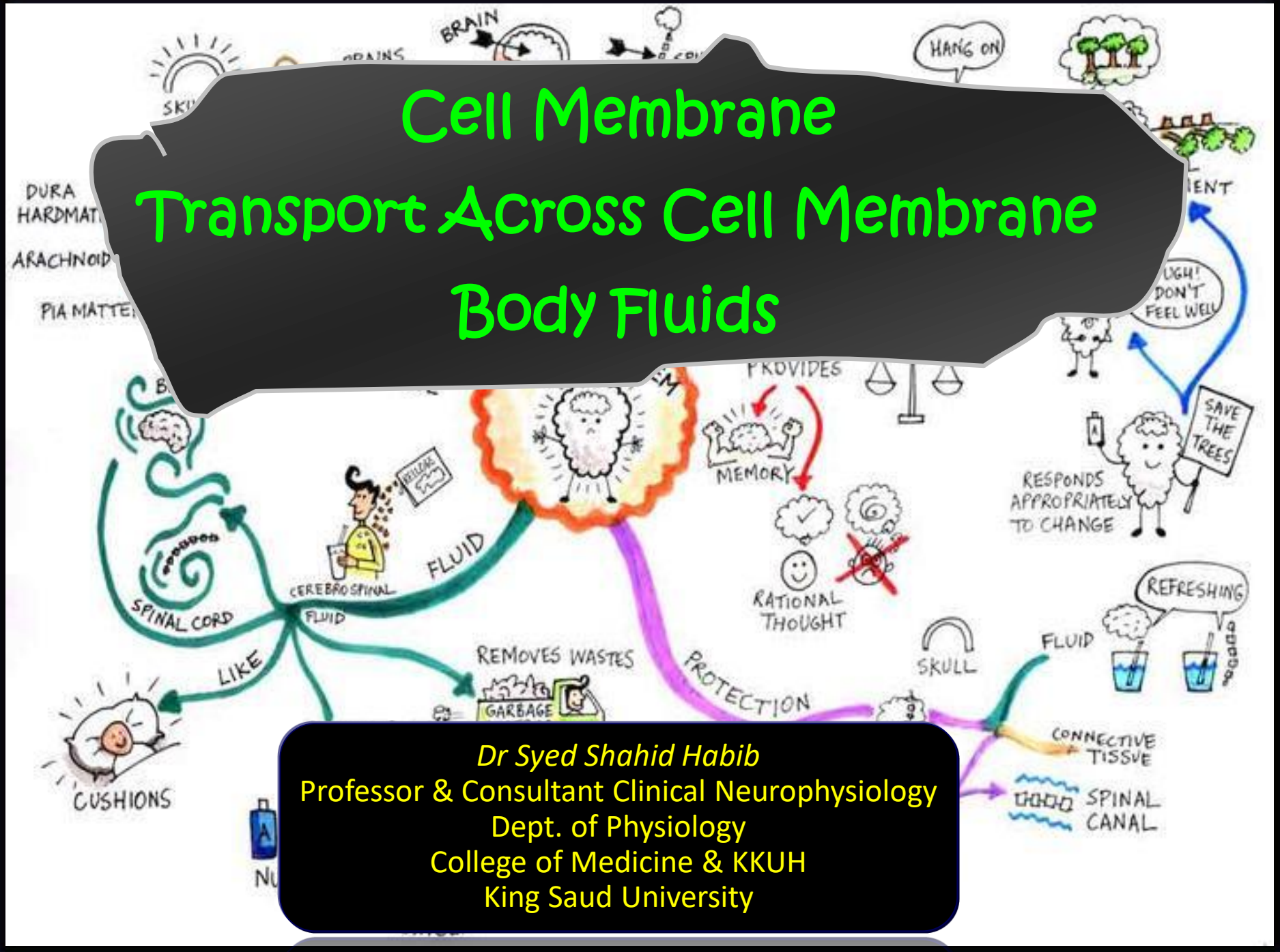
Cell Membrane
Transport Across Cell Membrane
Body Fluids



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OBJECTIVES

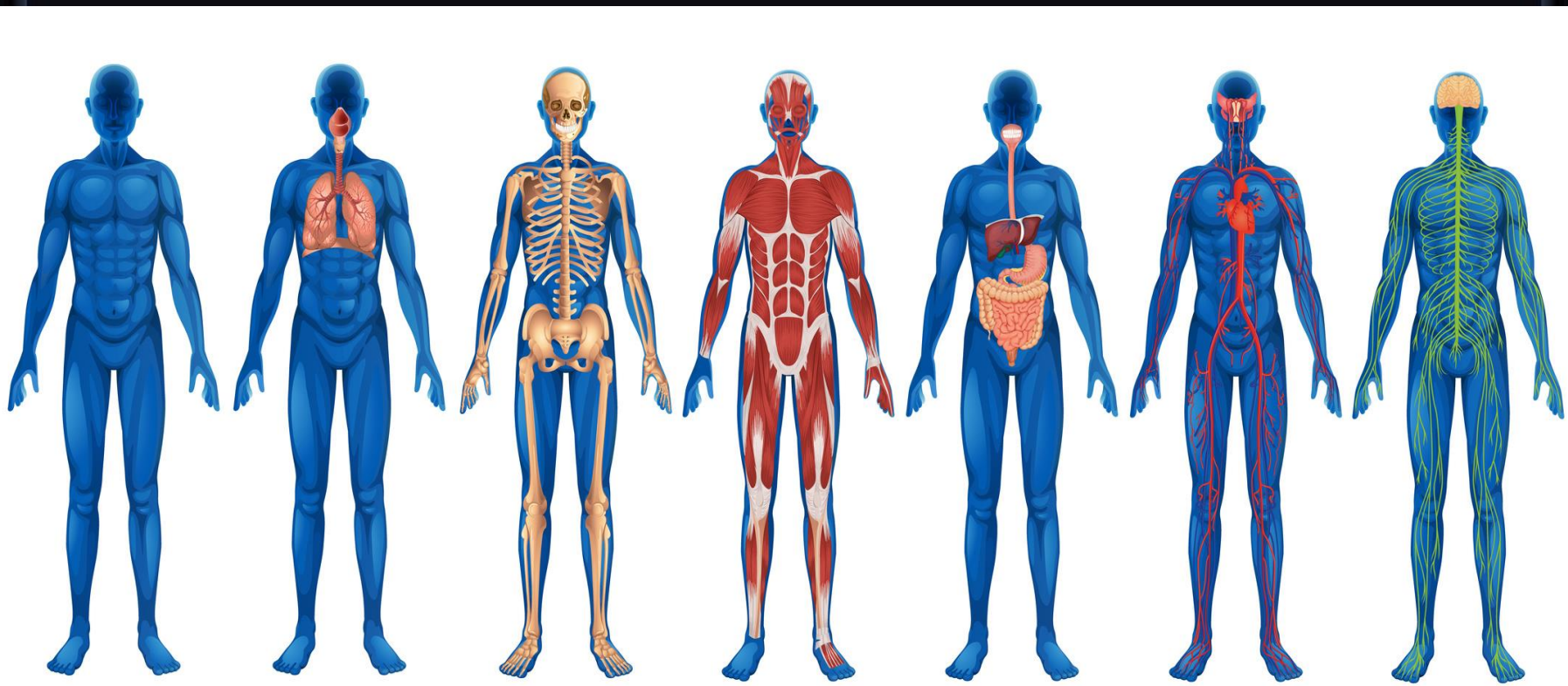
At the end of this lecture the student should be able to :

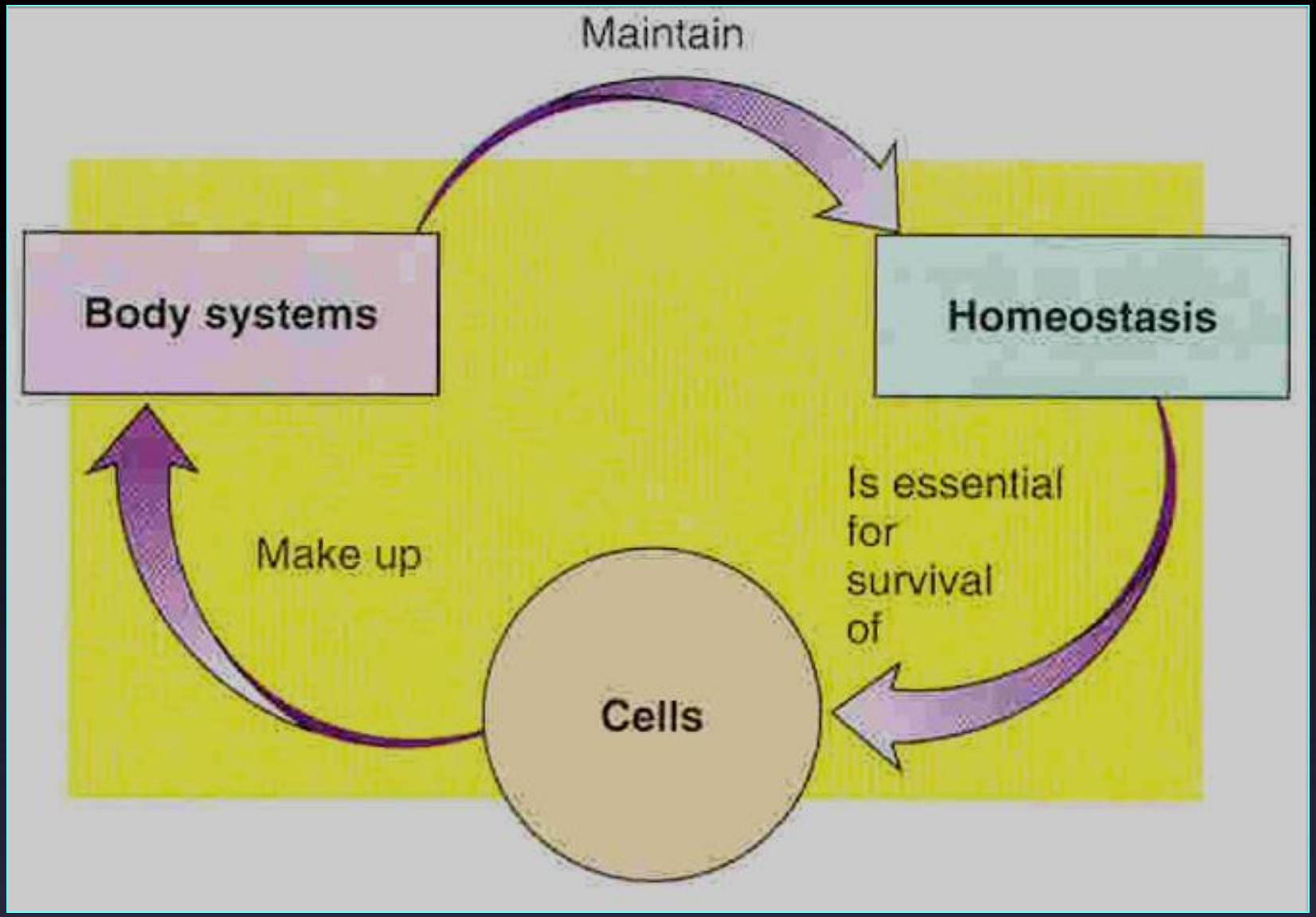
- Define Homeostasis and explain its control mechanisms
- Explain body fluid compartments
- Know and identify signs of dehydration.
- Describe the fluid mosaic model of membrane structure and function.
- Define permeability and list factors influencing permeability.
- Describe transport mechanisms across cell membrane and factors affecting these mechanisms

HOMEOSTASIS

Maintenance of nearly constant conditions in the internal environment.

American Physiologist Walter Cannon1929



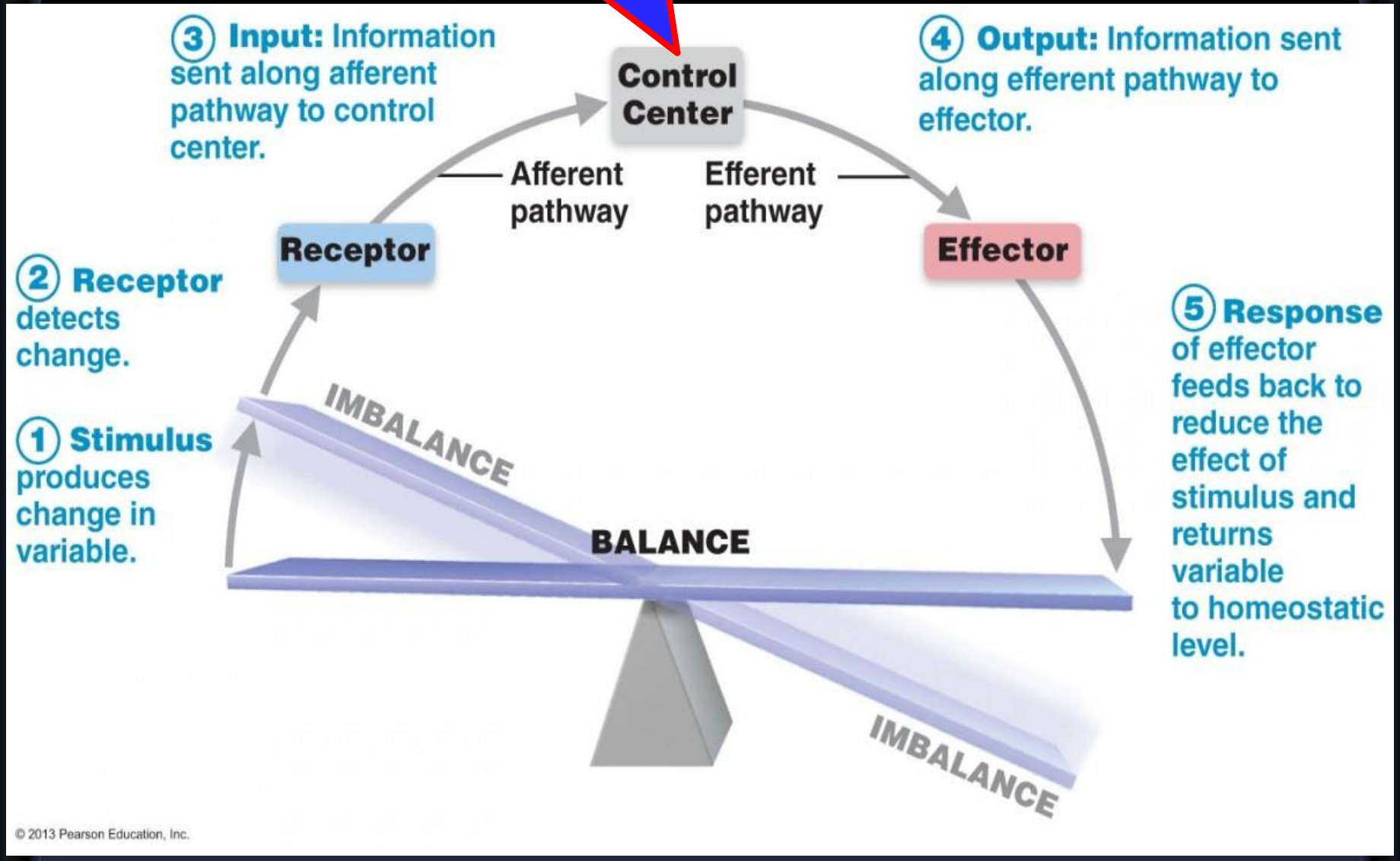

Maintain
Body systems
Homeostasis
Is essential for survival of
Make up
Cells

Homeostasis Control

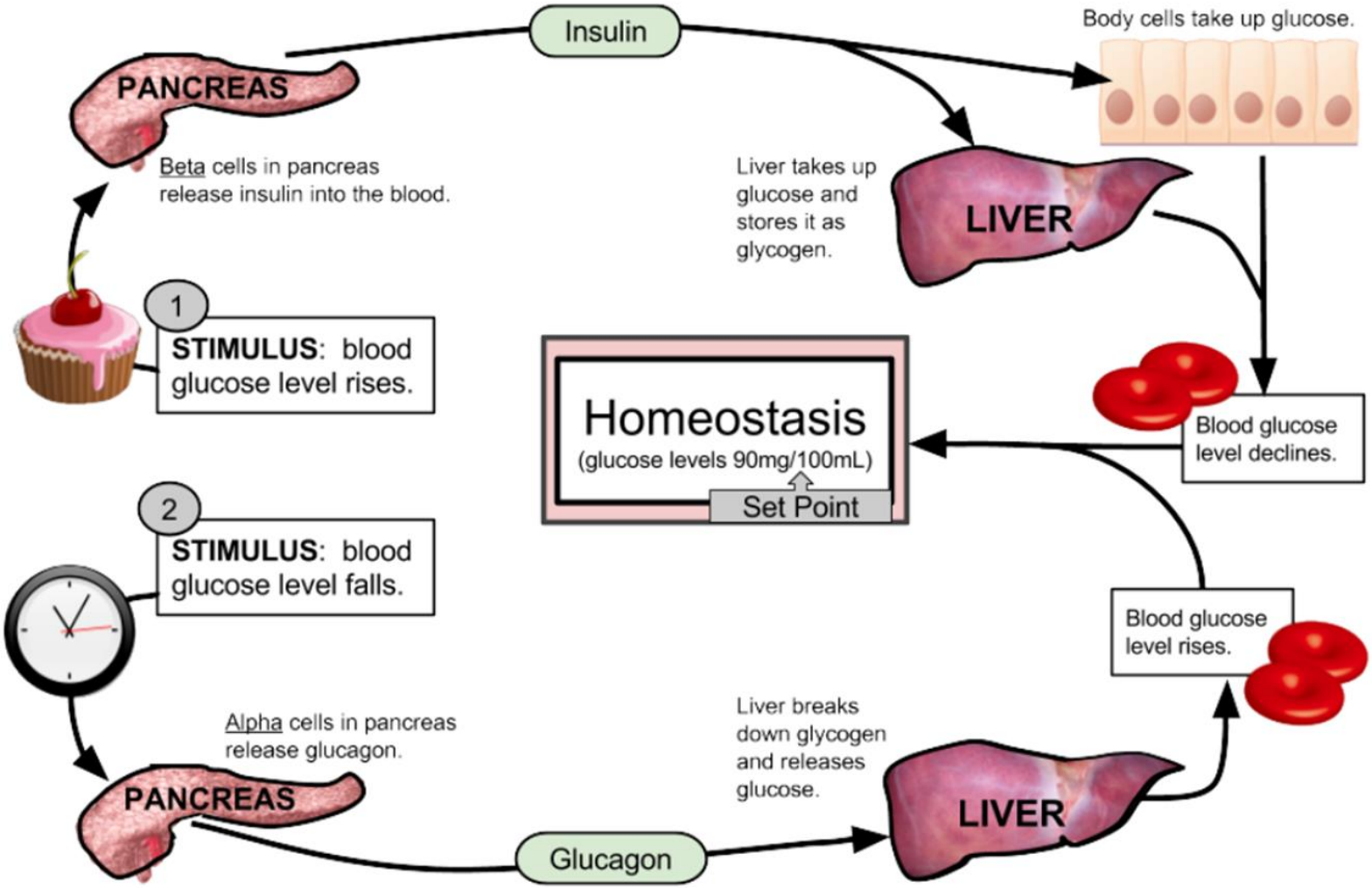
A loop system in which the system responds to perturbation either in the same direction (positive feedback) or in the opposite direction (negative feedback).

- **Negative feedback** is when the response diminishes the original stimulus.
- **Positive feedback** is when the response enhances the original stimulus.

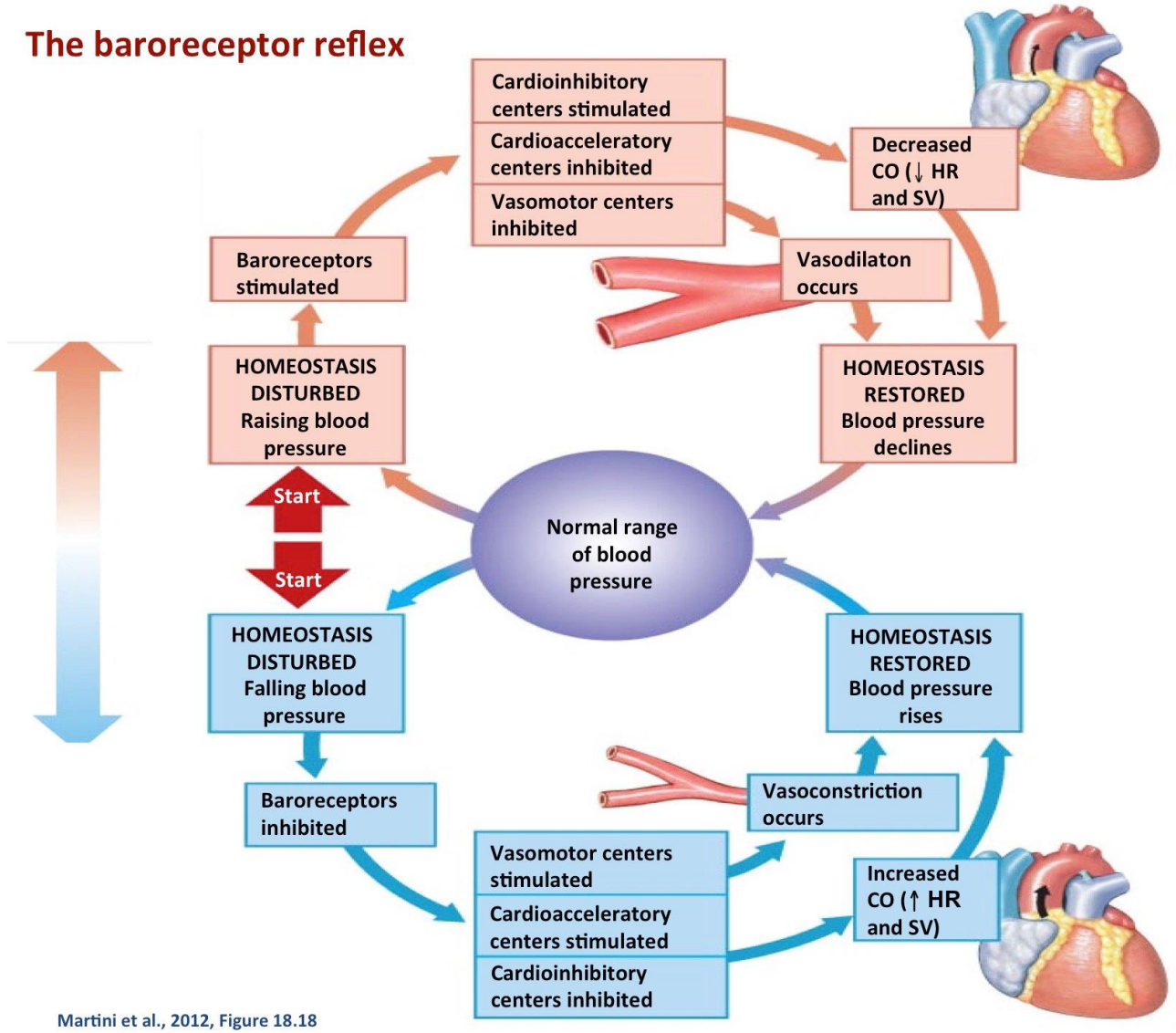
Determines the appropriate response



Negative feedback loop: Regulation of blood glucose



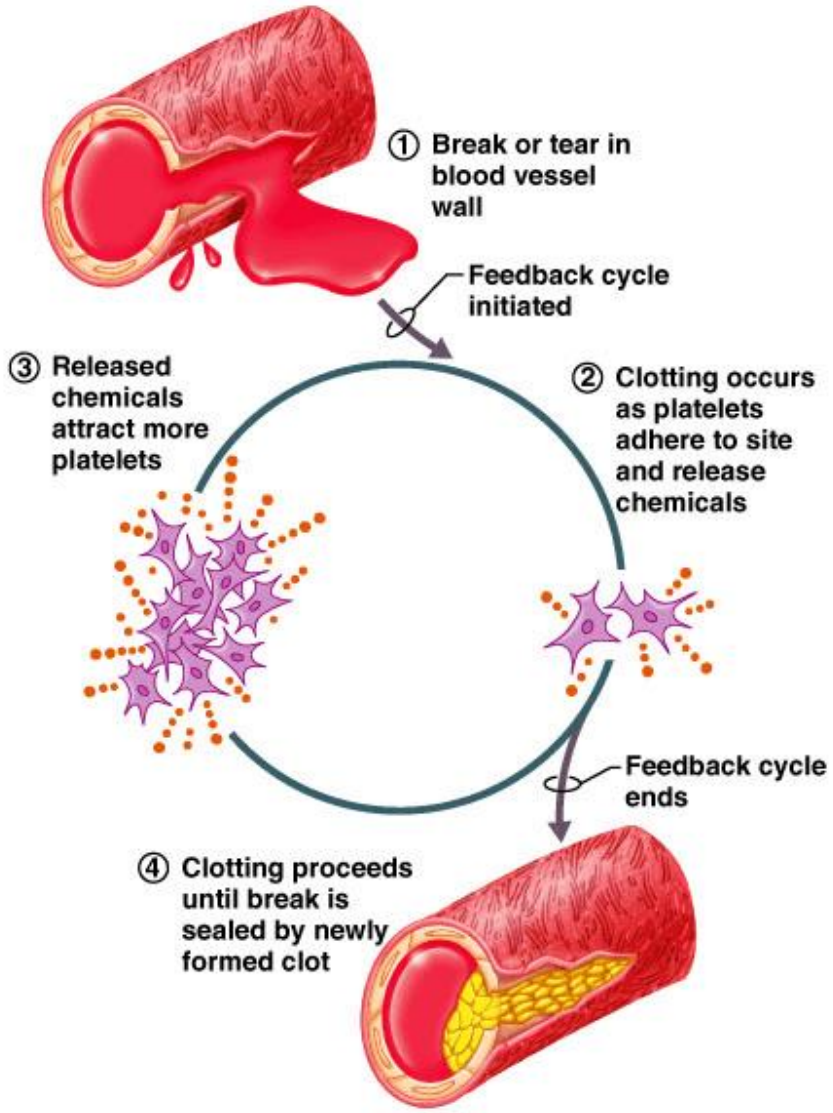
Nagtive feedback loop: Regulation of blood presssure

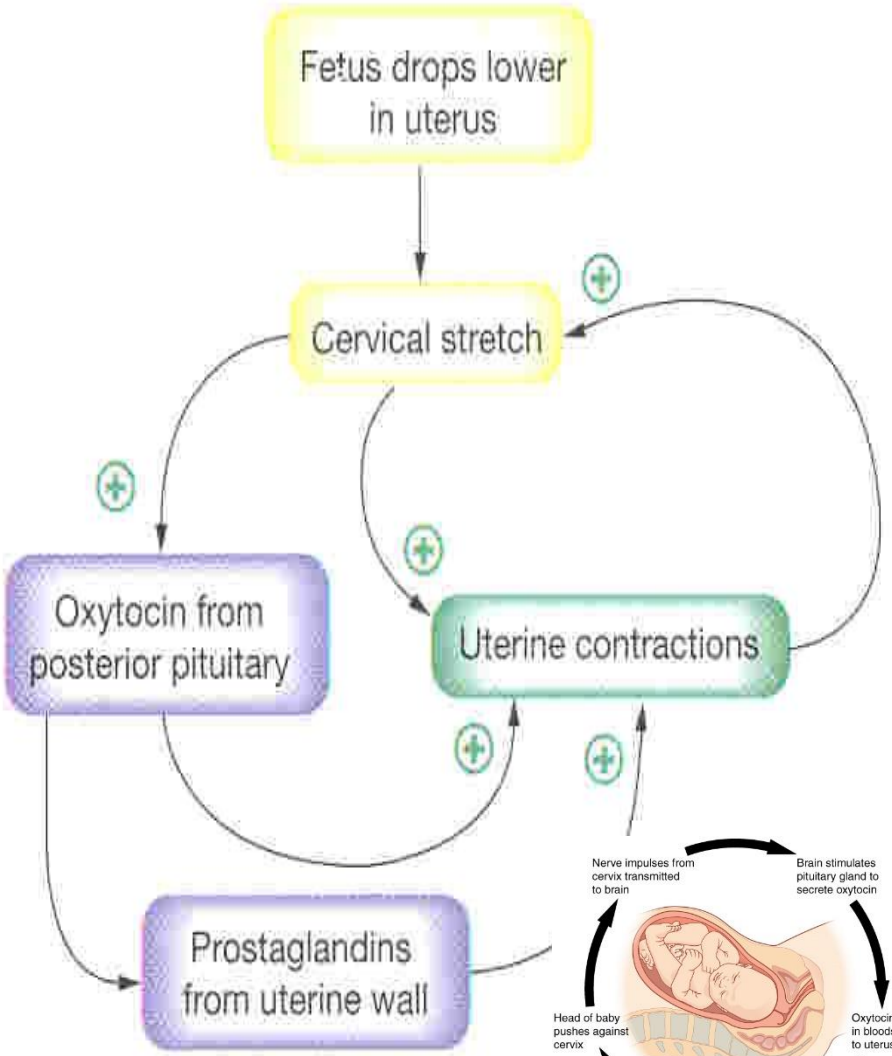


Martini et al., 2012, Figure 18.18

Positive feed back loop: blood clotting

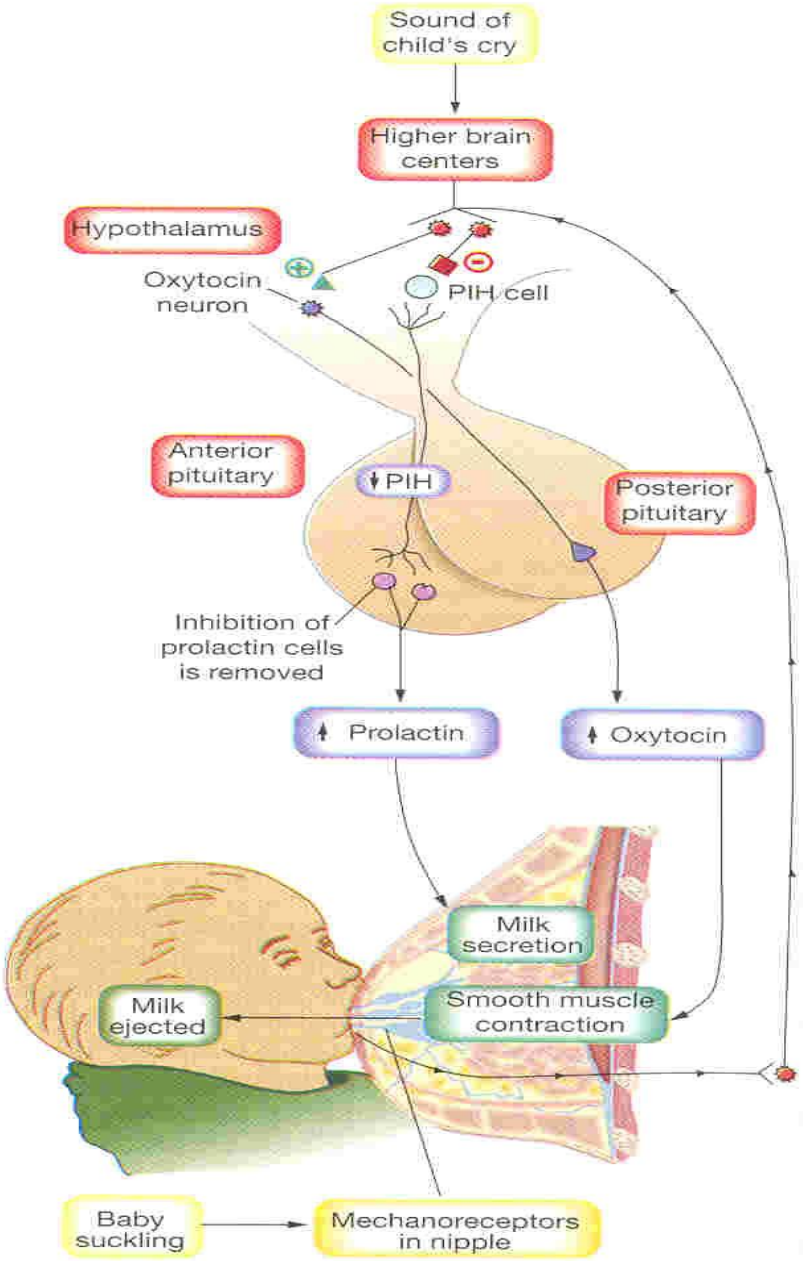
- The wall of the injured blood vessel releases chemicals that start the clotting process.
- Platelets in the blood begin to adhere to the wounded area and produce chemicals that attract more platelets.
- As the platelets continue to accumulate, more chemicals are released, and more platelets are drawn to the clot location.
- The clotting process is accelerated by the **positive feedback** until the clot is large enough to stop the bleeding.





The positive feedback loop of Parturition

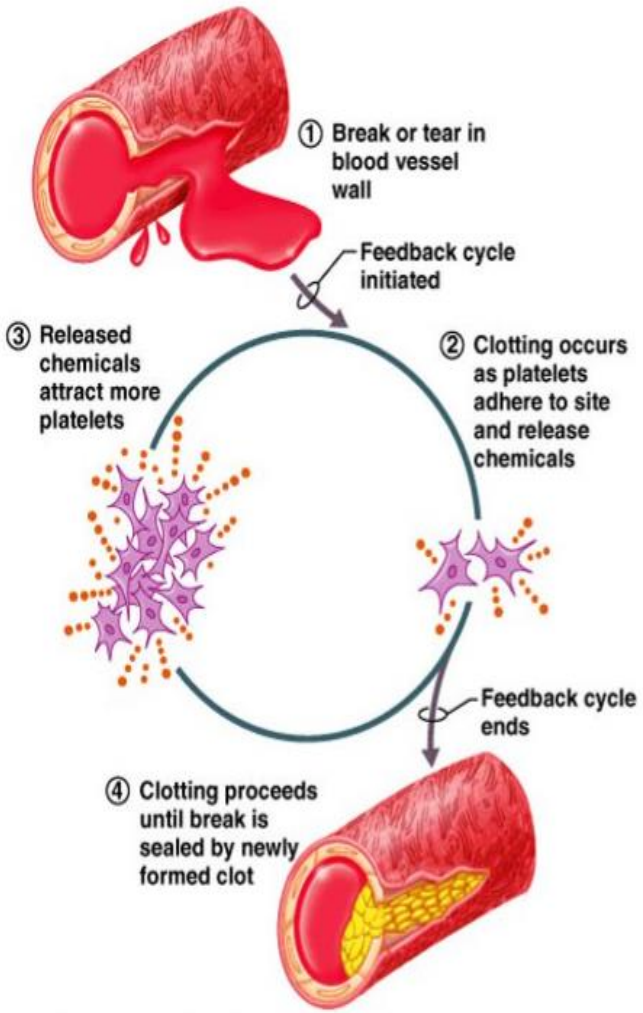
Stops when the fetus is delivered

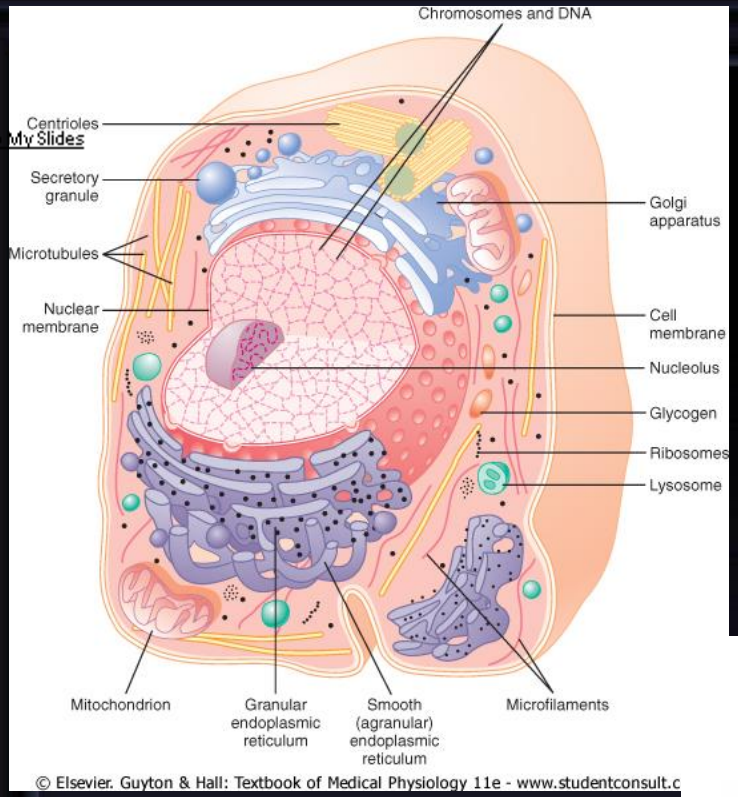


The positive feedback loop of Milk Let Down Reflex

Positive feed back loop: blood clotting

- The wall of the injured blood vessel releases chemicals that start the clotting process.
- Platelets in the blood begin to adhere to the wounded area and produce chemicals that attract more platelets.
- As the platelets continue to accumulate, more chemicals are released, and more platelets are drawn to the clot location.
- The clotting process is accelerated by the **positive feedback** until the clot is large enough to stop the bleeding.





CELL

A Busy Factory

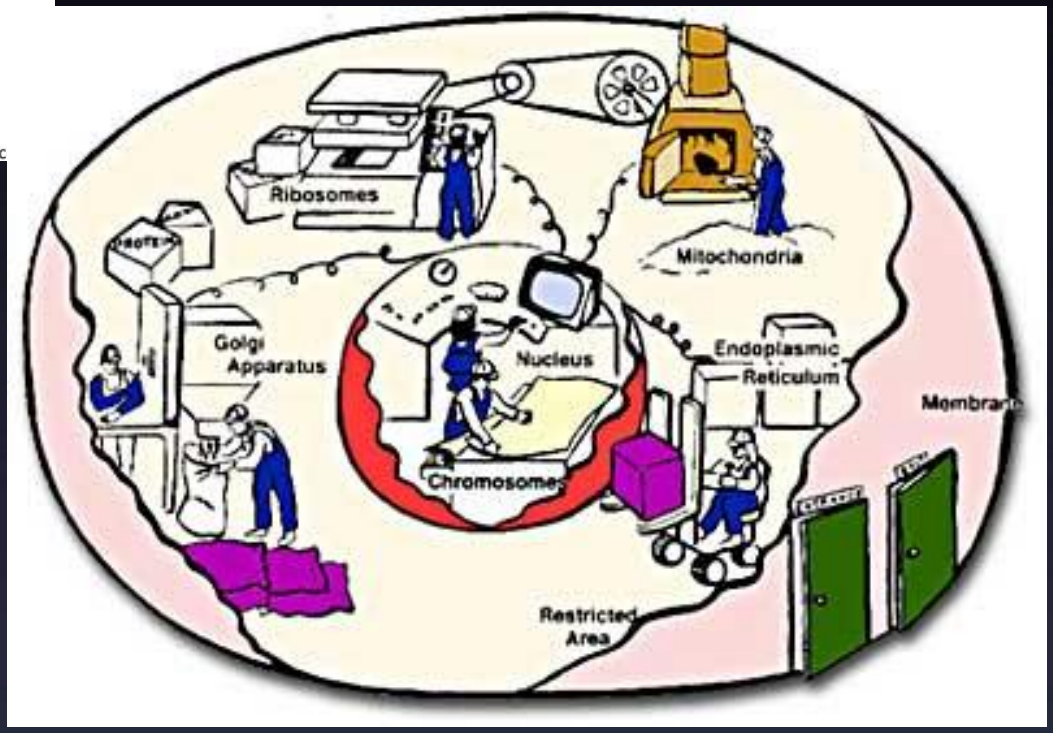
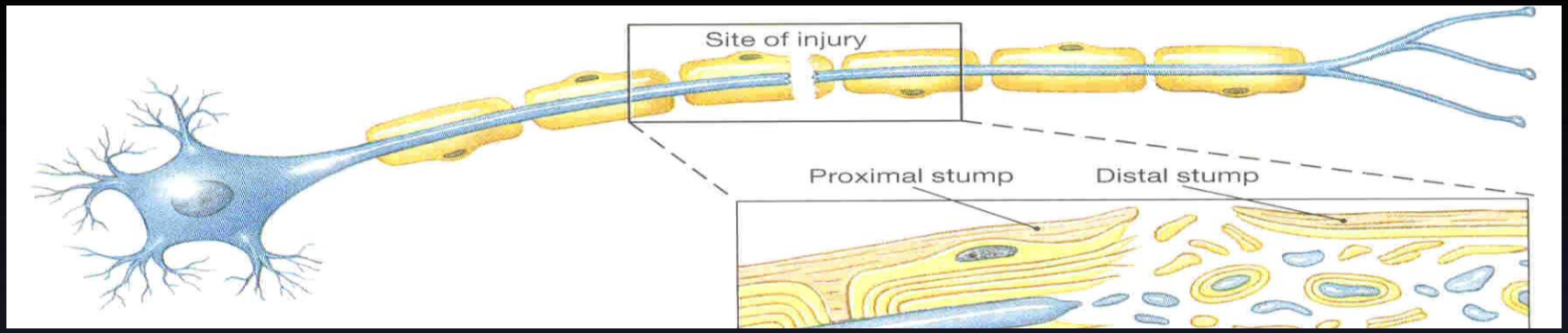


Table 3.1 Cellular Components: Structure and Function

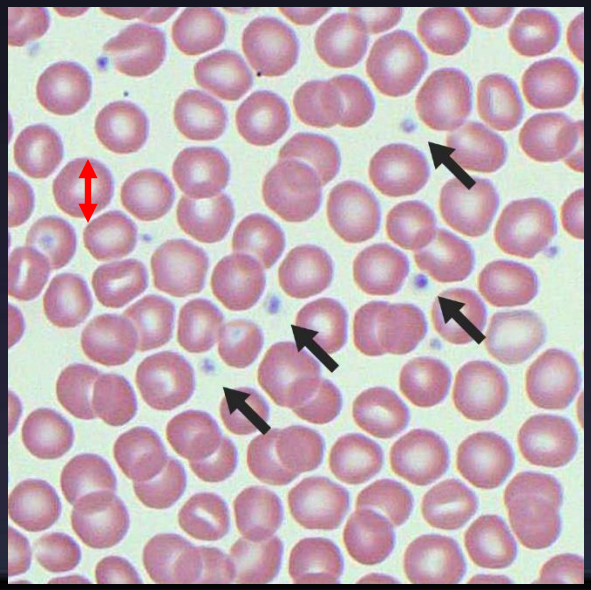
Component	Structure	Function
Plasma (cell) membrane	Membrane composed of double layer of phospholipids in which proteins are embedded	Gives form to cell and controls passage of materials into and out of cell
Cytoplasm	Fluid, jellylike substance between the cell membrane and the nucleus in which organelles are suspended	Serves as matrix substance in which chemical reactions occur
Endoplasmic reticulum	System of interconnected membrane-forming canals and tubules	Agranular (smooth) endoplasmic reticulum metabolizes nonpolar compounds and stores Ca^{2+} in striated muscle cells, granular (rough) endoplasmic reticulum assists in protein synthesis
Ribosomes	Granular particles composed of protein and RNA	Synthesize proteins
Golgi complex	Cluster of flattened membranous sacs	Synthesizes carbohydrates and packages molecules for secretion, secretes lipids and glycoproteins
Mitochondria	Membranous sacs with folded inner partitions	Release energy from food molecules and transform energy into usable ATP
Lysosomes	Membranous sacs	Digest foreign molecules and worn and damaged organelles
Peroxisomes	Spherical membranous vesicles	Contain enzymes that detoxify harmful molecules and break down hydrogen peroxide
Centrosome	Nonmembranous mass of two rodlike centrioles	Helps to organize spindle fibers and distribute chromosomes during mitosis
Vacuoles	Membranous sacs	Store and release various substances within the cytoplasm
Microfilaments and microtubules	Thin, hollow tubes	Support cytoplasm and transport materials within the cytoplasm
Cilia and flagella	Minute cytoplasmic projections that extend from the cell surface	Move particles along cell surface or move the cell
Nuclear envelope	Double-layered membrane that surrounds the nucleus, composed of protein and lipid molecules	Supports nucleus and controls passage of materials between nucleus and cytoplasm
Nucleolus	Dense nonmembranous mass composed of protein and RNA molecules	Produces ribosomal RNA for ribosomes
Chromatin	Fibrous strands composed of protein and DNA	Contains genetic code that determines which proteins (including enzymes) will be manufactured by the cell

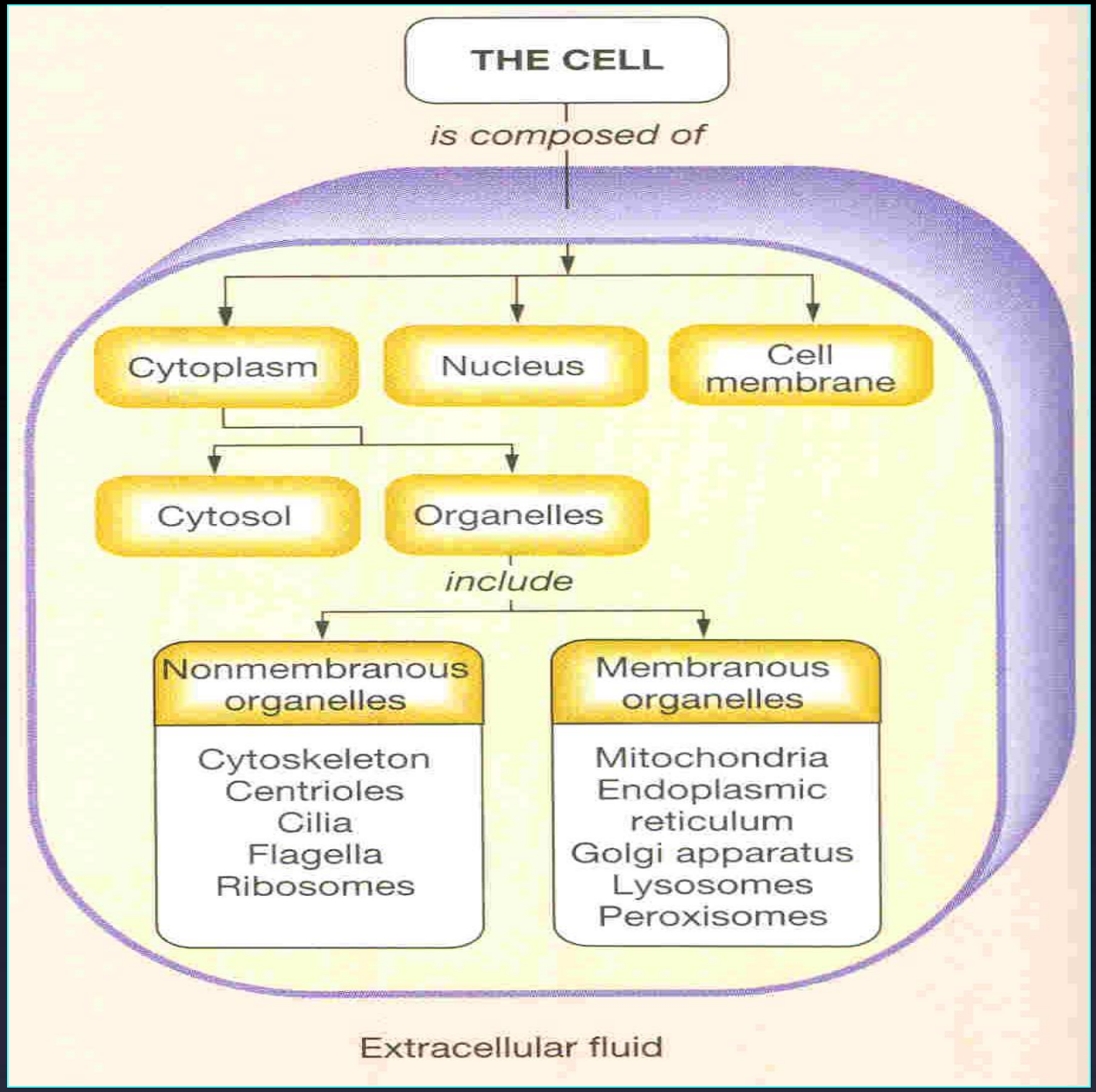
LARGEST AND SMALLEST CELL

SIZE : 1.5 meter



SIZE : 2-4um

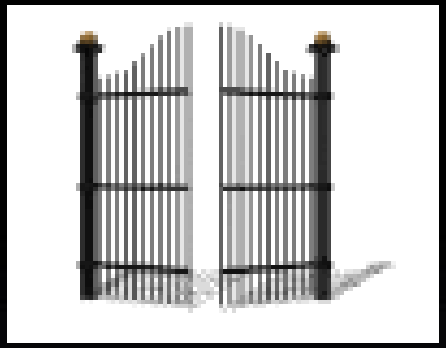



THE CELL
is composed of
Cytoplasm
Nucleus
Cell membrane
Cytosol
Organelles
include
Nonmembranous organelles
Cytoskeleton
Centrioles
Cilia
Flagella
Ribosomes
Membranous organelles
Mitochondria
Endoplasmic reticulum
Golgi apparatus
Lysosomes
Peroxisomes
Extracellular fluid

CELL COMPOSIOTION

- **Water 70-80 %**
- **Proteins 10-20 %**
- **Lipids 2 %**
- **Carbohydrates 1 %**
- **Minerals**

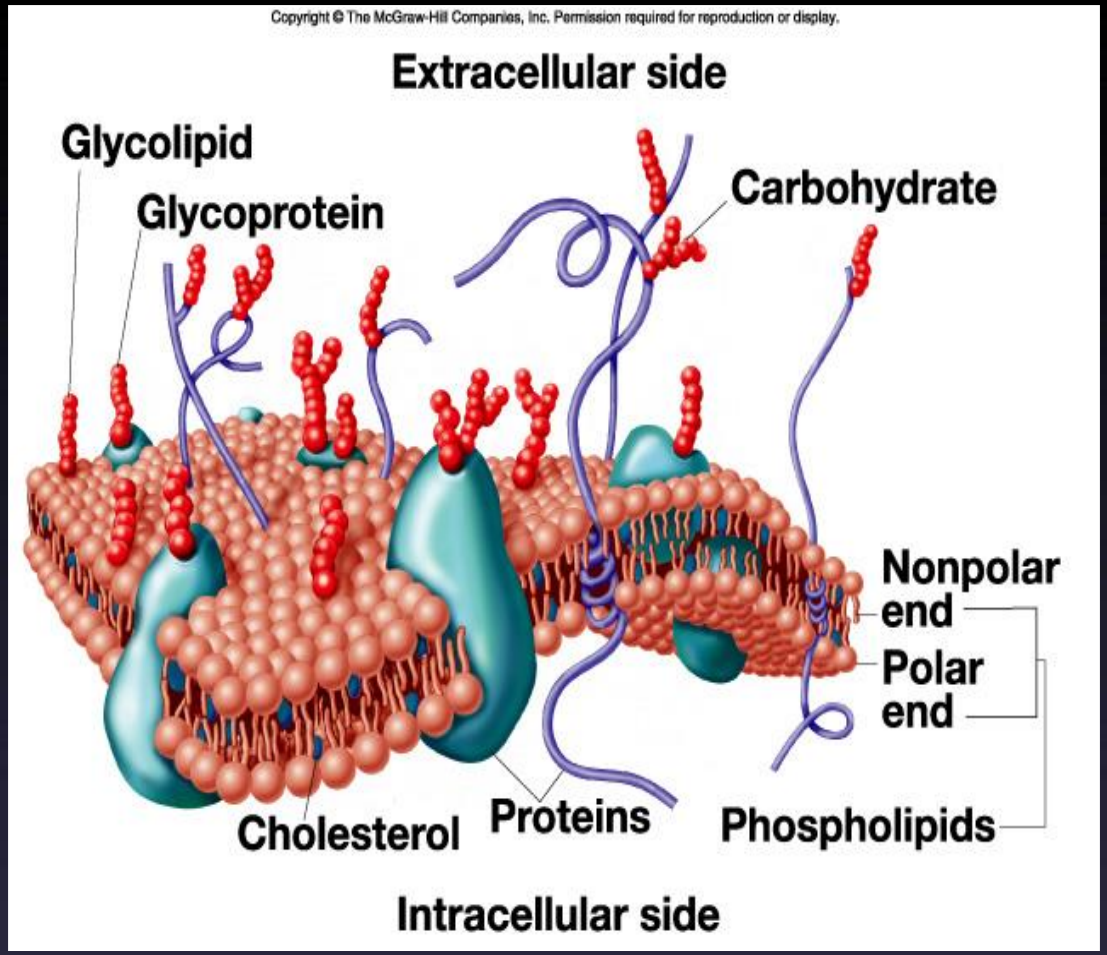
Plasma Membrane



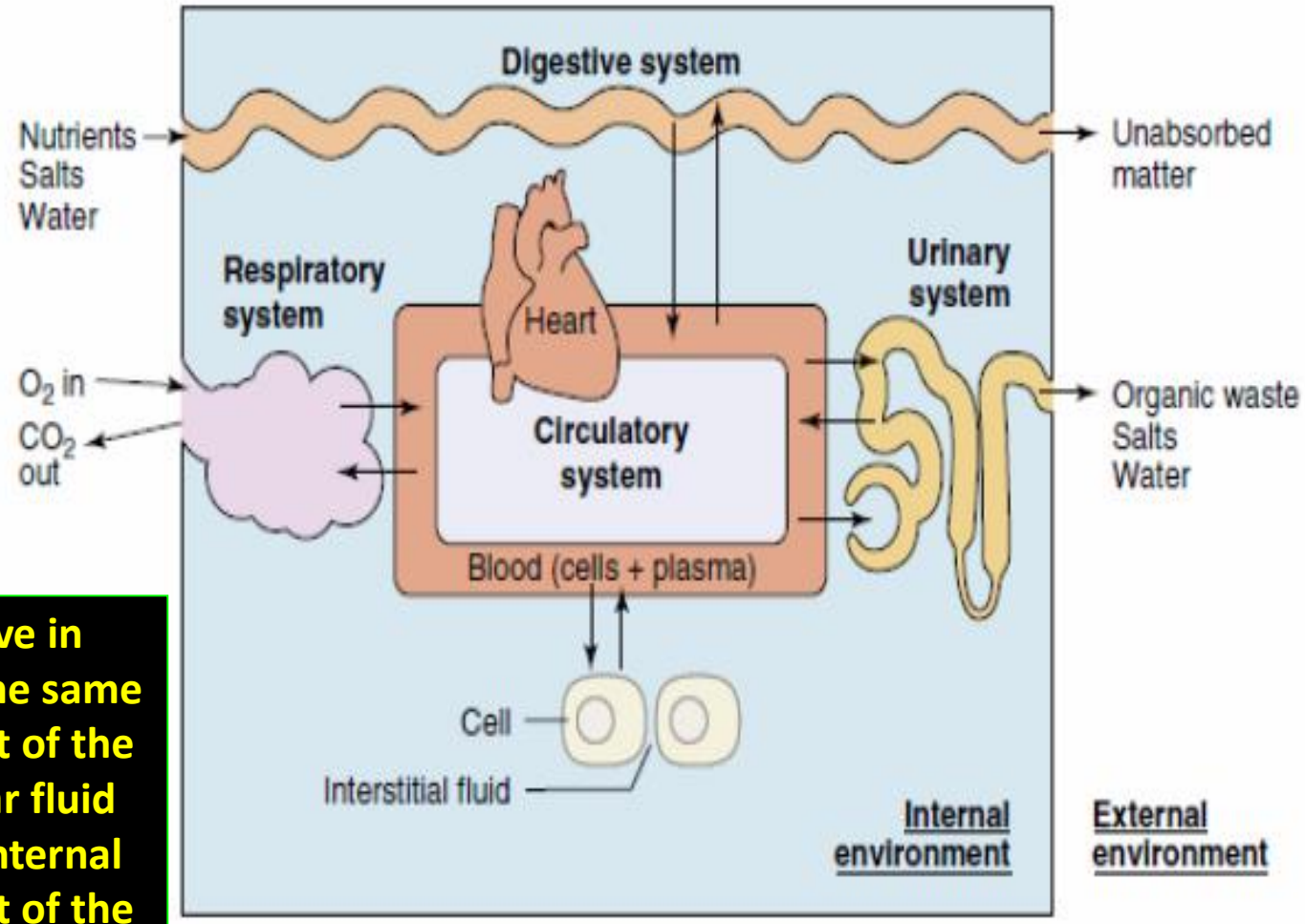
- Is **selectively permeable.**
- Composition:
  - **Double layer** of phospholipids due to hydrophobic/hydrophilic parts.
    - Restrict passage of H_20 and H_20 soluble ions.
  - **Proteins** span or partially span the membrane.
    - Provide structural support, transport molecules, serve as receptors.
  - **Negatively charged carbohydrates** attach to the outer surface.
    - Involved with regulatory molecules.

Cell membranes are like gates.

Plasma Membrane (continued)



EXTERNAL & INTERNAL ENVIRONMENT



All cells live in essentially the same environment of the extracellular fluid called the internal environment of the body

Exchanges of matter occur between the external environment and the circulatory system via the digestive, respiratory, and urinary systems. Extracellular fluid (plasma and interstitial fluid) is the internal environment of the body. The external environment is the air surrounding the body.

Fluids in the human body

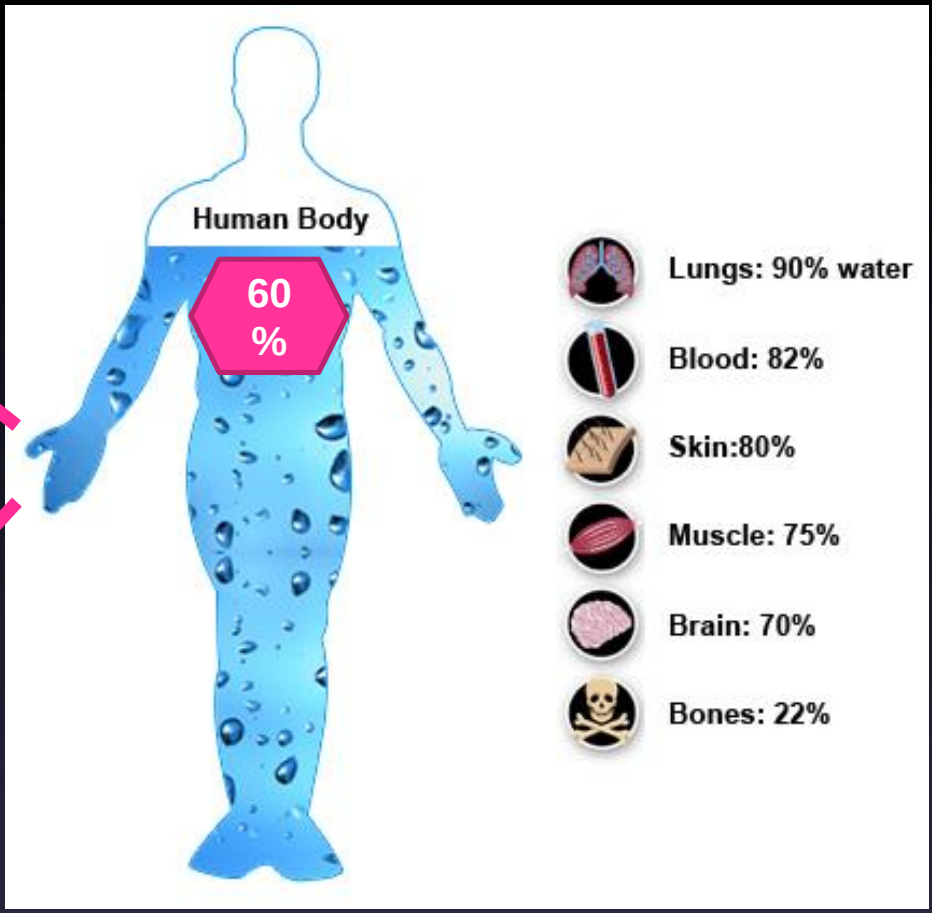
Extracellular fluid 1/3

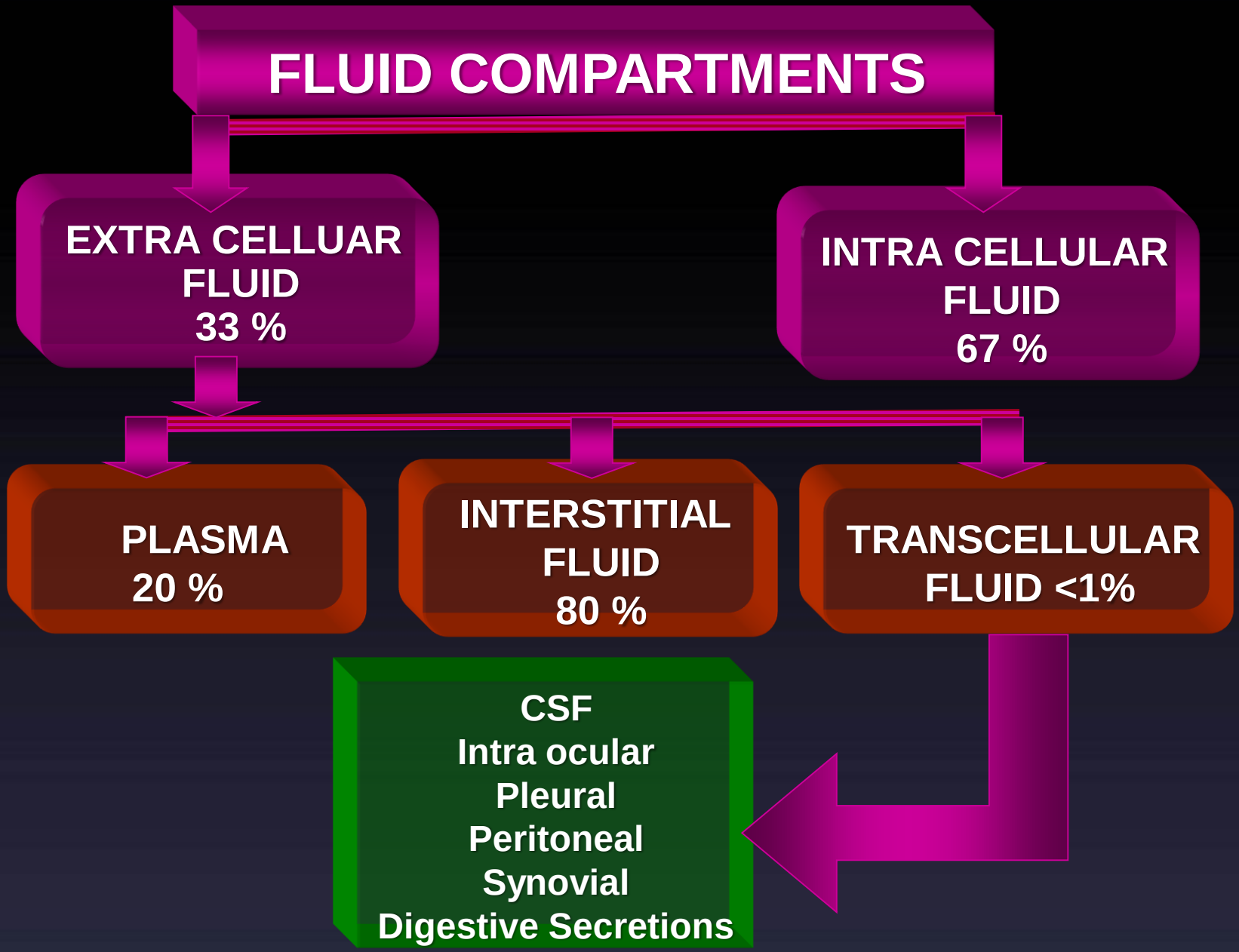
Interstitial Fluid 3/4

Transcellular Fluid & lymph 1%

Blood Plasma 1/4

Intracellular fluid 2/3




FLUID COMPARTMENTS
EXTRA CELLUAR FLUID 33 %
INTRA CELLULAR FLUID 67 %
PLASMA 20 %
INTERSTITIAL FLUID 80 %
TRANSCELLULAR FLUID <1%
CSF
Intra ocular
Pleural
Peritoneal
Synovial
Digestive Secretions

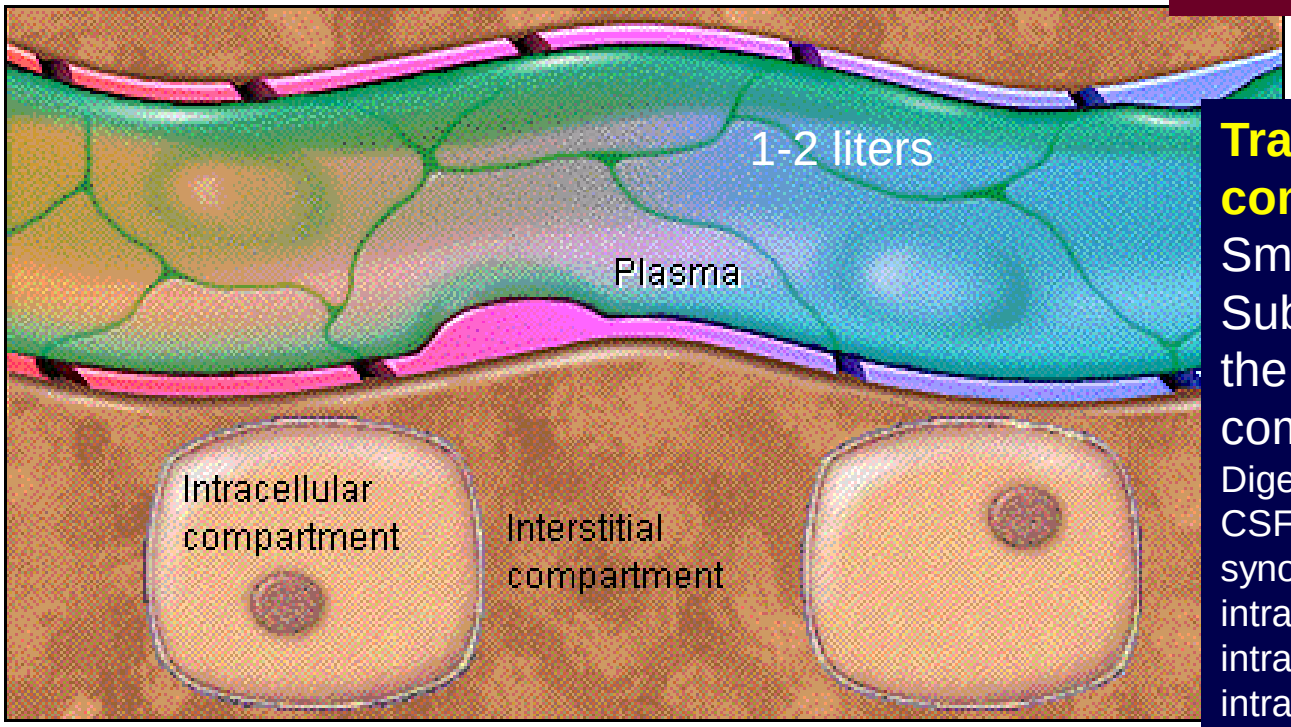
Fluid Compartments

The three major fluid compartments:

- **Intracellular fluid** (**ICF**) is the fluid within cells, also known as cytosol.
- **Extracellular fluid** (**ECF**) is the fluid found outside of cells.

There are two major kinds of extracellular fluid:

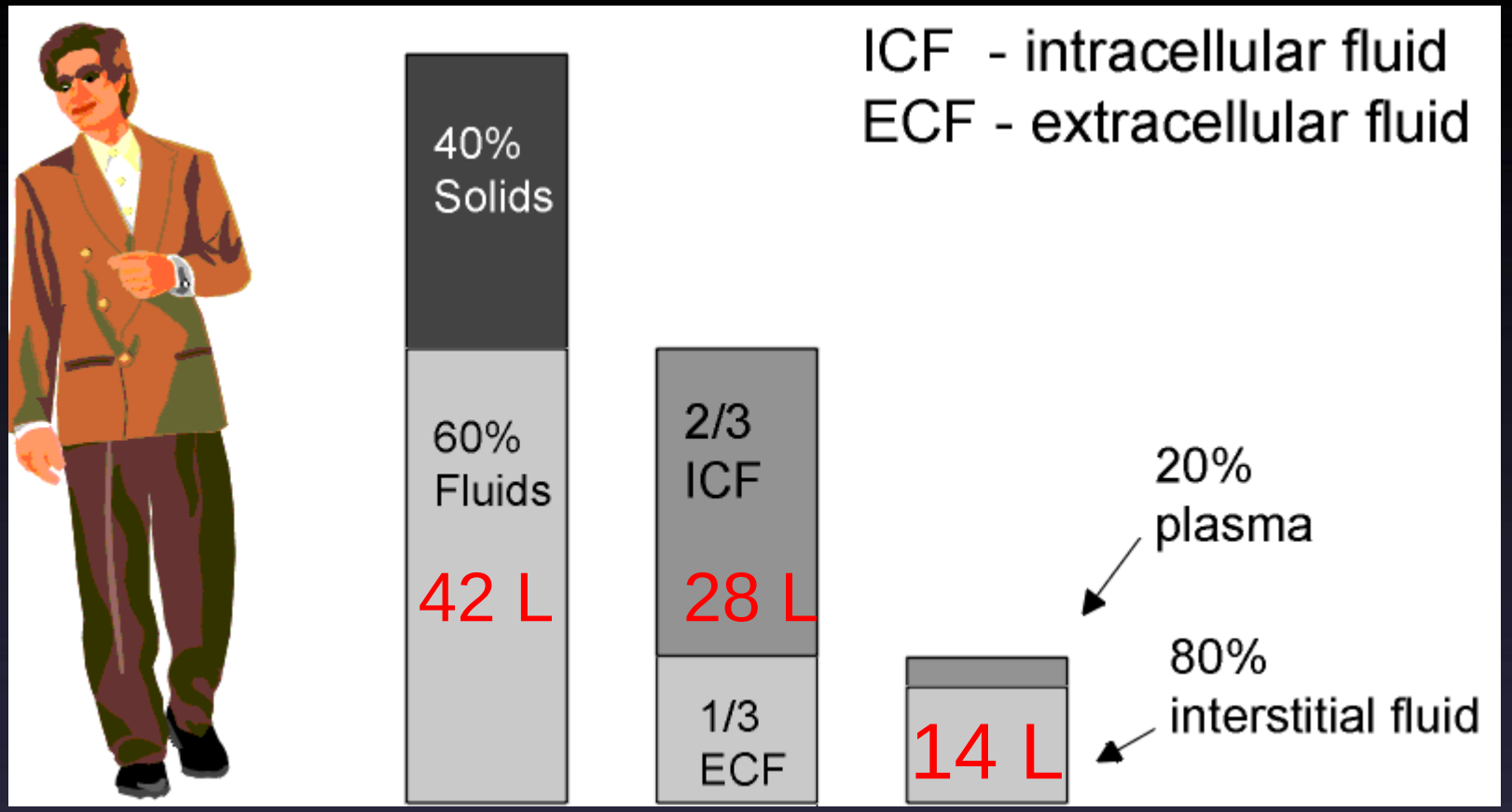
- **Interstitial fluid** is the fluid surrounding the cells.
- **Plasma** is the fluid component of blood.



For e.g:
TBW = 42L.
ECF = 14L.
ICF = 28L.
Plasma = 3.0 L.
Interstitial = 10.0 L.
Transcellular = 1.0 L

Trans cellular fluid compartment:
Small amount about1-2 L
Subset of E.C.F outside the normal compartments, e.g.
Digestive juices, C.S.F, mucus, CSF, GIT fluid, biliary fluid, synovial fluid, intrapleural fluid, intraperitoneal fluid, intrapericardial fluid and intraoccular fluid.

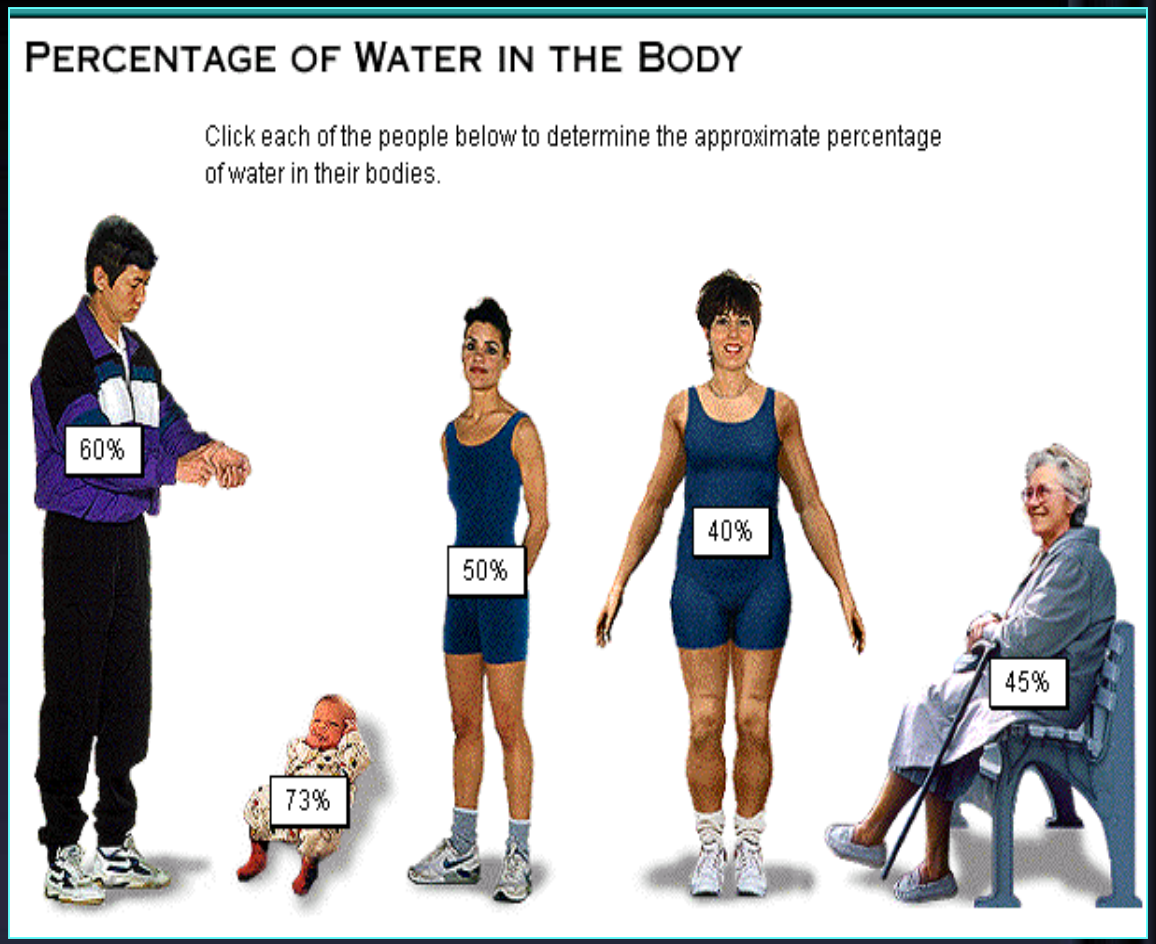
In a 70 kg adult man



FACTORS AFFECTING

Total Body Water varies depending on body composition:

- Infant: 73%
- Male adult: 60%
- Female adult fatty: 40%
- Female adult slim: 50%
- Effects of obesity ↓ water
- Old age 45%



FACTORS AFFECTING TBW

Physiological factors

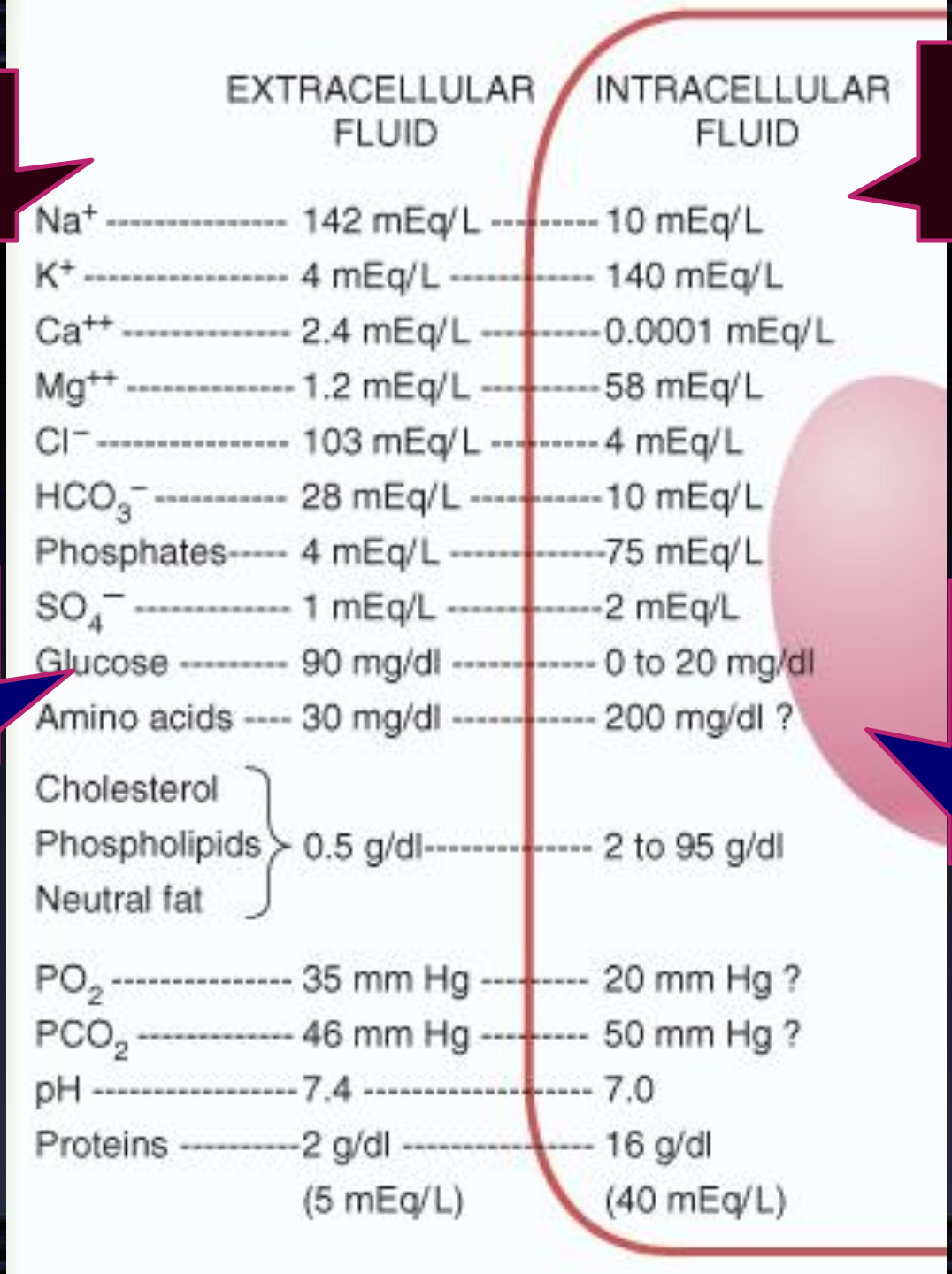
- Age
- Sex
- Body fat
- Climate
- Physical activity

Pathological factors

- Vomiting
- Diarrhea
- Diseases with excessive loss of water (DM, excessive sweating,….)
- Blood loss

ECF
Osmolality
300 mos/L

ICF
Osmolality
300 mos/L



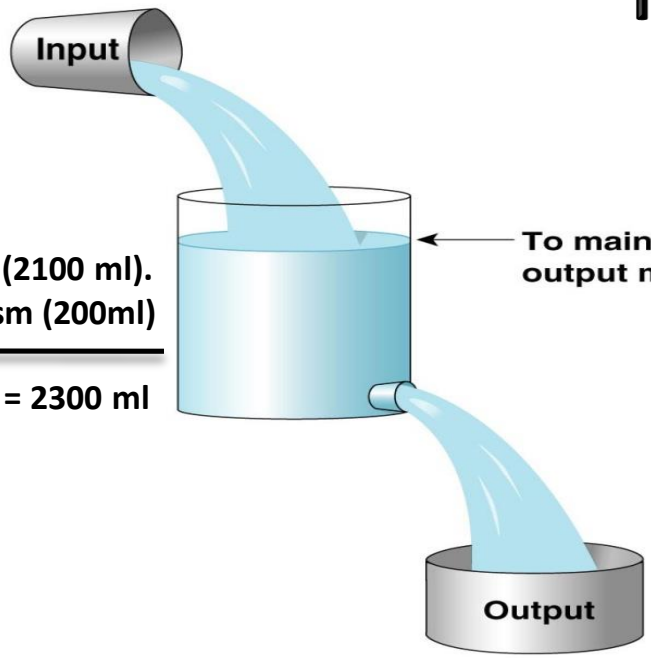
	EXTRACELLULAR FLUID	INTRACELLULAR FLUID
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{++}	2.4 mEq/L	0.0001 mEq/L
Mg^{++}	1.2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L
Phosphates	4 mEq/L	75 mEq/L
SO_4^-	1 mEq/L	2 mEq/L
Glucose	90 mg/dl	0 to 20 mg/dl
Amino acids	30 mg/dl	200 mg/dl ?
Cholesterol, Phospholipids, Neutral fat	0.5 g/dl	2 to 95 g/dl
PO_2	35 mm Hg	20 mm Hg ?
PCO_2	46 mm Hg	50 mm Hg ?
pH	7.4	7.0
Proteins	2 g/dl (5 mEq/L)	16 g/dl (40 mEq/L)

ECF
Charge
++++++

ICF
Charge
- - - - - -
-70 to -95 mv

Fluid Balance in the body

Input = output



Water intake:

- Fluids ingested (2100 ml).
- From metabolism (200ml)

Total intake = 2300 ml

Daily loss:

- Insensible loss (700 ml).
- Sweat (100 ml).
- Feces (100 ml).
- Urine (1400 ml).

Total loss = 2300 ml

Causes of dehydration

- Vomiting
- Diarrhoea
- Decrease water intake
- Increase water out put such as in diabetes
- Increase water loss such as in sweating

Signs of severe dehydration

- Not peeing or having very dark yellow pee.
- Very dry skin.
- Feeling dizzy.
- Rapid heartbeat.
- Rapid breathing.
- Sunken eyes.
- Sleepiness and lack of energy.
- confusion or irritability.
- Fainting.

VOLUME MEASUREMENT OF VARIOUS FLUIDS COMPARTMETNS

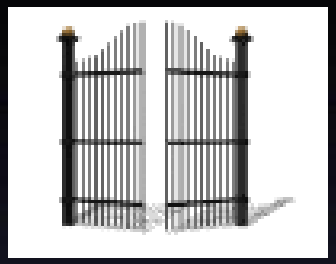
INTERSTITIAL FLUID

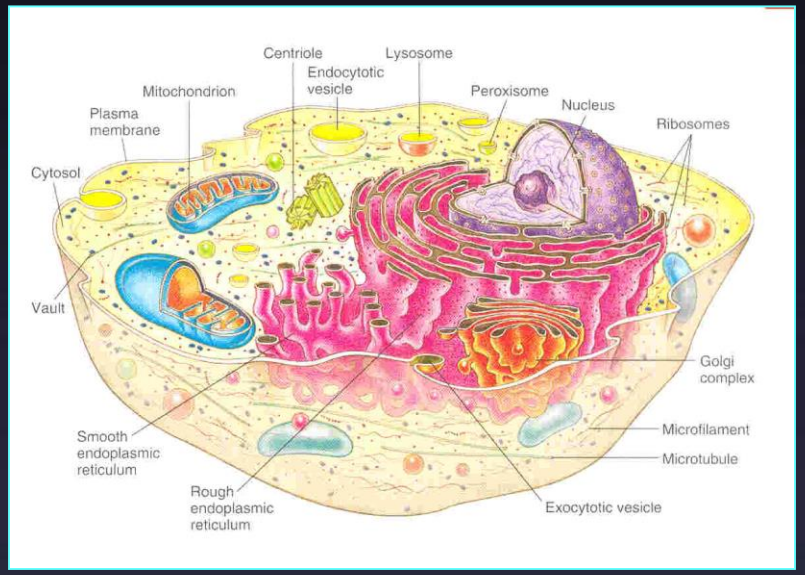
ECF – Plasma Volume

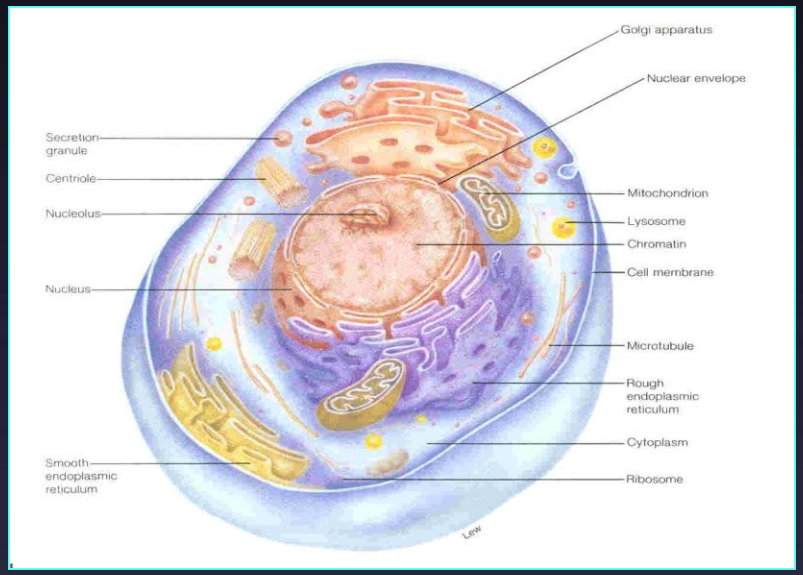
INTRACELLULAR FLUID

TBW – ECF

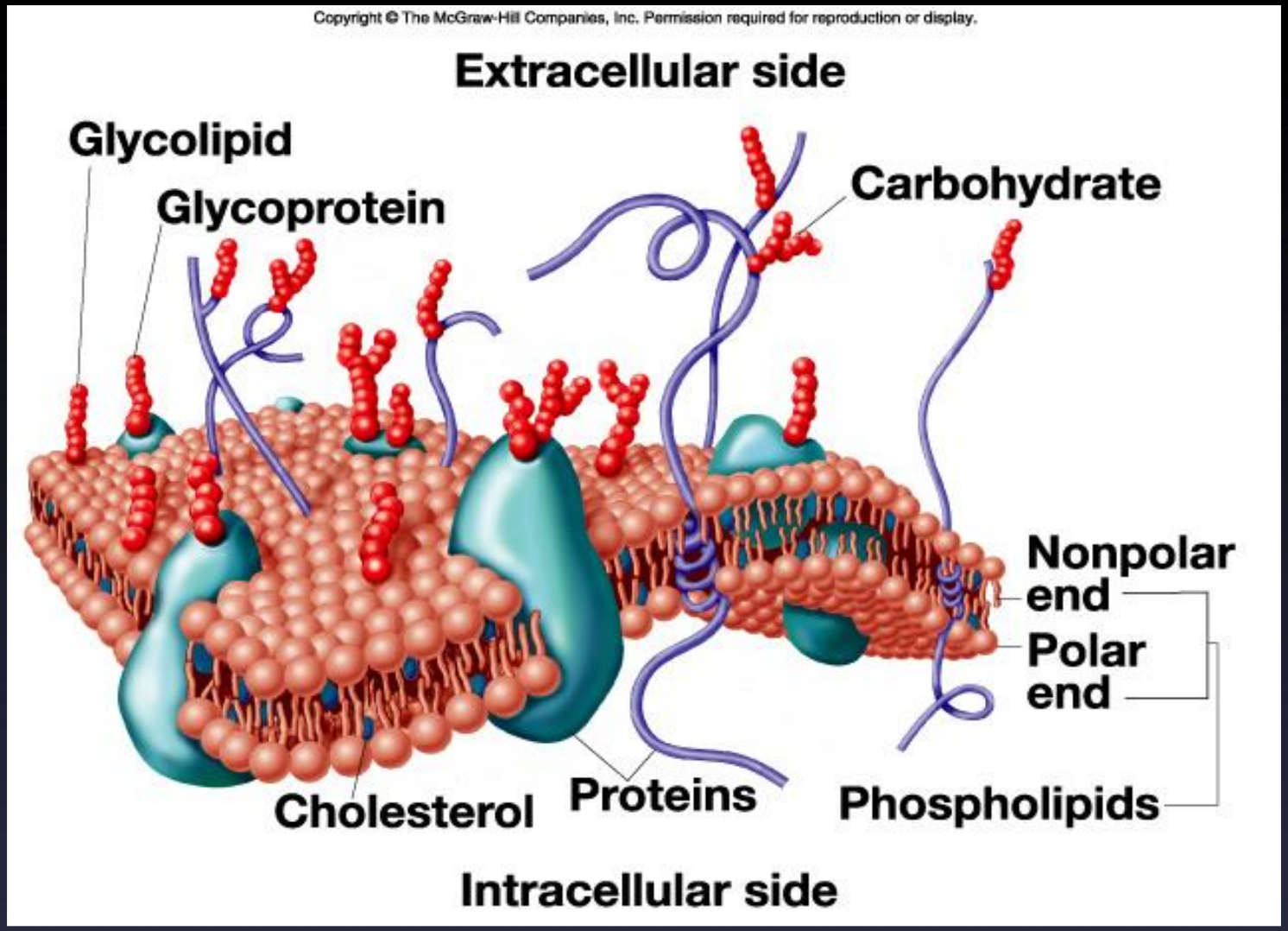
CELL MEMBRANE AND TRANSPORT MECHANISMS







Plasma Membrane (continued)



CELL MEMBRANE COMPOSIOTION

Proteins

1. Integral
2. Peripheral

Lipids

Phospholipids
Cholesterol
Other Lipids

Carbohydrates

Glycocalyx
1. Glycolipid
2. Glycoprotein

- Proteins 55 %
- Phospholipids 25 %
- Cholesterol 13 %
- Other Lipids 4 %
- Carbohydrates 3 %

Cell membrane proteins

Most of which are glycoproteins . they are of 2 types

1- the integral protein:

Provide structural channels (pores) through which water and water soluble substances esp. Ions can diffuse between the ECF and ICF.

Act as carriers proteins for substances that could not penetrate the lipid bilayer,

Others work as enzymes.

2- the peripheral proteins mainly on the inside of the membrane , and they are often attached to one of the integral proteins, function as enzymes,receptors or as other controllers of intracellular function.

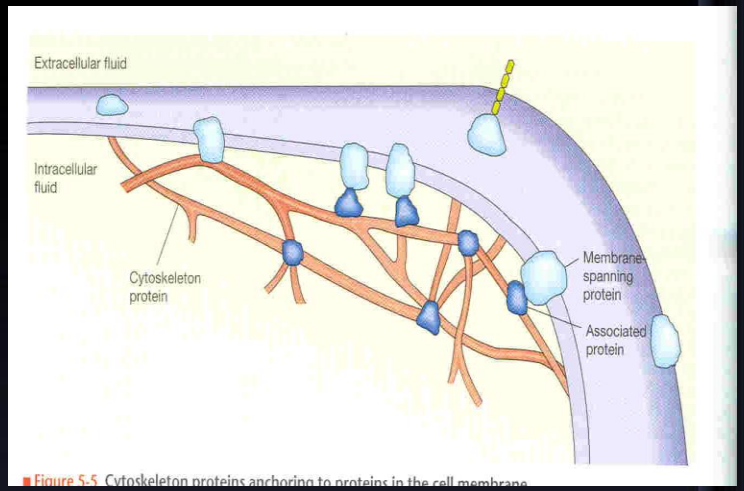
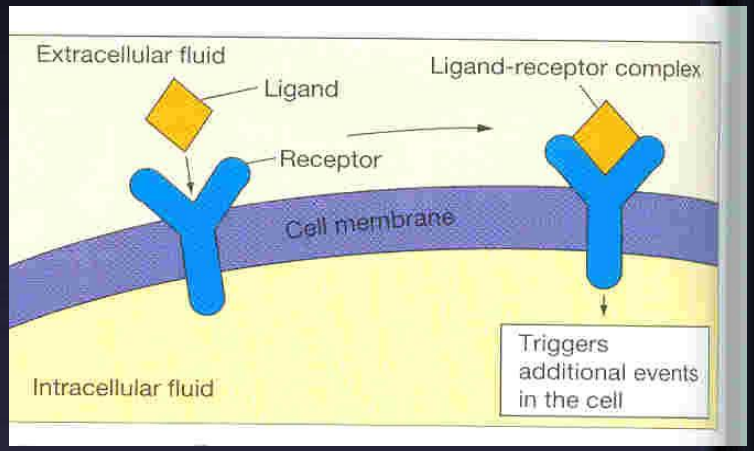


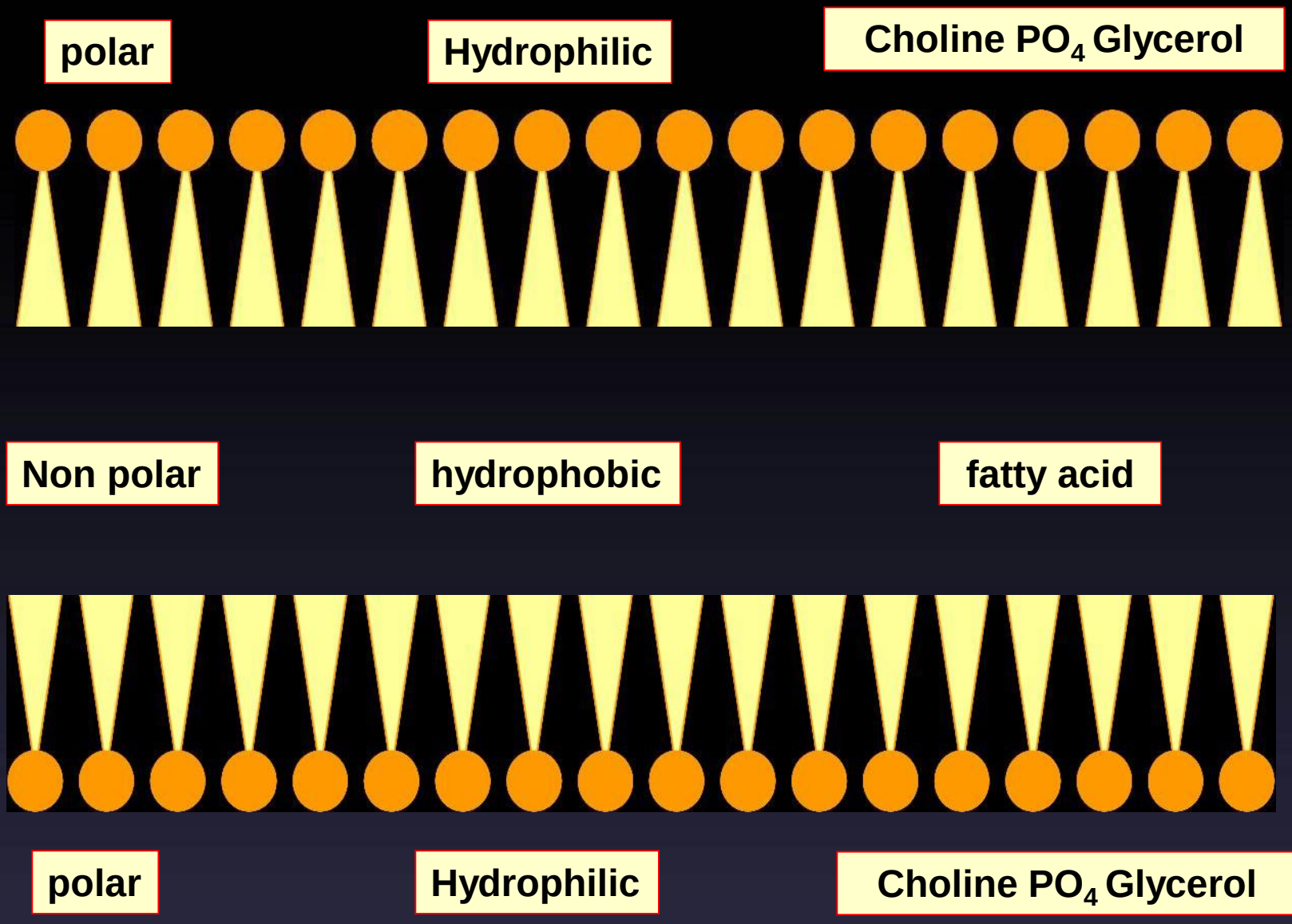
Figure 5-5 Cytoskeleton proteins anchoring to proteins in the cell membrane



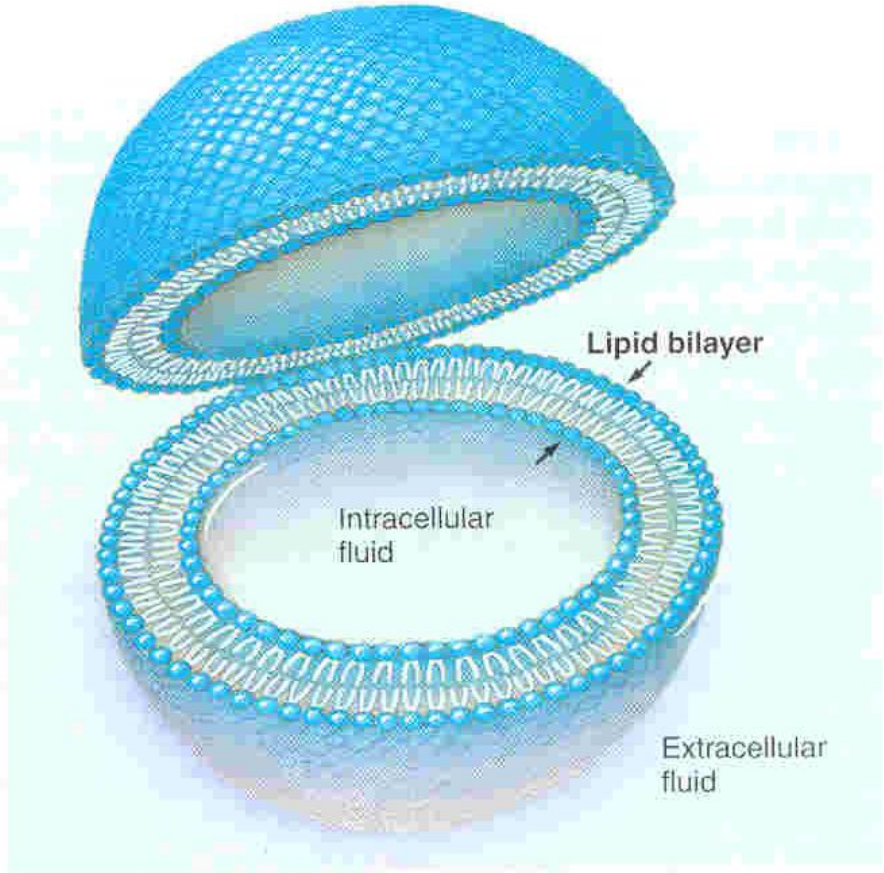
FUNCTIONS OF GLYCOCALYX

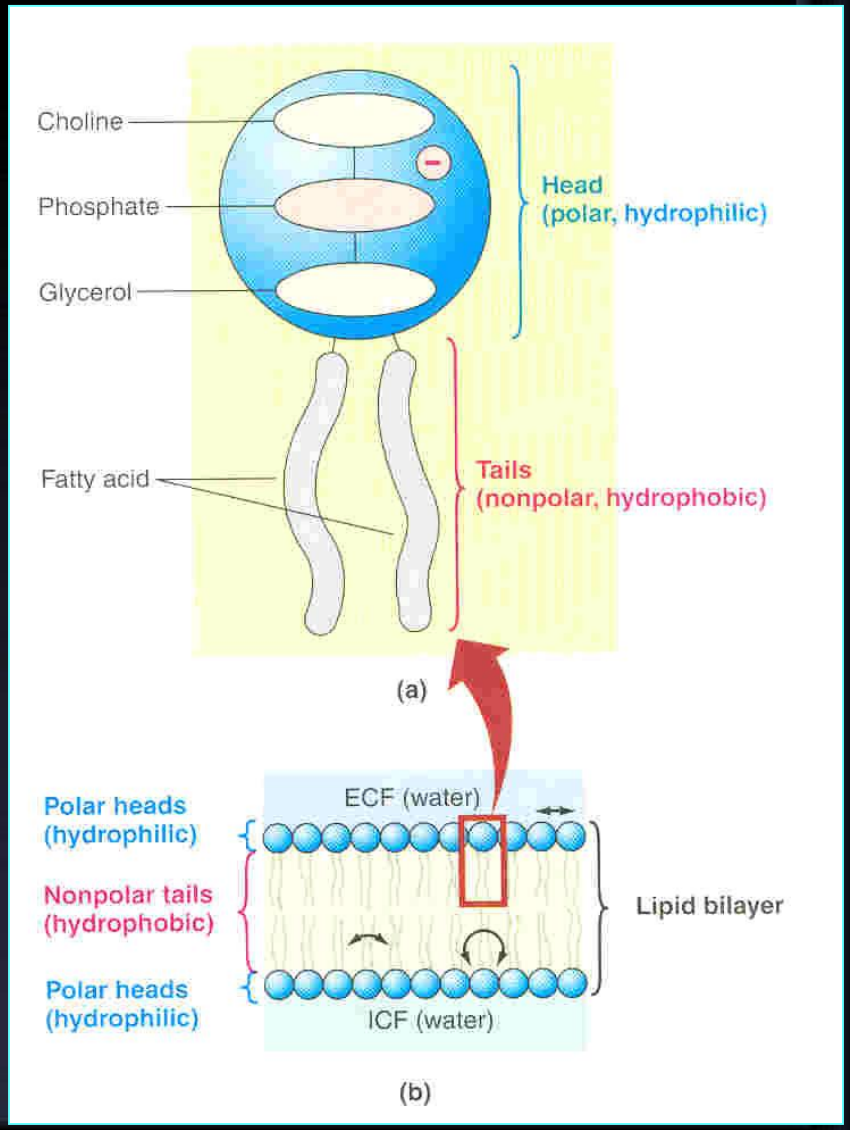
They are responsible for:

- Negative Charge on Cell Membrane that repels other negative objects
- Adhesion between Glycocalyx of different Cells
- Receptors
- Immune Reactions


polar
Hydrophilic
Choline PO_4 Glycerol
Non polar
hydrophobic
fatty acid
polar
Hydrophilic
Choline PO_4 Glycerol

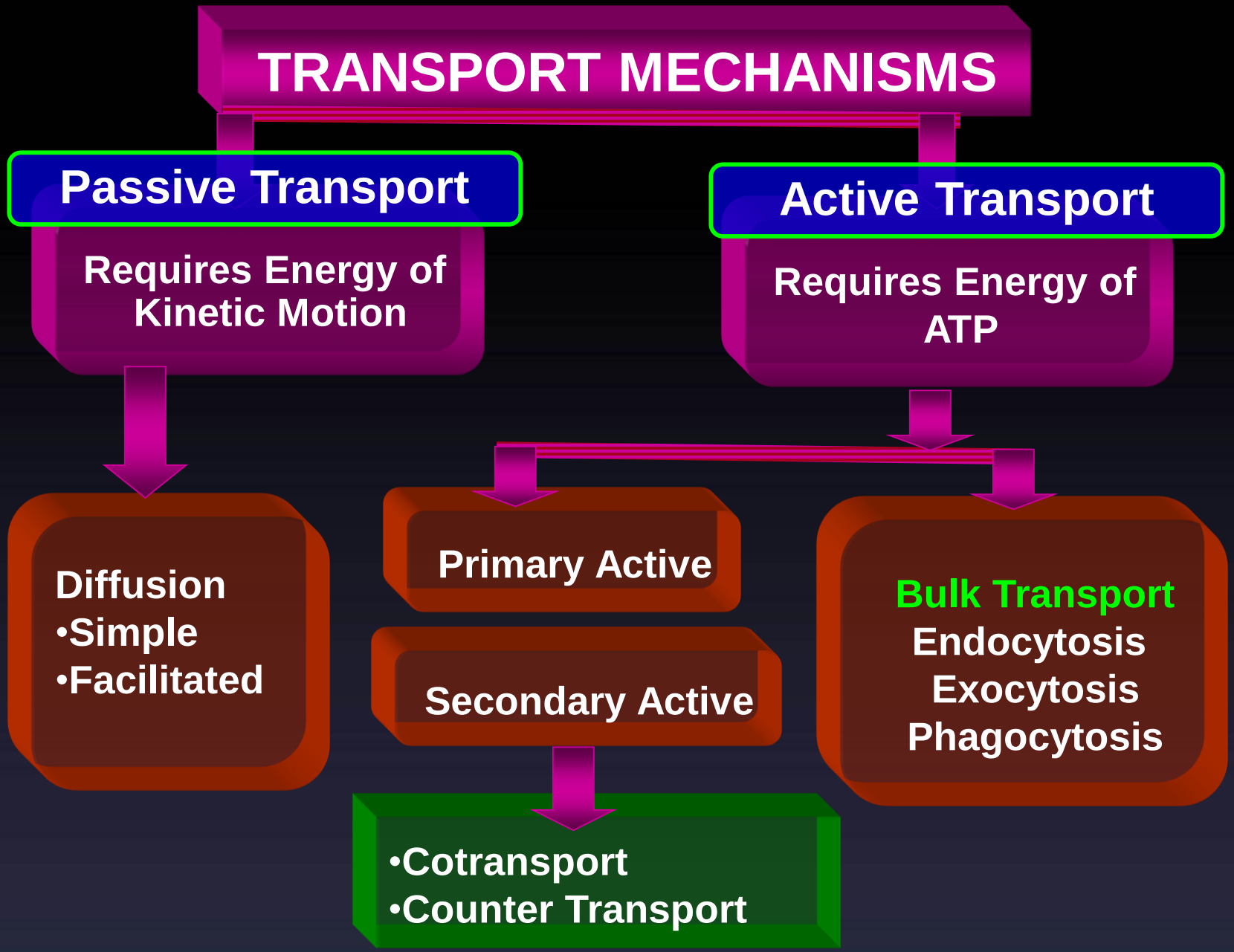
CELL MEMBRANE STRUCTURE





TRANSPORT MECHANISMS

- Cell membrane is selectively permeable to some molecules and ions.
- Not permeable to proteins, nucleic acids, and other molecules.


TRANSPORT MECHANISMS
Passive Transport
Requires Energy of Kinetic Motion
Active Transport
Requires Energy of ATP
Diffusion
•Simple
•Facilitated
Primary Active
Secondary Active
•Cotransport
•Counter Transport
Bulk Transport
Endocytosis
Exocytosis
Phagocytosis

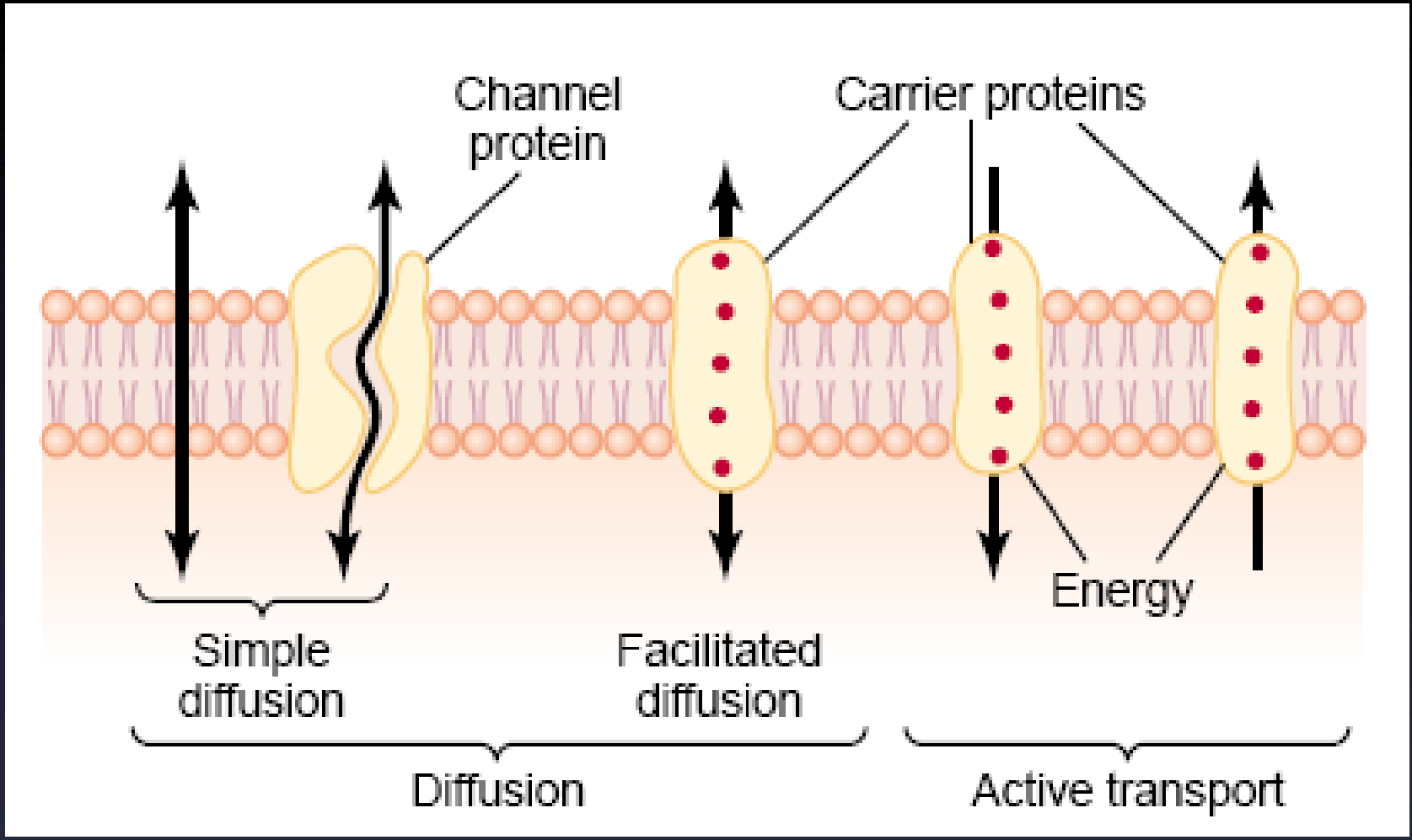
Categories of Transport Across the Plasma Membrane

- **Categorized by their energy requirements:**
  - **Passive transport:**
    - **Net movement down a concentration gradient. (High to low concentration)**
      - **Does not require metabolic energy of ATP.**
  - **Active transport:**
    - **Net movement against a concentration gradient. (Low to high concentration)**
      - **Requires ATP [Directly (Primary) Indirectly (Secondary)]**

Categories of Transport Across the Plasma Membrane

- **Mechanisms to transport molecules and ions through the cell membrane:**
  - **Carrier mediated transport:**
    - **Facilitated diffusion and active transport.**
  - **Non-carrier mediated transport.**
    - **Simple Diffusion and osmosis.**

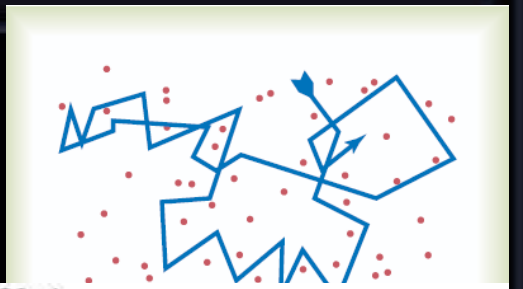
Categories of Transport Across the Plasma Membrane (continued)



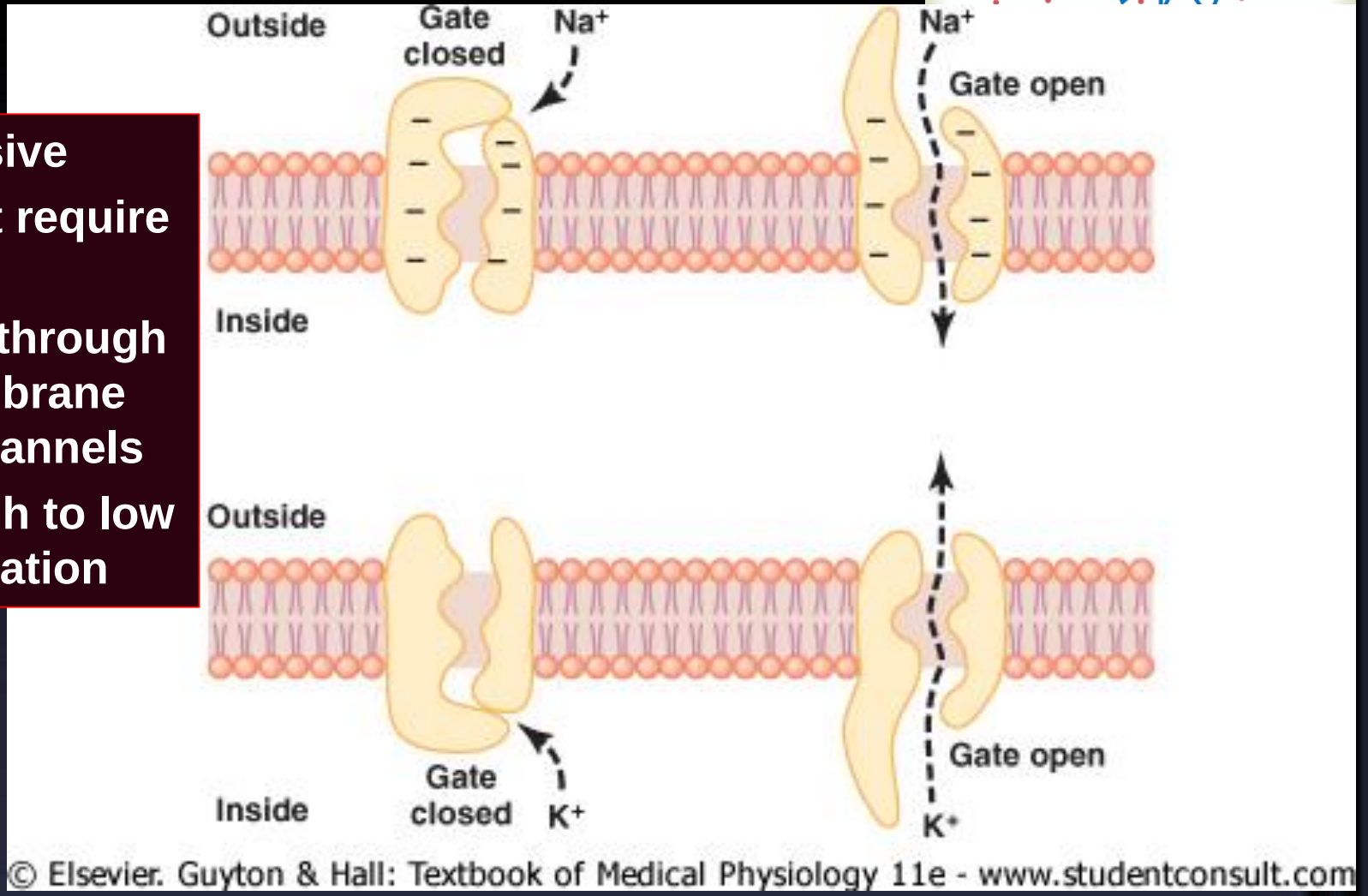
Diffusion

- Molecules/ions are in constant state of random motion due to their thermal energy.
  - Eliminates a concentration gradient and distributes the molecules uniformly.
- Physical process that occurs whenever there is a concentration difference across the membrane and the membrane is permeable to the diffusing substance.

Simple Diffusion



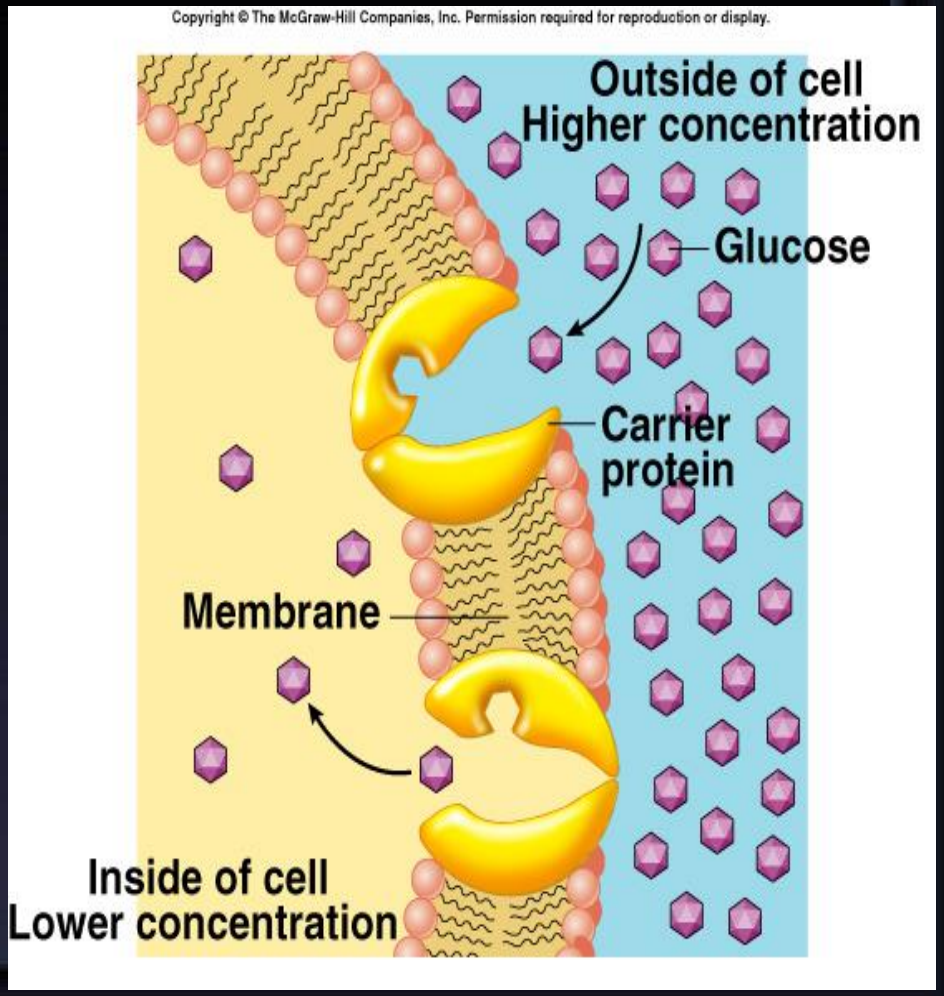
- It is Passive
- Does not require carrier
- Is either through cell membrane or ion channels
- From high to low concentration



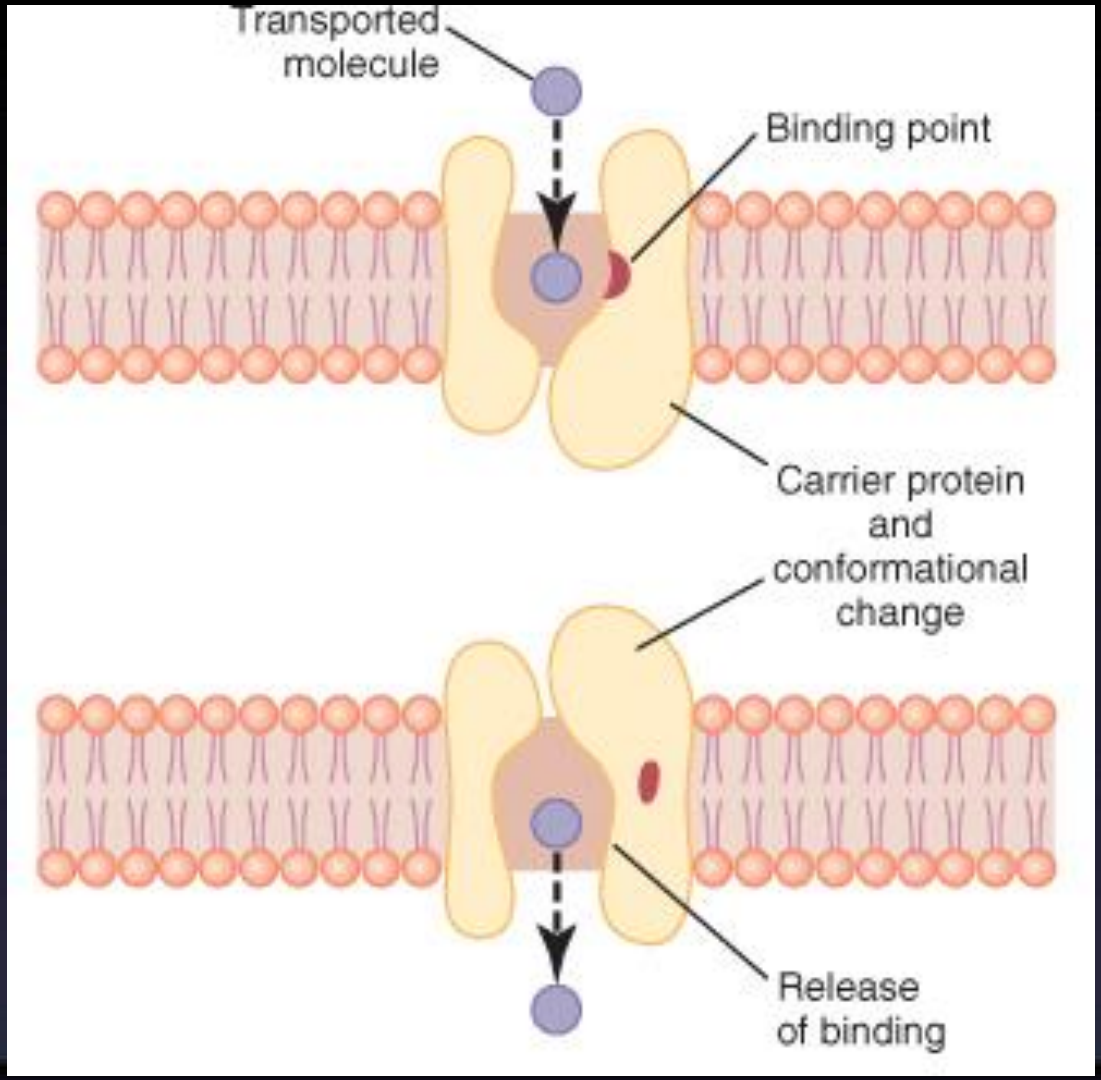
Facilitated Diffusion

It is Passive

- ATP not needed.
  - Powered by thermal energy of diffusing molecules.
- Involves transport of substance through plasma membrane down concentration gradient by carrier proteins.
  - Transport carriers for glucose designated as GLUT.



Facilitated Diffusion



Diffusion Through Plasma Membrane

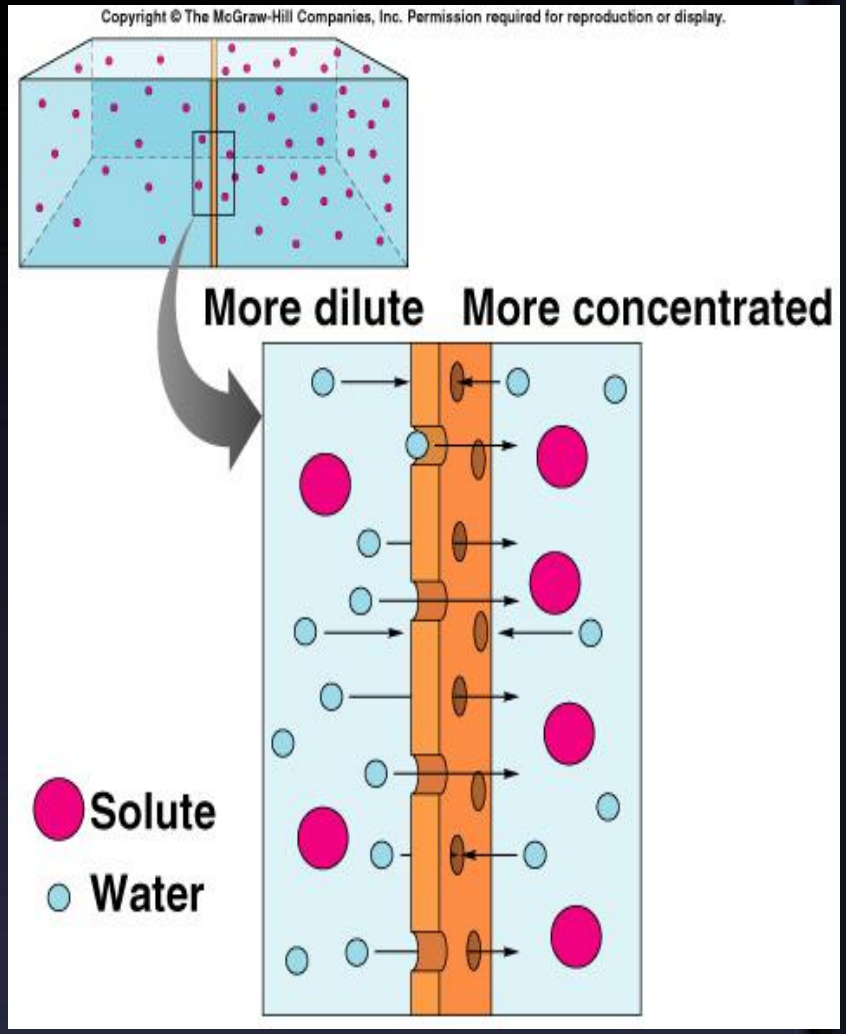
- **Cell membrane is permeable to:**
  - Non-polar molecules (0_2).
  - Lipid soluble molecules (steroids).
  - Small polar covalent bonds ($C0_2$).
  - H_20 (small size, lack charge).
- **Cell membrane impermeable to:**
  - Large polar molecules (glucose).
  - Charged inorganic ions (Na^+).

FACTORS AFFECTING NET RATE OF DIFFUSION

- **Permeability (Neuronal plasma membrane 20 x more permeable to K^+ than $Na^{+)}$**
  - **Thickness**
  - **Lipid Solubility**
  - **Protein Channels**
  - **Temperature**
  - **Molecular weight**
- **Surface Area**
- **Concentration Difference**
- **Electrical Potential**
- **Pressure Difference**

Osmosis

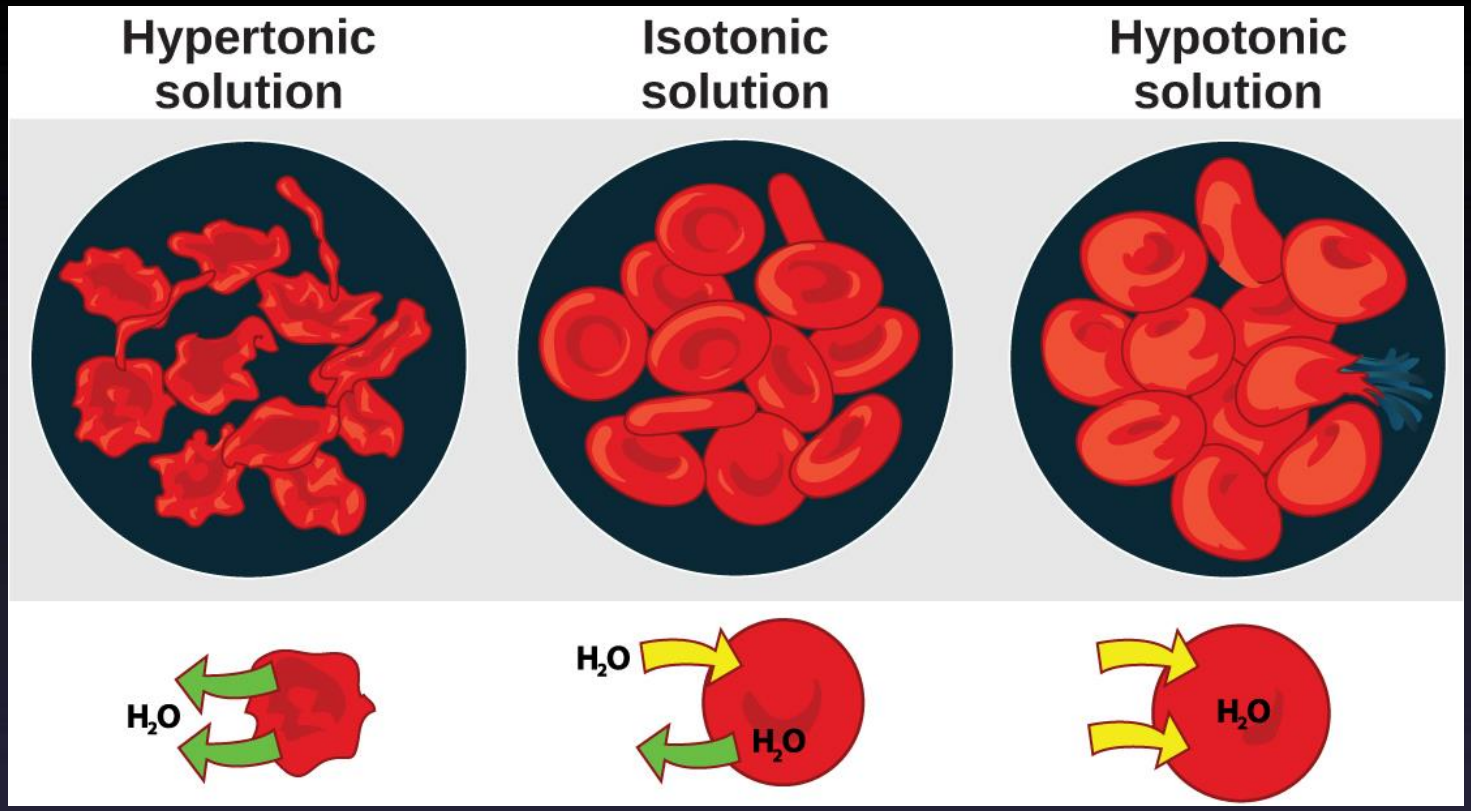
- Net diffusion of H_20 across a selectively permeable membrane.
- Movement of H_20 from a high[H_20] to lower [H_20] area until equilibrium is reached.
- 2 requirements for osmosis:
  - Must be difference in [solute] on the 2 sides of the membrane.
  - Membrane must be impermeable to the solute.
- Osmotically active solutes:
  - Solutes that cannot pass freely through the membrane.



Tonicity and its effect on movement of H_20

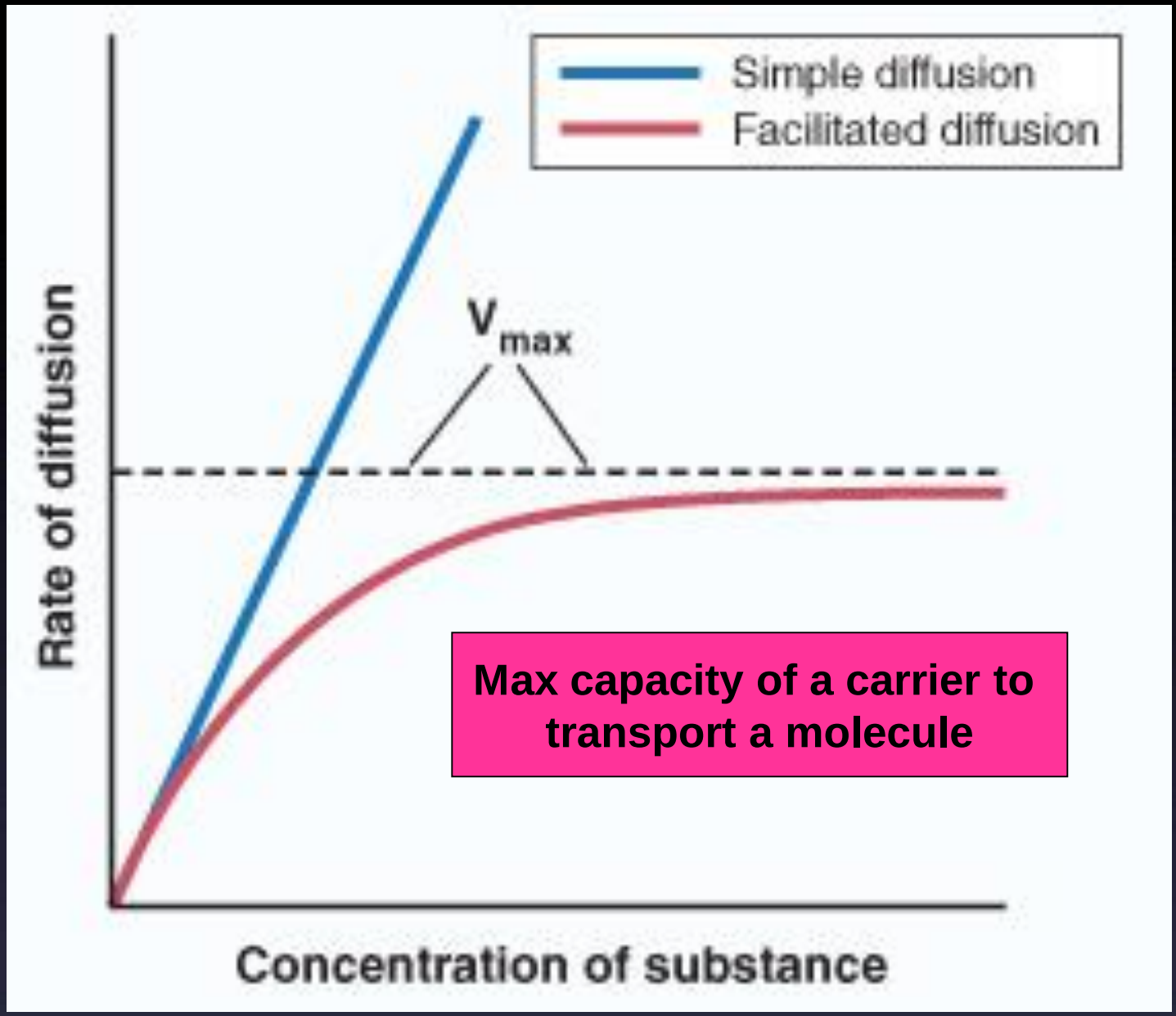
- **Isotonic:**
  - Equal tension omsolality (300 mosm/l) to plasma.
    - RBCs will not gain or lose H_20.
- **Hypotonic:**
  - Osmotically active solutes in a lower osmolality and osmotic pressure than plasma.
    - RBC will hemolyse.
- **Hypertonic:**
  - Osmotically active solutes in a higher osmolality and osmotic pressure than plasma.
    - RBC will crenate.

Effect of plasma osmolarity on Red Blood Cells (RBCs)

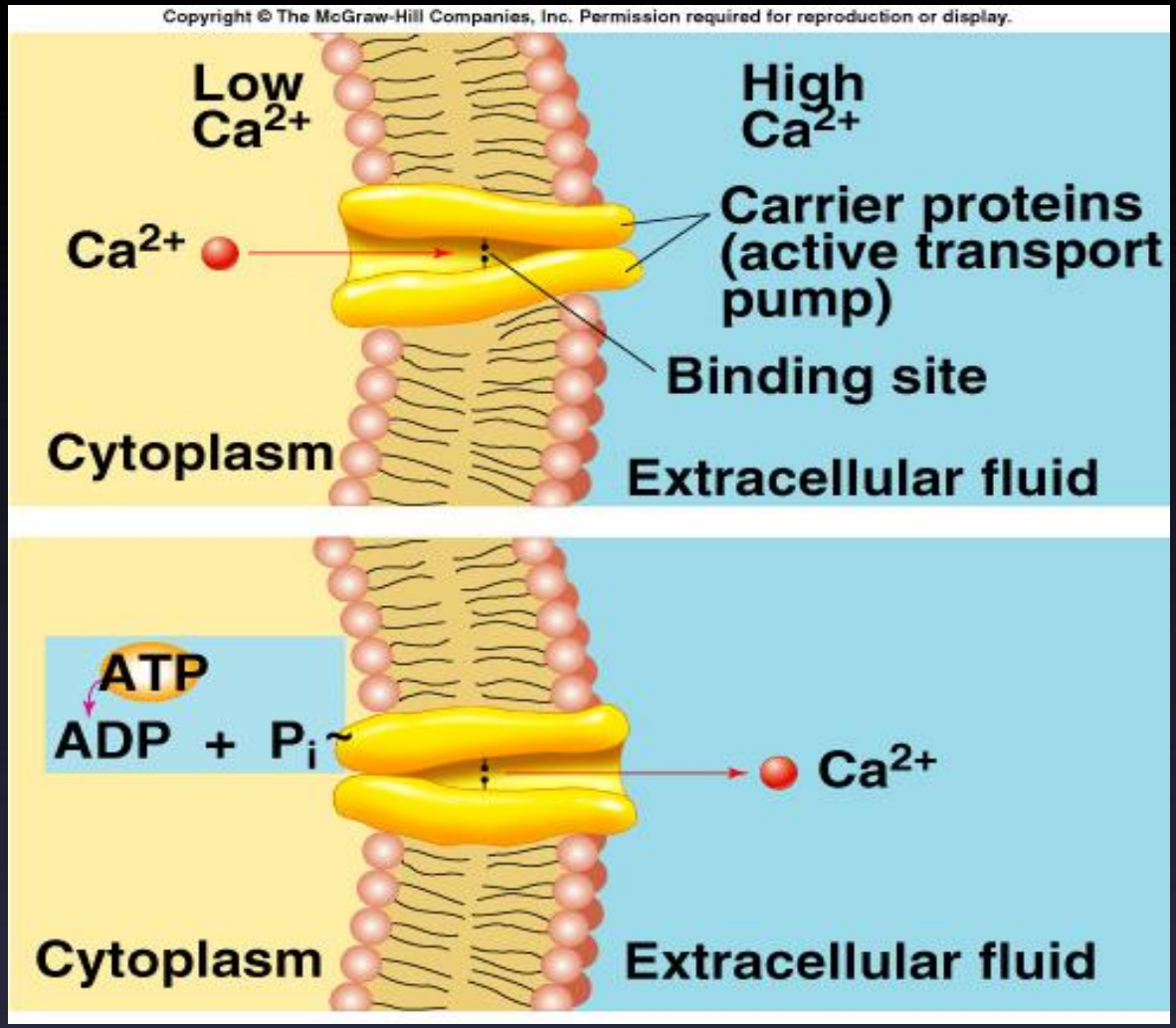


Plasma high in solutes ECF=ICF plasma low in solute

osmolarity

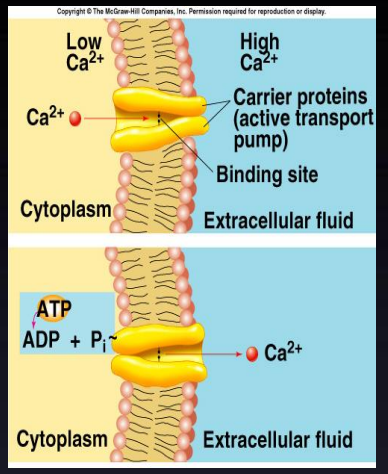

Simple diffusion
Facilitated diffusion
V_{max}
Rate of diffusion
Concentration of substance
Max capacity of a carrier to transport a molecule

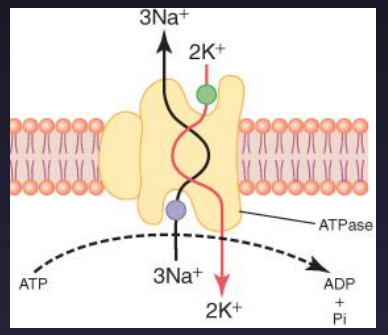
Primary Active Transport



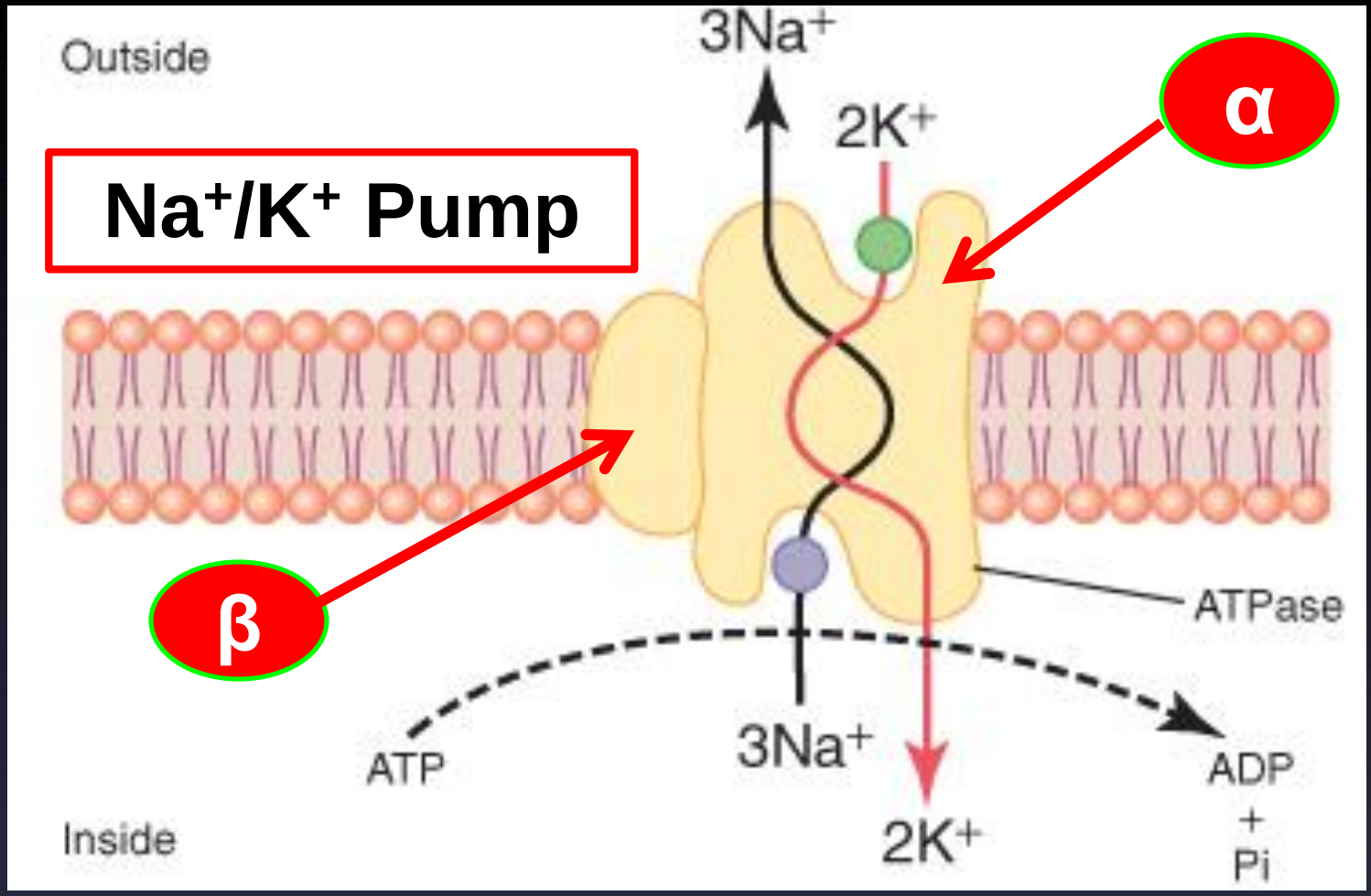
Primary Active Transport

- Hydrolysis of ATP **directly** required for the function of the pump for transport **against concentration gradient**.
- Molecule or ion binds to "recognition site" on one side of pump.
- Binding stimulates phosphorylation (breakdown of ATP) of carrier protein.
- Carrier protein undergoes conformational change.
  - Hinge-like motion releases transported molecules to opposite side of membrane.



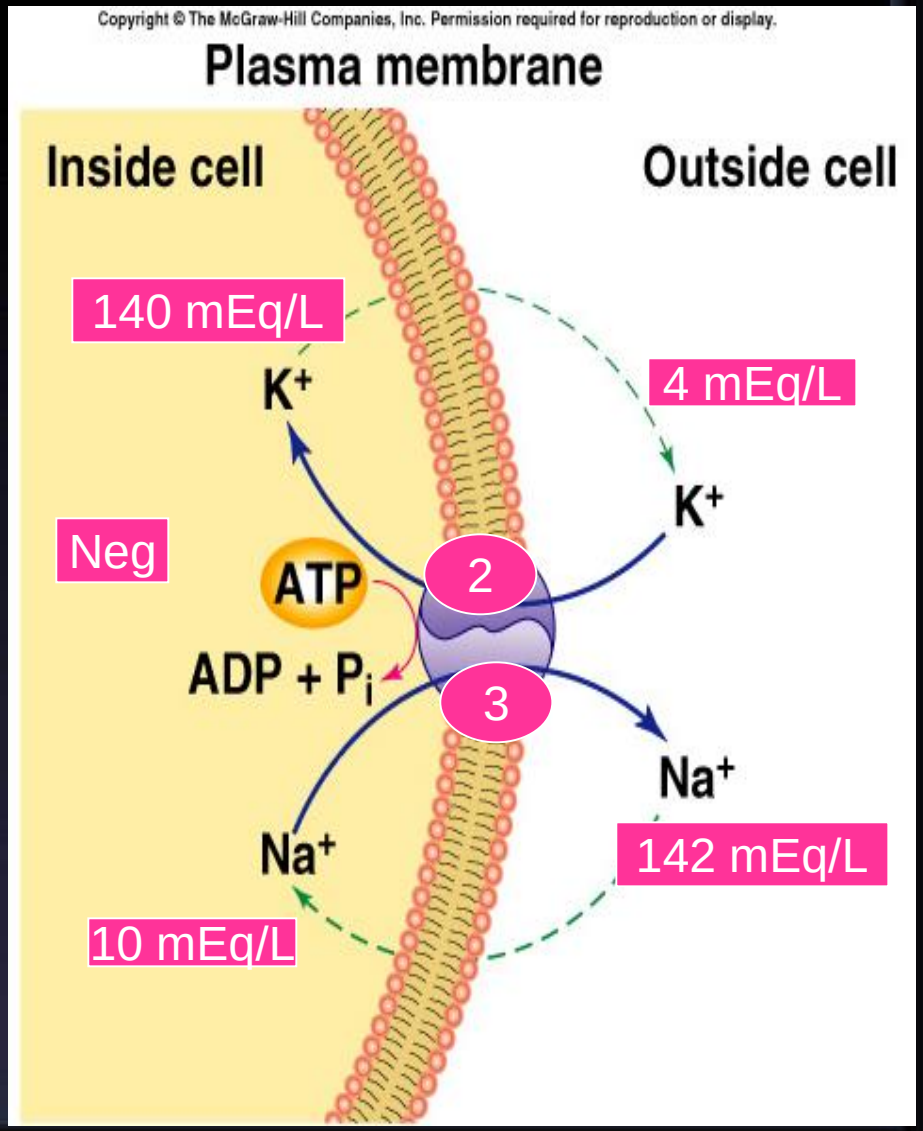


Primary Active Transport



Na^+/K^+ Pump

- Carrier protein is also an ATP enzyme that converts ATP to ADP and Pi.
  - Actively extrudes 3 Na^+ and transports 2 K^+ inward against concentration gradient.
- Steep gradient serves 4 functions:
  - Provides energy for "coupled transport" of other molecules.
  - Regulates resting calorie expenditure and BMR.
  - Involvement in electrochemical impulses.
  - Promotes osmotic flow.



Secondary Active Transport

Co Transport

Cotransport (Symport): Molecules or ion moving in the same direction as Na^+ Glucose cotransport.

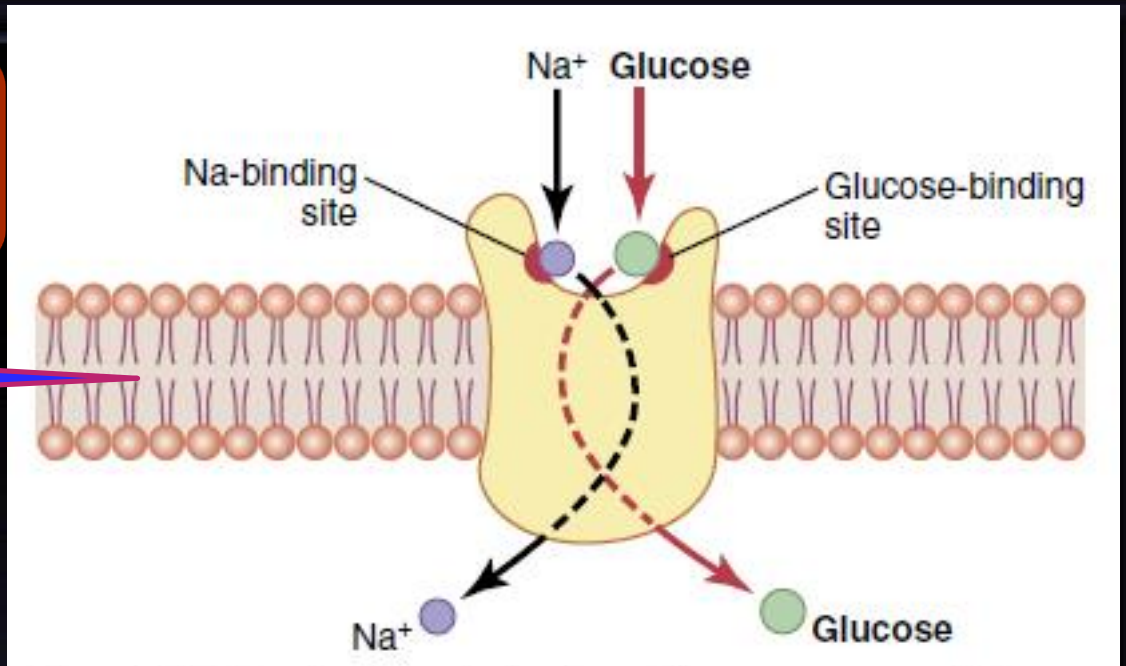
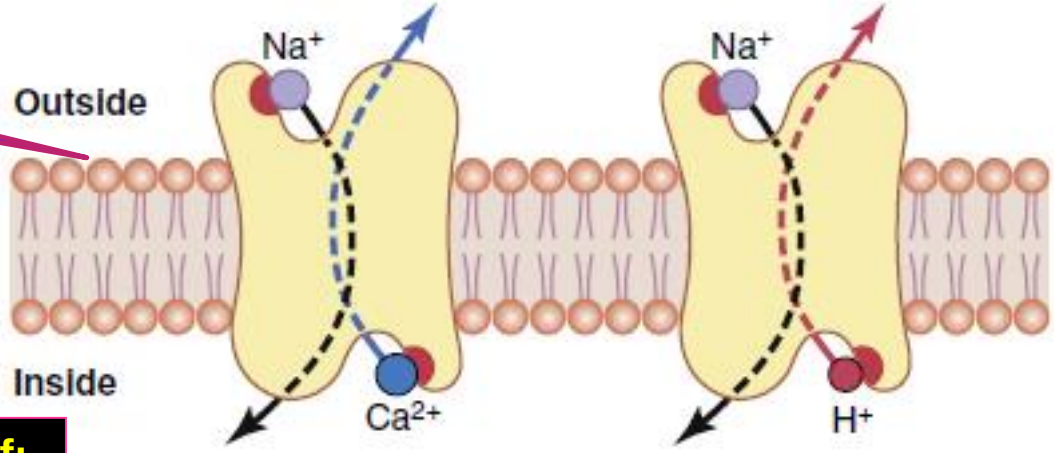


Figure 4-13 Postulated mechanism for sodium co-transport of glucose.

Counter Transport

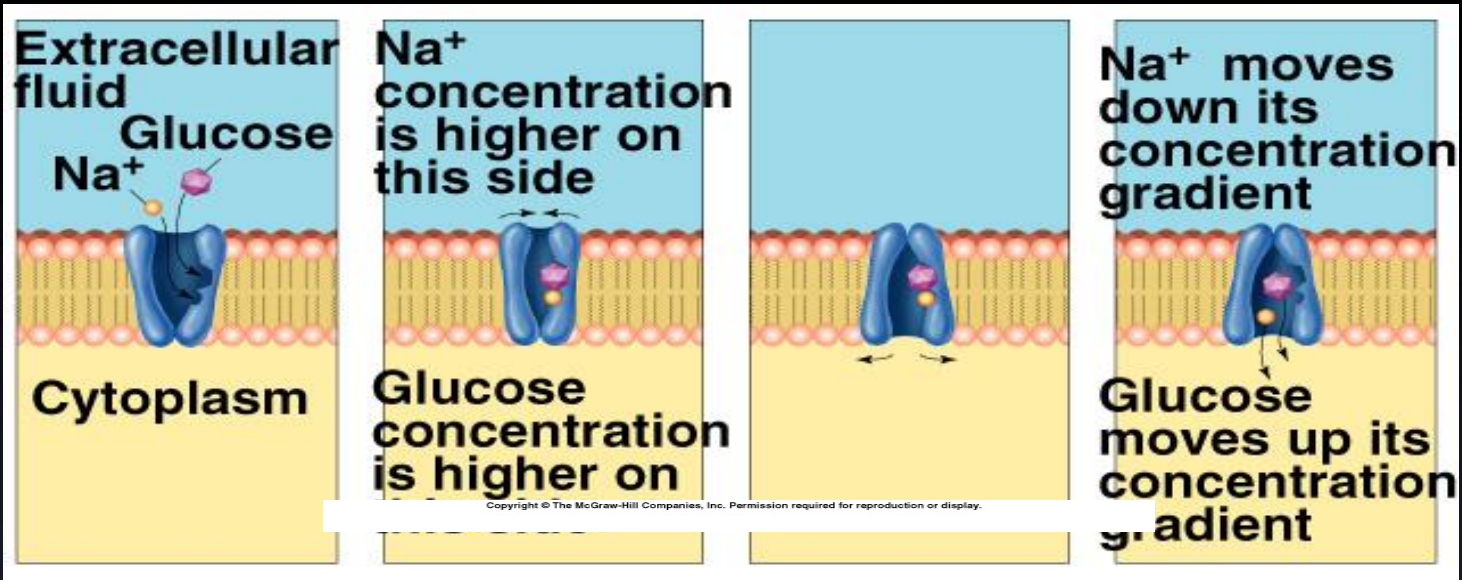
Countertransport (Antiport): Molecule or ion moving in the opposite direction of Na^+ H^+ counter transport.



ure 4-14. Sodium counter-transport of calcium and hydrogen ions.

Glucose transport is an example of:
Cotransport. & Facilitated diffusion.

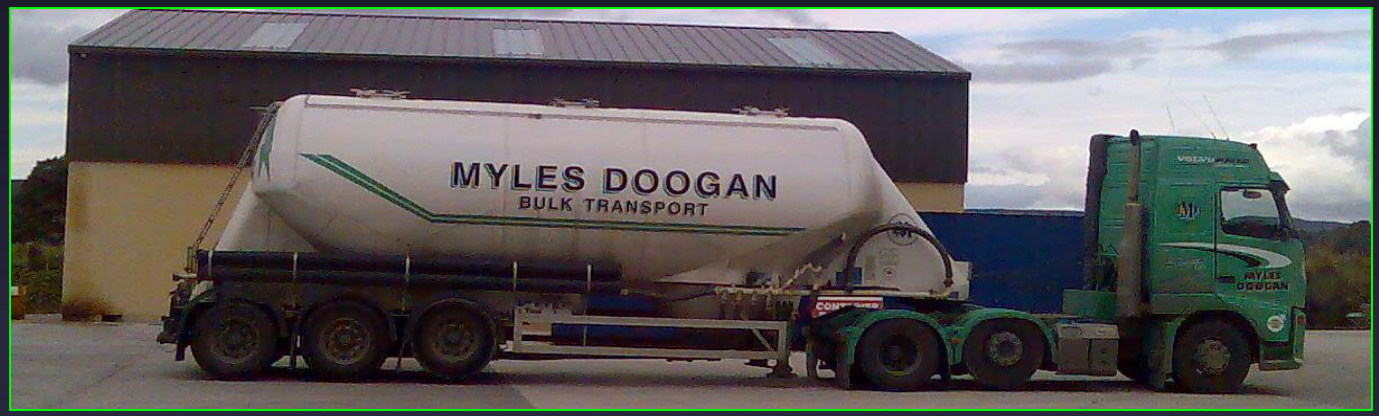
Secondary Active Transport

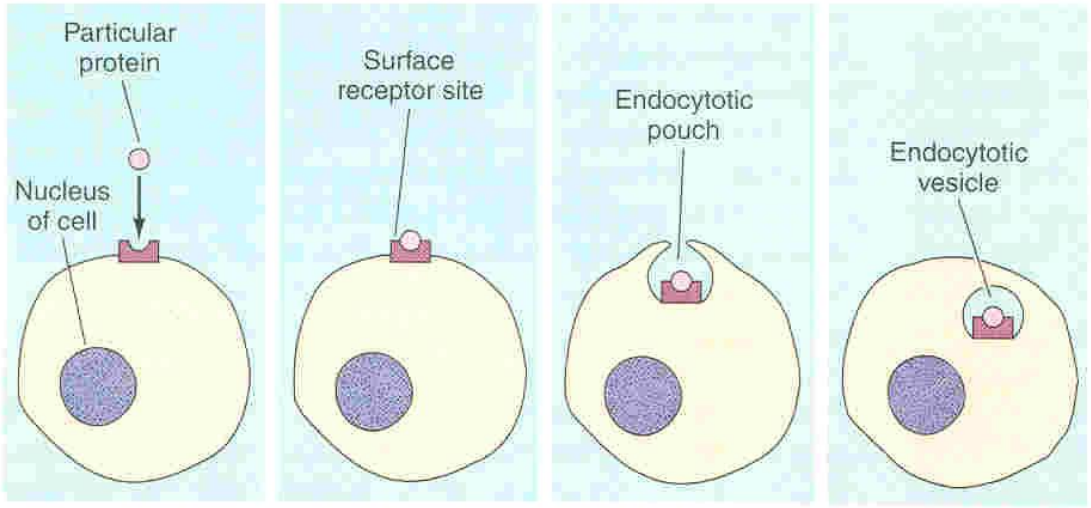


- Coupled transport.
- Energy needed for "uphill" movement obtained from "downhill" transport of Na^+.
- Hydrolysis of ATP by Na^+/K^+ pump required indirectly to maintain [Na^+] gradient.

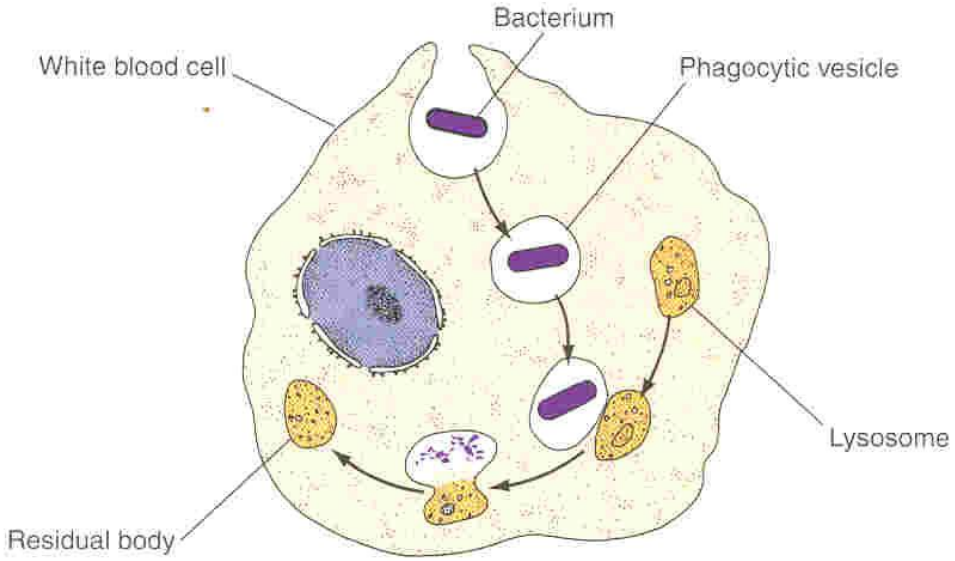
Bulk Transport

- **Movement of many large molecules, that cannot be transported by carriers, at the same time.**
- **Exocytosis:**
  - **Fusion of the membrane-bound vesicles that contains cellular products with the plasma membrane.**
- **Endocytosis:**
  - **Exocytosis in reverse.**
  - **Specific molecules can be taken into the cell because of the interaction of the molecule and protein receptor.**

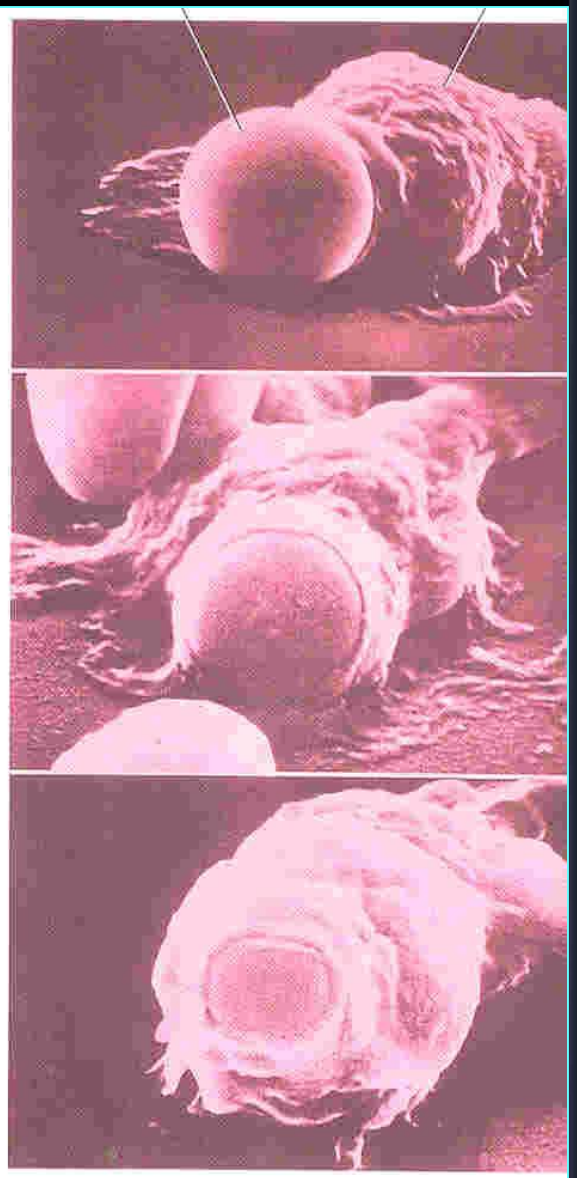




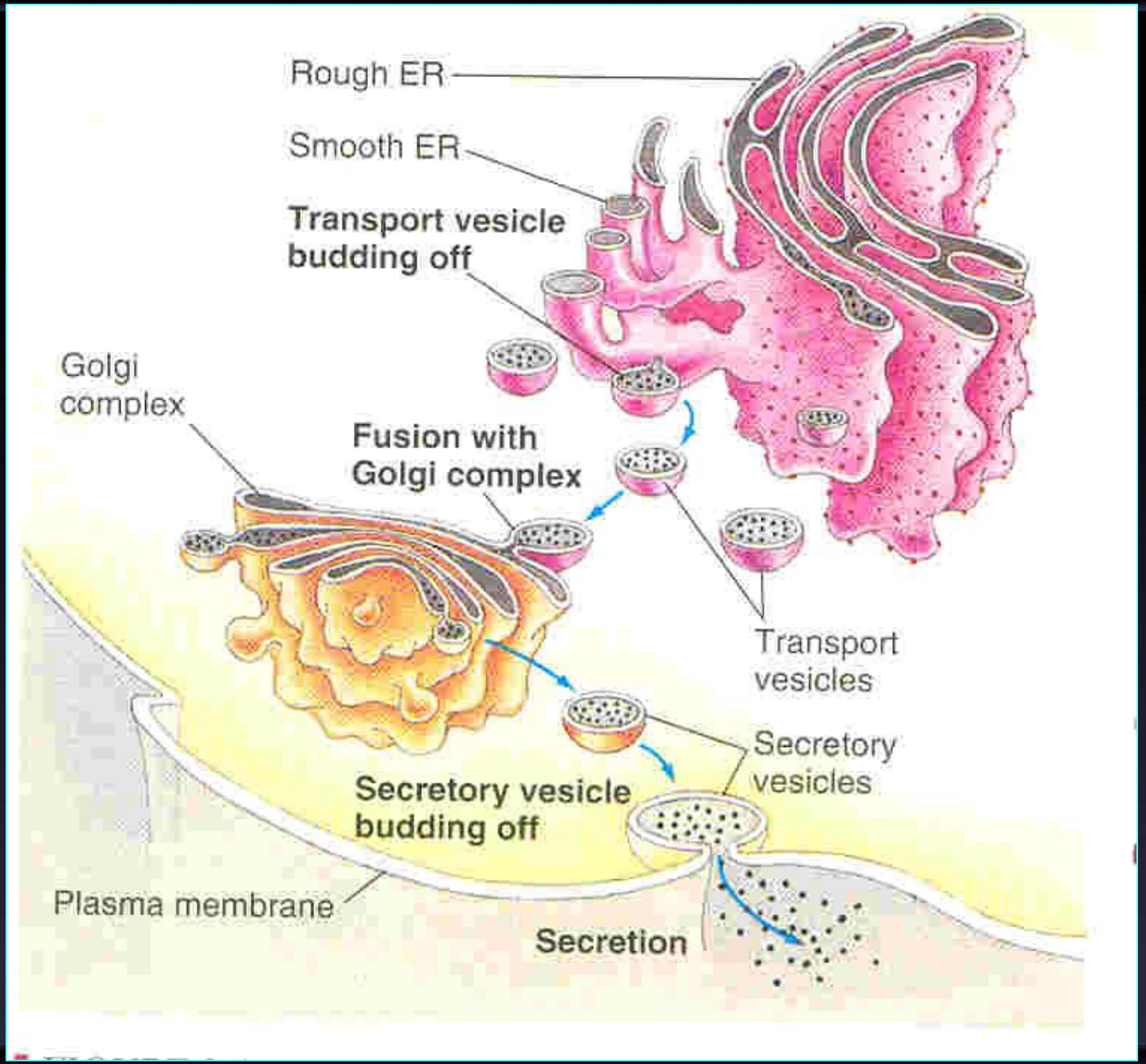
(a) Receptor-mediated endocytosis



(b) Phagocytosis



(c)


Rough ER
Smooth ER
Transport vesicle budding off
Golgi complex
Fusion with Golgi complex
Transport vesicles
Secretory vesicles
Secretory vesicle budding off
Plasma membrane
Secretion