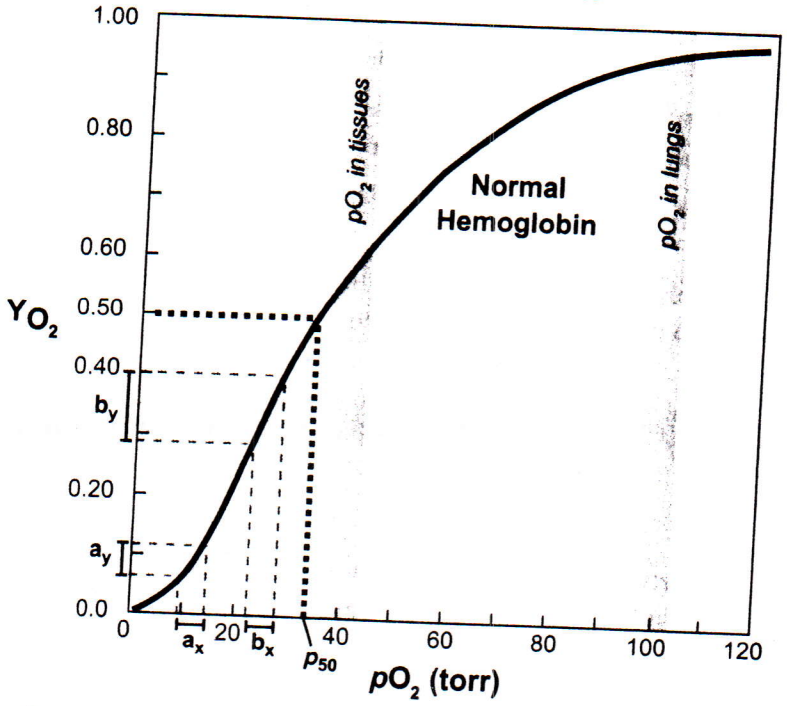
Plan

1. Form Structure/Function teams as instructed.
2. Answer the Critical Thinking Questions.
3. Prepare your spokesperson to share two discoveries your team made about the relationship between protein structure and function.

Model 1

The following figure depicts the oxygen binding curve for hemoglobin. Some textbooks use the symbol θ whereas others use Y_{O_2} in the formula for fractional saturation.

$$\theta \text{ or } Y_{O_2} = \frac{\text{Sites occupied}}{\text{Total available sites}}$$



Critical Thinking Questions

Part 1

1. What is plotted on the x-axis?

2. What does the pO_2 refer to in a solution like blood? In the blood, is there some O_2 bound and some unbound? What form of oxygen does the pO_2 refer to?

3. What is plotted on the y-axis?

4. When Y_{O_2} equals 1.0 how many oxygen molecules are bound to one hemoglobin molecule?

5. For the change in pO_2 on the x-axis labeled 'a_x' locate the corresponding change in Y_{O_2}. What is its label?

6. For the change in pO_2 on the x-axis labeled 'b_x' locate the corresponding change in Y_{O_2} What is its label?

7. Compare and contrast the change in pO_2 (ΔpO_2) for 'a_x' and 'b_x'.

8. Compare and contrast the change in Y_{O_2} (ΔY_{O_2}) for 'a_y' and 'b_y'.

9. Using the data from questions 7 and 8, describe how the Y_{O_2} changes with increasing pO_2 levels and use the term ***oxygen binding*** in your answer.

Information

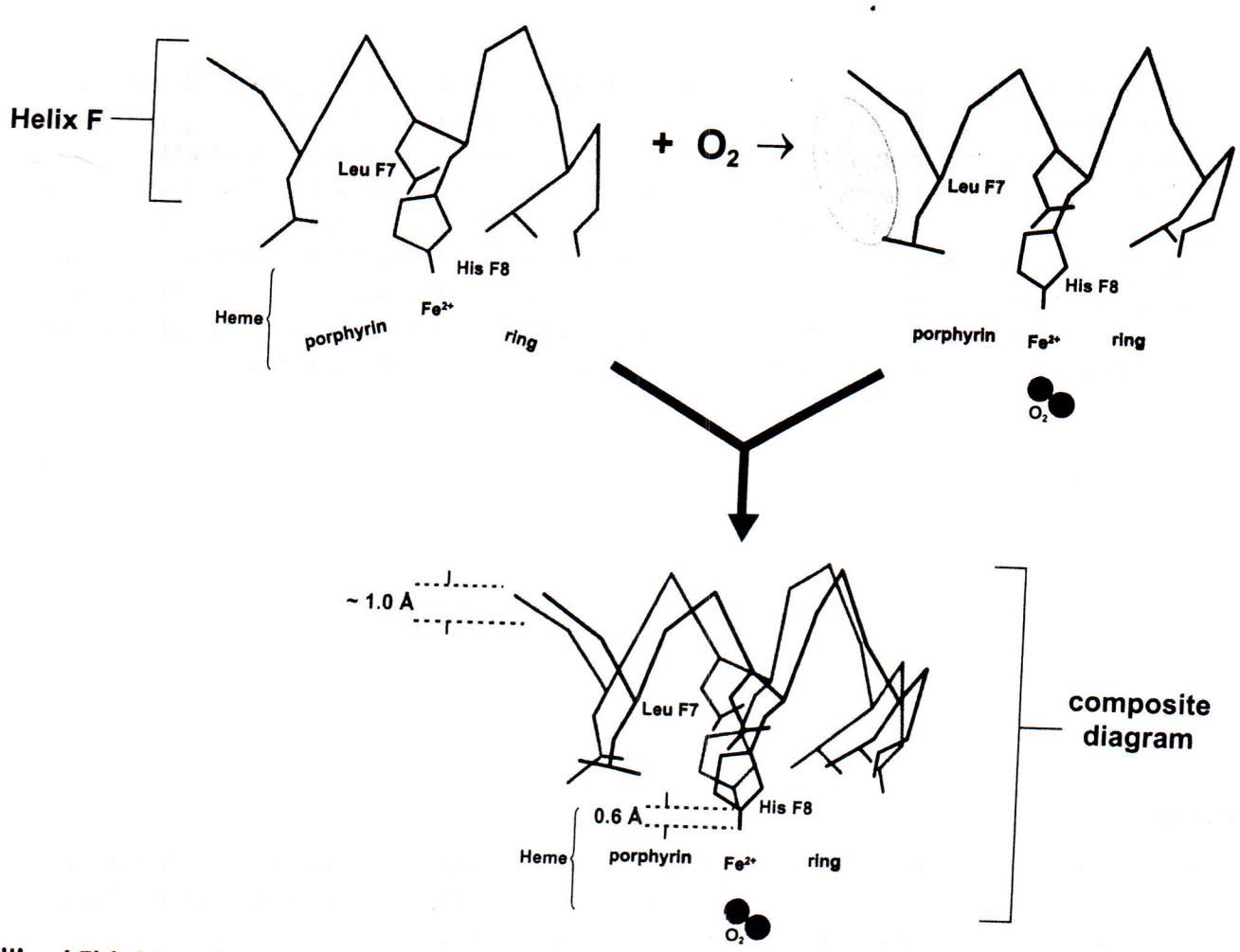
The positive change in hemoglobin saturation, Y_{O_2}, as more O_2 is present is called ***cooperative binding***. More oxygen is bound (Y_{O_2}) for a given change of pO_2 at high levels of O_2 than at low levels of O_2. This shows that hemoglobin has a greater affinity for oxygen when the partial pressure of oxygen is high and has a lower affinity when the partial pressure of oxygen is low. The binding of oxygen at one site affects the binding properties of oxygen at another site on the protein. This type of cooperativity is homotropic since oxygen binding at one site is affecting **oxygen** binding at another site. The term ***homotropic*** is used because the same ligand, oxygen, is involved at the multiple sites.

10. What is the function of hemoglobin? Be sure to account for role of loading and unloading of oxygen.

Part 2

Model 2

By convention the α helical segments of each hemoglobin subunit are labeled A through H. The nonhelical segments that connect between helices are labeled AB, BC, CD etc., which refer to the α helical segments being connected. Hemoglobin consists of 4 subunits named α_1, α_2, β_1 and β_2. The three-dimensional structure of the folded subunits is very similar even though the polypeptide sequences of the α chain and the β chain differ by more than 80% of the amino acids. The histidine labeled F8 in the figure below is the proximal histidine involved in coordination with the Fe^{2+} of the heme ring. In the α chain this is His 87 in the sequence, whereas in the β chain it is His 92 in the sequence. Both histidines are in the F Helix of their respective chain and therefore labeled F8.



Critical Thinking Questions

16. Describe the overall shape of the heme group, (porphyrin–Fe^{2+}–ring) without oxygen bound to Fe^{2+}.

17. Describe the overall shape of the heme group (porphyrin–Fe^{2+}–ring) with oxygen bound to Fe^{2+}.

18. When oxygen binds to the heme group, by how many angstroms does the Fe^{2+} appear to shift?

19. How far in Angstroms does the F8 histidine nitrogen appear to shift when oxygens binds to the Fe^{2+}?

20. Approximately how far in Angstroms does the Leu F7 appear to shift when oxygen binds to heme?

21. Approximately how far in Angstroms does Helix F appear to shift when oxygen binds to heme? What will happen to other helices in the subunit when helix F moves?

22. The binding of oxygen to the heme group results in flattening of the heme group and that event is communicated through the rest of the protein as Helix F of the alpha and beta chains changes position relative to the other helices and their respective subunits. This movement results in adjustments in the ion pairs at the interface between the α_1 and β_2 subunits and between the α_2 and β_1 subunits. The end result is a narrowing of the central channel of hemoglobin (the area in the center of the molecule). Therefore, structural changes within one subunit result in overall change in the quaternary structure of hemoglobin. Compare the affinity of hemoglobin for O_2 prior to the events described above and after those events. Make a generalization about hemoglobin structure as it relates to hemoglobin function. Your instructor may provide an animation depicting the described molecular events.

Information

In addition to O_2 binding, changes in other chemical conditions can result in changes in hemoglobin structure and function. Increases in blood H^+ result in oxygen binding curves for hemoglobin that are shifted to the right. The effect of H^+ can be understood in terms of the equilibrium:

$$H\text{-}Hb^+ + O_2 \rightleftharpoons Hb\text{-}O_2 + H^+$$

23. What is the pH of blood in the tissue and in the lungs and why does that difference in pH contribute to hemoglobin delivering oxygen? Use the equilibrium equation in your argument.