Biological Inorganic Chemistry
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Lecture 50
More nickel ion bearing enzymes

Hello, students. So, very good morning to everybody. So, we have reached to the end of our module 10. And this last lecture of this module will be devoted to the remaining part of our nickel enzymes. As I told you last time that we can have altogether six legal enzymes. So, we will be talking about the remaining three. Already we have discussed about other three.

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And there again we will talk about what important your nickel ion is and already we have learned that how the adjacent other metal ions center, so not nickel, the other metal ion center we have seen in case of urease we require the two metal ion centers, but both of them are nickel that means it is a homobimetallic system, but in this particular case we will now see you require a heterobimetallic system, because this hetero thing that means within a particular scaffold is very difficult to sometimes put two different metal ions.

Then we will see how again the inorganic sulfur can come into the play, because we will be bringing along with nickel, we will be bringing iron. So, not only iron, if you bring inorganic sulfur and the cysteine residues, we will be bringing the iron sulfur proteins also. We will see

also for the SODH enzyme that carbon monoxide dehydrogenase enzyme which whether it can assimilate nicely the carbon dioxide, and finally, we will see about the formation of methane is very important reaction based on your nickel enzyme.

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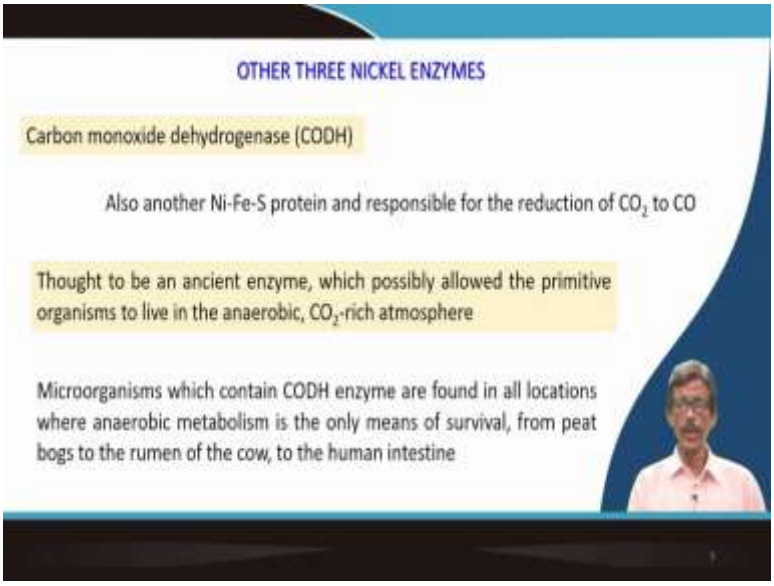

So, what are the remaining three nickel enzymes? We have seen that the fourth one is basically therefore your CODH is a carbon monoxide dehydrogenase thing. And as I just told you that if you have the nickel, you put other metal ion and you get a heterobimetallic system, but it should be supported by sulfur. So, where your sulfur will be? Whether it is coming from the protein chain or the each sulfur is inorganic sulfur.

And whether your sulfur is at the terminal point or sulfur is in between the nickel and iron, that means whether your sulfur center whether it is inorganic sulfur or organic sulfur is responsible for bridging these two metal ion centers. Because this particular thing when identified we know that this is required for the reduction or the conversion of CO2 to CO, because these are all one carbon centers.

And these one carbon species are very important that means the assimilation and the contribution towards the final carbon cycle that how these single systems that means the single carbon systems like your carbon dioxide or carbon monoxide can be incorporated over there. So, is thought to be an ancient anytime when we know that the system basically is dependent on the

corresponding environment which was available that means your carbon dioxide rich environment, because that time your dixygen was not there.

So, several microorganisms which can have your CODH enzyme and they are found in all locations whether it is aerobic or anaerobic in nature and definitely it can go for the corresponding metabolism and is the only means of survival, because they are surviving on not oxygen the way we survive, but they will be surviving on carbon dioxide, so from the peat bogs to the corresponding rumen of the cow to the human intestine.

So, the CODH will be everywhere and we can have this very typical reaction where we will be talking about the conversion of carbon dioxide what we produce in a different route from the assimilation of dioxygen molecule and burning of your say food material or the glucose compounds.

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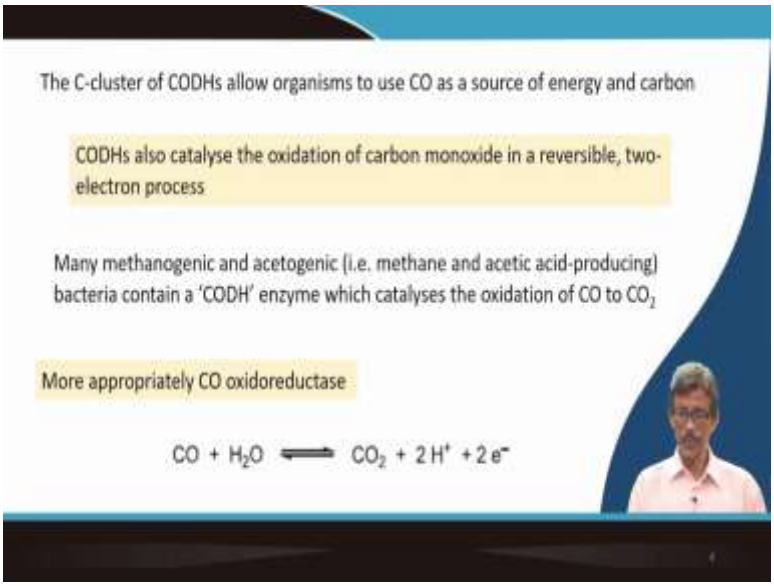

So, we can have many such units A cluster, B cluster, C cluster. So, we basically try to simplify our discussion, try to simplify our understanding in such a fashion that we can have the different types of things and where the nickel center is available.

So, if we consider that what has been identified that the C cluster of CODH is basically allowing the all the organisms to use carbon monoxide, not dioxide as a source of energy and carbon so if we get that particular information what we can understand now that these enzymes, and already

we have considered that these are nickel bound enzymes. So, people have struggled a lot. So, many years have gone to identify the presence of nickel in all these systems like your urease.

So, it basically responsible for the catalytic reaction where we can go for the reversible one that means the oxidation of now carbon monoxide is a two, is a reversible two electron process. So, you can go for the supply of the two electron for its oxidation. Now, if we consider that okay we will be able to produce that methyl function out of that, again it is a C1 molecule or you can produce a methane molecule, because CO, CO2, methane all you see all are C1 molecules.

If we can have some correlation between all these things by simple proton transfer, oxygen transfer and the redox reactions we will be happy. So, these enzymes that, many times you will find that these are not independent enzymes. They are dependent on some other function of the other enzyme. So, if we find that for the production of the methane and the acetic acid, the bacteria or the different bacteriums are basically responsible for your CODH enzyme and is going for your typical oxidation.

So, more appropriately, if we consider that we are talking about carbon monoxide, DH means your dehydrogenase, but carbon monoxide itself does not have any hydrogen. So, why we are talking this thing? So, is basically one particular idea that you can have that oxygen insertion and oxygen insertion is nothing but equivalent of the removal of H2. So, that way the nomenclature people used it. But if you are confused by looking at the name, more appropriately, we can call it as a CO oxidoreductase. That means you can go from CO to CO2 and CO2 to CO back.

So, that is the most fundamental chemical reaction what we will be talking this time for your CODH anytime that you have CO how you can oxidize it. You know from your again from your school days that water gas reactions, zip gas reaction and all these things, that is, if we just on the red hot coke, you will drop that steam, what happens, is the reaction of carbon with that of your water molecule. Here you have the reaction, so biochemical reaction between carbon monoxide and water molecule.

So, that water molecule is now you see interestingly is a very good oxidizing agent. This water molecule is supplying that oxygen is own and the only oxygen present in the water molecule can be supplied to your carbon monoxide molecule such that you can produce the CO2 molecule. So,

that gives you a very good example of your potential of oxidation of water molecule to give you. And while doing so you are also producing the corresponding proton and extra two electron.

So, if you are having, we know all the time when we produce some the proton and the electron and the oxide ion from the water molecule, we know that we can have for electron transfer. So, if you consume two electron for this particular reaction, you can have another two extra electron. So, all these things you have to manage nicely in this particular enzyme.

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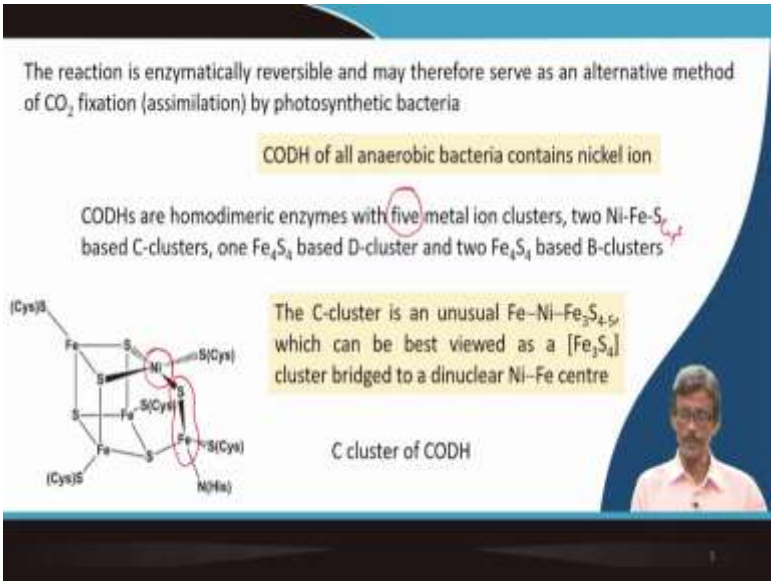

So, is enzymatically reversible as we are discussing that means you can reversibly go from to and fro business basically CO to CO2 and CO2 to CO. So, any direction is you put in the reversible sign for that and you can have, so if you can have some driving force from the left, it will go to the right and if there is another driving force from the right, it will come to the left. So, is basically related to our most important thing that your CO2 is a greenhouse gas.

Anything we burn, when we take our food also we are also producing carbon dioxide. So, if we can have certain type of this photosynthetic type of bacteria, we all know that in the photosynthesis we fix the CO2. So, similarly, these particular system or enzymes can be responsible for something where we find that these anaerobic bacteria they are surviving on CO2 and all such anaerobic bacteria of have this CODH family can have the nickel ion at their basic component or the active site component.

So, what is that particular structure of that particular enzyme? So, we see that the enzyme is the homodimeric enzyme, that means two equivalent part, not heterodimeric. So, two equivalent part of the enzyme is there. But when you see, when you try to find out even by solving the structure that how many metal ions are there. So altogether if we can have this number of metal ions there so we find that you can get it that all together you can have five metal ion centers.

So, when you detect because the position or the location of these five metal ions is very easy and location of this particular five metal ion is so important that you can initially detect the position of those five metal ion. So, basically what we are talking about is not a mononuclear nickel ion base thing but is typically aggregate.

So, our life is becoming more and more complex when we move from our life from the hemoglobin or the myoglobin. Hemoglobin was a little bit complicated, because it is a tetrameric unit of the myoglobin unit. So, when hemoglobin you talk, you have four iron centers. Similarly, when we think of all these things, the heteronuclearity is coming and you bring more number of metal ions apart from your nickel center.

So, if you take, already I told you that you have the nickel, you have the iron and you have the sulfide. So, the C cluster we are trying to analyze the C cluster. So, that means what can have the C cluster. So, it will have the adjacent one Fe4S4 ferredoxin molecule itself, based D cluster and two Fe4S4 based B clusters. So, you have many such Fe4S4 units for the electron supplyyou're your proton is available that can some part function as hydrogenase also.

So, what is the typical structure of this naming as C. So, C cluster of CODH is one particular part because you have the B cluster, you have the D cluster all are different. So, why we are focusing our attention on this C cluster? Because you have the active site. So, if you try to find that okay we know the four iron ferredoxin system, we know how the cysteine sulfur residues, how the inorganic sulfur that means the sulfide ions are there we know all these things.

Now, with that particular cluster you have to attach the nickel site. Therefore, when you try to bring the nickel site is not that the typical Fe4S4 unit is there. So, when you bring the nickel site what the biology can do for us is remove one of the iron center or at the beginning what you can have that you cannot have this particular thing as is not growing fully for your Fe4 unit, but it is going to Fe3 unit.

So, Fe3 unit when it is trying to attract the nickel center, you get Fe3 plus Ni, but you have to stabilize this nickel to the other coordination. So, your cysteine sulfur is coming, but it also has the inorganic sulfur. So, that is why what I was writing there that you can have also the whole unit that means you can have also Ni, FeS unit or Ni, S, Fe unit.

So, Ni is there, S is there and Fe is there. This S is your inorganic sulfur, not the terminal cysteine sulfur. But when you say that this sulfur, so you can consider that this is your terminal sulfur also. So, you can have also the terminal sulfur. So, remember all these things nicely such that you can understand the structure, you remember the structure and you can write the structure how it is growing.

So, on the Fe3 unit, you bring the nickel center, then to stabilize this particular entity, because nickel already have that particular fourth coordination site already. The nickel is brought over there by the cysteine from the other site. But how to stabilize it? How to clip it? So, for that clipping business you bring from my, this particular finger tip you bring the iron from there and nickel is here. So, you have to clip this particular two cases that you bring the iron.

Again it is supported by not only cysteine sulfur, but histidine nitrogen and take the help of the inorganic sulfur at the bottom. So, that basically gives us all these informations and we can able to write the corresponding structure, the C cluster having very unusual structure. You have iron, already we know that you can have that terminal iron. So, this iron is this iron.

Then nickel and Fe3S4 unit or some time Fe3S5 unit, because we are putting not only the four electron on the Fe3 unit, but also the fifth sulfur adjacent to your nickel center. So, you can have this particular the four as well as the five.

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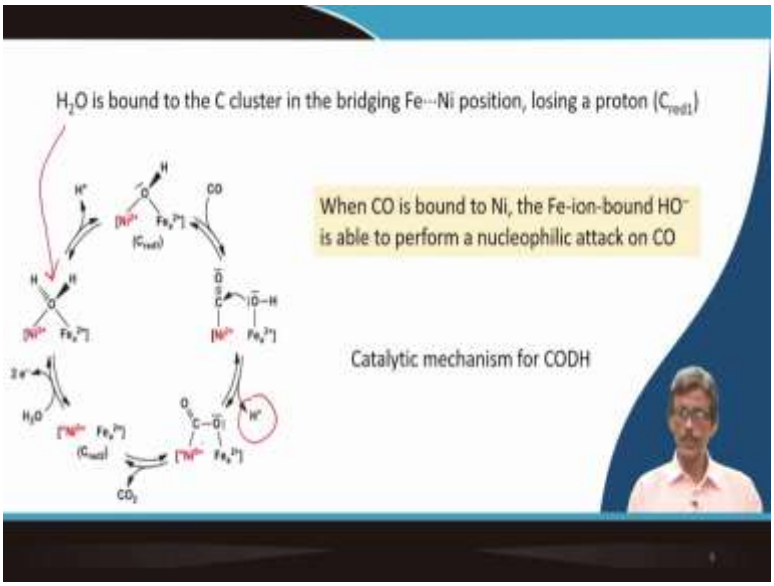

So, how it is working then? We know the reaction. We see that the carbon dioxide is producing your corresponding, carbon monoxide is reducing your carbon dioxide. So, you know the product. Your enzyme is known. Now, put the enzyme, allow the enzyme to work. But you will find that is a very fast reaction is happening. And through that fast reaction process you have to identify the different steps.

So, to identify the steps particularly if you have the simple water molecule as a very good ligand, the universal ligand always we call is there available to the C cluster and is available to the FeNi part. By doing so, it is losing a proton. And not only the proton, your C center is going for a reduction reaction. So, the cluster C in its reduced form one step reduction is reduced one so that is why C red 1. So, this is the entire cycle.

So, in a straightaway I am just writing this particular case. So, if you have this, how this water is there. So, what do you see that you bring this water over here, this is your water, we all know, we are discussing many times that you can have water having two lone pair of electrons and those two lone pair of electrons if those are supplied to your iron center as well as the nickel center you will have a bridging by the water molecule.

Then as I told you that you can have the corresponding loss of proton. We already considered that you can study that thing the loss of the proton. So, that means you are producing a hydroxido bridge between your nickel and iron center and that is your C red 1.

So, this C red 1 form is very useful for you and what we can find that whether you can have that bivalent nickel center, then carbon monoxide is coming and there was a huge debate whether you can have the electron transfer beforehand that means the nickel center can be reduced to nickel 1 and then your carbon monoxide can come and bind.

But it can so happen because we all know that the affinity for the nickel center towards carbon monoxide is more and more as you go down to the lower oxidation state that is why we know that the tetracarbonyl nickel center. But the affinity is well known. So, that is why people propose that particular thing at that time that if you go to the lower oxidation state, even people propose the zero oxidation state of the nickel center, then it nicely handled the carbon monoxide like your nickel tetracarbonyl formation.

So, if now because there are many debate for that, so one cycle is established then people established another cycle. So, if we consider, we are not going for the electron transfer first, let us see what happens if we take allow, because these are all unusual situation in the biology, because then biological system if you are forced to introduce the carbon monoxide and if you have some interaction on the nickel center, you can have the corresponding bonding interaction between the bivalent nickel even to that of your carbon monoxide center.

So, when you have this, because your COH particular part that means the corresponding C cluster is bridged by the hydroxide and when the carbon monoxide is coming, carbon monoxide will go for the ligand substitution reactions, the bridge will be lost and your hydroxido group will be transferred to your iron center.

And that iron center hydroxido group is the very good useful nucleophile and that nucleophile will come and attack that particular carbon monoxide molecule to convert it or transfer it that hydroxido group through deprotonation that means your H plus is going away from that hydroxido group you will be having with a carbonato complex, nothing but, sorry, carbon dioxide based compound.

So, this carbon dioxide can have, is again unusual situation that carbon dioxide can function as a bridging unit between the nickel center and the iron center and there you can talk about that, okay, I have reached to a nickel zero state. And then if you go through that particular reduced

form and the removal of the carbon dioxide from that particular entity you will having a nickel zero state. So, that is why you get a C reduced form.

Then now the water will come and again very quickly it can react with that particular part and regenerate the enzyme. So, CO2 is bound to the nickel center. Iron bound hydroxido group, what I discussed is, is performing that nucleophilic attack to your carbon monoxide molecule.

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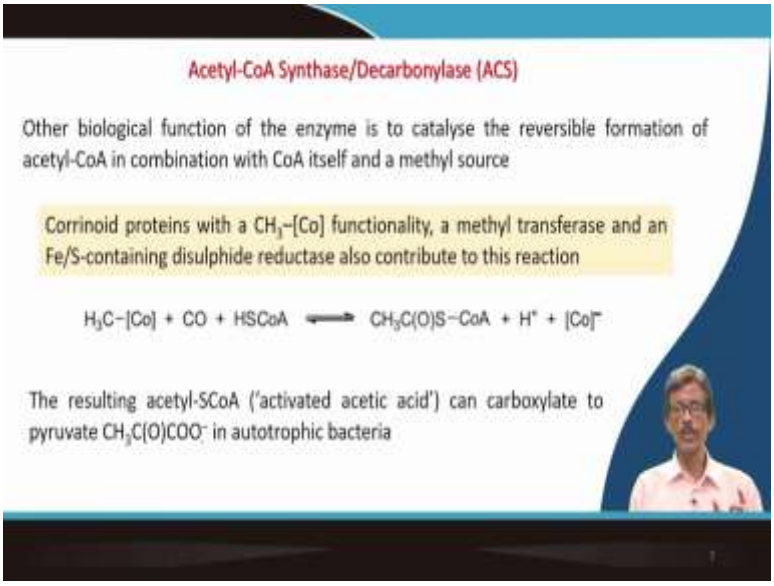

So, next we will go to another important molecule which we call as ACS is very easy to remember, acetyl coenzyme A synthase. We also know that that is related to some chemical society we call the American Chemical Society is well known is also known as ACS. But when we talk about that ACS to this ACS is acetyl group that means CH3CO function, some coenzyme is there and how we can utilize for the synthesis of that.

So, all biological functions and many other biological functions the enzyme is to catalyze the reversible formation of acetyl coenzyme A is not that the assimilation of CO and CO2, but you have to produce the CH3CO function which is a very useful function for that and is useful for your methyl source like your methylcobalamin we have seen earlier.

So, is basically a macro cyclic ring if you have. The corrinoid protein we have seen. The corrin ring we have seen for your methylcobalamin cases and your methyl transferase is there. We have

studied nicely. And then iron sulfur containing disulfide deductase if it is there and also can contribute to this particular reaction.

So, anything based on that corresponding one that means the methyl coenzyme if you have the corrinoid protein you can consider it as the corresponding not coenzyme you can consider, you can think of as the corresponding cobalt center, but is not the cobalt center is the methylcobalamin, not the cobalamin, it is the coenzyme.

So, if you go for that that if you have the methylcobalamin and you have the carbon monoxide and another coenzyme A is coming having a thiol function SH function dangling over there, so some reaction will be taking place there such that between the coenzyme and the methyl group you will be able to introduce the CO function which we already we are seeing that the CODH function. So, the working of, or the CODH function is also dependent on your ACS function.

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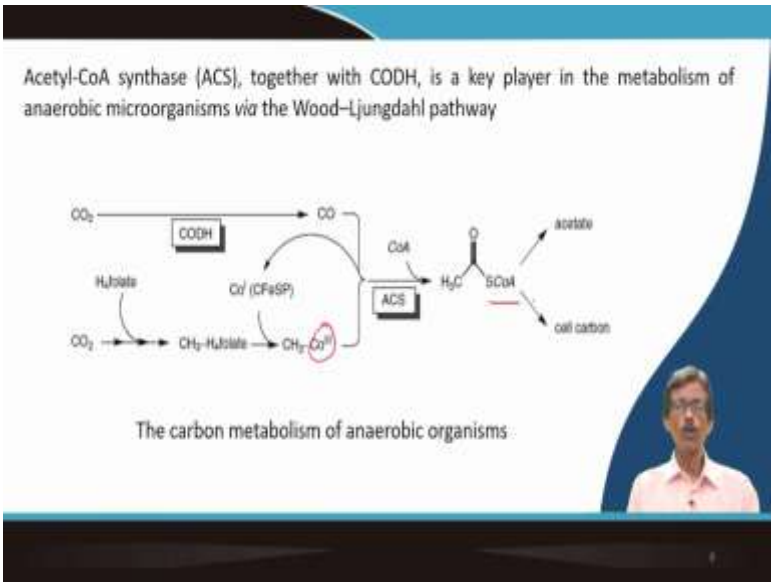

So, is go for the synthesis along with that CODH and is basically a metabolism pathway where the microorganisms are working and the pathway is known as Wood, that spelling can be the Ljungdahl, j is, can be silent, so Wood-Ljungdahl pathway. So, what is that pathway basically, how you can go? So, we have the carbon dioxide. We all know that carbon dioxide. We are also producing when we are burning our food material.

And if your CODH is involved, you will be able to produce CO, because that CO is required for the introduction of the corresponding CO within the corresponding function if it is a cobalt-based or if it is any other coenzyme based. So, do not be confused over here. Try to learn it nicely that whether you are handling a cobalt center, because when the oxidation state is known, it is a cobalt center or whether you have a different coenzyme because that is also abbreviated as C.

So, do not make any other type of confusion, whether is a cobalt center or is a coenzyme center, because most of the time we write that cobalt in italics form. Here you have written over there is the coenzyme A is the italics one.

So, we will be able to produce both these two groups that mean the assimilation of CO and CO2 and that taking care of the methyl you know that the CH3CO function is the acetyl function that is the most fundamental one for the formation of the acetate groups and also for the different types of cell carbon. So, this is basically the corresponding carbon metabolism pathway for any anaerobic organisms which are not dependent on O2 molecule.

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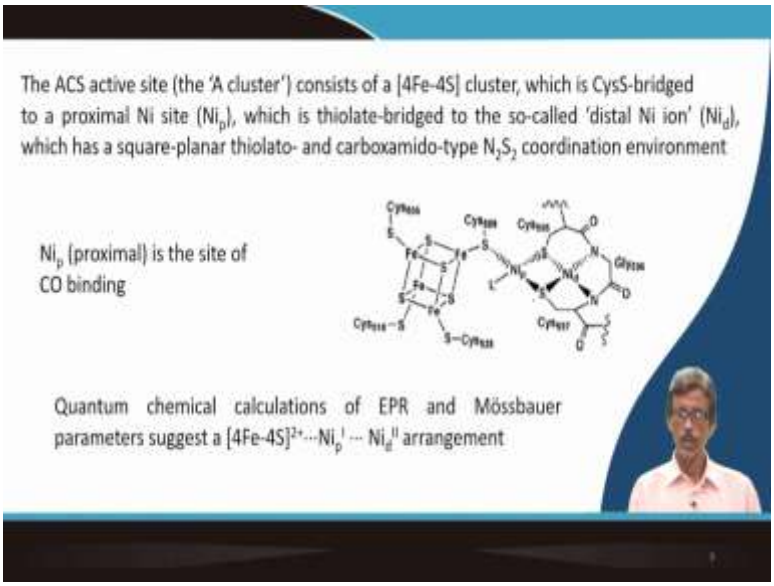

So, the active site of the A cluster consists of many, many clusters. You read it nicely that is why many lines I have written over there. But you have again a unique nickel center like that of your CODH. And how it is bind, that means the ligand environment when you identify the presence of that particular metal ion, we then next go for the identification of the peripheral ligands around that particular metal ion center.

Now, you see is closely related, but is a different type of thing, because Fe4S4 unit is the intact one, is not that Fe3 unit, but you can bring some cysteine residue in between and that cysteine residue is holding one nickel center, but you can have another nickel center. Label is not Ni1 and Ni2 like your urease. We have defined Ni1 and Ni2 for the urease molecule.

But in one case which is closed to your the Fe4 cluster is your proximal nickel is Nip and another one is the digital one having two different and the distinct coordination environment that you have to understand, because these are the final results given to you. People struggled a lot, scientists struggled a lot to determine the final structure of this particular molecule.

Until you do not have the structure, you cannot think of how the nickel is utilized for binding that particular species which is responsible for this conversion. Then when both these redox active metal ions are there the nickel center is there within the cluster as well as the two different nickel center. So, which one you can go for the corresponding transfer of electron.

So, not only the experimental findings from the measurements, but also the theoretical calculations based on quantum chemical calculations predicted us that this proximal nickel center is the active site having a bound L. L means the labile binding point or the labile coordination site which can be removed by your other incoming molecule which can function then as a active site.

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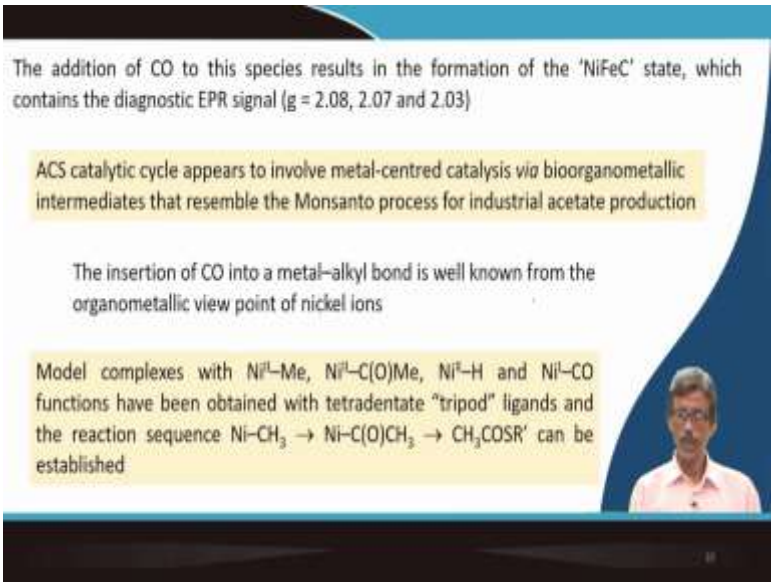

So, EPR thing can also help us to an understanding the type of spectrum is very closely spaced line. You have three lines. We all know the rhombic signal how it looks like. So, if you have the rhombic signal and if you have the very closely spaced, close to that of your DPPH value 2.08, 2.07 and 2.03 is diagnostic and characteristic for this particular environment.

So, it basically the cycle basically is appearing to involve the metal center or the metal ion centers to be specific via a bioorganometallic intermediate because we are talking about the metal ion and we are talking about the carbon. How we know about all these different things about the organometallic chemistry.

So, organometallic inorganic chemistry or the D metal ion based organometallic chemistry will always try to give some good idea how you can get a bond between the metal ion and the carbon center. So, if you are talking about carbon monoxide, if you are talking about carbon dioxide and then if you are talking about the corresponding methyl group or the acetyl function, all are involving the corresponding MC bond or in this particular case it is the nickel C bond, because the acetate production or any other thing is there famous Monsanto process is well known.

Is the industrially developed process that is why the name of the company is labeled to that. So, you have to go for the insertion of the carbon monoxide molecule over there and the metal ion alkyl bond is important and for this organometallic point of view is also important. So, what we can do basically. We can take, we go to the laboratory, prepare some model compounds, no biology nothing, no protein nothing.

You take some ligand which is basically mimicking, can mimic the environment of the system what we are looking for. So, to mimic that nickel environment we have seen that you can have the N2S2 environment. So, take N2S2 ligand, a tetradentate N2S2 ligand or two bidentate NS donor ligand.

So, whether it is a planar one, because if you go for the linear tetradentate ligand, the more chances are there that you can get a planar structure and then put the nickel. Then you try to go for whether I will be able to get the methyl compound or CO methyl compound or the hydride compound or the carbon monoxide compounds.

So, all these model compounds with a tripodal ligand, not the tetradentate, not the bidentate, but biology is always doing very good with that of your mimicking with the tripodal facially coordinated ligand. So, that tripodal ligand give all these reaction sequences and methyl can be converted to the acetyl function and acetyl can be transferred to some other group that means you can transfer the corresponding coenzyme functions.

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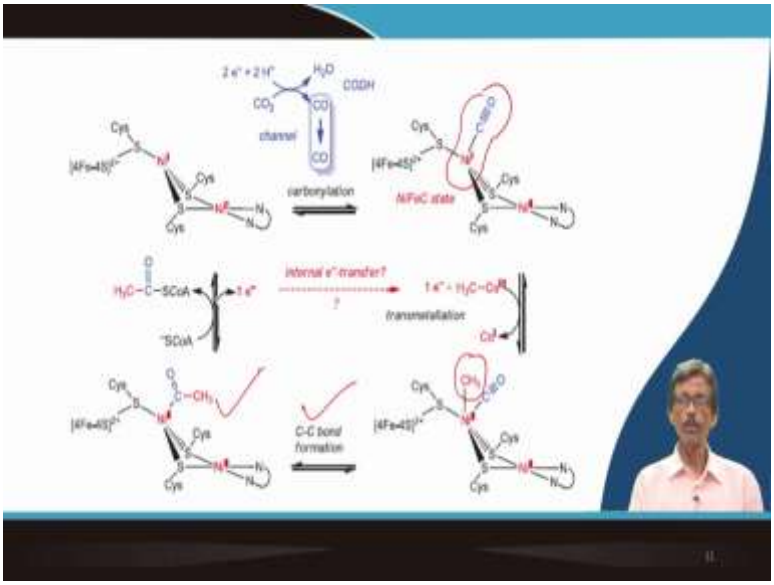

So, do not worry about this corresponding huge structure. But what we see that already we have seen that you can have the corresponding carbon monoxide bound thing and the carbon monoxide bound thing already we discussed a lot. So, you have the nickel center bound to this particular one. So, focus your attention on this particular part.

Then you see that while doing so you are able to put a methyl function over there. So, on the same metal ion center you are able to form two bonds, one bond is to the carbon monoxide and the second bond to the methyl function such that these two can interact nicely such that your methyl group can be converted to the acetyl function. So, that is the thing basically.

So, you go for the corresponding CC bond formation and you get the corresponding acetyl function. So, the other thing basically why you know the other part, because how you can have, what is the role of the other part, how the iron center is important, because in isolation you cannot think all these things, because in isolation if you think of is the typical laboratory based model chemistry.

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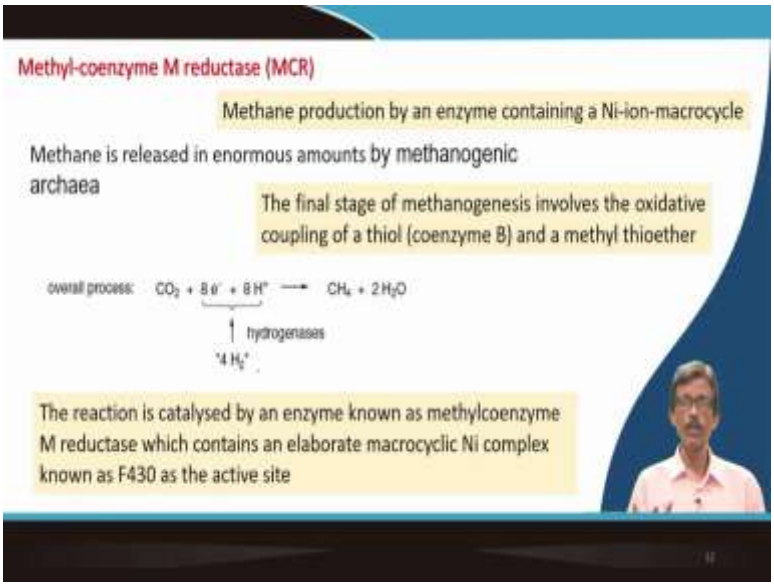

So, lastly, we will just quickly see the methyl coenzyme M reductase that is the last category of this nickel enzyme where we will be able to produce the methane. So, many methanogenic bacteria are involved and is the final stage, because where you are producing methane, because you need the methyl function or the methyl group attached to the nickel center if it is there, you just supply the proton and if your CH3 is released as CH3 minus you will get the methane.

So, the reaction was a complicated reaction. The transfer is eight electron and eight proton transfer and many hydrogenases are involved, because the equivalent number of that 4 H2 is supplied by the hydrogenases. That is why, why you require the presence of the iron centers over there.

So, we have the nickel complex and known as is the factor 430 because we know that the corresponding solid band of this macrocyclic ligands like the porphyrin can have a very good absorption that is why we have the cytochrome 450. Here we have the absorption as 430 nanometer.

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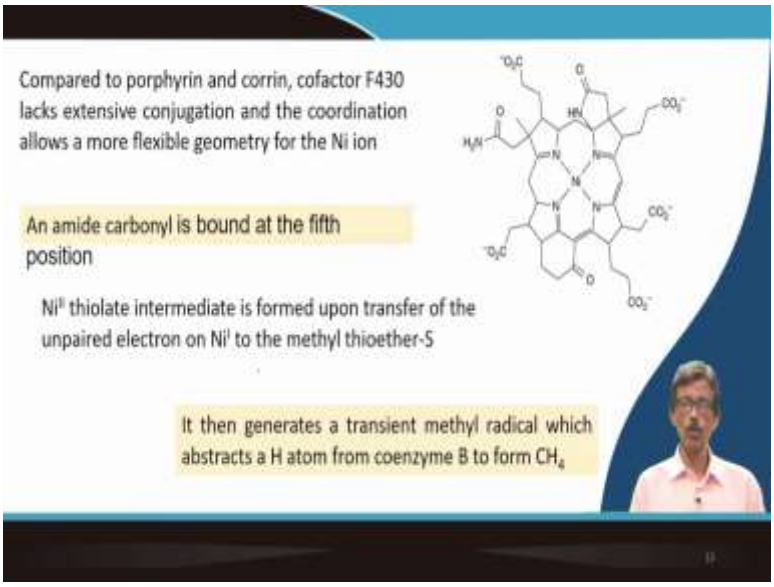

So, we can compare with the porphyrin and the corrin ring. So, this is the structure and how we can compare this particular structure with that of your porphyrin moiety and the corrin moiety with respect to that. So, you have the corresponding amide carbonyl bound to the fifth position and the nickel thiolet intermediate during that particular reaction. So, you can able to produce the transient methyl radical which abstracts the hydrogen atom from the coenzyme B which is the supplied last proton to your methane formation.

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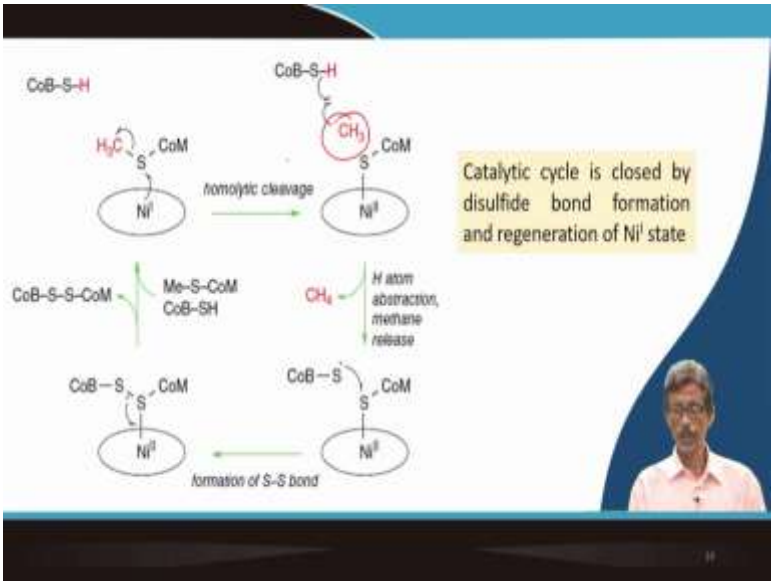

So, you have definitely the catalytic cycle is a very simple catalytic cycle. The coenzyme S is coming, binding to the nickel center, then another coenzyme B is there which is supplying that H and the formation of the corresponding methyl group there and the cleavage of that particular S methyl function on that giving you the methyl radical.

So, the production of this methyl radical is important, because this is the source of your methane formation. Then it take the hydrogen atom and you get this particular removal of this particular thing, methane is released and how you regenerate the corresponding original catalyst.

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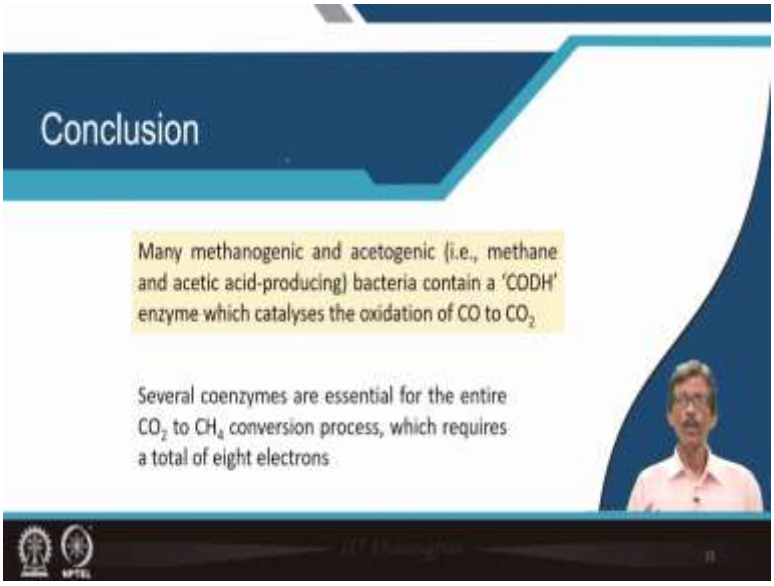

So, in conclusion what we can see that, methane we can consider, acetic acid we can consider, the bacteria is basically responsible for doing all these reactions. So, we have studied CODH enzyme and we have also studied how your CO can be converted to CO2. And then the CO2 how we can go forward CO2 to CH4 conversion where we are requiring eight electron transfer so definitely is a very complicated reaction compared to your photosynthetic reaction.

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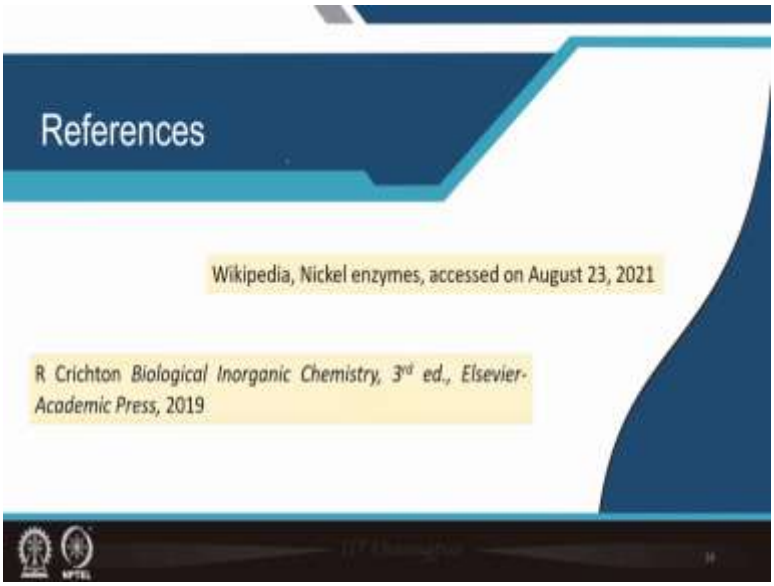

The references you start with the nickel enzyme and all other supporting things you can talk about or think about in the Wikipedia page and the book. So, thank you very much for your kind attention.