**Course Name: I think Biology**

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**W3L13_Biomolecules - Part II**

Hello and welcome to the I think biology NPTEL course. In this week, we are talking about the building blocks of biology. This lecture is on biomolecules. In the first part of this lecture, I spoke about nucleic acids and proteins. In the second part of this lecture, I will be talking about polysaccharides and lipids. Polysaccharides are made up of simpler molecules such as sugars or monosaccharides. And here we can look at the structure of glucose, which is the main sugar which is used in making polysaccharides. Glucose can exist in the straight chain form or in the ring form. And the ring form are of two types. You can have alpha or beta glucose.

And they differ from each other based on the position of the OH group which is attached to the carbon at the first position in the ring, which is shown here in blue. In alpha glucose, the OH group is below the plane of the ring. And beta glucose, it is above the plane of the ring. And this matters because the kinds of structures you can make using alpha glucose or beta glucose are very different. And the two main structures you will make are starch or cellulose.

Starch is a polymer of alpha glucose monomers. And they can have two kinds of linkages. They can either form the 1,4-glycosidic bond, which is basically two glucose molecules coming together in a dehydration reaction, which I spoke of earlier. And this will give you a linear polymer or a linear chain. You can also have a 1,6-glycosidic bond.

So this will lead to branching in the polymer such that you will have a more open structure. Cellulose is made up of beta glucose monomers linking in in the 1,4-glycosidic bond to give give a linear polymer. The difference being that if you look at the OH group, which has been highlighted in yellow, in starch, the OH group on the second carbon is all on the same side of the plane of the plane of the molecule. Whereas in cellulose, it is flipped in every alternate glucose monomer is flipped such that the OH group is on is on opposite sides of the plane of the molecule. And this allows cellulose to

make higher order structures because each cellulose molecule can hydrogen bond with another such cellulose molecule in order to get many fibers or many linear polymers coming together to form one fiber of cellulose.

So this also has other implications. The structure can impact the properties of the molecule. And we can think about this question as to why can we digest starch but not cellulose and look at it from a structural standpoint. This is a schematic of the structures you will find in the main polysaccharides found in plants and animals. So starch is made up of two polysaccharides, amylose, which is a linear polymer formed by the linking of 1,4-glycosidic alpha glucose bonds.

Amylopectin has both 1,4 and 1,6 bonds. So it is a branched structure. And so starch is a mixture of amylose and amylopectin. Glycogen which is a polysaccharide found in animal cells used for storage of glucose has a similar branched structure but it has it has more branches as compared to starch. And the reason is thought to be is in animal cells we do not store a lot of polysaccharides.

We only have small stores of glycogen. And we need to make fairly rapid use of this store upon demand. So if you have a more open structure, the hydrolysis of glycogen in order to generate glucose monomers will be faster as compared to starch. And that's the reason why it will have more branches and more of an open structure. Cellulose as I already said can form fibers which are basically hydrogen bonded cellulose molecules and then these fibers also come together to form larger structures called microfibers. And then these microfibers can form a mesh which will give very interesting properties to wood such that it has strength but also some elasticity. And this is what makes wood such a versatile material is the is the hierarchical structural build up of cellulose. There are also other polysaccharides which form part of the superstructure of wood but we're not going to go into that. Another class of polysaccharides are called glycosaminoglycans and here you can see that if you look at the repeating structure of the GAG it has a charge group in the form of NHO. And what this does is that it allows these polysaccharides to bind a lot of water molecules such that these interactions give them a very slimy feel.

And so these GAGs are found in mucus or snot and they're also find in found in synovial fluid where they're used for the lubrication of joints because they can entrap a very large quantity of water. Some well known GAGs are keratan sulfate, heparin, hyaluronic acid and chondroitin sulfate. And in fact some of these are sold as supplements and people with arthritis are urged to take either chondroitin sulfate or keratan sulfate in the hopes that it will build up these tissues where the joints are facing a lot of inflammation and degradation. Shown here is another kind of polysaccharide and this is a composite molecule. The image here has been produced using a technique called

atomic force microscopy but I won't go into the details of that but it allows us to visualize molecules at the atomic or even the molecular scale scale and look at their structure, the physical structure.

And aggrecan which is the molecule which is shown here is made up of a protein and polysaccharides. So it has a protein core and you can see that it's been marked here with the NN being shown and the CN being shown and then hanging off that protein core are many polysaccharides and there are so numerous that it gives a bottle brush appearance to this molecule. And the kinds of polysaccharides you can have can also be different. You can have keratin sulfate, you can have chondroitin sulfate and their numbers can also differ. So you can have a diversity in the kinds of polysaccharides which are attached to this protein core.

So again this molecule, aggrecan, is found in our joints and cartilage and it is used for cushioning and there is much work going on in studying the different states in which aggrecan is found. For instance in this particular study they looked at aggrecan in fetal tissues and mature tissues to find out what are the differences it undergoes during development. People are also looking at disease states such as arthritis and normal states to find out what are the changes happening to aggrecan in such conditions. So much interesting work is also happening on polysaccharides. Then let's move on to lipids.
Lipids come in three main classes of molecules. You have fatty acids, you have triglycerides and you have sterols. Fatty acids are long chain hydrocarbons and you can which end with a carboxylic group and the number of carbons in the chain can vary which can lead to a diversity of molecules. You can also have saturated fatty acids and unsaturated fatty acids. And there also you can have varying degrees of unsaturation.

So you can have molecules with one double bond or three double bonds to six double bonds and this can change the properties of the molecule. Then you can have a triglyceride which is basically a glycerol molecule to which you can attach fatty acids using an ester bond. So again depending on the kinds of fatty acids which are attached to the glycerol backbone you can product produce a variety of molecules. At the bottom of the slide I have shown a variation which we all know about which is a phospholipid. So phospholipid is also built on a glycerol backbone and it has two fatty acids hanging off the glycerol molecule and then one part of the molecule will have the phosphatidylcholine head which will make one particular kind of phospholipid which we are all familiar with.

Finally we also have sterols which are considered as lipids and they are ring structures and the most famous one that we are all aware of are is cholesterol which forms an integral part of our membranes and is also the building block for all our hormones.

Shown here is some more detail on these lipid structures. So you have starting from the left a glycerol phospholipid which I have already explained. Then you can also have glycerol lipids so instead of having a phosphate head it will just have an OH group hanging off the glycerol backbone. You can have sphingolipids which have an NH in the starting.

You can have fatty acids. I won't talk about polyketides or prenol lipids and you can have sterols. The other lipid which is shown here is a saccharolipid and I decided to show it because what I had mentioned earlier about composite molecules. So this is a molecule where you have a lipid attached to a polysaccharide and again this will have its own properties and will have its own functions in a particular location within the cell. So lipids have several functions within our bodies but one of the main functions is that they form membranes starting with the nuclear membrane, the ER Golgi and then ending with the plasma membrane. So you have this fantastic endomembrane system which ends in the plasma membrane.

And the plasma membrane and even the other membranes are formed of this lipid bilayer structure where you have two layers of lipids with the lipid tails interacting with each other and the heads of the lipids which are charged facing a watery environment. And so this allows us to demarcate the interior of the cell from the exterior. And so this phospholipid bilayer can be formed as sheets. So you can have a bilayer sheet. You can have spherical structures so you can have a liposome which is a lipid bilayer which is kind of folded up in the form of a sphere.

You can have a micelle which is just a single layer which is folded up into a sphere. So looking at the most famous and well-known form of these structures, you have the phospholipid bilayer in the form of the plasma membrane and shown here are also different kinds of proteins which can be embedded within this membrane. So the plasma membrane is not just composed of phospholipids but can also have proteins embedded in it. Going into a little bit more detail on plasma membranes, I thought we will try and update our picture of this plasma membrane. And shown here in figure A is a cross-section of a plasma membrane.

So you can have a diversity of lipids which will make up the lipid bilayer. So you can have unsaturated lipids and saturated lipids. And the composition of each leaflet, the upper leaflet and the lower leaflet of this lipid bilayer can be different. Apart from that you can have many proteins which can form part of the membrane. So you can have channel proteins, you can have receptor proteins, you have GPI anchored proteins, so these are proteins which are bound to lipids and so they can freely move.

You can have lipidated proteins, so they have lipid anchored in them and they extend across the membrane. Then you can have cholesterol which forms an integral part of the membrane and it changes the fluidity of the membrane. And so depending on the type of cell or the type of environment that the cell is exposed to, the amount of cholesterol will decide the fluidity of the membrane. And if you look at the image in B, you see a 3D version of the same picture shown in A. And the main thing to note here is that you can have different patches of lipids which form part of this lipid bilayer with many different proteins which are embedded in the membrane.

One last thing which we should talk about is actin fibers which are also now considered a part of this cell membrane. And so actually the lipid bilayer and this actin mesh which lies just below the bilayer forms a composite structure and in total gives the complete properties of the cell membrane. And so the actin meshwork provides some measure of structural integrity and strength to the cell membrane. But depending on the requirement, the meshwork can dissolve or degrade at a particular point and confer more fluidity to the cell membrane at that position. So say for instance a cell wants to put out a lamellipodium, then it can dissolve the actin meshwork at that point and allow the membrane to kind of flow in that particular location.

And then this meshwork can reform so that again the integrity of the membrane is maintained. So really we have to think about the cell membrane now as this very intricate and complicated structure consisting of many kinds of lipids, many different kinds of proteins, also many kinds of polysaccharides which can hang on off the lipids along with this actin meshwork just below the lipid bilayer. Here is another view of the lipid bilayer and this is for a vesicle. So vesicles are small structures which are used for transporting chemicals or other molecules from the cell to the membrane of the cell where they could be released. And you can also have traffic going in the opposite direction from the cell membrane into the interiors of the cell.

So this is the model of a synaptic vesicle. So these are vesicles which will travel on axons to the synapse and there they will release their cargo which is usually a neurotransmitter into the synaptic space. And this particular study found that vesicles have a very high protein component, over 50% of the vesicle was found to be made up of large number of different kinds of proteins which have been shown here. Again making the point that we really need to start updating our ideas of membranes from just the simplistic notion of a lipid bilayer. I will end my lecture by talking about an application related to lipids.

Post the second world war, the discovery of cortisone heralded a great advance in the treatment of arthritis. So there are reports of people who couldn't walk because of very

crippling arthritis. Upon being given cortisone, they could get up and start walking and move their fingers. So there was a lot of interest in the chemical synthesis of cortisone and the starting material that most chemical manufacturers were using at that point was basically bile salt bile salts which you would get animal tissue from slaughterhouses and then isolate the starting point for cortisone from that. And this was a very laborious method and would yield only very small amounts of cortisone and the number of steps you needed in the synthesis were quite large.

Then a company which was based in Mexico hit upon the idea of using plant sterols. So plants also make a variety of sterols for their own purposes and they started using a plant sterol called diosgenin which is found in the Mexican yam. And so if you look at the chemical structure of diosgenin, you can see that it also has this four-membered ring structure and then it also has these two extra rings. So diosgenin turned out to be an easier starting point for the synthesis of cortisone. And so this company called Syntex made cortisone from a plant-based sterol for the first time and they could make cortisone in much larger quantities and the chemical synthesis of cortisone was also a lot easier compared to the starting point which other companies were using.

So this allowed Syntex to start making cortisone using diosgenin and thus it could reach the market in much larger quantities than before. And then from the chemical synthesis of cortisone, it was but a short step to the chemical synthesis of reproductive hormones and so they also started to make progesterone which was then used for making the birth control pill. And this is really the start of a very long journey in terms of the design and synthesis of different kinds of molecules for birth control. And I would urge you to look up some of the work related to this.

I have given you one citation here. So with this, we will end our brief tour of biomolecules found in the cell and we can discuss this more in the tutorial and I look forward to seeing you there. Thank you.