Biological Inorganic Chemistry
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Lecture 53
Phosphorous

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Hello students, so good morning, everybody. So, today, we will just go for lecture number 53 considering phosphorus as your nonmetallic species in your biological world. So, how we can see the different phosphorus and the phosphorus related molecules particularly the anions. Because we are talking much about these anions, so what is the most important thing is that how chemistry can control the corresponding corrector or the reactivity of the phosphorus or the phosphorus bate anions then how the nature can take care of all these things through two different parts, that means, one is the biological part and another is the geological part.

So, together, we can have the biogeochemistry of phosphorus. So, it is also related to the corresponding point number 3 is the phosphorus cycle. So, we have when you have the phosphorus we are not talking in terms of the elemental phosphorus, that means, the element wise we know the red phosphorus, white phosphorus or the black phosphorus is not that the phosphorus-related species, which can give you some anions, and those anions how they are important for our biological world.

So, most important thing when we talk about phosphorus or the phosphate anions, we all know that the ATP molecules is our energy currency. So, how much ATP we synthesize daily and how much we consume and why this is so important. And also, if you consider that you have the phosphate anion.

And we all know in our body also including what are many protonating species are available, like the free amino acids and all these. So, if you are going to protonate the phosphate anion you will be ending up with that phosphoric acid HCPO4. So, it is not that we are producing the free phosphoric acid in our body or our fluid medium, but the corresponding anions are there and the protons are also available, so we can have some medium which is very much buffering in nature. Then finally the biomineralization process, which is also dependent on phosphorus. So, what are the phosphorus-related material we can have for our bone, for our teeth, we know appetite is the name of that particular mineral.

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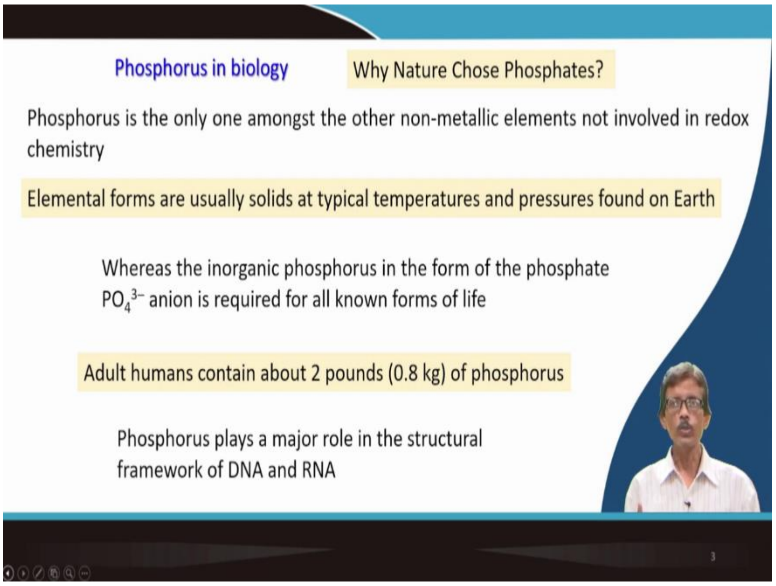

So, when you talk about the phosphorus in biological world, we always ask that why nature is considering these phosphates because this phosphate is very much important for our backbone for this ATP preparation and all these things. May not be so important in handling your dioxygen molecule, but some other enzymes are also dependent on all these things. So, when we talk about the nonmetallic elements in the biological world, so we think about the phosphorus after carbon, oxygen, hydrogen and nitrogen.

When we talk about that, whether it is involving very frequently in the redox chemistry that means electron transfer reactions is not, so it is stable in the highest oxidation state, that means, plus 5 oxidation state. But what do we know from our school days, the elemental form just now I told you the phosphorus has the element the tetramer the P4 phosphorus element, so elemental form is in the solid state.

So, geologists will come and say, oh, I know it from the mineral or the ore I can take out some phosphate rocks. So, those phosphate rocks when we treat those phosphate rocks, the phosphate rocks can give you the elemental phosphorus, but that is all in the solid state. So, in the standard temperature and pressure condition, water is available on the earth's crust or earth's surface, this phosphorus is present as in that solid state.

So, when this inorganic phosphorus we can go transforming it to the phosphate anion, and when we transfer it or transform it, that particular phosphate is required by all forms of life, so it's very important. So, as we considered earlier from our very beginning of our class, the average human body if it is 70 kg, how much phosphorus you can have in your body.

So, adult human basically contents have about two pounds of phosphorus that is about 0.8 kilogram that means 800 grams of phosphorus in your body. So, that phosphorus is your total phosphorus, whether that phosphorus is present in your teeth or that phosphorus present in your bone or that is in the corresponding ATP molecules.

But how we can correlate all these basically. The elemental phosphorus we do not have, but we have the another mineralized form which he considered as the biomineral. So, biomineral or biogenic mineral what we can have starting from there where we can think about the corresponding species or the compounds, which are important for our genetic information transfer that is your DNA and RNA molecule.

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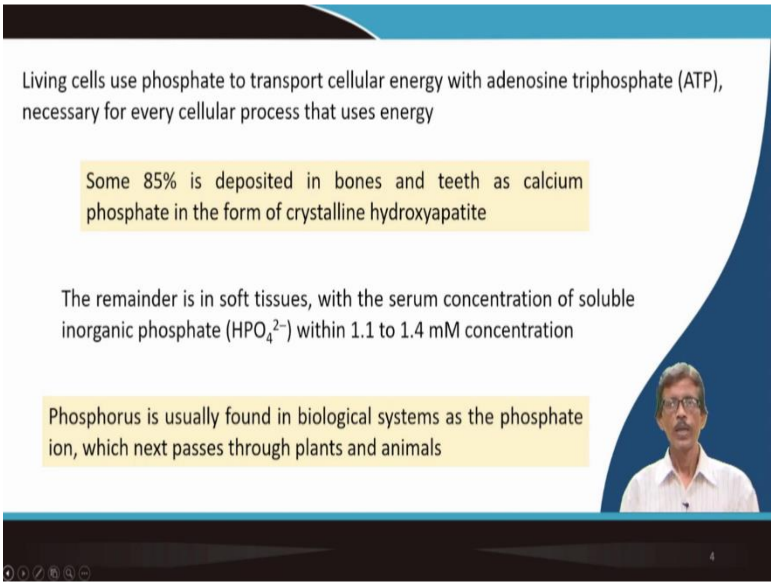

So, how the DNA and RNA molecules are also linked to the phosphorus or the phosphate anion? So, we have the living cells, they are utilizing phosphate to transport the cellular energy with the ATP molecules. So, we know that the phosphorylation reaction as well as the phosphorylation reaction is always taking place on the basic backbone of the adenosine triphosphate.

So, what you have? You have the nulceo base you have the sugar unit, then the phosphate unit. And then, if the phosphate unit can form the esters or diesters, we get the corresponding DNA and RNA molecule. So, all these are linked, but what we are trying to talk about today is that how you can think of only the phosphate your eyes are now centered on the phosphorus of the phosphate anion.

Like always, I say that a biological inorganic chemistry is basically devoted to many metal ions, but when we start our discussion about the non-metal ions like carbon, hydrogen and oxygen, so like that of your phosphorus, so, you should be able to tell that how the phosphorus is also important for your bio inorganic chemistry.

So, the cellular processes and also it gives the energy due to that of your teeth phosphorylation reaction and the production of many number of Pis, Pis are capital P small i is your inorganic phosphates. So, out of all these 85 percent is deposited in bones and teeth as calcium phosphate in the form of crystalline hydroxy apatite.

We know the powder form, if you have the calcium phosphate and if that is present in the powder form there is no so strong, but if you are able to crystallize it not only the pure calcium phosphate crystallization but you can have the hydroxy derived one or the fluoride derived one the fluorapatite and the hydroxyapatite, but along with some organic metrics, it can go for increasing its strength.

So, in terms of the corresponding phosphorus concentration, as well as the corresponding concentration of the inorganic phosphates, what do we can have in your blood or serum. So, all are present in the soft tissues and in the serum also, but that concentration is not very much, is only 1.1 to 1.4 millimolar concentration.

So, we have started our discussion about how much phosphorus you can have how much can be deposited 85 percent can be deposited as your bone and teeth formation, then the remainder, remainder is not crystallized, it is still in the solution. Because we get everything crystallized form from the solution. When you have the saturated solution, you go for the crystallization.

So, what is the remaining or the leftover solution concentration? It is not even in the molar concentration or something, but it is not even less that means they are not nanomolar but is the millimolar concentration is pretty high. So, pretty high concentration of these thing can manage all the biological reaction because always we know that the dependence of any particular chemical reaction is there on the concentration of the species available to you.

So, in the biological system, what is available as the phosphate ion and then slowly from your biogeochemical part if we think about the geochemistry is talking about on the soil and minerals and the rocks, then how the plant and the other animals can take up all these things particularly those herbivores, which are taking the plants as their food material. So, a plant gets that phosphate then those animals can also be taking that phosphates, so the phosphate cycle or the phosphorus cycle can continue in this manner.

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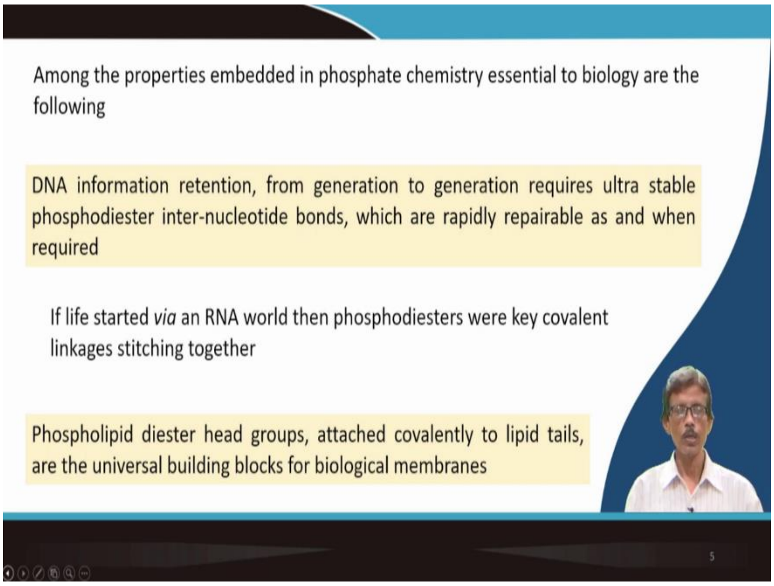

So, the properties what we can have with this particular phosphate, which are essential for many biological functions, so I am giving you the statements read the statement nicely such that you can have some good information about DNA, RNA, and how these ATP molecules and all these, so these are the basic understanding only. Why you should read phosphorous?

If somebody says that, we can go for the phosphorus chemical biology. What you are studying? Is phosphorus chemical biology. You will be thinking no it is very complicated one, is nothing complicated. You want to have the knowledge about the corresponding phosphorus bearing biomolecules only.

So, DNA information retention, where you retain the information from one generation to the other, you require a linkage which is phosphodiester linkage. So, you should know the constituent, you should know the chemical composition of all these molecules or the biomolecules, then, the corresponding structure. So, they all must have the phosphorus then we know that the phosphate can come but it is a diester thing.

So, if you have the phospho diester, it is the DNA or the RNA molecule. And rapidly repairable when required, that means, ATP, ADP, AMP and the phosphate transfer reactions and phosphorylation and dephosphorylation reactions are going on altogether. So, if we consider that one theory is there that our lives started from DNA.

So, if we consider that it is also true and if we add the DNA world, then the same phospodiester is again available and which is your covalent linkage stitching together the strands. So, this linkage is very important. So, then you have finally, the corresponding hydrogen bonding interactions from the nucleobases, but before that you have the backbone with that of your phosphate diester or phosphodiester linkage.

Finally, we will see also the phospholipids. What are phospholipids? We know lipids, but what are phospholipids? Whether you have a diester bond or not, and then you can have how the corresponding assembly of those lipids can give you the corresponding biological membrane.

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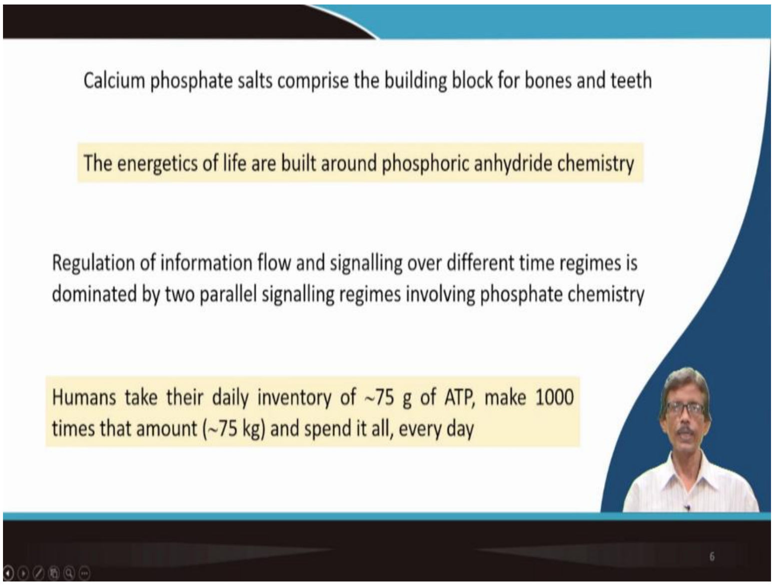

So, the calcium and calcium derives phosphate. So, whenever you have the phosphate we all know our body cannot restrict that okay calcium should not reach the phosphate. So, we have the corresponding approach of the calcium ions, which are cations the phosphate having three negative charges on the phosphate anion so is highly charged.

So, if they are coming together the chances are there, they can combine together and form the typical inorganic compound calcium phosphate. And that typical inorganic calcium phosphate compound will have very low solubility. So, when you have a corresponding concentration of these phosphates three phosphate anion in millimolar range 1.1 to 1.4 range, you can have also certain amount of calcium concentration in our body fluid, so they will come together combine and try to crystallize from the medium.

So, you can have the corresponding crystal growth for the bones, as well as on the, for the teeth. Then for the hydrolysis reaction ATP to ADP conversion or ADP to ANP conversion, we know, we will be able to release some free energy for that particular dephosphorylation reaction and we get the energy for that particular purpose.

Then we have the signaling. So, the information flow as well as signaling is also dependent on the phosphate chemistry. So, within this particular case also two parallel signaling regimes are the areas we can have. So, when we have certain amount of phosphorus available for not only your DNA and RNA molecules, but you think of only say ATP molecules.

So, when we have this much phosphorus in your body, we consider your body as a storehouse of your phosphorus base biomineral. It can be your teeth, it can be your bones, then you think about how much ATP you can have in your body. So, is the rule of thumb is very simple you will be able to remember the way I also remember the average human body is we consider as 70 kg or you can consider is a 75 kg, but you have only 75 grams of ATP, but it is cycling very fast, so it is very basically a catalytic molecule.

ATP to ADP to AMP is cycling back and forth. So, thousand times of that amount which is 75 kg of this. So, throughout the day, we will be able to make that means as an when required or when we need it we prepare. When you take the food material you have the glucose you have only the store of 75 grams of ATP, but that will cycle for thousand times. So, if the thousand times cycling is available, you will be able to produce an amount of total ATP which we require for our day long survival is about 75 kg again. So, it is easy to remember also.

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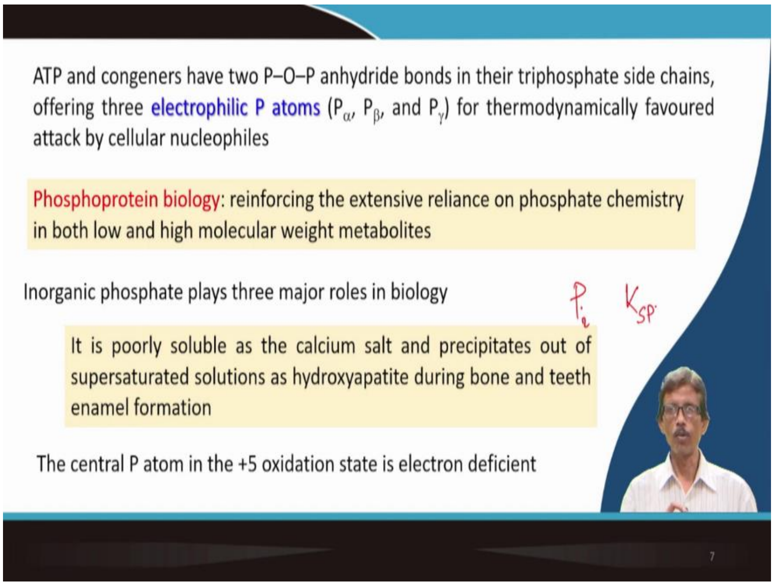

So, if you have the phosphorus and the phosphorus linkage so you will have the POP linkage, that means, diphosphate unit. How the diphosphate unit is formed, definitely, we have the anhydride PO of 1 and another PO will come making the POP bond, which is your anhydride bond is also for the triphosphate because ATP is a triphosphate molecule on the sidechain basically.

So, when you have the sidechain, you can have three P, one P close to that some part and the terminal Ps. So, you will have P alpha P beta and P gamma and which can have the corresponding thermodynamically favored attack by cellular nucleophiles. So, nucleophiles will come attach these links basically the chain, the three-membered chain and then can go for some very useful reactions.

So, not only the importance of the phosphorus in the biology, but several phosphoproteins also can take part in biological activities. What are phosphoproteins? So, phosphoproteins are not so complicated thing. Try to understand that whenever you have some OH function of alcohol, alcohol or the alkoxide ion you know that is a typical nucleophile it can attack the triphosphate or diphosphate to take up the phosphate group attached to that particular oxygen of your nucleophile.

So, the phosphorylation of the amino acids can also be possible to have. So, if you have the corresponding phosphorylation of the amine acid residues having some alcohol function, say the cerine the OH function is there. So, that particular part is getting phosphorylated, but you have the free amine function and the free carboxyl function. So, the free amine function as well as the free carboxyl function what you can have can give rise to the corresponding dipeptide, tripeptide and polypeptide and ultimately to protein formation. But you have the corresponding pendant phosphate group. So, those are basically your phosphoproteins.

So, there also we require the knowledge of phosphate chemistry for the understanding of the different metabolites, which can be of low molecular weight or can be high molecular weight. So, basically when we have the Pi capital P and small i, what do we write all the time which is your inorganic phosphate. So, that inorganic phosphate what you can have we consider, as Pi we write biologic in the biological world or the people who are because it is the abbreviated form. Very quickly you can understand easier inorganic phosphate.

So, is playing many roles. It is poorly soluble as calcium sulphate as just now, I told you that you can think about the corresponding calcium salt of the calcium phosphate. So, what we find? There we find, KSP the solubility product of the individual ion concentration that means, the individual ion concentration of or ionic product recall something. So, ionic product of the calcium concentration and ionic product of the phosphate concentration.

So, if your phosphate concentration is pretty high, which is in the range of 1.1 to 1.4 millimolar you will be able to get or reach this particular value of ionic product very quickly such that you can have the separation of hydroxyapatite for your bone and teeth enamel formation. So, the central phosphorus atom. In the phosphate is basically in the plus 5 oxidation state and is electron deficient so that is why it will attract many new profiles.

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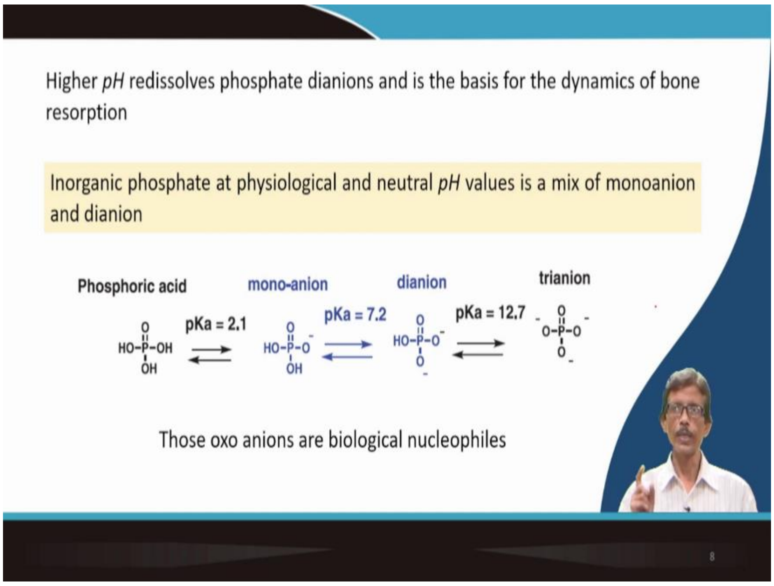

So, higher pH value basically if you have, that means, you have the calcium phosphate and you have a higher pH value, which redissolves the phosphate dianion, and is the basis for the dynamic bone resorption, basically resorption So, that dissolution, so is a continuous process because the bone we have, the corresponding repetition we know the growth of the bone we know is a dynamic process, but after some time is not the shrinking but it can have the corresponding bone density basically we call the loss of calcium, so it can have the corresponding leaching because it is always there like a mineral you have and you put inside a corresponding acidic environment.

So, in the acidic environment, which is less than only pH 7, so, you can have the dissolution of the basic anion so calcium can be leashed from that particular solid material. So, again the Pi can have thus a physiological role and neutral pH values is a mix of monoanion, dianion. So, what we can have if you have a neutral close to 7 pH value always we try to consider that our blood pH is only from 6.8 to 7.2 something like that is not our stomach pH which is close to 2 to 2.8.

So, what we can have, you see the phosphoric acid, which is the fully protonated form we can have which is H3PO4 but we can have the trianion at the end which is your PO43 minus, and you can have the involvement of 3pKa values particularly the pKa 7.2 which is the pKa 2 and the pKa 3 which is 12.7 these two are important.

So, in many times what we can see that you can have the corresponding oxo anions which are your biological nucleophile and these corresponding oxo anions can be protonated depending upon its available environment where you can satisfy the corresponding pKa value for dissociation of the proton.

So, if your pKa or the pH value of that particular medium is less than that of your 12 what you can think you will instead of getting the typical PO43 minus it will be protonated in the single step. Similarly, the second step also you can have the double protonation of the phosphate anion.

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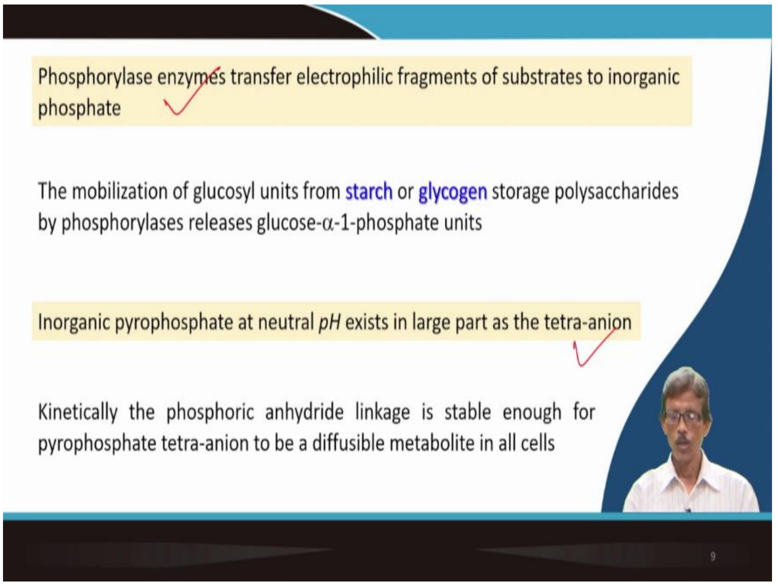

There then, again, we know that the enzymes the phosphorylase enzymes are there, and those phosphorylase enzymes can transfer many electrophilic fragments of substrate to inorganic phosphate. So, the work or the role of these engines, what these enzymes are doing basically? They basically control the reaction between the electrophilic fragment to the substrate to the inorganic phosphate, that means, it will attack either the oxygen center or the phosphorus center. Phosphorus center is having a charge of 5-plus, so it will have a demand for electron density, but oxygen having the charged one O minus so it will have the demand for the corresponding positive charge.

So, that is why within the system you can have a electrophilic side, as well as the nucleophilic side. So, we can have many such reactions, which can be controlled by different enzymes, which can also be metalloenzyme. So, one good thing we have studied from our school days again the glucose oxidation or the assimilation of the glucose for our energy production, where we produce large number of ATP molecules. But while doing so, we know that, we can have the glucose alpha 1 phosphate.

What does it mean basically? That means, you have the glucose, and we all know the glucose can have some groups can have aldehyde function, can have the alcohol function CH2OH function. So, if we are able to phosphorylate that alcohol function nicely, we get the phosphorylated glucose that is your nothing but your glucose alpha 1 phosphate. So, we can go for the phosphorylases reaction, and that phosphorylase reaction is basically controlled by this enzyme. So, this is your phosphorylase enzyme.

So, the mobilization of the glucosyl unit that means, you phosphate is there. Now, you think of in a different manner that you have the glucose unit attached to that phosphate. So, think of that movement of that glucose unit. So, whether we can take out that glucose the unit from the starch or from the glycogen, we know that in our body, the unused glucose which we are not burning immediately for our future use or future demand, it can be stored as the glycogen.

So, the glycogen is stored, which we all know as the polysaccharide because many times we take the disaccharide the sucrose, fructose, all these are disaccharides but also we take polysaccharides, but we cannot consume any amount of the starch. So, these polysaccharides you have to break so the hydrolysis is taking place and finally you get the glucose, and that glucose can be phosphorylated. So, all these energy transfer reactions are dependent on the transfer of the phosphates and sometimes the inorganic phosphates.

Then PPI the inorganic pyrophosphate that means, one more phosphate POP bond is there. At neutral pH exists in large part as tetra-anion So, if you have two phosphate units attached to it, so, altogether you can have many oxygens. So, those oxygens can be charged so you can have the tetraanion at a neutral pH value. So, whether you are removing that particular diphosphate unit or putting the diphosphate units in some other molecule is important.

Then kinetically the phosphoric anhydride linkage formation is stable enough for pyrophosphate tetra-anion information that is your all the four oxygen centers are charged that means those oxygen centers are charged to be diffusible metabolite in all cells. Since it is charged you have more charge, that means, you have more solubility. More solubility means that you can have the metabolites so you transferred those phosphates. My main intention at this point maybe, we want to move or we want to transfer those phosphates as the corresponding solubilized form in different metabolites. So, metabolites what gain, so metabolites are important for the burning of the glucose molecules forget the energy.

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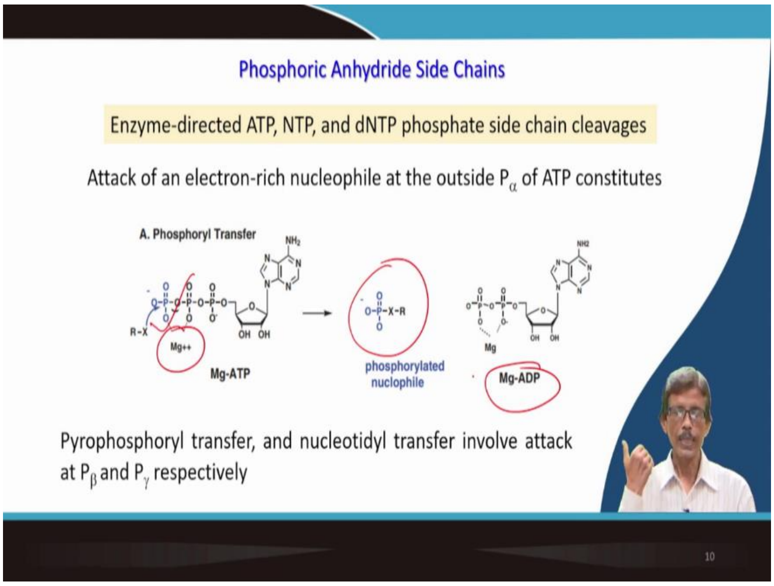

So, if you have this particular anhydride sidechain that means, POP bond is there, which enzyme can control for the formation of ATP, NTP, DNTP, phosphate sidechain, cleavage reaction. So, you have triphosphate then diphosphate then monophosphate. So, attack of an electron-rich nucleophile at the outside P alpha of ATP constant, so that means, the terminal phosphorus we can label it as the P alpha then you can have the P beta and then you can have the P gamma.

So, you see now that if you have the P alpha so this is your P alpha. So, when you attack the P alpha, we consider it as the phosphoryl transfer reaction because your RX which is your corresponding nucleophile which is coming and attacking your P alpha giving the corresponding phosphorylated nucleophile.

So, you can have the alcohol function, you can have the glucose function also, and this is the most simple reaction what you can think of for the corresponding phosphorylation reaction, and we consider that is the phosphoryl transfer reaction, which is also true for the typical ATP giving you ADP and the energy.

So, already we know that we require the corresponding coordination of the MG2 plus magnesium is binding then only you can have so magnesium is that still bound form. So, magnesium ADP is there, and you basically cleaving the corresponding phosphate group from there, so we are releasing some amount of energy.

Then the other two, that means, if you go for the beta, as well as the gamma phosphorus center one will be considered as the pyrophosphorene transport so two unit of the phosphate can be transferred, and the other one is, nucleotidyl transfer involve the attack on these two phosphorus centers.

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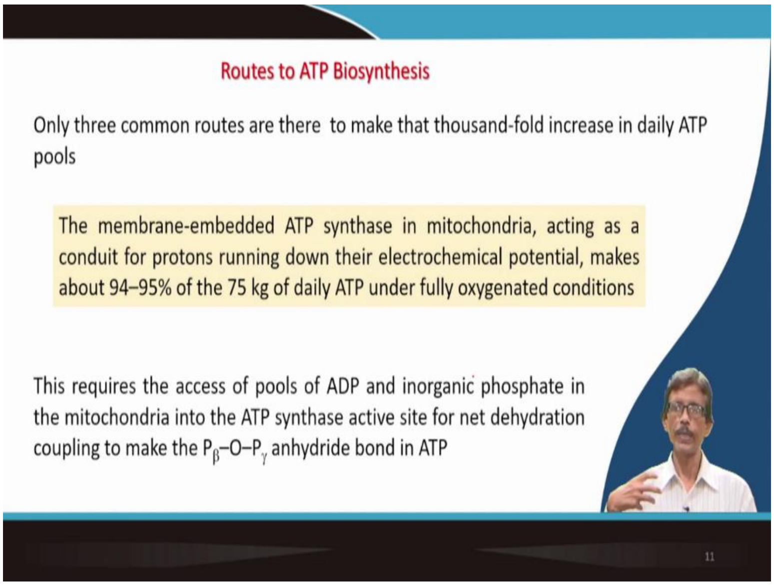

So, definitely, it will be related to your route for ATP biosynthesis and that ATP biosynthesis can have three common routes, and which can make many times like your corresponding production of your ATP, as I told you that you can have the throughout the day the 75 kg of ATP we are using with the 75 grams of ATP.

So, the membrane-embedded ATP you can have so, altogether, 94 and 95 percent of those amount of that amount of 75 kg of daily ATP requirement under fully oxygenated condition can have the proton, transfer potential protons running down from the electrochemical potential ATP synthesis are there for the synthesis of the ATP molecules, but for the breakdown which is required for your energy production which you get in your mitochondria.

So, it basically requires the access for the pool of ADP molecules inorganic phosphate in the mitochondria such that ATP synthase can work. And the corresponding net dehydration coupling to make a P beta OP gamma and anhydride bond in the ATP. So, ADP or ANP if you have you bring the phosphate, so you have the gamma, then you put the beta and then finally the alpha phosphorus center.

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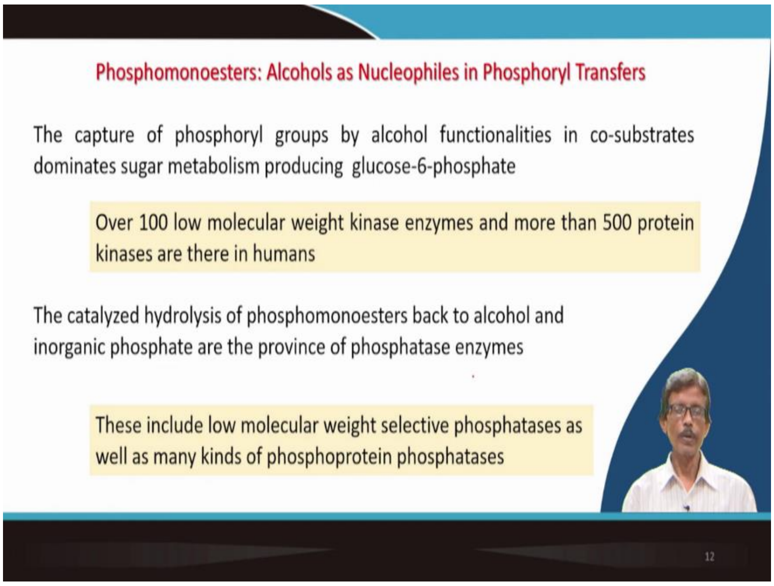

Then the phosphatemonoester, what are they, so bring alcohol as the nucleophile on your for the reaction. The first type of reaction what he considered as the phosphoryl transfer reaction and the group on the alcohol functionality that gives rise to your glucose 6 phosphate formation over 100 low molecular weight kinase enzymes are involved and 500 protein kinases. So, is a huge number. Do not worry about this numbers.

So, we are only trying to understand the basic reactions what you can have based on the phosphorus. You can have the hydrolysis or you can have the formation of the new POP bond. So, alcohols will come and many other charged species can come and bind to all these cases, so you can have the different low molecular weight, as well as high molecular weight of these phosphoproteins and the phosphatase will also be there which will be required for your hydrolysis.

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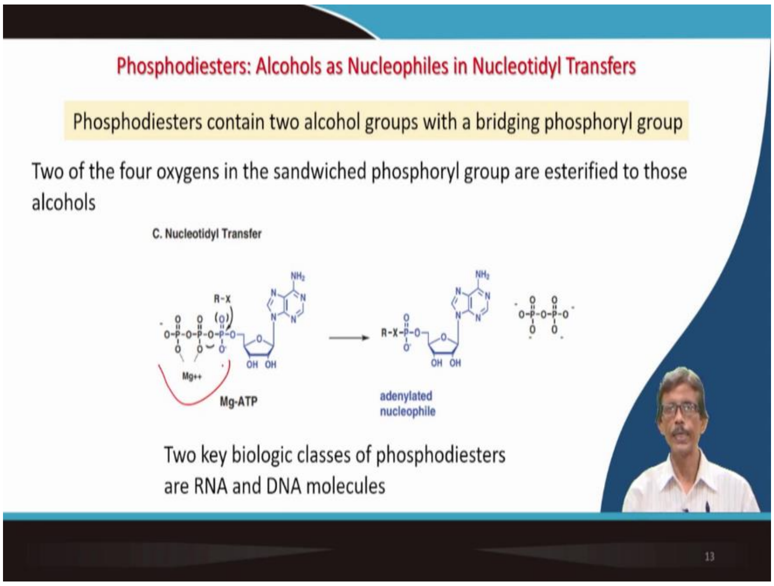

Then phosphodiester, the POP, and is required for your nucleotidyl transfers or nucleotidyl transfers. So, it can have two alcohol groups, which are bridging phosphoryl groups and those bleaching phosphoryl groups are basically like this now. So, now instead of attacking the first one you are attacking the third one.

Now, you see, the control of the magnesium ion is different. So, you have the adenylated nucleophile. So, if you have any alcohol part or anything, you can put one group to that particular group. So, these are very important reactions for these phosphodiester formations and the two key or key biology classes of phosphor diester or RNA and DNA molecule because you have the phosphate, and from two ends you have the corresponding ester formation.

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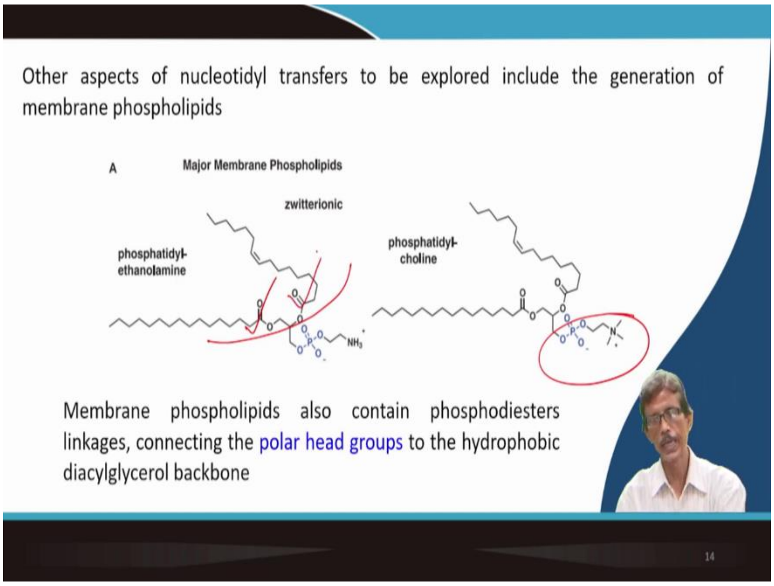

So, in other cases also the nucleotidyl will transport can be useful for your phospholipid formation. So, you have the backbone, then you bring this particular part. So, this is your lipid part and then you bring something else, which is your ethanolamine phosphate part. So, ethanolamine phosphate if you bring and attach to that particular, the central glycerol OH group or O miners group you get the phosphatidylethanolamine or you can bring the choline also the phosphorylated choline part to get that particular phospholipids.

So, membrane phospholipids are therefore, very important thing. Also, for the phosphorylation reaction and the dephosphorylation reaction, because you can have the polar head groups to the hydrophobic diacylglycerol backbone. So, this is one acyl backbone and this is a second acyl backbone and then you can have the phosphate backbone on the other side.

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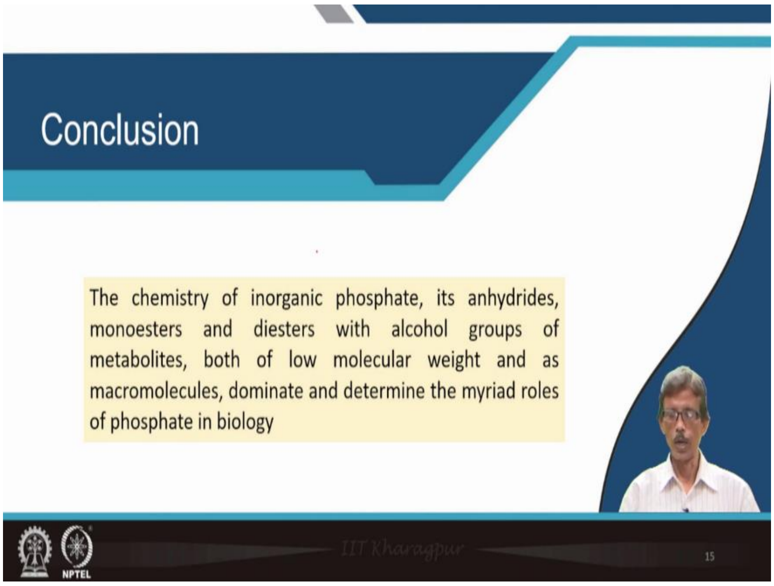

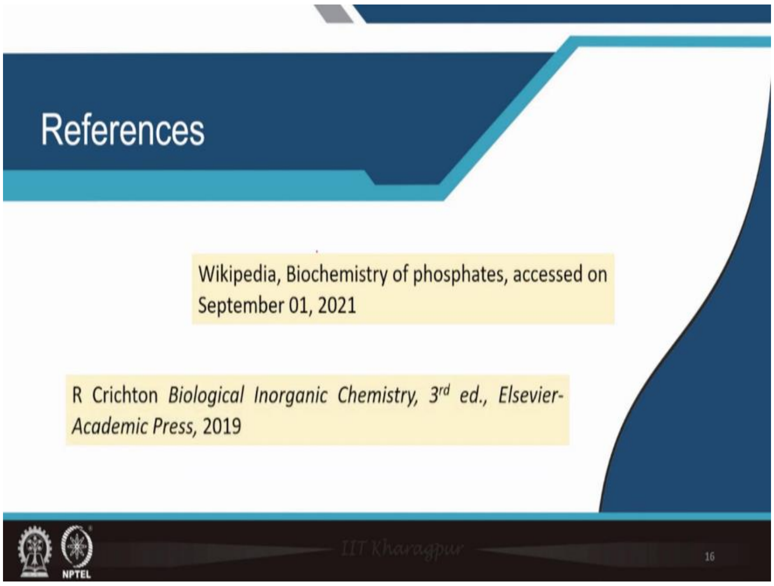

So, we have reached to the end, where we have seen that the chemistry of not phosphorus what we have learned from our school days again, inorganic phosphates it is anhydrous monoesters and diesters with alcohol groups or metabolites because we know the glucose. And if you burn it further, you can have them in alcohol, the pyruvic acids athletes and all these things, so, all metabolites are we have.

Low molecular weight, as the micro, macromolecules and they dominate and determine the myriad roles of phosphates in biology. So, all this chemistry basically, all this chemistry of phosphorylation and dephosphorylation reaction can give us many good informations related to our phosphate in biology world.

So, we basically can go typically for the biochemistry of phosphates within the page of phosphate or phosphorus you can have the in the Wikipedia page, but we look at the biochemistry part of the phosphates, and how, what are the biochemicals or macromolecules are biomolecules involving phosphorus. Then the book of Crichton. Then thank you very much for your kind attention.