Introduction to Physiology and Transport

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Syllabus: Introduction to Physiology (0501110)
FOR MEDICAL STUDENTS
Spring 2021

Subjects	Lect. No.	Pages in Guyton 14th	Pages in Guyton 13th
Introduction to Physiology: General outline of physiology. Homeostasis, control systems, negative & positive feedback mechanism	1	FM 3-9	**3-10**
Cell Membrane	2	FM 11-14	**11-14**
Units: moles, osmoles and equivalent. Osmosis and osmotic pressure	3	FM	
Transport-I (Passive) **A. Simple Diffusion** **B. Facilitated Diffusion** **C. Osmosis**	4	FM 45-52	**47-54**
Transport-II (Active) **A. Primary Active.** **B. Secondary Active: Co-and Counter-Transport** **C. Vesicular transport**	5-6	MK 52-56	**54-59**
Excitable Membranes: **Resting Membrane Potential: Origin And Determinants. Distribution Of Different Ions Across Cell Membranes**	7	MK 57-69	**61-74**
Electrochemical Equilibrium (Nernst Equation) As a Predictor For RMP **-E_{Na+}, E_{K+}, E_{Ca++}, E_{Cl-}** **-Other Equations Which Predict RMP: Goldman-Hodgkin-Katz Equation And Chord Conductance Equation**	8-9		
Autonomic Nervous System (I) Organization: Sympathetic and Parasympathetic	10	MK 729-740	**773-785**
Autonomic Nervous System (II)	11		
Body Water: Distribution & Measurements	12	MK 285-296	**305-316**
Abnormalities of body fluid volume regulation Hypo-osmotic dehydration & overhydration. Hyper-osmotic dehydration & overhydration. Edema (definition, types, difference between IC & EC edema).	13		
All or none versus graded potential	14	MK 560-562	**596-598**
Excitatory Post Synaptic Potential EPSP And Inhibitory Post Synaptic Potential IPS	15	MK 552-557	**587-592**
Basic neuronal circuits: Synapses: types, transmission of AP, neurotransmitters, facilitation, inhibition, summation, electrical events, processing, fatigue…etc. **Excitatory and Inhibitory postsynaptic potential**	**16-17**	**FM** **550-552** **563-570**	**584-587** **599-606**

Subjects	Lect. No.	Pages in Guyton 14th	Pages in Guyton 13th
- Neurotransmitters, types, synthesis, location (pre-and postgangelionic) - Receptors: types and location. - Adrenal medulla.	18		
Neurons: Types and classifications	19	FM 563-564	599-600
Microcirculation: Capillary Structure; Fluid Filtration (Forces) & Reabsorption - Starling Law Of Capillary Exchange - Lymphatic System	20-21	FM 177-186	189-198
Action Potential: Cardiac Action Potential (Fast Response AP) Vs Slow Response AP (The Pacemaker Concept)	22-23	FM 101-104 115-120	109-113 123-129
Receptors: types and adaptation - Membrane or intracellular - Ion channels - G-protein - Enzyme linked - Intracellular - Second messengers - cAMP and cGMP, Phospholipid - Calcium calmodulin and IRS	24-25	EZ 881-891	925-036
Signal Transduction (Regulation of cellular machinery) Extracellular regulators: nervous, endocrine, paracrine and autocrine	26-27	EZ 910-912 940-941	954-956 984-985
Steroids: Their Signal Transduction And Mechanism Of Action	28	EZ 926-927 931	970-971 976

Midterm Exam 40% and Final Exam 60%

Textbook: Guyton and Hall Textbook of Medical Physiology: 13th edition 2016

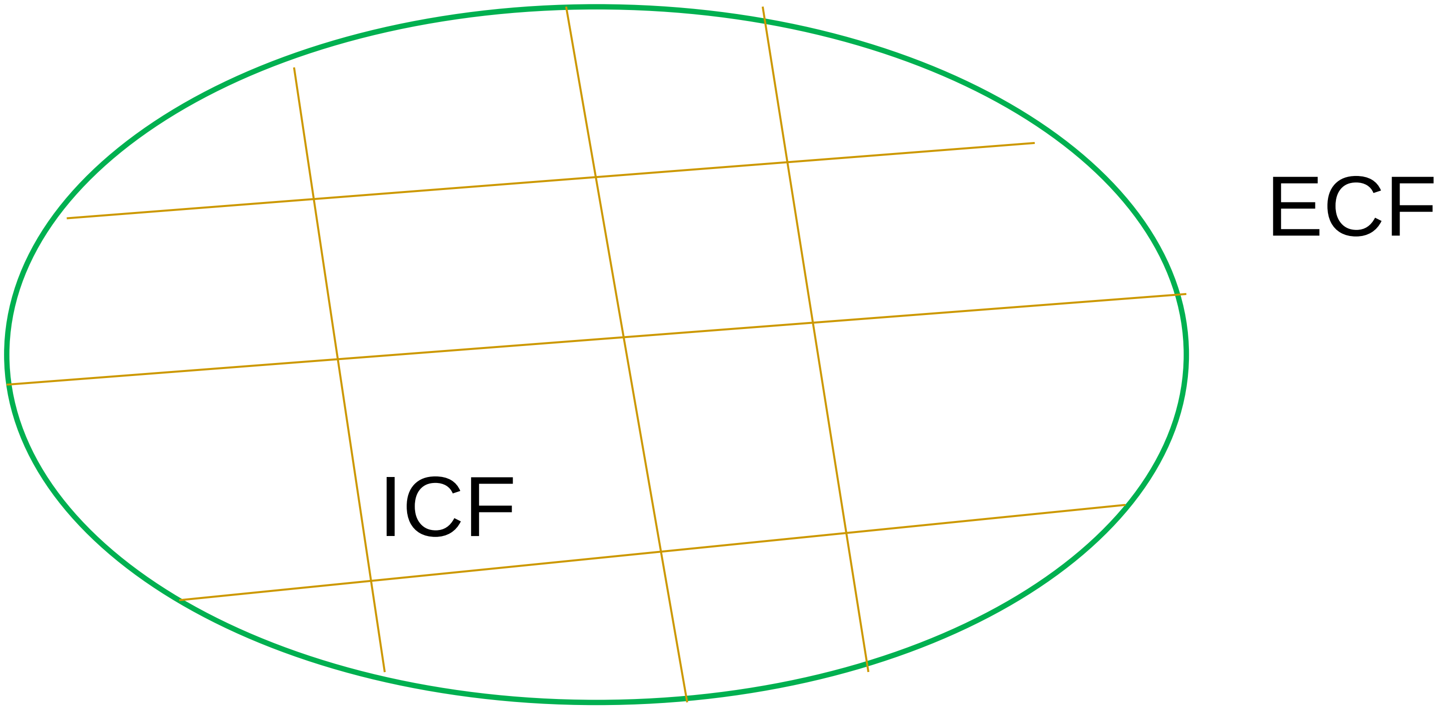
Anatomy and Physiology Defined

- Two branches of science that deal with body’s parts and function
  - **Anatomy**
    - The science of body structures and relationships
    - First studies by dissection (cutting apart)
    - Imaging techniques
  - **Physiology**
    - The science that is concerned with the function of the living organism and its parts, and of the physical and chemical processes involved.
    - The science of body functions

Zygot

Intracellular fluid =(ICF)

Extracellular fluid (ECF)



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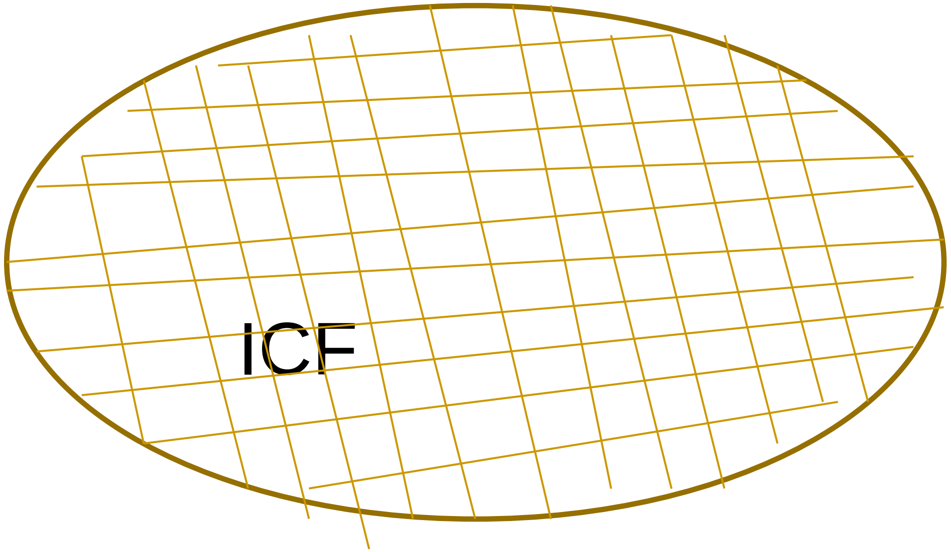


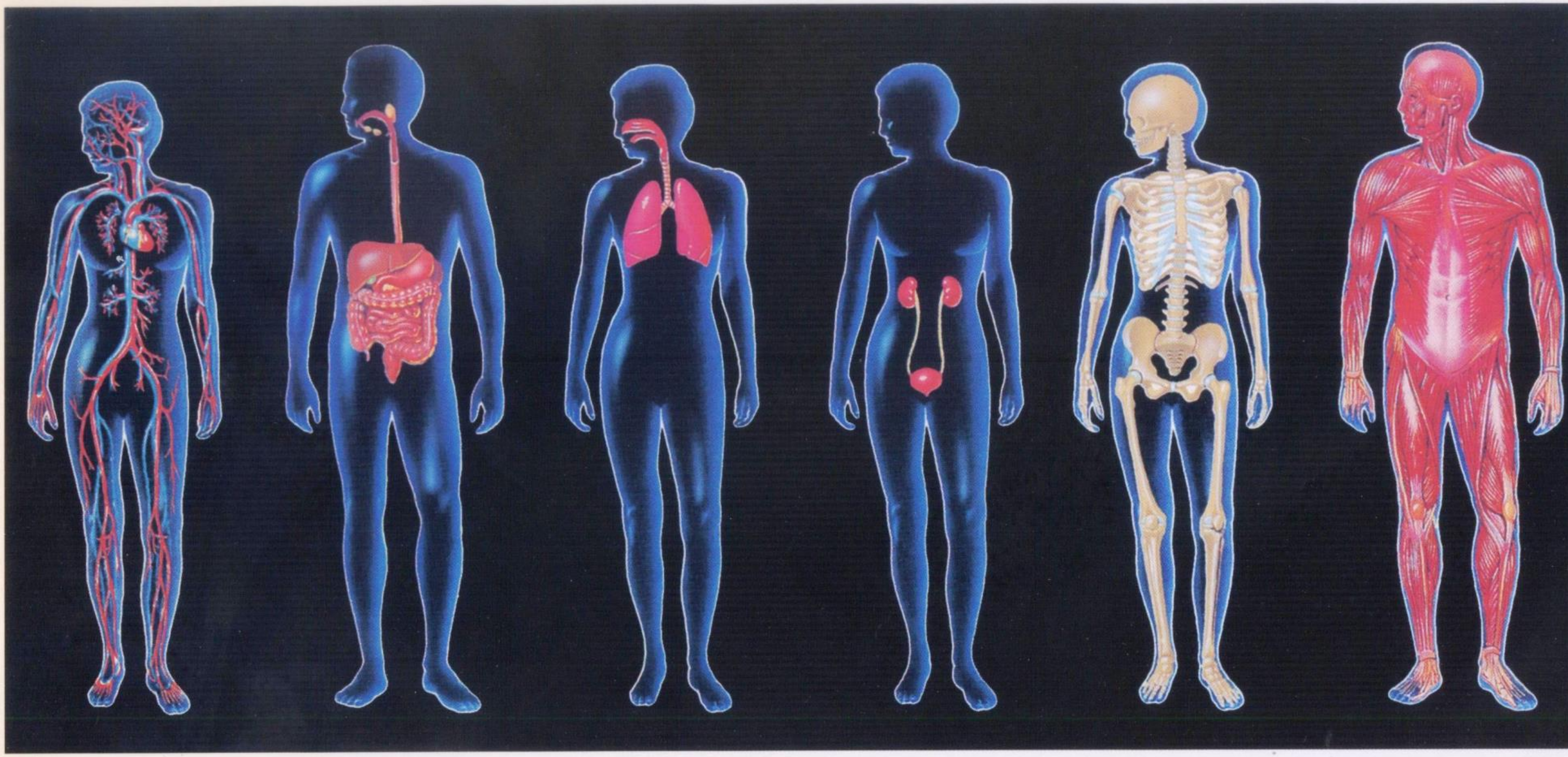
ECF

Emergence of systems to meet the need for supplying the cells with the nutrients it needs.

Levels of structural organization

- SYSTEM LEVEL
  - A **system** consists of related organs with a common function
  - Organ-system level
    - Digestive system breaks down and absorbs food
    - It includes organs such as the mouth, small and large intestines, liver, gallbladder, and pancreas
    - Eleven systems of the human body

Eleven organ systems of the human body, part 1



Circulatory system
heart, blood,
blood vessels

Digestive system
mouth, pharynx,
esophagus,
stomach,
small intestine,
large intestine,
salivary glands,
exocrine pancreas,
liver, gallbladder

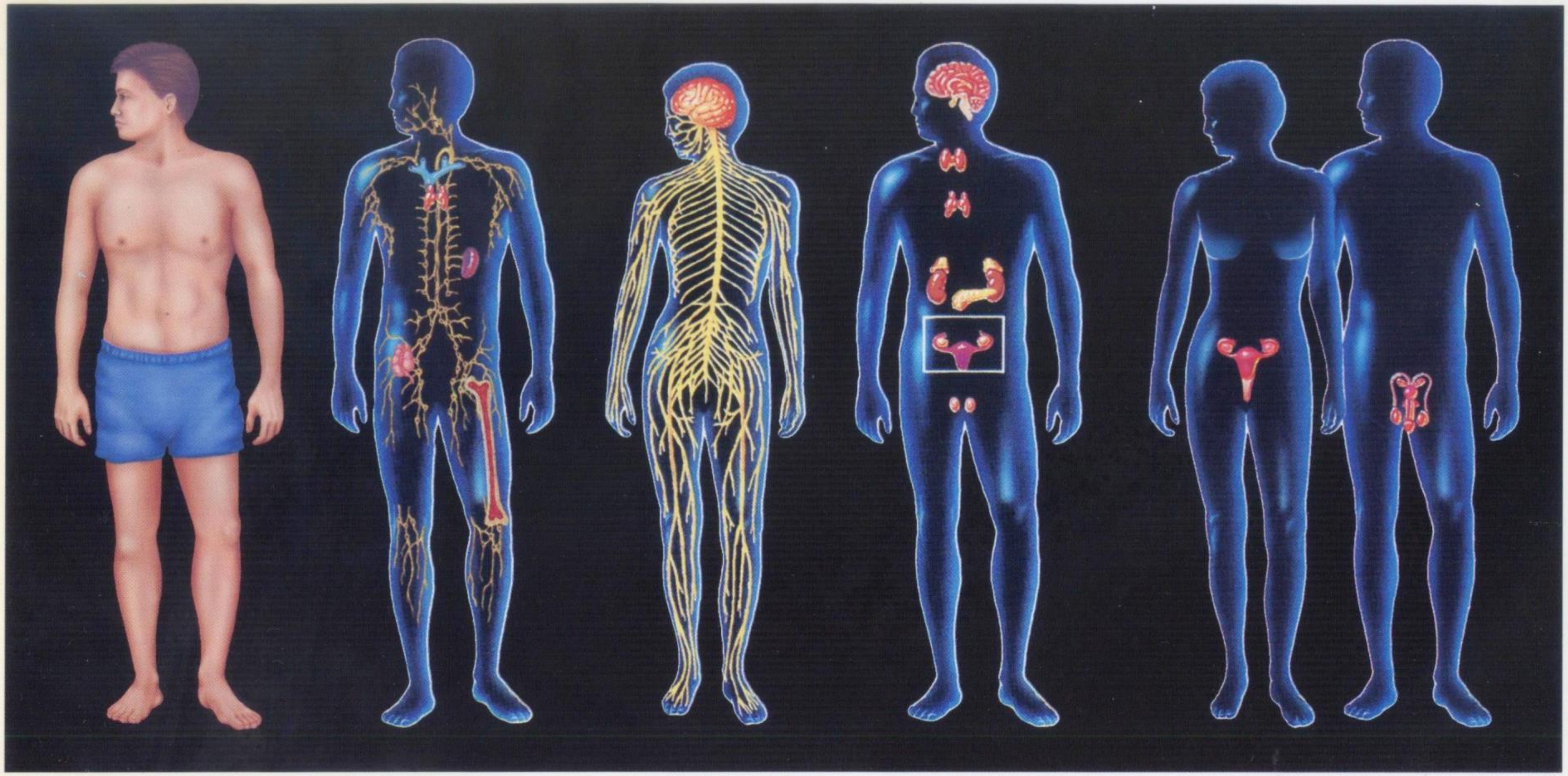
Respiratory system
Nose, pharynx, larynx,
trachea, bronchi, lungs

Urinary system
kidneys, ureters,
urinary bladder,
urethra

Skeletal system
bones, cartilage,
joints

Muscular system
skeletal muscles

Eleven organ systems of the human body, part 2



Integumentary system
skin, hair, nails

Immune system
lymph nodes, thymus, bone marrow, tonsils, adenoids, spleen, appendix, and, not shown, white blood cells, gut-associated lymphoid tissue, and skin-associated lymphoid tissue

Nervous system
brain, spinal cord, peripheral nerves, and, not shown, special sense organs

Endocrine system
all hormone-secreting tissues, including hypothalamus, pituitary, thyroid, adrenals, endocrine pancreas, gonads, kidneys, pineal, thymus, and, not shown, parathyroids, intestine, heart, and skin

Reproductive system
Male: testes, penis, prostate gland, seminal vesicles, bulbourethral glands, and associated ducts

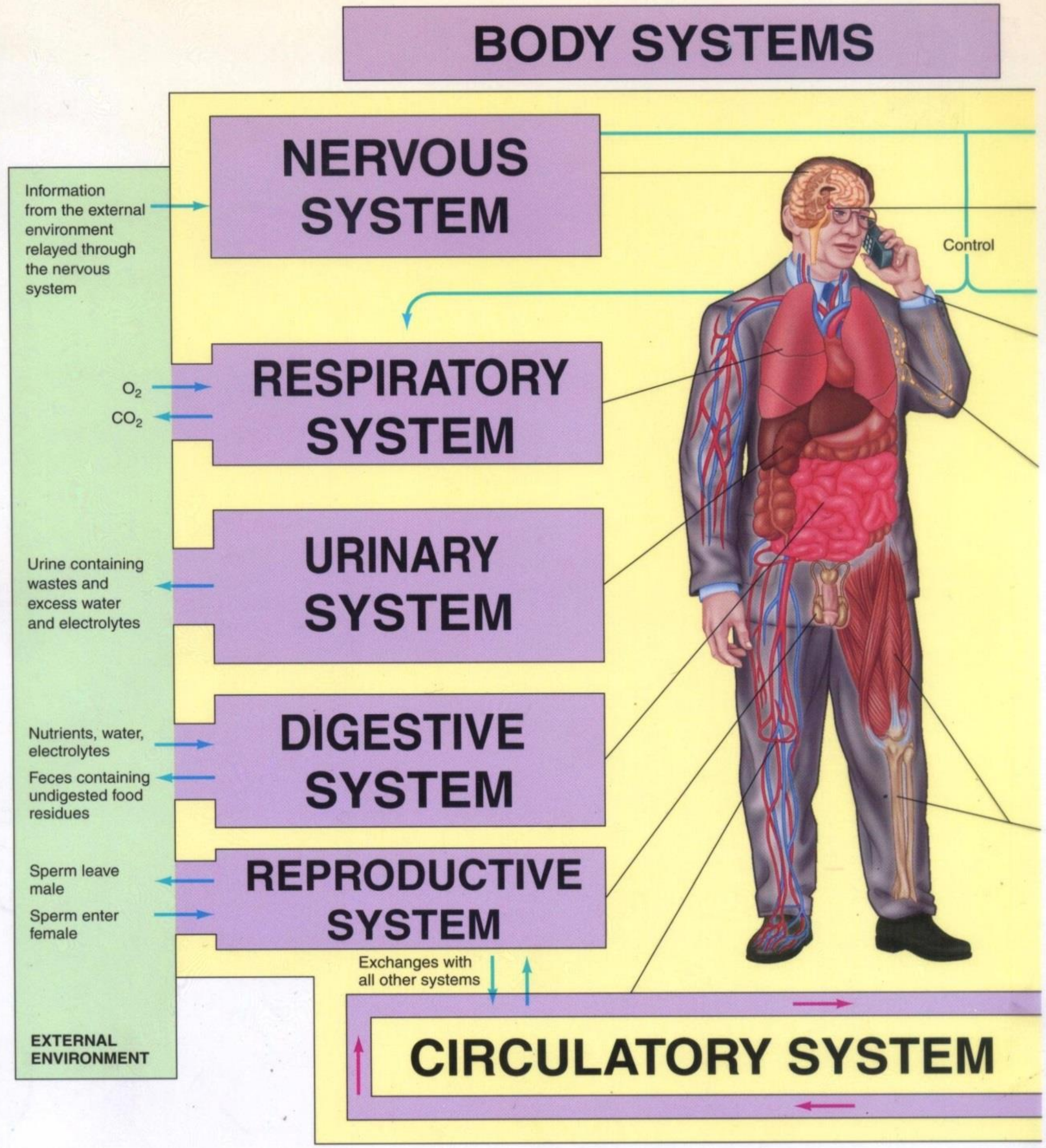
Female: ovaries, oviducts, uterus, vagina, breasts

Homeostasis

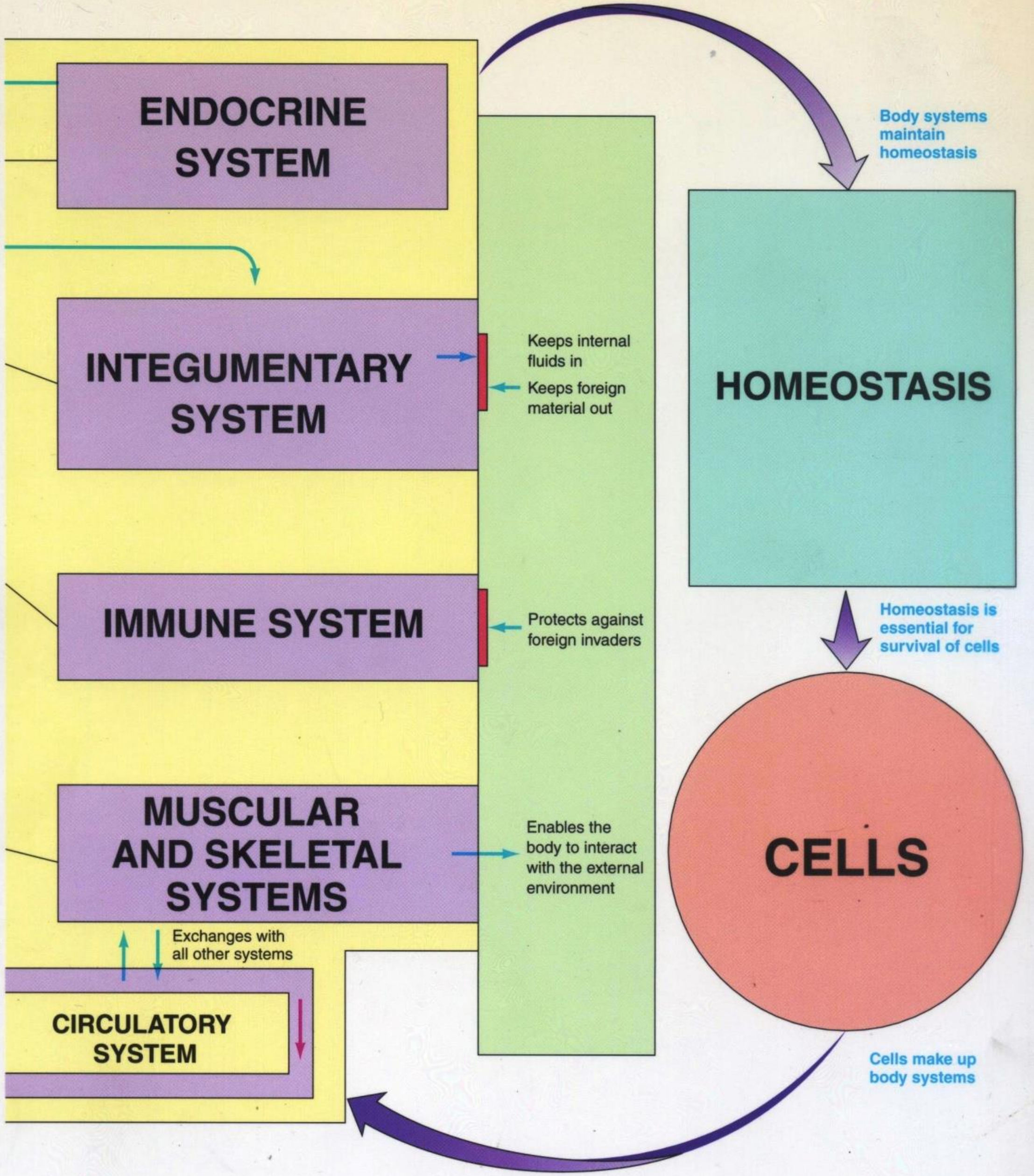
- A condition of **equilibrium** (balance) in the body's internal environment. Maintain an almost constant internal environment
  - Dynamic condition
  - Narrow range is compatible with maintaining life
  - Example
    - Blood glucose levels range between 70 and 110 mg of glucose/dL of blood
    - Whole body contributes to maintain the internal environment within normal limits

Figure 1.4

Body systems maintain homeostasis, part 1



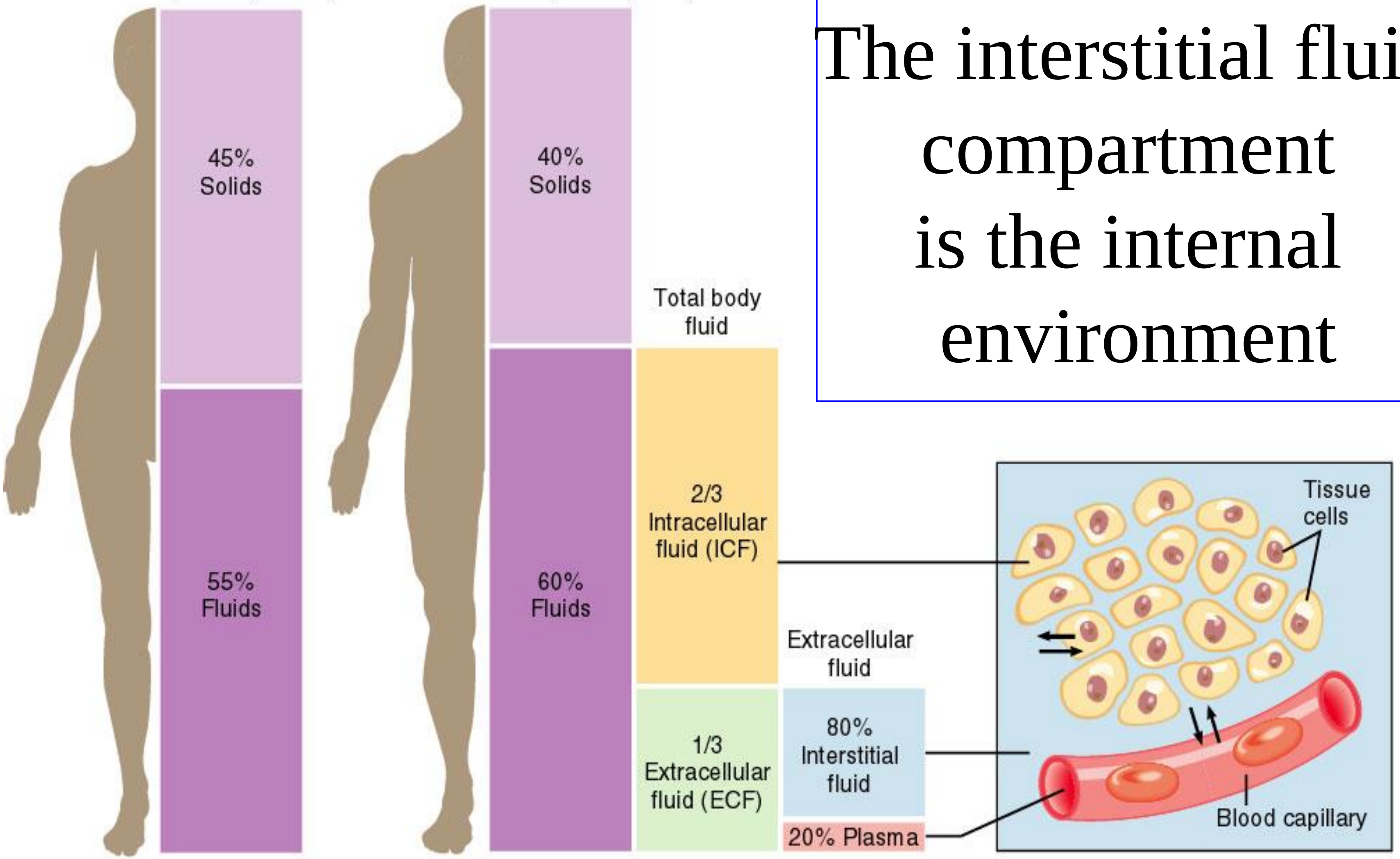
Body systems maintain homeostasis, part 2



Homeostasis and Body Fluids

- Maintaining the volume and composition of body fluids are important
  - **Body fluids** are defined as dilute, watery solutions containing dissolved chemicals inside or outside of the cell
  - **Intracellular Fluid (ICF)**
    - Fluid within cells
  - **Extracellular Fluid (ECF)**
    - Fluid outside cells
    - **Interstitial fluid** is ECF between cells and tissues

The interstitial fluid compartment is the internal environment



(a) Distribution of body solids and fluids in an average lean, adult female and male

(b) Exchange of water among body fluid compartments

27.01

Interstitial Fluid and Body Function

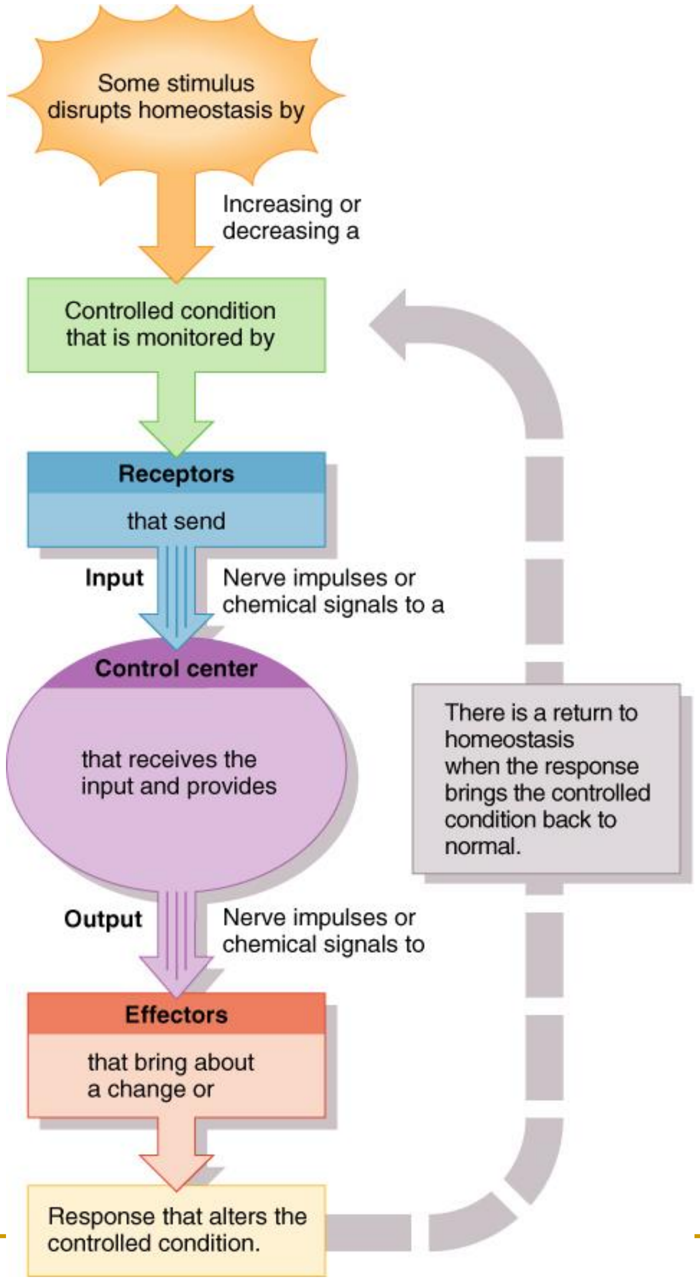
- Cellular function depends on the regulation of composition of interstitial fluid
- Body's internal environment
- Composition of interstitial fluid changes as it moves
    - Movement back and forth across capillary walls provide nutrients (glucose, oxygen, ions) to tissue cells and removes waste (carbon dioxide)

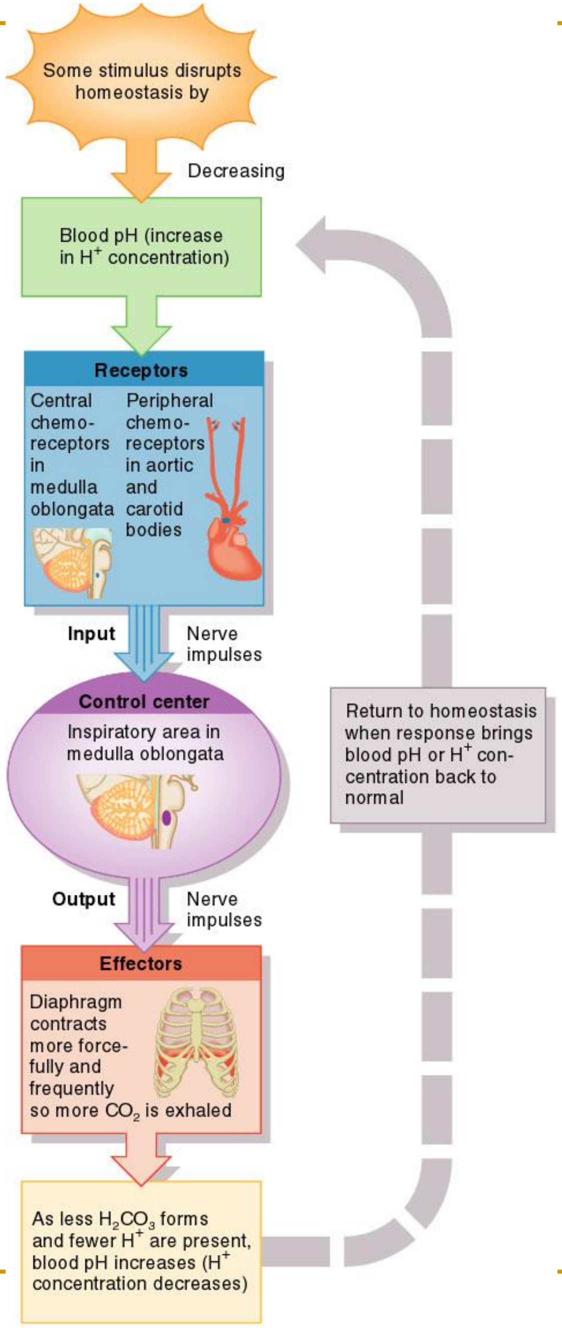
Control of Homeostasis

- Homeostasis is constantly being disrupted
  - **Physical insults**
    - Intense heat or lack of oxygen
  - **Changes in the internal environment**
    - Drop in blood glucose due to lack of food
  - **Physiological stress**
    - Demands of work or school
  - **Disruptions**
    - Mild and temporary (balance is quickly restored)
    - Intense and Prolonged (poisoning or severe infections)

Feedback System

- Cycle of events
  - Body is monitored and re-monitored
  - Each monitored variable is termed a controlled condition
- Three Basic components
  - Receptor
  - Control center
  - Effector




Some stimulus disrupts homeostasis by
Decreasing
Blood pH (increase in H^+ concentration)
Receptors
Central chemo-receptors in medulla oblongata
Peripheral chemo-receptors in aortic and carotid bodies
Input
Nerve impulses
Control center
Inspiratory area in medulla oblongata
Output
Nerve impulses
Effectors
Diaphragm contracts more force-fully and frequently so more CO_2 is exhaled
As less H_2CO_3 forms and fewer H^+ are present, blood pH increases (H^+ concentration decreases)
Return to homeostasis when response brings blood pH or H^+ con-centration back to normal

27.07

Feedback Systems

- **Receptor**
  - Body structure that monitors changes in a controlled condition
  - Sends **input** to the control center
    - Nerve ending of the skin in response to temperature change

Feedback Systems

- **Control Center**
  - Brain
  - Sets the range of values to be maintained
  - Evaluates input received from receptors and generates **output** command
  - Nerve impulses, hormones
    - Brains acts as a control center receiving nerve impulses from skin temperature receptors

Feedback Systems

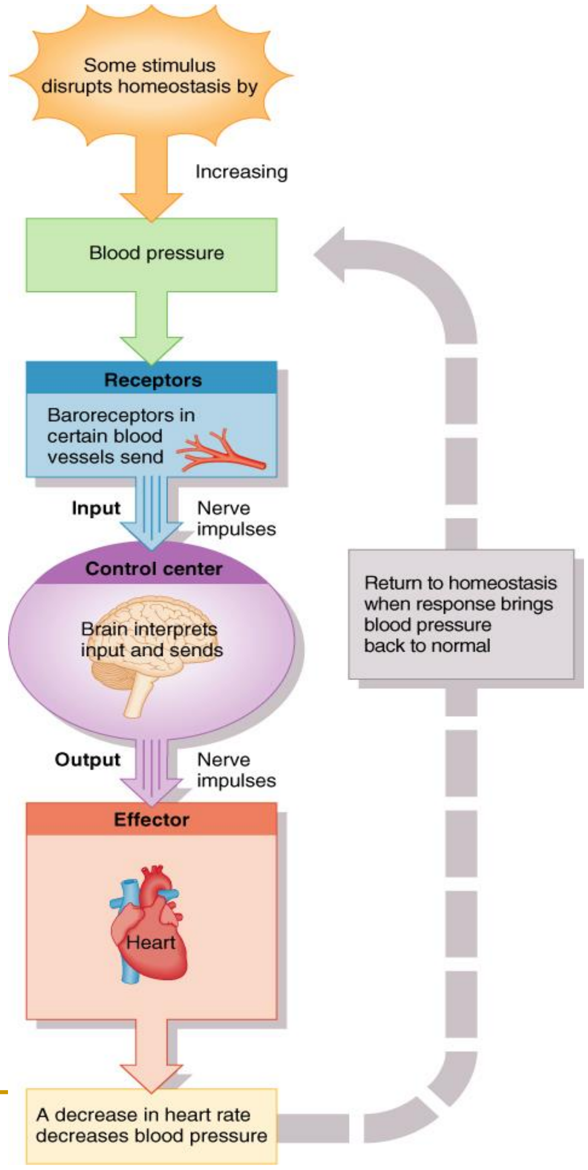
- **Effector**
  - Receives output from the control center
  - Produces a response or effect that changes the controlled condition
    - Found in nearly every organ or tissue
    - Body temperature drops the brain sends and impulse to the skeletal muscles to contract
    - Shivering to generate heat

Negative and Positive Feedback systems

- **Negative Feedback systems**
  - Reverses a change in a controlled condition
    - Regulation of blood pressure (force exerted by blood as it presses again the walls of the blood vessels)
- **Positive Feedback systems**
  - Strengthen or reinforce a change in one of the body's controlled conditions
    - Normal child birth

Negative Feedback: Regulation of Blood Pressure

- External or internal stimulus increase BP
  - Baroreceptors (pressure sensitive receptors)
    - Detect higher BP
    - Send nerve impulses to brain for interpretation
    - Response sent via nerve impulse sent to heart and blood vessels
    - BP drops and homeostasis is restored
    - Drop in BP negates the original stimulus



Positive Feedback: Blood Loss

- Normal conditions, heart pumps blood under pressure to body cells (oxygen and nutrients)
- Severe blood loss
  - Blood pressure drops
  - Cells receive less oxygen and function less efficiently
  - If blood loss continues
    - Heart cells become weaker
    - Heart doesn’t pump
    - BP continues to fall

Feedback Gain

A measure of the effectiveness of a feedback system

$$\text{Gain} = \frac{\text{Correction}}{\text{Error}}$$

Homeostatic Imbalances

- Normal equilibrium of body processes are disrupted
  - **Moderate imbalance**
    - Disorder or abnormality of structure and function
    - Disease specific for an illness with recognizable signs and symptoms
    - **Signs** are objective changes such as a fever or swelling
    - **Symptoms** are subjective changes such as headache
  - **Severe imbalance**
    - Death

Generalized Body Cell

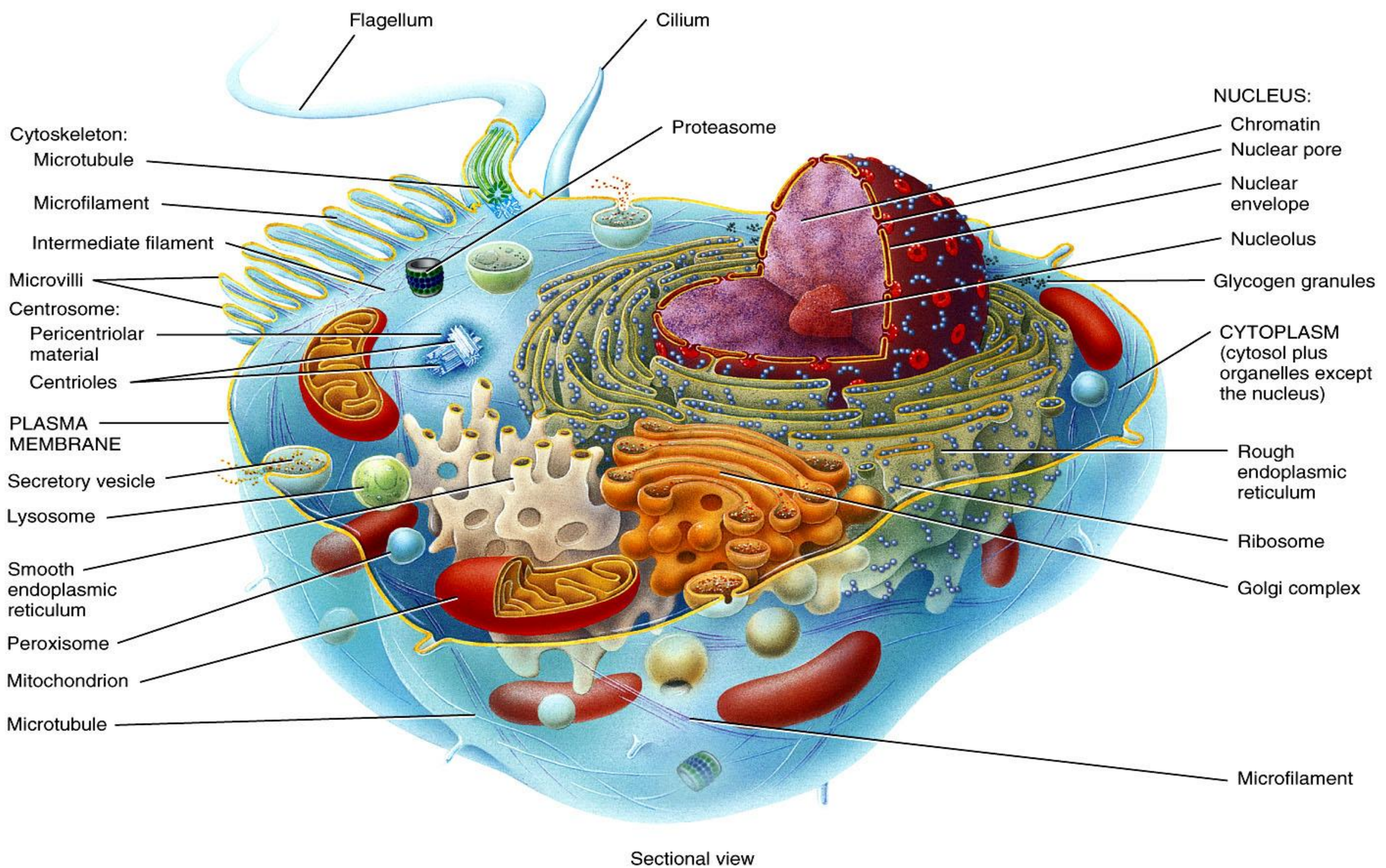


Figure 03.01 Tortora - PAP 12/e
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A Generalized Cell

1. Plasma membrane

- forms the cell's outer boundary
- separates the cell's internal environment from the outside environment
- is a selective barrier
- plays a role in cellular communication

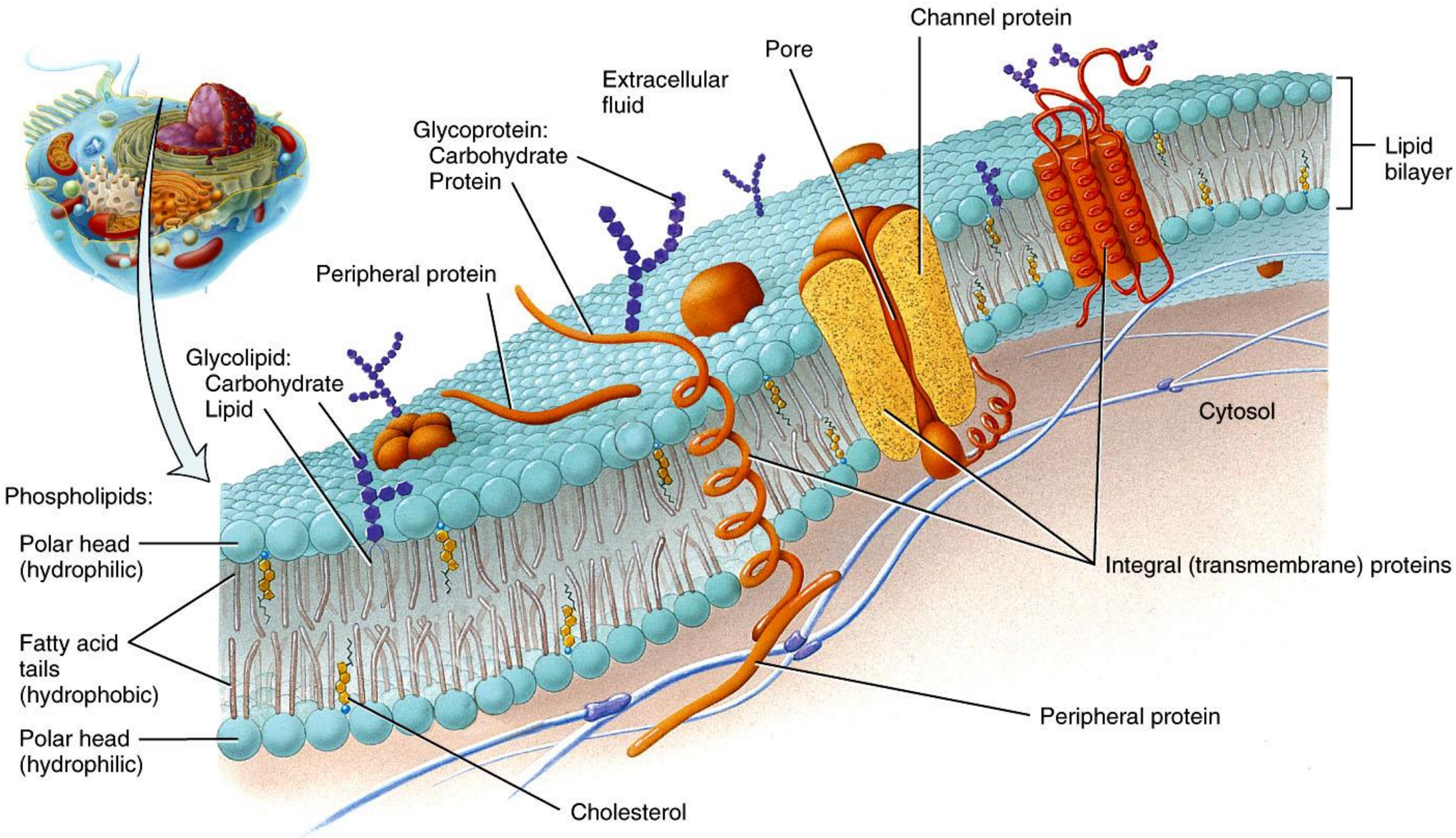
Plasma Membrane

- Flexible yet sturdy barrier
- The *fluid mosaic model* - the arrangement of molecules within the membrane resembles a sea of lipids containing many types of proteins
- The lipids act as a barrier to certain substances
- The proteins act as “gatekeepers” to certain molecules and ions

Structure of a Membrane

- Consists of a lipid bilayer - made up of phospholipids, cholesterol and glycolipids
- **Integral proteins** - extend into or through the lipid bilayer
- **Transmembrane proteins** - most integral proteins, span the entire lipid bilayer
- **Peripheral proteins** - attached to the inner or outer surface of the membrane, do not extend through it

Structure of the Plasma Membrane



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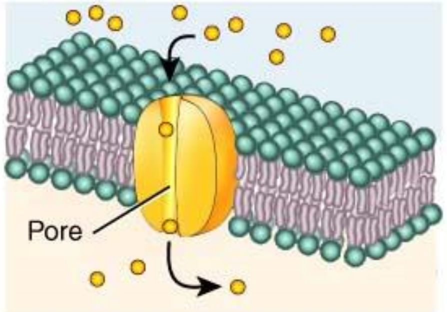
Structure of a Membrane

- **Glycoproteins -** membrane proteins with a carbohydrate group attached that protrudes into the extracellular fluid
- **Glycocalyx -** the "sugary coating" surrounding the membrane made up of the carbohydrate portions of the glycolipids and glycoproteins

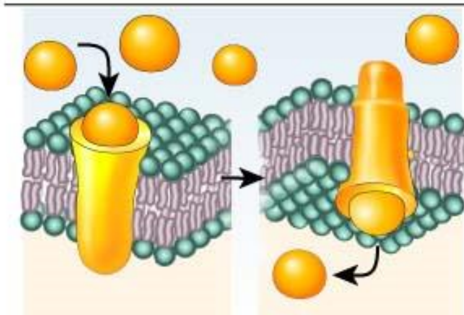
Functions of Membrane Proteins

- Some integral proteins are **ion channels**
- **Transporters -** selectively move substances through the membrane
- **Receptors** - for cellular recognition; a **ligand** is a molecule that binds with a receptor
- **Enzymes** - catalyze chemical reactions
- Others act as **cell-identity markers**

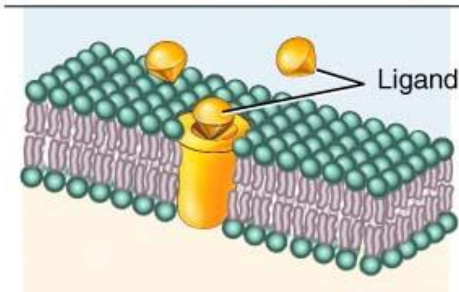
Extracellular fluid | Plasma membrane | Cytosol



Ion channel
Allows specific ion (●) to move through water-filled pore. Most plasma membranes include specific channels for several common ions.

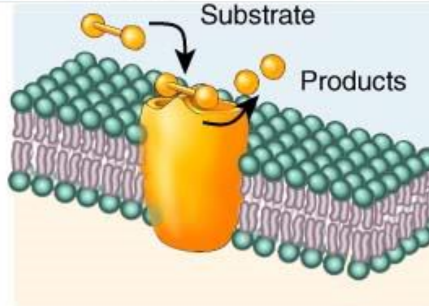


Transporter
Transports specific substances (●) across membrane by changing shape. For example, amino acids, needed to synthesize new proteins, enter body cells via transporters.

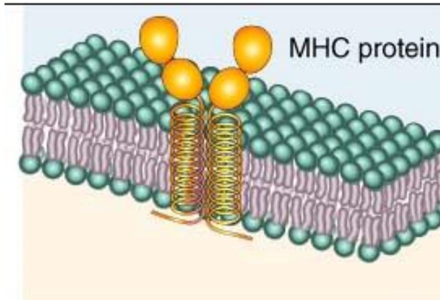


Receptor
Recognizes specific ligand (▼) and alters cell's function in some way. For example, antidiuretic hormone binds to receptors in the kidneys and changes the water permeability of certain plasma membranes.

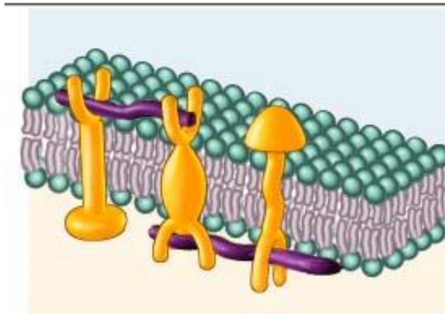
Extracellular fluid | Plasma membrane | Cytosol



Enzyme
Catalyzes reaction inside or outside cell (depending on which direction the active site faces). For example, lactase protruding from epithelial cells lining your small intestine splits the disaccharide lactose in the milk you drink.



Cell Identity Marker
Distinguishes your cells from anyone else's (unless you are an identical twin). An important class of such markers are the major histocompatability (MHC) proteins.



Linker
Anchors filaments inside and outside to the plasma membrane, providing structural stability and shape for the cell. May also participate in movement of the cell or link two cells together.

Membrane Permeability

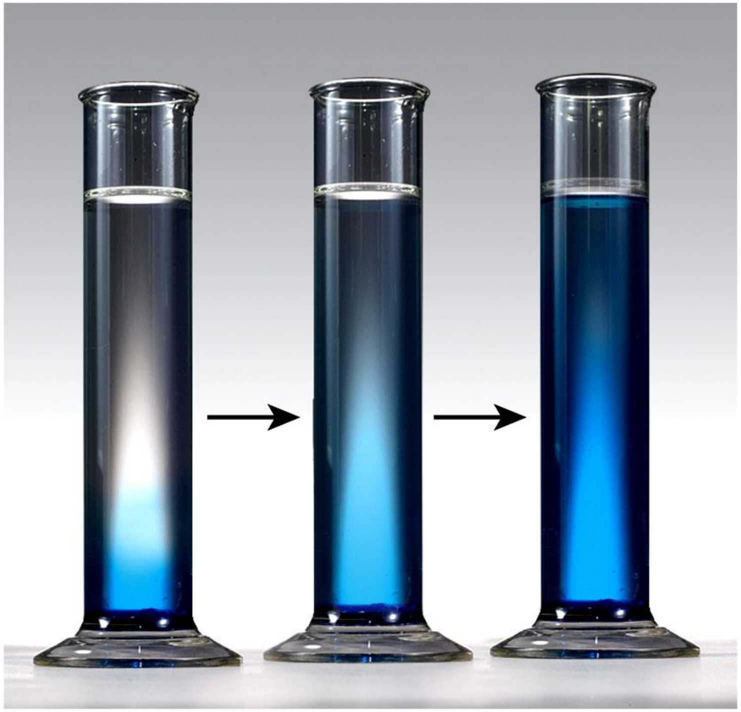
- The cell is either permeable or impermeable to certain substances
- The lipid bilayer is *permeable* to oxygen, carbon dioxide, water and steroids, but *impermeable* to glucose
- Transmembrane proteins act as channels and transporters to assist the entrance of certain substances, for example, glucose and ions

Passive vs. Active Processes

- Passive processes - substances move across cell membranes without the input of any energy; use the *kinetic energy* of individual molecules or ions
- Active processes - a cell uses energy, primarily from the breakdown of ATP, to move a substance across the membrane, i.e., against a concentration gradient

Diffusion

- Steepness of
- concentration gradient
- Temperature
- Mass of diffusing substance
- Surface area
- Diffusion distance



Beginning (a) Intermediate (b) Equilibrium (c)

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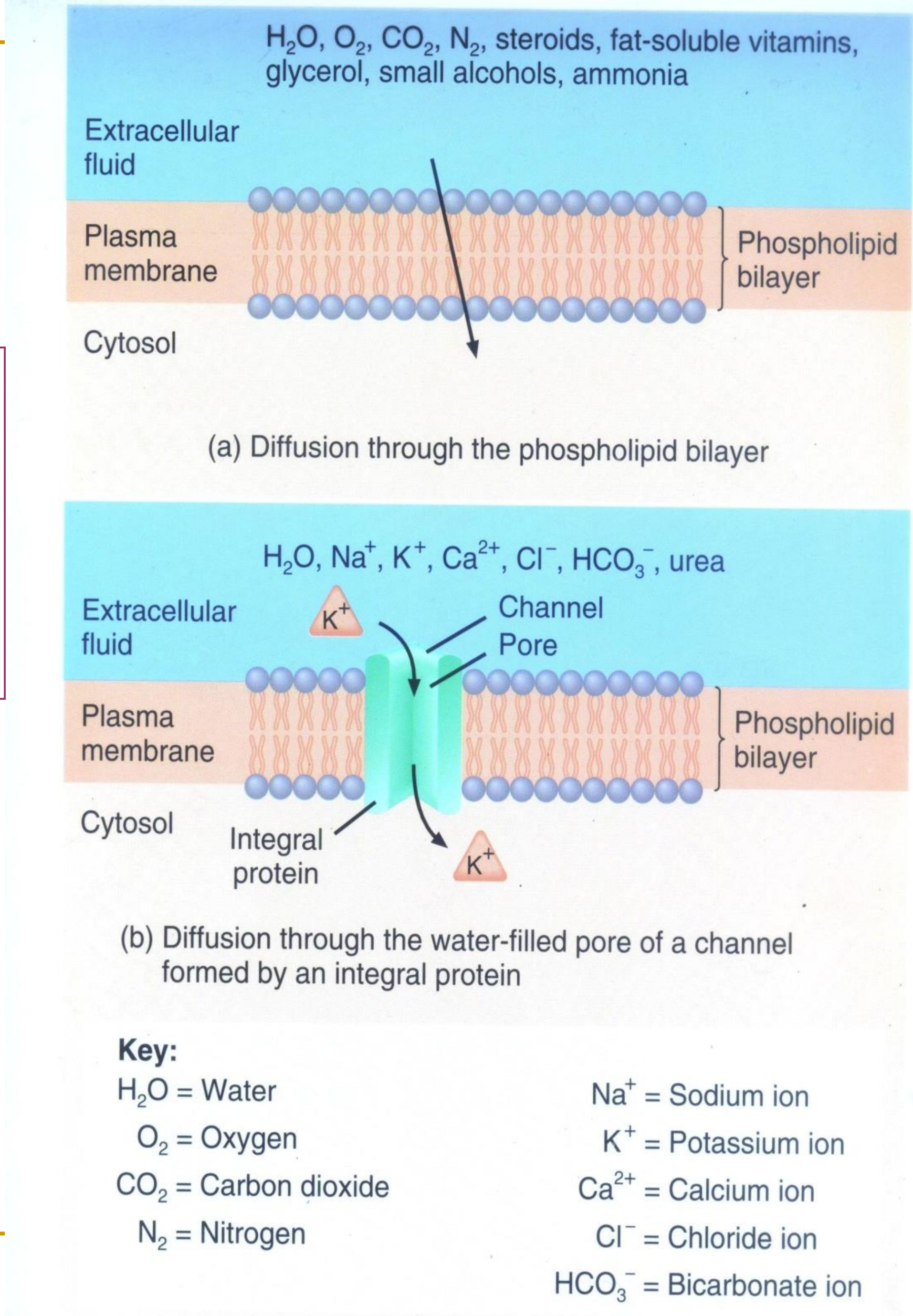
Simple diffusion through the membrane of lipid soluble substances



Diffusion Through the Plasma Membrane, Fig# 3.6a-b

Simple diffusion

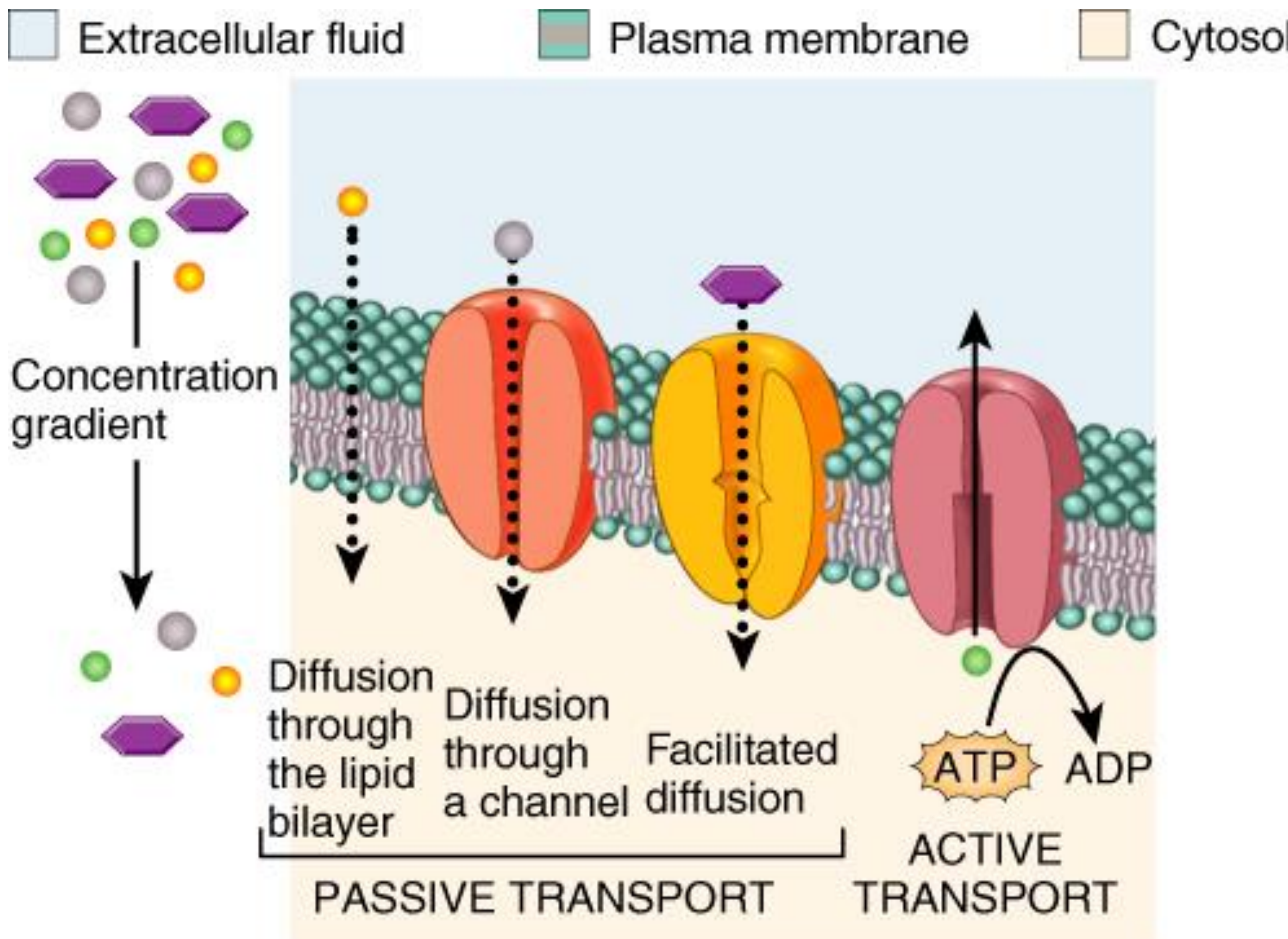
- Diffusion rate (J) is directly proportional to the concentration gradients and solubility in lipids. It is inversely proportional to the square root of the molecular weight and thickness of the membrane.

Fick's law of diffusion

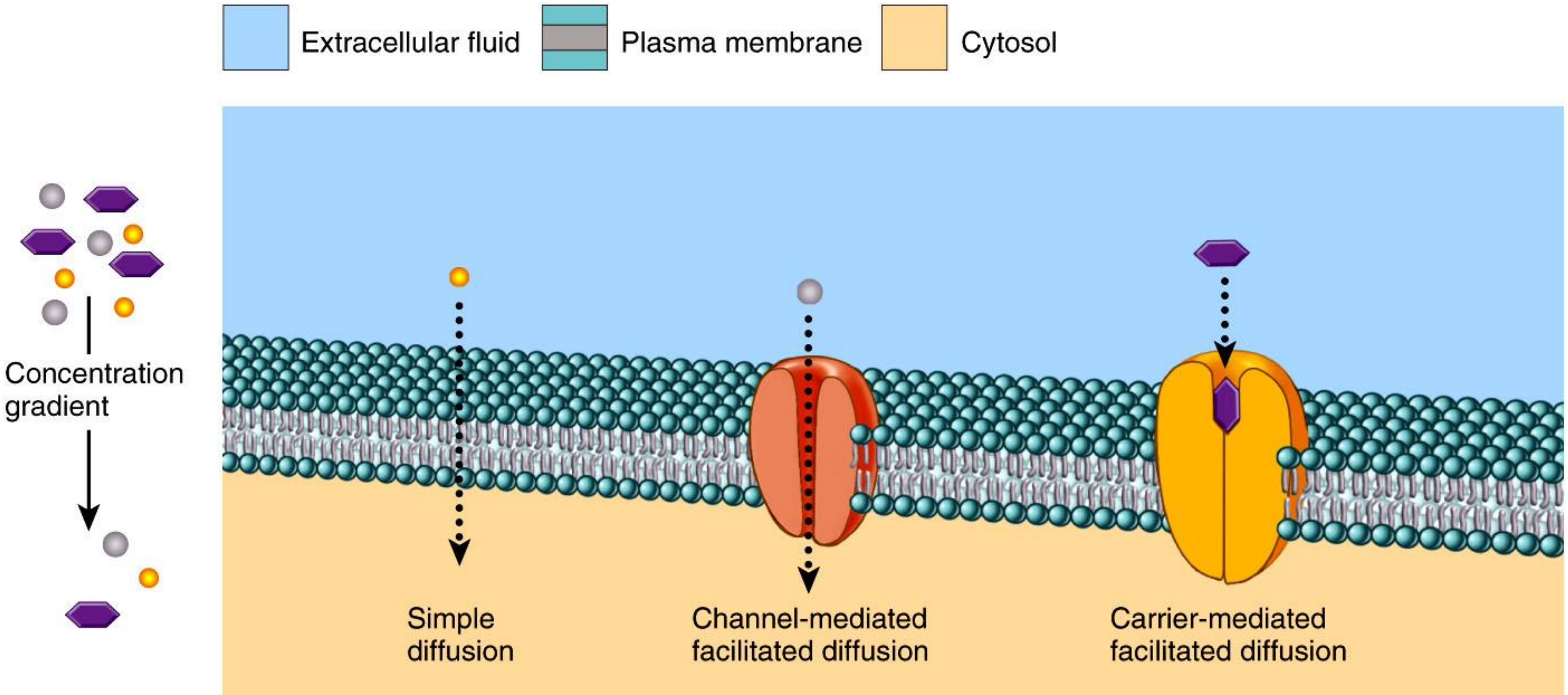
$J = P(C_2\text{-}C_1)*S$ where P=permeability in lipid

$(C_2\text{-}C_1)$= concentration gradient, S=surface area.

Or $J=DA*(\Delta C/ \Delta X)$, ΔC=concentration gradient, A=Area, ΔX=Thickness of the membrane, D=diffusion coefficient (depends on the solubility in lipids, molecular weight).


Extracellular fluid
Plasma membrane
Cytosol
Concentration gradient
Diffusion through the lipid bilayer
Diffusion through a channel
Facilitated diffusion
ATP
ADP
PASSIVE TRANSPORT
ACTIVE TRANSPORT

Simple Diffusion, Channel-mediated Facilitated Diffusion, and Carrier-mediated Facilitated Diffusion



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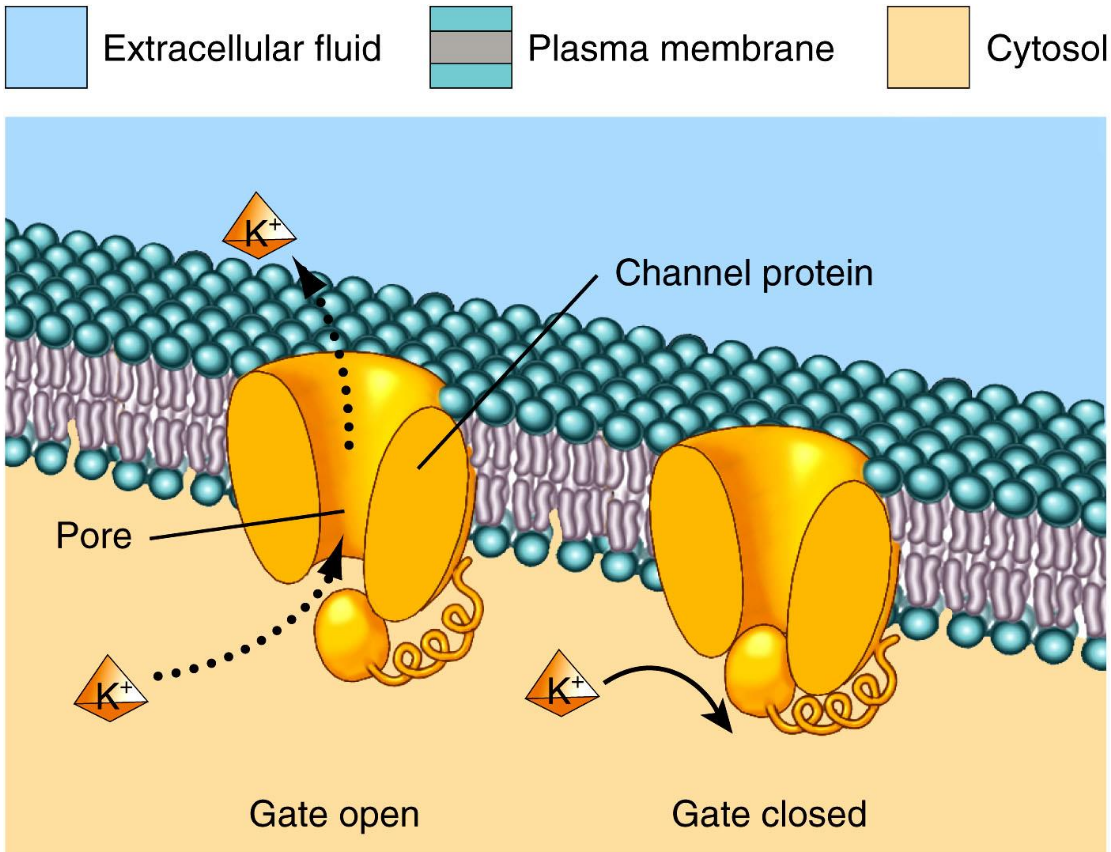
Channel-mediated Facilitated Diffusion of Potassium ions through a Gated K^+ Channel



Details of the K^+ channel

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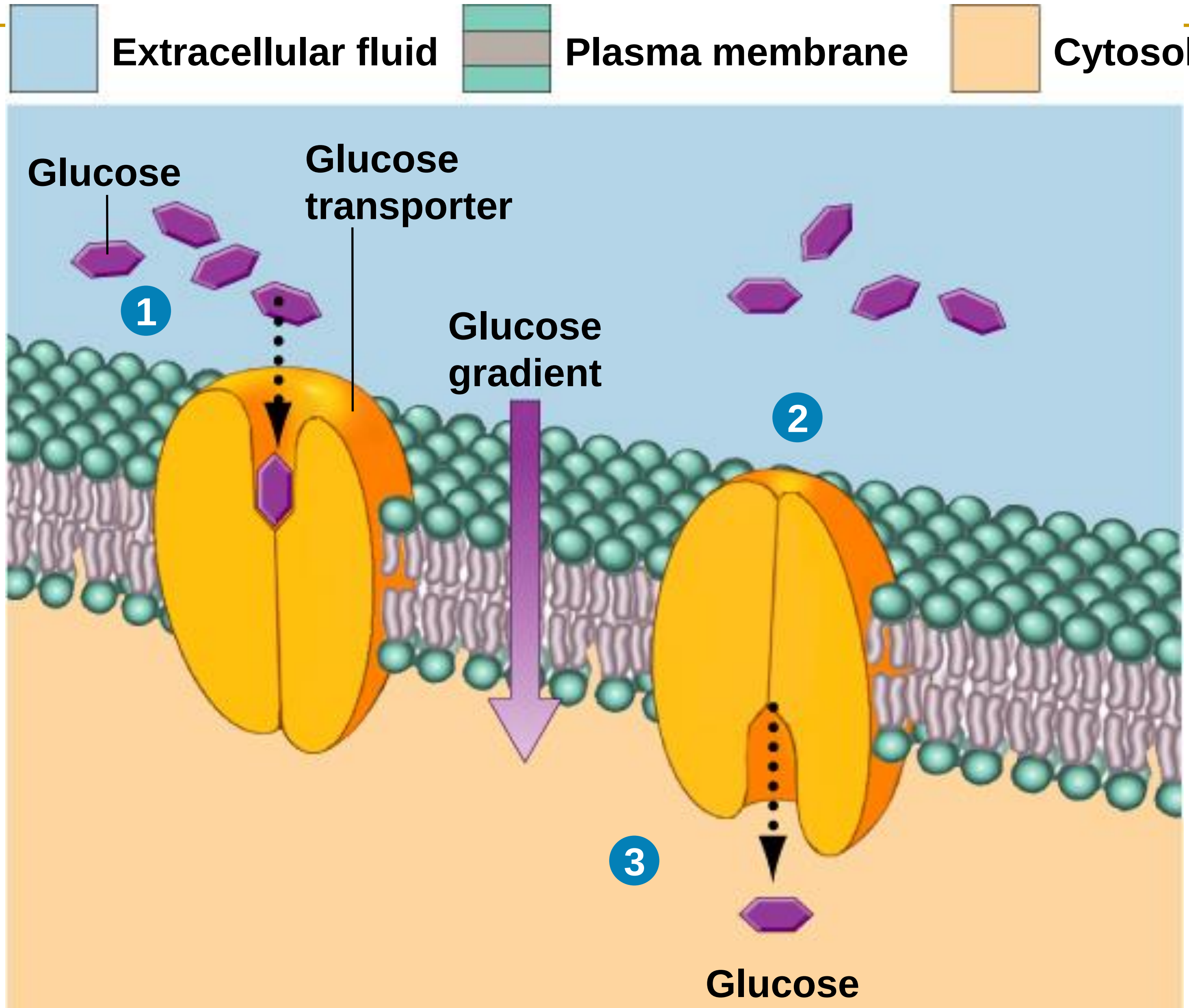
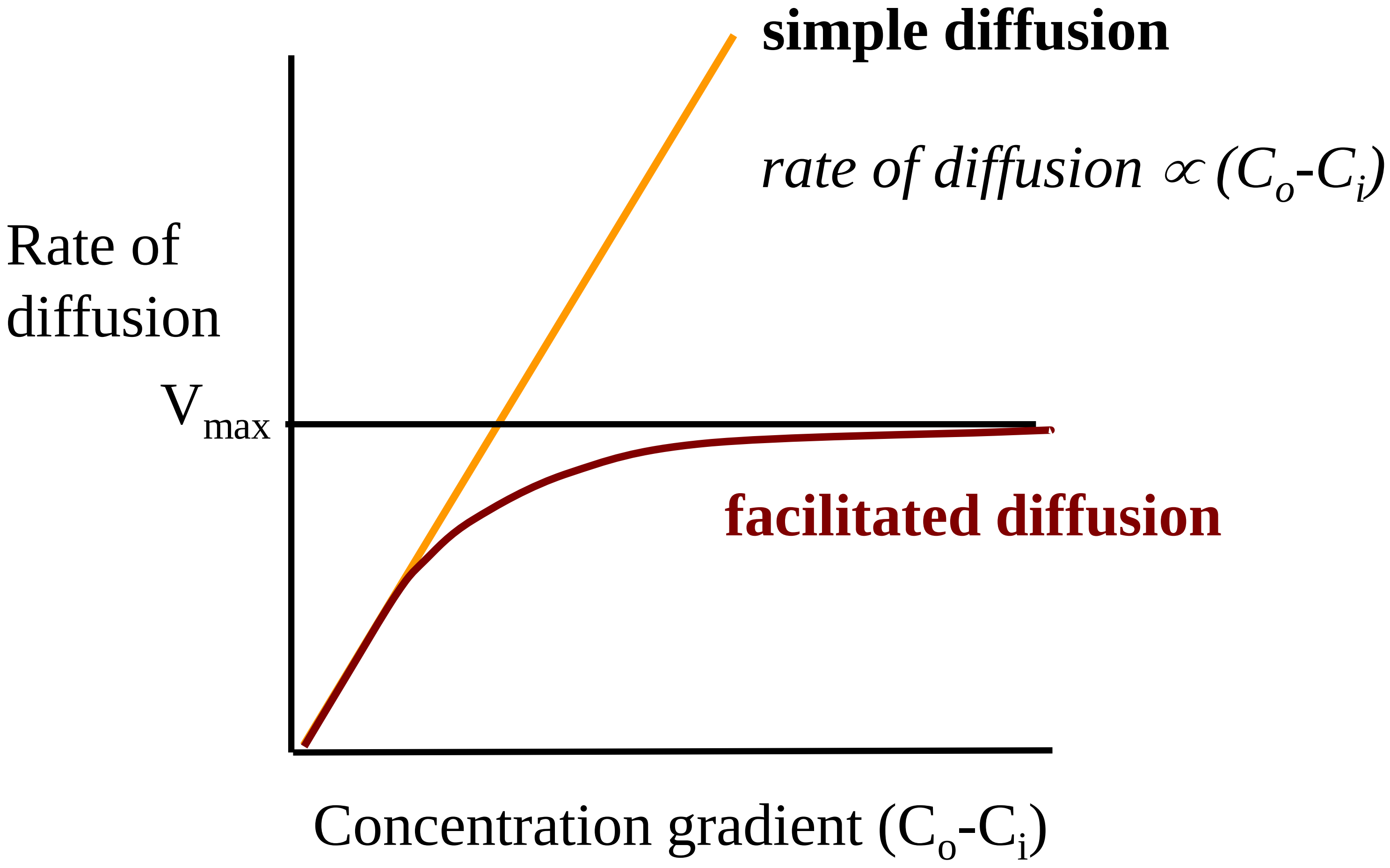


Carrier-mediated Facilitated Diffusion of Glucose across a Plasma Membrane

Simple diffusion

- Diffusion rate is directly proportional to the concentration gradients and solubility in lipids. It is inversely proportional to the square root of the molecular weight and thickness of the membrane.
- Facilitated diffusion is saturable because the binding sites are limited and has transport maximum

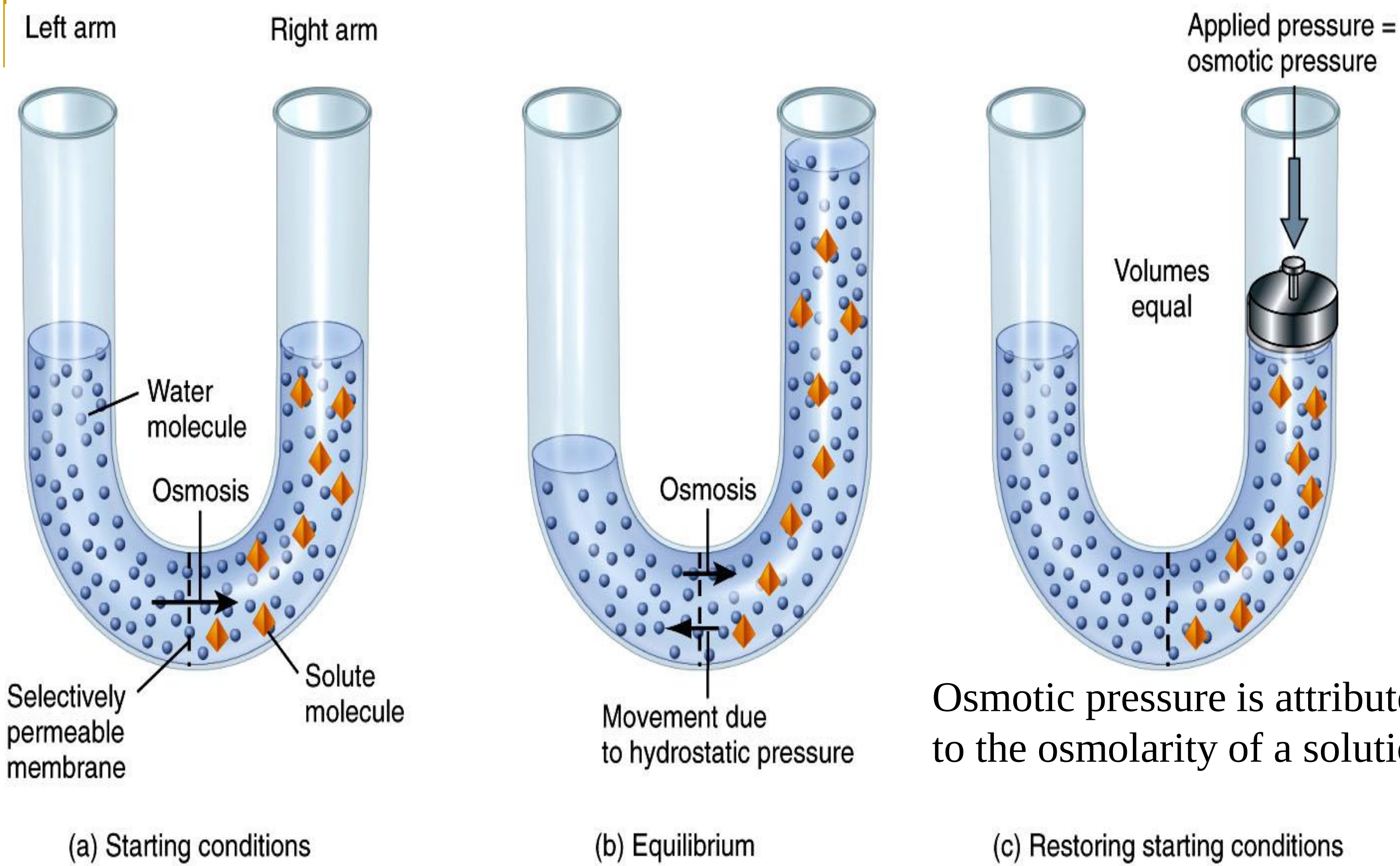


What limits maximum rate of facilitated diffusion?

Osmosis

- Net movement of water through a selectively permeable membrane from an area of high concentration of water (lower concentration of solutes) to one of lower concentration of water
- Water can pass through plasma membrane in 2 ways:

1. through lipid bilayer by simple diffusion
2. through aquaporins, integral membrane proteins



Osmotic pressure is attributed to the osmolarity of a solution

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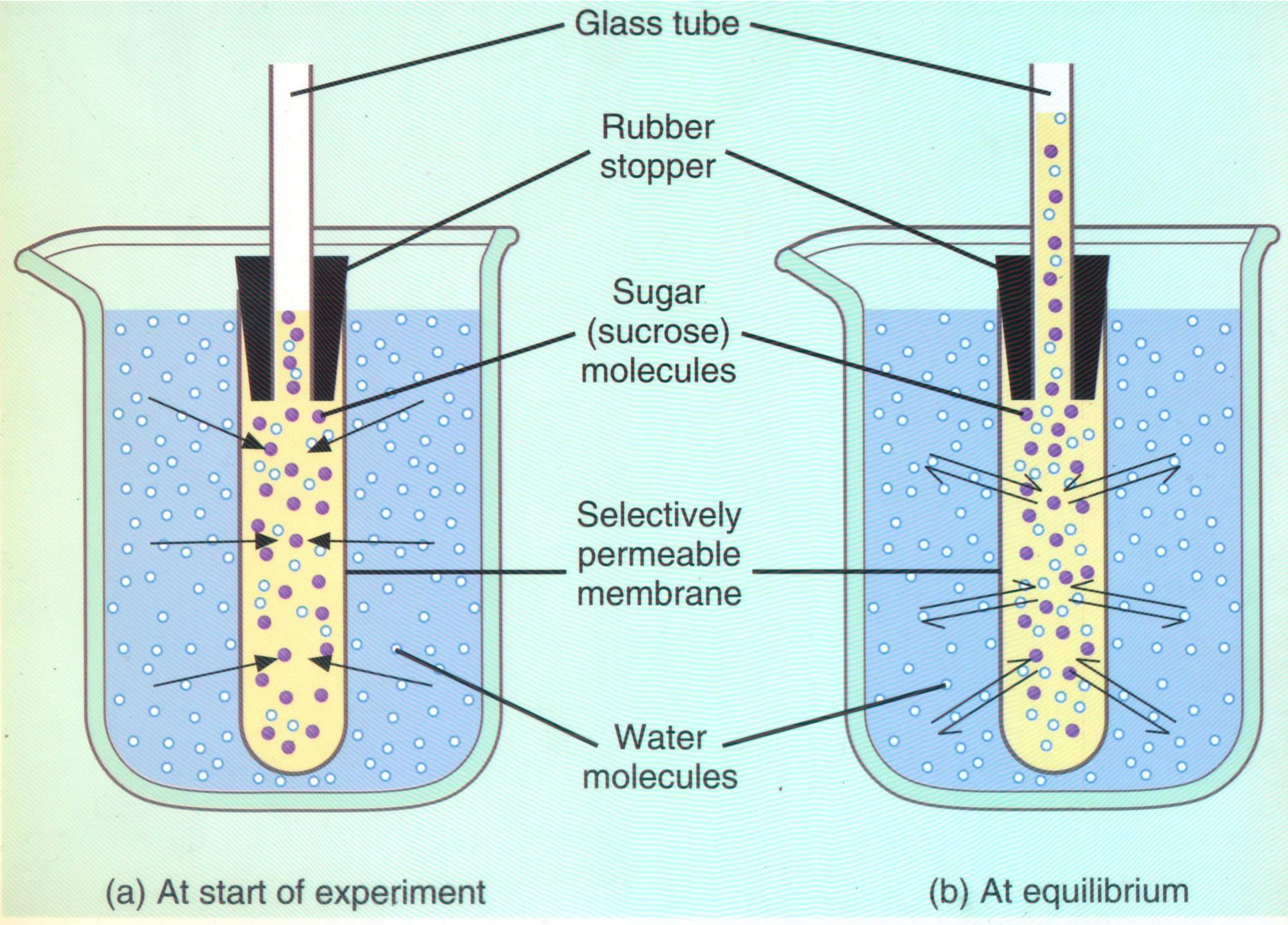


Principle of Osmosis, Fig# 3.7a-b

Osmotic Pressure and the factors on which it depends: Van't Hoffs Equation

- **All non penetrable solutes in a solution exerts osmotic pressure**
- According to Van't Hoff, osmotic pressure (π) depends on the molar concentration (n) of the solution and the temperature T in kelvin.

  $\pi = nRT$ where R is the gas constant

Osmotic pressure

- Osmotic pressure is higher when molar concentration is higher or temperature is higher and the molecular weight is lower
- Osmotic pressure depends mainly on the molar concentration or molarity of a solution
- Osmotic pressure is a colligative property, meaning that the property depends on the concentration of the solute but not on its identity

Osmotic pressure

- The osmotic pressure of an ionic solution is

$$\pi = i\ nRT$$

where "i" is the number of ions formed by dissociation per molecule

- The greater the no of ion/molecule when dissolved greater the osmotic pressure

Osmolarity/Osmolality

- To describe the total number of osmotically active particles per litre of solution term **osmolarity** is used
- The total number of osmotically active particles per kilogram of water the term **osmolality** is used
- Two solutions can have the same *molarity* but may have different *osmolarities*. E.g.

  OsM of 1 M glucose solution =1 OsM

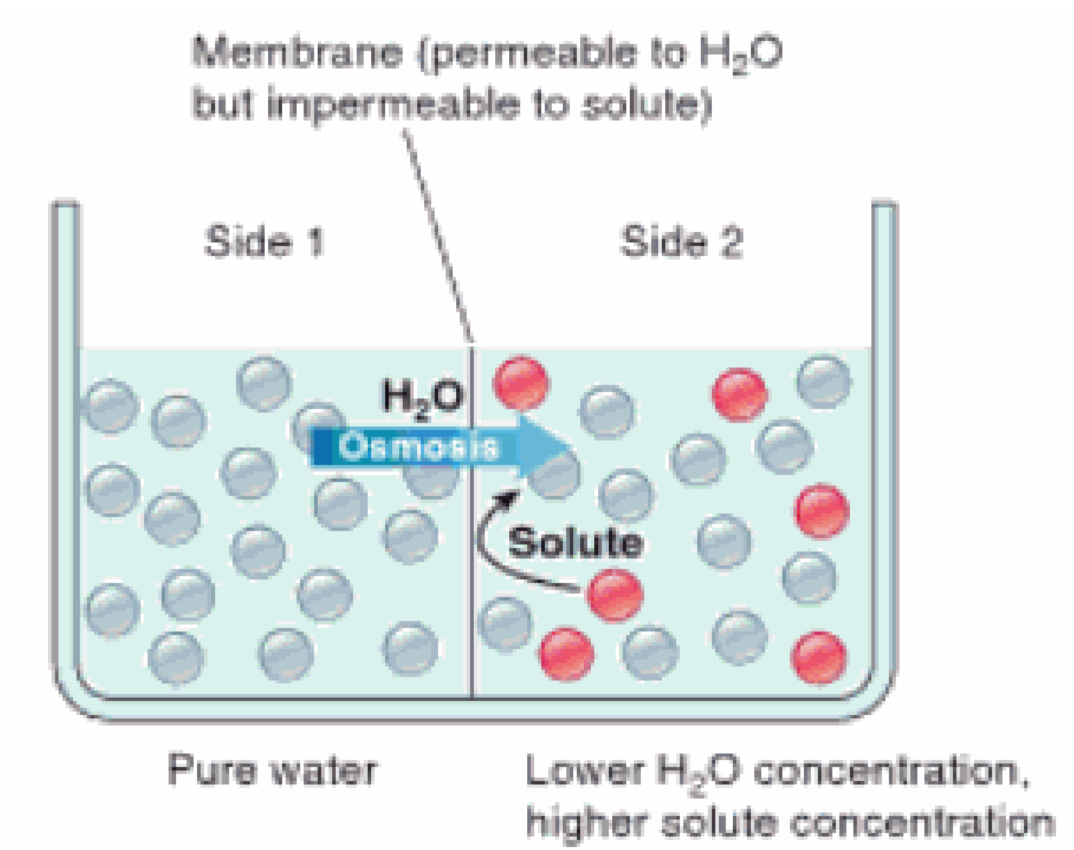
  OsM of 1 M NaCl solution = 2 OsM
- The higher the osmolarity, the greater the osmotic pressure of the solution.

Pressures of a solution

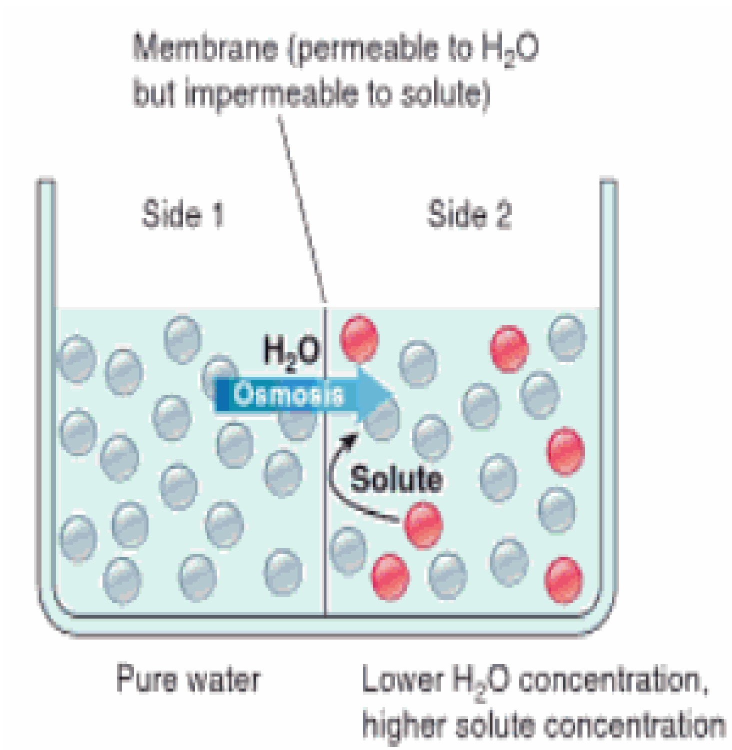
- **Osmotic pressure** (**the pulling pressure**) of a solution is the measure of tendency of a solution to pull water into it by osmosis because of the relative concentration of non penetrating solute and water
- **Hydrostatic pressure of a solution** is the pressure exerted by a stationary fluidic part of the solution on an object (semi permeable membrane in case of osmosis)
- Net hydrostatic pressure of a solution = hydrostatic pressure – osmotic pressure

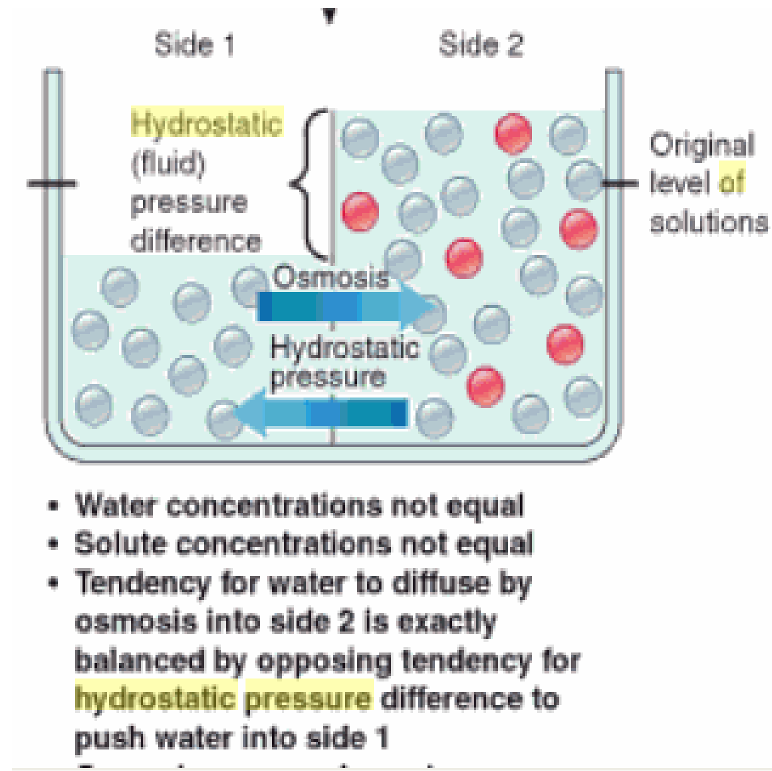
Example

- Separate pure water from a sugar solution with semi permeable membrane
- Both have same hydrostatic pressure
- Osmosis take water from side 1 to side 2 because solution on side 2 has greater pulling tendency



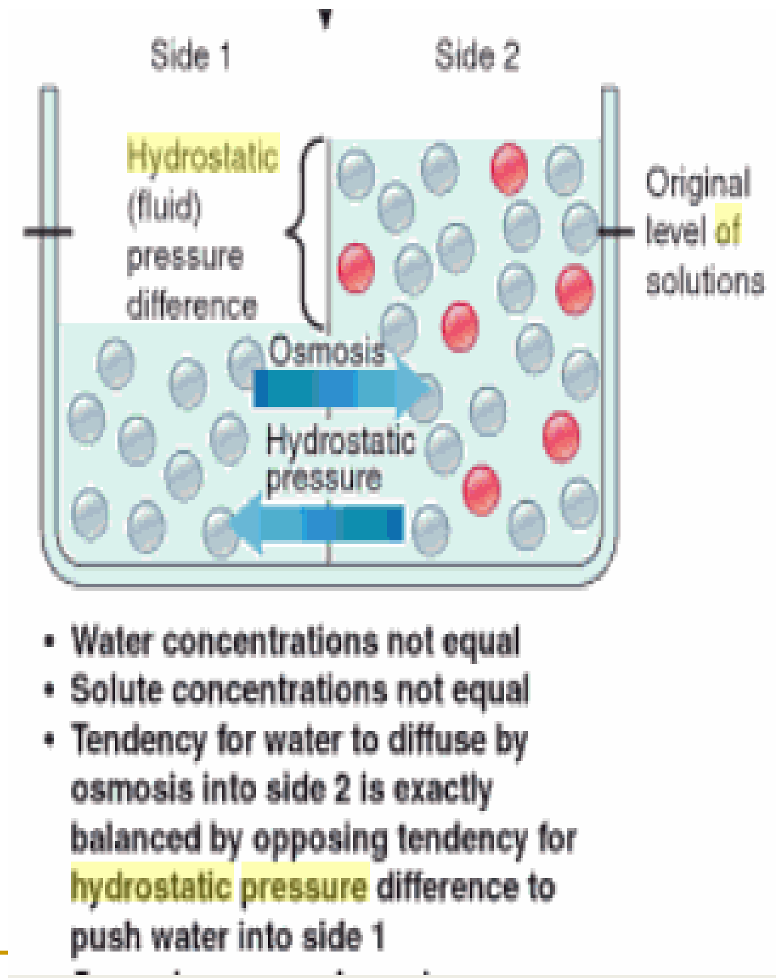
- Will all water go to side 2?
- No it stops after some time. This is the equilibrium state

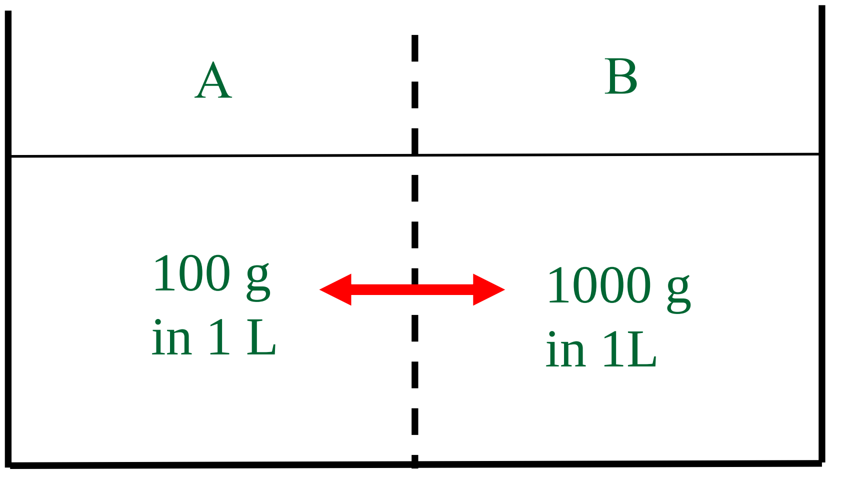




Equilibrium state

- As water moves by osmosis to side 2.
- Solution on side 2 has two tendencies now
- Tendency to push water back to side 1 due to greater hydrostatic pressure
- Tendency to pull water by osmosis back to side 2
- Equilibrium is achieved when tendency to pull water to side 1 and to push water into side 2 balances out





Solute A
Mw = 100

Solute B
Mw = 1000

Which solution has the greatest osmolarity?

Which has the greatest molar concn?

Which has the greatest number of molecules?

(6.02 x 10^{23} particles)

Relation between osmolarity and molarity

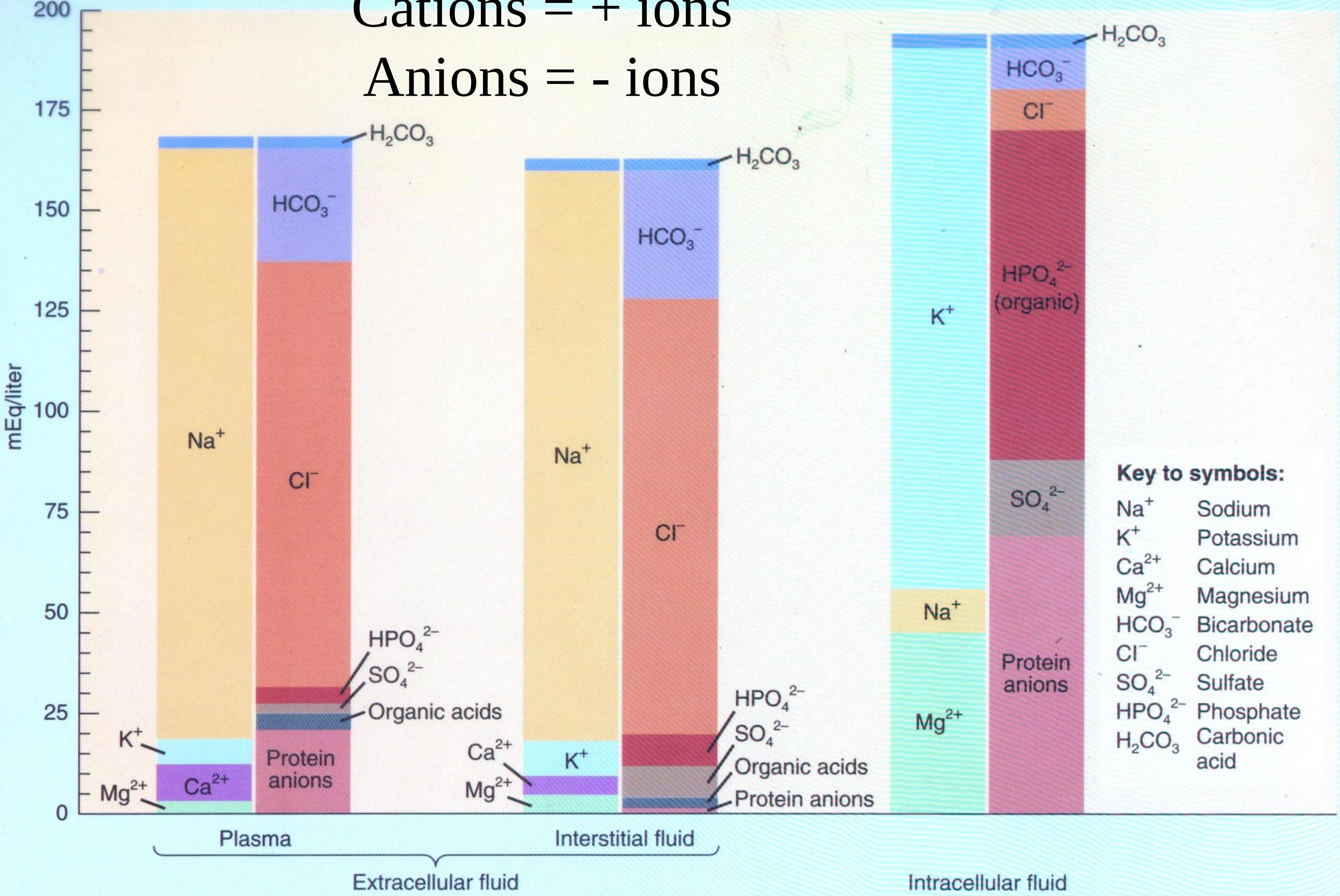
mOsm (millisomolar) = index of the concn
or mOsm/L of particles per liter soln

mM (millimolar) = index of concn of
or mM/L molecules per liter soln

150 mM NaCl = 300 mOsm

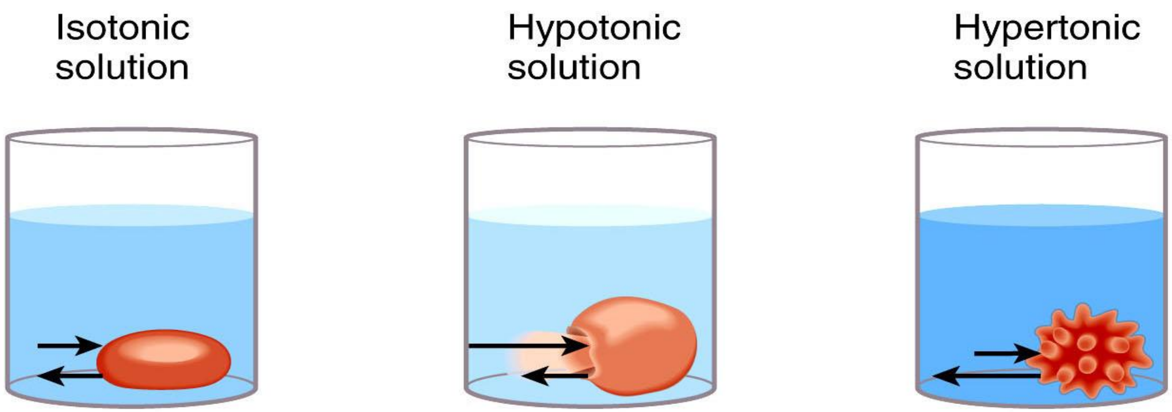
300 mM glucose = 300 mOsm

Cations = + ions
Anions = - ions

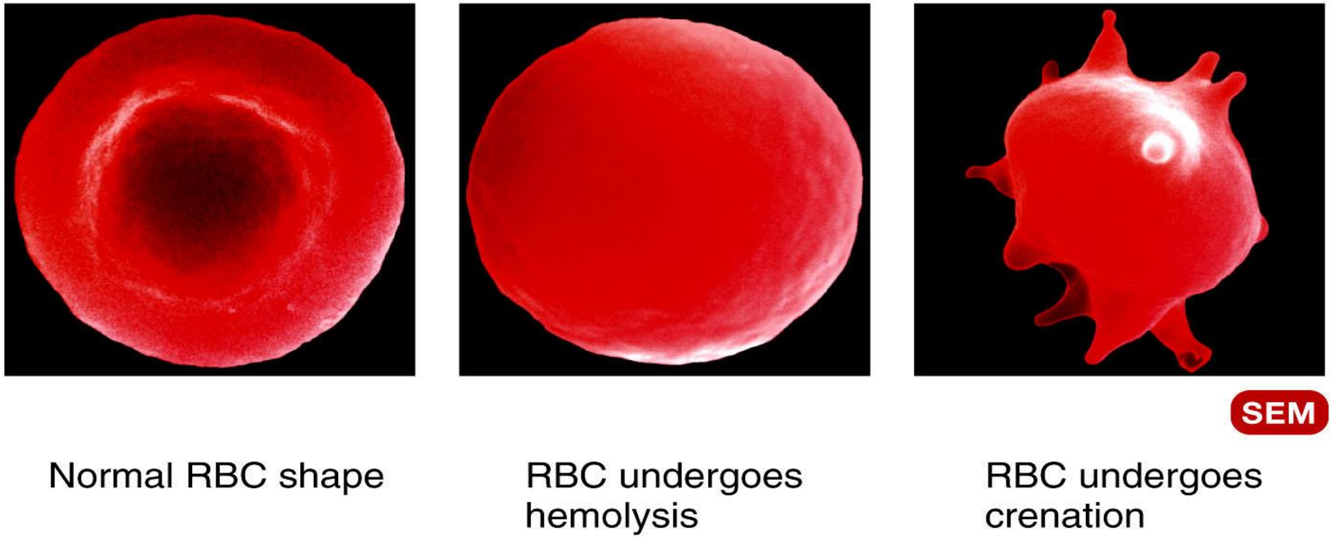


Comparison of Electrolyte and Protein Anion Concentrations in the Body Fluid Compartments,

Tonicity and its effect on RBCS



(a) Illustrations showing direction of water movement



(b) Scanning electron micrographs (all 15,000x)

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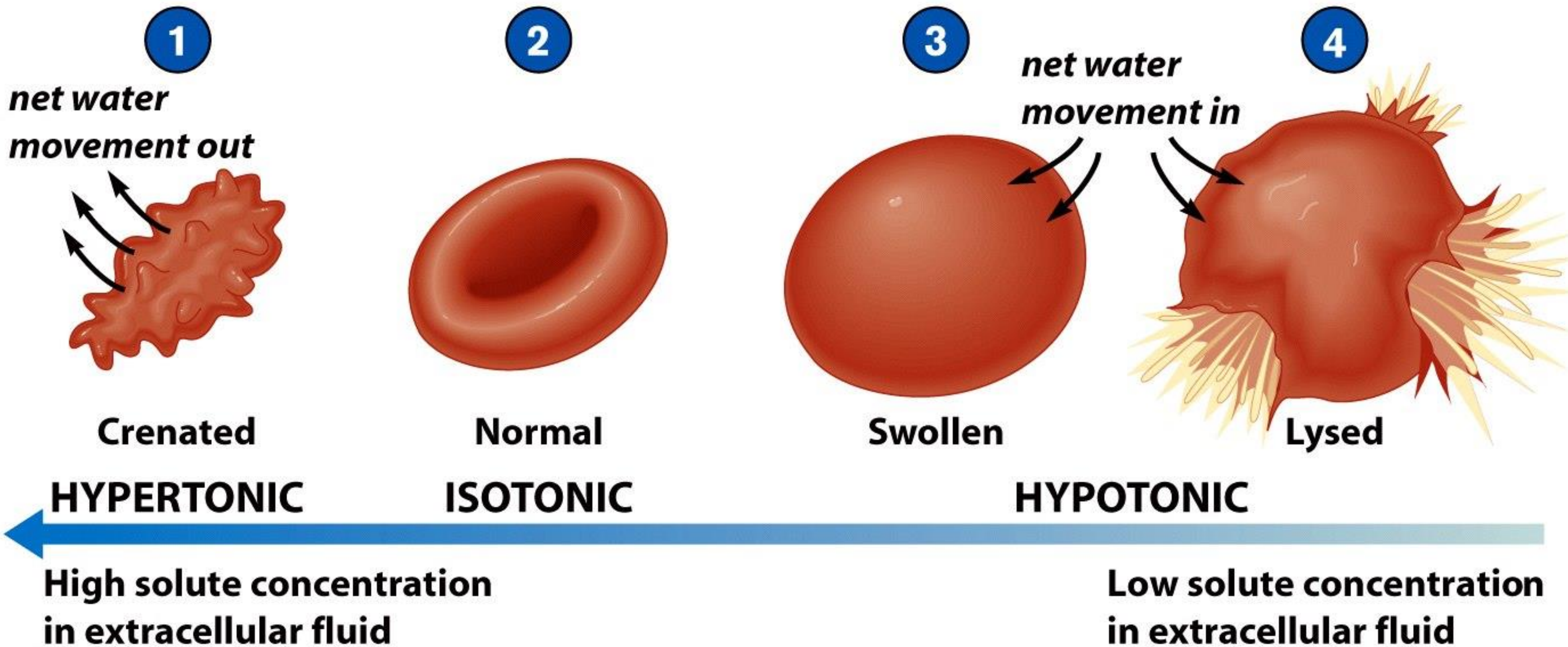
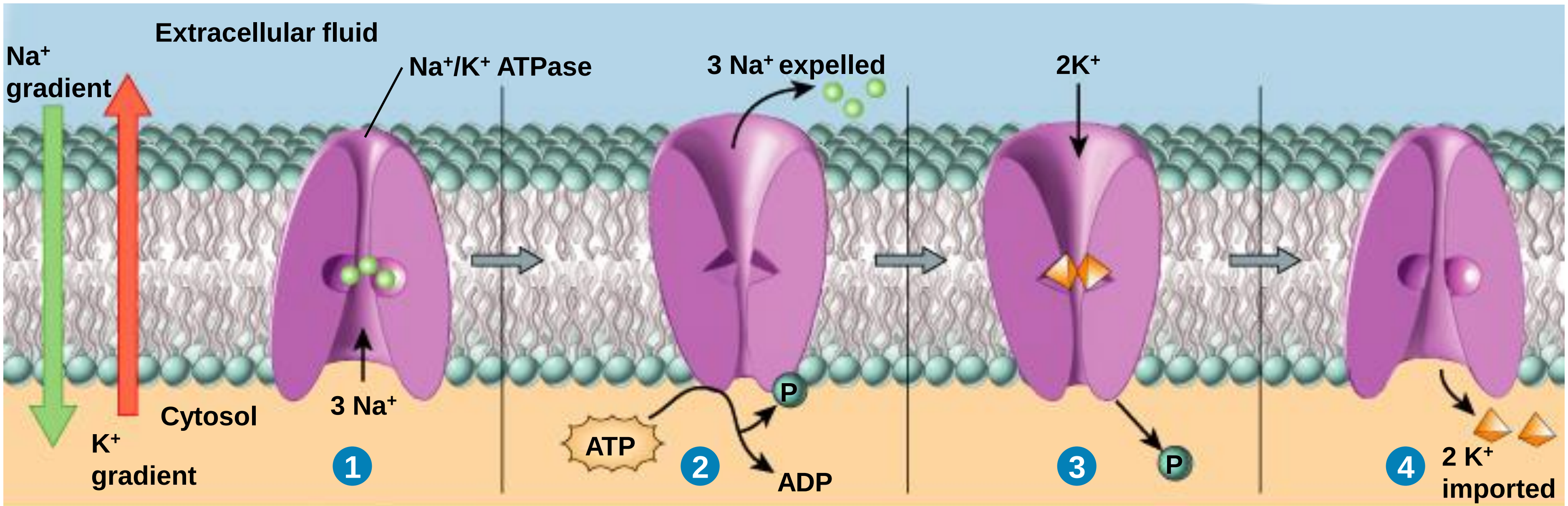

1
2
3
4
net water
movement out
net water
movement in
Crenated
Normal
Swollen
Lysed
HYPERTONIC
ISOTONIC
HYPOTONIC
High solute concentration
in extracellular fluid
Low solute concentration
in extracellular fluid

Active Transport

Solutes are transported across plasma membranes with the use of energy, from an area of lower concentration to an area of higher Concentration Sodium-potassium pump



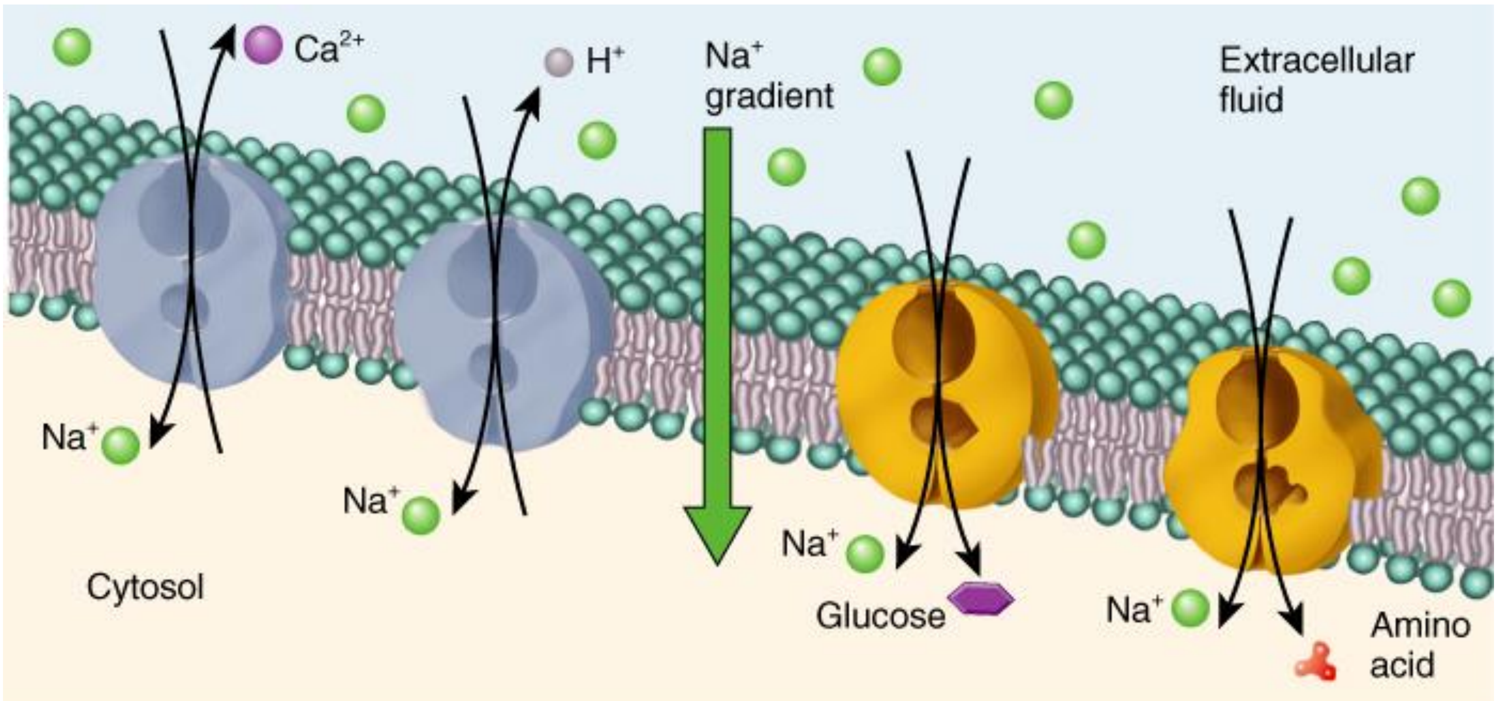
Active Transport

Primary Active Transport

- Molecules are "pumped" against a concentration gradient at the expense of energy (ATP)
  – *direct use of energy*

Secondary Active Transport

- Transport is driven by the energy stored in the concentration gradient of another molecule (Na^+)
  – *indirect use of energy*



(a) Antiporters

(b) Symporters

Saturation

- Similar to facilitated diffusion
- Rate limited by $\mathbf{V_{max}}$ of the transporters

Energetics

- Up to **90%** of cell energy expended for active transport!

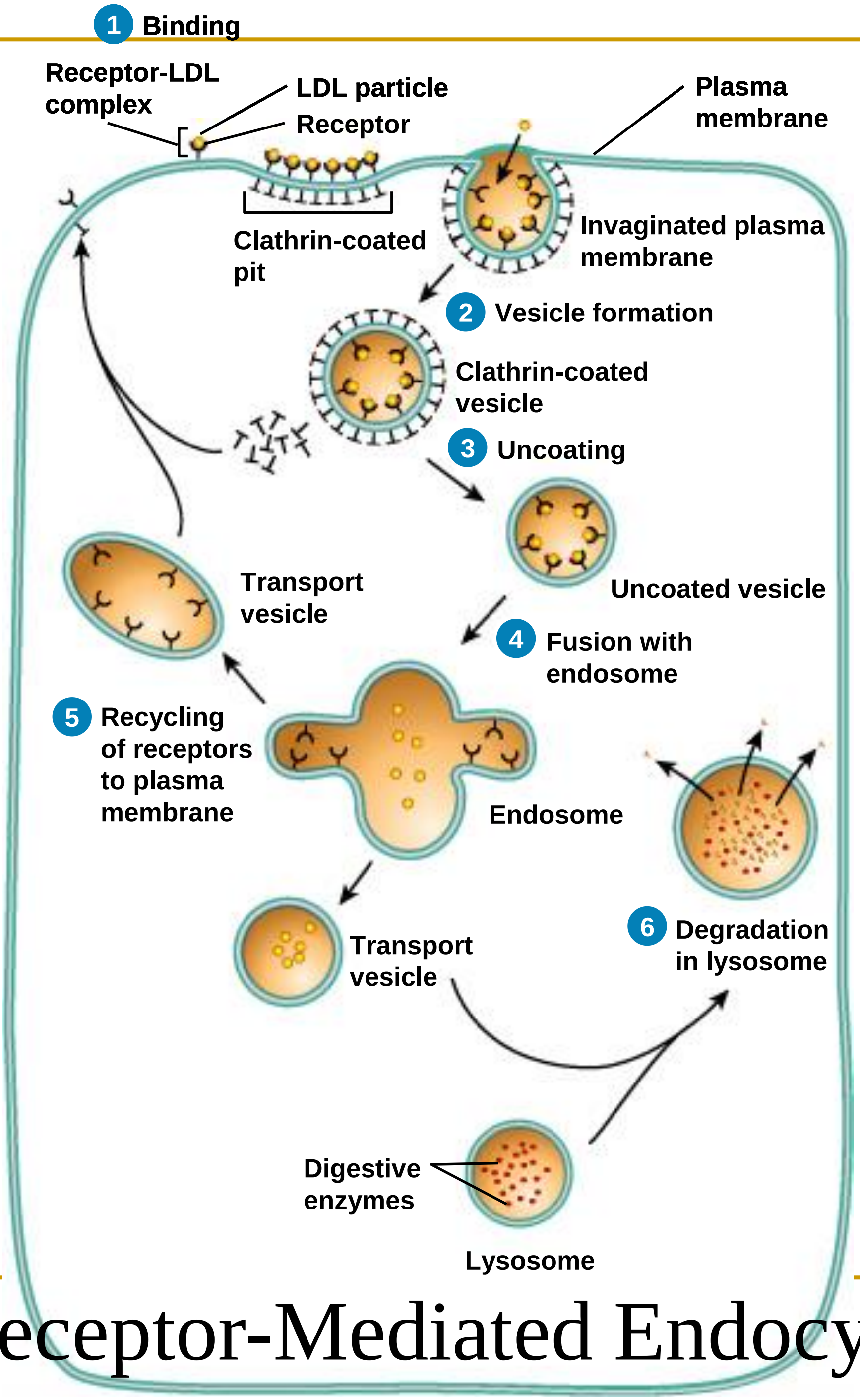
Transport in Vesicles

- **Vesicle** - a small spherical sac formed by budding off from a membrane
- **Endocytosis** - materials move into a cell in a **vesicle** formed from the plasma membrane

  three types: receptor-mediated endocytosis

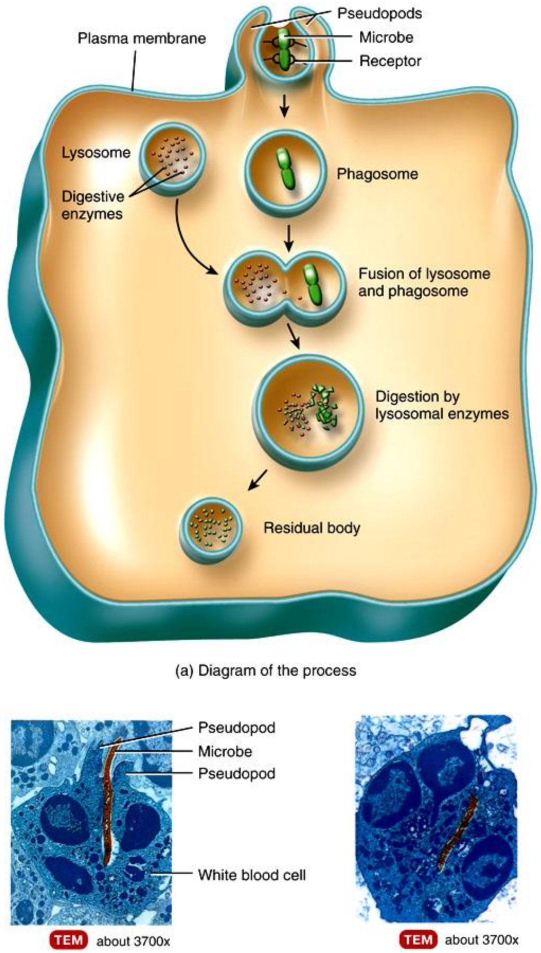
  phagocytosis

  bulk-phase endocytosis (pinocytosis)
- **Exocytosis** - vesicles fuse with the plasma membrane, releasing their contents into the extracellular fluid
- **Transcytosis** - a combination of endocytosis and exocytosis



Receptor-Mediated Endocytosis

Phagocytosis



(a) Diagram of the process

(b) White blood cell engulfs microbe

(c) White blood cell destroys microbe

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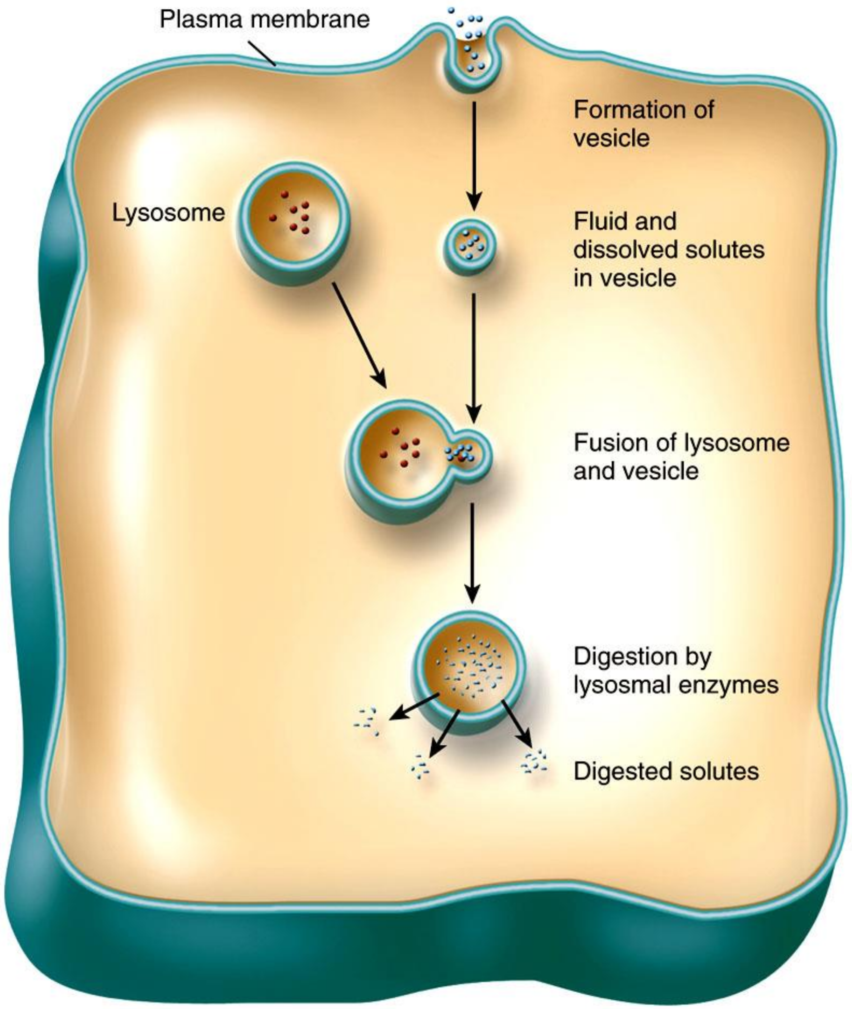
Bulk-phase Endocytosis



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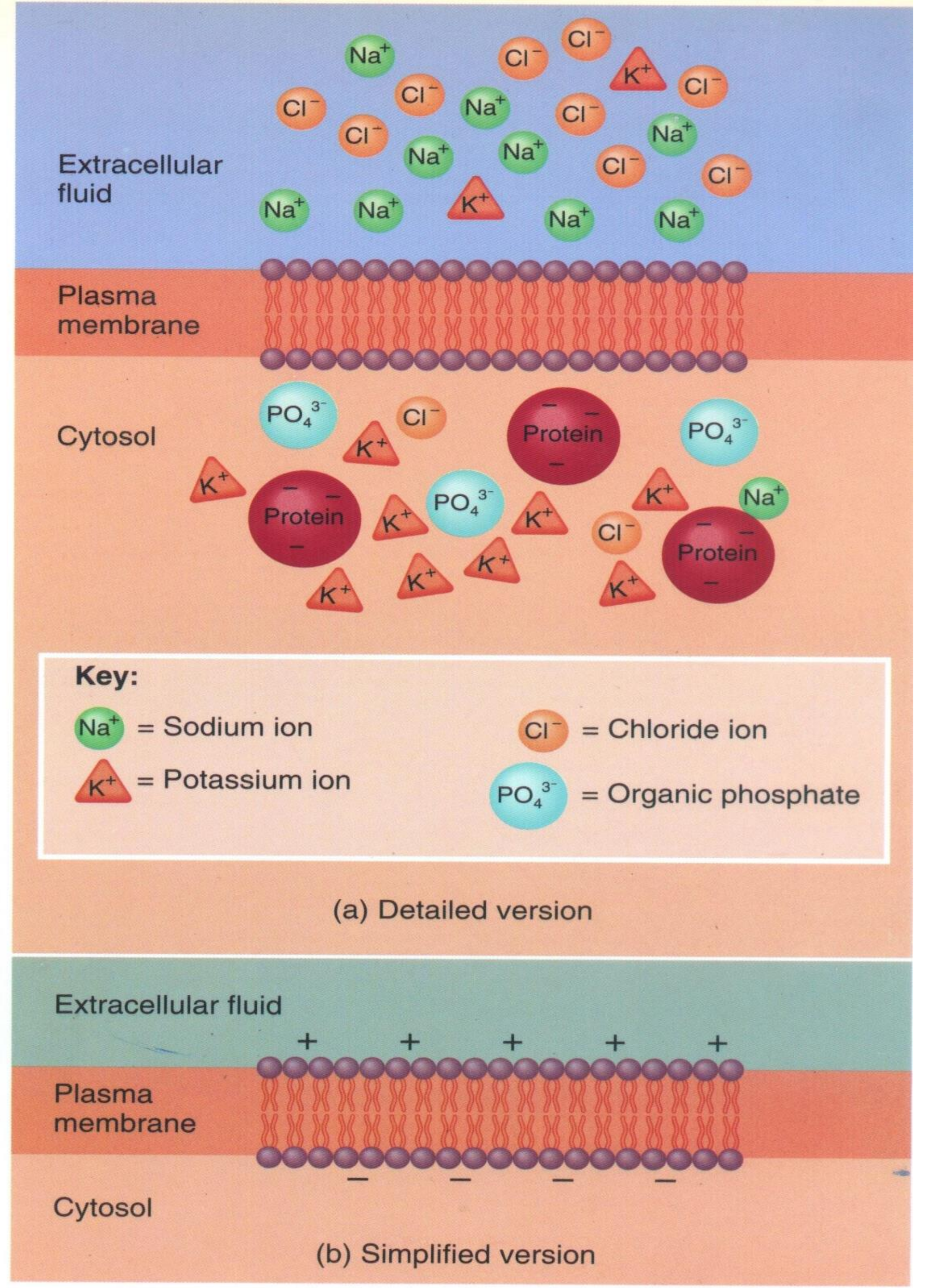
Resting Membrane Potential and polarization of cell membranes



Electrochemical Gradient, Fig# 3.4a-b

Thank You