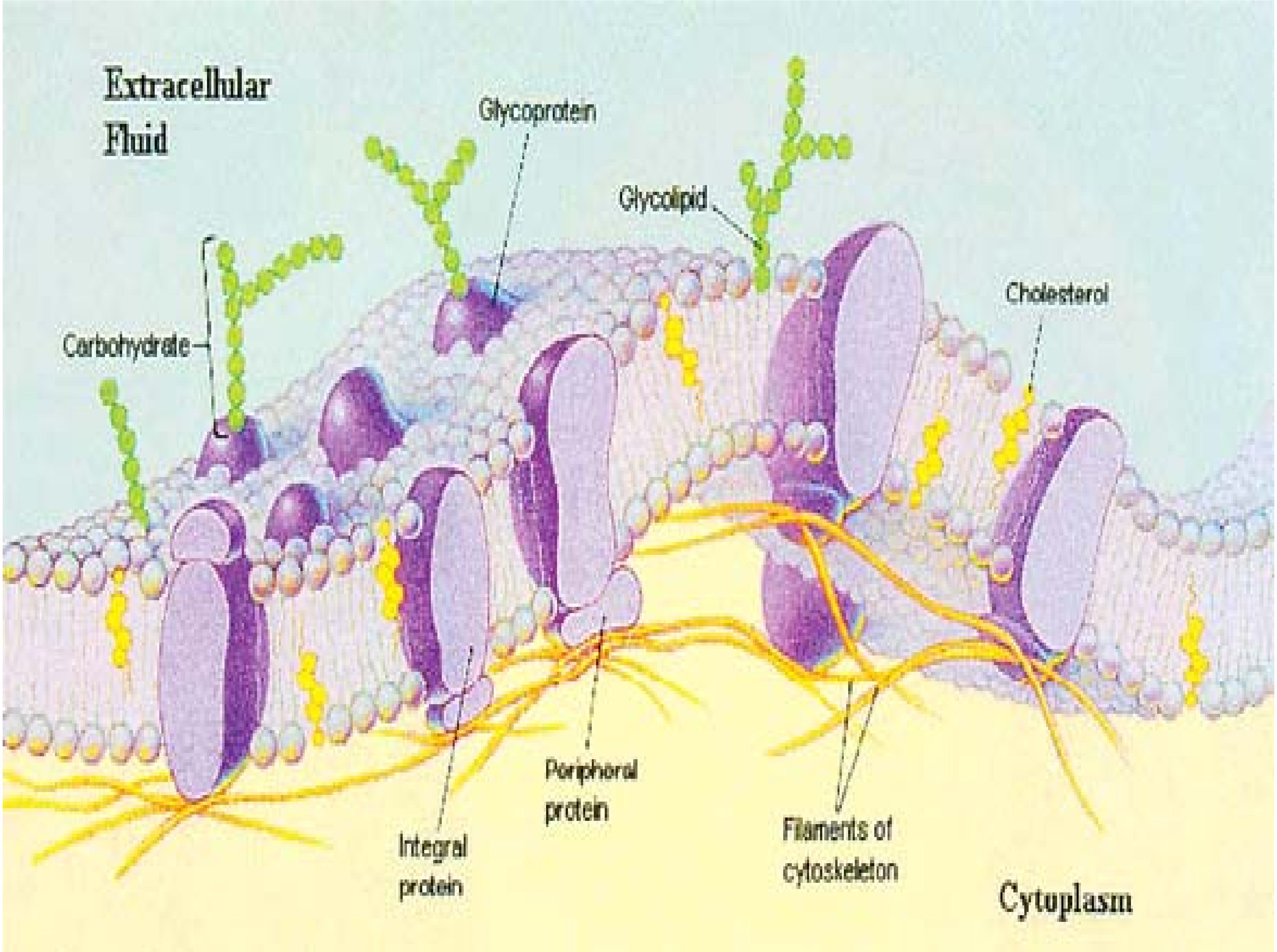
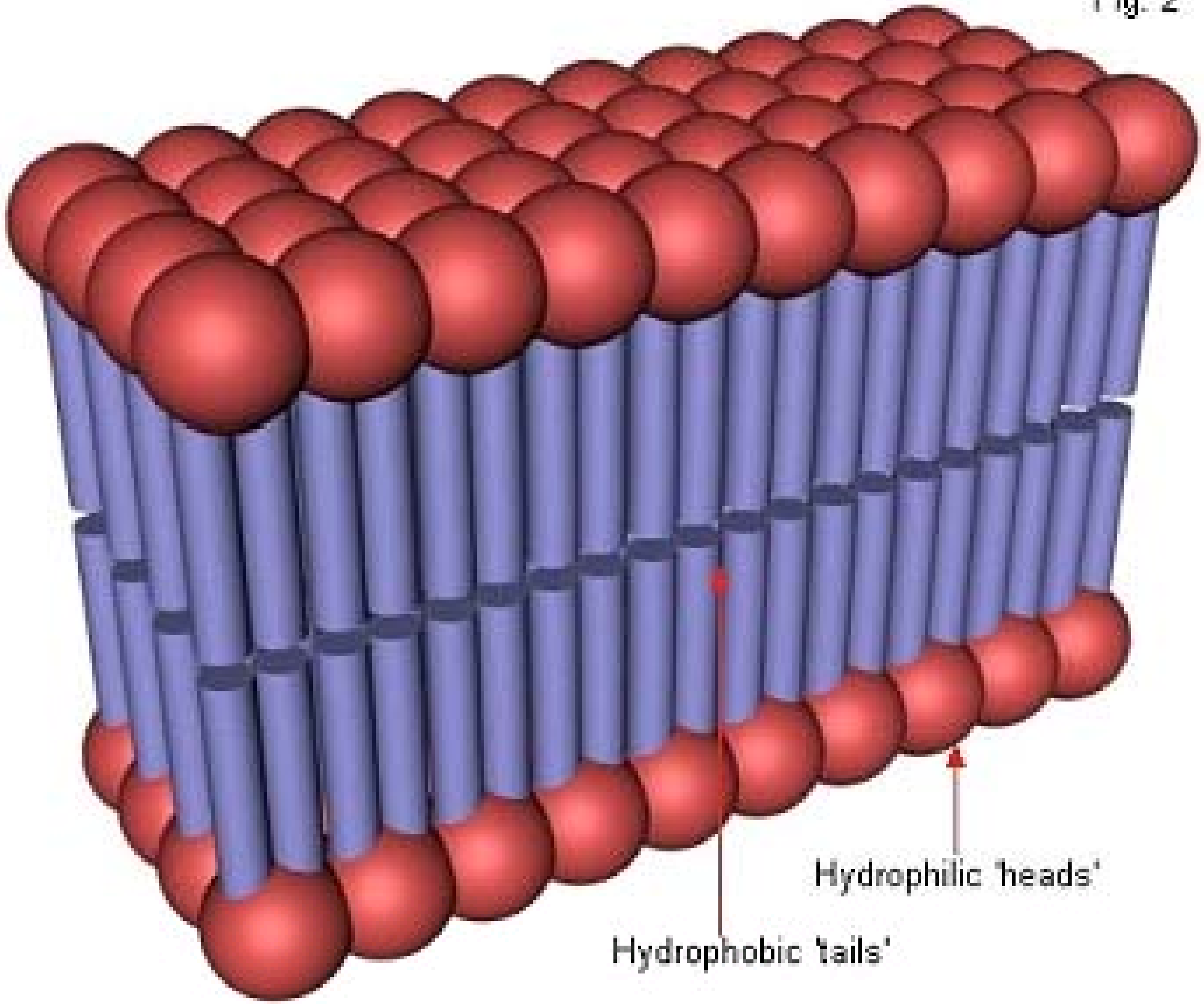
CELLULAR EXCHANGE

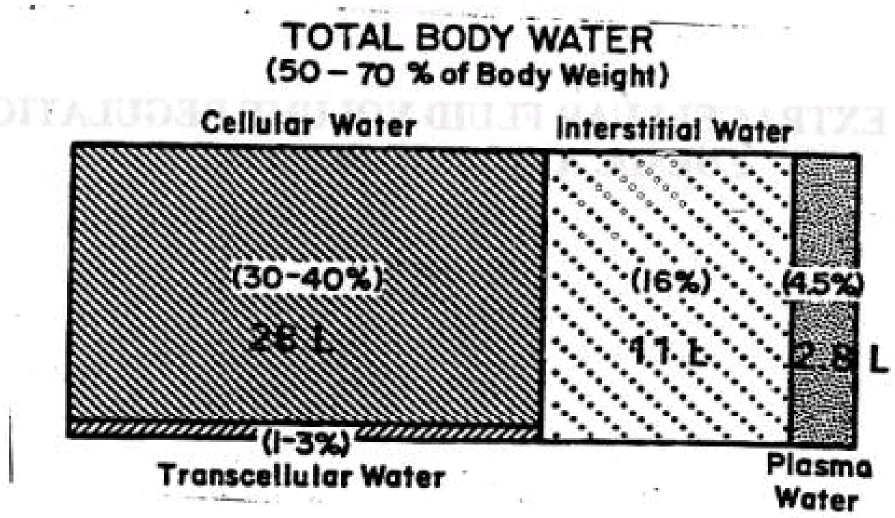
D.HAMMOUDI.MD



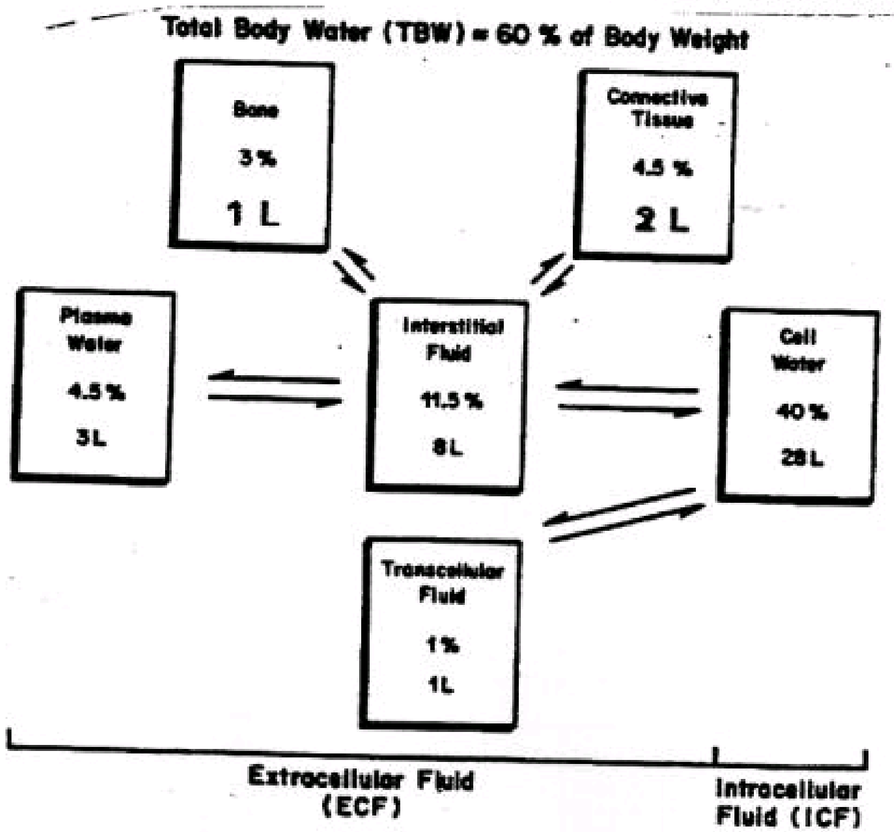
Extracellular Fluid
Glycoprotein
Glycolipid
Carbohydrate
Cholesterol
Peripheral protein
Integral protein
Filaments of cytoskeleton
Cytoplasm

Fig. 2





A more detailed examination of the distribution of the total body water is in the next slide:



Fluid within the body

- **Intracellular fluid** = ICF= 2/3 BODY WATER
- **EXTRACELLULAR FLUID** =ECF= 1/3 BODY WATER
- **INTERSTITIAL FLUID** =ISF=2/3 EXTRACELLULAR FLUID
- **Total blood volume** =plasma [extracellular volume] and the cellular elements of blood [red cells [intracellular fluid]

The body's water is effectively compartmentalized into several major divisions.

Intracellular Fluid (ICF) comprises 2/3 of the body's water.

- If your body has 60% water, ICF is about 40% of your weight.
- The ICF is primarily a solution of potassium and organic anions, proteins etc. (Cellular Soup!).
- The cell membranes and cellular metabolism control the constituents of this ICF.
- ICF is not homogeneous in your body. It represents a conglomeration of fluids from all the different cells

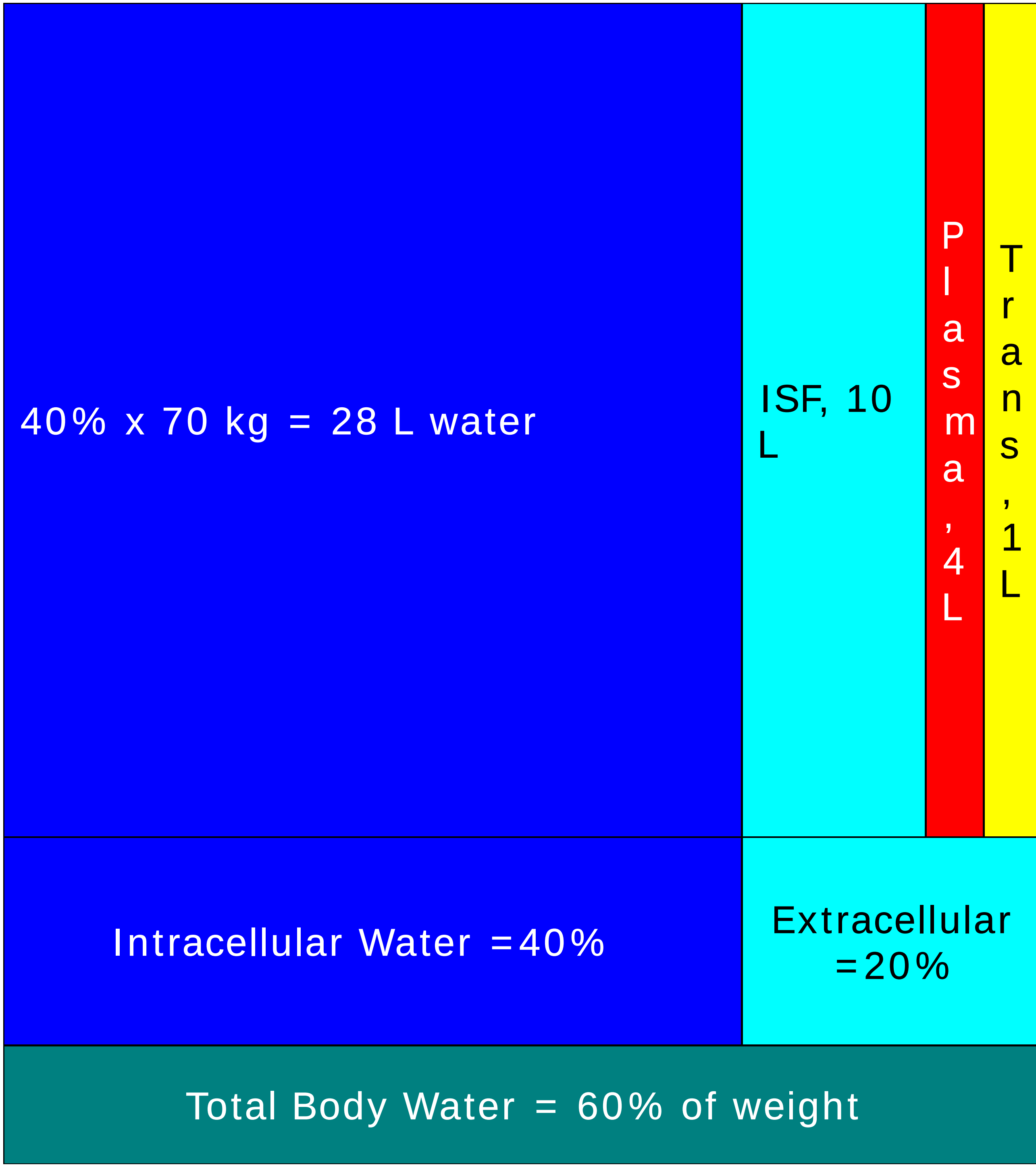
Extracellular Fluid (ECF) is the remaining 1/3 of your body's water.

ECF is about 20% of your weight.

The ECF is primarily a NaCl and $NaHCO_3$ solution.

The ECF is further subdivided into three subcompartments:

- **Interstitial Fluid (ISF)** surrounds the cells, but does not circulate. It comprises about 3/4 of the ECF.
- **Plasma** circulates as the extracellular component of blood. It makes up about 1/4 of the ECF.
- **Transcellular fluid** is a set of fluids that are outside of the normal compartments. These 1-2 liters of fluid make up the CSF, Digestive Juices, Mucus, etc.



The 60-40-20 Rule:
60 % of body weight is water
40% of body weight is intracellular fluids
20% of body weight is extracellular fluid

All the body's fluid compartments are in osmotic equilibrium (except for transient changes).

The ions and small solutes that constitute the ECF are in equilibrium with similar concentrations in each subcompartment.

The ECF volume is proportional to the total Na content.

Osmolarity measures the effective gradient for water **assuming that all the osmotic solute is completely impermeant.**

It is simply a count of the number of dissolved particles.

Therefore a 300 millimolar solution of glucose, a 300 millimolar solution of urea, and a 150 millimolar solution of NaCl each have the same osmolarity.

- **Tonicity** is a functional term that describes the tendency of a solution to resist expansion of the intracellular volume.
-
- Two solutions are **isosmotic** **when they have the same number of dissolved particles,** regardless of how much water would flow across a given membrane barrier.

- In contrast, two solutions are **isotonic** when they would cause no water movement across a membrane barrier, regardless of how many particles are dissolved.

Condition	Example	EC Fluid		IC Fluid	
		Osmolality	Volume	Osmolality	Volume
Hyposmotic expansion	excessive water intake	↓	↑	↓	↑
Hyposmotic contraction	salt wasting (Loss by kidneys)	↓	↓	↓	↑
Isosmotic expansion	IV infusion, edema	↔	↑	↔	↔
Isosmotic contraction	hemorrhage, burns	↔	↓	↔	↔
Hyperosmotic expansion	drink concentrated saline	↑	↑	↑	↓
Hyperosmotic contraction	severe sweating	↑	↓	↑	↓

Question: Explain how the plasma membrane is adapted to allow the substances which a cell needs to pass through.

•**Answer**: A plasma membrane consists of a **double layer of phospholipid molecules** arranged with their hydrocarbon chains inwards.
Fat-soluble and small molecules such as oxygen can diffuse through this bilayer.

• These molecules can pass through the gaps between the phospholipids.

•Water soluble molecules and ions make use of membrane proteins.

•Some of these proteins have pores in them. Ions often pass through these pores.

•Gates open and close regulating the passage of the ions.

•**Faclilitated diffusion and active transport make use of protein carriers.** These carriers have specific shapes which only allow certain molecules to fit them. A cell that needs to take up a lot of a particular substance will have a lot of one sort of carrier protein. Another cell which does not need so much may not have so much of that carrier. Active transport also uses the protein carriers but it allows substances to be taken up against the concentration gradient and is particularly useful when a cell needs a lot of a substance which is only present in small amounts in the surroundings. Active transport needs energy.

Diffusion

- Spontaneous movement of particles from an area of high concentration to an area of low concentration

- Does not require energy (exergonic)

- Occurs via random kinetic movement

- Net diffusion stops when concentration on both sides equal (if crossing a membrane) or when there is a uniform distribution of particles

    - Equilibrium is reached

    - Molecules continue to move, but no net change in concentration (hence the phase "net diffusion" above

    - Diffusion of one compound is independent to diffusion of other compounds

Factors Affecting Diffusion Across a Plasma Membrane

Diffusion directly through lipid bilayer

- The greater the lipid solubility of the diffusing particle, the more permeable the membrane will be
- All else being equal, smaller particles will diffuse more rapidly than larger particles
- **O_2, H_2O, CO_2 rapidly diffuse across lipid bilayer**

Diffusion of Hydrophilic Molecules Across a Plasma Membrane

- Plasma membrane is semipermeable
- **Water, while polar, is small enough to freely move across the plasma membrane**
- **Larger hydrophilic uncharged molecules, such as sugars, do not freely diffuse**
- Charged molecules cannot diffuse through lipid bilayer
- Ion channels and specific transporters are required for charged molecules and larger, uncharged molecules

Movement Across Membranes

1 - **Passive processes** - require no expenditure of energy by a cell:

•**Simple diffusion** = net movement of a substance from an area of high concentration to an area of low concentration.

The rate of diffusion is influenced by:

- **Concentration gradient**
- **Cross -sectional area through which diffusion occurs**
- **Temperature**
- **Molecular weight of a substance**
- **Distance through which diffusion occurs**

•**Osmosis** = diffusion of water across a semipermeable membrane (like a cell membrane) from an area of low solute concentration to an area of high solute concentration

•**Facilitated diffusion** = movement of a substance across a cell membrane from an area of high concentration to an area of low concentration.

•**Facilitated diffusion** = movement of a substance across a cell membrane from an area of high concentration to an area of low concentration.

This process requires the use of 'carriers' (membrane proteins).

In the example below, a ligand molecule (e.g., acetylcholine) binds to the membrane protein.

This causes a conformational change or, in other words, an 'opening' in the protein through which a substance (e.g., sodium ions) can pass.

Osmosis, the Passive Transport of Water

Osmosis = the diffusion of water across a semi-permeable membrane

Plasma membrane permeable to water but not to solute

Solute = dissolved particle
Solvent = liquid medium in which particles may be dissolved

Water moves from solution with lower concentration of dissolved particles to solution with higher concentration of dissolved particles

Water moves from dilute solution to concentrated solution

Osmotic potential is the total of all dissolved particles

Osmosis Examples in the Body

Salts and minerals from water are transferred through osmosis.

Water flows through the plasma membrane of cells and due to osmosis concentration of water, glucose and salt is maintained inside the body. Thus osmotic filtration is important in preventing cell damage.

Osmosis plays a very important role in human life as it helps in the proper functioning of the kidneys. It occurs in the kidneys to recover water from the waste materials of the body.

Kidney dialysis is also an example of osmosis.

It is for patients suffering from kidney diseases. In this process, the dialyzer removes waste products from a patient's blood through a dialyzing membrane, and passes them into the dialysis solution tank.

The red blood cells being larger in size cannot pass through the membrane and are retained in the blood.

Thus, by the process of osmosis waste materials are continuously removed from the blood.

Osmosis Examples in Daily Life

When your hands are immersed in dishwater for a long time, your skin looks bloated. This is an effect of osmosis.

When you pour salt onto a slug, water diffuses and slug shrinks as a result of osmosis.

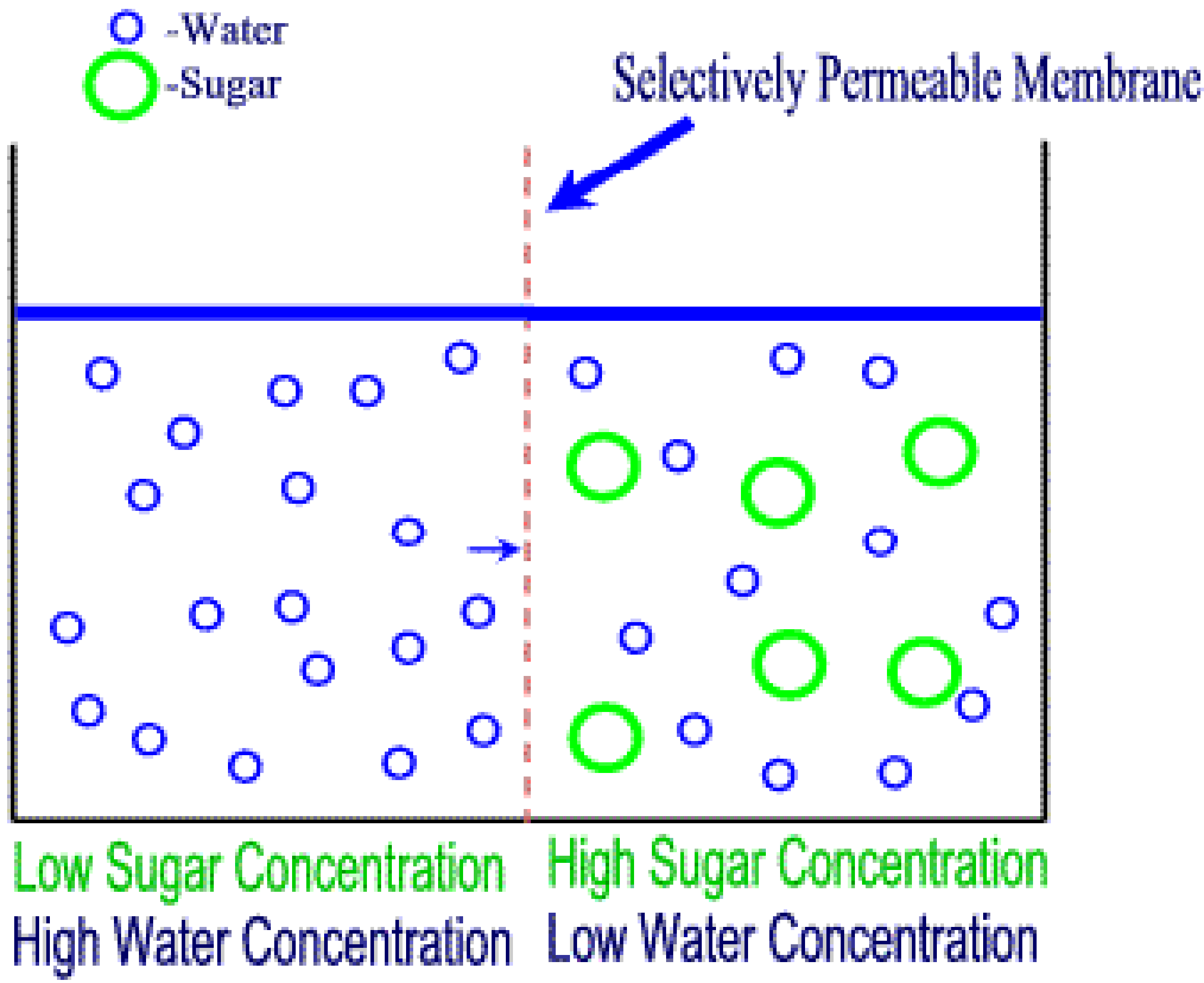
When you cook food and put sauce in the liquid part of your dish, some part of the solute moves inside the solid part of the food you are cooking. The solid part could be an egg, piece of meat but the sauce is made of solute and not water, so it will move into the food.

Osmosis also plays an important part in the body. It helps in the transfer of water and various nutrients between blood and fluid of cells.

Plants also use osmosis to take in water and minerals essential for its growth.

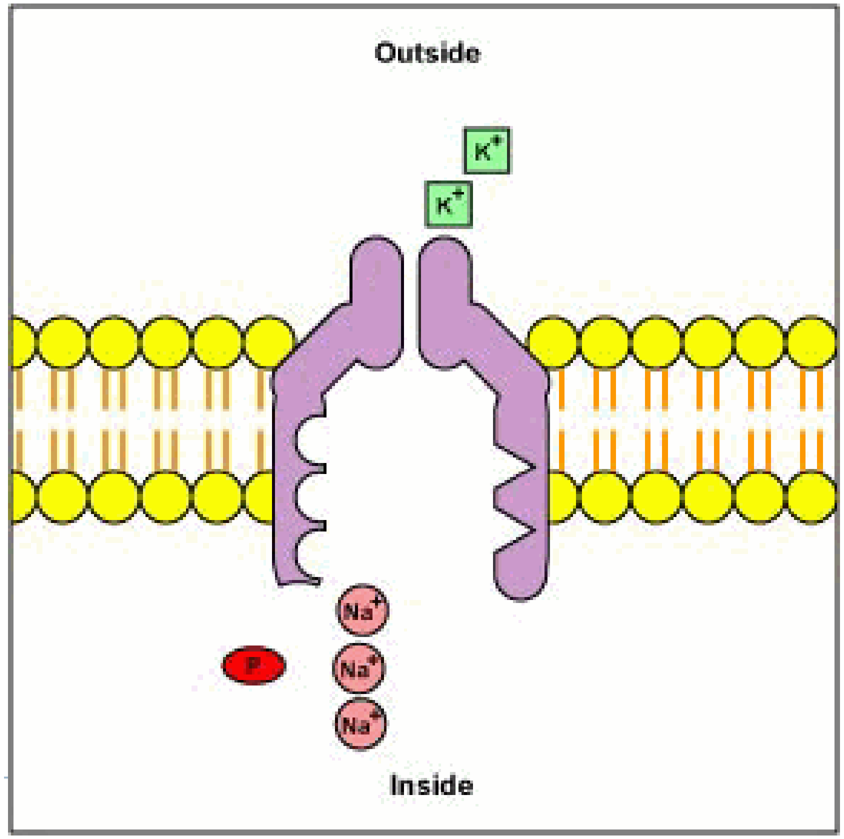
Reverse osmosis is a type of osmosis which is used to convert sewage water into clean drinking water. Have a look at reverse osmosis water purifier.

Osmosis

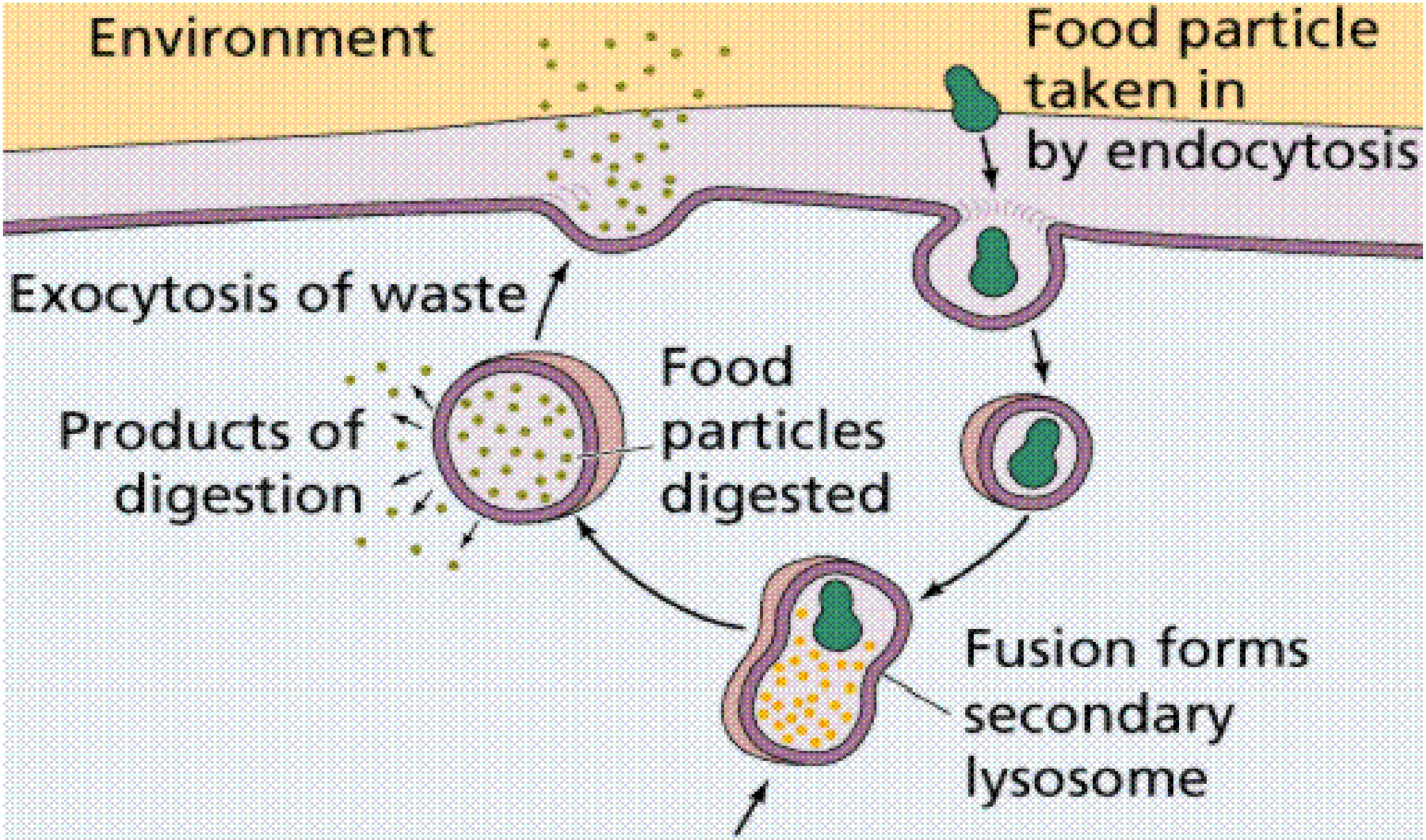

-Water
-Sugar
Selectively Permeable Membrane
Low Sugar Concentration
High Water Concentration
High Sugar Concentration
Low Water Concentration

2 - Active processes - require the expenditure of energy by cells:

Active transport = movement of a substance across a cell membrane from an area of low concentration to an area of high concentration using a carrier molecule



Endo- & exocytosis - moving material into (endo-) or out of (exo-) cell in bulk form



Passive Membrane Transport: Diffusion

- Simple diffusion – nonpolar and lipid-soluble substances
  - Diffuse directly through the lipid bilayer
  - Diffuse through channel proteins

PLAY Diffusion

Passive Membrane Transport: Diffusion

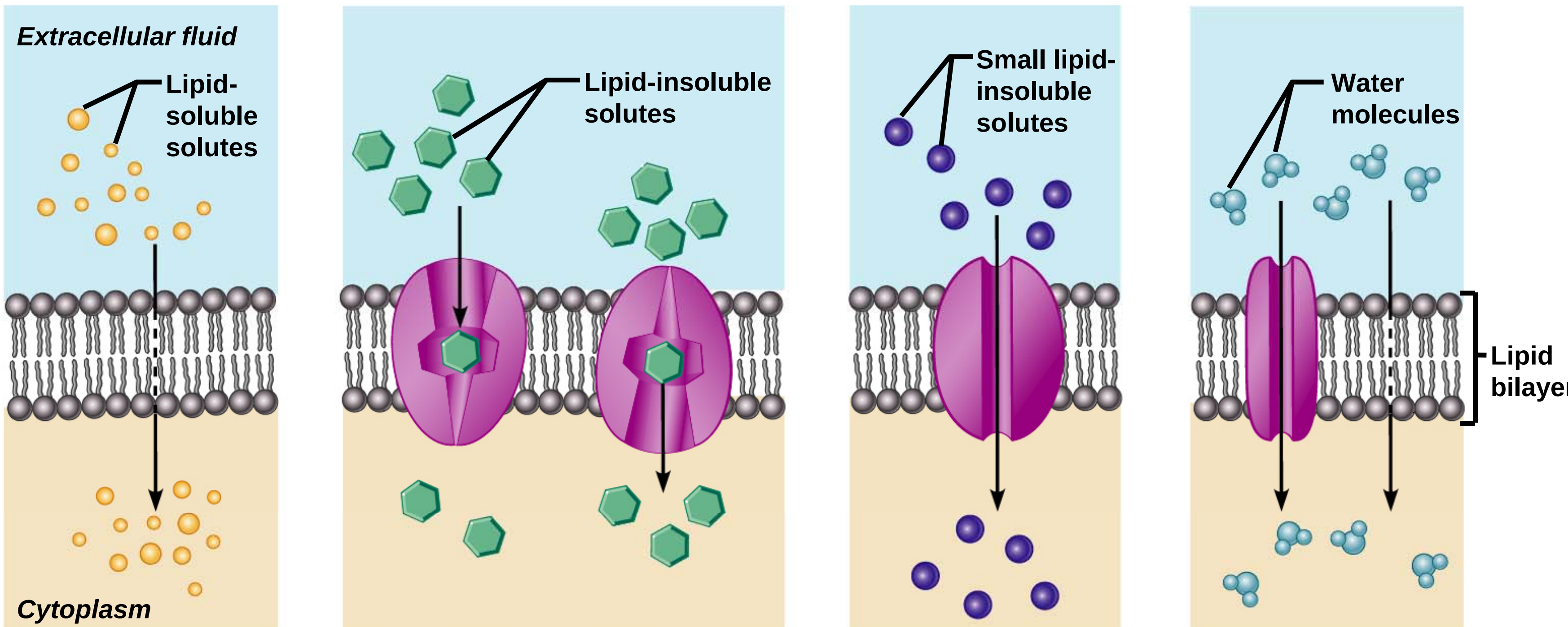
- Facilitated diffusion
  - **Transport of glucose, amino acids, and ions**
  - **Transported substances bind carrier proteins or pass through protein channels**

•Allows diffusion of large, membrane insoluble compounds such as sugars and amino acids
•Does not require energy (passive)
•Highly Selective
•Substance binds to membrane-spanning transport protein
•Binding alters protein conformation, exposing the other surface
•Fully reversible - molecules may enter the cell and leave the cell through the transport protein.
•Particles move from areas of high concentration to areas of low concentration.
•Movement rate of particles will saturate
  •Maximum rate limited by number of transporters
  •Once all transporters are operating at 100%, an increase in concentration will not increase rate

Carrier Proteins

- Are integral transmembrane proteins
- Show specificity for certain polar molecules including sugars and amino acids

Diffusion Through the Plasma Membrane



(a) Simple diffusion directly through the phospholipid bilayer

(b) Carrier-mediated facilitated diffusion via protein carrier specific for one chemical; binding of substrate causes shape change in transport protein

(c) Channel-mediated facilitated diffusion through a channel protein; mostly ions selected on basis of size and charge

(d) Osmosis, diffusion through a specific channel protein (aquaporin) or through the lipid bilayer

Figure 3.7

Diffusion Through the Plasma Membrane

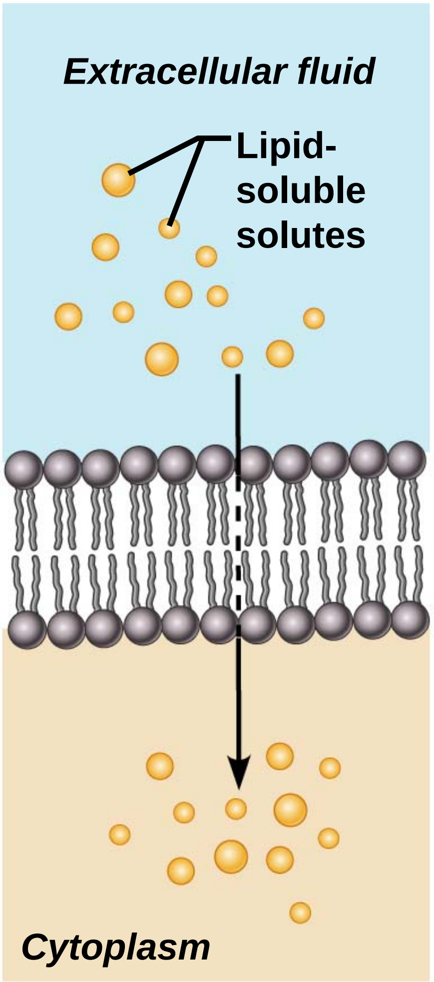


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Figure 3.7

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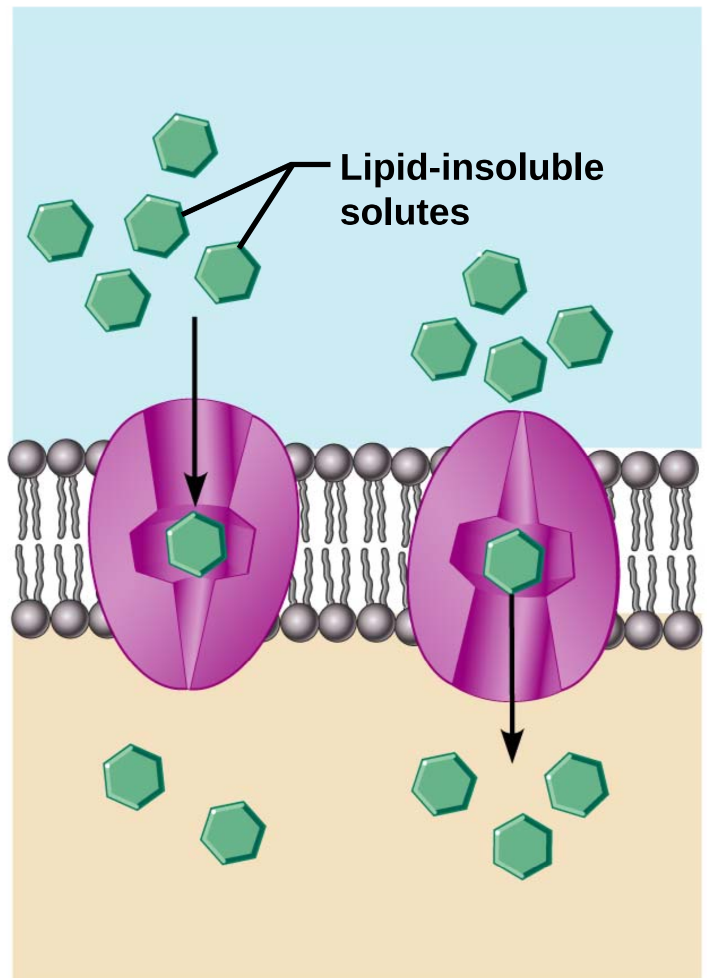
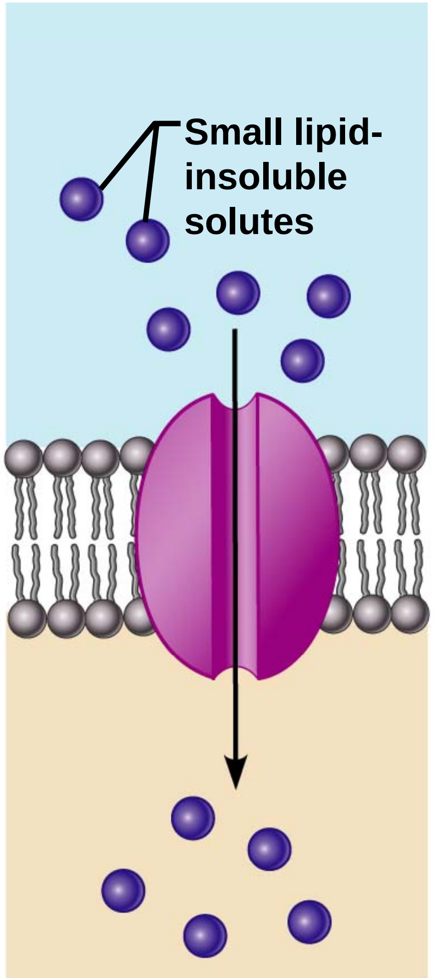


(b) Carrier-mediated facilitated diffusion via protein carrier specific for one chemical; binding of substrate causes shape change in transport protein

Figure 3.7

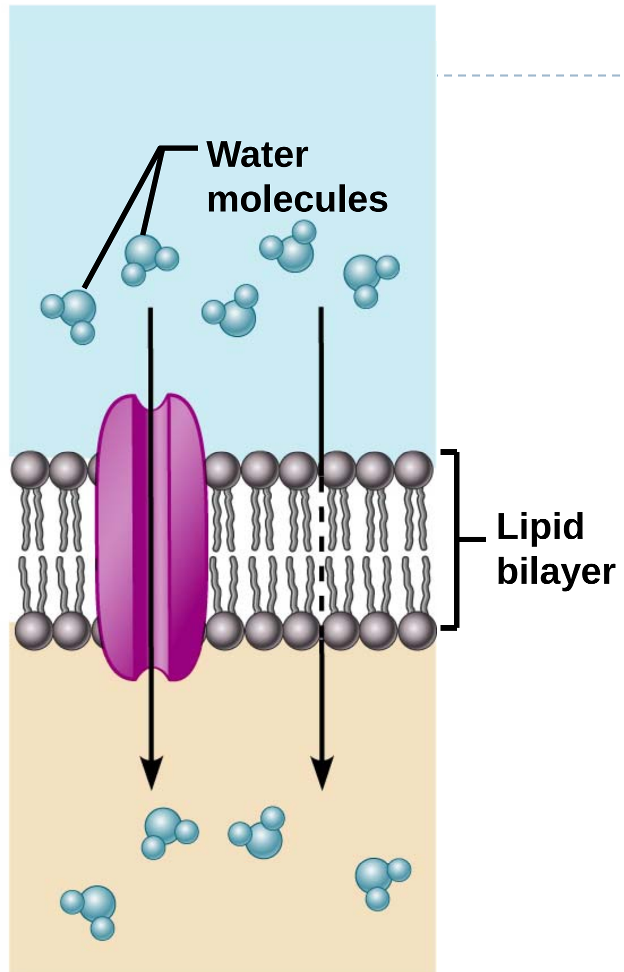
Diffusion Through the Plasma Membrane



(c) Channel-mediated facilitated diffusion through a channel protein; mostly ions selected on basis of size and charge

Figure 3.7

Diffusion Through the Plasma Membrane



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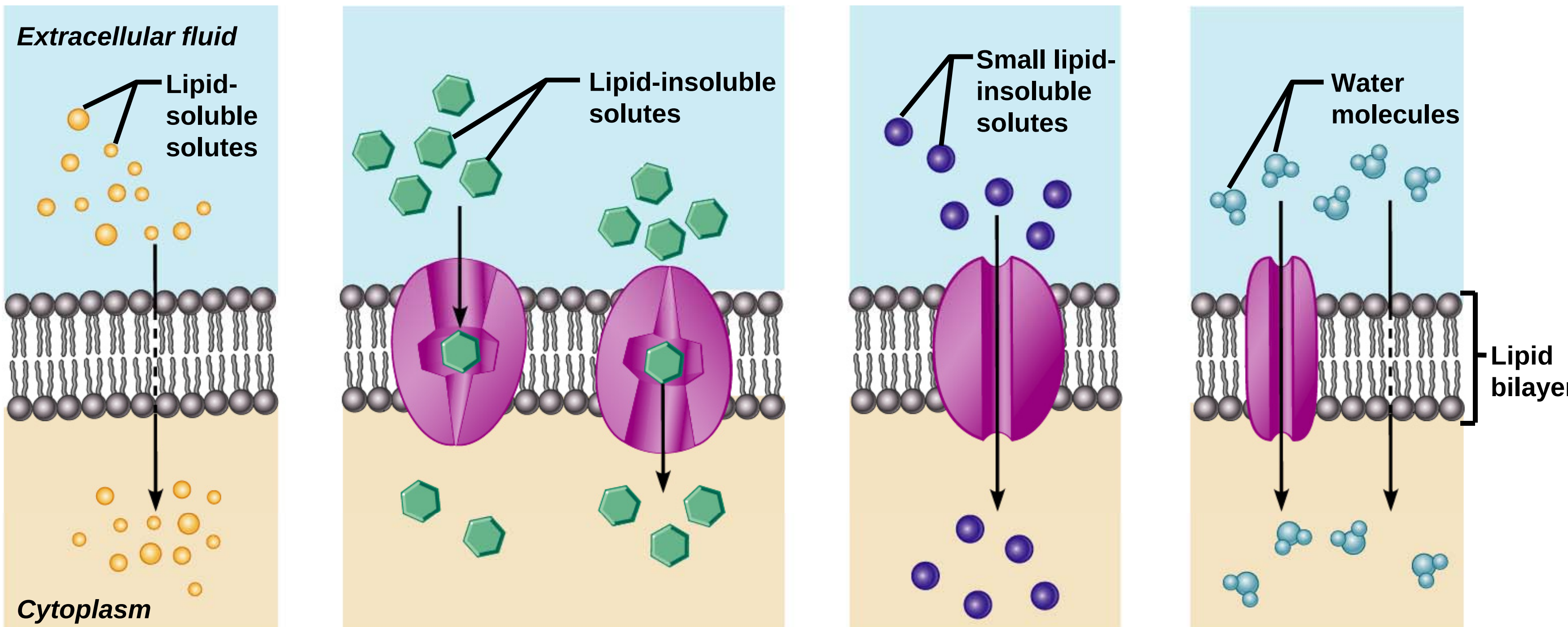
Diffusion Through the Plasma Membrane



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(d) Osmosis, diffusion through a specific channel protein (aquaporin) or through the lipid bilayer

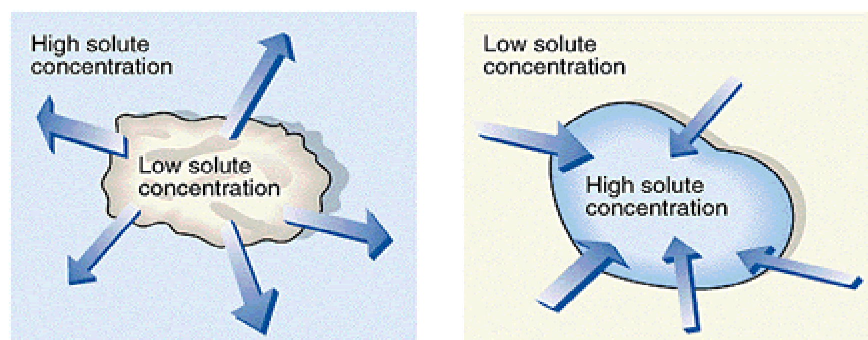
Figure 3.7

Passive Membrane Transport: Osmosis

- Occurs when the concentration of a solvent is different on opposite sides of a membrane
- Diffusion of water across a semipermeable membrane
- Osmolarity – total concentration of solute particles in a solution
- Tonicity – how a solution affects cell volume

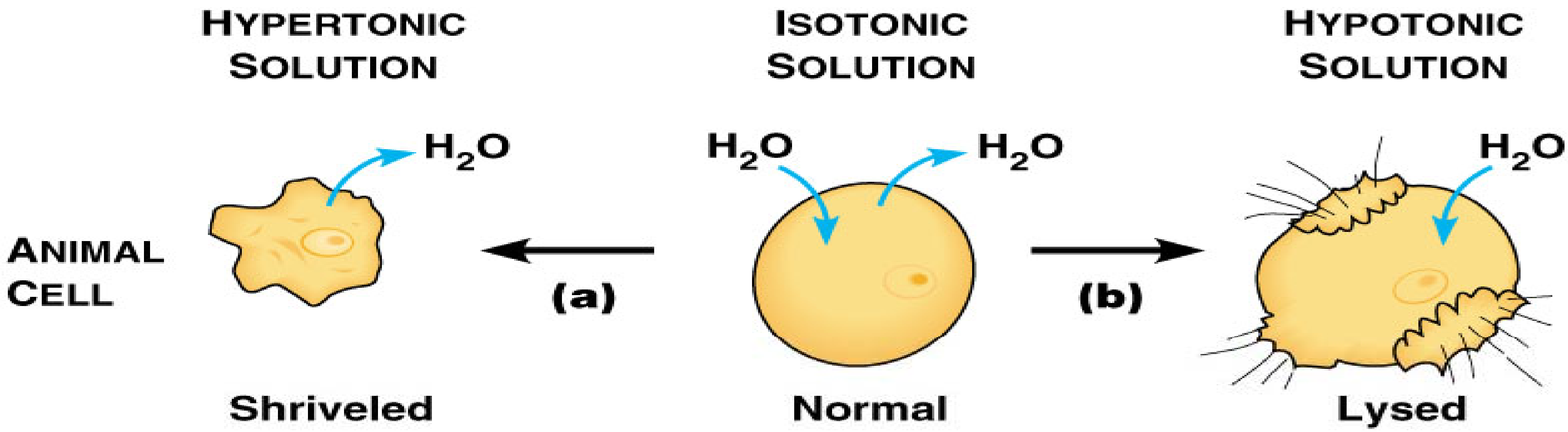
Solution Types Relative to Cell

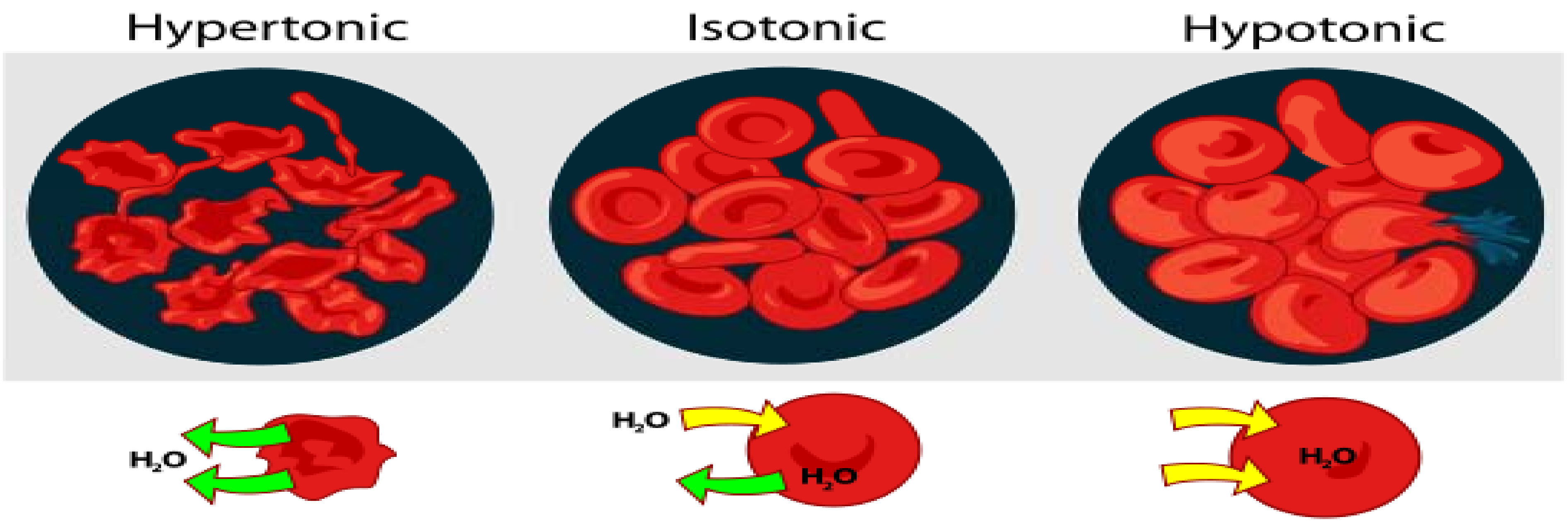
- **Hypertonic Solution:** Solute concentration higher than cell
  - More dissolved particles outside of cell than inside of cell
  - Hyper = more (think hyperactive); Tonic = dissolved particles
  - Water moves out of cell into solution
  - Cell shrinks
- **Hypotonic Solution:** Solute concentration lower than cell
  - Less dissolved particles outside of cell than inside of cell
  - Hypo = less, under (think hypodermic, hypothermia); Tonic = dissolved particles
  - Water moves into cell from solution
  - Cell expands (and may burst)
- **Isotonic Solution:** Solute concentration equal to that of cell
  - No net water movement

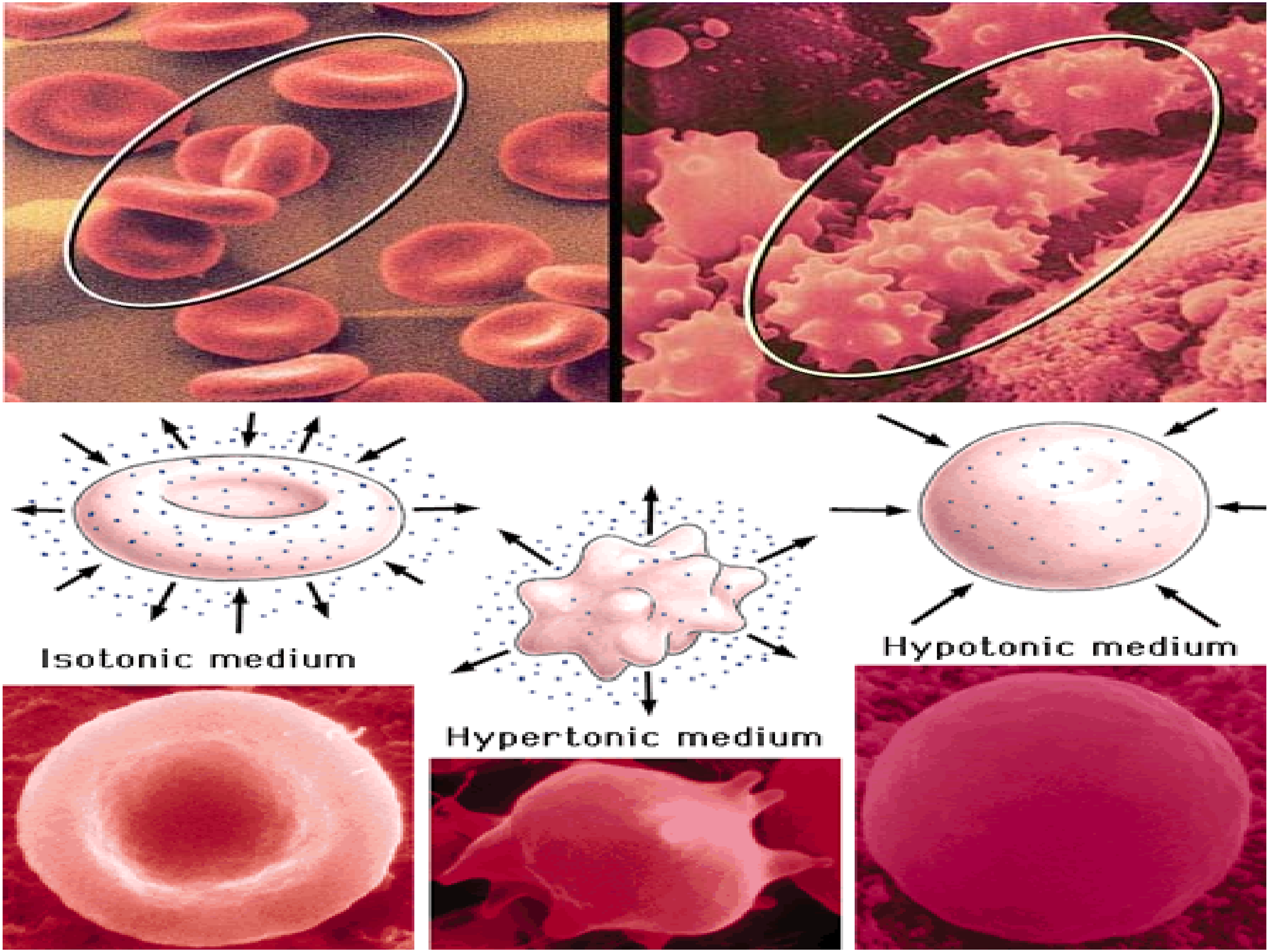


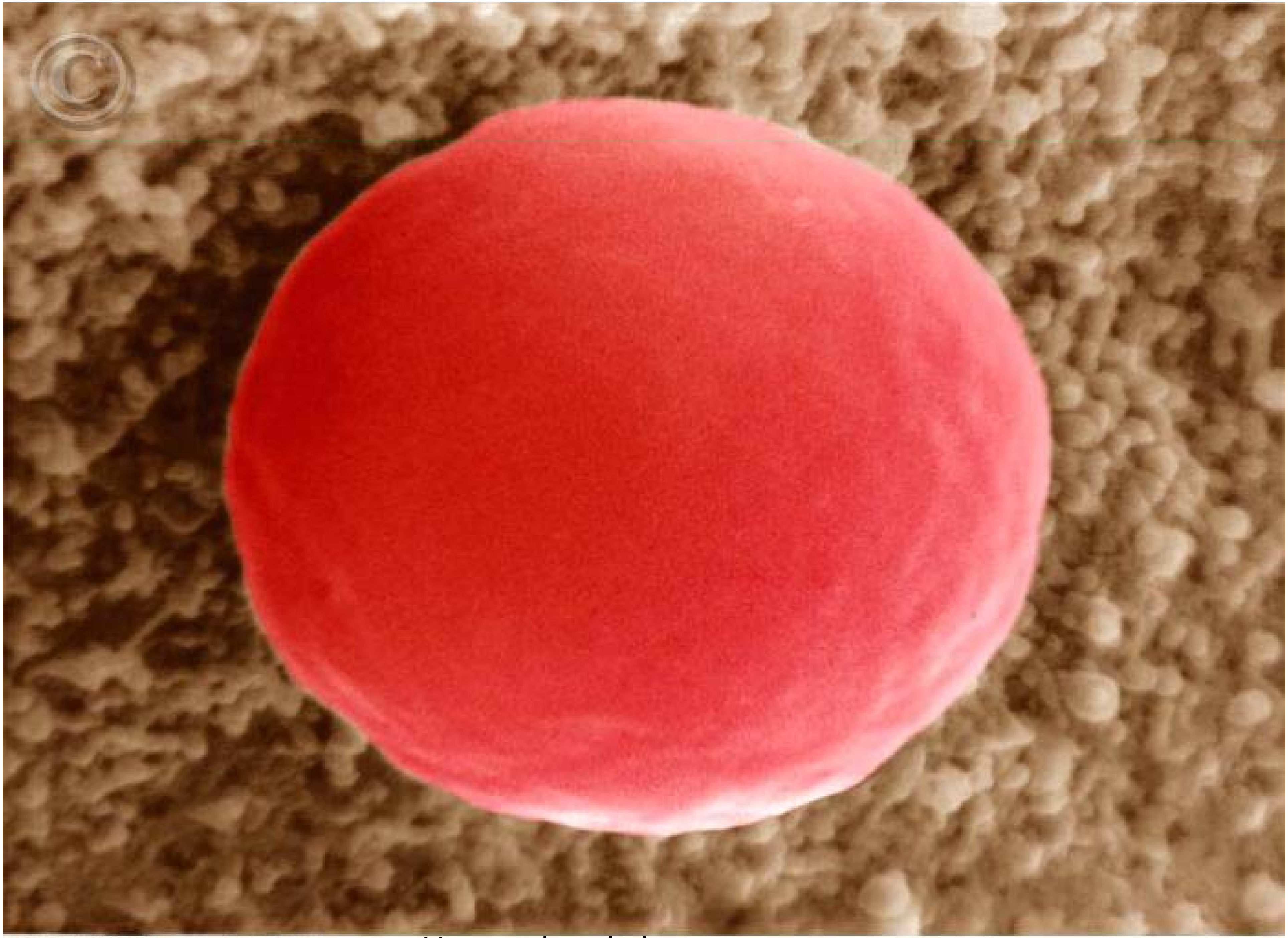
(a) (b)

Osmotic pressure affects cell shape and life

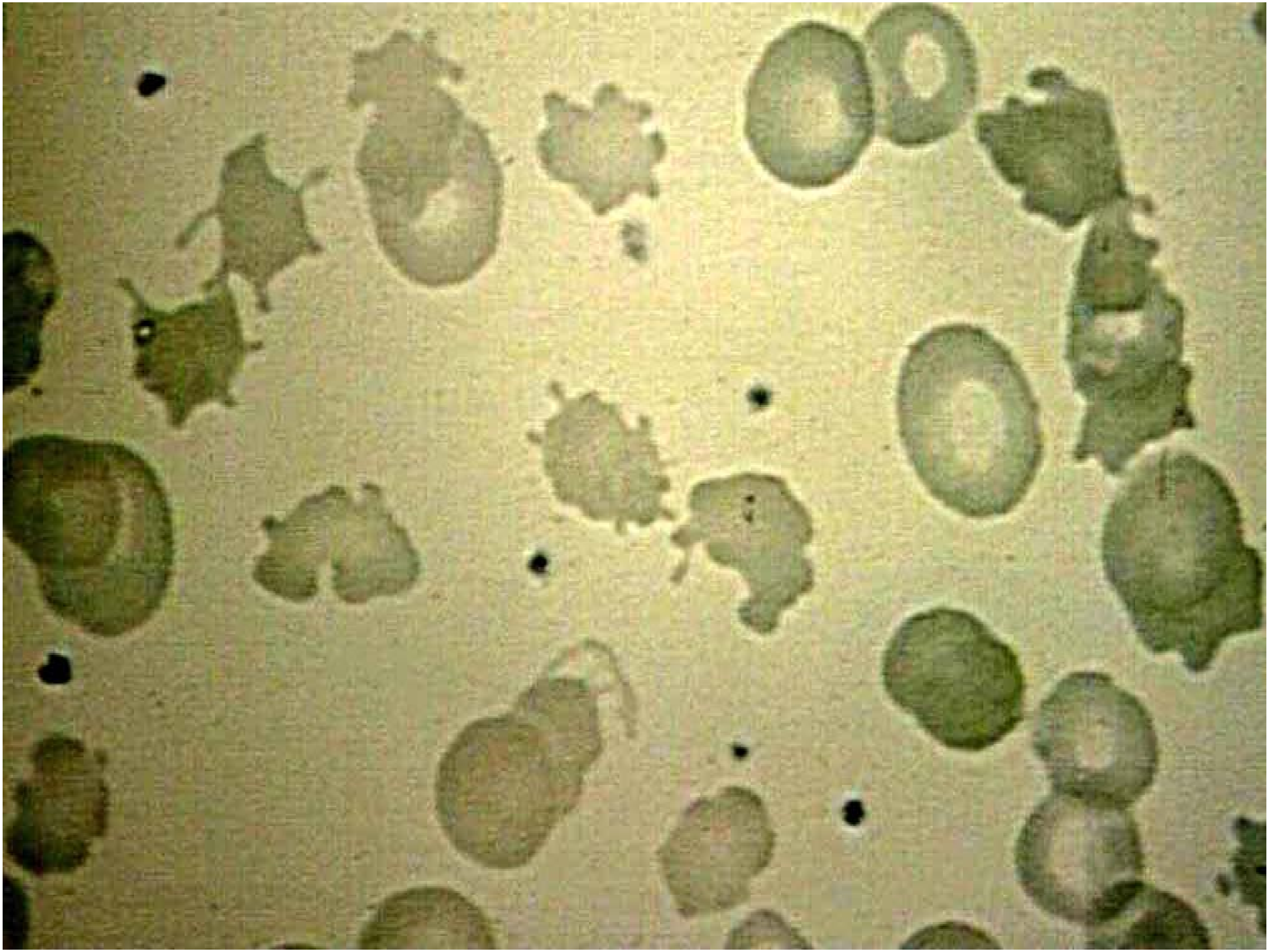





Isotonic medium
Hypertonic medium
Hypotonic medium



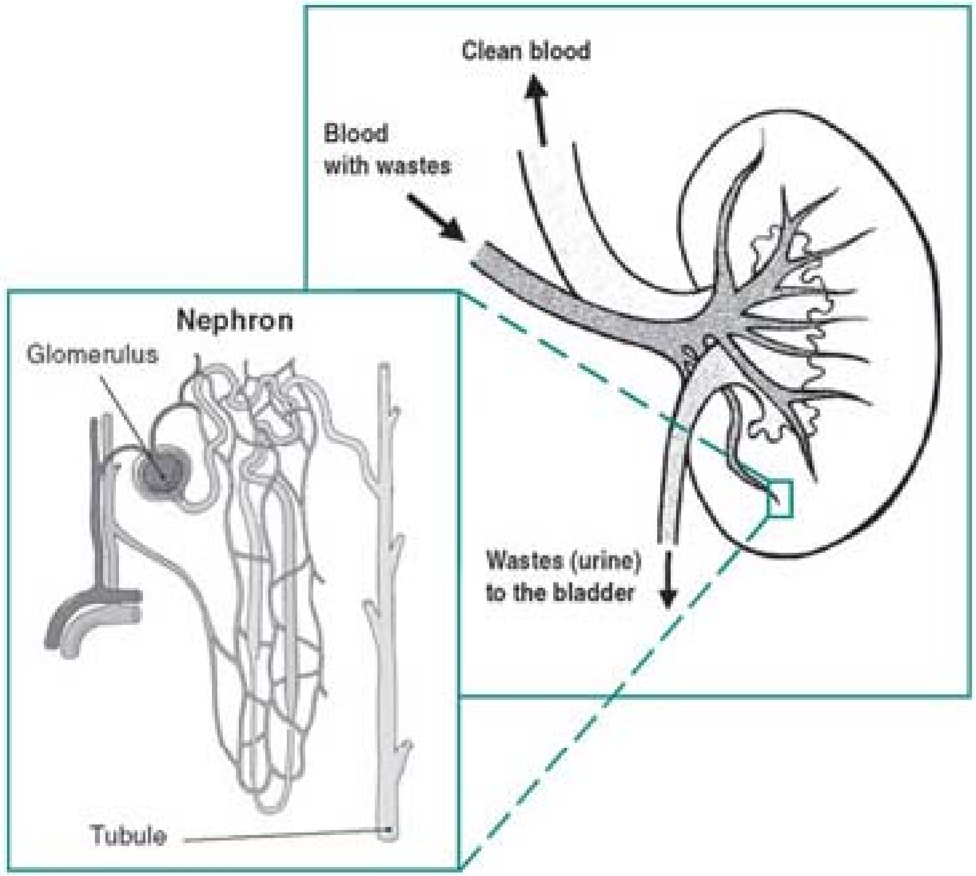
Hypotonic solution



Effects of Solutions of Varying Tonicity

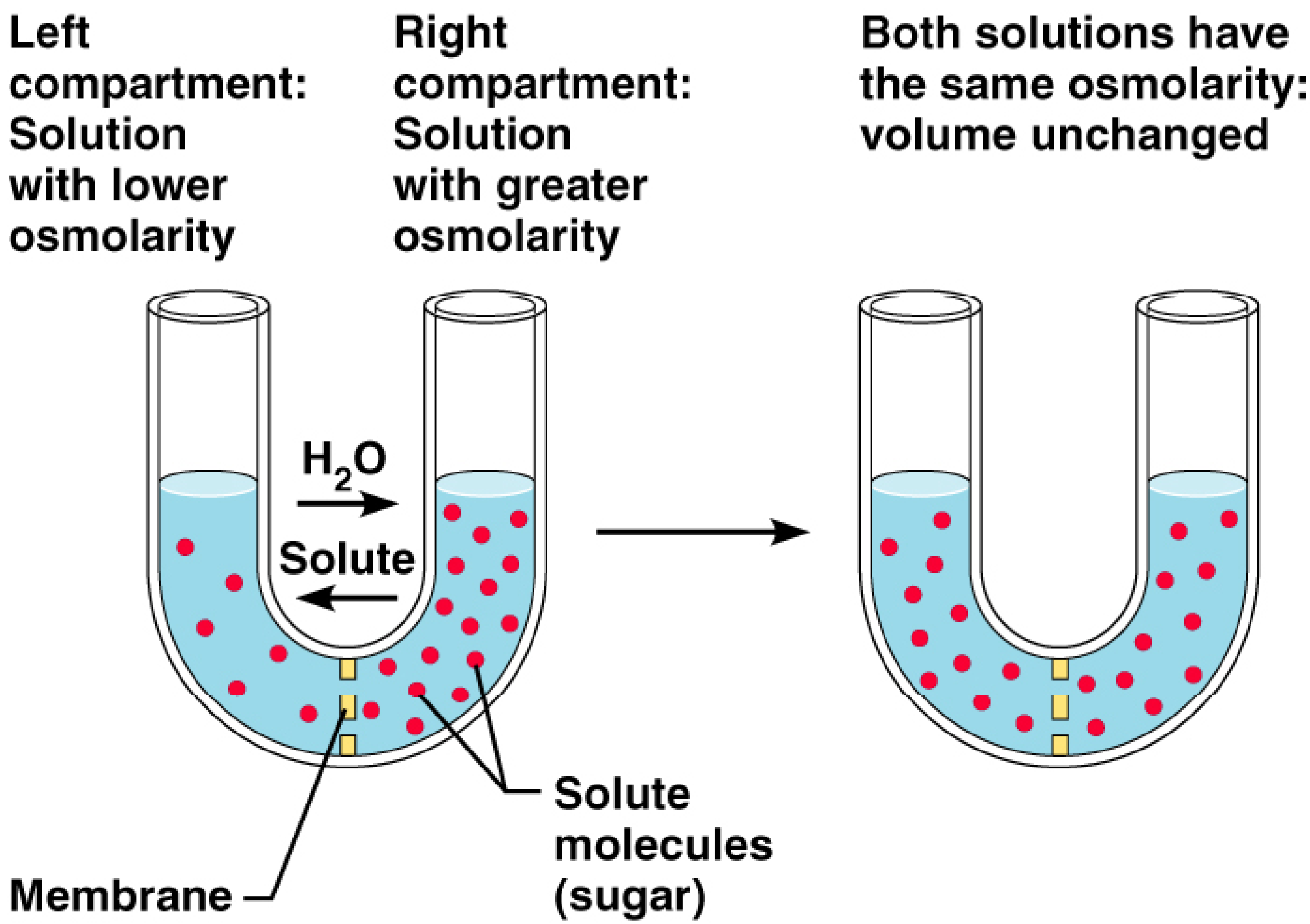
- **Isotonic** – solutions with the same solute concentration as that of the cytosol
- **Hypertonic** – solutions having greater solute concentration than that of the cytosol
- **Hypotonic** – solutions having lesser solute concentration than that of the cytosol

Why this is important biologically



Kidney function is dependent upon ion and water transport

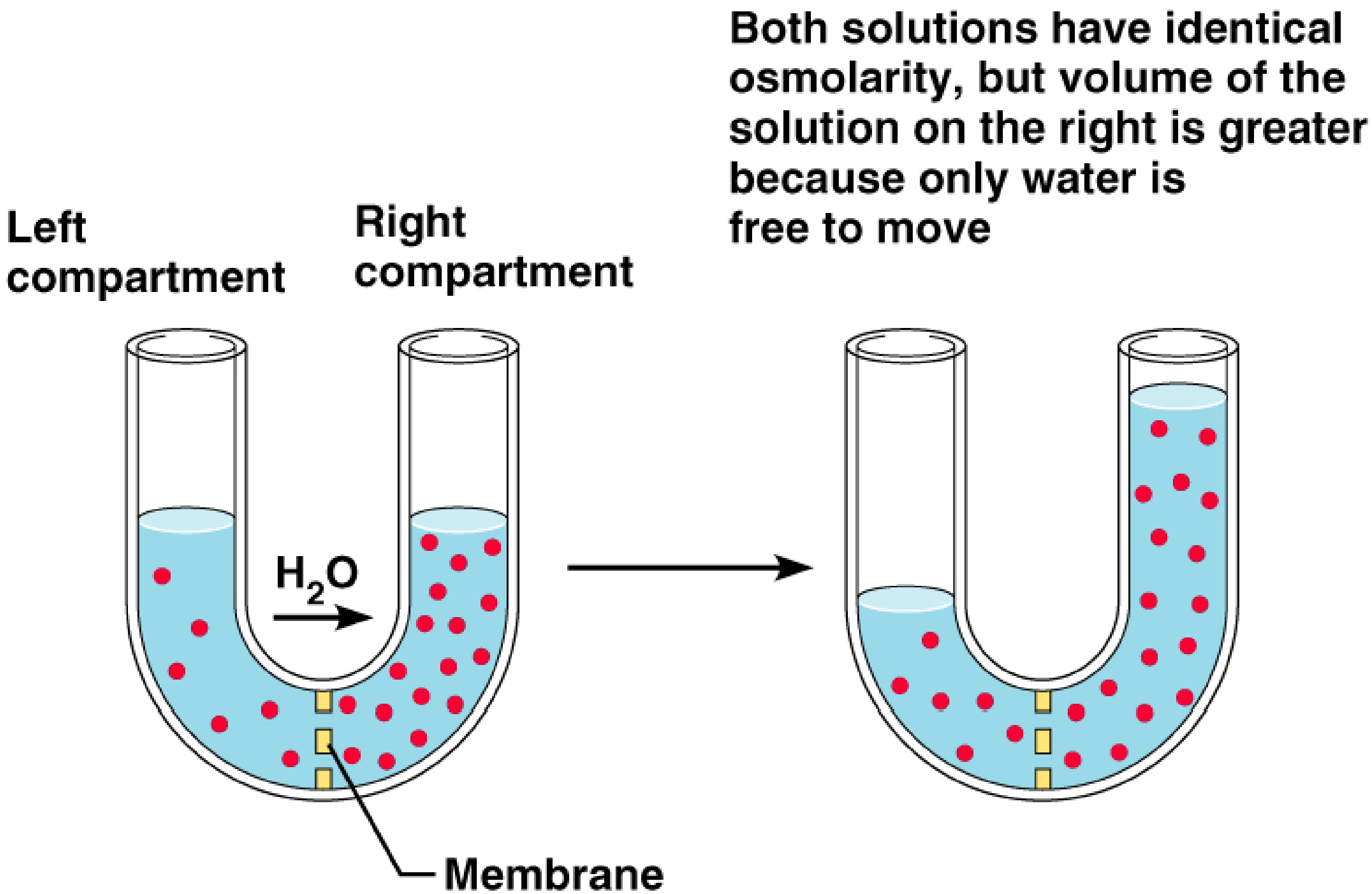
Effect of Membrane Permeability on Diffusion and Osmosis



(a) Membrane permeable to both solute molecules and water

Figure 3.8a

Effect of Membrane Permeability on Diffusion and Osmosis



(b) Membrane impermeable to solute molecules, permeable to water

Figure 3.8b

Passive Membrane Transport: Filtration

- The passage of water and solutes through a membrane by hydrostatic pressure
- Pressure gradient pushes solute-containing fluid from a higher-pressure area to a lower-pressure area

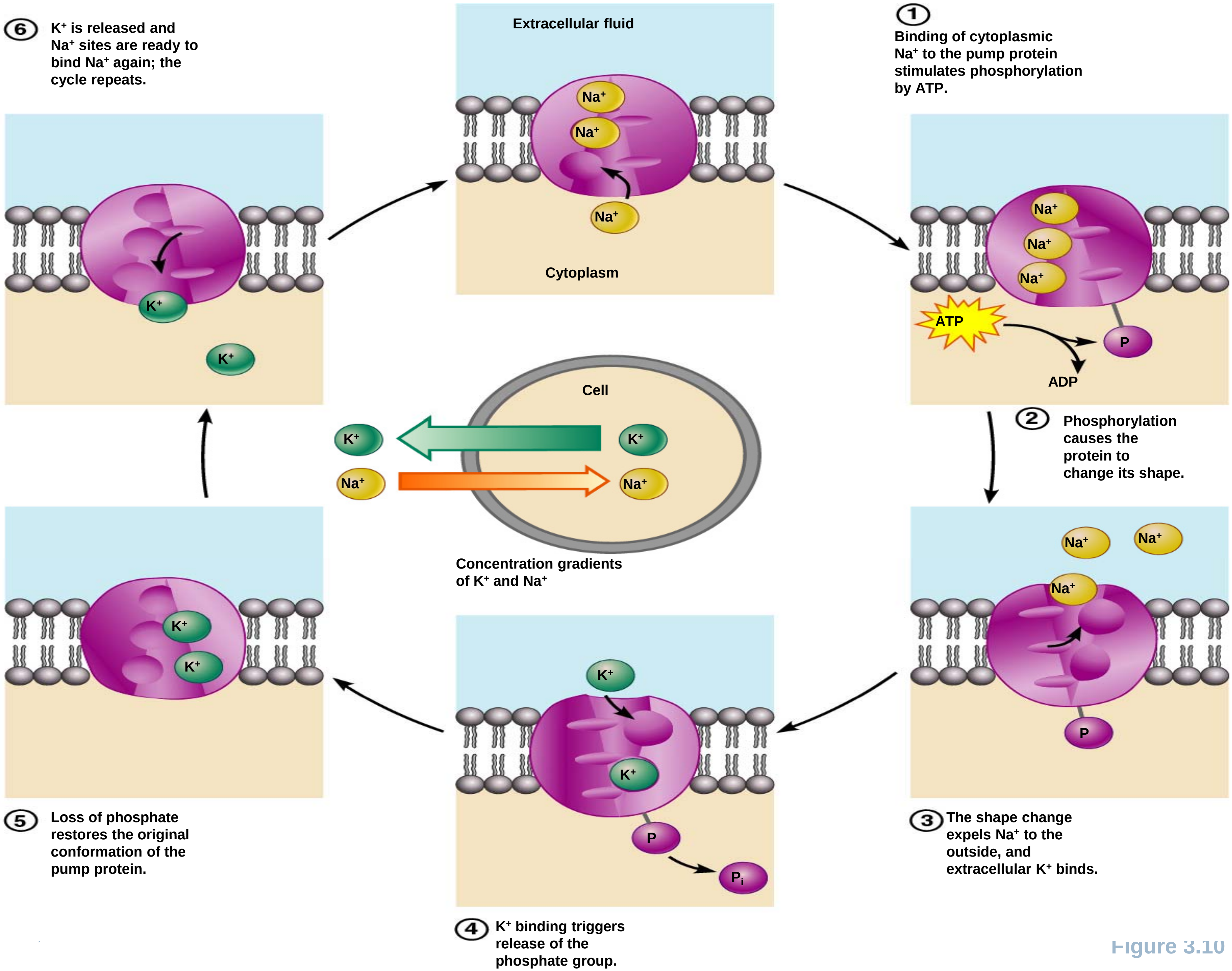

Extracellular fluid
Cytoplasm
Na+
Na+
Na+
1 Binding of cytoplasmic Na+ to the pump protein stimulates phosphorylation by ATP.
Na+
Na+
Na+
ATP
P
ADP
2 Phosphorylation causes the protein to change its shape.
Na+
Na+
Na+
P
3 The shape change expels Na+ to the outside, and extracellular K+ binds.
K+
K+
P
Pi
4 K+ binding triggers release of the phosphate group.
K+
K+
5 Loss of phosphate restores the original conformation of the pump protein.
K+
K+
6 K+ is released and Na+ sites are ready to bind Na+ again; the cycle repeats.
Cell
K+
K+
Na+
Na+
Concentration gradients of K+ and Na+

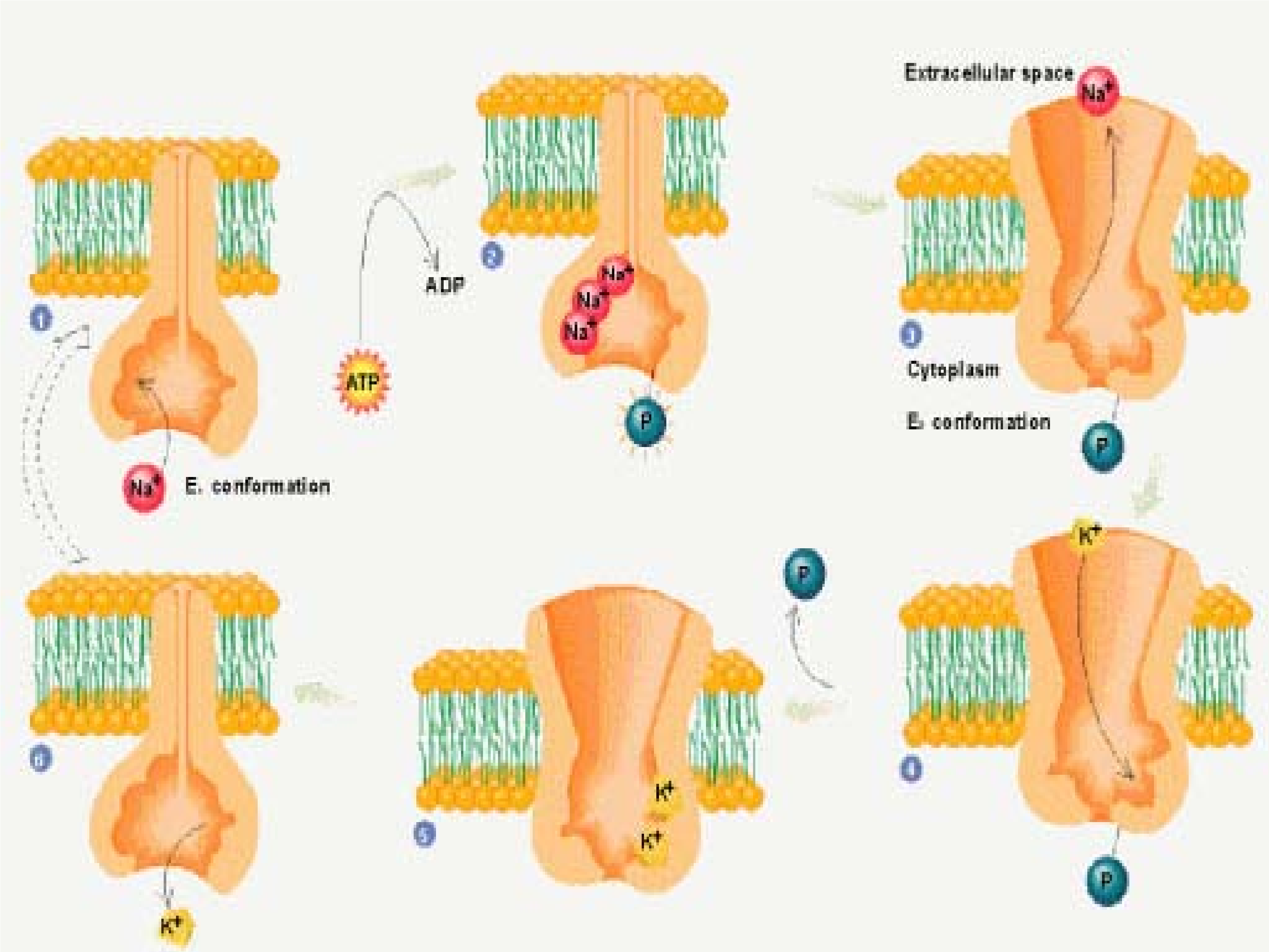
Figure 3.10

Active Transport

- Uses ATP to move solutes across a membrane
- Requires carrier proteins

The K^+ / Na^+ Pump: An Example of Active Transport

- Cellular [K^+] is low and [Na^+] is high - must pump K^+ in and pump Na^+ out
- K^+ and Na^+ transport require ATP energy
- Experimental evidence has shown that this pump will only work if [K^+] is high on outside and [Na^+] is high on inside.
- This pump works independent of concentration gradient
- The pump is an integral membrane protein
- Binds 3 Na^+ inside cell
- ATP is hydrolyzed and phosphate group transferred to protein
- when the pump is phosphorylated, its configuration changes and it opens up the Na^+ to the outside of the cell
- The Na^+ are released (the altered configuration does not favor the binding of Na^+)
- Two K^+'s from the outside now bind to the altered protein
- The binding of the K^+ causes the protein to lose its phosphate group
- Now that the phosphate group is gone, the altered protein reverts back to its original shape, which was open to the inside of the cell
- The original shape does not favor the binding of K^+, so these are released. Na^+ then binds to the protein and the process is repeated



Extracellular space
Cytoplasm
E. conformation
E. conformation
ATP
ADP
Na^+
K^+
P

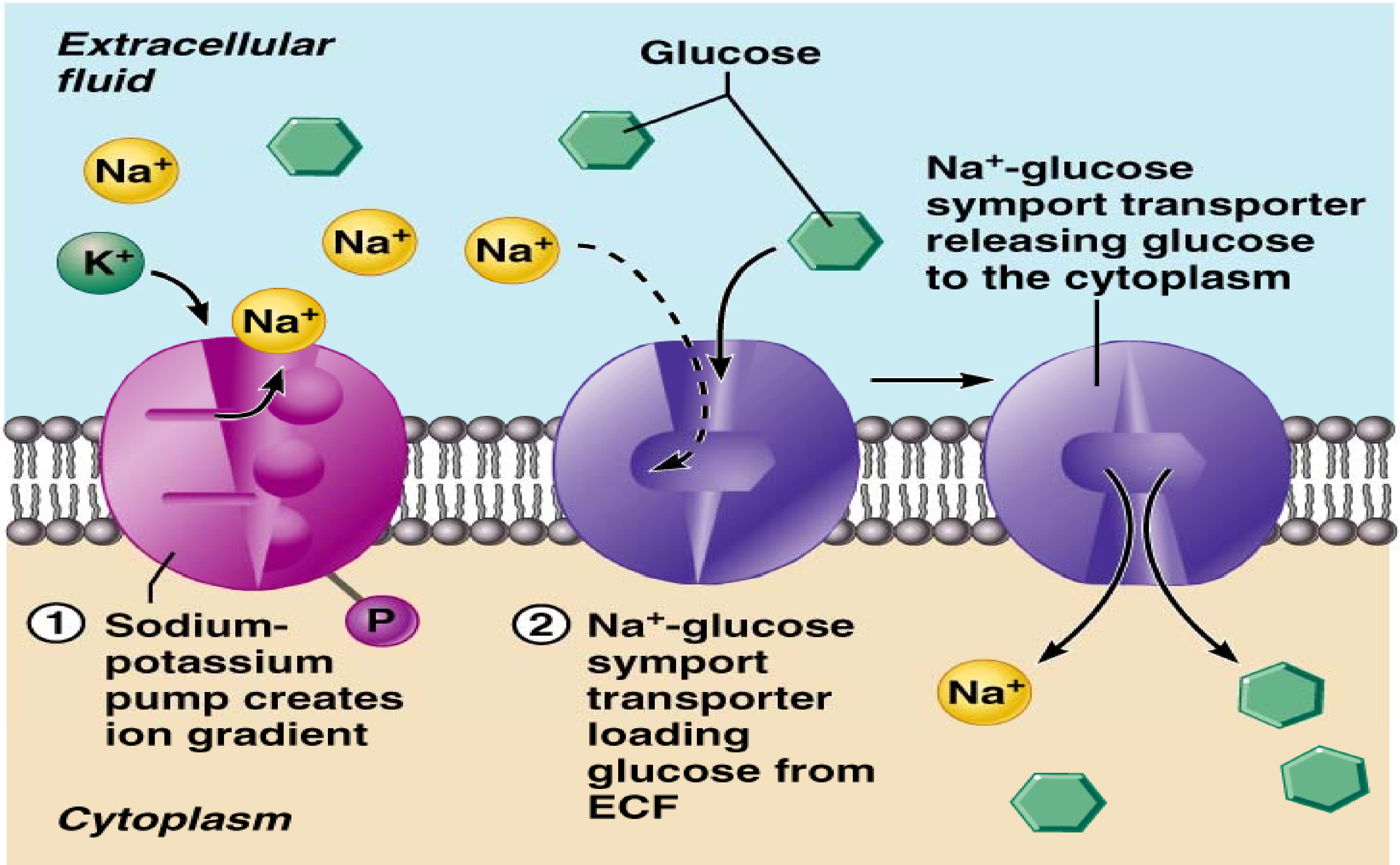
Types of Active Transport

- **Symport system** – two substances are moved across a membrane in the same direction
- **Antiport system** – two substances are moved across a membrane in opposite directions

Types of Active Transport

- **Primary active transport** – hydrolysis of ATP phosphorylates the transport protein causing conformational change
- **Secondary active transport** – use of an exchange pump (such as the Na^+-K^+ pump) indirectly to drive the transport of other solutes

Types of Active Transport



Vesicular Transport

- Transport of large particles and macromolecules across plasma membranes
  - Exocytosis – moves substance from the cell interior to the extracellular space
  - Endocytosis – enables large particles and macromolecules to enter the cell

Vesicular Transport

- **Transcytosis** – moving substances into, across, and then out of a cell
- **Vesicular trafficking** – moving substances from one area in the cell to another
- **Phagocytosis** – pseudopods engulf solids and bring them into the cell's interior

Vesicular Transport

- **Fluid-phase endocytosis** – the plasma membrane infolds, bringing extracellular fluid and solutes into the interior of the cell
- **Receptor-mediated endocytosis** – clathrin-coated pits provide the main route for endocytosis and transcytosis
- **Non-clathrin-coated vesicles** – caveolae that are platforms for a variety of signaling molecules

Exocytosis

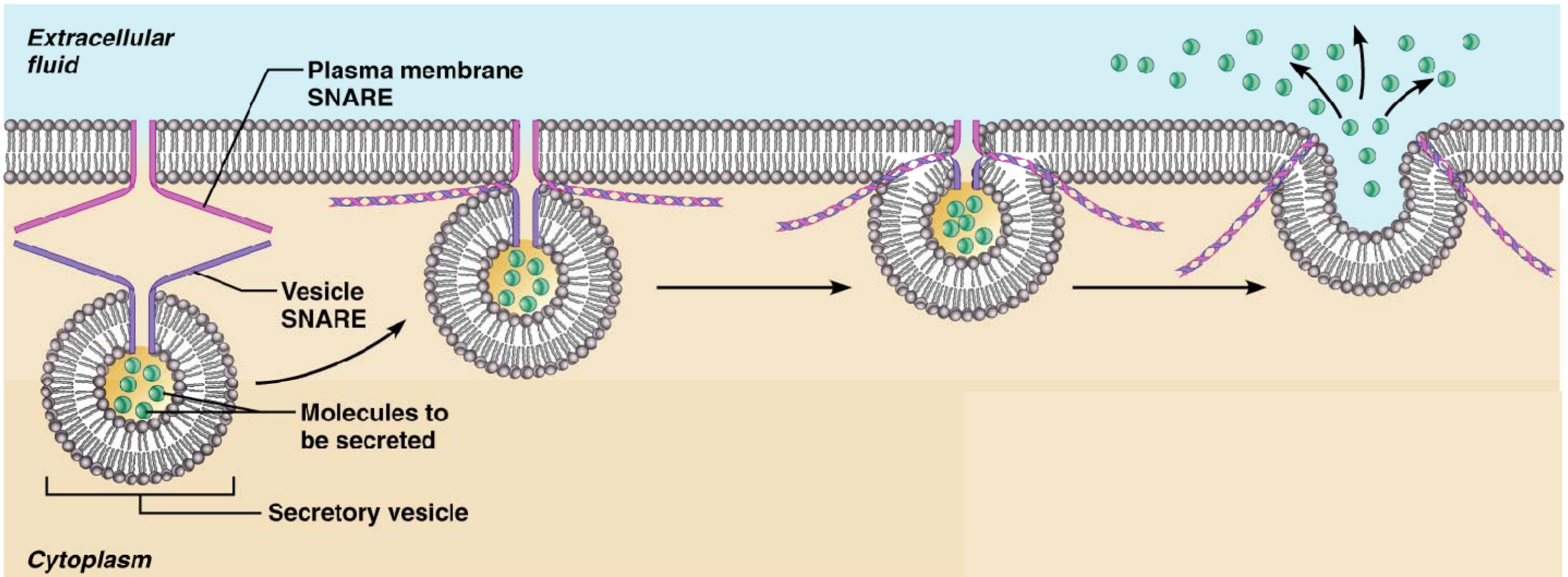
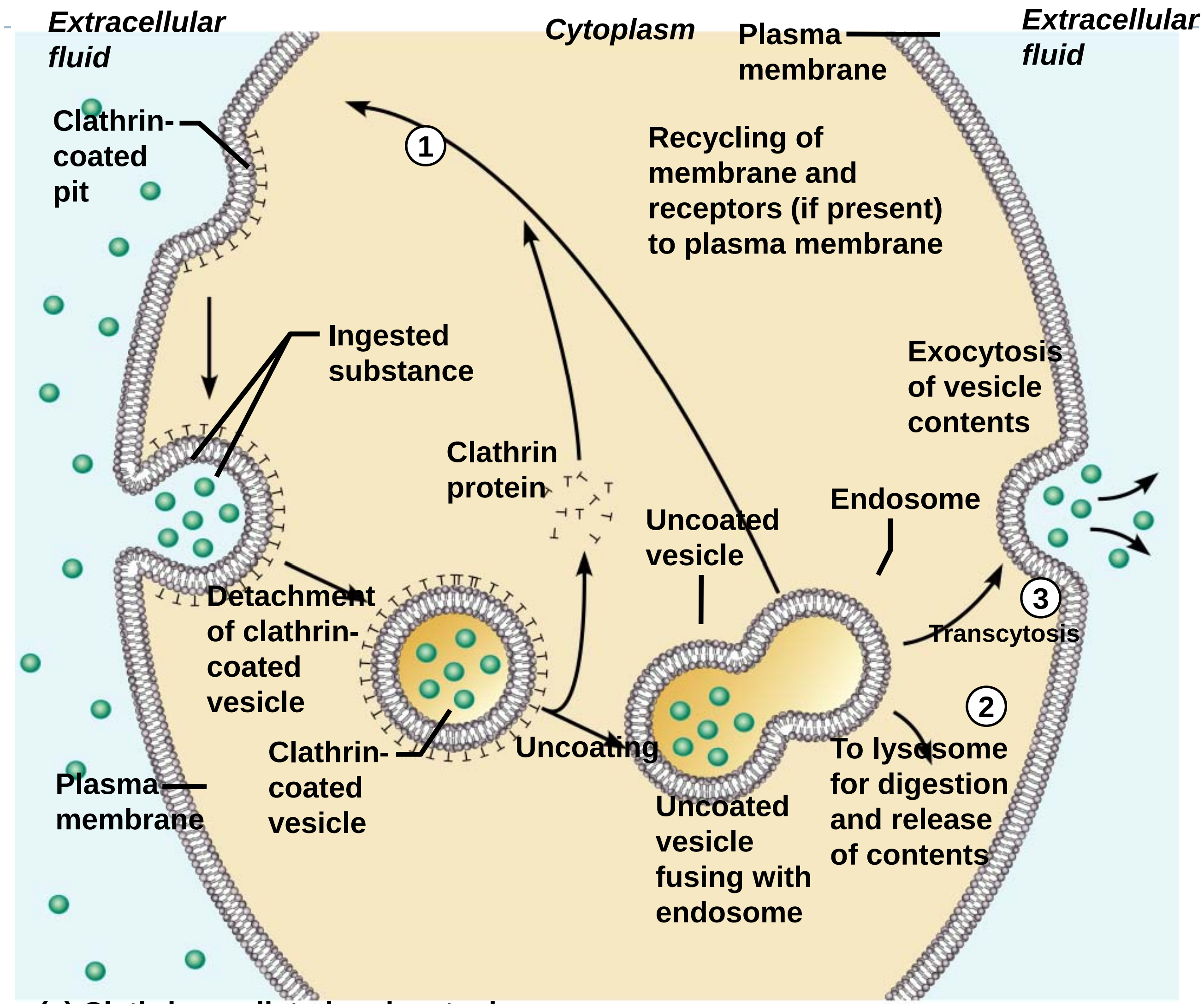


Figure 3.12a

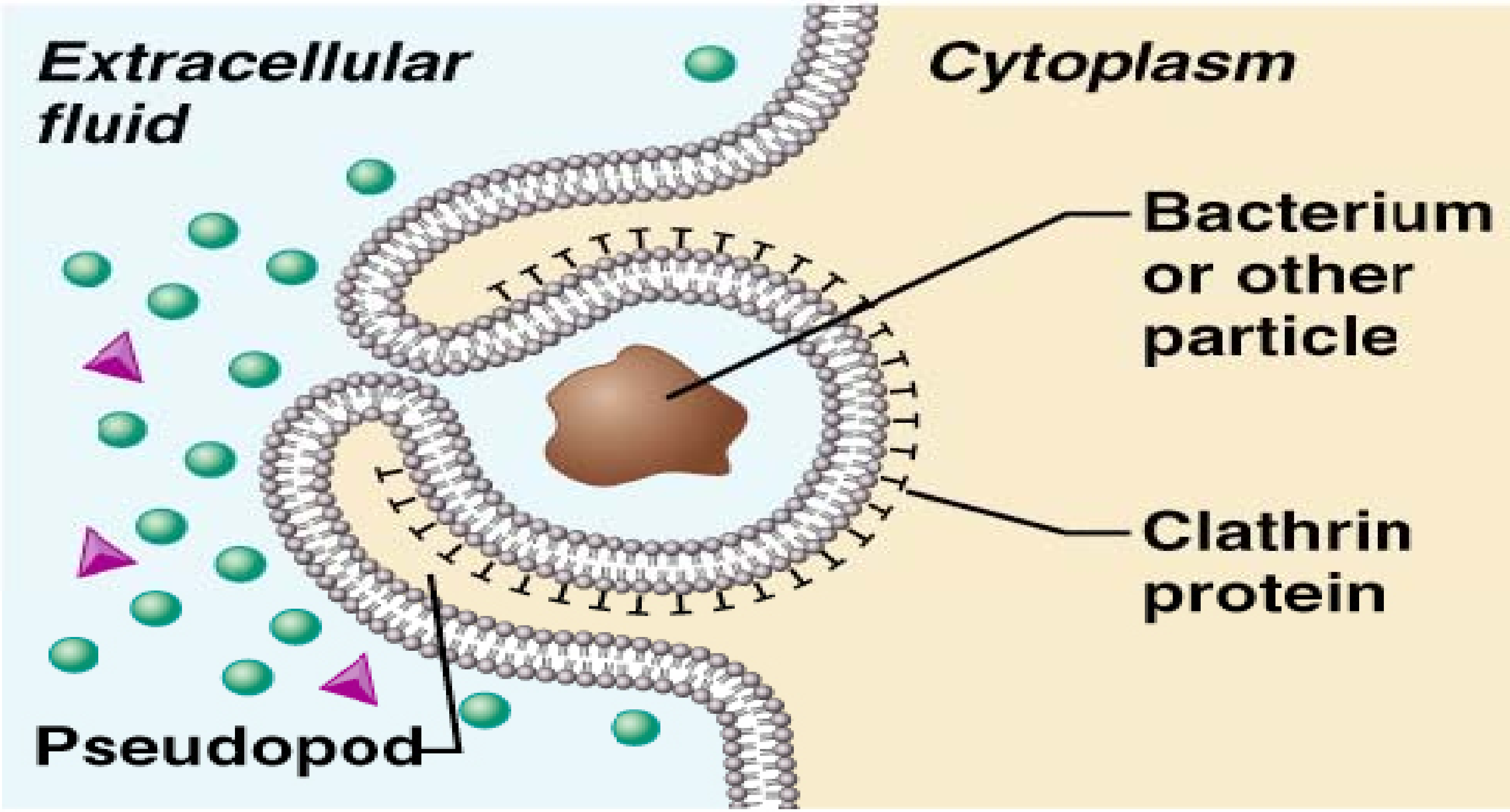
Clathrin-Mediated Endocytosis



(a) Clathrin-mediated endocytosis

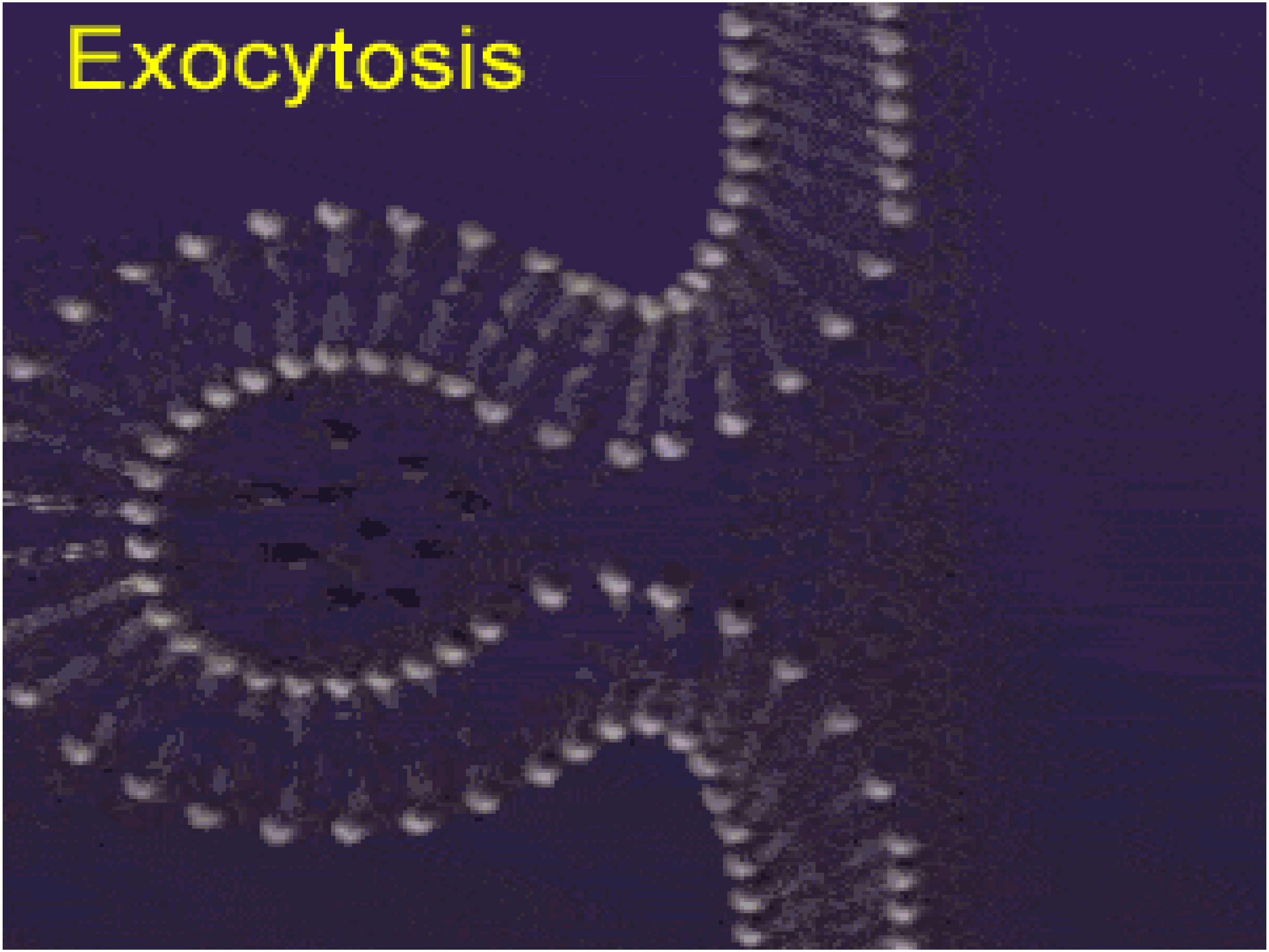
Figure 3.13a

Phagocytosis

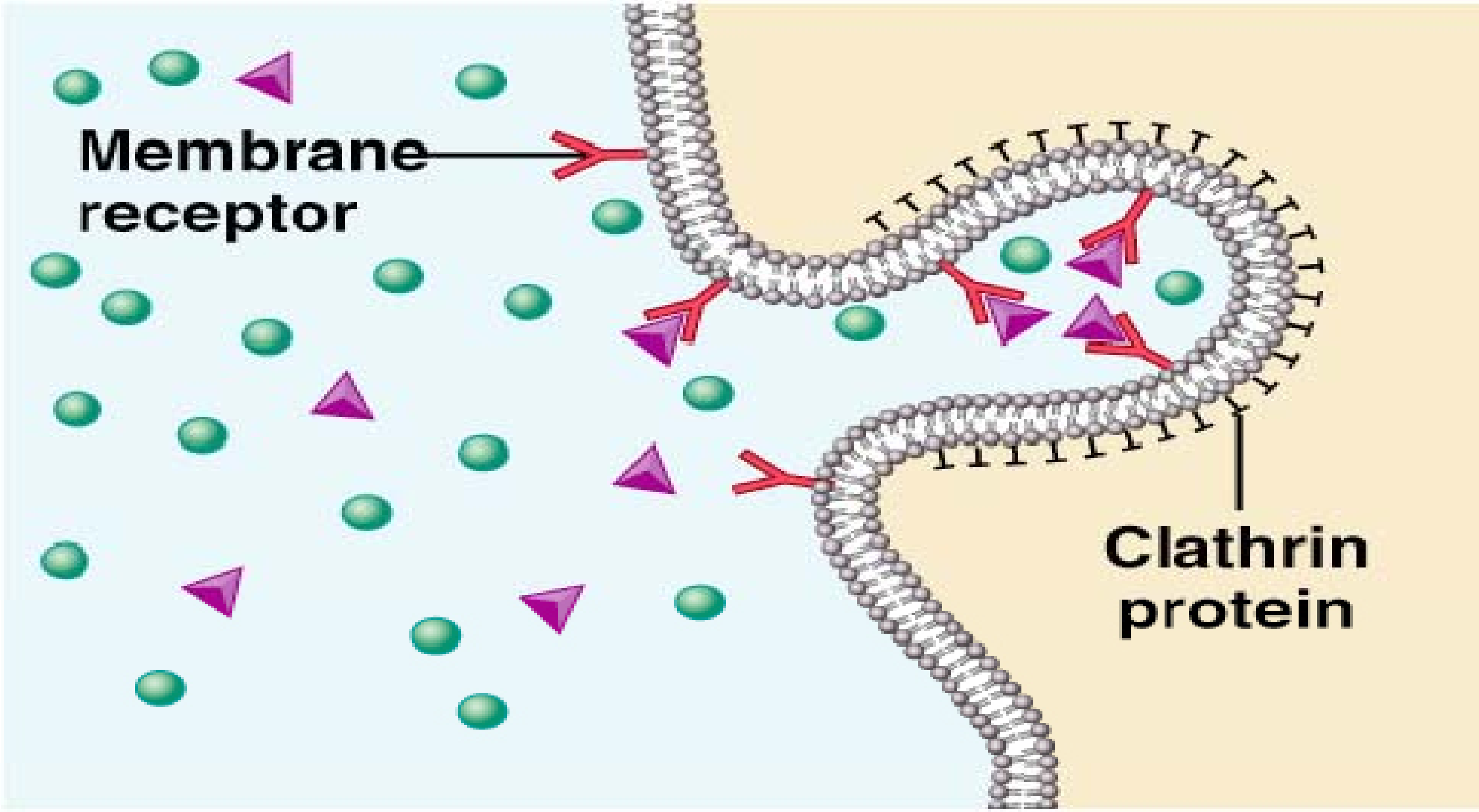


(b) Phagocytosis

Exocytosis



Receptor Mediated Endocytosis



(c) Receptor-mediated endocytosis

Passive Membrane Transport – Review

Process	Energy Source	Example
Simple diffusion	Kinetic energy	Movement of O_2 through membrane
Facilitated diffusion	Kinetic energy	Movement of glucose into cells
Osmosis	Kinetic energy	Movement of H_2O in & out of cells
Filtration	Hydrostatic pressure	Formation of kidney filtrate

Active Membrane Transport – Review

Process	Energy Source	Example
Active transport of solutes	ATP	Movement of ions across membranes
Exocytosis	ATP	Neurotransmitter secretion
Endocytosis	ATP	White blood cell phagocytosis
Fluid-phase endocytosis	ATP	Absorption by intestinal cells
Receptor-mediated endocytosis	ATP	Hormone and cholesterol uptake
Endocytosis via caveoli	ATP	Cholesterol regulation
Endocytosis via coatomer vesicles	ATP	Intracellular trafficking of molecules

Membrane Potential

- Voltage across a membrane
- Resting membrane potential – the point where K^+ potential is balanced by the membrane potential
  - Ranges from –20 to –200 mV
  - Results from Na^+ and K^+ concentration gradients across the membrane
  - Differential permeability of the plasma membrane to Na^+ and K^+
- Steady state – potential maintained by active transport of ions

Generation and Maintenance of Membrane Potential

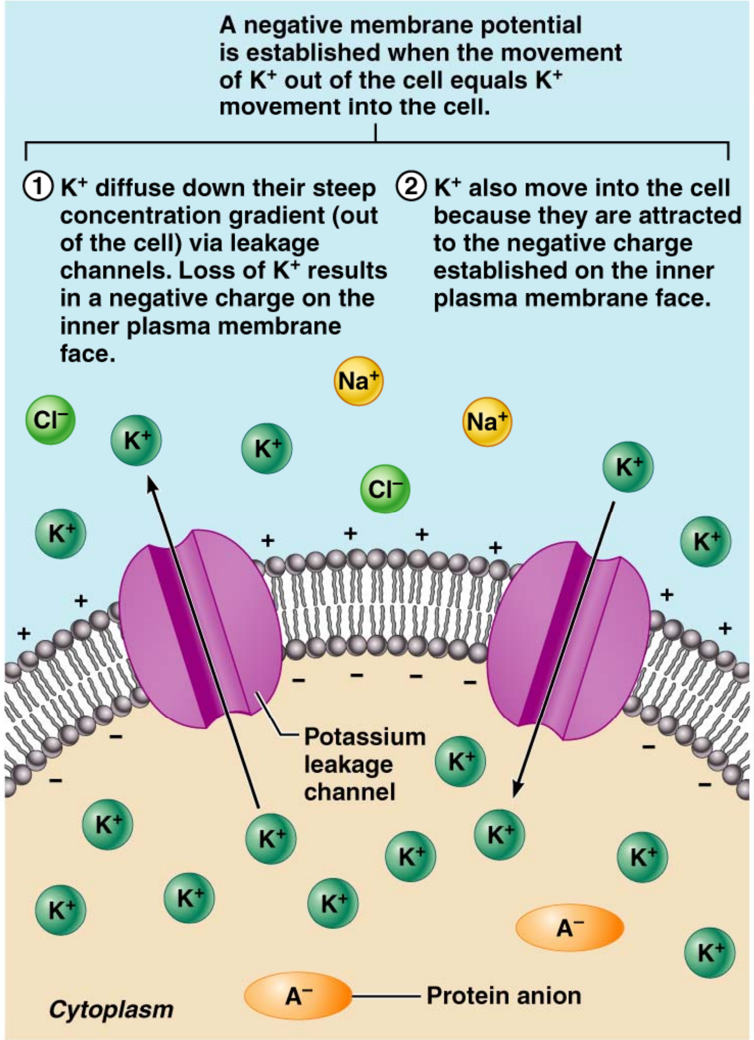
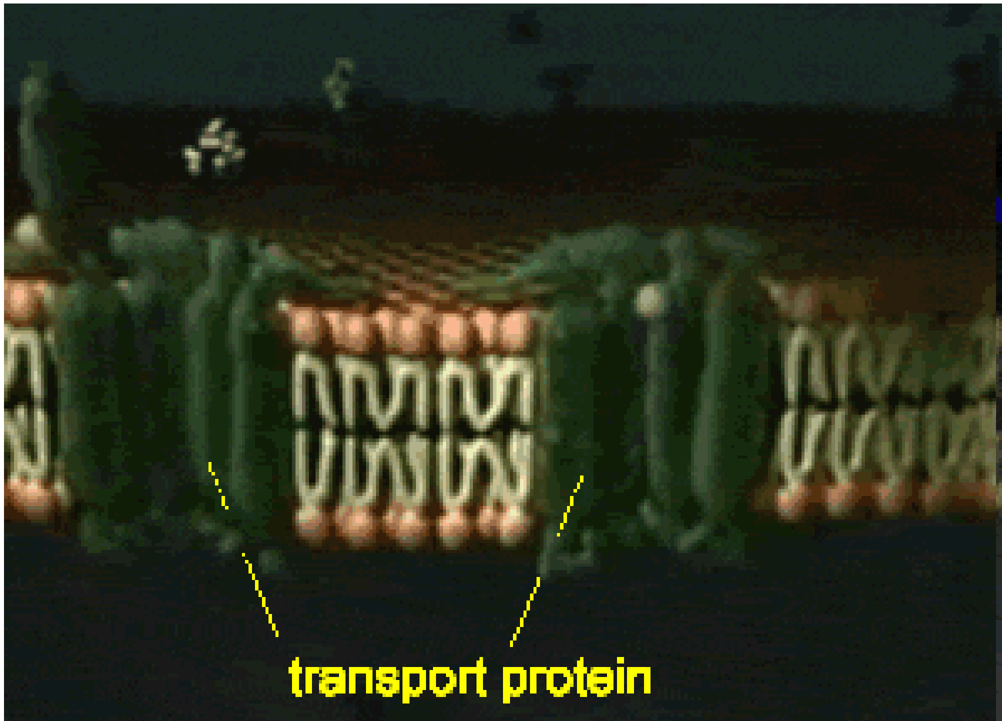
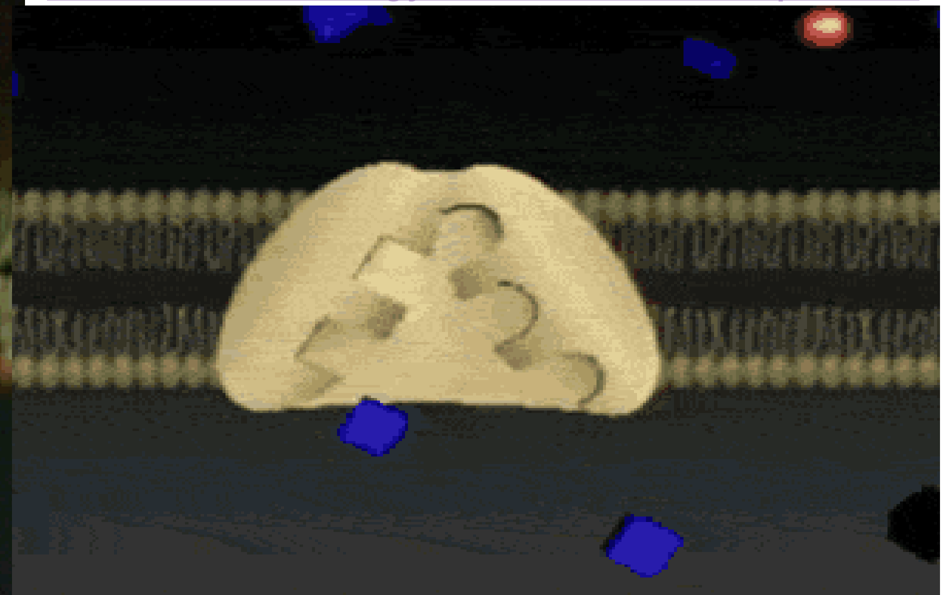


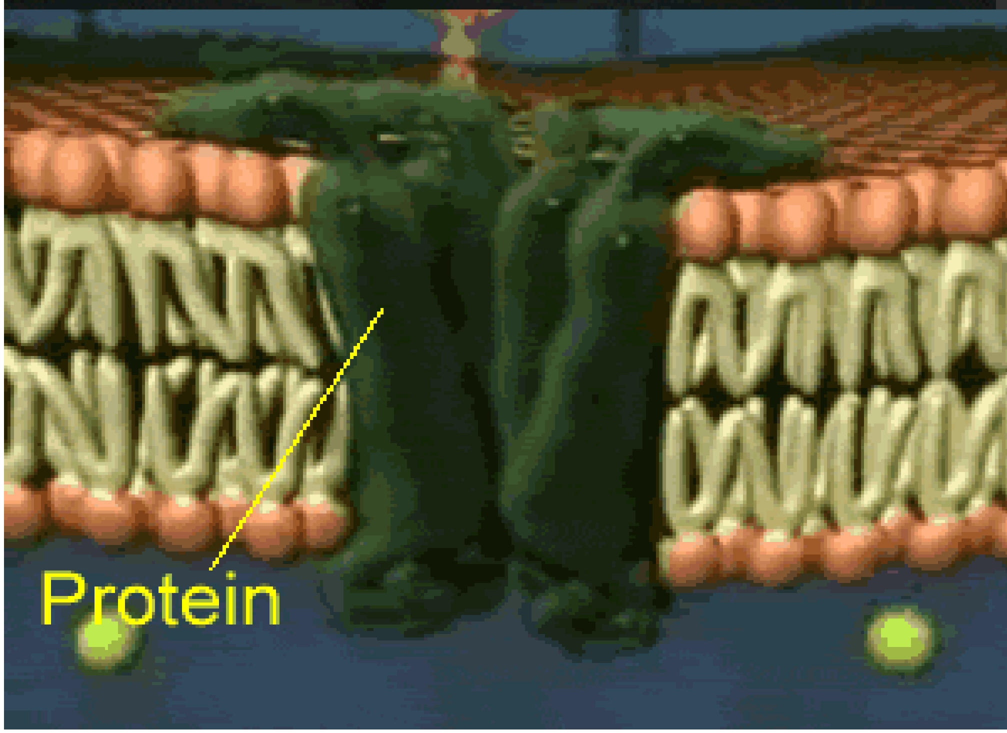
Figure 3.15

InterActive Physiology ®:
Nervous System I: The Membrane Potential



http://www.dynamicscience.com.au/tester/solutions/biology/cell/cellmbntrnspt.html





Exercise

- **How Will Water Move Across Semi-Permeable Membrane?**
- 1/Solution A has 100 molecules of glucose per ml
- Solution B has 100 moecules of fructose per ml
- How will the water molecules move?

- 2/Solution A has 100 molecules of glucose per ml
- Solution B has 75 moecules of fructose per ml
- How will the water molecules move?

- 3/Solution A has 100 molecules of glucose per ml
- Solution B has 100 moecules of NaCl per ml
- How will the water molecules move?

- 1/ There will be no net movement of water since the concentration of solute in each solution is equal

2/There will be a net movement of water from Solution B to Solution A until both solutions have equal concentrations of solute equal

3/ Each molecule of NaCl will dissociate to form a Na^+ ion and a Cl^- ion, making the final concentration of solutes 200 molecules per mil. Therefore, there will be a net movement of water from Solution A to Solution B until both solutions have equal concentrations of solute.

Cellular Communication

- **Signal Transduction Pathways**
- Chemical messages which elicit a response in cells server as a form of communication between cells
- Found in all cells
- Extremely conserved (similar) in widely different organisms (such as humans and yeast) leads one to believe that this evolved very early in the history of life
- **Local Communication**
- Used by cells to communicate to their immediate neighbors
- One cell secretes a signal molecule into the extracellular fluid which is picked up by the target cells
- One example of this is at the synapse of two neurons
- **Hormonal Signaling**
- Used by cells to communicate to other cells a great distance away (but still in the same organism)
- One cell secrets a signal molecule (hormone) into the blood system (if an animal) or into the extracellular fluid (if a plant)
- Only the target cells, however, will have the receptors necessary to elicit the response

The Three Stages of Cell Signaling - Reception, Transduction, Response

- **Reception**
  - A chemical message binds to a protein on the cell surface
- **Transduction**
  - The binding of the signal molecule alters the receptor protein in some way.
  - The signal usually starts a cascade of reactions known as a signal transduction pathway
- **Response**
  - The transduction pathway finally triggers a response
  - The responses can vary from turning on a gene, activating an enzyme, rearranging the cytoskeleton
  - There is usually an amplification of the signal (one hormone can elicit the response of over 10^8 molecules