Biological Inorganic Chemistry
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Lecture 34
Iron-Sulfur Proteins

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Hello Good Morning everybody. So, we were in iron ions in life processes and in this lecture which is number 34; we will talk about Iron-Sulfur Proteins. So, what we will do we will just bring the iron ions because we are throughout this module we are just learning about many things about iron starting from your hemoglobin to myoglobin. Then will bring basically the sulfur as your two types of different ligands.

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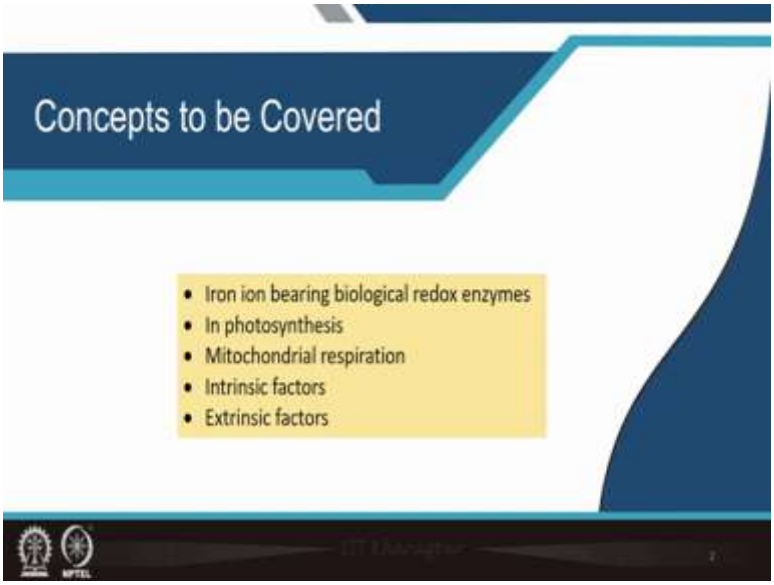

So, what are these? These are basically they will function as the electron transfer enzymes. So, all iron ions in these all these particular categories like your cytochromes will behave as typical iron sulfur; proteins of redox type. Then their participation in the photosynthesis there are many varieties of all these reactions will follow and definitely it will be related to the mitochondrial respiration and the two particular type of factors which can control the different E0 values as well as the rate of electron transfer that we will also see.

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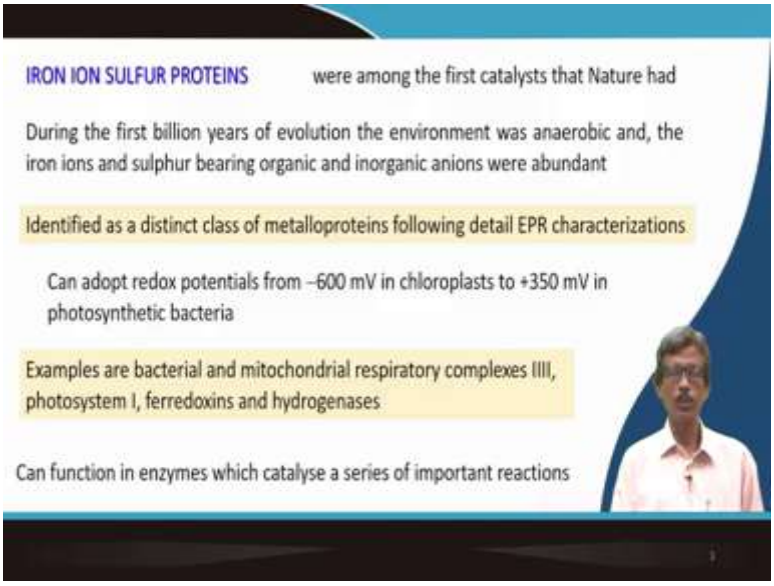

So firstly, we will start with that typical iron ion sulfur protein. So, what does it mean basically? So, when you say that you have iron center as well as you have different sulfur ligands or the sulfur donor groups are there. So, that particular entity sometime we write also Fe dash S. So, Fe dash s proteins or the iron sulfur proteins what we can find it because the historical it is also very important because these are a particular type of proteins and they also function as electron transfer enzymes.

Sometimes you can say or the electron transfer proteins and they are the first catalyst among the others which were discovered like your cytochromes and others the nature first identified these are the natural processes we get it at the first time. So, during a year of say several billion years time so like your geologists people who talk about the different billion years time and the evolution of this particular environment where we are sitting now.

How much you know about this particular environment which you all know now the oxidizing environment? Because you have the oxygen available, plenty of oxygen is there around your environment where you have also the iron center. So, when the system was not like that when it was an aerobic that means when air was not there and the iron ions and the sulfur bearing organic and inorganic ions were abundant also at that time.

So, if your oxygen was not there your environment was little bit reducing, so iron ions were there so because they are leaching from the iron metals basically from the iron ores also. So, when they come basically for giving you the different ions they will try to remain in the reduced state which is your the corresponding ferrous state. So, how we can identify it; what are the corresponding oxidation states; spin state all these problems always we know will be associated with your identification of iron as your iron center.

So, it can be your ferrous state, it can be your ferric state, it also can be in the high spin state and also it can be in the low spin state. So, all these metal of proteins bearing iron ions immediately we can characterize if we go through the electron paramagnetic resonance spectroscopy. So, EPR characterization will basically tell us whether you have a system where you have a particular type where capital S is equal to 0 that means the system is purely diamagnetic in nature.

And as we all know the diamagnetic system will not give you any EPR response. We at least we need a free radical type of unpaired electron so unpaired electron density or the spin density so

that will give rise to the corresponding paramagnetism due to the presence of the electron it can be on the metal centered electron or it can be also the ligand centered electron.

So, after initial characterization in terms of using EPR what we can follow is that let us have some about idea about the corresponding E0 values the thermodynamic redox equilibria is always there between these two states only is a very simple thing that we are talking only on iron in two states; the ferrous state as well as the ferric state. So, it can have a very high negative potential of minus 600 millivolt in chloroplasts.

So, you see the window now we are trying to stretch the window the redox window for electron transfer reactions. So, you can have the corresponding E0 value the thermodynamic potential for electron transfer as well as associated the rate or the rate of the electron transfer will also be important.

So, when you go for a positive potential when you talk about the oxidation of water molecule, we all know that in photosynthesis or in photosynthetic bacteria or to be precise in ps2 in photosystem 2 we can have a positive potential such that you are able to oxidize the water molecule to molecular oxygen.

So, you see there the potential can go up to plus 350 millivolt. So, if we are able to manipulate the ranges then we can see what are the different types of these iron sulfur proteins will be there whether you have a mononuclear system or a binuclear system or a multinuclear system and how you can change the corresponding environment. So, the basic idea in all these cases you have to determine the E0 values experimentally.

Then starting from your photosynthetic bacteria, we can have also the respiratory proteins, the bacterial as well as the mitochondrial respiratory complexes of say this not 4 is 3 complexes 3 then photosystem 1 ferredoxins and hydrogenases. So, all these are dependent on iron sulfur proteins; why? Because everywhere wherever you have a electron transfer reaction either you are talking about the reactions of the hydrogenases that you are reducing the protons or h plus ions to get hydrogen or you are assimilating dihydrogen to get the corresponding h plus.

More number of protons such that you can protonate certain specific spaces, places and the protonation of the corresponding anionic form of the protein chain sometimes. So, starting from

your hydrogenases we can have also the nitrogenases where you can go for the assimilation of dinitrogen molecule. They all are dependent on iron sulfur protein.

So, these reactions basically if you can have 5 to 10 reactions like the reduction of dinitrogen to the oxidation of hydrogen to the reduction of carbon monoxide or carbon dioxide always will find that this basic or ubiquitous proteins are there that means the iron sulfur proteins are always there.

Sometimes apart from your electron transfer reactions if we think that no I do not need to have the electron transfer but we are not changing much of this environment because some of these same type of iron centers in sulfur environment around sulfur you have so they can also function as catalysts or enzymes. So, there will be some important reactions that we will also see what are those important reactions what we can follow or what we can study in relation to that of your studies on iron sulfur proteins.

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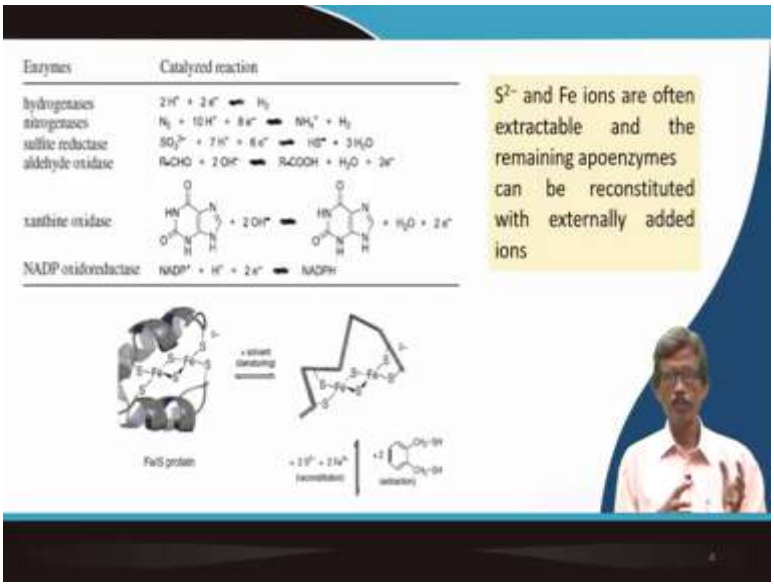

So, if we can have a huge number of these enzymatic reactions, so electron transfer reaction as well as the enzymatic reaction so hydrogenases are there that simple reaction what I just now uttered that you have the proton and when it is accepting electron it will be providing you the corresponding dihydrogen molecule or the reverse is also true the assimilation of dihydrogen molecule.

Then nitrogenase is also producing ammonia when it is protonated because plenty hydrogen ions are there in the system, so ammonium ions are produced. Then sulfide reductase, aldehyde oxidase, xanthine oxidase to up to NADP dependent oxido reductase or direct NADP oxido reductase reactions where your nadp is converting to your the reduced form NADPH. So, all these reactions what you find you have the corresponding active site.

So, active site may or may not be your iron site or any other metal on site but the electron donation like the reducing agent so biological reducing agent is your iron sulfur proteins at a particular type of or a particular range of electrode potential. So, is very important that is why because we all know that we can use many types of reducing agents in your organic chemistry reactions or the inorganic chemistry reactions.

Starting from your sodium borohydride, lithium aluminum hydride so only lithium hydride and many other reducing agents we use basically sometimes the hydrogen gas itself in presence of say Raney nickel we go for the reduction reactions. So, in all these cases they are functioning as the reducing agent that means at a particular potential if they are very strong we do not care about the potential value where the transfer is taking place for the electron.

But you see the right potential or the matching potential is here such that you see that the corresponding oxidase activity of your janthin is taking place or the aldehyde oxidation can take place to convert your aldehydes to your corresponding carboxylic acids. So, they all are dependent on this very simple type of iron sulfur proteins. So, one such example we have taken here is that you have the protein envelop and always I say that you can have the protein type of the.

So, you have the corresponding opening of the mouth, so the mouth opening is there such that you can have the entry of the corresponding iron ions and you have the sulfur the dangling sulfur groups are there. But interestingly here you see that it is 2 Fe 2s ferredoxin molecule is a dinuclear ferrydoxine molecule which had been inserted within the corresponding cleft or fold of the proteins one at the top and another as the bottom is not at the top and bottom but it is like basically enclosing the entire system like this.

Because you have to bring four cysteine in sulfur residues if on my finger tip if you have the cysteine sulfur residues. So, you have to bring this so you see that from this side is when is

opening is a jaw type of thing so it is opening up so you have two sulfur; thiol sulfur so you have these two thiol sulfurs and another end you have two thiol sulfur.

So, what you are doing basically we are basically trapping something which is nothing but your FeS the ferrous sulphide. The inorganic ferrous sulphide we are trying to trap inside a protein chain or inside a protein envelop that gives very good idea about the system what we are forming and if we have the whole system having a charge of 2 minus if you consider the cysteine sulfur residues having 1 s minus so four such is giving four negative charges and then two sulfides are again 2 plus 2; 4.

So 4 plus 4; 8 charges, 8 negative charges are there for this iron sulfur, two iron, iron sulfur ferrydoxine molecule then the overall charge if it is 2 minus then your iron centers are in the ferric-ferric state. So, this ferric-ferric or dipheric entity like your all other biomolecules we have seen iron is present in again another type of non-heme enzymes like your hemerethrin or other that particular methane mono-oxygenase and all these.

So, those are all di-iron states and you can have the dipheras and the pherospheric state. So, these are the 3 states but here interestingly we will see how many electron transfer can take place from this particular entity to go for another entity where you can have the reduced form and again another you can have the reduced form such that our basic idea is that you try to reduce the first iron center from ferric to ferrous and the second iron center again from ferric to ferrous.

But it is not always possible to individually think of about the metal ion center such that you can reduce all the iron sides to its lower oxidation state or you can go up for all of them for the upper oxidation state that means the trivalent state. But if you have the corresponding solvent if you give like dmso or dmf which are very thick solvent or heavy solvent and that can basically denature that means it can try to remove or if the solvent molecules will percolate inside the corresponding surroundings of this particular iron sulfur protein.

So, where we find that this particular environment will basically denature the thing and then you see the structure is changing the protein structure is changing, so you can have the tertiary structure of the protein and with the addition of the solvent you can just denature the thing and at the same time we can also weaken the binding of the cysteine sulfur residues or the cysteine sulfur donor groups.

Such that if you externally add some other thial groups so thial groups like this the bidented ligand so orthoxyl diethyl, so orthoxyl diethyl can be given such that it is again functioning as a bidented ligand but which is a synthetic bidented ligand not your protein bidented ligand. So, you can get it and you just remove that particular molecule so will be removing a synthetically isolated a model compound which we also can be prepared from laboratory work.

Because we are not depending on the protein environment or the protein coordination, we are depending on the some other ligands the bidentated diethyl ligands, so bident diethyl ligand can give rise to that particular di-iron ferredoxin molecule. So, after getting this again you put that solvent combination and all these things and we can have this the particular case that you can go for the corresponding removal of all these things or reconstitution also is possible.

If you take the ligand the laboratory prepared ligand and then these two anions like the anion as well as the cation the ferrous ion as well as the sulfide ion and will be able to make it. So, these two ions basically the sulfide ion as well as the iron ion or the ferrous iron can be extractable can be taken out and the remaining apoenzyme that without the metal ion as well as the most prominent anion which is your sulphide anion can you can have.

And further it can be reconstituted with externally added ions that means when you can take out then the protein apoenzyme is there so only apoenzyme you will be leaving behind. So, within that apoenzyme if you again put ferrous iron or sulphide ion will again reconstitute these things. So, that basically tells us the equilibrium process for this particular denaturation removal of the metal ion as well as sulphide anion as well as the corresponding reconstitution.

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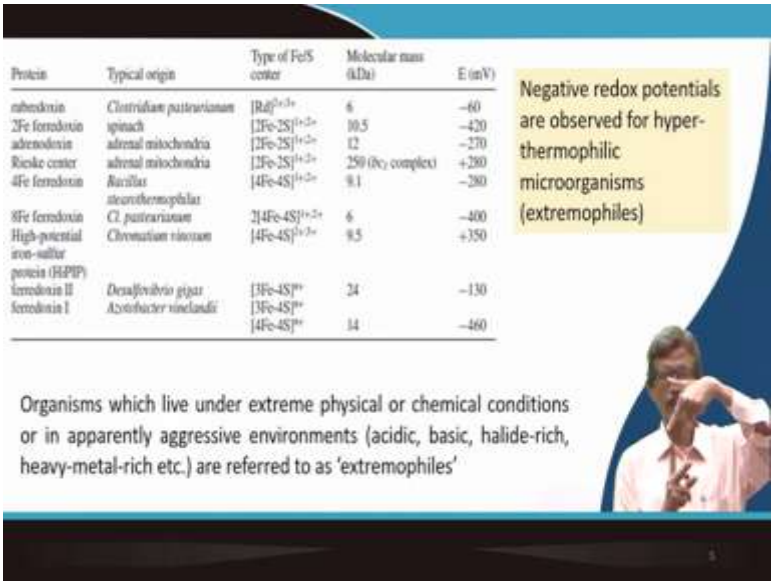

So, there are several organisms which live basically under extreme physical or chemical conditions and we call them as extremophiles because very drastic environment or aggressive environments what is written over there as highly acidic or the basic in the mines also, the acid mine drainages also or in basic condition sometimes very much highly halide rich that means chloride, bromide or fluoride rich and the heavy metal contamination is also there.

So, these organisms basically can survive if they are able to survive and if they can show some potential value for your iron centered electron transfer reaction that means the negative redox potential can also be observed for some hyper thermophilic microorganisms not in our body but also in some microorganisms which we consider or which we can classify as extremophiles because they can sustain the extreme environment.

There we find that starting from rubredoxin at the first entry to that of your ferrydoxine 1 in adiobacter vinalandi so you see the potential how much potential we can vary from minus 60 to minus 460 millivolt potential and in between you can have the rescue center which is there in the mitochondria adrenal mitochondria in our body also having a positive potential of plus 280 volt.

So, what we see now that the origin you can have the different types of proteins you can have and the cores are of similar type. When we talk about rubredoxin it will be the mononuclear iron sulfur protein having one iron center and four cysteine in sulfur group. So, all four are now

coming from the corresponding protein chain and which is coordinating the mononuclear iron side giving you the rubredoxin but you see the potential is only minus 60 millivolt.

So, rubredoxin in these two forms that means rd abbreviated as rd, rd 2 plus and 3 plus and molecular mass is also very less so it is a very short polypeptide chain. So, if you have a short polypeptide chain of only 6 kilo Dalton molecular weight so you will find that if you have the spiral type of thing so two of the cysteine is coming from the top and two are coming from the bottom and you have the spiral arrangement so you will be able to trap the iron center at the center of this particular loop.

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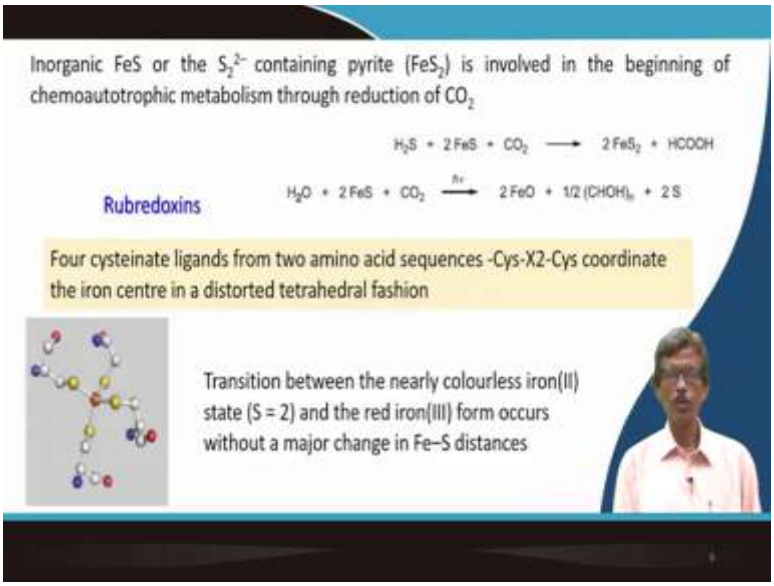

So, this potential is therefore very important and the corresponding reconstitution we can also be achieved like that of your inorganic iron sulphide where iron is in plus 2 and sulfur is in minus 2 state but sometimes the disulfide that means S2 2 minus only one charge per sulfur you see then FeS 2 iron pyrite we call so they are basically there as chemo autotrophic metabolism process so the reduction of Co2 and they are basically the source of iron as well as the different types of sulphide.

We are only talking about one type of sulfur that means the sulfide ion not that corresponding S2 2 minus but only S2 minus only. So, they are there so what are the reactions basically we can think of that ferrous sulphide can again further react with H2 S which is also plenty in that environment because you can have the corresponding sulfide ion and if acid is available the

proton is available it can react with that particular acid and give rise to the corresponding H2S production.

Similarly, that FeS can also be important in presence of your H nu also for the removal of the sulfur from the iron side and you can have the corresponding combination of the carbon material. So, the first example as I just now told you is your example for the rubredoxin and you have the four cysteine ligands and you have the cysteine residue and to x2 means two amino acid spacer.

So, if you have two amino acid spacer or x2 of that means that means you have one cysteine another cysteine and you have the spacer which is your x2. So, is basically functioning one half is functioning as a bidentate ligand and another half is the bi to another by dented ligand and that we all know that gives a very good tetrahedral arrangement around this particular iron side.

So, though we are showing that you have the separate cytidine residue but they are all connected from the top so when you go beyond this particular coordination site you can have the connectivity for these amino acid residues which are available for coordination to your Fe 2 plus.

So, what about this function whatever is the reactivity they are providing basically nearly colorless iron side because all we know about the ferrous ion in your typical iron salt the ferrous sulphate or the more salt we know friendly greenish in color but mostly it is nearly colorless in its color but when you oxidize it typically form the corresponding ferric ion because the sulfur is there and you can have the charge transfer transitions immediately such that the only the invisible spectra can identify in which oxidation state you are for the rubredoxin molecule.

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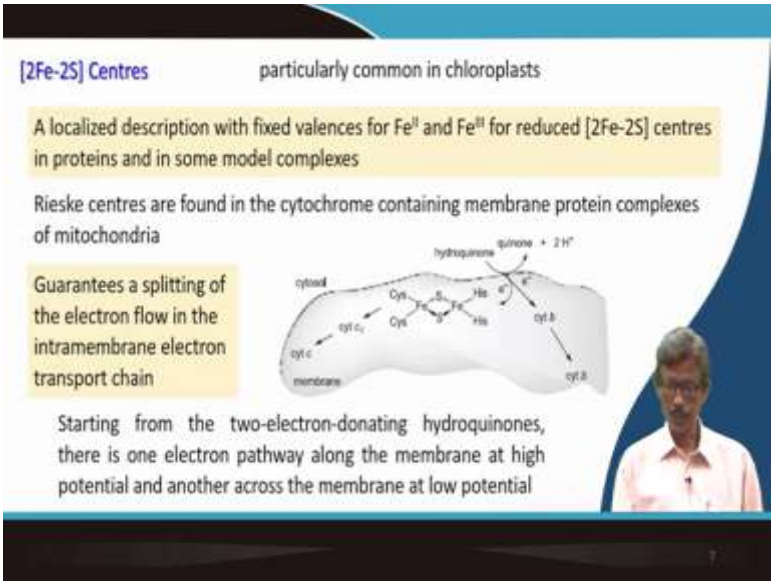

Then already we have seen how we get the 2 iron 2 sulfur system so we will just quickly go this particular part and we already seen that you can have a corresponding potential if you determine the potential in the chloroplasts. So, basically, whether you have a fixed balance state that means iron is in two state or another iron is in the ferric state when you go for oxidation of the ferrous-ferrous state or the di-ferrous state.

Is not like that a localized description can you can have but in most of the time is not a localized case for the protein environment is delocalized either you talk about the iron as 2.5, another iron is also 2.5 is very difficult to identify that which iron is your oxidized form and which iron is in the reduced form. Then we have seen that the example for the E0 value a positive potential value for the rieske center.

So, rieske centre is found in cytochromes containing membrane protein complexes of mitochondria. So, is basically it guarantees the splitting of the electron flow. So, we are talking about the electron flow in the mitochondria where you can have the intra membrane and the intra membrane electron transport chain. So, when it is there so you now connect where you have the corresponding iron sulfur ferredoxin molecule in between.

If you have the cytochrome c already we have seen that how we can talk about think about the cytochrome C to your cytochrome D. So, if you have this connectivity and in between you can have the hydroquinone converting to your quinone providing two electron transfer. So, that two

electron transfer is important from your hydroquinone giving quinone and two protons as well as two electrons.

Because if you are able to put those two electrons to your ferredoxin center and the right potential you can have such that you can accept those electrons to a diapheric 2 iron ferredoxin molecule immediately you will be able to reduce that to a di-ferrous state. So, then electron flow can take place depending upon your oxidation state whether it can go to the left side or it can go to the right side whether you have the oxidized form or the reduced form of this particular ferredoxin molecule.

So, you have the donating hydroquinone is there and now you can have one electron pathway along the membrane at high potential and another across the membrane at low potential. So, not only the two electron transfer can take place in one direction you can have one electron transfer in one direction another can be in the other direction. So, you have definitely a particular oxidation state of the ferredoxin molecule which will be useful for oxidizing one species at the left and reducing another species on the right.

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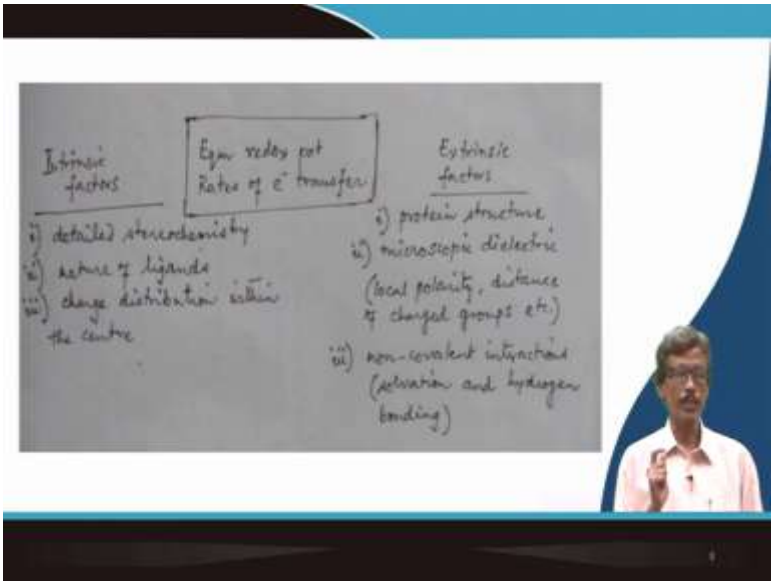

So, these things basically are determined by two quantities; one is the equilibrium redox potential, another is the rate of the electron transfer what we have seen in case of our cytochromes when we are talking about the cytochromes also. So, the extrinsic factors is the protein structure how good is your protein when you are provided with the cysteine residues.

Then the microscopic dielectric that means the local charge, polarity and the distances between the charge groups are the whether you have a positively charged part and a negatively charged species.

Then you can have the non-covalent interactions we all know that the secondary coordinate sphere interactions like your hydrogen bonding interactions where we always take the example for your nickel dmg complex. You have in the upper part you can have the corresponding hydrogen bonding interactions in your nickel dmg complex also.

Similarly; for a protein like complex structure, you can have also that particular system in your hand. Then the detailed stereochemistry nature of ligands and charge distribution within these centers are also important as your intrinsic factors.

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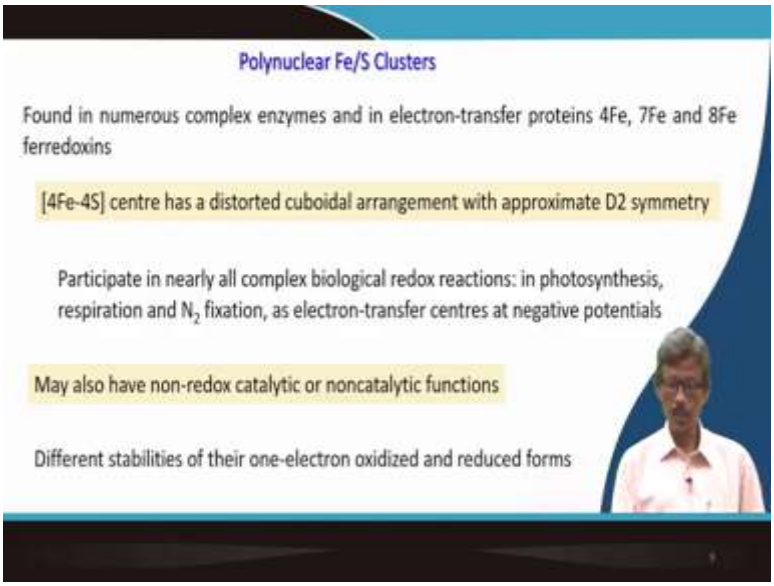

Then if we go for the polynuclear system polynuclear iron sulfur clusters how we get that. Numerous complex enzymes; so enzymes will be complex because your cluster is complex, starting from your 4 iron to 8 iron center how we get it so we already seen that you can have the 4 iron 4 sulfur center is a having a d2 symmetry not a tetrahedral symmetry because you have huge distortion.

Then you can have the nitrogen fixes also where you can have you see that the nitrogen can be trapped inside in some molybdenum base cofactor but which is again for its function dependent

on your iron sulfur proteins. But there are also which can be non-redox catalytic and non-catalytic also where you can you do not have the electron transfer reactions.

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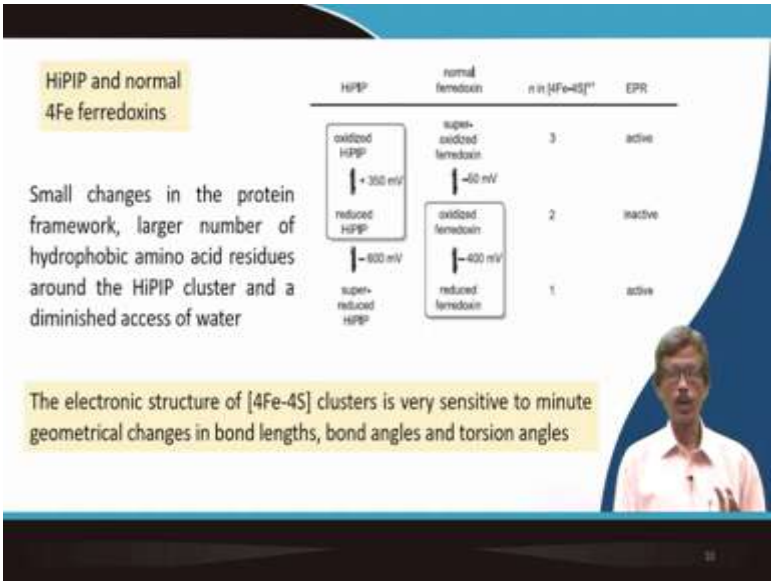

So, the different stabilities of this one electron oxidized form and the reduced form basically as important such that you can have a high potential and the normal 4 iron ferredoxin molecules. So, you can have one electron transfer for the high potential protein and one electron transfer for the low potential protein so these are the two accessible oxidation states what you can have depending upon your protein environment.

So, if you go for a small change in the protein framework or the protein environment your corresponding potential will change because you are exposing the hydrophobic part of the amino acid residues that means the polypeptide backbone for your high potential iron cluster iron protein cluster and a diminished access of water will also modify the corresponding E0 value. So, we can change the electronic structure by doing that corresponding typical structural reorganization then you can change the bond length, bond angles as well as the torsion angles.

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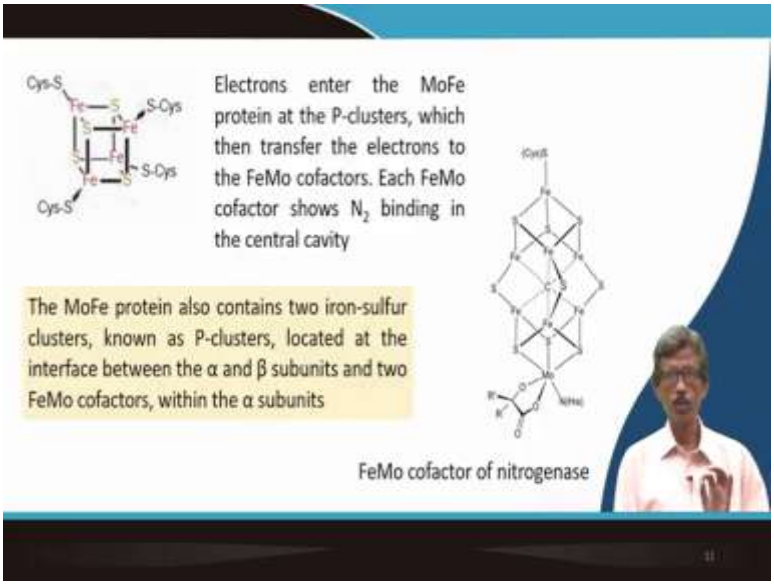

So, this is the very basic thing where you can have the 4 iron 4 sulfur proteins again utilizing the 4 cysteine sulfur residues what we are originally using for your rubredoxin molecule. So, you see how the self-assembly process can take place in the presence of your ferrous iron as well as sulfide anion because you can go for a bigger cofactor which is present in nitrogenous at the center you have the now the carbide which has recently been identified as the carbide ligand there where the center but that particular position can be occupied by your dinitrogen molecule also.

So, you can have p clusters this p cluster is important for your electron transport and then two sub units which are alpha beta sub units. So, we always know that these sub units are important and this iron molybdenum cofactor is important because of your nitrogen binding at the cavity.

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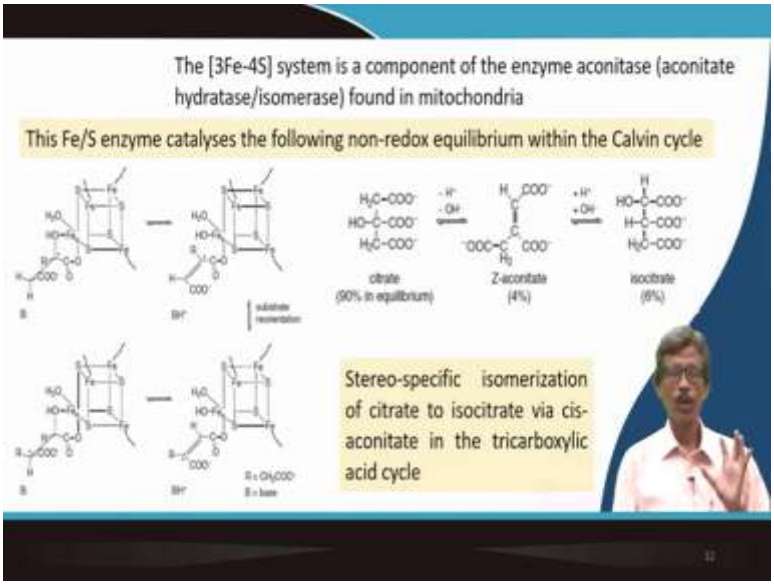

So, this particular 3 iron 4 sulfur system is the component of another example the last example what we are taking here now is that for the aconitase. So, is hydratase reaction that means is removal of some water molecule or hydrogen molecule from the system again addition of that such that you go for the isomeric product. So, non redox equilibrium you can have such that you can have a stereo specific isomerization between citrate and isocitrate which is important for our tricarboxylic acid cycle or kelvin cycle.

We know that what is kelvin cycle, so citrate is moving to isocitrate but here again the enzyme required is your iron sulfur protein 4 iron 4 sulfur protein. So, only one of the iron side which is not bound to your cysteine sulfur residue that is why you have 3 Fe 4 S system like that so one of the iron is basically coming afterwards and occupying that particular position and then your citrate group is also coming and binding to your system and then corresponding change the substrate reorientation.

Then the corresponding radical formation and then attachment of again the hydrogen dot or the hydrogen atom can take place such that you can reorganize these things such that you will end up at the end up you will be getting the isocitrate molecule.

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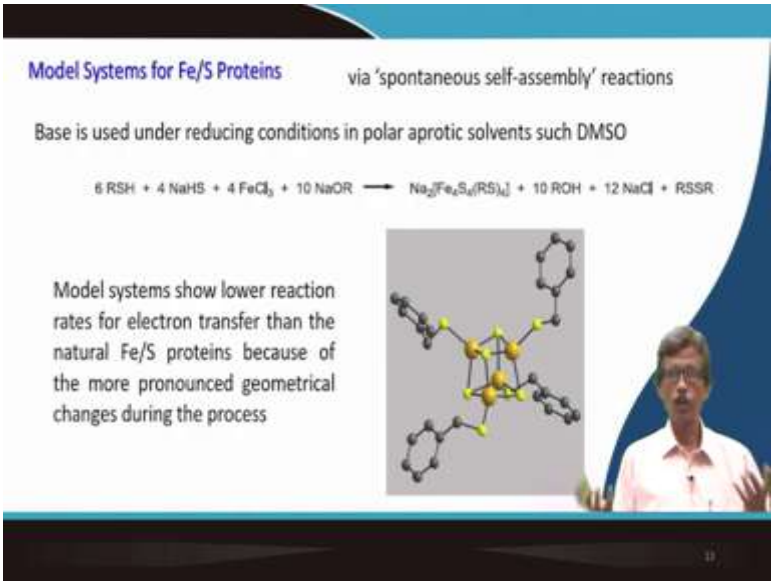

So, this is giving you the example for all these and we have already seen that how we can go for the model systems through extraction of the code from there or through some individual spontaneous self-assembly reactions by the ligand, the sulfur as well as the corresponding iron source.

If you take ferric chloride and RSH in presence of some NAHS you will be ending up with some salt which is a simple laboratory prepared model compound very much similar to that of your 4 iron 4 sulfur ferredoxin molecule. So, model systems we can have lower reaction rate we can study we can compare the properties the electronic structure, the final structure because the protein is not there your protein is substituted by some other ligand.

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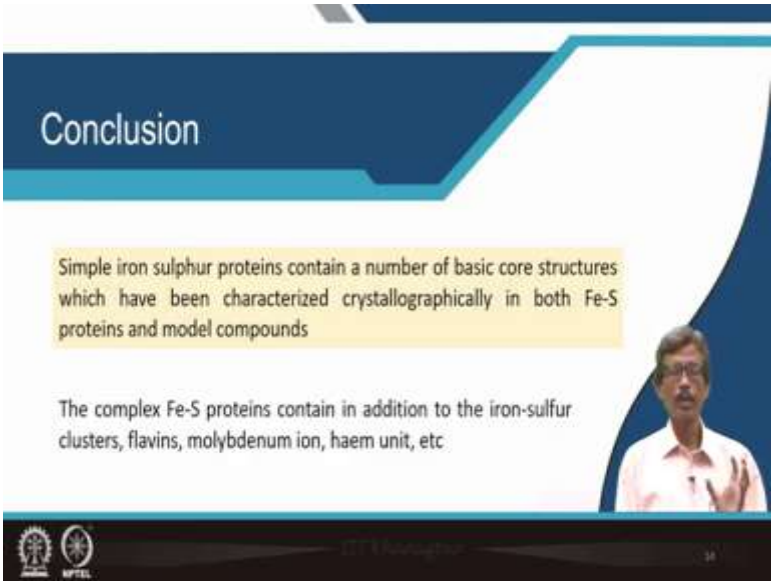

So, what we have seen so far that simple iron sulphide proteins contains number of basic core structures which can be characterized by crystallography and both the iron sulfur proteins and the model compounds we can compare such that when you move from the protein ligand system to our laboratory prepared artificial ligand system or simple organic molecule how much change is taking place such that you can have a new type of coordination chemistry can evolve out of these studies. And they also that iron sulfur proteins also contain not only iron sulfur but also flavins, we have seen molybdenum ions and the haem units.

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So, the Wikipedia page which you should search is your iron sulfur protein page and the book you should consult is the Robert Crichton’s book. Thank you very much for your attention.