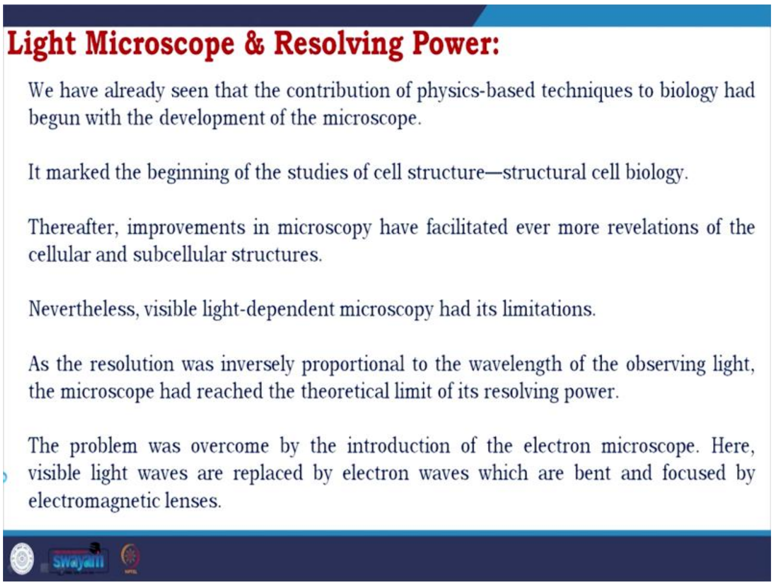
Structural Biology

Prof. Saugata Hazra
Department of Biotechnology
Indian Institute of Technology – Roorkee

Lecture 02
Introduction to Biological Macromolecules

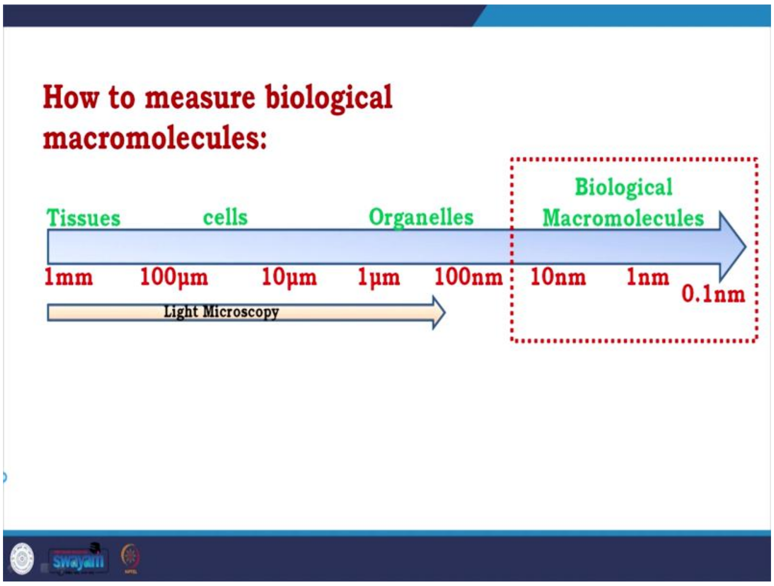
Hi everyone. Welcome to the Course on structural Biology. We are continuing towards the introduction. And I have talked about the history and evolution of Biology. Today will talk about biological macromolecules.

(Refer Slide Time: 00:47)



We talked about the light microscope and resolving power. You have already seen the contribution of the Physics technique to biology and begun the development of the microscope. It marked the beginning of the studies of cell structure the structural cell biology. After that, improvements in microscope have facilitated even more reflection of the cellular and subcellular structures. Nevertheless, visible light-dependent microscopy has its limitation of resolving power. As the resolution was inversely proportional to the wavelength of the observing light, the microscope had reached the theoretical limit of its resolving power. The problem could be overcome by introducing an electron microscope where visible light waves are replaced by electron waves that are bent and focused by electromagnetic lenses.

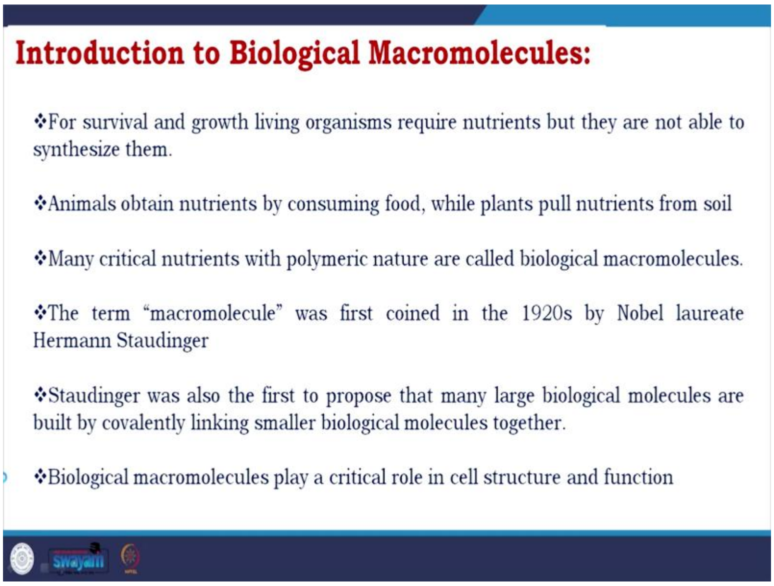
(Refer Slide Time: 02:00)



But let us take a look. When starting from an organism coming to an organ coming to tissues, cells, organelle, you will see that the tissues range within 1 millimetre 200 micrometres. The cells you are talking about continuously range from around 100 micrometres to 10 micrometres. Organelles are within the range of 1 micrometre to 100 nanometres. The biological macromolecule comes in between 10 nanometers to 0.1 nanometers.

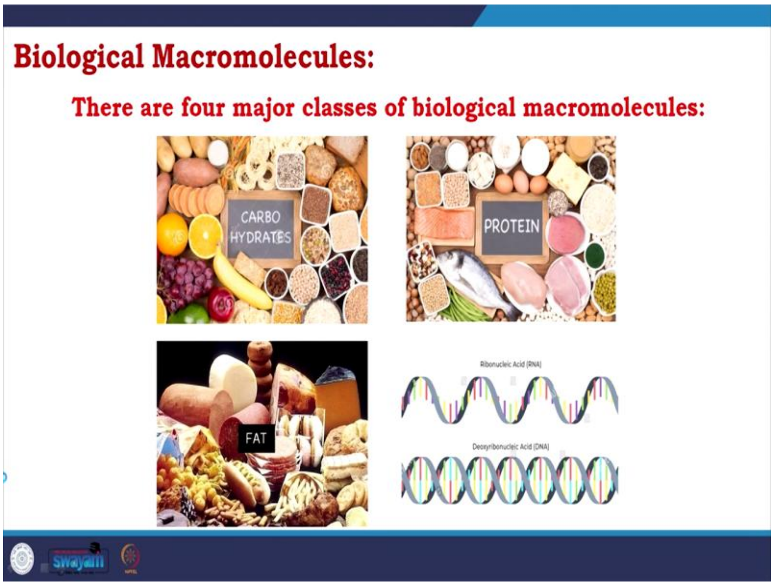
And you could easily see that light microscopy could not reach that area. So how to study them is what the structural Biology techniques talk about. But again, before going into them, we will try to look at those biological macromolecules, their basic properties, and all these things.

(Refer Slide Time: 03:08)



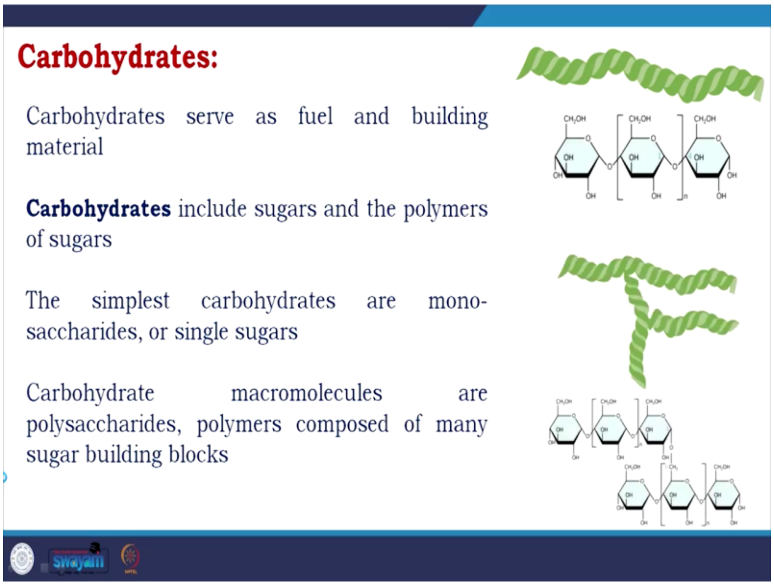
For survival and growth, living organisms require nutrients, but they cannot synthesize them. Animals obtain nutrients by consuming food, and plants pull nutrients from the soil. Many critical nutrients with polymeric nature are called biological macromolecules. The term macromolecule was first coined in 1920 by Nobel Laureate Harman Schrodinger. Schrodinger was also the first to propose that many large biological molecules are built by covalent linking smaller biological molecules together. He has introduced the concept of monomers to polymer formation of the biological relevant molecules. Biological macromolecules play a critical role in cell structure and function.

(Refer Slide Time: 05:22)



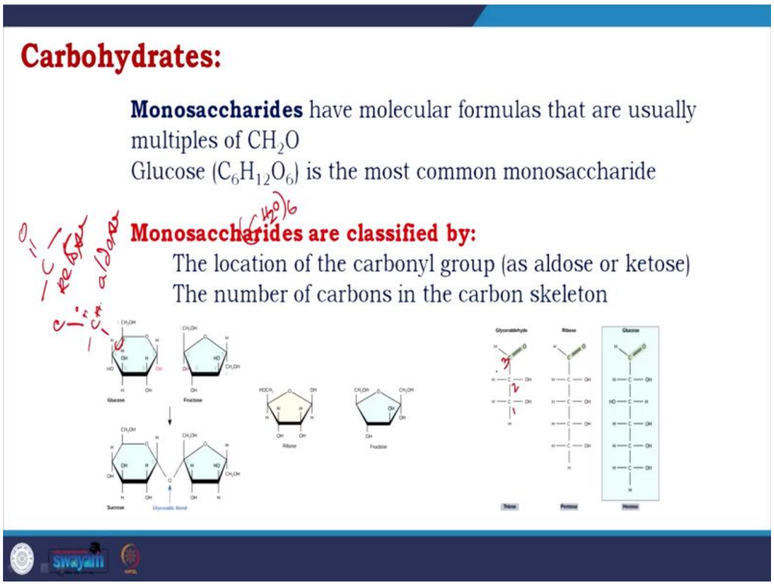
There are four major classes of biological macromolecules, which we will discuss. One Carbohydrate, protein, fat and nucleic acid, besides nucleic acid, comes in a different way carbohydrate, protein, fat is part of our daily diet.

(Refer Slide Time: 05:49)



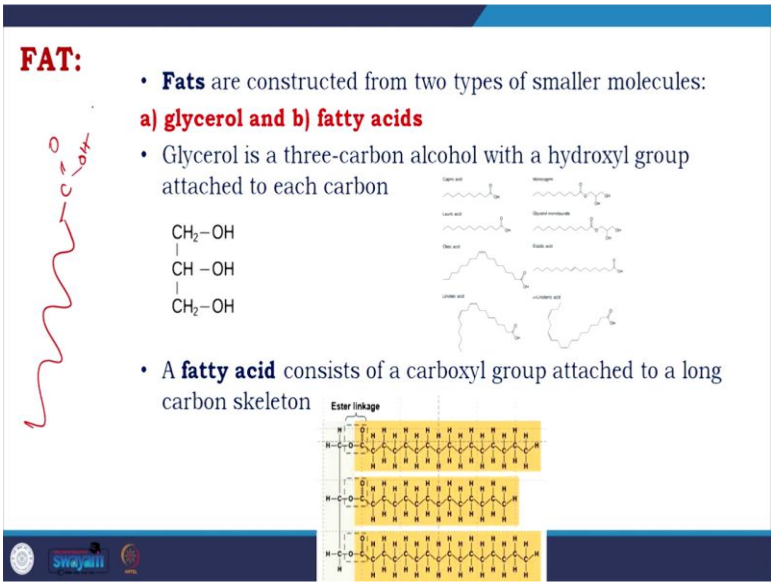
Let us start with carbohydrates. Carbohydrates serve as fuel and building material for the body. Carbohydrates include Sugars and the Polymers of sugars. The simplest carbohydrates are monosaccharides or single sugar. Carbohydrate macromolecules and polysaccharides polymers are composed of many sugar building blocks and that polymerization can be straight chain or branched chain. And that is one of the difficult things to study carbohydrates. If you look at this bonding, they could be formed in many ways. First, the monomers join to form polymer in units connected by a single bond. So when a single bond connects two units. They are freely rotatable, which means they could have generated every conformer. It is difficult to predict which conformer would be stable, but there are restrictions if there is a double or triple bond formation.

(Refer Slide Time: 08:06)



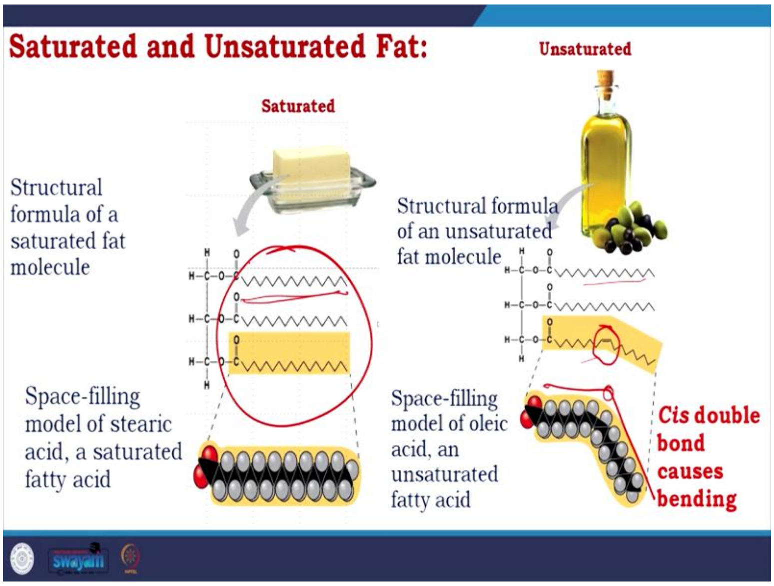
Monosaccharide: The molecular formulas usual multipliers by CH_2O. Glucose (C_6 H_{12} O_6) is the most common monosaccharide. Two ways classify monosaccharides—one with the location of the carbonyl (ketose and aldose). So you could see here glucose and fructose you will see the difference. Second, with the number of carbons in the carbon skeleton, if you see here 1 2 3 so, they are called triose. Glyceraldehyde is a triose. If it is five, they are called pentose. Ribose and deoxyribose are pentose. If it is six, they are hexose (glucose and fructose).

(Refer Slide Time: 09:42)



Fats are constructed from two types of smaller molecules glycerol and Fatty acid. Glycerol is the three-carbon alcohol with a hydroxyl group attached to each carbon. If fatty acid consists of a carboxyl group attached to a long carbon skeleton. A long carbon skeleton with C double bond OH. So if you look at Capric acid, lauric acid, maleic acid, linoleic acid, they are all examples of fatty acids. These fatty acids and glycerol fuse and form an ester linkage to form fat.

(Refer Slide Time: 10:44)

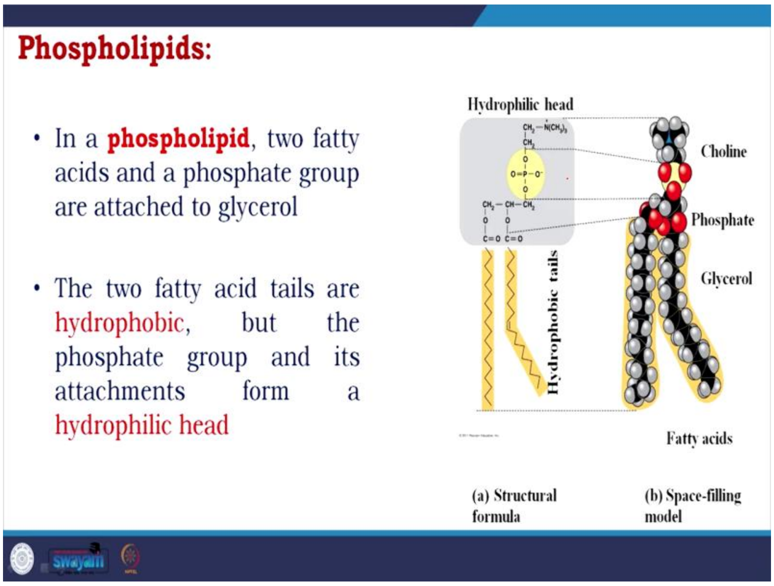


Fats are of 2 types saturated fat and unsaturated fat. While butter, which you regularly use at home, is an example of saturated fat, olive oil is a good example of unsaturated fat. Now, look at the structures, and there is a very interesting thing to observe. This is the structural formula of the saturated fat molecule. You see them when it is saturated; this goes straight. And this is the space-filling model.

These represent stearic acid. Here you see both saturated and unsaturated. You will see the double bond, and because of its presence, it is unsaturated. But more interestingly, you will see a neap there because the neap present reduced the membrane's dynamicity.

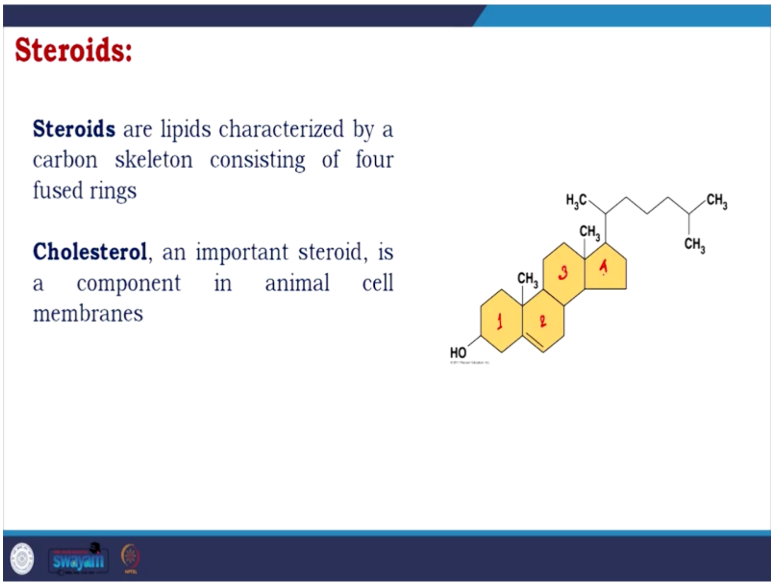
Whereas when it is having this bend, there are more dynamic results from your practical experience. You will find that butter is solidified in most conditions while olive oil is liquid in most temperatures, even if you keep them in the refrigerator. So this double bond is critical to define the nature of the fats. Now here another very interesting thing you have to keep in mind. These are about mono saturated. So for mono saturation, it comes and then has the double bond and then has a bend. But in the case of polyunsaturated, it will have a bend, but it will again have a bend. So, ultimately it would be getting the straight saturated like structure. So, saturated bad for dynamicity, and monounsaturated are good. Poly unsaturation, again giving the same scenario as saturation.

(Refer Slide Time: 14:05)



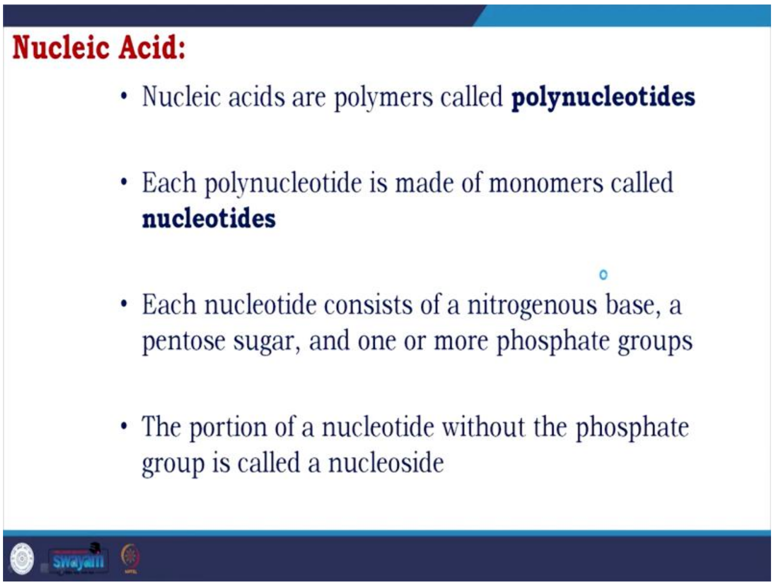
Two fatty acid and a phosphate group are attached to glycerol in phospholipids. Those two fatty acid tails are hydrophobic, as we know before, but the phosphate group and its attachment form a hydrophilic head. Because it is phosphate, it is not always that it would form a negative charge. In the presence of squalene which is present here. It shows a positive charge in the hydrophilic head, and in that way, phospholipids show a negative or positive charge creating the environment negative or positive.

(Refer Slide Time: 15:06)



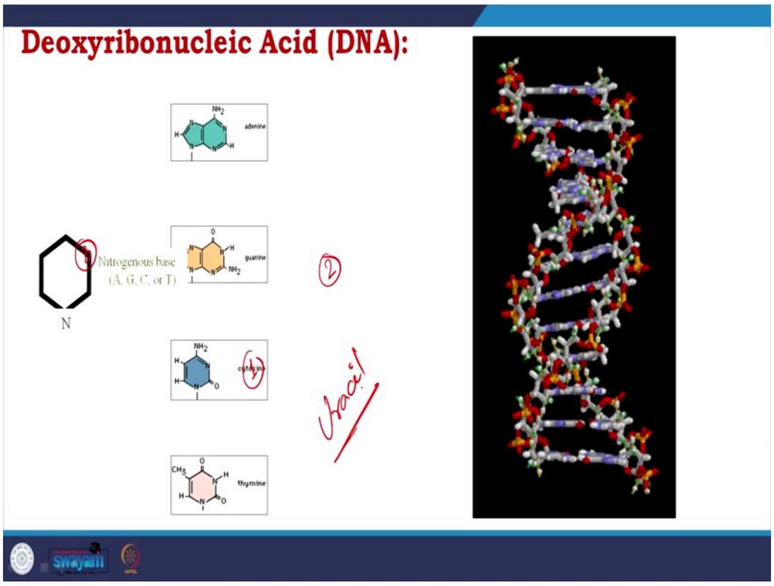
Steroids are lipids characterized by a carbon skeleton of four fused ring. The best example of steroid which are present in our body is cholesterol. It is an important steroid, is a component in animal cell membrane. Although cholesterol is essential in animals, high levels may contribute to cardiovascular disease.

(Refer Slide Time: 15:44)



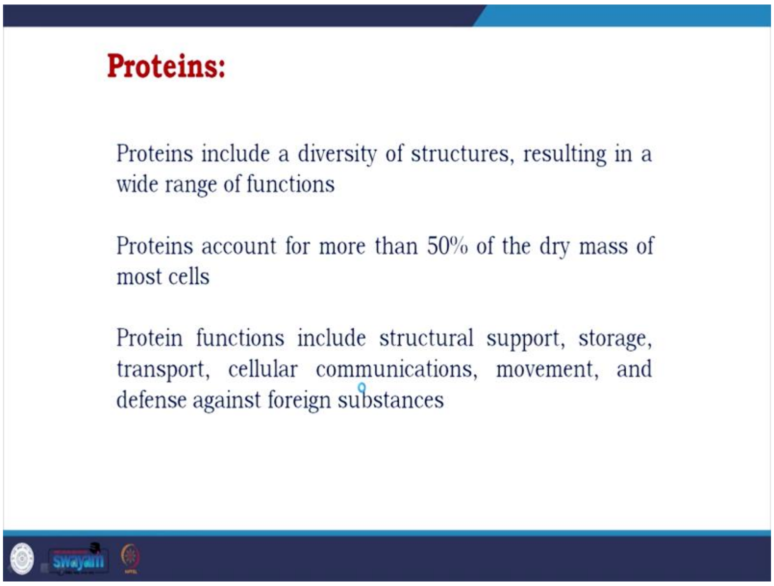
Nucleic acids are polymers called a polynucleotide. Each polynucleotide is made of monomers called nucleotides. Each nucleotide consists of a nitrogenous base, pentose sugar and phosphate groups. The portion of the nucleotides without the phosphate group is called the nucleoside.

(Refer Slide Time: 16:18)



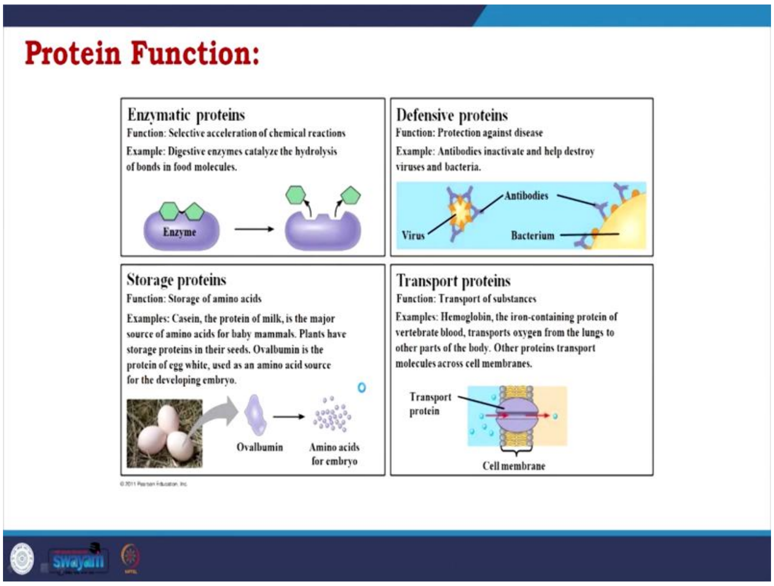
If you look at this animation, it will make it more clear. So there are three components sugar, nitrogenous base, and the phosphate group. The first one is sugar. The second one is the nitrogenous base, and the third is the phosphate group. They only differ in the nitrogenous base. In DNA, you get adenine, guanine, cytosine and thymine. Instead of thymine, you will get the Uracil in the case of RNA.

(Refer Slide Time: 17:02)



Proteins include diverse structures, resulting in a wide range of functions. Proteins account for more than 50% of the dry mass of most cells, and protein function include structural support, storage, transport, cellular communication, movement and defence against foreign substances.

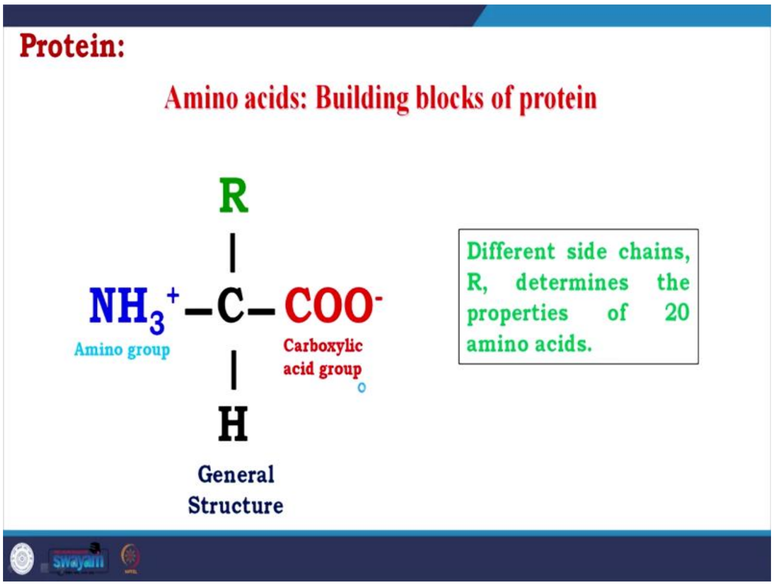
(Refer Slide Time: 17:40)



Proteins are generally of two types. One is called functional protein. They are also called enzymes. So enzymes are used for selective acceleration of chemical reactions. Very interesting if you think your body is a chemical factory, but your body has to maintain physiological conditions and temperature. So if you want to perform a reaction between A and B, you go to your chemistry lab and put A and B. You could put heat, temperature, pressure and other conditions so that the reaction proceeds in the forward direction.

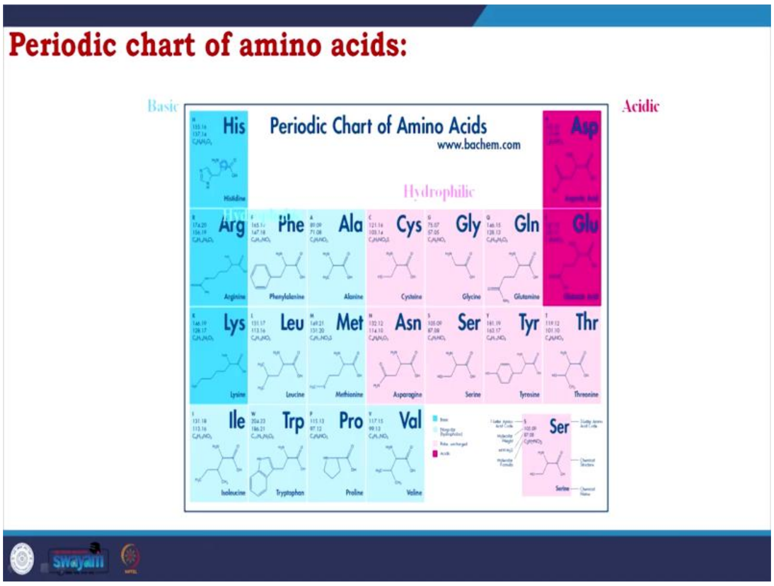
Your body cannot do that. You cannot take things, sit down in the oven, and burn yourself. So you have to accelerate by another way, and the other way is provided through the enzyme. Some proteins are involved in defence which protects against disease. For example, there are storage proteins, a function of amino acid storage. For example, casein, a milk protein, is the major source of amino acids for baby mammals. Plants have storage protein in their seeds. Ovalbumin is the protein of egg white used as an amino acid source for the developing embryo. Transport proteins, haemoglobin. People have studied myoglobin and haemoglobin in more detail. They are the crystallized proteins at the initial stage, and we got their structure.

(Refer Slide Time: 19:57)



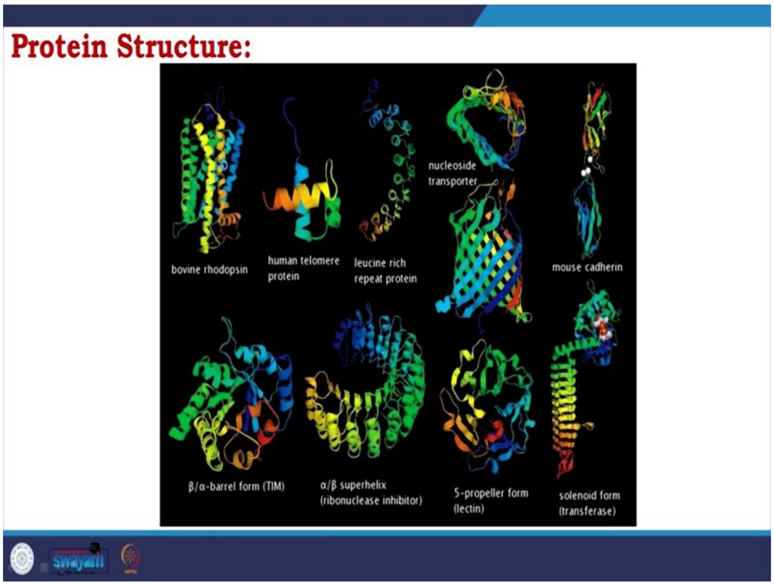
In the case of protein, the building blocks of proteins are amino acids. Here they have an amino group. They have a Carboxylic group. They have one hydrogen and one R, R means H. There are 20 different R's, so 20 different amino acids are there. Now, if you think about proteins developed by permutation and combination of 20 different amino acids, it gives a lot of diversity in character.

(Refer Slide Time: 20:43)



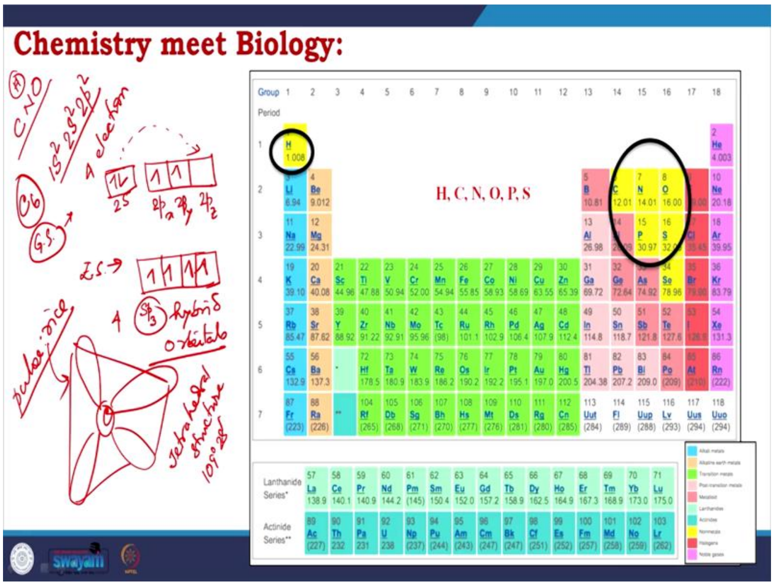
If you look at the basic part of this course, I will request you to read and memorize the chemistry of the protein. I will talk in detail, but to understand the beauty of how Biology is working, it is essential to remember where the chemistries are taking part. For that, you have to know all the chemistry of the amino acids. So, there are basic amino acids like histidine, arginine, lysine. There are acidic amino acids aspartate and glutamate—hydrophilic amino acids like glutamine asparagines. Glycine, serine, threonine and others are more hydrophobic.

(Refer Slide Time: 21:46)



Proteins form beautiful three-dimensional structures. What is the target of this course to study and understand? And Protein is the body's functional molecule, and you have to understand the three-dimensional structures they are developing. If you look at individual protein contents, very different three-dimensional structures and function.

(Refer Slide Time: 22:32)

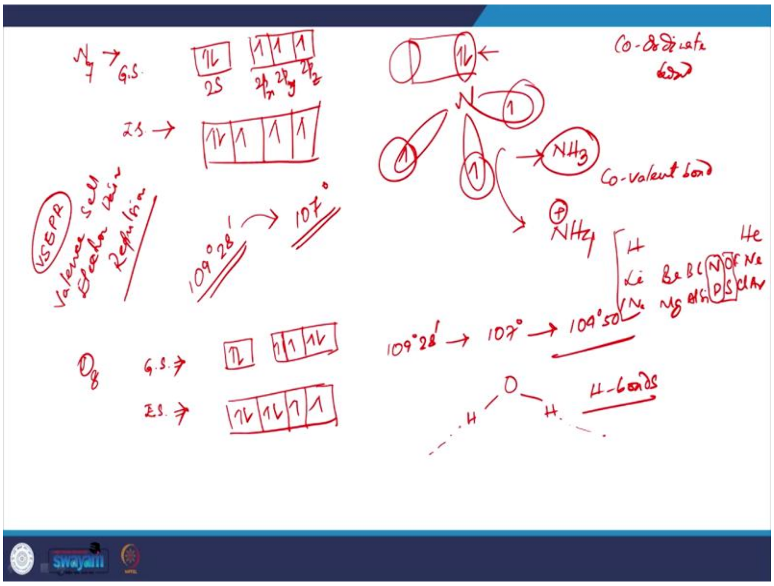


Chemistry meets Biology: This is the portion that is very, very interesting and critical. If you see the periodic table, only six elements, hydrogen, carbon, Nitrogen, Oxygen, Phosphorus and sulphur, they develop the entire Biology. And if you listen to me, I would say mostly the chemistry is developed by hydrogen, carbon, nitrogen and oxygen. So, it is very, very typical to know about their chemistry.

Starting with carbon because carbon develops the base of any biological molecule, is it the protein, be it carbohydrate, be it the macromolecules, cell everywhere. If you look at carbon, carbon has 6 electrons, so by electronic configuration $1S^2$ $2S^2$ $2P^2$, carbon has in its ground state four electrons, which are divided in the 2S, and there are two electrons here. In the excited state, these electron jumps here, and this process makes 4 electrons, 4 unpaired electrons, and not being S and P, they are all now SP$^{\cdot}$ So they create 4 SP^3 hybrid orbital's.

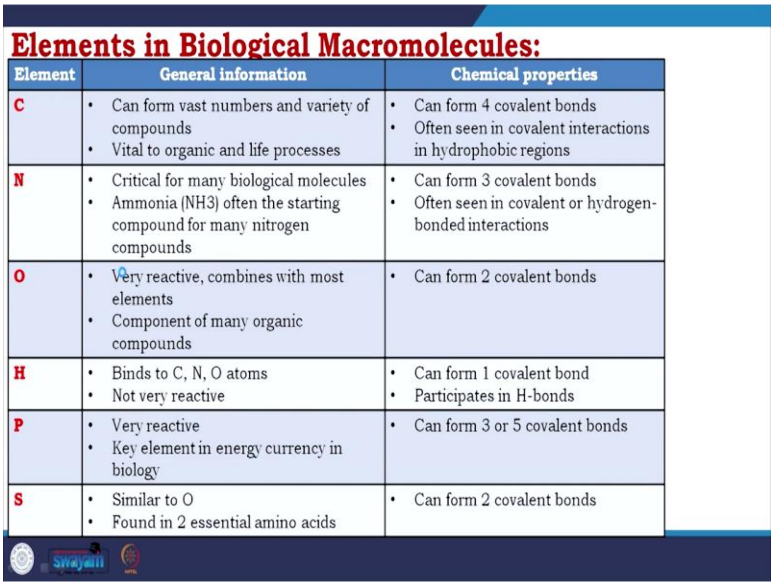
When we go to the protein part, we will look further at the peptide bond and talk about the SP_2 hybridized peptide bond.

(Refer Slide Time: 28:42)



Similar to carbon, nitrogen has 7 electrons. So in the ground state, it has 2S and 3 (2Px 2Py 2Pz). In the excited state, they will form 4 SP^3 hybridized orbitals again but one of them would contain a paired electron. So what would be the structure look like? This is the structure of a typical hydride of Nitrogen which is ammonia. This nitrogen is forming three bonds, introduced a lone pair here, so nitrogen would have three orbital's with single electrons with one lone pair. The single electrons would form a covalent bond with hydrogen, which will give NH_3. Can this lone pair form bond with hydrogen? Yes, but it would not be considered a covalent bond in that case. This should form a new type of bond, which is called a co-ordinate bond. In this co-ordinate bond, two electrons would be shared between hydrogen and nitrogen, and this will give nitrogen the ability to form a positive charge. So you can see now, this is the way the nitrogen would be looking. It have three hydrogens, but it could form an extra bond which is called a co-ordinate bond. The lone pair actually repel, there is a theory which is called valance cell electron pair repulsion theory, according to this, if there exists a lone pair, it will push the ripple the bonded angles. So from 109 degrees 28 minutes in carbon here, it would be reduced to 107 degrees approximately.

(Refer Slide Time: 38:31)

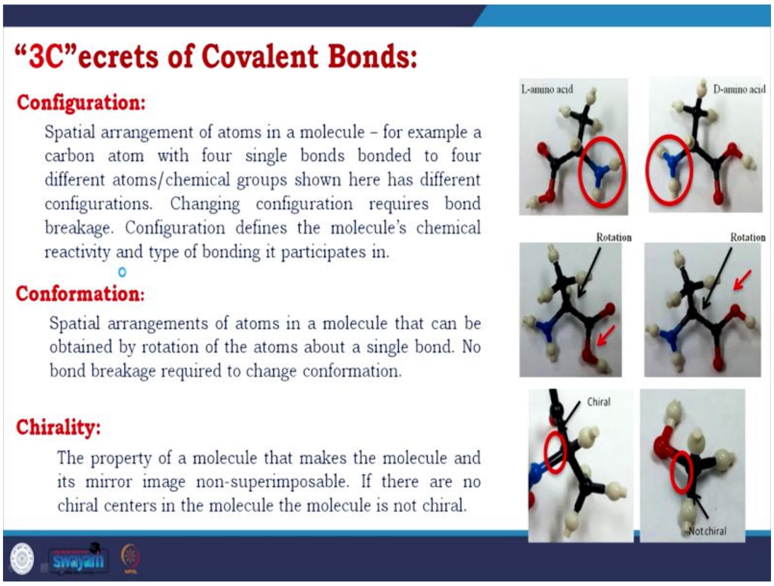


Elements in Biological Macromolecules:

Element	General information	Chemical properties
C	• Can form vast numbers and variety of compounds • Vital to organic and life processes	• Can form 4 covalent bonds • Often seen in covalent interactions in hydrophobic regions
N	• Critical for many biological molecules • Ammonia (NH3) often the starting compound for many nitrogen compounds	• Can form 3 covalent bonds • Often seen in covalent or hydrogen-bonded interactions
O	• Very reactive, combines with most elements • Component of many organic compounds	• Can form 2 covalent bonds
H	• Binds to C, N, O atoms • Not very reactive	• Can form 1 covalent bond • Participates in H-bonds
P	• Very reactive • Key element in energy currency in biology	• Can form 3 or 5 covalent bonds
S	• Similar to O • Found in 2 essential amino acids	• Can form 2 covalent bonds

So carbon can form a number and variety of compounds vital to organic and life processes. It can form four covalent bonds, which are often seen in covalent interactions and hydrophobic regions. Nitrogen is critical for many biological molecules, ammonia often the starting compound for many nitrogen compounds, can form 3 covalent bonds, often seen in covalent or hydrogen-bonded interaction. Oxygen, which is very reactive combined with most elements, a component of many organic compounds, can form two covalent bonds. Hydrogen binds to carbon, Nitrogen, Oxygen atom, not very reactive, can form 1 covalent bond, participate in hydrogen bonds which is extremely critical in biology. Phosphorus is a very reactive, key element in energy currency in Biology, which is ATP, forming 3 or 5 covalent bonds. Sulphur is similar to oxygen found in two essential amino acids, which are cysteine and methionine, and it can form two covalent bonds.

(Refer Slide Time: 39:41)

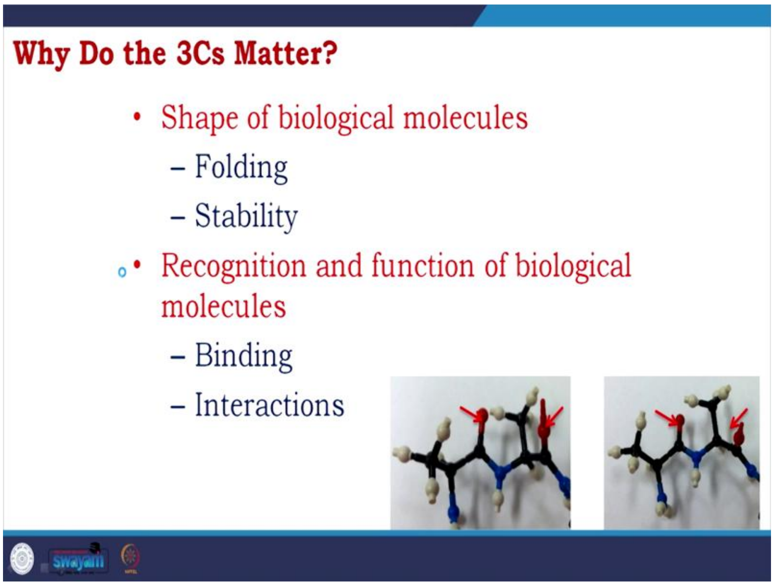


Now coming to a very interesting part, I call them three secrets of covalent bonds. It is very interesting to look at this basic part, which will be repeated in a huge way when we consider the macromolecule. The first thing is configuration. What is configuration? Configuration is the spatial arrangement of atoms in a molecule. For example, a carbon atom with four single bonds bonded to 4 different atoms shown in this picture has a different configuration. Changing configuration requires bond breakage. The configuration defines the molecules chemical reactivity and the type of bonding it participates in.

Coming to confirmation: If you see, you have to perform something called a rotation. So, if you have amino acids like this, if you look at this structure, this structure represents an amino acid called alanine.

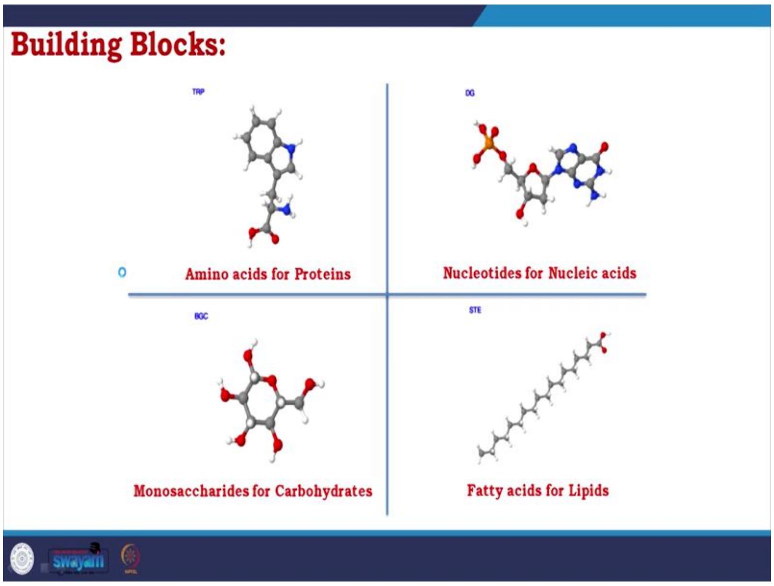
I have already explained Chirality, but if we have to understand, this is a molecule with four different groups connected to carbon. If I put hydrogen instead of one of these, it would lose its Chirality. So Chirality is the property of a molecule that makes the molecule and its mirror image non-superimposable, which we have discussed earlier.

(Refer Slide Time: 47:06)



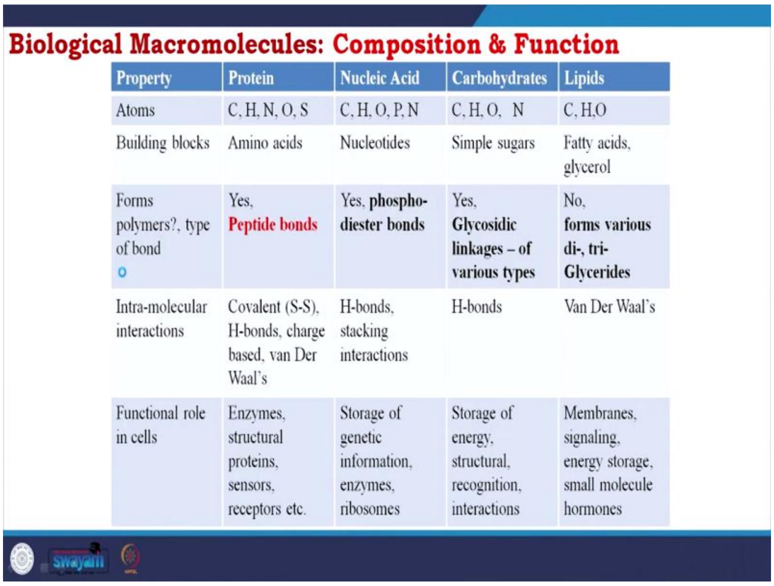
Why do the three secrets matter? The shape of biological molecules when we go for folding will be explained in more detail. When we discuss stability in protein engineering, we will discuss it in detail. Recognition and function of biological molecules have talked about the biasness of chirality to binding interaction because of these three secrets configuration, confirmation and chirality.

(Refer Slide Time: 47:37)



As we have already discussed, amino acids are building blocks of protein, and nucleotides are the building blocks of DNA and RNA. Monosaccharides are building blocks of carbohydrates. Glycerol and fatty acids are lipid or fat building blocks.

(Refer Slide Time: 47:59)



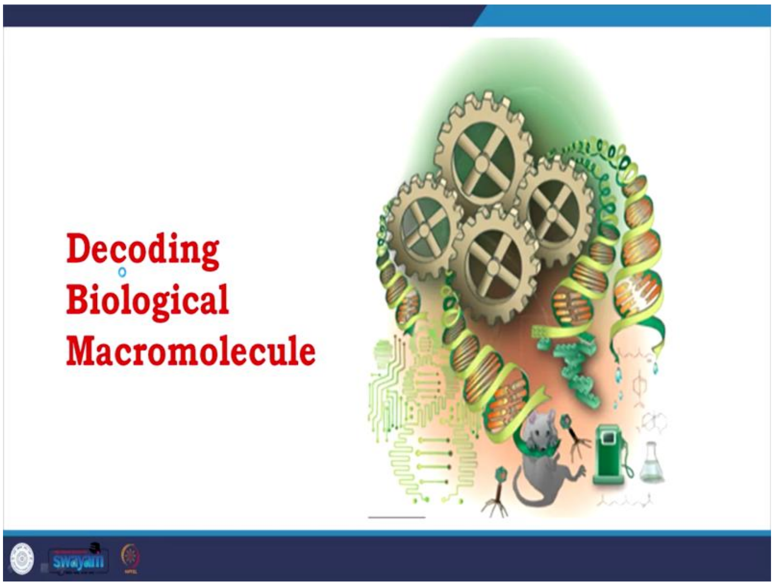
Biological Macromolecules: Composition & Function

Property	Protein	Nucleic Acid	Carbohydrates	Lipids
Atoms	C, H, N, O, S	C, H, O, P, N	C, H, O, N	C, H,O
Building blocks	Amino acids	Nucleotides	Simple sugars	Fatty acids, glycerol
Forms polymers?, type of bond	Yes, **Peptide bonds**	Yes, **phospho-diester bonds**	Yes, **Glycosidic linkages – of various types**	No, **forms various di-, tri-Glycerides**
Intra-molecular interactions	Covalent (S-S), H-bonds, charge based, van Der Waal's	H-bonds, stacking interactions	H-bonds	Van Der Waal's
Functional role in cells	Enzymes, structural proteins, sensors, receptors etc.	Storage of genetic information, enzymes, ribosomes	Storage of energy, structural, recognition, interactions	Membranes, signaling, energy storage, small molecule hormones

How the biological macromolecules do their composition and show the function? Protein uses the atoms of carbon hydrogen Nitrogen Oxygen and sulphur. Protein gets Phosphorus through phosphomodification. Nucleic acid use carbon, hydrogen, oxygen, phosphorus and nitrogen. Carbohydrates use carbon, hydrogen, oxygen, and nitrogen. Lipids use carbon hydrogen and oxygen. The building block for protein is amino acid, for nucleic acid is a nucleotide. For carbohydrate is simply sugar, and for lipid, it is fatty acids and glycerol. Can they form polymer? If yes, what is the bond type? Yes, it could form the polymer. The bond type is peptide bond for protein. Nucleic acid; The bond type is the phospo-diester bond. For carbohydrates, the bond type is glycosidic linkages. What are the intra-molecular interactions? For protein covalent bond, disulfide bond, hydrogen bonds, Van der Waals interaction, and all. For Nucleic acid; hydrogen bonding, and stacking interactions.

For carbohydrates, hydrogen bond, and lipids, mostly Van Der Waal's, and hydrophobic interaction. The functional role of the proteins is an enzyme, structural protein, sensory, receptors etc. Nucleic acid is storage of genetic information. It also works in the form of ribozymes. Carbohydrates function is storages of energy, structural formation recognitions, and interactions. The main function of lipids includes membrane formation, energy, and storage of small-molecule-like hormones.

(Refer Slide Time: 51:41)



Decoding the biological macromolecules would be extremely interesting because the first step is to look at a molecule to get the structure and understanding of its function.

We have discussed the biological macromolecules that have different properties and functions, the chemistry behind them, and their composition and comparatives.