Inorganic Chemistry of Life Principles & Properties
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Lecture – 60
Tutorials – Part IV & overall

Welcome you all to the more or less the last class in this particular course, but I will continue with the tutorial aspects that we have been discussing in the past three classes or so and then I will sum up the whole thing. So, let us look at the, a queries that are shown over there with under the zinc in biological system. I have completed up the copper in the previous class ok.

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In spite of the fact, that the zinc does not undergo a redox that means zinc 2 plus does not go to 3 plus does not go to 1 plus ok. It is involved in a variety of enzymes including oxidoreductases. So, there is a lot of enzymes are known, we know that, hydrolytic type, redox type. It does not undergo redox, but it the reaction product has oxidation reduction. How is that possible? So, how is that possible because, it does not undergo a redox, but it will utilize the help of another cofactor. For example, cofactor of NADH, so NADPH, which can act as a reducing agent, and that will help the zinc. So, that means, the zinc active center, and then NADPH center should be close in proximity, and should get triggered together, all that requires that one. For that you have enzyme has a mechanism,

therefore, the zinc is involved even in oxidoreductases. In spite of the fact, zinc itself does not undergo redox.

Let us look at the next one. In most of the zinc enzymes, there are one or more water molecules are always bound to the metal center, this is true, you look at any zinc enzyme you always find either one or more. And there are some more waters close by also other than the coordination, but we are talking about the ones which are at the coordination.

So, what do you think the role of such a water molecules, so why these waters? Generally speaking when you have a metal ion, and having a water molecule on that, if a substrate comes in straight away, the substrate would more or less displace this water molecule. So, that means, in the resting enzyme in most of the cases the water is present, and when the substrate comes the water will go away.

Or in some cases, this water gets activated. For example, zinc and that activation is supported by a general base like carboxylic group, which is sitting close by which will abstract a proton from your O H 2, which is bound to zinc. Therefore, you will form zinc hydroxy. So, the most common things are either to replace the coordination by an incoming molecule or to convert the water into hydroxide, which is a nucleophile this is most. In fact, that is true in many other cases as well, in many enzymes the metal center may not activate the water to O H, but they use it as the position to be filled in for the place of the substrate.

So, when the substrate comes that will vacate, so, in other words the substrate displaces this particular water molecule, and this is what happens even in zinc enzymes too. Let us get to the next question, how does the enzyme carbonic anhydrase converts the C O 2 into bicarbonate, so obviously, to convert C O 2 into bicarbonate you have to add one more O H minus, so this is clue has come already.

So, what is the mode by which it binds to the zinc center, and explain a how one establishes the binding mode unambiguously. See for example, let us say the carbonic anhydrase, now the C O 2 comes either C O 2 has to bind to the zinc center or it has to be in the close proximity, so that the zinc center can do some kind of a reaction. In fact, in case of the carbonic anhydrase what happens is, the C O 2 does not directly bind to the zinc center initially.

The C O 2 as such is recognized by the protein, and it holds it is held by certain hydrogen bond interactions. In such a way that the zinc or hydroxy is in close proximity to the carbon center of the C O 2, therefore, the carbon center of the C O 2 this the gets attacked by the O H. So, the that is electrophilic center is a carbon the nucleophile is O H. So, a zinc O H attacks at this, and as a result of that it will bind zinc O C O, that O also makes with the zinc another transition state. So, you have a transition state is being formed, and this breaks down in presence of the water and gives the carbonate ion.

So, what is required, carbon dioxide should be recognized, carbon dioxide should be held in the close proximity to what to zinc, and in the proximity of the zinc hydroxyl spaces, so that is how it happens ok. Let us look at another question, how does alcohol is converted to aldehyde product by the enzyme alcohol dehydrogenase, so this is the again dehydrogenase. Alcohol dehydrogenase this is what we were referring to oxidoreductase. So, obviously, directly the reactivity is not happening as a zinc redox, but zinc helps in one binding alcohol also activates in the neighbor residue the NADH.

Therefore the reaction occurs, and the oxidation takes place. So, what happens to human if this liver was not if this enzyme was not present in their liver, obviously, we know that when say somebody takes the alcohol we say all your liver gets affected, that means, we know that is it grows into the liver, and the liver where the reaction occurs. So, if this enzyme is not there, the alcohol will not be converted to the corresponding aldehyde. So, obviously, alcohol remains as a alcohol this is a dangerous, obviously. So, the and that means, one cannot consume alcohol, if this enzyme is not present in their body, in their liver, so obviously, is required to have to the alcohol to be utilized.

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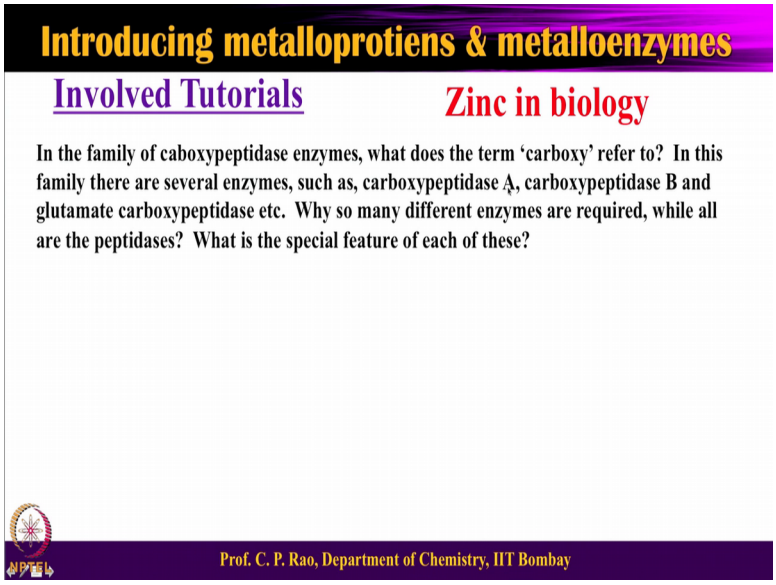

Let us look at one more query in this context of zinc in biology. In the family of carboxypeptidase enzymes, what is a term carboxy, referred to see? The carboxy here refers to the carbonyl part or the carbonyl N or the C terminal part of this. In this family there are several enzymes, such as carboxypeptidase, carboxypeptidase A, B and glutamate carboxypeptidase, so many things are there. So, why so many different enzymes are required, while all of these are? Yes, no doubt all of these are peptidases, but the enzyme has to recognize that particular peptide bond.

So, different kinds of the peptidases will recognize different types of the peptide bonds. What do we do typed peptide bond? All peptide bonds are same, but the one car C alpha on the left side, one C alpha on the right side, have got different R groups or same R group. So, therefore, that R group is the one which is differentiates. Suppose you have a aromatic moiety on this one, then a carboxy peptidase ok.

So, like that you have a negatively charged, positively charged you have a hydrophobic kind of thing. So, based on that different kinds of peptidases are required. So, therefore, the nature has developed variety of family of carboxy peptidases. And these are all the ones, which work based on the zinc ok, so ok.

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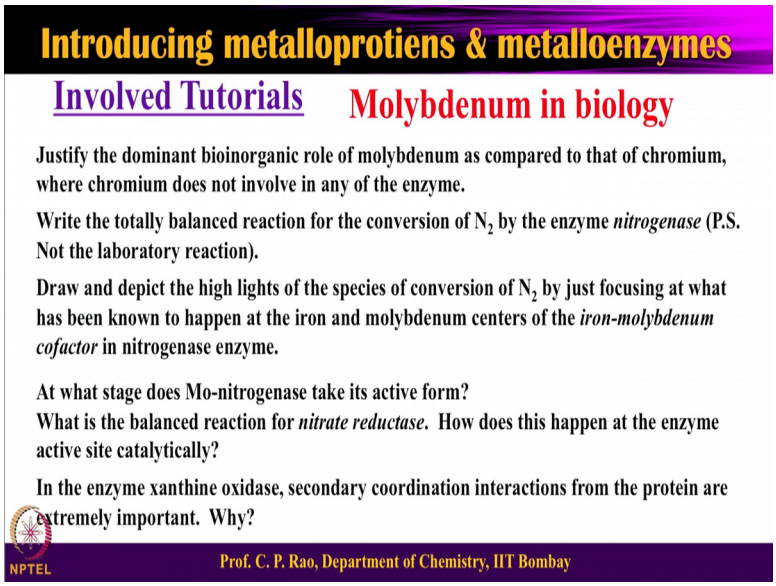

Let us move on to the topic on the molybdenum ok. So, the molybdenum ok, let us see some queries in that. Justify the dominant bioinorganic role of molybdenum ok, justify the dominant bioinorganic role of molybdenum that is played as compared to the chromium, where chromium does not involve in any of the enzyme. Why the question arises, is a chromium, molybdenum, tungsten, they are in the same family.

So, they are in the same family, why cannot one think that the, whatever the molybdenum is doing, why chromium has not done, it is a very interesting kind of thing. So, what do we need to think of we need to think of, because all these reactions the molybdenum are happening by their redox chemistry; by their oxophilic chemistry; by their oxo transfer chemistry. Now, if you use all these three points for molybdenum, all these three points for chromium, you will see the difference that the chromium does not have a suitable redox potentials as that of molybdenum because, in the enzymes as you will see later on, the enzyme will go from molybdenum 6 to molybdenum 5 to molybdenum 4.

Similarly, a chromium also has to go to chromium 6 to chromium 5 to chromium 4, and has to be stabilized. And the redox potentials have to pay about favor, also in the process oxygen should be added to the substrate, oxygen should be taken away from the substrate, which cannot happen by the chromium is not, so oxophilic as that of the molybdenum.

So, because of all these reasons the bioinorganic chemistry of molybdenum is more you know in the in the nature than that of the chromium. And in fact, no chromium is found still in any enzyme at all, because very strong reducing, very strong oxidizing, these characters of this chromium would be a disc favorable factor for itself not to be in the enzyme.

Let us look at the next question, write the totally balanced reaction for the con version of N 2 by the enzyme nitrogenase. Of course, here you have to take not a nitrogen reaction in a test tube or the nitrogen reaction by the an enzyme. Though the nitrogen requires six electrons, six proton, the enzyme requires eight electron, and eight protons and it gives not only 2 N H 3, but also gives H 2, and this hydrogen comes out first, and the enzyme is activated. And then only N 2 can get activated otherwise, it will not get activated.

So, therefore, total reaction by the enzyme must have both eight electrons, and eight protons. So, you can refer to my slides, and the lecture that I have give when you earlier. Let us look at the next one, draw, and depict the highlights of the species of conversion of an N 2 by just focusing at what has been known to happen at the iron and molybdenum centers of the iron-molybdenum cofactor in nitrogenase enzyme.

The nitrogen requires totally this enzyme requires eight electrons, eight protons. So, therefore, you have a each step, and first two electron, two protons will go as H 2, then the enzyme is ready to active accept the nitrogen. And the N 2 will be reduced by 1 electron, 2 electron, 3 electron, 4 electron and 5 electron, 6 electron. And correspondingly goes through all these intermediate steps, and then you have the final ammonia.

And there are different kinds of mechanisms, which I have given in the class, you can please look at that. At what stage there is a M O nitrogenase take its active form, I just now explained after the H 2 is evolved. What is the balanced reaction for the nitrate reductase, a nitrate to nitrite, nitrate to nitrite kind of thing, so it is basically reduction. So, correspondingly the electrons or taken in and one of the O goes as water. How does this happen at the enzyme active site catalytically, because initially the nitrate can bind to the molybdenum center, and then the molybdenum center undergoes redox, how many redox electrons are required here? Two electrons.

So, molybdenum 6 will go to molybdenum, molybdenum 4 will go to molybdenum 6, and the nitrate goes to nitrite. And then the enzyme, which is gone to 6 has to be read brought back to 4, and that is done by another system of enzymes like cytochromes, let us not worry about that at this stage for this question ok in the enzyme xanthine oxidase secondary ordinations interactions from the protein or extremely important one.

Yeah they are extremely important; because they have to recognize the substrate, when they recognize the substrate they will also favor its orientation. And if they are favoring orientation, the reaction can take place properly from the molybdenum center to that of the of the xanthine part of it.

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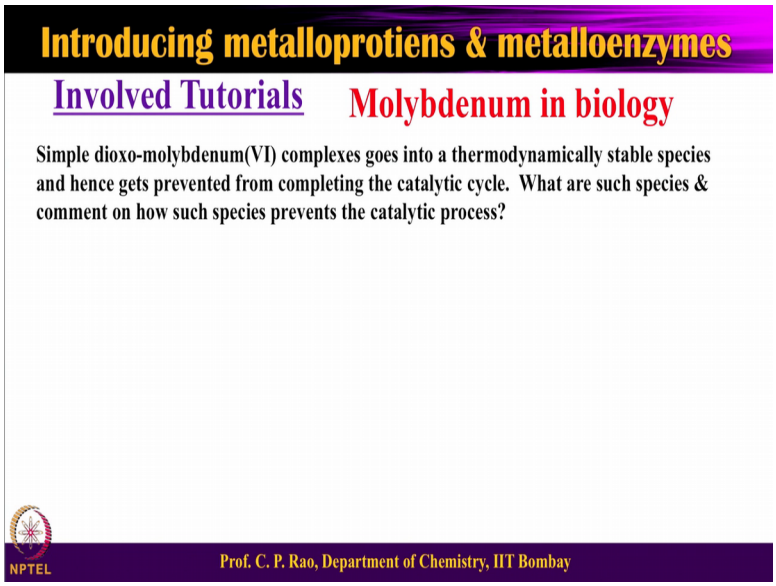

Let us look at some other also on the molybdenum. Simple dioxo molybdenum 6 complexes goes into a thermodynamically stable species, and hence, get prevented from completing the catalytic cycle. What are such species, and comment on a how such species prevents the catalytic process. What happens? If you take a simple dioxo molybdenum, and add some reducing agent with one electron, it will go to molybdenum 5, but such species two of such molybdenum fives can join together three oxo molybdenum. Just like I talk to you, when in case of the iron oxo oxygen bound species and reduced can get a iron oxo species.

Similarly, molybdenum oxo molybdenum with molybdenum 5, once that is formed it is irreversible, therefore, it prevents the catalytic cycle. So, what needs to be done, the

enzyme must be smart enough, that when it comes to the molybdenum 5 form no two molybdenum 5 unit should come closer, that means, protein should cover it up. And they will not form any kind of a dimer or mu oxo dimer ok. So, the species is the mu oxo dimer molybdenum 5, and you can easily find out this by the EPR spectroscopy etcetera. How much such species prevented here, yes once they are formed M O O, O M O O which is molybdenum oxo molybdenum with a bridged oxygen oxo molybdenum.

And this is the molybdenum 5 for each. So, this molybdenum 5 is a irreversible species therefore, catalysis is basically stopped ok. Let us look at some queries in the last part of the enzyme, that I talked to you on the mercury, and the talked to you on the selenium etcetera ok.

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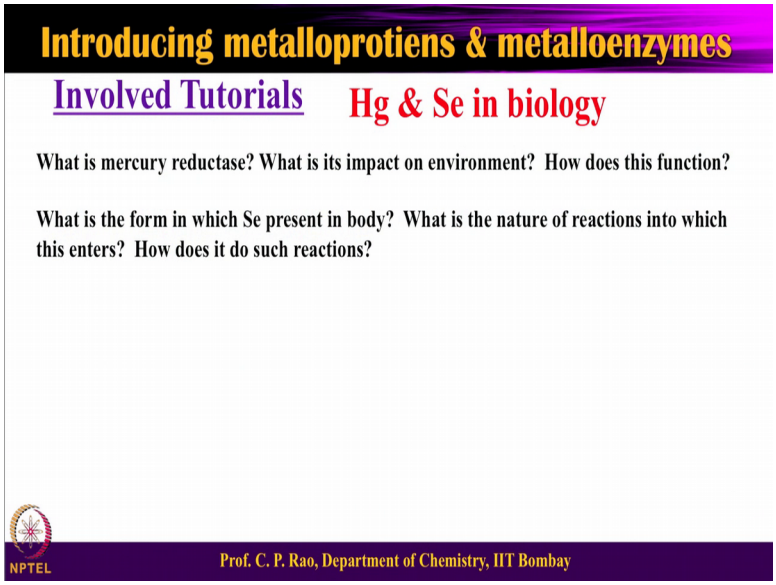

What is the mercury reductase? So, mercury reductase reducing the mercury, reducing mercury from mercury 2 plus to mercury 0 what is the impact on the environment? The mercury 2 plus, in fact, is a more dangerous species for the biological system. Mercury 0 is somewhat much less danger to the system that is why the mercury 2 plus toxicity is being reduced to mercury 0. In fact, this happens by enzyme called mercury reductase, this is present in a large number of a microorganisms.

Microorganisms obviously, are developed in the even in the environment. So, in the environment if we can create certain kind of a stimulation or the nutrients, these micro biology can grow, and these micro biology will generate the they will generate enzyme

called the mercury reductase, and that reductase will reduce mercury 2 plus to 0. How does this function? This enzyme is of course, is a complicated enzyme, but this enzyme works mostly on a thiol functions. Reduction is called cysteine oxidized cysteine is called cysteine or disulfide.

So, is a play chemistry play between the cysteine and disulfide, disulfide and cysteine. Cysteine is reduced form, disulfide in the oxidized form, so between these two, and that is how it happens ok. So, therefore, this is mainly play, so initially when mercury comes there are some systems, which will take up this mercury, but at that stage it will not happen, that will transfer to another site in the enzyme. As I explained in the class you can see the slide for that structures. And from there where the FAD, and NADH units are close by which will reduce the mercury 2 plus to 0, and oxidize the thiol functions into disulfide. And then that disulfide is again broken back into the thiol, so that your cycle is starting. So, this is how it functions in the biological systems ok.

What is the form in which selenium is present in the body? The selenium is not present as a selenium 0, is present present as a organo selenium, which is called selenocysteine. So, instead of sulfur assume S E everything else is same, and that kind of things, you know S S can bond to disulfur. Selenium and similarly, selenium can also bond with selenium with sulfur, selenium sulfur disulfide, the die seleno sulfide kind of thing. So, it can undergo whatever undergo is a undergo by the sulfide. So, therefore, this kind of the reactions occur in the selenium enzymes, where redox can occur as a selenium, and selenium with the hydrogen is called selenol just like a thiol, when it is have a hydroxy group S E O H, it is like equivalent to carboxylic kind of thing.

So, it can undergo all of these and as a result of this these enzymes called glutathione peroxidase. And thio redoxine thio redoxine reductase, and these all where the selenium part of the enzyme is involved. See I have gone through a large number of cases, and it is an idea of this tutorial is not to just give you the answers, but give you the approach along with the answer or approach and ask you to look at the at the slides, and this what I am done.

So, do not think that they for every case I give just the answer, no that is no use. Because, then that means, you have to mug, you should not mug, you should try to make yourself understand the subject. So, in effect what I have done. So, in effect what I have

done was, in the entire course I have done initially the teaching, the next part of that any in the teaching at every stage I every topic, I have made a conclusion for every super topic also I have made a conclusion kind of thing. And try to compare at each stage, it is a comparative way I have always been teaching ok. So, therefore, that is where I think it should be very stimulating things.

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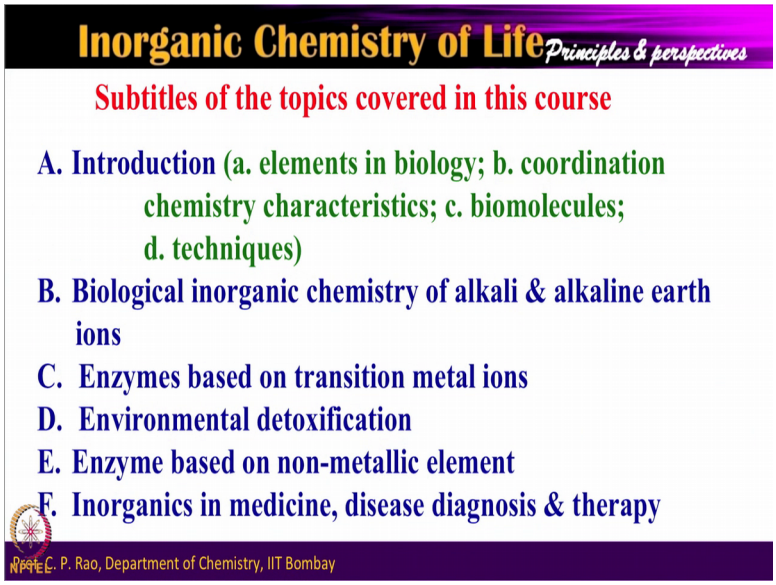

Subtopics I have concluded, super topics have concluded, and correlated also then at the end I have given something for 3, 4 hours I have given the highlights, which is again concluding every chapter that you studied earlier. Followed by that I have given last 4, 5 3, 4 hours the tutorials as how to address the question, I have told how to address; how to answer the questions by using the question itself by using our understanding of the thing itself; first we should coolly read the question; try to understand; try to see what with respect to the enzyme, what with respect to the chemistry point of view.

If you clump all of these, it will become the biological inorganic chemistry or inorganic chemistry for life. That is I have done the initial teaching part, teaching with the comparison to correlations and conclusions at every stage, super stage at the end of the thing, then towards the end I have also covered a large number of the tutorial problems given the approaches, how to look at this problem, how to make. Of course, I have given the answers also in a more or less almost every case except few, where you need to look at the exact slide for you to understand etcetera.

So, in the process I have done lot of introductory for 6, 7 hours, so which covers the general rules of elements in biology, then some coordination chemistry features or a biomolecules, protein synthesis kind of things, variety of techniques one of these I have given. Then I have taken aspects relevant to the alkali earth ions, biological perspectives, their biochemical aspects the binding strengths, and their trans binding versus transport relations, their transport things in the ATPases all those things I have been, case of cop the calcium the trigger functions are also in. Then I took a host of enzymes, transition metal based starting from titanium, because there is no enzyme, vanadium there are enzymes, chromium there are no enzymes.

So, therefore, I have not taken a manganese a lot of enzymes higher, there are a lot of large number of enzymes, cobalt large number of one only one enzyme, several enzymes, but one cofactor that is vitamin B 12, does a lot of reactions. Then nickel, lot of a different enzymes, and copper a lot of different enzymes, zinc also a lot of a different enzymes. Then I have gone to the molybdenum absolutely, large number of reactions, then I have talked to you mercury reductase, then I have talked to you selenium kind of thing too.

So, overall the more or less that is required to this, then I have talked to you an environment of detoxification, that is mercury reductase. Then I have talked to you a nonmetallic element like, selenium present in the glutathione peroxidase etcetera. Then I spent 3, 4 hours, or so on the inorganics in medicine maybe even more. And their disease diagnosis, and therapy aspects and thoroughly compare their effective things etcetera.

So, overall I try to build this course to suit inorganic chemistry of life, not just the bioinorganic chemistry, not just the biological inorganic chemistry, but inorganic chemistry of life. But at the level of principles and perspectives, because this is mainly targeted for masters, but as I said even the 3rd year B.Sc. students can be utilized, and a lot of Ph.D. students, it will be very useful thought provoking, and they can try to work on their research problems much more focused way.

Before I end my the last lecture, let me express my acknowledgments, see this whole task has been possible by the help of a large number of a large contingent of people. First and foremost is the NPTEL group, the NPTEL as a whole I thank them, the office staff as

well as the staff present at the studio, who have made all these things easy possible in the timeframe that we plan.

And more than this, I also need to acknowledge my course associates; I have had two course associates who also happens to be my own Ph.D. students, who are working in this similar area of a research, which concerned with this particular you know lecture series.

And They are the (Refer Time: 25:54) Narula and Srilatha Ponopally, I thank them very much for all the kind of support that they extended throughout the you know this recording of the all these lectures, making all the slides possible in a in a nicest form that it is. So, therefore, with this I would like to thank all the NPTEL, and my course associates. And more than that, I thank you all for you know taking up this particular course, of on Inorganic Chemistry of a Life Principles and Perspectives.

Thank you.