Inorganic Chemistry of Life Principles & Properties

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Lecture – 27
Role of Iron in life – Electron transfer

Welcome you all to the next class on Inorganic Chemistry of Life Principles and Perspectives. In the previous 3 to 4 classes we have or maybe even 4, 5 classes we have been looking at aspects relevant to oxygen, storage by myoglobin oxygen transport by hemoglobin.

Then we compared with the arthropod mollusks hemocyanin and hemorythrin aspects. Then followed by that we look at the iron transport by the transferrin; then we also looked at the iron stories by ferritin and once you have the storage or we also looked at the releases the iron from the stored protein. So, these are the aspects that we learned in the previous class.

Now, let us look at electron transport or electron transfer or electron passage kind of a phenomena, because this is absolutely important for most of the reactions either the electron is given electron is taken out which is carried by some enzymes. So, therefore, these are called electrons transport enzymes, of which we will look at iron case. We all we have electron transport enzymes based on iron we also have based on copper etcetera, but now in this particular topic we will look at those enzymes which are based on the iron.

So, when it comes to iron as I have already talked to you earlier iron is there in heme enzymes iron is there in non-heme enzymes, ok. So, we will have the electron transport phenomena explained taking an example of iron with a heme enzymes, I will also take examples where the iron the electron transfer is done by iron enzymes without having the heme which is called iron sulfur proteins.

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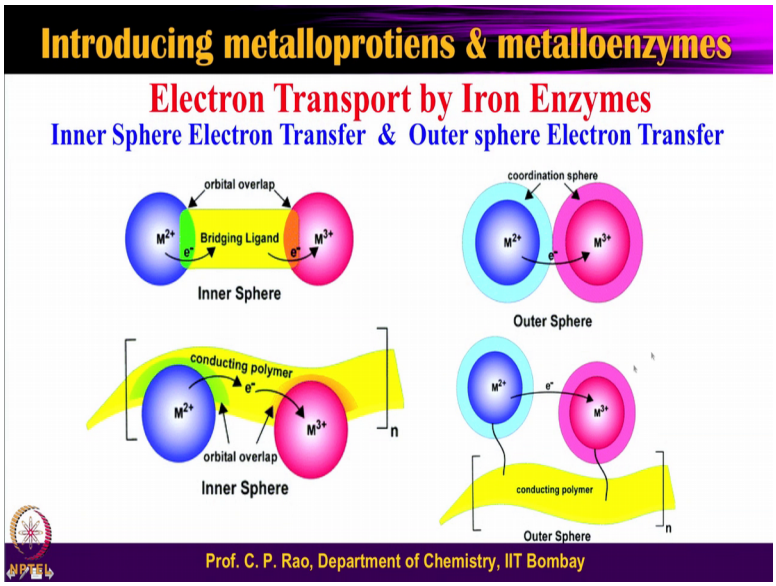

Let us look at what is in electron transfer what are the different processes. So, electron transfer is transferring an electron from a donor to an acceptor that is what is electron transfer is all about. Now so, let us look at this can happen by two means, one is called the inner sphere, other is called the outer sphere. So, let us look at what is inner sphere what we mean by that and what we mean by outer sphere.

Let us take the two systems here one is an M 2 plus it can be an ion it can be a coordination sphere it can be a complex and an M 3 plus is another complex. So, let us say the electron going from iron 2 plus to the M 3 plus complex then M 2 plus becomes M 3 plus and M 3 plus becomes M 2 plus and if this happens through a bridge ligand, so this bridge ligand will bring a overlap of orbitals between the donor on the left side and the acceptor on the right side, ok. So, the donor means electron donor acceptor means electron acceptor.

So, if such an electron if an electron transfer occurs through such a process it is called the inner sphere. What you can also have between the donor and acceptor, you can have a conducting medium and the conducting medium might act like a bridging ligand and therefore, the electron transfer takes place. So, all the figures that are shown on the left side in this particular slide corresponds to the electron transfer by inner sphere mechanism.

Now, what is outer sphere? Come to the right side you have one of the complex another complex, complex will have some ligands the ligand will have some pi kind of a cloud thing that is shown over here in the green portion, and here shown by the pink portion.

So, it is the overlap of the pi cloud of this donor complex with the pi cloud of the acceptor center and if that electron transfer takes place through that then you can call it as an outer sphere kind of a mechanism. Or you can also have some conducting medium conducting medium will overlap on one side with the donor, and the other side with the acceptor and allows by the kind of a electron transfer.

So, in either case you have a mostly it is a pi cloud of the complex of the donor with that of the complex of the acceptor overlapping and allowing the electron transfer or a medium where the pi cloud overlapping with the acceptor donor as well as with the acceptor. So, therefore, in effect that what we are trying to understand is electron transfer happening between the donor and acceptor is either bridge by a bridging ligand or through a kind of an outer sphere overlap. So, things can happen.

So, what all this communicate? It communicates something to do with the donor, something to do with the acceptor that means, their potentials and the medium how this is connected. So, therefore, we will come to that just in a while. Let us look at this electron transfer having said it goes from the donor which is shown by a bit orangish color and acceptor bit less oranges or more yellowish color.

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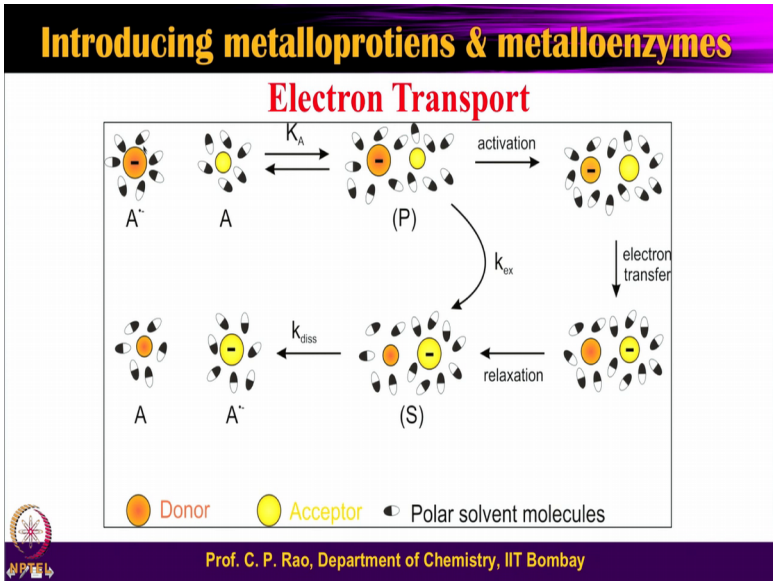

So, you have a donor, which is surrounded by the solvent and or ligands you can call it as and the acceptor which is surrounded by solvent or a ligands. So, now, you have a donor, acceptor and come in closer or forming a some kind of a complex. So, this complex is still we can say in the ground state. And this complex in the complex the donor and acceptor are very close in proximity therefore, this complexation itself can induce the electron transfer process.

So, if the electron transfer process takes place the donor will give away the electron acceptor will take the electron. So, the donor will lose the electron acceptor will gain the electron then you can see that it is made.

And now we have a complex which is the donor acceptor complex where the donor is oxidized and the acceptor is reduced and that is the complex what you have which is called S. So, the initial complex is called P the later complex is called S and this S complex has to break down back to this the donor and into the acceptor kind of a mode. And now the electron is lost from here is oxidized portion reduced portion. So, this is process is complete.

You can also have the ground state complex make get into a activated complex or transition state complex or active complex. How will it happen? It can happen by some change in the conformation, change in the structure of this particular ground state complex.

So, the ground state complex can undergo some conformational change a structural change and become activated complex and instead of having the electron transfer in the ground state the electron transfer would take in the activated complex. Now, this donor will give away the electron and donor gets oxidized and the acceptor accepts a electron and acceptor gets reduced.

Now, you have a different complex or activated complex and this can you know sort of rearrange back to a conformational state which is called the relaxation and then breaks down into this. So, you can see either from the ground state you can get a electron transfer or from an activated complex you can take electron.

So, you can have some kind of an activation through the through the some conformational changes relaxation through the other kinds of conformational changes.

So, now, we understand the electron transfer can happen I have written here is the solvent molecules, but you can take it as a coordination complex also or in an enzyme it can be the close proximity of the metal center that is also possible. So, you can take as a simple ion with the with the solvent molecules or a complex with the ligand molecules or protein where the protein metal ion is surrounded by the amino acids or heme centers, ok.

Now, if that is the case how do we visualize this? So, let us look at the visualization.

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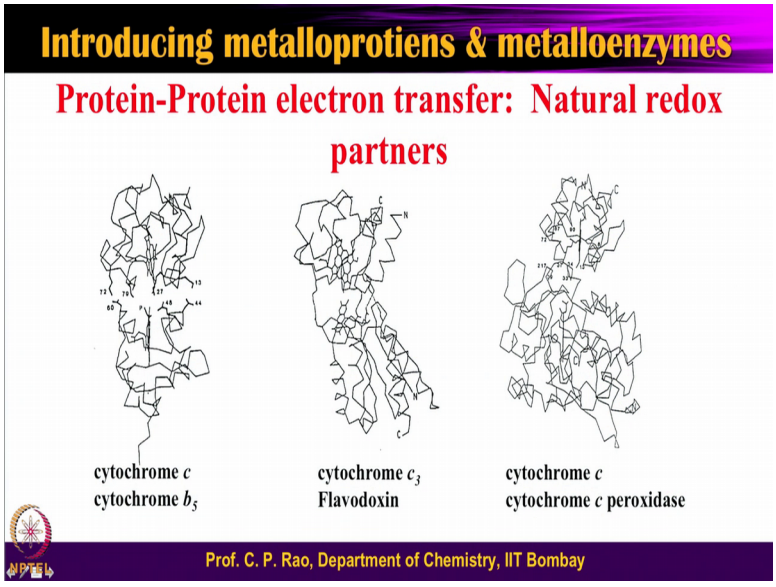

Let us take some natural partners. Now, we have gone from a conceptual level to a conceptual level where the two proteins, one protein act acting like a donor other protein acting like a acceptor now that is what we call it is a natural redox partners. So, redox partner means redox process partner is donor and acceptor.

Take this example, it has two components there is one protein in the top there is one protein in the bottom, ok. Now, these two proteins come closer and form a complex. So, what are these proteins? It is also written here one is cytochrome c, other cytochrome b 5. I will come bit later stage what is cytochrome c, where it is cytochrome b 5 do not be worried at all at this stage.

Now, these two form a complex and you could see this is the cytochrome c, it can be 5 and this is the region and you can see the region here is the heme and the region here is

the one which is containing that acceptance. So, the donor center heme acceptor center over here and so therefore, this region is the region which is important if the electron transfer should take place from this guy to this particular guy, ok.

So, and in the activated complex there will be some kind of reorganization, reorientation, the conformational change so that they come closer and they have a proper medium for electron transfer to take place. We can see another example too. So, you have a cytochrome c 3 and a flavodoxin, so the flavin moiety here on cytochrome c 3.

So, let us take this as a donor, this is an acceptor, this is one protein and this is the other protein, there are two different proteins are there. And they come closer and form a complex and this is the region where the protein electron transfer takes place. So, it is important. We can take another example cytochrome c and cytochrome c peroxidase or cytochrome c oxidase these kind of thing. So, you have a heme from cytochrome c, and you have a region here. So, this is the region which is important because this region should allow the electron transfer.

So, we have seen two proteins coming closer, one protein is a donor other protein is an acceptor they form some kind of a complex and this complex can go into activated stage through the some kind of a conformational changes. And now the complex is ready for electron transfer and electron transfer should be going through the kind of a medium that we have here. And then the donor will give the electron the acceptor will take up the accept a electron like the one which is explained in the previous two slides. So, it is exactly.

So, now I have shown some examples how the natural examples, how the enzymes will come closer, and form a kind of a complex this region is called the docked region, docked, docking region, so the region of docked region in this.

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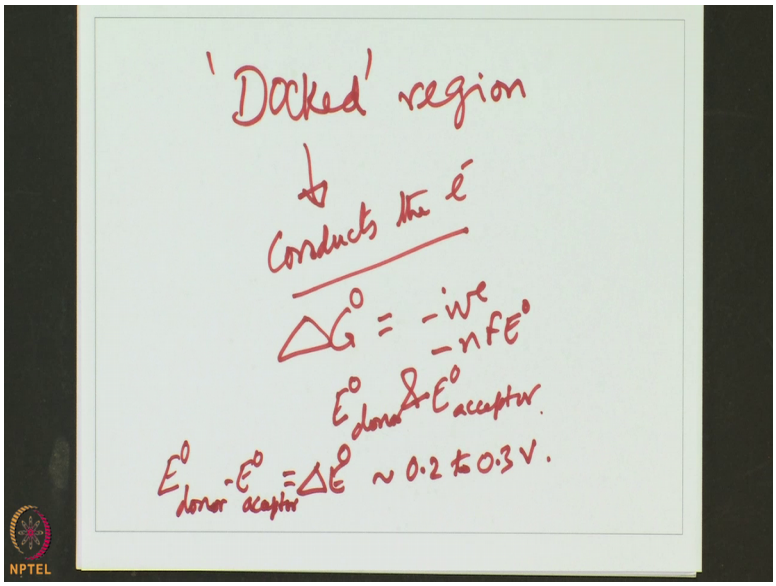

So, the two enzymes coming closer and you have the docked region. So, this docked region is important because this is the region which allows or conducts the electron. So, therefore, the properties of this docked region is important, between the two redox partners or two redox enzyme partners here, ok.

Now, we will next couple of slides let us look at some kind of thermodynamic parameters even the kinetic parameters of the electron transfer if it were to take place, ok. What are the factors that dry is the electron transfer? How does the potential energy curves look like?

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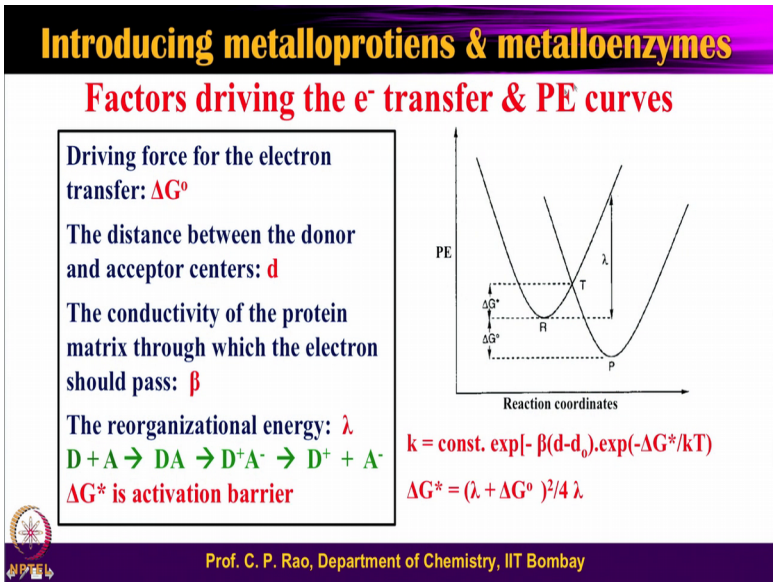

So, how will the electron transfer takes place? Obviously, electron transfer takes place from the thermodynamic considerations, thermodynamic consideration is nothing, but delta 0 and this is the one which is a driving factor. So, and if it is negative and it is spontaneous so, therefore, electron transfer takes place for that particular thing; So, this will be minus n FE naught, so therefore, negative or positive.

And this also depends on of course, this is what does this depend on this depends on the donor E naught of donor, E naught of acceptor and etcetera. So, therefore, it depends on the potential of the donor, potential of the acceptor very very essential and important. And it also depends on the a donor center to acceptor center distance which is shown as d. And the third factor is as I told you earlier there is a docked region in the docked region is there is in where the electron is conducting obviously, the medium conductivity is also important.

So, and then I told you when the two proteins come closer or two complexes come closer there will be some kind of a reconfirmation, reorganization, re-structural features happening. And that what is the expenditure that is energy that is required for such a thing to happen. And that is re-organization energy which is shown as a delta, ok.

So, you have a delta G naught which tells you whether the redox potentials of the donor and acceptor difference is good enough, because generally the redox potential difference is delta of E naught around 0.2 to 0.3 volts is good enough if a large then there the

reversibility is lost thermodynamic reversibility is not being found. So, therefore, that will not give a good redox couple.

So, to have a good redox process you should have the difference in the redox potentials of the donor versus the acceptor that is the winner in your 0.2 to 0.3. So, this is nothing, but E naught of donor minus E naught of acceptor and this is what we are referring to. So, I hope you understand that.

So, that means, in turn it depends on the redox potential of the donor, redox potentials the acceptor of course, the difference and how far they are donor to acceptor centers?. And what is the medium is a medium? Is good connecting not good connecting? And what is the energy required for reorientation?

So, all of these parameters this I have already explained donor acceptor, simple donor acceptor complex, and then it may be activated complex and then electronic transfer from donor and accepted by the acceptor and then those two separated. And this obviously, has an activation barrier. So, this activation barrier is dependent on what?

The activation barrier is dependent on the reorganizational energy and the delta G naught which is the driving force, ok. So, therefore, the formula is given lambda plus delta G naught whole square by 4 hundred lambda. So, therefore, the d is the activation barrier is also explained over here. So, therefore, rate of the electron transfer k is some constant forget about what exactly exponential of minus beta d minus d naught into exponential minus delta G star by kT.

So, d minus d naught is the actual distance between the two partners, the donor and acceptor in the ground state versus the donor and acceptor when it goes to the activated complex. So, that difference is the one which is what you have initial complex versus the complex that is formed in the activated that different. So, the distance should be smaller is good and the conductivity should be better is good and the lambda smaller is better. So, these kind of things will favor.

Now, let us look at the potential energy curve. So, if you look at the potential energy curve that you can see the potential energy versus the reaction coordinates or refers to the reactant profile. These are all obviously, we know that these are electron potential energy curves. So, these are basically the parabolas and this is for the product curve.

Now, let us see this reactant to the product difference in the y axis is the delta G naught, and this is the this will tell you the driving force whether the electron transfer is favorable or not favorable is understood from the delta G naught.

Now, from this the reactant where it has to climb, there is a cross section between the potential energy curve of the reactant and potential energy curve of the product there is a crossing point. So, this crossing point tells you the complex the ground state complex need to be activated prior to the electron transfer reaction taking place. So, therefore, the T here is the transition state or the activated complex and this has some energy and this shown over here delta G star.

So, delta G star is activation barrier or activation energy you can call either way activation energy activation barrier. So, the greater this value is a lower the reaction rate the catalytic rate, or the electron transfer rate. So, smaller is the better of course, in this one so that means, more energy transformation.

And what exactly in the lambda reorganization is? You take from these ground electronic state to the corresponding vibrational state corresponding to the product and that is the reorganization energy and this much of the reorganize. So, therefore, it is depends upon the conductivity, it depends upon the potential of the donor and acceptor, it depends upon the distance between the donor and acceptor, it is depends upon the reorganizational energy and depends upon the conductivity of the medium absolutely these are the points that you have to look at.

Now, let us look at I told you the smaller will have a greater rate etcetera. So, therefore, let us look at the cases where you have a the rate of the reaction the rate of the reaction versus the delta G naught. So, therefore, we can try to look at this particular comparison.

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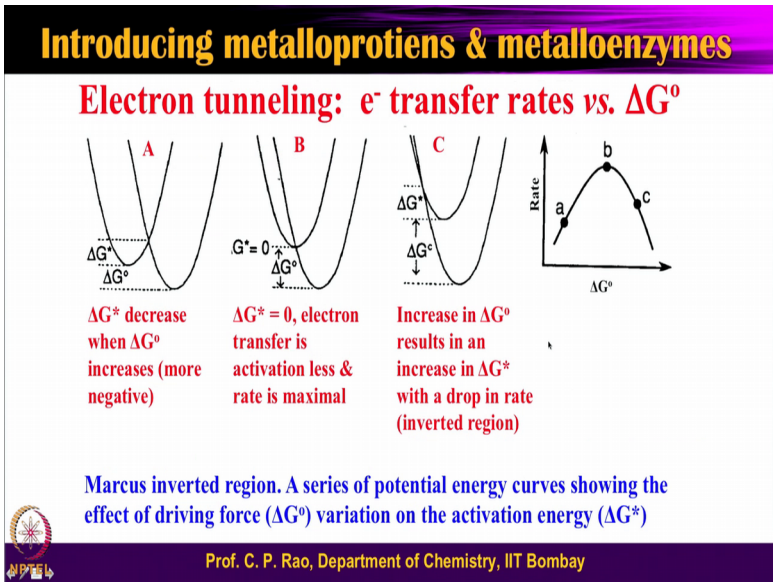

Now, here you see this is the delta G naught and this is the delta G star, ok. So, delta G star decrease when delta G naught increases because activation becomes less, and that will be the more negative and this will give let us say a rate like in a here. This rate is what? Electron transfer rate; What is this rate? Electron transfer rate is here, let us assume that that is there.

Now, let us club these two overlay so that the product curve is exactly at the center on the bottom of this particular reactant curve that means, the ground state itself is a transition state over itself is a activated complex. In other words the electronic transition straight goes into the activated complex and does not require any additional energy therefore, delta G star is 0, delta G star is 0. So, electron transfer is there is no activation barrier. So, in other words activation less so the rate should increase and you see that is going and it is a maximal it is the highest you cannot have any other thing.

Now, they take the third possibility this third possibility is it does interact, but not at this point, but it is some other point. So, this is the product curve this is a reactant curve and this is. So, this particular difference is increased. So, the delta G naught is now increased and delta G star is a in decreased. So, as I told you delta G star decreasing should give the reaction rate increase, but in this case because the delta G is not itself is going. So, increase in delta G naught again results in an increase in the delta G star with a drop in the rate, so this drop in the rate.

So, the rate of the reaction is lower and when delta G star is 0 goes up again goes down, so it will go like inverted region for this. So, this is referred as a Marcus inverted region. So, the driving force delta G naught and delta G star how does that determine so that means, you have an optimal or maximum energy electron transfer rate and either case you will have a lower electron transfer rates in this.

I think this is tells us that the one is that the two protein should come closer the donor part of the one protein acceptor part of the protein should come closer this will form a kind of a docked region you should make a complex. And this docked region should reorient, rearrange, reorganize into your complex of effective way where the electron transfer will take place. When I tell some example using this then you will understand better and that is where the whole system is involved.

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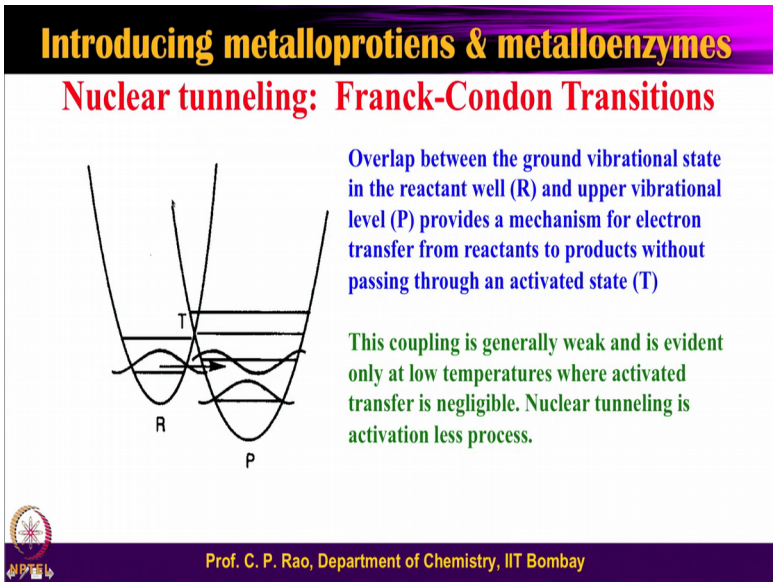

Now, let us look at the electron transfer when you say it electron transfer we always should be reminded of is something called Franck-Condon principle. What is the Franck-Condon principle in the Franck-Condon transitions?

So, you talk about the vertical transitions that is happening that is during the electron transition there is no nuclear coordinates moving or change in the nuclear coordinates. So, that is what is called the vertical transitions of that, ok. So, the overlap between the ground vibrational state in the reactant well and the upper vibration level provides a

mechanism for electron transfer from reactants to the products without passing through an activated state.

So, you can see that the vibrational state these are the excited vibrational state of the ground electronic to this one and this is matching with the product vibrational state which are higher. So, therefore, there is a direct transfer going to which is basically a kind of a nuclear tunneling kind of a process.

So, this kind of thing is generally not so strong, this kind of a coupling is very weak and this is for mostly at the low temperatures where the activated transfer is negligible. So, nuclear tunneling is activation less kind of a process. So, other cases you always have the activation barrier of this.

Now, this is what the basic I try to build for an electron transfer from a simple complex to your protein the protein docking versus their protein electron transfer things.

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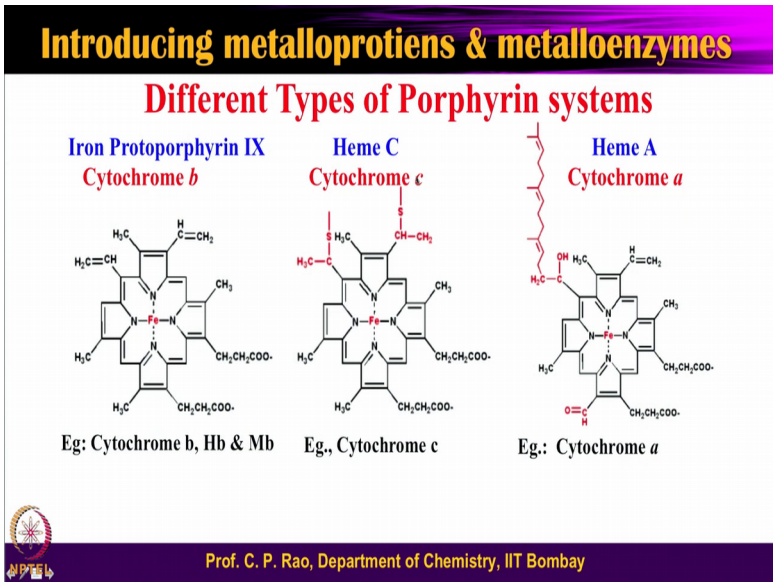

Now, let us look at examples for the case of some enzymes enzymes we take first the heme containing enzymes. I told you earlier when it came cytochrome b, cytochrome c I said I will explain you later and you can see those kind of things here. Cytochrome b, cytochrome c, cytochrome a etcetera what is the difference in this? The difference is some kind of a substitutions, nothing inside substitutions. So, here you have the muffles two and then the ethylene kind of a bridge.

Here you have S bridge. So, the thioether bridge with the thioether and that is connected to the protein that is connected, here it is not connected to the protein this part of it. Here this part of it is modified and connect with the protein and here this part is connected modified by this and then connected to the protein, ok. So, therefore, you have a one kind of a heme, another kind of a heme, another kind of a heme. Examples etcetera are given here where they are present.

So, why the nature has chosen like some modifications here, some modifications here, some modifications here? Any guess for that? That is reflected in the redox potential of the center of the iron.

So, therefore, the redox potential of this iron in this case we are different from the redox potential of the iron in this case, will be different from the redox potential of this iron in this case. And the redox potential is also influenced by protein that is surrounding the. So, one is by the kind of a deodorization you have other is by the influence of the protein. So, both together will influence the redox potentials.

So, redox potentials may become more negative, redox potentials may become more positive. So, we will come to that discussions in a while in that and so these are the kinds of things that we have in the proteins.

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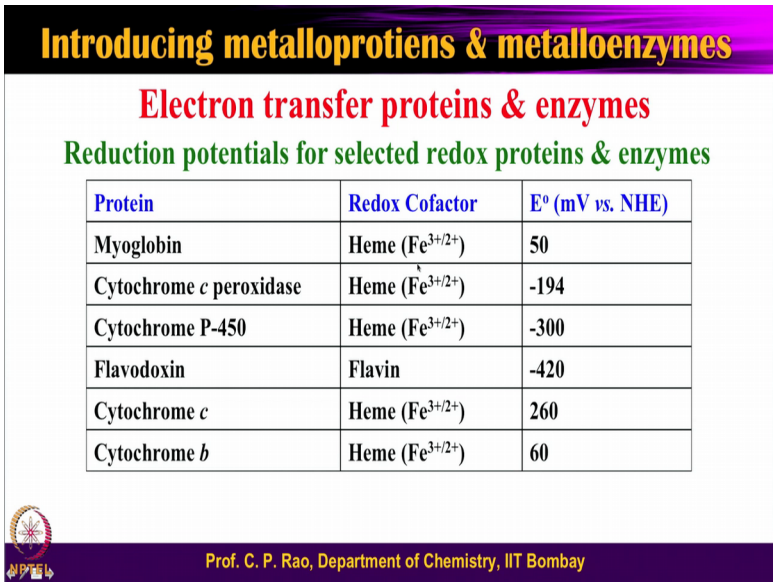

Let us look at some examples values of these redox potentials particularly in heme enzymes. Say myoglobin I mentioned to you that the there is a heme cytochrome b type of heme is there. So, you will have a redox potential of plus 50 millivolts.

You go to the cytochrome c, peroxidase minus 194, cytochrome p 450, you have the minus 300. The terminology of this will be explained later, the term why P-450 etcetera. Flavodoxin, flavin is the center minus 420, cytochrome c plus 260, cytochrome b plus 60, etcetera. So, all of these except this flavodoxin all of these are heme containing enzymes for a while you can keep this aside.

So that means, you have proteins with minus 300 and you have proteins plus there is a 260, 300. So, there is a window region of about 600 or more millivolts difference in the heme proteins itself. As I told you the iron center redox potential is modulated by the derivatization on the heme as well as the protein that is surrounding and that is why they go from minus 300 to plus 3 00 etcetera, etcetera.

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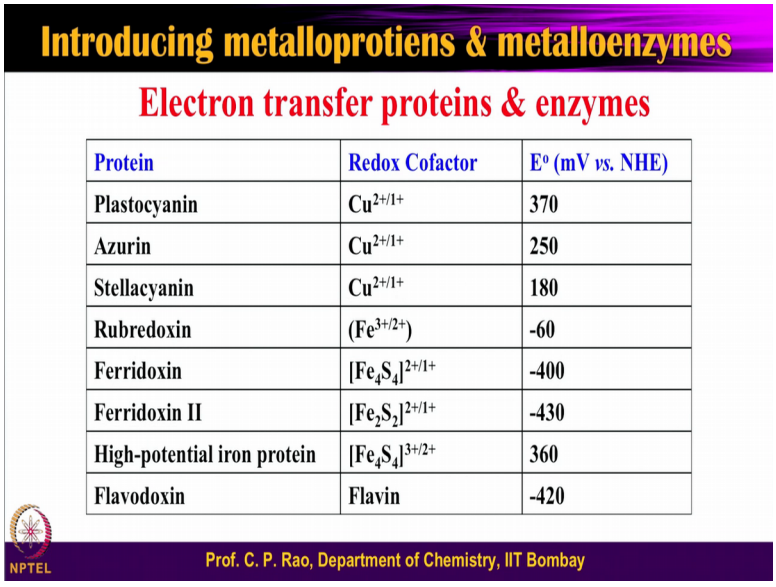

And it is true not only in the heme enzymes even if you take non-heme enzymes. Let us take some examples in this. First let us look at these bottom 1 2 3 4 5, and 1 2 3 4 the rubredoxin and ferridoxin, ferridoxin II, high potential iron protein, see minus 60, minus 400, minus 430, plus 360. The difference is around 800 millivolts. So, this is non-heme iron sulfur proteins. So, there is, so different protein here also what is bound to the iron

and what is the protein. So, both the thing that is bound to iron as well as the protein chain will be changing the redox potentials of this.

So, therefore, nature has chosen different kinds of heme derivatives different different kinds of non-heme derivatives where the electron transfer can takes place and it covers a large range of potential minus 400 to plus 400 millivolts.

We can also look at I will come to this much later stage copper. There are copper enzymes as I mentioned having different kinds of redox potentials. Then flavin will have minus 420. So, you can see that there is a lot of variation in this. So, I told you minus 400 to plus 400 around that vicinity around 800 millivolts or so.

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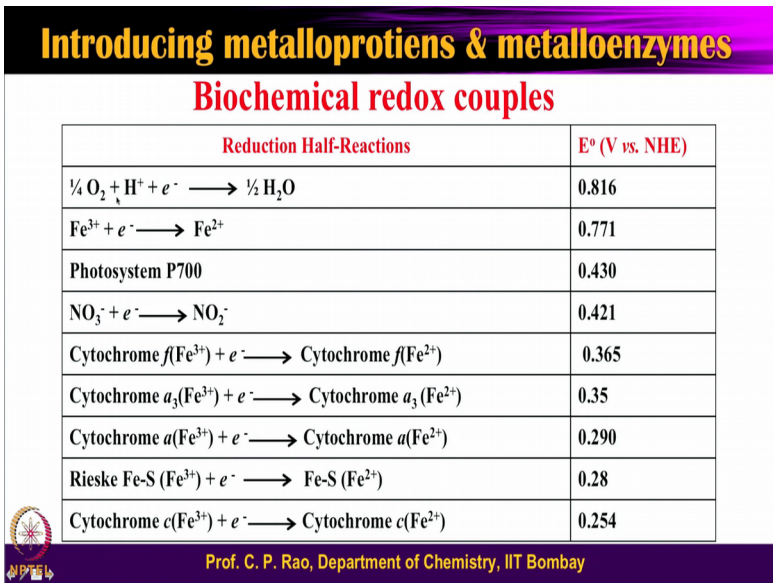

You can see some reactions oxygen reaction reduction to water oxygen reaction reduction to water is around 0.8 volts or 800 millivolts iron 3 plus to iron 2 plus is around 0.8, ok. And photosystem does not worry, nitrate to nitrite around 0.4 volt.

So, variety of cytochromes, going from iron 3 to iron 2, iron 3 to iron 2, iron 3 to iron 2 and they are all in the range of 0.36, 0.35, 0.29, 0.28 etcetera, cytochrome 0.25. So, you can see cytochromes see with little difference in it is range it goes from 0.25 to around 0.35, 0.36 kind of a potential.

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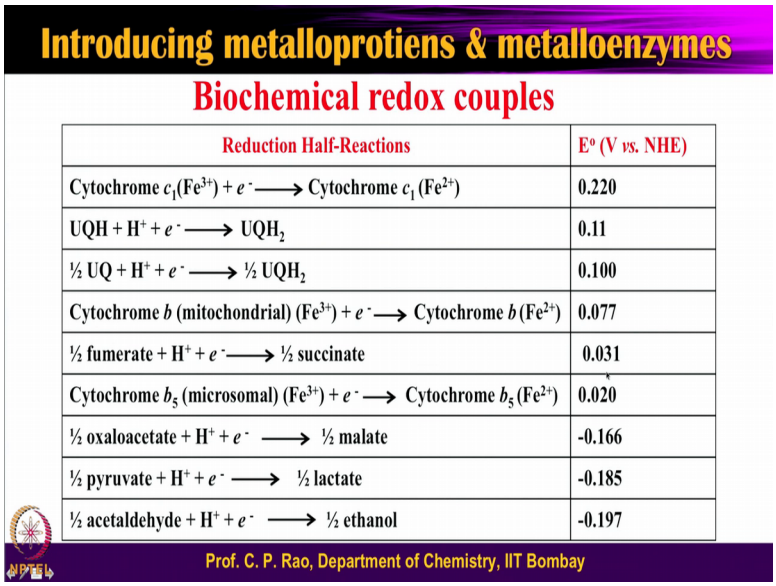

Reduction Half-Reactions	E^o (V *vs.* NHE)
Cytochrome $c_1(Fe^{3+}) + e^- \longrightarrow$ Cytochrome $c_1(Fe^{2+})$	0.220
$UQH + H^+ + e^- \longrightarrow UQH_2$	0.11
$\frac{1}{2}$ UQ + $H^+ + e^- \longrightarrow \frac{1}{2} UQH_2$	0.100
Cytochrome *b* (mitochondrial) $(Fe^{3+}) + e^- \longrightarrow$ Cytochrome *b* (Fe^{2+})	0.077
$\frac{1}{2}$ fumerate + $H^+ + e^- \longrightarrow \frac{1}{2}$ succinate	0.031
Cytochrome b_5 (microsomal) $(Fe^{3+}) + e^- \longrightarrow$ Cytochrome $b_5(Fe^{2+})$	0.020
$\frac{1}{2}$ oxaloacetate + $H^+ + e^- \longrightarrow \frac{1}{2}$ malate	-0.166
$\frac{1}{2}$ pyruvate + $H^+ + e^- \longrightarrow \frac{1}{2}$ lactate	-0.185
$\frac{1}{2}$ acetaldehyde + $H^+ + e^- \longrightarrow \frac{1}{2}$ ethanol	-0.197

And there are many other reactions which require positive reaction of potential. There are many reactions which require negative potentials minus 0.1,6 minus 0.18, minus 0.19. So, you can see 0.2 minus 0.3.

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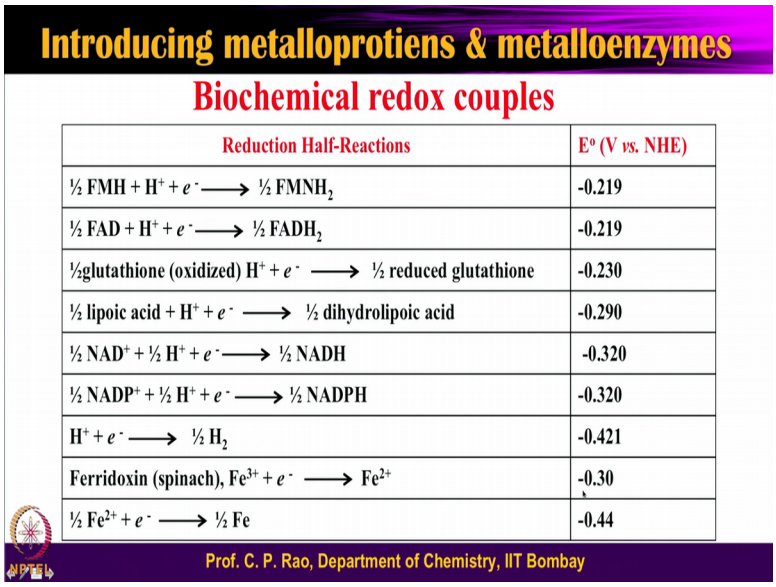

Reduction Half-Reactions	E^o (V *vs.* NHE)
$\frac{1}{2}$ FMH + $H^+ + e^- \longrightarrow \frac{1}{2} FMNH_2$	-0.219
$\frac{1}{2}$ FAD + $H^+ + e^- \longrightarrow \frac{1}{2} FADH_2$	-0.219
$\frac{1}{2}$glutathione (oxidized) $H^+ + e^- \longrightarrow \frac{1}{2}$ reduced glutathione	-0.230
$\frac{1}{2}$ lipoic acid + $H^+ + e^- \longrightarrow \frac{1}{2}$ dihydrolipoic acid	-0.290
$\frac{1}{2}$ $NAD^+ + \frac{1}{2} H^+ + e^- \longrightarrow \frac{1}{2}$ NADH	-0.320
$\frac{1}{2}$ $NADP^+ + \frac{1}{2} H^+ + e^- \longrightarrow \frac{1}{2}$ NADPH	-0.320
$H^+ + e^- \longrightarrow \frac{1}{2} H_2$	-0.421
Ferridoxin (spinach), $Fe^{3+} + e^- \longrightarrow Fe^{2+}$	-0.30
$\frac{1}{2}$ $Fe^{2+} + e^- \longrightarrow \frac{1}{2}$ Fe	-0.44

Now, you have seen a range of potentials going from plus 0.82 about minus 0.4 or so,. So, you have so many kind of a different potential range and you have seen the potentials that are there for these proteins are also from minus 400 to plus 400 even more so that

means, the proteins are capable of doing these reactions because their reaction potentials are also in the same range.

So, that is what I have explained you the basic concepts of the electron transfer and how it could happen in the protein protein. And some redox potentials, how these electron transfer proteins are spanning across the so many potential ranges etcetera.

So, I will in the next class I will get into some example both on the heme and non-heme and explain the mechanism of this, ok. So, wait for the next class.

Thank you very much.