Chem 241

Lecture 34

Announcement

Grading

.

Mistake we have class on the 3rd not 4th
May 3rd no lecture, review session

APRIL/MAY

M	T	W	T	F	S	S
19	20	21	22	23	24	25
26	27	28	29	30	1	2
3	4	5	6	7	8	9
10	11	12	13			

Recap

Exam 3

What the rest of the Periodic table was about

Bioinorganic Chemistry

Two fundamental chemical process

- The use of radiant solar energy to drive chemical reactions that produce oxygen and reduced organic compounds.
- The oxidation products of the above reactions.

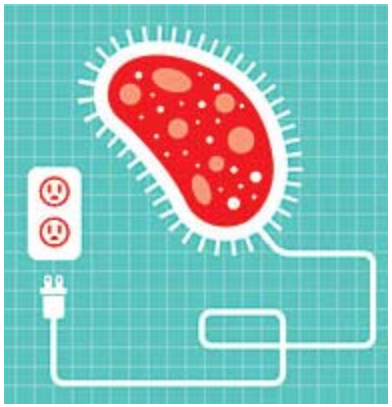
Interplay between kinetics and thermodynamics.

- Catalyst in the form of enzymes
- Metal-contain compounds

Organisms

Chemolithotrophic bacteria – get energy from various sources

$$2Fe^{2+} + [O] \rightarrow Fe_2O_3 + \text{energy}$$



Nitrifying bateria – use ammonia or nitrite

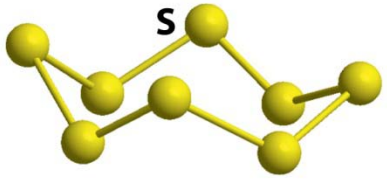
$$2\ NH_3 + [O] \rightarrow 2\ NO_2^- + 3\ H_2O + \text{energy}$$

$$NO_2^- + [O] \rightarrow NO_3^- + \text{energy}$$

Photolithotrophic – green sulfur bacteria and purple sulfur bacteria

$$8H_2S + [O] \rightarrow S_8 + 8H_2O + \text{energy}$$

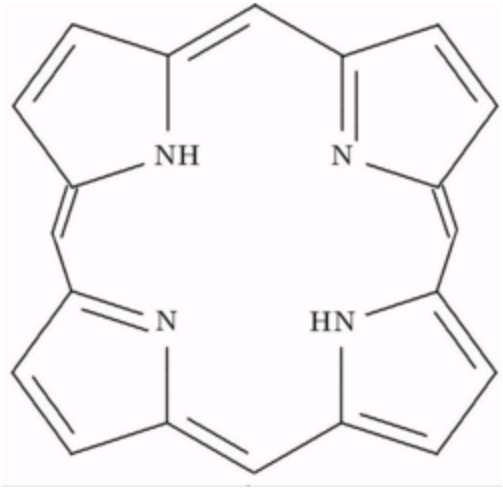
$$S_8 + 8H_2O + [O] \rightarrow 8SO_4^{2-} + 16H^+ + \text{energy}$$



Porphyrins

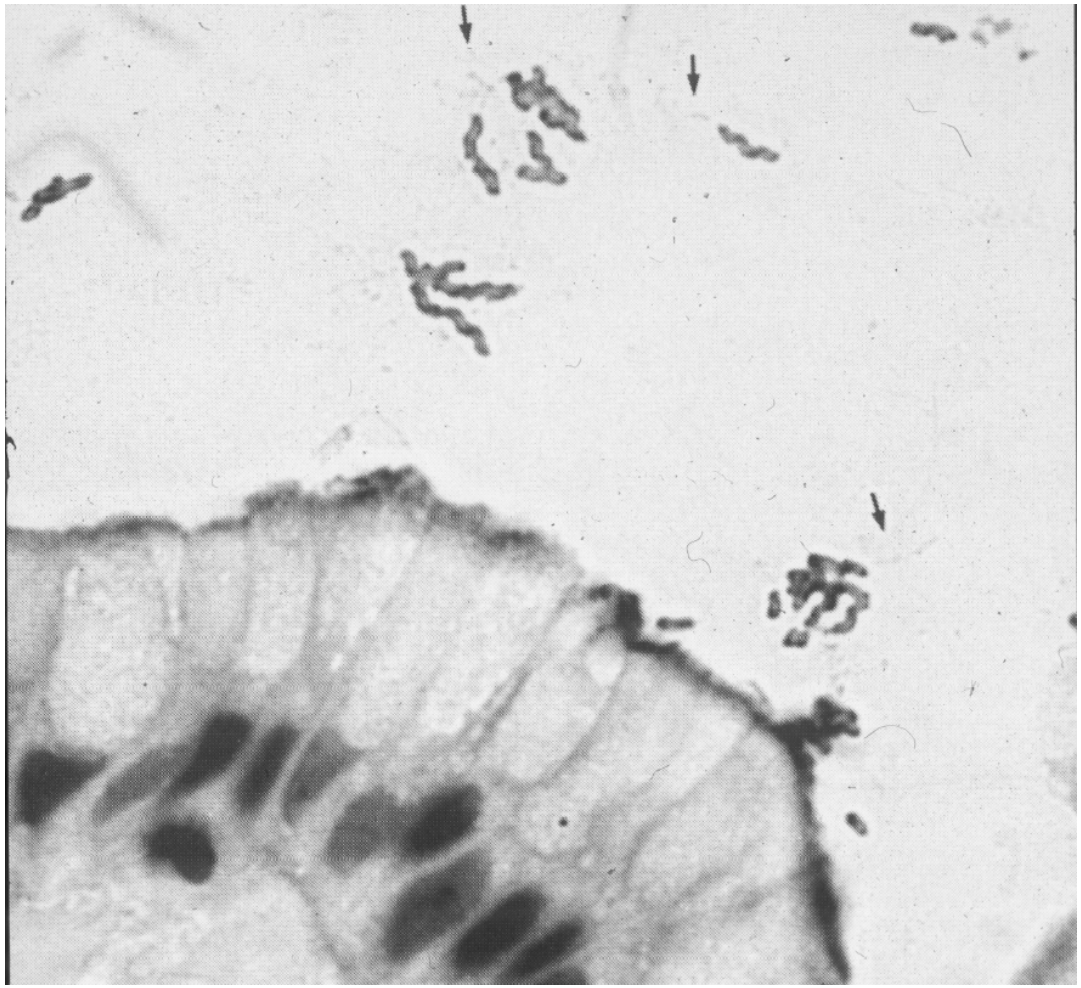
Biomolecules are often complex but at the heart of the beast are metals or metal coordination compound integrated into the structure.

Heme groups – iron chelated by a phorphyrin ring

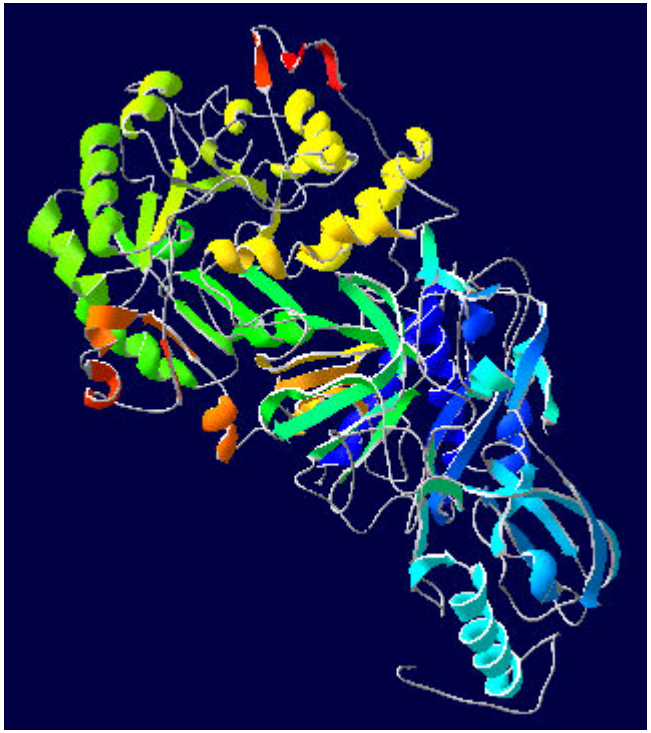


Kinetic formation, K_f , of phorphyrin complexes Cu^{2+} > Co^{2+} >Fe^{2+} > Zn^{2+}

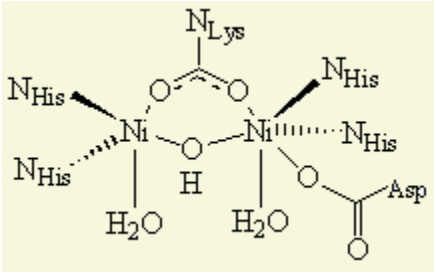
Helicobacter pylori

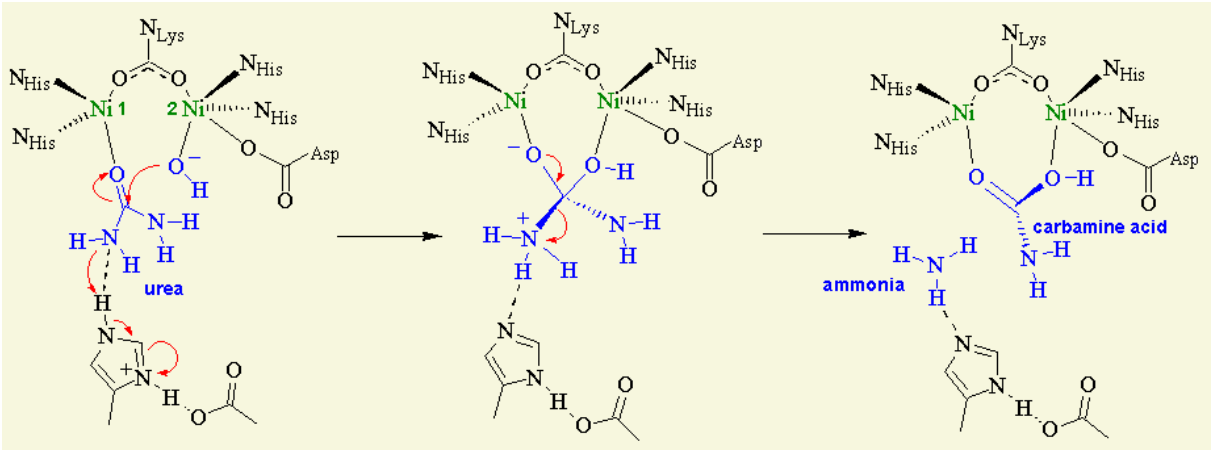


Urease

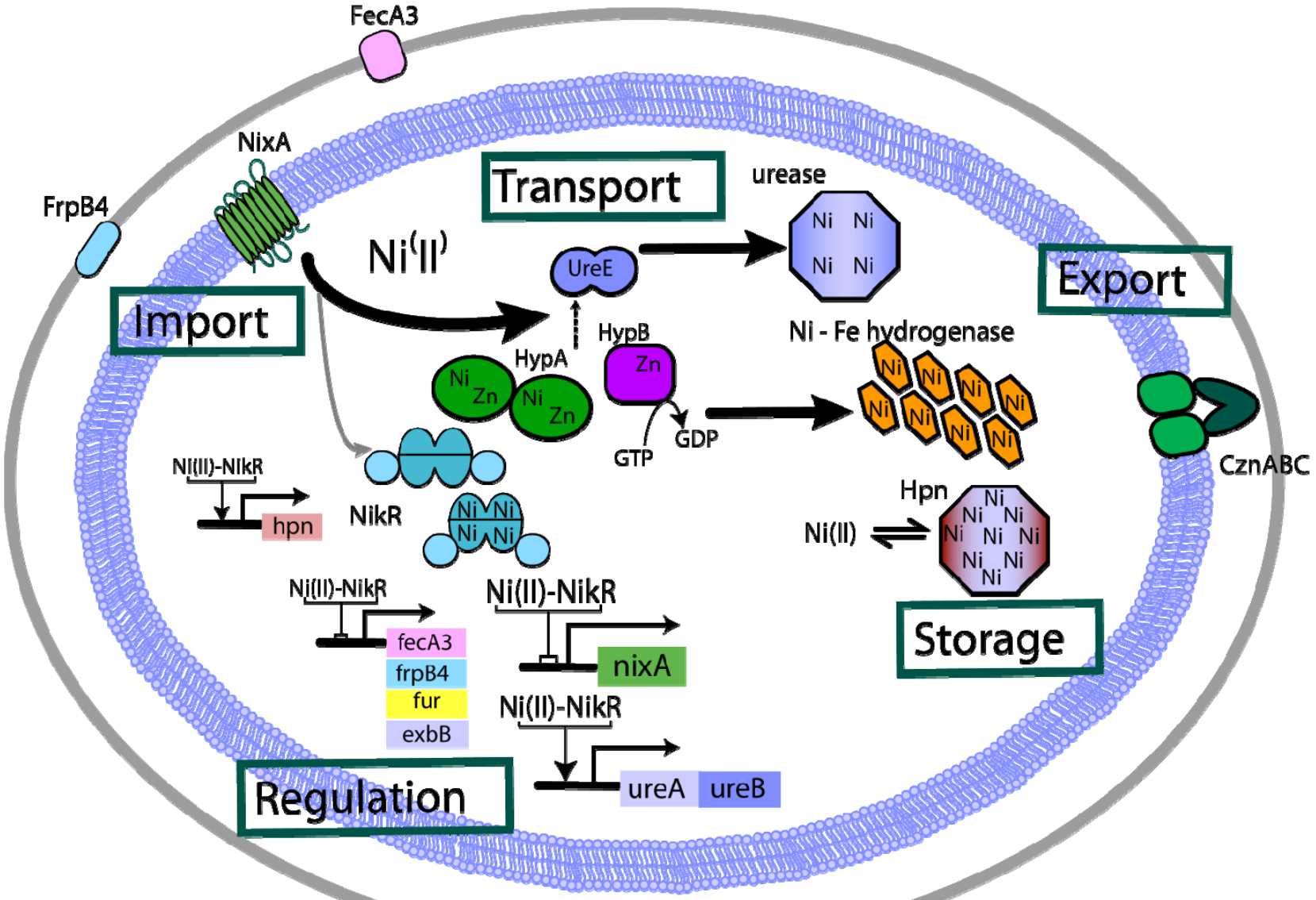


$$(NH_2)_2CO + H_2O \rightarrow CO_2 + 2NH_3$$





Traffic


FecA3
NixA
FrpB4
Transport
urease
Ni(II)
UreE
Import
Export
HypB
HypA
Ni - Fe hydrogenase
Zn
GTP
GDP
CznABC
Ni(II)-NikR
hpn
NikR
Hpn
Ni(II)
Ni(II)-NikR
Ni(II)-NikR
fecA3
frpB4
fur
exbB
nixA
Storage
Ni(II)-NikR
ureA
ureB
Regulation

NikR function is Ni-specific

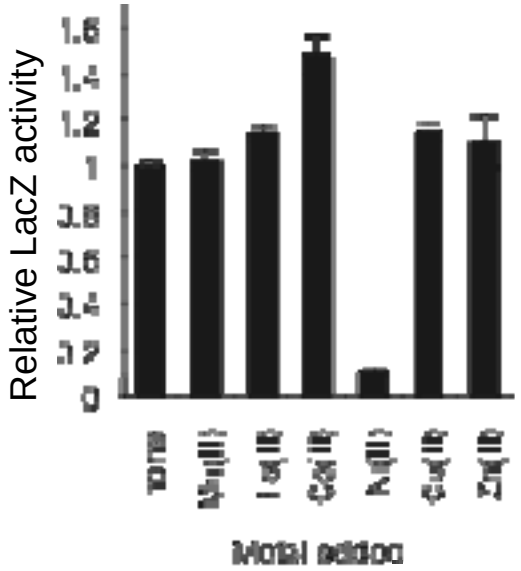
NikR can be activated for DNA-binding *in vitro* by other first row transition metals

Metal	$K_{d,\ M(II)}$	$K_{d,DNA}$
Co(II)	2 nM	11 nM
Ni(II)	1 pM	5 nM
Cu(II)	14 aM	3 nM
Zn(II)	1 pM	270 nM

Zamble and co-workers
Biochemistry (2004)

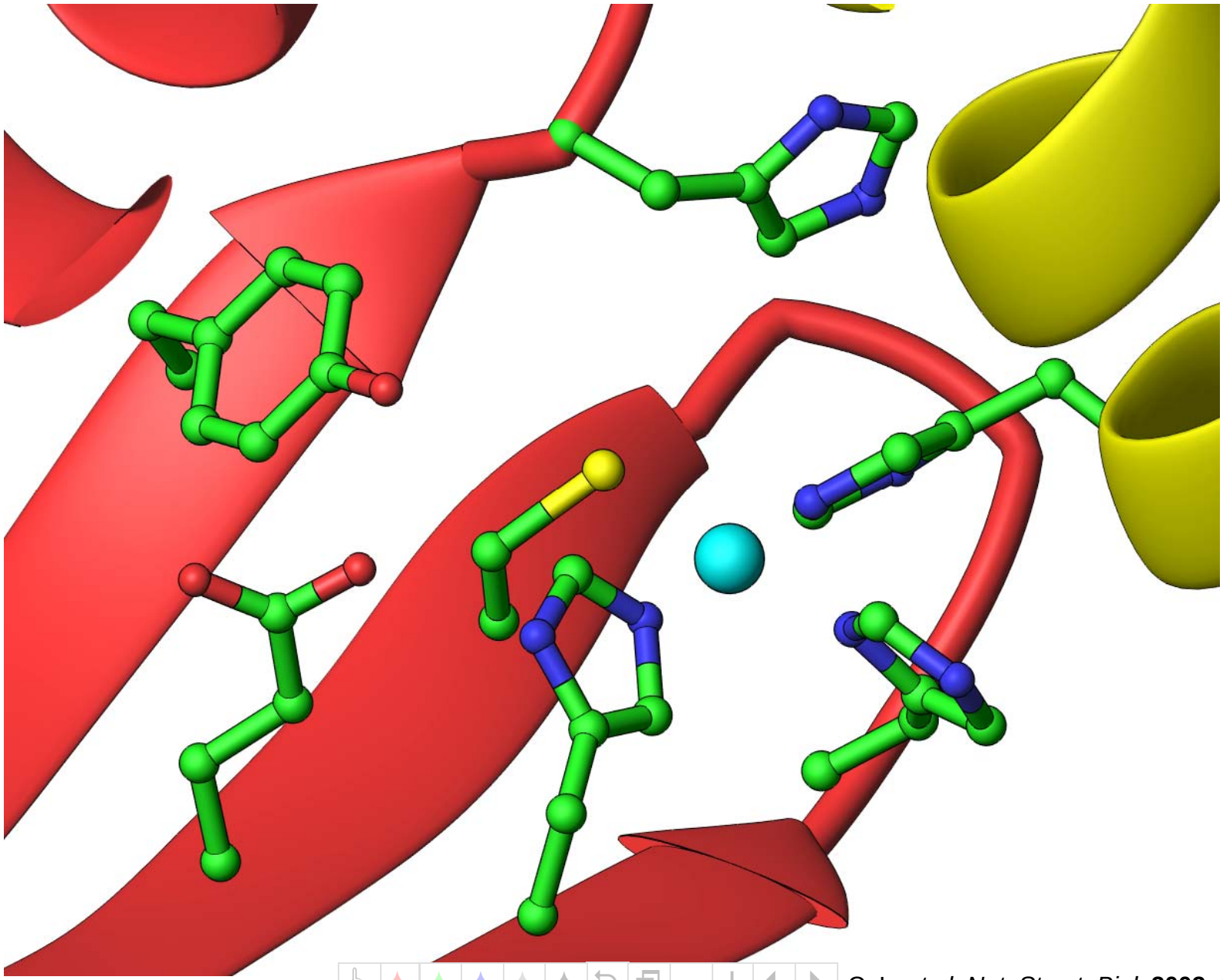
But the biological response (repression of P_{nik}) is completely Ni-specific.

P_{nik}-*lacZ* expression



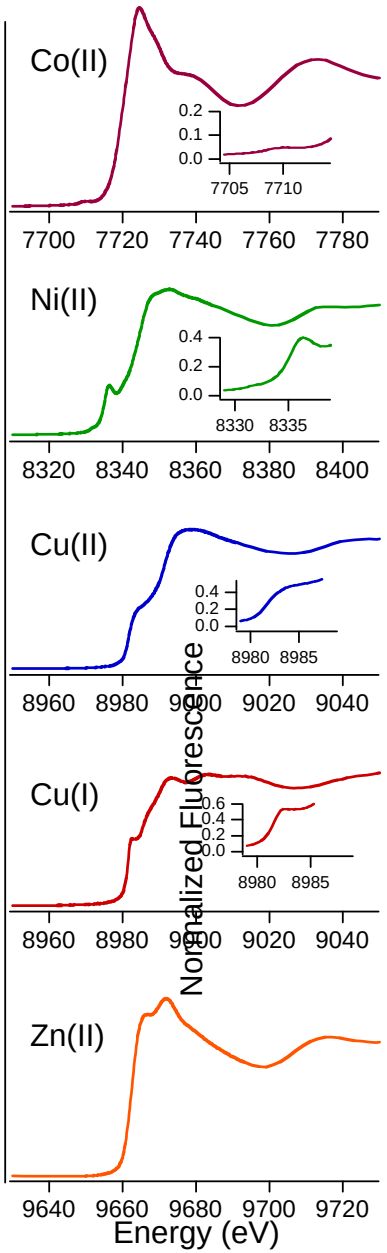
Schmitt *et al. J. Am. Chem. Soc.* **2007**, *129*, 5085.

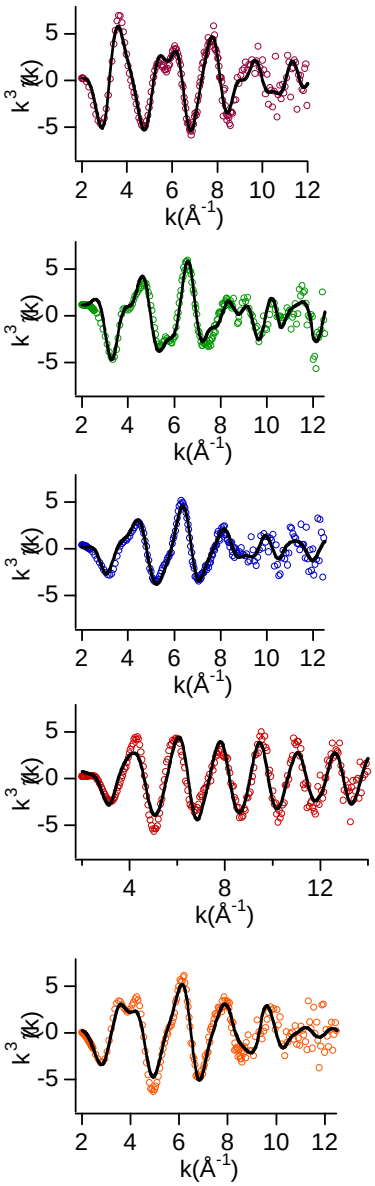
High-Affinity Nickel Site Structure



C. L. *et al. Nat. Struct. Biol.* **2003,** *10*, 794.

Metals bound to NikR have distinct structures

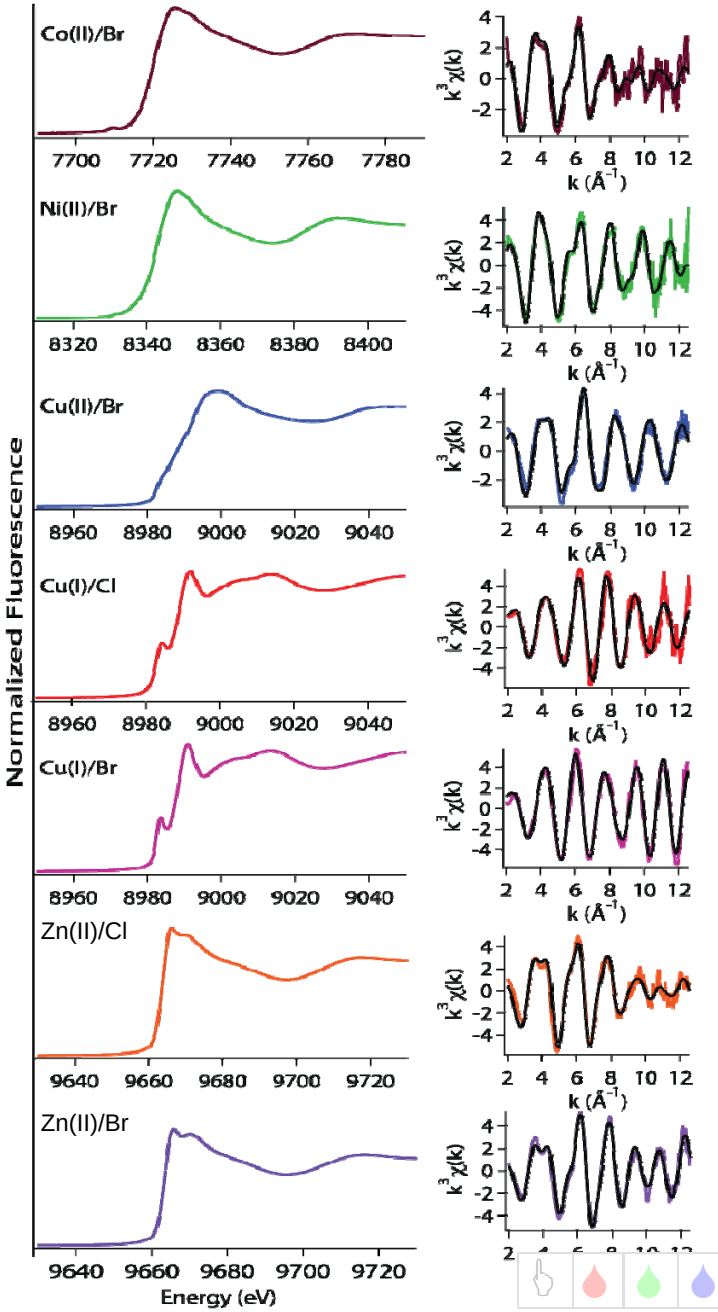




Metal	Geometry	CN	N[a]	r (Å)[c]
Co(II)	octahedral	6	3 Co-N_{His}	2.047(4)
			6 Co-C_{His}	2.959(10)
			3 Co-N/O	2.171(6)
Ni(II)	planar	4	3 Ni-N_{His}	1.905(3)
			1 Ni-S	2.130(6)
Cu(II)	planar	4	2 Cu-N_{His}	1.928(8)
			1 Cu-N/O	2.100(28)
			1 Cu-S	2.210(9)
Cu(I)	trigonal	3	1 Cu-N_{His}	2.130(16)
			1 Cu-N/O	2.036(14)
			1 Cu-S	2.279(5)
Zn(II)	tetrahedral	4	3 Zn-N_{His}	1.990(6)
			1 Zn-S	2.229(8)

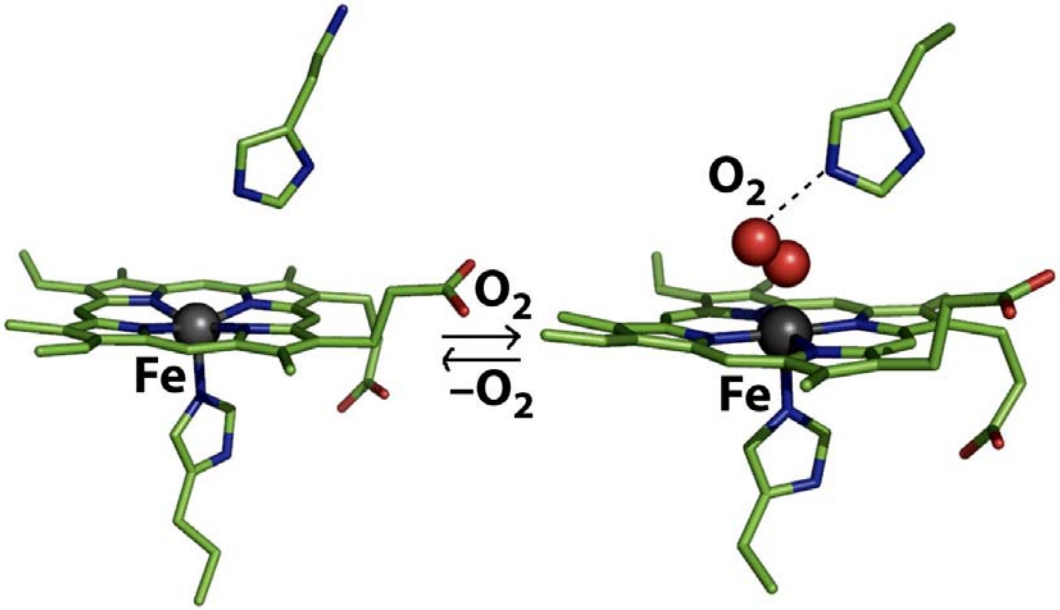
S. Leitch *et al. J. Am. Chem Soc.* **2007**, *129*, 5085.

EXAFS Analysis of WT RcnR complexes

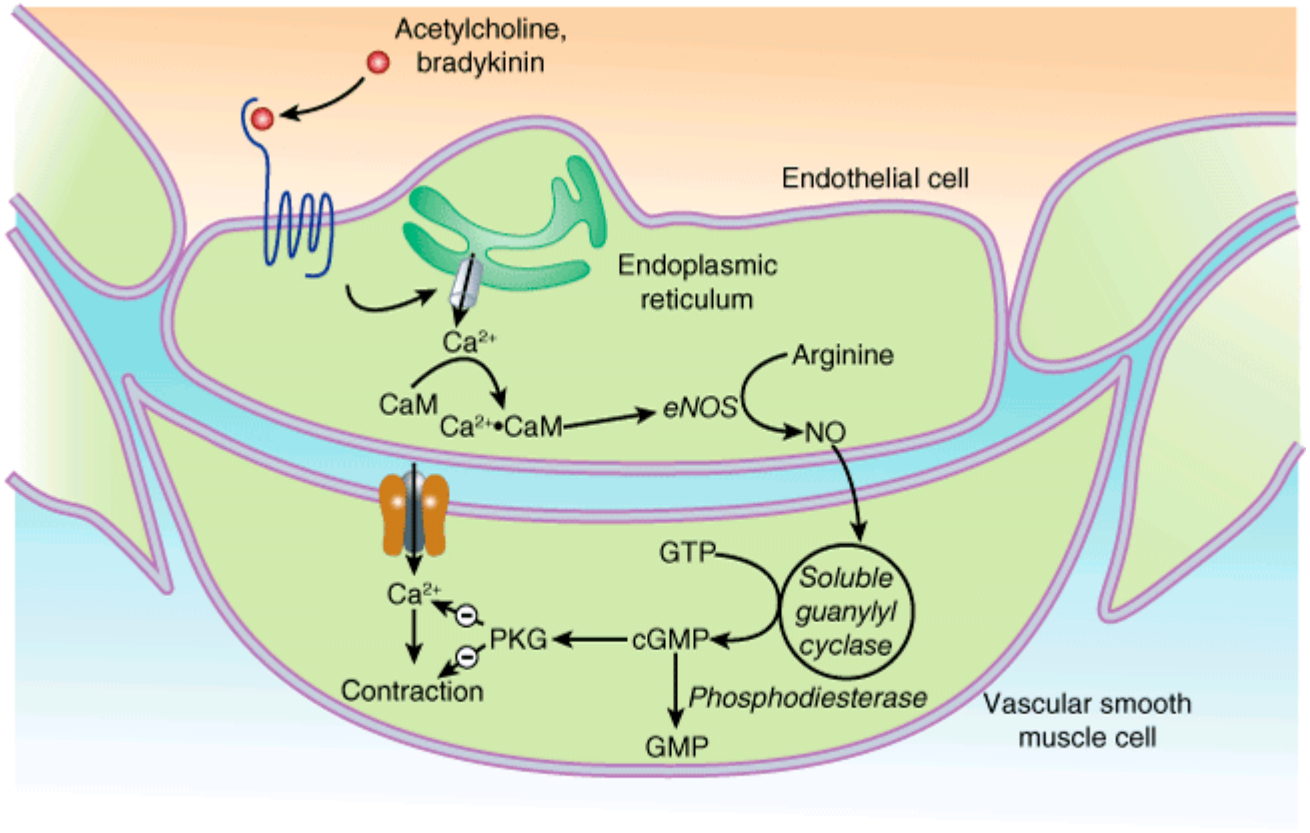


Sample	N	R(Å)	Geometry	CN
Co(II)NaBr	5 N/O (1 His)	2.05(1)	Octahedral	6
	1 S (Cys)	2.39(3)		
Ni(II)NaCl	5 N/O (1 His)	2.078(9)	Octahedral	6
	1 S (Cys)	2.62(3)		
Cu(II)NaBr	2N/O	1.971(9)	Planar	4
	1N/O (1 His)	1.89(2)		
	1 S (Cys)	2.18(2)		
Cu(I)NaCl	2 N/O	2.12(2)	Tetrahedral	4
	1 S (Cys)	2.31(1)		
	1 Cl-	2.74(2)		
Cu(I)NaBr	2 N/O	2.11(1)	Tetrahedral	4
	1 S (Cys)	2.30(6)		
	1 Br-	2.628(8)		
Zn(II)NaCl	2 N/O (1 His)	2.01(4)	Tetrahedral	4
	2 S (Cys + Cl-)	2.27(3)		
Zn(II)NaBr	2 N/O (1 His)	1.99(1)	Tetrahedral	4
	1 S (Cys)	2.31(5)		
	1Br-	2.371(8)		

Hemoglobin

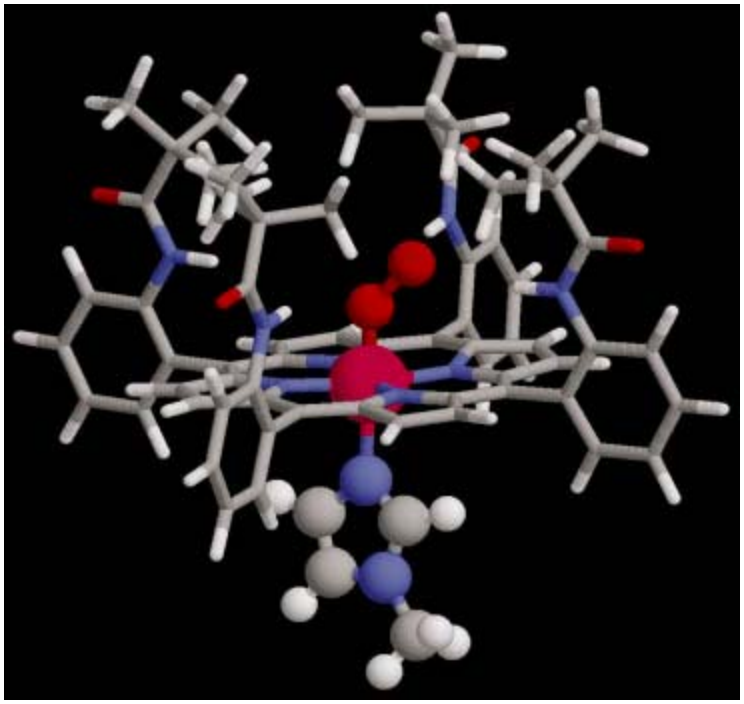


Endothelium-derived relaxing factor (EDRF)



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition:* http://www.accessmedicine.com

Picket fence



Picture representation

Cooperative effect