Q1. (25 Points)
The interaction energy between neutral atoms can be described by the Lennard-Jones potential, which is given by:

$V = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$, and F is –dV/dr

where V is the energy, F is the force, and r is the interatomic distance. Consider atoms with $\varepsilon$ = 1.23 kJ/mole and $\sigma$ = 3.82 Å.

(a) Consider two atoms that are 3.5 Å apart. Calculate the force on one of the atoms, using the Lennard-Jones potential. (20 points)

(b) What condition must the force satisfy for the energy of the two atoms to be at a minimum? (5 points)

a) $F = \frac{-dV}{dr}$

$= -\left(4\varepsilon\left(-12\sigma^{12}\left(\frac{1}{r}\right)^{13} - (-6)\sigma^{6}\left(\frac{1}{r}\right)^{7}\right)\right)$

$= -4\left(1.23\frac{kJ}{mol}\right)\left[-12(3.82\text{Å})^{12}\left(\frac{1}{3.5\text{Å}}\right)^{13} + 6(3.82\text{Å})^{6}\left(\frac{1}{3.5\text{Å}}\right)^{7}\right]$

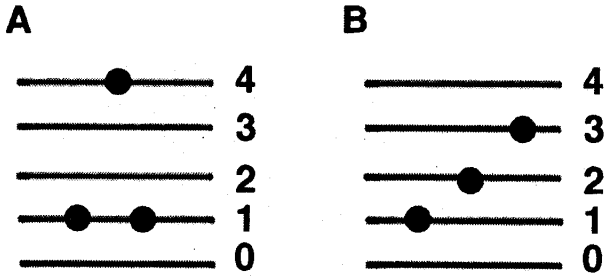
$= -4.92\frac{kJ}{mol}\left[-9.79\text{Å}^{-1} + 2.89\text{Å}^{-1}\right]$

$= 33.95\frac{kJ}{mol\text{Å}}$ $= 5.64\times10^{-23}\frac{kJ}{\text{Å}}$ per Atom

$= 5.64\times10^{-10}$ N

b) $\frac{dV}{dr} = 0$ and $\frac{d^2V}{dr^2} > 0$

Q 2. (25 points)
Consider a system of three identical and independent molecules, with energy levels that have values 0,1,2,3, ...(arbitrary units of energy).
Consider two states of the system, A and B, shown below. States A and B have equal energy (6 units). State A has one molecule in level 4 and two in level 1. State B has 1 molecule each in levels 1, 2 and 3. The multiplicity, W, of each state is given by N! / (n1! x n2! x n3! ...x nj! x....), where N is the number of molecules and nj is the number of molecules in state j.




(A) Calculate the relative probability of observing the molecules in configuration A over configuration B. (10 points)

State A : $N = 3 \quad n_0 = 0, n_1 = 2, n_2 = 0, n_3 = 0, n_4 = 1$

$$W_A = \frac{3!}{2!\,1!} = 3$$

State B $\quad N = 3 \quad n_0 = n_4 = 0 \quad n_1 = n_2 = n_3 = 1$

$$W_B = \frac{3!}{1!\,1!\,1!} = 6$$

Relative probability of observing the molecules in configuration A over B $= \frac{P_A}{P_B} = \frac{W_A}{W_B} = \frac{3}{6} = \boxed{\frac{1}{2}}$

(B) What is the change in entropy in going from state A to state B (assume $k_b$=1). (5 points)

$W_A = 3 \longrightarrow S_A = k_b \ln W_A = \ln 3$

$W_B = 6 \longrightarrow S_B = k_b \ln W_B = \ln 6$

$$\underline{\Delta S} = S_B - S_A = \ln 6 - \ln 3 = \underline{\ln 2}$$

Entropy increases in going from state A to state B.

Q2, continued.

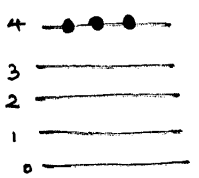
(C) Assume that the 3 molecules in the system have access to only the 5 energy levels shown above. When the total energy of all 3 molecules is increased to the maximum possible value, explain whether the entropy increases or decreases with respect to state B. (5 points).

Total energy = 12 units $n_0 = n_1 = n_2 = n_3 = 0$ $n_4 = 3$ $N = 3$

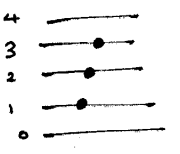
$$W = \frac{3!}{3!} = 1$$

$$S = k_B \ln W = 0$$

Entropy decreases with respect to state B.



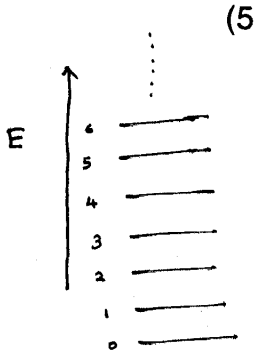

Ordered state




State B

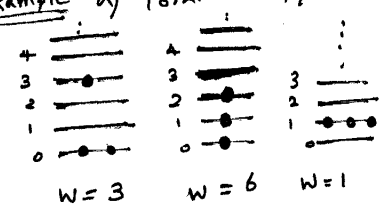
Disordered state.

(D) Next, assume that the system has an infinite number of possible energy levels of increasing energy. In this case, when the total energy of the 3 molecules is increased does the entropy always increase, or does it sometimes increase and sometimes decrease? Explain your answer. (5 points).



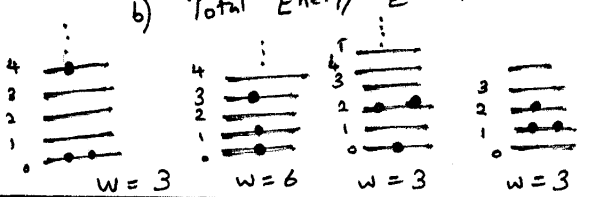

When the total energy of the 3 molecules is increased entropy always increases. Total # of configurations of the system with energy E increases as E is increased.

example a) Total energy $E = 3$




$\Rightarrow W_{total} = 10$ $S = k_B \ln W_{total} = \ln 10$

b) Total Energy $E = 4$



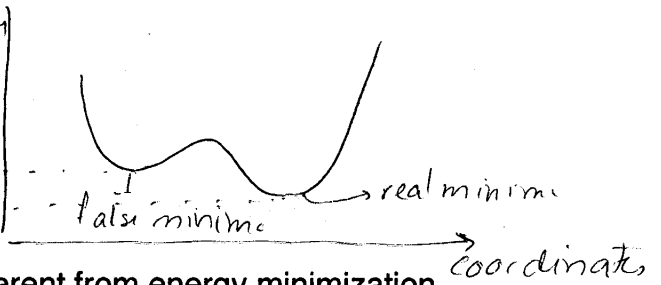

$\Rightarrow W_{total} = 15$ $S = k_B \ln W_{total} = \ln 15$

Q 3. (25 points)
Computer programs can easily minimize the energy of a molecule, such a protein. These programs work by changing the conformation of the molecule so that the potential energy of the molecule is at a minimum for such conformations.

(a) Explain why energy minimization fails to generate the properly folded and stable structure of complex molecules, such as proteins, starting from the unfolded structure (10 points).

Energy minimization works down the potential energy gradient surface to find the minimum. While this procedure works for very simple systems, it fails to do so for large ones.
Large systems potential energy surfaces contain several minima and only the lowest corresponds to the real equilibrium geometry.

Energy minimization gets trapped in false minima and can't find the real one, unless the starting configuration is realy close to the real one.




(b) How are molecular dynamics simulations different from energy minimization calculations? Can such simulations be used today to generate the folded structure of a protein? Explain your answer (10 points).

Molecular Dynamics (MD) take both Potential and kinetic energy into account. It moves particles in short intervals of time according to the Force acting on a given particle. The kinetic energy allows the simulation to scape from those false minima and, in principle, allows us to find the real one once the whole surface has been sampled.
For large systems the surface is just too big to be sampled easily. Moreover MD is limited by the size of the time step that it can use.
Because of that, in order to generate the folded structure of a protein would require a lot of computer time to finish.

(c) Is quantum mechanics used in the calculation of energies in computer programs used to simulate protein molecules? Explain your answer. (5 points)

Pure Quantum Mechanics is not used to solve the whole folding problem for proteins because it is too expensive. However Quantum Mechanics can be used to calculate either parts of the protein (using embedding methods) or even the parameters used to run other methods such as MD, or points in the potential energy surface.

Q4. (25 points)

Consider a system with just two energy levels, 1 and 2. The system has 1 mole ($6.0 \times 10^{23}$) molecules distributed between these two energy levels, $E_1$ and $E_2$.

$k_B = 1.38 \times 10^{-23}\ JK^{-1}$

$E_1 = 0.0\ J$,

$E_2 = 3.0 \times 10^{-21}\ J$,

$$Q = \sum_{i=1}^{2} e^{-E_i/k_bT} = 1 + e^{-E_2/k_bT}$$ → 0.7246376 → 0.4845

$p_2 = e^{-E_2/k_bT}/Q$, where p2 is the probability of finding a molecule in level 2.

(a) Calculate the total energy of the system at equilibrium at a temperature of T=300 K (state A) (15 points).

$E_{total} = \sum p_i E_i$

$p_2 = e^{-3\times10^{-21}\,J/(1.38\times10^{-23}\,J/K)(300K)} / 1 + e^{-3\times10^{-21}/(1.38\ldots)}$

$p_2 = 0.3263725$

$\therefore p_1 = 0.6736275$

$E = 0.9791175 \times 10^{-21}\ J$

$587.47\ J$

(c) Is quantum mechanics used in the calculation of energies in computer programs used to simulate protein molecules? Explain your answer. (5 points)

Q4. (25 points)

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$$Q = \sum_{i=1}^{2} e^{-E_j/k_bT} = 1 + e^{-E_2/k_bT}$$

$p_2 = e^{-E_2/k_bT}/Q$, where p2 is the probability of finding a molecule in level 2.

(a) Calculate the total energy of the system at equilibrium at a temperature of T=300 K (state A) (15 points).

$P_2 = \dfrac{e^{-\epsilon_2/k_B T}}{Q}$

$Q = 1 + e^{-\epsilon_2/k_B T}$

$= 1 + 0.485$

$= \dfrac{0.485}{1.485}$

$= 0.326$

Total $E_T = P_1 N_A \epsilon_1 + P_2 N_A \epsilon_2$

$= 0 + 0.326 \times 6.022 \times 10^{23} \times 3 \times 10^{-21}$

$E_T = 589.4\ J$

Question 4, continued.
(b) The energy of the system is doubled with respect to the energy in part (a), and the system is allowed to reach equilibrium. Calculate the new temperature of the system at equilibrium. (10 points)

New total $E_T = 1178.8\,J$

$E_T = p_2 N_A E_2$

$\therefore p_2 = 0.652$

$$p_2 = 0.652 = \frac{e^{-E_2/k_B T}}{1 + e^{-E_2/k_B T}}$$

$$\therefore 0.652 + 0.652\, e^{-E_2/k_B T} = e^{-E_2/k_B T}$$

$$0.3475\, e^{-E_2/k_B T} = 0.652$$

$$e^{-E_2/k_B T} = 1.876$$

$$-\frac{E_2}{k_B T} = \ln 1.876$$

$$T = \frac{-E_2}{k_B \ln(1.876)}$$

$T = -345\,K$

- END OF EXAM