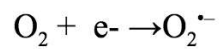


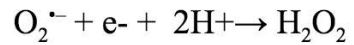
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11 Na Sodium 22.990		12 Mg Magnesium 24.305		3 3B 3B		4 4B 4B		5 5B 5B		6 6B 6B		7 7B 7B		8 8 VIII 8		9 9 VIII 8		10 10 VIII 8		11 1B 1B		12 2B 2B															
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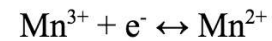
Reduction half reactions and their E°' values (at pH 7)



$$E^{\circ'} = -160 \text{ mV}$$

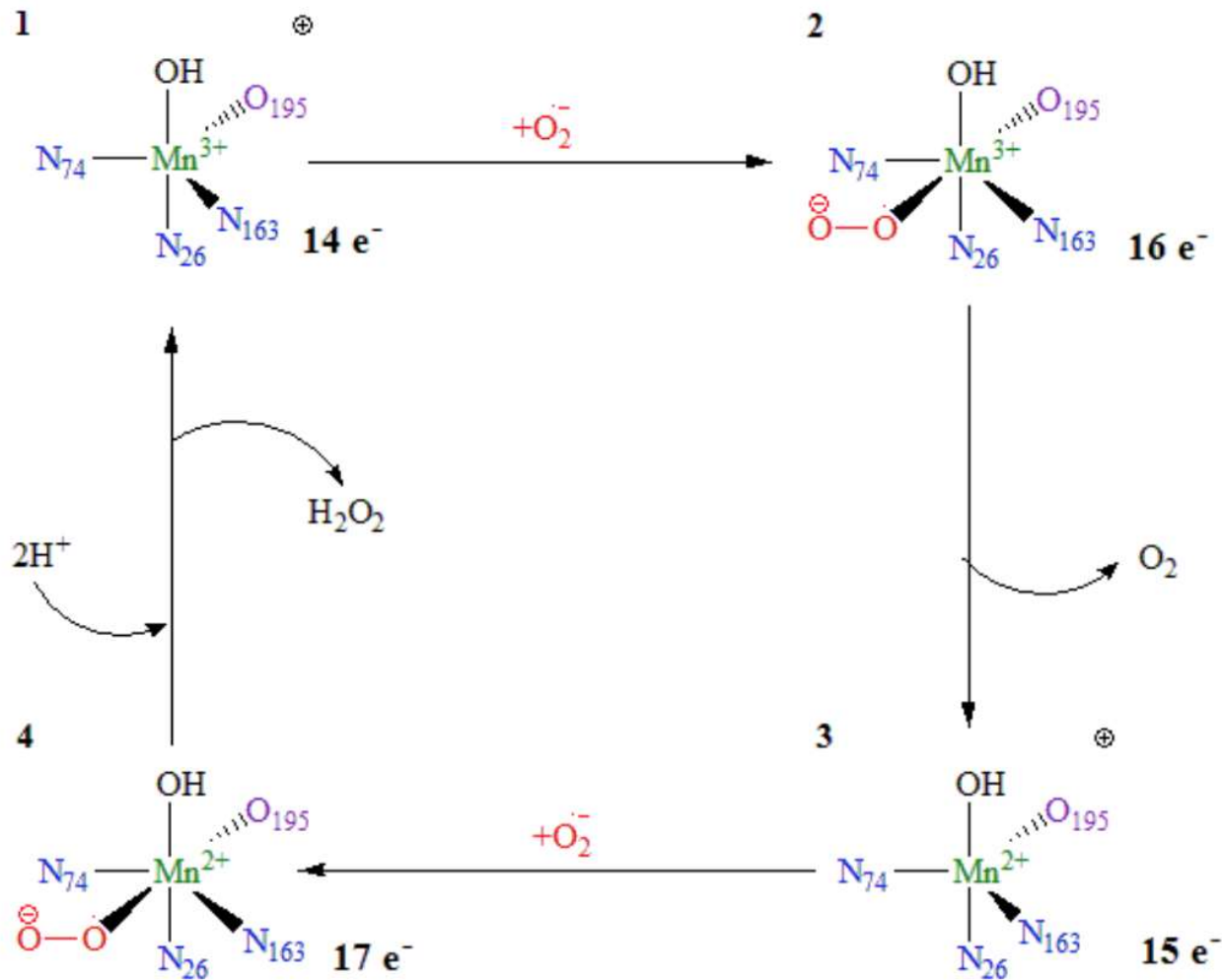


$$E^{\circ'} = +850 \text{ mV}$$

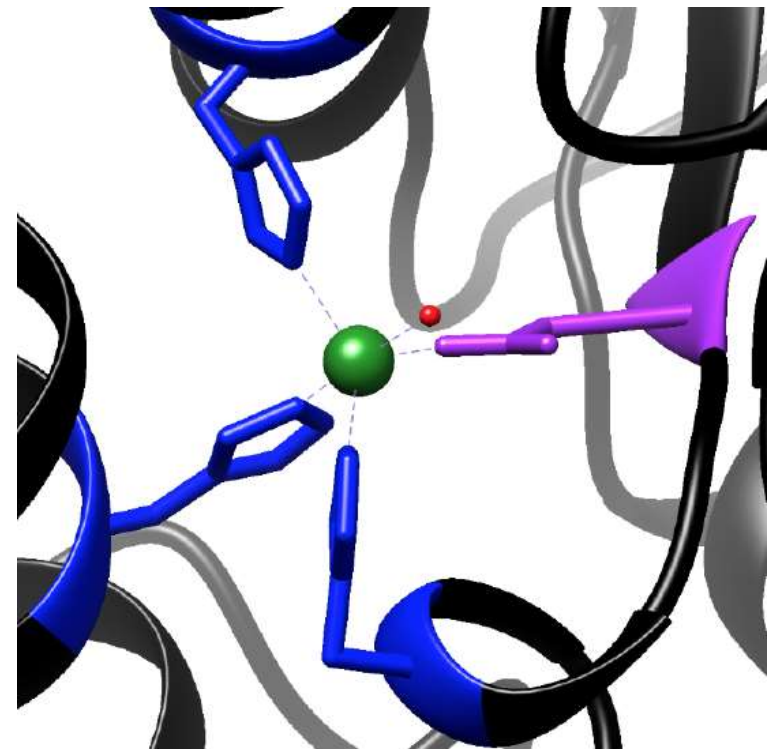


$$E^{\circ'} = +1,096 \text{ mV}$$

← outside of range



the MnSOD protein is thermodynamically favorable for the catalysis of superoxide to O_2 and H_2O_2



Superoxide Dismutase

MnSOD is a Redox Catalyst

The Mn superoxide dismutase (MnSOD) is the only SOD enzyme located in the mitochondrial matrix

Mitochondria reduces O_2 , producing an influx of $O_2^{\cdot -}$ radicals.

The Mn in SOD changes between its 3+ and 2+ oxidation states within the dismutase mechanism, consisting of two half-reactions. E

Electron exchange in metal complexes can happen by either an inner-sphere or outer-sphere mechanism.

In inner-sphere electron transfer, the metal cofactor is oxidized or reduced by a ligand bound directly to the metal.

In an outer-sphere mechanism, the metal is oxidized or reduced by a group not directly coordinated to the metal cofactor.

The catalysis of superoxide anions by MnSOD occurs by an inner-sphere mechanism

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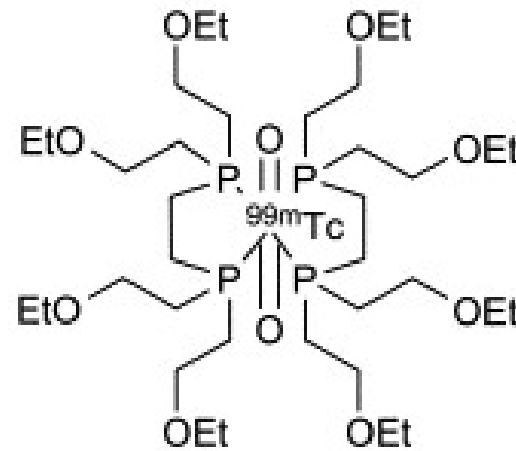
Technetium (specifically Technetium-99m)

widely used in nuclear medicine for diagnostic imaging of various organs, including the brain, heart, lungs, kidneys, and bones.

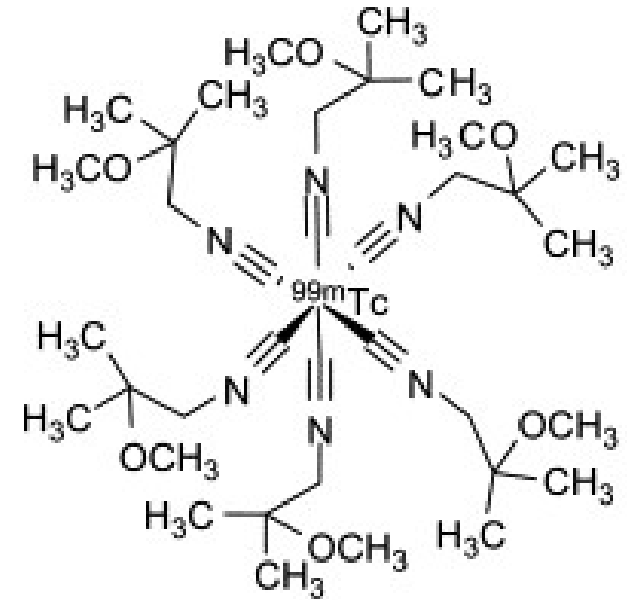
Its ideal properties for medical imaging include a 6-hour half-life, low-energy gamma ray emissions that are easily detected, and its ability to be attached to biologically active substances to target specific tissues.

Technetium-99m is the most common radionuclide for SPECT imaging and is used for conditions such as heart disease, kidney problems, and bone abnormalities.

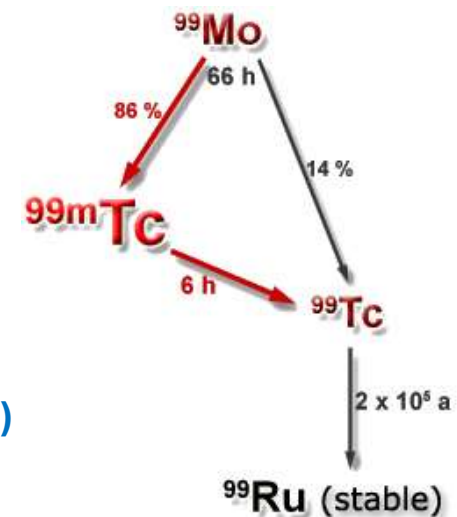
DuPont Radiopharmaceuticals -1989 FDA approval (same year as carboplatin)
(Cisplatin FDA approval 1978)



^{99m}Tc -Tetrofosmin



^{99m}Tc -Sestamibi



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Lanthanide Series

Actinide Series

Hemoglobin and Myoglobin

- These are conjugated proteins - A simple protein has only a polypeptide chain. A conjugated protein has a non-protein part in addition to a polypeptide component. Both myoglobin and hemoglobin contain heme.

- **Myoglobin** 17000 daltons (monomeric)

153 amino acids

- **Hemoglobin** 64500 daltons (tetrameric)

α -chain has 141 amino acids

β -chain has 146 amino acids

Iron in Hemoglobin binding O_2

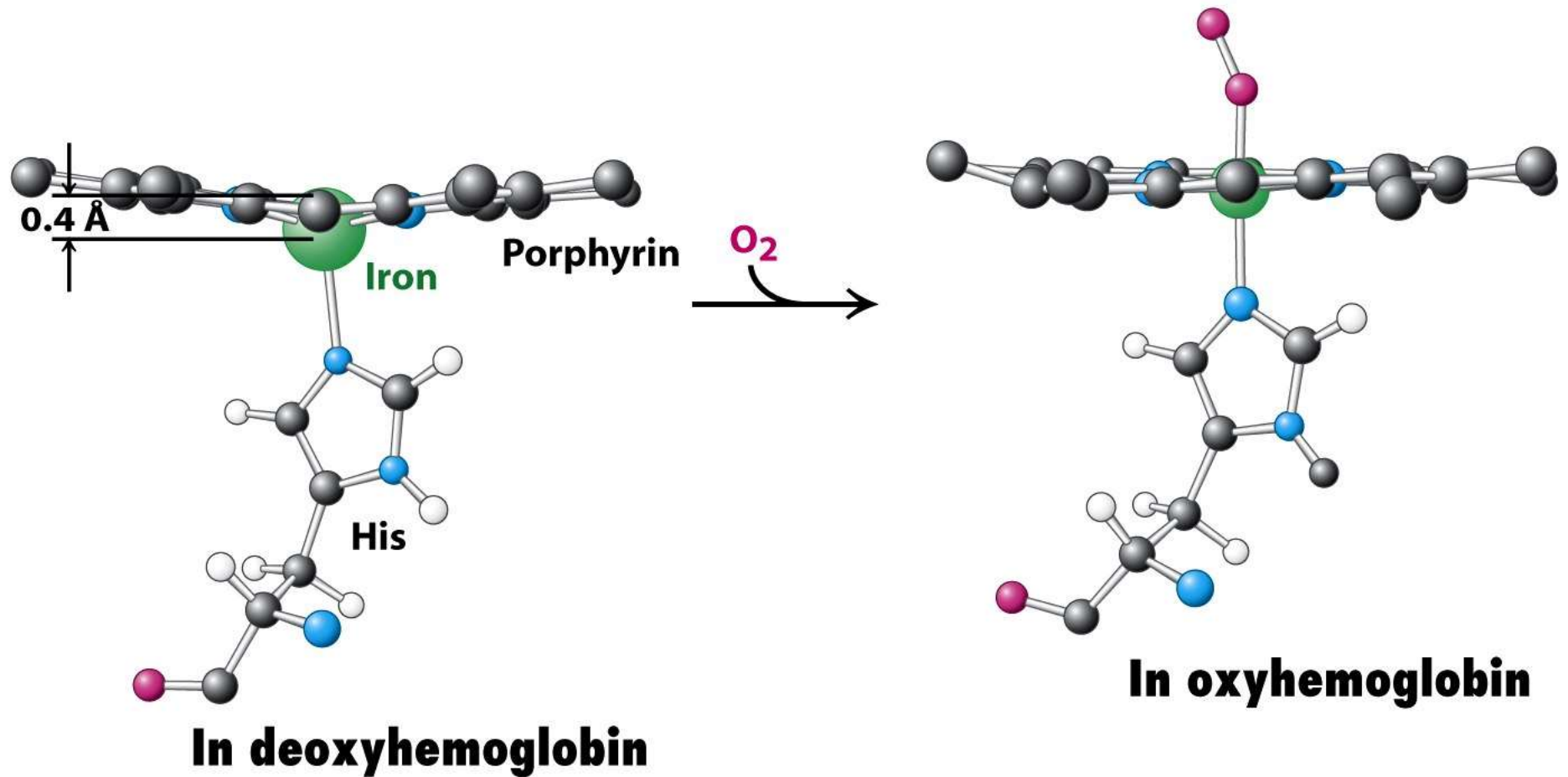
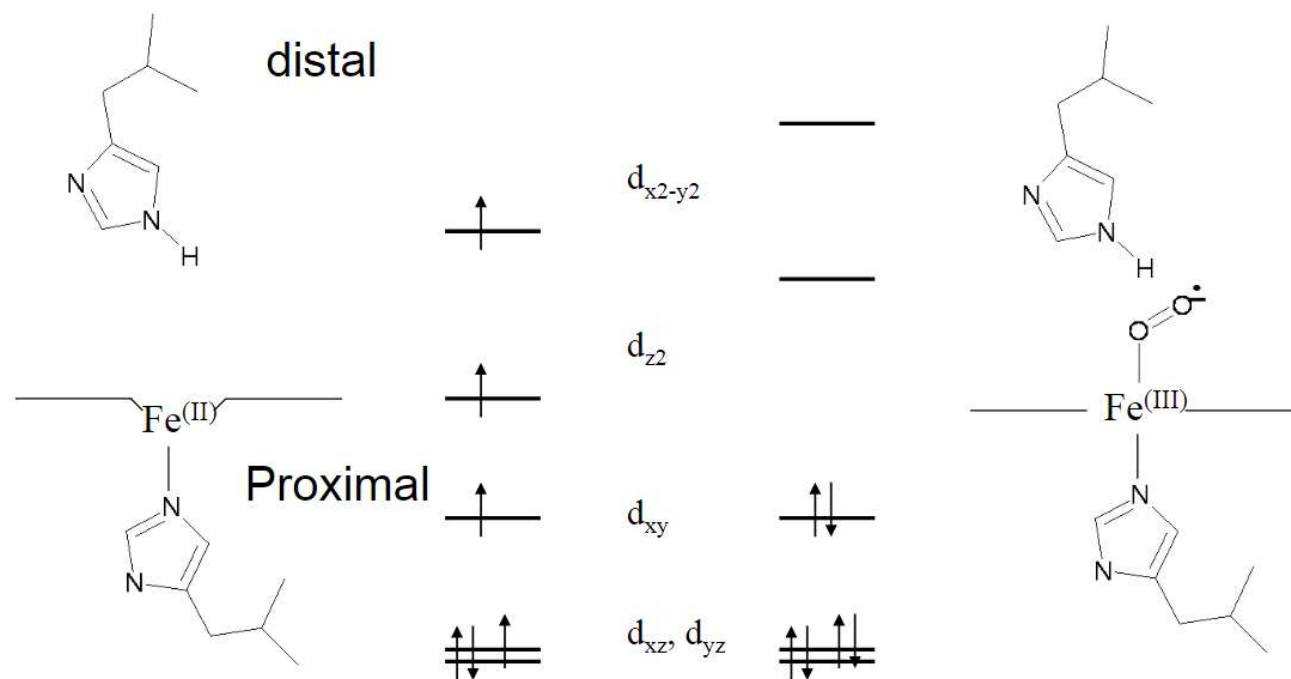


Figure 7-2
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Mode of O₂ Binding



Fe^{III}(HS) ionic radius = 78 pm

Fe^{III}(LS) ionic radius = 61 pm

Myoglobin O₂ Binding Properties



- Dissociation constant, $K_d = [\text{Mb}] [\text{O}_2] / [\text{MbO}_2]$

Few points to remember

- If K_d (dissociation) is higher, binding is weaker
- If binding curve is less steep, binding is weaker
- Half-saturation is the point where $[\text{O}_2] = K_d$:

$$K_d = [\text{Mb}] [\text{O}_2] / [\text{MbO}_2] = [\text{Mb}] K_d / [\text{MbO}_2]$$

$$K_d / K_d = [\text{Mb}] / [\text{MbO}_2] = 1 \quad \dots \quad [\text{Mb}] = [\text{MbO}_2]$$

Hemoglobin Cooperativity

The presence of several subunits alters the nature of the oxygenation curves entirely. As a consequence of a delicate interplay between the subunits, which is still only partially understood, the binding of oxygen is cooperative.

The affinity of a given heme for oxygen increases as the other hemes in the molecule are oxygenated. Consequently, the degree of saturation at first does not respond much to the pressure, then begins to rise abruptly. As the pressure continues to increase, the curve levels off and approaches asymptotically to 1, the full saturation value. The result is an S-shaped, or sigmoidal oxygenation curve.

Concerted, two state model

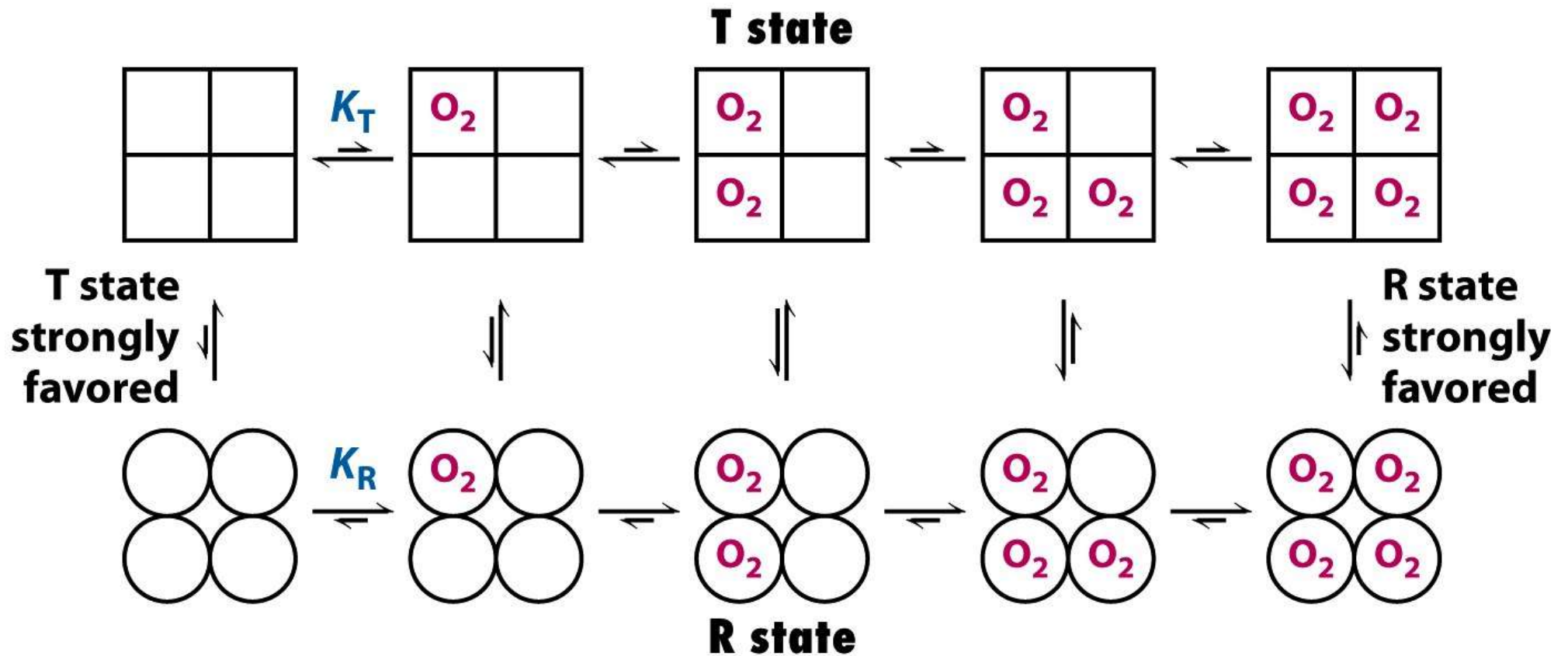


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Monod, Wyman & Changeux

R-state vs T-state Binding

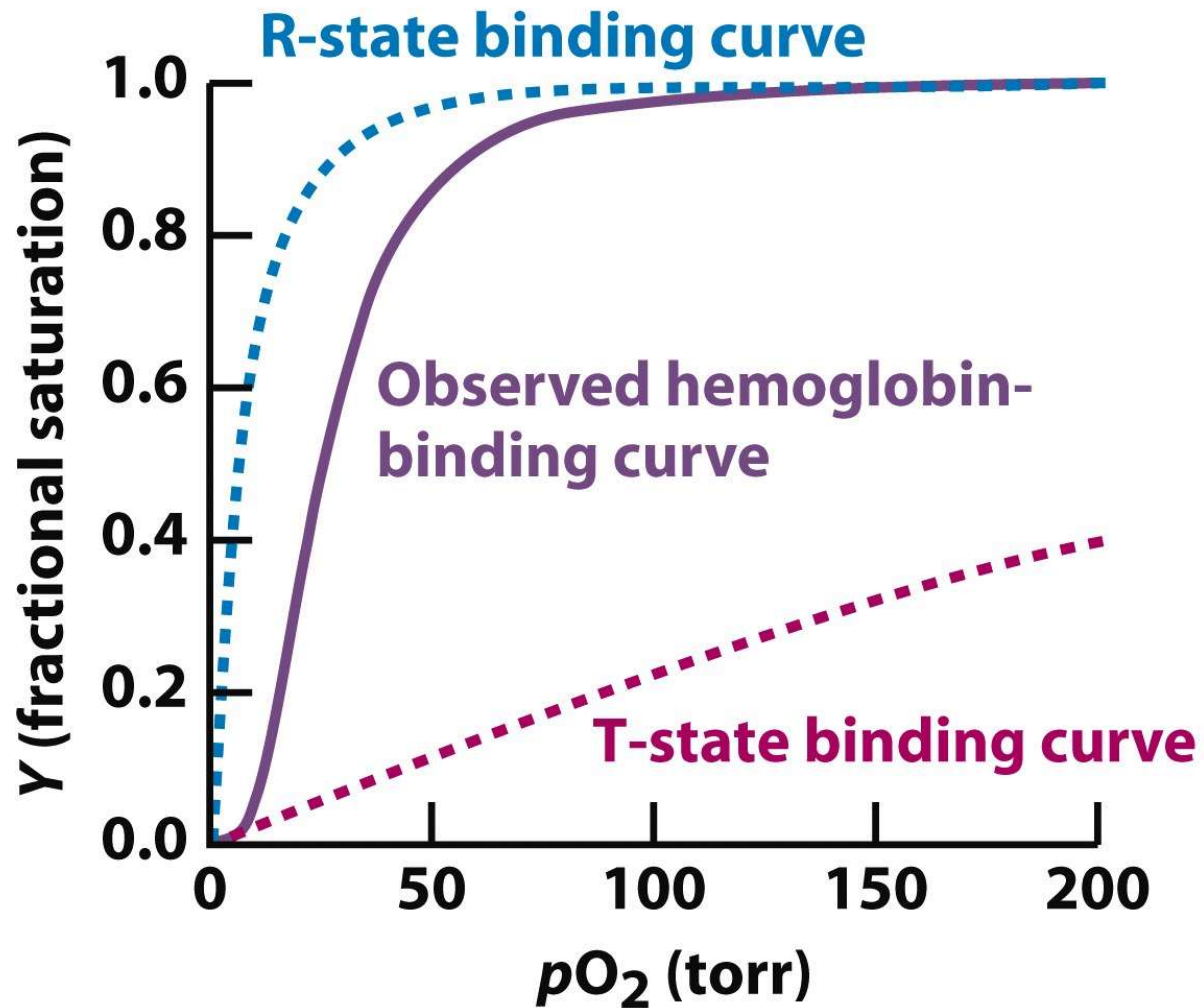


Figure 7-12
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➤ In oxygen-free Hb, the iron is in the bivalent state and has a high-spin configuration. The high-spin ion is too large to fit among the four porphyrin nitrogens and sits some .6 Å out of the heme plane toward the imidazole nitrogen (T state).

When the entry of oxygen, the metal reverts to low-spin state, shrinks, and moves toward the plane of the porphyrin (R state). This brief motion is believed to trigger a whole series of subtle changes in the arrangement of the subunits and to be responsible for many remarkable aspects of Oxygen-Hb equilibrium.

➤ The state of iron in oxyHb is to regard it as ferric-superoxide complex, with one-electron transferred to the oxygen.

If a decrease in pH shifts the O₂-Hb equilibrium in favor of deoxy-Hb,



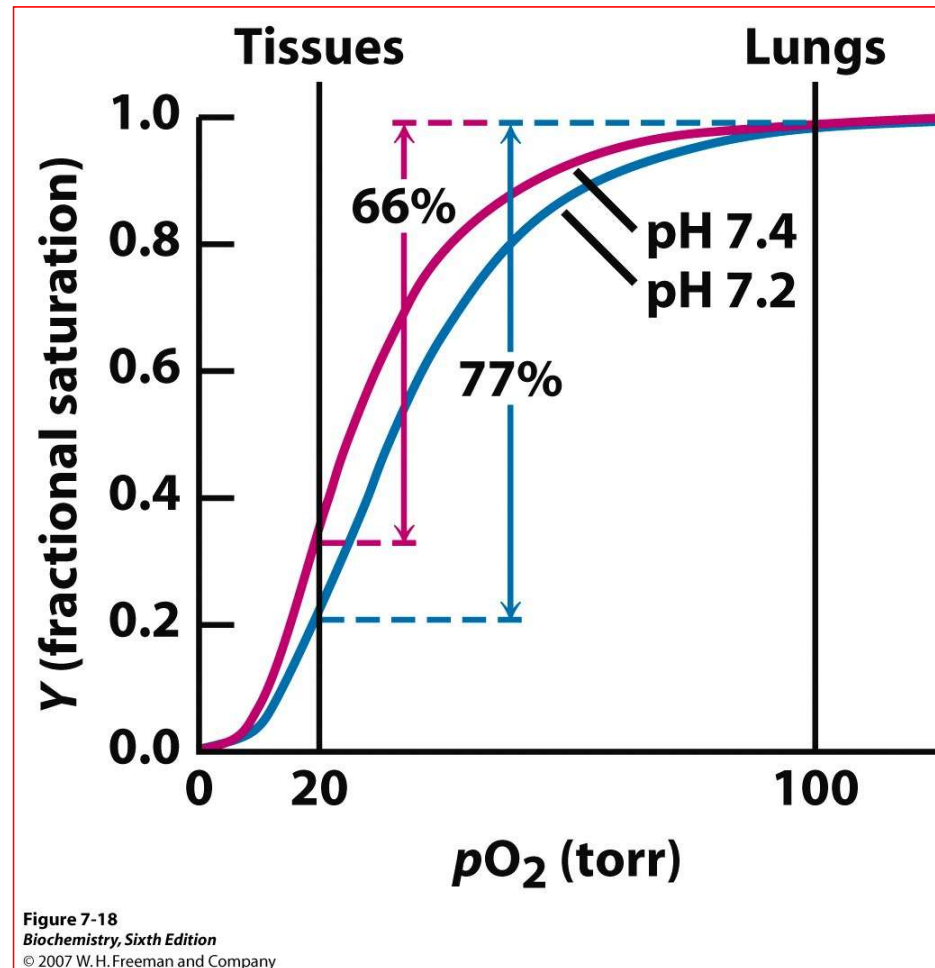
then according to Le Chatelier's principle, oxy-Hb (its surroundings) must be a stronger acid and deoxy-Hb (its surroundings) a stronger base.

An increase in pH leads to the production of oxy-Hb which, being a stronger acid, releases H⁺ ions.

The removal of H⁺ ions from surroundings by deoxy-Hb and their release by oxy-Hb facilitate the transport of CO₂.

The Bohr Effect

- Lowering the pH decreases the affinity of oxygen for Hb



The "**Bohr effect**" is a property of hemoglobin first described by the Danish physiologist Christian Bohr in 1904. Because of the Bohr effect, an increase in blood carbon dioxide level, a decrease in pH or increased temperature causes hemoglobin to bind to oxygen with less affinity.

This effect facilitates oxygen transport as hemoglobin binds to oxygen in the lungs, but then releases it in the tissues, particularly those tissues in most need of oxygen. When a tissue's metabolic rate increases, its carbon dioxide production increases. The carbon dioxide is quickly converted into bicarbonate molecules and protons by the enzyme **carbonic anhydrase**:



➤What happens in the lungs is the reverse of the situation in respiring tissues. The formation of oxyHb is accompanied with the release of protons. This converts the HCO_3^- to H_2CO_3 and CO_2 , which diffuses out of erythrocytes first into blood plasma, then to the environment.

The Bohr Effect

- ❖ Most of the CO_2 is transported as bicarbonate, which is formed within red blood cells by the action of carbonic anhydrase:



- ❖ The major portion of the Bohr Effect is due to the fact that increasing $p(\text{CO}_2)$ causes a decreased red cell pH (acidosis).
- ❖ A secondary part of the Bohr Effect is due to the fact that CO_2 reacts covalently with hemoglobin to form *carbamino*-hemoglobin which has a reduced O_2 affinity.



The bound *carbammates* form salt bridges that stabilize the T-form! (The **Tense**-form of hemoglobin possesses a lower O_2 affinity).

O₂ transport capability, a comparison

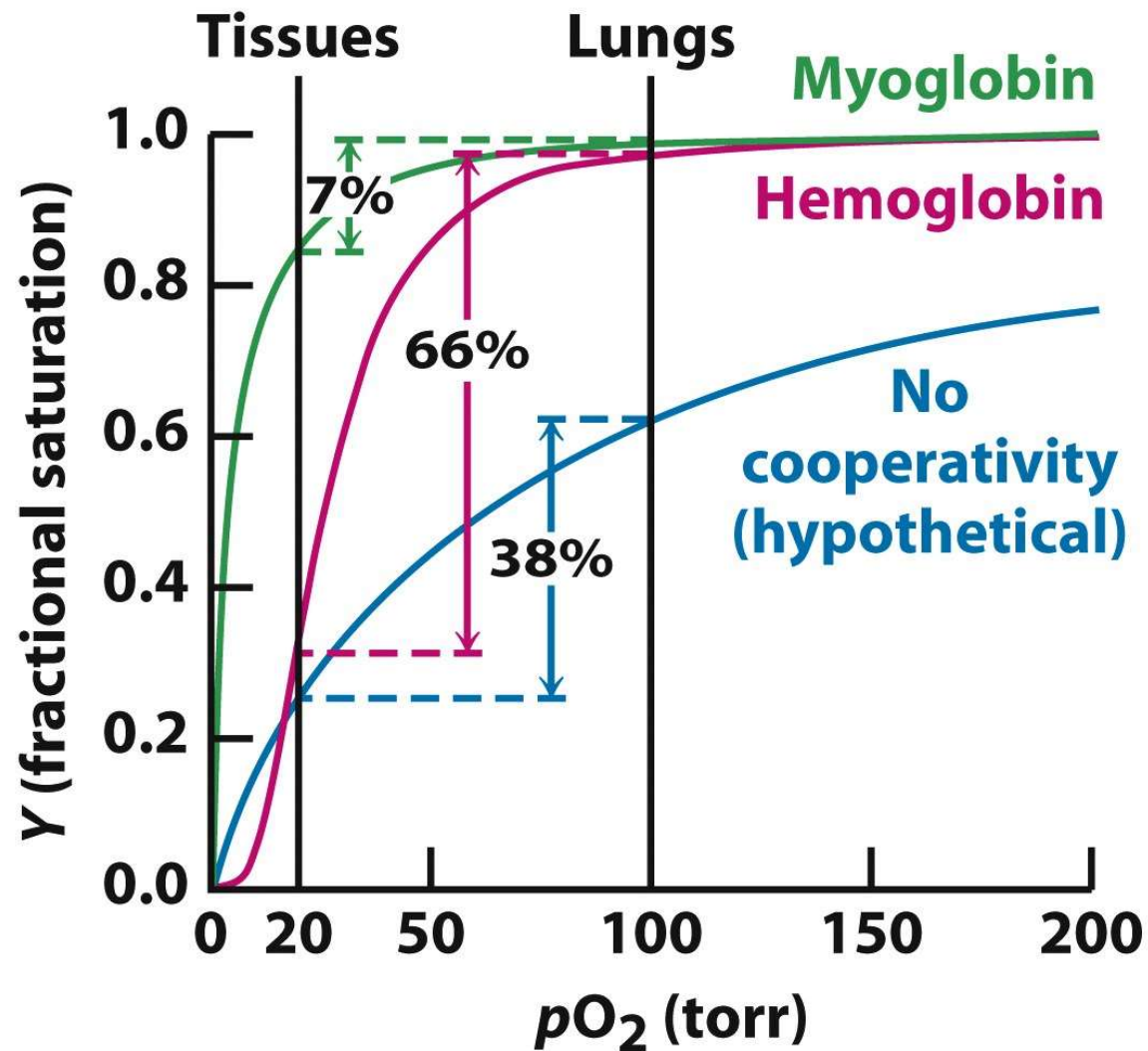


Figure 7-8
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