

PHYS 3511, Biological Physics, Assignment 4

Due Friday March 13, 2020. Read Philip Nelson's Biological Physics: Section 7.4 and 7.5. Read Class note on proteins and study powerpoint.

QUESTION 1 A large number of energetic cosmic-ray particles reach Earth's atmosphere continuously and knock electrons out of the molecules in the air. Once an electron is released, it responds to an electrostatic force, which is due to an electric field \mathbf{E} produced in the atmosphere by other point charges. Near the surface of Earth this electric field has a magnitude of $|\mathbf{E}| = 150 \text{ N/C}$ and is directed downward, as shown in Fig. 13.48. Calculate the change in electric potential energy of a released electron when it moves vertically upward through a distance $d = 650 \text{ m}$.

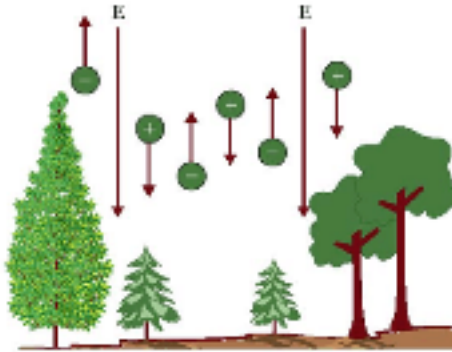


FIGURE 13.48

The electric energy of a test charge between two uniformly charged parallel plates is $E_{el} = q_{mobile} \frac{\sigma}{\epsilon_0} y$, and the magnitude of the electric field is $E = \frac{\sigma}{\epsilon_0}$.

QUESTION 2

Fig. 14.33 shows an electron at the origin that is released with initial speed $v_0 = 5.6 \times 10^6 \frac{m}{s}$ at an angle $\theta_0 = 45^\circ$ between the plates of a parallel plate capacitor of plate separation $D = 2.0 \text{ mm}$. If the potential difference between the plates is $\Delta V = 100V$, calculate the closest proximity of the electron to the bottom plate, d .

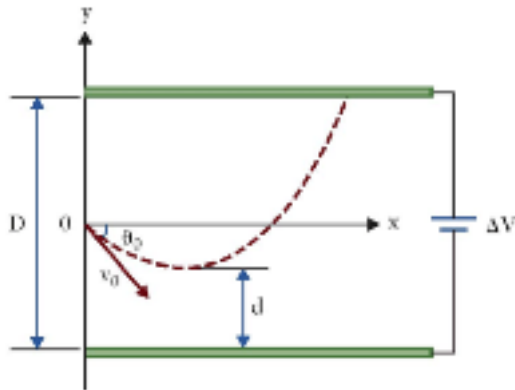


FIGURE 14.33

QUESTION 3 DNA in vivo. As discussed in class, DNA in cells are negatively charge, and are often modeled as a line charge with electric field strength $E = \frac{\kappa}{2\pi r\epsilon}$, where r is the distance from the line charge, $\epsilon = 80\epsilon_0$ is the dielectric constant in water, and κ is the charge per unit length (C/m). The electric field \vec{E} points towards the negatively charged DNA. Consider a single (+) counterion that is moved from a distance of a to R ($a < R$) from the line charge (DNA). The force on the charge is $F_e = -eE$, with the negative sign indicating that the force points toward the DNA. The change in internal energy ΔU equals negative the work done $\Delta U = -W_{a \rightarrow R} = -\int_a^R F_e dr = \int_a^R \frac{e\kappa}{2\pi r\epsilon} dr = \frac{e\kappa}{2\pi\epsilon} \ln\left(\frac{R}{a}\right)$. Using the idea that the entropy is $S = k_B \ln\Omega = k_B \ln(\pi r^2 l)$, where Ω is the volume accessible to the counterion located at a distance r away from the DNA, and l is the length of the DNA. As such the change in entropy in moving the counterion from distance a to R is $\Delta S = k_B \ln\left(\frac{\pi R^2 l}{\pi a^2 l}\right) = 2k_B \ln\frac{R}{a}$. A) Using the discussed information, **find the equation of the change in free energy $\Delta F = \Delta U - T\Delta S$.** B) If $\Delta F < 0$ then the (+) counterion would spontaneously move far away from the (-) DNA. Determine the condition for counterions to **distribute near** the DNA. C) Assume a DNA basepair has two negatively charge phosphate, and that the length of a basepair is 0.34 nm. Using the criterion of part B, determine the minimum temperature when the counterions will distribute about the DNA. **HINT:** For part B, find the condition for $\Delta F = 0$, and use $T = 300$ K, and determine κ , using the data that a bp of length 0.34 nm has a charge of $-2e$. The unit of κ , $\frac{C}{m}$.

QUESTION 4 Problem 7.7 from Philip Nelson's Biological physics
Effect of H-bonds on water

According to Section 7.5.1, the average number of H-bonds between a molecule of liquid water and its neighbors is about 3.5. Assume that these bonds are the major interaction holding liquid water together, and that each H-bond lowers the energy by about $9k_B T$. Find a numerical estimate for the heat of vaporization of water based on these ideas (see Problem 1.6), then compare your prediction to the actual value.

QUESTION 5 Electrophoresis In both part of this problem assume that the macromolecules are moving in a medium with the viscosity of water. A) Model a protein as a sphere of radius 2.5 nm, carrying a net electric charge of $q = 9e$, in pure water. If we apply an electric field $E = 4 \frac{V}{cm}$. How far will it move after 6 hours? B) In the experiment by Linus Pauling and coworkers, healthy hemoglobin and hemoglobin from patients with sickle-cell disease were evaluated with electrophoresis. An electric field of $E = 4.7 \frac{V}{cm}$ is applied for 20 hours, after which two bands appeared. It is known that the healthy cell is more negatively charged than the sickle cell. Assume that there is a charge difference of $-e$ and a cell diameter of $-7.5 \mu m$. What is the separation between the bands? Which band traveled farther? Repeat for $E = 20 \frac{V}{cm}$ and 48 hours? Comment.

QUESTION 6 Levinthal's Paradox two ways: The TrpCage protein is a 20 amino acid (aa) residue peptides that was at one time the fastest folding protein. It can fold from an unstructured unfolded **U** state to a compact native, **N**, state in $\tau_{fold} = 4\mu s$.

- A) Assume that each of the $N = 20$ amino acid (aa) of the TrpCage can assume 2 conformation leading to a total conformation of 2^N for the protein. Assume as Levinthal did, that the **N** state is associated with only **one** of these 2^N conformations. If it takes 1 picosecond = $10^{-12} s$ for an aa to change conformation, estimate the time it would take for the protein to reach the folded **N** state. Compare this with the actual folding time of $\tau_{fold} = 4\mu s$. **NOTE:**
- i) $2 = 10^{0.301}$; you should find that here the approximation is not too bad!
- B) In 2006, Rose et al presented a better theory (*Proc Natl Acad Sci USA* 103:1744– 1749, 2006), where it is argued that Ramachandran plots show that aa occupy **nine** distinct conformations. In this case the total number of conformation should be 9^N . Estimate the folding time and comment.

ANSWER: $10^7 s$

IMPORTANT POINT: Since the TrpCage is small it may be possible to do your calculation directly with a calculator. Also note $9 \sim 10^{0.954}$.

QUESTION 7 Debunking the Levinthal's Paradox with Thermodynamics: A thermodynamics study at $T = 25^\circ C$ of the **TrpCage** protein (a 20-residue protein) found that when the protein unfolds from the native state (N) to the unfolded state (U), $\Delta H = 56 kJ / mol$, and $\Delta G = 3 kJ / mol$, where $\Delta G = G_U - G_N$, with G_U and G_N being the Gibb's free energy of the U and N states, respectively.

- a) Calculate $\Delta S = S_U - S_N$, where S_U and S_N are the Gibb's entropy of the U and N states, respectively.

ANSWER: $178 J / K \cdot mol$

- b) Use the definition $S_i = R \ln \Omega_i$, with $R = 8.314 J / K \cdot mol$, where Ω_i is the number of conformation per protein. Assuming that the number of conformation of the native state is $\Omega_N = 1$, find the number of conformation for the unfolded state Ω_U .

ANSWER: 2×10^9 conformations

Use the Levinthal's argument, and assume that each conformation step, in the random search to go from the U state to the single-conformation N state, takes about a picosecond or $10^{-12} s$. Estimate the average folding time of the TrpCage. Compare this with the actual folding time of $t_{fold} = 4.0\mu s$.

QUESTION 8 Modified Levinthal's model. This question is based on the work of Leandro Martinez (Journal of Chemical Education, 2014, 91, 1918–1923). Assume that on average after a period of τ , each amino acid experience a perturbation in which will be in the **correct conformation (c)** with probability α , or be in the

incorrect conformation (i) with probability $1 - \alpha$. It can be shown that after a time t , the protein will be in the **unfolded (U) state** with probability $P_U(t) = (1 - \alpha^N)^{t/\tau}$, and that it will be in the **folded native (N) state** with probability: $P_N(t) = 1 - P_U(t)$. It can be shown that the folding time is the time, $t_{1/2}$ when the protein has a 0.5 probability of being in the N state gives: $0.5 = (1 - \alpha^N)^{t_{1/2}/\tau} \rightarrow t_{1/2} = \tau \frac{-0.693}{\ln(1 - \alpha^N)}$. For a

folding -funnel landscape (i.e. biased to the N state) we find $0.5 < \alpha < 1$.

A) For the TrpCage, assume $\tau = 10^{-12} s$, $t_{1/2} = \tau_{fold} = 4 \mu s$ the experimental folding time. Using $N = 20$ (number aa for TrpCage), calculate α .

ANSWER: $\alpha = 0.459$ Note that this is unusual as for most proteins $\alpha > 0.5$, but the TrpCage is not a natural protein. In fact it is much smaller than most proteins, which account for the unprotein-like answer that we get for question 4.

B) Assume that the probability of an aa being in the **c conformation** is

$P_c = \alpha = A \exp(-E_c / RT)$, where A is a constant, E_c the internal energy of the aa in the c conformation, and $R = 8.314 J \cdot K^{-1} \cdot mol^{-1}$ is the gas constant.

Similarly, the probability of an aa being in the **i conformation** is

$P_i = 1 - \alpha = A \exp(-E_i / RT)$, where A is a constant, E_i the internal energy of

the aa in the i conformation. Taking the ratio, $\frac{P_c}{P_i} = \frac{\alpha}{1 - \alpha} = \exp\left(-\frac{\Delta E_{ci}}{RT}\right)$, which

gives $\Delta E_{ci} = E_c - E_i = -RT \ln\left(\frac{\alpha}{1 - \alpha}\right)$. Use your answer from part A, to

calculate ΔE at room temperature for the TrpCage protein. Compare your answer to the result of part B of question 3. **NOTE:** For the comparison calculate ΔE of question 3 to internal energy per aa.

Partial Answer: you should get $\Delta E_{ci} > 0$.