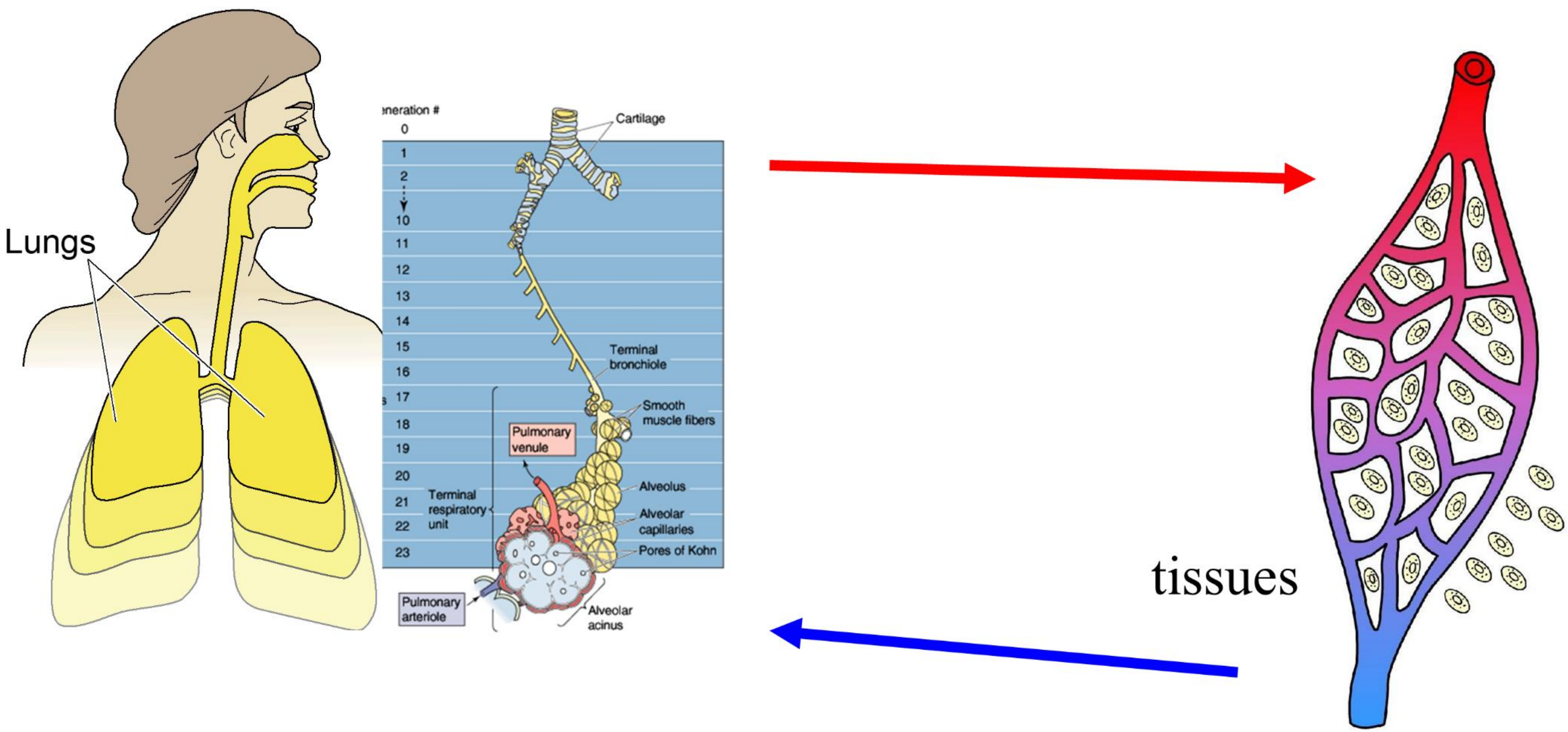
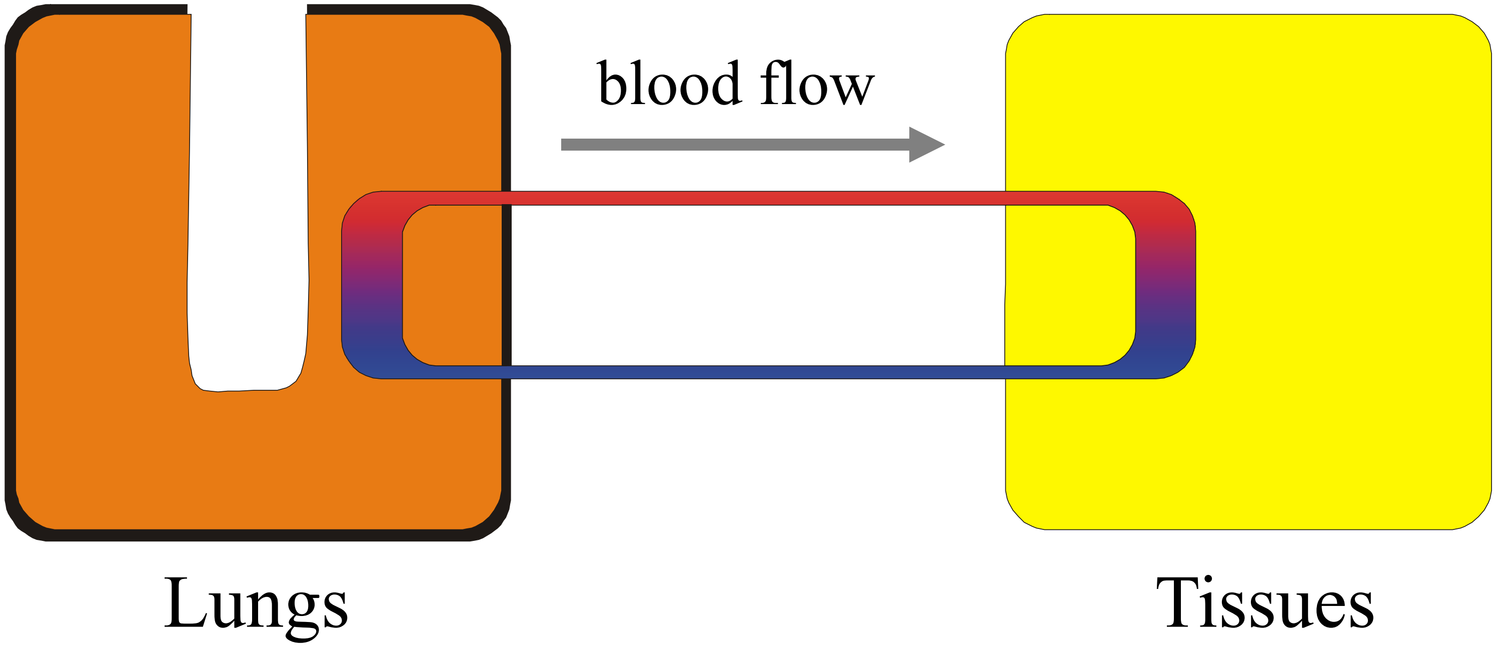


- The structure of the lungs and capillaries provides perfusion of liquid, maximizing gas transport while reducing flow volume.
- Blood serves as a perfusion fluid


blood flow
Lungs
Tissues

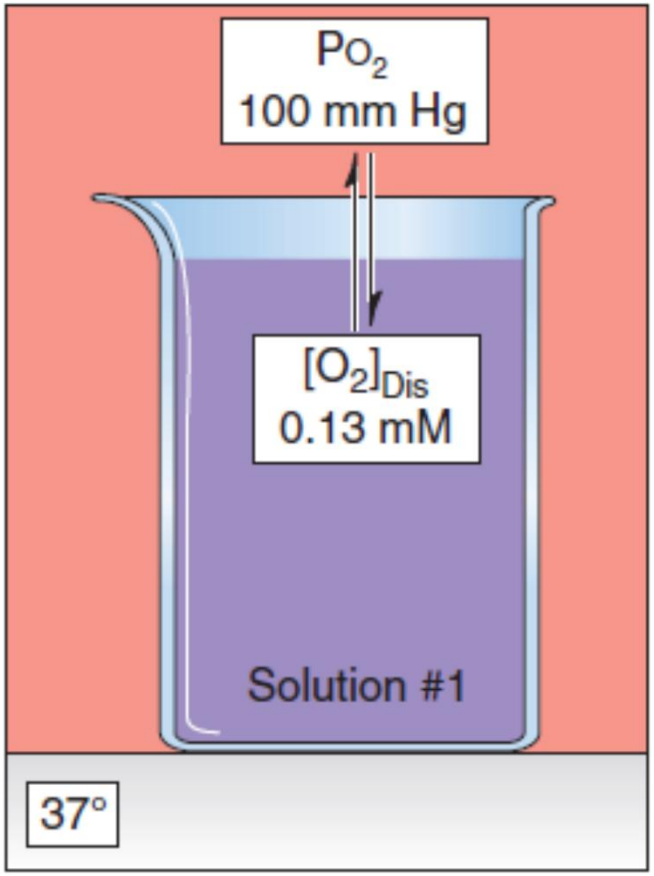
Henry's Law

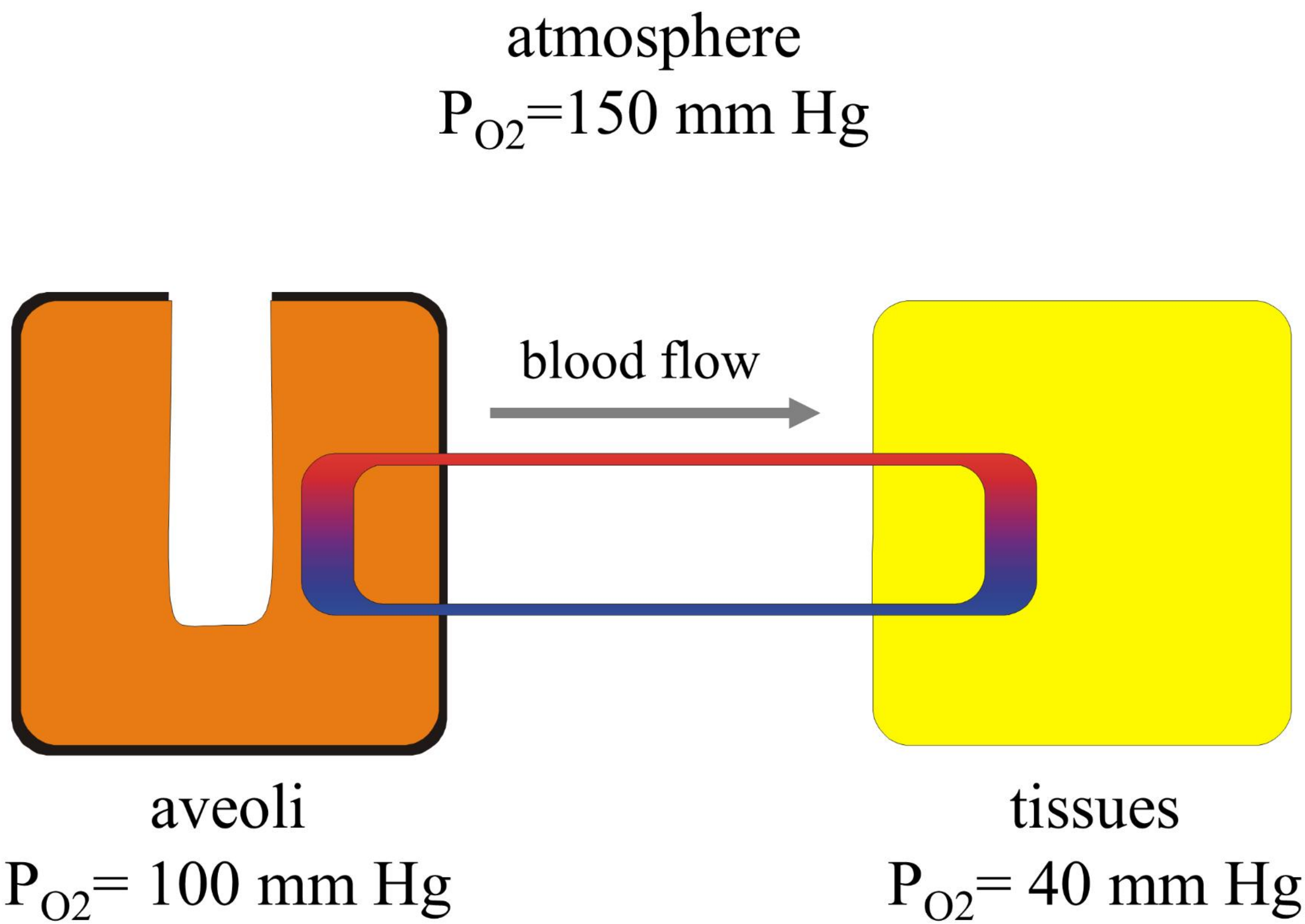
For a gas X at equilibrium between dissolved liquid and atmosphere:

$$[X] = s_x * P_x$$

s_x = solubility (conc./press.)
P_x = partial pressure (press.)

s_{O2} = 1.4E-6 M/mmHg




atmosphere
P_{O2}=150 mm Hg
blood flow
aveoli
P_{O2}= 100 mm Hg
tissues
P_{O2}= 40 mm Hg

Oxygen delivery rate

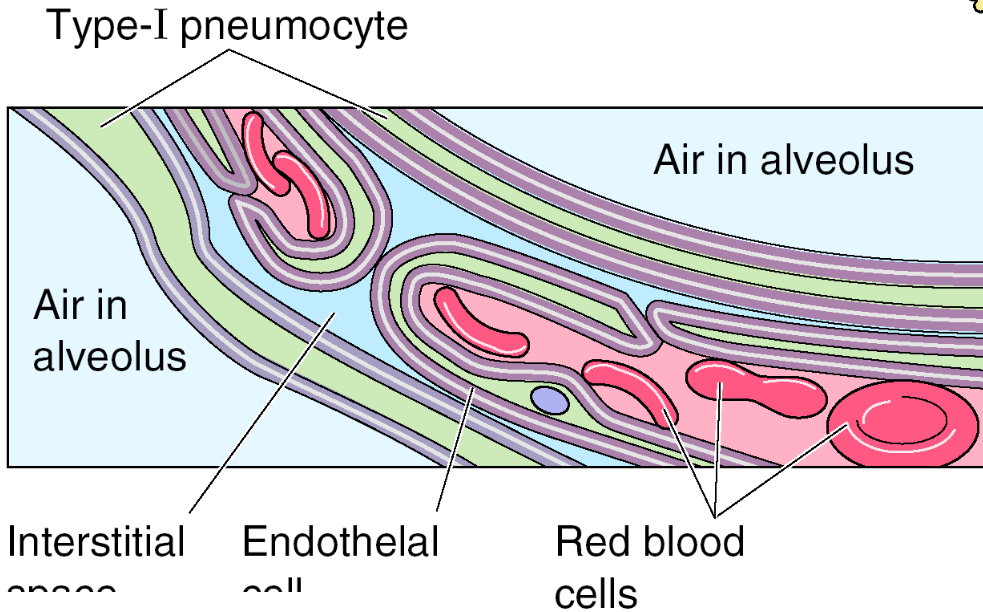
= (volumetric flow) * (oxygen delivery per volume)

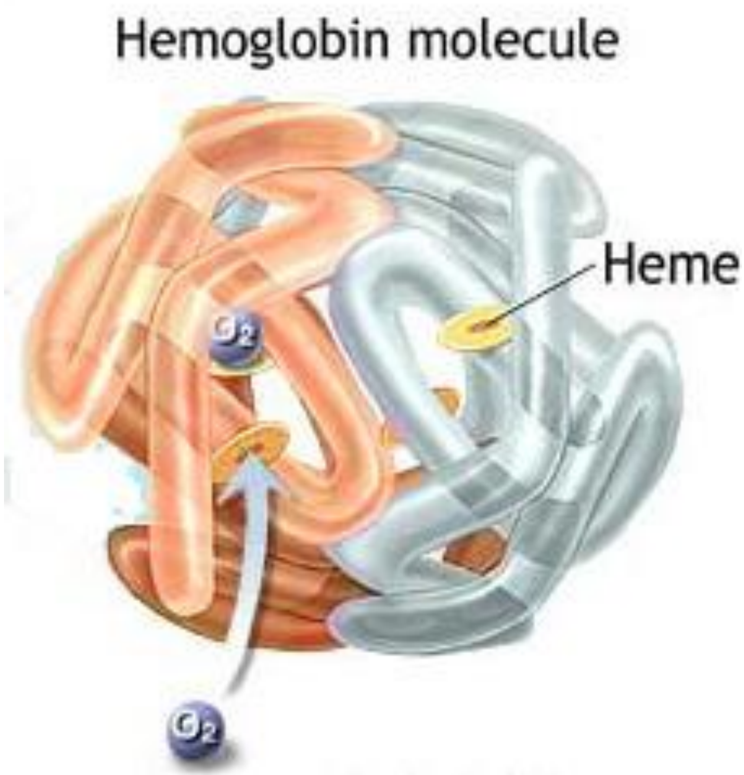
= (volumetric flow) * (solubility) * (change in pressure)

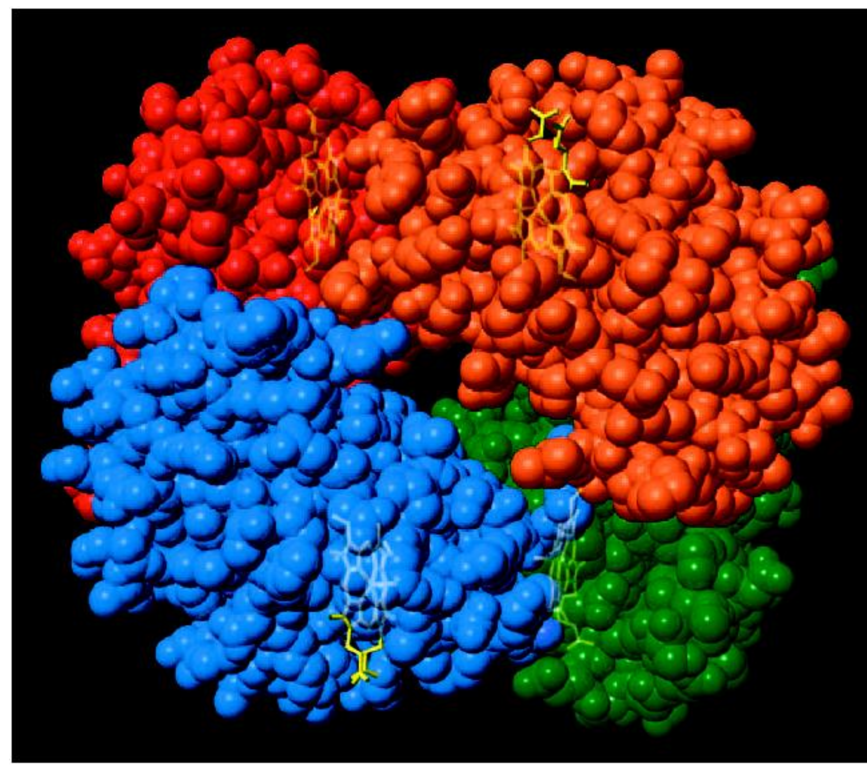
= (5 L/min) * (1.4E-6 M/mmHg) * (100 – 40 = 60 mmHg)

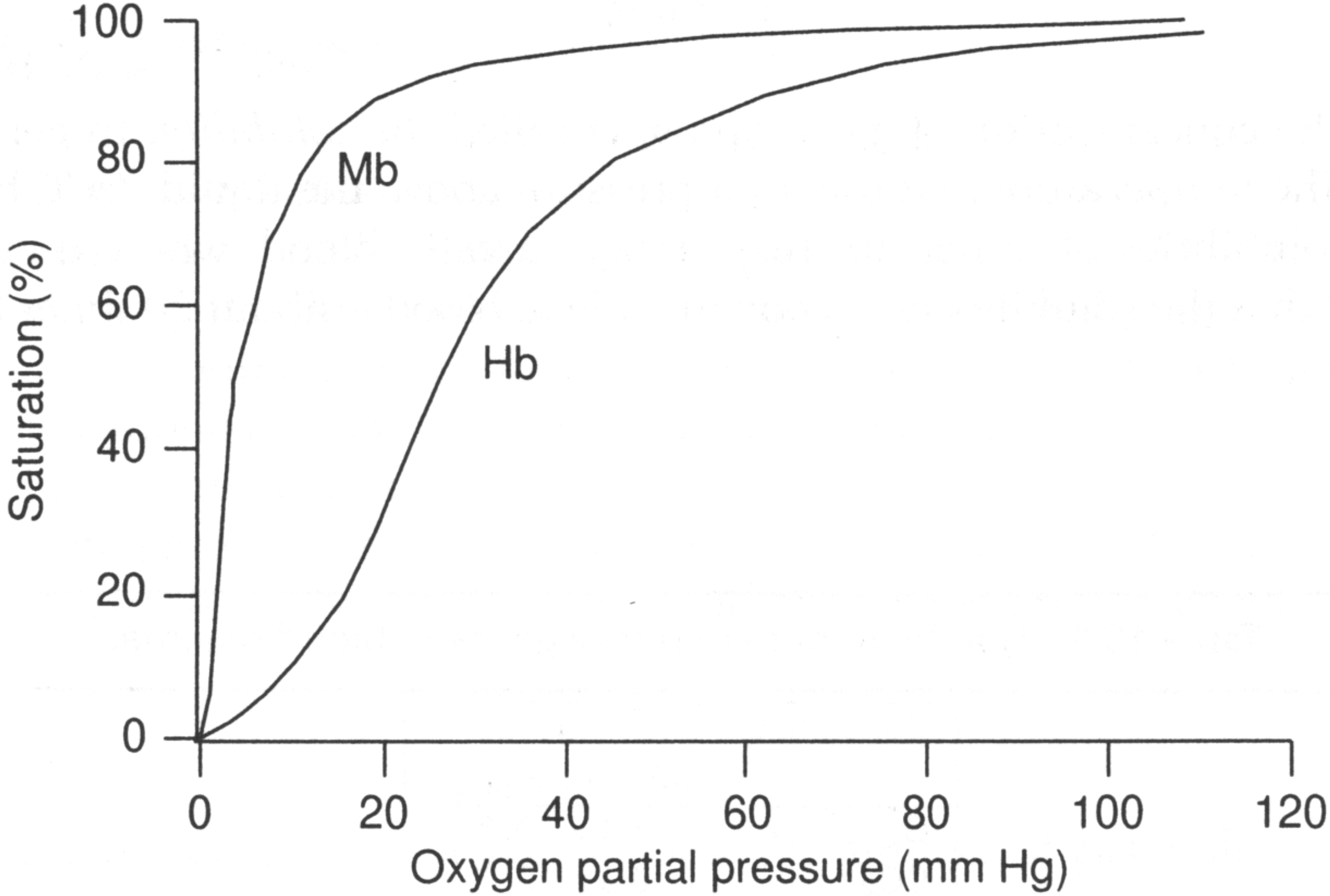
= 0.4 mmol/min

This is about 1/20 of oxygen demand


Type-I pneumocyte
Air in alveolus
Air in
alveolus
Interstitial
Endothelal
Red blood
cells


Hemoglobin molecule
Heme
O_2
O_2





100
80
60
40
20
0
Saturation (%)
Mb
Hb
0
20
40
60
80
100
120
Oxygen partial pressure (mm Hg)

Cooperative binding. One carrier with two ligands

$$S + C_0 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C_1 \qquad \frac{dc_1}{dt} = k_1 s c_0 - k_{-1} c_1 - k_2 s c_1 + k_{-2} c_2$$

$$S + C_1 \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} C_2 \qquad \frac{dc_2}{dt} = k_2 s c_1 - k_{-2} c_2$$

$$C_0 + C_1 + C_2 = C_T \qquad c_0 + c_1 + c_2 = c_T$$

$$c_1 = \frac{K_2 c_T s}{K_1 K_2 + K_2 s + s^2}$$

$$c_2 = \frac{c_T s^2}{K_1 K_2 + K_2 s + s^2} \qquad \text{Ligands} = 0 * c_0 + c_1 + 2c_2 = \frac{(K_2 + 2s) c_T s}{K_1 K_2 + K_2 s + s^2}$$

$$K_1 = \frac{k_{-1}}{k_1}; K_2 = \frac{k_{-2}}{k_2}$$

Independent binding sites, no cooperativity

$$c_1 = \frac{K_2 c_T s}{K_1 K_2 + K_2 s + s^2}$$

$$c_2 = \frac{c_T s^2}{K_1 K_2 + K_2 s + s^2}$$

$$\text{Ligands} = 0 * c_0 + c_1 + 2c_2 = \frac{(K_2 + 2s) c_T s}{K_1 K_2 + K_2 s + s^2}$$

$$K_1 = \frac{k_{-1}}{k_1}; K_2 = \frac{k_{-2}}{k_2}$$

$$K_1 = \frac{k_-}{2k_+}; K_2 = \frac{2k_-}{k_+}$$

or....

$$K = \frac{k_-}{k_+}; K_1 = K/2; K_2 = 2K$$

$k_1 = 2k_+$; $k_2 = k_+$

$k_{-1} = k_-$; $k_{-2} = 2k_-$

$$\text{Ligands} = \frac{2c_T (K + s) s}{K^2 + 2Ks + s^2} = 2\frac{c_T s}{K + s}$$

Infinite cooperativity

$$c_1 = \frac{K_2 c_T s}{K_1 K_2 + K_2 s + s^2}$$

$$c_2 = \frac{c_T s^2}{K_1 K_2 + K_2 s + s^2}$$

$$K_1 = \frac{k_{-1}}{k_1}; K_2 = \frac{k_{-2}}{k_2}$$

$$\text{Ligands} = 0 * c_0 + c_1 + 2c_2 = \frac{(K_2 + 2s) c_T s}{K_1 K_2 + K_2 s + s^2}$$

$K_1 \to \infty$, $K_2 \to 0$

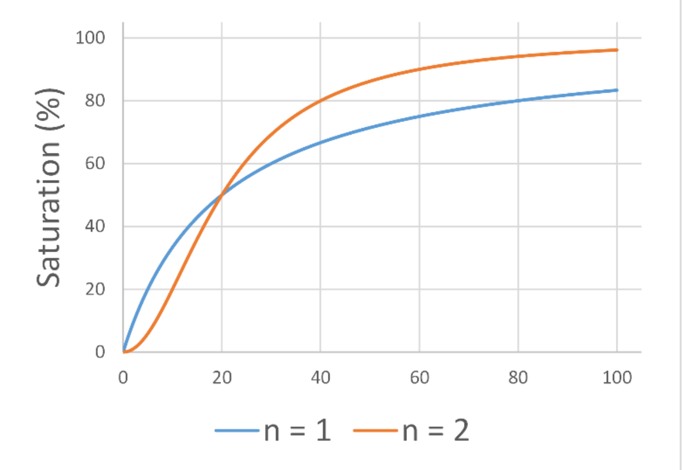
$$K_1 K_2 = \text{constant} = K_m^2$$

$$\text{Ligands} = \frac{2 c_T s^2}{K_1 K_2 + s^2} = \frac{2 c_T s^2}{K_m^2 + s^2}$$

Cooperativity and the Hill equation

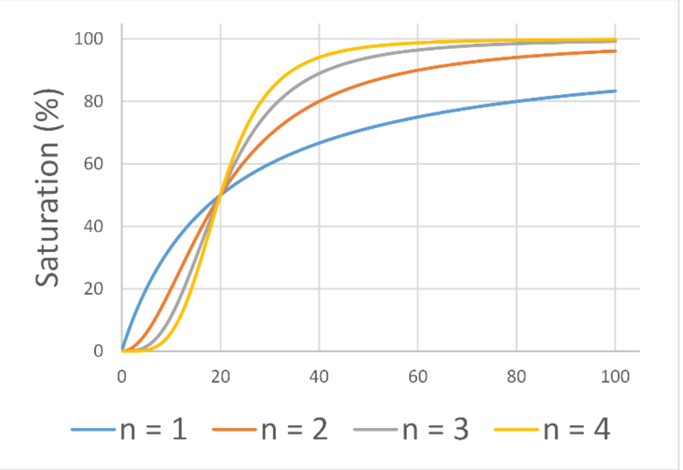
2 binding sites

	Independent sites	Infinite cooperativity
Ligands bound (concentration)	$2c_T\left(\dfrac{s}{K_M + s}\right)$	$2c_T\left(\dfrac{s^2}{K_M^2 + s^2}\right)$



m binding sites

	Independent sites	Infinite cooperativity
Ligands bound (concentration)	$mc_T\left(\dfrac{s}{K_M + s}\right)$	$mc_T\left(\dfrac{s^m}{K_M^m + s^m}\right)$

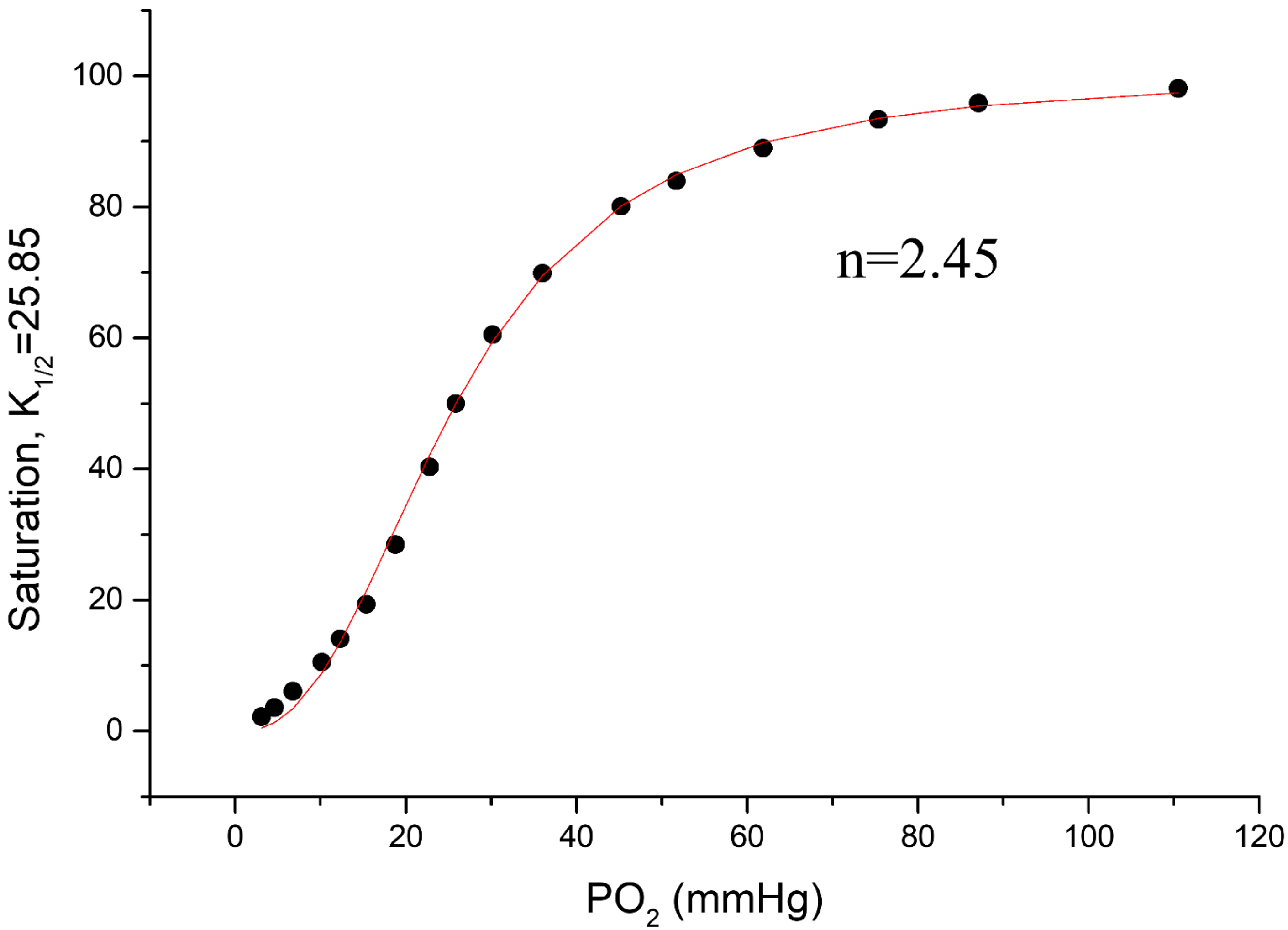


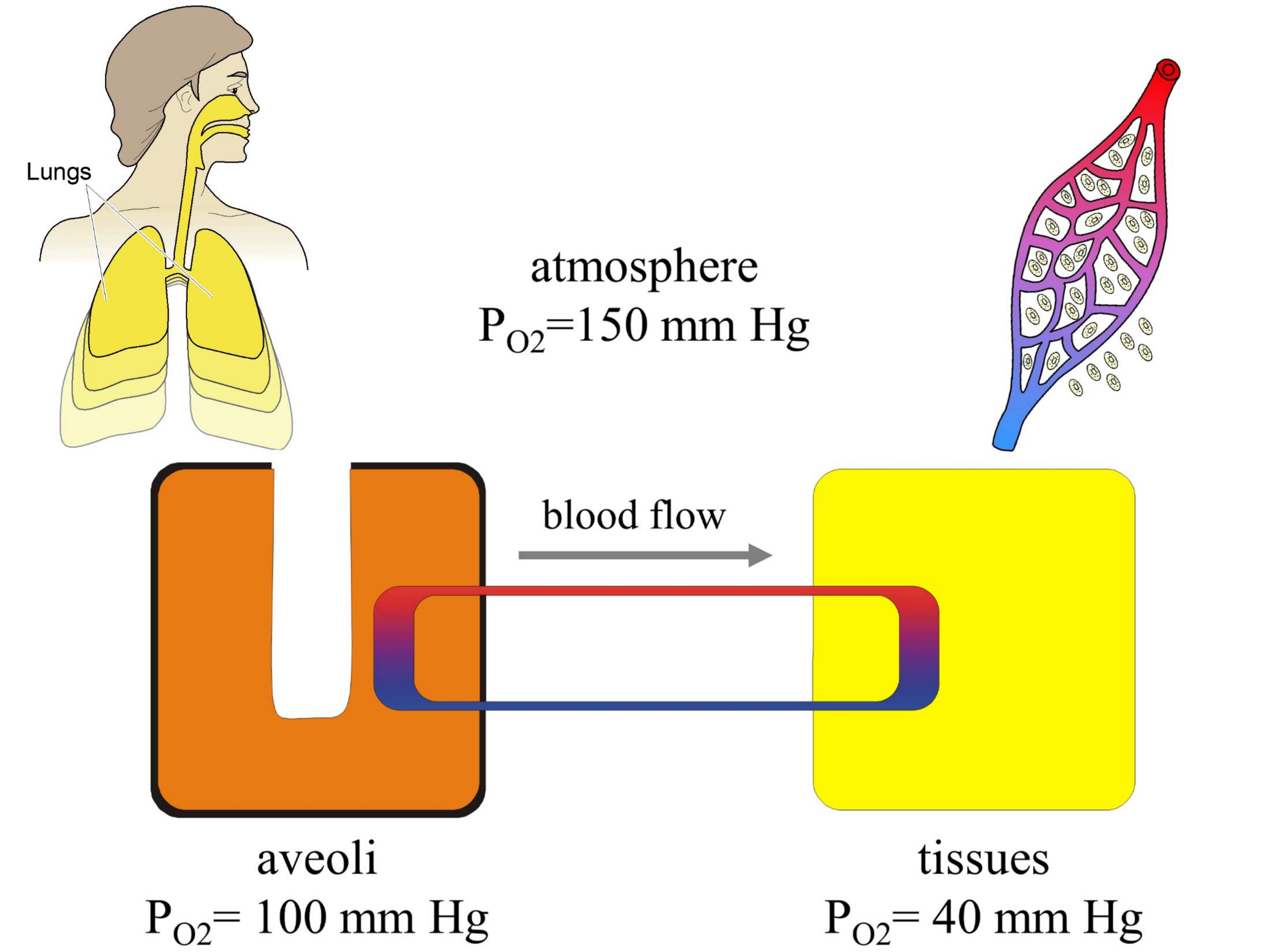
Hill equation

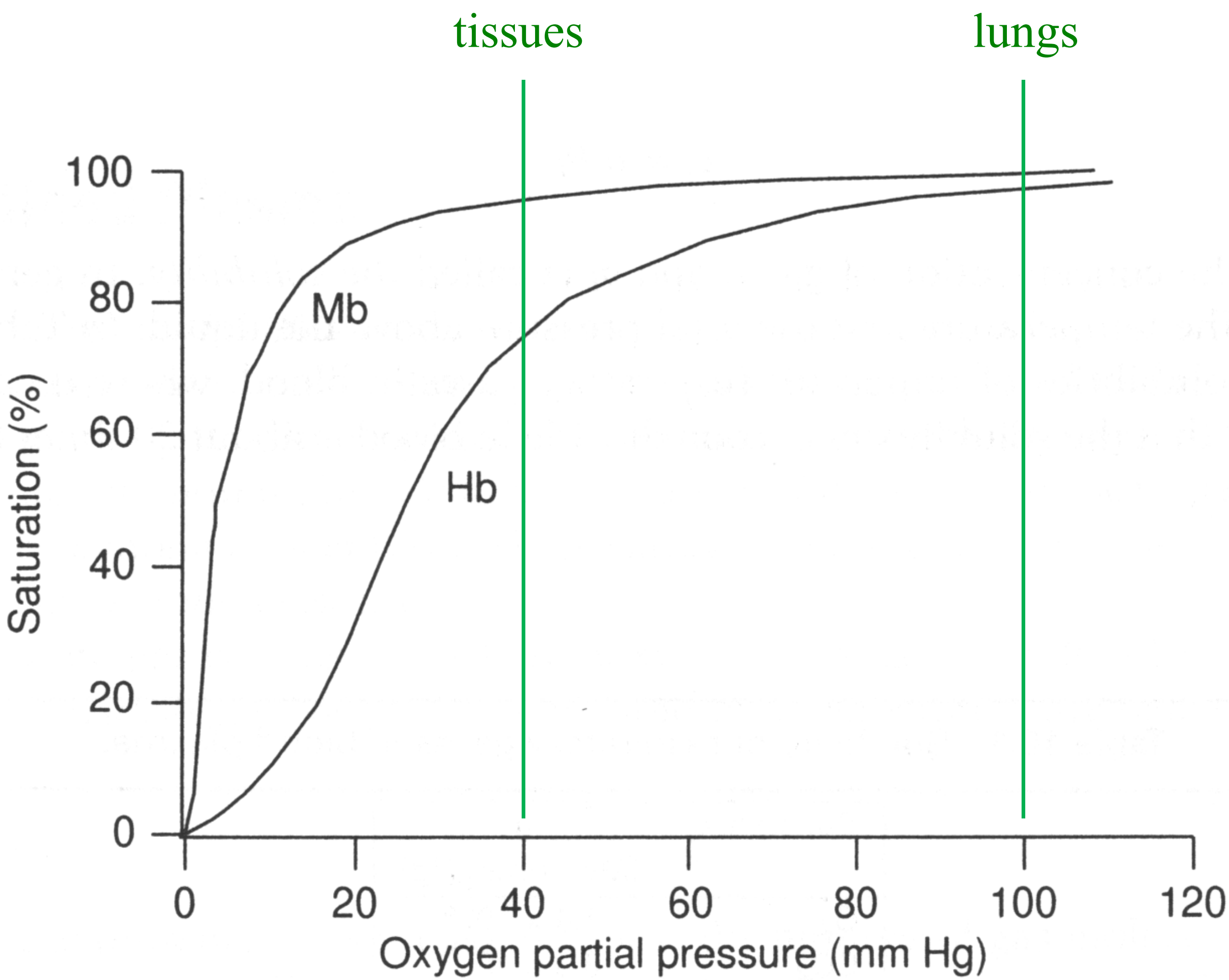
- m = binding sites
- n = Hill coefficient
  - n > 1 positive cooperativity
  - n < 1 negative cooperativity

$$\text{Ligands bound (concentration)} = mc_T\left(\frac{s^n}{K_M^n + s^n}\right)$$

Hemoglobin – Hill model




Lungs
atmosphere
P_{O2}=150 mm Hg
blood flow
aveoli
P_{O2}= 100 mm Hg
tissues
P_{O2}= 40 mm Hg

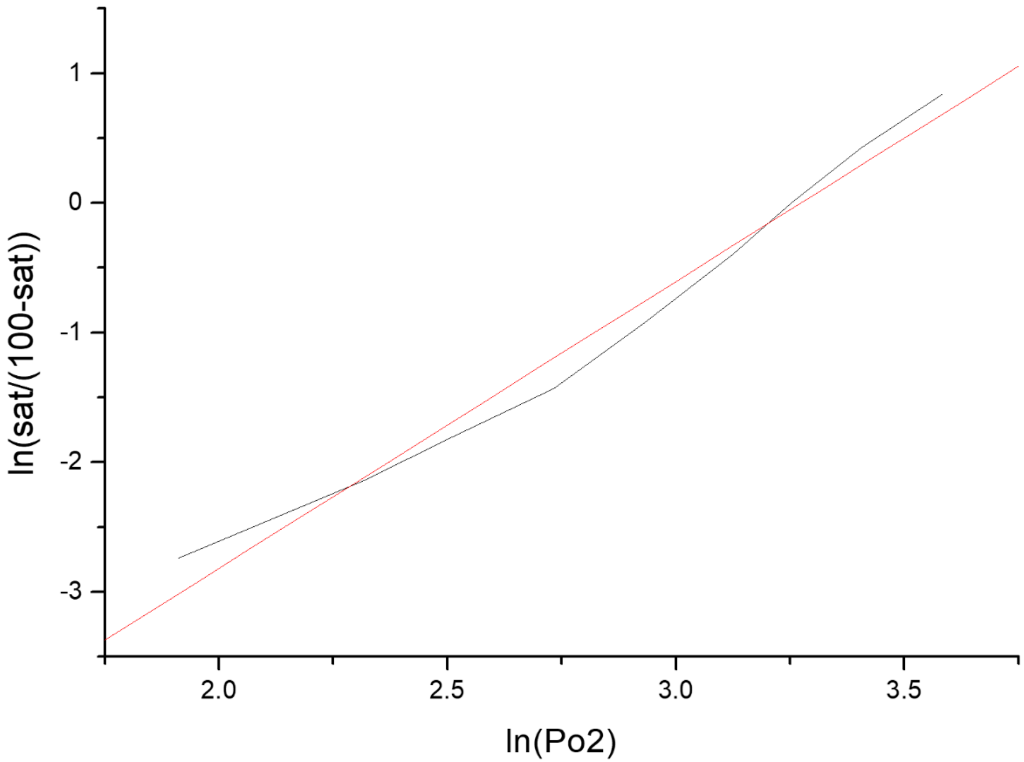

tissues
lungs
100
80
60
40
20
0
Saturation (%)
Mb
Hb
0
20
40
60
80
100
120
Oxygen partial pressure (mm Hg)

Hemoglobin – Hill plot

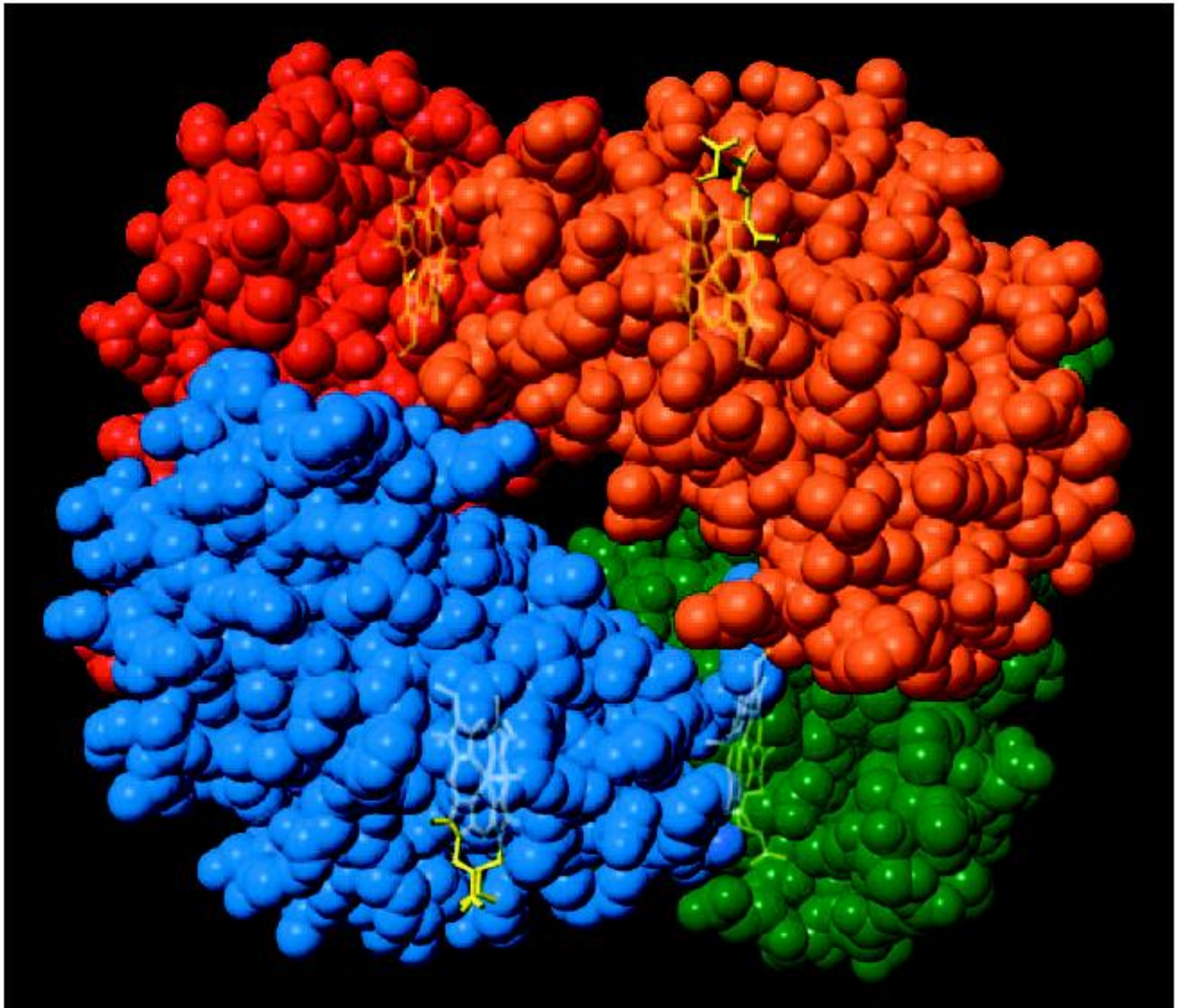
$$\text{Ligands} = (m * c_T) * \frac{s^n}{K_m^n + s^n}$$

$$\text{Saturation} = \frac{s^n}{K_m^n + s^n}$$

- plot ln(L/(Lmax-L)) vs ln(s)
- should be a straight line of slope n.

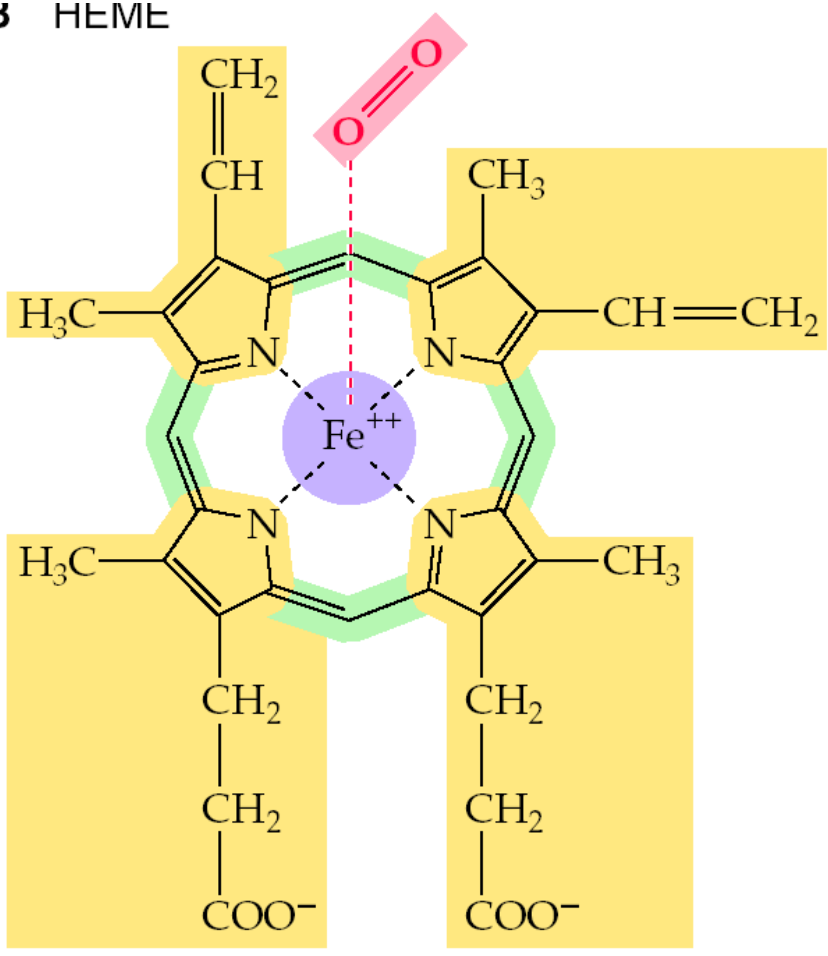


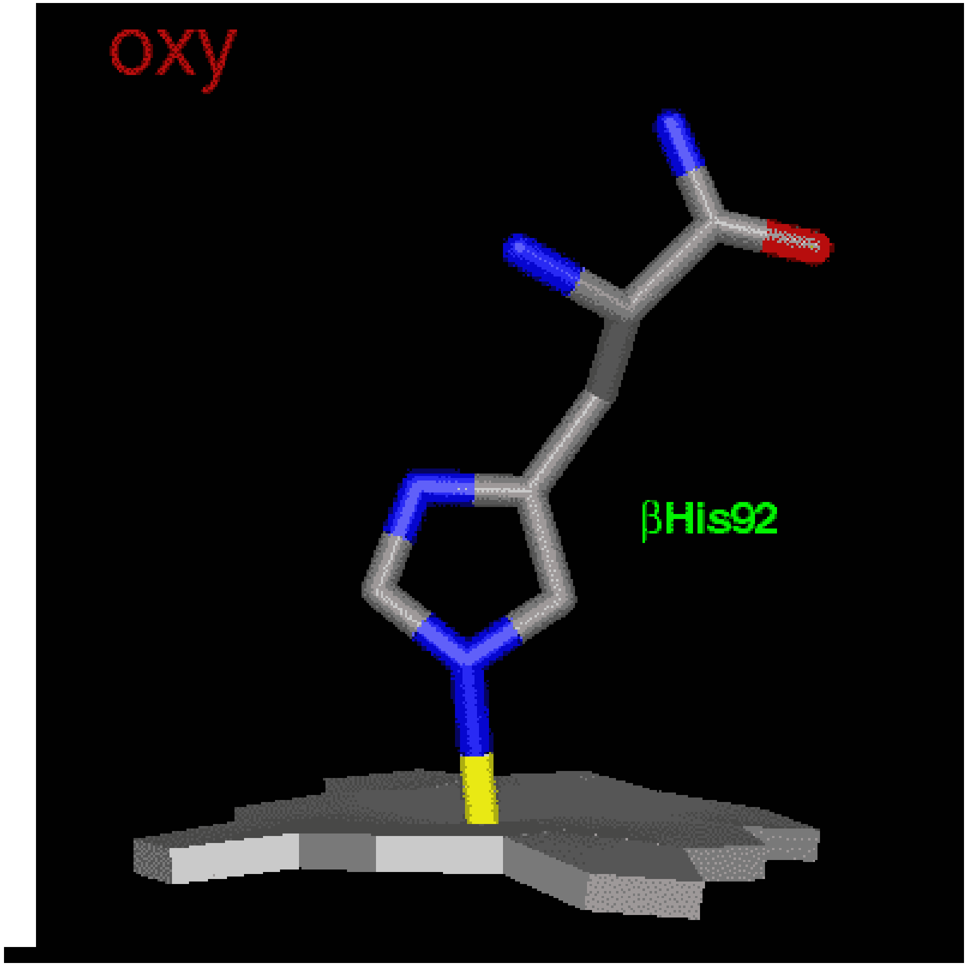
Hemoglobin



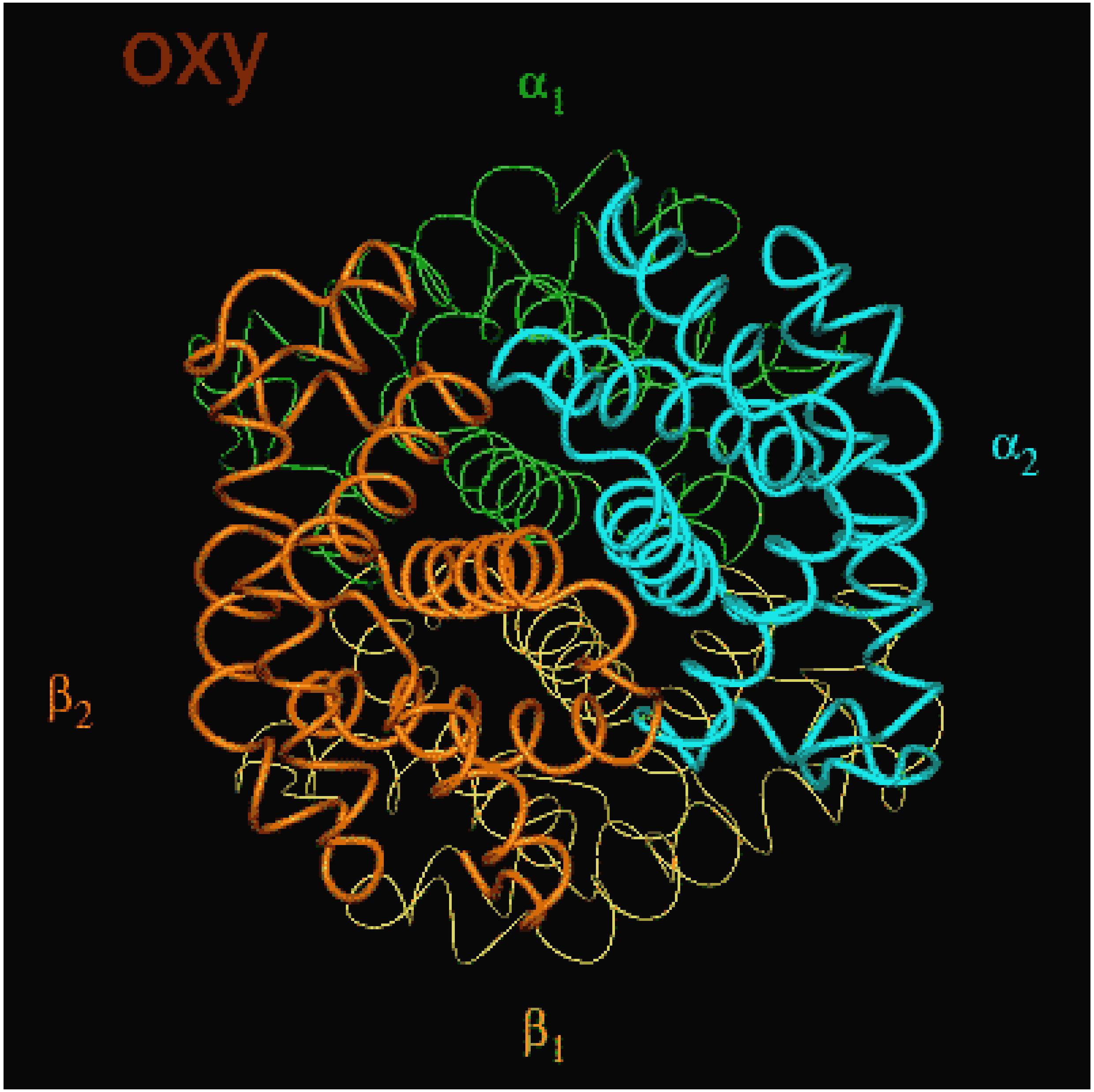
Heme response

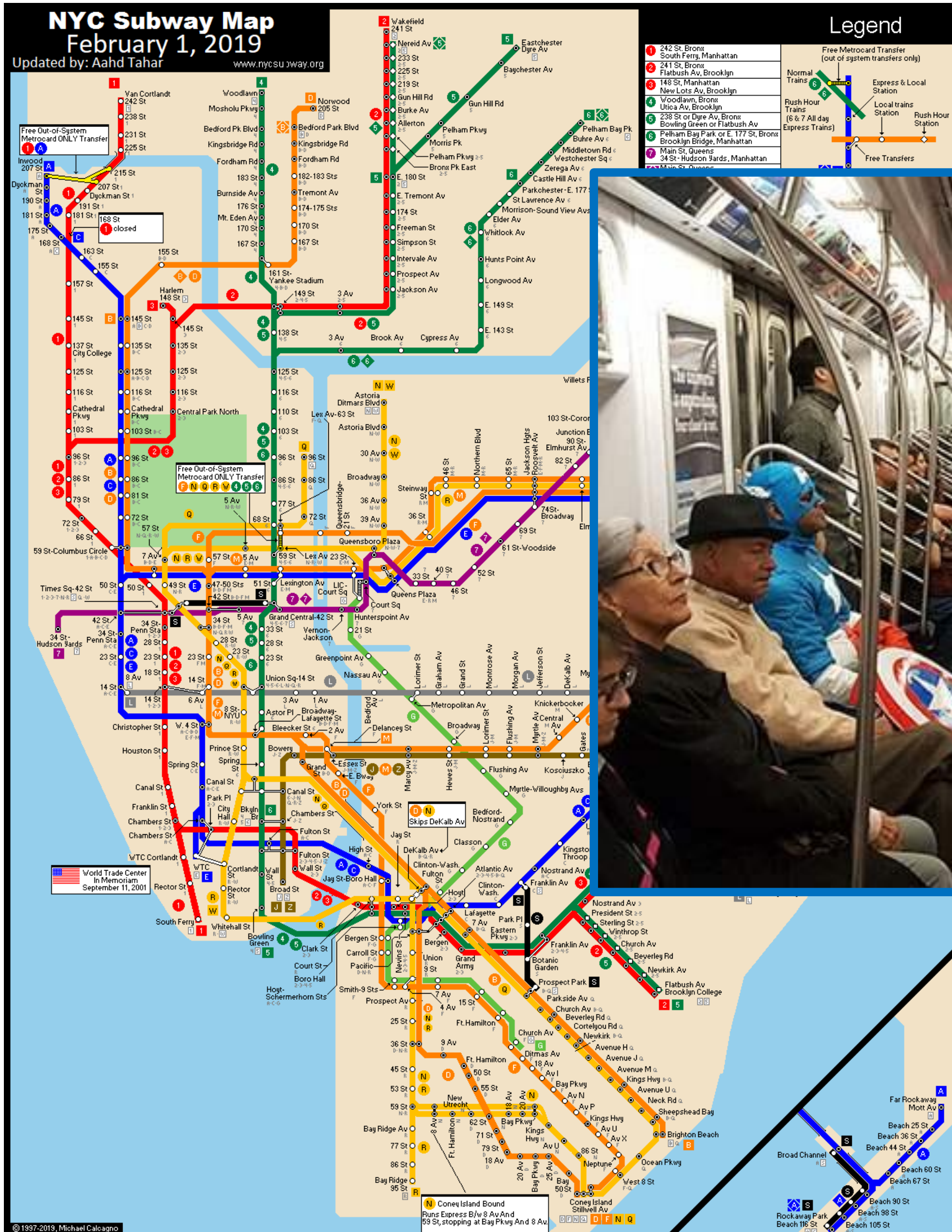
B HEME





Protein response

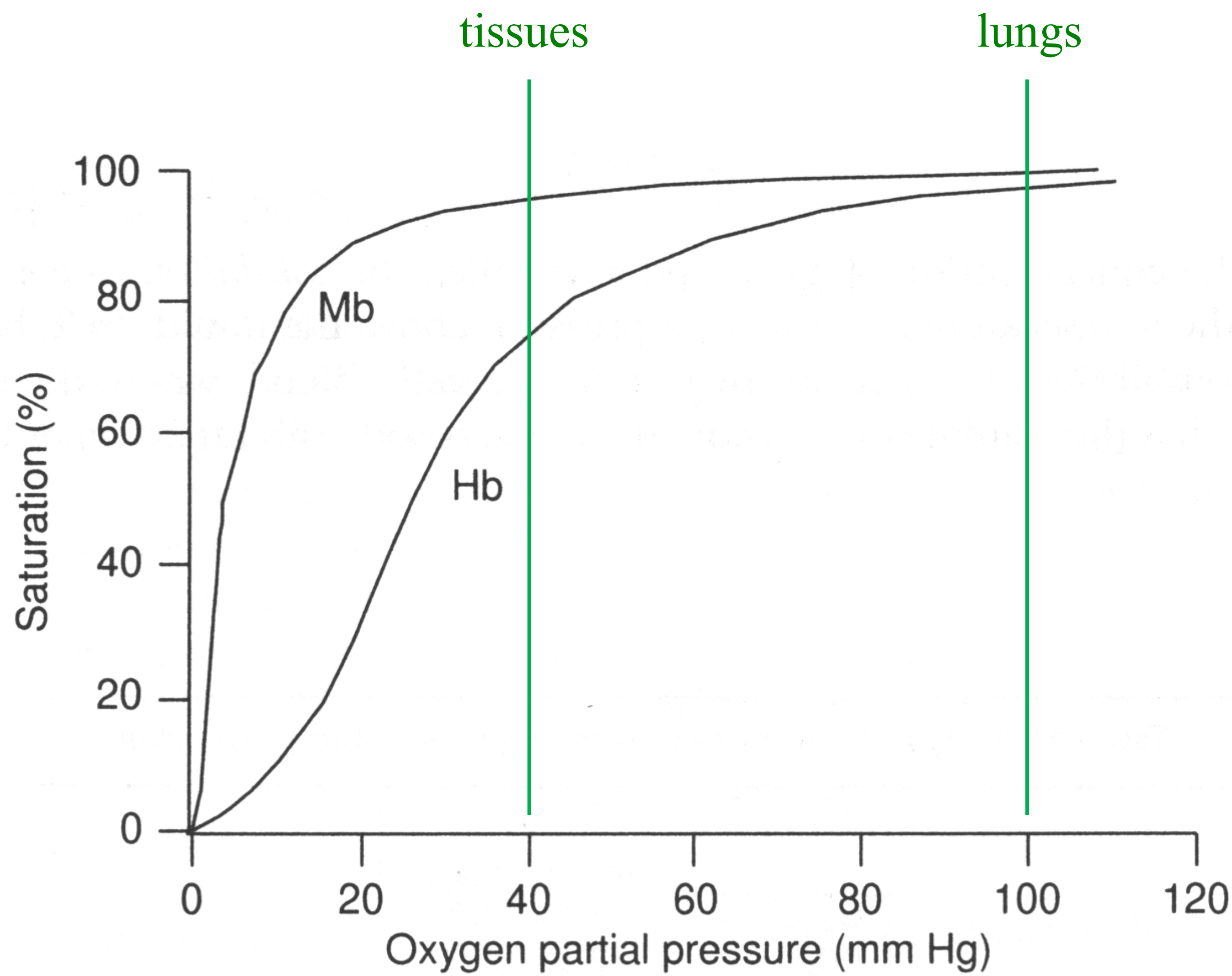




ere

tissues

$P_{O2} = 40$ mm Hg



tissues
lungs
100
80
60
40
20
0
Saturation (%)
Mb
Hb
0
20
40
60
80
100
120
Oxygen partial pressure (mm Hg)

CO_2 transport

- A problem similar to that posed for oxygen transport exists for carbon dioxide - dissoved gas is not enough.
- Carbon dioxide uses an additional mechanism:

$$CO_2 + H_2O \xleftrightarrow{slow} \underset{\text{(carbonic acid)}}{H_2CO_3} \xleftrightarrow{fast} \underset{\text{(bicarbonate)}}{HCO_3^-} + H^+$$

- About 90% of CO_2 is bound up in this manner
- The slow reaction is accelerated by enzymes, carbonic anhydrases.
- This transport comes at the introduction / manipulation of H^+; affects pH

CO_2 transport

$$pH=-\log([H^+])$$

Solution	**pH**
gastric secretions	0.7
Soda	2
Cytosol of a cell	7.2
Pancreatic fluid	8.1

Buffers

$$\mathrm{HA} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{H}^+ + \mathrm{A}^-$$

$$Ka = \frac{[H^+][A^-]}{[HA]} = \frac{k_1}{k_{-1}} = \text{dissociation constant}$$

$$pH = pKa + \log\left(\frac{[A^-]}{[HA]}\right)$$

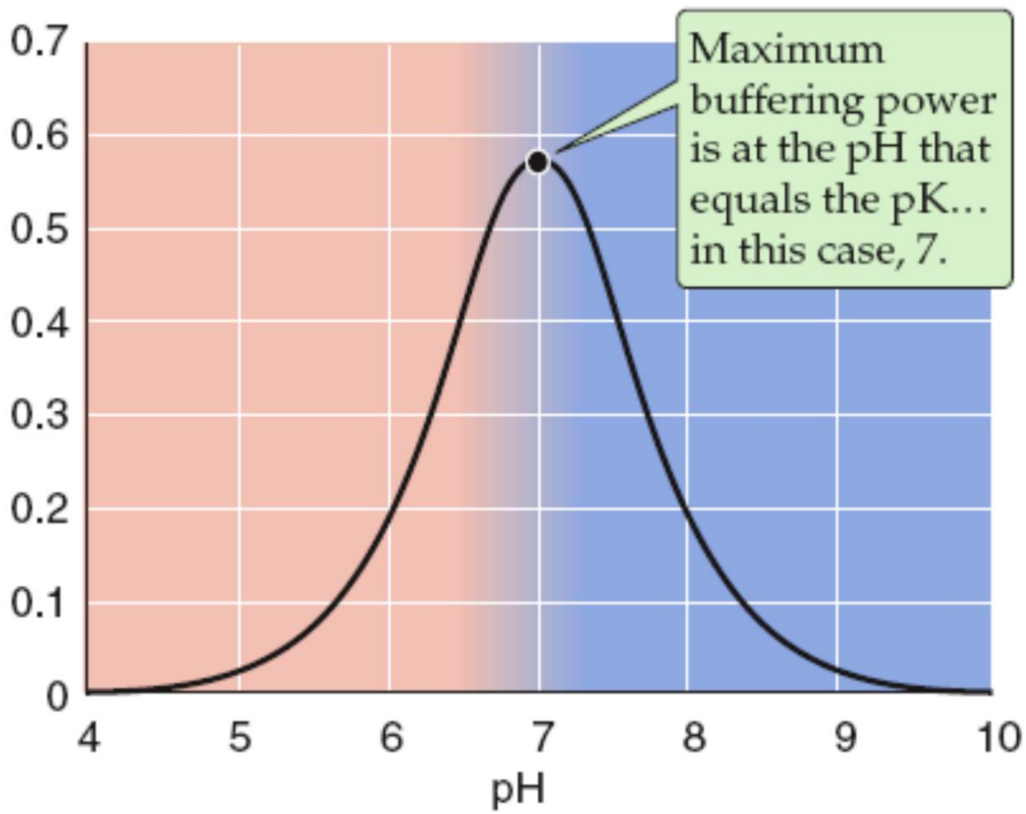
- Buffer Strength

$$\beta \equiv \frac{\Delta\,\text{strong base}}{\Delta \mathrm{pH}} = -\frac{\Delta\left|\text{strong acid}\right|}{\Delta \mathrm{pH}}$$

Buffer strength

- Closed system:

$$\beta_{closed} = 2.3[\mathrm{A}]_0 \frac{[H^+] * Ka}{([H^+] + Ka)^2}$$

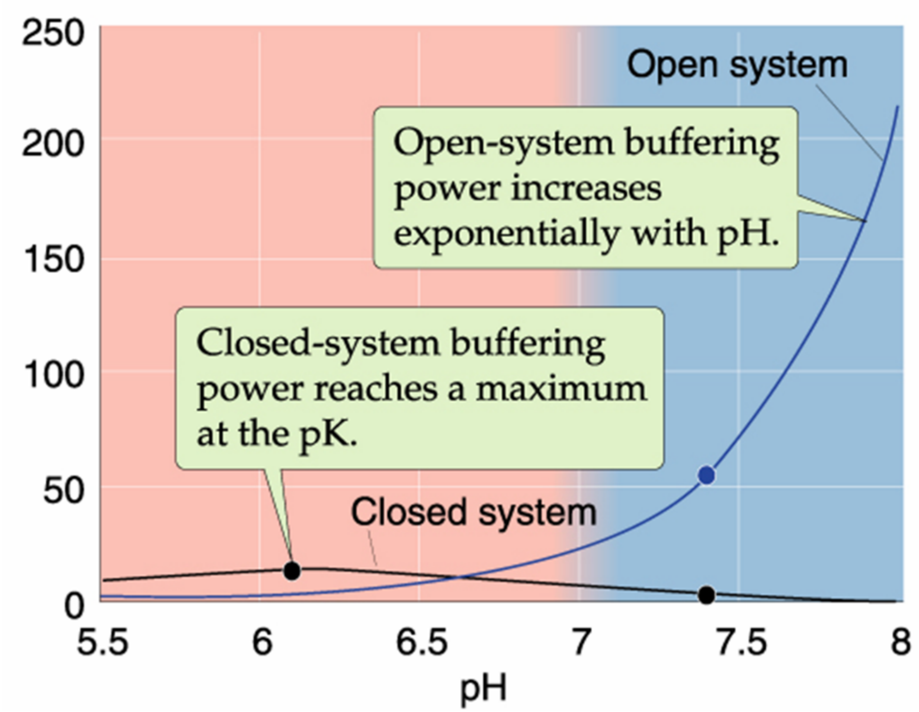


Buffer strength

- Bicarbonate open system
  - CO_2 exchanges with environment. If more is needed, it gets drawn from air. If some is created, it gets sunk into environment

$$CO_2 + H_2O \longleftrightarrow \underset{\text{(bicarbonate)}}{HCO_3^-} + H^+$$

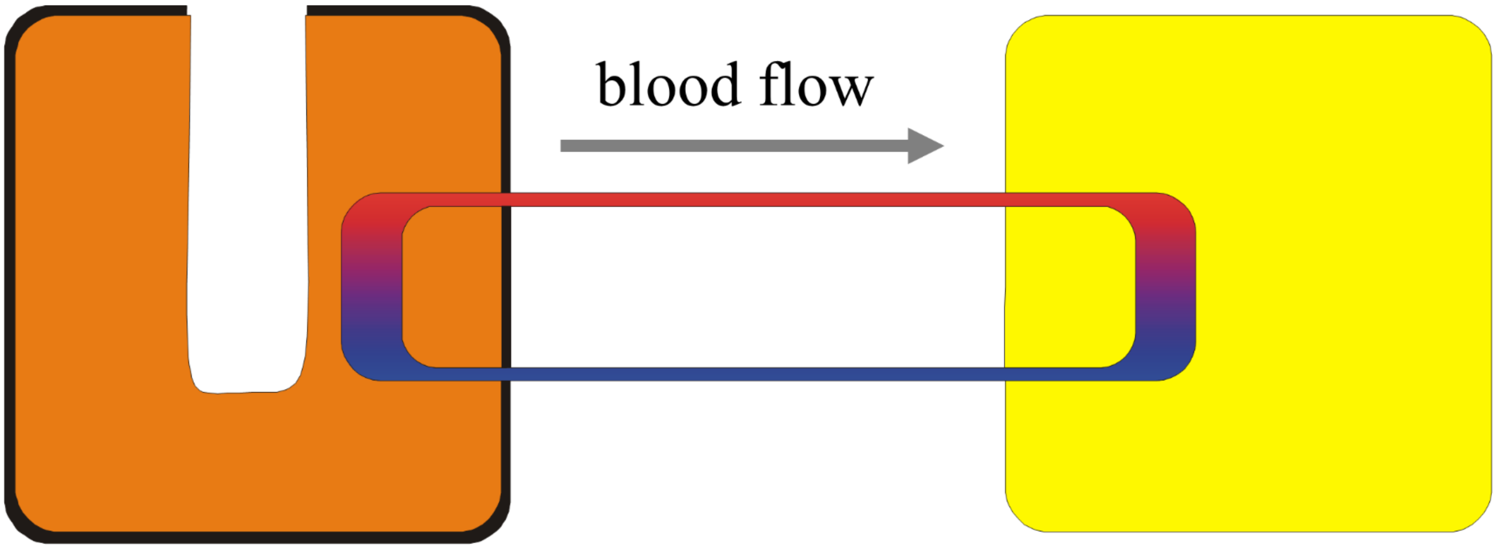
$$\beta_{open} = 2.3 * [HCO_3^-]$$



atmosphere

P_{O2}=150 mm Hg

P_{CO2}<1 mm Hg



aveoli

P_{O2}= 100 mm Hg

P_{CO2} = 40 mm Hg

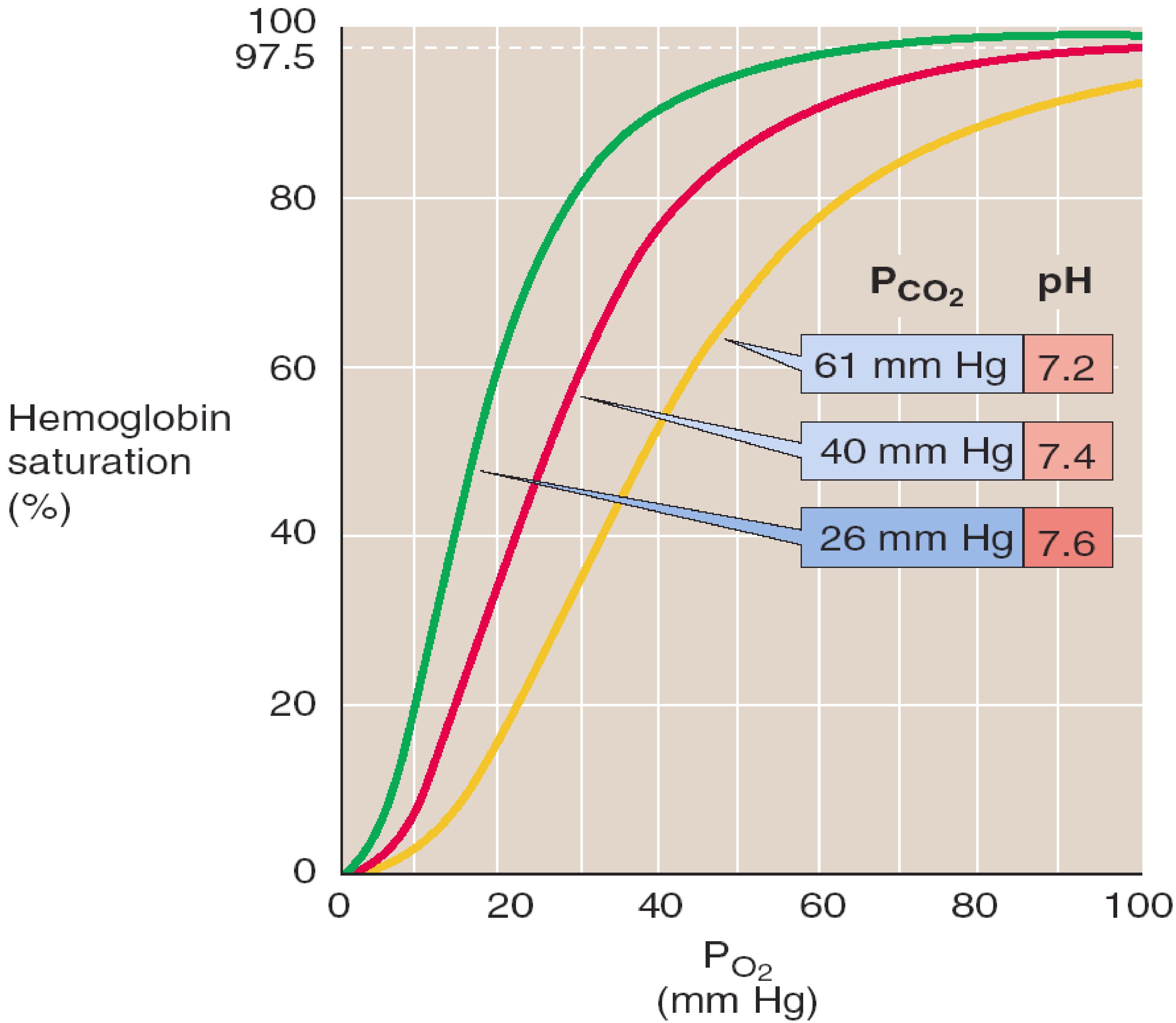
tissues

P_{O2}= 40 mm Hg

P_{CO2} = 46 mm Hg

s_{CO2} = 3.3E-5 M/mmHg

Bohr effect – response to pH



Response to CO_2