Bioinorganic Chemistry
Prof. Debashis Ray
Department of Chemistry
Indian Institute of Technology, Kharagpur

Lecture - 21
Nickel Enzymes-V

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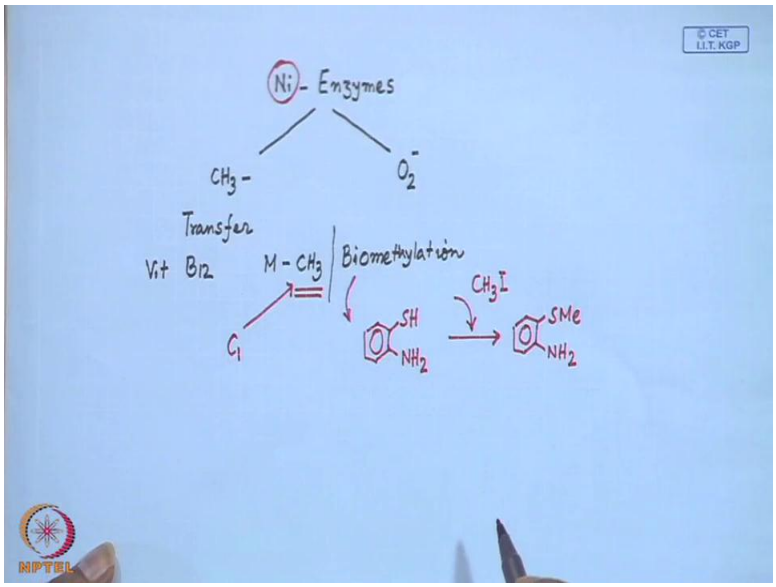

Yes, we will try to finish today about our nickel story. So, today we will talk about some other enzymes. There are other 2 enzymes which we will deal with the transfer of methyl group, in another case the condition where you can tackle the superoxide. So, which is talking about the transfer of methyl group, what we find in vitamin B 12 or several other places where, we can have the metal center which is attached to the methyl group. And we all know that this particular part of reactions which are very important and nature is also doing that kind of reaction we call it as some time as biomethylation. So, how the metal ion nickel now, in its most preferred oxidation states, how it can handle the transfer of methyl function from one particular unit to the other that will see.

And in this particular case, the biomethylation reaction that means the biological part is there and one more important part for this is that, we all know that any simple substrate like this, that means, is a very simple substrate and if we want to make it as S methyl 1. So, 2 amino thio phenol, 2 thio phenol if you want to get this S methylation so, something we have put there that means, similar to that of biomethylation reaction or that

some group like that some time how we can go for the methylation reaction in presence of methyl iodide .

So, if some mechanisms are there because this particular thing basically is a carbon, single carbon reagents, C 1 reagents. So, this can be produced for anything like carbon monoxide, carbon dioxide or anything. So, if this particular type of conversion can give you the formation of methyl function and that methyl group can be transferred nicely from one subject to other and if you just find that the involment of such nickel center is present we get something which we call it as a methyl-coenzyme M rediuctase.

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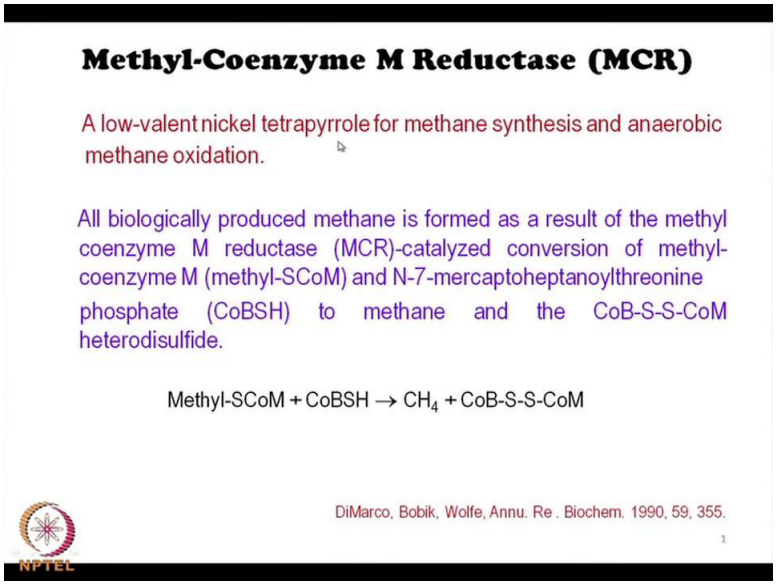

So, this is a big name but, still will find that the coenzymes is there which is giving some reaction which is M reductase function and the methyl transfer will be taking place. So, what is there at the back bone of the particular reaction is a low-valent nickel tetrapyrrole.

So, very basic identification or the very basic definition for the enzymes system tells us that, you have a nickel center plus the ligant attached to is a tetrapyrrole type of environment that means one particular square plan is occupied by 4 nitrogen atoms like any other phyrrole containing group and that nickel is there and that nickel it can stabilizes in that particular environment because you cannot have diosin of residue or any other type of residue which can stabilizes nickel in the normal oxidation states that means, plus 2 or in some higher oxidation states but, it can still stabilizes nickel in low

oxidation states. So, which is also very much important to know that even you can talk about the methyl cobalamin that vitamin B 12 systems had the C S C group attached to caballed center we always tried to have that particular metal center in low oxidation states that means, the coballat 1.

So, that particular center when it is nickel so, it is responsible for methane synthesizes well as some times anaerobic methane oxidation. So, basically this particular center can handle the methane synthesis and that particular thing what we find after that, that definitely some methyl groups attached to there and this methyl function if we can supply some hydrogen atom to eat it can produce nicely the CH 4. So, it is biologically how we produced this methane which is definitely a very important reaction because all shots of methanogenic bacteria they produce methane and in this particular reaction the terminal enzyme for that reaction is the methyl coenzyme reeducates which is MCR and that MCR catalyzed the conversion of coenzyme M.

So, this is your methyl coenzyme M. So, name tells you that it is a very good reagent for supplying your methyl, like your methyl iodide. If you go for providing some methyl group the methyl group from the methyl iodide so, you have your have use the some reducing agent and then, supply the methyl iodide like that of your S methalation reaction, the thiolmethylation reaction. So, in this particular case the methyl S coenzyme M which is reacting with is a big name through N-7-mercaptoheptanoylthreonine phosphate. So, will come what is the structure because at least from the name we should able to write down the structure of that the particular spices. So, this has also S H function. So, essentially what we are getting that this is basically S methyl compound like 2 amino thiphenol which is mentholated by methyl iodide.

So, which is a S methyl containing group and that S methyl containing group instead of supplying this methyl group to this S H, we have seen that this can also be a S H, S H on CoM. So, S methyl on CoM this can supply to its methyl group to this one that means the thionin phosphate function to make it CoB-S Me. And in other group what is happening there instead it can go because both of them the one is providing the methyl function and another is providing the hydrogen atoms giving rise to your methyl function and you have the oxidized form of this 2 coenzyme. So, one is there. So, if both of them are remaining in S minus and S minus and if we go for oxidation and we know that systeen systain conversion or any other type of conversion where, you can have a protein chain

we find large number of this type of reaction where, you can have the disulphide linkage formation.

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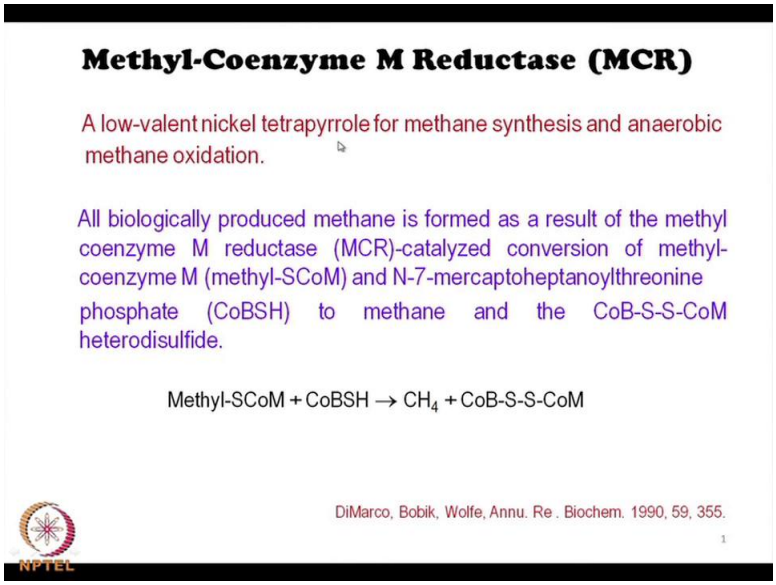

So, during the disulphide linkage formation between these 2 parts of these coenzymes we are able to produce the methane from the system. So, you have the nickel tetrapyrrole system and how we can provide the particular methyl group so, it should be. So, this reactions should be nickel center catalyzed, is not a direct reaction between this 2 but, it is a nickel catalyzed is reactions.

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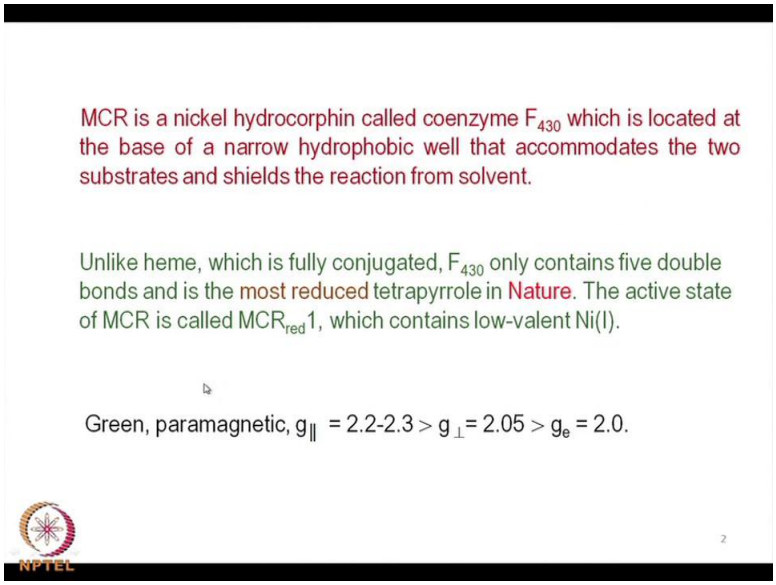

So, methyl coenzyme that reeducates methyl coenzyme reductase is nickel hydrocorphin, call it as hydrocorphin spices which is a tetrapyrrole system and we call it is the coenzyme F 430 which is well known like our cytrocrom P 450. So, you should able to identify this numbers. So, cytocrom P 450 was there in one form it can show the corresponding lamanax value at 450.

Similarly, this particular spices can also show is corresponding maximum absorption at 430 nanometer so, that why it is called coenzyme F. It is coenzyme factor which is responsible for the absorption at 430 nanometer due to the presence of the conjugation in the hydrophobic back bone. So, this is located based of a narrow hydrophobic well. So, this is the protein part narrow where it is located and some time it that accommodates to substrates and shields the reactions from solvent. That means, it is not directly reacting with the solvent that means the water molecule. Since, it is a preferring type of ligant we can identify the ligant forms in the metal center and then, its reactivity. So, unlike heme. So, in hemoglobin or in heme what we have the preferring which is really conjugated. But, in this particular case a 430 only contains 5 double bonds.

So, all together if you know that how many doubles bonds are there in the profile ending instead of that, that means the all together contain double bond but, instead of that 10 double bond in this f 430 you have 5 doubles bonds and this is the naturally available or naturally obtained spices where you can considered or you can tell this as the most reduced tetraprrole system. So, in case of vitamin B 12, in several are cases have, several other tetraprrole system including the photo system but, this is the most reduced form so, you do not have a extended conjugation for that. But, this particular nature has device certain mechanism for that the that is tetraprrole is well suited to bind your nickel center. And since it is a little bit reduced one and most one reduced one so, it will definitely have a packed structure and that packed structure or non panel structure what are we have discussed while talking to the profile and you can call back that also that how that bind is there when metallic is not there.

So, in the metal free form you have 2 nitrogen pointing towards downwards and 2 nitrogen upwards, we have seen a bold strait structure earlier. We have seen in case of profiling. So, this also have a different structure when in the free state and also in nickel bond state and that is definitely responsible for stabilizing the nickel preferably in nickel plus 1 nickel in plus 2 or in nickel plus 3 state. But, what is the corresponding active

state? The active state of MCR is called MCR reduced one, which contains basically low-valent nickel 1 that means, this particular one. So, to reduce this tetrapyrrole system is useful to stabilize your nickel in plus 1 oxidation states.

So, whenever the active site can identify in nature, it is a very difficult task to identify the corresponding oxidation states every time when saying that you never know whether the ligant system is oxidize or your metal system is reduce. So, people go for identifying these 2 things first. That means, first what is the color? There should be definitely a colored spices and in the paramagnetic one also. And when we go for this particular EPRS measurement will find that low-valent nickel 1 it has a catastic axies spectrum, you have g parallel and g perpendicular part for that particular spectrum and which is higher than the free electron g value. So, free electron g value which is very much closed to 2.0, which we can find sometimes that the standard reference material which is your DPPH. So, respect to DPPH dyphena picryl hydrazyl. You find that you have some values which are higher than that and you have a axel spectrum and which is catechist and for that of your nickel 1 center and sometimes by looking at the e p r spectrum, people can also find out whether this can have the another alternative for its paramagnetic state for this nickel that means, it can also be a trivalent nickel. But, it is not a trivalent nickel, this mono-valent nickel and this e p r signals are very much cathartic for that.

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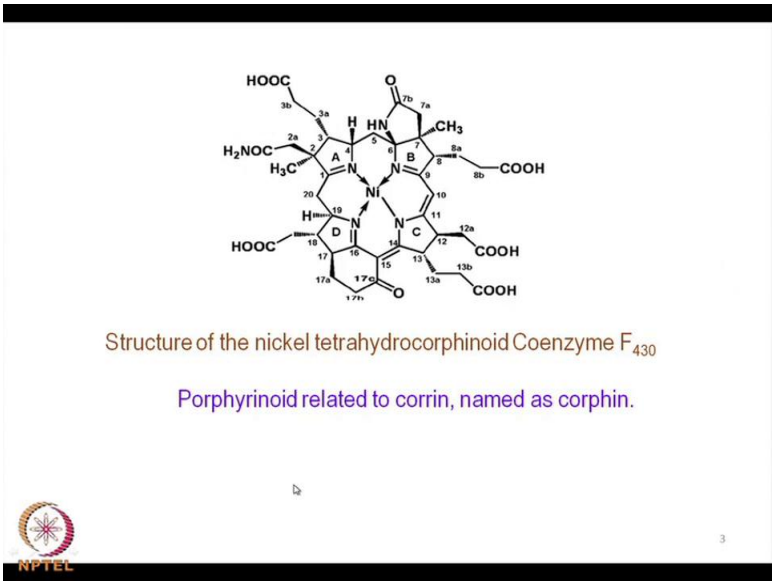

So, this is our structure. So, you have a reduced tetrahydrocorphinoid coenzyme form. So, this is the whole structure of the nickel tetrahydrocorphinoid coenzyme and F 430. So, you have this A B C D, these are the 4, 5 member tetraphyral rings.

And compare if you just never can see this things is always you should compare the corresponding conjugation or the unsaturation for the things. So, it is the most reduced one because you had not having 1 double bond here another double bond here and here 2 from here. So, 1 is missing, 1 double bond is missing here, 2 is missing from here and another is missing from this D group D ring. So, all together all 4, A B C D E they are losing 1 1 2 1 that means, all together 5 double bonds we are reducing to get this tetrahydrocorphinoid ring. And you have the similar type of amide and that corresponding carboxyl and substitutions for that. And also, one more thing is interesting, very much interesting compared to your tetrapyrral which is present in the him molecule is that you have all these 3 nitrogen which as shown as a arrow attach to the nickel center that means, they are all ternary nitrogen. Only this nitrogen is NH nitrogen. But, in case of perforin attached to the him function we have 2 NH groups there are there. So, when the ligant which call is a ligant basically in terms of the corresponding protonation level that in that case that means, in case of him we can considered it has H 2 L it has to hydrogen attached to L but, this is basically H L. So, one of his proton is available on this nitrogen. So, when you go for this basically the corresponding charge or in the deprotonated form, this ligant for is tetrahydrocorohinoid which we can level as L minus.

So, deprotonated form is L minus, not L 2 minus like that of your prophyrin. So, it is very easy to say from there are that is seen it is L minus we do not have access charge of the ligant system after deprotonation. It is very much situated for stabilizing nickel in a mono violent state. That means, in nickel mono violent state if you attach to it this to the entire system will be electro neutral. So, the electro neutrality also be a little bit driving force to stabilize in the low oxidation states but, if your ligant which is available on the porphyrin is already L 2 minus have already in deprotonated form depending upon the pH of that particular part immediately and that L 2 minus spices can have some tendency to stabilize this nickel or the iron center what we find in case of porphyrin to stabilize the metal center in plus 2 oxidation states. But, in this particular case you can stabilize nickel in plus one oxidation states.

So, you see that is very important like that of our peridin donor atom, whenever you have a ligant system or anything natural or unnatural spices which is going to bind your metal center if you have the peridin donor all 4 peridin donor groups. You can expect that you can get the corresponding metal center in low oxidation states that means you can compare the corresponding binding behavior pyridine expect to that of your phenol if it is phenol that means you have a tyrocinad. So, tyrocinad is when available from the protein chain it will always try to stabilized corresponding metal center in normal oxidation states or the high oxidation state but, when it is histriorin type of nitrogen that of our peridin like a hemocyanin all this cases you are stabilized particular center in low oxidation states like that of your copper plus 1 oxidation states what we gain in case of hemocyanin.

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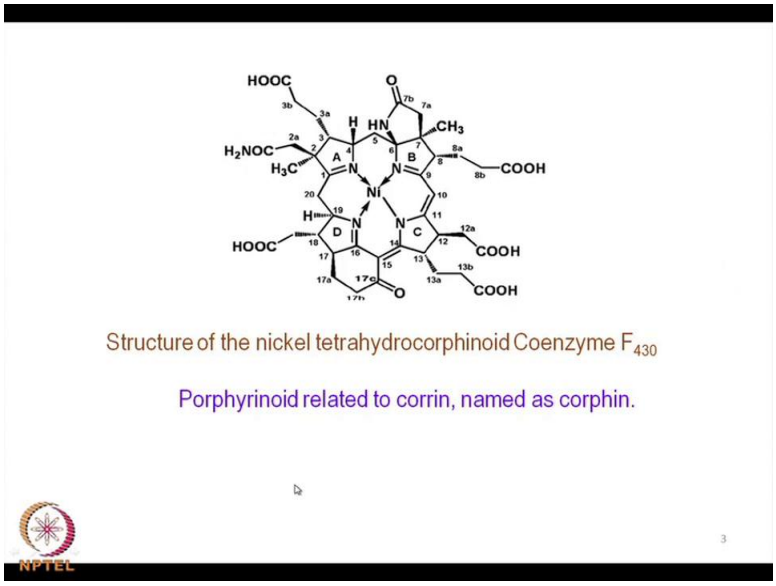

So, why it is corphinoid tetrahydrocorphinoid type that is means it is corpfin type corphinoid means is a corfin type. So, porphyrinoid related to corrin rings that means it has neither it has some similarity with porphyrin other part is similar to that of our according ring. So, very simple thing is that should be able to answer is always for that is for that you know now the micro cyclic ring profile, you know the corresponding micro cyclic ring corrin which is attach to the vitamin b12. Now, you get something which is in between porphyrin and corrin that is why is leveled as corpfin. So, if you draw the 3 structure that means the structure of porphyrinoid, the structure of corrin and the structure of corpfin then, you should be able to cordiality that how much similarity you

have with that of our corpfin, to that of our porphyrin and with that of our corrin. Because if look just at this particular ring this particular ring was also present not present in the porphyrin but, it was present in cornering. So, you should be able to cord late in that passion because all this groups because the nature is for giving you this particular thing. But, you can always you can have that information that in the catalytic activity your stabilizing nickel in plus 1 oxidation states but, is very difficult to make any unnatural tetraphyrrole which you can prepare in the laboratory to stabilized this particular compound so easily that means, the nickel compound in plus 1 oxidation states.

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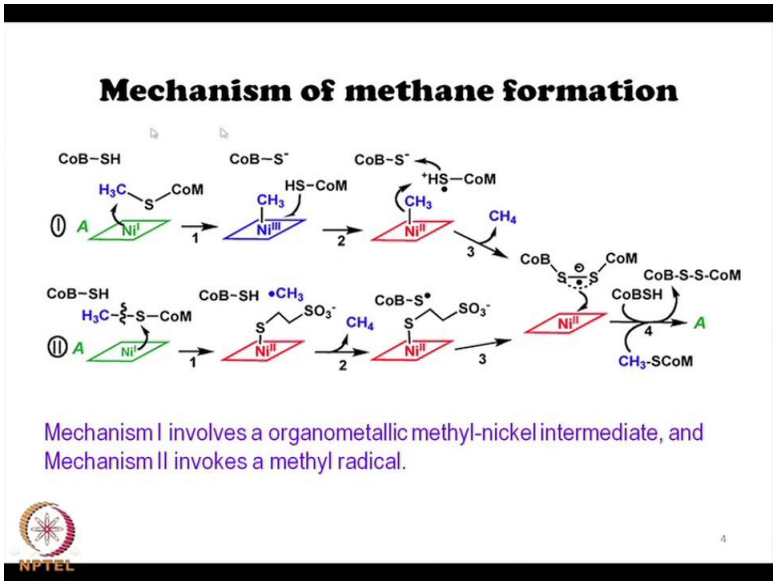

So, the mechanism also you can have the mechanism because you can have the different pathways and those mechanisms what tells us that you have to support one particular mechanism or a second alternative but, there are clues and there are some evidences which can support mechanisms 1 and mechanisms 2.

But, when we say that is a going through some reactions because there are large number of reactions not only for methyl but, involving in this coenzymes reduction that, 1 particular pathway is this and another particular pathway is this. So, distantly you can have to different mechanism and basically some time is very difficult to identify whether the particular mechanism is going through a organometallic pathway that means, like that of our vitamin b12, like that of our vitamin b12 you have a different spices where you

have a metal carbon bond that means that means that nickel methyl group is present. So, whether it is a going through a organometallic methyl nickel intermediate or another pathway where you can stabilize this particular pathway through the formation of methyl radical.

So, in the first case is very simple for any organic metallic catalytic path that means, you have this that means, the nickel 1 and this nickel 1 you just providing in a reagents which can supply your methyl group like that of our methyliodide. It is basically the same reaction what you can have if you are able to stabilized nickel in solution by using some reagent that means nickel what you can prepare with that of our microcyclic ligant, that nickel is prepared in the bi-valent nickel. So, nickel is in plus 2 oxidation states. So, what we will do in the second stage? We reduced it by say borohydride. So, when you reduced it by borohydride so that borohydrade spices or any other spices we can reduce a nickel center to nickel in plus 1 and in that particular state if you use some metallic agent like your coenzyme. So, that particular reagent it can be methyliodide.

So, if it is methyiodide is given immediately it can give you a corresponding mentholated form of your nickel and nickel is oxidizing to plus 1 to plus 3. So, this particular one that means this change is also taking outside our metal iron environment that methyl group is transferred to nickel center and this SH group that coenzyme B is providing this proton 2 this function and then, this particular thing this trivalent nickel which is not so stable that means, we are taking that advantage of the nickel can also form in plus 3 oxidation states. So, but this is a transiting existing so that is why we can have this 2 alternative that the transiting existing for nickel in high oxidation states and existing from methyl function as the radical this always happens. In the biological system if there are very much delocalized in the system and electro chemistry or any other thing measuring it in were in (( )). It is very difficult to identify the site of oxidation whether the corresponding oxidation that means the 1 is electron transfer for this spices from 2 to 3 whether it is taking for a center where it is metal center oxidation or it is a ligant center oxidation. So, nickel 3 forming it is going then in the next step then nickel center will be immediately reduced back. If the nickel center is reduced back what will happen? You can oxidize the surrounding. So, surrounding so it is going through a process where it can go for some inter action that means the thairadical. So, it will try to form a corresponding thairadical. But, it is not in a deprotonated form. If it is in the

deprotonated form you do not have to considered about the corresponding H plus but it is still protonated.

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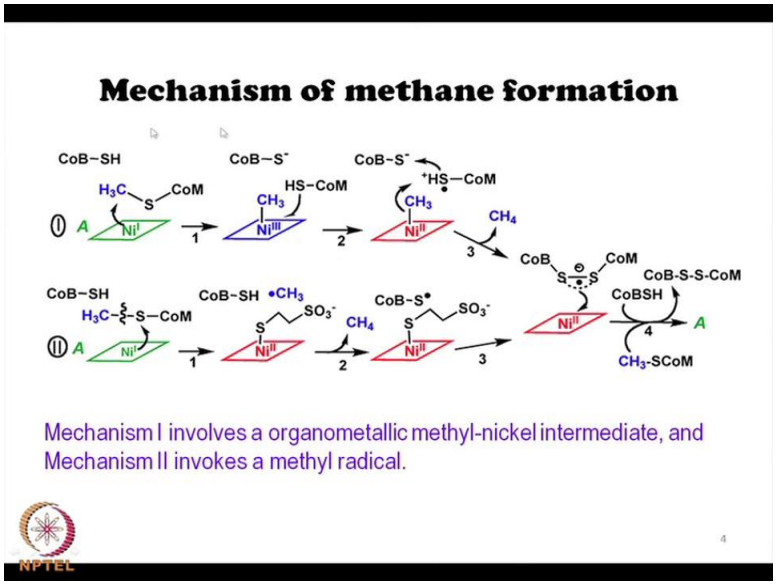

And in the protonated form you have this corresponding interaction. So, if it not deprotonated that form. And if this 2 groups that means surrounding nickel your methyl group is supplied to nickel center and this 2 groups now in close proximity that means, you have available sulfur sulfur ends from these 2 groups. And you have the available sulfur sulfur ends and you are trying to oxidizing it.

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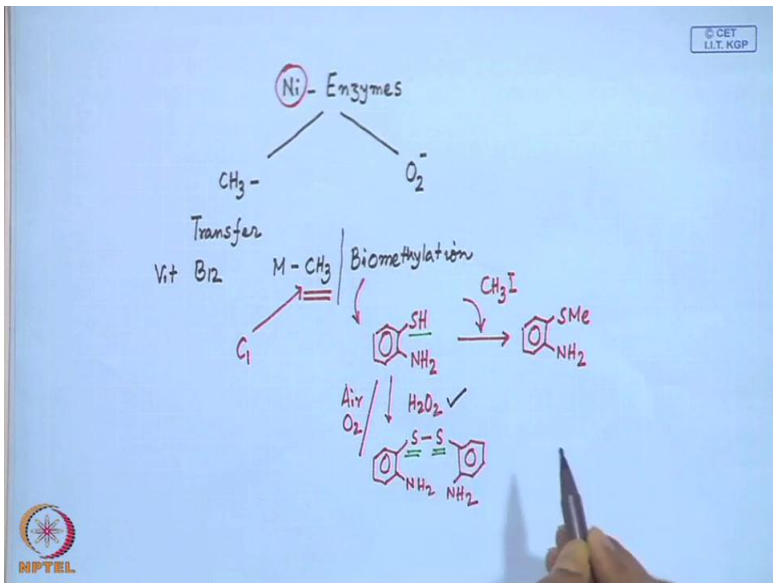

That means how we made this particular one? We all know that synthetically laboratory how we get this corresponding disulfide. This very easy to make. Sometime if you can keep the suitable condition. One important example is reagent is air from.

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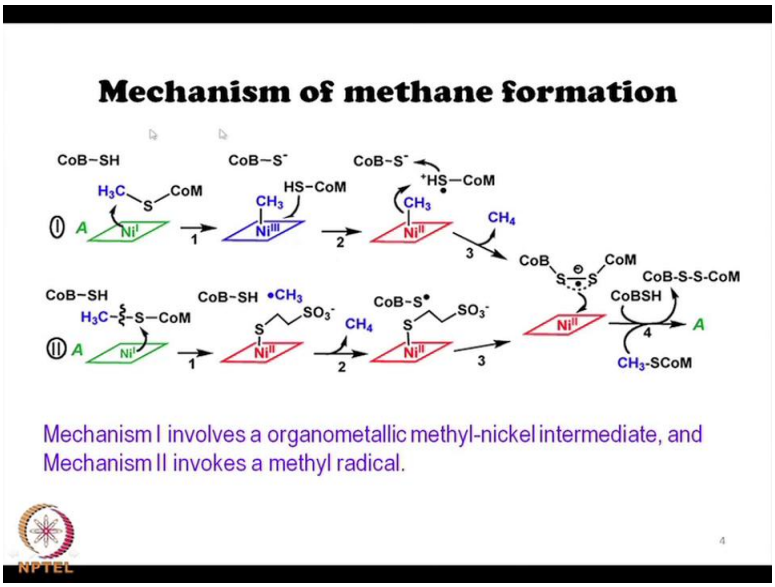

giving you oxygen or simple hydrogen peroxide. So, you get that hydrogen peroxide that you have some oxidizing agent. So, this oxidizing agent which is responsible for corresponding oxidation and this end, one end of this that means this particular S end. So, one end of this and another end of this if they are close of each other you get the corresponding disulfonate things. So, you have to have some oxidizing agent as well as you put one particular group close to the other function. So, this particular is not so deprotonated but, it is protonated form start interacting with another sulfur so this left on post to the other sulfur. So, you get some sulfur sulfur linkage over there and this particular one when you go for this so, this particular one is already removed and you get the methyl function.

But, the thing is that for the second mechanism that the state wise we should be able to tell in that way that, here if you have the instead of this methyl coordination you see. If you have a substrate and which is not so easy to considered that if you have a nickel center that means nickel 1 and you are using something that means, you have some group that means, you have when we talk about the for unnatural system the laboratory system that means you are providing methyl iodide and that methyl iodide is giving you

the methyl group to the nickel center. But, in this particular case you see in one case you have change of that you have a suitable condition where you get a organematallic intermitted that means, your methyl group from this particular end, the methyl group is your ligant. You are providing the methyl function to ligant for the nickel center.

But, at the same time when you go for this SH because that is why it is protonated for here. If it is protonated is binding property or binding potential to nickel is less but, if it is not protonated if it is going for that some cleavage only that means the carbon sulfur bond cleavage is taking place and sulfur is coming from there and this sulfur is definitely here the new ligant. So, this sulfur group can bind to your nickel center.

So, interestingly not so difficult for establishing which particular mechanism is operating for one system and which is not operated because here is you can have the metal carbon bond and here you have metal sulphite bond. And once you make this methyl radical so it is a radical path way and this will hydrogen atom forming the corresponding CH 4 that means, here it was producing methane in the third step, it is producing methane in the second step and your this end, this end is nothing but, your coenzyme m the entire molecule we can have because you have the corresponding charge on that sulphite function on the other end. So, this sulfur group is attaching over there. Now, is that you have the S dot over here. So, already you made this S dot and 1 sulfur is already bond to the nickel but, this a very difficult proposition that, your 1 sulfur end is bond to the metal center and this sulfur is in the radical form. So, now this 2 sulfur will start interacting to each other. So, now the new disulphite bond will starts forming between these 2 and it will be removed from the metal center. So, that removal from the metal center will give to this particular situation again and you go for this particular thing and here if you just provide this particular that means the cycle continuous again with methyl coenzyme m and CoB-SH.

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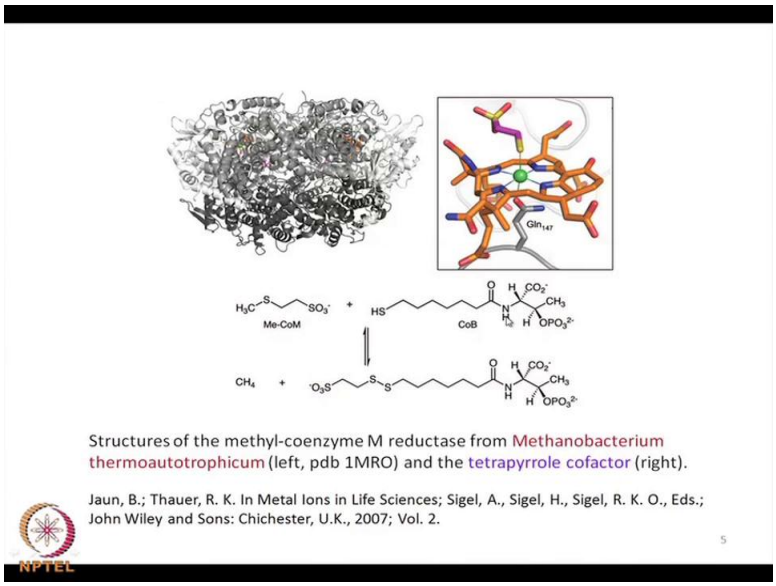

So, in CoB-SH what will see that particular spices that this the whole form. I told you a big name for that but that big name is nothing but, is not a very complex molecule but, you can have is a long chain because this the alkyl chain is little bit bigger compare to your coenzyme M and this bigger alkyl chain so forming your corresponding S S spices and your methyl group. So, definitely your methyl coenzyme M reductase what people had identified from this methanobacterium thermoautotrophicum. So, this is the source basically the methyl the methanobacterium thermoautotrophicum is a very complex molecule and people could identify this particular metal center because the metal is present. So, this particular center because you have so many channel, so many things and where that actual reaction is taking place is very difficult to identify sometime but, people could identify that you have the tetrapyrrole. This is your tetrapyrrole unit and that tetrapyrrole unit is responsible for this conversion and this particular part because once you find out particular part also. So, this is one part of that. So, is A P D H is the protein data bank. So, you have as a everything is available now a days this is from the protein data bank you can find out that thing. But, this particular part is interesting to ask that means there corresponding tetrapyrrole cofactor and when you have the nickel 1 it is basically that is why we all that we are talking about it tetrapyrrole because the enplane stabilization of the metal center is important and when we go for the other oxidation state that means, the nickel 1 or the nickel 3 you can have some interaction from the coordination number which is above the plane and other is below the plane.

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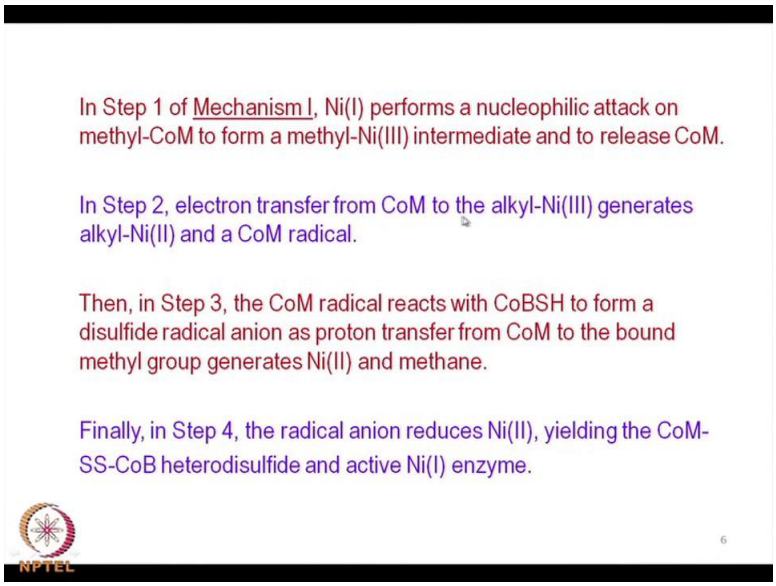

So, what we see that the steps basically what we I told you that is simple thing that mechanism 1 and mechanism 2. Already we have shown pictorially that, nickel 1 is basically performing the nucleophilic attach on the methyl coenzyme M and releases coenzyme M. In the second step all the steps are now written over here. Actually, the electron transfer from the alkyl nickel 3 which we have generated like that of your methyl cobalamin. So, alkyl nickel 3 portion is nothing but your methyl cobalamin type of thing and then, we produce nickel 2 plus 2 oxidation state attached to the alkyl and the CoM as the radical. And in the third step your CoB SH is taking up and your disulfide radical analysis forming there. It is not pure disulfide radical is formed. So, disulfide radical is formed as a photon transfer is talking place. So, sometimes without proton the disulfide attachment formation is important and sometimes this particular part which is attached to the proton is important also to proton transfer because all the cases we find that thyroal function is there. And that thyroal function can have the different protons level either it is protonated or it is not. When it is in the protonated form that is in the deprotonated from radical anion what is there that reduces the nickel 2 yielding the corresponding this hydro disulfide and nickel 2. It is then reduced back to your nickel 1. So, when you start transform here that is the step 1 to step 4. You are staring with the nickel 1 and you should able to complete the cycle and will end up with nickel 1 again back go back to your cycle again. So, this is for your mechanism 1.

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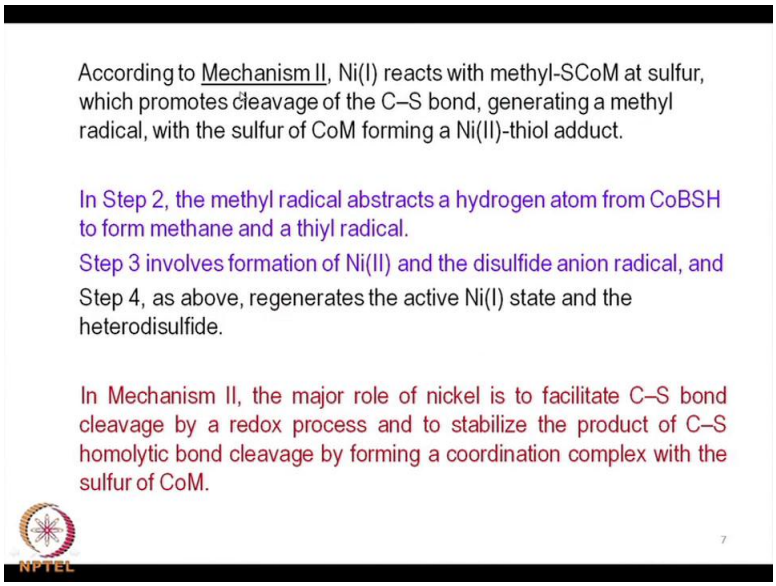

And similarly for the mechanism 2 also, the nickel 1 center reacts with methyal coenzyme at the sulfur and basically the difference for the mechanism 1 is that it promotes a corresponding C-S bond cleavage.

There we were talking about metal carbon bond formation. But, here you have the C-S bond cleavage and it is now generating the methyl radical. So, occasionally the homolatic cleavage for the corresponding C-S bond is so important that whether you are able to produce the corresponding methyl radical which is also true if you go through the detail of the corresponding reaction of the methyl cobalamin. So, methyl cobalamin we do some reaction sometimes we will find a cobalt is behaving as a catalyst and we are providing some good reagent as the methyl iodides so, reaction any reaction in that form. So, cobalt is there inside the bivalent cobalt and the cobalt 2 use some reducing agent like sodium borohydrate and use methyl iodide. So, definitely that path will go through a reduced form of the cobalt center which is basically activating your methyl function and that methyl function is responsible for transferring methyl group to any other substrate. So, same thing is also happening that in this particular case you do not have that particular reagent which has supplying in form of methyl iodide but, you have to have the corresponding C-S bond cleavage because this sort of C-S bond cleavage is there and that is…

So, this particular the C-S bond cleavage is important because sometimes we find that in this particular one is not like that nitrogen sulfur bond formation, it is the carbon sulfur bond formation and this cleavage is also very important. So, sometime we find that the metal is also required for this particular C-S bond cleavage here. So, then once you form the methyl radical you are should be happy that immediately if it attracts a hydrogen atom you will be able to form methane. So, for this particular pathway is little bit easier to convince that you are not involving nickel in plus 3 oxidation states. Why I am saying so, that sometime if you stabilize a particular metal center in senickel plus 2.

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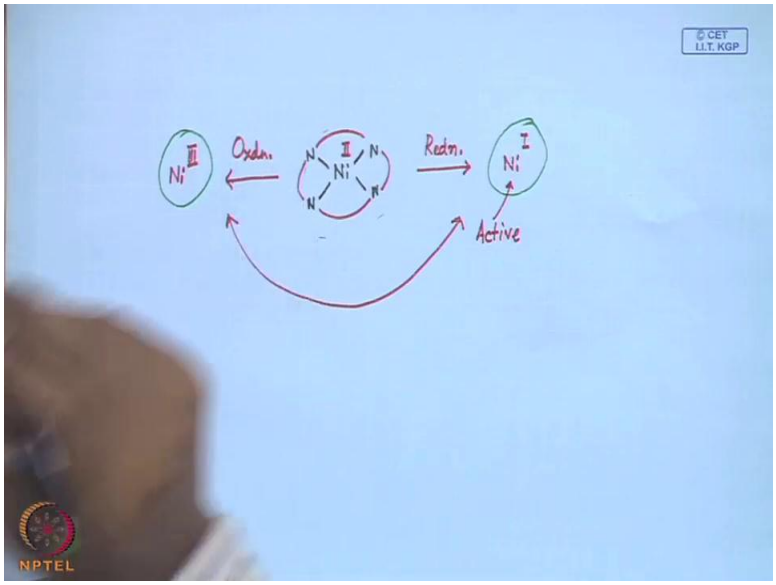

And that particular center when it is reacting. So, you have nickel site and you have 4 nitrogens attached to it which is a micro-cyclic range and initially, when it is forming that particular one that means nickel plus 2. And if we are talking something related to that we are going for reaction where you are stabilizing a particular center as plus 1. Nickel in the mono valent side which we are considering here it as the active oxidation state the corresponding active oxidation state. So, this is the reduction state we are talking and at the same time we are talking oxidation that means the first mechanism we are talking also 1 step that means talking oxidation nickel 2 to nickel 3 because we are talking something where you can consider these 2 steps as a 2 electron transfer step like that of your catalytic cycle will concern catalyst and so thing so many others involving palladium.

So, palladium is going from say, palladium 0 to palladium 2 or sometime if we use going from a corresponding oxidation state like nickel in 1 2 3. So, this particular environment whether it is little bit molecular environment in terms of the ligant and some other interaction like this super molecule environment in terms of the other non-covalent interaction of the hydrogen bounding which is required for stabilizing nickel in plus 2 oxidation state. So, it is important to know at that particular point the reduction is also visible and you can stabilize that means, you are not changing very much your environment, the coordination environment. You can stabilize the corresponding environment around nickel 1 but, sometimes it is very difficult to understand that it is also stabilizing the nickel in plus 3 oxidation state that means, the same environment if you do not go for little bit manipulation over the environment, is responsible for stabilizing all 3 oxidation state of nickel that means nickel in plus 1, nickel in plus 2, nickel in plus 3.

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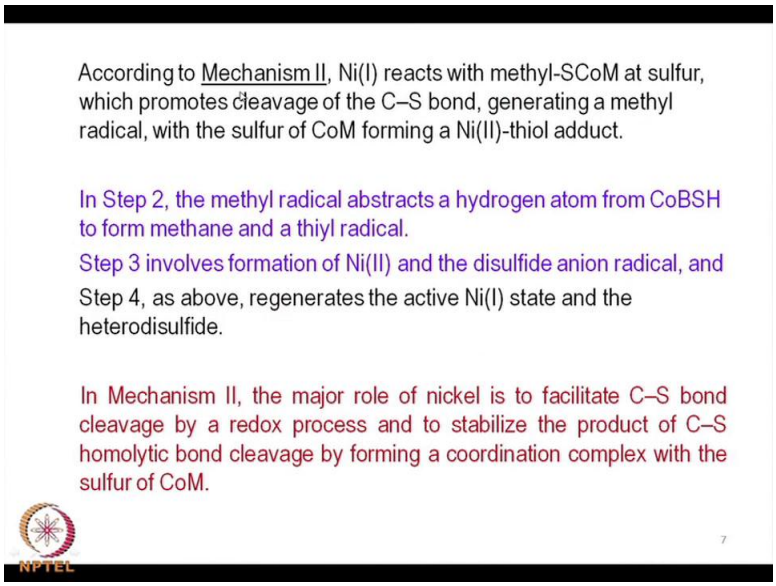

Instead of that if you go for considering the corresponding reaction that means mechanism where, this particular mechanism we are not involving the nickel in the plus 3 oxidation state. Instead we are converting it to a methyl radical. So, oxidation is taking place on the organic part and we are giving getting something which is the methyl radical. So, these two alternatives also teaches something you should be very much careful while taking all these things that which particular part can go for whether you consider you organic part is oxidizing or your metal center is oxidizing. So, when the

radical is formed and the methane is forming from there and you get this same thiyl radical that means the sulfur.

So, electron transfer can take place involving your carbon center that means the formation of your methyl function either in the radical from, in some other form then, metal center and the sulfur center. So, the involvement of the sulfur group is also important for all these typical electron transfer reactions. So, you have the nickel 2 and the disulfide anion radical and this disulfide anion radical is reacting with nickel 2 species giving rise to nickel 1 and the heterodisulfide. So, this particular mechanism 2 is therefore plays a major role of nickel into facilitate C-S bond cleavage and definitely the C-S bond cleavage is not that the very simple bond cleavage when you talk interms of the organic chemistry we nicely say that we are making some C-S bond, bond formation and bond cleavage reaction what we are ignoring sometime. What redox process is? The identification of this redox process is so important that in the biological system the redox process is involving there and you are talking something where you can go for the corresponding C-S bond cleavage and to stabilize the product for the C-S humalitive bond cleavage and forming a coordination complex with the sulfur of CoM. That means you are getting ultimately you are stabilizing this particular center.

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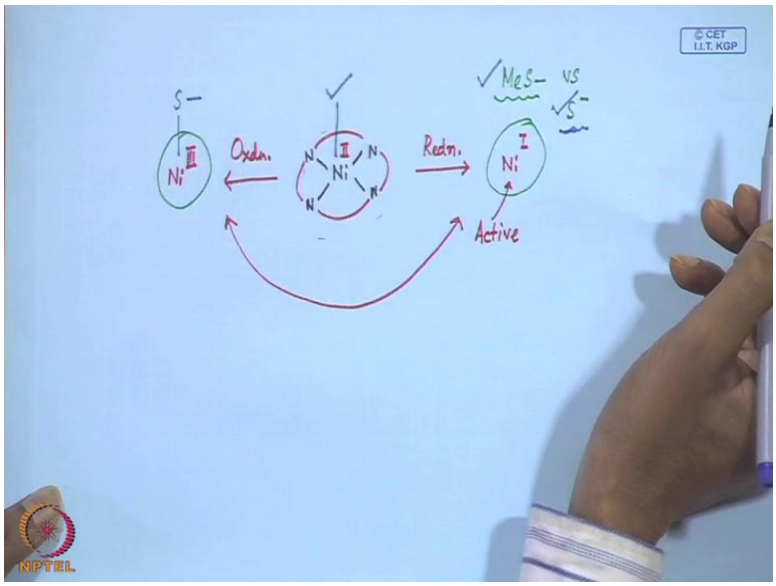

That means, when we find these that means, if you can the product that means where we are talking about the corresponding environment is a methyl sulfide. So, that if you can

little bit recall for the different cyto-chromes where we are talking about the cyto-chrome and the iron center, the coordination of these that means the coordination of S methyl with that of S minus.

So, when you have a neutral S methyl function you always accept that it can stabilize the nickel in plus 2 oxidation state and plus 1 oxidation state. But, when you are able to produce a S minus species that means you produce you get some charge on these because you have some different affinity for nickel in plus 1 oxidation state, plus 2 oxidation state and plus 3 oxidation state for different forms of these groups. But, you cannot change this particular environment what we are thinking about, we are thinking about this particular part that means what is going to coordinate from the apical site and what is forming there from that change. So, sulfur interaction when you get that thing so, you can have the choice for binding of this S methyl function and the coordination of the S minus. So, when it is in the deponent form it defiantly can stabilize nickel in plus 3 oxidation state.

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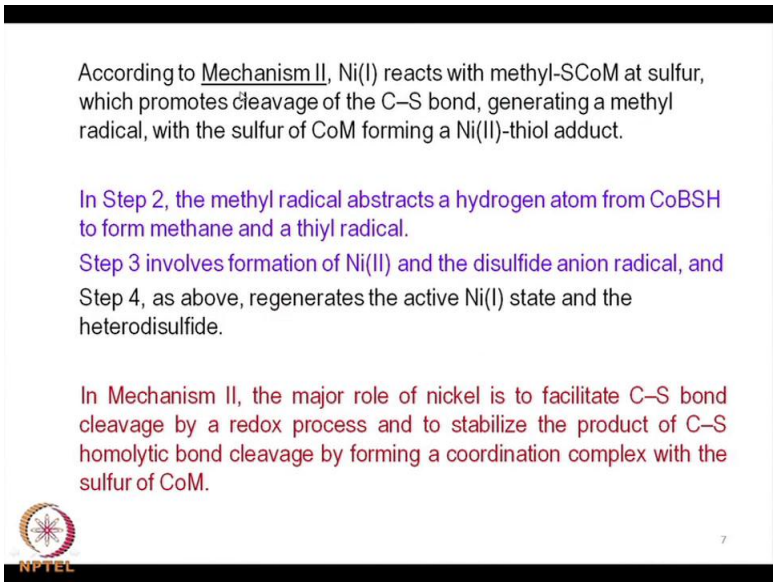

So, this particular state not only the C-S bond cleavage but, also the formation of the corresponding coordination compound around nickel and the corresponding binding of sulfur is also important because sulfur is provided by both CoM and CoB.

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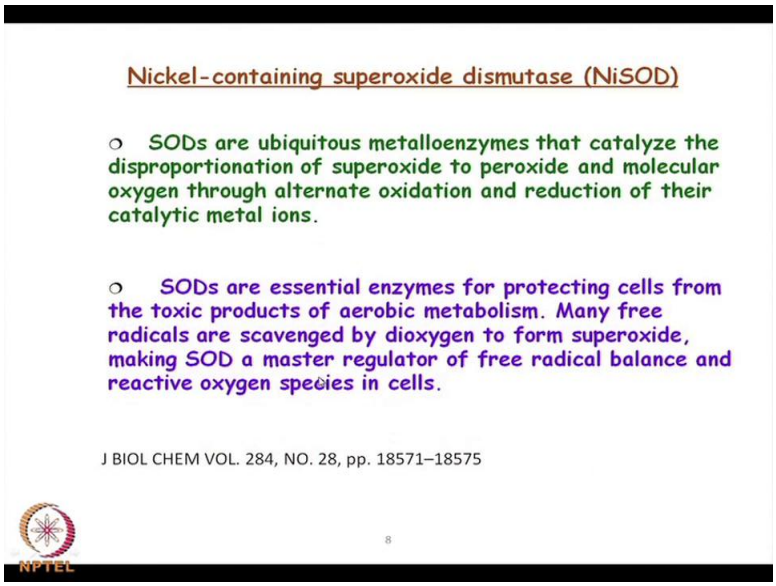

So, next we will just go for the last species which we just today we will finish basically is your super oxide dismute is what we have seen earlier.

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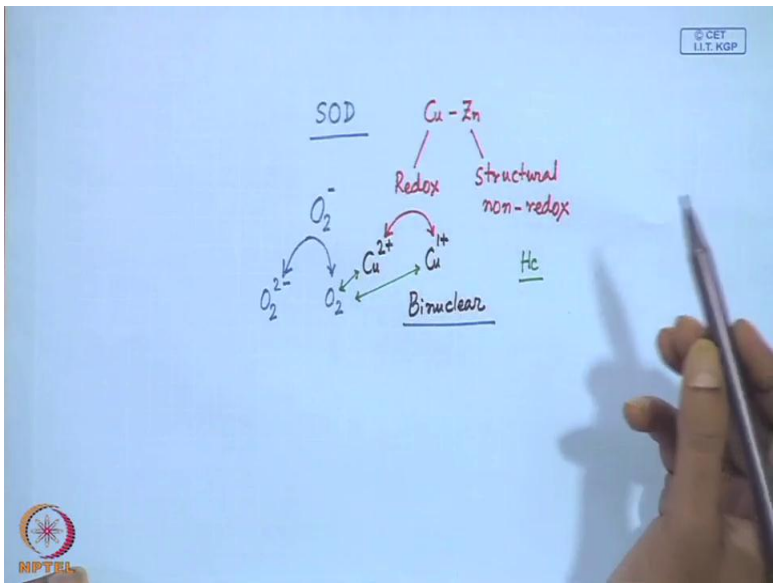

The simplest example we know but, it is not that you should know only the simplest example which was based on copper and zinc. And where the copper zinc super oxide dismuted we are talking about that one particular part, the zinc part was structural part is giving you a definite structure for the copper environment and which is also a non redox part and copper is our redox part.

So, this particular copper when it is in the redox part so the electron transfer from the super oxide anion. So, super oxide anion the electron transfer can take place for a corresponding redox based on copper 2 plus and copper 1 plus. So, this is little bit a complex one because if when you talk interms of the both of the copper presence of the copper and zinc and they all are there and this copper and zinc is present over there. And this particular part is responsible for structure. So, you have a binuclear system and for that binuclear system one part is the redox part and another one part is your non redox part.

But, definitely that part which is there that means the zinc. Zinc is responsible for giving you the corresponding reactivity pattern for this particular copper center. So, copper you have the corresponding electron transfer and that electron is basically going to your superoxide anion. So, that super oxide and iron ion how you can go for this particular copper. So, whatever we say they are that means that you already we already know that how the super oxide is dismutes reaction it will go for peroxide and O 2 formation. So, this peroxide and O 2 is therefore, is very important and what you should know that this is the binding behavior that means, this particular interaction that means, interaction of copper 2 dioxygen or copper 1 with dioxygen that we have seen in case of our hemocyanin part that hemocyanin part we all study due to the interaction of copper of center with that of your dioxygen molecule because that time your dioxygen molecule was your carrier molecule. Carrier molecule for copper but, this immediately establishes that your copper center can go and interact with your O 2 molecule. And if is interacting and if there is some overlap, good overlap of these and you can go for corresponding electron transfer so, what happens that you can give the extra electron from this copper 1 which is reduced form you can transfer these electron to O 2 to make it O 2 minus that means, it is changing to super oxide that happens also your hemoglobin molecule. So, metal in the low oxidation state and you have the O 2. So, one part of the system then there is one part of this particular molecule you can get based on the copper.

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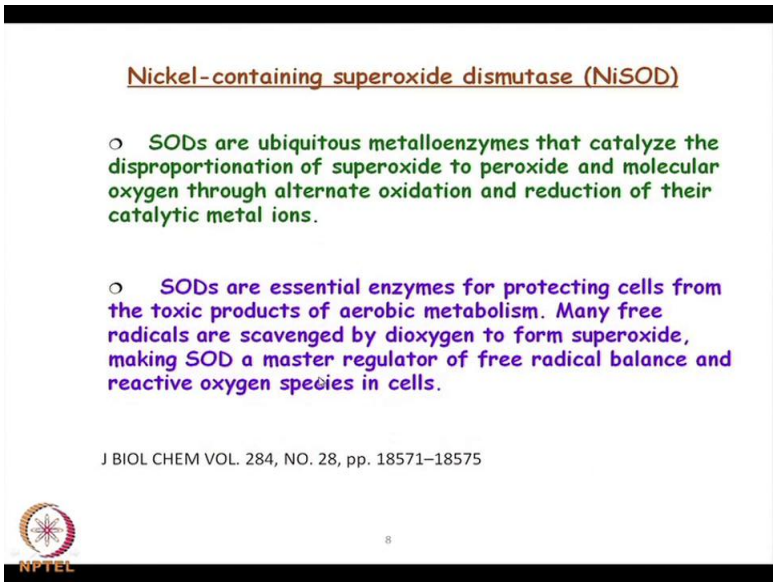

So, in other cases you can have superoxide dismutase based on manganese also. So, you all know starting from all these families that means the manganese bearing superoxide dismutase then, copper zinc binuclear superoxide dismutase. In all these cases we find that it is available everywhere is a very good metal enzyme that catalyzed disproportionate of superoxide and peroxide and molecule oxygen gain through alternate oxidation reduction of the catalytic metal ions. So, atleast it should have a site that means you should have sight where you have identified the corresponding catalytic metal ions. So, this catalytic metal sight is very important otherwise you can get the corresponding because reaction is based on the simple superoxide dismutase reaction. That means, if you have a catalytic metal ion that means you have 2 corresponding form that means the metal can be stabilize in 2 oxidation states and it is corresponding coordination geometry because it should support the corresponding coordination geometry for the metal ion in low oxidation state as well as the higher oxidation state.

So, these all we known as be a very useful enzymes for protecting cells from toxic products of aerobic metabolism. So, whenever you talk or whenever you discuss all these things related to your oxygen transport and oxygen storage, you should always think of something that when you talk about the dioxygen carrier molecules, we should always think of something that where your metal center is getting oxidized and you can supply some extra radical to the dioxygen molecule and the dioxygen molecule can be reduce to superoxide or any other free radical cases. So, we should have very useful mechanism

for good free radical scavengers. So, free radical scavengers should also be there to perform the superoxide making the superoxide dismutase is master regulator for any kind of free radical balance and another species we call it as ROS the reactive oxygen species.

In biological system wherever you go the cells can have the ROS. So, different ROSs are there. So, all these reactive oxygen species are there and how we can control, how we can regulate the corresponding concentration of these reactive oxygen species and the typical concentration of different free radicals that can be encountered by that nickel bearing enzymes. So, nickel that is why play an important role is playing so many other role starting from your uriage that it can also give rise to some redox reactivity, when it was present with urious you do not find any electron transfer behavior it is only a hydrolytic mechanism. So, any kind of such reaction that means that is your phosphate type of activity also, if you have a phosphate type of activity you can considered only a non redox hydrolytic path. So, nickel is so unique metals entire that in biological system it is performing both the 2 reactions that means, in a non hydroxide of hydrolytic pathway also we can go for some other pathway which is based on electron transfer.

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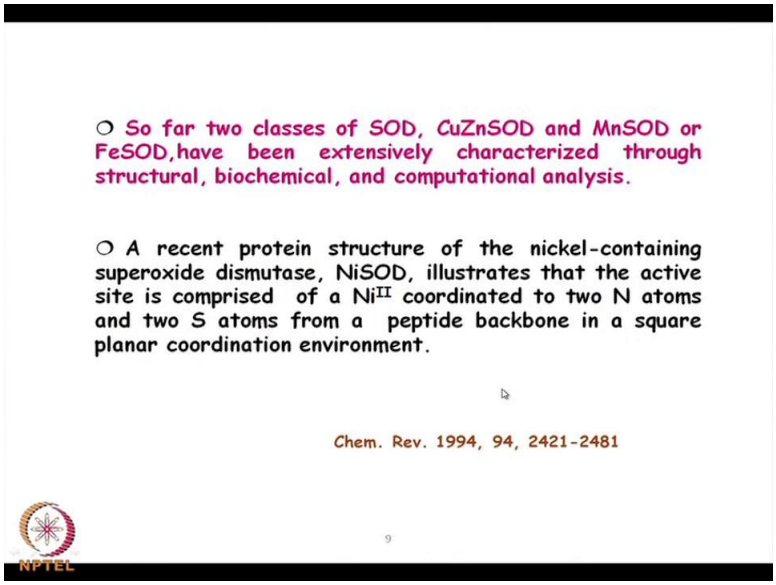

So, this super oxide this meant is already I told you that is a copper zinc super oxide dismutase and manganese is there and sometimes very few iron superoxide dismutase have also been identified. So, once you find these thing that means you have copper that means the copper is a redox center, manganese also redox center and also your iron is

also redox center. Only thing is that it is different from one form to the other that is your coordination environment is different that means ligant parts are different. If your ligant part is different you get a bimetallic system. If your ligant part is suitable for binding manganese because the metal ions is CSM which is also a very important factor, that why you are getting a corresponding superoxide dismutase based on manganese only. You have large number of different metal ion pool why this superoxide dismutase what has been identified, what has been characterized at manganese SOD. It is not taking up nickel to it is sights because this ligant part that means the biological ligant part the protein part as some good affinity and CSM for manganese. It will only attract manganese. So, this SOD, this manganese SOD in dibinate form that means without metal center it will not bind copper, it will not bind zinc or it will not bind iron. So, it is very much specific to the metal center. So, large numbers of characterized people have done through structural identification of the bio chemical reactions and theoretical fitting of all these data and all these. Sometime calculations also tell you this particular part can go for very basic reaction because this superoxide dismutase reactions all other reactions are very basic reactions. So, this is not a very old story for that the nickel superoxide dismutase has been identified mostly the last 20 years. So, when people have identified this SOD that the active sight comprised. So, immediately you can identify this particular sight whether your nickel sight is in plus 1 oxidation state, plus 2 oxidation state or plus 3 oxidation state and this co ordinate to 2 nitrogen atoms 2 sulfur atoms from a peptide backbone in a square planar coordination environment. Is not a corresponding environment which is octahedral in nature because nickel 2 once you have you always tempted to think that this nickel 2 can have other alternative coordination environment that means octahydral coordination environment.

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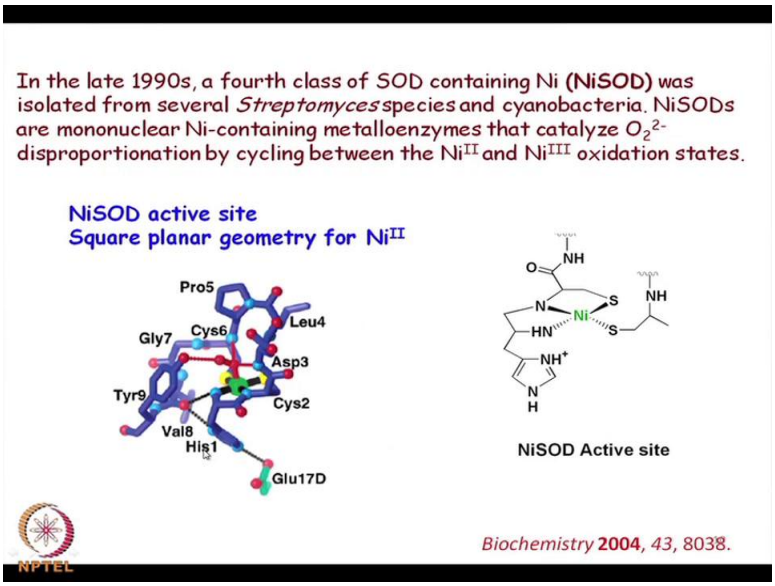

And this nitrogen binding in sulfur binding if you can able to identify the typical nature for the individual atom is what type of nitrogen it is and what type of sulfur atoms from the protein backbone or the protein chain then, in N 2 and S 2 environment. N 2 and S 2 environment, N 2 S 2 environment in several in other biological systems we have found in carbon monoxide dehydrogen is also. I told you that if you have N 2 S 2 environment it can be very nicely feted for you tetra valent hydrovalent environment as well. But, in this particular case you have a square environment. So, in late 1990s basically it has the it has been identified and is a definitely is a nickel containing metal enzyme that catalyze the corresponding disproportions are O 2 minus by cycling between nickel 2 and nickel three oxidation state. So, you see when we compare this particular system with other system that is not the cycling of nickel 2 between nickel 2 and 3 or nickel 2 and 1 is also important. So, identification that point only. Your catalytic cycle is operating between nickel 2 and 1 or nickel and 3 which is also important and that is being dictated by the environment. If you have a sulfur environment and this sulfur environment of thiolated environment that means S minus environment. So, if you have S minus environment for that and this is a nickels S O de-active side. So, if you have a corresponding environment of this thiolatesulfur, what you think that this are highly a responsible for its corresponding stabilizing your nickel in the plus 3 oxidation state. It can stabilize your oxide hydroxide it can stabilize nickel in higher oxidation state. So, in this environment if its cycles between this 2 and 3 you can that your nickel environment is in the thiolated environment and it is in the square panel coordination geometry in the native form.

And these are the typical ends which are providing the corresponding small polypeptide chain like of thing that means, if you have this corresponding aminus its site chains and all this. So, this is the environment to this yellow groups your sulfur ends and this 2 lightly a blue color is your nitrogen ends and you have the green nickel centre. So, when you have this square panel environment immediately it tells something that always like your micro cyclic and environment, the square panel environment, when you talk about nickel we always think of that is a square panel environment which is well suited for your micro cyclic environment as well. So, you that apical site available for interacting your substrate molecule or your superoxide O 2 or peroxide molecule. So, your apical site is available for interacting with that and transferring electron to that particular species through that apical site.

So, identification of this particular species and its corresponding cycle for this 2 oxidation state was very much important to identify nickel as an active site of nickel peroxide dismutase, which is typically different from your copper zinc super oxide dismutase. So, you have something that means if you have the thiol coordination over there and if you some other group because this particular thiol coordination to nickel also allows a breezing motive. It can also breeze some other moral centre of other nickel site what that is also not happening over here this is happy with a mononuclear system. So, you have to identify the centre as a mono nuclear one are that mononuclear centre is giving you that particular reaction to your superoxide.

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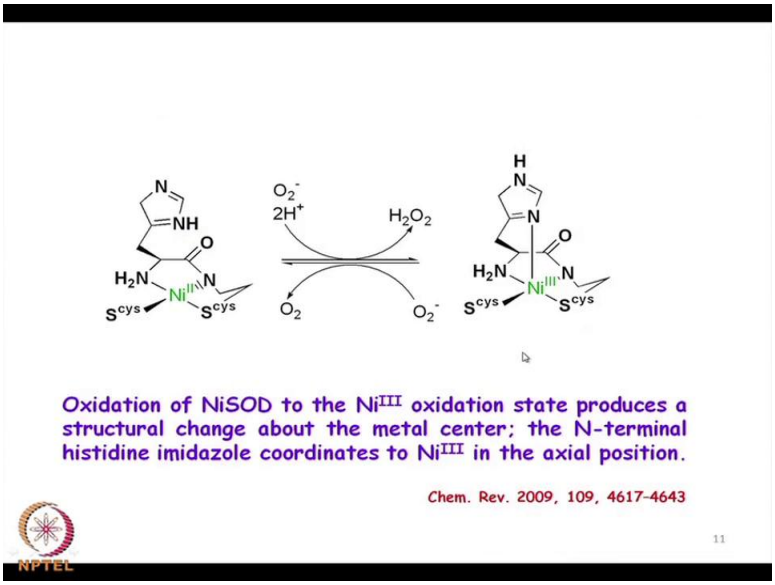

So, this is the thing that oxidation of that particular super oxide to plus 3. So, if also recalls you something that your palladium site or any other catalytic site. So, these are the corresponding systin residues and when you have so you just providing your superoxide. So, this superoxide group is providing use a superoxide. Superoxide is a 1 electron donor. So, this superoxide is giving you this particular one is taking place or it this in this particular this is 1 electron donor and this particular it is 1 electron acceptor. So, when it is acceptor electron it goes to peroxide and basic interest peruses is that it is oxidizing your nickel centre it is going for trivalent nickel and that trivalent nickel is always preferring for coordination for a fifth coordination site on also a 6 coordination site.

So, once you makes this in nickel plus 3 oxidation state, you can go and you can identify you can correct rise by means of your epr spectra and that epr spectra will immediately tell you that you have oxidize your nickel centre to nickel trivalent state and that trivalent state is stabilized and this dangling part of this protein chain. So, this is this trident ligant what we have soon in our pervious slide that, this trident part you have and you have a dangling group involved their and this dangling group is providing your coordination this nitrogen. So, wherever some other group is available. So, nickel is in the trivalent state is therefore, stabilized. So, when these group this nitrogen, not this NH nitrogen, this nitrogen. So, tertiary nitrogen is coming and coordinating to your nickel centre though you can have every long nickel nitrogen is bond in the apical site but, still you have some interaction.

So, this particular inbuilt ligant environment not that your solvent is coming over there it is attaching to this particular centre but, your inbuilt ligant what is available over there which is providing some donor groups and in encapsulating your trivalent state nicely and is bearing stabilized. So, when this 4 coordinated centre is available you get this, you go for a fifth coordination for this particular nitrogen form this pended group. So, this site is available for 5 coordination and this species when it is going because this cycling back. So, to and fro it is cycling. So, your another superoxide molecule will come into picture. So, this superoxide molecule will go and bind through this sixth coordination position. So, 6 site is available. So, this vacant site it is available, your this superoxide it is available for attacking this nickel and its transferring to O 2 minus and it is providing that electron to the trivalent nickel and that trivalent nickel is going back to nickel 2.

So, this is the thing that how this particular so the same species why you have seen the disproportion is in the reaction in the same superoxide anion is responsible for electron donation as well as electron acceptance to the nickel centre and that is very important because electro chemically if you measure the cyclic voltamogram, you should know the corresponding e 0 value for this transfer from nickel 2 to nickel 3. So, that potential is also useful to know that which particular potential reason we can have the corresponding transfer of these 2 electrons form superoxide to hydrogen peroxide and superoxide to dioxygen.

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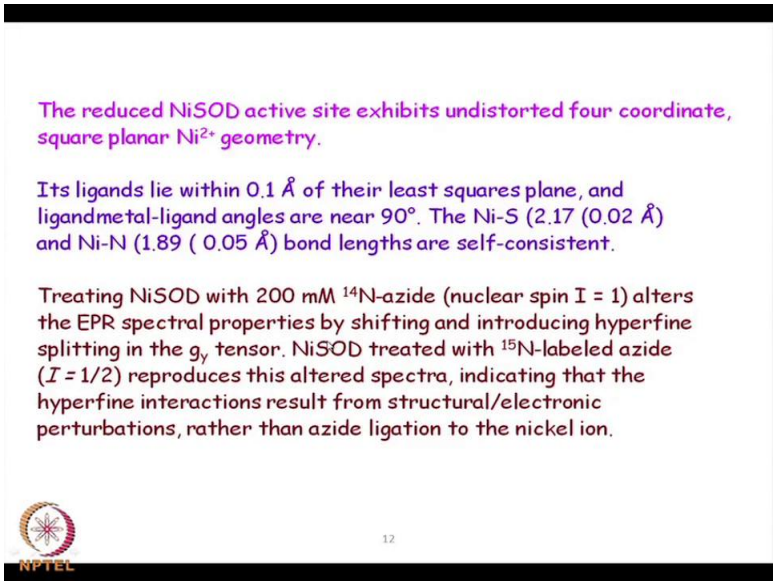

So, this basically gives us something that you get all this information for long distances or this apical binding and salt distances for vessel binding.