Biological Inorganic Chemistry
Professor Debashis Ray
Department of Chemistry
Indian Institute of Technology, Kharagpur
Lecture - 2
Metallobiosite Structures

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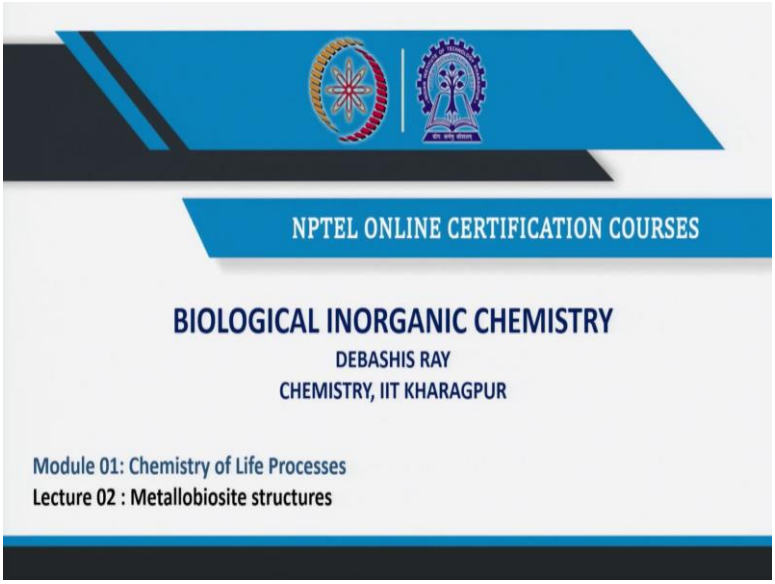

Hello, welcome back, good morning to everybody again. So, we were talking about the chemistry of life processes. So, what are the most important thing what we can understand is that already we have discussed that we can have several metal ions in different categories in different important metallobiomolecules.

So, those important biomolecules if we consider that we have like your haemoglobin and myoglobin, so all the time throughout our entire course, basically, one two or three examples I will be citing every day or every time, is that, that you can have a site and now, we have seen that you can grow the entire site through some intervention of the protein molecule, then some small molecule like the porphyrin ring, we can consider as the ligand.

And we all know what is porphyrin, like your myoglobin molecule if your porphyrin is there and that porphyrin is your ligand system and that porphyrin is being utilised to trap your iron, what is happening then? Why we are calling this lecture number two as the metallobiosite structures.

That means, not only the binding of your O2 molecule to that of your iron centre is important, what we should know the entire structure of the metallobiosite, if at the tip of this my finger, if you have iron, sitting iron over here and you have the porphyrin ring surrounding it. So, we

should definitely know what is known by your typical structure. We all know, why we should be knowing the structure?

Because the important thing is that the iron centre is present in your myoglobin and haemoglobin and the O2 molecule is coming, O2 molecule is trying to interact with the deoxy form, when oxygen is not present, we call it as a deoxyhaemoglobin or deoxymyoglobin will try to interact with that particular iron site.

So, whether that FeO bond will form or not, and how the entire system, the entire environment can help you, whether you can get the typical form of oxymyoglobin or oxyhaemoglobin, directly from that simple coordination of O2, that oxygen molecule, which is available in your air, that O2 molecule to that of your deoxy form of these two important molecules, the deoxymyglobin or deoxyhaemoglobin. So, the metallobiosite structure is therefore, very important, and we will find that how we can find this.

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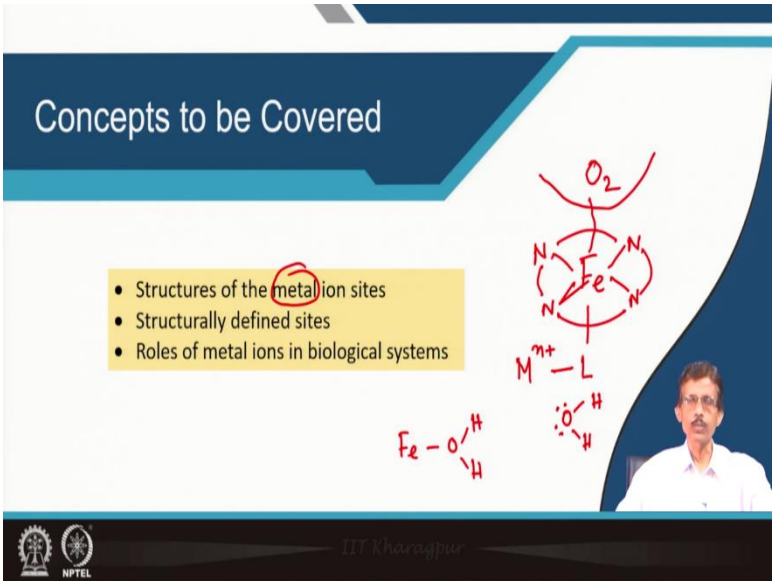

So, the concepts what will be trying to cover here is the structures of the metal ion sites, which is important. That the structure of the metal ions sites are important, then the structurally defined sites also. And finally, the roles of metal ions in these biological systems. So, if we consider that what I told you just now that if you have iron and this particular iron, what you can have, that this iron is forming four bonds and those four bonds basically, if you they are coming from the four nitrogens of porphyrin ring, that we all know.

So, we are trying to know basically that what sort of coordination is taking place and we very simply we say all the time that if you have metal ion, which is Mn plus interacting with your

ligand giving you that particular bond, which is nothing but your coordinate bond, because we all know that if you have water molecule like this, O H H we all know it has two lone pair of electrons and another two lone pair of electrons and if these two lone pair of electrons are donated to the metal ion centre like that of iron, simply.

So, you can have one of the lone pair if it is donated, we can get a Fe O bond from your iron coordinated to a simple water molecule. Now, why we should know all these system that means all these structures? Because what we are talking, we are trying to understand is your this particular coordination site. So, this particular one will be reserved for the protein interaction, the globin chain will come and bind from the fifth coordination site and your O2 molecule basically will come from the sixth sites.

So, that is why all the time we should know about the corresponding structure of all these metallobiosites in metallobiomolecules such that we can something we can correlate which is your structure with that of your activity. What activity we should know, so, first that you have to have the growth of the molecule, then we should know the structure, then only you will be able to tell that whether your O2 will come to bind that particular system that means, if you have two system one is your deoxymyoglobin, another is the oxymyoglobin.

Now, you know that definitely in deoxy form, this O2 will not be there, O2 is out. But in the oxy form of myoglobin and haemoglobin your O2 will come and try to bind to this particular iron site from that particular point. So, in this particular class, basically, we will try to cover about this thing and also, we will try to understand the how the metal ions is functioning for this O2 interaction, that means, the metal ion will try to activate the dioxygen molecule.

Otherwise, we do not get that particular reactivity from that O2 molecule itself, the O2 what is there in our environment, what is there in our air is not coming and interacting with the food molecule to give you the energy, the energy currency the ATP molecules without any kind of intervention from your haemoglobin or myoglobin molecules.

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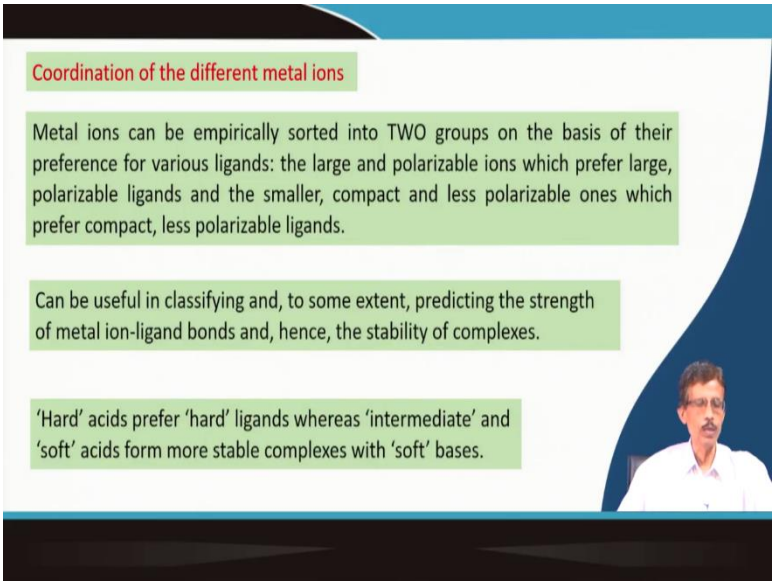

So, the different types of coordination, the coordination bond formation, we all know that the what sort of coordination we can have. So, these coordinations basically the metal ions are responsible like that of water molecule, water molecule will come and coordinate to the metal ion centre. So, when he considered these that the different metal ions are basically important for this particular type of coordination.

So, in which category your O2 molecule will come and which category your water molecule will come, and if we now consider that the coordination of water molecule is the inherent property or inherent behaviour, when your Fe3 plus is present in your blood, in your biological fluid or even in your test tube, whether you are forcing this particular coordination if the water molecules are available around your Fe3 plus ion.

So, how we can consider, if we consider the coordination of iron, the coordination of copper and coordination of zinc. So basically, we will be talking about two groups on the basis of their preference for various ligands. So, already we are considering this oxygen only your O2 of your dioxygen molecule or oxygen of water molecule.

Now, if your nitrogen is coming, because already we discussed about the nitrogen from the porphyrin ring and the nitrogen from the globin chain. So, whether they are going for the coordination equally well to that particular iron centre, that we should know. So, the preference for various ligands, how it is being controlled is that the large and polarizable ions which prefer large polarizable ligands that means, the bigger ligands and the smaller compact and less polarizable ions will prefer the compact ligand.

So, these are of similarity choice basically, if you iron centred Fe3 plus is a smaller and compact and less polarizable, it will definitely attract the smaller anion of the smaller groups. So, these are very much useful in classifying and to some extent predicting the strength of the metal ion bonds and hence the stability of the complexes. Because once we go for these particular interactions, that means the coordination of water molecules to Fe3 plus, if Fe3 plus is present in your test tube, so long Fe3 plus is there in your iron environment of water.

Definitely 6 bonds immediately 6 bonds are forming 6 coordinate bonds are forming over there making Fe H2O whole 6 3 plus, the hexaco iron 3 species, which is always we can have if you add some ferric chloride in a test tube of water. So will consider them as the hard acids, that hard acids prefer hard ligands, that Fe3 plus, if Fe3 plus is hard it will prefer the hard ligand like O minus or O2 minus.

Whereas we can have the intermediate strength between hard and soft and the soft donors as well as soft acceptors for this. So, this is your HSAB principle, we already learnt it from your school days and the college days also.

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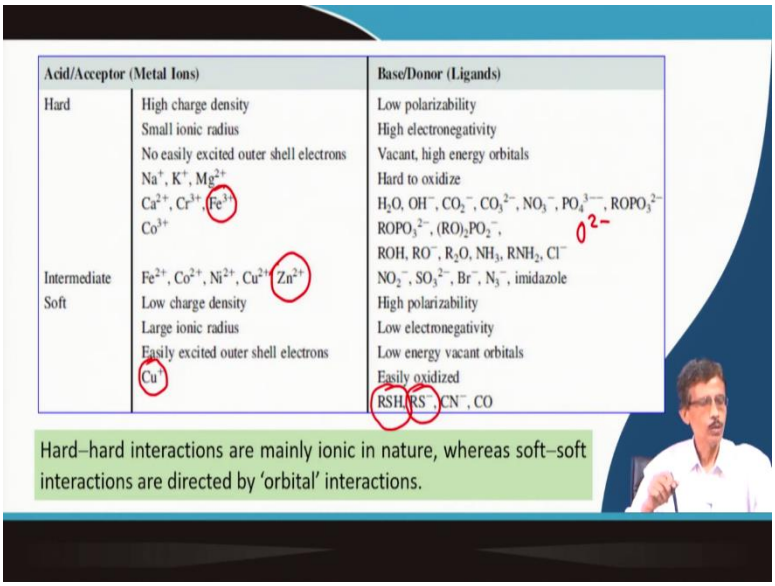

So, hard and soft acid base theory, HSAB theory is equally well applicable to all these metal ions. So, metal ions are nothing but metal ions are electron donor acceptors. So, those are acids like Fe3 plus. So, you can have high charge density for that small ionic radius not or no easily available excited outer cell electrons like that of your sodium plus to cobalt 3 plus.

So, this sodium plus to cobalt 3 plus. So, definitely we can have these and whatever we have just turned that if you have these Fe3 plus. So, you see that Fe3 plus, which is under category

of hard, so what will it prefer, it will prefer the binding of your water molecule, it will prefer the binding of your hydroxide ion. Similarly at some point also it can bind to your O2 minus molecule, O2 minus system or O2 minus anion also.

So, the hard system, so when you have the sodium because some point of time will be also discussing the coordination of sodium as well as the potassium ion. So, what sort of ligand we can have, whether the same porphyrin, the porphyrin is a macro cyclic ligand, where you can have 1, 2, 3, 4 nitrogens, is the planar macrocyclic molecule.

And within it you are putting iron inside, inside the cavity, cavity of the porphyrin ring. Whether the sodium or why sodium is not going there and coordinating to that particular thing. So, this is a different story will be talking about afterwards also. So, the corresponding donors basically they can have the low polarizability, high electronegativity, vacant high energy orbitals, such that you can have this matching orbitals.

Donor orbitals as well as acceptor orbitals, we all know from the molecular orbital theory, that you can have this donor acceptor compatibility and if you have these donor acceptor compatibility, you can have nice overlap of the orbitals such that you can form the molecular orbitals. And the molecular orbitals can have all these electron pairs which are being donated from the donors. Donors are what? Donors, are your water molecule, donors are your dioxygen molecule, donors can be your hydroxide ion and donors can be your oxide ion as well.

So, those donors can donate those electron pairs to the iron centre and such that what ultimately, we are looking for, we are ultimately looking for that bond, that iron and oxygen bond. Similarly, we can have the intermediate soft. So, Fe2 plus they can have these and the softer ones also the softer one like that of your copper 2 plus. So, like your table for the metal ions, the in the metallobiomolecules thing, you should also remember all these things.

So, when you have the copper 1 plus, so, they will definitely prefer that thiolate ion or the free thiol molecule R-SH, is the thiol molecule. So, this sort of coordinations, we can classify it for these types of categories and is also very much important to know what the hard-hard interactions, the soft-soft interactions.

Because the harder interactions are ionic in nature, whereas soft-soft interactions are directed by orbital interactions, the formation of the molecular orbitals, and the corresponding

occupancy of those orbitals by the electrons, which are being donated by your donor molecules.

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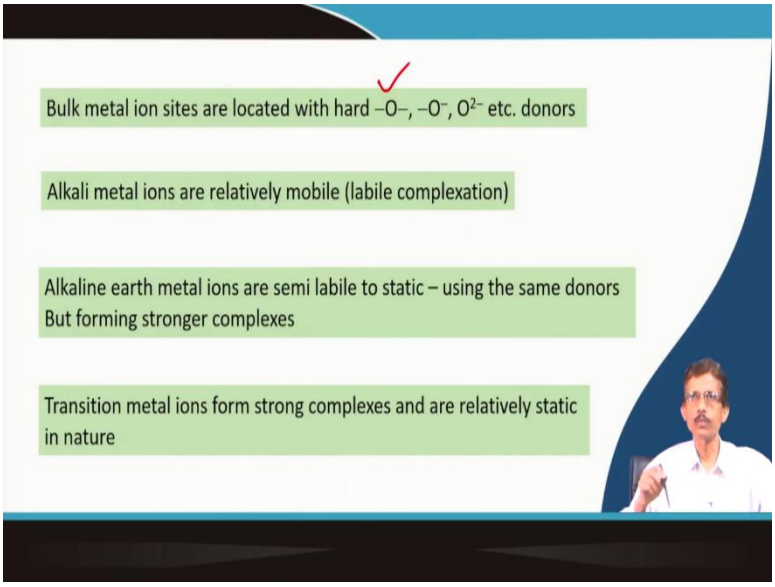

So, the bulk metal ion sites are located with that of your hard, O is ether, O2 bonds is the ether molecule that means R-O-R. So, is that methyl O methyl is the methyl ether dimethyl ether or diethyl ether, we can add then hydroxide ion which is deprotonated form of alcohol or phenol and O2 minus is your water molecule deprotonated water molecule. So, these can function as the donors to your bulk metal ion sites like calcium of all these things.

And alkali metal ions are relatively mobile, so they can go for only the labile complexation behaviour. So, in this particular case, the labile complexation is very important, that means, if your binding is not so strong that we are not talking in terms of the transition metal ions, in your school days, on your early college days also you have learned the coordination chemistry with respect to the 3d metal ions, we have learned only the coordination chemistry of 3d metal ions.

So, when you are dissolving ferric chloride in water, we are getting the corresponding complex pieces of the hexaco iron and that hexaco iron species is basically their complexed form. But when you have the sodium chloride in it is this another test tube containing water. Do you have any idea what species you can have there, whether the same hexaco species or something else that you always ask that why we are talking about, what we are learning about only the dissolution of ferric chloride in water.

So, we will talk all these things because you have, can have a relatively mobile system and your oxygen donor that means, this first category of these donor that means that thioether donor can also come and interact with your sodium ions at the potassium ions. What about alkaline earth? The magnesium and calcium they are semi labile to static using the same donors but forming a little bit stronger complexes compared to your alkali metal ions.

But finally, the 3d metal ions, they form strong complexes, definite complexes and the coordination number as well as oxidation number if is known. They give you some static configuration and they are relatively static in nature. That is why the iron present in your, this particular systems of myoglobin and haemoglobin when iron forming four bonds with the porphyrin nitrogens, then the fifth bond with the nitrogen of the globin chain, and then the sixth bond with the O2.

So, it will definitely give you a geometry, the coordination geometry which will be, we know the most preferred coordinates in geometry is the octahedral geometry when your coordination number is 6. So, with the coordination number of 6, you will be getting octahedral geometry. So, whatever structure and whatever function will be talking about, will be thinking about will all move around with that particular geometry.

So, we will have the octahedral geometry and with that octahedral geometry, you have to think of the O2 binding, you have to think of the function of the cytochromes, can have to think of the corresponding metalloenzymes also the bearing iron. So, iron, you have seen that iron is present in so many places.

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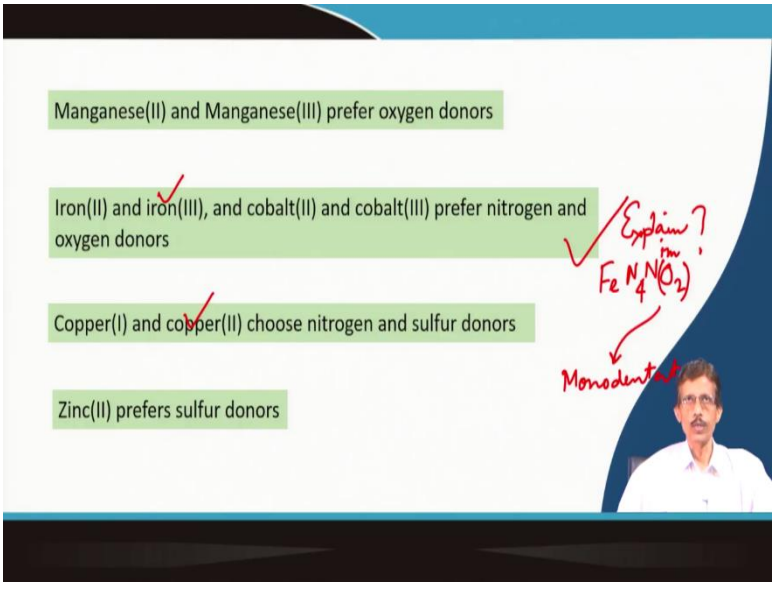

Then we can have manganese II and manganese II they also prefer oxygen donors iron II, III and cobalt II, III prefer nitrogen and oxygen. So, that is why you give the clue over here, that if I say that this is the statement based on the HSAB principle, and if I ask you now, that whether you will be able to explain it or not, the way I explained it.

So, how you explain it? You have to explain it in such a way that you have to put these iron centre that means Fe3 plus in that particular category is properties and all these, these are the atomic or ionic properties. And based on that whether it can have some preference for nitrogen and oxygen such that we can have the corresponding Fe coordination, Fe4 nitrogen from the porphyrin.

Fifth nitrogen from the imidazole donor of the globin chain, then you have the O2 molecule is not O2 is the monodentate, so, is the monodentate ligand, so is the monodentate. So, 4 plus 1, 5 then 6, so 6 coordination sites are fulfilled. So, those 6 coordination sites will give you the corresponding deoxy form of your haemoglobin or myoglobin.

Then copper slowly we are moving from the in the periodic table from left to the right. So, we are moving towards the end before zinc, but copper in two oxidation states, they prefer nitrogen and they prefer as well as sulphur. So, that is the very important class of molecules.

So, when we will be considering the hemocyanin, side by side with that of your haemoglobin will see there that you can have the corresponding coordination of copper with that of your not only nitrogen but also O2 also. So, the O can also come for this particular copper, which copper form of copper is your copper II.

So, between these two metal ions also, that copper II and copper ion your corresponding hardness or softness are also different. So, they will definitely have in a particular environment, the choices because the mixed ligand environment you are also modulating the corresponding character of your metal ion site.

Due to that coordination also like that of your coordination from the porphyrin to that of your bare Fe3 plus when it is bound to the porphyrin your character is changing and that change corrector of this particular iron site will tell us that whether it will attract another nitrogen or another oxygen.

So, that is the most important judgement over there where we can find out all these things. So, zinc also again, it can prefer nitrogen as well as sulphur, because zinc is the bigger one is

a 3d ten cistern, all the d levels are filled and it also like to have the corresponding coordination with that of your sulphur donors.

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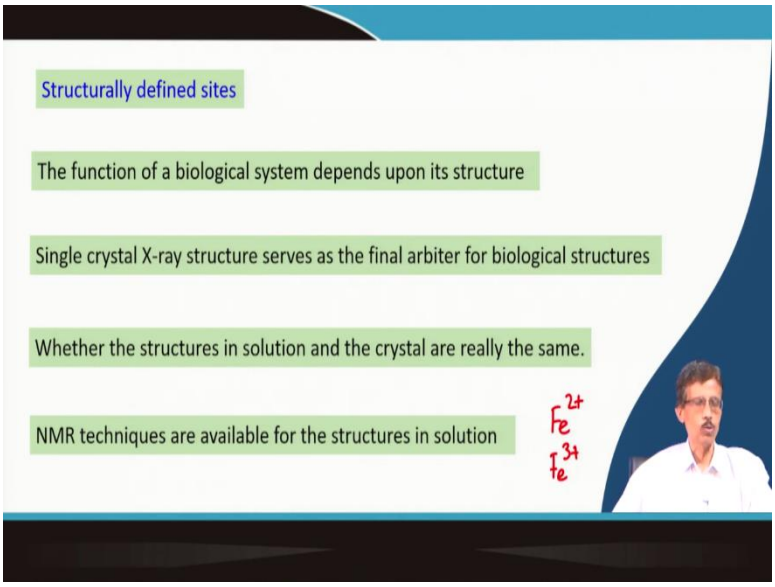

So, this all these informations that what they are being, they are trying to have it. So, we must have the structurally defined states then. What are those states basically? So not only the structure around the metal ion like iron, the hexacoordination around that iron centre, but also, we try to know the entire structure of the metallobiomolecule like the protein crystallography, is a very complex thing.

But we the inorganic chemist or the coordination chemistry will try to see the molecule from the point of view of understanding at the point where iron is present. So, the function of a biological system therefore depends on the structure that is why the structure function relationships we all know and a single crystal X ray structure analysis, so many times will be talking about the methods the physical methods, what we can use to understand the structures as the final arbiter for biological structure determination.

So, definitely it is the protein crystallography which can ultimately or finally determine the whole structure of these molecules. Whether the structures in solution and the crystal are really the same, that is the important thing because we are talking about something where your biomolecules are swimming or biomolecules are floating in the fluids or the solution system.

But, at the same time, when we are trying to find out the structure, it is the crystals, the crystallised form we are talking about, so we have to correlate these two. So, if the single

crystal X ray structure determination can find out the actual structure in the solid state. So, that gives us the solid-state structure of those biomolecules or the biological structures. So, what about we should know about the corresponding solution structure.

So, NMR, Nuclear Magnetic Resonance techniques will be then useful to understand to know the corresponding structures in solution, which is very important. That can also tell us whether the crystalized structure is preserved in solution also, but again it will be a difficult thing because this NMR technique does not go all the time nicely with that of your paramagnetic metal ion centres.

So, we all know that the Fe2 plus and Fe3 plus, so they have unpaired electrons. So, if you have a Fe2 plus and Fe3 plus having the unpaired electrons, so the paramagnetically shifted, the contacts shifted signals you can have. So, those contact shifted signals can be there, and those signals can be very difficult to find out or difficult rationalize in some point of time, but if it is zinc, which is a diamniotic centre metal ion centre. So, for the zinc protein structures in solution can be very well or very easily understandable to us.

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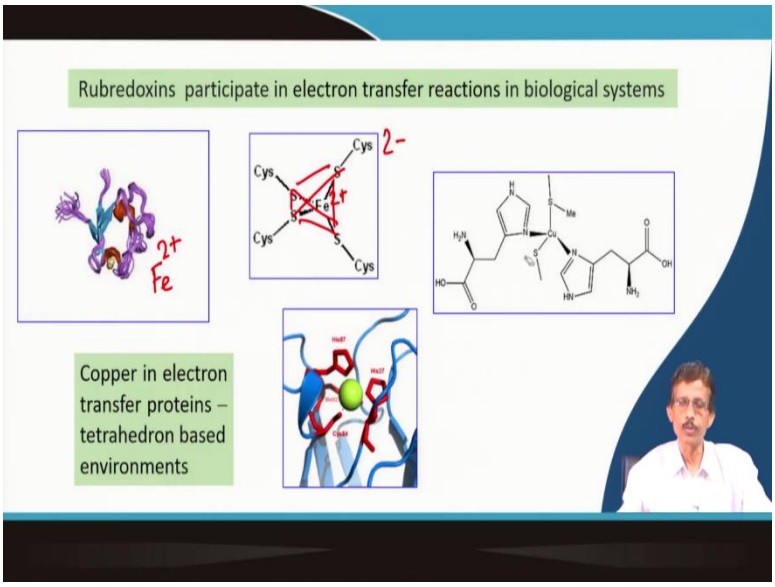

So, what do you find then that you have to have the corresponding molecule and will be talking about some names only now, we are bringing some simple molecules what we can have that of your rubredoxins. So, rubredoxins what you can have, what is that rubredoxin? Because the function is known and long back or many years back basically people first identified the molecule it is showing some electron transfer behaviour.

Then they identify that what metal ion is present over there, whether iron is present, copper is present or zinc is present that is important. So, identification of the metal ion like that of your identification of any unknown sample. The chemistry starts with that only the analytical chemistry part what we talk about, the identify the corresponding metal or the metal ion in the system.

So, in that particular case what we you find, that if you have the rubredoxin and that rubredoxin is therefore with you, and that rubredoxin basically is therefore is a huge structure. So, this is the protein crystallographic understanding and that protein crystallographic understanding will give us that particular structure is a huge structure.

So, is a protein part is there, but what do we try to find out what we should know that if I say that no, that analysis the chemical analysis or biochemical analysis as told us that we can have a iron site and also, we do not know whether you have a ferrous iron or a ferric iron which is present, where that iron is centre is. And sometime it is easy to understand and easy to find out that particular metal ion in a huge protein structure.

Because the methodology what we follow the singles for the single structure determination the heavy atom method, one method is there because the electron density around iron centre will be more compared to your carbon, compared to your nitrogen or the oxygen or the sulphur. So, iron will be detected first.

So, that will immediately tell us whether you are having a single iron centre or a double iron centre or more than that. So, to locate that particular iron centre, you see these red spears and all these spheres will be coming there and that structure can be found out nicely if you know the structure.

So, the coordination environment which is also important, the coordination environment then determined as FeS4, you have iron and 4 sulphur, the organic sulphur, the amino acid is your cysteine sulphur. So, when 4 cysteine sulphurs are coming and coordinating to your iron site and your iron is say your ferrous iron, what geometry will be getting, that also you will be able to find out from the structure determination.

If you zoom the structure and if you are able to go to this particular point, what is that particular environment of the coordination sphere made up of 4 sulphur atoms or sulphur donors. So, the environment is S4, 4 sulphur, thiolate sulphurs all are charged. So, the overall charge will be there if you have a complex of this type of thing, if you have Fe2 plus here like

that, if it is Fe2 plus 4 sulphurs are giving 4 negative charges. So overall, the compound or the system will have a charge of 2 minus.

But interestingly what you will be able to make out from here is the corresponding tetrahedral geometry. So, this is your tetrahedron around iron. So, that particular tetrahedral iron geometry is important to find out from that particular structure. Similarly, if you have the copper, copper in electron transfer proteins, and again a tetrahedral geometry based on environment.

So, you find out so if you zoom it, this is the rubredoxins structure, if you zoom it more, you will be able to find out the histidine residues which are imidazole ring, imidazole ring around this copper site. So, like this you will be able to draw it also in a plain piece of paper. This is the corresponding amino acid part from this that mean the histidine residues of the protein part.

So, this is protein, this is part of the protein not that these finishing over here, amino acid we are showing the amino acid histidine residue, but they are part of the bigger protein chain and the copper environment bound to one thiolate and another thioether sulphur, this is the methionine SME group.

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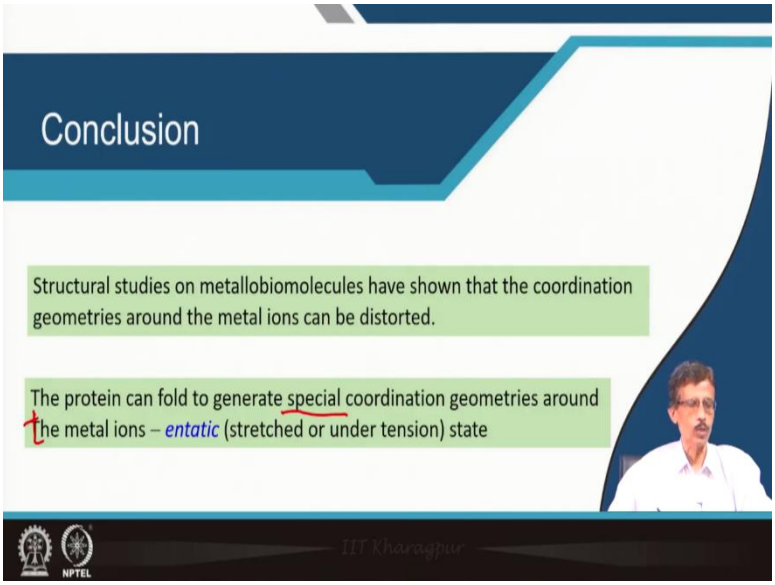

So, these particular determinations and the structures basically tell us all these information. So, what we can conclude over here from this particular class is that the structural studies are important. And these structural studies give us many informations of these metallobiomolecules, which is showing some very important coordination and the geometry.

Because at the centre whether your iron is in tetrahedral geometry or in octahedral geometry like that of your haemoglobin and myoglobin is important. Similarly, the metal ion copper in a particular oxidation state the cupric copper, copper 2 plus or cuprous copper, copper 1 plus coordinating to some donor atoms available around it is important.

And then finally, the structure will also tell us that the huge protein chain there are say 150 amino acids or 200 amino acids forming the polypeptide chain. So, there are this particular thing is mainly the governing the entire structure. So, they will force on the donor atoms such that you can have huge amount of distortions.

So, the protein can fold the protein folding. In our future classes will be seeing the protein folding and how the protein folding is important to manipulate the coordination around these metal ions. So, those can fold to generate a special coordination geometries which are neither tetrahedral or not a square planar geometry say for a coordination number of 4.

So, it will give rise to spatial coordination geometry around the metal ions. So, it will be a small t, not the capital T's, metal ions giving you an entatic state and that entatic state is important which is a stretched state and under tension, which is giving rise to all these reactivities. So, a distorted structure we are looking for, we will be looking for a distorted structure which will be functionally more active.

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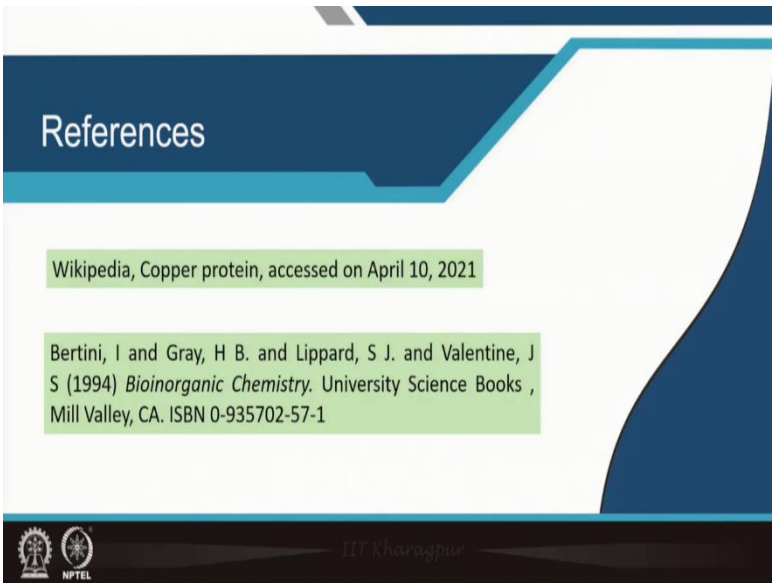

So, definitely will be going for so is a very well available area of references I most of these classes, I will just give you that if you are reading something quickly go to the Wikipedia page and search for the copper proteins. And then one book which is on Bioinorganic

Chemistry by Bertini, Gray, Lippard and Valentine. So, is a huge book, but the part what you are looking for, that you can consult that you can see also. So, thank you very much. Thank you all.