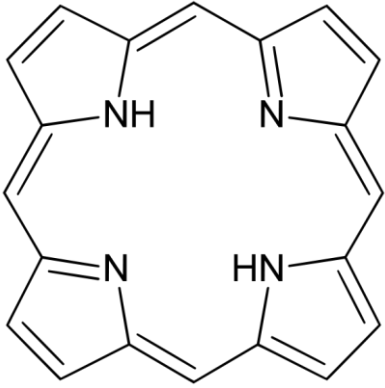# General Chemistry: Inorganic section

Instructor: Dr. Prakash Chandra Mondal

**Department of chemistry**

Lecture: 5

Coordination Complexes in Biological Systems

Porphin

Porphyrins are heterocyclic macrocycles that are composed of four pyrroles. They form coordination complexes with metal ions and are found to be biologically relevant.

Aerobic cellular respiration occurs in our body (using oxygen), in which glucose reacts with oxygen, forming ATP (source of energy) that can be used by the cell.

$$C_6H_{12}O_6 + 6\ O_2 \longrightarrow 6\ CO_2 + 6\ H_2O + 36\ ATP$$

Energy from ATP
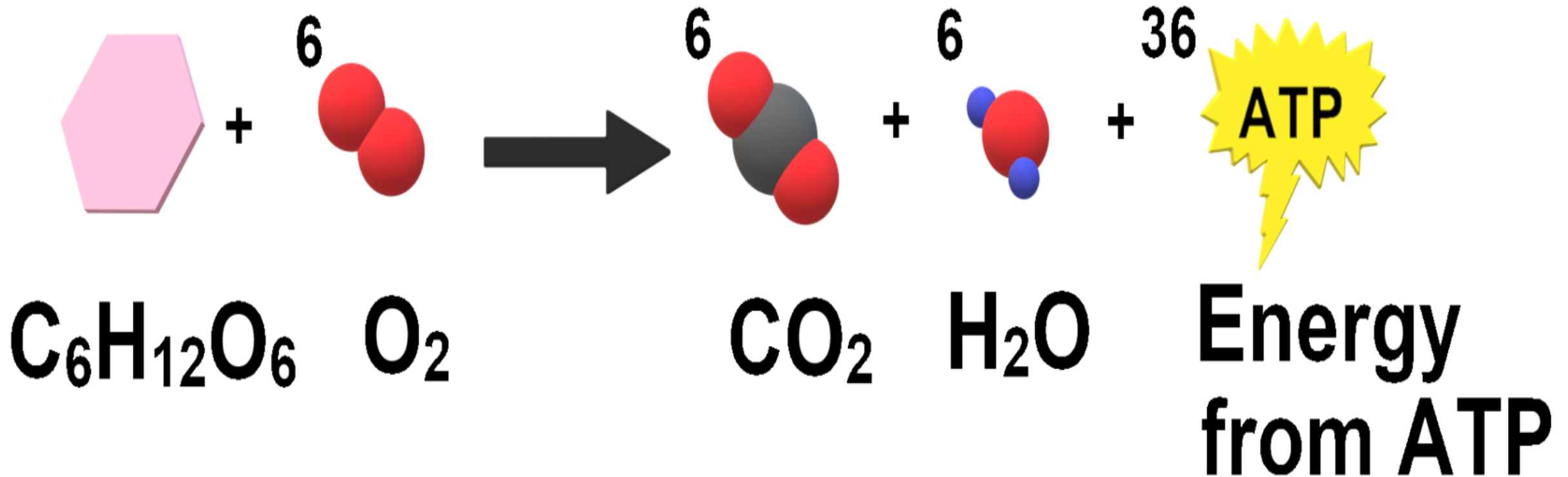
Bioinorganic chemistry

Bioinorganic chemistry deals with the role of metal ions in biological functions such as oxygen transport

The metals like Na^+, K^+, Fe^{2+}, Co^{2+}, Mg^{2+}, Ca^{2+}, Zn^{2+} play important roles in several biological functions.

O_2 is only marginally soluble (<0.0001 M) in blood plasma at physiological pH

Our bloodstream contains about 150 g/L of hemoglobin which is an effective oxygen carrier.

Once the Hb-O_2 complex reaches the tissue that consumes oxygen, the O_2 molecules are transferred to another protein, myoglobin which transports oxygen through the muscle tissue

Hb and Mb in the human body
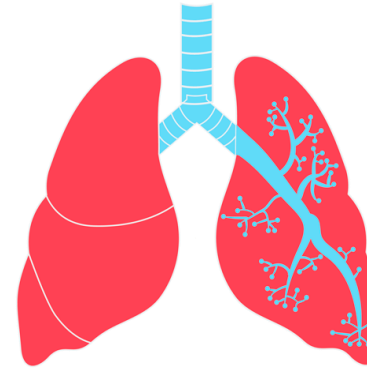
More Hb

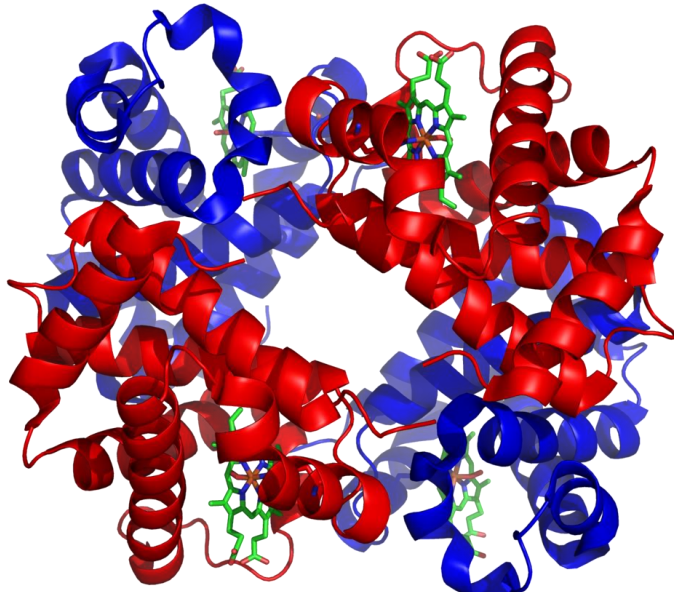Found in RBC

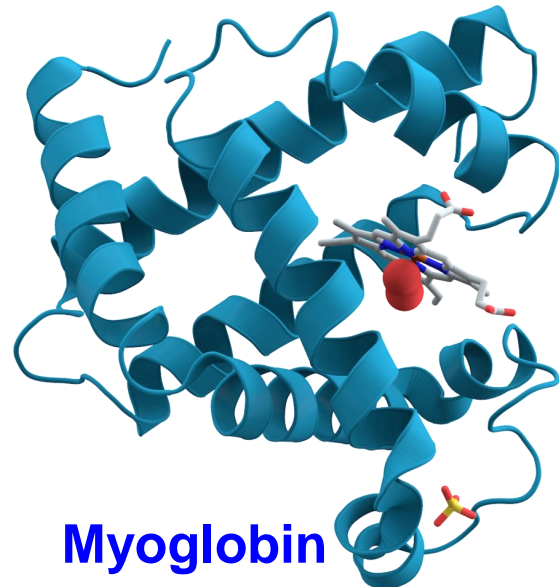(36%)

O_2 transport

(lungs to tissue)

More Mb

Found in muscle cells

Release O_2 in the cells

Myo/Hemo-globin – Oxygen Transporter

Hemoglobin

Myoglobin

BASIS FOR COMPARISON	HEMOGLOBIN	MYOGLOBIN
Number of chains	Haemoglobin has 4 chains of two different types- alpha and beta, delta, gamma, or epsilon (depending on the type of hemoglobin).	It contains single polypeptide chains.
Type of structure	A tetramer.	A monomer.
Binds	Binds CO_2, CO, NO, O_2 and H^+.	Binds to O_2, tightly and firmly.
Their presence	Systemically all over the body.	In muscles cells.
Types of curve	Sigmoid binding curve.	Hyperbolic curve.
Also known as	Hb.	Mb.
Role	Haemoglobin is transported along with blood to whole body and carry oxygen.	Myoglobin supplies oxygen to muscles only, which is helpful at the starving time of oxygen.
Concentration in blood	High in RBC.	Low.

**Notice that the hemoglobin is essentially a tetramer of myoglobin.**

Oxygen Binding to Myoglobin

The two sides of the heme plane are called the proximal side (nearer the plane) and the distal side (away from the center of the body).
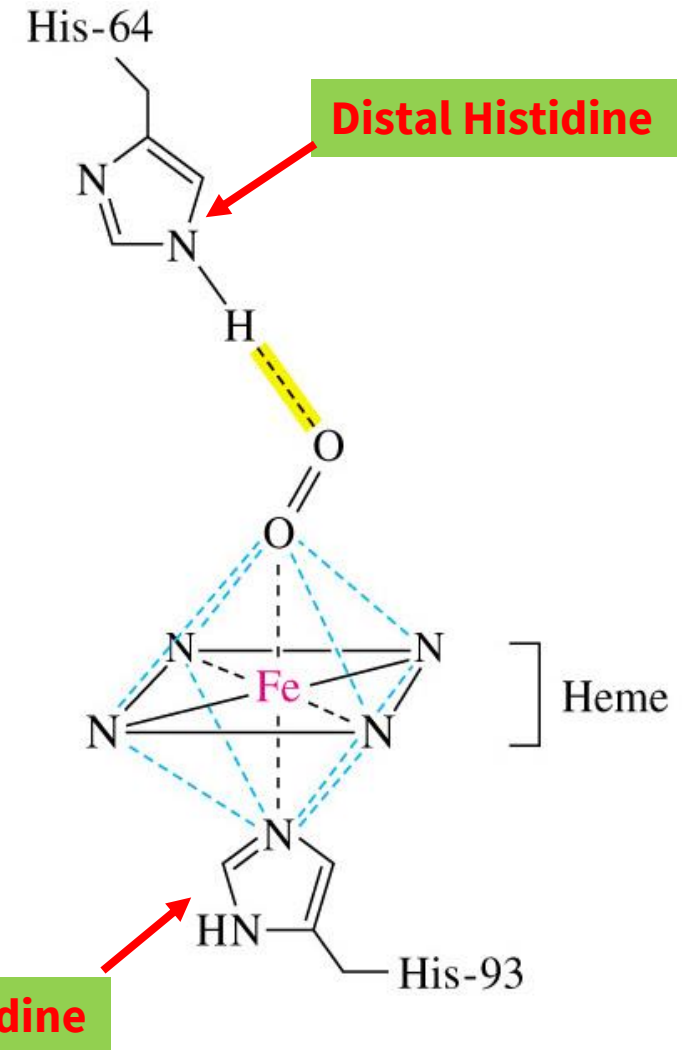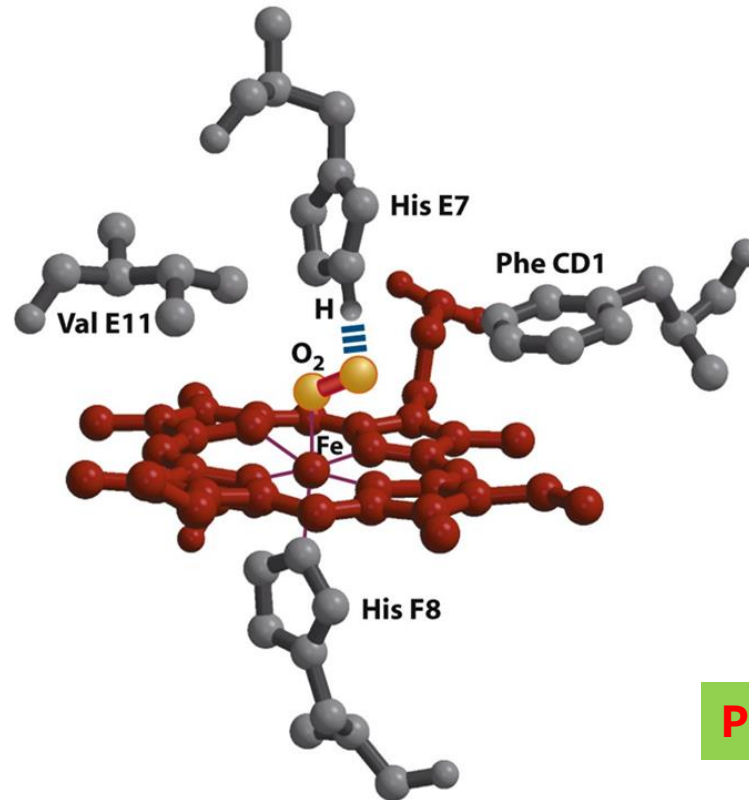
His 93 (proximal his) binds directly to iron.

His 64 (distal his) stabilizes the O_2 binding site.

O_2 is hydrogen bonded to the imidazole N-H of the distal histidine.
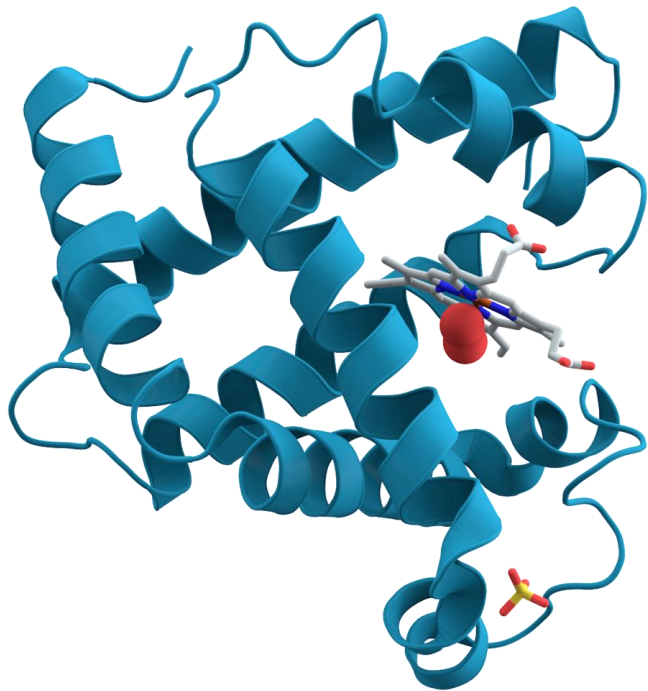
Myoglobin

**His 64 stabilizes bound O_2 by hydrogen bonding and inhibits CO**
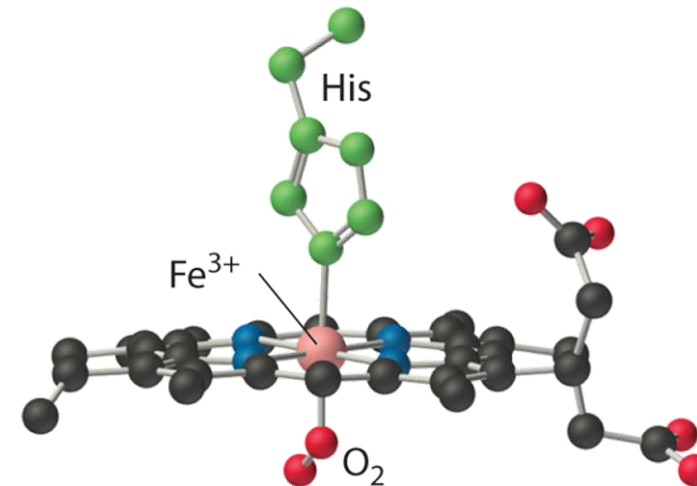
Structural Changes in Myoglobin Upon O_2 Binding

- **The coordination number of Fe^{2+} in deoxyhemoglobin is five, with square pyramidal geometry.**

- **In the absence of oxygen binding, Fe^{2+} is out of the heme plane. Upon the oxygen binding, it pulls the Fe into the heme plane.**

- **Ferrous ion in deoxyhemoglobin is in high-spin and lies approximately 40 pm out of the heme plane towards the proximal side giving a "dome shape" to heme.**

- **The spin state of Fe(II) changes from high spin to low spin resulting in a concomitant decrease in size, now Fe-centre properly fits into the heme cavity. It also pulls the proximal histidine towards the heme plane.**
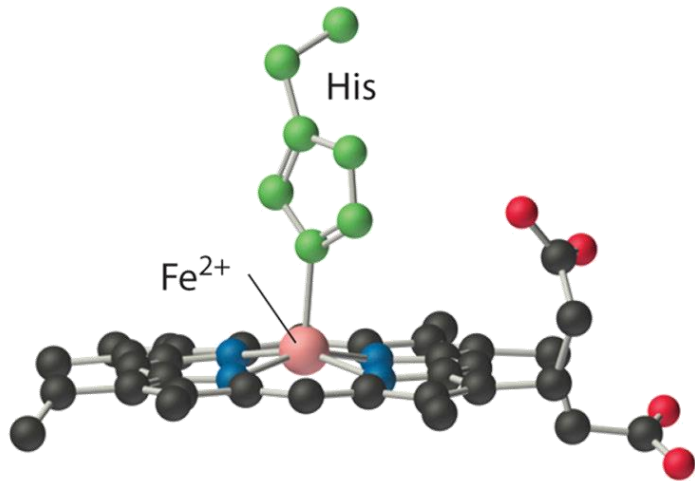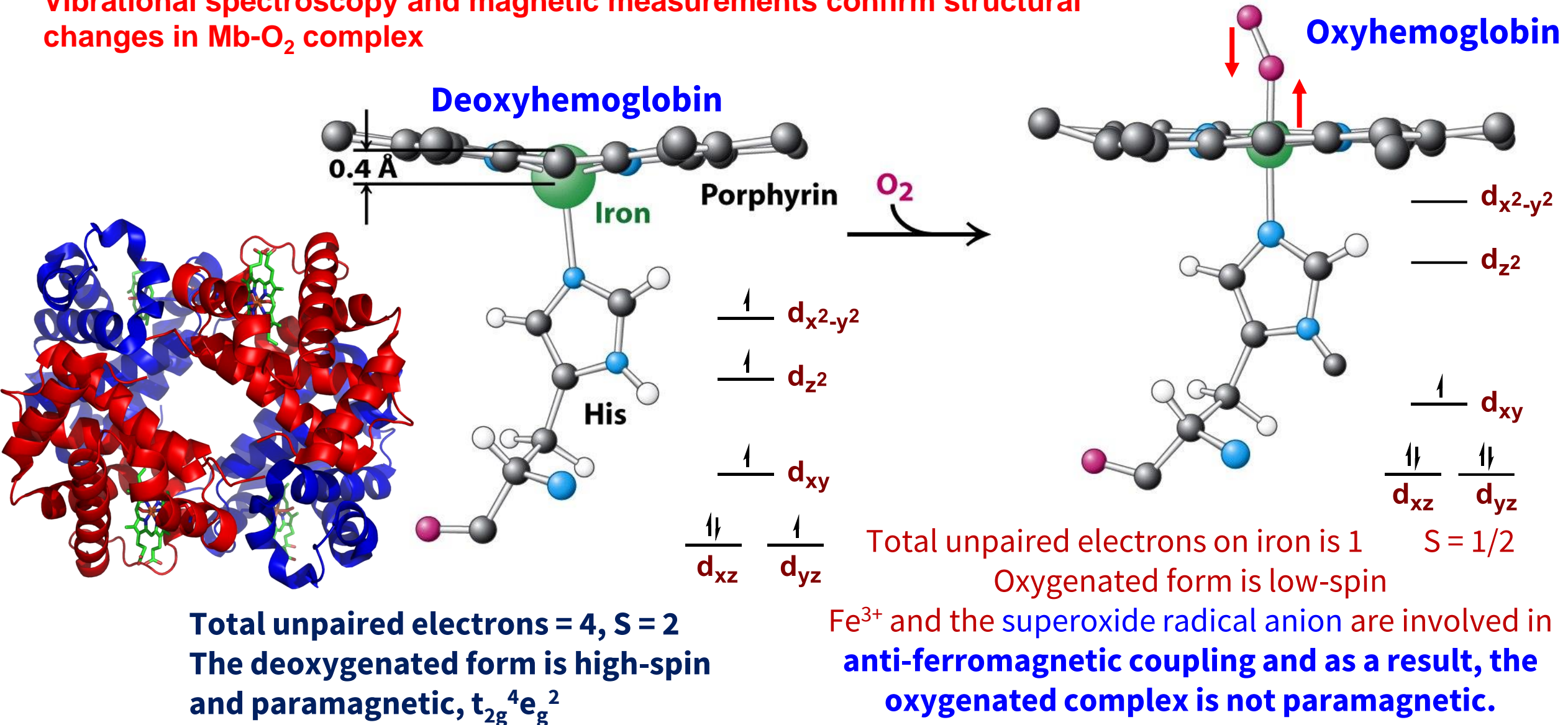

dome shape

(a) Deoxymyoglobin

(b) Oxymyoglobin

Structural Changes in Myoglobin Upon O_2 Binding

Vibrational spectroscopy and magnetic measurements confirm structural changes in Mb-O_2 complex

Oxyhemoglobin

Deoxyhemoglobin

0.4 Å

Iron

Porphyrin

O_2

His

$d_{x^2-y^2}$

d_{z^2}

d_{xy}

d_{xz} d_{yz}

$d_{x^2-y^2}$

d_{z^2}

d_{xy}

d_{xz} d_{yz}

Total unpaired electrons = 4, S = 2
The deoxygenated form is high-spin and paramagnetic, $t_{2g}^4 e_g^2$

Total unpaired electrons on iron is 1   S = 1/2
Oxygenated form is low-spin
Fe^{3+} and the superoxide radical anion are involved in **anti-ferromagnetic coupling and as a result, the oxygenated complex is not paramagnetic.**

Oxygen Binding Curve for Hb and Mb

- Unlike Mb, Hb displays a sigmoidal binding curve. The curve indicates that the affinity of Hb for oxygen is lower than that of Mb! At low-pressure

- Hb must be able to bind oxygen in the lungs

and it must be able to release oxygen in capillaries

- If Hb behaved like Mb, very little oxygen

would be released in capillaries

- The sigmoid, cooperative oxygen binding

 the curve of Hb makes this possible!

- Myoglobin has a high affinity for O_2.

- Allows myoglobin to act as an O_2 storage reserve.

- It releases O_2 when pO_2 becomes low indicating O_2 depriva

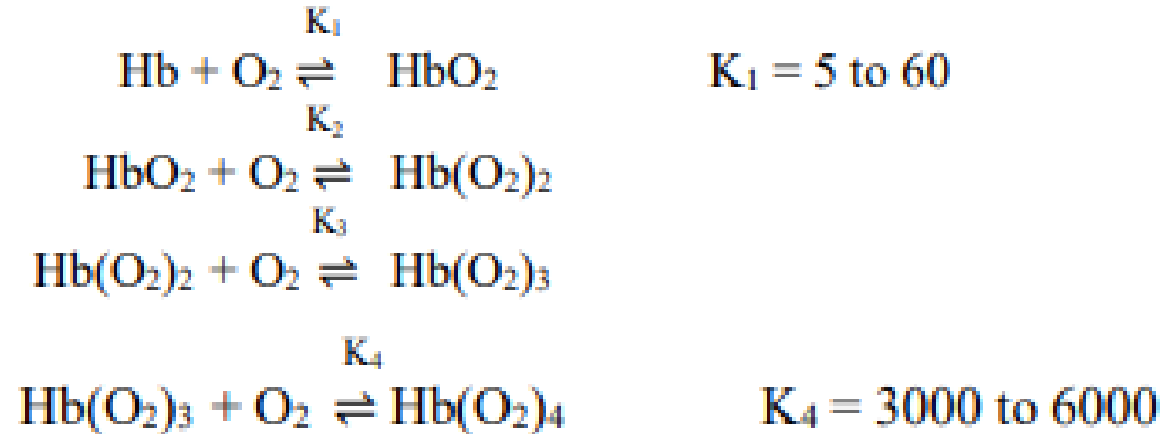**P_{50} = 2.8 Torr for Mb; 26 Torr for Hb**
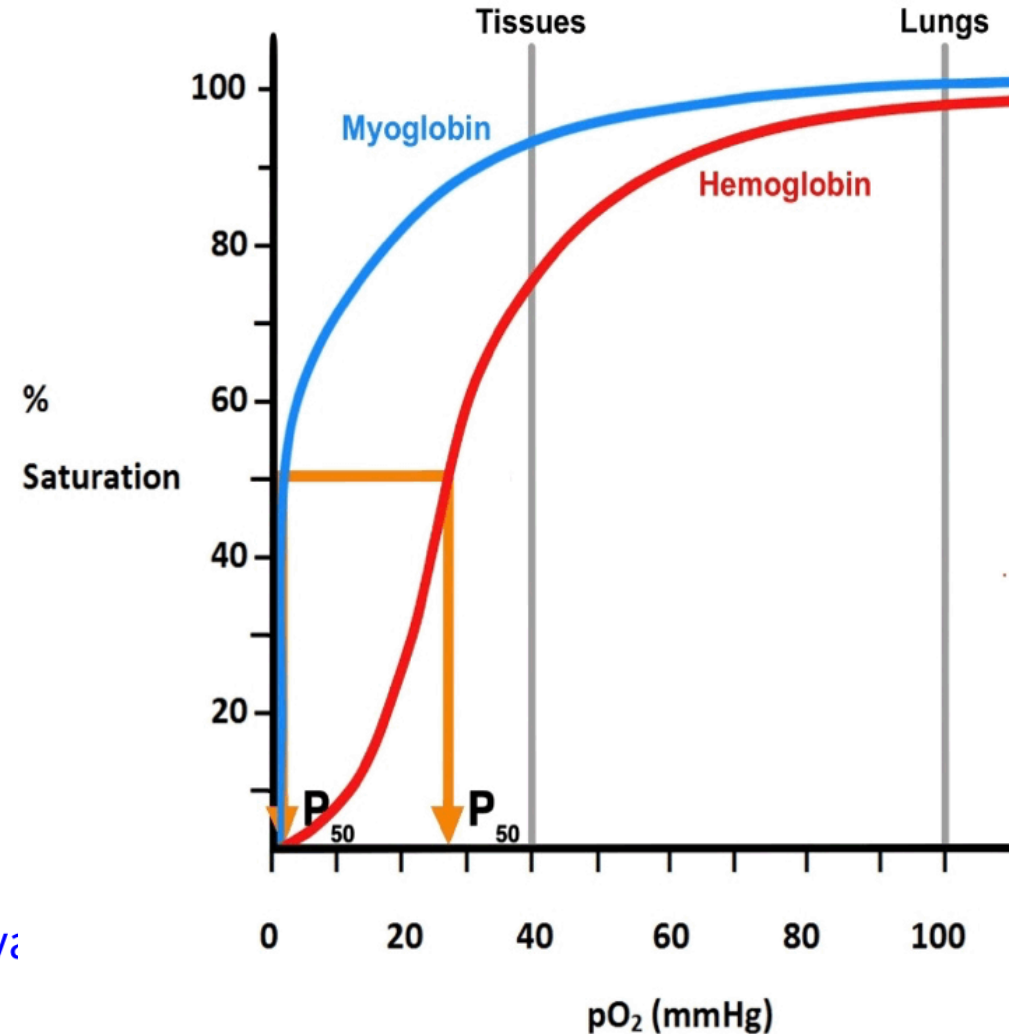
p_{50} refers to the pressure at which Mb or Hb is 50% bound to dioxygen (O_2)

Tissues   Lungs

Myoglobin

Hemoglobin

% Saturation

P_{50} P_{50}

pO₂ (mmHg)

8

Cooperative effect in O2 binding

One of the most important features of hemoglobin is the cooperative effect in dioxygen binding.

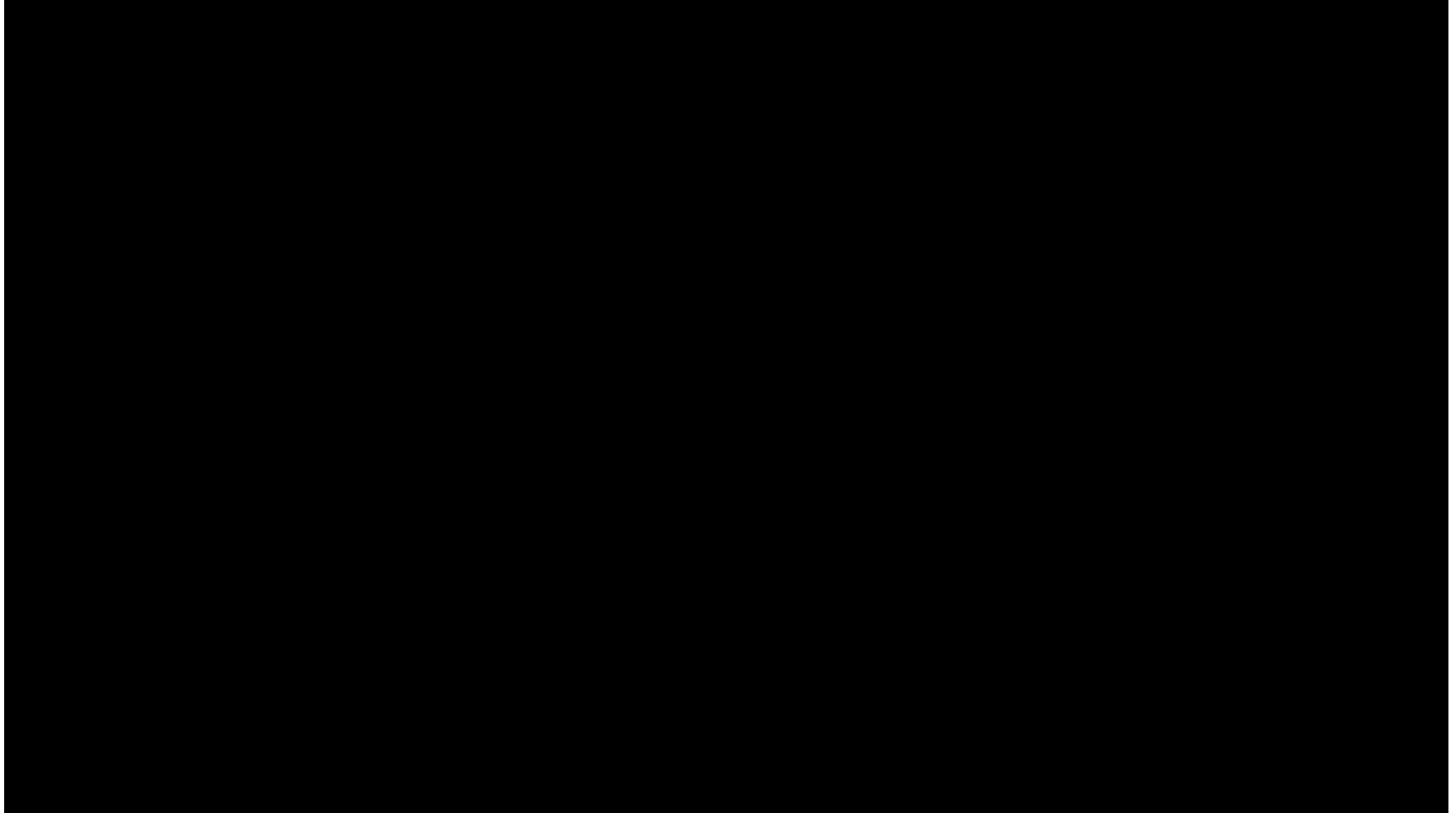**One hemoglobin molecule can bind to a maximum of four O_2.**

$$Hb + O_2 \underset{}{\overset{K_1}{\rightleftharpoons}} HbO_2 \qquad K_1 = 5 \text{ to } 60$$

$$HbO_2 + O_2 \underset{}{\overset{K_2}{\rightleftharpoons}} Hb(O_2)_2$$

$$Hb(O_2)_2 + O_2 \underset{}{\overset{K_3}{\rightleftharpoons}} Hb(O_2)_3$$

$$Hb(O_2)_3 + O_2 \underset{}{\overset{K_4}{\rightleftharpoons}} Hb(O_2)_4 \qquad K_4 = 3000 \text{ to } 6000$$

where K_1, K_2, K_3 and K_4 are the the stepwise formation constants for the binding of O_2 to hemoglobin.

These formation constants follow the order $k_1 < k_2 < k_3 < k_4$

The binding of dioxygen to hemoglobin enhances the binding of the next dioxygen.

The binding of the first dioxygen is the most difficult one, and the fourth dioxygen is bound most readily and tightly.

Can the color of blood be blue?

Can the color of blood be blue?

- Hemocyanin... ...ods.
- The active s... ...dues,
- When deoxy...
- Molecular ox...
- Cu(I) is oxid...
- The oxygen... ...fashion

Deoxyhemoc...

Horseshoe crab blood: the miracle vaccine ingredient that's saved millions of lives

By Katie Pavid
First published 3 December 2020
Last updated 15 January 2021

During 2020, COVID-19 vaccines were created in record time.

Nature plays a huge part in the medicines we rely on every day. And when it comes to vaccines, we have horseshoe crabs and their blood to thank for keeping us safe.

Horseshoe crabs are older than the dinosaurs. They've been around for 450 million years, which means they watched the rise and fall of millions of other species, and survived ice ages.

As well as being incredible 'living fossils', they have also helped to keep most of us alive. If you have ever had a vaccine, chances are that it was tested for safety using horseshoe crab blood. And they're about to save even more lives, because they're playing their part in the creation of a Covid-19 injection.
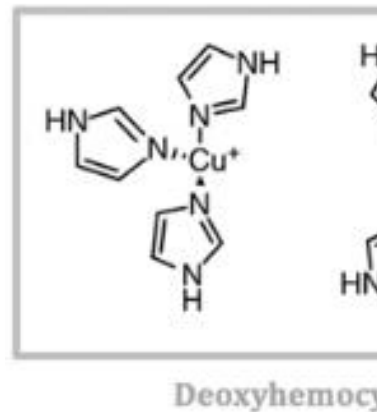
...osts 12 lakh INR

Cu●●●Cu distance decreases by 1.0 Å in oxyhaemocyanin (Cu^I●●●Cu^I = 4.6A Å vs. Cu^{II}●●●Cu^{II} = 3.6A Å

Question Time !!

Why human blood is red?

Why to Study Organometallic Chemistry?

Paul Ehrlich (1908)
OrganoArsenic compound

V Grignard and P Sabatier (1912)
Grignard Reagent

K. Ziegler and G. Natta (1963)
Ziegler Natta Polymerization

G. Wilkinson and E. Fischer (1973)
Sandwich Compounds

H.C.Brown and G. Wittig (1973)
Hydroboration/Olefination

R. Hoffman and K. Fukui (1981)
Reaction Mechanism

Knowles, Noyori and Sharpless (2001)
Asymmetric Catalysis

Chavin, Grubbs and Shrock (2005)
Olefin Metathesis

Suzuki, Negishi and Heck (2010)
Cross-coupling

Why to Study Organometallic Chemistry?

- **Organic Synthesis: Organometallic complexes allow many powerful synthetic organic transformations that can't be accomplished without metals, including Heck, Suzuki, asymmetric hydrogenation reactions.**

- **Bulk Chemical Synthesis and Catalysis: Huge industrial importance to organometallic processes, including commodity chemicals such as plastics.**

- **Materials Science: Many organometallic compounds are used in advanced materials applications including organic light-emitting diodes, organic electronics.**

- **Bioinorganic Chemistry: Some overlap, such as with Vit. B12, hydrogenase, carboxylase, etc.**

- **Energy Science: The emerging subfield of catalysis.**

Introduction to Organometallic Compounds

An Organometallic Compound contains at least one M—C bond

Common ligands in organometallic compounds: CO, NO, N_2, PR_3, H_2

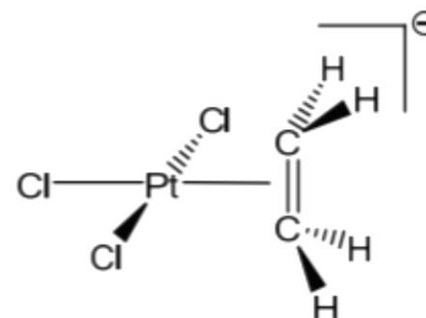**Both σ and π bonding between Metal and Carbon occur**

Zeise's Salt was synthesized in 1827 $K[Pt(C_2H_4)Cl_3] \cdot H_2O$

- Confirmed to have $H_2C=CH_2$ as a ligand in 1868.

W. C. Zeise (1827): 1st organometallic transition metal complex

$$K_2PtCl_6 + EtOH \longrightarrow K^+ \begin{bmatrix} Cl & Cl \\ & Pt \\ Cl & \end{bmatrix}^{\ominus} + H_2O + KCl$$

Zeise'sches Salz
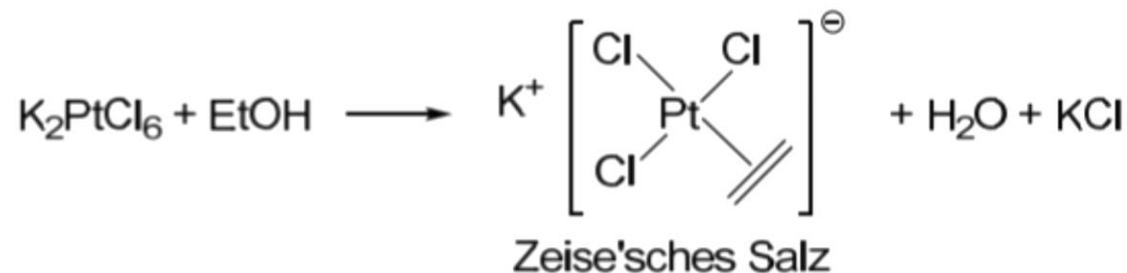
contested by J. Liebig: *Liebigs Ann. Chem.* **1837**, 23, 1

Molecular structure of $K[PtCl_3(C_2H_4)]\cdot H_2O$
(*Inorg. Chem.* **1975**, 14, 2653)

History of Organometallic Compounds

- **Ni(CO)$_4$ synthesized in 1890 (Ludwig Mond of Brunner Mond & Co.)**

L. Mond (1890): 1st Binary Transition metal carbonyls

$$Ni + 4\,CO \longrightarrow Ni(CO)_4 \quad (T = 25\ ^{\circ}C,\ p = 1\ bar)$$

b.p.: 34 $^{\circ}$C
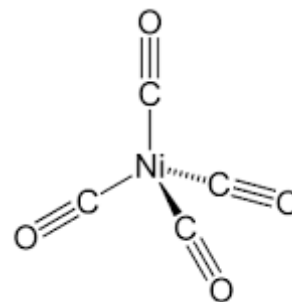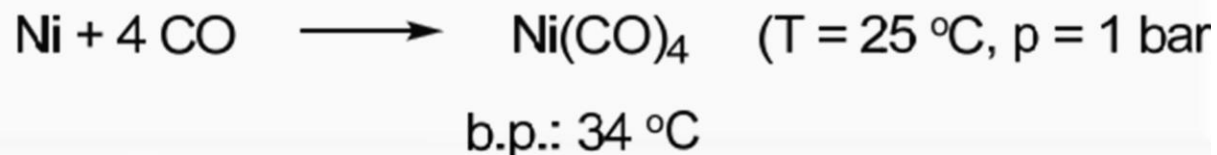
The oxidation state for nickel is zero because the Ni-C bonding electrons come from the C atom.
Ni–C and C–O distances have been calculated to be 1.838 Å and 1.141 Å, respectively

- Grignard Reagents (X-Mg-R) synthesized about 1900

$$R \!-\! X \xrightarrow[\text{Et}_2\text{O or THF}]{\text{Mg}} R \!-\! MgX$$
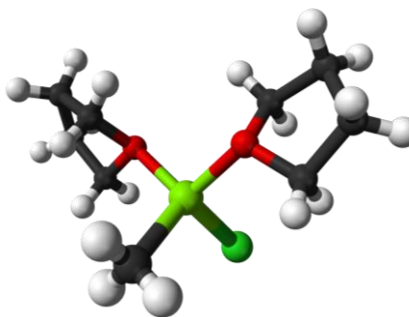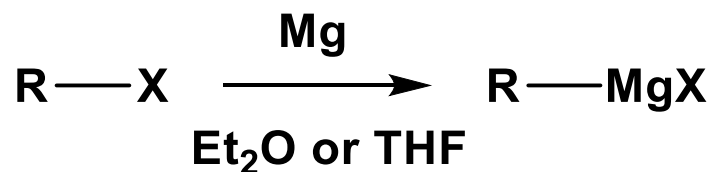
Usually, the Grignard reagents are expressed as R-Mg-X, but in fact, the magnesium(II) center is tetrahedral due to the coordination with Lewis basic solvents, E.g., bis-adduct of methylmagnesium chloride and THF.

**Victor Grignard**
Nobel prize in 1912

History of Organometallic Compounds

- **1951: Ferrocene was accidentally discovered by Keally and Pauson, and Miller and co-workers. The actual structure was proposed by Wilkinson and Fischer which led to the development of metallocene chemistry and they received Nobel Prize in 1973 (Wilkinson and Fischer).**

FeCl$_3$

Fulvalene

Fe(0) + N$_2$

NR$_3$

C$_{10}$H$_{10}$Fe
Cp2Fe, "Ferrocene"
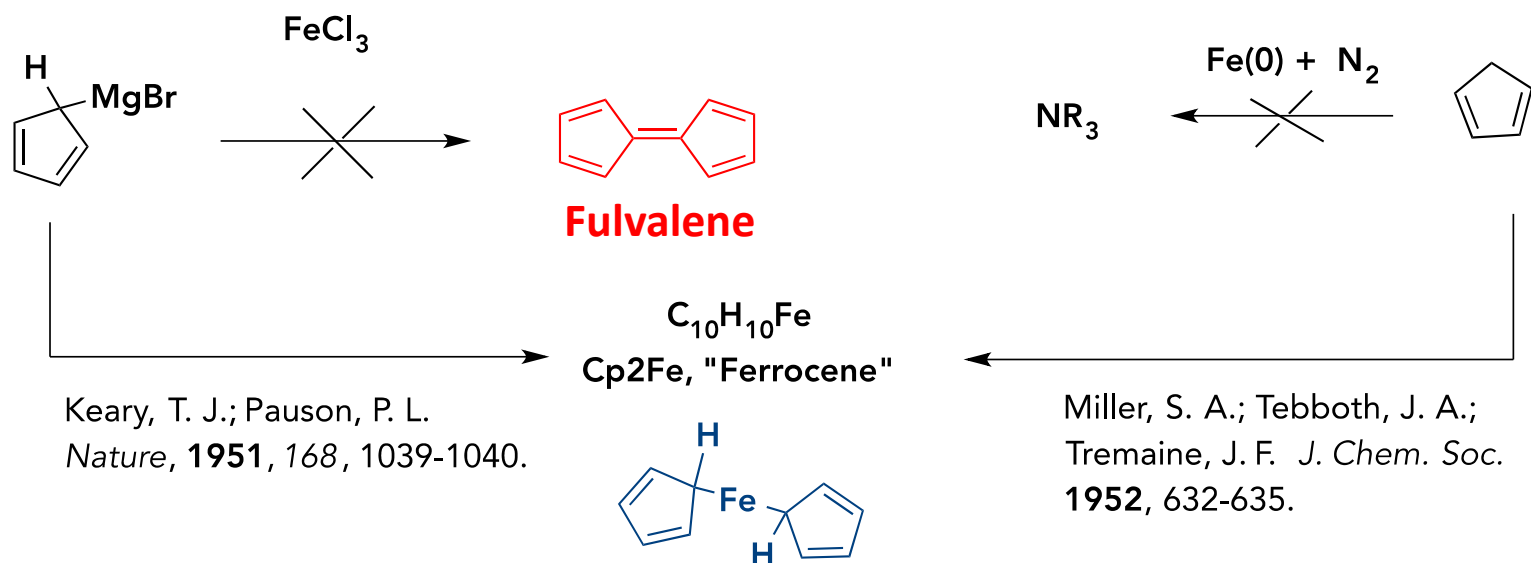
Keary, T. J.; Pauson, P. L. *Nature*, **1951**, *168*, 1039-1040.

Miller, S. A.; Tebboth, J. A.; Tremaine, J. F. *J. Chem. Soc.* **1952**, 632-635.

Modern Organometallic Chemistry Begins After this Discovery
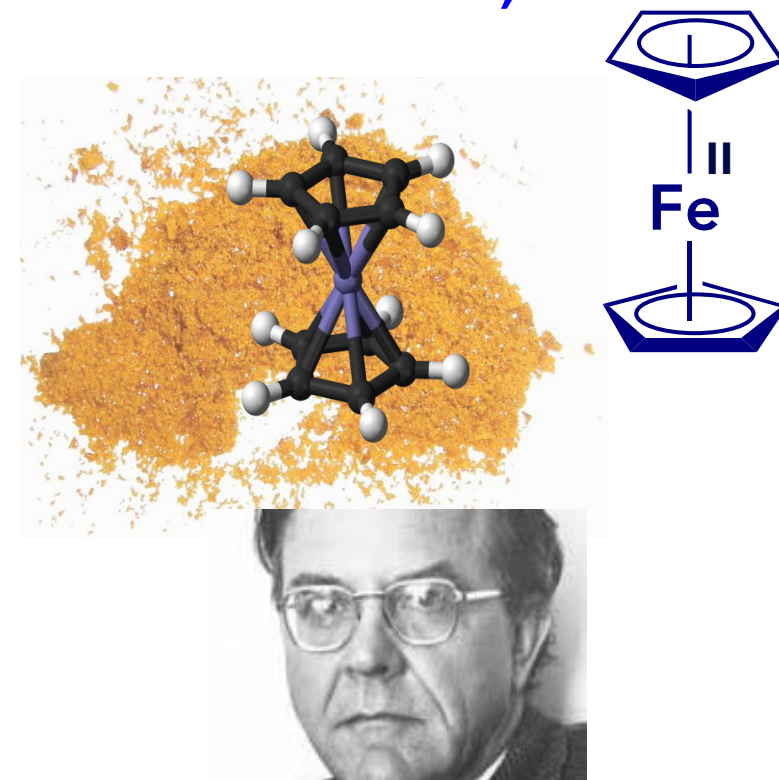
Geoffrey Wilkinson Nobel prize in 1973

Terminology: Hapticity (η)

η^x "eta-*x*" was originally developed to indicate how many uninterrupted and *contiguous* donor atoms of a π-system were coordinated to a metal center. **_Hapticity_** is another word used to describe the bonding mode of a ligand to a metal center. An η^5-cyclopentadienyl ligand, for example, has all five carbons of the ring bonding to the transition metal center.

η^x values for all-carbon based ligands where the x value is odd usually indicate *anionic* carbon ligands (*e.g.*, η^5-Cp, η^1-CH_3, η^1-allyl or η^3-allyl, η^1-CH=CH_2). The no. of electrons donated (ionic method of electron counting) by the ligand is usually equal to **x + 1**. Even η^x values usually indicate *neutral* carbon π-system ligands (*e.g.*, η^6-C_6H_6, η^2-CH_2=CH_2, η^4-butadiene, η^4-cyclooctadiene). The no. of electrons donated by the ligand in the even (*neutral*) case is equal to **x**.

Ferrocene

η^5-Cp	η^3-Cp	η^3-allyl	η^1-allyl
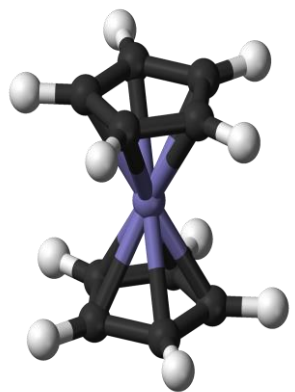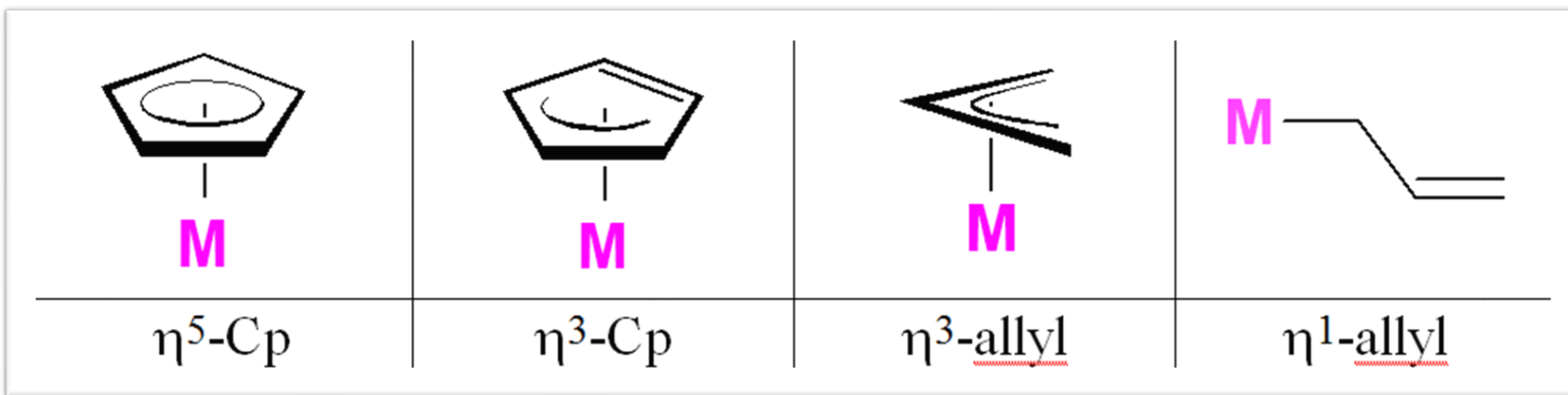
The 18 Valence Electron Rule

Electron counting is an important tool to judge whether a given compound is stable or not.

You must be familiar with the octet rule for the second-row elements. The 18-electron rule is analogous formulation for transition elements (with many exceptions!).

For thermodynamically stable complexes, the number of ligands attached to a metal will be such that the sum of the number of electrons donated by the ligands plus the valence electrons on the metal will be "18"

Why 18? It is the maximum number of electrons that can be accommodated by One {ns}, three {np}, and five {(n-1)d} orbitals (2 + 6 +10 =18).

Structures that have this preferred count are called electron-precise.

Structures that have less than 18 electrons are termed as "coordinatively unsaturated" (they are electron-deficient species and have room for more ligand(s))

Methods for Counting Electrons

- The first method is called the "ionic method" which considers charges on the metal ion and ligands to calculate the number of electrons.

- The second method is called the "**neutral atom method**".

  We will follow only the **ionic method** to avoid any confusion

  How to count electrons?

- Determine the oxidation state of the transition metal center(s) and the metal centers resulting in d-electron count. To do this one must:

  $$[Ni(CO)_4]$$

  - a) Note any overall charge on the metal complex
  - b) Know the charges of the ligands bound to the metal center (ionic ligand method)
  - c) know the number of electrons being donated to the metal center from each ligand (ionic ligand method)

- Add up the electron counts for the metal center and ligands.
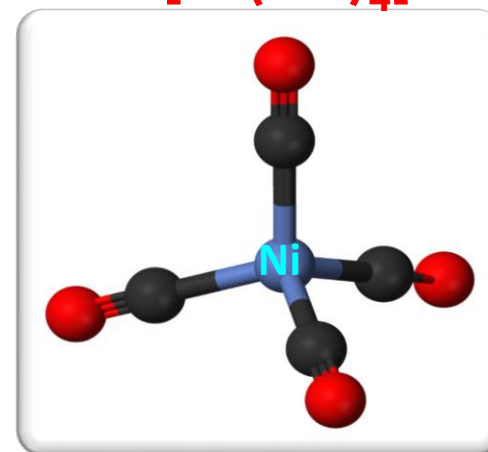
Common Ligands and Electrons Contributed

- **Electron Counting**
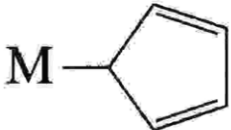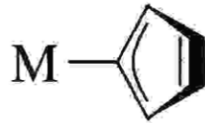
  a) **Common ligands are assigned an electron count and charge.**

  b) **The overall charge on the complex must equal the total charge on ligands plus the charge on the metal; this helps determine the d-electron count of the metal.**

  c) **Add up all electrons from metal d orbitals and ligands to find the total electron count.**

Ligand	Method A
H	2 (H^-)
Cl, Br, I	2 (X^-)
OH, OR	2 (OH^-, OR^-)
CN	2 (CN^-)
CH_3, CR_3	2 (CH_3^-, CR_3^-)
NO (bent M—N—O)	2 (NO^-)
NO (linear M—N—O)	2 (NO^+)
CO, PR_3	2
NH_3, H_2O	2
=CRR' (carbene)	2
H_2C=CH_2 (ethylene)	2
CNR	2
=O, =S	4 (O^{2-}, S^{2-})
η^3-C_3H_5 (π-allyl)	2 ($C_3H_5^+$)
≡CR (carbyne)	3
≡N	6 (N^{3-})
Ethylenediamine (en)	4 (2 per nitrogen)
Bipyridine (bipy)	4 (2 per nitrogen)
Butadiene	4
η^5-C_5H_5 (cyclopentadienyl)	6 ($C_5H_5^-$)
η^6-C_6H_6 (benzene)	6
η^7-C_7H_7 (cycloheptatrienyl)	6 ($C_7H_7^+$)

Varying Hapticity = Varying Electron Contribution

Number of bonding positions	Formula	Name	
1	η^1-C_5H_5	monohaptocyclopentadienyl **2 electron donor**	M— (structure)
3	η^3-C_5H_5	trihaptocyclopentadienyl **4 electron donor**	M— (structure)
5	η^5-C_5H_5	pentahaptocyclopentadienyl **6 electron donor**	M— (structure)

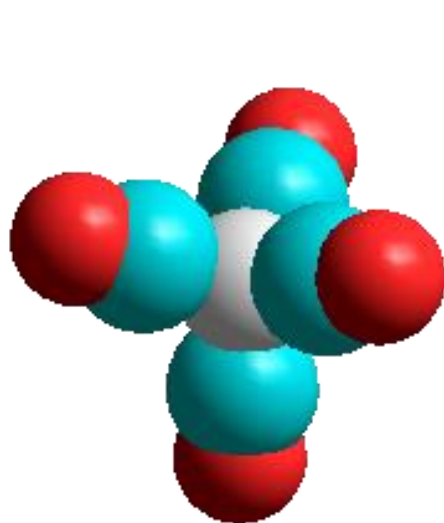**A molecule can have the same ligand but with different hapticities**

η^5-cyclopentadienyl

OC‴Fe—H
OC

η^1-cyclopentadienyl
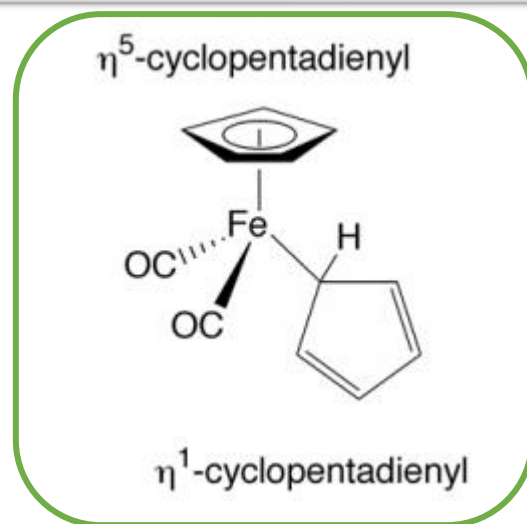
The allyl anion has similar attributes

η^3-allyl	η^1-allyl
M	M
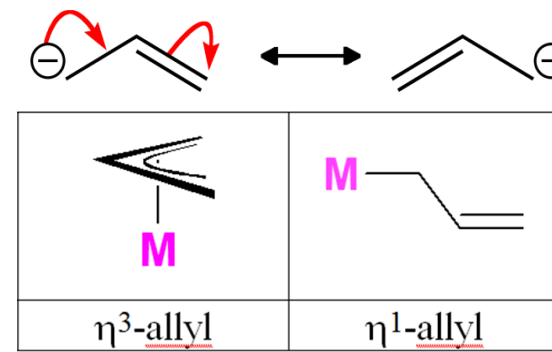
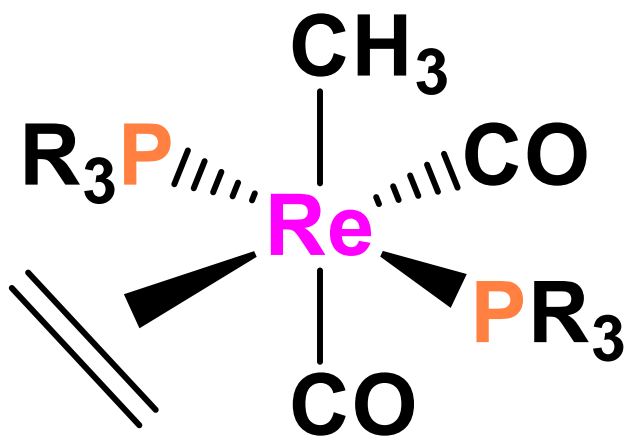**4 electron donor**   **2 electron donor**

22

Metal-Carbonyl Complexes

- **The carbonyl ligand forms a huge number of complexes with metal ions, most commonly in low oxidation states, where it binds to the metal through its C-donor, as in the complexes below, where all the metal ions are zero-valent:**

| $[Ni(CO)_4]$	$[Fe(CO)_5]$	$[Cr(CO)_6]$
Ni(0), d^{10} = 10e$^-$	Fe(0), d^8 = 8e$^-$	Cr(0), d^6 = 6e$^-$
4 x CO = 8e$^-$	5 x CO = 10e$^-$	6 x CO = 12e$^-$
18 e$^-$	**18 e$^-$**	**18 e$^-$**
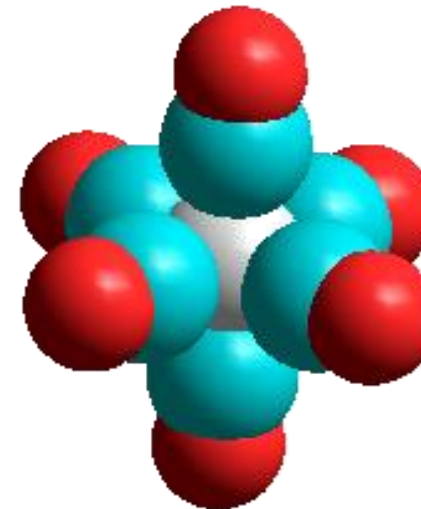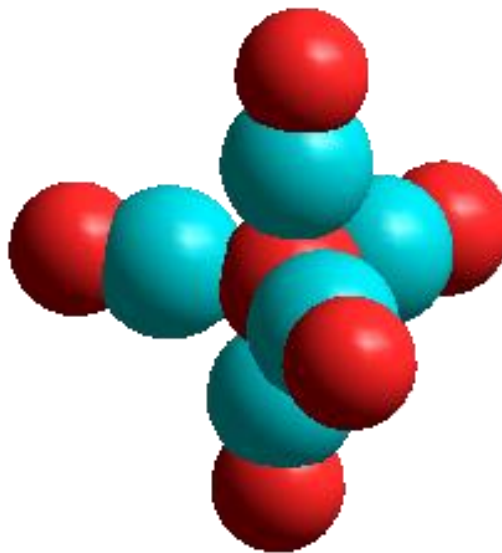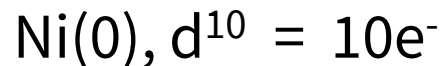
Example: A Simple Case

- There is no overall charge on the complex
- There is one anionic ligand (CH_3^-, methyl group)
- The Re metal atom must have a +1 charge to compensate for the one negatively charged ligand. So the Re is the in the +1 oxidation state. We denote this three different ways: Re(+1), Re(I), or Re^I.

Re(+1), d^6	6e$^-$
2 PR$_3$	4e$^-$
2 CO	4e$^-$
CH$_3^-$	2e$^-$
CH$_2$=CH$_2$	2e$^-$
Total:	**18e$^-$**

Example: Somewhat Tricky!

1) There is no overall charge on the complex

2) There is one anionic ligand ($C_3H_5^-$, allyl)

3) The top ligand is NOT a MeCp$^-$! It is a neutral diene that has a H attached to the methyl-substituted ring carbon. This is a neutral 4e$^-$ donor.

4) Because the complex is neutral and there is one anionic ligand present, the Rh atom must have a +1 charge to compensate for the one negatively charged ligand. So the Rh atom is in the +1 oxidation state.
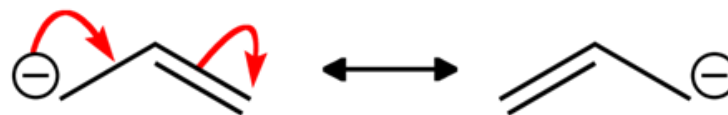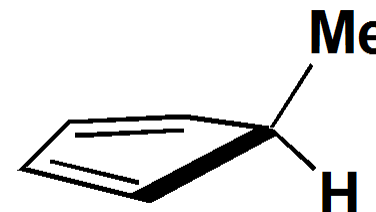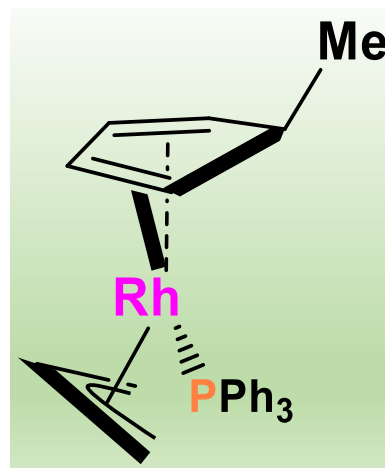

|	
Rh(+1), d^8	8e$^-$
PR$_3$	2e$^-$
η^4-C$_5$H$_5$Me	4e$^-$
η^3-C$_3$H$_5^-$	4e$^-$
Total:	**18e$^-$**

18 Electron Rule Explains Some Observations

- The compound $Mn_2(CO)_{10}$ exists but $Mn(CO)_5$ does not.

- A species such as $[Mn(CO)_5]$ would have only 17 e^-.

- Each Mn contributes one electron to the valence shell of the other Mn, giving the metal-metal bonded species $[(CO)_5Mn-Mn(CO)_5]$. To check on the 18-electron rule, we look at one metal at a time:

$[Mn_2(CO)_{10}]$

Mn-Mn bond

Mn

Mn
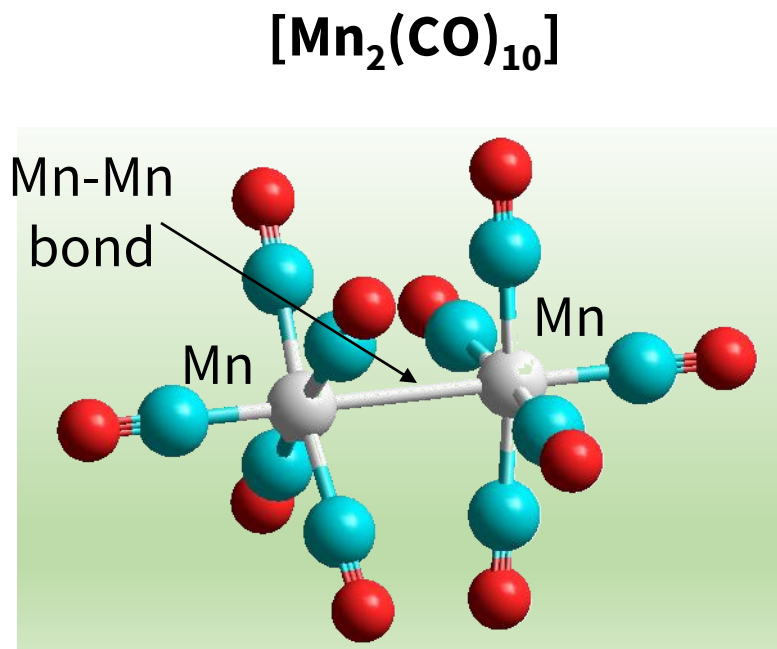
$Mn(0), d^7$	=	7 e^-
5 C≡O	=	10 e^-
Mn-Mn	=	1 e^-

18 e^-

Bridging Carbonyl Ligands

$[Co_2(CO)_8]$

bridging carbonyls
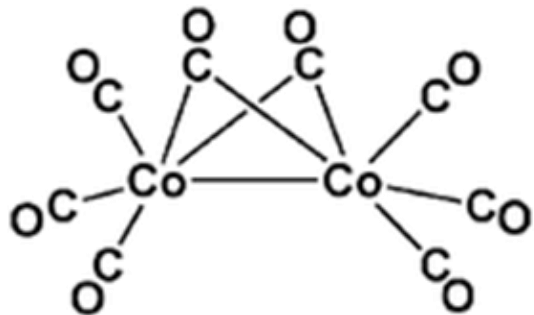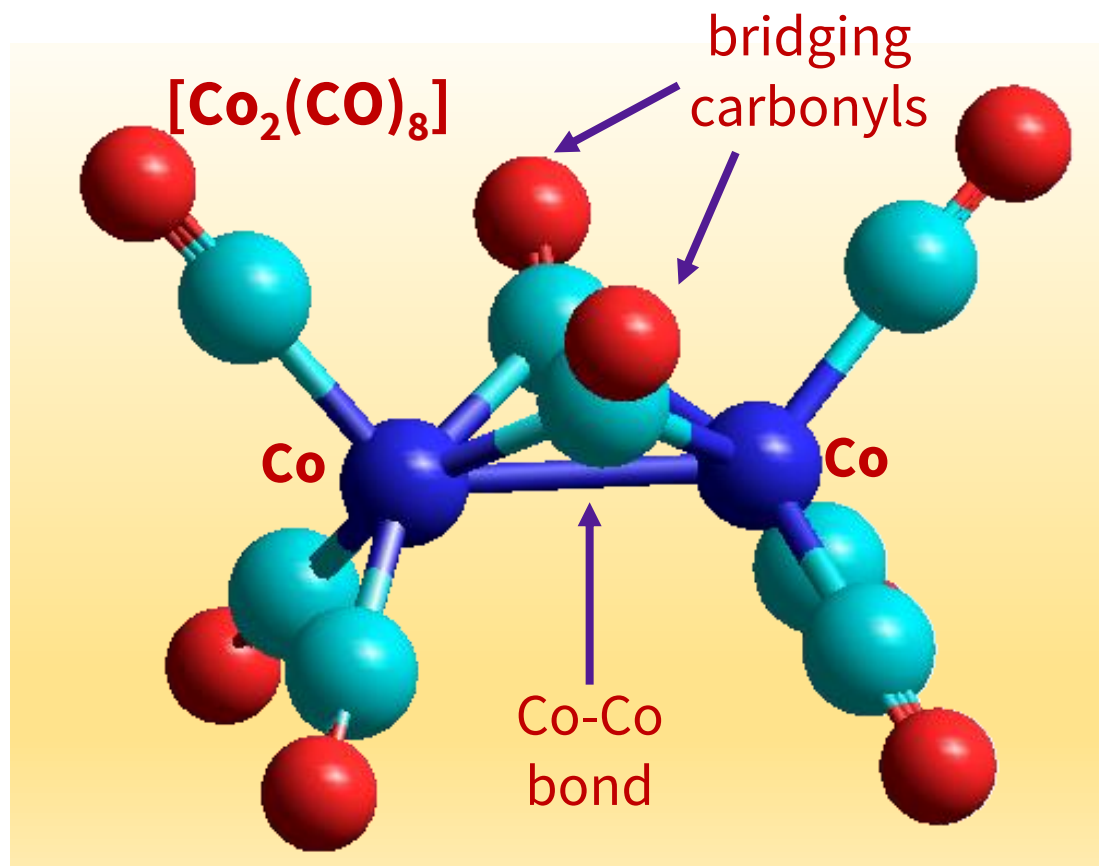
Co   Co

Co-Co bond

- **Carbonyls may form bridges between two metals, where they donate one electron to each metal in working out the 18-electron rule.**

- In $[Co_2(CO)_8]$, each Co has three terminal CO's, two bridging CO's, and a Co-Co bond:

Co(0), d^9	=	$9e^-$
3 CO's	=	$6e^-$
2 bridged μ-CO's	=	$2e^-$
Co-Co bond	=	$1e^-$
		$18e^-$

Exceptions to 18 Electron Rule

d^3	d^4	d^5	d^6	d^7	d^8	d^9	d^{10}	$d^{10}s^1$
21 Sc Scandium	22 Ti Titanium	23 V Vanadium	24 Cr Chromium	25 Mn Manganese	26 Fe Iron	27 Co Cobalt	28 Ni Nickel	29 Cu Copper
39 Y Yttrium	40 Zr Zirconium	41 Nb Niobium	42 Mo Molybdenum	43 Tc Technetium	44 Ru Ruthenium	45 Rh Rhodium	46 Pd Palladium	47 Ag Silver
57 La Lanthanum	72 Hf Hafnium	73 Ta Tantalum	74 W Tungsten	75 Re Rhenium	76 Os Osmium	77 Ir Iridium	78 Pt Platinum	79 Au Gold

Early Transition Metals
16e- and sub-16e-configurations are common
Coordination geometries higher than 6 relatively common

Middle Transition Metals
18e- configurations are common

Coordination geometries of 6 are common

d^6

Late Transition Metals
16e- and sub-16e-configurations are common
Coordination geometries of 5 and lower are common:
d^8 = square planar

MeTiCl$_3$, **8e⁻**;

Me$_2$NbCl$_3$, **10e⁻**;

WMe$_6$, **12e⁻**;

Pt(PCy$_3$)$_2$, **14e⁻**;

[M(H$_2$O)$_6$]$^{2+}$ (M = V, **15e⁻**; Cr, **16e⁻**; Mn, **17e⁻**; Fe, **18e⁻**),

CoCp$_2$, **19e⁻**;

NiCp$_2$, **20e⁻**;