# Biochemistry fundamentals

## BIOS 1006

## 17 June 2025

## Objectives

- Know all definitions.

- Know the basic atoms that comprise biological systems. (CHNOPS)

- Describe why carbon is ideal for forming the skeleton of biomolecules.

- Name and draw the common functional groups found in biomolecules.

- 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.

- Describe the properties of water that make it an ideal solute for life.

- Describe the properties of hydrogen bonds and what is required for them to be formed.

- 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.

- Describe Lennard-Jones plots and use them to describe and predict interactions between molecules.

- Describe the hydrophobic effect and van der Waals interactions and describe their different roles in biomolecular structure.

- Describe the properties and principles of buffers and buffering capacity.

- Calculate the pH from the concentration of $H^+$ and vice versa.

- Calculate the pH, pKa or the amounts of acid and conjugate base using the Henderson-Hasselbalch equation.

- Predict protonation state of a group based on it pKa and the buffer pH.

- Describe the physiologically important buffers.

# Definitions

**dipole moment ($\mu$)** separation of charges due to differences in electronegativity

**electrostatic** involves charges

**functional groups** specific groups of atoms within molecules that are responsible for the molecule's characteristic chemical reactions

**hydrophobic** "water hating"

**solute** in a solution, dissolved in a solvent

**solvent** in a solution, dissolves the solute

**van der Waals distance/radius** the distance where the attractive and repulsive forces between two nonbonded atoms are equal

**weak interactions** weaker, transient interactions that are additive and can become stronger

# The biological building blocks
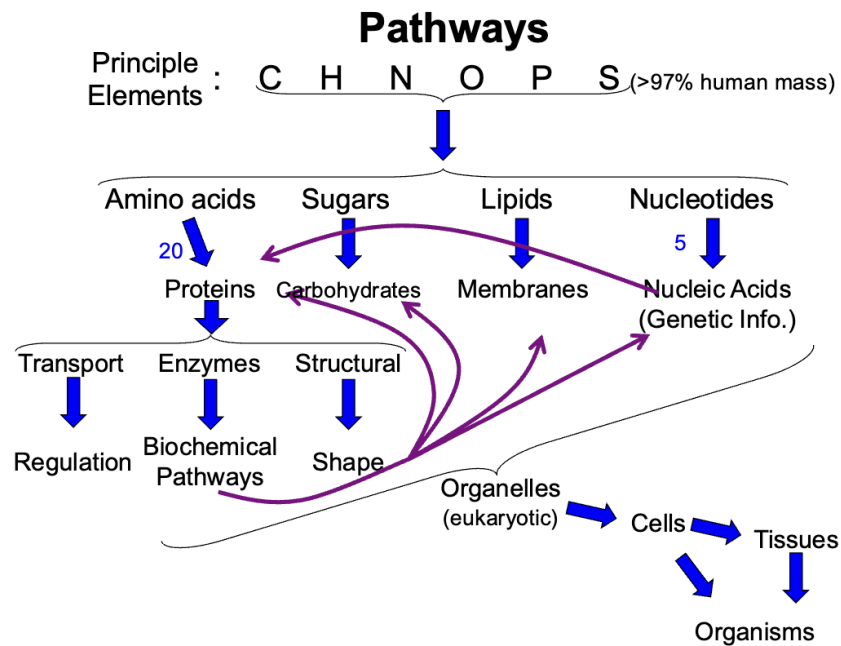


## Functional groups
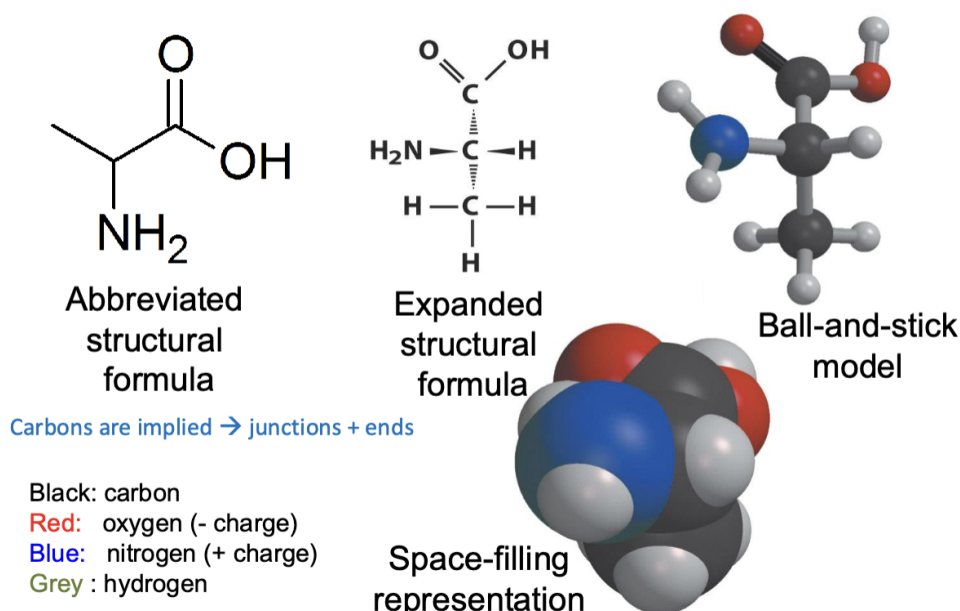
(R denotes a generic hydrocarbon chain)

Memorize!

| Family Name | Group Structure | Group Name | Significance |
|---|---|---|---|
| Alcohol | R—OH | Hydroxyl | Polar (and therefore water-soluble), forms hydrogen bonds |
| Aldehyde | $\overset{\displaystyle O}{\underset{\displaystyle R-C-H}{\|\|}}$ | Carbonyl | Polar, found in some sugars |
| Ketone | $\overset{\displaystyle O}{\underset{\displaystyle R-C-R'}{\|\|}}$ | Carbonyl | Polar, found in some sugars |
| Acids | $\overset{\displaystyle O}{\underset{\displaystyle R-C-OH}{\|\|}}$ | Carboxyl | Weakly acidic, bears a negative charge when it donates a proton |
| Amine | R—NH$_2$ | Amino | Weakly basic, bears a positive charge when it accepts a proton |
| Amide | $\overset{\displaystyle O}{\underset{\displaystyle R-C-NH_2}{\|\|}}$ | Amido | Polar but does not bear a charge |
| Thiol | R—SH | Thiol | Easily oxidized; can form —S—S— (disulfide) bonds readily |
| Ester | $\overset{\displaystyle O}{\underset{\displaystyle R-C-O-R'}{\|\|}}$ | Ester | Found in certain lipid molecules |
| Alkene | RCH=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 → amide**
- **Aldehyde** has carboxyl at the **end**; **ketone** has it in the **middle**

## Representations of molecules



O

OH

NH₂

**Abbreviated structural formula**

Carbons are implied → junctions + ends

Black: carbon
Red:   oxygen (- charge)
Blue:  nitrogen (+ charge)
Grey : hydrogen

O      OH
 \\   /
   C
   ⋮
H₂N — C — H
   |
H — C — H
   |
   H

**Expanded structural formula**

**Ball-and-stick model**

**Space-filling representation**

## 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: $\alpha$, $\beta$, and $\gamma$ based on which carbon is attached to the amine (closest to the central carbon is $\alpha$, next is $\gamma$, etc.)
- $\alpha$ amino acid (most common): **amine** attached to $\alpha$ **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 ($H_2O$): 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), $sp^3$ 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

- Int**ra**molecular forces

    - Ionic bonds

    - Covalent bonds

- Int**er**molecular 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:

$$F = \frac{1}{4\pi\varepsilon_0}\frac{q_1 q_2}{\varepsilon_r r^2}$$

    - $F$ is interaction strength

    - $q_1$ and $q_2$ are signed charges

    - $r$ is the distance between centers

    - $\varepsilon_r$ is the dielectric constant
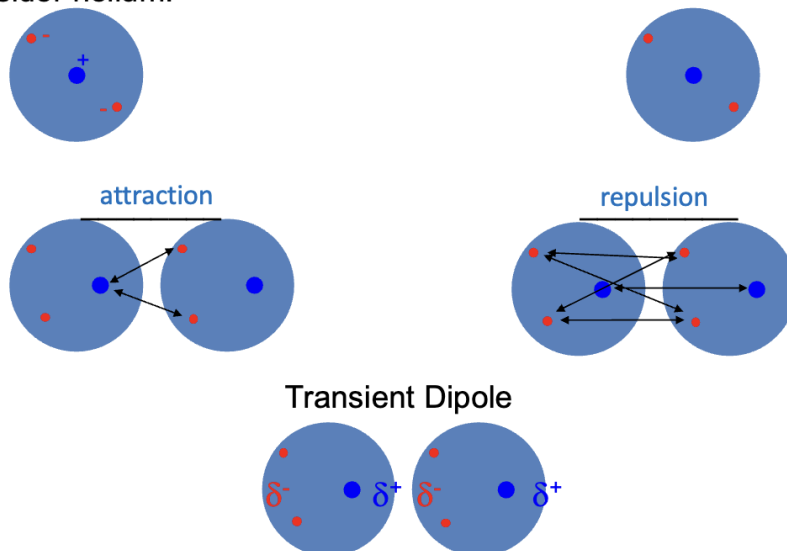
    - All others are constants

- 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** ($\mu$)
- Three types
  - **Dipole-dipole interactions** (fixed dipoles)
  - **Dipole-induced dipole interactions** (fixed dipole and nonpolar)
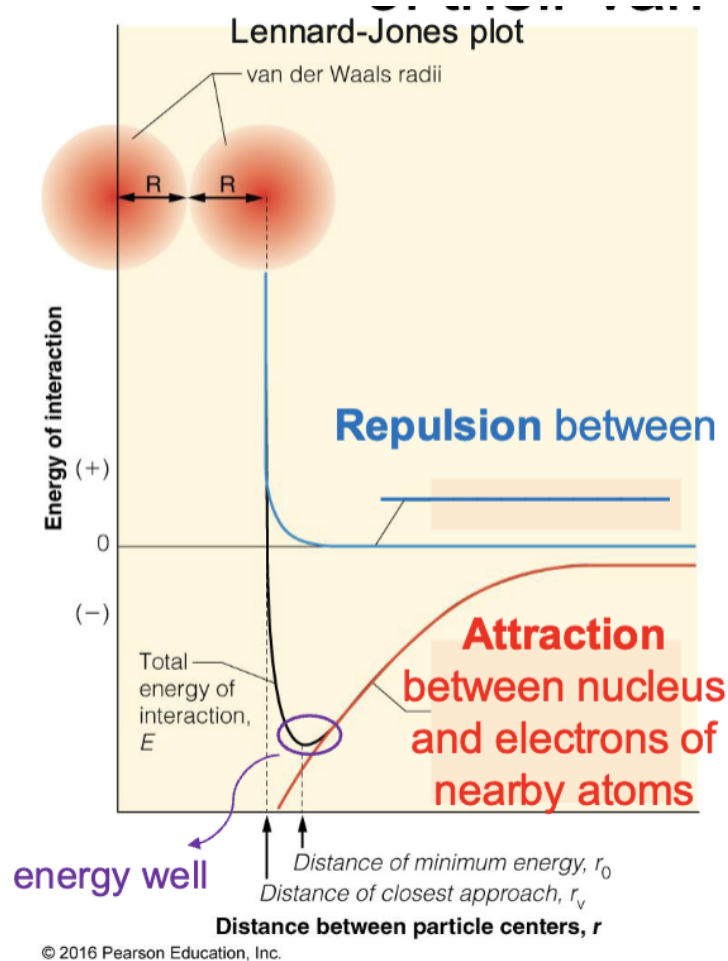  - **Induced dipole-induced dipole interactions (London Dispersion)** (nonpolar and nonpolar)

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

Consider helium:

attraction

repulsion

Transient Dipole

$\delta^-$ $\delta^+$ $\delta^-$ $\delta^+$

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
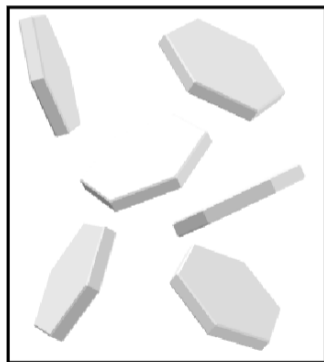
## Hydrophobic molecules

- 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
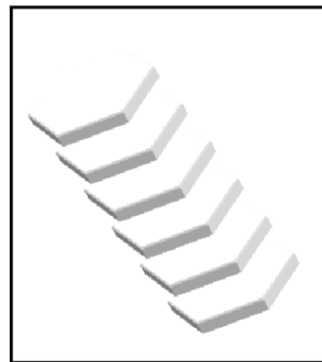
## Hydrophobic effect vs. van der Waals

### Hydrophobic Effect



Forces hydrophobic
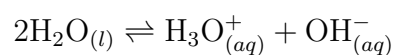molecules into a box

### Van der Waals
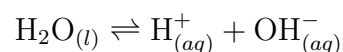


Arranges molecules
in the box

## 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:

$$2H_2O_{(l)} \rightleftharpoons H_3O^+_{(aq)} + OH^-_{(aq)}$$

For simplicity:

$$H_2O_{(l)} \rightleftharpoons H^+_{(aq)} + OH^-_{(aq)}$$

**Dissociation constant formula**

$$K_w = [H^+][OH^-] \tag{1}$$

**Calculation of pH and pOH**

$$pH = -\log[H^+] \tag{2}$$

$$pOH = -\log[OH^-] \tag{3}$$

## 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**

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

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

$$K_a = \frac{[H^+][A^-]}{[HA]} \tag{5}$$