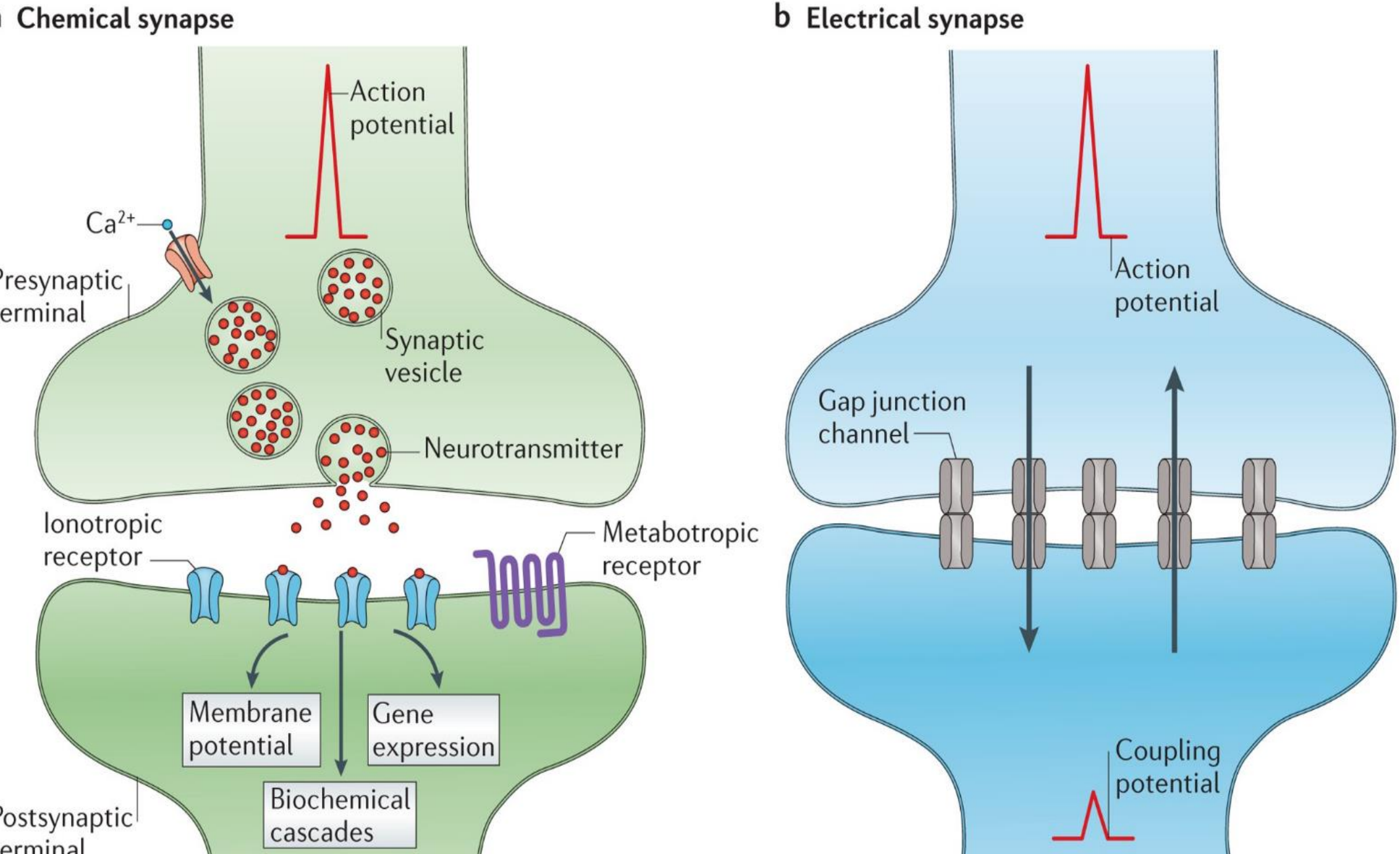
-The rise in Ca^{2+} concentration causes synaptic vesicles—the presynaptic **organelles that store neurotransmitters**—to fuse with the presynaptic **plasma membrane and release their contents into the space between the pre- and postsynaptic cells.**

-Although it is not yet understood exactly how Ca^{2+} triggers exocytosis, **specific proteins on the surface of the synaptic** vesicle and elsewhere in the presynaptic terminal evidently mediate this process.

SITES OF CHEMICAL SYNAPSES

-Chemical synapses are biological junctions through which neurons' **signals** ⊙ **can be sent to each other and to non-neuronal cells such as those** in muscles or glands. -

Chemical synapses allow neurons to form circuits within the central nervous system. They are crucial to the biological computations that underlie perception and thought. They allow the nervous system to connect to and control other systems of the body.


Chemical synapse
Action potential
Ca2+
Presynaptic terminal
Synaptic vesicle
Neurotransmitter
Ionotropic receptor
Metabotropic receptor
Membrane potential
Gene expression
Biochemical cascades
Postsynaptic terminal
b Electrical synapse
Action potential
Gap junction channel
Coupling potential

QUESTIONS

1- which is the main cause of resting membrane potential?

Na diffusion through passive channels (a

Na diffusion through voltage gated channels (b

K diffusion through passive channels (c

Ca diffusion through voltage gated ca channels (d

Protein diffusion through the cell membrane (e

2- WHICH IS THE MAIN CAUSE OF DEPOLARIZATION PHASE OF NERVE ACTION POTENTIAL?

Movement of k outside the nerve cell (a

Na K pump (b

Chloride influx (c

Increased permeability of the cell to Na (d

Movement of K inside the nerve cell (e

3-DURING THE SLOW PHASE OF DEPOLARIZATION :THE FIRING LEVEL OCCURS AT WHICH OF THESE VALUES?

-55mv (a

+35mv (b

-70mv (c

0mv (d

-65mv (e

4- IN RAPID DEPOLARIZATION THE OVERSHOOT OCCURS AT WHICH OF THESE VALUES?

-90mv (a

0mv (b

+35mv (c

-55mv (d

+70mv (e

5- WHICH IS THE MAIN CAUSE OF REPOLARIZATION IN NERVE ACTION POTENTIAL

Na influx (a

Na k pump (b

Ca pump (c

Cl influx (d

Beginning of k efflux (e

6- WHICH IS THE CAUSE OF REDISTRIBUTION OF IONS INSIDE AND OUTSIDE THE NERVE CELL AT THE END OF ACTION POTENTIAL?

K efflux (a

Na influx (b

Na k pump (c

Ca pump (d

Cl influx (e

7-

WHICH IS THE VELOCITY OF CONDUCTION OF NERVE IMPULSE BY SALTATORY CONDUCTON?

10 meter per second (a

120 meter per second (b

2 meter per second (c

50 meter per second (d

70 meter per second (e

8-WHICH IS THE TRIGGER OF RELEASE OF THE CONTENTS OF PRESYNAPTIC VESICLES IN CHEMICAL SYNAPSES?

Ca influx inside the nerve terminal (a

Na influx inside the nerve terminal (b

Rise of K level inside nerve terminal (c

Chloride exit outside the nerve terminal (d

Na efflux outside the nerve terminal (e

SHORT ESSAY QUESTIONS

1-Define RMP ,mention its value and describe its causes

2-Mention the three basic types of ion channels

3-Define action potential and describe its phases

4-Compare between chemical and electrical synapses as regard the

- Define sites of expression and mechanism of transmission