Introduction into Biochemistry

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Course information

- Recommended textbooks
  - Marks' Basic Medical Biochemistry: A Clinical Approach 6th Edition, by Michael Lieberman (Author), Alisa Peet MD (Author), 2023
  - Biochemistry 8th edition by Mary Campbell (Author) and Shawn Farrell (Author)

- Online:

  https://themedicalbiochemistrypage.org/

- Instructors
  - Prof. Nafez Abu Tarboush
  - Prof. Mamoun Ahram

Outline

- Introduction
- Acids and bases, pH, and buffers
- Macromolecules
  - Carbohydrates, lipids, amino acids, peptides, and proteins
- Protein structure-function relationship
  - Part I: Fibrous proteins: collagen, elastin, and keratins
  - Part II: Globular proteins (plasma proteins, myoglobin, hemoglobin, and immunoglobulins)
  - Part III: Regulation of hemoglobin
- Enzymes
  - structural features and classification, kinetics, mechanisms of regulation, cofactors
- Protein purification and analysis

Biochemistry & chemical composition of living organisms

Biochemistry = understanding life

- Know the chemical structures of biological molecules
- Understand the biological function of these molecules
- Understand the interaction and organization of different molecules within individual cells and whole biological systems
- Understand bioenergetics (the study of energy flow in cells)

Biochemistry in medicine:

- ***explains all disciplines***
- ***diagnose and monitor diseases***
- ***design drugs (new antibiotics, chemotherapy agents)***
- ***understand the molecular bases of diseases***

You do not have to know biochemistry to be a physician, but it makes you an elite physician if you do

Chemical elements in living creatures

- The human body is composed mainly of ~30 elements.
- Four primary elements: carbon, hydrogen, oxygen, and nitrogen (96.5% of an organism's weight)
- Then, calcium and phosphorus (that’s 98.5%).
- Others exist in trace amounts but are essential, elements (mostly metals).

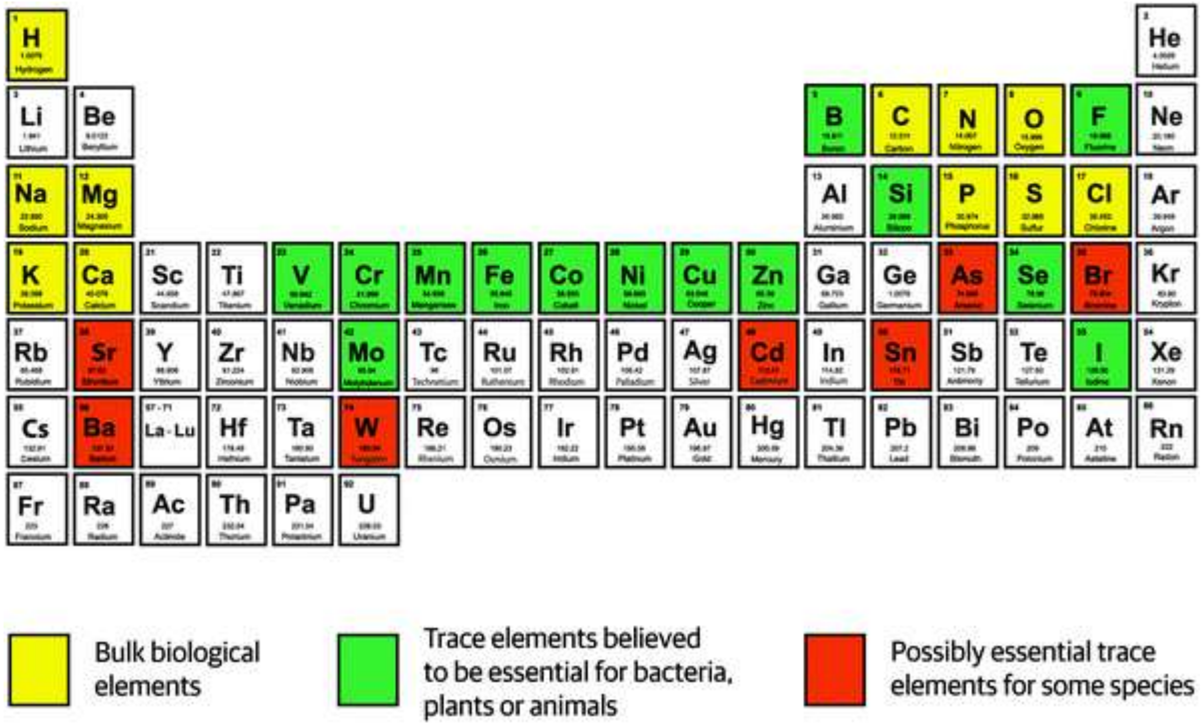


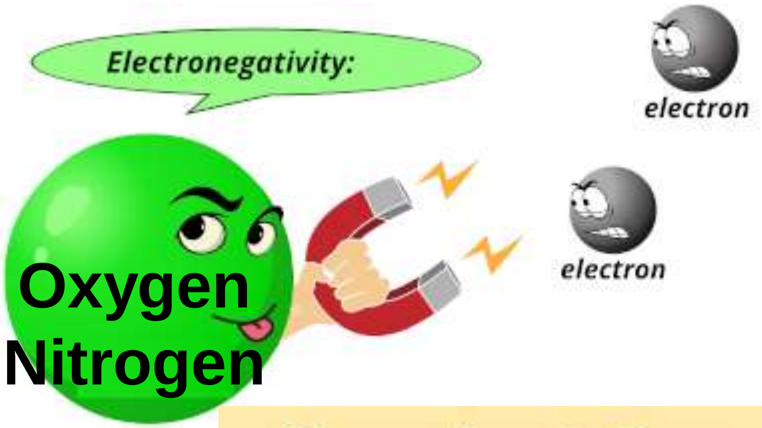
TABLE 2.1 Elements of the Human Body

Name	Symbol	Percentage of Body Weight
Major Elements (Total 98.5%)		
Oxygen	O	65.0
Carbon	C	18.0
Hydrogen	H	10.0
Nitrogen	N	3.0
Calcium	Ca	1.5
Phosphorus	P	1.0
Lesser Elements (Total 0.8%)		
Sulfur	S	0.25
Potassium	K	0.20
Sodium	Na	0.15
Chlorine	Cl	0.15
Magnesium	Mg	0.05
Iron	Fe	0.006

Trace Elements (Total 0.7%)			
Chromium	Cr	Molybdenum	Mo
Cobalt	Co	Selenium	Se
Copper	Cu	Silicon	Si
Fluorine	F	Tin	Sn
Iodine	I	Vanadium	V
Manganese	Mn	Zinc	Zn

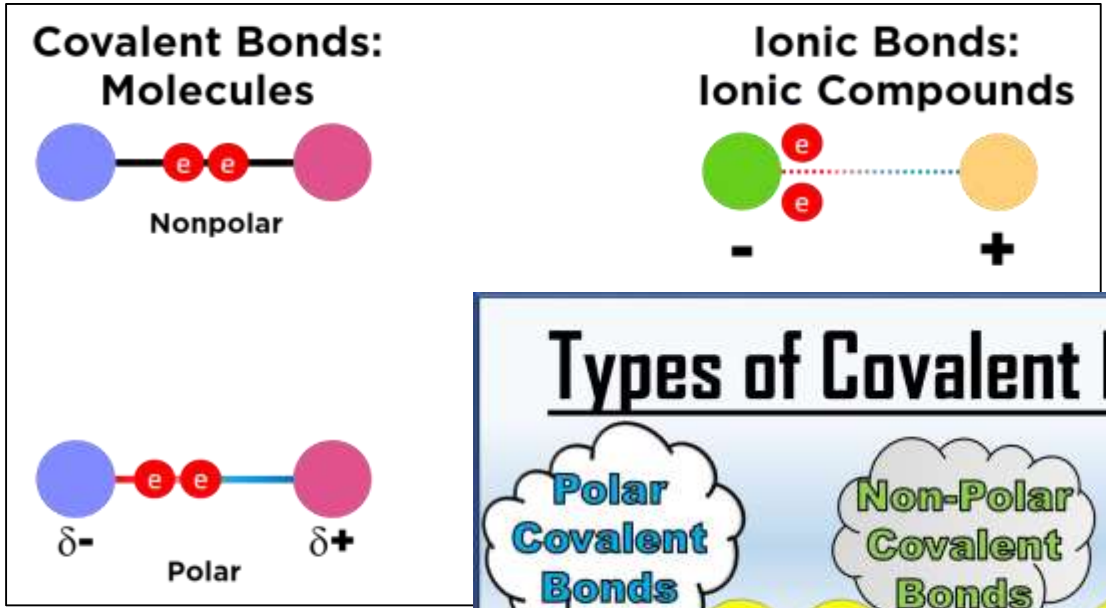
Important terms

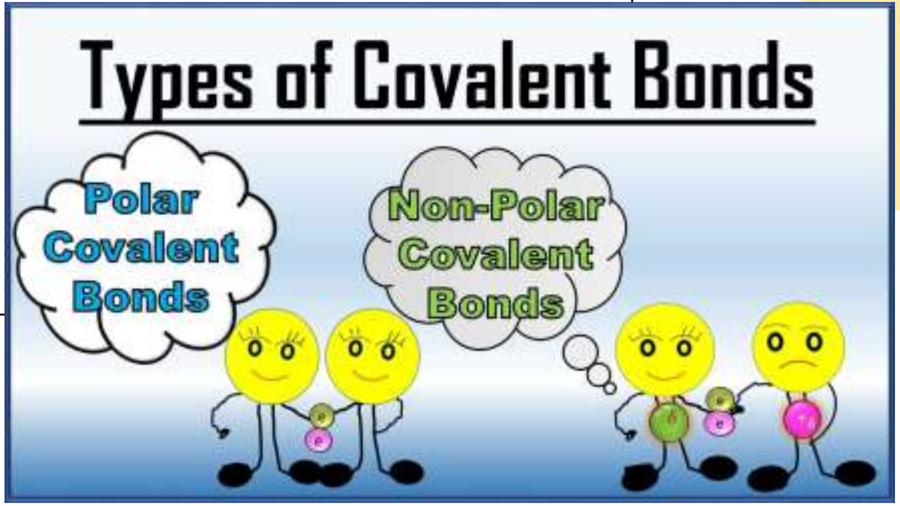
- Electronegativity
- Covalent bonds
  - Polar vs. non-polar covalent bonds
  - Single vs. multiple
- Nucleophile vs electrophile

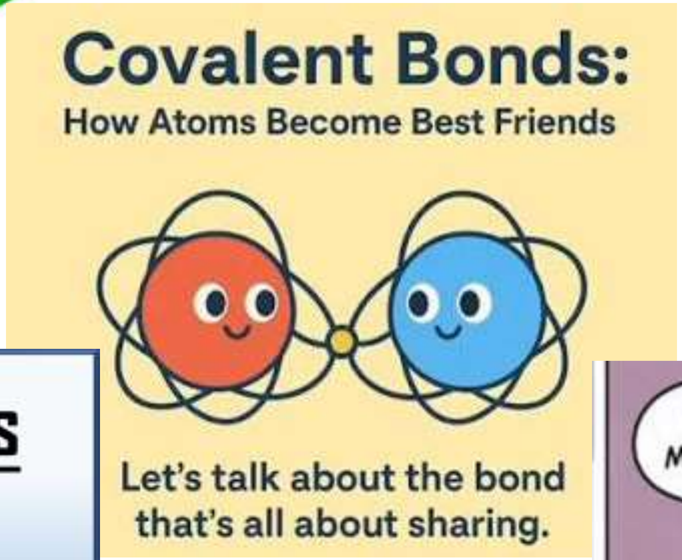


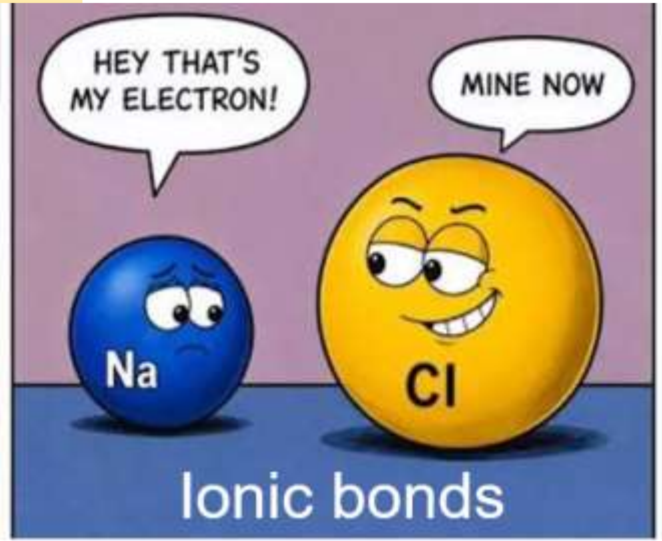
Hydrogen

Carbon



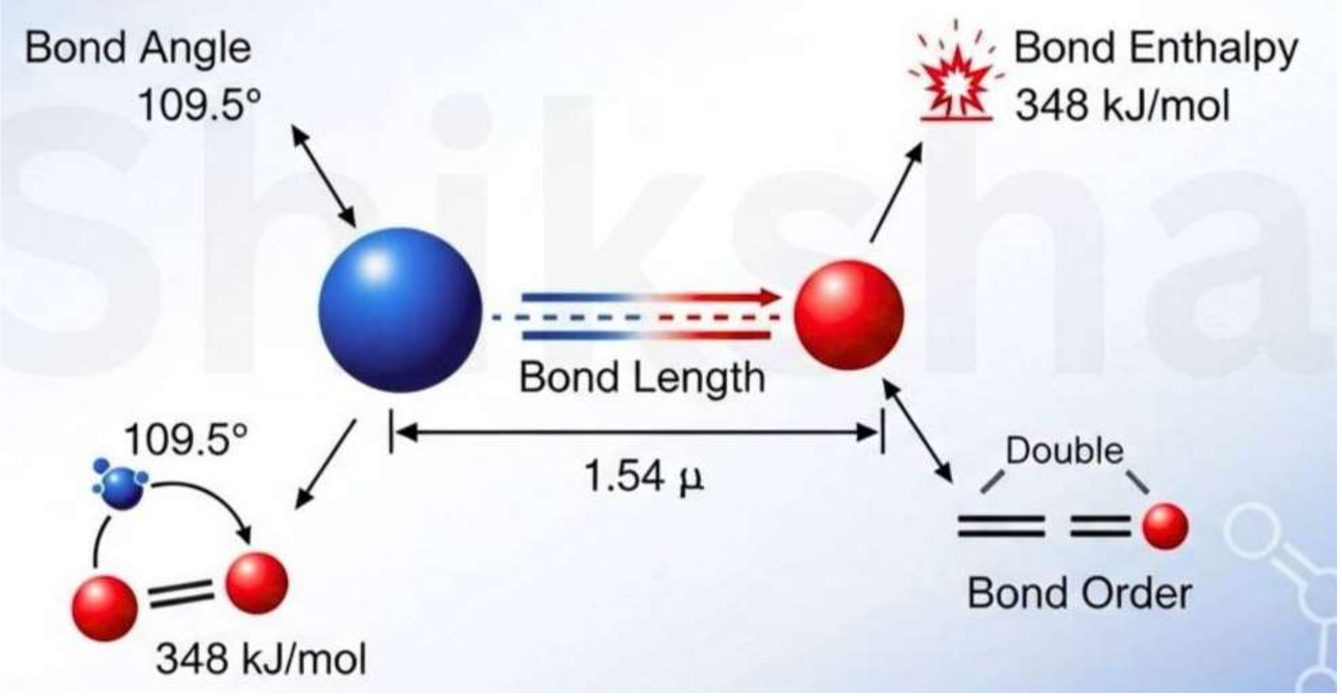






Important properties of covalent bonds

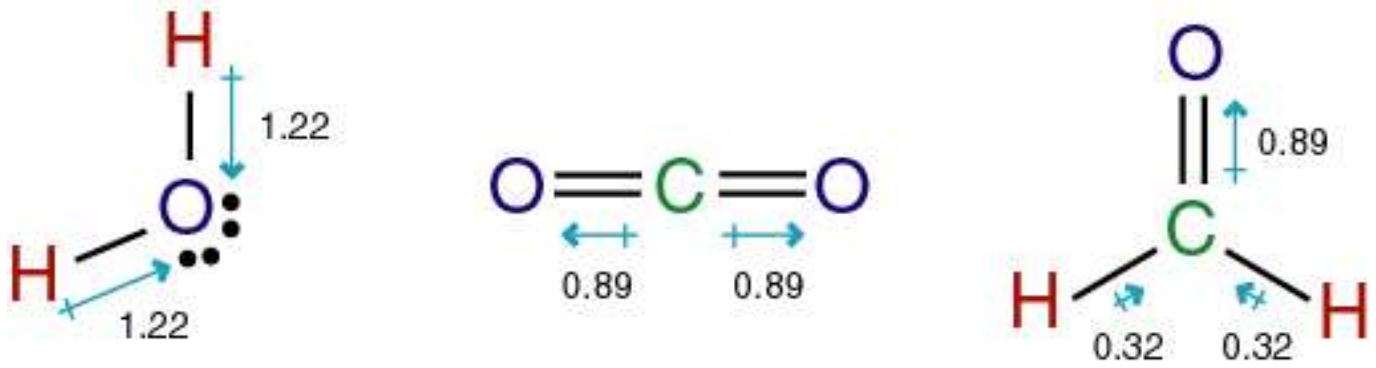
Bond Length	Distance between nuclei of bonded atoms
Bond Angle	Angle between two bonds at central atom
Bond Enthalpy	Energy to break one mole of bonds in gaseous state
Bond Order	Number of shared electron pairs (bonds) between atoms
Bond Polarity	Unequal sharing of electrons between atoms



Polarity of covalent bonds

- Covalent bonds in which the electrons are shared unequally in this way are known as polar covalent bonds. The bonds are known as “dipoles”.
    - Oxygen and nitrogen atoms are electronegative
    - Oxygen and hydrogen
    - Nitrogen and hydrogen
    - Not carbon and hydrogen

Both water and CO_2 contain polar bonds, but only water is a polar molecule. Why?



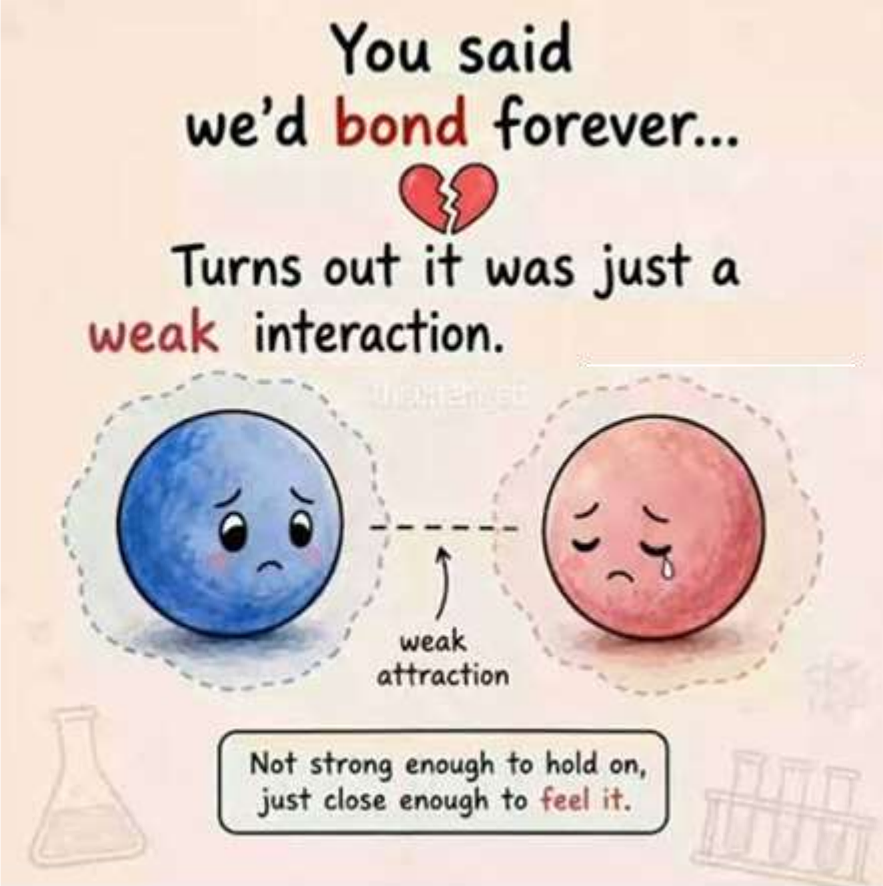
Non-covalent interactions

Electrostatic interaction

Hydrogen bonds

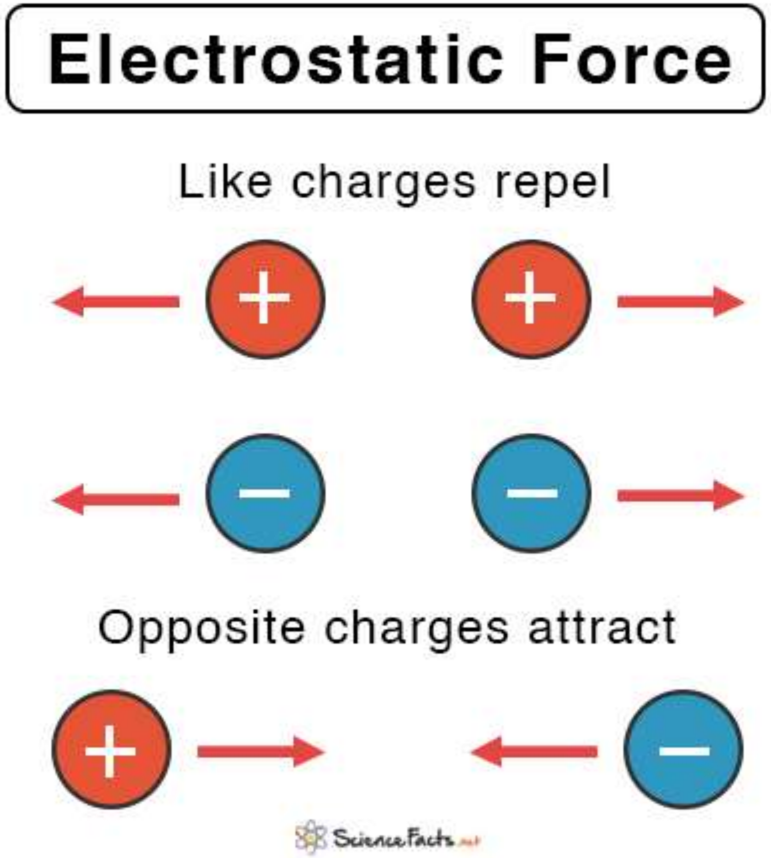
Van der Waals

Hydrophobic interactions

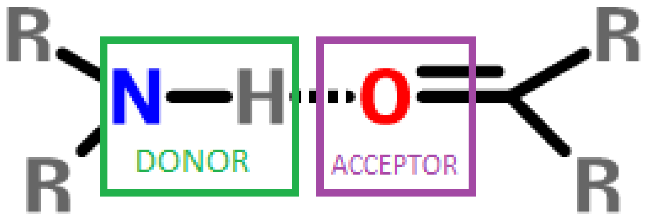


Electrostatic interactions

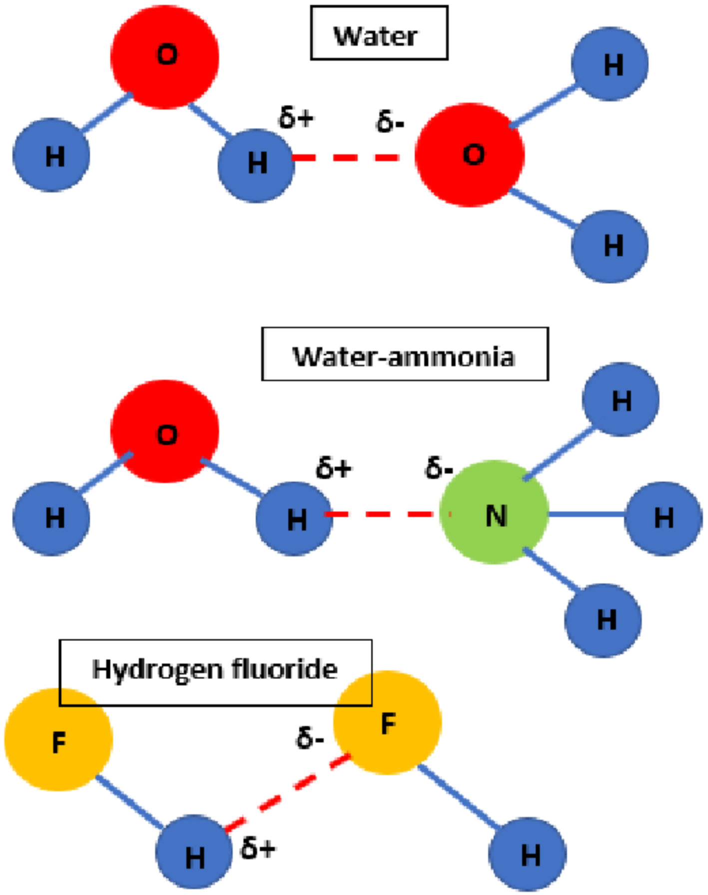
- Also called, charge-charge interactions:
  - They are formed between two charged particles.
  - These forces are quite strong in the absence of water.



Hydrogen bonds

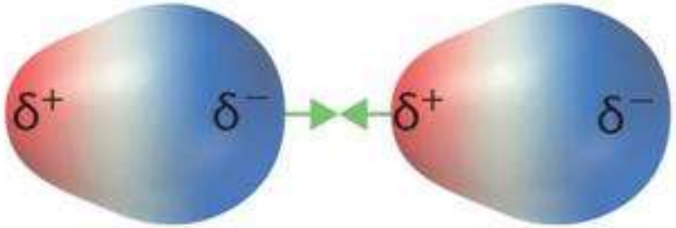


- A hydrogen bond is a strong, non-covalent dipole-dipole attraction between a hydrogen atom (called a donor) that is covalently bonded to a highly electronegative atom, and another electronegative atom (called an acceptor) with a lone pair of electrons.
- These bonds typically form with the elements nitrogen, oxygen, or fluorine.

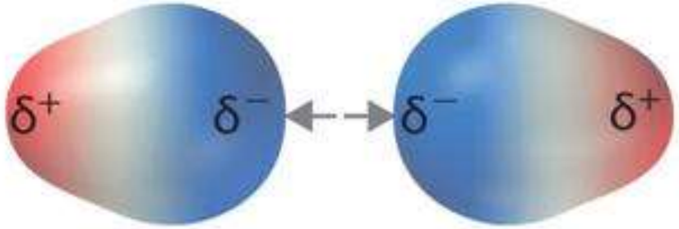


van der Waals attractions

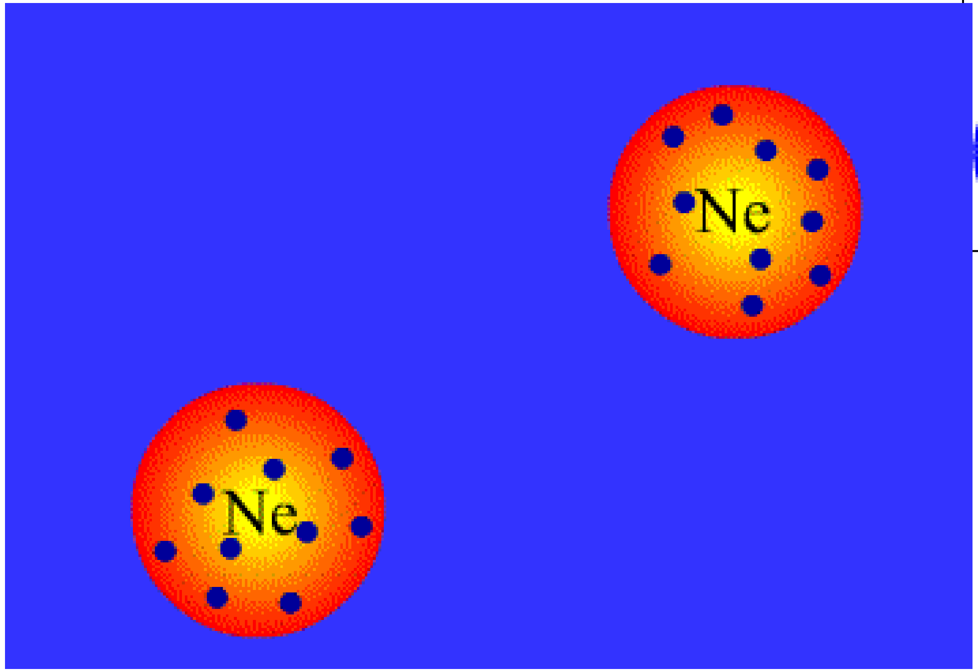
- Unequal distribution of electronic charge around an atom at any time resulting in attractive and repulsive forces.
- The strength of the attraction is affected by distance.

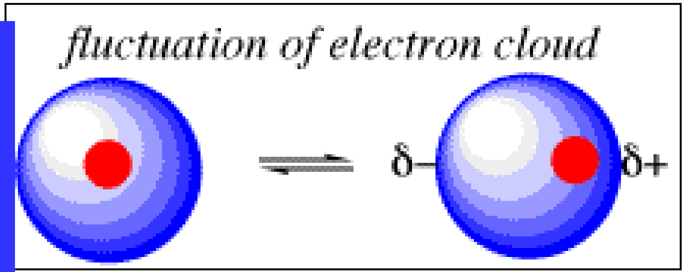


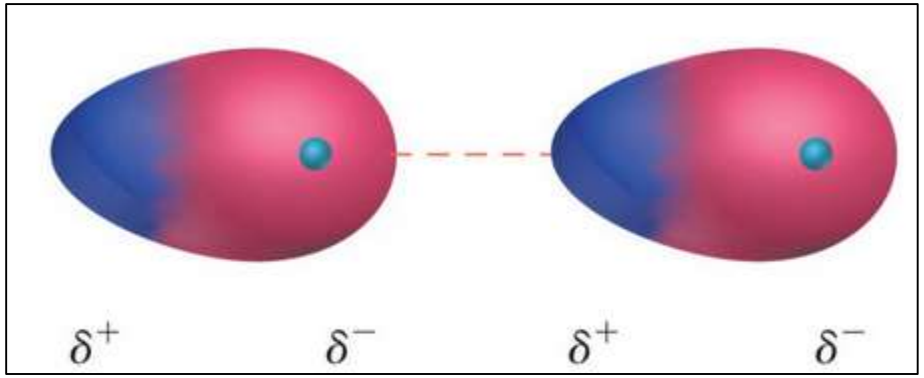
(b) Attraction



(d) Repulsion

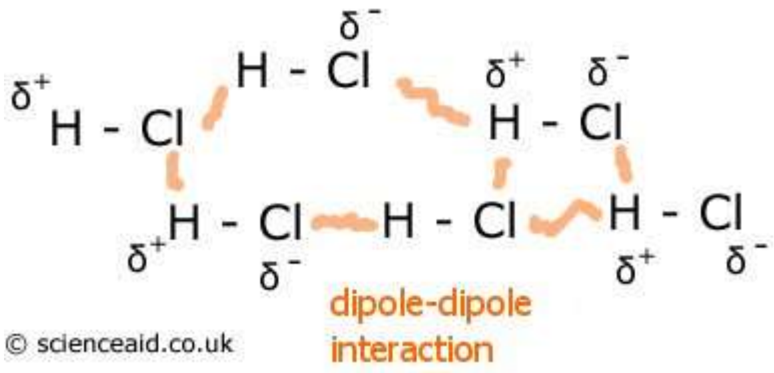


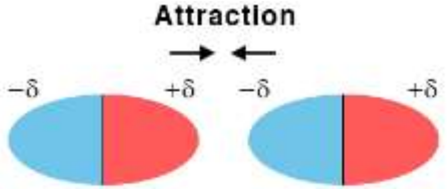


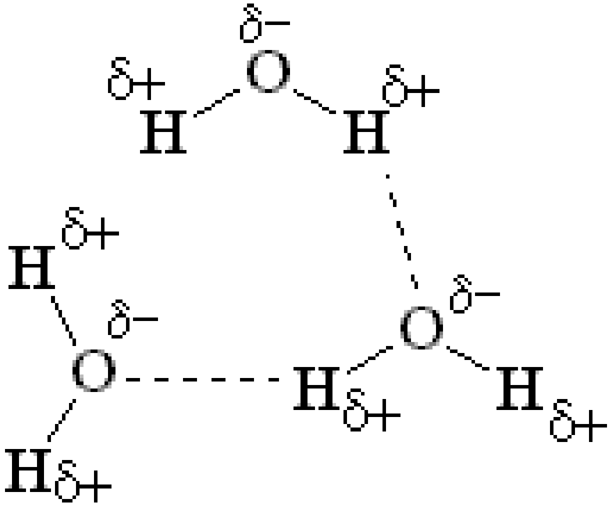


Note others:

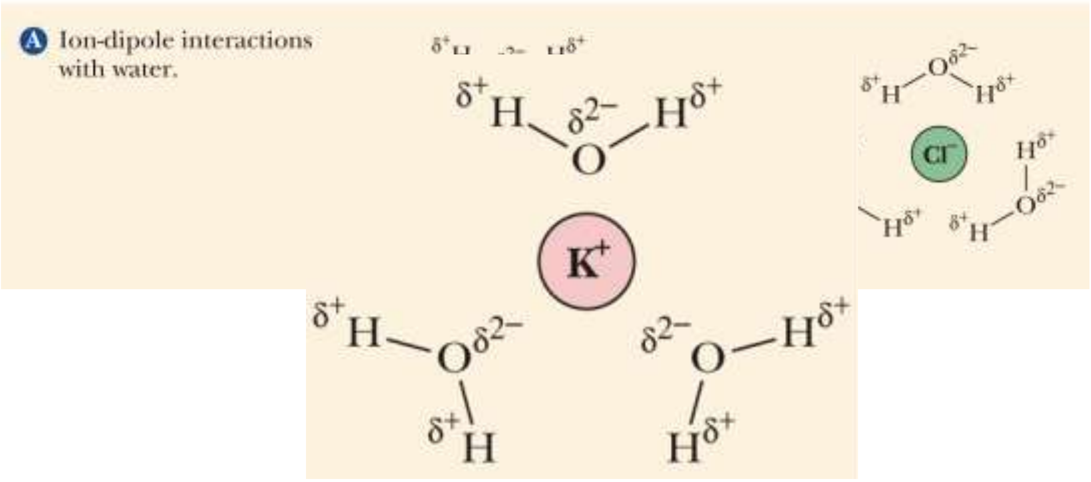
Dipole-dipole interaction





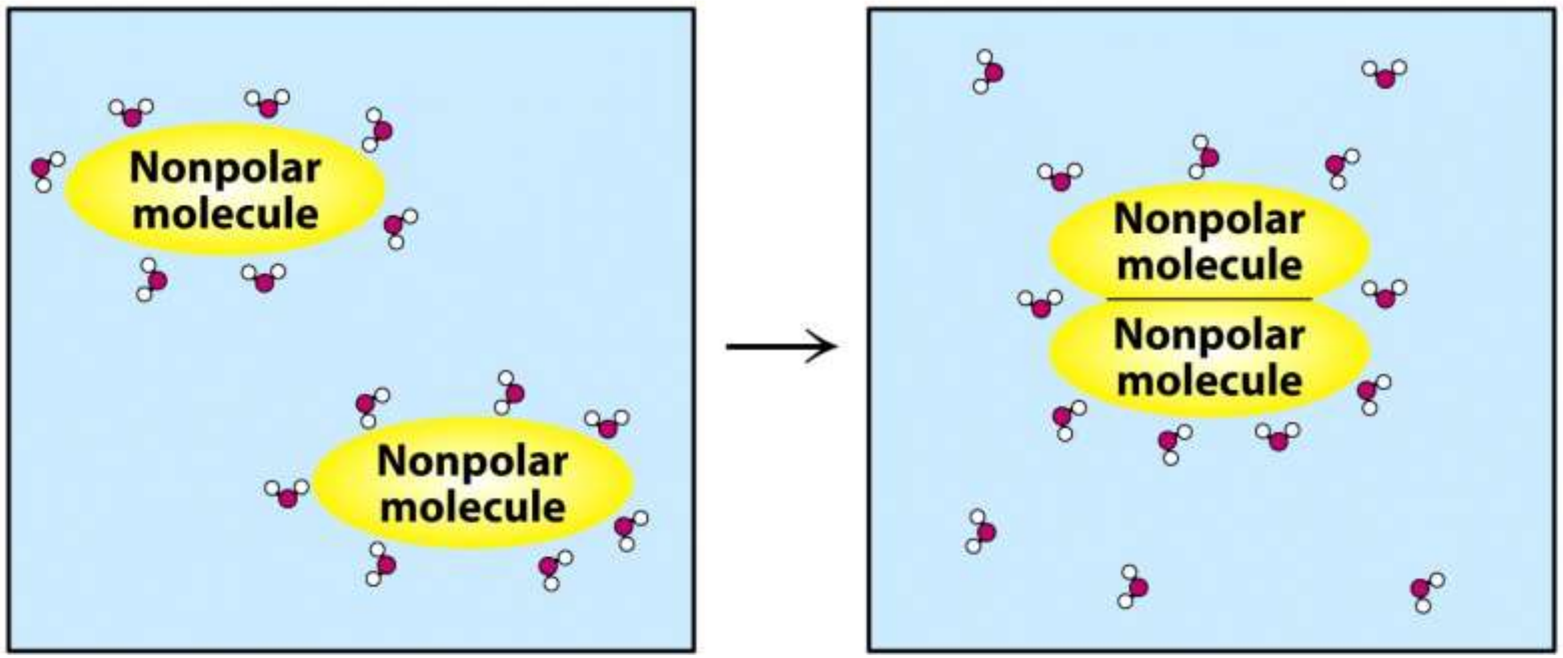


Dipole-charge interaction



Hydrophobic interactions

- Self-association of nonpolar compounds in an aqueous environment to minimize the unfavorable interaction with water molecules.
- It is not that nonpolar molecules are attracted to each other; it is driven by water molecules naturally bonding with one another, excluding the nonpolar substances.



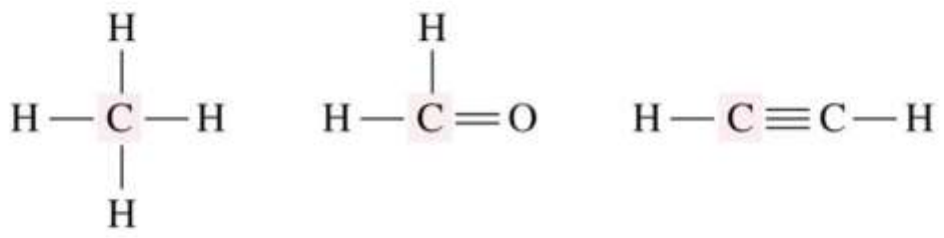
Properties of noncovalent interactions

- Reversible
- Relatively weak
- Can be either attractive or repulsive
- Molecules interact and bind specifically.
- Noncovalent forces significantly contribute to the structure, stability, and functional competence of macromolecules in living cells.
- Involve interactions both within the biomolecule and between it and the water of the surrounding environment

Carbon

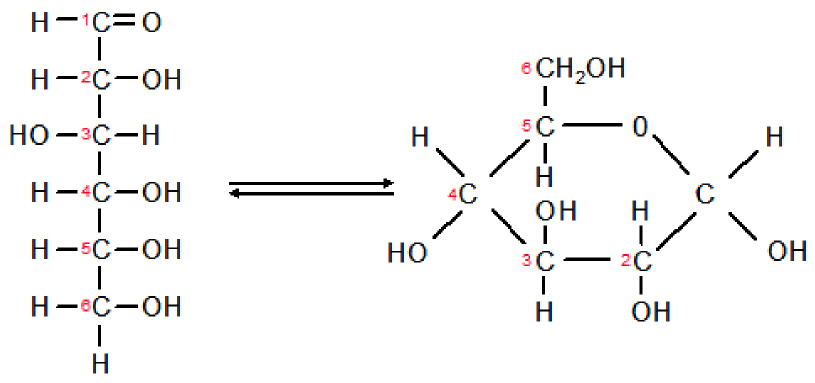
The road to diversity and stability

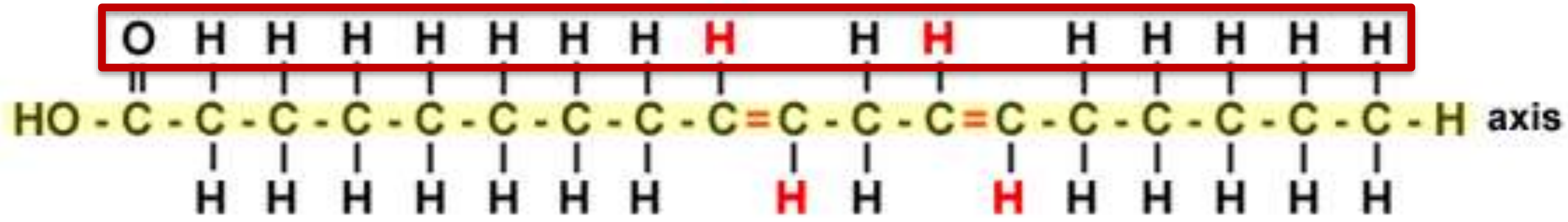
Properties of carbon (1)



CH_4 (methane) CH_2O (formaldehyde) C_2H_2 (acetylene)

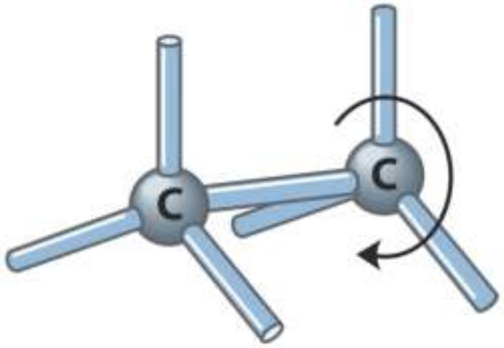
- It can form four bonds, which can be single, double, or triple bonds.
- Each bond is very stable.
  - strength of bonds: triple > double > Single)
- They link C atoms together in chains and rings.
  - These serve as a backbones.

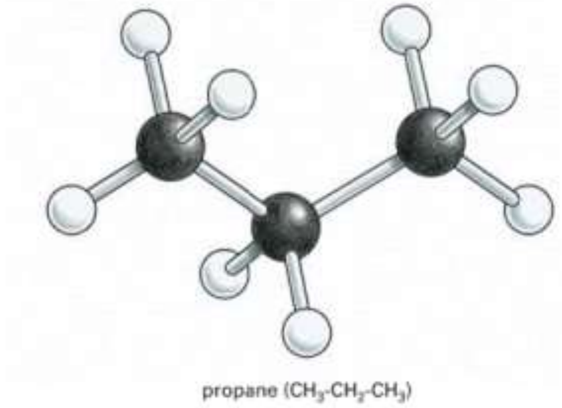


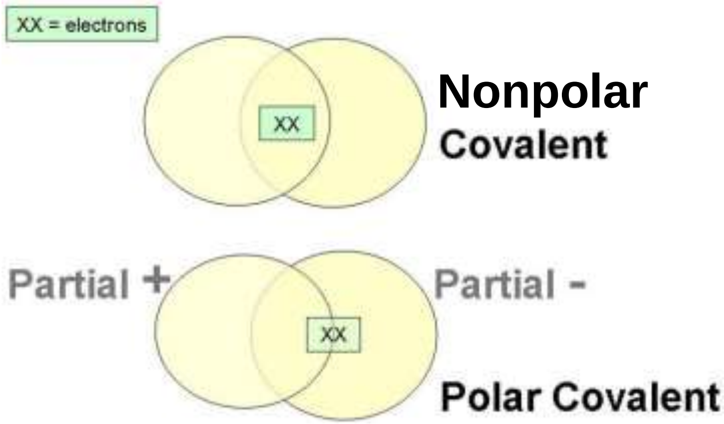


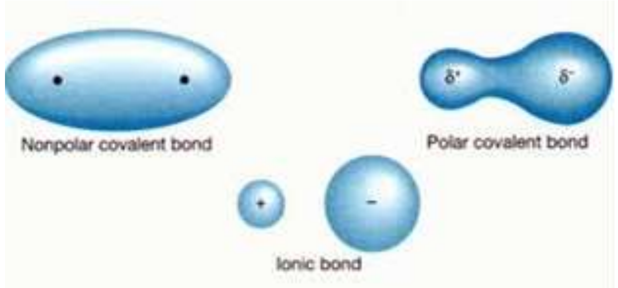
Properties of carbon (2)

- Carbon bonds have angles giving molecules three-dimensional structures.
- In a carbon backbone, some carbon atoms rotate around a single covalent bond producing molecules of different shapes.
- The electronegativity of carbon is between other atoms.
    - It can form polar and non-polar molecules.
- Pure carbon is not water soluble, but when carbon forms covalent bonds with other elements like O or N, the molecule that makes carbon compounds is soluble.





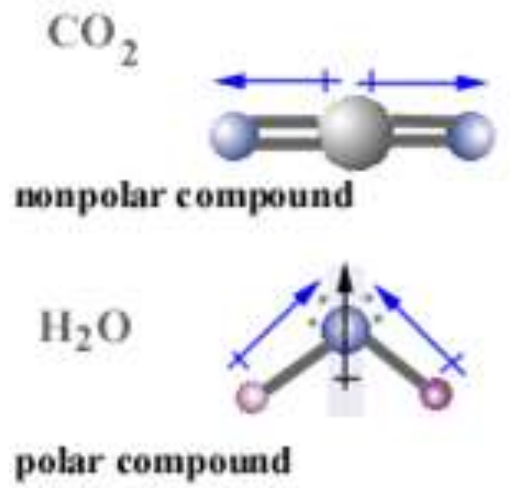


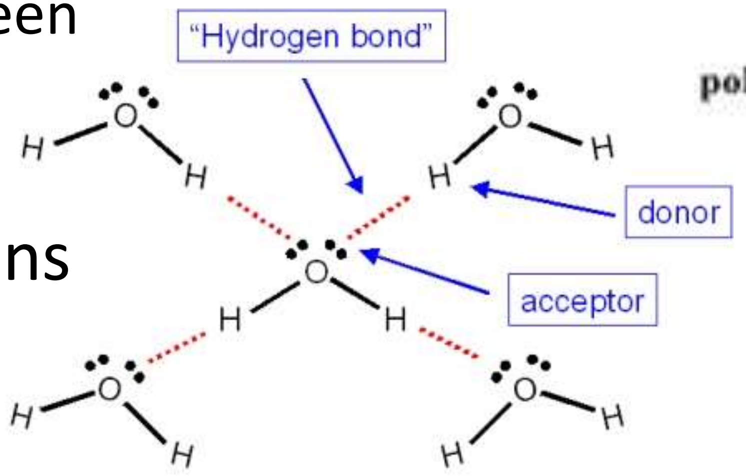


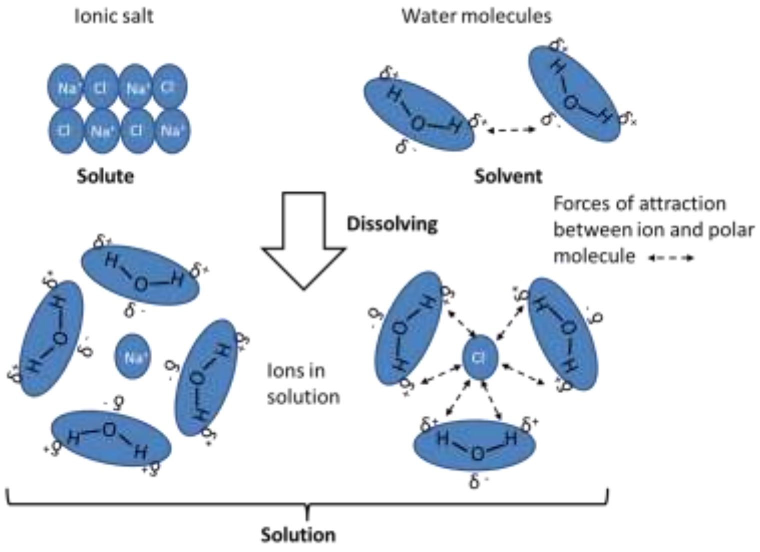
Water

Properties of water (1)

- Water is a polar molecule as a whole because of:
  - the different electronegativities between Hydrogen and oxygen
  - It is angular.
- It can form dipole-dipole interactions and dipole-charge interactions.
- Water is highly cohesive.
- Water molecules produce a network.
- Water is an excellent solvent because It is small, and it weakens electrostatic forces and hydrogen bonding between polar molecules.

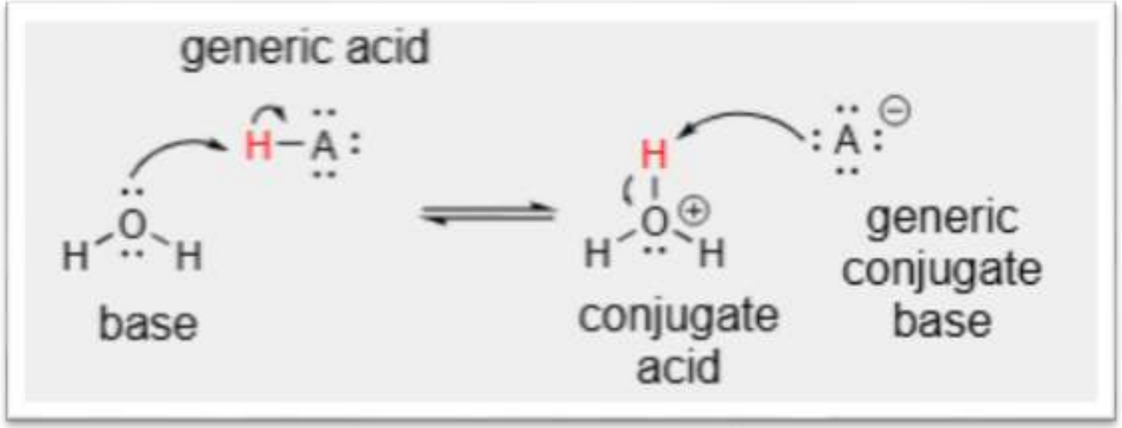


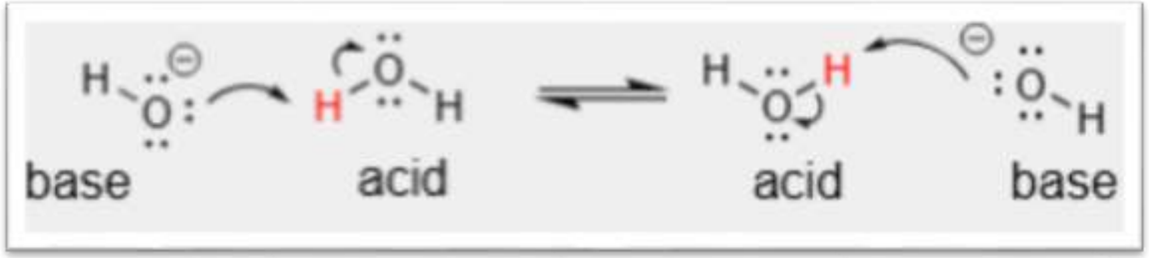




Properties of water (2)

- It is reactive because it is a nucleophile and an electrophile.
  - A nucleophile is an electron-rich molecule that is attracted to positively-charged or electron-deficient species (electrophiles).





Properties of water (3)

- Water molecules are ionized to become a positively-charged hydronium ion (or proton), and a hydroxide ion:

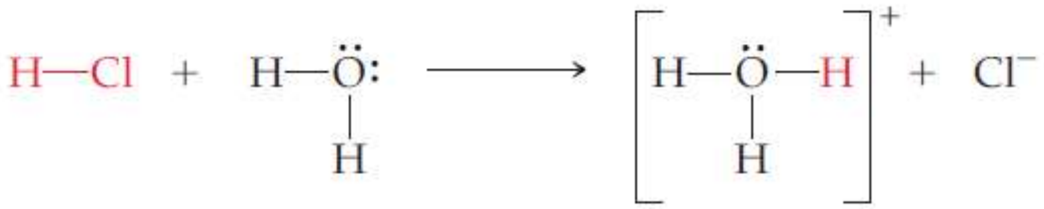
$$H_2O + H_2O \rightleftharpoons H_3O^{\oplus} + OH^{\ominus}$$

Note: $H_3O^+ = H^+$

Acids and bases

Types of acids and bases

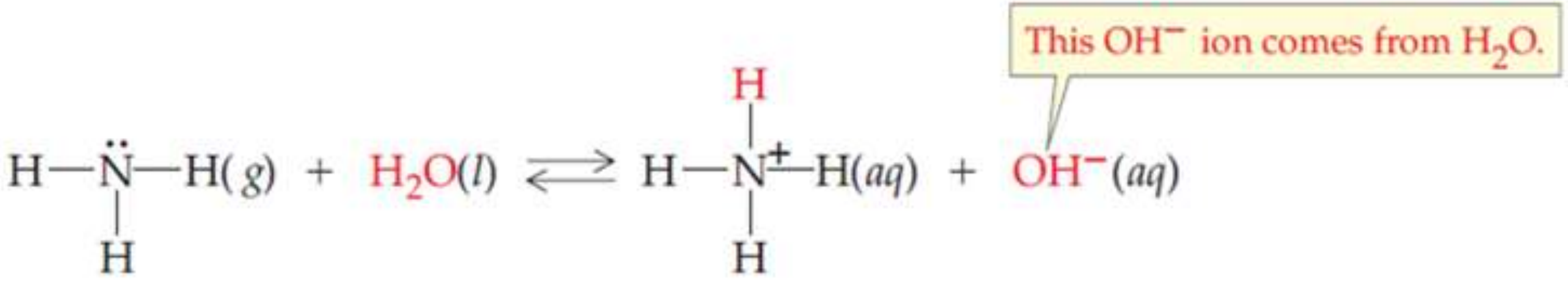
- Acid: a substance that produces H^+ when dissolved in water
  - H^+ reacts with water-producing hydronium ion (H_3O^+).
  - (Cl^-) is a conjugate base.



- Monoprotic acid: HCl, HNO_3, CH_3COOH
- Diprotic acid: H_2SO_4
- Triprotic acid: H_3PO_3

- Base: a substance that produces OH^- when dissolved in water or accepts a proton (H^+) from an acid.
  - Na^+ or NH_4^+ is a conjugate acid.

$$NaOH \longrightarrow Na^+ + {}^-OH$$



Water = amphoteric

- Substances that can act as an acid in one reaction and as a base in another are called **amphoteric substances.**
  - **Example: water**
- With ammonia (NH_3), water acts as an acid because it donates a proton (hydrogen ion) to ammonia.

$$NH_3 + H_2O \leftrightarrow NH_4^+ + OH^-$$

- With hydrochloric acid, water acts as a base.

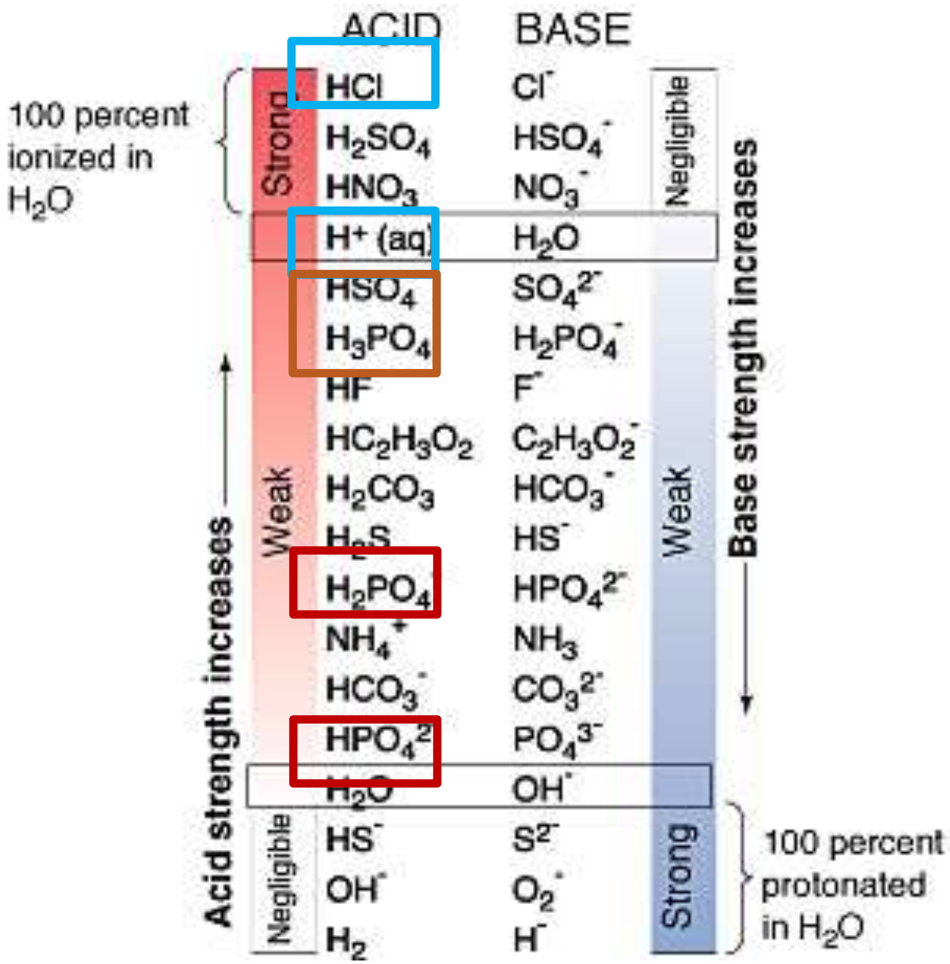
$$HCl + H_2O \rightarrow H_3O^+ + Cl^-$$

Ampho = 'both' or 'dual'

Acid/base strength

- Acids differ in their ability to release protons.
  - Strong acids dissociate 100%.
- Bases differ in their ability to accept protons.
  - Strong bases have a strong affinity for protons.

- For multi-protic acids (H_2SO_4, H_3PO_4), each proton is donated at different strengths.



Rule

- The stronger the acid, the weaker the conjugate base.
- Strong vs. weak acids
  - Strong acids and bases are one-way reactions

$$HCl \rightarrow H^+ + Cl^-$$

$$NaOH \rightarrow Na^+ + OH^-$$

  - Weak acids and bases do not ionize completely

$$HC_2H_3O_2 \leftrightarrow H^+ + C_2H_3O_2^-$$

$$NH_3 + H_2O \leftrightarrow NH_4^+ + OH^-$$

Equilibrium constant and acid dissociation constant

- Acid/base solutions are at constant equilibrium.
- We can write equilibrium constant (K_{eq}) for such reactions

$$HA \longleftrightarrow H^+ + A^-$$

$$K_a = \frac{[H_3O^+] \cdot [A^-]}{[HA]}$$

Note: $H_3O^+ = H^+$

- The value of the K_a indicates the direction of the reaction.
  - When K_a is greater than 1, the product side is favored.
  - When K_a is less than 1, the reactants are favored.

What is pKa?

$$pK_a = -\log K_a$$

TABLE 2.4 Dissociation constants and pK_a values of weak acids in aqueous solutions at 25°C

Acid	K_a(M)	pK_a
HCOOH (Formic acid)	1.77×10^{-4}	3.8
CH_3COOH (Acetic acid)	1.76×10^{-5}	4.8
$CH_3CHOHCOOH$ (Lactic acid)	1.37×10^{-4}	3.9
H_3PO_4 (Phosphoric acid)	7.52×10^{-3}	2.2
$H_2PO_4^{\ominus}$ (Dihydrogen phosphate ion)	6.23×10^{-8}	7.2
HPO_4^{2-} (Monohydrogen phosphate ion)	2.20×10^{-13}	12.7
H_2CO_3 (Carbonic acid)	4.30×10^{-7}	6.4
$HCO_3^{\ominus}$ (Bicarbonate ion)	5.61×10^{-11}	10.2
$NH_4^{\oplus}$ (Ammonium ion)	5.62×10^{-10}	9.2
$CH_3NH_3^{\oplus}$ (Methylammonium ion)	2.70×10^{-11}	10.7

TABLE | 9.4 K_A AND pK_A VALUES FOR SELECTED ACIDS

Name	Formula	K_a	pK_a
Hydrochloric acid	HCl	1.0×10^{7}	−7.00
Phosphoric acid	H_3PO_4	7.5×10^{-3}	2.12
Hydrofluoric acid	HF	6.6×10^{-4}	3.18
Lactic acid	$CH_3CH(OH)CO_2H$	1.4×10^{-4}	3.85
Acetic acid	CH_3CO_2H	1.8×10^{-5}	4.74
Carbonic acid	H_2CO_3	4.4×10^{-7}	6.36
Dihydrogenphosphate ion	$H_2PO_4^{-}$	6.2×10^{-8}	7.21
Ammonium ion	NH_4^{+}	5.6×10^{-10}	9.25
Hydrocyanic acid	HCN	4.9×10^{-10}	9.31

Molarity of solutions

- Solutions can be expressed in terms of its concentration or molarity.
- Moles of a solution are the amount in grams in relation to its molecular weight (MW or a.m.u.).

$$\text{moles} = \text{grams} / \text{MW}$$

- A molar solution is where the number of grams equal to its molecular weight (moles) in 1 liter of solution.

$$M = \text{moles} / \text{volume (L)}$$

- Since (mol = grams / MW), you can calculate the grams of a chemical you need to dissolve in a known volume (L) of water to obtain a certain concentration (M) using the following formula:

$$\text{grams} = M \times \text{volume (L)} \times \text{MW}$$

- Acids and bases can also be expressed in terms of their normality (N) or equivalence (Eq).

Exercise

- How many grams do you need to make 5M NaCl solution in 100 ml (MW 58.4)?

grams = 58.4 x 5 M x 0.1 liter = 29.29 g

Equivalents

- When it comes to acids, bases, and ions, it is useful to think of them as equivalents.
- An equivalent is the number of moles of hydrogen ions that an acid can donate.
  - or a base can accept.
- For ions, one **equivalent (Eq) is** equal to the number of ions that carry 1 mol of charge.

Examples

- For acids:
  - 1 mole HCl = 1 mole $[H^+]$ = 1 equivalent
  - 1 mole H_2SO_4 = 2 moles $[H^+]$ = 2 equivalents
    - 1 eq of H_2SO_4 = ½ mol (because 1 mole gives two moles of H^+ ions)
- For ions:
- One equivalent of Na^+ = 23.1 g, One equivalent of Cl^- = 35.5 g, One equivalent of Mg^{2+} = (24.3)/2 = 12.15 g

- **The typical concentration of Mg^{2+} in blood is 3 mEq/L. How many milligrams of Mg^2+ are in 250 mL of blood?**

Exercise

- Calculate milligrams of Ca^{2+} in blood if total concentration of Ca^{2+} is 5 mEq/L.

- 1 Eq of Ca^{2+} = 40.1 g/2 =20.1 g

- Grams of Ca^{2+} in blood =
- = (5 mEq/L) x (1 Eq/1000 mEq) x (20.1 g/ 1 Eq)
- = 0.1 g/L
- =100 mg/L

Electrolytes

- Electrolytes are electrically-charged minerals when dissolved in water, such as sodium, potassium, chloride, calcium, magnesium, phosphate, and bicarbonate.
- They are vital for various bodily functions such as nerve and muscle function, fluid balance, acid-base balance, and blood pressure.
- Heavy and continuous diarrhea from conditions such as cholera can result in dehydration and very low sodium levels in the body [hyponatremia).
- Heavy sweating during strenuous exercise can also lead to dehydration and loss of electrolytes.

Molarity and equivalents

Equivalents = n x M x volume (L)

One equivalent of any acid neutralizes one equivalent of base.

Based on the equation above, since *x* eq of an acid is neutralized by the same *x* eq of a base, then (n x M x vol) of an acid is neutralized by (n x M x vol) of a base.

Titration

- Titration means that we add an acid to a base slowly.
- At one point during titration, the acid and the base neutralize or cancel each other.
  - *In other words, "to titrate" means "to neutralize".*
- At the point of neutralization, the concentration of H^+ is equal to the concentration of OH^-.
- The best way to calculate how much acid is needed to neutralize a base (or the opposite) is to calculate the equivalents (not mere M, vol, or n).

Problem 1

10.92 Titration of a 12.0 mL solution of HCl requires 22.4 mL of 0.12 M NaOH. What is the molarity of the HCl solution?

- Note that each one produces 1 mole of the ions (H^+ or OH^-), so 1M of HCl is equal to 1M of NaOH.

Eq of base = Eq of acid

n x M1 x Vol1 = n x M2 x Vol2

1 x 0.12 x 22.4 =1 x M2 x 12

M2 = (0.12 x 22.4) / 12

M2 = 0.224 M

What are the equivalents for each one of them?

Problem 2

10.93 What volume of 0.085 M HNO_3 is required to titrate 15.0 mL of 0.12 M $Ba(OH)_2$ solution?

- Note that 1 mole of HNO_3 produces 1 mole of H^+, but 1 mole of $Ba(OH)_2$ produces 2 moles of OH^-. In other words, the n is different.
- Also, remember that Equivalents = n x M x volume (L), where n is the number of charges or the number of H+ (or OH-) the acid or base can produce or accept.

What are the equivalents for each one of them?

Eq of acid = Eq of base

N x M1 x Vol1 = n x M2 x Vol2

1 x 0.085 x Vol = 2 x 0.12 x 15

Vol = (2 x 0.12 x 15) / 1 x 0.085

Vol = 42.35 mL

Antacids

$$CaCO_3 + 2\ HCl \rightarrow CaCl_2 + H_2O + CO_2$$
$$NaHCO_3 + HCl \rightarrow NaCl + H_2O + CO_2$$
$$Al(OH)_3 + 3\ HCl \rightarrow AlCl_3 + 3\ H_2O$$
$$Mg(OH)_2 + 2\ HCl \rightarrow MgCl_2 + 2\ H_2O$$

- Alkaline compounds (neutralize HCl)
- They reduce stomach acidity and provide relief from heartburn and indigestion (dyspepsia).
- They reduce the digestion of proteins by pepsin (pH 1-2 vs. 3.5-5).
- Examples: Magnesium Hydroxide, Aluminum Hydroxide, Calcium Carbonate, Sodium Bicarbonate

Ionization of water

- Water dissociates into hydronium (H_3O^+) and hydroxyl (OH^-) ions.
- For simplicity, we refer to the hydronium ion as a hydrogen ion (H^+) and write the reaction equilibrium as:

$$H_2O \rightleftharpoons H^+ + OH^-$$

Equilibrium constant

- The equilibrium constant Keq of the dissociation of water is:

$$K_{eq} = \frac{[H^{\oplus}]\,[OH^{\ominus}]}{H_2O}$$

- The equilibrium constant for water ionization under standard conditions is 1.8 x 10^{-16} M.

Kw

- Since there are 55.6 moles of water in 1 liter, the product of the hydrogen and hydroxide ion concentrations results in a value of 1 x 10^{-14} for:

$$K_{eq} = \frac{[H^{\oplus}][OH^{\ominus}]}{H_2O} \longrightarrow \underline{K_{eq}(55.5\ M)} = [H^{\oplus}][OH^{\ominus}]$$

- This constant, Kw, is called the ion product of water

$$K_w = [H^{\oplus}][OH^{\ominus}] = 1.0 \times 10^{-14}\ M^2$$

$[H^+]$ and $[OH^-]$

- For pure water, there are equal concentrations of $[H^+]$ and $[OH^-]$, each with a value of 1×10^{-7} M.
- Since Kw is a fixed value, the concentrations of $[H^+]$ and $[OH^-]$ are inversely changing.
- If the concentration of H^+ is high, then the concentration of OH^- must be low, and vice versa. For example, if $[H^+] = 10^{-2}$ M, then $[OH^-] = 10^{-12}$ M