Helix-coil transition (continued)

So, now let's go back to the start, and ask how to set up the problem when there are **interactions** between the units of the polymer. We will limit ourselves to nearest neighbor interactions, and this will give us the one dimensional Ising model. Much of the methodology will remain the same as above with no interactions, and it is interesting to see the differences.

We make the following definitions for the models shown below: A helical unit that is neighboring a helical unit to its immediate right has a statistical weight of "s", and a helical unit that is neighboring a coil state on its right has a statistical weight of sσ (where σ often has a value of 10^{-3}-10^{-4}; this means that a helical state bordering a coil state to its right is much less likely than a helix state that borders a "helix" unit to its right).

The **coil state** of a unit has a statistical weight of "1" - that is, the coil state defined the zero of free energy.

The partition function for a "N" dimensional polymer is:

$$Z_N = \mathbf{e}\mathbf{W}^N\mathbf{e}^+ = \begin{pmatrix} 1 & 1 \end{pmatrix} \begin{pmatrix} p^{hh} & p^{hc} \\ p^{ch} & p^{cc} \end{pmatrix}^N \begin{pmatrix} e_1^+ \\ e_2^+ \end{pmatrix}$$

Note we are writing the Nth power of the matrix; as before we are using e=(1 1), because this row vector will pick up all the terms in the matrix into a sum. The right vector we can find as follows. The last matrix on the right belongs to the Nth element of the chain. This unit in the chain is special, because there is no polymer element to its right. So, we will assume that the element will act as though it always has a "coil" state to its right. This is not necessary, but probably close to the real case, and it makes the examples easy to write down. This means there are only two states we have to worry about for this rightmost unit, and these statistical weights are: p^{hc} and p^{cc}. Note the following multiplication:

$$\begin{pmatrix} p^{hh} & p^{hc} \\ p^{ch} & p^{cc} \end{pmatrix} \begin{pmatrix} 0 \\ 1 \end{pmatrix} = \begin{pmatrix} p^{hc} \\ p^{cc} \end{pmatrix}.$$

This gives a column vector where the possible states are the elements of the vector we want for the rightmost unit. So, we will define

$$\begin{pmatrix} e_1^+ \\ e_2^+ \end{pmatrix} = \begin{pmatrix} 0 \\ 1 \end{pmatrix}.$$

Look at the case (for an example) where the chains can only open up from the right end; that is, we will not allow a coil state to be followed (on the right) by a helix state – the polymer is constrained to "open up" – from a helix to a coil state - from the right end). We can write down the whole partition function:

$$Z_N = \begin{pmatrix} e_1 & e_2 \end{pmatrix} \begin{pmatrix} p^{hh} & p^{hc} \\ p^{ch} & p^{cc} \end{pmatrix}^N \begin{pmatrix} e_1^+ \\ e_2^+ \end{pmatrix} = \begin{pmatrix} 1 & 1 \end{pmatrix} \begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix}^N \begin{pmatrix} 0 \\ 1 \end{pmatrix}$$

We want to use the following diagonalization procedures:

$$Z_N = \mathbf{e}\mathbf{W}^N\mathbf{e}^+ = \mathbf{e}\left(\mathbf{T}\mathbf{\Lambda}\mathbf{T}^{-1}\right)^N \mathbf{e}^+ = \mathbf{e}\mathbf{T}(\mathbf{\Lambda})^N\mathbf{T}^{-1}\mathbf{e}^+ = \mathbf{e}\mathbf{T}\begin{pmatrix} \lambda_1^N & 0 \\ 0 & \lambda_2^N \end{pmatrix}\mathbf{T}^{-1}\mathbf{e}^+$$

The **_eigenvalues_** of the matrix

$$\begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix}$$

are

$$\lambda_1 = s \,, \lambda_2 = 1 .$$

To get the diaganolized matrix and its inverse (T and T^{-1}) we need the eigenvectors .

$$\begin{pmatrix} \xi_1^i \\ \xi_2^i \end{pmatrix}$$

$$\begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix} \begin{pmatrix} \xi_1^i \\ \xi_2^i \end{pmatrix} = \lambda_i \begin{pmatrix} \xi_1^i \\ \xi_2^i \end{pmatrix} ;$$

they are, in normalized form, as follows:

$$\begin{pmatrix} \xi_1^1 \\ \xi_2^1 \end{pmatrix} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

and

$$\begin{pmatrix} \xi_1^2 \\ \xi_2^2 \end{pmatrix} = c_1 \begin{pmatrix} (s\sigma) \\ (1-s) \end{pmatrix}$$

, where

$$c_1 = \sqrt{\frac{1}{(1-s)^2 + (s\sigma)^2}}$$

check if they are really eigenvectors, and to which eigenvalues they belong:

.

$$\begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix} \begin{pmatrix} 1 \\ 0 \end{pmatrix} = s \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

and

$$\begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix} \begin{pmatrix} (s\sigma) \\ (1-s) \end{pmatrix} = 1 \cdot \begin{pmatrix} s\sigma \\ 1-s \end{pmatrix}$$

So, now all you have to do, is find the diaganolizing matrix, and its inverse, and use the equation:

$$Z_N = \mathbf{e}\mathbf{W}^N \mathbf{e}^+ = \mathbf{e}(\mathbf{T}\mathbf{\Lambda}\mathbf{T}^{-1})^N \mathbf{e}^+ = \mathbf{e}\mathbf{T}(\mathbf{\Lambda})^N \mathbf{T}^{-1}\mathbf{e}^+ = \mathbf{e}\mathbf{T}\begin{pmatrix} s^N & 0 \\ 0 & 1 \end{pmatrix}\mathbf{T}^{-1}\mathbf{e}^+$$

<u>Lets work it out longhand for N=3 (three units) without the eigenvectors</u>:

$$Z_N = \begin{pmatrix} 1 & 1 \end{pmatrix} \begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix} \begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix} \begin{pmatrix} s & (s\sigma) \\ 0 & 1 \end{pmatrix} \begin{pmatrix} 0 \\ 1 \end{pmatrix}$$

$$= \begin{pmatrix} 1 & 1 \end{pmatrix} \begin{pmatrix} ss(s\sigma) + s(s\sigma) + (s\sigma) \\ 1 \end{pmatrix} = \begin{matrix} ss(s\sigma) & + s(s\sigma) & +(s\sigma) & +1 \\ hhh & hhc & hcc & ccc \end{matrix}$$

$$\frac{\sigma(s-1)\left(s^3 + s^2 + s\right)}{(s-1)} + 1 = \frac{\sigma s}{(s-1)}\left(s^3 - 1\right) + 1$$

Now lets solve the general matrix equation for N sites; we need the T, T^{-1} matrices:

$$T = \begin{pmatrix} 1 & c_1(\sigma s) \\ 0 & c_1(1-s) \end{pmatrix}$$

and

$$T^{-1} = \frac{1}{[c_1(1-s)]} \cdot \begin{pmatrix} c_1(1-s) & -c_1(\sigma s) \\ 0 & 1 \end{pmatrix} = \begin{pmatrix} 1 & -\sigma s \big/ (1-s) \\ 0 & \dfrac{1}{[c_1(1-s)]} \end{pmatrix}$$

You should check if $\mathbf{TT^{-1}} = \mathbf{1}$. Now we can form the **_whole partition function_**:

$$Z_N = \mathbf{eT}\begin{pmatrix} s^N & 0 \\ 0 & 1 \end{pmatrix}\mathbf{T^{-1}e} = \begin{pmatrix} 1 & 1 \end{pmatrix}\begin{pmatrix} 1 & c_1(\sigma s) \\ 0 & c_1(1-s) \end{pmatrix}\begin{pmatrix} s^N & 0 \\ 0 & 1 \end{pmatrix}\begin{pmatrix} 1 & -\sigma s \big/ (1-s) \\ 0 & \dfrac{1}{[c_1(1-s)]} \end{pmatrix}\begin{pmatrix} 0 \\ 1 \end{pmatrix}$$

$$= \begin{pmatrix} 1 & 1 \end{pmatrix} \begin{pmatrix} 1 & c_1(\sigma s) \\ 0 & c_1(1-s) \end{pmatrix} \begin{pmatrix} -s^N \sigma s \big/ (1-s) \\ \dfrac{1}{[c_1(1-s)]} \end{pmatrix} = \begin{pmatrix} 1 & 1 \end{pmatrix} \left(\left\{ (\sigma s)s^N \big/ (s-1) - (\sigma s) \big/ (s-1) \right\} \atop 1 \right)$$

$$= (\sigma s)s^N \big/ (s-1) - (\sigma s) \big/ (s-1) + 1$$

$$Z_N = \frac{(\sigma s)}{(s-1)}\left(s^N - 1\right) + 1$$

This is the **general expression for our partition function** in a compact notation. Compare to the above simple derivation of just three sites.

Let's look at the formal calculations using this expression for the partition function:
First, we calculate the experimental parameter that is usually measured, and this is the average fraction of units in the helix state,

$$\theta = \frac{\langle \#h \rangle}{N}.$$

$$\theta = \frac{1}{N} \frac{\partial \ln Z_N}{\partial \ln s} = \frac{1}{N} \cdot \frac{\frac{(s\sigma)}{s-1}\left[\left(s^N - 1\right)\left\{1 - \left(\frac{s}{s-1}\right)\right\} + Ns^N\right]}{Z_N}$$

This starts to look messy, and we do not want to get bogged down in numerical calculations and approximations. Let's leave the general case, and the matrix calculations, and look at an example of a very short chain, to see the **influence of the cooperativity**.

Take a 4mer.
Configuration Statistical Weight (S.W.) S.W. when $\sigma = 10^{-4}$ and s=10

hhhh σs^4 1

hhhc σs^3 10^{-1}

hhcc σs^2 10^{-2}

hccc σs 10^{-3}
cccc 1   1

   Z_N=2.111

So we see that the only *two states* that are *contributing* are the hhhh and the cccc states <u>even when about half the units are in the helix state</u>. Note that s=10 where for almost half occupancy! – it is far from the s=1 value where there is ½ occupancy for the individual unit (no cooperativity) case. This is partially due to the short chain, in addition to the cooperativity. As the chains get longer, the steepness of the transition increases, and the ½ point of the transition approaches s=1 (when N is *very* large). Actually, for our zipper model with N=4, ΔG_{hc}/RT=*ln*(s)=*ln*(10)=2.3, rather than zero, as it is for the independent unit case when θ=1/2.

Let's calculate the exact occupancy. First because this model is so easy, we can write the partition function by inspection, actually (sorry about all the matrix calculations).

$$Z_N = \sigma \sum_{i=1}^{N} s^i + 1$$

.

The fraction units in the helix state is (show this):

$$Z_N = \left(\frac{\sigma s}{s-1}\right)\left(s^N - 1\right) + 1 \quad ;$$

and

$$\theta = \frac{1}{N}\frac{\partial \ln Z_N}{\partial \ln s} = \frac{\sigma}{N Z_N}\sum_{i=1}^{N} i s^i \quad .$$

If we just calculate this for the sum where N=4 and using the above parameters for s and σ, we get θ=0.511. You should compare this value to the case of independent sites! For the independent sites, only 4.5% would be in the **hhhh** and **cccc** state *together* when θ≈0.5 – all the rest would be in the intermediate states, because there are so many ways to arrange these intermediate states on the polymer chain.

So we see why one makes the "***two-state***" approximation. In this approximation we have

$$Z_N = 1 + \sigma s^N$$

and

$$\theta = \frac{\sigma s^N}{1 + \sigma s^N}$$

this is just like a series reaction A<->I_1<-> I_2<-> I_3...<->B, where the intermediates are at such low concentration, that one can make the approximation that the reaction proceeds in only one step, with an overall equilibrium constant equal to the multiplication of all the individual ones: the reaction is then: A<->B, with

$$K_{overall} = \prod_{i=1}^{N} K_i$$

,

and $K_1 = s\sigma$, and all others are equal to s.

Then

$$\theta = \frac{K_{overall}}{1 + K_{overall}} = \frac{\sigma s^N}{1 + \sigma s^N}.$$

This is usually a very good approximation for small chain lengths.

Here are some examples of this type of "zipper" transition for different lengths and for different cooperativities.

First , here are examples of θ for N=4,6,8,and 10, where we have used the values σ=10^{-4}, and we are using the two-state approximation. This is a good approximation for short enough chains (N small), and for small enough σ (great enough cooperativity) – this is the case for these values for which the curves are calculated.
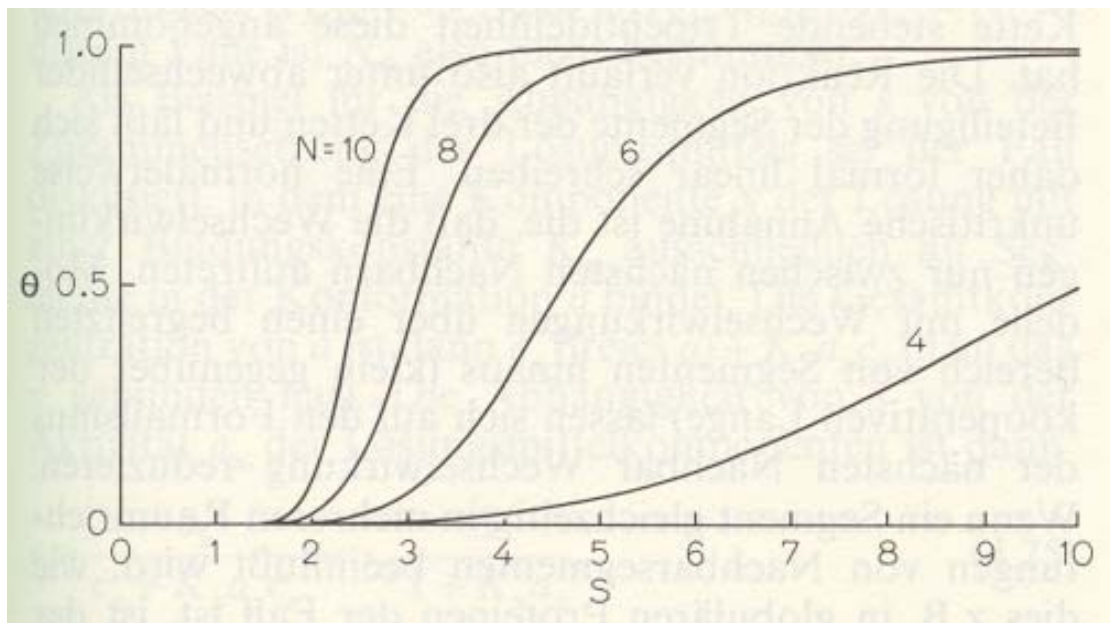
Note how the transition gets sharper as N increases, and the $\theta = 1/2$ point decreases, and for N=10, is about at s=2. Because this is never a good approximation for very long chains, we will never approach the limit of $\theta=1/2$ at s=1, with this approximation. But note the difference to the *individual polymer-unit* approximation; there,

$$\theta = \frac{s}{1+s},$$

and the $\theta=1/2$ point is **always at $\sigma=1$**, and it can get as sharp as we want.

Now look at the **"infinite-chain"** limit, using different values for the cooperativity (i.e. different σ values). This is shown for a little different model, where we allow neighboring units in states "ch" as well as in "hc" (the above example was for just the "hc" case. We state this without any proof – you can calculate this yourself; it is easy. The result is:

$$\theta = \frac{1}{2}\left(1 + \frac{s-1}{\sqrt{(s-1)^2 + 4\sigma s}}\right)$$
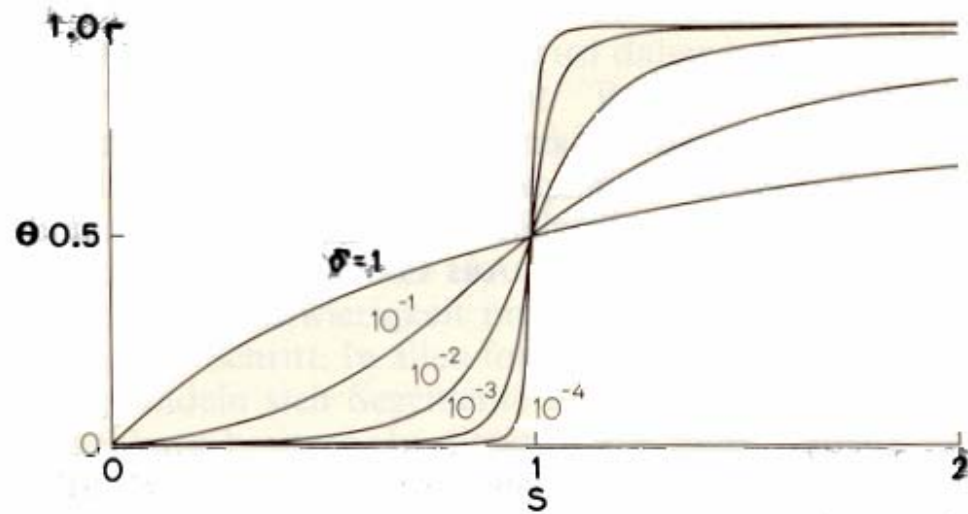
Another interesting parameter is the average length> of an unbroken helix segment, $\langle N_h \rangle$:

$$\langle N_h \rangle = \frac{\theta}{1-\theta} \frac{1}{\sqrt{\sigma s}} \frac{1}{2}\left(1 + s + \sqrt{(1-s)^2 + 4\sigma s} \right);$$

when $\theta = 1/2$, then $\langle N_h \rangle_{\theta=0.5} = 1 + \sigma^{-1/2}$ This is the "cooperative length", and shows the

limit of cooperativity in the one-dimensional chain, and in the case at hand, where $\sigma=10^{-4}$, this is about 100 units. So, there are long sequences of alternating "h" and "c" regions for the case of high cooperativity. For very long chains, this varies with the value of σ. For an uncooperative transition ($\sigma=1$) the average sequence length of "h" states at $\theta=1/2$ is 2 (this is quite a difference). So we see that the presence of such cooperativity, which arises from the polymer nature of the units, will make a very large difference in the nature of the type of small "polymer machines" that nature can make.

This is actually the basic reason why such complex entities can be made in biological systems, and sets the stage for the extremely wide variety (essentially infinite) of conformations (and of very *specific* conformations) of proteins, and nucleic acids, which are needed for a functioning biological system. And this arises simply from *nearest neighbor interactions*.