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Introduction into Biochemistry

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
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  - Dr. Diala Abu Hassan

Outline

- Introduction
- Acids and bases, pH, and buffers
- Macromolecules
    - Carbohydrates, lipids, and 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***

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).

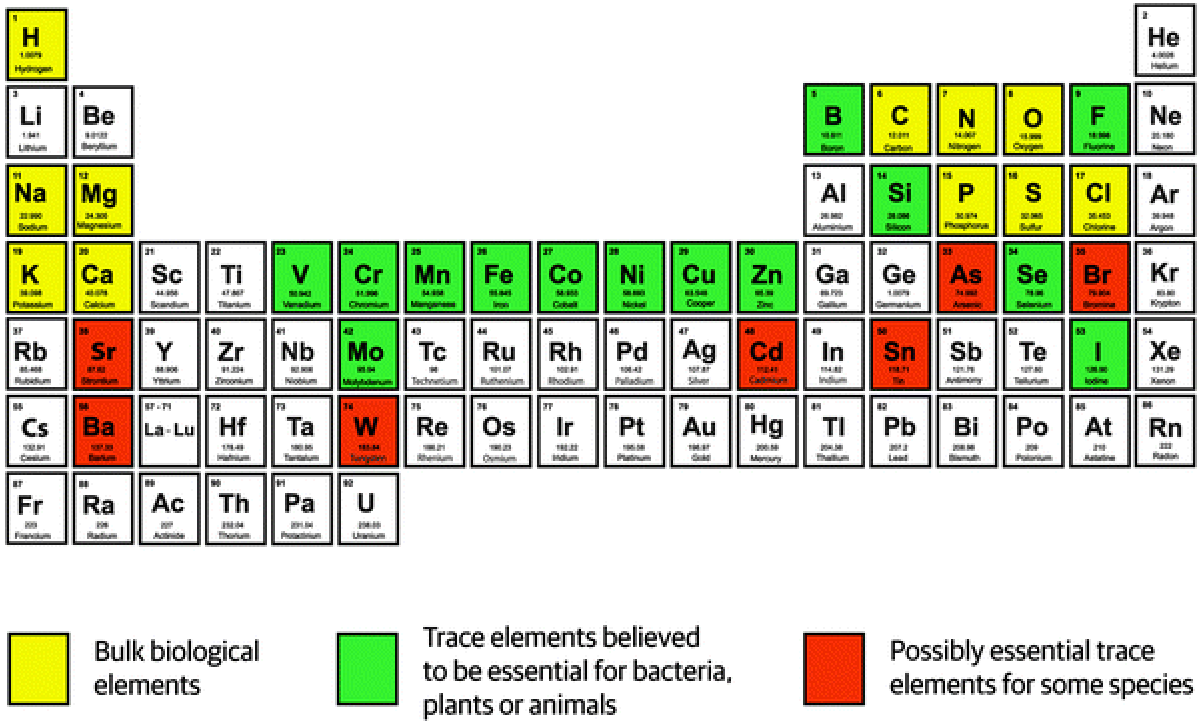
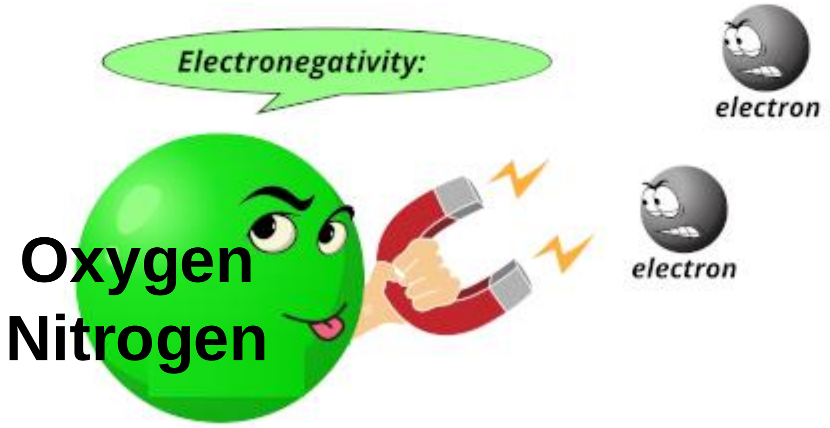


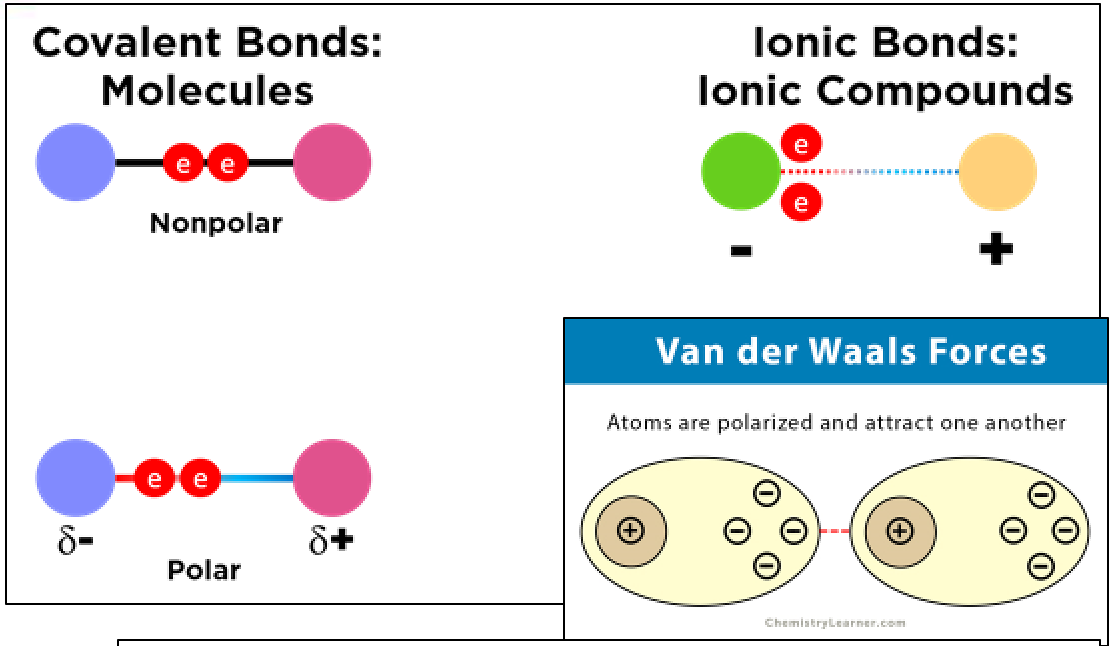
TABLE 2.1 Elements of the Human Body

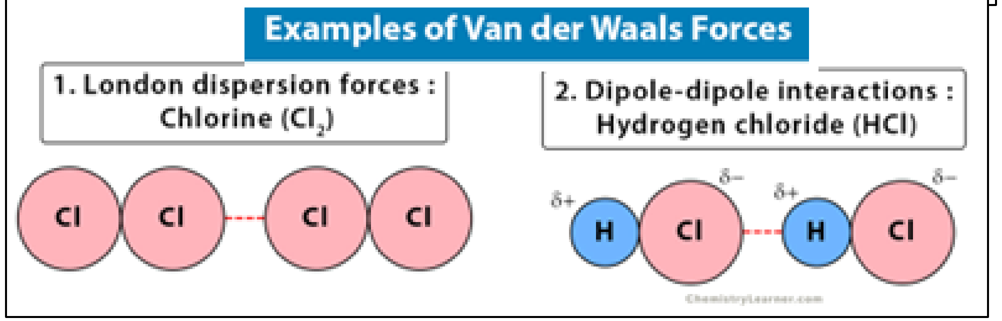
Name	Symbol		Percentage of Body Weight
Major Elements (Total 98.5%)			
Oxygen	O		65.0
Carbon	C		18.0
Hydrogen	H		10.0
Nitrogen	N		3.0
Calcium	Ca		1.5
Phosphorus	P		1.0
Lesser Elements (Total 0.8%)			
Sulfur	S		0.25
Potassium	K		0.20
Sodium	Na		0.15
Chlorine	Cl		0.15
Magnesium	Mg		0.05
Iron	Fe		0.006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

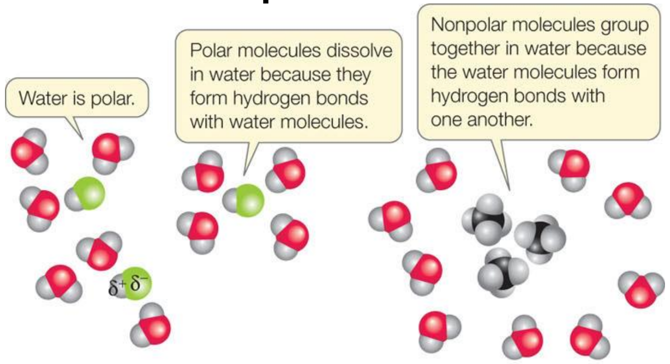
Important terms

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







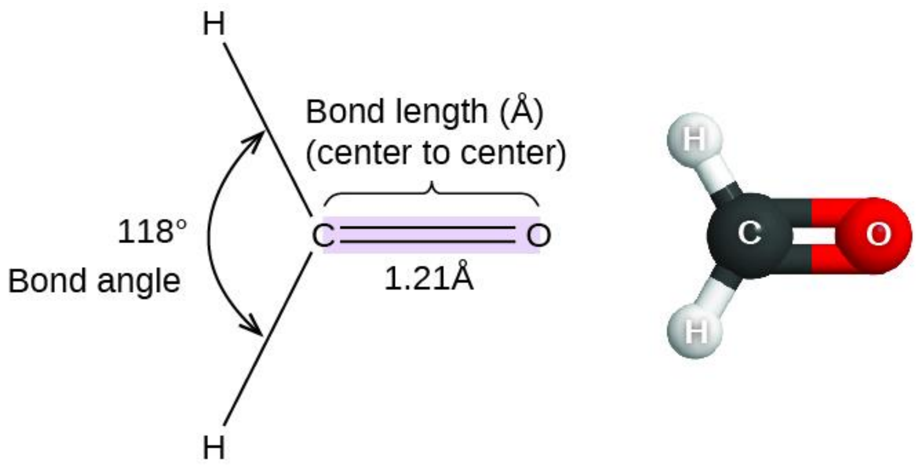


(A) Hydrophilic
(B) Hydrophobic

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

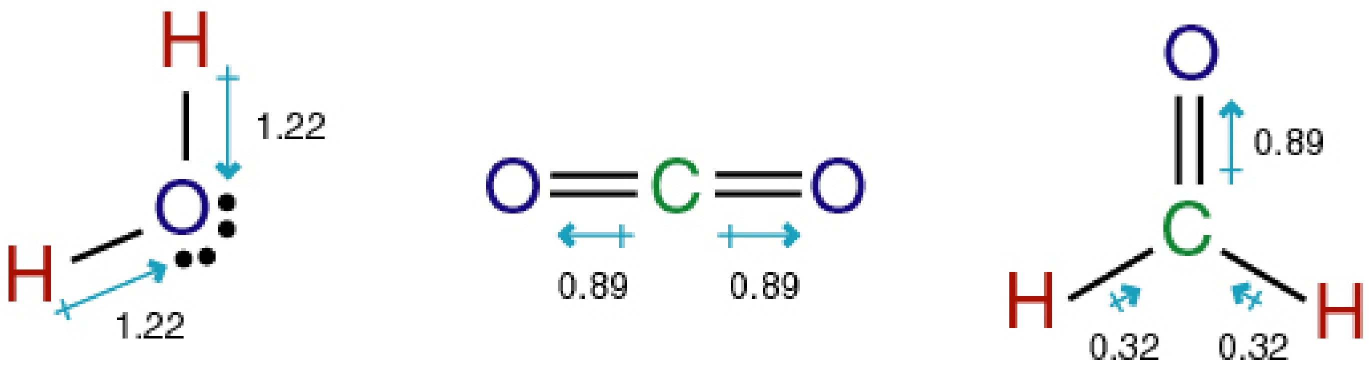
- The three-dimensional structures of molecules are specified by the bond angles and bond lengths for each covalent linkage.



Polarity 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

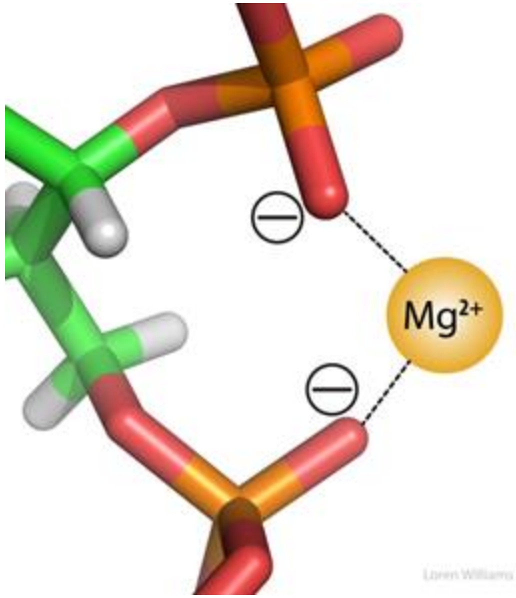
Both water and CO_2 contain polar bonds, but only water is a polar molecule.

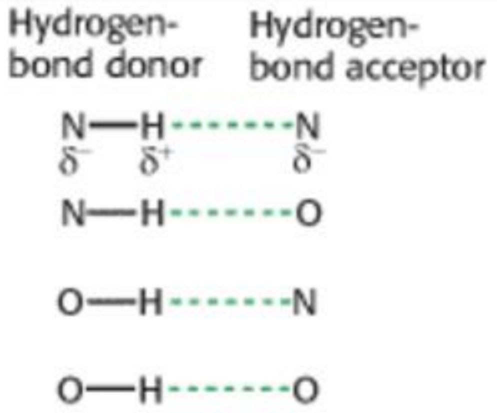


What are non-covalent interactions?

- They are reversible and relatively weak.

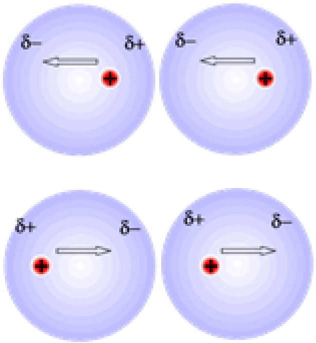
Electrostatic interactions (charge-charge interactions):
- **They are formed between two charged particles.**
- **These forces are quite strong in the absence of water .**





Hydrogen bonds

A hydrogen atom is partly shared between two relatively electronegative atoms (a donor and an acceptor).

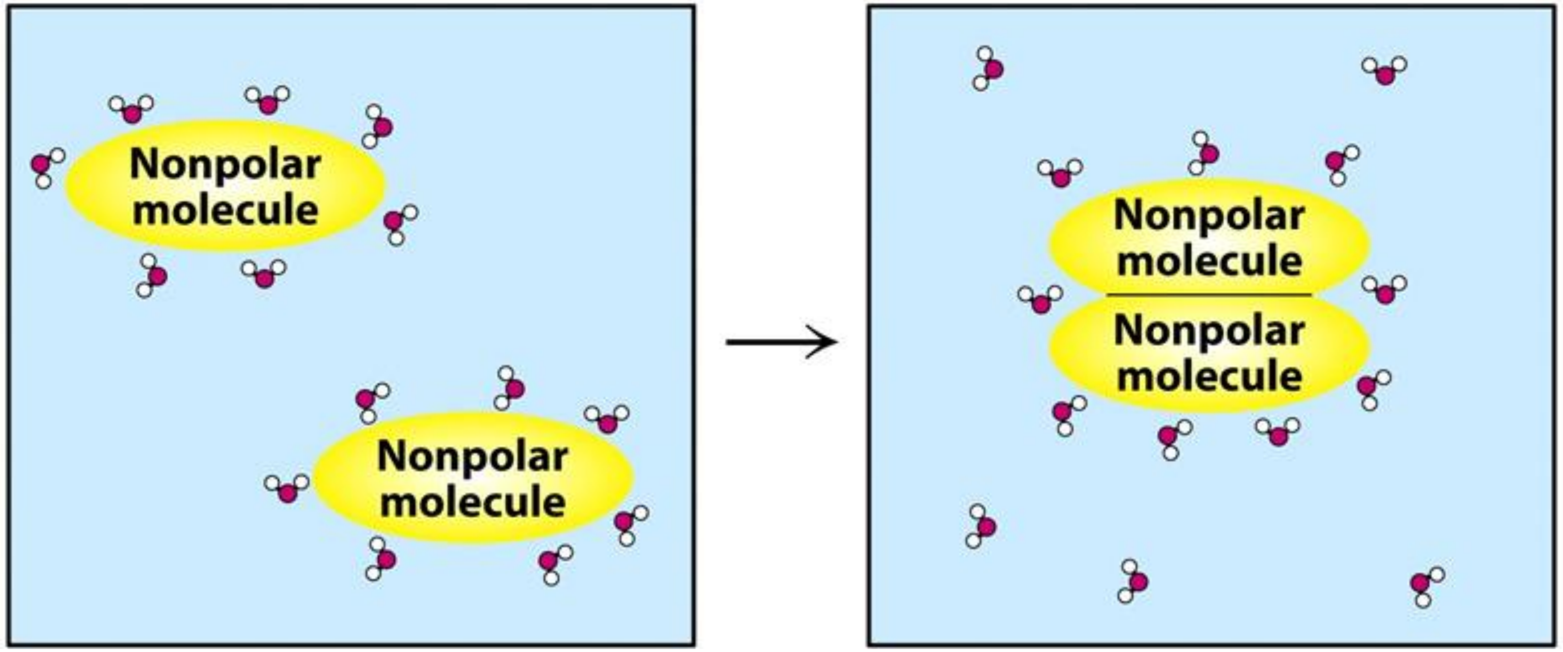


van der Waals interactions

Unequal distribution of electronic charge around an atom changes with time.
The strength of the attraction is affected by distance.

Hydrophobic interactions

- Self-association of nonpolar compounds in an aqueous environment
- Minimize unfavorable interactions between nonpolar groups and water



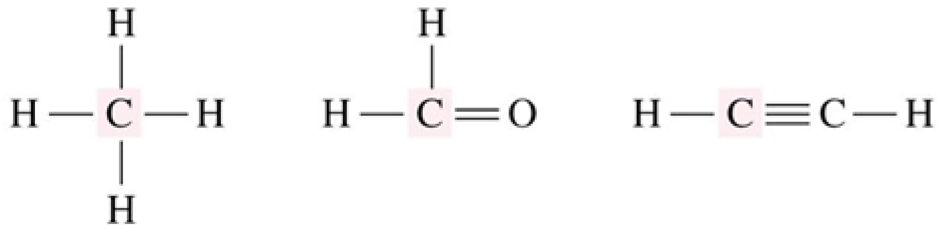
Properties of noncovalent interactions

- Reversible
- Relatively weak
- Molecules interact and bind specifically.
- Noncovalent forces 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

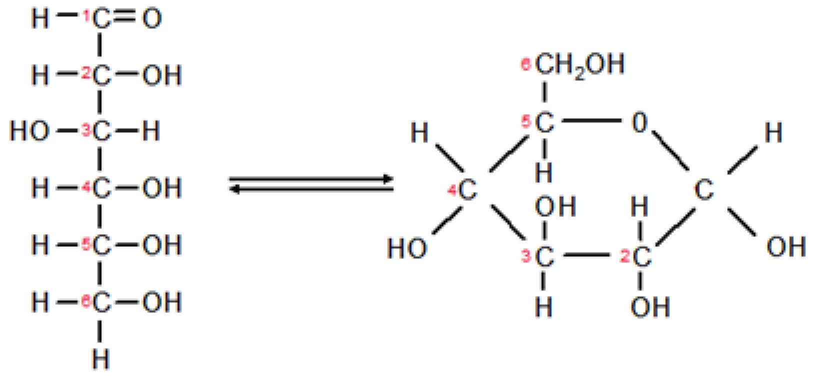
The road to diversity and stability

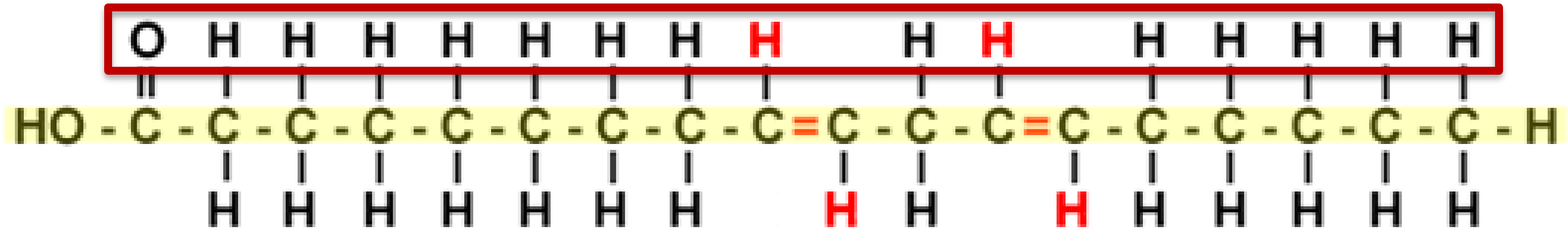
Properties of carbon (1)



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

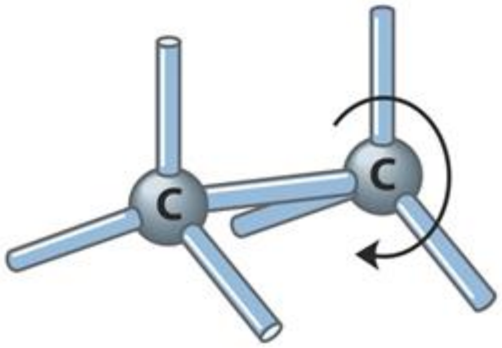
- It can form four bonds, which can be single, double, or triple bonds.
- Each bond is very stable.
  - strength of bonds: triple > double > Single)
- They link C atoms together in chains and rings.
  - These serve as a backbones.

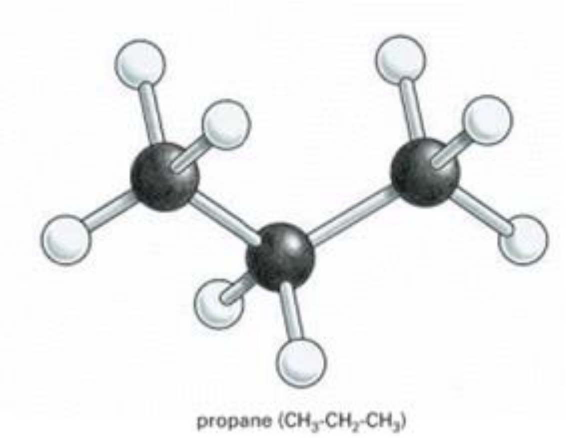


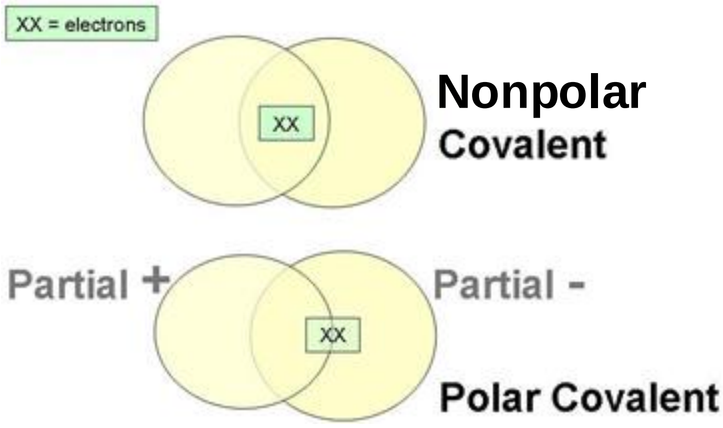


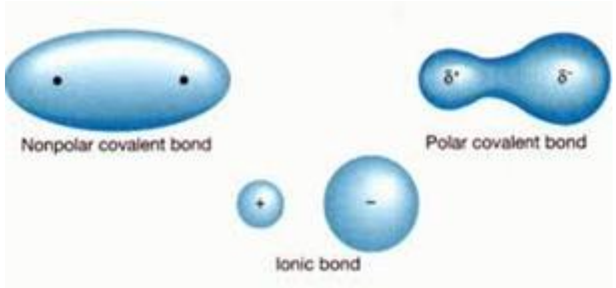
Properties of carbon (2)

- 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.



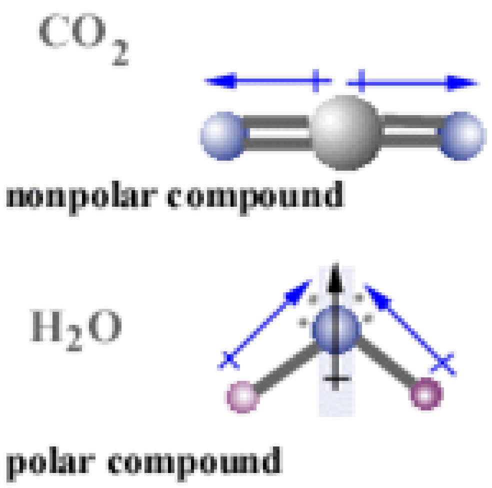




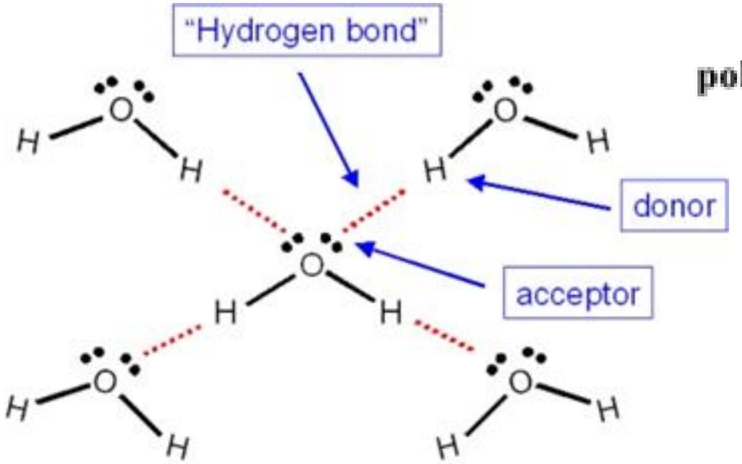


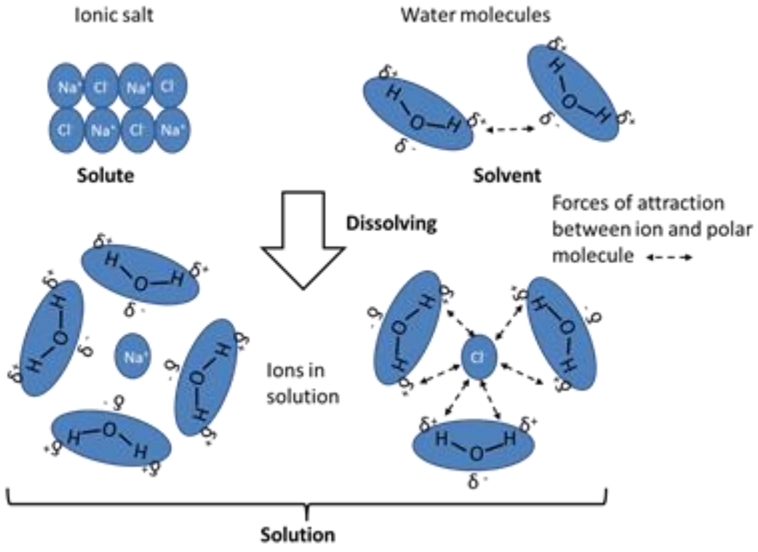
Water

Properties of water (1)



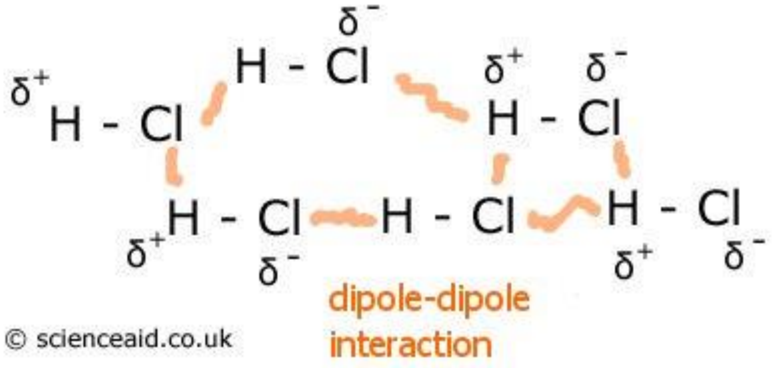
- Water is a polar molecule as a whole because of:
  - the different electronegativities between Hydrogen and oxygen
  - It is angular.
- Water is highly cohesive.
- Water molecules produce a network.
- Water is an excellent solvent because It is small, and it weakens electrostatic forces and hydrogen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

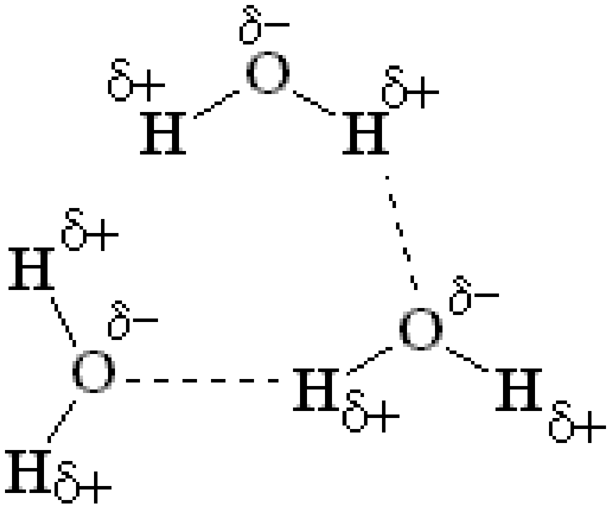




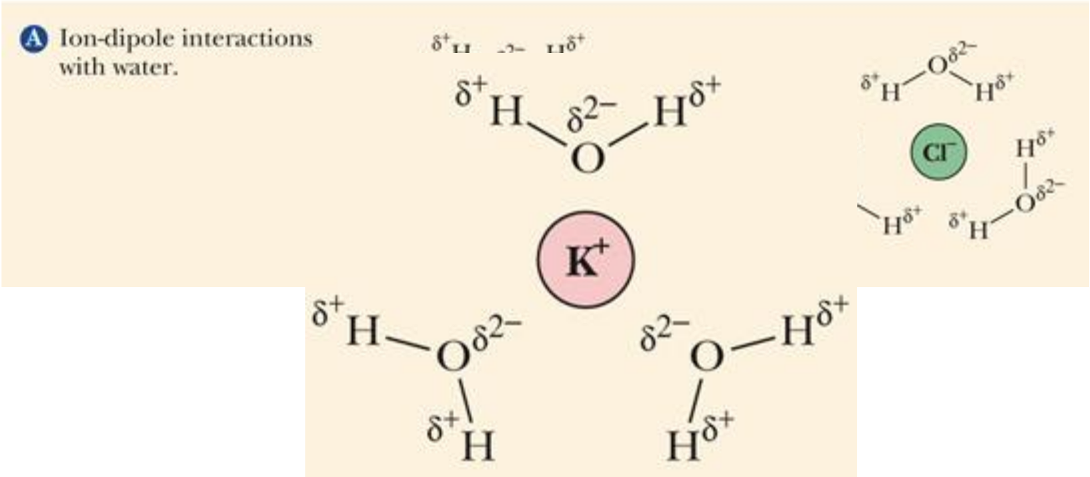
Note

Dipole-dipole interaction



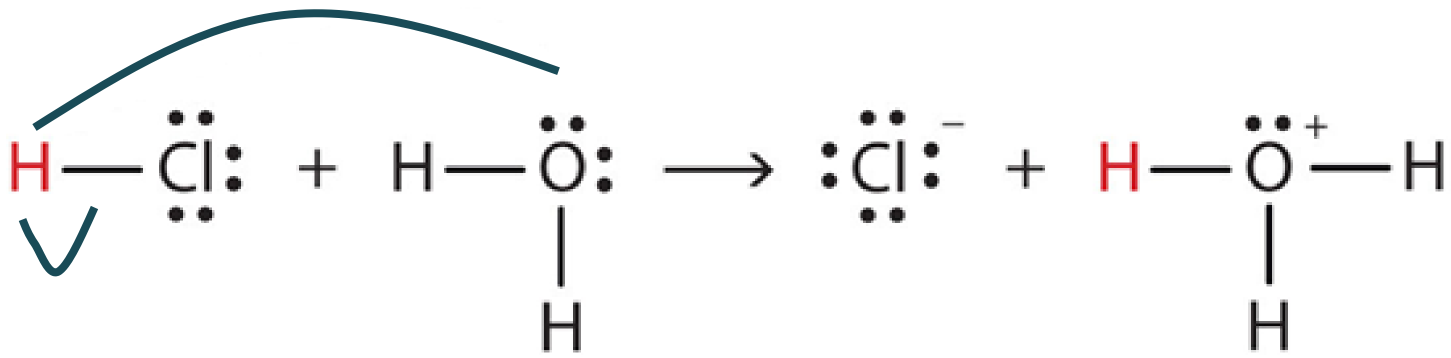


Dipole-charge interaction



Properties of water (3)

- 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).



Properties of water (4)

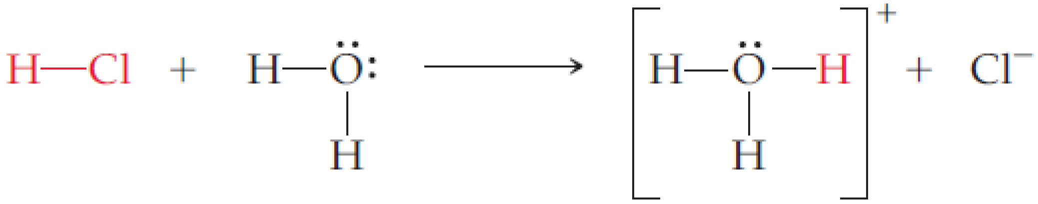
- Water molecules are ionized to become a positively-charged hydronium ion (or proton), and a hydroxide ion:

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

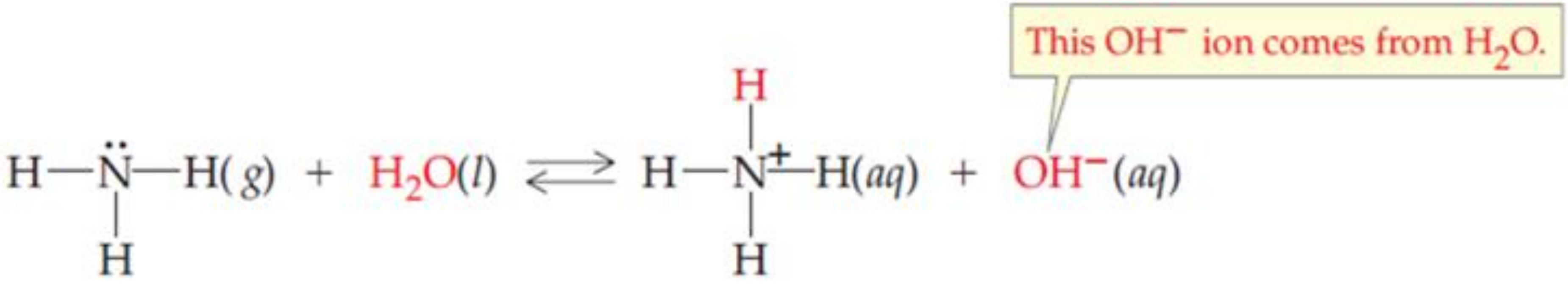
Note: $H_3O^+ = H^+$

Types of acids and bases

- Arrhenius acids and bases
- Acid: a substance that produces H+ when dissolved in water
  - H+ Reacts with water-producing hydronium ion (H_3O^+).



- Base: a substance that produces OH^- when dissolved in water.



Types of acids and bases

- The Brønsted-Lowry acid: any substance (proton donor) able to give a hydrogen ion (H^+-a proton) to another molecule.
  - Monoprotic acid: HCl, HNO_3, CH_3COOH
  - Diprotic acid: H_2SO_4
  - Triprotic acid: H_3PO_3

- Brønsted-Lowry base: any substance that accepts a proton (H^+) from an acid.
  - $NaOH$, NH_3, KOH

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'

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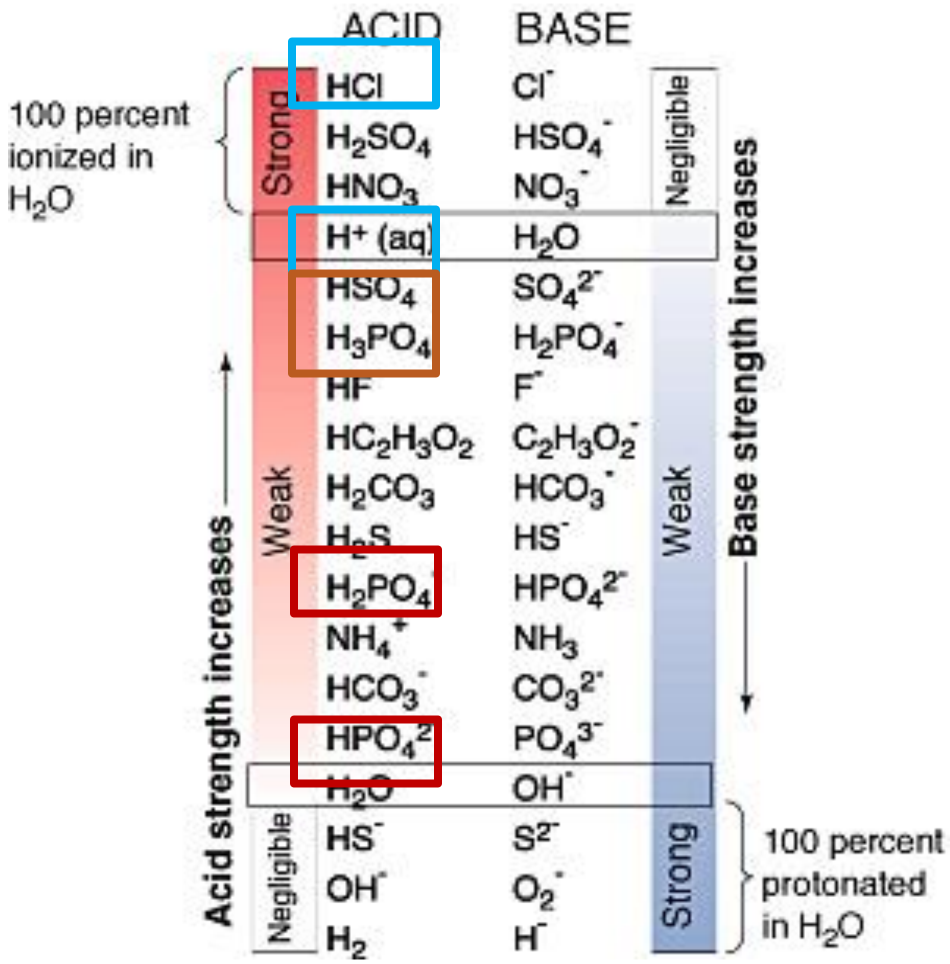
Acid/base strength

- 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
$HPO_4^{2\ominus}$ (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 amount of moles of hydrogen ions that an acid can donate .
  - or a base can accept.
- A 1 g-Eq of any ion is defined as the molar mass of the ion divided by the ionic 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)

Remember: One equivalent of any acid neutralizes one equivalent of any base.

- 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

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.

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 M1 x 12= 1 x 0.12 x 22.4

M1 = (0.12 x 22.4) / 12

M1 = 0.224 M

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.**
- Titration means that we 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.

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

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 1.8×10^{-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:

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

- 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