BioInorganic Chemistry
Chemistry 3391B

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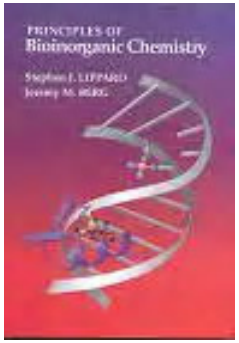
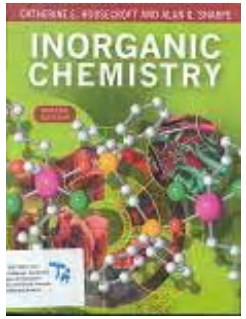
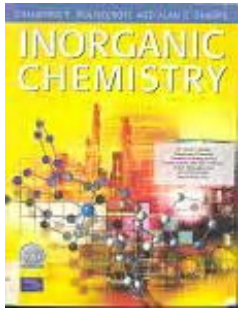
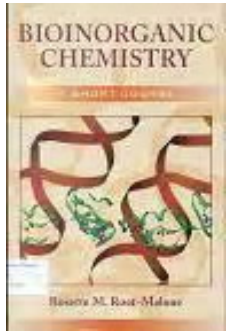
B) Important chemistry and special inorganic chemistry for bioinorganic chemistry

1. Periodic table
   a. Elements, transition metals, trends, electronic configurations, d orbitals
   b. Hard and Soft metals and Ligands
   c. Sizes of cations, atoms, anions; size to charge ratio
2. Metal-Ligand complex formation
   a. Special molecules that bind metals
      1. Ligands – special features of ligands
      2. Shapes of complexes
   b. Equilibrium constants
      1. K_F
      2. Chelate effect
      3. K's for multiple Ligands
      4. pK_a









Recommended text Books

Principles of Bioinorganic chemistry by Lippard & Berg. TAYSTK QU 130.L765 1994 (On heavy demand (2-hour loan) at the Taylor Library and in the book store.)

**Bioinorganic chemistry: a short course by Roat-Malone. QU130.R628b (On heavy demand (2-hour loan) at the Taylor Library and in the book store.)

Bioinorganic chemistry: inorganic elements in the chemistry of life: an introduction and guide by Kaim and Schwederski. (On heavy demand (2-hour loan) at the Taylor Library.)

The biological chemistry of the elements: the inorganic chemistry of life by da Silva and Williams. QU4.S586b 2001 (On heavy demand (1-day loan) at the Taylor Library)

File revision information: Date last revised: R18-hijK - Filename: 3391B-B-2018-INORG-R18-reduced-heme-moved--fghijK.doc

To start then

1. Periodic table
   i. Elements, transition metals, trends, electronic configurations, d orbitals
   ii. Hard and Soft metals and ligands
   iii. Sizes of cations, atoms, anions; size to charge ratio

Summary : This section provides the background necessary to understand the following scenarios:

1. Zn exists as the 2+ cation only and binds to sulfur in cysteine as well as to nitrogen in histidine but Na exists only as the 1+ cation and never binds to cysteines, rather preferentially to oxygen in water, and even better, to oxygen in carboxylic acids, the O^-.
2. The electronic configuration of each element and its place in the Periodic Table controls its chemistry.
3. For metals in Groups 3-12 (V – Zn) the key to the chemical properties is the arrangement of the 5 3d orbitals** and the electron distribution in the d-orbitals.
4. Equilibrium is a thermodynamic property that tells us energetically which way the reaction will go but not how fast.
5. The chelate effect is very important as biological reactions benefit from the enhancement in binding constant. Reaction rates tell us how fast the reaction takes place.

**By "arrangement", I mean the energy of each of the 5 3d orbitals when the metal is part of a complex – see slide 41.

L-B	R-M	K-S	In Housecroft 2nd ed.	Problems to do
1-2			See ch. 1, p 20-21; Ch. 20, p 557-564.	If blank – see later

Some of the many different Porphyrin rings in biology - see LB 131

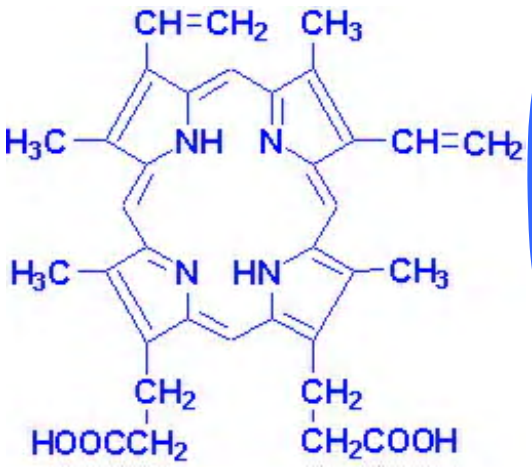
Heme= iron protoporphyrin IX

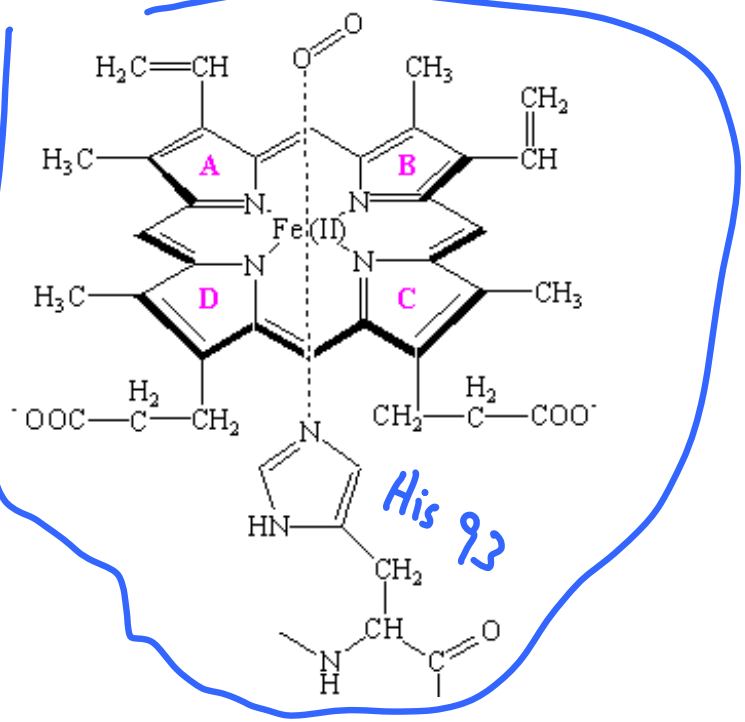
freebase

protoporphyrin IX

-see next slide

how to memorize



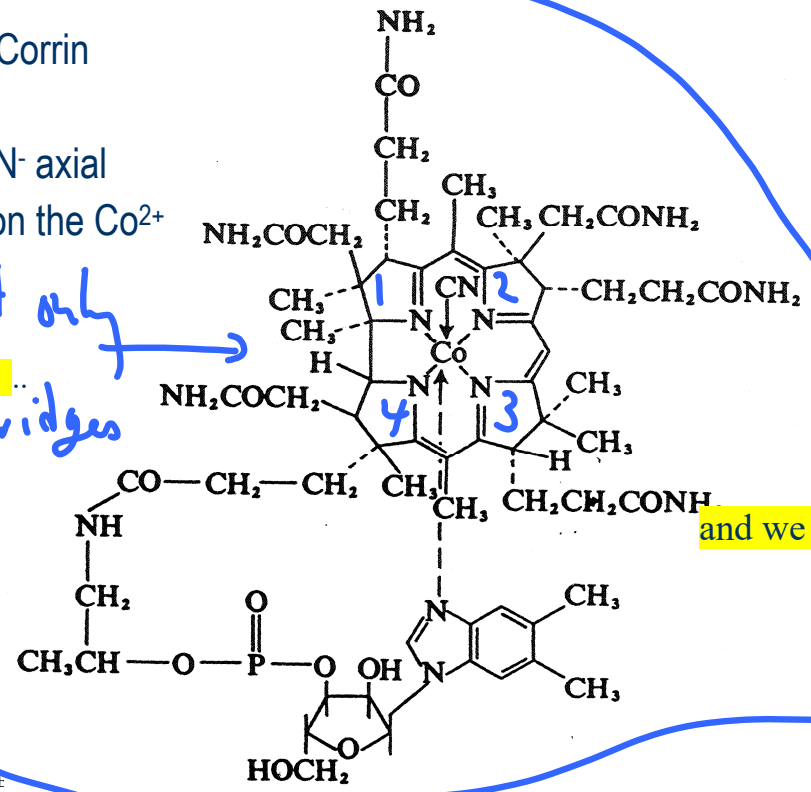


Cobalt Corrin

Vit B12

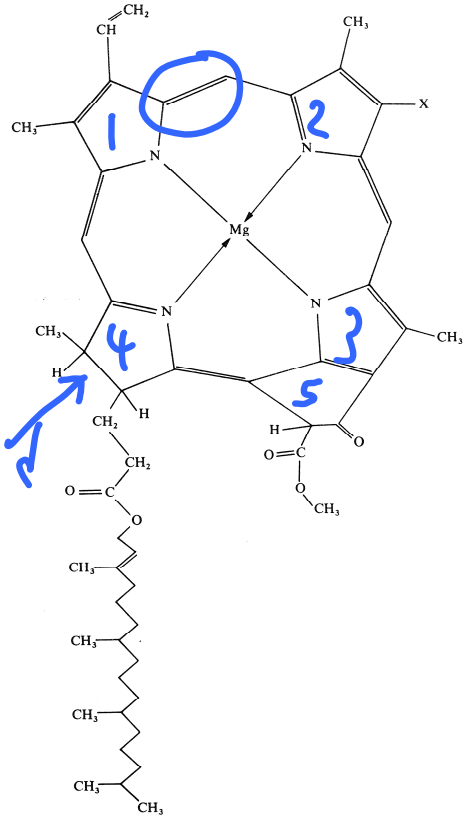
Note CN^- axial ligand on the Co^{2+}

but only 1150 ... 3 bridges



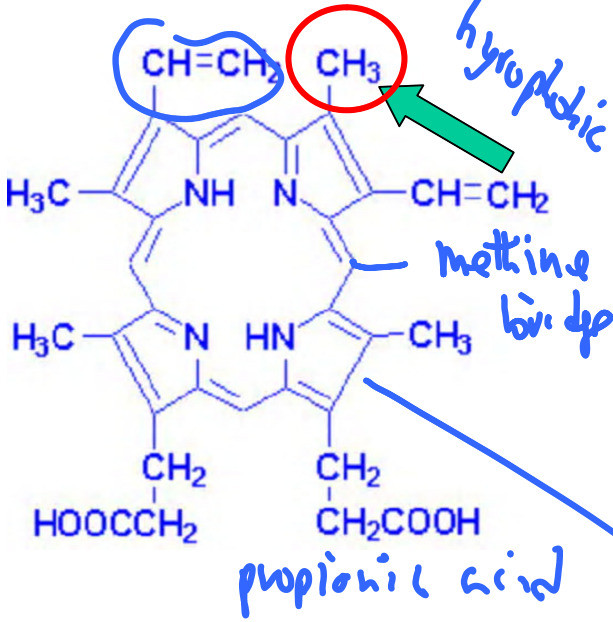
and we must draw what??

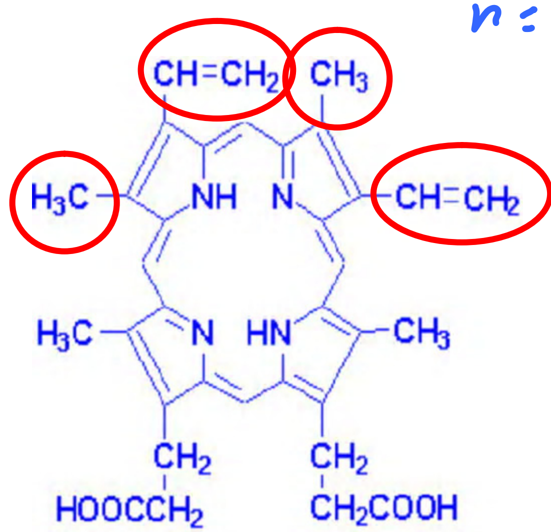
Chlorin in chlorophyll →

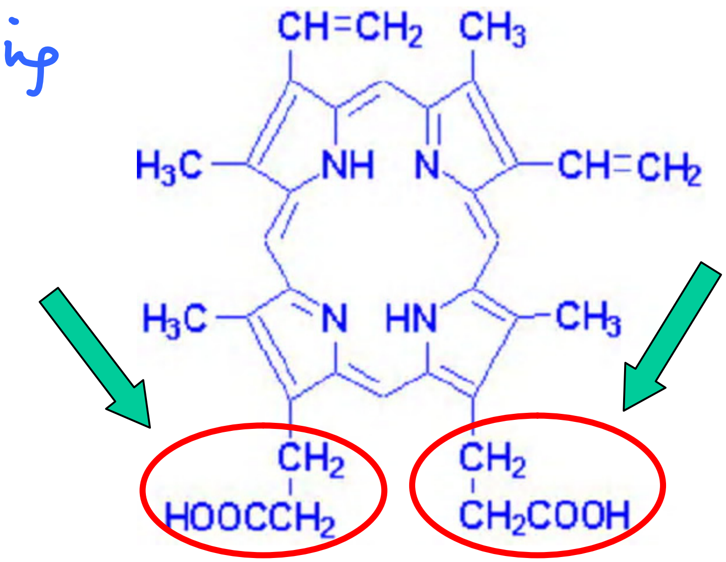


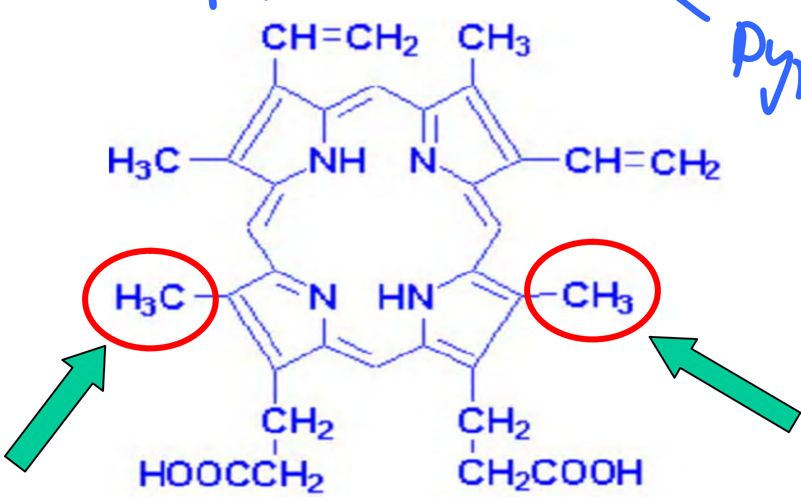
vinyl methyl 18 π electrons = aromatic ring
n = 4

How to remember how to draw PPIX

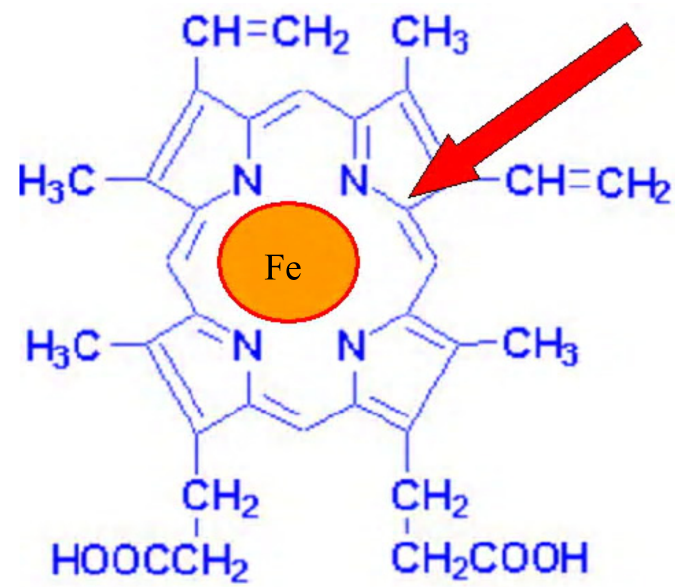








pyrrole



Iron protoporphyrin IX – usually called ‘heme’ – Fe can be 2+, 3+ or 4+
Key to heme proteins – see myoglobin, hemoglobin, catalase, and many others – variations in the peripheral groups are found in proteins like cytochrome c. Many here proteins use the imidazole nitrogen (HIS) for the ‘proximal’, 5th position amino acid.

The Periodic Table…

1. We know about Rows and Columns
2. Rows: Periods – generally the only link is the same (s, p) or 1 less (d) valence shell is being filled – so these elements are of similar size (always decreasing) BUT their properties are completely different.
3. The columns indicate the Atomic Orbital (AO) being filled 1 & 2 –s; 3-12 (d) (or (f)); 13-18 p
4. GROUPS – have numbers & names

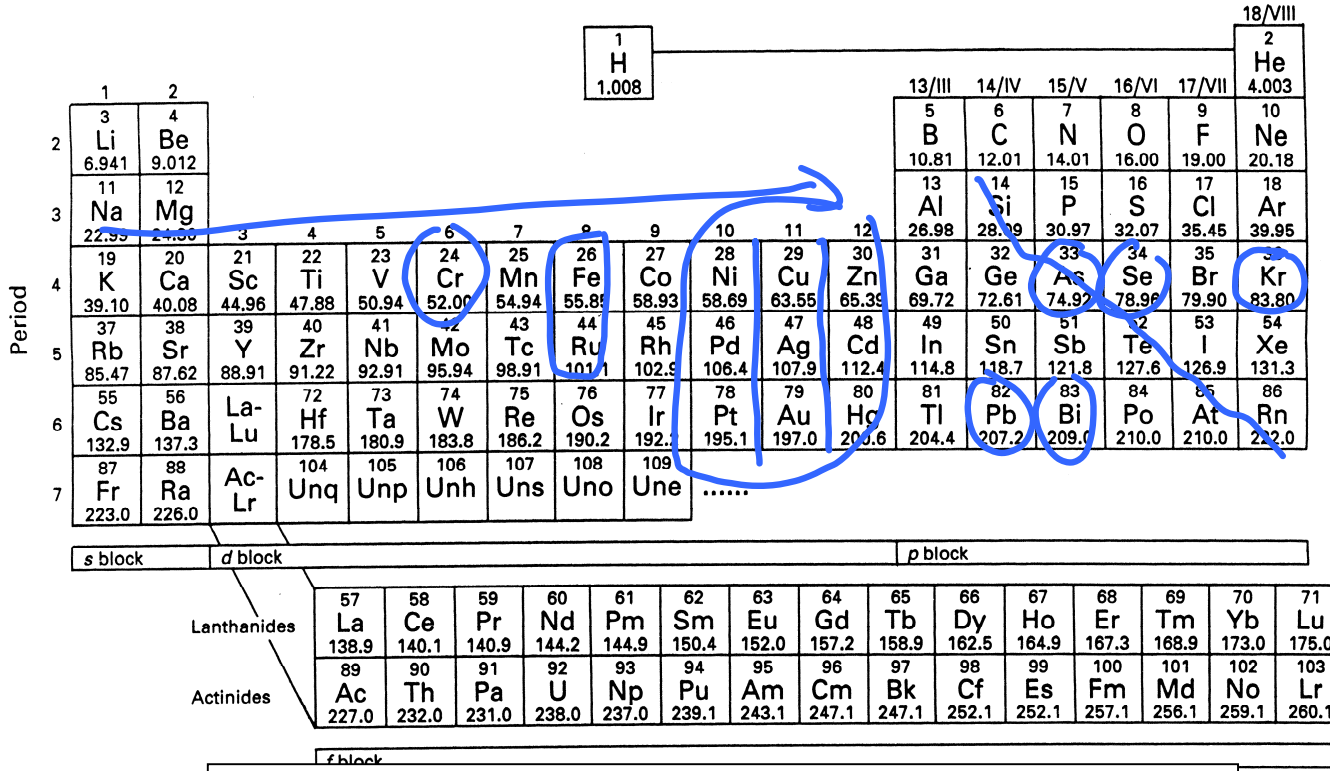
Alkali metals (1) Alkaline earths (2) Chalcogens (16), Halogens (17) (18) Rare gases

All MAIN groups (13-18)

8. Groups 3-12 –d-block elements called either Transition Metals or d-block metals (dbMs) – see →
9. Major groups we will study (learn) 1, 2, 12, 17 + all the others see below…

So where are our key metals? Next slide

The Periodic Table



→ Why not all called Transition Metals? Well, the definition requires at least 1 d-electron. So, many oxidation states (which ones?) and Zn^{2+} don't fit. D-block metal (dbM) includes all elements groups 3-12.

L-B	R-M	K-S	Problems to do
1-2			Check – Housecroft & Sharpe Inorganic Chemistry 2nd Ed – p 20 -

Learn this table

a table like this on the

These are the metals that are found throughout biology and for which we know the oxidation state and some of the complexes that form.

For a metal complex, we need to know:

1) The oxidation state of the metal in the complex
2) The electronic configuration of this oxidation state
3) The electron distribution if this a dbM – we need to know which 3d orbitals the electrons occupy – to do this we need to know:
4) The 3d splitting pattern for that geometry
5) The ligand field strength(s)* of the ligands
6) Determine whether the electrons are spin parallel or paired up (high or low spin)

*essentially the electron donor strength

Hard/ Int/Soft? Complete later	Preference for ligand donor group?	M	+1	+2	+3	+4	Example of molecules in biology	Example species where this molecule is found
		Na	+1				Nerves all cell membranes	all arganisms
		Mg		+2			Chlorophyll; ATP activation	Plants and all organisms
		K	+1				Nerves – cell membranes	All organisms
		Ca		+2			Muscle action – bone formation – shell formation	
		Sc						
		Ti						
		V		+2				
		Cr			+3		+6 – highly toxic +3 insulin production	humans
		Mn		+2				
		Fe		+2	+3	+4	Hemoglobin – myoglobin; +3 and + 4 catalase	mammals
		Co	+1	+2	+3		Vit B12 (CN^-)	All mammals
		Ni		+2				
		Cu	+1	+2			Hemocyanin – superoxide dismutase ($O_2^- \rightarrow H_2O_2$) Cytochrome oxidase	Invertebrates – lobsters, crabs – blue blood; mammals
		Zn		+2			Carbonic anhydrase (1 Zn per molecule)	mammals
		Cd		+2			+2 – toxic	
		Hg	0 and +1	+2			0 & +1 & +2 and methylated (CH_3Hg^+) – all toxic – worst is methylHg^+	
		Pb		+2		+4	+2 & +4 – both toxic	
		As			+3		+3 (& +5) – toxic	

Comparison of cations and anions

We can identify the biologically important elements from Group 1 and 2 , dBM and Group 13, 14, 16 and 17.

The size to charge ratio is important in biological coordination chemistry

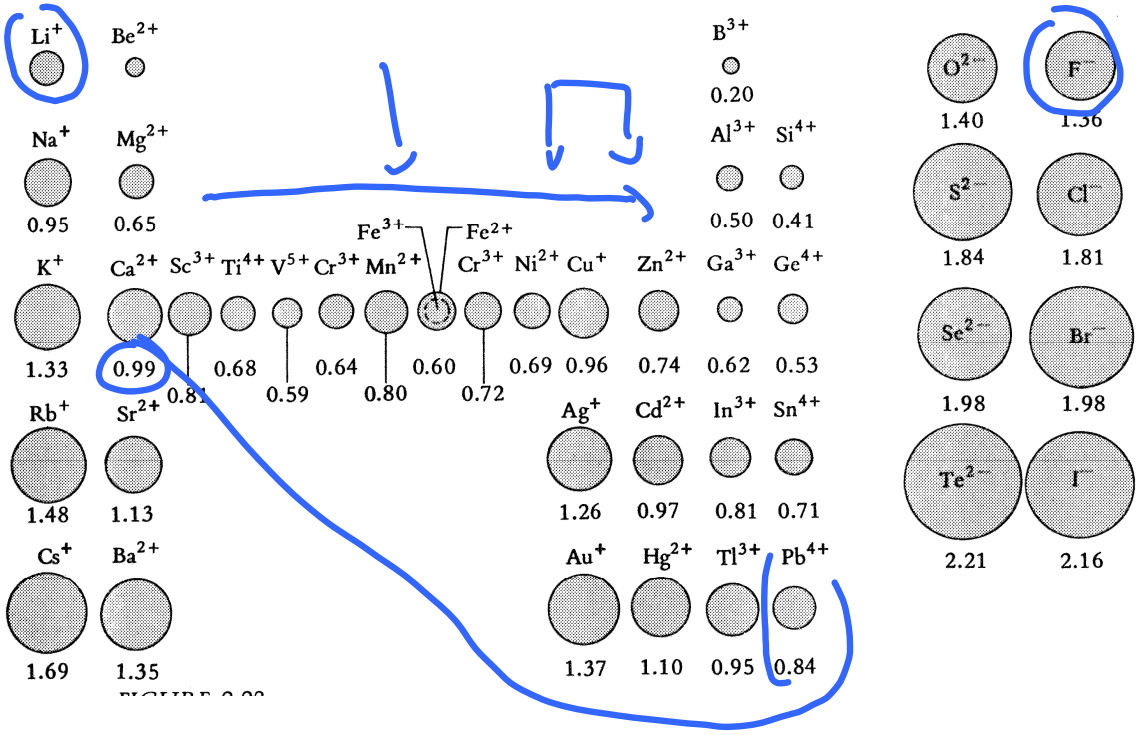
Biological ligands recognise metals often by the charge/size ratio alone

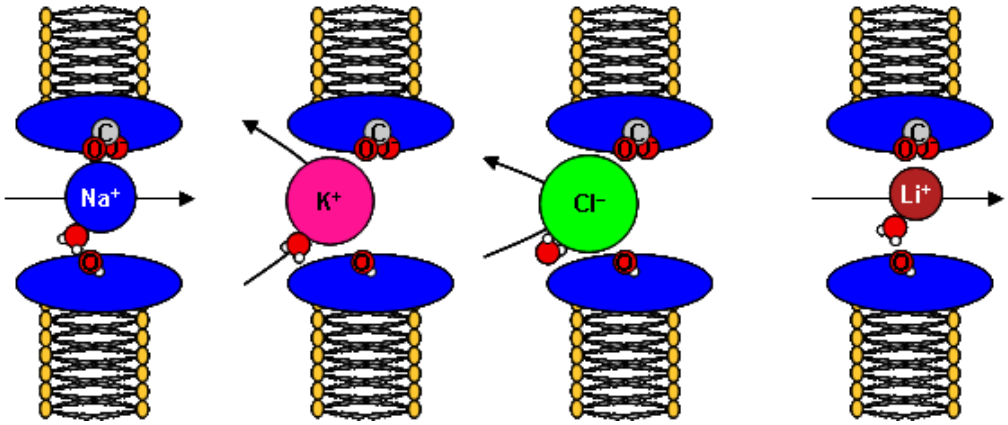
Trends:

1. Down the groups – always larger whether neutral, cation or anion because of the extra protns and neutrons and core electrons.
2. Across rows: different trends not so easy – track the 1st IE - high IE=smaller.
3. The greater the positive charge = smaller; negative charge = larger.
4. So Ca^{2+} is smaller than ……
5. And S^{2-} is larger than ……..
6. BUT d-block metals (dBM) all about the same.

This fig also emphasizes that isomorphous replacement can take place – substitute one cation for a cation of the same size – Pb^{2+} for Ca^{2+}.

Needs **hard-soft** rules followed though. So less likely to substitute Cd^{2+} for Ca^{2+} - why not? (See below)





This is a description of how an enzyme pump that pumps 2 K^+ into a cell and pumps 3 Na^+ out of a cell works. This is a 'passive' mechanism. We will see more complex mechanism in the Biology unit (section 3). See also the cyclic polyethers and the antibiotics – valinomycin as synthetic examples of ion selectivity based on size.

Special molecules that bind metals

Ligands – special features of ligands

1. Control the function of the metal
2. Change the shapes of complexes
3. There is an effect of shape on the energies of 3d orbitals (dbM's)
4. Equilibium reactions – the equilibrium constant, K_B
5.

Ligands – special features of ligands

(i) Biologically important ligands

N- (as R_2N:)

S- (as RS:R and RSH and RS^-)

O- containing (as RC=O:, RO:R, ROH, and esp RO^-)

and also water

OK – let us look at a typical small complex

(ii) Chelating ligands used to detoxify metals

BAL - soft (S)

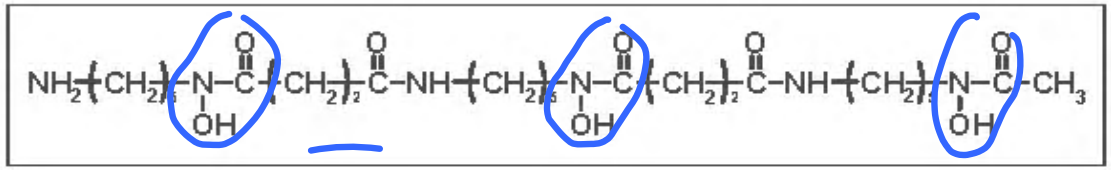
D-penicillamine – medium (N)

EDTA – hard (O)

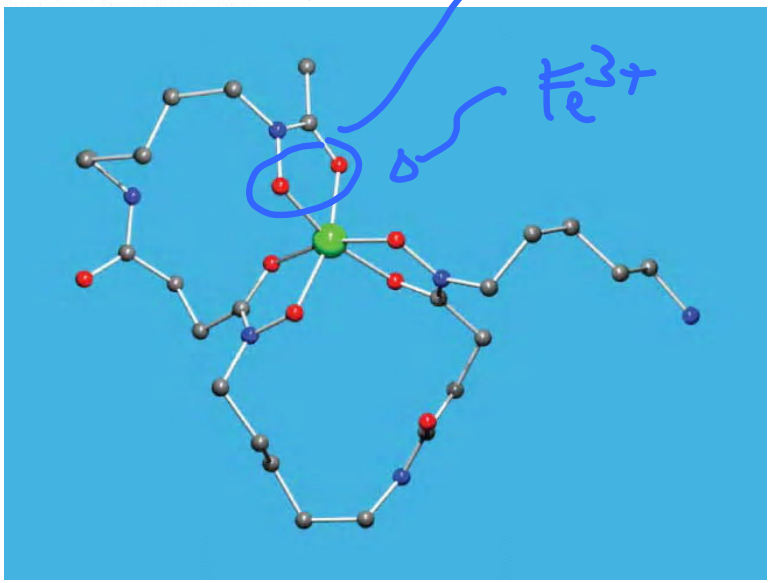
Desferrioxamine B see LB p 13-14 – hard (O)

(All these structures coming)

And note – later in "Chelators" in "Toxic Metals"



Desferrioxamine B



Desferrioxamine B complex with Fe(III) used to remove excess iron in humans – a hexadentate chelator

3103

Hard-Soft Metals and Ligand atoms

1. Pearson Hard-Soft (Acid-Base) theory applied to metals and ligands – a critically important aspect of biological metal-based chemistry
2. Ca … Mg… Co… Cu ..
3. But, Cu^{+} and Hg^{2+} are really soft
4. So bind preferentially with ?
5. Although the metals are the same in biology, the ligands include amino acid side groups – come back to here once we have covered the amino acid section and add in the amino acids that bind metals –
6. remembering that uncharged N is intermediate, so binds all metals.

Need to know –

Table 2. Classification of Hard and Soft Acceptors and Donors [3]

Acceptor		
Hard	Intermediate	Soft
H^+, Na^+, K^+, Be^{2+}, Mg^{2+}, Ca^{2+}, Mn^{2+}, Al^{3+}, Cr^{3+}, Co^{3+}, Fe^{3+}, $As(III)$ As^{3+} (with RO^-)	Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}	Cu^+, Ag^+, Au^+, Tl^+, Hg^{2+}, CH_3Hg^+ As^{3+}(with RS^-) Cd^{2+}
Donor		
H_2O, OH^-, F^-, Cl^-, PO_4^{3-}, SO_4^{2-}, CO_3^{2-}, O^{2-}	Br^-, NO_2^-, SO_3^{2-}	HS^-, S^{2-}, RS^-, CN^-, SCN^-, CO, R_2S, RSH
		Cys Met

As^{3+} is confusing because it is really a metalloid – so has both ionic and covalent properties – when covalently bound to RS^- is acting as a soft metal. When bound to oxides, then is hard.

L-B	R-M	K-S	Problems to do
21-23; 24-25	Table 1.7, p 6	P 15; also 13-20 generally	Which metals do you predict will bind to metallothionein? See Fig 2.1 in L-B – why – search the web – what other metals bind to metallothionein??

1 Tu. 13th Feb.

Are there any systematic ways of predicting which metal binds to which ligand?

In synthetic chemistry, it's not too easy - change the conditions and almost any ligand will coordinate any metal, BUT in biology, nature took the easy way out most of the time, or, why take chances and - take the easy route and react ligand sand metals that always react together...

Hard acid - Soft base theory

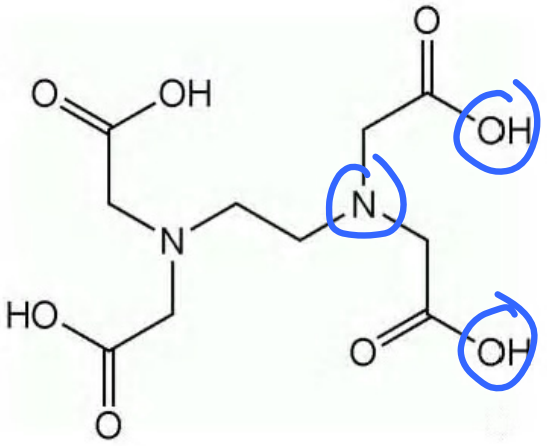
Hard acids react with hard bases and

Soft acids react with soft bases

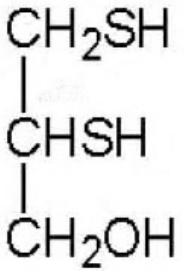
And intermediate acids and bases? Well, they react with everything.

Extremes - very hard, why?

Very soft, why?



$EDTAH_4$



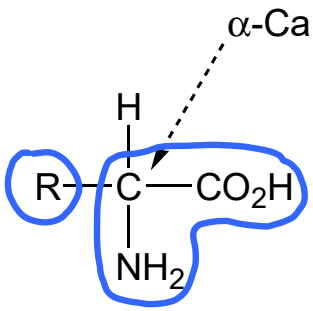
BAL

must know page

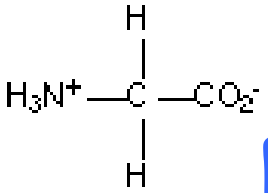
Biological Ligand molecules

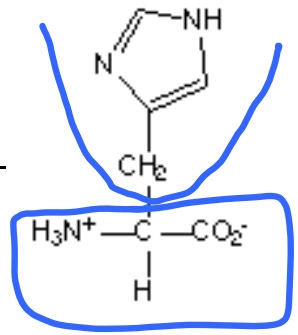
Excellent source for information http://en.wikipedia.org/wiki/List_of_standard_amino_acids

We'll jump ahead by bringing in those amino acids likely to bind metals as well here.



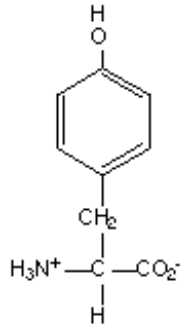
GLYCINE





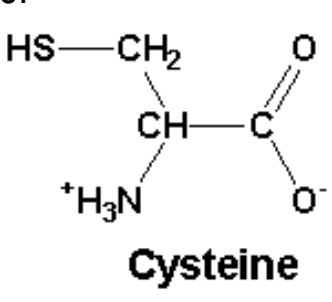
HISTIDINE

HIS - imidazole group N



TYROSINE

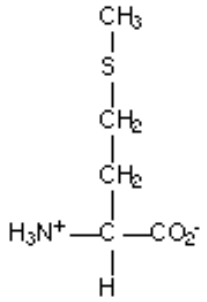
TYR O



Cysteine

CYSTEINE

CYS S



METHIONINE

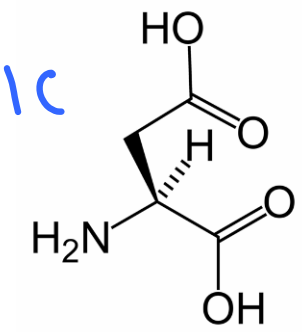
MET S

Oxygen from Asp – aspartic acid and

Which are the donor atoms?

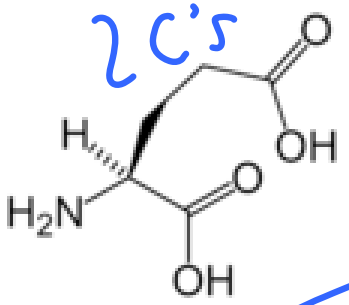
Hard, Int or Soft?

Then there are these biological ligands:



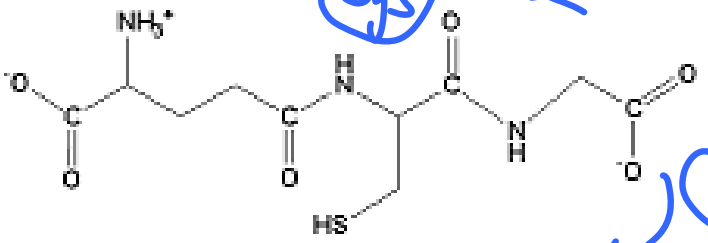
1C

Glu, glutamic acid



2 C's

cys



Glutathione

2 GSH

2-

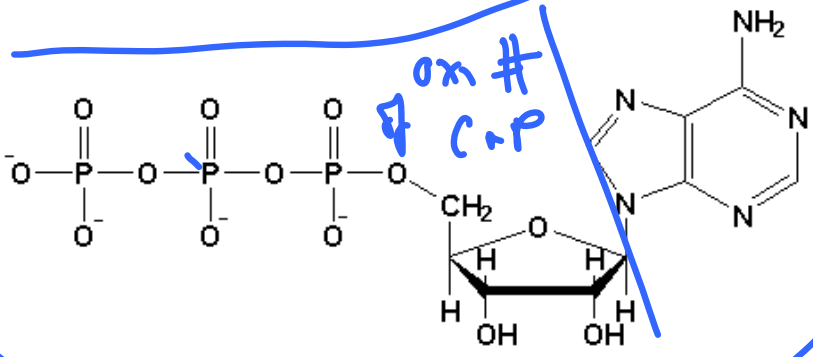
1- 1-

GSSG

2+

2+

ox # of ATP

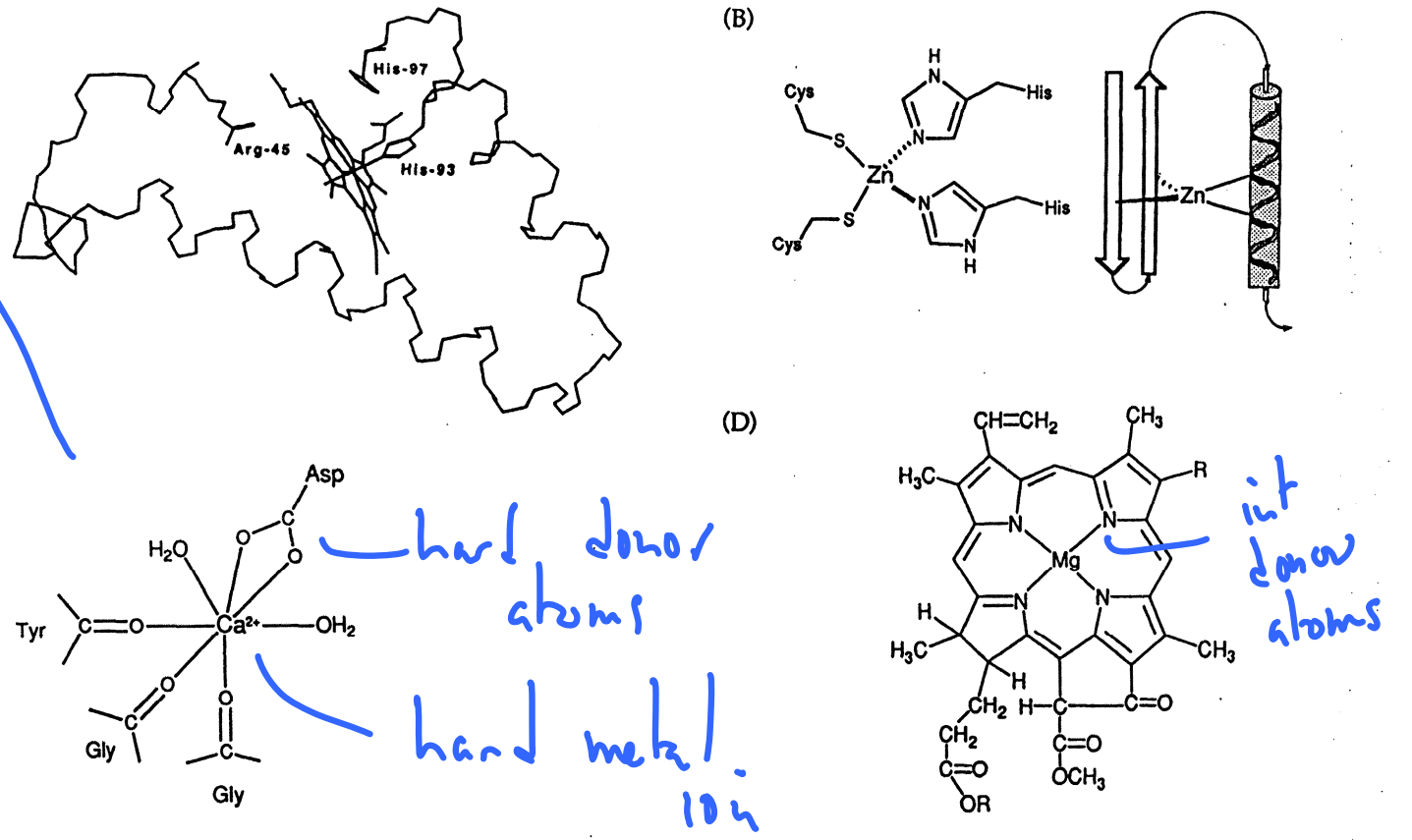


Adenosine triphosphate (ATP)

L-B	R-M	K-S	Problems to do
22 44; 46; 47		15-16; 16-38 everything about ligands,and metals, and rings; also 3d splitting	If blank – see later

Structural form of the metal changes the function (from before)

1. Coordination by **ligands** – ligands are either neutral with nonbonding pairs (like NH_3) or anions like OH^- to stabilize the metal cation.
2. The more oxidized the metals, the more anionic the ligands have to be.
3. Biological LIGANDS – see after Hard-Soft slide – we must relate Hard-Soft character to the metal cation and the ligand



hard donor atoms

hard metal ion

int donor atoms

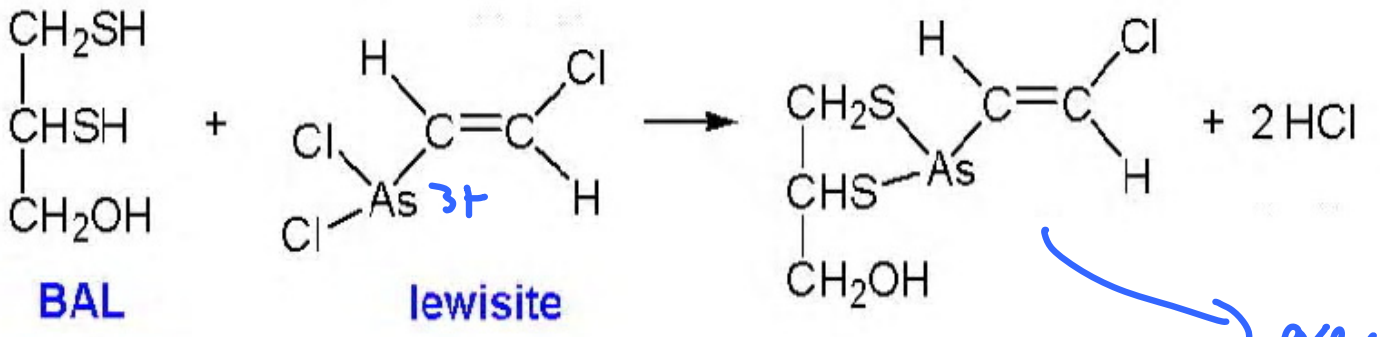
Figure 1.15 Coordination modes for metal binding to metalloproteins and peptides. (A) The heme prosthetic center and a portion of the backbone in myoglobin. (B) Bound Zn^{2+} in a zinc finger. On the right the portion of the protein backbone that forms the "finger" is traced. Figure 1.19 gives more details on such schematic diagrams. (C) The metal-binding domain of a Ca^{2+}-activated enzyme (phospholipase A_2) showing coordination of a chelating carboxylate, two water molecules, and three backbone carbonyls. (D) Chlorophyll from the light-harvesting complex of the photosynthetic reaction center.

What are the ligands – the atoms next to the metals in these examples? Write out the molecules without the metals in B, C and D. You'll need to check your biochemistry book for the amino acids – also coming in 3 lectures here.:

L-B	R-M	K-S	Problems to do

Recall arsenic poisoning in shell fish

So, how does BAL work with Lewisite?



excreted.

Chelation in action .... Didentate attachment of the BAL to the As

Nature 156, 616-619 (24 November 1945) | doi:10.1038/156616a0

British Anti-Lewisite (BAL)

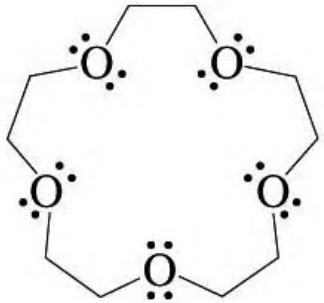
R. A. PETERS , L. A. STOCKEN & R. H. S. THOMPSON

Abstract

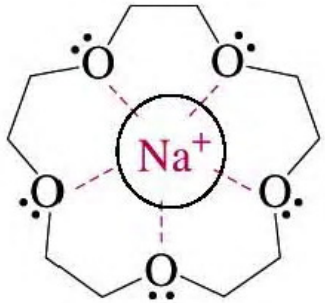
IN the first fortnight of the War (1939) fundamental research was initiated in the Oxford Department of Biochemistry by Peters and carried out under his direction by a group of workers as an extra-mural research with the support of and for the Chemical Defence Research Department, Ministry of Supply; the object was to find antidotes for vesicants, both arsenical such as lewisite (CH.Cl: CH.As.Cl_2) and also those of the mustard gas type. In this brief review, the main facts are given about the discovery of the antidote to lewisite known as *BAL*, owing to its medical importance; more detailed papers based upon the original reports are being prepared. An attempt is made to include the more relevant work from elsewhere and also to focus the main stages in this discovery, as this may prove useful in planning future work of this type.

How do cyclic polyethers "crown ethers" work?

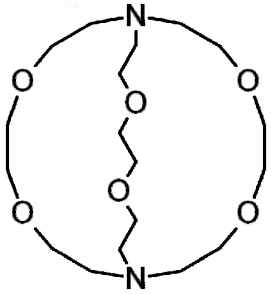
Na^+
guest
Na^+ 1.80Å

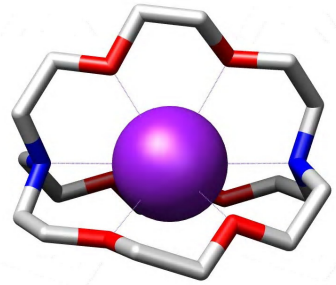


host
[15]-crown-5
cavity diameter = 1.7–2.2 Å



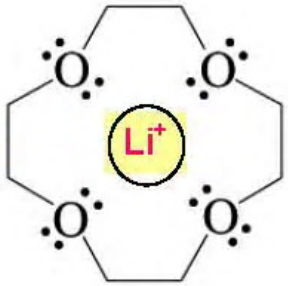
inclusion compound





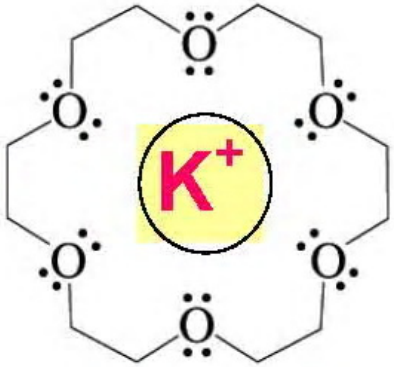
[2.2.2]cryptand

Li^+ 1.20Å

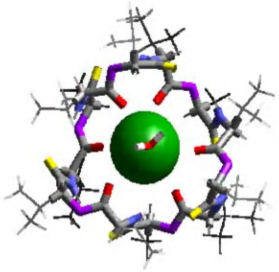


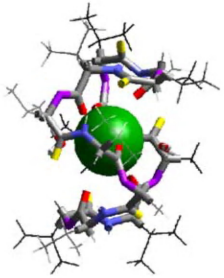
[12]-crown-4
cavity diameter = 1.2–1.5 Å

K^+ 2.66Å

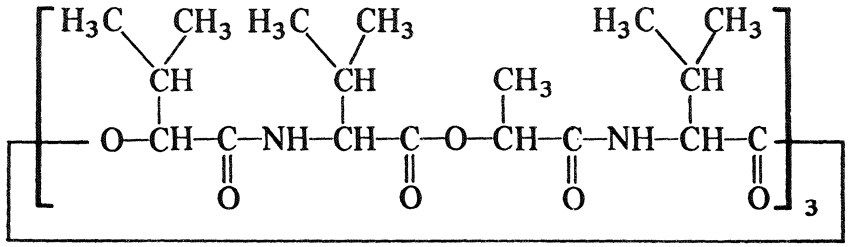


[18]-crown-6
cavity diameter = 2.6–3.2 Å





antibiotics that function to disrupt the membrane transport



Valinomycin

Special molecules that bind metals:

Shapes of complexes

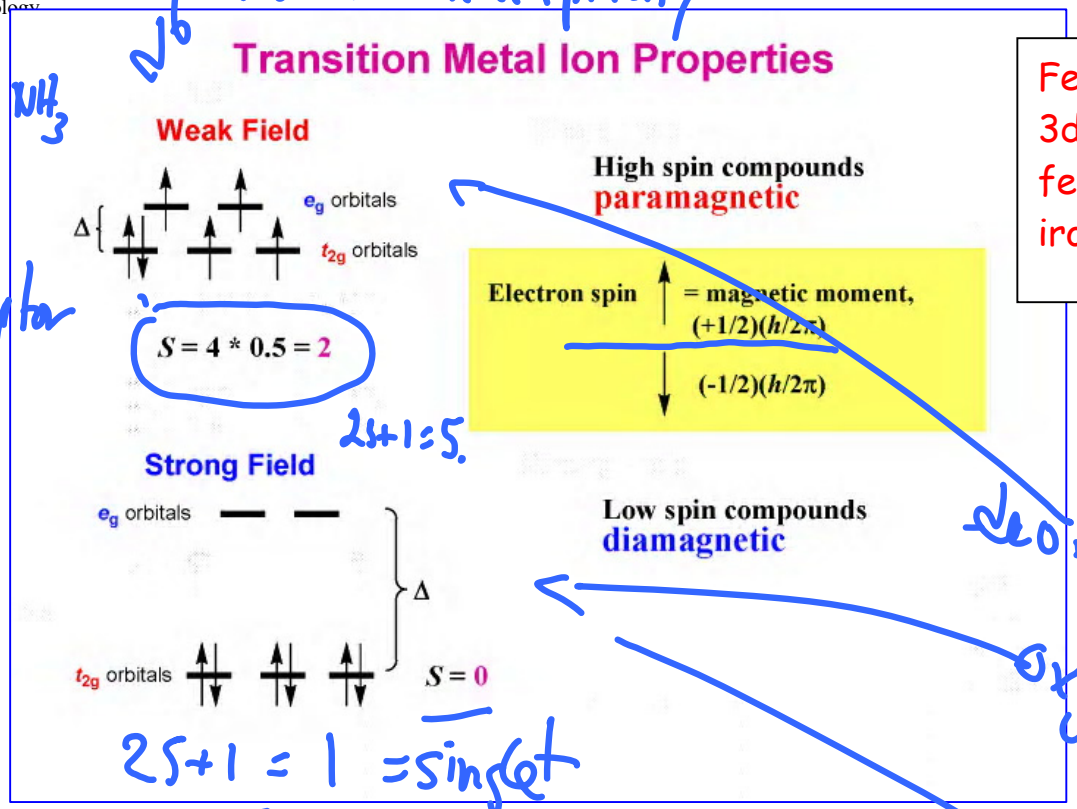
1. Forming complexes is the key to many biologically important reactions.
2. In fact even metals not thought to form well-defined complexes (Group 1 & 2), preferring to exist as isolated ions, <u>are always</u> surrounded by water – a shell of 6 – 8 water molecues, and in their biological passage – these molecules are transported often into and then out of of cells, these transporters or pumps have tuned groups to bind to the metals – **hard metals so hard attaching atoms – a good guess would be?**
3. Group 1 and 2 metals maintain osmotic pressure across membranes, this same atom is part of an enzyme molecule used to move these metals through a lipid bilayer that is the membrane.
4. On the other hand, the dBMs are always coordinated to something – being transported or functioning. The chemical nature of the attached ligands and the shape **<u>control function.</u>**
5. We are interested in:
    a. The possible shapes of complexes that form
    b. The atoms that bind the metals and the molecule that inludes those atoms – the ligands
    c. The effect this shape has on the atomic orbitals of the coordinated metal – most significantly, the effect on the 5 3d orbitals of the dBMs
    d. The binding constants, the K_F, showing especially the relative bind strengths. (In a competition, the metal with the greater K_F will win the ligand!)
    e. The form of the ligand depends on its state in acidic, neutral and basic conditions, this is controlled by pK_a.

Effect of ligand field strength on the splitting of the 3d orbitals.

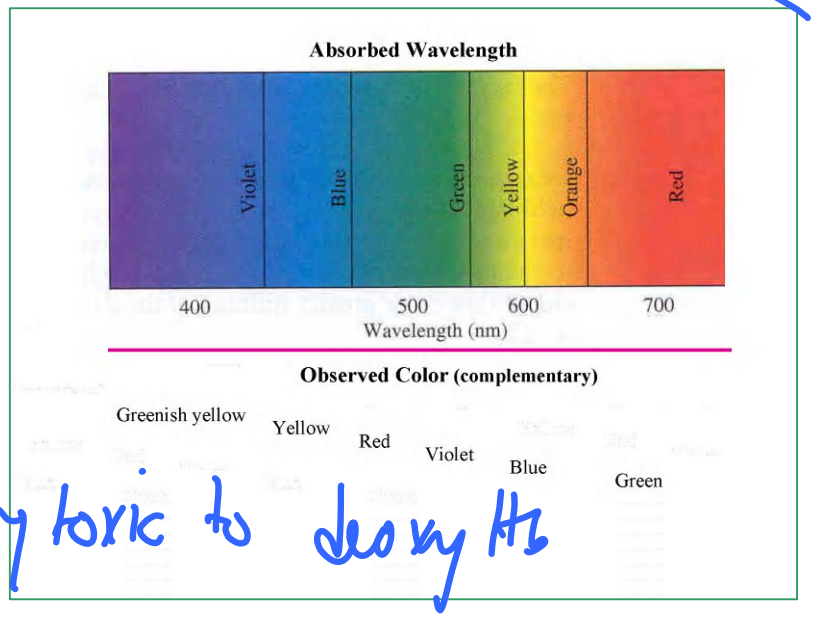
Weak field ligands

1. Strong field ligands
2. Why is this important for us to understand?
3. Myoglobin & Hemoglobin
4. There is a theoretical basis – not for us in detail – just 4 examples, "The Spectrochemical Series"
5. Weak field: fluoride, hydroxide – intermediate: water and oxides, RO^-,- Strong field: cyanide, carbon monoxide
6. (H&S p 559)
7. What does all this have to do with biological molecules? Well, the field strength controls the availability of electrons and whether the molecule is going to be DIAMAGNETIC OR PARAMAGNETIC – and we will see this in the colours. Paramagentic metals are a problem in biology = RADICALS

L-B	R-M	K-S	Problems to do
288 - Hb			If blank – see later



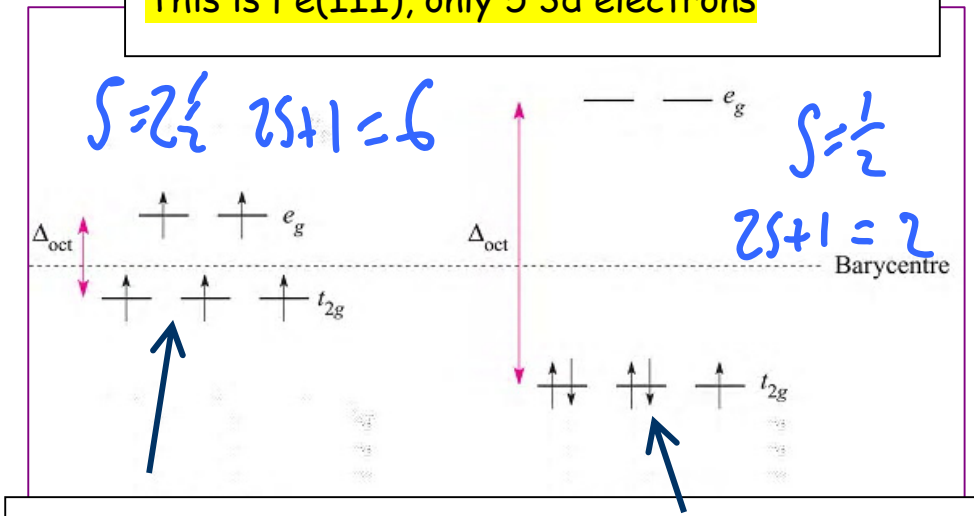
Fe^{2+}
$3d^6$
ferrous iron

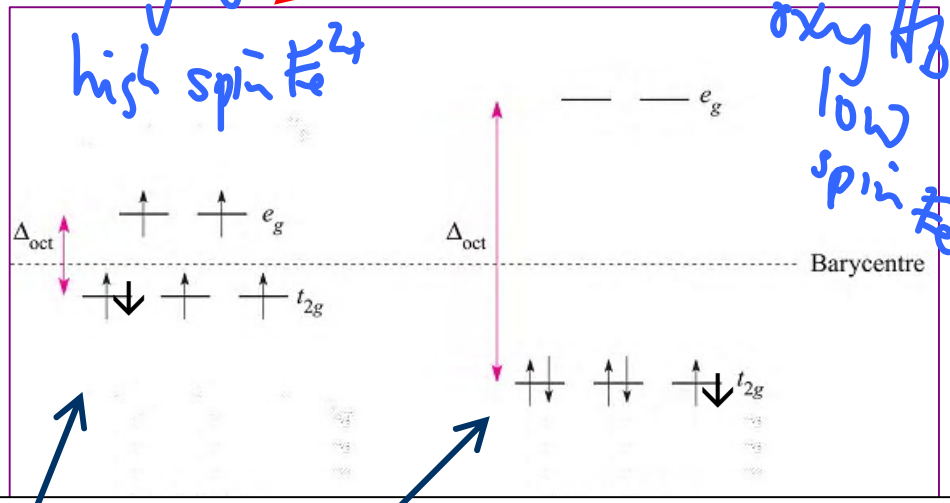


Fe(III) has 5 3d electrons: $3d^5$ and is always paramagnetic whereas Fe(II) has 6 3d electrons and is only paramagentic when high spin. Intermediate spin is also possible – how? What is the value of S? (Found? In heme proteins – HRP and cyt c'?). Low spin Fe(II) is always diamagnetic (needs what type of axial ligand?)

For Fe(II) - add 1 electron! To make 6 here

This is Fe(III), only 5 3d electrons





Weak field (F^-, OH^-, intermediate H_2O and also 1 N from HIS plus H_2O)

Strong field CN^-

Weak field (2 x H_2O and also 1 N from HIS plus H_2O)

Strong field - dioxygen with HIS-N in 5th position and His-N plus CO

Fe(III) always unpaired electrons, therefore, always paramagnetic Fe(II) only paramagnetic if high spin - low spin is diamagnetic

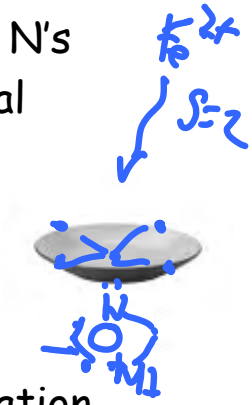
The Spectrochemical Series (for Chem 3391B)

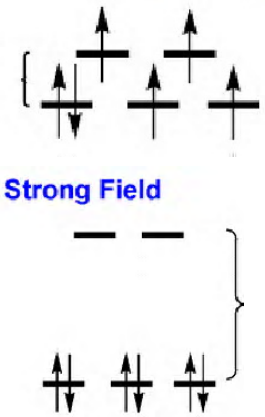
σ + π donor σ only σ + π acceptor

Weak F^- OH^- RO^- (RCOOH) Int H_2O NH_3 Strong PPIX-4N's O_2 CN^- CO

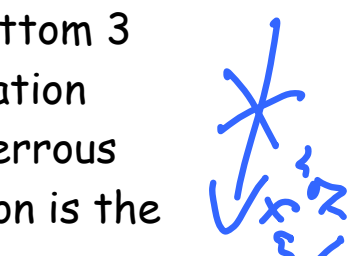
A quick (very quick) primer in the dioxygen chemistry of hemoglobin –see Hb section --

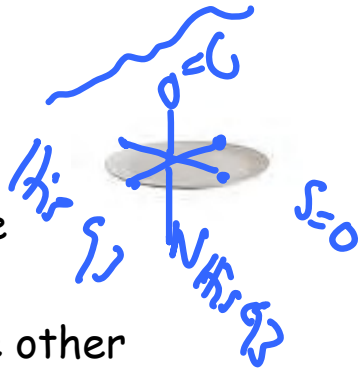
1) DEOXYhemoglobin (in the veins) has 1N from imidazole (proximal, or 5th position), 4 N's from the protoporphyrin IX ring (the heme ring) and nothing in the 6th position or distal position. Because of this (5-coordination not 6 = Weak Field) the 6 electrons in Fe^{2+} adopt a High Spin electronic configuration ($4x+\frac{1}{2}$ =sum of spins= 2). High Spin Fe^{2+} is larger than Low Spin Fe^{2+} so does not fit into the hole in the heme ring – the ferrous ion pops out of the ring a bit on the side of the proximal histidine.





When oxygen binds – this makes the OXYhemoglobin and the 6 coordination exerts a Strong Field, the energy gap between the top 2 and the bottom 3 3d orbitals increases, and the electrons pair up = Low Spin configuration (S=0).. Low Spin Fe2+ IS SMALLER THAN High Spin Fe2+ so the ferrous iron moves back into the plane of the ring. (An alternative explanation is the the electron distribution in oxyHb/oxyMb= Fe(III) + O_2^-.) How does all this movement control oxygenation? Well, there are four hemes in hemoglobin, and they are all connected through a hydrogen bond network. When the Fe drops out of the plane it pushes the Histidine down, this mechanically moves the protein. So, all the other hemes 'know' that one heme is not in the DEOXY-or sprung state. Conversely, when the Fe picks up the dioxygen, movement back into the plane pulls the attached Histidine and 'tells' the other hemes that it is now oxygenated. This 'spring-loaded' effect also has the property of delaying oxygenation until there is plenty of dioxygen available – so all 4 heme groups can pick up oxygen at once and then travel fully oxygen-loaded to the muscles.

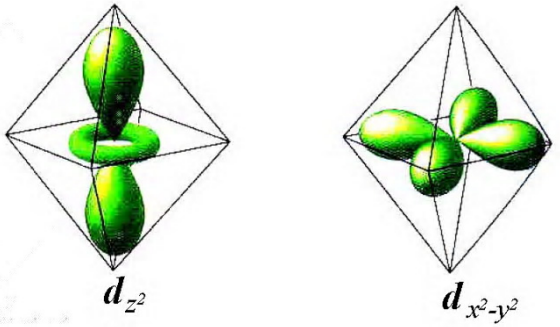


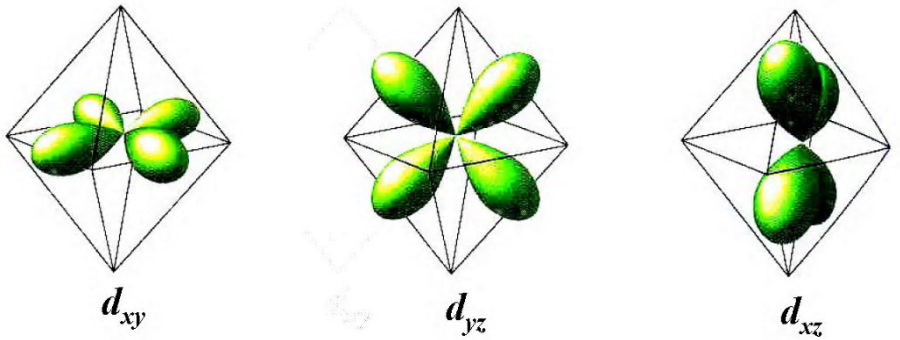


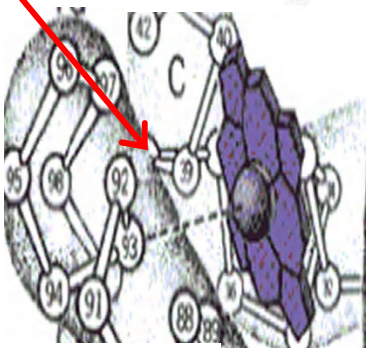
3d orbital arrangements –1 – the shapes of the 5 3d orbitals (2=the energies)

1. The lobes of the electron density in the 5 3d orbitals point at the vertices of the octahedron
2. The number of electrons in the 3d orbitals in each orbital and whether they are all the same spin (high spin) or paired up (low spin) changes the size of the cation.
3. Many dbM complexes form octahedral shapes (ML_6) the 3d orbitals will interact with those attached ligands – for example, look at the heme group in myoglobin – 6 ligands bind to the Fe^{2+}.
4. This is the basis of the dioxygen binding of myoglobin and hemoglobin because the energies of each 3d orbital (there are 5 here) can be different and depends on the ligand (or no ligand) attached. Here we have 4 the same – N's on the protoporphyrin IX ring (PPIX) or heme ring, 1 N from HisF8 or His93 histidine imidazole side chain, and 1 empty spot (the 6th position) for water, or dioxygen or CO – but tight because of HisE7.
5. To memorize – the 3d shapes and the alingment of His93 connected to the Fe –heme and the O_2 and CO in Myoglobin.

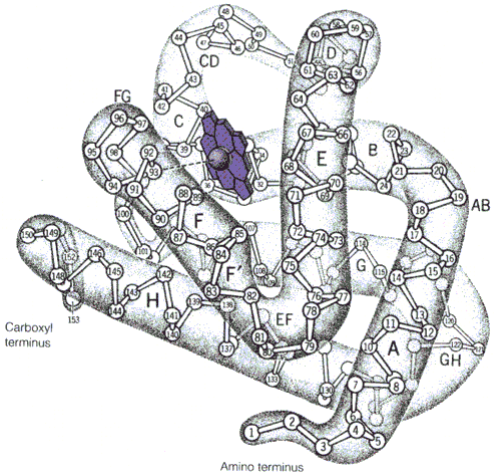
His F8, means 8th amino acid in helical coil F (6th). We will call it His93. meaning 93rd amino acid from the N-terminal. HisE7 is His64. So where is His E7

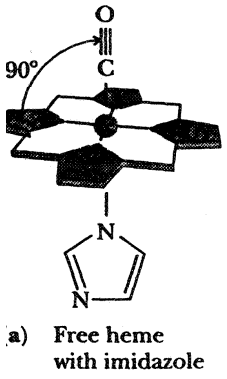




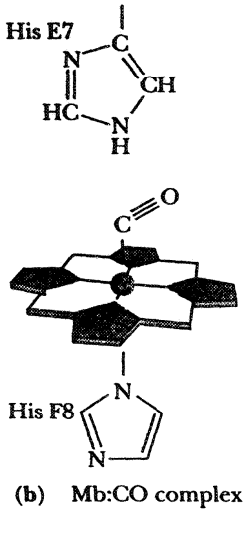


Find the 6 ligand s- 5 are N's, the 6th is the dioxygen – O_2 – see below RHS

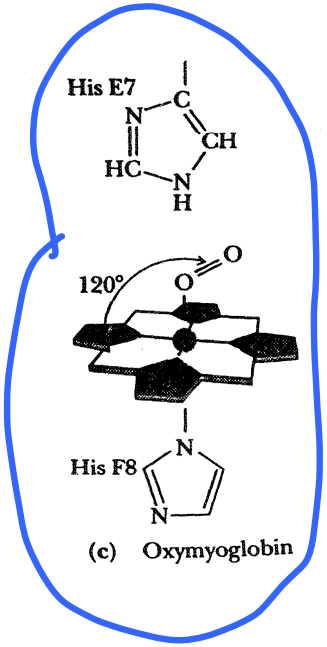




(a) Free heme with imidazole



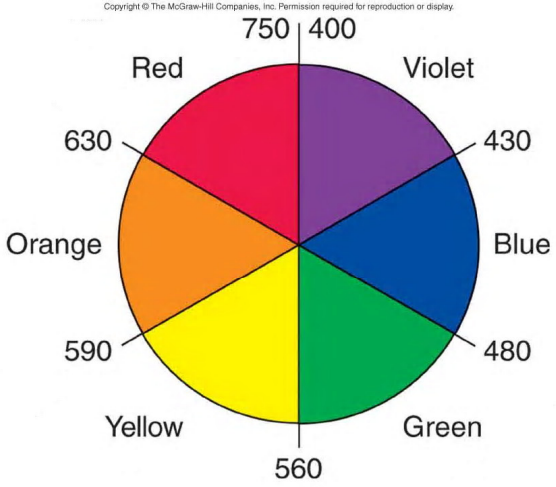
(b) Mb:CO complex



(c) Oxymyoglobin

Table 23.11 Relation Between Absorbed and Observed Colors

Absorbed Color	λ (nm)	Observed Color	λ (nm)
Violet	400	Green-yellow	560
Blue	450	Yellow	600
Blue-green	490	Red	620
Yellow-green	570	Violet	410
Yellow	580	Dark blue	430
Orange	600	Blue	450
Red	650	Green	520



The most important ligand and molecule – OXYGEN

1. First because oxygen in its many forms mammalian existence we need to look at h forms are interconnected.

2. The electrochemical potentials are onl A second molecule or atom must be conne the 2 ½ potentials must be positive for th react.

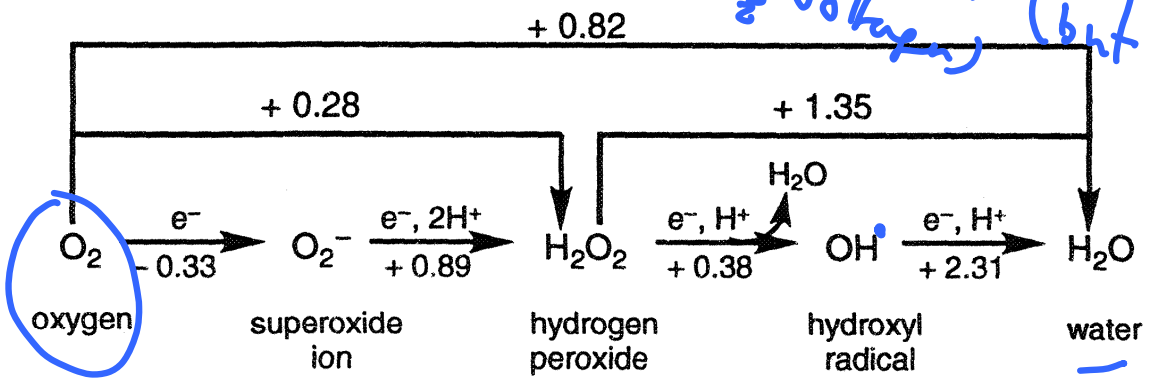


Chart 8.1

3. Electrochemical potentials are thermodynamically controlled – there is no information on the rate of the reaction – luckily! Why luckily? Consider what humans are made of and the composition of gas surrounding us…

Which biological molecules are involved with the oxygen species shown here?

(Cu, Zn) Superoxide dismutase (SOD) – breaks up O_2^{--} —to H_2O_2
(Fe(III)-Fe(IV))Catalase – breaks up H_2O_2 – to O_2 and H_2O

(Fe(II)) Hemoglobin – transports O_2
(FE(II)) Myoglobin – stores O_2

Equilibrium – what does it mean?

$aA + bB \rightleftharpoons cC + dD$

$K_F = \dfrac{[C]^c[D]^d}{[A]^a[B]^b}$

but $K_F = \dfrac{k_{+1}}{k_{-1}}$ the specific rate constants.

at equilibrium $k_{+1}[A]^a[B]^b = k_{-1}[C]^c[D]^d$

ie this is a dynamic process.

$A \xrightarrow{k} (+)$

$\text{Rate} = \dfrac{dc}{dt} = k[A][B]$

Really reactions are much simpler than the above:

$A + B \rightleftharpoons C$ bimolecular

Equilibrium – specifically step-wise vs cumulative equilibrium constants.

*nomenclature:

$A + B \rightleftharpoons AB_1 \quad K_1 = \dfrac{[AB_1]}{[A][B]}$

$AB_1 + B \rightleftharpoons AB_2 \quad K_2 = \dfrac{[AB_2]}{[AB_1][B]}$

etc.
etc.

Cumulative:

$A + 2B \rightleftharpoons AB_2$

$\beta_2 = \dfrac{[AB_2]}{[A][B]^2} = K_1 K_2$

T.O.→

$A + 3B \rightleftharpoons AB_3$

$\beta_3 = \dfrac{[AB_3]}{[A][B]^3} = K_1 K_2 K_3$

T.O.→

Equilibrium

How does the type of ligand affect K_F?

Generically, the more donor atoms on the ligand the greater K_F will be – the "chelate effect."

Polydentate ligands – bind to metals with more than one donor atom.

oxalate $^{-}O{=}C{-}C{=}O^{-}$ (ox) EDTA

porphyrins

(see next slides)

– all because of $\Delta G^\circ = -RT \ln K$

$= \Delta H^\circ - T\Delta S^\circ$

ΔH° we know – $T\Delta S^\circ$?

Key

Equilibrium "chelate effect"

$\Delta G^\circ = -RT \ln(K)$ (units: $\ln = 2.303 \log_{10}$)

$= \Delta H^\circ - T\Delta S^\circ$

heat of formation enthalpy

if ⊖ve: if ΔS°: ⊖ve

⊕ve: ⊕ve

$T = K^\circ$

$0^\circ C = 273\,K$

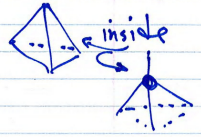
if ΔS° is very positive (J/mol/K) then ΔG° – very negative + $K \gg\gg 1$ … 10^6 10^{10} 10^{40}!

eg siderophores that capture Fe^{3+}

Examples

$[Cd(H_2O)_4]^{2+} + 4NH_3 \rightleftharpoons [Cd(NH_3)_4]^{2+} + 4H_2O$

CN = 4 Tetrahedral



Cumulative binding constant

$\beta_4 = \frac{[Cd(NH_3)_4]^{2+}[H_2O]^4}{[Cd(H_2O)_4]^{2+}[NH_3]^4}$

H_2O is solvent so is not included in the value → $\beta_4 / [H_2O]^4$

Kn stepwise:

$[Cd(H_2O)_4]^{2+} + NH_3 \overset{K_1}{\rightleftharpoons} [Cd(H_2O)_3(NH_3)]^{2+} + H_2O$

etc.

Generally, $K_1 > K_2 > K_3 > K_4$ and $\beta_4 = K_1K_2K_3K_4$

Equilibrium
The chelate effect

Consider Ni^{2+} really $[Ni(H_2O)_6]^{2+}$

$[Ni(H_2O)_6]^{2+} + 6NH_3 \overset{\beta_6}{\rightleftharpoons} [Ni(NH_3)_6]^{2+} + 6H_2O$

7 species — 7 species

What happens if we use EDTA? (NOO NOO)

$[Ni(H_2O)_6]^{2+} + EDTA^{4-} \rightleftharpoons [Ni(EDTA)]^{2-} + 6H_2O$

2 — 7

ΔS = ⊕ ve — ΔS ⊕ ve?

Then $-T\Delta S$ is large.

Equilibrium "chelate effect"

β_6	$[Ni(NH_3)_6]^{2+}$	4.0×10^9	$\log_{10}\beta_6 = 8.61$
=			
	(large? $[Co(NH_3)_6]^{2+} \approx 4 \times 10^{33}$)		
β_1	$[Ni(EDTA)]^{2-}$	3.6×10^{18}	
β_3	$[Ni(en)_3]^{2+}$	2.1×10^{18}	(?)

ΔS effects for these 3?

Chelate effect $\frac{\beta_3 (en)_3}{\beta_6 (NH_3)_6}$ $\frac{\beta_1 (EDTA)}{\beta_6 (NH_3)_6}$

β_3 β_6 β_1 β_6

Equilibrium "chelate effect"

$[Cd(H_2O)_4]^{2+} + 2en \rightleftharpoons [Cd(en)_2]^{2+} + 4H_2O$

If $\Delta S^\circ = -60.70$ kJ/mole

$\Delta H^\circ = -56.48$ kJ/mole

$T = 25\,^\circ C = 298$ K $\quad R = 8.314$ J/K

Calculate β_2, ΔS°

($\approx 4.4 \times 10^{10}$; $+14.2$ J/K)

Expectations from the material in this unit	
1	Know your way round the Periodic Table – esp elements of bio-interest in Groups 1, 2, 14-17. Which are these elements? What are the configurations of the row 2 and 3 metals we are interested in? Know the orbital shapes and labels s, p, and d What is special about the ionization energies across the rows? How does this change the characteristics of the element wrt forming compounds? What happens to the size of elements when oxidized? Reduced? What is a ligand? How is it defined? Why do the hard metals lie on the LHS of the Periodic Table? And the soft metals are? And the hard ligands? And the sift ligands? What are the distinguishing features of all these types of species?
2	Predict good ligand atoms for the following dications**: Zn, Cd, Hg – which amino acids would be prime targets? And Mg, Ca – what about Pb? (See ch. 17 in K&S) **what does this mean?
3	What is BAL? Why was it used in the 1st and 2nd World Wars? What is the L in BAL? What is EDTA? What does it bind best? Why? And, deferrioxamine B – what is it? Why would you be given this as a drug? What is special about the polyether molecules? How would they 'work' in a biological system? Match the following metal ions to the preferred amino acids: K, Zn, Cd, Cu as +1.
4	Identify those amino acids most likely to bind metals – which atoms bind directly to the metal in these molecules? Be able to draw and recognise protoporphyrin IX
5	How do the 3d orbitals split? What effect does this have on the arrangement of electrons? Which of the compounds of oxygen shown in slide 1079 are important to an organism? Which would be toxic? See R-M p 205 for a start on this
Study questions Using books, the Internet and lectures – explain how dioxygen binding takes place in the heme protein myoglobin in terms of the 3d orbitals and d electron configuration	