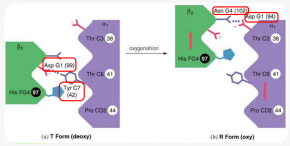
Hemoglobin

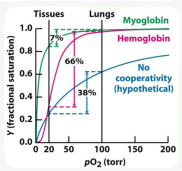
Definition & Prosthetic Group

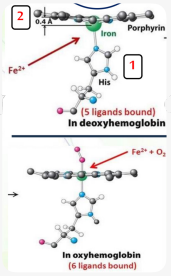
- Proteins with Heme
  - Hemoproteins
- Prosthetic Group
  - Tightly Bound Non-Polypeptide Unit
    - Essential for Function
  - Organic or Inorganic
    - Vitamins, Sugars, Lipids
      - Organic
    - Metal Ions
      - Inorganic



Hemoglobin Structure

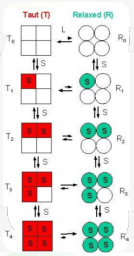
- Globular Protein
  - Allosteric
  - Tetramer
- Composed of
- Subunits
  - Two Alpha (α) Chains
    - 141 Amino Acids
      - Arg141
    - Valine as First Amino Acid
  - Two Beta (β) Chains
    - 146 Amino Acids
      - His146
    - Valine as First Amino Acid
- Contains
- Histidine Residues
  - Proximal Histidine
    - Covalent Bond with Iron
  - Distal Histidine
    - Gatekeeper
    - Hydrogen Bond with Oxygen
  - Plays a Role in
- Structural Changes
  - Tense (T) State
    - Low Affinity for Oxygen
  - Relaxed (R) State
    - High Affinity for Oxygen





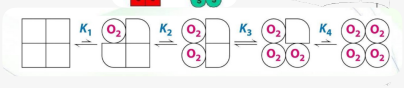
Oxygen Binding & Allosteric Effect

- Oxygen Binding
  - Iron's Sixth Coordinate
    - Induces Structural Change
  - Heme Flattening
    - Dome-shaped to Flat
- Allosteric Effect
  - T to R Transition
    - Breaking Electrostatic Interactions
    - Increased Oxygen Affinity
  - Positive Cooperativity
    - Easier Binding of Subsequent Oxygen Molecules

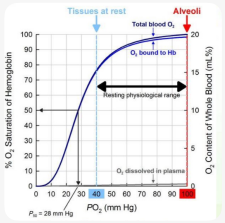


Cooperativity Models

- Concerted (MWC) Model
  - Two States: T & R
    - Simultaneous Conformational Change
  - Increased Occupancy Favors R State
- Alternative Model
- Sequential (KNF) Model
  - Independent Subunit Changes
    - Induced Fit
  - Multiple Intermediate States



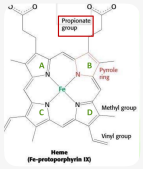
Enables



Heme Structure

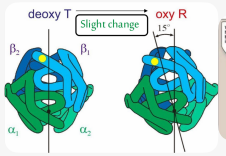
- Protoporphyrin IX + Iron (Fe2+)
  - Contains
  - Complex
  - Hydrophobic
- Porphyrin
  - Planar Structure
    - Four Pyrrole Rings
  - Substituents
    - Two Substituents per Pyrrole
    - Propionate Groups
      - Hydrophilic
- Iron Binding
  - Central Location
    - Four Covalent Bonds
  - Six Coordinates of Binding
    - Fifth with Proximal Histidine
    - Four within Heme
    - Sixth with Oxygen

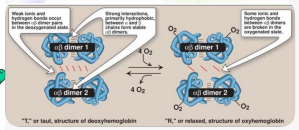
Iron binds to the heme molecule at its center through four covalent bonds



Subunit Interactions

- Dimer of Dimers
  - (α-β)2
- Strong Hydrophobic Interactions
  - Between α & β
- Weaker Electrostatic Interactions
  - Between αβ & αβ Dimers





Oxygen Distribution

- High Affinity in Lungs
  - R State
- Low Affinity in Tissues
  - T State
  - Oxygen Release
- Sigmoidal Saturation Curve
  - Allosteric Behavior

Hemoglobin has a high affinity for oxygen in the lungs and a low affinity in the tissues, allowing for efficient oxygen delivery.

Developmental Transition of Hemoglobins

- Embryonic Stage
  - Transition to
  - Hemoglobin Gower 1 (ζ2ε2)
    - Yolk Sac
    - High Oxygen Affinity
- Fetal Stage
  - Transition to
  - Fetal Hemoglobin (α2γ2)
    - High Oxygen Affinity
- Adult Stage
  - Hemoglobin A1 (α2β2)
    - Major Adult Hemoglobin
  - Hemoglobin A2 (α2δ2)
    - Minor Adult Hemoglobin
  - Glycosylated Hemoglobin (HbA1c)
    - Diabetes Biomarker

	Hemoglobin A1C (HbA1c)	Fasting Blood Sugar Test	Random Blood Sugar Test
Normal	< 5.7%	< 100mg/dL	N/A
Prediabetes	5.7 – 6.4%	100 – 125 mg/dL	N/A
Diabetes	≥ 6.5%	> 125 mg/dL	≥ 200 mg/dL