

Bio Inorganic Chemistry

Chapter 31

Outline

- 1. Very important terms of coordination chemistry
- 2. General aspects of bioinorganic chemistry
- 3. Coordination for uptake, transport and storage (Fe)
- 4. Hard ions: Na^+ , K^+ , Mg^{2+} , Ca^{2+} 5. Cobalamines
- 6. Metals in Photosynthesis
- 7. Fe in bio systems
- 8. Function of Zn
- 9. Fixation of nitrogen

Coordination compound (complex)complex)--basics

- Central atom is bound to unexpectedly large number of ligands•
- Usually discrete species in solution and solid•
- Examples: $K_4[Fe(CN)_6]$, $CoCl_2 \cdot 6 H_2O$ •

Coordination compound (complex)complex)--basics

- Properties of central atoms (transition metals):•
- Large charge/radius ratio•
- Variable oxidation states (d-electrons available)
- Meta stable high oxidation states, s-electrons are removed first

Coordination compound (complex)complex)--basics

- Compounds are often paramagnetic (unpaired electrons)
- Formation of colored ions and compounds
- Compounds with profound catalytic activity
- Formation of stable complexes (Lewis acids)
- Trend to metal-metal bonding (clusters, not important in biology)

Coordination compound (complex)complex)--basics

- Properties of ligands
- Monodentate or
- poly dentate ligand•
- Ambi dentate ligands (nitro-, nitrito)

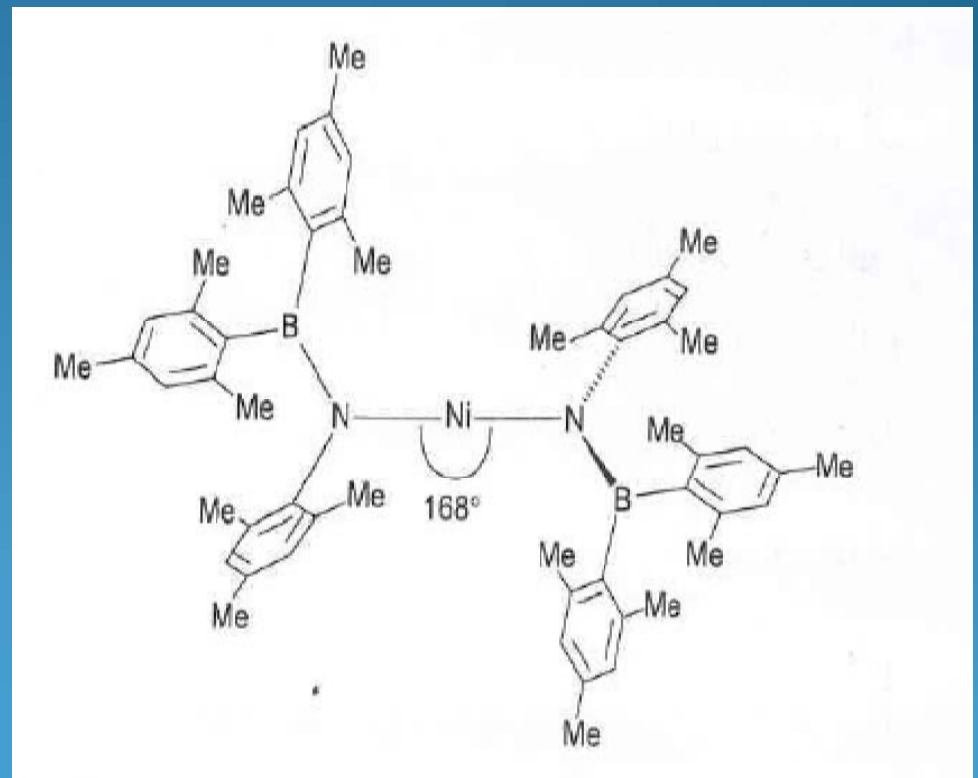
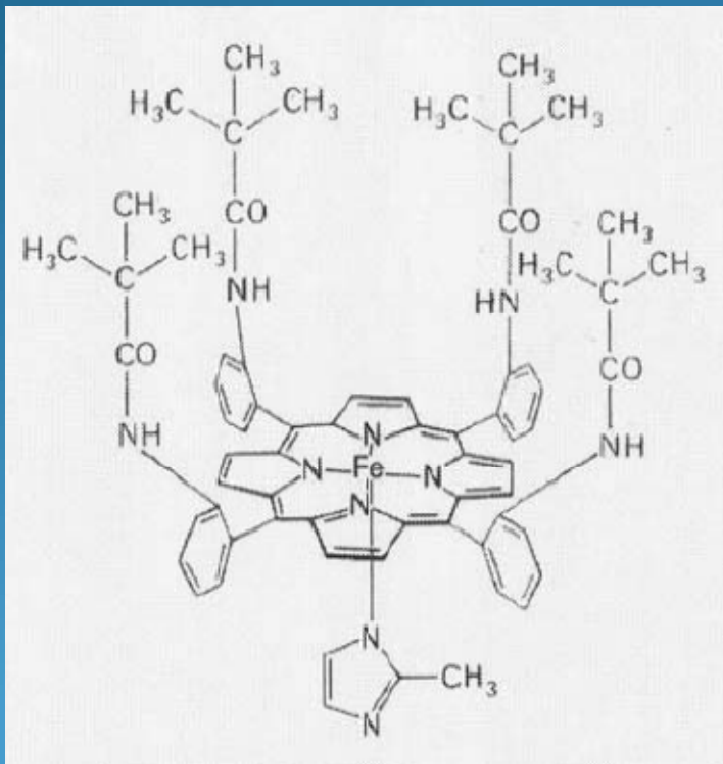
Coordination number

Coordination number--examples

- Higher CN's are favoured:
- Complexes containing central atoms of the periods 5 and 6, small ligands (size)
- Single bonds metal-ligand (see MnO_4^- ...)
- On the left of a row of the d-block (size and small number of d-electrons)
- Central atoms with a high oxidation number (size and small number of d-electrons)

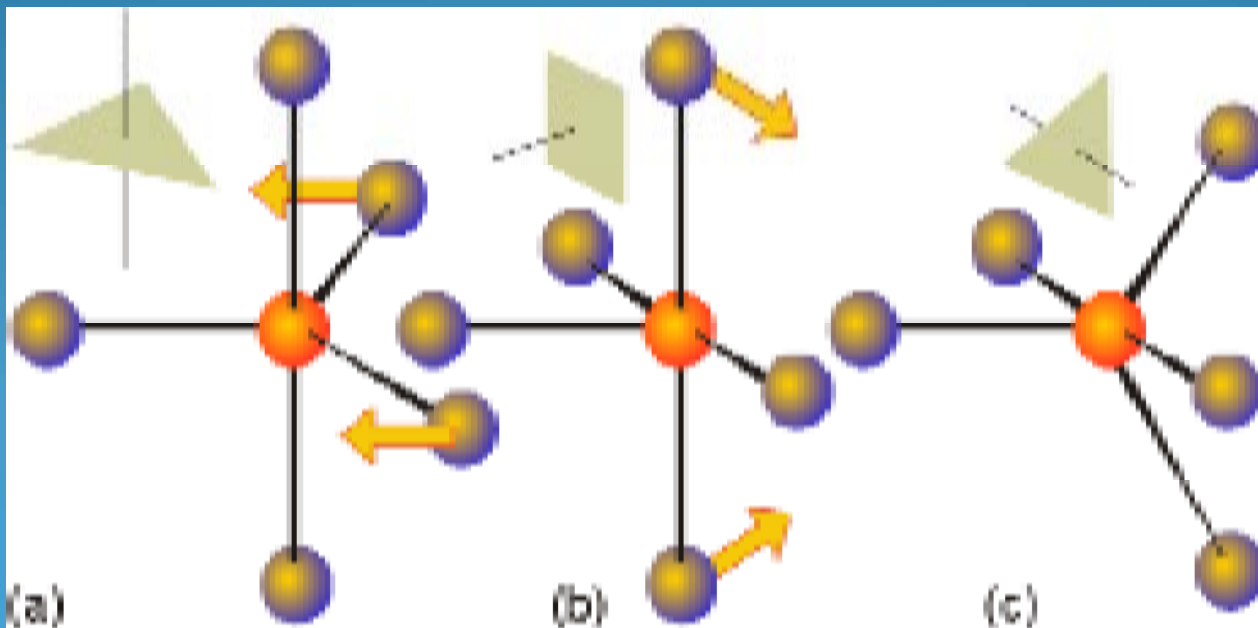
- CN 2: linear (Cu^+ , Ag^+ , Au^+ , Hg^+)
- CN 3: trigonal planar (HgI_3^- , $[\text{Pt}(\text{P}\{\text{C}_6\text{H}_5\}_3)_3]$)
trigonal pyramid
- CN 4: tetrahedron ($[\text{Al}(\text{OH})_4]^-$, $[\text{Cd}(\text{CN})_4]^{2-}$)
square planar (d8, $[\text{PtCl}_4]^{2-}$, $[\text{AuF}_4]^-$)
bisphenoidal (ψ -trigonal bipyramid, $[\text{AsF}_4]^-$,
 $[\text{SbCl}_4]^-$)
- tetragonal pyramid (ψ -octahedron)
- CN 5: trigonal bipyramid ($\text{Fe}(\text{CO})_5$, $[\text{SnCl}_5]^-$)
 - tetragonal pyramid

Coordination Number-examples



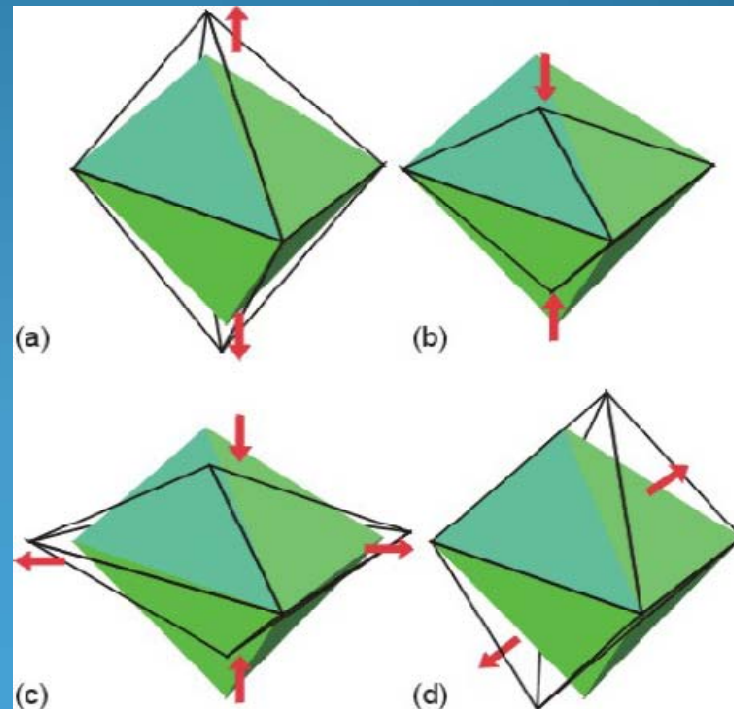
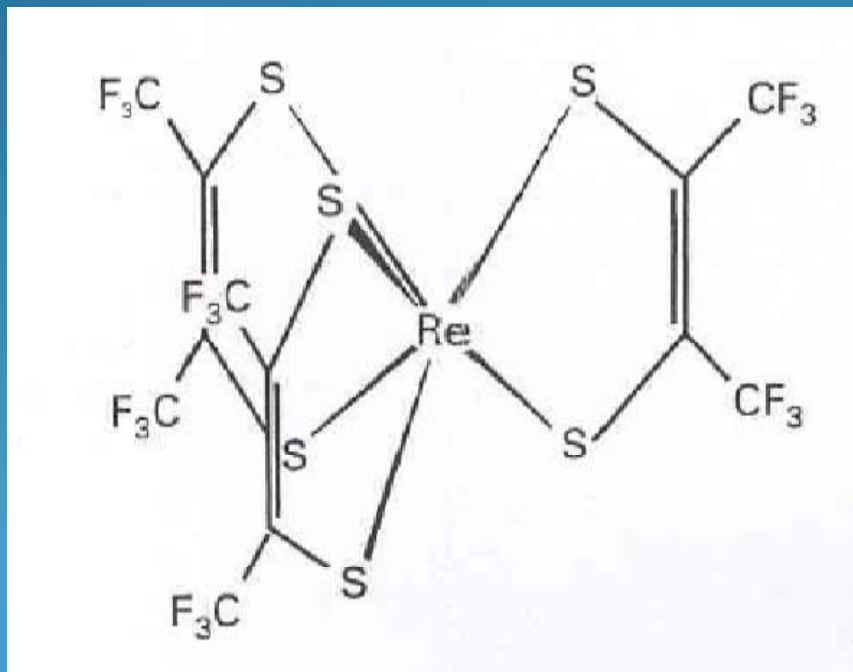
Coordination number-examples

- Pseudorotation
- Exchange of a- and e-ligand, see MgATpase
- $[\text{Ni}(\text{CN})_5]^{3-}$: b) and a) in crystal structure
- $\text{Fe}(\text{CO})_5$: fast pseudorotation in solution



Coordination number-examples

- CN 6:
- octahedron ($[\text{Cr}(\text{H}_2\text{O})_6]^{3+}$, $[\text{Fe}(\text{CN})_6]^{3-}$)
- distorted octahedron
- Trigonal prism

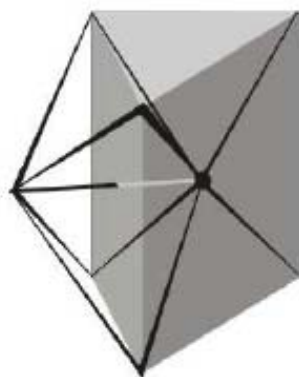
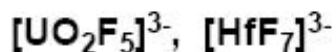


Coordination number-examples

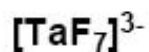
• CN 7:



pentagonal bipyramid



monocapped trigonal prism

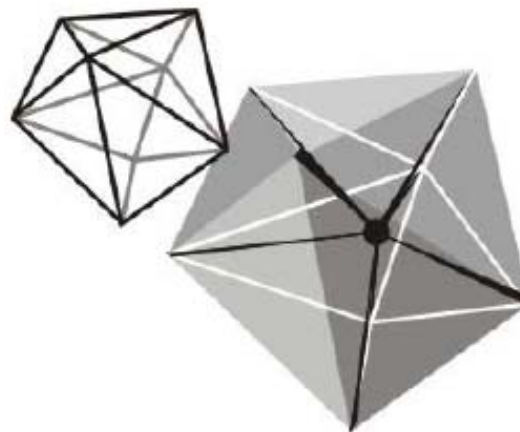
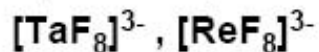


monocapped octahedron

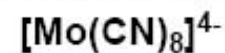


• CN 8: cube ($[\text{UF}_8]^{3-}$)

square antiprism



dodecahedron



Isomerism

- Two or more molecules or ions have the same molecular formula but the atoms are arranged differently
- The structures of isomers are not super imposable
- Isomers have different physical (color) and/or chemical properties.

Isomerism

- Stereoisomerism
- Optical isomerism:
- Enantiomers
- Geometrical isomerism:
- cis-, trans; meridional, facial
- Structural isomerism
- Ionization isomerism ($[\text{CoCl}(\text{NH}_3)_5]\text{SO}_4$ / $[\text{CoSO}_4(\text{NH}_3)_5]\text{Cl}$)
- Coordination isomerism ($[\text{Co}(\text{NH}_3)_6]$ $[\text{Cr}(\text{CN})_6]$ / $[\text{Cr}(\text{NH}_3)_6]$ $[\text{Co}(\text{CN})_6]$)
- Linkage isomerism (cyano/ isocyano)

Periodic table of life

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	Ac															

Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Metals

Essential elements for humans (daily requirement: 25 mg)

Non metals

Presumably essential elements

Symptoms of deficiency:

Mg (muscle cramps), Fe (anemia), Mn (infertility)

• Toxic effects in case of high doses (therapeutic width)

• Occurrence of non essential elements (e.g. Rb: 1.1 g / 70 kg) and of contaminations (e.g. Hg)

Functions of “inorganic elements”

- Assembly of structures (DNA, biomineralization), endo-and exoskeletons. **Ca, Mg, Zn, Si**
- Information carriers (muscle contractions, nerve function). **Na, K, Ca, Mg**
- Activation of enzymes. **Mg, Ca**
- Formation, metabolism and degradation of organic compounds by Lewis acid/base catalysis. **Zn, Mg**
- Transfer of electrons (energy conversion), **FeII/FeIII/FeIV**, stable due to bioligands
- Uptake, transport, storage and conversion of small molecules
- O₂: **Fe, Cu** (conversion), **Mn** (generation)
- N₂: **Fe, Mo, V** (conversion to ammonia)
- CO₂: **Ni, Fe** (reduction to methane)

Most prominent “bioelements”

- Na^+, K^+ : Electrolytes
- Mg^{2+} : Chlorophyll, energy production (ATP \rightarrow ADP), skeleton
- Ca^{2+} : muscle functions, Hydroxylapatite $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$, CaCO_3
- $\text{V}^{\text{IV/V}}$, $\text{Mo}^{\text{IV/VI}}$, $\text{W}^{\text{IV/VI}}$, $\text{Mn}^{\text{II/III/IV}}$, $\text{Fe}^{\text{II/III}}$, $\text{Ni}^{\text{I/II/III}}$, $\text{Cu}^{\text{I/II}}$: electron transfer
- Fe and Cu: transport and storage of oxygen
- Fe^{II} , Fe^{III} : Magnetite (Fe_3O_4)

Role of the metallic elements

- The metallic elements play a variety of roles in biochemistry. Several of the most important roles are the following:
 1. *Regulatory action is exercised by Na^+ , K^+ , Mg^{2+} , and Ca^{2+} . The flux of these ions through cell membranes and other boundary layers sends signals that turn metabolic reactions on and off.*
 2. *The structural role of calcium in bones and teeth is well known, but many proteins owe their structural integrity to the presence of metal ions that tie together and make rigid certain portions of these large molecules, portions that would otherwise be only loosely linked. Metal ions particularly known to do this are Ca^{2+} and Zn^{2+} .*
 3. *An enormous amount of electron-transfer chemistry goes on in biological systems, and nearly all of it critically depends on metal-containing electron-transfer agents. These include cytochromes (Fe), ferredoxins (Fe), and a number of copper-containing "blue proteins," such as azurin, plastocyanin, and stellacyanin.*

Most prominent “bioelements”

- **Co:** Cobalamine, e.g. Vitamin-B₁₂
- **Zn²⁺:** Enzymes, zincfinger(gen. transcription), stabilization of proteins
- **Si^{IV}:** bones; SiO₂/silicagel
- **P^V:** Hydroxylapatite, ATP, cell membrane, DNA
- **Se-^{II}:** Selenocysteine
- **F⁻:** Fluorapatit(Ca₅(PO₄)₃F) teeth; **Cl⁻:** besides HCO₃⁻-most important free anion, **I⁻:** hormones of the thyroid, radiation therapy

Terms related to bioinorganic chemistry

- Active center: Location in an enzyme where the specific reaction takes place
- Allosteric enzyme:
- Can bind a small regulatory molecule that influences catalytic activity
- Apo-enzyme:
- An enzyme that lacks its metal center or prosthetic groups
- •ATP: Adenosine 5'-triphosphate•
- Biomembrane: Sheet like assemblies of proteins and lipids (bilayer)
- Calmodulin: Ca binding protein involved in metabolic regulation
- Carbonic anhydrase: Zn-containing enzyme that catalyzes the reversible decomposition of carbonic acid to carbon dioxide and water
- Charge-transfer complex: An aggregate of two or more molecules in which charge is transferred from a donor to an acceptor.
- Chlorin: 2,3-Dihydroporphyrin, reduced porphyrin with two non-fused saturated carbon atoms (C-2, C-3) in one of the pyrrole rings.
- Chlorophyll: Magnesium complex of a porphyrin in which a double bond in one of the pyrrole rings (17-18) has been reduced. A fused cyclopentanone ring is also present

- **Cluster**: Metal centers grouped close together which can have direct metal bonding or through a bridging ligand, e.g. ferredoxin
- **Cobalamin**: Vitamin B₁₂, substituted corrin-Co(III) complex
- **Coenzyme**: A low-molecular-weight, non-protein organic compound (often a nucleotide) participating in enzymatic reactions
- **Cofactor**: An organic molecule or ion (usually a metal ion) that is required by an enzyme for its activity. It may be attached either loosely (coenzyme) or tightly (prosthetic group).
- **Cooperativity**: The phenomenon that binding of an effector molecule to a biological system either enhances or diminishes the binding of successive molecules, e.g. hemoglobin
- **Corrin**: Ring-contracted porphyrinderivative that is missing a carbon
- **Cytochrome**: Hemeprotein that transfers electrons, and exhibits intense absorption bands. The iron undergoes oxidation-reduction between oxidation states Fe(II) and Fe(III).
- **Cytochrome C-oxidase**: The major respiratory protein of animal and plant mitochondria. It catalyzes the oxidation of Fe(II)-cytochromec, and the reduction of dioxygen to water. Contains two hemes and three copper atoms, arranged in three centers.

- **Cytochrome P-450**: General term for a group of heme-containing monooxygenases. The reaction with dioxygen appears to involve higher oxidation states of iron, such as Fe(IV)=O .
- **Desferrioxamine (dfo)**: Chelating agent used world-wide in the treatment of iron overload conditions, such as hemochromatosis and thalassemia.
- **Dismutase**: Enzyme that catalyzes a disproportionation reaction.
- **Entatic state**: A state of an atom or group which has its geometric or electronic condition adapted for function. Derived from entasis (Greek) meaning tension.
- **Enzyme**: A macromolecule that functions as a biocatalyst by increasing the reaction rate.
- **FeMo-cofactor**: An inorganic cluster found in the FeMo protein of the molybdenum-nitrogenase, essential for the catalytic reduction of N_2 to ammonia.
- **Ferredoxin**: A protein containing more than one iron and acid-labile sulfur, that displays electron-transfer activity but not classical enzyme function.
- **Ferritin**: An iron storage protein consisting of a shell of 24 protein subunits, encapsulating up to 4500 iron atoms in the form of a hydrated iron(III) oxide.

- **Heme**: A near-planar coordination complex obtained from iron and dianionic porphyrin•
- **Hemerythrin**: A dioxygen-carrying protein from marine invertebrates, containing an oxo-bridged dinuclear iron center•
- **Hemocyanin**: A dioxygen-carrying protein (from invertebrates, e.g. arthropods and molluscs), containing dinuclear type 3 copper sites•
- **Hemoglobin**: A dioxygen-carrying heme protein of red blood cells
- **HiPIP**: High-Potential Iron-sulfur Protein (ferredoxin). Cluster which undergoes oxidation-reduction between the $[4Fe-4S]^{2+}$ and $[4Fe-4S]^{3+}$ states
- **Holoenzyme**: An enzyme containing its characteristic prosthetic group(s) and/or metal(s)•
- **Ion channel**: Enable ions to flow rapidly through membranes in a thermodynamically downhill direction after an electrical or chemical impulse. Their structures usually consist of 4-6 membrane-spanning domains. This number determines the size of the pore and thus the size of the ion to be transported
- **Ionophore**: A compound which can carry specific ions through membranes
- **Ion pumps**: Enable ions to flow through membranes in a thermodynamically uphill direction by the use of an energy source. They open and close upon the binding and subsequent hydrolysis of ATP, usually transporting more than one ion towards the outside or the inside of the membrane

Terms related to bioinorganic chemistry

- **Metalloenzyme**: An enzyme that, in the active state, contains one or more metal ions
- **Mitochondria**: Cytoplasmic organelles, produce ATP by oxidative phosphorylation
- **Myoglobin**: A monomeric dioxygen-binding heme protein of muscle tissue, structurally similar to a subunit of hemoglobin
- **Photosynthesis**: A metabolic process in plants and certain bacteria, using light energy absorbed by chlorophyll and other photosynthetic pigments for the reduction of CO₂, followed by the formation of organic compounds

Terms related to bioinorganic chemistry

- **Plastocyanin**: An electron transfer protein, containing a type 1 copper site, involved in plant and cyanobacterial photosynthesis, which transfers electrons to Photosystem 1•
- **Iron Sulfur protein**: An iron-sulfur protein of the mitochondrial respiratory chain, containing a [2Fe-2S] cluster•
- **Rubredoxin**: A single iron-sulfur protein, function as an electron carrier•
- **SOD**: superoxide dismutase, catalysis of disproportionation of superoxide
- **Substrates**: A compound that is transformed under the influence of a catalyst
- **Trace elements**: Elements required for physiological functions in very small amounts, e.g. Co, Cu, F, Fe, I, Mn, Mo, Ni, Se, V, W, and Zn

Terms related to bioinorganic chemistry

- **Type 1,2,3 copper**: Different classes of copper-binding sites in proteins, classified by their spectroscopic properties as Cu(II). Type 1, or blue copper centers the copper is coordinated to at least two imidazole nitrogens from His and one sulfur from Cys. In type 2, or non-blue copper sites, the copper is mainly bound to imidazole nitrogens from His. Type 3 copper centers comprise two spin-coupled copper ions, bound to imidazolenitrogens
- **Zinc finger**: A domain, found in certain DNA-binding proteins, comprising a helix-loop structure in which a zinc ion is coordinated to 2 -4 Cysulfurs, the remaining ligands being His

Principle of complementarity

- The active sites of enzymes tend to be more complementary to the transition states than they are to the actual substrates
- Preformation of the transition state by strained enzyme (entactic state)
- Energy aspect: small activation energy,
- statistical aspect: more productive encounters between reaction partners,
- Kinetic aspect: faster reaction

Cyclic ligands—Porphyrin complexes

- Unsaturated tetradentate macrocyclic ligands
- Coordination of otherwise labile divalent metal ions
- Porphyrin complexes: chelate-effect and size selective as host
- Porphyrin: very stable, Hückel-aromatic ($18 \text{ e}^- = 4n + 2$), colored



Porphyrin

Hemoglobin
Myoglobin
Peroxidases } Fe



Chlorin

Chlorophyll (Mg^{2+})
Tunichlorine (Ni^{2+})



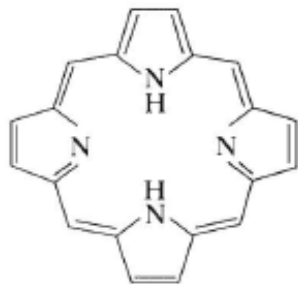
Corrin

Cobalamin (Co^{2+})

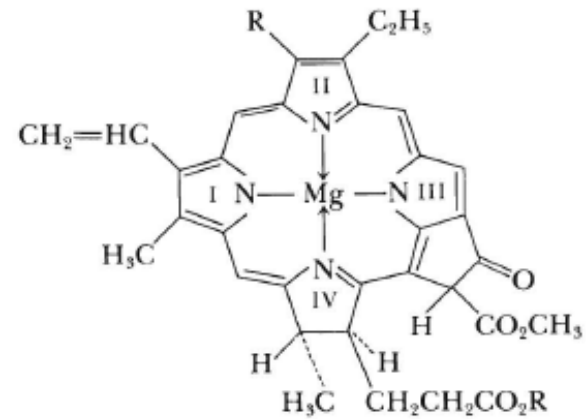


Metallaporphyrin
complex

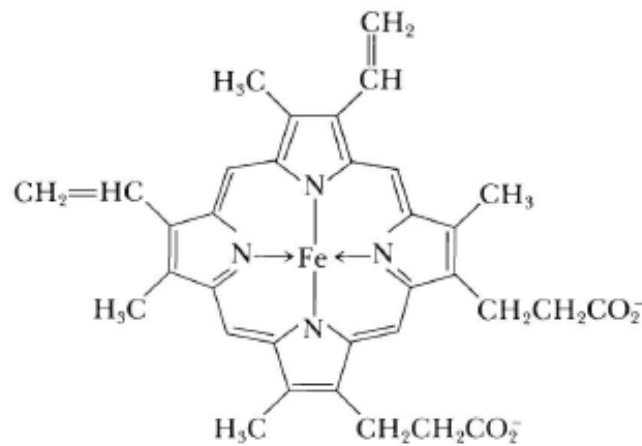
Porphyrins



(a)

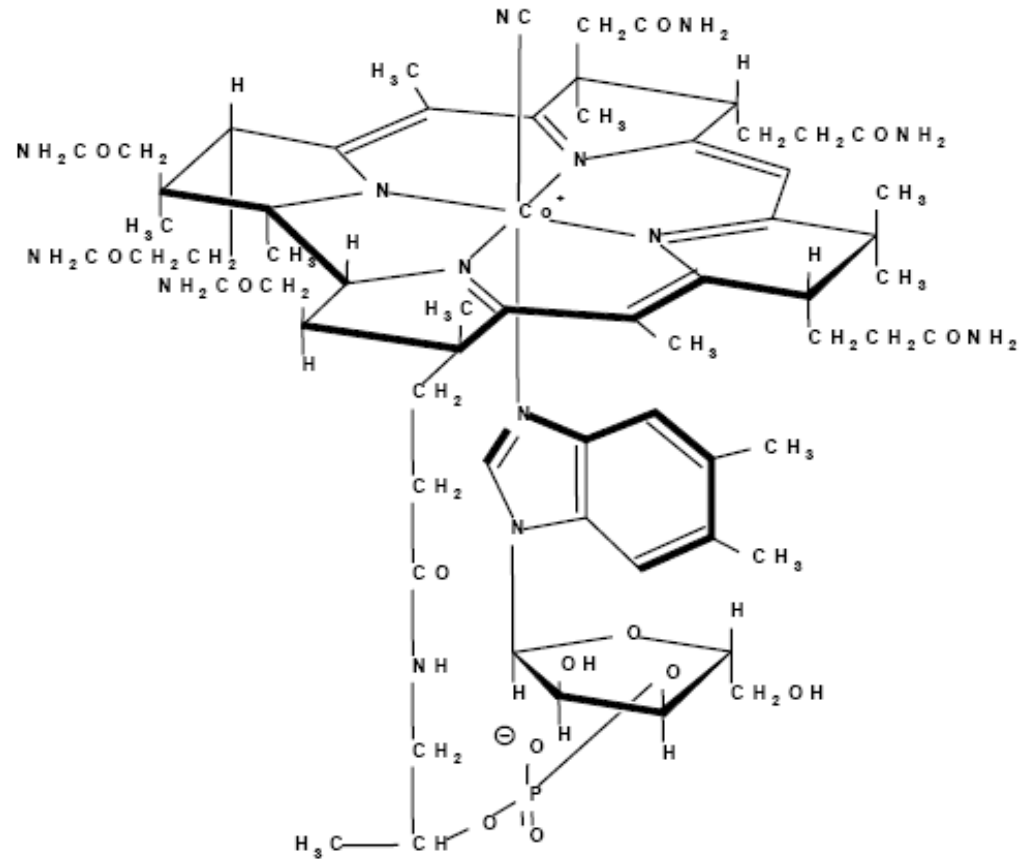
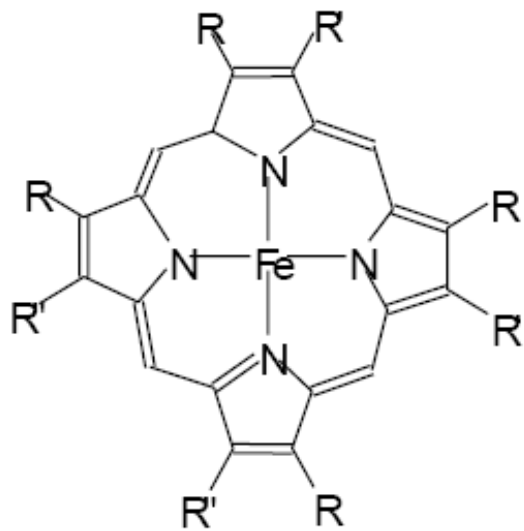


(b)



(c)

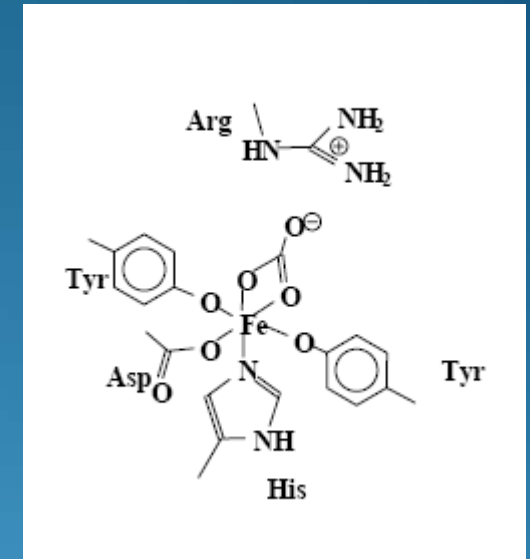
Cyclic ligands—Porphyrin complexes



Vitamine B₁₂

Fe in proteins

- Transport: Transferrin
- Coordination of Fe by carboxy- and phenolate groups of residues
- Uptake of two Fe(III) and one HCO_3^-
- Stability of complexes decrease with decreasing pH
- High affinity of Apotransferrin, protection against infections
- Not very specific (Cr^{3+} , Al^{3+} , Cu^{2+} , Mn^{2+} ...)
- Release of Fe(III): Reduction to Fe(II) and binding by porphyrine

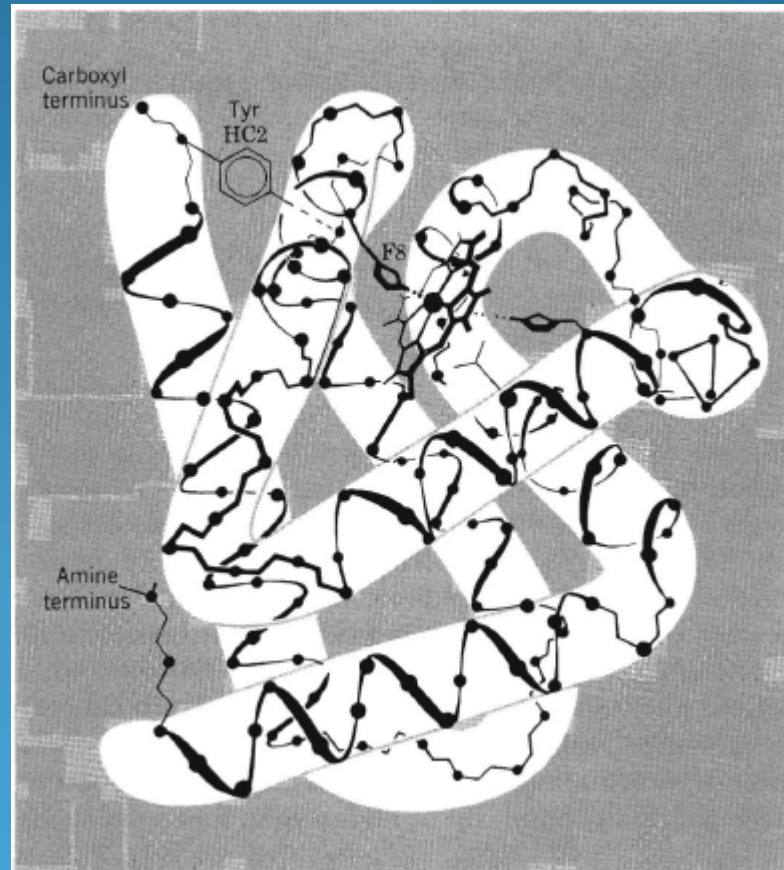


Fe in proteins

- Storage: Ferritin
- High symmetry of Apoferritin: F_{432}
- *Hollow sphere built from proteins (inner dia.: ~ 7 nm, outer dia. ~ 13 nm)*
- *Capacity: up to 4500 Fe^{3+} , biomineralization(?)*
- *Carboxylate groups for Fe(III) binding, core-structure related to Ferrihydrite $Fe_{10}O_6(OH)_{18}$*
- *Exchange via channels (dia. 1nm), tuning of hydrophilic/hydrophobic character via residues*
- *Release of Fe as Fe(II) via hydrophilic channels*

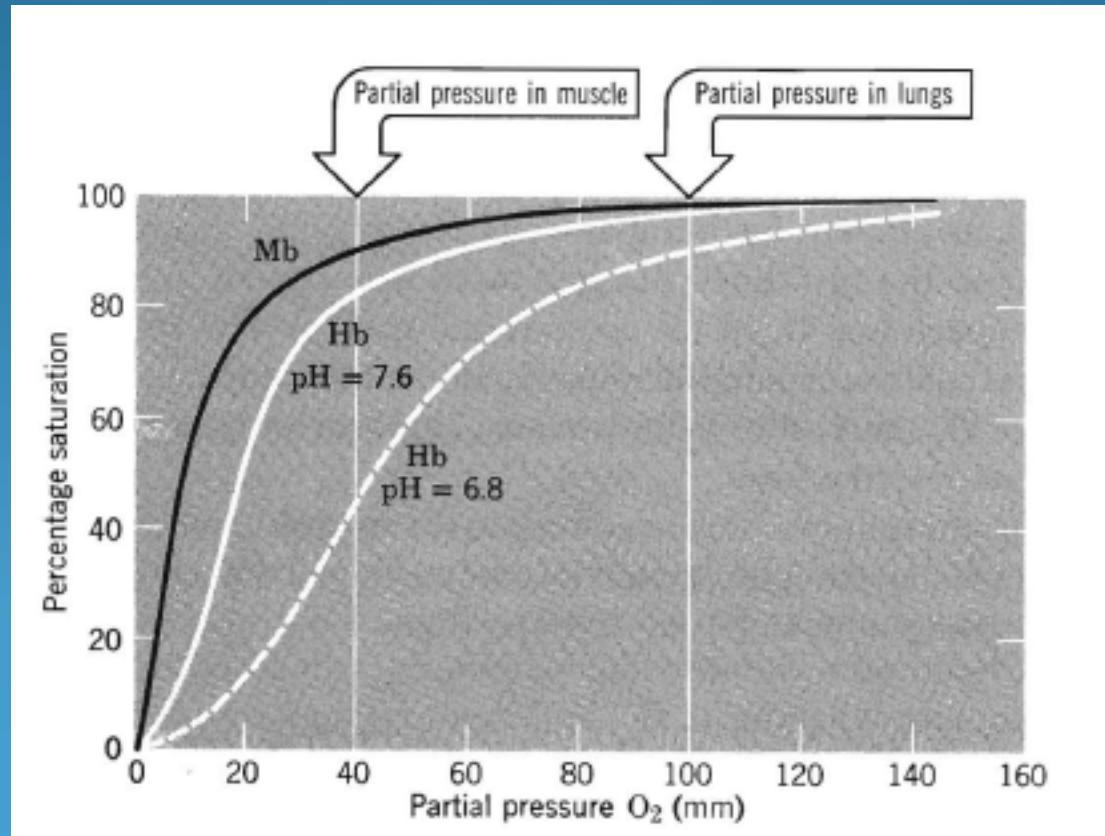
Fe in proteins

- Hemoglobin

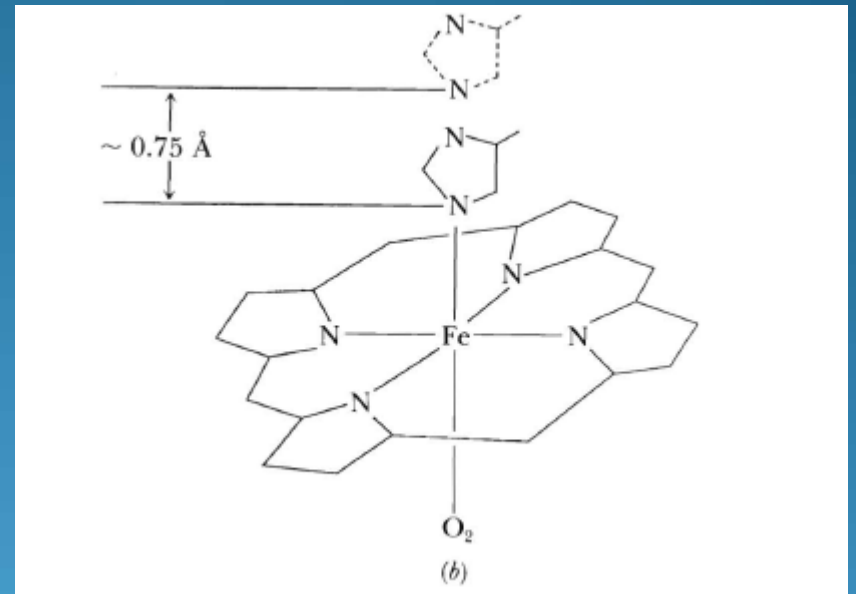
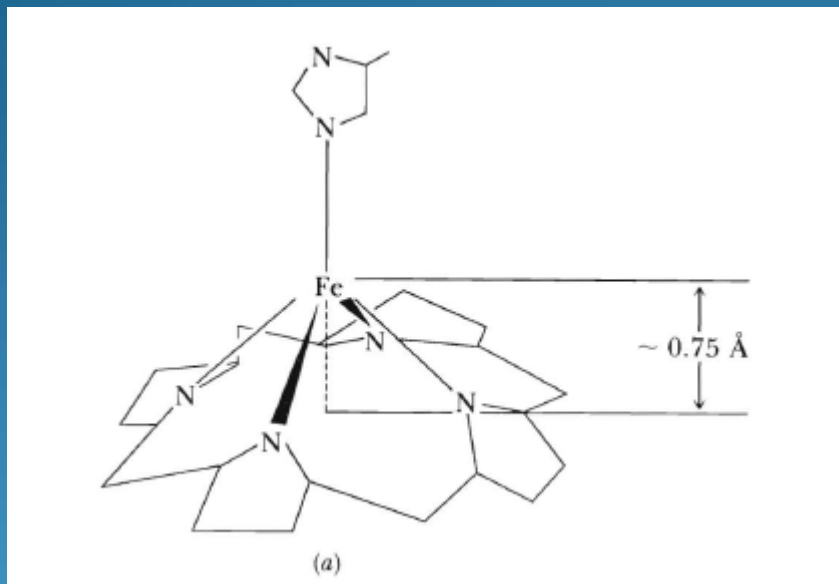


Hemoglobin - Myoglobin

- Bohr effect



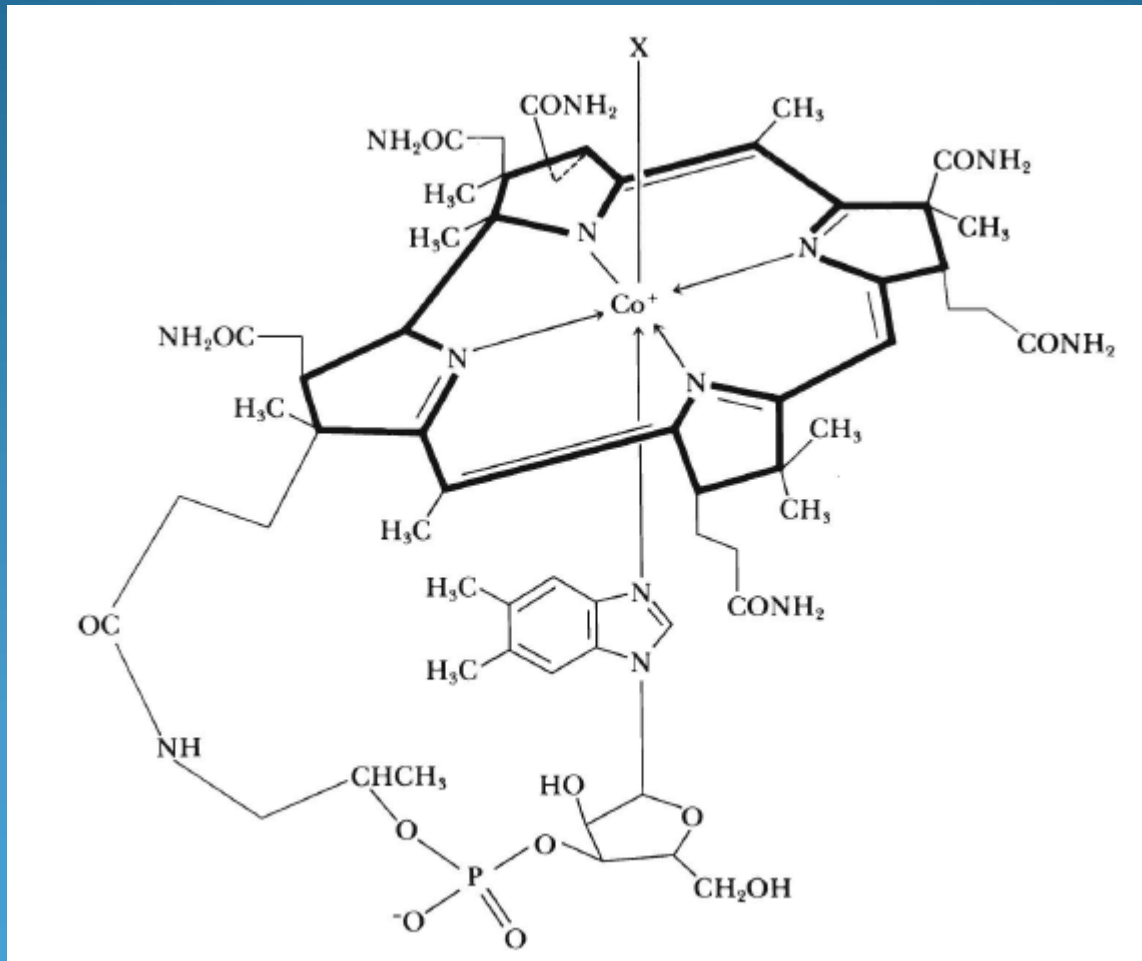
Bohr Effect



The Bioinorganic chemistry of Cobalt

- The best-known biological function of cobalt is its intimate involvement in the coenzymes related to vitamin B₁₂
- It consists of four principal components:
 1. A cobalt atom.
 2. A macrocyclic ligand called the *corrin ring*, which bears various substituents. *The essential corrin ring system is shown in bold lines. It resembles the porphine ring, but differs in various ways, notably in the absence of one methine (=CH-) bridge between a pair of pyrrole rings.*
 3. A complex organic portion consisting of a phosphate group, a sugar, and an organic base, the latter being coordinated to the cobalt atom.
 4. A sixth ligand may be coordinated to the cobalt atom. This ligand can be varied, and when the cobalt atom is reduced to the oxidation state +1, it is evidently absent.

Structure of Cobalamin



Cobalamine

- The cobalamins can be reduced in neutral or alkaline solution to give cobalt(II) and cobalt(I) species, often called B_{12r} and B_{12s} respectively.
- powerful reducing agent
- decomposing water to give hydrogen and B_{12r}
- reductions can apparently be carried out *in vivo* by *reduced ferredoxin*.
- cyano- or hydroxocobalamin is reduced, the ligand (CN- or OH-) is lost, and the resulting five-coordinate cobalt(I) species reacts with ATP in the presence of a suitable enzyme to generate the B₁₂ coenzyme.

Nitrogen fixation

- *Nitrogenases*
- *Consist of 2 proteins*
 - *A Fe protein*
 - *A MoFe protein*
- *Each of them is inactive*
- *Mixing them makes them active*
- The Fe-protein consists of two identical subunits that clasp a ferredoxin unit (Fe_4S_4) between them by forming Fe-S bonds to two cysteine residues in each subunit.

Nitrogen fixation

- The MoFe-protein, so-called because it contains both molybdenum and iron.
- X-ray crystallographic study revealed a metal cluster arrangement
- The structure is still somewhat inaccurate and one of the bridging groups (Y) has not yet been conclusively identified.

