1. [20 points] Describe/discuss/explain the mechanism(s) by which oxygen is transported from alveoli to cells (in tissue).

In normal circumstances alveolar partial pressure $PAO_2 \approx 100$ mmHg and the O_2 in the blood coming back from the tissue to the pulmonary capillary has a partial pressure $P_{O2} \approx 40$ mm Hg so there is a pressure gradient for oxygen to diffuse across the tissue barrier from the alveolus space into the pulmonary blood. A very small amount of oxygen is dissolved: for each mm Hg of P_{O2}, there is 0.003 ml O_2.100 ml^{-1} of blood, and most of O_2 binds to hemoglobin to form oxyhemoglobin: HbO_2. O_2 is then carried over by the blood which becomes part of the systemic circulation and ends up at the tissue capillaries. Because mitochondria of the cells are utilizing oxygen, there is a pressure drive from the erythrocyte to the plasma to the interstitial fluid to the cell so oxygen goes down the pressure gradient and diffuses into the cells: O_2 comes off hemoglobin as dissolved O_2, diffuses off the red blood cell into the plasma and from the plasma into the interstitial fluid to be consumed in cell mitochondria.

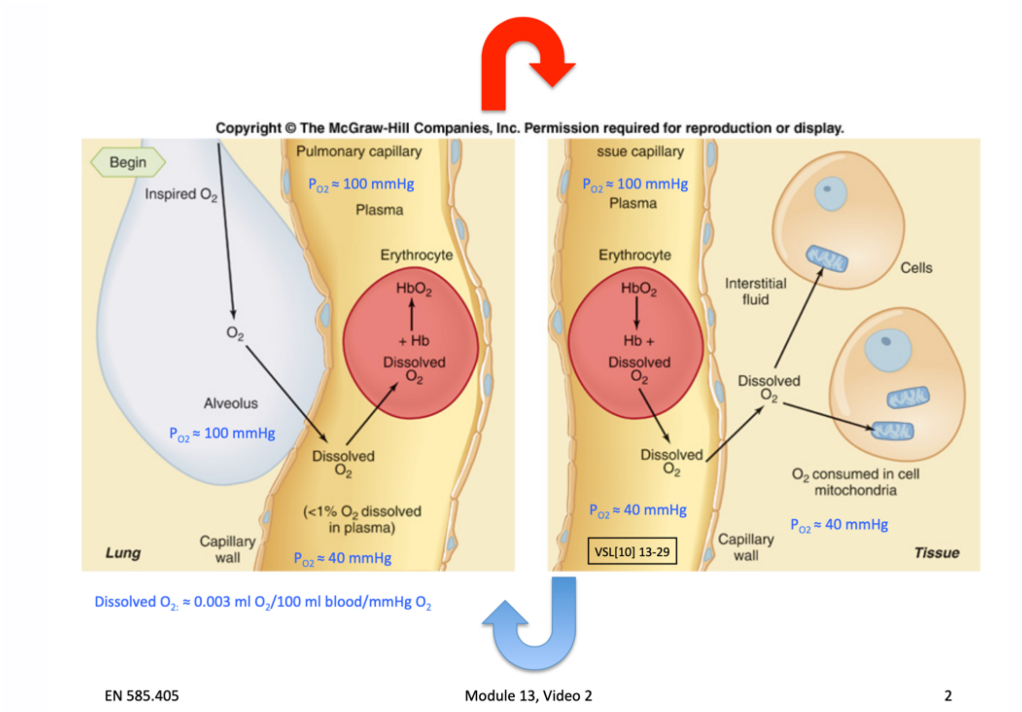

Figure 1

2. [20 points] Describe/discuss/explain the mechanism(s) by which carbon dioxide is transported from cells (in tissue) to alveoli.

Cells produce CO_2 and there is a pressure gradient to drive CO_2 to diffuse from the cells to the interstitial fluid and to diffuse across the tissue barrier into the blood plasma ($PCO_2 \approx$ 46 mm Hg in the interstitial fluid, tissue capillary $PCO_2 \approx$ 40 mm Hg). CO_2 is carried into the blood in three forms:

- *dissolved* in the plasma or the red blood cell
- *bicarbonate* HCO_3^- which is formed by the following sequence:
  $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$
  The first reaction is slow in the plasma but fast within the red blood cell because of the presence of the carbonic anhydrase (CA). HCO_3^- diffuses into the plasma and to maintain charge balance a chloride ion moves in (chloride shift).
- *carbamino compounds* which are formed by the combination of CO_2 with proteins, the most important being the amino groups of hemoglobin to form carbaminohemoglobin (for simplicity noted $HbCO_2$)

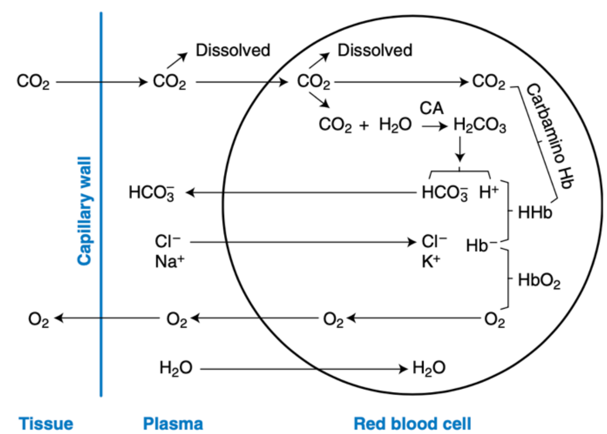

Figure 6.5. Scheme of the uptake of CO_2 and liberation of O_2 in systemic capillaries. Exactly opposite events occur in the pulmonary capillaries.

Figure 2, West[10] p.94

Among the three forms just described, under which carbon dioxide is transported from the cells to the lung, the predominant mechanism is in the form of bicarbonate $HCO3^-$. When the blood enters the pulmonary capillary the $PCO_2 \approx$ 46 mm Hg and the PCO_2 in the alveolus is about 40 mmHg, the pressure gradient drives CO_2 off the pulmonary capillary: the reverse reactions previously described happen, $HCO3^-$ and H^+ combine to produce H_2CO_3, which then dissociates to CO_2 and H_2O, also $HbCO_2$ generates Hb and free CO_2. Free CO_2 diffuses then across the blood gas barrier into the alveolar air to be exhaled.

3. [20 points] Describe/discuss/explain the effect(s) of increased temperature and of increased acidity on the oxygen - hemoglobin saturation curve. Describe/ discuss/explain the physiologic significance of such effect(s).

As the blood moves from the pulmonary capillary to the tissues, temperature is increased because of the heat produced by tissue metabolism. The P_{CO2} is increased because of the CO_2 entering the blood from the tissues which increases acidity or H^+ concentration (or a decrease in pH). The more metabolically active a tissue, the greater its P_{CO2}, H^+ concentration, and temperature, so conditions are less favorable for hemoglobin to bind O_2, and as it passes through the tissue capillaries, hemoglobin has a decreased affinity for oxygen.

Increased temperature decreases hemoglobin's affinity for oxygen by altering its conformation. Carbon dioxide and H^+ decrease hemoglobin's affinity by combining with the globin portion of hemoglobin and altering the conformation of the hemoglobin molecule.

As a net result, less oxygen can bind to hemoglobin reducing hemoglobin saturation with O_2, and the oxygen-hemoglobin saturation curve is shifted to the right by an increase in temperature or increase P_{CO2}, or H^+ concentration (figure 3).

"Therefore, hemoglobin gives up even more oxygen than it would have if the decreased tissue capillary P_{O_2} had been the only operating factor."

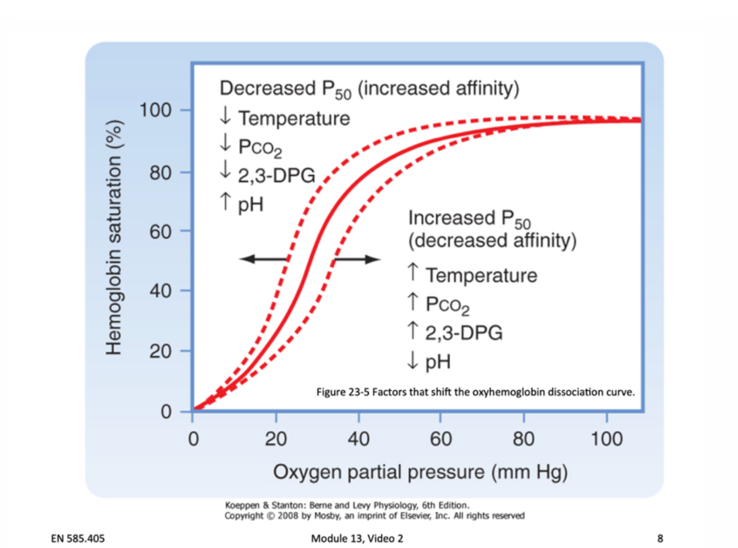

Figure 3

We gradually transitioned from one oxygen-hemoglobin saturation curve at $PO_2 \approx 100$ mm Hg, $PCO_2 \approx 40$ mmHg, about 100% O2 saturation of Hb at the pulmonary capillary toward, when reaching the tissue's capillary, an oxygen – hemoglobin saturation curve corresponding to $PCO_2 \approx 46$ mmHg: hemoglobin releases more oxygen during passage through the tissue's capillary providing cells additional oxygen (figure 4).

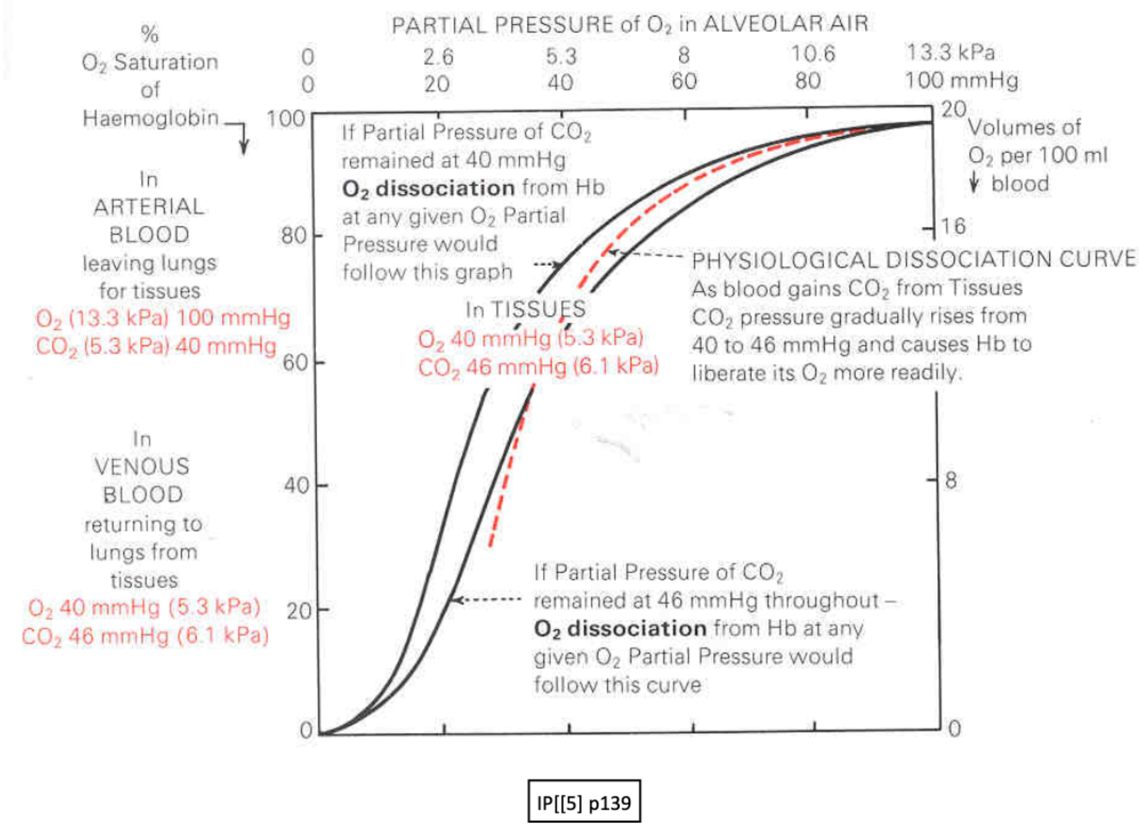

Figure 4