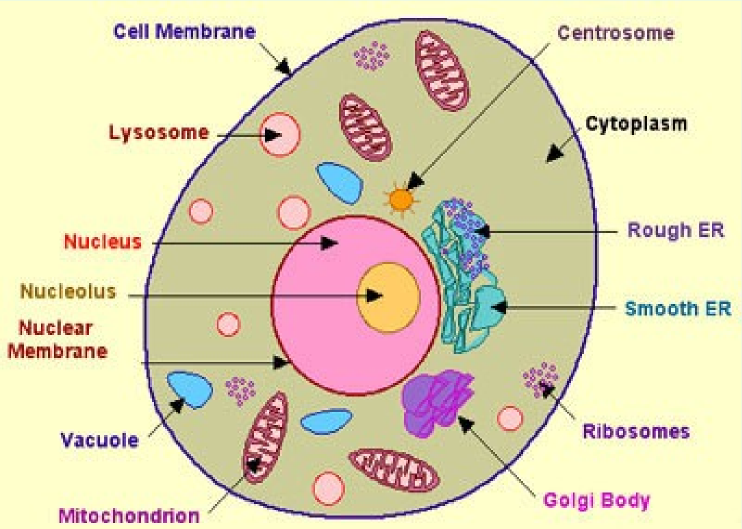
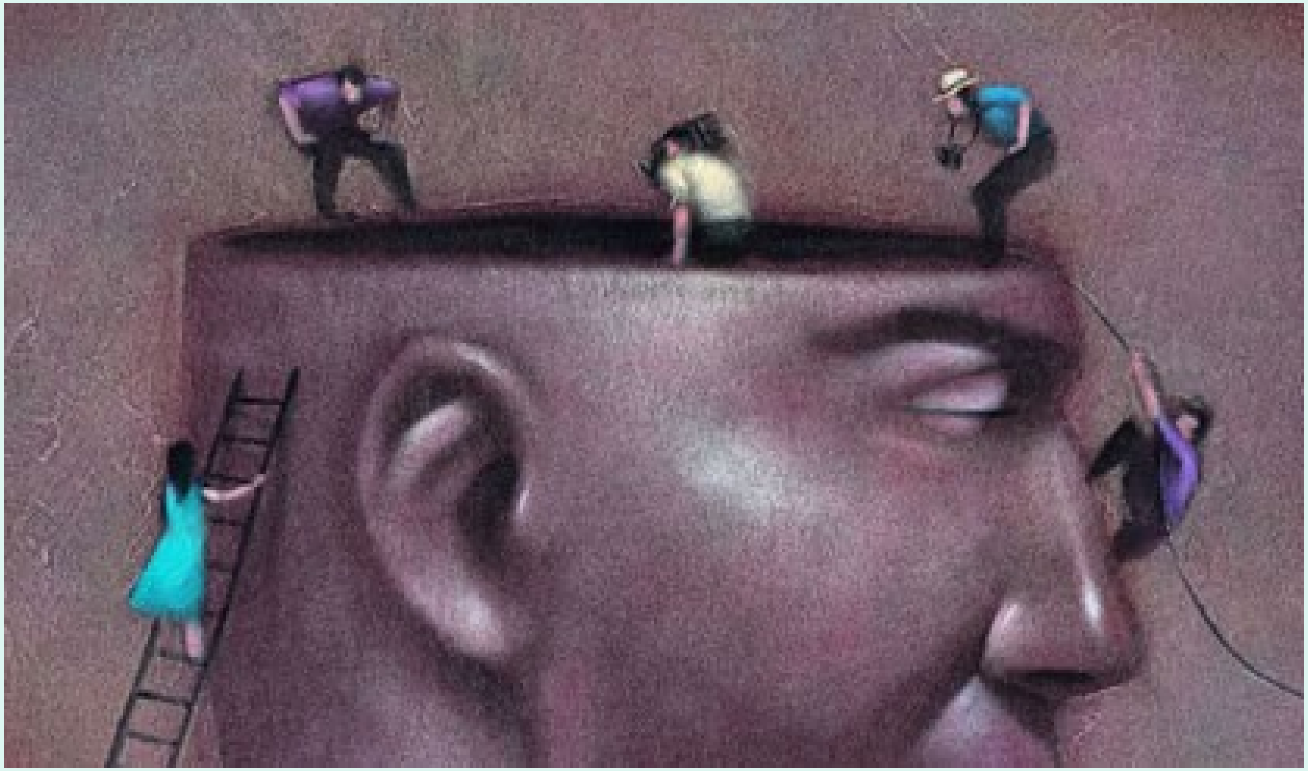
HUMAN PHYSIOLOGY





PHYSIOLOGY

- The term *physiology* originated from a Greek root *Physiologikos* meaning discourse on natural knowledge.
- It was introduced by the French physician *Jean French* in 1552.
- Physiology is a tripod science, its three legs being *Physics, Chemistry* and *Anatomy.*

The purpose of physiology

- The whole purpose of physiology is to explore the normal functioning of the living organisms - their principles, their mechanism, and their control.
- The functional unit of the body is the *cell* and a group of similar cells constitute a *tissue,* a group of tissues form a *system.*

SYSTEMS

In order to understand the functions of the body, it is convenient to divide them into the following systems:

Haemopoietic system;

Reticulo-Endothelial and Lymphatic systems;

Skeletal and Muscular systems;

Nervous system and Special senses;

Circulatory system;

Respiratory system;

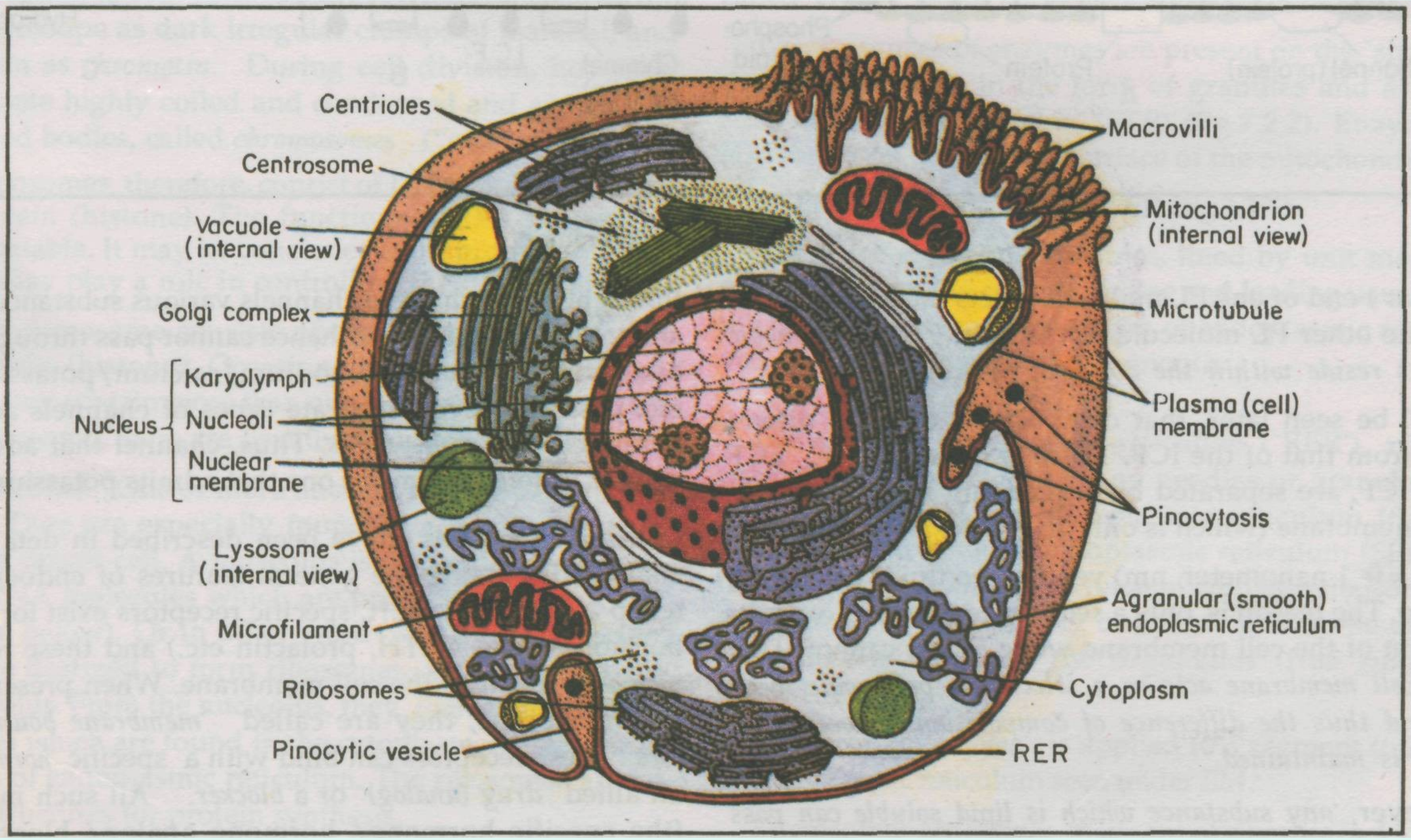
Digestive system and Metabolism;

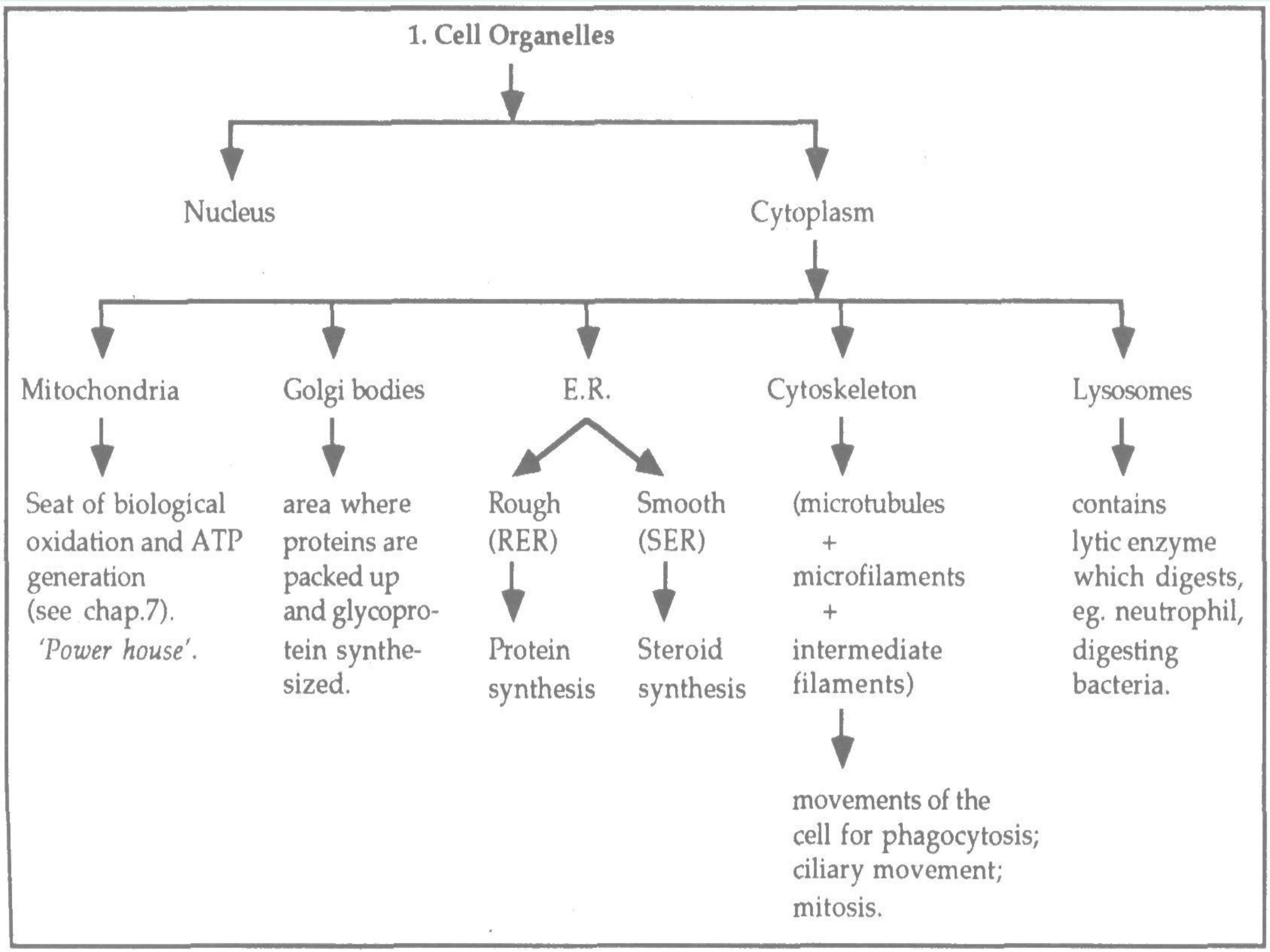
Excretory system;

Endocrine and Reproductive systems.

CELL

- The basic living unit of the body is the cell, and each organ is an aggregate of many different cells held together by intercellular supporting structures. The entire body contains about 100 trillion cells.
- Each type of cell is specially adapted to perform one or a few particular functions. Although the many cells of the body often differ markedly from each other, all of them have certain basic characteristics that are alike.


Centrioles
Centrosome
Vacuole (internal view)
Golgi complex
Karyolymph
Nucleus
Nucleoli
Nuclear membrane
Lysosome (internal view)
Microfilament
Ribosomes
Pinocytic vesicle
Macrovilli
Mitochondrion (internal view)
Microtubule
Plasma (cell) membrane
Pinocytosis
Agranular (smooth) endoplasmic reticulum
Cytoplasm
RER


1. Cell Organelles
Nucleus
Cytoplasm
Mitochondria
Golgi bodies
E.R.
Cytoskeleton
Lysosomes
Seat of biological oxidation and ATP generation (see chap.7). 'Power house'.
area where proteins are packed up and glycoprotein synthesized.
Rough (RER)
Smooth (SER)
Protein synthesis
Steroid synthesis
(microtubules + microfilaments + intermediate filaments)
movements of the cell for phagocytosis; ciliary movement; mitosis.
contains lytic enzyme which digests, eg. neutrophil, digesting bacteria.

ECF & ICF

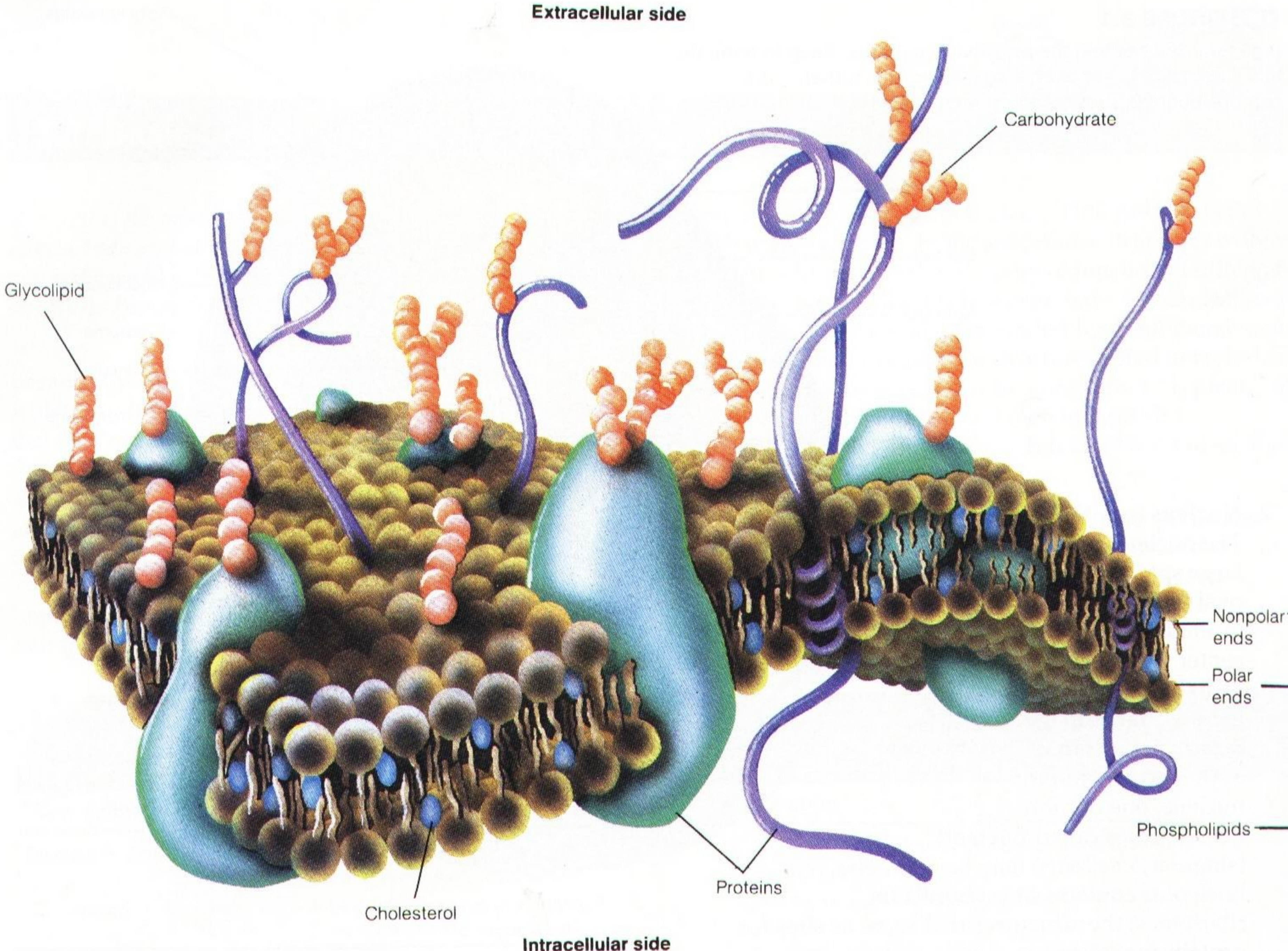
- About 56% of the adult human body is fluid.
- Although most of this fluid is inside the cells and is called *intracellular fluid*, about one third is in the spaces outside the cells and is called *extracellular fluid*.
- This extracellular fluid is in constant motion throughout the body. It is rapidly transported in the circulating blood and then mixed between the blood and the tissue fluids by diffusion through the capillary walls.
- In the extracellular fluid are the ions and nutrients needed by the cells for maintenance of cellular life.

ECF

- The extracellular fluid contains large amounts of sodium, chloride, and bicarbonate ions, plus nutrients for the cells, such as oxygen, glucose, fatty acids, and amino acids. It also contains carbon dioxide that is being transported from the cells to the lungs to be excreted, plus other cellular products that are being transported to the kidneys for excretion.

ICF

- **The intracellular fluid differs significantly from the extracellular fluid; particularly, it contains large amounts of potassium, magnesium, and phosphate ions instead of the sodium and chloride ions found in the extracellular fluid.**
- **Special mechanisms for transporting ions through the cell membranes maintain these differences.**

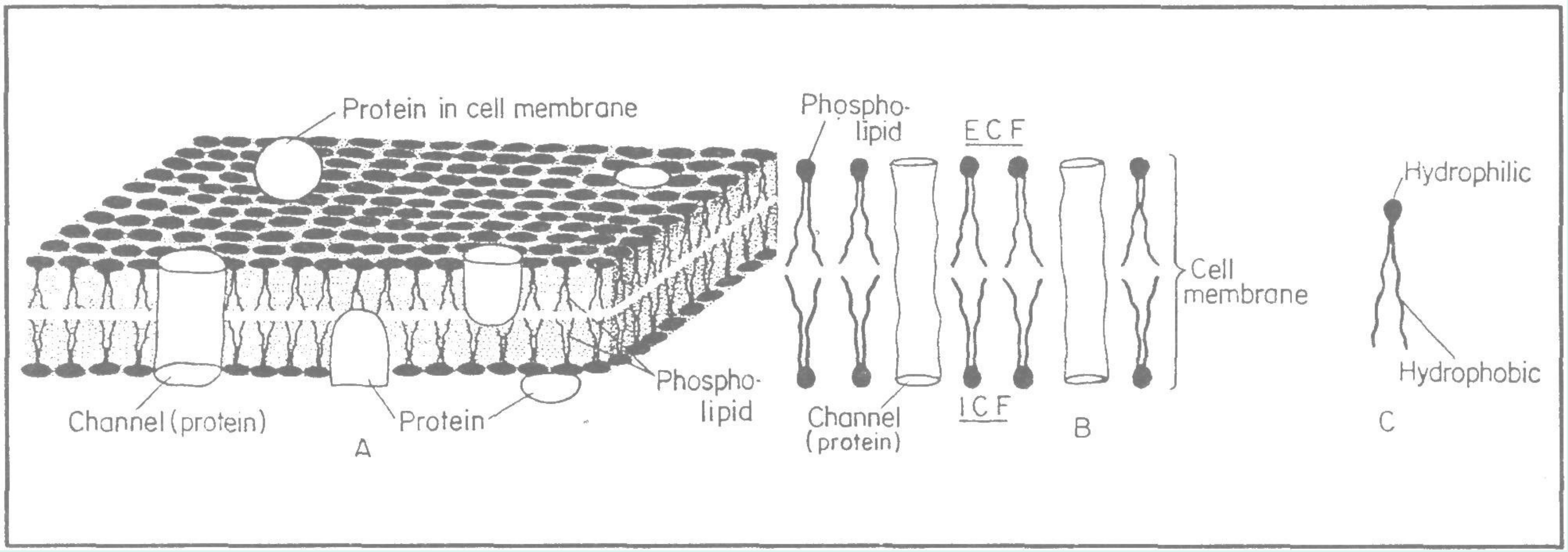


Extracellular side
Carbohydrate
Glycolipid
Nonpolar
ends
Polar
ends
Phospholipids
Proteins
Cholesterol
Intracellular side

CELL MEMBRANE

- The cell membrane consists mainly of two layers of phospholipid (PL) molecules and in between protein molecules are present.
- Phospholipids are polar molecules. They have two ends, one hydrophilic (water soluble) the other hydrophobic (water insoluble). The hydrophilic end is the polar and the hydrophobic one is non polar.

CELL MEMBRANE

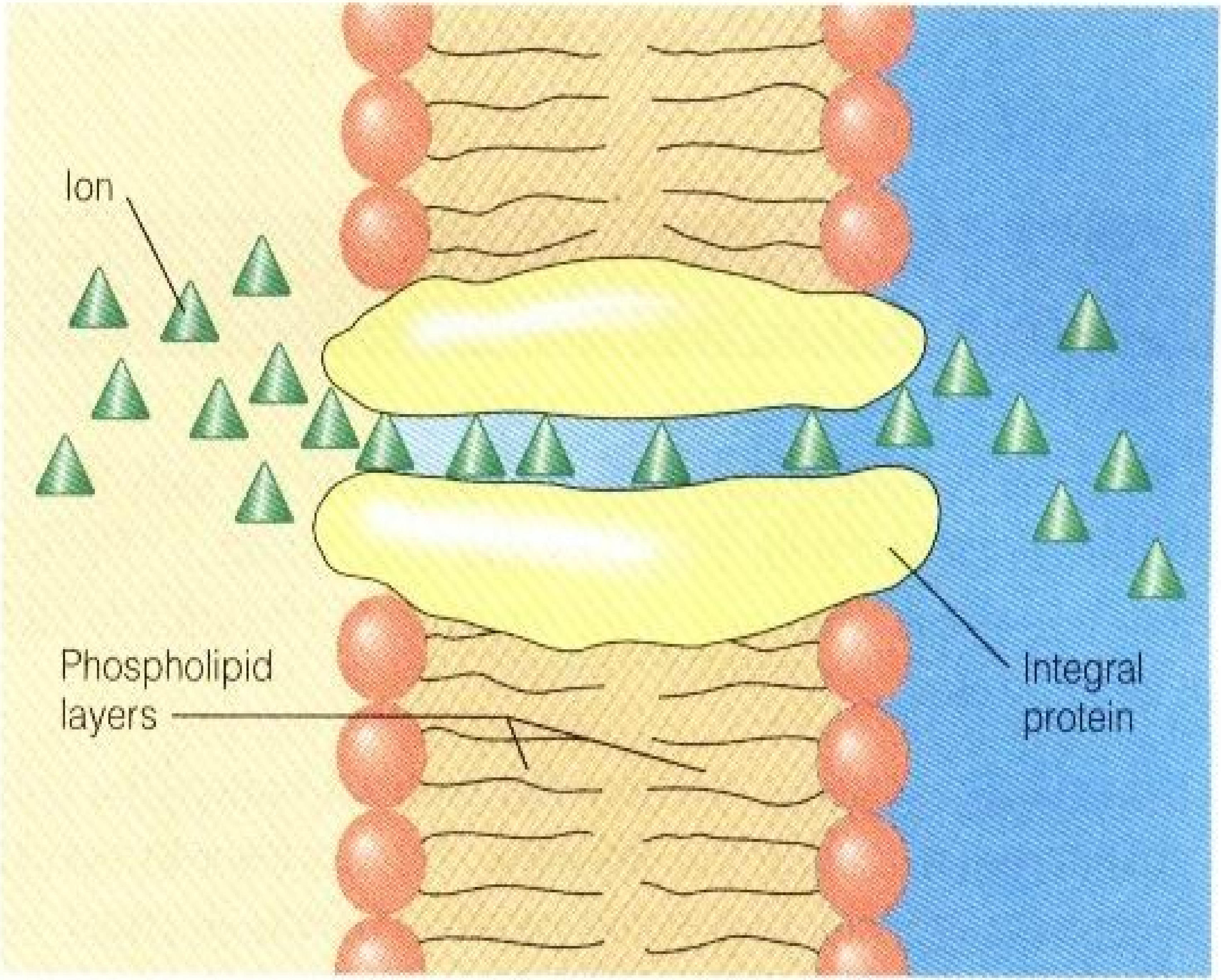


INTEGRAL & PERIPHERAL PROTEINS

- Proteins of the cell membrane are divided into two groups:

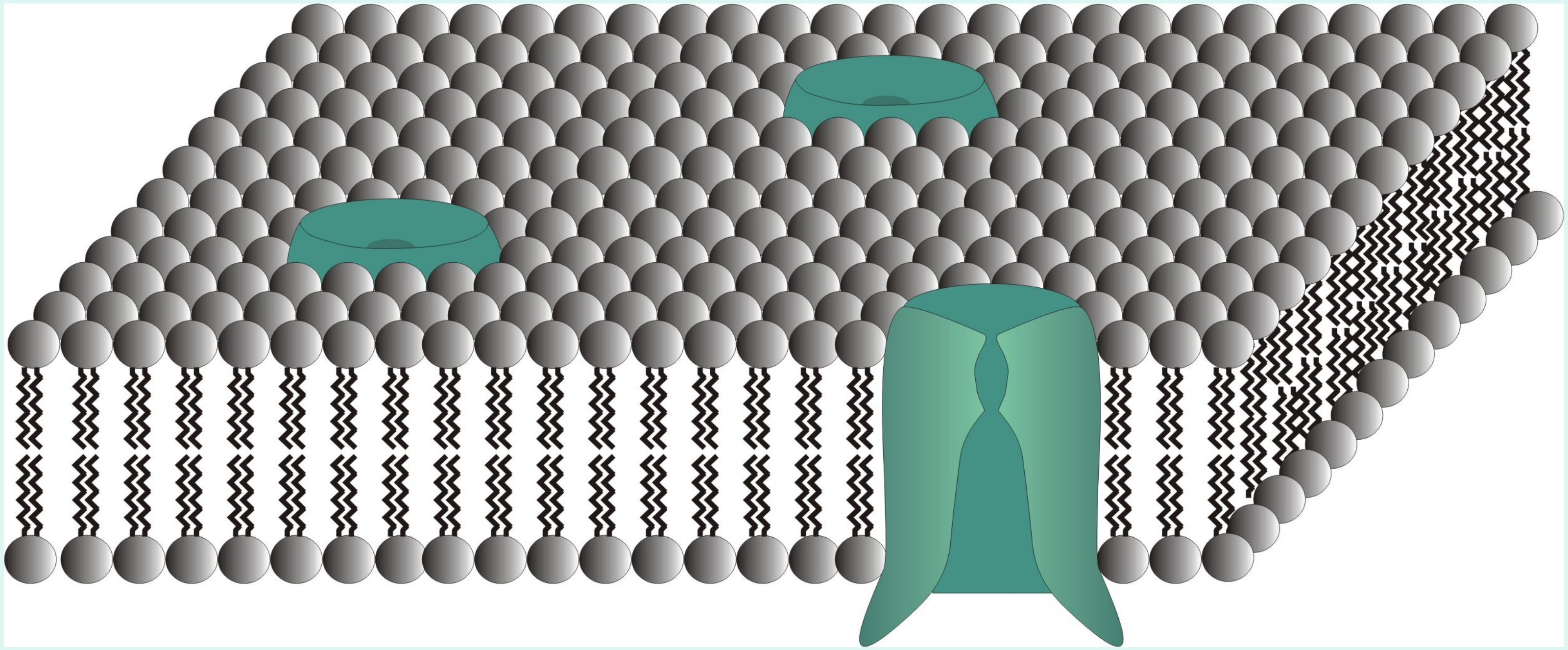
  1) the integral proteins (transmembrane protein like channel proteins)

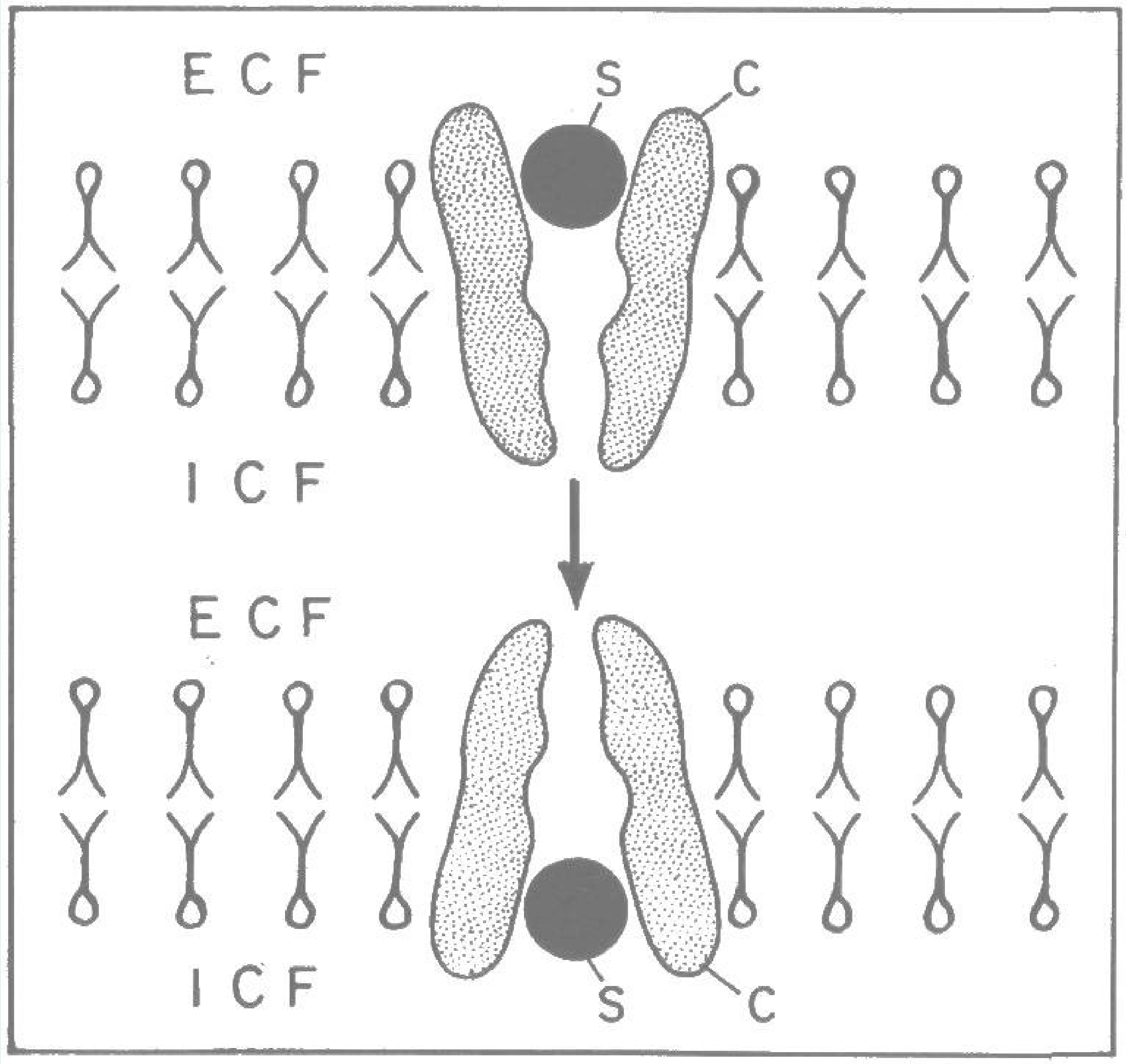
  2) the peripheral proteins (can be removed from the cell membrane without it damaging).
- Proteins in the cell membrane can be (1) an ion channel (channel protein), (2) a receptor protein, (3) an enzyme, (4) carrier protein.

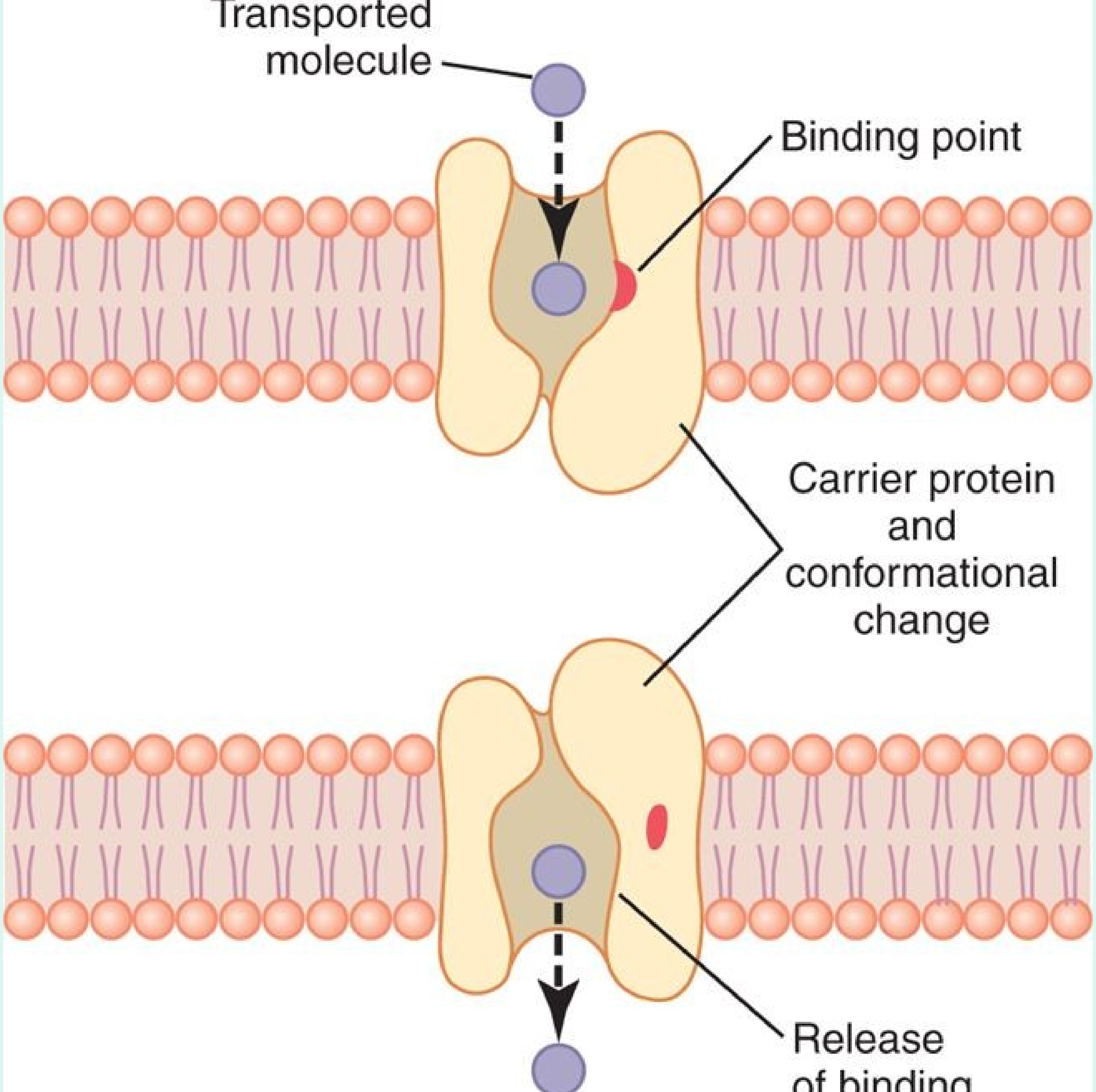

Ion
Phospholipid
layers
Integral
protein

CHANNEL PROTEIN

- The channels in the cell membrane are usually closed, but when an action potential passes over them or a specific chemical (eg, acetyl choline - ACh) comes in its contact, it opens.
- When it opens, it causes a communication to develop between the ECF and ICF. There are specific channels like Na-channel, K-channel, Ca-channel and so on.




ECF
S
C
ICF
ECF
ICF
S
C



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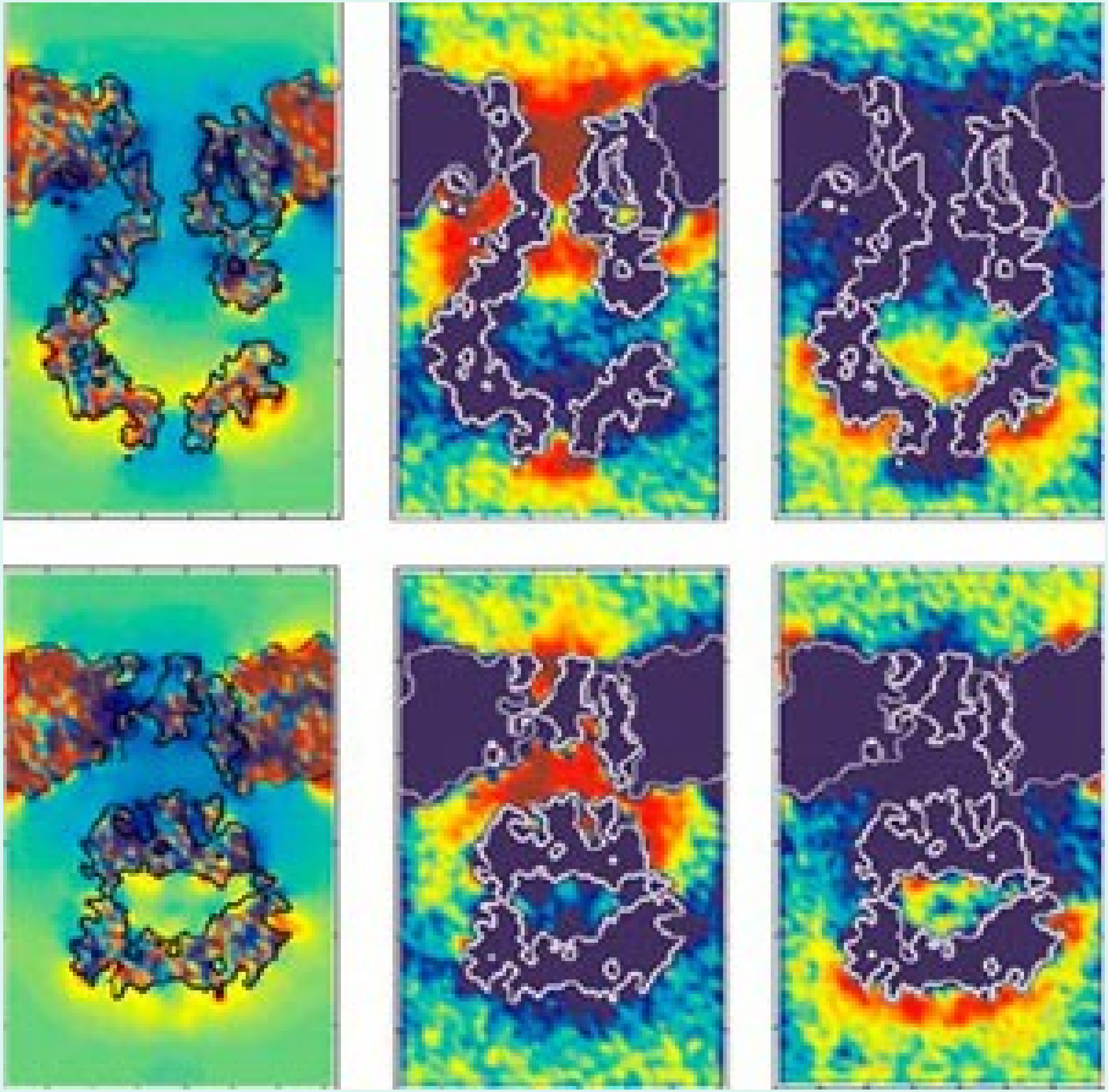
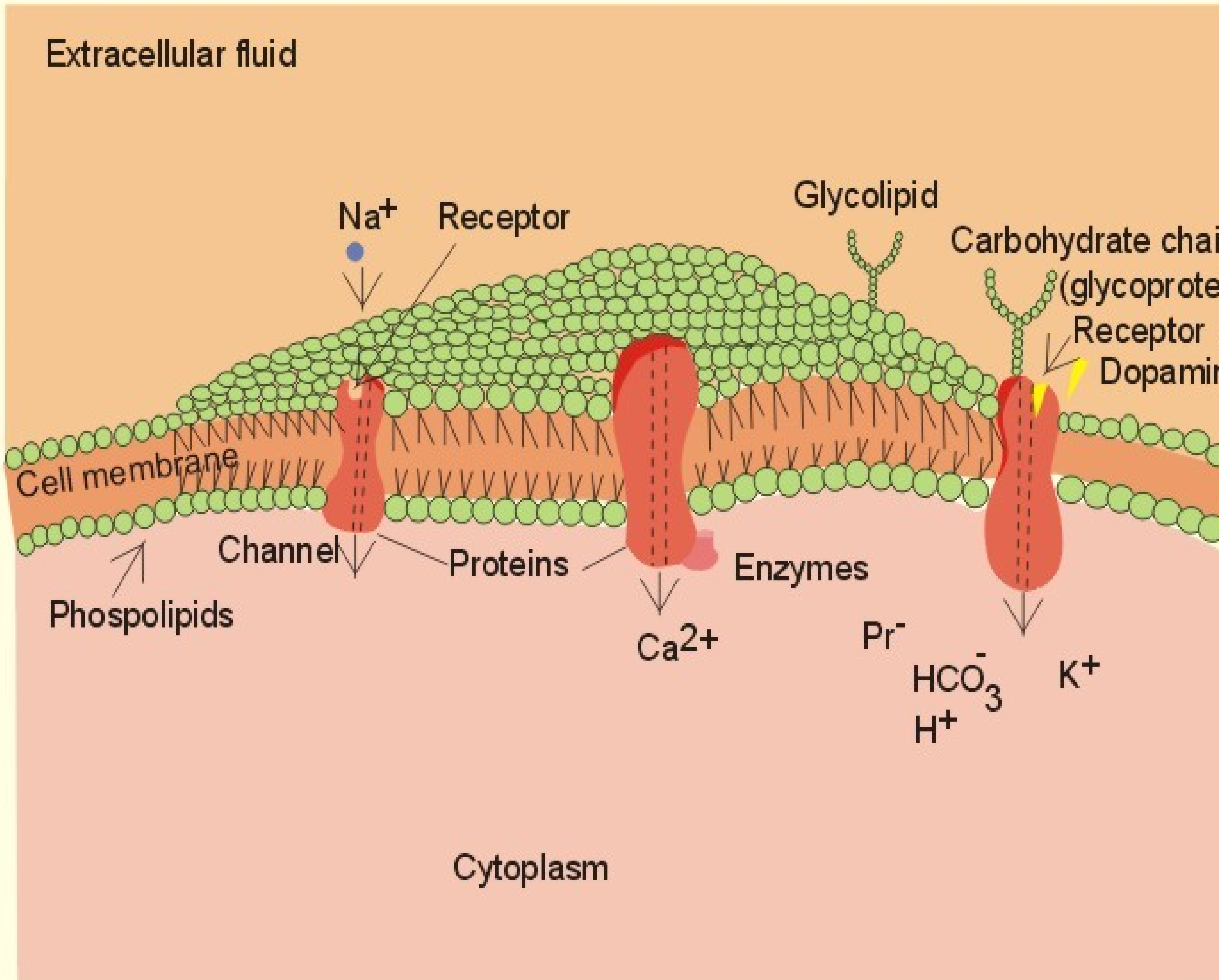


RECEPTOR PROTEIN

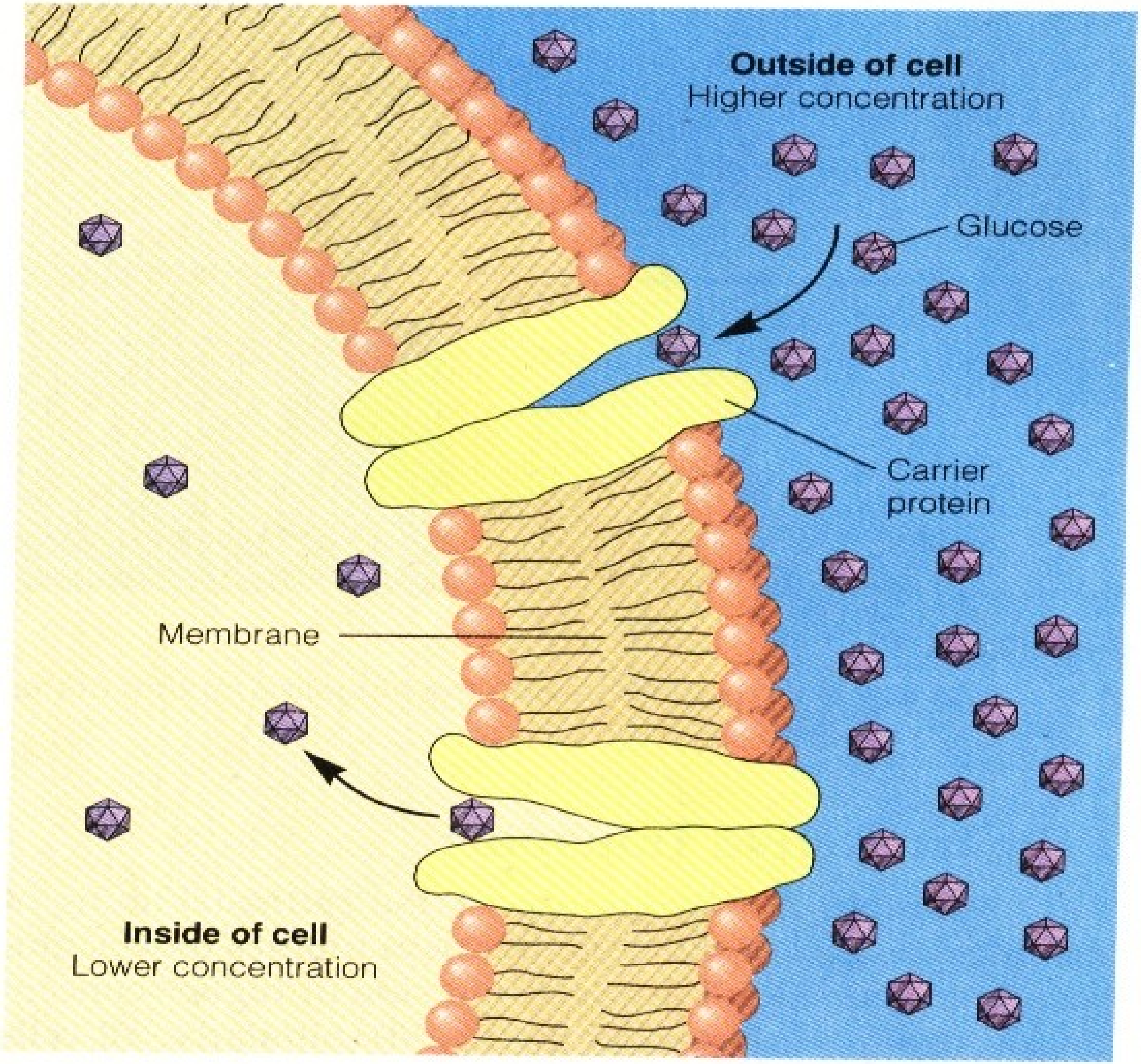
- **Receptors are proteinaceous compounds.**
- **A receptor can combine with a highly specific molecule. (Thus, the receptor for insulin hormone will combine with insulin but not with any other molecule.)**
- **After the combination of receptor with the specific chemical molecule for which it has affinity, a *receptor-ligand complex* is formed - the cell is activated or inhibited (the specific chemical molecule is called ligand).**

Model Of A Cell Membrane

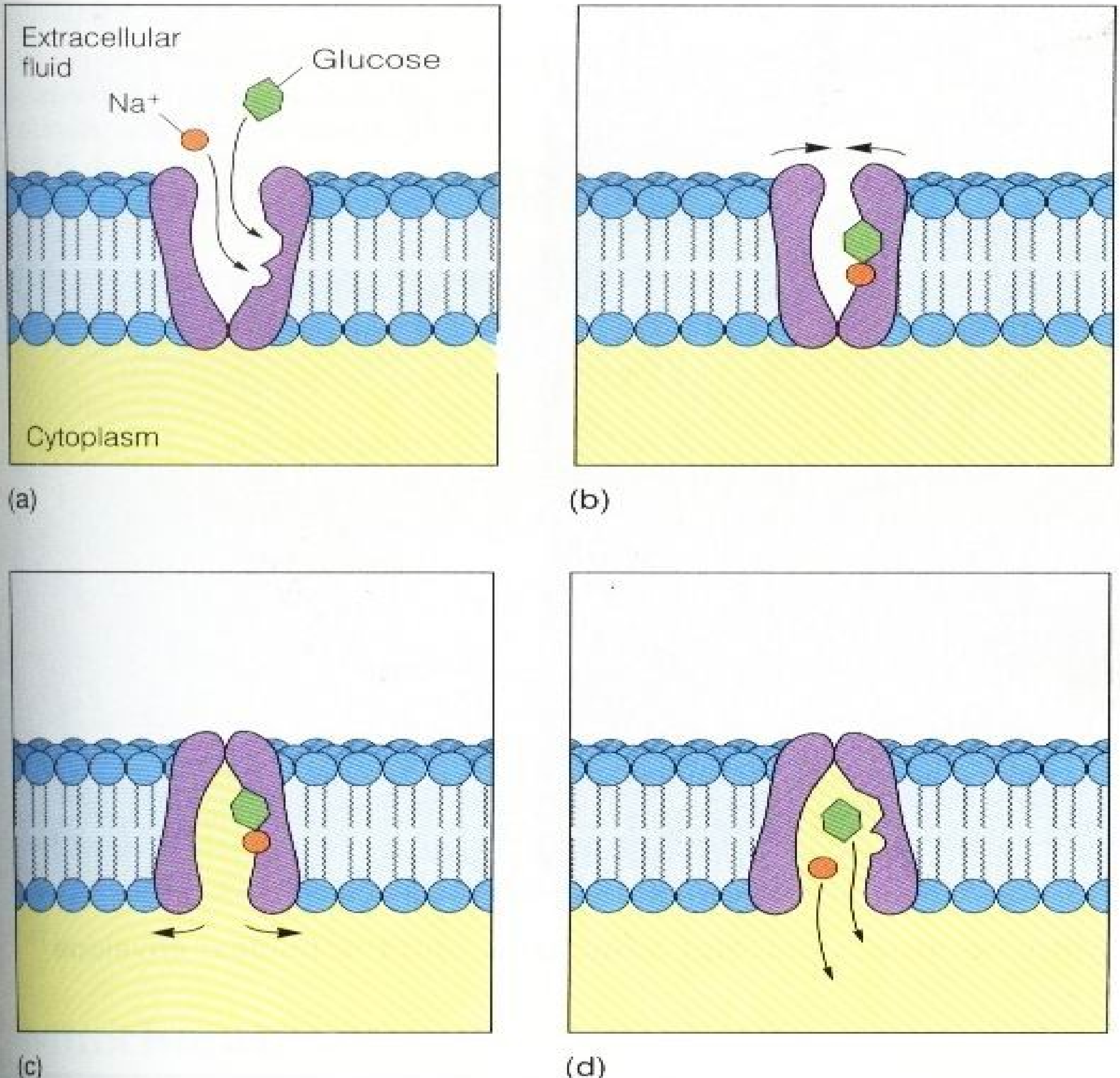


CARRIER PROTEIN

- A carrier protein is an «integral protein» of the cell membrane. It has affinity for a specific chemical molecule. For example, glucose transport across the cell occurs via carrier. There is a carrier protein in the cell membranes of many cells, which can (because it has affinity for glucose) catch a glucose molecule.



Outside of cell
Higher concentration
Glucose
Carrier protein
Membrane
Inside of cell
Lower concentration



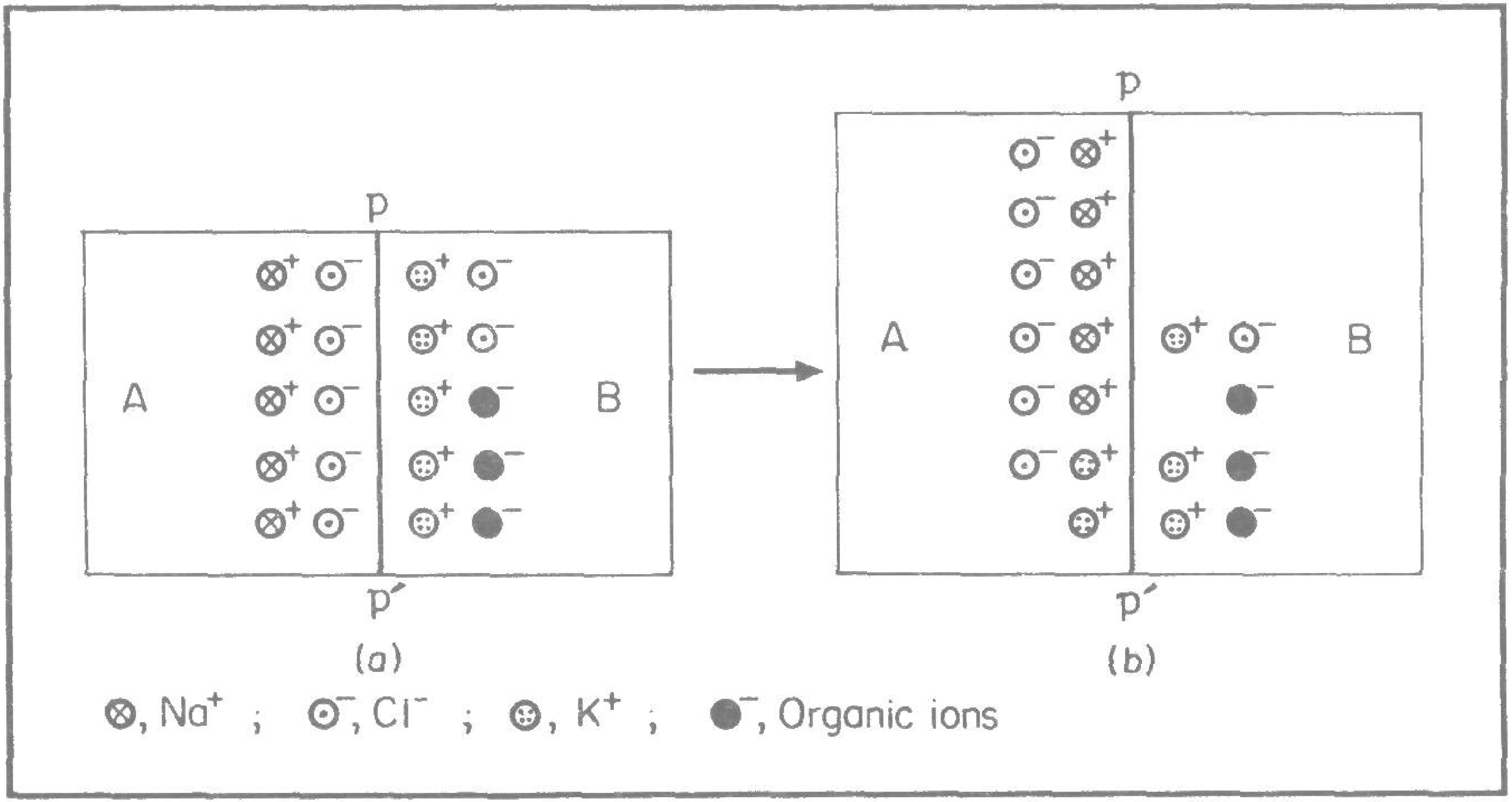
Extracellular fluid
Glucose
Na+
Cytoplasm
(a)
(b)
(c)
(d)

PASSAGE OF MOLECULES THROUGH THE CELL MEMBRANE

- The major mechanisms of cell membrane crossing by different molecules include:
    1) diffusion,
    2) mediated transport,
    3) endocytosis-exocytosis,
    4) osmosis.

DIFFUSION

- Diffusion has two subgroups:
  1) lipid diffusion (also called, simple diffusion)
  2) diffusion through the channels.
- In diffusion molecules move according to chemical gradient (ie, molecules from a solution of higher concentration move towards a solution of lower concentration).

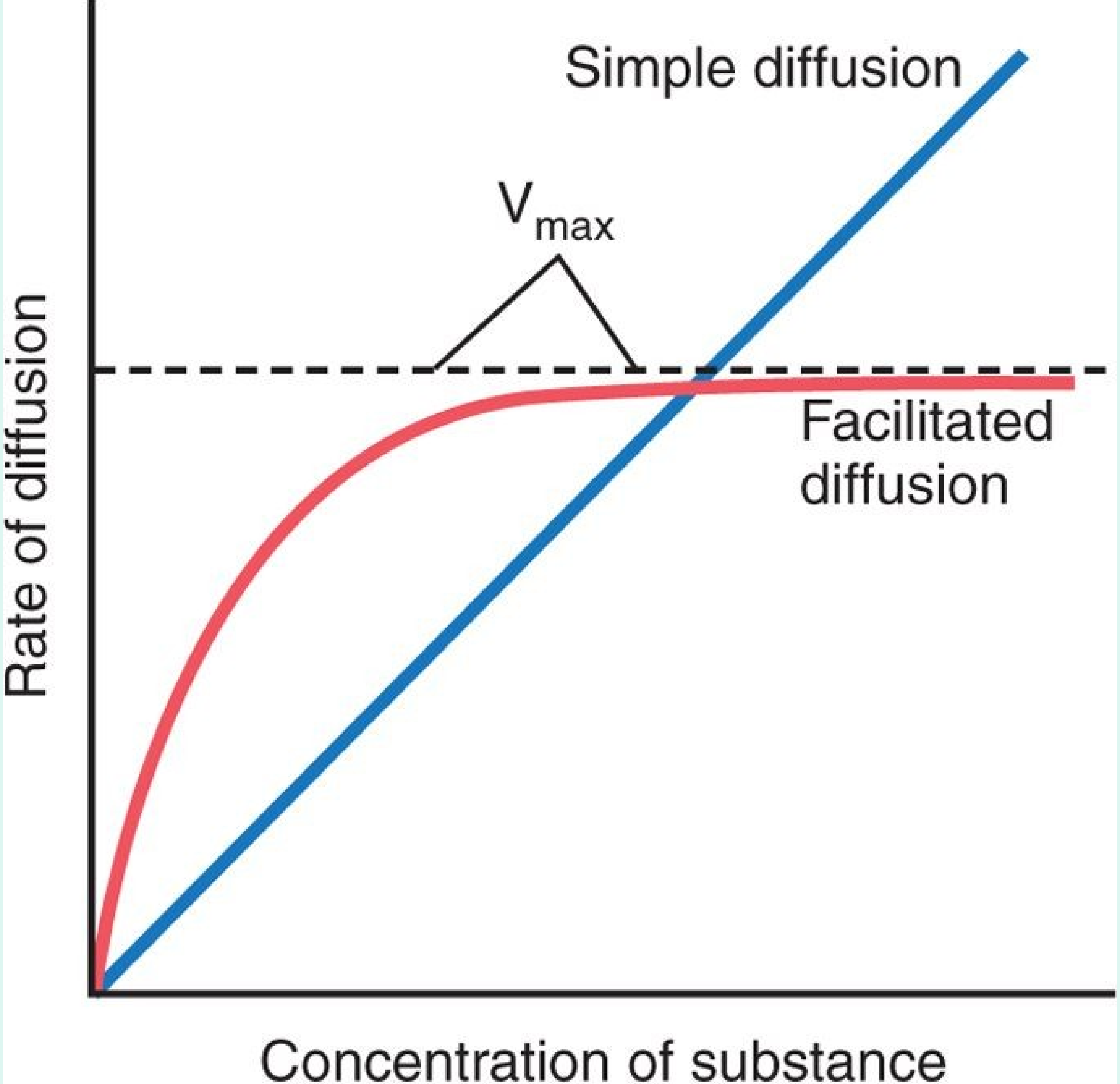

p
A
B
p′
(a)
p
A
B
p′
(b)
⊗, Na+ ; ⊙⁻, Cl⁻ ; K+ ; ●⁻, Organic ions

LIPID DIFFUSION (simple diffusion)

- Molecules which are soluble in fat (lipid) can cross the cell membrane easily. Many molecules, all lipid soluble, like CO_2, O_2, steroid hormones, many drugs enter or leave the cell by this way.
- Non lipid soluble materials like electrolytes (Na, K, Ca), glucose, amino acids can not use this route.

DIFFUSION THROUGH CHANNELS

- The channels, while the cell is at rest, remain closed. But these channels open when they are properly stimulated. This stimulus can be (1) electrical or (2) chemical.
- Channels which open when subjected to electrical stimulus are called «voltage gated channels». Those channels which open due to action of chemicals (neurotransmitters, hormones) are called «ligand gated channels».



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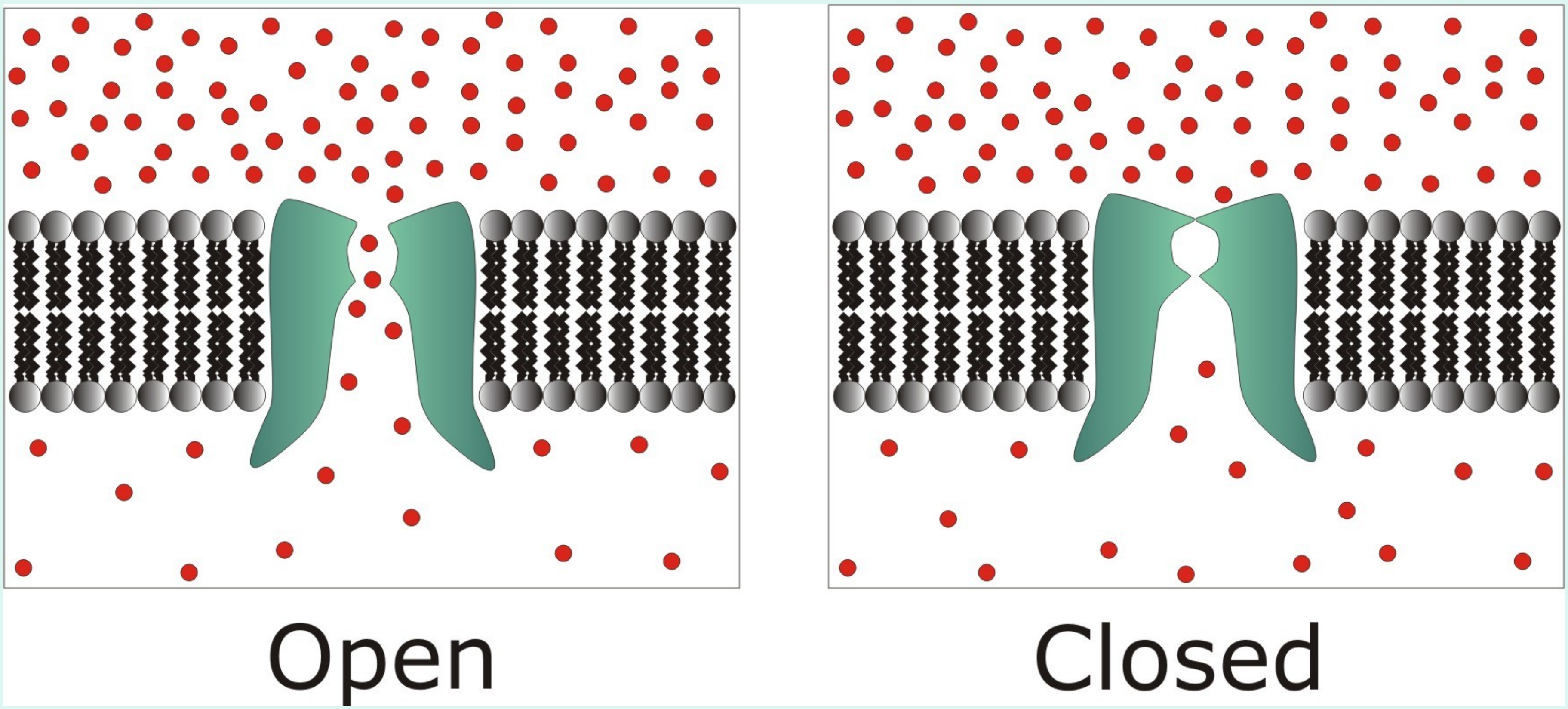
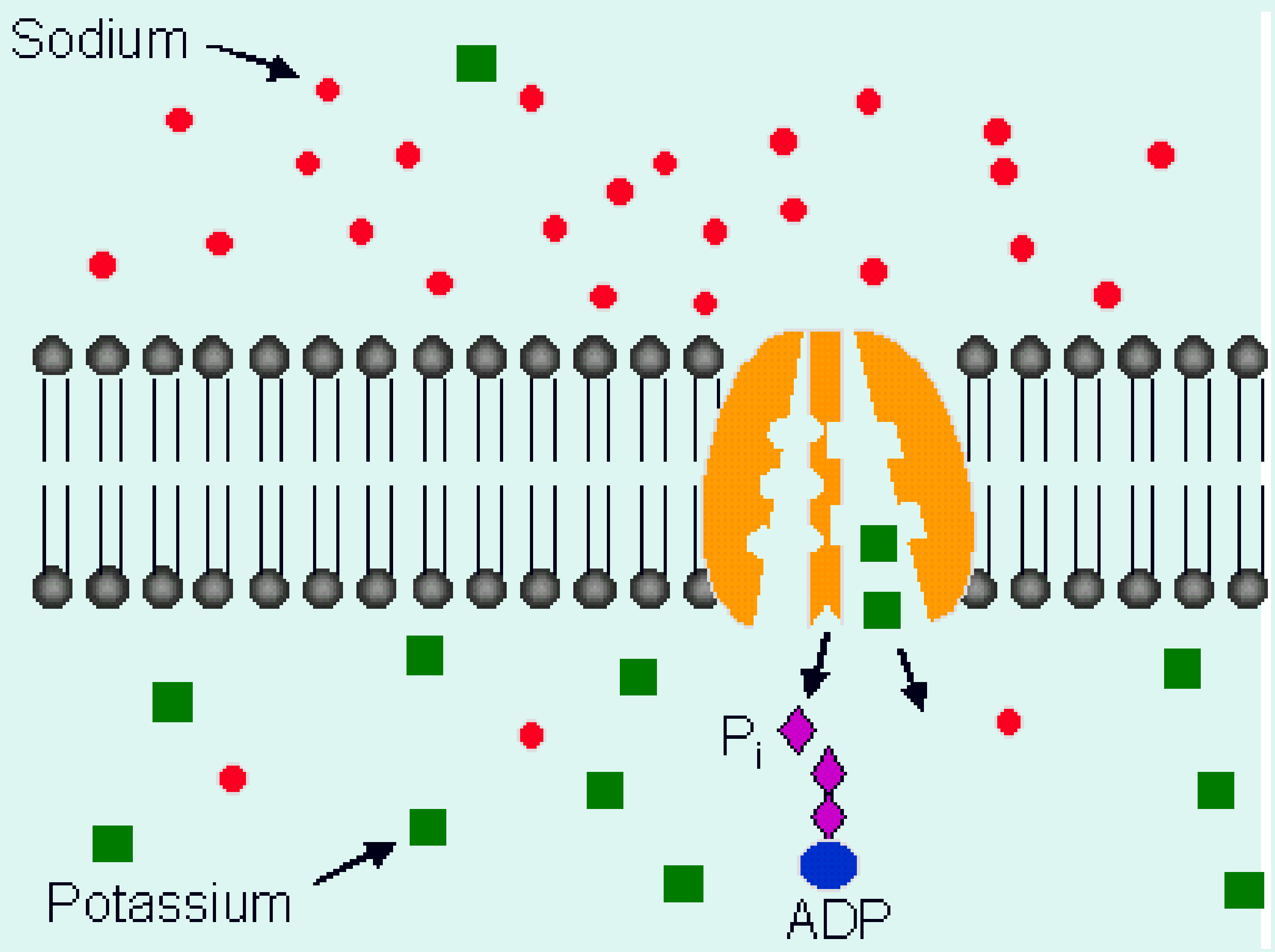
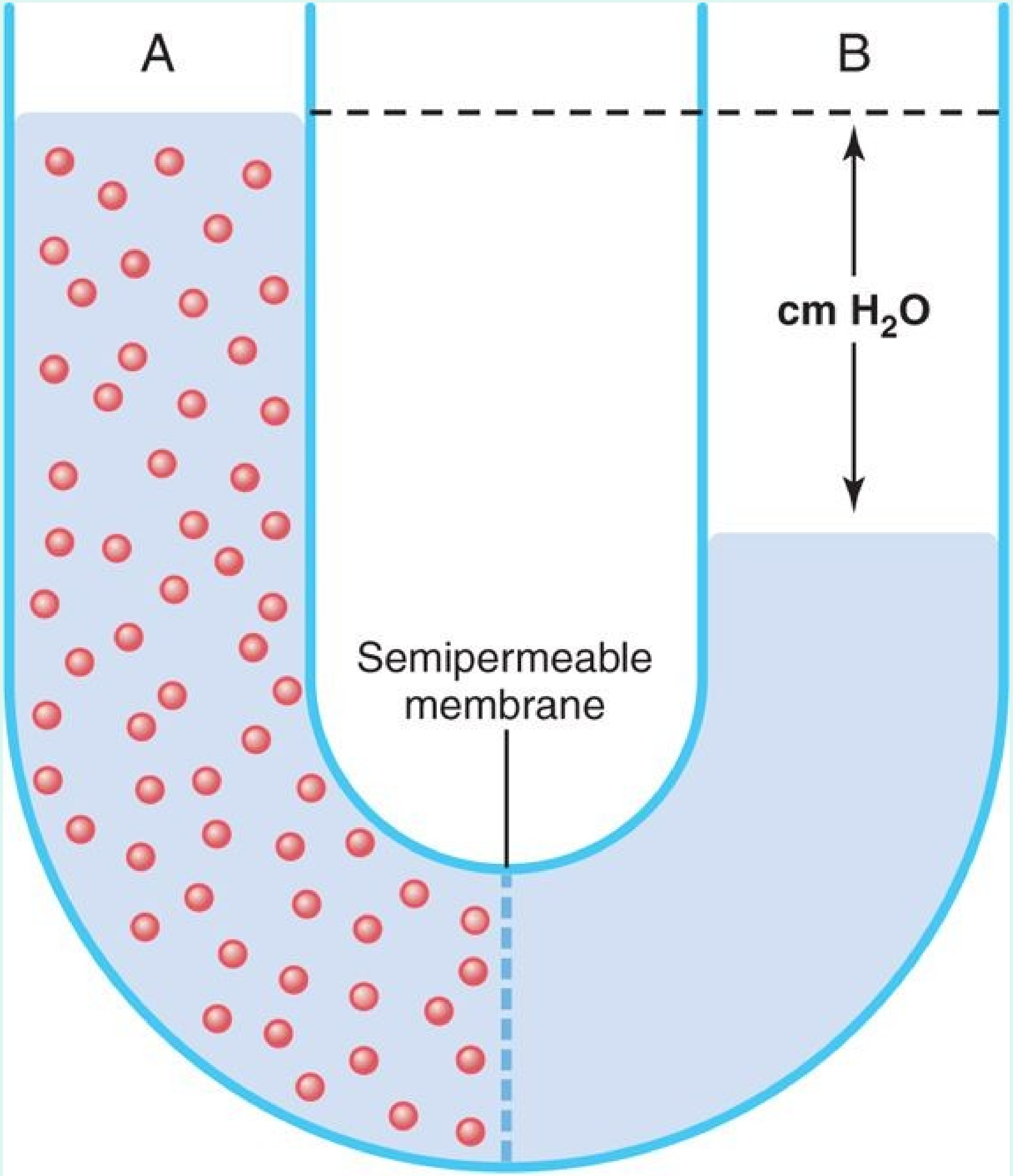

Open
Closed


Sodium
Pi
ADP
Potassium



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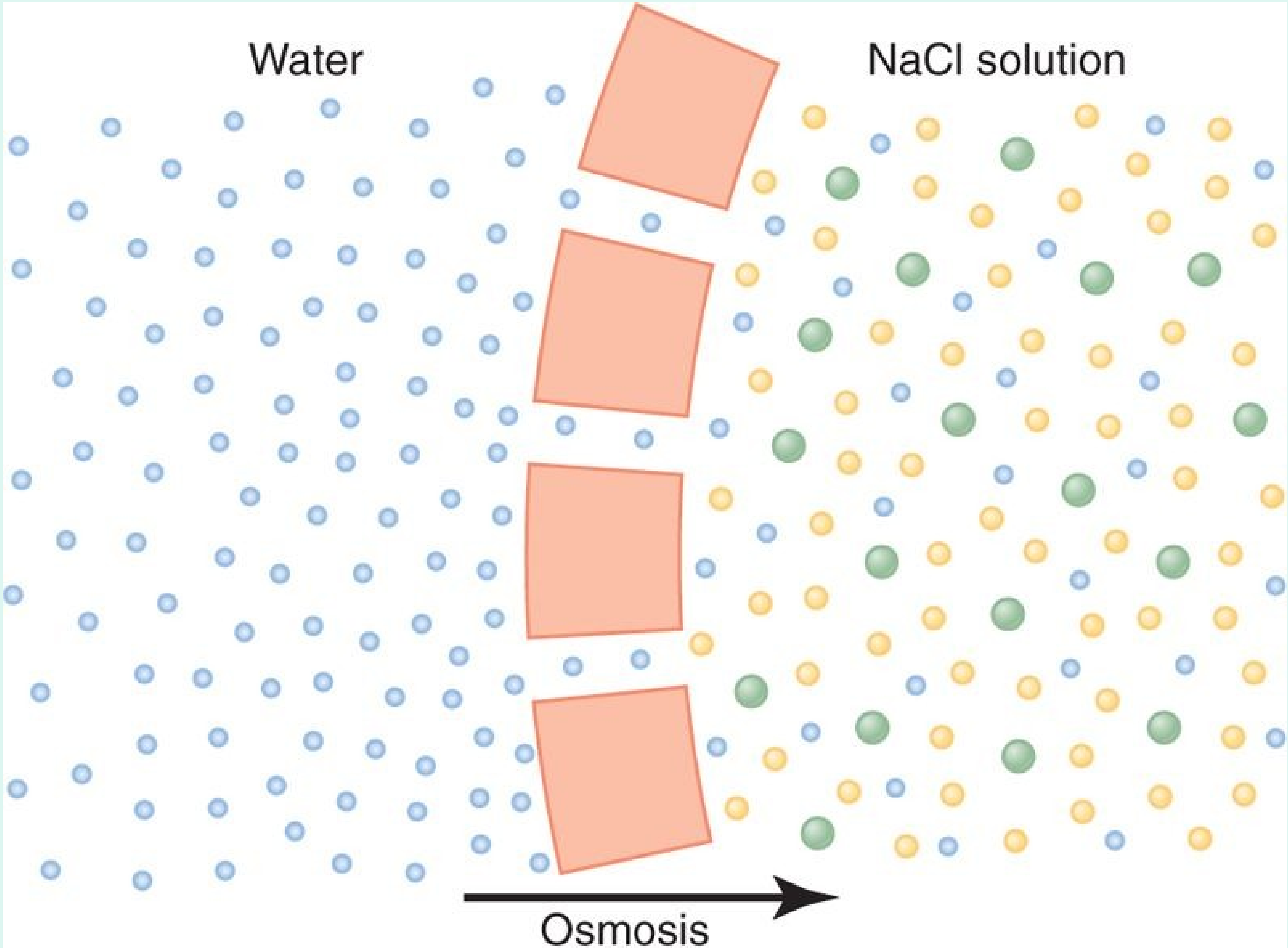

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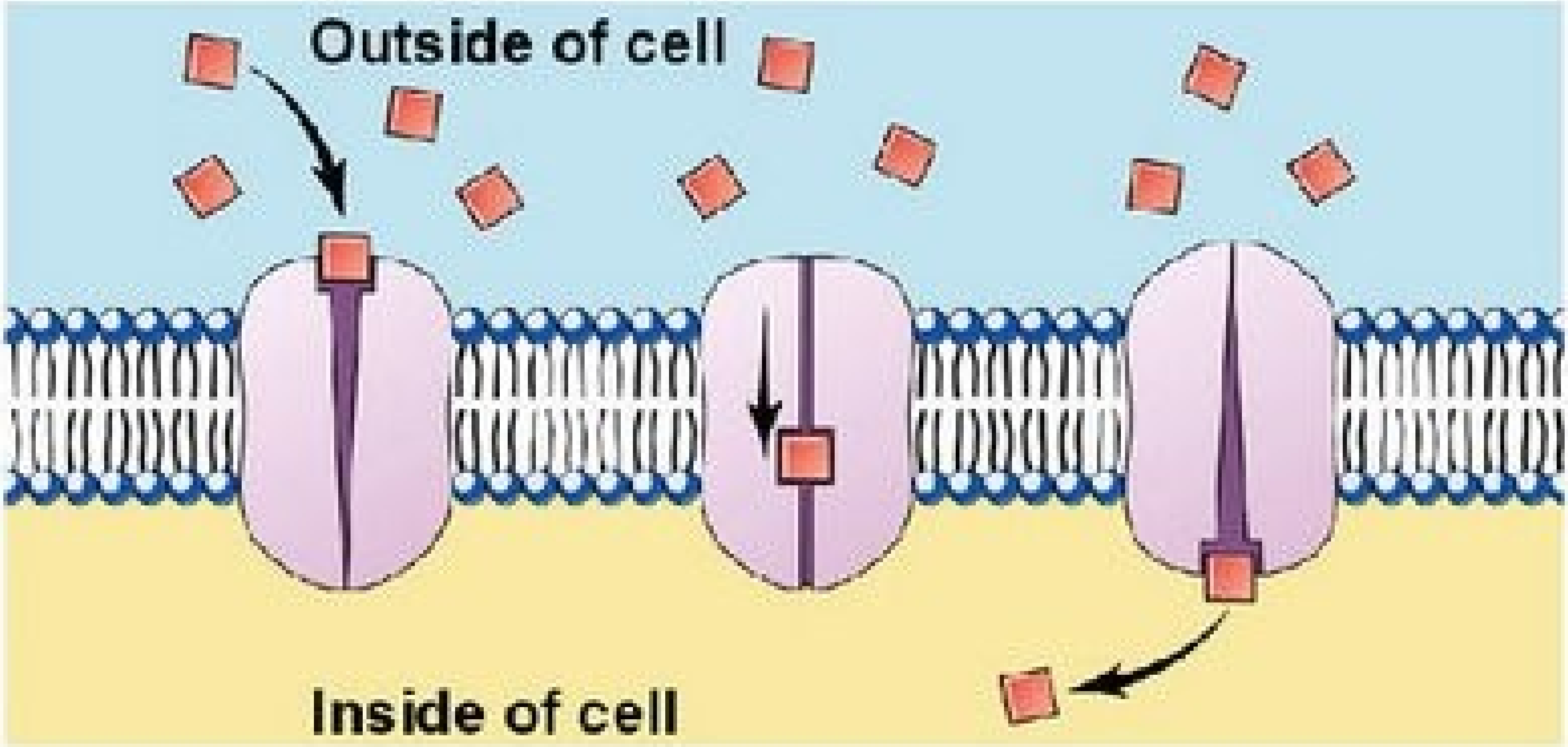
MEDIATED TRANSPORT

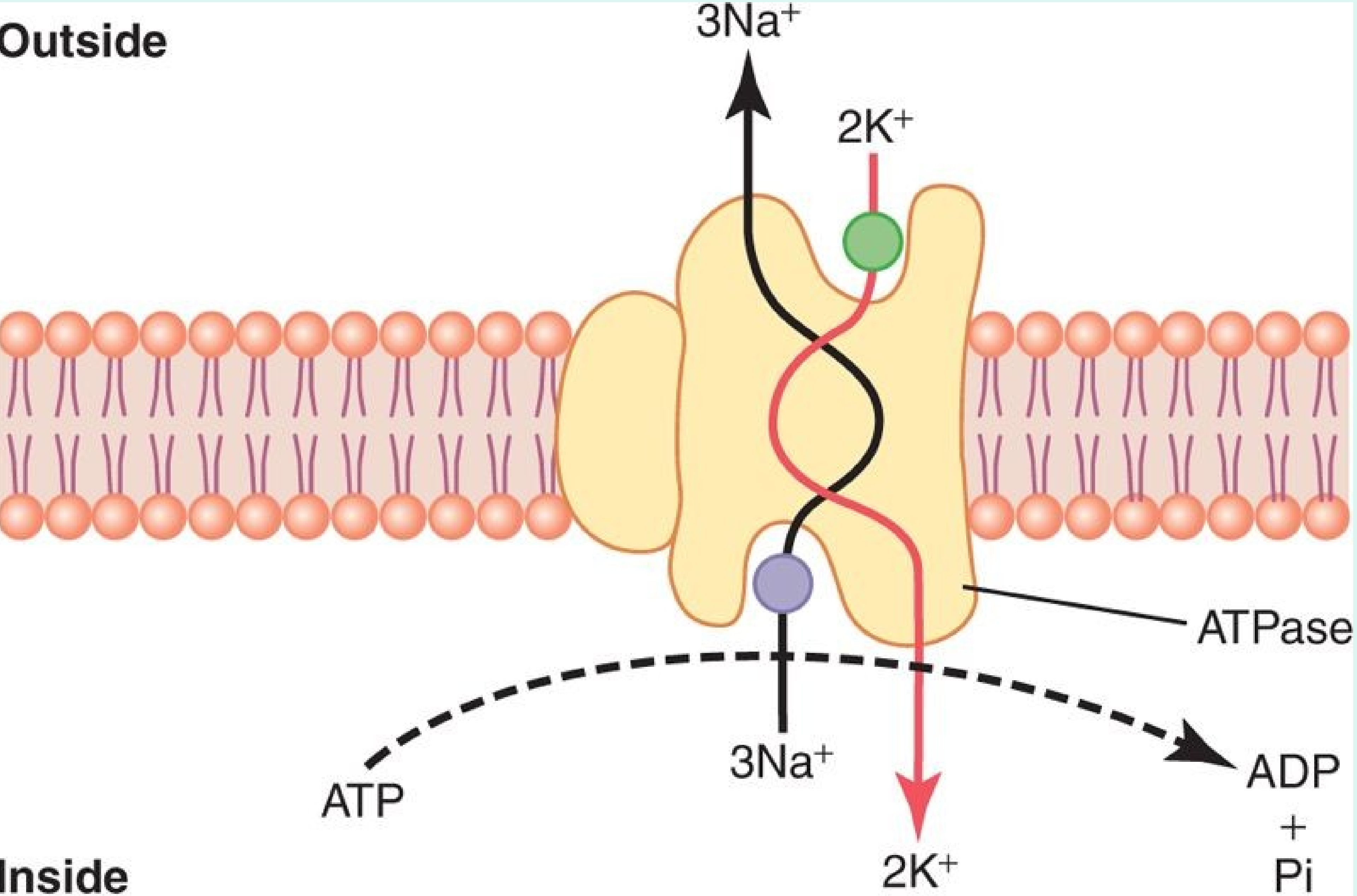
- Some substances (eg. glucose, amino acids) are not soluble in fatty medium or can not pass through channels because of their big size. Such substances cross the cell membrane by mediated transport (also called «carrier mediated transport»).
- Some electrolytes like Na, K are transported as they can move from higher concentration to lower concentration.

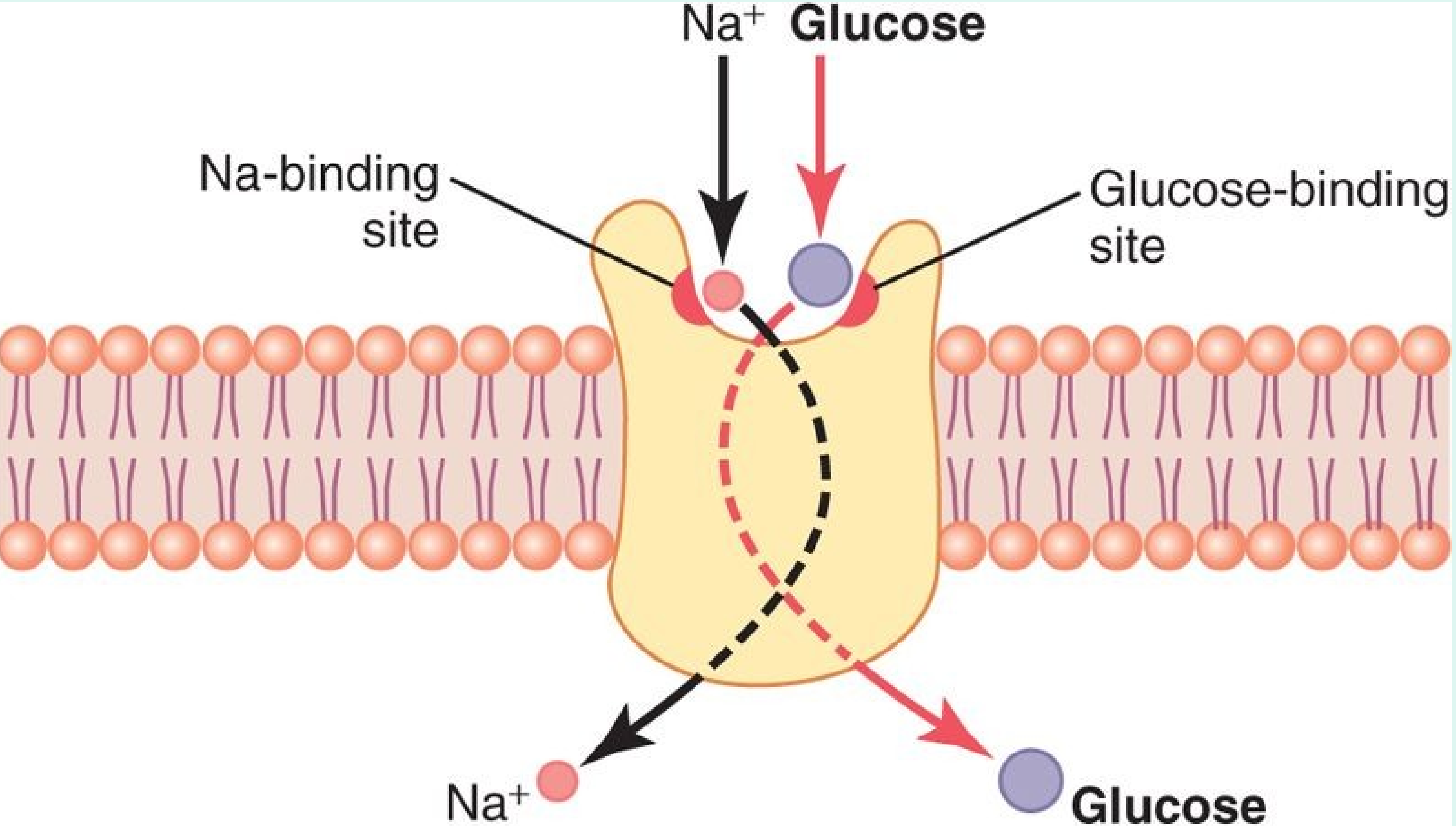
CARRIER MEDIATED TRANSPORT

- Carrier mediated transport has two major classes: (1) facilitated diffusion and (2) active transport (primary active transport and secondary active transport).
- In facilitated diffusion, the movement of molecule is «downhill», ie, it moves from higher to lower concentration.
- In active transport the movement of molecule is «uphill» i.e., it moves from lower to higher concentration (for this, expenditure of energy is required).

Facilitated Diffusion




Outside
3Na+
2K+
ATPase
ATP
3Na+
2K+
ADP
+
Pi
Inside



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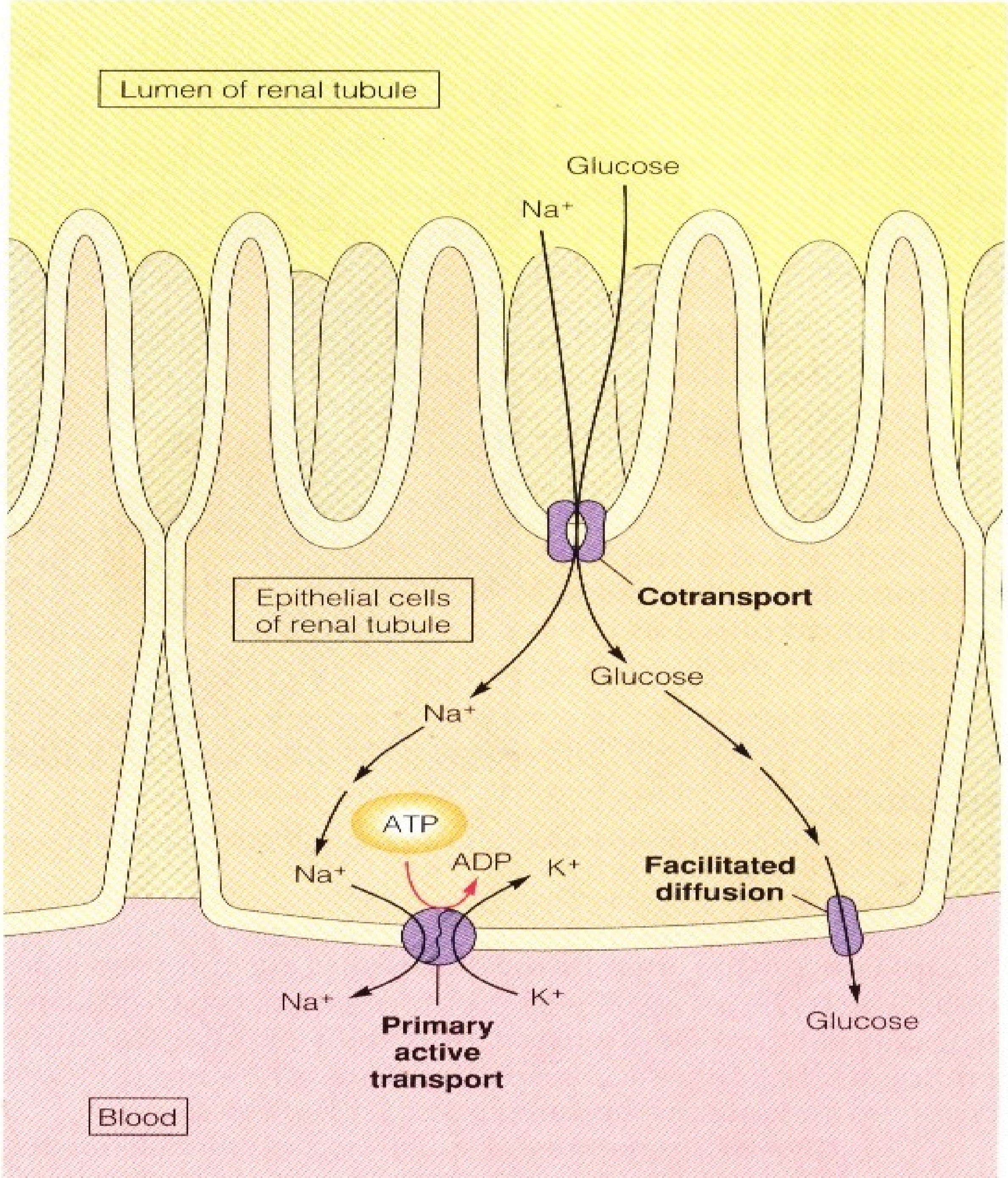
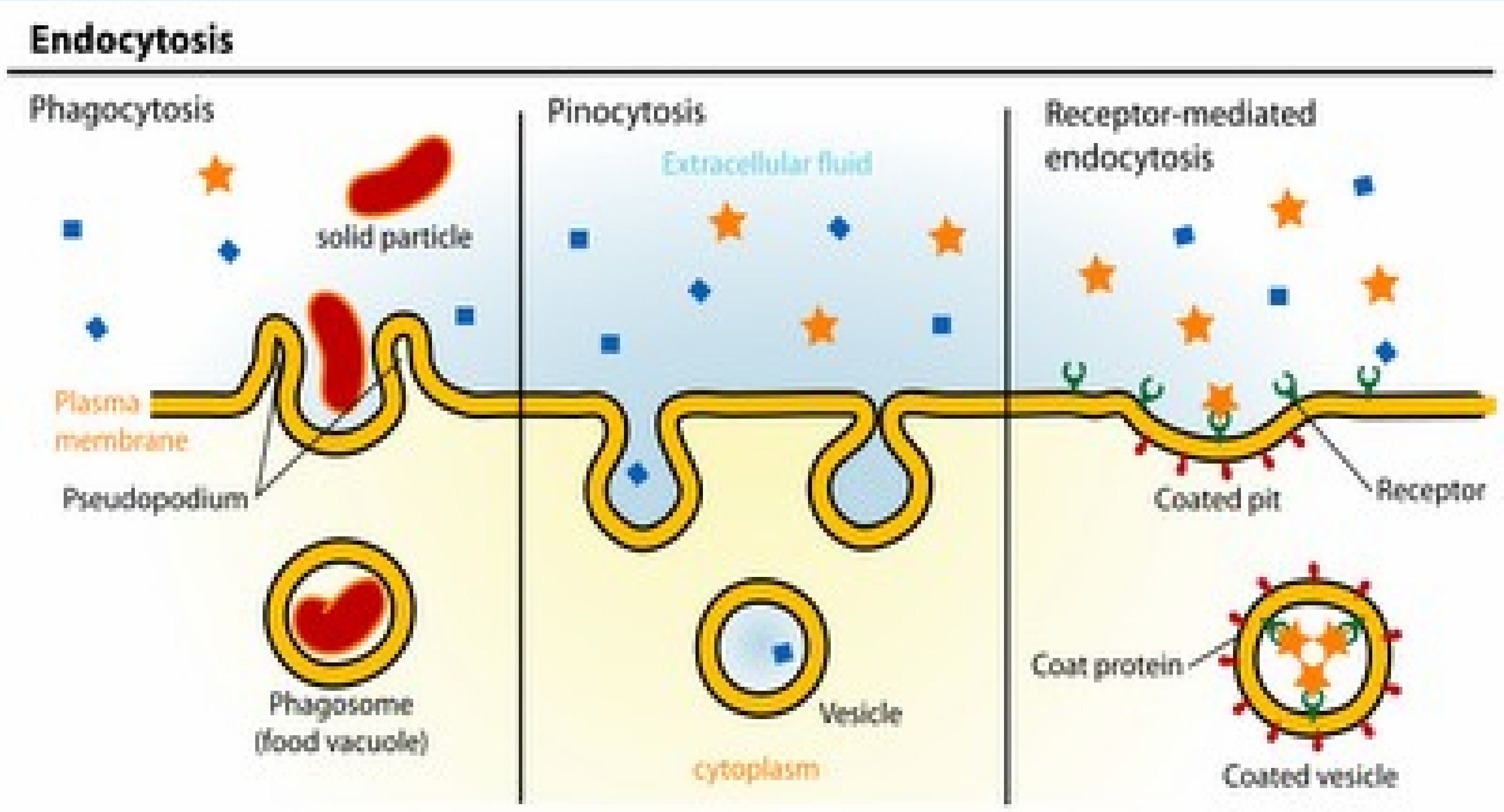

Lumen of renal tubule
Glucose
Na+
Cotransport
Epithelial cells of renal tubule
Glucose
Na+
ATP
ADP
Na+
K+
Facilitated diffusion
Na+
K+
Primary active transport
Glucose
Blood

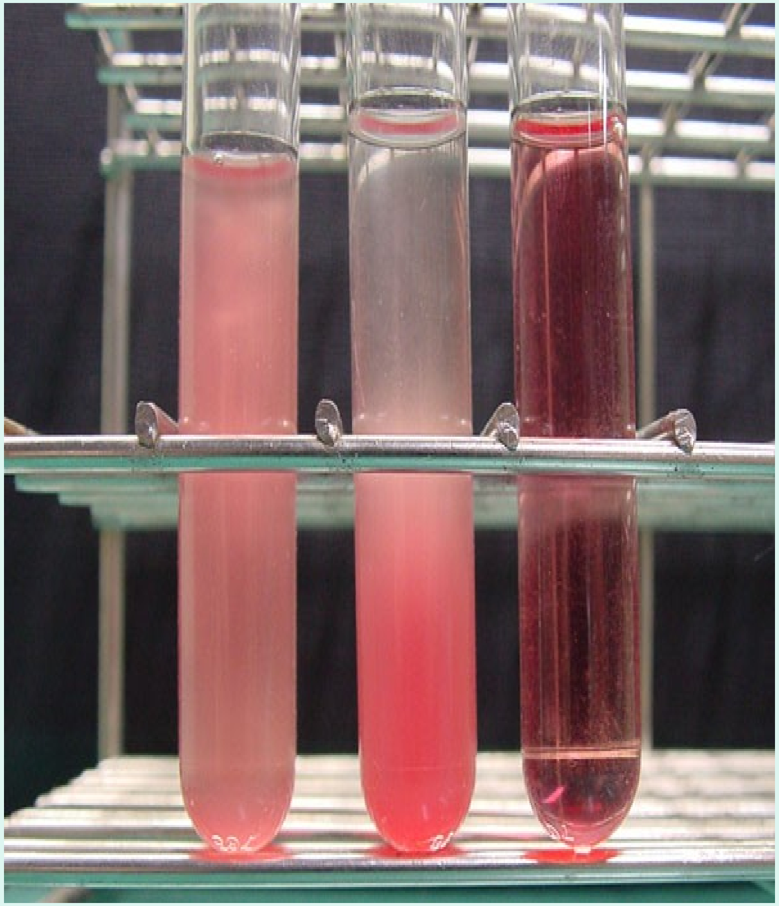
ENDOCYTOSIS-EXOCYTOSIS

- There are two major subgroups of endocytosis: (1) pinocytosis and (2) phagocytosis.
- When the matter is a small fluid droplet, the process is called pinocytosis («drinking» by the cell) and when it is cellular debris or bacteria, it is called phagocytosis («eating» by the cell).


Endocytosis
Phagocytosis
Pinocytosis
Receptor-mediated endocytosis
Extracellular fluid
solid particle
Plasma membrane
Pseudopodium
Phagosome (food vacuole)
Vesicle
cytoplasm
Coated pit
Receptor
Coat protein
Coated vesicle

OSMOSIS

- The osmosis is a phenomenon in which water flows across a biological membrane from lower concentration to higher concentration.
- Imagine that a RBC is suspended in plain water. Cell membrane of the RBC is a selectively permeable membrane. Water enters the RBC. As result, RBC swells and bursts (the so-called *hemolysis*).



OSMOTIC PRESSURE OF THE PLASMA PROTEINS

- At arterial end, fluid from the plasma leaves the capillary to enter the tissues. This fluid contains glucose, amino acids etc. At venous end fluid from the tissue carrying waste products enter the capillary. This movement of fluid is dependent primarily on two factors: (1) capillary blood pressure and (2) osmotic pressure of the plasma proteins.

PHYSIOLOGICAL SALINE

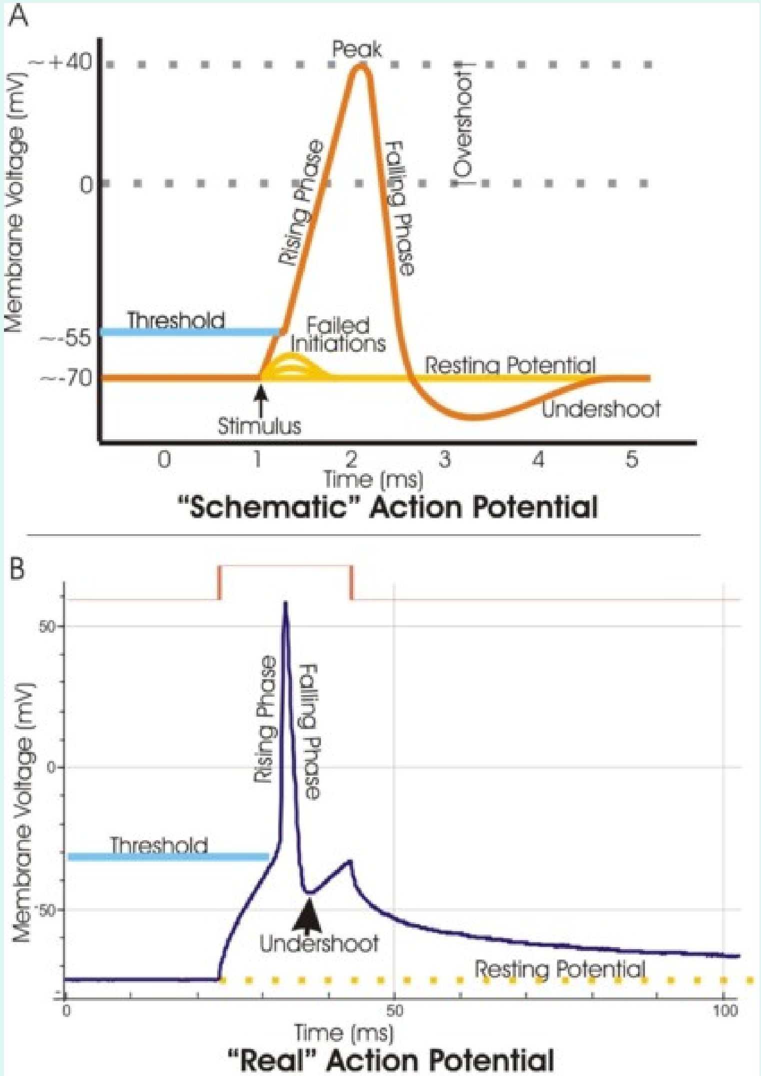
- The physiological (normal) saline contains 0.85 (or 0.9) gm of NaCl per 100 ml.
- Solutions which have weaker molar strength than normal saline are called hypotonic saline.
- Those solutions which have stronger osmolar strength than normal saline are called hypertonic saline.

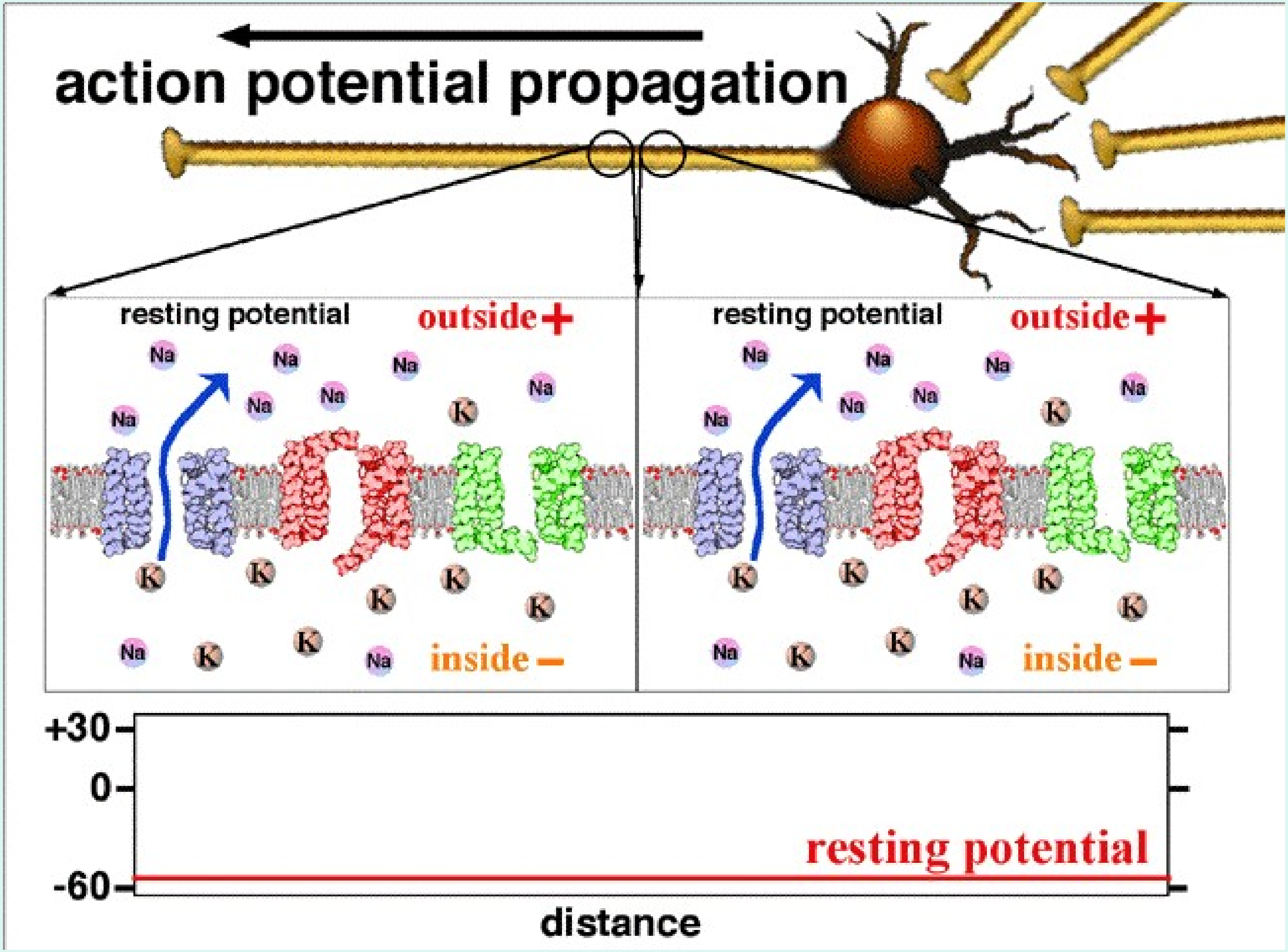
MEMBRANE POTENTIAL

Membrane potential is of two major kinds:

1) resting membrane potential (found when the cell is at rest)

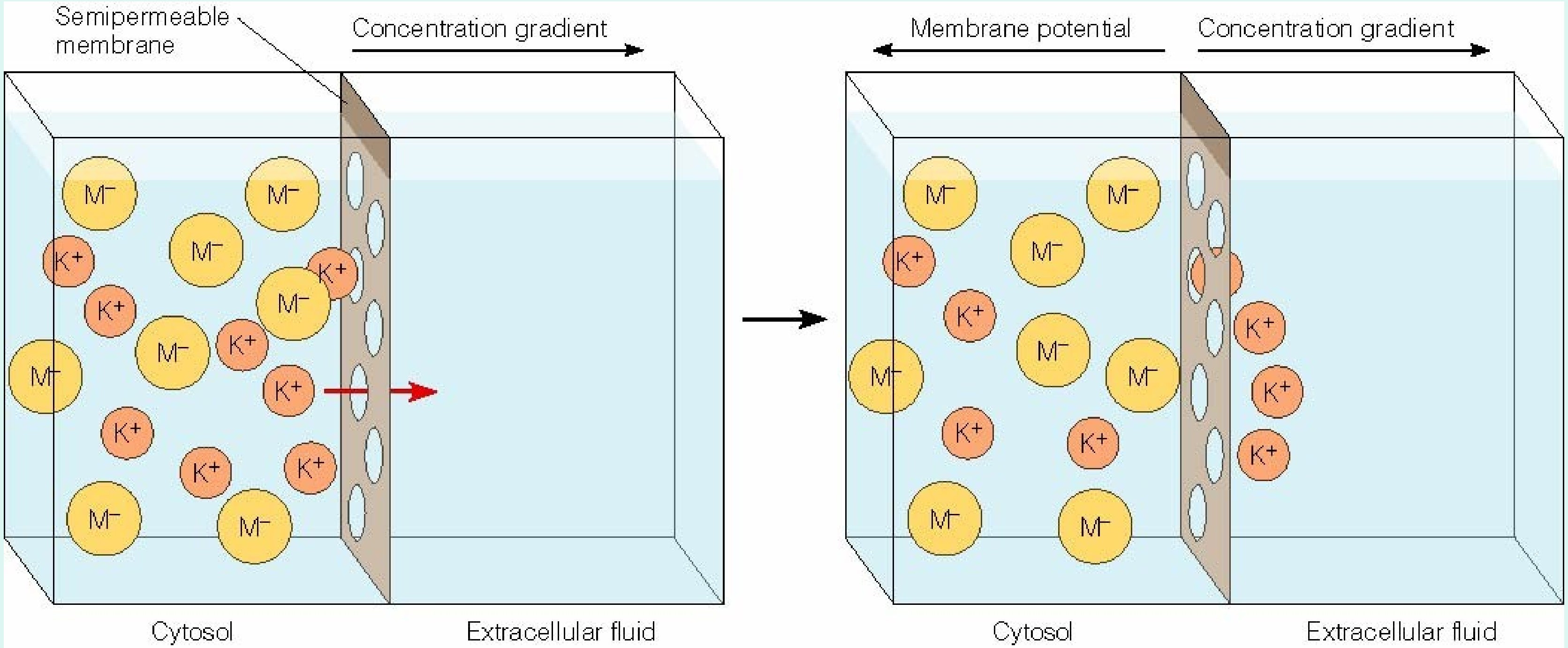
2) action potential (found when the cell is active).




action potential propagation
resting potential
outside +
Na
K
inside –
resting potential
outside +
inside –
+30
0
-60
resting potential
distance

RESTING MEMBRANE POTENTIAL

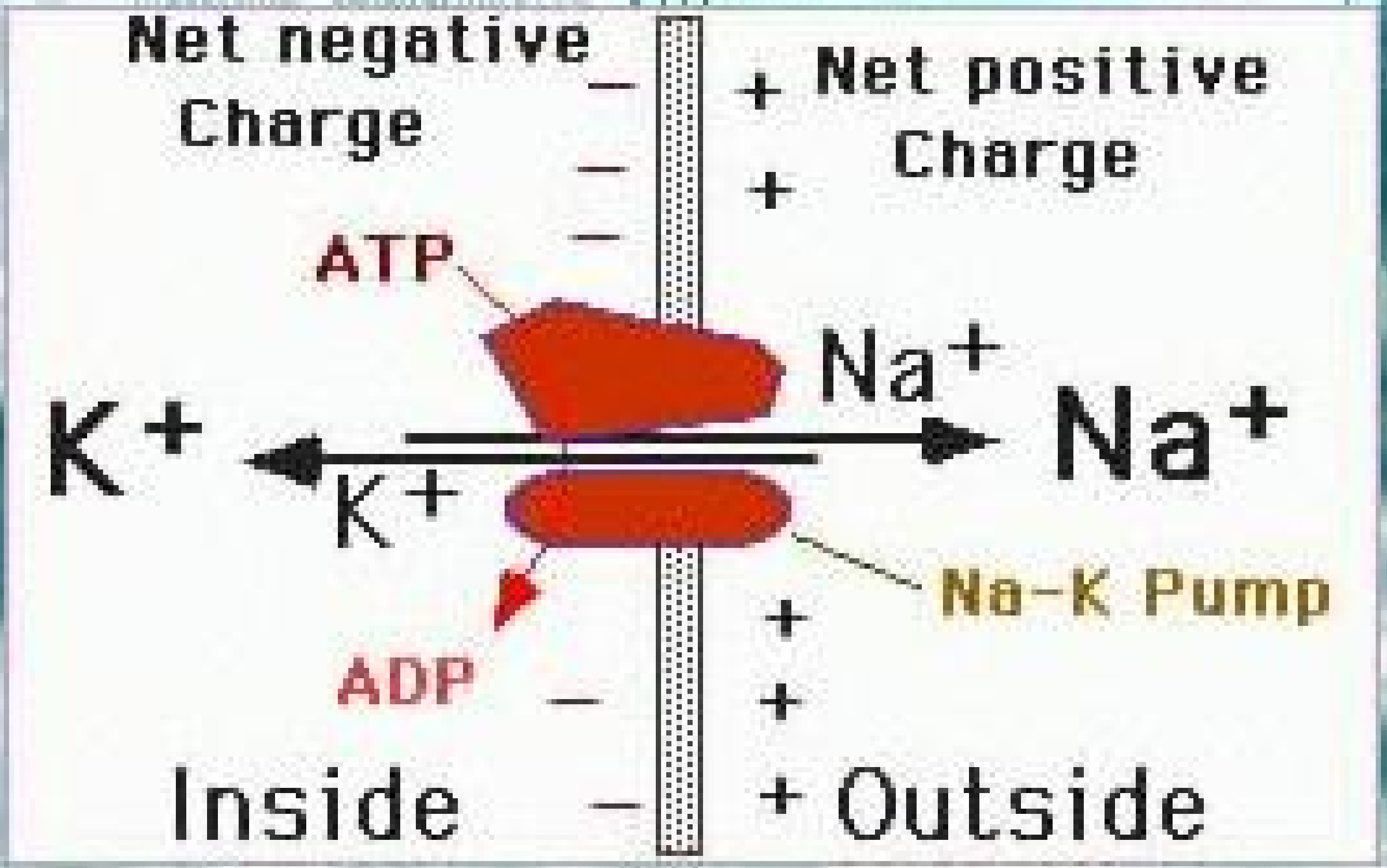
- **Both in the ICF and ECF there are plenty of ions. Normally, each cation (eg. Na, K) is matched by one anion (eg. Cl, HCO3) so that electroneutrality is maintained.**
- **While just inside the membrane, anions (negatively charged particles) are in excess.**
- **The magnitude of potential difference across the cell membrane of a resting cell, is called the "*resting membrane potential*" (RMP).**



Semipermeable membrane
Concentration gradient
M⁻
K+
Cytosol
Extracellular fluid
Membrane potential
Concentration gradient
Cytosol
Extracellular fluid

RMP

- The cell membrane at rest is permeable to K. So, K diffuses out along concentration gradient. Due to loss of positive charges, the inside of the cell becomes negative.
- The anions inside the cells are mostly large molecules like proteins, phosphates, and can not pass out.
- The chloride is permeable but can not go out against its concentration gradient, so can not influence the negativity (its permeability is also less).
- Na (the other prevalent cation) is impermeant to the cell membrane at rest, therefore the inside remains negative.


Net negative Charge
Net positive Charge
ATP
Na+
K+
Na+
K+
Na-K Pump
ADP
Inside
Outside

RMP

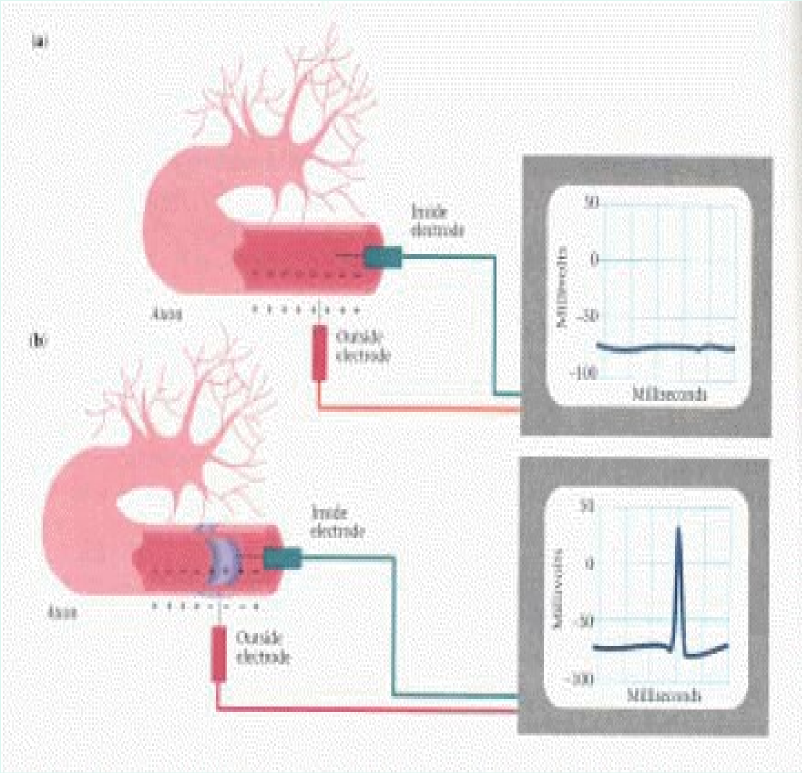
- When the number of K going out down the concentration gradient becomes equal to the number of K coming in due to electrical gradient, an equilibrium is reached.
- These ions are distribute along the membrane with the positive charges outside and the negative charges inside; while both the ECF and ICF as a whole remain electrically neutral.
- The value of RMP is in the range of -70 mV to -90 mV (the negative sign indicates the polarity of the inside of the membrane).

RMP

- Na, K, and Cl all can move across the membrane at rest but at different rates.
- K can pass easily through its leak channels which are always open. The strong and persistent tendency of K efflux makes the inside of the membrane negative.
- The tendency of Na is to enter the cell. This is firstly because the inside is negative and Na is a positive ion, secondly, the concentration of Na in ECF is many times higher than the its concentration in ICF.
- But Na can not pass through the leak channels because of its higher effective diameter along with the water molecules attached to it. The voltage-gated Na channels are also closed at rest. So, Na entry is negligible.
- Movement of Cl also occurs but it is transient and insignificant.
- When these forces are overwhelmed, the MP is reversed and action potential develops.

ACTION POTENTIAL

In resting state inside of the cell remains negative in respect to the outside, this is called *polarised state*. If this polarised state in an excitable cell like nerve or muscle is disturbed by a stimulus, then the MP changes in a specific manner due to movement of various ions leading to *depolarisation* of the cell.

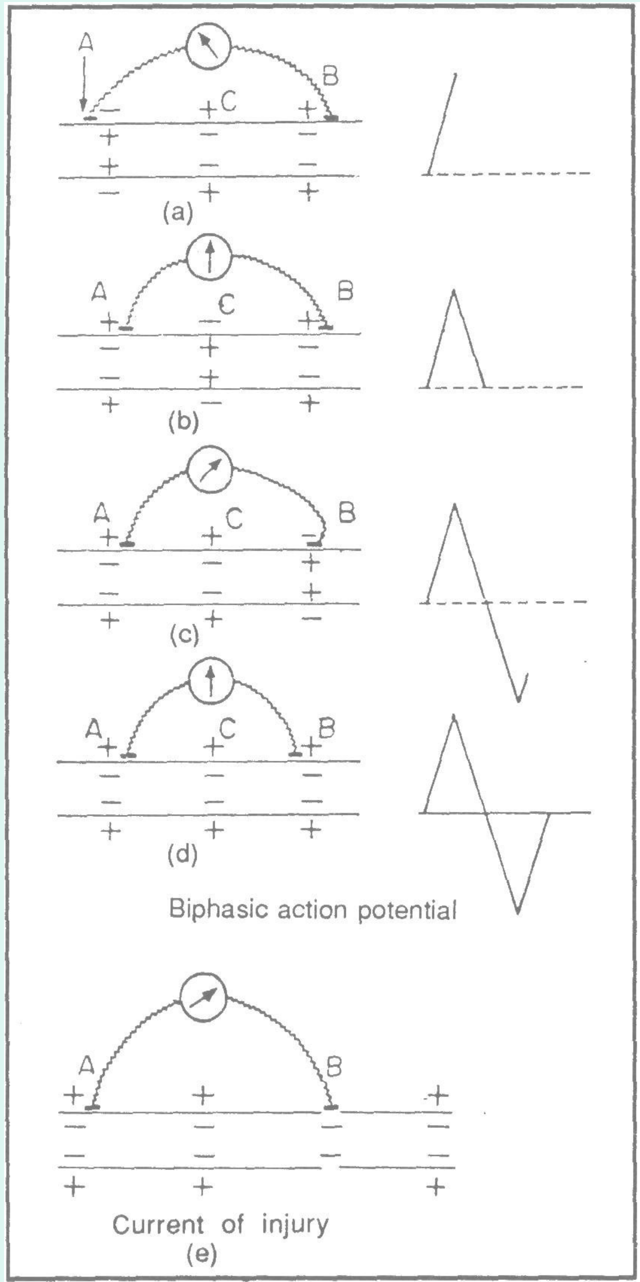


STIMULUS & THRESHOLD

- A stimulus may be physical, thermal, chemical, mechanical or electrical in nature. The stimulus which is just sufficient to produce an AP (i.e., to depolarise) an excitable cell or tissue is called a threshold stimulus.
- Stimuli stronger than this threshold stimulus is called suprathreshold and stimuli weaker than this are called subthreshold stimuli.
- A subthreshold stimulus will not be able to stimulate a tissue but a suprathreshold stimulus will of course stimulate.
- To be stimulated a more excitable tissue needs a less strong stimulus and a less excitable tissue - a stronger stimulus.

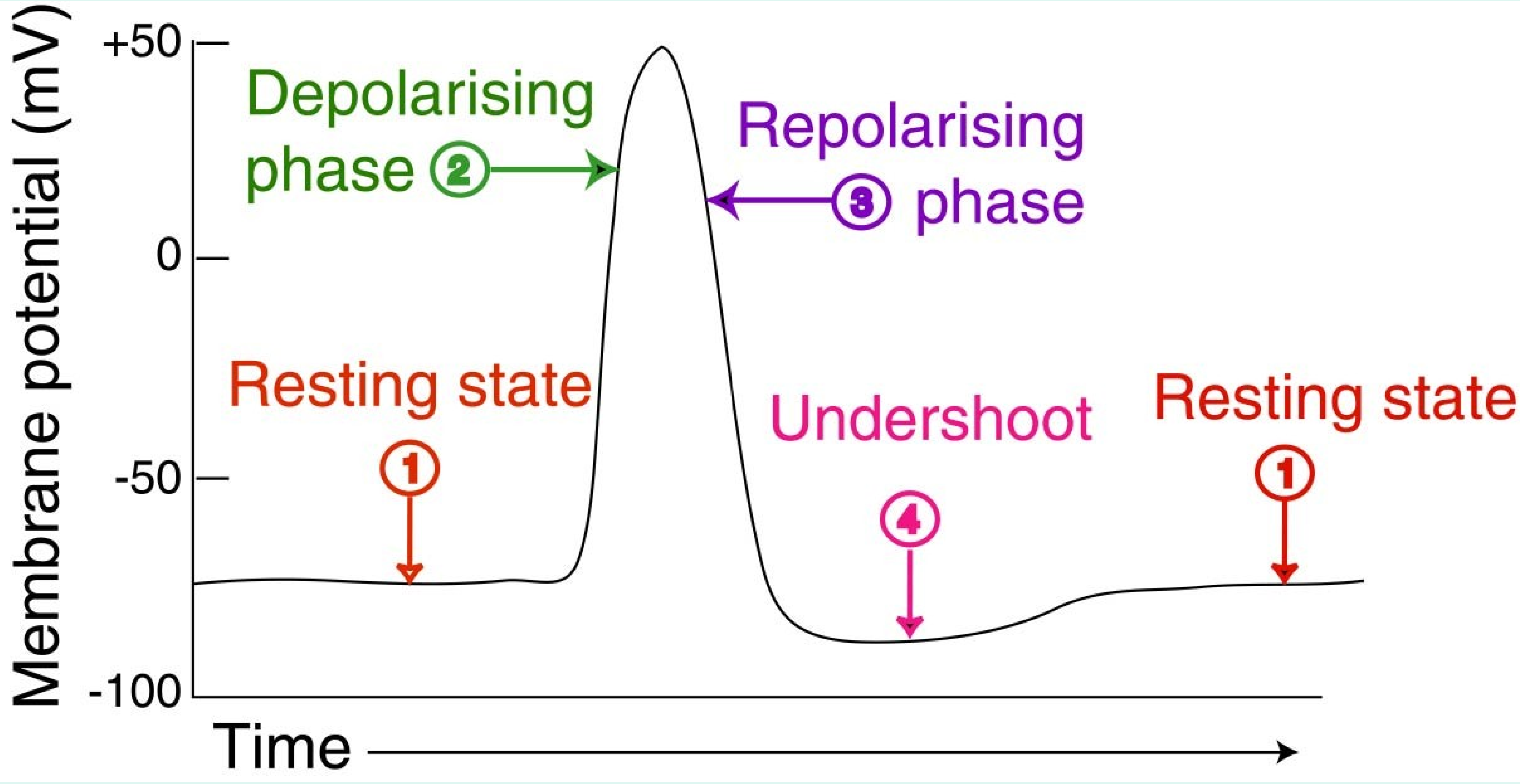
AP

- **A typical AP is seen when a nerve or a muscle fibre is stimulated by a threshold stimulus. When the stimulus is applied after some delay (latent period), there is a gradual change of MP towards "0" up to a point. This point is called firing potential (as the membrane fires at this MP).**



AP

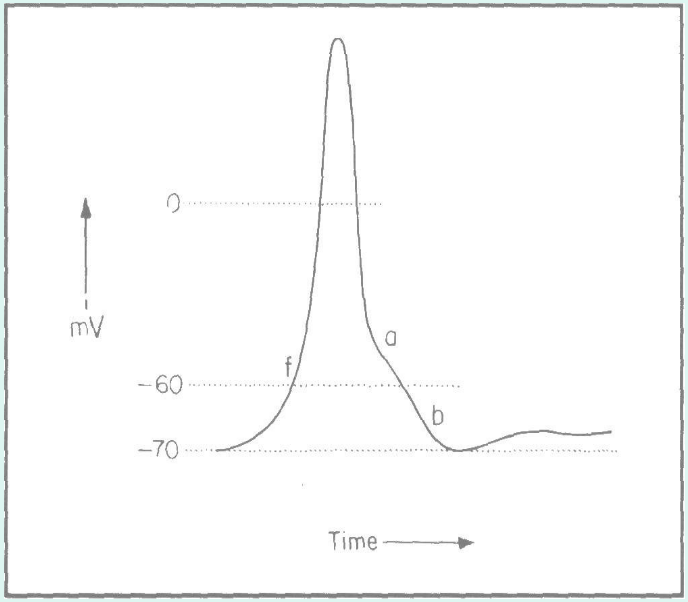
- Then a sharp change is seen and MP rapidly goes towards “0” and crosses the “0” line to become positive (+35 mV). At this point, the inside of the cell has become positive in respect to the outside. Now, the cell is said to be depolarised.
- Then the MP changes in reverse direction, towards the resting value or RMP. At first it returns very quickly - called rapid repolarisation and then slowly - called negative, after potential or after-depolarisation.

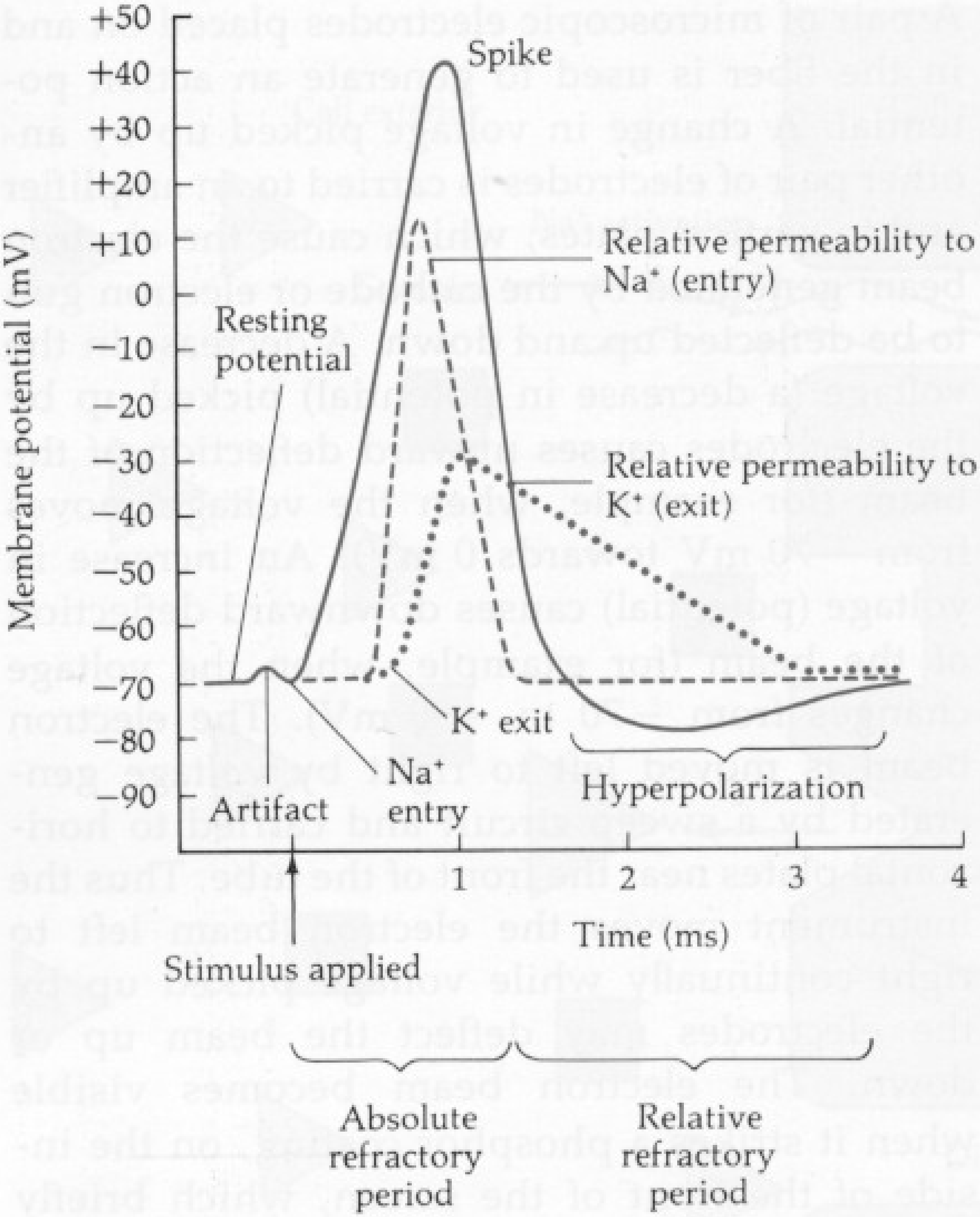


Membrane potential (mV)
+50
0
-50
-100
Depolarising phase ②
Repolarising ③ phase
Resting state ①
Undershoot ④
Resting state ①
Time

AP

- After this the MP goes below the original potential (i.e, more negative than RMP). This stage is called positive after potential or after-hyperpolarisation.
- Lastly it comes back to RMP. A pointed peak of the graph, due to depolarisation and rapid repolarisation is called spike.



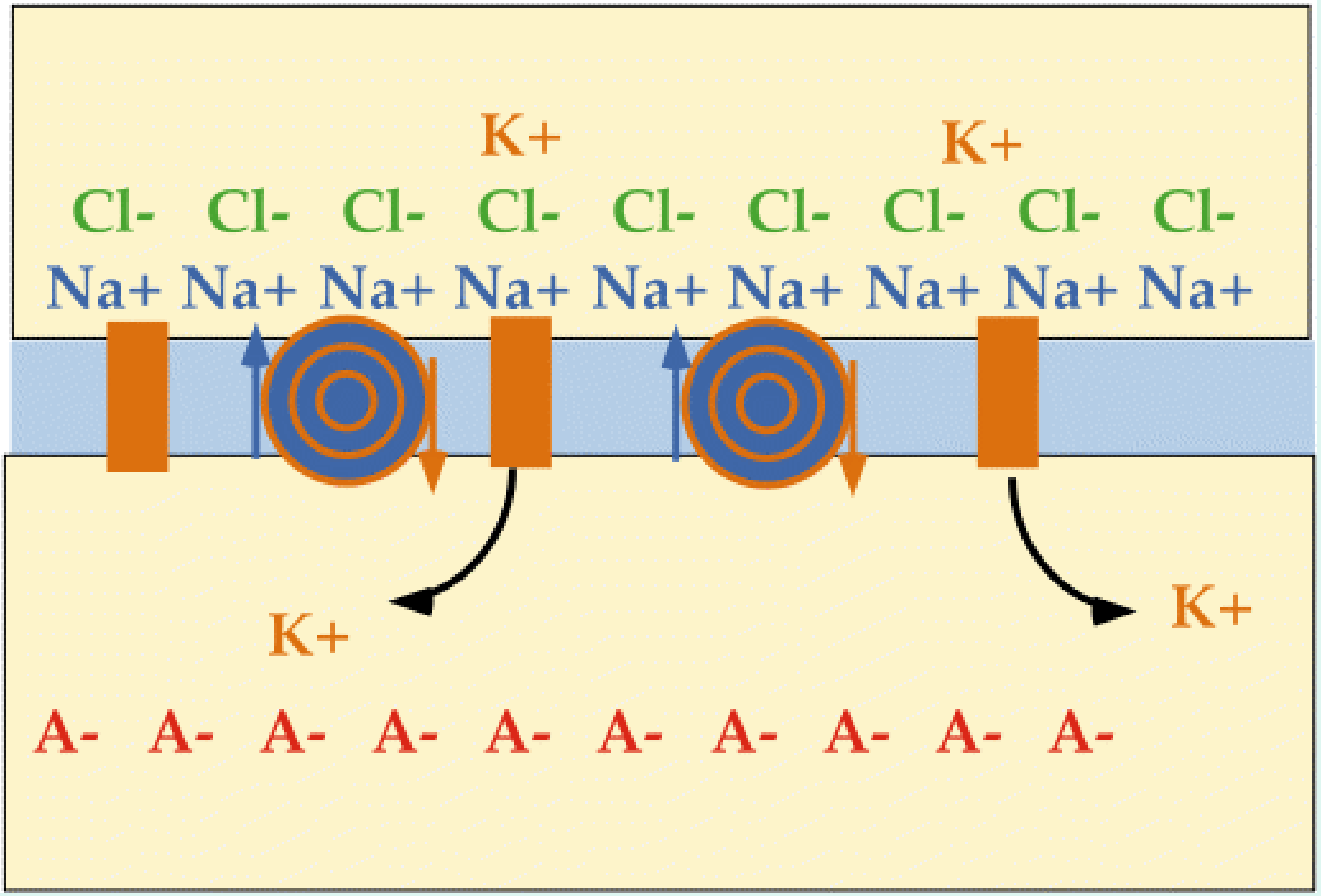


+50
+40
+30
+20
+10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
Membrane potential (mV)
Spike
Relative permeability to Na⁺ (entry)
Relative permeability to K⁺ (exit)
Resting potential
K⁺ exit
Na⁺ entry
Artifact
Hyperpolarization
1
2
3
4
Time (ms)
Stimulus applied
Absolute refractory period
Relative refractory period

AP: IONIC MECANISMS

- After the application of the stimulus, some time is required before any appreciable change occurs in the MP. This period is called *latent period* due to application of stimulus MP is lowered and Na channels (voltage-gated) in the membrane start opening.
- Na enters the cell and reduces the MP further. This lowering of MP opens up more Na channels. It continues in a positive feed back manner (i.e., more Na enters more Na channels open up) up to a point and the MP reaches a critical value - *firing potential*.
- Then there is opening of maximum number of Na channels. It leads to explosive Na entry and the rapid upshot of MP and depolarisation. So, the MP is now positive, the cell is depolarised and the cause of this depolarisation is explosive Na entry.

MEMBRANE POTENTIAL
How does it get there?
CHANNELS & PUMPS!



Neuronal Transmembrane Potentials

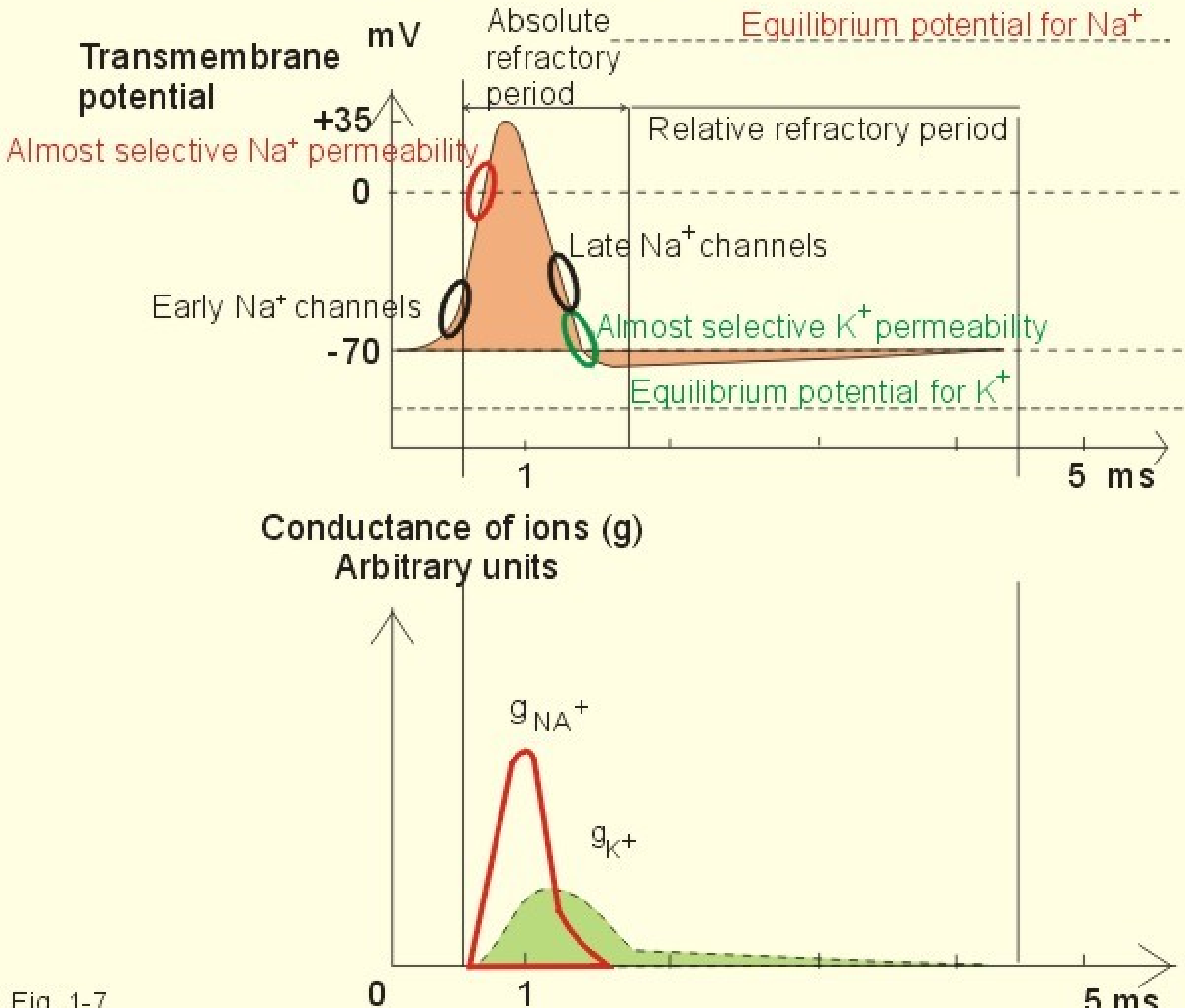
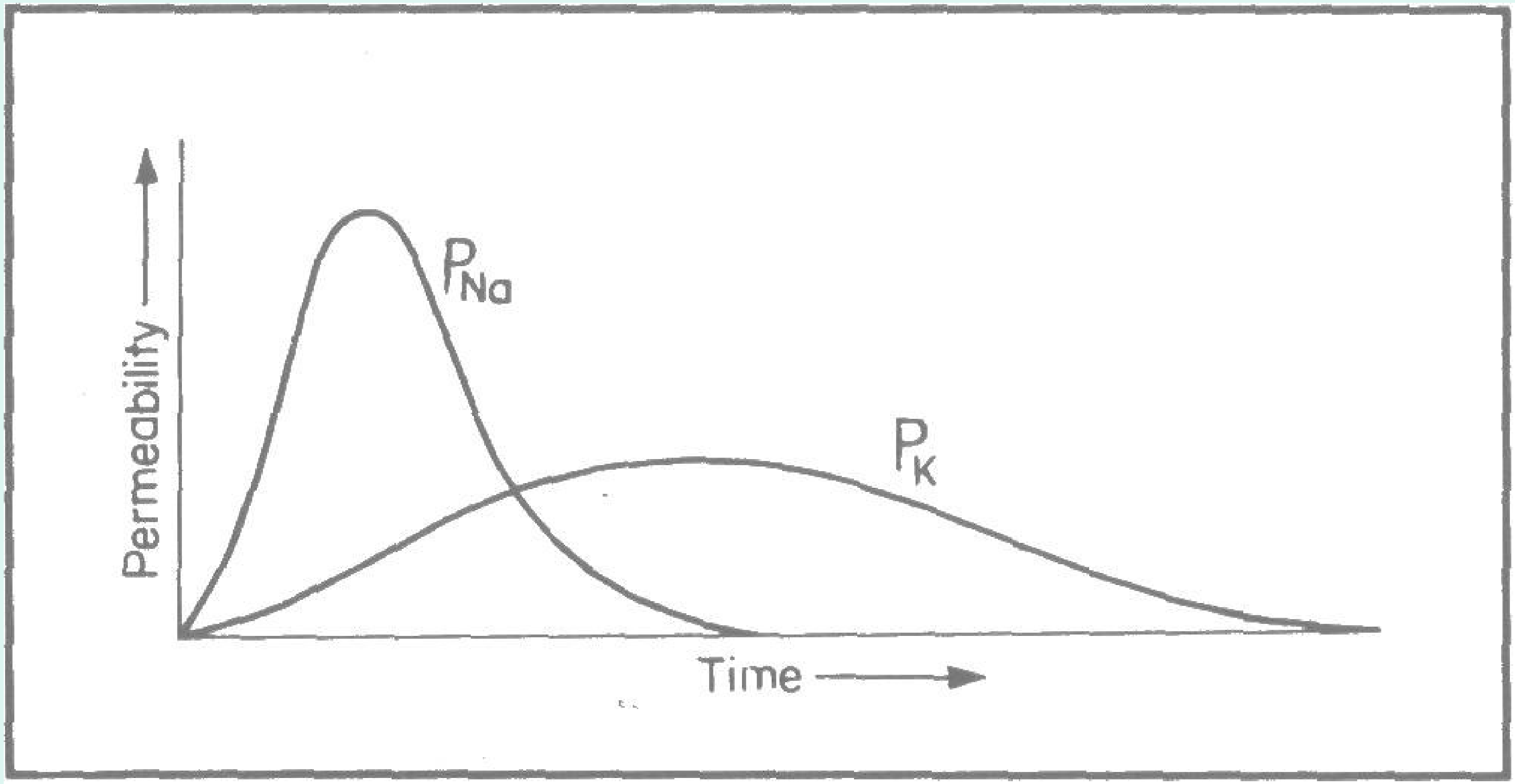


Fig. 1-7

KMc

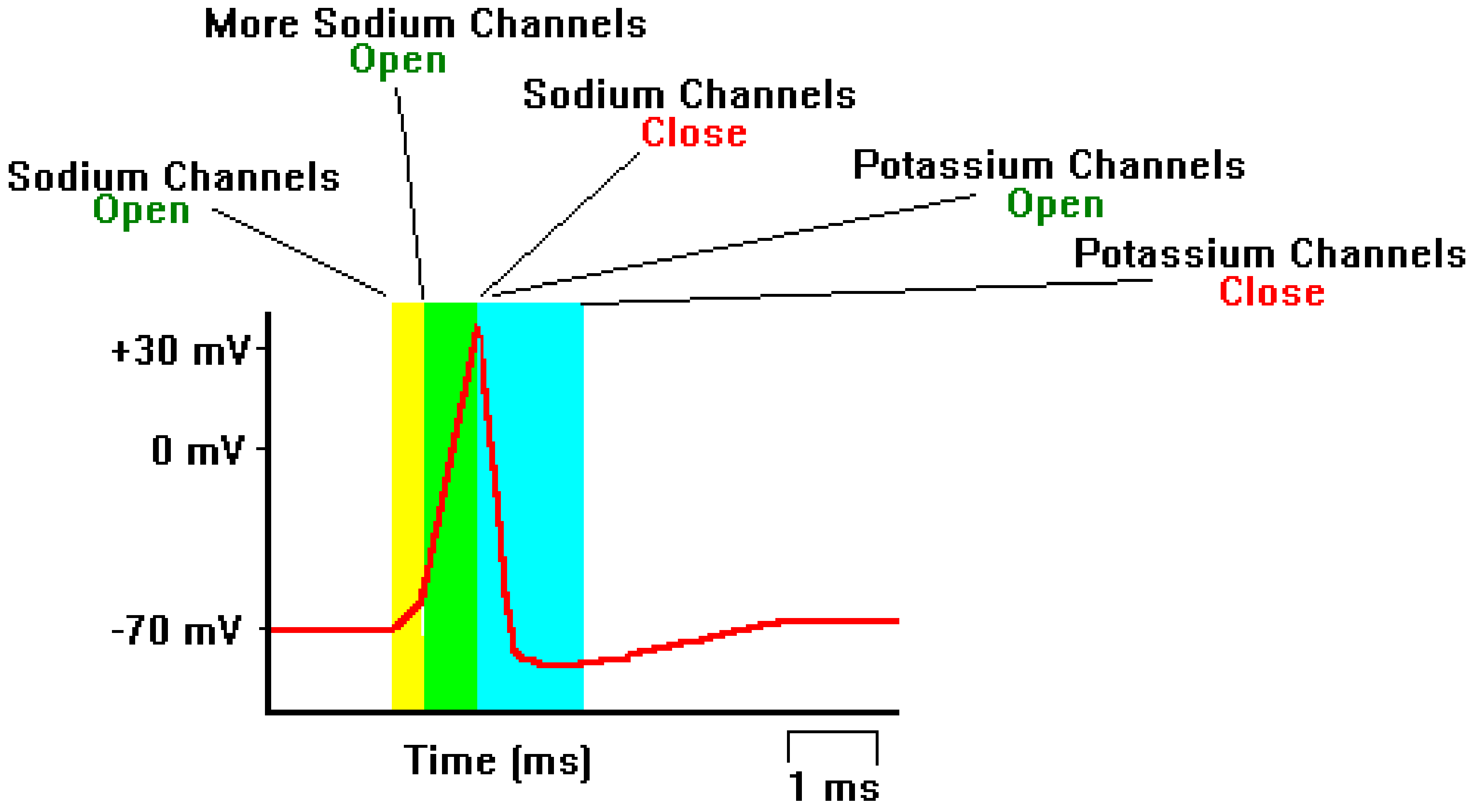
AP: IONIC MECANISMS

- Some K channels are always open, but with the start of decrease of MP, plenty of voltage-gated K channels open up and K leaks to the outside rapidly.
- This is helped by positivity of the inside and MP is rapidly restored.
- This results in rapid repolarisation and the K exit is called rectification current.


Permeability
P_{Na}
P_K
Time

AP: IONIC MECANISMS

- After this, the inside becomes negative and K efflux slows down resulting in after depolarisation.
- The process continues due to late closure of the voltage-gated K channels and there is over correction of MP; this causes the after-hyperpolarisation.
- Later on, the MP comes to the original level. Therefore, Na permeability increases first. Initially it is low but is very high after the firing potential.
- The K permeability starts increasing with the start of depolarisation but the rate is slower. It is highest during rapid repolarisation. Increased K permeability is continued for prolonged time.
- During one AP a very small number of ions changes side (the cell loses some K and gains some Na) and in a cell many action potentials can form without rest.



More Sodium Channels
Open
Sodium Channels
Close
Sodium Channels
Open
Potassium Channels
Open
Potassium Channels
Close
+30 mV
0 mV
-70 mV
Time (ms)
1 ms

Neuronal Transmembrane Potentials

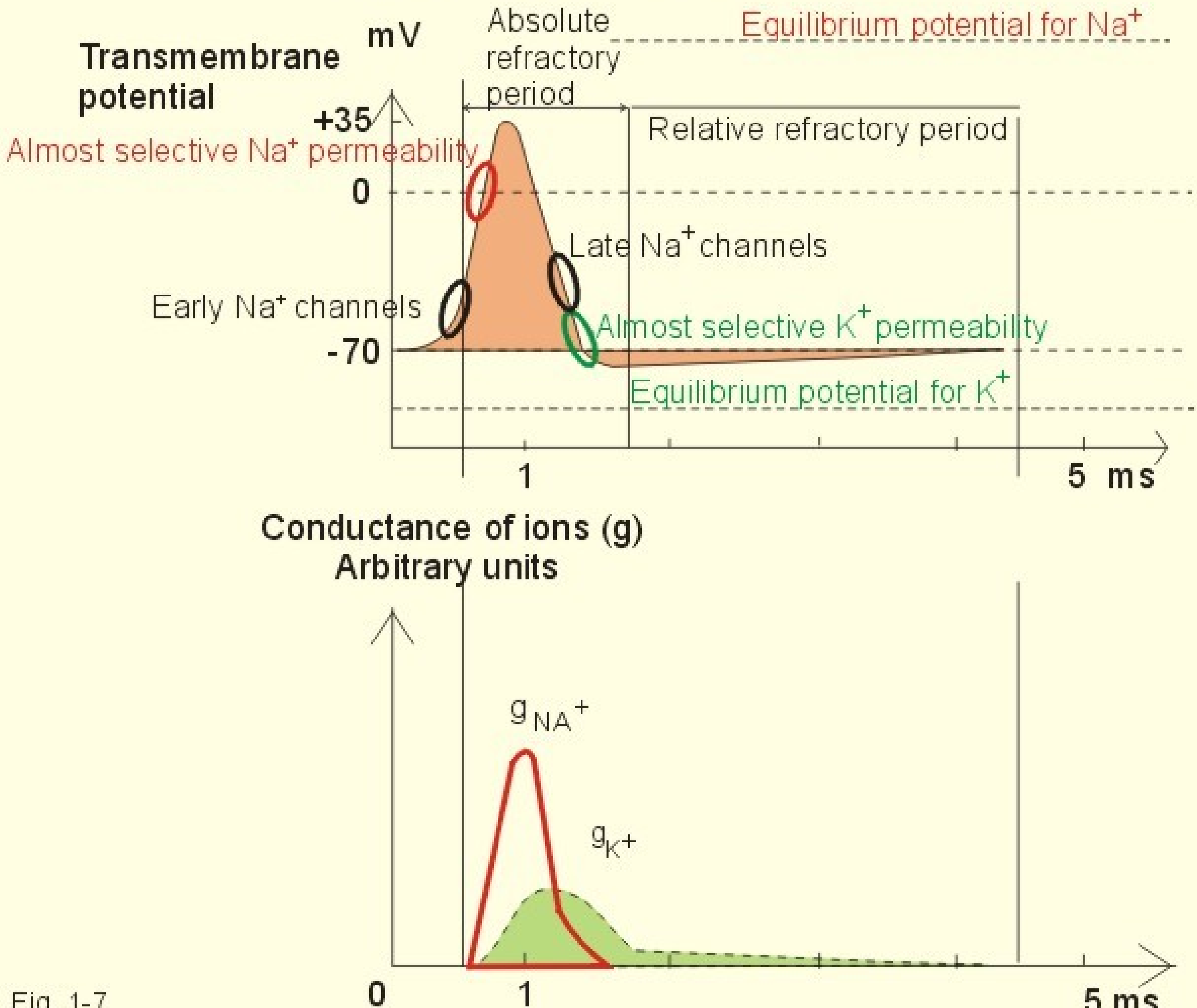
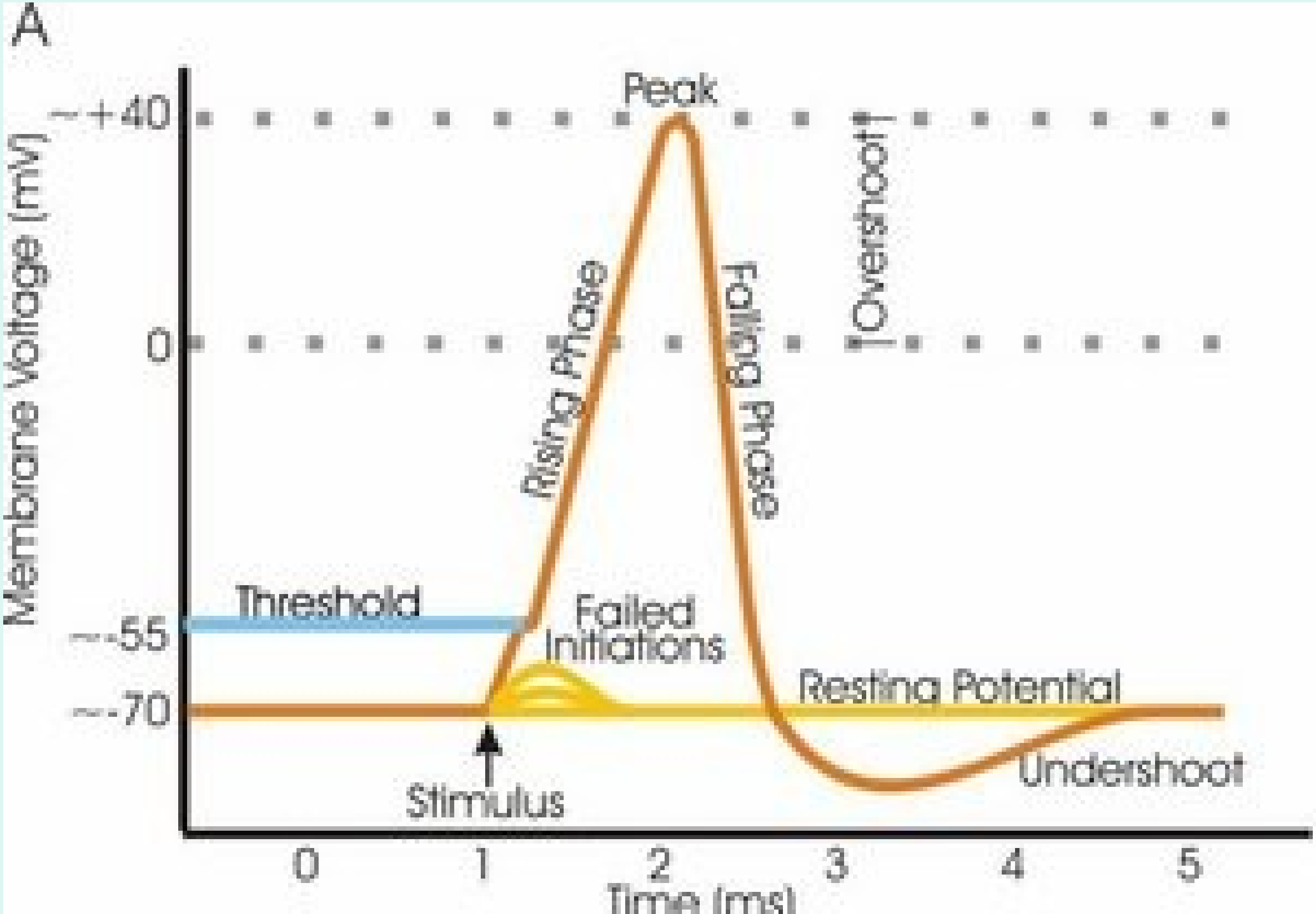


Fig. 1-7

KMc



"Schematic" Action Potential

Thank You
For Your Attention!