Metals in Biology
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Lecture – 01
Importance of Metals in Biology

Hello, welcome everyone, we will discuss Metal in Biology or principles of bio inorganic chemistry. I am Debabrata Maiti from IIT Bombay, the book we are trying to follow from this course metals in biology is that of principles of bioinorganic chemistry by Stephen J. Lippard and Jeremy M. Berg. Well as you know this course is mainly going to be about the metals not about you not about me, but by metals, what is the role of metal ions in biological system are they just spectator or they have crucial role to play? I think all of you understand perhaps metal has very important role to play.

We have two major avenues of study and that is to understand the roles of naturally occurring inorganic elements which is metal in biology. As you may know by weight more than 50 percent of living species or matter is inorganic, metal ion at the core of biomolecules controls many key life processes. They can be used as drugs as well as probes there are many metal ions that you are perhaps already familiar with playing a important role as drugs. We will see the mechanism of their accent and how they are modulating the overall activity.

Today in today's class mainly we will try to discuss how metal ions are taken up by our body, what metals are taken up, how different metals are assembled inside the biological system. More importantly how do cells regulate metal ion concentration so called homeostasis, what or how do the metal ions fold biopolymers, how is the correct metal ion inserted into its site? We will also try to see slowly different hydrolytic enzymes wherein metal ions plays a key role in hydrolysis reaction and metal is essentially acting as Lewis acid of course, you are familiar with metals playing a crucial role in our respiratory systems such as hemoglobin right that is found in biology.

We will also discuss in this course metal proteins which are involved in just the electron transfer nothing else, just one electron transfer processes. We also will see atom and group transfer such as simply oxygen transfer or oxygen activation and then utilize the oxygen from air for different substrate hydroxylation chemistry. Hydrogenas

bioorganometallic chemistry essentially other many different other metalloenzymes such as nitrogenase and many others that we will discuss. We have metal ions as medicine as we are mentioning also metalloneurochemistry or metallo metals in zinc nitric oxide others and others where it is playing a crucial role, we will also discuss the role of protein in these metal active sites. So, let us first look at what we have seen or learned may have already a little bit and that is these are different metal ions that is present and playing a crucial role in respiration right.

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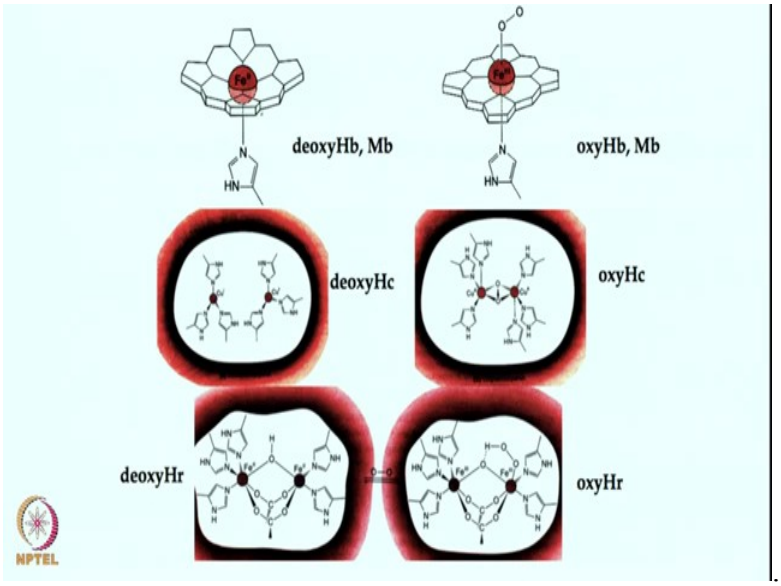

So, there are three different oxygen carriers which are distinct and known in biology the top one is deoxy hemoglobin on the left hand side where you have a porphyrin centers which is playing the key role. There is a iron (II) active site in the top one and the axial ligand is histidine as you know it is a imidazole part of imidazole is appended from the histidine and the axial side. There is oxyhemoglobin where oxygen is bound with the iron center to give oxyhemoglobin or oxymyoglobin.

We have when we do not have such a thing present such as these are these porphyrin iron centers are not present in some of the species then we have these di-copper iron centers which is ligated by 3 histidine unit on each of the copper center. We have these 2 copper center binding with the oxygen, so that is how the oxygen binds in an side-on geometry copper dioxygen species this is a completely reversible process. So, is the top one completely reversible process in this case Fe^{2+} is getting oxidized to Fe^{3+}. In this case 2

copper(I) centers getting oxidized to 2 Cu^{2+} center in and oxygen is reduced to peroxo by 2 electron one from each of these copper center.

Where even hemoglobin myoglobin or hemocyanin is not there we have this hemoerythrin or deoxy-hemerythrin which is responsible for the oxygen carriers in biological system. Each of these iron centers are supported by histidine in the first case these are 3 histidine in the second case there are 2 histidine. These pictures are taken from that principles of bioinorganic chemistry book by Stephen Lippard and Jeremy Berg. We have then once again these 2 iron center bridged by 2 carboxylate bridge 2 carboxylate moiety we have the oxygen activation at one of these centers to give these you know reversible binding between the deoxy hemerythrin and oxy hemerythrin, right.

Over all then we have different respiratory enzyme which is responsible for carrying oxygen from let us say in a human from the lungs to different part of the body. These hemoglobin or these porphyrin containing iron center that you just have seen a moment ago plays a crucial role in keeping us alive by transporting binding and transporting oxygen to deliver it at every possible position in our body keeps us alive, so these are respiratory metalloenzyme.

So, metal as you can see plays a very important role already right what within 2-3 minute of the class we realized that metals has importance in biological setup, right. Well as you have seen we have metal ion such as iron in hemoglobin supported by a bioinorganic chip called porphyrin. Porphyrin is a flat molecule, right. It has four nitrogen centers which is coordinating the iron both is in +2 state as well as its +3 state, of course higher oxidation states are also possible, but not in hemoglobin myoglobin cases.

Now, it is also a reversible oxygen binding; that means, it can bind with oxygen although electron transfer happens Fe^{2+} goes to Fe^{3+} during the process, but it is a completely reversible process. Therefore, once it has to release oxygen is not released as a reduced species one electron reduced species, but it is in native form in the dioxygen form it is getting delivered in different parts of the body since iron oxygen activation process is completely reversible in nature.

You let us just take a look at the porphyrin centers we have seen that it is a chip which is supporting the metal ion, but more importantly it has different peripheral carboxylate and axial ligand such as imidazole which is part of the histidine plays a crucial role in the

process. You should start drawing the porphyrin ring and practice how to overall draw it clearly without losing your slip you should must practice that.

Now, let us look at different electron transfer protein there are major metal units in electron transfer protein which are known as iron sulfur cluster, they are involved in electron transfer or electron relay process. So, they act as the relay station, many different such relay stations are there some of them are right over here.

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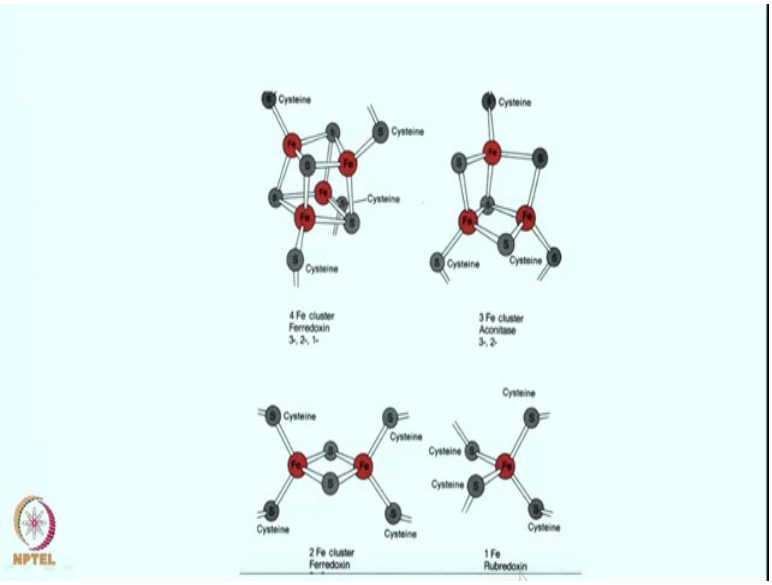

As you can see these are different iron sulfur cluster we have 4 iron sulfur clusters where this is a four iron clusters Ferredoxin iron are in different oxidation state three iron cluster Aconitase. We are once again iron are in different state we have two iron cluster ferredoxin which is once again a key center for electron transfer. Also we can have one iron Rubredoxin once again it is playing a key role in electron transfer processes.

Now, not only iron sulfur cluster there are other metal center even the porphyrin contouring center cytochrome C where one porphyrin ring and 1 iron center and 2 histidine on the two axial sites are responsible for the electron transfer. There are many other different metal centers involved in the electron transfer process they are doing just nothing else, but electron transfer process is getting facilitated by this center.

Now, of course, the question might be in your mind what is the necessity of these electrons and what is the role of the metal in the process? Well we will come back to

those queries little later as we go along in this course or of course, when we talk metal in biology or metals in biology we must be thinking about let us say sodium metal Na^+ K^+ there are channels right.

So, there are passive diffusion and ion specific channels to regulate or to modulate the concentration of metal ions in the cell or even outside the cell. So, all these are ion channels and there are selectively or they are selectively getting accumulated at a particular site of our body. And therefore, we need to see about these different metal ions how they are getting in and how they are getting controlled overall in the process.

Well at this point metal ions channeling or concentration maintenance can be done very precisely and scientists have understood to a decent level how these processes are happening. These are the lot of biological system being already studied and conclusion being that we have very simple principle behind controlling the concentration of metal ions such as sodium potassium in the cell and outside the cell.

Another interesting part of the bioinorganic chemistry or metals in biology is the organometallic chemistry, even the sensitive organometallic chemistry can be feasible inside our body that is quite amazing you know it perhaps. For example, Vitamin B12 we have a cobalt center which is supported by 4 nitrogen just like porphyrin right molecule and we have also a cobalt active cyano bond cobalt cyanide is involved in Vitamin B12 also we have different bio organometallic units.

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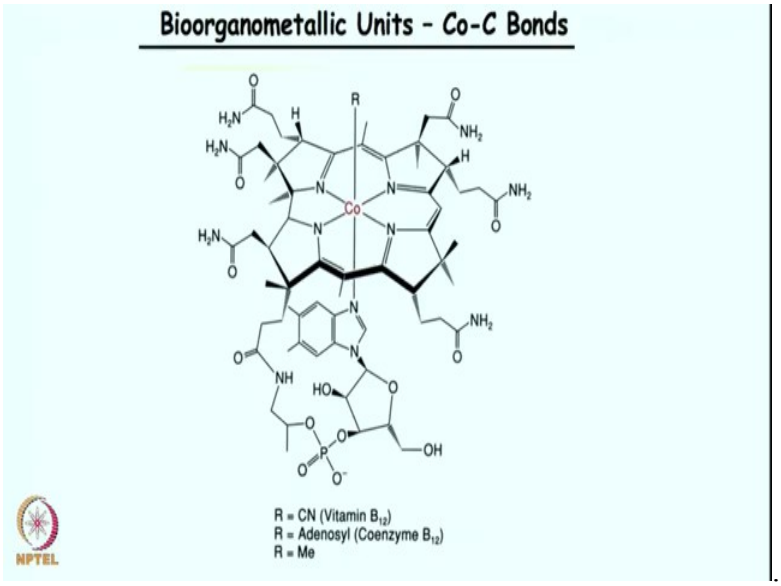

Let us see this you know this vitamin b 12 where you have a cobalt cyano bond.

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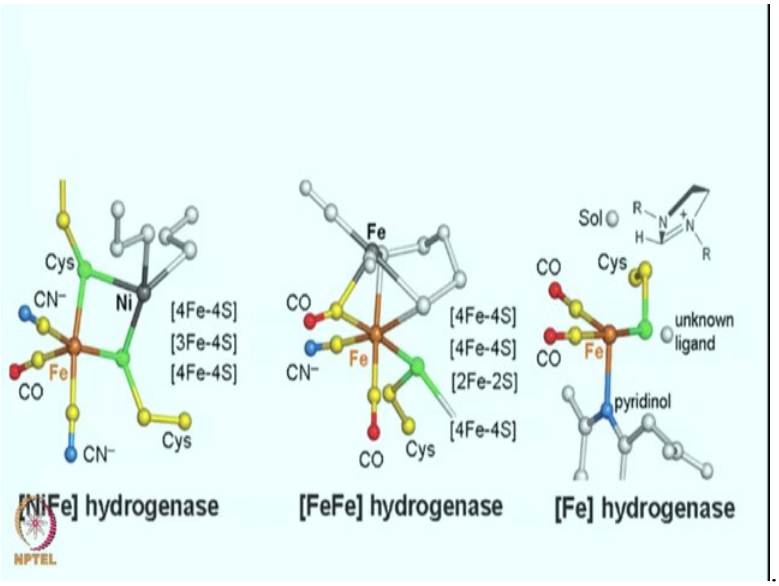

We also have these different bio organometallic you need such as nickel iron hydrogenas; iron hydrogenas and iron different other hydrogenases are also present. These are nothing but a great example of the organometallic species in our biological system which is quite fascinating I would say. Well as you know there are metal ions also present in many life saving drugs or very crucial drugs that indirectly or directly saves our lives. For instance we have different you know platin series of drug cisplatin carboplatin we have also our enough in barium sulfate which is involved for the gastrointestinal X ray contrast enhancement, but lithium carbonate also involved in the manic depression.

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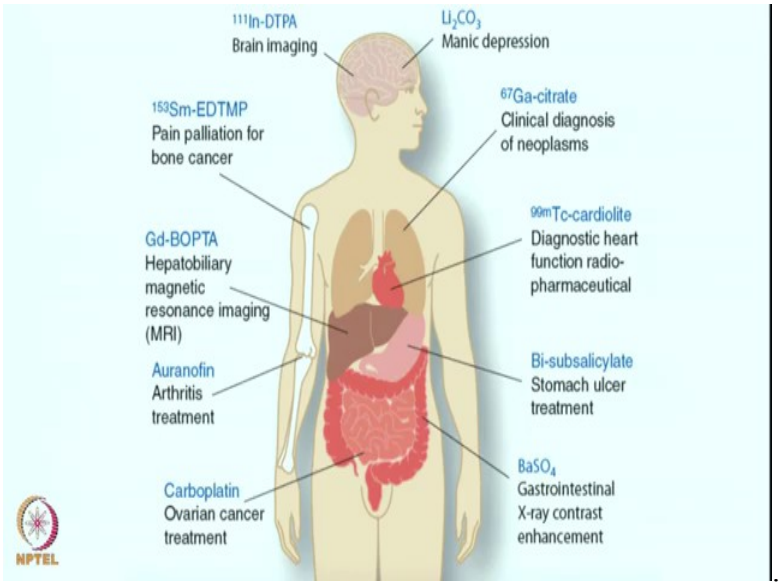

Here in some of the drugs in different part of the body as they have used, but all of them have one thing common that they are metal based and there is a ligand which holds the metal ions into these. Therefore overall I hope what we will be discussing in this class is how metal ions play a crucial role in our body, what metals are used, how they are taken up, and how they are assembled in our body, how do cells regulate metal ions concentration. How do metal ions fold a biopolymer which is having clear implications in several diseases amyloid beta peptide are responsible for their folding misfolding responsible for parkinson disease, alzheimer diseases and more importantly how is the correct metal ion inserted into it is site why not lets say for example, zinc is getting into the porphyrin site of myoglobin we have also different hydrolytic enzymes right which where metal is acting as a Lewis acid catalyst. As you have briefly seen metal can act as a electron transfer site oxygen chemistry both the reversible oxygen binding for oxygen transport and utilizing this oxygen for doing interesting synthetic transformations such as hydroxylation or even in other cases halogenation chemistry, even where oxygen has a role for halogenation chemistry such as chlorination and bromination. We have different hydrogenase enzyme, nitrogenase enzyme all these will be discussing subsequently in different classes under this course metals ions in biology where we are trying to discuss the principles of bioinorganic chemistry.

So, I hope in the first class the overall overview of this course is the importance of the metal ions in biology and to realize that more than 50 percent of our body weight is

metals. Metal ions are present in many different places of our body perhaps almost everywhere if more than 50 percent it is of our body weight that has to be in many different places and there must be a role a crucial role they are playing in our biological system.

We will see how they control these biological processes, how these metal ions concerned controls the biological processes, what is the mechanism of action. A lot of these studies are of course, still undergoing we have some understanding better understanding we will take perhaps decades centuries. But slowly we are realizing how we perform, how even our mood swing, what is the role of metal in that of course, a number of diseases more importantly are also associated with the presence, excess, folding, miss folding induced by the metal ions all these things we will be learning in the subsequent classes.

We will see you in the next class start studying I think as I mentioned the one of the book that you can follow and some of the slides which we will be discussing over here are made from these Lippards bioinorganic Lippards and Bergs bioinorganic chemistry and in other sources available in the internet or different other sources overall, we will try to discuss briefly and try to impress upon you that how important the metal ions are in our daily life.

With this let me come back to you and say you goodbye for the first class and we will be back in the second class soon. Thank you very much keep studying bioinorganic chemistry metal ions in biology.

Thank you.