Inorganic Chemistry of Life Principles & Properties
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Lecture - 59
Tutorials - Part III

Welcome you all to the next class on Inorganic Chemistry of Life Principles and Perspectives. So, in the previous two-three classes, we have been going through the tutorial queries, where I am giving insights into that. Of course, also referring you to look back into what I taught in the class. So, we were in the half way with the iron in biological system, let us start looking at some more queries in iron in biology ok.

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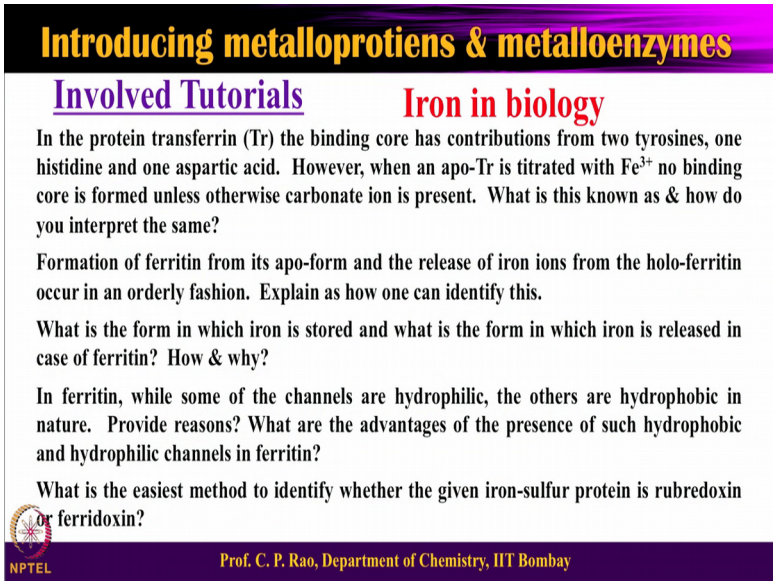

So, in the let us look at this particular query. In the protein transferrin, it is transfer in a protein. The binding core has contribution from two tyrosine, one histidine and one aspartic acid. So, this is which means this is a primary coordination core.

However, when an apo transferrin is titrated with iron 2 plus no binding core is formed unless otherwise the carbonate ion is present. So, what is this, and how do one interpret this one ok. If you look at the fully formed protein structure, you will find very nicely from the crystal structure is understood that the transferrin the ion center is bound to two tyrosines, and two histidines, and even aspartic acid.

So, now you take the transferring, remove the ion. When you start adding the ion it will never form the transferrin protein, because of the absence of the carbonate, so carbonate is required. So, when you add carbonate, what will happen, when you add carbonate, it will form the core actual core. So, that is the iron core for the transferrin.

So, why because the carbonate acts like a allosteric factor. So, allosteric means allo is other, steric is stereo form other stereo form that means it affects under stereo forms of this protein. So, with that it will close the core and makes the iron to be present in the transferrin core, and make an enzyme.

So, there is where so this is known as allosteric factor, and this is the reason why. Otherwise is the core is open when the carbonate is there it will lock it lock the core. So, therefore, you have the primary coordination core is being completely locked, and that ok.

Let us come to the next question formation of ferritin from its apo form, and the release of the iron ions from the holo ferritin occur in an orderly fashion explain how. You know that the ferritin core is a huge is about 70 to 80 angstrom diameter about 7 to 8 nanometers diameter. And therefore, about 4500 iron atom ions can sit inside this core. See if that many can sit in there inside the core obviously, you have to have a method; you have to have a pro forma; you have to have a fashion by which this can be connected. And these are chemical species; these are charged species therefore, you require.

See, if you want to put two ion ions one next to the other both a cationic, they will ripple. So, how will you do, put something in between, let us say an oxo or a phosphate something of that kind, then the oxo will be negative charge, then this negative charge can compensate their positive repulsion and can bring together. And all this thing will go in a very nice orderly fashion. So, as it goes insigne you will attach one to the next to the next to the next the whole thing get. When you are releasing again the last one will come out first, then the next one the next one the next one. There are some more queries where I will give more deep responses to how it happens etcetera ok.

What is the form in which ion is store, and what is the form in which ion is released in case of ferritin, and how and why. See the transport when it brings it is always in the iron 2 plus, and the when the iron 2 plus goes it goes through the channels, and goes inside.

When it goes inside and binds to the carboxylic framework then it will get oxidized. For oxidation O 2 is also used ok and when you want to reduce when you want to release again ion which is oxidized form of the ion. Oxidized form of the ion is breached by oxo and phosphate groups there for it will not easily come out. Also you know that ion 3 is less labile then iron 2. Therefore, you need some reducing agents, which will reduce the iron 3 plus to iron 2 plus. And once it becomes iron 2 plus it is mobile and labile it will come out, that is kind of thing ok.

Let me let me bring your attention to the next question, in ferritin. While some of the channels are hydrophilic others are hydrophobic in nature provide the reasons. Why some of them should be hydrophilic, some of them hydro hydrophobic very simple. Without even knowing any aspect of it can tell that means, there are some hydrophilics it will hydrophilic loving groups either to go in or to come out.

Similarly, some hydrophobic kind of groups to go in or to come out, that is precisely the reason. The channels are there to take in or channels are there to take it out. What are the advantages of the presence of such hydrophobic and hydrophilic channels in meriden yes. There are several advantages, because what is required you have to have iron 2 plus to go inside; you have to have some O 2 should go inside. You have to have reducing agents to go inside, and to reduce and take it out.

So, therefore, entry and exit of all this, and the iron entry and exit; as well as the hydrophobic; as well as an oxygen entry; so all of these uses either the hydrophilic or the hydrophobic channel therefore, both of these are essential. And you can get all the details from the information that I have given in the class ok.

Let us come to the next question. What is the easiest method to identify, whether the given iron sulfur protein in rubredoxin a or the ferridoxin. So, what is the easy method to identify a something is missing the inorganic sulfur or sulfide. So, what is the easier method to identify sulfide ions, whether given iron sulfur protein is rubredoxin or ferridoxin ok.

So, how do you find in the rubredoxin there is no S 2 minus; in the ferridoxin there is S 2 minus. And if you add mineral acid the S 2 minus will come as H 2 S, and the smell itself will tell you that there is a inorganic sulfide. In the rubredoxin you take, and add HCL

nothing will happen no smell will come, because there is no sulfide ion very simple no spectrometer is required you can do that.

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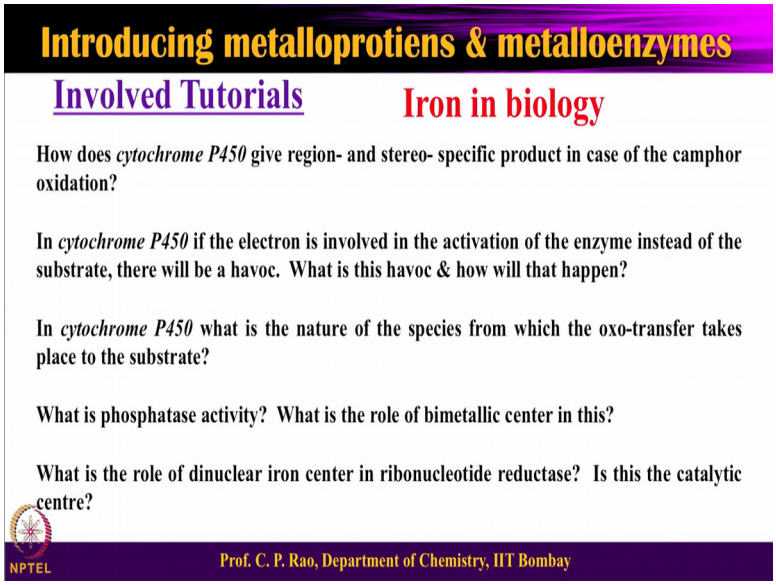

Let us look at some more iron ion iron in biology how cytochrome P 450 give regio, and stereospecific product in case of camphor. Camphor oxidation I have already shown in the class as you know the camphor is held by the secondary interactions the protein at the cavity above the porphyrin heme level such that that particular carbon is poised exactly on top of the ion center. Why, because that iron center will become ferial oxo. And that oxo group will go from there to the carbon center, and also the direction.

So, since the position and direction both are fixed by the protein in arranging the substrate exactly over the iron center therefore, this is where you get the regio and stereo selectivity ok. Come to the next question, in cytochrome P450 if the electron is involved in the activation of the enzyme, instead of this substrate there will be a havoc. What is this havoc how will this happen ok.

So, let us look at the query the of this one in cytochrome P450, if the electron is involved in the activation of the enzyme, instead of the substrate. So, substrate is conform or any kind of other thing, and if that happens. Then what we say is its really going to be a dangerous part. Why is it dangerous, because once the enzyme is activated by one electron reduction. This electron can be given to the O 2, and the O 2 can become O 2 minus dot. And you know the O 2 minus dot is superoxide and this dangerous it can

oxidize the substrate. It can oxidize the enzyme itself, because the substrate is not there ok.

So, therefore, the enzyme as chosen that it is activated only when the substrate comes not by the electron ok. Let us get to the next question in cytochrome P450 what is the nature of the species formed which a involved in transferring the oxygen or oxo species to the substrate. Is the ion center which will become ferriloxo, and it is the ferriloxo which is, oxidized from the ion which is which transfers the oxygen.

What is the phosphatase activity? Why is that there are two metals in this. So, what is the role of the bimetallic center. So, the phosphatase activity purple acid phosphatase, and you have alkaline phosphatase to in purple acid phosphatase, it is mainly iron in the alkaline phosphatases it is zinc ions these are all the die nuclear centers.

So, in the phosphatase activity in the phosphatase activity means, the phosphate high ester hydrolysis; so hydrolyzing the phosphate ester that is where thing is. So, what is the role of the two metal centers one or the metal center will be useful in binding the phosphate moiety, the other one is useful for providing a nucleophilic attack on the ester. So, that the ester gets hydrolyzed. So, one is for binding are these for catalysis activity. So, both are together as a bio nuclear.

Come to the next question, what is the role of dinuclear center in ribonucleotide reductase. We have seen in the dinuclear role in phosphatase. So, is it the same in this case. So, is this the catalytic center the role of dinuclear say ion in ribonucleotide reductase is not same as that the phosphatase. Because no substrate binds to the iron, and no second iron will be acting as a catalyst. Its role is what I am sure if you look back you would see, that to stabilize a radical on the tyrosine. That tyrosine radical will trigger the reaction basically.

So, therefore, in case of the ribonucleotide reductase the iron neither provides a position for binding the substrate, nor second iron provides any utility of catalytic activity at all ok. So, therefore, the di iron center present in the ribonucleotide is not the catalytic center, it is stabilizes the tyrosine radical, and reaction occurs elsewhere in another sub unit of this. Where this radical is transferred to a thigh al radical, and from there actually the reaction takes place at the center where nucleotides are bound. So, hope you understand the things.

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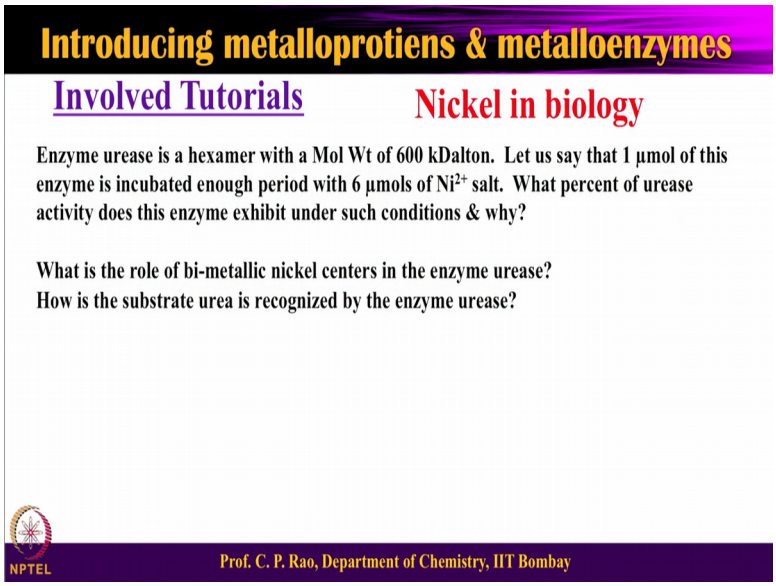

Let us look at some additional questions, this questions based on the Nickel in biology enzyme urease is a hexamer with a molecular weight of 600 kilo Dalton. Let us say that 1 micro mole of this enzyme is incubated enough period with 6 micro moles of nickel 2 plus salt. What percent of urease activity does this enzyme exhibit under such conditions, and why? See if you look back, also given in the question is hexamer, 600 kilo Dalton about 100 kilo Dalton for each monomer. And you know each monomer has got one center of the new nickel center one dinuclear nickel center, this is a dinuclear nickel center ok.

So, if you use one mole of enzyme, what does it mean; there is six equivalence of subunits. So, it is basically 6 mole of nickel 2 plus, and that is what is you understand that. So, the entire one mole micro mole is a of protein is saturated with the nickel 6 moles.

So, what percent of urease? So, how much moles of a nickel is required actually, for 1 mole of micro mole of enzyme. Because each center is dinuclear there are 6 centers 6 into 2 12, but what will you give it only 6. So, that means, you get only three of them.

So, therefore, the percentage is the reaction what percentage the urease activity does this enzyme exhibit, it is 50 percent under such conditions in that. So, you put all 12 micro moles then the whole thing, all 6 centers or occupied by nickel and then you have a nickel enzyme functioning fully well.

What is the role of bi-metallic nickel center in this enzyme urease? How is the substrate urea is recognized by the enzyme urease? This is more or less like the kind of an answer I gave for dinuclear manganese center present in or dinuclear ion center present in phosphatase.

So, what is the he tell there one of the ion center is providing a space for binding; other ion center is providing a nucleophile to attack, and thereby you have a cleavage, exactly the same. So, one of the nickel center is useful for binding the urease the C O moiety of the of the urea. The other one provides it is an attack, and this therefore, you have a cleavage of the ammonia. Finally, you have to you have to cleave the urea to get ammonia, and the corresponding carbonate equivalent one, because the water is also involved. You can see the reaction in the thing.

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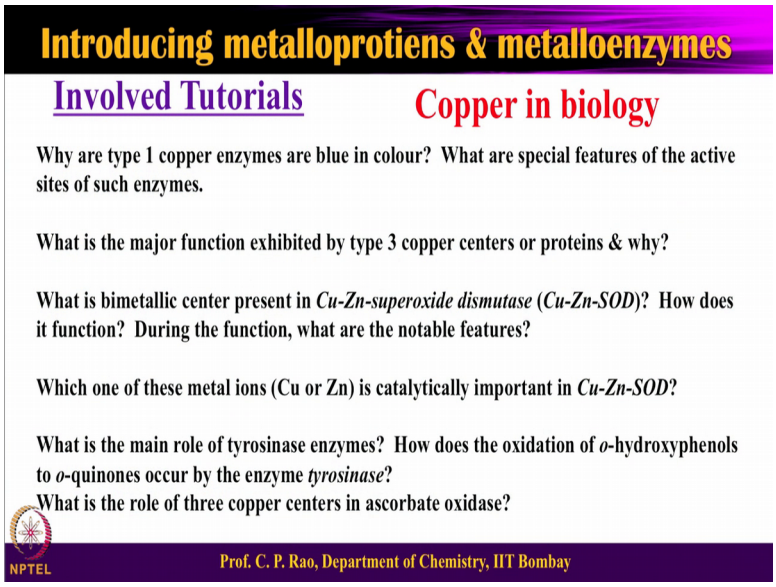

Let us look at the next one in the copper; the copper in biological systems. Why are the type 1 copper enzymes a blue in color? What are the special features of these enzymes at the active site. So, whenever you look at the inorganic compounds, and you look at some kind of color the two reasons, one is either through the D D transition or through the charge transfer transition. The kind of a transition that you expect here will not mean the D D transition will not be in the visible region therefore, it is the charge transfer.

So, where the charge transfer from, if you are aware this has a cysteine and methionine, therefore, it is a thiolate function or sulfidal function or thio function. Therefore, it is

from the thio or thiolate to the copper center charge transformer. And that is what is found.

What is the major function exhibited by type 3 copper centers in proteins and why? First of all the type 3 copper center is a dinuclear center. And di nuclear center the moment comes in the mind, if one should think of both the metal centers for a redox purpose, giving one one electron. In fact, copper 2 can go to copper 3; copper 3 can go to copper 2, so 1 electron. So, therefore, 2 such copper centers; 2 electrons. Therefore, 1 can expect a 2 electron redox process.

So, for a O 2, 2 electron redox processes is O 2 2 minus. So, the major function exhibited by the type 3 is activating the oxygen, and then followed by your oxygen transfer etcetera takes place ok.

Let us look at the next one. What is the bimetallic center present in copper zinc superoxide dismutase (Cu-Zn-SOD)? How does this function? During the function, what are the notable features? What is the bimetallic center present in the copper zinc superoxide dismutase? It is copper, and the zinc it is there in the name. How does it function? Can you expect zinc to undergo redox no it is a redox silent, and it is always note as zinc 0, zinc 2 plus. So, zinc 2 plus will never change whereas, copper can go between copper 2 plus and copper 1 plus.

In some situations copper 3 plus is also possible, but not here. So, copper 2 plus, copper 3 plus. So, therefore, it is basically the copper undergoing redox will bring the redox to the zinc is present in that. So, that means, zinc is should be a silent element or it could be a what you can call it is instructional element, and copper is a functional element. So, the functional is occurring it, the copper and the structure is stabilized by the zinc. The question is not there, but I will pose how do you know that it is the various catalytic other is structure.

Suppose you replace the structural element of 1 by another the activity may not get affected to its too much extent. On the other hand if I happen to replace the catalytic element a catalytic ion the catalysis will go down dramatically. So, therefore, you can easily make out what it is. This is not there in this question, but I am posing another question on the spot now. Which one of the metal ions copper zinc is catalytically

important already explained to you the previous it is a copper which is, catalytically important zinc is structurally.

What is the main role of tyrosinase enzymes? How does the oxidation of ortho hydroxy phenols to ortho quinone occur by the enzyme tyrosinase? Ok, Tyrosine is tyrosine oxidation so that means, these basically oxidizes the tyrosines, they can oxidize the aromatics all these kinds of things. So, these are tyrosines kind of enzymes,. And this enzyme has got 2 copper centers with 3 3 histidines and copper one, no bridging.

Now, when the oxygen comes in the picture the oxygen will be activated, between the two coppers by giving one electron each. And making it to O 2 2 minus and coppers will all get oxidized to the corresponding copper to copper 2 plus. The tyrosine or hydroxy phenols which bind at the copper center will be oxidized by this one. In fact, this kind of a thing is a is a chain kind of reaction records in the biological system. And such things are always found to lead to when so many enzymes work to lead to something called melanin formation. You know skin tanning etcetera cut fruits brownishing etcetera.

So, what is the role of the copper centers in ascorbate oxidase. There are 3 copper centers what is the role type 1 copper provides electron transfer, type 2 pots mediates, type 3 activates oxygen, and this oxygen is further broken, and you form the oxygen with a tri center; one, type 2 copper; two type 3 coppers. So, it will become a kind of a bridge species where the type 2 copper will help. So, type 1, type 2, type 3 coppers ok.

We have some more questions, I will take in the last class that is the next in the next class, I will take the remaining tutorials and sum it up.

Thank you very much.