University of Washington
Department of Chemistry
Chemistry 453
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Lecture 10. 1/28/15

A. The Bragg-Zimm Model for Helix-Coil Transitions

- The Zipper model agrees with experimental data well if the protein is not too large. If the protein is large, a number of helical sequences may initiate at remote location in the protein. In this limit, the zipper model no longer works.
- To address structural transitions in larger proteins, a more realistic model is required. The Bragg-Zimm model relaxes the requirement that the C-to-H transition only occurs adjacent to a preexisting H domains.
- In the Bragg-Zimm model, H states do not have to occur in contiguously, but non-contiguous H states are energetically unfavorable and thus are statistically weighted less in the partition function.
- The following rules apply in the Bragg-Zimm model:
  1. Like the Zipper model, the Bragg-Zimm model is parameterized by s and σ. The parameter s again is an equilibrium constant that characterizes $C \overset{s}{\rightleftharpoons} H$ such that s=[H]/[C].
  2. The parameter σ is called the nucleation parameter. A statistical weight of σs is assigned if the H is next to a C or is the first H in the sequence. If H occurs next to another H its weight is s.
  3. In proteins s is typically slightly greater than 1. The parameter σ varies between 0.001 and 0.0001.
- Using these rules we can construct the statistical weights for all eight possible trimer sequences and the partition function. Table 9.1 gives the trimer sequences and the weights.

Trimer Sequences	CCC	HCC	CHC	CCH	CHH	HHC	HCH	HHH
Statistical Weights	1	σs	σs	σs	σs^2	σs^2	$\sigma^2 s^2$	σs^3

Table 10.1: Bragg-Zimm Model: statistical weights for the eight possible trimer sequences.

- The partition function is simply constructed as in the other models using the statistical weights in table 9.1:

$$q = q_0\left(1+3\sigma s+2\sigma s^2+\sigma^2 s^2+\sigma s^3\right) = q_0\left(1+\sigma\left(3s+2s^2+\sigma s^2+s^3\right)\right) \qquad (10.1)$$

- Note the differences between the partition function for the zipper model versus the Bragg-Zimm model: the HCH intermediate is disallowed in the zipper model and allowed in Bragg-Zimm...but it has a “probability” of $\sigma^2 s^2$ q_0/q
- As before it is now possible to calculate the fractional helicity. Let s=1.00, σ=0.0600;

$$f_H = \frac{\langle n\rangle}{3} = \frac{s}{3q}\frac{\partial q}{\partial s} = \frac{s}{3q}\frac{\partial}{\partial s}\left[1+3\sigma s+2\sigma s^2+\sigma^2 s^2+\sigma s^3\right]$$

$$= \frac{s}{3q}\left[3\sigma+4\sigma s+2\sigma^2 s+3\sigma s^2\right] = \left(\frac{1}{3}\right)\left(\frac{3\sigma s+4\sigma s^2+2\sigma^2 s^2+3\sigma s^3}{1+3\sigma s+2\sigma s^2+\sigma^2 s^2+\sigma s^3}\right)$$

$$= \left(\frac{\sigma}{3}\right)\left(\frac{3s+4s^2+2\sigma s^2+3s^3}{1+\sigma\left(3s+2s^2+\sigma s^2+s^3\right)}\right) = \left(\frac{0.0600}{3}\right)\left(\frac{3+4+2(0.0600)+3}{1+(0.0600)(3+2+0.0600+1)}\right) \qquad (10.2)$$

$$= (0.0200)\left(\frac{10.12}{1+(0.0600)(6.06)}\right) = \frac{0.202}{1.36} = 0.149$$

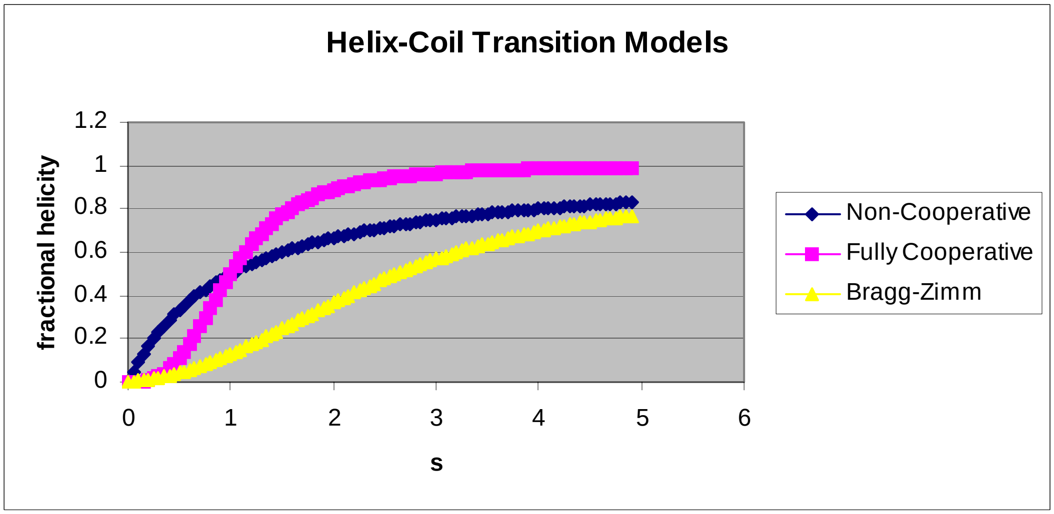
- Recall in the last lecture that when we worked this problem for the zipper model the result was virtually the same. The Zipper and Bragg-Zimm models will not differ much for small s because the amount of HCH, for example, will not be large at small s. The two theories will differ more when s becomes large.
- The Bragg-Zimm Model was used to calculate the theory lines (solid lines) in Figure 10.1.
- In general the fully cooperative model rises too fast to simulate data. As $\sigma \to 0$ the helix is destabilized and longer chains (i.e. larger N) are required to stabilize the helix.
- As $\sigma \to 1$ the Bragg-Zimm model approaches the non-cooperative model.
- 

Figure 10.1; Comparison of Non-cooperative, fully cooperative (equation 6.10) and Bragg-Zimm (equation 9.5) for N=3 and σ=0.05.

B. The Bragg-Zimm Partition Function: Matrix methods

- Three of the models that we have covered for helix-coil transitions have relatively simple expressions for the partition functions:
    - Non-cooperative:

$$q = q_0\left(1+\sum_{k=1}^{N}\frac{N!}{(N-k)!k!}s^k\right) = q_0(1+s)^N \tag{10.3}$$

    - Fully Cooperative:

$$q = q_0\left(1+s^N\right) \tag{10.4}$$

    - Zipper:

$$q = q_0\left(1+\sigma\sum_{k=1}^{N}(N-k+1)s^k\right) = \frac{\sigma s^2\left(s^N+Ns^{-1}-(N+1)\right)}{(s-1)^2} \tag{10.5}$$

- Given the partition function q for each model equation 10.3-10.5) we can determine the fraction of monomer that are helical from

$$f_H = \frac{\langle n\rangle}{N} = \frac{1}{N}\frac{s}{q}\frac{\partial q}{\partial s} \tag{10.6}$$

- The Bragg-Zimm model is more complicated than these other models in that it uses a set of rules to construct a partition function. These rules are:
    - If a C monomer follows a another C monomer, it is weighted by 1 in the partition function
    - If a C monomer follows a H monomer, it is weighted also by 1 in the partition function
    - If a H monomer follows a C it is a nucleation step and is weighted by σs.
    - If a H monomer follows another H it is a propagation step and is weighted by s.
        - These four rules are compiled into a statistical weight matrix $\underset{\sim}{M}$ which has the form:

$$\underset{\sim}{M} = \begin{array}{c} C \\ H \\ \\ \end{array}\!\!\begin{array}{c}\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix} \\ \begin{array}{cc} C & H \end{array}\end{array} \tag{10.7}$$

    - The matrix $\underset{\sim}{M}$ is used in the following calculation to generate the partition function.
- For N=1:

$$\frac{q}{q_0} = (1,0)\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}\begin{pmatrix} 1 \\ 1 \end{pmatrix} = 1+\sigma s \tag{10.8}$$

- For N=2;

$$\frac{q}{q_0} = (1,0)\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}\begin{pmatrix} 1 \\ 1 \end{pmatrix} = 1 + 2\sigma s + \sigma s^2 \tag{10.9}$$

- For N=3:

$$\frac{q}{q_0} = (1,0)\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}\begin{pmatrix} 1 \\ 1 \end{pmatrix} = (1,0)\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}^3\begin{pmatrix} 1 \\ 1 \end{pmatrix} \tag{10.10}$$

$$= 1 + 3\sigma s + 2\sigma s^2 + \sigma^2 s^2 + \sigma s^3$$

- Matrix algebra techniques show that for a N-long polymer where N is very large:

$$\frac{q}{q_0} = (1,0)\begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}^N\begin{pmatrix} 1 \\ 1 \end{pmatrix} \approx \frac{\lambda_1^N (1-\lambda_2)}{\lambda_1 - \lambda_2} \tag{10.11}$$

where $\lambda_{1,2} = \dfrac{s+1 \pm \sqrt{(s-1)^2 + 4\sigma s}}{2}$ and in general $\lambda_1 > \lambda_2$

  - Equation 10.11 is valid only for very large N.
  - When N is very large

$$\ln q = \ln \lambda_1^{N+1} + \ln(1-\lambda_2) - \ln(\lambda_1 - \lambda_2) \approx N \ln \lambda_1 \tag{10.12}$$

  - When the fraction helicity is calculated we can simplify even more. Using the definition of f_H and the expression for q in equation 10.11...

$$f_H = \frac{\langle n \rangle}{N} = \frac{s}{N}\frac{\partial \ln q}{\partial s} \approx s\frac{\partial}{\partial s}[\ln \lambda_1] = \frac{s}{\lambda_1}\frac{\partial \lambda_1}{\partial s} \tag{10.13}$$

- Conclusion: For the Bragg-Zimm model when N is very large:

$$f_H \approx \frac{s}{\lambda_1}\frac{\partial \lambda_1}{\partial s}$$

where $\lambda_1 = \dfrac{s+1+\sqrt{(s-1)^2 + 4\sigma s}}{2}$ *and* $\dfrac{d\lambda_1}{ds} = \dfrac{1}{2}\left(1 + \dfrac{s-1+2\sigma}{\sqrt{(s-1)^2 + 4\sigma s}}\right)$