Cell Physiology

Prepared by

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* Historical background:

- In 1665, the term **cell** was first coined by the English man **Robert Hooke** when he saw the cells of cork.

- In 1838, an English botanist, **Robert Brown** found a small body in the cell and called it the nucleus.

- In 1840, a German zoologist, **Purkinje** gave the name the protoplasm to the cell content.

- In 1861, another German zoologist, **Max Schultz** **defined the cell** as a mass of protoplasm containing a nucleus.

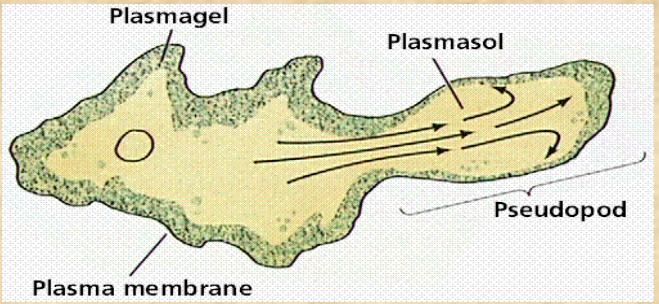
* Further development in the field of biochemistry as well as the development of a new physical and chemical techniques had allowed us to identify the ultrastructure of the cell.

The cell is:

The functional (basic) unit

Of

living matter



i.e.,

In a simple and complex living organisms, each cell can perform various attributes of life such as metabolism, growth, reproduction, reaction to stimuli,… etc.

Therefore,

if we are to understand the way that living organisms function, we must understand

CELL PHYSIOLOGY

Cellular life cycle

Cellular life cycle:

= The life cycle of a cell extends from mitosis of origin till mitosis of division.

1) May last only 10-30 hours.

Reproduction is **rather rapid** e.g., depressed cells such as cells of BM, gut epithelium and germinal layer of skin.

2) May extend for many years:

Reproduction is **slow e.g.,** cells smooth muscles.

3) May extend over the entire lifetime of the animal:

Reproduction is repressed and does not occur at all e.g., nerve cells and striated muscle cells,

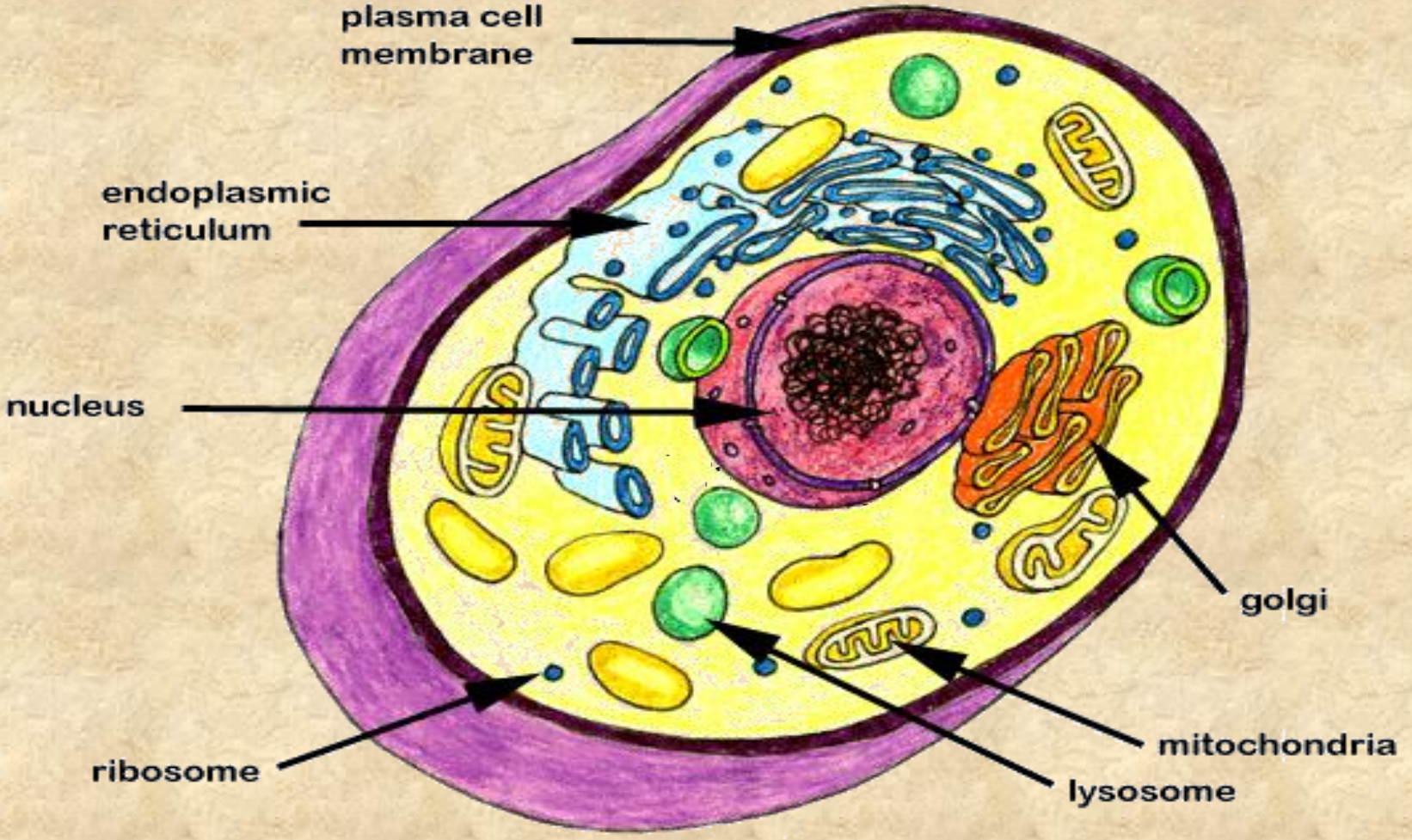
Chemical components of the cell:

Chemical analysis of the cell revealed that it is composed of a number of **different chemical substances (organic and inorganic) organized in an aqueous solution.**

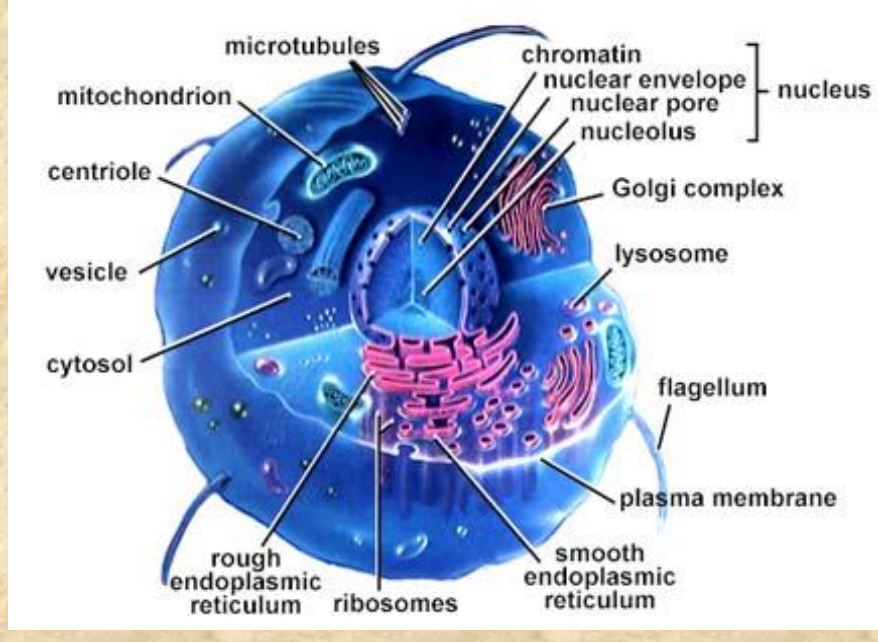
Most animal cells is composed mainly of:

- **80% water.**
- **15% protein.**
- **3% fat.**
- **1% carbohydrates**
- **while, electrolytes make up the remaining 1%.**

Cell structure



Cell structure:



A typical cell consists of :

(1) Cell membrane = Plasma membrane

= A delicate membrane , enclosing

(2) Protoplasm:

- protoplasm of the nucleus is called Nucleoplasm.
- remaining protoplasm of the cell is called cytoplasm

(3) Nucleus:

Located near the center and it is enclosed by a membrane called **nuclear mambrane.**

Components of the cytoplasm:

Within the cytoplasm we can observe several discrete objects called:

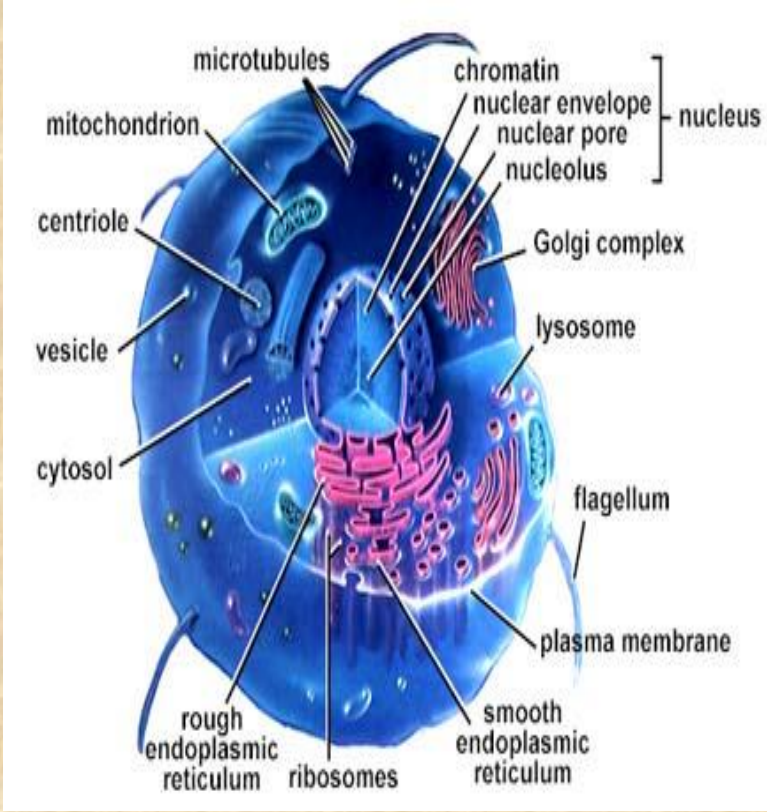
1- Cell organelles (tiny organs): e.g.,

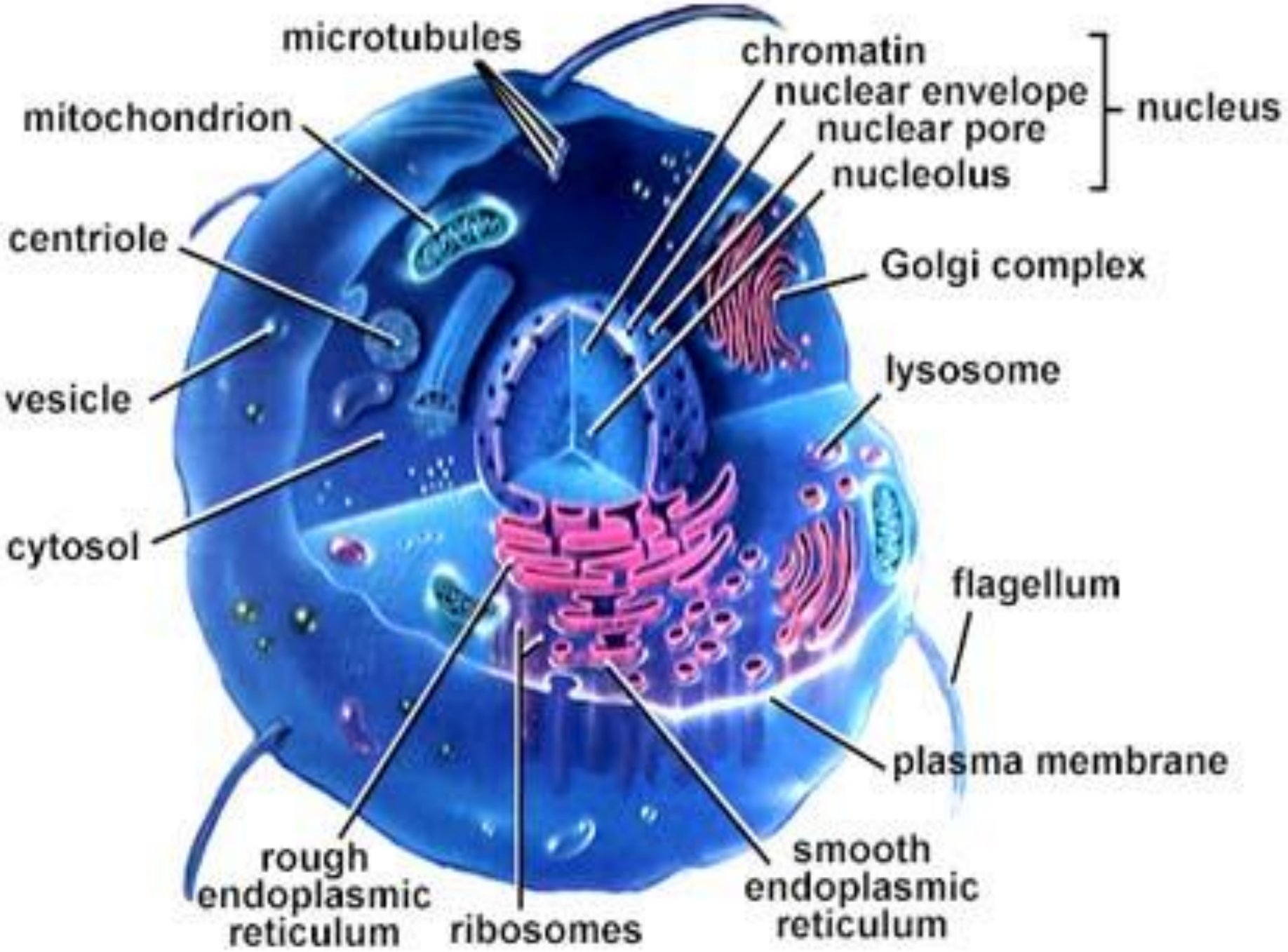
- mitochondria - lysosomes,
- endoplasmic reticulum, - Golgi complex,
- centrioles (centrosomes) - fibers.

2- Inclusions (= non living substances**)**

e.g., - proteins, - carbohydrates
- lipids - pigments
- crystals - secretory granules.

,




microtubules
mitochondrion
centriole
vesicle
cytosol
chromatin
nuclear envelope
nuclear pore
nucleolus
nucleus
Golgi complex
lysosome
flagellum
plasma membrane
rough endoplasmic reticulum
ribosomes
smooth endoplasmic reticulum

Shape of the cell:

*** Cells may shaped like rods, spiral, rectangular, spheres, ….ets.**

- **Shape of the cell is delicated by its function** i.e.,

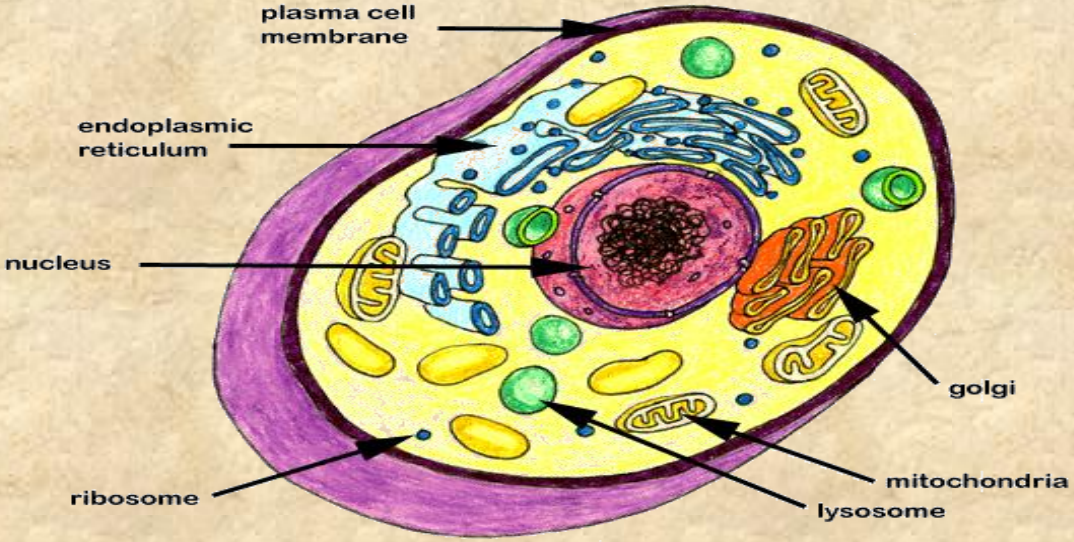
  - Human blood cells are saucer shaped and fairly flat → to permit the ready transfer of O2 and CO2

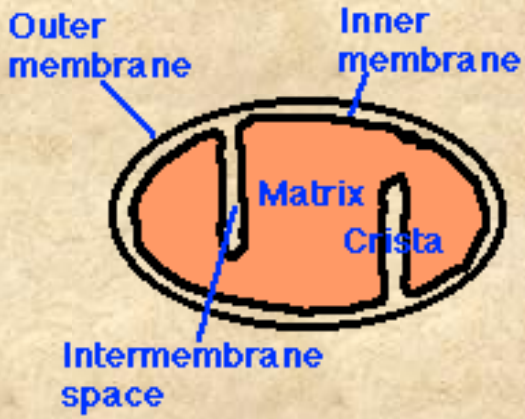
  - Nerve cells have long thin extensions → to transmit massages.

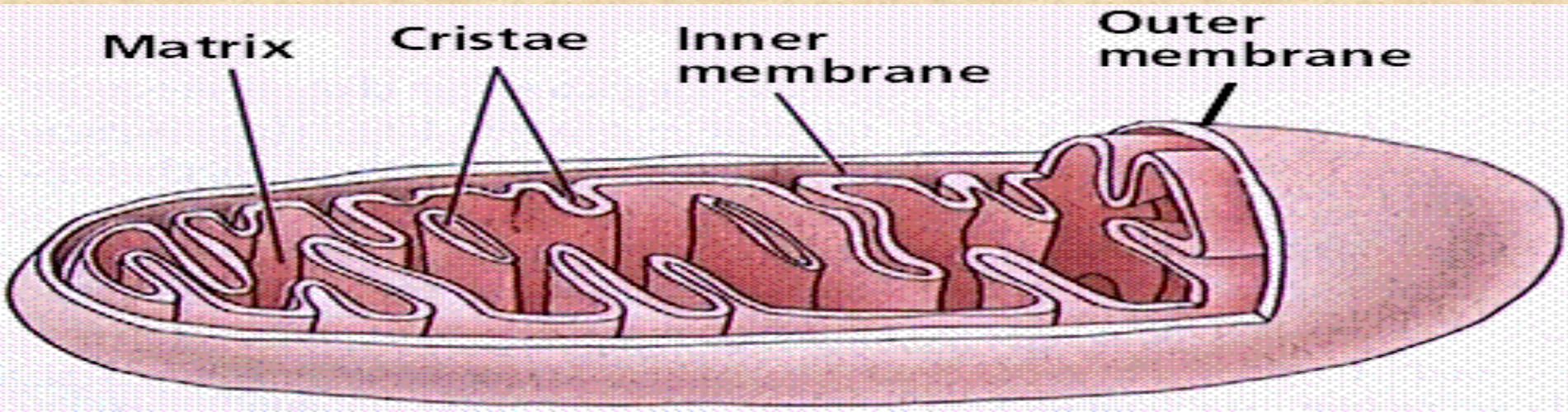
Size of the cell:

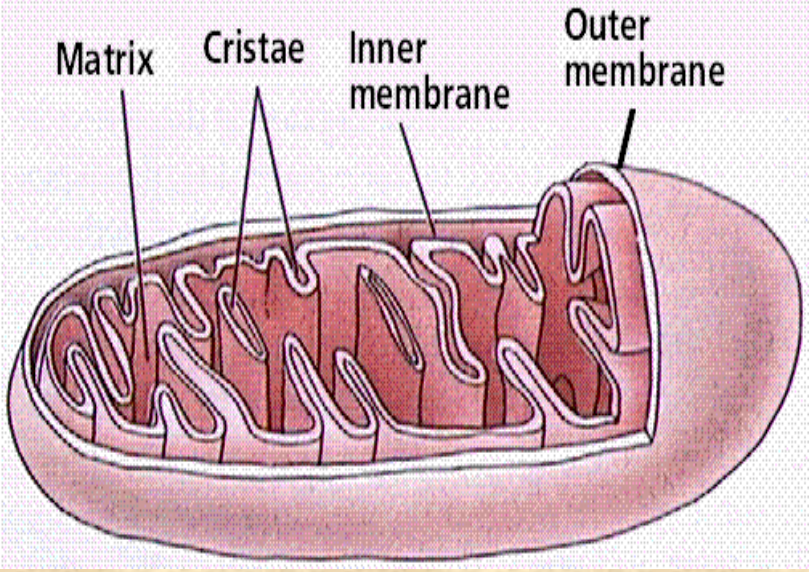
Ranges from few microns **in diameter to that of an ostrich egg** (which may reach the size of an orange)

Mitochondria (Mitochondrion)


plasma cell membrane
endoplasmic reticulum
nucleus
golgi
ribosome
mitochondria
lysosome


Outer membrane
Inner membrane
Matrix
Crista
Intermembrane space


Matrix
Cristae
Inner membrane
Outer membrane



Structure of mitochondria:

(A) Two (lipid bilayer-protein) membranes:

1- An outer membrane:

- Smooth
- Enclosing an intracristeal space that is filled with enzymes and raw material for mitochondrial reaction.

2) An inner mmebrane:

- Highly folded to form shelves (cristae) onto which oxidative enzymes are attached e.g., NADH dehydrogenase, succinate dehydrogenase, cytochrome c reductase, cytochrome c oxidase and ATP synthase

(B) Inner cavity:

- Filled with matrix containing large amounts of dissolved enzymes which are necessary for extracting energy from nutrient e.g., **enzymes of the citric acid cycle, fatty acid oxidation and mitochondrial nucleic acids.**

Size and shape of mitochondrion:

- Varies from:

few hundred nanometer in diameter and globular shape

to

large as 1-7 micrometer in diameter and filamentous shape.

Number of mitochondria/cell:

- Varies from less than 100 up to several thousands.
- Depending on the amount of energy required by the cell.

Therefore,

Heart, muscle and liver cells contain numerous number of mitochondria.

Distribution within the cell:

Mitochondria tend to migrate to move like amoebae (contract and relax) to be concentrated at portions of cells where the metabolic processes and energy production are high.

Function of mitochondria:

Power house of the cell i.e.,

- Oxidation of nutrients forming CO_2, H_2O and Energy.

- The liberated E is used to synthesizes a high energy substance called Adenosine triphosphate (ATP) which is then available to

power cellular functions

Mitochondrial replication:

Self replicative = one mitochondrion can form a second one, a third one and so on whenever there is a need in the cell for increased amounts of ATP.

This process depends on:

1) Mitochondrial DNA:
   - double stranded and circular
   - plays a role similar to DNA of the nucleus but with a specific genetic code
2) Mitochondrial RNA (ribosomal, messenger and transfer) but each is specific to the mitochondria.
3) proteins and lipids of mitochondria and cytoplasm:
   which are incorporated into mitochondria as they enlarge and bud off to form new mitochondrion.

N.B: Some protein synthesis occurs in the mitochondria on mitochondrial ribosomes that are different than cytoplasmic ribosomes. Other mitochondrial proteins are made on cytoplasmic ribosomes

Endoplasmic reticulum

Endoplasmic reticulum:

= Network of tubular and vesicular structures interconnected with each other.

Formed of:

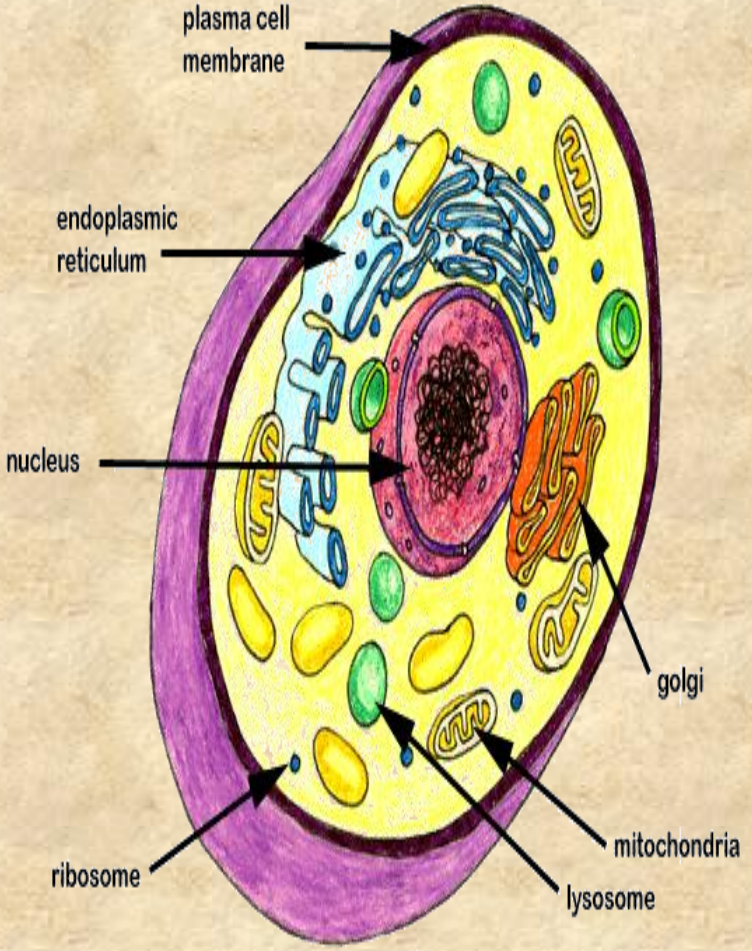
Lipid- protein membranes similar in structure to the cell membrane and continuous with it

- Various substances can move from cell membrane via these tubules to the nucleus.

Types:

1- Rough endoplasmic reticulum:

2- Smooth endoplasmic reticulum:



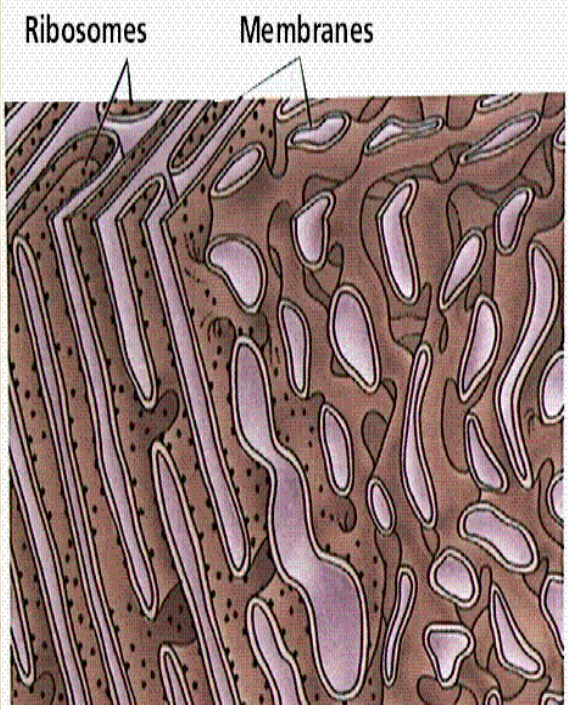
Rough endoplasmic reticulum:

Function:

Protein synthesis? Their outer surfaces are studied with granules of RNA (called Ribosomes) which play a major role in protein synthesis e.g., hormones, enzymes, antibodies

NB:

Rough ER is connected to the nuclear envelope through which the messenger RNA (mRNA) travels to the ribosomes



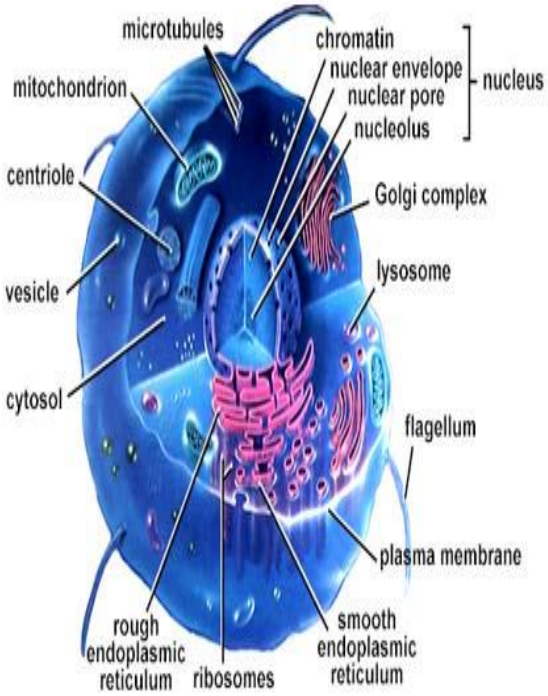
Smooth (Agranular) endoplasmic reticulum:

Function:

1- Synthesis of steroid and phospholipids.

2- Metabolism and detoxification of substances in the liver.

3- Excitation-contraction coupling in skeletal muscle.



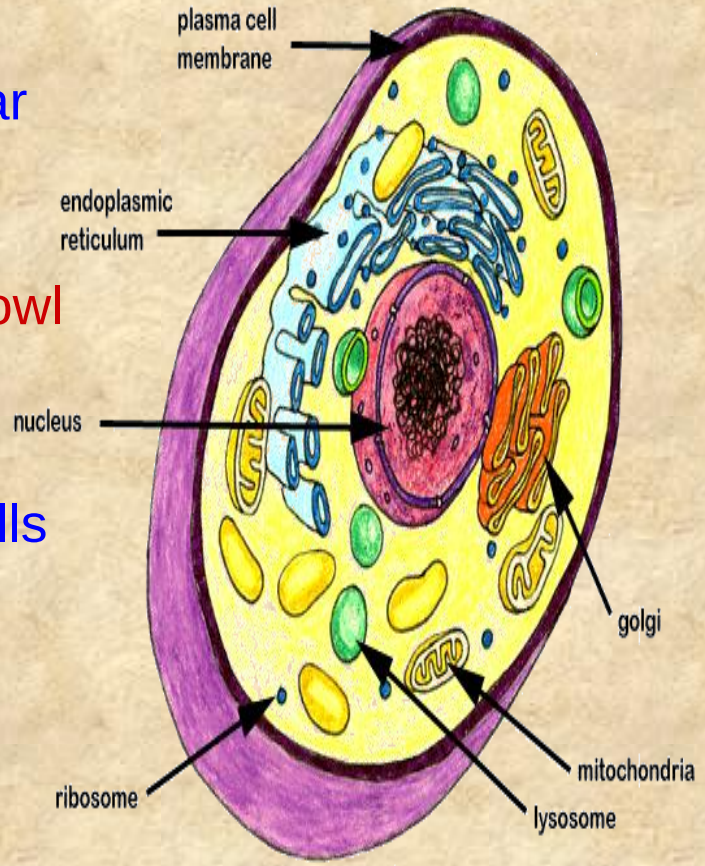
Golgi complex

Golgi apparatus (GA):

= Rows of flattened sacs, usually present near the nucleus.

- GA was first seen by the Italian anatomist; Camillo Golgi (1983), in the brain cells of owl and later in the nerve cells of cat.

- It is always very prominent in secretory cells e.g., cells of sweet glands or endocrine glands.



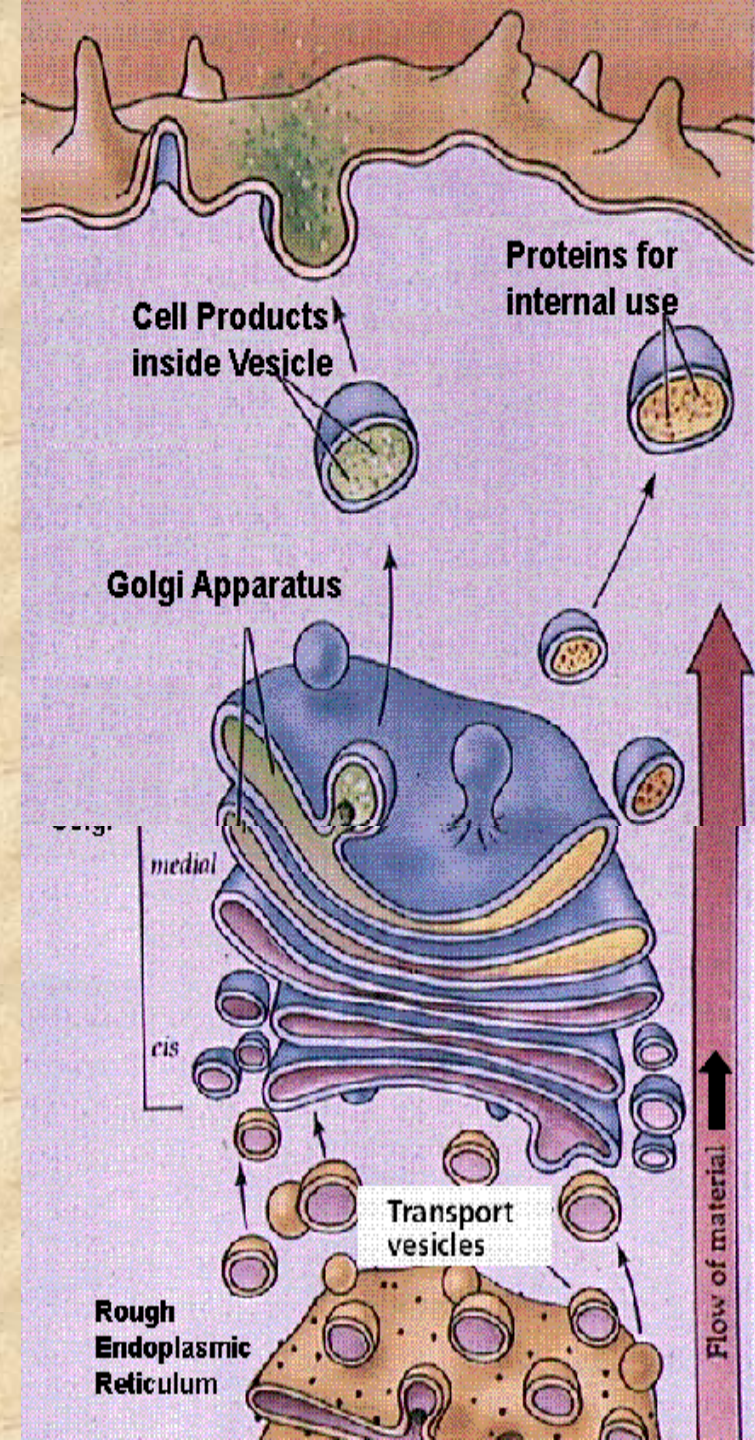
Function of GA:

1- Package, concentration and storage of secretory products from rough ER:

Proteins made within the rough ER→ bud off in transport vesicles → fuse with the membrane of GA → components of the vesicles are further modified, concentrated and packaged → by the time they bud off as vesicles on the opposite side of the GA.

2- Participates in production of hydrolytic enzymes for lysosomes.

3- Site of glycoprotein (CHO+Protein) synthesis



Lysosomes

= Large (0.05 to 0.5 micron) , irregular membrane bound vesicles containing more than 40 hydrolytic enzymes.

- **Lysosomal enzymes:**

= synthesized on the rough ER → transferred to the Golgi for modification and packaging → segregate to form lysosomes.

- e.g.

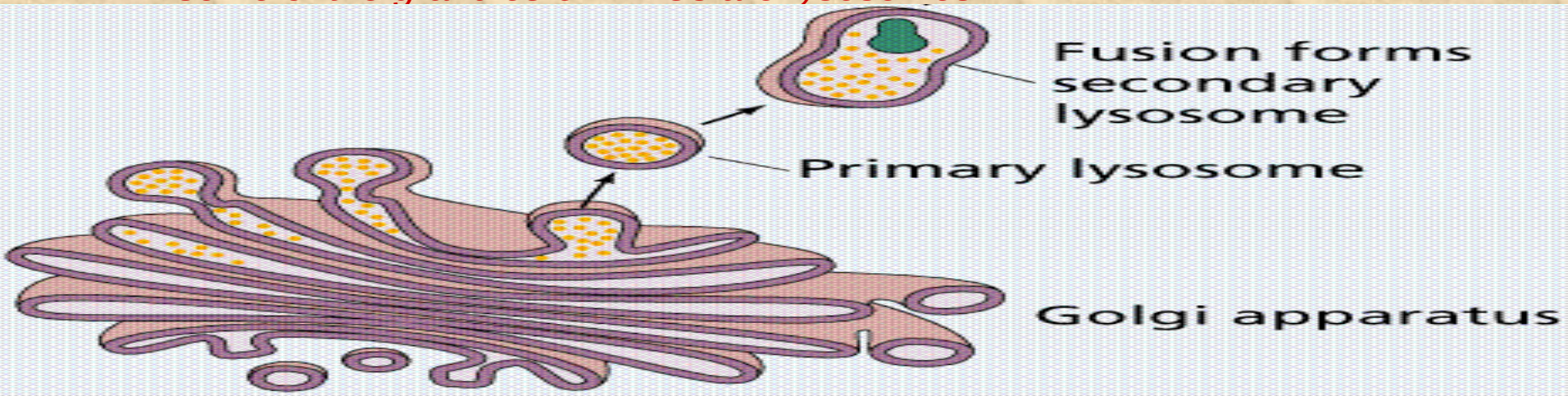
,- acid phosphatase - ribonuclease, deoxyribonuclease,
- proteases - lipases - sulfatases

- These enzymes function optimally at pH 5 and are mostly inactive at the pH of the cytosol (7.2).

- **Limiting membrane:**

keeps the digestive enzymes separate from the cytoplasm → protects the cell from digesting itself.

N.B: some of the granules of WBCs are lysosomes.



Function of lysosomes:

Digestive system of the cell?

more numerous in cells performing phagocytosis.

1- Digestion of large particles that enter the cell:

Exogenous substances e.g., bacteria

↓

engulfed by the cell

↓

a membrane-limited vacuole (phagosome=phagocytic vacuole).

↓

come into contact with lysosomal membane and fuse with each other forming one body

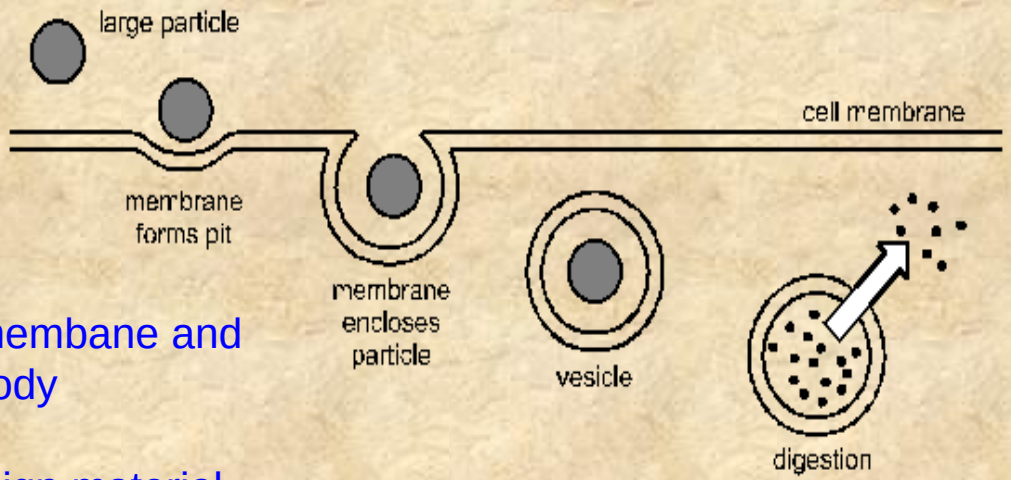
↓

The lysosomal enzymes digest foreign material

↓

end products of digestion

1) Diffuse out of the vacuole into the cytoplasm (warm-out product),
2) while the remaining indigestible residue is eliminated by exocytosis.



2- Digestion of warm-out product:

lysosomes also engulf warm-out products forming autophagic vacuoles.

3- Digestion of cell itself (autolysis):

- **When a cell die:** lysosome membrane ruptures→ lysosomal enzymes become free within the cell and cause autolysis
- **In multicellular animal,** many cells constantly form, live for short period of time and then die e.g., liver cells. Therefore, autolysis is an efficient method of riding the body of debris.

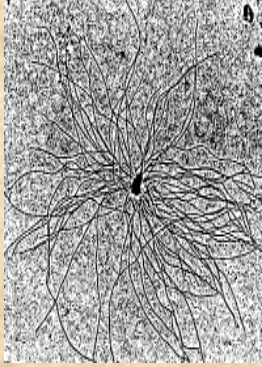
4- Digestion of substances external to the cell:

= exocytosis of a pocket of enzymes is released from a lysosomes outside the cell to destroy the surrounding structures e.g.,

* Fertilization: sperm penetrate the protective coat of the ovum

* Osteolysis: osteoclast cells destroy bone

Centrosome:



= Condensed protein of cytoplasm, which is usually attached to the outside of the nucleus.

- By Ordinary microdcope:

Usually the centrosome is **inconspicuous** in cells except during **cell division**

- By electron microscope:

C**entrosome appears to be made up of two short cylindrical structures called centrioles** arranged at right angle to each other.

Function:

1- During mitosis:

the two centrioles moves to opposite poles of the cell to become organizing centers for the mitotic spindle, which is made of microtubules.

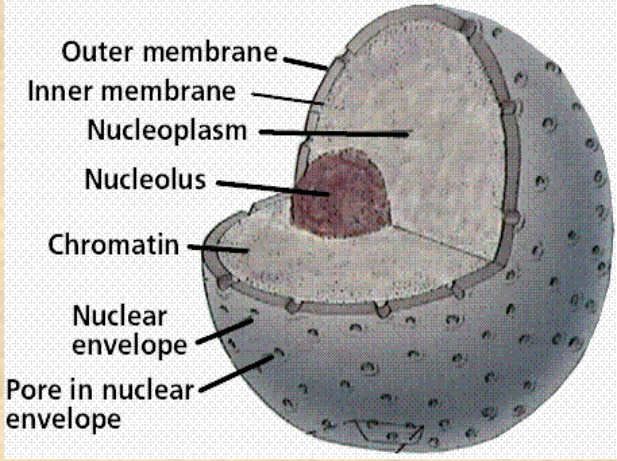
2- During spermiogenesis:

Centriole, lie just posterior to the nucleus, divided into two centrioles (proximal and distal). The distal centriole develops to form axial filament of the tail.

NB: ***In certain types of cells e.g., Nerve cells there is no centriole and so they do not divide.***

Nucleus

Nucleus



= Spherical, sometimes elongated structure surrounded by nuclear envelope (nuclear membrane)

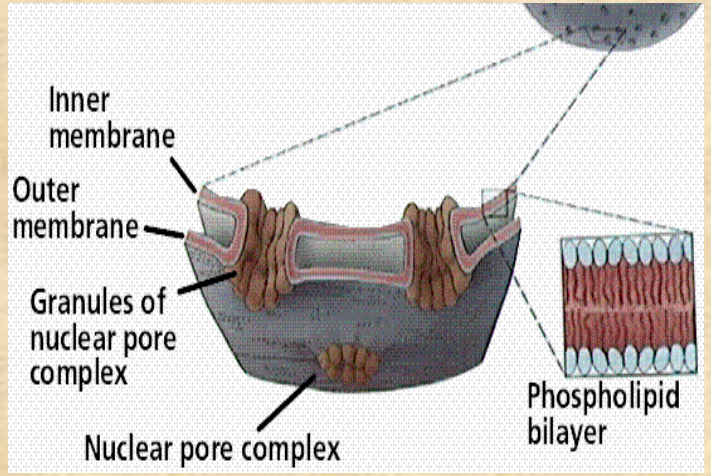
Nuclear membrane:

- nearly similar in structure to plasma membrane

- contains numerous pores for the transport of large macromolecules and ribosomal subunits to the cytoplasm

- is often attached with ribosomes at the outside membrane

- is sometimes continuous with the rough ER.



Function of nucleus:

Contains the genetic material; **Chromatin**

Chromatin:

= coiled DNA bound to basic proteins called histones and some less well defined non-histone proteins

Membranous structures of the cell

Membranous structures of the cell

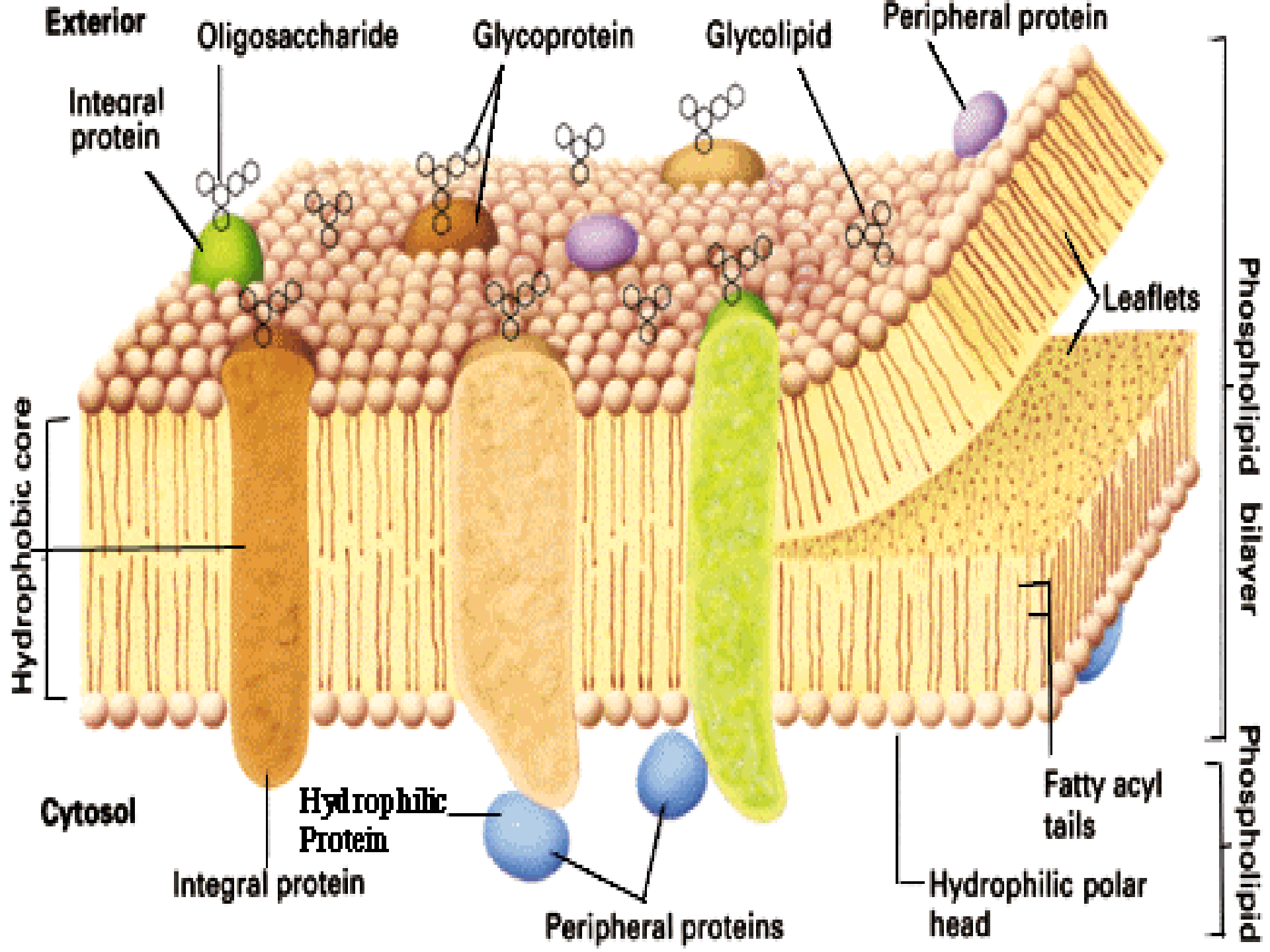
Include:

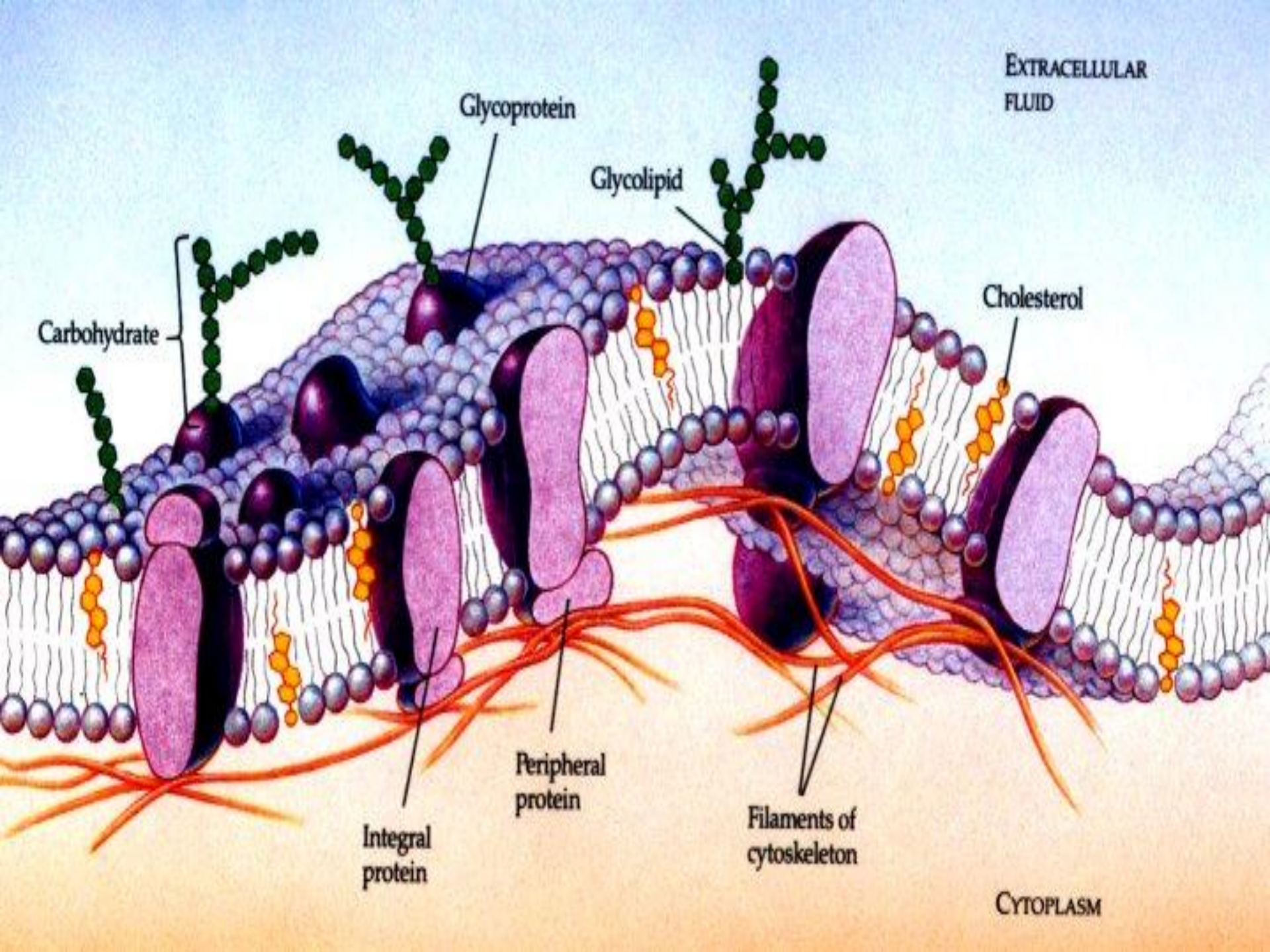
1- Cell membrane = Plasma membrane:
semipermeable membrane surrounding the cell.
2- Nuclear membrane:
surround the nucleus.
3- Intracellular membranes:
surround the cytoplaasmic organelles

Although, these membranes vary in considerably in their structure they have certain common features:

1- They are generally 7.5 nm (75 angstrom) **thickness**.
2- **Chemically**, they are made up of:
50-55% → protein
29% → lipids
13% → sterols (e.g., cholesterol)
3% → carbohydrates.

Cell membrane
= Plasma membrane


Exterior
Oligosaccharide
Glycoprotein
Glycolipid
Peripheral protein
Integral protein
Leaflets
Phospholipid bilayer
Hydrophobic core
Cytosol
Hydrophilic Protein
Integral protein
Peripheral proteins
Fatty acyl tails
Hydrophilic polar head
Phospholipid


Extracellular fluid
Glycoprotein
Glycolipid
Carbohydrate
Cholesterol
Peripheral protein
Integral protein
Filaments of cytoskeleton
Cytoplasm

Plasma membrane

- Semi-permeable envelop (surround)) the cell

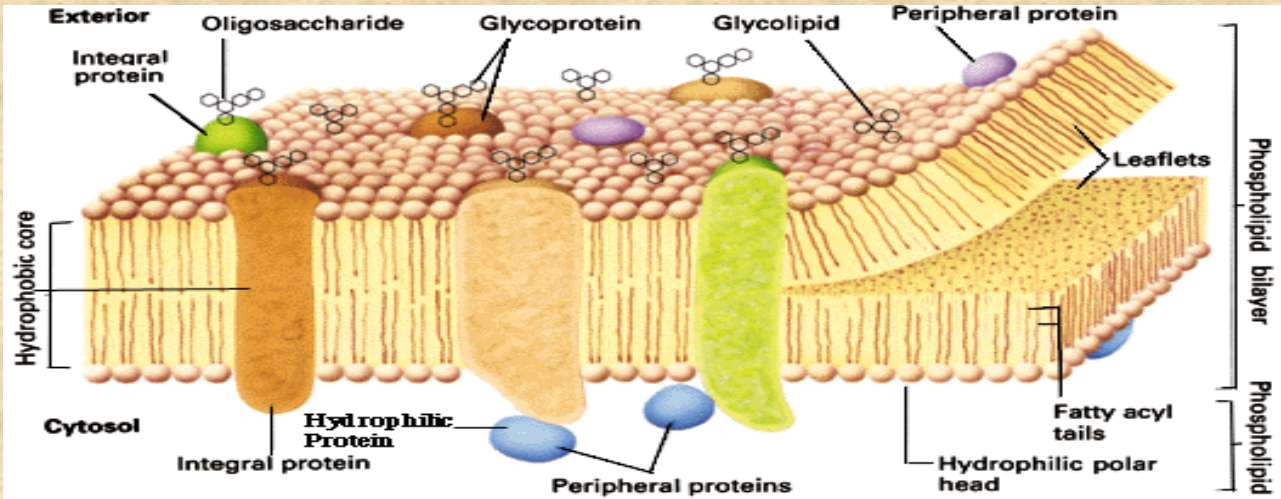
Structure of cell membrane:

(a) Light microscope:

Cell membrane is not visible.

(B) Electron microscope: (fluid-mosic model)

Two lipid layers in which protein molecules are suspended or floating

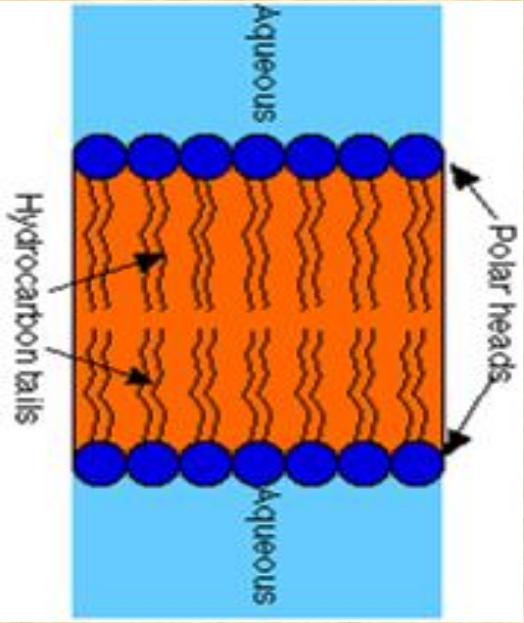


(I) Lipid bilayers:

- The major lipid in the cell membrane is:

a) Phospholipid (phospahtidyl choline and phospahtidyl ethanolamine)

b) cholesterol (N.B., bacterial cell do not contain cholesterol).



Phospholipid molecule:

Shape: resembles **clothspin i.e.,**

* **Head end** (Phospahte group)
  - charged (polar)
  - hydrophilic
  - present in the inner and outer surface
* **Tail portion** (Two fatty acid chains):
  - non charged (non polar)
  - hydrophobic.
  - present in the interior

Dynamic activity of lipid layer:

The phospholipid molecules exhibit a continuous lateral motion around their longitudinal axises but:

1) within the constant arrangement i.e.,
head on the inner and outer surfaces while, the tail (FAs) in the inner.

2) do not slip from one side to the other

Functions of c.m. lipids:

1- Importance for the fluidity of C.m.:

The hydrophilic ends interact with water (aquaous environment) on either sides of the c.m. while, the hydrophobic ends inteacts with themselves to form a **closed self sealing structure.**

2- Aid in the selective permeability character of the cell membrane:

= permeable to non polar substances and impermeable to polar substances. This is due to **t**he arrangement of the phosphate groups on the inner and outer surfaces while, the FAs chain in the interior explain (maintain).

3- Keep flexibility and dynamic activity of the c.m.:

Through the motion of phospholipid molecules???. Thus helping the cell to changes its shape.

4- Cholesterol molecules: give toughness to c.m together with their effect on c.m. permeability

5- Glycolipid molecules functions as:

- recognition sites and so help in cell to cell adhesion.
- important for self-differentiation and immune response.

(II) Protein molecules:

- Protein constitute 50-55% of the mass of c.m. The more active the cell the more its protein content in c.m.

Types:

1- Separate protein:

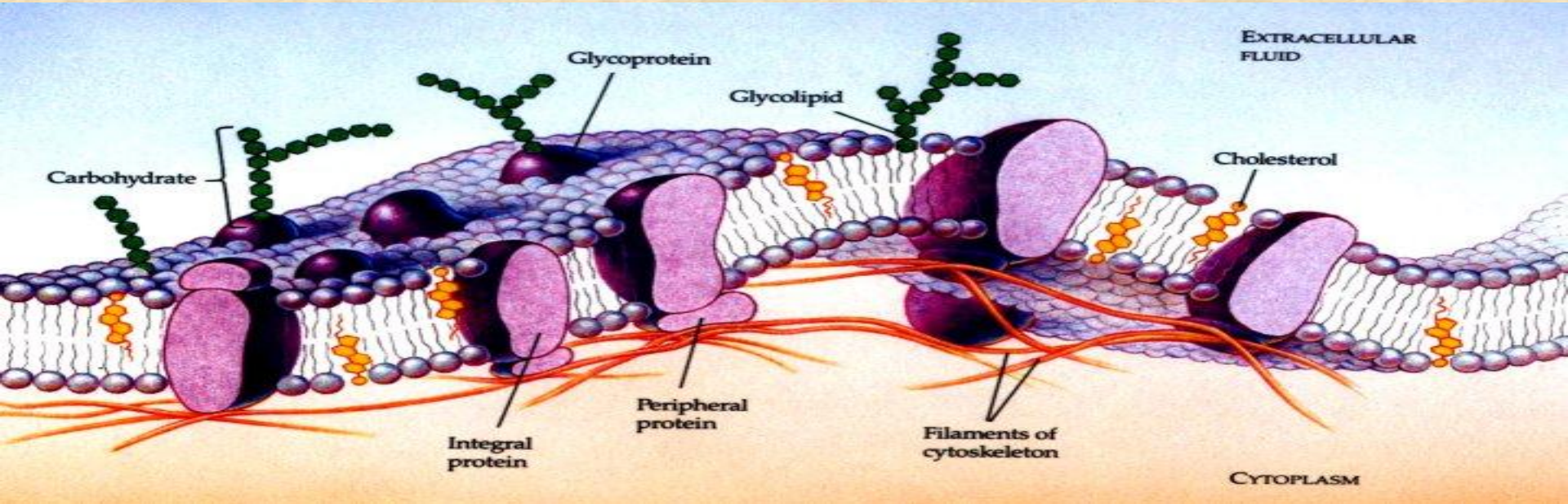
= protein that float and still embedded in the fat layer.

2- Integral protein:

= protein that extends completely (or half the way) through the cell membrane

3- Peripheral protein:

= Stud or attach the inside or outside of the cell membrane



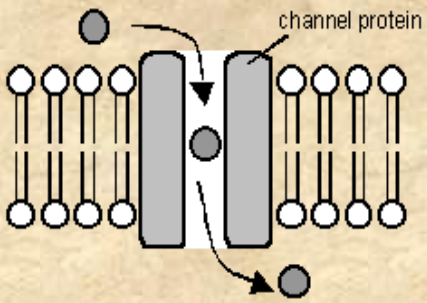
Functions of c.m. Proteins

1- Act as a structural protein:

i.e., have the ability to change their shape (configuration changes) to form protein channels of various shape and diameter

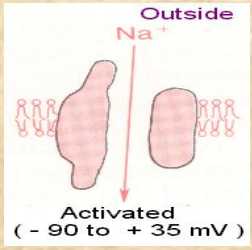
Protein channels:

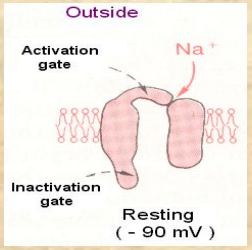
(A) Non-gated (open all times): allows passage of ions all time



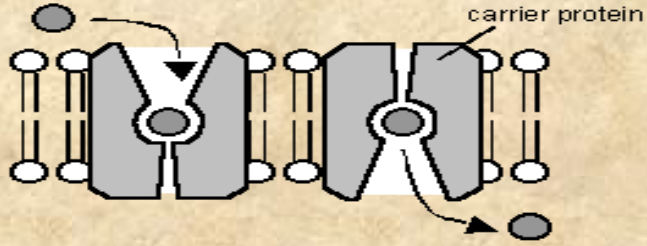
(B) Gated: (during rest → closed, while during activity→ opens)

1) Voltage-gated: sensitive to electric changes in c.m





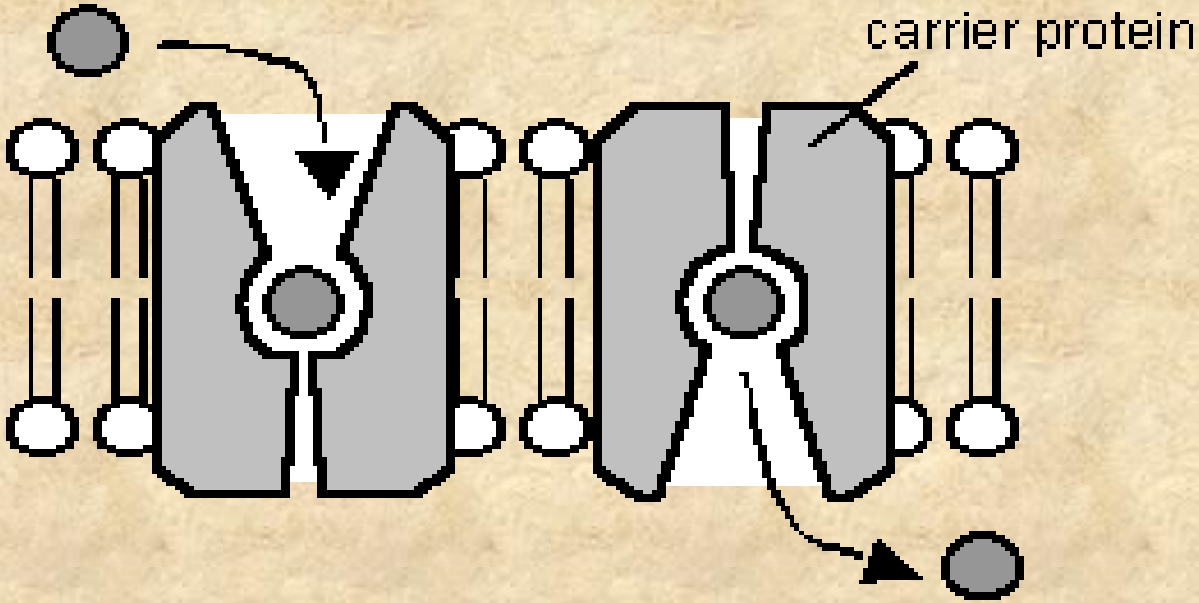
2) Ligand-gated: sensitive to ligand (substance that activates a specific receptors on c.m).



2-Carrier for large molecules in case of facilitated passive diffusion i.e., according to concentration gradient)

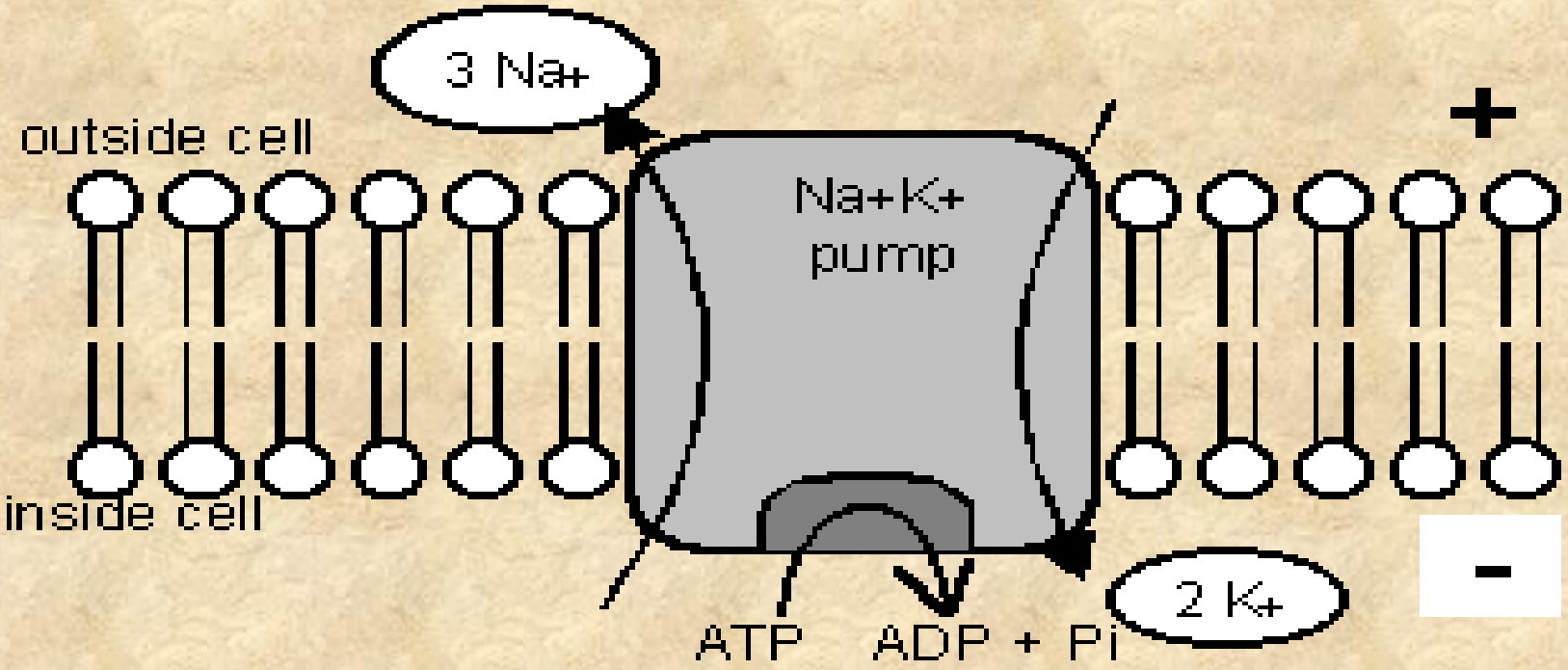
e.g., glucose transportation

Glucose attaches to specific site (protein receptors) which is then activated → undergo configuration changes → channel form → transport inside the cell.



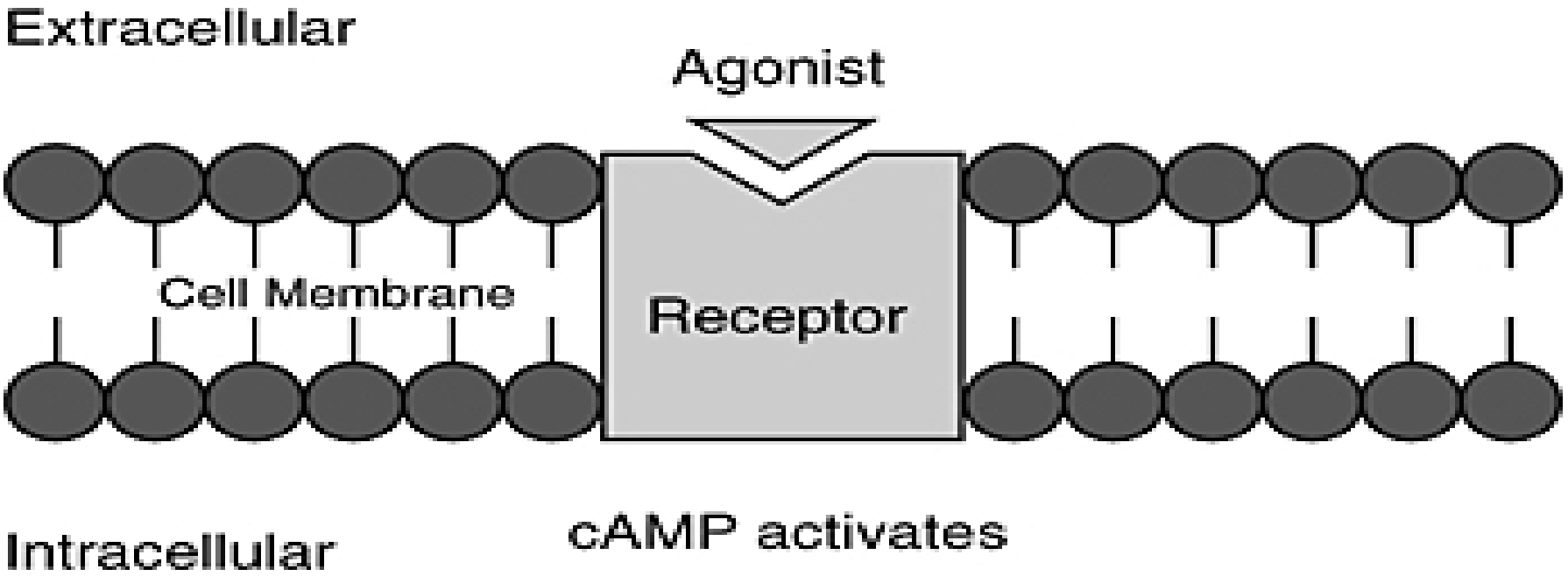
3- Carrier of substances in case of active transport (against conc gradient):

e.g., Na+-K+ pump



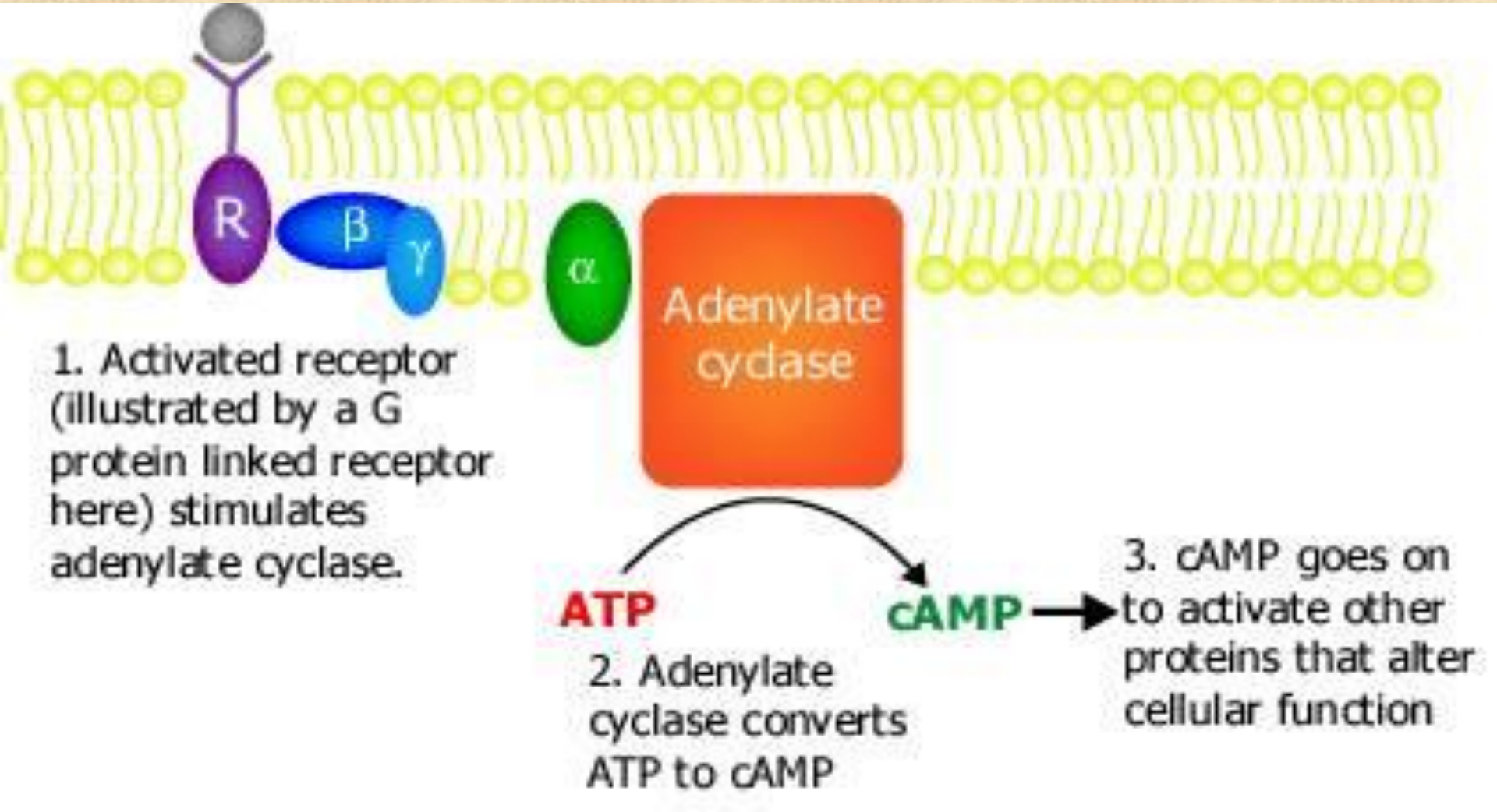
4- Function as receptor on cell membrane and nuclear membrane:

Certain ligand (e.g., neurotransmitter, hormone, drug., …etc) binds to specific protein receptor → initiates physiologic response



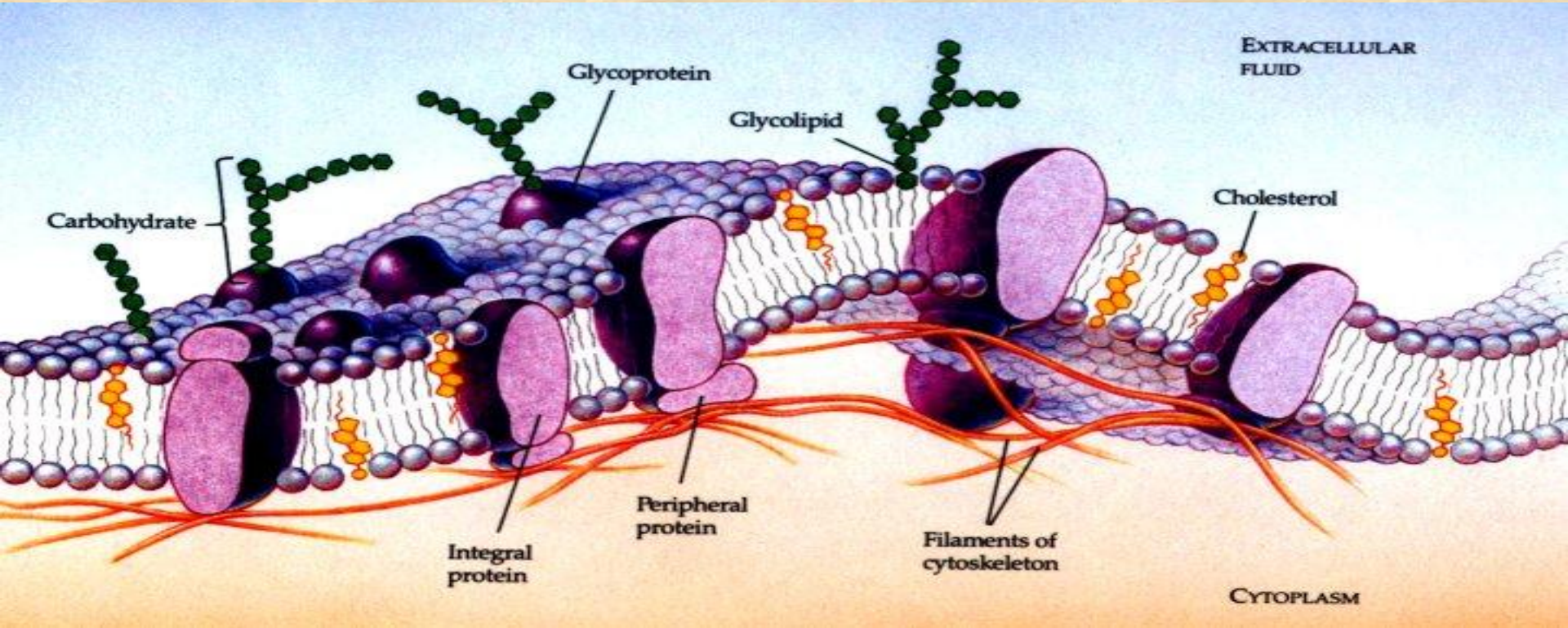
5- Function as enzymes:

e.g., ATPase, Adenylcyclase, …etc.



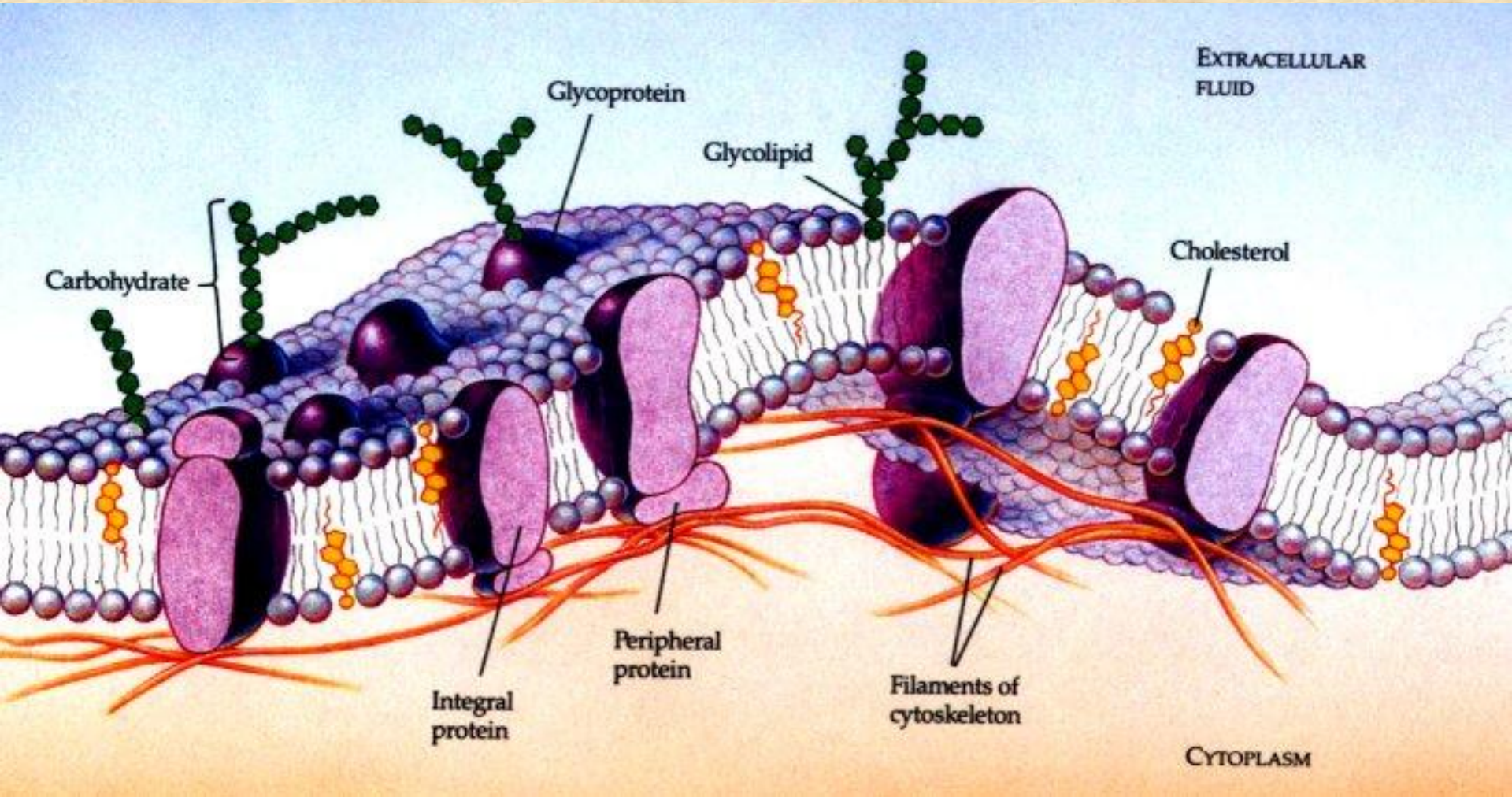
6- Glycoprotein formation:

- Ag-Ab reaction



7- Formation of cytoskeleton of the cell:

Cytoskeleton = systems of fibrils (microtubules, microfilaments, …etc) made of protein→ maintain structure of the cell in place.



8- Formation of intercellular connection:

(A) Tigh junction:

(B) Gap (or channel) junction:

(C) Cell adhesion molecules:

(A) Tight junction:

Protein molecules projects to form ridges (half from one cell and half from the other) → adhere strongly to obliterate the space between the two cells

e.g., apical margins of epithelial cells of intestine and renal tubules.

(B) Gap (or channel) junction:

- The inter cellular space narrows from 25 nm to 3 nm.

Protein molecules (in cm of one cell) arrnge itself in

a hexagonal manner to form what is called **Connexon** surrounding a channel

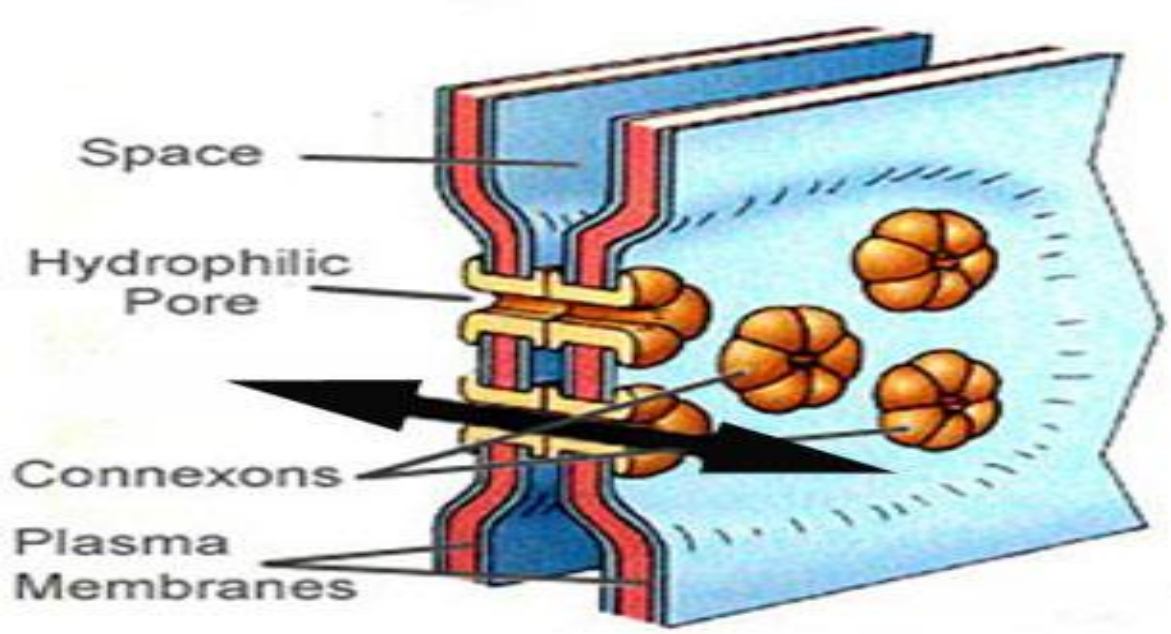
↓

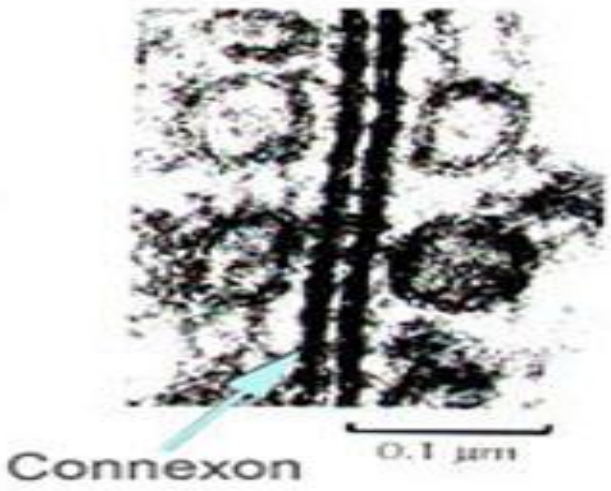
which will be in line with corresponding connexon of the neighboring cell

↓

allows transfer of ions and other molecules from one cell to another.

- e.g., neuromuscular junction.

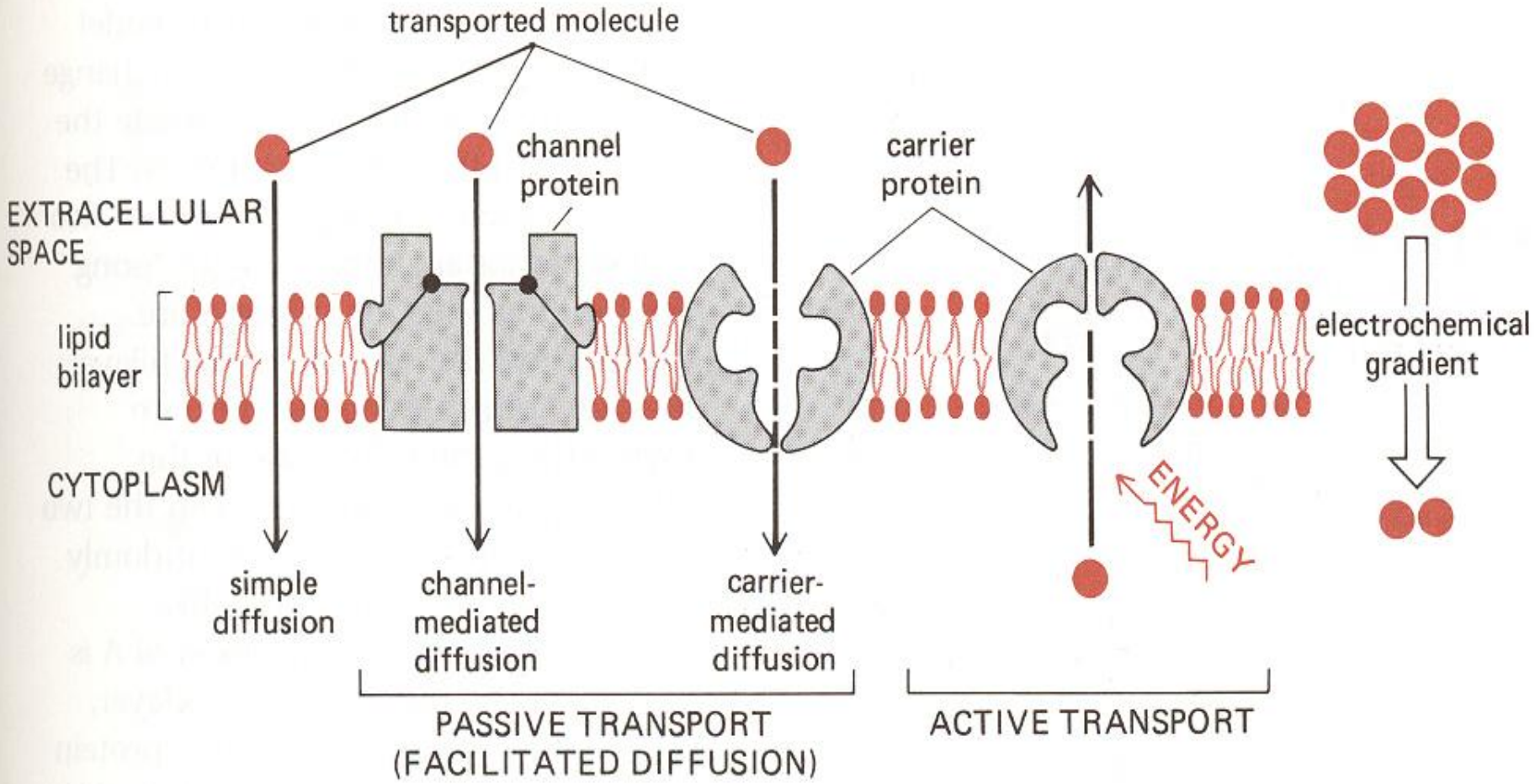




(C) Cell adhesion molecules:

Responsible for adhesion of cells to the basal lamina.

Transport across the cell membrane


transported molecule
channel protein
carrier protein
EXTRACELLULAR SPACE
lipid bilayer
CYTOPLASM
electrochemical gradient
ENERGY
simple diffusion
channel-mediated diffusion
carrier-mediated diffusion
PASSIVE TRANSPORT (FACILITATED DIFFUSION)
ACTIVE TRANSPORT

Cell membranes act as barrier to most substances??

↓

Materials are concentrated inside cells

- There are five main methods by which substances can move across a **cell membrane**:

1- Simple Passive Diffusion (or Lipid Diffusion)

2- Osmosis (Simple Passive Diffusion of H_2O)

3- Facilitated Passive Transport

4- Active Transport

5- Vesicles (endocytosis and exocytosis).

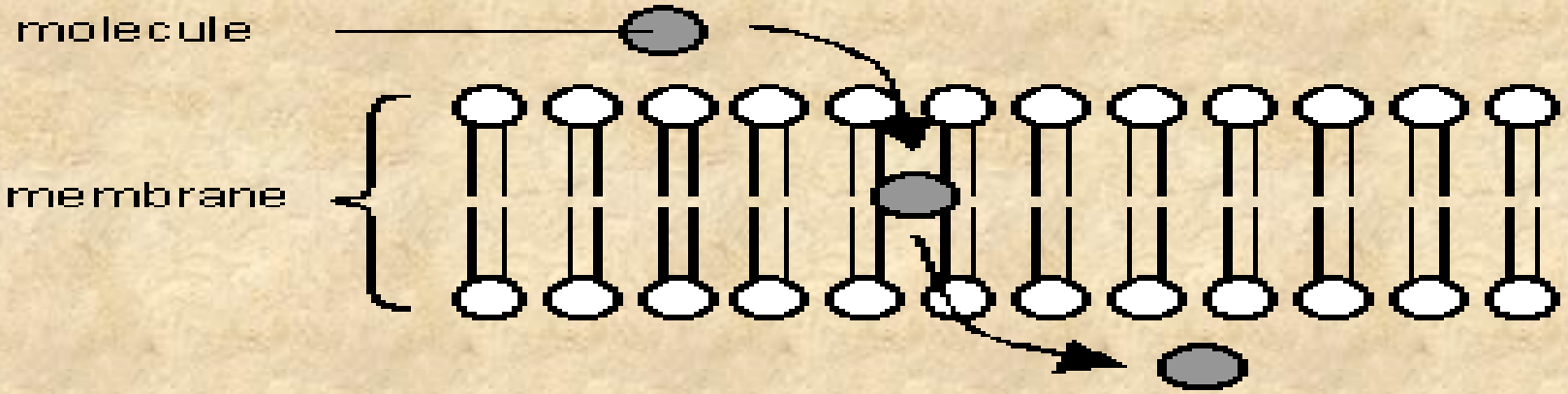
(1) Simple Passive Diffusion (Lipid diffusion):

= Substance can diffuse (according to concentration gradient) directly through the lipid bilayer part of the **membrane**, e.g.,

- lipid-soluble molecules such as steroids,
- very small molecules such as H_2O, O_2 and CO_2 .

- Characterized by:

- Passive = no energy is involved
- Simple = no carrier protein is required
- Movement of molecules occurs according to conc gradient



(2) Osmosis (Simple Passive Diffusion of Water):

= diffusion of **WATER** across a **membrane**.

- Water molecules can diffuse freely across a **membrane**, but always **down** their concentration gradient,

i.e., water diffuses from a dilute to a concentrated solution.

N.B:

Osmosis= It is a normal lipid diffusion (= simple passive diffusion),

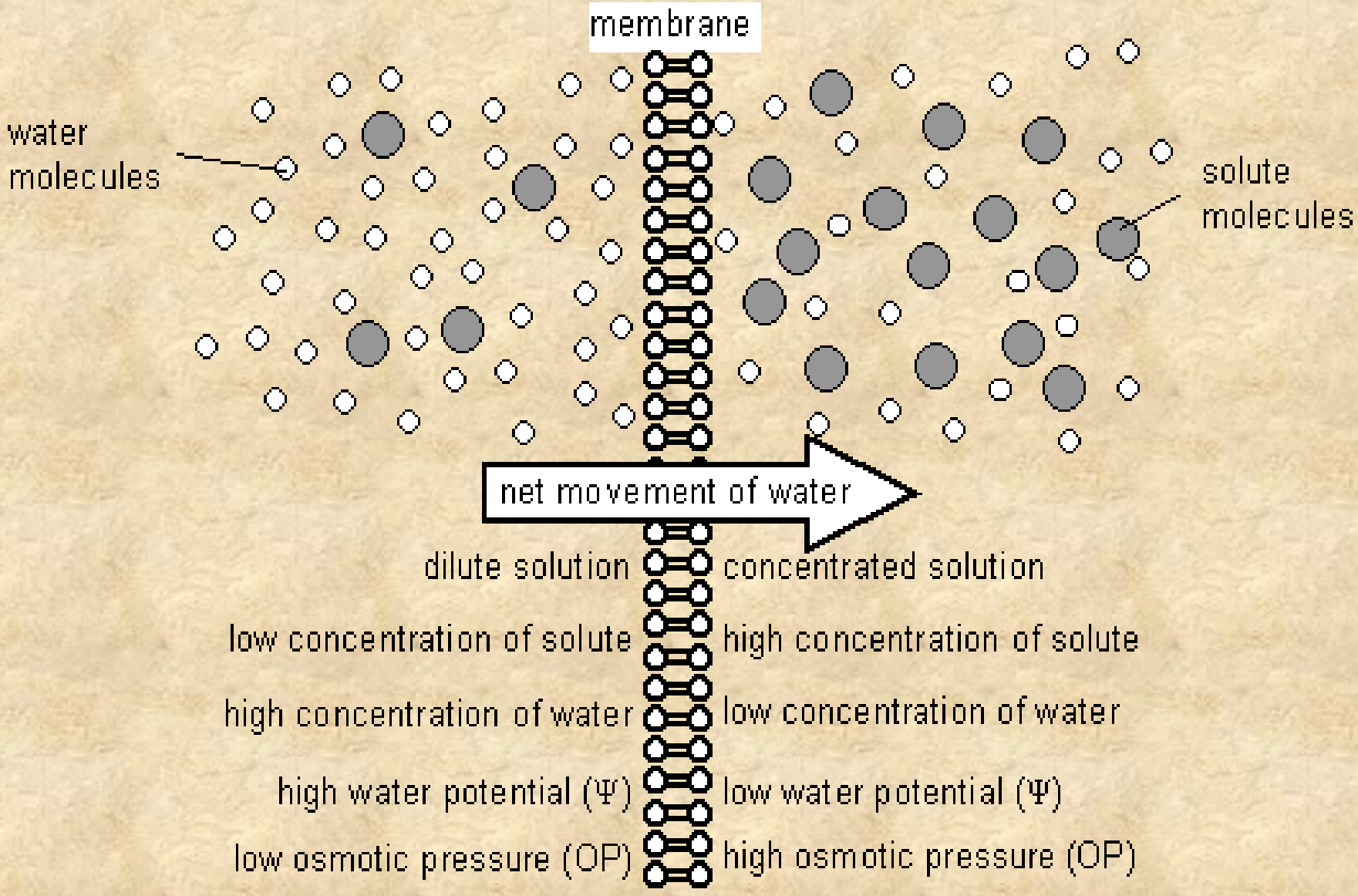
but since water

is so important and so abundant in cells

(its concentration is about 50 M),

the diffusion of water has its own name;

Osmosis.


membrane
water molecules
solute molecules
net movement of water
dilute solution
concentrated solution
low concentration of solute
high concentration of solute
high concentration of water
low concentration of water
high water potential (Ψ)
low water potential (Ψ)
low osmotic pressure (OP)
high osmotic pressure (OP)

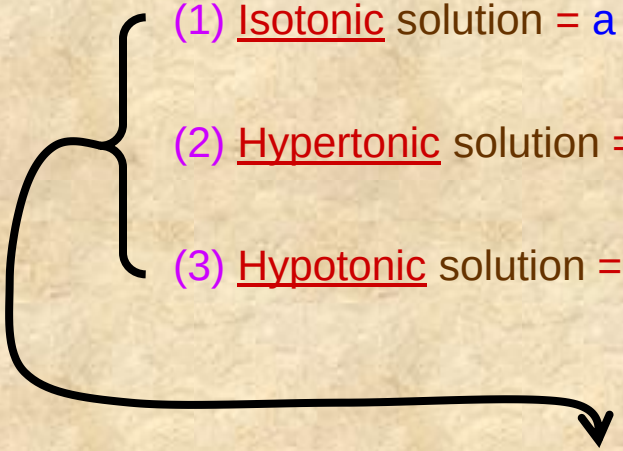
Cells and Osmosis.

- There are three possible concentrations of solution to consider:

(1) Isotonic solution = a solution of equal OP (or concentration) to a cell

(2) Hypertonic solution = a solution of higher OP than a cell

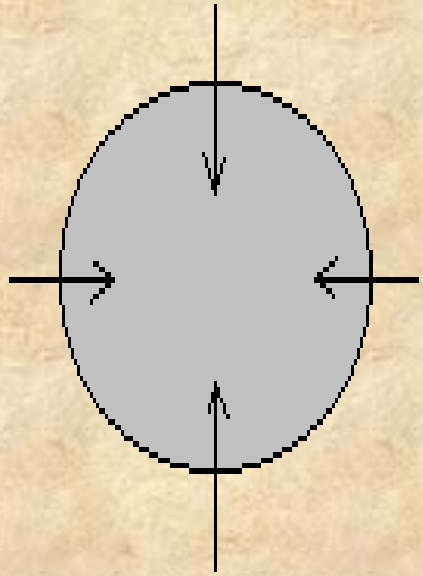
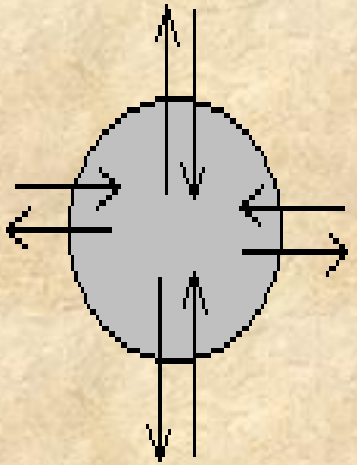
(3) Hypotonic solution = a solution of lower OP than a cell



The concentration (or OP) of the solution that surrounds a cell

Will affect the state of the cell

due to osmosis.

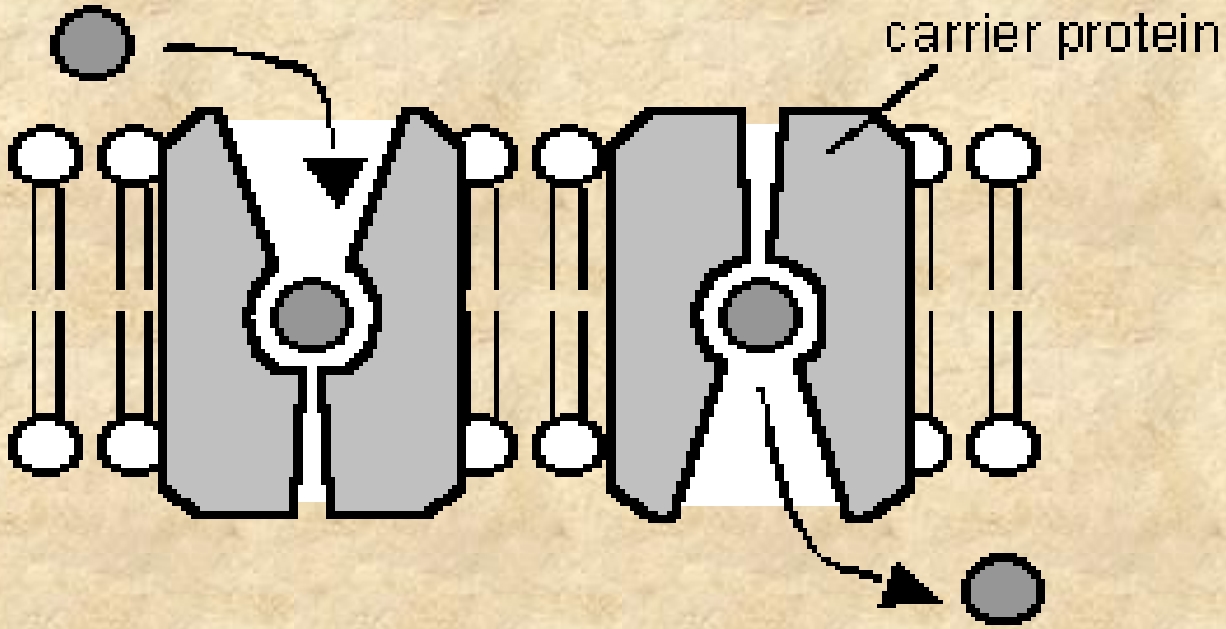
Hypotonic solution	Isotonic solution	Hypertonic solution
		
water enters, cell swells and may burst (lysis).	no net movement of water, cell normal size	water leaves, cell shrinks and crenates

(3) Facilitated Passive (carrier mediated) transport:

= transport of substances across a **membrane according to concentration gradient** by a trans-**membrane** protein molecule, e.g., glucose transportation

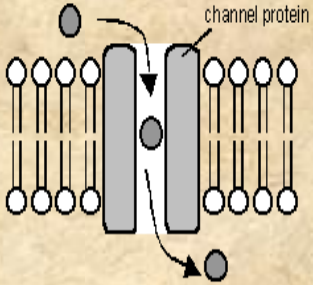
Characterized by:

- Passive: no energy is involved
- Facilitated (or carrier mediated): require a specific transport protein
- Movement of molecules occurs according to conc gradient



- Kinds of transport proteins:

(1) Channel Proteins:

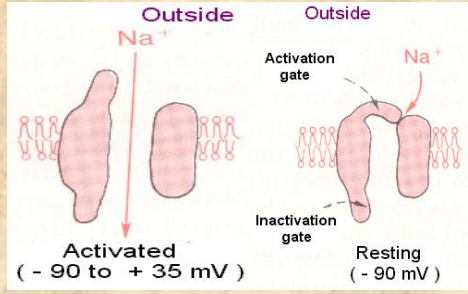


(A) **Non-gated (open all times):** allows passage of ions all times
e.g., water-filled pore or channel in the **membrane**.

(B) **Gated:** (during rest → closed, while during activity→ opens)

1) Voltage-gated: sensitive to electric changes in C.m

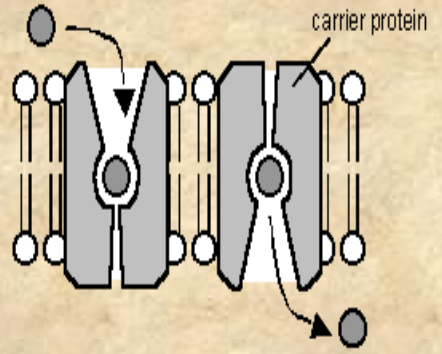
2) Ligand-gated: sensitive to ligand (substance that activates a specific receptors on c.m).



(2) Carrier Proteins:

= binding site for a specific solute.

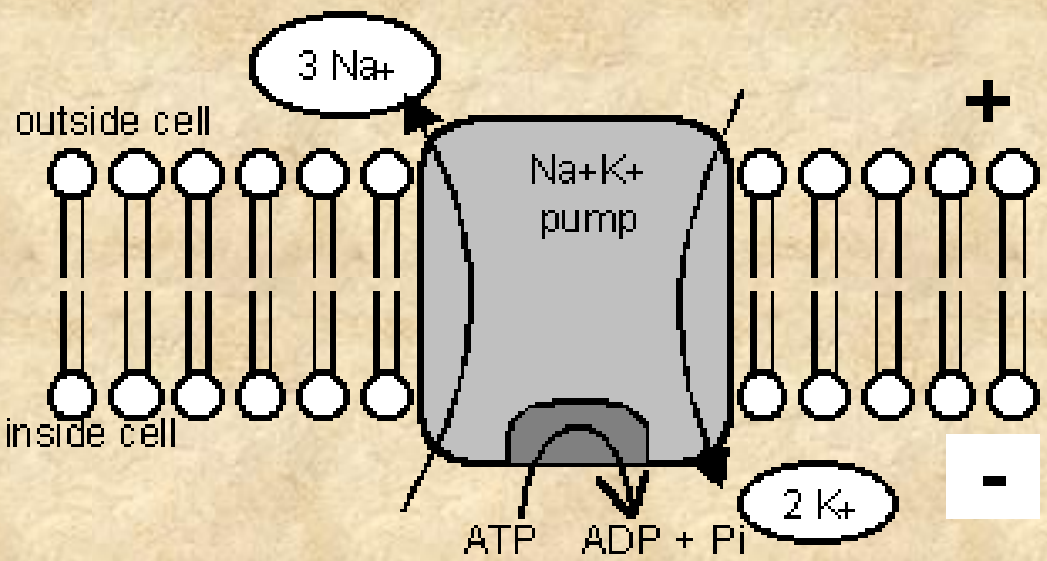
Bind to the substance
(where it is present at a high concentration)
↓
transport and release it to the other side of the cell membrane
(where it is present at low concentration)



(4) Active transport:

= Pumping of substances (against conc gradient) across a membrane by a trans-membrane protein molecule.

e.g., Na+-K+ pump.



Characterized by:

- Active : requires energy that derived from splitting of ATP by ATPase enzyme into ADP, Phosphate (Pi) and E

- Requires a specific transport protein: protein binds a substance (on one side of the **membrane**) → undergos configuratory shange → release the substance to the other side.

- Pumping: movement of molecules occurs against the conc gradient

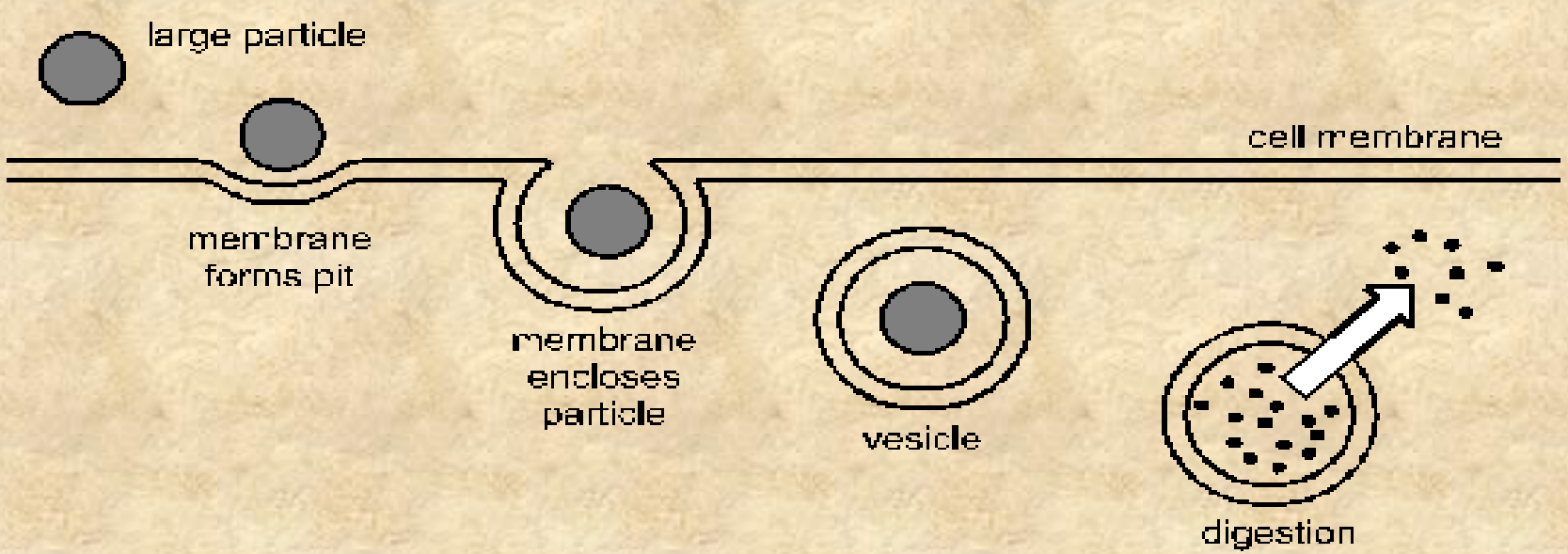
(5) Endocytosis (pinocytosis and phagocytosis):

Endocytosis = transport of materials **into a cell** i.e.,

Materials are enclosed by a fold of the **cell membrane**, which then pinches → shut (separates) to form a closed vesicle. Such vesicle is usually digested

a) Pinocytosis (cell drinking) = Materials and the vesicles are small such as a protein molecule.

b) Phagocytosis (cell eating) = Materials are large such as a white blood cell ingesting a bacterial cell.



(6) Exocytosis

= Reverse of endocytosis.

= Transport of materials out of a cell

e.g., Hormones and digestive enzymes are secreted by exocytosis from the secretory cells of the intestine and endocrine glands

- Materials to be released outside the cell, it must be first enclosed in a **membrane** vesicle, usually from the RER and Golgi Body.

N.B:

Sometimes materials:

can pass straight through cells **without making contact with the cytoplasm**?

by being taken in by endocytosis at one end of a **cell** and passing out by exocytosis at the other end.


Thanks