**Introduction**
**Bioinorganic Chemistry**
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**Lecture – 1**

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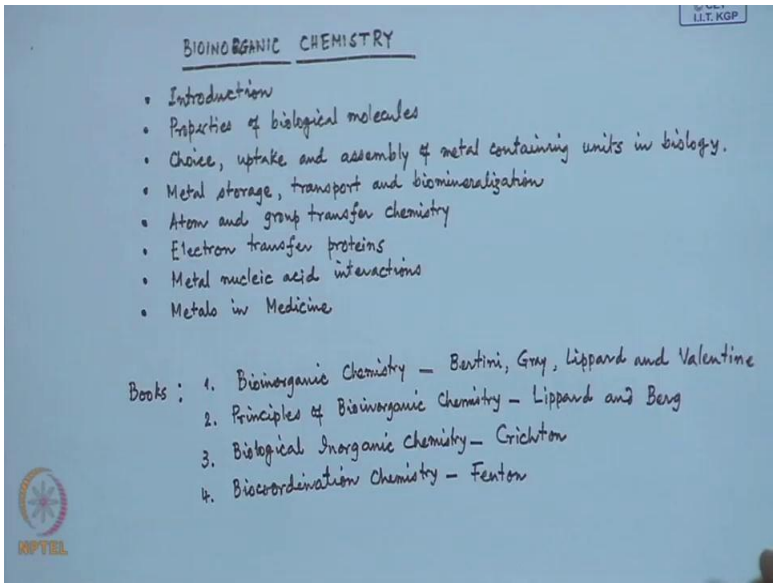


Hello. So, in this class we will be talking about some basic aspects of bioinorganic chemistry, and which will be covered with in this first class particularly, introduction which we will deal with some of the basic aspects, but little bit we know and some more will be covering in this class, and related to the second one is the properties of biological molecules, and these properties are basically different from what we know about the typical molecules, where we have something where we know that the basic skeleton is made up of say your carbon, hydrogen, nitrogen and all these, and most of the time we will be talking about since then organic part of this will be covering as starting with the metal ion.

Suppose we have the hemoglobin, where we have the iron, and that metal part if we just simply considered, and if you considered that the metal is coordinating with the some of your important ligands, we can considered this as the bio codes in chemistry in that way. So, how these properties of all these biological molecules are different from that of our simple typical small molecules, where you have one metal ion, and several ligands.

So, if the source is different; that means, if the metal source is all the biological source, and the ligands are all biological source, and when they are interacting, and how they are following, whether they are completely different from what we know, from our laboratory knowledge, that how they are giving some metal complex, and how they are forming in our life process. So, the next one we will just covered that choice uptake and assembly of metal containing units in biology, where we will see that how, the nature has a typical choice process, such that it can, take the particular metal ion, or some non metal species, for its typical action, and how it can take for its utilization, and finally, the assembly of metal containing units.

Assembly is the typical process, where we can have. Suppose a metal centre is there, and when it is coordinating to the biological ligands or biogenic ligands, but the source is biological only, and that is forming some unit what we call as the metal ligand assembly. So, you have one metal, and depending upon its demand or coordination environment or the nature of the metal center, it can bind either two ligand or it can bind four ligand, or it can bind six ligands, together around the metal center, but these particular assembly process, what we will be talking there, when we have one particular metal center, and a molecular unit is functioning for some important reactions.

Suppose we know little bit about that hemoglobin or myoglobin system, where we consider that the iron center is there, and some of the donor groups are there surrounding the metal center, and forming a mono nuclear unit, but if we go beyond that; that means, the mononuclear system is giving through some bridging ligand to a binuclear system or that binuclear unit is thought the taking of another center giving your tri nuclear unit, because this is important to know, where we know that the assembly of metal containing units, how we can have, because we are utilizing these metal sorts, say iron from our body, but we are taking this particular iron from our dietary sources, from our food material, and that iron is going to our body. And we are slowly absorbing those iron, and how this is basically related to our laboratory knowledge, that where we use some metal, we take some primorigen bottle. You have the ligand already synthesized, but for in our body, or in plant system, or in any other living system, we do not have all these things. So, you should have the source of the metal, as well as the source of the ligand.

So, how we get all these metal centers, we metal centers we are getting from the food material. So this uptake is important in that way, how the system is taking of that iron,

and that iron will be utilized for some useful purpose. Suppose that iron is utilized for our blood synthesis, or hemoglobin synthesis, but for that particular synthesis what we need. we need the metal, as well as some ligand, say porphyrin ligand, but you should have the source for the porphyrin, as well as the source for the iron, but you cannot wait, till you reach the corresponding available iron site.

That means, you have to wait for food material, what will be taking, or iron source direct iron source we are taking some time, as some iron tonics or something, but you have to wait for the hemoglobin synthesis, or all these things, but the hemoglobin synthesis is a regular process, throughout the day, and throughout the month or throughout the year. We are continuously synthesizing that thing. So, we should have some regular source, and that regular source, we will deal with after that what should be your iron store house, how you can store iron in our body.

So, for that purpose also, we should have some specific mechanism, where we can absorb the iron, from your food material, or any other source, and that iron is taken off by some small ligands or some groups, and that is there, and it is transferred from one particular part to the other part, and that part is responsible for storing that iron; that means, the store house of the iron. So, that is why this particular, the assembly process is important, because in that assembly process we stored large number of iron items. So, the next one which we will be talking about is the therefore, your metal storage then transport and biomineralization. So, you can store the metal centers, it is not only true for iron, it can be true for zinc, it can be true for copper, because only three four metal ions we know, they are concentration is very high in our body, and those metal ions are useful.

So, you should some store house, but only what we know so far about iron only, but we do not know in detail that how the zinc is stored in our body, or copper is stored in our body, but in the recent developments of the recent studies what we are studying now a days, because throughout your life, as we are going older and older, suppose after 70 years or after 80 years or after 60 years, how these store house of this metal ions are behaving. Are all them are utilized for your blood synthesis, or they are doing some degenerative process in our body, that people are talking.

People started enquiring all these things, how these two diseases will talk about little bit afterward; the Alzheimer diseases and Parkinson disease, why those two diseases are related to the accumulation of your metal ions in your brain. So, not only that when you we take the food, and for the stomach the metal ions are accumulating, we are accumulating, then slowly through your serum or the blood stream, it is moving through the through your entire body, and ultimately little bit of that for our neurological processes or generating the neurotransmitters, is going to our brain also.

So, for that particular purpose what we see that, metal storage transport and biomineralization. We know all how nature is doing for our us, how the nature is storing the metal ions, in a old or mineral fashion. This is that, the same thing the bio mineralization term will be discussing afterwards, that how the biological system is also responsible for some type of that mineralization process.

We know iron in the nature, we know that they are available in the form of hematite, magnetite, and all other iron ore, from your school days you are learning all these things, but in our body how they are getting stored, from the free supply of the ions. The supply of those ions in the Fe2 plus or Fe3 plus, and those are then stored in our body, in some typical form, and that particular form will considered as your biomineral. Next we will just talk about the atom and group transfer chemistry. This is nothing but how we can transfer one particular atom, or a particular group, from one system to the other. The way we know that the iron center is responsible for accepting our oxygen molecule, when we get the oxy hemoglobin, or oxy myoglobin molecule.

So, the entire thing is that, here is a dioxygen molecule, which is getting attached to your metal center, and dioxygen is behaving as a ligand, but in this particular case, what we see that, the atom and group transfer. So, in the biological systems, if we sign that the iron center is there, and that iron center, if we have that particular iron center, which is attached to the dioxygen molecule and that dioxygen molecule afterwards.

If you confined some mechanism is there, and it is happening in our living system also, that if you have a oxygen oxygen cleavage. we know there is a very strong bond there, that oxygen oxygen double bond is there, but if you are able to claim that, such that you can mix something, where if you have the F e o system, the ferial system or the F e o oxy system, which is very much similar to that of our typical of some other metal center's

that we all know, that the venal dial system or the moleupdia system, and how these oxygen's are transferred, because these oxygen is utilized for making some important transformations, and making some important molecules, that these oxygen whether that particular oxygen say, for some example that corresponding reaction, what we know that the insertion of the oxygen atom, say in some C H bond, what we call as a oxygen in insertion and reaction and for that oxygen. Insertion and reaction what we use, we use some par acids, or some the agent, some chloroperbenzoic acid or a diesel benzene.

So, that oxygen is getting transformed to some of all these organometallic type compound, but if in the biological system that is also required, that we have to transfer that oxygen from one system to another, and that particular thing is basically activated by the metal center. So, metal oxo systems, most of these cases, we will talking about to the metal not nitrogen or sulphur all other case. So, will talk little bite about this metal oxygen system, and how we can accept that oxygen; that means, you have the pure system, where you have the metal center, this talking up all these oxygen.

So, you are getting that particular oxo complex, and afterwards that oxo complex is transferring that oxygen, for oxidizing some others species. next we will be talking about that electron transfer proteins. So, all these things, because we are talking about iron. So, why iron is so important, because we know much about the iron center, starting from your blood, your cytochromes and all other system, and some of these metal centers, when we consider that this is a basically a consideration for the center, where you have the metal centers which are either redox active or redox inactive, like zinc and iron.

So, some of these reactions, some of these characterization, and some of these properties, it will be typically related to zinc, where you cannot get the some electron or you cannot put some electron to the system, but if it is a system which is iron based, and we all know that the iron is settling very easily between is plus two oxidation state, and plus three oxidation state. So, you can take off large number of electrons from the system, or you can put large number of electrons to that particular system, because which is very much required, when we try to oxidize, or reduce a particular system.

Suppose we try to reduce dioxygen molecule, for our assimilation, for our food oxidation. We try to reduce dioxygen molecule to water, so we have to supply for electrons in the same passion. In the photosynthesizes also, we try to oxidize the water

molecule to get the dioxygen molecules. For all these electron transfer reaction, and the molecules which are default in all these radox process, will be talking about this electron transfer, but they are from protein origin, so biological molecules which can supply electron, and which can take up electrons.

So, they are oxidoreductases, so they can provide for your oxidation reactions, and they can also provide your reduction reactions. then towards the end of this course, will basically talking about metal nucleic acid interactions, where we will see that, we all know that the component for the D N A R N A, all these the nucleic acid the nuclear tides, and the nucleosides and all, but how they are interacting with the metal, whether the metal has some role to play, for the different reactions related to your D N A and the R N A molecules. and lastly will talk about, the metals in medicine which is very important, because some of these metal containing important compound we can use as medicine, but before that we should know little bit about something ,where the metal center is directly involved for some of our diseases. So, than only we can find whether it is a your c split anticancer molecules or not, how we know that.

That means, if we know that the function of this particular platinum complex, and all these reactions, how it can help that the metal center is required, and two of these donor groups are coming from your D N A molecule or the any other living molecules, and they are doing something, where you can stop the propagation of the tumor growth, or any other growth system or whether those metal centers, can be involved whether that you are using a redox active metal center, or in redox inactive metal center, that for the d n a cleavage action. For that what we need, that we have now the D N A we can consider that D N A as a very big ligand molecule, because we know all the donors groups available, and metal is very useful to bind we all know that. It is all the time which is, nothing is there available to the metal center, it can bind to water molecule. So, it can bind to water molecule, and that water molecule after deponent, it can have a corresponding hydroxide complex.

So, in that particular form, that whether nothing is available, you can have a metal center which; that means, the availability of the metal center, close to your all these nucleic acids, or the medicinal molecules is a important, but if that particular water molecule can be substituted, by some of the donor groups from the medicine, or from the nucleic acid. So, metal will all be interacting, with all these useful groups. So, that will see how the

metals are interacting with nucleic acid, as well as the medicine. So basically some useful books will just cover, or you just study you can have, those books number one is, your bioinorganic chemistry Bertini Gray Lippard and Valentine. Second one is, Principles of Bioinorganic Chemistry by same Lippard and Berg. Third one is biological inorganic chemistry by Crichton and last one is also related to these and very handy book is bio coordination chemistry by Fenton.

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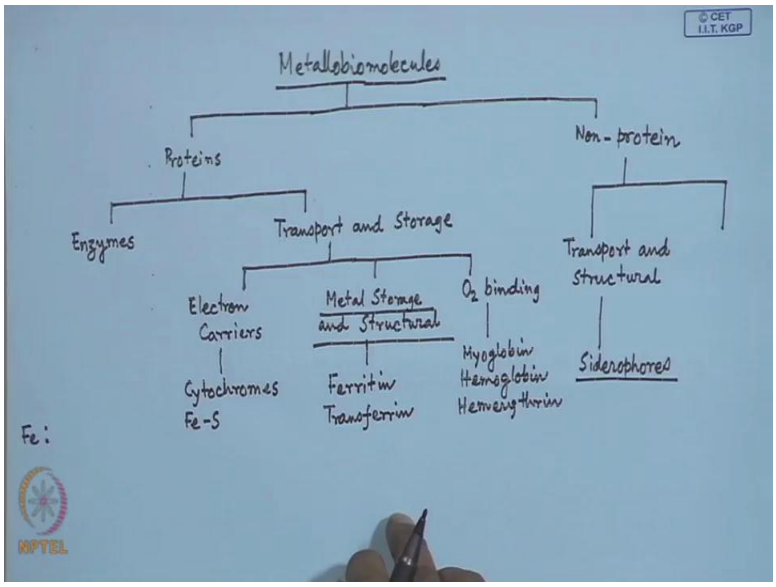


So, the basic classification for all these molecules; that means, whether we can have a typical metallo biomolecule And these metallo biomolecules you have the metal center and; obviously, will be talking about those metal centers, and will always referred, where ever you go, and where ever you study all these things, that how these metallo biomolecules are classified, depending upon their function.

So, there are certain aspects that metallo biomolecules, you can classified as per there functional behavior, as there metal ion content, because when we look from a inorganic chemist in point of view or codeine chemist point of view, how you see, a particular metallo biomolecule. A biologist can see from its biological site, his eye is well trained, well expertise eyes of biology, but when I see, or you see that from a cortisone chemist site, that you will first look at the metal center, and you will always try to gathered information related to that metal center, and that is why you always interested to those molecules only.

We are not taking any system, where you have a system, some enzymes, and some protein molecules, where no such metal centered is there, but these groups, like this metallo biomolecules. You have some metalloenzymes, why we are taking all these things, because we know the property of these metal ions. We know how they are coordinating to the water center, if you have the water as the ligand, or if you have the ammonia as the ligand or any other small groups as the ligands, because we know how these metal can interacting, because the bonding pattern, then the detail chemical pattern, or the chemistry pattern, chemical bonding is known with the respect to that particular metal center. So for ours, for this particular type of class, it is very easy to classify all these, with respect to the metal center. If I ask you that how many of these metallo biomolecules you know, related to that particular metal center, say iron.

Next we know, we should know the what are the different structures, because when you have the iron site in a test tube, in laboratory class if you say iron in your test tube, and then you put the ligand, any ligand starting from your water; the most simplest possible ligand is the water molecule, two ammonia or any other complex ligand system. You immediately tell me, no this is from me a corresponding octahedral compound, or tetra hydra compound, or something which is a dinuclear compounds, but all these cases you do not know that detail structure. So, once you identify the metal center, next thing what we try to know, is the corresponding structure, because the structure is all the time very important, when you go for complex ligand system. So we will see that your ligand is not a simple ligand now your ligand is not water molecule, your ligand is not ammonia molecule simple, but they are complex.

So, when you have a complex ligand system, and you put that metal on that system, but what is happening, the metal will always try to find its available donor side. Suppose iron is there, and it is you having a complex ligand system. So, iron will try to coordinate to the available donor item, whether it is nitrogen or oxygen or sulphur. So, the organic part, that organic complex molecule or biological origin, will have to find out that how many oxygen are there, how many nitrogen are there or how many sulphur groups are there.

So, immediately those groups will come close to iron, and if they are falling at a bonding distance of 2 Armstrong or so they will try to form some bonds, but if you are available donor groups are less than those required numbers, say we are looking for a octohydrol

complex for iron, but the available groups are less; that means, available groups are four, or available groups are three what will happen, your iron will bound to the that particular organic ligand, and you will have some vacant positions, and those vacant positions are very useful, because in the laboratory you cannot control all these things. Once you dissolve the iron or salt in water, in a test tube what will you find that you are getting a hexaco complex of iron two, or iron three.

You cannot say that, I have something; that means, only three water molecule are coordinated to the metals center, and remaining three are not there, but in the biological system, to know the structure, we will find that those three groups from the that organic part of the molecule, is coming and attaching to the iron center, and you are having three vacant sites. If it is in the water system, because most of the time we will be talking about water, in our living system it is water system.

So, they are all will be coordinated by water molecule. So, the next thing once you identify the metal center, next thing you should look at the corresponding structures, and for that metal is playing an important role. All the time what we are talking so much about all these metal enzyme, because protein crystallography is a huge subject, is a vast subject, and that protein crystallography when we try to get the corresponding crystal. So, we used x ray do for the structure determination, and for that structure determination we always see, that some x ray is used, and the diffraction patterns we are getting, but the first thing that you should have the right sample, and that right sample is in the crystallized form.

So, all these biological samples, divide of metal center, they are all of biological origins, typical organic molecules, and some time those organic molecules have very big. They are trapping huge amount of water molecules, or some other molecules. So, it is very difficult to crystallize those molecules for x-ray diffraction, but if it is there metal enzyme or metal containing molecule. So, that particular system, that assembly of the metal and the biological ligand, it is easy to crystallized, and during that structure determinants, it is also easy to identified, without taking the help of the other spectroscopic properties, or the spectroscopic determinations for the metal ligand distances, or the metal ligand size. You can find out or you can locate from the diffraction pattern precisely the metal center. The first thing what we can do, because the

atomic mass is very high for the metal. So, that particular technique is known as the heavy atom method, you can locate the metal precisely, and very accurately.

So, that is why it is giving you a useful structure, if you do not know the detailed structure. Suppose the detailed structure of your hemoglobin molecule, or the myoglobin molecule, but if you have a diffraction pattern, and which you can partially solve, you can find out or you can determine the structure, which is your immediate impartment of the iron, and that gives us some idea that we can find out, the immediate impartment of the iron, and which is also very important to know, the function of the metal, related to your function of the hemoglobin, or the function of the myoglobin. So, three things we can together we know, to identify the metal center. Then you know the structure, and then how this particular structure, is related to your functions, different functions. So, this metallo biomolecule. So, there is atypically we all know that, one part you have the protein part, and another is the non protein part.

And in the protein part, you can have the enzymes, and when you have the metal center, they are all your metal enzymes, and these protein parts can be further subdivided into two, and the other part is your transport and storage, and this transport, because we will focus our attention here only, because we are lot elaborating the entire subclass of all these things, because if you know all these classifications initially, you can tell what particular type of metallo biomolecule we are dealing with, and how these metallo biomolecules are related to some the names of this molecules. So, if you have these transport, and storage in terms of electrons. They are basically electron carriers; that mean, you can have large amount of electron, and these protein molecules featured important for these; that is they are basically your metallo biomolecules, and those metallo biomolecules are protein in nature, and they can be useful for transport and storage of electrons.

So, these are basically electron transfer molecules, and those molecules we all know, they are the examples are your cytochromes. So, what are cytochromes, from this chart, or this table you can have, that what are cytochromes, you can able to tell, that they are electronic carrier they are a transport and storage type, because they can tunneling electron, they can store electron, and they are in protein nature, they are of metallo biomolecules type, so in these cytochromes as well as your iron sulphur proteins.

So, when we identify, what I was telling you, that when you identify these centers, that what are your iron sulphur proteins; that means, when your name is there, you can immediately tell that is iron is there and sulphur is there, but the metal center is present is your iron, but for the cytochromes also, you have the iron centered present there, and now the next one is important and we will start from there basically, which is your metal storage, and structural. So, how we can utilize these protein molecules, to trap your metal ions, and those trapped metal ions can be stored.

So, we will have a store house of these metal ions, and this storing of these metal ions can also be utilized for your different structural pattern also. So, under this category we will consider two of these molecules; one is your ferritin. So, these ferritin molecules are basically your metal storage system, where we can store our metal ions. In our body also, we stored these metal ions as ferrtin molecule so, how you get these ferrtine molecule?. So, ferrtine molecules we will have a huge protein envelop, and within that protein envelope, you can store large amount of iron centers.

So, basically this particular, if the details studies known, and if you can know that how these transferritin molecules are forming there. You can tell little bit about the process, what we considered as your biomineralization process. So, huge protein envelope is available, and you are supplying one after another forms your food material, the iron site, and that iron is going from one particular place suppose your intestine or some other place, to the site where you have the ferrtin molecules are not that is distributed throughout your entire body.

At some location it is there and that location how you carry this. So, what you should know first, whether the molecules which are responsible for carrying these iron centers, or how they are stored. So, these two are related, so that the transport as well storage of these iron site they are for therefore, related, how you can utilize those molecules. There will be some protein molecules which will be utilized for transferring your iron site from one point to the other, and once you transferred that there something is available again, which can store your metal center. So, that is there. So, one such molecule is ferrtin, and another is transferrin. So, name immediately tells us such that, this is responsible for your transfer of iron. So, that is why it is transferring, and your F e is your iron, ferritin is also related to your iron site and. So, these two are related for your metal storage and structural once. So, these we will discuss next, and for completion of this particular

transport and storage, with respect to electron carrier, with respect to metal storage and structure, and the third one is o two binding, that little bit we all know.

This oxygen binding, and this oxygen binding is also related to your transport and storage, how you transfer oxygen dioxygen molecule, and how you store dioxygen molecule, because there we all know, that we have this for O 2 binding, we have the myoglobin molecule, we have the hemoglobin molecule, we have the hemerythrin molecule. And from the non protein part, one part will take, because for, what will discussed in possible.

In the next class is our division from this non protein part; one is your transport and structural, and this is very important, that we have moved from a protein part to a non protein part. So, it may not be related to mammals, or human system. It can be to your planned system, or it can be to your bacterial system, how the bacteria is utilizing, because we all know that, we are also all the time we should know, little bit about this bacterial part of their metal assimilation, because the bacterial infection, always we are suffering, the pathogenic bacteria, how it can be controlled, not only through medicine, but also from your balanced for the metal iron.

So, bacterial thing and all these things, they basically utilize the non protein molecule, for their transport and structural part related to your iron. So, that iron basically, for this transport and structural part, we have molecules like siderophores. So, those siderophores, they are all iron bearing molecule. So, those iron bearing molecule, they give basically the siderophores, but these siderophore molecules are not protein molecules, they are small molecular weight molecules, and those molecules are utilized by the bacteria, for transferring that iron from one site to the another, and to know the detail of this siderophores is very important, because they utilize some useful structure. So when people determined the structural.

People know this structure of all this molecules. The siderophore groups they are basically very good ligand system, where one particular part is providing a bidentate part, and three of these groups are attached to a micro cyclic ring type of thing, and they are basically trapping that iron and transferring one from one part to the other. So, basically these things will see first, that the ferritin molecule, the transferring molecule,

and the siderophores. And for that particular thing, and will just simply go for, that how this particular metal ions play important role for some of our bio chemical processes.

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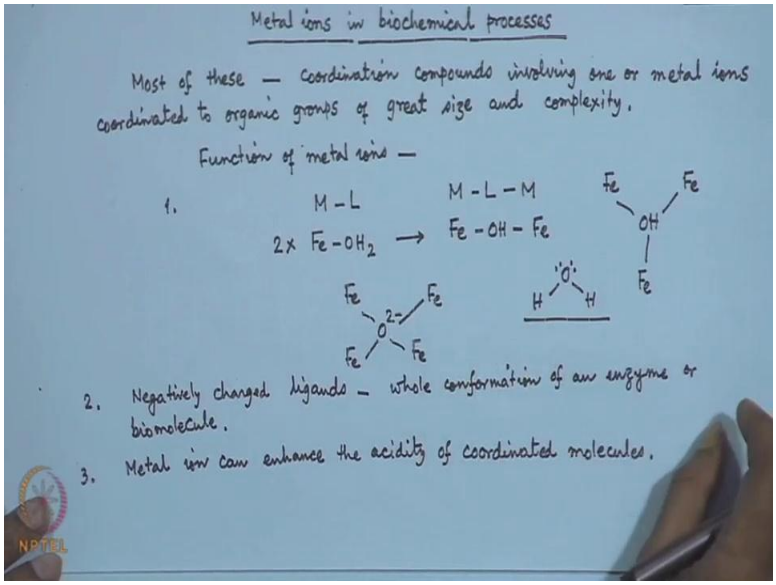


So, most of these are coordination compounds, involving one or more metal ions coordinated to organic groups of great size and complexity. So, we all interested to know, the function of these metal ions. So, for that particular thing, that you have the metal and the ligand system. So, when you have something, that you have the ligand, it can also function as a bridge to two metal centers. So, the way we know that if you can have, iron bound to water, at the same time you can have, in the deported form of the water, you get F e O H F e system. So, for this particular purpose when two such thing; that means, when two of these, interacting to this forming a bridge system. So, you have the bridging group. So, how they are forming, because this iron is there, you have water coordinated, and we need to deponate this one particular water molecule, and one water molecule for the second iron center, is leaving. So, that o h is giving you that bridge system.

So, in a complex situation, what we can get for that this o h group, when they are bound to your iron site, depending upon the available loan pair of electrons, because you have these water molecules, where we know that water molecules all have two loan pair of electrons, and those two loan pair of electrons can form two coordinate bonds, but the neutral water molecule is not strong enough, to bridge that particular unit, where you

have two metal centers. So, if they go for depotenation, and that depotenation will help to provide you charge on the group, so in a negative charge species like that O H minus. Similarly sometime what we find to know or detect any metal centre, which is bound to your hydroxide group, can be very easily identified, if you are able to find that, there are certain groups where iron is bound to your o h group. So, any spectroscopic technique which can be useful to identify these F e O H bound or F e O H F e unit, which will be useful to know this particular motive.

So, this particular motive can further be extended. So, when you remove this water molecule from here, another proton from this water molecule, you get the hydroxide group, and that hydroxide group with a charge, have three loan pair of electrons. So, it can go basically for a triangular motive. So, in this particular case, this we are slowly moving towards to know that the, how these ferritin assembly is taking place. So, if you have, because all the mineralization process also we know in a similar fashion, the mineralization process is also taking place; that means, the hydroxide are formed first, and then hydroxide are transferring to the typical oxides, whether it is F e 2 o 3 or F e 3 o 4 type, and those hydroxides forming your corresponding oxides, if you knew the typical mineral. So, in the bi mineralization process, or during ferritin formation, how this O H groups are useful, to give you a huge cluster, because if this growth is continuing, with O H you can attach three iron centres, and if it is o 2 minus, it can attach 4 F e centers.

So, is another typical motive for the growth, or for the assembly process, and those assembly processes what we are getting all these thing, from the simple ligand, which is your water molecule. So, in this particular fashion, that the bridging groups or the ligands can change the whole configuration. If this is one, this is two. So, binding to these negatively charged functional groups or ligands, change the whole conformation of an enzyme or bio molecule. And during that process what is happening there. That through coordination metal ion can enhance, the acidity cannot see. It can enhance the acidity of coordinated molecule, which is very important. When iron is bound to your water molecule, we all know that this particular p k is changing, so p k is getting lowered.

So, some acidic water molecule attached to the iron centre, so that immediately goes for depotenation. So, in the system itself, you are getting that iron centre which is attached to the hydroxide, when hydroxide is forming, starting from one iron centre to two iron centre to three iron centre, and this hydroxide group is attached to three iron centers. So,

because further lowered, and that particular one will undergo for the depotenation, and you get a oxide o based system. So, that basically give you that how you bring four metal centers together and that particular thing going further, because you have the other vacant sites from each and every iron site. So, that all this can also be occupied by water molecule, or the hydroxide groups, and you can go for a corresponding polymerization process in that fashion.

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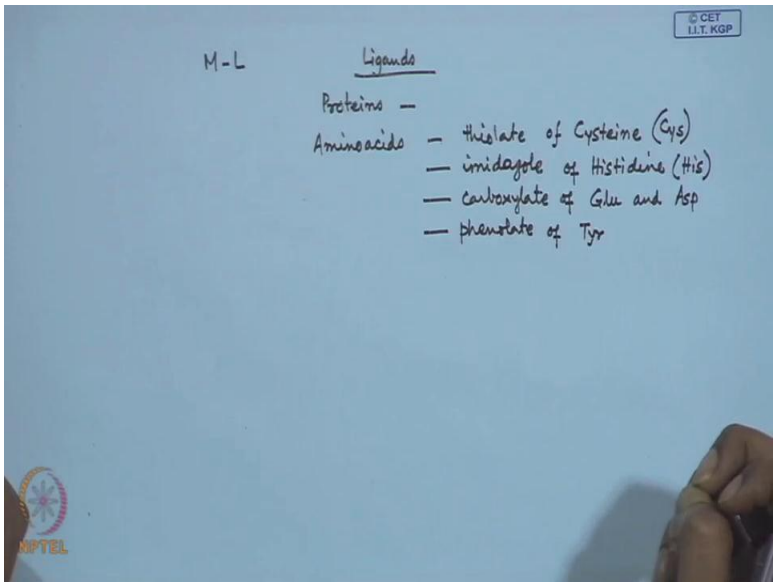


So, during this particular behavior, what we see that the metal plus ligand system, and in the biological system, most of these ligands what will be getting, from the proteins basically. From these proteins what we will get, and these amino acids, different amino acids; say from this particular thiolate or cysteine, then you can have imidazole of histidine, carboxylate of glutamate, and aspatate, and phenolate of tyrosines. So, these are few examples for those groups, that when you have the ligand structure, and those ligands are protein origin, and you have some amino acids, so all this polypeptide chains, bearing those amino acids. So, always you have the amide backbone, and from those amide backbones you can have the pendent groups available, and those pendant groups like your cysteine, histidine, tyrocine all these things, they are dropping down from the backbone.

So, depending upon the structure; suppose you have the corresponding primary structure, secondary structure tertiary structure of the protein, you can have some useful donor

groups available, from sulphur, nitrogen, oxygen of the carboxyl group and the tyrocine from the phenolate unit, those are available for binding the metal centre. So, this particular thing. So, in the next class will see that how these all these ligand systems, and the metal centre are useful for giving you a particular assembly, when we talk about the different ferritin molecules, how ferritin groups will be formed. So, you have a long polypeptide chain, and those polypeptide chains, whether they should be available for direct iron binding or not, that you should know first. So, from the very beginning of this classification of this metal, and the ligand system from the biological origin, because the ligands are all from biological system, and they are basically made up of the different amino acids.

So, when they are coiled around, to giving you a typical shape, and available donor groups if they are available from this long polypeptide chain, they will be coordinated to the middle centre. And in other case this particular one what we find that, divide of the metal centre we get something which is, the apoferritin part, when you do not have the metal centre. So, this apoferritin part ,and if we talk about the transferring molecule, the apo transferring part, how these protein structures are there, and how these protein structures are changing, through metal binding or metal coordination. So, that will see from there, that how it can grow, from the typical point of view of your metal, coordinating to your ligand system.

Thank you.