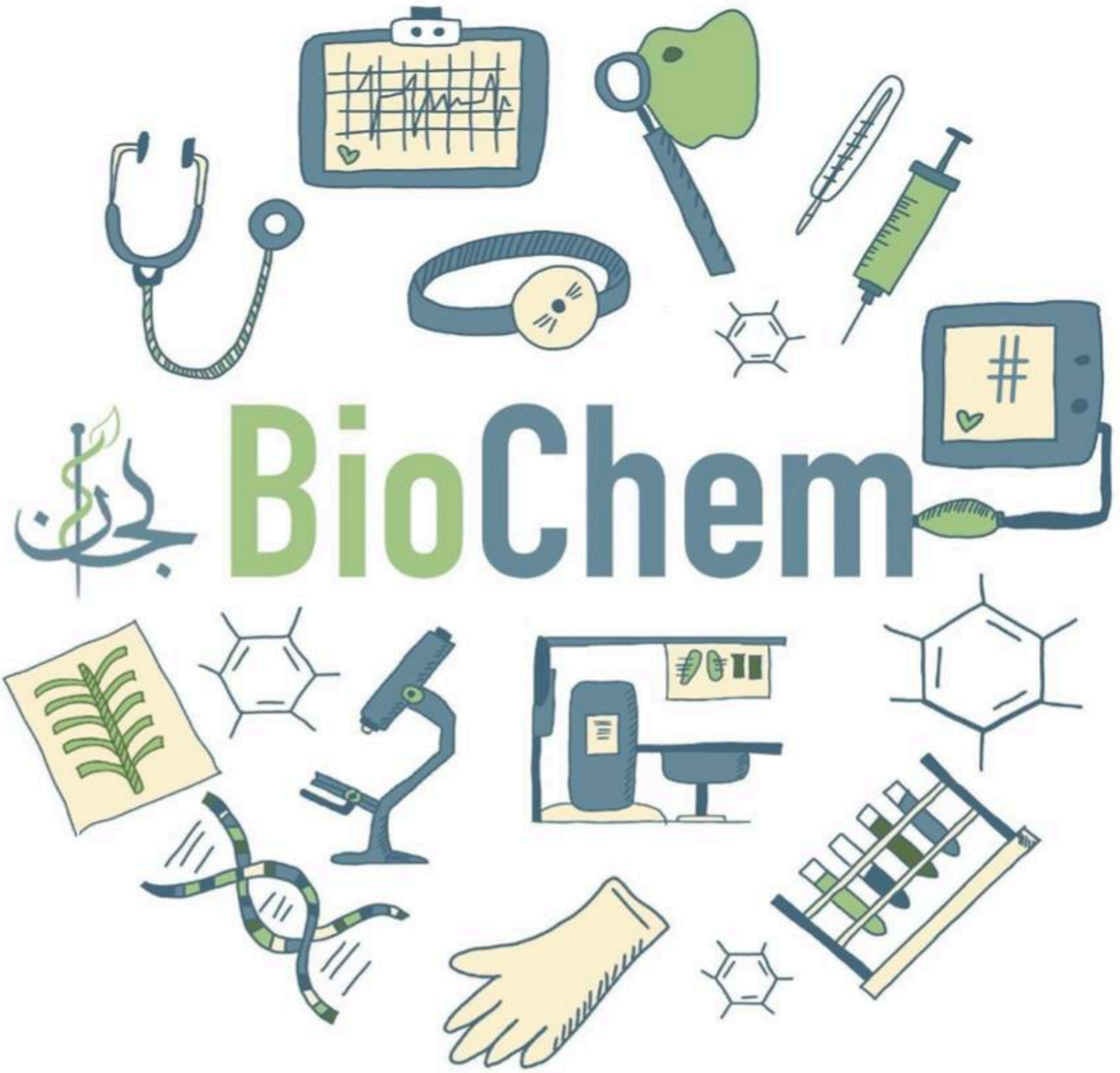

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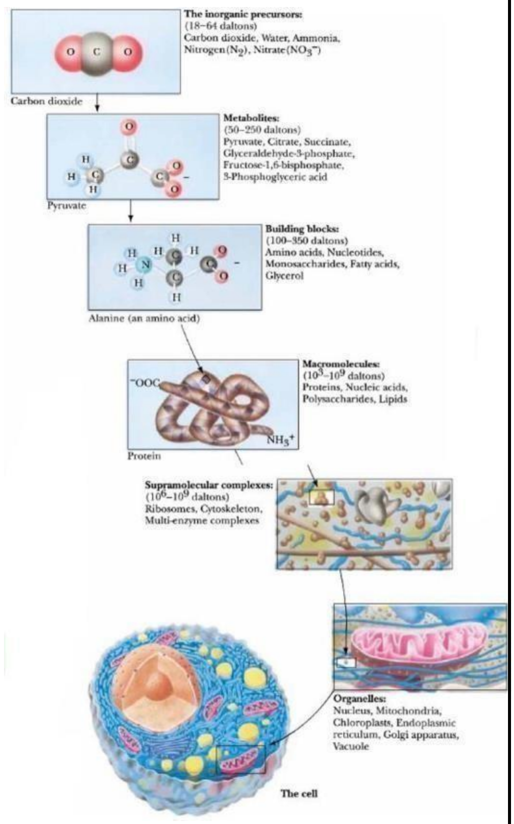
❖ Introduction to Biochemistry



- What is Biochemistry?

Biochemistry is the science concerned with studying the various molecules that occur in living cells and organisms (such as: humans, plants, animals, etc.) and their chemical reactions (how do they interact with each other).

The word biochemistry is made up of two parts; Chemistry: refers to the chemical compounds are their reactions, and Bio: refers to the biological system we are studying the reactions at. (Cell, tissue, organ or organ system, because simply, we mainly consist of atoms, atoms groups form compounds, chemical compounds form macromolecules which form organelles, which form cells then tissues and the whole organism.

- Why do we study Biochemistry?

It's the base for so many sciences and future treatments.

1. Know the chemical structures of biological molecules.
2. Understand the biological function of these molecules.

(Determining the structure will help us in knowing the function because biological molecules mainly own a specific structure to function in a specific way, i.e., they never possess a structure without a purpose.)

3. Understand interaction and organization of different molecules within individual cells and whole biological systems (for e.g.: what reactions can happen? What are the possible products?) and what changes can be done on these interactions (for e.g.: ordering them, stopping them, increasing reaction rate, ……).
4. Understand bioenergetics (the study of energy flow in cells). Studying how energy stored in the bonds of molecules gets converted from one type to another.

Understanding how molecules interact in normal conditions and how do they interact in a certain disease or abnormality, you're going to know how to deal with this disease or how to treat it.

For example: Diabetes type 1 (in this disease patients suffer from deficiency of insulin), knowing the structure of insulin will enable us to synthesize it and give it to the patients as a treatment.

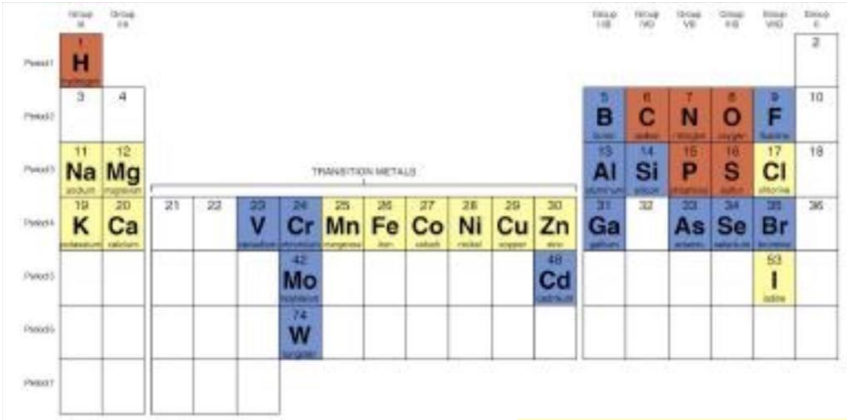
So how do we use Biochemistry in medicine?

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

❖ Chemical elements in living creatures:

Different types of elements are present in our cells (as organisms).

Living organisms on Earth are composed mainly of 31 elements (as shown in the table).



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

Four primary elements (Most abundant elements): Carbon, Hydrogen, Oxygen, and Nitrogen,

96.5% of an organism's weight.

The second group includes sulfur and phosphorus come in the 2nd tier until we finally reach metal ions known as Trace Elements, those elements are important even though they are not present in large quantities.

Most biological compounds are made of only SIX elements: C, H, O, N, P, S. Others are minor, but essential, elements (mostly metals).

❖ Covalent Bonds:

Atoms mentioned earlier form molecules, in which covalent bonds connect their atoms, known as covalent molecules.

Covalent bonds are chemical bonds that involve the sharing of electron pairs between atoms (no full loss and gain of electrons happen).

As we studied before, covalent bonds have a lot of types, such as single, double, and triple covalent. C-C, C-H, C-O, C-N, etc. are examples on covalent bonds, etc.

- Important properties of bonds:

1- **Bond strength**: amount of energy that must be supplied to break a bond. (The stronger the bond, the more energy we need)
2- **Bond length**: the distance between two nuclei, which depends on atoms size, bond type(single, double, triple). Also, bond strength is related to bond length, longer bonds are weaker, while shorter bonds are stronger.
3- **Bond orientation**: bond angles determining the overall geometry of atoms, and the geometry in its turn determines the function.

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

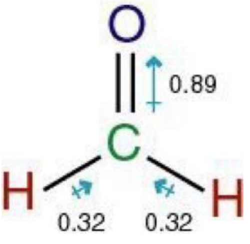
❖ Polarity of Covalent Bonds

Elements forming covalent bonds have different abilities to attract electrons towards them **(electronegativity).** Atoms having high electronegativity (O & N for example) will attract electrons toward them, which results in a partially negative charge, while atoms having low electronegativity will have a partially positive charge. **(Look at the example bellow)**

Covalent bonds, in which electrons are shared unequally (having electronegativity difference), are known as polar covalent bonds or “dipoles” .

Theses covalent bonds can be either between the same type of atom and between different types as well, so we get polar and non-polar covalent bonds.

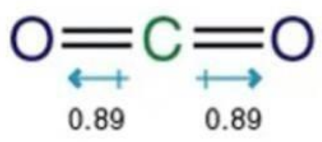
Polar covalent bonds occur between atoms with high electronegativity difference , non-polar covalent bonds occur between atoms with zero (similar atoms) or very low difference in electronegativity.



so, if we look at this example, we notice that there’s a high difference in electronegativity between C & O, and since the electronegativity of Oxygen is much higher, the bond electrons will be closer to O rather than to C, so the O is going to get partial –ve charge (δ-) and the C is going to get partial +ve charge (δ+).

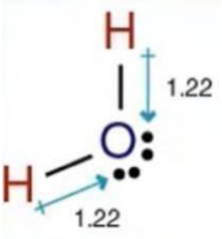
The bond between C-H is considered to be non-polar covalent, since the difference in electronegativity between them is so small (one third the difference between C-O), so there won't be any δ- or δ+ at all.

Polarity describes both bonds & molecules:



The geometry plays an important role in the molecule polarity, notice that the C-O bonds in the molecule are polar, but the whole molecule is NOT, why?

Because the best way to distribute O atoms around C atom and maintaining them as far as possible is linearly(180°).According to this, 2 oxygen atoms of equal electronegative pull the electron density from carbon from either direction. Thus, net pulling =0.



lone pair of electrons on the Oxygen atom are going to repulse due to negative charges. To prevent this, molecule bents which gives them more space, which means that molecule is not linear and H atoms don't oppose each other. According to this, pulling forces are not canceled and molecule is polar.

❖ Non-covalent interactions

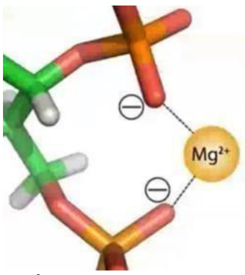
These are connections between molecules in which there are no shared electrons between molecules (different than covalent bonds)

They occur between molecules and not between atoms of a molecule, unless molecule is large.

They are quick, reversible (form and break all the time and only last for very short time) and weak interactions

There are different types of non-covalent interactions:

1. **Electrostatic interactions** (charge-charge interactions) also called Ionic interactions.

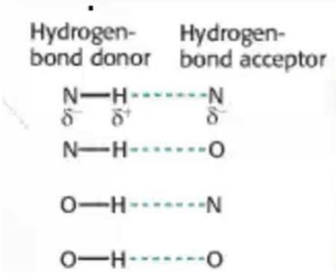


They are interactions between charged particles whether they have full or partial charge, different charges attract while similar charges repel. These forces are quite strong in the absence of water.

The larger the charges of the particles are, the larger the attraction and repulsion forces according to Coulomb's law. $F = k\frac{q_1 q_2}{r^2}$

2. **Hydrogen bonds:**

a special type of Electrostatic interactions (it's considered electrostatic because there are partial charges involved) also it can be considered as an independent type of interactions

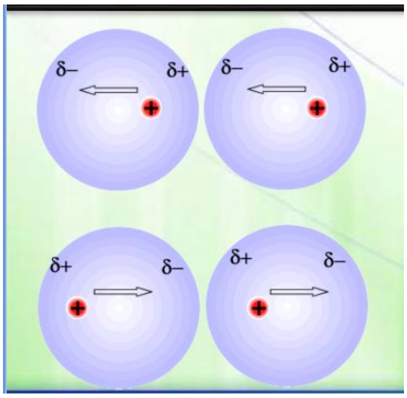


A hydrogen atom is partly shared between two relatively electronegative atoms (a donor and an acceptor). Hydrogen bond forms between a Hydrogen atom connected to a highly electronegative atom (hydrogen becomes + charged) and a negatively charged atom on another molecule.

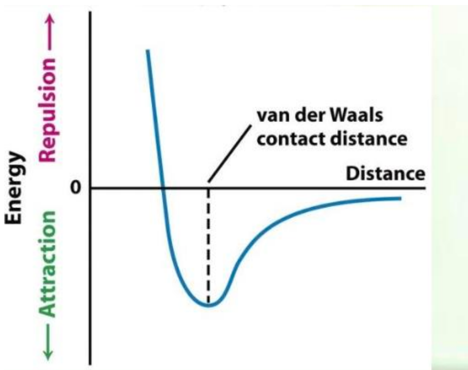
The donor partially donates the hydrogen atom and the acceptor accepts the hydrogen partially.

3. **Van der Waals interactions**:

This interaction results from the movement of electrons present in orbits around the nuclei of an atom. At a specific time, electrons will move to a certain point making it relatively more negative, while other sides will be relatively more positive. When two or more atoms come closer to each other, the local negative areas in some atoms will be attracted to the local positive areas in other atoms.



The strength of the attraction is affected by distance.

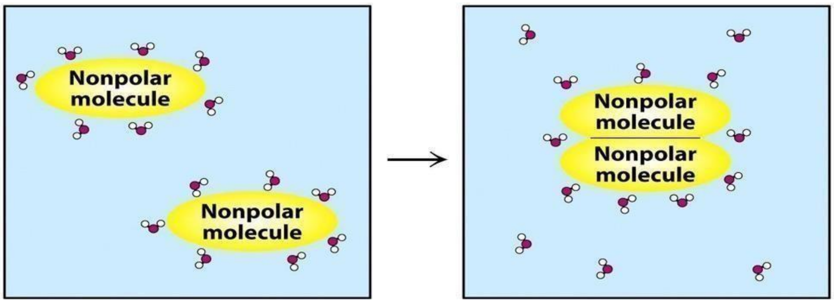


Note: Hydrogen bonds and some ionic interactions are the STRONGEST, and Van der Waals are the WEAKEST

3-Hydrophobic interactions:

-Not true interactions. They are the forces that drive hydrophobic or non-polar molecules. away from polar or aqueous environment and associates them together.

-Minimize unfavorable interactions between non polar groups and water.
Example: when you throw oil on a surface of water, the oil droplets will accumulate and aggregate as one big droplet in a short amount of time. This happens due to the forces responsible for minimizing interactions with water (hydrophobic interactions)



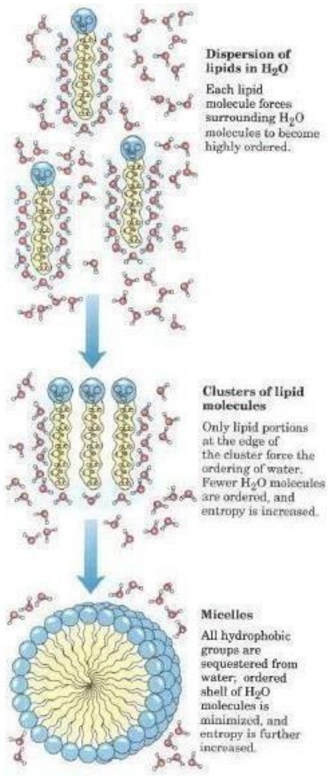
Hydrophobic interactions and micelle formation:

*Recall: amphipathic molecules are molecules containing both polar and non-polar parts in its structure.

-When mixing amphipathic and water molecules, water molecules will try to form interactions around each of these amphipathic molecules but this reaction is unstable due to the presence of the hydrophobic tails.

-The **hydrophobic interactions** would aggregate/accumulate these molecules and get them in line next to each other as you can see in the picture

*Blue part from the outside(polar region) and yellow part from the inside(nonpolar region)



-The interactions between hydrophobic part and water become less but are still present the sides and the bottom, thus cluster remains unstable.

-So, for a complete isolation of the hydrophobic part of these molecules from the aqueous environment, molecules will form a bowl or a cage like structure called micelle

-This structure is stable, as Water molecules can now surround the polar part of the micelle structure and form hydrogen bonds whereas hydrophobic tails are hidden in the core of the micelle, away from water molecules.

To sum up, Hydrophobic interactions minimize unfavorable interactions between non polar groups and water by forming micelle.

Hydrophobic interactions are very important when removing grease (which is hydrophobic).

while washing hands or dishes using soap and water.

- Grease and fat molecules are going to be stuck in the middle of the micelle because they are hydrophobic. So, when you wash off the soap, the grease will be removed because it's stuck inside the micelle structure.

Properties of non-covalent interactions:

-**Reversible** (they break and form spontaneously with a short life)ex: the lifetime of a hydrogen bond is a nano second only.

-**Relatively weak when compared to the covalent bonds**. 1-30 kj/mole vs 350 kj/mole in c-c bond.

-**Molecules interact and bind specifically** (they require special conditions for interactions to occur).

Ex: Molecules should be properly oriented and close enough to each other for any interaction to occur, and for ionic interactions to occur, molecules should possess similar or different charges.

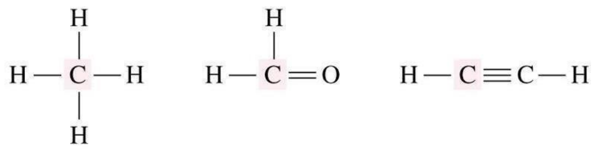
-Non covalent forces, even though weak, but the presence of large quantities significantly contribute to the structure stability, and functional competence of macromolecules in living cells.

-**Can be either attractive or repulsive** (ionic interactions between different charges are attractive and repulsive between similar charges)

-**Involves interactions both within the biomolecule** (ex: hydrogen bonds in large molecules), **and between it and water in the surrounding environment** (ex: hydrophobic interactions).

Carbon and its properties:

-Carbon atoms have 6 e^- around nucleus, with 4 electrons in the last orbit. Thus, it is a tetravalent atom and can formfour bonds, which can be single, double, or triple bonds.

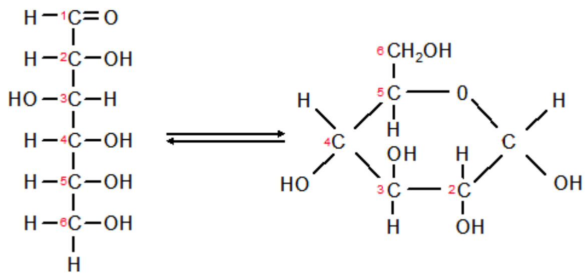


CH_4 (methane) CH_2O (formaldehyde) C_2H_2 (acetylene)

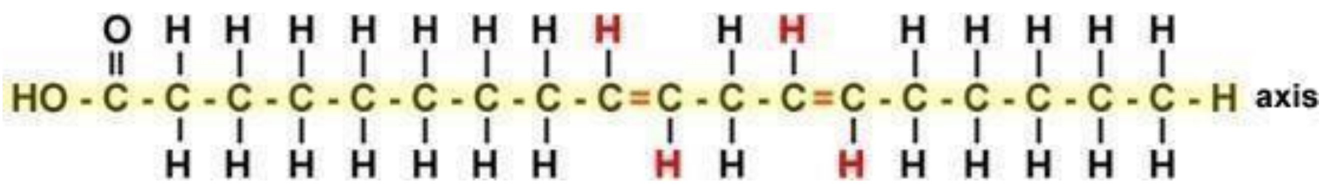
-Each bond is very stable.

-Carbon bonds have different length(single> double> triple), strength(triple> double> single), and get oriented in space in different orientations and would create a wide range of shapes.

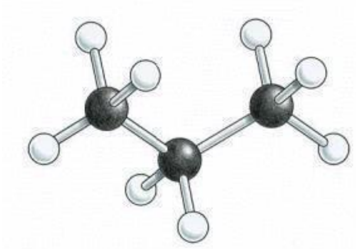
-They link c atoms together in chains and rings. these serve as backbones for organic molecules.(linear or ring)



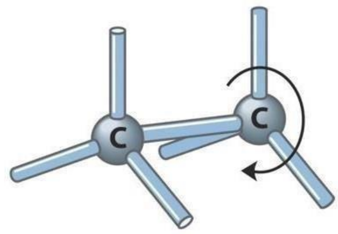
-They can interact and form bonds with different types of atoms or the same type.



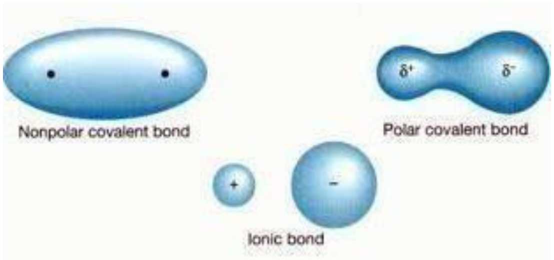
-Carbon bonds have angles giving molecules three-dimensionalstructure which is related to their function.
the angle depends on the type of bond and the presence of unshared electrons,
-In a carbon backbone, some carbon atoms rotate around a single covalent bond producing molecules of different shapes (isomers).

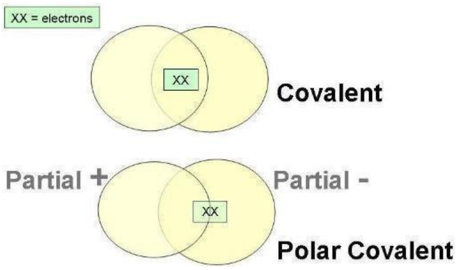

propane (CH_3-CH_2-CH_3)

*Why can’t they rotate around double or triple bonds?
due to their rigidity, movement would be restricted, in addition to their planar structure.



-The electronegativity of a carbon is between other atoms.
it can form polar (ex: when it binds to a highly electronegative atoms) and nonpolar (ex: when it is binds to hydrogen) 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 the carbon skeleton (backbone), that contribute to organic molecules diversity and differences in functions and properties.

They determine the class of the compound (C-C double bond for alkenes, Hydroxyl (OH) group for alcohol, Carbonyl (COH) for aldehydes, etc. ...).

Another example is phosphoric acid derivates. Molecules in which phosphate groups are added in different numbers, which is an important reaction during metabolism in our cells.

Class of Compound	General Structure[a]	Functional Group Structure	Functional Group Name	Example
Alkane	RCH_2-CH_3	$-C(H)-C(H)-$	Carbon–carbon and carbon–hydrogen single bonds	H_3C-CH_3
Alkene	$RCH=CH_2$	$>C=C<$	Carbon–carbon double bond	$H_2C=CH_2$
Alcohol	ROH	–OH	Hydroxyl group	CH_3OH
Thiol	RSH	–SH	Thiol or sulfhydryl group	CH_3SH
Ether	R–O–R	–O–	Ether group	CH_3-O-CH_3
Amine[b]	RNH_2, R_2NH, R_3N	$-N<$	Amino group	H_3C-NH_2
Imine[b]	R=NH	$>C=N-H$	Imino group	$(H_3C)_2C=NH$
Aldehyde	R–C(=O)–H	–C(=O)–H	Carbonyl group	$CH_3C(=O)H$
Ketone	R–C(=O)–R	–C(=O)–	Carbonyl group	$CH_3C(=O)CH_3$
Carboxylic acid[b]	R–COOH	–C(=O)–OH	Carboxyl group	$CH_3C(=O)OH$
Ester	R–C(=O)–OR	–C(=O)–OR	Ester group	$CH_3C(=O)-OCH_3$
Amide	$R-C(=O)-NH_2$	–C(=O)–N(H)–H	Amide group	$CH_3C(=O)-NH_2$
Phosphoric acid[b]	HO–P(=O)(OH)–OH	HO–P(=O)(OH)–OH	Phosphoric acid group	HO–P(=O)(OH)–OH
Phosphoric acid ester[b]	R–O–P(=O)(OH)–OH	–O–P(=O)(OH)–OH	Phosphoester group or phosphoryl group	$CH_3OP(=O)(OH)-OH$
Phosphoric acid anhydride[b]	R–O–P(=O)(OH)–O–P(=O)(OH)–OH	–O–P(=O)(OH)–O–P(=O)(OH)–OH	Phosphoric anhydride group	$CH_3O-P(=O)(OH)-O-P(=O)(OH)-OH$
Carboxylic acid–phosphoric acid mixed anhydride[b]	R–C(=O)–O–P(=O)(OH)–OH	–C(=O)–O–P(=O)(OH)–OH	Acyl-phosphoryl anhydride	$CH_3C(=O)-O-P(=O)(OH)-OH$

[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.

Water:

Why is water important to our bodies?

1-Around 60% of our body is water, and 70-85% of the weight of a typical cell.

2-Is a solvent of many substances our bodies need such as glucose, ions, etc.

to clarify: when a substance is dissolved in water it becomes easier to transport them from one side to another, water also acts a medium for reactions as it facilitates collisionbecause the dissolved molecules move more easily so they have a higher chance of interacting with each other.

3- Acts as a medium in which acids and bases release their chemical groups to maintain a constant cellular environment or homeostasis.

4- essential buffer that maintains PH.

*Point 3 and 4 will be discussed in later lectures.

5- Temperature regulation (keeping it at a certain range) due to its high specific heat capacity (it requires a high amount of energy to change its temperature)

6-A participant in many biochemical reactions. (Act as a participant in reactions)

Water distribution in body compartments:

*Example: an average man who weighs 70kg will have 40 liters of water, distributed as 25 liters intracellularly and 15 liters extracellularly. Extracellular fluid is further distributed into 10 liters of interstitial fluid and 5 liters of blood and a small amount for lymph.

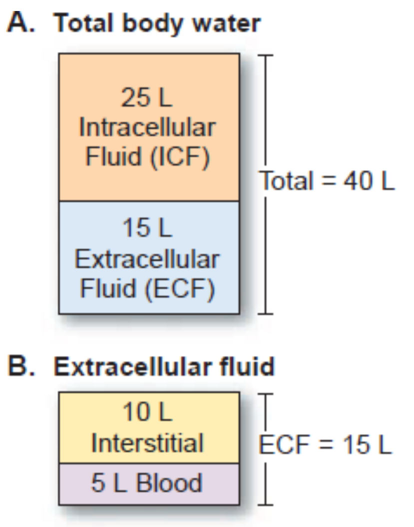


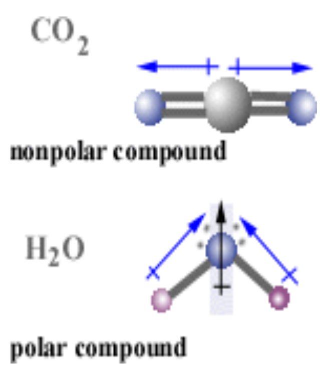
FIG. 4.2. Fluid compartments in the body based on an average 70-kg man.

Properties of water:

1- **Water is a polar molecule as a whole because of:**

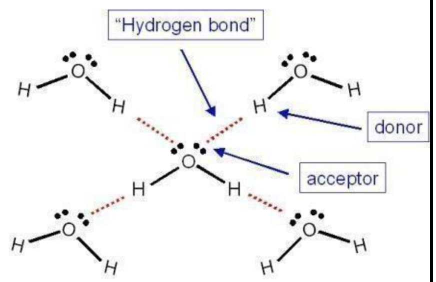
a) The different electronegativity between hydrogen and oxygen

b) It is angular(As said before, water molecules have two unshared pairs of electrons that causes the bending of the molecule and results in an angle between the hydrogen and oxygen, leading to the formation of a polar molecule because the forces are not completely in opposite directions so they don't cancel out.



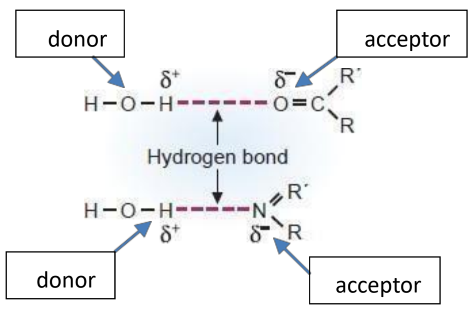
2- **Water is highly cohesive** due to the formation of hydrogenbonds which causes point 3.

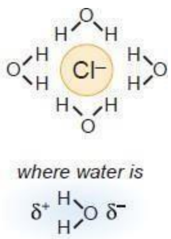
3- **Water molecules produce a network** (in this case, the oxygen atom is the hydrogen acceptor, and the hydrogen itself acts as a hydrogen donor).

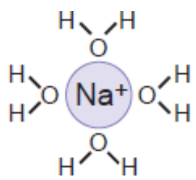


4- **Water is an excellent solvent** because it is small and it weakens electrostatic forces and hydrogen bonding between polar molecules

*Dissolution is a process of hydrogen bond formation between water molecules and a different type of solute with water acting as a doner and solute as acceptor.

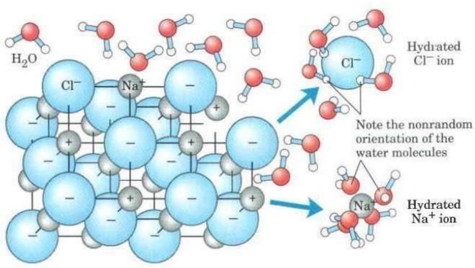




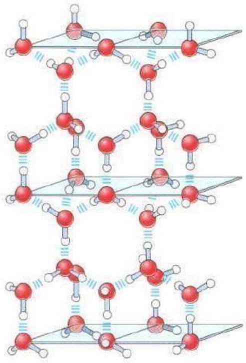


Dissolution of ionic compounds like NaCl, we start with a solid organized crystal in water, water molecules will start to interweave in between the Na+ and Cl- causing them to dissolve away from the crystal, which result in ionizing them. Then water molecules will form hydration shells around both ions, that have different sizes and shapes.

Oxygen (which has a partial negative charge) is going to be close to the Na+ whereas Hydrogen (which has a partial positive charge) would be closer to the Cl-.



Hydrogen bonds between water molecules:



Average number of H-bonds in liquid water at 10°C is 3.4, while in ice crystals it’s 4.

***What do we mean by a 3.4 hydrogen bond?**

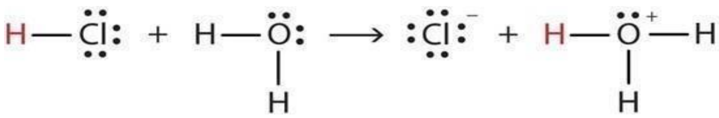
There is no 0.4 hydrogen bond. Hydrogen bonds form and breaks all the time in a nanosecond; however, each water molecule is surrounded by 3.4 hydrogen bonds as an average in liquid state.

*As temperature increases, molecules will gain more energy (kinetic energy will increase), therefore, molecules will move faster and get away from each other so, **the distance increases** in between , thereby making the formation of hydrogen bonds harder whereas in lower temperature, the water molecules are organized in crystals so they have little to no mobility which causes the formation of many hydrogen bonds. (More temperature=less hydrogen bonding)

5- It is reactive because it is a nucleophile

As we said before, water molecules may contribute as a participant in reaction, they act as **nucleophile**

A nucleophile is an electron-rich molecule that is attracted to positively-charged or electron-deficient species (electrophiles). (Nucleo: derived from nucleus, Phile: likes)



*A water molecule has two unshared pairs of electrons making it highly electron-rich and nucleophilic, causing it to attack **positively charged** atoms or molecules such as hydrogen.

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

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

Ionizing one water molecule will gives off OH- and H+ (if 2 water molecules are ionized, it gives off OH- and H3O+)

This will be important when we talk about acids and bases in later lectures.

Water and thermal regulation:

water's structure allows it to resist sudden and large temperature changes.

The thermal regulation and resistance are due to:
1- high thermal conductivity thus, water facilitates heat dissipation from high energy consumption areas into the body water pool. The heat doesn't just stay in small heatedareas in your body, it's conducted and shared by all the water in your body).

2- high heat of fusion, so large drop in temperature is needed to convert liquid water to ice. (Not only does water resist an increase in temperature, but it also resists a decreasein temperature and crystallization into ice).

3- high heat capacity and heat of vaporization; large amount of energy is absorbed when liquid water (sweating) is converted to a gas and evaporates from the skin, that's why we feel a cooling effect

Specific heat is the amount of energy required to raise/decrease the temperature of 1g of a substance by 1 degree Celsius.

Heat of vaporization is the amount of energy required to convert 1g of water from the liquid state to the gas state.

Example: if you go outside and it is 50 degrees Celsius your body will not reach that temperature because much of it is going to get dissipated to raise the temperature of the water in the body by a very small amount of increase (water inside the body requires large quantities of heat to change its temperature).
furthermore, when you're sweating, water which is a major constituent of sweat absorbs a very large amount of heat on your skin and evaporates leaving a cooling effect.

To summarize: when sweating increases, evaporation increases this means that the molecules of water on your skin are getting energy so they move faster, break hydrogen bonds and reduce their number resulting in evaporation and the cooling effect that you can feel.

↓ Temperature → ↑ H-bonds

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