Body Fluids:

1) **Water**: (universal solvent)

Body water varies based on age, sex, mass, and body composition.

- $H_2O \sim 73\%$ body weight
  - Low body fat;
  - Low bone mass

- $H_2O (♂) \sim 60\%$ body weight
- $H_2O (♀) \sim 50\%$ body weight
  - $♀ = \uparrow$ body fat / $↓$ muscle mass

- $H_2O \sim 45\%$ body weight
Body Fluids:

1) **Water**: (universal solvent)

**Total Body Water**
- **Volume = 40 L**
  - (60% body weight)

**Intracellular Fluid (ICF)**
- **Volume = 25 L**
  - (40% body weight)

**Extracellular Fluid (ECF)**
- **Volume = 15 L**
  - (20% body weight)

**Plasma**
- **Volume = 3 L**

**Body Fluids:**

2) **Solute**

A) **Non-electrolytes**
- (do not dissociate in solution – neutral)
  - Mostly organic molecules
    - (e.g., glucose, lipids, urea)

B) **Electrolytes**
- (dissociate into ions in solution – charged)
  - Inorganic salts
  - Inorganic / organic acids
  - Proteins

**Units for measuring [solute]:**

A) **mole / liter (mol / L)**
- mole = 6.02 x 10^{23} molecules
  - A glucose concentration of 1 mol / L has
    6.02 x 10^{23} glucose molecules in 1 L of solution

B) **osmoles / liter (osmol / L)**
- osmole = # of particles into which a
  solute dissociates in solution
  - 1 mol / L of NaCl is equal to 2 osmol / L
    because NaCl dissociates into two particles

C) **equivalents / liter (Eq / L)**
- equivalent = # of moles x valence
  - 1 mol / L of CaCl_{2} equates to 2 Eq / L of Ca^{2+}
    and 2 Eq / L of Cl^{-} in solution

D) **pH** (used to express H^{+} concentration)
- pH = -\log_{10} [H^{+}]
  - A [H^{+}] of 6.5 x 10^{-8} Eq / L equates to a pH of 7.19
Body Fluids:

2) **Solutions:**

- The solute composition varies greatly between the ECF and ICF

Each body fluid compartment has the same concentration, in mEq/L, of positive ions (cations) and negative ions (anions)

(Principle of Macroscopic Electroneutrality)

The total solute concentration (osmolarity) is the same in ICF and ECF

(water moves freely across cell membranes)

*HOWEVER*

<table>
<thead>
<tr>
<th>Substance</th>
<th>ECF (mEq/L)</th>
<th>ICF (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>140</td>
<td>14</td>
</tr>
<tr>
<td>K⁺</td>
<td>4</td>
<td>120</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>2.5</td>
<td>1 x 10⁻⁴</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>105</td>
<td>10</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>pH</td>
<td>7.4</td>
<td>7.1</td>
</tr>
<tr>
<td>Osmolarity (mOsm/L)</td>
<td>290</td>
<td>290</td>
</tr>
</tbody>
</table>

The differences in solute concentration across cell membranes are created and maintained by transport mechanisms in cell membranes
Cell Membrane Structure:

**Fluid mosaic model**

A) **Lipid bilayer**
   - Phospholipids (amphipathic)
   - Functional barrier

B) **Integral proteins**
   - Transport proteins
   - Pore / channel proteins
   - Anchor proteins (CAMs)
   - Receptor proteins

C) **Peripheral proteins**
   - Anchor proteins
   - Enzymes

**Transport Mechanisms:**

Simple Diffusion:
Substances diffuse directly through membrane or through channel (no interaction with protein)

Factors affecting net diffusion (flux):

1) Concentration gradient ($C_A - C_B$)
   - $\uparrow$ concentration gradient = $\uparrow$ flux

2) Partition coefficient (K)
   - $K = \frac{[\text{solute}] \text{ in oil}}{[\text{solute}] \text{ in water}}$
   - $\uparrow K = \uparrow$ flux

3) Thickness of membrane ($\Delta x$)
   - $\downarrow$ thickness = $\uparrow$ flux

4) Size of solute molecule
   - $\downarrow$ size = $\uparrow$ flux

5) Viscosity of medium
   - $\downarrow$ viscosity = $\uparrow$ flux

6) Surface area (A)
   - $\uparrow$ surface area = $\uparrow$ flux

Guyton & Hall (Textbook of Medical Physiology, 12th ed.) – Figure 2.3
Transport Mechanisms:

**Simple Diffusion:**
Substances diffuse directly through membrane or through channel (no interaction with protein)

- Downhill transport
- Lipid bilayer

Determining rate of net diffusion:

\[
J = PA (C_A - C_B)
\]

- \( J \) = Net rate of diffusion (mmol/sec)
- \( P \) = Permeability (cm/sec)
- \( A \) = Surface area for diffusion (cm^2)
- \( C_A \) = Conc. of solution A (mmol/L)
- \( C_B \) = Conc. of solution B (mmol/L)

* Includes K, D, and membrane thickness

**Facilitated Diffusion:**
Substances interact with carrier proteins (conformational/chemical changes)

- Downhill transport
- Lipid bilayer

Characteristics of carrier-mediated transport: Saturation

**Stereospecificity:**
- Recognize specific molecular isomers

<table>
<thead>
<tr>
<th>D-glucose</th>
<th>L-glucose</th>
</tr>
</thead>
</table>

**Competition:**
- Recognize chemically-related solutes

<table>
<thead>
<tr>
<th>D-glucose</th>
<th>D-galactose</th>
</tr>
</thead>
</table>

Chemical gradient
Transport Mechanisms:

**Saturation:**

Rate of Diffusion

\[ \text{Rate of Diffusion} = \frac{\text{Concentration of Substance}}{V_{\max}} \]

**WHY?**

- **Simple diffusion**
  - Increase # of carrier proteins

- **Facilitated diffusion**
  - Process takes time

**Transport maximum** \( (T_{\text{Max}}) \)

Ultimately, all carriers actively involved in shuttling substances

---

**Primary Active Transport:**

Energy derived from the breakdown of ATP is directly coupled to the transport process

**Other examples:**
- \( \text{Ca}^{2+} \) pump
- \( \text{H}^+ / \text{K}^+ \) pump

**Na\(^+ / \text{K}^+ \) Pump:**

- **Outside**
  - \( \text{Na}^+ \): 142 mEq/L
  - \( \text{K}^+ \): 4 mEq/L

- **Inside**
  - \( \text{Na}^+ \): 10 mEq/L
  - \( \text{K}^+ \): 140 mEq/L

Two sub-units:
- \( \alpha \) subunit
- \( \beta \) subunit

**Guyton & Hall (Textbook of Medical Physiology, 12th ed.) – Figure 4.8**

**Guyton & Hall (Textbook of Medical Physiology, 12th ed.) – Figure 4.11**
**Transport Mechanisms:**

**Primary Active Transport:**
Energy derived from the breakdown of ATP is directly coupled to the transport process.

**How much energy is required for active transport?**

It depends on the strength of the concentration gradients being established…

Energy (cal/osmole) = $1400 \log (C_1 / C_2)$

- $10x = 1400 \text{ cal}$
- $100x = 2800 \text{ cal}$

May require 60–90% of cell's energy!

**Secondary Active Transport:**
Energy derived from concentration gradient established by primary active transport.

**A) Cotransport (symport)**
Solutes transported in the same direction across membrane.

Both solutes required for transporter to function

---

Costanzo (Physiology, 4th ed.) – Figure 1.7
**Transport Mechanisms:**

- **Uphill transport** (metabolic energy required)

**Lipid bilayer**

**Secondary Active Transport:**

Energy derived from concentration gradient established by primary active transport

**B) Countertransport (antiport)**

Solute transported in opposite directions across membrane.

Both solutes required for transporter to function.

---

**Prescription Drug:**

**Cardiac glycosides** are a class of drugs that inhibit Na⁺/K⁺ pumps.

**Digitalis**

A cornerstone for the treatment of heart failure (↑ cardiac contractility)

**Common foxglove**

*Digitalis purpurea*
Osmosis:

Movement of water across a semi-permeable membrane due to differences in solute concentrations.

Osmosis depends on the osmolarity of the two solutions in question:

\[ \text{Osmolarity} = g \cdot C \] (mOsm / L)

- \( g \) is the number of particles per mole in solution (Osm / mol)
- Takes into account whether there is complete or partial dissociation
- \( C \) is concentration (mmol / L)

- Isosmotic: Solutions with same osmolarity
- Hyperosmotic: Solution with ↑ osmolarity
- Hyposmotic: Solution with ↓ osmolarity

Osmotic pressure (\( \pi \)) depends on:

1. Concentration of osmotically active particles
2. Ability of solute to cross membrane

\[ \pi = g \cdot C \cdot \sigma \cdot R \cdot T \]

- \( \pi \) is Osmotic pressure (atm)
- \( g \) is # of particles per mole in solution (Osm / mol)
- \( C \) is Concentration (mmol / L)
- \( \sigma \) is Reflection coefficient (varies from 0 – 1)
- \( R \) is Gas constant (0.082 L – atm / mol – K)
- \( T \) is Absolute temperature (K)

25.5 L = atm / mol

Guyton & Hall (Textbook of Medical Physiology, 12th ed.) – Figure 4.10
Osmosis:

Reflection coefficient: Ease at which a solute crosses a membrane

\[ \pi = g \, C \, \sigma \, R \, T \]

Tonicity: The effective osmotic pressure between two solutions

Isotonic:

Net water movement from a hypotonic solution to a hypertonic solution

Costanzo, Physiology, 4th ed.) – Figure 1.10