

生物無機化学

Bioinorganic Chemistry

Part 2

3章 酸素輸送タンパク質

3-1ヘモグロビン

3-2ヘムエリトリン

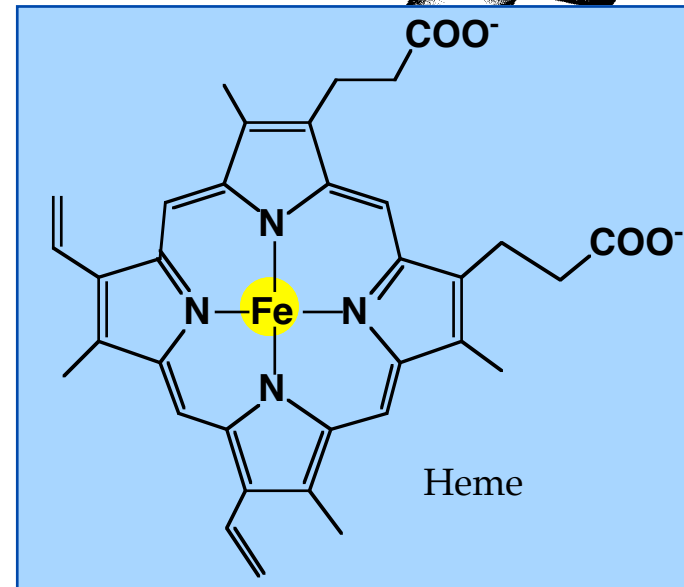
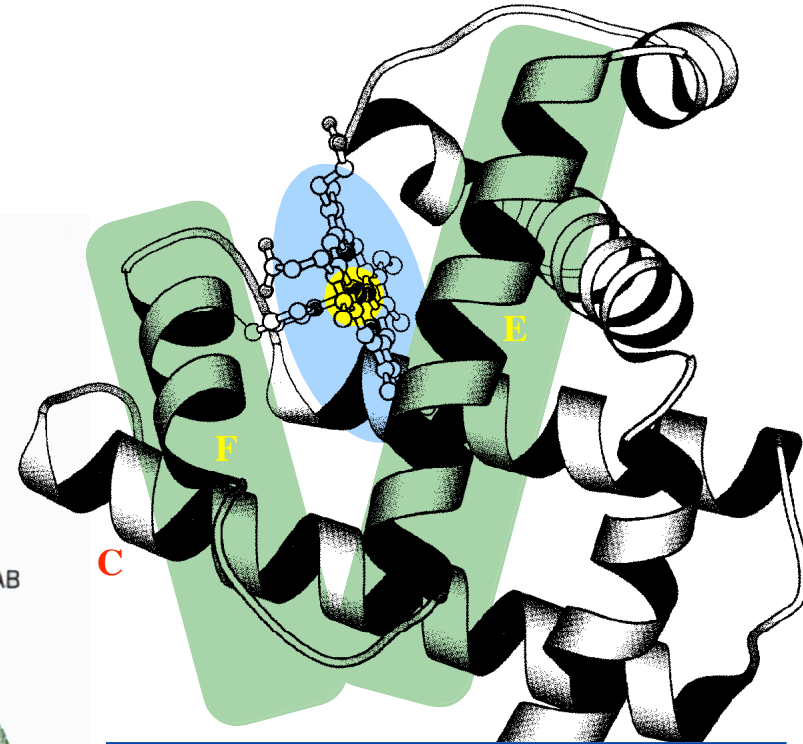
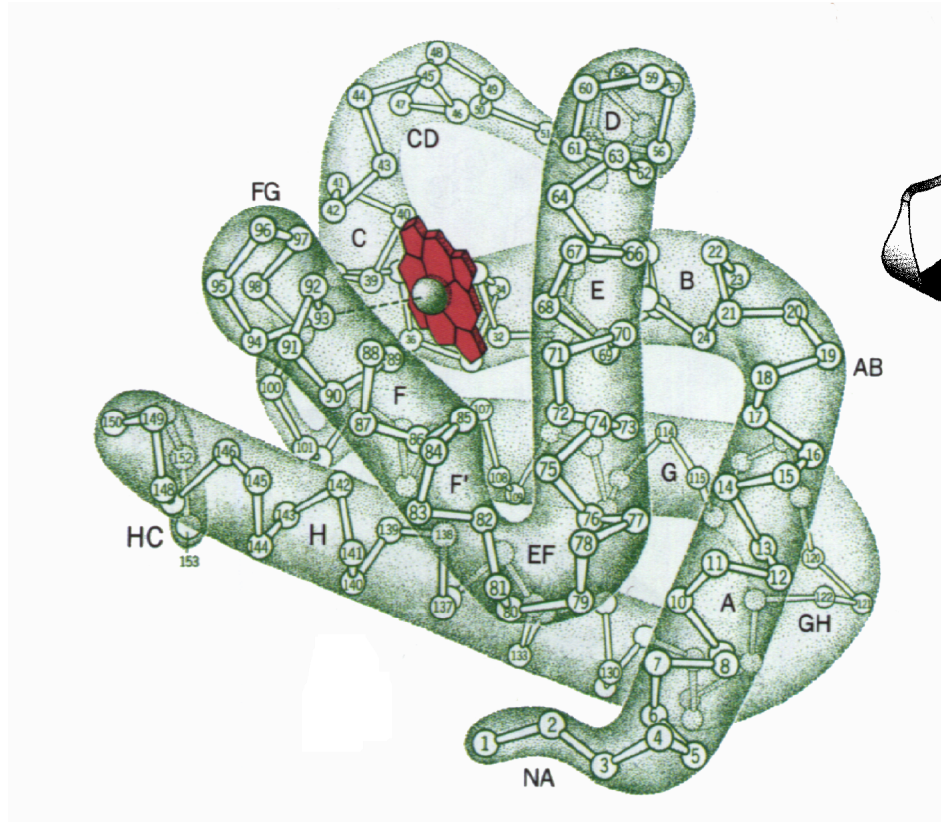
3-3ヘモシアニン

酸素輸送タンパク質

Dioxygen Carrier Proteins

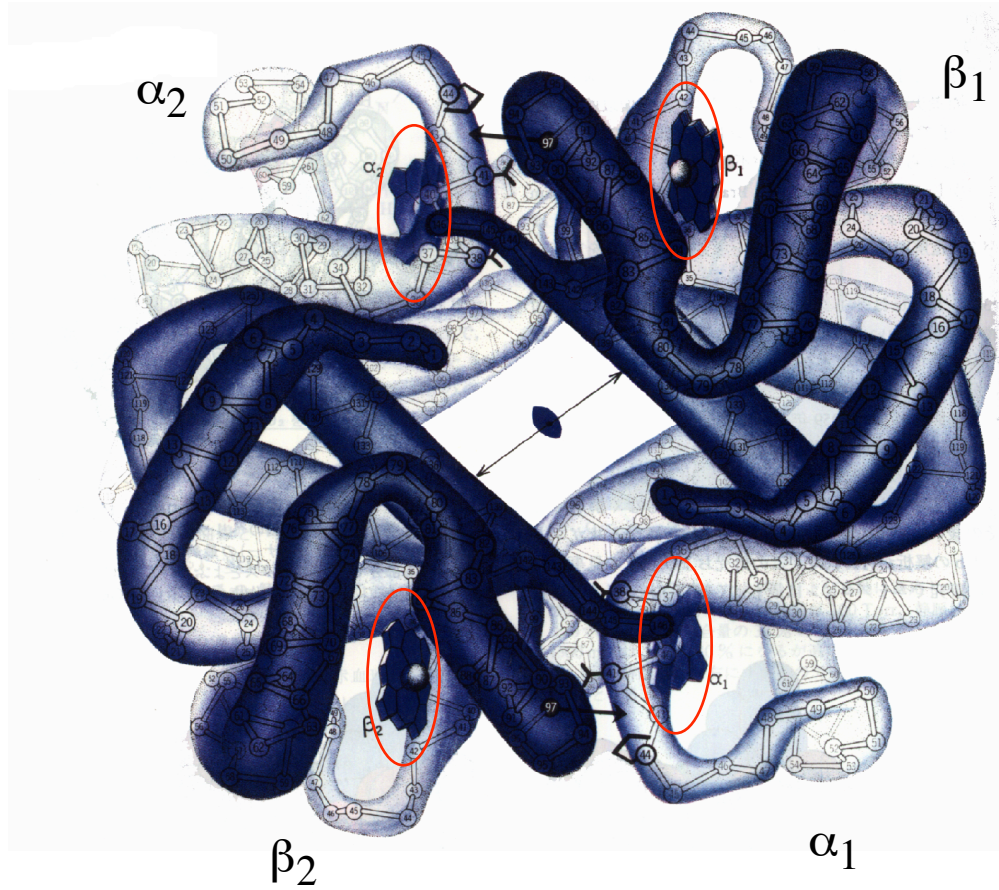
	ヘモグロビン	ヘムエリトリン	ヘモシアニン
proteins	Hemoglobin (Hb)	Hemerythrin (Hr)	Hemocyanin (Hc)
metal	Fe-porphyrin	dinuclear Fe	dinuclear Cu
oxidation state	(II)/(III)	(II)/(III)	(I)/(II)
deoxy/oxy			
metal:O ₂	Fe : O ₂	2Fe : O ₂	2Cu : O ₂
source	all vertebrate many invertebrates	marine invertebrates	arthropods mollusks
color, oxy-form	red	violet-pink	blue
color, deoxy-form	red-purple	colorless	colorless
coordination	porphyrin	protein side chains	protein side chains
Mw	65 kDa	108 kDa	400-20000 kDa
number of subunits	4	8	many
	ミオグロビン Myoglobin (Mb)		

ミオグロビン(Mb)の構造

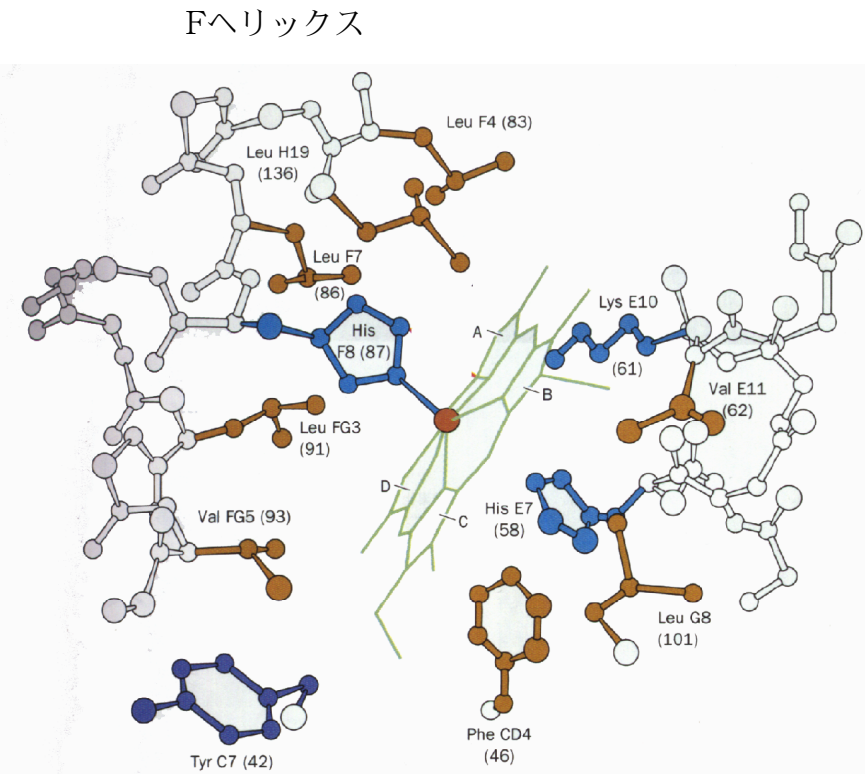


マッコウクジラのみオグロビン(Mb)のX線結晶構造
153アミノ酸残基, A-H 8個のヘリックス構造
(ヴォート)

ヘモグロビン(Hb)の構造

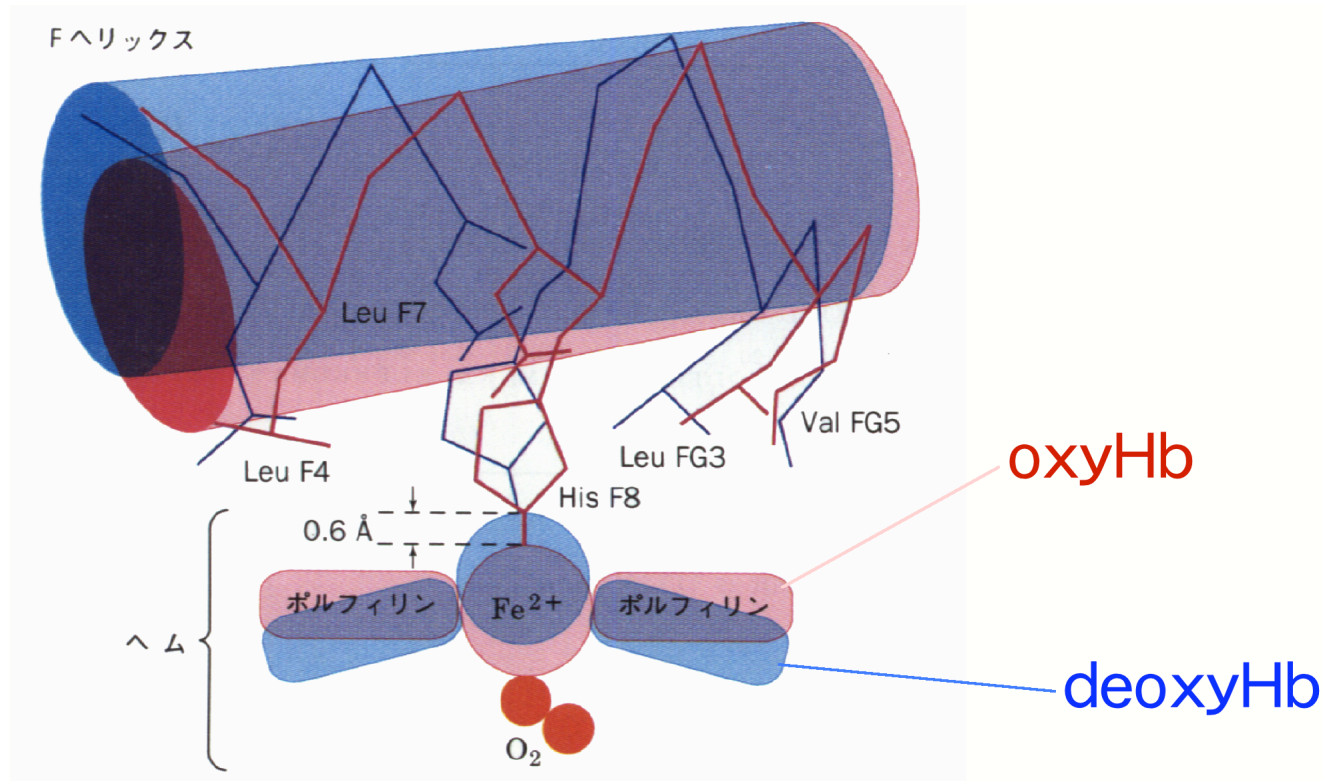


デオキシヘモグロビンの結晶構造
 $\alpha_2\beta_2$ サブユニット四量体

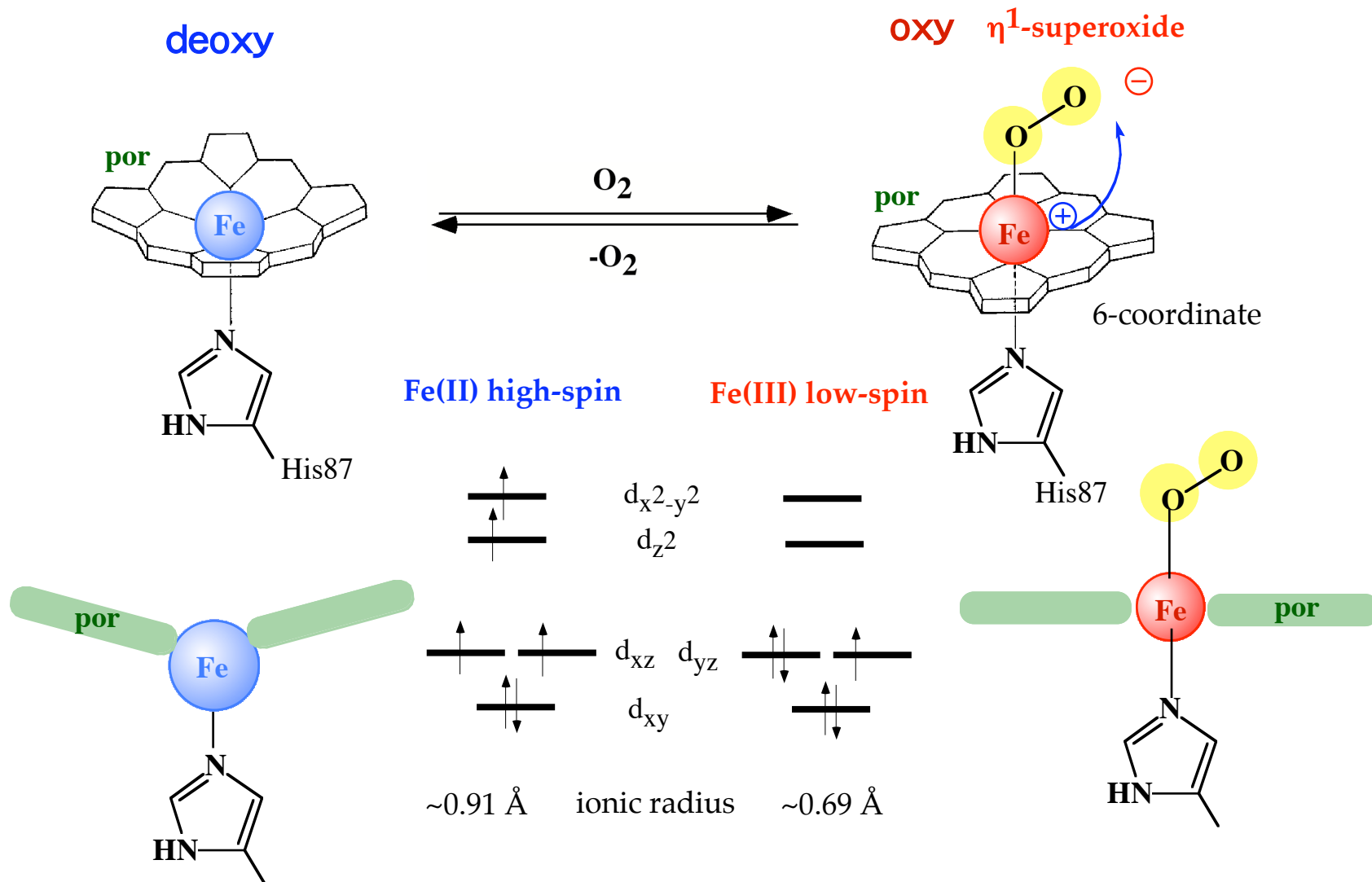


deoxyHb α 鎖のへム周辺の構造 (T状態)


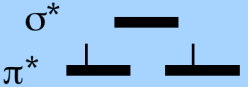


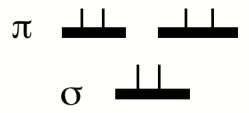
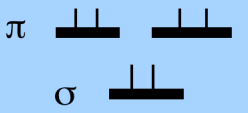
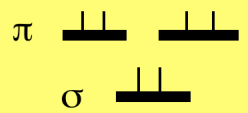
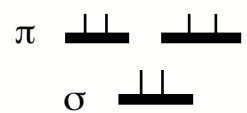
酸素結合に伴う誘起適合 (Induced Fit)



酸素結合に伴う誘起適合 (Induced Fit)



Electronic Structures and Vibrational and Geometrical Properties of Dioxygen Derivatives

	O_2^+	O_2 dioxygen	O_2^- superoxide	O_2^{2-}
				
				
bond order	2.5	2.0	1.5	1.0
d_{O-O} (Å)	1.12	1.21	1.33	1.49
ν_{O-O} (cm ⁻¹)	1905	1580	1097	802

Hbにおける酸素結合の協同性 (1)

アロステリック効果

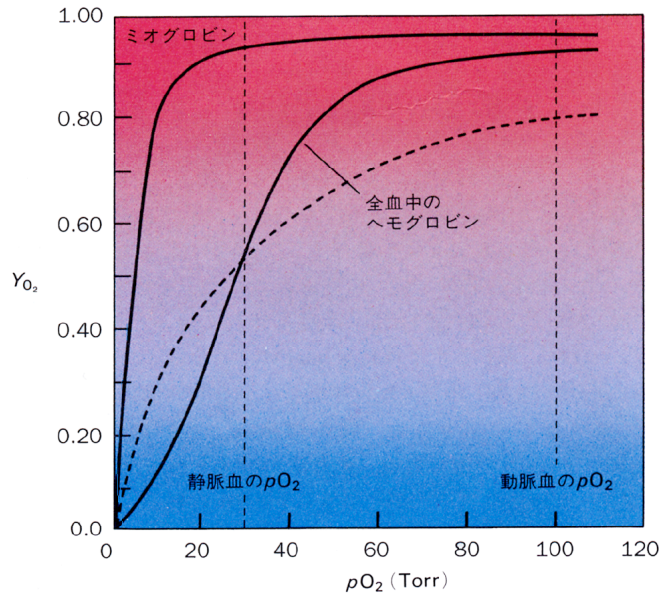
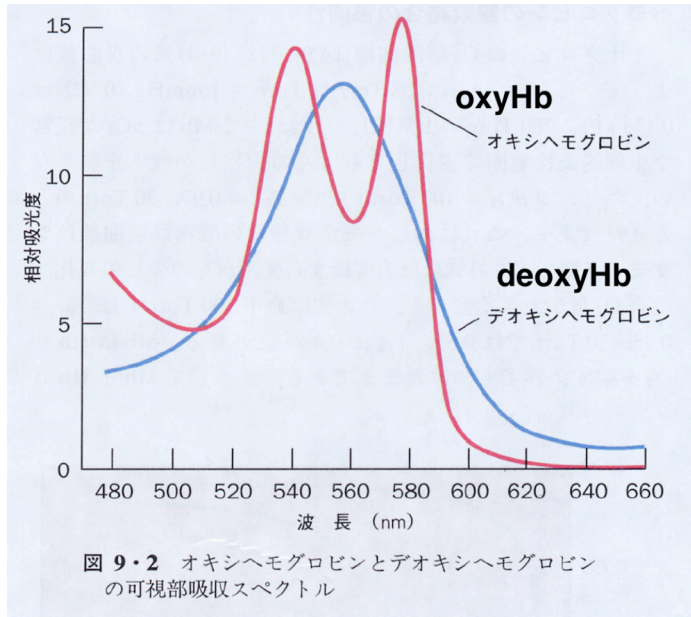
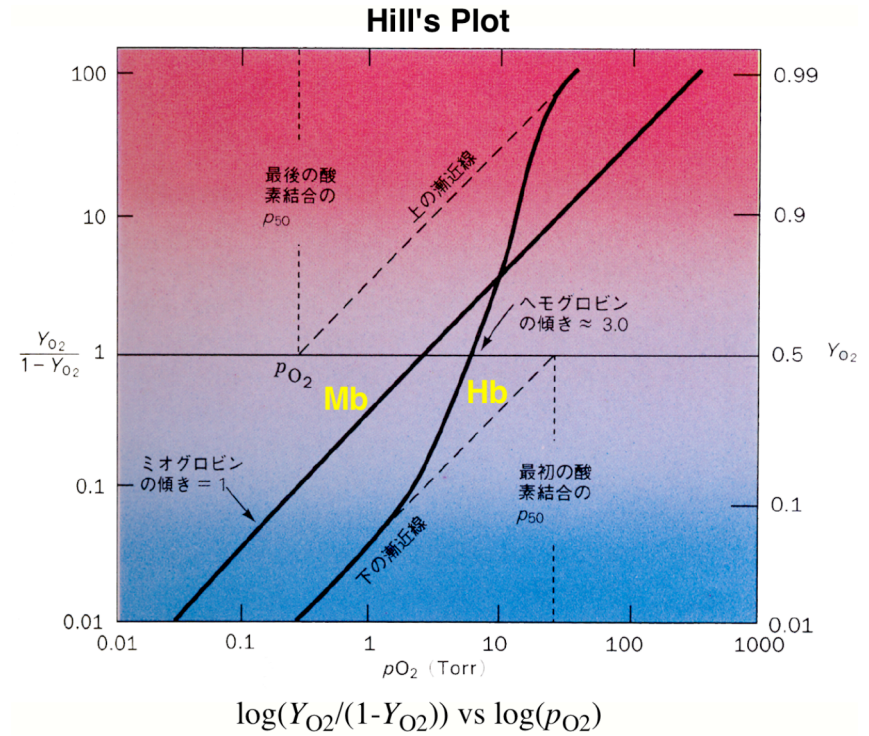


図 9・3 Mbと全血中のHbの酸素解離曲線。ヒトの動脈および静脈の pO_2 (平地の値)も示す。破線はHbと同じ p_{50} (26 Torr)値の場合の単純解離曲線



Hbにおける酸素結合の協同性 (2) アロステリック効果

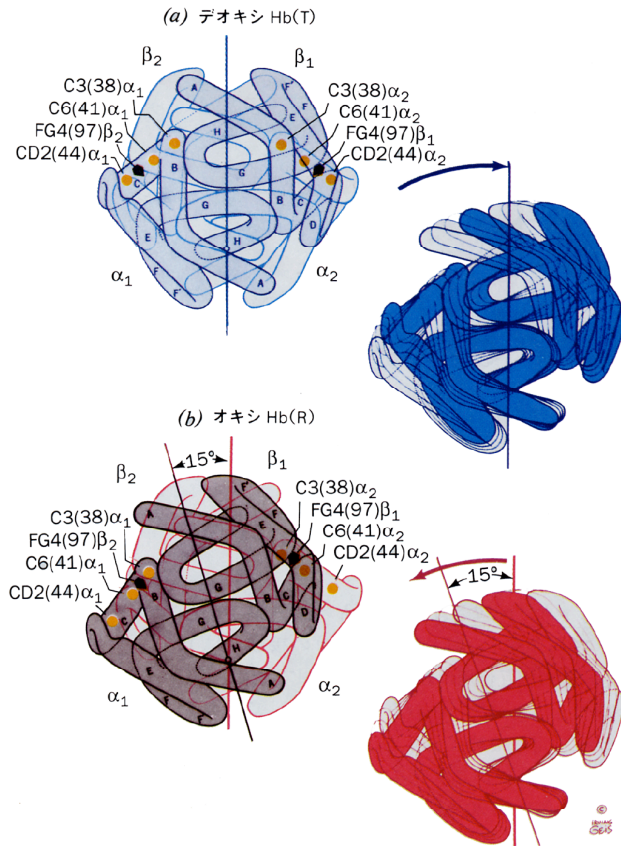


図 9・14 デオキシ Hb(a) とオキシ Hb(b) の四次構造差の概略、酸素化すると $\alpha_1\beta_1$ (色つき), $\alpha_2\beta_2$ (輪郭) 両プロトマーが右側に示すようにそれぞれ一つの単位として互いに 15° ほど回転する。分子の対称性は保たれる。His FG4 β (五角形) が $\alpha_1\text{-}\beta_2$, $\alpha_2\text{-}\beta_1$ 接触面で Thr C3 α , Thr C6 α , Pro CD2 α (黄) の間で位置を変えることに注意。この図は図 9・13 を横から見た形 [図の著作権 © by Irving Geis]

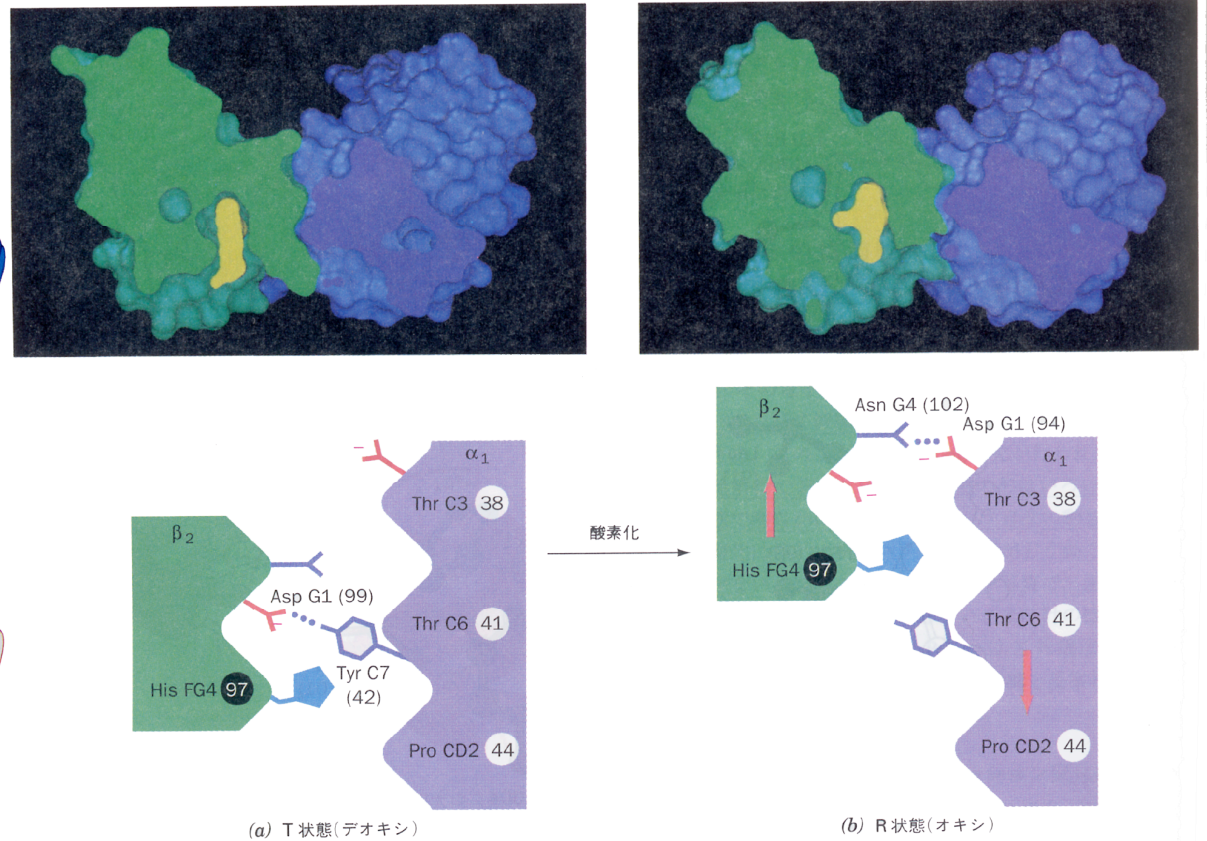
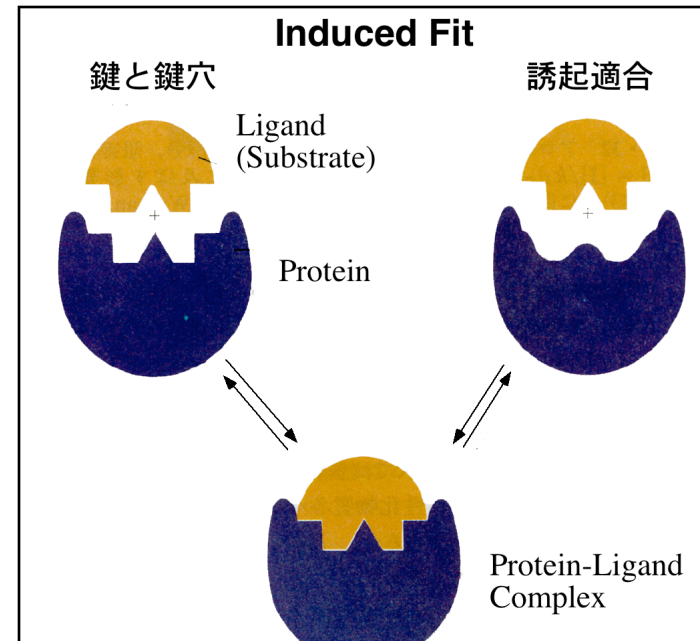
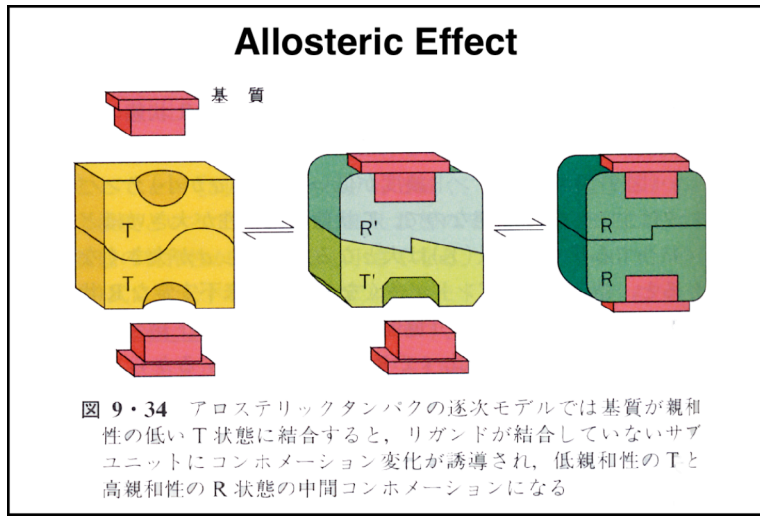
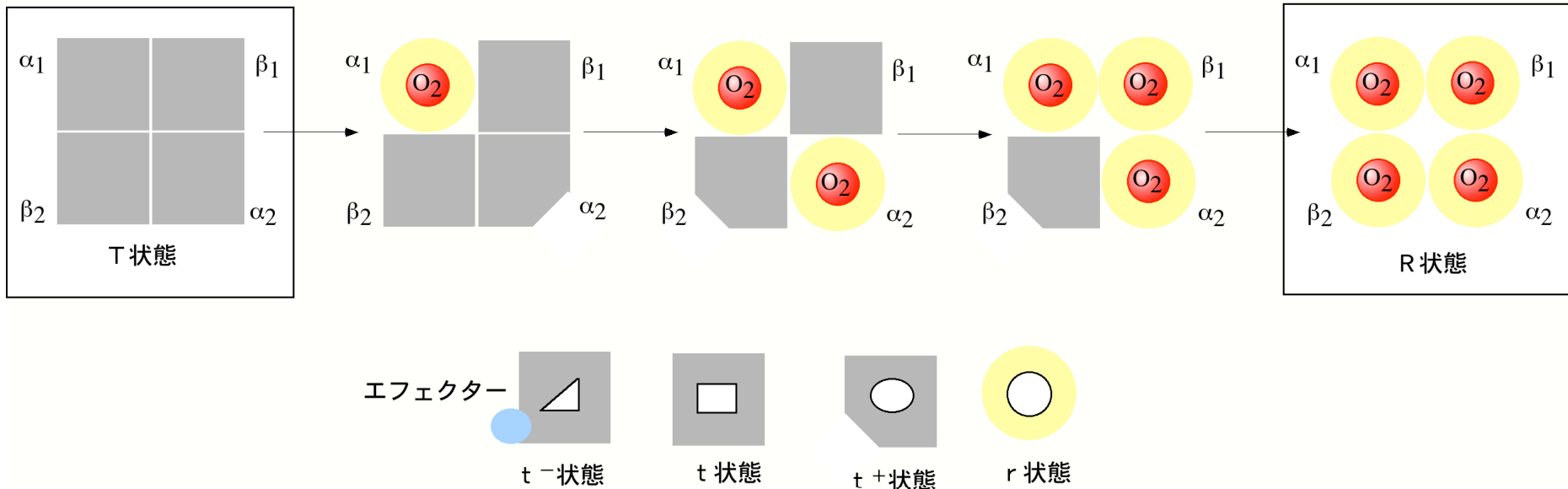


図 9・17 $\alpha_1\beta_2$ 二量体の断面図。(a) T 状態、(b) R 状態。 $\alpha_1\beta_2$ 二量体を $\alpha_1\text{C}$ と $\beta_2\text{FG}$ の接触面がみえるように 2 回対称軸に対し垂直に切断したところ。T \rightarrow R 遷移では途中で安定状態なしに両者が切り換わる。サブユニット同士はどちらの状態でも別の水素結合により結合している。図 9・13、図 9・14、図 9・19 も同じ変化を別の表し方で示す [Michael Pique, Research Institute of Scripps Clinic, San Diego, California の好意による]

Hbにおける酸素結合の協同性 (3)

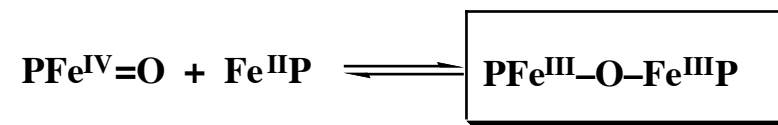
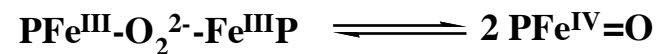
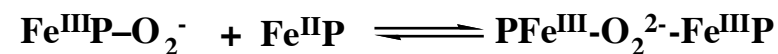
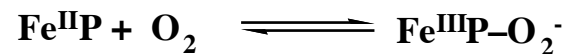


ヘモグロビンの場合の概念図

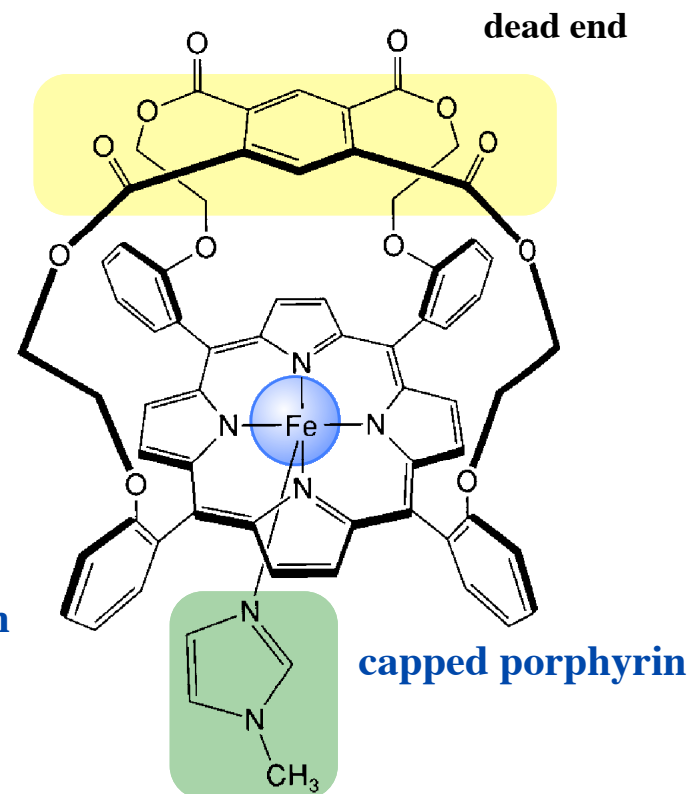
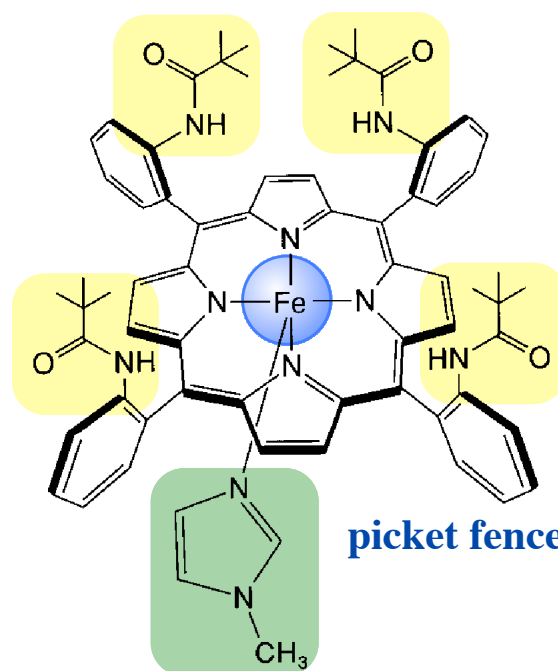


Model Compounds for Hb and Mb

Normal Porphyrin Fe(II) Complexes

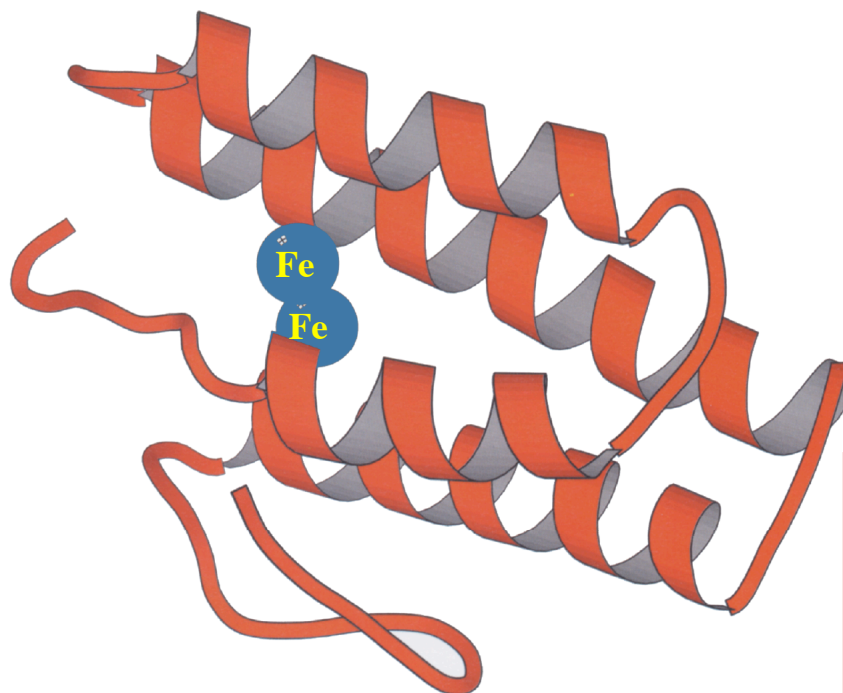


Reversible Dioxygen Binding



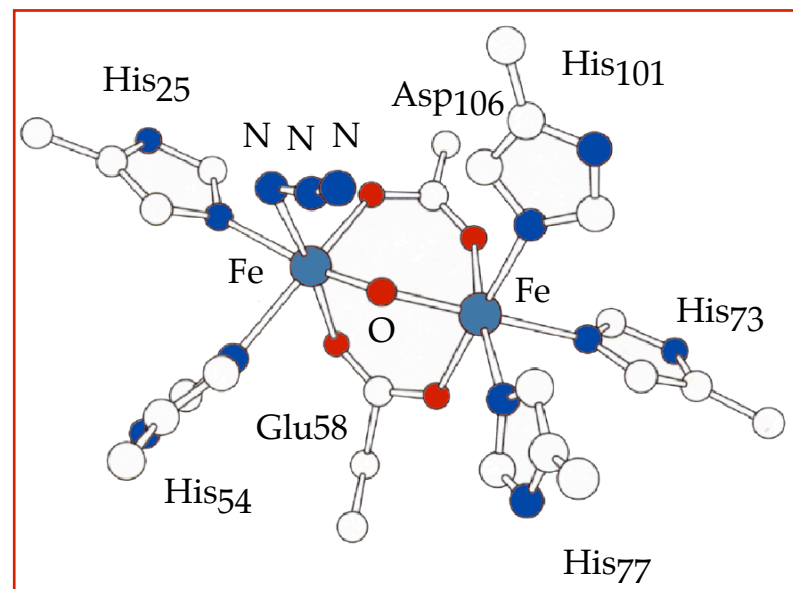
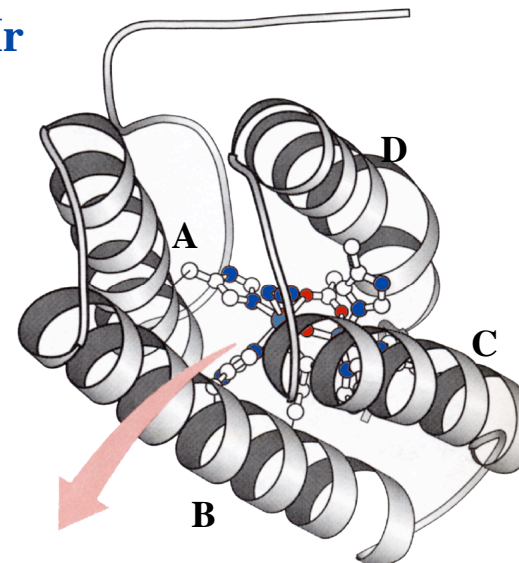
Structures of Hemerythrin (Hr)

deoxyHr

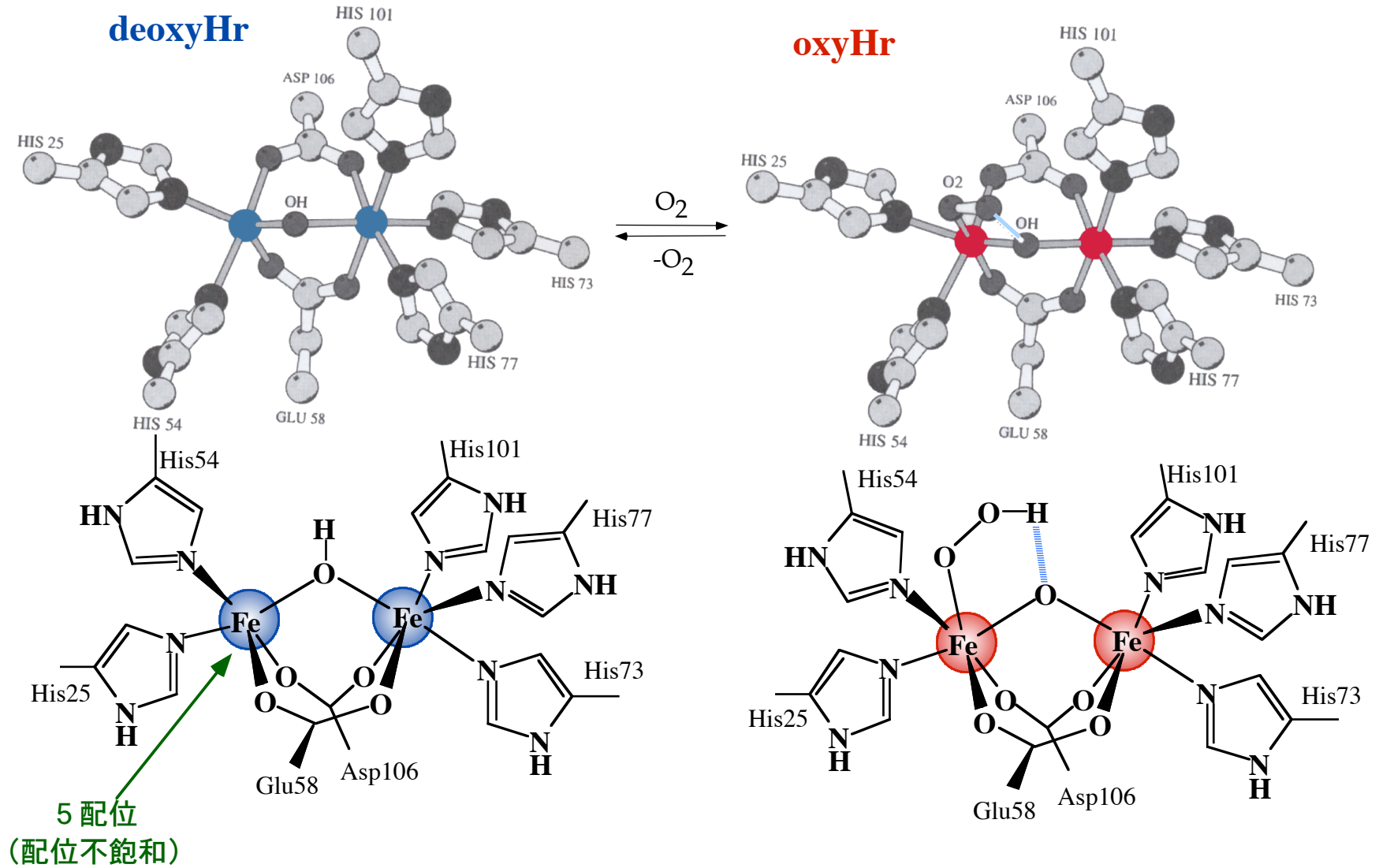


Octamer
108 kDa

azidometHr

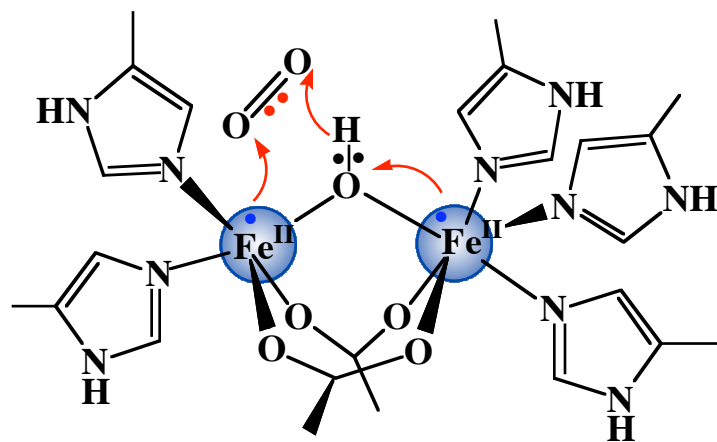


Dioxygen Binding Mode of Hemerythrin (Hr)



Structural and Spectral Parameters of deoxy- and oxyHr

deoxyHr



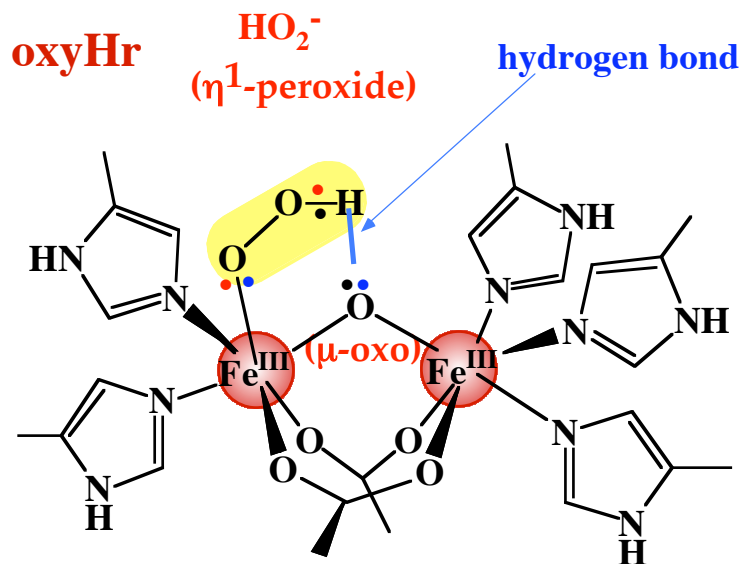
Fe(II)⋯Fe(II) colorless

$$\begin{aligned} M \cdots M &= 3.57 \text{ \AA} \\ M-OH &= 1.98 \text{ \AA} \\ M-O-M &= 128^\circ \end{aligned}$$

Mossbauer

$$\begin{aligned} \delta &= 1.14 \text{ mm s}^{-1} \\ qs &= 2.76 \text{ mm s}^{-1} \end{aligned}$$

oxyHr



Fe(III)⋯Fe(III) violet

$$\begin{aligned} M \cdots M &= 3.24 \text{ \AA} \\ M-O &= 1.82 \text{ \AA} \\ M-O-M &= 128^\circ \end{aligned}$$

Mossbauer

$$\begin{aligned} \delta &= 0.48, 0.52 \text{ mm s}^{-1} \\ qs &= 1.00, 1.92 \text{ mm s}^{-1} \end{aligned}$$

$$\lambda = 330, 360^{\text{sh}} \text{ nm (LMCT)}$$

$$\nu_{\text{O-O}} = 844 \text{ cm}^{-1}$$

$$\nu_{\text{Fe-O-Fe}} = 486 \text{ (sym), } 757 \text{ (asym) cm}^{-1}$$

Electronic Structures and Vibrational and Geometrical Properties of Dioxygen Derivatives

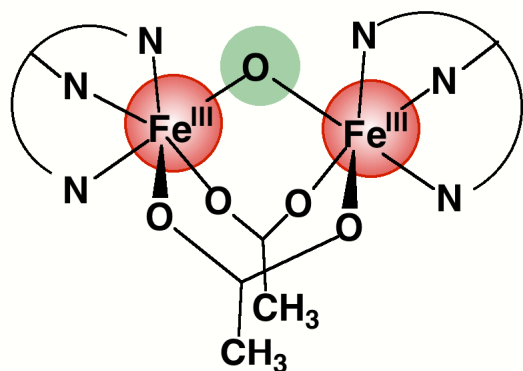
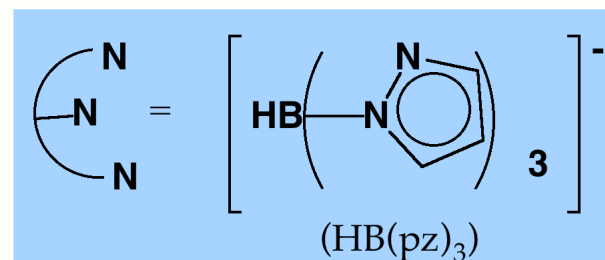
	O_2^+	O_2 dioxygen	O_2^- superoxide	O_2^{2-} peroxide
bond order	2.5	2.0	1.5	1.0
d_{O-O} (Å)	1.12	1.21	1.33	1.49
ν_{O-O} (cm ⁻¹)	1905	1580	1097	802

Model Compounds for Oxyhemerythrin (oxyHr)



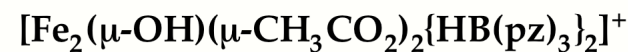
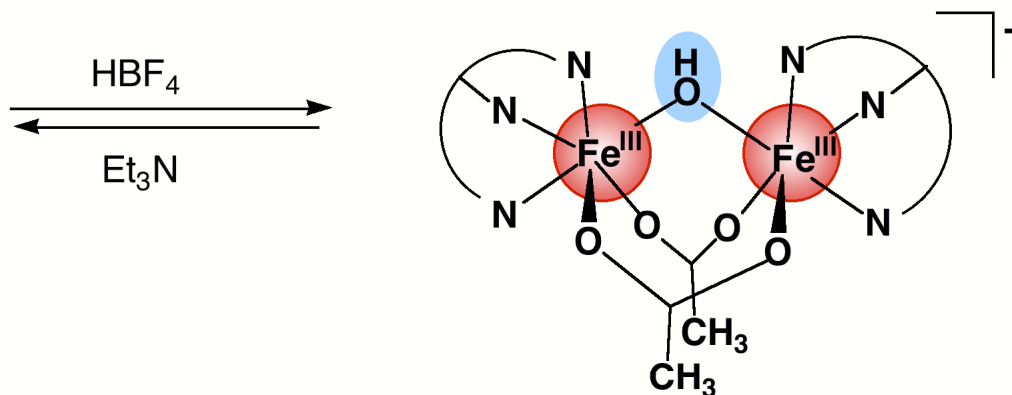
in H₂O

Spontaneous Self-Assembly



Fe...Fe = 3.145(1) Å dark green

Fe-O_{oxo} = 1.784 Å

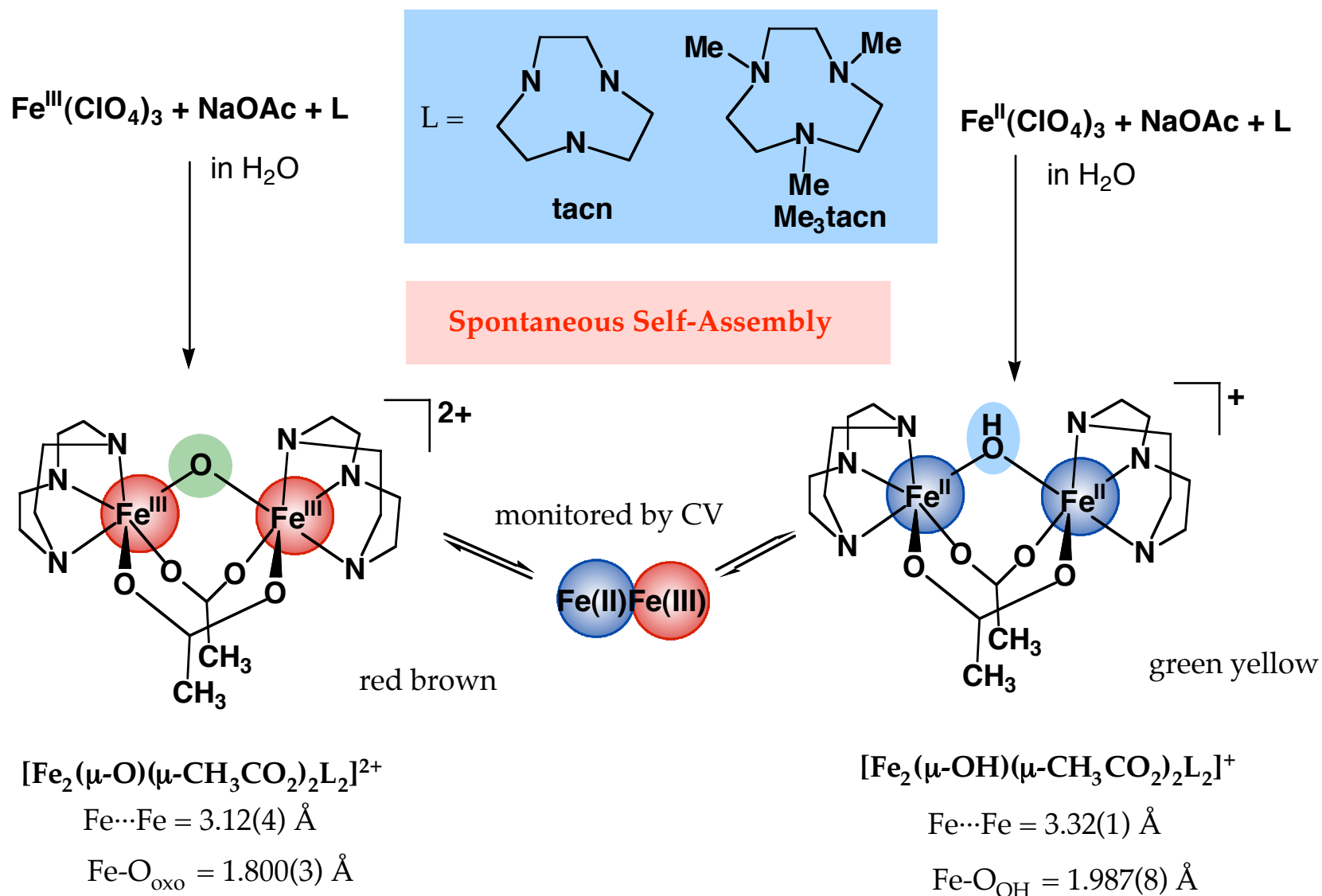


Fe...Fe = 3.439(1) Å orange

Fe-O_{OH} = 1.956 Å

Lippard et al, *J. Am. Chem. Soc.*, **1983**, 105, 4837; **1984**, 106, 4632; **1984**, 106, 3655

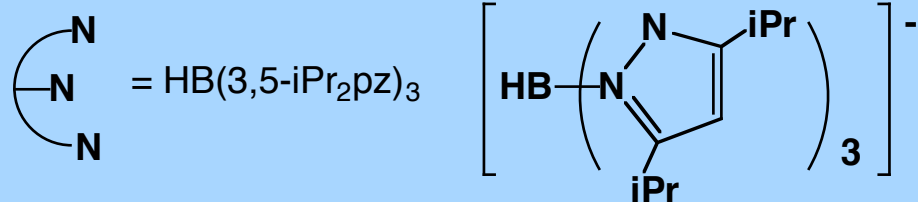
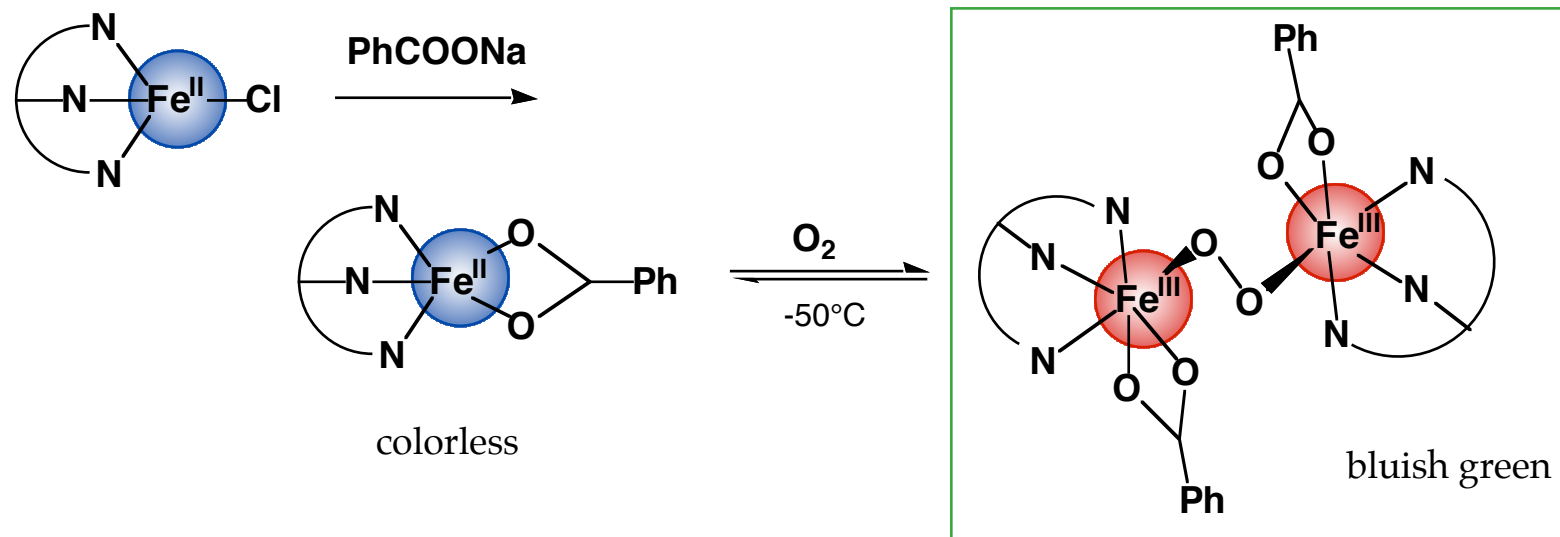
Model Compounds for Oxy- and Deoxyhemerythrin (oxy-, deoxyHr)



Wieghardt et al, *Angew. Chem. Int. Ed. Engl.*, **1984**, 22, 727; **1985**, 24, 778

Wieghardt et al, *J. Am. Chem. Soc.*, **1987**, 109, 7387

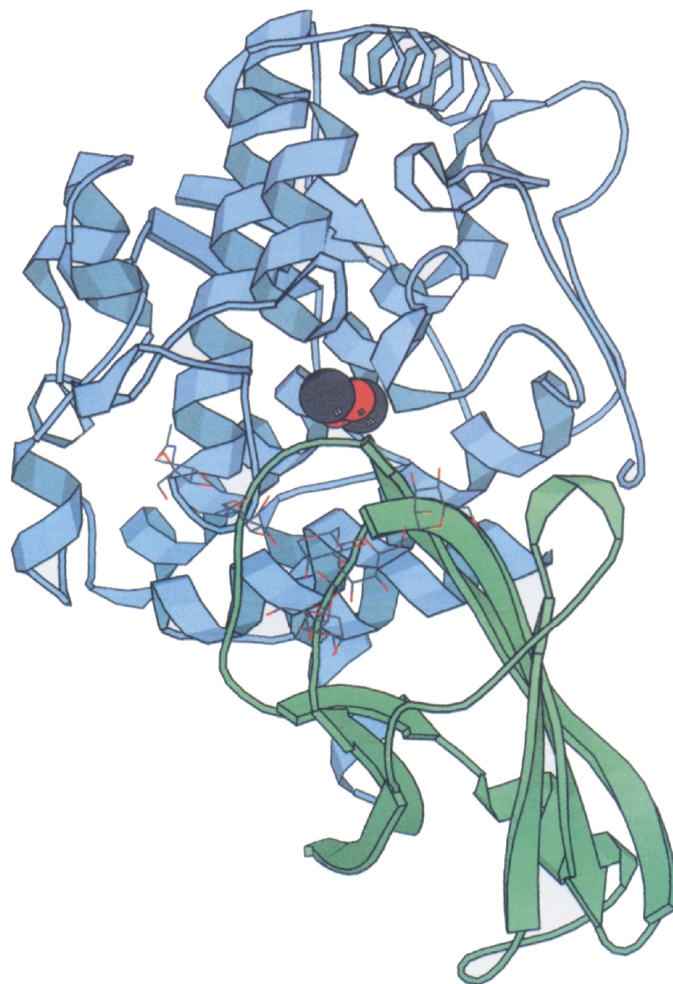
Model Compound for Dioxygen Binding by Dinuclear Fe Core



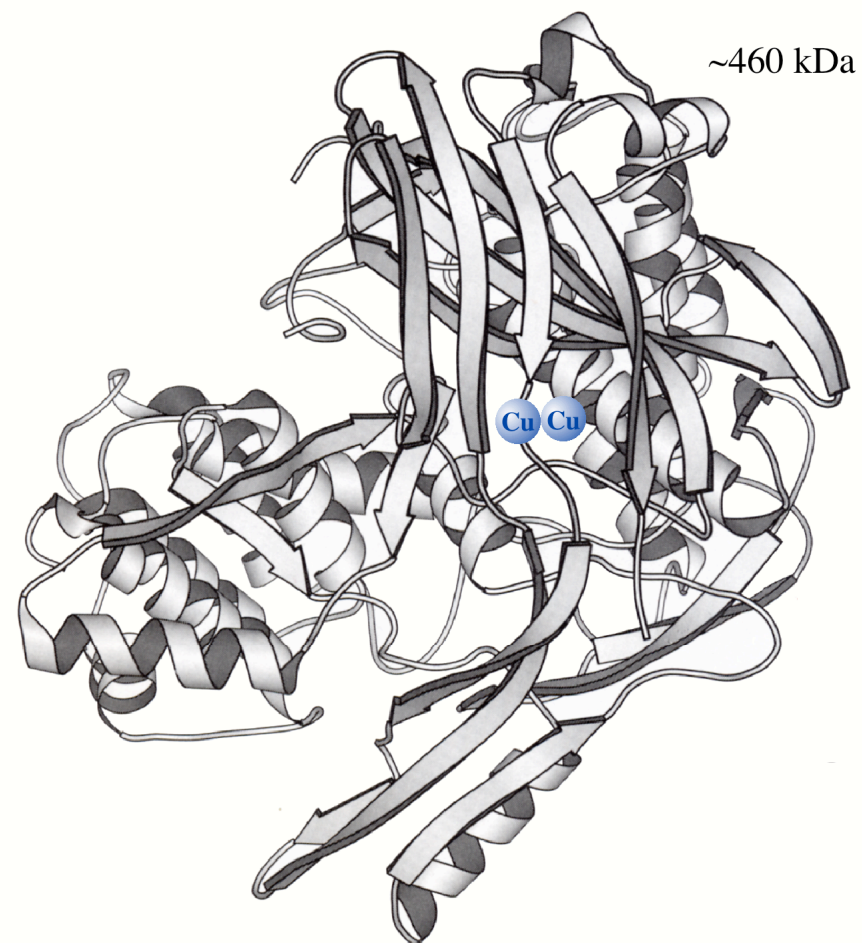
Kitajima, Que et al, *J. Am. Chem. Soc.*, 1994, 116, 9071

Hemocyanin (Hc)

OxyHc (from *Octopus defleini*)

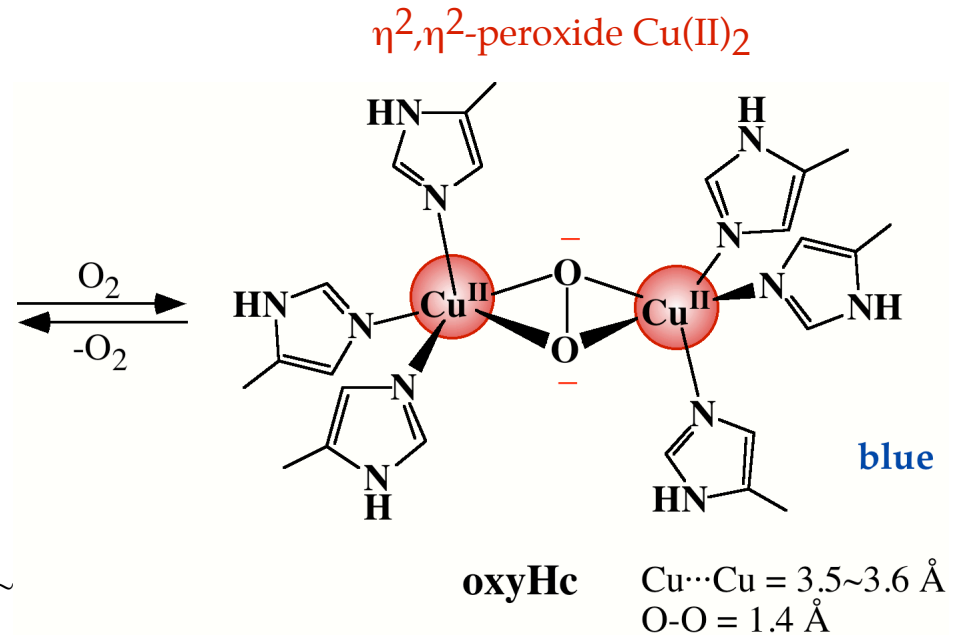
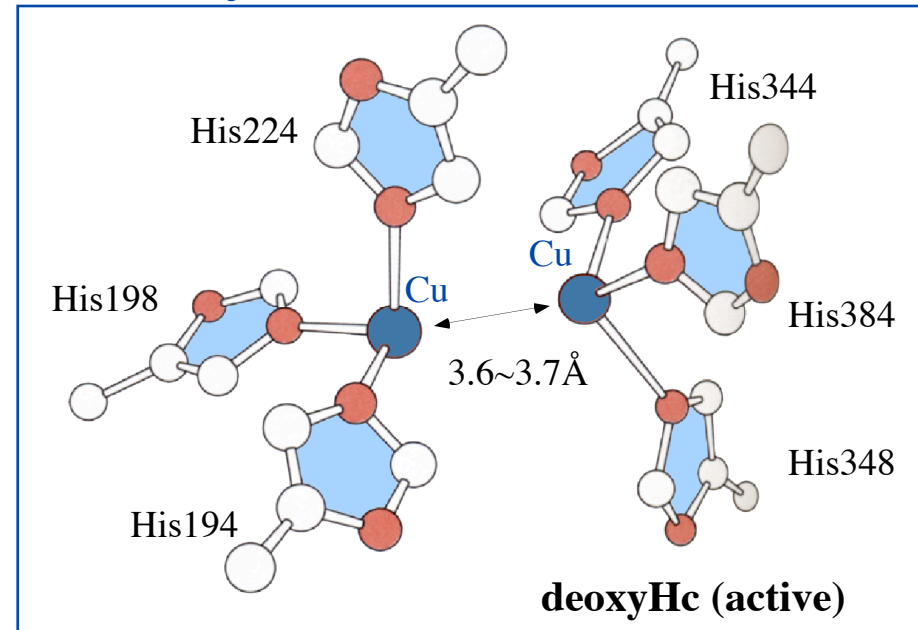
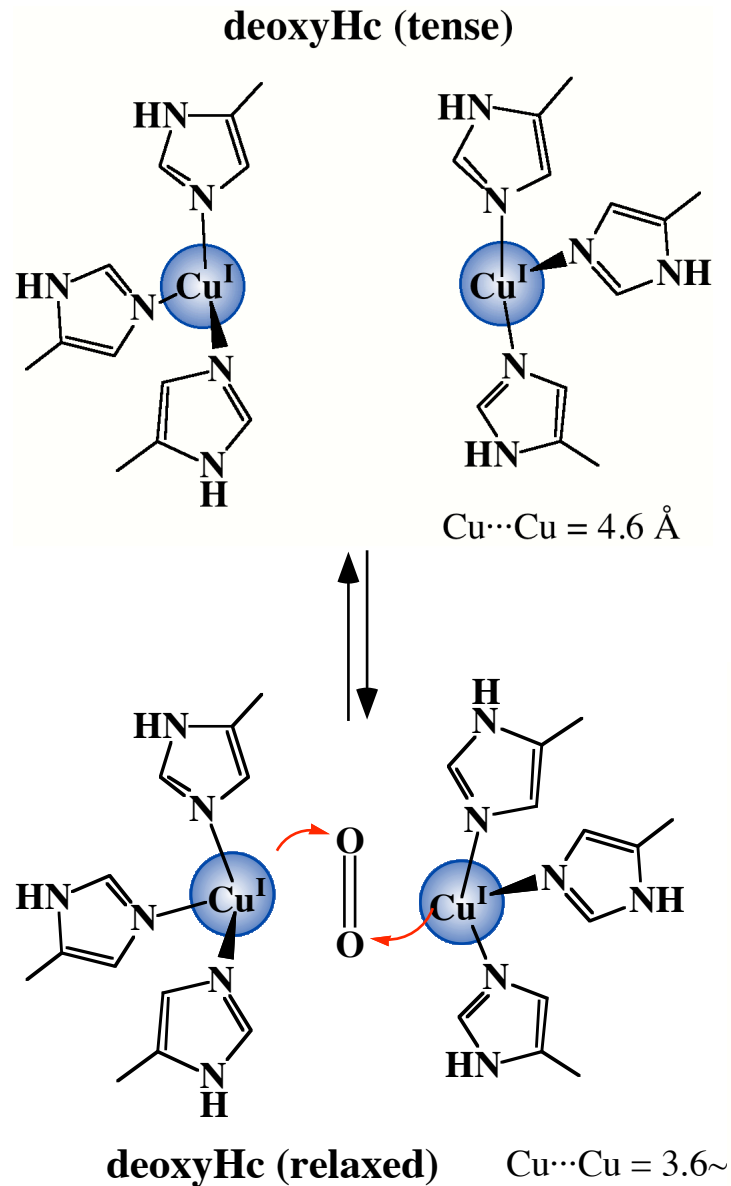


deoxyHc (from *Panulirus interruptus*)

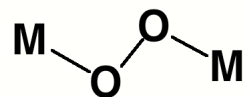
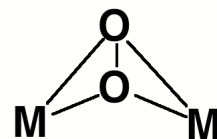
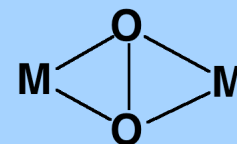


Gaykema et al, *Nature*, **1984**, 309, 23
 Volbeda et al, *J. Mol. Biol.*, **1989**, 209, 249 etc

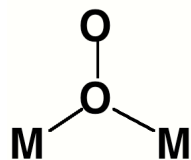
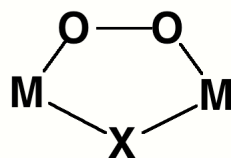
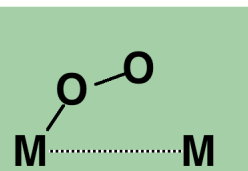
Active Sites of Hemocyanin



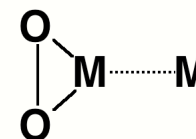
Coordination Behavior of Peroxide Ion on Dinuclear Core

 $\mu\text{-}\eta^1,\eta^1$  $\mu\text{-}\eta^2,\eta^2$
(bent) $\mu\text{-}\eta^2,\eta^2$
(planar)

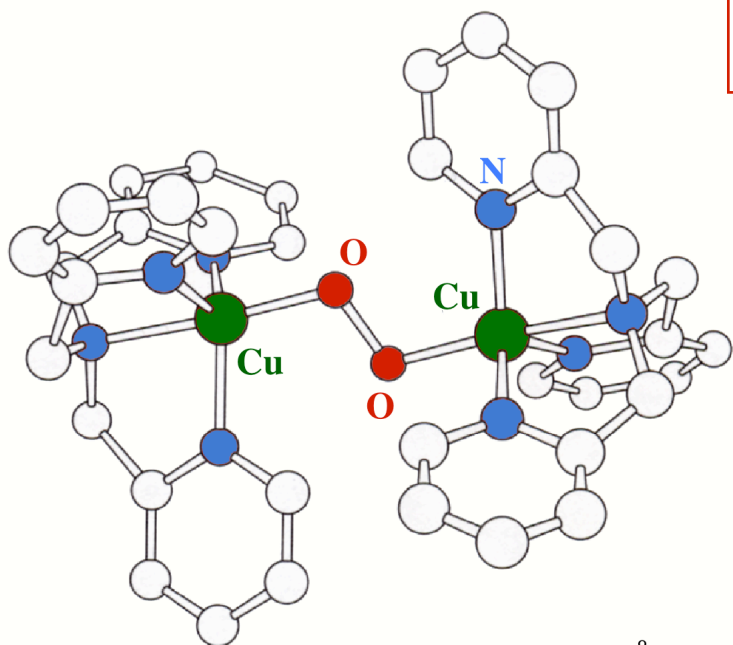
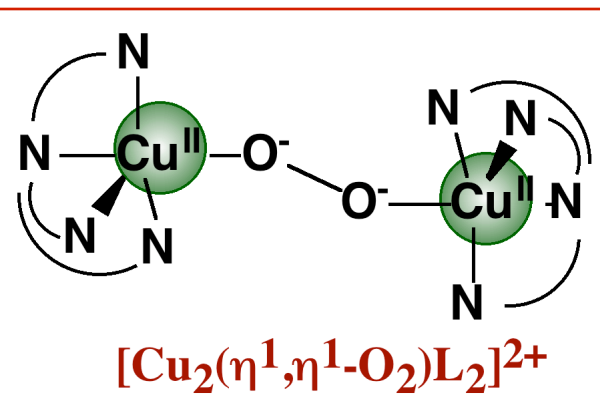
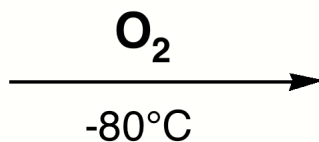
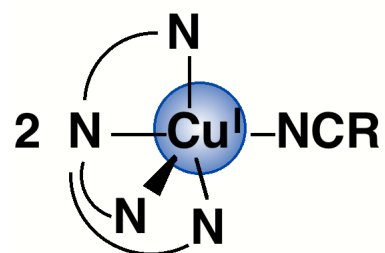
Hc

 $\mu\text{-}\eta^1$  $\mu\text{-}\eta^1,\eta^1$  η^1

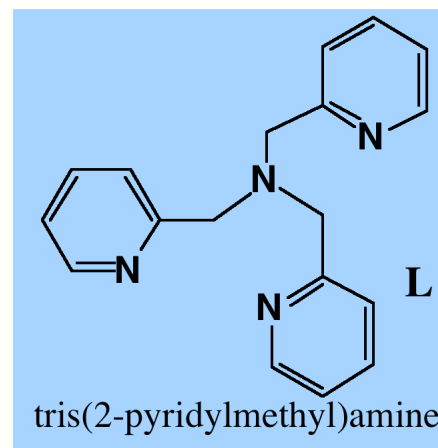
Hr

 η^2

Dioxygen Binding by Cu(I) Model Compound

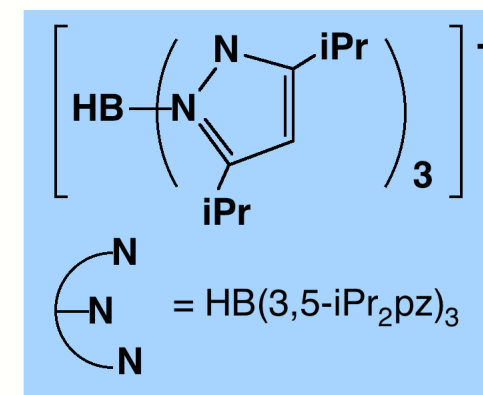
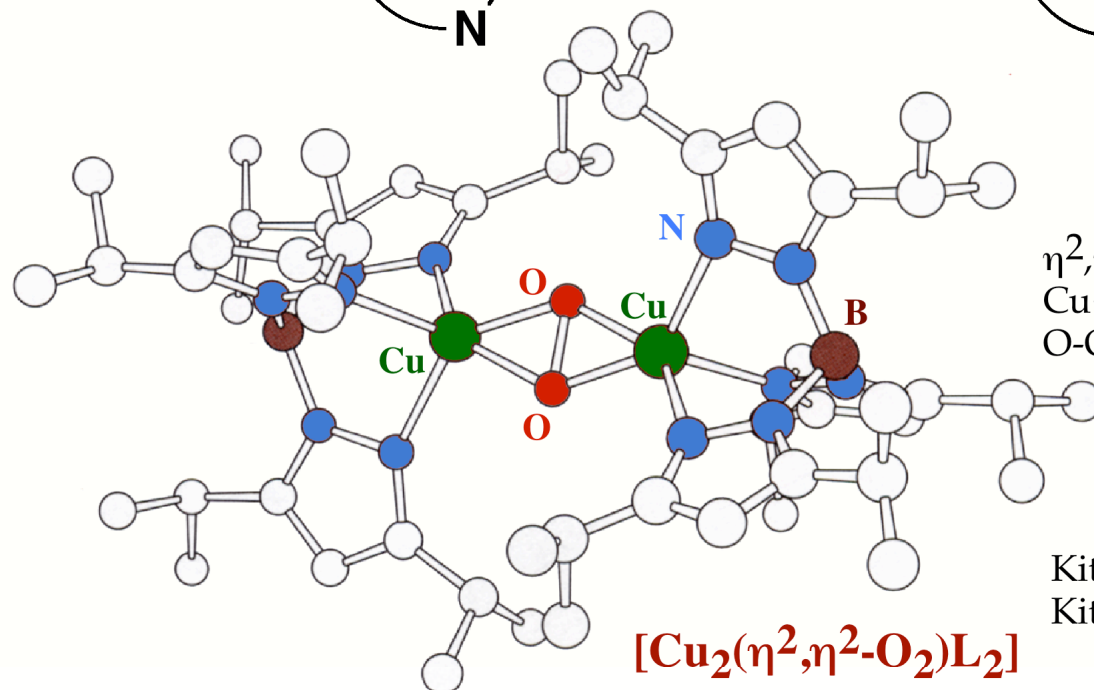
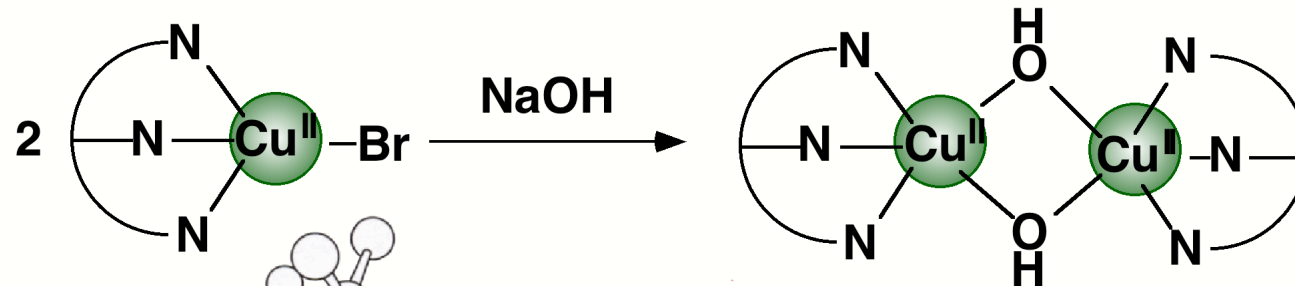
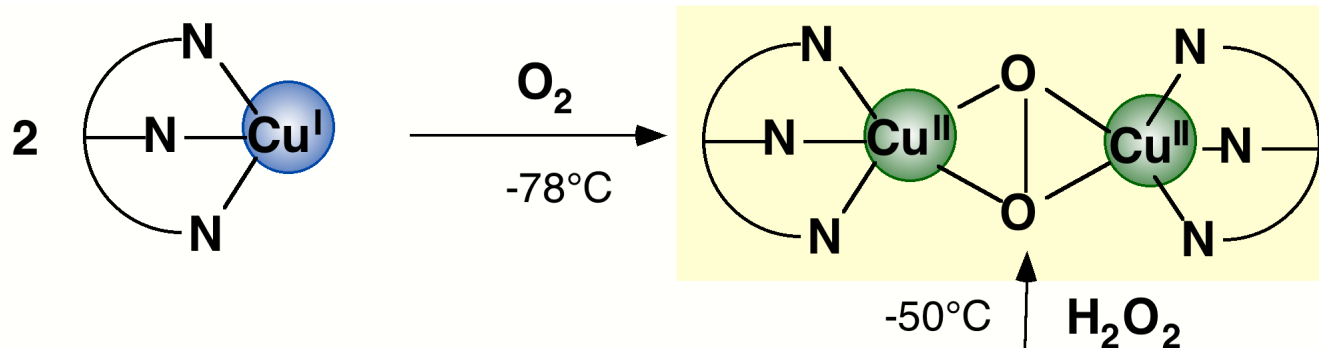


$\text{Cu}\cdots\text{Cu} = 4.359(1) \text{ \AA}$
 $\text{O}-\text{O} = 1.432(6) \text{ \AA}$



Karlin et al, *J. Am. Chem. Soc.*, **1988**, *110*, 3690
 Karlin et al, *Acc. Chem. Res.*, **1989**, *22*, 241

Dioxygen Binding by Cu(I) Model Compound



Kitajima et al, *J. Am. Chem. Soc.*, **1989**, 111, 8975

Kitajima et al, *J. Am. Chem. Soc.*, **1992**, 114, 1277

FIN