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Textbook of
BIOCHEMISTRY
for Medical Students

As per the Competency-based Medical Education Curriculum (NMC)

Diagnostic testing for COVID -19 included

Highlights
- Thoroughly revised & updated
- Key concepts & summary included
- Richly illustrated
- Updated Long & Short Qs and Essay Qs
- New MCQs and Case studies

DM Vasudevan
Sreekumari S
Kannan Vaidyanathan

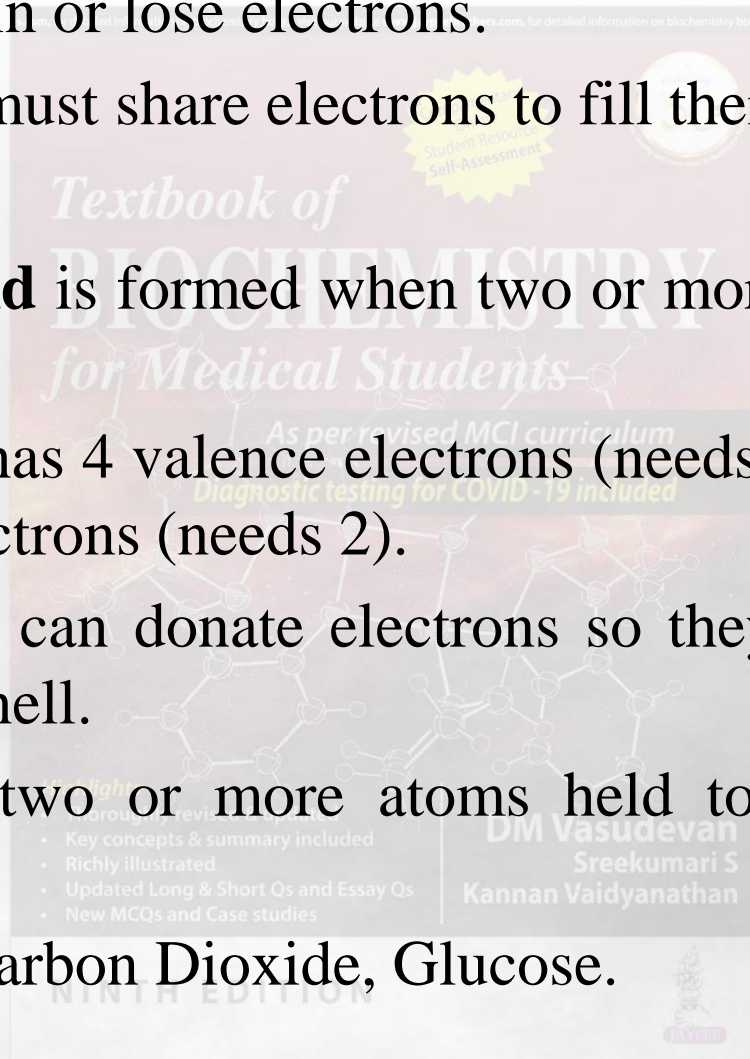**TENTH EDITION**

Chapter 1
Biochemical Perspectives to Medicine

Textbook of
# BIOCHEMISTRY
for Medical Students
By D.M. Vasudevan et al

T E N T H
E D I T I O N

- Not all atoms gain or lose electrons.

- Many elements must share electrons to fill their valence shells.

- A **Covalent Bond** is formed when two or more atoms share pairs of electrons.

  - Ex: Carbon has 4 valence electrons (needs 4) and Oxygen has 6 valence electrons (needs 2).

  - Neither atom can donate electrons so they share pairs to fill the valence shell.

- A **Molecule** is two or more atoms held together by covalent bonds.
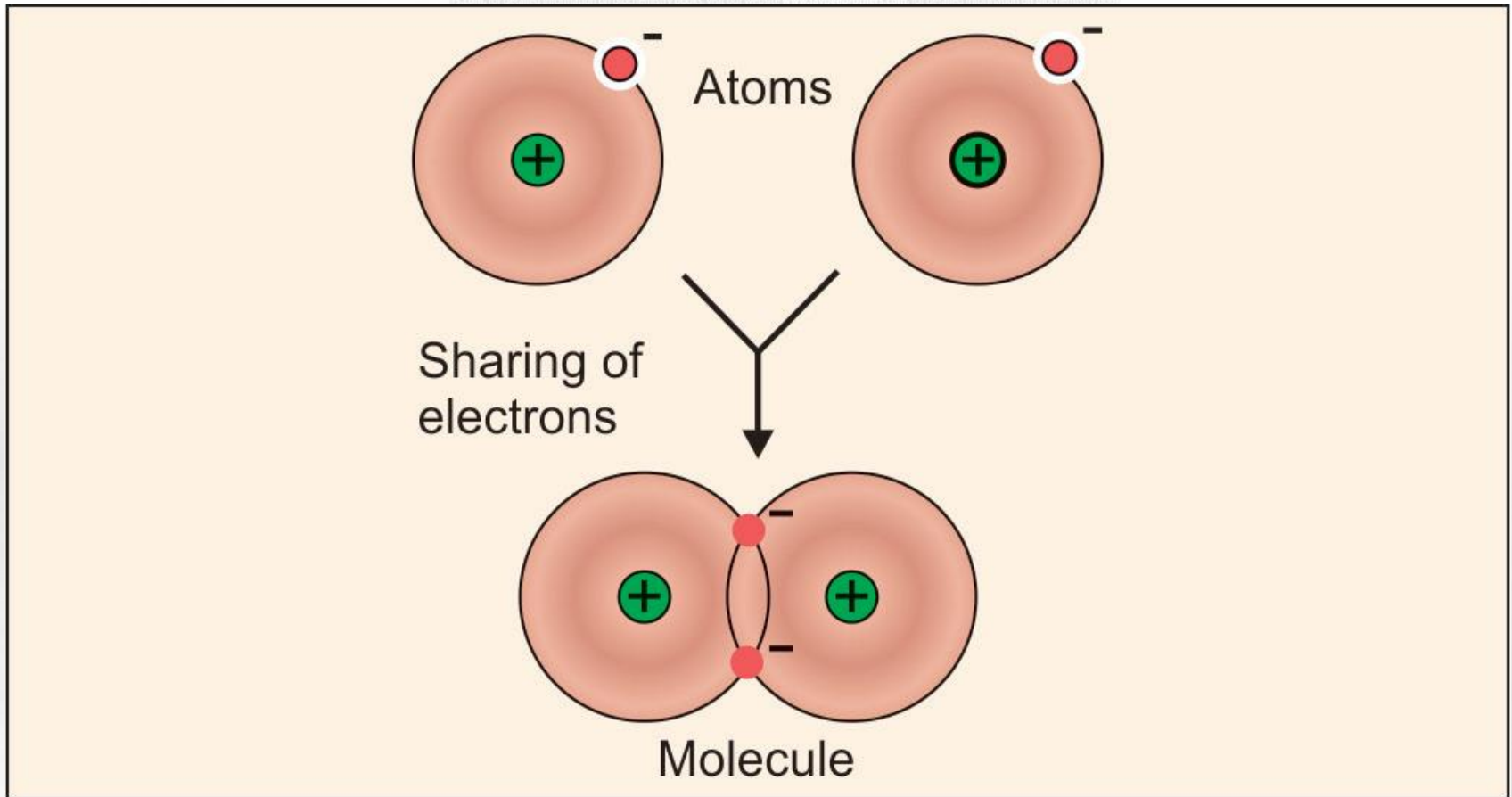
  - Ex: Water, Carbon Dioxide, Glucose.
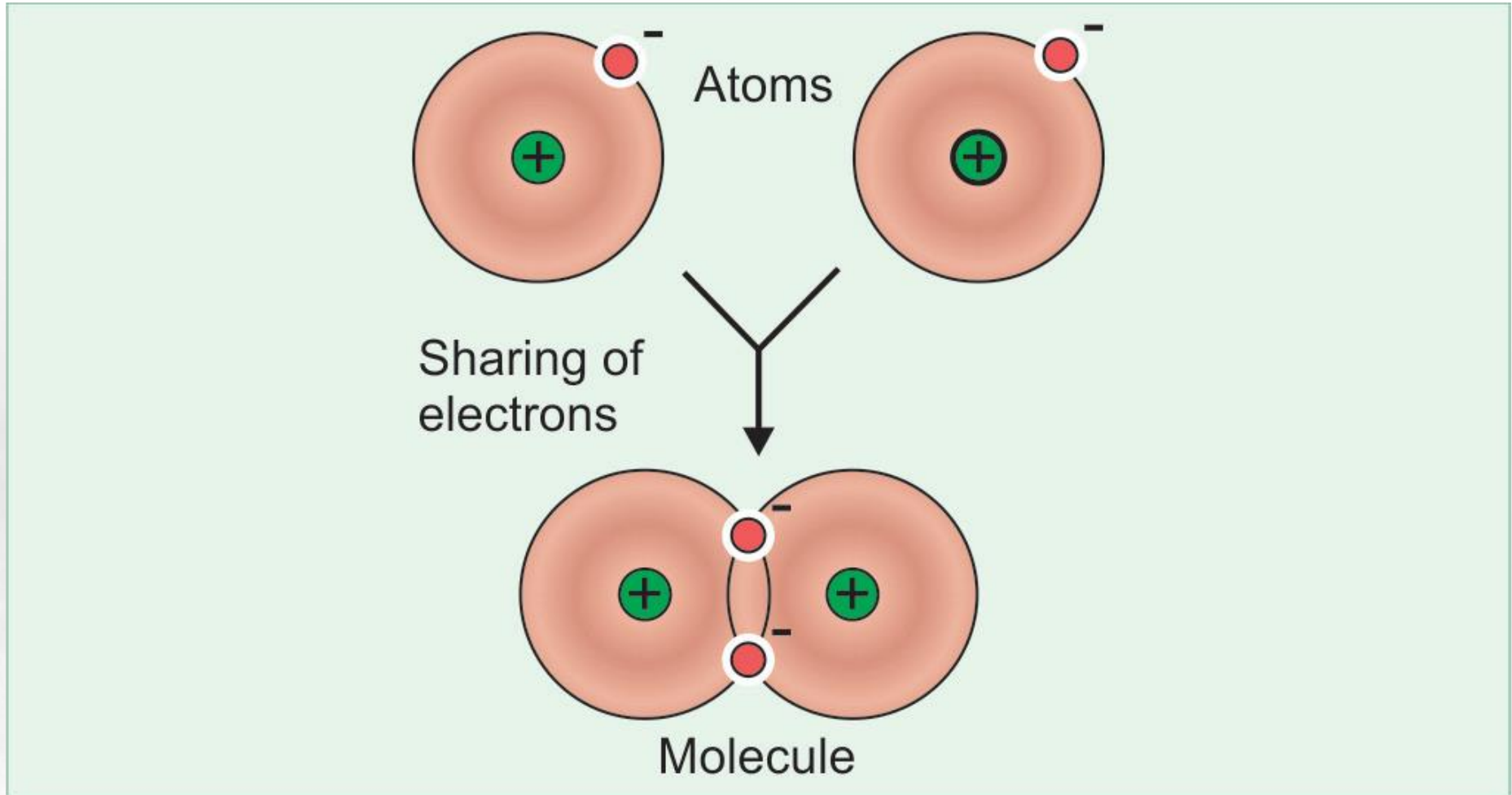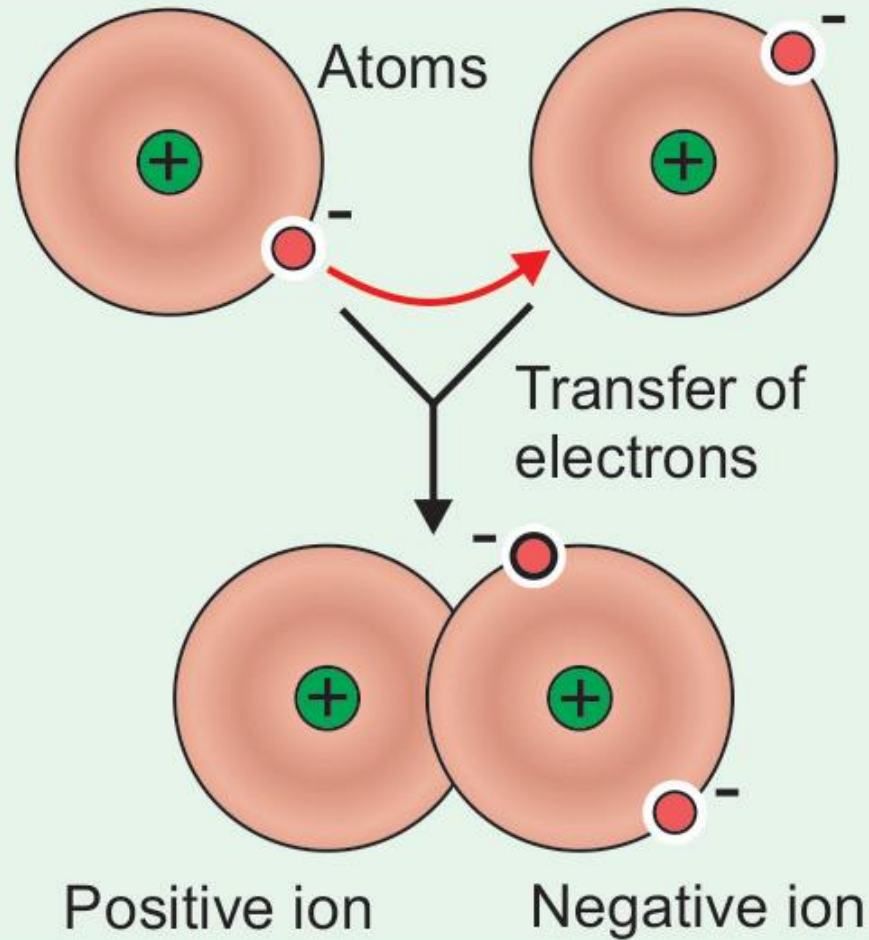
Covalent bond.

Ions form when Atoms Gain or Lose Electrons

- An **Ion** is an atom that has gained or lost one or more electrons.
- An Ion forms because an atom is more stable when its outermost energy level is full; the gain or loss of electrons allows this to occur.
- Some ions are positively charged (those that lose electrons)
- Some ions are negatively charged (those that gain electrons).
- An **Ionic Bond** form through the electrical force between oppositely charged ions.
  - Ex: Salt is an ionic bond between sodium and chlorine.
  - Chlorine (Cl) has 7 valence electrons (needs 1) and Sodium (Na) has 1 valence electron (need to get rid of it)
  - Sodium donates its electron to chlorine forming an ionic bond that creates salt.
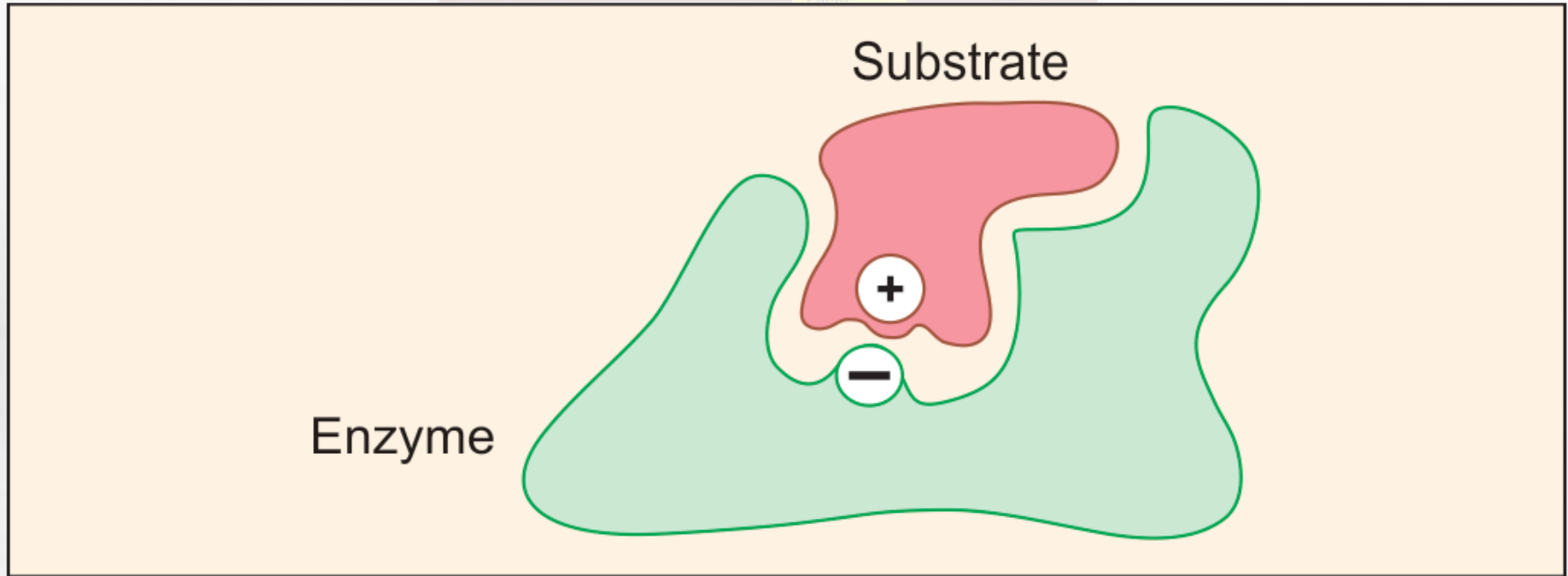
Molecules contain covalent bonds

Ionic bond.

Fig. 1.13. Ionic bonds used in protein interactions
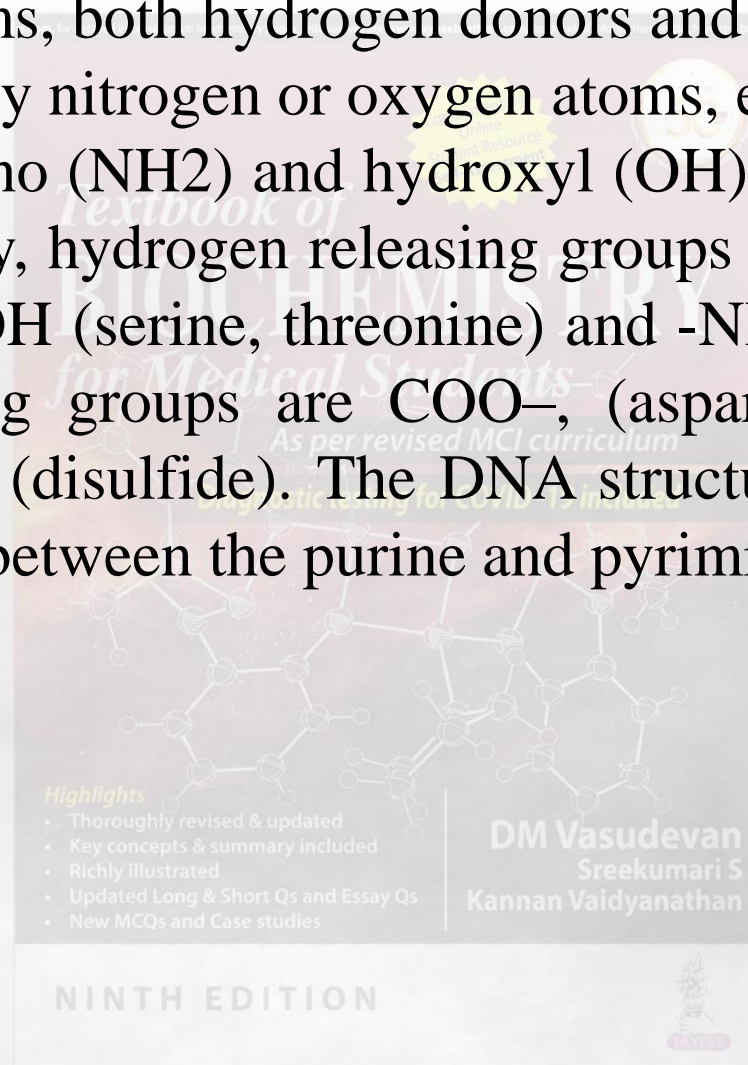
Water and Hydrogen Bonds

- Water is a **Polar Molecule**, this means that is has a slightly positive end and a slight negative end (like a magnet).

- Polar molecules form when atoms in a molecule have unequal pulls on the electrons they share.

- Other molecules, called nonpolar molecules, do not have these charged regions.

- Opposite charges of polar molecules interact to form **Hydrogen Bonds**.

- **A Hydrogen Bond** is an attraction between a slightly positive hydrogen atom and a slightly negative atom.

- **Hydrogen Bonding** is very common in water, but also occurs in other molecules.

Properties Related to Hydrogen Bonding

In biological systems, both hydrogen donors and acceptors are usually nitrogen or oxygen atoms, especially those atoms in amino (NH2) and hydroxyl (OH) groups. With regard to protein chemistry, hydrogen releasing groups are –NH (imidazole, indole, peptide); -OH (serine, threonine) and -NH2 (arginine lysine). Hydrogen accepting groups are COO–, (aspartic, glutamic) C=O (peptide); and S–S (disulfide). The DNA structure is maintained by hydrogen bonding between the purine and pyrimidine residues.
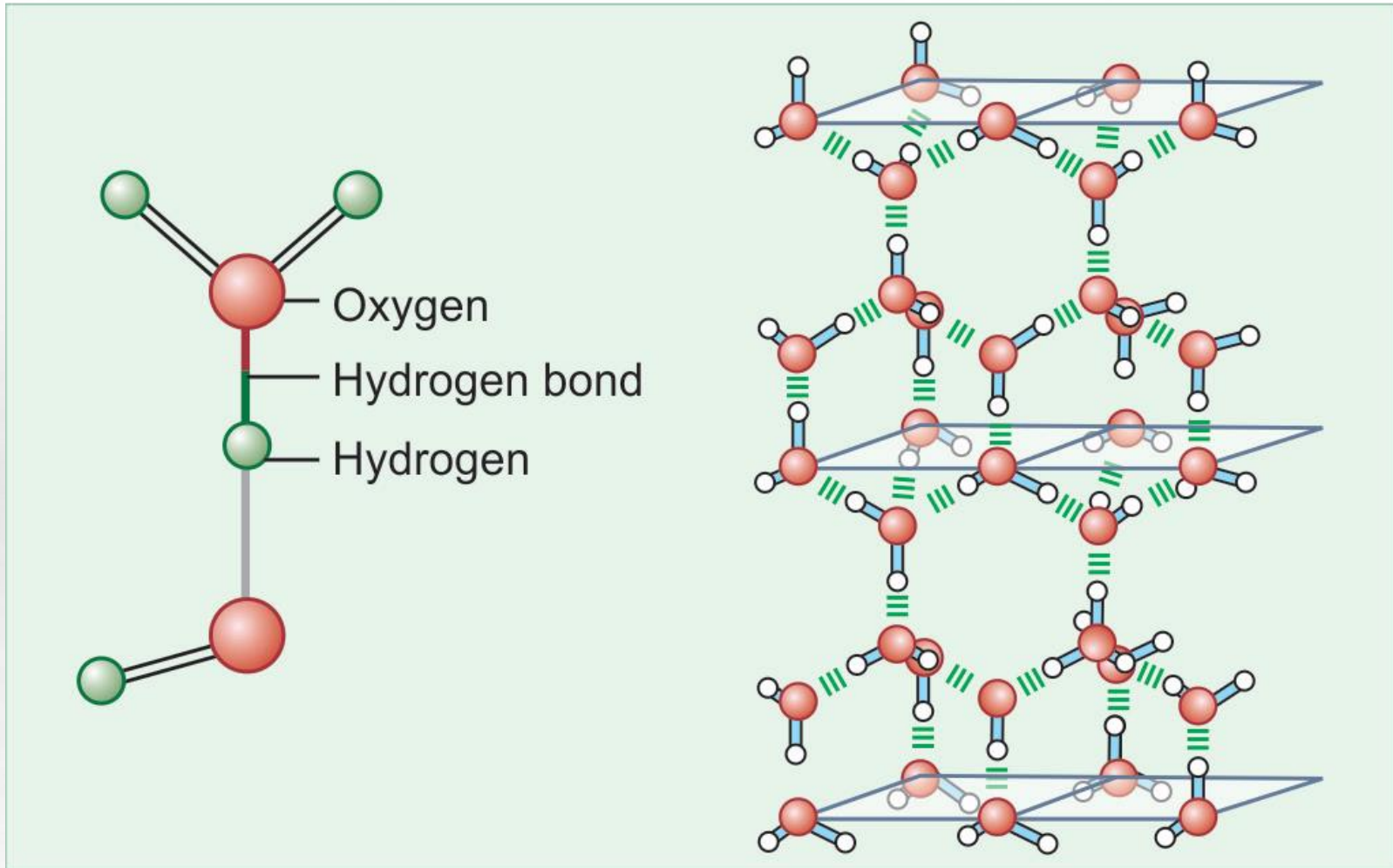
Water molecules hydrogen bonded.
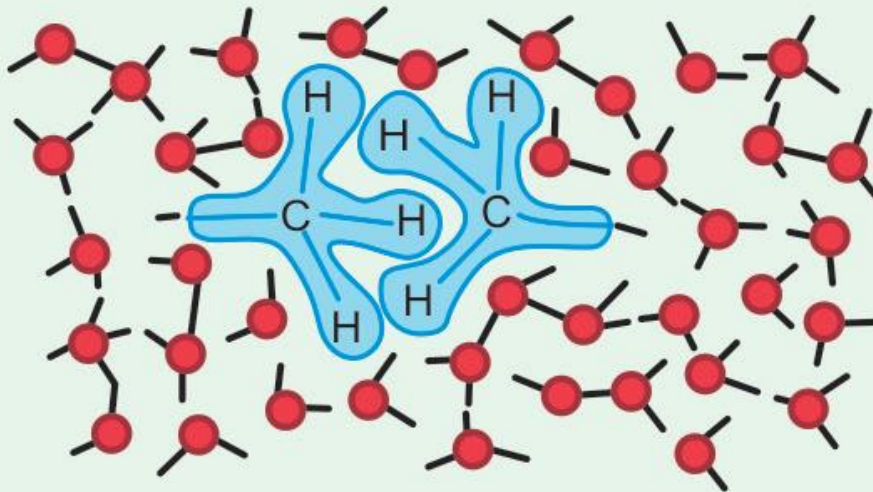
Hydrophobic Interactions

Nonpolar groups have a tendency to associate with each other in an aqueous environment; this is referred to as hydrophobic interaction. These are formed by interactions between nonpolar hydrophobic side chains by eliminating water molecules. The force that causes hydrophobic molecules or nonpolar portions of molecules to aggregate together rather than to dissolve in water is called the "hydrophobic bond". This serves to hold lipophilic side chains of amino acids together. Thus, nonpolar molecules will have minimum exposure to water molecules.
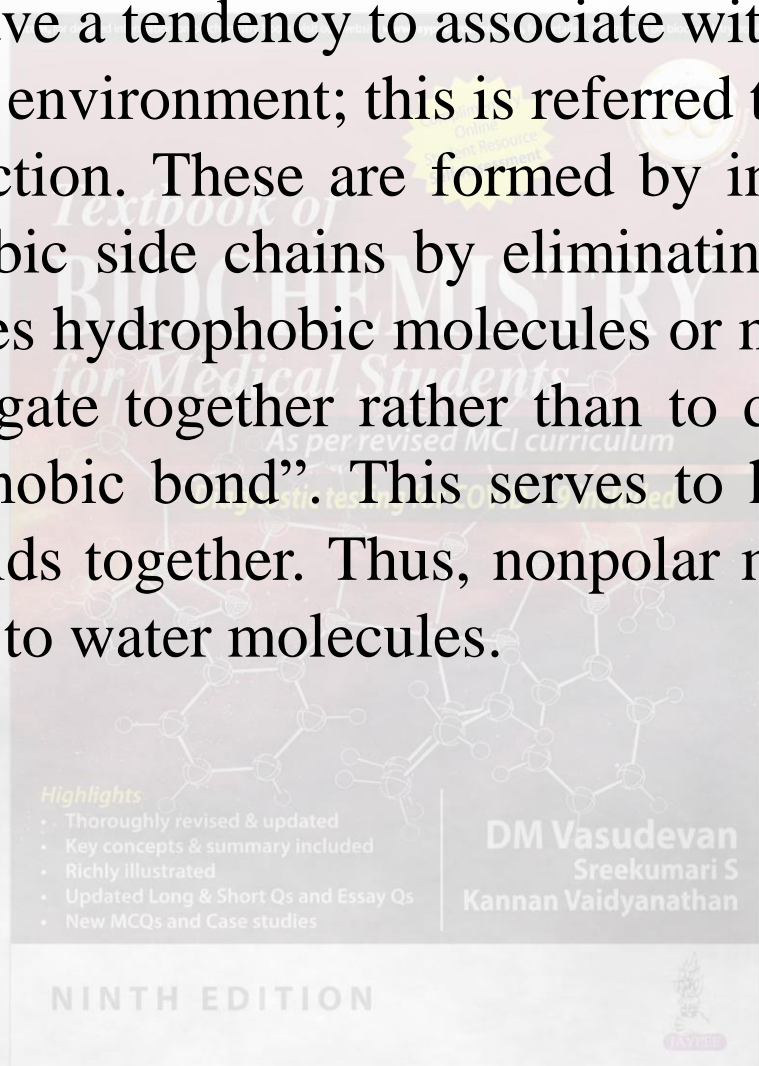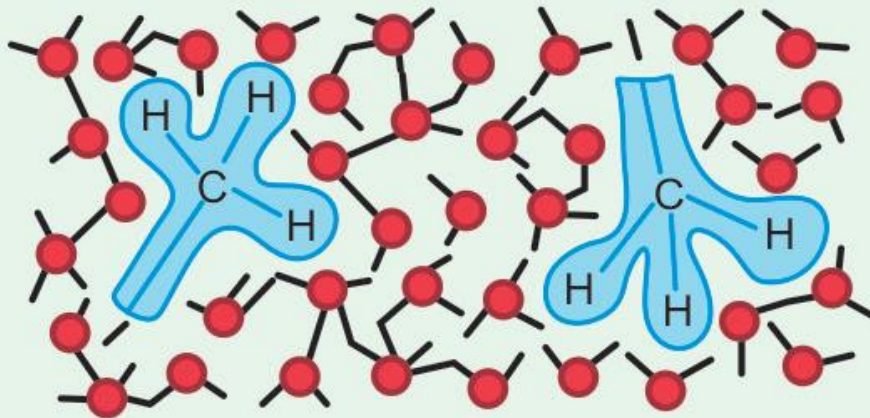
(A) Two hydrophobic molecules surrounded by water molecules

(B) When two hydrophobic molecules come together, surrounding water molecules are minimal

Hydrophobic interaction.

Van der Waals Forces

These are very weak forces of attraction between all atoms, due to oscillating dipoles. These are short range attractive forces between chemical groups in contact. This force will drastically reduce, when the distance between atoms is increased. Although very weak, van der Waals forces collectively contribute maximum toward the stability of protein structure, especially in preserving the nonpolar interior structure of proteins.
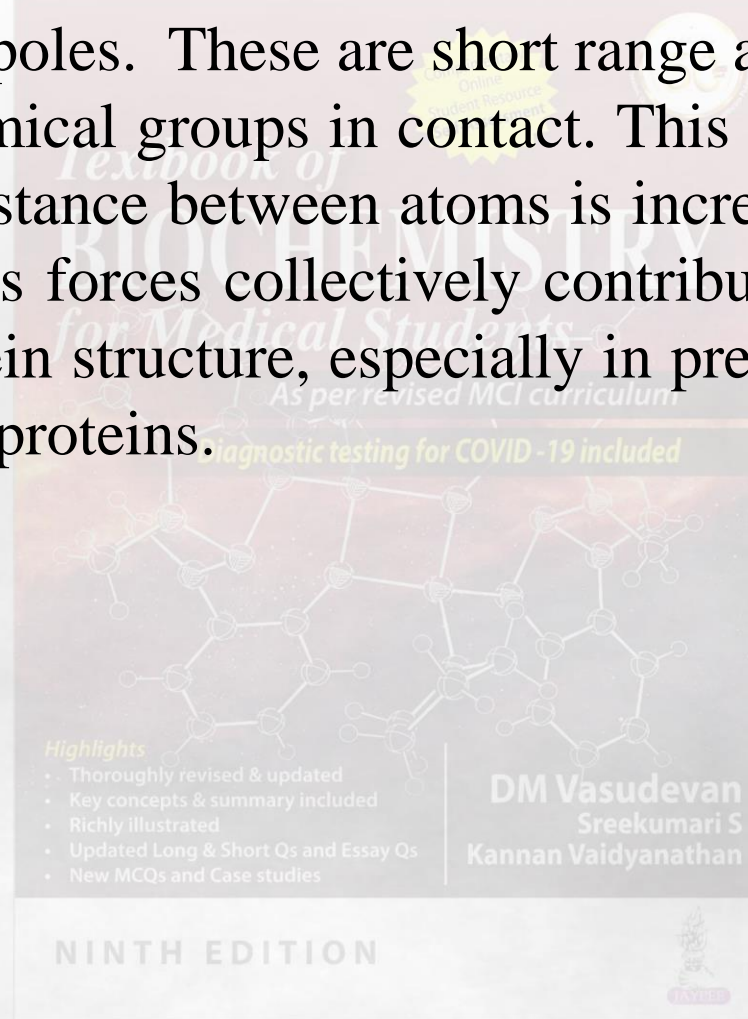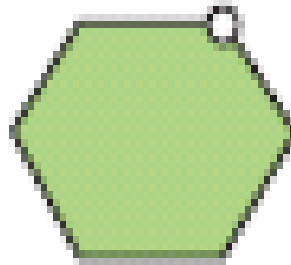
Four Main Types of Carbon-based Molecules are found in Living Things

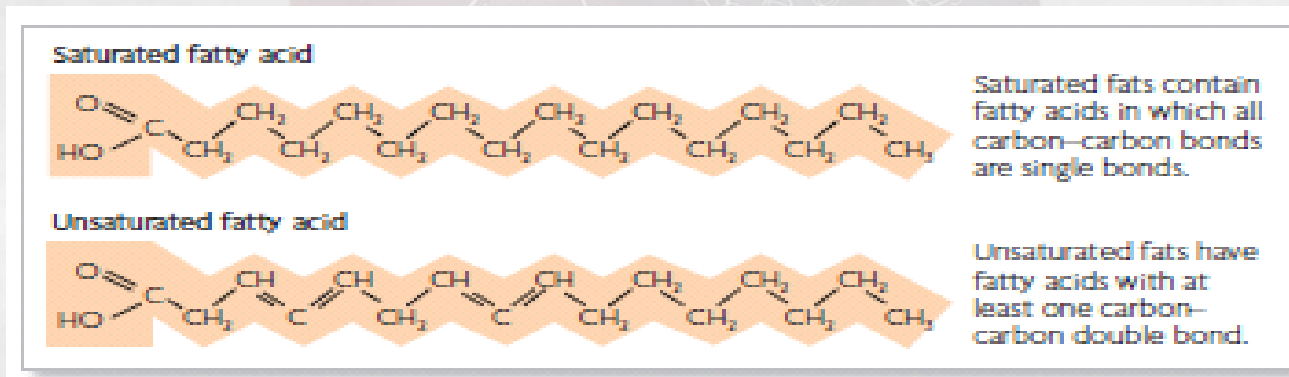| Monomer	Polymer	Examples
Monosaccharides (simple sugars)	Polysaccharides	Glucose, Fructose, Starch
Triglyceride (3 fatty acids and a glycerol)	Lipids	Fats, oils, and waxes.
Amino Acids	Protein	Muscle, hair, nails
Nucleotides	Nucleic Acids	DNA, and RNA
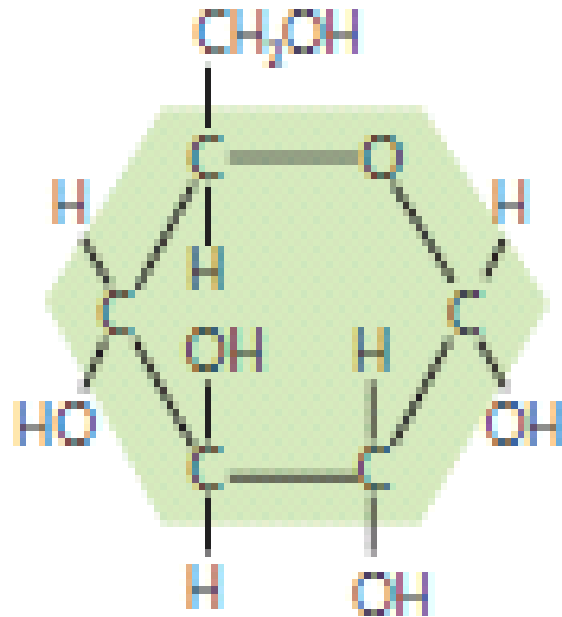
Glucose ($C_6H_{12}O_6$) can be ring shaped and is often shown as a simplified hexagon.

- **Carbohydrates** are molecules composed of carbon, hydrogen, and oxygen in a **1:2:1 ratio**.

- These include sugars and starches.

- Carbohydrates serve as the Main energy source for living things.

Lipids

- **Lipids** are nonpolar molecules that include fats, oils, wax, and cholesterol.
- Lipids make up the cell membrane (phospholipids).
- Lipids provide protection and insulation for the cell.
- Lipids can also be used as an energy source.
- The main types of Lipids are Saturated and Unsaturated Fats.
  - **Saturated Fats** – contains all single bonds and is a solid at room temperature.
  - **Unsaturated Fats** – contain at least one double bond and are liquids at room temperature.

Saturated fatty acid

Saturated fats contain fatty acids in which all carbon–carbon bonds are single bonds.

Unsaturated fatty acid

Unsaturated fats have fatty acids with at least one carbon–carbon double bond.

Proteins

- A Protein is a polymer made of **monomers called amino acids**.

- Amino Acids are molecules that contain Carbon, Hydrogen, Oxygen, Nitrogen, and sometimes Sulfur.

- Organisms use 20 different amino acids to build proteins.

- Amino acids are held together by **peptide bonds**.

Amino Acid Structure

Hydrogen

Amino

Carboxyl

R-group (variant)
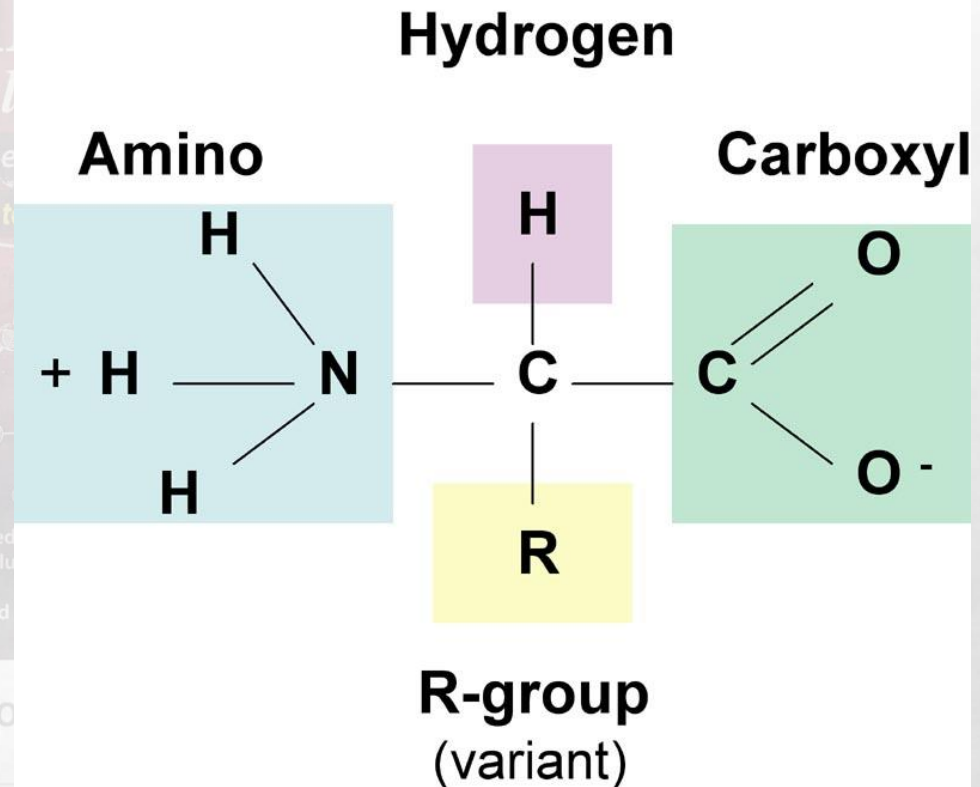
Nucleic Acids

- **Nucleic Acids** are polymers that are made up of monomers called nucleotides.

- A nucleotide is composed of a sugar, a phosphate, and a nitrogen base. Ex: **DNA and RNA**

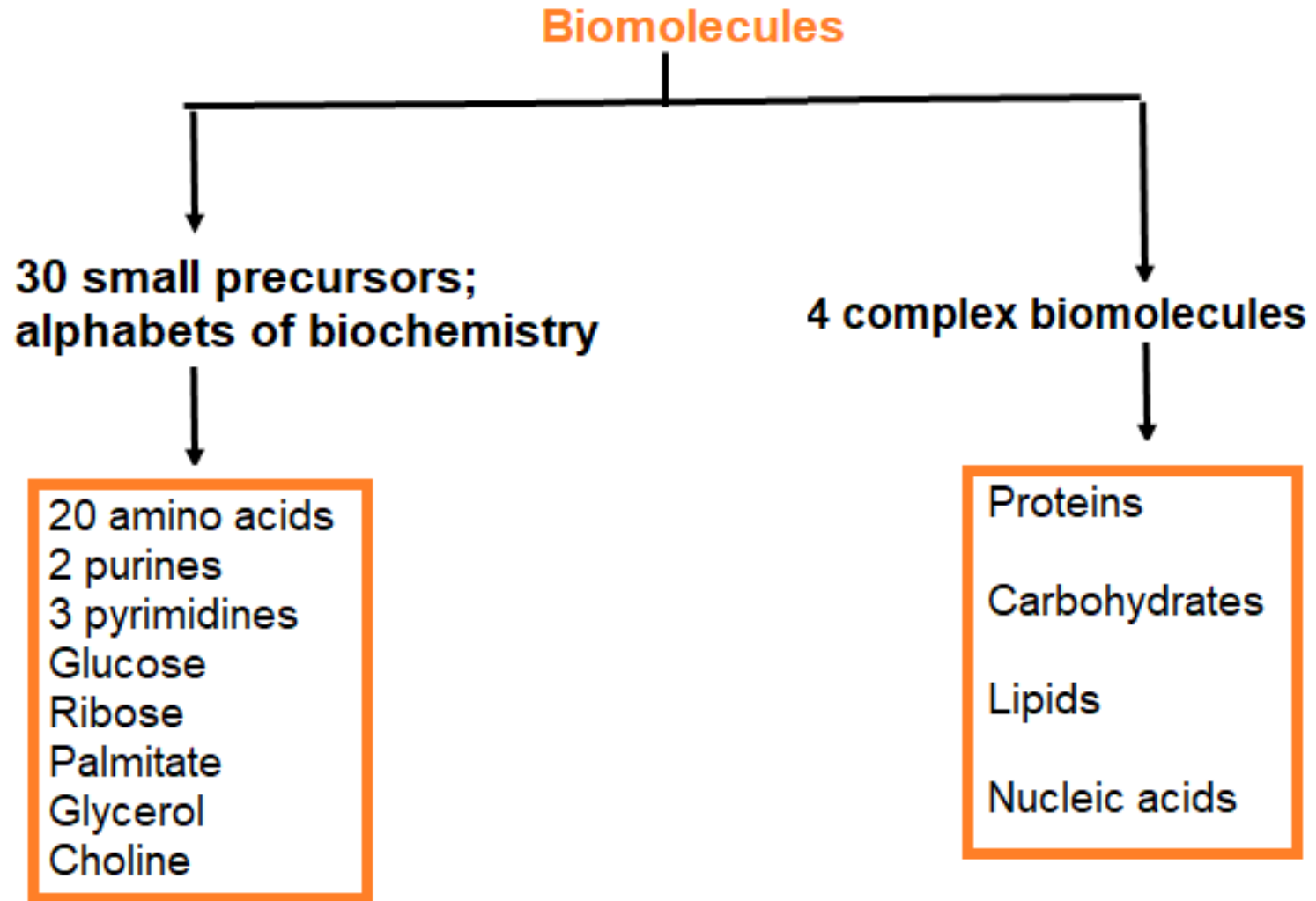- Nucleic Acids create the detailed instructions for creating proteins.

A nucleotide

Phosphate

Pentose Sugar

Nitrogenous Base (A,T,C or G)

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Biomolecules

| 30 small precursors; alphabets of biochemistry	4 complex biomolecules
20 amino acids 2 purines 3 pyrimidines Glucose Ribose Palmitate Glycerol Choline	Proteins Carbohydrates Lipids Nucleic acids

Reactants, Products and Bond Energy

- **Reactants** are the substances that go into a chemical reaction.

- **Products** are the substances created by the reaction.

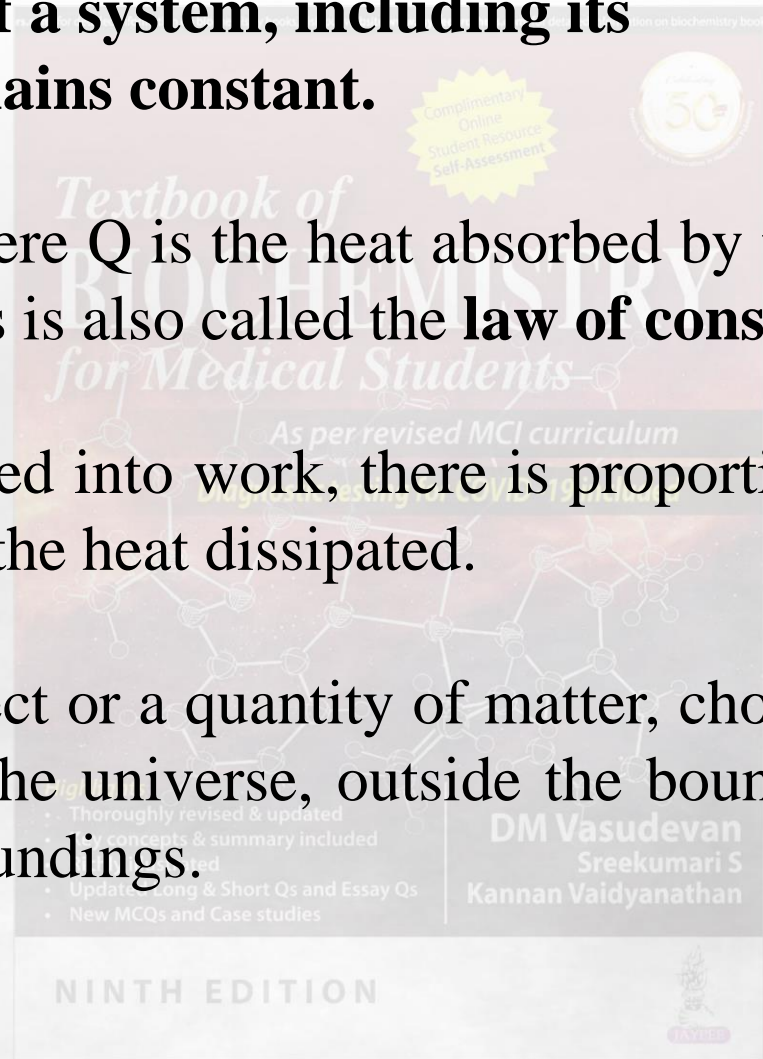- $6O_2 + C_6H_{12}O_6 \rightarrow 6CO_2 + 6H_2O$
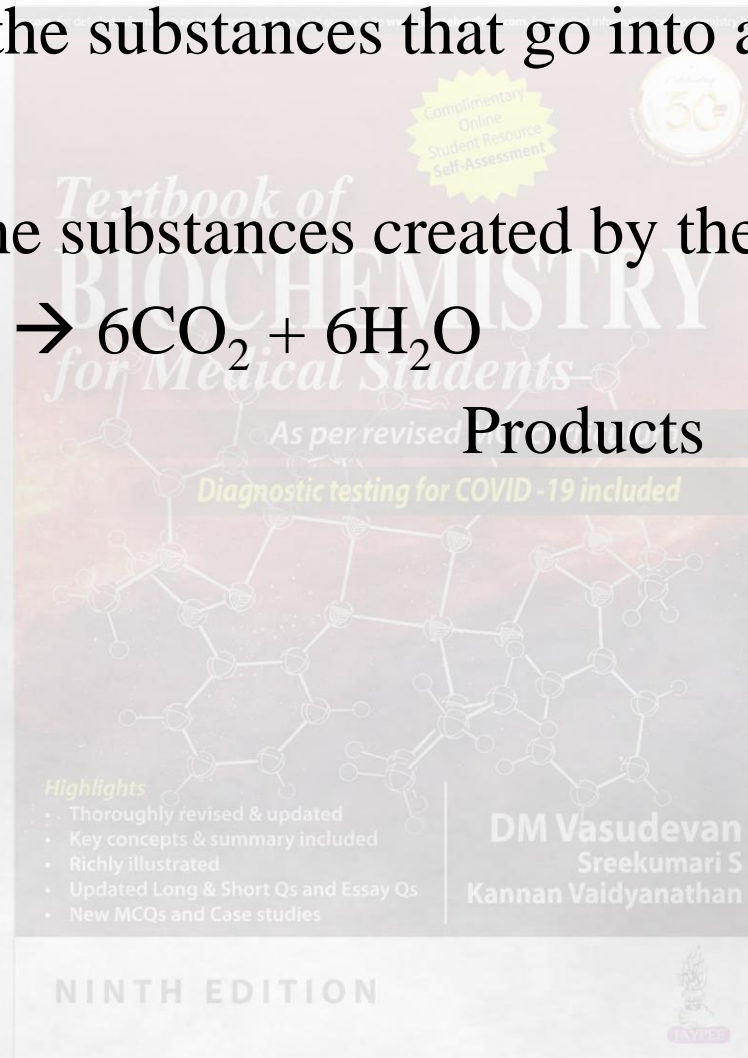
  Reactants   Products

The total energy of a system, including its surroundings, remains constant.

Or, ΔE = Q–W, where Q is the heat absorbed by the system and W is the work done. This is also called the **law of conservation of energy**.

If heat is transformed into work, there is proportionality between the work obtained and the heat dissipated.

A system is an object or a quantity of matter, chosen for observation. All other parts of the universe, outside the boundary of the system, are called the surroundings.

The total entropy of a system must increase if a process is to occur spontaneously. A reaction occurs spontaneously if DE is negative, or if the entropy of the system increases.

Entropy (S) is a measure of the degree of randomness or disorder of a system. Entropy becomes maximum in a system as it approaches true equilibrium.

Enthalpy is the heat content of a system and **entropy** is that fraction of enthalpy which is not available to do useful work.

A closed system approaches a state of equilibrium. Any system can spontaneously proceed from a state of low probability (ordered state) to a state of high probability (disordered state).
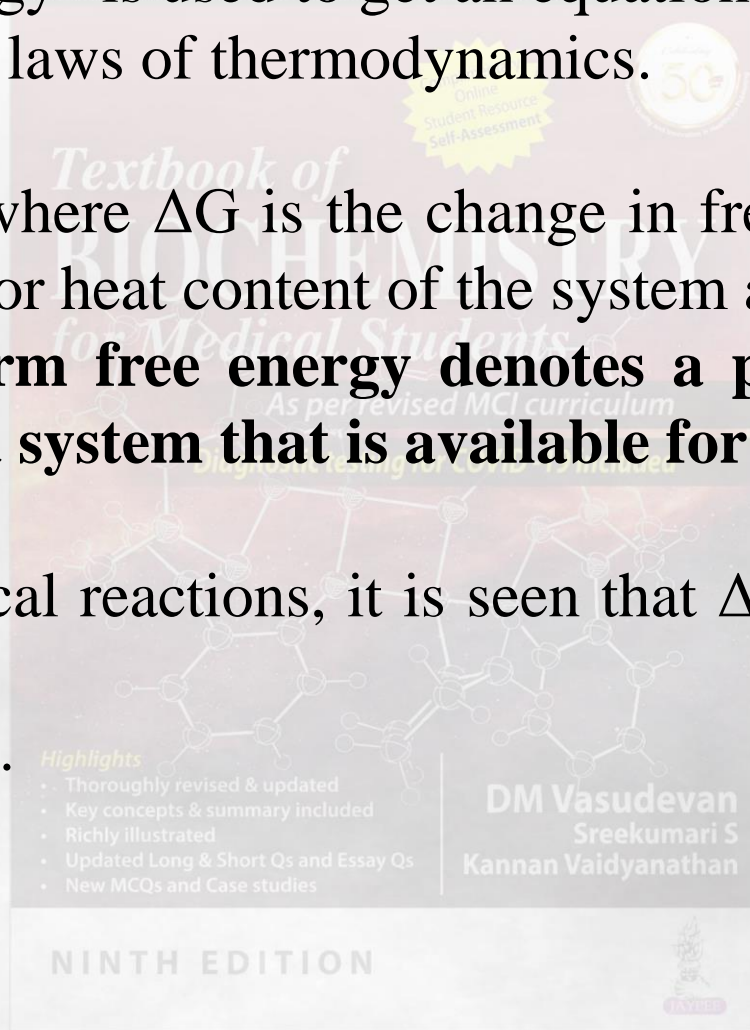
Gibbs Free Energy Concept

The term "free energy" is used to get an equation combining the first and second laws of thermodynamics.

$\Delta G = \Delta H - T\Delta S$, where ΔG is the change in free energy, ΔH is the change in enthalpy or heat content of the system and ΔS is the change in entropy. **The term free energy denotes a portion of the total energy change in a system that is available for doing work.**

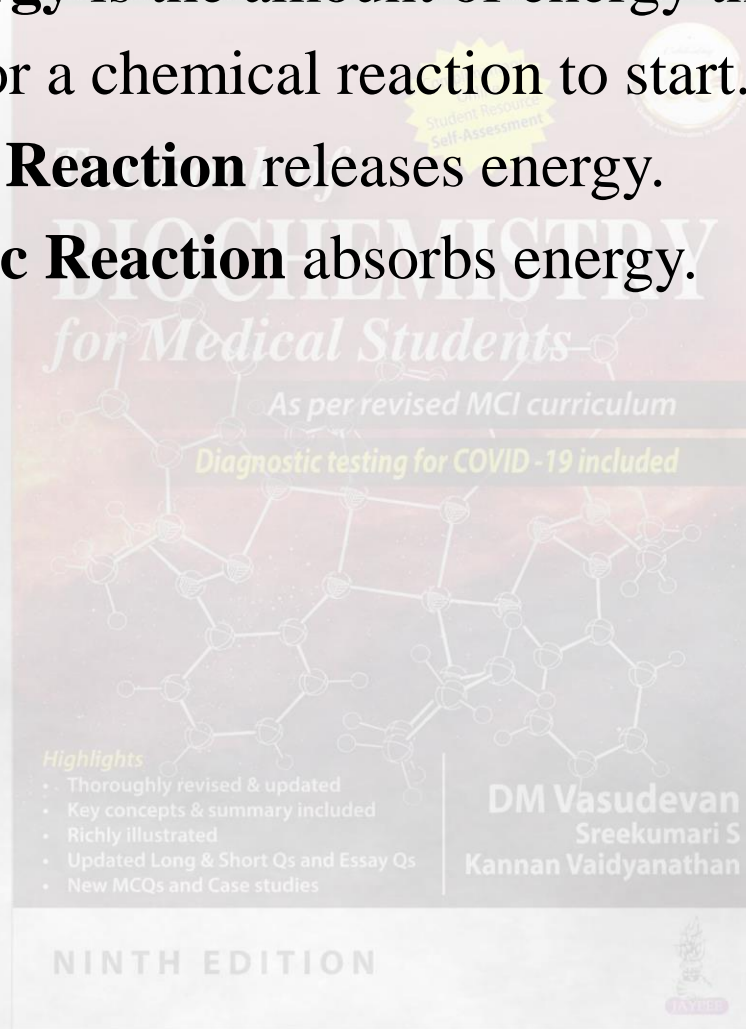For most biochemical reactions, it is seen that ΔH is nearly equal to ΔE.

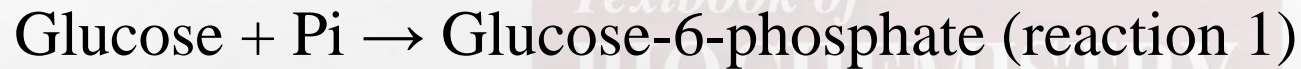So, $\Delta G = \Delta E - T\Delta S$.

- **Activation Energy** is the amount of energy that needs to be absorbed for a chemical reaction to start.

- An **Exothermic Reaction** releases energy.

- An **Endothermic Reaction** absorbs energy.

Energetically unfavorable reaction may be driven forward by coupling it with a favorable reaction.

Glucose + Pi → Glucose-6-phosphate (reaction 1)
ATP + H2O → ADP + Pi (reaction 2)
Glucose + ATP → Glucose-6-phosphate + ADP (3)

Reaction 1 cannot proceed spontaneously. But the 2nd reaction is coupled in the body, so that the reaction becomes possible. For the first reaction, $\Delta G0$ is +13.8 kJ/mole; for the second reaction, $\Delta G0$ is –30.5 kJ/mole. When the two reactions are coupled in the reaction 3, the $\Delta G0$ becomes –16.7 kJ/mole, and hence the reaction becomes possible.
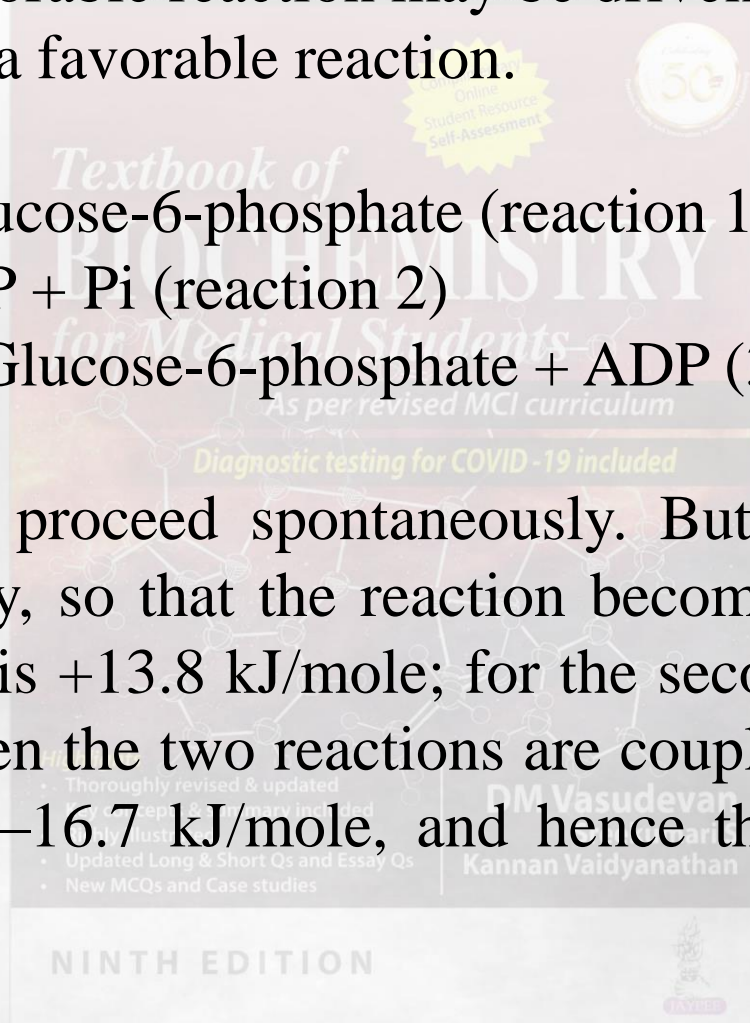
Donnan Membrane Equilibrium

When two solutions are separated by a membrane permeable to both water and small ions, but when one of the compartments contains impermeable ions like proteins, distribution of permeable ions occurs according to the calculations of Donnan.

NaR, which will dissociate into Na+ and R–. Then Na+ can diffuse freely, but R– having high molecular weight cannot diffuse. The right compartment contains NaCl, which dissociates into Na+ and Cl–. Both ions can diffuse freely. Thus, if a salt of NaR is placed in one side of a membrane, at equilibrium

$$Na+ \times R- \times H+ \times OH- = Na+ \times OH- \times H+$$
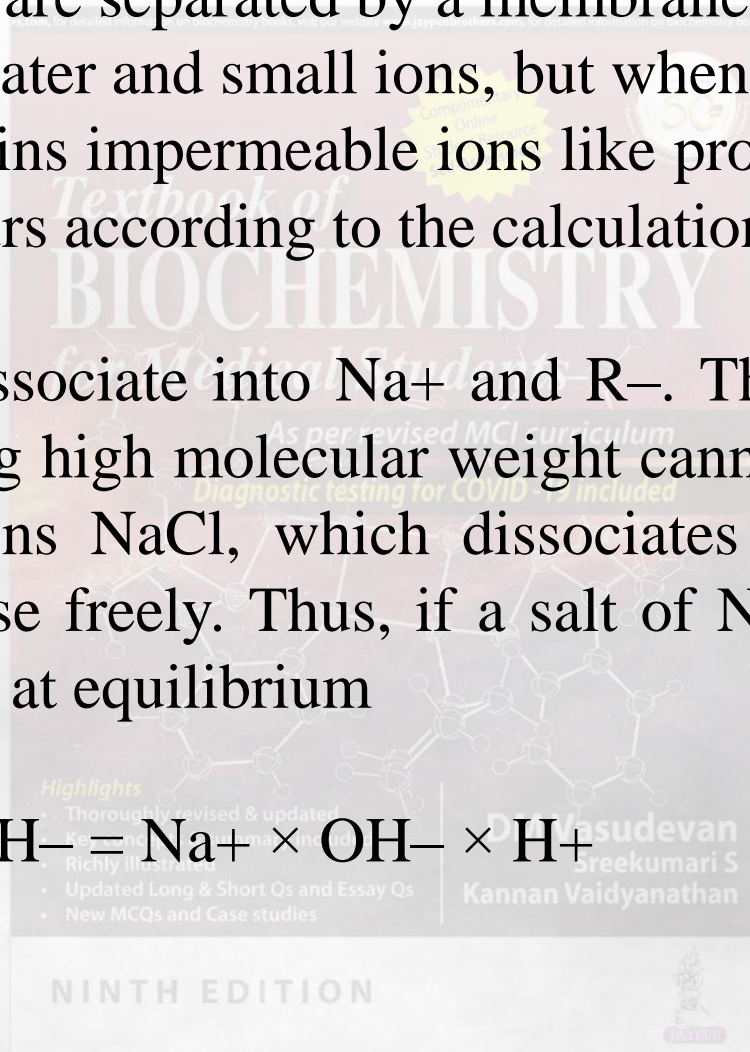
Initially five molecules of NaR are added to the left compartment and 10 molecules of NaCl in the right compartment and both of them are ionized. When equilibrium is reached, the distributions of ions are shown. According to Donnan's equilibrium, the products of diffusible electrolytes in both the compartments will be equal, so that

$[Na+] L \times [Cl–] L = [Na+] R \times [Cl–] R$

If we substitute the actual numbers of ions, the formula becomes 9 × 4 in left = 6 × 6 in right

Donnan's equation also states that the electrical neutrality in each compartment should be maintained.

In other words the number of cations should be equal to the number of anions, such that in left compartment: $Na+ = R- + Cl-$; substituting: $9 = 5 + 4$.

In right compartment: $Na+ = Cl-$; substituting: $6 = 6$

The equation should also satisfy that the number of sodium ions before and after the equilibrium are the same; in the given example, initial $Na+$ in the two compartments together is $5 + 10 = 15$; after equilibrium also, the value is $9 + 6 = 15$.

In the case of chloride ions, initial value is 10 and final value is also $4 + 6 = 10$.
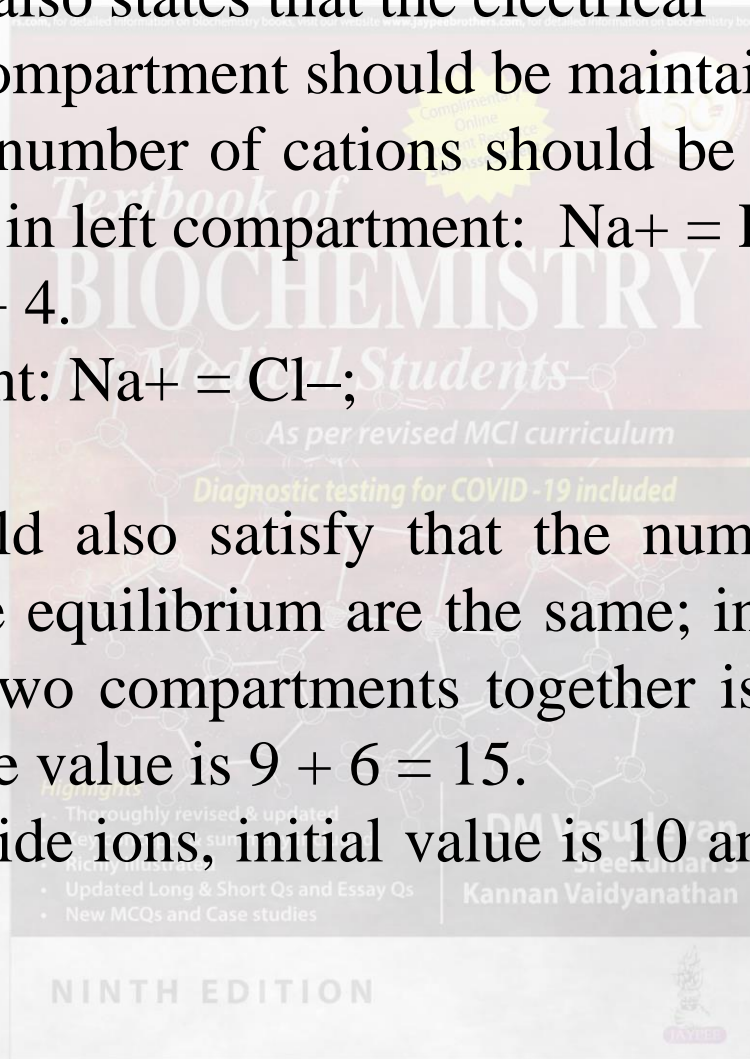
Donnan membrane equilibrium.
(A) initial condition; (B) after reaching the equilibrium.

In summary, Donnan's equations satisfy the following results:

1. The products of diffusible electrolytes in both compartments are equal.

2. The electrical neutrality of each compartment is maintained.

3. The total number of a particular type of ions before and after the equilibrium is the same.
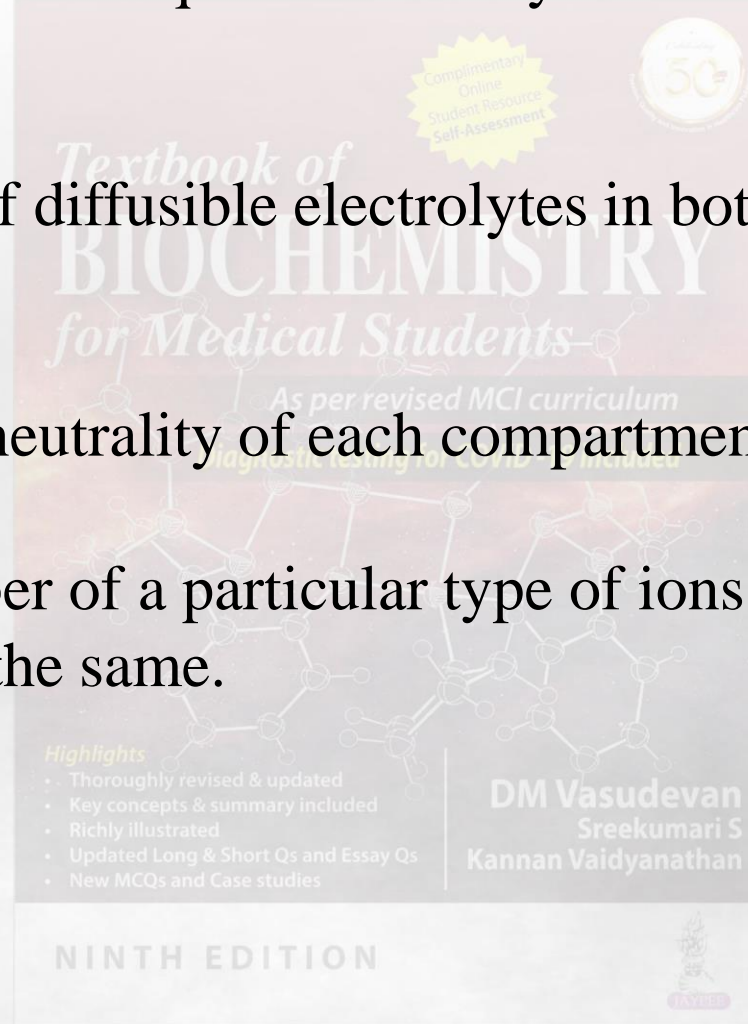
Clinical Applications of Donnan's Equation

The total concentration of **solutes in plasma** will be more than that of a solution of same ionic strength containing only diffusible ions; this provides the net osmotic gradient.

The lower pH values within tissue cells than in the surrounding fluids are partly due to the concentrations of negative protein ions within the cells being higher than in surrounding fluids.

The pH within red cells is lower than that of the surrounding plasma is due, in part, to the very high concentration of negative non-diffusible hemoglobin ions. This will cause unequal distribution of H+ ions with a higher concentration within the cell.

The chloride shift in erythrocytes and higher concentration of chloride in cerebrospinal fluid (CSF) are also due to Donnan's effect.
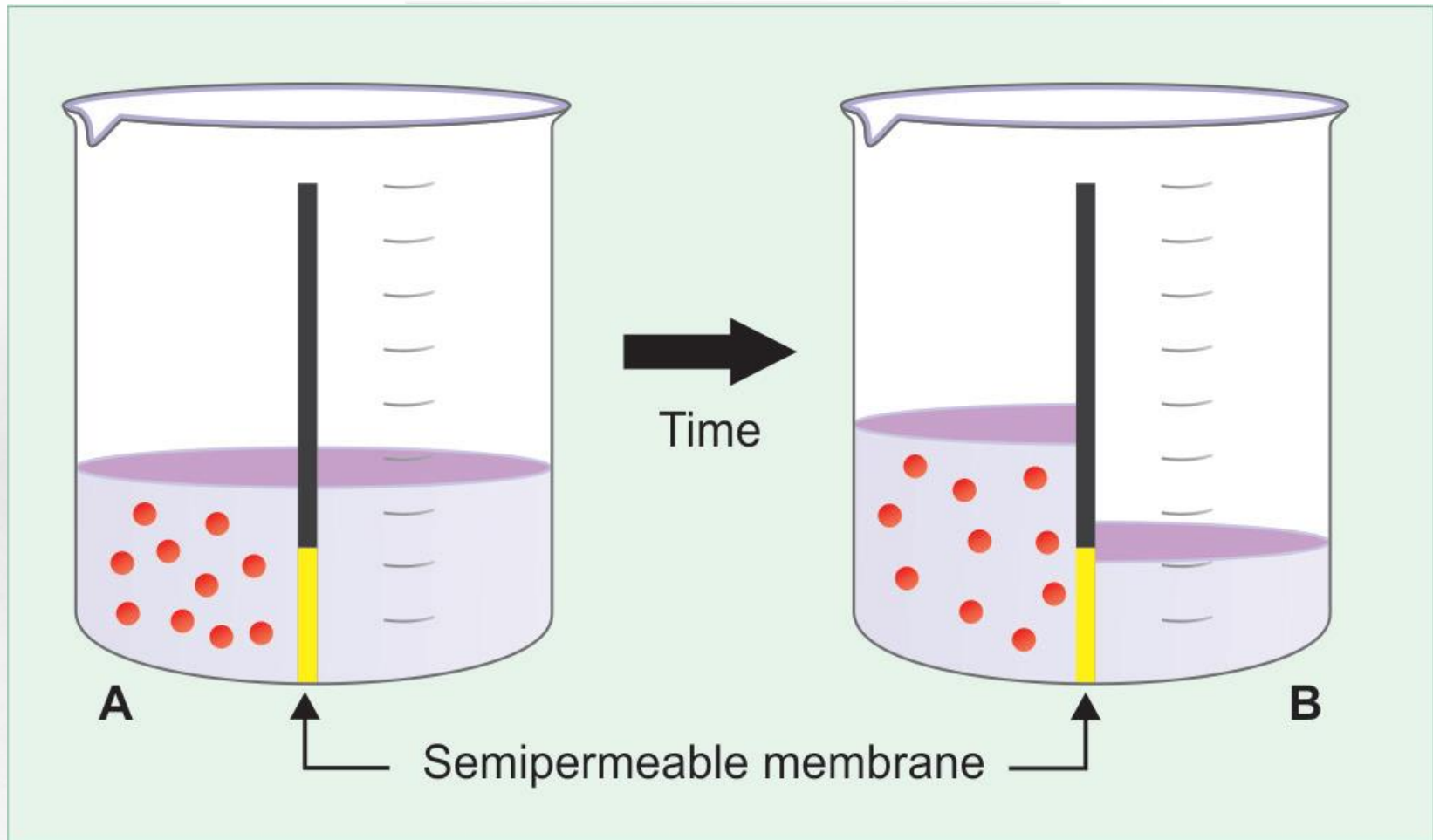
Osmosis

Osmosis is an important property of particles in solution. Osmosis is the spontaneous net movement of solvent molecules through a semipermeable membrane into a region of higher solute concentration, in the direction that tends to equalize the solute concentrations on the two sides.

In other words, it is also the flow of a solvent from a more dilute solution to a relatively concentrated solution through a semipermeable membrane. Osmosis is the movement of a solvent across a semipermeable membrane toward a higher concentration of solute. Osmosis is a passive movement. In biological systems, the solvent is water.
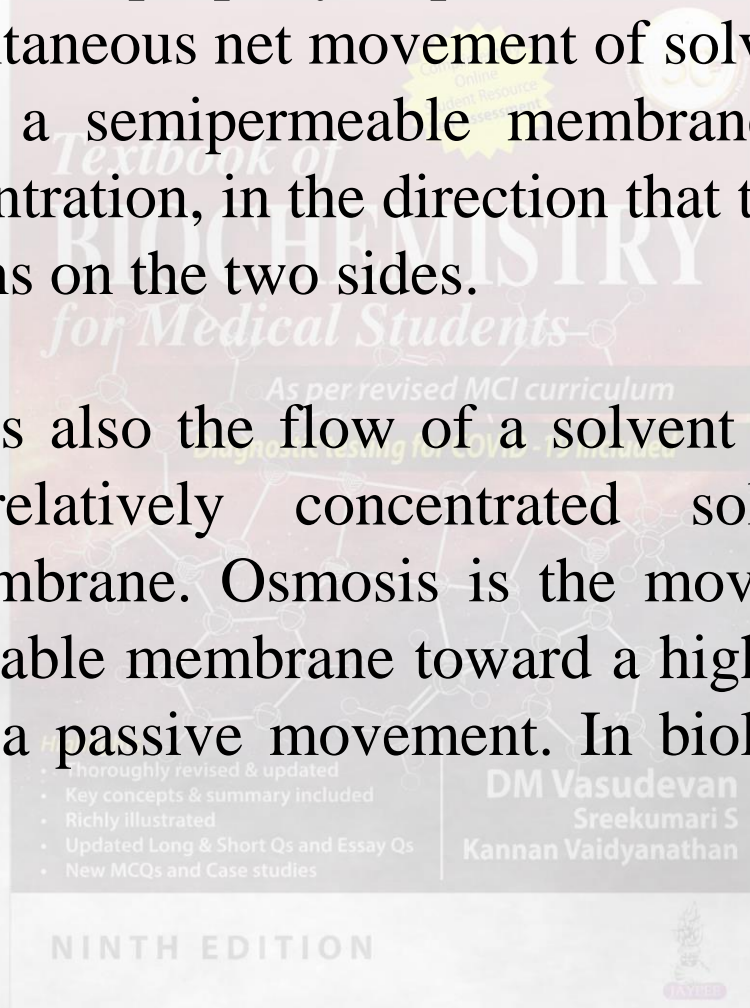
Osmosis. (A) Initial condition; (B) After reaching the equilibrium.
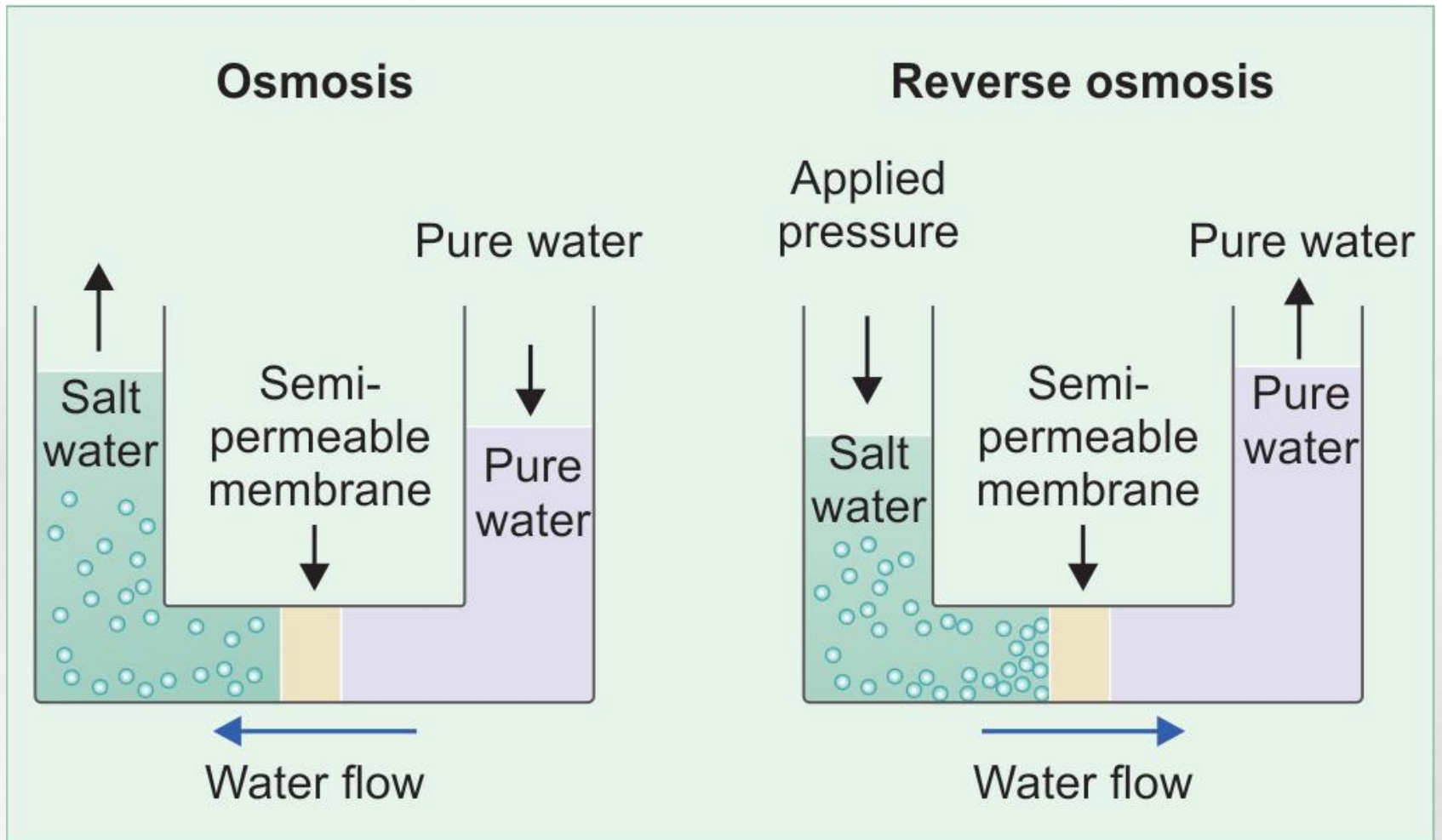
Reverse Osmosis.

Osmotic Pressure

Osmotic pressure is defined as the external pressure required to be applied so that there is no net movement of Solvent across the membrane. Osmotic pressure is a **colligative property**, meaning that the osmotic pressure depends on the molar concentration of the solute but not on its identity. The force per unit area, or pressure, required to prevent the passage of water through a selectively permeable membrane is the measurement of osmotic pressure.
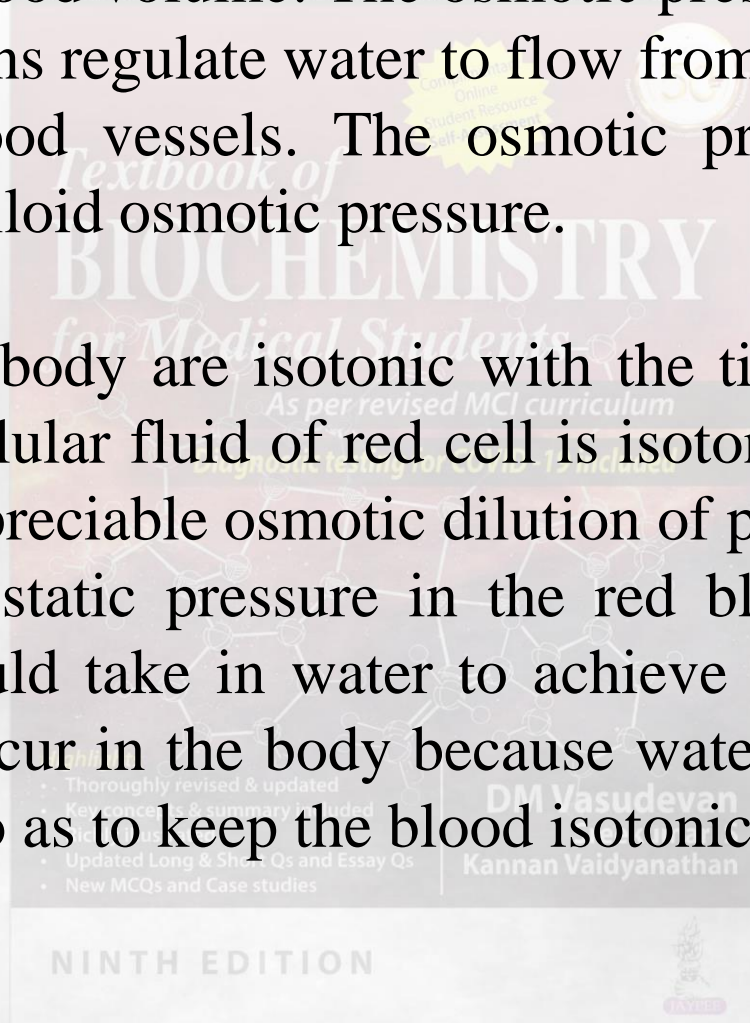
The osmotic pressure of a solution is directly proportional to the concentration of the solute and in turn depends on the number of molecules or ions contained in the solution.
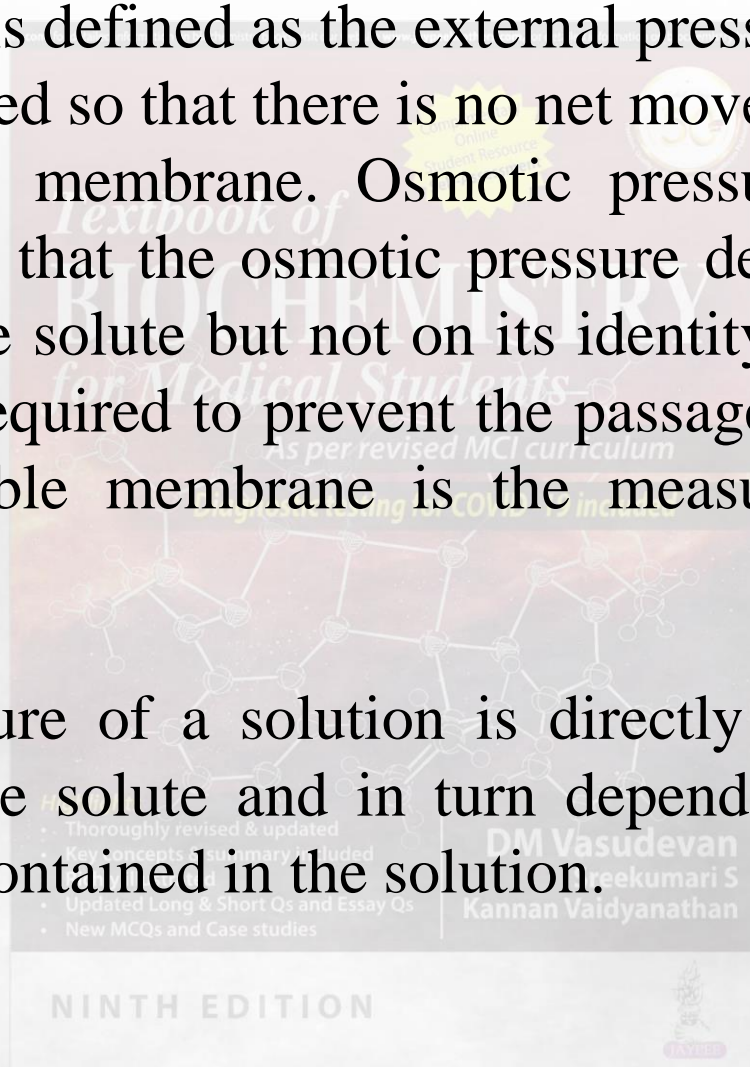
1. Regulation of blood volume: The osmotic pressure of plasma proteins regulate water to flow from interstitial fluid to the blood vessels. The osmotic pressure of protein is referred to as colloid osmotic pressure.

2. The cells in the body are isotonic with the tissue fluid and blood plasma. (Intracellular fluid of red cell is isotonic with 0.92% NaCl solution). An appreciable osmotic dilution of plasma would create a dangerous hydrostatic pressure in the red blood cell (RBC) and cells, which would take in water to achieve osmotic equilibrium. This does not occur in the body because water or salt are excreted by the kidneys so as to keep the blood isotonic with the cells.

3. Destruction of RBC by **hemolysis**: When RBC is placed in a hypotonic solution, the red cells swell, owing to water passing into the cell osmotically (**endosmosis**). If the solution is sufficiently hypotonic, the cell may even rupture with the cell content diffusing into the surrounding fluid. This is called hemolysis. If the RBCs are placed in hypertonic solution, water passes out of the cell (exosmosis) and RBCs will shrink. This process is called **crenation**.

4. Absorption (passive diffusion) of nutrients from the gastrointestinal tract.

5. Fluid interchange in various compartments of the body follows the principle of osmosis. Water moves spontaneously depending on osmotic pressure.

6. Biological membranes are semipermeable. They are impermeable to large polar molecules, such as proteins and polysaccharides, while being permeable to nonpolar hydrophobic molecules like lipids as well as to small molecules by diffusing across the phospholipid bilayer via aquaporins (small transmembrane proteins similar to ion channels).

Osmosis is the primary means by which water is transported into and out of cells. The pressure of a cell is largely maintained by osmosis across the cell membrane between the cell interior and its relatively hypotonic environment.
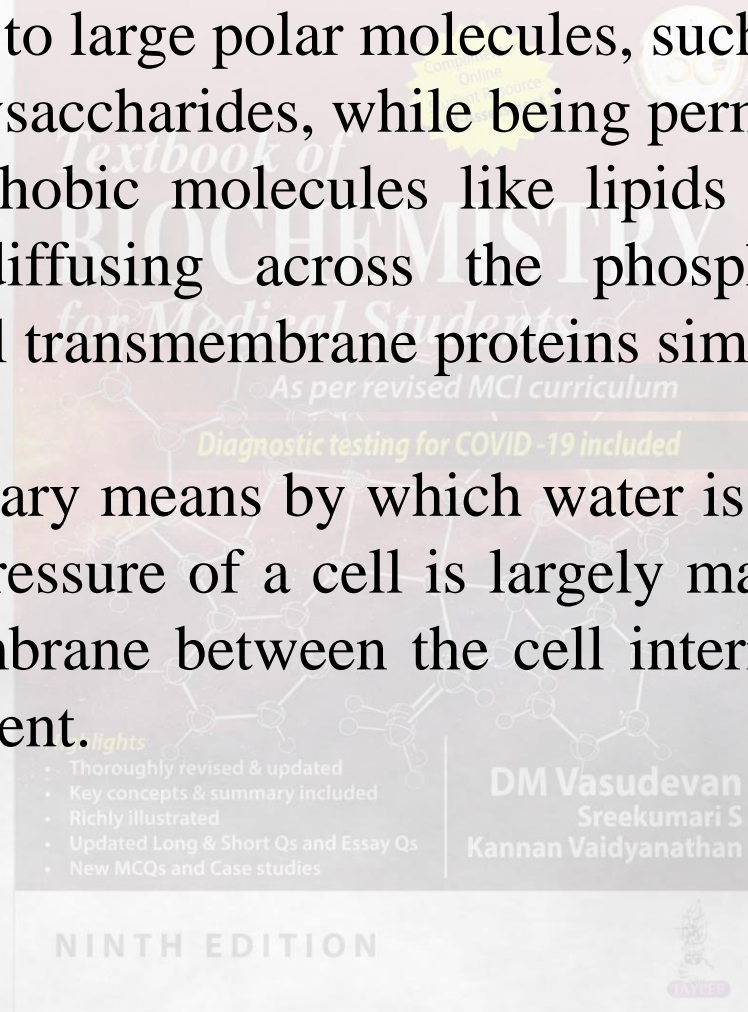
Clinical Importance of Dialysis

1. Separation of proteins from small solutes.

2. Formation of biological ultrafiltrates such as interstitial fluid, cerebrospinal fluid, glomerular filtrate.

3. Dialysis by artificial kidney. Acute or chronic loss of function of kidney is a threat to life and requires removal of toxic waste products and restoration of body fluid volume and composition toward normal. This can be accomplished by dialysis with an artificial kidney. In acute renal failure an artificial kidney may be used to tide the patient over, until the kidneys resume their normal function. Dialysis cannot bring back the normal body fluid composition into completely normal state. It cannot replace all the multiple functions performed by the kidney.

An equivalent is the amount of a substance that reacts with (or is equivalent to) another substance in a given chemical reaction. The mass of an equivalent is called its equivalent weight.

Equivalent weight is the mass of a substance in grams that combines with or is chemically equivalent to eight grams of oxygen or one gram of hydrogen. The equivalent weight is calculated as the molecular weight divided by the valence.
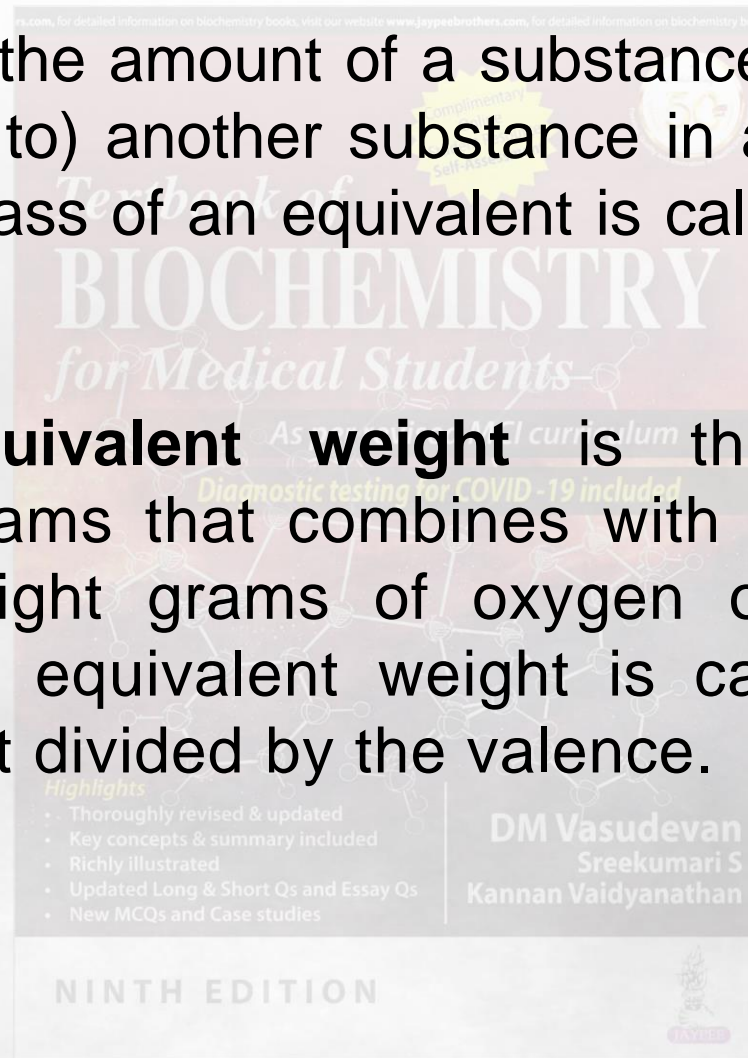
Equivalent Weight

In clinical practice, it is routinely described in terms of milliequivalents (meq or mEq). This is especially common for the measurement of compounds in biological fluids; for instance, the healthy level of potassium in the blood is defined between 3.5 and 5.0 mEq/L.

A certain amount of univalent ions provides the same amount of equivalents while the same amount of divalent ions provides twice the amount of equivalents. For example, 1mmol of Na^+ is equal to 1 mEq, while 1 mmol of Ca^{++} is equal 2 mEq.
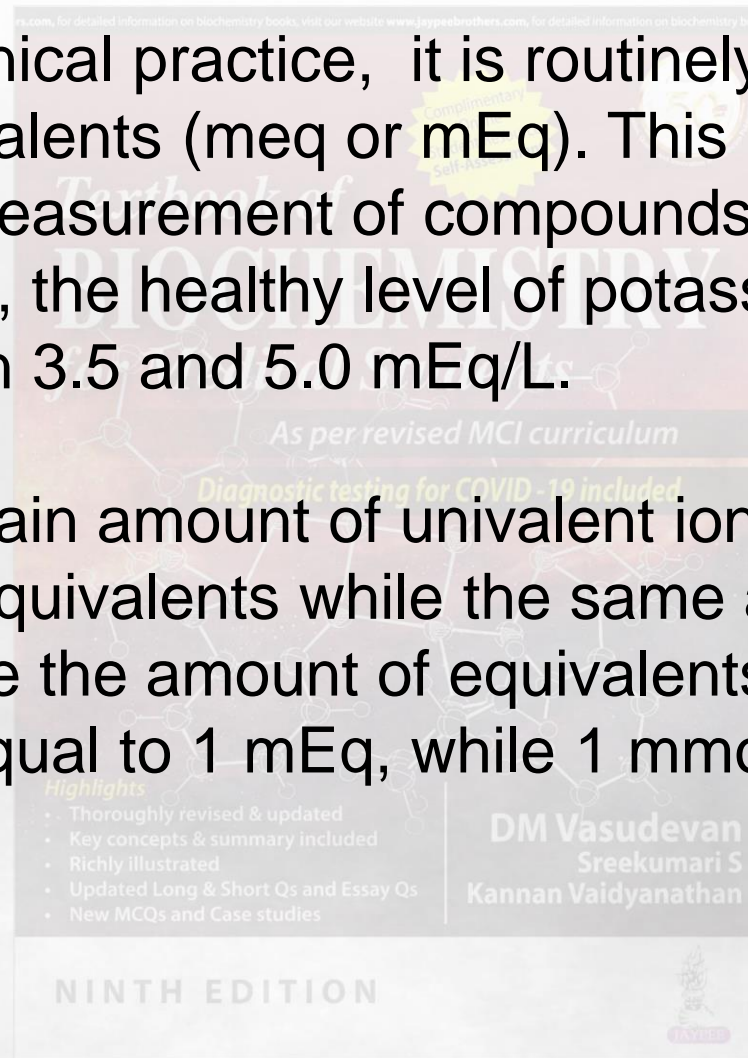
Molecular weight (mol.wt) is the average mass of a molecule of a compound compared to $\frac{1}{12}$ the mass of ^{12}C (carbon-12). (By definition, the weight of isotope of ^{12}C is equal to 12)

Molecular mass or molecular weight is the mass of a molecule. It is calculated as the sum of the atomic weights of the constituent atoms.

Atomic and molecular mass values are expressed in the unit of "Dalton" or "D".
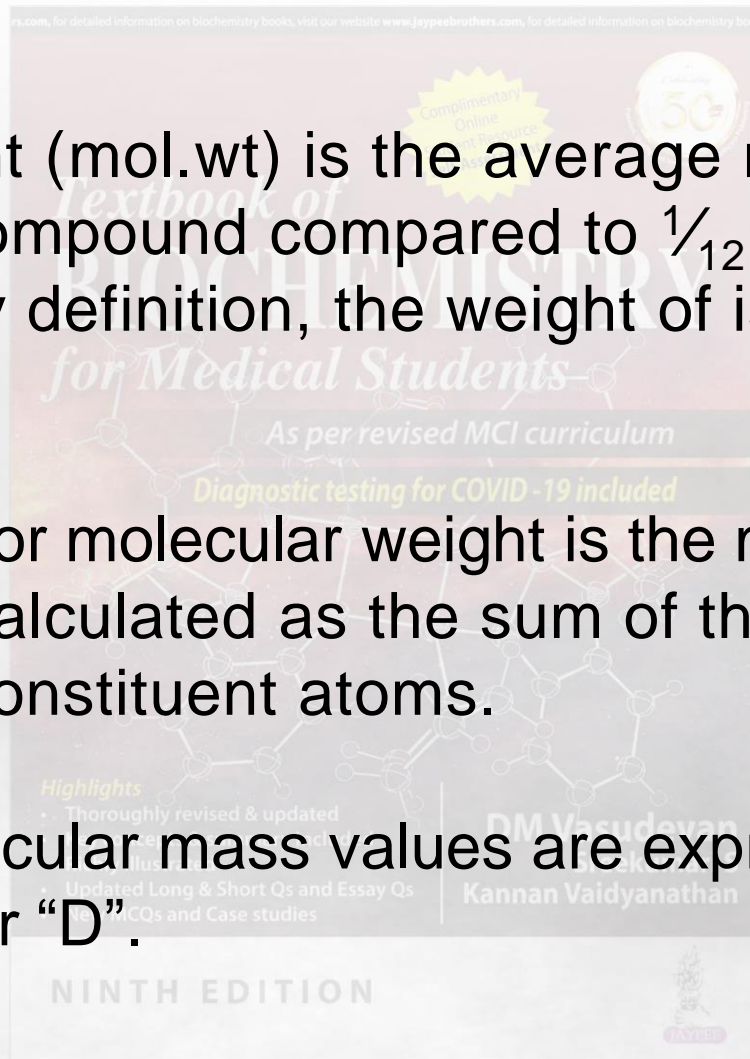
A **mole** is the unit of amount of pure substance in the International System of Units (SI units) that contains the same number of atoms as there are atoms in exactly 12 grams of the isotope carbon 12 (^{12}C). The mole is abbreviated as "mol".

Molarity : The concentration of a solution is commonly expressed by its molarity, which is defined as the number of moles of the dissolved substance per litre of solution.