

## Chapter 2

2.1. If no bias then 50:50, but if one or both isomers are autocatalytic then simple rate equation indicates that steady state solution converges to one of the isomer populations, relevant to D/L sugars since all natural sugars are in D form. Evolutionary pressure to select one of the isomer over the other depends upon what the isomer binds to in the cell e.g. is that structure isomer-dependent or not.

2.2 (a) ca.  $6.3 \times 10^{-18}$  kg or  $\sim 6.3 \times 10^{-15}$  g (assume mostly water in cell to get total mass). (b) Assuming roughly equal numbers of all four bases indicates mean Mw of 0.265 kDa per base. Using result from (a) implies  $\sim 14.3 \times 10^6$  bases, or  $\sim 7,200$  kbp, then 0.34 separate per bp implies contour length of  $\sim 2.4$  mm.

2.3 If you tally up all one-base changes there are 134 which do not change the amino acid coded for, implying no effect on evolutionary fitness, or  $134/576=23\%$  of one-base mutations have no effect, or  $0.23 \times 55\% = 13\%$  of the DNA sequence has changed without affecting the amino acid sequence, and 42% has changed with consequent changes in the amino acid sequence. This roughly accounts for the observation. There are other more complex factors also e.g. there may also be posttranslational modification of mRNA.

2.4 Assume total mass of protein in cell is  $\sim 20\%$  as stated in chapter text, and assume E. coli has a mass roughly equivalent to a sphere of diameter 1 micron as per answer to Question 2.2, and assume mean amino acid Mw is  $\sim 137$  Da as given also, indicates total number of amino acids per cell of  $\sim 3.2 \times 10^6$  residues. Assume 3 nucleotides per amino acid residues implies  $\sim 9.5 \times 10^6$  residues. If range of transcription speed of RNAP is 20-90 nucleotides per second then this would take  $\sim 5$ - $20 \times 10^5$  seconds or a mean of  $\sim 20 \times 10^3$  min. This suggests there are  $\sim 1,000$  active RNAP molecules in the cell at any one time since all of this protein would need to be replicated in one 20 min cell doubling time, and this output of mRNA can be amply accommodated for translation into peptides/protein by the  $\sim 20,000$  ribosomes present per cell.

2.5 Force is  $-\text{grad}(\text{potential energy})$ . Force is vector so we need to consider up magnitudes and directions of total force, but potential energy can be summed as a scalar and then a final calculation at end to calculate total force vector, and so is computationally more efficient to do this way.

2.6 Van der Waals interactions are due to dispersion-steric forces, modeled by  $-\text{grad}$  of Lennard-Jones potential, or  $12A/r^{13} - 6B/r^7$ . When this is zero  $r=r_m=(2A/B)^{1/6}$  and  $U=V_m=A/(2A/B)^{12/6} - B/(2A/B)^{6/6} = B^2/4A - B^2/2A = -B^2/4A$ , so  $B=2A/r_m^6 = -B^2/2V_m r_m^6$  or  $B=-2V_m r_m^6$  and  $A=Br_m^6/2 = -V_m r_m^{12}$ , so  $U=-V_m((r_m/r)^{12} - 2(r_m/r)^6)$

2.7 (a) Energy required to break a single H-bond is  $\sim 5k_B T$ , so mismatch energy difference equivalent to breaking either 2(AT or TA) or 3 (CG or GC) H-bonds, so if equal proportion of A, T, C, G then mean number of H-bonds to break is 2.5, mean energy of  $\sim 12.5k_B T$ . Probability of this transition given by Boltzmann factor  $\exp(-12.5k_B T/k_B T)$  or  $10^{-5} - 10^{-6}$ , which is roughly as observed. (b) Total 'diploid' genome (i.e. chromosomes from each parent) is  $2 \times 3 \times 10^9$ , or  $\sim 6 \times 10^9$  bp. Thus probability or error equivalent to  $1/(6 \times 10^9)$  or  $\sim 2 \times 10^{-10}$ . This is much smaller than (a), due to error checking mechanisms in living cell correcting for many mismatches (typically using alternative strand in DNA double helix as a template).

2.8 Typical transmembrane voltage  $V$  is ca.  $-200\text{mV}$ , so free energy change in moving charge  $q$  through  $V$  is simply  $Vq$ , or  $3.2 \times 10^{-20} \text{ J}$ , or  $\sim 8 k_B T$  at room temperature. The activation barrier for spontaneously translocating across intact lipid bilayer membrane is ca. an order of magnitude higher if substitute in values to electrical self energy of  $q/8\pi\epsilon_0\epsilon_r$ , – to prove this consider energy to charge up a spherical capacitor of capacitance  $C = CV^2/2 = 1qV$  where  $V$  is indicate electrostatic potential energy. For spherical shall, using Gauss's law,  $V=Q/4\pi\epsilon_0\epsilon_r$ , result follows.

If sodium ions allowed to translocate freely across pores into water 'reservoir' of much larger volume than cell, then all sodium ions will be lost from cell, equivalent to  $VC$  where  $V$  is volume of cell and  $c$  is initial concentration of sodium ions, which assuming cell is perfect sphere gives  $V=5.2 \times 10^{-16} \text{ m}^3 = 5.2 \times 10^{-13} \text{ L}$ ,  $c=150\text{mM}$ , so number of ions is  $\sim 4.6 \times 10^{10}$  ions.

2.9 (a) Energy per mole released from 38 ATP is  $38 \times 18k_B T \times \text{Avogadro's number}$  which is  $38 \times 18 \times 1.38 \times 10^{-23} \times 300 \times 6.02 \times 10^{23} = 1705 \text{ kJ mol}^{-1}$ . Thus efficiency is  $\sim 1705/2870$  or  $\sim 59\%$ . (b) Length scale of bacterial cell  $\sim 1$  micron, so volume  $\sim 10^{-18} \text{ m}^3$  or  $10^{-15} \text{ L}$ . Number of glucose molecules  $\sim 5 \times 10^3 \times 10^{-15} \times 6.02 \times 10^{23} = 3 \times 10^6$  molecules, equivalent to  $\sim 2$  billion  $k_B T$  of energy, much greater than required transition energy for molecular processes in cell, so cell breaks this down into smaller manageable chunks of single ATP chemical potential energy.

2.10 (a) Same as answer to Question 2.8 or  $\sim 8 k_B T$ . (b) Sum of two half reactions (see Equations 2.1 and 2.2), gives electrochemical voltage  $E$  total for reaction =  $-0.315 - (-0.166) = -0.149\text{V}$ , free energy change per mole given by  $-nEq$ ,  $n=2$  as  $2 \text{ H}^+$  transferred, giving  $4.8 \times 10^{-20} \text{ J} = 4.8 \times 10^{-20} / (1.38 \times 10^{-23} \times 300)$  or  $\sim 12 k_B T$ . Three molecules of  $\text{NAD}^+$  per TCA cycle, so  $\sim 36 k_B T$  total available, or  $\sim 4 \text{ H}^+$  pumped per TCA cycle, assuming majority of chemical potential energy available from  $\text{NAD}^+$  coupled to proton pumping (i.e. negligible loss as heat). (c) Use Equation 2.4 and assume  $\Delta G=0$  if no loss of heat, and  $\Delta G_0$  is under 'standard' conditions for everything apart from  $\text{pH}=7.5$ , gives  $[\text{NADH}]/[\text{NAD}^+] = ([\text{Malate}]/[\text{Oxaloacetate}][\text{H}^+])\exp(-\Delta G_0/k_B T)$ . From chapter we are told the concentrations of oxaloacetate and malate are kept relatively low in the cell at  $50 \text{ nM}$  and  $0.2 \text{ mM}$ , The concentration of protons is given by difference in concentration between  $\text{pH}7.5$  and standard conditions of  $\text{pH}7 = 10^{(7-7.5)} = 0.32 \text{ M}$ . Substituting in these values gives  $[\text{NADH}]/[\text{NAD}^+] \sim 0.08$  – i.e.  $>$  an order of magnitude excess of  $\text{NAD}^+$ , the low concentration of oxaloacetate drives forwards the whole TCA cycle.

2.11 Quite possibly

2.12 Bacteria (mainly in gut).

2.15 Variation as proportion of mean in height is much greater than the variation due just to bp spontaneous mutation of probability  $\sim 1$  in  $10^9$ , so the 'phenotype' variation is due to more than just spontaneous genetic mutation (many factors).

2.16 After  $n$  dilutions, if  $I$  out of  $T$  ( $=9$ ) cultures are infected then number  $N$  of virus molecules in original  $1\text{mL}$  volume of undiluted culture is  $(T/I)10^n$  from simple probability considerations if just one virus is required to infect a culture and assuming that  $I < T$  (i.e. not 'saturated' with excess viruses) and  $I > 0$  (i.e. there is at least one virus particle present). So taking average from  $10^{\text{th}}$  and  $11^{\text{th}}$  dilutions suggests  $N = ((6/9)10^{10} + (2/9)10^{11})/2 = 1.4 \times 10^{10}$  viruses, in  $1\text{mL}$ . Thus in  $1\text{L}$  there are  $1.4 \times 10^{13}$  viruses, which is a molarity of  $1.4 \times 10^{13} / (6.02 \times 10^{23}) = 2.3 \times 10^{-11} \text{ M}$