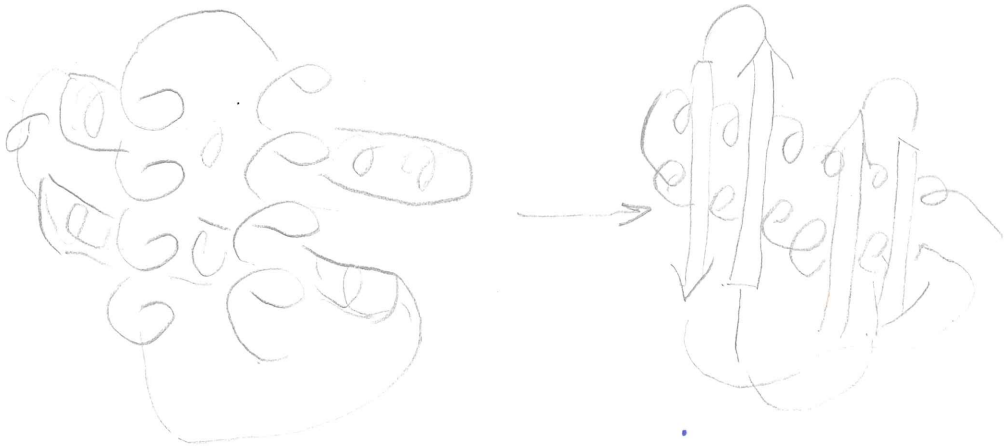
Chapter 7: Hemoglobin: Portrait of protein in action

Chapter 4

30 structure of proteins

* Structure-function relationship of protein

prion protein: Mad cow Disease
Spongiform encephalopathy
Kuru - Creutzfeldt-Jakob Disease



PrP^C
cellular form

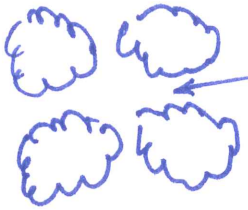
PrP^{SC}
Scrapie form
infectious
cross species

* primary Structure: amino acid sequence

* Secondary Structure: α-helix
β-sheet
demains (supersecondary structure)

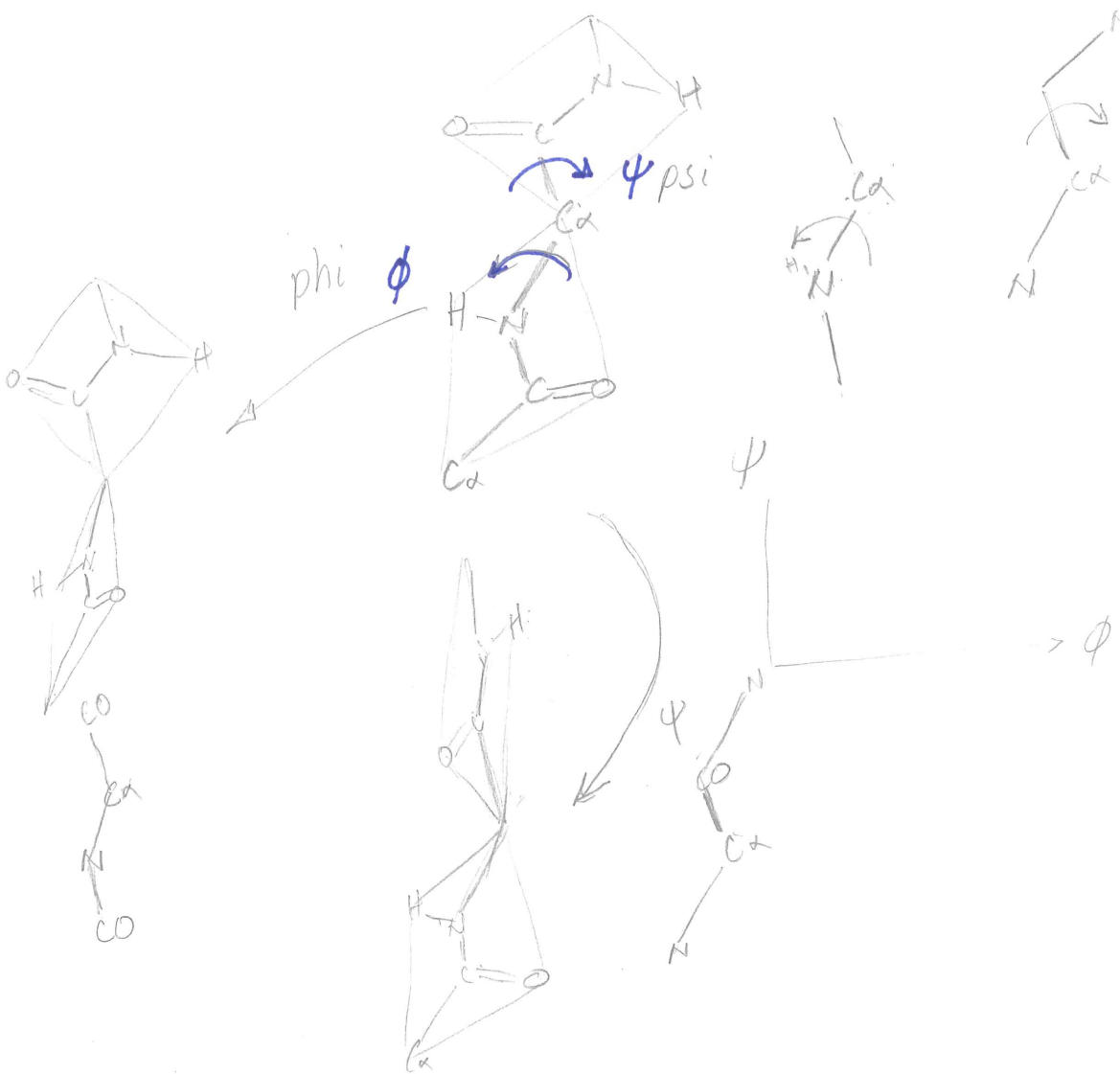
Tertiary Structure : side-chain + ~~pos~~ prosthetic group

Quanternary Structure : multi-subunit protein



Non-covalent bond
1. H-bond
2. electrostatic attraction
3. hydrophobic interaction

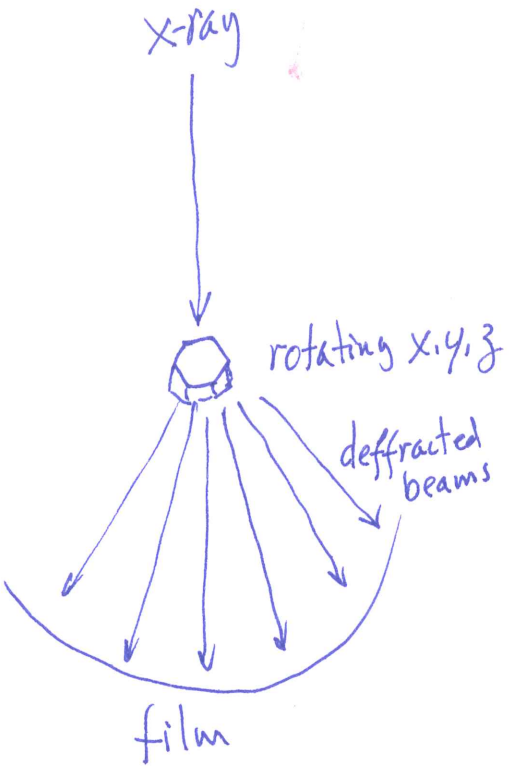
* Secondary structure
periodic Structure in protein backone

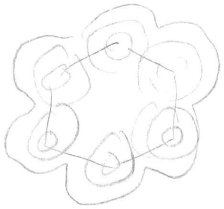


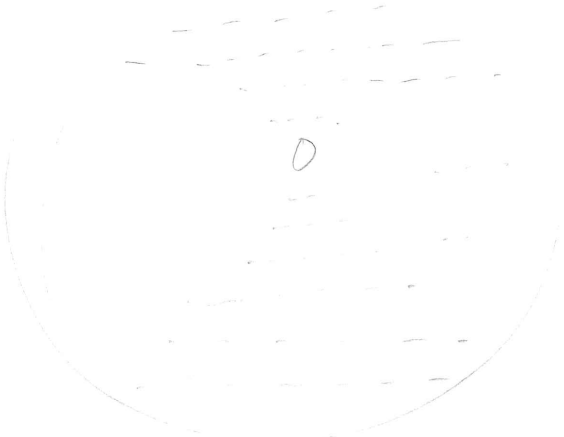
protein 3D structure Determination

X-ray crystallography ~~technique~~

Saturate solution
↓
Single crystal
↓
diffractometer 繞射
↓
diffraction pattern
Fourier Transform (Image construction)
↓
Electron density
↓
3D structure

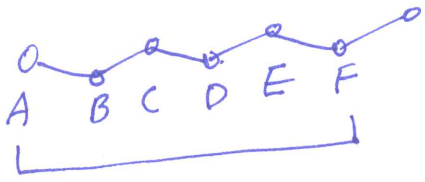


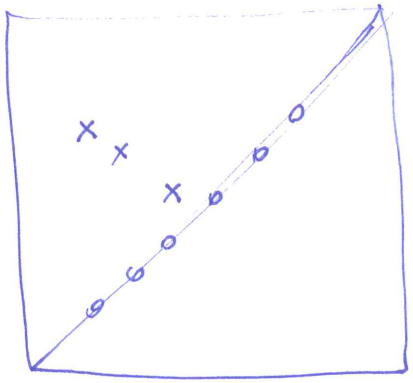


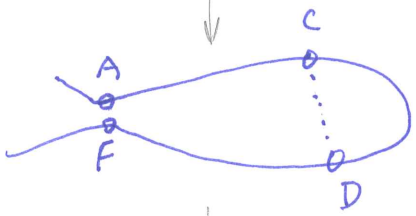


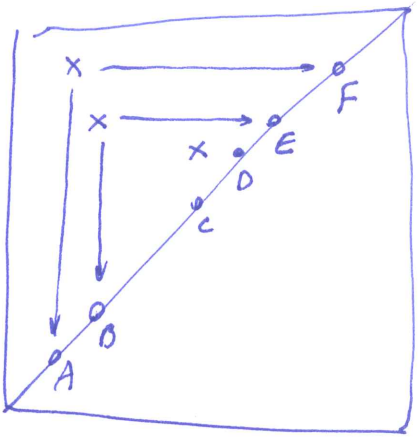
diffraction pattern in film

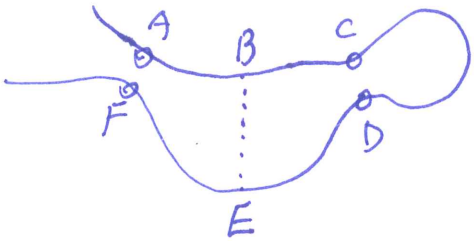
NMR Spectroscopy : NOEs (Nucleus Overhauser Effect)

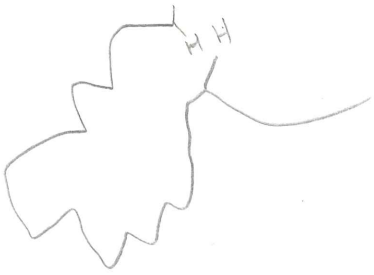


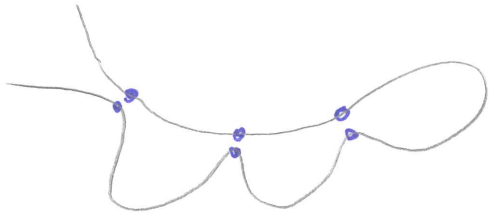


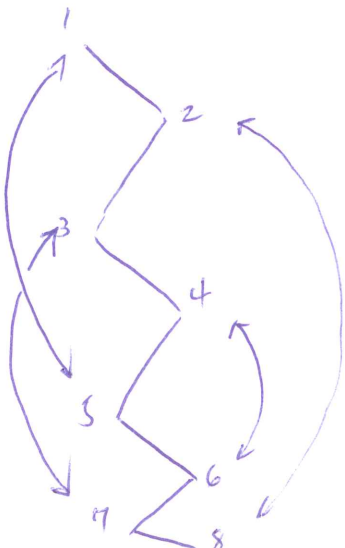


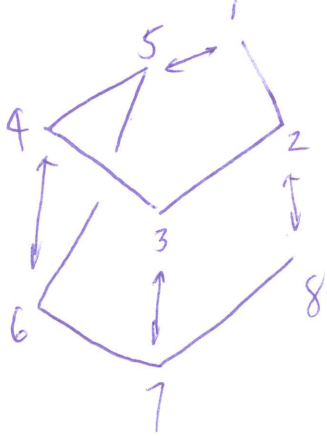






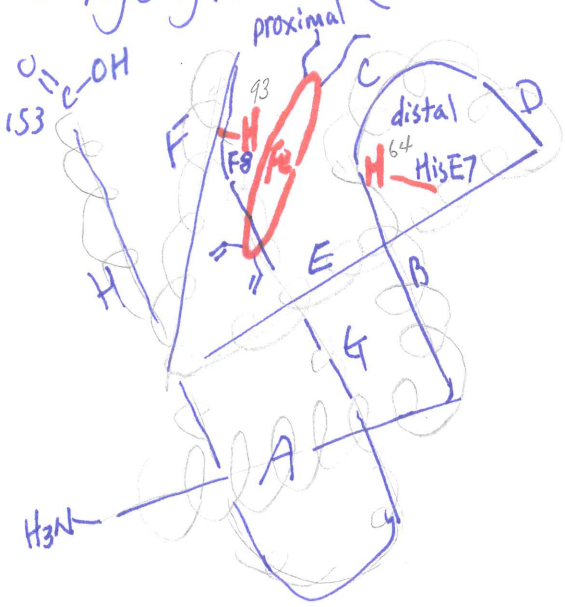


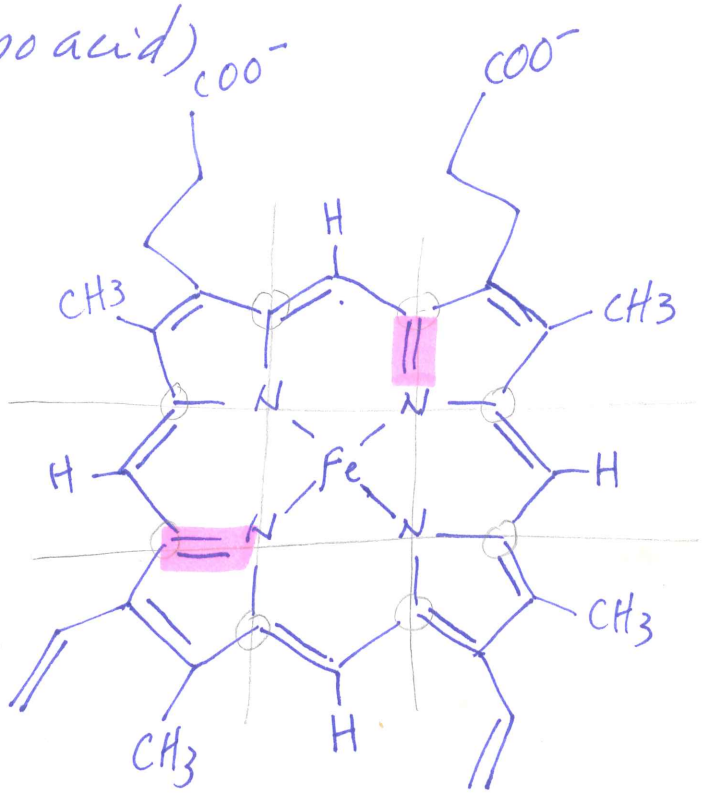




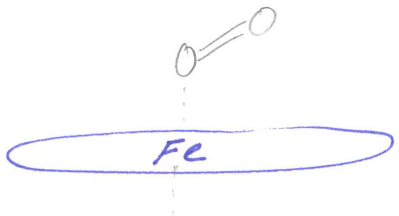
Hemoglobin

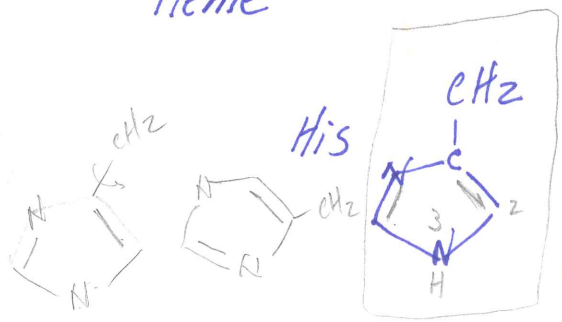
Myoglobin (153 amino acid)

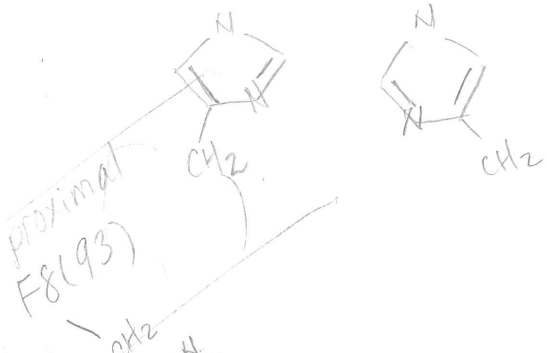


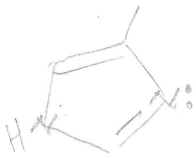


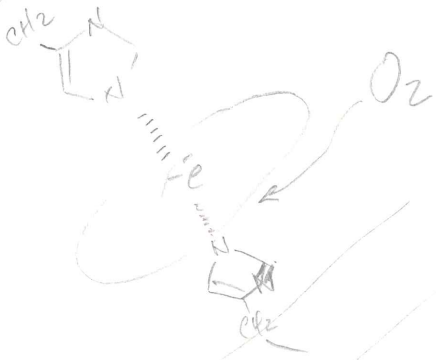
Heme

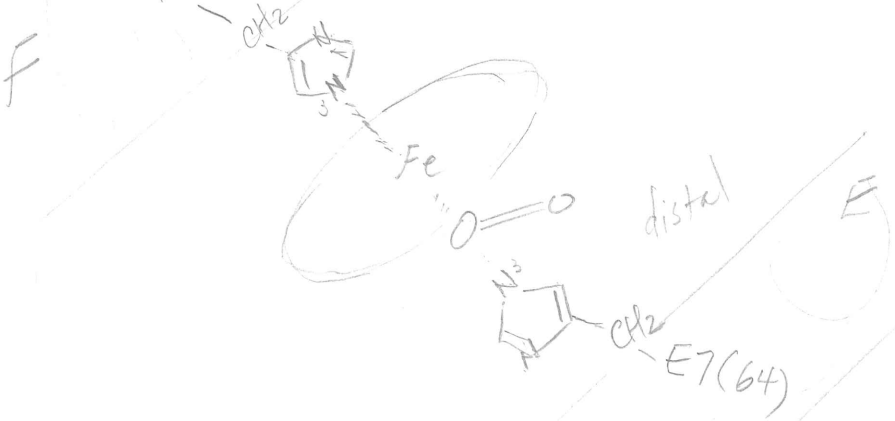




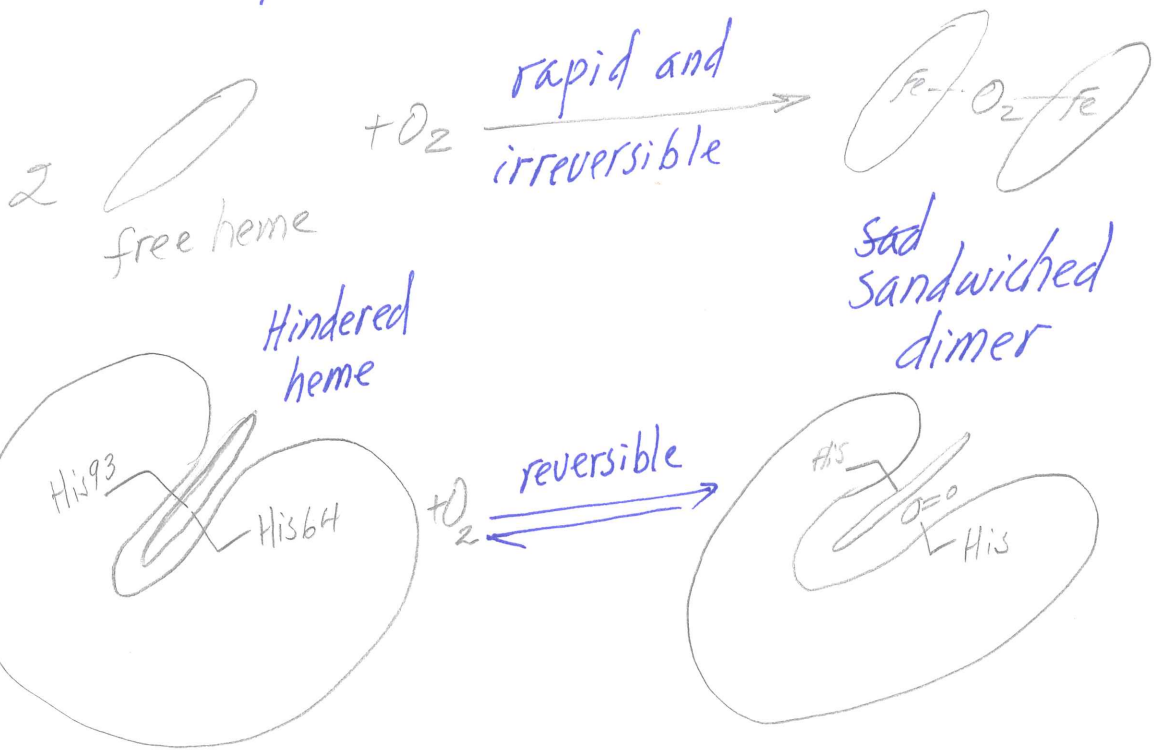




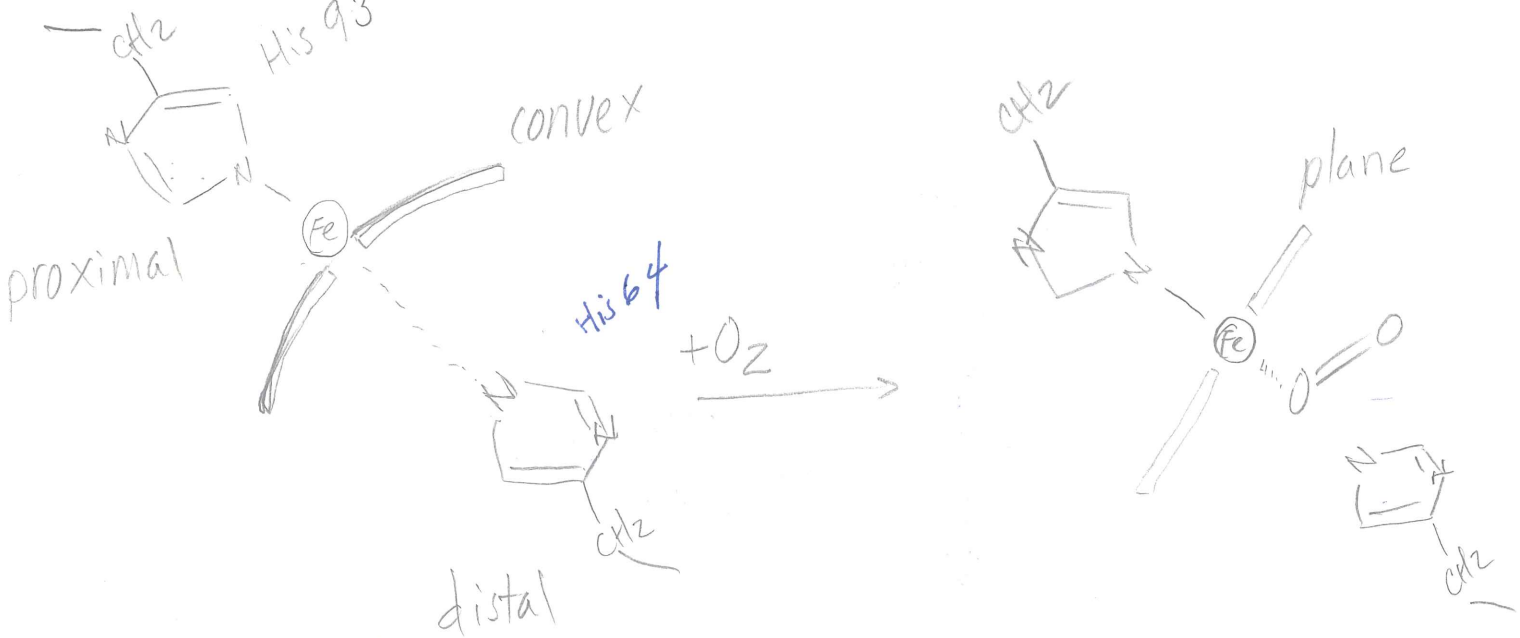




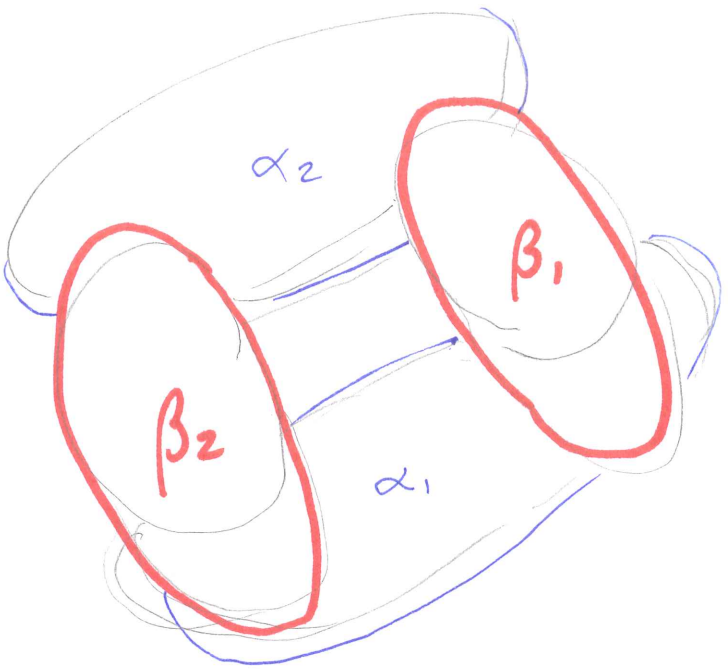
Hindered Heme enviroment is essential for O_2 transport and storage



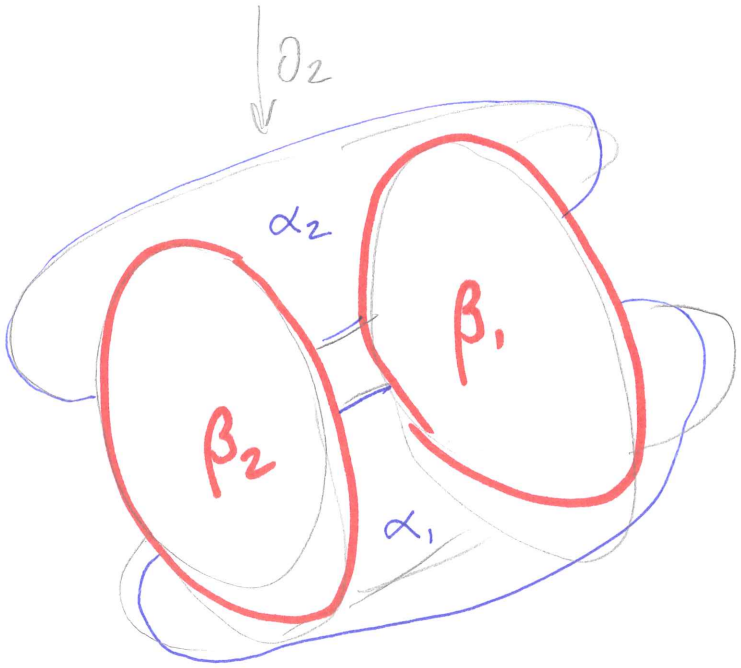
Hemoglobin



deoxy



de-oxy Hemoglobin

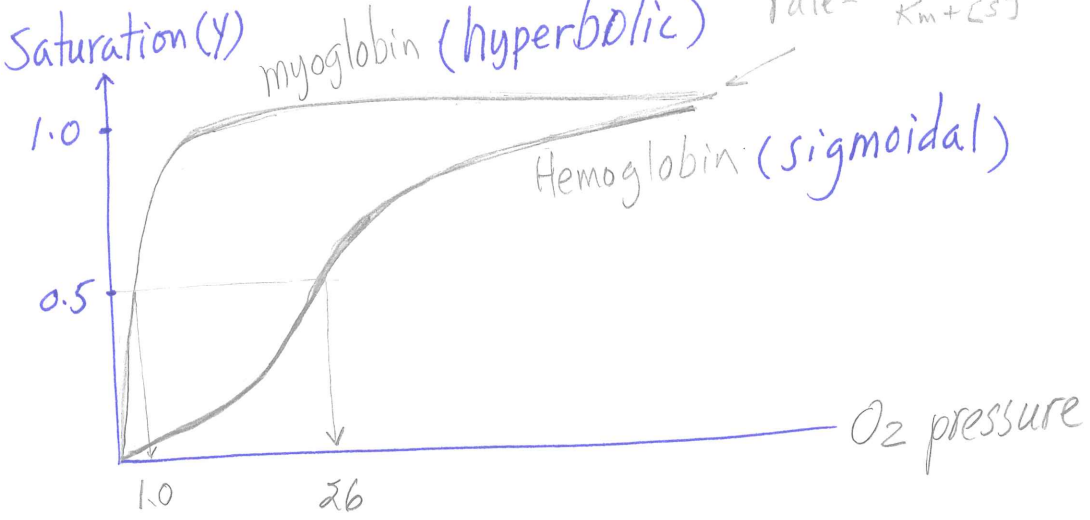


Oxy-Hemoglobin

Cooperativity of Hemeglobin

① $[S] \ll K_m$
② $[S] \gg K_m$
③ $[S] = K_m$

$$\text{rate} = \frac{V_{max}[S]}{K_m + [S]}$$



Oxygen dissociation curve

① hyperbolic / sigmoidal

② Myoglobin > Hemoglobin

$$MbO_2 \overset{K}{\rightleftharpoons} Mb + O_2$$

$$Y = \frac{[MbO_2]}{[MbO_2] + [Mb]}$$

③ Myoglobin: $Y = \frac{PO_2}{PO_2 + P_{50}}$ Michaelis-Menten

Hemoglobin: $Y = \frac{(PO_2)^n}{(PO_2)^n + (P_{50})^n}$ Hill

$$Hb(O_2)_n \rightleftharpoons Hb + nO_2$$

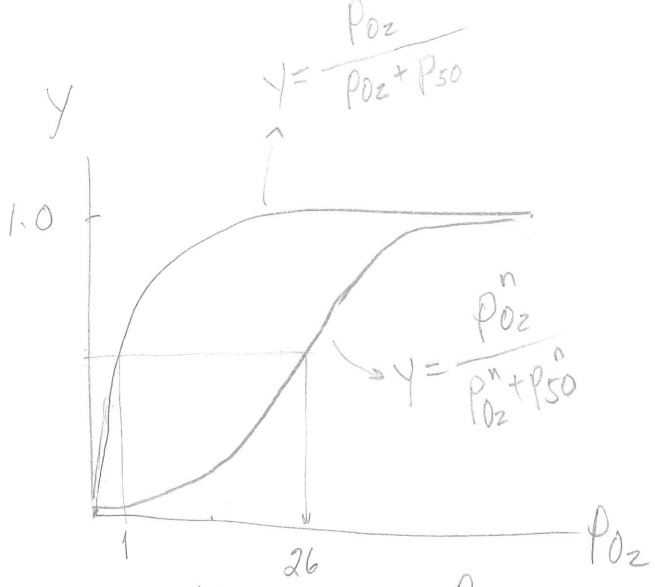
$$K = \frac{[Mb][O_2]}{[MbO_2]}; \quad Y = \frac{[MbO_2]}{[MbO_2] + [Mb]}$$

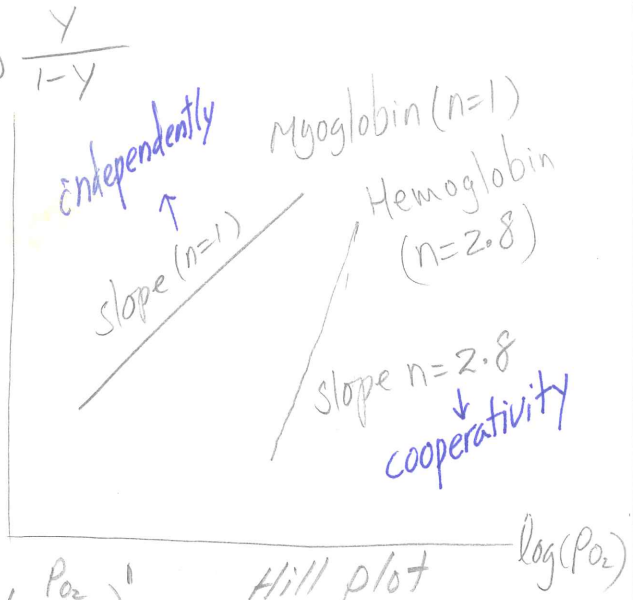
$$[O_2] = K\frac{[MbO_2]}{[Mb]}$$

$$[MbO_2] = \frac{[O_2][Mb]}{K}$$

$$Y = \frac{\frac{[O_2][Mb]}{K}}{\frac{[O_2][Mb]}{K} + \frac{[Mb]K}{K}} = \frac{[O_2]}{[O_2] + K}$$

$$Y = \frac{[O_2]}{[O_2] + K} = \frac{PO_2}{PO_2 + P_{50}}$$





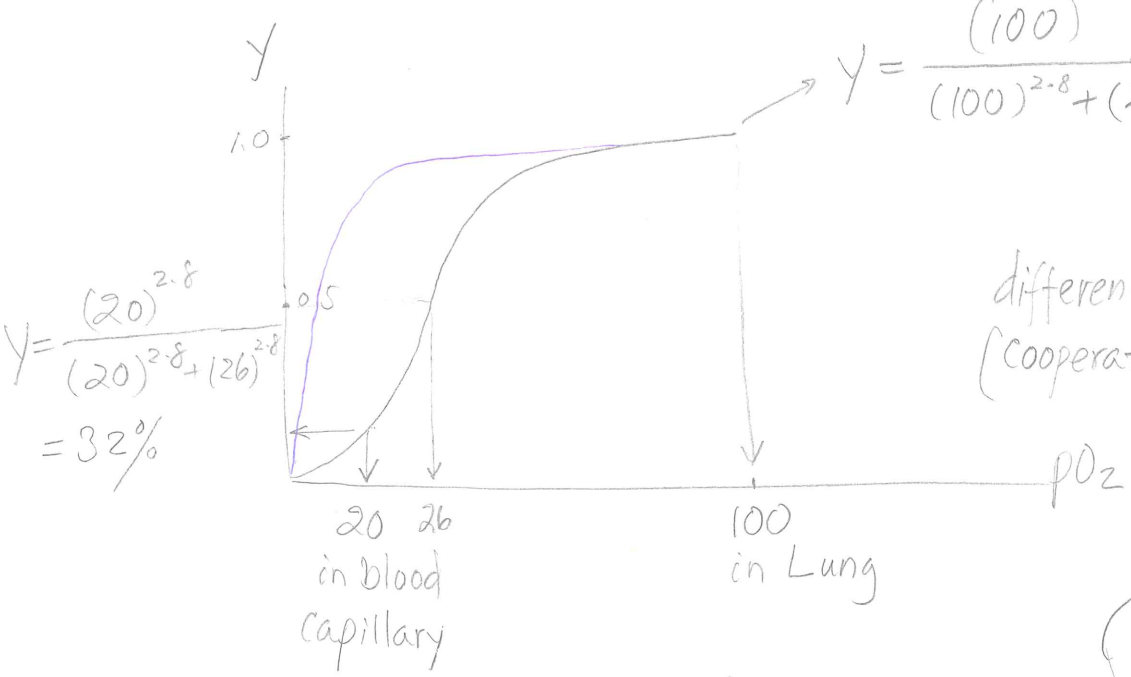
Hill plot

Myoglobin: $Y = \frac{P_{O_2}}{P_{O_2} + P_{50}} \Rightarrow \frac{Y}{1-Y} = \left(\frac{P_{O_2}}{P_{50}}\right)^1$

Hemoglobin $Y = \frac{P_{O_2}^n}{P_{O_2}^n + P_{50}^n} \Rightarrow \frac{Y}{1-Y} = \left(\frac{P_{O_2}}{P_{50}}\right)^n$

$$\log \frac{Y}{1-Y} = n \log\left(\frac{P_{O_2}}{P_{50}}\right)$$

Example of O_2 transfer w/ cooperativity



difference of $Y = (98 - 32)\% = 0.66$
(cooperativity $n = 2.8$)

If non-Cooperativity ($n=1$)

Lung: $Y = \frac{100'}{100' + 26'} = 0.79$

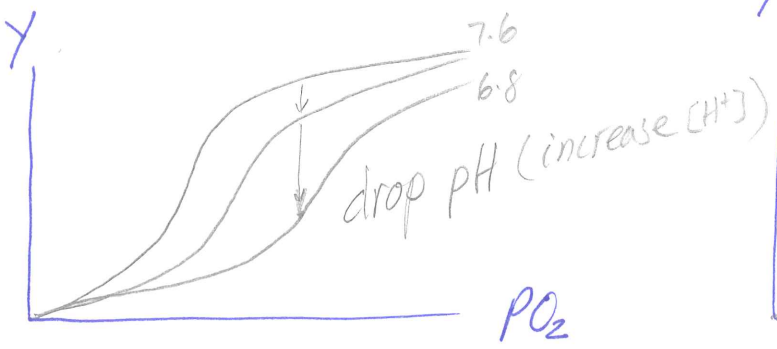
blood: $Y = \frac{20'}{20' + 26'} = 0.43$

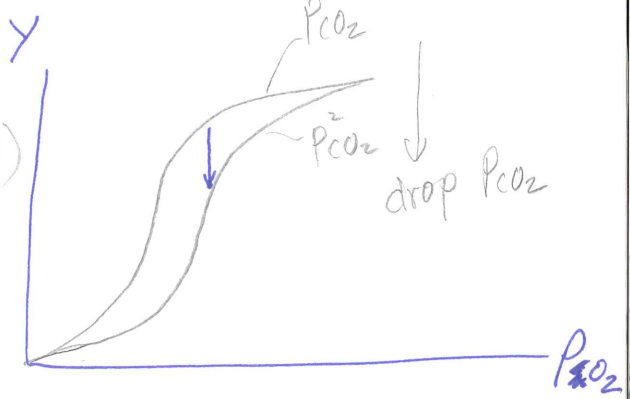
(driving force) difference $= 0.38$

O_2 transfer from Lung → blood

differences $\frac{0.66}{0.38} = 1.8$ different

Bohr effect (H^+ & CO_2)





$HbO_2 + H^+ + CO_2 \longrightarrow O_2 + Hb\begin{matrix}-CO_2\\-H^+\end{matrix}$

metabolically active tissue (contracting muscle) or respiring tissue

releasing

BPG (2,3-bisphosphoglycerate) binding