CONCEPT: HILL EQUATION

Cooperative Ligand-Binding in Allosteric Proteins

●In 1913, before any knowledge Hb's structure existed, Archibald _____ studied Hb's cooperative O_2-binding.

●Recall: *Coefficients* in a reaction (#'s in *front* of molecules) are included into K_d as _____.

●From this, it *SEEMS* that for proteins with an "*n*" number of **L**-binding sites, the PL-reaction & equations for K_d & θ will be:

$$P + \_\_L \rightleftharpoons PL\_\_$$

$$K_d = \frac{[P][L]^{\_\_}}{[PL\_\_]}$$

$$\theta = Y = \frac{[L]^{\_\_}}{[L]^{\_\_} + K_d^{\_\_}}$$

n = # of **L**-binding sites on a protein.

The Hill Equation

●The equation above for θ can be algebraically rearranged & reformatted to get the _____ *Equation*.

□ This algebraically rearranged *Hill Equation* resembles the equation of a _____ (y = mx + b).

□ *Hill Equation* allows for the graphing of **PL**-Binding data on a *linear* plot called the *Hill* _____.

Equation of a Line: $y = mX + b$

Hill Equation: $\log\left(\frac{\theta}{1-\theta}\right) = n \log([\ \ ]) - n \log(\ \ )$

Hill Constant (n_H) & Cooperativity

●Contrary to what it *SEEMS*, experimental data shows the equations above must replace "n" with the _____ *constant* (n_H).

□ *Hill constant* or *Hill coefficient* (n_H): the *degree of* _____ of a **L**-binding reaction.

□ A protein's *affinity* for its ligand (K_d) is affected by *cooperativity* and therefore the Hill constant (n_H).

□ n_H is ALWAYS a value between 0 & the *maximum* number of **L**-binding sites on a protein (n): 0 ≤ _____ ≤ _____.

Hill Constant (n_H) ($0 \le n_H \le n$)	Degree of Cooperativity
n_H ____ 1	_____ cooperativity.
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CONCEPT: HILL EQUATION

When $n_H = n$

●*Hill constant* (n_H) can ONLY equal number of **L**-binding sites (n) under _____ circumstances:

1 Protein displays NO cooperativity (ex. _____). **2** Protein *ONLY* follows *Concerted Model* of cooperativity.

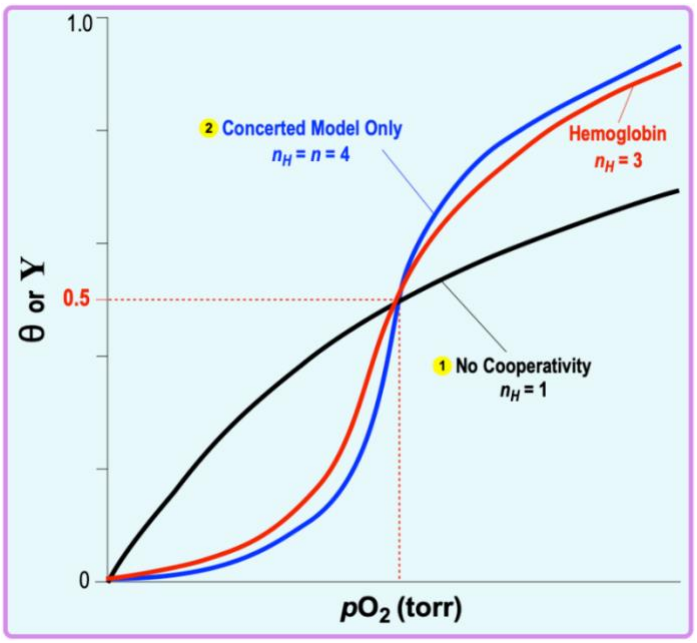
Hb's $n_H \neq$ Hb's n

●Recall: Hb's O_2-binding behavior is explained via a _____ of *concerted* & *sequential* models.

□ In its cooperative state, Hb's Hill constant ranges from 2.8 to 3 ($n_H \approx$ ____) even though it has 4 **L**-binding sites (n = 4).

EXAMPLE: Assuming Hb's K_d = 26 torr, calculate the fractional saturation of Hb at pO_2 = 100 torr & Hill coefficient (n_H) = 3.

a) 1.4
b) 0.59
c) 0.98



PRACTICE: At a CO_2 partial pressure of 5 torr, the p_{50} value for hemoglobin is 26 torr. What is the fractional saturation when n_H = 3 and pO_2 = 25 torr, a typical venous oxygen partial pressure?

d) 1.1 c) 0.12 e) 0.47
e) 0.68 d) 0.88

PRACTICE: What is Hb's fractional saturation when p_{50} = 26 torr, n_H = 3, and pO_2 = 100 torr, a typical pO_2 in the lungs?

a) 0.65 c) 0.89 e) 0.33
b) 1.6 d) 0.98