

### Coil to Globule Transition:

This follows “Giant Molecules” by Alexander Yu. Grosberg and Alexei R. Khokhlov (1997).

The Flory Krigbaum expression for the free energy of a self-avoiding chain is given by,

$$F(R) = \frac{z^2 V_0 (1 - 2\chi) kT}{2R^3} + \frac{3R^2 kT}{2zl^2} = U(R) - TS(R) \quad (1)$$

Equation (1) can be rewritten using the coil expansion coefficient,  $\alpha$ ,

$$\alpha^2 = \frac{R^2}{R_\theta^2} = \frac{R^2}{zl^2} \quad (2)$$

$$F(\alpha) = \frac{z^{1/2} B kT}{2\alpha^3 l^3} + \frac{3\alpha^2 kT}{2} = U(\alpha) - TS(\alpha) \quad (3)$$

where B is the second virial coefficient,

$$B = V_0 (1 - 2\chi) \quad (4)$$

Finding the minimum in the free energy expression, equation (3), yields the most probable value for  $\alpha$ ,

$$\alpha \sim \left( \frac{z^{1/2} B}{l^3} \right)^{1/5} \quad (5)$$

The virial expansion of the enthalpic interactions is given by,

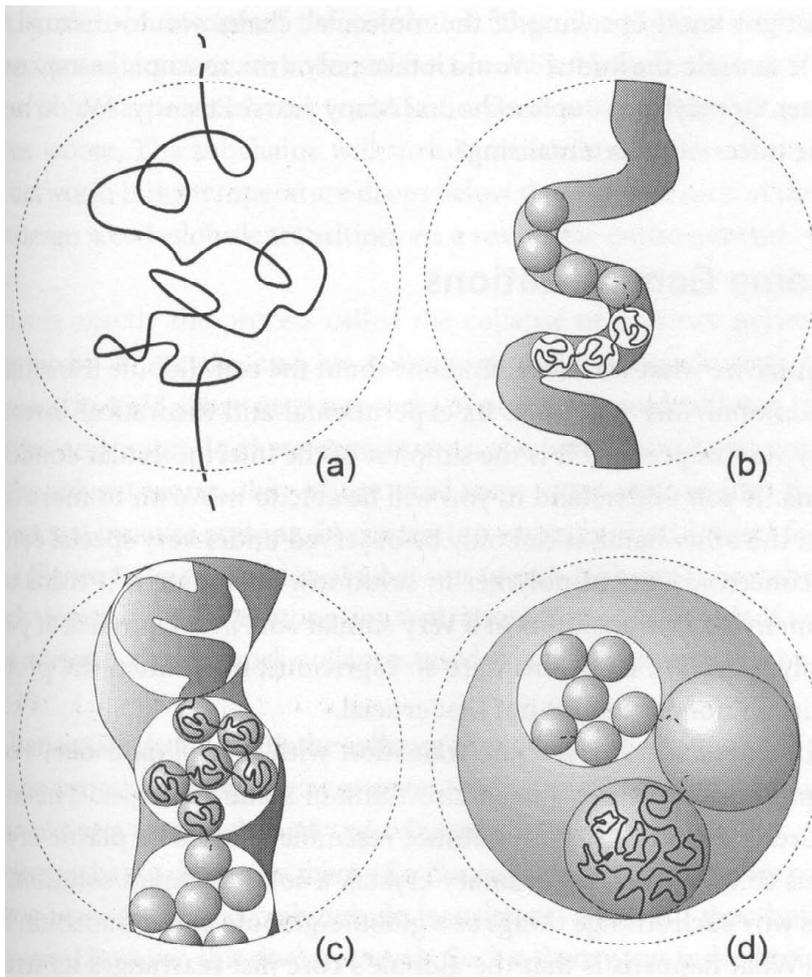
$$U(\alpha) = V_{Coil} kT [n^2 B + n^3 C + \dots] \approx V_{Coil} kT n^2 B \sim \frac{kTR^3 B z^2}{R^6} = \frac{z^{1/2} B kT}{2\alpha^3 l^3} \quad (6)$$

where n is the segmental density in the coil and  $V_{Coil}$  is the volume of the coil. The second virial coefficient describes binary interactions and the third virial coefficient describes ternary interactions. In dilute conditions we can ignore the higher order interactions and use only the second virial coefficient.

The Flory-Krigbaum approach is calculated for coil expansion,  $\alpha \geq 1$ , and for dilute conditions. This means that  $\chi \leq 1/2$  or  $T \geq 2\Delta\epsilon/k$  or  $\theta$ . When  $T < \theta$  the coil will collapse. This occurs when a protein folds, DNA folds into the nucleosome and chromosome, and when RNA folds. Polyelectrolytes and charged gels can also show coil collapse into a globular (3-d) state. Polymer physics can describe this behavior using functions extended from the original approach of Flory and Krigbaum by Stockmayer, Lifshitz and others. First, in coil collapse the third virial

coefficient,  $C$  in equation (5), is retained because the concentration is higher in the collapsing coil. Under this condition the second virial coefficient,  $B$  in equation (4) is negative but the third virial coefficient is positive. This is because, according to Grosberg and Khokhlov, “in general the higher the order of interaction the wider the range where they are effectively repulsive (positive)” since the volume excluded is proportional to the number of interacting particles (repulsive part) while the attraction (from charge or hydrophobic/hydrophilic interactions or van der Waals interactions) are related to surfaces and are proportional to  $m^{2/3}$ .

Grosberg and Khokhlov’s figure 8.6 shows a model for chain collapse that explains the entropic behavior in terms of blobs of  $g^*$  chain units associated with a confined chain. We can consider the collapsed chain as composed of  $z/g^*$  collapsed blobs each with an energy  $kT$ .



**FIGURE 8.6**  
A few initial stages of the coil-globule transition. This looks self-similar! (Compare with what we write about self-similarity in Chapter 10). Source: Courtesy of S. Nechaev.

The entropy part of equations (1) and (3) also changes in coil collapse. The coil must fit into a size  $R^* = \alpha z^{1/2} l$ . We consider an ideal chain that could fit in this size. This chain would have a mass  $g^*$  such that  $g^* = R^{*2}/l^2$ . The chain is composed of  $z/g^*$  segments that can fit in the collapsed coil size  $R^*$ . The entropy associated with confinement of the coil is composed of  $z/g^*$  chains each of which contributes  $kT$  to the entropy so,

$$[-TS(\alpha)]_{\text{Confinement}} \sim kT \frac{z}{g^*} = kT \frac{zl^2}{R^2} = \frac{kT}{\alpha^2} \quad (7)$$

In the absence of confinement (coil collapse) the expression was,

$$[-TS(\alpha)]_{\text{Expansion}} \sim kT\alpha^2 \quad (8)$$

and a sum of these terms (approximation),

$$-TS(\alpha) = [-TS(\alpha)]_{\text{Confinement}} + [-TS(\alpha)]_{\text{Expansion}} \sim kT(\alpha^2 + \alpha^{-2}) \quad (9)$$

The total expression for the free energy of a collapsing coil is given by the sum of equation (9) and equation (6) including the third virial coefficient,

$$F(\alpha) \sim kT(\alpha^2 + \alpha^{-2}) + \frac{kTBz^{1/2}}{2\alpha^3 l^3} + \frac{kTC}{\alpha^6 l^6} \quad (10).$$

Which works for both expansion and collapse. Finding the minimum in this free energy yields the most probable value for  $\alpha$ , (equivalent of equation (5)),

$$\alpha^5 - \alpha = x + y\alpha^{-3} \quad (11)$$

where x is related to B and is given by,

$$x = K_1 B z^{1/2} / l^3 \quad (12)$$

and y is related to C and is given by,

$$y = K_2 C / l^6 \quad (13).$$

If  $\alpha$  is small you can neglect the terms on the left hand side of equation (11) and solve for R,

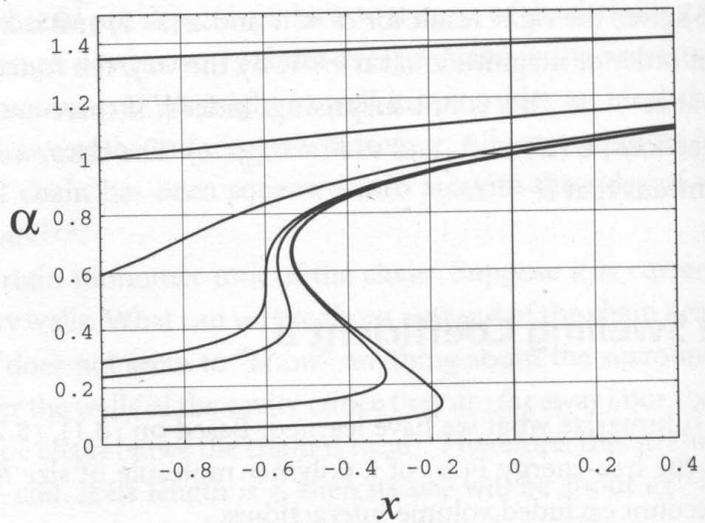
$$R \sim \alpha z^{1/2} l \sim \left( \frac{-C}{B} \right)^{1/3} z^{1/3} \quad (14)$$

so the structure is 3-d or globular. Other interesting features of equation (11) including its prediction of a collapse transition, under certain conditions, are made by Grosberg and Khokhlov.

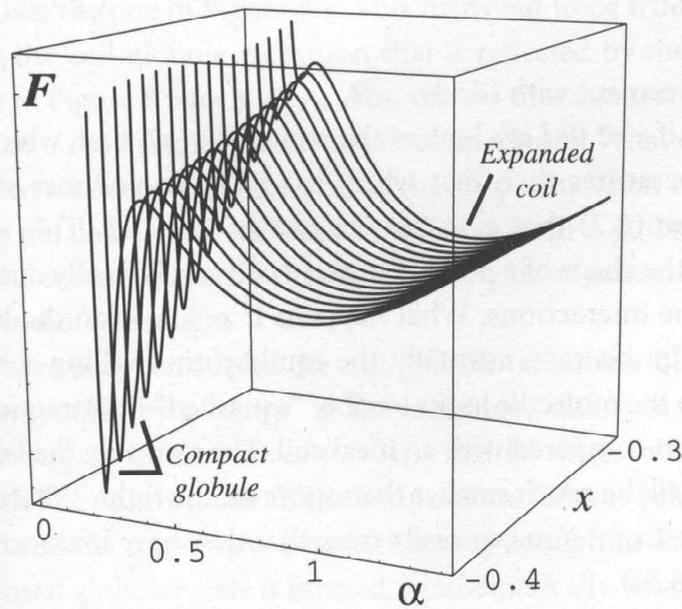
Equation (11) can be understood by plotting the coil expansion factor,  $\alpha$ , versus the reduced temperature function x for fixed values of y as shown in Figure 8.3 from Grosberg and Khokhlov reproduced below. In this figure, at large y the chain is flexible and the coil only slightly collapses on cooling (smaller x). The theta temperature occurs at x = 0. For rigid chains with a small value for y, the curve shows three values for a given x just below the  $\theta$ -temperature.

Equation (11) corresponds to points where the derivative of the free energy is 0. These can be minima or maxima and when 3 points are seen for a given  $x$  this reflects two minima separated by a maxima. So for these values a transition is observed from a coil state for large  $\alpha$ , to a globular state reflected by 3d structures as indicated by equation (14).

**FIGURE 8.3**  
 The dependence  $\alpha(x)$  given by equation (8.7) for different values of  $y$ ; from top to bottom, the curves correspond to the following values of  $y$ : 10, 1, 0.1, 1/60, 0.01, 0.001, 0.0001.

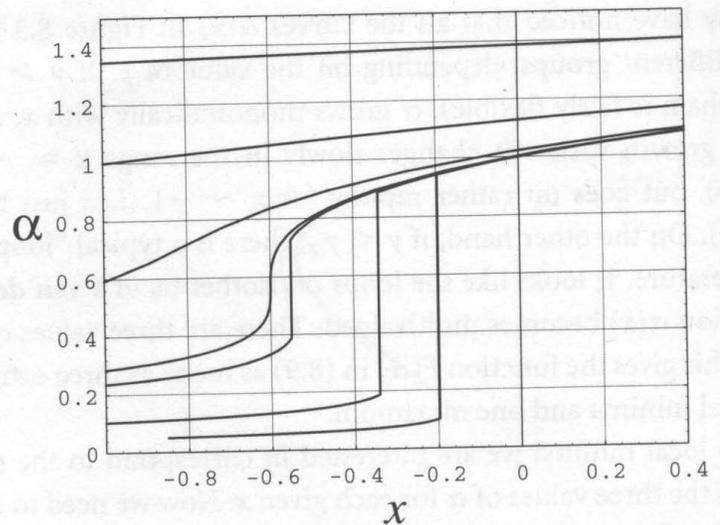


For fixed values of  $x$  we can plot the free energy, equation (10), as a function of  $\alpha$ , Figure 8.4 from Grosberg and Khokhlov reproduced below. This clearly shows two minima and a maxima. For any value of  $x$  there is a global minimum associated with the thermodynamically most favored state, either a coil or a globule. The  $\alpha$  for the most favored state can be mapped as a function of  $x$ , Grosber and Khokhlov's Figure 8.5 below, for the values of  $y$  used in Figure 8.3.



**FIGURE 8.4**  
 The dependence  $F(\alpha)$  in the case where  $\alpha(x)$  is multivalued. As  $x$  changes (which can be controlled by, say, temperature change), the shape of the  $F(\alpha)$  dependence changes such that one minimum gets deeper at the expense of the other. Deeper minimum corresponds to the more stable state. For this figure, we choose the value  $y = 0.001$ .

**FIGURE 8.5**  
 The curves  $\alpha(x)$  in Figure 8.3 are multivalued at some  $x$ ; in this figure, one solution is selected for each  $x$  such that the values of  $\alpha(x)$  correspond to the absolute minimum free energy for every  $x$ . The values of  $y$  are the same as in Figure 8.3.



For rigid chains (chain persistence versus chemical diameter) a dramatic transition is seen between the coil and globule states. This is a first order transition (a discrete transition). For flexible chains (in terms of the persistence versus chemical diameter) the chain shows a gradual, continuous transition with no discrete change in size.