Chapter 4 細胞及環境的互動

4-1　細胞外環境

4-2　細胞間的溝通

✓ 4-3　物質通過細胞膜的運輸方式

4-4　細胞的興奮性

Transport Across Membranes

- **What membranes do**
  - --Separate material: ICF / ECF
  - --Allow exchange of material: ICF / ECF
- **Why transport is important**
  - --Obtaining O_2 and nutrients
  - --Getting rid of waste products
- Membrane is **selectively permeable**
  - --Permeable = to pass through
  - --Selective = restrictive
- Membranes allow the transport of some substances, but not others

Transport Across Membranes

- The **lipid** bilayer (**nonmediated transport**)
  --small, nonpolar, uncharged molecules
  --ions and charged or polar molecules (x)
- Transmembrane **proteins** (**mediated transport**)
  --ion channels
  --transporters
- Macromolecules are unable to pass through the plasma membrane except by **vesicular transport**

ECF / ICF Composition Differences

Solute	ICF (mM)	ECF (mM)
K^+	140.0	4.0
Na^+	15.0	145.0
Mg^{2+}	0.8	1.5
Ca^{2+}	$<0.001^{\dagger}$	1.8
Cl^-	4.0	115.0
HCO_3^-	10.0	25.0
P_i	40.0	2.0
Amino acids	8.0	2.0
Glucose	1.0	5.6
ATP	4.0	0.0
Protein	4.0	0.2

Driving Forces: *Chemical* and *Electrical* forces = *Electrochemical* force

Chemical Driving Force

- Characteristics

  --Concentration gradient = ΔC

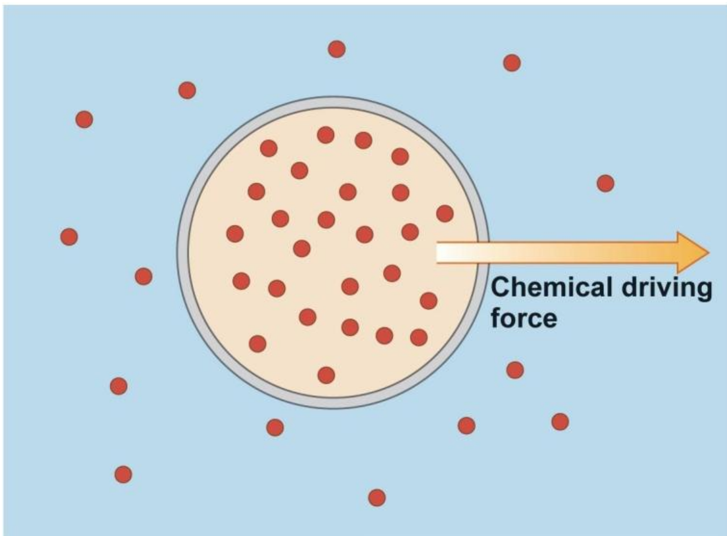
  --Gradient "pushes" particles from higher to lower concentration

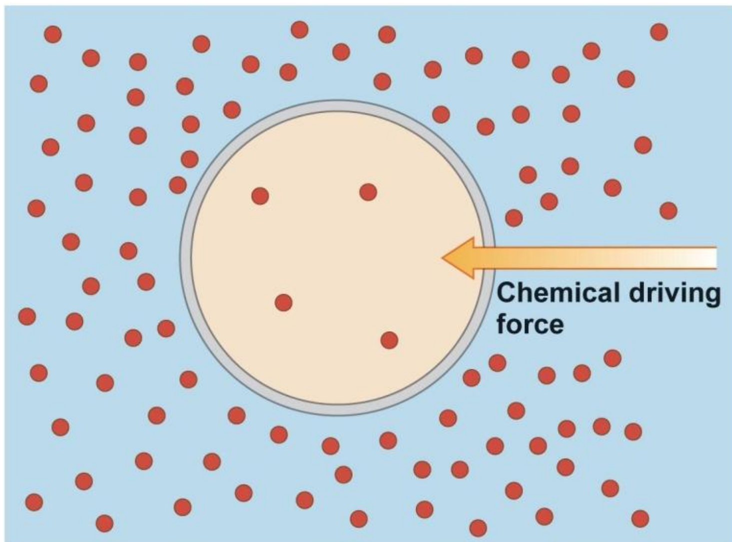
  --Force acts from higher to lower concentration

- *Direction* of chemical driving force

  --Down the chemical gradient

  --From higher to lower concentration ($\Delta C \uparrow$, driving force $\uparrow$)





Electrical Driving Force

- Membrane potential (V_m)

  --Due to unequal distribution of anions and cations across cell membrane

  --Charge separation = source of energy

- Magnitude of V_m = Strength of force

  --Usually measured in millivolts (mV)

  --Has a polarity (reference is ICF)

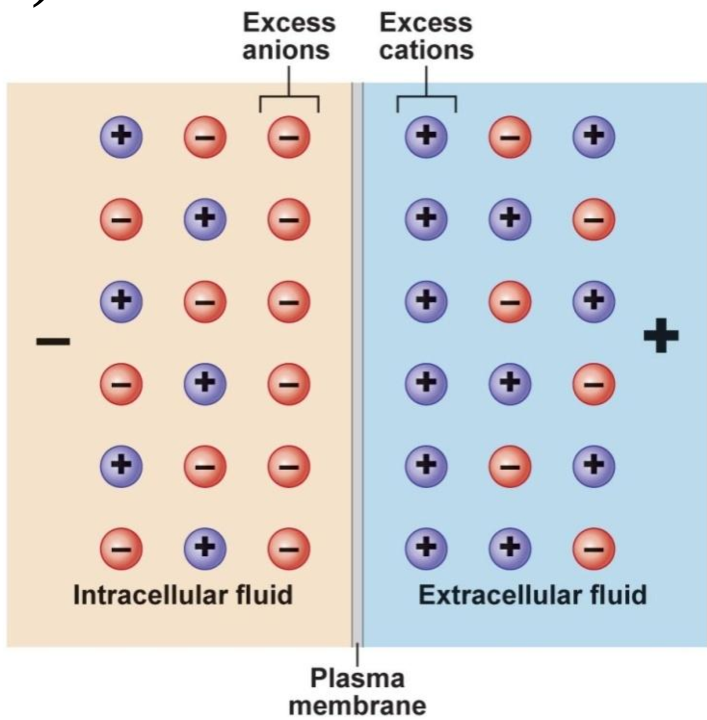
- Principles

  --Opposite charges attract

- Direction of force depends on

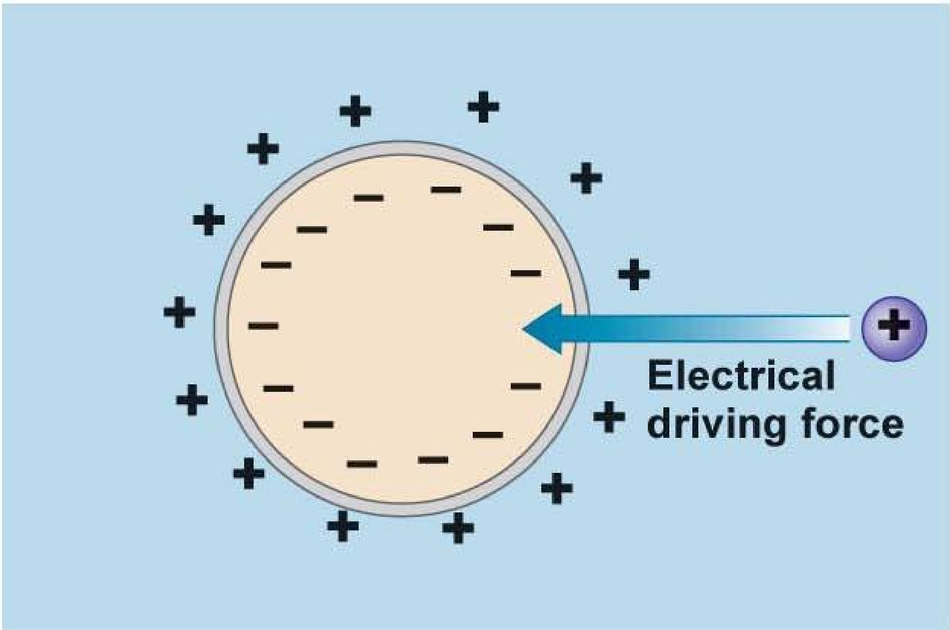
  --Polarity of cell

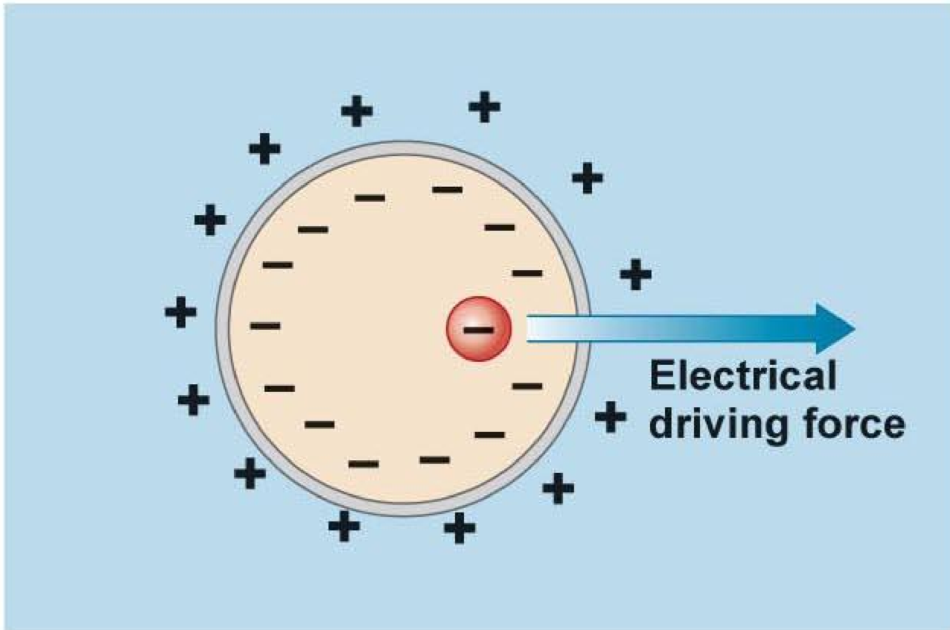
  --Charge on particle



Electrical Driving Force

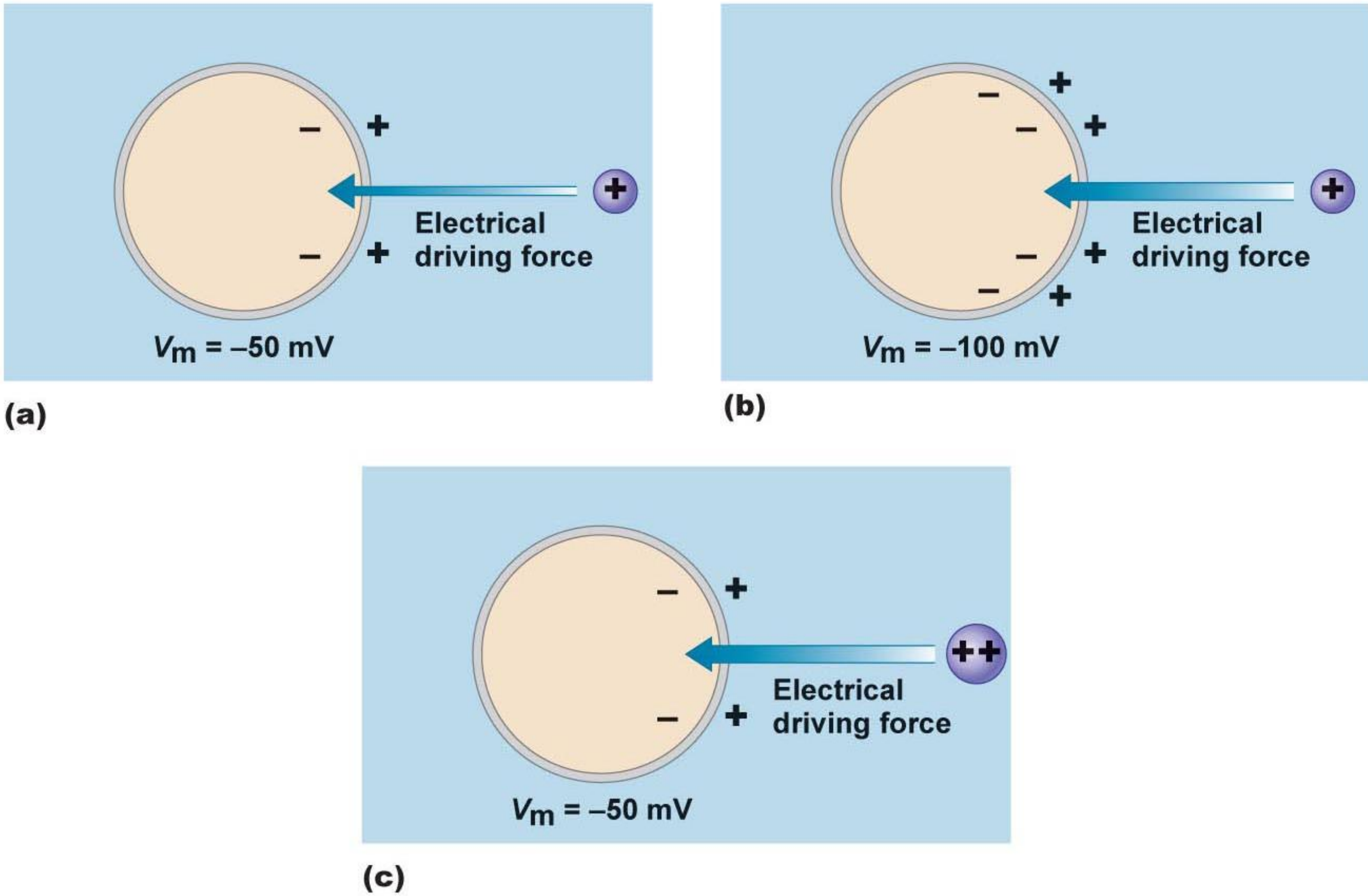
- *Direction* of force depends on
  - --Polarity of cell
  - --Charge on particle





Electrical Driving Force

- *Magnitude* of force depends on
  - --Strength of V_m
  - --Amount of charge on particle



Electrochemical Driving Force

- *Total* force acting on particles = ***Sum*** of chemical and electrical forces
- If chemical and electrical forces act in ***same*** direction

  --Electrochemical force acts in the direction of <u>each</u>

  --Magnitude = sum of chemical force and the electrical force
- If chemical and electrical forces act in ***opposite*** directions

  --Electrochemical force acts in direction of the <u>stronger force</u>

  --Magnitude = larger force minus smaller

Membrane Transport

- ***Passive (Physical) Processes:***

-- **Simple diffusion**

-- **Facilitated diffusion**

-- **Osmosis**

-- **Filtration**

- ***Active (Physiological) Processes:***

-- **Active transport**

-- **Endocytosis & Exocytosis**

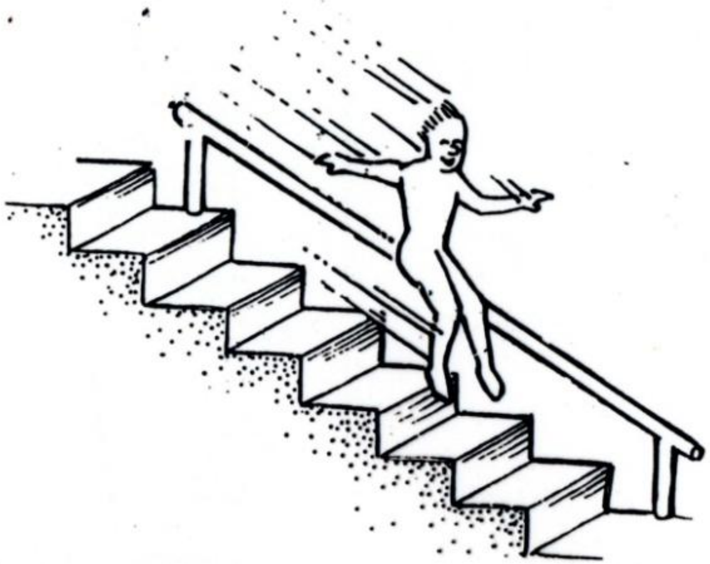
-- **Transcytosis**

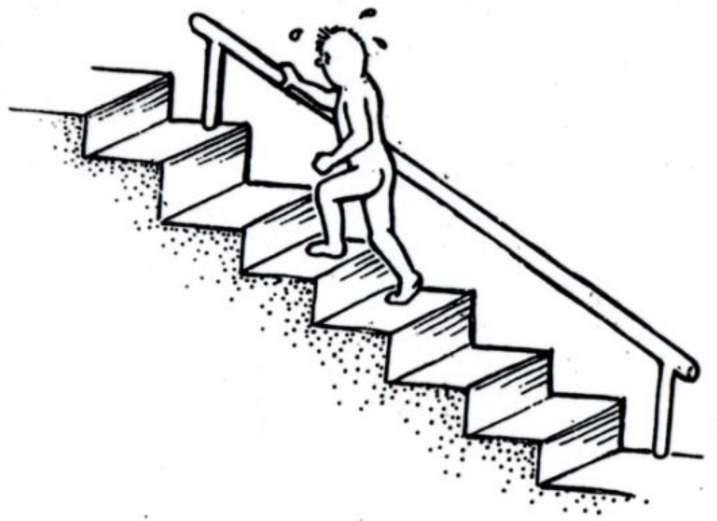
Membrane Transport

- ***Carrier-mediated (mediated):***
  - **--Facilitated diffusion**
  - **--Active transport**

- ***Noncarrier-mediated (nonmediated):***
  - **--Simple diffusion of lipid-soluble molecules**
  - **--Simple diffusion of water = osmosis**
  - **--Simple diffusion of ions through nonspecific channels**

Membrane Transport





Passive Transport

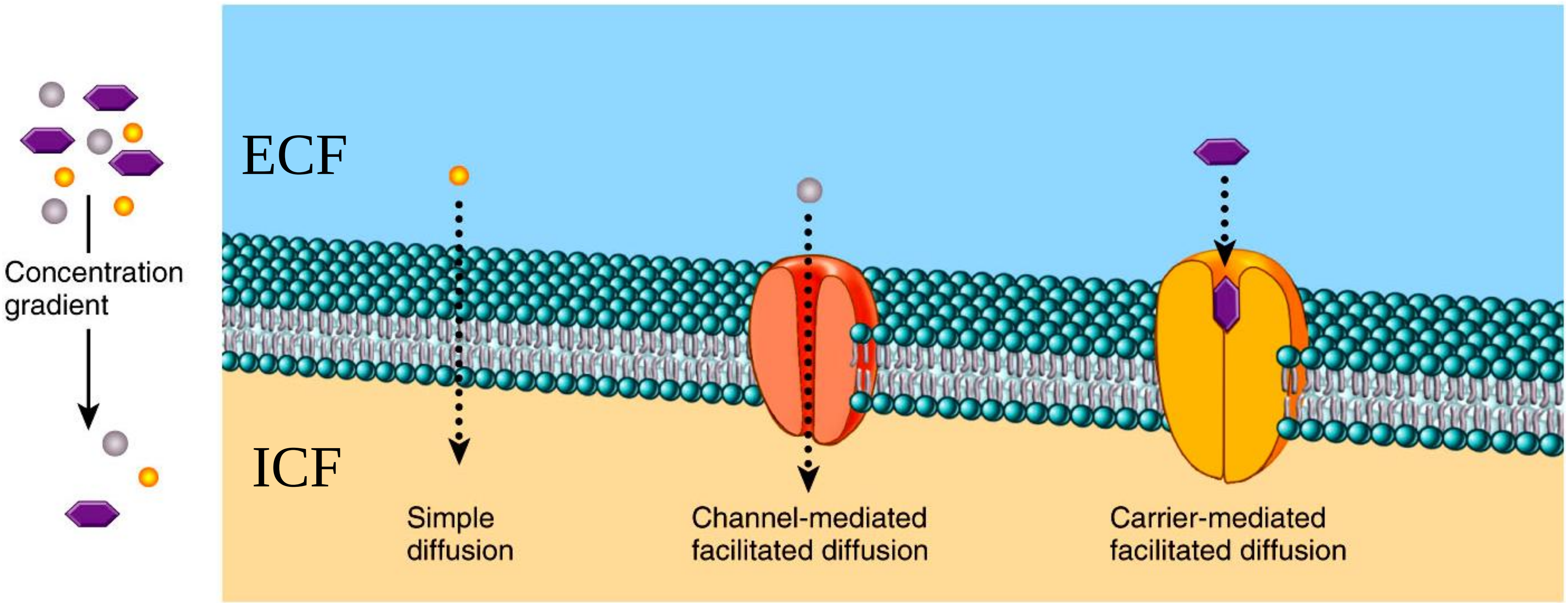
- ✓*Spontaneous*
- ✓*No energy is required*
- ✓*Downhill movement*

Active Transport

- ✓*Not spontaneous*
- ✓*Requires energy*
- ✓*Involves a pump (membrane protein)*
- ✓*Uphill movement*

Passive Transport

- **Three types of passive processes are**
  - **--diffusion through the lipid bilayer**
  - **--diffusion through ion channels**
  - **--facilitated diffusion (transporters = carriers)**

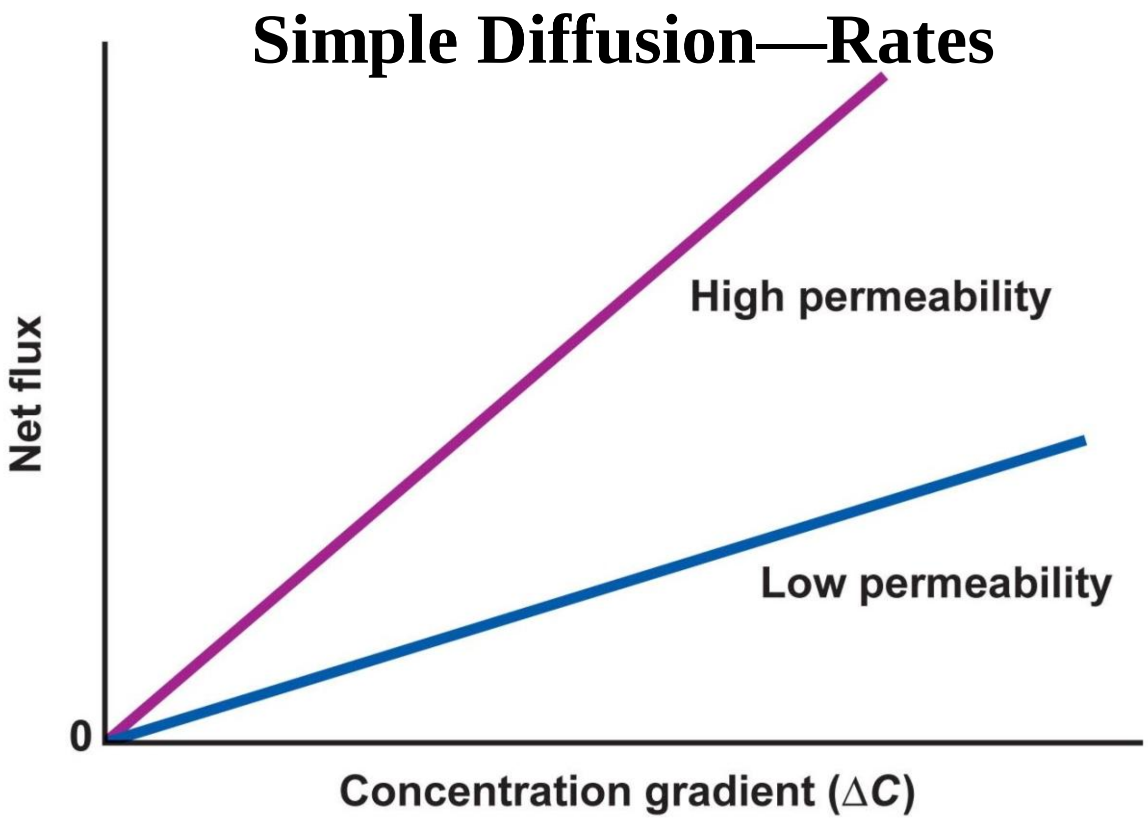


Diffusion through the Lipid Bilayer (Simple Diffusion)

- ***Diffusion*** **is the random mixing of particles that occurs in a solution as a result of the kinetic energy of the particles**
- **Diffusion rate across plasma membranes is influenced by several factors:**
  - --Steepness of the concentration gradient
  - --Surface area (pulmonary, intestinal, capillaries, etc.)
  - --Diffusion distance
  - --Membrane permeability ($P_{Na} < P_K$)
  - --Temperature
  - --Size or mass of the diffusing substance

Simple Diffusion

- Factors influencing membrane permeability:
  - --Lipid solubility of diffusing substance
  - --Size and shape of diffusing particle
  - --Temperature
  - --Thickness of membrane



Fick's Law of Diffusion

Factors Influencing the Rate of Net Diffusion of a Substance across a Membrane (Fick's Law of Diffusion)

FACTOR	EFFECT ON RATE OF NET DIFFUSION
↑ Concentration gradient of substance (ΔC)	↑
↑ Permeability of membrane to substance (P)	↑
↑ Surface area of membrane (A)	↑
↑ Molecular weight of substance (MW)	↓
↑ Distance (thickness) (ΔX)	↓

Modified Fick's equation:

$$\text{Net rate of diffusion (Q)} = \frac{\Delta C \cdot P \cdot A}{MW \cdot \Delta X}$$

$$\left[\frac{P}{\sqrt{MW}} = \text{diffusion coefficient (D)}\right]$$

$$\text{Restated } Q \propto \frac{\Delta C \cdot A \cdot D}{\Delta X}$$

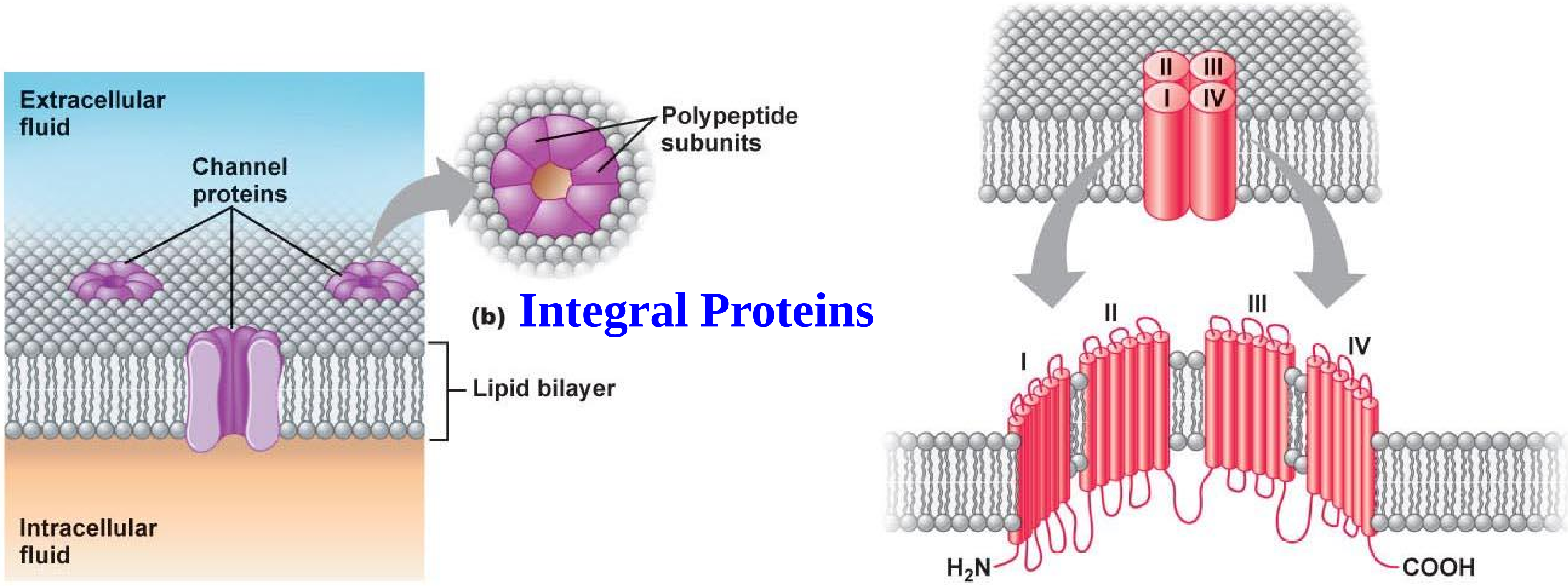
Diffusion through the Ion Channels

- Passive transport through a channel
- Characteristics of a channel

  --Transmembrane protein

  --Functions like a passageway or pore

  --Substance specific (small, inorganic ions=hydrophilic)



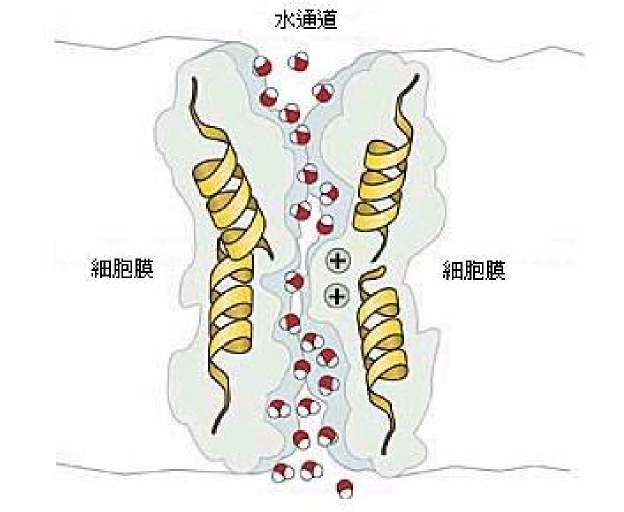
(a)

(b) Integral Proteins

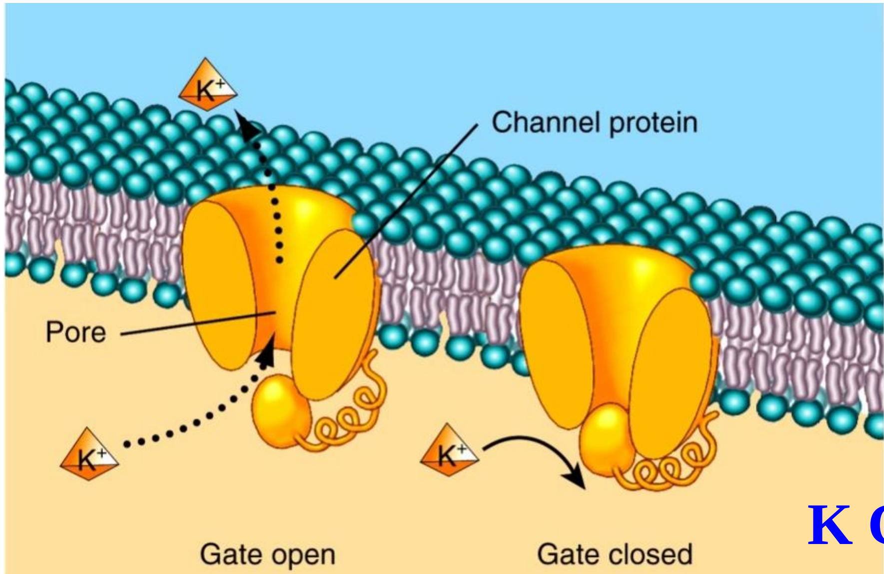
(c) Na Channel

Types of Channels

- Diffusion of water through **aquaporins**



- Diffusion through **ion channels**
  - --**Leak** channels
  - --**Gated** channels
- Factors affecting rate of transport
  - --Transport rate of each channel
  - --Number of channels in membrane



K Channel

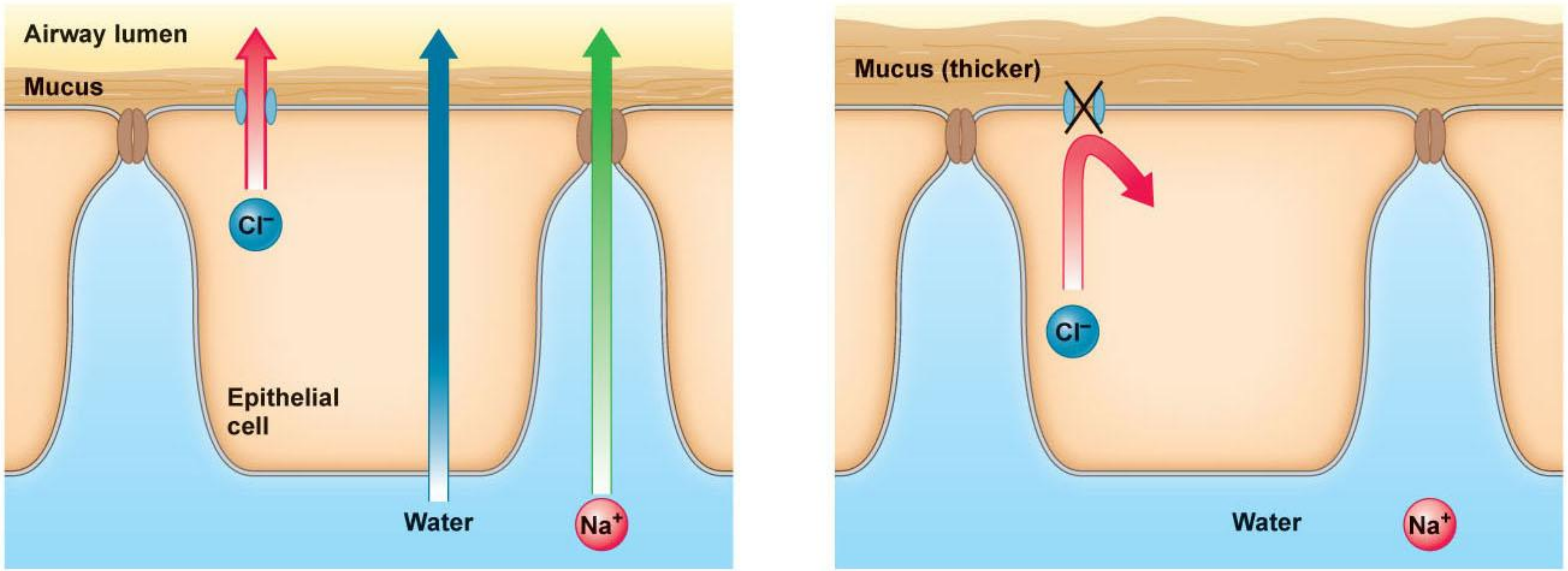
Types of Gated Channel

1. Receptor-operated Channels =Ligand or chemical-gated Channels
2. Voltage-sensitive Channels =Voltage-gated Channels
3. Stretch-activated Channels =Mechanically-gated Channels

比較項目	化學閘門通道	電位閘門通道	機械閘門通道
定義	由化學訊息分子決定開關的通道	由膜電位大小決定開關的通道	由機械刺激決定開關的通道
分布	視網膜感光細胞、運動終板膜	神經細胞、肌肉細胞、腺體細胞	內耳基底膜毛細胞
舉例	ACh、麩胺酸、天門冬胺酸、γ- 胺基丁酸、甘胺酸等化學閘門通道	電位閘門 Na^+ 通道、電位閘門 K^+ 通道、電位閘門 Ca^{2+} 通道	機械閘門 K^+ 通道
開放結果	局部電位 (local potential)	動作電位 (action potential)	感受器電位 (receptor potential)

Clinical Application: Cystic Fibrosis

- Cystic fibrosis is caused by a defective gene that produces an abnormal chloride ion (Cl^- channels) transported
- The disease affects the respiratory, digestive, urinary, and reproductive systems

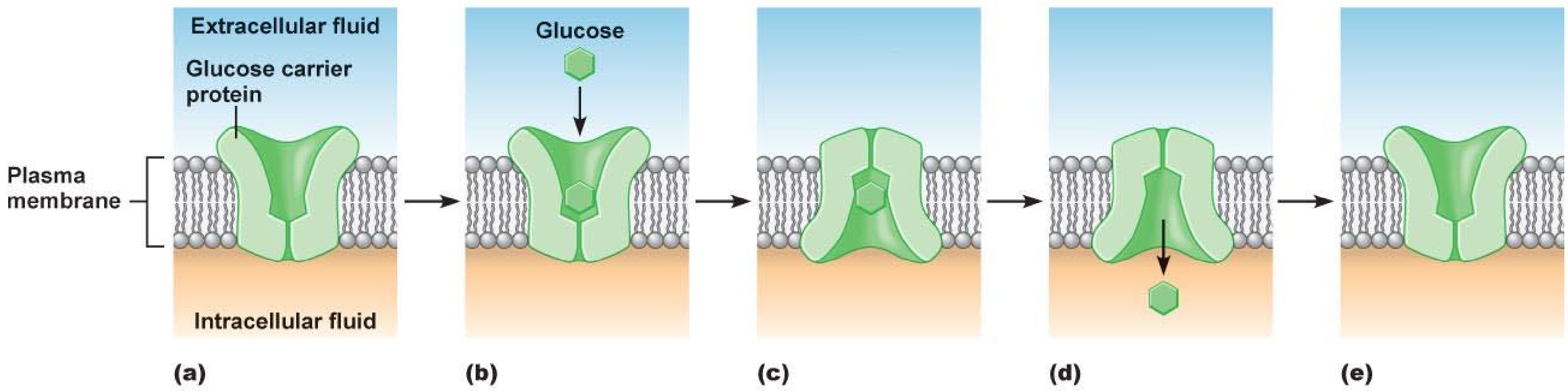


(a) Normal solute and water transport

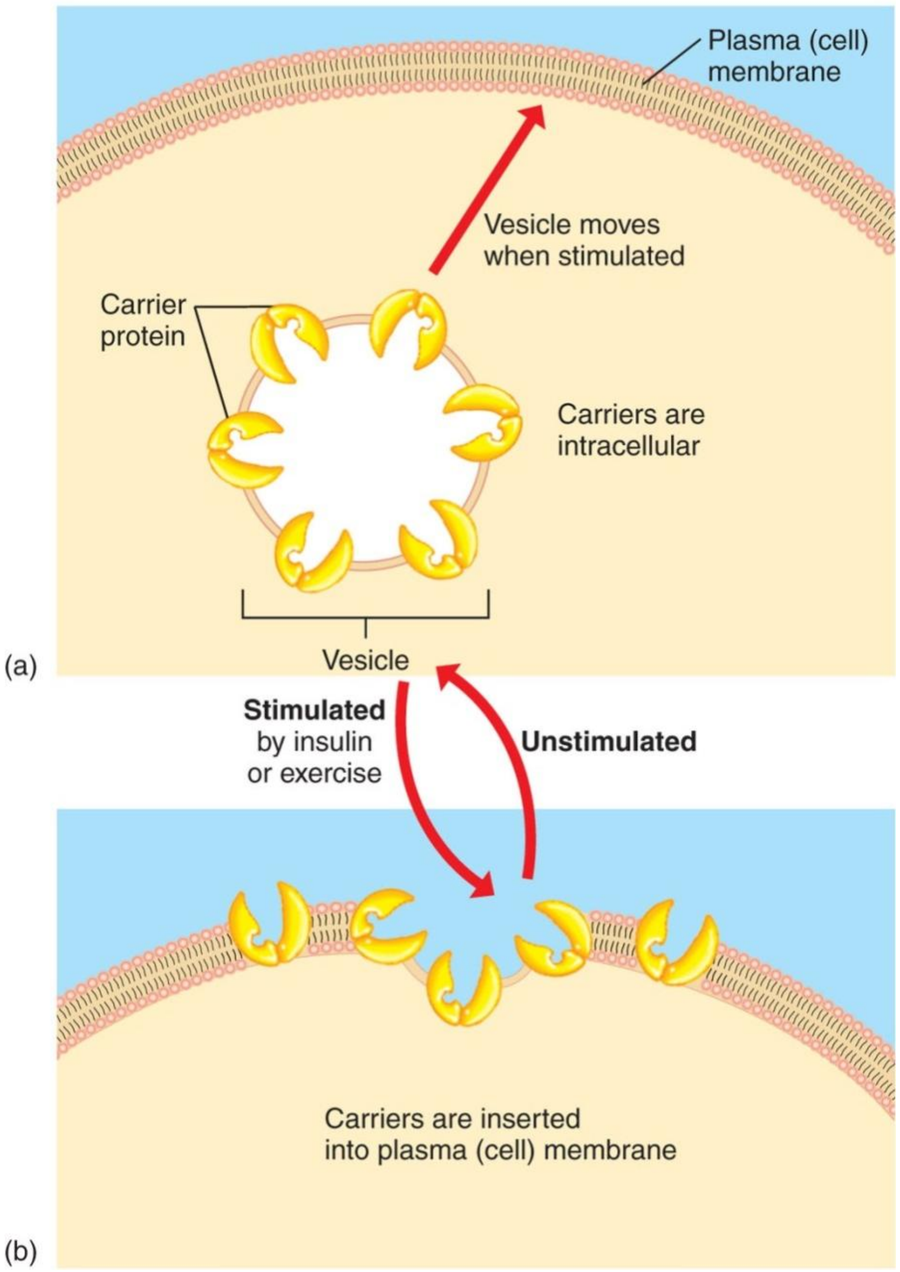
(b) Defective solute and water transport in cystic fibrosis

Facilitated Diffusion

- Passive transport through transporter (carrier-mediated)
- Characteristics of a transporter
  - --Transmembrane protein
  - --Has binding sites for specific particles (***Specificity***)
  - --Binding occurs one side at a time (***Competition* & *Saturation***)
  - --Random conformational changes



GLUT4/muscle cells & adipocytes



GLUT4/muscle cells & adipocytes

Facilitated Diffusion

- Factors affecting rate of transport
  - --Rate of transport of each carrier
  - --Number of carriers in membrane (transport maximum)
  - --Concentration gradient

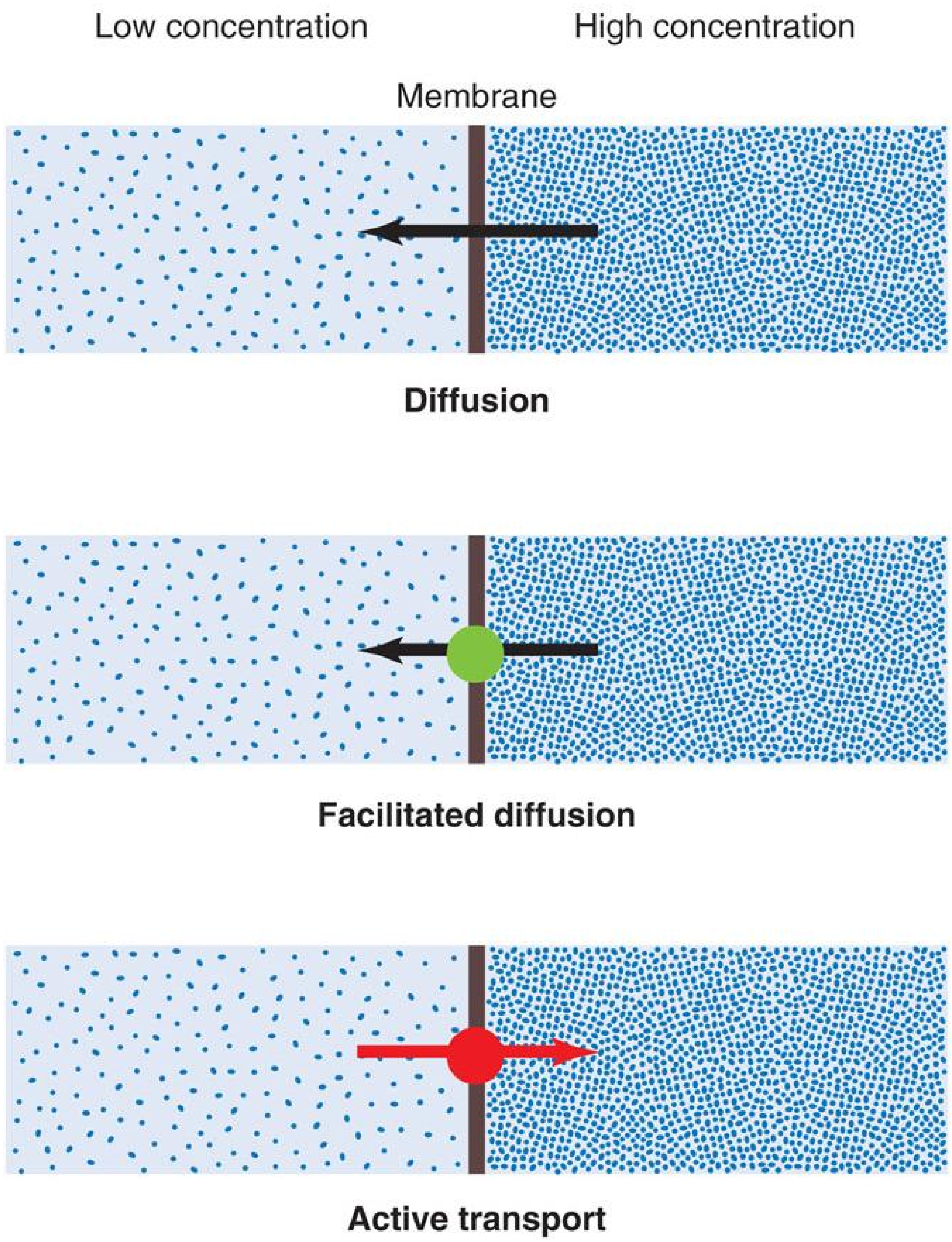
glucose, fructose, galactose, and some vitamins

Human Glucose Transporter (GLUT)

Isoform	Location	Function(s)
GLUT1	Placenta, brain (BBB), muscle, RBC	Basal glucose transporter isoform for cellular metabolism and glucose transport
GLUT2	Pancreatic β-cells, liver, small intestine	High capacity, low affinity isoform. Act as a glucose sensor
GLUT3	Neural, small intestine	High affinity isoform. Role in neuronal glucose transport (metabolism)
GLUT4	Skeletal muscle, adipose tissue, heart	Insulin-responsive isoform. Expressed only in insulin-responsive cells/tissues. Translocation to plasma membrane upon insulin stimulation
GLUT5	Small intestine, brain, muscle, adipose tissue	Fructose transporter

Types of Diffusion

比較項目 \ 擴散方式	簡單擴散	促進性擴散
運輸速率	慢	快
飽和性	無	有
專一性	無	有
經由膜蛋白運輸	不需要	需要
順濃度梯度／順電位梯度	是	是
耗能情形	不耗能	不耗能
對通道阻斷劑或接受器競爭性抑制物的敏感性	不強	強



Carrier-Mediated Transport
-Facilitated Diffusion
-Active Transport

Active Transport

--*Nonspontaneous*

--*Requires cell energy*

--*Involves a pump*

--*Movement is uphill*

Active Transport

- **Movement of polar or charged substances against their concentration gradient**

  --energy-requiring process

  - energy from hydrolysis of ATP (primary active transport)
  - energy stored in an ionic concentration gradient (secondary active transport)

- **Characteristics of a Pump**

  --A type of membrane protein (integral)

  --Function as transporter and enzyme (ATPase)

  --Can harness energy (40% of cellular ATP)

  --Have specific binding sites

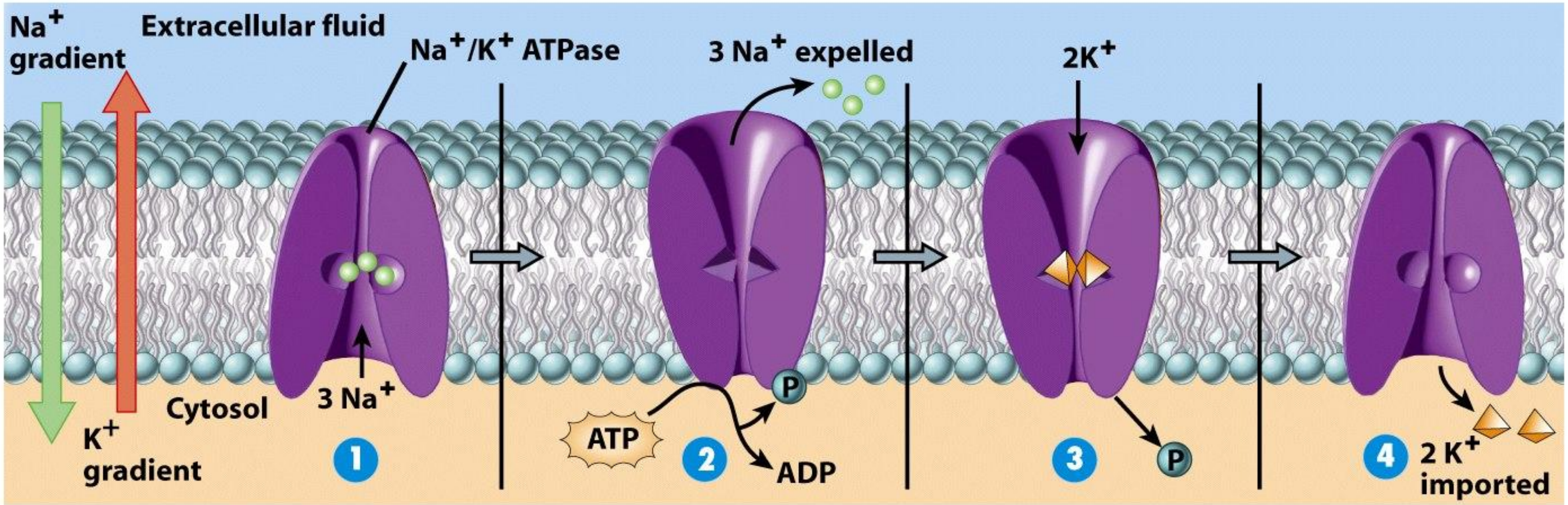
  --Demonstrate saturation

  --Works against concentration gradient

Primary Active Transport

--Energy is usually from ATP hydrolysis

--Na^+/K^+ ATPase (pump) most common example



- ✓ ***H-K pump/stomach***
- ✓ ***Ca pump/muscle cell or sER***

Na^+/K^+ Pump

- **Found in all body cells**
- **ATPase enzyme that pumps 3 Na^+ out of the cell and 2 K^+ into the cell (conc. difference)**
- **Serves three functions:**

--Provides energy for secondary active transport (coupled transport) of other molecules

--Produces electrochemical impulses in neuron and muscle cells

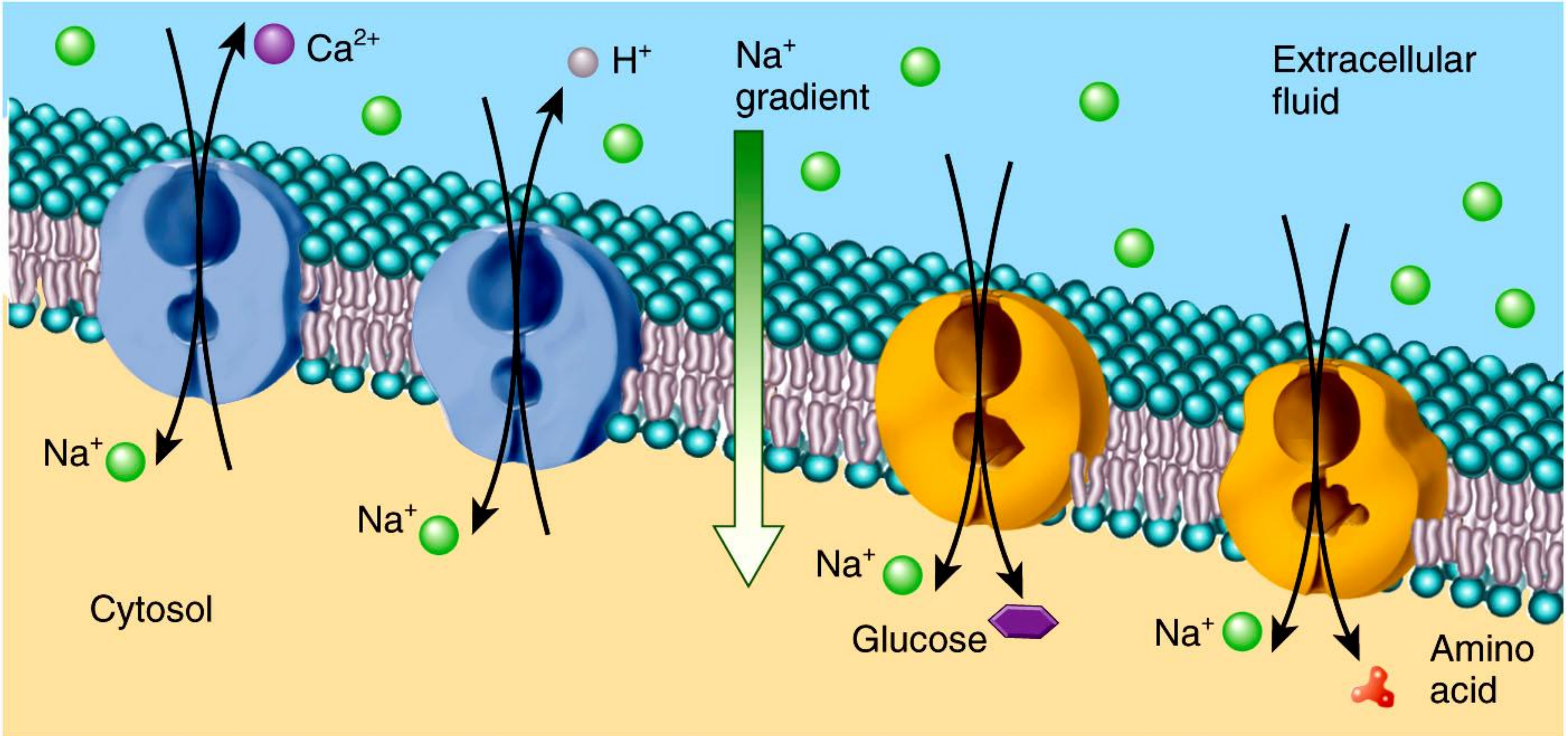
--Maintains osmolality

Secondary Active Transport (Coupled Transport)

--Energy released from ion diffusion (Na conc. gradient)

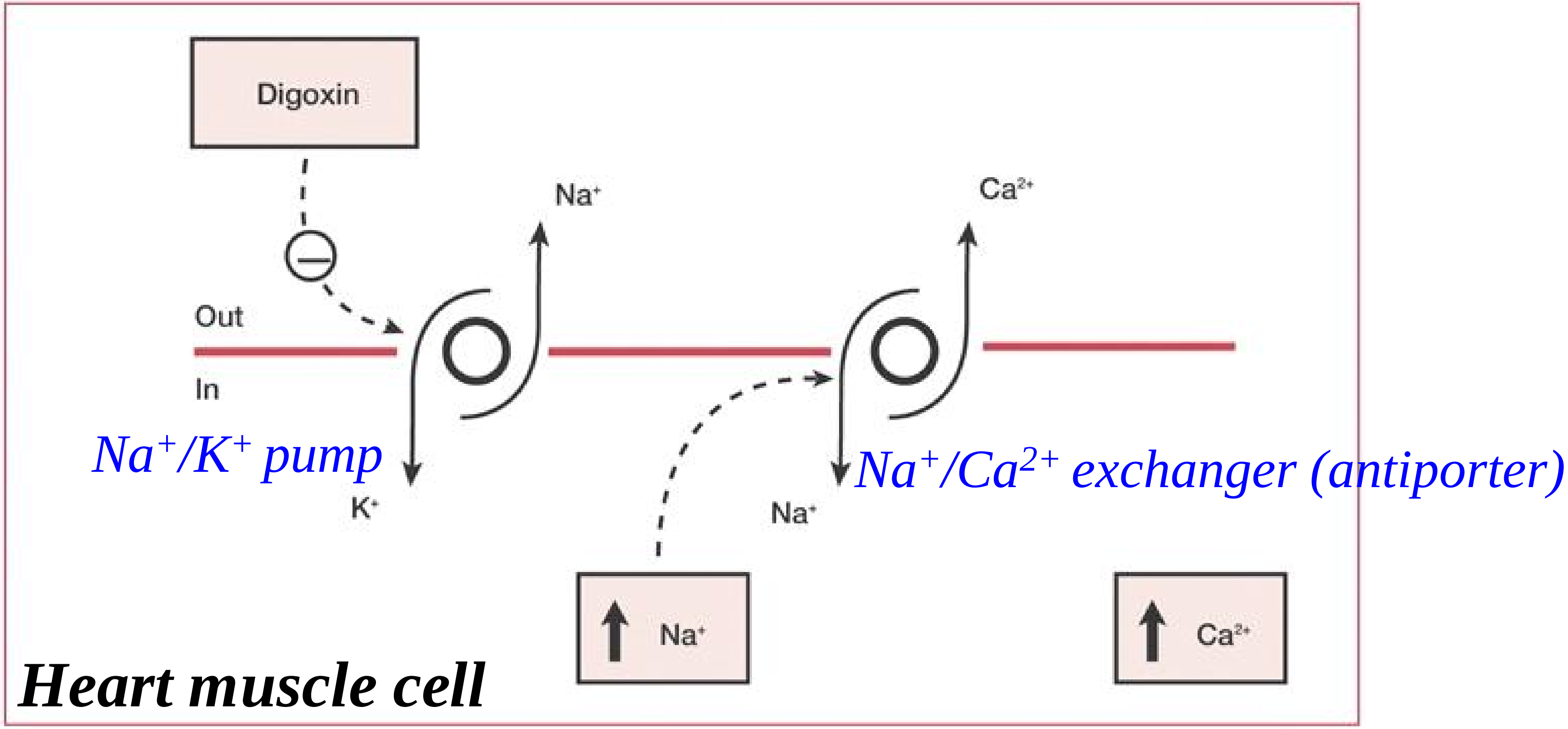
--Energy drives a pump

--Diffusion results from previous active transport of ion



Countertransport (antiport) *Cotransport (symport)*

Clinical Application: Digitalis

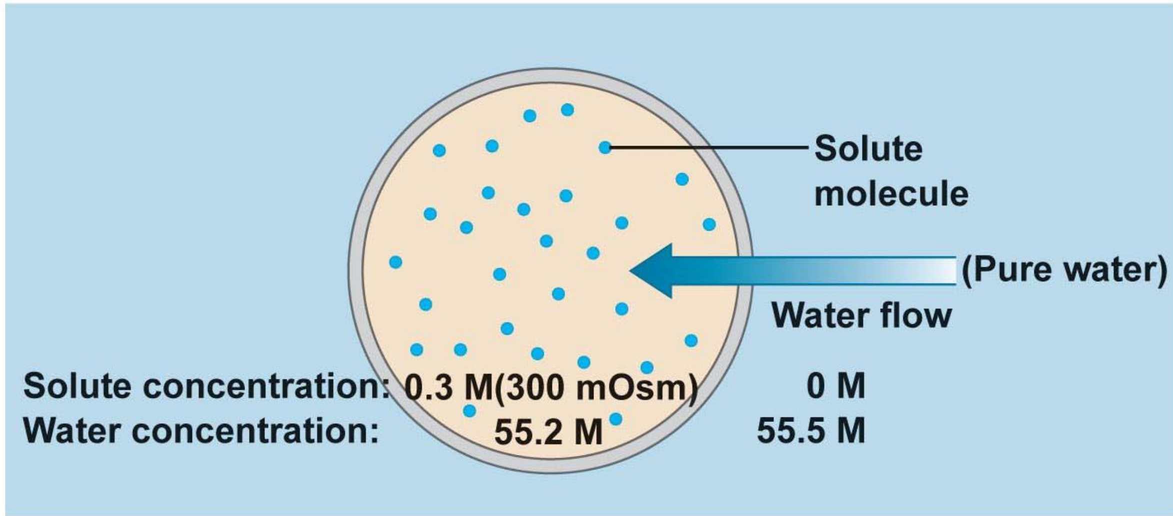


Membrane Transport

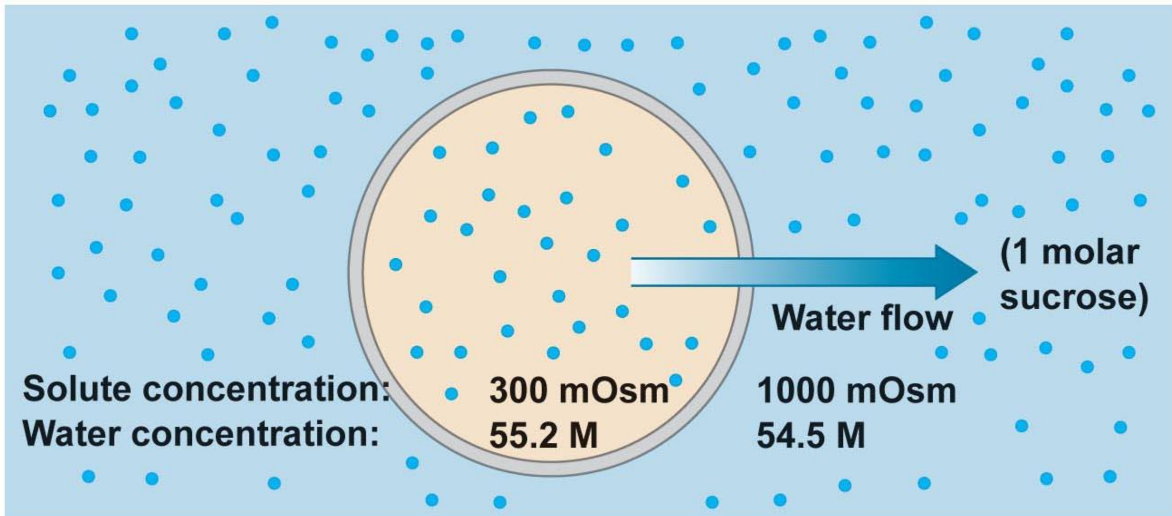
	SIMPLE DIFFUSION	MEDIATED TRANSPORT			
		Passive transport		Active transport	
		Channel	Facilitated diffusion	Primary	Secondary
Direction of net flux	Down electrochemical gradient	Down electrochemical gradient	Down electrochemical gradient	Up electrochemical gradient	Up electrochemical gradient
Transport protein required?	No	Yes, ion channel	Yes, carrier	Yes, pump	Yes, pump
Requires energy?	No	No	No	Yes	Yes
Energy source	(Not applicable)	(Not applicable)	(Not applicable)	ATP or other chemical energy source	Electrochemical gradient of another solute
Saturation?	No	Sometimes	Yes	Yes	Yes
Specificity?	No	Yes	Yes	Yes	Yes
Character of transported substance	Hydrophobic (nonpolar)	Hydrophilic (ionized or polar)	Hydrophilic (ionized or polar)	Hydrophilic (ionized or polar)	Hydrophilic (ionized or polar)
Examples	Fatty acids, O_2, CO_2	Inorganic ions (Na^+, K^+, Cl^-, Ca^{2+})	Organic molecules (glucose)	Inorganic ions (Na^+, K^+, H^+, Ca^{2+})	Organic molecules and inorganic ions (glucose, amino acids, H^+, Ca^{2+})

Osmosis

- Net diffusion of water
- Characteristics
  - --Always passive
  - --Unaffected by membrane potentials
  - --Driven by water gradient
  - --Membrane permeable to water, but impermeable to the solute



(a)



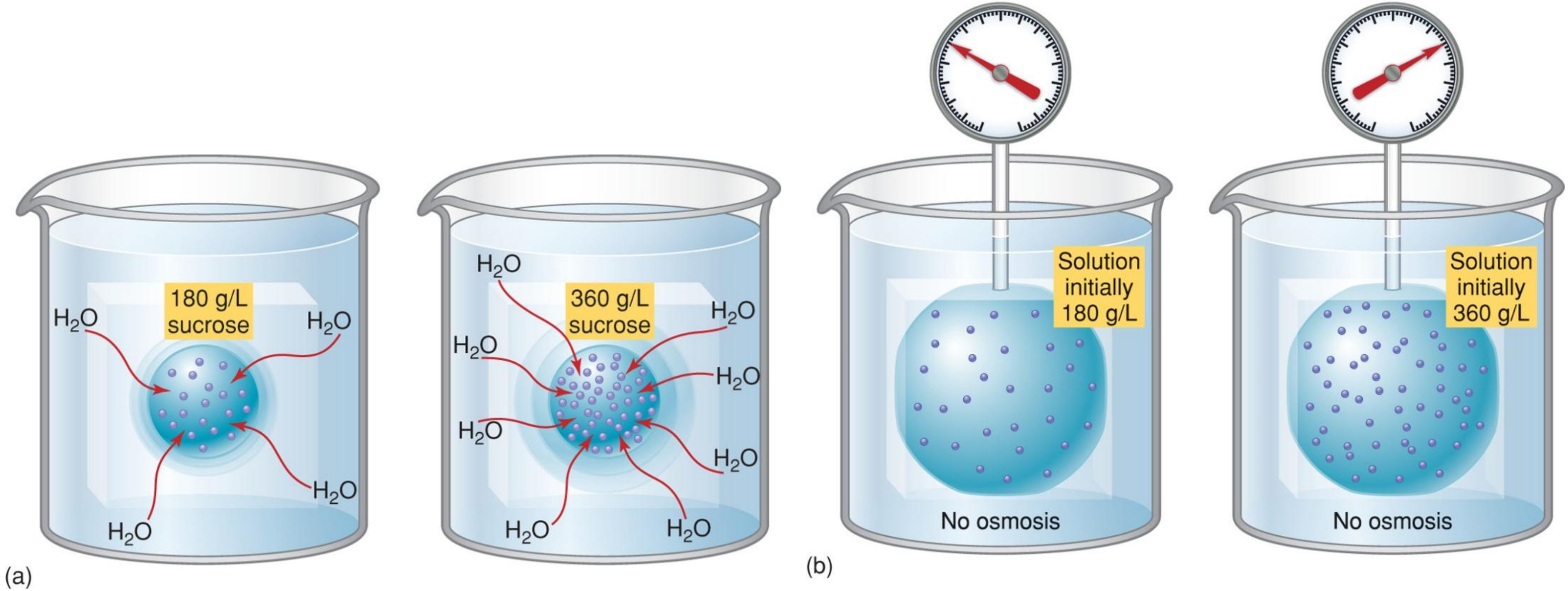
(b)

Osmosis

- **Osmolarity**
  - --Total solute concentration of a solution
  - --Solute particle — displaces water
  - --Milliosmole (mOsm)
    - ➢1/1000 of an osmole
    - ➢Used in physiology
    - ➢ICF and ECF is around 300 mOsm

Osmotic Pressure

The force surrounding a cell required to ***stop osmosis***



✓Used in place of osmolarity
✓Reflects total solute concentration
✓Ability to "pull" water

Tonicity

- Plasma has the same osmolality as a 0.3M (5%) glucose or a 0.15M (0.9%) NaCl solution

  --These solutions are considered **isosmotic** to plasma

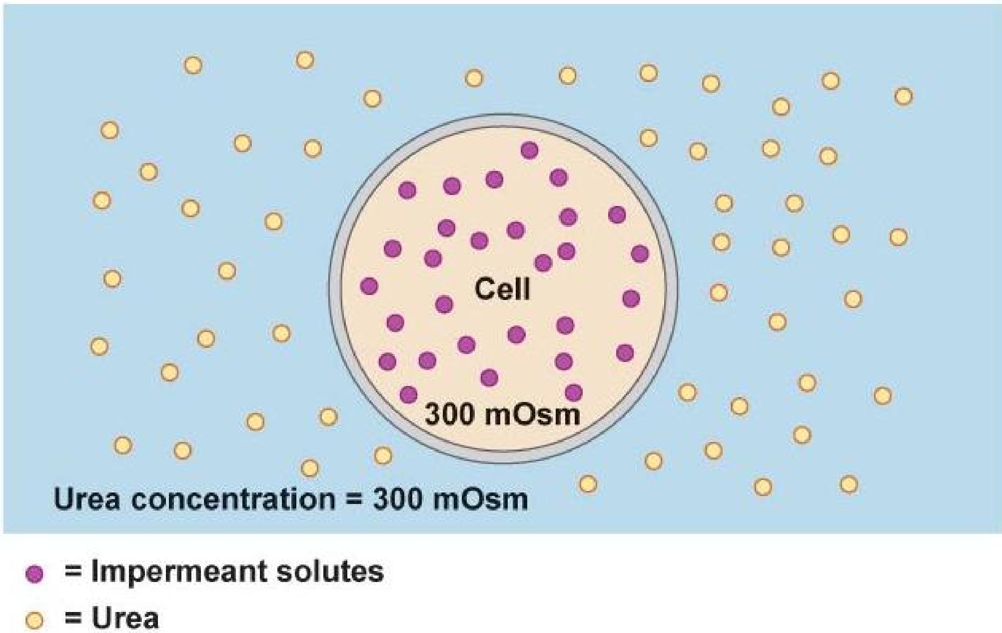
- **Tonicity** is the effect of a solute concentration on the osmosis of water

  --If a membrane separates a 0.3M glucose solution and a 0.15M NaCl solution, there will be no net movement of water = **isotonic**

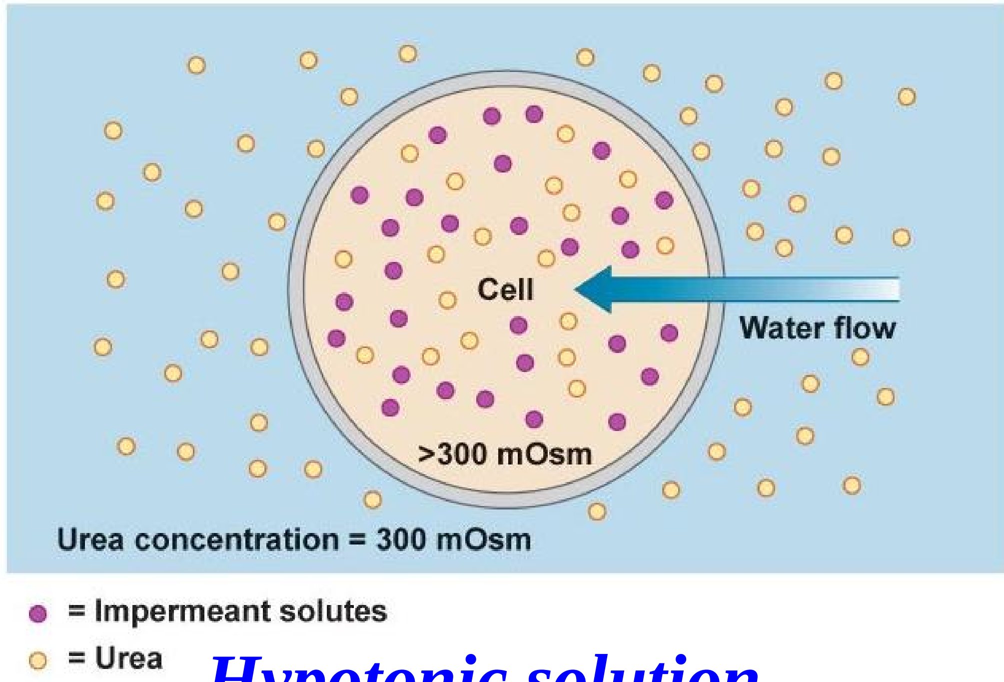
- Tonicity takes into account the permeability of the membrane to the solutes. <u>If the solutes can cross the membrane, the tonicity will change</u>

  --If you place RBCs in a 0.3M solution of urea, the tonicity will not be isotonic. Urea can cross into the RBCs and draw water with it

  --These cells will eventually burst

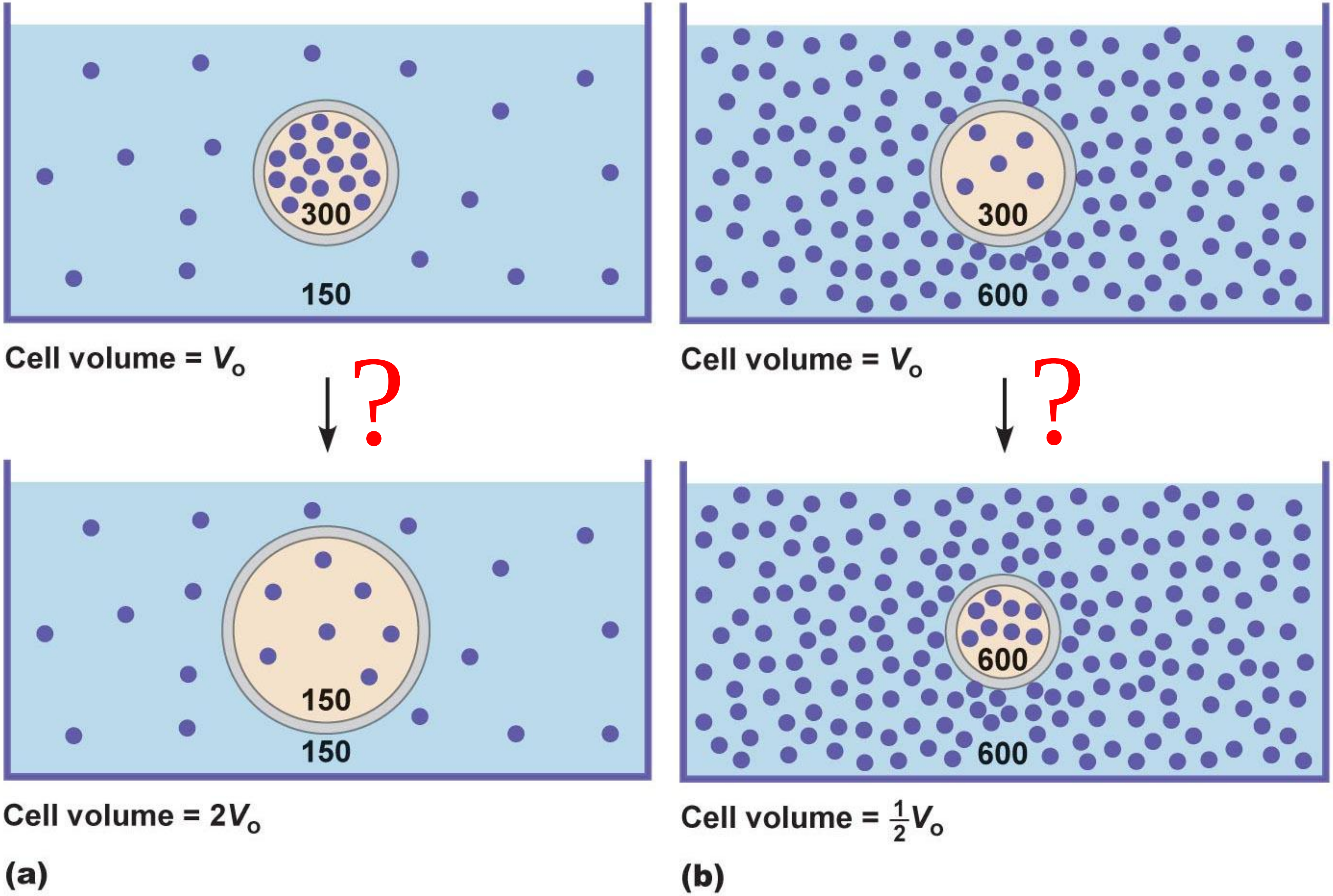


(a) *Isotonic solution*



(b) *Hypotonic solution*

Extracellular Osmolarity & Cell Volume



Osmolarity and Tonicity

Terms	Definitions and solute concentrations
Osmolarity	Total concentration of permeant and impermeant solutes
Iso-osmotic*	300 mOsm (permeant + impermeant)
Hypo-osmotic*	Less than 300 mOsm (permeant + impermeant)
Hyperosmotic*	Greater than 300 mOsm (permeant + impermeant)
Tonicity	Concentration of impermeant solutes relative to intracellular fluid
Isotonic*	300 mOsm (impermeant)†
Hypotonic*	Less than 300 mOsm (impermeant)†
Hypertonic*	Greater than 300 mOsm (impermeant)†

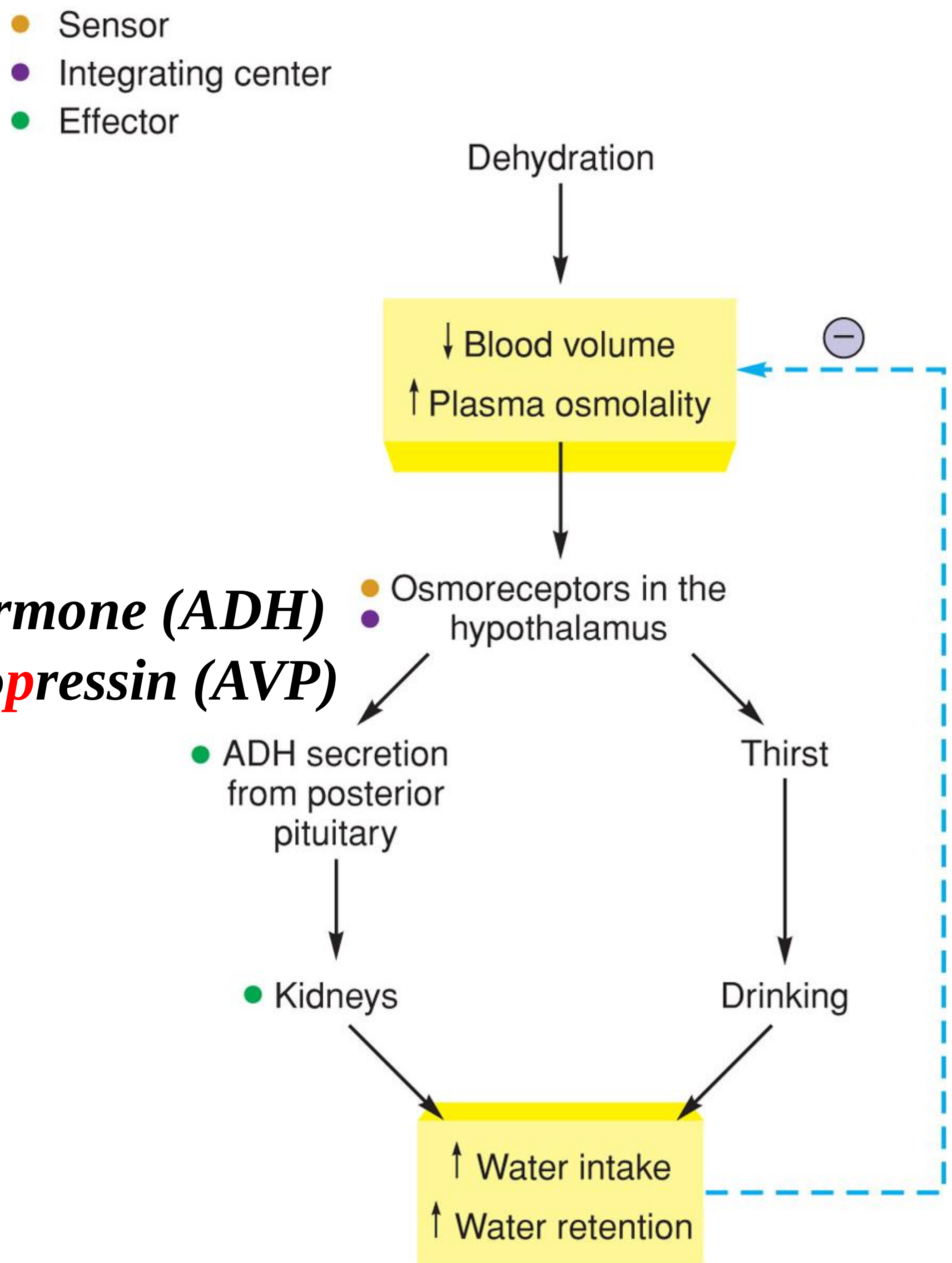
*These designations are relative to a cell containing 300 mOsm solutes, which are assumed to be impermeant.

†Permeant solutes may or may not be present.

Regulation of Blood Osmolality

***A**nti**d**iuretic **h**ormone (ADH)*

*= **A**rginine **v**aso**p**ressin (AVP)*



Transport via Vesicles
Requires ATP

- **Endocytosis** – large materials move into a cell in a **vesicle** formed from the plasma membrane

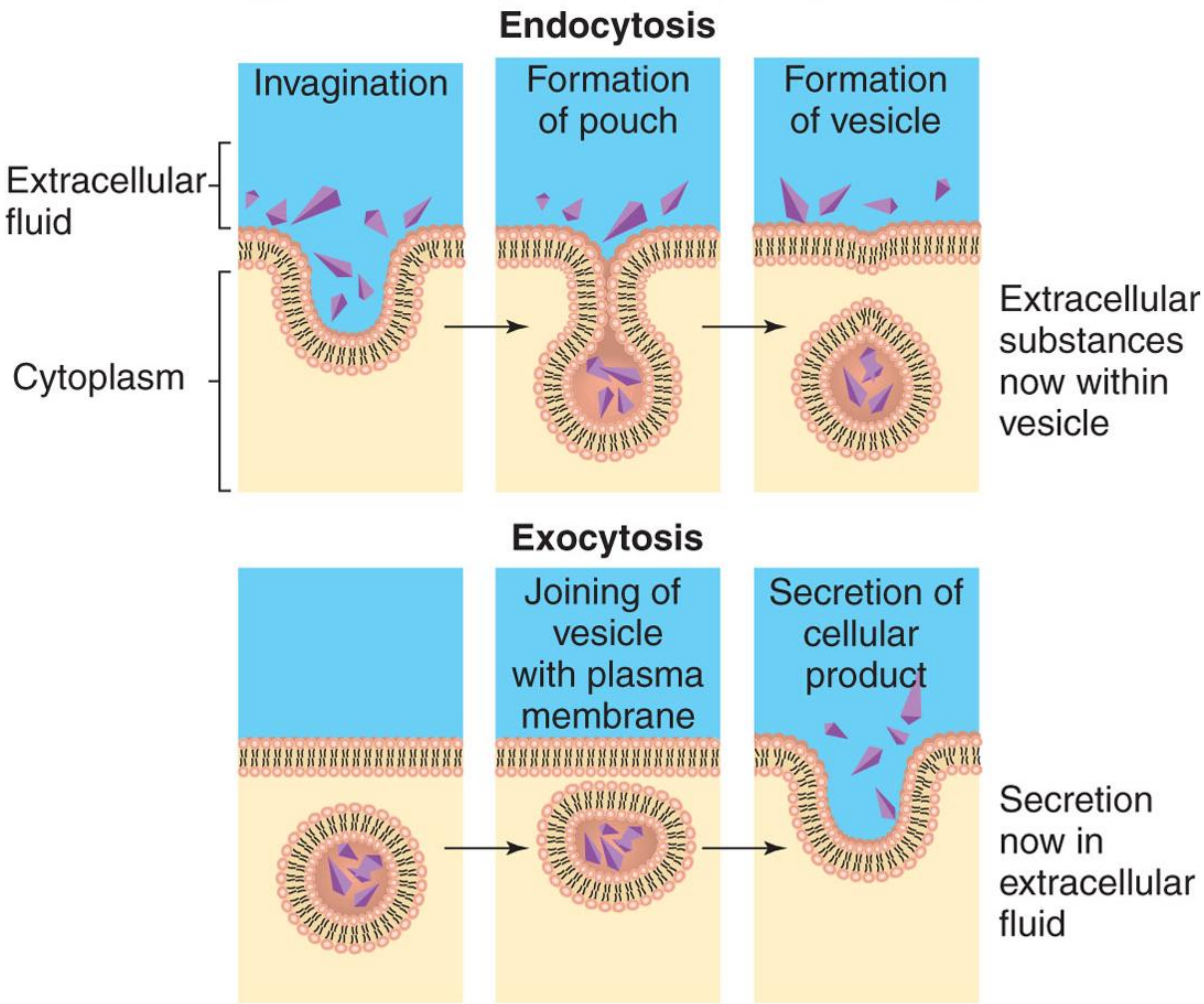
  --three types: *Pinocytosis*

  Phagocytosis

  Receptor-mediated endocytosis

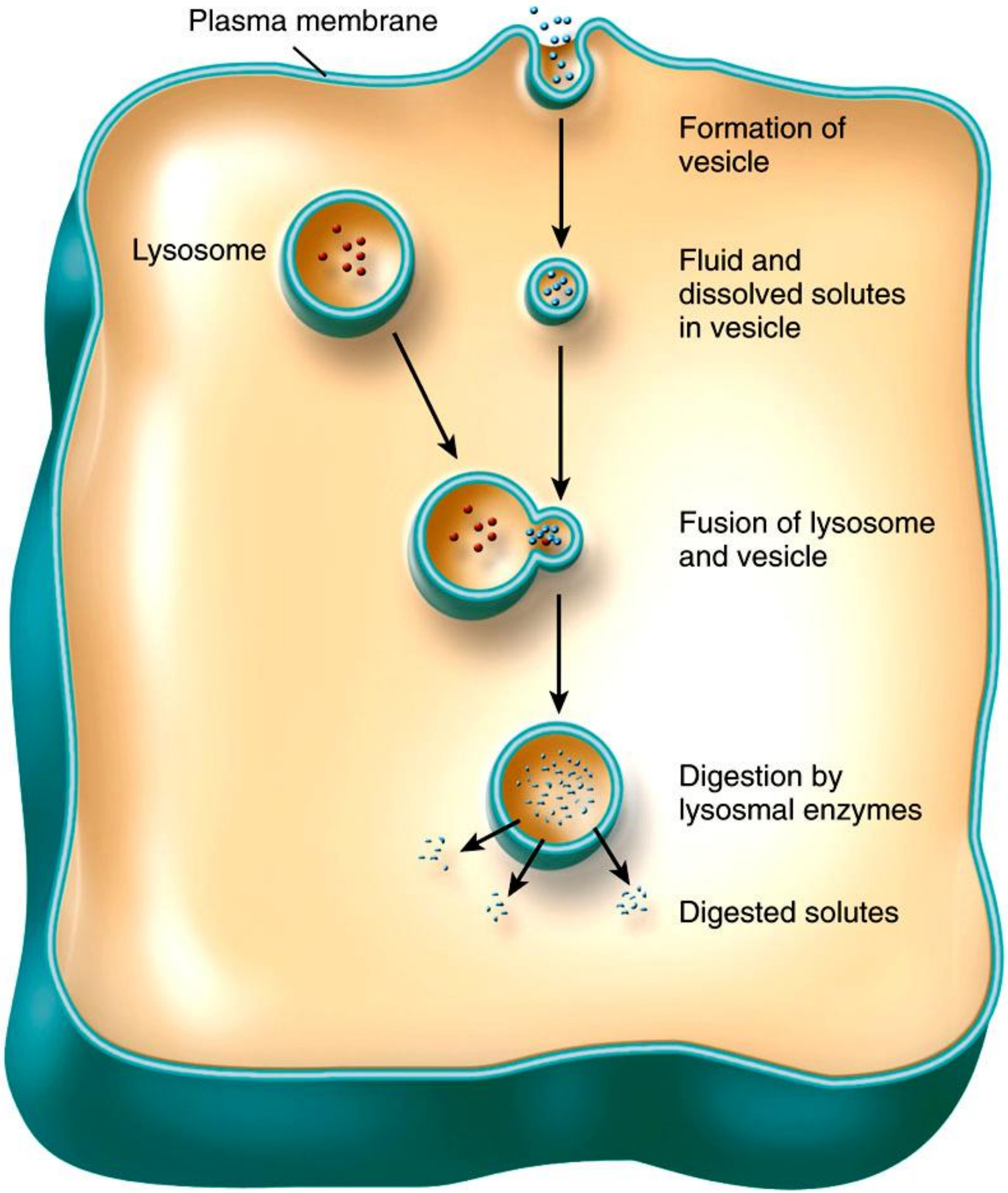
- **Exocytosis** - **vesicles** fuse with the plasma membrane, releasing their contents into the extracellular fluid (ex. proteins, hormones, and neurotransmitters)
- **Transcytosis** - a combination of endocytosis and exocytosis

Endocytosis & Exocytosis

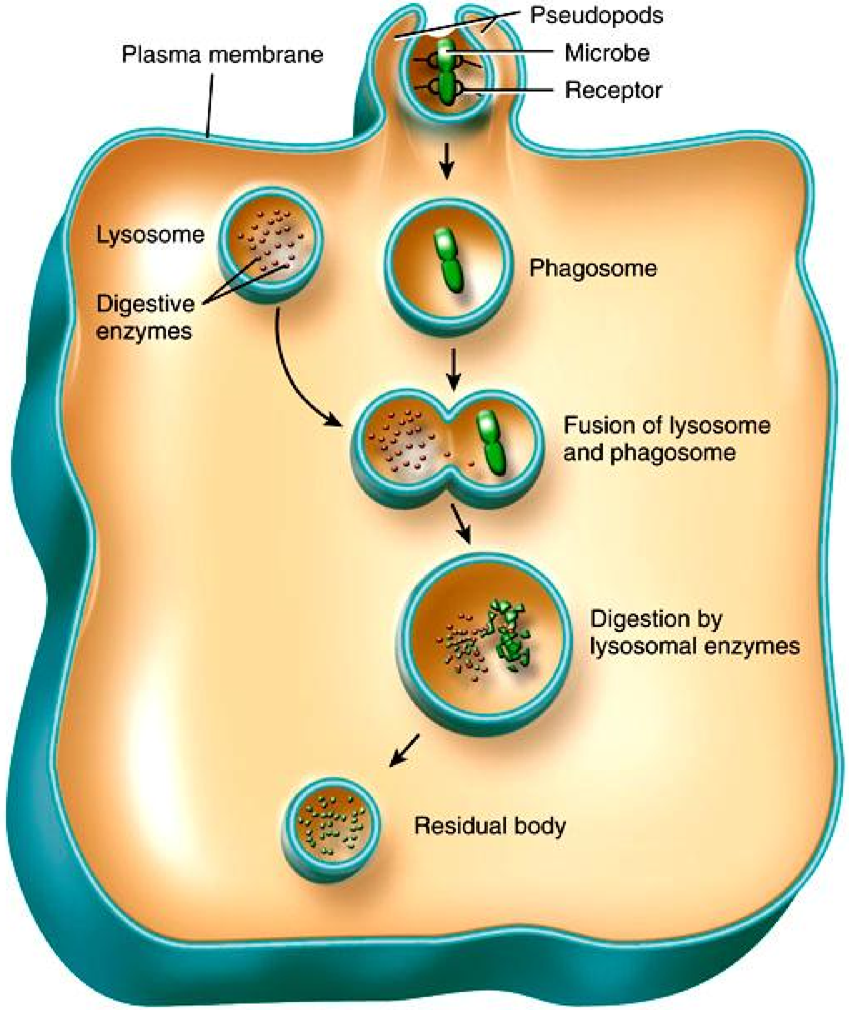


Pinocytosis

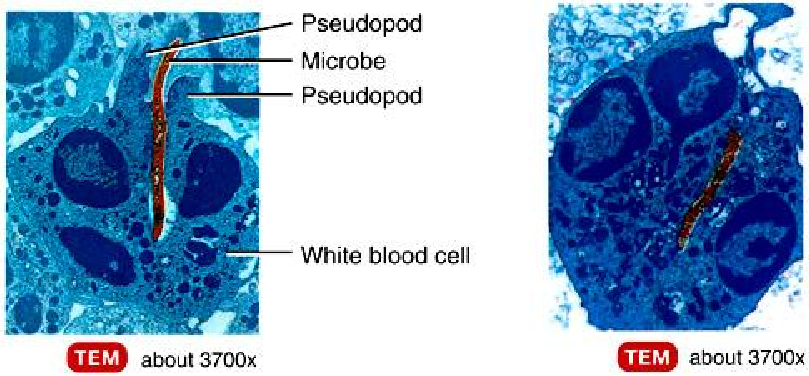
Dissolved molecules



Phagocytosis



(a) Diagram of the process

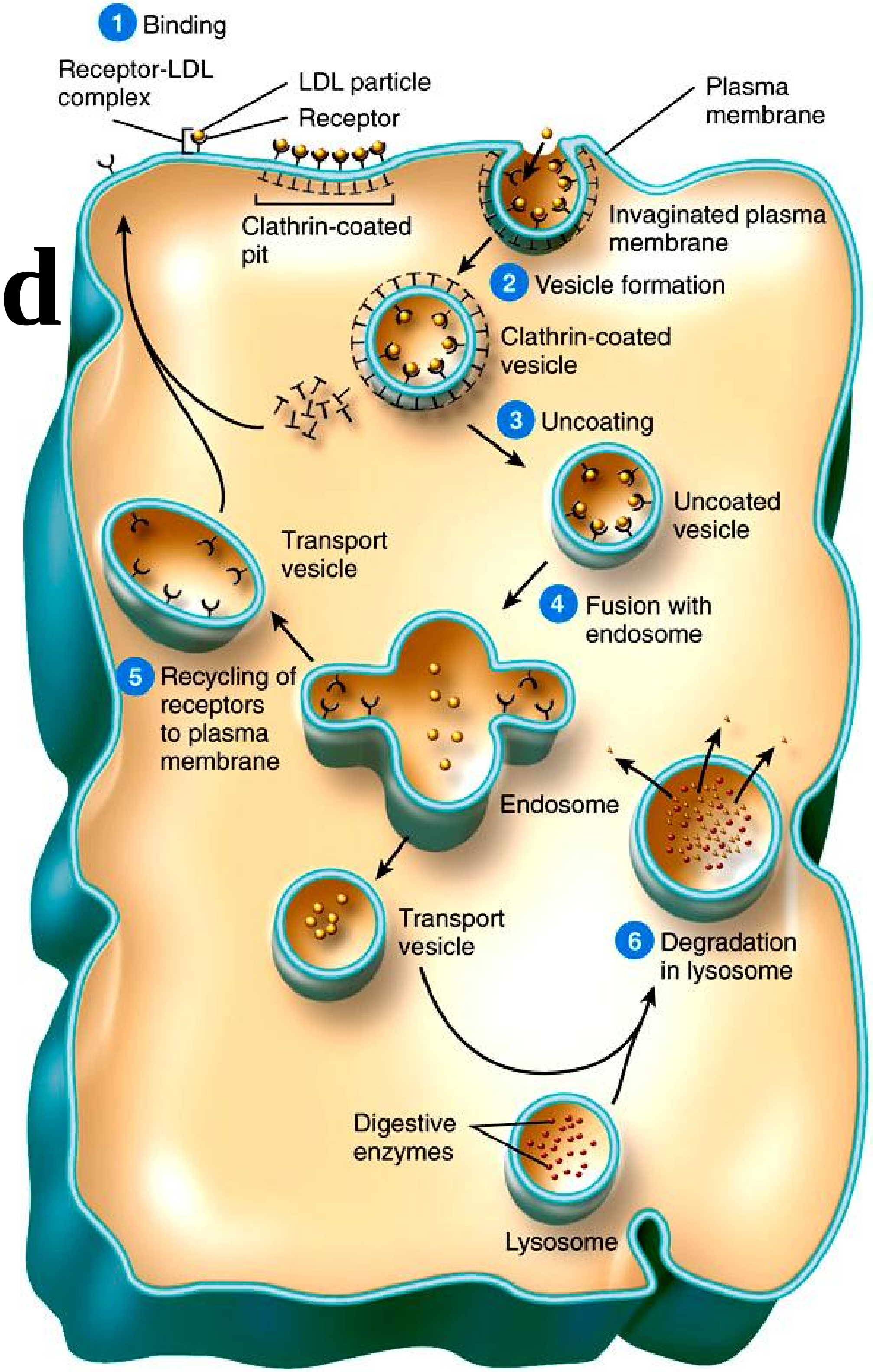


(b) White blood cell engulfs microbe

(c) White blood cell destroys microbe

Receptor-Mediated Endocytosis

- ✓*LDL particles*
- ✓*Some viruses*
- ✓*Antibody*
- ✓*Vitamin*
- ✓*Transferrin etc.*



Transcytosis