Bioinorganic Chemistry

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Lecture - 01
Bio-inorganic Chemistry: General Introduction and Prospects

A warm welcome to Bio-inorganic Chemistry Course. Let me introduce first myself. This is Dr. S P Rath, professor in the Department of Chemistry at IIT, Kanpur.

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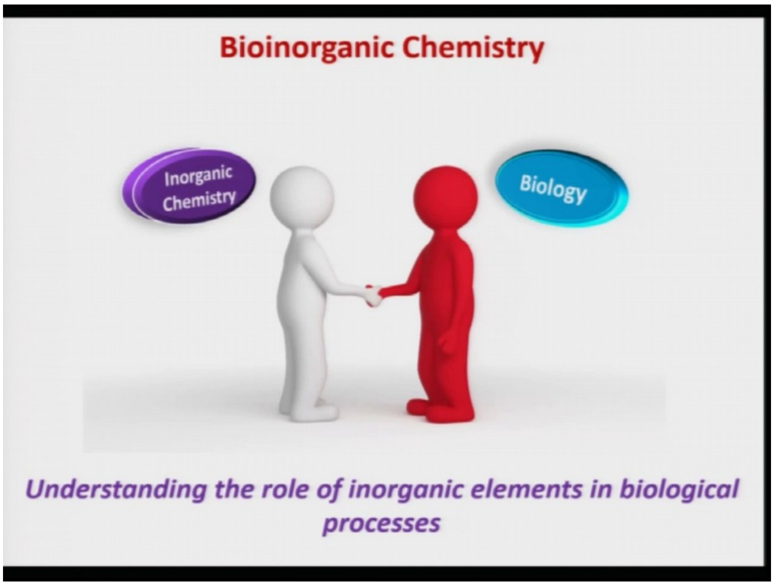

Bioinorganic Chemistry

Understanding the role of inorganic elements in biological processes

And the bio-inorganic chemistry is a meeting point of chemistry and biology, and this has been designed to understand the role of inorganic elements in biological processes.

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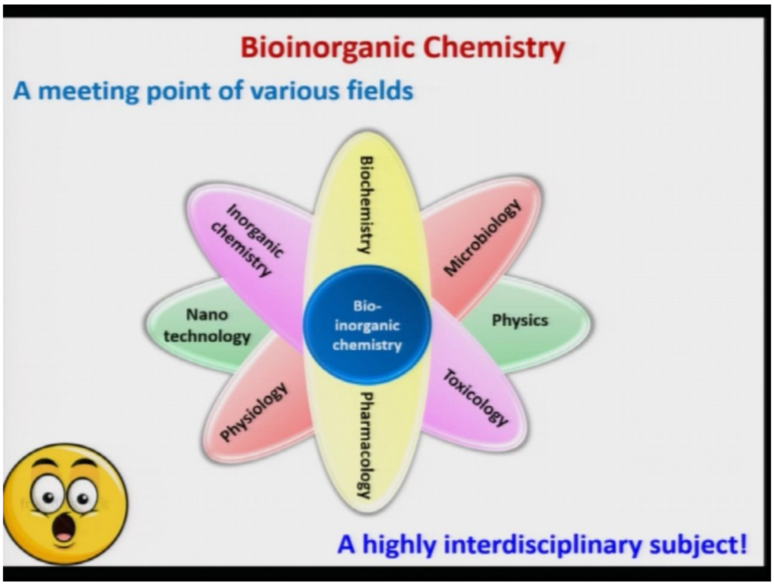
Bioinorganic Chemistry

A meeting point of various fields

A highly interdisciplinary subject!

And this bio-inorganic chemistry is a highly interdisciplinary subject and meeting point of various field like inorganic chemistry, physics, biochemistry, microbiology, nanotechnology, physiology, pharmacology, etc.

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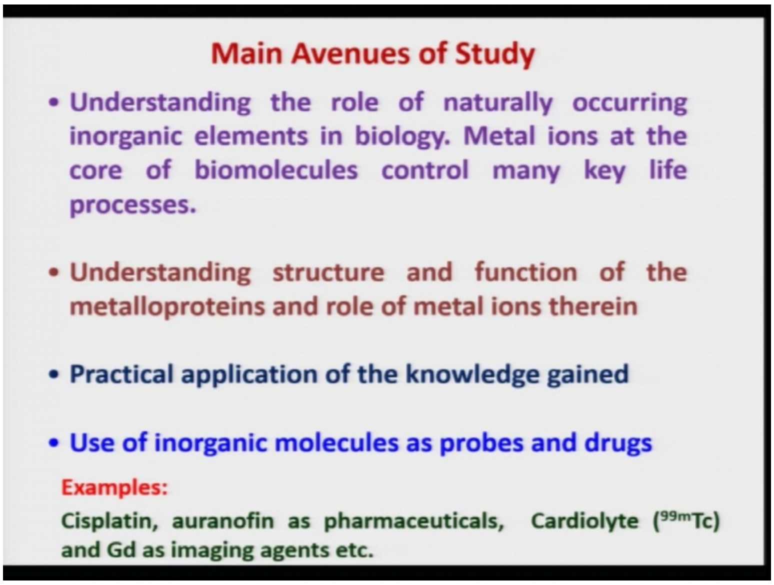
Main Avenues of Study

- Understanding the role of naturally occurring inorganic elements in biology. Metal ions at the core of biomolecules control many key life processes.
- Understanding structure and function of the metalloproteins and role of metal ions therein
- Practical application of the knowledge gained
- Use of inorganic molecules as probes and drugs

Examples:

Cisplatin, auranofin as pharmaceuticals, Cardiolyte (^{99m}Tc) and Gd as imaging agents etc.

The main avenues of this study would be understanding the role of naturally occurring inorganic elements in biology. Metal ions at the core of biomolecules control many key processes. Understanding structure and function of the metalloenzymes and roles of metal ion therein. Practical application of the knowledge gained and use of inorganic molecules as probes and drugs. For example, cisplatin, auranofin, cardiolyte, several such examples are there.

I will now take a joy ride to highlight what would be showcased in the next few hours of my journey in this short course of bio-inorganic chemistry. Please note that only few selected topics will be chosen to cover during this short time.

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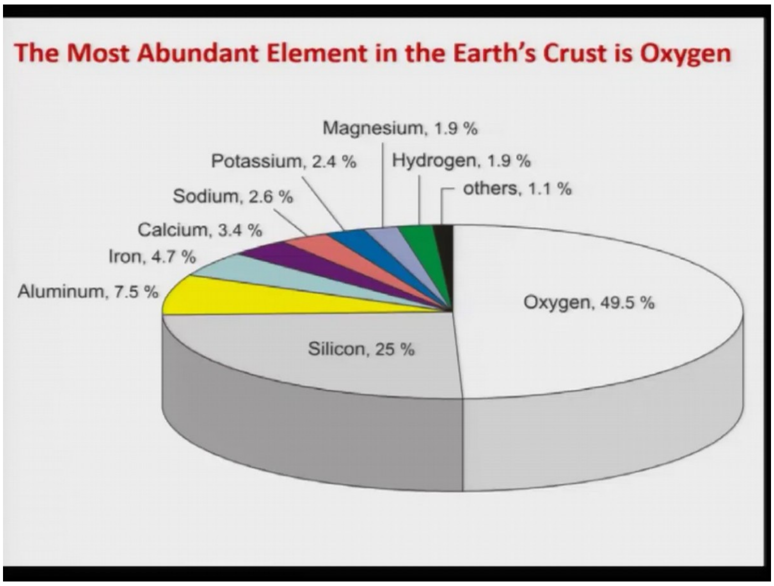

The Most Abundant Element in the Earth's Crust is Oxygen

The most abundant element in the earth crust is oxygen.

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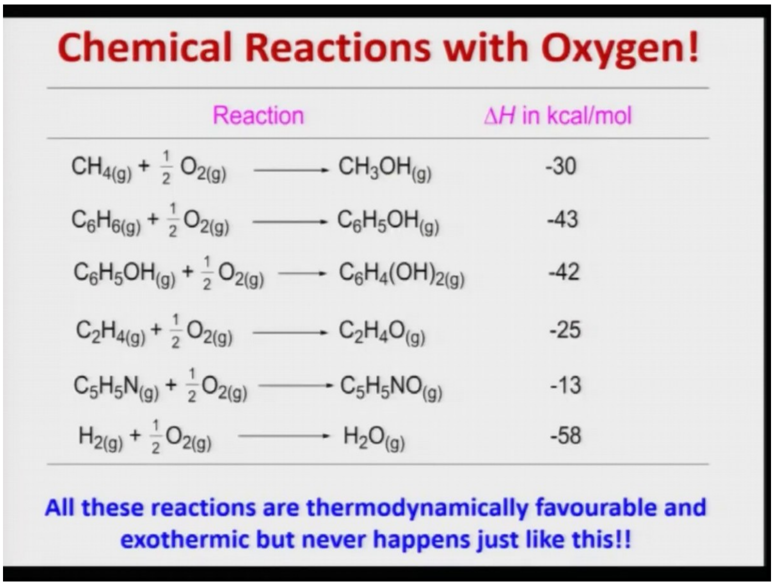

Chemical Reactions with Oxygen!

Reaction	ΔH in kcal/mol
$CH_{4(g)} + \frac{1}{2} O_{2(g)} \longrightarrow CH_3OH_{(g)}$	-30
$C_6H_{6(g)} + \frac{1}{2} O_{2(g)} \longrightarrow C_6H_5OH_{(g)}$	-43
$C_6H_5OH_{(g)} + \frac{1}{2} O_{2(g)} \longrightarrow C_6H_4(OH)_{2(g)}$	-42
$C_2H_{4(g)} + \frac{1}{2} O_{2(g)} \longrightarrow C_2H_4O_{(g)}$	-25
$C_5H_5N_{(g)} + \frac{1}{2} O_{2(g)} \longrightarrow C_5H_5NO_{(g)}$	-13
$H_{2(g)} + \frac{1}{2} O_{2(g)} \longrightarrow H_2O_{(g)}$	-58

All these reactions are thermodynamically favourable and exothermic but never happens just like this!!

And you see there are there can be many chemical reactions with oxygen, however, all these reactions are thermodynamically favorable and exothermic. However, it never happens just like mixing.

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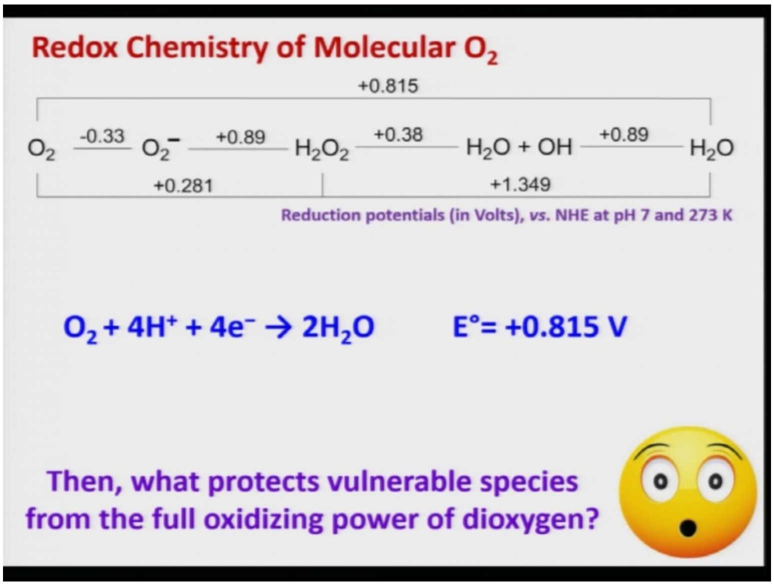

Redox Chemistry of Molecular O_2

Reduction potentials (in Volts), *vs.* NHE at pH 7 and 273 K

$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$ $E° = +0.815$ V

Then, what protects vulnerable species from the full oxidizing power of dioxygen?

The redox chemistry of molecular oxygen is shown over here and the most important reactions is when dioxygen converts to water with the help of 4 proton and 4 electron, with a redox potential of 0.815 Volt.

The reduction potential of the 4 electron reduction of dioxygen is a measure of great oxidizing power of dioxygen. If this being so, then what protects vulnerable species from the full oxidizing power of dioxygen.

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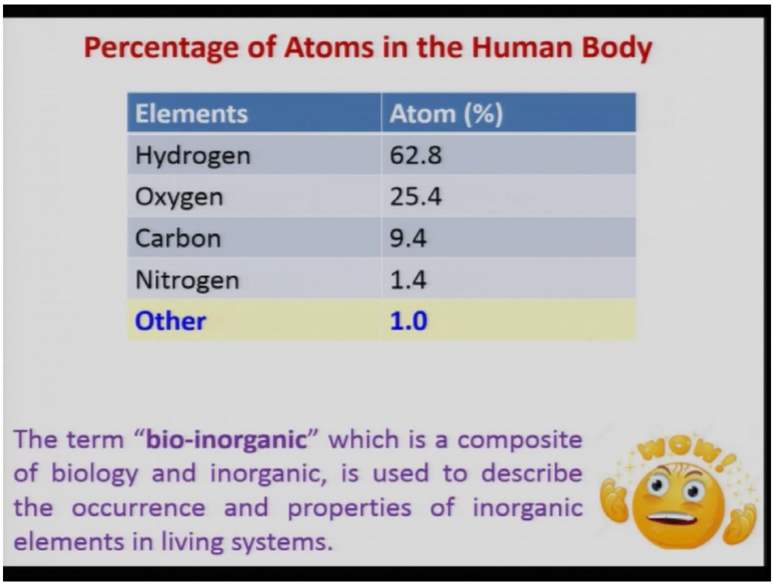

Percentage of Atoms in the Human Body

Elements	Atom (%)
Hydrogen	62.8
Oxygen	25.4
Carbon	9.4
Nitrogen	1.4
Other	**1.0**

The term “**bio-inorganic**” which is a composite of biology and inorganic, is used to describe the occurrence and properties of inorganic elements in living systems.

The percent of atoms in human body is shown over here. As you can see that hydrogen is around 62.8 percent, oxygen 25.4, carbon 9.4, nitrogen 1.4 and other elements together is just 1 percent. At first sight the idea of inorganic chemistry associated with life may appear to be rather narrow field of study, as we tend to think of living matter as being just organic. However, it is a fact that without certain inorganic elements no organism could exist.

The term bio-inorganic which is a composite of biology and inorganic, is used to describe the occurrence and properties of inorganic elements in living system, and these elements are extremely important for our day-to-day life.

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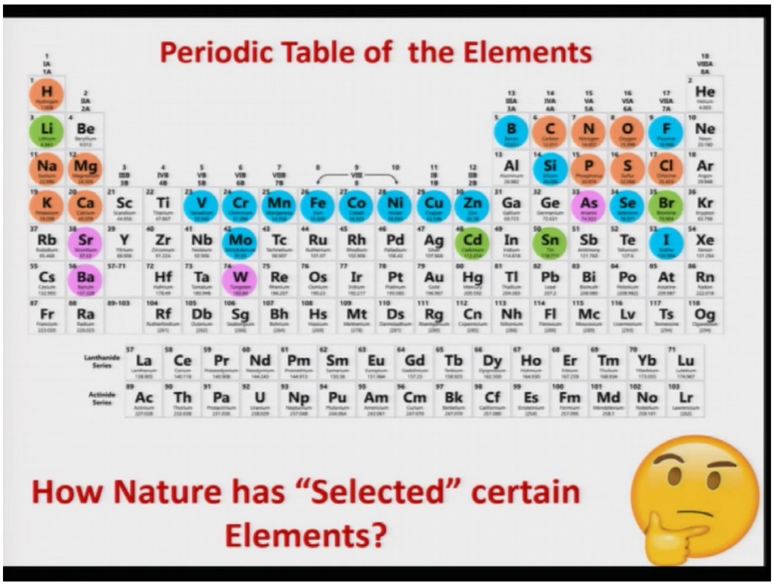

Periodic Table of the Elements

How Nature has "Selected" certain Elements?

I have shown here the periodic tables of element, and as one can see that some of these elements are highlighted blue, green, pink, brown. The brown color is for the elements which are present in bulk amount in biological system. Then the blue one, which is believed to be the essential for a wide range of bacteria, plants and animals including humans. Then green, which is for elements that may possibly we essential for some species. Whereas, pink is for those elements which are believed to be essential for some species. As you can see, that most of the elements are not even used in biology.

Now, we will discuss that how nature has selected only certain elements from large number of elements presents in the periodic table.

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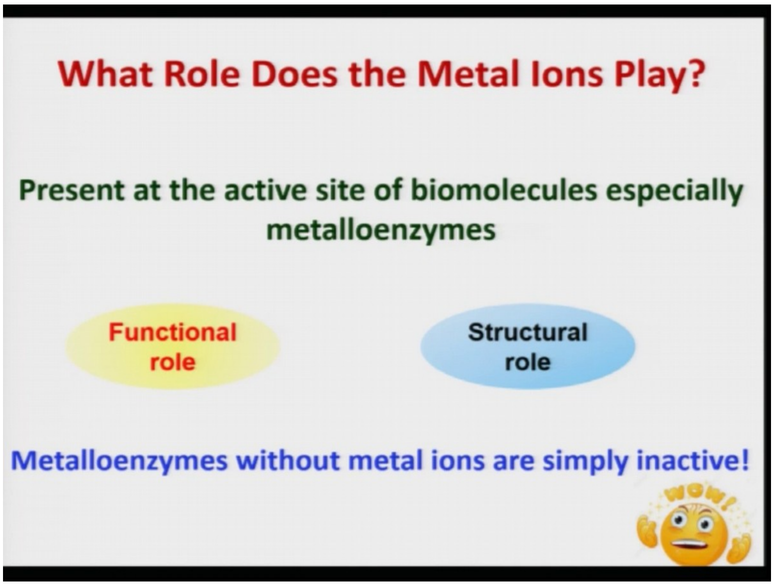

What Role Does the Metal Ions Play?

Present at the active site of biomolecules especially metalloenzymes

Functional role

Structural role

Metalloenzymes without metal ions are simply inactive!

Now, what role does the metal ions play? The metal ions are present at the active site of biomolecules, specially metalloenzymes, and they have been doing as a some functional role as also structural role. However, metalloenzymes without metal ions are simply inactive.

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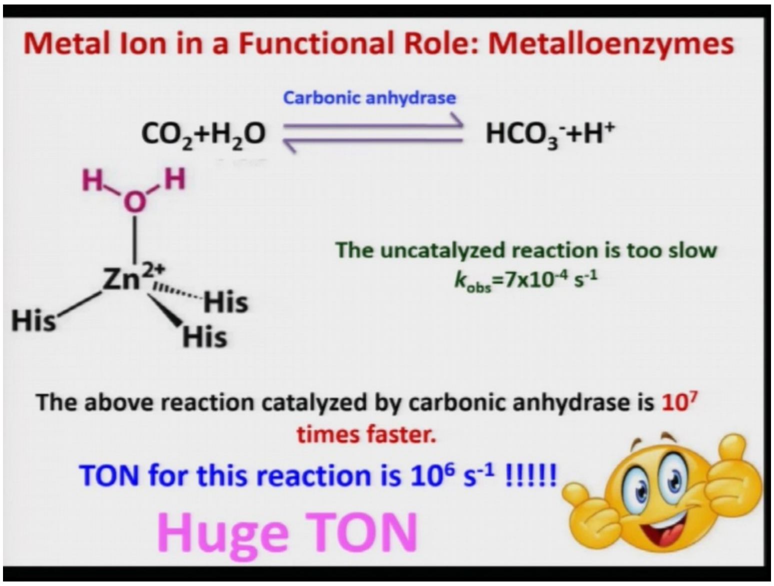

Metal Ion in a Functional Role: Metalloenzymes

$CO_2 + H_2O \underset{}{\overset{\text{Carbonic anhydrase}}{\rightleftharpoons}} HCO_3^- + H^+$

The uncatalyzed reaction is too slow

$k_{obs} = 7 \times 10^{-4}\ s^{-1}$

The above reaction catalyzed by carbonic anhydrase is 10^7 times faster.

TON for this reaction is $10^6\ s^{-1}$!!!!!

Huge TON

I will now show you a example of a metal ion in a functional role. Say carbonic anhydrase is actually responsible for conversion of carbon dioxide and water to bicarbonate, and H^+. And this is the active site structure of carbonic anhydrase where you can see that three histidines are ligated, and the fourth position is occupied by weak water ligand.

The uncatalyzed reaction is too slow; it is just 7 x 10^{-4} s^{-1}. The above reactions when it is catalyzed by carbonic anhydrase is 10^{7} times faster, turnover number of this reaction is 10^{6} s^{-1}, huge turnover number. We will discuss that how this enzyme actually increases the rate of these reactions.

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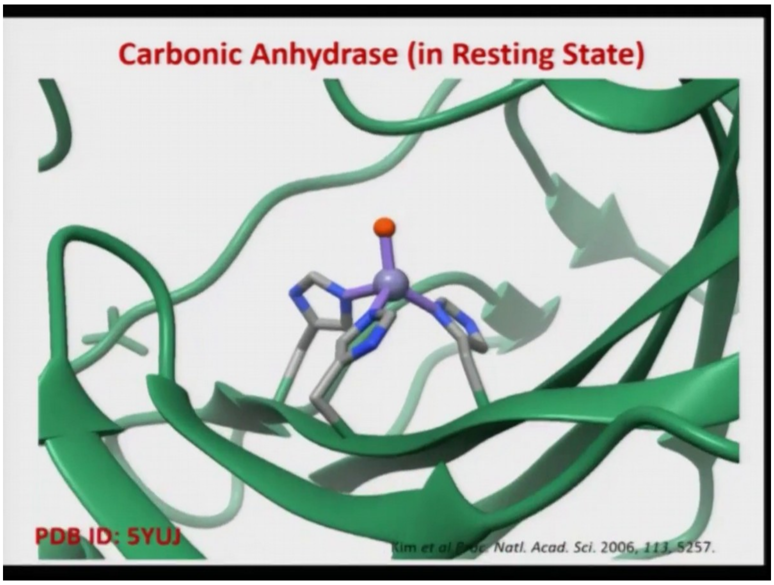

Carbonic Anhydrase (in Resting State)

PDB ID: 5YUJ

Kim et al Proc. Natl. Acad. Sci. 2006, 113, 5257.

X-ray structure of carbonic anhydrase is shown over here. You see that there is a huge protein chains wrapping around this molecule and inside this protein this zinc ion is sitting. And, once we remove this protein chain you can see the active site structure of this carbonic anhydrase.

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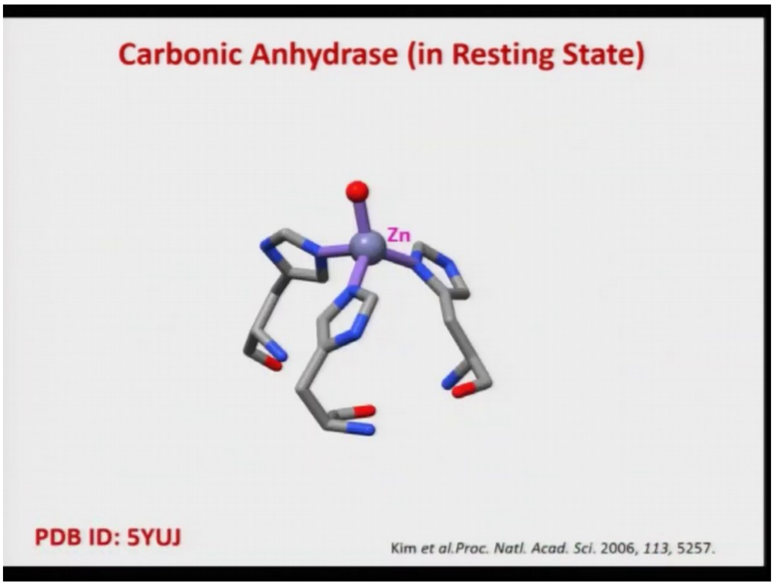

Carbonic Anhydrase (in Resting State)

PDB ID: 5YUJ

Kim *et al.Proc. Natl. Acad. Sci.* 2006, *113*, 5257.

Now, you will see that how the metal ion is responsible for its conversion to bicarbonate.

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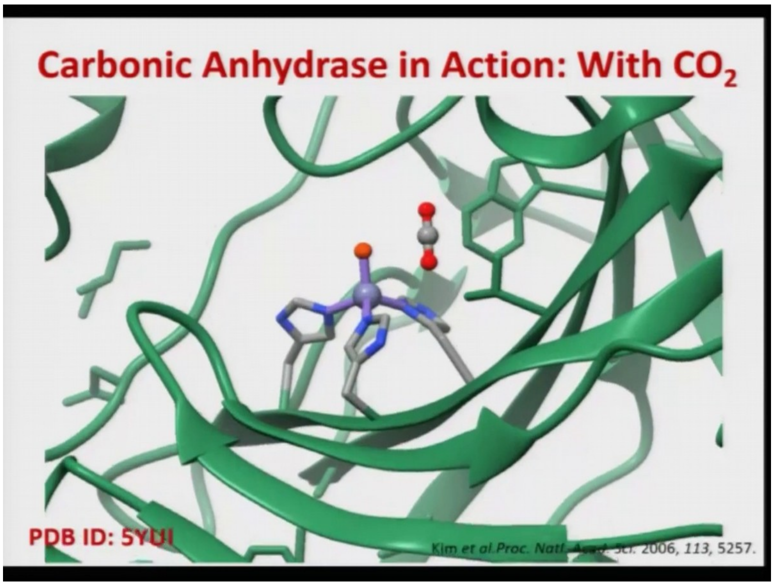

Carbonic Anhydrase in Action: With CO_2

PDB ID: 5YUI

Kim *et al.Proc. Natl. Acad. Sci.* 2006, *113*, 5257.

This is the protein structure with carbon dioxide as a substrate. You see that carbon dioxide is sitting over there.

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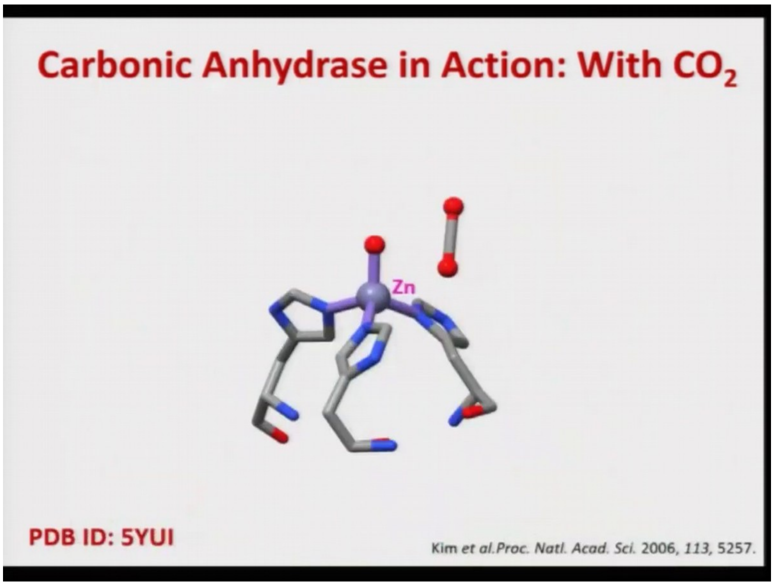

Carbonic Anhydrase in Action: With CO_2

PDB ID: 5YUI

Kim *et al.Proc. Natl. Acad. Sci.* 2006, *113*, 5257.

Again, once I removed this protein chains you can see that carbon dioxide is sitting close to metal center.

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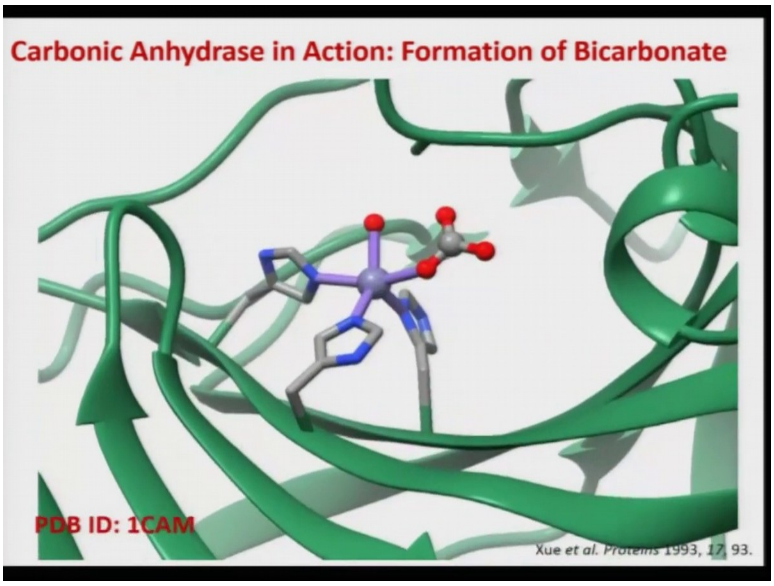

Carbonic Anhydrase in Action: Formation of Bicarbonate

PDB ID: 1CAM

Xue *et al. Proteins* 1993, *17*, 93.

And this is also the protein structure of carbonic anhydrase and formation of bicarbonate is clearly visible.

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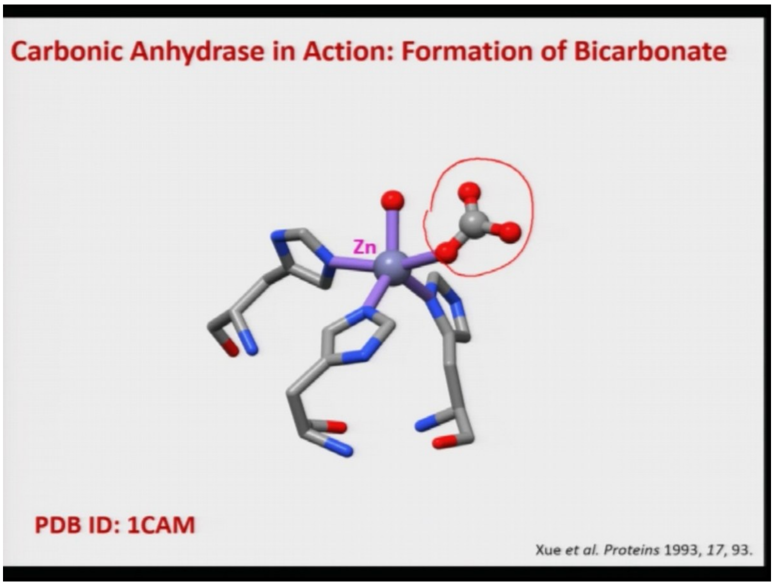

Carbonic Anhydrase in Action: Formation of Bicarbonate

PDB ID: 1CAM

Xue *et al. Proteins* 1993, *17*, 93.

And once I remove this protein chains you can see that the bicarbonate is formed over here and this is ligated to the zinc metal center. So, you can see yourself that how zinc is responsible for this transformation of carbon dioxide to bicarbonate.

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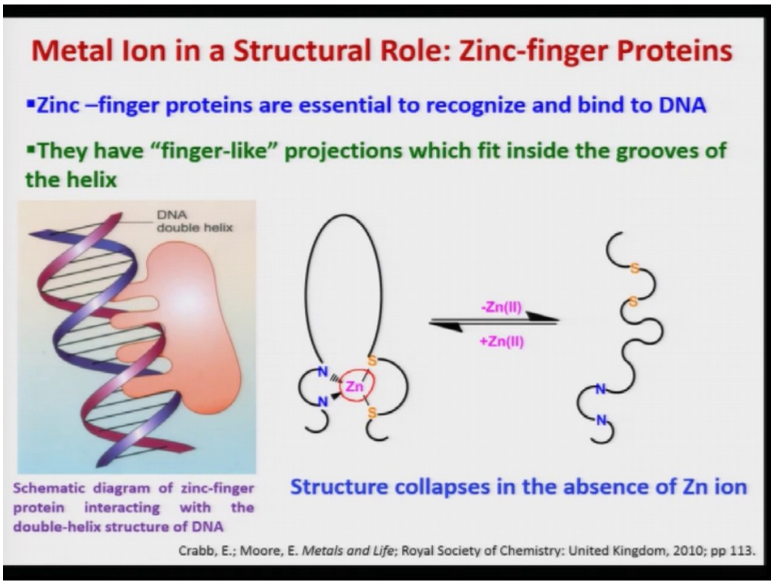

Metal Ion in a Structural Role: Zinc-finger Proteins

- **Zinc –finger proteins are essential to recognize and bind to DNA**
- **They have "finger-like" projections which fit inside the grooves of the helix**

Schematic diagram of zinc-finger protein interacting with the double-helix structure of DNA

Structure collapses in the absence of Zn ion

Crabb, E.; Moore, E. *Metals and Life*; Royal Society of Chemistry: United Kingdom, 2010; pp 113.

I will now show you a metal which is in a structural role, zinc finger protein. Now, zinc finger proteins are essential to recognize and bind to DNA. They have finger like projection which fit inside the grooves of the helix. As one can see that this is the polypeptide chain and zinc is sitting inside with ligated with nitrogen and sulfur. Now, once you remove the zinc the entire structure collapse. So, this suggests that how crucial the zinc metal ion is.

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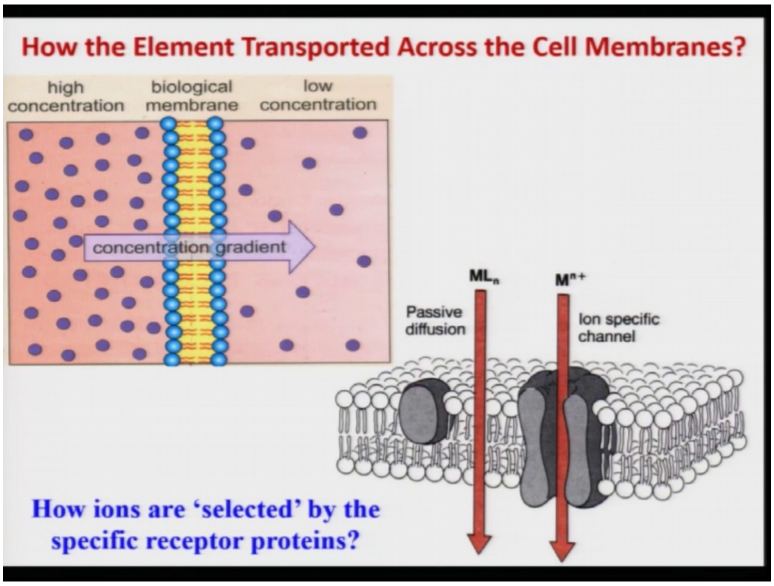

How the Element Transported Across the Cell Membranes?

How ions are 'selected' by the specific receptor proteins?

Now, question is that how the elements transported across the cell membrane. So, you can see that the elements in high concentration comes through the biological membrane to the low concentration very easily, across the concentration gradient. This is passive transport. Now, if the elements have to go to the opposite direction, like from low concentration to high concentration, you must need an energy to do that because it is not spontaneous though this is called active transport.

Now, elements like iron, zinc, copper, molybdenum comes inside the cell against the concentration gradient, since their concentration increases by many thousand folds inside the cell. It would be interesting to discuss how the specific receptor proteins allows only some selected elements to come inside the cell. So, it can be passive diffusion, it can be through an ion specific channel. But it would be very selective, so that not every element can come inside the cells. So, we will be talk about how ions are selected by the specific receptor proteins.

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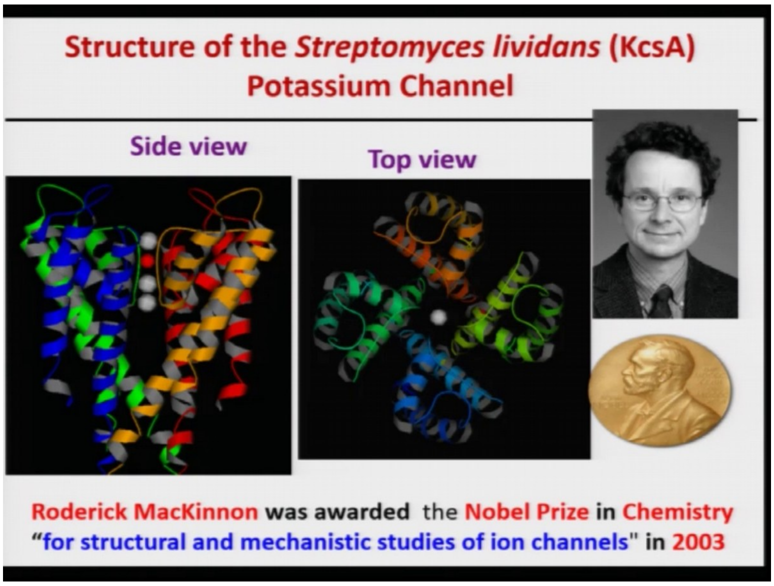

Structure of the *Streptomyces lividans* (KcsA) Potassium Channel

Side view

Top view

Roderick MacKinnon was awarded the **Nobel Prize** in **Chemistry** **"for structural and mechanistic studies of ion channels"** in **2003**

For example: this potassium channels is shown over here. And this is very much specific for the potassium and it only allows potassium to go through this channel and Roderick Mackinnon was awarded the Nobel Prize in Chemistry in 2003, for structural and mechanistic study of ion channels. So, we will be discussing all these in details in my subsequent lectures.

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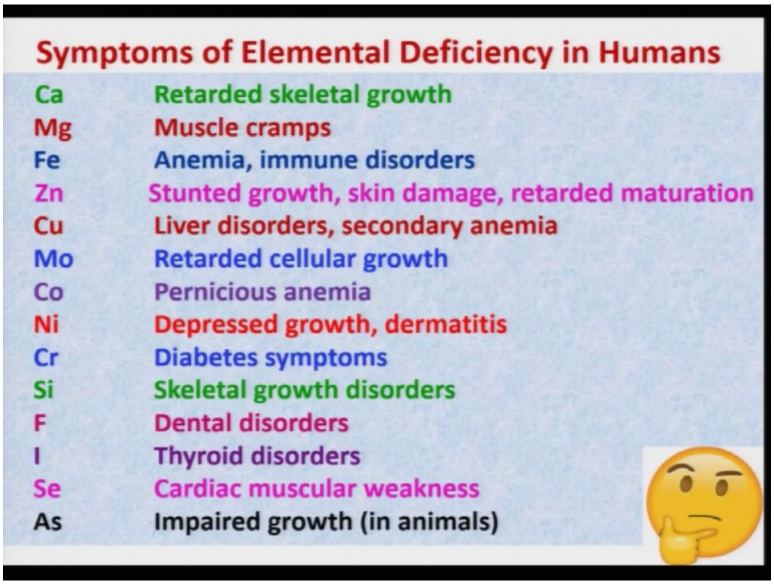

Symptoms of Elemental Deficiency in Humans

Ca	Retarded skeletal growth
Mg	Muscle cramps
Fe	Anemia, immune disorders
Zn	Stunted growth, skin damage, retarded maturation
Cu	Liver disorders, secondary anemia
Mo	Retarded cellular growth
Co	Pernicious anemia
Ni	Depressed growth, dermatitis
Cr	Diabetes symptoms
Si	Skeletal growth disorders
F	Dental disorders
I	Thyroid disorders
Se	Cardiac muscular weakness
As	Impaired growth (in animals)

Now, I have shown here the symtoms of element deficiency in humans. As you can see that large number of deficiencies or diseases can happen once you have a deficiency of a particular element. For example, calcium that is retarded skeletal growth; magnesium, iron, zinc, copper, molybdenum, cobalt, nickel, chromium, silicon, chlorine, iodine, selenium, arsenic: all these elements have to be present within a certain concentration range. If it is present in more concentration or less concentration than the desire amount then one would be having diseases, and some of these symptoms are tabulated over here.

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Effects of Metal Deficiency in Human

Now, some of these effects of metal deficiencies are shown over here.

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Medicines to Supplement Metal Deficiency

And if you have the deficiency you have to take medicines to supplement those metals, and go to the doctor and doctor will write this medicines indeed.

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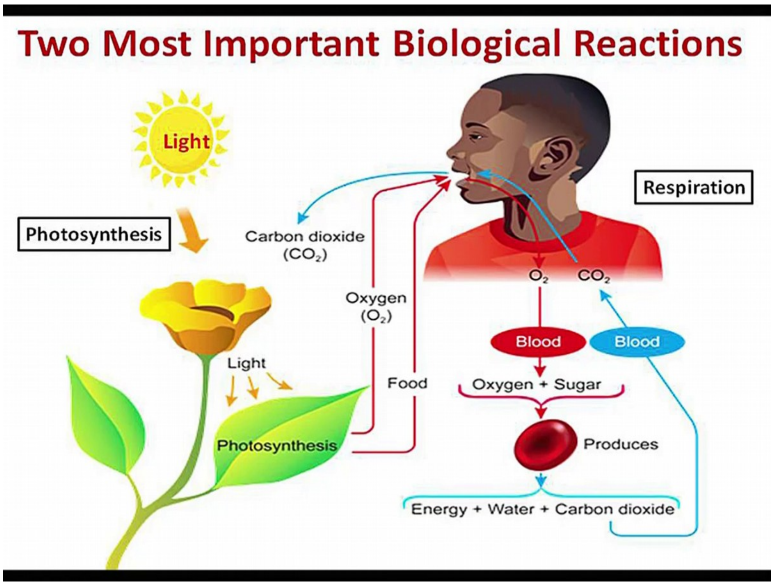

Two Most Important Biological Reactions

Now, two most important biological reactions are shown here. For example, that we take dioxygen and dioxygen is being circulated in the blood and it releases lots of energy and carbon dioxide during the respiration. And this carbon dioxide transported through blood goes out of our body, and it is being utilized by green plant and in presence of light they undergo a photosynthesis reactions and it liberate oxygen which we inhale. So, this is being the cycle of two important reaction, one is photosynthesis, another one is respiration.

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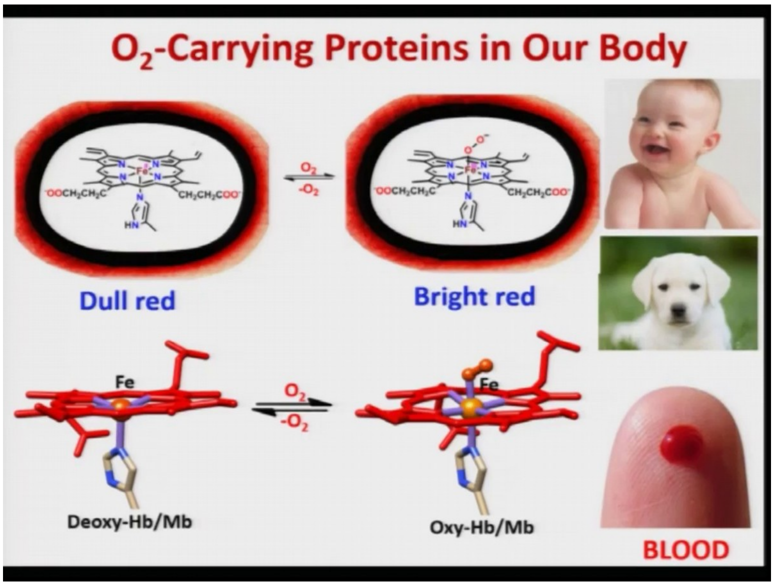

O_2-Carrying Proteins in Our Body

Now, the dioxygen carrying proteins are shown here in hemoglobin and myoglobin in our body, and as you can see that deoxyhemoglobin and deoxymyoglobin which is 5 coordinated convert to 6 coordinated upon dioxygen binding and Fe(II) getting oxidized to Fe(III), whereas, dioxygen getting reduced to superoxides.

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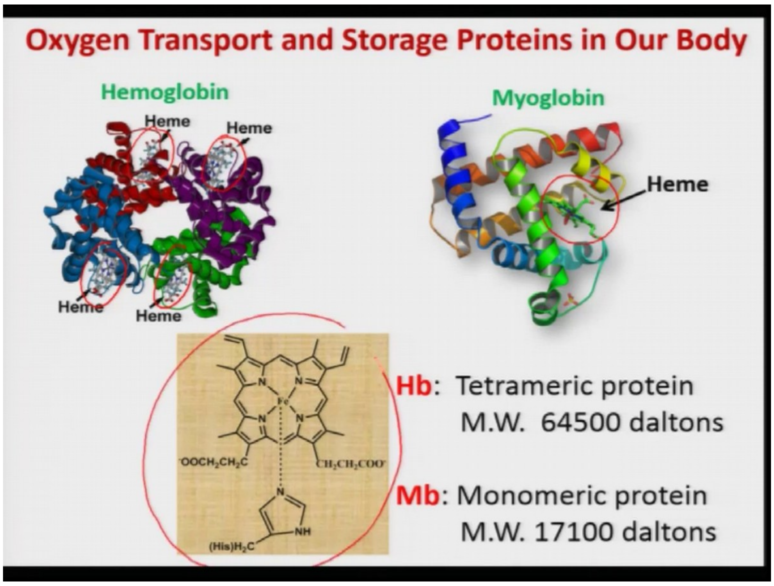

Oxygen Transport and Storage Proteins in Our Body

Hb: Tetrameric protein
M.W. 64500 daltons

Mb: Monomeric protein
M.W. 17100 daltons

Now, hemoglobin and myoglobin are responsible for this dioxygen transport and storage in our body. However, hemoglobin is tetrameric in nature. As you can see that these heme centers are here 1 2 3 4, however, huge proteins are wrapping around this heme centers. Similarly, myoglobin there is only one heme centers and basically the structure of this heme center is shown over here.

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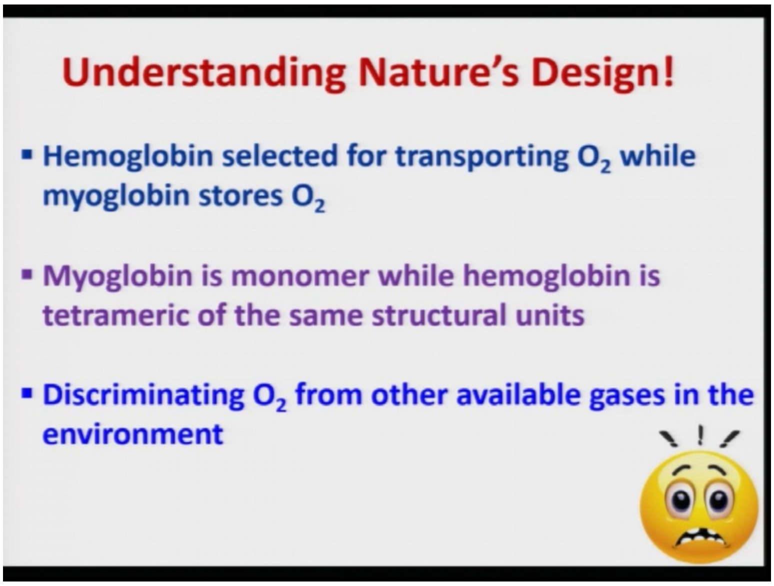

Understanding Nature's Design!

- Hemoglobin selected for transporting O_2 while myoglobin stores O_2
- Myoglobin is monomer while hemoglobin is tetrameric of the same structural units
- Discriminating O_2 from other available gases in the environment

This being the case now, we need to understand that how nature design this molecules. The hemoglobin selected for transporting oxygen while myoglobin stores oxygen. Myoglobin is monomer while hemoglobin is tetramer of the same structural units. Discriminating oxygen from other available gases in the environment; so, we will be talking all this and try to understand the nature's design.

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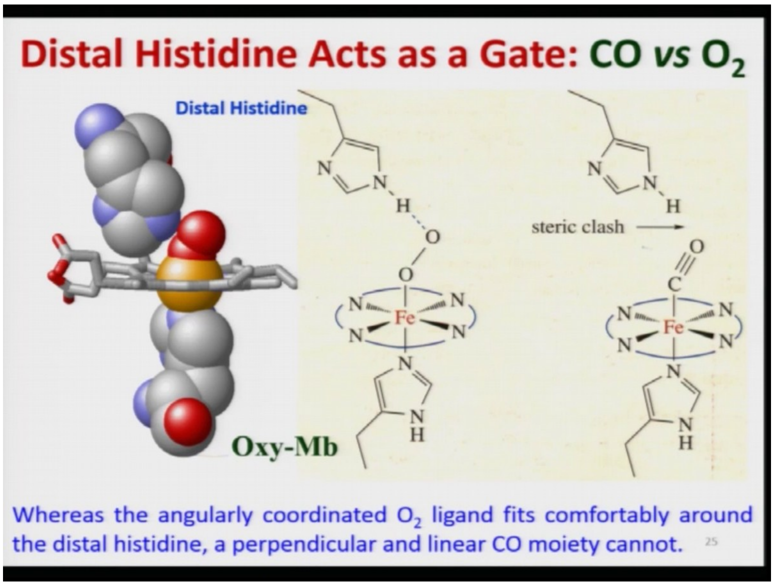

Distal Histidine Acts as a Gate: CO *vs* O_2

Whereas the angularly coordinated O_2 ligand fits comfortably around the distal histidine, a perpendicular and linear CO moiety cannot.

For example: this distal histidine which is not ligated directly to the iron center is responsible for discriminating between carbon monoxide and oxygen. As one can see that this distal histidine while facilitating the angular coordination of dioxygen comfortably, while the perpendicular and linear carbon monoxide moiety cannot bind like this it is forced to have in a angular fashion.

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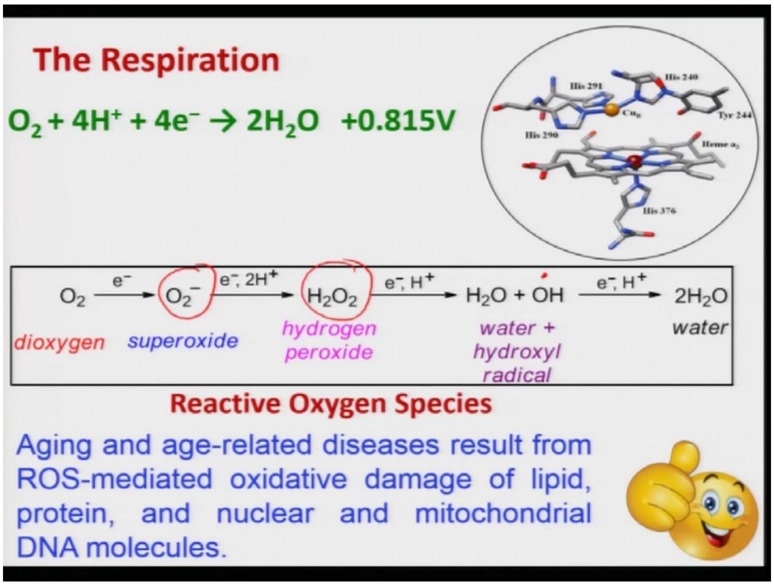

The Respiration

$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O \quad +0.815V$

$$O_2 \xrightarrow{e^-} O_2^- \xrightarrow{e^-,\,2H^+} H_2O_2 \xrightarrow{e^-,\,H^+} H_2O + \dot{O}H \xrightarrow{e^-,\,H^+} 2H_2O$$

dioxygen superoxide hydrogen peroxide water + hydroxyl radical water

Reactive Oxygen Species

Aging and age-related diseases result from ROS-mediated oxidative damage of lipid, protein, and nuclear and mitochondrial DNA molecules.

In the respiration, the most important transformations that happens is dioxygen convert to water with the help of 4 proton and 4 electron. Dioxygen completely reduced in this way. However, if it is reduced partially, what would happen? So, dioxygen after one electron reduction converts to superoxides, superoxide then convert to peroxides, peroxides after reduction converted to water and OH radical and OH radical converts to water.

As you can see that partial reduction produces superoxide, peroxides, hydroxyl radical, these are actually called reactive oxygen species and very harmful for our biological system. And this reactive oxygen is responsible for aging and age related disease in our body.

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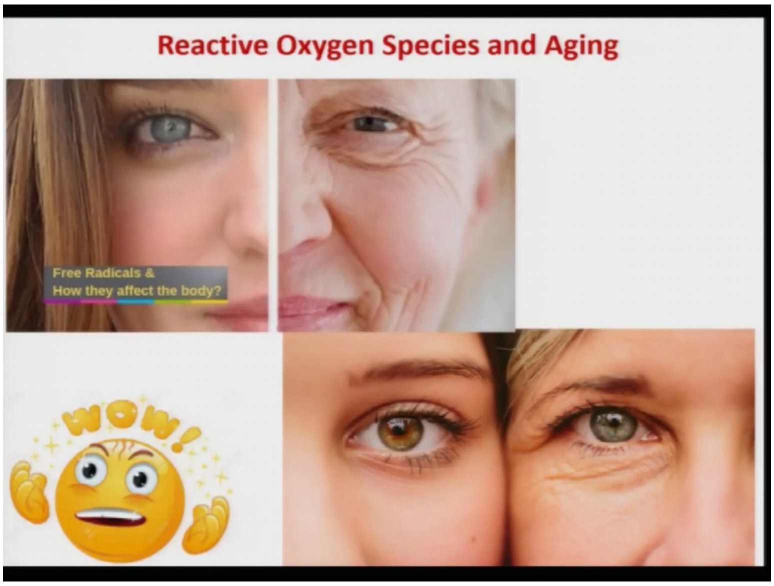

Reactive Oxygen Species and Aging

So, I have shown here how reactive oxygen species actually changes our faces.

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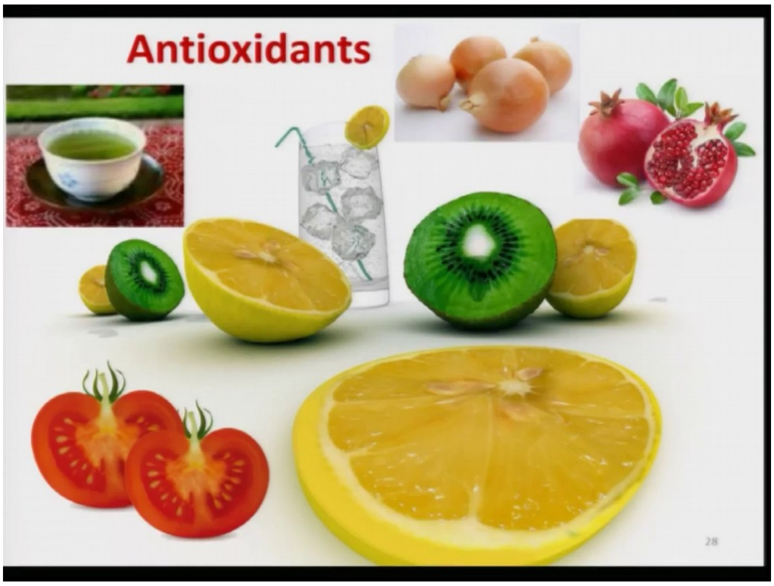

Antioxidants

And, these antioxidants are also there to fight against this reactive oxygen species. And some of these food items are shown here which are strongly antioxidant which destroy those Ros the reactive oxygen species.

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And this is what one can use at home without losing much. You can stay teen also at very old age.

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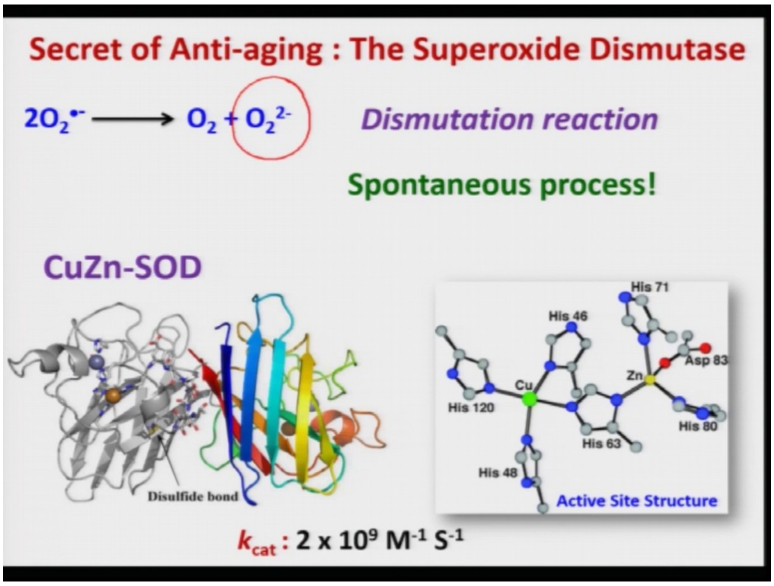
Secret of Anti-aging : The Superoxide Dismutase

$2O_2^{\bullet-} \longrightarrow O_2 + O_2^{2-}$ *Dismutation reaction*

Spontaneous process!

CuZn-SOD

k_{cat} : 2×10^9 M^{-1} S^{-1}

Now, secret of anti-aging agent is superoxide dismutase; as one can see the superoxide getting converted to oxygen and O_2^{2-} peroxide. However, this is a dismutation reaction, means this is a spontaneous process, thermodynamically feasible, ΔG negative. Now, this being the case, why nature design enzyme called superoxide dismutase? This is because the rate of these transformations has increased enormously. It becomes 2 x 10^9

$M^{-1}s^{-1}$. And that is the reason why nature has designed an enzyme because superoxides are extremely poisonous. However, the super oxides also produce peroxides which is another poisons.

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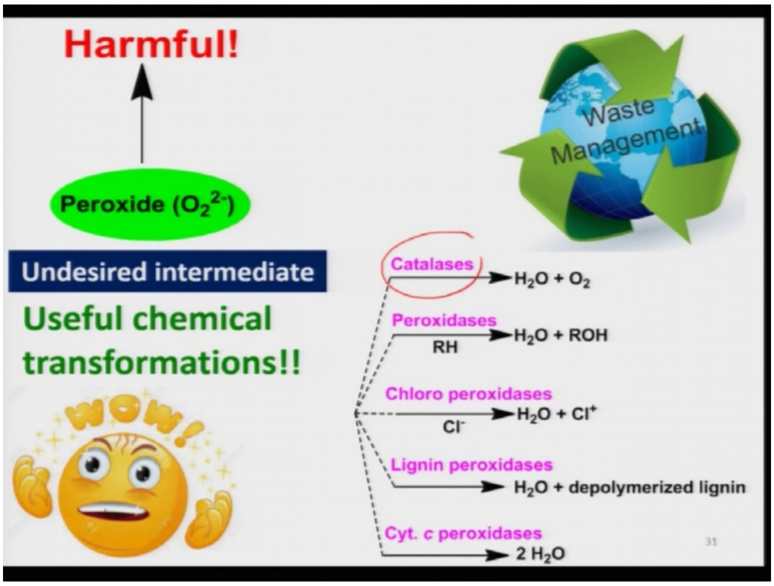

Harmful!

Peroxide (O_2^{2-})

Undesired intermediate

Useful chemical transformations!!

Catalases $\rightarrow H_2O + O_2$

Peroxidases $\xrightarrow[RH]{} H_2O + ROH$

Chloro peroxidases $\xrightarrow[Cl^-]{} H_2O + Cl^+$

Lignin peroxidases $\rightarrow H_2O$ + depolymerized lignin

Cyt. *c* peroxidases $\rightarrow 2\,H_2O$

Now, this peroxides is undesired, and also extremely harmful. However, nature utilized this undesired product harmful product, so something very useful. And some of the enzymes such as catalase, peroxidase, chloro-peroxidase, lignin peroxidase, cytochrome c peroxidases there are lots of enzymes which actually converts this undesired intermediate into something very useful molecules in our biological system. Now, what could be the better waste management than this?

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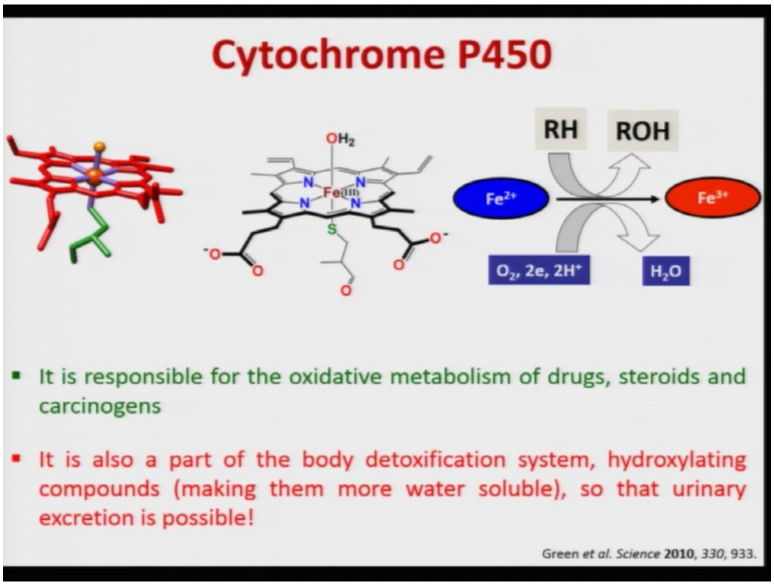

Cytochrome P450

- It is responsible for the oxidative metabolism of drugs, steroids and carcinogens
- It is also a part of the body detoxification system, hydroxylating compounds (making them more water soluble), so that urinary excretion is possible!

Green *et al. Science* **2010**, *330*, 933.

Cytochrome P450 is another very important enzymes in our body which is responsible for oxidative metabolism of drugs, steroids and carcinogen. It actually protect our body from toxification and hydrolyzed undesired compound, so that it can excrete through our body.

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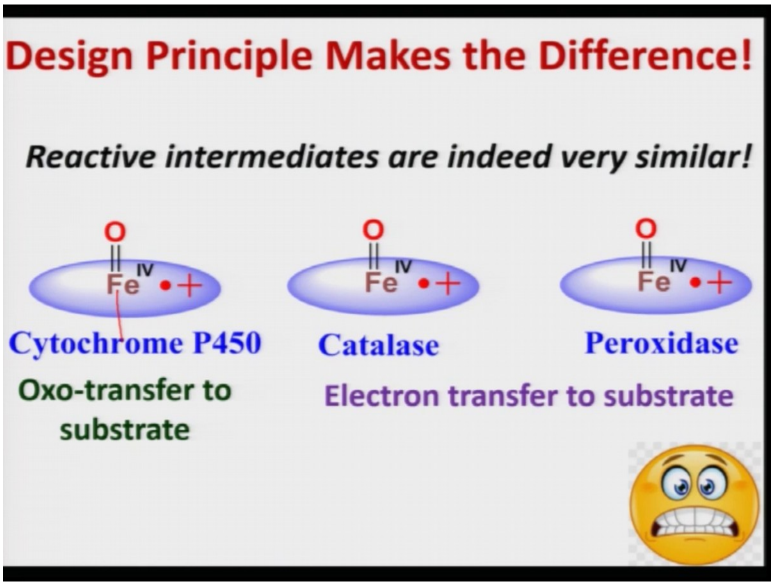

Design Principle Makes the Difference!

Reactive intermediates are indeed very similar!

Cytochrome P450 — **Oxo-transfer to substrate**

Catalase **Peroxidase** — **Electron transfer to substrate**

Now, the cytochrome P450 catalyst and peroxidase all go through a highly reactive intermediates that is called Fe(IV) oxo-species, and they are all similar only difference is their axial coordination. The 6th position is occupied, in some cases it is histidine, in some cases it is tyrosine, in some cases it is cysteine. However, their structures are indeed very similar. Now it is very surprising to see that their activity is very different. For example, in cytochrome P450 it is actually responsible for oxo-transfer to substrate while catalase andperoxidase, it is electron transfer to substrate. It is interesting to see that how design principle makes all these differences in reactivity.

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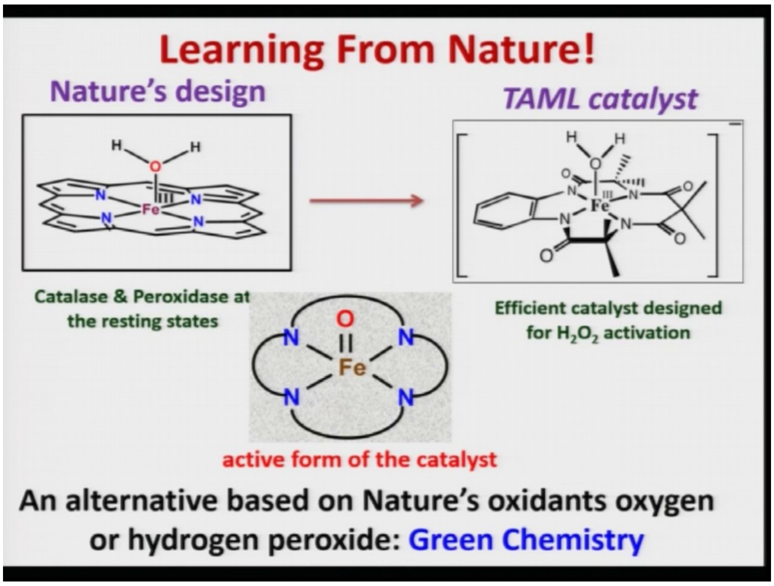

Learning From Nature!

Nature's design

TAML catalyst

Catalase & Peroxidase at the resting states

Efficient catalyst designed for H_2O_2 activation

active form of the catalyst

An alternative based on Nature's oxidants oxygen or hydrogen peroxide: Green Chemistry

We have also learnt from nature and implemented the knowledge, gained for the betterment of our day to day life. Catalase and peroxidase at resting state is like this, and one of our friend from US (United States) has made this biofriendly catalyst TAML which is doing miracles in cleaning large number of pollutants from our environment. He also indeed earns huge amount of money out of that. The active form of this catalyst is the same for both biology and bio-catalyst. This is an alternative based on nature's oxidant, oxygen or hydrogen peroxide.

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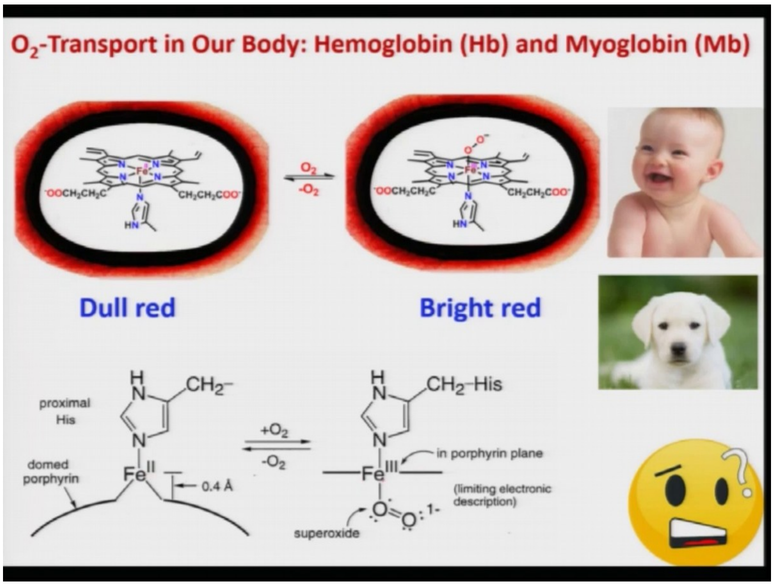

O_2-Transport in Our Body: Hemoglobin (Hb) and Myoglobin (Mb)

Dull red

Bright red

Now, as I have discussed that in our body hemoglobin and myoglobin is responsible for oxygen transport in our body. Now, what is exactly happening? That Fe(II) converted to Fe(III), while dioxygen reduced to superoxide and once this dioxygen leaves this Fe(III) converts back to Fe(II) again. So, this is completely reversible which is happening all the time in our body.

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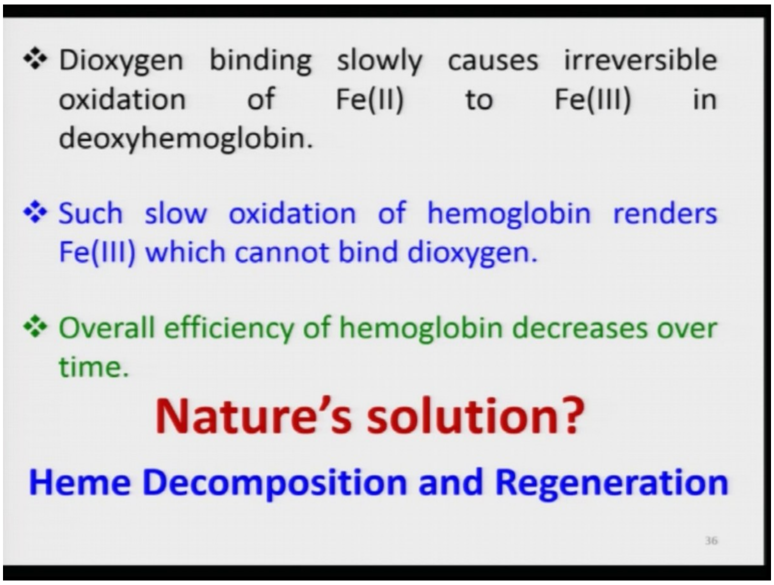

- Dioxygen binding slowly causes irreversible oxidation of Fe(II) to Fe(III) in deoxyhemoglobin.
- Such slow oxidation of hemoglobin renders Fe(III) which cannot bind dioxygen.
- Overall efficiency of hemoglobin decreases over time.

Nature's solution?

Heme Decomposition and Regeneration

Now, dioxygen binding slowly causes irreversible oxidation of Fe(II) to Fe(III) in deoxyhemoglobin, and in that way the overall efficiency of hemoglobin decreases over the time. Now, what is the nature solution for it? Yes, nature has a solution. So, heme decomposition and regeneration of the blood is what is the solution. And we all know that red blood cell lasts only for 120 days.

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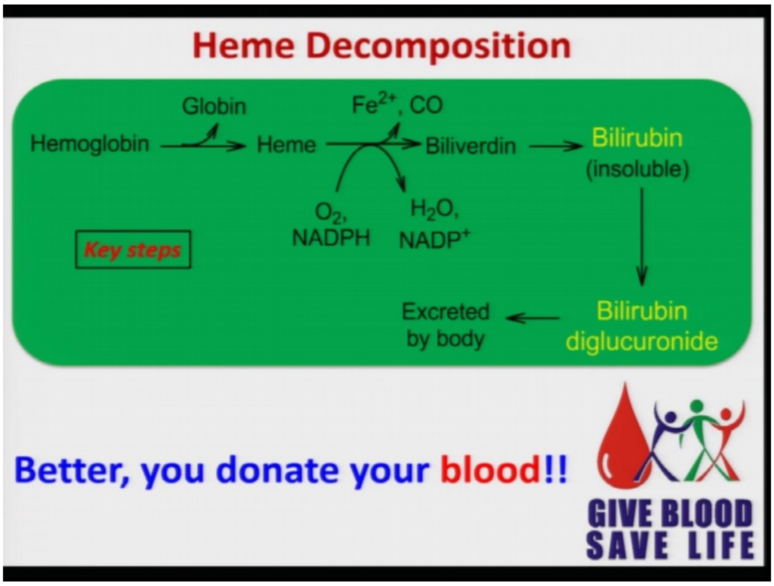

Heme Decomposition

Better, you donate your blood!!

So, this is what that heme decomposition process catalyzed by heme oxygenase is, like hemoglobin converted to biliverdin, bilirubin, which is yellow in color however, insoluble. Then bilirubin converted to bilirubin diglucuronide and which excrete through urine. So, this is what is happening all the time. And it is better that you donate your blood, otherwise it undergo this types of decomposition process all the time.

As I have already said that red blood cell has lifespan of only 120 days and after that it decomposes. So, this is what is happening. And, it is a spontaneous process. If you have disbalance then this bilirubin which is yellow in color will be deposited on the body and creates this jaundice.

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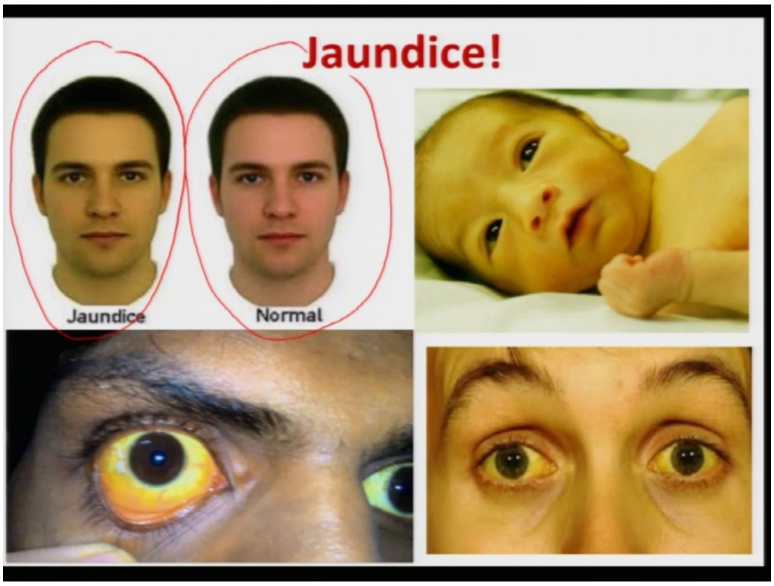

Jaundice!

You can see this normal person is shown over here, however, the person which is having jaundice which is his body color turns yellow and you can see this is a very common disease in our life, if it is not spontaneous.

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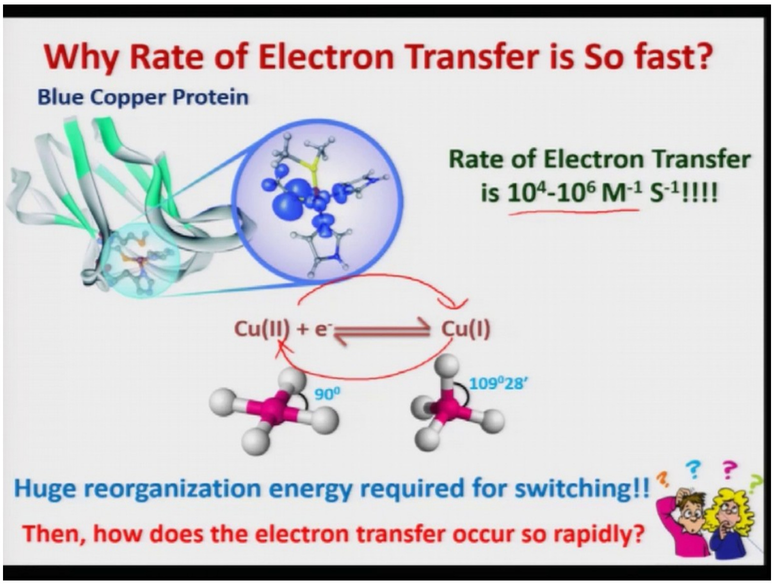

Why Rate of Electron Transfer is So fast?

Blue Copper Protein

Rate of Electron Transfer is 10^4-10^6 M^{-1} S^{-1}!!!!

$Cu(II) + e^- \rightleftharpoons Cu(I)$

Huge reorganization energy required for switching!!

Then, how does the electron transfer occur so rapidly?

Now, I will be talking that why the rate of this electron transfer is so fast in some of these enzymatic proteins or enzymatic system. I am showing here a blue copper protein, an example where the rate of electron transfer is increased to 10^8 to 10^{10} times faster. In this blue copper protein the rate is 10^4 to 10^6 $M^{-1}S^{-1}$. However, what is happening in blue copper protein? This Cu(II) converts to Cu(I) and Cu(I) releases one electron convert to Cu(II). So, Cu(II) become Cu(I) and Cu(I) become Cu(II); so, one takes electron, one release electron. So, this is what is happening.

During this process there is a huge structural reorganization energy required. Say Cu(II) is 4 coordinated species always square planar. Cu(I) which is d^{10} system it prefers tetrahedral. Now, converting a square planar to tetrahedral and tetrahedral to square planar, there is a huge reorganization energy required and these slows down the rate of electron transfer. Now, this being the case, then how the electron transfer in blue copper protein increases to 10^8 to 10^{10} times faster. So, we will talk about all these in details.

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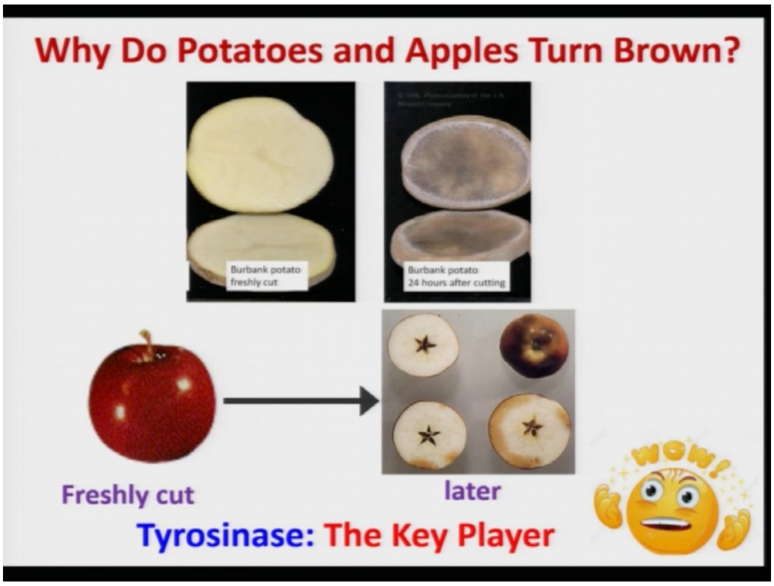

Why Do Potatoes and Apples Turn Brown?

Freshly cut

later

Tyrosinase: The Key Player

You must have seen that potato and apple turns brown, if you cut it and keep it for few hours and this is because that the surface is getting protected out of this brown color. And the enzyme which is responsible for this browning of the surface is tyrosinase. We will talk about in details the mechanism of this brown color and how tyrosinase is actually responsible for converting this apple and potato to brown.

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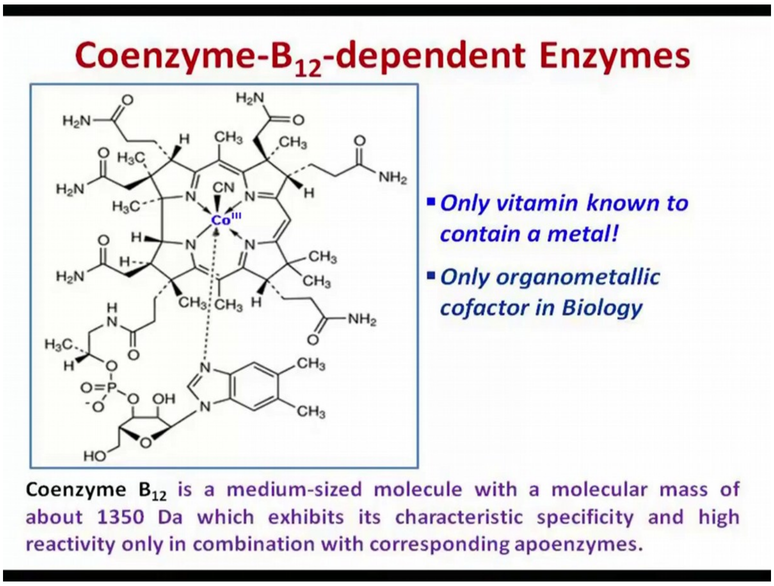

Coenzyme-B_{12}-dependent Enzymes

- *Only vitamin known to contain a metal!*
- *Only organometallic cofactor in Biology*

Coenzyme B_{12} is a medium-sized molecule with a molecular mass of about 1350 Da which exhibits its characteristic specificity and high reactivity only in combination with corresponding apoenzymes.

The coenzyme B_{12} dependent enzymes is shown here. Basically, coenzyme B_{12} is a medium sized molecule with a molecular mass of about 1350 dalton, which exhibits it characteristic, specificity and high reactivity only in combination with corresponding apoenzymes. And as you can see that this vitamin B_{12} is the only vitamin known to contain a metal; and also now we will look at the design and nature selection of the metal and the macrocycle.

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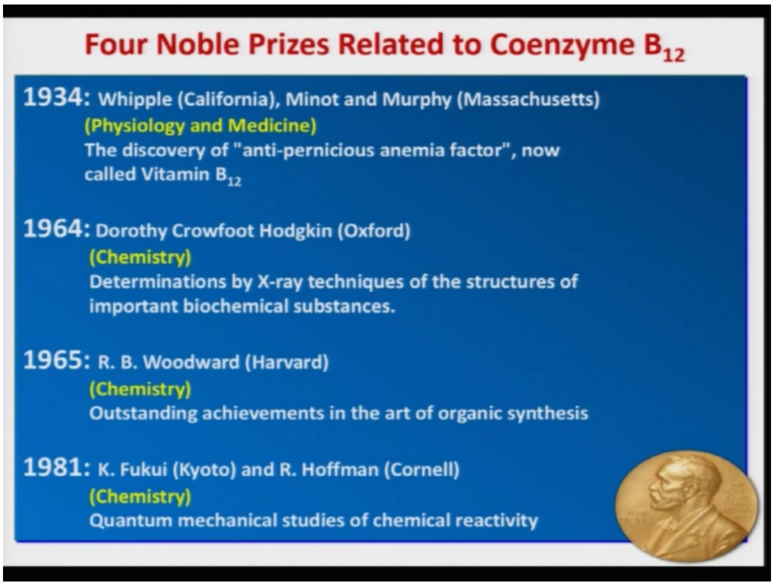

Four Noble Prizes Related to Coenzyme B_{12}

1934: Whipple (California), Minot and Murphy (Massachusetts)
(Physiology and Medicine)
The discovery of "anti-pernicious anemia factor", now called Vitamin B_{12}

1964: Dorothy Crowfoot Hodgkin (Oxford)
(Chemistry)
Determinations by X-ray techniques of the structures of important biochemical substances.

1965: R. B. Woodward (Harvard)
(Chemistry)
Outstanding achievements in the art of organic synthesis

1981: K. Fukui (Kyoto) and R. Hoffman (Cornell)
(Chemistry)
Quantum mechanical studies of chemical reactivity

This coenzyme B_{12} is so important that 4 Noble Prize was awarde. In 1934, Whipple, Minot, Murphy got the Noble Prize for the discovery of anti-pernicious anemia factor. Now, we call vitamin B_{12}. 1964, Dorothy Hodgkin, see solved the X-ray structure of this complicated molecule. 1965: Woodward for its outstanding achievements in the art of organic synthesis. 1981: Fukui and Hoffman for quantum mechanical studies of chemical reactivity. You all know that woodward-Hoffman rules how important it is for pericyclic reactions.

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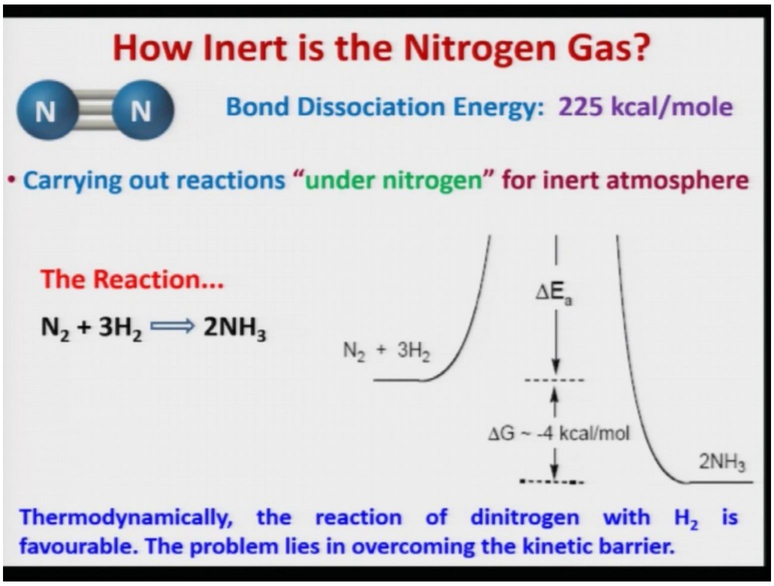

How Inert is the Nitrogen Gas?

Bond Dissociation Energy: 225 kcal/mole

- Carrying out reactions "under nitrogen" for inert atmosphere

The Reaction...

$N_2 + 3H_2 \Longrightarrow 2NH_3$

Thermodynamically, the reaction of dinitrogen with H_2 is favourable. The problem lies in overcoming the kinetic barrier.

Now, how inert is the nitrogen gas? This nitrogen bond dissociation energy is very high, 225 kcal/mol. Indeed, we run our reactions under nitrogen assuming that it will maintain inert atmosphere. The reaction this $N_2 + 3H_2$ gives rise to 2 molecule of ammonia, it is also thermodynamically favorable, but the kinetic barrier is too high as one can see out of this diagram.

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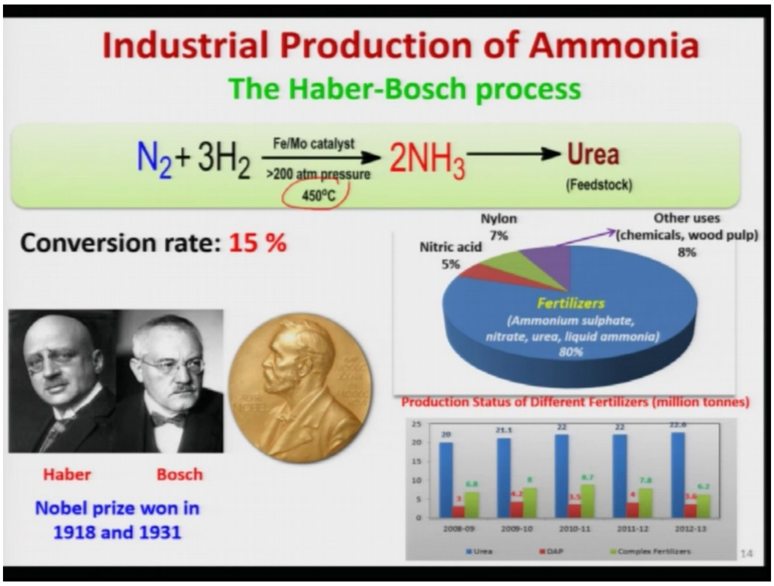

Industrial Production of Ammonia

The Haber-Bosch process

$$N_2 + 3H_2 \xrightarrow[\substack{>200\text{ atm pressure}\\ 450^{\circ}C}]{\text{Fe/Mo catalyst}} 2NH_3 \longrightarrow \text{Urea}$$

(Feedstock)

Conversion rate: 15 %

Haber Bosch

Nobel prize won in 1918 and 1931

Production Status of Different Fertilizers (million tonnes)

Indeed, the industrial production of ammonia which is popularly known as the Haber Bosch process is N_2 + $3H_2$ converts to ammonia which eventually transformed to urea. This ammonia requires a very drastic condition of more than 200 atmospheric pressure, 450 ˚C temperature and iron molybdenum catalyst. At urea is very important for our farmers. It has been used as a fertilizers. And the Haber and Bosch got Noble Prize in 1918 and 1931, respectively. Conversion rate is only 15%.

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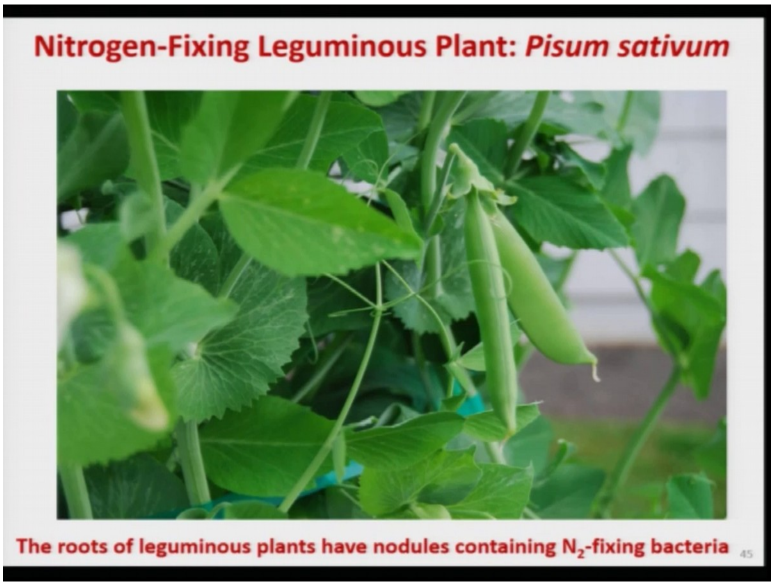

Nitrogen-Fixing Leguminous Plant: *Pisum sativum*

The roots of leguminous plants have nodules containing N_2-fixing bacteria

Now, in contrast if you look at the biological catalyst nitrogenase, this is the leguminous plant.

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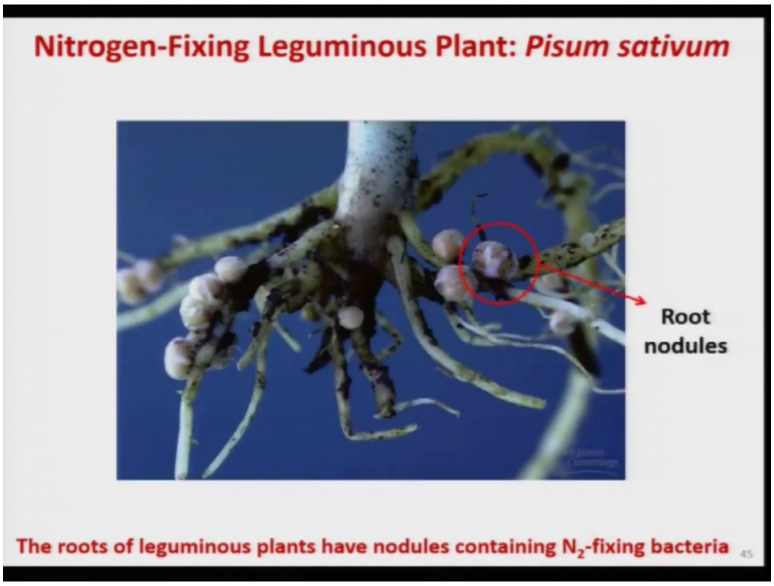

Nitrogen-Fixing Leguminous Plant: *Pisum sativum*

The roots of leguminous plants have nodules containing N_2-fixing bacteria

And, this is the root nodules have those nitrogenase which silently fixes the aerial nitrogen converting them to ammonia and fertilizers.

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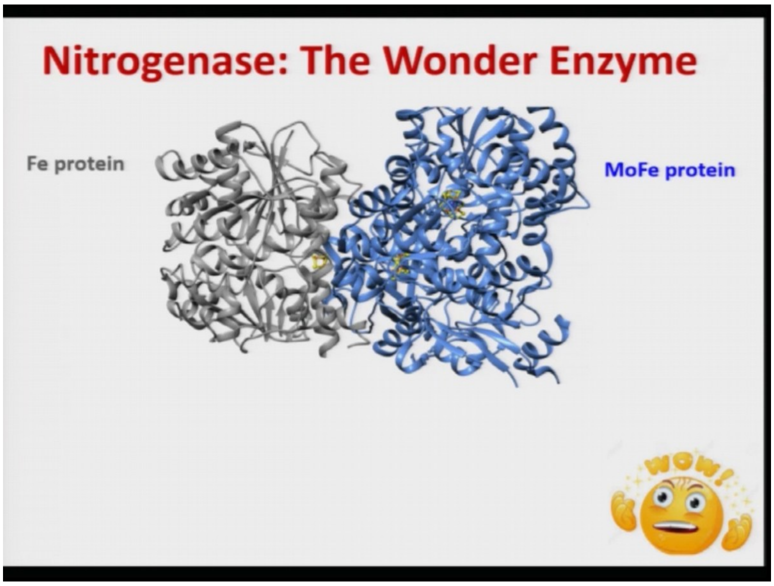

Nitrogenase: The Wonder Enzyme

So, the nitrogenase is this enzyme has this iron protein and iron molybdenum protein.

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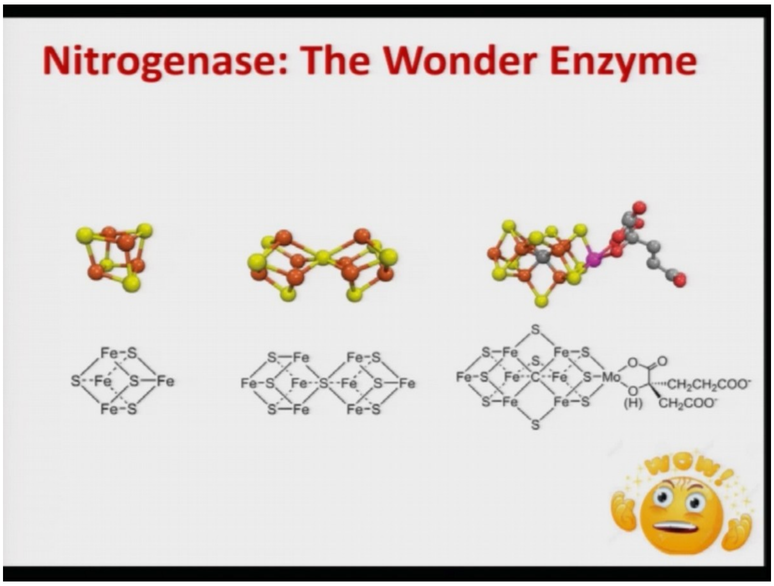

Nitrogenase: The Wonder Enzyme

And, once you remove the protein, as you can see this iron sulfur clusters and iron molybdenum clusters are actually responsible for fixing the aerial nitrogen and converting them to ammonia and other useful products. We will discuss in details in the subsequent lectures.

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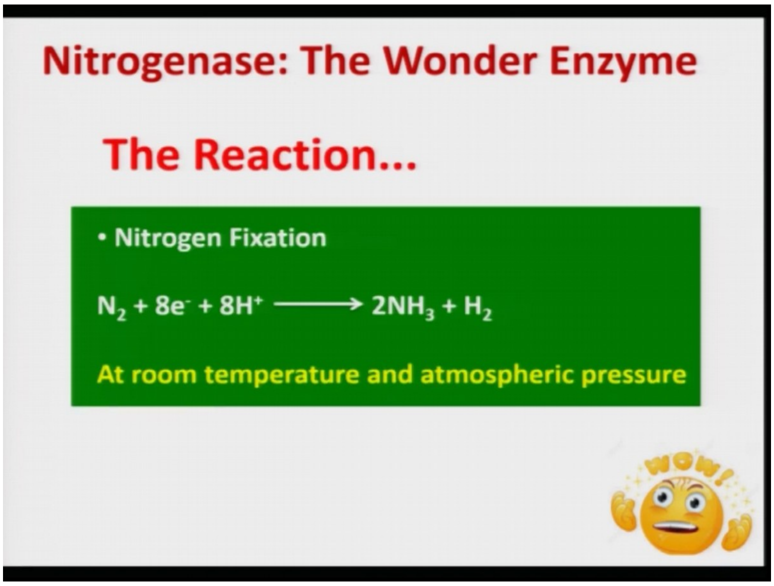

Nitrogenase: The Wonder Enzyme

The Reaction...

- Nitrogen Fixation

$N_2 + 8e^- + 8H^+ \longrightarrow 2NH_3 + H_2$

At room temperature and atmospheric pressure

So, the reaction which is actually happening is converting aerial nitrogen to ammonia at room temperature and normal atmospheric pressure. So, it is interesting to see that how aerial nitrogen can so easily be fixed, and so easily be utilized and we will be discussing these in details, in subsequent lectures.

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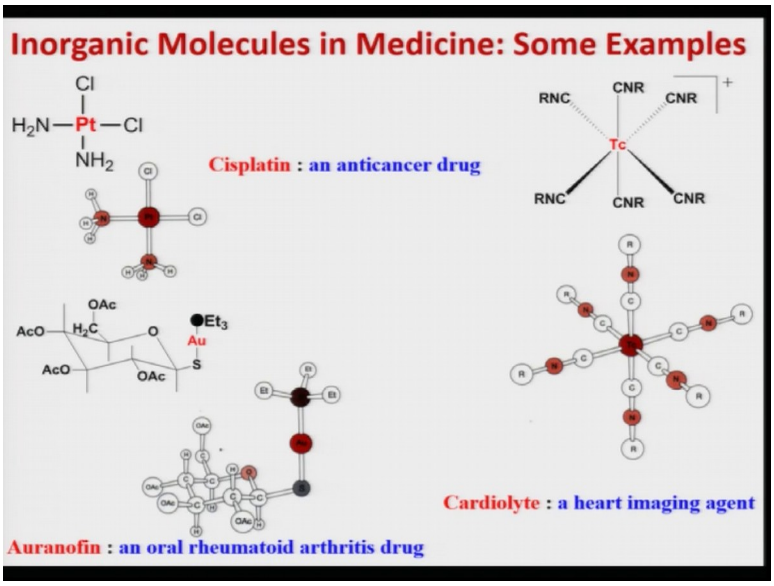

Inorganic Molecules in Medicine: Some Examples

Cisplatin : an anticancer drug

Cardiolyte : a heart imaging agent

Auranofin : an oral rheumatoid arthritis drug

Now, I will also talk about the inorganic molecules used in medicines. And some of these examples popular examples are shown over here. This is cisplatin which is an anti-cancer drug. Auranofin, which is arthritis drug; cardiolyte, it is an imaging agent. There are many such molecules which are used in medicine, and I will be talking all details in my lectures. And, I hope our journey would be very pleasant, and you will all enjoy going through this course.

Thank you so much for your attention.