Química de Coordinación (1)

UNAM 2023

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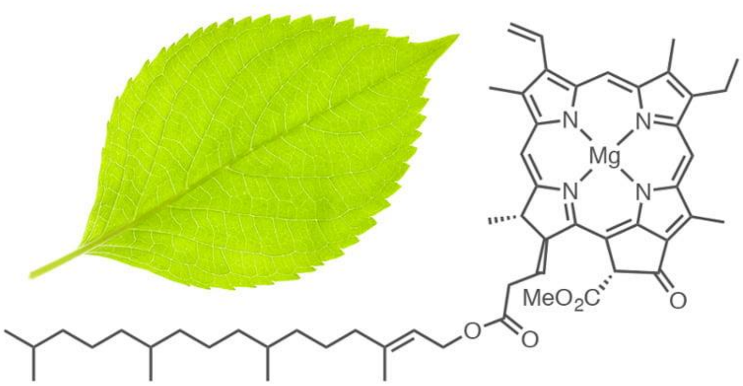
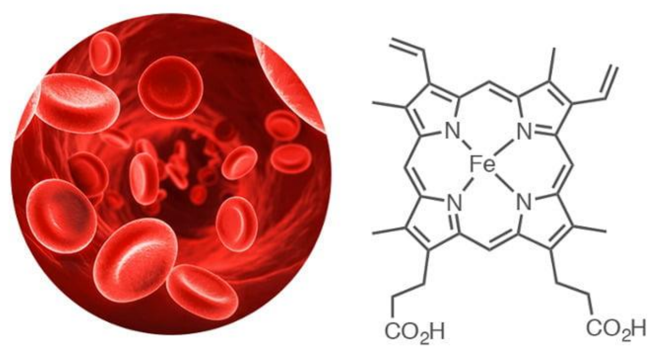
https://www.researchgate.net/profile/Peter-Kroneck

Iones metálicos en sistemas vivos
Metaloenzimas y Metaloproteínas

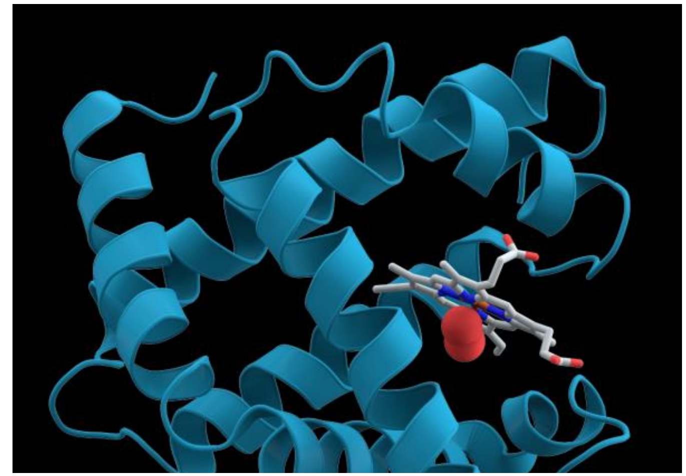
Chlorophyll a

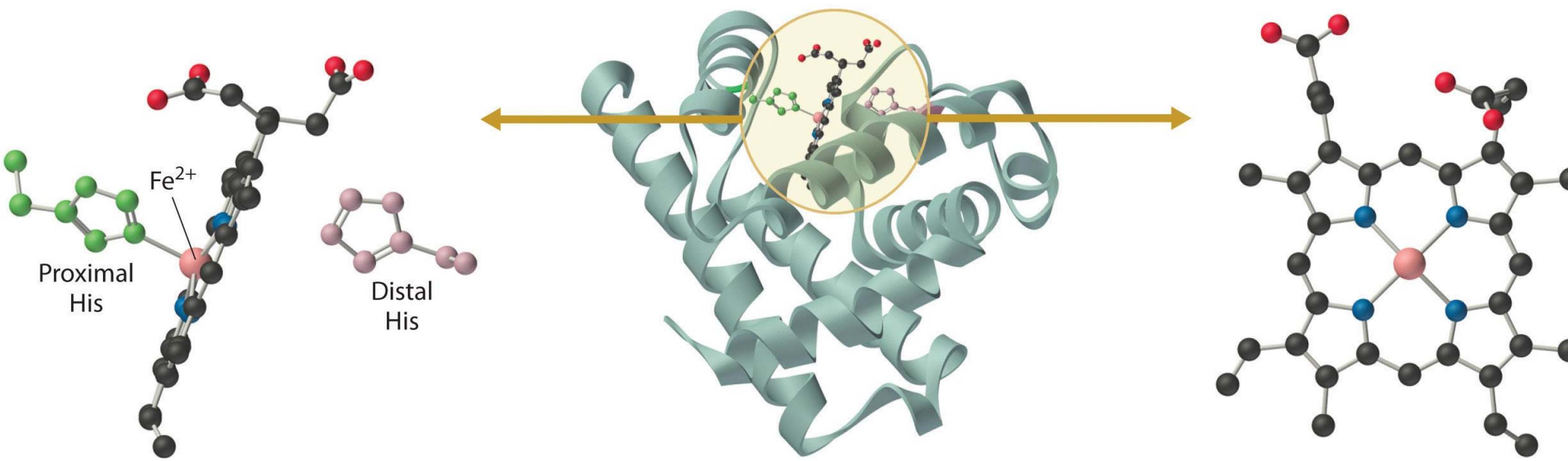


Heme b



Pregunta: Qué es esto?





Side view   Myoglobin with heme   Heme 90° rotation

Trayendo química inorgánica a vida..

Biochemistry
Physiology

Biogeochemistry

Molecular Biology

Biophysics

Química de Coordinación Bioinorgánica

Microbiology

Environmental Chemistry

Spectroscopy

Structural Biology

Catalysis

Physical Chemistry

Medical Chemistry/Toxicology

Bibliografia Basica y Complementaria

J. J. R. Fraústo da Silva, R. J. P. Williams, 2001
The biological chemistry of the elements, Oxford University Press

R. R. Crichton, 2008, 2012 y 2019
Biological Inorganic Chemistry, Elsevier

I. Bertini, H. B. Gray, S. J. Lippard, J. Selverstone Valentine
Bioinorganic Chemistry, 1994
https://espanol.libretexts.org/Quimica/Qu%C3%ADmica_Inorg%C3%A1nica/Libro%3A_Qu%C3%ADmica_bioinorg%C3%A1nica_(Bertini_et_al.)
https://libretexts.org/index.html

E. R. Featherston, J. A. Cotruvo, 2021 (Review)
The biochemistry of lanthanide acquisition, trafficking, and utilization
Biochim Biophys Acta, Molecular Cell Research *1868*, 118864
https://doi.org/10.1016/j.bbamcr.2020.118864

Sitios Web Importantes

https://www.ebi.ac.uk/pdbe/

comprehensive database of published protein structures

http://www.webelements.com

periodic table of the elements including useful information on each element

https://www.alphafold.ebi.ac.uk/AlphaFold

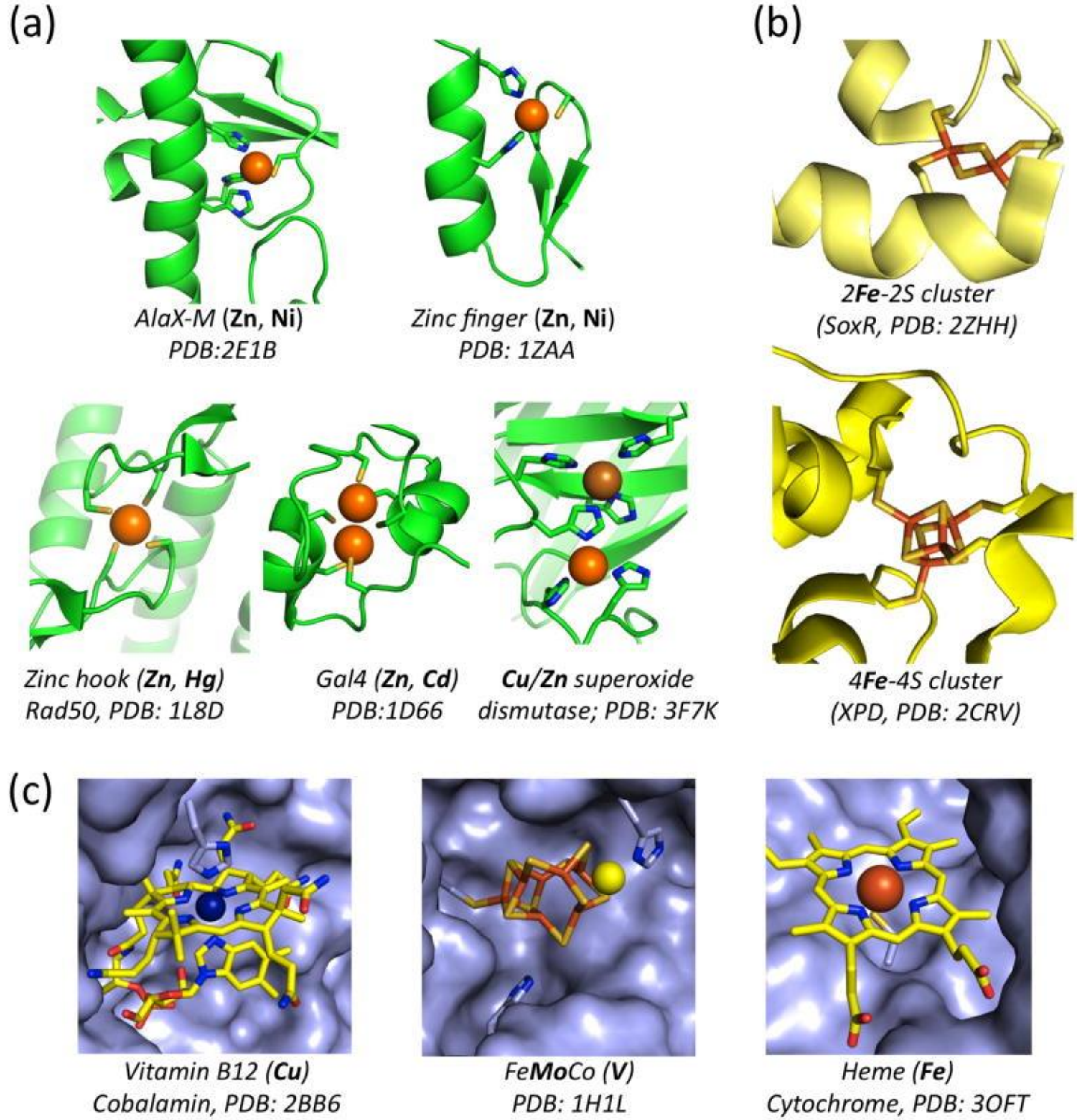
Protein Structure Database (DeepMind and EMBL-EBI)

https://esmatlas.com/

Open atlas of predicted metagenomic protein structures

PDB Database

- **PDB = Protein Data Bank**
  https://www.rcsb.org/; type PDB number in search field
- **1A70 (for Ferredoxin)**
- **3SBP (for Nitrous Oxide Reductase)**

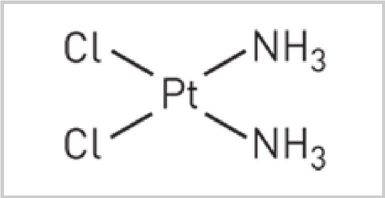

(a)
AlaX-M (Zn, Ni)
PDB:2E1B
Zinc finger (Zn, Ni)
PDB: 1ZAA
Zinc hook (Zn, Hg)
Rad50, PDB: 1L8D
Gal4 (Zn, Cd)
PDB:1D66
Cu/Zn superoxide
dismutase; PDB: 3F7K
(b)
2Fe-2S cluster
(SoxR, PDB: 2ZHH)
4Fe-4S cluster
(XPD, PDB: 2CRV)
(c)
Vitamin B12 (Cu)
Cobalamin, PDB: 2BB6
FeMoCo (V)
PDB: 1H1L
Heme (Fe)
Cytochrome, PDB: 3OFT

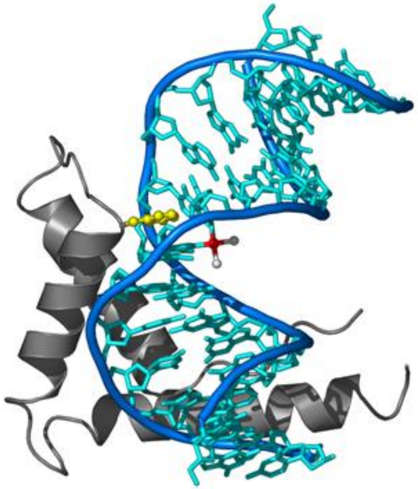
Metales y Vida: la Química de Coordinación de la Naturaleza

"El uso de metales para tratar dolencias humanas se remonta al menos al quinto siglo a. de J.C., y el estudio y la imitación de metales en la biología son un sujeto vibrante hoy"

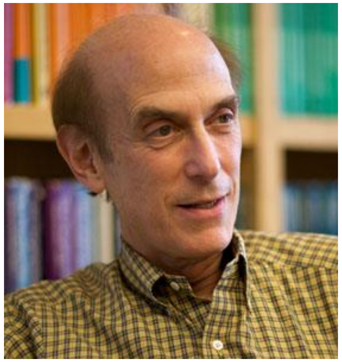
Stephen Lippard, J Am Chem Soc (2010), 132, 141689-14693

B. Rosenberg et al., (1965) Nature, 205, 698 - 699





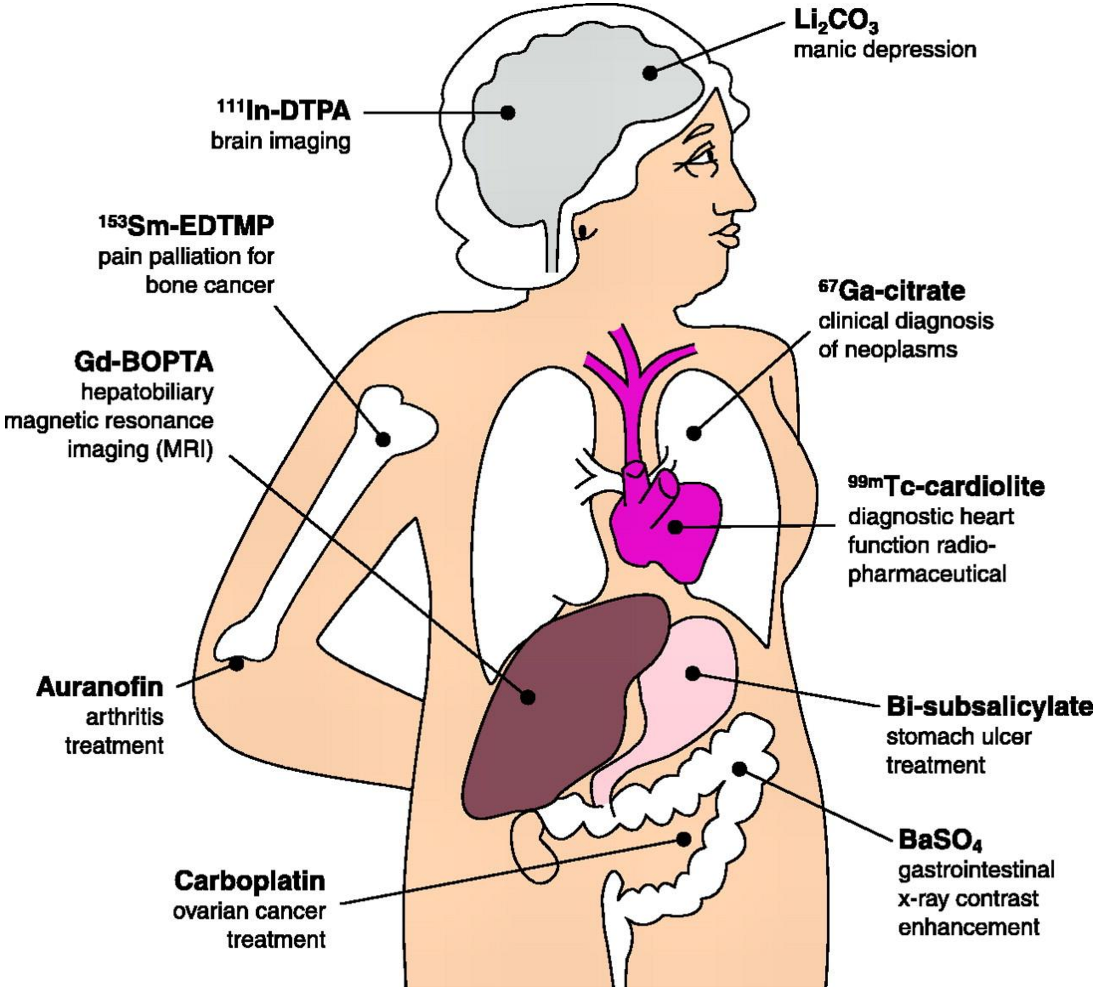
Cisplatin-DNA adduct bound to HMGB1. Cisplatin shown as red and white spheres; DNA is shown in blue; HMBG1 shown as grey cartoon with intercalated phenylalanine shown as yellow spheres. Image credits: Michael S. McCormick.



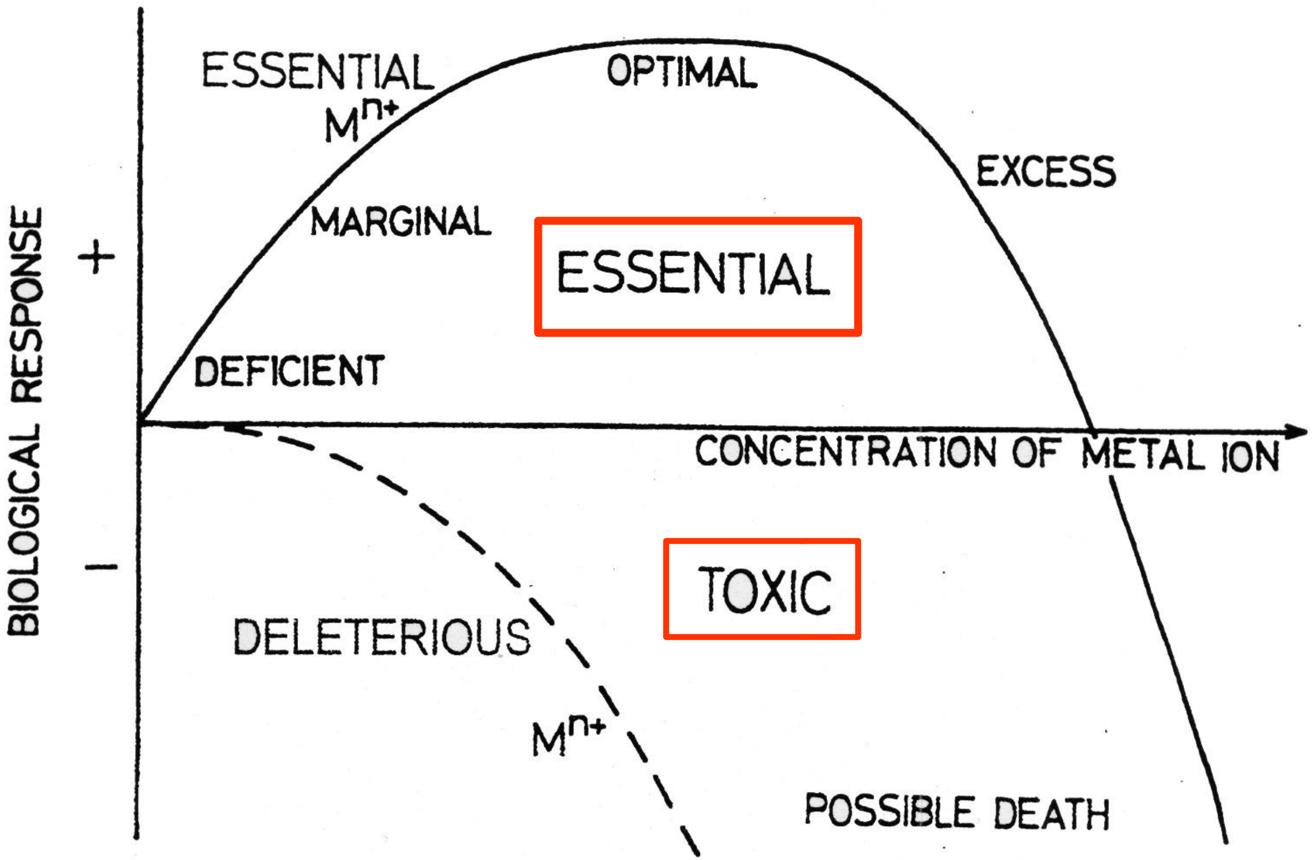
Metales en Medicina – Aplicaciones

"Uno de los desafíos de diseñar medicinas basadas en el metal es equilibrar la toxicidad potencial de una formulación activa con el impacto positivo sustancial de estos recursos terapéuticos y diagnósticos cada vez más comunes"

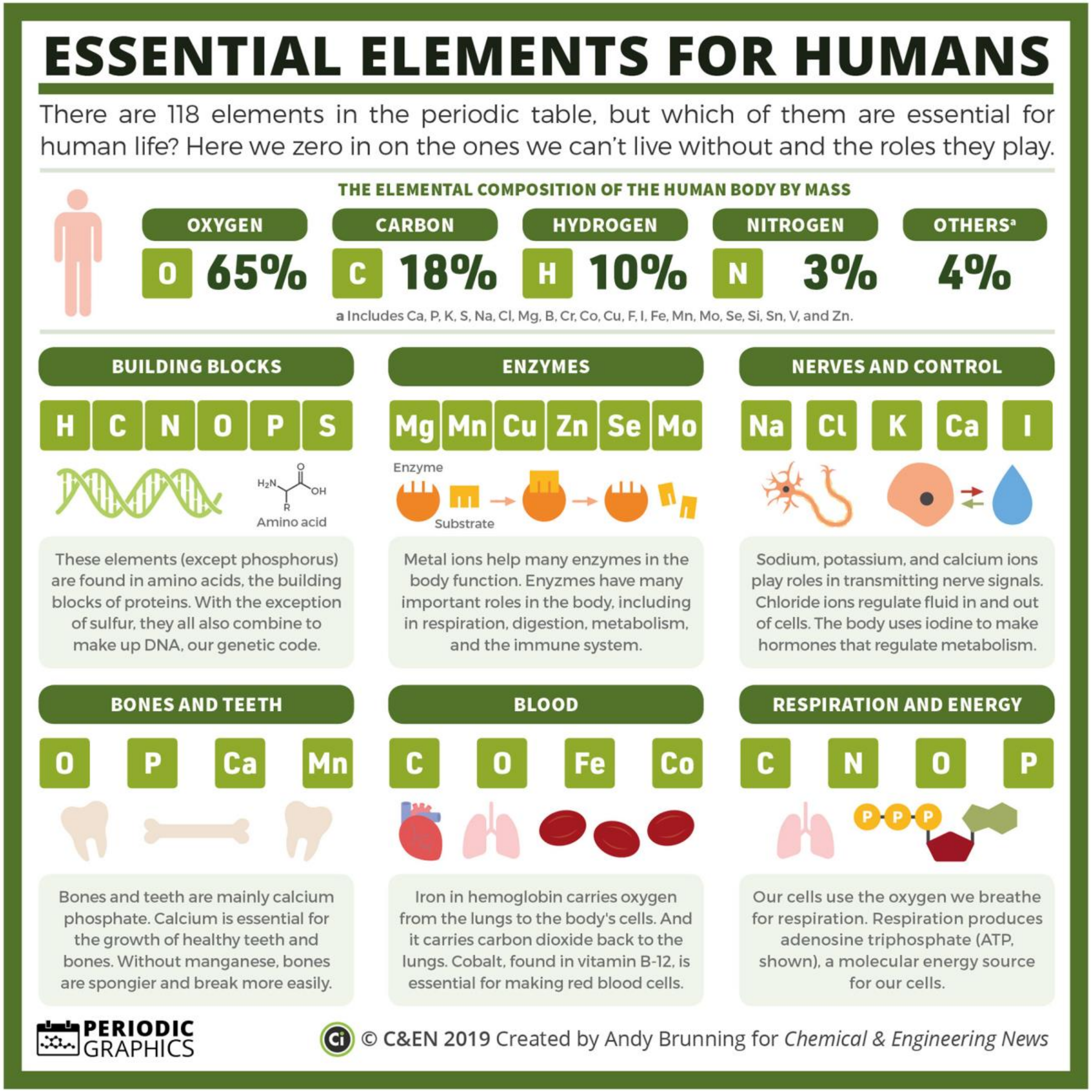
K.H. Thompson, C. Orvig (2003) Science 300, 936-939



Bertrand Diagram
Relación dosis-función

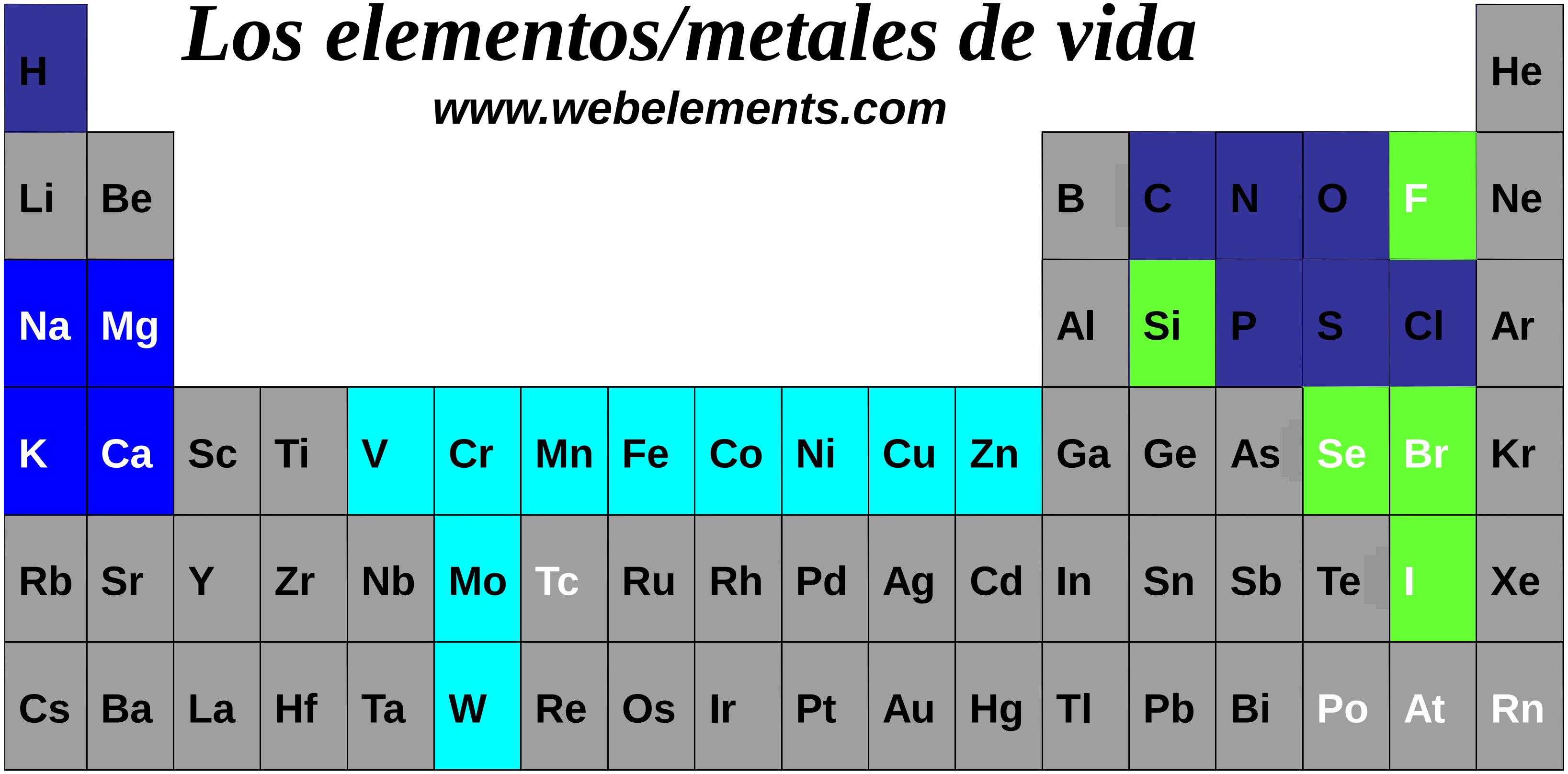


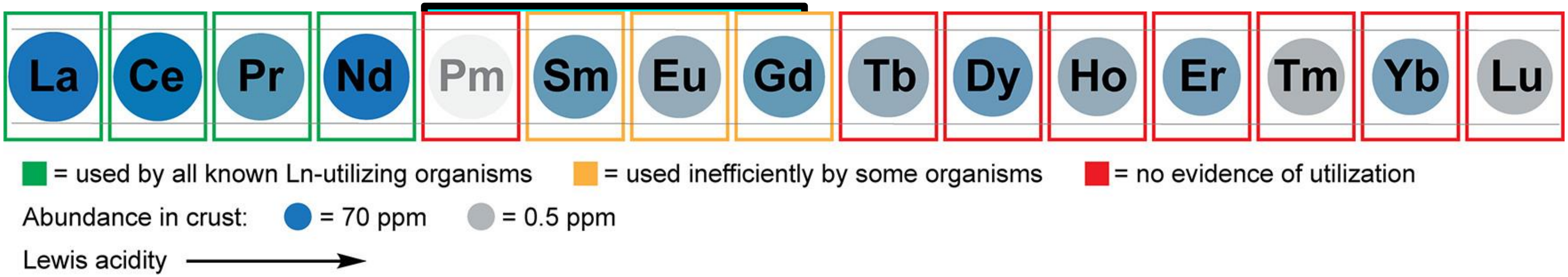
Biological response dependence on the concentration of an essential nutrient (solid curve) and of a deleterious substance (dashed curve)


ESSENTIAL ELEMENTS FOR HUMANS
There are 118 elements in the periodic table, but which of them are essential for human life? Here we zero in on the ones we can't live without and the roles they play.
THE ELEMENTAL COMPOSITION OF THE HUMAN BODY BY MASS
OXYGEN
O 65%
CARBON
C 18%
HYDROGEN
H 10%
NITROGEN
N 3%
OTHERS[a]
4%
a Includes Ca, P, K, S, Na, Cl, Mg, B, Cr, Co, Cu, F, I, Fe, Mn, Mo, Se, Si, Sn, V, and Zn.
BUILDING BLOCKS
H C N O P S
Amino acid
These elements (except phosphorus) are found in amino acids, the building blocks of proteins. With the exception of sulfur, they all also combine to make up DNA, our genetic code.
ENZYMES
Mg Mn Cu Zn Se Mo
Enzyme
Substrate
Metal ions help many enzymes in the body function. Enyzmes have many important roles in the body, including in respiration, digestion, metabolism, and the immune system.
NERVES AND CONTROL
Na Cl K Ca I
Sodium, potassium, and calcium ions play roles in transmitting nerve signals. Chloride ions regulate fluid in and out of cells. The body uses iodine to make hormones that regulate metabolism.
BONES AND TEETH
O P Ca Mn
Bones and teeth are mainly calcium phosphate. Calcium is essential for the growth of healthy teeth and bones. Without manganese, bones are spongier and break more easily.
BLOOD
C O Fe Co
Iron in hemoglobin carries oxygen from the lungs to the body's cells. And it carries carbon dioxide back to the lungs. Cobalt, found in vitamin B-12, is essential for making red blood cells.
RESPIRATION AND ENERGY
C N O P
P P P
Our cells use the oxygen we breathe for respiration. Respiration produces adenosine triphosphate (ATP, shown), a molecular energy source for our cells.
PERIODIC GRAPHICS
© C&EN 2019 Created by Andy Brunning for Chemical & Engineering News

Los elementos/metales de vida

www.webelements.com





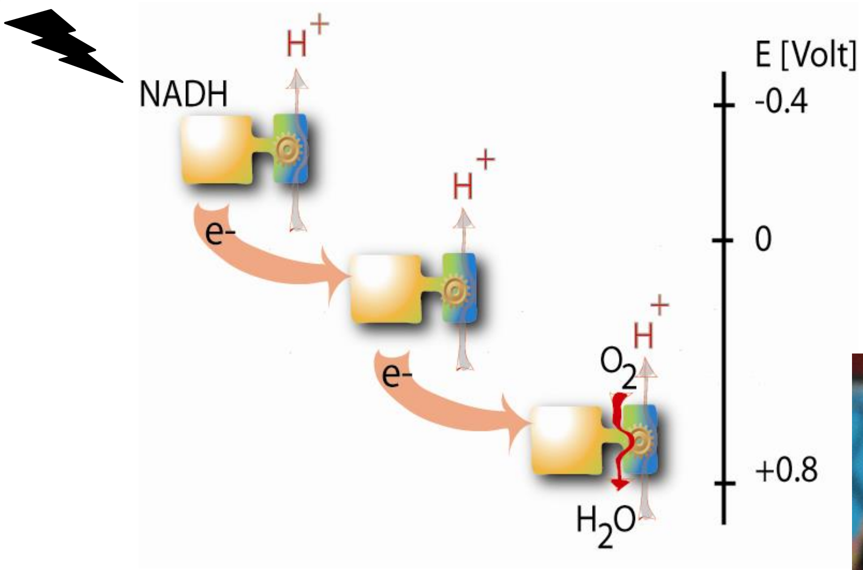
Mo: 9 mg

METAL DE TRANSICION

Por qué investigan metales en la biología?

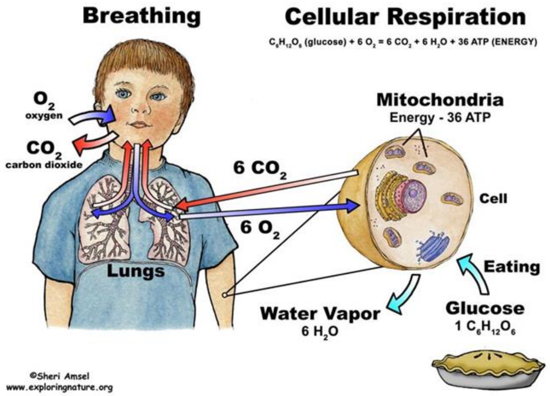
- **Hay apenas cualquier proceso importante en la naturaleza que no depende de un <u>ión</u> metálico; ~ 1/3 de las proteínas del genoma humano dependen de <u>iones</u> metálicos**
- **Dos ejemplos importantes:**
- **Catálisis ácida y baja**
- **Química de redox – Transferencia de protones y electrones (conservación de energía)**

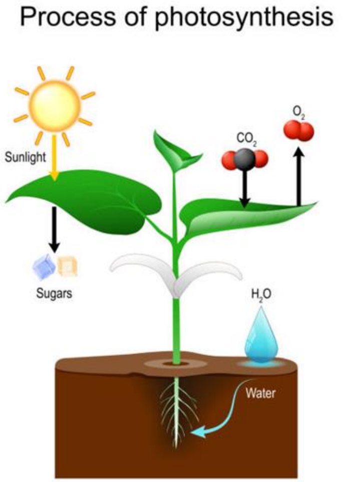
Transferencia de protones y electrones
Conservación de energía (Brazil 2014)

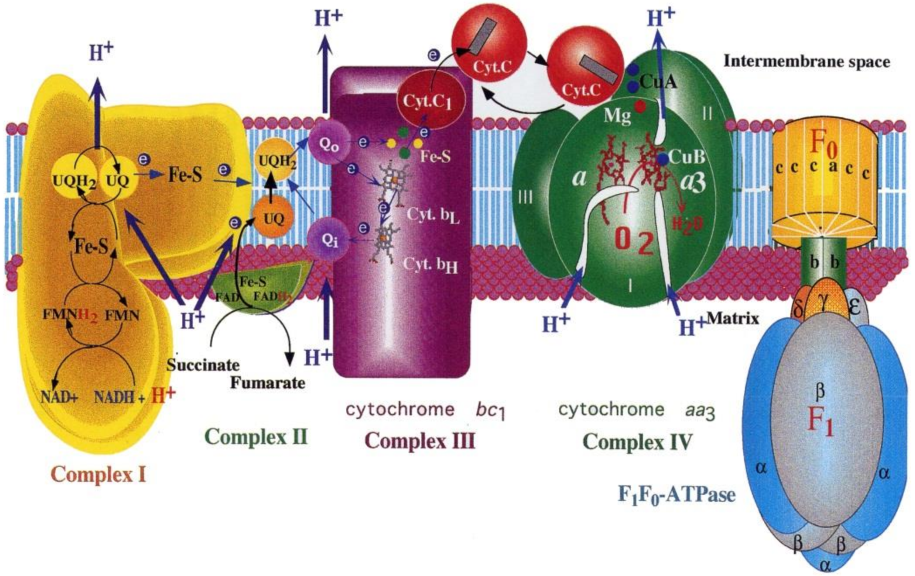


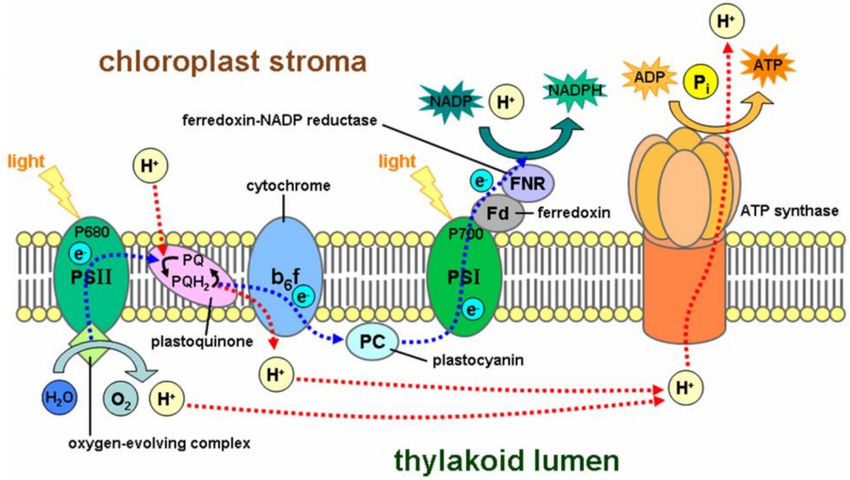
$$\Delta G^{o\prime} = -nF\Delta E^{o\prime}$$

Respiración de Mitochondrial & Síntesis de Centro de Reacción Fotosintética de ATP – Transferencia de electrón/protón Conectada – Fuerza de Protonmotive

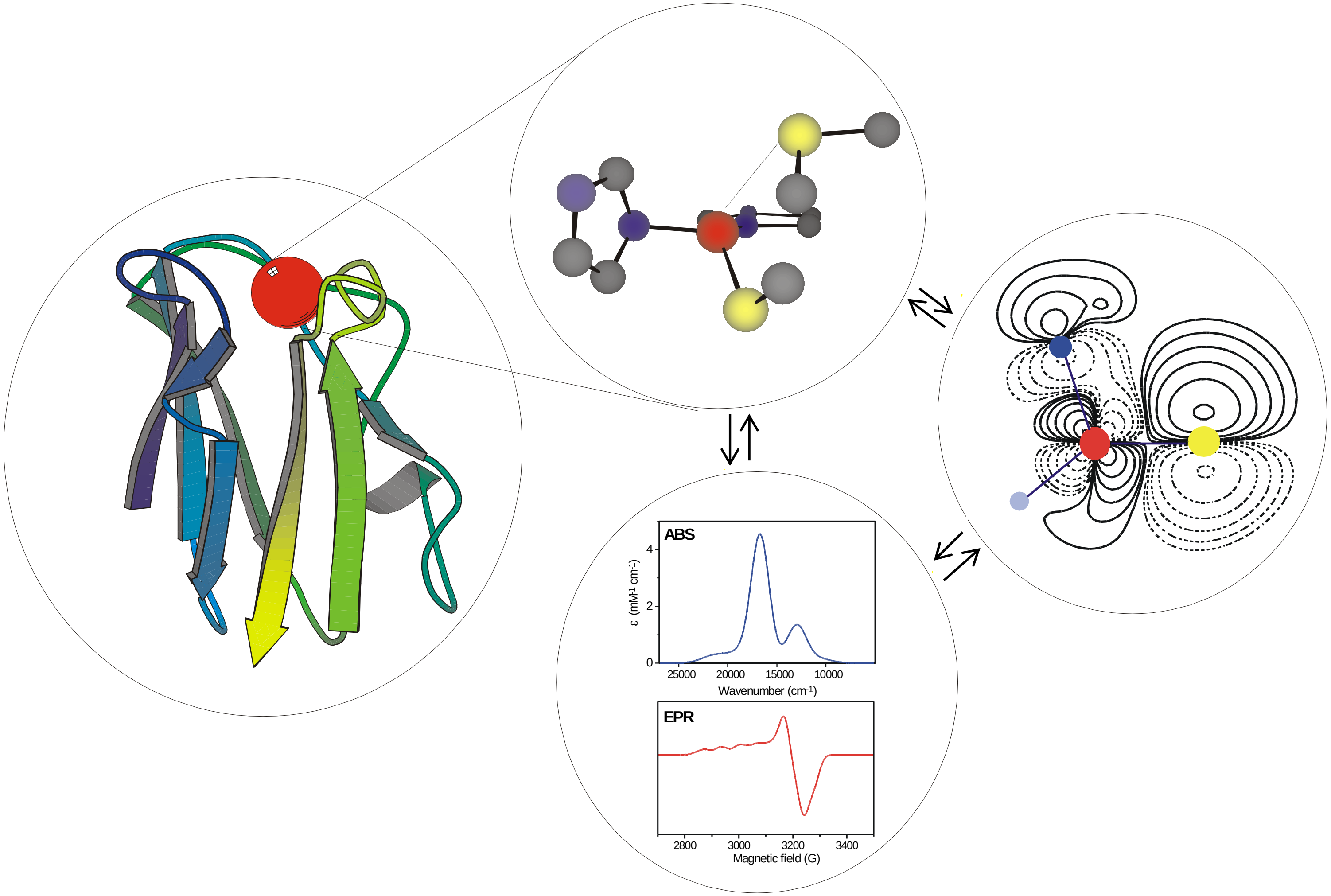








Objetivo: Estructura 3D/Electrónica Función/Mecanismo de Acción



Por qué (transición) iones de metal ?

- **<u>Positively Charged</u>**
  - **Lewis Acids**
  - **Stabilization of Anions**
- **<u>Loosely Bound Electrons</u>**
  - **Redox Active**
  - **Multiple Redox States**
  - **Easily tunable Redox Potential**
- **<u>Redox/Acid Base Chemistry</u>**

- **<u>Open Shell Systems</u>**
  - **No Problems with Spin Restriction**
- **<u>Sterochemically Flexible</u>**
  - **Large Variety of Structures.**
  - **Little Reorganization**
  - **Facile Ligand Addition/Dissociation**
- **<u>Facilitate Reactions of Bound Ligands</u>**

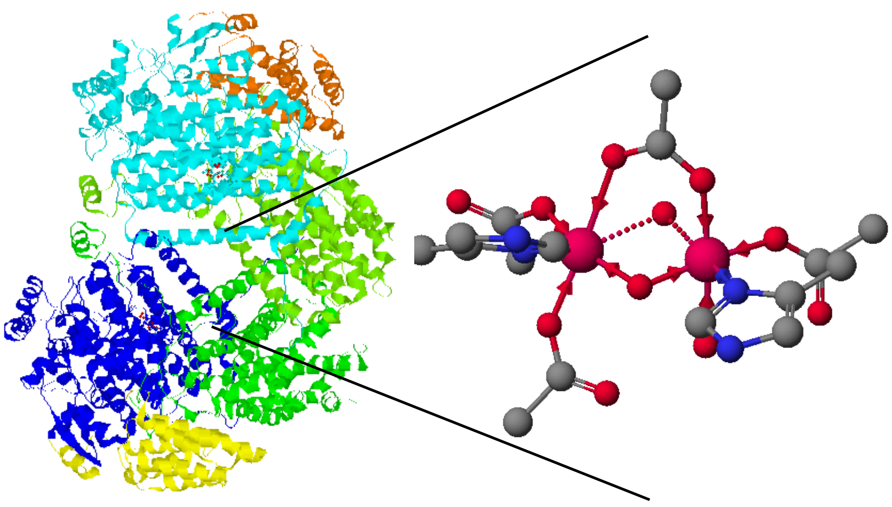
Propiedades básicas de un complejo de la proteína metálico

Chem. Rev. 1996, 96, 2239-2314 (1996) RH Holm, P Kennepohl, E I Solomon, Structural and Functional Aspects of Metal Sites in Biology

Prot-L| --------M

δ- δ+

strong attraction

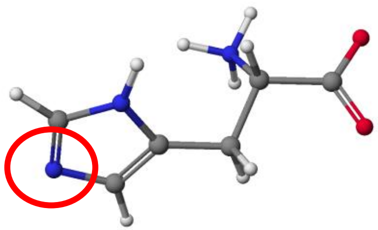


$CH_4 + O_2 + 2e^- + 2H^+ \rightarrow H_3COH + H_2O$

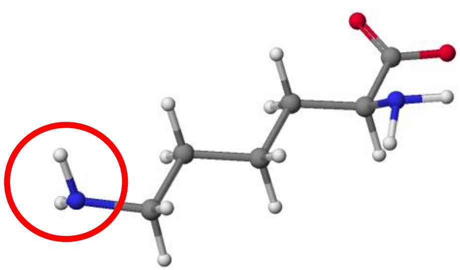
Química en el Centro Catalítico (Sitio activo) de la Enzima de Hierro Metano Monooxigenasa

Ligantes en proteínas – residuos del aminoácido

N

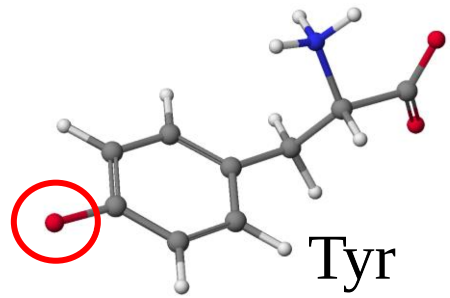


His

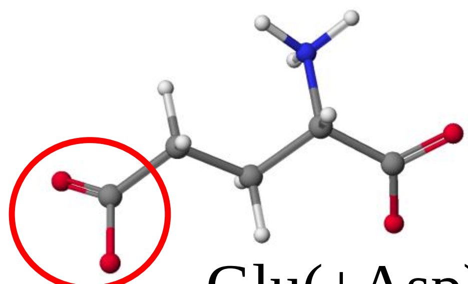


Lys

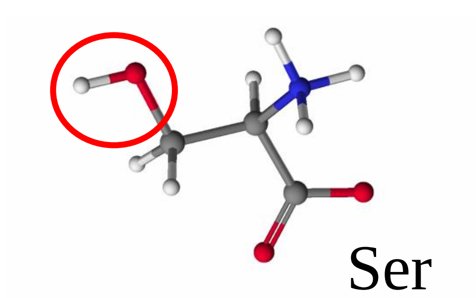
O



Tyr

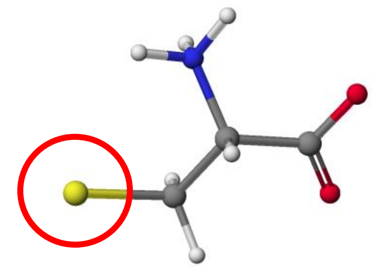


Glu(+Asp)

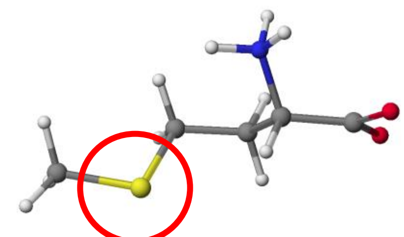


Ser

S

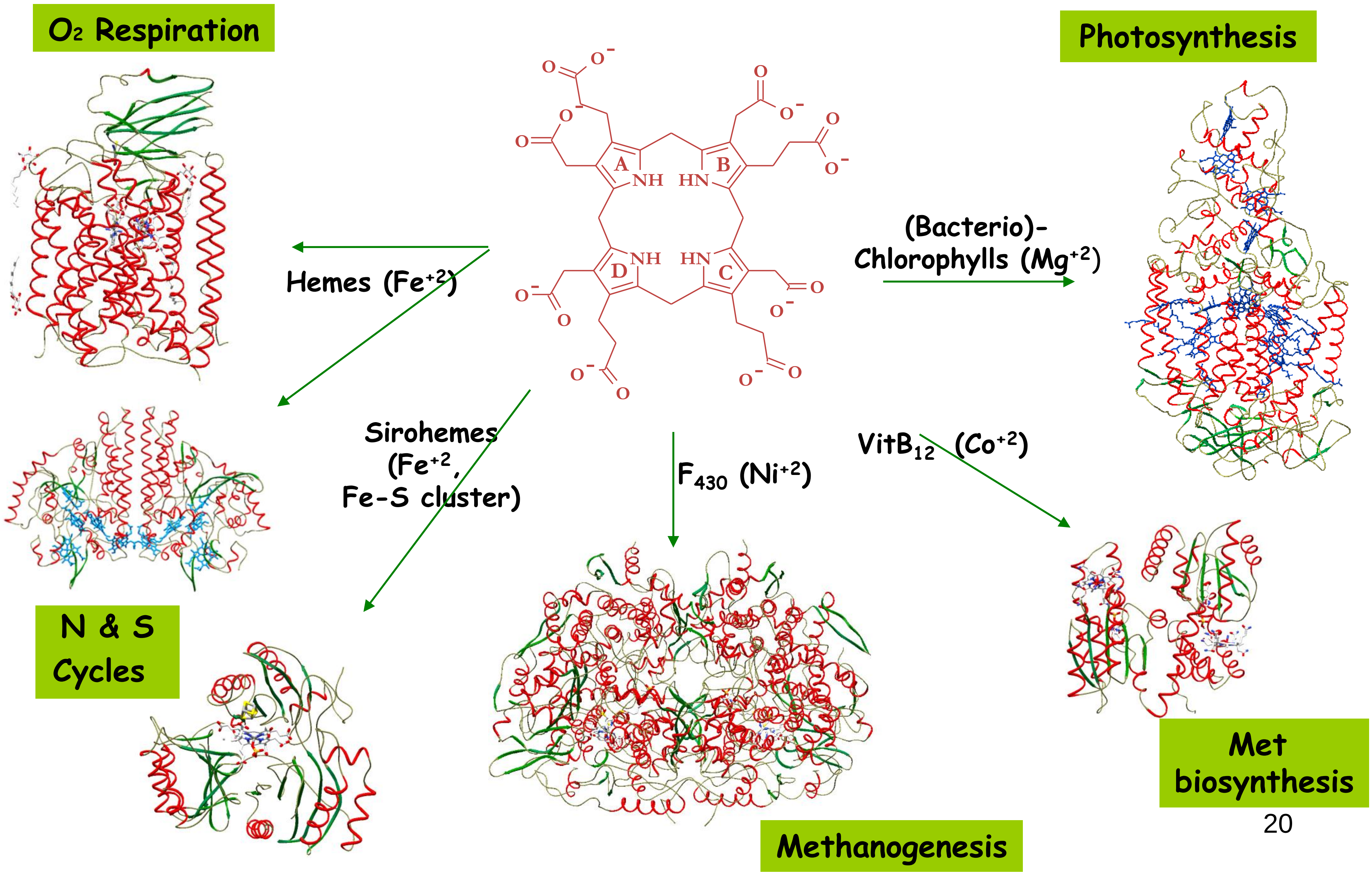


Cys



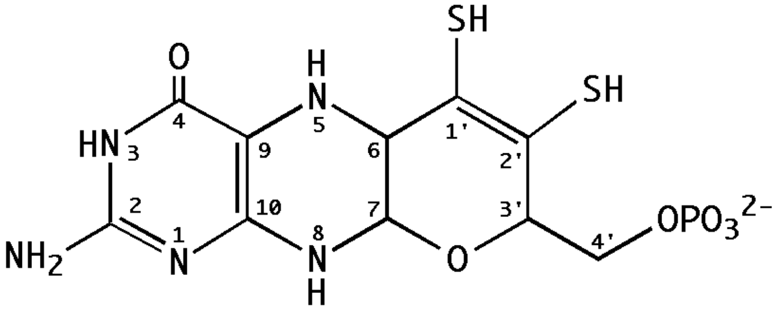
Met

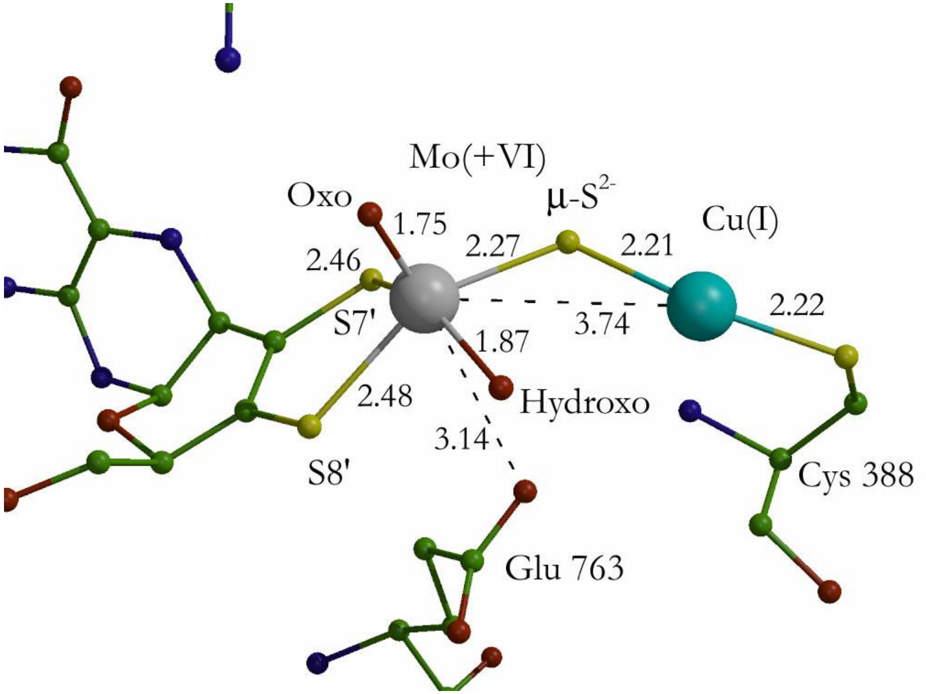
Tetrapirrol está compuesto por 4 unidades de pirrol (porfirinas y ftalocianinas; clorofila, citocromos, pigmentos biliares y vitaminas)



Molybdopterin, un ligante que liga el Mo y el W

JOURNAL of BIOLOGICAL CHEMISTRY (2009) Vol. 284, p. e10, N Kresge, R D Simoni, R L Hill: The Discovery and Characterization of Molybdopterin - the Work of K. V. Rajagopalan





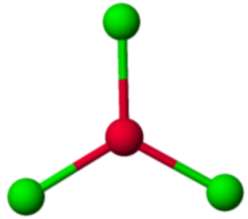
Mo-S-Cu Cluster in CO Dehydrogenase from *Oligotropha carboxidovorans*

$CO + H_2O \rightarrow CO_2 + 2\ H^+ + 2e^-$

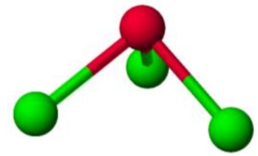
H Dobbek et al., Proceedings National Academy of Sciences/USA, 99, 15971-15976 (2002)

Geometría – Número de Coordinación

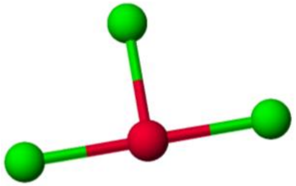
3



Trigonal

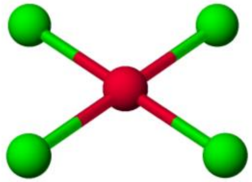


Trigonal pyramidal

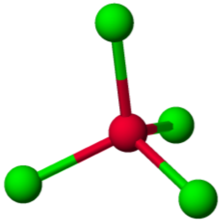


T-shape

4

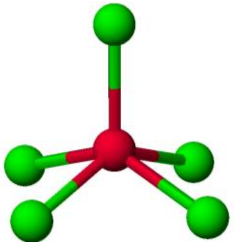


Square planar

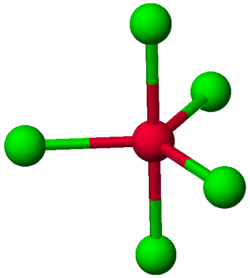


Tetrahedral

5

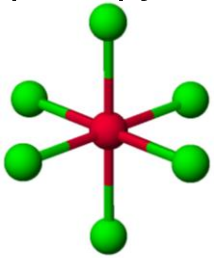


Square pyramidal



Trigonal bipyramidal

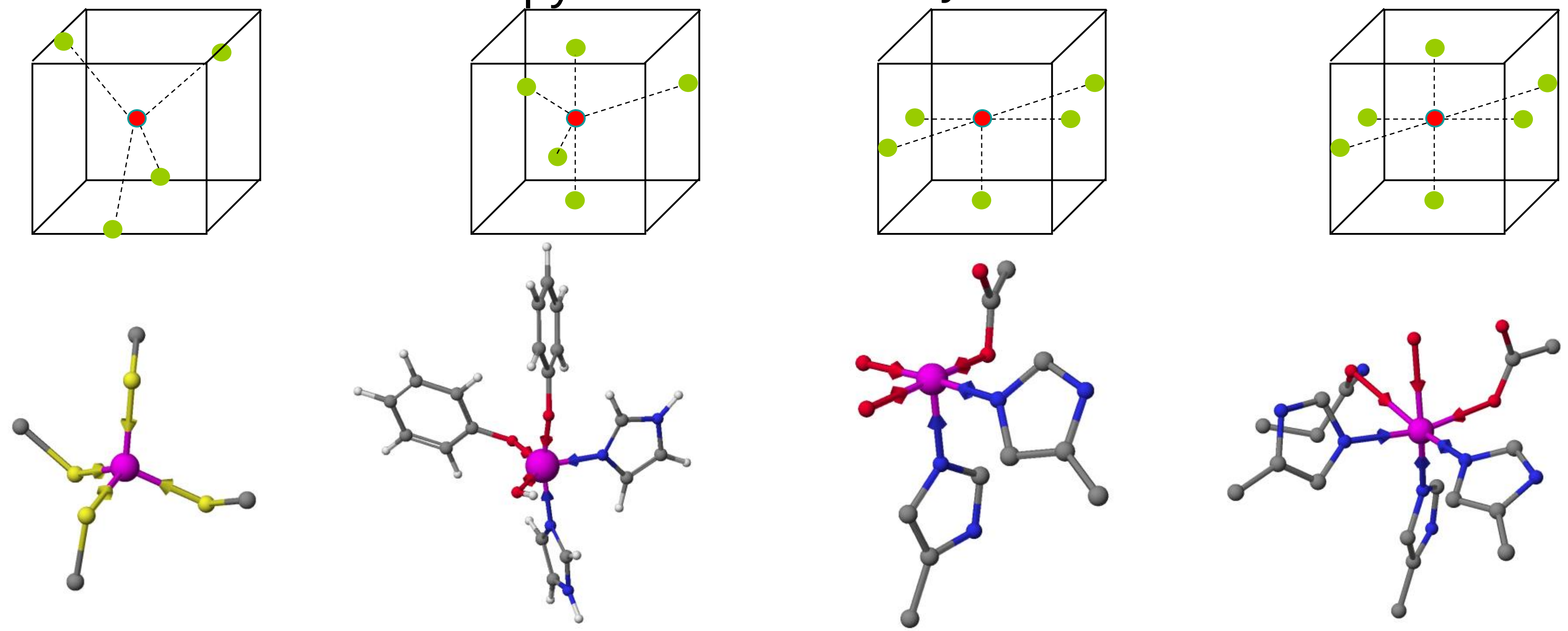
6



Octahedral

Geometría es importante: Proteínas de Hierro

Tetrahedron | Trigonal Bipyramide | Tetragonal Pyramide | Octahedron

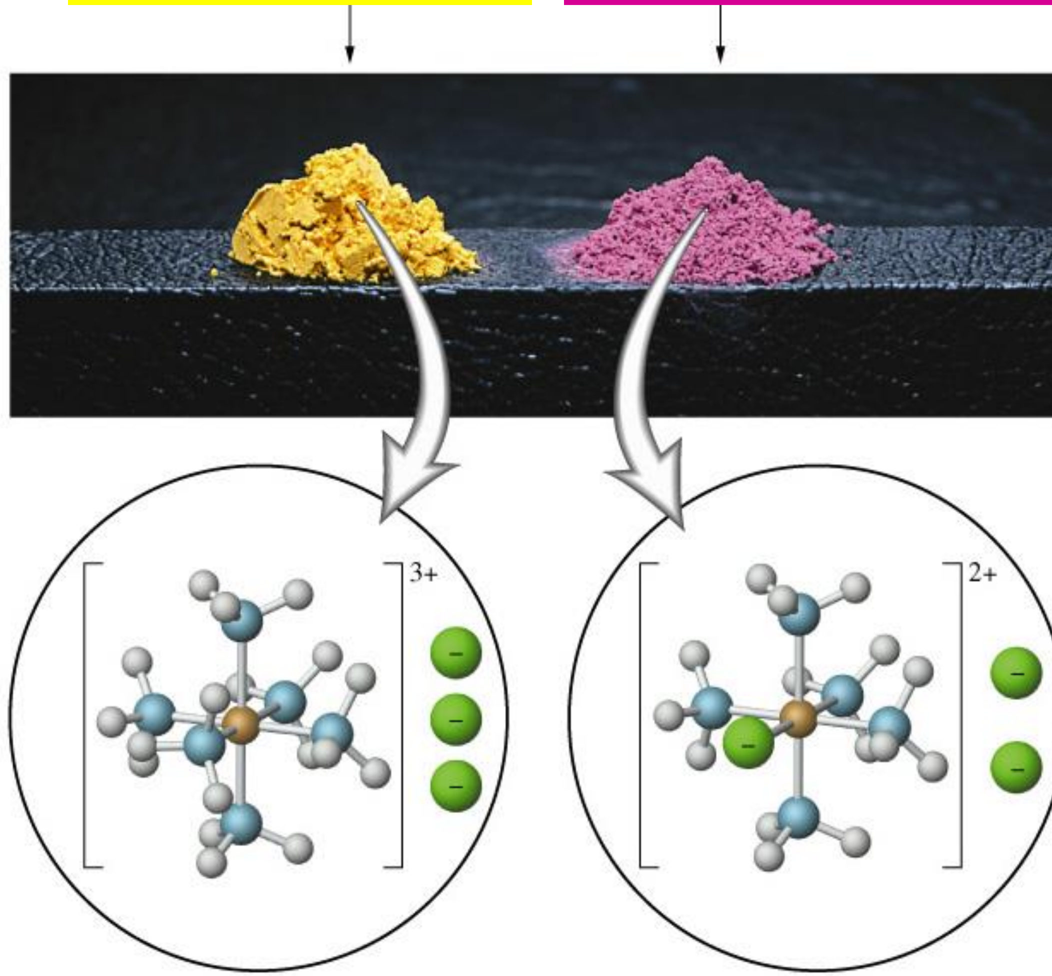


Rubredoxin | 3,4-Protocatechoate Dioxygenase | Tyrosine Hydroxylase | Lipoxygenase

El Solomon, *et al.* (**2000**), Chem. Rev., 100, 235–350

Color y Magnetismo

$Co[(NH_3)_6]Cl_3$ $Co[(NH_3)_5Cl]Cl_2$

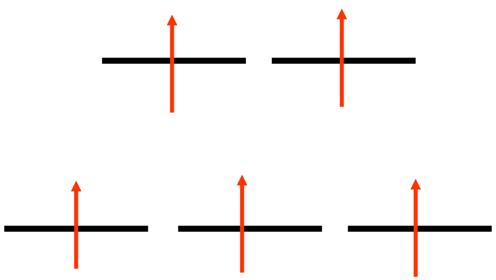


Alfred Werner (University of Zürich/CH, Nobel Prize in Inorganic Chemistry, 1913)

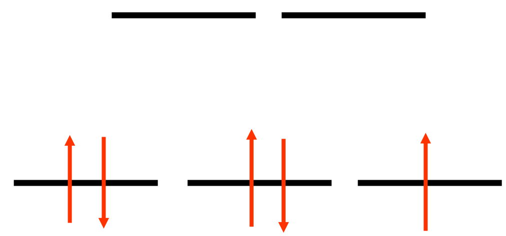
Color y Magnetismo

Estados de spin variables de centros metálicos

For a d^5 configuration, Fe(III)



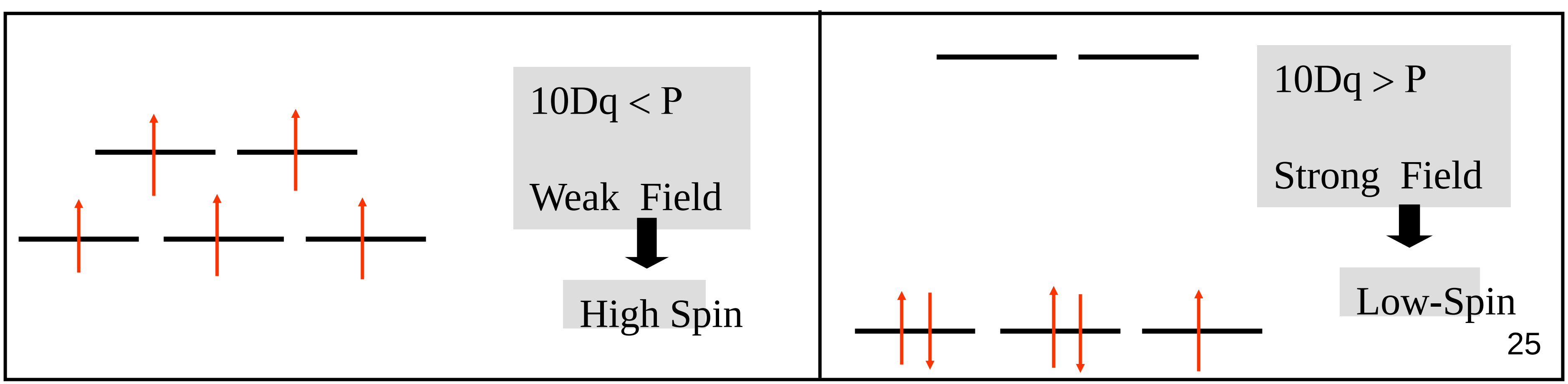
OR



High-Spin, S= 5/2

Low-Spin, S= 1/2

Depending on the METAL ION ENVIRONMENT, balance of Crystal Field Splitting, 10Dq and Spin-Pairing Energy, P



Metales – Funciones biológicas

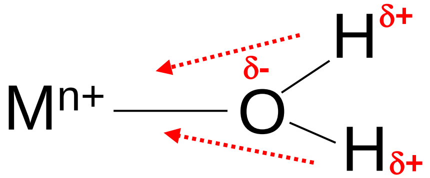
Metal (Ion)	Function, Enzymes
Na	Charge Carrier, Osmolysis/equilibrium
K	Charge Carrier, Osmolysis/equilibrium
Mg	Structure, ATP/ThDP Binding, Photosynthesis,...
Ca	Structure, Signaling, Charge Carrier
V	Nitrogen Fixation, Haloperoxidases, O_2 Carrier
Cr	***Unknown! (glucose metabolism ???)***
Mo	Nitrogen Fixation, Oxidoreductase, O-Transfer
W	Oxidoreductases, Acetylene Hydratase
Mn	Photosynthesis, Oxidases, Structure,...
Fe	Oxidoreductases, O_2 Transport + Activation,e^--Transfer,...
Co	Oxidoreductases, Vitamin B_{12} (Alkyl Group Transfer)
Ni	Hydrogenase, CO Dehydrogenase, Hydrolases, Urease
Cu	Oxidoreductases, O_2 Transport, e^- -Transfer
Zn	Structure, Hydrolases, Acid-Base Catalysis...

Estados de la oxidación de metales en biología

Metal	Valence state (Electron configuration)
Na	Na(I)
K	K(I)
Mg	Mg(II)
Ca	Ca(II)
V	V(V)=(d^0), V(IV)=(d^1), V(III)=(d^2)
Cr	Cr(III)=(d^3),Cr(IV)=(d^2),Cr(V)=(d^1)
Mo	Mo(III)=(d^3),Mo(IV)=(d^2),Mo(V)=(d^1), Mo(VI)=(d^0)
W	W(IV)=(d^2) ,W(V) =(d^1), W(VI)=(d^0)
Mn	Mn(V)=(d^2),Mn(IV) =(d^3),Mn(III) =(d^4),Mn(II) =(d^5)
Fe	Fe(V)=(d^3), Fe(IV)=(d^4),Fe(III)=(d^5),Fe(II)=(d^6), Fe(I)?=(d^7)
Co	Co(III)=(d^6), Co(II)=(d^7), Co(I)=(d^8)
Ni	Ni(III)=(d^7), Ni(II)=(d^8), Ni(I)=(d^9)
Cu	Cu(III)=(d^8), Cu(II)=(d^9), Cu(I)=(d^{10})
Zn	Zn(II) =(d^{10})

Exogenous Ligantes

	Ligand	pK_a
Acid/base	$H_2O/OH^-/O^{2-}$	14,~34
	HCO_3^-/CO_3^{2-}	10.3
	HPO_4^{2-}/PO_4^{3-}	12.7
	H_3CCOO^-/H_3CCOOH	4.7
	HO_2^- /H_2O_2	11.6
	NH_3 /NH_4^+	9.3
	N_3^- /N_3H	4.8
	F^-, Cl^- Br^-, I^-/XH	3.5, -7, -9, -11
Neutral	O_2, CO, NO, RNC	

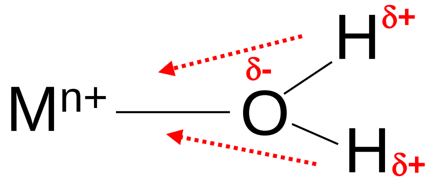


Modulación de pK_a

$$H_2O + M^{n+} \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} HO^- \text{-} M^{n+}$$

Metal	pK_a
none	14.0
Ca^{2+}	13.4
Mn^{2+}	11.1
Cu^{2+}	10.7
Zn^{2+}	10.0

4 orders of magnitude !



Control cinético

$$[M^{n+}(H_2O)_m] \underset{+H_2O}{\overset{-H_2O}{\rightleftharpoons}} [M^{n+}(H_2O)_{m-1}]$$

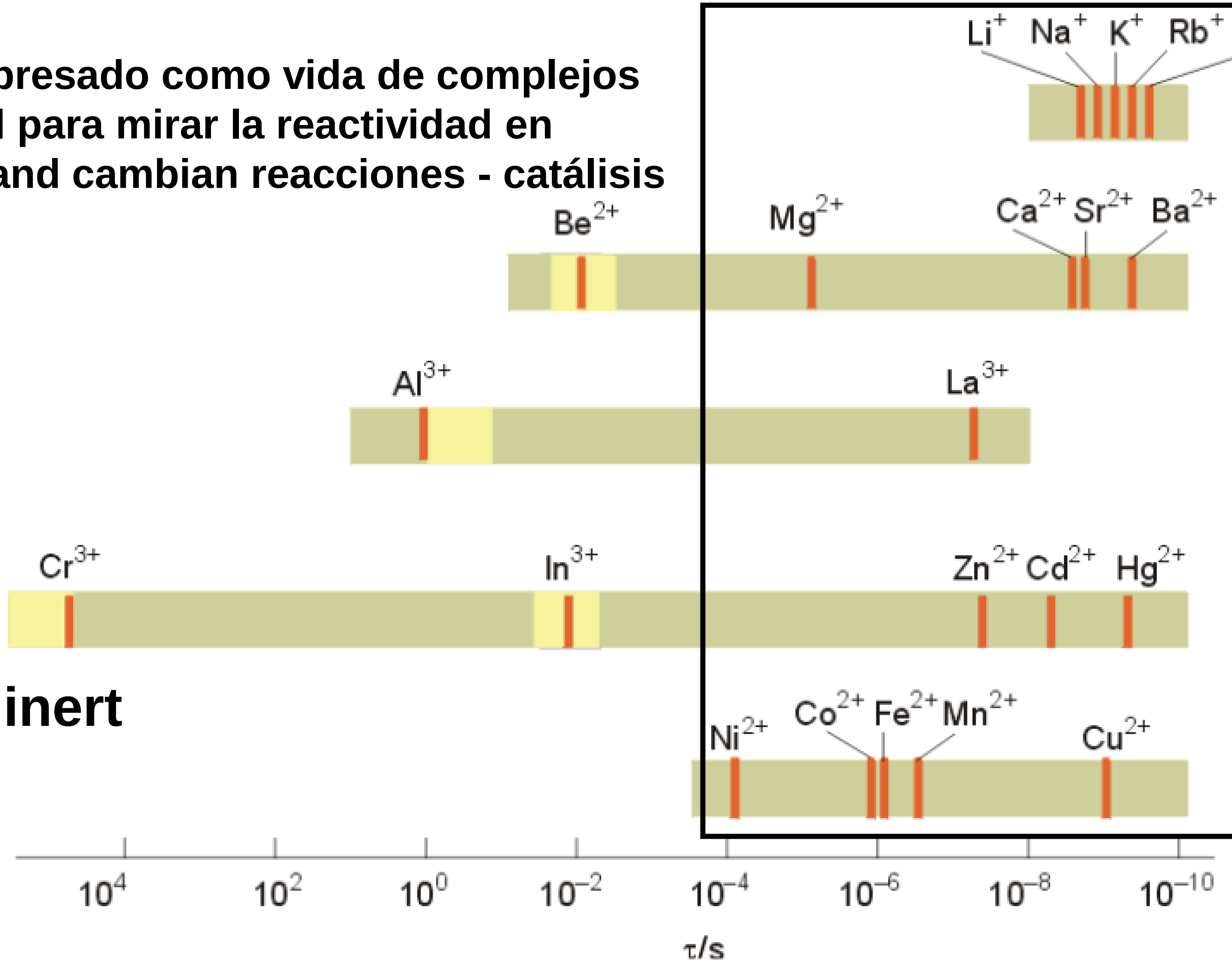
Metal	k (s^{-1})
K^+	1×10^9
Ca^{2+}	3×10^8
Mn^{2+}	2×10^7
Fe^{2+}	4×10^6
Co^{2+}	3×10^6
Ni^{2+}	4×10^4
Fe^{3+}	2×10^2
Co^{3+}	$<10^{-6}$

15 orders of magnitude!

Velocidades de cambio de H_2O

M. Eigen, Nobel Prize Lecture 1967

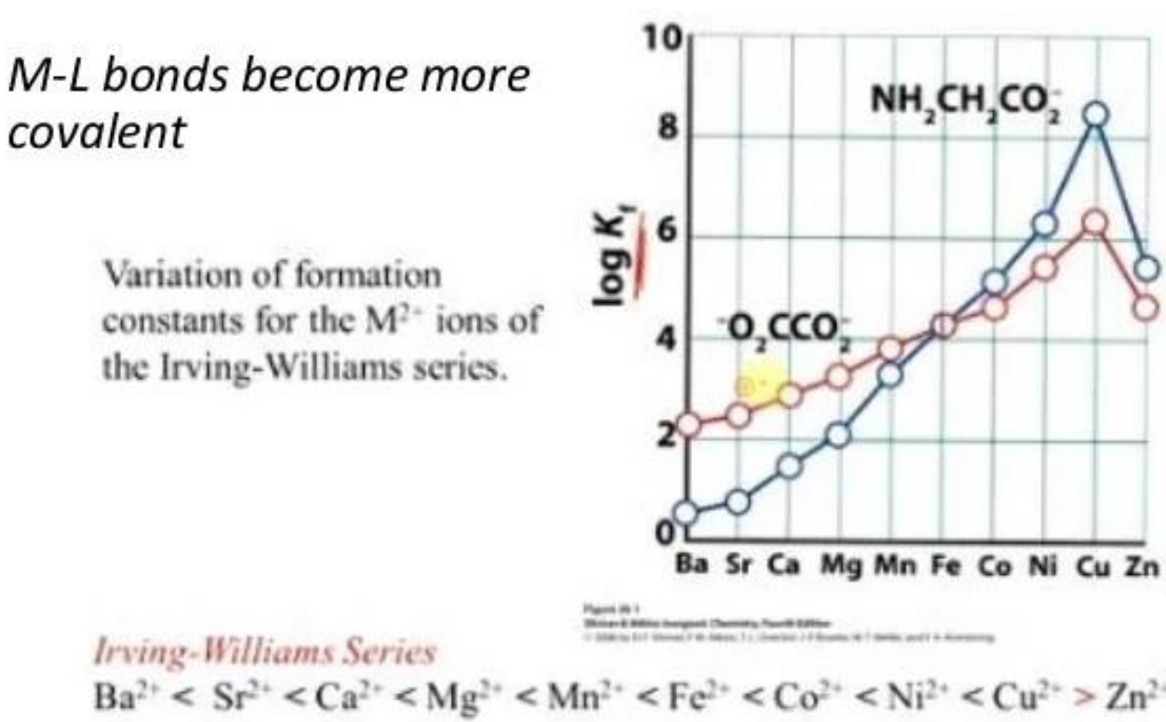
Expresado como vida de complejos
Útil para mirar la reactividad en ligand cambian reacciones - catálisis



labile

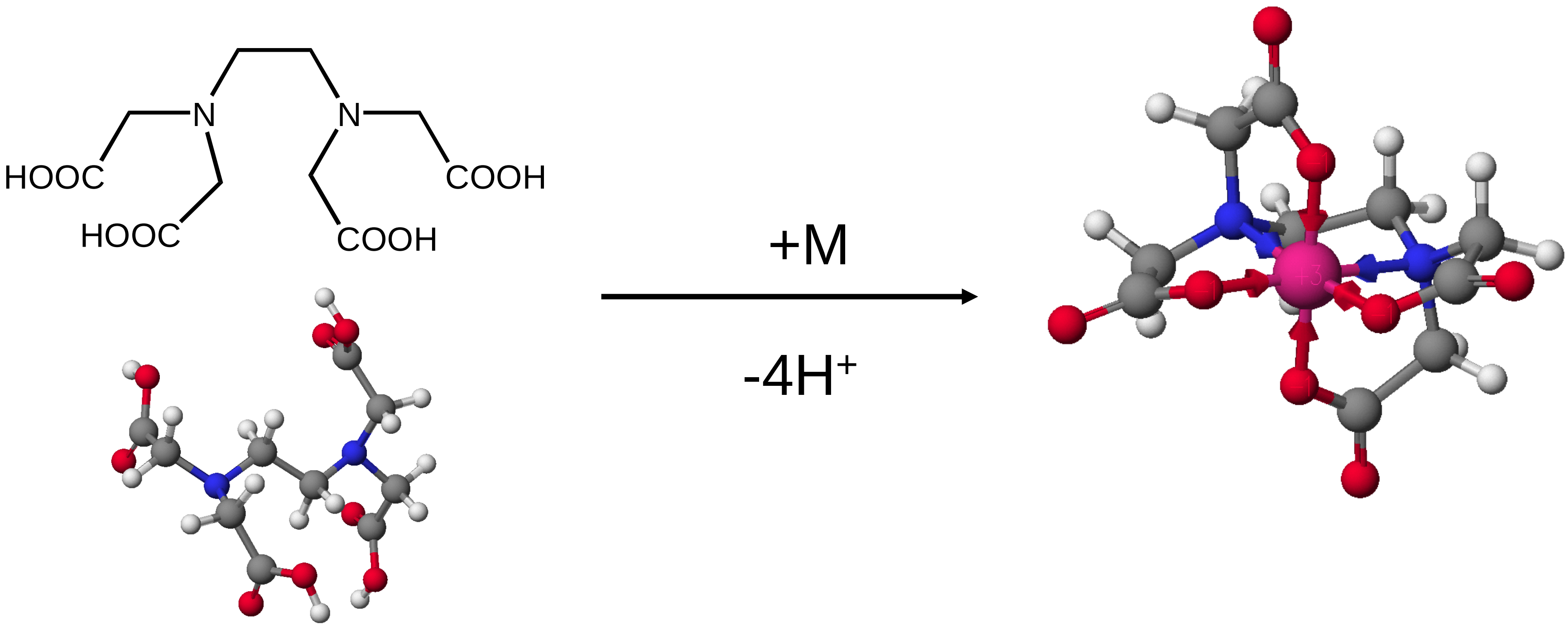
Estabilidad de complejos del ión metálicos
Irving-Williams Series

H. Irving, R. J. P. Williams (1953) J.Chem.Soc. 3192-3210



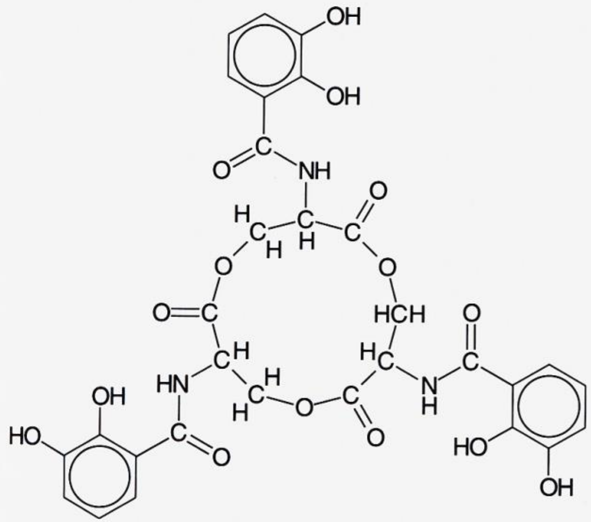
Stability order for high-spin divalent metal ion complexes: Maximum at Cu(II), Minimum at Mn(II)

Strong chelating ligand: EDTA

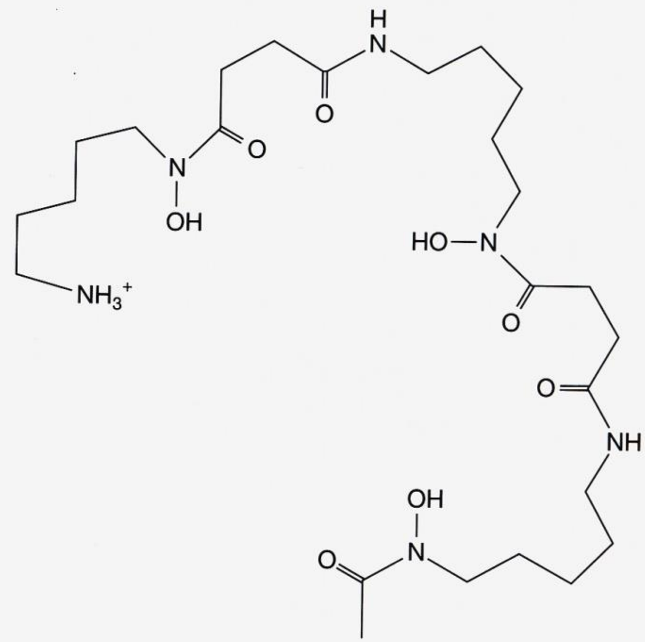


Hexadentate Ligand => strong complexing agent; can be applied to remove metal ions from biological samples (proteins, nucleic acids).

Biological Chelate: Siderophores



(a) Enterobactin

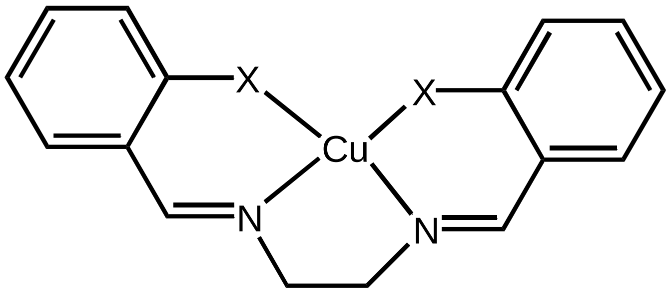


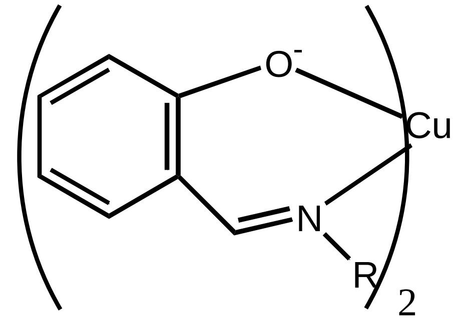
(b) Desferrioxamin

Extremely stable complex of Enterobactin/Fe^{3+} K~ 10^{49}

Release of Fe through a) degradation of ligand, or b) protonation and reduction to Fe^{2+} which binds much weaker to the siderophore.

Modulación de Redox Potentials $E_{1/2}$





$X{=}O^{-}$: $E_{1/2}$ = -1.21 V

$X{=}S^{-}$: $E_{1/2}$ = - 0.83 V

R=CH_3 : $E_{1/2}$ = -0.90 V

R=C_2H_5 : $E_{1/2}$ = -0.86 V

R=*i*-Pr : $E_{1/2}$ = -0.74 V

R=*t*-Bu : $E_{1/2}$ = -0.66 V

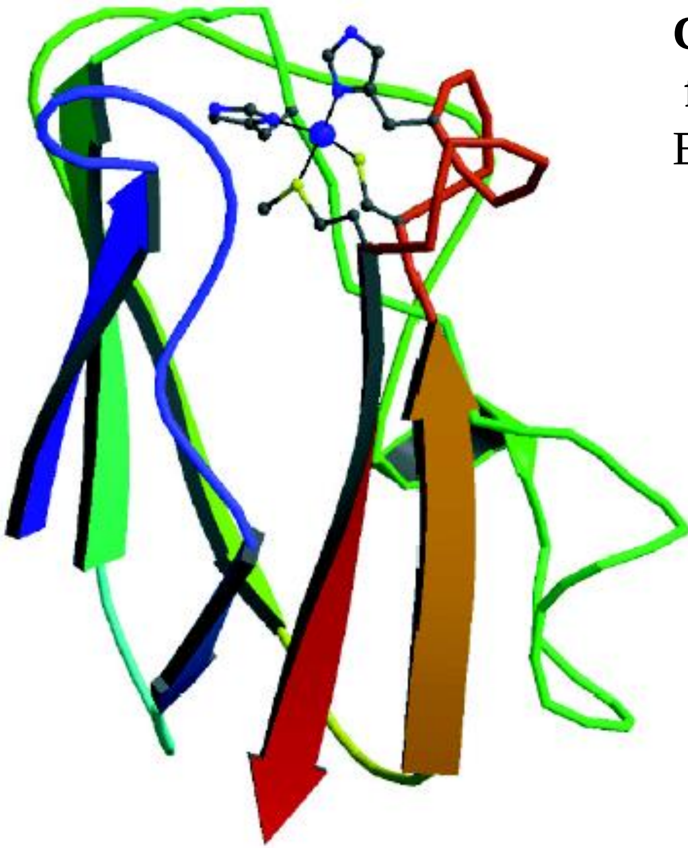
RS^{-} stabilizes Cu(I) state

Positive Potential

El obstáculo de Steric fuerza la geometría tetrahedral, stabilizes Cu(I)

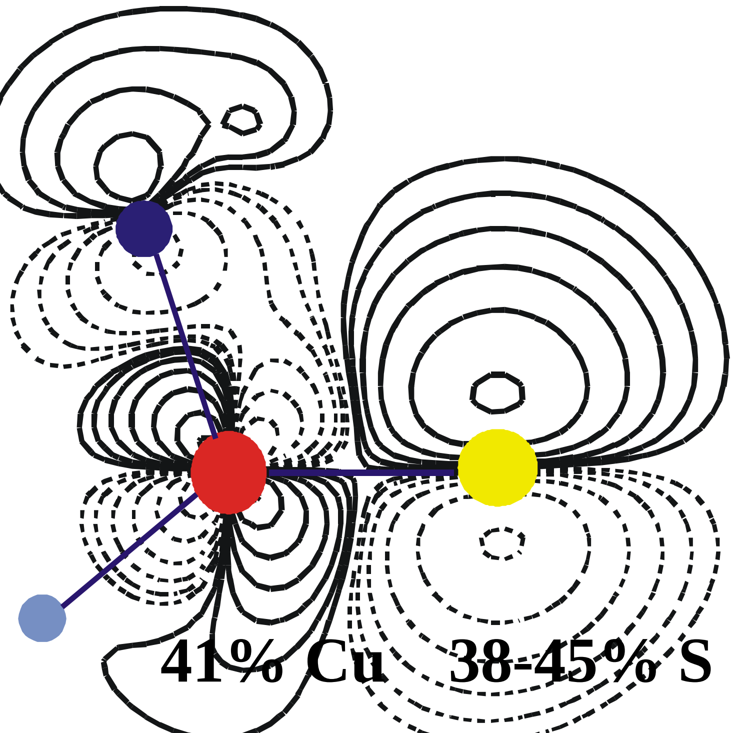
Metal Site 1: Blue Cu Site (Plastocyanin)

Function: Electron Transfer/Photosynthesis



Covalent Cu-Cys π-bond is mainly responsible for its unique properties

EI Solomon, Inorg. Chem. 2006, 45, 8012-8025

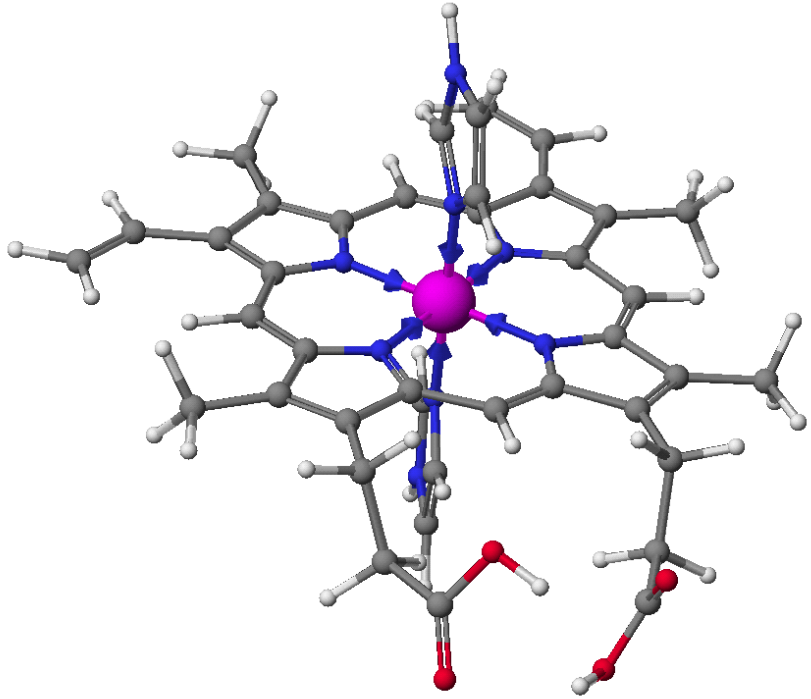


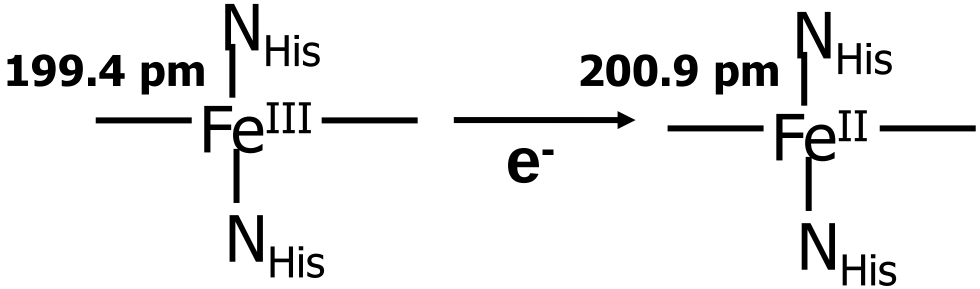
PDB Code: 1PLC
HC Freeman, 1978

Cu(II) Spin-Distribution

Metal site 2: Heme Fe

Function: Electron Transfer/Respiration





Reorganization energy $\propto \Sigma(\Delta R_{ML})^2$

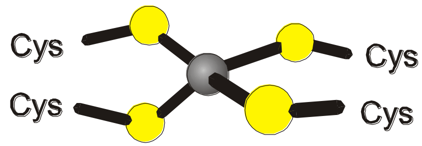
In Cytochromes ≤ 4-5 kcal/mol

Sigfridsson, E.; Olsson, M.H.M.; Ryde, U. (**2001**) *J. Phys. Chem. B*, 105, 5546

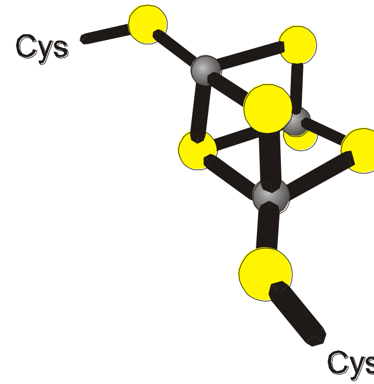
Metal Site 3: Iron – Sulfur centers (FeS)

Function: 1-Electron Transfer (and Catalysis)

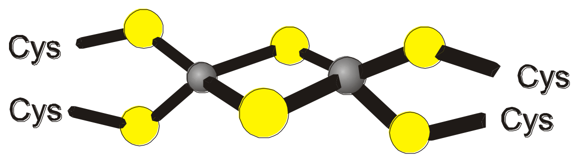
Rubredoxin



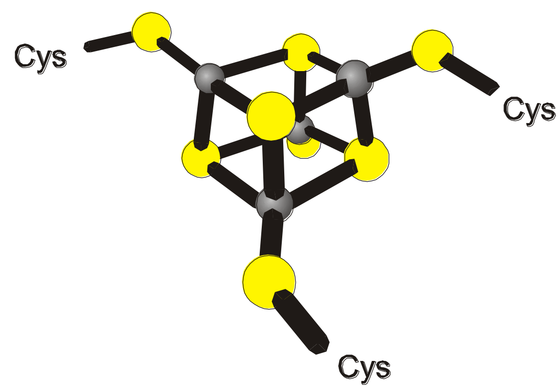
[3Fe-4S]



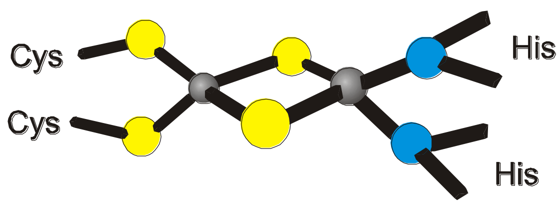
[2Fe-2S] Ferredoxin



[4Fe-4S]

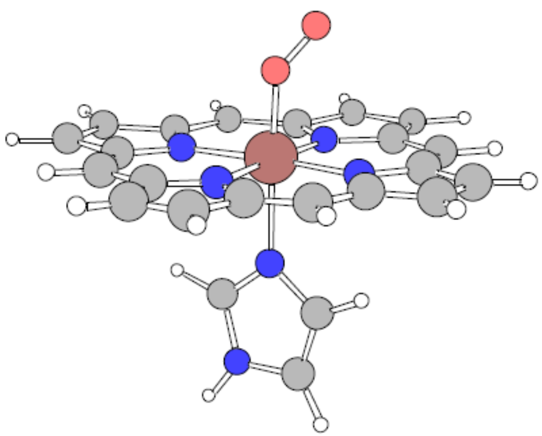


[2Fe-2S] Rieske center

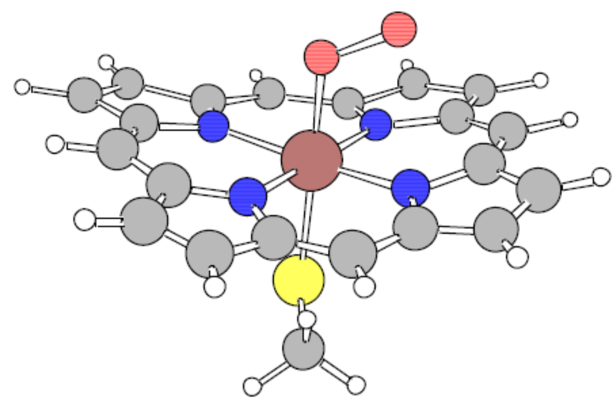


Trans-Effect - Modulación de reactividad

A ligand X *trans* to a second ligand Y can influence the stability of the M-Y bond. With X being a strong Lewis base, the M-Y bond will be weakened



Myoglobin
Axial Histidine
O_2 Transport



Cytochrome P450
Axial Cysteine
O_2 Activation

$RH + O_2 + 2H^+ + 2e^- \rightarrow R\text{-}OH + H_2O$

Proteínas modulan las Propiedades de Iones Metálicos

Coordination number

– The lower the higher the Lewis acidity

Coordination geometry

– Proteins can dictate distortion

– Distortion can change reactivity of metal ion

Weak interactions - Second Shell Effects

– Hydrogen bonds to bound ligands

– Hydrophobic residues: dielectric constant can change stability of metal-ligand bonds