Goal: Derive average fractional occupancy assuming a non-cooperative model. Then derive the fractional occupancy assuming a simple cooperative model.

If we set up the hemoglobin so that we can exchange particles between the system and reservoir, the Boltzmann Factor becomes the Gibbs Factor.

$$e^{-\beta(E(s)-\mu N_s)}; \ \beta = \frac{1}{kT}$$

Where E is the energy of the system, defined by:

$$E = \varepsilon \sum_{\alpha=1}^{4} \sigma_\alpha$$

N_s is the number of particles in the state, and μ is the chemical potential. Then we can use the Grand Partition Function:

$$\mathcal{Z} = \sum_s e^{-\beta(E(s)-\mu N_s)}$$

Which implies the probability of the state denoted by $P(s)$ is:

$$P(s) = \frac{1}{\mathcal{Z}} e^{-\beta(E(s)-\mu N_s)}$$

Then the average fractional occupancy can be defined as follows:

$$\langle N \rangle = \sum_s (N_s)(P(s)) = \sum_s N_s \frac{e^{-\beta(E(s)-\mu N_s)}}{\mathcal{Z}}$$

Note that:
$$\frac{1}{\beta}\frac{\partial}{\partial\mu}[\ln \mathcal{Z}] = \frac{1}{\beta}\frac{1}{\mathcal{Z}}\frac{\partial\mathcal{Z}}{\partial\mu} = \langle N \rangle$$

So:
$$\langle N \rangle = \frac{1}{\beta}\frac{\partial}{\partial\mu}\ln \mathcal{Z}$$

The binding sites of hemoglobin has the following states, if we assume a non-cooperative model:

# Binding Sites	# Configurations	Configuration Notation
0	1	E
1	4	O_1, O_2, O_3, O_4
2	6	$T_1, T_2, T_3, T_4, T_5, T_6$
3	4	H_1, H_2, H_3, H_4
4	1	F

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If we assume a non-cooperative model, then we only need to look at the states individually using the Grand Partition Function $\mathcal{Z}$ (split on two lines for readability):

$$\mathcal{Z} = \sum_s e^{-\beta(E(s)-\mu N_s)}$$

$$\mathcal{Z} = e^{-\beta\left(E(\overline{E})-\mu N_{\overline{E}}\right)} + \sum_{i=1}^{4} e^{-\beta\left(E(\overline{O_i})-\mu N_{\overline{O_i}}\right)} + \sum_{i=1}^{6} e^{-\beta\left(E(\overline{T_i})-\mu N_{\overline{T_i}}\right)}$$

$$+ \sum_{i=1}^{4} e^{-\beta\left(E(\overline{H_i})-\mu N_{\overline{H_i}}\right)} + e^{-\beta\left(E(\overline{F})-\mu N_{\overline{F}}\right)}$$

However, we know the values of $E(s)$ and N_s.

State	$E(s)$	N_s
E	0	0
O	1	1
T	2	2
H	3	3
F	4	4

This means if we call the energy of the system ε, then State $E(\overline{T}) = 2\varepsilon$, for example. So we can simplify $\mathcal{Z}$ to:

$$\mathcal{Z} = 1 + 4e^{-\beta(\varepsilon-\mu)} + 6e^{-2\beta(\varepsilon-\mu)} + 4e^{-3\beta(\varepsilon-\mu)} + e^{-4\beta(\varepsilon-\mu)}$$

$$\frac{\partial \mathcal{Z}}{\partial \mu} = \beta[4e^{-\beta(\varepsilon-\mu)} + 12e^{-2\beta(\varepsilon-\mu)} + 12e^{-3\beta(\varepsilon-\mu)} + 4e^{-4\beta(\varepsilon-\mu)}]$$

Since we're given that:

$$\langle N \rangle = \frac{1}{\beta}\frac{\partial}{\partial \mu}\ln \mathcal{Z} \Rightarrow \langle N \rangle = \frac{1}{\beta}\frac{1}{\mathcal{Z}}\frac{\partial \mathcal{Z}}{\partial \mu}$$

So:

$$\langle N \rangle = \frac{1}{\beta}\frac{\beta[4e^{-\beta(\varepsilon-\mu)} + 12e^{-2\beta(\varepsilon-\mu)} + 12e^{-3\beta(\varepsilon-\mu)} + 4e^{-4\beta(\varepsilon-\mu)}]}{1 + 4e^{-\beta(\varepsilon-\mu)} + 6e^{-2\beta(\varepsilon-\mu)} + 4e^{-3\beta(\varepsilon-\mu)} + e^{-4\beta(\varepsilon-\mu)}}$$

$$\langle N \rangle = \frac{4e^{-\beta(\varepsilon-\mu)} + 12e^{-2\beta(\varepsilon-\mu)} + 12e^{-3\beta(\varepsilon-\mu)} + 4e^{-4\beta(\varepsilon-\mu)}}{1 + 4e^{-\beta(\varepsilon-\mu)} + 6e^{-2\beta(\varepsilon-\mu)} + 4e^{-3\beta(\varepsilon-\mu)} + e^{-4\beta(\varepsilon-\mu)}}$$

Note that this equation only holds for the non-cooperative model for hemoglobin (Assuming $J = 0$). If we assume a simple cooperative model, our energy equation changes slightly. This simple model only takes into account cooperation between pairs.

$$E = \varepsilon \sum_{\alpha=1}^{4} \sigma_\alpha + \frac{J}{2} \sum_{(\alpha,\gamma)} \sigma_\alpha \sigma_\gamma$$

If we assign $E(s)$ again as we did prior, then instead of having simply $\delta\varepsilon$ for some δ, we would have some J term mixed in. We can solve for these using logic:

State	ε	J	$E(s)$
E	0	0	0
O	1	0	ε
T	2	1	$2\varepsilon + J$
H	3	3	$3\varepsilon + 3J$
F	4	6	$4\varepsilon + 6J$

This occurs since for States E and O, there are not two states occupied to have cooperation. Then we have 1 cooperation pair for two binding sites, 3 cooperation pairs for three binding sites, and 6 cooperation pairs for four binding sites.

Once again, we can use the Grand Partition Function.

$$\mathcal{Z} = 1 + 4e^{-\beta(\varepsilon-\mu)} + 6e^{-\beta(2\varepsilon-2\mu+J)} + 4e^{-\beta(3\varepsilon-3\mu+3J)} + e^{-\beta(4\varepsilon-4\mu+6J)}$$

$$\mathcal{Z} = 1 + 4e^{-\beta(\varepsilon-\mu)} + 6e^{-2\beta(\varepsilon-\mu)-\beta J} + 4e^{-3\beta(\varepsilon-\mu)-3\beta J} + e^{-4\beta(\varepsilon-\mu)-6\beta J}$$

Once again, we can use the equation for $\langle N \rangle$ and solve:

$$\langle N \rangle = \frac{1}{\beta}\frac{1}{\mathcal{Z}}\frac{\partial \mathcal{Z}}{\partial \mu}$$

$$\langle N \rangle = \frac{4e^{-\beta(\varepsilon-\mu)} + 12e^{-2\beta(\varepsilon-\mu)-\beta J} + 12e^{-3\beta(\varepsilon-\mu)-3\beta J} + 4e^{-4\beta(\varepsilon-\mu)-6\beta J}}{1 + 4e^{-\beta(\varepsilon-\mu)} + 6e^{-2\beta(\varepsilon-\mu)-\beta J} + 4e^{-3\beta(\varepsilon-\mu)-3\beta J} + e^{-4\beta(\varepsilon-\mu)-6\beta J}}$$

Note: Although not shown here, a similar logic follows for cooperation between three and four binding sites. Also like earlier, the β cancels out.

To start modeling, we can adopt parameters in the form of $j = e^{-\beta J}$ and $x = \mathcal{C}e^{-\beta(\varepsilon-\mu_0)}$, where $\mathcal{C}$ is a parameter representing a ratio of concentrations, thus changing μ to μ_0. This has no effect on the modeling.

$$\langle N \rangle = \frac{4x + 12x^2 j + 12x^3 j^3 + 4x^4 j^6}{1 + 4x + 6x^2 j + 4x^3 j^3 + x^4 j^6}$$

This is the equation we will use to model fit. When working with the non-cooperative model, we will assume $j = 1$ (i.e. $J = 0$).