INTRODUCTION TO BIOCHEMISTRY:

BIOCHEMISTRY IN MEDICINE:

- Explains all disciplines
- to Diagnose and monitor diseases
- to Design drugs (new antibiotics, chemotherapy agents)
- to Understand the molecular bases of diseases

CHEMICAL ELEMENTS IN ORGANISMS:

Element	Comment
First Tier	
Carbon (C)	Most abundant in *all organisms*
Hydrogen (H)	
Nitrogen (N)	
Oxygen (O)	
Second Tier	
Calcium (Ca)	Much less abundant but found in *all organisms*
Chlorine (Cl)	
Magnesium (Mg)	
Phosphorus (P)	
Potassium (K)	
Sodium (Na)	
Sulfur (S)	
Third Tier	
Cobalt (Co)	Metals present in small amounts in *all organisms* and essential to life
Copper (Cu)	
Iron (Fe)	
Manganese (Mn)	
Zinc (Zn)	
Fourth Tier	
Aluminum (Al)	Found in or required by *some organisms* in trace amounts
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)	

Total Elements = 31

Atoms are NOT valuable unless they *interact* with each other to form molecules

BONDS:

*Properties of Bonds:

-Bond Strength; the amount of energy needed to break the bond.

-Bond Length; the distance between two nuclei.

Factors:

- The size of the nuclei of the atoms contributing to the bond
- The type of bond whether it's a single bond, double bond or triple bond

Relation between Length & Strength of a certain Bond:

Longer = Weaker

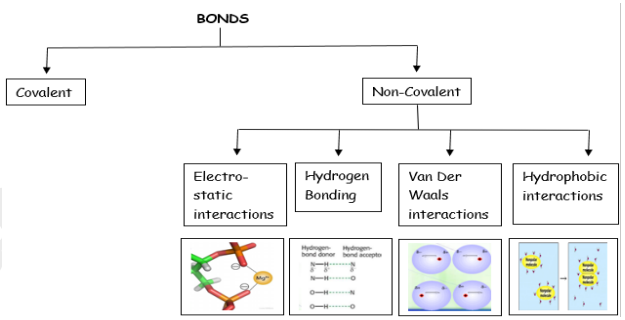
Shorter = Stronger

-Bond Orientation: bond angles determining the overall geometry of atoms in a molecule.

Factors:

- The sizes of atoms
- The types of bonds
- The orientation in space
- The number and types of bonds they can make with each other

*Types of Bonds:



◊ Covalent Bond:

When electrons are neither in the 1st atom nor the 2nd one, but shared (either equally or unequally) between both of them.

If sharing is equal, the bond is non-polar. **i.e.** H-H

If sharing is unequal;

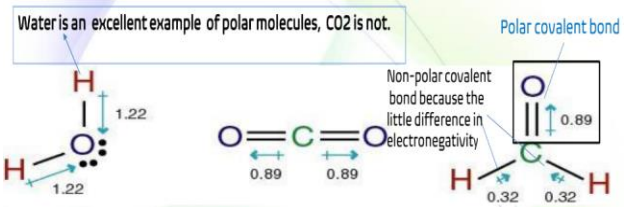
If ΔElectronegativity is low, the bond is non-polar. **i.e.** C-H

If ΔElectronegativity is high, the bond is polar. **i.e.** O-H / N-H

Bonds are known as "dipoles".

RECALL:

Electronegativity: The tendency of an atom to attract electrons of the bond.



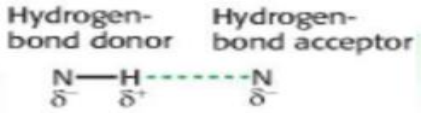
NOTE:
Do Not Be Confused between polarity of a bond & polarity of a molecule (the overall polarity of all bonds).
i.e. CO_2
C=O is a polar bond
O=C=O is a non-polar molecule

◊ Non-Covalent Bond Interactions:
Are a type of connections between molecules where no electrons are shared.
They're interactions based on attraction and repulsion, that is made between different molecules, it's not between atoms of the same molecules -unless it is a very large molecule-.

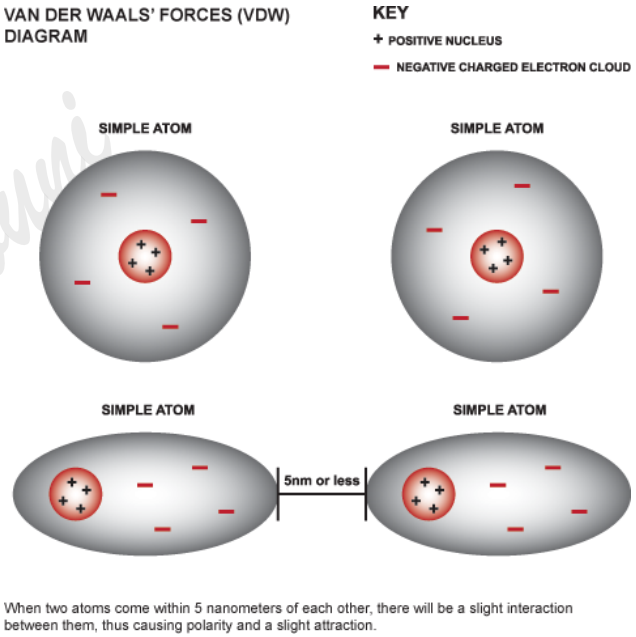
- Properties of Non-Covalent Interactions:
-Reversible
-Relatively weak (1-30 KJ/mole vs. 350 KJ/mole in C—C bond)
-Molecules interact and bind specifically
-Noncovalent forces significantly contribute to the structure, stability and functional competence of macromolecules in living cells
-Can be either attractive or repulsive
-Involve interactions both within the biomolecule and between it and the water of the surrounding environment

•Electrostatic Interactions (Charge-Charge Interactions):
-They are formed between two charged particles
-These forces are quite strong in the absence of water
-They can be: (full-full/ full-partial/ partial-partial)

•Hydrogen Bond:
<u>It is a special case of electrostatic interactions</u>.
The first molecule must involve a hydrogen atom which is covalently bonded to highly EN atom in the same molecule. This hydrogen (partially positive) must be associated by a hydrogen bond with a highly EN atom (partially negative) in another molecule.
NOTE:
The molecule which has this hydrogen is called **donor** and the other is called **acceptor**

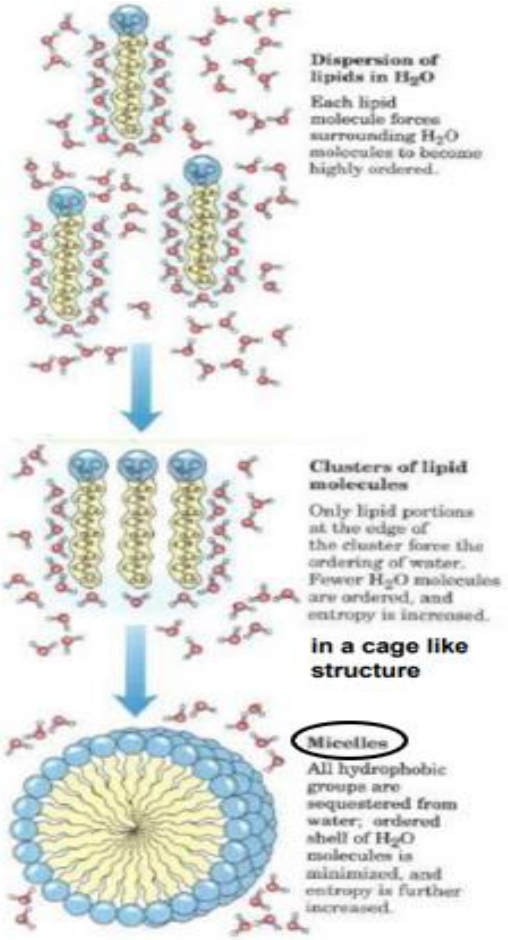


•Van Der Waals Interactions:



When two atoms come within 5 nanometers of each other, there will be a slight interaction between them, thus causing polarity and a slight attraction.

•Hydrophobic Interactions:
Self-association of nonpolar compounds in an aqueous environment (The forces that drive 2 separated droplets of oil in a surface of water to come together forming one big droplet).
-Not true interactions
-Minimize unfavorable interactions between nonpolar groups and water

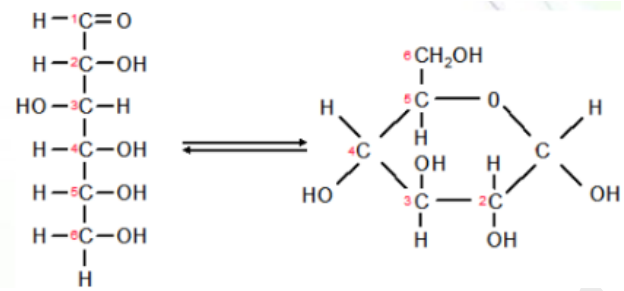


CARBON:

***Properties of Carbon:**

•**It** can form four bonds, which can be; single < double < triple bonds. Each bond is very stable.

Carbon can form bonds with other **C** atoms in chains and rings. These serve as backbones.



•**Carbon bonds** have angles giving molecules 3D structure.

Some **carbon atoms** rotate around a single covalent bond producing **isomers**.

Factors:

-The type of bond

-The presence /absence of unshared electron pairs

•**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 resulting molecule is soluble.

FUNCTIONAL GROUPS:

Class of Compound	General Structure[a]	Functional Group Structure	Functional Group Name	Example
Alkane	RCH_2-CH_3		Carbon-carbon and carbon-hydrogen single bonds	H_3C-CH_3
Alkene	$RCH=CH_2$		Carbon-carbon double bond	$H_2C=CH_2$
Alcohol	ROH		Hydroxyl group	CH_3OH
Thiol	RSH		Thiol or sulfhydryl group	CH_3SH
Ether	R–O–R		Ether group	CH_3-O-CH_3
Amine[b]	RNH_2 R_2NH R_3N		Amino group	H_3C-NH_2
Imine[b]	R=NH		Imino group	
Aldehyde			Carbonyl group	
Ketone			Carbonyl group	
Carboxylic acid[b]	R–COOH		Carboxyl group	
Ester			Ester group	
Amide			Amide group	
Used in Phospho-rylation Phosphoric acid[b]			Phosphoric acid group	
Phosphoric acid ester[b]			Phosphoester group or phosphoryl group	
Phosphoric acid anhydride[b]			Phosphoric anhydride group	
Carboxylic acid–phosphoric acid mixed anhydride[b]			Acyl-phosphoryl anhydride	

[a] R 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.

NOTE:

The presence of different compounds with different reactions is due to the presence of functional groups.

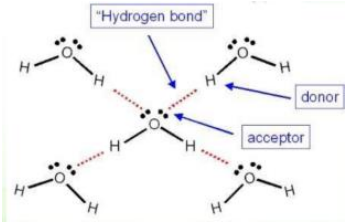
WATER:

***Properties:**

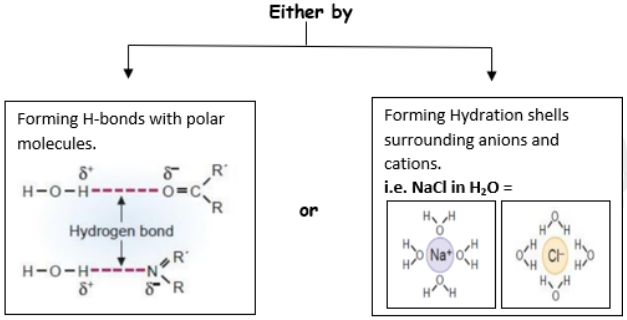
•**Water** is a polar molecule, because;
The different electronegativity between Hydrogen and oxygen.
It is angular.

•**It** is highly cohesive.

•**Water molecules** produce a network by interacting with each other through hydrogen bonds.



•**It** is an excellent solvent because it is small, and it weakens electrostatic forces and hydrogen bonding between polar molecules.



◊ H-Bonding:

-H-bond (X—H----A) is stronger if;
A is O, N or F **& X** is O, N or F

-Average number of H-bond in ice crystals is 4, **while in liquid water at 10 °C** is 3.4. [There is no 3.4 hydrogen bond, there is a half-life of the hydrogen bond that is a round nanosecond, so they form and break all the time]

-Number of H-bonds decrease with higher temperatures

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

•Water molecules are ionized to become a positively charged hydronium ion [H_3O^+] (or proton) and a hydroxide ion [^-OH].

***Importance:**

•~60% of our body is water, 70-85% of the weight of a typical cell

•A solvent of many substances our bodies need such as glucose, ions, etc.
[Important in Transport**]**

•Acts as a medium in which acids and bases release their chemical groups to maintain a constant cellular environment or homeostasis.
(This facilitates reactions allowing ligands to move freely**)**

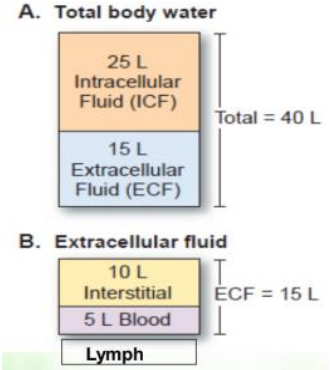
•A participant in many biochemical reactions (Not just as a medium).

•Essential buffer that maintain pH

•Temperature regulation - high specific heat capacity; maintaining the temperature in a certain range

[Water Structure Resists Temperature Changes, because of;
-High thermal conductivity
-High heat of fusion
-High heat capacity and heat of vaporization**]**

***Water in Our Bodies:**



ACIDS AND BASES:

DEFINING ACIDS AND BASES:

***Acid Definition:**

-Arrhenius: a substance that produces H+ when dissolved in water.

-Bronsted-Lowry: Proton donor substance
-Lewis: Electron acceptor substance

***Base Definition:**
-Arrhenius: a substance that produces ^{-}OH when dissolved in water.
-Bronsted-Lowry: Proton acceptor substance
-Lewis: Electron donor substance

WHAT ABOUT WATER ??
It is an *amphoteric* [NOT amphipathic] substance;
it acts as an **acid** if reacted with **base**

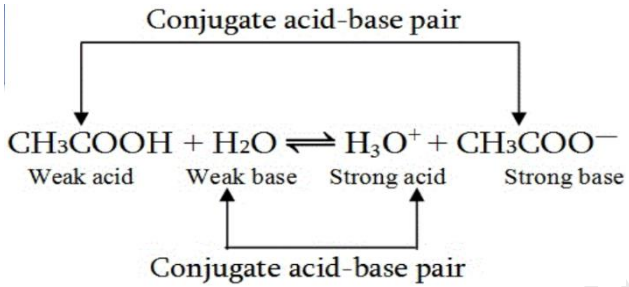
$NH_3 + H_2O \leftrightarrow NH_4^+ + OH^-$

it acts as a **base** if reacted with **acid**

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

TYPES OF ACIDS [According to *Number of Protons (H+)*]:
Monoprotic acid: HCl, HNO_3, CH_3COOH
Polyprotic acid;
Diprotic acid: H_2SO_4
Triprotic acid: H_3PO_3

CONJUCATED ACID-BASE PAIR:



The stronger the acid, the weaker the conjugate base and vice versa.

NOTE:
- Strong acids and bases are one-way reactions

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

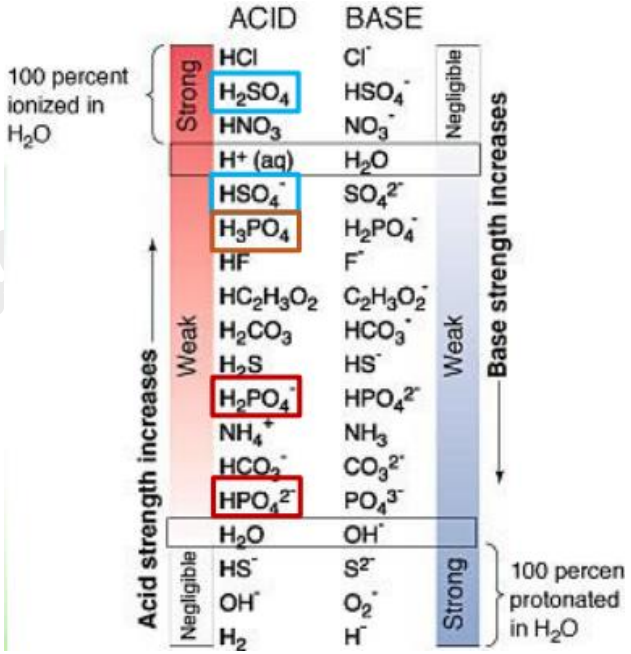
$NaOH \rightarrow Na^+ + OH^-$

- Weak acids and bases do not ionize completely

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

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

STRENGTH OF ACIDS AND BASES:
***Description:**
-Acid Strength: Acid ability to release (donate) protons.
-Base Strength: Base ability to accept protons.



***Calculations:**
-Acid Strength: By calculating K_a; the higher the K_a, the stronger the acid.

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

If K_a > 1, the products side is favored.
If K_a < 1, the reactants side is favored.
[For simplicity, K_a is converted into **pK_a**, which = -log K_a**]**

↑ K_a ↓ pK_a ↑ Strength

-Base Strength: By calculating K_b; the higher the K_b, the stronger the base.

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

If K_b > 1, the products side is favored.

If K_b < 1, the reactants side is favored.

[For simplicity, K_b is converted into **pK_b**, which = -log K_b**]**

↑ K_b ↓ pK_b ↑ Strength

EXPRESSION OF SOLUTIONS:

***Molarity:**

Number of moles per liter.

moles (mol) = grams / MW

Molar (M) = moles / volume

grams (g) = M x mol x volume

***Equivalents:**

A measuring unit.

1 Eq of a strong Acid = 1 mol of H^+

i.e.

1 Eq of HCl = 1 mol of H^+ = 1 mol of HCl

1 Eq of H_2SO_4 = 1 mol of H^+ = 1/2 mol of H_2SO_4

1 Eq of a strong Base = 1 mol of ^-OH

i.e.

1 Eq of NaOH = 1 mol of ^-OH = 1 mol of NaOH

1 Eq of $Ca(OH)_2$ = 1 mol of ^-OH = 1/2 mol of $Ca(OH)_2$

1 gEq of an Acid = x grams (g) of this acid that gives 1 mol of H^+

i.e.

1 gEq of HCl →

(1 mol of H^+ = 1 mol of HCl) x 36.5 g/mol

= 36.5 g

1 gEq of H_2SO_4 →

(1 mol of H^+ = 1/2 mol of H_2SO_4) x 98 g/mol

= 48 g

1 gEq of a Base = x grams (g) of this base that gives 1 mol of ^-OH

i.e.

1 Eq of NaOH →

(1 mol of ^-OH = 1 mol of NaOH) x 40 g/mol

= 40 g

1 Eq of $Ca(OH)_2$ →

(1 mol of ^-OH = 1/2 mol of $Ca(OH)_2$) x 74 g/mol = 37 g

NOTE:

1 Eq of any acid neutralizes 1 Eq of any base.

1 gEq of an ion = MW / ionic charge

i.e.

1 gEq of Na^+ = 23.1 g

1 gEq of Cl^- = 35.5 g

1 gEq of Mg^{+2} = (24.3)/2 = 12.15 g

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

***Normality:**

Normality = Eq / volume

[Conc. Of a solution, expressed in equivalents**]**

RECALL:

Molarity = mol / volume

[Conc. Of a solution, expressed in moles**]**

◊ Normality and Molarity:

N = n x M, where;

n: number of moles of H^+/^-OH provided by 1 mol of the acid/base, respectively.

M: Molarity

i.e.

3M H_2SO_4 = (2x3=6) N H_2SO_4

1M $Ca(OH)_2$ = (2x1=2) N $Ca(OH)_2$

Exercise

- What is the normality of H_2SO_4 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

N = M x n = 0.33 x 2 = 0.66 N

NOTE:
The normality of a solution is NEVER less than the molarity. [N >= M]

◊ Normality and Equivalents:
N = Eq / L
RECALL:
"1 Eq of any acid neutralizes 1 Eq of any base"
BUT 1 mol of any acid cannot always neutralize 1 mol of any base.
Thus, in terms of Neutralization (Titration):
M1 x vol1 = M2 x vol2
Can only be applied when the ratio between donated H^+ & donated ^-Oh is 1 : 1.
i.e. HCl, NaOH / H_2SO_4, $Ca(OH)_2$

While; N1 x vol1 = N2 x vol2
Can be applied in any case.

Exercises:

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?

Ratio is 1:1
M1 x vol1 = M2 x vol2
M1 x 12.0 = 0.12 x 22.4
M1 (HCl) = 0.224 M

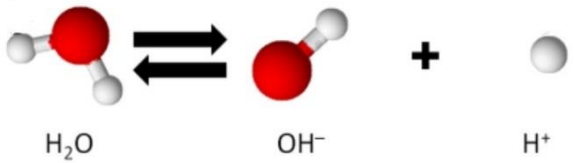
What volume of 0.085 M HNO_3 is required to titrate 15.0 mL of 0.12 M $Ba(OH)_2$ solution?

Ratio is NOT 1:1
N1 x vol1 = N2 x vol2
(n1xM1) x vol1 = (n2xM2) x vol2
(1x0.085) x vol1 = (2x0.12) x 15.0
vol1 (HNO_3) = 42.35 ml

Titration of a 10.0 mL solution of KOH requires 15.0 mL of 0.0250 M H_2SO_4 solution. What is the molarity of the KOH solution?

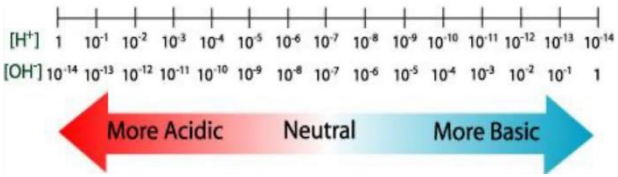
Ratio is NOT 1:1
N1 x vol1 = N2 x vol2
(n1xM1) x vol1 = (n2xM2) x vol2
(1xM1) x 10.0 = (2x0.025) x 15.0
M1 (KOH) = 0.075 M

IONIZATION OF WATER:
***The Reaction:**



***K_{eq} and K_w:**
RECALL:
K_{eq} is the value that shows us the where the reaction tends to go.
For A + B → C + D; K_{eq} = [C][D] / [A][B]
H_2O → $H^+ + {}^-OH$; K_{eq} = $[H^+][^-OH] / [H_2O]$
NOW;
measured:
$[H^+] = [^-OH]$ (Because both are produced simultaneously) = 1.0×10^{-7} M
calculated:
1) $[H_2O]$ -in 1 L- = 1000ml = 1000g;
if x 1/18 mol/g
$[H_2O]$ = 55.5 M
2) **K_{eq}** = $[H^+][^-OH] / [H_2O]$ = 1.8×10^{-16} M

BUT, What is K_w ??
K_w is the ion product of water **meaning that** what is the conc. of the ions produced by the dissociation of water or in other solutions.
Thus;
K_w = $[H^+] \times [^-OH]$ = 1.0×10^{-14} M^2
For other solutions, and since K_W is a fixed value, the concentration of $[H^+]$ and $[^-OH]$ are *inversely* changing.

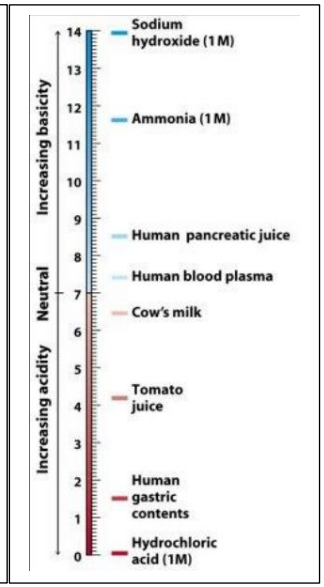


THE POWER OF HYDROGEN (pH):

***Relation between pH, ^{-}OH and H^{+}:**

TABLE 2.3 Relation of $[H^{\oplus}]$ and $[OH^{\ominus}]$ to pH

pH	$[H^{\oplus}]$ (M)	$[OH^{\ominus}]$ (M)
0	1	10^{-14}
1	10^{-1}	10^{-13}
2	10^{-2}	10^{-12}
3	10^{-3}	10^{-11}
4	10^{-4}	10^{-10}
5	10^{-5}	10^{-9}
6	10^{-6}	10^{-8}
7	10^{-7}	10^{-7}
8	10^{-8}	10^{-6}
9	10^{-9}	10^{-5}
10	10^{-10}	10^{-4}
11	10^{-11}	10^{-3}
12	10^{-12}	10^{-2}
13	10^{-13}	10^{-1}



***How to Calculate pH?**

pH = $-\log_{10}[H^{+}]$

Thus, we need to have $[H^{+}]$

Exercises:

Calculate pH for:

0.01 M of HCl

0.01 M of HCl = N / n; where n = 1

→ *0.01 N of H^{+}*

pH = $-\log_{10}[0.01] = 2$

0.01 M of H_2SO_4

0.01 M of H_2SO_4 = N/n; where n = 2

→ *0.02 N of H^{+}*

pH = $-\log_{10}[0.02] = 1.7$

0.01 N of H_2SO_4

0.01 N of H_2SO_4 = 0.01 N of H^{+}

pH = $-\log_{10}[0.01] = 2$

0.01 N of NaOH

0.01 N of NaOH = 0.01 N of ^{-}OH

→ **10^{-2} $[^{-}OH]$ -- 10^{-12} $[H^{+}]$**

pH = $-\log_{10}[10^{-12}] = 12$

---

1 x 10^{-11} M of HCl

0.1 M of acetic acid (CH_3COOH)

Cannot be determined unless we have K_a, because it is a weak acid.

***Exercises Considering K_a, K_b and pH:**

Find the K_a of a 0.04 M weak acid HA whose $[H^{+}]$ is 1 x 10^{-4}.

$K_a = [A^{-}][H^{+}] / [HA]$

$K_a = [H^{+}]^2 / [HA]$

$K_a = 10^{-4} \times 10^{-4} / 0.04$

$K_a = 2.5 \times 10^{-7}$

What is the $[H^{+}]$ of a 0.05 M $Ba(OH)_2$?

$[^{-}OH]$ = 2 x 0.05 = 0.10 M = 1 x 10^{-1} M

$[H^{+}]$ = 1 x 10^{-14} / 1 x 10^{-1} = 1 x 10^{-13} M

The $[H^{+}]$ of a 0.03 M weak base solution is 1 x 10^{-10} M. Calculate pKb.

$[H^{+}]$ = 1 x 10^{-10} M

$[^{-}OH]$ = 1 x 10^{-14} / 1 x 10^{-10} = 1 x 10^{-4} M

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

$K_b = [^{-}OH]^2 / [B]$

$K_b = 10^{-4} \times 10^{-4} / 0.03$

$K_b = 3.33 \times 10^{-7}$

pK_b = $-\log K_b = 6.48$

***Determination of pH:**

◊ Acid – Base Indicators:

- Litmus paper (least accurate)

[Red – Acid / Blue – Base]

-Universal indicator

◊ pH Value Indicators:

-An electronic pH meter (most accurate)

***pH for Some Substances:**

The pH of Various Common Fluids

Fluid	pH
Household lye	13.6
Bleach	12.6
Household ammonia	11.4
Milk of magnesia	10.3
Baking soda	8.4
Seawater	8.0
Pancreatic fluid	7.8–8.0
Blood plasma	7.4
Intracellular fluids	
Liver	6.9
Muscle	6.1
Saliva	6.6
Urine	5–8
Boric acid	5.0
Beer	4.5
Orange juice	4.3
Grapefruit juice	3.2
Vinegar	2.9
Soft drinks	2.8
Lemon juice	2.3
Gastric juice	1.2–3.0
Battery acid	0.35

NOTE: One-unit difference between substance X and substance Y **means** 10-fold difference in $[H^+]$, **because** pH scale is a *logarithmic scale*.

HENDERSON-HASSELBALCH EQUATION

***Equation:**

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

***Derivation:**

$$Ka = \frac{[H+][A-]}{[HA]}$$

Now, taking negative log on both sides of the equation gives:

$$-\log K_a = -\log\frac{[H+][A-]}{[HA]}$$

OR

$$-\log K_a = -\log[H^+] + (-\log\frac{[A-]}{[HA]})$$

By definition,

$$-\log K_a = pK_a \text{ and } -\log[H^+] = pH$$

Thus,

$$pK_a = pH - \log\frac{[A-]}{[HA]}$$

This equation is then arranged to form the Henderson Hasselbalch equation as:

$$pH = pK_a + \log\frac{[A-]}{[HA]}$$

***pK_a Definition According to Henderson-Hasselbalch Equation:**

It is the pH where 50% of acid is dissociated into conjugate base.

BUFFER SYSTEM:

***What is a Buffer?**

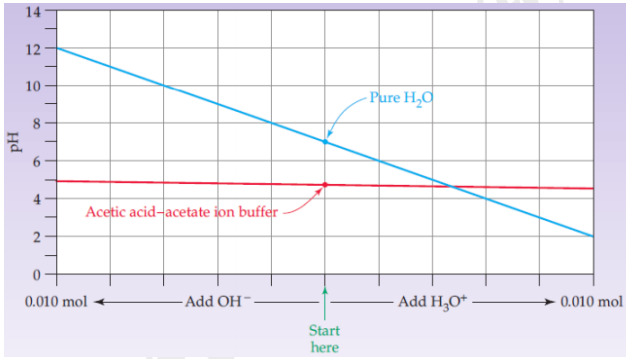
A solution that resist changes in pH by changing reaction equilibrium.

***What is it Composed of?**

A weak acid/base with its salt.

-Equal amounts-

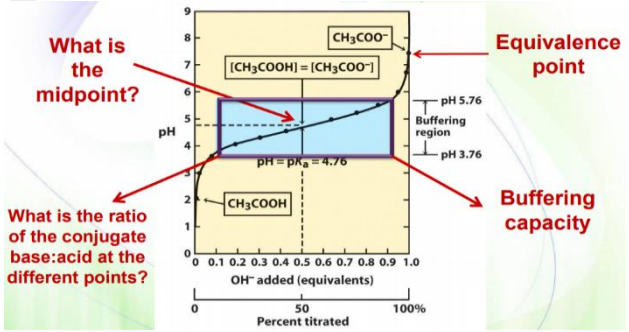
***Buffer vs. Pure Water: Resisting pH Change**



Pure water cannot maintain the pH of a solution, while **Buffer systems** can.

***Titration Curve:**

◊ for Monoprotic Acid (Acetic Acid):



NOTE:

For monoprotic acid, there is only 1 midpoint.

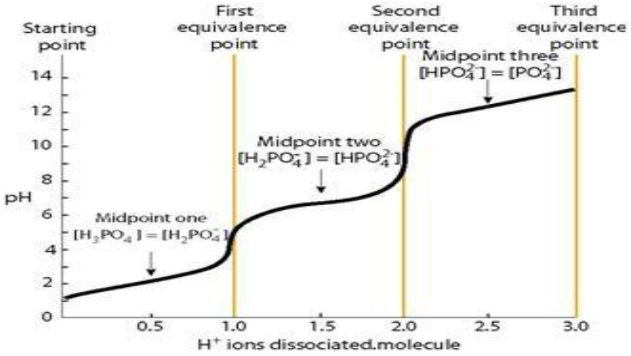
For diprotic acid, there are 2 midpoints.

For triprotic acid, there are 3 midpoints.

NOTE:

The Equivalence Point is not always equal to 7, **it depends on** the type of acid/base reacted.

◊ for Polyprotic Acid (Phosphoric Acid):



***Choosing the Right Buffers:**

-The Ability of a Buffer to Function depends on:

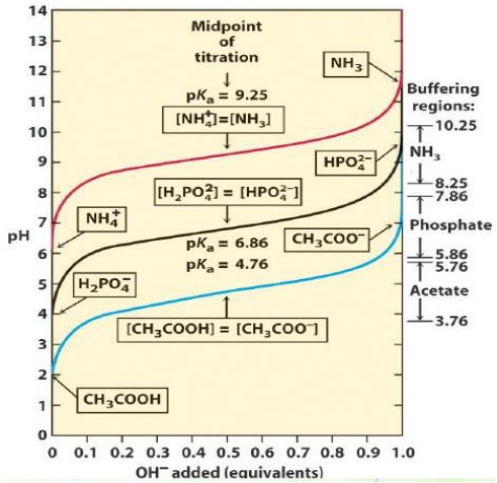
1) Buffer Concentration;

It will not affect the **buffering capacity,** but it will affect the **ability to resist the changing in the PH.**

more conc., more resistance, less pH change

2) Buffering capacity (Buffering Range):

It highly depends on pK_a of the buffer **and** the desired pH value.



Exercises:

Calculate the pH of a buffer containing:

•0.1M HF & 0.12M NaF? (K_a= 3.5x 10^{-4})

$pK_a = -\log K_a = 3.46$

pH = $pK_a + \log([F^-]/[HF]) = 3.54$

•0.1M HF and 0.1M NaF, when 0.02M HCl is added to the solution?

$pK_a = -\log K_a = 3.46$

[HF] = 0.1 + .02 (because of more H^+ thus more F^- + H^+ thus more HF)

$[F^-]$ = 0.1 - .02 (because of loss of F^- to new H^+)

[HF] = .12

$[F^-]$ = .08

pH = $pK_a + \log([F^-]/[HF]) = 3.28$

A) What is the concentration of 5 ml of acetic acid knowing that 44.5 ml of 0.1 N of NaOH are needed to reach the end of the titration of acetic acid?

N (NaOH) x vol = N (CH_3COOH) x vol

0.1 x 44.5 = N (CH_3COOH) x 5

N (CH_3COOH) = 0.89

but; N = n x M

→ M = N / n

M (CH_3COOH) = 0.89 / 1 = 0.89 M

B) Calculate the normality of acetic acid.

"N (CH_3COOH) = 0.89"

What is the pH of a lactate buffer that contain 75% lactic acid and 25% lactate? (pK_a = 3.86)

[lactate]: [lactic acid] = 25: 75 = 1: 3

pH= $pK_a + \log([\text{lactate}]/[\text{lactic acid}]) = 3.38$

What is the pK_a of a dihydrogen phosphate buffer when pH of 7.2 is obtained when 100 ml of 0.1 M NaH_2PO_4 is mixed with 100 ml of 0.1 M Na_2HPO_4?

1st Method:

pH = $pK_a + \log([Na_2HPO_4]/[NaH_2PO_4])$

but, $[NaH_2PO_4] = [Na_2HPO_4]$, **thus log** = 0

pK_a = pH = 7.2

2nd Method:

$[NaH_2PO_4]$ = 0.1 M x 100ml = 0.01 mol

$[Na_2HPO_4]$ = 0.1 M x 100ml = 0.01 mol

$[H^+]$ = $10^{-pH} = 10^{-7.2} = 6.3 \times 10^{-8}$ mol

$K_a = [H^+]x[Na_2HPO_4] / [NaH_2PO_4]$

$K_a = 6.3 \times 10^{-8}$

pK_a = 7.2

A) Dissolving 0.02 moles of acetic acid CH_3COOH (pK_a = 4.8) in water gave 1 liter of the solution. What is the pH?

$pK_a = -\log K_a$, **thus;**

$K_a = 10^{-pka} = 10^{-4.8} = 1.58 \times 10^{-5}$

$K_a = [H^+]x[CH_3COO^-] / [CH_3COOH]$

$K_a = [H^+]^2 / [CH_3COOH]$

$[H^+]$ = $\sqrt{(K_a \times [CH_3COOH])} = 5.6 \times 10^{-4}$ mol

pH = $-\log [H^+] = 3.25$

B) To this solution was then added 0.008 moles of concentrated (NaOH). What is the new pH?

(In this problem, you may ignore changes in volume due to the addition of NaOH)

(NaOH will react with CH_3COOH; less $[CH_3COOH]$ & more $[CH_3COO^-]$)

$[CH_3COOH]$ = .02 - .008 = .012 mol

$[CH_3COO^-]$ = .00056 + .008 = 8.56×10^{-3} mol

pH = $pK_a + \log([CH_3COO^-]/[CH_3COOH])$

pH = 4.65

***Buffers in the Human Body:**

-Carbonic acid-bicarbonate system (blood [Extracellular])

-Dihydrogen phosphate/ monohydrogen phosphate system [Intracellular]

i.e. ATP, glucose-6-phosphate, bisphosphoglycerate (RBC)

-Proteins

i.e. Hemoglobin in blood, other proteins in blood and cells

1) Carbonic Acid – Bicarbonate Buffer System:

-Mechanism:

CO_2 from body tissues is transported to the lungs where it interacts with H_2O.

$$CO_2 + H_2O \xrightarrow[\text{In RBCs}]{\text{carbonic anhydrase}} H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

This system -along with other systems- maintain blood pH around **7.4**.

When the blood becomes acidic (H^+ increases abnormally), the respiratory rate increases, thus it gets rid of CO_2 fast and decreases the formation of H_2CO_3 thus H^+.

When the blood becomes basic (H^+ decreases abnormally), the respiratory rate decreases, thus it gets rid of CO_2 slowly and increases the formation of H_2CO_3 thus H^+.

NOTE: The renal system is also involved in regulating the pH through reabsorbing HCO_3^-, so it increases or decreases the rate of absorption according to the change in H+ concentration.

<u>Explain</u>: pK_a of the bicarbonate buffer is 6.1 so the capacity ranges between (5.1-7.1) and we know that the blood pH is 7.4 (outside the buffering capacity).

- We are dealing with an open system
- Relatively high concentration of HCO_3^- in the ECF (24mmol/L)
- Physiological control:

CO_2 by the lungs

HCO_3^- by the kidneys

NOTE:

More H^+, more interaction with HCO_3^-, more H_2CO_3, more CO_2, more exhalation

More ^-OH, more interaction with H_2CO_3, more HCO_3^-, less CO_2, less exhalation

MEDICAL SIGNIFICANCE:

***Acidosis:**

-means that blood pH < 7.35

-Causes:

Metabolic Causes:

◊ Starvation:

When the sugar is broken down, there will be some acetyl CoA going to Krebs cycle producing energy.

When burning fats, there will be a very large amount of acetyl CoA, some of them will get into Krebs and the rest will form keto acids.

Thus, starvation is caused when we start relying on meat, fats and proteins as a source of energy (NO USE of sugars)

HOW?

1- When you eat a meal, the glucose conc. in the blood increases

2- Insulin is secreted to bind cells and get the sugar into them

3- Excess sugar is stored in the liver as glycogen

4- Decreasing glucose conc. in the blood

5- After a while, all the sugar is consumed and you will feel hungry

6- Your body starts breaking down glycogen (almost first 10-18 hours) and lipids (fat)

7- Breaking fats releases large amounts of acetyl CoA which will activate the synthesis of ketone bodies or keto acids **(lower pH)**

◊ Uncontrolled Diabetes:

1- No insulin
2- No absorption of glucose from blood
3- Cells think that the body needs energy
4- Breaking fats
5- Release of large amounts of acetyl CoA which will activate the synthesis of ketone bodies or keto acids **(lower pH)**

Respiratory Causes:

◊ Asthma / Emphysema

1- People with this problem cannot exhale CO_2 very well
2- CO_2 stays more in their lungs
3- CO_2 reacts with water forming carbonic acid which dissociates into bicarbonate and H^+
4- more H^+ **(lower pH)**

***Alkalosis:**

-means that blood pH > 7.45

-Causes:

Metabolic Causes:

◊ Hypokalemia:

Kidneys try to compensate the loss of K^+ by reabsorbing K^+ and excreting H^+ in the collecting ducts to maintain the electrical balance. **(less H^+ → higher pH)**

Respiratory Causes:

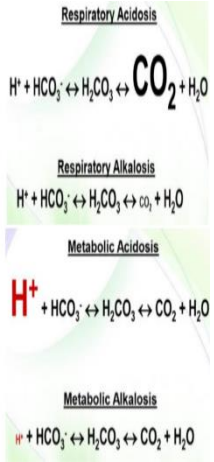
◊ Climbing High Altitudes / Anxiety:

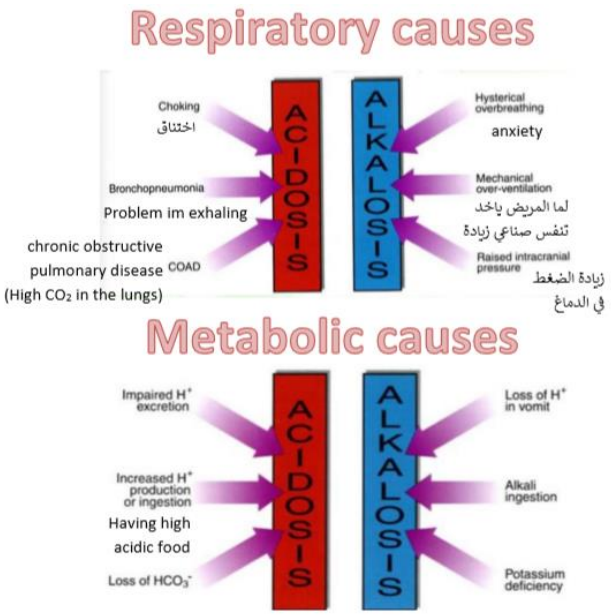
1- more exhalation than inhalation
2- less CO_2
3- less interaction with H_2O
4- less production of H_2CO_3
5- less production of HCO_3^- & H^+
(higher pH)

WRAP UP:

In the respiratory acidosis or alkalosis, the problem is the CO_2. In the acidosis, we have high conc. of CO_2 → high conc. of acid. In the alkalosis, we have low conc. of CO_2 (it is mostly exhaled) → low conc. Of acid.

In the metabolic acidosis or alkalosis, the problem is the H^+. In the acidosis, we have high conc. of H^+ → high conc. of acid. In the alkalosis, we have low conc. of H^+ → low conc. Of acid.





***How Does our Body Compensate the Change in the pH?**

If the problem is metabolic (change in H^+ conc.), we will have respiratory compensation whether it is hyperventilation or hypoventilation (change in CO_2 conc.).

If the problem is respiratory (change in CO_2 conc.), we will have metabolic (renal) compensation (change in HCO_3^-).

Cause Response

$H^+_{(aq)} + HCO_3^-{}_{(aq)} \rightleftharpoons H_2CO_3{}_{(aq)} \rightleftharpoons H_2O_{(l)} + CO_2{}_{(g)}$

	pH	pCO_2	HCO_3^-
Resp. acidosis	Normal But<7.40	↑	↑
Resp. alkalosis	Normal but>7.40	↓	↓
Met. Acidosis	Normal but<7.40	↓	↓
Met. alkalosis	Normal but>7.40	↑	↑

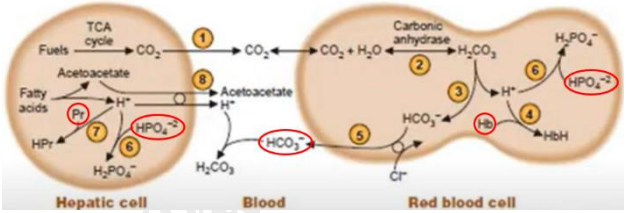
NOTE:
Complete vs. Partial Compensation
In Complete Compensation, the action of the body will be enough to get the pH back to its normal value.
In Partial Compensation, the action of the body will NOT be enough to get the pH back to its normal value.

[Both have the same procedure**]**

2) Dihydrogen phosphate-monohydrogen phosphate system (intracellular):
-It consists of ($H_2PO_4^-/HPO_4^{-2}$).
-It is the most important buffer inside the cells because of having phosphate group.
-Examples (molecules having phosphate):
ATP, glucose-6-phosphate, bisphosphoglycerate (RBC).

3) Proteins:
One amino acid called **histidine** can act as a **buffer** under the physiological conditions of a blood pH 7.4, **because** the side chain of this amino acid **(imidazole)** has a pKa (7.1) that is very close to the pH of the blood.
This group (imidazole) keeps the pH by acting as a base accepting proton (protonation) then donating protons (deprotonation) according to the environment.

[As histidine increases = more efficient buffer**]**
Hemoglobin in blood contains 38 histidine molecules, each one could be protonated or deprotonated depending on the situation.
Other proteins like albumin in the blood or other proteins in the cell have different numbers of histidine and they could act as buffers.
NOTE: Buffer Proteins do not exist only extracellularly, instead, there are some acting intracellularly.



EXERCISES WRAP UP:

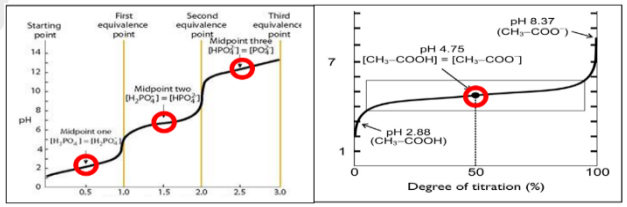
RULES AND LAWS:
***K_w** = $[H_3O^+] \times [^-OH] = 10^{-14}$
Thus, $[H_3O^+]$ = $10^{-14} / [^-OH]$

***$[H_3O^+]$** = 10^{-pH}
Thus, pH = $-\log[H_3O^+]$

***K_a** = $[H^+]x[A^-] / [HA]$
***K_a** = 10^{-pka}
Thus, pK_a = $-\log K_a$

***K_b** = $[^-OH]x[BH^+] / [B]$
***K_b** = 10^{-pkb}
Thus, pK_b = $-\log K_b$

***pH** = $pK_a + \log([A^-]/[HA])$
Thus, pH = pK_a, where;
$[A^-] = [HA]$



***moles (mol)** = grams / MW
***Molar (M)** = moles / volume
***grams (g)** = M x mol x volume

***Eq and gEq:**
1 Eq of a strong Acid = 1 mol of H^+
1 Eq of a strong Base = 1 mol of ^-OH
1 gEq of an Acid = x grams (g) of this acid that gives 1 mol of H^+
1 gEq of a Base = x grams (g) of this base that gives 1 mol of ^-OH

***Normality** = Eq / volume
***Normality** = M x n

*M1 x vol1 = M2 x vol2
Can only be applied when the ratio between donated H^+ & donated ^-Oh is 1: 1.
*N1 x vol1 = N2 x vol2
Can be applied in any case.