**Biological Inorganic Chemistry**
**Professor. Debashis Ray**
**Department of Chemistry**
**Indian Institute of Technology, Kharagpur**
**Lecture No. 06**
**Coordination of peptide building blocks**

Hello everybody so now we will see about the examples of different biological ligands. So, how the biological ligands now will come into the picture of our discussion where we can talk about the coordination of the different peptide building blocks. So, we all know that how the peptides are forming the peptide bonds are forming.

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So, we will be discussing here that the different amino acids. Whether the simple amino acid can function as the ligand or not that we should know. And also that this particular one where we can have this understanding that you have the glycine. So, NH2 CH2 COH whether that simple glycine if you go to the laboratory glycine is available in the market you can buy it and you can see the coordination behaviour of glycine.

But when you go to the biological world in the biological field you will find that the glycine can be a component or a part of the polypeptide chain. So, how that glycine can function towards coordination. Then the different donor groups in the amino acids we will see. And we will find that these amino acid can function as the ligand.

So, as the glycine in some synthetic work also the glycine can function as the ligand and part of the polypeptide chain how it can function. Whether that can so any kind of coordination and most importantly the last one the pendant groups. So, you have the amino acid and the

amino acid backbone is there in one end you have the NH2 function in another end you have the COH function.

In between you have R which is the alpha carbon of the amino acid backbone. So, these R function can be of different types. So, what are those different groups we can have and whether those different groups can be available for the coordination to your different available metal ions.

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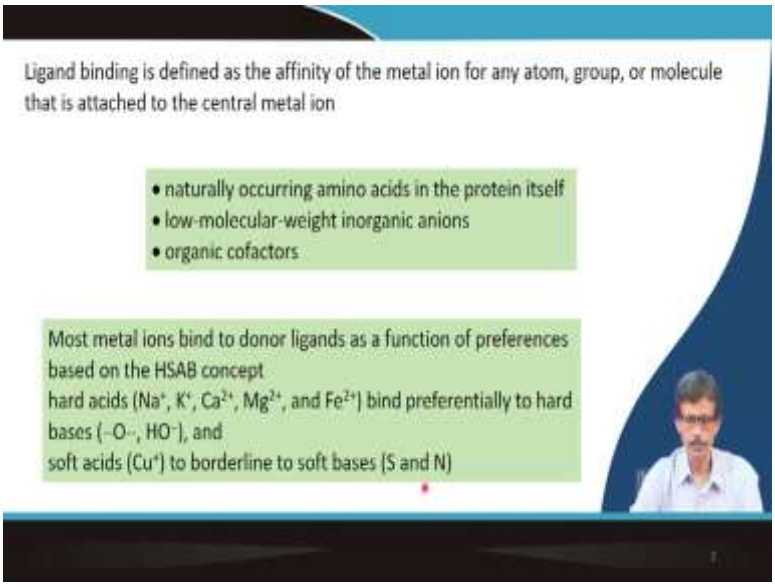


We will see. So, the ligand binding basically how we can define we define it as the affinity of the metal ion for any atom group or molecule that is attached to the central metal ion. So, basically what we get there that you have the central metal ions. So, any neutral group neutral molecule like that of your water or any other atom like chloride, bromide can also go for your bonding with iron center or some time a typical group.

They perk loaded group CLO 4 minus whether that perk loaded group will come and coordinate to your metal ion center that we have to see. Because in many cases you can have many such anionic groups and anionic groups means like your phosphate your biological phosphate we all know now that your DNA molecule your RNA molecule you have the phosphate groups. So, those phosphate groups whether those phosphate groups can function as a ligand or a part of the ligand or the ligand entity.

So, you have that charged species so the group of those atoms phosphorus and oxygen and the charged species. So, we will be talking about the naturally occurring amino acids those are 20 number. So, 20 such amino acid we will be dealing here in this particular class in the

protein itself. So, how the polypeptide is forming and what are the donor groups available for metal ion coordination.

And then low molecule inorganic anions like that of your perk loaded that of your phosphate or any other thing because phosphate can be inorganic phosphate you called Pi capital P small i substrate which is an inorganic phosphate that means is typical phosphate like your an iron of the phosphoric acid you have phosphoric acid which is H3PO4. And if you go for the corresponding anion formation is PO 4 3 minus.

So, that is inorganic phosphate but if you attached with some carbon some alkyl function or organic backbone on that phosphate or a sugar molecule or a part in the DNA or the RNA molecule you know those are inorganic phosphates. And sometimes we will talk about the inorganic cofactors whether these are organic cofactors and whether those organic cofactors can be useful for coordination or not.

So, here we will see that the most metal ions will try to bind or accept those ligands as per your HSAB principle. We have discussed earlier also once again we are seeing that if you have from sodium to iron 2 plus iron not 3 plus so they are also hard. The sodium, potassium, calcium, magnesium and iron they are hard so they obviously prefer the hard donor basis that means ether oxygen. Both the two sides you have the R r.

So, R O R is the ether group or sometimes you have the O any function on the phenyl thing. So, that can basically coordinate to your sodium or potassium or calcium and magnesium and sometimes these are also have the iron 2 plus, like way you know you have the crown ethers. Crown ethers like the your (())(5:44) just now what we have discussed instead of NH function if you have that ether functions O CH2 CH2 O CH2 CH2 O and you complete the cycle.

So, that particular O3 macro cyclical ligand can bind sodium, can bind potassium, can bind magnesium. But if you have soft acids copper is copper 2 plus is not soft is the borderline one. So, if you have the soft acid of copper 2 1 plus the reduced copper the cuprous copper it has either sometimes is the bottom line basicity or sometimes soft basis they will attract sulphur and nitrogen sulphur is soft and nitrogen is under borderline category.

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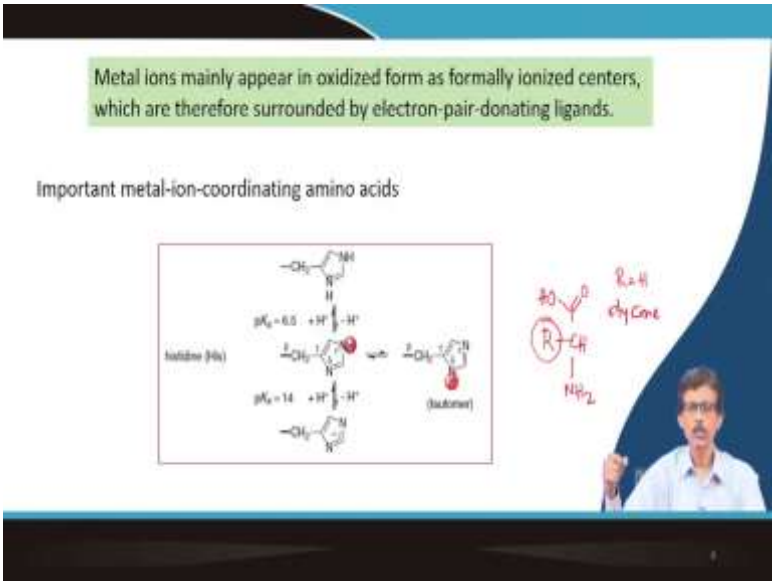


So, you can have the complete matching of these metal ions with the donor groups. But when they are appeared as oxidized as formally organized centers. Which are therefore surrounded by electron pair donating ligand so it is charged. It will attract the electron pair or it will charge the negative end of the molecule which can function as a ligand. So, important metal ion coordinating amino acids what we can have now.

So one by one so we have chosen some examples only how we can use these examples for this particular case that you have the histidine. So, that histidine basically gives us this particular one so this is the function r. So, this particular function if you can have so this particular function of R and this particular function what do you find that R is there. So, if you are the R and you have the backbone.

So, you have the CH you have the NH2 you have the acid function. We know that the glycine when R is equal to H it is glycine. Now this particular group can play some important role for metal ion coordination. So, one such example is your histidine. So, this histidine basically giving us that particular information where we get that how these R function is now your this particular case your R is now this CH2 and then another hydro cyclic ring.

These hydro cycling is nothing but your imidazole ring we call one carbon spacer between a penta cycle 5 atoms 2 of them are hetero, 2 of them are nitrogens. So, what do you get here that these 2 nitrogens can have some pKa value. So, 1 pKa value is 6.5. It can go for the corresponding change in this particular one and another is the pKa 14 when you can have the corresponding deprotonation at that particular point.

So, if you find that this particular one that means you have the corresponding tautomeric form. So, this particular tautomeric form is giving rise to this particular one. So, you have the port donation. So, this pKa for the protonation of these stutzeri nitrogen and this is deprotonation. So, in one case you have the protonated form and another case you have the deprotonated form and these two are the possibilities.

Then you have since then you have this carbon is your alpha carbon on the backbone. So, you have the beta then gamma then delta and epsilon. So, these two nitrogens basically is that they are the tautomer. So, you can have the nitrogen so these two are the tautomers. So, either this nitrogen can have hydrogen or this nitrogen can have the hydrogen. So, following deprotonation one of the nitrogen will be charged and the charged nitrogen will be available to your coordination to your metal ions center.

So, if you can have a big chain we will be seeing that in case of your myoglobin molecule. The globin chain will clump and the globin is a very big chain 150 Forbes or like that amino acid residues are there. And it will have one particular important that histidine residue and that histidine residue will be giving your nitrogen for coordination to our iron center for that particular case it is functioning as a mono dented ligand.

In our previous class we are talking about the synthetic ligand which is available to your thallium can so a mono dented coordination with the coordination number of 1. Similarly, the globing chain containing histidine residue can function as a mono dentated ligand towards your iron center in myoglobin in haemoglobin.

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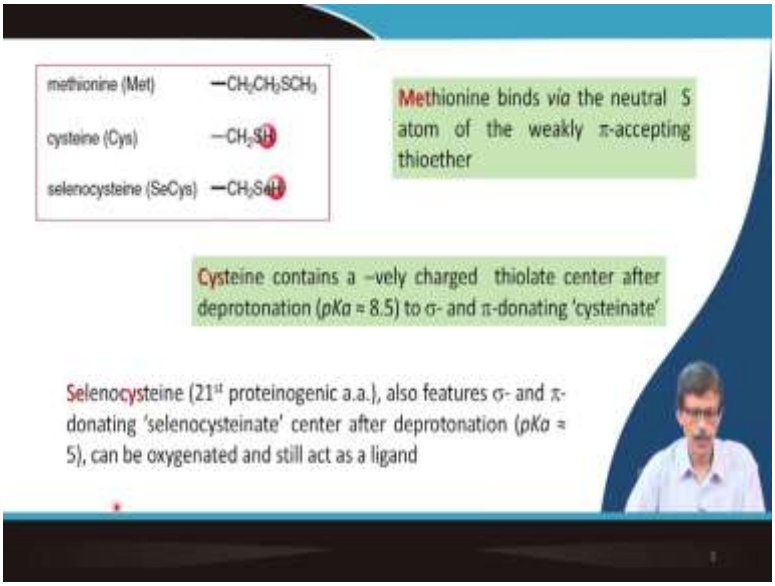

Then we can have others that means the methionine cysteine and selenocysteine. So, what we have seen that in this particular case how this methionine the cysteine and selenocysteine can coordinate. So, we know this is your like your ether this is thioether S methal. So, both the two ends you can have carbon S in between left carbon and right carbon so it is a thioether. But if these two are SH and this is SCH.

So, methionine binds via the neutral sulphur atom of the weekly pi accepting thioether without donor. This thioether donor is weakly pie accepting in nature. So, the nature of this coordination is important for this particular case. And we see that for the case of cysteine which is containing a negatively charged thiolate center after deprotonation. And through that deprotonation at a pKa value of 8.5.

It can function as both sigma donor as well as pi donating ligand. So, is a sigma and pi donating cystenate cysteineto cystenate. And it is abbreviated as CYS for the whole name of the cysteine. So, CYS is the name of the amino acid. So, if it is bound to the iron center in iron sulphur proteins will find that the cysteine will form an FeS bound. Then we can have the selenocysteine apart from your 20 list of 20 amino acids.

This is the twenty first proteinogenic amino acid and it can also like that of your cysteine can have both sigma as well as pie donating capacity. I am giving you the selenocysteine at an iron which can bind to your metal ion center. And after deprotonation it can be oxygenated and still can act as a ligand. So, if the sulphur can be oxygenated giving you is SO bound. So, directly like nitrogen giving you an oxide sulphur can also give you sulphone or sulfoxide.

We all know one oxygen and two oxygen. So, in sulfoxide so dimethylsulfoxide we all know is a very good solvent. So, is dimethyl sulphur so dimethyl sulphide and if sulphide is getting SO it is dimethylsulfoxide. So, that particular DMSO can is well known as a very good ligand. So, if these amino acid residues can be oxygenated or oxidized. It can still function as a very good ligand. Similarly, your selenocysteine.

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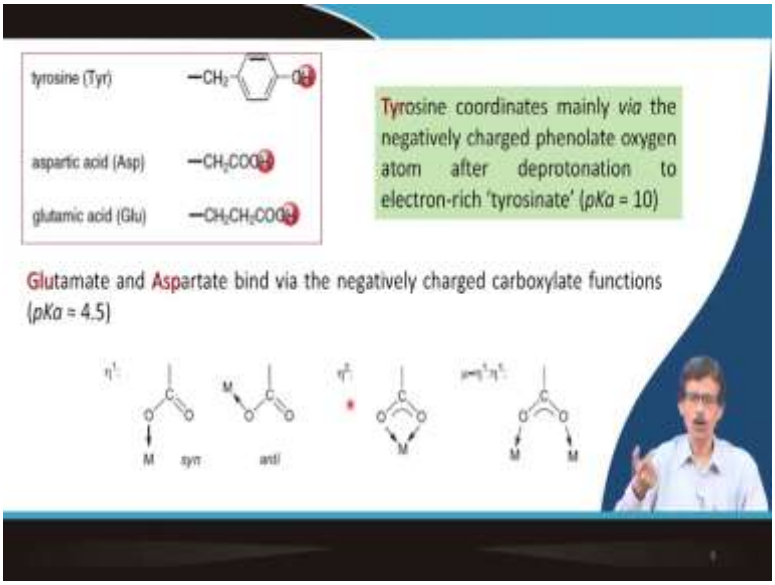


Then we can have the tyrosine residue, tyrosine has the odd group is CH2 PH OH function. Then aspartic acid and the glutamic acid and this tyrosine residue what you can have that if you see that this particular group is the pendant group and this is also a pendant group from the carboxy ends. And we will find here that after deprotonation so because the left hand side what you can have you can have this chain the polypeptide chain is here.

But after this polypeptide chain which you can have the coiling. So, coiling is going on from left to right and in between you have the pendant group. So, if you have the tyrosine amino the residue is the tyrosine residue. So, what you can have you can have the phenyl unit CH2 phenol is nothing but connected to your web CH2 function and the phenol part para phenol para hydroxy group to that have of your CH2 function.

So, is basically the pendant point. So, this pendant group after deprotonation you get something which is phenolate ion. And this if O minus can be available for metal ion coordination because it is coming down from the chain. So, chain is calling out chain is basically pulling from there and so this distance will be getting due to the presence of the phenol ring. And your metal ion here say.

So, if the metal ion so it can form a metal ion oxygen bond of that of your tyrosine residue. So, the tyrosine basically coordinates via the negatively charged phenolate at oxygen. If it is deprotonated that red part of the H can be deprotonate is nothing but a phenol all know is the weak acid. And you can have the charge and the deprotonation to the electron rich tyrosinate anion is forming with pKa value obtain only is the very weak acid.

So, the residue will be considered as the Tyr. So, that Tyr in the polypeptide chain, chain can be available to coordinate to your metal ion center. Then what about the other two which are based on the acidents. So, these acidents are not your primary carboxyl groups which are available in the amino acid backbone. This is the second carboxyl at end. So, those are the pendant groups like that of your phonology end.

So, the aspartic acid and the glutamic acids giving you the corresponding anions through deprotonation because these are acidic functions like your acetic acid. So, they can quickly deprotonate so most of the time in the biological pH. The pH in the micro environment the local environment of the metal ion they can remain as your corresponding anionic form that means the glutamate form or the aspartate form.

And they can bind through the carboxyl end now. So, from phenol end or the phenolate group it can coordinate to your carboxyl at end. How it can form the different bonds basically. So, that is a very typical coordination and we should have to go back to your coordinate and chemistry class basically standard codes in chemistry classes. Where we know that nomenclature the eta the hapto nomenclature for coordination.

So, when one of the oxygen so this particular oxygen you see the one of the oxygen. So, is not delocalized between this two oxygen also one is only charged. Since the localized charge on one of the oxygen of the carboxy end if it is O minus that O minus can coordinate to the metal ion center. So, what do we get then that this particular bond is forming and since these two oxygens on the same side and they are the other oxygen which is not coordinating.

But it is on the same side of that so the lone pair so you can have these lone pair over here. And the other lone pair on this particular side like your water molecule we have seen that the water molecule you can have this is the tip of this disease oxygen. You can have one oxygen lone pair directing to at this side and another is directing towards that side.

So, like that also you can have the lone pair over here and another lone pair of here when it is coordinating to this lone pair it is a syn coordination eta 1 syn, syn eta 1 coordination but when it is coordinating to the other lone pair it will be the anti eta 1 anti-coordination. Similarly, if it is in the collating form is a difficult one because it is forming a four membered ring to the metal ion center until and unless you have a bigger metal ion it will not form a collecting coordination with a four membered ring.

So, if it is formed it will be a eta two type of population. But the most interestingly and most importantly the mu eta 1 eta 1 coordination on the same side of the two metal ion centers. Which is syn in coordination and that syn in coordination is basically is going there. And basically we can have this particular coordination to these metal ions centers in such a fashion that though anti lone pairs anti lone pairs are not available and coordinating to the metal ion center only the cysteine.

So, this carboxylate function is basically coordinating two metal ions centers like that of the simple metal ion salt to you know like your copper acetate. From your school days you will are studying that particular structure and the geometry of the typical copper procedure which is the diamond. You have one copper acid copper center at the top and then at the bottom.

And then you can have the four acetate bridges you have a square plan at the top and another square plan at the bottom. And that each and every points the vertices of the square plan is connected by this sort of mu eta 1 eta 1 syn mu eta 1 eta 1 coordination and basically it is clipping these two copper plans CuO4 plans.

And then you can have two water molecules one at the top and another at the bottom. This is the structure of the copper acetate. So, these amino acid can also play a very useful role because it can vary from one coordination type to the other. So, you can have labial environment or changing partner from one metal ion to the other or from one species to the other it can form.

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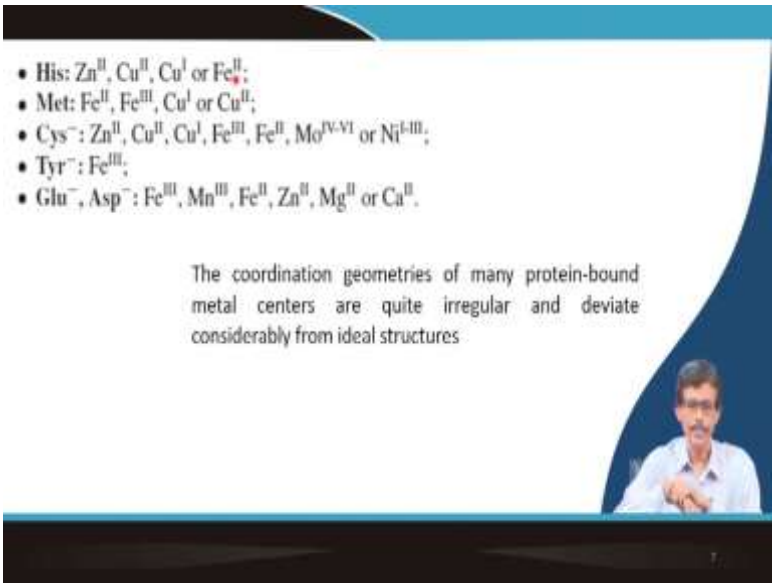

So, the matching point what are the matching species you can have that if you have the amino acid residue as histidine. If you can amino acid residue as the glutamate and anion or the aspartic at anion. So, what are the corresponding metal ions. So, this is roughly some examples basically you can have think of like these and you can have talk in terms of if you have histidine.

And if you have metal and center is Zinc which particular biomolecule will that talking about if it is histidine and copper what biological molecule we are thinking and talking about. Histidine towards iron 2 is the histidine of globin. If it is histidine of the globin so the globin can function as a mono dentate ligand and that mono dentate ligand of histidine from the globin chain can coordinate to the fifth chords inside after fortified in coordination.

So, for firing you can have 4 nitrogen at the tip of my 4 fingers. So, these are the 4 at the center you have the iron so this is the thing. Then I add from the bottom your that particular nitrogen from the histidine residue is coming and coordinating to that particular iron site. So, that is the histidine coordination for your myoglobin that is the histidine coordination for your hemoglobin.

Similarly, the methionine, the cysteinate coordination, the tyrosinate coordinates and glutamate and aspartate coordination for the different metal ions. So, they can also give rise to different geometries from the many protein bound metal ion centers are quite irregular and deviate considerably from the ideal structure.

Because what you can have the distortions you have a very big backbone backbone of the protein chains. So, those backbone of the protein chains are there. And you can have the corresponding strained coordination and that strain coordination is due to that you can have that R functions of the amino acid residues. And those R functions of the amino acid residues are coming and coordinating to the metal ion center.

But it is not that of your free water molecules are free ammonia or free ethuline di amino molecule. What do we get in your test tube or the reaction flux or the volumetric flux or the any other reaction vessel. That these particular thing are now restricted to have the restricted moment is not the free water molecule or not the free ammonia molecule will come and coordinate to your metal ion center.

So, you will have many such distortions like the distortions what we have seen the tacon substituted by 3 ethyl groups. So, 1 and 3 ring is different to that of your S3 ring.

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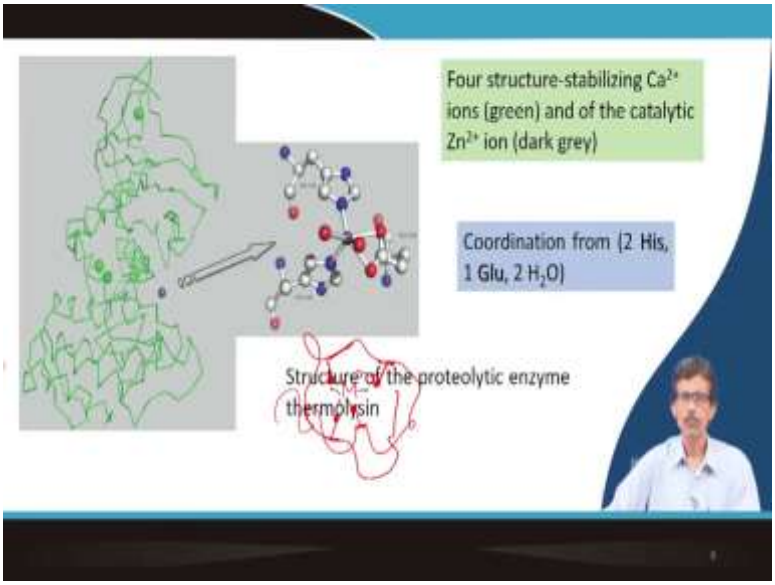


Similarly, these geometries basically can give rise to all these things all these facts in a very difficult fashion that how you get a very big molecule. So, the protein crystallography or the protein structure will basically give us that particular information where we find that what we get this particular thing that means this particular metal ions center. So, if you have this particular metal ions center as your m n plus and the huge molecule you can have.

Then this huge molecule the huge backbone basically these backbones are nothing but your basically the peptide backbone. The polypeptide chain what you can have so this polypeptide chain is there and you can have some pendant groups. You can have some pendant groups from the polypeptide chain. You can have some pending growth from this polypeptide chain and you can have some pendant group from this polypeptide chain.

Now if you can have some donor groups the nitrogen oxygen or the sulphur from these ends. They will try to form basically they will try to form now the different bonds. If 4 such groups are available, what we find? That you can have a geometry due to a coordination number of 4 only. It can be a square plan, it can be a tetrahedron, or it can be distorted tetrahedron, or a distorted square plane.

So, the example which is given over here is not only telling us that you can have this particular spear. So, spear said nothing but your corresponding groups which are your metal ions. So, the metal ion centers you can have. So, these metals ion center for from it is nothing but the structure of the proteolytic enzyme thermolysin.

So, is a proteolytic so the leases of the protein chain is responsible by this particular enzyme which is thermos lysine we all know is very much relevant to us also in our body also it is there. And where you can have the Zinc is your catalytic site is the dark grey spear. So, this is your Zinc and apart from that you can have other sides which are the calcium side so 1 2 3 4 calcium sides you can have.

So, what the role of calcium is flame so calcium is also coordinating and zinc is also coordinated into the donor groups. So, we have classified the donor groups which are available for coordination to your calcium. And which are available for to your zinc coordination. So these two not will be mixed up. So, the positions which are available for your zinc coordination is reserved for zinc. And the coordinates and pocket which is available for your calcium which is also reserved for your calcium.

So, we will get this particularly very useful structure and we will be able to locate the position of calcium as well as position of the zinc. But the this particular lytic function or the lysis function or the hydrolysis function is done by the zinc. So, what do we get here you see that this particular coordination the coordination what we are getting from two histidine one glutamate residues and two water molecules.

So, you have two water molecules. So, these water molecules bound to the zinc center they are better nucleophile compared to that of your free water molecules. So, the metal and activated water molecules will be superior nucleophile for your any kind of hydrolysis reactions. So, the thermolysin are very useful catalysts for these hydrolysis reactions.

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So, what we have seen in this particular class we can summarize in that way also. That the attractions of individual amino acid side chains the metal ions are attracting those side chains to certain oxidation states of metal ions are often characteristic resulting in a typical selectivity pattern that so I am telling the pockets are reserved for calcium and pockets are reserved for zinc.

Then individual oxidation states of these bio metal ions favoured the corresponding coordination environment. So, zinc coordination environment will be typically different from the calcium environment. Similarly, the iron coordination environment is different not only it is the reference of the metal and for a particular type of coordination arrangement or coordinates in geometry.

But also the structure of the protein environment or the protein envelope if your protein structure is a very big one and it is much more complicated. It will try to distort the environment very nicely such that you can have a more distorted environment around that particular metal ion. So, what we will see from here that this distortion is important. And one point we have discussed also that highly distorted state is useful for this activity.

So, the biological environment what we can have with regard to that of your metal ion that particular environment always try to have a distorted environment. Such that your reactivity will be higher if you have more symmetric arrangement your reactivity would be less. So, that is the corresponding conclusions what we have gathered from this particular part.

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Then we can have the references that Wikipedia on amino acids and the book of Crichton. So, thank you all for your presence and for your attention. Thank you very much.