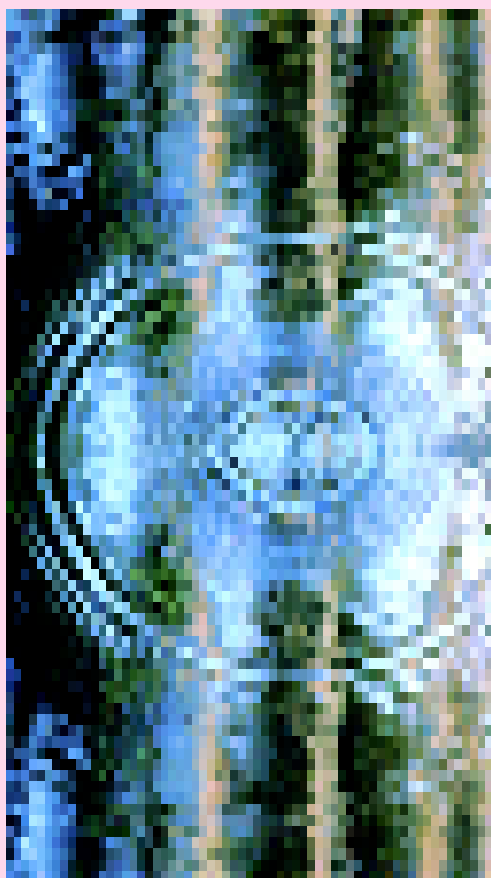


Cytoplasmic Matrix

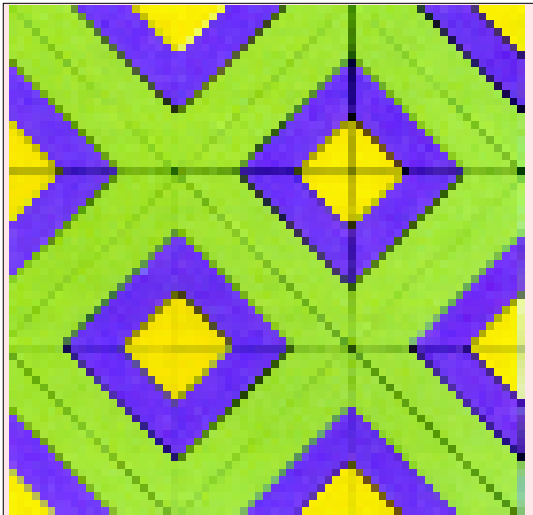
(Chemical Organization of the Cell)



All of life is conditioned by the chemistry of water.

Cells, tissues and organs are composed of chemicals, many of which are identical with those found in non-living matter, while others are unique to living organisms. The study of chemical compounds found in living systems and reactions in which they take part is known as **biochemistry**. Studies of the structure and behaviour of individual molecules constitute **molecular biology**. If the 'secret of life' is to be found anywhere it is in these molecules (**Roberts**, 1986).

In fact, all living systems are subject to the same physical and chemical laws as are non-living systems. Within the cells of any organism, the living substance, or **protoplasm**, is itself comprised of a multitude of non-living constituents : proteins, nucleic acids, fats (lipids), carbohydrates, vitamins, minerals, waste metabolites, crystalline aggregates, pigments, and many others, all of which are composed of molecules and their constituent atoms. The *protoplasm is alive because of the highly complex organization of these non-living substances and the way they interact with one another*. This is just like a watch which is a timepiece only when all of its gears, springs,



Like small geometric units can be combined into higher-order patterns similarly the properties of a living thing emerge from the precise arrangement of component parts: atoms, molecules, cell parts, cells and so on.

and bearings are organized in a particular way and interact with one another. Neither the gears of a watch nor the molecules in protoplasm can interact in any way that is contrary to universal physical laws. Consequently, the more completely we can understand the functioning of protoplasm and its constituents on the basis of chemical principles, the more completely we can understand the phenomenon of life.

As already described in Chapter 3, the **cytoplasmic matrix** or **cytosol** is the fluid and soluble portion of the cytoplasm that exists outside the organelles (**Suzuki et al.**, 1986). In this chapter the physical and chemical nature of the cytosol will be described.

PHYSICAL NATURE OF CYTOSOL (OR CYTOPLASMIC MATRIX)

The cytosol (cytoplasmic matrix) is a colourless or greyish, translucent, viscid, gelatinous or jelly-like colloidal substance. It is heavier

than water and capable of flowing. In past, there has been a lot of controversy about the physical nature of the matrix. Different workers advanced different theories about the physical characteristics of the matrix. Their theories can be represented as follows :

1. Reticular theory suggests that the matrix is composed of reticulum of fibres or particles in the ground substances (Fig. 4.1 A).

2. Alveolar theory was proposed by **Butschili** in 1892 and according to it, the matrix consists of many suspended droplets or alveoli or minute bubbles resembling the foams of emulsion. (Fig. 4.1 B).

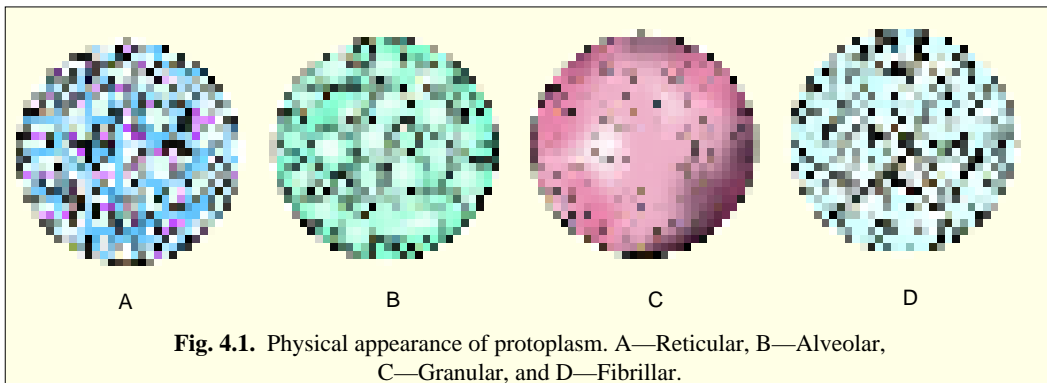


Fig. 4.1. Physical appearance of protoplasm. A—Reticular, B—Alveolar, C—Granular, and D—Fibrillar.

3. Granular theory was propounded by **Altmann** in 1893. This theory supports the view that the matrix contains many granules of smaller and larger size arranged differently. These granules were known as bioplasts (Fig. 4.1 C).

4. Fibrillar theory was proposed by **Fleming** and it holds that the matrix is fibrillar in nature (Fig. 4.1 D).

5. Colloidal theory has been forwarded very recently after the electron microscopical observations of the matrix. According to the recent concept, the matrix is partly a true **solution**, partly a **colloidal system**.

A **solution** is a mixture of liquid called **solvent** and any chemical substance in solid or liquid state, called **solute**. In a solution the particles of solute should be less than 1/10,000 millimetre in diameter. The solution part of the matrix consists of water as solvent in which various solutes of biological importance such as glucose, amino acids, fatty acids, electrolytes, minerals, vitamins, hormones and enzymes remain dissolved.

A **colloidal system** can be defined as a system which contains a liquid medium in which the particles ranging from about 1/1,000,000 to 1/10,000 millimetre in diameter, remain dispersed. Thus, the colloidal state is a condition in which one substance, such as protein or other macromolecule, is dispersed in another substance to form many small phases suspended in one continuous phase. In this way every colloidal system consists of two phases : a **discontinuous** or **dispersed phase** and a **continuous** or **dispersion phase**. Whole of the protoplasm (cytoplasm + nucleoplasm) is a colloidal solution, because the main molecular components of protoplasm— proteins—show all characteristics of the colloidal state. Proteins form stable colloids because, firstly, they are charged ions in solution that repel each other, and, secondly each protein molecule attracts water molecules around it in definite layers.

Phase Reversal

Cytosol (cytoplasmic matrix) like many colloidal systems, shows the property of **phase reversal**. For example, gelatin particles (discontinuous phase) are dispersed through water (continuous phase) in a thin consistency that is freely shakable (Fig. 4.2 A). Such a condition is called a **sol**. When the solution cools, gelatin now becomes the continuous phase and the water is in the discontinuous phase. Moreover, now the solution has stiffened and becomes semisolid and is called a **gel**.

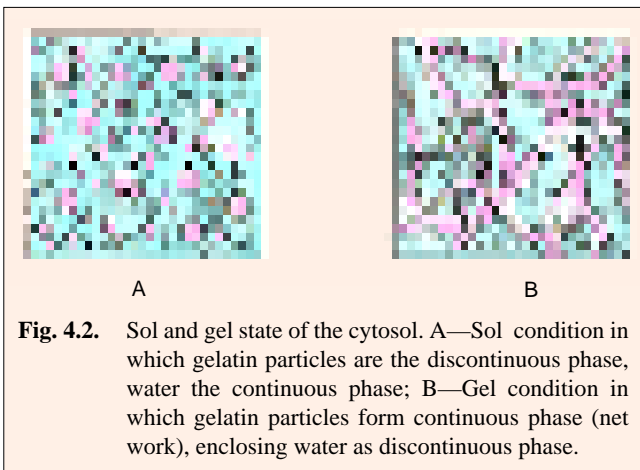


Fig. 4.2. Sol and gel state of the cytosol. A—Sol condition in which gelatin particles are the discontinuous phase, water the continuous phase; B—Gel condition in which gelatin particles form continuous phase (network), enclosing water as discontinuous phase.

In gel state the molecules of colloidal substance remain held together by various types of chemical bonds or bond between H—H, C—H or C—N. The stability of gel depends on the nature and strength of chemical bonds. Heating the gel solution will cause it to become sol again, and the phases are reversed. Under the natural conditions, the phase reversal of the cytosol (cytoplasmic matrix) depends on various physiological, mechanical and biochemical activities of the cell.

CHEMICAL ORGANIZATION OF CYTOSOL (OR CYTOPLASMIC MATRIX)

Chemically, the cytoplasmic matrix is composed of many chemical elements in the form of atoms, ions and molecules.

Chemical Elements

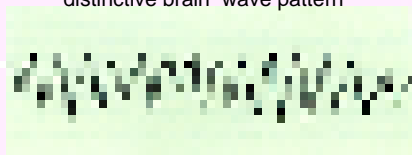
Of the 92 naturally occurring elements, perhaps 46 are found in the cytosol (cytoplasmic matrix). Twenty four of these are considered essential for life (called **essential elements**), while others are present in cytosol only because they exist in the environment with which the organism interacts. Of

72 CELL BIOLOGY

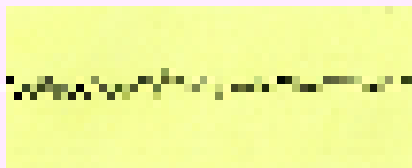
the 24 essential elements, six play especially important roles in living systems. These **major elements** are carbon (C, 20 per cent), hydrogen (H, 10 per cent), nitrogen (N, 3 per cent), oxygen (O, 62 per cent), phosphorus (P, 1.14 per cent) and sulphur (S, 0.14 per cent). Most organic molecules are built with these six elements. Another five essential elements found in less abundance in living systems are calcium (Ca, 2.5 per cent), potassium (K, 0.11 per cent), sodium (Na, 0.10 per cent), chlorine (Cl, 0.16 per cent) and magnesium (Mg, 0.07 per cent). Several other elements, called **trace elements**, are also found in minute amounts in animals and plants,



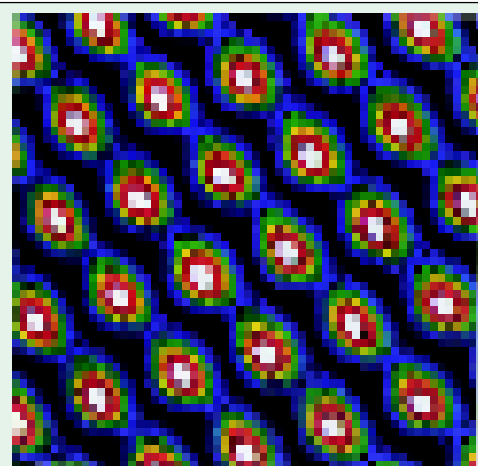
(a) a person meditating; has a very distinctive brain wave pattern



(b) The brain wave pattern of the same person while not meditating



Ions, Nerve impulses and Meditation. Na^+ are crucial to electrical activity in the brain, which can be monitored and recorded.



All matter is composed of atoms. Photo of individual atoms on the surface of a silicon crystal developed by tunneling microscopy.

but are nevertheless essential for life. These are iron (Fe, 0.10 per cent), iodine (I, 0.014 per cent), molybdenum (Mo), manganese (Mn), Cobalt (Co), zinc (Zn), selenium (Se), copper (Cu), chromium (Cr), tin (Sn), vanadium (V), silicon (Si), nickel (Ni), fluorine (F) and boron (B).

Ions

The cytoplasmic matrix consists of various kinds of ions. The ions are important in maintaining osmotic pressure and acid-base balance in the cells. Retention of ions in the matrix produces an increase in osmotic pressure and, thus, the entrance of water in the cell. The concentration of various ions in the intracellular fluid (matrix) differs from that in the interstitial fluid. For example, in the cell K^+ and Mg^{++} can be high, and Na^+ and Cl^- high outside the cell. In muscle and nerve cells a high order of difference exists between intracellular K^+ and extracellular Na^+ . Free calcium ions (Ca^{++}) may occur in cells or circulating blood. Silicon ions occur in the epithelium cells of grasses. The free ions of phosphate (primary, H_2PO_4^- and secondary, HPO_4^-) occur in the matrix and blood. These ions act as a buffering system and tend to stabilize pH of blood and cellular fluids. The ions of different cells also include sulphate (SO_4^-), carbonate (CO_3^-), bicarbonate (HCO_3^-), magnesium (Mg^{++}) and amino acids. Cellular functions of certain ions have been tabulated in Table 4-1.

Table 4-1. Cellular functions of certain ions. (Source : Sheeler and Bianchi, 1987).

Element	Ionic form present	Functions
1. Molybdenum	MoO_4^{2-}	Cofactor or activator of certain enzymes (<i>e.g.</i> , nitrogen fixation, nucleic acid metabolism, aldehyde oxidation).
2. Cobalt	Co^{2+}	Constituent of vitamin B_{12} .
3. Copper	Cu^+ , Cu^{2+}	Constituent of plastocyanin and cofactor of respiratory enzymes.
4. Iodine (Heaviest trace element)	I^-	Constituent of thyroxin, triiodothyronine and other thyroid hormones.
5. Boron	BO_3^{3-} , $\text{B}_4\text{O}_7^{2-}$	Activates arabinose isomerase.
6. Zinc	Zn^{2+}	Cofactor of certain enzymes (<i>e.g.</i> , carbonic anhydrase, carboxypeptidase).
7. Manganese	Mn^{2+}	Cofactor of certain enzymes (<i>e.g.</i> , several kinases, isocitric decarboxylase).
8. Iron	Fe^{2+} , Fe^{3+}	Constituent of haemoglobin, myoglobin and cytochromes.
9. Magnesium	Mg^{2+}	Constituent of chlorophyll; activates ATPase enzyme.
10. Sulphur	SO_4^{2-}	Constituent of coenzyme A, biotin, thiamine, proteins.
11. Phosphorus	PO_4^{3-} , H_2PO_4^-	Constituent of lipids, proteins, nucleic acids, sugar phosphates, nucleoside phosphates.
12. Calcium	Ca^{2+}	Constituent of plant cell walls; matrix component of bone tissue; cofactor of coagulation enzymes.
13. Potassium	K^+	Cofactor for pyruvate kinase and K^+ -stimulated ATPase.

Electrolytes and Non-electrolytes

The matrix consists of both electrolytes and non-electrolytes.

(i) Electrolytes. The electrolytes play a vital role in the maintenance of osmotic pressure and acid base equilibrium in the matrix. Mg^{2+} ions, phosphate, etc., are good examples of the electrolytes.

(ii) Non-electrolytes. Some of minerals occur in matrix in non-ionizing state. The non-electrolytes of the matrix are Na, K, Ca, Mg, Cu, I, Fe, Mn, Fl, Mo, Cl, Zn, Co, Ni, etc. The iron (Fe) occurs in the haemoglobin, ferritin, cytochromes and some enzymes as catalase and cytochrome

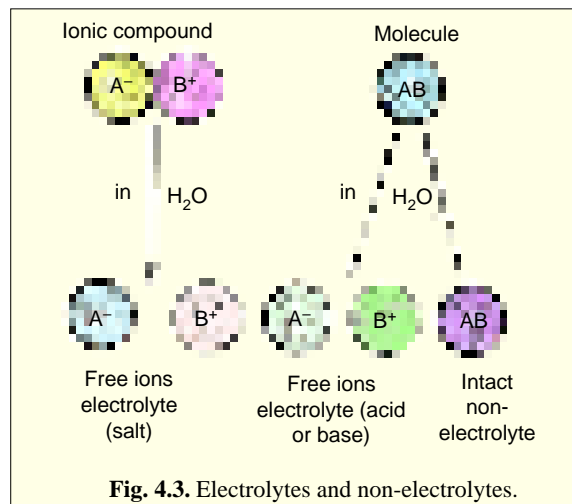


Fig. 4.3. Electrolytes and non-electrolytes.

oxidase. The calcium (Ca) occurs in the blood, matrix and the bones. The copper (Cu), manganese (Mn), molybdenum (Mo), zinc (Zn) are useful as cofactors for enzymatic actions. The iodine and fluorine are essential for the thyroid and the enamel metabolism, respectively.

TYPES OF COMPOUNDS OF CYTOSOL

Chemical compounds are conventionally divided into two groups : **organic** and **inorganic**. Organic compounds form 30 per cent of a typical cell, rest are the inorganic substances such as water and other substances.

Table 4-2. The approximate percentage composition of the human body (Source : Roberts, 1986).

Substance	Percentage
1. Water	65
2. Protein	18
3. Fat	10
4. Carbohydrate	5
5. Other organic	1
6. Inorganic	1

INORGANIC COMPOUNDS

The inorganic compounds are those compounds which normally found in the bulk of the physical, non-living universe, such as elements, metals, non-metals, and their compounds such as water, salts and variety of electrolytes and non-electrolytes. In the previous section, we have discussed a lot about the inorganic substances except the water which will be discussed in the following paragraph.

Water

The most abundant inorganic component of the cytosol is the water (the notable exceptions are seeds, bone and enamel). Water constitutes about 65 to 80 per cent of the matrix. In the matrix the water occurs in two forms, viz., **free water** and **bound water**. The 95 per cent of the total cellular water is used by the matrix as the solvent for various inorganic substances and organic compounds and is known as **free water**. The remaining 5 per cent of the total cellular water remains loosely linked with protein molecules by hydrogen bonds or other forces and is known as **bound water**.

The water contents of the cellular matrix of an organism depend directly on the age, habitat and metabolic activities. For instance, the cells of the embryo have 90 to 95 per cent water which decreases progressively in the cells of the adult organism. The cells of lower aquatic animals contain comparative high percentage of the water than the cells of higher terrestrial animals. Further the percentage of water in the matrix also varies from cell to cell according to the rate of the metabolism.

Molecular structure of water. The special physical properties of water are found in its molecular structure. Water is formed by the combination of hydrogen and oxygen through the formation of covalent bonds, in which atoms by sharing pairs of electrons, become linked together (Fig. 4.4). Covalent bonds are strong chemical bonds between atoms and contain a relatively large amount of chemical energy (110.6 kilocalories/Mole or 462 kilojoules/Mole). In Figure 4.4 hydrogen is shown with its one electron which it may share with an oxygen atom. Each oxygen atom has two electrons which it may share with two hydrogen atoms.

Unique physical properties of water and their biological utility. There are several extraordinary properties of water that make it especially fit for its essential role in the protoplasmic systems (*i.e.*, cytosol or matrix). Some of the unique properties of water are the following :

1. Water as a solvent.

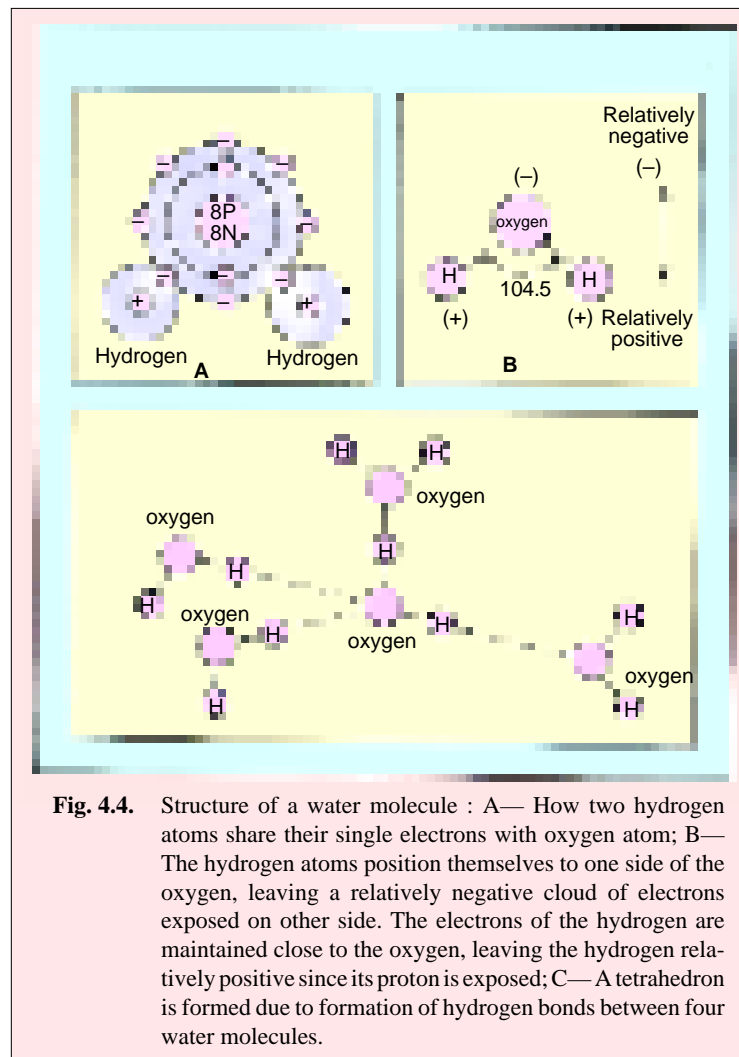
Water is most stable yet versatile of all solvents. Water's properties as a solvent for inorganic substances as mineral ions, solids, etc., and organic compounds such as carbohydrates and proteins, depend on water's dipole nature. Because of this polarity, water can bind electrostatically to both positively and negatively charged groups in the protein. Thus, each amino group in a protein molecule is capable of binding 2.6 molecules of water. The solvency is of great biological importance because all the chemical reactions that take place in the cells do so in aqueous solution. The water also forms the good dispersion medium for the colloidal system of the matrix.

2. Water's thermal properties. Water is the only substance that occurs in nature in the three phases of solid, liquid and vapour within the ordinary range of earth's temperatures. Water

has a **high specific heat** : it requires 1 calorie (4.185 joules) to elevate the temperature of 1 gram of water by 1°C (such as from 15 to 16°C). Such a high thermal capacity of water has a great moderating effect on environmental temperature changes and is a great protective agent for all life.

Water also has a **high heat of vaporization**. It requires more than 540 calories (2259 joules) to change 1 gram of liquid water into water vapour. Thus, water tends to have a remarkably high boiling point (100°C) for a substance of such low relative molecular mass. Were it not for this lucky accident, it is likely that liquid water would never have existed on earth and would have been lost to outer space. Further, for terrestrial plants and animals, cooling produced by the evaporation of water is an important means of getting rid of excess heat. Moreover, at the other temperature extreme, large amounts of energy (335 joules or 80 cal per gram) must be lost for water to be converted from the liquid to the solid state. This is called **heat of fusion**. Water's melting point being 0°C.

Another important property of water from a biological standpoint is its unique **density behaviour** during change of temperature. Most liquids become continually more dense with cooling.



Water, however, reaches its maximum density at 4° C and then becomes lighter with further cooling. Therefore, ice floats rather than settling on the bottom of lakes and ponds. This protects the aquatic life from freezing.

3. Surface tension. Water has a **high surface tension**. This property, caused by the great cohesiveness of water molecules, is important in the maintenance of protoplasmic form and movement. Despite its high surface tension, water has **low viscosity**, a property that favours the movement of blood through minute capillaries and of cytoplasm inside cellular boundaries.

Molecules dissolved in water, lower its surface tension and tend to collect at the interface between its liquid phase and other phases.

This may have been important in the development of the plasma membrane, and certainly plays an important role in the movement of molecules across it.

4. Transparency. The water is transparent to light, enabling the specialized photosynthetic organelles, the chloroplast, inside the plant cell to absorb the sunlight for the process of photosynthesis.

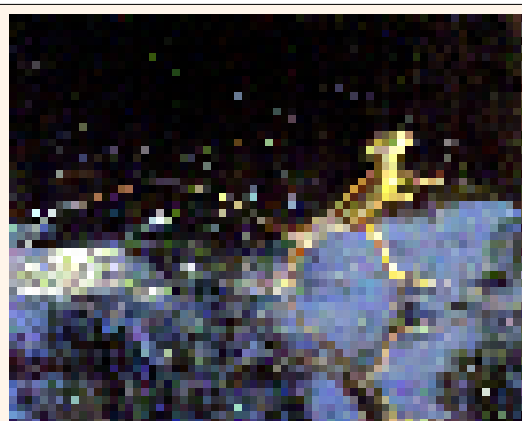
ORGANIC COMPOUNDS

The chemical substances which contain carbon (C) in combination with one or more other elements as hydrogen (H), nitrogen (N), sulphur (S), etc., are called **organic compounds**. The organic compounds usually contain large molecules which are formed by the similar or dissimilar unit structure known as the **monomers**. A monomer (Gr., *mono*=one, *meros*=part) is the simplest unit of the organic molecule which can exist freely. Some organic compounds such as carbohydrates occur in the matrix as the monomers. The monomers usually link with other monomers to form **oligomers** (Gr., *oligo*=few or little, *meros*=part) and **polymers** (Gr., *poly*=many, *meros*=part). The oligomers contain small number of monomers, while the polymers contain large number of monomers. The oligomers and polymers contain large-sized molecules or macromolecules. When a polymer contains similar kinds of monomers in its macromolecule it is known as **homopolymer** and when the polymer is composed of different kinds of monomers it is known as the **heteropolymer**.

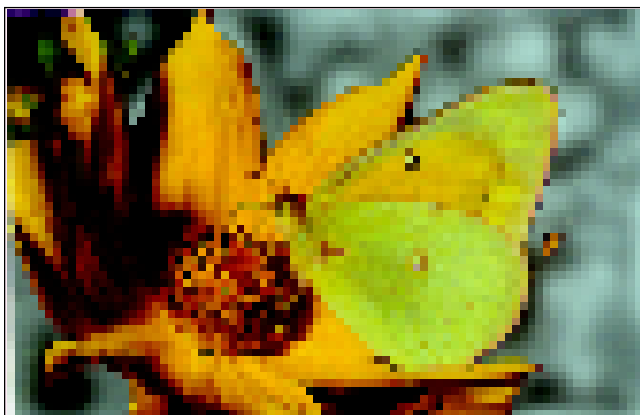
The main organic compounds of the matrix are the carbohydrates, lipids, proteins, vitamins, hormones and nucleotides.

Carbohydrates

The carbohydrates (L., *carbo*=carbon or coal, Gr., *hydro*=water) are the compounds of the carbon, hydrogen and oxygen. They form the main source of the energy of all living beings. Only green part of plants and certain microbes have the power of synthesizing the carbohy-



A basilisk lizard runs across a pond, putting the water's surface tension to good use.



Simple sugars: Many animals consume sugar like this butterfly consuming nectar, a solution rich in glucose.

drates from the water and CO_2 in the presence of sunlight and chlorophyll by the process of photosynthesis. All the animals, non-green parts of the plants (*viz.*, stem, root, etc.), non-green plants (*e.g.*, fungi), bacteria and viruses depend on green parts of plants for the supply of carbohydrates.

Chemically the carbohydrates are polyhydroxy aldehydes or ketones and they are classified as follows :

A. Monosaccharides (Monomers), B. Oligosaccharides (Oligomers), and C. Polysaccharides (Polymers).

A. Monosaccharides. The monosaccharides are the simple sugars with the empirical formula $\text{C}_n(\text{H}_2\text{O})_n$. They are classified and named according to the number of carbon atoms in their molecules as follows :

(i) **Trioses** contain three carbon atoms in their molecules, *e.g.*, glyceraldehyde and dihydroxy acetone.

(ii) **Tetroses** contain four carbon atoms in their molecules, *e.g.*, erythrose and erythrulose.

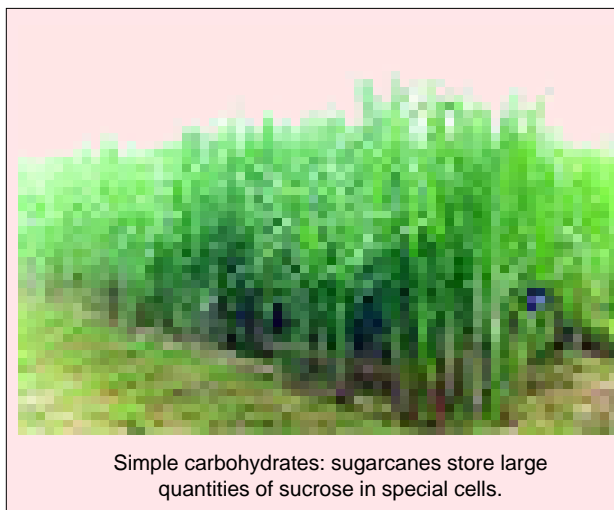
(iii) **Pentoses** contain five carbon atoms in their molecules, *e.g.*, ribose, ribulose, deoxyribose, arabinose and xylulose.

(iv) **Hexoses** contain six carbon atoms in their molecules, *e.g.*, glucose, mannose, fructose and galactose.

(v) **Heptoses** contain seven carbon atoms in their molecules, *e.g.*, sedoheptulose.

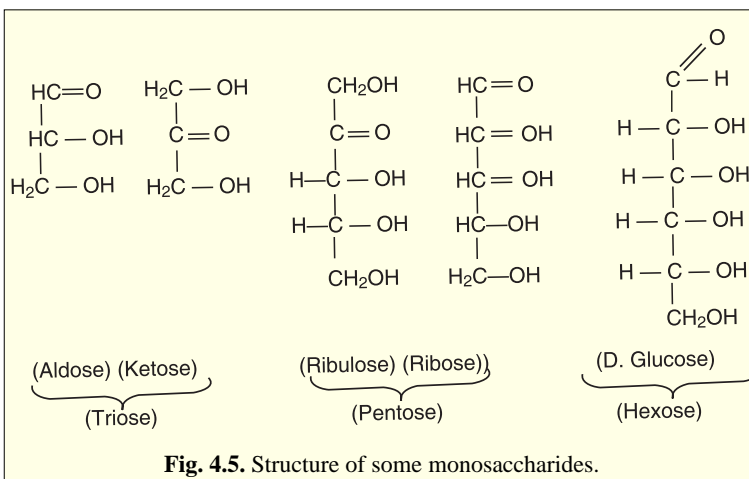
The monosaccharides usually exist as isomers. For example, three hexose sugars—glucose, fructose, and galactose, contain the same number of carbon, hydrogen and oxygen atoms (*i.e.*, $\text{C}_6\text{H}_{12}\text{O}_6$), but they are different sugars because of different arrangements of the atoms within the molecules. Glucose and galactose are **optical isomers** or **stereoisomers**. If a carbon atom is present in a molecule which has four different chemical groups bonded to it, the groups can be arranged in two distinct spatial arrangements about the carbon atom (such a carbon atom is often called **asymmetric carbon atom**). These two different arrangements are known as the **mirror-images** and a convenient example of such mirror-image structures are the two human hands which are identically structured but which cannot be superimposed on each other. The two isomers are designated as 'D' or 'L' by analogy to D- and L- glyceraldehyde, which are aldotrioses.

Most of the monosaccharides are optically active, meaning that their asymmetric carbon (s) cause the rotation of plane of polarised light. Molecules that rotate the plane of polarization to the right, as one faces the light source, are called **dextrorotatory** and are designated **d** or (+), while the opposite case is **levorotation**, designated **l** or (-). It is important to remember that the capitals D and L refer to structure, whereas the lower case **d** and **l** refer to optical activity established before the structure could be determined (see **Dyson**, 1978). Thus, one sees references to D (+) -glucose, also called dextrose, and D (-) -fructose, also called levulose.

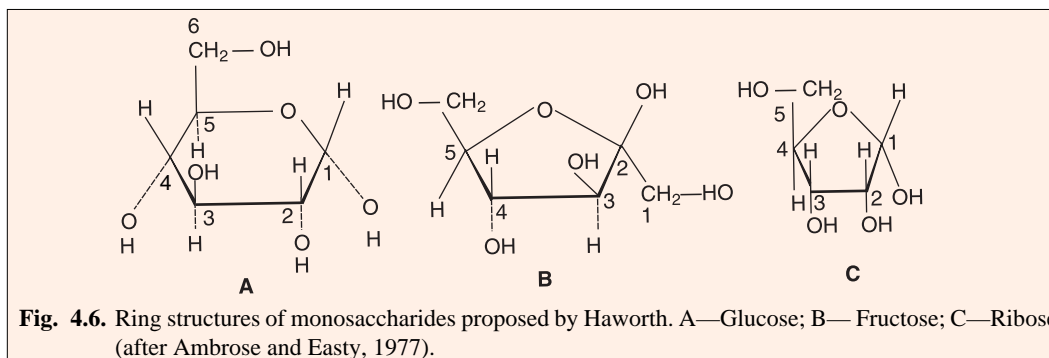


Simple carbohydrates: sugarcanes store large quantities of sucrose in special cells.

Further, for the sake of simplicity, sugars can be represented in a linear straight chain form (Fig. 4.5). In fact, however, the more important configuration is the cyclic one; it is an isomer having an oxygen bridge between two of the carbons. Ring formation introduces a new asymmetric carbon at position one. The stereochemistry of monosaccharides is such that the ring formed is either



five- or six- membered; a seven-membered ring would involve too much strain. In pentose (five-carbon) sugars such as ribose, a five-membered **furanose ring** is formed. In hexoses such as fructose and glucose, a six-membered **pyranose ring** is formed (Fig. 4.6). A useful way of representing the ring-structures of sugars was proposed by **Haworth** (1927). The pyranose or furanose ring is considered to be in the plane perpendicular to the plane of the paper; thus, in gluco-pyranose, carbon atom 2 and 3 are in front of the paper, and carbon atom 5 and the ring oxygen lie behind the plane of the paper. The substitute groups are either above or below the plane of the ring (see **Ambrose** and **Easty**, 1977).

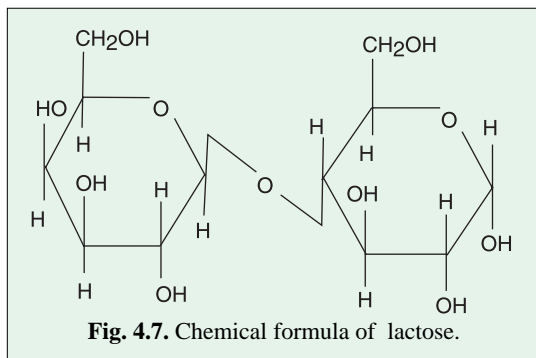


The monosaccharides are the monomers and cannot split further or hydrolysed into the simpler compounds. The pentoses and hexoses are the most abundantly occurring monosaccharides of the matrix.

The pentose sugar, **ribose** is the important constituent molecule of the ribonucleic acid (RNA) and certain coenzymes as nicotinamide adenine dinucleotide (NAD), NAD phosphate (NADP), adenosine triphosphate (ATP) and coenzyme A (CoA). Another pentose sugar the **deoxyribose** is the important constituent of the deoxyribonucleic acid (DNA). The **ribulose** is a pentose sugar which is necessary for photosynthetic mechanism.

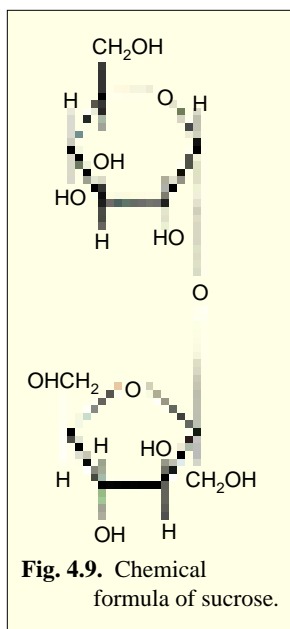
The **glucose**, a hexose sugar, is the primary source of the energy for the cell. The other important hexose sugars of the matrix are the fructose and galactose.

B. Oligosaccharides. The oligosaccharides consist of 2 to 10 monosaccharides (monomers) in their molecules. The monomers remain linked with each other by the **glycosidic bonds** or **linkages**. Certain important oligosaccharides are as follows :



sucrose and maltose occur mainly in the matrix of plant cells, while the lactose occurs exclusively in the matrix of animal cells. The molecules of sucrose are composed of D-glucose and D-fructose. The molecules of maltose consist of two molecules of D-glucose. The molecules of lactose are composed of two monomers, *viz.*, D-glucose and D-galactose. Like monosaccharides all disaccharides are sweet, soluble in water and crystallizable.

C. Polysaccharides. The polysaccharides are composed of ten to many thousands monosaccharides as the monomers in their macromolecules. Their empirical formula is $(C_6H_{10}O_6)_n$. The molecules of the polysaccharides are of colloidal size having high molecular weights. The polysaccharides can be hydrolysed into simple sugars.



The **nutrient polysaccharides** serve as reserves of monosaccharides and are in continuous metabolic turnover. Included in this group are **starch** (plant cells and bacteria), **glycogen** (animal cells), **inulin** (plants such as artichokes and dandelions) and

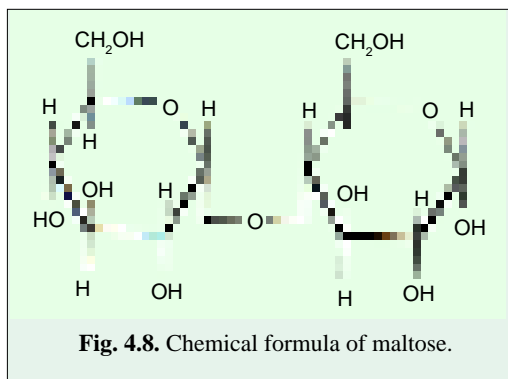
(i) **Disaccharides** contain two monomers, *e.g.*, sucrose, maltose, lactose, etc.

(ii) **Trisaccharides** contain three monomers, *e.g.*, raffinose, mannotriose, rabinose, rhaminose, gentianose and melezitose.

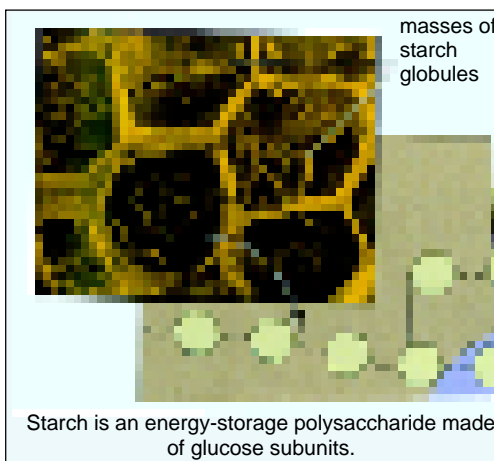
(iii) **Tetrasaccharides** contain four monomers, *e.g.*, stachyose and scordose.

(iv) **Pentasaccharides** contain five monomers, *e.g.*, verbascose.

The most abundant oligosaccharides of the animal and plant cells are the disaccharides such as sucrose, maltose and lactose. The su-



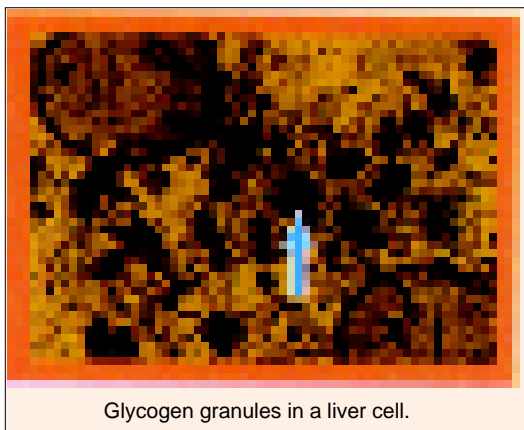
Polysaccharides can be divided into two main functional groups : the structural polysaccharides and the nutrient polysaccharides. The **structural polysaccharides** serve primarily as extracellular or intracellular supporting elements. Included in this group are **cellulose** (found in plant cell wall), **mannan** (a homopolymer of mannose found in yeast cell walls), **chitin** (in the exoskeleton of arthropods and the cell walls of most fungi and some green algae), **hyaluronic acid**, **keratin sulphate** and **chondroitin sulphate** (these three are found in cartilage and other connective tissues) and the **peptidoglycans** (in bacterial cell wall).



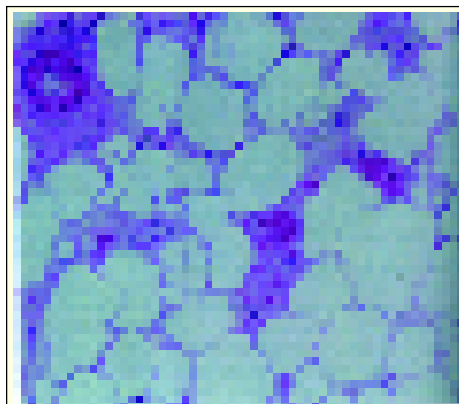
paramylum (an unbranched nutrient and storage homopolymer of glucose found in certain protozoa, *e.g.*, *Euglena*).

Molecules of some polysaccharides are **unbranched** (*i.e.*, linear) chains whose structure may be ribbon-like or helical (usually a left-handed spiral). Other polysaccharides are **branched** and, like many proteins, assume a globular form.

On the chemical basis, the polysaccharides can be divided into two broad classes: the homopolysaccharides and the heteropolysaccharides.



Glycogen granules in a liver cell.



T.S of adipose cells of a mammal where fat is stored.

Homopolysaccharides. The homopolysaccharides contain similar kinds of monosaccharides in their molecules. The most important homopolysaccharides of the matrix are the starch, glycogen, paramylum and cellulose.

(a) Starch. Starch is a nutrient, storage polysaccharide of plant cells (*e.g.*, potato tubers). It usually occurs in cells in the form of **grains** or **granules** (they are located inside the

spherical plastids). Starch granules contain a mixture of two different polysaccharides, amylose and amylopectin, and the relative amounts of these two polysaccharides vary according to the source of the starch. **Amylose** is an unbranched 1→4 polymer of glucose and may be several thousand glycosyl

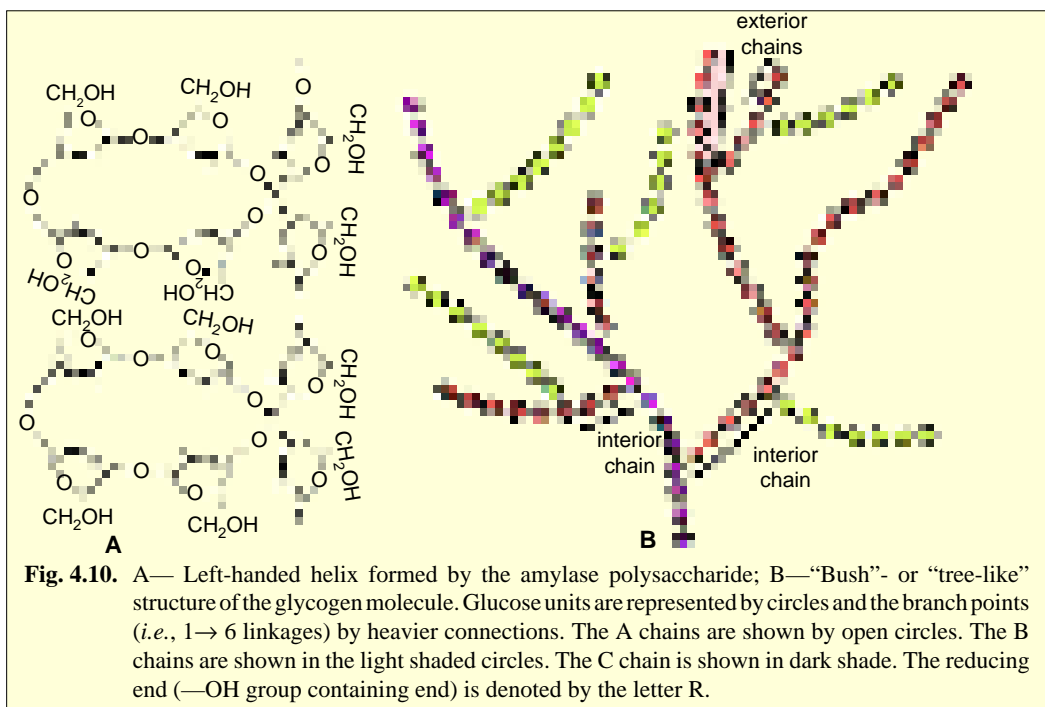
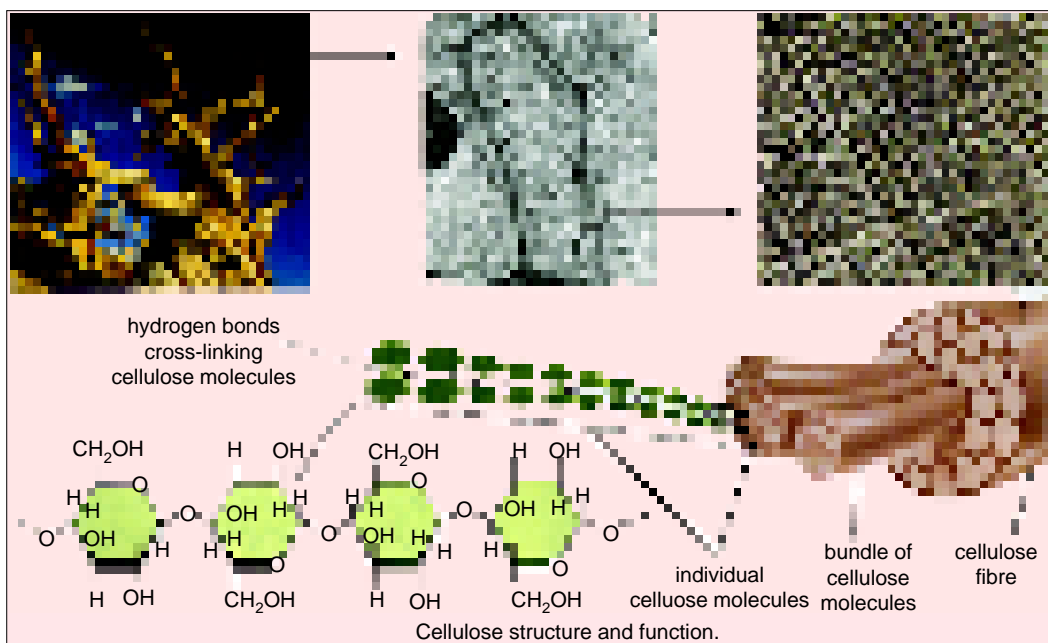
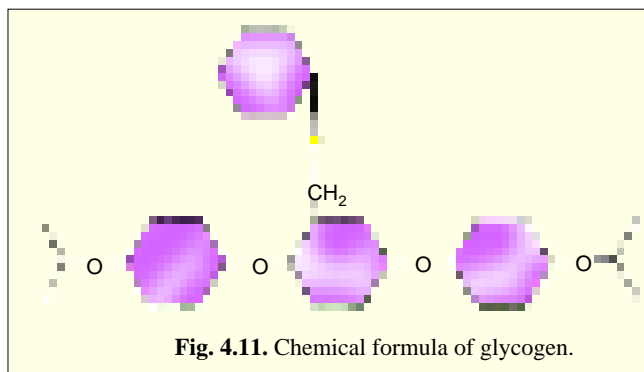


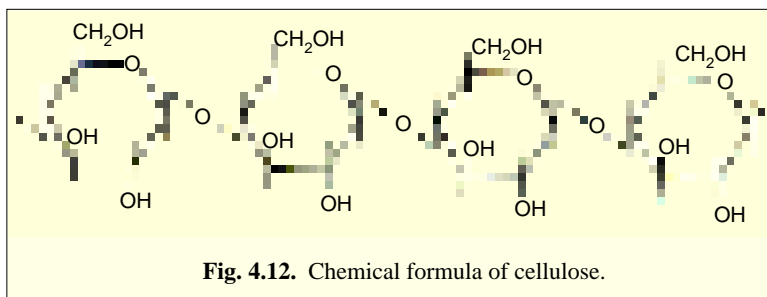
Fig. 4.10. A— Left-handed helix formed by the amylose polysaccharide; B—“Bush”- or “tree-like” structure of the glycogen molecule. Glucose units are represented by circles and the branch points (*i.e.*, 1→6 linkages) by heavier connections. The A chains are shown by open circles. The B chains are shown in the light shaded circles. The C chain is shown in dark shade. The reducing end (—OH group containing end) is denoted by the letter R.

units long. The polysaccharide chain exists in the form of a left-handed helix containing six glycosyl residues per turn (Fig. 4.10 A). The familiar blue colour that is produced when starch is treated with iodine is believed to result from the coordination of iodine ions in the interior of the helix. (In fact, such a colour reaction occurs when helix contains minimum six helical turns or 36 glycosyl units). **Amylopectin** is glycogen-like and is a branched polysaccharide containing many 1→4- and few 1→6-linked glucosyl units.

(b) Glycogen. Glycogen or animal starch is a branched, nutrient, storage homopolysaccharide of all animal cells, certain protozoa and algae. It is particularly abundant in liver cells and muscle cells of man and other vertebrates. Glycogen is more soluble than starch and exists in the cytoplasm as tiny granules. Glycogen molecules exist in a continuous spectrum of sizes, with the largest molecules containing many thousands (*e.g.*, 30, 000) of glucose or glycosyl units. Each glycogen molecule consists of long, profusely branched ('bush'-or 'tree-like' structure; Fig. 4.12B) chains of α -glucose molecules. The glycosidic bonds are established between carbon 1 and 4 of glucose (*i.e.*, α -1→4 linkages) except at the branching points, which involve linkages between carbon 1 and 6 (*i.e.*, α -1→6 linkages) (Fig. 4.11). A glycogen molecule contains three types of chains— A, B and C. There is only one **C chain** which bears many B and A chains and ends in the free reducing group (*i.e.*, carbon 1 of glucose at the end of C chain bears a hydroxyl or OH group). The **B chains** are attached directly to C chain and bear one or more **A chains**. The A chain may also be linked to the C chain.

(C) Cellulose. Cellulose is most common and abundant biological product on earth. It is a major component of cell walls of plants and is also found in the cell walls of algae and fungi. Cellulose is an unbranched (straight) structural polysaccharide of glucose in which the neighboring monosaccharides are joined by β -1→4





glycosidic bonds. Chain lengths vary from several hundred to several thousand glycosyl units (e.g., in the algae *Valonia*, a single molecule of cellulose may contain more than 20,000 glycosyl units). In a cellulose molecule successive pyranose

rings are rotated 180° relative to one another so that the chain of sugars takes on a “flip-flop” appearance (Fig. 4.12). Due to this, the OH groups of sugar molecules stick outwards from the chain in all directions which can form hydrogen bonds with OH groups of neighbouring cellulose chains, thereby establishing a kind of three-dimensional lattice. Thus, in plant cell walls 2000 cellulose molecules are organized into cross-linked, parallel **microfibrils** (having 25 nm diameter), whose long axis is that of the individual glucose chain.

(d) Chitin. Chitin is an extracellular structural polysaccharide found in the cell walls of fungal hyphae and the exoskeleton of arthropods. The chemical structure of chitin is closely related to that of cellulose; the difference is that the hydroxyl group of each number 2 carbon atom is replaced by an acetamide group. Hence, chitin is an unbranched polymer of **N-acetylglucosamine** containing several thousand successive aminosugar units linked by β -1 \rightarrow 4 glycosidic bonds.

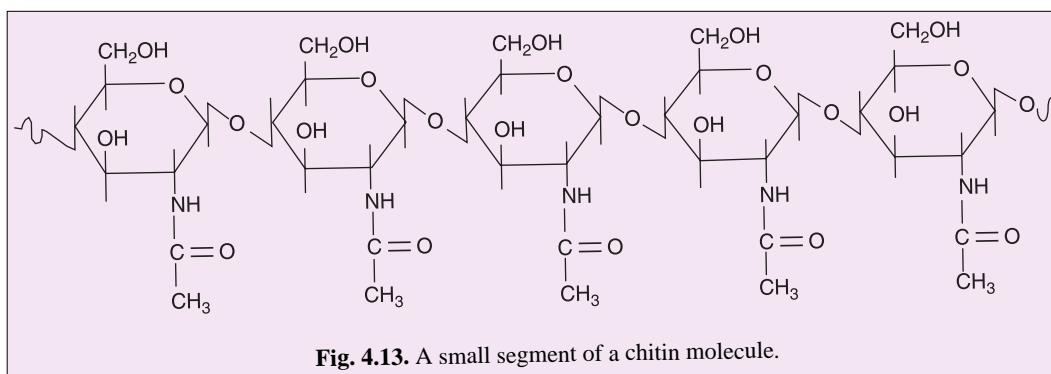
The plant cells besides containing starch and the cellulose contain other polysaccharides such as xylan, alginic acids (algae), pectic acids, inulin, agar-agar and hemicellulose. Of these, some polysaccharides provide mechanical support to the cell, while others are used as stored food material.

Heteropolysaccharides. The polysaccharides which are composed of different kinds of the monosaccharides and amino-nitrogen or sulphuric or phosphoric acids in their molecules are known as heteropolysaccharides. The most important heteropolysaccharides are as follows:

(a) Hyaluronic acid, keratin sulphate and chondroitin sulphate. Cartilage tissue contains the related acidic heteropolysaccharides such as hyaluronic acid, kera-



Tough, slightly flexible chitin supports the otherwise soft bodies of arthropods and fungi.



tin sulphate and chondroitin sulphate. **Hyaluronic acid** is an unbranched heteropolysaccharide containing repeating disaccharides of **N-acetylglucosamine** (or D-glucosamine) and glucuronic acid. In addition to cartilage, hyaluronic acid is also found in other connective tissues, in the synovial fluid of joints, in the vitreous humor of the eyes, and also in the capsules that enclose bacteria.

Keratin sulphate, like hyaluronic acid, is a repeating disaccharide forming an unbranched chain. Each disaccharide unit of the polysaccharide consists of **D-galactose** and **sulphated N-acetylglucosamine**. It is found in cartilage and cornea.

Chondroitin sulphate is a repeating disaccharide consisting of alternating **glucuronic acid** and **sulphated N-acetyl galactosamine** residues. It is found in cartilage, bone, skin, notochord, aorta and umbilical cord.

(b) Heparin. Heparin is a blood anticoagulant and found in the skin, liver, lung, thymus, spleen and blood. Its molecule contains the repeated disaccharide units, each having **D-glucuronic acid** and **D-glucosamine**.

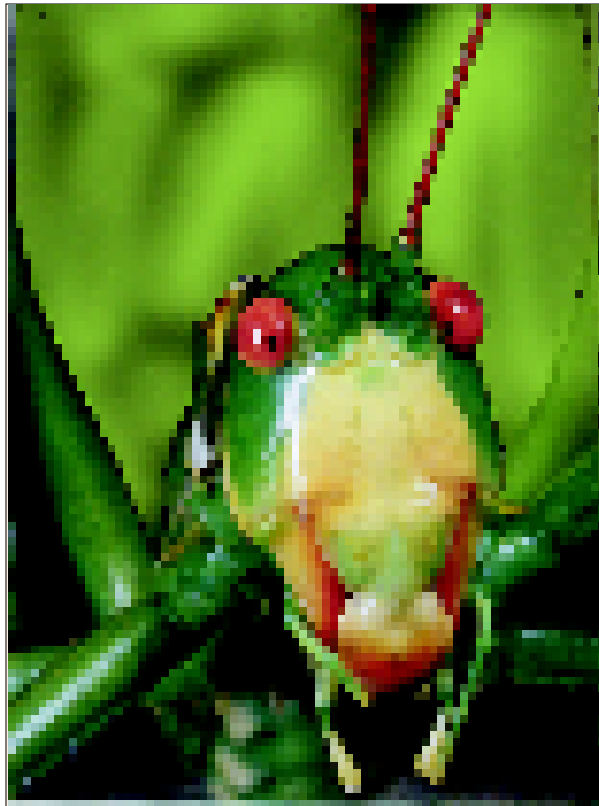
(c) Proteoglycans, glycoproteins and glycolipids. Polysaccharides also occur in covalent combination with proteins and lipids, to form the following three types of molecules :

(i) Proteoglycans. The molecules of proteoglycans consist of much longer portion of polysaccharide and a small portion of protein. They are also called **mucoproteins** (**De Robertis** and **De Robertis, Jr.**, 1987). The proteoglycans are amorphous and form gels which are able to hold large amounts of water.

The **cartilage proteoglycan** is found extracellularly in cartilage and bone. In its molecule, strands of protein, called **core protein**, extend radially from a long, central hyaluronic acid molecule. In each core protein strand, three carbohydrate bearing regions may be identified. The first region contains numerous oligosaccharides, the second region contains keratin sulphate chains and the third region contains chondroitin sulphate chains. This arrangement gives cartilage its resilience and tensile strength.

(ii) Glycoproteins (or **glycosaminoglycans** or **mucopolysaccharides**). In these molecules, the carbohydrate portion consists of much shorter chains which are often branched. Glycoproteins serve diverse roles in cells and tissues and include certain enzymes, hormones, blood groups, saliva, gastric mucin, ovomucoids, serum, albumins, antibodies or immunoglobins (see Table 4.3).

(iii) Glycolipids. These molecules are covalent combinations of carbohydrate and lipid. The carbohydrate portion may be a single monosaccharide or a linear or branched chain. Glycolipids form the component of most cell membranes, *e.g.*, cerebrosides and gangliosides.



Chitin is a primary component of the glistening outer skeleton of this grasshopper.

Table 4-3. Carbohydrate content of glycoproteins (Source : Sheeler and Bianchi, 1987).

Glycoprotein	Percentage of carbohydrate	Function
1. Ovalbumin	1	Hens-egg food reserve
2. Follicle-stimulating hormone (FSH)	4	Hormone
3. Fibrinogen	5	Blood coagulation protein
4. Transferrin	6	Iron transport protein of blood plasma
5. Ceruloplasmin	7	Copper transport protein of blood plasma
6. Glucose-oxidase	15	Enzyme
7. Peroxidase	18	Enzyme
8. Luteinizing hormone	20	Hormone
9. Heptoglobin	23	Haemoglobin-binding protein of blood plasma
10. Erythropoietin	33	Hormone
11. Mucin	50–60	Mucus secretion
12. Blood-group glycoprotein	85	Unknown

Lipids (Fats)

The lipids (Gr., *lipos*=fats) are the organic compounds which are insoluble in the water but soluble in the non-polar organic solvents such as acetone, benzene, chloroform and ether. The cause of this general property of lipids is the predominance of long chains of aliphatic hydrocarbons or benzene ring in their molecules. The lipids are non-polar and hydrophobic. The common examples of lipids are cooking oil, butter, ghee, waxes, natural rubber and cholesterol. Like the carbohydrates, lipids serve two major roles in cells and tissues : 1. They occur as constituents of certain structural components of cells such as membranous organelles; plant pigments such as **carotene** found in carrots and **lycopene** that occurs in tomatoes; vitamins like A, E and K; menthol and eucalyptus oil; and (2)

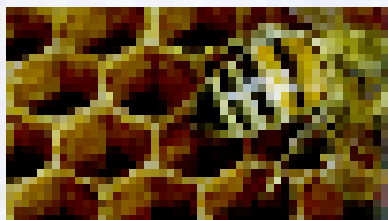
they may be stored within cells as reserve energy sources. Like the starch and glycogen, fat is compact and insoluble and provides a convenient form in which energy-yielding molecules (the fatty acids) can be stored for use when occasion arises.

Lipids are all made of carbon, hydrogen and sometimes oxygen. The number of oxygen atoms in a lipid molecule is always small compared to the number of carbon atoms. Sometimes small amounts of phosphorus, nitrogen and sulphur are also present. Natural fats and oils are compounds of **glycerol** (*i.e.*, glycerine or propane-

1, 2, 3 triol) and **fatty acids**.

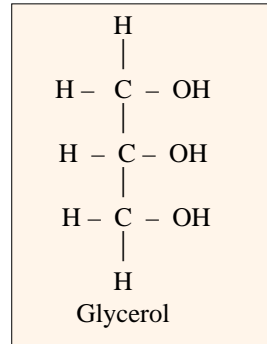


(a) Fat is an efficient way to store energy.



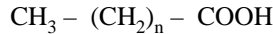
(b) Wax is a highly saturated lipid.

They are esters which are formed due to reaction of organic acids with alcohols. There is only one kind of glycerol : its molecular configuration shows no variation and it is exactly same in all lipids. The formula of glycerol is $C_3H_8O_3$ and following is its molecular structure :



Fatty acids. A fatty acid molecule is **amphipathic** and has two distinct regions or ends: a long **hydrocarbon chain**, which is **hydrophobic** (water insoluble) and not very reactive chemically, and a **carboxylic acid group** which is ionized in solution (COO^-), extremely **hydrophilic** (water soluble) and readily forms esters and amides. In neutral solutions, salts of the fatty acids form small spherical droplets or **micelles** in which the dissociated carboxyl groups occur at surface and the hydrophobic carbon chains project towards the centre. In cells, the fatty acids only sparingly occur freely; instead, they are esterified to other components and form the saponifiable lipids.

A fatty acid molecule may be either saturated or unsaturated. The **saturated fatty acids** consist of long hydrocarbon chains terminating in a carboxyl group and conform to the general formula :

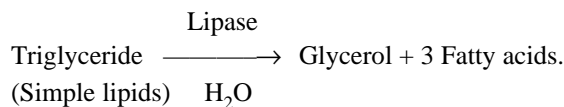


In nearly all naturally occurring fatty acids, n is an even number from 2 to 22. In the **saturated fatty acids**, most commonly found in animal tissues, n is either 12 (*i.e.*, **myristic acid**), 14 (*i.e.*, **palmitic acid**) or 16 (*i.e.*, **stearic acid**). In **unsaturated fatty acids**, at least two but usually no more than six of the carbon atoms of the hydrocarbon chain are linked together by double bonds ($-\text{C} = \text{C}-$), *e.g.*, **oleic acid**, **linoleic**, **linolenic**, **arachidonic** and **clupanadonic acids**. Double bonds are important because they increase the flexibility of the hydrocarbon chain, and thereby the fluidity of biological membranes. Unsaturated fatty acids predominate in lipids of higher plants and in animals that live at low temperatures. Lipids in the tissues of animals inhabiting warm climates contain larger quantities of saturated fatty acids.

Essential fatty acids. Some animals, especially mammals, are unable to synthesize certain fatty acids and, therefore, require them in their diet. They are called **essential fatty acids** and include linoleic acid, linolenic acid and arachidonic acid. Such essential fatty acids have to be obtained from plant material by the animal.

Types of lipids. The lipids are classified into three main types : 1. simple lipids, 2. compound lipids and 3. derived lipids.

1. Simple lipids. The simple lipids are alcohol esters of fatty acids :

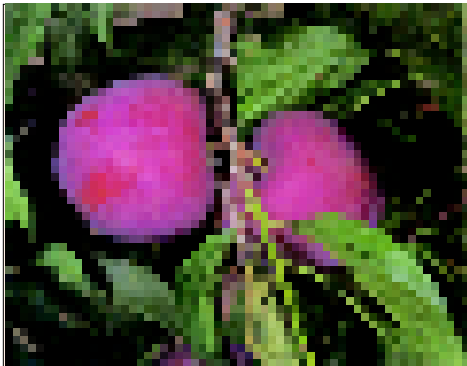


Simple lipids are also of following two types :

(a) Neutral fats (Glycerides or triglycerides). They are triesters of fatty acids and glycerol. Neutral fats represent the major type of stored lipid and so accumulate in the cytoplasm.

(b) Waxes. Waxes have a higher melting point than neutral fats and are the esters of fatty acids of high molecular weight with the alcohol except the glycerol. The most important constituent alcohol of the molecules of waxes is the **cholesterol**, *e.g.*, bees wax.

2. Compound lipids. The compound lipids contain fatty acids, alcohols and other compounds as phosphorus, amino-nitrogen carbohydrates, etc., in their molecules. Some of the compound lipids are important structural components of the cell, in particular of cell membranes. The compound lipids of the cell are of the following types :



Waxes give plums their delicate whitish bluish and help keep citrus fruit juicy.

tail regions pack together very closely facing the air and their head groups are in contact with the water (Fig. 4.14). Two such films can combine tail to tail to make a phospholipid sandwich or self-sealing **lipid bilayer**, which is the structural basis of cell membranes.

Various membranes of cell contain the following four types of phospholipids : **1. phosphatidyl choline** or **lecithin**; **2. phosphatidyl ethanolamine** or **cephalin**; **3. phosphatidyl serine**; and **4. phosphatidyl inositol**. The other important phospholipids of the matrix are the phosphoinositides (occur mostly in the cells of liver, brain, muscle and soyabean), plasmalogens and isositides. Plasmalogens are a special class of phospholipids which are especially abundant in the membranes of nerve and muscle cells and are also characteristic of cancer cells.

Liposomes. When aqueous suspensions of phospholipids are subjected to rapid agitation by using ultrasound (*i.e.*, insonation), the lipid disperses in the water and forms **liposomes** or **lipid vesicles**. Liposomes are small spherical bodies (25 nm to 1 μm in diameter) whose surface is formed by a bilayer of phospholipid molecules enclosing a small volume of the aqueous medium. They exhibit many of the permeability properties of natural membranes, *i.e.*, water soluble small molecules or ions can be enclosed by the liposomes and they can also traverse the lipid bilayer of latter. Recently, liposomes have been found to have great therapeutic promise, since, they can be used as vectors for the transfer of specific drugs, proteins, hormones, nucleic acids, ions or any other molecule into the specific types of animal cells. The contents of the liposomes can enter the target cells by two routes : 1. The liposomes can attach to the surface of target cells and may fuse with the plasma membrane, following which their contents are released into the cytosol or cytoplasmic matrix. 2. The entire liposomes may be endocytosed and degraded intracellularly (see **Sheeler** and **Bianchi**, 1987).

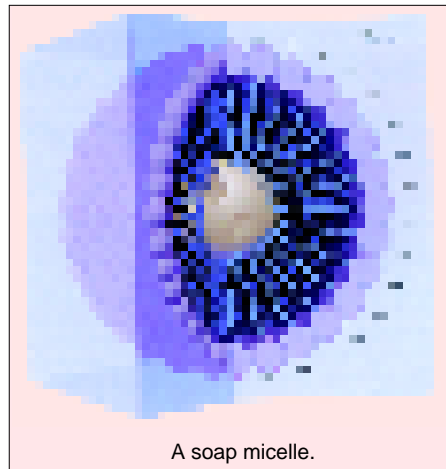
(ii) Sphingolipids. The sphingolipids occur mostly in the cells of the brain. Instead of the glycerol, they contain in their molecules amine alcohol (sphingol or sphingosine). For instance, the myelin sheaths of the nerve fibres contain a lipid known as **sphingomyelin** which contains sphingosine and phospholipids in its molecules.

(iii) Glycolipids. The glycolipids contain in their molecules the carbohydrates and the lipids. The matrix of the animal cells contains two kinds of glycolipids, *viz.*, cerebrosides and gangliosides.

(a) Cerebrosides. The cerebrosides contain in their molecules sphingosine, fatty acids and

(i) Phospholipids (or Glycerophos-phatides).

Such type of lipids form the major constituent of cell membranes. In a molecule of phospholipid two of the —OH or hydroxyl groups in glycerol are linked to fatty acids, while the third —OH group is linked to phosphoric acid. The phosphate is further linked to a hydrophilic compound such as **ethanolamine**, **choline**, **inositol** or **serine**. Each phospholipid molecule, therefore, has hydrophobic or water-insoluble tail which is composed of two fatty acid chains and a hydrophilic or water-soluble polar head group, where the phosphate is located. Thus, in effect the phospholipid molecules are detergents, *i.e.*, when a small amount of phospholipid is spread over the surface of water, there forms a monolayer film of phospholipid molecules; in this thin film,



A soap micelle.

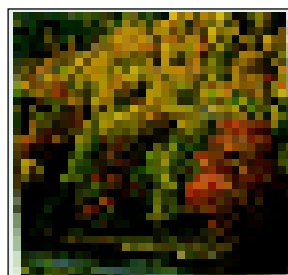
galactose or glucose. The cerebrosides are the important lipids of the white matter of the cells of brain and the myelin sheath of the nerve. The important cerebrosides are the kersin, cerebrin, nervon and oxynervons.

(b) Gangliosides. The gangliosides have complex molecules which are composed of sphingosine, fatty acids and one or more molecules of glucose, lactose, galactosamine and neuraminic acid. The gangliosides occur in the grey matter of the brain, membrane of erythrocytes and cells of the spleen. Gangliosides act as **antigens**.

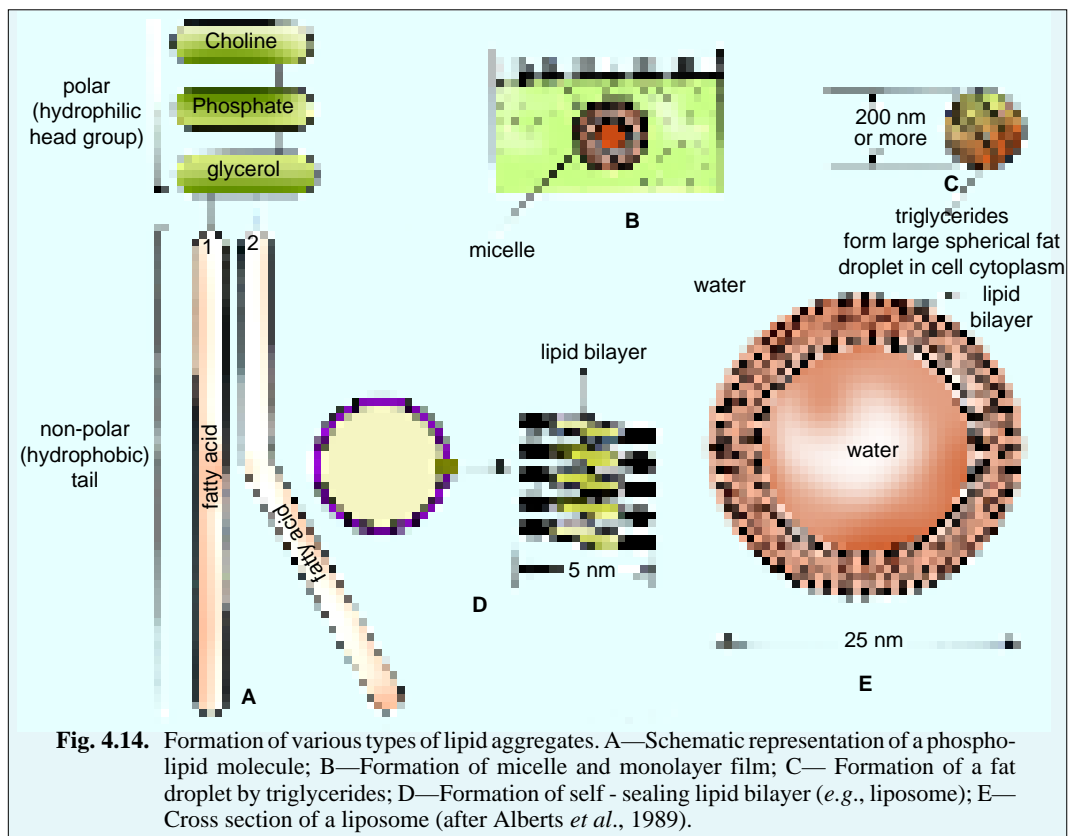
One type of ganglioside, called **GM2**, may accumulate in the lysosomes of the brain cells because of a genetic deficiency that results in the failure of the cells to produce a lysosomal enzyme that degrades this ganglioside. This condition is called **Tay-Sachs disease** and leads to paralysis, blindness and retarded development of human beings.

3. Derived lipids (or Nonsaponifiable lipids). Some type of lipids do not contain fatty acids in their constituents and they are of following three types :

A. Terpenes. The terpenes include certain **fat-soluble vitamins** (e.g., vitamins A, E and K), **carotenoids** (e.g., photosynthetic pigments of plants), and certain **coenzymes** (such as coenzyme Q or ubiquinone). All the terpenes are synthesized from various numbers of a five-carbon building block, called **isoprene unit** (Fig. 4.17). The isoprene units are bonded together in a head-to-tail organization. Two isoprene units form a **monoterpene**, four form a **diterpene**, six a **triterpene**, and so on. The monoterpenes are responsible for the



Chlorophyll present in green plants are responsible for making them autotrophs.



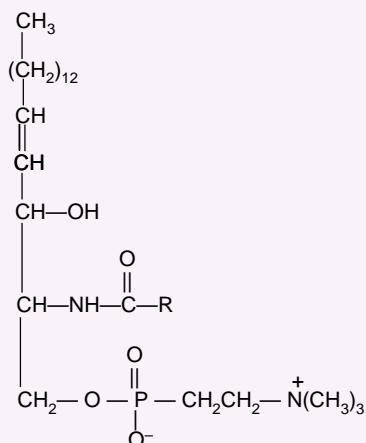


Fig. 4.15. General chemical formula of sphingomyelin.

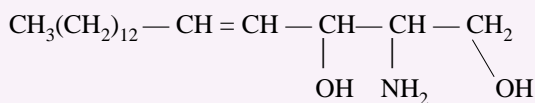


Fig. 4.16. Chemical formula of sphingosine.

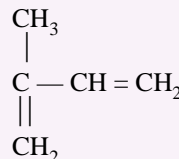


Fig. 4.17. Isoprene.

characteristic odours and flavours of plants (*e.g.*, **geraniol** from geraniums, **menthol** from mint and **limonene** from lemons). **Dolicol phosphate** is a **polyisoprenoid** (*i.e.*, long chain polymer of isoprene) and is used to carry activated sugars in the membrane-associated synthesis of glycoproteins and some polysaccharides.

The **carotenoids** are the compound lipids and they form the pigments of the animal and plant cells. There are about 70 carotenoids occurring in both types of cells. The important carotenoids of cells are the α , β and γ carotenes, retinene, xanthophylls, lactoflavin in milk, riboflavin (vitamin B₂), xanthocyanins, coenzyme Q, anthocyanins, flavones, flavonols and flavonones, etc. Chemically all carotenoids are long-chain isoprenoids having an alternating series of double bonds. They are synthesized by plant tissues and are located in the chloroplast lamellae to help in light absorption during photosynthesis. In animal cells, carotenoids serve as precursors of vitamin A.

The **chlorophylls** are essential photosynthetic green pigments of the chloroplasts. A chlorophyll molecule (Fig. 6.18) consists of a **head** and a **tail**. The head consists of a **porphyrin ring** or **tetrapyrrole nucleus** from which extends a hydrophobic tail which is made up of a 20-carbon grouping, called the **phytol**. Phytol (C₂₀H₃₉) is a long straight-chain alcohol containing a single double bond. It may be regarded as a hydrogenated carotene (vitamin A). The porphyrins (Gr., *porphyr* = purple) are complex carbon-nitrogen molecules that usually surround a metal, *i.e.*, it is formed from four pyrrol rings linked together by methane bridges and metal atom (Mg or Fe) is linked to pyrrol

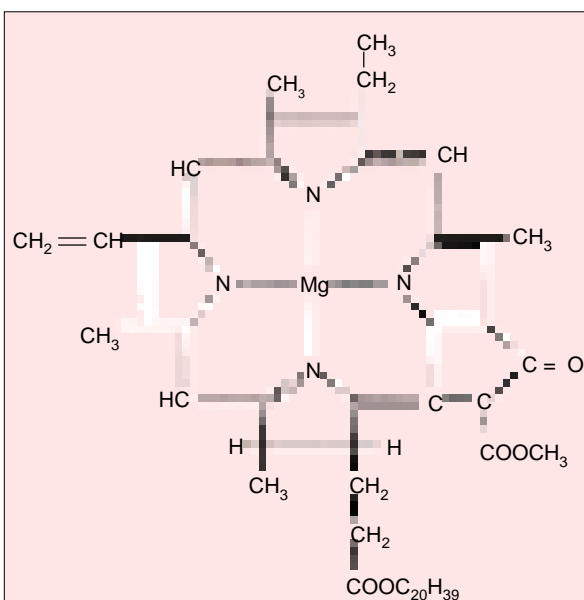


Fig. 4.18. Chemical formula of chlorophyll.

rings. In chlorophyll molecule, the porphyrin surrounds a magnesium ion, while in haeme of **haemoglobin**, it surrounds an iron ion (Fig. 4.19). Many other pigments of animal cells such as **myoglobin** and **cytochromes** have porphyrin rings in their molecules.

B. Steroids. The steroids consist of a system of fused cyclohexane and cyclopentane rings. All are derivative of **perhydro - cyclopentano - phenanthrene**, which consists of three fused cyclohexane rings and a terminal cyclopentane ring (Fig. 4.20). Steroids have widely different physiological charac-

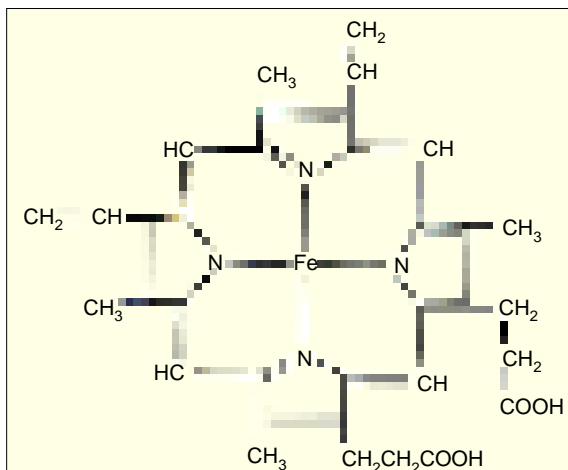


Fig. 4.19. Chemical formula of haeme portion of haemoglobin.

ergosterol and **stigmasterol** found in plants. Cholesterol (Fig. 4.21) is found in the plasma membrane of many animal cells and also in blood, bile, gallstone, brain, spinal cord, adrenal glands and other cells. It is the precursor of most steroid sex hormones and cortisones. **7-dehydro-cholesterol** is found in the skin where it is responsible for the synthesis of vitamin D in the presence of sunlight. **Ergosterol** is also a precursor of vitamin D.

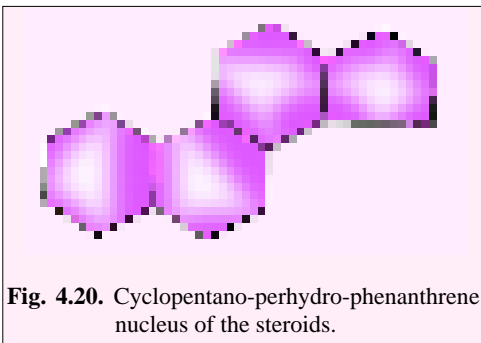


Fig. 4.20. Cyclopentano-perhydro-phenanthrene nucleus of the steroids.



Some body builders endanger their health by taking 'steroids'.

teristics. For example, some steroids are **hormones** (e.g., sex hormones such as estrogen, progesterone, testosterone and corticosterone) and affect cellular activities by influencing gene expression. Some steroids are **vitamins** (e.g., vitamin D₂) and influence the activities of certain cellular enzymes. Some steroids (e.g., cholic acid) are fat emulsifier found in the bile.

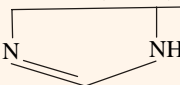
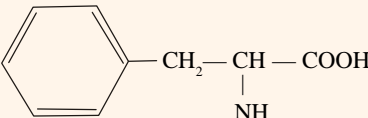
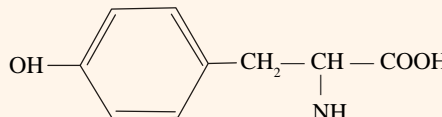
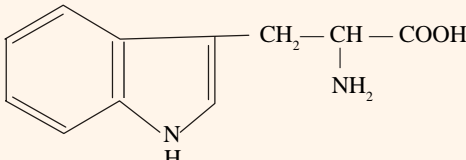
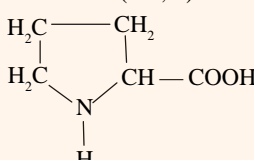
Alcohols of the steroids are called **sterols**. The common examples of the sterols are **cholesterol** found in animals and



Cholesterol plug in artery

C. Prostaglandins. Hydroxy derivatives of 20-carbon polyunsaturated fatty acids are called **prostaglandins**.

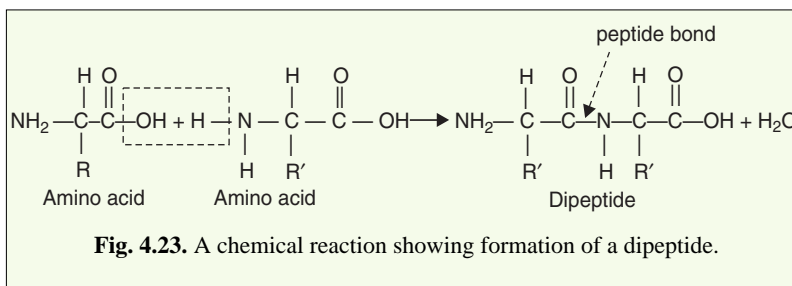
They are found in human seminal fluid, testis, kidney, placenta, uterus, stomach, lung, brain and heart. There are sixteen or more different prostaglandins, falling into nine classes (PGA, PGB, PGCPGI). Their main function is binding of hormones to membranes of the target

Group of amino acid	Name of the amino acids, symbols and chemical formulae
<p>IV. Hydroxyl containing amino acids.</p>	<p>9. Arginine (Arg, R)</p> $\begin{array}{c} \text{NH} \\ \\ \text{H}_2\text{N}-\text{C}-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$
	<p>10. Histidine (His, H)</p> $\begin{array}{c} \text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$ 
	<p>11. Serine (Ser, S)</p> $\begin{array}{c} \text{HO}-\text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$
	<p>12. Threonine (Thr, T)</p> $\begin{array}{c} \text{CH}_3-\text{CH}-\text{CH}-\text{COOH} \\ \quad \\ \text{OH} \quad \text{NH}_2 \end{array}$
	<p>13. Cysteine (Cys, C)</p> $\begin{array}{c} \text{HS}-\text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$
<p>V. Sulphur containing amino acids.</p>	<p>14. Methionine (Met, M)</p> $\begin{array}{c} \text{CH}-\text{S}-\text{CH}_2-\text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$
<p>B. Aromatic amino acids.</p>	<p>15. Phenylalanine (Phe, F)</p> 
	<p>16. Tyrosine (Tyr, Y)</p> 
	<p>17. Tryptophan (Try, W)</p> 
<p>C. Secondary amino acids.</p>	<p>18. Proline (Pro, P)</p> 

Group of amino acid	Name of the amino acids, symbols and chemical formulae
D. Amino acid amides.	19. Asparagine (Asn, N) $\begin{array}{c} \text{NH}_2 \\ \\ \text{O}=\text{C}-\text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$
	20. Glutamine (Glu, Q) $\begin{array}{c} \text{NH}_2 \\ \\ \text{O}=\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}-\text{COOH} \\ \\ \text{NH}_2 \end{array}$

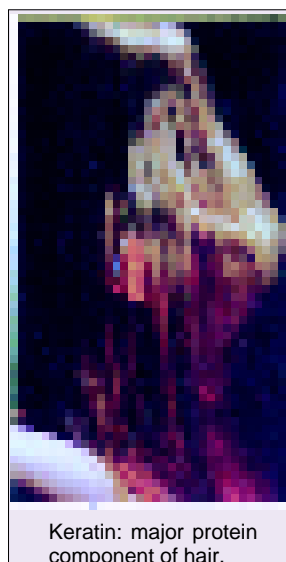
In certain amino acids R group is either a hydrogen atom (*e.g.*, glycine, the simplest amino acid) or a hydrophobic aliphatic (*e.g.*, leucine) or aromatic (*e.g.*, phenylalanine) hydrocarbon. In other cases, R group contains either an extra carboxyl group or an extra amino group or its equivalent. Glutamic acid and aspartic acid each have an extra carboxyl (—COOH) group. Lysine and arginine both contain an additional amino group or equivalent structure. Histidine also contains a N group. Other amino acids such as serine and tyrosine have hydroxyl groups in their side chains. Of a particular importance is the amino acid cysteine which possesses a thiol (SH) group.

2. Formation of proteins. Because a molecule of the amino acid contains both basic or amino (—NH₂) and acidic or carboxyl (—COOH) group, it can behave as an acid and base at a time. The



molecules of such organic compounds which contain both acidic and basic properties are known as **amphoteric molecules**. Due to amphoteric molecules, the amino acids unite with one another to form complex and large pro-

tein molecules. When two molecules of amino acids are combined then one amino acid molecule combines with the carboxylic (—COOH) group of other amino acid and the loss of a water molecule takes place. This sort of condensation of two amino acid molecules by —NH—CO linkage or bond is known as **peptide linkage** or **peptide bond**. A combination of two amino acids by the peptide bond is known as **dipeptide**. When three amino acids are united by two peptide bonds, they form **tripeptide**. Likewise, by condensation of few or many amino acids by the peptide bonds the **oligopeptides** and **polypeptides** are formed respectively. The various molecules of polypeptides unite to form the **peptones**, **proteases** and **proteins**. Thus, protein macromolecules are the polymers of many amino acid monomers. The size (molecular weight), shape, and function of proteins are determined by the number, type and distribution of the amino acids present in the molecule. Proteins occur in a wide spectrum of molecular sizes from small molecules such as the hormone ACTH (or adrenocorticotrophic hormone) which consists of only 39 amino acids and has a molecular weight of 4500, to extremely large proteins such as haemocyanin (an invertebrate blood pigment) which consists of 8200 amino acids and has a molecular weight greater than 900,000 (see Table 4.5 for additional examples).



2. Types of proteins. Many different methods have been used to classify proteins, no method of their classification being entirely satisfactory :

(1) Classification based on biological functions. According to their biological functions, proteins are of two main types :

1. Structural proteins which include **keratin**, the major protein component of hair (cortex), wool, fur, nail, beak, feathers, hooves and cornified layer of skin; and **collagen**, abundant in skin, bone, tendon, cartilage and other connective tissues.

Table 4-5.

Molecular weight and amino acid content of some proteins (Source : Sheeler and Bianchi, 1987).

Protein	Number of amino acids	Molecular weight
1. Adrenocorticotrophic hormone (ACTH)	39	4,500
2. Insulin	51	5,700
3. Ribonuclease	124	12,000
4. Cytochrome-c	140	15,600
5. Horse myoglobin	150	16,000
6. Trypsin	180	20,000
7. Haemoglobin	574	64,500
8. Urease	4,500	473, 000
9. Snail haemocyanin	8, 200	910,000

2. Dynamic or functional proteins which include the enzymes that serve as catalysts in metabolism, hormonal proteins, respiratory pigments, etc.

(2) Classification based on shape of proteins. According to the shape or conformation, two major types of proteins have been recognized :

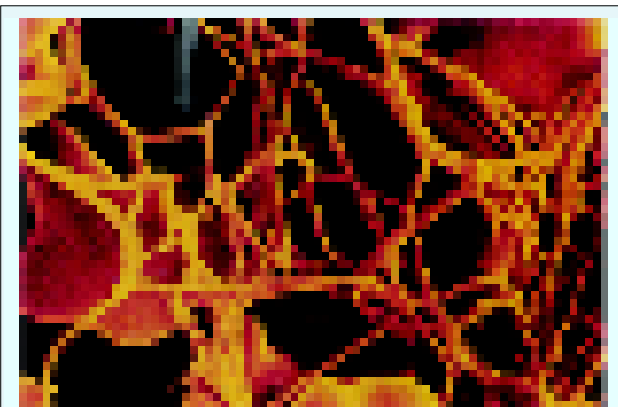
(a) Fibrous proteins. Fibrous proteins are water-insoluble, thread-like proteins having greater length than their diameter. They contain secondary protein structure and occur in those cellular or extracellular structures, where strength, elasticity and rigidity are required, *e.g.*, collagen, elastin, keratin, fibrin (blood-clot proteins) and myosin (muscle contractile proteins).

(b) Globular proteins. Globular proteins are water-soluble, roughly spheroidal or ovoidal in shape. They readily go into colloidal suspension. They have tertiary protein structure and are usually functional proteins, *e.g.*, enzymes, hormones and immunoglobulins (antibodies). Actin of micro- filaments and **tubulins** of microtubules are also globular proteins (see **Alberts et al.**, 1989).

(3) Classification based on solubility characteristics. According to this criterion proteins can be classified into two main types :

(A) Simple proteins. These proteins contain only amino acids in their molecules and they are of following types :

(i) Albumins. These are water soluble proteins found in all body cells and also in blood stream, *e.g.*, **lactalbu-**



Fibrin threads and red blood cells are clearly visible in this blood clot.

min, found in milk and **serum albumin** found in blood.

(ii) **Globulins**. These are insoluble in water but are soluble in dilute salt solutions of strong acids and bases, *e.g.*, **lactoglobulin** found in milk and **ovoglobulin**.

(iii) **Glutelins**. These plant proteins are soluble in dilute acids and alkalis, *e.g.*, **glutenin** of wheat.

(iv) **Prolamines**. These plant proteins are soluble in 70 to 80 per cent alcohol, *e.g.*, **gliadin** of wheat and **zein** of corn.

(v) **Scleroproteins**. They are insoluble in all neutral solvents and in dilute alkalis and acids, *e.g.*, keratin and collagen.

(vi) **Histones**. These are water soluble proteins which are rich in basic amino acids such as arginine and lysine. In eukaryotes histones are associated with DNA of chromosomes to form nucleoproteins.

(vii) **Protamines**. These are water soluble, basic, light weight, **arginine** rich polypeptides. They are bound to DNA in spermatozoa of some fishes, *e.g.*, **salmine**, of salmon and **sturine** in sturgeons.

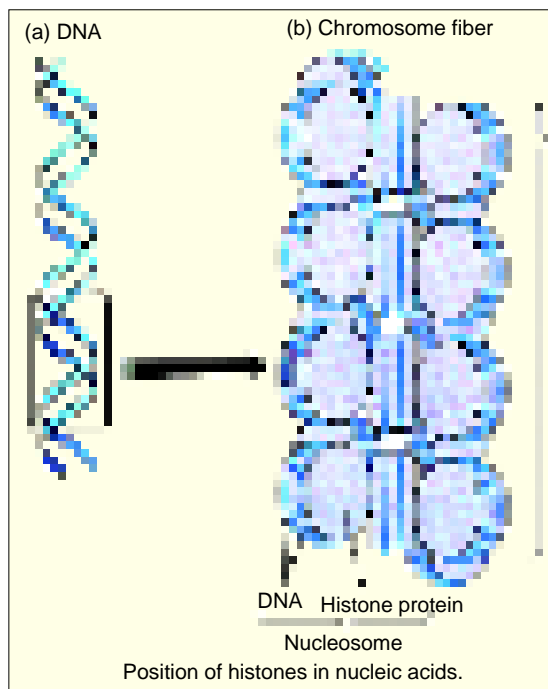
(B) **Conjugated proteins**. These proteins consist of simple proteins in combination with some non-protein components, called **prosthetic groups**. The prosthetic groups are permanently associated with the molecule, usually through covalent and/or non-covalent linkages with the side chains of certain amino acids. Conjugated proteins are of following types :

(i) **Chromoproteins**. Chromoproteins are a heterogeneous group of conjugated proteins which are in combination with a prosthetic group that is a pigment, *e.g.*, respiratory pigments such as **haemoglobin**, **myoglobin** and **haemocyanin**; **catalase**, **cytochromes**, **haemerythrins**; visual purple or **rhodopsin** of rods of retina of eye and yellow enzymes or **flavoproteins**.

(ii) **Glycoproteins**. Glycoproteins are proteins that contain various amounts (1 to 85 per cent) of carbohydrates. Of the known 100 monosaccharides, only nine are found to occur as regular constituents of glycoproteins (*e.g.*, glucose, galactose, mannose, fucose, acetylglucosamine, acetylgalactosamine, acetylneuraminic acid, arabinose and xylose). Glycoproteins are of two main types : 1. **Intracellular glycoproteins** which are present in cell membranes and have an important role in membrane interaction and recognition. They also serve as antigenic determinants and receptor sites.

2. **Secretory glycoproteins** are **plasma glycoproteins** secreted by the liver ; **thyroglobulin**, secreted by the thyroid gland ; **immunoglobulins** secreted by the plasma cells ; **ovoalbumins** secreted by the cells of oviduct of hen ; **ribonucleases** and **deoxyribonucleases**. **Mucus** and **synovial fluid** are also glycoproteins with lubricative properties.

(iii) **Lipoproteins**. Lipid containing proteins are called **lipoproteins**. Their lipid contents are 40 to 90 per cent of their molecular weight and this tends to affect the density of the molecule. There are four types of lipoproteins : 1. **High density lipoproteins (HDL)** or α -lipoproteins; 2. **Low density lipoproteins (LDL)** or β -lipoproteins ; 3. **Very low density lipoproteins (VLDL)** or pre- β -lipoproteins; and 4. **Chylomicrons**. Lipoproteins include some of the blood plasma proteins, various types of membrane proteins, lipovitellin of egg yolk and proteins of brain and nerve tissue.



(iv) **Nucleoproteins.** Nucleoproteins are proteins in combination with nucleic acids (DNA and RNA). However, these proteins are not true conjugated proteins since the nucleic acid involved cannot be regarded as prosthetic groups. Nucleoproteins are of two types : 1. **Histones** which are quite similar in all plants and animals. Their highly basic nature accounts for the close associations histones form with the nucleic acids. Histones are involved in the tight packing of DNA molecules during the condensation of chromatin into chromosomes for the mitosis. 2. **Nonhistones** have great heterogeneous amino acid composition and are acidic in nature. They have selective combination with certain stretches of nuclear DNA and, thus, are involved in the regulation of gene expression.

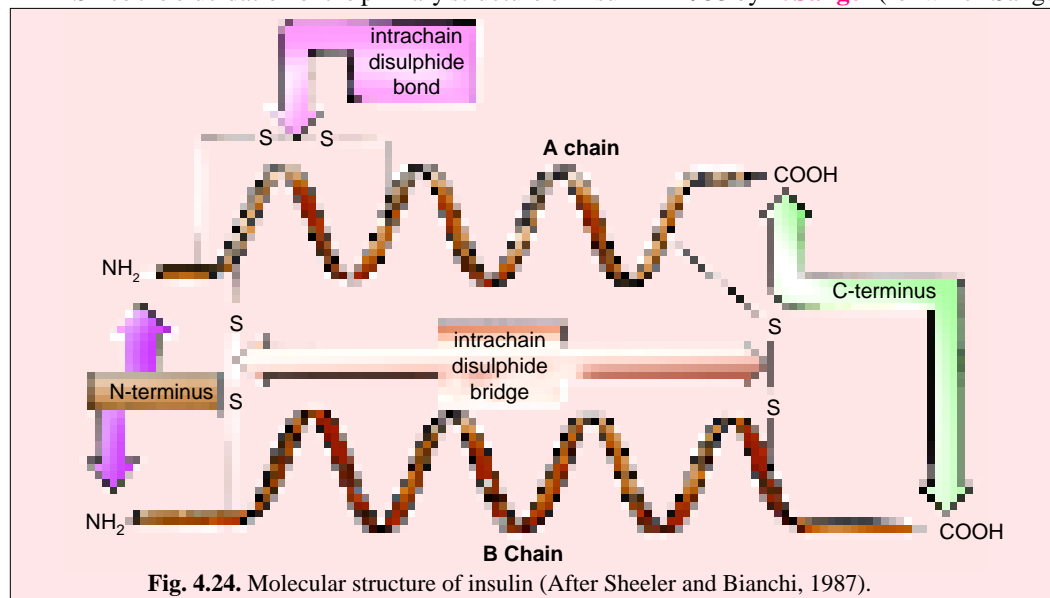
(v) **Metalloproteins.** Metalloproteins are proteins conjugated to metal ions which are not part of the prosthetic group, e.g., **carbonic anhydrase** enzyme contains zinc ions and amino acids in its molecule; **caeruloplasmin**, an oxidase enzyme containing copper; and **siderophilin** contains iron.

(vi) **Phosphoproteins.** Phosphoproteins are proteins in combination with a phosphate group, e.g., casein of the milk and ovovitellin of eggs.

3. Structural levels of proteins. The protein as synthesized on the ribosome is a linear sequence of amino acids, polymerized by the elimination of water between successive amino acids to form the peptide bond, and existing as a randomly coiled chain without specific shape and possessing no biological (*i.e.*, catalytic) activity. Within seconds of synthesis being completed, the protein folds into a specific three-dimensional form, which is the same for all molecules of the same type of protein and which now is capable of doing catalysis. According to their mode of folding the following four levels of protein organization have been recognized :

(a) **Primary protein structure.** The primary protein structure is defined as the particular sequence of amino acids found in the protein. It is determined by the covalent peptide bondings between amino acids. Primary structure also includes other covalent linkages in proteins, for example the linkages that may exist between sulphur atoms of cysteine amino acids located in the chain of the protein insulin. The first protein to have its primary structure determined was of insulin, the pancreatic hormone that regulates glucose metabolism in mammals. Insulin has a molecular weight of 5,800 daltons and contains 51 amino acids. Insulin consists of two polypeptide chains of 21 and 30 amino acid residues, called the A and B chains, respectively (Fig. 4.24). (An **amino acid residue** is that which is left when the elements of water are split out during polymerization).

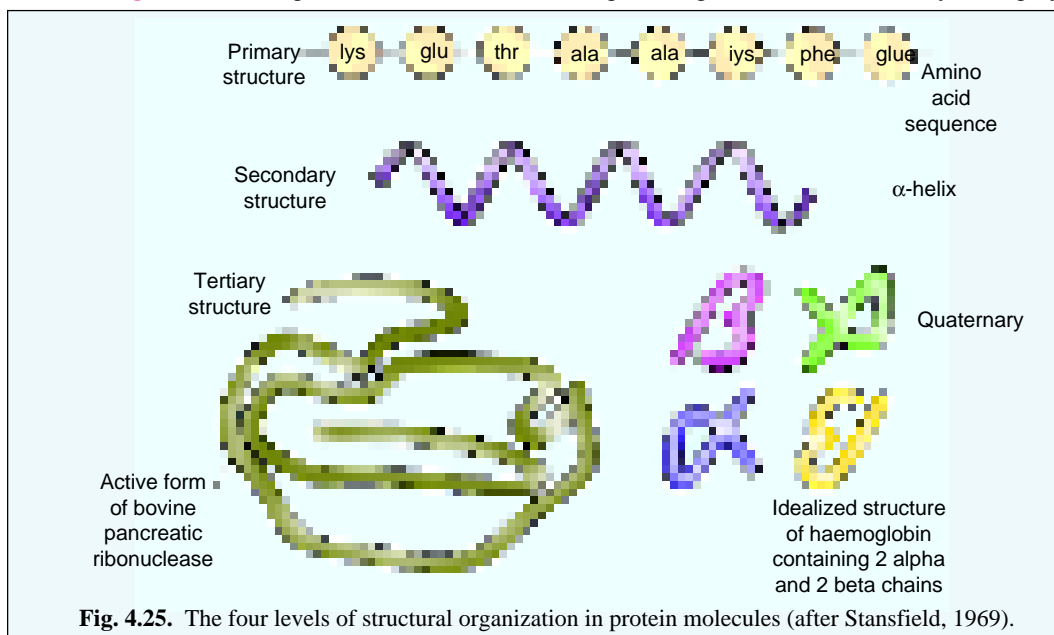
Since the elucidation of the primary structure of insulin in 1953 by **F. Sanger** (for which Sanger



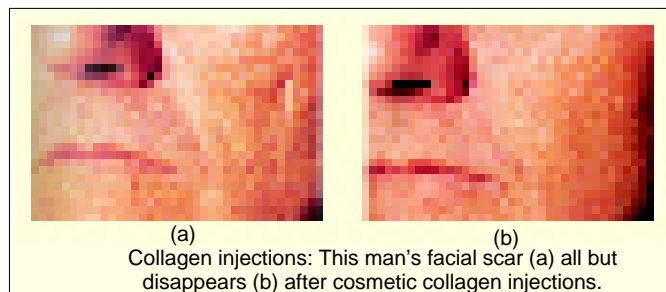
received a Nobel Prize), several hundred proteins have been fully sequenced. Among the fully sequenced proteins are ribonuclease and nearly 100 types of haemoglobin. For example, **Stein** and his coworkers established the amino acid sequence (*i.e.*, primary structure) of the enzyme **ribonuclease**. This enzyme is produced by the pancreas and secreted into the small intestine where it catalyzes the hydrolytic digestion of polyribonucleotide chains (RNA). The ribonuclease consists of a single 124 amino acid polypeptide having a molecular weight of about 12,000.

(b) Secondary protein structure. Secondary structure of the protein is any regular repeating organization of the polypeptide chain. There are three types of secondary protein structure: (1) **Helical structure** (*e.g.*, α -keratin and collagen); (2) **Pleated sheet structure** or **β -structure** (*e.g.*, fibroin of silk); and (3) **Extended configuration** (*e.g.*, stretched keratin). Most fibrous proteins have secondary structure. In globular protein, too, it is not uncommon for half of all the residues of each polypeptide to be organized into one or more specific secondary structures.

Collagen. The collagens (the source of leather, gelatin, glue, etc.) are a family of highly



characteristic fibrous proteins found in all multicellular animals (*e.g.*, in connective tissues). They are secreted by the fibroblasts constituting most abundant (up to 25 per cent of total body's proteins) proteins of mammals. The characteristic feature of collagen (or **tropocollagen**) molecules is their stiff, triple-stranded helical structure (which was discovered by **Rich**, **Crick** and **Rama-chandran**). Three collagen polypeptide chains are left-handed α -helices or alpha chains, each is about 1000 amino acid residues long. These chains are wound around one another in a regular superhelix to generate a rope-like collagen or tropocollagen molecule which is about 300 nm long and 1.5 nm is diameter (Fig. 4.26).

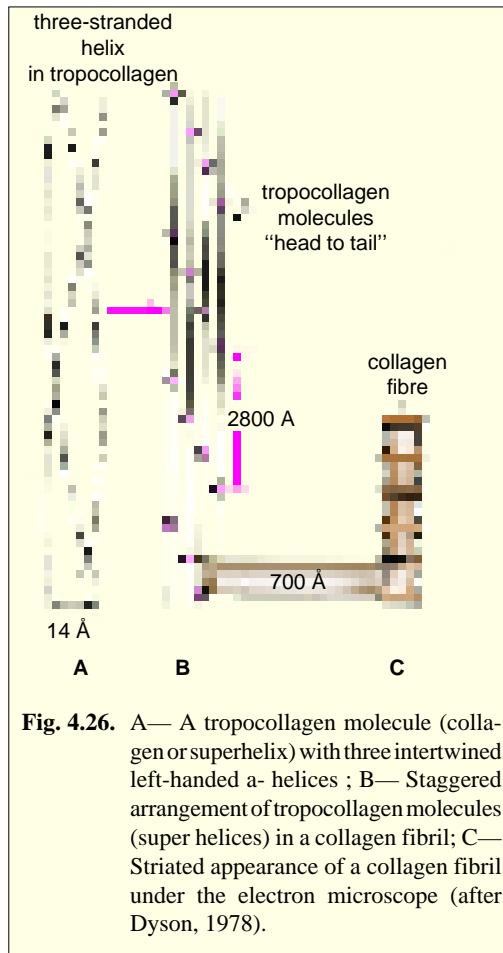
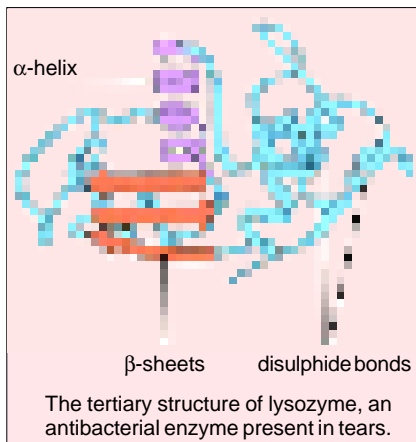


Collagens are exceptionally rich in **proline** (and **hydroxyproline**; both accounting for more than 20 per cent of collagen's amino acids) and **glycine**. Other dominant amino acids of collagens are **lysine** and **alanine**.

So far, about 20 distinct collagen-chains have been identified, each encoded by a separate gene. About 10 types of triplet-stranded collagen molecules have been found to assemble from various combinations of 20 types of α -chains. The best defined are types I, II, III and IV. **Type I collagen** is present in the dermis, tendons, ligaments, bone, cornea, dentine of teeth and internal organs and accounts for 90 per cent of body's collagen. **Type II collagen** is present mainly in cartilage, intervertebral disc, embryonic notochord and vitreous humour of eye. **Type III collagen** occurs in skin, cardiovascular system, gastro-intestinal tract and uterus. **Type IV collagen** is present in basal laminae or basement membranes of epithelia. Type I, II and III collagens are the fibrillar collagens showing typical striated fibres. Type IV collagen lacks a distinct fibrillar structure.

The individual collagen polypeptide chains (α -chains) are synthesized on membrane bound ribosomes and injected in the lumen of ER as larger precursors, called **pro- α -chains**. These precursors have distinct polarity, containing terminal propeptides at their N- and C- terminus. Each pro- α -chain then combines with two others to form a hydrogen-bonded, triple stranded helical molecule, called **procollagen**. Such a procollagen of fibrillar collagens (I, II, and III) is secreted from the fibroblast in the extracellular space. Due to enzyme action its terminal propeptides are removed and the procollagen is converted into a **tropocollagen molecule**.

Many tropocollagen molecules spontaneously assemble into the ordered arrays, called **collagen fibrils**. The collagen fibrils are thin (10 to 300 nm in diameter), cable-like structures, many micrometres long, exhibiting cross-striations every 67 nm and are clearly visible in the electron microscope. The collagen fibrils often aggregate into larger bundles which can be seen in light microscope as **collagen fibres**. Type IV collagen molecules assemble to form a sheet-like **meshwork** that constitutes a major part of all basal laminae (Martin *et al.*, 1985, Burgeson, 1988).



(C) Tertiary protein structure. Tertiary protein structure refers to a more compact structure in which the helical and non-helical regions of a polypeptide chain are folded back on themselves. This structure is typical of globular protein structure, in which it is the non-helical region that permits the folding. The folding of a polypeptide chain is not random but occurs in a specific fashion, thereby imparting certain steric (*i.e.*, three-dimensional) properties to the protein. For example, in enzymes folding brings together **active amino acids**, which are otherwise

scattered along the chain, and may form a distinctive cavity or cleft in which the substrate is bound.

The complete tertiary structure of a protein can only be deduced by a laborious analysis of X-ray scattering patterns from crystals. The first protein to have its secondary and tertiary structure determined was **myoglobin**, a 153-amino acid, oxygen-binding protein found primarily in red muscle and largely responsible for the colour of that tissue. The work was done at Cambridge under the direction of **J.C. Kendrew** (1961). Although at some points the polypeptide chain does have secondary structure (alpha-helical structure), the chain is mainly characterized by seemingly random loops and folds.

In a tertiary protein the polypeptide chain is held in position by weak secondary bonds which are of different types such as **ionic bonds** (or electrostatic bonds or salt or salt bridges); **hydrogen bonds**; **hydrophobic bonds** and **disulphide bonds**.

(d) Quaternary protein structure. In proteins that are composed of two or more polypeptide chains, the quaternary structure refers to the specific orientation of these chains with respect to one another and the nature of the interactions that stabilize this orientation. The individual polypeptide chains of the protein are called **sub-units** and the active protein itself is called **multimer**. While multimeric proteins containing up to 32 subunits have been described, the most common multimers are **dimers**, **trimers**, **tetramers**, **pentamers** (*e.g.*, RNA polymerase) and **decamers** (*e.g.*, DNA polymerase III) (Table 4-6). If the protein consists of identical sub-units, it is called **homopolymers** and is said to have **homogeneous quaternary structure**, *e.g.*, the isozymes H_4 and M_4 of lactic dehydrogenase (LDH), enzyme phosphorylase and L-arabinose isomerase. The enzyme β -galactosidase consists of four identical polypeptide chains. Lastly, when the sub-units of the protein are different, the protein is called **heteropolymer** and is said to have a heterogeneous quaternary structure, *e.g.*, haemoglobin and immunoglobulins. Quaternary proteins are usually joined by hydrophobic forces. Hydrogen bonds, ionic bonds and possibly disulphide bonds may also participate in forming quaternary structures.

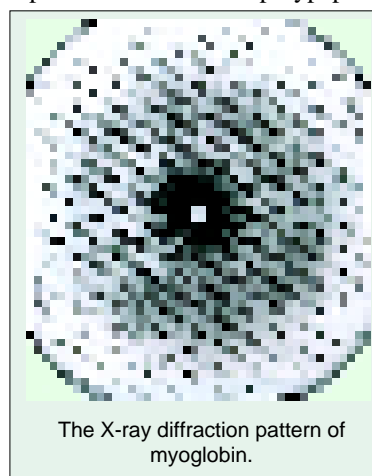


Table 4-6.

Subunits and molecular weight of some multimer proteins (Source : **Sheeler and Bianchi, 1987**).

Protein	Molecular weight	Number	Subunits Designation	Molecular weight
1. Haemoglobin A (human)	64,500	4	Alpha chains (2) Beta chains (2)	15,700 16,500
2. Lactate dehydrogenase	135,000	4	A chain (0 to 4) B chain (4 to 0)	33,600 33,600
3. Immunoglobulin G	150,000	4	Light chains (2) Heavy chains (2)	25,000 50,000
4. Tryptophan synthetase (<i>E.coli</i>)	150,000	4	Alpha chains (2) Beta chains (2)	29,500 45,000
5. Aspartate transcarbamylase	306,000	12	C chains (6) R chains (6)	34,000 17,000
6. L-arabinose isomerase (<i>E.coli</i>)	360,000	6	(identical)	60,000
7. Apoferritin (iron storage protein)	456,000	24	(identical)	19,000
8. Thyroglobulin	670,000	2	(identical)	3,35,000

Some Examples of Tertiary and Quaternary Proteins

(i) **Ribonuclease. C.B. Anfinsen** initiated and confirmed the notion that, acting in concert, the specific primary structure of a polypeptide and the innate properties of the side chains of its amino acids cause the polypeptide to spontaneously assume its biologically active tertiary structure. In 1972, he got the Nobel Prize for this definitive work. **Anfinsen** identified four disulphide bridges in the ribonuclease protein, suggesting that the enzyme is highly folded (Fig. 4.25). As is the case with almost all enzymes, the catalytic activity of ribonuclease depends on the maintenance of a particular three-dimensional shape. In concentrated solutions of β -mercaptoethanol and urea, the disulphide bridges of the enzyme are broken and the resultant unfolding of the polypeptide chain is accompanied by a loss of enzyme activity. The enzyme is said to be **denatured**. If the β -mercaptoethanol and urea are removed by dialysis and the denatured ribonuclease reacted with oxygen, the four disulphide bridges re-form spontaneously, and essentially all the catalytic activity of the protein is restored. Similar observations have been made with other proteins, that is, they are capable of spontaneously re-establishing their biologically active tertiary (or even quaternary, *e.g.*, haemoglobin) structure after having undergone extensive molecular disorganization.

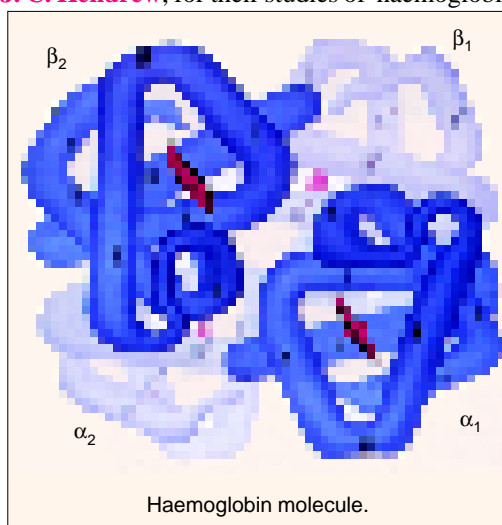
(ii) **Haemoglobin.** Haemoglobin is one of the fully sequenced protein. Our present understanding of the structure and function of haemoglobin is the outcome of 50 years of research of **M. F. Perutz**. He got the Nobel Prize in 1962, along with **J. C. Kendrew**, for their studies of haemoglobin and myoglobin.

The haemoglobin is a conjugated globular protein, that is, it contains some non-protein part. In all but the lowest vertebrates, haemoglobin is a tetramer (a heteropolymer). In lampreys, however, haemoglobin is monomeric, that is, it contains a single globin chain like the myoglobin. In humans, most common type of haemoglobin is haemoglobin A (HbA), which consists of 574 amino acid residues and has a molecular weight of 64,500. Its secondary, tertiary and quaternary structure is typical of all higher vertebrate haemoglobins. The protein portion of the haemoglobin molecule, called **globin**, is composed of four polypeptide chains, each of which is also globular in shape. The four globin chains consist of two identical pairs : two **alpha chains** (141 amino acids each) and two **beta chains** (146

amino acids each). The non-protein portion of haemoglobin consists of four iron-containing haem groups, one associated with each of the four globin chains. Nineteen of the twenty biologically important amino acids are included in the globin of haemoglobin.

Haemoglobin molecule is highly symmetric; it can be divided into two identical halves, each consisting of an $\alpha\beta$ - dimer. The complete tetramer is similar to a mildly flattened sphere having a maximum diameter of about 5.5 nm. The four polypeptide chains are arranged in such a way that unlike chains have numerous stabilizing interactions, whereas, like chains have few. A cavity about 2.5 nm long and varying in width from about 5 to 10 Å passes through the molecule along the axis. Each globin chain envelops its haem group in a deep cleft.

(iii) **Immunoglobulins.** The ability to resist infection by pathogens (viruses, bacteria and other unicellular parasites) and by multicellular endoparasites, is called **immunity**. Specific immune response function by recognizing particular chemical structures, known as **antigens**—on the surface



of invading cells. An antigen can be a protein, lipid, carbohydrate or any other molecule. These antigens interact with protein molecules produced by the host, the **immunoglobulins**, which bind the antigen in much the same way as an enzyme binds its substrate. Specific **immune responses involve many different types of cells. One type, the B-lymphocyte or B-cell**, is capable of producing **free immunoglobulins**, called **antibodies**.

An immunoglobulin (Ig) molecule is a Y-shaped heteropolymer and is composed of two identical **H (heavy)** polypeptide chains

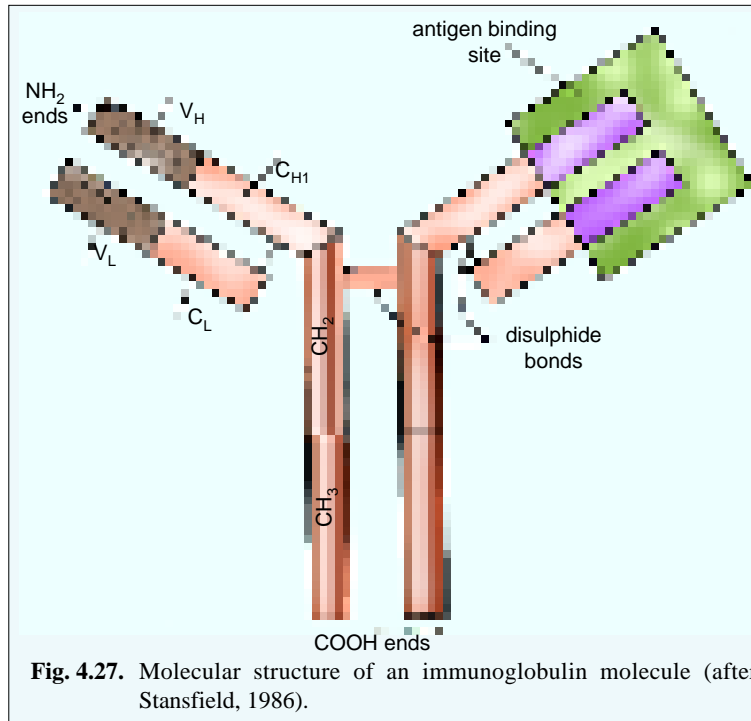
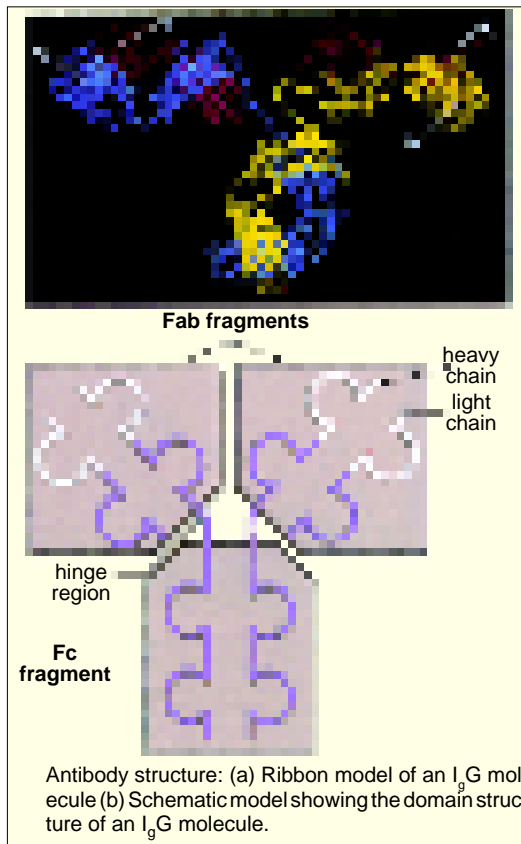


Fig. 4.27. Molecular structure of an immunoglobulin molecule (after Stansfield, 1986).



and two smaller identical **L (Light)** polypeptide chains (Fig. 4.30). Heavy chains contain antigenic determinants in the “tail” (carboxyl) segments by which they can be classified as Ig G, Ig M, Ig A, Ig D or Ig E. Light chains can likewise be typed as kappa or lambda. Within a H chain class or L chain type, these segments exhibit very little variation in primary structure from one individual to another and are called **constant regions (C)**. The amino ($-NH_2$) ends, however, are extremely diverse in primary structure, even within a class and are called **variable (V) regions**. The V_H and V_L regions together form two **antibody-combining sites** (called **antigen - binding sites**) for specific interactions with homologous antigen molecules. The C_H region consists of three or four similar segments, presumably derived evolutionarily by duplication of an ancestral gene and subsequent modification by mutations; the similar segments are called **domains** and are labelled CH_1 , CH_2 , CH_3 , etc. A mature lymphocyte (plasma cell) produces antibodies with a single class H chain and a single type of L chain, hence, also a single antigen-binding specificity. The first antibodies produced by a developing plasma cells are usually of class Ig M.

Enzymes

The cytoplasmic matrix and many cellular organelles contain very important organic compounds known as the **enzymes**. The word enzyme (Greek. "in yeast") had been proposed by **Kuhne** in 1878. The enzymes are the specialized proteins and they have the capacity to act as catalysts in chemical reaction. Like the other catalysts of chemical world, the enzymes are the catalysts of the biological world and they influence the rate of a chemical reaction, while themselves remain quite unchanged at the end of the reaction. The substance on which the enzymes act is known as **substrate**. The enzymes play a vital role in various metabolic and biosynthetic activities of the cell such as synthesis (anabolism) of DNA, RNA and protein molecules and catabolism of carbohydrates, lipids, fats and other chemical substances. The enzymes of the matrix and cellular organelles are classified as follows :

1. Oxireductases. The enzymes catalyzing the oxidation and reduction reaction of the cell are known as oxireductases. These enzymes transfer the electrons and hydrogen ions from the substrates, *e.g.*, hydrogenases or reductases, oxidases, oxygenases and peroxidases.

2. Transferases. The enzymes which transfer following groups from one molecule to other are known as transferases : one carbon, aldehydic or ketonic residues, acyl, glycosyl, alkyl, nitrogenous, phosphorus containing groups and sulphur containing groups.

3. Hydrolases. These enzymes hydrolyse a complex molecule into two compounds by adding the element of the water across the bond which is cleaved. These enzymes act on the following bonds—ester, glycosyl, ether, peptide, other C–N bonds, acid anhydride, C–C, halide and P–N bonds. Certain important hydrolase enzymes are the proteases, esterases, phosphatases, nucleases and phosphorylases.

4. Lysases. The lysase enzymes add or remove group to or from the chemical compounds containing the double bonds. The lysases act on C–C, C–O, C–N, C–S and C–halide bonds.

5. Isomerases. These enzymes catalyse the reaction involving in the isomerization or intramolecular rearrangements in the substrates, *e.g.*, intramolecular oxidoreductases, intramolecular transferases, intramolecular lysases, cis-trans-isomerases, racemases and epimerases.

6. Ligases or synthetases. These enzymes catalyze the linkage of the molecules by splitting a phosphate bond. The synthetase enzymes form C–O, C–S, C–N and C–C bonds.

According to the chemical nature of the substrate the enzymes have also been classified as follows:

1. Carbohydrases, 2. Proteases (endopeptidases and exopeptidases), 3. Amylases, 4. Esterases, 5. Dehydrogenases, 6. Oxidases, 7. Decarboxylases, 8. Hydrases, 9. Transferases, and 10. Isomerases.

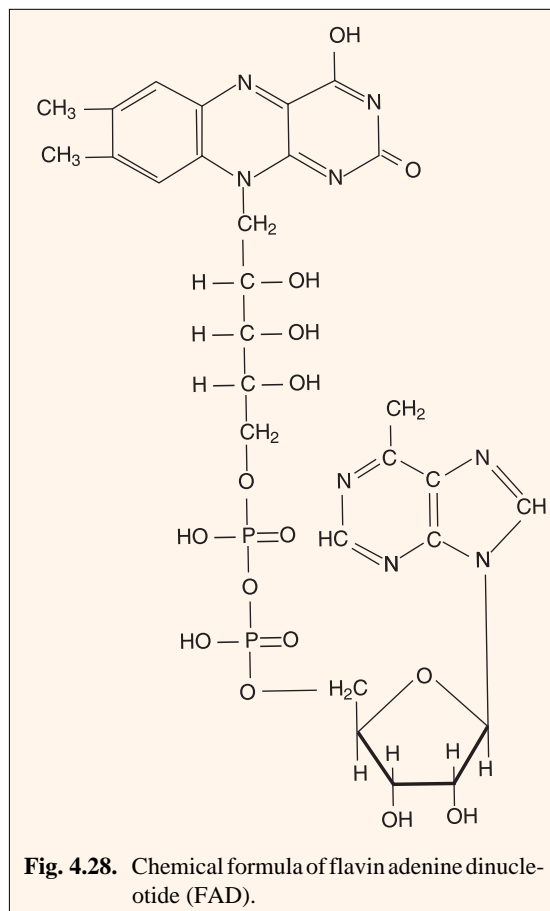


Fig. 4.28. Chemical formula of flavin adenine dinucleotide (FAD).

The enzymes are **specific** in action and many factors such as pH, temperature and concentration of the substrate affect the rate of the activity of enzymes. Certain enzymes occur in the inactive form (called **proenzymes** or **zymogens**) and these are activated by other enzymes known as **kinases** to perform catalytic activities. Likewise, the enzyme **trypsinogen** of the pancreatic cells is activated in the intestine by the enzyme **enterokinase** and the enzyme **pepsinogen** of the Chief cells of the stomach is activated by the **hydrochloric acid** which is secreted by parietal cells.

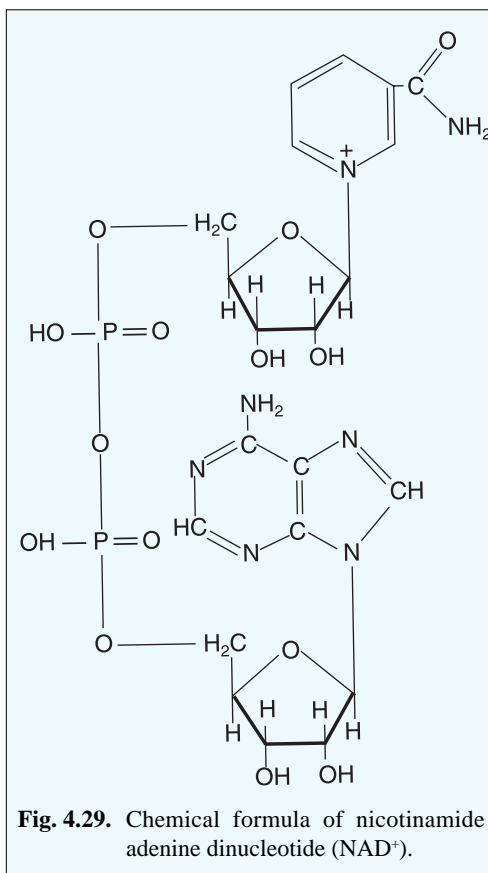
Prosthetic Groups and Coenzymes

Certain enzymes such as **cytochromes** are the conjugated proteins and contain prosthetic group as **metalloporphyrins** complex in their molecules.

Certain enzymes cannot function singly but they can function only by the addition with the small molecules of other chemical substances which are known as **coenzymes**. The inactive enzyme (which cannot function singly) is known as the **apoenzyme**. The apoenzyme and coenzyme are collectively known as **holoenzyme**. For instance, the enzyme **hydrogenase** is an apoenzyme which can function either with the coenzyme NAD^+ or NADP .

Some important coenzymes or cofactors are as follows :

1. Nicotinamide adenine dinucleotide (NAD) or Diphosphopyridine nucleotide (DPN),
2. Nicotinamide adenine dinucleotide phosphate (NADP) or Triphosphopyridine nucleotide (TPN),
3. Flavin adenine mononucleotide (FAM),
4. Flavin adenine dinucleotide (FAD),
5. Ubiquinone (coenzyme Q or Q),
6. Lipoic acid (LIP or S_2),
7. Adenosine triphosphate (ATP),
8. Pyridoxyl phosphate (PALP),
9. Tetrahydrofolic acid (CoF),
10. Adenosyl methionine,
11. Biotin,
12. Coenzyme A (CoA),
13. Thiamine pyrophosphate (TPP),
14. Uridine diphosphate (UDP).

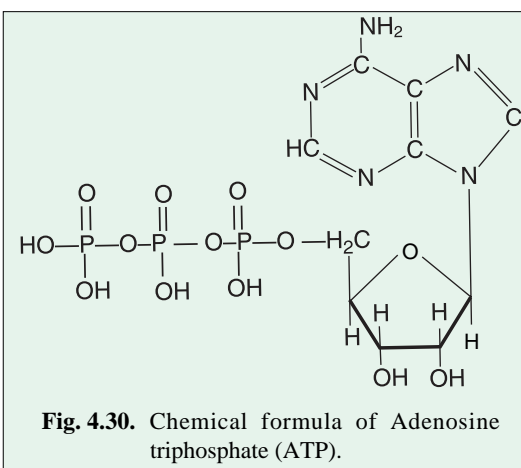


Isoenzymes

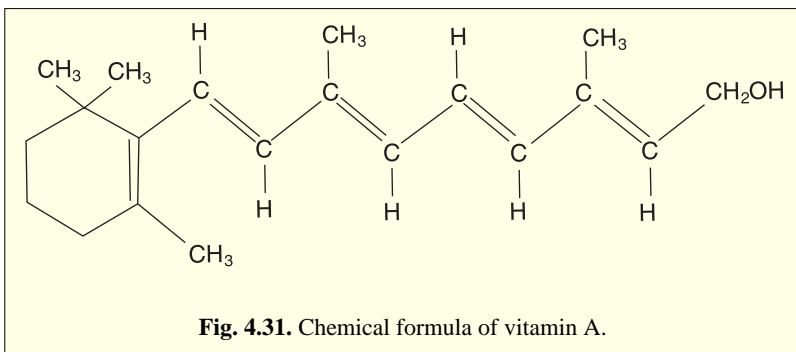
Recently, it has been investigated that some enzymes have similar activities and almost similar molecular structures. These enzymes are known as **isoenzymes**. The isoenzymes have relation with the heredity (**Latner** and **Skillen**, 1969, and **Weyer** 1968). There are about 100 isoenzymes in the cell, e.g., lactic dehydrogenase (LDH) occur in the form of five identical isoenzymes.

Vitamins

The vitamins are organic compounds of diverse chemical nature. They are required in minute amounts for normal growth, functioning



and reproduction of cells. The vitamins play an important role in the cellular metabolism and act as the enzymes or other biological catalysts in the various chemical activities of the cell. Their importance for the animals has been reported by **Hopkins, Osborne, Mendal**, and **McCollum** (1912–1913). **Funk** (1912) demonstrated the presence of basic nitrogen in them and gave the name “vitamins” meaning vital amines to them.



The animal cell cannot synthesize the vitamins from the standard food and so they are taken along with the food. Their deficiency in the cell causes metabolic disorder and leads to various diseases. For example, the deficiency of ascorbic acid (Vitamin C) inhibits procol-

lagen helix formation. Normal collagens are continuously degraded by specific extracellular enzymes, called **collagenases**. In scurvy, the defective pro- α -chains that are synthesized, fail to form a triple helix and are immediately degraded. Consequently, with the gradual loss of the pre-existing normal collagen in the matrix, blood vessels become extremely fragile and teeth become loose in their sockets. This implies that in these particular tissues degradation and replacement of collagens is relatively fast. For example, in bones, the ‘turnover’ of collagen is very slow, *i.e.*, in bone, collagen molecule persists for about 10 years before they are degraded and replaced (see **Alberts et al.**, 1989). The vitamins of utmost biological importance have been tabulated in Table 4-7.

Hormones

Hormones are the complex organic compounds which occur in traces in the cytoplasm and regulate the synthesis of mRNA, enzymes and various other intracellular physiological activities. The most important hormones are growth hormones, estrogen, androgen, insulin, thyroxine, cortisone, and adrenocortical hormones, etc. These hormones are synthesized by the ductless or endocrine glands and transported to various cells of multicellular organisms by blood vascular system. In cells they regulate various metabolic activities. For example, the ecdysone hormone has been found to form puffs (Balbiani rings) in the giant chromosomes of insects. The hormones activate or depress the gene at the

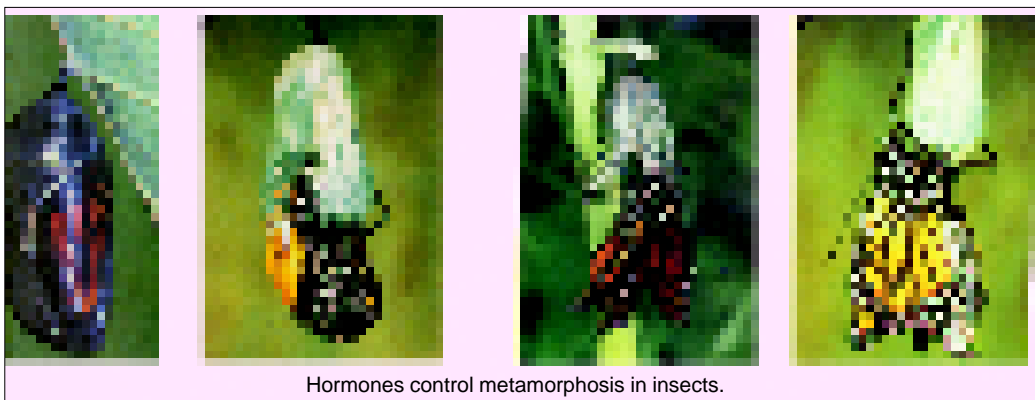
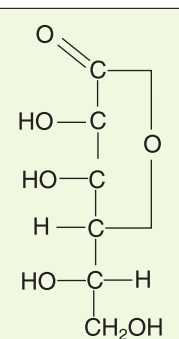


Table 4-7. Vitamins and their characteristics.

Vitamin	Daily requirement	Sources	Functions	Diseases and symptoms caused by lack of vitamin
Fat Soluble Vitamins				
1. Vitamin A (Retinol)	750 μ gm	Animal fats (fish liver oil, egg-yolk, milk, butter, cheese); palm oils; red peppers; dark green leafy vegetables (spinach, methi, cabbage); yellow vegetables (carrot, pumpkin) and yellow fruits (mango, papaya).	Stored in liver; maintain general health and vigour of epithelial cells.	1. Skin becomes dry and scaly and so does cornea of eyes causing xerophthalmia or 'dry eye'; 2. Night blindness or nyctalopia (inability to see in dimlight).
2. Vitamin D (Calciferol)	200 IU (5 μ gm)	Fish liver oils, liver, egg-yolk, butter, fresh milk; also produced by our body when skin-cholesterol is exposed to ultra-violet rays of sunlight.	Involved in intestinal absorption of calcium and phosphorus and in calcium metabolism and bone formation.	1. Rickets in children; 2. Osteomalacia in adults.
3. Vitamin E (Tocopherol)	Trace amounts (15 IU)	Vegetable oils (especially polysaturated fatty acids); wheat germ oil; egg-yolk; green leafy vegetables; tomato; milk and butter.	Inhibit catabolism (<i>i.e.</i> , oxidation) of certain fatty acids of cellular membranes.	Hemolytic anemia due to oxidation of unsaturated fats resulting in abnormal structure and function of mitochondria, lysosomes and plasma membrane of cells.
4. Vitamin K (Naphthoquinone)	Trace amounts	Naturally produced by intestinal bacteria; liver; fresh green vegetables (spinach, cabbage, cauliflower).	Required for the formation of prothrombin (an essential component of blood-clotting).	Haemorrhage or bleeding in new-born infants; scurvy-like symptoms (blood takes longer to clot).
Water Soluble Vitamins				
5. Vitamin B (Thiamine)	1.3 mg (boys) 1.2 mg (girls)	Yeast; whole cereals (<i>e.g.</i> , unpolished rice); pulses; oil-seeds, soyabean; nuts (especially groundnut); liver, pork, sea food, green leafy vegetables.	1. Essential for synthesis of acetylcholine; 2. Rapidly destroyed by heat. 3. Carbohydrate metabolism.	1. Beriberi . Partial paralysis of smooth muscle of gastrointestinal tract; paralysis of skeletal muscles, atrophy of limbs. 2. Polyneuritis .
6. Vitamin B ₂ (Riboflavin)	1.6 mg (boys) 1.4 mg (girls)	Peas, beans, milk, egg-white, liver, kidney, germinated cereals and pulses, growing green leafy vegetables.	Forms the coenzyme FAD which is involved in metabolism of carbohydrates and proteins.	1. Blurred vision, cataract and corneal ulceration; 2. Dermatitis (inflammation of skin); 3. Cheilosis (cracking of skin at the corners of mouth and scaling of lips).

Vitamin	Daily requirement	Sources	Functions	Diseases and symptoms caused by lack of vitamin
7. Niacin (Nicotinic acid)	18 mg (boys) 15 mg (girls)	Meat, liver, fish, chicken, yeast, whole grain, peas, beans, pulses, nuts (ground-nuts) potato, tomato, green vegetables, germinated seeds and milk (Maize is deficient in niacin).	1. Forms the coenzyme NAD which is involved in energy-releasing reactions; 2. In lipid metabolism inhibits production of cholesterol and help in fat breakdown.	Pellagra , a disease characterised by three D's-dermatitis, diarrhoea and dementia (psychological disturbance).
8. Vitamin B ₆ (Pyridoxin)	1.5–2 mg	Liver, meat, fish (salmon), whole cereals, yellow corn, legumes, tomatoes, yoghurt.	1. Forms coenzymes involved in amino acid metabolism in brain; 2. Involved in fat metabolism.	1. Convulsions; 2. Dermatitis of eyes, nose and mouth; 3. Retarded growth.
9. Folic acid	50–100 mg	Green leafy vegetables, germinated pulses, eggs, liver.	1. Essential for synthesis of DNA. 2. Overcooking destroys it.	Macrocytic anaemia (production of abnormally large red blood cells).
10. Biotin (Vitamin H)	0.3 mg	Yeast, liver, egg-yolk, milk, kidneys.	Acts as coenzyme in metabolism of carbohydrates, fatty acids and nucleic acid.	1. Mental depression; 2. Muscular pain, fatigue; 3. Dermatitis; 4. Nausea.
11. Vitamin B ₁₂ (Cyanocobalamin)	0.2–1.0 μ gm	Liver, kidney, meat, fish, eggs, milk, cheese	Acts as coenzyme necessary for DNA synthesis, red blood cell formation, growth and nerve function.	1. Pernicious anaemia; 2. Malfunctioning of nervous system.
12. Vitamin C (Ascorbic acid)	40 mg	Amla, guava, citrus fruits (lime, lemon, orange), tomatoes, green leafy vegetables (cabbage, <i>chauli</i> and cauliflower).	1. Promotes protein synthesis (collagen), wound healing and iron absorption; 2. Protects body against infections; 3. Rapidly destroyed by heat.	Scurvy. A disease characterised by swelling of gums, multiple haemorrhages, anaemia and weakness.

particular locus on the chromosome. Thus, hormones serve to coordinate the various activities concerned with a particular function, *e.g.*, the hormone ecdysone controls moulting and metamorphosis in insects (**Beermann**, 1965).

In mammalian liver cells, the enzymes which convert glucose into glycogen are regulated by the hormone insulin which is synthesized by β -cells of the islets of Langerhans in the pancreas. Moreover, the hormone thyroxine, a secretion of thyroid gland, activates the enzyme phosphorylase to form glucose phosphate from the glycogen.

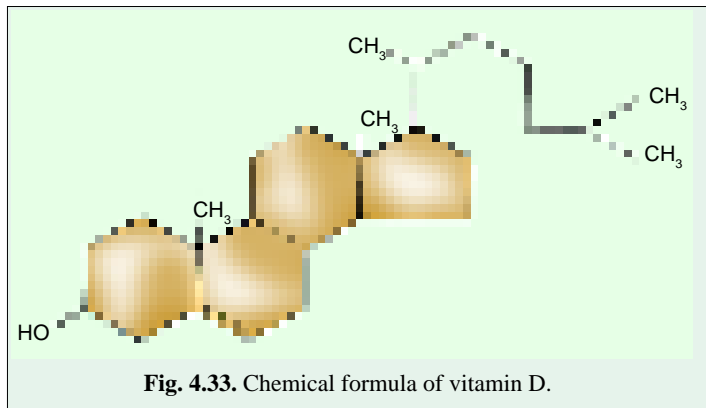


Fig. 4.33. Chemical formula of vitamin D.

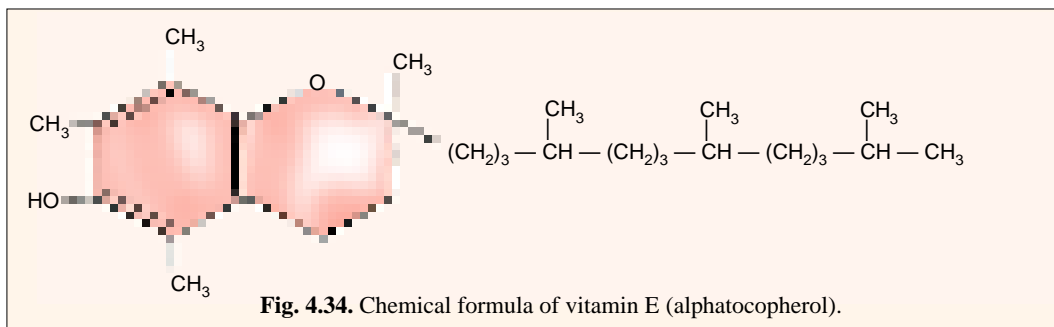
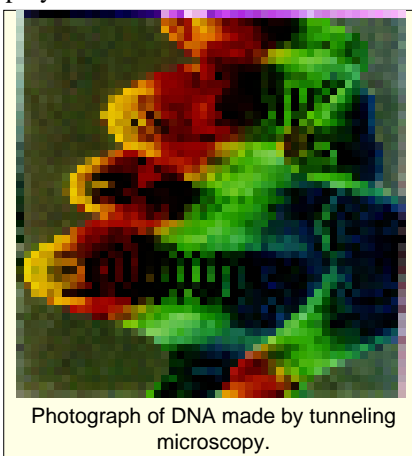


Fig. 4.34. Chemical formula of vitamin E (alphatocopherol).

Nucleic Acids

The nucleic acids are the complex macromolecular organic compounds of immense biological importance. They control the important biosynthetic activities of the cell and carry hereditary informations from generation to generation. There occur two types of nucleic acids in living organisms, *viz.*, **Ribonucleic acid (RNA)** and **Deoxyribonucleic acid (DNA)**. Both types of nucleic acids are the polymers of the nucleotides. A nucleotide is composed of nucleoside and phosphoric acid. Even the



Photograph of DNA made by tunneling microscopy.

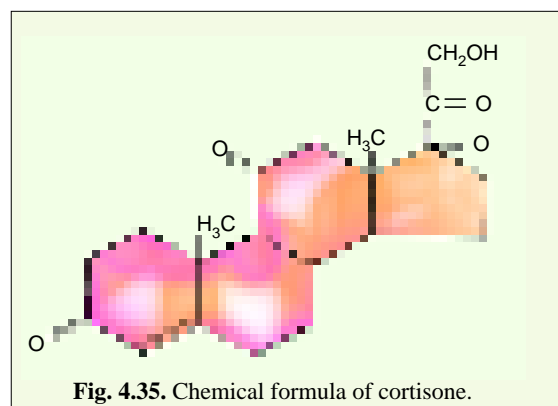


Fig. 4.35. Chemical formula of cortisone.

nucleoside is composed of the pentose sugars (Ribose or Deoxyribose) and nitrogen bases (Purines or Pyrimidines). The **purines** are **adenine** and **guanine** and the **pyrimidines** are the **cytosine**, **thymine** and **uracil**. The cytoplasmic matrix contains only RNA, while DNA exclusively remains concentrated in the nucleus.

The DNA and RNA have almost similar chemical compositions except a few differences. Both have been compared in Table 4-8.

PROPERTIES OF CYTOPLASMIC MATRIX

The matrix is a living substance and it has following physical and biological properties :

Physical Properties

The most of the physical properties of the matrix are due to its colloidal nature and these are as follows :

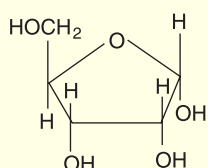


Fig. 4.36. Chemical formula of ribose sugar.

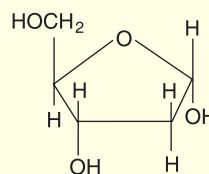


Fig. 4.37. Chemical formula of deoxyribose sugar.

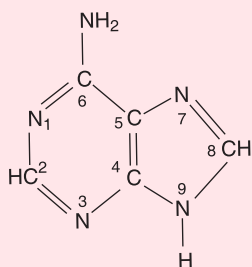


Fig. 4.38. Chemical formula of adenine.

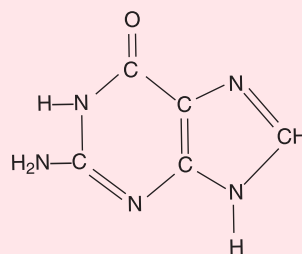


Fig. 4.39. Chemical formula of guanine.

1. Tyndall's effect. When a beam of strong light is passed through the colloidal system of the matrix at right angles in the dark room, the small colloidal particles which remain suspended in the colloidal system, reflect the light. The path of the light appears like a cone. This light cone is known as **Tyndall's cone** because this phenomenon has been first of all reported by **Tyndall** (1820—1893) in colloids.

2. Brownian movement. The suspended colloidal particles of the matrix always move in zig-

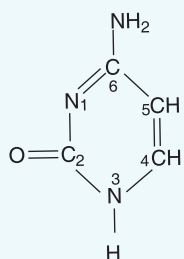


Fig. 4.40. Chemical formula of cytosine.

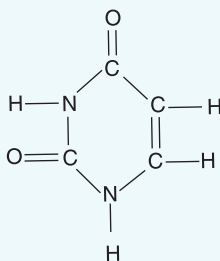


Fig. 4.41. Chemical formula of uracil.

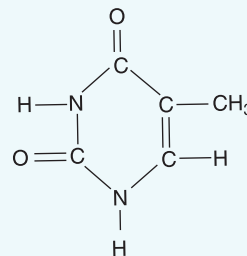


Fig. 4.42. Chemical formula of thymine.

zag fashion. This movement of molecules is caused by moving water molecules which strike with the colloidal molecules to provide motion to them. This type of movement was first of all observed by Scottish botanist **Robert Brown** in 1827 in the colloidal solution. Therefore, such movements are known as **Brownian movement**. The Brownian movement is the peculiarity of all colloidal solutions and depends on the size of the particles and temperature.

Table 4-8. Comparison of DNA and RNA.

DNA	RNA
1. It contains pentose sugar known as deoxyribose.	1. It contains pentose sugar called the ribose.
2. The molecule contains the phosphoric acid (phosphate) molecule which connects various sugars with one another.	2. The molecule contains the phosphoric acid (phosphate) molecule which connects various sugars with one another.
3. The nitrogen bases are : (i) Purines —adenine and guanine. (ii) Pyrimidine —cytosine and thymine.	3. The molecule contains following nitrogen bases in its molecule: (i) Purines —adenine and guanine. (ii) Pyrimidines —cytosine and uracil.
4. Molecules have four nucleotides as deoxyadenosine monophosphate, deoxyguanosine monophosphate, deoxycytidine monophosphate and thymidine monophosphate.	4. Molecules have four nucleotides as adenosine monophosphate, guanosine monophosphate, cytidine monophosphate and uridine monophosphate.
5. The molecule contains a double stranded helix structure in which many nucleotides remain arranged in pair.	5. The molecules consist of single chain of polynucleotides.
6. DNA is a genetic material and occurs in chromosomes, nucleoplasm and mitochondria, etc.	6. RNA is a carrier of genetic informations and it plays very significant role in the mechanism of protein synthesis. It mostly occurs in nucleolus, nucleoplasm and cytoplasm.

3. Cyclosis and amoeboid movement. Due to the phase reversal property of the cytoplasmic matrix, the intracellular streaming or movement of the matrix takes place. This property of intracellular movement of matrix is known as the **cyclosis**. The cyclosis usually occurs in the sol-phase of the matrix and is effected by the hydrostatic pressure, temperature, pH, viscosity, etc. The intracellular movements of the pinosomes, phagosomes and various cytoplasmic organelles such as the lysosomes, mitochondria, chromosomes, centrioles, etc., occur only due to cyclosis of the matrix. The cyclosis has been observed in most animal and plant cells.

The amoeboid movement depends directly on the cyclosis. The amoeboid movement occurs in the protozoans, leucocytes, epithelia, mesenchymal and other cells. In the amoeboid movement the cell changes its shape actively and gives out cytoplasmic projections known as **pseudopodia**. Due to cyclosis matrix moves these pseudopodia and this causes forward motion of the cell.

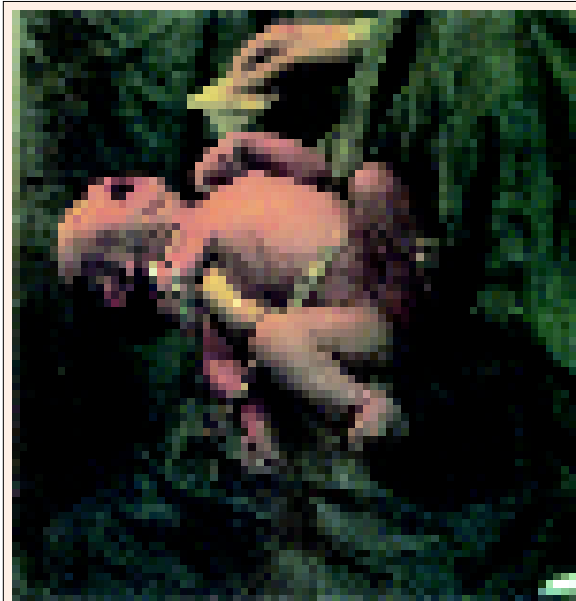
4. Surface tension. The molecules in the interior of a homogeneous liquid are free to move and are attracted by surrounding molecules equally in all directions. At the surface of the liquid where it touches air or some other liquid, however, they are attracted downward and sideways or inward, more than upward; consequently they are subjected to unequal stress and are held together to form a membrane. The force by which the molecules are bound is called the **surface tension** of the liquid. The cytoplasmic matrix being a liquid possesses the property of surface tension. The proteins and lipids of matrix have less surface tension, therefore, occur at the surface and form the membrane, while the chemical substances such as NaCl have high surface tension, therefore, occur in deeper part of the matrix.

5. Adsorption. The increase in the concentration of a substance at the surface of a solution is known as adsorption (L., *ad*=to, *sorbex*=to draw in). The phenomenon of adsorption helps the matrix to form protein boundaries.

6. Other mechanical or physical properties of matrix. Besides surface tension and adsorption, the matrix possesses other mechanical properties, *e.g.*, elasticity, contractility, rigidity and viscosity which provide to the matrix many physiological utilities.

7. Polarity of the egg. The colloidal system due to its stable phase determines the polarity of the cell matrix which cannot be altered by centrifugation of other mechanical means.

8. Buffers and pH. The matrix has a definite pH value and it does not tolerate significant variations in its pH balance. Yet various metabolic activities produce small amount of excess acids or bases. Therefore, to protect itself from such pH variation the matrix contains certain chemical compounds as carbonate-bicarbonate system known as **buffers** which maintain a constant state of pH in the matrix.



Surface tension: A baby's first breath is facilitated by a special coating called a surfactant, which the lungs secrete. This material acts much like a detergent to decrease the surface tension of the fluid layer lining the lungs. Without the surfactant hydrogen bonds in the water lining the small sacs of the lungs would pull water molecules together so tightly that the sacs would collapse.

Biological Properties

The matrix is a living substance and it has following biological properties :

1. Irritability. The irritability is the fundamental and inherent property of the matrix. It possesses a sensitivity to stimulation, an ability to transmission of excitation and ability to react according to stimuli. The heat, light, chemical substances and other factors stimulate the cytoplasmic matrix to contract.

2. Conductivity. The conductivity is the process of conduction or transmission of excitation from the place of its origin to the region of its reaction. The matrix of nerve cells possesses the property of the conductivity.

3. Movement. The cytoplasmic matrix can perform movement due to cyclosis. The cyclosis depends on the age, water contents, heredity factors and composition of the cells.

4. Metabolism. The matrix is the seat of various chemical activities. These activities may be either constructive or destructive in nature. The constructive processes such as biosynthesis of proteins, lipids, carbohydrates and nucleic acids are known as **anabolic processes**, while the destructive processes such as oxidation of foodstuffs, etc., are known as **catabolic processes**. The anabolic and catabolic processes are collectively known as **metabolic process**.

5. Growth. Due to the secretory or anabolic activities (Gr., *anabolism*= a throwing up) of the cell, new protoplasm continuously increases in its volume. The increase in the volume of the matrix causes into the growth of the cell which ultimately divides into daughter cells by the cell division.

6. Reproduction. The cytoplasm has the property of asexual and sexual reproduction.

REVISION QUESTIONS

1. What is cytoplasmic matrix ? Describe various theories regarding the physical nature of the matrix. Also discuss various properties of the matrix.
2. What is the structural basis for the unique properties of the water molecule ? How do the properties of water make it of importance to living systems ?
3. How would you define carbohydrates ? What are the major classes of carbohydrates ? How do the polysaccharides differ from the protein macromolecules ?
4. What are the major classes of lipids and what types of functions are served by them ?
5. Give the structure of triglyceride.
6. Name two porphyrins and give their functions.
7. What is the general formula of amino acids ?
8. What are primary, secondary, tertiary, and quaternary levels of protein structure ? What types of chemical bondings are responsible for each of these structural levels ? Which of the structural levels play a fundamental direct role in protein functioning ?
9. Describe the molecular structure of the following proteins : collagens, haemoglobin and immunoglobulin.
10. Write an essay on immunity and immunoglobulins.
11. How would you define an enzyme ? Describe some main types of enzymes.
12. Give structural formula of ribose and deoxyribose sugars.
13. What are three components of a nucleotide ?
14. List the nitrogenous bases which occur in DNA and RNA.
15. Enumerate the differences between DNA and RNA.
16. Write short notes on the following :
 - (i) Amino acids ;
 - (ii) ATP ;
 - (iii) Vitamins ;
 - (iv) Hormones ;
 - (v) Nucleic acids ;
 - (vi) Brownian movement ; and
 - (vii) Cofactor.