Please use in room 153. You may borrow for up to 1 hour for copying. Thanks AR

Key

Additional Problems: Oxygen Transport

1) $Y = \frac{pO_2^n}{pO_2^n + P_{50}^n}$ $n = 1$, $P_{50} = 1.00$ torr, $pO_2 = 2.43$ torr

or $pO_2 = 5.5$ torr

$Y = \frac{2.43}{2.43 + 1.00} = \underline{0.708}$ $Y = \frac{5.5}{5.5 + 1.0} = \underline{0.85}$

2) $n = 2.8$, $P_{50} = 26$ torr $pO_2 = 15.0$ torr or 87.5 torr

$Y = (15.0)^{2.8} / (15.0)^{2.8} + (26)^{2.8}$ | $Y = (87.5)^{2.8} / (87.5)^{2.8} + (26)^{2.8}$

$Y = \underline{0.18}$ | $Y = \underline{0.97}$

3) a) $\Delta Y = Y_{lungs} - Y_{tissues} = \frac{100^{2.8}}{100^{2.8} + 26^{2.8}} - \frac{20^{2.8}}{20^{2.8} - 26^{2.8}} =$

$= 0.98 - 0.32 = \underline{\underline{0.66}}$

b) ~~100 molecule~~ of Hb is 400 subunits or 400 O_2-binding sites. On average, 98% of these sites will fill in the lungs, + only 32% will remain filled after passing through tissues. So the capacity to deliver O_2 is 66% of the number of carrier sites: $400 \times .66 = 264$ O_2 molecules.

264 mmole O_2 delivered per 100 mmole Hb tetramer.

4. a) noncooperative ⇒ $n = 1$ $\Delta Y = \frac{100}{100 + 26} - \frac{20}{20 + 26} = \underline{0.35}$*

b) Mutations at subunit interfaces might affect cooperativity. But because of the complexity of the cooperative mechanism, it's hard to rule out other sites. Probably not surface residues or heme-binding residues

*transport reduced by about half

5. a) $n = 2.8$ $P_{50} = 10$ torr

$$\Delta Y = \frac{100^{2.8}}{100^{2.8} + 10^{2.8}} - \frac{20^{2.8}}{20^{2.8} - 10^{2.8}} = 0.99 - 0.87 = \underline{0.12}$$

(transport reduced by about 80%)

b) Mutation at BPG binding site might lower affinity for BPG, thus lowering P_{50}.

6. See next page

6. a) $Y_A = \frac{a}{a+P_{50}}$ $\quad Y_B = \frac{b}{b+P_{50}}$ $\quad$ Let $P = P_{50}$ (to save writing)

$$\Delta Y = \frac{a}{a+P} - \frac{b}{b+P} = \frac{a(b+P) - b(a+P)}{(a+P)(b+P)}$$

now, simplify:

$$\Delta Y = \frac{\cancel{ab} + aP - \cancel{ab} - bP}{ab + aP + bP + P^2} = \frac{P(a-b)}{P^2 + P(a+b) + ab}$$

take derivative with respect to P. (a and b are constants) ☆

$$\frac{d\,\Delta Y}{dP} = \frac{(P^2 + P(a+b) + ab)(a-b) - P(a-b)(2P + a + b)}{(P^2 + P(a+b) + ab)^2}$$

If $\frac{x}{y} = 0$ then $x = 0$, so $\frac{d\,\Delta Y}{dP} = 0$ if the numerator $= 0$.

$$(a-b)\left[P^2 + P(a+b) + ab - 2P^2 - aP - bP\right] = 0$$

if $a \neq b$, then $a - b \neq 0$, so term in brackets $= 0$. (If $a = b$, no net transport anyway.)

$$P^2 + \cancel{P(a+b)} + ab - 2P^2 - \cancel{P(a+b)} = 0$$

or $\quad -P^2 + ab = 0$

or $\quad P^2 = ab \quad P = \sqrt{ab}$.

b) For lungs-to-tissues, $a = 100$, $b = 20$.,

$P = \sqrt{100 \cdot 20} = 45$

The P_{50} of Hb may be a compromise between what is optimal for 100 torr-to-20-torr transport + other functions, such as response to pH change.

☆ Because $\frac{d}{dx}\left(\frac{f(x)}{g(x)}\right) = \frac{g(x)\frac{d}{dx}(f(x)) + f(x)\frac{d}{dx}(g(x))}{(g(x))^2}$