

Hemoglobin and Myoglobin

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OVERVIEW

Globular proteins

- Compact proteins that are approximately spherical in shape

Hemoproteins

- Specialized proteins that have prosthetic heme group

Prosthetic groups

- Non-protein molecules that are essential to biological function

HEME GROUP STRUCTURE

- Porphyrin ring with iron center (Fe^{2+})

Fe^{2+} coordinates 6 bonds:

- 1-4. Four planar nitrogen atoms (of porphyrin ring)
- 5. Proximal histidine
- 6. Oxygen

MYOGLOBIN

- Skeletal and cardiac muscle
- Reservoir for oxygen
- Single polypeptide with 8 [alpha helix](#) segments

- One heme group
- Distal histidine holds oxygen in place

HEMOGLOBIN

- [Red blood cells](#)
 - Supplies body's tissues with oxygen
- 4 polypeptides (instead of one): each subunit resembles myoglobin structure
 - [Tetramer](#): with 2 alpha-beta dimers
- Strong hydrophobic interactions: stabilize alpha-beta dimer
- Weak ionic and H-bonds: between dimers

T-form hemoglobin

- "Taught" or "tense" form: polypeptides restricted in movement
- Deoxygenated form: oxygen affinity is low

R-form hemoglobin

- "Relaxed" form: weaker ionic and H-bonds between dimers
- Oxygenated form: oxygen affinity is high

COOPERATIVE BINDING

- Conformational change between T-form and R-form hemoglobin

Myoglobin does not exhibit cooperative binding: only one oxygen binding site* – One oxygen binds hemoglobin subunit – Binding disrupts inter-dimer bonds: causes conformational change – Change in 3D structure increases oxygen affinity of remaining subunits

DISSOCIATION CURVE

- % oxygen saturation vs. oxygen partial pressure (torr)
- Cooperative binding produces sigmoidal binding curve
- pO₂ in body's tissues: 30 torr
- pO₂ in lungs: 100 torr

Hemoglobin

- Half saturated at 30 torr (body's tissues): responds to O₂ availability

Myoglobin

- Hyperbolic curve (simpler binding pattern corresponds to single heme)
- High affinity for O₂
- Binding properties correspond to role in oxygen in storage (not oxygen delivery)
- Early curve: exercising muscle; plateau: muscle at rest

CLINICAL CORRELATION

Fetal hemoglobin

- Dissociation curve to the left of adult hemoglobin
- Greater affinity for O₂: O₂ transfer from maternal hemoglobin to fetus

FULL-LENGTH TEXT

- Here we will learn about hemoglobin and myoglobin, the two major oxygen carrying proteins in humans.
- To begin, start a table to learn some key features of these proteins.
- Denote that they are globular; they are almost spherical in shape.
- Denote that they are hemoproteins, which are specialized proteins that have a prosthetic heme group.
- Prosthetic groups are non-protein molecules that are essential to biological function.
- Denote that myoglobin is found in skeletal and cardiac muscle, and that it functions as a reservoir for oxygen in these cells.
- Denote that hemoglobin is found in red blood cells, and supplies the body's tissues with oxygen.

We will start by learning the prosthetic heme group of hemoglobin and myoglobin.

- Draw an iron center (Fe^{2+}).

- Write that iron coordinates 6 bonds total, and that it lies at the center of a porphyrin ring.

- Porphyrins are large, complex ring structures. We will include only a portion of heme's porphyrin ring in our diagram.

- Now, show that our iron center binds four nitrogens in one plane.

- Show that the nitrogen of a histidine group forms the fifth bond.

- This histidine is a proximal amino acid residue in the protein portions of both hemoglobin and myoglobin.

- Show that oxygen is the sixth bond iron coordinates with.

- Finally, draw a porphyrin ring surrounding the four planar nitrogens.

Now, let's draw hemoglobin and myoglobin. We will start with myoglobin.

- Draw a single polypeptide and indicate that it comprises 8 alpha-helix segments.

- Draw a representative heme group:
 - Specify an iron center and a porphyrin ring.

- Now, show that the iron in the heme group is bound to the following:
 - A histidine of one of the alpha helices in myoglobin (specify it as the proximal histidine).
 - Oxygen.

- Next, show that oxygen is held in place by the histidine of another alpha helix in myoglobin (specify it as the distal histidine).

- Note that the hydrogen in histidine binds oxygen, while the nitrogen binds the positively charged iron.

Now, let's draw hemoglobin, which comprises four polypeptides instead of just one.

- Draw a dimer in which each subunit contains a heme group.

- We draw a simplified version, but indicate that each subunit closely resembles myoglobin's tertiary structure.

- Label each subunit alpha and beta.

- Show that strong hydrophobic interactions stabilize the dimer.

- Next, draw an identical dimer below this one.

- Indicate that weak ionic and hydrogen bonds stabilize this dimer's interaction with the one above it.

- Thus, hemoglobin is a tetramer with four subunits.

- Its actual three-dimensional structure is more complex, but we will not worry about that, here.

- Now, label this tetramer the T-form for "taut" or "tense," in which the polypeptide chains are restricted in their movement.

- Indicate that this is hemoglobin's deoxy form; its oxygen affinity is low.

- Next, redraw the tetramer, but do not draw the ionic and hydrogen bonds just yet.

- Next, show that the heme groups are bound to oxygen. We leave out the stabilizing histidines for clarity.

- Now, draw a representative weak ionic and hydrogen bond between the two dimers.

- Indicate that oxygen disrupts these bonds.

- Show that this is the R-form for "relaxed."
- The weaker ionic and hydrogen bonds allow the subunits to move slightly in this state.

- Indicate that this is hemoglobin's oxy form; its oxygen affinity is high.
- Draw reversible arrows to represent the conformational change between the T-form and R-form hemoglobin molecules.

Next, let's elaborate on this conformational change.

- We call it cooperative binding.
- Step 1: One oxygen binds a hemoglobin subunit.
- Step 2: this binding disrupts inter-dimer bonds, which causes a conformational change.
- Step 3: this change in hemoglobin's three-dimensional structure increases the remaining subunits' affinities for oxygen.

Why doesn't myoglobin exhibit cooperative binding?

- Because it only has one heme group, and thus only one oxygen binding site.
- Myoglobin is fully saturated when bound to one oxygen; its affinity cannot increase when there are no additional oxygen binding sites.

Now, let's compare the binding properties of both myoglobin and hemoglobin by drawing their dissociation curves. These curves measure their relative affinities for oxygen.

- Draw a graph and label the x-axis oxygen partial pressure (torr).
- Number it 0 to 120.

Now, let's label some key values.

- Show that 30 torr is approximately the partial pressure of oxygen in the body's tissues.
- Show that 100 torr is approximately the partial pressure in the lungs.

- Next, label the y-axis % oxygen saturation and number it 0 to 100; we will use it to compare the oxygen binding patterns of both hemoglobin and myoglobin.

Now let's draw the oxygen binding curve for hemoglobin and myoglobin. Start with hemoglobin.

- Draw a sigmoidal curve that plateaus just below 100% saturation.
- Write that cooperative binding produces this sigmoidal shape; as one oxygen molecule binds, hemoglobin's affinity for additional oxygen increases, and its percent saturation rapidly increases.
- Show that hemoglobin reaches half saturation in the peripheral tissues; it responds to oxygen availability and releases it when partial pressure is low.

Now, for myoglobin.

- Draw a hyperbolic curve to the left of the hemoglobin curve, a much simpler binding pattern that corresponds to myoglobin's single heme group.
- Indicate that myoglobin has a high affinity for oxygen, and does not release it until the partial pressure is very low.
- These binding properties correspond to myoglobin's role in oxygen storage.
- Label the early portion of the curve "exercising muscle" and the plateau "Muscle at rest."
- Write that myoglobin releases oxygen in response to the muscle's immediate needs.
- In contrast, write that hemoglobin's cooperative binding allows it to respond to changes in oxygen availability.
- As a clinical correlation, show that the fetal hemoglobin dissociation curve is to the left of the adult hemoglobin curve.
- Why? It has a greater affinity for oxygen to facilitate oxygen transfer from the maternal hemoglobin to the fetus; fetal oxygen supplies come from the mother.