Inorganic Chemistry of Life Principles & Properties

Prof. C. P. Rao
Department of Chemistry
Indian Institute of Technology, Bombay

Lecture – 04
Biomolecules

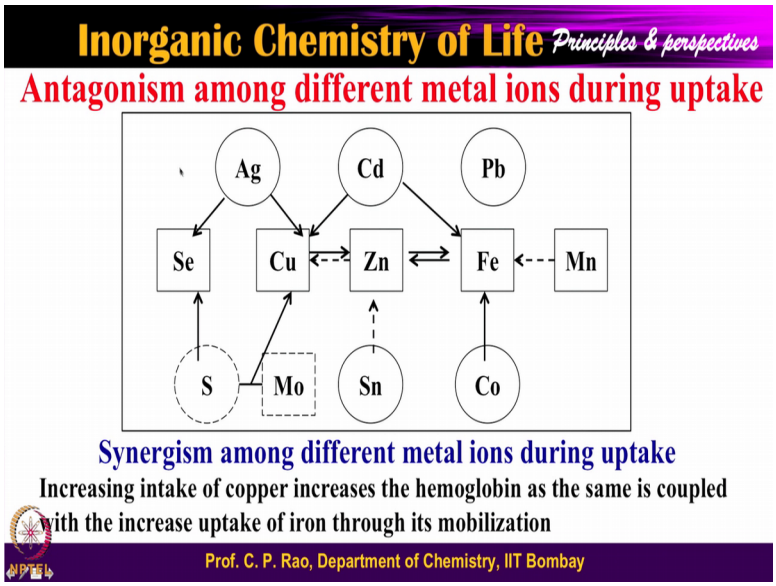
Welcome back to the next lecture on Inorganic Chemistry of Life Principles and Perspectives. Let us get a bit of recapitulation of what we have looked it in the past few lectures. So, what I talk to you hopefully you got impressed on that is that, the inorganic element or species should be a part of the biological system. Number 2 is exhibiting a function, number 3 concentration of the elements are important of the essential phrase and essential ultra trace elements, higher concentration is a problem which is called toxicity lower concentration is also a problem, which is called efficiency; we have looked at all these.

So, there is a certain level of concentration of each of these ultra trace as well as trace essential elements to be present to have a healthy life of a any life being, it could be human or other. So, that is another aspect; the third is only certain elements have been picked up by the nature not entire 118 elements of the periodic table.

The reasons probably could be not just the concentration of these present in the earth crust, rather their coordination chemistry properties, their thermodynamic properties like stability crystal field stabilization energies, their kinetic properties like kinetic controls, reactivity, liability etcetera. So, therefore, the coordination chemistry, liability and stability these are some of the important terms, which I will be covering a bit later 1 or 2 lectures from now. So, I will be covering that ok.

Now, so having said there are yeah I also have explained to you in the previous lecture absorption. So, absorption example I have taken was the iron. So iron absorption where human, from human to the intestine from intestine to blood ok. So, when these kind of thing happen, it is not that only one element is absorbed, we have several elements which absorbed simultaneously.

(Refer Slide Time: 02:38)



So, in such a case there could be positive kind positive kind of an interaction, there could be a negative kind of interaction between element x with respect to the element y or with respect to element z. Assuming that element x, y and z are being absorbed. So, let us say there are 3 or 4 several elements are absorbed by the body, then when they absorb there is a inter interactions. These interactions can be negative, these interactions can be positive. So, what is negative, what is positive?

So, negative is as follows let us say when the element x is taken more and more by the tissue, the y is taken less and less by the tissue. So, when concentration of x is increasing means concentration of the y is decreasing such a kind of thing is called what I am referring as a negative interaction and this as a name in the literature which is called Antagonism.

So, x increases y decreases, the absorption levels that is called antagonism. Now the second possibility which you can easily guess is that, x increases y also increase so; that means, x and y both the concentrations increased parallel together ok. So, that is referred as Synergism.

So, antagonism; synergism, now this we are talking about 2 elements, but there can be several elements which are taken up, and we have seen totally there almost about a dozen elements, which are ultra-trace and ultra-trace elements. So that means, all these trace and ultra-trace elements can be in dynamic equilibrium, they can be competing with

something either in a positive way or in a negative manner and that is what is shown in this particular. So, please kindly have a focus at this particular slide and let us take one example.

Take copper-zinc. Copper and zinc there is a line, a solid line connecting this and there is an arrow from copper to zinc; what does this mean? This means as the concentration of the copper increases, the concentration of the uptake of the concentration of the zinc decreases and this is what is what is antagonistic.

Now what is the reverse? The reverse is a broken line arrow; that means, as the uptake of zinc is increasing concentration of the uptake of zinc is increasing, the concentration of the copper is not so much affected, there is a little difference is there. So, that x is explained by broken line and solid line. So, solid line means they are coupled strongly, the weak line means they are coupled weakly; these the broken line.

And arrow directions means from left to the right towards the arrow; that means the one which is antagonistic into that direction. So, copper to zinc. So, similarly you can see a silver to copper. So, as the concentration the silver keep increasing by the organism taking, the copper gets decreased similarly cadmium uptake increases that will affect the copper uptake ok. You take another example zinc versus iron. So, zinc increase will affect the iron, iron increase will affect the zinc equally well ok.

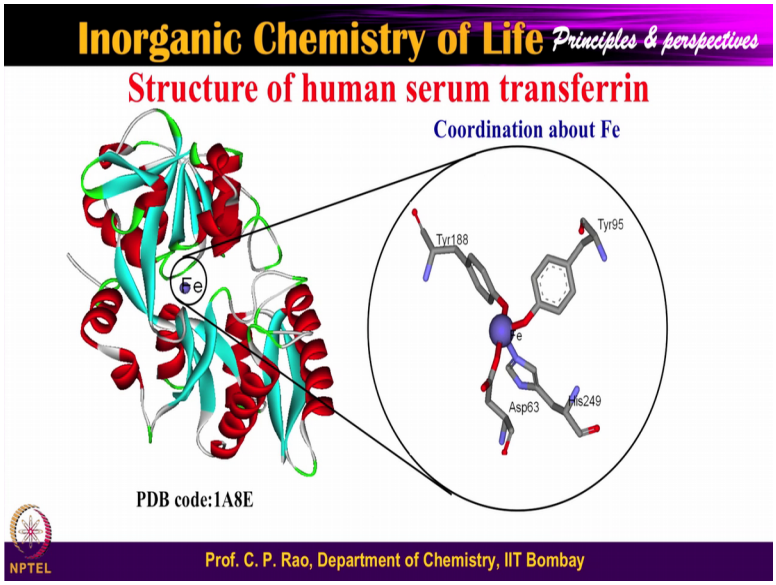
So, like that you can see all these kinds of a thing. So, in other just let me give one example for the synergistic part. So, synergistic for example, as you increase the copper, the as the organism takes more and more copper salts a copper ions into the body what happens? The iron the hemoglobin is increasing. So, the hemoglobin; that means, iron uptake is increasing ok. So, the iron uptake is increasing in this ok.

So, therefore, we have seen antagonistic parts, we have also seen synergistic part. So, copper iron relation is synergistic, copper zinc is antagonistic, zinc iron is antagonistic, but copper iron is synergistic. For example, manganese increase, do affect iron absorption but not so, strongly. Cobalt uptake will definitely affect the iron, but the iron uptake does not affect the cobalt because there is no arrow in this direction reverse direction.

So, molybdenum in the form of sulfides can affect copper. So, more and more bundle of sulfides and less and less copper being taken in it. So, these are the kinds of things so; that means, so, it is a very complicated equilibrium over competitive equilibria existing in the body, when they are absorbed by the body by the tissue ok. So, this is not while eating this is when it is absorbed by the by the intestines, when it is absorbed by the blood when it is released to the blood that competition can be understood ok.

So, I hope you understand that. So, having too many in the in this particular in a periodic table, the elements which are essential and ultra-trace element ultra-trace elements. So, both these affect the inter concentrational uptake. So, copper will antagonistically affect the zinc, zinc and iron will antagonistically affect each other that is the kind of thing that we have. So, this is a very interesting kind of a phenomena. So, this leads to internal increase and as well as decrease in this; that is why balancing is required. So, that is why you need daily supplements of each of this ion as I mentioned earlier ok.

(Refer Slide Time: 08:48)



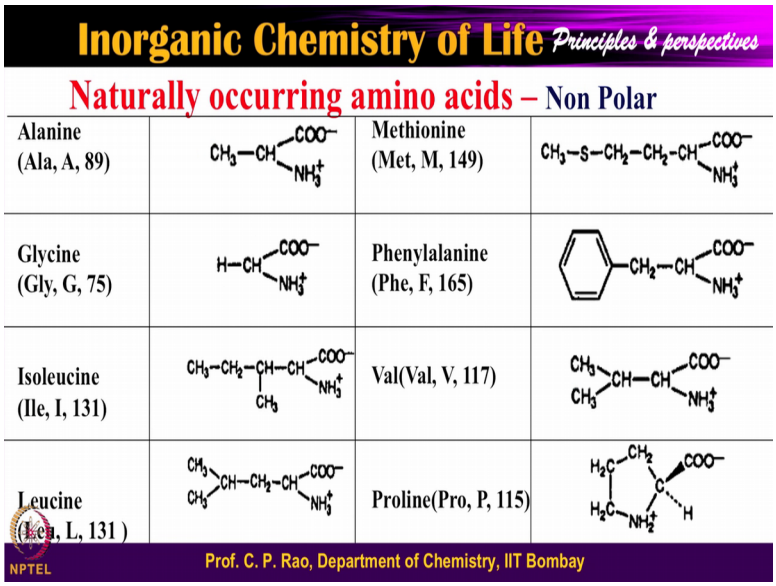
Let us look at go back and look at what we have seen earlier. So, this is one of the example I have shown that is called the transferrin; transferrin this is a whole thing is protein, this is a iron.

Now, if I zoom the iron region is here. So, the blue centre is the iron and you have some connectivity with the red, some connected with the blue the red etcetera. So, what are these? This is a side chain of the tyrosine, this is a side chain of the tyrosine, this is the

side chain of the histidine, this is the side chain of the aspartic. I will explain you the amino acids bit later and then it will become much more clearer what I am trying to say ok.

So, let us look at the aspects what are the amino acids. In the previous slide I mentioned when you look at the when you focus at the iron centre, there is a tyrosines 2 tyrosines one histidine one carboxylic, which is coming from the aspartic. So that means the iron ion is connected to the phenolate of the tyrosine, phenolate of the tyrosine, nitrogen of the imidazole of the histidine and carboxylic of carboxylate oxygen of the aspartic. So that means amino acids are capable of binding to these metal ion centers.

(Refer Slide Time: 10:16)



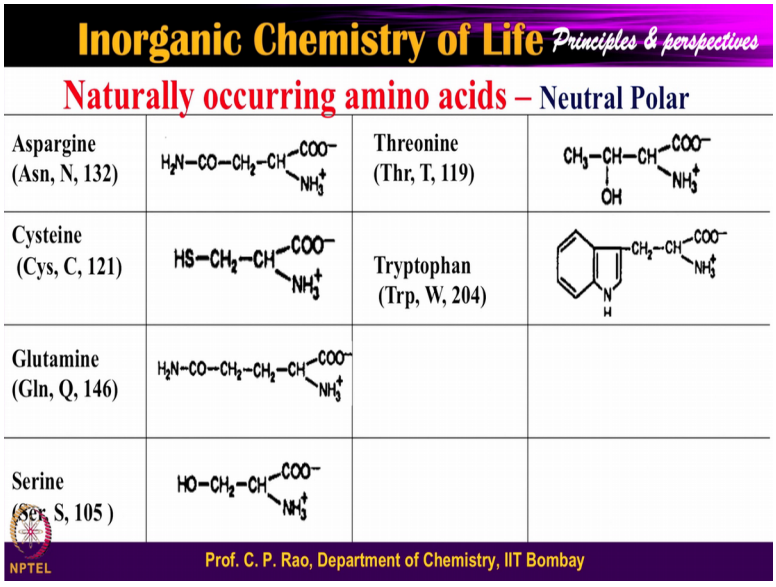
So, let us look at for a while, what are the kinds of side chains you have. So, let us look at the side chains. So, we need to look at the side chains because these are the side chains which are left out for binding, not the main chain; the alpha carboxylic alpha amino these are involved in the peptide bond formation.

So, what is left? What is left is only the side chains. So, therefore, let us put some effort in looking at the side chains. So, one of the side chain here alanine is the methyl group, a glycine hydrogen, isoleucine this is the brittle kind of a moiety, the leucine butyl but isobutyl kind of moiety etcetera. So, these are all non-polar as you know metal, butyl all these kinds of things are non polar. And in some amino acids you have the S CH 3 group

and you have a phenyl group, you have a propyl group, you have a 5 membered kind of a group.

So, all of these side chains are non-polar. So, all of these side chains have no specific affinity or ligating centre if one were to consider to bind it to the metal ion. They can only add to the hydrophobicity, but they will not be able to add anything to the binding part of it. So, one part of the amino acids non polar amino acids we have looked at and we have looked at their side chains.

(Refer Slide Time: 12:04)

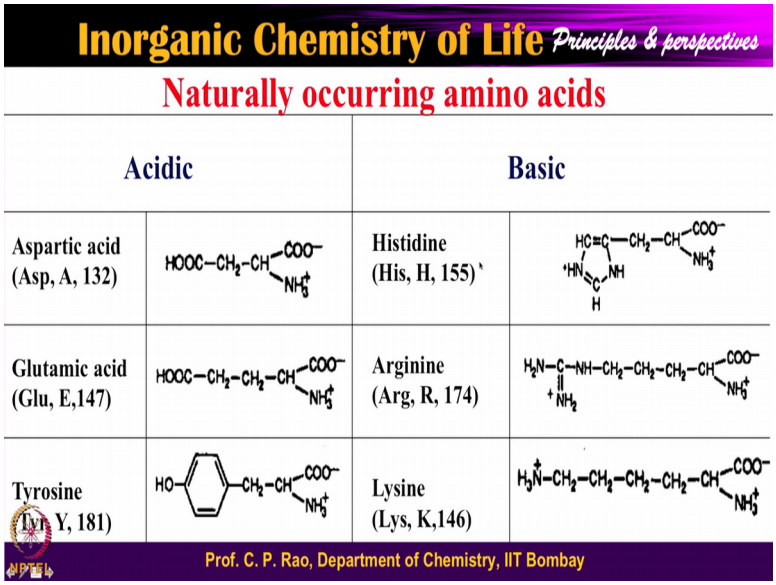


Let us look at some other amino acids. So, here we have a polar, but they are neutral non charged neutral means non charged ok there is no charge involved in this. So, therefore, you have for example, here you can see that there is a CO N H 3 group. Now C O is a dipole N H 2 is a dipole. So, therefore, you have a polarity of this and here CH 2 SH; SH is a dipole CH is also a dipole. So, therefore, you have a polarity and you can see in this CO N H 2 and CH 2 OH. So, these are asparagine, cysteine, glutamine and the serine. So, these are the 4; look at on this side we have CH CH 3 1 OH, so obviously, this is a dipole. So, this is a polar.

And we have the ring indole kind of a ring again you have a dipole. So, therefore, all this dipoles are leading to the polarity of the molecule ok. So, in the previous case we have only the alkyl or aryl groups. So, which gives the hydrophobicity, which are non-polar

and in this particular case we have a polar, in other words we have a groups which are a dipole and therefore, dipole gives the polarity.

(Refer Slide Time: 13:36)



Now, look at a few more which are charged. So, the charge will come a little differently when you are really looking at; these are called acidic type, these are called basic type. So, the acidic we have aspartic acid, glutamic acid and tyrosine and basic is you have a histidine, ah we have a arginine, we have a lysine and these are mainly the charged species and these are non-charged, but acidic because you can see carboxylic group and when this carboxylic group looses the proton it becomes carboxylate, it is an excellent group for binding to transition metal ions.

In fact, if you have ever studied the coordination chemistry, you would see lot of examples are coming basically from the carboxylate kind of a moieties a lot of examples will come. And this is glutamic the difference is only one CH 2 group extra, in glutamic as compared to aspartic. And here if you lose this proton then becomes a phenolate then you know the phenyl. So, these are all acidic protons acidic groups and this on the right side you have the basic groups in the right side you have the basic groups ok.

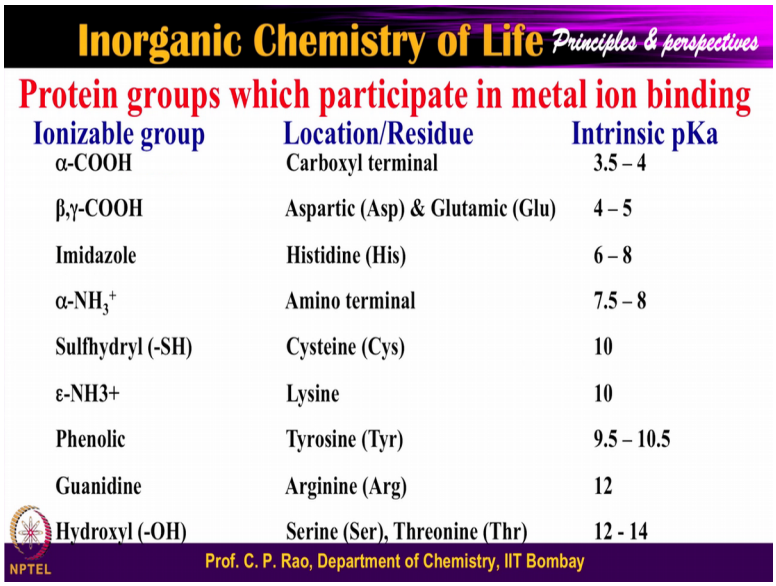
And this when it loses the proton it becomes neutral and it will bind happily, if it this also when it loses the proton it can bind happily, also here too or they can also bind to negatively charged pieces. So, this positive you can bind to the negatively charged thing.

So, they can either bind to the negatively charged pieces or lose the proton and bind to the metal center; either here or here or here these are called histidine, arginine and lysine.

Now, we have seen amino acids based on their side chains, one is polar and non-polar ok side chains where you have a alkyl l then we have polar some kind of a dipoles are attached then we have acidic and basic and then we have some with the positively charged where when the proton goes away, then they are ready to bind to the system. So, I hope you can have a look at after this lecture, these kinds of things how they can bind where they can bind etcetera. We are referring to only the side chain not the main chain part.

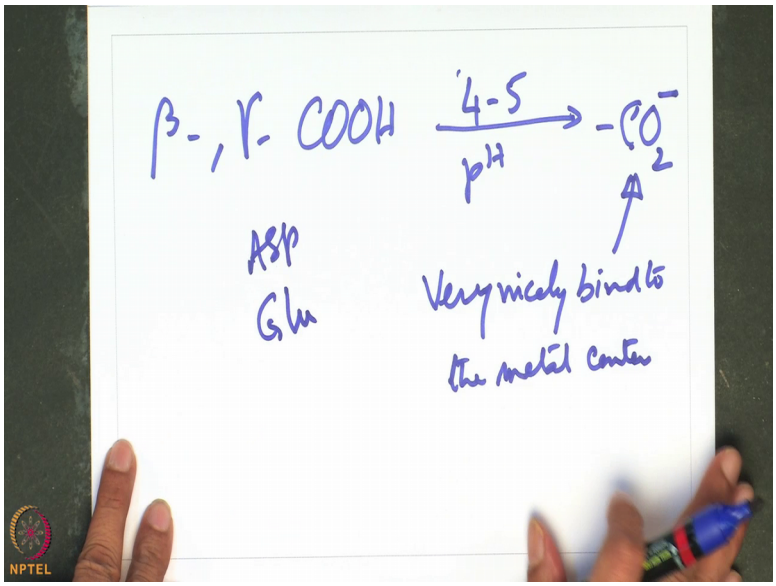
So, please ignore this because these 2 are utilized in binding due to the peptide in formation of the peptide bond.

(Refer Slide Time: 16:10)



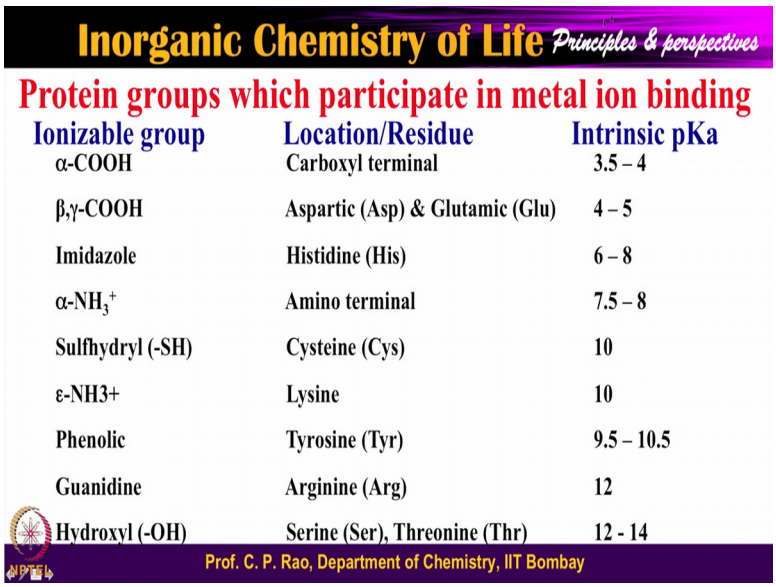
So, having looked at the amino acids of this I also said some of the side chains are legating centers and they can happily bind, some of them cannot bind let us look at those, which can bind. So, here this particular table tells which are those things can bind ok. So, this is not from the binding alpha COOH pollute and beta and gamma these are coming from aspartic and glutamic. So, they can deprotonate at a pH 4 to 5; that means, when the local pH in the biological system is 4 to 5, they can still be in COOH is converted into COO minus.

(Refer Slide Time: 17:00)



So, what you will find in this is the beta and gamma kind of a COOH groups ok. So, when the pH is 4 to 5 pH, so they or as a carboxylate and this can very nicely bind to the metal center. So, this is a ligane and ligating center ah this. So, this can come from aspartic, this can come form glutamic acid. So, you have imidazole. So, in the imidazole you have histidine ok.

(Refer Slide Time: 17:46)

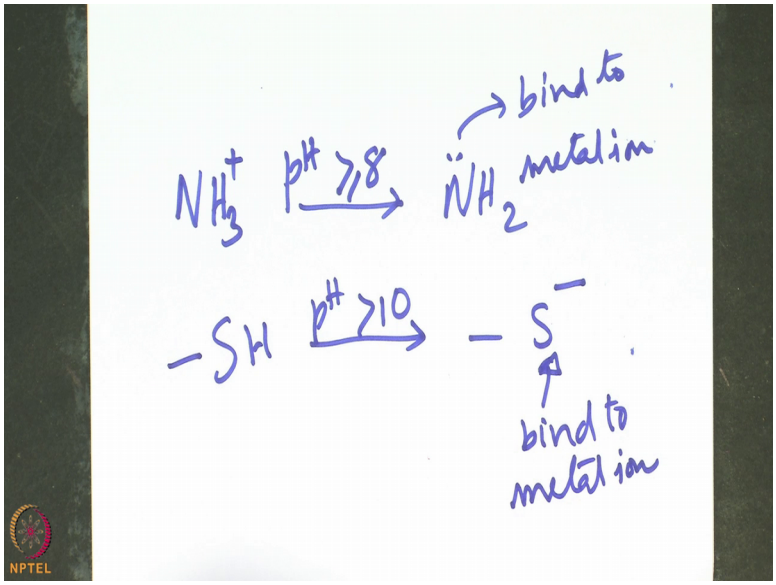


So, histidine is there; the histidine can lose its NH proton in the 6 to 8 pKa or pH. So, at this stage this is active to bind to the metal centers, this can very nicely bind to the metal

centers imidazole and then if you have a ammonium ion you require little bit more basic condition to be removed.

So, if you have that you remove you can increase the pH, then it will be. So, that it means in those regions the proteins where the pH is around 7.5 to 8, even the ammonium ion can bind because it is no more ammonium ion and it is basically amine.

(Refer Slide Time: 18:39)



So, it is like this any kind of an NH 3 plus can at greater pH can become NH 2 and this can bind to metal. So, when pH is greater than or equal to 8 ok then you have sulfhydryl function; it requires a bit more, basic can pKa is 10 only around 10 this can form the thiolate. So, suppose you can write this is as SH so, SH at pH greater than 10 can become S minus.

So, this can bind to metal ion ok, so, as you can see that ok. Next one is ammonia ion. So, ammonium ion can also lose this proton and then tyrosine phenolic, which is around 9 and half to 10 and half can bind guanidinium, which is a cation at pH 12, it will lose the proton and then it will form the in neutral and neutral can bind to.

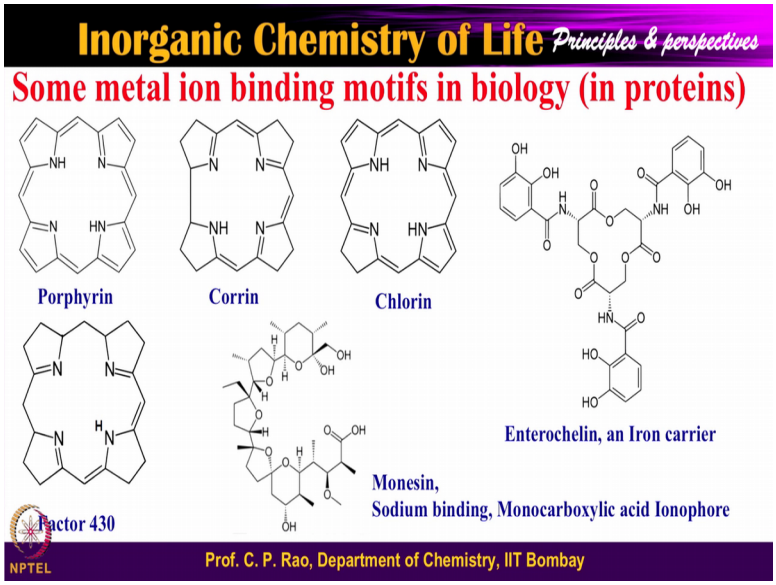
And then when you have serine or threonine then you have a OH, and this OH can be taken out the at 12 to 14 pH. Now in a while I will explain you how one can visualize and understand this. So, what you have seen now is that, you have seen some of them

can be deprotonated 3.5 to 4, some of them bit above 4-5, some of them around 6 to 8, some of them around 10, some of them around 12, some of them around 12 to 14.

So, what do you understand from this; that means, to remove the proton from that particular group as you go down from here to here, it is bit difficult which means you require more and more basic condition and is go this direction reverse and less and less, even it acidic pH the carboxylic can be something like 4 to 5 pH; what is 4 to 5 pH? It is basically an acid. So, 4 to 5 pH is acidic pH. Even in the acidic pH glutamic and aspartic acid as long as the pKa pH is greater than 4 or 5 it will be present in the form of COO minus, it is what you should understand.

So, go from up from top to bottom from you go from top to bottom in this here. So, it is becoming difficult to remove the proton. So that means, what this tells you carboxylate always bind so easily, they followed by then the amine centers or imidazole centers, then followed by the sulfhydryl center or tyalate and then followed by the alcoholic centers. So, alcoholic OH are the weakest systems requires strong base for you to remove that ok.

(Refer Slide Time: 22:04)



So, what we have seen till now is that, all those side chains shown in the previous case are capable of binding to the metal ions and therefore, they are called the ligating centers and then you get some coordination kind of a situation, they bind to the coordination coordinating situations into this one's ok. So that means, the aspartic is capable of binding to the metal center, glutamic is capable of binding to the metal center, histidine is

capable of binding to the metal center, cysteine is capable of binding to the metal center, lysine is capable of binding to metal center, tyrosine is capable of binding to the metal center, arginine is capable of binding to the metal center hydroxyl like serine and threonine, but not at the same pKa, they require different kinds of pKa levels in the system. So, therefore, that is where. So, therefore, in the proteins you have a different pockets, the pockets pKa will be different. So, therefore, you can expect the such a kind of things to bind to the metal center ok.

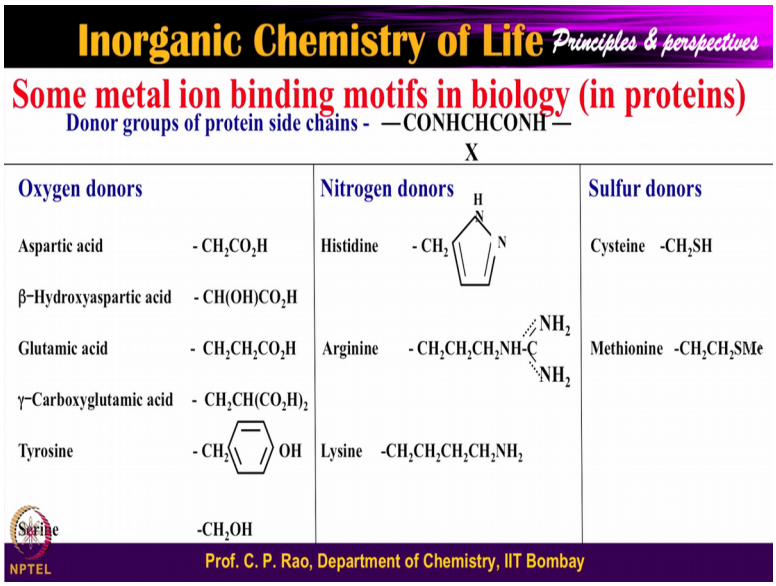
So, and also there are some additional kind of a motifs we find in the biological systems, other than the side chains. For example, these are given here; porphyrin, corrin, chlorin this is not nothing to do the Cl, this chlorin is a term, but this is found for nickel enzymes, some of the nickel enzymes and then also factor 430, these 2 are found in the found for the nickel, corrin is found for the cobalt, the porphyrins are found for the ion.

So, these are mainly for ion enzymes, cobalt enzymes, nickel enzymes ok. So, therefore, sometimes the metal ion can be bound to these also, these are called special motifs. So, the metal ion is bound to these and this is in turn bound to the protein or peptide ok. There are some other things that we see here. So, this is called iron carrier this is a enterochelin enterobacktin all this kinds of molecules. Such kind of molecules are used by certain microorganisms, these microorganisms require iron for their growth. What they do is they ooze out there these kind of a molecule into the medium and from the medium they capture the iron ions, and they captured iron ions are brought inside the body in this one ok.

So, that is very interesting kind of thing. So, first of all it oozes out the microorganism and whatever the iron in the surrounding will be captured is capturing is in chemistry is called bound, it is called complexation, in chemistry the capture means complexation.

And this capture or complex one will go back inside the cell ok. And there are some molecules which are used by the biological systems as the iron transporters; this particular example here shown is referred as a monesin, and this is a sodium binding protein, it will take in and out in some of the species. So, as an ionophore you can see typically this has some groups ok. So, look at that. So, this has typically some ether kind of oxygen's, maximum number of ether kind of oxygen's and that is very well suited for sodium binding, I will come to this later bit later stage to explain you high this ok.

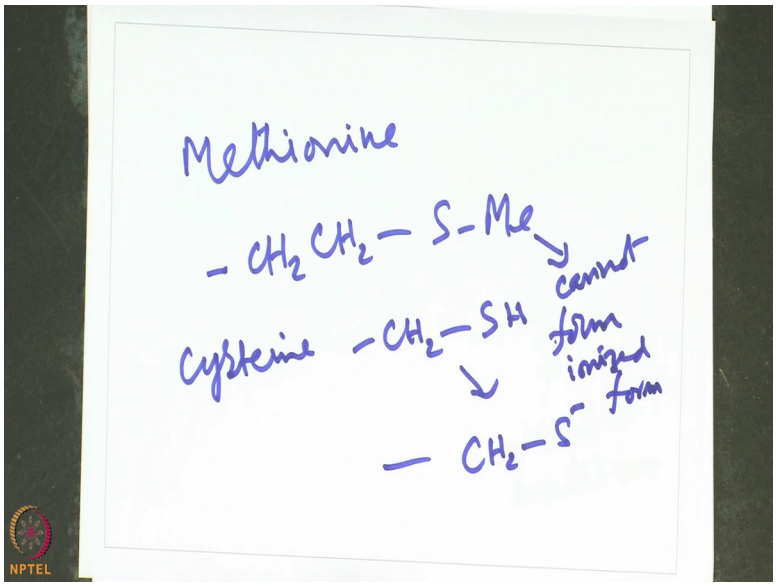
(Refer Slide Time: 25:49)



So, let us compile back all these the metal binding motifs in biology; aspartic acid so on and gultamic acid and this were tyrosines, and histidine, arginine, lysine and cysteine and methionine, then you have serine also here. So, you can see carboxylic kind of things binding, then phenolic OH binding, alcoholic OH binding and then imidazole nitrogen binding and then guanidinium group binding, then amine group binding, then SH group binding and SH group this is methionine; this is this is SMe.

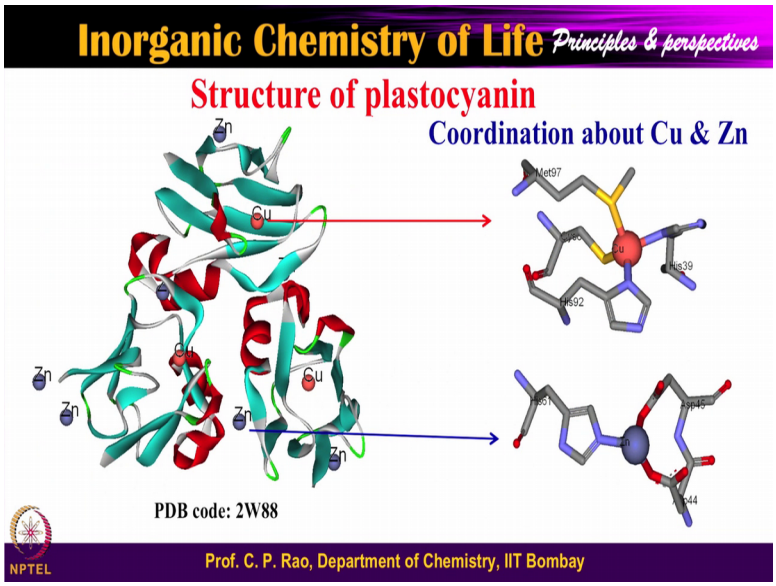
So, therefore, it will not that ionize it will bind to the loan pair. So, methionine case is something different, methionine case it is a different.

(Refer Slide Time: 26:54)



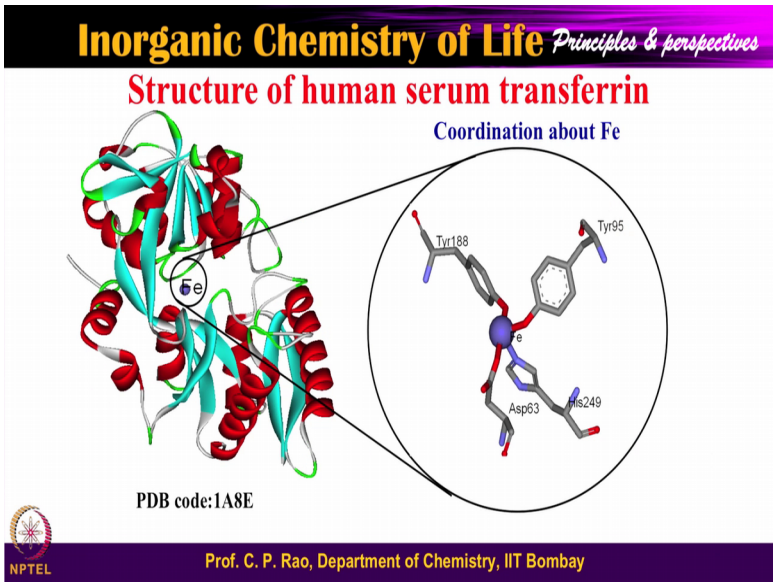
So, in methionine you have this you have CH 2, CH 2 SMe and in cysteine, you have CH 2 SH ok. So, this can get ionized it can form CH 2 S minus, but this cannot form ionized form ok.

(Refer Slide Time: 27:33)



So, what we have tried to tell you is till now is that, is that the ion is present in the metalloprotein and this ion is bound to the neighbors of the amino acids.

(Refer Slide Time: 37:28)



For example, you can see here in the transferrin it is bound to 2 tyrosines, one histidine, one aspartic and a glutamic. In this case is a plastocyanin let us not worry about what this is, there are 2 ions one is a copper, other is a zinc. Copper is bound by a one methionine, one cysteine, one the histidine, another histidine here and the zinc is bound by carboxylic aspartic and histidine. So; that means, what we are seeing is that in case of this metalloenzymes the metal portion gives a kind of a coordination complex.

So, what you understand now? So, the metal ion forms a coordination complex with a side chains of this amino acids ok. Let us summarize what we learn in this particular lecture. This particular lecture we have learn, the ion absorption is competitive between different ions and they could be antagonistic they could be synergistic that is one of the aspect that we have seen.

Then the next part we have seen was that these metal ions are bound by the side chains and the side chain deprotonation binding is dependent on the pKa. For carboxylic it is pKa could be low for nitrogen it is little high, for thiol it is little bit higher and for guanidinium ammonium ions is much higher and pH for alcoholic OH is much higher.

So, they can all bind to the metal centers. So, they are more the amino acids like tyrosine, tryptophan, aspartic, glutamic, cysteine and serine all these kinds of amino acids are capable of binding to the metal centers. Therefore, the metal center in metalloproteins is basically a kind of a coordination complex. If you look at the first portion it is like a

coordination complex and so, at this stage, we will slightly shift and see a broader focus of the metalloproteins and metalloenzymes and their presence.

Thank you.