Introduction to Biochemistry

Summer 2024/2025

Course information

- Recommended textbooks
  - Marks' Basic Medical Biochemistry: A Clinical Approach 5th Edition, by Michael Lieberman (Author), Alisa Peet MD (Author), 2018
  - Biochemistry 8th edition by Mary Campbell (Author) and Shawn Farrell (Author)
- Online:
  - https://themedicalbiochemistrypage.org/
- Instructors
  - Prof. Nafez Abu Tarboush

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 and address the function of biological 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

- Four primary: carbon, hydrogen, oxygen, & nitrogen
- Others exist in trace amounts but are essential, elements (mostly metals)

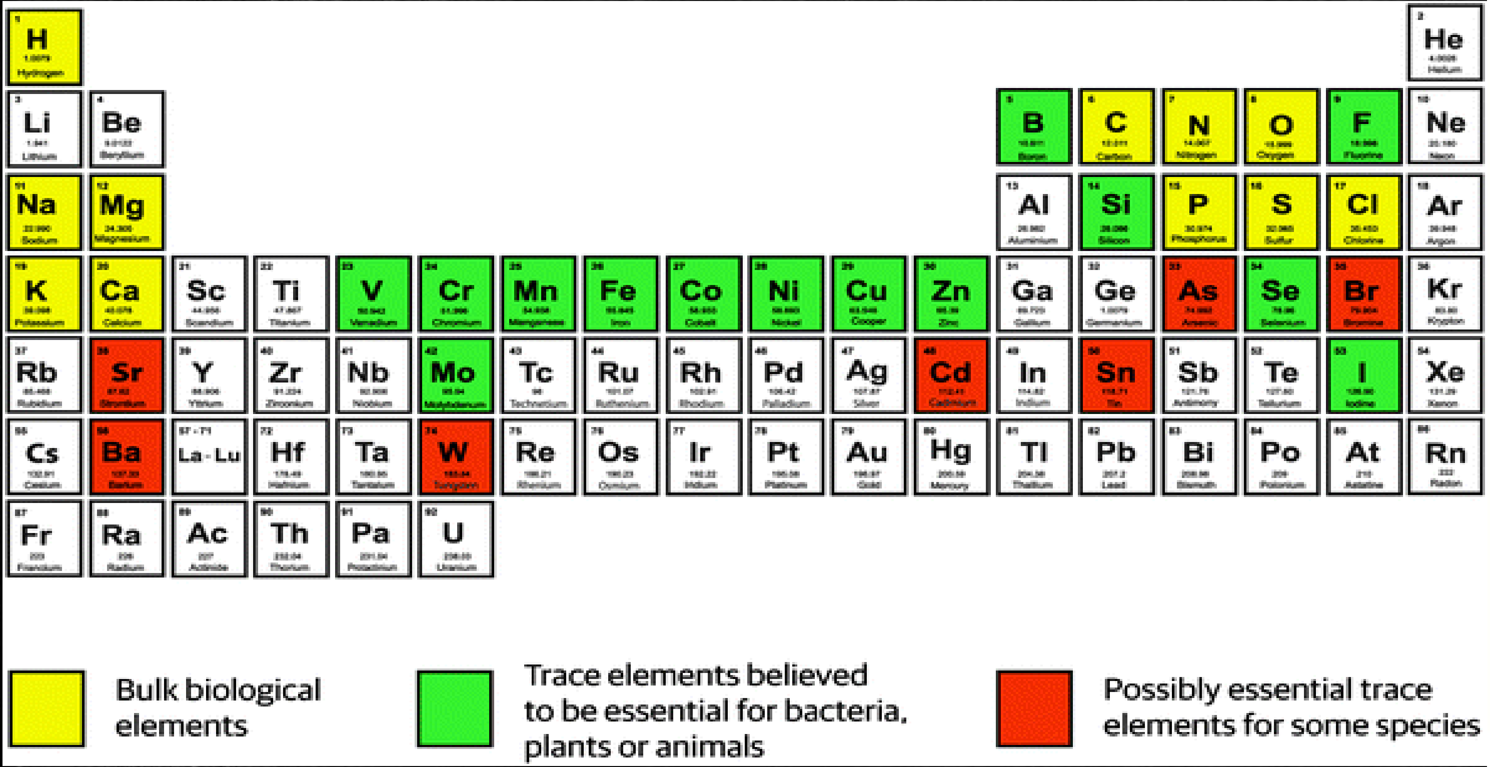


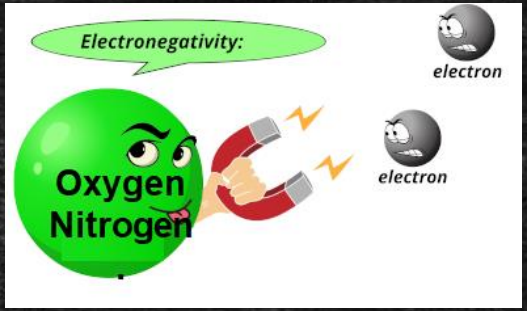
TABLE 2.1 Elements of the Human Body

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

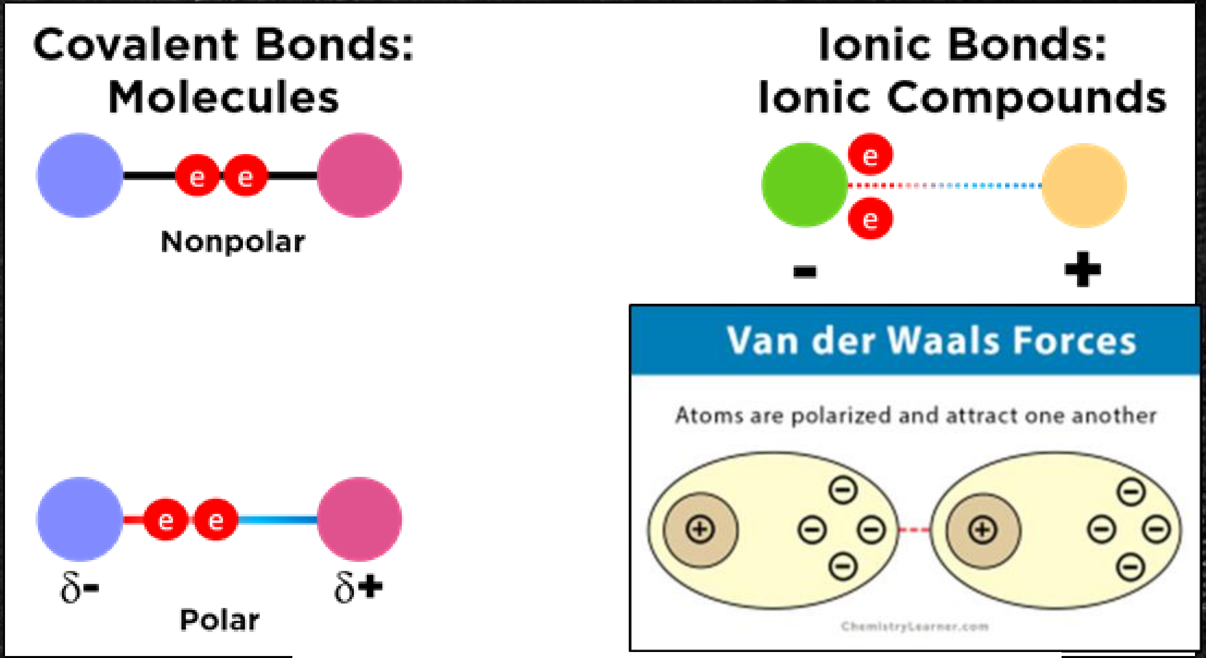
Trace Elements (Total 0.7%)

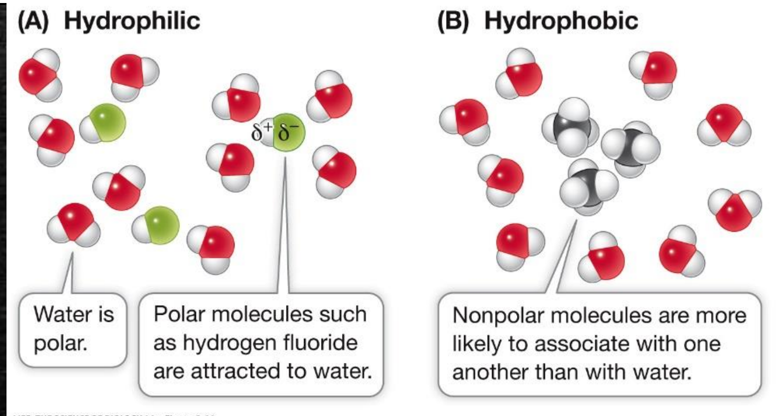
Chromium	Cr	Molybdenum	Mo
Cobalt	Co	Selenium	Se
Copper	Cu	Silicon	Si
Fluorine	F	Tin	Sn
Iodine	I	Vanadium	V
Manganese	Mn	Zinc	Zn

Important terms



- Electronegativity
- Covalent bonds
  - Polar vs. non-polar
  - Single vs. multiple
- Non-covalent interactions
  - Electrostatic interactions
  - Hydrogen bonds (donor and acceptor)
  - Van der Waals interactions
  - Hydrophobic interactions
    - Hydrophobic versus hydrophilic molecules
  - Nucleophile vs electrophile

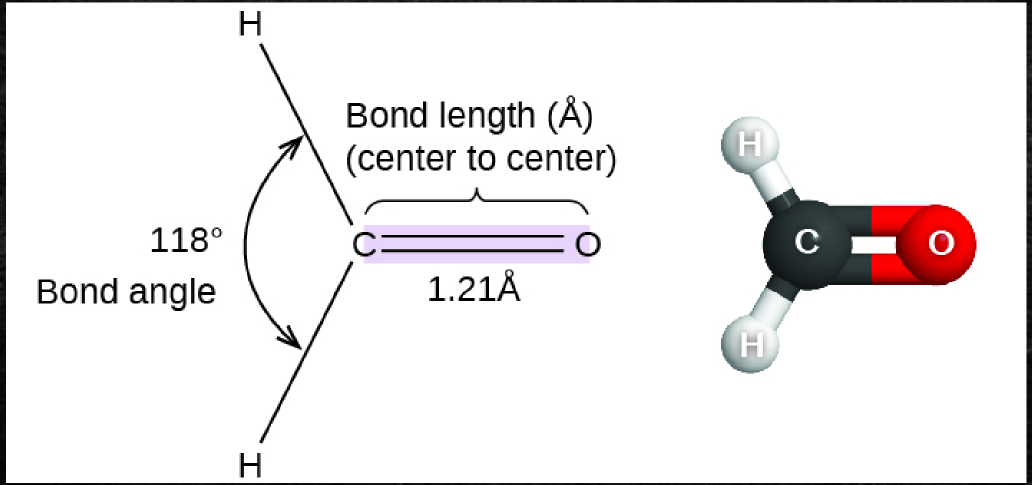




LIFE: THE SCIENCE OF BIOLOGY 11e, Figure 2.11

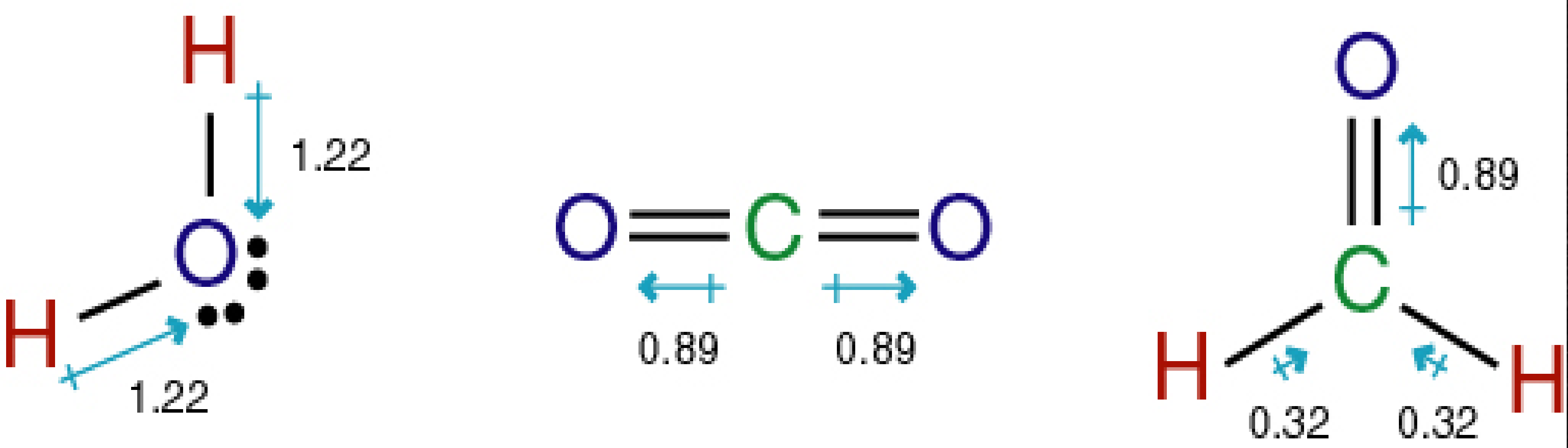
Important properties of bonds

- Bond strength (amount of energy that must be supplied to break a bond)
- Bond length: the distance between two nuclei
- Bond orientation: bond angles determining the overall geometry of atoms
- The three-dimensional structures of molecules are specified by the bond angles and bond lengths for each covalent linkage.



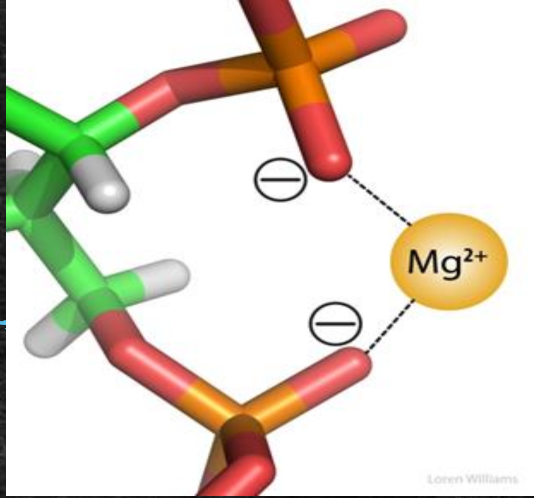
Polarity

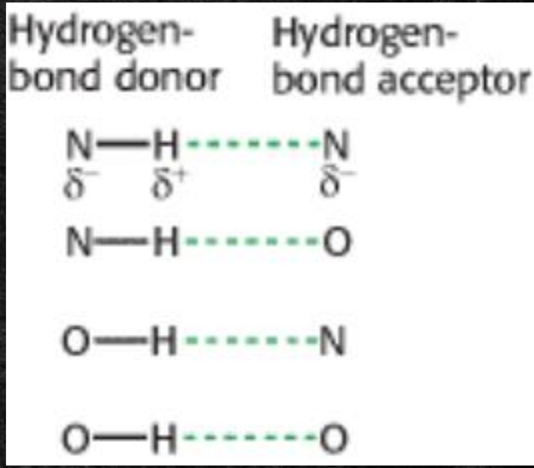
- Electrons are shared unequally = “dipoles”
- Both water and CO_2 contain polar bonds, but only water is a polar molecule. Why?

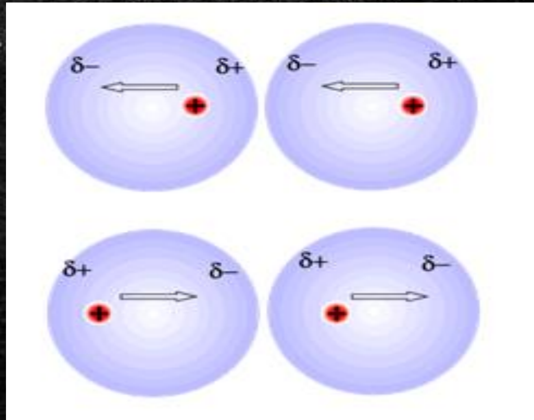


What are non-covalent interactions?

- They are reversible and relatively weak
- Electrostatic interactions (charge-charge interactions):
  - Quite strong in the absence of water
- Hydrogen bonds
  - Shared between a donor and an acceptor
- Van der Waals interactions
  - Unequal distribution of electronic charge around an atom changes with time
  - The strength of the attraction is affected by distance

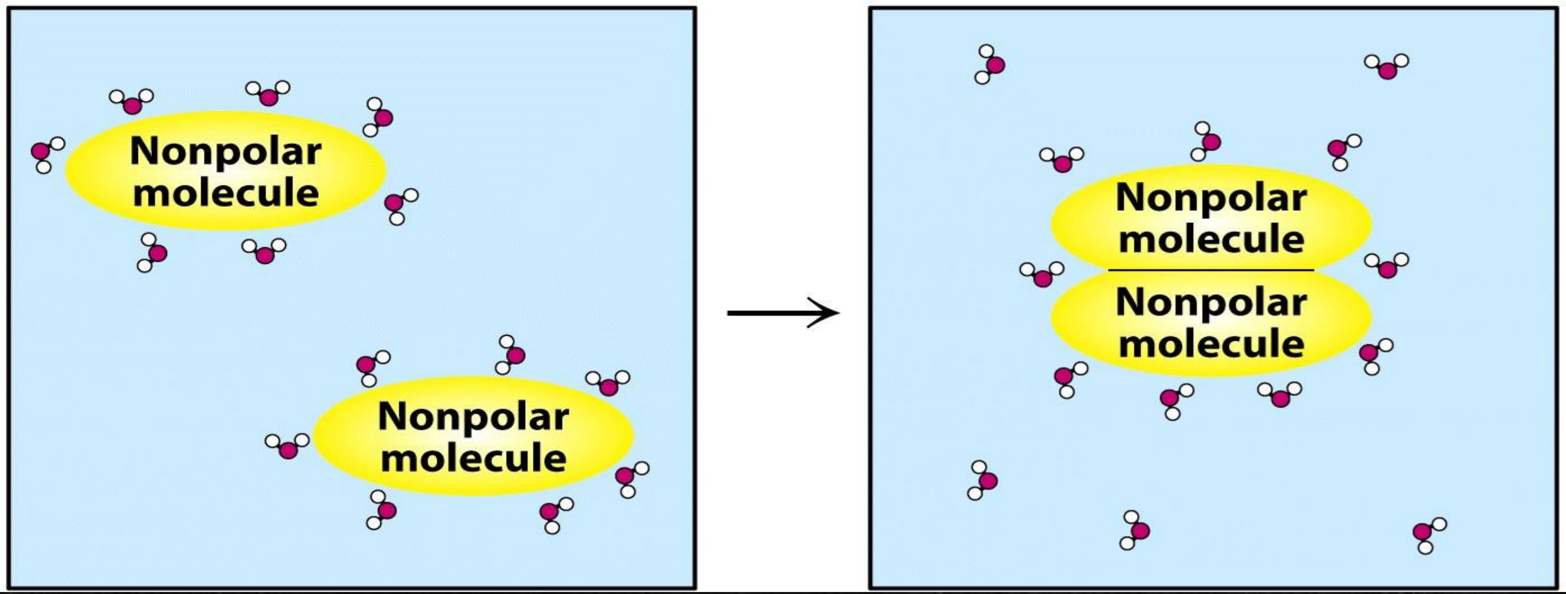


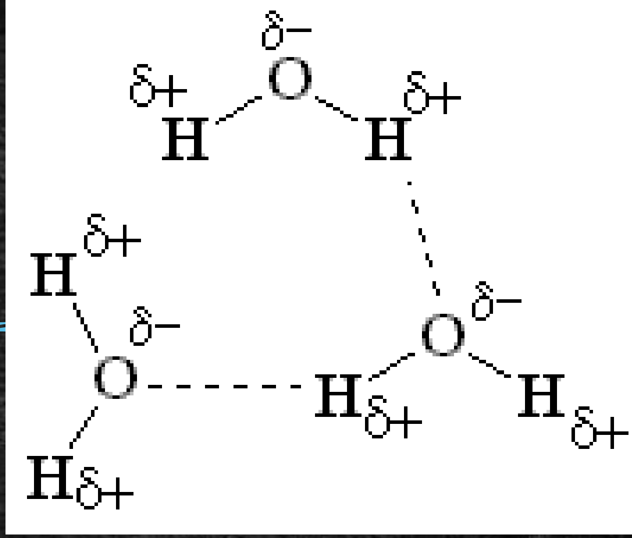


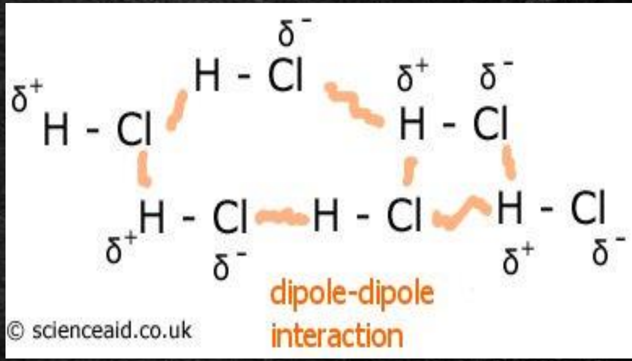


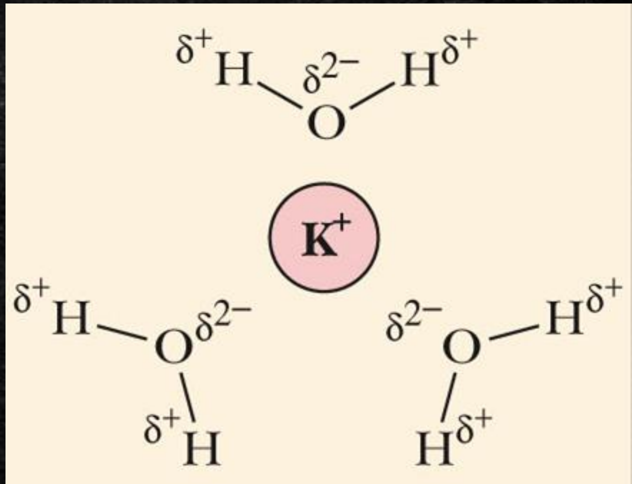
What are non-covalent interactions?

- Dipole-dipole interaction
- Dipole-charge interaction
- Hydrophobic interactions
  - Self-association of nonpolar compounds in an aqueous environment









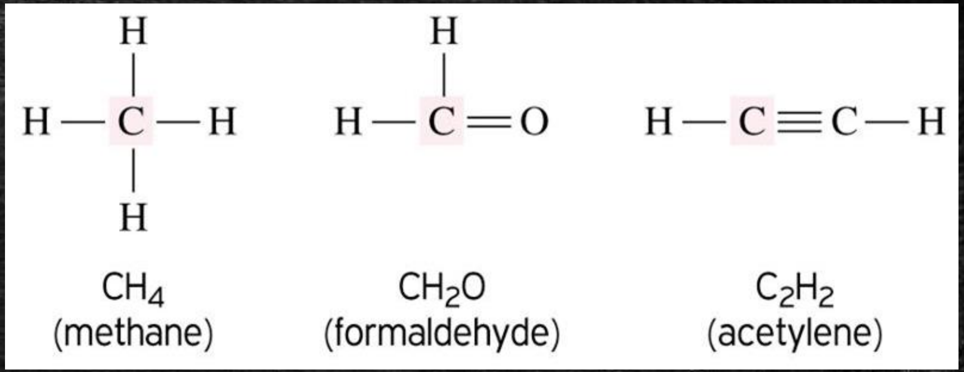
Properties of noncovalent interactions

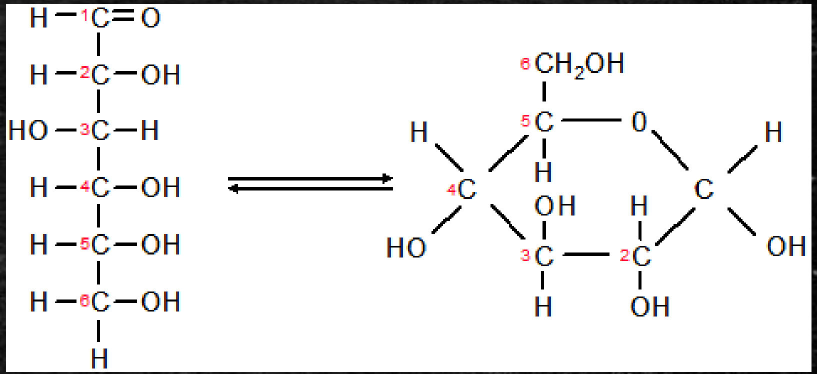
- Reversible
- Relatively weak
- Molecules interact and bind specifically
- Significantly contribute to the structure, stability, and functional competence of macromolecules in living cells
- Can be either attractive or repulsive
- Involve interactions both within the biomolecule and between it and the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

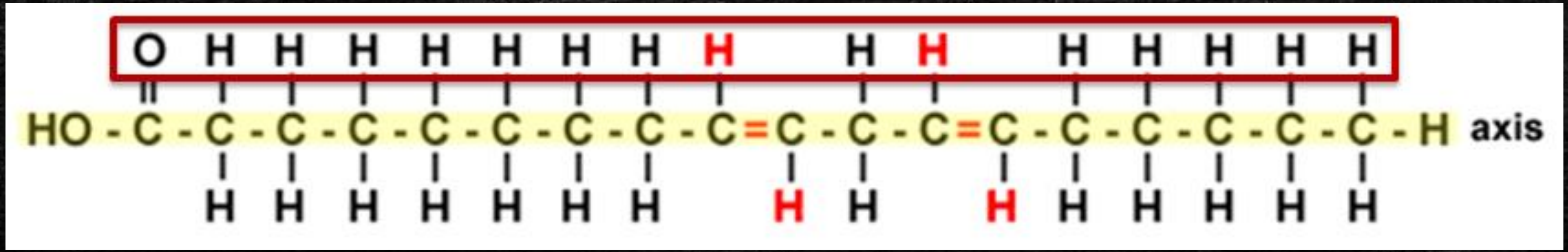
Carbon

Properties of carbon (1)

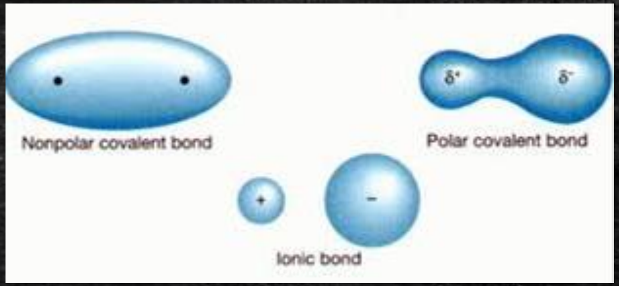
- It can form four bonds
- Single, double, or triple bonds
- Bonds are very stable
- They link C atoms together in chains and rings
  - These serve as backbones



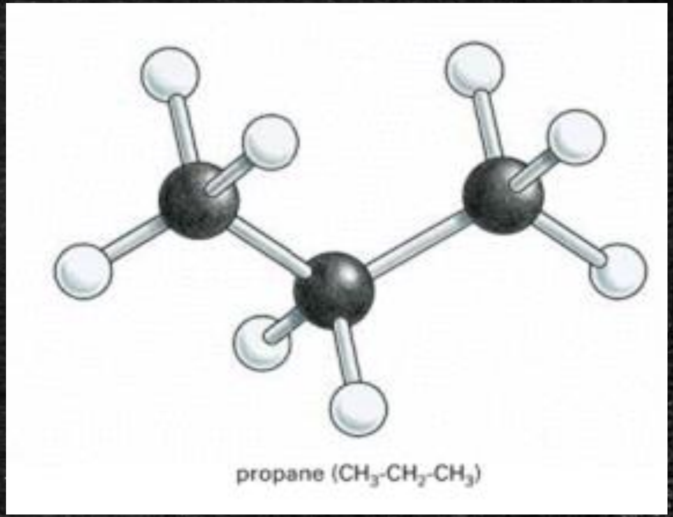


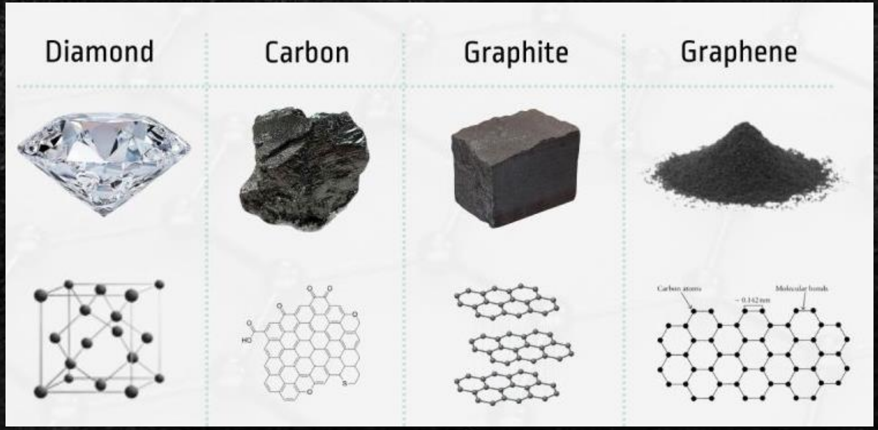


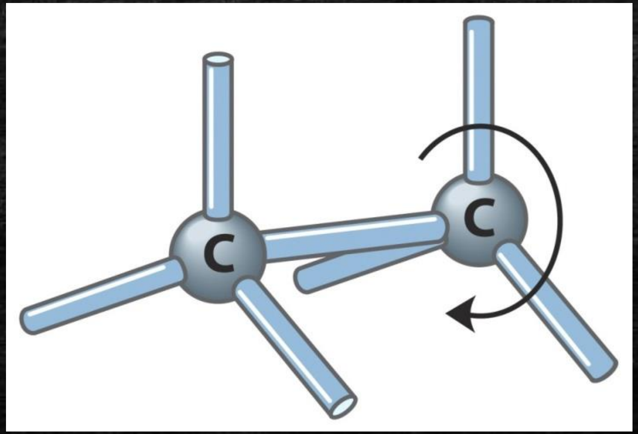
Properties of carbon (2)

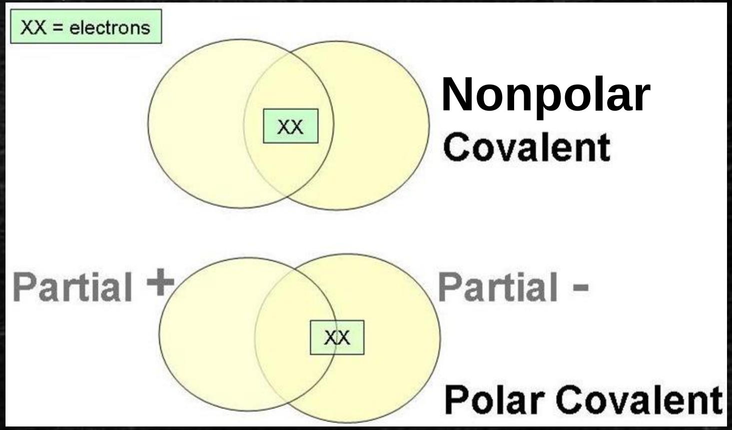


- Three-dimensional structures (angles)
- Rotation (molecules of different shapes)
- Electronegativity (between others):
  - It can form polar and non-polar molecules
- Pure carbon is not water soluble (graphite, diamond)





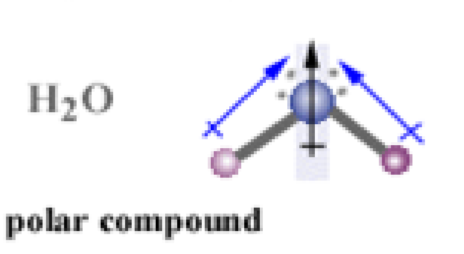




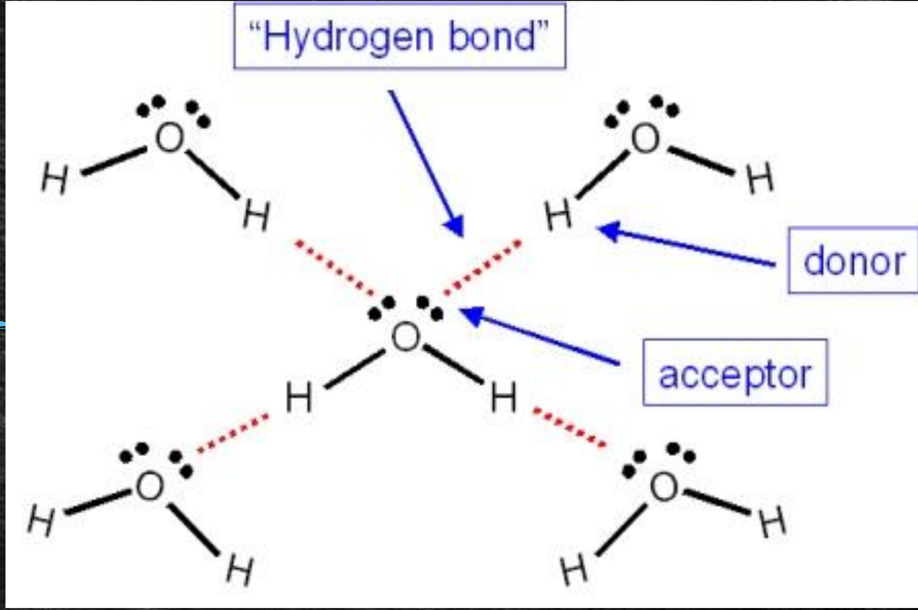
Water

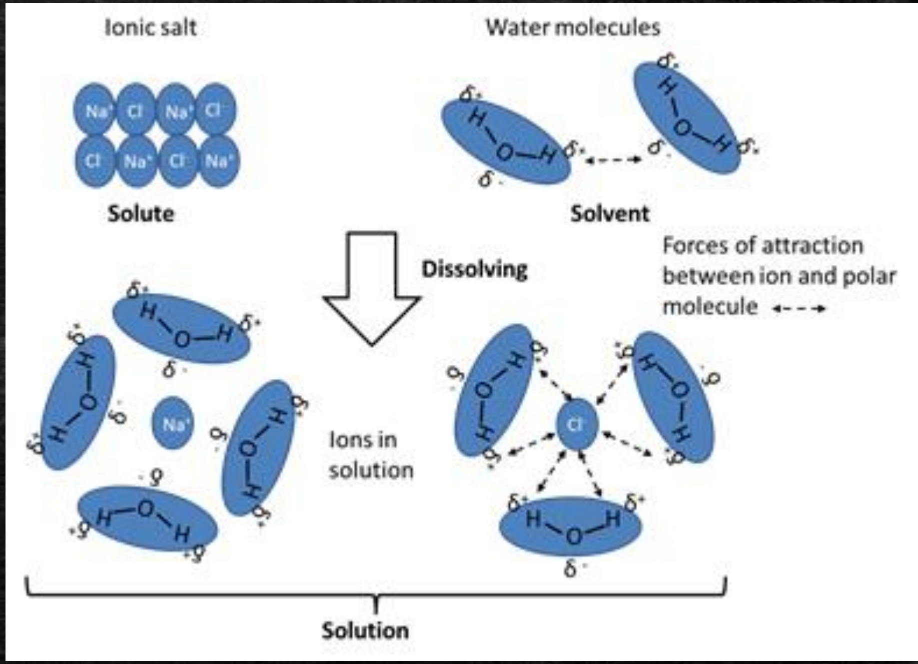
Properties of water (1)

- Polar
- Angular



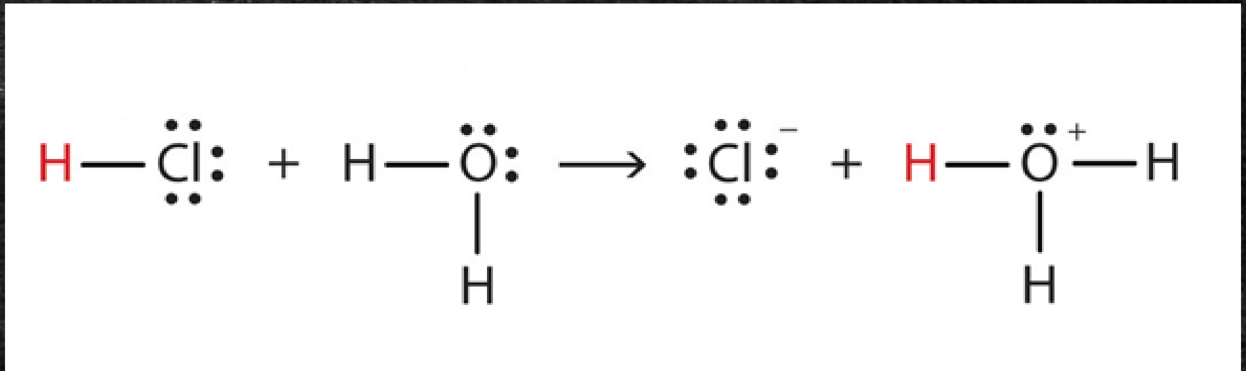
- Dipole-dipole interactions and dipole-charge interactions
- Highly cohesive
- produces a network
- Water is an excellent solvent
  - Small
  - Weakens electrostatic forces and hydrogen bonding between polar molecules





Properties of water (2)

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



- It can be ionized

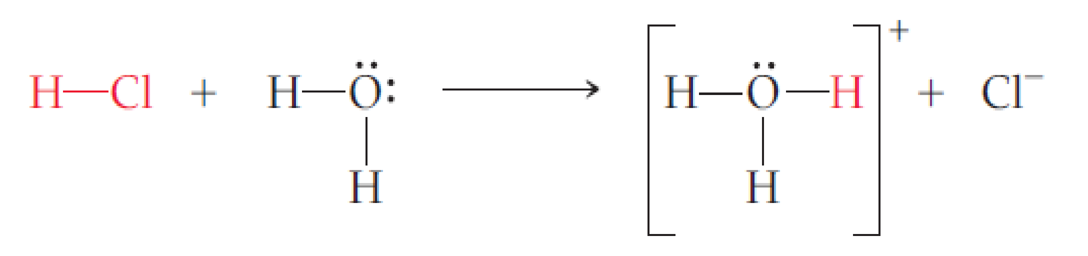
$$H_2O + H_2O \rightleftharpoons H_3O^{\oplus} + OH^{\ominus}$$

Note: $H_3O^+ = H^+$

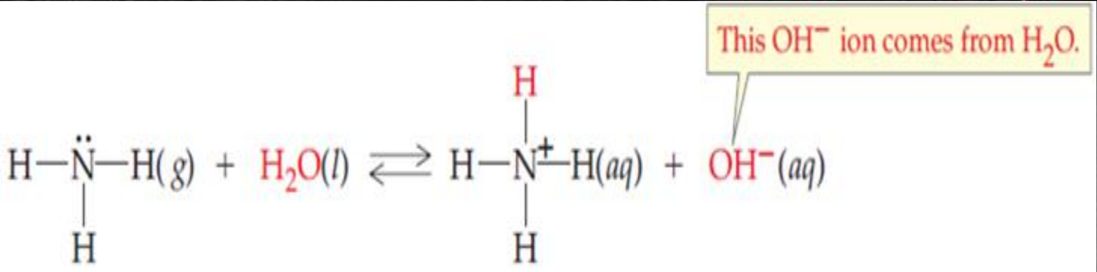
Acids and bases

Definitions and terms

- Acid:
  - A substance that produces H^+ (H_3O^+) when dissolved in water or reacts with other substances
  - Monoprotic acid: HCl, HNO3, CH3COOH
  - Diprotic acid: H_2SO_4
  - Triprotic acid: H_3PO_3



- Base:
  - A substance that produces OH^- when dissolved in water or accepts H^+ when reacts with other molecules
  - NH_3



Water = amphoteric

- Ampho = 'both' or 'dual'
- Substances that can act as an acid in one reaction and as a base in another
- With ammonia (NH_3), water acts as an acid because it donates a proton (hydrogen ion) to ammonia

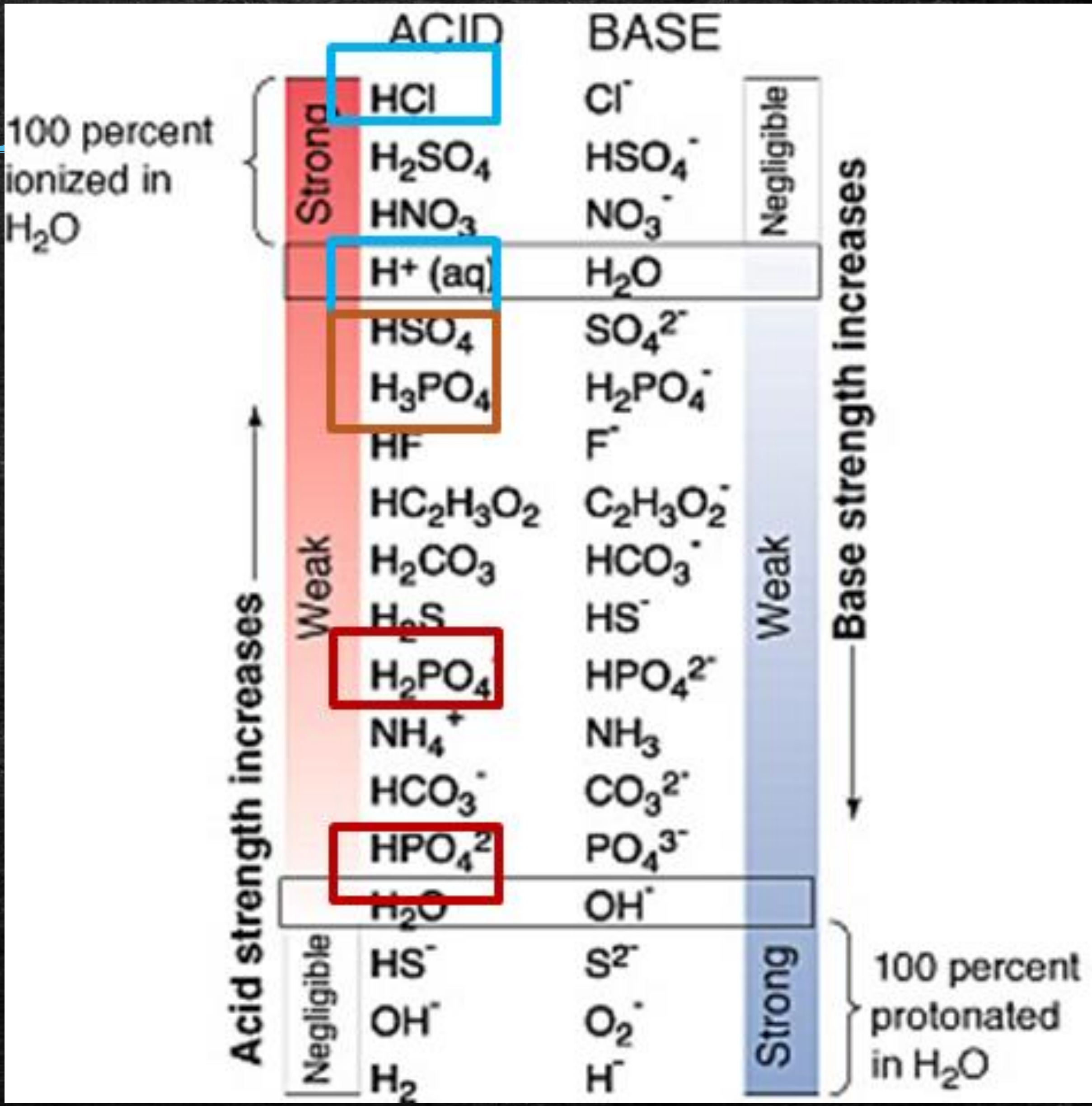
$$\mathbf{NH_3 + H_2O \leftrightarrow NH4^+ + OH^-}$$

- With hydrochloric acid, water acts as a base

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

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 acids and bases are one-way reactions

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

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

- 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
  - Equilibrium constant (Keq) for such reactions

$$HA \leftrightarrow H^{+} + A^{-}$$

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

  - Value of the Ka indicates the direction of the reaction

Ka vs. pKa

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

$$pK_a = -\log K_a$$

Measurements of acids and bases

Molarity

- Measurement of concentration
- Moles = grams / MW
- M = moles / volume (L)
- Grams = M x volume (L) x MW
  - 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

- 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.
- 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:
  - 1 eq of Na+ = 23.1 g, 1 eq of Cl- = 35.5 g, 1 eq of Mg2+ = (24.3)/2 = 12.15 g

Problems to solve

- How many equivalents are in the following:

(a) 5.0 g HNO_3

(b) 12.5 g $Ca(OH)_2$

(c) 4.5 g H_3PO_4

- 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.
- *Note: atomic weight of Ca^{+2} is 40.1 grams/mole*

  – 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

- Electrically-charged minerals when dissolved in water
- Sodium, potassium, chloride, calcium, magnesium, phosphate, and bicarbonate
- Vital for various bodily functions such as nerve and muscle function, fluid balance, acid-base balance, and blood pressure
- Heavy and continuous diarrhea can result in dehydration and very low sodium levels in the body (hyponatremia)
- Heavy sweating leads 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
- Basis of titration (neutralization)

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?

Eq of base = Eq of acid

$n \times M_1 \times Vol_1 = n \times M_2 \times Vol_2$

$1 \times 0.12 \times 22.4 = 1 \times M_1 \times 12$

$M_1 = (0.12 \times 22.4) / 12$

$M_1 = 0.224$ M

Problem to solve

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.

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)
- Reduce stomach acidity and providing relief from heartburn and indigestion (dyspepsia)
- Reduce digestion of proteins by pepsin (pH 1-2 vs. 3.5-5)
- Examples: Magnesium Hydroxide, Aluminum Hydroxide, Calcium Carbonate, Sodium Bicarbonate

Ionization of water

- For simplicity, we refer to the hydronium ion as a hydrogen ion (H^+) and write the reaction equilibrium as:

Water undergoes <u>Self Ionisation</u>

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

or

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

Equilibrium constant

- The equilibrium constant K_{eq} 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 1.8×10^{-16} M.

The ion product of water (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 1×10^{-14} for:

$$K_{eq}\,(55.5\ M) = [H^{\oplus}]\,[OH^{\ominus}]$$

- This constant, Kw, is called the ion product for 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