

Biophysics PS 1.

1. (A) Spring $k = 5 \times 10^5$ dyne/cm

10^5 dyne = 1N, so

$k = 500$ N/m

$U_{\text{spring}} = \frac{1}{2} k A^2$ for amplitude A , so $U_{\text{spring}} = \frac{1}{2} k_B T \rightarrow$

$\frac{1}{2} k A^2 = \frac{1}{2} k_B T \rightarrow \boxed{A = \left(\frac{k_B T}{k} \right)^{1/2}}$

Plugging in $k_B T = 4.1$ pN nm (from PBoC p. 169) gives

$$A = \left(\frac{4.1 \text{ pN} \cdot \text{nm}}{500 \text{ N/m}} \right)^{1/2} = \left(\frac{4.1 \times 10^{-12} \text{ N} \times 10^{-9} \text{ m}}{500 \text{ N/m}} \right)^{1/2}$$

$$= \left(\frac{4.1}{5} \times 10^{-23} \text{ m}^2 \right)^{1/2} = \left(\frac{41}{5} \times 10^{-24} \text{ m}^2 \right)^{1/2} = 3 \times 10^{-12} \text{ m}^2$$

$\boxed{A = 0.03 \text{ \AA}}$

(B) A typical C-C covalent bond is 1 or 1.5 Å, so 0.03 Å is indeed a very small amount of stretch: 3% or so.

(C) Since the spring energy term in the force field eqⁿ is $K_r r^2$, we want $\boxed{K_r = \frac{1}{2} k}$. Putting in numbers,

$$K_r = \frac{1}{2} (500 \text{ N/m}) = 250 \frac{\text{N} \cdot \text{m}}{\text{m}^2} \times \left(\frac{10^{-10} \text{ m}}{\text{Å}} \right)^2 = 2.5 \times 10^{-18} \frac{\text{J}}{\text{Å}^2}$$

Since 1 cal = 4.2 J, $1 \text{ J} = \frac{1}{4.2} \text{ cal} \times \frac{10^{-3} \text{ kcal}}{\text{cal}} \times \frac{6 \times 10^{23}}{\text{mole}} = 1.4 \times 10^{20} \frac{\text{kcal}}{\text{mol}}$

So $K_r = 2.5 \times 10^{-18} \frac{\text{J}}{\text{Å}^2} \times \frac{1.4 \times 10^{20} \text{ kcal/mol}}{\text{J}} = 3.5 \times 10^2 \frac{\text{kcal/mol}}{\text{Å}^2} = \boxed{3500 \frac{\text{kcal/mol}}{\text{Å}^2}}$

should be 350 kcal/mol/Å²

$$2. (A) \quad 4\Delta \left(\left(\frac{r_0}{r} \right)^{12} - \left(\frac{r_0}{r} \right)^6 \right) \leftrightarrow \frac{A_{ij}}{r^{12}} - \frac{B_{ij}}{r^6}, \text{ so}$$

$$A_{ij} = 4\Delta r_0^{12} \text{ and } B_{ij} = 4\Delta r_0^6$$

(B) The equilibrium position is the minimum of E . This occurs when $\frac{dE}{dr} = 0$, ie

$$0 = \left. \frac{dE}{dr} \right|_{r=r_{eq}} = 4\Delta \left(-12 \left(\frac{r_0}{r_{eq}} \right)^{13} \frac{1}{r_0} + 6 \left(\frac{r_0}{r_{eq}} \right)^7 \frac{1}{r_0} \right), \text{ or}$$

$$2 \left(\frac{r_0}{r_{eq}} \right)^{13} = \left(\frac{r_0}{r_{eq}} \right)^7 \rightarrow \boxed{r_{eq} = \sqrt[6]{2} r_0}$$

$$\begin{aligned} E_{min} &= E(r_{eq}) = 4\Delta \left(\left(\frac{r_0}{\sqrt[6]{2} r_0} \right)^{12} - \left(\frac{r_0}{\sqrt[6]{2} r_0} \right)^6 \right) \\ &= 4\Delta \left(\frac{1}{4} - \frac{1}{2} \right) = -\Delta \rightarrow \boxed{E_{min} = -\Delta} \end{aligned}$$

(c) $r_{eq} = 4 \text{ \AA}$ and $E_{min} = -0.150 \text{ kcal/mol}$.

$$(i) \quad \Delta = -E_{min} = \boxed{0.150 \text{ kcal/mol}}$$

$$r_0 = 2^{-1/6} r_{eq} = \frac{4}{\sqrt[6]{2}} \text{ \AA} = \boxed{3.6 \text{ \AA}}$$

$$(ii) \quad A_{ij} = 4\Delta r_0^{12} = 4(0.150 \text{ kcal/mol})(3.6 \text{ \AA})^{12} = \cancel{2.5 \times 10^6 \text{ kcal/mol}}$$

$$\boxed{A_{ij} = 2.5 \times 10^6 \frac{\text{kcal}}{\text{mol}} \text{ \AA}^{12}}$$

$$B_{ij} = 4\Delta r_0^6 = 4(0.150 \frac{\text{kcal}}{\text{mol}}) \frac{(4 \text{ \AA})^6}{2} = \boxed{1.2 \times 10^3 \frac{\text{kcal}}{\text{mol}} \text{ \AA}^6}$$

3(A) From lecture,

$$k_B = 1.4 \times 10^{-23} \text{ J/K}$$

$$T_{\text{folding}} = \left(\frac{\ln 2}{2}\right) \frac{\epsilon}{k_B}, \text{ so}$$

$$\epsilon = \left(\frac{\ln 2}{2}\right) k_B T_{\text{folding}} = \left(\frac{\ln 2}{2}\right) \left(1.4 \times 10^{-23} \frac{\text{J}}{\text{K}}\right) (273 + 100 \text{ K})$$

$$= \left(\frac{\ln 2}{2}\right) 373 (1.4 \times 10^{-23} \text{ J}) \times \frac{1 \text{ cal}}{4.2 \text{ J}} \times \frac{10^{-3} \text{ kcal}}{\text{cal}} \times \frac{6 \times 10^{23}}{\text{mol}}$$

$$= \left(\frac{\ln 2}{2}\right) \cdot \frac{373 \cdot 1.4 \cdot 6}{4.2} \times 10^{-3} \frac{\text{kcal}}{\text{mol}} = \boxed{0.26 \frac{\text{kcal}}{\text{mol}}}$$

(B) For $\epsilon = 18 \frac{\text{cal}}{\text{Å}^2}$, and assuming that a single H-P contact is responsible for burying $\frac{1}{4}$ of the $4\pi R^2$ surface area, we want

$$\left(18 \frac{\text{cal}}{\text{Å}^2}\right) \cdot \frac{1}{4} (4\pi R^2) = 0.26 \frac{\text{kcal}}{\text{mol}}, \text{ so}$$

$$R^2 = \left(\frac{0.26 \text{ kcal}}{\text{mole}}\right) \frac{1}{\pi} \left(\frac{\text{Å}^2}{18 \text{ cal}}\right) \times \left(\frac{\text{mole}}{6 \times 10^{23}}\right) \cdot 10^3 \frac{\text{cal}}{\text{kcal}}$$

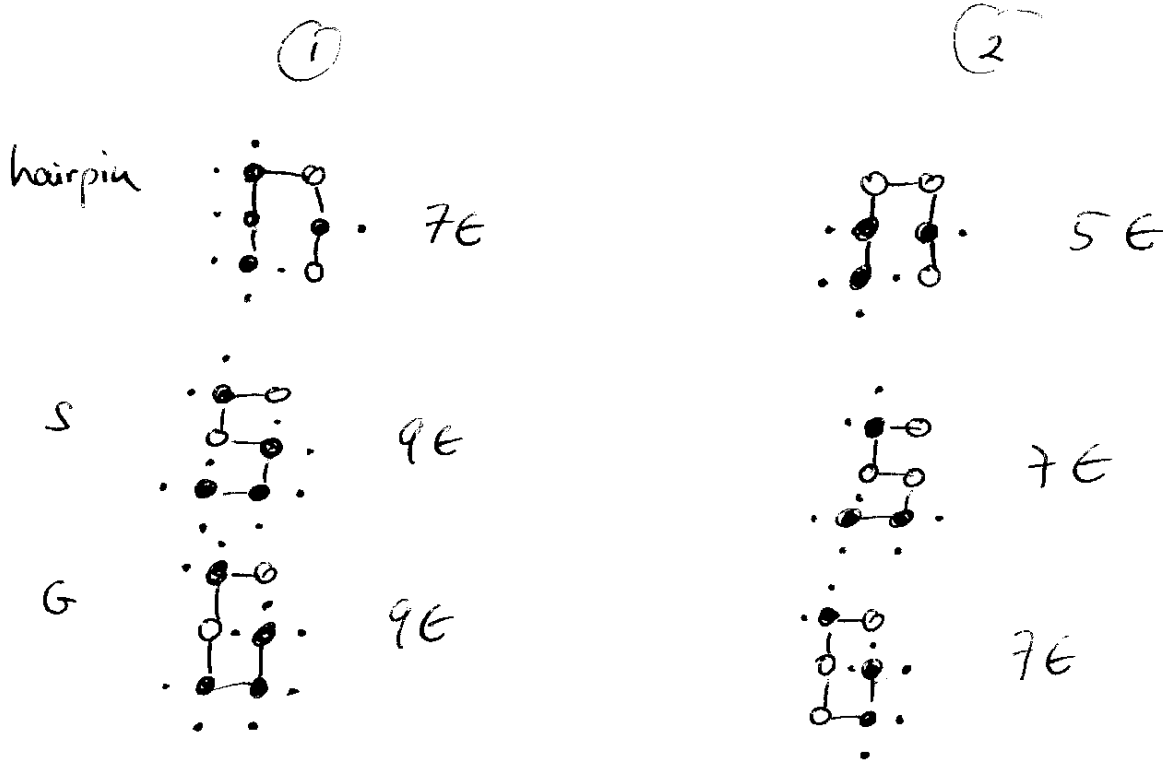
$$= \left(0.26 \frac{\text{kcal}}{\text{mol}}\right) \frac{1}{\pi} \frac{\text{Å}^2}{18 \text{ cal/mol}} = \left(\frac{260}{18\pi}\right) \text{Å}^2 = 4.6 \text{Å}^2$$

$$\boxed{R = 2.1 \text{ Å}}$$
 This is pretty small - mainly b/c

the mapping from H-P object to the "real world" is complicated, so ϵ isn't the same as a 3D hydrophobic energy.

4 (A) ~~The~~ The sequences are $\bullet \bullet \bullet \circ \bullet \circ$ (1)
 and $\bullet \bullet \circ \circ \bullet \circ$ (2)

Threading them gives (w/ a dot for each H-P contact)



(i) From above, hairpin is lowest energy state so it will dominate at low T.

(ii) for (1) $G_{\text{hairpin}} = 7E - k_B T \ln 1$

$G_{\text{other}} = 9E - k_B T \ln 2$

Hairpin is the lowest free energy when

$7E < 9E - k_B T \ln 2$ or

$T < \left(\frac{2}{\ln 2}\right) \frac{E}{k_B}$

for (2) $G_{\text{hairpin}} = 5E - k_B T \ln 1$

$G_{\text{other}} = 7E - k_B T \ln 2$

$5E < 7E - k_B T \ln 2 \rightarrow T < \frac{2}{\ln 2} \frac{E}{k_B}$
 as before.

7.6 Toy model of protein folding

A four-residue protein can take on the four different conformations shown in Figure 7.21. Three conformations are open and have energy ϵ ($\epsilon > 0$), and one is compact, and has energy zero.

(a) At temperature T , what is the probability, p_o , of finding the molecule in an open conformation? What is the probability, p_c , that it is compact?

(b) What happens to the probability p_c , calculated in (a), in the limit of very large and very low temperatures.

(c) What is the average energy of the molecule at temperature T ?

(a) The weights of each of the three open states is $\exp(-\beta\epsilon)$, while the weight of the compact state is 1 (since it has zero energy). The partition function is $Z = 1 + 3 \exp(-\beta\epsilon)$ while the probabilities of finding the "protein" in the open and closed states are

$$p_o = \frac{3 \exp(-\beta\epsilon)}{Z}, \text{ and } p_c = \frac{1}{Z}. \quad (7.104)$$

(b) The high temperature limit corresponds to $\beta \rightarrow 0$ in which case $p_c \rightarrow 1/4$, as expected since in this case all 4 states are equally likely. In this case the thermodynamic state of the protein is solely determined by entropy.

On the other hand, in the low temperature limit when $\beta \rightarrow \infty$, $p_c \rightarrow 1$, which means that the protein will assume the lowest energy state. In this case equilibrium is determined by minimizing the energy.

(c) The average energy is $U = \epsilon p_o + 0 p_c$ and therefore

$$U = \frac{3\epsilon \exp(-\beta\epsilon)}{3 \exp(-\beta\epsilon) + 1}. \quad (7.105)$$

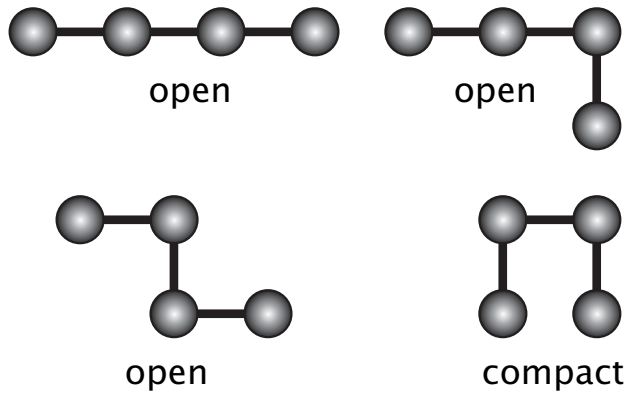


Figure 7.21: Toy model of protein folding showing four different conformations. (Adapted from example 8.2 of K. Dill and S. Bromberg, *Molecular Driving Forces*, New York: Garland Science, 2003.)

At high temperatures this expression reduces to $U = 3\epsilon/4$, while at low temperatures $U = 0$.