Lecture 1

Introduction into Biochemistry

تذكر أن الأمة جريحة وأنها بحاجة لك أنت..

نعم أنت، فكن على قدر المسؤولية

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APPROVED
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Course information

- Recommended textbooks
  - Marks' Basic Medical Biochemistry: A Clinical Approach 5th Edition, by Michael Lieberman (Author), Alisa Peet MD (Author), 2018
  - Biochemistry 8th edition by Mary Campbell (Author) and Shawn Farrell (Author)

- Online:

  https://themedicalbiochemistrypage.org/

- Instructors
  - Prof. Mamoun Ahram
  - 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

such as sugars, proteins, and fats.

- Know the chemical structures of **biological molecules**
- Understand the biological function of these molecules
- Understand the interaction and organization of different molecules, such as collagen or the constituents of the plasma membrane, within individual cells and whole biological systems
- Understand **bioenergetics** (the study of energy flow in cells)

The structure of a biological molecule is intimately linked to its function.

For example, regarding enzymes (which stimulate reactions), each enzyme has a structure that is best suitable to help it perform its biological function.

(1) Usage and (2) Transfer of energy

e.g., eating, digestion, absorption, transporting via blood, supplying cells, specific reactions inside the cell, etc.…

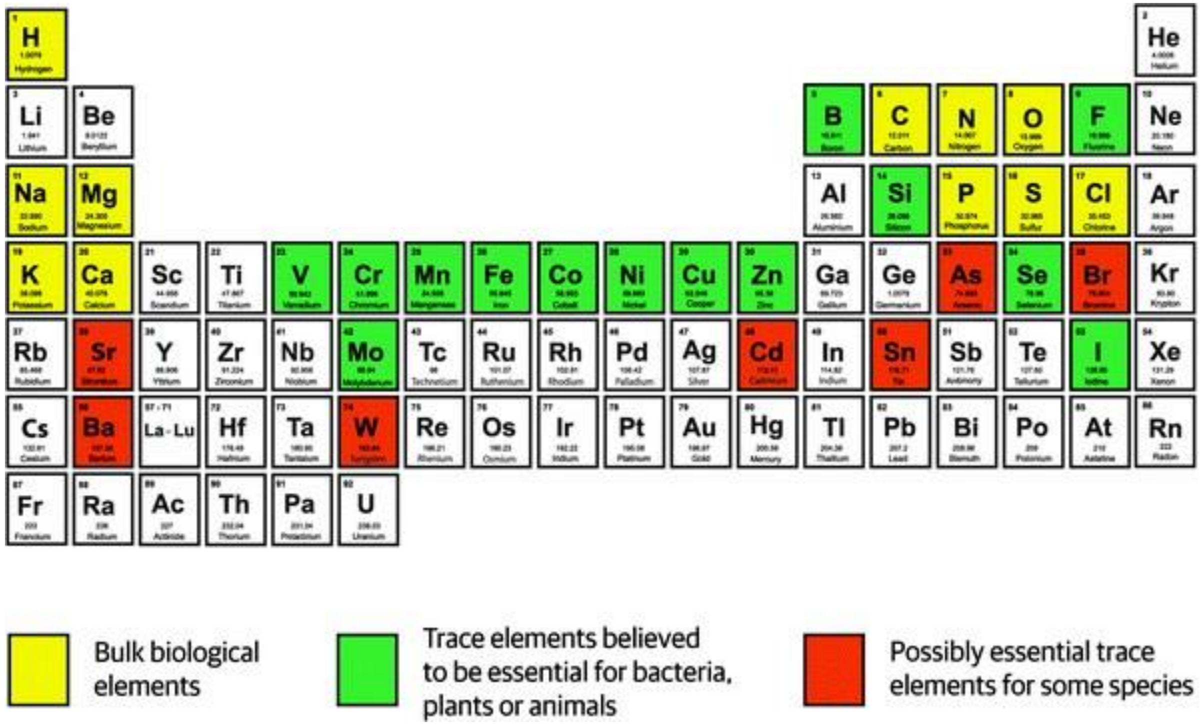
Biochemistry in medicine:

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

Biochemistry, unlike anatomy or pathology, is not essential for normal physicians, but is important for elite ones!
Biochemistry is the molecular basis of diseases and is essential for developing new treatments and drugs.

Chemical elements in living creatures

- The human body is composed mainly of about 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). Iodine is important for the function of the thyroid gland.



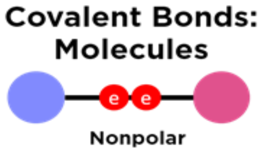
Take a look on those tables

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

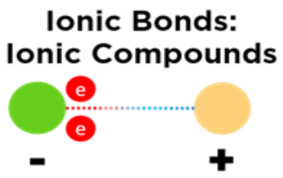
Electronegativity is the ability of an atom to attract electrons to itself. **Oxygen and nitrogen**, for example, have very high, **carbon** has intermediate, and **hydrogen** has weak electronegativity.

- Electronegativity
- Covalent bonds are made by sharing valence electrons
  - Polar (e.g., O-H) vs. non-polar covalent bonds (e.g., C-C)
  - Electrons "spend more time" near the nucleus of the atom with the highest electronegativity
  - Because electrons "spend more time" near the atom with the higher electronegativity, this atom acquires a partial negative charge, and the other atom, which has a lower electronegativity, acquires a partial positive charge.
  - Single vs. multiple: Single, double, or triple bonds



Neutral

Partial Charges



Full "Real" charges

Non-covalent Interactions *between molecules;* **not bonds**

They are more important in biochemistry and there are 4 of them

1. Electrostatic interactions, between (+,-) “real” charges

   e.g., between a positive ion and a negative ion (different from ionic bonds)

2. Hydrogen bonds (donor and acceptor), between (+,-) partial charges

   e.g., in HCl, between H (partial +) and Cl (partial -) **in 2 different molecules**

   Donor (must have hydrogen) — Acceptor (negative charge)

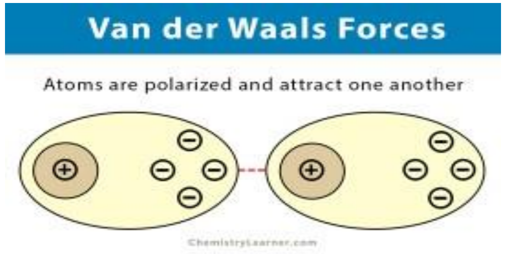
3. Van der Waals interactions

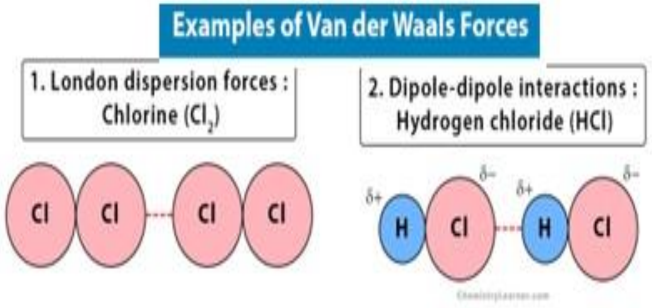
   Occurs due to electrons getting momentarily unevenly distributed between the atoms creating partial charges which are **always changing**.

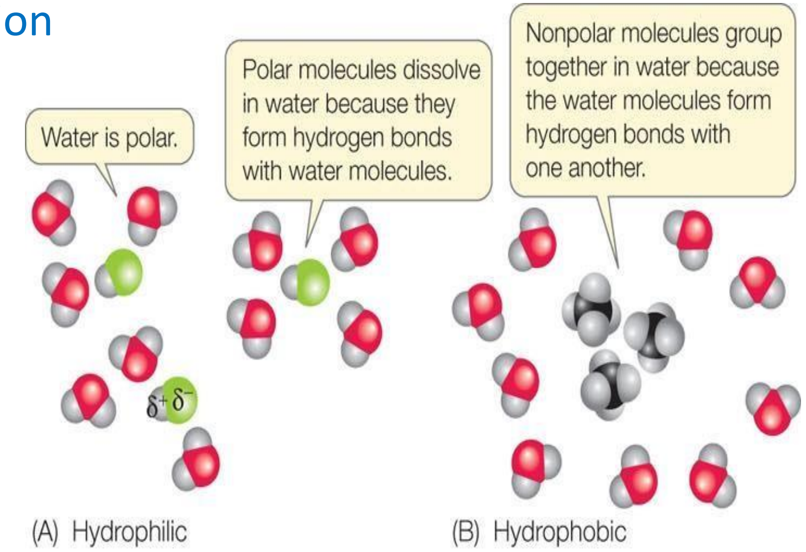
   One is not enough, but collectively, they can make for stable strong interaction between large molecules such as proteins stabilizing a specific structure

4. Hydrophobic interactions

   Occurs between nonpolar covalent molecules





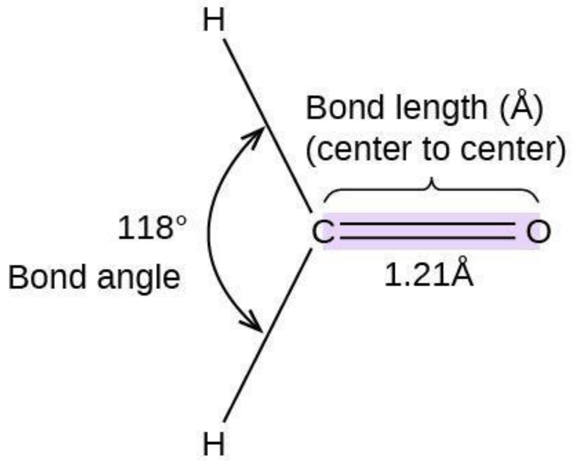


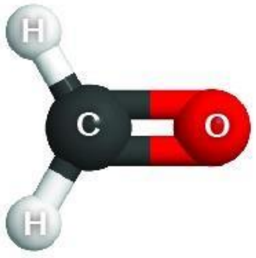
- Hydrophilic (polar) attracting water is energy favorable
- Hydrophobic (nonpolar) attracting water is energy unfavorable
- Nucleophile (electron-rich) and electrophile (electron-poor)

Important properties of covalent 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 in space (3D not 2D)
- The three-dimensional structures of molecules are specified by the bond angles and bond lengths for each covalent linkage.

A carbon-carbon bond is considered a strong bond because it needs a high amount of energy to be broken.





For a given pair of atoms,
The **single bond** is the weakest and longest while the **triple bond** is the strongest and shortest.
The **double bond** is in between.

Polarity of covalent bonds and molecules

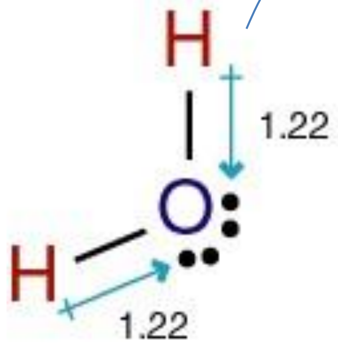
- Covalent bonds in which the electrons are shared unequally in this way are known as polar covalent bonds. The bonds are known as “dipoles”.
  - Oxygen and nitrogen atoms are electronegative
  - Oxygen and hydrogen
  - Nitrogen and hydrogen
  - Not carbon and hydrogen

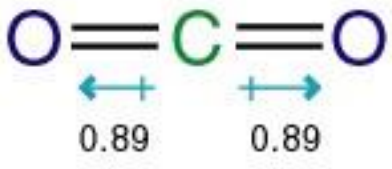
In a water molecule, an O atom is covalently bonded to 2 H atoms. Since the electronegativity of O is greater than that of H, each O-H bond is polar with O carrying a partial (+) charge and the 2 H each carrying a partial (-) charge. Since the geometry of the water molecule is asymmetric, the overall molecule is polar because the 2 polar bonds do not cancel each other.

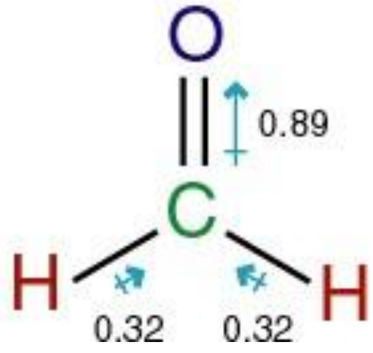
We can decide if a molecule is polar or not by trying to divide it by an imaginary line.

If there is a line which divides it into a part with net partial (+) charge and another part with a net partial (-) charge, the molecule is **polar**. Otherwise, it is **nonpolar**.

Both water and CO_2 contain polar bonds, but only water is a polar molecule.
The 2 C=O bonds cancel out in CO_2.

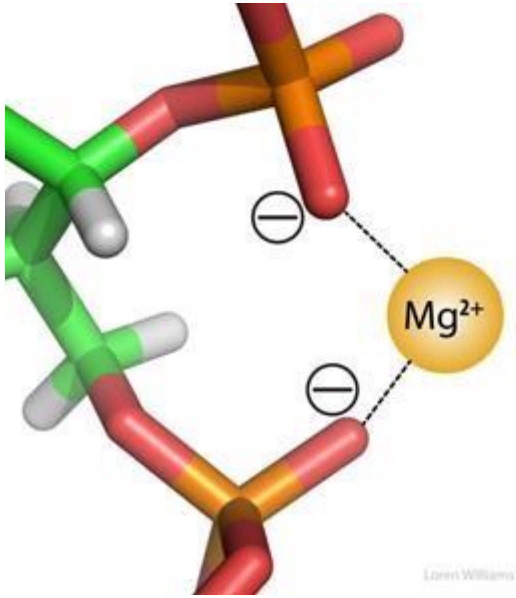






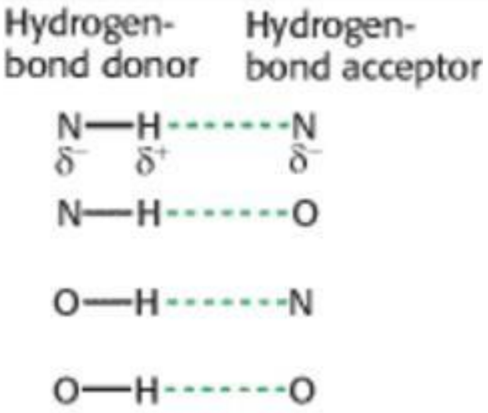
What are non-covalent interactions?

- They are reversible and relatively weak.



Electrostatic interactions (charge-charge interactions):

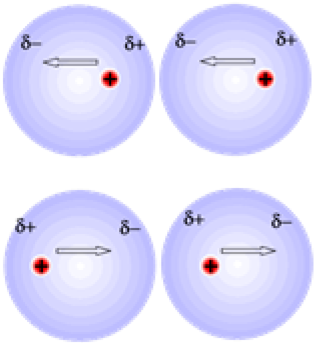
- **They are formed between two charged particles.**
- **These forces are quite strong in the absence of water.**



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.

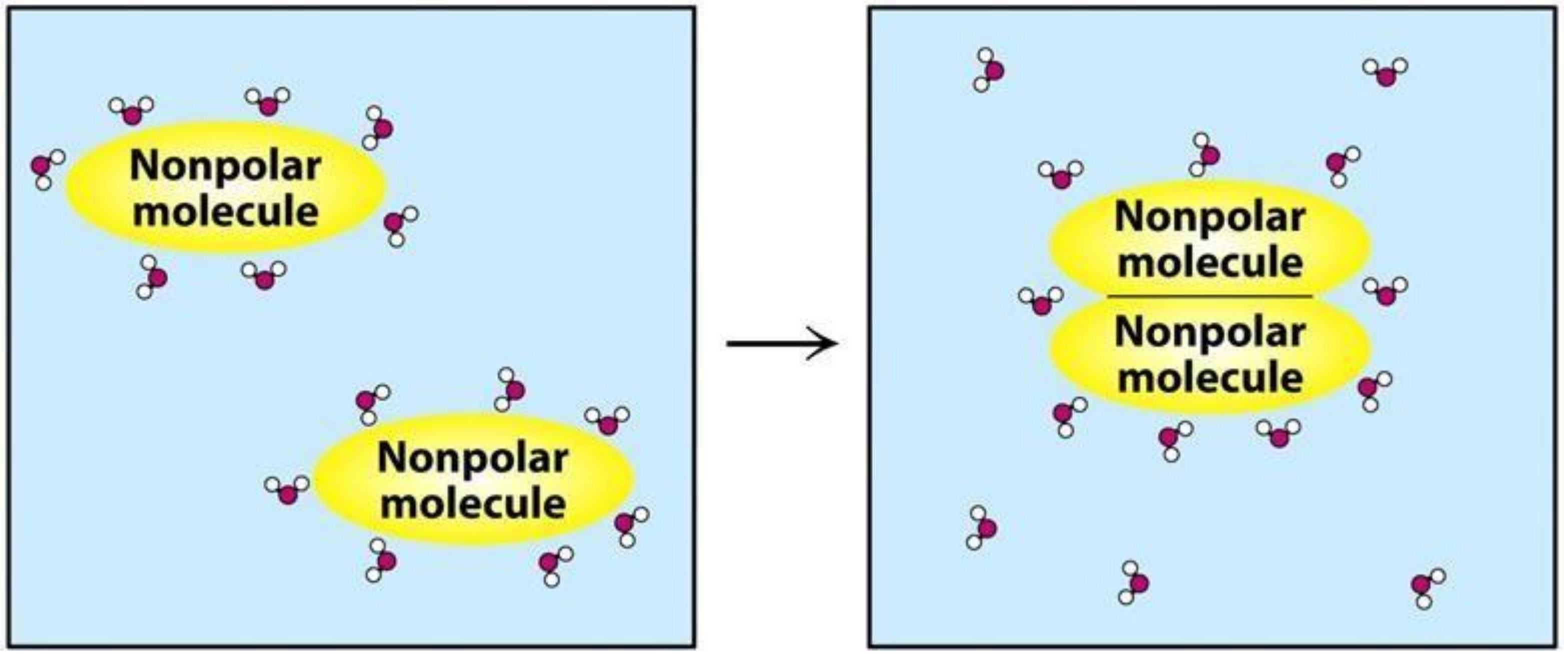
The strength of the attraction is affected by distance.

Hydrophobic interactions

- They determine the whole structure of molecules (as we will see later).
- Self-association of nonpolar compounds in an aqueous environment
- Minimize unfavorable interactions between nonpolar groups and water

When nonpolar (hydrophobic) molecules are in aqueous solution, they come close together because they share the trait of “hydrophobicity”.

They prefer the interaction with another similar nonpolar molecule over the interaction with water, which is polar.



Properties of noncovalent interactions

- Reversible (at any moment, it can be broken and another one formed)
- Relatively weak

Ionic bonds (e.g., in salts) need considerable energy to be broken, but less than the energy needed to break covalent bonds. **Other interactions are dramatically weaker.**

- Molecules interact and bind specifically

Interactions between partial charges are not random, but are governed by many factors

- Noncovalent forces (attraction and repulsion) significantly contribute to the structure, stability, and functional competence of macromolecules in living cells.
- Can be either attractive or repulsive

The structure forms based on that (+,+ or -,-) repels each other and that (+,-) attracts each other.

- Involve interactions both within the biomolecule and between it and the water of the surrounding environment

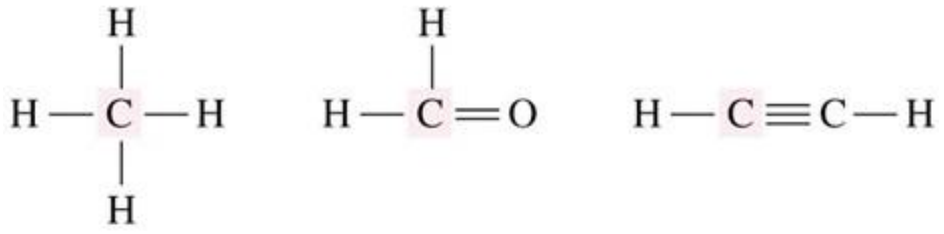
Carbon

The road to diversity and stability

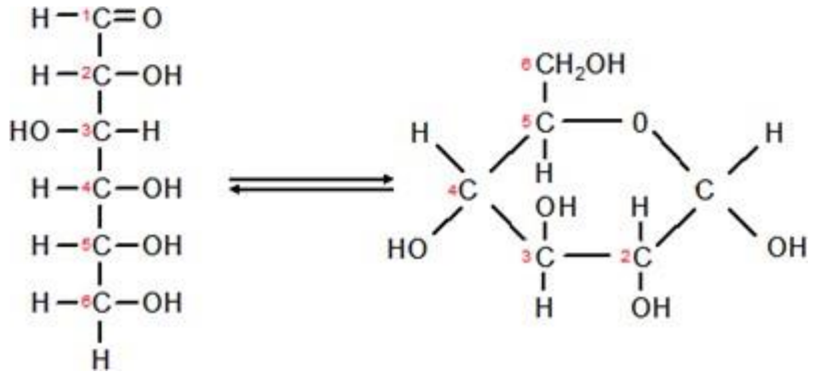
Carbon → Diversity → Life

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.



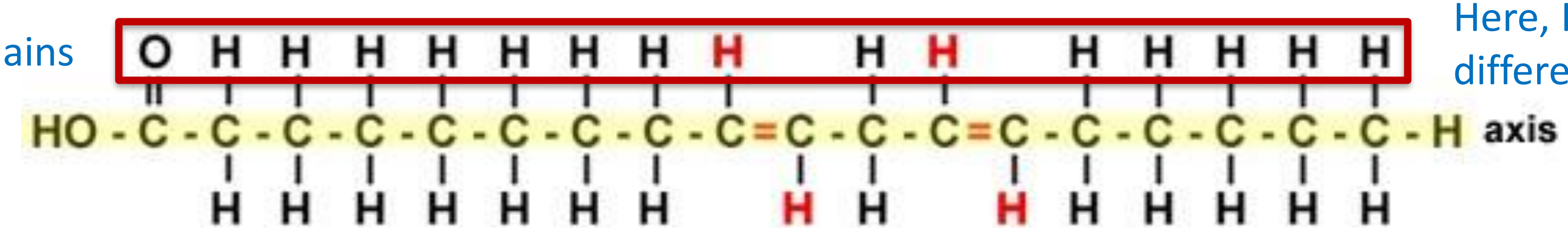
CH_4 (methane) CH_2O (formaldehyde) C_2H_2 (acetylene)



Both are glucose forms

Side Chains

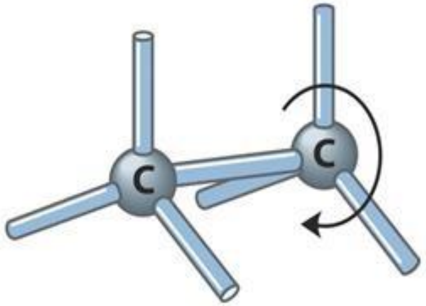
Backbone

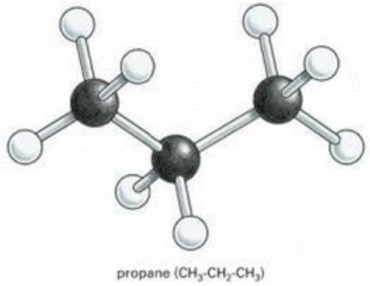


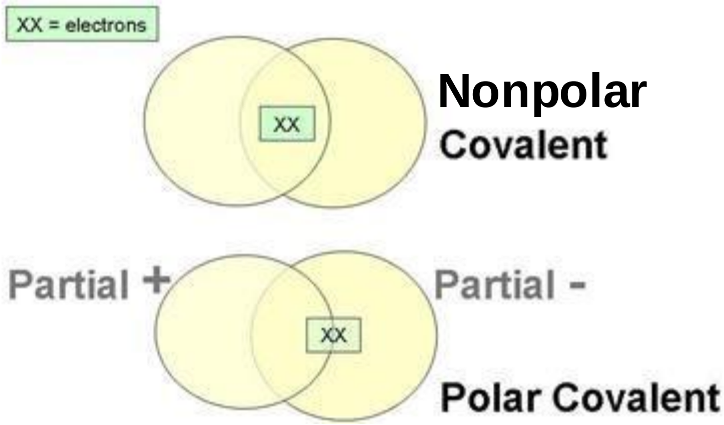
Here, H and O; different → diversity!

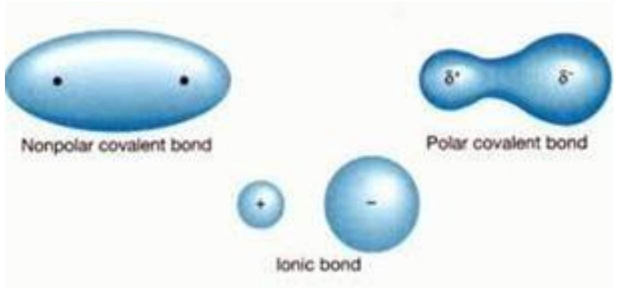
Properties of carbon (2)

- Carbon bonds have angles giving molecules three-dimensional structures.
  Diversity here is due to different special arrangement of atoms governed by the surrounding environment (e.g., water, oil, or alcohol).
- 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 (intermediate, polar bonds with O, and nonpolar bonds with H).
  - 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.







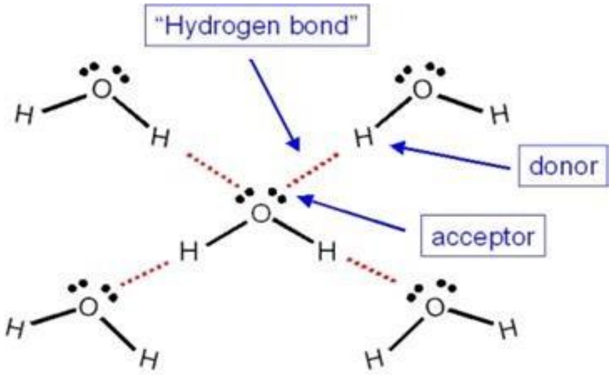


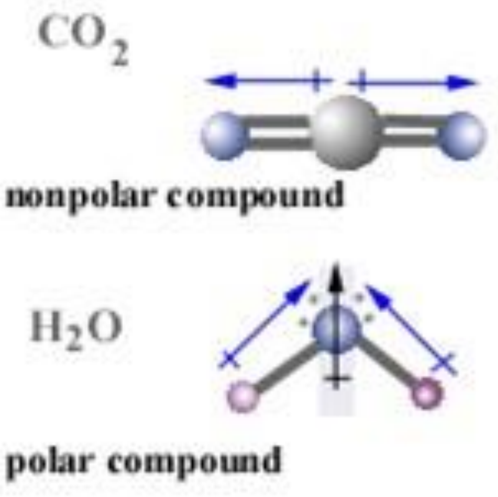
Water

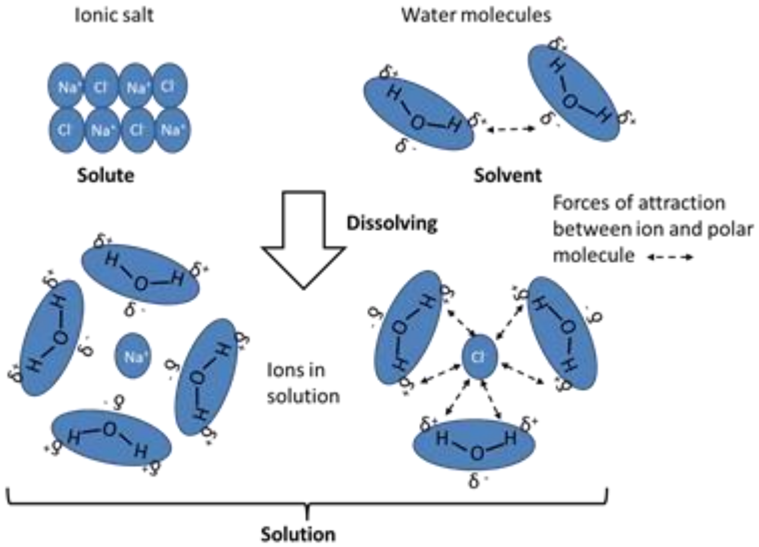
Properties of water (1)

- Water is a polar molecule as a whole because of:
  - the different electronegativities between Hydrogen and oxygen
  - It is angular (asymmetrical).
- Water is highly cohesive.

  A water molecule can form H-bonds with 4 molecules. This cohesive trait enables water to resist the gravity force in plants for example.
- 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.





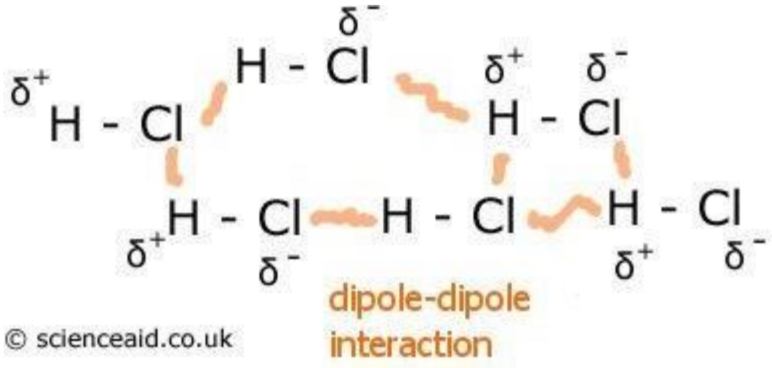


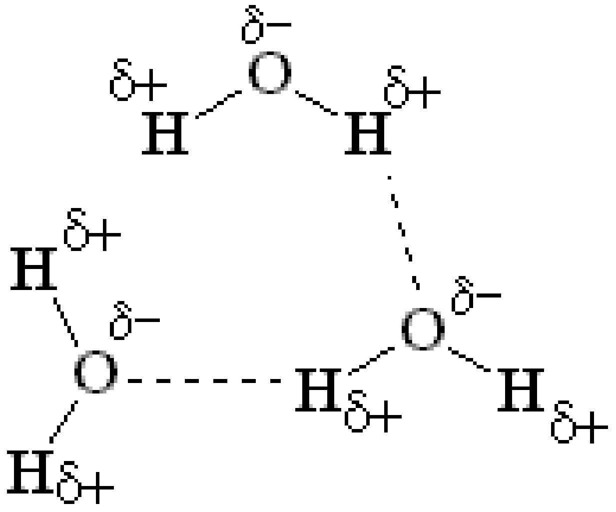
Water can make electrostatic forces with opposite "real" or partial charges on solute molecules.

Note

Dipole-dipole interaction

2 opposite partial charges

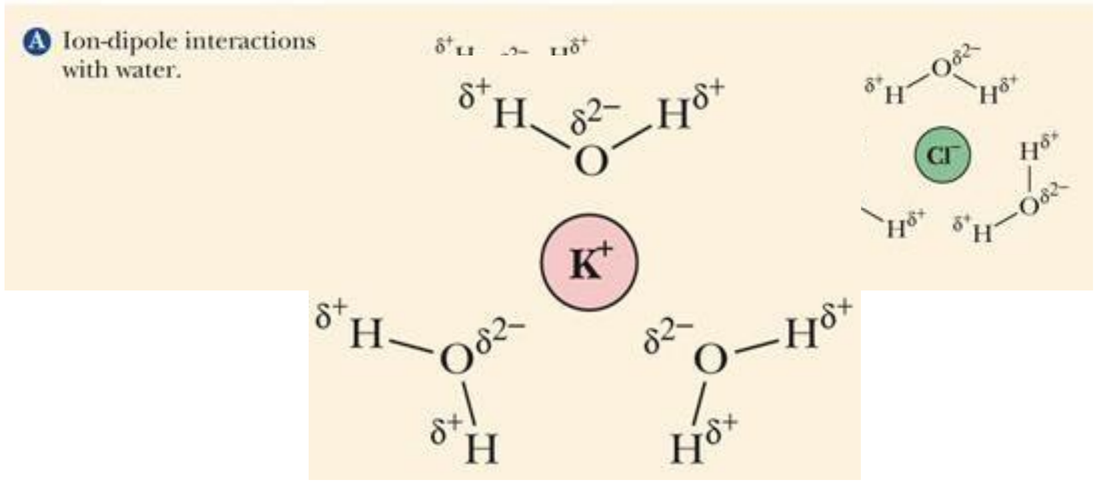




→ The doctor here considered the H-Cl bond to be a hydrogen bond!!

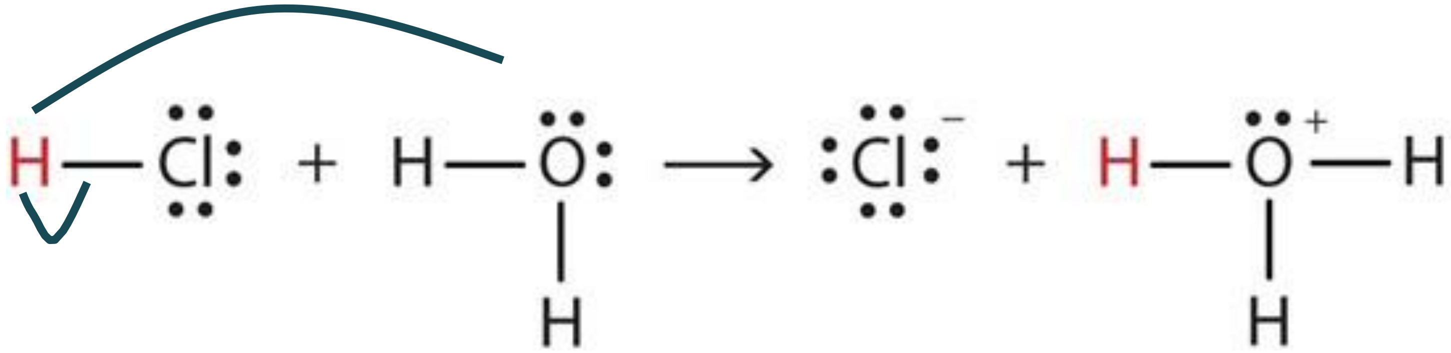
Dipole-charge interaction

Partial with “real” charge



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).



The reaction above is favorable because (1) the water molecule is a nucleophile due to the presence of lone pairs (partial negative charge) on the oxygen atom and (2) the hydrogen has a partial positive charge.

This is why enzymes bind to their substrates inside the 3D structure (in the active site) such that surrounding water (reactive nucleophile) does not interfere in the catalyzed reaction.

Properties of water (4)

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

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

Water we drink is a mixture of mainly H_2O molecules and some H^+ (H_3O^+) and OH^- ions.

Note: $H_3O^+ = H^+$

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V1 → V2			
V2 → V3			
V3 → V4			

Additional Resources:

1. Campbell textbook:
   - sec. 2.1 (Water and Polarity)
   - sec. 2.2 (Hydrogen Bonds)

رسالة من الفريق العلمي:

بداية فصل جديد..
قد لا يكون الأكثر راحة

ومن لا يحب صعود الجبال
يعش أبد الدهر بين الحفر