Chapter 2

Intermolecular forces in physical biochemistry

Intermolecular forces and state of matter

- In **solids,** the intermolecular forces are very strong, and the constituent particles are closely packed. That is why; solids are incompressible and have high density.
- In **liquids**, the intermolecular forces are strong enough to keep the particles tied upon to each other but not strong enough to keep them in fixed positions. This is why; liquids can flow and do not have a definite shape.
- In **gases**, the intermolecular forces are negligible (extremely weak), and the constituent particles are free to move. As a result, gases, can occupy any space available to them.

Solids can be divided in to two distinct classes:

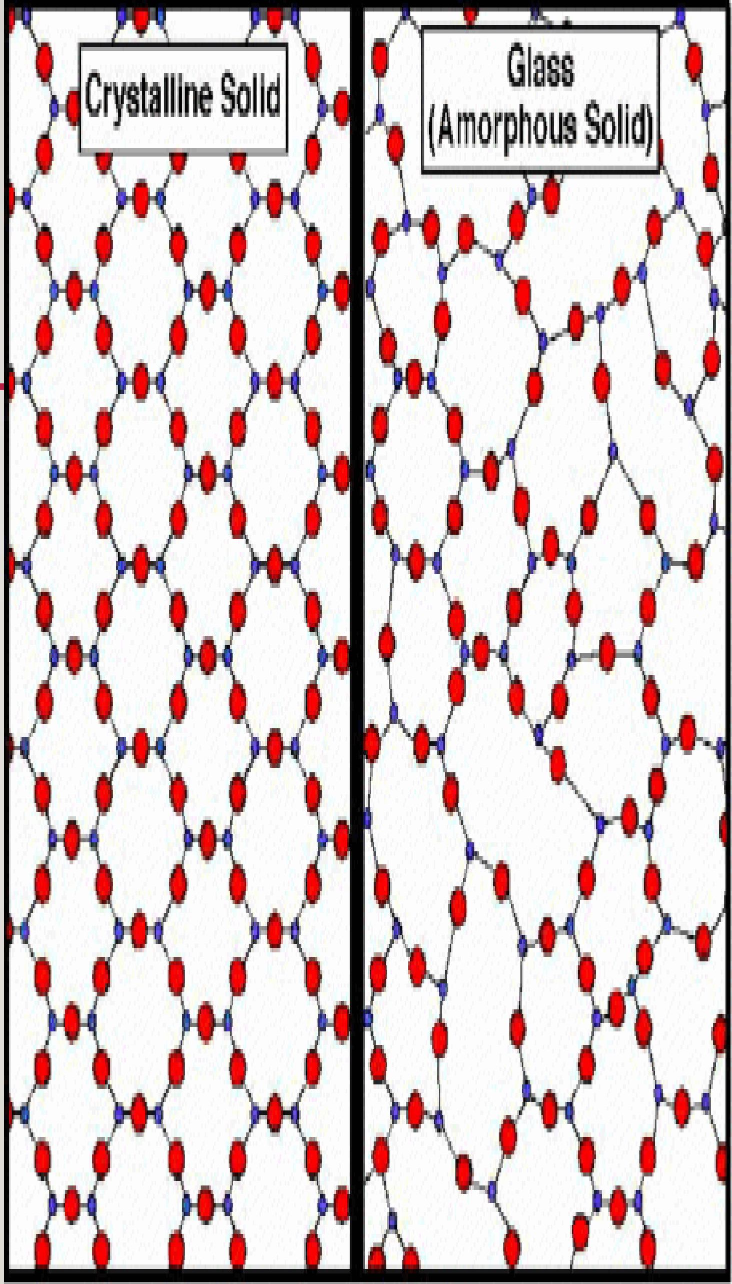
1) Crystalline solids

Ordered arrangement of atoms, ions, or molecules. They can form a regular repeating three-dimensional structure called a crystal lattice. Examples of pure substances that are crystalline solids at room temperature and pressure are iron metal, diamond, and table salt (NaCl) and sugar.

2) Amorphous solids

Random arrangements of atoms, ions, or molecules

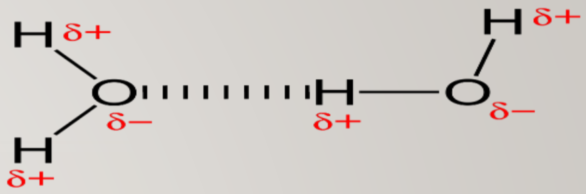
Examples of amorphous solid such as synthetic fibers, plastics, and glasses.



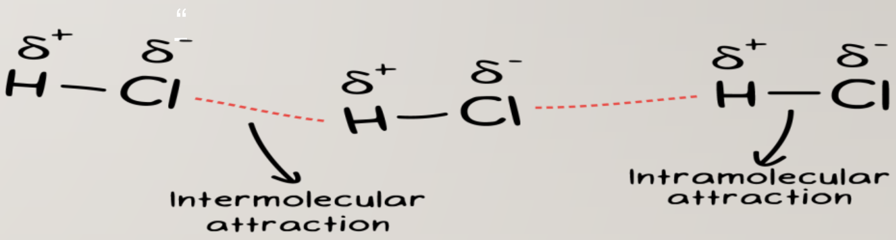
There are 2 types of attraction in molecules

1. **Intermolecular forces** are attractive forces **between** molecules. ***(Example: water molecule to water molecule***

Intermolecular forces (IMFs) are the **forces** which mediate interaction between molecules.



2. **Intramolecular forces** hold atoms together ***within*** in a molecule. ***(Example: H to O bond within a water molecule).***



THE IMPORTANCE OF KNOWING THE INTERMOLECULAR FORCES IN PHYSICAL BIOCHEMISTRY

1-Intermolecular forces play a major role in determining the physical and chemical properties of biomolecules.

2-It is the central to the most critical processes of biochemistry such as protein conformation and enzyme activity or DNA base-pairing.

3-The physical properties of melting point, boiling point, vapor pressure, evaporation, viscosity surface tension, and solubility are related to the strength of attractive forces between molecules.

I-Chemical Bonds

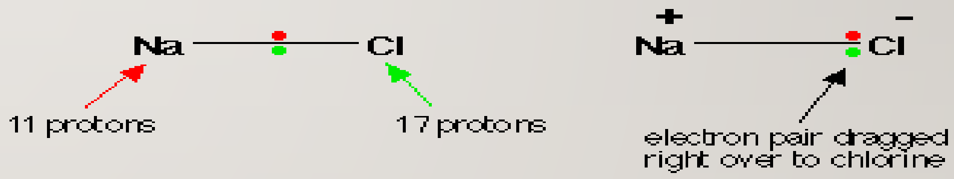
- When atoms are joined together as a result of electronic interaction, the force that holds them together is called a chemical bond.

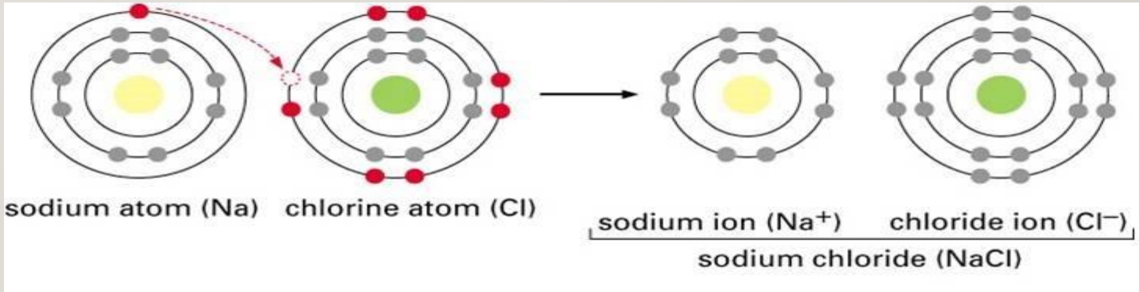
- Several characteristics are associated with bonds like; **bond strength**, **the maximum number of bonds an atom can make**, **the bond angle**, and **the freedom of rotation permitted by the bond.**

- Types of bonds

I- Ionic bond

- It is formed when electrons are first transferred from one atom to another and the ions thus formed are bound together by electrostatic attraction.
- The ionic bond is considerably weaker than the covalent bond.
- Ionic substances are formed when an atom that loses electrons relatively easily react with an atom that has a high affinity for electrons. ex. metal-nonmetal compound

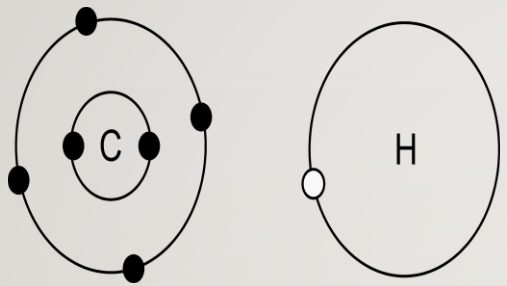




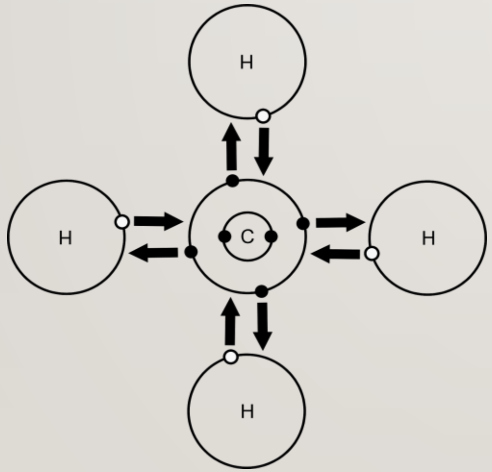
2- Covalent bond

- A single covalent bond is formed when two atoms share a pair of electrons.
- In a covalent bond the number of electrons that are available to be shared is definite; hydrogen can form only one covalent bond and carbon only four as in *methane* (CH_4).

The Methane Molecule (CH_4)



Both carbon and hydrogen atoms have an incomplete outer shell.



One carbon atom shares four electrons with the hydrogen atoms.

Each hydrogen atom shares one electron with the carbon atom.

The sharing of a pair of electrons constitutes a single covalent bond.

Therefore, four covalent bonds are formed.

The process of sharing electrons is known as **covalent bonding.**

In order to achieve a full outer shell...

Hydrogen atom needs one electron

Carbon atom needs four electrons

Nitrogen atom needs three electrons

Oxygen atom needs two electrons

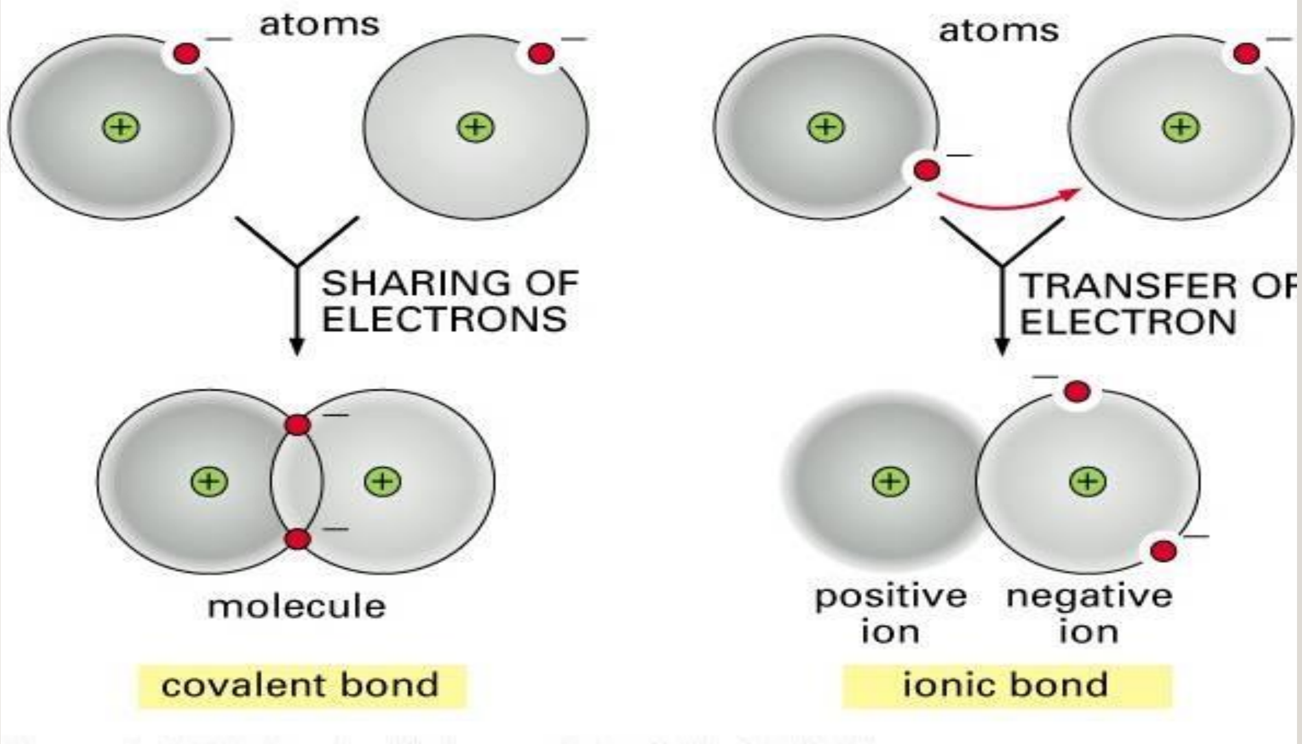
Fluorine atom needs one electron

Neon atoms already have a full outer electron shell.

Covalent Bond and Ionic Bond

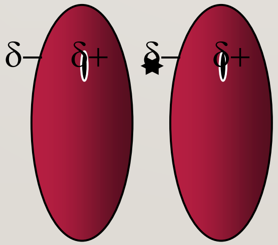
Ionic bond: electron transfer

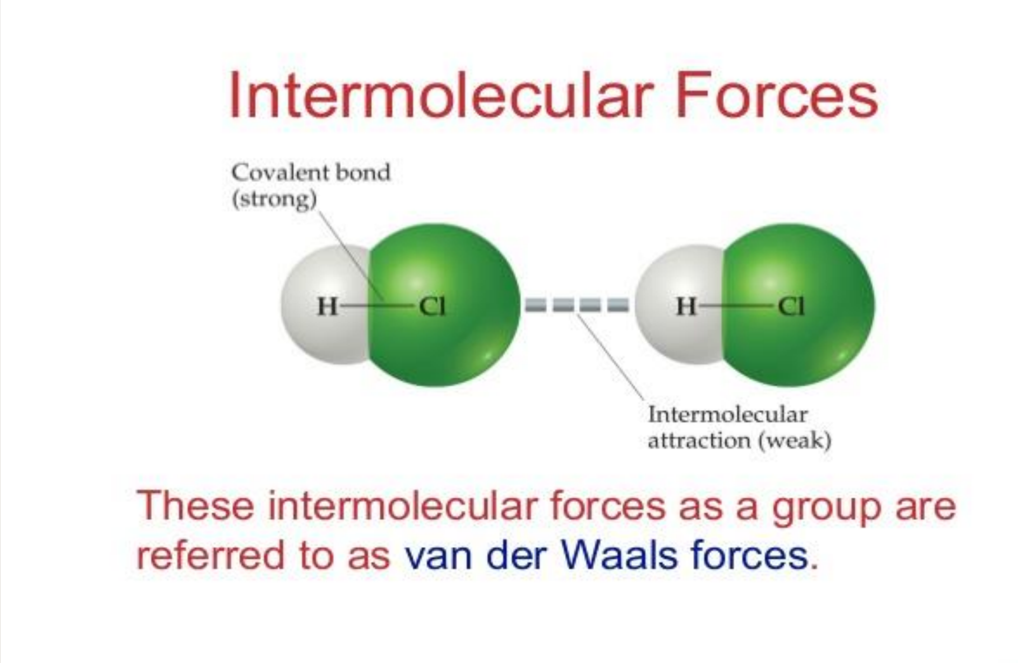
Covalent bond: electron sharing



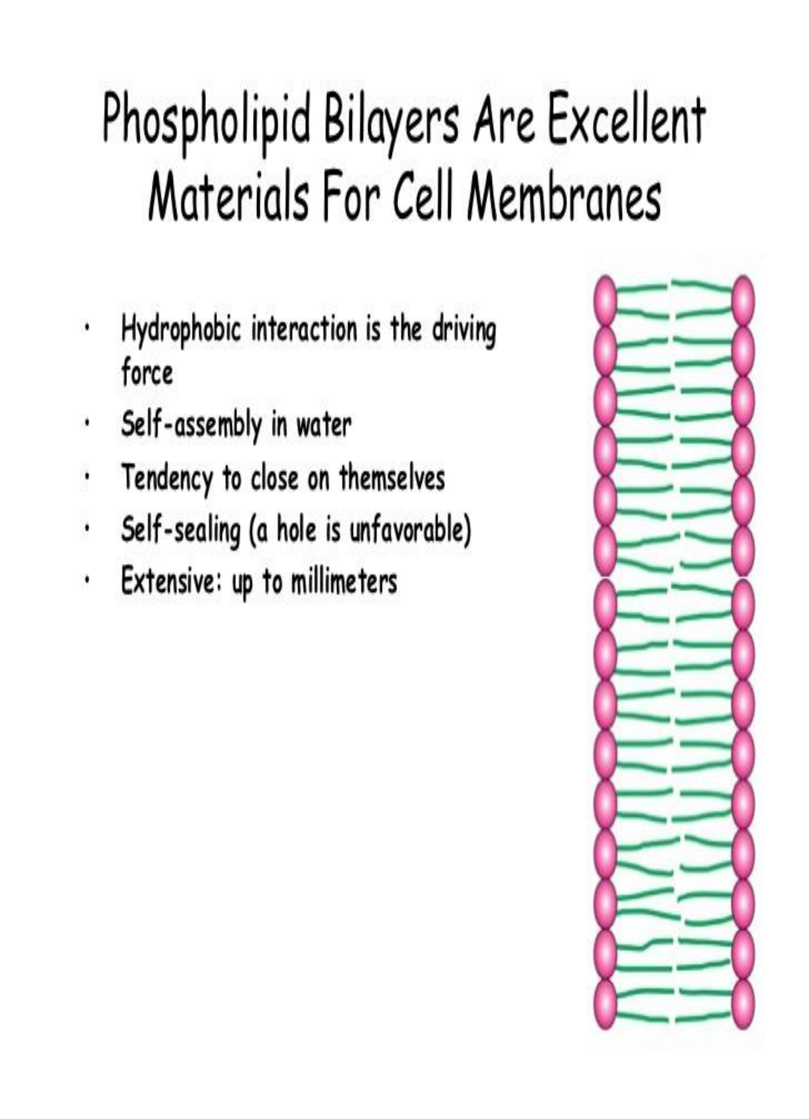
3- Van der Waals forces

- They are nonspecific forces that are present when atoms come close to each other.
- Van der Waals force are created by the fluctuating charge distributions caused by the nearness of molecules. When atoms get very close, they experience a repulsive or attractive forces. Van der Waals forces are relatively weak compared to normal chemical bonds, but play a fundamental role in fields as diverse as structural biology.
- Although Van der Waals forces are weak, they are often the **only** attractive force between molecules.



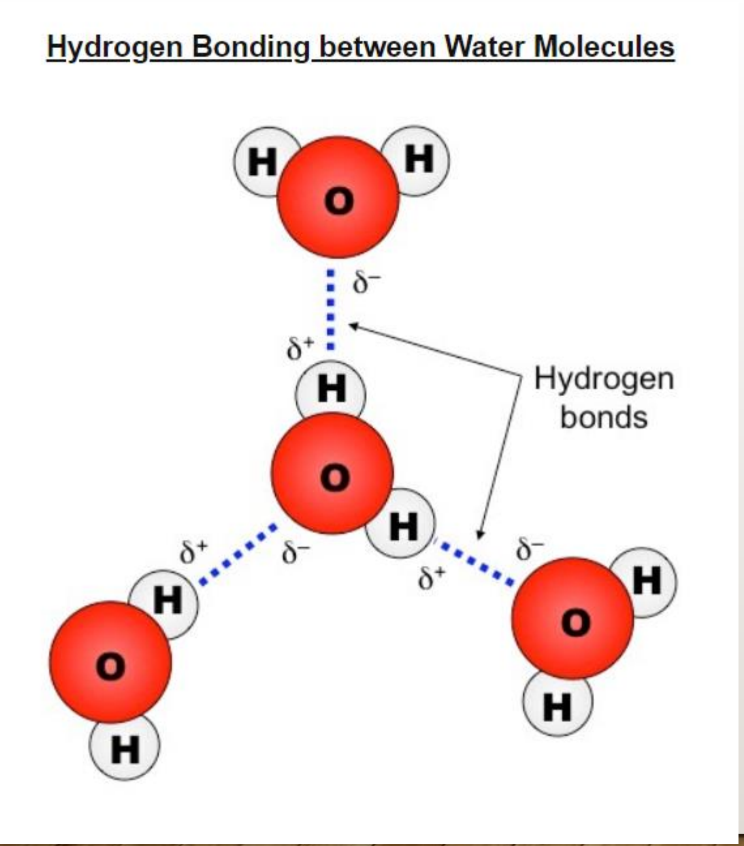


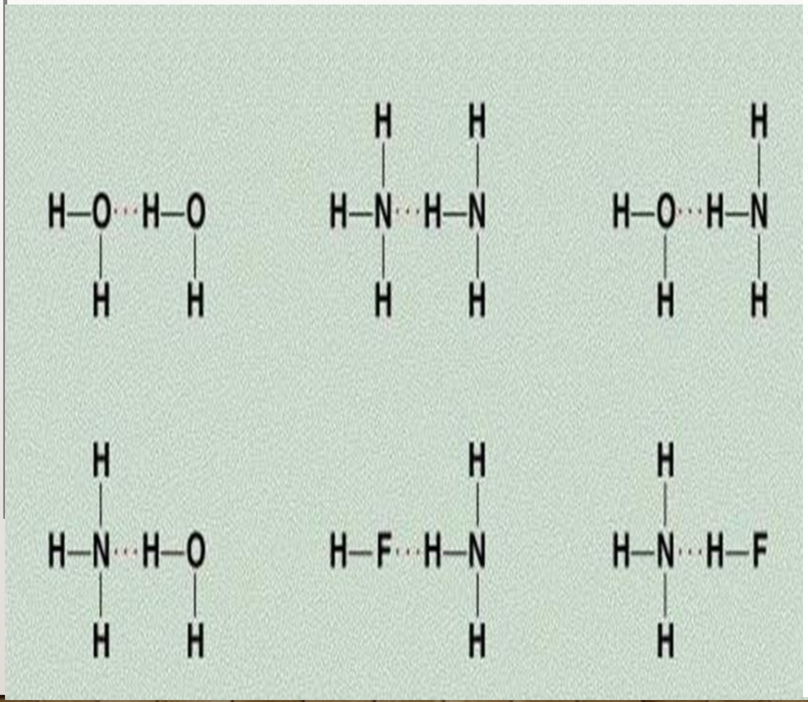
4–Hydrophobic interactions describe the relations between water and hydrophobes (low water-soluble molecules and non polar). Hydrophobes usually have a long chain of carbons that do not interact with water molecules. The mixing of fat and water is a good example of this particular interaction. The common misconception is that water and fat doesn’t mix because the Van der Waals forces that are acting upon both water and fat molecules are too weak. The behavior of a fat droplet in water has more to do with the enthalpy and entropy of the reaction than its intermolecular forces.

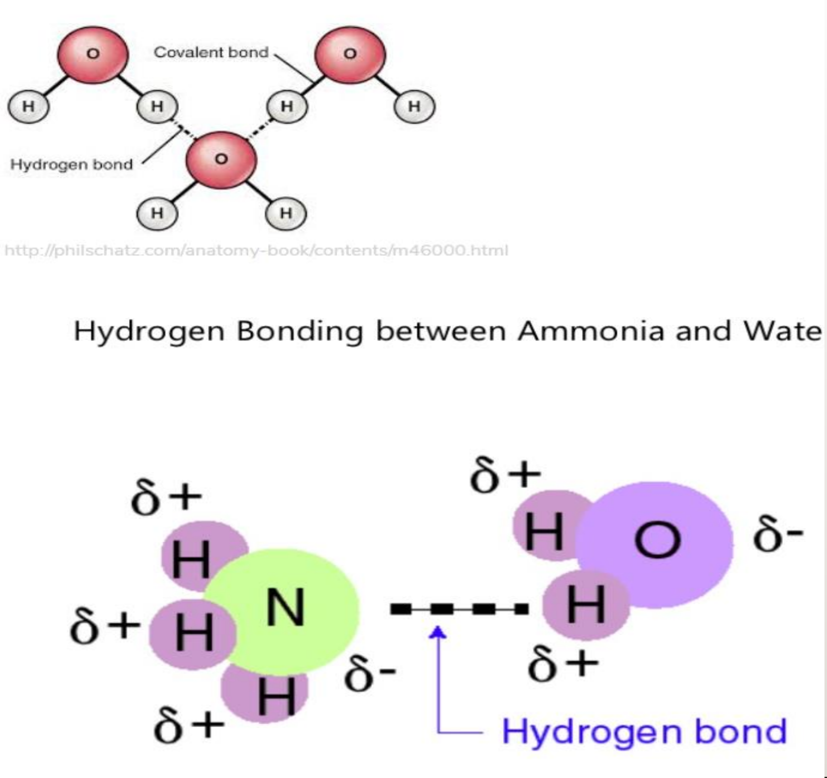


5 Hydrogen bond

It is very important bond in biological macromolecules. It is also a weak bond and arises when a covalently bound hydrogen atom that has some positive charge encounters a covalently bound acceptor atom (one with a negative charge). The most important hydrogen bonds in biological systems are those in which the bonds is between H and O or between H and N atoms. They are stronger than van der Waals forces.





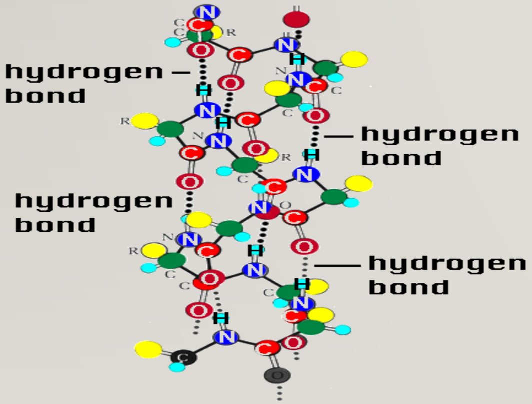


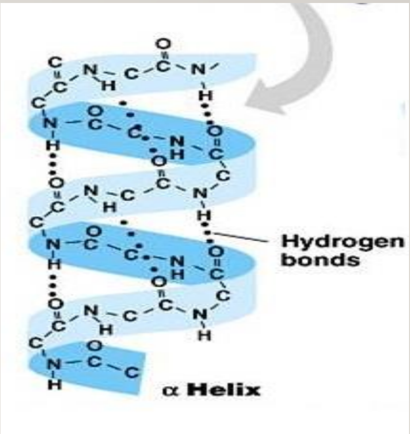
H-BONDS IN PROTEINS

H-bonds contributing to structure and folding.

α-helix

- It is a spiral structure resulting from hydrogen bonding between one peptide bond

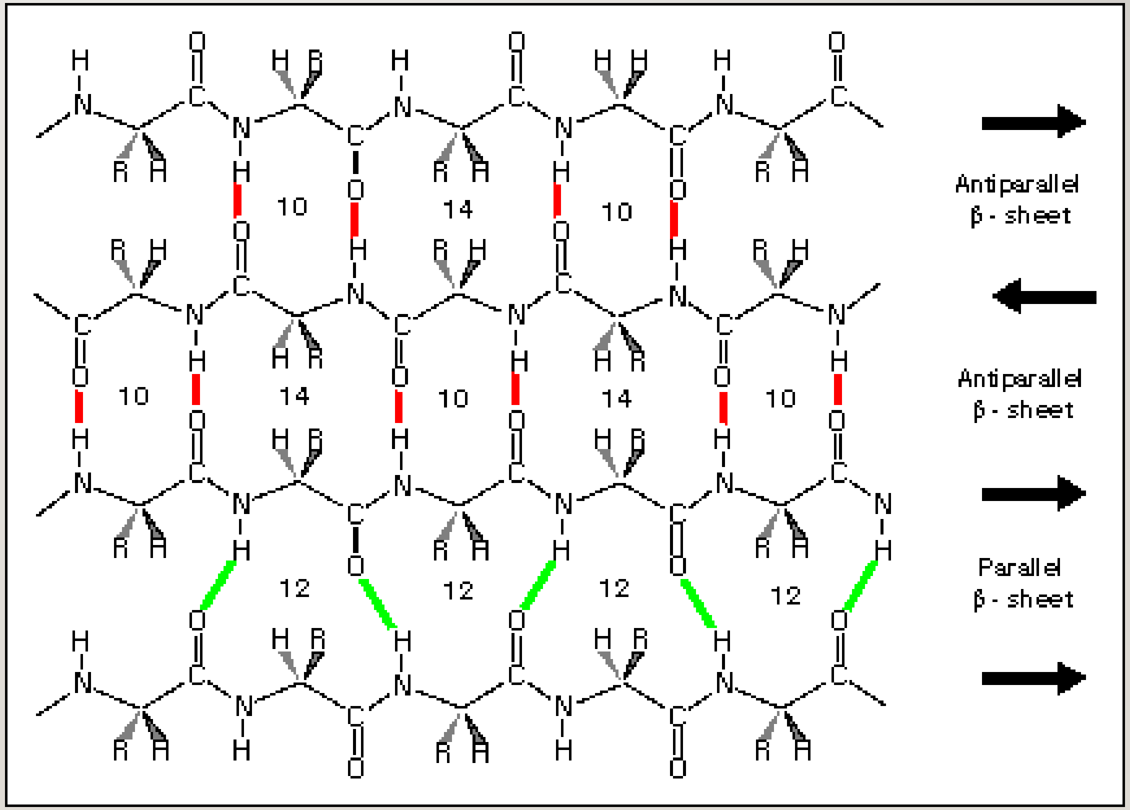




β-sheets: hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain.

Antiparallel β-sheets

Parallel β-sheets



Making and breaking bonds

- In a chemical reaction, the bond formation involves a change in energy. The stronger the bond, the greater is the energy released when the bond forms.

$$A + B \longrightarrow AB + \text{Energy}$$

- Chemical bonds may also be broken often by heat energy or by collisions. If a bond is broken, the energy required is equal to the energy released upon formation of that bond.

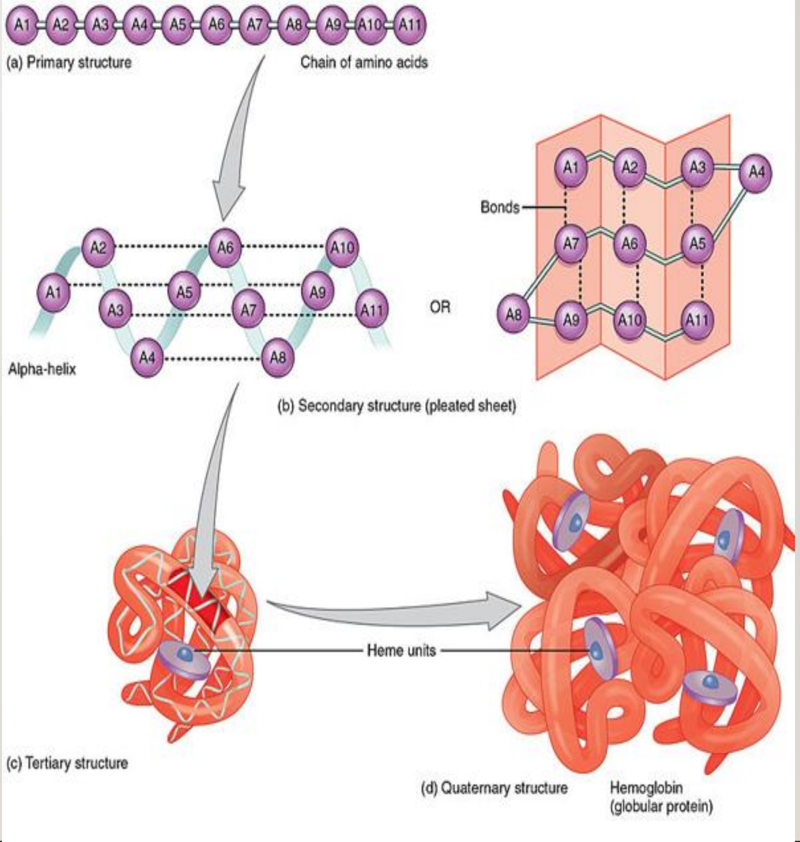
$$AB + \text{Energy} \longrightarrow A + B$$

Bonds and the molecular shapes

The weak bonds are important in determining the shapes of molecules. The shapes of many molecules is automatically determined by the distribution of covalent bonds. Double and triple bonds are rigid and don't permit rotation around the bond. Molecules having single covalent bonds permit parts of the molecule to rotate around those bonds.

INTERMOLECULAR FORCES AND PROTEIN STRUCTURE

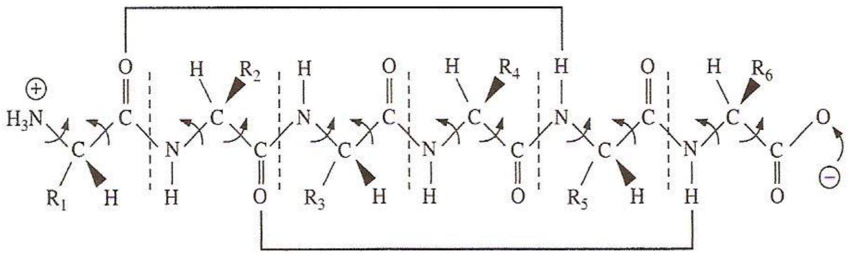
- Proteins are polypeptides of 20 naturally occurring amino acids.
- Amino acids are linked by amide bonds from the carboxyl group of one amino acid to the amino group of the next
- *The sequence of amino acid residues in a polypeptide is called* ***primary structure***
- *The polypeptides fold into different* ***secondary structures*** held together by hydrogen bonds and other non covalent interactions



- Level 1: bond between a.a making peptide bond (primary sequence)

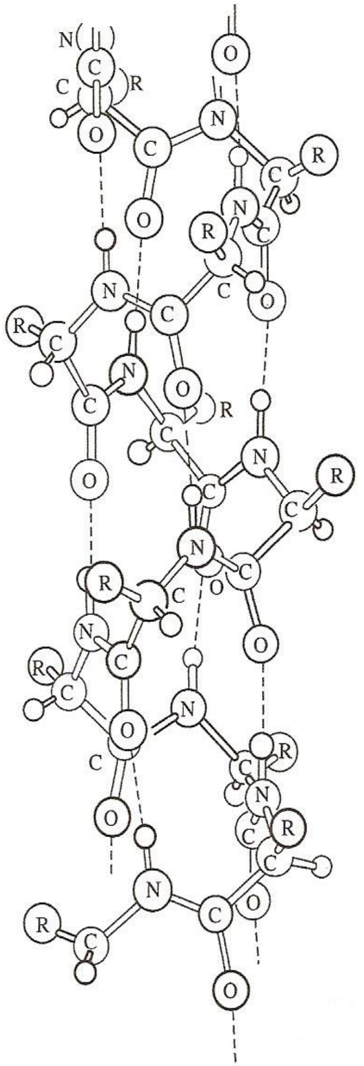
- Level 2 :backbone hydrogen bond

Level 3 : van dar Waal
disulfide bridge
electrostatic attraction
hydrophobic attraction



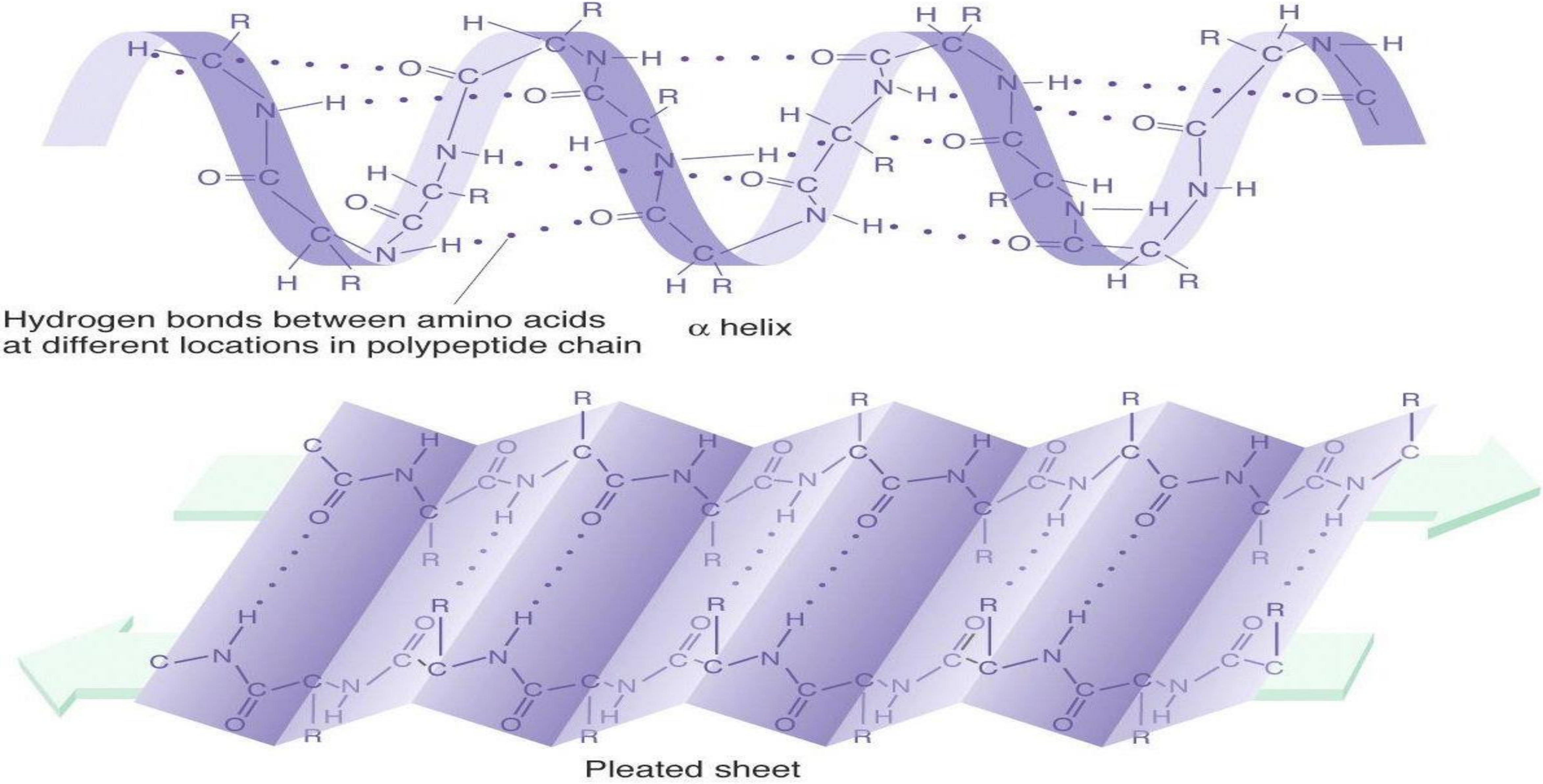
▲ FIGURE 3.4

A polypeptide chain. Residues are commonly numbered by starting from the amino terminal. The residues in the polypeptide chain are separated by dotted lines, and the arrows show the two bonds (on either side of each α-carbon) around which rotation can occur. The two long lines joining a carbonyl oxygen to an amide hydrogen 4 residue units away on its carboxyl terminal side represent hydrogen bond formation in an α-helix structure (see figure 3.5).



▶ FIGURE 3.5

The α-helix. The structure shown here is the right-handed conformation commonly found in proteins. [From Linus Pauling, *The Nature of the Chemical Bond* (Ithaca, NY: Cornell University Press, 1960, p. 500). Copyright © 1939 and 1940, 3d ed. © 1960 by Cornell University. Used by permission of Cornell University Press.]


Hydrogen bonds between amino acids at different locations in polypeptide chain
α helix
Pleated sheet

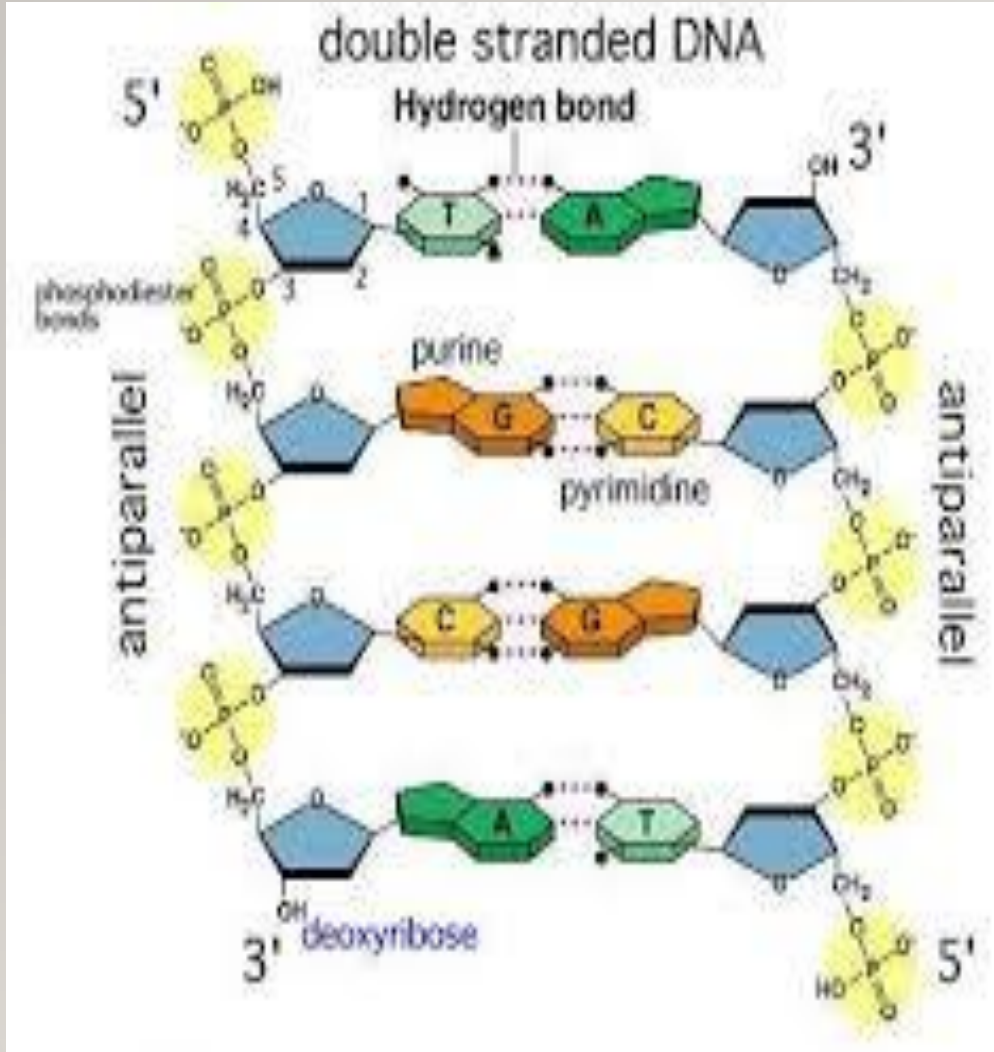
- The different folded conformations of a polypeptide depend on rotation about the two single bonds attached to the amide group
- **α-helix is a common secondary structure element in proteins**.
- Folding is a spontaneous process that is mainly guided by hydrophobic interactions, formation of intramolecular hydrogen bond and van der Waals forces.

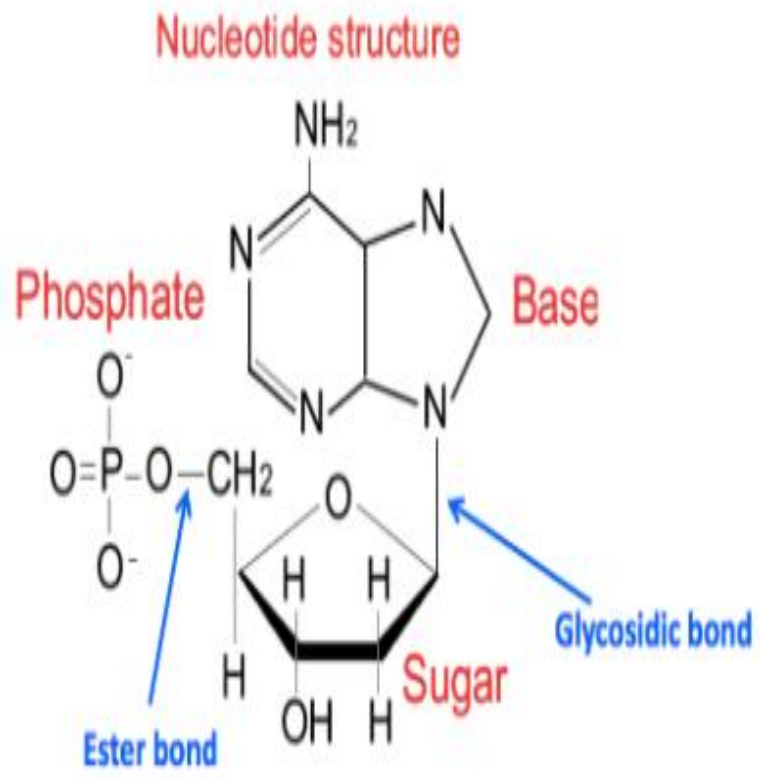
Intermolecular Forces Of Nucleic Acids

Nucleic acids are polynucleotides of four naturally occurring nucleotides. The nucleotides are composed of a sugar group connected to one of four bases and to a phosphate group.

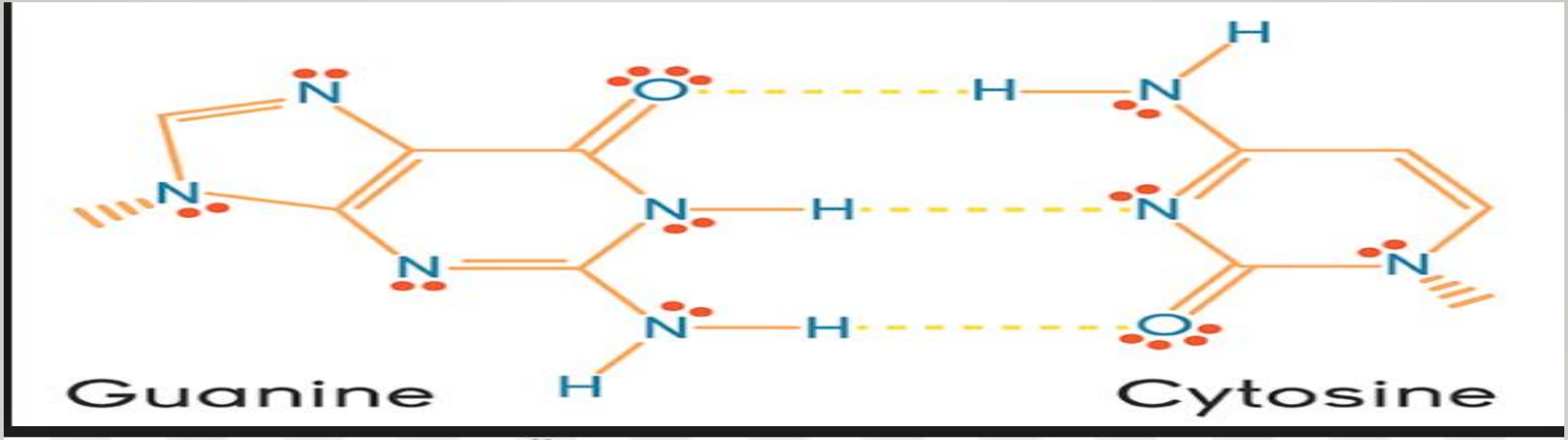
Nucleotides are linked by phosphodiester bonds (fig.). *The sequence of the bases in the polynucleotide is the primary structure*.

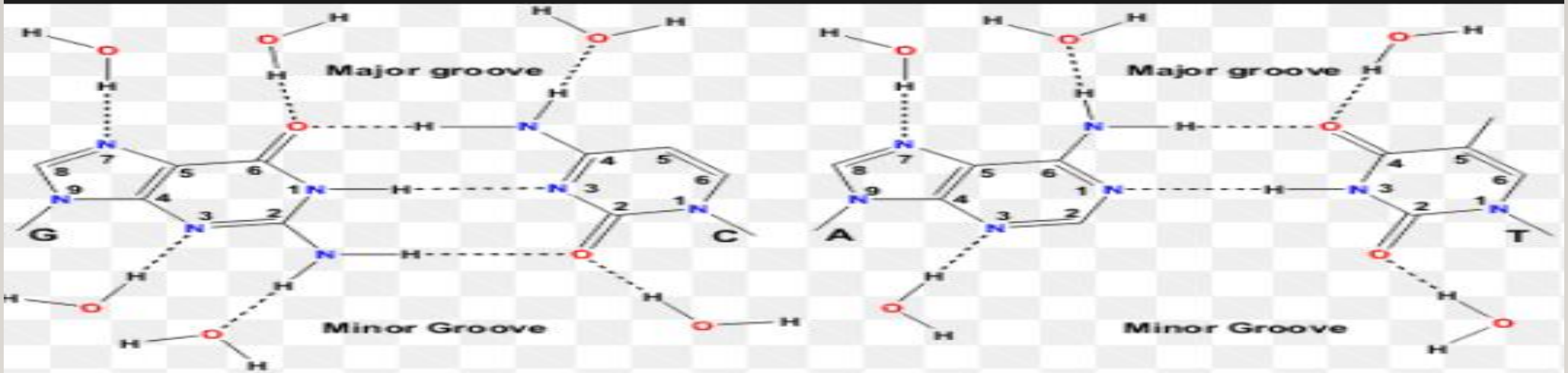
<u>The stacking of the base pair, one above the other, plus the hydrogen bonds between bases provide the stabilizing enthalpy and free energy of the helix</u>



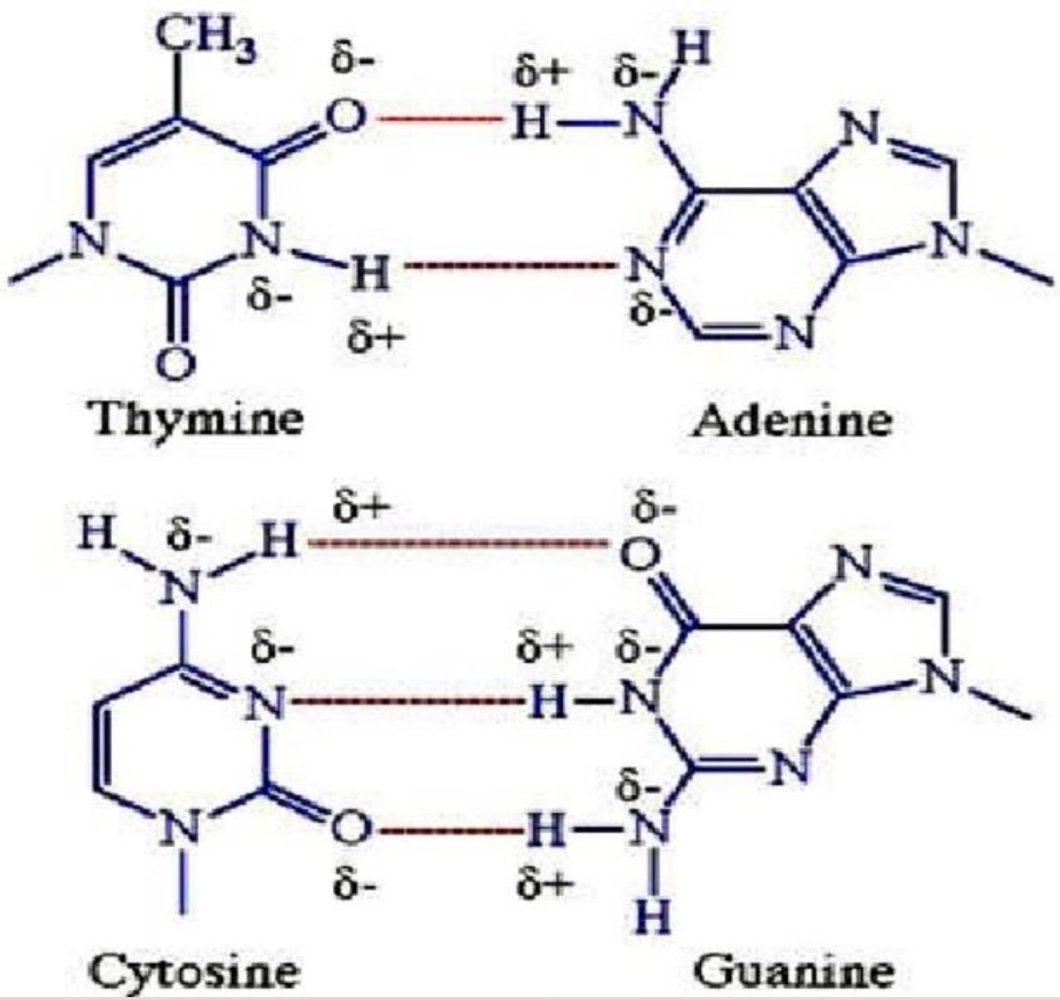


- Ester bonds and Glycosidic bond or N-glycosidic bond


Guanine
Cytosine

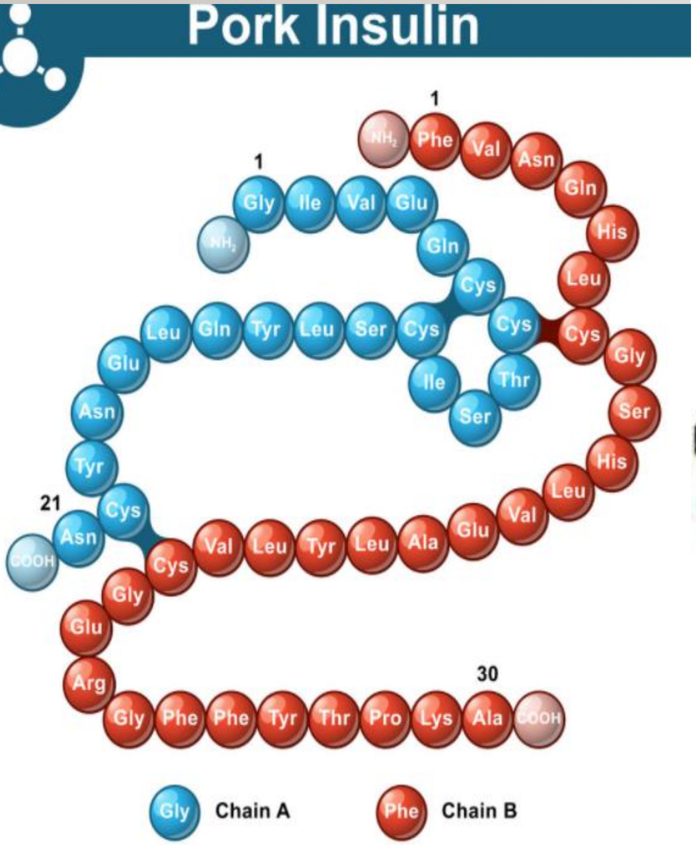

Major groove
Major groove
G
C
A
T
Minor Groove
Minor Groove

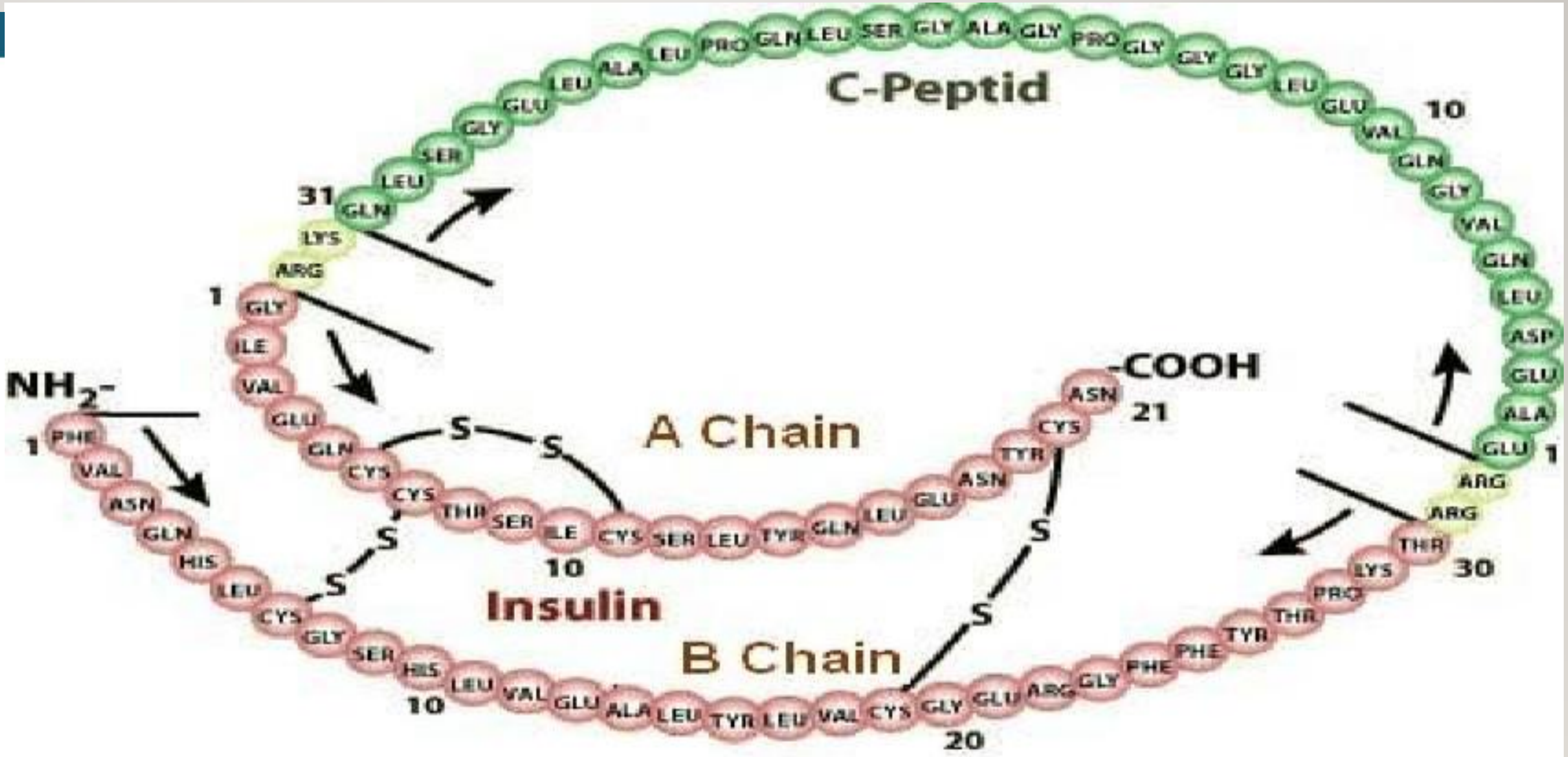
Hydrogen Bonds in DNA



- Here are the two diagrams outlining where the hydrogen bonds are within DNA (red lines).
- Base A and T are held together by two hydrogen bonds (an O-H and N-H bonds)and bases G and C are bonded together by three hydrogen bonds (2 O-H bonds and 1 N-H bond).
- The different number of Hydrogen bonds ensure that the bases link together correctly

<u>Structure of human pro-insulin</u>. 82-polypeptide hormone consisting of the A chain (21 a.a.) and the B chain (30 a.a.) linked by two disulfide bridges (Cys7A–Cys7B / Cys20A–Cys19B). One more intrachain disulfide bond is located between Cys6–Cys11 within the A chain (Murray et al, 2003).



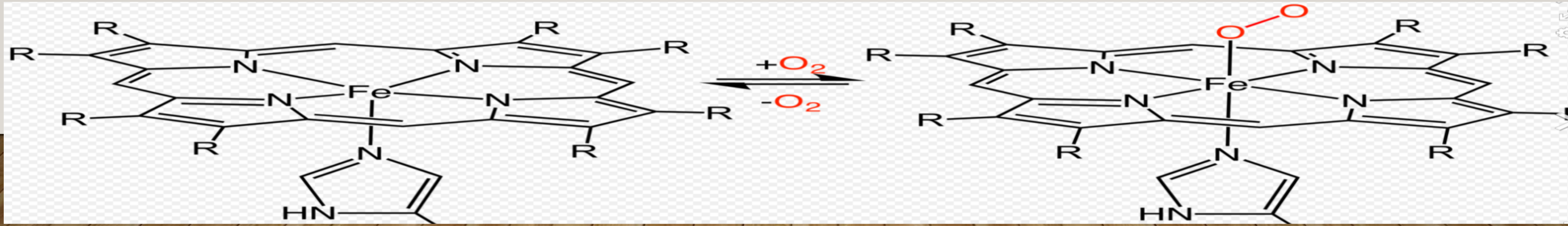


Myoglobin and hemoglobin

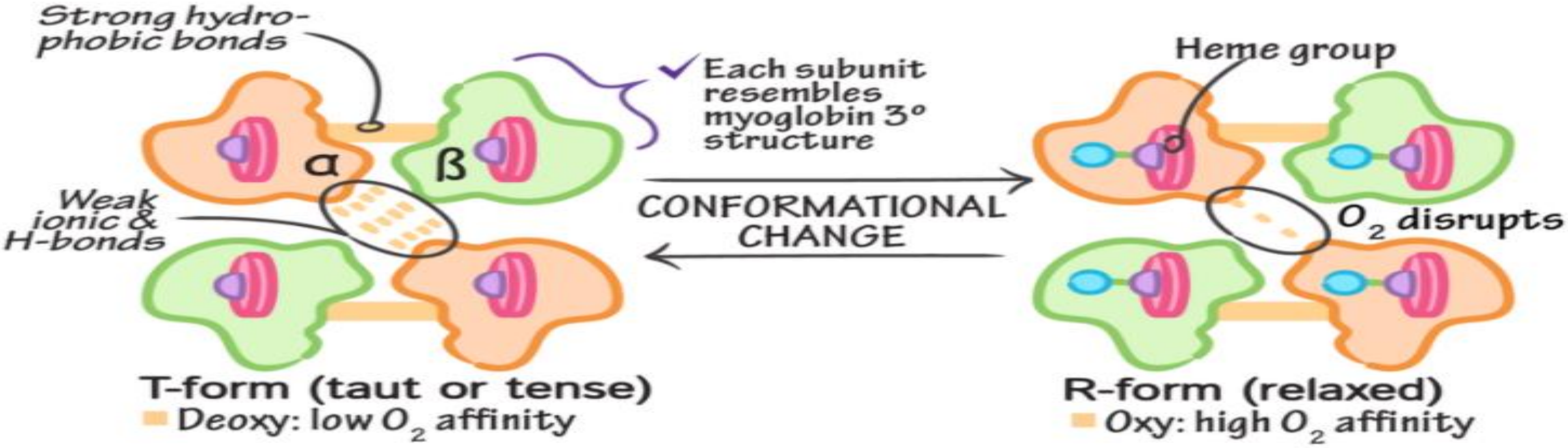
THEY are much alike in their action toward oxygen.
All body cells require oxygen for metabolism, but unfortunately, oxygen is non-polar and not soluble in the aqueous blood. The problem then becomes, how do you get oxygen to the tissue cells?
Hemoglobin is used to transport oxygen in the blood in red blood cells to tissue cells where it is used directly. Myoglobin is present in skeletal muscles as an extra storage protein to enable muscles cells to have a readily available supply of oxygen.
The hemoglobin molecule is made up of four polypeptide chains: two alpha and two beta chains . The alpha and beta chains have different sequences of amino acids, but fold up to form similar three-dimensional structures. The four chains are held together by noncovalent interactions. There are four binding sites for oxygen on the hemoglobin molecule, because each chain contains one heme group. The iron atom in heme binds to the four nitrogens in the center of the protoporphyrin ring.

Heme:

Hemoglobin and myoglobin both a have group called "heme", which is at the heart of the protein structure.
. It is made from a a series of nitrogen five member cyclic rings, that are further joined to each other by more rings.
At the center of the heme group is the **iron +2** metal ion. The nitrogen atoms bind to the iron ion through what are called coordinate covalent bonds. This means that ,unlike normal covalent bonds where each atom contributes one electron for the bond, that the nitrogen contributes both electrons for the coordinate covalent bond. The oxygen molecule will ultimately bind to this iron ion also using a coordinate covalent bond.



Hemoglobin



Cooperative Binding

1. One O_2 binds a hemoglobin subunit
2. O_2 binding disrupts inter-dimer bonds
3. ↑ O_2 affinity of remaining subunits

Applications of Intermolecular Forces

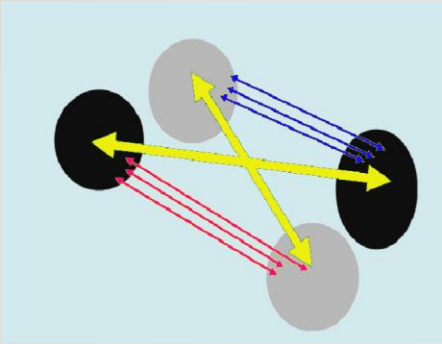
Liquid properties

Properties of liquids are related to the INTERMOLECULAR FORCES OF ATTRACTION in various liquids.

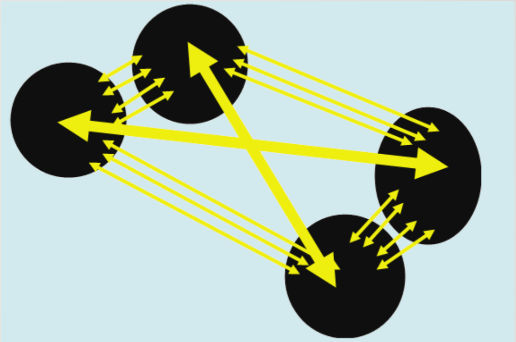
- Surface tension
- Capillary action
- Boiling point

I -SURFACE TENSION

- Molecules at the surface (exposed to air) are attracted inward.
- This creates a force in the surface that tends to minimize the surface area.
- The surface tension of a liquid is related to the amount of energy needed to increase its surface area per unit



The force between the molecules of different substance is known as **Adhesive force.**



The force between the molecules of the same substance is known as **Cohesive force.**

- At liquid-air interfaces, surface tension results from the greater attraction of liquid molecules to each other (due to cohesion) than to the molecules in the air (due to adhesion).
- What are the causes of surface tension?
- The surface tension is caused by the effect of the intermolecular forces that exist in the interface.

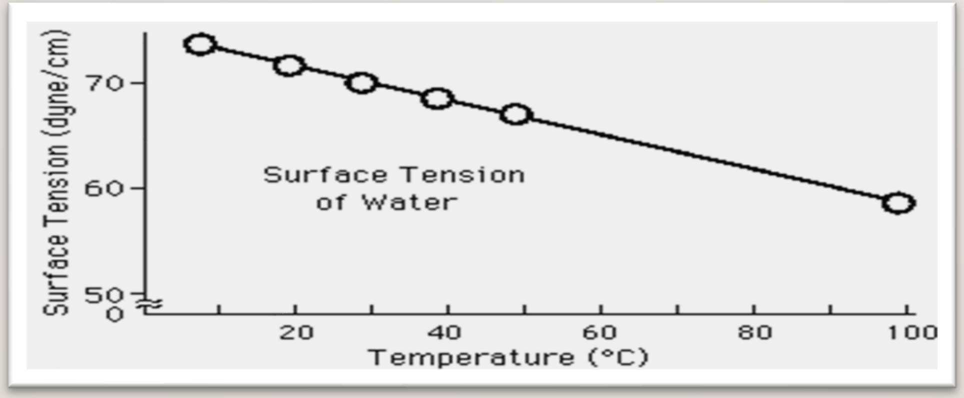
<u>Factors affecting surface tension</u>

The surface tension ***depends on :***

***The nature of the liquid**

Liquids whose molecules have *strong intermolecular* attraction forces have *high surface tension*

***Temperature: as** the temperature of the liquid increases, the surface tension decreases



The figure shows that the surface tension decreases with increasing temperature, this is due to cohesion forces decrease with increasing thermal agitation.

SURFACE TENSION EXAMPLES (BIOLOGICAL SIGNIFICANCE) APPLICATION

1-Clinical test for jaundice

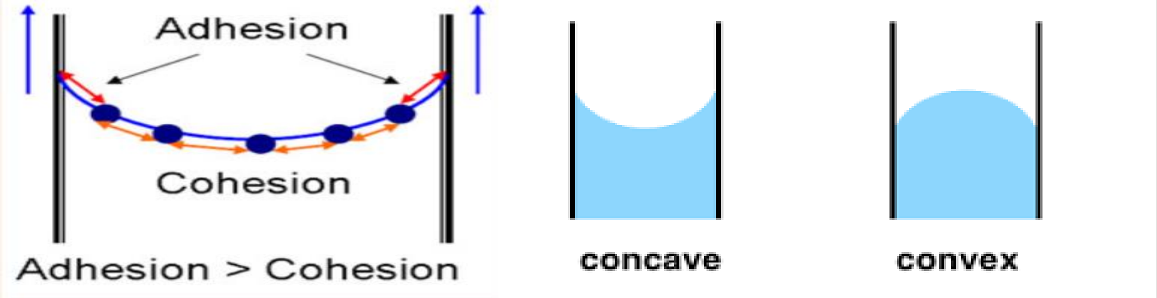
Normal urine has a surface tension of about 66 dynes/cm but if bile is present (a test for jaundice), it drops to about 55.

In the hay test, powdered sulfur is sprinkled on the urine surface. It will float on normal urine, but sink if the S.T. Is lowered by the bile.

2- **Surface tension disinfectants**

Disinfectants are usually solutions of low surface tension. These allow them to spread out on the cell walls of bacteria and disrupt them. One such disinfectant, S.T.37, its low surface tension compared to the 72 dynes/cm for water.

2- Capillary action



Capillary action is the property of some liquids to rise in narrow glass tubes (capillary tubes)

- Capillary action rises due to the two forces; adhesion and cohesion.
- Adhesive forces attract the liquid to the wall of the tube, while cohesive attract the liquid to it self

The meniscus is the curve in the upper surface of a liquid close to the surface of the container or another object, caused by surface tension. It can be either convex or concave, depending on the liquid and the surface

3- boiling point

Higher the intermolecular forces between the liquid particles, harder it is for it to escape into the vapor phase, ie., you need more energy to convert it from liquid to the vapor phase, in other words, higher its boiling point.

At sea level, pure water boils at 100 °C and freez at 0 °C.