Introduction to Complex Biological Systems
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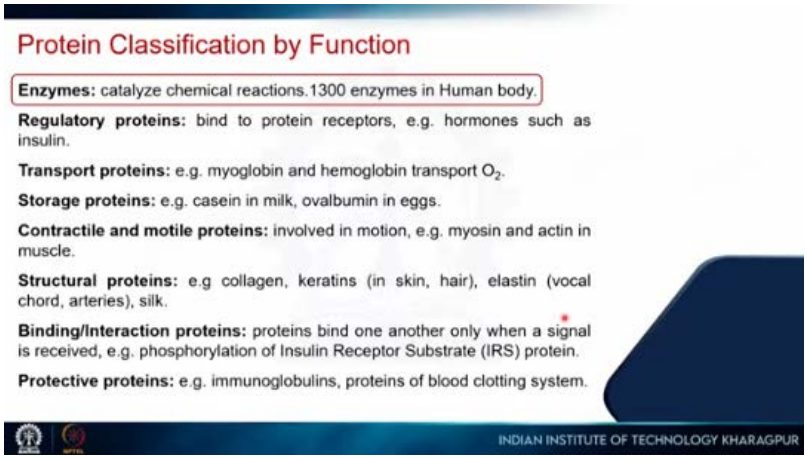
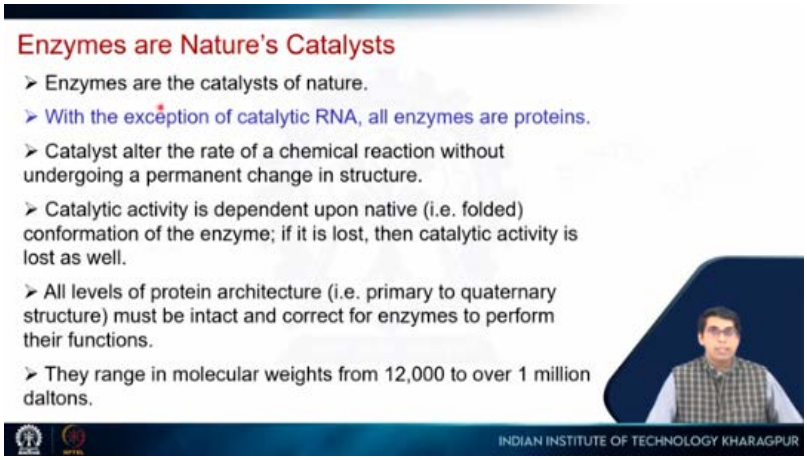
Lecture 31
Vitamins and introduction to bioenergetics

Welcome to the Week 7 lectures of Introduction to Complex Biological Systems. So this week, we are going to discuss metabolism, which is the harnessing of energy in living systems. In today's lecture, I will discuss vitamins and also give an introduction to bioenergetics. So in the fourth week of lectures, we saw that enzymes are one class of proteins.

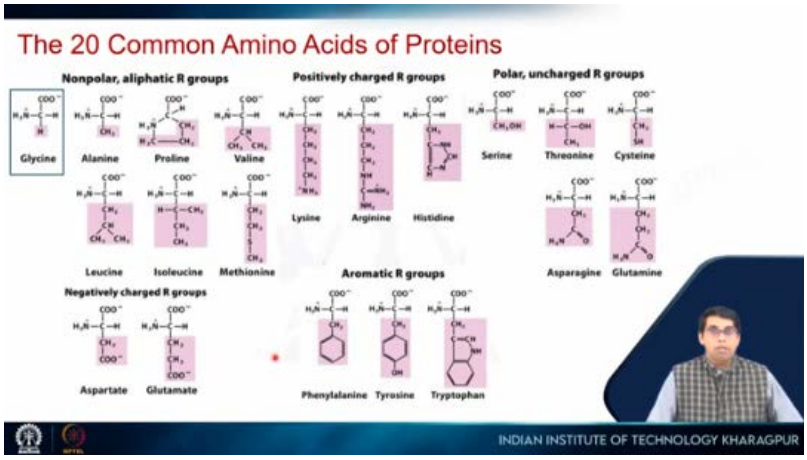


So in Week 3, we learned about proteins and saw that there are all these different types of proteins and in Week 4, we focused on this one particular type of protein which are enzymes, and enzymes are biological molecules that catalyze chemical reactions. So it turns out that there are almost 1300 enzymes. These are approximate numbers.

There are this many enzymes in our body, and they catalyze all sorts of chemical reactions. So what are enzymes? These are nature's catalysts. We saw that RNA can also catalyze reactions, but enzymes are the ones. So most enzymes are proteins and then we learned about all the properties of enzymes. We saw that enzymes have an active site, and this active site is where the actual chemistry happens. Now, since enzymes, or most enzymes, are proteins, they are made up of these 20 amino acids and if you look at these amino acids, we do see different types of functional groups in their side chains.



For example, we have these aromatic side chains, we have these negatively charged side chains, we have positively charged side chains, we have hydrophobic groups, and we have polar groups. So we have all these different types of functional groups. But when we are thinking about catalyzing certain chemical reactions, it turns out that these functional groups are not enough. They are enough to form a scaffold, which is the structure of the protein to fold into three-dimensional space. But the active site chemistry might require some additional functional groups and these functional groups are provided by some other small molecules, which can bind to the active site of an enzyme. They can bind covalently or non-covalently. So these are called cofactors. What are cofactors? Cofactors bind the active site of an enzyme and help in substrate binding or catalysis.

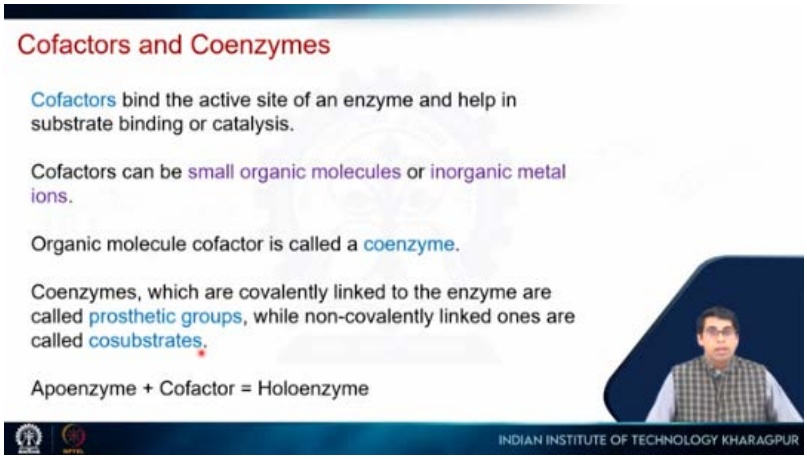


Cofactors can be small organic molecules or inorganic metal ions like magnesium ion, zinc ion, and so on, or they can be small organic molecules. So, in today's lecture, I am going to focus mostly on these small organic molecules. When these cofactors are organic

molecules, they are called coenzymes. Coenzymes that are covalently linked to the enzyme are called prosthetic groups. So, they can be directly bound to the enzyme via a covalent bond or they can be bound in the active site without any covalent bond.

So, they might be hydrogen bonds or hydrophobic interactions and things like that. So, in such cases, when it is non-covalently linked, the coenzyme will be called a co-substrate. When the cofactor is an organic molecule, it is called a coenzyme. When the coenzyme is covalently linked, it is called a prosthetic group and when it is non-covalently linked, it is called a co-substrate.

So, these are the nomenclatures that are used. Now, the enzyme is a protein, let us say, and the polypeptide chain without the cofactor will be called the apoenzyme. When the cofactor is bound in its active site, it is called a holoenzyme. So, what are these coenzymes? Coenzymes are organic molecules that are derived from vitamins.



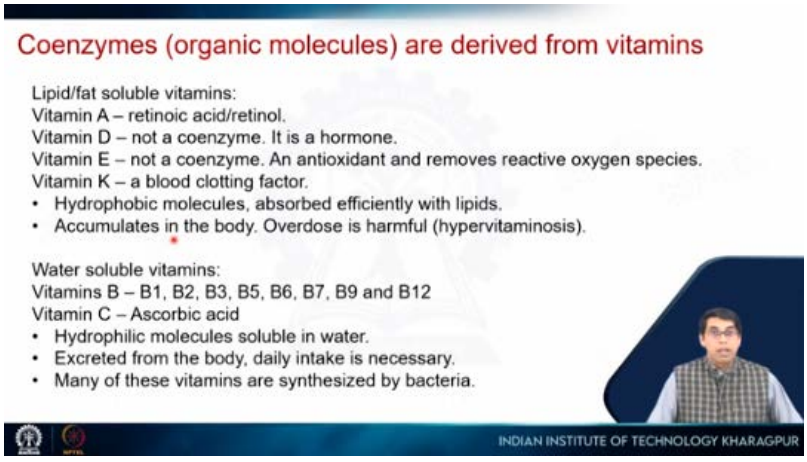
So there are all sorts of vitamins that we take regularly through our diet, and these diets undergo certain chemical reactions to eventually form these coenzymes. It turns out that vitamins can be classified into two groups based on their solubility. So we can group them as water-soluble vitamins and fat-soluble vitamins. So fat-soluble vitamins are mainly of four types. Vitamin A, which is also called retinoic acid or retinol.

Vitamin D, it is not exactly a coenzyme; it is a hormone. Vitamin E, again, it is not a coenzyme; it is an antioxidant, and it removes reactive oxygen species. So this is something

very important because reactive oxygen species can create all sorts of damage in our cells. Vitamin K, it's an important blood clotting factor.

So the common feature of all these vitamins is that they are hydrophobic molecules. So they are absorbed efficiently with lipids. So they are fat-soluble. Now, since they are hydrophobic, they will accumulate in the body because they are not soluble in the water medium that is present inside most of our cells, which means that overdose can be harmful. These molecules accumulate in the body, which means that overdose can be harmful. So, this is called hypervitaminosis. We'll look at the example of vitamin A, and vitamin A is something that is important for vision. Now, if you take too much vitamin A, then it can actually impair vision. So, that is one of the challenges or problems with these fat-soluble vitamins.

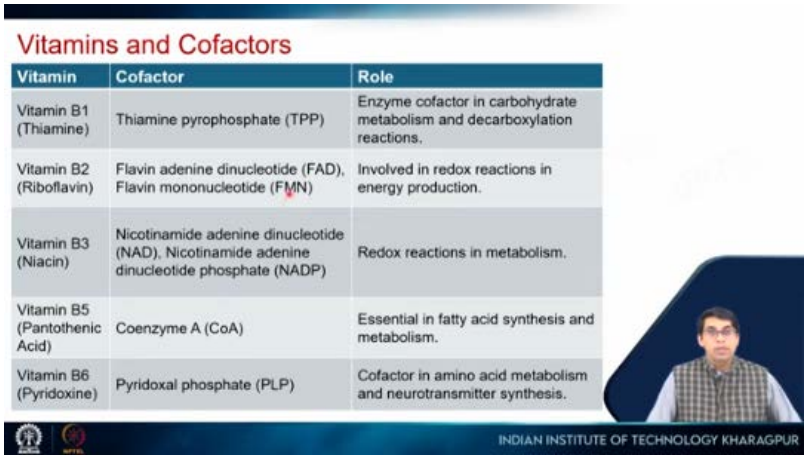
The other classes of vitamins are water-soluble vitamins and they are vitamin B and vitamin C. So, vitamin B comes in all these different flavors. So, B1, B2, B3, B5, B6, B7, B9, and B12. I will discuss these vitamins in more detail in the next few slides. Vitamin C is also called ascorbic acid.



So, these are hydrophilic molecules. So, they are soluble in water, which means that they are also excreted out very easily. So, these vitamins are something that we have to take regularly. So, daily intake is necessary. Many of these vitamins are also synthesized by bacteria.

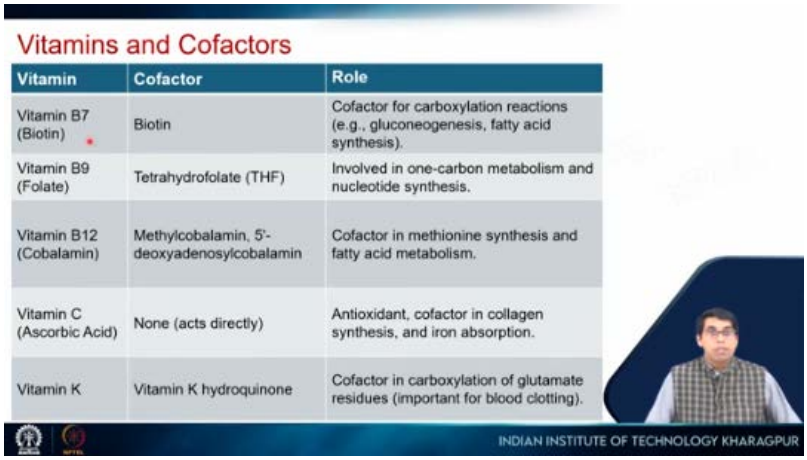
So, let us look at this vitamin B. B1 is also called thiamine, and the cofactor form of this vitamin is thiamine pyrophosphate or TPP. It acts as a cofactor in carbohydrate metabolism and decarboxylation reactions. We will see examples of TPP in this week's lectures. Vitamin B2 is also called riboflavin. It comes in two forms.

One is flavin adenine dinucleotide or FAD. The other one is flavin mononucleotide or FMN. These molecules or cofactors are involved in redox reactions in energy production processes. We will see a lot of these flavin molecules in the next few lectures this week. Vitamin B3 or niacin also comes in two forms.



One is nicotinamide adenine dinucleotide or NAD, and the second one is its phosphorylated form, which is NADP. These are also involved in redox reactions in metabolism. We are going to see FAD, NAD, and NADP, these molecules a lot in the lectures this week. Vitamin B5 is called pantothenic acid. It is the coenzyme A, which is essential in fatty acid synthesis and metabolism.

We will see some examples of coenzyme A in the next few lectures. Vitamin B6, or pyridoxine, the cofactor form is pyridoxal phosphate, or PLP. It is an important cofactor in amino acid metabolism and neurotransmitter synthesis. Vitamin B7 is biotin. It is a cofactor for carboxylation reactions, for example, gluconeogenesis.

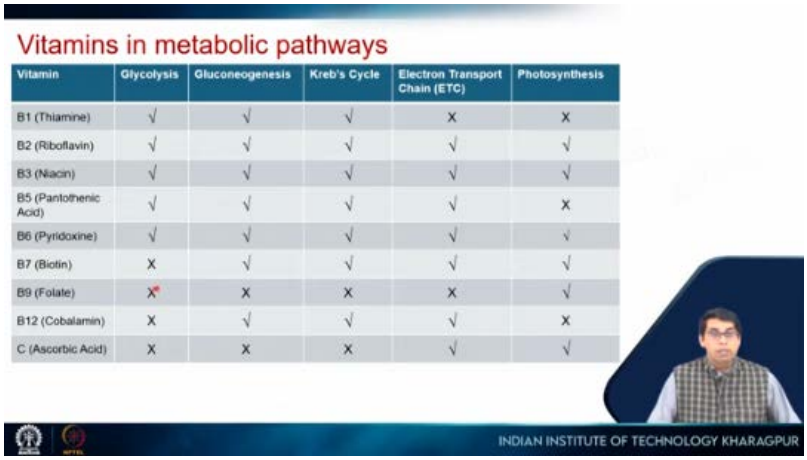


So we will see gluconeogenesis in the next lecture and also fatty acid synthesis. B9 is folate. The cofactor form is tetrahydrofolate. It is involved in one-carbon metabolism and nucleotide synthesis. B12 is cobalamin.

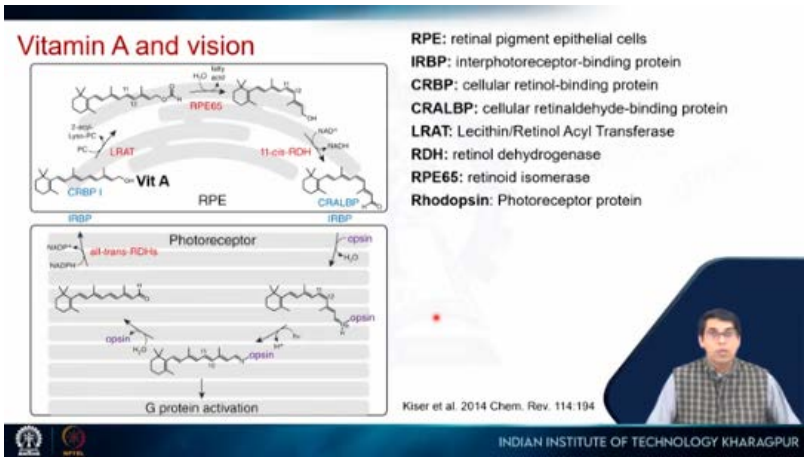
Again, it comes in at least three different forms: methylcobalamin, adenosylcobalamin, or cyanocobalamin. Next, I will discuss this in more detail in the next slide. So it is a cofactor in methionine synthesis and also in fatty acid metabolism. Vitamin C is called ascorbic acid. So it is not a cofactor; it acts directly.

It's also an antioxidant, and it acts as a cofactor in collagen synthesis and iron absorption. Vitamin K, the cofactor form, is vitamin K-hydroquinone. It's a cofactor in the carboxylation of glutamate residues, which is important in blood clotting. So here, what I have done is I have made a table. So, I have listed all the vitamins in this column and these are the different columns where I have listed important processes that I'm going to discuss in the lectures this week. So, what I have done is check whether a particular vitamin is involved in a particular process. If it is, then I have put a tick mark. If it is not, then I put a cross mark.

So, this gives you a single-glance picture, where you can see the involvement of these vitamins in these important metabolic processes. So, let us look at the example of vitamin A. I am not going to discuss all the vitamins. I am just going to discuss vitamin A and vitamin D for the fat-soluble vitamins.



So, vitamin A is this. So, this is all-trans retinol, and this gets converted to all-cis retinol. So, this is the actual retinol. So, let us start from here. So, this is the retinol. This retinol is then bound to a particular membrane protein, which is called rhodopsin. So, this is the architecture of the eye. So, these are all the. So, what you see here, RPE, is the retinal pigment epithelial cells.



So, these are the pigment cells inside your eye and this retinol is an important molecule which is responsible for vision. So here, the molecule is connected to rhodopsin via a Schiff base kind of. So, this NH, what you see here, is coming from a lysine side chain of this protein.

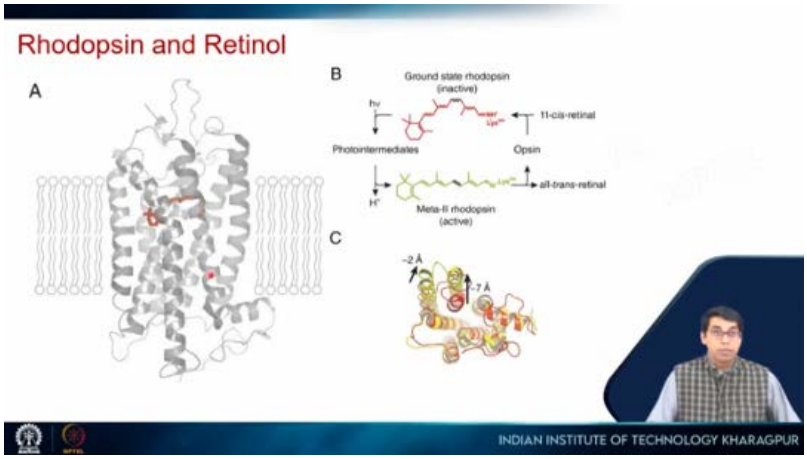
So it is bound to the protein. Now when we see something, light falls and causes a change in the conformation of this molecule. So if you look at this position, this is carbon number 11 and carbon number 12. The two carbons next to it are on the same side. So this form is called the cis form.

So that is why it is 11-cis. So that's the cis form. When light falls on this molecule, it creates a transition from cis to trans. So now you see 11 and 12 are here, but the two carbons are on opposite sides of the double bond. So there is a cis to trans conformational change, which is triggered by light.

When this happens, you can see that the shape of the molecule changes, and that causes a change in the conformation of the protein, which is the signal that is now transmitted to the brain and converted to an image. So this is how light is converted to a physical signal in the protein, which is further transmitted. Now you have the trans form, which has to be further converted into the cis form, and this is done via these processes. So then this whole cycle keeps repeating. So again, now you have the cis form.

This cis form, when light falls, converts to trans. That message is again transmitted via the protein and then again, this cis molecule is converted, and this trans molecule is converted back to cis. So this is called the vision cycle. So let us look at the protein.

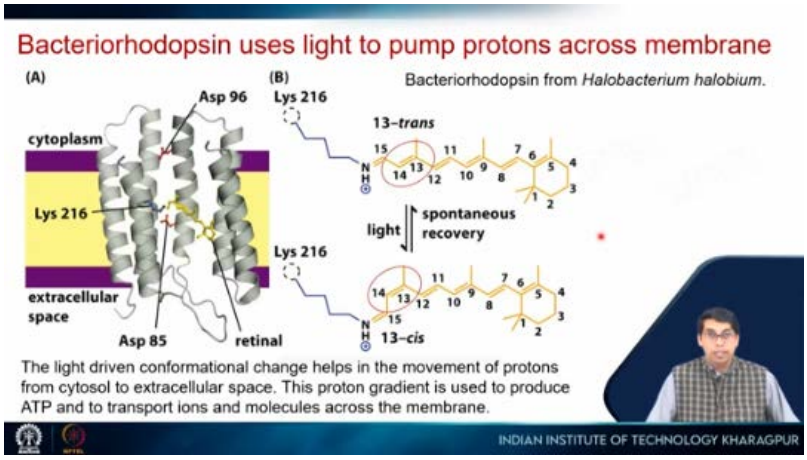
So this is rhodopsin, and you can see that it is a membrane-bound protein, and the retinol molecule is bound somewhere here. So it is an all alpha-helix protein. This is the cis form. So this is 11-cis retinol, and it is bound to this protein opsin or rhodopsin. When light falls, it gets converted to this trans form.



This trans form, since it is bound to the protein here, actually changes the conformation of the protein. So these alpha helices which are present, if we look from the top, then you can see the arrangement of the alpha helices here. So in the red, when the molecule is red, you

can see the red alpha helices and when the molecule is yellow, you can see the yellow alpha helices and you can see that this alpha helix, the red one, moves from this to this. There is a big shift in the alpha helix, and it is almost 7 angstroms. Similarly, this other alpha helix moves by almost 2 angstroms. So there is a major conformational change upon this cis-to-trans change triggered by light in the retinol molecule. So the change in retinol triggers a change in rhodopsin, and then that change is further transmitted, resulting in vision.

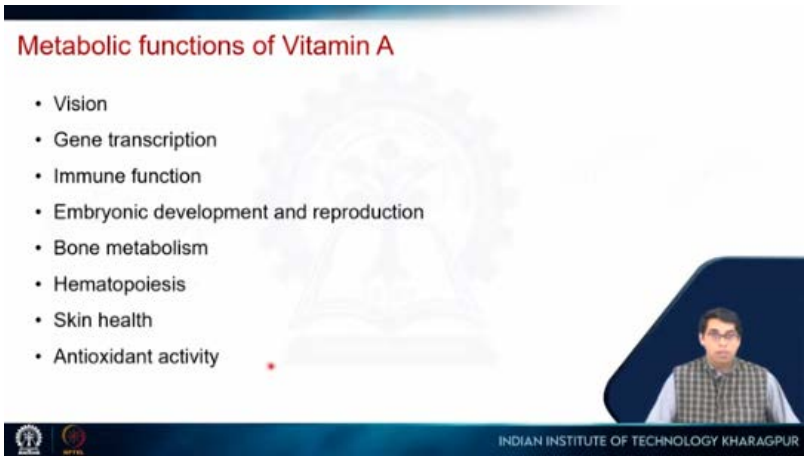
So this is something that we have previously seen. So I'll show you that slide again. So we have already seen this in the Week 3 lecture. I think that was the last lecture of Week 3, where I discussed membrane proteins.



So we saw this bacterial rhodopsin. So this protein, which binds this exact same molecule which is retinol and there also, this cis-to-trans conversion happens because of light. When this conversion happens, it results in a change in the conformation of this molecule and that change in conformation of the molecule is used to drive protons from one side to the other side of this membrane. So in that case, bacteriorhodopsin uses light-driven conformational change to create movement of protons. So this proton gradient is used to produce ATP. So light energy is used to create the proton gradient, and then the proton gradient is used to create ATP, which is the energy currency.

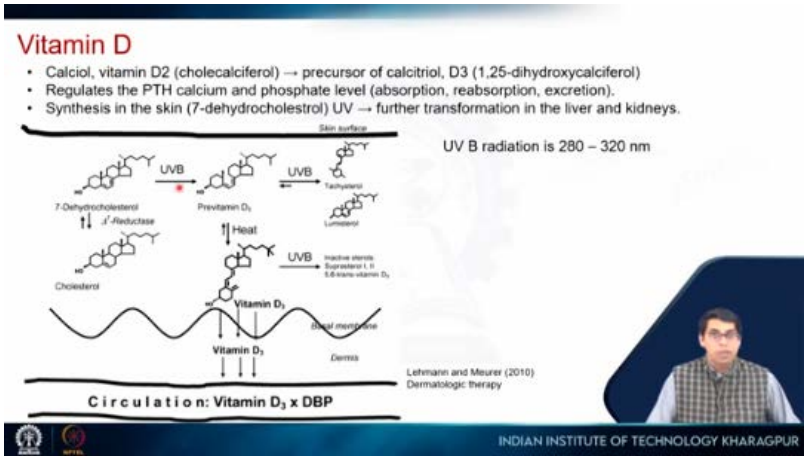
So that was in bacteria. In our case, we are using the same reaction to see. So we are converting it into information. We are converting it into vision. So this is something that you will see quite often in biology that very similar processes have been reused for different purposes.

So it will be more evident when I talk about evolution in next week's lecture. So what are the metabolic functions of vitamin A? Vision is one primary function that we have already discussed. Apart from that, it is also involved in gene transcription, immune function, embryonic development and reproduction, bone metabolism, hematopoiesis, which is the formation of all the blood cells, skin health, and antioxidant activity. So it is involved in many, many processes.



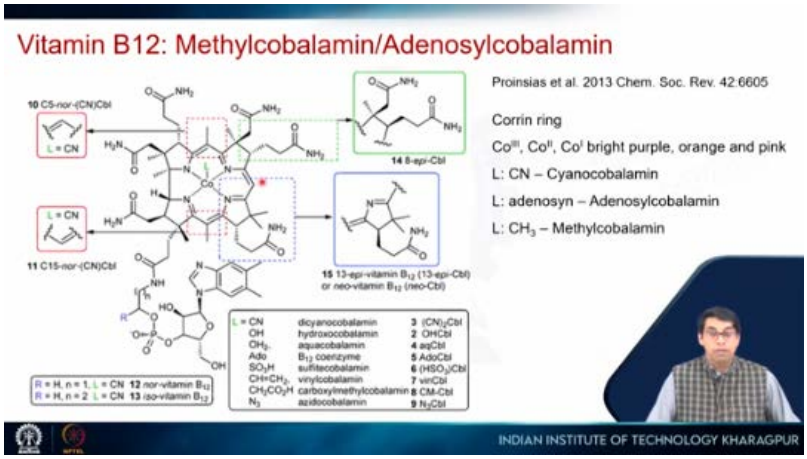
The other example that I will take up for the fat-soluble vitamins is vitamin D. So, vitamin D is formed from cholesterol. So, this is the structure of cholesterol and what you will see is that it gets converted to this 7-dehydrocholesterol. So, why dehydro? Because there is a double bond that is formed here. So, that's a dehydrogenase reaction. So, it's a reduction reaction. Now, when UV light is incident upon this molecule, a certain light-sensitive reaction happens.

So, there is a ring-opening reaction that happens here. You can see that a ring-opening reaction happens. Now, this is pre-vitamin D3, but this is not a very stable molecule because there is steric hindrance. So, there is steric obstruction at this position. So, just using thermal energy, this molecule gets converted into this molecule. So this is cis, and it gets converted into trans and this is your vitamin D3. So it is synthesized from cholesterol, but again, light plays an important role in the synthesis of vitamin D3. So we actually need UV radiation.



That is why vitamin D3 synthesis happens in the skin. It is further transformed in the liver and kidneys. So this UV B radiation is in the range of 280 to 320 nanometers. So, that is why sunlight is important for the production of vitamin D3.

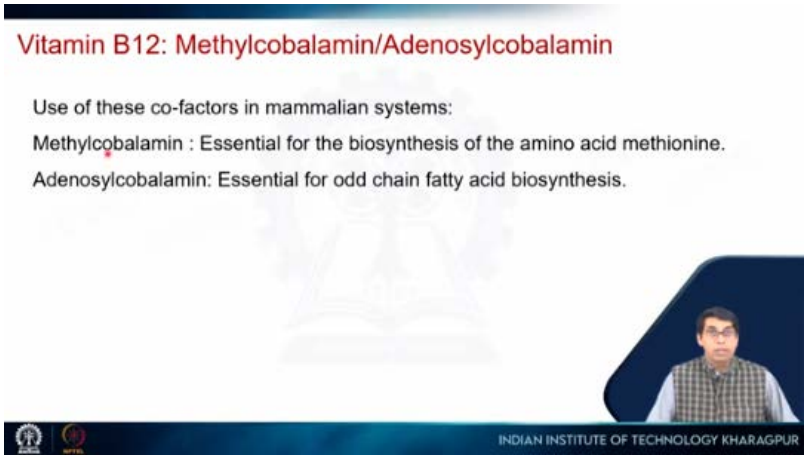
So, this is vitamin B12. This is a fat-soluble, and this is a water-soluble vitamin. So I have taken up this example of vitamin B12 because it is one of the most complex structures that you will see for a vitamin. This is something that you might have seen before. So we have seen in the case of hemoglobin, the porphyrin ring.



This is a similar ring, but it is not a porphyrin. It is called a chlorin ring and in this case, there is a cobalt ion sitting at the center. And again, it is not a very planar structure. It is not a planar structure like the porphyrin ring.

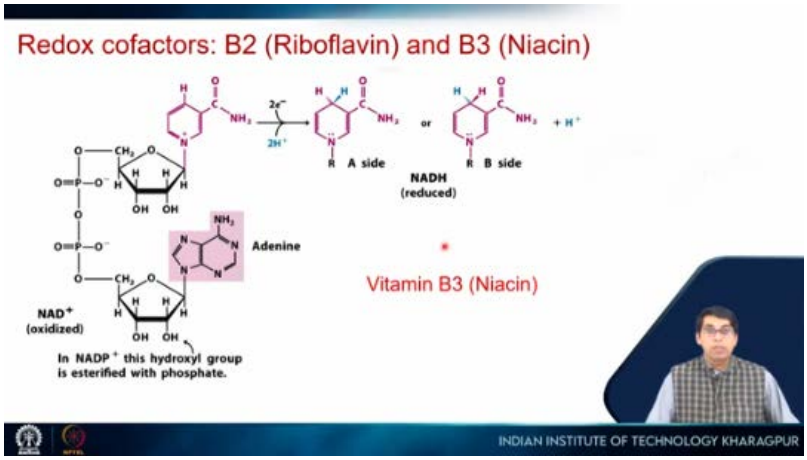
So on one end, there is this ligand. In the case of hemoglobin, it was oxygen. In this case, this ligand can be of a different type. So some of those are listed here. I will talk mostly about these three.

So if that ligand is a cyanide group, then it is called cyanocobalamin. If it is an adenosyl group, then it is called adenosylcobalamin and if it's a methyl group, then it is called methylcobalamin. So these two are the active forms of the vitamin that act as cofactors and in all these forms, this cobalt undergoes or it is present in these different types of oxidation states. So it can be cobalt 3, cobalt 2, or cobalt 1 and then, of course, it can participate in oxidation-reduction reactions. So, what is the function of vitamin B12? Methylcobalamin is essential for the biosynthesis of the amino acid methionine.



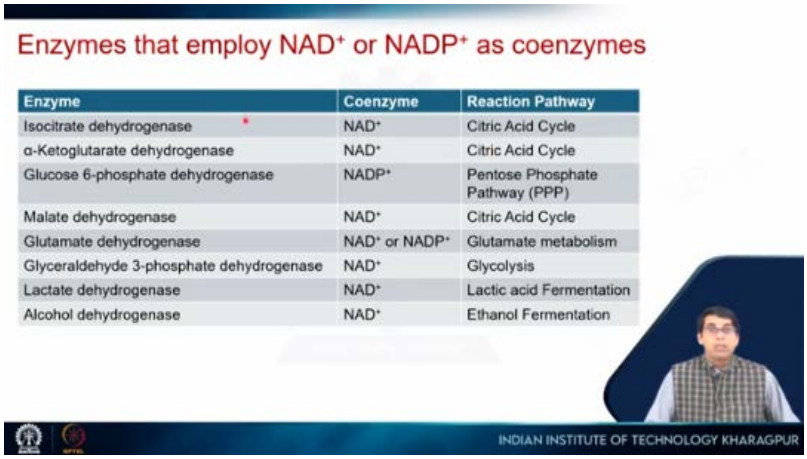
So, the terminal methyl group is supplied by this cofactor. Adenosylcobalamin is essential for the odd-chain fatty acid biosynthesis. So, there are two more vitamins which we will see. I'm mentioning them here specifically because we will see a lot of these vitamins in the next few lectures. So, one is vitamin B2 or riboflavin, and the other one is vitamin B3 or niacin.

So, this is the structure of vitamin B3 or niacin. So, what you see here is this is a nicotinic ring and then here, there is adenine. So, most of this remains constant. So, we are not going to discuss much about this because this is not where the actual chemistry happens. The chemistry happens here. So this and this. So these are the, this is the oxidized form. This is the oxidized form and this is the reduced form. Now this is NAD^+, this molecule when it gets reduced, it becomes NADH.



If we have a phosphate group at this position, then this is called $NADP^+$. So, if there is no phosphate, it is NAD^+; if there is phosphate, it is $NADP^+$. Similarly, when it gets reduced, if there is no phosphate, it will be NADH. If there is a phosphate, it will be called NADPH.

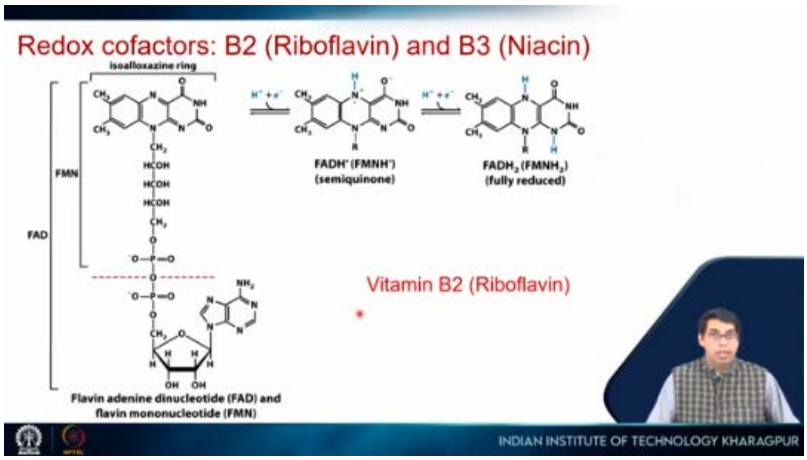
So these are the two forms of vitamin B3 or niacin. So that is the cofactor. We will see that NAD^+ and NADH or $NADP^+$ and NADPH are involved in oxidation-reduction reactions. So enzymes that employ NAD^+ or $NADP^+$ as coenzymes. Isocitrate dehydrogenase.



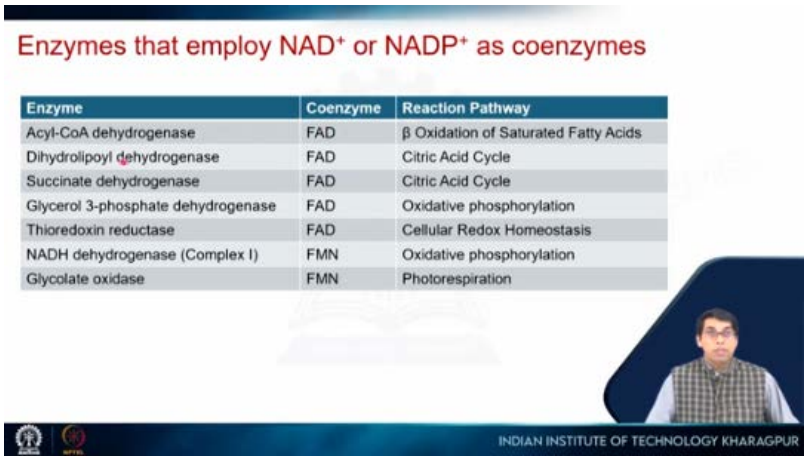
We will see NAD^+ in the citric acid cycle. This will come in the third lecture this week. Alpha-ketoglutarate dehydrogenase, again in the citric acid cycle. Glucose 6-phosphate dehydrogenase, this is $NADP^+$, it will be present in the pentose phosphate pathway, so that will be the next lecture. Malate dehydrogenase, again in the citric acid cycle.

Glutamate dehydrogenase, glutamate metabolism. Glyceraldehyde 3-phosphate dehydrogenase in glycolysis, this will be the next lecture. Lactate dehydrogenase, alcohol

dehydrogenase in lactic acid fermentation or ethanol fermentation. So you will see that these are all oxidation-reduction reactions. The next one is riboflavin, vitamin B2 and in the case of riboflavin, again, we have this group, and we are not going to talk much about this adenine group. But this group isoalloxazine ring. So, this is the one that is important. So, this one can undergo one-electron reduction or two-electron reduction.

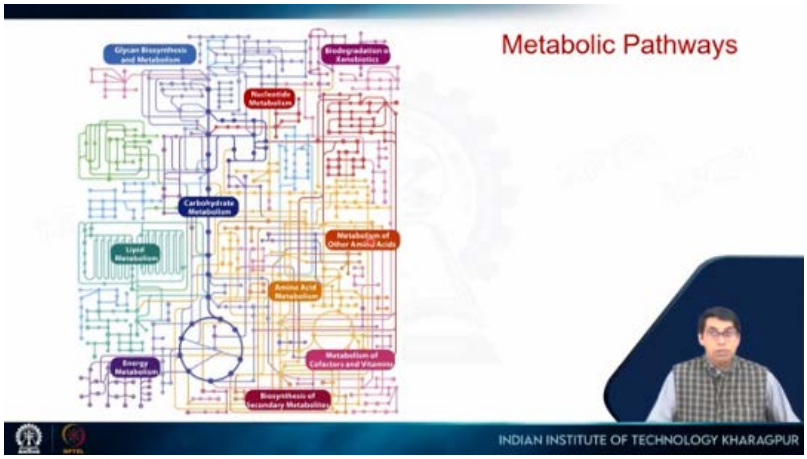


So, this is different from this, different from niacin. So, in the case of niacin, it is always a two-electron reduction. But in the case of flavin, it can be a one-electron reduction or a two-electron reduction. So, it can catalyze more, and it has more nuance. Thus, it can catalyze a greater variety of oxidation-reduction reactions. So, we are going to see a lot of this FAD and FMN. So, acetyl-CoA dehydrogenase, which is present in the oxidation of saturated fatty acids. Dihydrolipoyl dehydrogenase, succinate dehydrogenase, both in the citric acid cycle, so Week 3.



Glycerol 3-phosphate dehydrogenase, oxidative phosphorylation, so it will come later this week. Thioredoxin reductase, again later this week. NADH dehydrogenase, oxidative phosphorylation, glycolate oxidase, and photorespiration. So, we are going to see all of these processes in the lectures this week.

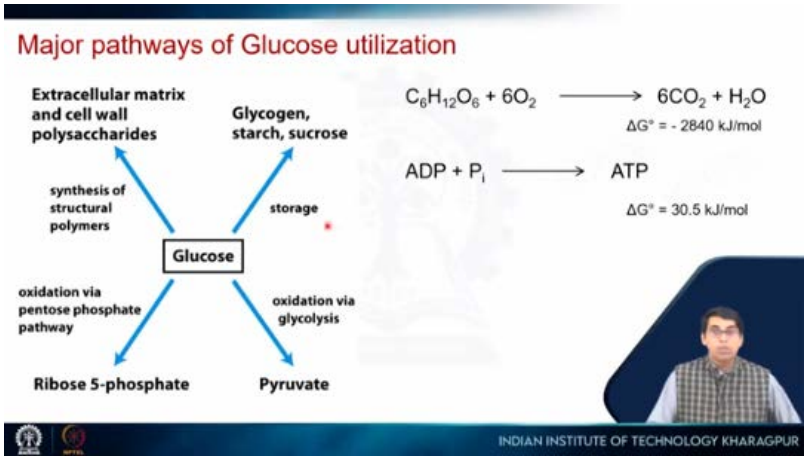
We will come across these coenzymes and these enzymes. I will end by showing you this complex diagram. So this is something that is called a metabolic pathway. In this diagram, each point is some molecule, and each line is the conversion of that molecule to another molecule. So, for example, if you follow this to this, this is converted to some other metabolic molecule, and this conversion will be catalyzed by some enzyme.



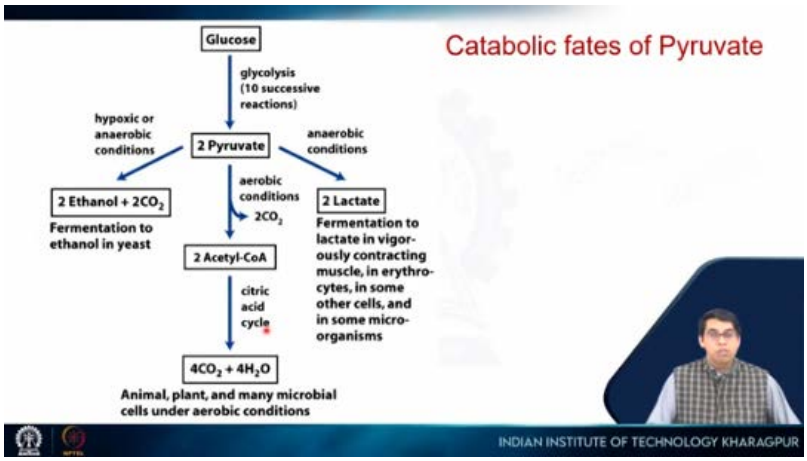
So every line will, in essence, represent a molecule. A chemical reaction which is catalyzed by some enzyme. We are going to look at glycolysis in the next lecture, and we are going to look at the citric acid cycle in lecture 3. So, briefly, in glycolysis, what happens is we are going to look at the formation of pyruvate from glucose.

So glucose is a very high-energy molecule; the combustion of glucose results in, so if you use oxygen, if you oxidize glucose, you will get carbon dioxide and water, and you will get a release of a very high amount of energy. But if we just burn glucose, most of this energy will be lost as heat energy, which we cannot use much. What nature does, or what metabolism does, is it takes this glucose molecule and proceeds through these oxidation reactions in a stepwise manner, and while it does that, it will keep on harnessing the energy that comes out and will also make important molecules, important metabolic molecules.

So we are going to see that in the next few lectures, and we will see what happens to this pyruvic acid.



Glucose forms pyruvic acid and from pyruvic acid, we will go into the citric acid cycle and then all molecules are synthesized while these processes occur. So we are going to discuss all of this in more detail in the next lecture.



These are the books that I have followed for this lecture. So you can refer to these books. Thank you.

REFERENCES

Following books may be referred to

- Lehninger Principles of Biochemistry
- Biochemistry (Lubert Stryer)
- Molecular Biology of the Cell (Alberts)
- Molecular Cell Biology (Lodish)