

Biochemistry fundamentals

BIOS 1006

17 June 2025

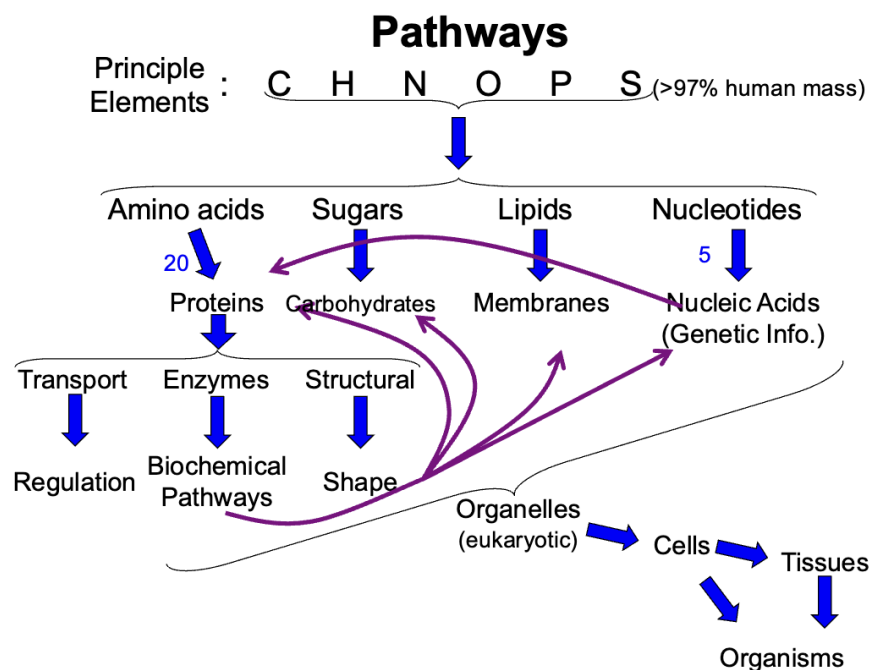
Objectives

- Know all definitions.
- Know the basic atoms that comprise biological systems.
 - CHNOPS (carbon, hydrogen, nitrogen, oxygen, phosphorus, sulphur)
- Describe why carbon is ideal for forming the skeleton of biomolecules.
 - Carbon is flexible
 - Can form 4 covalent bonds
 - Carbon can form single, double, and triple bonds
 - Forms chains, branched chains, and rings
- Name and draw the common functional groups found in biomolecules.
 - Hydroxyl -OH (alcohol)
 - Carbonyl C=O (ketone C=O (carbonyl in the middle) vs aldehyde -CHO)
 - Carboxyl -COOH (acids)
 - Amino -NH_2 (amine)
 - Amido -C(=O)NH_2 (amide)
 - Sulfhydryl -SH (thiol)
 - Phosphate -PO_4^{3-} (phosphate)
 - Ester -COOR (ester)
- Recognize different molecular representations and draw abbreviated and expanded structural formulae.
- Describe the four basic building that comprise biological systems, their different sub-classifications, and the four major classes of biomolecules that they form. Identify to which class of the four basic building blocks a small molecule belongs or is related.

- Amino acids → polypeptides (proteins)
- Lipids (fatty acids) → triglycerides, phospholipids, steroids, membranes
- Carbohydrates (sugars) → polysaccharides
- Nucleotides → nucleic acids (DNA, RNA)
- Describe the properties of water that make it an ideal solvent for life.
 - Polarity
 - High heat of vaporization
 - Hydrogen bonding
 - Cohesion and adhesion
 - Less dense as a solid
 - High specific heat
 - Neutral pH
- Describe the properties of hydrogen bonds and what is required for them to be formed.
 - Strongest van der Waals interaction
 - Collinear orientation
 - Electrostatic interaction
 - Individually weak but collectively strong
 - Dynamic
 - Requires a donor (N-H, O-H, F-H) and acceptor (has free lone pair)
- Describe the three types of “weak” interactions, the types of groups that participate in these interactions and the role they play in solvation and biomolecular structure.
 - Three types of weak interactions: **hydrogen bonds, dipole-dipole interactions, London dispersion forces (LDFs)**
 - Hydrogen bonds: occur when a hydrogen atom covalently bonded to an electronegative atom (N-H, O-H, F-H) interacts with another electronegative atom bearing a lone pair of electrons. Water forms extensive hydrogen bonds with polar solutes, aiding in their dissolution. In biomolecular structure, H-bonds stabilize protein secondary structures (alpha helices and beta sheets) and DNA base pairing.
 - Dip-dip interactions: occur between fully charged ions or between ionized groups of opposite charge. Water stabilizes ions by surrounding them with its polar molecules (ion-dipole interaction), helping salts dissolve. Salt bridges in proteins help stabilize tertiary and quaternary structures.

- LDFs (induced dipole-induced dipole): weak, transient interactions arising from induced dipoles between closely packed nonpolar atoms or molecules. Poorly solvated in water and are not very stable.
- Describe Lennard-Jones plots and use them to describe and predict interactions between molecules.
 - When molecules are far apart (large radius), there is no interaction
 - As they approach each other, attraction appears. The most stable configuration is at the equilibrium point.
 - When molecules are too close together and reach past the van der Waals radius, repulsion occurs. Molecules are unstable.
- Describe the hydrophobic effect and van der Waals interactions and describe their different roles in biomolecular structure.
 - The hydrophobic effect is the tendency of nonpolar molecules to aggregate in aqueous solutions to minimize their exposure to water. This is driven by an increase in entropy of the water molecules surrounding the hydrophobic groups.
 - Van der Waals interactions are weak, transient interactions that occur between nonpolar molecules. They are additive and become stronger when many of them are present.
- Describe the properties and principles of buffers and buffering capacity.
 - Buffers consist of a weak acid and its conjugate base or a weak base and its conjugate acid
 - Resist changes in pH when acids or bases are added
 - Buffering capacity is greatest when the concentrations of the weak acid and its conjugate base are equal
- Calculate the pH from the concentration of H^+ and vice versa. (See 2 for the formula.)
- Calculate the pH, pKa or the amounts of acid and conjugate base using the Henderson-Hasselbalch equation. (Use ICE tables, pH, pKa, and the ratio of concentration between the conjugate base and acid)
- Predict protonation state of a group based on its pKa and the buffer pH.
- Describe the physiologically important buffers.
 - Bicarbonate buffer system $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$
 - Phosphate buffer system $H_2PO_4^- + H_2O \rightleftharpoons H_3O^+ + HPO_4^{2-}$
 - Protein buffer system (amino acids can act as weak acids or bases)
 - Ammonia buffer system $NH_3 + H^+ \rightleftharpoons NH_4^+$

The biological building blocks



Functional groups

(R denotes a generic hydrocarbon chain)

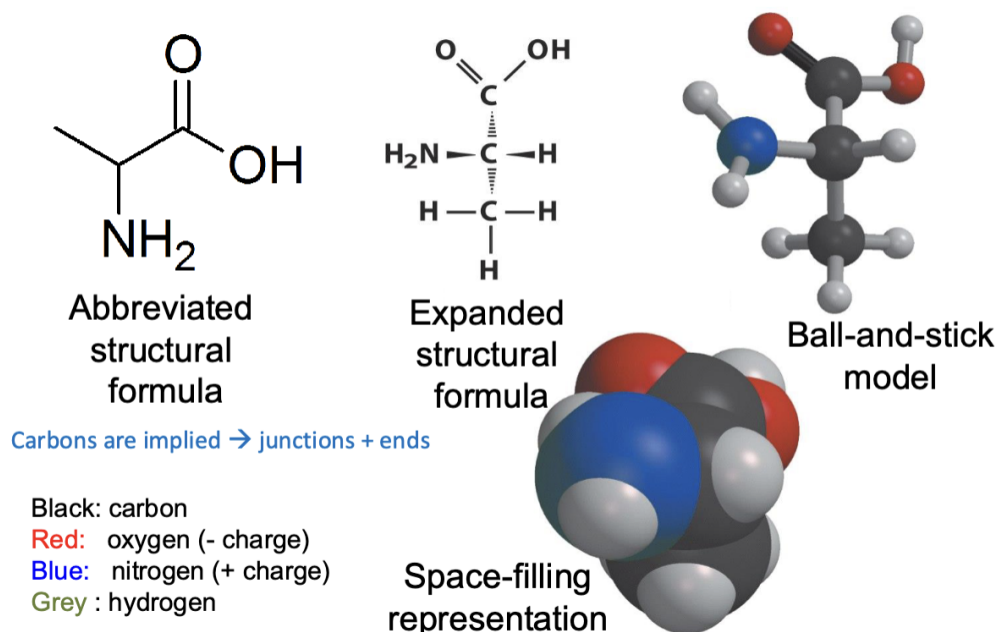
Memorize!

Family Name	Group Structure	Group Name	Significance
Alcohol	$\text{R}-\text{OH}$	Hydroxyl	Polar (and therefore water-soluble), forms hydrogen bonds
Aldehyde	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{H} \end{array}$	Carbonyl	Polar, found in some sugars
Ketone	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{R}' \end{array}$	Carbonyl	Polar, found in some sugars
Acids	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{OH} \end{array}$	Carboxyl	Weakly acidic, bears a negative charge when it donates a proton
Amine	$\text{R}-\text{NH}_2$	Amino	Weakly basic, bears a positive charge when it accepts a proton
Amide	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{NH}_2 \end{array}$	Amido	Polar but does not bear a charge
Thiol	$\text{R}-\text{SH}$	Thiol	Easily oxidized; can form $-\text{S}-\text{S}-$ (disulfide) bonds readily
Ester	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{O}-\text{R}' \end{array}$	Ester	Found in certain lipid molecules
Alkene	$\text{RCH}=\text{CHR}'$	Double bond	Important structural component of many biomolecules (e.g., found in lipid molecules)

+ phosphate (PO_4^{3-})

- Hydroxyl + carbonyl \rightarrow carboxyl
- Amine + carbonyl \rightarrow amide
- Aldehyde has carboxyl at the **end**; **ketone** has it in the **middle**

Representations of molecules



The four major classes

Amino acids

- Hundreds of naturally occurring forms
- Defined by the presence of amine and carboxylic acid groups
- Classified based on the proximity of these groups
- Three different classes: α , β , and γ based on which carbon is attached to the amine (closest to the central carbon is α , next is γ , etc.)
- α amino acid (most common): **amine** attached to α **carbon** (1 away from the central carbon), carboxyl and an **R group** (side chain, 20 different common types)
- **Peptide** or **amide** bonds link amino acids together (form amide group with the carboxyl group + amine group)

Sugars (carbohydrates)

- Molecules containing carbonyl and hydroxyl functional groups
- Two classes: **ketose** and **aldose** sugars (carbonyl in the middle = ketose, at the end = aldose, same as functional groups)
- Hydrated carbons
- Very hydrophilic

Lipids

- Soluble in hydrophobic solutions
- Do not polymerize but form higher order structures
- Fatty acids

Nucleotides

- 3 basic components: phosphate group(s), ribose, nitrogenous base
- Polymerize into: DNA (deoxyribose, adenosine, cytosine, guanine, thymine); RNA (ribose, adenosine, cytosine, guanine, uracil)
- **Purines** (2 rings) and **pyrimidines** (1 ring)
- Mnemonics: “Pure As Gold” (adenine and guanine are purines) and “CUT the Py” (cytosine, thymine, and uracil are pyrimidines)

Water (H₂O): the biological solvent

Physical properties of water

- Solvent characteristics
- Non-compressible
- Chemical stability
- Biochemical reactant
- Hydration of molecules
- Participates in biomolecular interactions
- Ice floats
- High boiling and freezing temperatures
- High heat of vaporization
- High specific heat capacity
- High surface tension
- Dissolves molecules with ionizable or polarizable functional groups but cannot dissolve nonpolar or hydrophobic molecules

Molecular properties of water

- **Tetrahedral** electron geometry (104.5 degrees), sp³ hybridized, 0.99 Å from H to O
- Electronegativity results in the formation of **polar bonds**
- Forms **hydrogen bonds** (hydrogen is attracted to the lone pair electrons of an oxygen from another molecule)

Properties of hydrogen bonds

- **Oxygen, nitrogen, and fluorine** can form hydrogen bonds (very electronegative)
- Require a donor (has H attached) and acceptor (has free lone pair)
- Hydrogen bonds in between casual interaction and covalent interaction in terms of proximity
- Both covalent and electrostatic properties
- Collinear orientation (present in a straight line)
- Other orientations possible but not as strong
- Electrostatic interaction

- Atoms involved share electrons
- In liquid water, 3.4 neighbors on average (4 in ice)
- Hydrogen bonds can be disrupted by water

Weak interactions

- Weak interactions are constantly being formed and broken between biomolecules (more transient)
- Additive (can become strong)
- Essential for rapid communication
- Allows for flexibility
- Three types of weak electrostatic interactions
 - **Salt bridges** (ionic)
 - **Van der Waals interactions**
 - **Hydrogen bonds**

Relative strengths of interactions

Strongest to weakest

- Intramolecular forces
 - Ionic bonds
 - Covalent bonds
- Intermolecular forces (IMFs)
 - Ionic interactions and salt bridges
 - Van der Waals forces:
 - * Hydrogen bonds
 - * Dipole-dipole interactions
 - * London dispersion forces (LDFs)

Salt bridges and ionic interactions

- One positive interacting with one negative with full electrical charges (ionic bonds are NOT salt bridges)
- Interaction strength calculated from Coulomb's law:

$$F = \frac{1}{4\pi\epsilon_0} \frac{q_1 q_2}{\epsilon_r r^2}$$

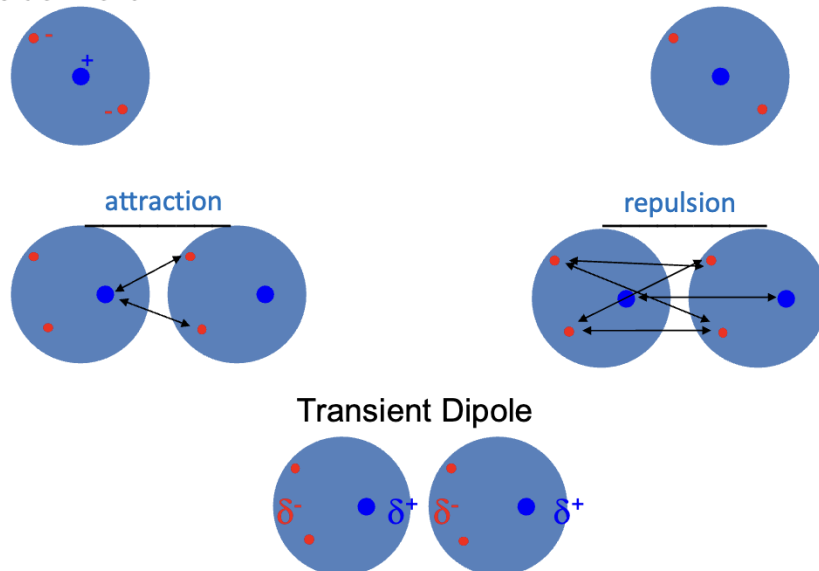
- F is interaction strength
- q_1 and q_2 are signed charges
- r is the distance between centers
- ϵ_r is the dielectric constant
- All others are constants
- Water is good at breaking ionic bonds
- **Hydration shells** prevent ionic bonds from reforming

Dipole interactions

- Occur between molecules that have or can adopt a **dipole moment** (μ)
- Three types
 - **Dipole-dipole interactions** (fixed dipoles)
 - **Dipole-induced dipole interactions** (fixed dipole and nonpolar)
 - **Induced dipole-induced dipole interactions (London Dispersion)** (nonpolar and nonpolar)

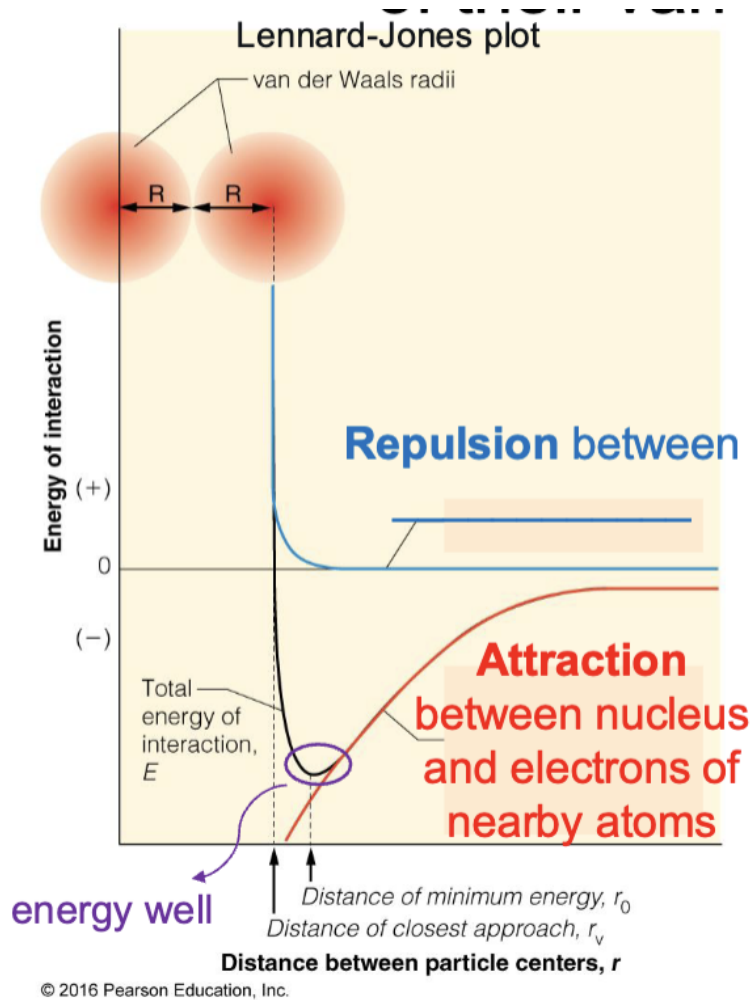
LDFS: a type of van der Waals interaction between non-polar molecules

Consider helium:



Electrons are constantly moving creating transient dipoles in nonpolar molecules

Lennard-Jones plot



Atoms come together until they reach the **van der Waals distance/radius** at which point they begin to repel each other

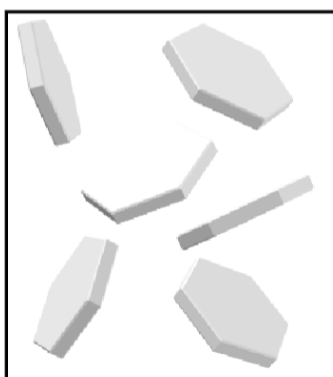
Hydrophobic molecules

- Oil and water do not mix - oil is hydrophobic
- Hydration shells will still form, but they are not stabilized
- The separation of water and hydrophobic molecules is driven by the **hydrophobic effect**
- Favorable because there is an increase in **entropy**
- Second law of thermo: All spontaneous processes result in an overall increase of entropy in the universe ($\Delta S_{\text{universe}} > 0$)

- Nonpolar-nonpolar - shell of hydration, but less water that forms the shell. More water ends up in the system, increasing water entropy and increasing overall entropy (energetically favorable)
- The overall entropy increases when only one cage is formed
- Hydrophobic effect drives the folding of proteins
- **Hydrophobic R-groups are forced into the core; hydrophilic R-groups form a shell** around the hydrophobic core. **Van der Waals forces organize amino acids** in the core
- Molecules with hydrophilic and hydrophobic “sides” (example: phospholipids) forming micelles and bilayers

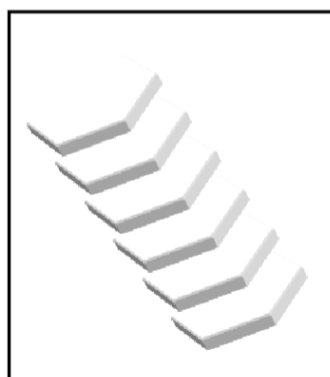
Hydrophobic effect vs. van der Waals

Hydrophobic Effect



Forces hydrophobic molecules into a box

Van der Waals

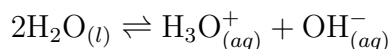


Arranges molecules in the box

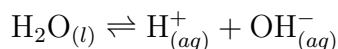
pH

- Hydrogen ions (H^+ , “protons”) can be gained or lost by some functional groups changing the properties of functional groups
- pH is tightly regulated by the body at 7.4
- A change greater than 0.5 pH units can lead to coma or death

A small amount of water ionizes:



For simplicity:



Dissociation constant formula

$$K_w = [\text{H}^+][\text{OH}^-] \quad (1)$$

Calculation of pH and pOH

$$\text{pH} = -\log[\text{H}^+] \quad (2)$$

$$\text{pOH} = -\log[\text{OH}^-] \quad (3)$$

Acids and bases

- **Brønsted acids** are H^+ donors
- **Brønsted bases** are H^+ acceptors
- A **strong acid** or **strong base** is **completely ionized** in water ($A + B \rightarrow C + D$)
- **Weak acids** are **incompletely ionized** in aqueous solutions ($A + B \rightleftharpoons C + D$)
- Charges depend on the functional group
- Acid becomes conjugate base; base becomes conjugate acid
- Weak acid and its conjugate bases reach equilibrium in solution

Acid dissociation formula

$$K_a = \frac{[\text{H}^+][\text{conjugate base}]}{[\text{weak acid}]} \quad (4)$$

Larger K_a (dissociation constant) = stronger acid

ICE table (for weak acids only)

Initial	100 mmol	0	0
Change	-X	+X	+X
End	100 mmol - X	+X	+X

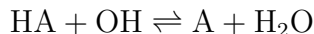
Le Châtelier's Principle

The degree to which a weak acid is dissociated depends on the pH of the system (if you decrease something, how does equilibrium shift?)

$$K_a = \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]} \quad (5)$$

Titration

A strong/weak acid or a strong/weak base is always titrated with a **strong acid/base** (neutralization reaction)



- **Equivalence point** occurs when **all HA is neutralized**
- **Half equivalence** happens in the buffer region (flat part before the equivalence point) halfway between the start and the equivalence point, where $\text{pH} = \text{pKa}$ and the concentration of the weak acid is equal to the concentration of the conjugate base
- Buffering is best on the flat part of the curve
- pH (potential of hydrogen) = pKa (strength of weak acid)

Henderson-Hasselbach equation for weak acid/conjugate base or weak base/conjugate acid:

$$\text{pH} = \text{pKa} + \log \frac{[\text{A}^+]}{[\text{HA}]} \quad (6)$$

Maximum buffering capacity when $[\text{HA}] = [\text{A}^-]$

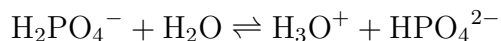
Buffers

A buffer resists changes in pH. Buffers form weak acid/conjugate base or weak base/conjugate acid pairs.

Bicarbonate buffer is one of the more important buffers in blood.



Phosphate buffer is important in cells, particularly intracellular fluids.



Proteins have ionizable side chains that can act as buffers. Haemoglobin, for example, helps maintain the pH of blood.