

Inorganic Chemistry of Life Principles & Properties
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Lecture - 38
Role of Copper in life - General perspectives

Welcome you to the next class in the Inorganic Chemistry of Life Principles and Perspectives. In the last three classes, we have looked at the enzymes or based on the nickel which really contributed to the life genesis itself going from a carbon monoxide atmosphere which is reducing atmosphere to that of the one what we enjoy today.

Now, we move on to next set of enzymes. So, enzymes based on the copper.

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Introducing metalloproteins & metalloenzymes

**Biological Inorganic Chemistry of
Copper**

Copper enzymes

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So, let us look at the biological inorganic chemistry of the copper; copper enzymes.

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Introducing metalloproteins & metalloenzymes		
Main Classes of Copper Proteins		
Proteins	Where Found	Biological Function
“Blue” electron carriers Azurin, Plastocyanin Stellacyanin, Ume cyanin	Algae, green leaves and other plants	Electron Transfer (Photosynthesis)
“Blue” Oxidases (reducing O_2 to H_2O) Laccase	Tree, Fungal	Oxidation of Phenols and diamines
Ceruloplasmin	Human, animal serum	Weak oxidase activity Fe and Cu transport
Ascorbate Oxidase	Plants	Oxidation of L- Ascorbic acid
Superoxide dismutase	Red blood cells	O_2^- detoxification
Cytochrome c oxidase	Mitochondria	Terminal oxidase

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Before we go more into the details of the copper enzymes, their functions, let us look at a bit information on the classes; various classes of these copper proteins or copper enzymes, one of the major class of this particular copper proteins is called Blue Copper proteins and these Blue Copper proteins because they are blue in color. I will explain in a while why they are in blue color and the main function of these proteins is the electron transfer. The variety of such things are there like Azurin, Plastocyanin, etcetera, etcetera, I will come back to that in a while.

So, they are found in Algae, green leaves, plants, many kinds of systems that we have and then we also have another set of enzymes, class of enzymes called Blue Oxidizes. These Blue Oxidizes contain one of these Blue electron transfer protein plus some oxidizing center as well. So, these are there ok. So, both of these; so, these are like Laccase, like Ceruloplasmin, aspo ascorbic Ascorbate Oxidase, etcetera. So, these are found in fungal, animal, human, plants, all kinds of things are there.

So, these have got one of them is the electron transfer, blue protein where the blue color is coming from and then the redox center for the other part of it. So, this can be involved in a rea variety of reactions oxidations of phenol and ascorbic acid many of these things ok.

So, and some of them are also involved in the transport phenomena too. We will come to that little later. Let us see another class of enzymes of copper which are referred as

copper based superoxide dismutase and we have studied several times, the Superoxide dismutase enzymes; the main function is to remove the O_2^- which is superoxide. So, detoxifying the superoxide these are present in the red blood cells and you see would see that this is a di bi metallic enzyme with one copper and one zinc where the copper is a functional, zinc is non functional, rather structure, we will get into all of those, then we also have another class of proteins; copper proteins where Cytochrome-C oxidase which is obviously, Mitochondrial one and this is nothing, but Terminal oxidase of this.

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Introducing metalloproteins & metalloenzymes

Main Classes of Copper Proteins

Proteins	Where Found	Biological Function
“Non Blue” Oxidases (reducing O_2 to H_2O_2) Amine Oxidase Galactose Oxidase	Most animals	Elastin, Collagen formation
Oxygen Carrier Hemocyanin	Molluscs and arthropods	Oxygen Transport
Copper monooxygenases Phenol o-monoxygenase (Tyrosinase) Dopamine β -Hydroxylase	Animal skin, Insects and plants Adrenals	Tyrosine oxidation pigment (melanin) Converts dopamine to norepinephrine
Copper Dioxygenases Quercetinase	Fungal	Quercetin oxidative cleavage,

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Besides these, we also have non blue oxidizers. That means there is no Blue Copper protein present in this, and these are called Non Blue Copper oxidizes. This reduces O_2 to H_2O_2 and this Amine Oxidase Galactose Oxidase, these are some of the examples of the Non Blue Oxidizes.

So, this means that they do not have the blue colored centers that were there for the earlier case. These are found in animal molds, etcetera. So, and they are involved in the collagen formation, Elastin formation, oxidizing the Galactose. So, many of these kind of reactions come to another class of proteins which is the Oxygen Carrier. We have already seen the Oxygen Carrier proteins earlier and we have also combined and compared between the Hemoglobin and Hemocyanin. So, there we have seen a di copper center, these are involved in oxygen transport and these are present in the Molluscs and

arthropods and we have said at the time because of the presence of these ones, the their blood is blue and we looked at all these; when we were talking about the oxygen transport by the by the by the protein of Hemoglobin systems and we compared as well.

So, and you also have like in the iron monooxygenase and the Dioxygenase monooxygenase. So, that will add only one oxygen and the dioxygen will add both the dioxygens are the O₂ and some of the corresponding things are shown here Tyrosine Oxidation and it will give some form of the oxidized which will further convert into melanin. So, dopamine to norepinephrine; so, these are this is happens in the brain of the human and the for Dioxygenase Querceti oxidative cleavage these are present in the fungal.

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Several other copper enzymes

Copper Enzyme	Biological Function
Aminoacid oxidase	Deamination of primary amines
Catechol oxidase	Synthesis of melanin
Dopamine-β-monooxygenase	Noradrenaline synthesis
Protein-lysine 6-oxidase	Collagen and elastin cross-linking
Peptidylglycine monooxygenase	α-Amidation of neuropeptides
Lysyl oxidase	Strengthens connective tissues
Metallothionein	Radical scavenging, metal transport

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So, now, we have seen a large number of different kind of enzymes having Blue Copper protein. It is simple electron transfer; electron transfer with oxidase properties, then we have seen non Blue Copper and with the oxidase properties and we also have seen somewhere all these together are present so many kind of a different kinds of the things.

So, here we see that a few additional other kinds of things. So, amin Aminoacid oxidase, Catechol oxidase, Dopamine-oxo-monooxygenase, Lysine oxidase, Peptidylglycine monooxygenase, Lysyl oxidase, Metallothionein; so, variety of these things are there in the copper enzymes. So, it is going to be very huge story, then we need to go try to understand one by one its properties, etcetera.

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Deficiency syndromes of some copper enzymes	
Enzyme	Important Function
Ceruloplasmin	Decreased circulating copper levels, iron deficiency
Cytochrome-C oxidase	Hypothermia, muscle weakness
Dopamine β -hydroxylase	Hypothermia, neurological defects
Lysyl oxidase	Laxity of skin and joints
Peptidylglycine- α amidating monooxygenase	Neuroendocrine defects
Superoxide dismutase	Diminished protection against oxidative stress

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Now, what will happen when you have i in the beginning stages, I have explained metal ion need and efficiency and excess kind of a that is doses deficiency excess kind of syndromes? Now if you look at the definitions of copper; deficiency of copper can lead to the decreased circulating copper levels, then it will make the iron deficiency also and that will if it leads to the Ceruloplasmin, this is the kind of a function, it can lead to the deficiency of building Cytochrome-C oxidase, then that will become that will lead to hypothermia and muscle weakness, if the copper deficiency leads to Dopamine beta-hydroxylase deficiency, then Hypothermia, neurological defects like that so; that means, a number of copper based enzymes will be affected as a result of the deficiency of the copper ions. So, this enzyme can get affected; this, this, this, this, this.

So, all of these will have corresponding, for example, if the copper oxide; copper based Superoxide dismutase is a enzyme is affected because of the low concentrations of the copper in the cellular concentrations, then what will happen? This enzyme will be low in concentration. If this enzyme is low in concentration, it will not be able to protect the cells from oxidative stress so many things are possible. So, all this is because the ion is deficient. Therefore, the corresponding enzymes are not being developed as the corresponding enzymes are not developed the corresponding functions are not shown. So, this is how one needs to attach one to the other ok.

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Type I Copper proteins

- Thiolate ligand to Cu(II) charge transfer – Intense Blue colour of Cu(II) state ($\text{CysS}^- \rightarrow \text{Cu}^{2+}$)
- Asymmetrical Cu site (distorted trigonal-pyramidal, distorted 4-coordinated)
– Unusual EPR properties
- Arbitrary subunit division – plastocyanins, pseudoazurins, amicyanins etc.

azurins, amicyanins, pseudo-azurins and plastocyanins have similar copper coordination by two His, one Cys and one Met residue.

- Type I copper protein Functions – Electron transfer

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So, let us look at this is the Blue Copper proteins and these are also referred as a type one copper proteins type one, this one has nothing to do with the copper oxidation state one, it has nothing to do with the copper one oxidation state. So, type one copper proteins which are nothing with the Blue Copper proteins, I said they are give intense blue color and simply the blue color is coming because of a charge transfer the charge transfer from cysteinyl sulfur to Cu 2 plus. So, this is the kind of thing where you find and the in this kind of a proteins, the copper side is distorted either distorted tetrahedral distorted 4 coordinate or distorted 5 coordinate trigonal bipyramidal.

So, and they show depending upon these unusual EPR properties. So, you have different kinds of a subunits into these plastocyanin, pseudoazurin, amicyanin, all of these are called the Blue Copper proteins and the azurins, amicyanins, pseudo-azurins, plastocyanins, they have a similar kind of a copper coordination. So, their coordination is two histidine, one cysteine, one methionine; I will come into more details of the coordination sphere, a bit later after I cover type one, type two, type three and other types of protein, then I will come explain you the actual coordination transfer.

So, what is the function of these kinds of proteins? The main function these proteins type one copper proteins is electron transfer.

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Type II Copper proteins

- The copper centres - square planar or pyramidal coordination, containing oxygen and/or nitrogen ligation.
- The Cu(II) is EPR active, with a 'normal' signal. There is no intense blue color.
- Ex . copper/zinc superoxide dismutase, dopamine β -monooxygenase, galactose oxidase and the various copper-containing amine oxidases.
- Some members of this last group may also contain a modified amino-acid residue

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So, we will see; how they do the electron transfer, etcetera, etcetera, now having looked at some general features of type one, let us look at the general features of type two, then will which is the type three; we will see combined types, we will see all new kinds of types, then we will go into details of each one of this.

In the type two, you have a kind of a close to a square planar or a square pyramidal kind of a coordination containing oxygen, nitrogen, no thiol group, there is no thiol is involved, therefore, there is no charge transfer, therefore, there is no blue color. So, these are Non Blue Copper oxidizes. So, the copper two is EPR active with a normal signal and there is no intense blue color at all.

So, copper zinc superoxide dismutase dopamine, monooxygenase, galactose, I have shown you these; some of these examples in the in the table that I given you a couple of slides before. So, galactose, oxidase, copper containing amine oxidase, all of these will contain type two copper, type two copper, type two copper proteins, these are all referred as.

In some other cases, some of the cases, it is not only the side chain of the protein is binding, there is some modified version of the side chains of the protein, they act as a cofactors. So, I will again explain this when I come to the story of the type two copper proteins ok.

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Type III Copper proteins

- In this group a pair of copper atoms comprise a dinuclear centre, with no EPR activity
- The best known example of an enzyme containing a single Type 3 centre is tyrosinase (catechol oxidase, EC 1.10.3.1).
- This protein contains a metal centre which is a structural analogue of the dinuclear copper centre in hemocyanin.



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Then type three copper proteins; these are not from one single copper ion, these are from two copper ions, it is called dinuclear copper center and these are there is no EPR activity, this is referred as type three; this is found in number of enzymes like tyrosinase, catechol oxidase, etcetera, alone in tyrosinase, along with other centers in the catechol oxidase, a in the catechol oxidase and the other kinds of enzymes too.

So, this protein contains a metal center which is structural analog of the hemocyanin, in a hemocyanin, you form dicopper center, here also you will find dicopper center.

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Multi-Copper Oxidases

There are several proteins with catalytic activity that contain Types 1, 2 and 3 centres.

These include L-ascorbate oxidase, laccase and ceruloplasmin (ferro-oxidase), the latter two having aromatic diamine and diphenol oxidase activity.

Type 2 and Type 3 copper centres could be juxtaposed.

L-ascorbate oxidase, a trinuclear copper site is present, consisting of a type 3 copper site, very close (3.9 Å) and possibly bridged to a type 2 copper site . Ceruloplasmin functions as a ferro-oxidase and the Fe(III) produced in this reaction can then oxidize the same substrates as laccase.



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Multi-Copper Oxidases; aware it will have type 1 we have type 2, it will also have type 3 together. So, that is what is called Multi-Copper Oxidases. the function is oxidation redox properties of this and there are several kind of coppers of which one is type 1 which is being Blue Copper protein type 2 non blue center, but oxidase property type 3 is a dicopper center and all these three can also function. So, these are all present in ceruloplasmin, laccase ascorbate oxidase, all of these have got type 1, type 2, type 3 centers, they function in a coordinated manner ok.

So, for example, here L-ascorbate oxidase; a tri nuclear copper site is present, it is a consisting of a type 3 copper site which is very close to the type 2 copper site. They; it therefore, it became 2 plus 1; 3 coppers, then far away from this, there is a type 1 also far away from this which is about 15 to 20 angstroms away from this, you have a type 1 also.

So, the Ceruloplasmin functions as ferro-oxidase and the iron three produced in this reaction can then oxidize the same substrate as laccase. So, you do not need to so much worry about this point of it. So all that you need to understand from this particular slide is that you have a type 1, you have a type 2, you have a type 3, you have enzymes where all of these are also present together whenever type 1 is present, it will have the blue color ok, even if other things do not give the blue color, there are other special type of copper centers are there.

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Copper Centers in Cytochrome Oxidase

Two unique copper centres in cytochrome-c oxidase.

The first copper center isolated metal ion and has been referred to as Cu_A (also known as Cu_I)

The second copper center is part of a dinuclear centre with cytochrome a_3 .

It has been referred to as Cu_B (also known as Cu_II , Cu_3).

The ascriptions Cu_A and Cu_B are most frequently used.

There is a striking similarity between two of the Cu centres of N_2O reductase and Cu_A



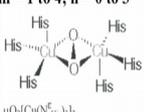
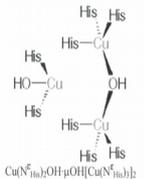
Which are present in Cytochrome-C oxidase and these are referred as copper A where the one of the copper is isolated metal ion refer to copper A and some places will be written as copper small d, it is a capital A.

The second copper center is a part of the dinuclear center with cytochrome a 3 and this is referred as copper B; Cu B ok, Cu a 3 is all. So, Cu A, Cu B are the most frequently used terminology. So, there is a striking similarity between the two of the copper centers in the N 2 O reductase nitrous oxide reductase, we will not look under the copper system, we have already look at under the iron case. So, we will not look at that, but just say that there is a similarity between the copper centers, the N 2 O reductase and the copper A; copper A is present in the cytochrome oxidase, copper B is also a present in a cytochrome oxidase. So, copper A center, copper B center. So, these are special centers besides the type 1, type 2, type 3.

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Copper centers: Type II & III & together

$Cu(NHis)_mR_n$ R = O or S ligands, m = 1 to 4; n = 0 to 3  $\mu O_2[Cu(NHis)_4]_2$	Four or Five CN Catechol oxidase Haemocyanins Tyrosinase	Type II Type III
 $Cu(NHis)_3OH\mu OH[Cu(NHis)_2]$	Blue oxidases Ascorbate oxidase Ceruloplasmin Laccase	Trinuclear center Type II + Type III

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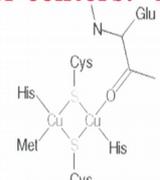
So, all these we have and you can see, they are just the simple structures of these; the type 2 as you can see there, it has no thiol group histidines and some other groups they could be 4, they can be 5 in some cases, 4 coordinates in some cases 5 coordinate.

And type 3 has got this kind of thing hemocyanin in we have already seen, this is oxidized hemocyanin in Blue Copper oxidizes where this is a type 2 type and this is a type 3 and there is one type 1 away from it. So, with this is coupled. So, type 2 and type 3. So, this portion is type 2, this portion is type 3, it is together.

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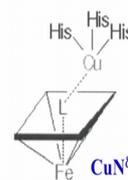
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Copper centers: Type A & B (cytochrome c oxidase)



Cu_A
Cytochrome *c* oxidase
N₂O reductase

$Cu_2(N^{\delta}_{His})_2O^{\delta}_{Glu}S^{\delta}_{Met}(\mu S^{\gamma}_{Cys})_2$



Cu_B
Cytochrome *c* oxidase
Ubiquinone oxidase

$CuN^{\delta}_{His}(N^{\epsilon}_{His})_2L$ L=bridging ligand between Cu_B and Fe of Haem a₃

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And now, we are talking about A B type; A B types are here; type A in Cytochrome-C oxidase and type B in again in the cytochrome B oxidase, but away from C oxidase. So, these are all the kind of a centers that you have. Now what we have looked at? We have looked at the type 1, type 2, type 3.

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Classification of biological copper centers

	Mononuclear		Dinuclear		Tetranuclear
Type	Type 1	Type 2	Type 3	Cu _A	Cu _Z
UV-Vis Spectrum	Strong absorption~ 600nm & (in some proteins 450nm)	Weak absorption~ 700nm	Weak absorption~ 700nm	Strong absorption~ 480 & 530nm	Strong absorption~ 640nm
EPR Spectrum	4-lines spectrum	4-lines spectrum	Non detectable	7 lines spectrum	2x4-lines spectrum
Common ligands	His, Cys, (Met)	His, Asp, (Tyr)	His, (Tyr)	His, Cys, (Met)	His, S ²⁻
Geometry	Distorted tetrahedral	Distorted tetragonal	Tetragonal	Trigonal planar	m ₄ -S ²⁻ tetracopper cluster
Examples	Azurin, Plastocyanin	Superoxide dismutase	Hemocyanin tyrosinase	Cyt C oxidase NO ₂ reductase	NO ₂ reductase

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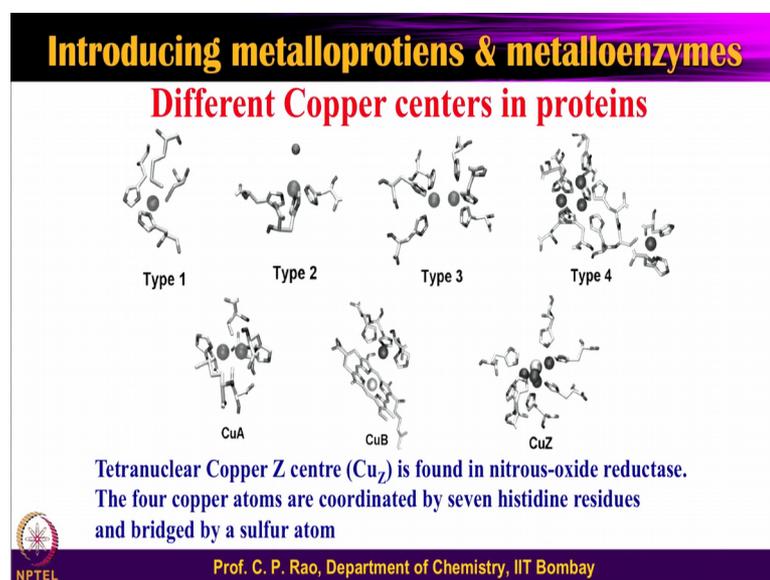
Copper A, copper B and we have not looked at the copper Z. There is another one coppers Z is also there which is tetranuclear, copper B is the from the dinuclear case in this way.

So, these are some characteristics are given. They are all have absorptions in the more or less in the visible region and the absorptions go from 450 to seven hundred. So, 450 to 480 to 530 to 640 to 700; so; that means, your coordination course are changing from one to the other to the other. Their emission spectra are shifted into the visible region in these ones you can see and the type 1; the 4 line EPR, type 2 4 line EPR, type 3; no, you cannot detect non EPR. copper A has 7 line EPR, copper Z has 2 into 4 line because that is the further coupled into that line spectrum. So, that is a referred as a 2 into 4 line spectrum. So, you have initially 4 lines each of the 4 lines each of the line is further divided into two lines ok.

So, the common kind of ligands are what? Histidine, Cysteine and Methionine in this case and here there is no Cysteine in type 2 and there is no Cysteine in type 3 too as you can see that; copper A has gone and copper Z has got a sulfido. So, they have the distorted tetrahedral in some cases; trigonal bi pyramidal distorted tetragonal distorted tetragonal all these kinds of geometries you can go through all these examples.

So, now we got familiarized with type one.

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And with type two, with type 3, type 1, type 2 are mono copper center and type 1 has got not only histidines, it has got one methionine, one cysteine, that is the reason why you get the blue color into these ones and then you have the type 2; no cysteines, no methionines, no blue color, but still 1 copper center and type three the 2 copper centers

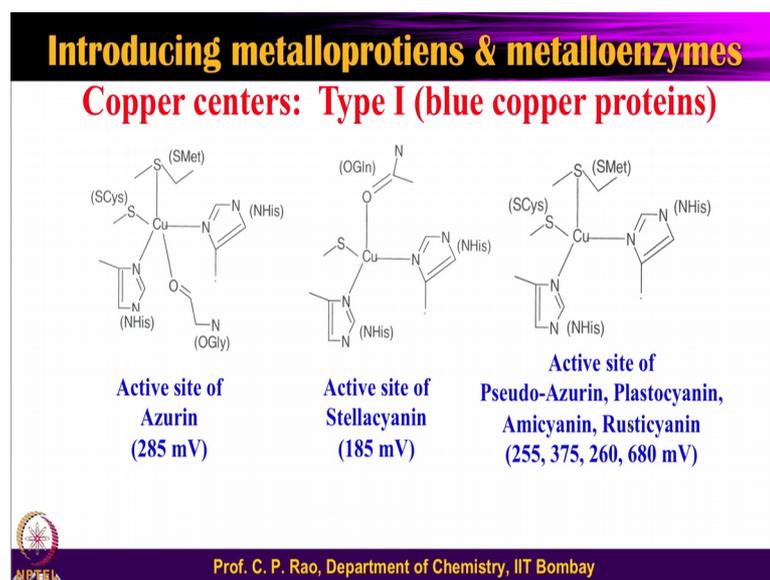
that you have and no cysti no cysteines, no blue color from this and then the one 4 which is having all 3

Now, we are referring it as a type 4, you see these 2 coppers are referred as type 4, this copper is referred as type 2 very away from it which is called the type 1. So, it has one type 1, one type 2, one type 3; these two are within 3 to 4 angstroms and this is about 15-20 angstroms away from this and these are all of these is we know very well its electron transfer and this is redox oxidative reductive type and this can even activate the dioxygen too here substrate can bind as well; so, electron transfer O₂ oxy activation and substrate binding all three together in one; so, it is called oxidases.

Now, the other thing just lately we have looked at copper A center, copper B center, both of these are present in Cytochrome-C oxidase and copper Z center where 4 copper centers are there and this is where you have the 4 copper centers; these tetranuclear copper Z center is found in nitrous oxide reductase and the 4 copper atoms are coordinated by 7 histidines and bridged by a sulfur atom, you can see that the one here that is the sulfur atom here and these are the 4 coppers here and there are some histidines are bond to this.

So this; we may not be looking into the more details of the thing because these are not very well understood in terms of the mechanism, but they are there the very well; now what we have seen; you have sufficiently large things thing that you could see the copper is involved in a variety of enzymes; type 1, type 2, type 3, type 4 is nothing, but summation of type 1, type 2, type 3 and copper A, copper B and copper Z. So, these are the things. So, type one is Blue Copper type 2 oxidase, type 3, it can activate the O₂ and it is a dicopper center, type 4 has got all these type 1, type 2 and type 3 all the three together as you can see here and all the three type 2 is here, type 3 is here, type 1 is here and copper A and copper B which are in the Cytochrome-C oxidase and this is the copper Z ok.

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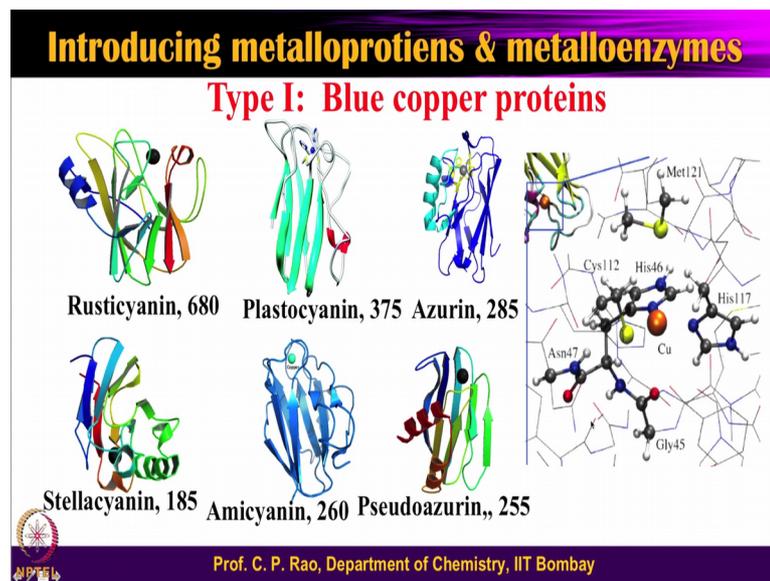
Having looked at the general classifications general, you know type of copper centers, let us go more specific; let us take to start with type 1 copper centers, these are also referred as Blue Copper centers, these are also referred as electron transfer copper proteins whether you say electron transfer, copper protein, whether you say Blue Copper protein or whether you say type 1 proteins; all of them are one and the same. So, do not get confused. So, I will be using different terminology at different stages. So, type one is same as Blue Copper protein is same as the electron transfer copper proteins.

Now, you can see one of them; here active site of that; other one active site of that other; like this. So, what we need to see; the one in the middle, you have a 2 histidines, 1 SME methionine and this is the glutamine and here 2 histidines, 1 methionine and 1 cysteine. This will be very strongly blue color and all of these because of the thiol, the charge transfer from copper 2 plus thiol to the copper 2 plus center.

So, this is a 5 coordinated is roughly trigonal bipyramid distorted this is distorted tetrahedral. This is also distorted here. So, you have generally 4 and 5 coordination of this. So, azurin and you see that the redox potentials are changing 285, 185, 255, 375, 260, 680. That means, the lowest here is 185, the highest here is 685; around 680. So, a difference is about 500 millivolts. So, by changing the coordination of course, is not sufficient enough and this is the protein also probably must be making a absolute contribution to the redox potential.

So, this so, what is the advantage having so much different with so that you can do variety of redox reactions using this one. So, electron transfer can be transferred from one to the other to the other to the other very efficiently when you have different redox potentials that you have in this enzyme ok. So, you can see that.

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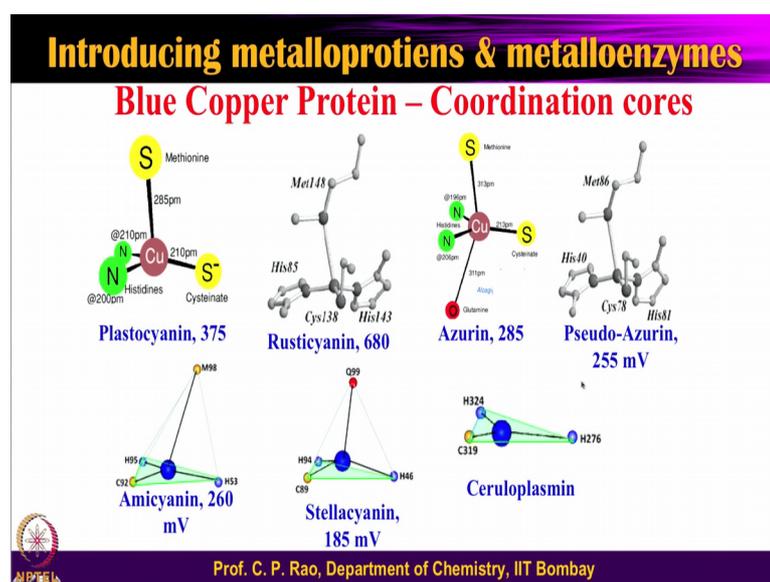


Now, the same thing; let us look at the enzymes, let us look at the enzymes. So, we have look at the enzyme here, this is a an enzyme and this is the copper center, this is an enzyme, this somewhere here is a copper center, this is an enzyme somewhere here is a copper center as you can see that somewhere here is a copper center. So, you can see here, somewhere here is a copper center, somewhere here is a copper center, somewhere here is a copper center.

So, in all these proteins, protein has a lot of a structure and in towards roughly towards terminal some of them a bit more exposed than the other they are all towards the end of the protein. So, this protein roughly can be taken as cylindrical and towards the end you have this copper center.

So, this is a protein with 680 millivolts, 375 millivolts, 285 millivolts, etcetera, etcetera, one example you can see here this is your copper, this is your asmethyl and this is your cysteine, this is one of the histidine, this is other histidine. So, two histidines and one methionine, one cysteine and the remaining protein; you can see here very nicely you can see the protein here.

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If you look at the closely these ones; you can see the coordination sphere very nicely very nice very good and very good here. So, you can see all these coordination spheres. So, either the highly distorted, you can see there are very highly distorted tetrahedral also highly distorted trigonal bipyramid, you see why highly distorted, you can see this S Cu S angle is very very acute a kind of an angle; so all these kinds of things there.

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Copper centers: Type I (blue copper proteins)

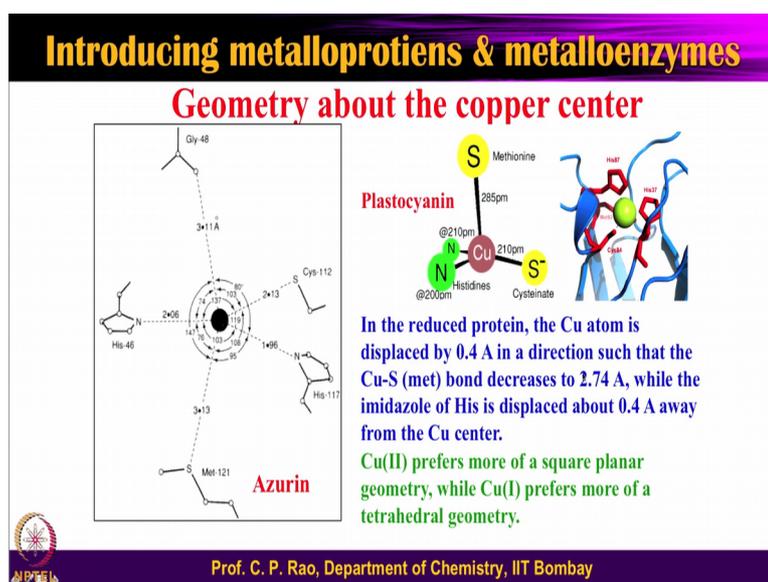
Protein	Redox (mV)	Residues at binding site	Sources of enzyme with PDB code
Plastocyanin	375	His37, Cys84, His87, Met92	Populus sp. (4PCY)
Rusticyanin	680	His85, Cys138, His143, Met 148	Thibacillus Ferrooxidans (1A3Z)
Stellacyanin	185	His46, Cys89, His95, Met98	Cucumis Sativus (1JER)
Amicyanin	260	His53, Cys92, His95, Met98	Paracoccus Denitrificans (1AAC)
Azurin	285	Gly45, His46, Cys112, His117, Met121	Pseudomonas Aeruginosa (1BEX)
Pseudoazurin	255	His40, Cys78, His81, Met86	Achromobacter Cycloclastes (1BQK)

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So, the same thing is shown here which are the residues binding. So, this is not very essential, you can always look at whenever you think like that this, I already explained to

you, explained to you that the redox potential change a lot though the though the coordination changes only somewhat so; that means, both the coordination is contributing to this redox potential as well as the protein conformation is contributing to the redox potential.

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So, if you see closed by this copper; one of the copper one cent type 1 case this is azurin, this is the trigonal, this is the bipyramidal kind of things that you can see highly distorted and you can look at a plastocyanin, you see, this copper 2 sulfur bond thiolate bond is 2.85; a 285 pico meter is nothing, but 2.85 angstrom which is very far away far away and, but forms a coordination.

So, therefore, such kind of a distortion; why such a kind of distortion is nature have chosen, there is something that one needs to look at that yes we will look at that. Now see the copper this protein what is its function electron transfer. So, electron transfer means it can go between copper can go between 2 plus and 1 plus in the oxidized state it is copper 2 plus in the reductase copper 1 plus again back to oxidized copper two plus back reduced copper 1 plus.

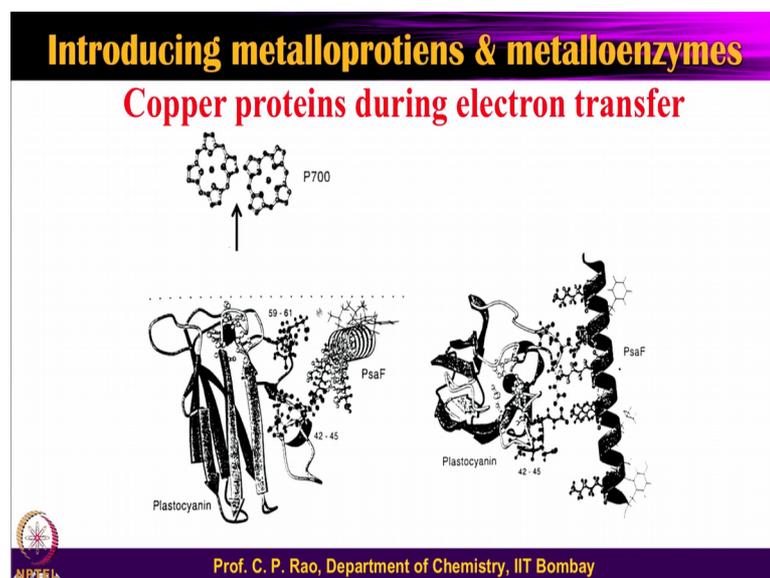
So, therefore, one electron transfers. So, it is going between copper 1 and copper 2. So, when you this is from the oxidase protein. Now when you go to the reduced protein crystal structure is known this distance is brought down from 2.85 to 2.7475 and this is

moved a little bit further away and this is a little bit dropped this bit little bit moved towards this.

So, there is a lot of change in the geometry of this and these are connected to the protein. So, when the geometry changes here, this will change the protein conformation. So, therefore, the protein conformation is coupled with this geometry changes which is coupled with redox. So, redox copper 1, copper 2 is coupled with these changes in this geometry parameters which in turn is converted which in turn is changing the protein conformation. So, therefore, protein conformations are very much influential in this.

Now, why is this so much distorted? As I said, you need to go through a copper 1 plus and copper 2 plus and as you know very well the copper 1 plus prefers more of a tetrahedral copper 2 plus prefers more of a square planar. So, therefore, you have somewhere in between this particular geometry is neither square planar nor a tetrahedral geometry. So, because of the infinite between the amount of reorganization required or reorganization energy required including the redox is very minimal and that is the reason why the protein has chosen such a kind of a prot elect a kind of a geometry in this too you can see that.

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Now, how will it do the electron transfer? It will join with another protein or the receptor or other counterpart of the biological system and this is from your plastocyanin and there is a overlap of these things or some other kinds of antennas where the electron transfer.

So, the electron transfer I explained to you very well when I this is initially introduced topic of the in under the ion; where I talk to you for the iron sulfur proteins as well as I have talked to you cytochromes; prior to that I introduced to you the 2 proteins come closer; the one is giving a electron, other is taking the electron, vice versa, they come there is a reorganization of this and then the electron transfer taking place between them either from the through a in the trans elect inner sphere electron transfer or outer sphere electron transfer many times, you will have a outer sphere electron transfer and that is the kind of thing that you can see here too and so that is where we have the electron transfer part of this we have.

So, therefore, I have started explain to you the different classes like type one type two type 2, type 4, copper A, copper B, copper Z kind of things and I have started with type one electron transfer how the electron transfer is phesyl because of the distorted geometry during the 1 copper one copper two and the protein electron transfer is very efficient to the other biological proteins.

Thank you very much.