

1. (i) Before ligand binding:

O				O
	O			
		O		
			O	
O				O

After ligand binding:

O				O
	O			
			O	
O				O

Entropy: $S = k_b \ln W$, $k_b = 1.381 \times 10^{-23} J/K$.

Let subscript 0 represent before ligand binding and subscript 1 represent after ligand binding.

$$W = \frac{\Omega!}{L!(\Omega! - L!)}$$

$$W_0 = \frac{25!}{7!18!} = 480,700$$

$$W_1 = \frac{25!}{6!19!} = 177,100$$

$$S_0 = k_b \ln 480700 = 13.08k_b = 1.806 \times 10^{-22} J/K$$

$$S_1 = k_b \ln 177100 = 12.08k_b = 1.668 \times 10^{-22} J/K$$

- (ii)
- $\Delta S = S_1 - S_0$
- . Using the S values from part (i),

$$\Delta S = (12.08 - 13.08) \times k_b$$

$$\Delta S \approx k_b = 1.381 \times 10^{-23} J/K$$

- (iii) From part (ii), the entropy change is negative which is **unfavourable**. However, ligand binding could still be spontaneous if the entropic loss could be balanced by lower binding energy.
- (iv) Let $\varepsilon_{sol}, \varepsilon_b$ be the energies of solution and ligand binding, respectively. There are $L = 7$ ligands available to bind. The partition function weights are:

$$\text{Before ligand binding case: } W_0 e^{-\frac{L\varepsilon_{sol}}{k_b T}} = 480700 e^{-\frac{7\varepsilon_{sol}}{k_b T}}$$

$$\text{After ligand binding case: } W_1 e^{-\frac{(L-1)\varepsilon_{sol} + \varepsilon_b}{k_b T}} = 177100 e^{-\frac{6\varepsilon_{sol} + \varepsilon_b}{k_b T}}$$

Equating the weights and isolating for $\varepsilon_{sol} - \varepsilon_b$,

$$\begin{aligned}
 W_0 e^{-\frac{7\varepsilon_{sol}}{k_b T}} &= W_1 e^{-\frac{6\varepsilon_{sol} + \varepsilon_b}{k_b T}} \\
 \frac{W_0}{W_1} &= e^{-\frac{(6\varepsilon_{sol} + \varepsilon_b)}{k_b T} - (-\frac{7\varepsilon_{sol}}{k_b T})} \\
 \frac{W_0}{W_1} &= e^{\frac{\varepsilon_{sol} - \varepsilon_b}{k_b T}} \\
 \varepsilon_{sol} - \varepsilon_b &= k_b T \ln \frac{W_0}{W_1} \\
 \varepsilon_{sol} - \varepsilon_b &= k_b T \ln \frac{480700}{177100} \\
 \varepsilon_{sol} - \varepsilon_b &= k_b T
 \end{aligned}$$

Therefore, ligand binding energy needs to be $1k_b T$ less than solution energy to counter the entropic loss.

2. From Fig. 7.21 in the textbook, $\varepsilon = 2k_b T$ and $\Delta\varepsilon = 0; -2k_b$; and $-4k_b T$.

The grand partition function is:

$$Z = 1 + 2e^{(-\beta(\varepsilon_T - \mu))} + e^{(-\beta(2\varepsilon_T - 2\mu))} + e^{-\beta\varepsilon}(1 + 2e^{-\beta(\varepsilon_R - \mu)}) + e^{-\beta(2\varepsilon_R - 2\mu)}$$

Rearranging to group terms by ligand molecules bound,

$$Z = [1 + e^{-\beta\varepsilon}] + [2e^{-\beta(\varepsilon_T - \mu)} + 2e^{-\beta(\varepsilon + \varepsilon_R - \mu)}] + [e^{-\beta(2\varepsilon_T - 2\mu)} + e^{-\beta(\varepsilon + 2\varepsilon_R - 2\mu)}] \quad (1)$$

Writing expressions for p_0 , p_1 and p_2 ,

$$p_0 = \frac{1 + e^{-\beta\varepsilon}}{Z} \quad (2)$$

$$p_1 = \frac{2e^{-\beta(\varepsilon_T - \mu)} + 2e^{-\beta(\varepsilon + \varepsilon_R - \mu)}}{Z} \quad (3)$$

$$p_2 = \frac{e^{-\beta(2\varepsilon_T - 2\mu)} + e^{-\beta(\varepsilon + 2\varepsilon_R - 2\mu)}}{Z} \quad (4)$$

Let $\Delta\varepsilon = \varepsilon_R - \varepsilon_T$, such that $\varepsilon_R = \Delta\varepsilon + \varepsilon_T$. Substituting $\varepsilon_R = \Delta\varepsilon + \varepsilon_T$ into (1),

$$Z = 1 + e^{-\beta\varepsilon} + 2e^{-\beta(\varepsilon_T - \mu)} + 2e^{-\beta(\varepsilon + \Delta\varepsilon + \varepsilon_T - \mu)} + e^{-\beta(2\varepsilon_T - 2\mu)} + e^{-\beta(\varepsilon + 2\Delta\varepsilon + 2\varepsilon_T - 2\mu)} \quad (5)$$

Similarly, substituting $\varepsilon_R = \Delta\varepsilon + \varepsilon_T$ into (2)-(4),

$$p_0 = \frac{1 + e^{-\beta\varepsilon}}{Z} \quad (6)$$

$$p_1 = \frac{2e^{-\beta(\varepsilon_T - \mu)} + 2e^{-\beta(\varepsilon + \Delta\varepsilon + \varepsilon_T - \mu)}}{Z} \quad (7)$$

$$p_2 = \frac{e^{-\beta(2\varepsilon_T - 2\mu)} + e^{-\beta(\varepsilon + 2\Delta\varepsilon + 2\varepsilon_T - 2\mu)}}{Z} \quad (8)$$

Let $x = \frac{c}{c_0} e^{-\beta(\varepsilon_t - \mu_0)}$. Rewriting (5)-(8) in terms of x ,

$$Z = 1 + e^{-\beta\varepsilon} + 2x(1 + e^{-\beta(\varepsilon + \Delta\varepsilon)}) + x^2(1 + e^{-\beta(\varepsilon + 2\Delta\varepsilon)}) \quad (9)$$

$$p_0 = \frac{1 + e^{-\beta\varepsilon}}{Z} \quad (10)$$

$$p_1 = \frac{2x(1 + e^{-\beta(\varepsilon + \Delta\varepsilon)})}{Z} \quad (11)$$

$$p_2 = \frac{x^2(1 + e^{-\beta(\varepsilon + 2\Delta\varepsilon)})}{Z} \quad (12)$$

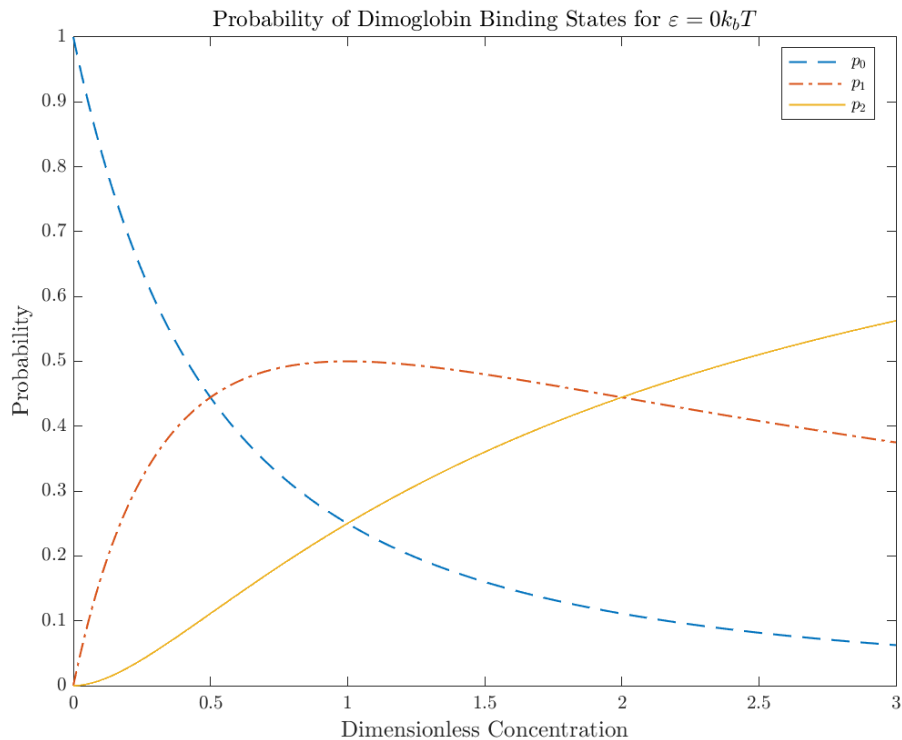
By definition, $\beta = \frac{1}{k_b T}$. From the question, $\varepsilon = 2k_b T = 2\beta^{-1}$. Substituting β, ε into (9)-(12),

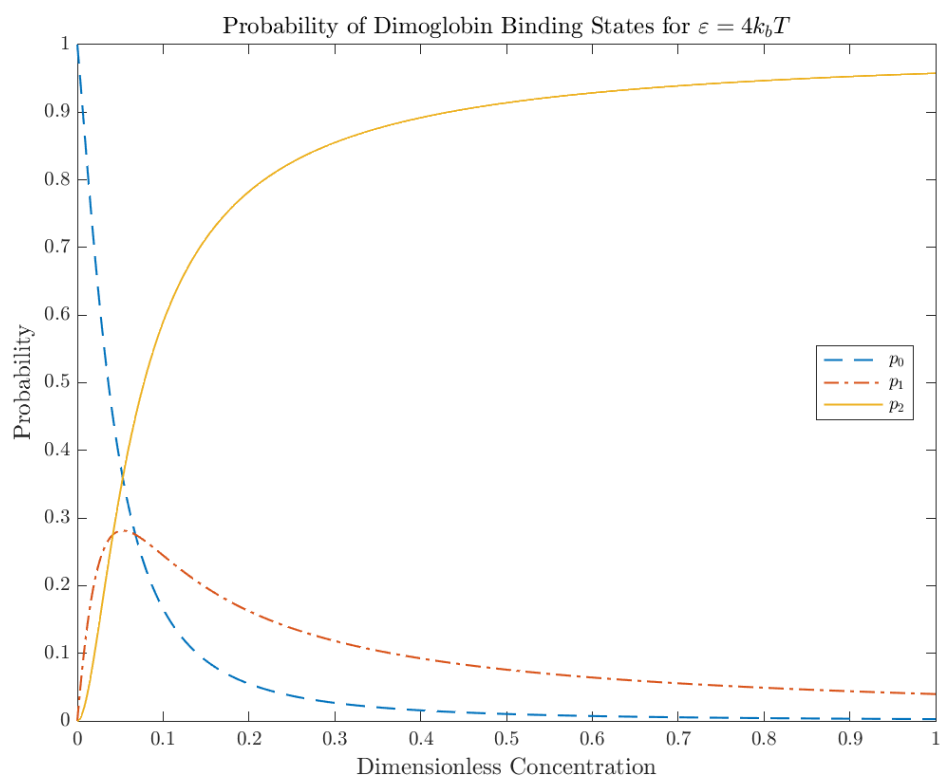
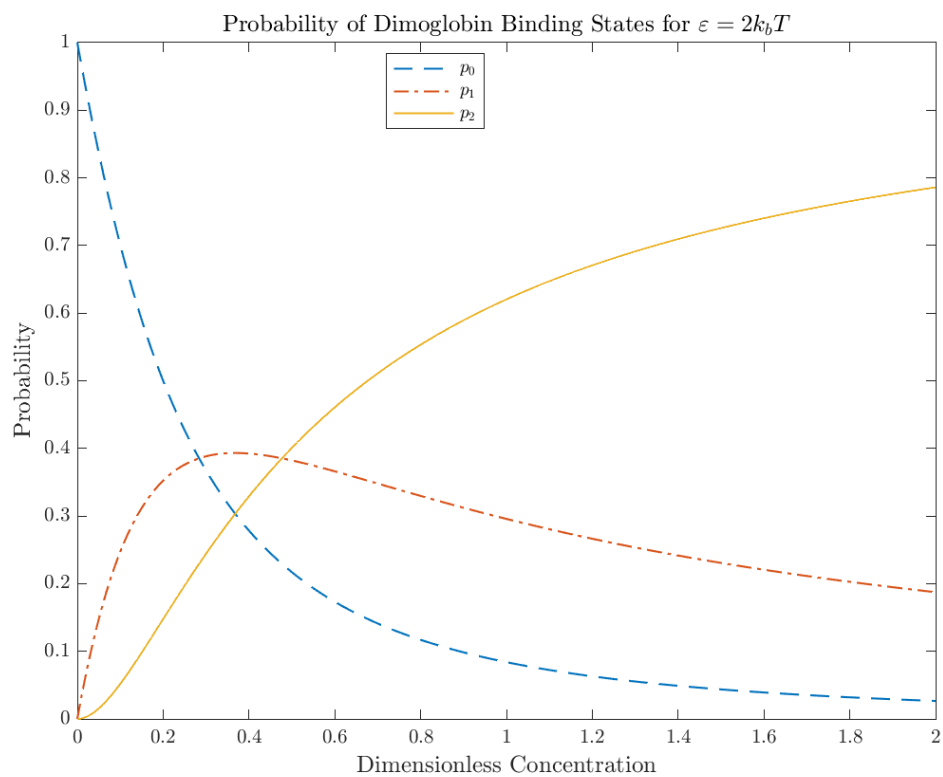
$$Z = 1 + e^{-2} + 2x(1 + e^{-(2 + \frac{\Delta\varepsilon}{k_b T})}) + x^2(1 + e^{-(2 + \frac{2\Delta\varepsilon}{k_b T})}) \quad (13)$$

$$p_0 = \frac{1 + e^{-2}}{Z} \quad (14)$$

$$p_1 = \frac{2x(1 + e^{-(2 + \frac{\Delta\varepsilon}{k_b T})})}{Z} \quad (15)$$

$$p_2 = \frac{x^2(1 + e^{-(2 + \frac{2\Delta\varepsilon}{k_b T})})}{Z} \quad (16)$$





3. (a) This protein has 3 possible open conformations and 1 possible closed conformation. At temperature T :

- i. The energetic weight for the open conformation is $e^{-\frac{\epsilon}{k_b T}}$. Since there are 3 open conformations with the same energetic weight, these 3 conformations can be summed up into a total open weight, $3e^{-\frac{\epsilon}{k_b T}}$
- ii. The energetic weight for the closed conformation is $e^{-\frac{0}{k_b T}} = 1$. Since there is only one closed conformation, the total closed weight is 1.
- iii. The partition function is the sum of the two total weights,

$$Z = 1 + 3e^{-\frac{\epsilon}{k_b T}}$$

Therefore, the probability p_o of finding the protein in an open conformation is:

$$p_o = \frac{3e^{-\frac{\epsilon}{k_b T}}}{1 + 3e^{-\frac{\epsilon}{k_b T}}} = \frac{3e^{-\frac{\epsilon}{k_b T}}}{Z}$$

The probability p_c of finding the protein in a closed conformation is:

$$p_c = \frac{1}{1 + 3e^{-\frac{\epsilon}{k_b T}}} = \frac{1}{Z}$$

- (b) The behaviour of p_c at very low and very high temperatures can be examined using limits:

$$\begin{aligned} \lim_{T \rightarrow \infty} p_c &= \frac{1}{4} \\ \lim_{T \rightarrow 0} p_c &= 1 \end{aligned}$$

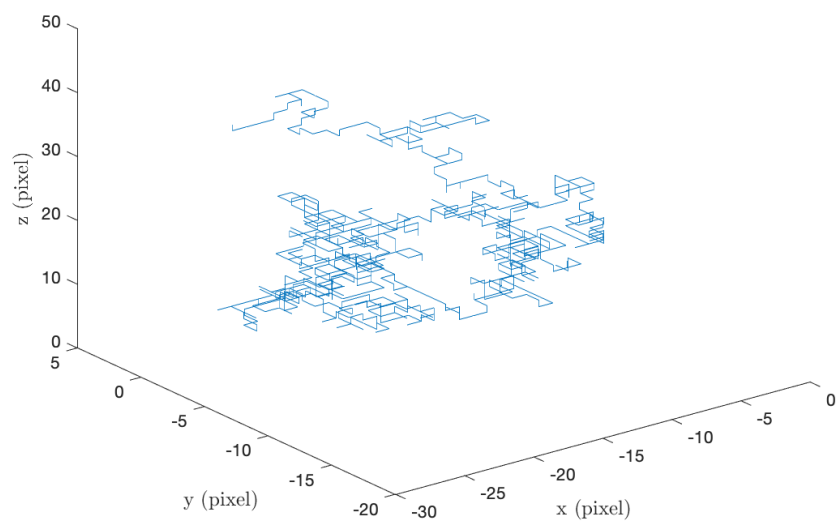
Therefore, at very high temperatures, p_c approaches 0.25 and the protein would be equally likely in any of the 4 conformations. At very low temperatures, p_c approaches 1 and the protein would only be found in the closed state.

- (c) The average energy of the molecule at temperature T is:

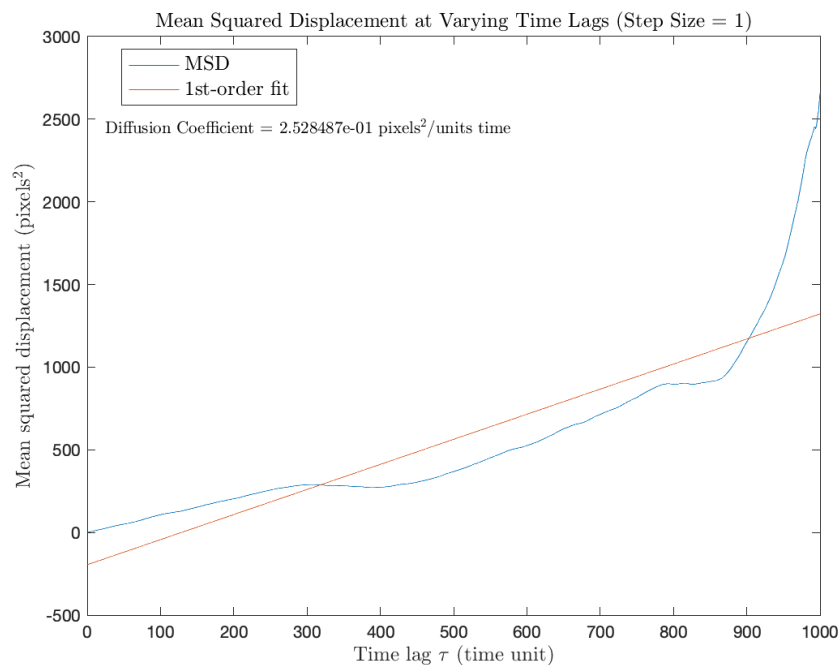
$$\langle E \rangle = \sum_i \epsilon_i p_i = \epsilon p_o + 0 p_c = \frac{3\epsilon e^{-\frac{\epsilon}{k_b T}}}{1 + 3e^{-\frac{\epsilon}{k_b T}}} = \frac{3\epsilon e^{-\frac{\epsilon}{k_b T}}}{Z}$$

4. (a) See figure below.

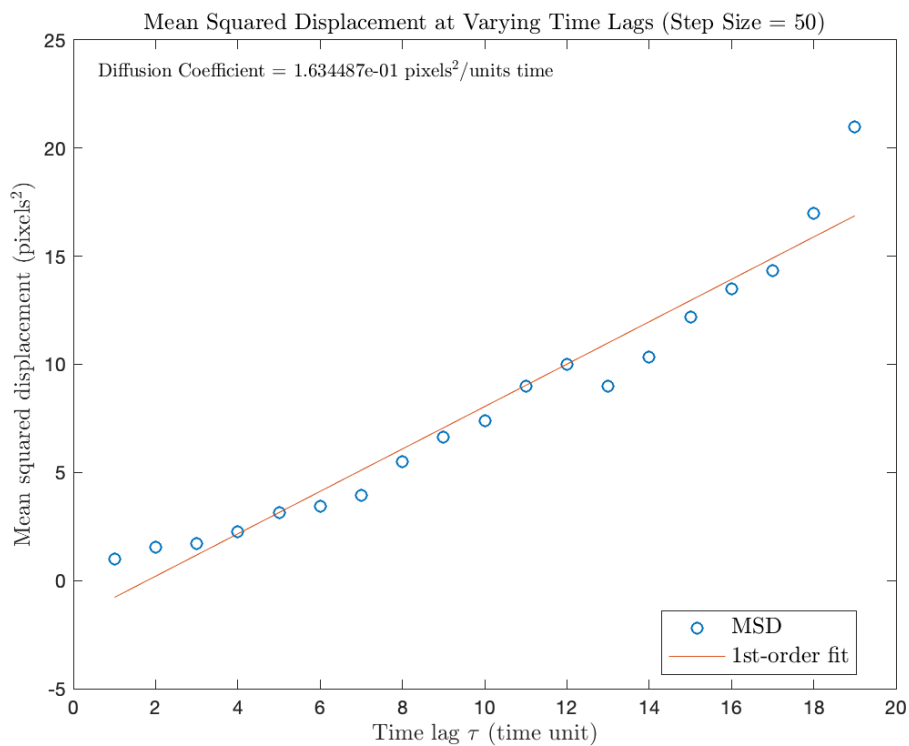
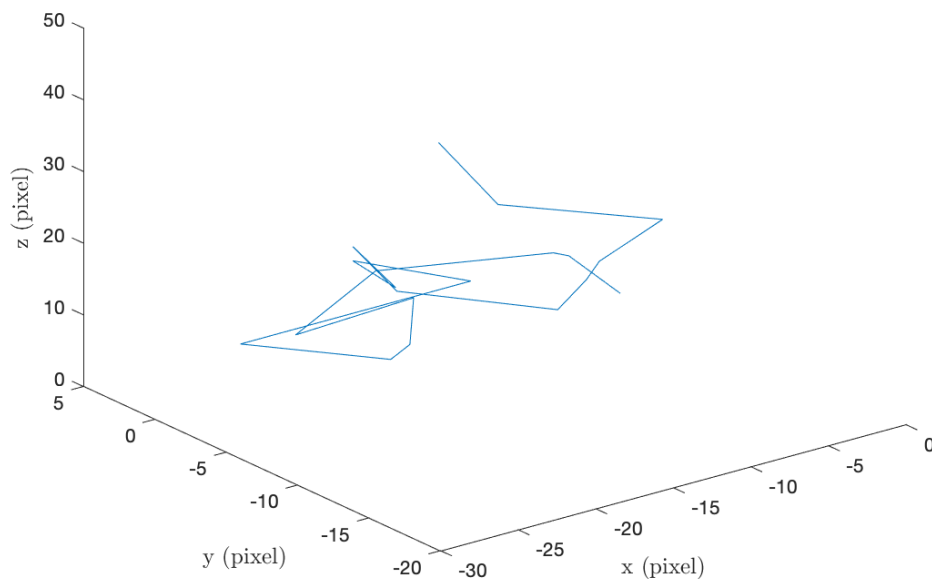
3D Random Walk Trajectory for N = 1000 Steps (Step Size =1)



- (b) See figure below. Diffusion coefficient is $\frac{1}{6}$ of the slope of the linear fit. Here, the diffusion coefficient is $2.528 \times 10^{-1} \text{ pixels}^2/\text{unit time}$.



3D Random Walk Trajectory for N = 1000 Steps (Step Size = 50)



(c) See figure below. The diffusion coefficient here is $1.634 \times 10^{-1} \text{ pixels}^2/\text{unit time}$. It is within the same order of magnitude as in 4(b).

(d) See figure below.

