Introduction to Biomolecules
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Lecture – 17
Bioenergetics (Part 2/2)

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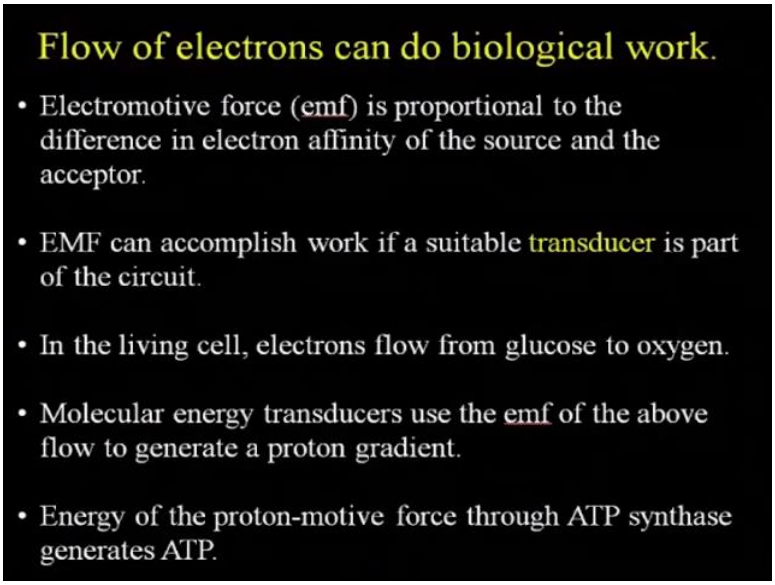

So, in the last class we were discussing about how in biology most of the energy transfer is via oxidation reduction reactions and then was talking about the free energy that is available is actually is a reflection of the kind of bonds and the kind of atoms that are bonded and as an example we saw how the phosphoric acid esters in ATP how that is a high energy molecule and how hydrolysis of ATP can release free energy and so on.

We saw about thioester all that. So here we are going to focus primarily on the electron transfer related thing. I think I sort of explained this, but for continuity sake I will begin here once more. So, when you have a molecule which is having low affinity for electrons and you have another molecule that readily accepts electron then the electron one would donate and another one will accept.

And this electron transfer will happen with a force that is equivalent to the difference in the relative affinity for the electrons between these two molecules. So, this is what happens in an electrochemical battery. At one electrode you might have a chemical species that readily donates electron and at the other electrode you might have a species that readily accepts.

Now if you have a wire connecting the two, then there will be an electron flow and because the difference in the potential between the two electrodes we will determine the force of this flow that can be used to do a work if you have a suitable transducer. The transducer is an important thing here. So, in living cells the electrons like this is one major example, it is not just electrons flow only from glucose and only to oxygen.

So, this is a major example therefore here it is there as an example. So, electrons flow from glucose to oxygen often times to discuss biochemistry we will keep our conceptual centering on the carbohydrate chemistry particularly glucose because this is the major molecule involved and the metabolic conversions of glucose is what is the best understood in terms of mechanisms of enzymes involved, etc.

And the molecular energy transducers use the emf of the above flow to generate a proton gradient. This we will learn at length when we go to oxidative phosphorylation. This is pretty much the summary of the whole thing. So, when the glucose has low affinity for electron and oxygen has high affinity, so it flows from glucose to oxygen and earlier I have told you that this happens in step wise like in a waterfall.

You do not allow the entire water to fall on one windmill at the bottom of the waterfall, you can have stepwise falling and therefore you can have multiple water mills from the top of the waterfall to the bottom and each one could produce sufficient mechanical energy to drive a function. So similarly, from glucose to oxygen it is like from the top of the water fall to the bottom of the waterfall it does not directly fall.

There are intermediate carriers from glucose to a next relatively high affinity electron acceptor and then from that to relatively higher one next one and so on there are multiple things between these two. And then each one of them you have a transducer and the way the energy transduced here is to push protons against concentration gradient across a membrane. So, you end up building a proton gradient.

And then when the proton once you create a place where proton gradient proton concentration is higher, then another place and when the proton passes down its concentration gradient that energy released is used to make ATP. So, this is how the energy from glucose

finally ends up making ATP. So chemical energy basically is converted from one form to another form of chemical energy this is what happens.

So, since this is the central concept of how it happens in biology, we need to pay attention to this electron transfer and therefore we will visit very briefly two basic concepts of electrochemistry now.

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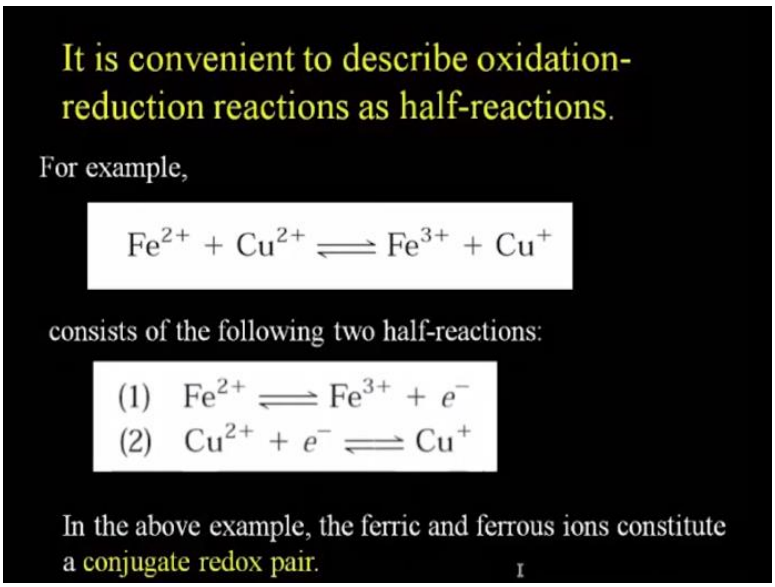

So, these oxidation reduction reactions where you have this oxidation losing electron or reduction accepting electron. So, these are convenient to consider them as half reactions. So, the following gives you an example of what is a half reaction. So, let us see here ferrous becomes ferric, cupric becomes cuprous. One is oxidized, another is reduced. So that you can consider as two separate reactions.

One is this ion ferrous becoming ferric by losing an electron, so this is getting oxidized, it lost an electron. So that alone we consider as one half of this complete reaction. And in the second half this one accepts the electron and gets reduced cupric to cuprous. So here this ferrous ferric behaves more like to get an analogy, not exactly the same but as an analogy acetic acid acetate you have a weak acid and its conjugate base.

So, you have a weak acid and its conjugate base as a pair. Very similarly here you have this something that can lose an electron, meaning this gets oxidized. So, this is a reducing species here and this is something that can get reduced, means this is an oxidizing species. So, reducing oxidizing species together from a pair and that we call as conjugate redox pair. So in

terms of the acid, we talk about the proton losing and proton accepting ability and those two species as one conjugate acid base pair.

So do not confuse that with this, they are not identical. Here it is losing electron. If there is a concomitant loss of proton or acceptance of proton that is a different story. Here the discussion or the naming is purely centered on whether a given species loses an electron or accepts an electron and the donor acceptor of electrons they form a redox pair. So that is how the conjugate acid base pair is different from a redox pair.

So, you have a one redox pair here, another redox pair here. Let us say this is at one electrode of a battery and this is at the other electrode of a battery and if this is something that would be having less affinity for electrons this has more affinity for electron. Then if the two electrodes are connected by wire electron will automatically flow from one electrode to other electrode. So that is the basis for what happens in the electron transfer based oxidation reduction reactions.

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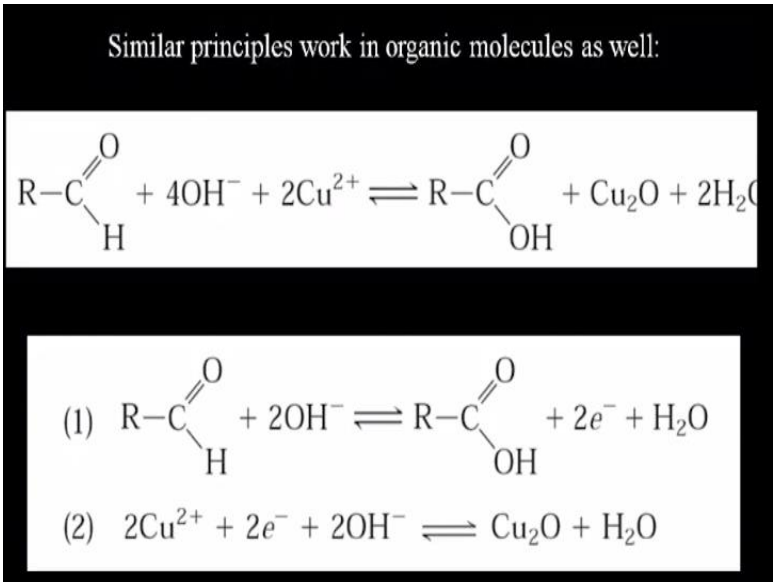

So very similar principle applies in biology as well. Like for example here you take the aldehyde group, so this is getting oxidized to carboxylic acid and the electrons ultimately come from this hydroxyl ion. So here in the process copper gets oxidized as well. So, what is reduced this is the hydroxyl group becoming H 2 O, so that is the reduction. So now this you can write as two redox pairs.

One aldehyde and the hydroxyl group and then the two electrons being released and in the second step the two electrons are transferred to the two cupric to become cuprous oxide because this uses two copper molecules you balance the equation by having two copper ions here. So, you can have again very similar logic as what we saw in the previous one, the same logic happens here except that here we have brought in organic molecules.

And this is what happens in living systems. So, in living systems the energy is actually not purely in terms of rearranging bonds alone, so it is actually electron transfer molecules have high or low affinity for electrons and therefore electro chemistry principles apply here.

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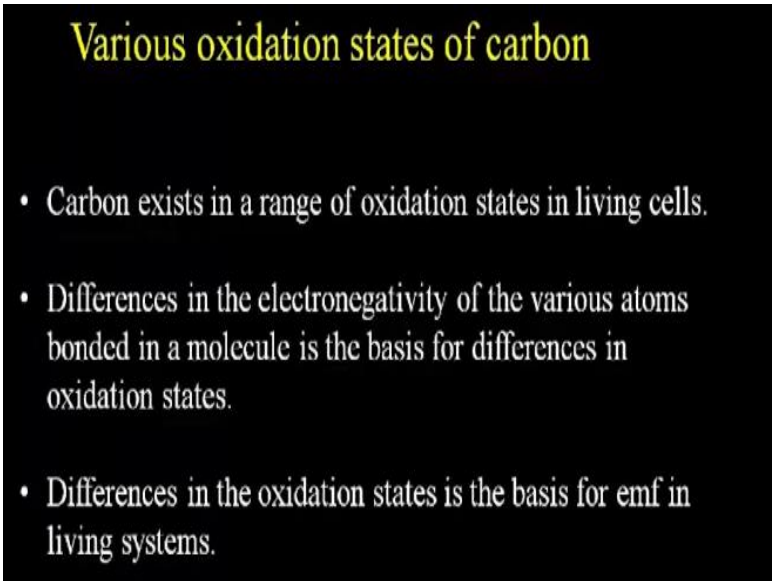

So before we move further, we are going to look at this carbon's oxidation state once more. We have already paid attention to this when at the very beginning when we considered 5 kinds of reactions in one of them in the oxidation reduction, we looked at how carbon have multiple oxidation states. We will revisit that once more in the next slide.

Then differences in the electronegativity of various atoms bonded in a molecule is the basis for oxidation state difference. So, this will come as we go through examples. So primarily it is all due to the electronegativity of the atoms and that is where the high affinity low affinity comes.

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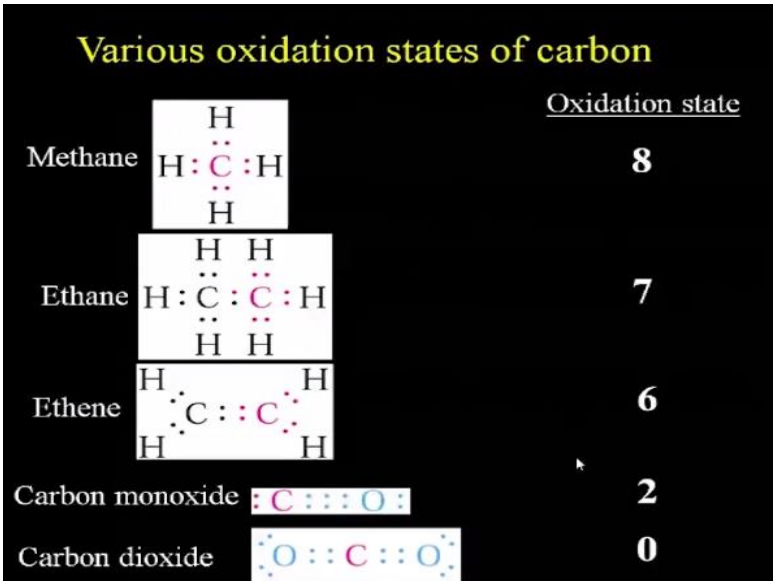

So first let us go and look at the carbon's oxidation state. So that has the key to understand how one molecule may be like at the swimming pool in water and another molecule could be at the six feet tall diving board. So, you take methane for example. So, in methane if you look at it, carbon is more electronegative than hydrogen, so therefore carbon has more claim on the paired electrons and this is the highly reduced state of carbon.

So that we call as oxidation state 8. It is primarily counting the number of electrons that are bonded with the other molecules. So here the type of bond and the type of atoms that is where its energy is or that is where its electron affinity comes to. So here if you look at it so here the electron affinity the carbon has more hold on 8 electrons and that is because of the kind of atom it is bonded to, here it is hydrogen.

Next if you look at ethane here one of the shared electron pair is with another carbon. So, this carbon is not going to behave like hydrogen it is going to behave like carbon and as a result this carbon does not have that much claim on one of those electrons that otherwise it would have had. So, it is slightly more oxidized compared to methane. So, there is no oxygen in the picture here. So, oxidation-reduction is primarily here we are viewing it in the nature of affinity for electrons.

So here affinity for electron is slightly reduced, further reduced when it is a double bond here, it has lost claim on one more electron pair. And when you go to carbon monoxide so you actually you have charge here. So, with oxygen being strongly electronegative compared to

carbon now it does not have that much claim, so it falls to 2. So, for the simplicity sake I have not included the examples between this but the book has example for 5, 4, 3 all of them.

And in the most oxidized form carbon dioxide the carbon actually has no claim on any of the electrons that it claimed in methane. So, this is the most oxidized form. So here what I want you to remember is in each one of these molecules the electron affinity varies. So, this carbon has the maximum reduced state like claim on maximum number of electrons. Here it has the least, basically 0 here.

So, these are the 8 oxidation states of carbon and the energy the relative affinity primarily therefore comes from. Now we will understand this bullet better. Differences in the electronegativity of various atoms bonded in a molecule is the basis for the differences in the oxidation state of that given molecule. So, oxidation state of methane versus oxidation state of carbon dioxide.

So, methane can give up electrons that has the lowest affinity for electron it can readily give electrons. Whereas oxygen in carbon dioxide we call it as fully oxidized because it just cannot give up any more electrons. It has the highest electron affinity there the 2 oxygen atoms. So, therefore electron can flow from methane to carbon dioxide but not the opposite and the basis for this is the relative electronegativity.

Like if you have carbon bonded to hydrogen, nitrogen, phosphorus, sulfur, oxygen. So, depending on that the relative affinity will keep changing because the electronegativity of these atoms vary oxygen being the strongest and hydrogen being the lowest. And these differences in the electronegativity coming from the differences in the oxidation state therefore is the basis for generating this electron motive force in living system. So that is how energy flow happens in the living system.

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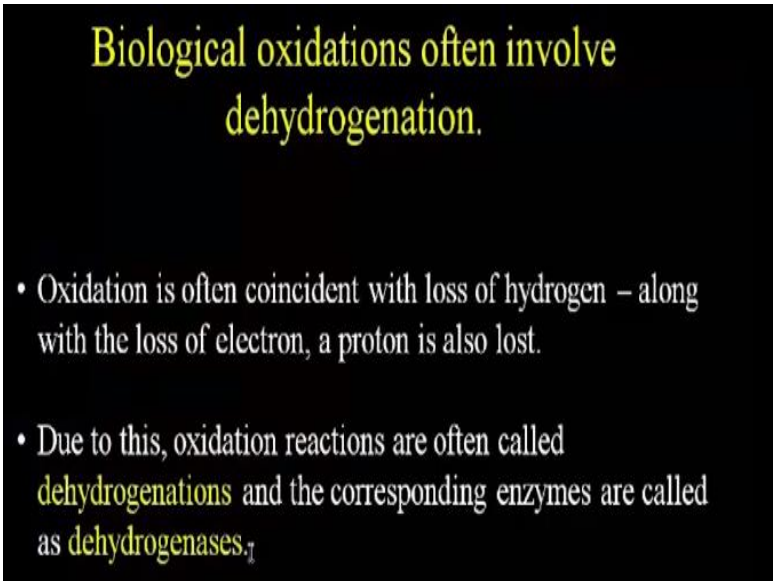

So now we will actually go into seeing the biological oxidations and reductions one step at a time. The actual reaction will take still few more lectures, so we just make a beginning here. So, oxidation is often a coincidence in biology with the loss of hydrogen. So, it is usually an electron along with a proton. So, the proton concomitantly being lost we do not pay attention here.

We pay attention primarily to electron because that is where the difference in affinity for electron is where we get this EMF, we get that free energy. So usually happens as a loss of hydrogen that is the form in which we lose electron. Meaning when we lose an electron, we also lose a proton. So therefore, the oxidations are usually dehydrogenations meaning you are losing a hydrogen.

Removing your hydrogen that is why dehydrogenation like dehydrating when you lose water dry up you call dehydrating. So similarly, when you lose hydrogen you call dehydrogenation and the corresponding enzymes are dehydrogenases.

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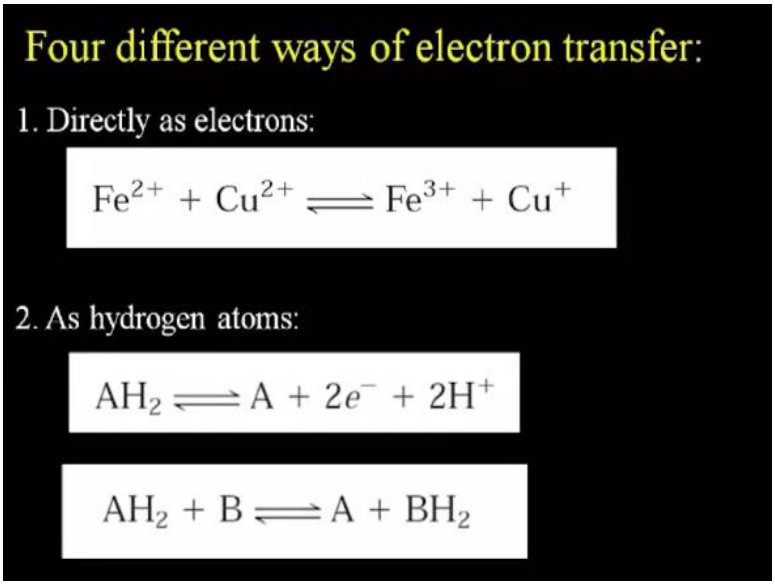

So now we will look at the various base in which electron transfer happens. One directly as electrons as we saw in the examples of iron and copper ions and second way is hydrogen atoms like you lose here 2 hydrogen atoms but in the form of, sorry you lose 2 electrons but in the form of 2 hydrogen atoms. These 2 protons also go. So, this is a typical dehydrogenation.

So here this is another example. So here this is losing hydrogen and this gains hydrogen. So, this is like the half reaction for this, only one half is written.

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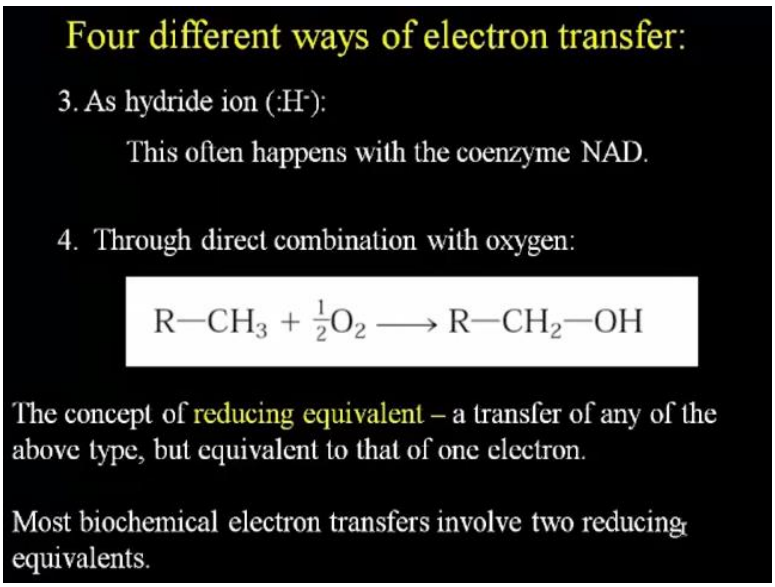

And the third which often happens in electron transfer chain is hydride ion. So, what actually happens here is you lose 2 electrons and a proton. You do not lose 2 electron and 2 proton that would be losing 2 hydrogens, instead here you lose an extra electron 2 electrons and a

proton and as a result that resulting ion hydride ion has a negative charge because it has one extra electron compared to the proton number.

And this is the form in which it happens with that cofactor which is NAD. So we will learn in detail about it a few slides later today itself. And the fourth one is combining with oxygen, so here you do not visibly formally see an electron coming out and electron going to another one the acceptor insert directly or combination with oxygen. So, this gets hydroxylated, so methane becomes methyl hydroxide here, so this is one way.

So, these are the four ways directly as electrons, as hydrogen atom, as hydride ion and fourth by combination with oxygen. So here only the oxidation state is changed or altered without formal electron transfer like here instead of having all 4 valences with hydrogen here one of them is with an oxygen and therefore that pair shared with carbon that is the carbon is sort of oxidized by partially losing it to this. Here you do not have a formal electron transfer.

So, in all these we talk about electron transfer and we can introduce a quantitative term called reducing equivalent so which is equivalent to the transfer of one electron regardless of what is the mode in which electron is transferred. It could be any one of the four but the equivalent of one electron transfer, we call as one reducing equivalent. Biochemical reactions usually involve 2 hydrogen atoms as in dehydrogenation reactions.

So usually, they involve two reducing equivalents. One reducing equivalent equals to the transfer of one electron.

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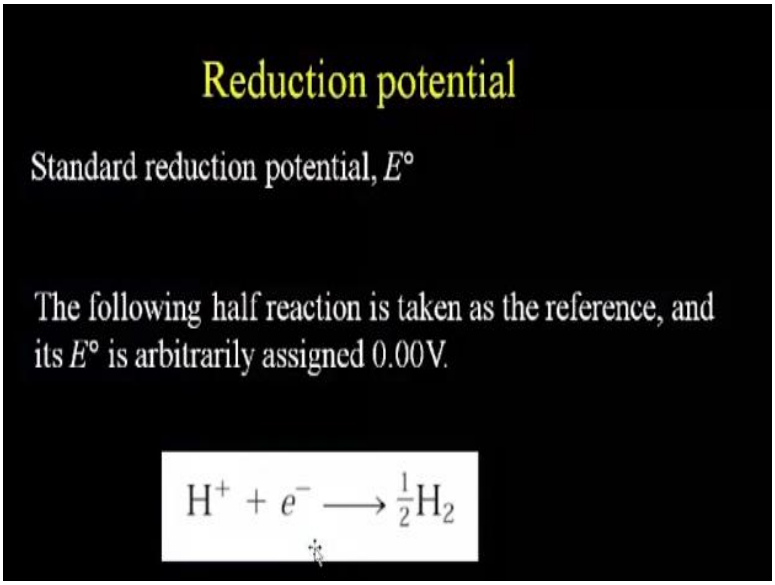

So now we are going to talk about a concept called the reduction potential. So, reduction potential is actually the potential of a molecule to take up or give electrons. It is basically defining affinity for electron in a different way. So, for example the reduction potential for one molecule is low means it would readily lose electrons. If the reduction potential for one molecule is very high means it has high affinity for electrons.

So, it is not going to get readily oxidized anymore, it is not going to lose electrons. So then within reduction potential, we define a term called standard reduction potential. So standard reduction potential means when everything is at one molar concentration at temperature 25 degrees and if it is gas it is at a certain partial pressure which is taken as the standard that value will be there and when we are going to look at the fuel cell in the next slide.

And this standard reduction potential is arbitrarily assigned as 0 volts for this particular half reaction that is proton taking up a electron to become hydrogen atom and this electron acceptance by this or this one going to donate this we take it as the reference and this is taken as the this hydrogen's standard reduction potential, everything else is compared with this.

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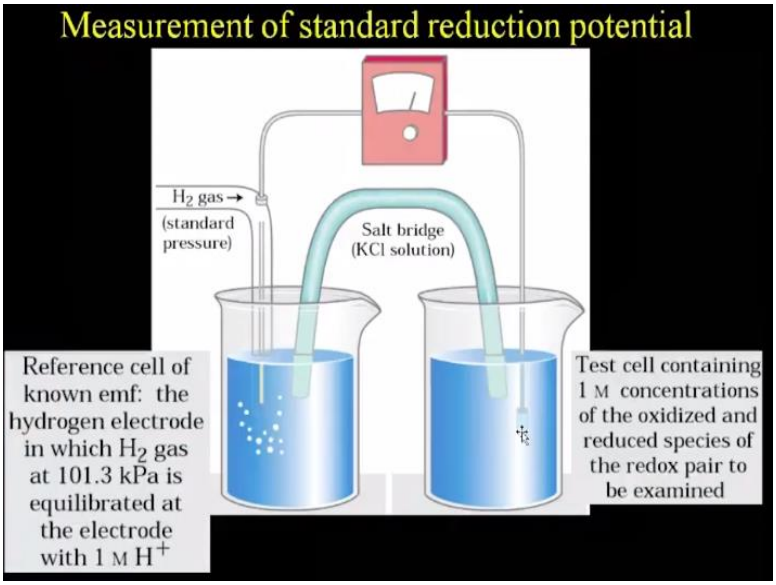

So now for example if I am going to take another redox pair and I use this hydrogen as this reaction in the other one that is connected by a wire. So, the salt bridge allows for exchange of the ions between the two. So now to have the standard reduction potential when it is gas you have 101.3 kilo pascals. So, when you have that pressure of the gas that is taken for the standard electron potential. So here the proton concentration will be 1 molar.

If it is not gas if it is something dissolved, then it is 1 molar concentration. So, the reduction potential when the concentration is 1 molar and temperature is 25, then you call it as standard reduction potential. So, when you have hydrogen gas under standard pressure when this is in standard reduction potential situation now against that you measure the other one. So, if whatever you have here if this has a high affinity for electron higher affinity than this, then the electrons will flow through this.

And you can have a meter here and that can measure and tell you the difference between the two. So that is how you measure the standard reduction potential for any redox pair by keeping that pair at 1 molar concentration, then only it will be its standard reduction potential.

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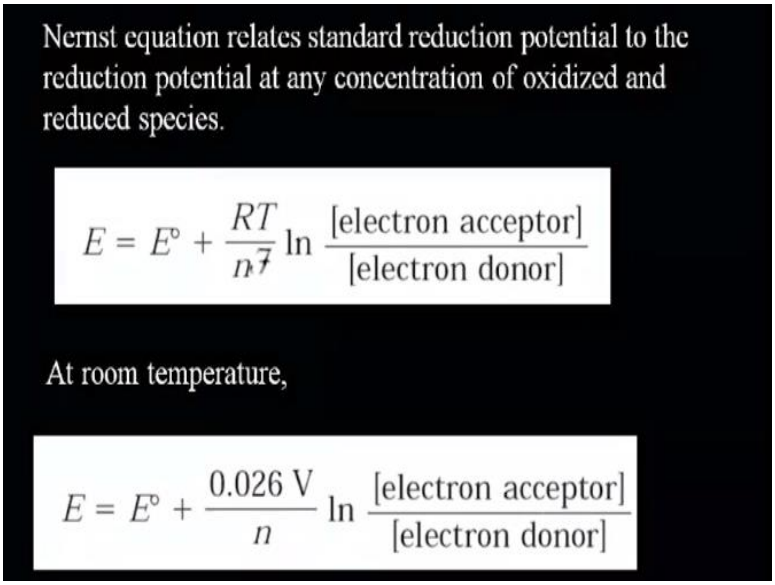

So now fine I understand this electron affinity difference and therefore differences in reduction potential and you call standard reduction potential when it is 1 molar concentration or if it is gas 101.3 kilopascals all that is fine. But how does it connect to free energy? So, my interest is how do I get the energy out of these molecules? So that is where now we are going. So now how do I calculate the reduction potential at a given concentration?

I only understand concentrations, how do I calculate that? So that is given by Nernst equation. So, reduction potential E equals standard reduction potential of that particular pair then this relationship natural logarithm of electron acceptor by electron donor. So normally we take the reduction potential of the electron acceptor and then we take that as a ratio of in the numerator and in the denominator we have electron donate donor.

So, the high reduction potential versus low reduction potential. So, at room temperature you if you substitute the value, Faraday's constant number of electrons involved in this transfer and they substitute the value of gas constant on absolute temperature then it simplifies to this. So, these are constant, so therefore that value is that the number of electrons would depend on what is your redox pair.

Now biochemists normally in addition to this 1 molar concentration and standard pressure, etc., they will also talk about the pH.

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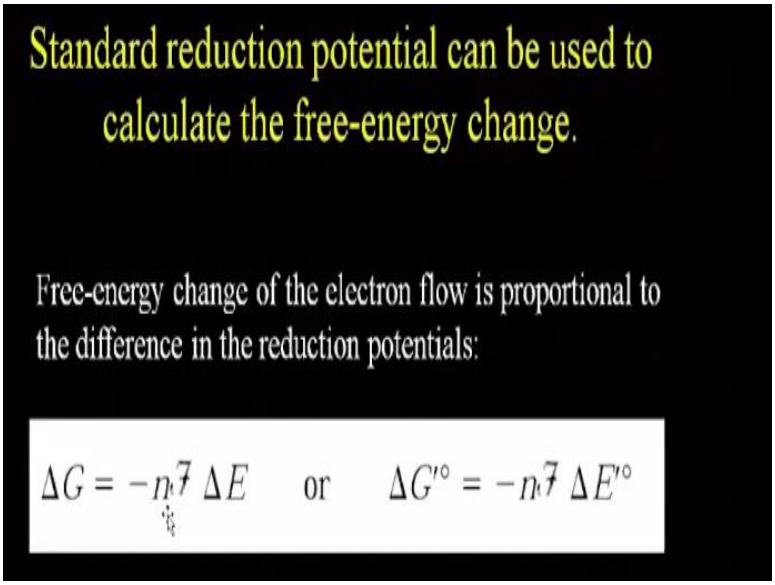

And when the whole thing if you consider at pH 7 you introduce this prime as well. So, for the biochemists the standard reduction potential will be the E prime and this 0 symbol degree symbol denotes the standard reduction potential. So standard reduction potential at pH 7 is what this prime and this degree symbol both together indicate. Now the Nernst equation allows you to calculate the reduction potential at any concentration provided you know the standard reduction potential for that particular pair.

And once you have calculated that reduction potential for any concentration based on this relationship you will get the delta G. So, the relationship between the reduction potential difference and the delta G is given by this equation minus number of electrons times Faraday's constant and the difference in the reduction potential. So here the difference comes from between this and this, acceptor and donor, so that is where the difference comes.

So, if the concentrations are given using this equation you will be able to calculate the reduction potential for that given concentration for that redox pair. And when you have for example in this instead of a hydrogen if I am having another redox species let us say redox pair 1, redox pair 2, then the difference between the two like once you have calculated E for both of them, the difference between the two will be the delta G.

And normally we calculate the delta E by subtracting the acceptor, the higher reduction potential from that you subtract the one with the lower electron potential so that is the direction for the subtraction here to get the delta E. So for the standard one, you will use this standard and pH 7. So, this is for any concentration.

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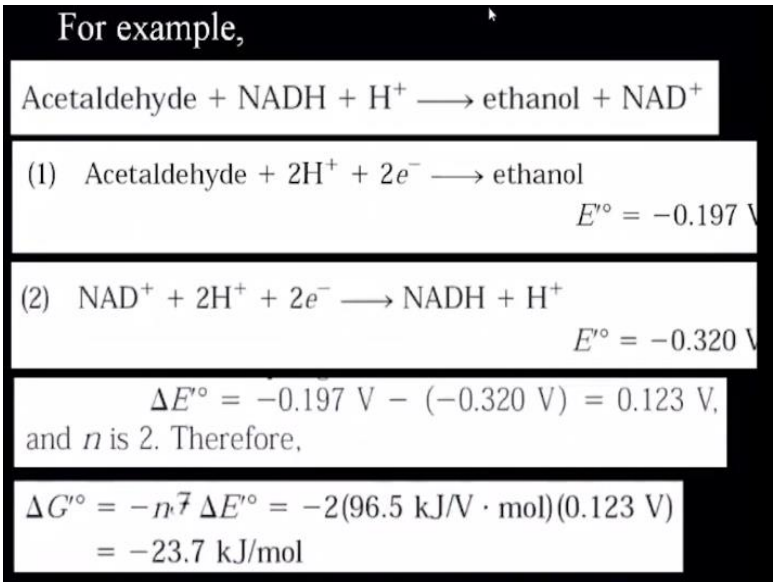

So here is an example. So, you have acetaldehyde getting oxidized to ethanol. So, this is the typical reaction that happens in yeast fermentation to produce alcohol. Acetaldehyde is reduced to ethanol or ethanol is oxidized to acetaldehyde. So, if you remember the competitive inhibition in enzymes we were talking about this. So, we were talking about alcohol dehydrogenase oxidizing methanol to formaldehyde.

And the formaldehyde being toxic and we used ethanol as a competitor with methanol in that particular example. It is the same reaction we are looking at here. So, it is a dehydrogenation, If you take ethanol we are going to learn about NADH and NAD chemical species, this can be oxidized and this can be reduced. So, say ethanol gets dehydrogenated so this has taken a hydride ion that is 2 electrons and 1 proton.

And therefore one proton is left out into the medium and ethanol is oxidized to acetaldehyde and vice versa this gets reduced. So here first we calculate for this redox pair ethanol and acetaldehyde. So here the transfer is 2 electron 2 hydrogen transfer, the number of electrons, n in that equation will be 2. So here the standard reduction potential at pH 6, meaning these two being at the 1 molar under the pH of the solution is 7 at that time this is the value calculated using this equation.

And same thing for NAD is this and now we take the delta. When we take the delta we take the one that has the high affinity for electron acceptor and that is acetaldehyde here and from that we subtract this. So this is negative, this is also a negative. So therefore, you end up

getting + 0.123 volt. And this when you now substitute in this equation for connecting the G and E, then you get –23.7 kilojoules per mole.

So, joules per mole is the unit for this and this is a negative free energy change meaning this is favorable. This reaction will happen. So when you have electron transfer in this manner acetaldehyde and ethanol redox pair with NADH and NAD+ you will have NAD getting reduced and it proceeds with negative free energy change meaning energy is available to do work if you have a transducer attached to it. So, this is how you would calculate this. So, if any of this is not clear, you should interrupt and ask questions.

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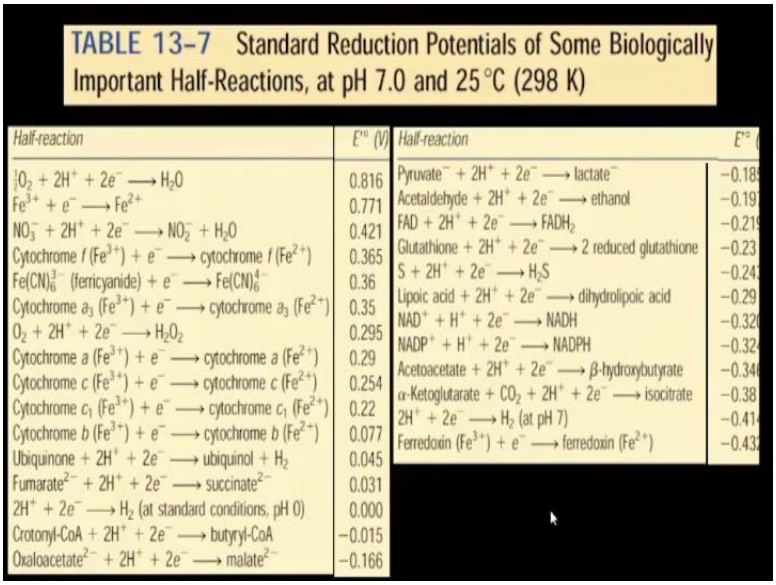

TABLE 13–7 Standard Reduction Potentials of Some Biologically Important Half-Reactions, at pH 7.0 and 25 °C (298 K)

Half-reaction	E'° (V)
$\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$	0.816
$Fe^{3+} + e^- \longrightarrow Fe^{2+}$	0.771
$NO_3^- + 2H^+ + 2e^- \longrightarrow NO_2^- + H_2O$	0.421
Cytochrome *f* $(Fe^{3+}) + e^- \longrightarrow$ cytochrome *f* (Fe^{2+})	0.365
$Fe(CN)_6^{3-}$ (ferricyanide) $+ e^- \longrightarrow Fe(CN)_6^{4-}$	0.36
Cytochrome a_3 $(Fe^{3+}) + e^- \longrightarrow$ cytochrome a_3 (Fe^{2+})	0.35
$O_2 + 2H^+ + 2e^- \longrightarrow H_2O_2$	0.295
Cytochrome *a* $(Fe^{3+}) + e^- \longrightarrow$ cytochrome *a* (Fe^{2+})	0.29
Cytochrome *c* $(Fe^{3+}) + e^- \longrightarrow$ cytochrome *c* (Fe^{2+})	0.254
Cytochrome c_1 $(Fe^{3+}) + e^- \longrightarrow$ cytochrome c_1 (Fe^{2+})	0.22
Cytochrome *b* $(Fe^{3+}) + e^- \longrightarrow$ cytochrome *b* (Fe^{2+})	0.077
Ubiquinone $+ 2H^+ + 2e^- \longrightarrow$ ubiquinol $+ H_2$	0.045
Fumarate^{2-} $+ 2H^+ + 2e^- \longrightarrow$ succinate^{2-}	0.031
$2H^+ + 2e^- \longrightarrow H_2$ (at standard conditions, pH 0)	0.000
Crotonyl-CoA $+ 2H^+ + 2e^- \longrightarrow$ butyryl-CoA	−0.015
Oxaloacetate^{2-} $+ 2H^+ + 2e^- \longrightarrow$ malate^{2-}	−0.166

Half-reaction	E'°
Pyruvate$^-$ $+ 2H^+ + 2e^- \longrightarrow$ lactate$^-$	−0.18
Acetaldehyde $+ 2H^+ + 2e^- \longrightarrow$ ethanol	−0.19
FAD $+ 2H^+ + 2e^- \longrightarrow FADH_2$	−0.21
Glutathione $+ 2H^+ + 2e^- \longrightarrow$ 2 reduced glutathione	−0.23
$S + 2H^+ + 2e^- \longrightarrow H_2S$	−0.24
Lipoic acid $+ 2H^+ + 2e^- \longrightarrow$ dihydrolipoic acid	−0.29
$NAD^+ + H^+ + 2e^- \longrightarrow$ NADH	−0.32
$NADP^+ + H^+ + 2e^- \longrightarrow$ NADPH	−0.32
Acetoacetate $+ 2H^+ + 2e^- \longrightarrow \beta$-hydroxybutyrate	−0.34
α-Ketoglutarate $+ CO_2 + 2H^+ + 2e^- \longrightarrow$ isocitrate	−0.38
$2H^+ + 2e^- \longrightarrow H_2$ (at pH 7)	−0.41
Ferredoxin $(Fe^{3+}) + e^- \longrightarrow$ ferredoxin (Fe^{2+})	−0.43

So this is a table, simply you do not need to memorize any of this. This is just to give an idea. There are multiple redox pairs in biology and for each of them this standard reduction potential at pH 7 has been calculated and those are given here.

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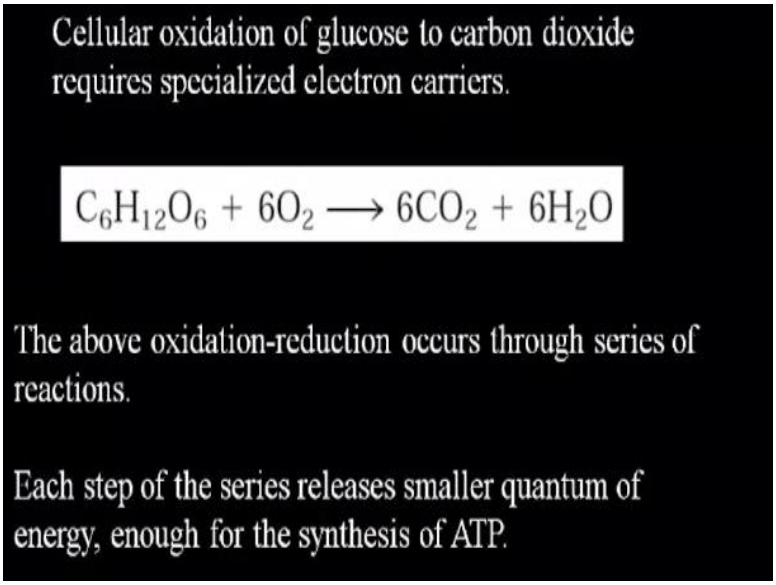

So now with this refreshing the memory of your electrochemistry which I am sure you have learnt at least on two three occasions previously let us go and see the biological oxidation. So, this is not like as some smaller waterfall as acetaldehyde and ethanol. This is like really tall waterfall. So, the electron flow from this to this happens in multiple steps and in each step the electron is being temporarily carried by molecules that we call as electron carriers.

The chemistry or the chemical structure of those molecules enable them to function as electron carriers meaning they can reversibly undergo oxidation reduction. So, this is a new idea though there are things called electron carriers. So today we will see one example as we go through. So, the above is once more I am reiterating through a series of reactions. Each step of the series releases smaller quantum.

And that quantum is sufficient to provide the required energy for ATP formation plus releasing some into the environment as heat to satisfy the second law of thermodynamics. So that is the quantum that comes from the individual steps of the series. So, therefore the series each step is calibrated through the process of evolution of this process such that the energy from each step is sufficient to make an ATP.

Let us say you have a turbine and that is only going to make 1 megawatt electricity and total available in a waterfall is to make 1 gigawatt, then you make a 1000 intermediate step and in each step you put your small 1 megawatt turbine on the way. So, therefore at the end you make 1 gigahertz out of it, instead if you put the 1 megawatt at the bottom of the waterfall you will only get the 1 megawatt. The rest your 999 you are going to lose.

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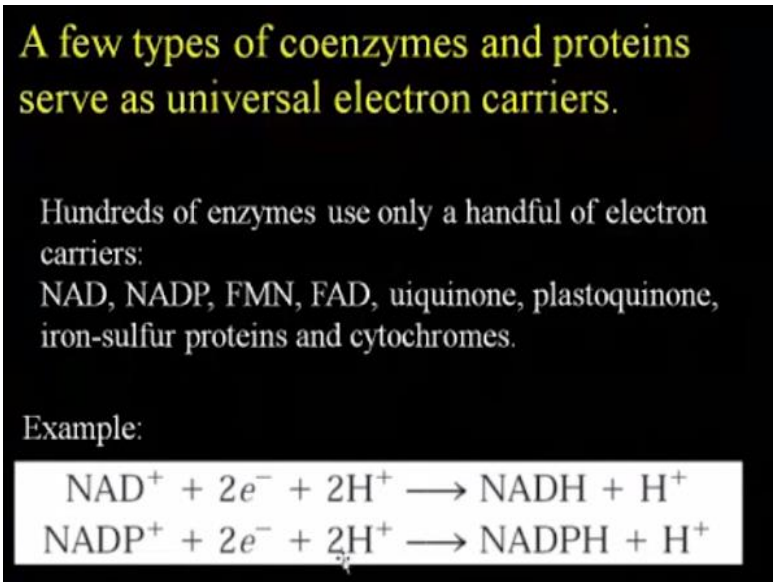

So now we get to those electron carriers. So, a few types of coenzymes and proteins serve as universal electron carriers. Meaning from variety of molecules they can accept electrons and they can donate more electrons to variety of acceptors. And you have hundreds of reactions but we only use a handful of electron carriers. You do not have a whole lot to memorize here. So, biology in that sense requires a lot less to memorize than mathematics because here we deal with a few simple things.

And the theme repeats and reoccurs and again and again. So, for example if I have to memorize the table of 20 times 20 starting from 1 time 1, then I have whole lot of things to memorize, but here you do not have that much to memorize. So, biology requires very little memorizing, but memorizing is very important to be a learned scholar. So, anyone who is going to object to learning structures I am already precluding that by saying this.

So, what are these handful of electron carriers? NAD we just saw. So, we will have a very close look at it and appreciates the beauty of that molecule. NADP is actually NAD which is phosphorylated at one part of it, otherwise they both functions very similarly although the enzymes are specific. Some enzymes that use NAD do not use NADP and vice versa, but there are enzymes that can use both. Then you have another one called FMN, another one called FAD.

These two are related, they both have the F. Then you have ubiquinone specialized to work in membranes it is a hydrophobic, plastoquinone similar to ubiquinone but functions in

photosynthesis. Then iron-sulfur proteins, they have a cluster of iron and sulfur ions coordinated in the proteins and they help in electron transform, we will see this when we go to electron transport chain. And then cytochromes, these are proteins.

So, these are like pigments like the one we saw, we actually have seen when we were learning about vitamin E, vitamin K, etc. That time we learned about ubiquinone and plastoquinone, same lipid molecules. So, these also familiar, when we see the structure you will recognize that. So, you have coenzymes and proteins. So, these are coenzymes and these two are proteins. So example we take NAD.

So. NAD to indicate the oxidized state we use plus sign, it does not mean it has a net positive charge, same with NADP can take a hydride ion meaning 2 electrons and 1 proton to become NADH. So, this is hydride, has taken therefore 1 proton goes into the medium. So, when it is getting oxidized 1 proton comes from the medium, it donates 2 electrons but only 1 proton, same with this.

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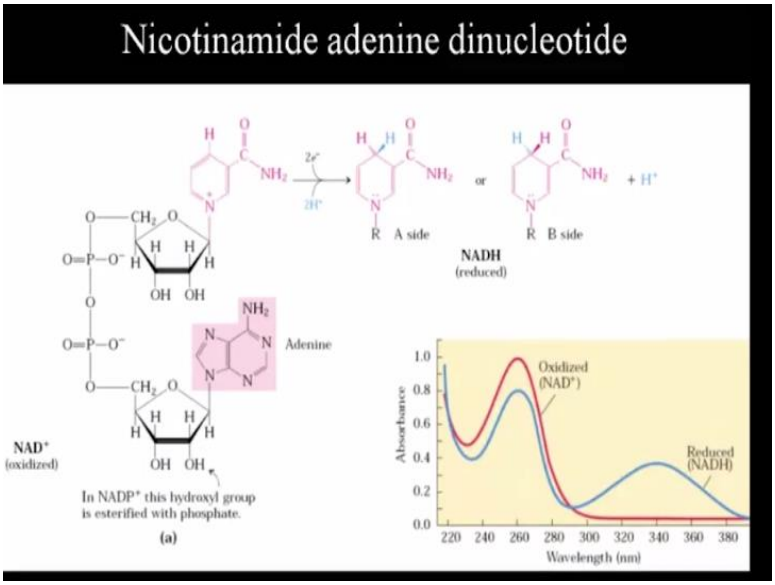

So here is the structure of nicotinamide adenine dinucleotide that is what is NAD. This structure you already know. So adenine, one of the nitrogenous bases in nucleotides in our DNA and RNA and we know the ribose sugar already we learned this. We also know the phosphate, nucleotide meaning these three together, very early lectures we have learned. So, there is no new thing here.

The only thing is you have another ribose that is in phosphodiester bond just like in nucleic acids. The only thing is here it is both are with the fifth carbon instead of 3 and 5. In nucleic acids you have had 5 attached to the 3. Here it is 5, 5 and a new nitrogenous phase that is this nicotinamide. So, nicotinamide adenine dinucleotide, two nucleotides so you call dinucleotide in this phospho anhydride bond it is not with the hydroxyl group as an ester this is inorganic anhydride acid-acid.

So nicotinamide adenine then dinucleotide, it is two nucleotides. This alone you will call one nucleotide, this alone you will call one nucleotides, therefore this dinucleotide. So now the electron carrying capacity comes from this structure, this pyridine ring. This nitrogen can either be deficient in one electron or can be reduced. So here it takes a hydride ion and loses the charge and it has those 2 electrons of the hydride is shown as two dots and the proton into the medium.

And theoretically speaking that hydrogen atom that it takes can be either in this side like facing one side or the other. So, one is A side, another is B side. Chemically it makes no difference at all, but we have enzymes that either catalyze the A side transfer or B sided transfer and the preferences could be as high as 10 power 7. Like for example one enzyme may prefer A to B at a ratio of 10 power 7.

Meaning out of 10 power 7 molecules it worked on A will be that many for one of the B or vice versa. So, the enzyme show preference but chemically it does not make difference, it could be on either side. So, this one since it carries the additional hydrogen we call as NADH. This is stable and reduced form, so no charge shown in notation. You just write NADH, but when it is oxidized you write NAD +.

And this plus is not the net charge of all of them see here your negative charge all that. It only indicates this nitrogen. The focus is only on this electron carrying part of it for the reversible oxidation reduction. And they have a characteristic absorption, only the reduced species absorbs at 340 and these characteristics is often used to measure whether it is in the oxidized form or reduced form or what is the ratio of the two.

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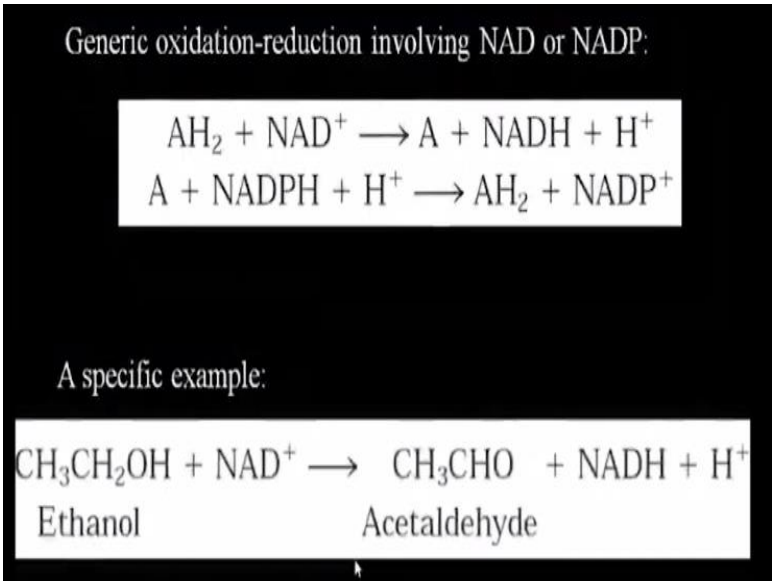

So this is a generic example. So you have like we just saw acetaldehyde. So, this is like ethanol becoming acetaldehyde or vice versa. In the process NAD gets reduced or oxidized in the opposite direction. So, this is just for convenience for the oxidizing part they have shown NADPH. So, it happens to be either one of the two in both directions. So here you have the same specific example that we just saw ethanol getting oxidized and NAD + getting reduced. So, this is a typical dehydrogenation reaction.

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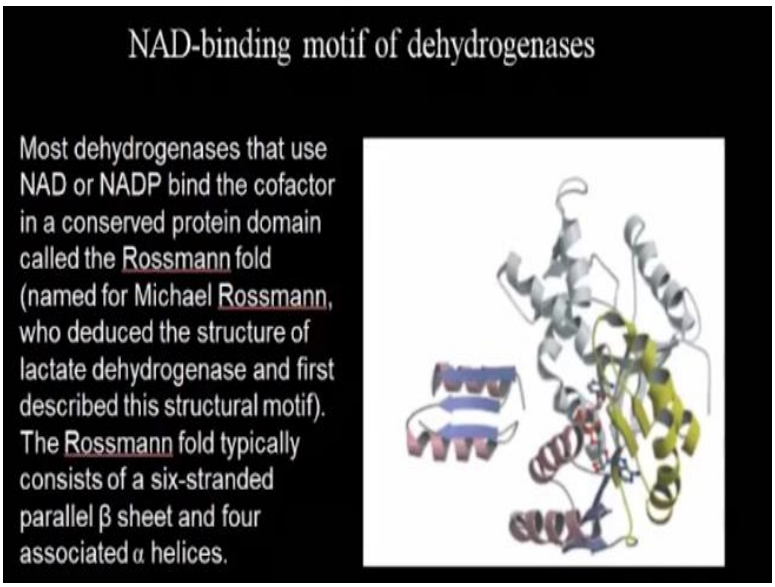

And so NAD is or NADP is present in the active site of enzymes that is why we call this as a coenzyme. It is not a metal, therefore we do not call cofactor. It is a complex organic molecule we call it as coenzyme. And this is loosely bound to the enzyme. So after getting oxidized or reduced, it can freely diffuse out of an enzyme and it can be taken up by another oxidation-reduction enzymatic reaction.

So it is not a prosthetic group. And the large number of enzymes use NAD. Now it is a very common thing, this is not like an exception that we are trying to learn here. And these have a typical conserved protein domain that binds NAD and that domain looks like this diagram on the left. So, this is only showing half of it. So, the actual concerted domain that we call as Rossmann ford because Rossmann is the one who discovered this structure, he deduced the structure of this in lactate dehydrogenase.

So, lactate dehydrogenase is the one that gives some pyruvic acid or lactate. So when you exercise like for example when you go for a fast run, your muscle cells cannot really completely convert glucose all the way to carbon dioxide, instead it gets into an intermediate pyruvate and whatever energy you get from glucose oxidation to pyruvate that is used. But the pyruvate gets reduced to lactic acid.

And that lactic acid buildup in our muscles is why you get muscle pain when you run long distance very fast and that lactic acid needs to be then again oxidized to pyruvate and then pyruvate gets finely accessed to carbon dioxide. So, this is an important enzyme in muscles lactate dehydrogenase. It reversibly converts lactic acid pyruvate and vice versa. So in that he deduced the structure, but this is a conserved motive found in all oxidation reduction enzymes that use NAD as a cofactor.

So, this contains typically 6 beta sheets, so these are arrows, blue color arrow here, with the 4 alpha helices I told you this is half structure, so it only has 3 and 2. So this is a full molecule with this ball and stick thing here is the NAD bound there in the three-dimensional ribbon model of the enzyme.

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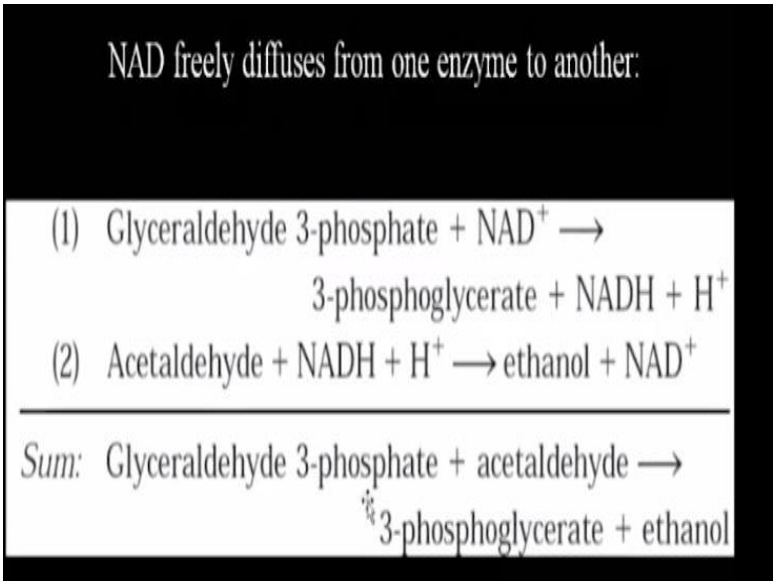

So, it freely diffuses. For example glyceraldehyde 3-phosphate getting oxidized to 3-phosphoglycerate. This is a reaction glycolysis, so we will see that in the sequence then it will make sense. And in this process NAD gets reduced. So, electron transfer has happened from this to this in hydride form and then this freely diffuses out of this enzyme glyceraldehyde 3-phosphate dehydrogenase and like that from many other things too.

Then you have a pool of NADH in the cytoplasm and that can be used by alcohol dehydrogenase to reduce acetaldehyde into ethanol. So, remember here carbon is double bond with acetaldehyde aldehyde carbon, carbonyl carbon, here it is hydroxyl. So it is a double bond with oxygen, so lesser oxidation state, here single bond OH. So, this is a more reduced. So therefore, this is getting oxidized.

And the electron for that is coming from this NAD, NADH + H+ and it has lost a hydride and then it becomes NAD+. So, it can diffuse from one enzyme to another enzyme. So the sum therefore for us is glyceraldehyde 3-phosphate is oxidized. So here aldehyde becomes carboxylic. So in aldehyde one is the double bond O and another is with hydrogen, here one is with double bond O another one is hydroxide. So the bond there is COH instead of CH. So that is why this is relatively oxidized compared to this.

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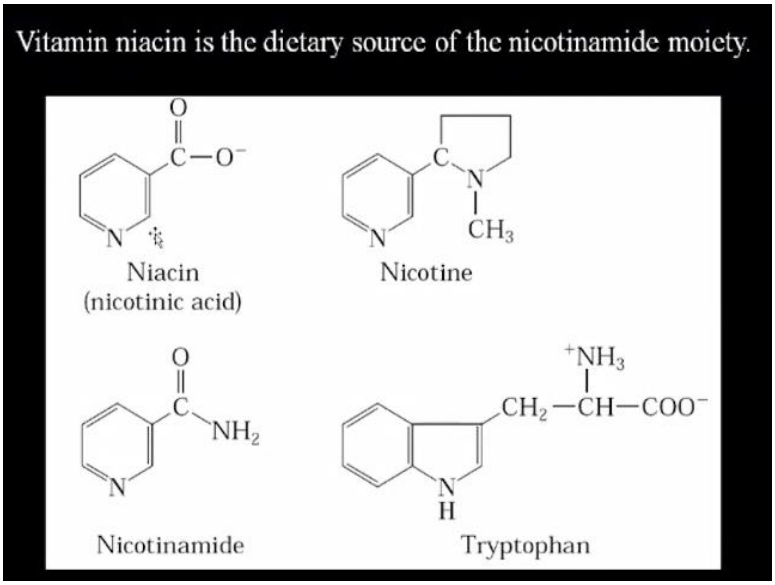

Now a little bit slightly relaxed discussion compared to the heavy electron based chemistry. So where do we get this NAD. So, looks like if this is a central electron carrier and this electron transfer is the way we get energy, so then this molecule seems to be very crucial. So where do we get it from? So essentially, we get it from tryptophan. This tryptophan is one of the 20 amino acids that is the source for producing this nicotinamide and nicotinic acid.

So, both of this can be readily converted to the nicotinamide of or NAD or NADP. So originally it was isolated from nicotine and that is why this name comes nicotinamide or nicotinic acid or niacin. So this is the water-soluble vitamin niacin. So far you have seen lipid soluble vitamins ADEK, so this is our first water soluble vitamin we are seeing. So, you have heard about vitamins earlier, so this is one of the B complex vitamins.

So if I can make from tryptophan then why it is a vital molecule? Why are you calling vitamin? That is because the conversion of tryptophan to nicotinamide or niacin is not sufficient enough for our need and sometimes the protein source in your food for example if you are eating a lot of corn or corn-based diet you will not get much tryptophan. So therefore, you need it in the food that is why it is an essential molecule and that is niacin.

So what happens if you do not have niacin enough in the food that we will see in the next class. So primarily tryptophan is the source, but that is not sufficient, so it has to be there in the food in the form of niacin which is a B complex vitamin and that is where from you get this portion in NAD which is an essential electron carrier. I will stop here. Tomorrow we will look at the niacin deficiency, etc., and we will move to the next electron carrier.