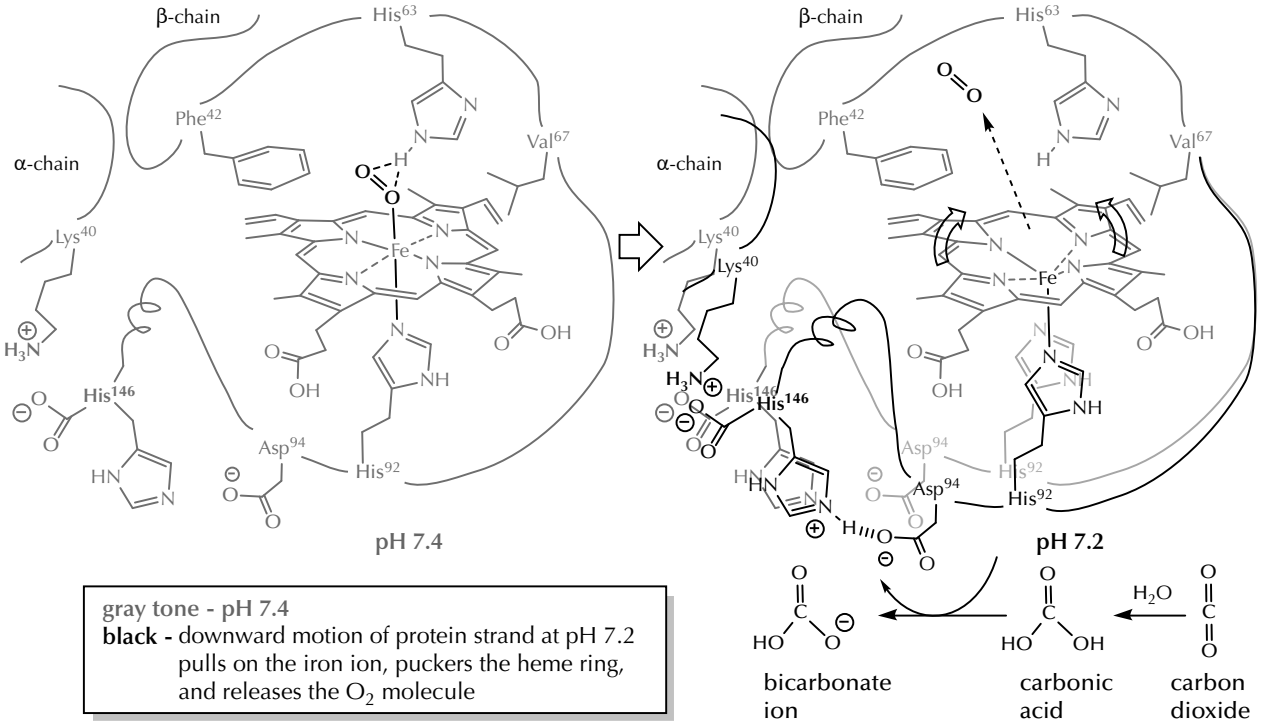
Figure 1803

Deoxygenation of hemoglobin at the cells.



(1) The His^{146} protonation causes a conformational change in the β-chain that is particularly significant near Asp^{94}, and because Asp^{94} is only residue away from His^{92}, the conformational effect from protonation is transmitted as movement of the iron ion in the protoporphyrin ring. The protonation and hydrogen bond formation bring His^{146} and Asp^{94} closer together, and the resulting movement tugs on His^{92} and pulls the iron atom below the plane of the protoporphyrin ring, causing the ring to pucker upwards. The puckering of the ring as the iron atom pulls away is enough of a change to release the oxygen molecule.

(2) The motion of the C-terminal His^{146} also moves the α-chain because of the ionic interaction between His^{146} (β-chain) and Lys^{40} (α-chain). At the same time that the protonation of a histidine is taking place over in the beta-chain to change its conformation and release oxygen, the second motion of the α-chain, due to the movement of Lys^{40}, causes the release of the second oxygen atom from hemoglobin to take place faster than the first one.

To restate the second item, above: The release of the first oxygen molecule, which is motivated by the change in pH, also causes a conformational change in a nearby chain that increases the rate of the second oxygen molecule's release. And then, the cumulative effect of those two chains is transmitted to a third, which is also being protonated, and the release of the third molecule is faster, still, followed by another amplification of the conformational changes, resulting in the release of the fourth oxygen molecule.

Take a moment to think about the wonderfully subtle action of this molecular machinery. As the hemoglobin, loaded up with four oxygen molecules, moves into an area in need of oxygen, and that need is signaled by the slight decrease in pH which accompanies the production of carbon dioxide (meaning that oxygen is being actively used, and so more is needed). Protonation of the loaded hemoglobin causes a cascade of conformational changes that serially accelerate the loss of each oxygen molecule. Another small molecule (2,3-bisphosphoglycerate) becomes ionically associated with the vacated hemoglobin, helping to stabilize it in this empty, unloaded form, for its trip back to the lungs.