DEBRE MARKOS UNIVERSTY SCHOOL OF MEDICINE DEPARTMENT OF MEDICAL PHYSIOLOGY

INTRODUCTION TO MEDICAL PHYSIOLOGY

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What is Human Physiology

- Branch of biomedical sciences that deals with **normal body function.**
- It is sometimes called the science of regulation of physiologic parameters of the body.
- **Fields of Physiology** range from simple viral physiology, bacterial physiology, cellular physiology to the most complex human physiology

Why do we learn Physiology?

- To explain the physical and chemical factors that are responsible for the origin, development, and progression of life.
- To diagnose and treat abnormalities (pathologies).
  - Once we have known the normal physiologic phenomena, it is not difficult to detect abnormalities.

Historical background

- Physiology is an experimental science to which a number of scientists contributed a lot.
- **William Harvey in 1628:-** Described the direction of **blood circulation** and other aspects of circulatory system.
- **Claude Bernard:-** 100 years ago French physiologist described that every cell in the body is bathed with the fluid (Extra cellular fluid). ECF contains all the needed substances for cells.
- Cells are capable of living ,growing, and performing their special functions as long as the proper concentrations of oxygen, glucose, different ions, amino acids, fatty substances, and other constituents are available in this internal environment.

Historical background...

- **Walter Cannon**, another great physiologist of the 1st half of 19th century, termed the maintenance of constant conditions in the ECF as homeostasis
  - ✓ *Essentially all organs and tissues of the body perform functions that help maintain these constant conditions.*
- Physiology as a quantitative science which all physiological parameters are expressed in numbers and units
- Physiology has a strong link with disciplines like:
  - *Anatomy*
  - *Biochemistry*
  - *Pathology*
  - *Pharmacology*
  - *Physics etc*

Homeostasis

- The term homeostasis mean that maintenance of static or constant conditions in the internal environment (ECF) of the body.
- To maintain homeostatic environment *all organs and tissues* use Feedback control system.

For example

- ✓ Lungs maintain the normal concentration of respiratory gases in blood.
- ✓ The CVS transports required substances and removes waste products,
- ✓ The kidneys maintain constant ionic concentration
- ✓ GIT maintains internal environment by providing nutrients ,water and electrolytes to the body.

Homeostasis…

- Extracellular fluid is transported through all parts of the body in two stages.
  - Movement of blood through the body in the blood vessels.
  - Movement of fluid between the blood capillaries and the intercellular spaces between the tissue cells.

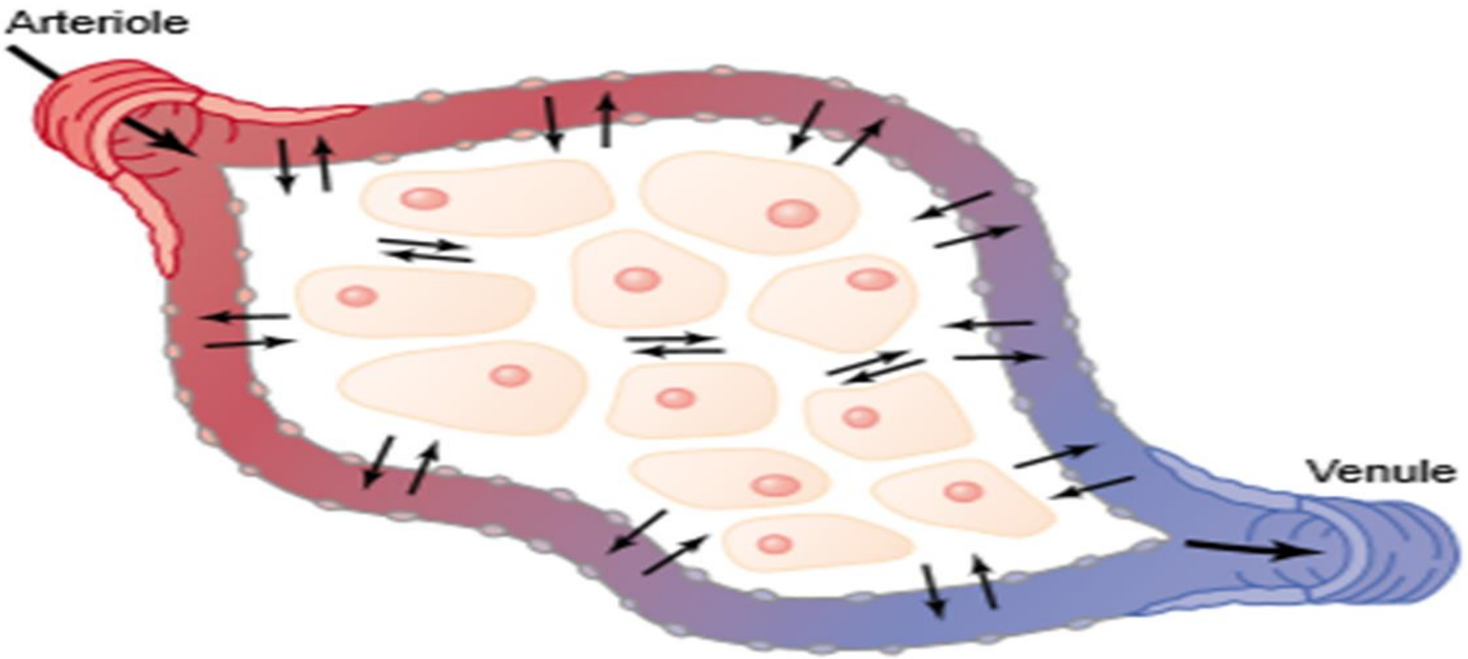


Fig. Diffusion of fluid and dissolved constituents through the capillary walls and through the interstitial spaces.

Regulatory systems of homeostasis

- The two systems in the body designed for controlling homeostasis:

    1. Nervous system

    2. Endocrine system

1. The nervous regulatory mechanism

- The nervous system regulates body functions through generation of action potential and release of neurotransmitters.
- To bring about complete communication among various structures of the body NS act through reflex arc.

The nervous regulatory mechanism…

- Reflex arc is a pathway of neural reflex. It composed of five structures:

1. Receptors (change detectors and transducers)

2. Sensory system (carries nerve signal to the integrating center)

3. Integrating center (evaluates the information and gives feedback)

4. Motor system (carries information away from the integrating center)

5. Effectors (receive motor feedback and accordingly act which result desirable biological responses)

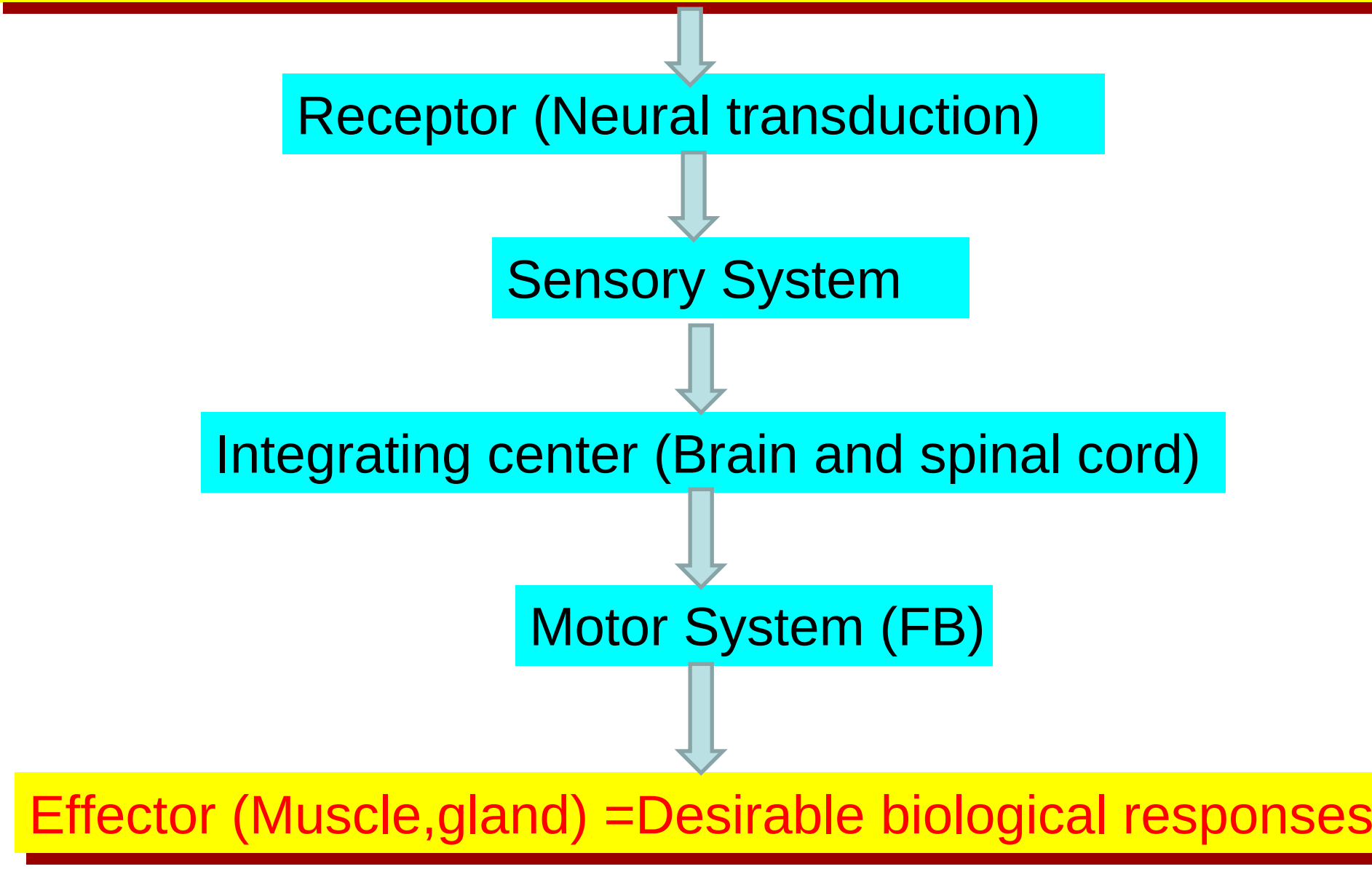


Fig. Reflex Arc

Regulatory systems of homeostasis cont'd…..

2. The hormonal regulatory mechanism

Hormones are chemical messengers secreted by endocrine glands, and transported via blood to the target organs including other glands.

Examples:

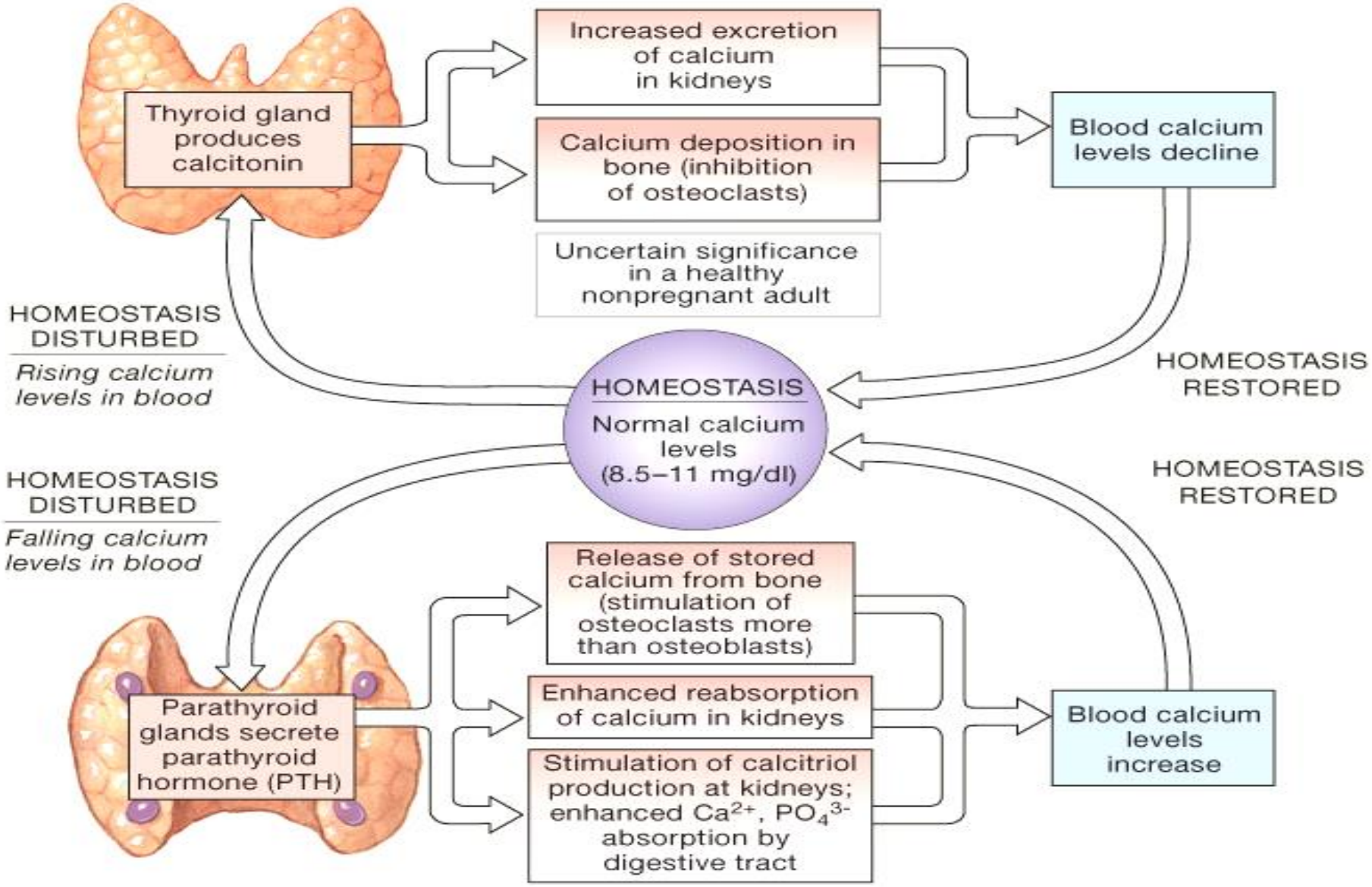
Parathyroid glands secrete parathyroid hormone → to the kidneys, bone and small intestine = ↑[Ca2+]

Aldosterone from adrenal cortex → to the kidneys, intestine ⇨ ↑ [Na+]

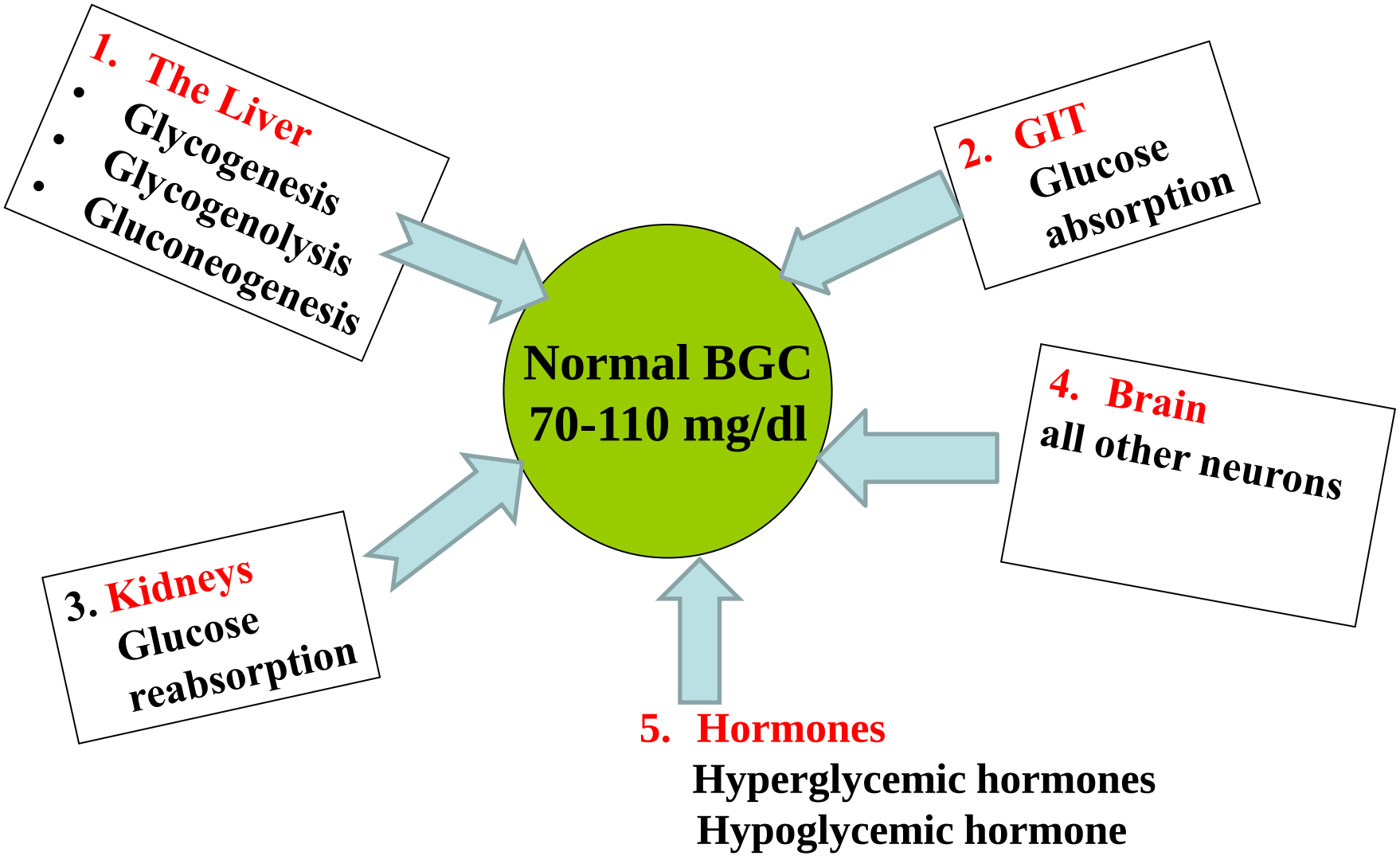
Anti-diuretic hormone (ADH) causes water retention from the kidneys and intestine.

An organism is said to be in a state homeostasis when its internal environment contains an optimum amount of nutrients, gases, electrolytes, water, hormones, enzymes and temperature.

Ca^{2+}homeostasis



Blood glucose homeostasis



Regulatory systems of homeostasis cont'd…..

Common Properties Of Hormones And Neurotransmitters

- Both are released in small amount
- Both have receptors on the target organs
- Both act by altering their target organs
- Both work towards common goal →Homeostasis

But there are differences

- Nervous regulation is faster but hormones is slower
- Nervous effects are diffused but hormones is mostly localized

Some important Homeostatic Values

Body fluid volume (40 L)	ECF = 15L ICF = 25L
Osmolality	300 mosm/L (285 – 300 mosm/L)
PH	7.35 – 7.45
Blood Gases	PCO_2 = 40 – 46 mm Hg PO_2 = 40 – 104 mm Hg
Body Temperature	36.3 – 37.1^{O}C
Electrolytes (ECF)	Ca^{2+}=10 mg/dL or 5 meq/L or K^+ = 4 meq/L Na^+= 142 meq/L Cl^-= 103 meq/L HCO_3^- =27 meq/L

Waste Products	Bilirubin =0.5 mg/dl Creatinine =0.6 – 1.5 mg/dL BUN = 8 – 25 mg/dl Uric acid (s) Women = 2.3 – 6.6 mg/dL Men = 3.6 – 8.5 mg/dL
Blood Glucose level	FBG: 70 – 110 mg/dl RBG: 70 -200mg/dl
Hemodynamics	Systolic pressure = (90 – 140 mm Hg) Diastolic pressure = (60 – 90 mm Hg) Pulse pressure = 40 mm Hg Mean ABP = 96 mm Hg Pulmonary AP = 25/10 Cardiac output = 5 L/min Blood Flow = 5 L /min
Plasma cells	RBC count = 4.6 -5.2 millions/mm^3 WBC count = 5000-11,000/mm^3 Hb =12-16g/dl in F, 14-18 g/dl in M

Feedback control mechanisms of the homeostasis

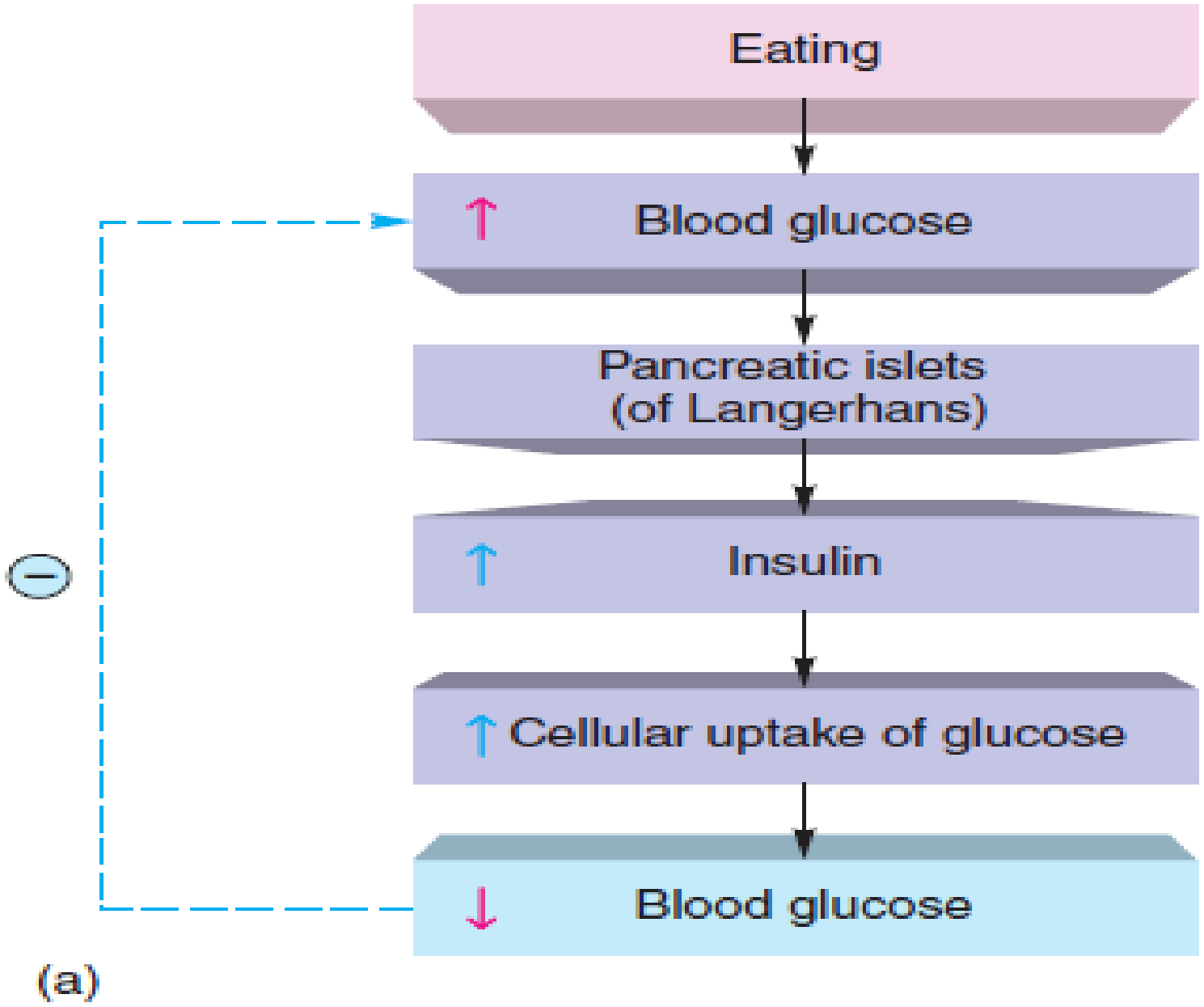
- Feedback control mechanism is a means by which our body tries to maintain its homeostatic environment
- There are two types of feed back mechanisms:

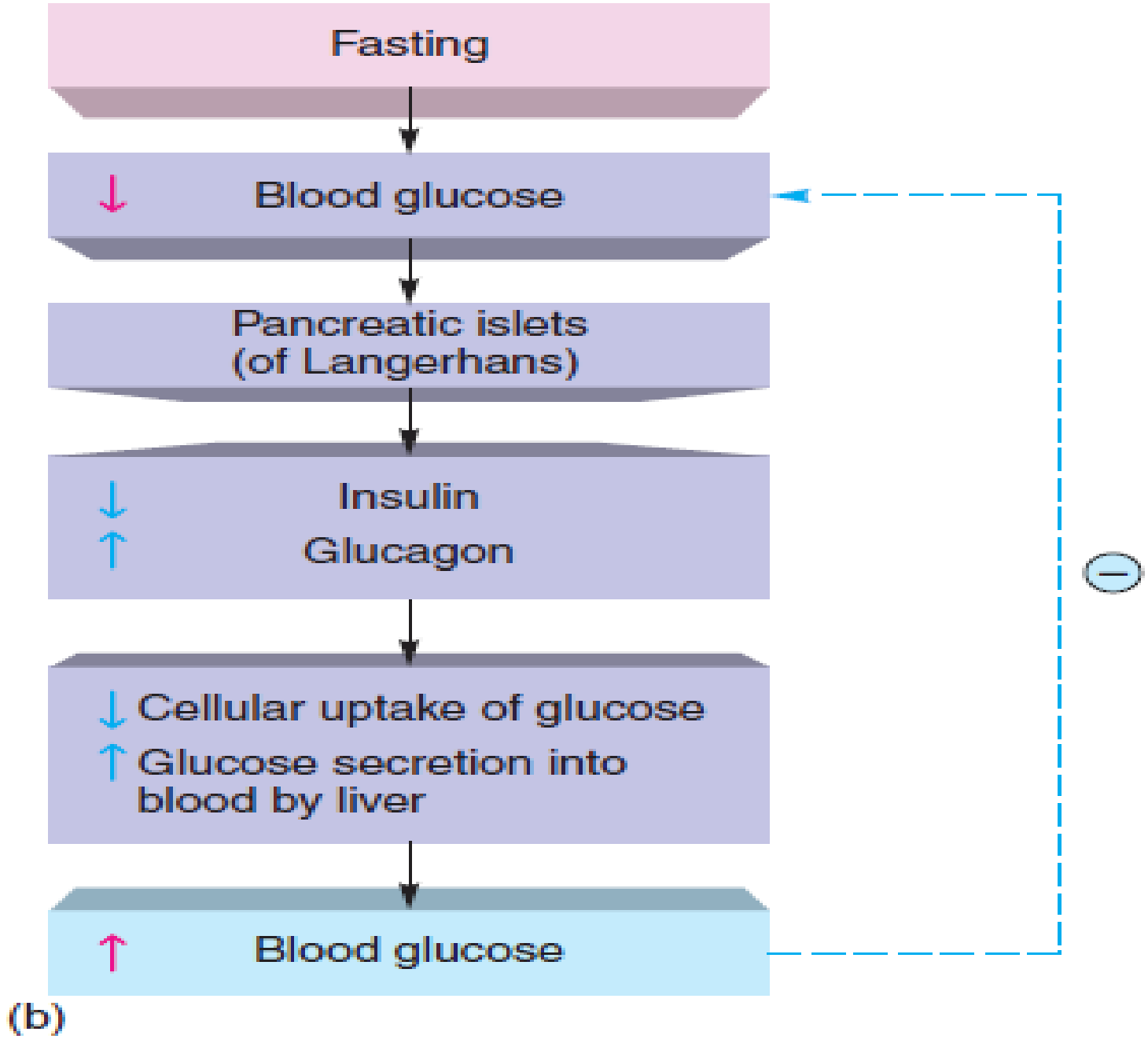
  A. Negative Feedback Mechanism (NFM)

  B. Positive Feedback Mechanism (PFM)

1. Negative Feedback Mechanism(NFM

- It works by producing an effect which **opposes the previous** condition (the initiating stimulus) of the organ.
  - ✓ For example: If the P_{CO2} is increased in the blood, the NFM stimulates the respiratory center, which has an effect on decreasing P_{CO2} in blood to normal via increasing respiratory rate.
- In general, if some factors (parameters) become **excessive or too little,** a control system initiates the NFM, which consists of a series of changes that return the factors toward certain mean values (set point or normal values), thus, **maintaining homeostasis**.


Eating
↑ Blood glucose
Pancreatic islets
(of Langerhans)
↑ Insulin
↑ Cellular uptake of glucose
↓ Blood glucose
⊖
(a)


Fasting
↓ Blood glucose
Pancreatic islets
(of Langerhans)
↓ Insulin
↑ Glucagon
↓ Cellular uptake of glucose
↑ Glucose secretion into blood by liver
↑ Blood glucose
⊖

(b)

The Positive Feedback Mechanism (PFM)

- It works by producing an effect which **enhances or repeats** the same action like that of the starting stimulus. It also called **vicious circle** and disturbs the internal environment and cause disease and death.

For example, if a person suffers from a heart attack that damages the heart function, then the heart pumps less amount of blood to the tissues including the heart muscle and brain. Because the heart muscle does not get sufficient nutrients and O_2, the activity of the heart becomes weaker and weaker and the weaker the heart the lesser blood is pumped and then death may occur.

Examples of the PFM

1. **Blood clotting** is an example of a very valuable use of PF

2. **Generation and propagation of the action potential**.

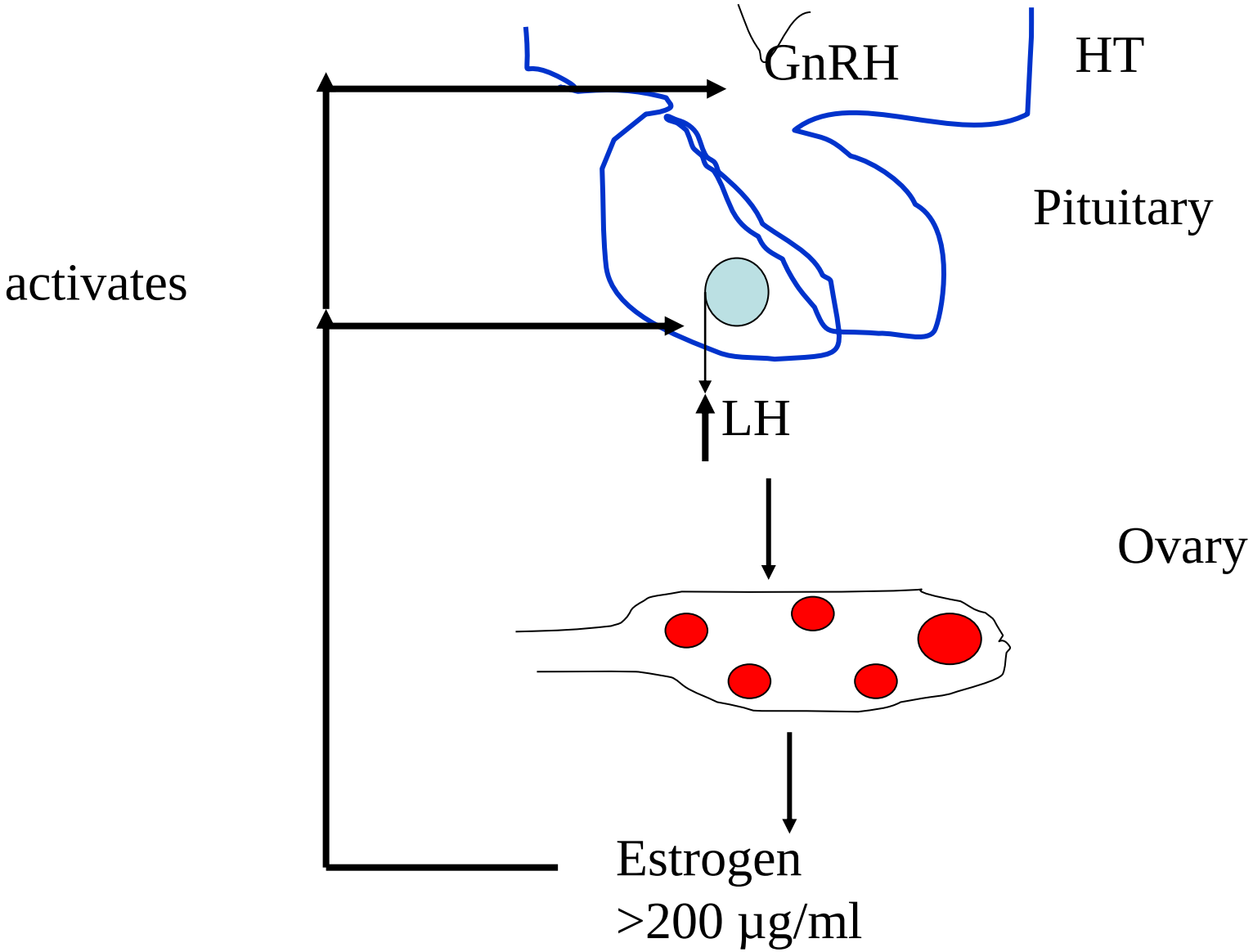
   ✓ Stimulated nerve fiber → opening of Na^+ channels → entry of few Na^+ stimulates the opening of more and more Na^+ channels.

3. **Labor during child birth**

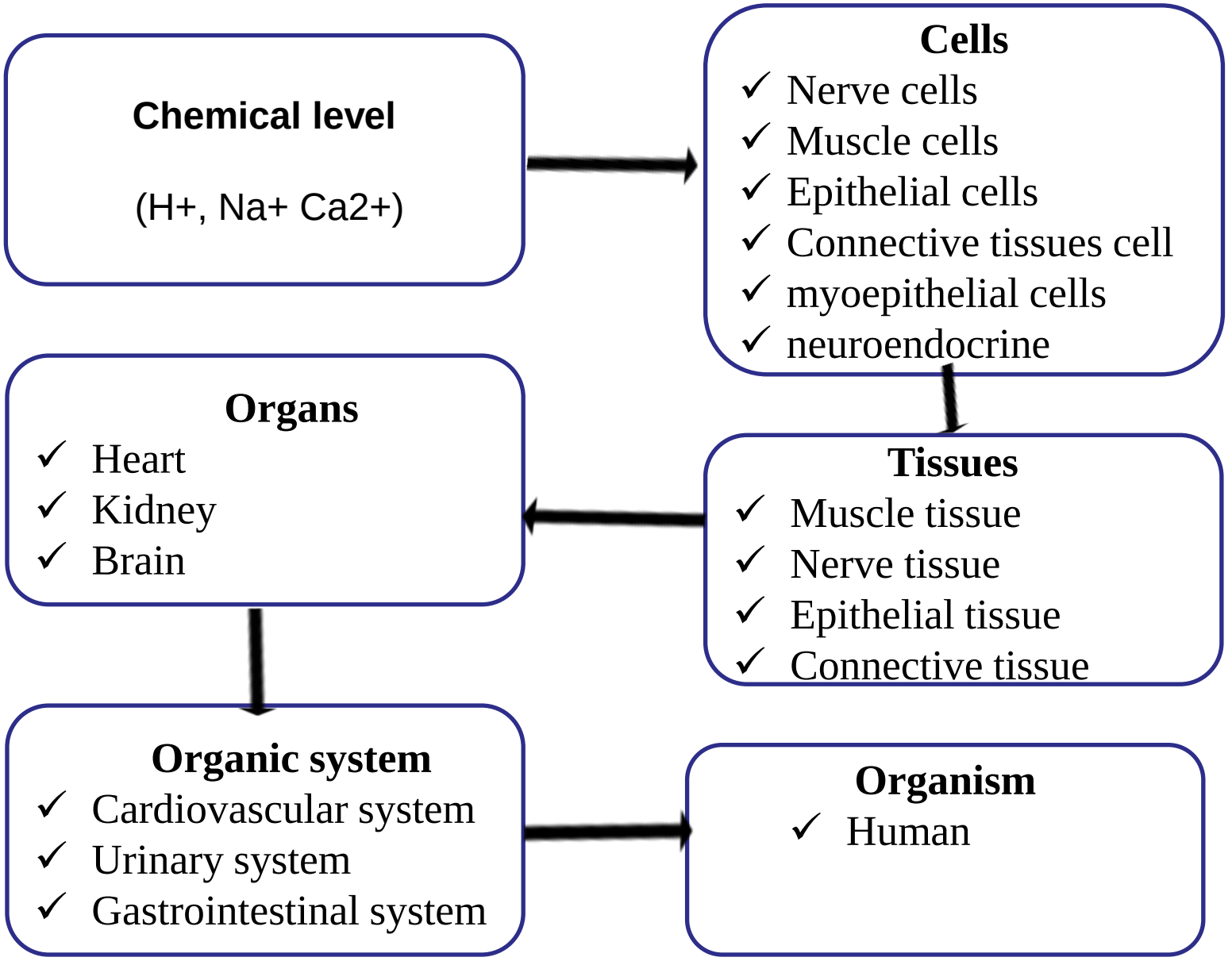
   Uterine contraction is enhanced as the head of the baby stretches the cervix →generation of action potentials →AP reaches H →another AP →posterior pituitary → release of oxytocin into the blood →contraction of uterine muscle →more and more stretching and more and more contraction. The only way to stop this kind of phenomenon is by removing the stimulus

4. **LH-surge:** immediately before ovulation.

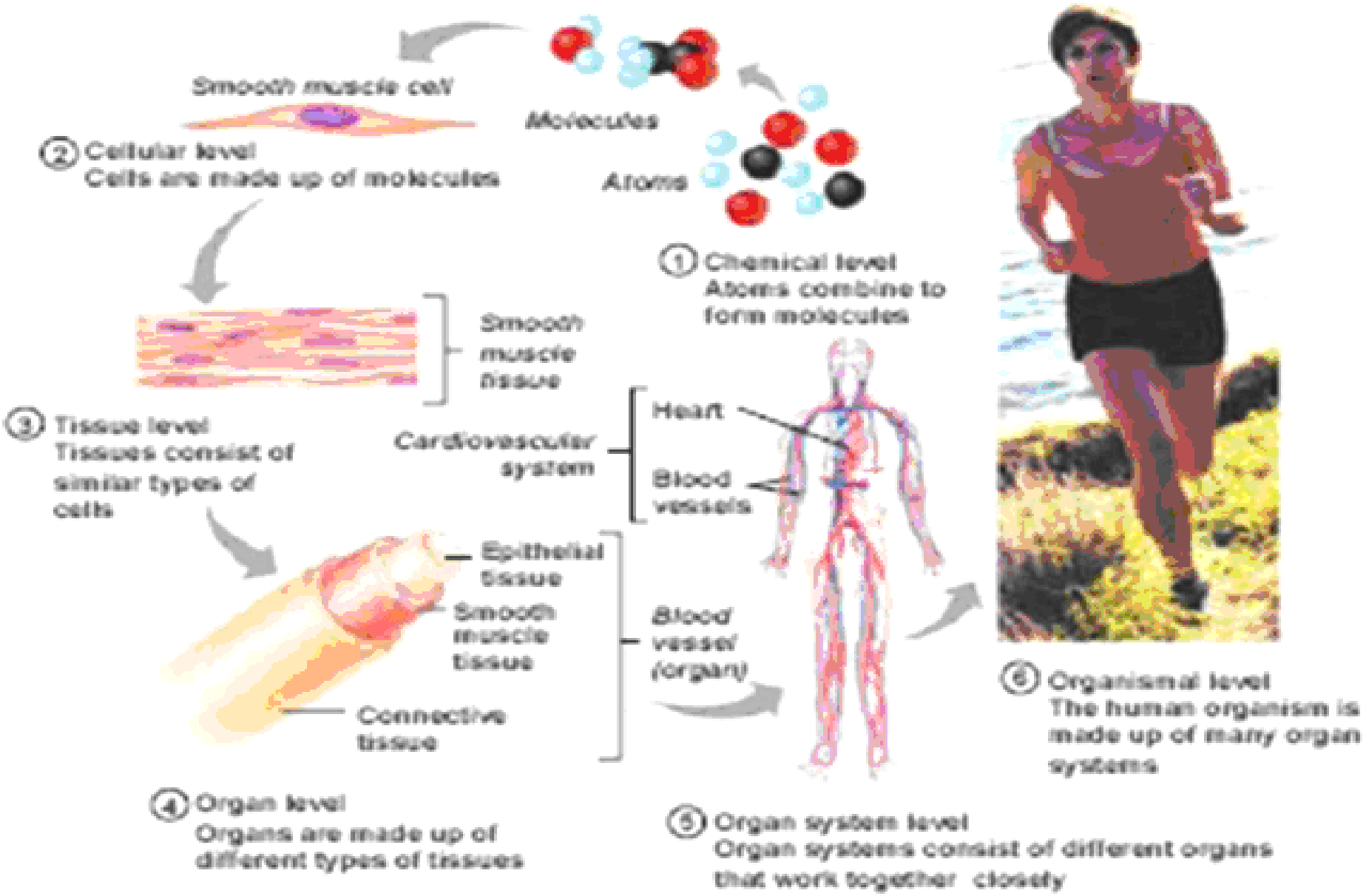
LH surge: the positive feedback mechanism



Structural levels of organization of human body



Structural levels of organization



Cell physiology

- **Cells** are functional & structural units of the body

There are tow types of cells:

A. Cells without typical nucleus = prokaryotes

B. Cells with nucleus = eukaryotes

Cell physiology….

- **Prokaryotes: (Eg. bacteria)**
  - Smaller (1-10 μm)
  - No cytoskeleton
  - Generally no membrane-bound organelles
  - RNA and protein synthesis in same compartment
  - Small circular chromosome
  - Generally very small & unicellular

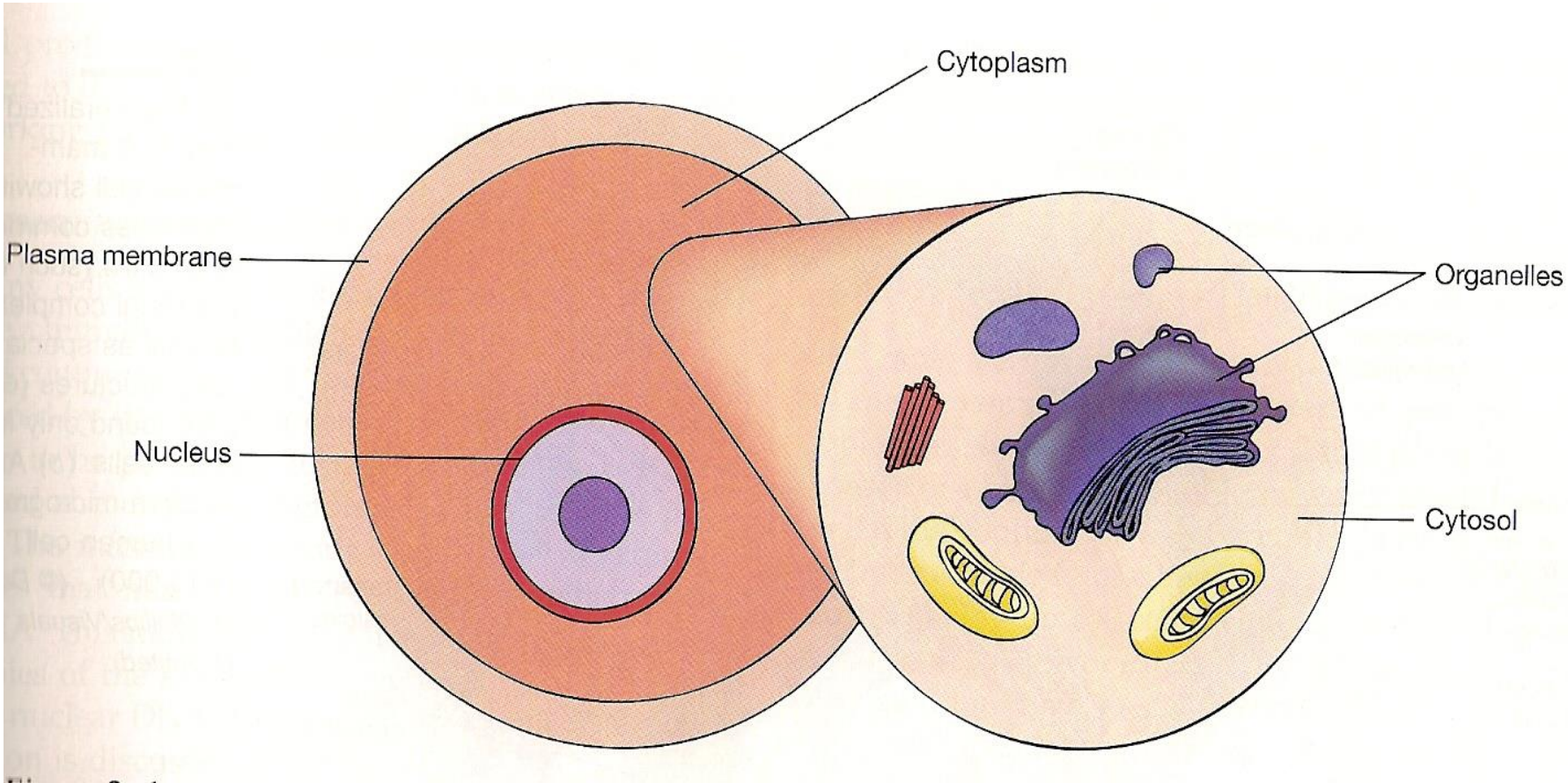
No nucleus

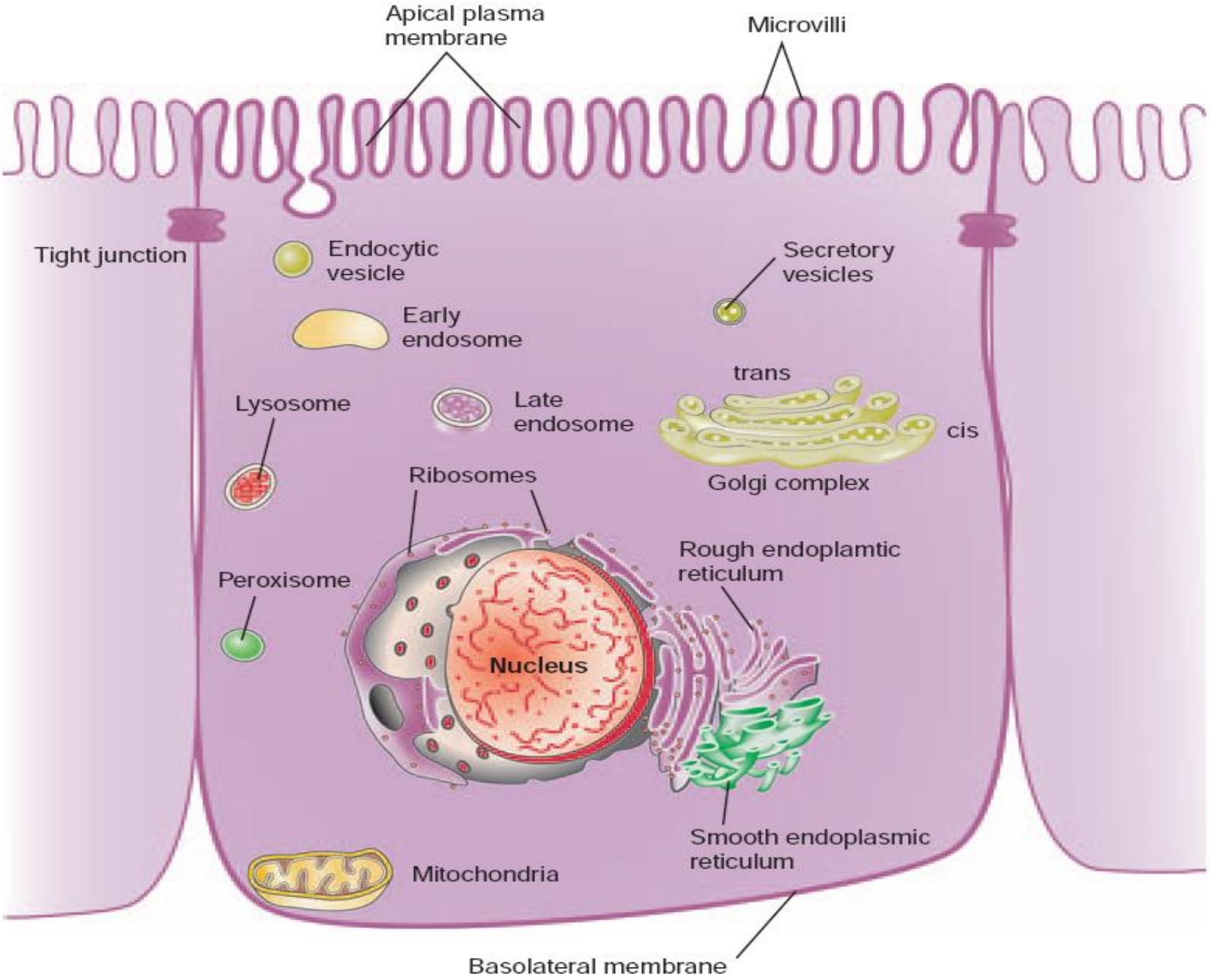
- **Eukaryotes:**
  - Genetic material mostly in nucleus
  - Larger (10-100 μ m)
  - Cytoskeleton present
  - Membrane-bound organelles present
  - RNA synthesis in nucleus, protein synthesis in cytoplasm

Cell Structures and Function

3 principal parts:

- Plasma (cell) membrane
- Cytoplasm (contains organelles)
- Nucleus




Apical plasma membrane
Microvilli
Tight junction
Endocytic vesicle
Secretory vesicles
Early endosome
trans
Lysosome
Late endosome
cis
Golgi complex
Ribosomes
Rough endoplamtic reticulum
Peroxisome
Nucleus
Smooth endoplasmic reticulum
Mitochondria
Basolateral membrane

Generalized cell

Components of cells

1. A typical cell has two parts: nucleus and cytoplasm.
2. Nucleus is separated from the cytoplasm by a nuclear membrane
3. The cytoplasm is separated from the surrounding fluid (ECF) by the plasma membrane

The different substances that make up the cell are collectively called

protoplasm. Protoplasm is composed of five basic substances:

1. Water
2. Electrolytes
3. Proteins
4. Lipids
5. Carbohydrates.

The plasma membrane

- It is a sheet-like structure that surrounds (encloses) the cell, separating the cellular contents from the ECF.
- It is entirely composed of proteins and lipids in a ratio of 55:43 respectively, and only 3% of carbohydrates.

Percent proportion:

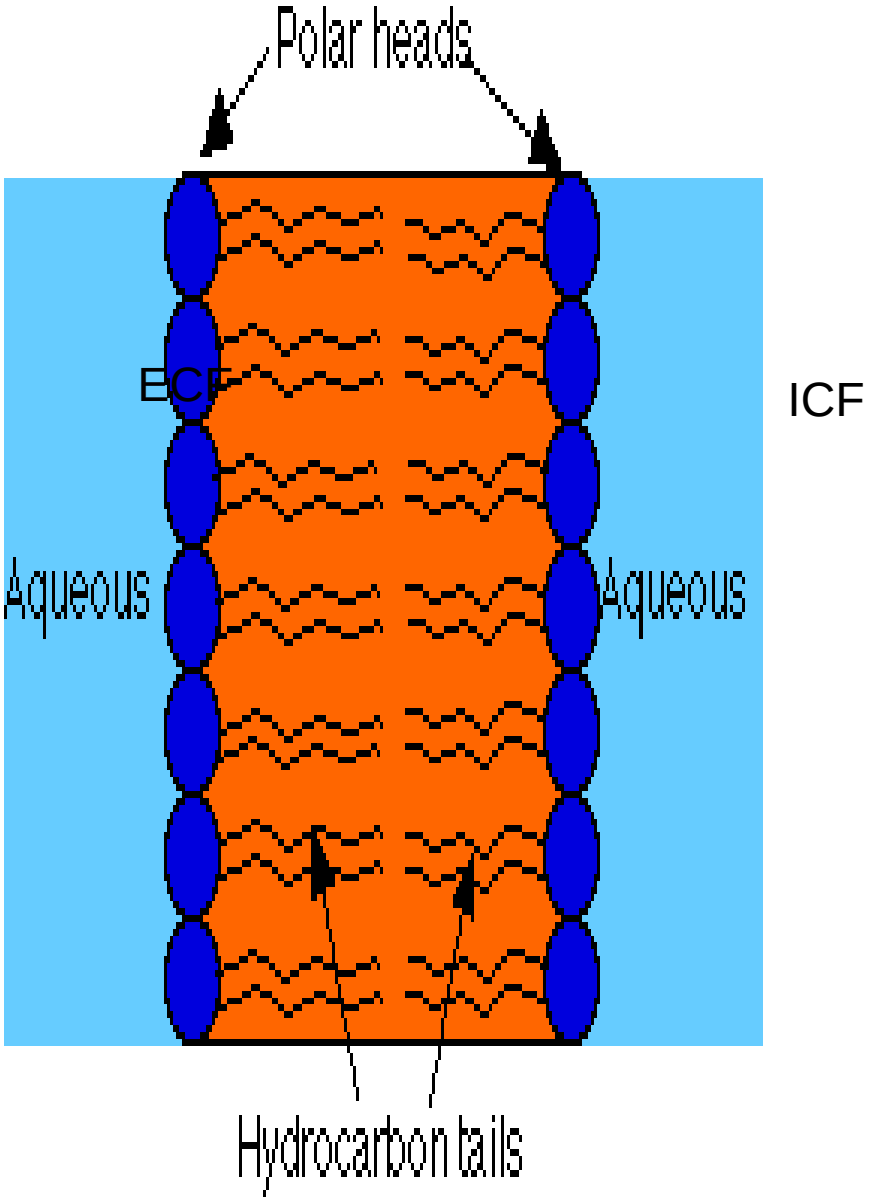
1. **Proteins: 55 %**
2. **Lipids: 42 %** →
   - Phospholipids ⇒ 25 %
   - Cholesterol ⇒ 13 %
   - Neutral tats ⇒ 4 %
3. **Carbohydrate: 3 %**

★ The level of cholesterol determines rigidity of the membrane.

Function of the plasma membrane

1. Separates cellular contents from the ECF
2. Regulates the passage of substances in and out.
    - It is semi-permeable allowing some substances to pass through it excluding others. This creates unequal distribution of ions on both sides of the membrane.
3. It provides receptors for NTs, hormones and drugs.
4. It is a means of cell to cell contact.
5. Plays an important role in the generation and transmission of electrical impulse in nerves and muscle.
6. Involved in the regulation of cell growth and proliferation.

Lipid component of the cell membrane

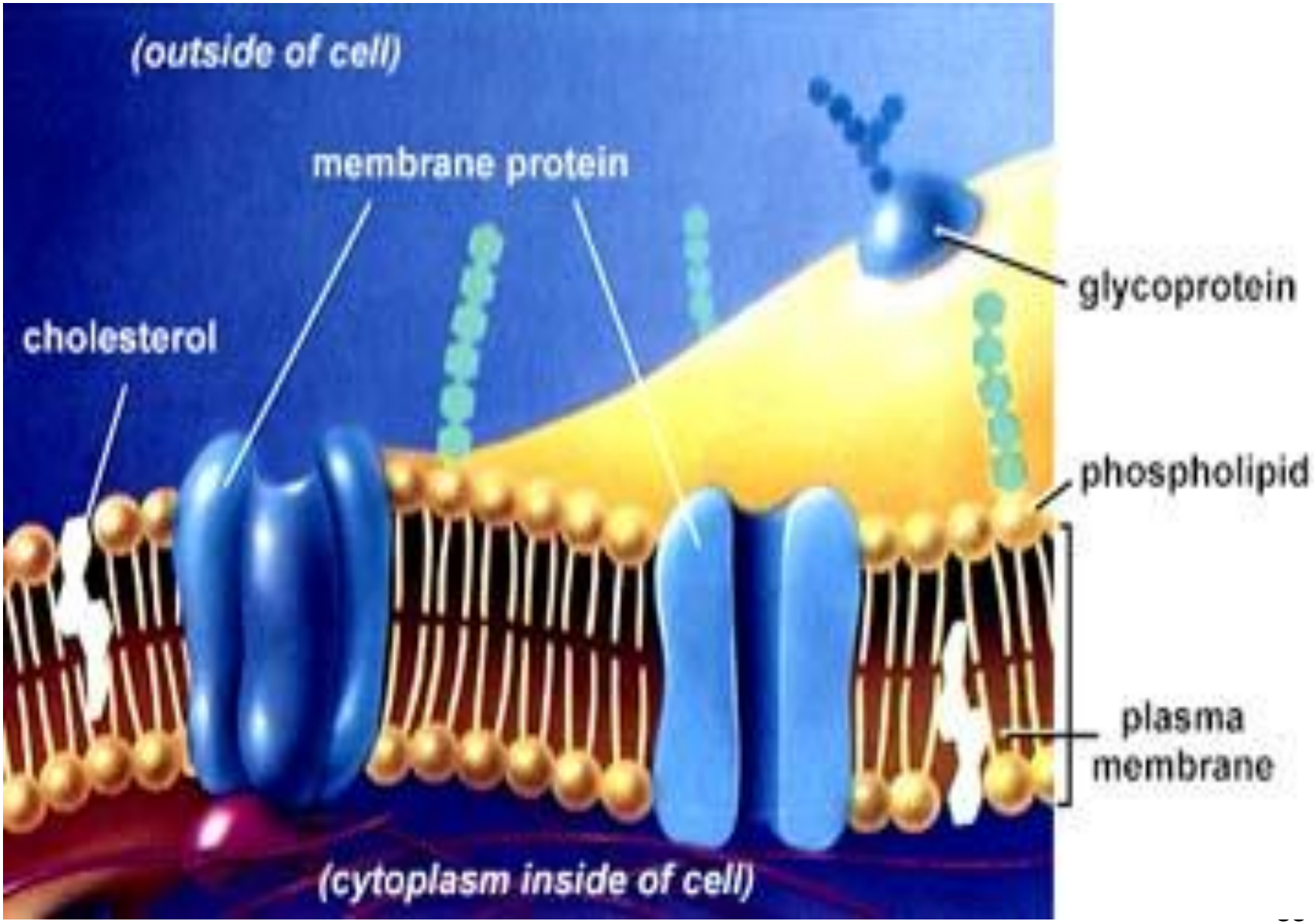


- ✓ A plasma membrane is a fluid in its nature, according to the fluid Mosaic model of the membrane.
- ✓ The cell membrane consists of an organized arrangement of proteins, lipids and CHOs
- ✓ The major lipids are phospholipids such as **phosphatidyl choline** and **phosphatidyl-ethanolamine**, and **cholesterol**.
- ✓ Lipids form the basic structure of the membrane.
- ✓ The lipid molecules are arranged in two parallel rows, forming a lipid bilayer.

The plasma membrane…

- It is believed that globular proteins are embedded in the lipid bilayers and that these proteins participate in the transport of lipid-insoluble particles through the plasma membrane, some integral proteins act as **carriers and channels**.
- The cell membrane is surrounded by a cell coat or glycocalyx, which is made up of glycolipids and glycoproteins.
- It uses the site of hormonal **receptors and antigenic activity** in blood groups.
- The phospholipids component is organized into a **double layer** with their hydrophobic (tail) and polar (hydrophilic) heads.

The plasma membrane…



The plasma membrane…

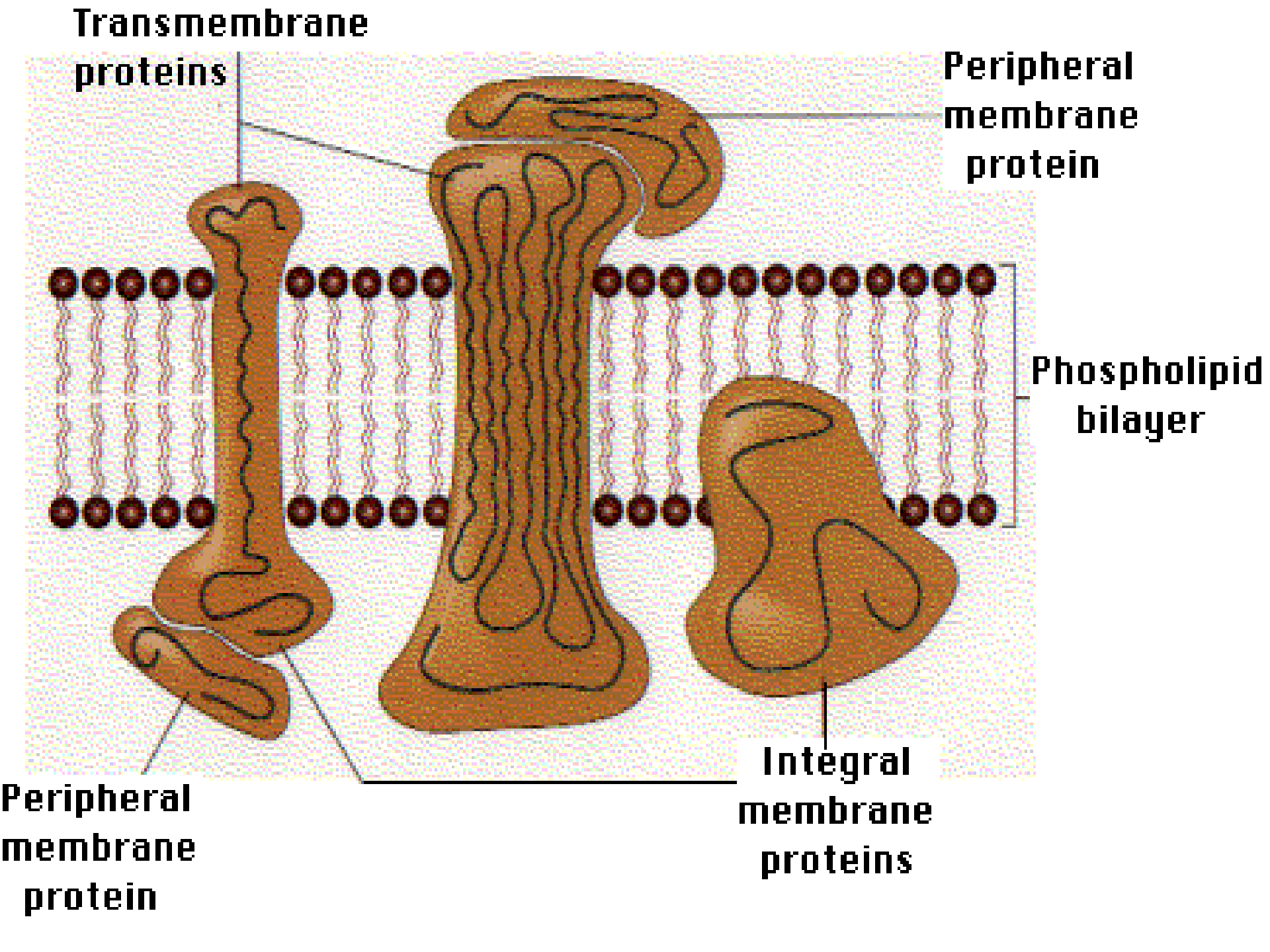
- The physical orientation of the lipid bilayer structures is that the hydrophilic ends of the lipid molecules line up facing the ICF and ECF.
- The hydrophobic tails of the molecules face each other in the interior of the bilayer.
- The lipid bilayer portion of the cell membrane is impermeable to water and water soluble substances such as ions, glucose, urea and others.
- Fat soluble substances such as O_2, CO_2, N_2, alcohol and drugs can diffuse through the membrane.

Membrane proteins

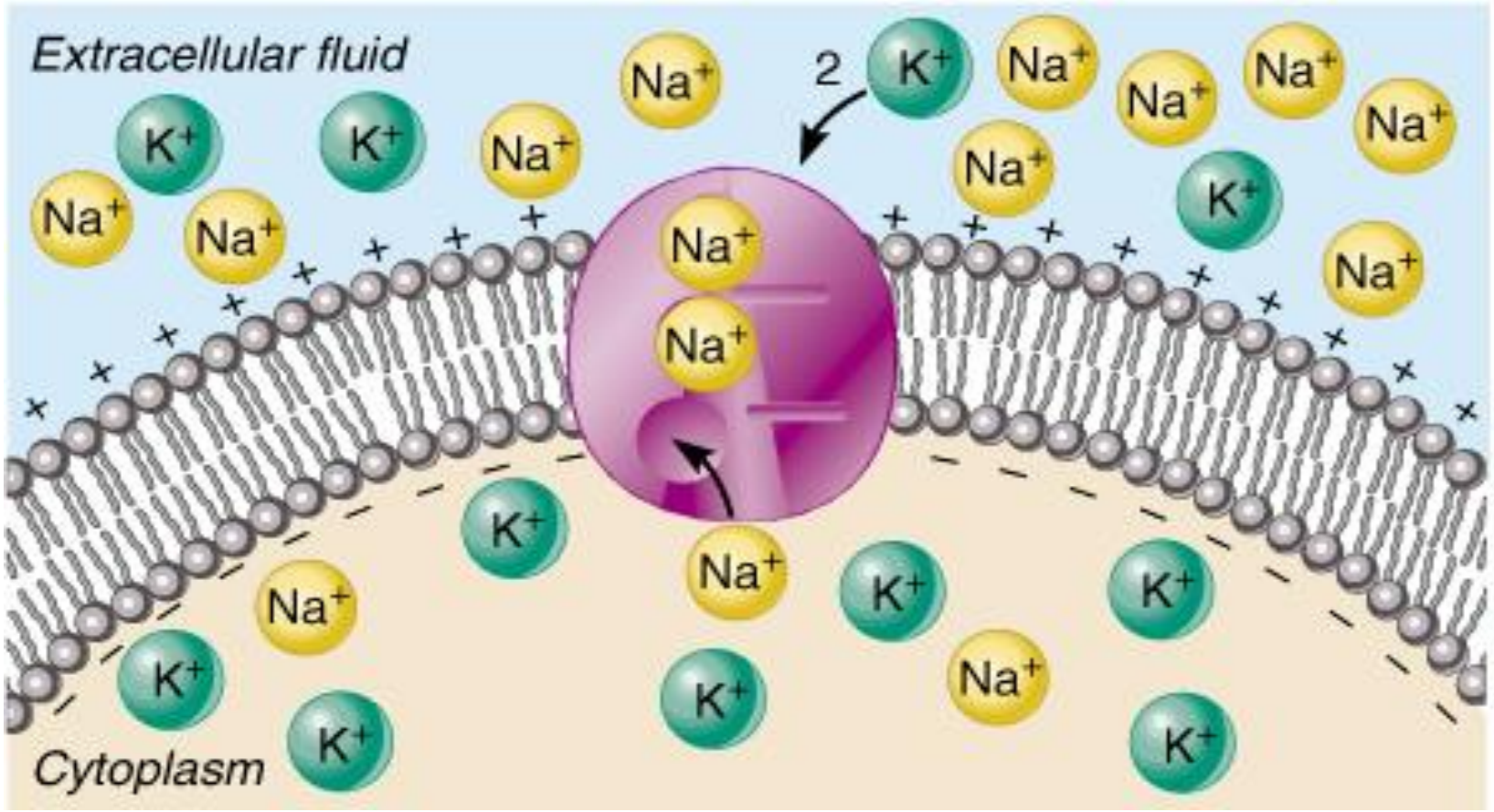
Integral and Peripheral proteins

A. **Integral or intrinsic proteins:** interdigitated in the hydrophobic center of the lipid bilayer.

- Transmembrane proteins are integral proteins that span the entire bilayer.
- Transmembrane proteins serve as:
  1. Channels through which ions pass
  2. Carriers which actively transport materials across the bilayer e.g. glucose
  3. Pumps which actively transport ions
  4. Receptors for neurotransmitters and hormones
- Integral proteins that are present only on one side of the membrane, serve primarily as enzymes.


Transmembrane proteins
Peripheral membrane protein
Phospholipid bilayer
Peripheral membrane protein
Integral membrane proteins

Membrane proteins: channels



Membrane proteins (cont'd)

B. Peripheral or extrinsic proteins: bind to the hydrophilic polar heads of the lipid or on integral proteins.

- Peripheral proteins that bind to the intracellular surface contribute to the cytoskeleton.
- Peripheral proteins that bind to the external surface contribute to the glycocalyx (a cell coat that is composed of glycolipids and glycoproteins to cover the cell membrane)
- Extrinsic protein not use for Channel ,Carrier but use as receptor & enzymes

Membrane carbohydrates

- Attached invariably on the outside surface of the membrane, binding with protruded integral proteins and lipid, they form glyco-proteins and glyco-lipids (glycocalyx).
- They play a role in
  1. Immune reaction (antigenical importance)
  2. Cell to cell attachment
  3. Act as receptors for NTs, hormones and drugs

Cytoplasm

- is the portion of the cell found between nucleus and cell membrane
- contains organelles and cytosol
- Cytosol is the fluid portion of cytoplasm
- Organelles are specialized compartments or subunit within a cell that has a specific function
- An organelle is usually separately enclosed within its own plasma membrane.

The nucleus

- The nucleus is the control center for the cells.
- It contains the genes, which are units of heredity.
- Chemically each gene consists of highly compressed DNA in the form of chromosomes
- Genes control cellular activity by determining the type of **proteins**, **enzymes, and other substances that are made by the cell**.
- The nucleus is also the site of RNA synthesis.

The nucleus (cont'd)

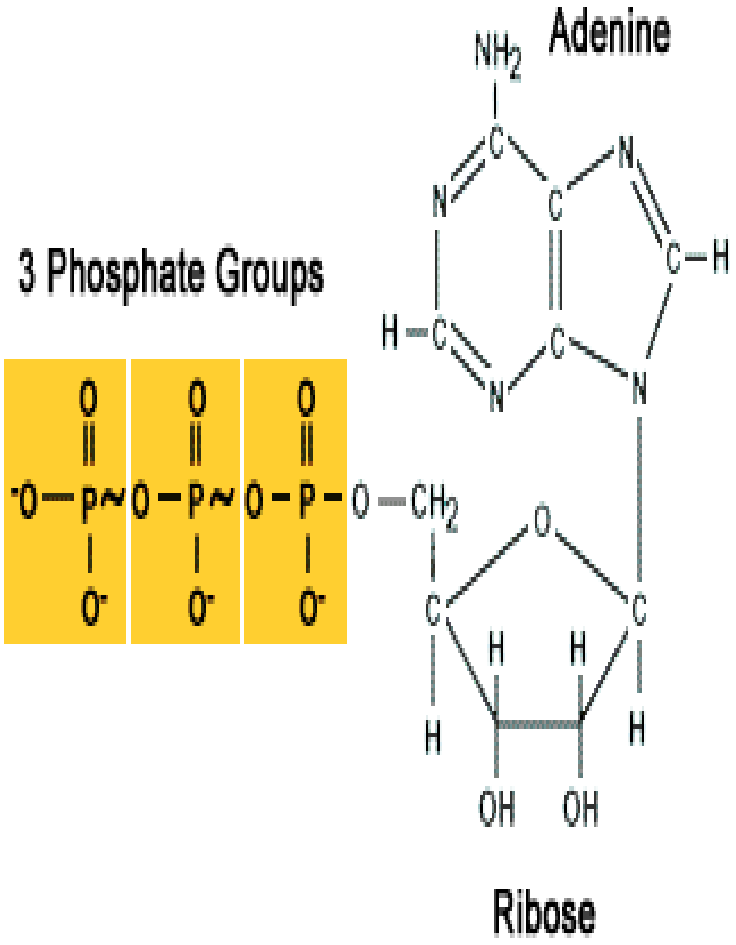
- There are three kinds of RNA
  - Messenger RNA (mRNA), which carries the instruction from DNA for protein synthesis to the cytoplasm
  - Ribosomal RNA (rRNA), which moves to the cytoplasm where it becomes the site of protein synthesis.
  - Transfer RNA (tRNA), serves as an amino acid transporter system within the cell for protein synthesis.
- Nucleotides are composed of nitrogen containing bases purine (A, G) and pyrimidin (C, T) as well as deoxyribose sugar conjugated by phosphate.

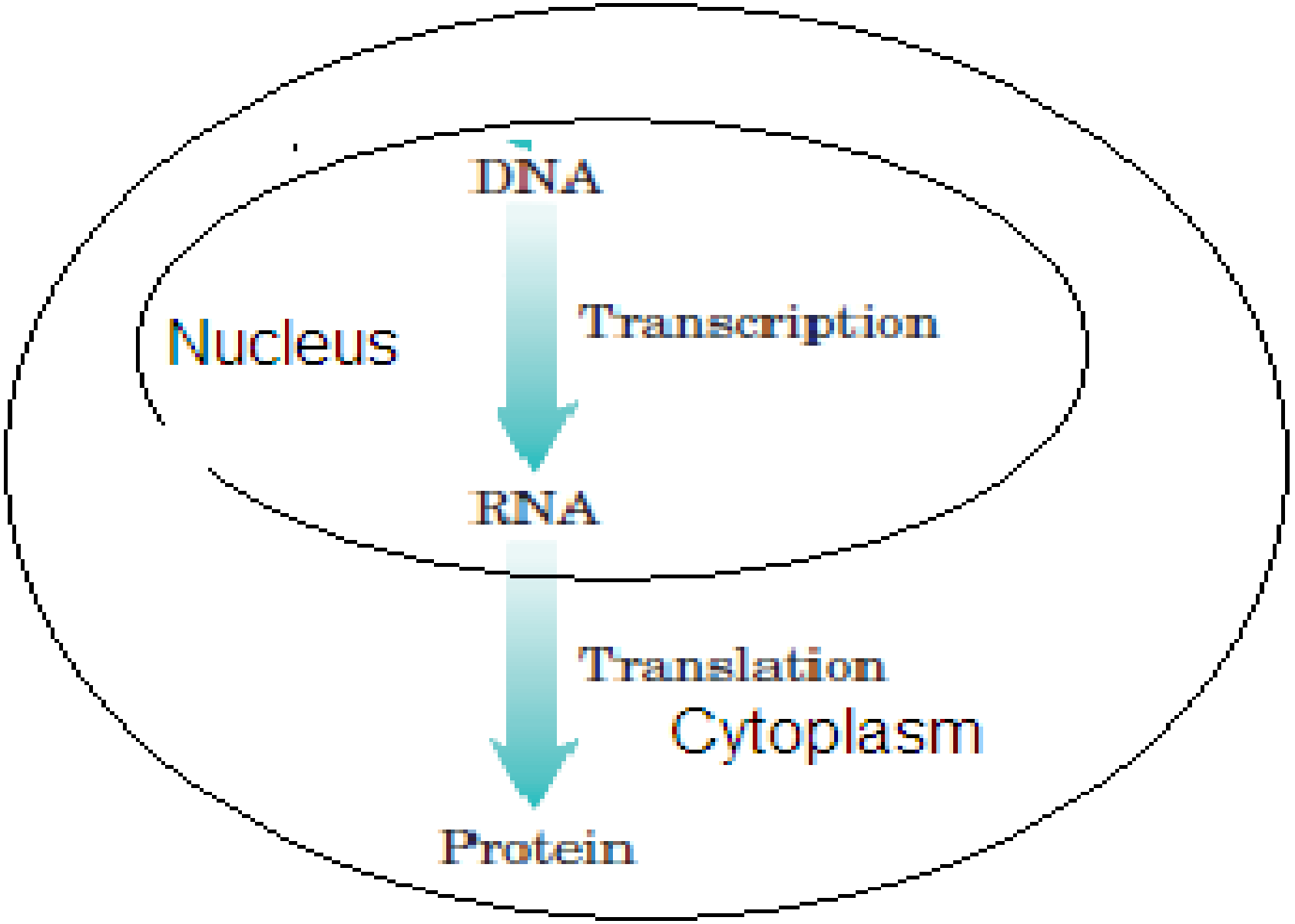
The nucleus (cont'd)

- In RNA, the pyrimidin base T is replaced by U and the 5-carbon sugar is ribose.
- In addition to the chromatin, the nucleus contains one or two round bodies called **nucleoli for** rRNA synthesis.
- The nuclear contents are surrounded by a double walled **nuclear membrane**.
- The pores present in this membrane allow fluids, electrolytes, RNA, and other materials to move between the nuclear and cytoplasmic comportments.

Function of nucleotides

1. Building units of nucleic acid DNA, RNA
2. High energy molecules (ATP, GTP)
3. Biosynthetic mediators (UDP-glycogen)
4. Regulator of chemical reaction in the cell e., g,. cAMP
5. Act as coenzyme (NAD, FAD)




DNA
Nucleus
Transcription
RNA
Translation
Cytoplasm
Protein

Cellular organelles

- inner organs of the cell. These include the ribosomes, endoplasmic reticulum (ER), Golgi apparatus, mitochondria, lysosomes, peroxisomes and the cytoskeletal system (microtubules and microfilaments).

Ribosomes:

- Are the sites of protein synthesis in the cell
- Small particles composed of rRNA and proteins
- Found in two forms: attached to the wall of ER or as free ribosomes.

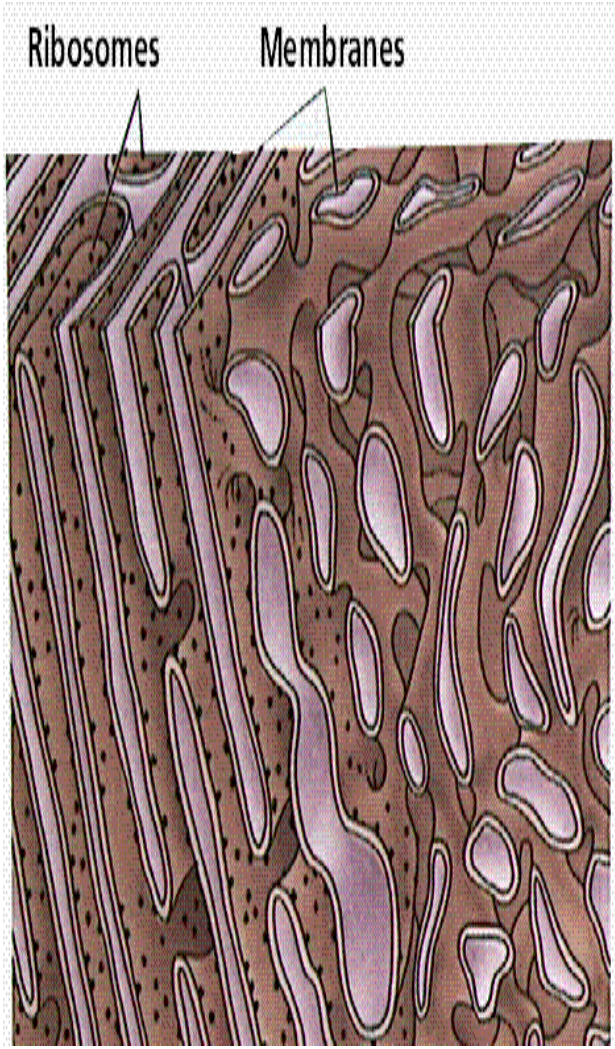
- Free ribosomes are found in two forms
  - Scattered in the cytoplasm
  - Clustered (aggregated) to form functional units called polyribosomes

Endoplasmic Reticulum (ER)

- It is an extensive membranous structure that connects various parts of the inner cell.
- ER is also connected with the nuclear membrane.
- There are two types of ER: rough ER and smooth ER.
- The rER is associated with ribosomes.
- The function of rER is to segregate proteins that are being exported from the cell.
- rER is the site of protein synthesis

Endoplasmic reticulum (ER)

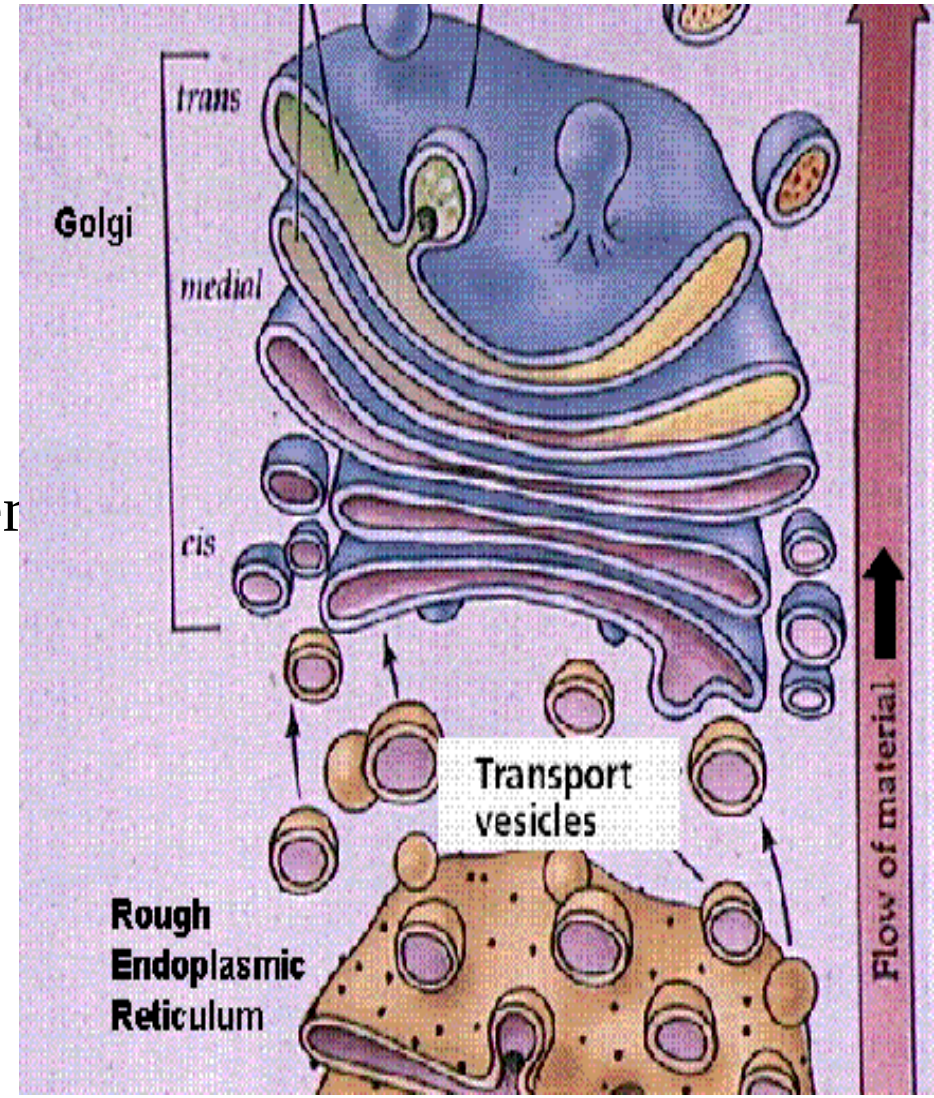
- The sER is free of ribosome.
- Function of sER varies in different cells.
- The sarcoplasmic reticulum of skeletal and cardiac muscle cells are forms of sER.
- Calcium ions needed for muscle contraction are stored and released from the sarcoplasmic reticulum of muscle cells.
- In the liver, the sER is involved in glycogen storage and drug metabolism.
- ER can synthesize a group of drug metabolizing enzymes called microsomal system.
- Function of sER:-
  1. Glycogen storage
  2. Calcium storage
  3. Lipid biosynthesis
  4. Drug metabolism (detoxify)



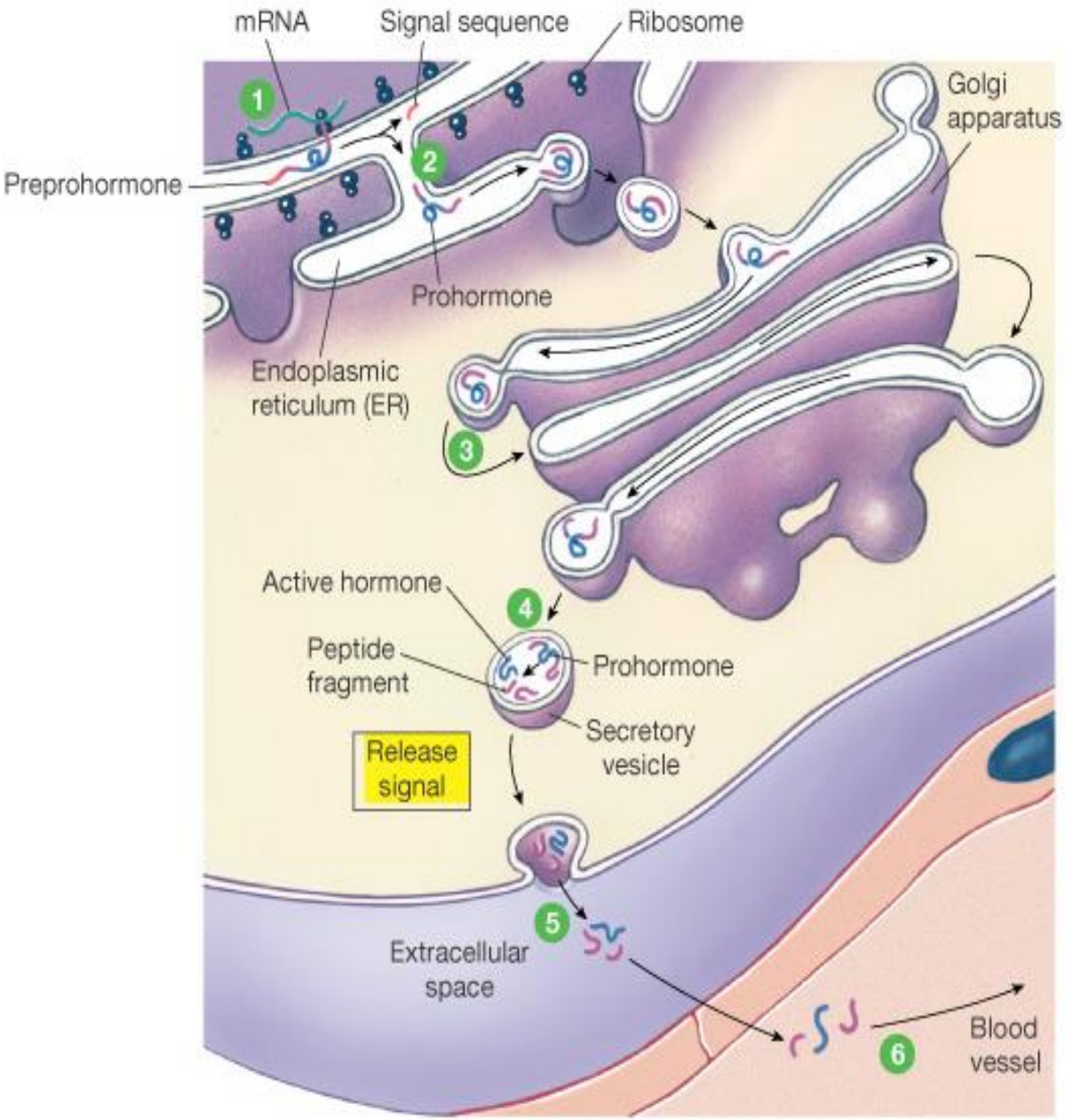
Endoplasmic reticulum (rER and sER)

Golgi Complex

- The Golgi complex consists of flattened membranous saccules and cisterns that communication with the ER and acts as a receptacle for hormones and other substances that the ER produces.
- It then modifies and packages these substances into secretory granules.



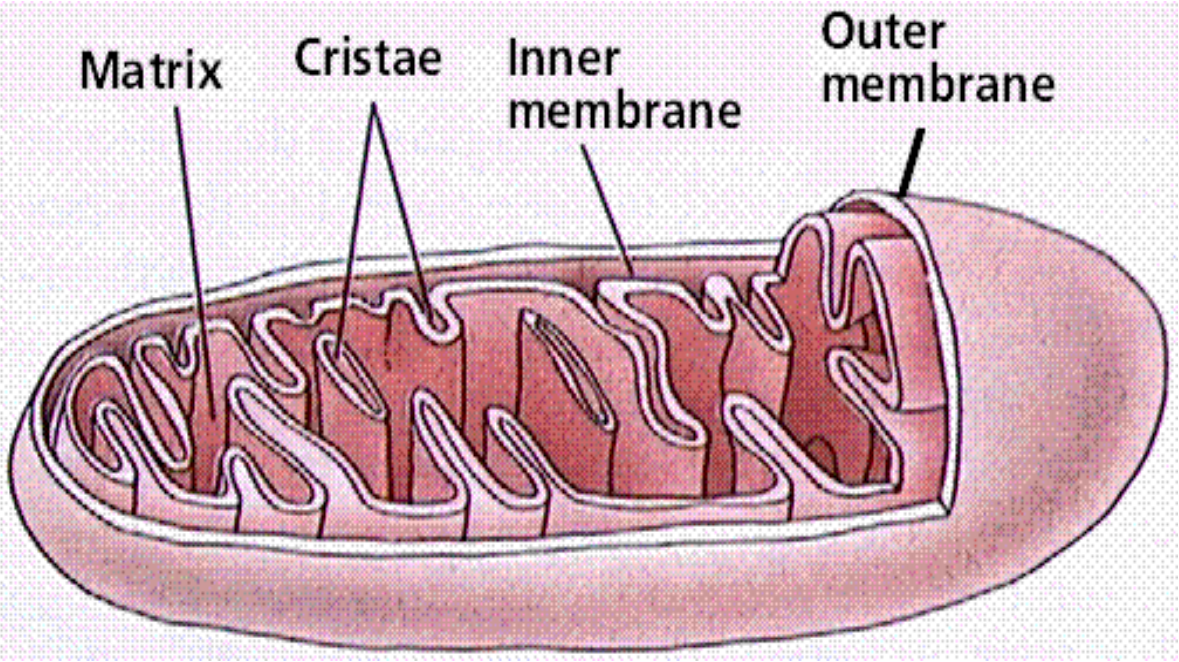
Rough ER and Golgi complex



1. Messenger RNA on the ribosomes of the ER binds amino acids into a peptide chain called a **preprohormone**. The chain is directed into the ER lumen by a **signal sequence** of amino acids.
2. Enzymes in the ER chop off the signal sequence, creating an inactive **prohormone**.
3. The prohormone passes from the ER through the Golgi apparatus.
4. Secretory vesicles containing enzymes and prohormone bud off the Golgi. The enzymes chop the prohormone into one or more active peptides plus additional peptide fragments.
5. The secretory vesicle releases its contents by exocytosis into the extracellular space.
6. The hormone moves into the circulation for transport to its target.

Mitochondria

- The mitochondria are literally the “power plants” of the cell, capable of producing the energy rich compound ATP, which is required for various cellular activities.
- The mitochondria require oxygen to produce energy (ATP) from food stuffs.

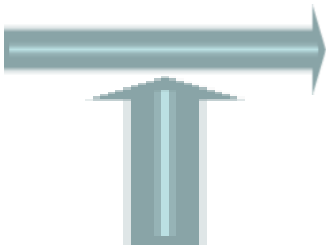


Lysosomes

- Lysosomes are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm.
- The lysosomes provide an intracellular digestive system that allows the cell to digest
  - Damaged cellular structures,
  - Food particles that have been ingested by the cell, and
  - Unwanted matter such as bacteria.
- It is surrounded by a typical lipid bilayer membrane and is filled with large numbers of small granules 5 to 8 nanometers in diameter, which are protein aggregates of as many as 40 different hydrolase (digestive) enzymes.
- The membrane surrounding the lysosome prevents the enclosed hydrolytic enzymes from coming in contact with other substances in the cell and, therefore, prevents their digestive actions.

Peroxisomes

- Also called small bodies
- Spherical in shape
- Surrounded by single membrane
- Have protective role in that they secrete chemical that converts harmful substances into harmless
- e.g., Catalase produced by peroxisomes change H2O2 to H2O and O2

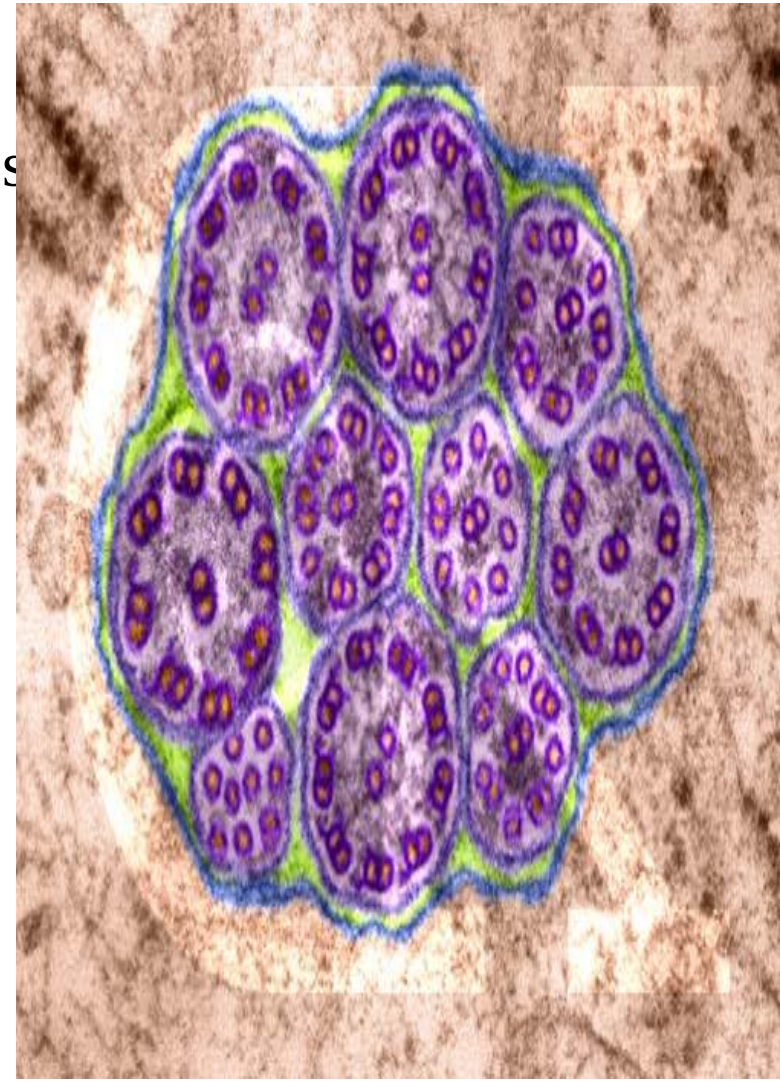


Cytoskeletal system of the cell

- They are microfilaments and microtubules, rigid threadlike structures dispersed through out the cytoplasm.

Function of cytoskeletal system:

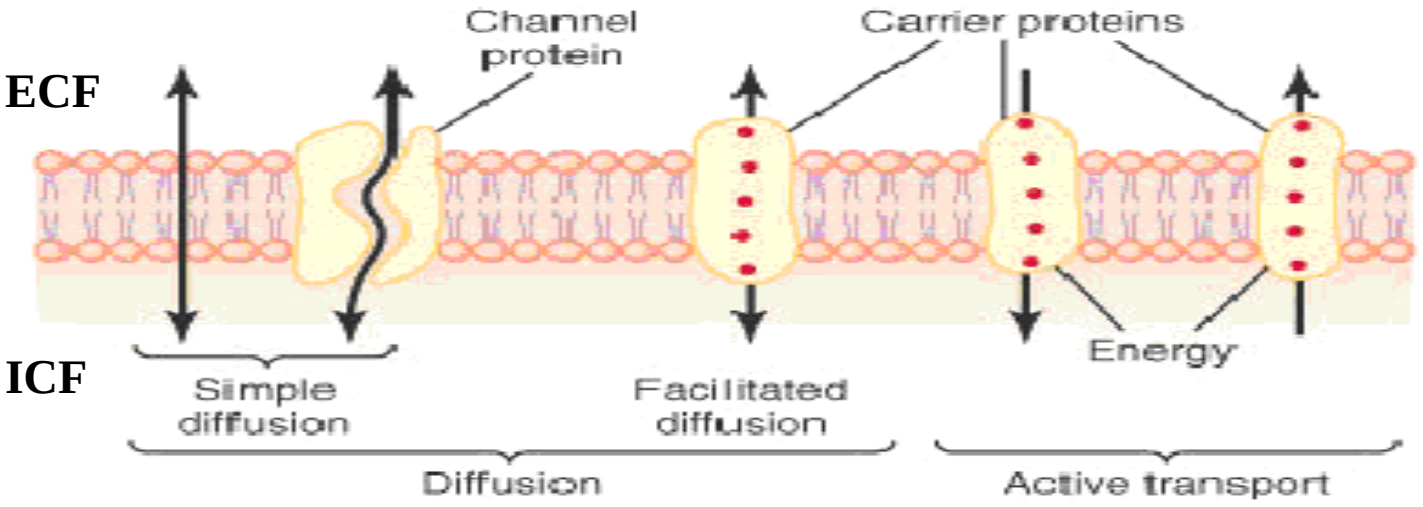
1. Maintain shape of the cells. eg. Neurofibrils in axon
2. Serve as a transport system for the movement of compounds and organelles within the cell. eg axoplasmic transport
3. Construct the mitotic spindle eg. Centroils
4. Provide for the support and movement of cilia and flagella
5. Cell to cell contact: to fasten cell membranes together



Microtules organized as 9+2 doublets

Transport through the cell membrane

- Substances are transported through the cell membrane by:
  1. Simple diffusion
  2. Osmosis
  3. facilitated diffusion
  4. active transport (1° and 2°) and
  5. vesicular transport mechanisms.
     - ✓ Endocytosis
     - ✓ Exocytosis



Simple Diffusion

- Diffusion is passive movement of substances down their concentration gradient.

- Factors affecting the net rate of diffusion
  - Lipid solubility of the subs
  - Membrane permeability
  - Concentration difference or Pressure difference
  - Electrical potential difference of ions
- Membrane permeability is affected by
  - Membrane Thickness
  - Lipid solubility
  - No of ion channels per unit area
  - Temperature: ↑T = ↑ thermal motion of molecule⇨↑permeability
  - MW

Simple Diffusion

- Rate of diffusion is determined by the following factors summarized in the formula shown below.

- Rate of diffusion = $\frac{S.\ A.\ T.\ C}{\sqrt{D}\ MW}$

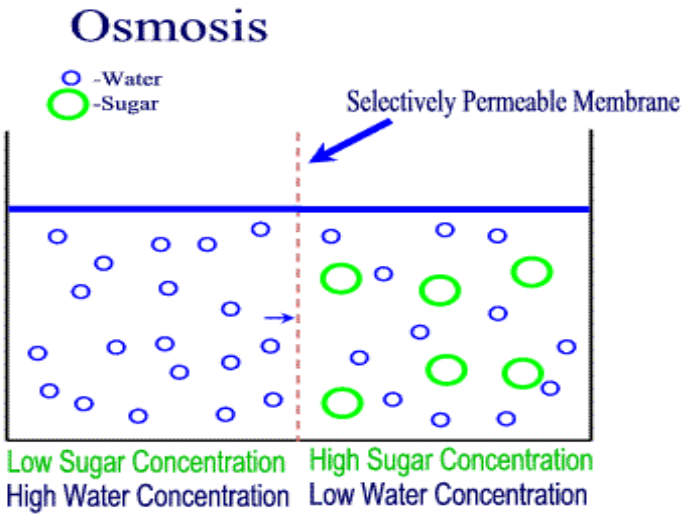
Where,

C	=	Change of concentration
S	=	Solubility in lipid
A	=	Surface area of the membrane
T	=	Temperature
D	=	Distance or membrane thickness
MW	=	Molecular wt of substances

- Examples: Substances that are transported by simple diffusion are CO_2, O_2, alcohol, lipid soluble drugs and ions through specific channels.

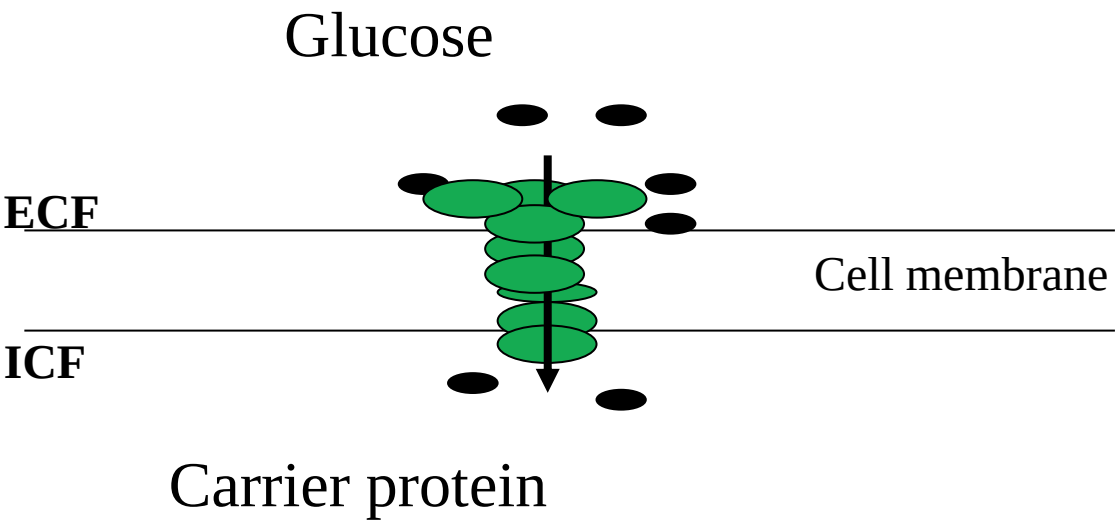
Osmosis

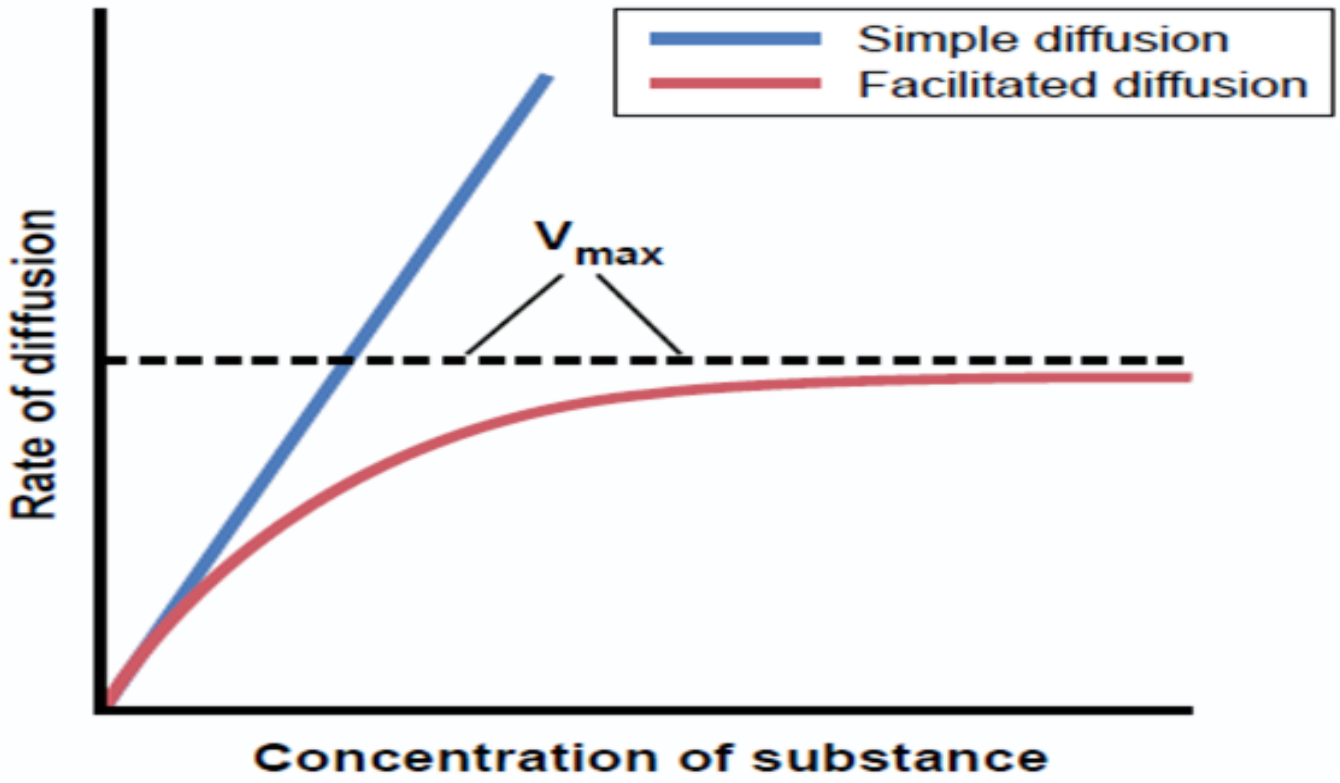
- It is the power of movement of H_2O from an area of higher amount of water to an area of lower amount of water through the semi permeable membrane.
- The direction of movement of water is governed by the amount of osmoticaly active particles (solutes).
- The pressure that opposes osmosis of water is called osmotic pressure
- H2O molecules have very small (0.3 nm) in diameter, so that they can not traverse the lipid bilayer simply. Instead they pass through specific water channels called **aquaporins**: Five aquaporins (AQ1….AQ5) have been identified in the body.



Facilitated diffusion

- Carrier mediated transport
- Carriers are saturable, do not need energy
- Transports substances down their concentration gradient
- Examples: transport of glucose, proteins. (Macromolecules)





Effect of concentration of a substance on rate of diffusion through a membrane by simple diffusion and facilitated diffusion. This shows that facilitated diffusion approaches a maximum rate called the V_{max}.

Active transport

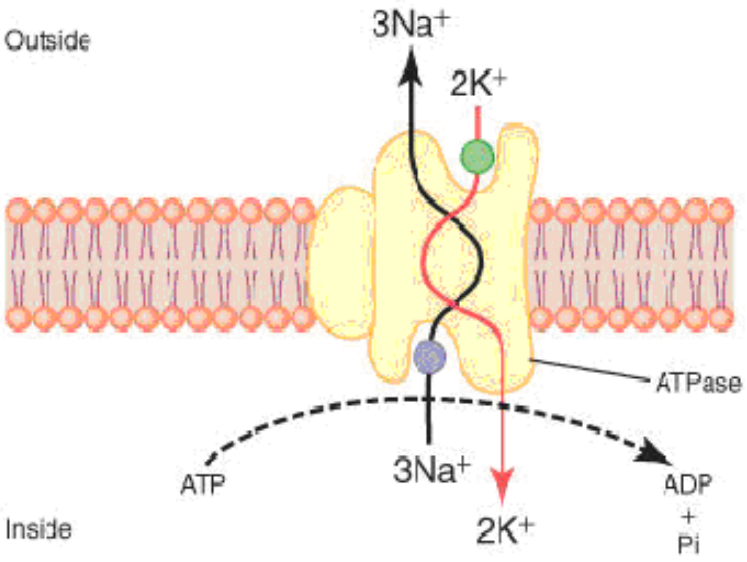
- Substances are transported against concentration, electrochemical gradient, up hill direction.
- Used for the transport of Na^+, K^+, Ca^{2+}, Fe^{2+}, H^+, Cl^-
- Consumes energy in the form of ATP

Primary active transport

- Carrier protein is involved
- Consumes energy from ATP
- Carrier protein is anti-porter

Common examples

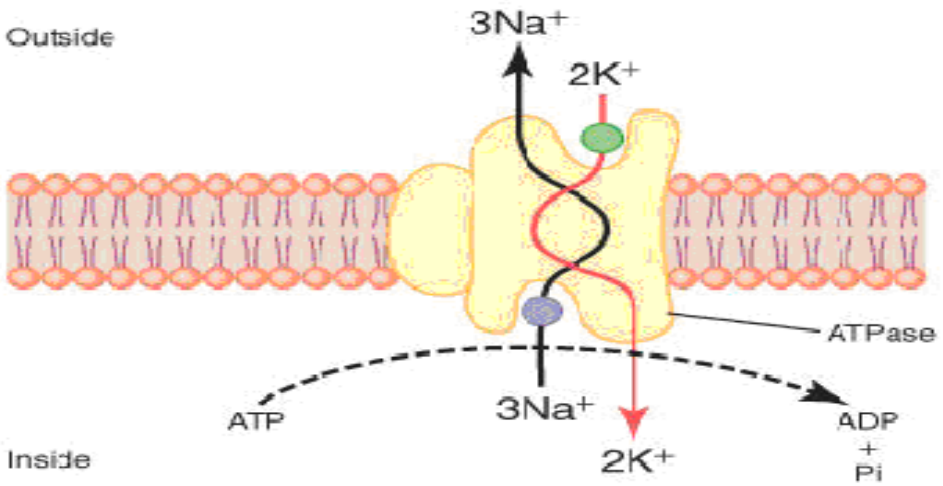
1. **Na+ - K+ ATPase**
2. **H+ - K+ ATPase**
3. **Ca2+ ATPase**



Active transport: Na+ - K+ ATPase

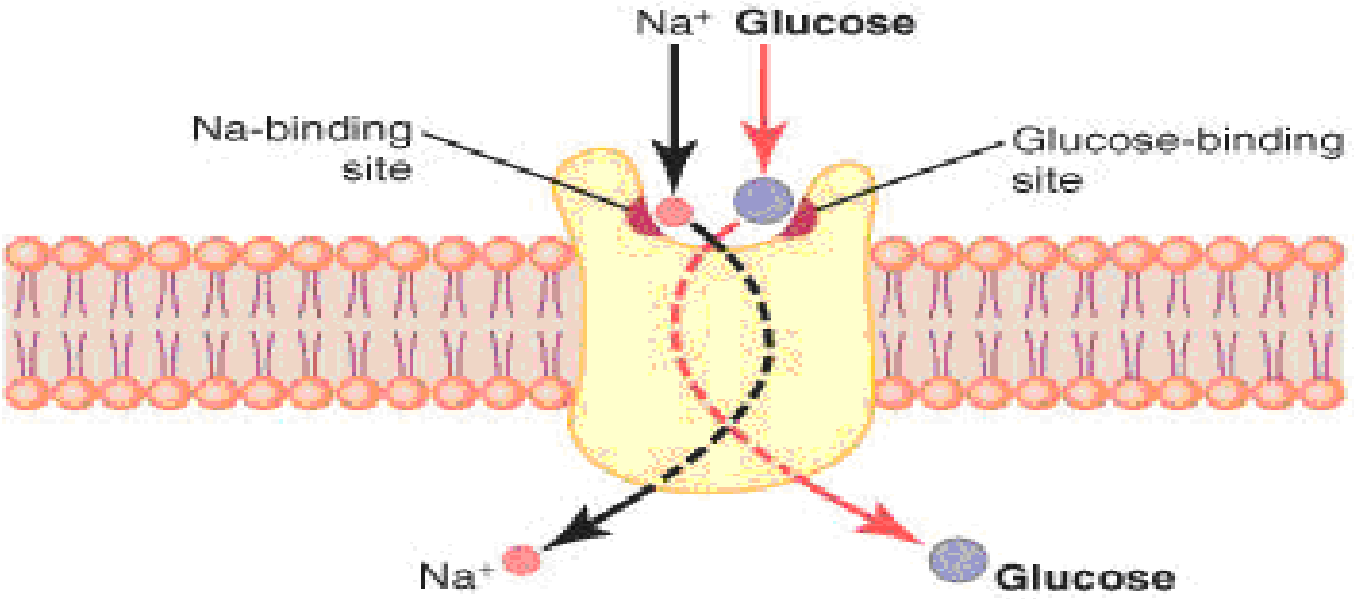
Na-K-Pump

- It pumps $3Na^+$ outward and $2K^+$ inward
- It maintains ↑Na outside and ↓K+ inside
- It maintains electropositive outside and electronegative, inside.
- Na+ - K+ pump is a carrier protein that is made up of two subunits. It has 3 binding sites for Na+ inside
- It has 2 binding sites for K+ on the outside
- It has ATPase activity inside. ATP = ADP + ---P + energy.
- Energy brings conformational change of the pump so that Na+ pumped outward and K+ inward.



Secondary active transport

- Carrier protein is involved
- Consumes energy, but not ATP
- Carrier protein is symporter

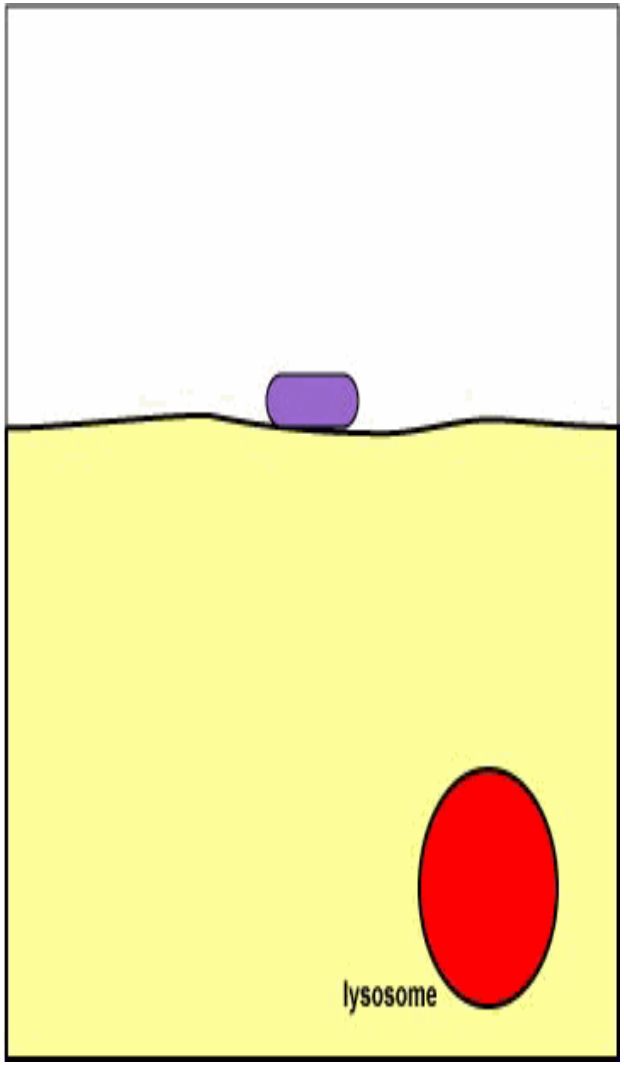


- **Uniport carriers:** Carry single substance to one direction
- **Antiport carriers:** Carry two substances in opposite directions
- **Symport carriers:** Carry two substances into the same direction

Vesicular transport

There are two types:

1. Endocytosis:
   Pinocytosis
   phagocytosis
2. Exocytosis



Cell Junctions (Intercellular Connections)

- Multicellular organisms (eg. human) exist because cells are able to bind to each other
- Cells may adhere either directly ***to each other in cell-cell adhesion*** or ***to extracellular components*** that provide a structural framework for cell binding
- The binding of cells to the ECM is termed cell matrix or cell-substratum adhesion
- Cell adhesion is not just a structural element that binds things together, it is also a highly dynamic process

Cell Junctions (Intercellular Connections)…

- Molecules that mediate cell adhesion are called **cell adhesion molecules** (CAMs)
- The majority, but not all, of CAMs belong to one of four protein families:
  - Cadherins
  - Immunoglobulin (Ig) family,
  - Selectins (**Selectins** are Calcium-dependent, Cell to Cell Surface Carbohydrate Binding Proteins**.**
  - Integrins (are receptors that mediate attachment between a cell and the tissues surrounding it,

Cell Junctions (Intercellular Connections)…

- CAMs are transmembrane proteins and have:

  1. An extracellular domain that participates in adhesion,
  2. A transmembrane domain that anchors the protein in the cell membrane,
  3. A cytoplasmic domain that mediates attachment to the cytoskeleton

- Adhesive binding by adhesion molecules may be either homophilic, meaning that the molecule binds to another of the same type, or heterophilic, meaning that binding is to a molecule of different type
- Cell-cell and cell-matrix junctions are diverse in structure and they do more than physical binding

Cell Junctions (Intercellular Connections)…

Four main functions of cell-cell and cell-matrix junctions are:

i . Anchoring junctions (adheres, desmosomes, hemidesmosomes)

ii. Occluding junctions (tight junctions)

iii.Channel forming junctions (gap junctions)

iv. Signal relaying junctions (chemical synapses and immunological synapses)

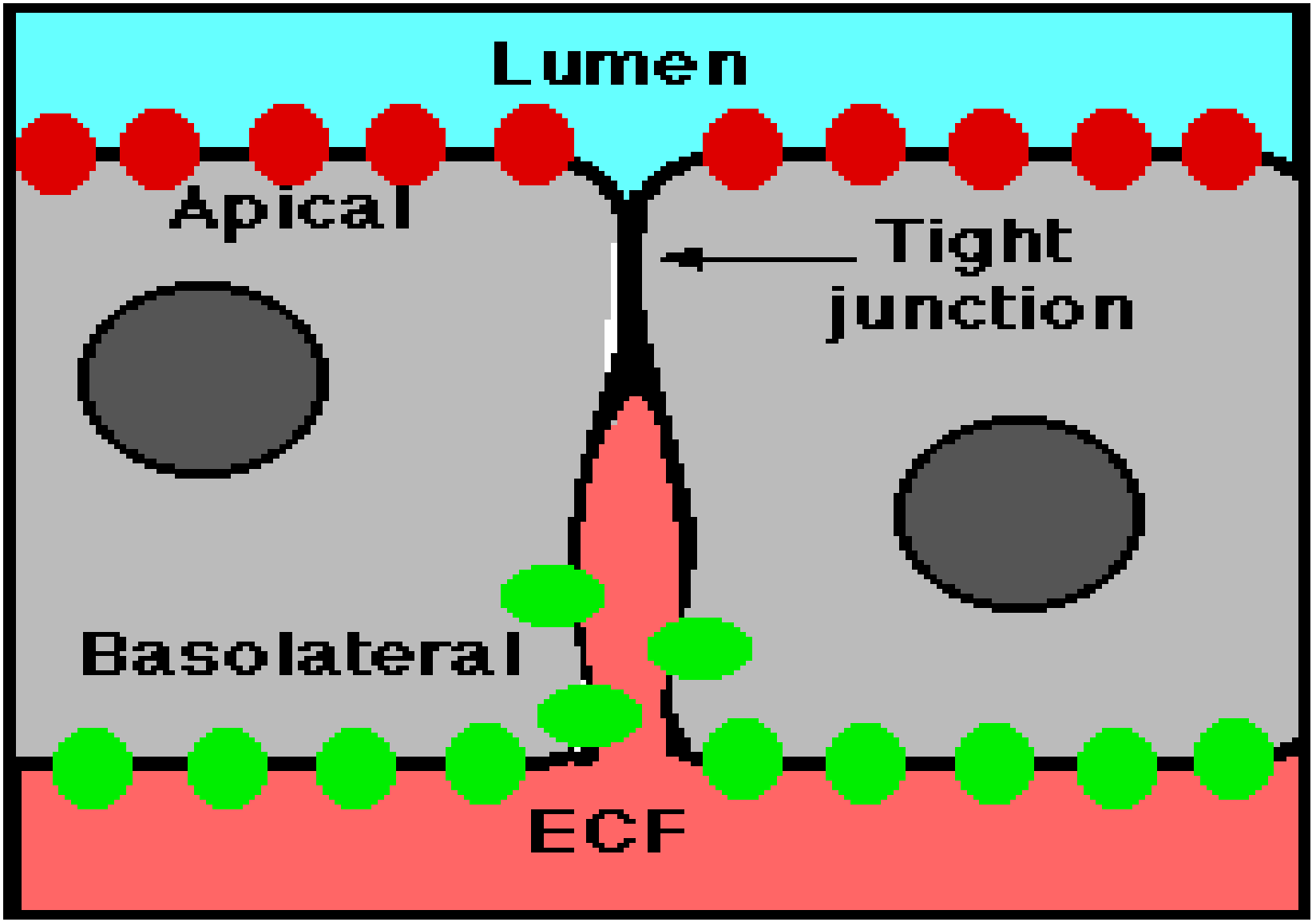
1. Tight Junctions

- Regulate paracellular permeability and cell polarity (spatial differences in the shape, structure, and function of cells).
- Are made up of ridges—half from one cell and half from the other—which adhere so strongly at cell junctions that they almost obliterate the space between the cells
- Surround the apical margins of the cells in epithelia such as the intestinal mucosa and the walls of the renal tubules
- Permit the passage of some ions and solute in between adjacent cells (paracellular pathway)
- Spaces between cells or, more precisely regulate the permeability of these spaces selectively

1. Tight Junctions…

- Prevent the movement of proteins in the plane of the membrane, helping to maintain the different distribution of transporters and channels in the apical and basolateral cell membranes that make transport across epithelia possible
- act as “fences” to separate the molecules in the apical and basolateral membranes, thus helping to maintain cell polarity
- The transmembrane components of tight junctions are the proteins occludin and claudin
- In the cytoplasm occludin and claudin interact with the actin cytoskeleton through attaching cell proteins

Tight junction….



2. Desmosomes…

- Are spotlike or punctate junction
- Maintain tissue integrity by providing ***strong intercellular adhesion*** and acting as a link between the cytoskeletons of adjacent cells
- are linked to keratin intermediate filaments inside the cell, then extend across the plasma membrane to associate with identical cadherins of an adjacent cell
- Abundant in skin, heart, neck of uterus where they are needed to withstand mechanical stress

3. Adherens junctions

- ☛ Provide strong mechanical attachments between adjacent cells
- ☛ The primary function of the adherens junction is ***cell-cell adhesion***
- ☛ *C*adherins linked to actin microfilaments in the cytoplasm extend out of the cell and bind to cadherins of an adjoining cell
- ☛ Found in the heart and epithelial tissue

4. Gap junctions (Communicating junctions)

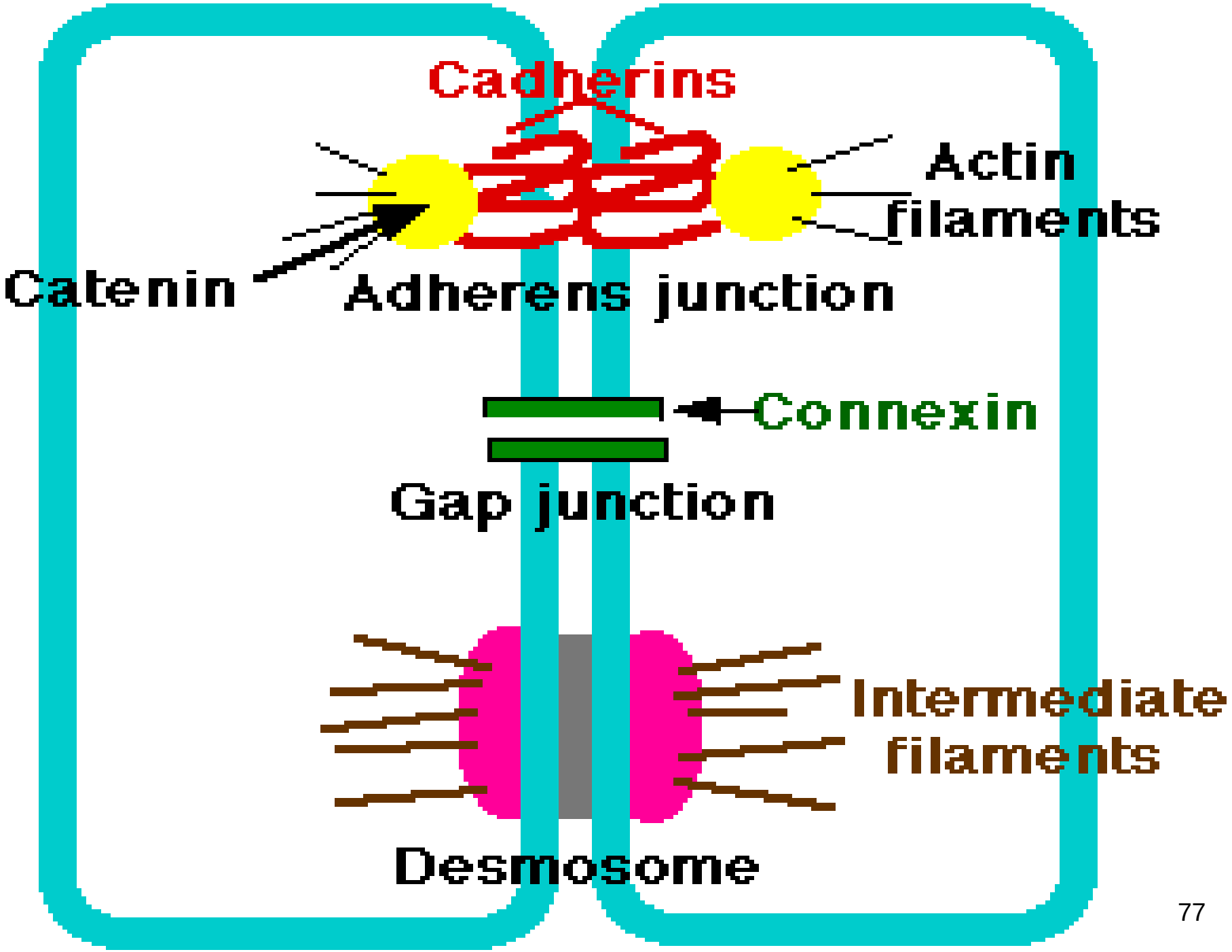
☛ The principal function of the gap function is cell-cell communication (exchange of small molecules and ions between the cells)

☛ Formed by two connecting transmembrane protein rings called **connexins (gap junction proteins)** embedded in cell membrane of adjacent cells

☛ The protein forms tiny fluid-filled tunnels that connect neighboring cells

☛ The tunnels allow passage of water, small solutes, but not macromolecules (proteins, nucleic acids) from one cell to the other

☛ In cardiac muscle and smooth muscle electrical impulse flows from cell to cell through gap junction

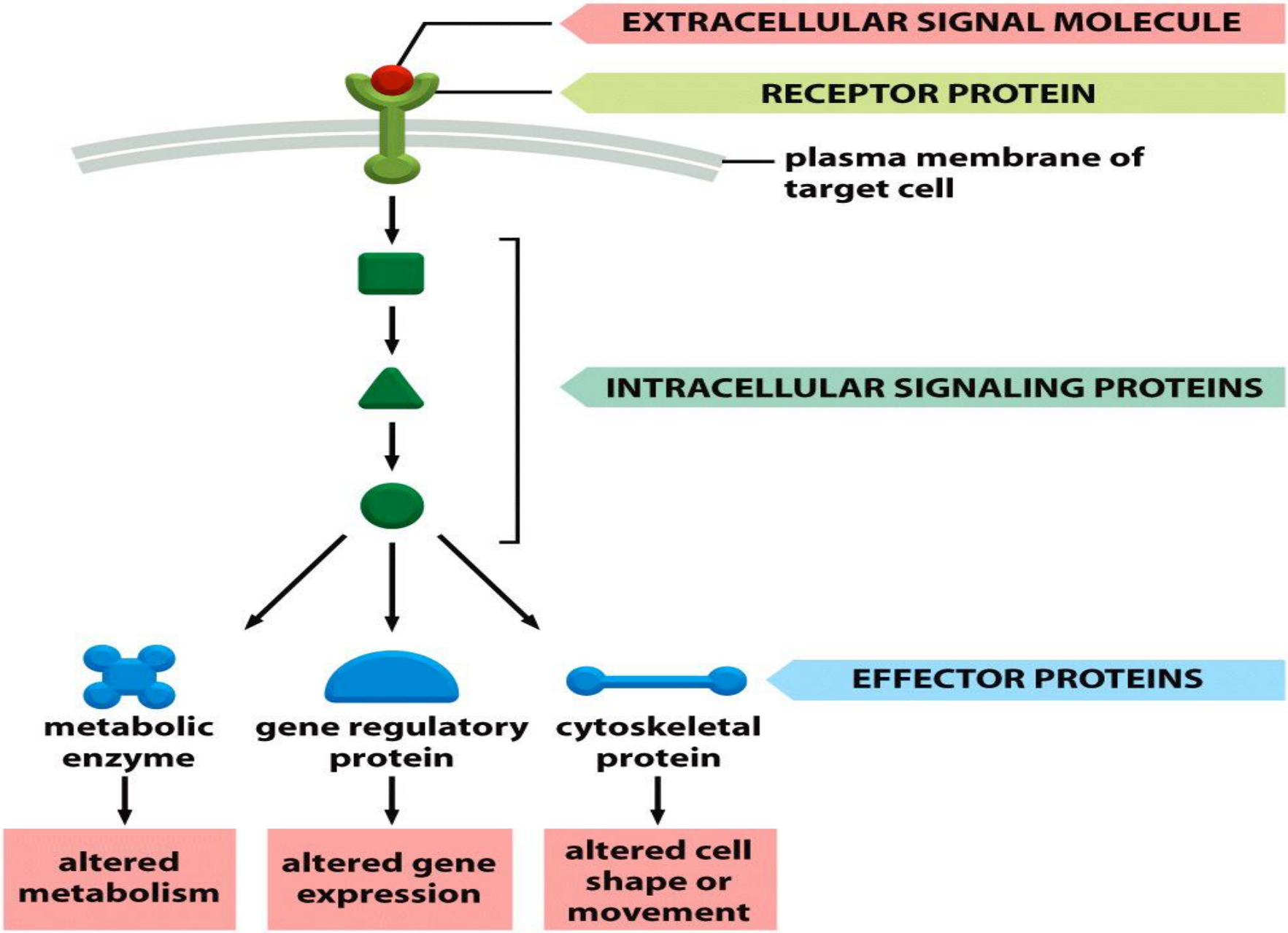

Cadherins
Actin
filaments
Catenin
Adherens junction
Connexin
Gap junction
Intermediate
filaments
Desmosome

INTERCELLULAR SIGNALING

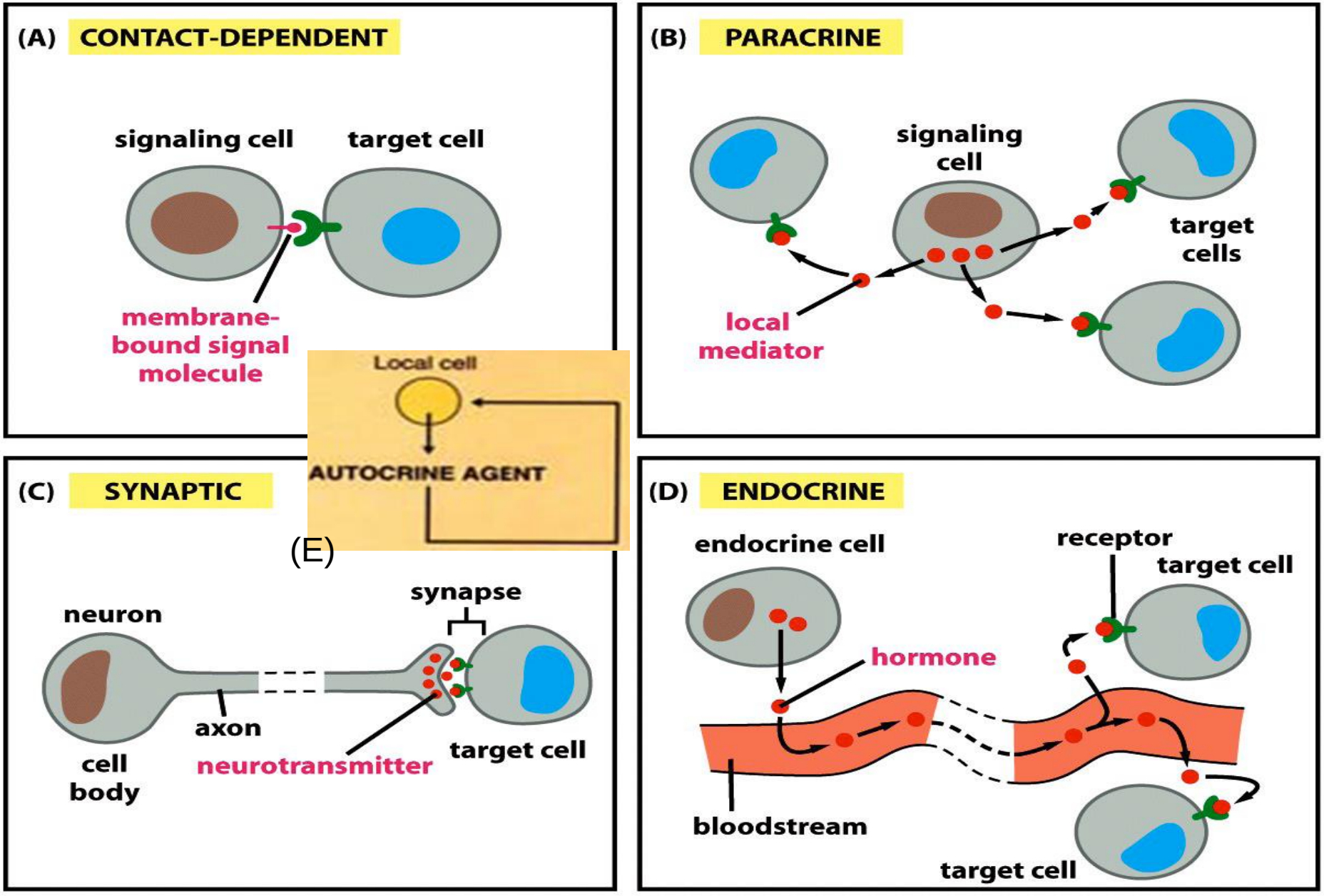
Cells need to be able to communicate to other cells and respond to environmental changes

For multi-cellular organisms, cell-cell communication is important

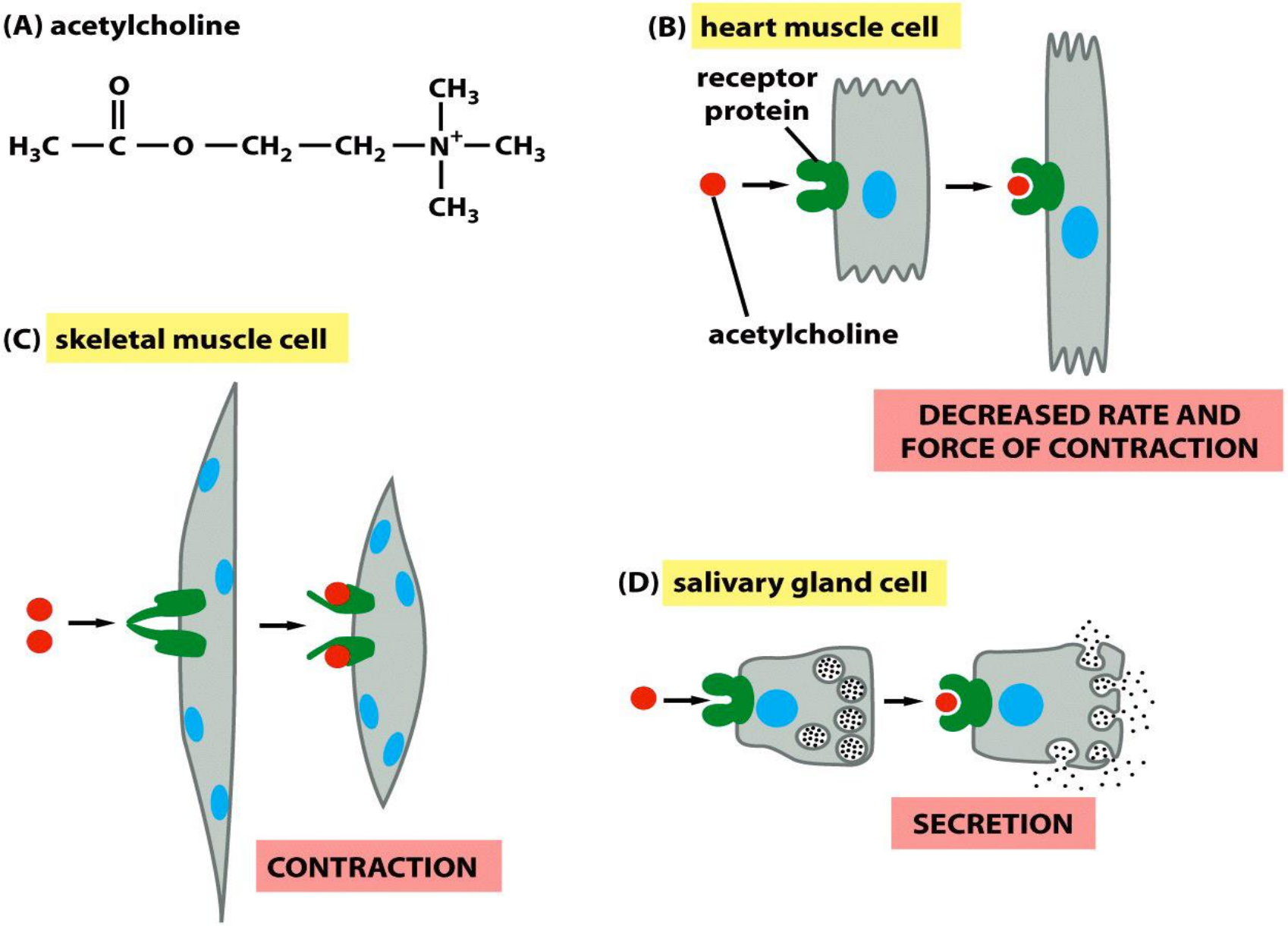
For unicellular organisms, they need to be able to respond to physical and chemical changes in their environment



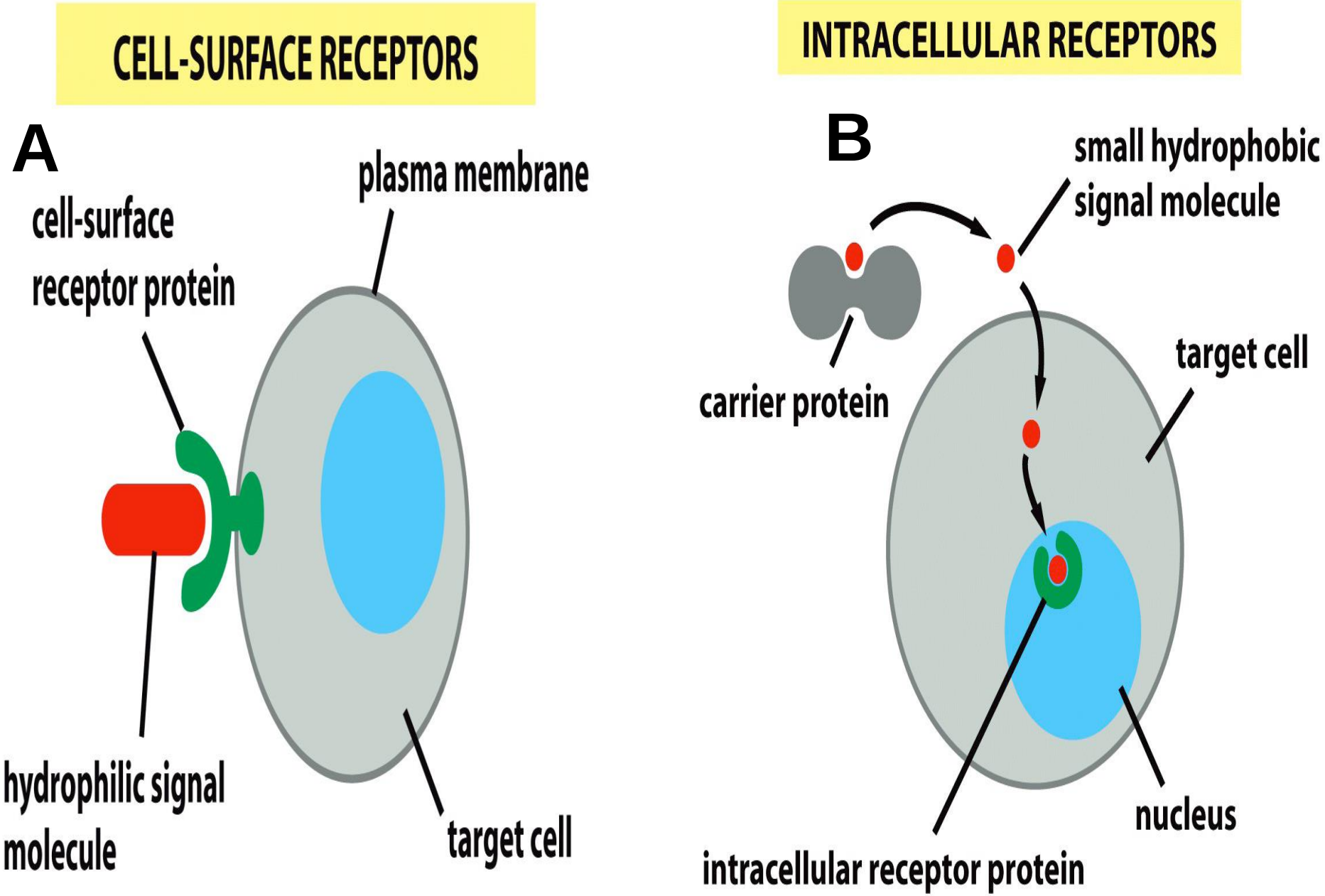
Ultimate effects of cell signaling



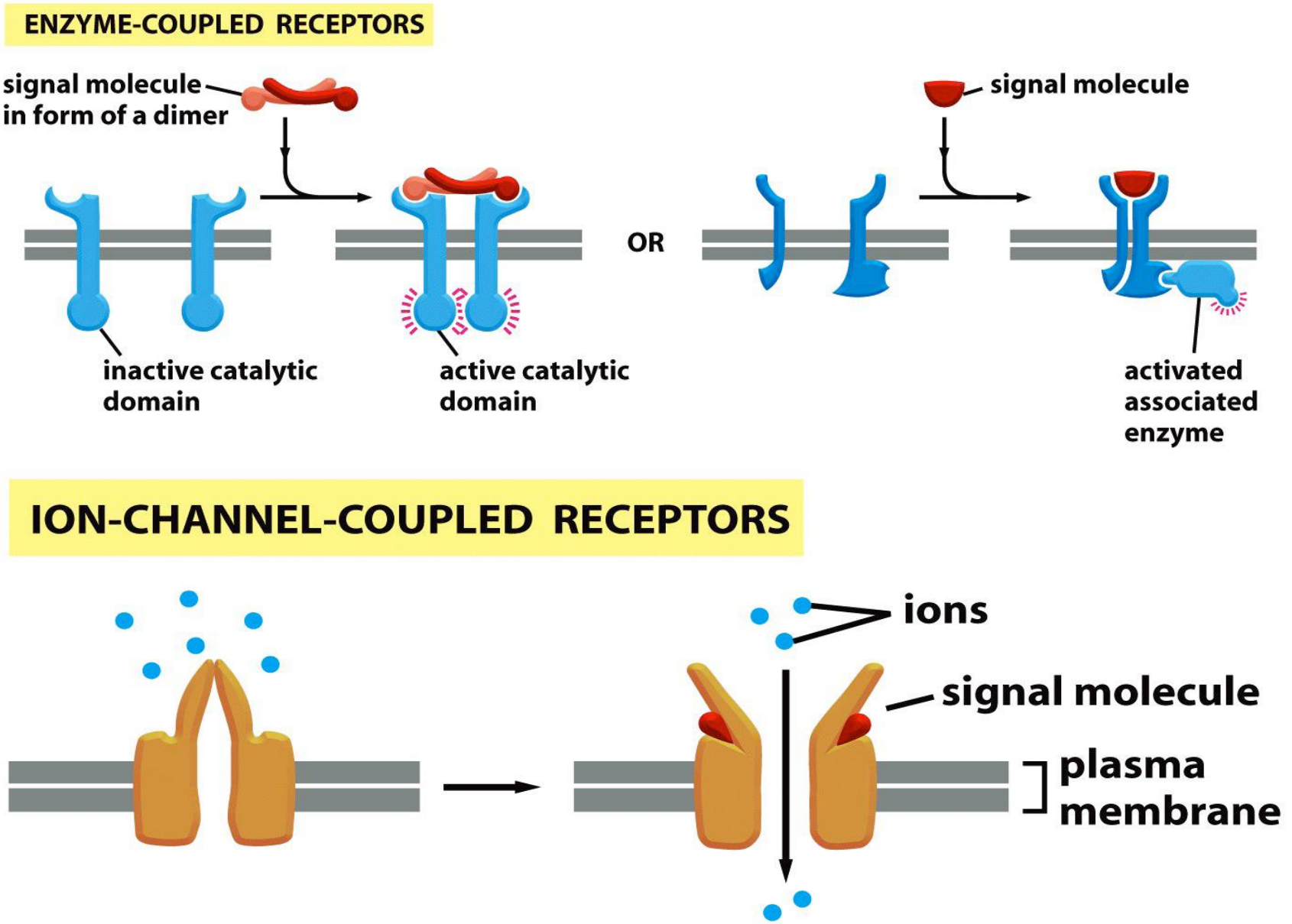
Five forms of intercellular signaling (Cell-cell communication)



Same signal can cause different reactions depending on the target cell



Cell-surface receptor versus intracellular receptor



Major types of cell surface receptors

Fluid environment of the body

- 60% of human body is made up of fluid
  - Sex; adult men ~ 60% of total body weight
    adult women ~ 55% of total body weight
  - Age; neonate ~ 70% of total body weight
    > 60 years men ~52%, women 46% of total body weight
- Body fluid is distributed in 2 compartments

1. Intracellular fluid compartment (ICF) : two thirds of the body water

2.Extracellular fluid compartment (ECF): one third of the body water

ICF

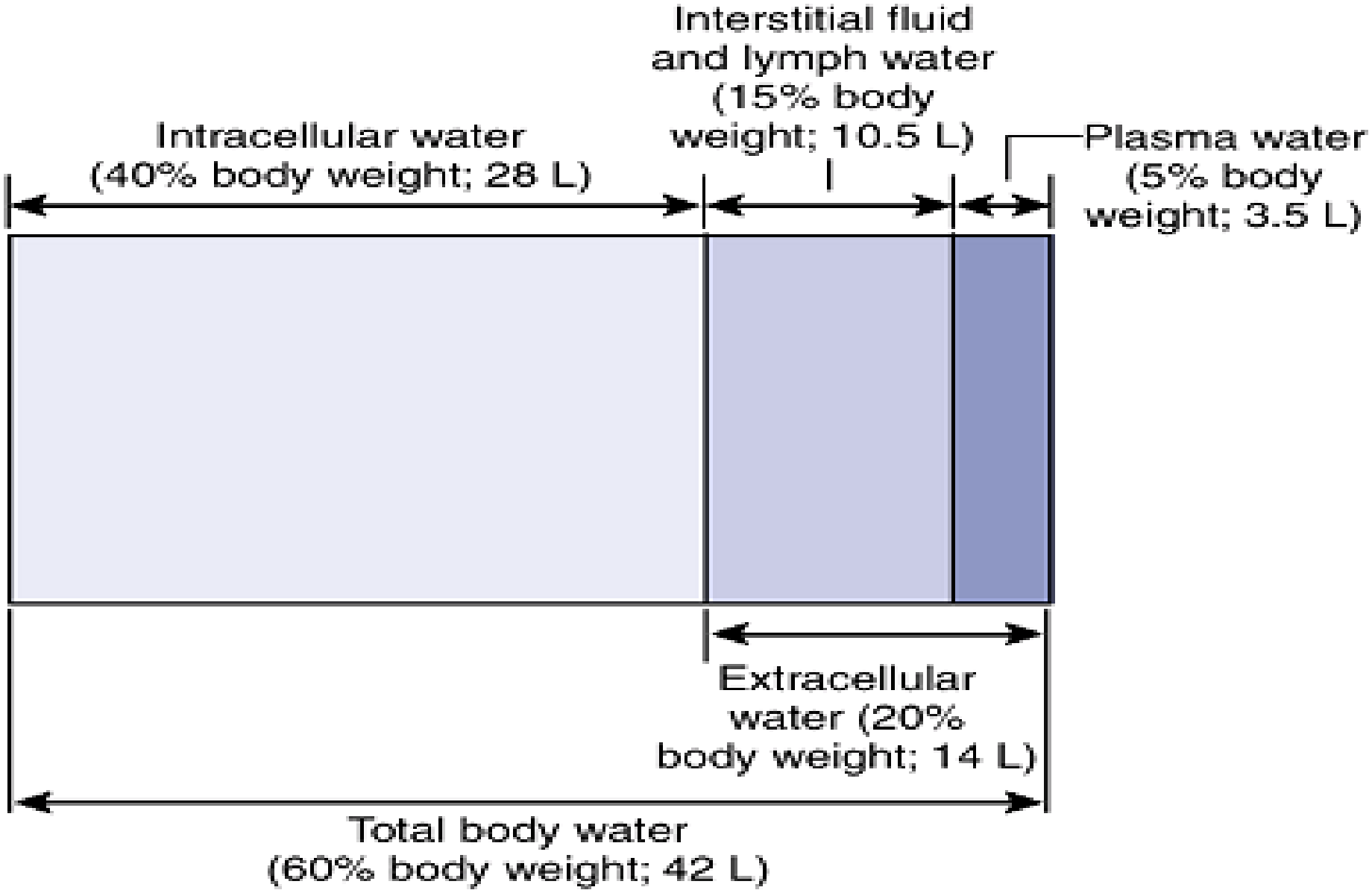
- Water
- High K^+, Po_4^{3-}, Mg^{2+}
- Nutrients, gases
- Hormones

ECF

- Water
- High Na^+, Cl^- , Ca^{2+} and HCO_3^-
- Nutrients: glucose, aa, lipids
- Gases: O_2, CO_2
- Hormones, Enzymes

Body fluid compartment cont'd……..

- These two fluid compartments differ strikingly in terms of their electrolyte composition
- But the fluid compartments solute concentrations (osmolarity) are normally equal (no an osmotic difference between cells cytoplasm and ECF)
- The ECF further subdivided into two major sub compartments:
  - ✓ The interstitial fluid and lymph, comprises three fourths of the ECF
  - ✓ The blood plasma, comprises about one fourth of the ECF
- The blood plasma, interstitial fluid, and lymph are nearly identical in composition, except for the higher protein concentration in the plasma



Distribution of body water compartments in an average adult man weighing 70 kg

Body fluid compartment cont'd……

- In addition to above mentioned, ECF compartment includes transcellular fluid that amounts to about 1% to 3% of body weight
- Transcellular fluids include cerebrospinal fluid, aqueous humor of the eye, secretions of the digestive tract and associated organs (saliva, bile, pancreatic juice), renal tubular fluid and bladder urine, synovial fluid, and sweat
- Transcellular fluids are not plasma ultrafiltrates (as are interstitial fluid and lymph); so they have a distinct ionic composition

Constituents of Extracellular and Intracellular Fluids

- Ionic composition of plasma and interstitial fluid is similar (plasma and interstitial fluid are separated by highly permeable capillary membranes)
- Higher concentration of protein in the plasma than in interstitial fluid
  - ✓ Intracellular fluid is separated from the extracellular fluid by a cell membrane (highly permeable to water but not to most of the electrolytes in the body)
  - ✓ Intracellular fluid contains large amounts of potassium and phosphate ions plus moderate quantities of magnesium and sulfate ions
  - ✓ The intracellular fluid contains only small quantities of sodium and chloride ions and almost no calcium ions

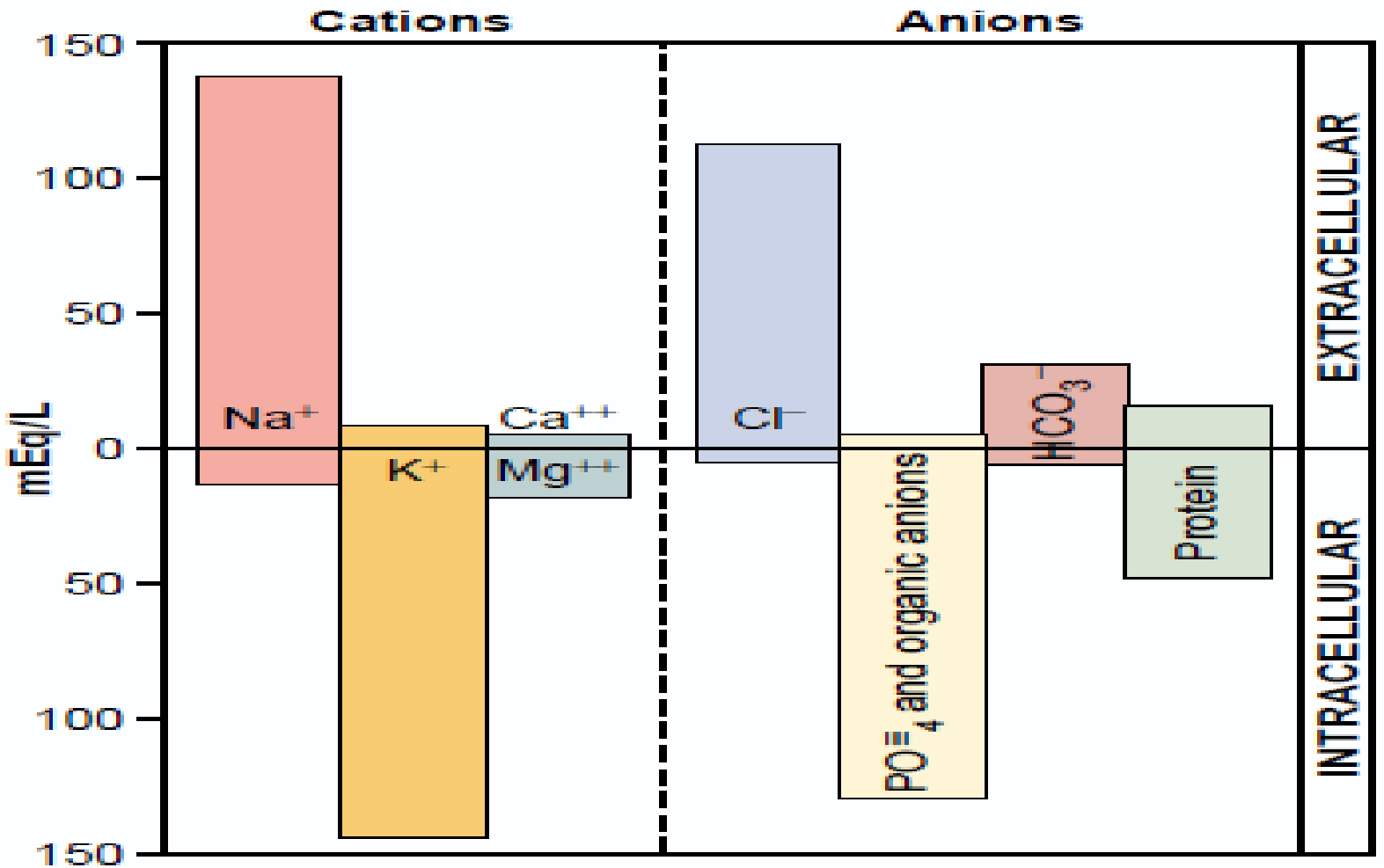


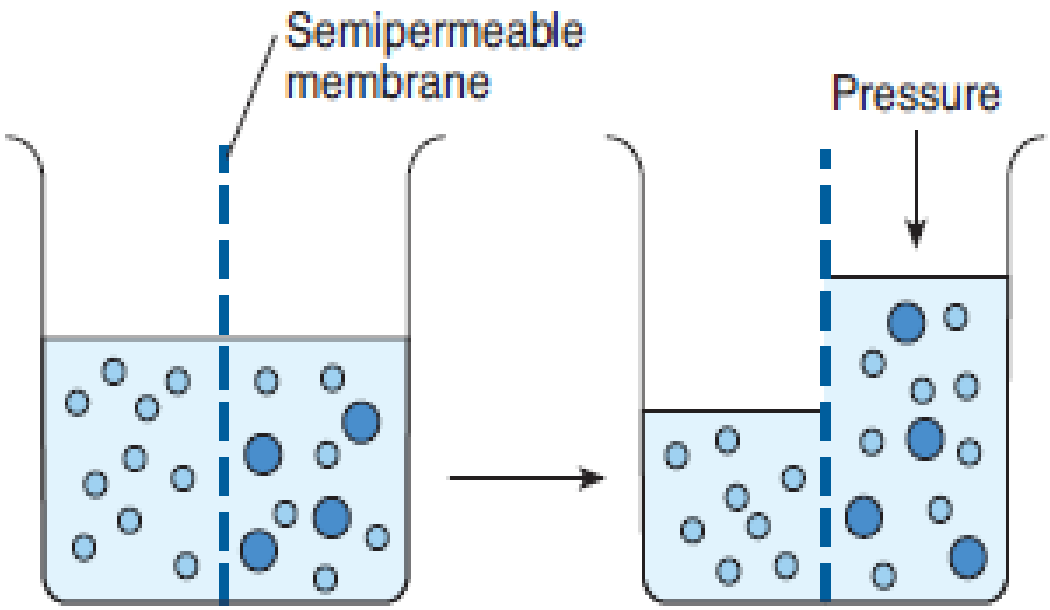
Fig. Major cations and anions of the ICF and ECF

Water Balance

- People normally stay in a stable water balance; that is, water input and output are equal
- Body fluid volume is kept remarkably constant
- Daily intake of water:
  - Ingested in the form of liquids and water in the food, 2100 ml/d
  - Synthesized in the body due to oxidation of nutrients, 200 ml/day
- Daily loss of body water:
  - Insensible water loss 700 ml/day
  - Fluid loss in sweat, 100 ml/day
  - Water loss in feces, 100 ml/day
  - Water loss by the kidneys (urine), 1400 ml/day
- The most important means by which the body maintains a balance between water intake and output is by controlling the rates at which the kidneys excrete water (0.5 L/day to 20 L/day)

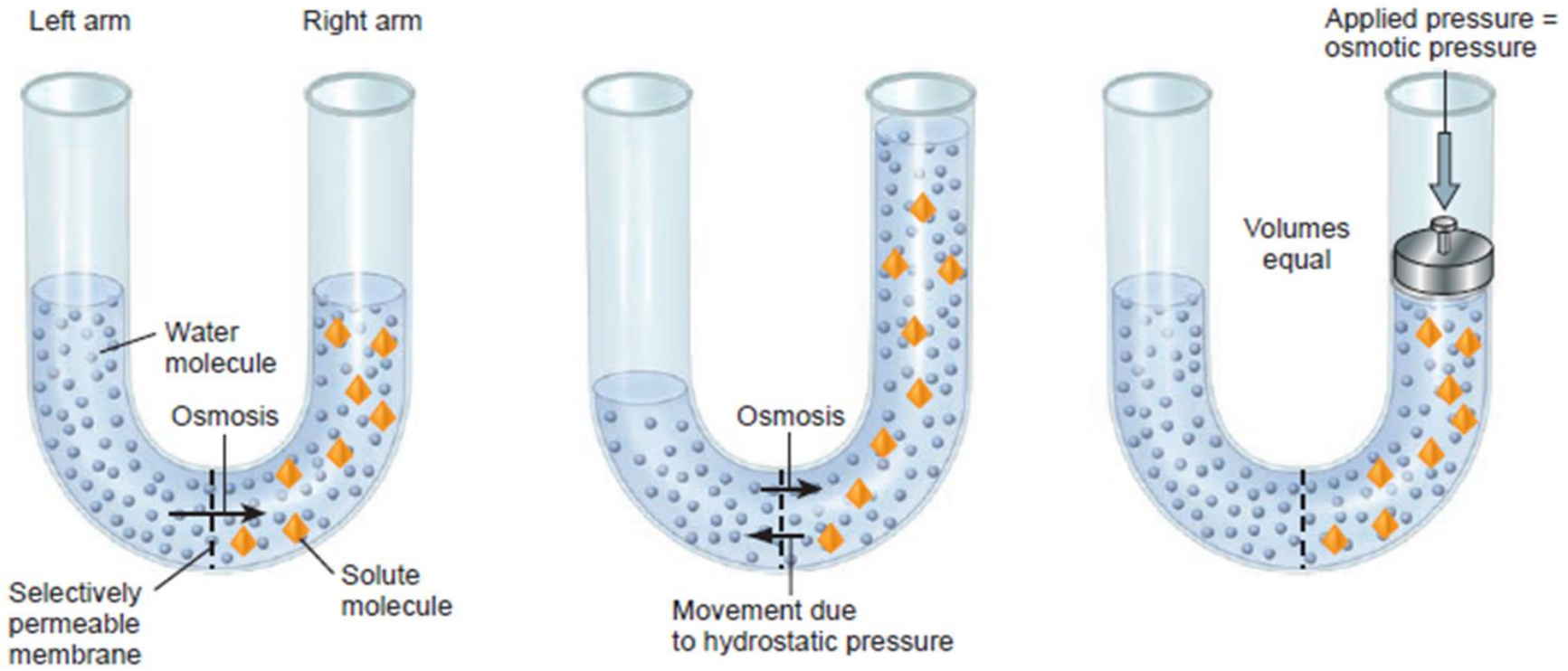
Osmosis and Osmotic Pressure

Osmosis is the net diffusion of water across a selectively permeable membrane from a region of high water concentration to one that has a lower water concentration



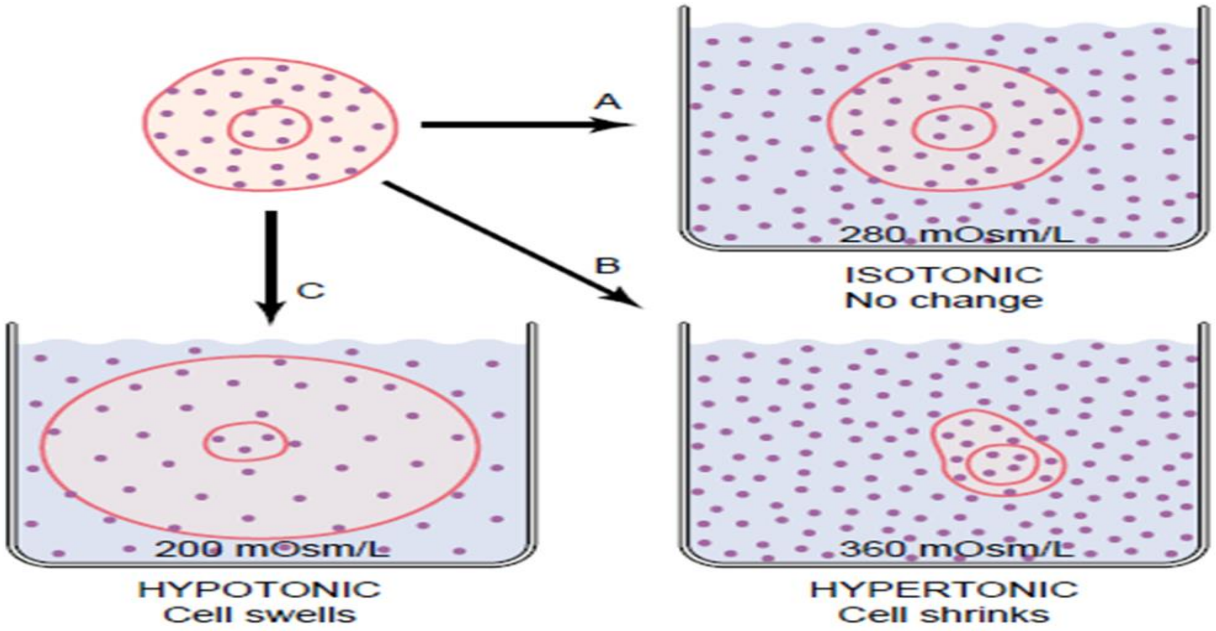
Osmosis from area of high water concentration to low water concentration

- The tendency for movement of water molecules to a region of greater solute concentration (low water concentration) can be prevented by applying pressure to the more concentrated solution The pressure necessary to prevent water migration is the **osmotic pressure** of the solution



Isotonic, Hypotonic, and Hypertonic Fluids

- Cell is placed in **Isotonic** solution (280-300mOsm/L) the cells will not shrink or swell because the water concentration in the intracellular and extracellular fluids is equal.eg. ***0.9 % sodium chloride***.
- Cell is placed into hypotonic solution *(*<282 mOsm/L) → diffusion of water into the cell → swelling of the cell.
- Cell is placed in a solution (>282 mOsm/L) water will flow out of the cell into the extracellular fluid, while the cell **shrinks.**



THNAK YOU