Circular Dichroism and Mossbauer Spectroscopy for Chemists

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Lecture – 15
Chirality and biology - V

Hello and welcome to this new segment of CD spectroscopy and Mossbauer spectroscopy for chemist. My name is Arnab Datta and I am an associate professor in the department of chemistry at IIT. Bombay. So, previously we are looking into different symmetry elements that can be present in molecules and try to connect those symmetry elements to it is properties and one of the property just stood out it is the chirality.

So, today we are going to look into a little bit more details in chirality.

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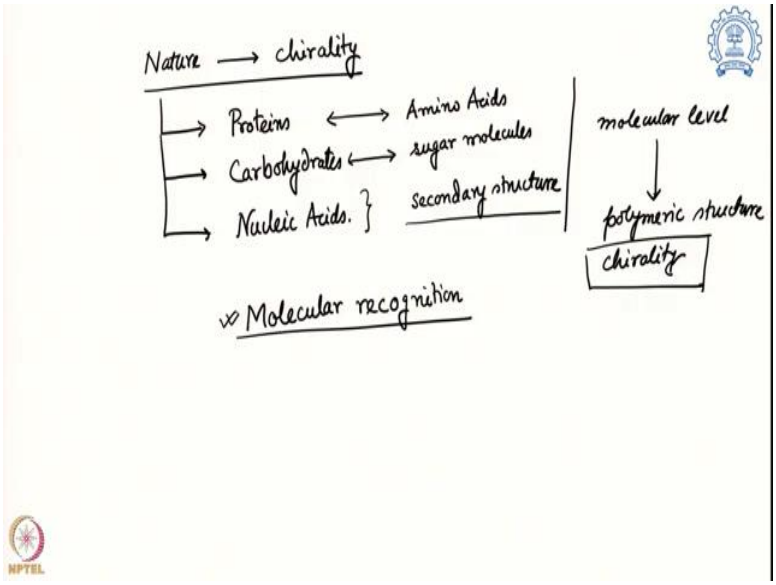

So, we have already looked into chirality and we found in nature chirality is a crucial factor and this chirality is present in most of the typical bio molecules including proteins, carbohydrates and nucleic acid and we have found these proteins are actually made out of amino acids which are itself chiral, carbohydrates also the sugar molecules of different kinds and they are also chiral in nature.

Whereas nucleic acid they are made out of this adenine, threonine and all those different nucleosides and nucleotides. Those are itself not chiral but when they create the secondary structure those are chiral in nature. So, all together we found that in this biomolecules from the molecular level to the large scale polymeric structure the chirality is playing a

huge role and why this particular chirality is maintained so natively in this bio molecules?

One of the important answers we got is the molecular recognition. So, as you have looked into the different molecules and how they behave and how they interact with the different molecules present around it. We found this molecular recognition is one of the important factors which actually say how the life is going on. So, if we try to answer what is life in a very broad perspective, we found that we can define it like there are multiple chemical reaction happening but in a synchronous way.

So, they kind of know which reaction we need to perform? Which reaction we need to shut off? And which reaction we need to prefer? So, how this molecules can detect can sense which reaction they should go forward with and over there come this particular term molecular recognition and chirality is an important part of this molecular recognition so that we are going to look into in much more detail format in this particular segment.

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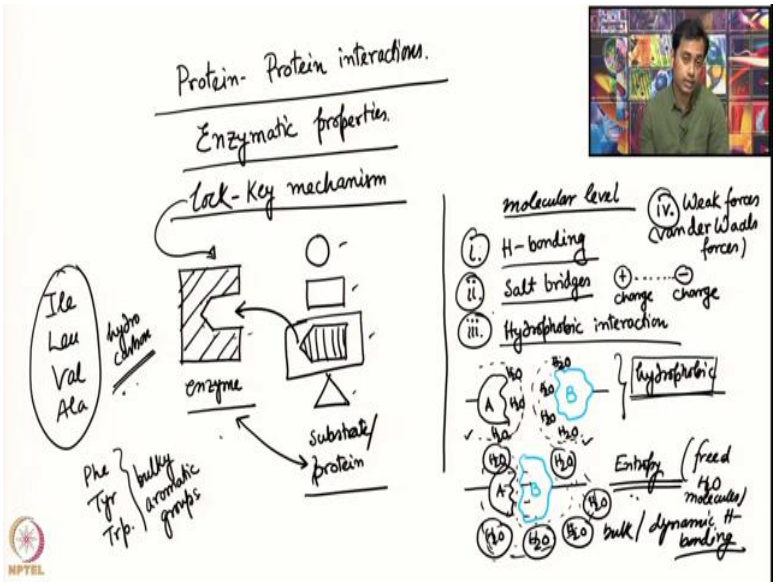

So, one of this molecular recognition that we can think about is for the protein-protein interaction and one of the major portion of the protein-protein interaction is enzymatic properties, when the enzymes are reacting and most of us learn this particular term lock and key mechanism that has been followed vividly for this enzyme. So, how it actually works? See, if I want to draw a cartoon picture of that and say this is one portion of my protein structure and here my reaction will occur.

So, this is one of the protein say this is the enzyme part. So, now if I put different kinds of systems to it, out of all this only this one present over here fits exactly to this

side. So that means we can have different keys but only one of them fit to this key. So, over here this is actually cartoon picture we say the different shapes like sphere, square this particular shape or triangle. Only this particular shape over here that I have drawn only this one fits very nicely to this enzyme and that is the lock and key mechanism we are talking about.

Now, over here when you talk about this protein-protein interaction is going how it is recognized, we want to learn a little bit more like what is the fundamental aspect remain in this particular lock and key mechanism? So, if we look closely at the molecular level and try to figure it out what are the different interactions is actually going on over there? We found this enzyme and say this is the substrate which can be also another protein.

What are the different interactions goes between this substrate and enzyme? And over here we found at molecular level there are different possibilities. So, the first one is hydrogen bonding so, we have enzyme which is made out of the amino acids and in the earlier classes we have gone through, what are the different amino acids possible? And over there one of the important factors was the backbone which actually contains the amide bond and also the sides chain and the R groups present in all the different kinds of amino acid.

But there are particular functionalities which can actually lead to the formation of hydrogen bonding. So, this hydrogen bonding can define like which particular molecules it would like to be preferring so that it can forms a very good nice hydrogen bonding network over there around this core. So, after hydrogen bonding the other one comes to our picture is called the salt bridges.

So, salt bridges are nothing but over here what happens? There are two different parts of the molecules are coming. One molecule creates a positive charge and the other segment creates a negative charge and then they create a electrostatic interaction which is favourable in nature. So, for an example arginine, lysine those kind of amino acids with their side chain they can create this positive charge.

Whereas, aspartate, glutamate they create the carboxylic acid group which is negative in charge. So, if you bring those two different types as arginine, lysine and aspartate, glutamate together you are going to get a very nice electrostatic interaction which is known as the salt bridges. So that is one of the other common factor comes over here. The third one comes into this picture is hydrophobic interaction.

So, typically when we talk about the salt bridges or hydrogen bonding they are favoured in a hydrophilic environment, where there are water or polar media around it. So, they actually create an influence around the groups which likes to be in hydrogen bonded or salt vision network. However, there are different amino acids for an example phenylalanine, tyrosine, tryptophan all those groups which actually contains a very bulky aromatic groups around it.

And along with that we have also got isoleucine, leucine, valine even alanine. This kind of amino acid which produces hydrocarbon chain as a side chain so, those kind of groups hydrocarbon chain or bulk aromatic groups creates a lot of hydrophobicity and this hydrophobic interaction also can play a role. So, how this hydrophobic interaction plays a role? To give you an idea over here.

I am showing you say there is a hydrophobic group present over here this is group A which is hydrophobic in nature and now say there is another group coming over here B which is also hydrophobic in nature. So, both this are hydrophobic group. Because we are talking about a protein atmosphere which is present in a save system so, there will be some water around it. So, before their interaction this molecule A and this molecule B will be interacting a lot of water.

Now, this water molecules around this A and B are not really stabilized because A and B as we just said hydrophobic in nature so, they are non polar. So, they are not having very good interaction with the water molecules which is polar in nature and to stabilize it. So, in this particular format of A and B both of them are really unstable there is not much enthalpic support to establish this interaction.

However, if I put A and B close together now, what happens? All this water molecules that was present in between now they can leave and go outside. So, they are relieved from their original position and what is the consequence of that? So, when these two hydrophobic groups comes close together and releases the previously interlinked water molecules they got released.

So, this water molecule can go into the bulk and do a dynamic hydrogen bonding network which is present in the bulk solution specially in water. Previously, it cannot do that because it has to interact with A and B, how much inactive or destabilized it is? However, when we put this A and B together those water molecules got released. So, this water can stick together and create this dynamic hydrogen bonding and the same time previously this water molecules are bound.

So, they cannot move around because there is not much interaction going on between this hydrophobic group and the water. But when we talk about the water molecules over here due to this dynamic hygiene morning water molecules can go in different places very nicely. So that creates an entropy and this entropy factor is coming because of this freed water molecules and this particular water molecules actually creates the overall gives free energy negative.

So that is why hydrophobic interaction is favourable in nature not only because A and B actually have some interaction in between them which is possible through pipe interaction and all those things. But the major contributor to that in a polar solvent or aqua solvent is the release of the bound water molecule and creates the bulk water. So that entropic factor drives it and that is why hydrophobic interaction is quite a stabilizing interaction.

And that also plays a role when we are talking a molecular level interaction during two enzymes or two proteins. So, over there hydrogen bonding solvents and hydrophobic interaction also play an important role. And the last one also play an important role, is the weak forces. Weak forces I mean Vander Waals forces so, the molecules can be hydrophobic chemically non polar invertor and but at the same time they can create some instantaneous dipole moment which can interact.

So, it can be a dipole induced dipole or induced dipole induced dipole interaction which actually creates some interactions between the proteins. So, among this these four are the crucial interactions which actually creates a bonding interactive system around two proteins and that is actually create this particular interactions possible. With that now, we know that yes, these are the interaction possible hydrogen bonding, salt bridges, hydrophobic interaction even weak forces coming into the foray.

But why this particular shape dependency? This forces can define like how stable and how destabilized I am but how they define this shape dependency? So that is coming next.

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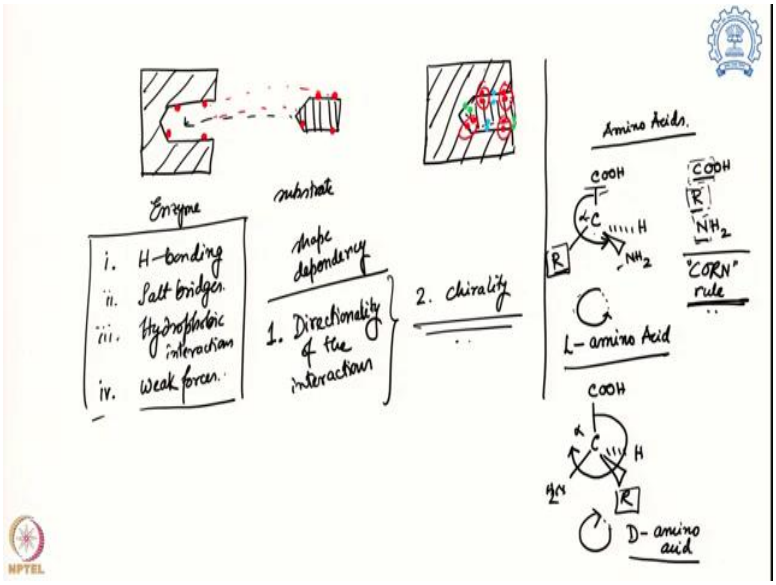

So, over here I am drawing this part one more time. So, this is one of the enzymatic core area where my substrate is going to come and bind and say the substrate is nothing but one of the other protein segment and this is going to come and bind over there and it feeds very nicely so, we now know that there are particular factors like hydrogen bonding, salt bridges, hydrophobic interaction and last.

But not the least the weak forces, actually define how they are going to interact? So, these are the tools by which the enzyme and subset going to interact but why this particular shape dependency? Because, that is a crucial factor why it is a lock and key mechanism. So, this lock and key mechanism is coming from this shape dependency and the shape dependency come from two different factors.

First directionality of the interactions so now, say over here in this particular molecule, over here I have some particular groups which can do hydrogen bonding. So, in that respect I would like to put over here in my molecule some corresponding groups over here. So that they can support this hydrogen bonding network on this molecule. So, over there you can see if this molecule goes over there, It can creates interaction between them so, let me draw that one more time.

Once it is getting form the bond and say over here is other protein coming and over here, I have this hydrogen bonding diodes where they can create a nice pairing between the groups through this hydrogen bonding. So, this positioning of the hydrogen bonding ensures that yes this molecule has to be entering in this particular way and it is supporting the overall shape of the system and this system can go forward even for salt bridges or say hydrophobic interactions.

So, all these kind of different interactions are possible so, all those together come here and ensure that the molecule goes to a particular different direction. With respect to all those things dictionary of the interactions, the other thing come into the picture is the chirality that also defines how your molecule is going to interact particular through this lock and key mechanism? And that is coming from the natural amino acids and their integral chirality.

So, any amino acids we have drawn that earlier. So, we will draw that one more time is the alpha carbon of the amino acids again and over there this is the carboxylic acid, so, this is the NH_2 group, I mean group this is the R group and hydrogen is the backward. So that is the definition of alpha carbon which connects the both amine group, carboxylic acid and the R group and also in hydrogen and over here in this tetrahedral geometry when I am showing it.

I will put this hydrogen on the back side and then look into the carboxylic acid, R group and nitrogen which is above the plane of the paper or on the plane of the paper and try to connect how this carboxylic acid group the R group and NH_2 groups are connected. So, carboxylic, R group and NH 2 group. When if we took the first two letters of carboxylic acid R for the side chain, N for the amine, we get is a CORN.

So, this is why it is known as a CORN rule which says that how do you define the positioning of the carboxylic acid R group and amine group in a three dimensional space. Where, I am putting the hydrogen on the backside in a tetrahedral geometry showcasing of the alpha carbon and over here you can see carboxylic acid R group and amine group. How I am moving? I am moving like this. So, it is a left hand motion, so that is why it will be called as an L amino acid.

Similarly, carboxylic acid of another alpha carbon, put the hydrogen on the back and now swap the places between amine and R group and over here the CORN rule, you can say it is going the other direction is going on the right hand side rotatory reaction. So that is why it is known as the D amino acid. So, this is the L amino acid and this is the D amino acid and that is how they interact between themselves and this particular D amino acid what we are showing over here, will behave differently than the L amino acid.

Because you can see although the groups are same carboxylic acid, R group or amine group the orientation is different. Where is the R group, on the right hand side or the left hand side? And depending on that they would also create an additional directionality during this interaction and which would create particular phase on this enzyme, binding site or

from the substrate that they would prefer to bind on that particular phase and that also creates an another dimension to this lock and key mechanism.

So, with respect to that we can say yes, lock and key mechanism actually works and over here the different functionalities that is actually creating that one obviously is the directionality of this different interaction. But it is also complemented by the chirality which ensures the molecule has a particular phase during this particular interaction.

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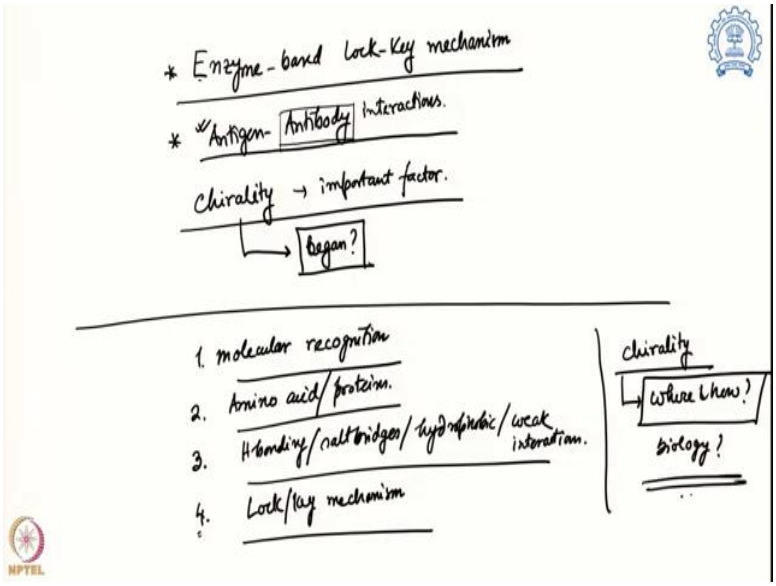

With respect to that the other particular motion other than this enzyme based lock and key mechanism. One of the other example of such interaction is antigen antibody interaction and we have learned this term a lot over the past few years, antigen and antibody interaction whereas antibody is a complex molecule which contains both hydrophobic and hydrophilic interactive regions and which also contains carbohydrate and proteins.

And those things comes and interacts with this antigen which can be different molecules, small part of the protein or even small organic or inorganic molecules and over there the amino acids or carbohydrate molecules present in this antibody they play a huge role on detecting this particular antigen. So that once one antigen comes into the system our antibody can detect it and can create a signalling mechanism so that we know yes, this antigen has arrived.

So that we can trigger whatever the safety precautions we can get from the cellular mechanism. So that is why antigen antioxidant interactions is very much important and it is again is actually executed with the respect of all the different interaction and also the chirality present in the molecule. So, with that two things gone from our hand. Now,

the question comes to our mind we know that chirality is one of the important factors.

But the question is where does this chirality begin? So, you start questioning the origin of chirality. Because so far we know we are seeing chirality from the beginning of the life even for a very simple single cell systems like amoeba they also have chirality because their proteins are made out of the chiral amino acid molecules. Now, the question is where all those things kind of began and can we understand how this particular system actually originated?

So that we can have an idea, how this chirality is playing a huge role in this particular factor? So that we will cover in the next segment. So, in this particular segment we have covered so far the molecular recognition and how amino acid and proteins can come together and create this molecular recognition factors. Third we will also learn about all the hydrogen bonding, salt bridges, hydrophobic interaction and weak interaction.

So, those are the common factors which are going to come into the play and we look into details of this lock and key mechanism and how that works in biology? So, these are the things we have learnt so far. And then we throw a question that chirality is one of the tool for this molecular recognition but where and how this chirality come into the biology? So that was the question that we are going to answer in the next segment. So, with respect to that would like to conclude this particular segment over here. Thank you very much.