

Introduction into Biochemistry

Dr. Mamoun Ahram Summer 2018

Course information



- Recommended textbooks
 - Biochemistry; Mary K. Campbell and Shawn O. Farrell, Brooks Cole; 7th edition
- Instructors
 - Dr. Mamoun Ahram
 - Dr. Nafez Abu Tarboush
 - Dr. Diala Abu Hassan

Recommended websites



- NCBI Bookshelf: (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books)
- The Medical Biochemistry Page: (http://web.indstate.edu/thcme/mwking/home.html)
- Biochemistry, Garret and Grishan, Second Ed.: http://web.virginia.edu/Heidi/home.htm

Outline (Ahram + Abu Hassan)



- Introduction
- Acid, base, and pH
- Macromolecules and carbohydrates
- Lipids
- Amino acids
- Polypeptides and proteins structure
- Protein structure-function relationship (part I: fibrous proteins)
- Protein structure-function relationship (part II: globular proteins)

Outline (Ahram + Abu Tarboush)



- Enzymes (introduction)
- Enzymes (kinetics)
- Enzymes (mechanism of regulation)
- Enzymes (cofactors)
- Protein analysis

Office hours for Dr. Ahram



- Location: School of Medicine, Building 1, first floor
- Time: Daily 11-1 (I prefer by appointment)
- Note: If I am not in my office, then try the lab in the first floor. Simply ask for me.



Introduction into biochemistry & Chemical composition of lving organisms

Dr. Mamoun Ahram Lecture 1

References

- This lecture
- Campbell and Farrell, Page 35-43



Biochemistry = understanding life

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

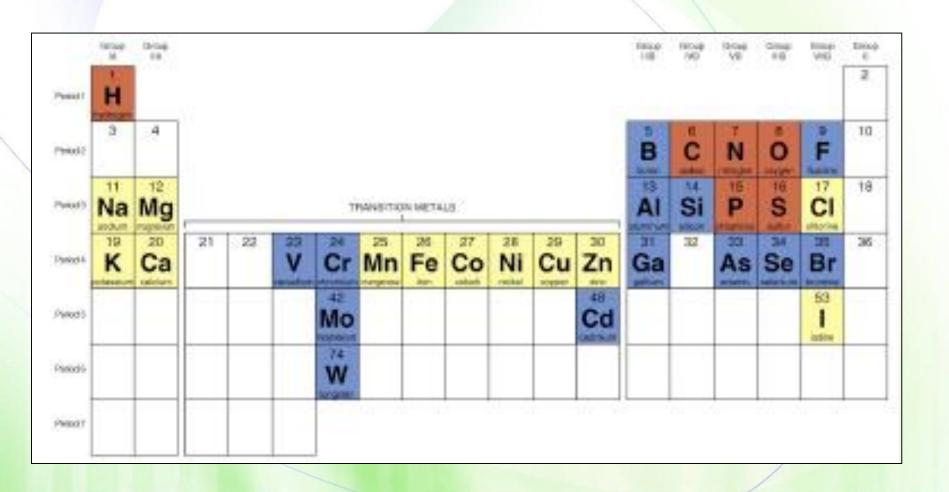
Biochemistry in medicine:

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

Chemical elements in living creatures

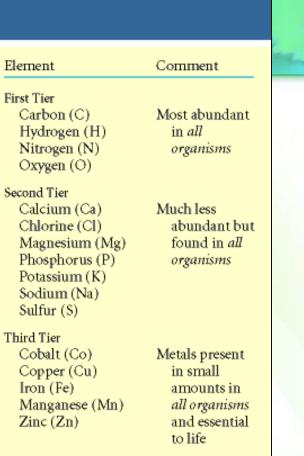


Living organisms on Earth are composed mainly of 31 elements



Abundant elements

- Four primary elements: carbon, hydrogen, oxygen, and nitrogen
 - 96.5% of an organism's weight
- The second groups includes sulfur and phosphorus
- Most biological compounds are made of only SIX elements: C, H, O, N, P, S
- Others are minor, but essential, elements
 - Mostly metals





Aluminum (Al)
Arsenic (As)
Boron (B)
Bromine (Br)
Chromium (Cr)
Fluorine (F)
Gallium (Ga)
Iodine (I)
Molybdenum (Mo)
Nickel (Ni)

Selenium (Se)

Silicon (Si) Tungsten (W) Vanadium (V) Found in or required by some organisms in trace amounts



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
 - Backbone of a molecule
- Nucleophile versus electrophile

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

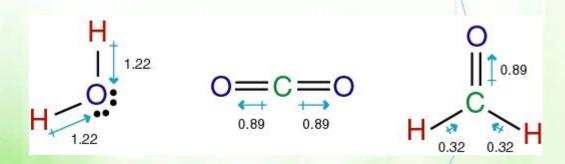
The three-dimensional structures of molecules are specified by the bond angles and bond lengths for each covalent linkage

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

Water is an excellent example of polar molecules, but not CO₂.



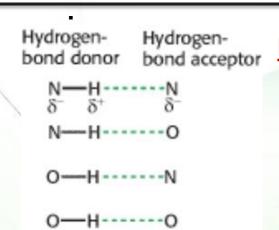
What are non-covalent interactions?



They are reversible and relatively weak.

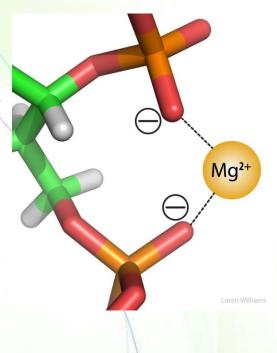
Electrostatic interactions (charge-charge interactions):

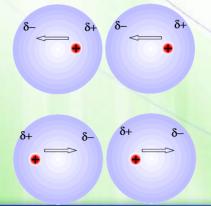
- They are formed between two charged particles.
- These forces are quite strong in the absence of water



Hydrogen bonds

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

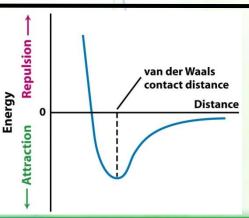




van der Waals interactions

Unequal distribution of electronic charge around an atom changes with time.

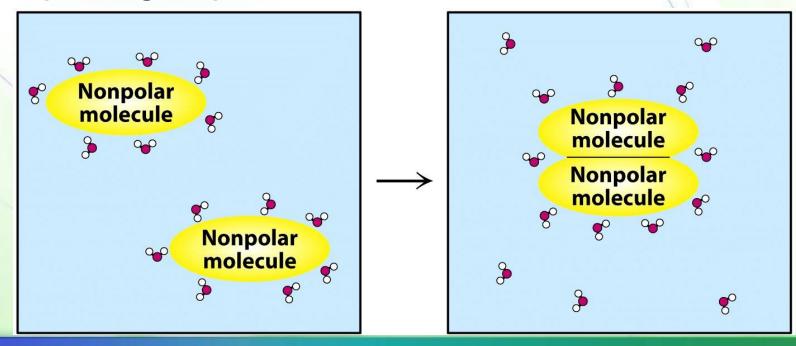
The strength of the attraction is affected by distance.



Hydrophobic interactions



- Not true bonds
- Self-association of nonpolar compounds in an aqueous environment
- Minimize unfavorable interactions between nonpolar groups and water



Properties of noncovalent Interactions



- Reversible
- Relatively weak. 1-30 kj/mole vs. 350 kj/mole in C—C bond
- 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.

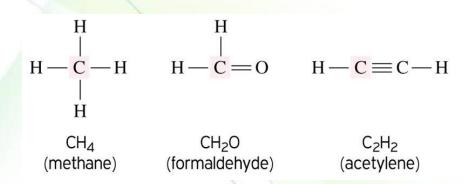
Carbon

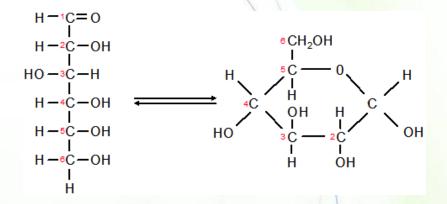
The road to diversity and stability

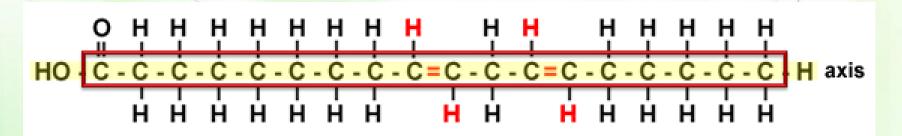
Properties of carbon (1)



- 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.



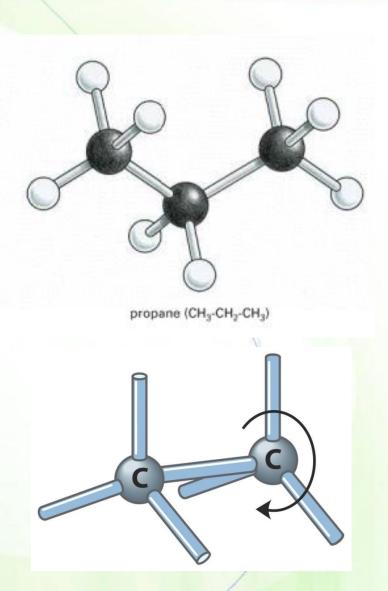




Properties of carbon (2)



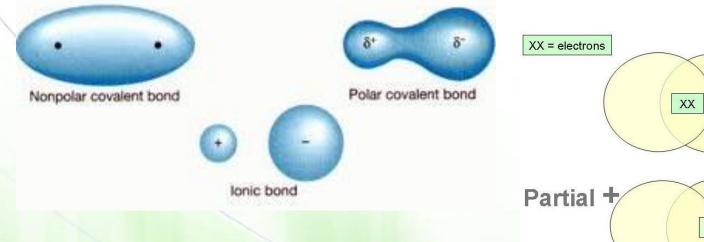
- Carbon bonds have angles giving molecules threedimensional structure.
- In a carbon backbone, some carbon atoms rotate around a single covalent bond producing molecules of different shapes.

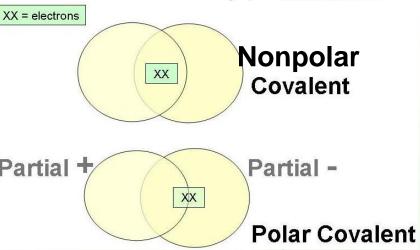


Properties of carbon (3)



- 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 to be soluble.





Functional groups (Groups of atoms attached to a carbon skeleton)



Class of Compound	General Structure ^a	Functional Group Structure	Functional Group Name	Example
Alkane	RCH ₂ -CH ₃	н Н І С-С- 1	Carbon-carbon and carbon-hydrogen single bonds	H ₃ C-CH ₃
Alkene	$RCH=CH_2$	C=C	Carbon-carbon double bond	$H_2C = CH_2$
Alcohol	ROH	-OH	Hydroxyl group	CH ₃ OH
Thiol	RSH	−SH	Thiol or sulfhydryl group	CH ₃ SH
Ether	R-O-R	-o-	Ether group	CH ₃ -O-CH ₃
Amine ^b }	RNH ₂ R ₂ NH R ₃ N	-n<	Amino group	H ₃ C-NH ₂
Imine ^b	R=NH	C=N-H	Imíno group	H_3C $C=NH$
Aldehyde	O ∥ R−C−H	О - - - -	Carbonyl group	CH ₃ C H
Ketone	$\stackrel{ m O}{\parallel}$ $R-C-R$	O -C- O	Carbonyl group	O CH₃CCH₃
Carboxylic acid ^b	RСООН	 ~С−ОН	Carboxyl group	сн³с он



Ester	O R-C-OR	O -C-OR	Ester group	O ∥ CH₃C−OCH₃
Amide	O R-C-NH ₂	O H -C-N H	Amide group	O CH ₃ C-NH ₂
Phosphoric acid ^b	O HO-P-OH OH	О НО—Р—ОН ОН	Phosphoric acid group	O HO—P—OH OH
Phosphoric acid ester	R-O-P-OH OH	O -O-P-OH - OH	Phosphoester group or phosphoryl group	O CH₃OP—OH OH
Phosphoric acid anhydride ^b	O O O	O O 	Phosphoric anhydride group	O O
Carboxylic acid-phosphoric acid mixed anhydride ^b	O O 	О О -C-О-Р-ОН ОН	Acyl-phosphoryl anhydride	О СН ₃ С-О-Р-ОН ОН

^aR refers to any carbon-containing group.

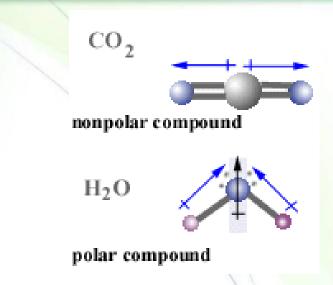
^b These molecules are acids or bases and are able to donate or accept protons under physiological conditions. They may be positively or negatively charged.

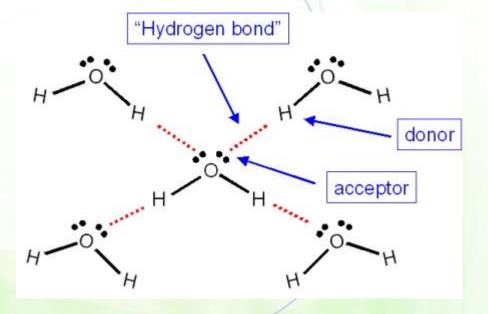
Vater

Properties of water (1)



- Water is a polar molecule as a whole because of:
 - the different electronegativitiy between Hydrogen and oxygen,
 - It is angular.
- Water is highly cohesive.
- Water molecules produce a network.

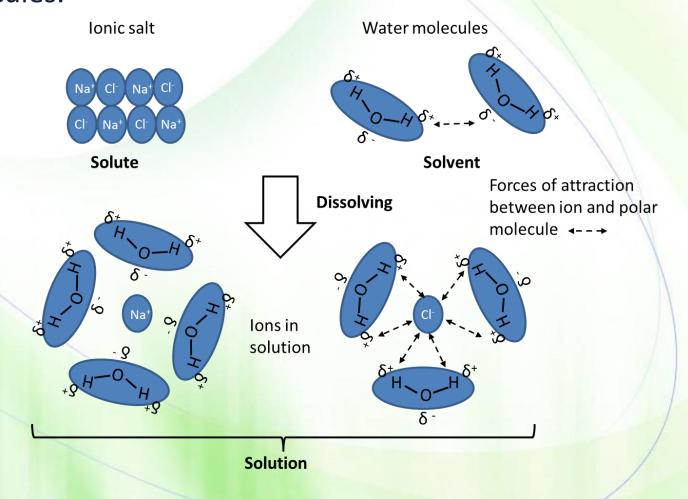




Properties of water (2)



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

$$\begin{array}{c|c} \delta^{+}H & CI & H^{\delta^{+}} \\ \delta^{-}H & CI & H^{\delta^{+}} \\ \delta^{2^{-}}O & H^{\delta^{+}} & O^{\delta^{2^{-}}} \\ H^{\delta^{+}} & \delta^{+}H & O^{\delta^{2^{-}}} \end{array}$$

$$\delta^{+}H \underbrace{\delta^{2-}H^{\delta^{+}}}_{O}H^{\delta^{+}}$$

$$\delta^{+}H \underbrace{O^{\delta^{2-}}\delta^{2-}O^{-}H^{\delta^{+}}}_{\delta^{+}H}$$

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 positivelycharged hydronium ion (or proton), and a hydroxide ion:

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

Brønsted-Lowry acids and bases



- Acid: a substance that produces H⁺ when dissolved in water
 - H⁺ Reacts with water producing hydronium ion (H3O+).

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

$$H = \ddot{N} - H(g) + H_2O(l) \iff H - \ddot{N} + H(aq) + OH^-(aq)$$
 $H = \ddot{N} - H(g) + H_2O(l) \iff H - \ddot{N} + H(aq) + OH^-(aq)$

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, HNO₃, CH₃COOH
 - Diprotic acid: H₂SO₄
 - Triprotic acid: H₃PO₃
- Brønsted-Lowry base: any substance that accepts a proton (H+) from an acid.
 - NaOH, NH₃, KOH

Water is an amphoteric substances



- Substances that can act as an acid in one reaction and as a base in another are called amphoteric substances.
- Example: water
- With ammonia (NH₃), water acts as an acid because it donates a proton (hydrogen ion) to ammonia.

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

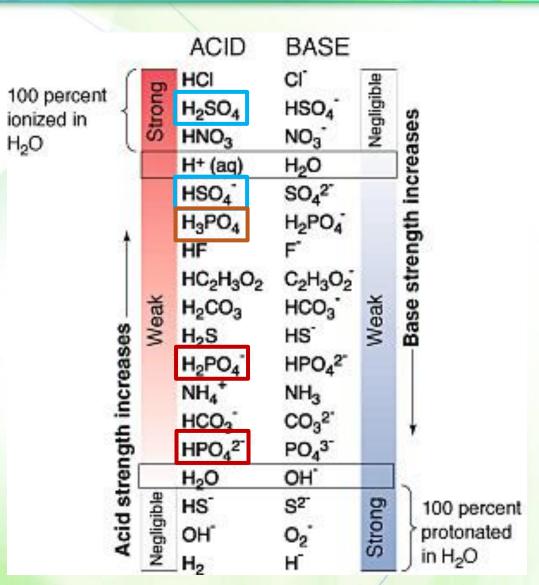
With hydrochloric acid, water acts as a base.

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

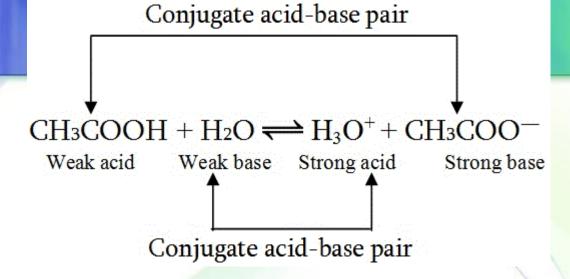
Acid/base strength



- Acids differ in their ability to release protons.
 - Strong acids dissociate 100%
- Bases differ in their ability to accept protons.
 - Strong bases have strong affinity for protons
- For multi-protic acids (H₂SO₃, H₃PO₄), 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

$$HCI \rightarrow H^+ + CI^-$$

NaOH \rightarrow Na⁺ + OH⁻

Weak acids and bases do not ionize completely

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

 $NH_3 + H_2O \leftrightarrow NH_4^+ + OH_2^-$



Equilibrium constant



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

$$K_a = \frac{[{
m H_3O^+}] \cdot [{
m A}^-]}{[{
m HA}]}$$
 Note: H₃O⁺ = H ⁺

- The value of the K_a indicates direction of 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	$K_{\mathbf{a}}(\mathbf{M})$	pK _a
HCOOH (Formic acid)	1.77×10^{-4}	3.8
CH ₃ COOH (Acetic acid)	1.76×10^{-5}	4.8
CH ₃ CHOHCOOH (Lactic acid)	1.37×10^{-4}	3.9
H ₃ PO ₄ (Phosphoric acid)	7.52×10^{-3}	2.2
H ₂ PO ₄ [⊕] (Dihydrogen phosphate ion)	6.23×10^{-8}	7.2
HPO ₄ (Monohydrogen phosphate ion)	2.20×10^{-13}	12.7
H ₂ CO ₃ (Carbonic acid)	4.30×10^{-7}	6.4
HCO ₃ [⊕] (Bicarbonate ion)	5.61×10^{-11}	10.2
NH ₄ [⊕] (Ammonium ion)	5.62×10^{-10}	9.2
CH ₃ NH ₃ ⊕ (Methylammonium ion)	2.70×10^{-11}	10.7

TABLE | $9.4~K_A$ AND pK_A VALUES FOR SELECTED ACIDS

Name	Formula	Ka	рKa
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 ₃ CH(OH)CO ₂ H	1.4×10^{-4}	3.85
Acetic acid	CH ₃ CO ₂ H	1.8×10^{-5}	4.74
Carbonic acid	H ₂ CO ₃	4.4×10^{-7}	6.36
Dihydrogenphosphate ion	$H_2PO_4^-$	6.2×10^{-8}	7.21
Ammonium ion	$\mathrm{NH_4}^+$	5.6×10^{-10}	9.25
Hydrocyanic acid	HCN	4.9×10^{-10}	9.31
Hydrogencarbonate ion	HCO ₃ ⁻	5.6×10^{-11}	10.25
Methylammonium ion	CH ₃ NH ₃ ⁺	2.4×10^{-11}	10.62
Hydrogenphosphate ion	HPO_4^{2-}	4.2×10^{-13}	12.38

Base dissociation constant (K_b)





$$BH^+ \stackrel{\longrightarrow}{\longleftarrow} B + H^+$$

$$B + H_2O \longrightarrow BH^+ + OH^-$$

$$K_a = \frac{[B][H^+]}{[BH^+]}$$

$$K_b = \frac{[BH+][OH^-]}{[B]}$$

TABLE 7.3 Values of K_b for Some Common Weak Bases

Name	Formula	Conjugate Acid	$K_{ m b}$
Ammonia	NH ₃	NH ₄ ⁺	1.8×10^{-5}
Methylamine	CH ₃ NH ₂	CH ₃ NH ₃ ⁺	4.38×10^{-4}
Ethylamine	$C_2H_5NH_2$	$C_2H_5NH_3^+$	5.6×10^{-4}
Aniline	$C_6H_5NH_2$	$C_6H_5NH_3^+$	3.8×10^{-10}
Pyridine	C_5H_5N	$C_5H_5NH^+$	1.7×10^{-9}

Expression



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

Molarity of solutions



We know that moles of a solution are the amount in grams in relation to its molecular weight (MW or a.m.u.).

A molar solution is one in which 1 liter of solution contains the number of grams equal to its molecular weight.

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

$$grams = M \times vol \times MW$$

Exercise



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

grams = $58.4 \times 5 M \times 0.1 \text{ liter} = 29.29 \text{ g}$

Equivalents (acids/bases and ions)



- When it comes to acids, bases and ions, it is useful to think of them as equivalents.
- 1 equivalent of a strong acid contains 1 mol of H⁺ ions, and 1 g-Eq of an acid is the mass in grams that contains 1 mol of H⁺ ions.
- Similarly, 1 equivalent of a strong base contains 1 mol of OH⁻ ions, and 1 g-Eq of a base is the mass in grams that contains 1 mol of OH⁻ ions.
- For ions, a 1 g-Eq of any ion is defined as the molar mass of the ion divided by the ionic charge.

Examples



- 1 mol HCl = 1 mol [H⁺] = 1 equivalent
- \bullet 1 mol H₂SO₄ = 2 mol [H⁺] = 2 equivalents
- One equivalent of Na⁺ = 23.1 g
- One equivalent of Cl⁻ = 35.5 g
- One equivalent of $Mg^{+2} = (24.3)/2 = 12.15 g$

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

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 =

- $= (5 \text{ mEq/L}) \times (1 \text{ Eq/1000 mEq}) \times (20.1 \text{ g/ 1 Eq})$
- $= 0.1 \, g/L$
- =100 mg/L

Normal solutions



Normality (N) considers both the molarity of the solution and the equivalent content of the acid or base.

N= n x M (where n is an integer)

For an acid solution, n is the number of H⁺ provided by a formula unit of acid. Similarly, for a base solution is the number of OH⁻ a base can donate.

Example



- 3 M H₂SO₄ solution is the same as a 6 N H₂SO₄ solution
- 1 M Ca(OH)₂ solution is the same as a 2N Ca(OH)₂ solution

Remember!

The normality of a solution is NEVER less than the molarity

Exercise



What is the normality of H₂SO₄ solution made by dissolving 6.5 g into 200 mL? (MW = 98)?

```
M = mol / MW or M = grams / (MW x vol)
= 6.5 g / (98 x 0.2 L)
= 6.5 / 19.6
= 0.33
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$$N = M \times n = 0.33 \times 2 = 0.66 N$$

Normality and equivalents



$$\frac{\text{Normality (N)}}{\text{Liters of solution}} = \frac{\text{Equivalents of acid or base}}{\text{Liters of solution}}$$

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

Problems



- 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?
- 10.93 What volume of 0.085 M HNO₃ is required to titrate 15.0 mL of 0.12 M Ba(OH)₂ solution?
- 10.94 Titration of a 10.0 mL solution of KOH requires 15.0 mL of 0.0250 M H₂SO₄ solution. What is the molarity of the KOH solution?

Hint: If number of H⁺ (OH⁻) is different, convert M to N, find the answer in N, then convert N to M.

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?

$$M1 \times Vol1 = M2 \times Vol2$$

$$0.12 \times 22.4 = M2 \times 12$$

$$M2 = (0.12 \times 22.4) / 12$$

$$M2 = 0.224 M$$



10.93 What volume of 0.085 M HNO₃ is required to titrate 15.0 mL of 0.12 M Ba(OH)₂ solution?

Convert M to N first N of $HNO_3 = 1 \times 0.085 = 0.085 \text{ N}$ N of $Ba(OH)_2 = 2 \times 0.12 = 0.24$

N1 x Vol1 = N2 x Vol2 0.24 x 15 = 0.085 x Vol2 Vol2 = (0.24 x 15) / 0.085 Vol2 = 42.35 mL

Apply same method for third question

Ion product of water



$$\mathrm{HA}(aq) + \mathrm{H}_2\mathrm{O}(l)
ightleftharpoons H_3\mathrm{O}^+(aq) + \mathrm{A}^-(aq)$$
 $\mathrm{A}^-(aq) + \mathrm{H}_2\mathrm{O}(l)
ightleftharpoons HA(aq) + \mathrm{OH}^-(aq)$

$$K_{\rm a} \cdot K_{\rm b} = \left(\frac{[{\rm H}_3{\rm O}^+] [{\rm A}^-]}{[{\rm H}_A]}\right) \left(\frac{[{\rm H}_A] [{\rm OH}^-]}{[{\rm A}^-]}\right)$$

$$= [H_3O^+][OH^-]$$

$$=K_{
m W}=1.0 imes10^{-14}$$
 at 25 $^{\circ}{
m C}$

Ionization of water



- Water dissociates into hydronium (H₃O⁺) and hydroxyl (OH⁻) ions.
- For simplicity, we refer to the hydronium ion as a hydrogen ion (H⁺) and write the reaction equilibrium as:

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

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:

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

This constant, Kw, is called the ion product for water.

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

[H₁] and [OH₁]



- For pure water, there are equal concentrations of [H⁺] and [OH⁻], each with a value of 1 x 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.

