Oxygen Binding

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Introduction

- Respiratory proteins bind O_2
  - Myoglobin (Mb)
    - Found in vertebrate muscle
    - Stores oxygen in the muscles
    - Relays O2 from the capillaries to the muscle cells
  - Hemoglobin (Hb)
    - Found in human blood
    - Transports oxygen from lungs to tissues
    - Gives red blood cells their color

- Hemocyanin (Hc)
  - Found in arthropods and mollusks
  - Transports oxygen
  - Binds O_2 cooperatively O_2:2Cu
- Hemerythrins (Hr)
  - Found in inverterbrates
  - Transports oxygen
  - Binds O_2 O_2:2Fe

Structural Differences

- Mb and Hb
  - Contain mononuclear active sites
  - Contain a heme where the Fe is located
- Hc and Hr
  - Contain binuclear active sites
  - Do not contain a heme

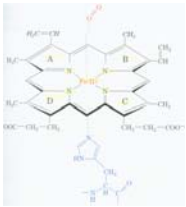
Other Oxygen Carriers

- Leghemoglobin
  - Found in plants
  - Supply oxygen to the nitrogen-fixing bacteria that colonize root nodules
- Chlorocruoin
  - Found in some annelids (e.g. earthworms)
  - Supply oxygen to tissues via blood

Myoglobin

- First protein structure determined by x-ray crystallography
  - 153 residues
  - Dimensions: 44X44X25 Å

Myoglobin



- Heme group
  - Porphyrin derivative with 4 pyrrole groups
  - Fe^{II} in the center of the heme
    - Coordinated by 4 porphyrin N atoms and 1 N from histidine side chain
    - Oxygen acts as sixth ligand
  - Between E and F helices

Myoglobin

- When exposed to oxygen
  - Fe^{II} irreversibly oxidized to Fe^{III}
  - Protein portion prevents this oxidation

$$Mb + O_2 \leftrightarrow MbO_2$$

Hemoglobin

- Structure determined by X-Ray Crystallography
  - 18% of the residues are identical to those in myoglobin
  - Has exact C_2 symmetry and pseudo symmetry
  - Dimensions: 64x55x50 Å
  - Tetrametric protein with quaternary structure $\alpha_2\beta_2$
  - Hemes are 25-37 Å apart

Hemoglobin

- Two conformational states according to Perutz mechanism
  - T-state (Conformation of deoxy-hemoglobin)
  - R-state (Conformation of oxy-hemoglobin)
  - Shift from T to R state upon binding O_2

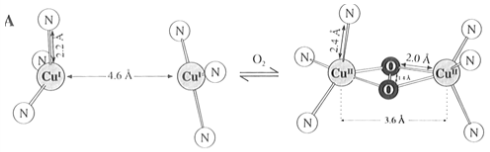
Perutz Mechanism

- T-State
  - Porphyrin ring is dome shaped
  - Fe position out of porphyrin ring
  - Proximal His and Helix F raised
- R-State
  - Porphyrin ring is flat
  - Fe position in the plane of the porphyrin ring
  - Proximal His and Helix F lowered to follow Fe

Cooperativity

- The binding of ligand to one site affects the binding of additional ligands to the other sites
- Hemoglobin
  - O_2 binding is highly, not infinitely, cooperative
    - First O_2 binds independently
    - Fourth O_2 binds with a 100 fold greater affinity than the first

Hemocyanin Mechanism

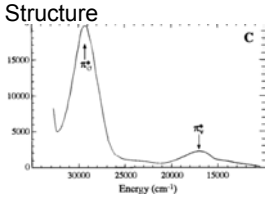


Hc Physical Properties

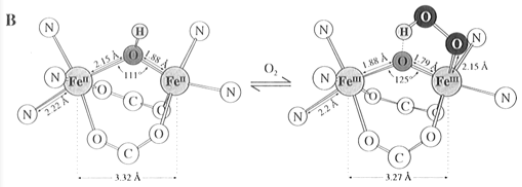
- Some coopertivity
  - Factors affecting oxygen bonding
    - pH
    - Presence of Ca^{2+}
    - Cu-Cu distance
    - Jahn-Teller effect

Hc Physical Properties

- Spectroscopy
  - Low Energy CT Transition
  - O-O Stretching Frequency
  - Determination of Structure



Hemerythrin Mechanism



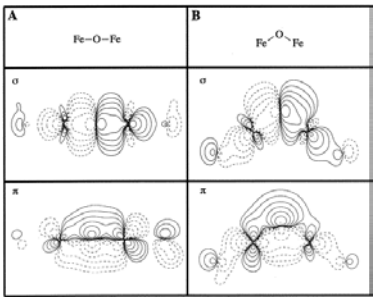
Hr Physical Properties

- Limited cooperativity
  - Geometry limited due to bridging ligands
- Spectroscopy
  - Crystallography
  - EXAFS

Dioxygen-Metal Bond

- Linear vs. Bent
  - Linear
    - Bond has Fe^{III} d character resulting in a short, strong bond
    - Oxygen π orbitals and iron d π orbitals interact
  - Bent
    - Oxygen pi bond loses iron d character
    - Increases net electron density on oxo ligand

Linear vs. Bent



References

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- Voet, D.; Voet, J.G.; Pratt, C.W. *Fundamentals of Biochemistry*; John Wiley and Sons: New York, NY, 2002, pp 162-171.