Metals in Biology
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Lecture – 06
Electron Transfer (ET) in living systems

Hello welcome back to Metals in Biology. Today, we will discuss electron transfer in living systems and the book to follow is Principles of Bioinorganic Chemistry by Lippard and Berg. So, lot of schemes, figures are taken from this book and also the lecture notes of professor Lippard ok.

So, as you know, electron transfer is required to be happening in number of cases in our biological system. All over biological system 1 electron, 2 electrons, 3 electrons or even 4 electron processes are required. At a time only 1 electron transfer is usually preferred well without electron transfer certain catalytic cycle cannot be completed. So, therefore, electron the simplest reagent I would say plays a key role in many biological processes.

Electron transfer as well as proton transfer usually they are coupled together and that is how they control the redox potential. Often we see that there are metals involved into these electron transfer processes.

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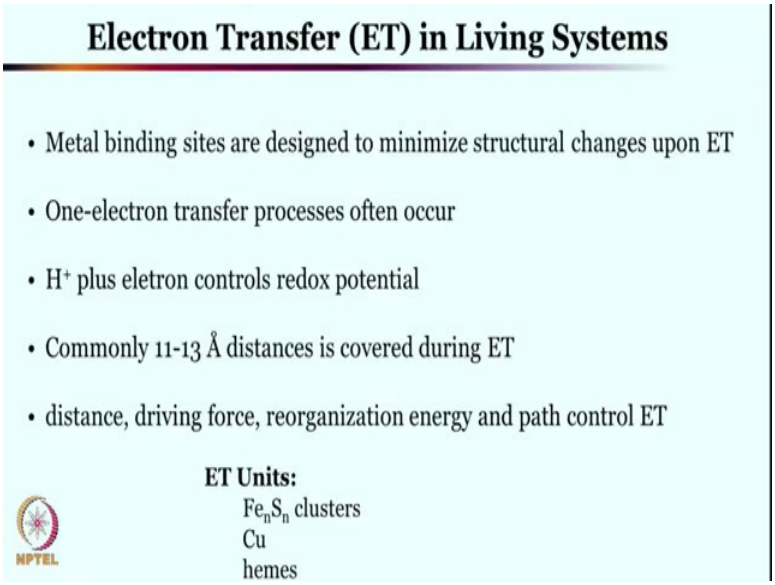

One of the major criteria that we will see today for the metal center containing electron transfer site is simply before and after electron transfer, there should not be too much reorganizational energy. So, the energy of the system before electron transfer and after electron transfer will remain almost constant.

So, therefore, metal binding sites are designed in such a way so, that they can minimize structural changes upon electron transfer. As I mentioned 1 electron transfer processes often occurs so, if let us say you need a multiple electron for a given system, 1 electron at a time will be transferred not 2 electrons 3 electrons or 4 electrons at a time will be transferred ok. So, it is going to be a stepwise electron transfer processes for the multi electron processes.

Well electron transfer can happen through bond or through space. In biological system often it is up to 11 to 13 angstrom distance can be covered for the for the electron transfer processes ok. Of course, larger electron transfer or longer electron transfer distance can be also possible, we might will not be discussing those too much, but it is also possible to transfer electron over long distances much more than 11 to 13 angstrom.

A number of parameters is controlling the electron transfer rate, that includes the distance between the origin and the delivery site; the driving force, reorganizational energy and the path by which the electron transfer happening. So, once again the distance between the donor and acceptor, the driving force and the reorganizational energy before and after electron transfer of course, the pathway by which it is going or it is happening that also will also vary.

Today mainly we try to keep it very brief on the electron transfer processes on the iron sulfur clusters, copper centers as well as the hemes centers. So, we will see a number of iron sulfur clusters are present for the electron transfer site or as a electron transfer site. Similarly copper centers can also participate in electron transfer. Of course, these are all going to be the redox active metal center and that is why they are participating in the electron transfer processes.

We can also have heme iron center participating just as electron transfer processes. One of the common thing for these electron transfer centers is they are not directly participating into the main reaction or the main process. If it is a synthetic transformation they are not actually involved into that except they just provide that electron ok. If it is

just the electron transfer, then only these species come into the picture otherwise they are not really involved too much of the synthetic chemistry or the chemical transformation that happens in the biological system these are only electron transfer site.

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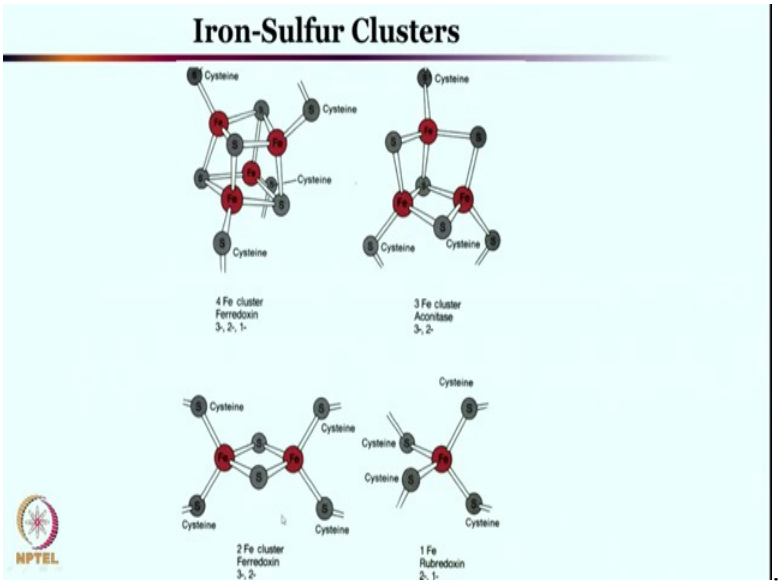

Let us look at some of the iron sulfur clusters. Well these are the most popular one, these are include these includes mononuclear iron center, dinuclear iron center, 3 iron center and 4 iron center. So, these clusters can be named in different ways; this is rubredoxin, this is ferredoxin which has 2 iron cluster between them it is bridged by sulfide as you can see over here for rubredoxin 1 iron center these are thiolate or cysteine bound iron center and for these cases iron is getting oxidized to iron 3 and it is settling between iron 2 and 3 for the electron transfer processes.

For these cases, these are two different iron centers and bridged by 2 sulfide of course the terminal ligands are also sulfur containing cysteine residue of the protein backbone. If you look at this one this is one of the age of the cubane is missing, you have 1 2 3 iron center bridged by the 4 sulfide unit 1, 2, 3 and 4. Each of the iron center is also supported by the cysteine thiolate or S minus center. So, overall these are quite fascinating center as well. So, we have finally, 4 iron center bridged by the sulphide and also supported by the cysteine ok.

So, this 4 iron cluster center also known as ferredoxin, 3 iron cluster center also known as aconitase and these are different overall charges that can they can have during and

after the electron transfer processes. Just one thing, you must have noticed that these are very solid and rigid structures, not too much is going wrong in this system. We will see that in a moment why these are so, effective for the electron transfer processes.

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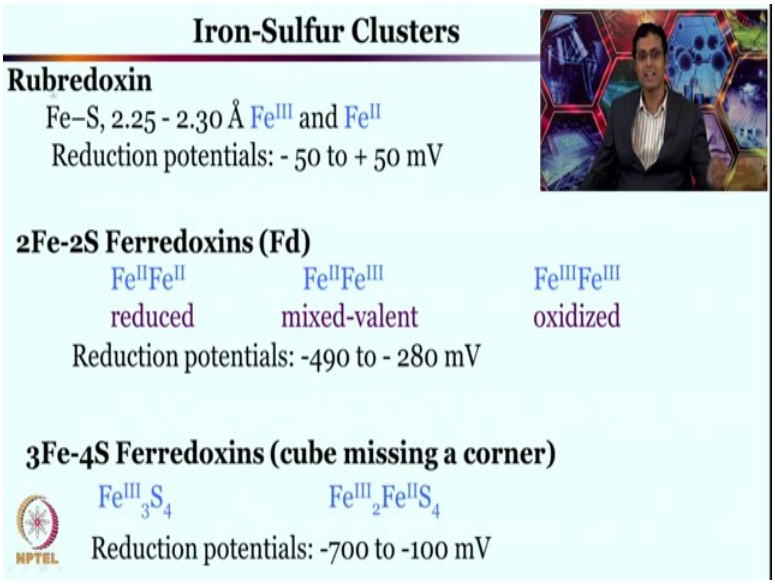

Well before getting into that let me discuss briefly on the rubredoxin, which is a mono iron center you have 1 iron and once 1 iron sulfur distance these are S coming from this cysteine moiety iron sulfur distant any of these we are looking at, the bond distance is usually 2.25 to 2.30 angstrom and we are looking for the oxidized and the reduced form these are the 2 form by which the electron transfers are happening. After electron transfer from this site it gets oxidized to iron 3 and once again it accepts 1 electron and result in iron 2 plus formation reduction potential is in the range of minus 50 to 50 millivolt for this short of rubredoxin system.

So, whenever these reduction potential matches and if these centers are available, then these centers can actually provide one electron to the delivery center or the acceptor to the acceptor. As we were discussing there are 2 iron 2 sulfur center which are known as ferredoxin, now these the reduced form of the ferredoxin will contain iron 2 plus and iron 2 plus this is fully reduced form and the fully oxidized form would be iron 3 plus and iron 3 plus. Obviously, there is a state in between these reduced and oxidized form where one of the iron is in plus 2 state and another is in plus 3 step. So, this is for

ferredoxin, reduction potential for these processes vary from minus 490 to minus 280 millivolt in this reduction potential range these iron sulfur clusters are operative.

We have seen another one this cube missing corner 3 iron 4 sulfur ferredoxin, you have 3 iron 3 plus centers 3 plus centers along with the S 4 S 4 unit and as you can imagine that these center can be reduced further, this is completely oxidized form and this can be reduced to iron 3 2 and iron 2 S 4. So, one of the iron is getting reduced to iron 2 plus reduction potential for this for this system varies from minus 700 to minus 100 milli volt.

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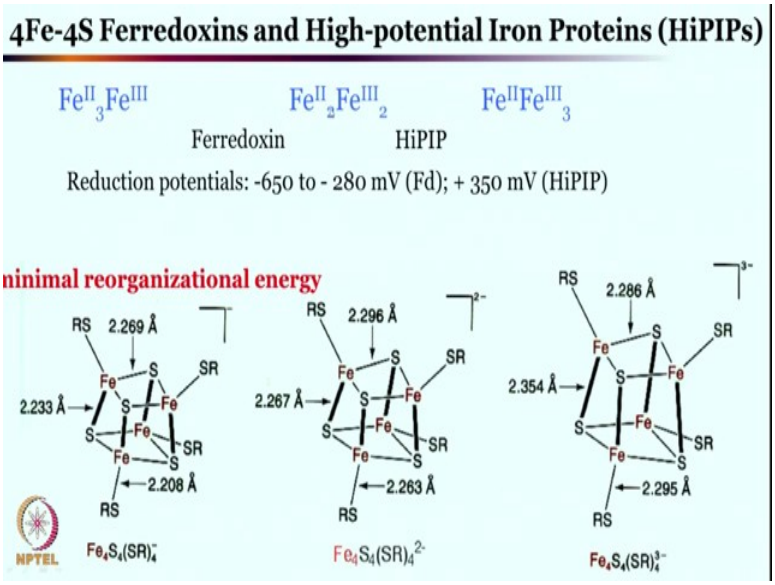

We have seen 4 iron 4 sulfur also and that is over here, that is also known as ferredoxin and these are also high potential iron proteins and these settles between that 2 sorry 3 iron 2 plus state and 1 iron 3 plus state. It can be oxidized to 2 of them 2 of them being in iron 2 plus and 2 of them in iron 3 plus further oxidation of one of these iron 2 plus leads to only 1 iron 2 plus form being formed as your large iron 3 plus 3 of them is remaining ok.

So, these are the iron sulfur clusters which are participating in the electron transfer processes and their reduction potential varies from minus 60 minus 650 to minus 280 millivolt region and this is the range where these 4 iron 4 sulfur cluster occurs.

But most importantly I think we must realize that why this sort of cluster any of those clusters are very effective for the electron transfer process and that is precisely due to the

fact that before and after electron transfer, there is minimum reorganizational energy involved during this process. So, before and after electron transfer things remain as much same as possible.

For instance if you see this is Fe 4 S 4 SR 4 minus and in these cases as you can see this is overall 1 minus charge if you add one more electron to this system. So, overall you get 2 minus charge; if you add one more electron to the system overall, you get 3 minus charge. So, 1 minus 2 minus 3 minus effectively these centers remained same.

So, one more electron addition to these leads to this compound, one more electron addition to this compound leads to this compound. But irrespective of what electron transfer is happening you see this iron sulfur bond just to pick up one of them these are having crystal structure all 3 of them. And this is this distance is iron sulfur distances be being noted as 2.233 angstrom whereas, after 1 electron reduction this distance become 2.267 angstrom which is essentially meaning that this iron sulfur distance really did not change at all or nothing you cannot really say that there is any change, and from there on. If you add within one more electron these 2.267 angstrom distance between iron and sulfur changes to only 2.354 angstrom.

So, virtually these iron sulfur distance remain constant throughout the process and therefore, despite these electron transfer processing processes happening in here, there is very little reorganizational energy that is required from transforming one species into other.

So, this is once again one of the key phenomenon for the electron transfer processes and electron transfer centers which are nothing, but metal of enzymes, but these metal of enzymes remained so, solid and so, well organized that that electron transfer processes does not bother them too much. So, it remains a completely reversible process and they are able to do these chemistry effortlessly and that is what counts a lot ok. In often in nature the processes are so, efficient and so, simple that that synthetic chemist cannot even really think show so, lightly about these processes ok.

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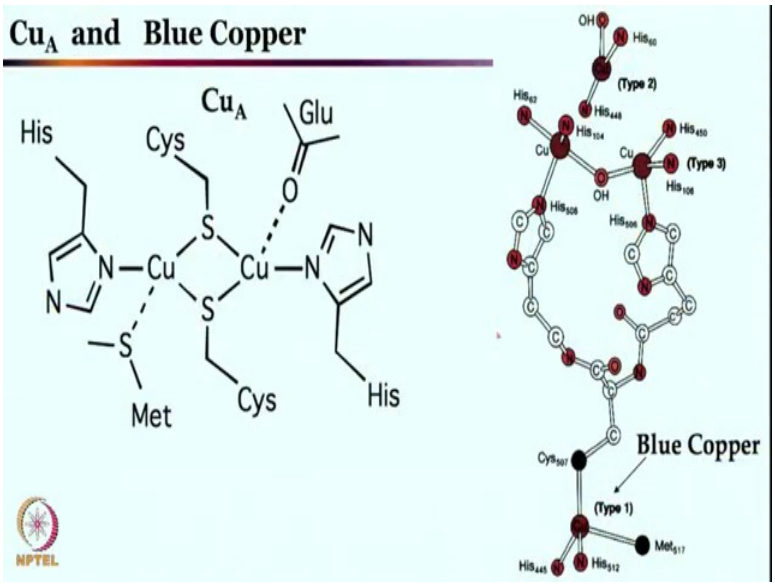

Well, we have other centers. So, far you have seen the iron sulfur clusters being the electron transfer site, but then its not limited, electron transfer is not limited to the iron sulfur cluster there are many other centers. For example, there is this copper A center, just buildup of copper no iron sulfur over here just copper and sulfur as you can see each of the copper is having a cysteine sulfur linkage and they are the bridging one.

These are the bridging one between the 2 copper center and one of the terminal is once again methionine which is a copper sulfur bond, and the copper pa copper ba or glycine in intermediate also over there, as you can see each of them are also at attached with histidine moiety. Overall it is a dimeric copper center which is which is bridged by the cysteine moiety 2 cysteine moiety and before once again before and after electron transfer this remains pretty much the same.

So, the core of the structure did not change at all during and before and after the electron transfer processes ok. Not only these die copper containing copper A centers are responsible for the electron transfer processes, there are other centers where also we can see that the major activity or the only activity they carry out is the is that of an electron transfer. Another, the series of copper species or another type of copper species is called blue copper that you can see over here. Over here in the blue copper which is also known as type one copper center and these are having 2 histidine and 1 methionine and 1 cysteine ligation and the copper center.

So, this is tetra coordinated copper center and that is over here as you can see it is going to be tetrahedral in nature. So, this is blue copper center that is particularly because these complexes copper 2 complexes copper sulphur charge transfer absorption are quite strong and these charge transfer copper sulphate results charge transfer is giving rise to the blue color of these species ok.

This is the active site of ascorbate oxidase here not only one copper center you have other total 3 copper centers are involved, 2 of them are the bridging one which are bridged by the hydroxyl, these 2 copper center each of them are having 3 histidine in them and they are exchanging or communicating the spin through the hydroxy. So, the EPR spectrum of these actually become EPR silent due to the super exchange right.

Now, in the ferromagnetic coupling right these are these are coupled through coupled these 2 copper center are coupled through anti ferromagnetic exchange and therefore, the EPR becomes silent and in addition to the type 1. So, these are called type 3 copper centers which are bridge with each other or bridge and communicated with communicating with each other there is yet another type of copper center which is known as the type 2 copper.

Here you have 2 histidine and 1 OH coordination from the from the protein backbone. Like overall then it is a 3 different type of types of copper overall total 4 copper; these 2 are same this is different this is different. So, ascorbate oxidase is quite an interesting enzyme, you see 3 different types of copper center and over all 4 copper centers are there. It is also known as multicopper oxidases. So, these are capable of converting oxygen into water that is fascinating, we will see in some classes later that oxygen to water is one of the most fascinating reaction known in the domain of biological and bio inorganic chemistry and this chemistry this oxygen to water transformation chemistry is quite complicated with these with these copper centers. There remained controversy in this area there are no generalized mechanism and that tendency can be supported by this ascorbate oxidase so far.

So, much more study is required to get the details about the process wherein oxygen is converted into water by utilizing this copper center. Obviously, there are other metal law enzymes which are also capable of converting oxygen into water one such spaces that is

known so, far or one such center that is known so far is methanemonooxygenase. We will discuss that later ok.

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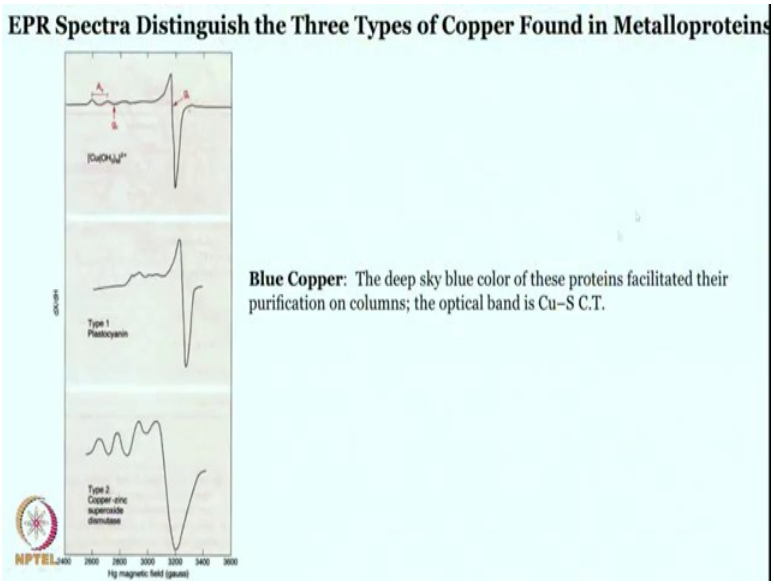

Moving on; so, as you have seen that these copper centers are distinct. So, this is cop EPR spectra for copper hexaaqua complex and there is this type 1 copper that is for plastocyanin. This is type 2 copper centers which are for copper zinc superoxide dumi dismutase mainly observed the type 1 copper. So, far you have seen shown these blue copper centers which are tetra coordinated as you have seen over there, these are having very distinct copper EPR as you can see over here. These three with types of copper can be very easily distinguishable by the EPR spectroscopy. As I was mentioning this is for the blue copper, blue copper centre that is the type 1 copper center over here and type 3 is EPR silent and type 2 is the one we have shown over here.

Now, this blue copper piece species also are very very active in the UV-visible spectra, where as strong absorption speak is observed and which gives rise to the blue color of this copper center and by a by these characteristics blue color. One can easily pretty easily isolate this compound by simple column chromatography technique ok.

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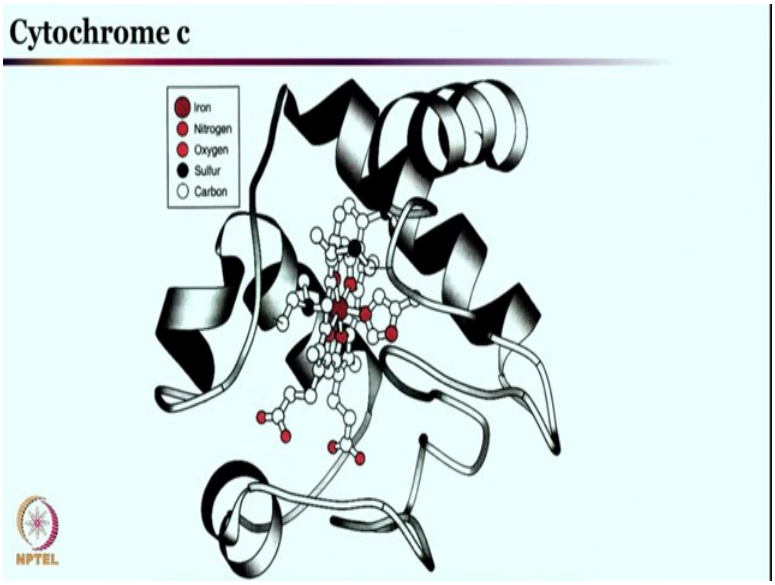

Moving on, it is not only limited to the iron sulfur cluster the electron transfer processes I mean. Electron transfer processes as you have seen are predominantly controlled by the iron sulfur cluster, but there is also the copper center as you also have seen the copper A site and the blue copper site and a and again one of the fascinating center for the for electron transfer processes nothing else just the electron transfer processes in cytochrome C. Just to remind you this cytochrome-C is completely different ka compared to cytochrome C oxidase which we will see later. The cytochrome C oxidase is the enzyme which participates in converting oxygen to water also, but then that is some for the discussion for some other day.

Cytochrome C. This cytochrome C has only one in heme iron center and their axial ligands are methionine and histidine, these 2 ligands are axially attached with this heme iron center as you can see over here. So, the porphyrin heme, iron in the middle from one axial site it is the methylene and from the other axial site, it is the histidine that is bound with it. This is coordinatively saturated and this is why perhaps why it cannot react with oxygen. It does not react with anything it is just acting as a stationary center for the electron transfer processes; if the iron center gets oxidized and reduced that is it. So, iron 2 plus and iron 3 plus for the electron transfer processes.

So, in these centers all the these centers we have discussed so, far iron sulfur cluster, copper di copper center and the di copper cop center known as the copper a as well as the

blue copper centers all and the cytochrome C all of them are capable of transferring one electron at a time and that is what they do contribute towards the active chemistry or active site chemistry of a given metal or enzyme, that they that these are linked with. Of course, these electron transfer sites are linked with a bigger transformation or bigger processes whenever or wherever that is happening.

If you are looking at carefully these centers are going to be a low spin center ok. So, you have a heme iron center and the 2 ligands are there.

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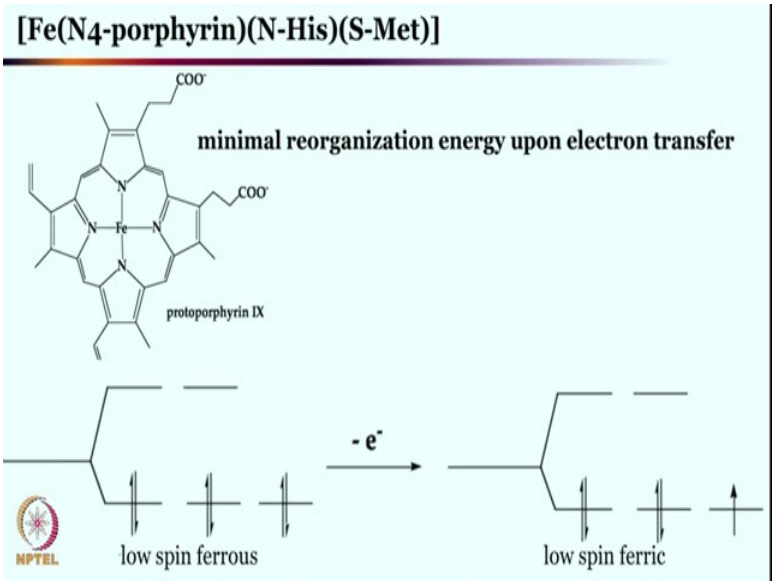

So, it is a hexa coordinated heme center. If you if you once again notice that these are also designed in such a way so, that so, that the energy upon electron transfer remains almost reorganized. So, these remain minimum or these minimum reorganization energy upon electron transfer essentially drives them for the desired electron transfer process ok.

So, there is there is the drawing for the protoporphyrin 9 for your these heme iron centers, as you can see the these are also having 2 axial centers as we have seen in the in the last slide, where we see that a methylene and histidine is linked. So, this methylene and histidine linked iron center will be nothing, but the low spin. So, this is a very good ligand porphyrin itself is a very good ligand, but in addition there is methylene and histidine which are strong field ligand all of them put together, it would be a low spin iron complex low spin iron 2 plus complex it is a iron 2 plus is a d6 electronic configuration.

So, t2g6 2 2 electron each if you are transferring an electron from these systems. So, iron 2 plus is ox getting oxidized to iron 3 plus that would be to be low spin ferric, overall then it is going to be t2g5 it is a low spin and therefore, you see that that this electron remains in the t2g level there is no transfer or transfer of electron from the eg level and therefore, the change in the size or the overall reorganization energy is rather minimum for this short of centers.

Once again these can only act as one electron transfer processes at a time or these can participate in one electron transfer processes at a time, and the main key important things to remember that they have the they have been evolved in such a way so, that the so, that and they minimize that the organizes an energy upon electron transfer ok.

So, to sum up for this for this class today, I hope you able to see that there are many different electron transfer side depending on the need and the reduction potential that is required for a given transformation. We have seen different various iron sulfur cluster let us say for at least 4 different type of iron sulfur cluster, you have seen which is participating in the electron transfer processes. There are 1 iron sulfur center one 2 iron sulfur center and 3 iron sulfur center as and the 4 iron sulfur centers.

These structure as you have seen in the case of the Cubane structure for the 4 iron 4 sulfur cluster, the crystal structure clearly shows that before and after electron transfer there is essentially nothing changing for this for this cluster and therefore, this rock solid character of this site before and after electron transfer make them more suitable for these processes, there is no reorganization almost no reorganizational energy reorganizational energy required for these processes and making them feasible making the electron transfer feasible without much hassle.

Not only the iron sulfur cluster you have just seen the porphyrin iron center ligated with 2 ligand such as histidine and the methylamine is also capable of transferring electron, this center is called cytochrome C in addition to that there is just copper or copper only system such as copper A and the blue copper center, which are having characteristic UV-visible and EPR spectra nonetheless these are capable of transferring one electron at a time and these are these are pretty good pretty good electron transfer side and they are very much valued in the active site chemistry that we will see in the subsequent classes.

Keep studying and once again the main book to follow would be Lippard and Berg you can read from any other book of your choice, professor Kiams book is also great. Please do keep studying from different chapters of these books we will see you soon.

Thank you very much.