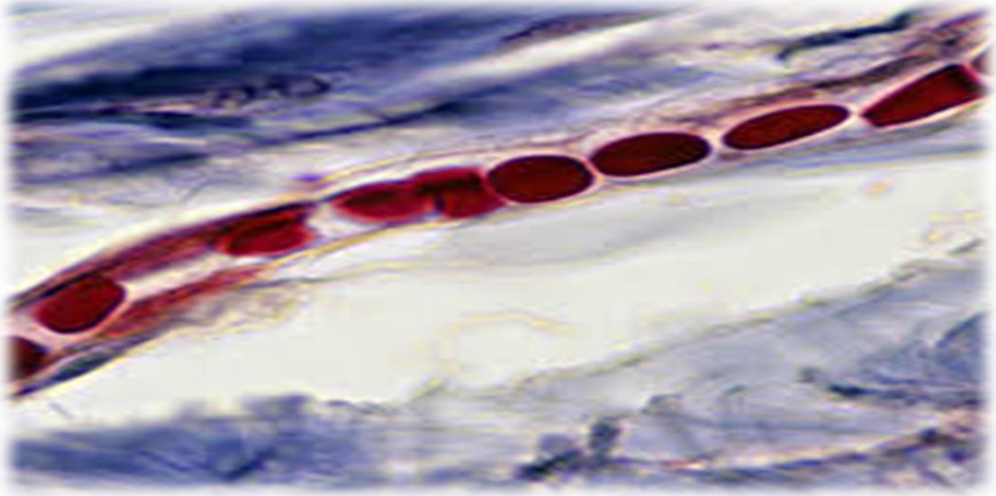

Fluid Exchange Between Body Compartments

Tissue Biology and Introduction to Human Embryology (MED 114)

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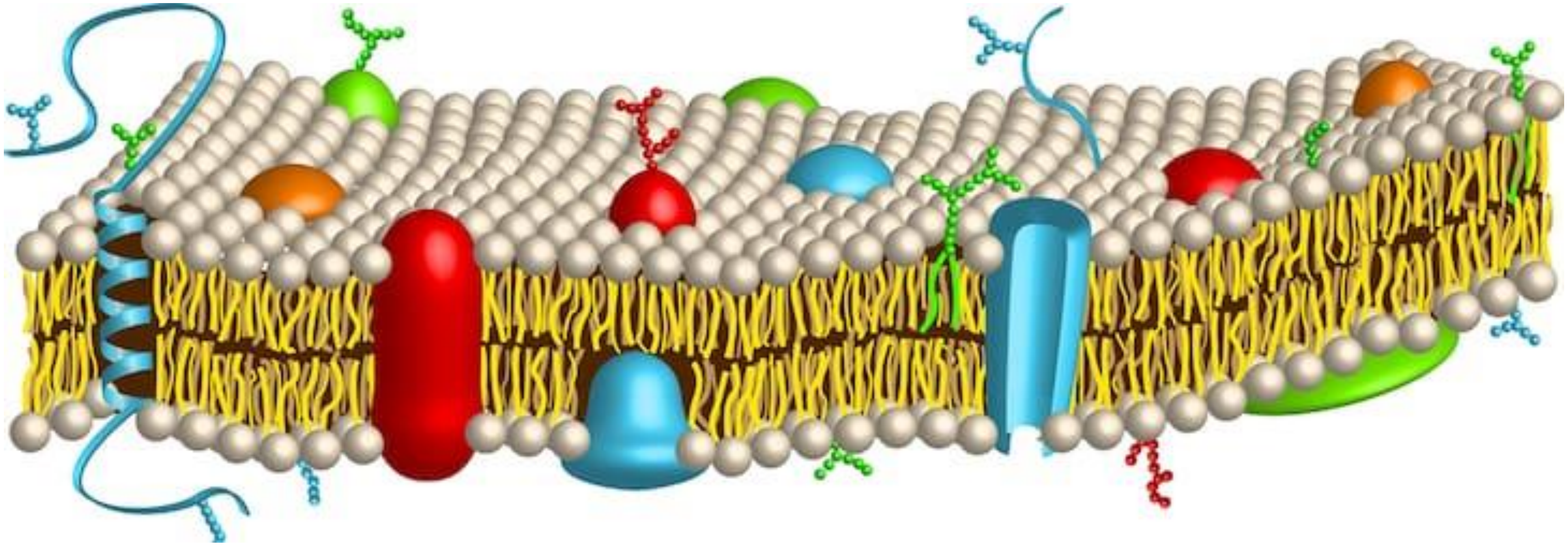
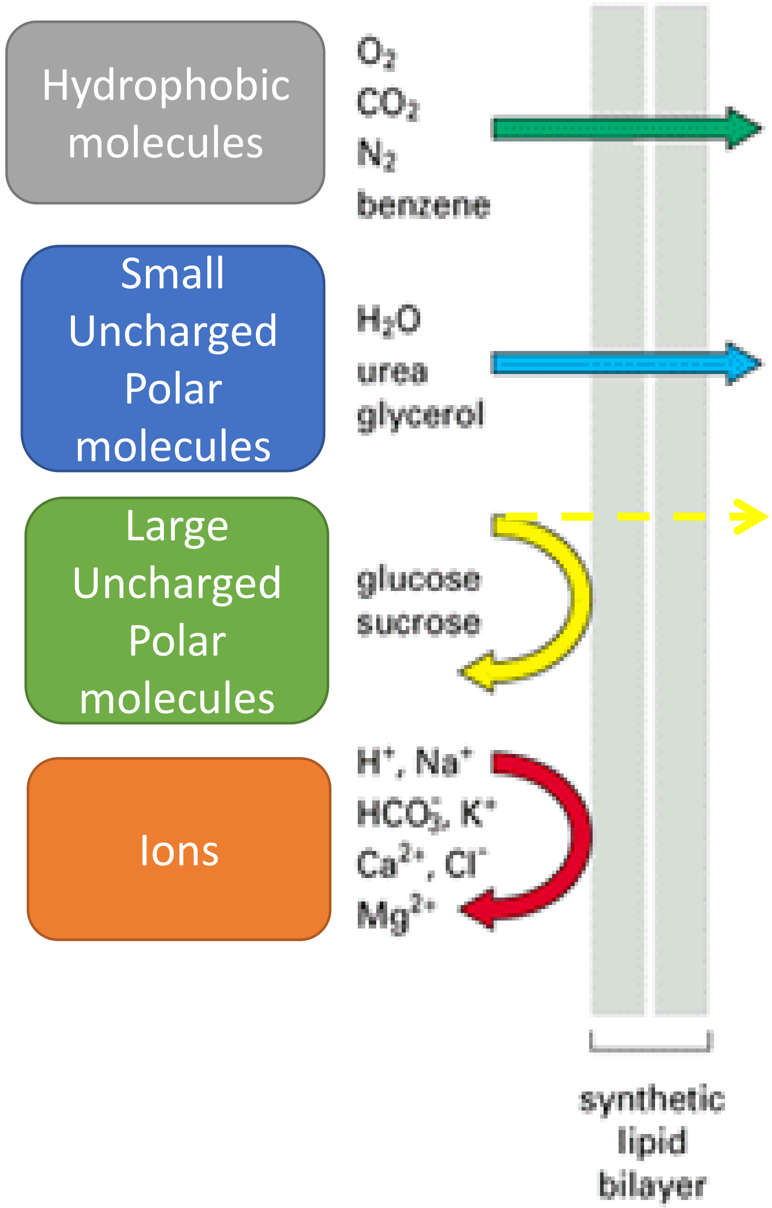
Basic structure of the cell membrane

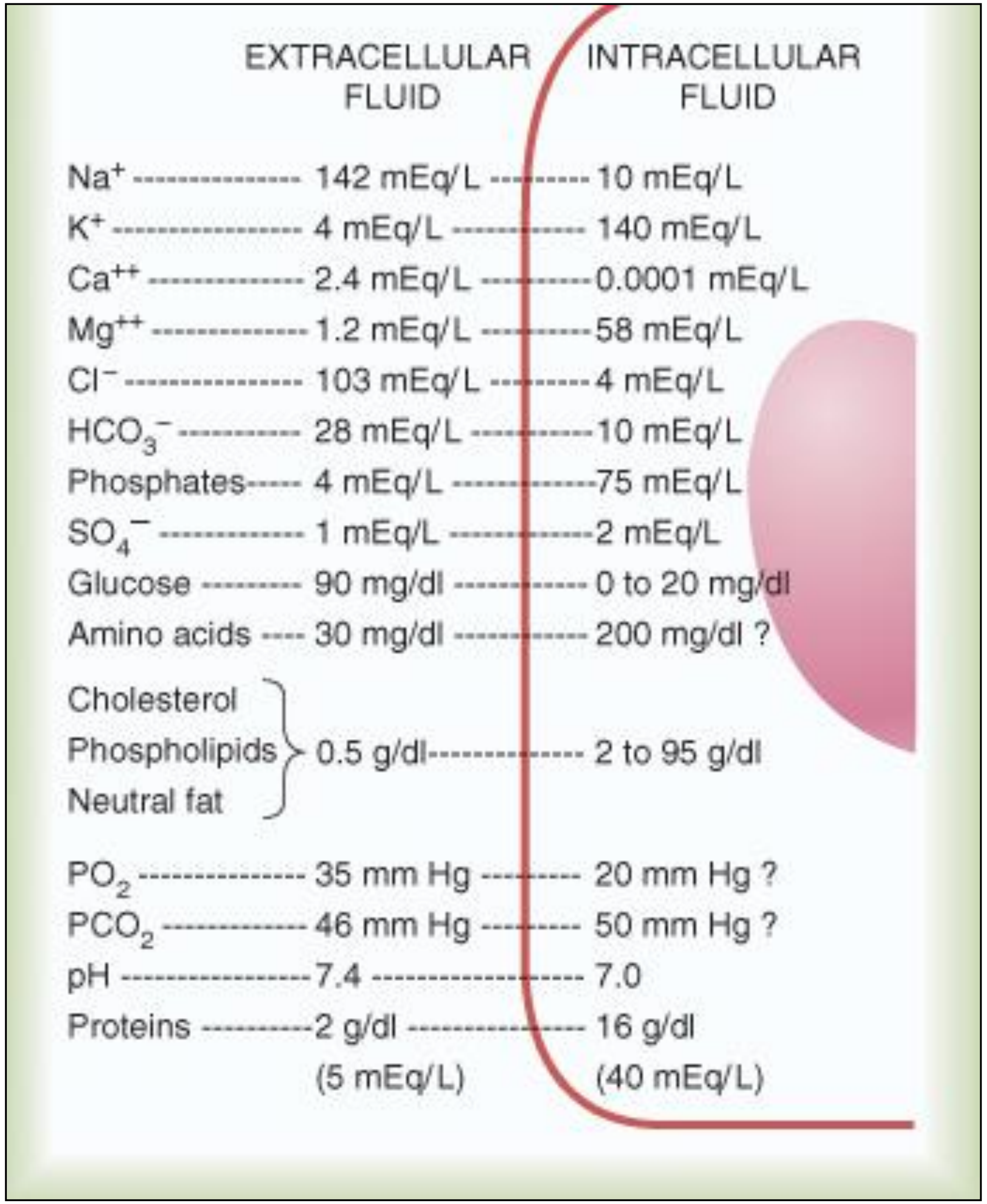


Transport of substances accross cell membranes

Because of their hydrophobic internal parts, lipid bilayer:

- is **permeable** to
  - Small, uncharged, polar molecules
  - Hydrophobic molecules
  - Gases
- is **impermeable** to
  - Charged molecules (e.g. Na^+, Cl^-, K^+, Ca^{2+})
  - Large water soluble molecules (e.g. Proteins, nucleic acids, sugars, nucleotides etc.)
- **Selective permeability**

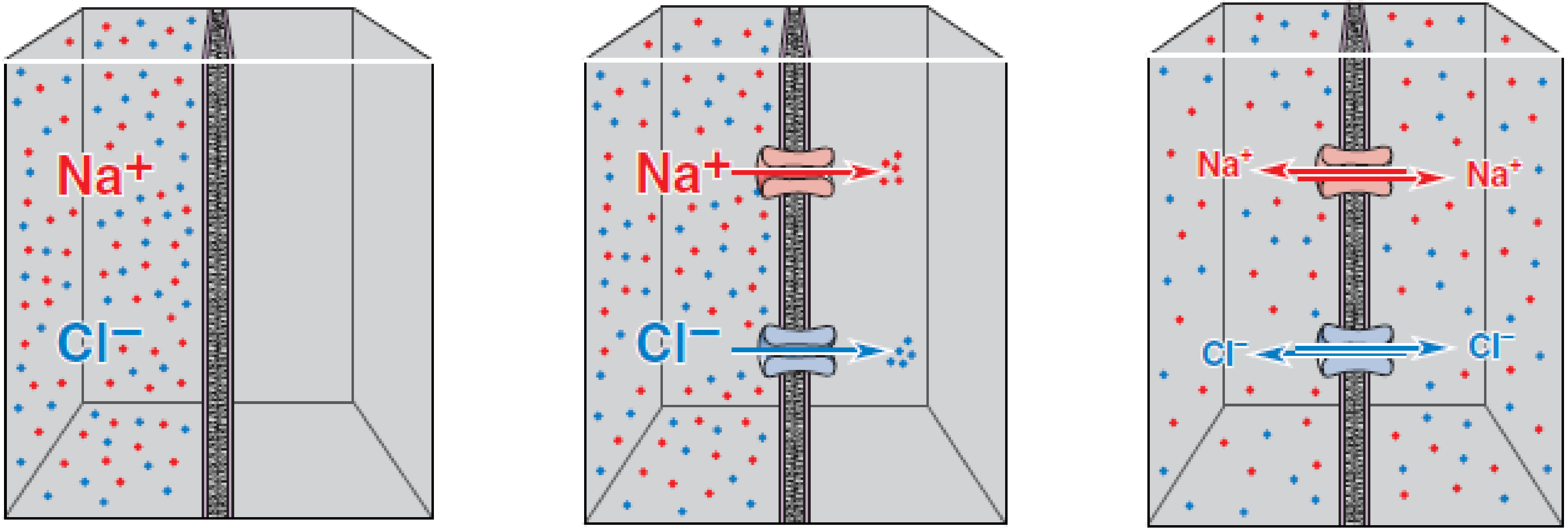




	EXTRACELLULAR FLUID	INTRACELLULAR FLUID
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{++}	2.4 mEq/L	0.0001 mEq/L
Mg^{++}	1.2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L
Phosphates	4 mEq/L	75 mEq/L
$SO_4^{=}$	1 mEq/L	2 mEq/L
Glucose	90 mg/dl	0 to 20 mg/dl
Amino acids	30 mg/dl	200 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)

Guyton and Hall Textbook of Medical Physiology, 13th Ed

Diffusion



The movement of ions across the membrane by diffusion, therefore, happens when

✓ The membrane has channels permeable to the ions

✓ There is a concentration gradient across the membrane.

Movement of Water between different fluid compartments

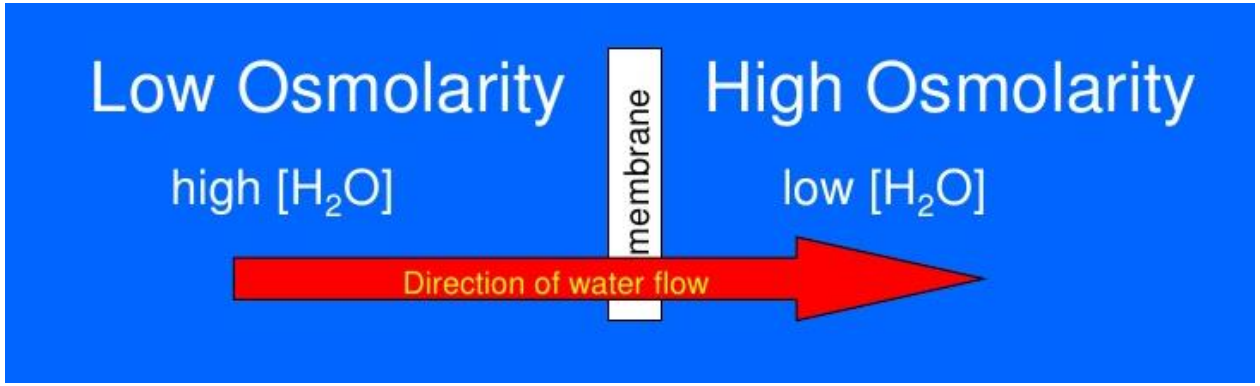
- The pathways and driving forces for this water movement are different across cell membranes, in comparison to the capillary walls.
- Movement of water between the ICF and ECF compartments, across cell membranes, occurs through aquaporins expressed in the plasma membrane.
- The driving force for this water movement is an osmotic pressure difference. The osmotic pressure of both the ICF and ECF is determined by the molecules/ions present in these fluids.

Osmosis

- Net diffusion of water across a membrane
- Aquaporins: Water channels
- Different numbers in different membranes and the numbers can be altered in response to various signals

Osmolarity

- The total solute concentration of a solution
- 1 osmol (osm) = 1 mol of solute particles
  - 1 M glucose= 1 osm
  - 1 M NaCl=2 osm



Tonicity

- For two fluids separated by a semipermeable membrane, the one with lower solute concentration is *hypotonic*, and the one with higher solute concentration is *hypertonic*
  - Water diffuses from hypotonic to hypertonic

- *Isotonic* fluids have the same solute concentration

- The osmolarity of the extracellular fluid is normally in the range of 285–300 mOsm
- Because water can diffuse across plasma membranes, water in the intracellular and extracellular fluids will come to diffusion equilibrium.
- At equilibrium, therefore, the osmolarities of the intracellular and extracellular fluids are the same—approximately 300 mOsm.

Osmolarity of the intracellular fluids 300 mOsm

- Isotonic = 300 mOsm
- Hypertonic > 300 mOsm
- Hypotonic < 300 mOsm

Osmotic Pressure

- When a solution containing solutes is separated from pure water by a *semipermeable membrane* (a membrane permeable to water but not to solutes), the pressure that must be applied to the solution to prevent the net flow of water into it is known as the osmotic pressure of the solution.

- Osmolarity ↑ Osmotic pressure ↑

- Represents the amount of pressure that would have to be applied to a solution to prevent the net flow of water into the solution by osmosis

Isotonic Solutions

150 mM NaCl

300 mOsm NaCl (0.9% NaCl)

300 mM glucose

300 mOsm glucose (5% glucose)

Ringer lactate

- **Treatment of fluid loss**

- Plasma proteins exert an osmotic force of about 25-28 mmHg to pull the interstitial fluid from tissues into the blood: **Colloid osmotic pressure** or **Oncotic pressure**

- **Hydrostatic pressure** refers to force that is exerted by the fluid inside the blood capillaries against the capillary wall.

Interstitial Fluid Return by the Lymphatic System

- Network of tiny vessels intermingled among capillaries
- After entering the lymphatic system by diffusion, the fluid is called lymph; its composition is about the same as that of interstitial fluid
- Disruptions in lymph flow often result in fluid accumulation, or edema

Transport of small molecules and ions

A) Passive transport

- Simple diffusion
- Facilitated diffusion
  - **Pores** (un-gated channels)
  - **Channel proteins** (gated pores)
  - **Carrier proteins** (permeases)
  - Osmosis

B) Active transport

- ATP dependent (Primary active transport)
- Dependent on ion gradients (Secondary active transport)

A) Passive Transport: **No energy required**

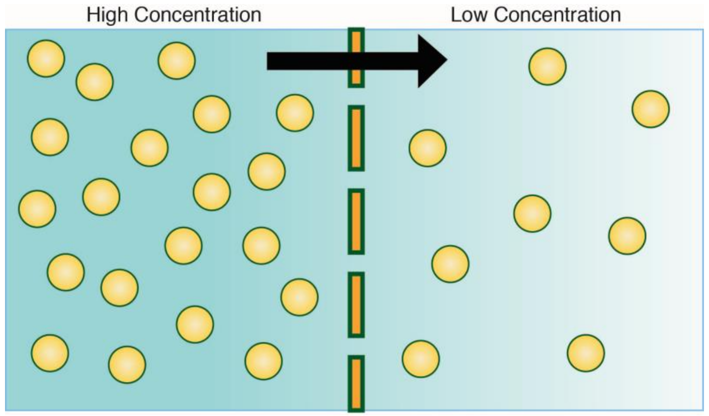
1) Simple diffusion
2) Facilitated diffusion

Direction and driving force of transport

Uncharged molecules
The concentration difference of the molecule on both sides of the membrane:
In the direction of the concentration gradient

Molecules with a net charge
Concentration gradient+
Electrical potential difference=
In the direction of the electrochemical gradient

1) Simple diffusion



Hydrophobic molecules

Small Uncharged Polar molecules

O_2, CO_2, H_2O, alcohol, steroid hormones etc.

Cooper. The Cell: A molecular approach, 2nd edition

2) Facilitated diffusion

Integral Membrane Proteins

i. Pores (ungated channels)

ii. Channel proteins (gated pores)

iii. Carrier proteins (transporters, carriers, permeases)

✓ They are found in all biological membranes and in very different forms.

✓ Each protein carries a specific group of molecules (eg. **sugars, amino acids, ions**).

Large Uncharged Polar molecules

Charged molecules
Ions

2) Facilitated diffusion

✓No external source of energy is provided.

✓Molecules travel across the membrane in the direction determined by their concentration gradients / the electric potential across the membrane.

✓High → Low

Large Uncharged
Polar molecules

Charged
molecules
Ions

Pores (ungated channels)

- Both sides are always open
- Aquaporins

B) Active Transport: **REQUIRES ENERGY**

- ✓Transport against electrochemical gradient
- ✓Require specialized proteins
- ✓From low conc. to high conc.
    1. ATP hydrolysis (Primary active transport)
    2. Ion gradient (Secondary active transport)

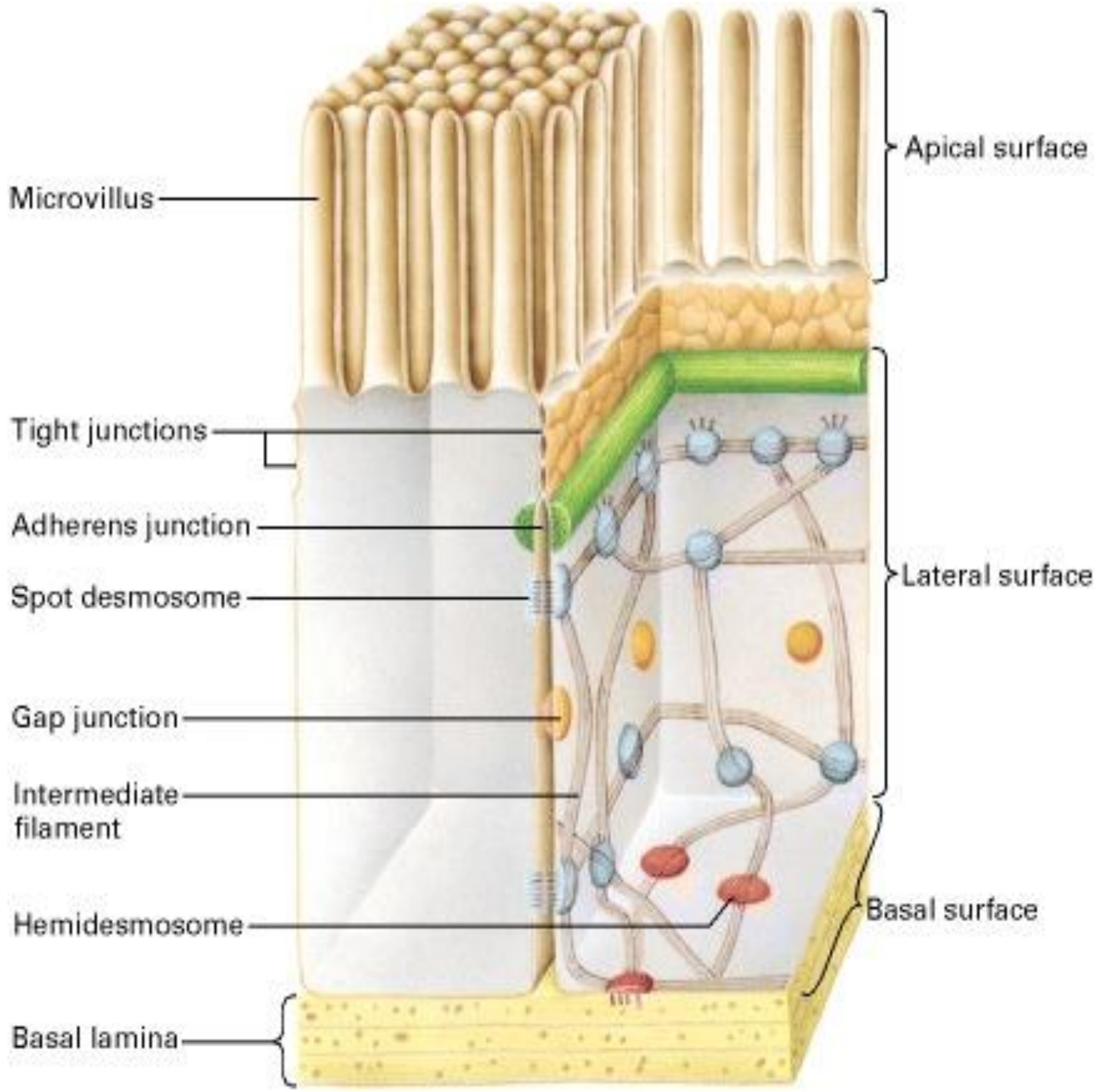
Alberts et al. Molecular Biology of the Cell, 5th edition

Na^+-K^+ ATPase (Na^+-K^+ pump)

- ATP-driven pump
- Member of a P-type pump family.
- Extremely important in maintaining intracellular and extracellular concentration differences of sodium and potassium.
- A typical animal cell uses 1/3 of its energy for this pump to work.
- The Na + gradient it creates
  - Transport of many nutrients across the membrane
  - Regulation of cytosolic pH
  - Regulation of osmolarity

2. Ion greadient_driven pumps: Secondary active transport

Epithelial cells are highly polarized



Transport of molecules across epithelium

- **Paracellular transport:** H_2O and small molecules
- **Transcellular transport:** Passing directly through the cell
- **Transcytosis:** Passing through the cell by vesicles

Transport of glucose in the small intestine epithelium

- ✓ **Na^+-K^+ ATPase** localized to the basolateral membrane
- ✓ Symporter SGLT1 restricted to the apical membrane: **Na^+/glucose symporter**
- ✓ **Uniporter GLUT5** restricted to basolateral membrane

Movement of water across an epithelium

- Net movements of water across an epithelium are dependent on net solute movements.
- The active transport of Na+ across the cells and into the surrounding interstitial spaces produces an elevated osmolarity in this region and a decreased osmolarity in the lumen.
- This leads to the osmotic flow of water across the epithelium in the same direction as the net solute movement.
- The water diffuses through aquaporins in the membrane (transcellular pathway) and across the tight junctions between the epithelial cells (paracellular pathway).