

Answer all questions. Answers should be brief and to the point and all important statements/assumptions should be clearly stated/explained.

Section I (Multiple Choice Questions)

1. The minimum number of entities required to generate an oscillatory biological circuit is (1)

- a) 2
- b) 3
- c) 1
- d) 4

Ans: a

2. Calculate the Reynold's number for a fish of size 10 cm swimming through water at a speed of 1 m/s. Assume viscosity of water to be 1 cP. (1)

- a) 10^3
- b) 10^5
- c) 10^6
- d) 10^4

Ans: b

3. Assuming diffusion constant of a small molecule in water to be $10^{-9} \text{ m}^2/\text{s}$, calculate how much distance the molecule will wander in a minute. (1)

- a) 1 m
- b) 6 μm
- c) 500 nm
- d) 600 μm

Ans: d

4. For a (μ , p, T) ensemble, chemical equilibrium requires (1)

- a) thermal equilibrium
- b) mechanical equilibrium
- c) both a & b
- d) none of these

Ans: c

5. The maximum volume of a rectangular box subject to the constraint surface area = 1/3 is (1)

- a) 1/27
- b) 1/9
- c) 1/81
- d) 1/3

Ans: Give full marks if student have used right approach.

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SECTION II

6. Calculate the diffusion coefficient (D) of a protein (in units of $\mu\text{m}^2/\text{sec}$) whose diameter is 5 nm at a temperature of 300 K. Assume the viscosity of the solution to be 1 cP. Estimate the time it takes for the protein to diffuse the distance of 10 cm. For molecular motors that hydrolyze ATP and move along the cytoskeletal filament with a speed of 1 $\mu\text{m}/\text{sec}$, how long does it take to reach 10 cm? After what time does directed motion become more efficient than diffusion?

(2+2+2+2)

Solution:

$$D = kT/6\pi\eta a$$

a) At room temperature, $kT = (4.1 \text{ pN}\cdot\text{nm}) / (6\pi \cdot 10^{-2} \text{ g/cm}\cdot\text{sec}) \cdot 2.5 \text{ nm} = 87 \mu\text{m}^2 / \text{sec}$

In 3D, $r^2 = 6Dt$

Hence, $t = r^2/6D = (10 \text{ cm})^2 / (6 \cdot 87 \cdot 10^{-7} \text{ cm}^2/\text{sec}) = 2 \cdot 10^7 \text{ seconds}$

The protein will take $2 \cdot 10^7$ seconds to traverse a 10 cm distance if its motion is solely diffusion driven.

b) When the velocity generated by the molecular motors is 1 $\mu\text{m}/\text{sec}$, the protein would travel the distance of 10 cm in 10^5 seconds.

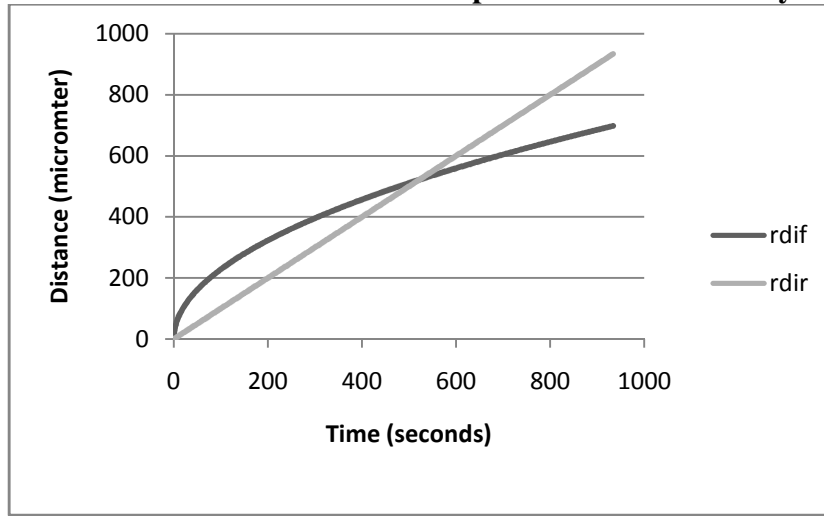
c) $r_{\text{dif}} = (6Dt)^{1/2}$

$r_{\text{dir}} = vt$

Now, when $t = t^*$, $r_{\text{dif}} = r_{\text{dir}}$

Hence $6D/v^2 = t^* = 522 \text{ seconds}$

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7. If we have an mRNA that is needed at the level of ten copies per cell on average and the half-life of the mRNA in cytoplasm is ten minutes, then what fraction of the time will the gene remain active? Assume that the polymerase makes RNA at a rate of 20b/sec, that the original message is 6000 bases long, and that the next polymerase can start after the previous polymerase has moved 500 bp.

(4)

Answer:

Half-life of 10 minutes means that 5 of 10 molecules will be degraded and system needs constant supply of 5 molecules every 10 minutes.

$L=6000$ bp, rate of synthesis is $v=20\text{bp/s}$, so time of synthesis is $T=L/v=300\text{s}$.

Time between moment of transcription initiations $t=500\text{bp}/v=25\text{s}$.

5th copy of RNA will be start to be synthesized in 100th second after beginning of synthesis of the first RNA molecule, and will finish synthesis in next $T=300\text{s}$, so cycle for synthesis of 5 molecules is $t+T=400$ s. And the gene should be activated $400\text{s}/10\text{min}=\sim 66\%$ of time.

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8. Figure to the right represents the replication process of fly DNA.

Estimate the fraction of total fly DNA represented in the adjoining micrograph picture. Size of the total fly DNA is 1.8×10^8 base pairs. Also estimate the number of DNA polymerase molecules in a eukaryotic cell of a fly. There are 8 replication forks in the micrograph. Estimate the DNA length between fork 4 and 5. Start counting from bottom of the figure. The speed with which a replication fork moves is 40 bp/s. Estimate the time taken for the forks to collide.
(2+2+2+2)

Solution

a) Number of base pairs = 1.8×10^8 base pairs = $1.8 \times 10^8 \times 3.4 \text{ \AA} = 6 \times 10^4 \text{ \mu m}$.

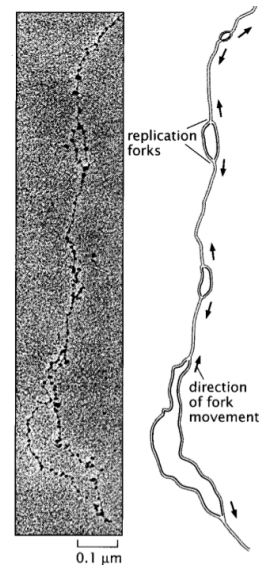
Approximate length of DNA shown in the figure is 1.3 μm .

Hence, the fraction of DNA shown = 2×10^{-5} fraction

b) Here we see 8 forks in 2×10^{-5} fraction of DNA. Also, each fork has 2 DNA Polymerases working. Hence, for the total length of DNA to be replicated, $16 \times 1/2 \times 10^{-5} = 8 \times 10^{-5}$ DNA polymerases will be used.

c) Distance between fork 4 and 5 is approximately 0.3 μm = 10^3 base pairs. Assuming the rate to be 40bp/s, two forks moving in opposite directions will work at 80bp/s. Thus, it will take 12 seconds for the two forks to collide.

d) Assuming that the forks are homogeneously distributed across the length of the DNA, the time taken for replication to complete is 12 seconds. The mean distance between forks being 0.3 μm .



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9. Prove that maximum entropy for constant average energy (i.e., $\langle E \rangle = \sum p_i E_i$) predicts $p_i = e^{-E_i/k_B T}$ where p_i is the probability associated with i 'th state and E_i is the corresponding energy requirement. (6)

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$$q, S = -k_B \sum p_i \ln p_i \quad U = \sum p_i E_i$$

$$dU = \sum E_i dp_i \text{ (as microscopic energy states depend on } V \& N, \text{ but not on } T)$$

$$dF = dU - Tds \quad \sum p_i = 1$$

Thus, we want the probability distribution that satisfies $dF = 0$ s.t. $\sum p_i = 1$. The constraint can be written as $\alpha \sum dp_i = 0$ where α is the Lagrange Multiplier.

$$\text{Thus we have, } \sum [E_i + k_B T (1 + \ln p_i) + \alpha] dp_i = 0$$

$$\Rightarrow \ln p_i = -E_i/k_B T - \alpha/k_B T - 1$$

$$p_i = \frac{e^{-E_i/k_B T - (\alpha/k_B T) - 1}}{e}$$

$$\sum p_i = 1 \Rightarrow p_i = \frac{e^{-E_i/k_B T}}{Z} \quad \text{where } Z = \sum e^{-E_i/k_B T}$$

Full Marks: 50

Total Time: 120 mins

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10. Derive the expression for entropy (S) of a system in terms of the average energy ($\langle E \rangle$), the temperature (T) and the partition function (Z). (6)

$$\begin{aligned}
 10. \quad S &= -k_B \sum p_i \ln p_i \\
 p_i &= \frac{e^{-\beta E_i}}{Z} \quad \text{where } \beta = \frac{1}{k_B T} \\
 \text{Thus,} \quad S &= -k_B \sum \left\{ \frac{e^{-\beta E_i}}{Z} \right\} \left\{ -\beta E_i - \ln Z \right\} \\
 \Rightarrow S &= -k_B \sum \frac{e^{-\beta E_i}}{Z} \times E_i \\
 &\quad + k_B \sum \frac{e^{-\beta E_i}}{Z} \ln Z \\
 &= k_B \times \frac{1}{k_B T} \sum p_i E_i \\
 &\quad + k_B \frac{\ln Z}{Z} \sum e^{-\beta E_i} \\
 &= \frac{\langle E \rangle}{T} + k_B \frac{\ln Z}{Z} \times Z \\
 &= \langle E \rangle / T + k_B \ln Z \\
 \text{Thus,} \quad &\boxed{S = \langle E \rangle / T + k_B \ln Z}
 \end{aligned}$$

11. Write the differential form of the fundamental equation of entropy. Assuming $dU = TdS - pdV + \sum_{j=1}^N \mu_j dN_j$, determine the expression for entropy $S(V)$ for an ideal gas ($pV = NkT$). How would the entropy change if the volume doubles? (6)

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$$11. \text{ we have } dU = TdS - PdV + \sum \mu_i dN_i$$

$$\Rightarrow dS = \frac{dU}{T} + (P/T)dV - \sum \mu_i/T dN_i$$

$$\text{Thus, } \left. \frac{\partial S}{\partial V} \right|_{U, N} = P/T$$

$$\text{For an ideal gas, } PV = NkT$$

$$\Rightarrow P/T = Nk/V$$

$$\text{Thus } \frac{\partial S}{\partial V} = Nk/V$$

$$\Rightarrow S = Nk \ln V$$

$$\text{Thus } S_2/S_1 = \frac{\ln V_2}{\ln V_1}$$

$$\frac{S_2}{S_1} = \frac{\ln 2V_1}{\ln V_1} = 1 + \frac{\ln 2}{\ln V_1}$$

12. In an experiment, dimerization of two single protein molecules was investigated. The dimer was found to have two states with protein molecules either 3 nm apart or 2 nm apart. Assuming the interaction energy is given by $k(x - x_0)^2$, where x is the distance between the two protein molecules, $x_0 = 2\text{ nm}$ and $k = 1\text{ k}_B\text{T/nm}^2$, calculate the partition function and probabilities associated with the two states. Repeat the above three calculations assuming $k = 0$. (6)

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12.

There are two states,

E_1 (state 1, 3 nm apart)

$$= k [(3-2)^2] = k = 1 k_B T$$

E_2 (state 2, 2 nm apart) $= 0$

$$Z = e^{-E_1/k_B T} + e^{-E_2/k_B T}$$

$$= e^{-1} + e^0 = 1 + e^{-1}$$

$$p_1 = \frac{e^{-1}}{1 + e^{-1}} \quad p_2 = \frac{1}{1 + e^{-1}}$$

$$p_1 < p_2$$

when $k = 0$,

$$E_1 = E_2 = 0 \Rightarrow p_1 = p_2 = 1/2$$

13. Consider a thought experiment of melting double-stranded DNA. Imagine a 3 base pair (bp) DNA at temperature T . The DNA can be in one of the following two states: (i) all base pairs are

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intact. (ii) two base pairs are broken, and one is intact. Calculate entropy for each state. If energy associated with each base pair formation is $100 k_B$, which of the states will be preferred at temperatures of $T=100$ K and $T=1000$ K, respectively? (6)

13. State 1 = all base pairs are intact

$$W_1 = 1$$

State 2 = 2 bp's are broken

$$W_2 = 3 \quad \left(\begin{array}{|c|} \hline \text{---} \\ \hline \text{---} \\ \hline \end{array}, \begin{array}{|c|} \hline \text{---} \\ \hline \text{---} \\ \hline \end{array}, \begin{array}{|c|} \hline \text{---} \\ \hline \text{---} \\ \hline \end{array} \right)$$

$$S_1 = k_B \ln 1 = 0 \quad S_2 = k_B \ln 3$$

$$F_1 = E_1 - TS_1 = 300 k_B - T \quad F = \text{Free Energy}$$

$$F_2 = E_2 - TS_2 = 100 k_B - k_B T \ln 3$$

At $T=100$ K, $F_2 = -0.09 \times 100 k_B < F_1$
 At $T=1000$ K, $F_2 > F_1 \Rightarrow$ State 1 is preferred at 1000 K