Inorganic Chemistry of Life Principles & Properties
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Lecture – 16
Role of Alkali, Alkaline earth elements in life

I welcome you to the next class of the Inorganic Chemistry of Life Principles and Perspectives. So, far we have tried to complete most of the introductory items, which are necessary to build this particular course. Now as a part 2 kind of a thing we will start looking at each of the metal ions, which is important in the biological system and the corresponding proteins or enzymes and look at their function with more details than what we have seen initially.

So, as a continuation in that let us start with first alkali alkaline earth ions, because these are mainly the kind of a ions, which either involve with a weak kind of an interaction with the enzymes they activate the enzymes by the weak interactions and all they are involved in a kind of a charge neutralization other kinds of functions as well.

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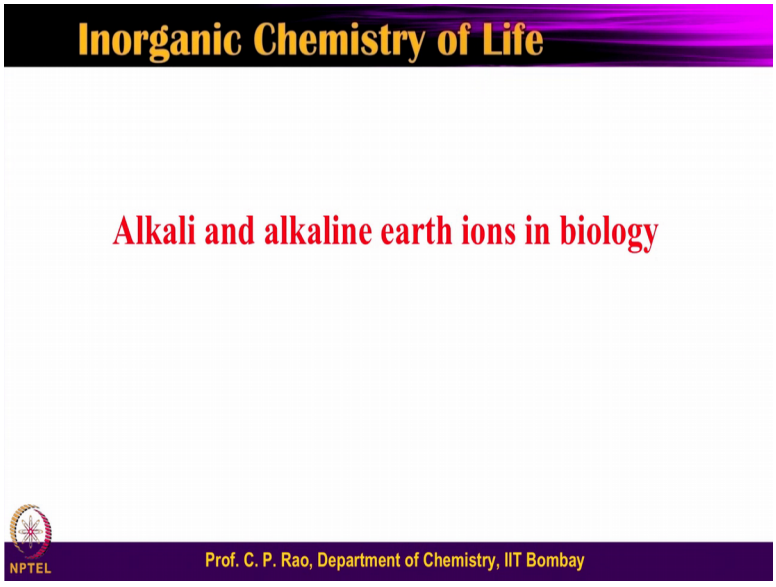

Let us start with alkali alkaline earth ions also these appear as the first elements that we come across when you look at the periodic table. So, we I have already talked to you earlier, the kinds of ion there are involved in the biological system.

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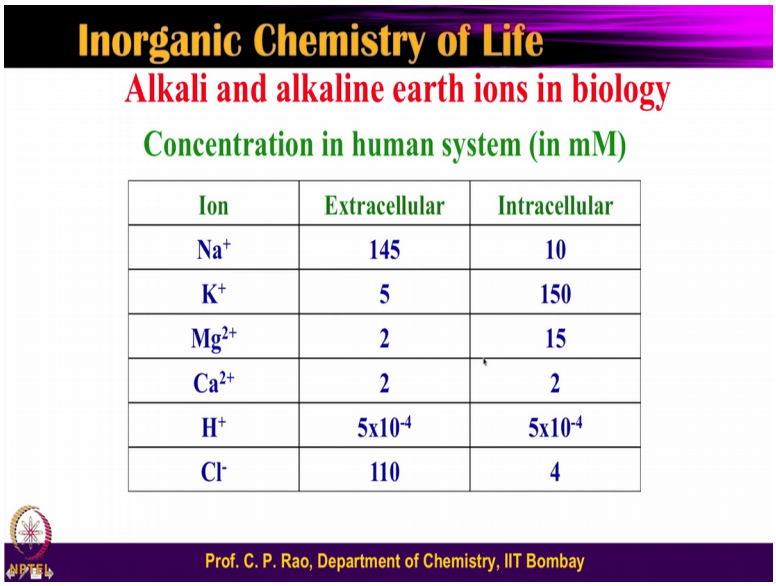

Ion	Extracellular	Intracellular
Na^+	145	10
K^+	5	150
Mg^{2+}	2	15
Ca^{2+}	2	2
H^+	$5x10^{-4}$	$5x10^{-4}$
Cl^-	110	4

Of which if you look at alkali alkaline earth, what are the important alkali alkaline earth ions in the biological system? The alkali alkaline earth ions in the biological systems which are important, which are important in the life processes or sodium potassium among the alkali and magnesium calcium among the alkaline earth ions.

Therefore, it is very appropriate to look at their concentrations in the human system or human tissue or we can categorize cell inside, which is called intracellular cell outside, which is called the extracellular. So, let us look at the concentration of these ions extracellular and intracellular.

So, very interestingly if you look at these ones you will see, the sodium having 145, these are all in millimolar outside the cell only 10 millimolar inside the cell. If you look at potassium it is more or less reverse, the 5 millimolar in the extracellular and 150 millimolar in intracellular. So, what does this how do we try to understand?

Already we do that there are a huge number of enzymes, which are inside the cell they are activated by the potassium ions. Those proteins are activated by potassium ions therefore, the concentration of these potassium ion inside the cell is very high and also important we will come to do in a while, their concentrations from inside versus outside has to be maintained, that brings in something called transport which are good explain very soon.

Now so, what do we see among the sodium and potassium? Sodium is large outside the cell, potassium is large inside the cell. So, which means the proteins intracellular proteins are mostly activated by potassium as compared to the sodium; that you will accept where I show the enzymes the involvement of whether a sodium or potassium you know just in a while you will certainly appreciate that ok.

The next aspect we look at is magnesium and calcium, you can see that magnesium and calcium magnesium as a 2 millimolar extra or 15 millimolar, intra calcium has got both inter extra or intra almost the same. So, these are another aspect, this aspect is there is a greater concentration of magnesium ions inside the cell as compared to that other calcium ion. In fact, we know that there are a large number of calcium activated proteins calcium triggered proteins inside the cell, in spite the concentration of the calcium is low.

So, this means this provides a challenge to the system, the biological system to the nature how do you come over because magnesium may activate a calcium protein, because the magnesium concentration is high. So, which means nature has to circumvent this kind of a phenomena by another method which I will explain very soon.

Though the concentration of the calcium 2 process is very small compared to that of the magnesium 2 process plus inside the cell, calcium proteins are not activated by magnesium ions though its concentration is high because of special modification that the nature has taken in those proteins ok. I will explain that. So, what kind of modification generally carboxylates are added to the protein. So, more carboxylates go by the 2 calcium rather than to the magnesium I will explain this better later.

Now concentration of proton concentrations and chloride concentrations all there. So, these are important phenomena to maintain the concentrations inside versus outside. See the chloride outside is large proton concentration more or less same both inside at the outside too. So, therefore, these inside versus outside the cell, concentration of these ions had to be maintain that is what is actually happening by these transport systems.

Before we go to the transport systems let us look at some properties of these ions. First let us look at the properties the alkali ions I know that the only lithium and sodium.

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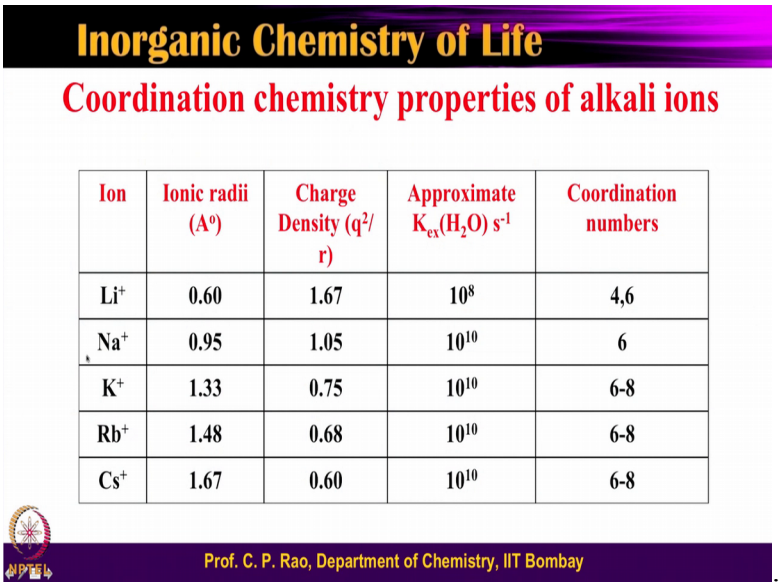

Sodium and potassium are essential are important in the context of biological systems, lithium role is not still showed by any protein, but lithium is in as kind of a essential trace element. Of course, the rubidium and cesium or not the biological elements, but it will just look at some alkali the properties, correlation properties like ionic size as you go ionic radii if you look at 0.6 0.95 or 0.3. So, it increases as I expect.

It we are not going to the details of this, how we it increases etcetera that will be shown explained in your 11th and 12th standard chemistry courses, a charge density. Because as the as the size increases, the denominator charge density means charge square by r. So, r is your radius. So, therefore, as the radius goes up the value of the charge will go down and the charge density will go down because charge is same for all of them 1; 1 square is 1, 1 by this, 1 by that, 1 by that, 1 by that etcetera. So; that means, you have more charged it is the lithium as compared to sodium as compared to potassium etcetera this will definitely influence the reactivity.

Now, exchange reactions; we already talked about the liability. The liability is basically ganged it gauged understood by the water exchange between the outer of the coordination sphere versus inside the coordination sphere inside coordination sphere versus outside. So, between the outside to inside exchange is the one which is. So, if you look at lithium you have very high kind of thing 10 power 8 sodium 10 power 10 potassium and rubidium.

So, what is the size this is increased its almost the same. So, these are all at a diffusion rates. So, the reactivities are quite good and kind of coordinations, lithium can show most of the time 4 occasionally very occasionally less frequently 6, the sodium who shows more frequently 6 and can potassium can show 6 occasionally 7 and 8 and similarly rubidium and cesium. But we are not so, much interested in rubidium cesium, we are interested basically sodium and potassium in these things. So, as you can see the size decrease charge density decrease, the rate of exchange of interactions and the coordination numbers these are some important.

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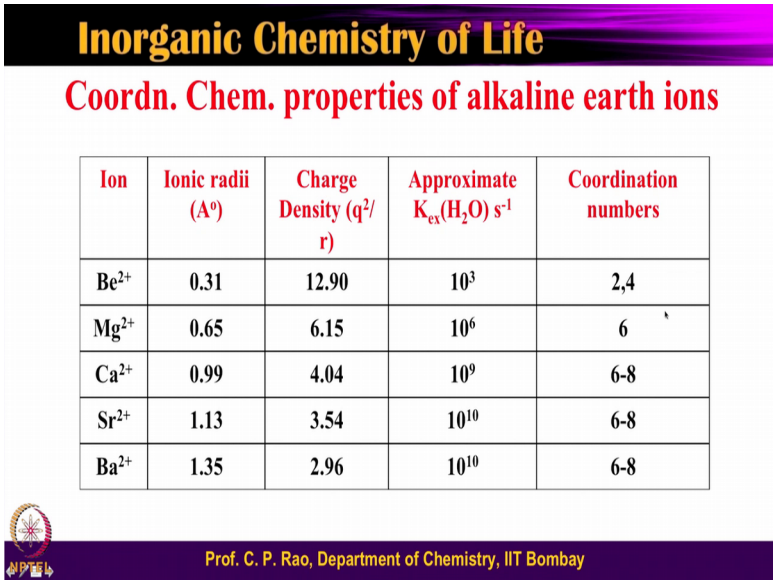

So, having looked at the alkali ions, let us look at alkaline earth ions. Again we know all among the alkaline earth ions beryllium, magnesium, calcium, strontium, barium; what are important in the biological systems, magnesium and calcium. So, you go from very small size the beryllium, to bit considerable size to magnesium 2 larger size and large and larger similarly charge; obviously, will decrease now.

And now you can see, but very small size very small exchange rate. For magnesium its a reasonably good 10 power 6 is a reasonably good range, calcium 10 power 9 and if you go to beyond. So, 10 power 6 to 10 power 9 there coordination numbers be really was not important because of highly reactive ion and that not present in the biological systems, what is present is magnesium 2 present a calcium 2 plus. Magnesium most of the time shows 6, calcium shown most of the 6 occasionally 7 very rarely 8 2. So,

therefore, 6, 6, 7 and 8 these are some important properties that we need to understand utilize during our studies.

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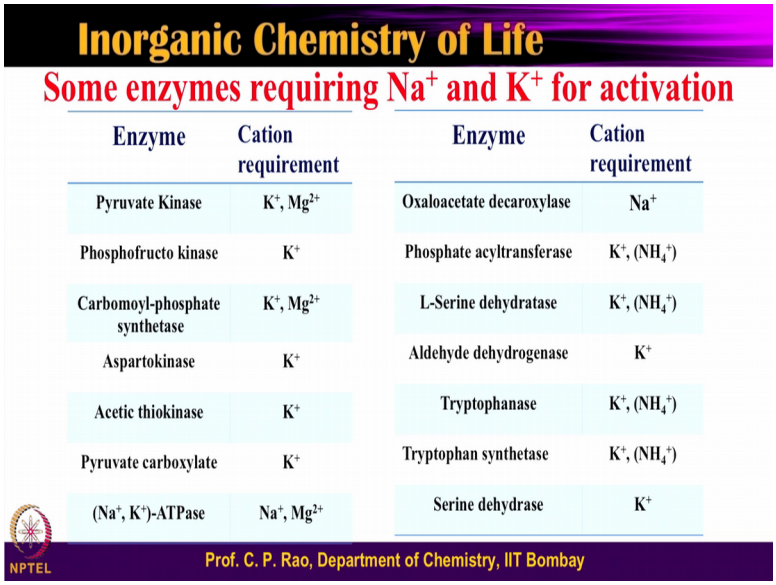

As I told you in the earlier slide, that the concentration the potassium is very high inside the cell whereas, for sodium it is very high outside the cell and I also mentioned as a result of that many of the proteins are activated inside the cell by potassium not by sodium. So, that you can see here, there are several enzymes. Do you need to remember all this? No not at all. How do you understand this? By the class; it is called Kinase, it s called synthetase; kinase, thiokinase, a part of kinase, carboxylase, decarboxylase etcetera transferase, hydratase or dehydratase, dehydrogenase. So, try to see the classes these classes are all we have learned we have heard all of them. What is important to learn is so potassium ion, potassium ion, potassium ion, potassium ion, potassium ion, potassium ion; only sodium and sodium here, potassium, potassium in this.

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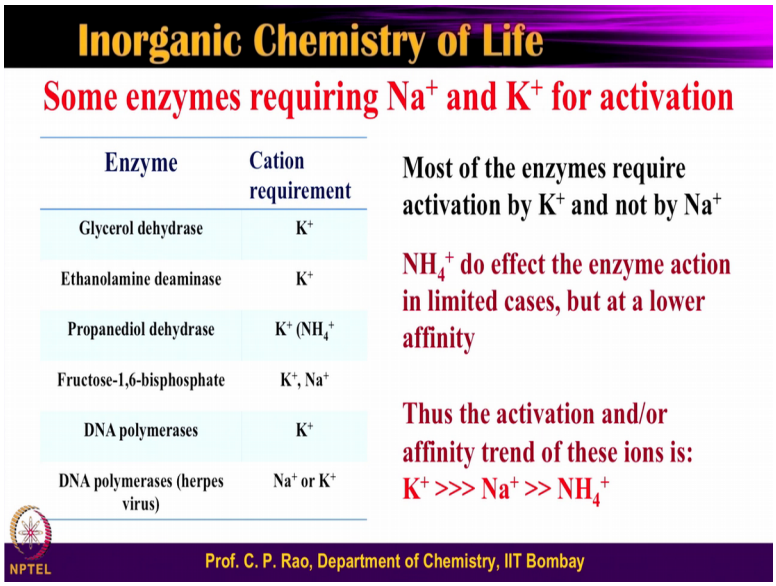

So, you can see that and if you go to the next you will see mostly potassium potassium. So, what you have seen? Among all these enzymes the enzymes of kinases phosphatases, carboxylases, decarboxylases, dehydratases all of these are synthetases primarily it is the potassium plus, in a few cases sodium plus, and there are some bracketed values or shown bracketed species are shown some ammonia. Some of the species can be activated even by ammonium ions in that to. So, therefore, what is their relative activations? If we look at all these enzymes, the maximum activation of the intracellular proteins are activated by the potassium and not by sodium, a few of sodium and if you take ammonium ion do effect it enzyme action very limited cases, but affinity is very low. So, you can forget simply ammonium ion roll. So, look at only a potassium and sodium ion rolls.

Now thus the activation of the proteins or the affinity of binding of these potassium and sodium either way you can explain. You could talk about the their affinity binding affinity or their activation levels of the enzymes either way the thread is potassium is for far superior than sodium, which is superior than that of the ammonium.

So, of course, we are very much interested in the potassium sodium and if you see the potassium and sodium, I have shown three greater than symbols. Potassium is greater than further greater than greater than sodium plus so; that means, the potassium is more very much more important in the enzymes present in the intracellular biological systems

therefore, that is very appropriate to take its granted that the most of the intracellular proteins are activated by the potassium not by the sodium only a few of them.

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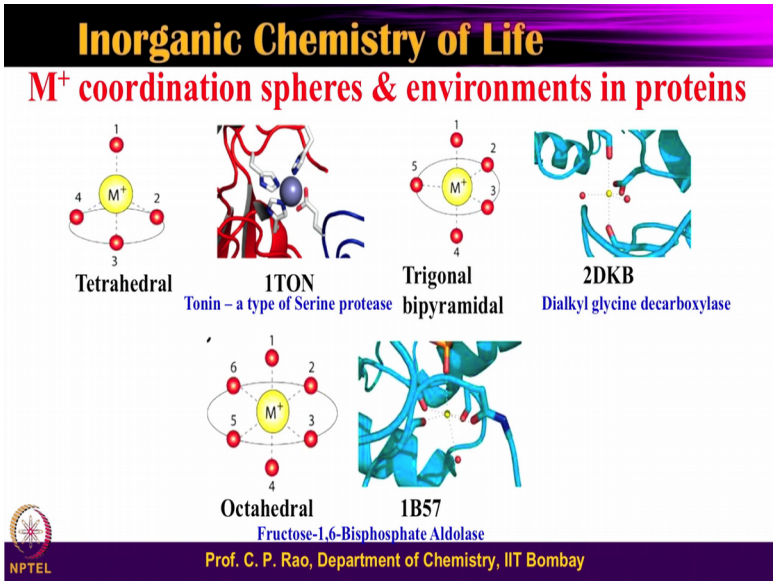

When they activate these enzymes, how do they look like in terms of their binding, in terms of their coordination ok? So, coordination's we know already we have studied in the geometries; the 4 coordination, the 5 coordination, the 6 coordination, the 7 coordination, the 8 coordination all of these we have looked at in the earlier stage of this particular course.

Now, if you look at some of these we are talk about M plus. So, plus means, it could be a sodium plus, it could be a potential plus. I have given some examples different enzymes do not need to remember at all. So, here is one of the enzyme where an m plus ion mostly in the sodium ion kind of thing is involved with 4 dearest Niebuhr oxygen's and they are all interacting by ion dipole. The oxygen is a dipole; oxygen center is a dipole the Na plus or k plus is an ion. So, ion dipole interactions and you know these interactions are not as strong as the covalent ones, they are weak interactions and that is how it is present here you can see that there are oxygen's where they are coming from we will explain a they while.

I take another example this Dialky glycine decarboxylase. In this case there are five coordination with respecting M plus, this is by three of them in the trigonal, the 2 of the base is the axial trigonal bipyramidal kind of a situation.

Take another one where we have a octahedral 6 oxygens you can see, that another octahedral 6 oxigens you can see that another fructose one 6 bisphosphate aldolase. So, this is a different enzyme.

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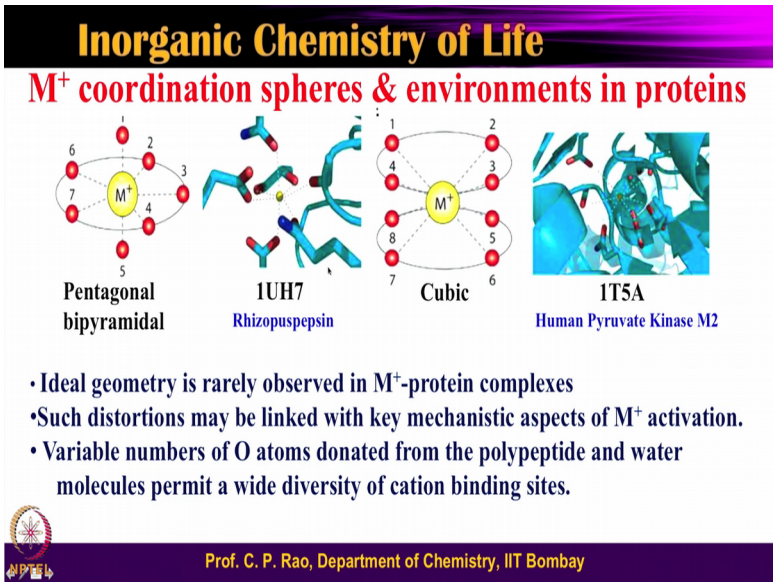

Many of the enzymes have got various sodium centers sodium binding positions, potassium binding positions or specific binding positions to. Take some more examples, this is seven coordination look a pentagonal bipyramid and the example is shown over through, I had eight coordination is a cubic kind of thing 4 of the top 4 on the bottom and the example is shown like this.

So, what are we seeing in all these cases, metal ions is bound to 4 5 6 7 8 oxygen centers number 1; and the geometries or not perfect at all, the are not ideal they are all the geometries which are distorted. You know distortion when it comes to we always think is not good, distortion is very good for bound breaking and bond breakage; bound breakage and bond breakage is very important for catalysis, for reactivity. So, therefore, distorted geometries should not be underestimated, should be given enough importance because they are important in the catalysis too.

So, ideally geometry is rarely observed most of the distorted geometries, these such distortions we have importance in their function in their mechanism of activating the enzymes. So, that is what I told you they are more important for an activity, for function, for catalysis. And then mostly oxygen centers where are the oxygen's are coming from.

The oxygen are coming from the peptide carbonyl oxygen, the oxygen's are coming from side chain carboxylate oxygens, the oxygen's are coming through water oxygen these are the main sources for the oxygen.

Nevertheless all of these alkali ions sodium and potassium, in the biological systems more or less exclusively bonded by oxygen atoms more or less exclusively bonded by oxygen's with maybe a few exceptions. So, let us not worry about those exception for mostly that is the kind of thing that we have.

So, let us look at the same taking one example dialkyl glycine decarboxylase. Decarboxylase you can understand you are removing the carboxylic group that is what it is decarboxylation kind of thing.

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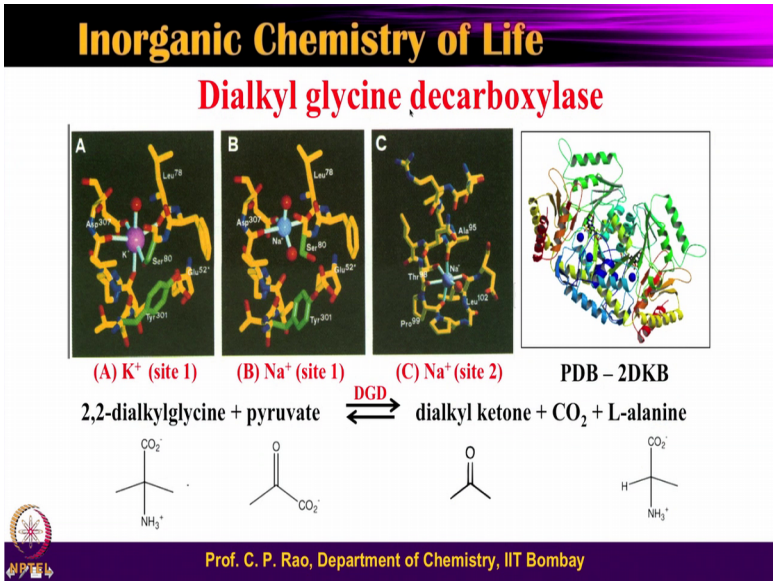

So, there is a carboxylic group which you are removing its called decarboxylate. This enzyme has a site 1, in the site 1 here the potassium is binding, there is a enzyme with the site 1 can also be bound by the sodium plus and there is a site 2, which is below here we can be bound by the sodium.

So, site 1 potassium, site 1 sodium, site 2 sodium like this. So, you have different sites are involved in the enzymes, these are these are bounded by these are interacted by the sodium and potassium, but more or less all of these are by sodium and potassium only when you talk about the (Refer Time: 17:32) valent cations two other alkali alkal alkali

ion is involved in the biological processes, the protein structure is showed over there here you can see the helices ribbons etcetera these are the ions which are bounded there.

Let us take this particular example, what it does? You take a 2 prime dialkyl glycine; that means, glycine is CH 2 and that instead of 2 hydrogens 2 methyl groups take 1 methyl group 1 methyl group. So, this is what is called 2 dialkly glycine and it presence is the pyruvate, you can see that pyruvate CH 3 CO COO minus is a basically propionic acid, but the 1 of the carbon is oxidized to ketone.

So, its kind of a that pyruvate this under this enzyme, dia glycine decarboxylase when it acts on these particular substrates it will convert it will convert this into oxidized form here carbon. So, becomes your ketone and the CO 2 is knocked out, the CO 2 will go away and the remaining part will make it to an alanine because it is going to react with the other bolicular framework of this one. So, therefore, you did this amidiation and then get this particular thing.

So, dialkyglycine implies pyruvate is converted by this enzyme to ketone, acetone, CO 2 and alanine anything now you understand. So, the further exact role of this is not a part of this particular course we do not need to really worry occasionally we will explain their activities in various things too. So,. So, I think that will make a kind of a situation for alkali ions, let us look at alkaline earth ions. What are the alkaline earth ions? Alkaline earth ions important or magnesium and also important is calcium.

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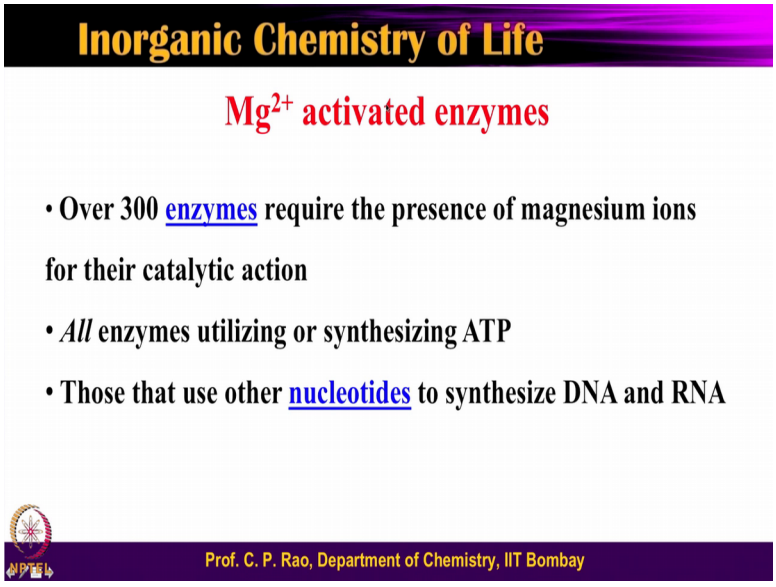

So, if you look at the magnesium situation, we have seen that the magnesium concentration is about 15 millimolar in cell and its about 2 millimolar for calcium. So, magnesium is quite well prevalent in various ways.

There are 300 enzymes which required the presence of magnesium ions for their catalysis in some way or the other magnesium ions are important there. There are enzymes where enzymes may utilize the ATP, enzymes we synthesize the ATP. In both of these cases the magnesium 2 plus is a must without the magnesium 2 plus ATP synthesis, ATP hydrolysis does not take place that you have to keep it mind throughout the course this.

So, there is a lot of enzymes which require the magnesium 2 plus ions and is also involved in other nucleotides to synthesize DNA RNA, but at the level of the enzyme. So, there are large number of enzymes which are activated by magnesium 2 plus at the magnesium 2 plus is involved in activating in doing that function.

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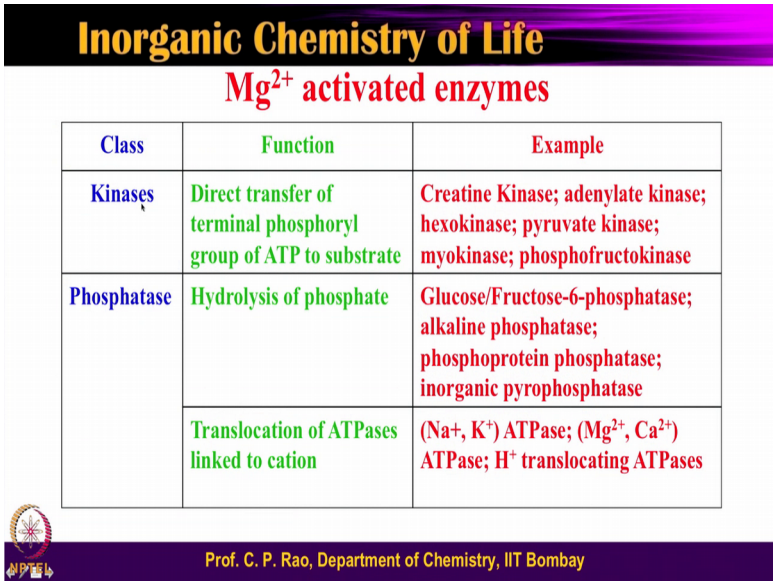

What kind of functions on the magnesium? They are kinases already talked to you what is the kinase? Kinase is nothing, but phosphorylation, they do phosphorylation, the bring some phosphoryl or phosphate kind of moiety and act of the substrate.

Phosphatase there already the phosphate is there you hydrolyze that and remove it. So, hydrolysis of the phosphate moiety is basically the phosphorylation or adding the

phosphate group etcetera these are all examples not so important, there are several examples are there. So, so many kinds of examples in here you could always look at just for a completeness I have given this. So, like Creatine Kinase, adenylate kinase etcetera.

So, the kinases are they directly transfer the phosphoryl group to the protein its call also called phosphorylation phosphatase is a hydrolysis. So, you basically bring the phosphate moiety one of this one ok.

So, there are. So, translocation of ATPases linked to the cation that is also taking from 1 position, the phosphoryl moiety to another position that also there or you can also have phosphate moiety shifted from 1 side to the other side as well due to the phosphate phosphorylation dephosphorylation. So, these things happen because of the phosphorylation and dephosphorylation, these are made part of sodium potassium ATPase magnesium calcium ATPase, these are called ATPase pups which work to maintain the balance the ion concentration across the membrane across the cell inside versus outside.

This sometimes these are also connected by the proton transfer 2. So, ion transfer, proton transfer, cation transfer, proton transfer it could be alkali ions or it will be alkaline earth ions. So, all of these, s o, these are the involved in phosphate transfer etcetera with this.

There is a mutases are there. So, between different substrates the phosphoryl transfer.

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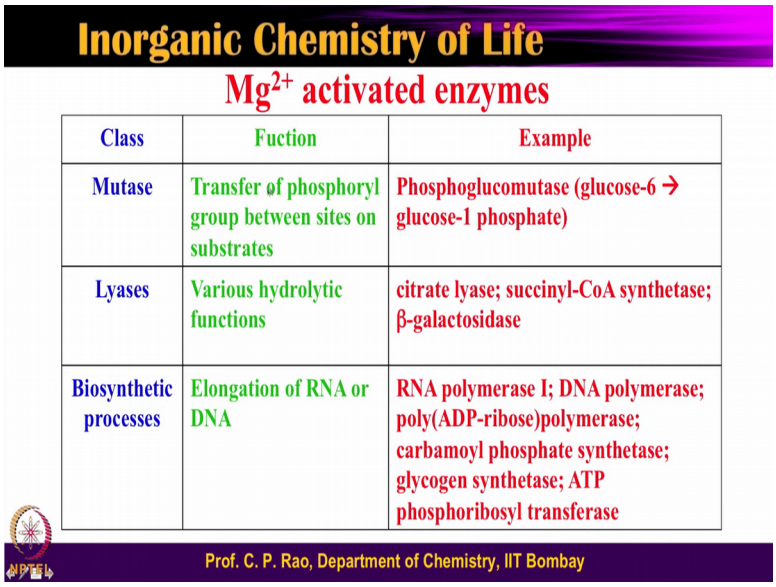

So, phosphoglucomutase, so glucose 6 to glucose 1 phosphate 6 position to 1 position kind of thing. So, you are going from 1 to the other. So, it is a kind of isomerizing, it is a kind of an isomerizing too. So, we take from one place and particular another place. So, overall composition is the same, but the position is different therefore, there other properties are different.

Lyases, so, hydrolytic functions there are different kinds of hydrolysis. By a synthetic process, because you add things, you elongate things it can be polymerases, it could be synthetases. So, all these kinds of proteins like kinases, phosphatases, mutases, lyases, the synthetase or polymerases you know all the cases the magnesium ions are required absolutely.

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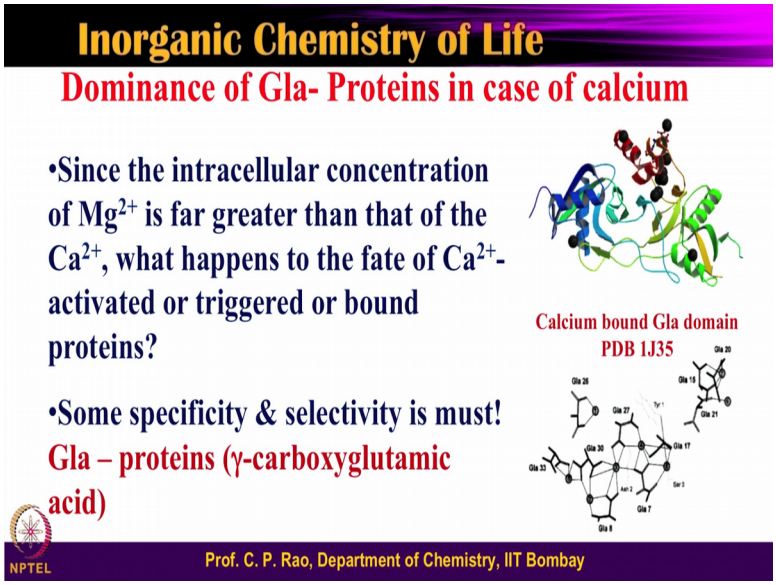

Now let us look at the calcium ion case. As I told you just a while ago that, the concentration magnesium 2 plus is quite large in the inside the cell as compared to that of the calcium 2 plus. So, magnesium 2 plus concentration is 15 millimolar while the calcium 2 plus concentration, 2 millimolar is about 7 2 about order of magnitude high. But there are large number of calcium containing proteins inside the cell, and therefore, the question is that can the consume proteins or enzymes be activated by magnesium.

If it does then it is a great danger you know why because the calcium or magnesium be activate within the enzymes or calcium and start doing calcium role that is a greater disadvantage, because that cannot be triggered functions. So, therefore, calcium proteins

must evolved differently in the inside the cell as compared to that which is activated by the magnesium 2 plus.

For this the nature has done very wisely by adding some carboxylic groups to the to the amino acid side chains like side chains and glutamic acid, aspartic acid to the add some carboxyl groups. Already there is one carboxylic group in glutamic in aspartic, but the in post translational modification for the calcium proteins, the additional carboxylic group is added and such kind of added proteins are called Gla proteins, they have gamma carboxyglutamic acid; that means, glutamic acids are modified with one additional carboxy group.

So; that means, what? You have a center you see that a lot of these things are carboxyl groups, there is a carboxylic group, there is a carboxylic group, there is a carboxylic group, there is a carboxylic group, so all these carboxylic groups. So, therefore, you have a carboxylic rich regions in proteins of the calcium and such regions are not present in the magnesium. So, therefore, a clear cut difference is coming in case of a calcium protein versus the magnesium proteins. Therefore, calcium proteins cannot be activated by magnesium ions even though the magnesium concentration is tenfold greater than that of the calcium concentration.

Now, you understand, you understand why the calcium proteins are not activated are not controlled, are not regulated by the magnesium ions, though the magnesium concentration is almost tenfold excess, tenfold greater inside the cell as compared to calcium. It is because the nature has modified the proteins that are present by adding the carboxyl group 2 its side chains and such addition of the carboxylic groups brings to gamma carboxylic glutamic acid from a simple glutamic acid.

That will create in proteins a regions, which are very highly carboxylic rich; that means, calcium is highly carboxylic fillic whereas, magnesium is not carboxylic fillic, it prefers more of a ether like oxygen's, water like oxygen's, carbonyl like oxygen's and a little bit of carboxylic, but not as much. Whereas, calcium will prefer more of a carboxylic like oxygen's, therefore, calcium does not touch the magnesium proteins, magnesium ions does not touch the calcium proteins even though they are living together inside the cell that is absolutely important information.

. So, further let us look at we have looked at in case of magnesium 2 plus what are the kinds of functions, we will seen kinases phosphatases, mutases, synthetases, pulverizes etcetera let us look at in case of calcium 2 plus.

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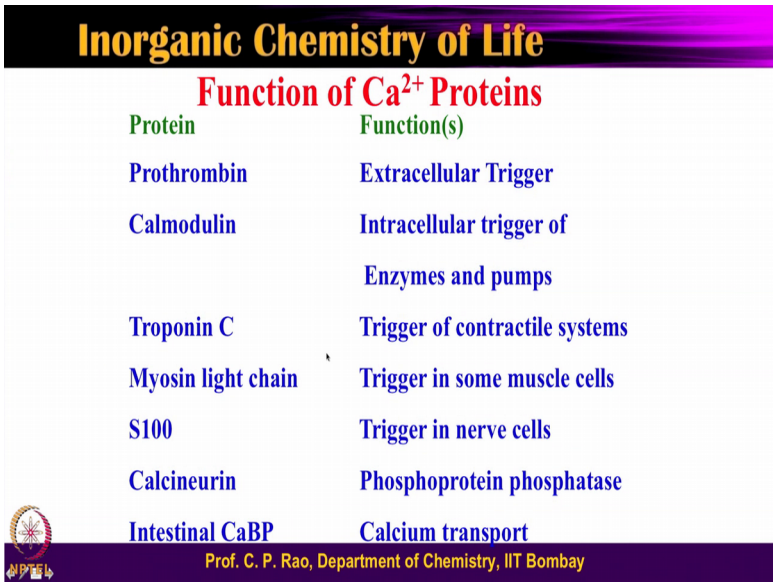

In the calcium 2 plus your calcium 2 plus has got several kinds of a functions like a trigger functions ok. So, enzyme and pumps contractile systems, muscle systems nerve cells phosphatase activities, transport activities is you can see all of these these are the names of the enzymes which are having that function prothrombin extracellular trigger, calmodulin intracellulars trigger it will trigger the functions so; that means, concentration the calcium controls that particular protein for their function.

So, the enzyme and function triggers the troponin C, triggers and contractile systems, trigger in muscle cells some it triggers in nerve cells, phosphoprotein phosphatase and calcium transport.

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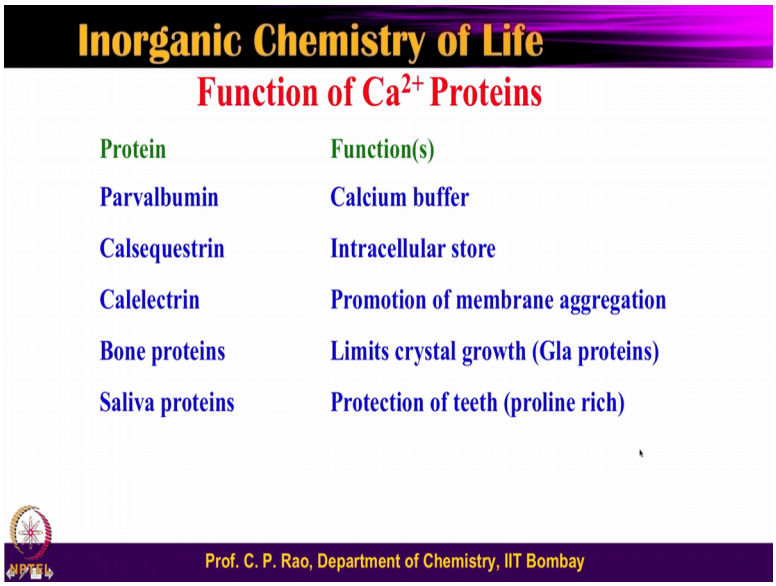

Let us look at some more, these are calcium buffer actions are also important because concentrates are important therefore, calcium buffer action is important sub case where there is a calcium low, this buffer protein will add, calcium high concentration buffer protein will take up. So, therefore, that is a important thing, that will happen in the biological systems in the cells then store calsequestrin sequestering be sequestering the ion storage, can calelectrin promotion in membrane aggregation because mambrane potentials etcetera in both proteins Gla proteins therefore, they are forming the crystal like..

And you know in the te protection of the teeth. So, there is a proline rich kind of a proteins are there, which are controlled by the calcium to give these are called the saliva proteins. So, various kinds of things that you can see in the calcium binding proteins.

So, let us look at since these are there, what kind of they have a binding constants a binding ability stability.

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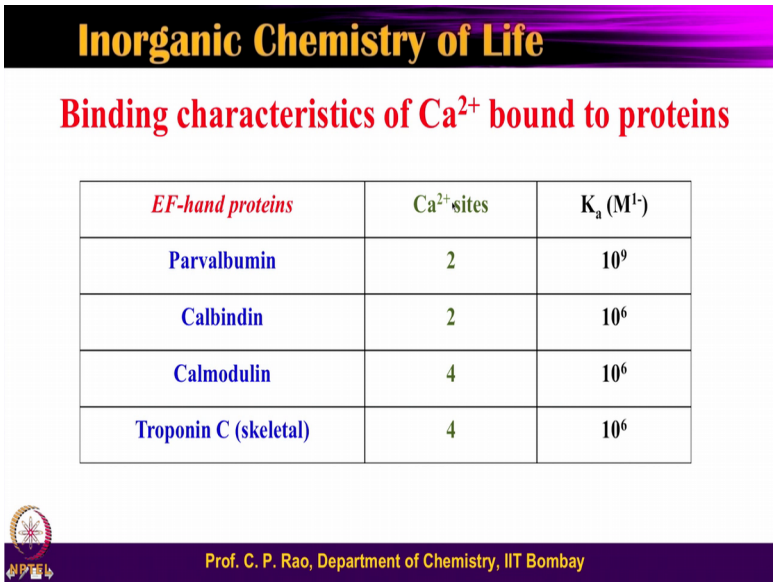

EF-hand proteins	Ca^{2+} sites	K_a (M^{1-})
Parvalbumin	2	10^9
Calbindin	2	10^6
Calmodulin	4	10^6
Troponin C (skeletal)	4	10^6

Some other binding proteins of the calcium, they are 10 power 9, some other 10 power 6. So, they have there are parvalbumin there are 2 calcium sites calbindin to calcium sites calbindin 4 calcium sites troponin there are 4 calcium sites. So, these all 10 power nine and 10 power 6.

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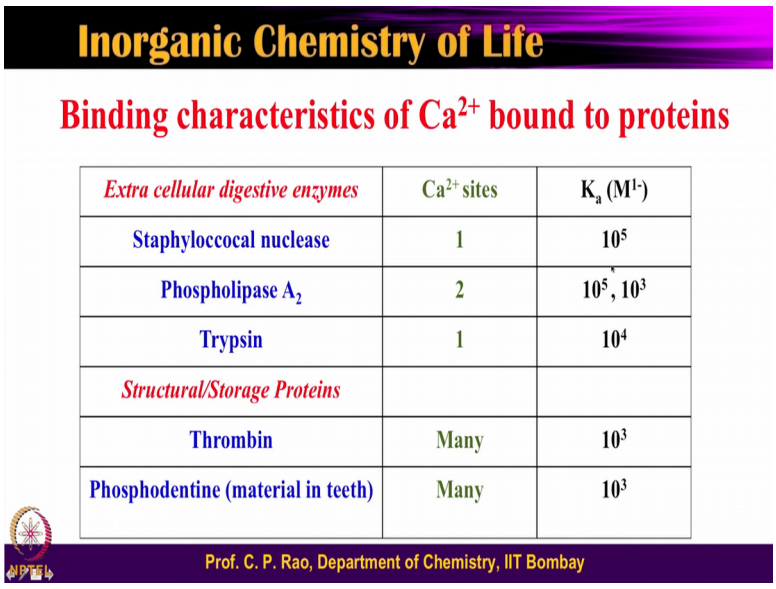

Extra cellular digestive enzymes	Ca^{2+} sites	K_a (M^{1-})
Staphyloccocal nuclease	1	10^5
Phospholipase A_2	2	10^5, 10^3
Trypsin	1	10^4
Structural/Storage Proteins		
Thrombin	Many	10^3
Phosphodentine (material in teeth)	Many	10^3

Let us look at some more; these are the there is one calcium site staphylococcal nuclease, calcium 1 site which is ten power 5, the phospholipase A 2 there are 2 sites, 10 power 5

for one case, 10 power 3 and trypsin 10 power 4 and there are thrombin and phosphodentine material in teeth 10 power 3.

So, what we have seen? 10 power 3 up to 10 power 9.

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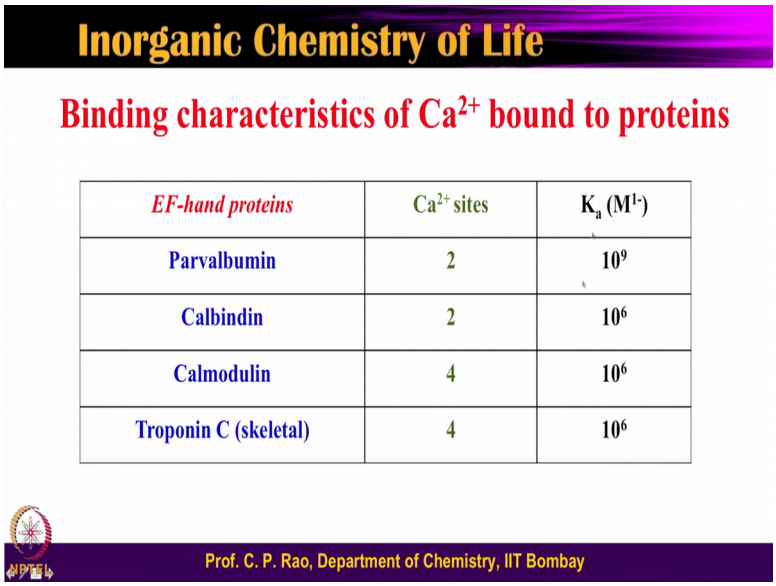

So, here 10 power 9 as you go 10 power 6 and split 10 power 5, 10 power 3 so on. So, there is a great range of binding strength. So, this is the strength of the calcium why calcium can interact to show trigger functions, can show other kinds of functions as well in the enzymes of this and the to sum up of all this.

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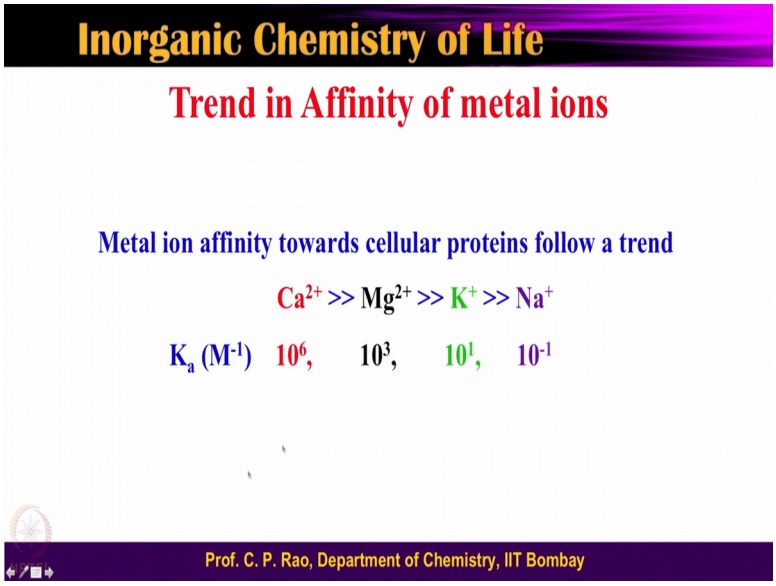

Let us look at the binding strengths of all these metal ions. So, the metal ion affinity towards the cellular proteins, if you take calcium, magnesium, potassium and sodium calcium is much greater than magnesium is much greater that potassium is much greater than sodium. 10 power 6 to 10 power 3 to 10 power minus 1, so, the average. So, about 1000 fold difference, about 100 fold difference, about 100 fold difference. So, that is the one of the real critical point that one needs to keep in mind different affinities triggering the proteins very much differently and I will come to more properties of this in the next class.

Thank you very much.