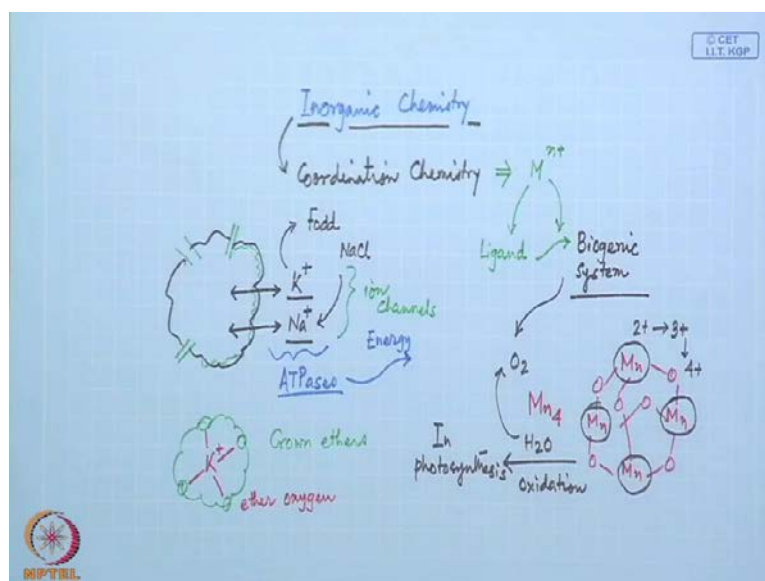


Coordination Chemistry
Prof. Debashis Ray
Department of Chemistry
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Lecture - 40
Biological Inorganic Chemistry

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Good evening everybody. So in this last class, we will just discuss something about the biological aspects of coordination chemistry, and broadly speaking when we talk about the total inorganic chemistry, and we find that some part of this particular sub-discipline of chemistry can be devoted to coordination chemistry. And in these lectures we were focusing our attention where we see that how coordination chemistry of several metal centers which is present in some oxidation state M plus can interact with different ligand systems and provide some interesting properties to the system. And today's class we will find that how this ligand system, if we just move this ligand system from typical laboratory prepared molecules to biogenic system, we get the corresponding thing which is the biological part of the coordination chemistry.

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Biological coordination chemistry

The overlapping area of coordination chemistry and biochemistry which focuses the mutual relationship between these two sub-disciplines, with spotlight upon the function of metal complexes in living systems, including the transport, speciation and, eventually, mineralisation into inorganic materials, and including the use of metal complexes in **medicinal therapy and diagnosis**.

The species can be metal ions (such as K^+ , Fe^{2+} and Fe^{3+}), composite ions (e.g. molybdate), coordination compounds (like **cisplatin** and **carbonyltechnetium**), or inorganic molecules such as CO , NO , O_3 . Medicinal inorganic chemistry on the one hand, and **biomineralisation** on the other hand, are important integral parts.

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So, we considered this as the entire area as the biological coordination chemistry and where we should have everybody should have some very basic idea about the coordination chemistry. So, the coordination chemistry is an integral part for dealing with these biological molecules and biologists would also know little bit of this sort of chemistry; otherwise it is very difficult to explain what is happening there involving large number of important metal ions and metalloids and nonmetals.

So, what we see that this is basically an overlapping area of coordination chemistry and biochemistry which basically focuses the relationship between these two sub-disciplines and focus their attention for the metal complexes in living systems; that means the entire living system can give us the corresponding ligand system and that ligand system can bind to the metal ions which are available biologically also because from the different food materials or other sources we get the metal ions into the living system.

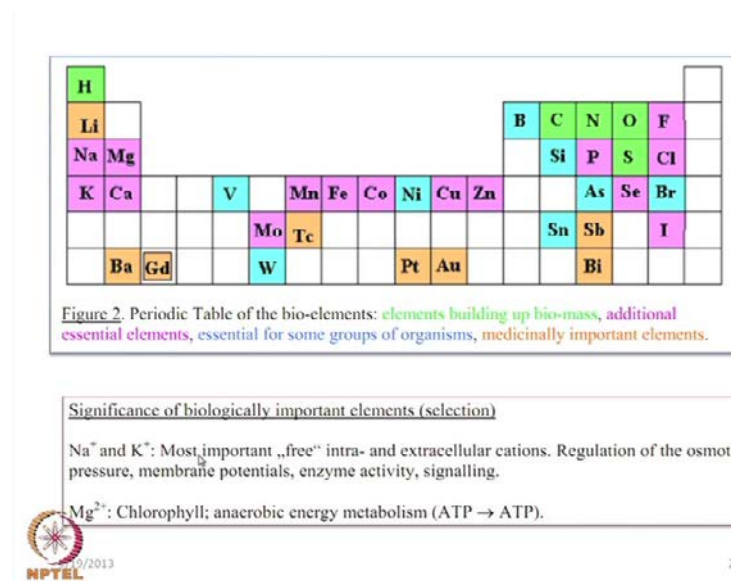
So, these metal ions when they enter into the living system, they go from one part to the other and they involved in the transport mechanism of these metal ions. Then they are involved in speciation that some metal ions are important for some molecules, others are not and ultimately it can go for typical storing of the metal ions in some of part of our bodies, say liver in the human system or in some other crystallite form in other animals and birds, etcetera. So, mineralization can also take place and the mineralization of inorganic materials not only the small molecules, but the big material type of thing is

also important. And lastly these molecule some of these good molecules we all know nowadays in the area of say some point of the general knowledge that some of these metal containing molecules are important drug such as cisplatin you all know that can be involved; that means that metal complex can be involved in medicinal therapy and diagnosis some imaging techniques can be done with these metal centers.

So, these species can be some of these as the metal ions starting from our potassium sodium balance; potassium and sodium is important in different ATP areas also, then iron which is important in our myoglobin and hemoglobin molecules in our cytochromes. And in some cases they can be some composite ions like molybdates; instead of molybdenum centre we can have different number of oxygen groups as to the molybdenum centre making this as the molybdate centre. So, this molybdate centre can also be a very good important species for OXO-transfer reactions. So, this particular compound as I just now told you that the cisplatin molecule which is platinum bearing metal complex and sometime the carbonyl technetium.

So, technetium where carbon monoxide is your good ligand can function as a very good medicinal molecule. In that way the small inorganic molecule such as the well known toxic gas like carbon monoxide, then nitric oxide, then ozone; they all can go and bind to the metal centre and function as very good ligand. So, the other part of this subject, the medicinal inorganic chemistry, we can have at one hand and bio-mineralization process where mineralization can take place in the living system where large amount of iron, say which is not utilized immediately for blood synthesis can be stored in our body and can function as integral part of the living system.

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So we will see that from the entire periodic table, if we just focus some of these systems because it is not possible to cover all these things but we can classify them in terms of their some groups. So these groups basically starting from sodium to iodine, they are essential elements which can function as some nice important reactions in the living system such as iron in blood, cobalt in vitamin B 12 and all these things. So, out of the entire periodic table we can have some of these elements and we consider them as bio-elements and these bio-elements can range from the elements which are being utilized as the biomass; that means the molecules which are responsible for making the typical bio-molecules, the carbohydrates, the glucose, the nucleic acids and all these to the medically important elements.

Some of these medically importance is the technetium which is a very good imaging agent, then Antimony and Bismarck they are also some though they are toxic element wise or the iron wise, they are toxic to the living system, but they can be utilized for some important functions to our system. So, how we select these metal ions or these different bio-elements for the important functions what nature can do for us; one such is the sodium and potassium ion. So, we know that within a cell system always we can have some balance for the transfer of potassium ion and sodium ion. So, we will have a different concentration of sodium ion outside the cell and a different concentration inside the cell. And we only consume sodium ion as sodium chloride, but the potassium what we get from the different food material, it is coming from the food material and they are

basically important in different ATP uses where ATP molecules are getting hydrolyzed to give rise to some amount of energy.

So, energy is generated with the use of these ATP uses and some of these ATP uses can function only with the potassium and the sodium ion. And these potassium and sodium ions are important because through these passage and all these things we can have some channels therefore, and they basically play some important role in ion channels. So, whenever we do some of these reactivity how these potassium and how because these are some biological membrane and how these biological membrane are being crossed by potassium and sodium and how they are bound. So, that way some important molecules we know that the crown ether type of molecules where you have several number of oxygen donors. So, if we have crown ether in our hand so instead of only hydrated form of these potassium and sodium, we can have potassium interacting with the ether oxygen. So, these are the ether oxygen groups.

Similarly, some biological molecules are available to trap this potassium and pass these biological membranes to take this potassium ion which is required for our activity within the cell. So, it is important therefore the sodium and potassium is therefore important in the free form and in the bound form for intra- and extracellular cations. So, some of these cations are present in large amount or the concentration is higher outside the cell and some having higher concentration inside the cell, they basically regulate also the osmotic pressure, they maintain the ionic potential or the membrane potential where they are separated by some membrane. They also responsible for enzyme activity like that of our ATP uses activity and sometimes the signaling also it can go for. Similarly the divalent non-transition metal ion like magnesium $2+$ plus the bivalent magnesium which is all we know as present in chlorophyll which can show some corresponding reaction for the storing the energy from the sun, for conversion of carbon dioxide and water to the glucose molecule in the photosynthesis.

So, the energy from the sunlight in the form of H news it can be trapped and that H new that energy can be transferred for the fixation of carbon dioxide and water molecule within the glucagon systems during photosynthesis. And it is also utilized for anaerobic energy metabolism when oxygen is not required and we can go for ATP to ADP; this is ADP, adenosine triphosphate to adenosine biphosphate conversion; that means one

inorganic phosphate group is being released and that can be converted for this transfer for energy transduction.

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Ca^{2+} : Signalling, muscle contraction, enzyme regulation. Main inorganic part of the endoskeletons (bones, teeth, enamel: hydroxyapatite; $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$). Exoskeletons of mussels, shells, corals, sea urchins etc: aragonite or calcite; CaCO_3 .

$\text{V}^{\text{IV/V}}$, $\text{Mo}^{\text{IV/VI}}$, $\text{W}^{\text{IV/VI}}$, $\text{Mn}^{\text{II/III/IV}}$, $\text{Fe}^{\text{II/III}}$, $\text{Ni}^{\text{II/III}}$, Cu^{II} : active centres in electron-transport (redox) enzymes, oxygenases, dismutases.


Fe and Cu: Transport of oxygen.

Fe^{III} : Iron-storage proteins (ferritins).

$\text{Fe}^{\text{II}} + \text{Fe}^{\text{III}}$ in magnetite (Fe_3O_4): orientation of magnetobacteria, pigeons, bees in Earth's magnetic field.

Co: Synthases and isomerases (cobalamines, e.g. vitamin- B_{12}); methylation of inorganics.

Zn^{2+} : In the active centre of hydrolases, carboanhydrase, alcohol dehydrogenase, synthases; genetic transcription (zinc fingers), stabilisation of tertiary and quaternary structures of proteins; repair enzymes.



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So we see that other ions like after magnesium, we have calcium. So, calcium like sodium and potassium can be involved in signaling process; that means sometime it can show that calcium concentration is higher in one part and calcium concentration is low in the other part. Then it is involved in muscle contraction, enzyme regulation and main inorganic part is for endoskeletal formation; that means the formation of bones, the teeth the bone enamel and all these cases the common molecule or the common compound what is forming is $\text{Ca}_5\text{PO}_4\text{OH}$ which is known as hydroxyapatite. So, this particular material is there which has covered our teeth as the enamel material. But for that particular system synthesis is required in the presence of right amount of calcium in the living system.

Then exoskeleton of muscles, the cells, the corals, the sea urchins, etc where most of them are found from calcium carbonate which are another form of calcite the mineral calcite we know; the nature is giving us in the form of that calcite and aragonite also. So, this basically gives us something that in living system we can store this calcium as in some mineral form and that we can consider it as the corresponding bio-mineralization process. Then coming to the transition metal ions, large numbers of transition metal ions

are involved and showing some activity in this bioinorganic chemistry where vanadium to copper is involved there and not only all these metal ions.

But due to the electron transfer mechanisms or involvement of these metal ions in the redox enzymes such as cytochromes, cytochrome oxidase and all these cases they involved in different oxidation states; vanadium such as in plus 4 and plus 5 oxidation state, molybdenum when it is between plus 4 and plus 6 oxidation state; that means it can go for two electron transfer as well as the OXO transfer. So, the oxygenases; that means the transfer of oxygen from one group to the other from the molybdenum centre to the sub-step can take place with the change in the oxidation state of molybdenum from plus 4 to plus 6. In a similar fashion tungsten can also function between these two oxidation state; manganese we all know manganese can be easily go from a bivalent state to a tetravalent state and one such manganese cluster is known which is manganese 4 and four such manganese centers are there which are bridged by OXO in a fashion like this, where this tetranuclear complex is responsible for water oxidation in photosynthesis.

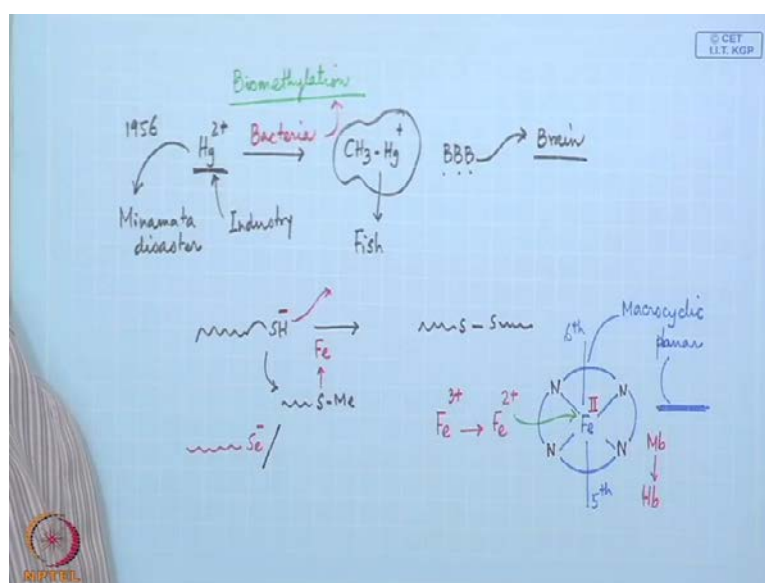
So, manganese when present, so four such manganese centers are present in this complex adamantane type of structure. But this manganese oxidation state can settle between 2 plus to 3 plus to 4 plus; that means electron transfer can take place where this water can give rise to the evolution of dioxygen molecule. So manganese, then iron, then nickel and copper, they are present in several dismutase's and oxygenases such as copper along with zinc is present in super oxide dismutase's where the generation of super oxide from the dioxygen molecule can be encountered and it can go for disproportionation reaction to water and hydrogen peroxide sometime and ultimately the catalases and peroxidases can destroy the accumulated hydrogen peroxide into the system.

Then these two metal ions; that means, iron and copper can also involve in transport of oxygen; this particular one will see in detail for hemoglobin and myoglobin molecule also in our body copper is present in hemocyanin molecule for dioxygen transfer. So, these two metal ions are very important for the electron transfer as well as electron storage. In the same way these two metal ions can be involved for dioxygen transport and dioxygen storage. Then there are some molecules which are ferritin molecules which can be utilized for iron storage in proteins for the bio-mineralization process where iron is getting stored; whatever iron we get, we get slowly the different concentration of these iron from the food material and that particular iron ferritin has taken up that iron and it is

stored in some other form. And that particular storehouse of iron will be utilized for the synthesis of some important bio molecule such as cytochromes or hemoglobin or myoglobin.

Then both the two oxidation states of iron; that means the iron 2 and iron 3, they are present in magnetite's such as Fe_3O_4 which are present in bacteria and they are showing some magnetic property such that they can show the direction when this bacteria can move from one side to the other. Then home coming pigeons also, bees also, they can see or they can fill the corresponding earth's magnetic field due to the presence of these Fe_3O_4 crystallites within their body. Then cobalt, the cobalt in different oxidation states such as cobalt in plus 1, cobalt in plus 2 and cobalt in plus 3 can be utilized for the generation of cobalamines and vitamin-B 12 and sometimes the methylation of inorganic systems.

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So, these cobalt systems are utilized for the generation of, say, biomethylation reaction. So, one such important reaction is the biomethylation reaction where we see that a particular metal ion, say, mercuric ion and is well known for several years are around 1956; we have seen the corresponding Minamata disaster in Japan seaway where the poisoning effect of mercury from some industrial effluent. So, industry was responsible for the release of huge amount of mercury in the sea water, but some bacterial intervention was there. So, bacteria was available in sea water sea bacteria particularly

for this particular biomethylation reaction where the Hg 2 plus is converted to methyl mercury.

So, this particular one having some metal carbon bond can be considered as an organometallic species but which is much more deadly than the mercuric ion itself. Because it has some other property the lyophilic property is changing and it can cross the corresponding BBB what we all know which is known as blood brain barrier. So, there is a barrier. So, membrane is there and that membrane cannot be crossed by in mercuric state but it can be crossed by methyl mercury and it can be accumulated inside the brain of the human being those who are consuming this water or it was contaminated within the fish which is available in that particular areas seawater of that particular area.

So, this particular molecule can be accumulated in the brain and that would be neurotoxic to the human being and large amount of death case was reported in that particular area for this disaster. Then we have the non-transition metal ion like zinc 2 plus; it is forming the corresponding active centre for different hydrolyses responsible for hydrolyses reaction. Then carboanhydrase reaction, then alcohol dehydrogenase reaction, different synthasases reaction and genetic transcription reactions such as different zinc fingers bound to twelve units and the stabilization of tertiary and quaternary structure of the proteins some interaction with the zinc centre and repair enzymes. So, zinc can also play some important role in all these biological molecules.

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Si^{IV} ("silicate"): Involved in the built-up of bones. In the form of SiO₂/silica-gels as support in monocotyledonous plants (like grass) and the shells of diatoms.

P^V (phosphate): Constituent in hydroxi- and fluorapatite (Ca₅(PO₄)₃(OH/F)); energy metabolism (ATP), NADPH, activation of organic substrate; phospholipids in cell membranes; phosphate esters (DNA, RNA,...).

Se^{-II}: Selenocystein in special enzymes (e.g. glutathionperoxidase)

F⁻: Fluorapatite (Ca₅(PO₄)₃F) in dental enamel

Cl⁻: Along with hydrogencarbonate the most important free anion.

I⁻: Constituent of thyroid hormones (such as thyroxine).

Then some memb group elements like silica as silicates; they are responsible for building our bones, then silica-gels and silica support in this different grass and plants and the cells of diatoms they are present. Then phosphorus as we have seen just now that along with calcium phosphorous is also an important constituent for the generation of this fluorapatite system for the dental enamel, then the formation of adenosine triphosphates also. So, all inorganic phosphates what we are forming in the biological system such as the different lipid molecules we know the glycerol is forming the different esters with the long chain carboxyl acids and that esters can sometime be forming from the corresponding phosphate groups and they are phosphate esters. So, phosphor glycerides are known and formations of those phosphor glycerides are nothing but the incorporation of the phosphorous into the living organism. Then they are also responsible for the activation of organic substrates.

Then this is the thing that the formation of phospholipids in cell membrane because one of the most important constituent for the cell membrane is the different phospholipids and phospholipids are being found from the different acids, the glycerol and the corresponding phosphoric acid part which is generated through the accumulation of this phosphorous. And then the different phosphate esters because the deoxyribonucleic acids and the corresponding ribonucleic acids, the RNA and DNA molecules, all bear the different phosphate groups. Then selenium like that of our cystein molecule because the cystein we know that is a typical amino acid. So, is a very important amine acid bearing some SH group which play some important role and where this S can be oxidized from S S linkage, then it can go for methylation S methyl unit for the corresponding amino acid like methionine.

So, they all play some important role because they all are very good ligand because this can go for binding to the iron centre. Similarly, this after deprotonation forming S minus can go for binding some important metal ions. So, when we just substitute this particular end by selenium unit and that is also a corresponding selenocystein unit and that selenocystien unit also gives rise to some important reactions to the biological system. So, it is a special enzyme; when it is being substituted by cystein molecule by selenium such as glutathionperoxidase, so glutathion formation which is a very important anti-oxidant molecule in our system. So, for that we can have the corresponding peroxidase

activity; that means some reducing environment we can have if we have that corresponding peroxidase.

So, this glutathionperoxidase contains selenium. Then after calcium, we have phosphorous and after that we have the fluorine. So, fluorine is also an important constituent for the formation of this dental element and fluorine can play some important role along with the availability of calcium and phosphorous. Then chloride ion along with hydrogen carbonate, the most important free anion. Because when we consume dioxygen molecule in our body after food burning, we produce carbon dioxide and that carbon dioxide is getting converted to bicarbonate anion and that bicarbonate anion has one negative charge.

Similarly Cl minus also have someone negative charge and while we tackle the sodium ion and the potassium ion; we can also tackle the corresponding counter anion such as bicarbonate anions and Cl minus for the balance. Then I as I minus that iodide ion in thyroid hormone preparation such as thyroxine, iodine am being incorporated in the phenyl ring; that is why we all the time we consume some iodized salt. Instead of sodium chloride we can have also some sodium iodide in our system such that we can have right amount of thyroxine in our body.

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Medicinal relevant elements (selection):

Li^+ : Treatment of bipolar disorder (maniac depression) and hypertension.

Gd^{3+} : Contrast agent in magnetic resonance tomography of soft tissues.

BaSO_4 : Contrast agent for X-ray tomography. Sun protection.


$^{99\text{m}}\text{Tc}$ (a metastable γ -emitter; $t_{1/2} = 6 \text{ h}$): Radio diagnostics (bone cancer, infarct risk, ...)

Pt^{II} : Chemotherapy (e.g. with cisplatin *cis*- $[\text{Pt}(\text{NH}_3)_2\text{Cl}_2]$) of cancer (ovaria, testes)

Au^{I} : Therapy of rheumatic arthritis.

Sb^{III} : Treatment of inflammatory skin pimples like acne.

Bi^{III} : Treatment of gastritis.

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Then the last category of molecules that is for medical imaging and medical diagnosis and for the medicine. So, some of these metal ions will be useful for medically relevant


element such as lithium, gadolinium barium, and technetium. Lithium for maniac depression, gadolinium for imaging for magnetic resonance imaging, barium sulphate for contrast X-ray tomography and sometime sun lotion and technetium having some isomer which is 99 minute lifetime where you have which is a gamma-emitter.

So, which is a metastable species with atomic number 99 atomic weight 99; so, which can be utilized for diagnosis in bone cancer and some other cases also. Then platinum as cisplatin is a drug molecule for cancer chemotherapy, gold as in rheumatic arthritis drug, then antimony for the inflammatory skin pimples like acne because antimony is also known as the first molecule which has been prepared by person known as Upen Brahmahchari who made this from urea stibamine molecule for the black fever treatment, then bismarck for treatment of gastritis.

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Essentiality of elements is defined by

- (1) A physiological deficiency appears when the element is removed from the diet**
- (2) The deficiency is relieved by the addition of that element to the diet**
- (3) A specific biological function is associated with the element**

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So, we see that there are several essential elements in our hand and those essential elements which can show some physiological deficiency appears when the element is removed from the diet. So, if we do not take that element that metal ion such as iron, such as zinc, such as copper, we see some disorder in our system. So, it is a condition where we call that this particular element should be essential and we should have some balance with those elements. Then the deficiency is relieved by the addition of that element in that diet. So, if somebody is deficient in iodine, somebody is deficient in iron, somebody is deficient in calcium; we should put those elements in the diet chart. So,

these elements can have also some important biological function which it can show when it is associated with some important functions such as oxygen transfer, oxygen accumulation and oxygen utilization for the energy outcome.

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Transition metal ions commonly are not present in a free form, but rather coordinated (complexed) to ligands.

In particular, this applies to metal ions in the active centres of enzymes or otherwise integrated into peptides and proteins.

Examples for the respective ligands are listed below (N-functional: peptide moiety, porphinogenes, histidine; O-functional: tyrosinate, serinate, glutamate and aspartate; S-functional: cysteinate and methionine).

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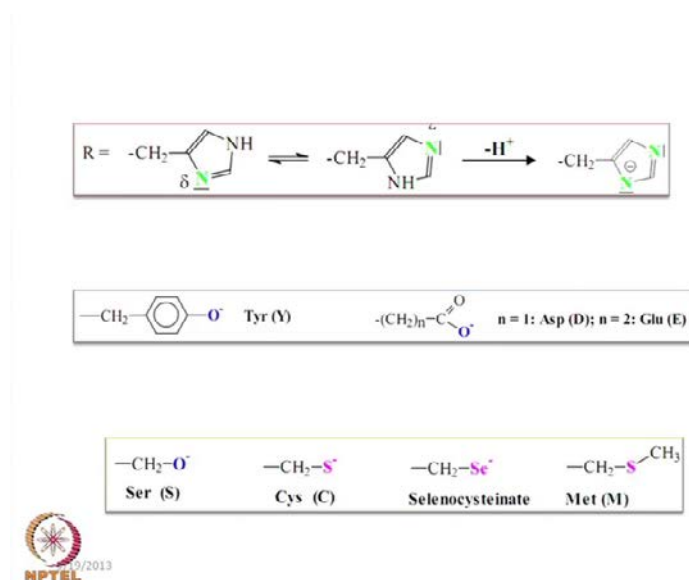
So, several of these transition metal ions such as iron, such as copper, such as cobalt, they are present in free form and sometimes they are coordinated to the ligands because they cannot remain as the corresponding aqua complexes; instead of those aqua complexes they can be complexed with the ligand. So, we must know the corresponding nature of these ligands, what are those ligands which we can handle. So in the active centers in the enzymes, you can have the peptides and proteins and all these peptides and proteins all we know that they have CO NH groups and those CO NH groups can be utilized for binding the metal centre because the amide group has oxygen donor as well as the nitrogen donor. So, any of these donor atoms can function as the useful donor group for metal coordination.

So, if we just go for these peptides and proteins in the biological molecules. So, the amine acids are coming into the picture and those amine acids first of all giving rise to the amide backbone but apart of that amide backbone, depending upon the corresponding substitutions, the R function which is present in those amino acid can also be a good pendant group to bind the metal ion such as tyrosine; tyrosine has a phenol unit. So, phenol unit after deprotonation can give rise to the phenol oxygen and that phenol

oxygen can go and bind to the metal centre. So, there are some groups available which can function as very good ligands such as nitrogen bearing; that means the peptide, the porphyrinogenes, the histidines, then oxygen bearing is tyrosine's, the serine molecule itself and the glutamate an aspartate, then sulphur function from cystein and methionine.

So, we can have all this possibilities and we can have from biogenic ligand, nitrogen oxygen and sulphur donors from these ligands. So, this is the amide part which can give rise to this nitrogen as the charge ion after deprotonation of this NH group. So, when this nitrogen is charged, this nitrogen can go and bind to the metal centre; otherwise we have the corresponding oxygen which is charged or oxygen lone pair can be utilized for the metal coordination.

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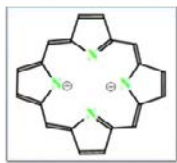


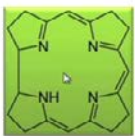
Then we can have the individual unit; this is the individual part that the hydrocyclic ring attached to the histidine amino acid. So, when our part of the histidine is individual part. So, it can have different tautomeric forms. After deprotonation of this nitrogen also this is the N H function and this is the N function only but initially this nitrogen can go for; that means the delta nitrogen can go for metal coordination. But if you have the deprotonation, then this nitrogen in the charged form can bind to the metal centre and in some cases when the charge is zero colors between these two nitrogen atoms, we can go for bridging such as we find a super oxide dismutase; between copper and zinc this group is present, this one binds copper centre and this one binds the zinc centre.

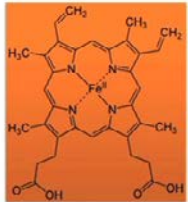
So, this particular unit can function as a bridging group between copper and zinc in the biological system. Then this is a tyrosine unit what I was just telling now is the phenol unit is present, this O minus can bind to the metal centre, then aspartic acid and the glutamic acid having the carboxyl and in this carboxyl oxygen with a charged which is blue in color can go for metal coordination. Then serine group can also give rise to the corresponding oxygen donor from the alcohol end. So, this is similar to that of the methoxy or ethoxy coordination to the metal centre edge. Then cysteine sulphur in S minus form, in selenocysteine through selenium which is the analog of the cysteine unit and metonine through thioether sulphur which is neutral sulphur and this neutral sulphur can bind to the different metal centers.

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Macrocycles








Corrin is the heteromacrocylic compound related to substituted derivative that is found in vitamin B₁₂. Its name reflects that it is the "core" of vitamin B₁₂ (cobalamins).

A heme group consists of an iron ion held in a heterocyclic ring, known as a porphyrin.


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Then we can have another interesting group of molecules which are the known as the different metallocycles and this metallocycles are form when we can have a macrocycles. So, a cyclic ligand we can have where, say, four nitrogen donor atoms are available and that nitrogen can give rise to a cyclic unit. So, this can bind to the metal centre, the second one, the third one and fourth one also. So if we have iron at the centre, we have a corresponding macro cyclic ligand and this particular one is basically a planar molecule which is planar after metal ion coordination. So, we can have also the vacant sides from fifth coordination and from the sixth coordination. So, this basically gives rise to the corresponding macrocyclic structure, one such is the porphyrin unit. So, this particular

five member nitrogen bearing ring we all know from the basic organic chemistry knowledge that this is the porphyrin unit, this is a second porphyrin.

So, if four such groups; that means the four such pyrrole units can be connected. If we can connect four such pyrrole units through some methine bridge, we get the corresponding macrocyclic unit as the corresponding cyclic one which can bind to the metal centre such as iron and if we just look at the entire molecule, this nitrogen is the tertiary nitrogen, but this is secondary having NH function this has also NH function. So, after deprotonation the ligand can give rise to two negative charges. So, if we have a bivalent metal ion it can nicely bind to the bivalent metal ion giving a neutral metal ligand complex. So, one such important biological thing is that the basic skeleton is there. Further to the basic skeleton we can have also these groups attached as the corresponding substitutions on the pyrrole unit.

So, pyrrole units have some substitutions and regular substitutions like the methyl group and the other groups and some propionic acid group is also there and the deprotonation of these propionic acid groups also play some important role for oxygen transfer, because this particular unit is the basic unit for our blood which is our myoglobin unit or the hemoglobin unit where this iron centre is responsible for dioxygen coordination. So, the coordination chemistry plays an important and the vital role for oxygen binding and oxygen transfer in the living system in our body also. So, when iron is attached to this particular macrocyclic ring; that means the porphyrin ring, we call it as the heme group. So, that is why the name comes for hemoglobin also; heme plus globin unit give rise to the hemoglobin unit.

So, heme group consists of an iron ion held in a heterocyclic ring known as the porphyrin. So, this is our porphyrin ring. When porphyrin ring in plane go for binding to iron in the ferrous state; that means the iron two, it give rise to the heme group. So, there are also several other group which is also known as the heteromacrocyclic compound; hetero macro cyclic means this is forming from carbon, hydrogen and the hetero atom is the nitrogen. So, which is related to this particular porphyrin ring, but it is found in vitamin B 12. Its name reflects that it is the code of vitamin B 12 and the cobalamine molecule. So, when we have the vitamin B 12 molecule, another macro cyclic ring can go and function as a very good important biological ligand to bind the metal centre which is now instead of iron is now cobalt.

So, like that protein chain like that polypeptide chain we have these groups of ligands which are also biologically found. So, it is available in the living system. So, such thing is this which is little bit different from this one, but again some reduced pyrrole units are there and which is known as the corrin ring. This is different from that porphyrin ring and in this case we have a four such methylene unit, so this one, two, three, four carbons atoms are there, but here we do not have such linkage; it is a direct connection between these to reduce pyrrole unit. So, it basically gives a different type of environment or different type of cavity for metal coordination; that is why the cobalt centre which is present with this particular ring is of different type compared to that of iron centre.

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Iron, when taken up with the food and processed in the mouth (chewing, admixture of saliva) is mostly present in its ferric (Fe^{3+}) form and thus gets into the gastro-intestinal tract as Fe^{3+} . In case of an intact milieu in the small intestines, ferric iron is reduced to its ferrous form (Fe^{2+}).

Only in this oxidation state can iron be absorbed by the epithelium cells of the mucosa. For transfer to the blood serum, reoxidation to Fe^{3+} is necessary.



So, macrocyclic rings also play some important role for this biological coordination chemistry, then if we come for a particular metal centre like iron. So, iron we take up with the food material we chew it and we mix it with the saliva and when it is processed, we take some amount of free iron in our mouth and mostly it is present in the ferric form because iron cannot be present as the ferrous form because the saliva and during chewing it can be converted, it can be oxidized by the oxygen available in there to the ferric form and thus it enters into the gastrointestinal tract as ferric ion. So, whatever iron we consume as our food material, we consume it as the ferric ion and in the intact form it goes to the small intestine and ferric iron there is reduced to the ferrous form. So, once it can go for a reduced environment. So when the reduced environment is available, it can go for an electron transfer.


So if we present for this, how we incorporate this iron the ferrous iron into the p porphyrin ring for the synthesis of myoglobin and four such myoglobin units can bind to each other to give you the hemoglobin molecule. So, whatever iron we are consuming as Fe 3 plus in small intestine, it is reduced to Fe 2 plus and after reduction it is being carried to the porphyrin ring for the coordination. So, this reduction is important. So, some important groups of molecules are also available for this sort of reduction. So, in the ferric state it can be absorbed by the epithelium cells of the mucosa. So, when it is transferred in the bloods serum, it is required to reoxidize to ferric form wherever it is required; otherwise it is only present in the ferrous form.

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The oxidation $\text{Fe}^{2+} \rightarrow \text{Fe}^{3+}$ in the mucosa is catalysed by a copper enzyme (ceruloplasmin, containing seven copper centres: $\text{Cu}^+ \rightarrow \text{Cu}^{2+}$).

The Fe^{3+} ions are then taken up by apotransferrin (H_2Tf); simultaneously, carbonate is coordinated to iron. $\text{Fe}^{3+}\text{-Tf}$ is the transport form for iron.

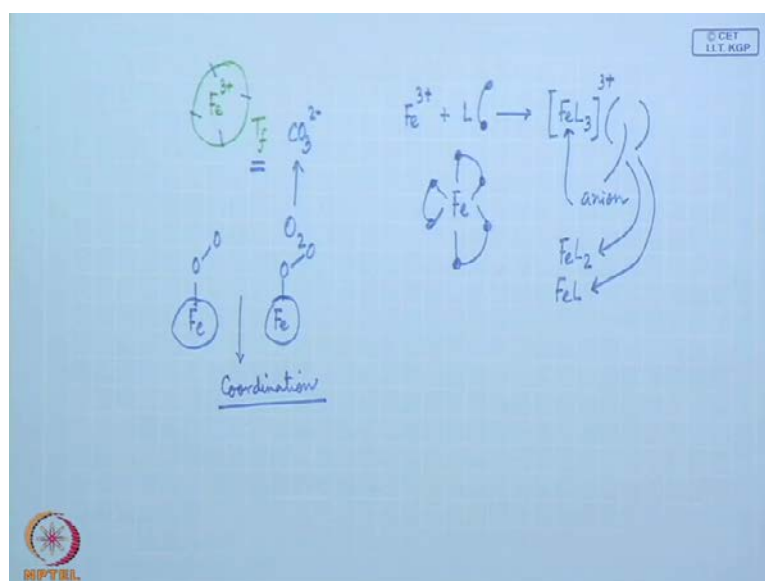
The iron-loaded **transferrin** delivers iron to sites of potential use (e.g. incorporation into protoporphyrin IX and generation of haemoglobin), or stored in iron storage proteins (**ferritins**).

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So, the oxidation of this; that means the ferrous to the ferric form in the mucosa in some cases is also catalyzed by the copper enzymes. So, for good assimilation of iron is not that with we have some deficiency in iron, we have some shortage of iron. We do not have much iron in our body; we do not take much iron in our food material through our food material, but the thing is that for right assimilation of this iron we need also copper. So, copper enzymes such as ceruloplasmin which is a cluster type of arrangement not a mononuclear system; it has seven copper centers present and such a cluster type of arrangement can give rise to a transfer of electron if each and every centre can give rise to one electron. So, all together it can give rise to seven electrons from the seven copper centers which is present in this ceruloplasmin molecule to convert the corresponding iron of that same number to the ferric form.

So, the redox between the redox chemistry involving this coordination chemistry because all this coppers are bound to the ligand system is important for the corresponding redox chemistry for the iron which is being stored and saved in our body for the synthesis of some right number of useful molecules. So, when these ferric ions are taken up by some groups of molecules which are known as apotransferrin. So, transferrin molecules are nothing but apotransferrin means without the metal centre. So, this is basically some part of the biological system some protein part of the biological system which are functioning as a good ligand or big macromolecular ligand system. So, the big macromolecular ligand system when it goes for iron binding, we find that apotransferrin after coordination of ferric ion give rise to the transfer in molecule but that binding is not so easy, because one carbonate anion is required for the coordination of iron to give us the corresponding ferric transferrin molecule in the transport system which is required for iron transport.

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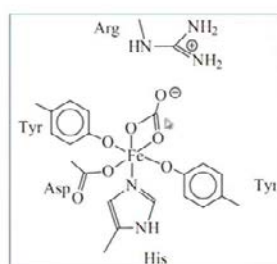


So, ferric transferrin Fe^{3+} is incorporated within the transferrin molecule and this transferrin molecule tells us that we can have this incorporation; that means we can have some donor points available for the carbonate ion such as that what we know that when we do some coordination chemistry of ferric ion with some ligand, we get something that we have FeL_3 type of complex but if the L is a neutral one; if L is not providing any charge to the system, so we have 3 plus charge. So, for charge balance we need some anions. So, anion is required for charge balance, but this particular anion is not going for

coordination to this iron centre because this iron centre is coordinatively saturated; it has octahedral coordination if L is a bidentate ligand like ethylenediamine or bipyridine. So, we can have the coordination of these six like this. So, what we get that if we have some vacancy; that means if we can form some $Fe L_2$ molecule or $Fe L$ molecule, then these anion can come and bind directly to the metal centre what is happening in case of this transferrin molecule with the use of CO_3^{2-} which we are producing in plenty after consumption of dioxygen molecule.

So, when dioxygen molecule is getting consumed is forming the carbonate anion we get the generation of right amount of carbonate anion and that carbonate anion is basically helping for trapping the iron by the apotransferrin molecule. So, the iron loaded transfer in delivers iron to the sides of potential use that where we use for it is synthesis such as hemoglobin, but if it is not utilized in a full form; that means the entire amount of iron what is available through iron loaded transfer in is not consumed for hemoglobin production; that means the right amount of protoporphyrin IX is not available for coordination, then the excess amount of iron will be stored in ferritin molecules and these are known as the corresponding storage protein for ferritin.

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The Fe^{3+} -carbonate-transferrin complex. Coordination of carbonate(2-) is supported by salt interaction with an arginine residue in the protein pocket.



So, what we see that the transfer what we get for that transferrin molecule is this that we have these four coordination donor atoms from aspartic acid, the tyrosine end and the other tyrosine end and the histidine groups from the polypeptide chain. So, the

polypeptide chain is providing four useful donor groups; three of them are oxygen and another is nitrogen. So, the biogenic ligand of apotransferrin has O₃N character. So, O₃N donor atoms from the apotransferrin can be utilized for the iron coordination or iron binding, but it can satisfy four coordination sites.

So, we need the binding of carbonate. So, whatever thing is happening there and this carbonate is also stabilized by some hydrogen bonding interactions or ion pair interaction from some arginine side end of this transfer in molecule and this charged end is stabilized through some ion pair interaction. But what we basically get here is that instead of iron in the ferric form we are basically putting the entire iron carbonate unit. So, basically a molecule which is iron carbonate is being stored inside the transferrin molecule. So, the iron carbonate transferrin complex is this which has coordination of carbonate which is supported by salt interaction or ion pair interaction or hydrogen bond interaction with the arginine residue in the protein pocket. So, protein pocket has this particular side chain in this particular direction and in that direction only carbonate can go and approach our iron site.

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Ferritins are iron storage proteins, built up of a hollow protein sphere (apo-ferritin, M = 450 kDa, 24 subunits of 163 amino acids each) with an outer diameter of 130 and an inner diameter of 70 Å. The inner surface of this capsule is lined with carboxylate functions, which can coordinate Fe³⁺. Up to 4500 Fe³⁺ can be taken up.

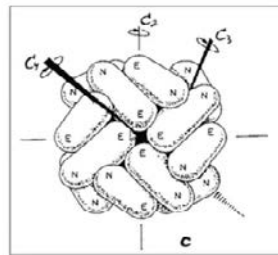
The various iron centres are connected by bridging oxido and hydroxido groups very much as in the colloidal form of ferric hydroxide or the mineral goethite. The overall composition of the iron nucleus is 8FeO(OH)·FeO(H₂PO₄).



So, this basically gives rise to the development of the storage proteins, the storage molecules; the ferritins are the storage molecules where we have the iron storage and which is a very hollow protein types of structure and the protein sphere is forming with the apoferritin molecule and with an outer diameter of 130 to 70 Å and it can go

for coordination of ferric ion and up to large number of ferric ion; that means 4500 ferric ion can be taken up by this ferritin molecule. So, the various iron centers are connected by bridging oxido and hydroxido groups. So, whatever iron is stored this molecular formula this can be $8 \text{ FeO OH FeO H}_2 \text{ PO}_4$. So, from the outer surface we can have from the lipid layer the phosphate units, but otherwise the basic structure is basically a bio-mineralization process where iron is getting stored by oxohydroxido core formation. So, oxo and hydroxido groups are important for the generation of the colloidal ferric hydroxide similar to that of mineral goethite and the overall composition is given by this particular formula.

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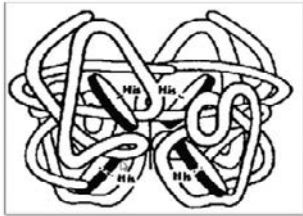


Subunit structure and channels of C₂, C₃ (for iron exchange with the surroundings) and C₄ symmetry




So, what we get there that this ferritin molecule is basically giving rise to the corresponding this type of largest type of thing where we have 24 sub units; this protein subunits are there and inside this we have the corresponding mineral code and that mineral code is there and we have the subunit structure and channels of C₂ and C₃ symmetry and for iron exchange with the surrounding. So, channels of C₂ and C₃ symmetry these two symmetric points the C₂ point and C₃ points are the utilized for iron binding and the C₄ symmetry is for iron removal from the system. So, we get the corresponding iron exchange, because some of these channels are available for iron incorporation and one channel is responsible for iron removal from the system; that means one particular channel is hydrophilic in nature and the other channel is hydrophobic in nature.

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Schematic view of haemoglobin (a tetramer, mainly $\alpha_2\beta_2$ in adults; there is one haeme group per subunit).

In the pulmonary alveoli, O_2 is taken up by haemoglobin (Hb, $M = 65$ kDa; Fig. 5); at saturation, 1 L of blood can dissolve ca. 200 ml of oxygen.



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So, this particular case give rise to the development of the generation of the hemoglobin molecule what we have seen that the corresponding hemoglobin molecule which is basically a tetramer of four such units and the histidine groups from the glowing part is connected to the iron centers. So, this is one iron centre, this is another iron centre, this is third and this is the fourth iron centre for the hemoglobin molecule. So, this is the view of the hemoglobin molecule and where we have a tetrameric structure of $\alpha_2\beta_2$. So, basically a quaternary structure quaternary protein structure and one heme group per subunit. So, this is one heme group, this is another heme group, this is the third and this is the fourth one. So when we consume this in our pulmonary alveoli, O_2 is taken up by the hemoglobin. So, this is when O_2 is not there; this is the form where we have the deoxyhemoglobin form and when we have the saturation and one liter of blood can dissolve up to 200 ML of oxygen.

So, huge amount of iron can be stored and in all these cases, this is the thing that if you have all individual groups and we basically go for this O_2 coordination and one liter of blood can store 200 ML of this oxygen and all are due to the typical metal ion coordination. So, the coordination chemistry is basically an important and vital role for this iron storage as well as iron for the coordination of the dioxygen molecules. So, we have this. So, when all these four are forming this particular dioxygen molecule attached to this individual iron centre, we have the corresponding oxyhemoglobin form and that

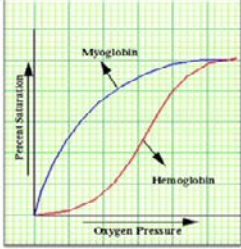
oxyhemoglobin from can transfer the dioxygen molecule to other molecule for the food burning.

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After transport of O₂ by haemoglobin in the blood stream, the oxygen is transferred to tissue myoglobin (Mb). As shown in Figure, Mb has a higher affinity to O₂ than Hb.

In the deoxy form of Hb, Fe²⁺ is in its high-spin state and thus exhibits a paramagnetism corresponding to four unpaired electrons.

The diameter of high-spin Fe²⁺ is 92 pm; the Fe²⁺ ion thus is too large to fit into the space left by the four N-functions of the protoporphyrin.



The sigmoidal shape of hemoglobin's oxygen-dissociation curve results from cooperative binding of oxygen to hemoglobin.



So, this transport of oxygen by hemoglobin can go for the blood stream and we have the right amount of this dioxygen molecule and that dioxygen molecule is stored in the myoglobin. And this storing process is basically given by the equilibrium between the deoxy form of the hemoglobin and the deoxy form of the myoglobin and Fe²⁺ in this deoxy form is in high-spin state and in showing paramagnetism and it corresponds to four unpaired electrons and its diameter is 92 picometer and Fe²⁺ thus is too large to fit in the pocket of the protoporphyrin which is a planar macrocyclic ring and above which your Fe²⁺ is sitting. And that Fe²⁺ when binds to the dioxygen, we can have two different types of oxygenation curves. One is for the hemoglobin which is basically a shift and we call it as a sigmoidal curve and another is of corresponding different type which is different from that of the sigmoidal curve and due to this thing we know that they have the corresponding difference in oxygenation reaction.

So, whatever oxygen is stored in this hemoglobin is transferred to the myoglobin because hemoglobin has some different affinity which can be oxygenated easily at low partial pressure compared to the myoglobin molecule; that is why we go for transfer of oxygen molecules from hemoglobin to myoglobin. So, the sigmoidal shape of the hemoglobin is therefore giving rise to the corresponding oxygen dissociation curve and that basically


giving us the corresponding cooperative binding of the dioxygen molecule by the hemoglobin.

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Actually, Fe^{2+} is displaced from the plane spanned by the porphyrin by 40 pm towards the proximal His; cf. Fig. 6; resulting in a watch glass bulge of the porphyrin, i.e. a tensed situation.

Consequently, deoxy-Hb is termed T (for tensed) form. On uptake of oxygen, the iron spin state converts to low-spin, resulting in a reduction of its diameter to 75 pm (Fe^{2+} , no unpaired electrons) or 69 pm (Fe^{3+} , 1 unpaired electron), respectively.

The iron ion now moves into the plane of the porphyrin (R form; R = relaxed).



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So, this basically give us something that iron 2 plus is displaced from the plane which is spanned by the porphyrin ring and is going towards the corresponding ball shaped of the porphyrin for oxygen coordination and is in the tensed form. As a result the deoxyhemoglobin is termed as T form and on uptake of oxygen iron spin converts to the low-spin and the reduction of its diameter is from 75 picometer to 69 picometer and having no unpaired electron with unpaired electron respectively for this transfer. And this basically gives rise to the thing that due to this transfer, iron is basically moved from the plane of the porphyrin, so the tensed form is converted to the relaxed form and these two forms are very much important for the transfer of oxygen to our cell system for the food burning.

Thank you very much.