chapter

1

The Foundations of Biochemistry

1. The Size of Cells and Their Components

(a) If you were to magnify a cell 10,000-fold (typical of the magnification achieved using an electron microscope), how big would it appear? Assume you are viewing a "typical" eukaryotic cell with a cellular diameter of 50 μm.

(b) If this cell were a muscle cell (myocyte), how many molecules of actin could it hold? (Assume the cell is spherical and no other cellular components are present; actin molecules are spherical, with a diameter of 3.6 nm. The volume of a sphere is $4/3\ \pi r^3$.)

(c) If this were a liver cell (hepatocyte) of the same dimensions, how many mitochondria could it hold? (Assume the cell is spherical; no other cellular components are present; and the mitochondria are spherical, with a diameter of 1.5 μm.)

(d) Glucose is the major energy-yielding nutrient for most cells. Assuming a cellular concentration of 1 mM, calculate how many molecules of glucose would be present in our hypothetical (and spherical) eukaryotic cell. (Avogadro's number, the number of molecules in 1 mol of a nonionized substance, is 6.02×10^{23}.)

(e) Hexokinase is an important enzyme in the metabolism of glucose. If the concentration of hexokinase in our eukaryotic cell is 20 μM, how many glucose molecules are present per hexokinase molecule?

Answer

(a) The magnified cell would have a diameter of $50 \times 10^4\ \mu\text{m} = 500 \times 10^3\ \mu\text{m} = 500$ mm, or 20 inches—about the diameter of a large pizza.

(b) The radius of a globular actin molecule is 3.6 nm/2 = 1.8 nm; the volume of the molecule, in cubic meters, is $(4/3)(3.14)(1.8 \times 10^{-9}\ \text{m})^3 = 2.4 \times 10^{-26}\ \text{m}^3$.*

The number of actin molecules that could fit inside the cell is found by dividing the cell volume (radius = 25 μm) by the actin molecule volume. Cell volume = $(4/3)(3.14)(25 \times 10^{-6}\ \text{m})^3 = 6.5 \times 10^{-14}\ \text{m}^3$. Thus, the number of actin molecules in the hypothetical muscle cell is

$$(6.5 \times 10^{-14}\ \text{m}^3)/(2.4 \times 10^{-26}\ \text{m}^3) = 2.7 \times 10^{12}\ \text{molecules}$$

or 2.7 trillion actin molecules.

**Significant figures:* In multiplication and division, the answer can be expressed with no more significant figures than the least precise value in the calculation. Because some of the data in these problems are derived from measured values, we must round off the calculated answer to reflect this. In this first example, the radius of the actin (1.8 nm) has two significant figures, so the answer (volume of actin = $2.4 \times 10^{-26}\ \text{m}^3$) can be expressed with no more than two significant figures. It will be standard practice in these expanded answers to round off answers to the proper number of significant figures.

3. Genetic Information in *E. Coli* DNA The genetic information contained in DNA consists of a linear sequence of coding units, known as codons. Each codon is a specific sequence of three deoxyribonucleotides (three deoxyribonucleotide pairs in double-stranded DNA), and each codon codes for a single amino acid unit in a protein. The molecular weight of an *E. coli* DNA molecule is about 3.1×10^9 g/mol. The average molecular weight of a nucleotide pair is 660 g/mol, and each nucleotide pair contributes 0.34 nm to the length of DNA.

(a) Calculate the length of an *E. coli* DNA molecule. Compare the length of the DNA molecule with the cell dimensions (see Problem 2). How does the DNA molecule fit into the cell?

(b) Assume that the average protein in *E. coli* consists of a chain of 400 amino acids. What is the maximum number of proteins that can be coded by an *E. coli* DNA molecule?

Answer

(a) The number of nucleotide pairs in the DNA molecule is calculated by dividing the molecular weight of DNA by that of a single pair:

$$(3.1 \times 10^9 \text{ g/mol})/(0.66 \times 10^3 \text{ g/mol}) = 4.7 \times 10^6 \text{ pairs}$$

Multiplying the number of pairs by the length per pair gives

$$(4.7 \times 10^6 \text{ pairs})(0.34 \text{ nm/pair}) = 1.6 \times 10^6 \text{ nm} = 1.6 \text{ mm}$$

The length of the cell is 2 μm (from Problem 2), or 0.002 mm, which means the DNA is (1.6 mm)/(0.002 mm) = 800 times longer than the cell. The DNA must be tightly coiled to fit into the cell.

(b) Because the DNA molecule has 4.7×10^6 nucleotide pairs, as calculated in (a), it must have one-third this number of triplet codons:

$$(4.7 \times 10^6)/3 = 1.6 \times 10^6 \text{ codons}$$

If each protein has an average of 400 amino acids, each requiring one codon, the number of proteins that can be coded by *E. coli* DNA is

$$(1.6 \times 10^6 \text{ codons})(1 \text{ amino acid/codon})/(400 \text{ amino acids/protein}) = 4{,}000 \text{ proteins}$$

4. The High Rate of Bacterial Metabolism Bacterial cells have a much higher rate of metabolism than animal cells. Under ideal conditions some bacteria double in size and divide every 20 min, whereas most animal cells under rapid growth conditions require 24 hours. The high rate of bacterial metabolism requires a high ratio of surface area to cell volume.

(a) Why does surface-to-volume ratio affect the maximum rate of metabolism?

(b) Calculate the surface-to-volume ratio for the spherical bacterium *Neisseria gonorrhoeae* (diameter 0.5 μm), responsible for the disease gonorrhea. Compare it with the surface-to-volume ratio for a globular amoeba, a large eukaryotic cell (diameter 150 μm). The surface area of a sphere is $4\pi r^2$.

Answer

(a) Metabolic rate is limited by diffusion of fuels into the cell and waste products out of the cell. This diffusion in turn is limited by the surface area of the cell. As the ratio of surface area to volume decreases, the rate of diffusion cannot keep up with the rate of metabolism within the cell.

(b) For a sphere, surface area = $4\pi r^2$ and volume = 4/3 πr^3. The ratio of the two is the surface-to-volume ratio, S/V, which is $3/r$ or $6/D$, where D = diameter. Thus, rather than calculating S and V separately for each cell, we can rapidly calculate and compare S/V ratios for cells of different diameters.

$$S/V \text{ for } N. \textit{ gonorrhoeae} = 6/(0.5\ \mu\text{m}) = 12\ \mu\text{m}^{-1}$$

$$S/V \text{ for amoeba} = 6/(150\ \mu\text{m}) = 0.04\ \mu\text{m}^{-1}$$

$$\frac{S/V \text{ for bacterium}}{S/V \text{ for amoeba}} = \frac{12\mu\text{m}^{-1}}{0.04\ \mu\text{m}^{-1}} = 300$$

Thus, the surface-to-volume ratio is 300 times greater for the bacterium.

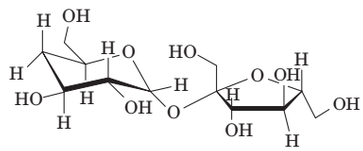
Data Analysis Problem

14. Sweet-Tasting Molecules Many compounds taste sweet to humans. Sweet taste results when a molecule binds to the sweet receptor, one type of taste receptor, on the surface of certain tongue cells. The stronger the binding, the lower the concentration required to saturate the receptor and the sweeter a given concentration of that substance tastes. The standard free-energy change, $\Delta G°$, of the binding reaction between a sweet molecule and a sweet receptor can be measured in kilojoules or kilocalories per mole.

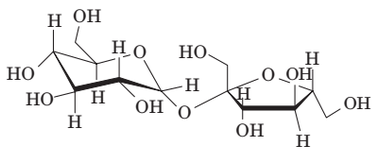
Sweet taste can be quantified in units of "molar relative sweetness" (MRS), a measure that compares the sweetness of a substance to the sweetness of sucrose. For example, saccharin has an MRS of 161; this means that saccharin is 161 times sweeter than sucrose. In practical terms, this is measured by asking human subjects to compare the sweetness of solutions containing different concentrations of each compound. Sucrose and saccharin taste equally sweet when sucrose is at a concentration 161 times higher than that of saccharin.

(a) What is the relationship between MRS and the $\Delta G°$ of the binding reaction? Specifically, would a more negative $\Delta G°$ correspond to a higher or lower MRS? Explain your reasoning.

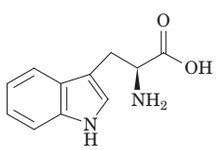
Shown below are the structures of 10 compounds, all of which taste sweet to humans. The MRS and $\Delta G°$ for binding to the sweet receptor are given for each substance.



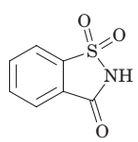
Deoxysucrose
MRS = 0.95
$\Delta G° = -6.67$ kcal/mol



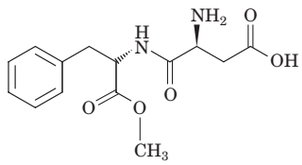
Sucrose
MRS = 1
$\Delta G° = -6.71$ kcal/mol



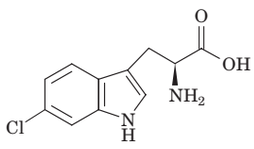
D-Tryptophan
MRS = 21
$\Delta G° = -8.5$ kcal/mol



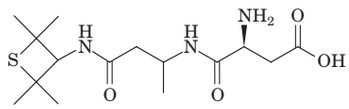
Saccharin
MRS = 161
$\Delta G° = -9.7$ kcal/mol



Aspartame
MRS = 172
$\Delta G° = -9.7$ kcal/mol



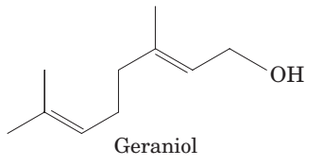
6-Chloro-D-tryptophan
MRS = 906
$\Delta G° = -10.7$ kcal/mol



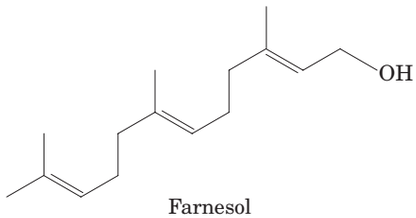
Alitame
MRS = 1,937
$\Delta G° = -11.1$ kcal/mol

can be used to create a stable emulsion in a mixture that contains up to 75% oil. Mayonnaise, too, is an emulsion created with egg yolks, with an oil:vinegar mixture in a 3:1 ratio.

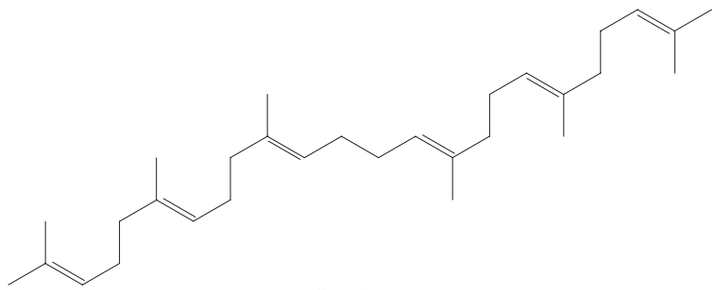
4. Isoprene Units in Isoprenoids Geraniol, farnesol, and squalene are called isoprenoids, because they are synthesized from five-carbon isoprene units. In each compound, circle the five-carbon units representing isoprene units (see Fig. 10–22).



Geraniol

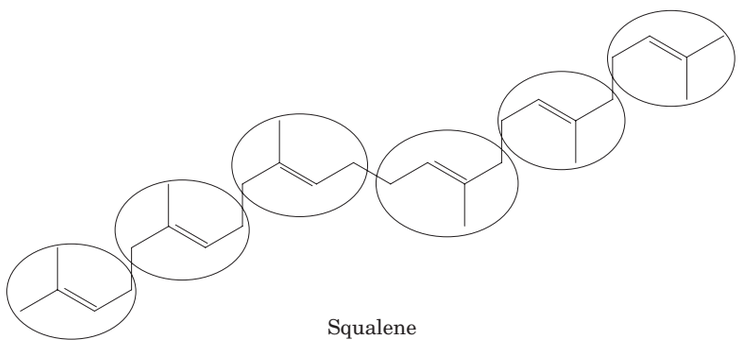


Farnesol



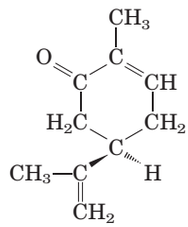
Squalene

Answer

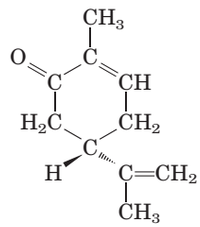


Squalene

5. Naming Lipid Stereoisomers The two compounds below are stereoisomers of carvone with quite different properties; the one on the left smells like spearmint, and that on the right, like caraway. Name the compounds using the RS system.



Spearmint



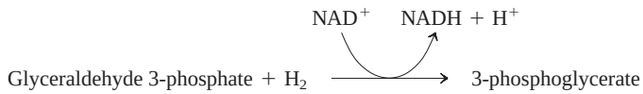
Caraway

Answer Spearmint is (*R*)-carvone; caraway is (*S*)-carvone.

9. Equivalence of Triose Phosphates ^{14}C-Labeled glyceraldehyde 3-phosphate was added to a yeast extract. After a short time, fructose 1,6-bisphosphate labeled with ^{14}C at C-3 and C-4 was isolated. What was the location of the ^{14}C label in the starting glyceraldehyde 3-phosphate? Where did the second ^{14}C label in fructose 1,6-bisphosphate come from? Explain.

Answer Problem 1 outlines the steps in glycolysis involving fructose 1,6-bisphosphate, glyceraldehyde 3-phosphate, and dihydroxyacetone phosphate. Keep in mind that the aldolase reaction is readily reversible and the triose phosphate isomerase reaction catalyzes extremely rapid interconversion of its substrates. Thus, the label at C-1 of glyceraldehyde 3-phosphate would equilibrate with C-1 of dihydroxyacetone phosphate ($\Delta G'^\circ = 7.5$ kJ/mol). Because the aldolase reaction has $\Delta G'^\circ = -23.8$ kJ/mol in the direction of hexose formation, fructose 1,6-bisphosphate would be readily formed, and labeled in C-3 and C-4 (see Fig. 14–6).

10. Glycolysis Shortcut Suppose you discovered a mutant yeast whose glycolytic pathway was shorter because of the presence of a new enzyme catalyzing the reaction



Would shortening the glycolytic pathway in this way benefit the cell? Explain.

Answer Under anaerobic conditions, the phosphoglycerate kinase and pyruvate kinase reactions are essential. The shortcut in the mutant yeast would bypass the formation of an acyl phosphate by glyceraldehyde 3-phosphate dehydrogenase and therefore would not allow the formation of 1,3-bisphosphoglycerate. Without the formation of a substrate for 3-phosphoglycerate kinase, no ATP would be formed. Under anaerobic conditions, the net reaction for glycolysis normally produces 2 ATP per glucose. In the mutant yeast, net production of ATP would be zero and growth could not occur. Under aerobic conditions, however, because the majority of ATP formation occurs via oxidative phosphorylation, the mutation would have no observable effect.

11. Role of Lactate Dehydrogenase During strenuous activity, the demand for ATP in muscle tissue is vastly increased. In rabbit leg muscle or turkey flight muscle, the ATP is produced almost exclusively by lactic acid fermentation. ATP is formed in the payoff phase of glycolysis by two reactions, promoted by phosphoglycerate kinase and pyruvate kinase. Suppose skeletal muscle were devoid of lactate dehydrogenase. Could it carry out strenuous physical activity; that is, could it generate ATP at a high rate by glycolysis? Explain.

Answer The key point here is that NAD^+ must be regenerated from NADH in order for glycolysis to continue. Some tissues, such as skeletal muscle, obtain almost all their ATP through the glycolytic pathway and are capable of short-term exercise only (see Box 14–2). In order to generate ATP at a high rate, the NADH formed during glycolysis must be oxidized. In the absence of significant amounts of O_2 in the tissues, lactate dehydrogenase converts pyruvate and NADH to lactate and NAD^+. In the absence of this enzyme, NAD^+ could not be regenerated and glycolytic production of ATP would stop—and as a consequence, muscle activity could not be maintained.

12. Efficiency of ATP Production in Muscle The transformation of glucose to lactate in myocytes releases only about 7% of the free energy released when glucose is completely oxidized to CO_2 and H_2O. Does this mean that anaerobic glycolysis in muscle is a wasteful use of glucose? Explain.

Answer [PP_i] is high in the plant cell cytosol because the cytosol lacks inorganic pyrophosphatase, the enzyme that degrades PP_i to 2 P_i. Plants are unique in this regard. Animal cells have pyrophosphatase in their cytosol, and [PP_i] is therefore kept too low for PP_i to be a useful phosphoryl group donor.

15. Regulation of Starch and Sucrose Synthesis Sucrose synthesis occurs in the cytosol and starch synthesis in the chloroplast stroma, yet the two processes are intricately balanced. What factors shift the reactions in favor of **(a)** starch synthesis and **(b)** sucrose synthesis?

Answer

(a) Low levels of P_i in the cytosol and high levels of triose phosphate in the chloroplast favor formation of starch.

(b) High levels of triose phosphate in the cytosol favor formation of sucrose.

16. Regulation of Sucrose Synthesis In the regulation of sucrose synthesis from the triose phosphates produced during photosynthesis, 3-phosphoglycerate and P_i play critical roles (see Fig. 20–26). Explain why the concentrations of these two regulators reflect the rate of photosynthesis.

Answer 3-Phosphoglycerate is the primary product of photosynthesis; [P_i] rises when light-driven synthesis of ATP from ADP and P_i slows. The concentrations of these two metabolites thus provide clues to the energetic state of the leaf cell. When photosynthesis is occurring at a high rate, [P_i] drops and [3-phosphoglycerate] rises; in the dark, [P_i] rises and [3-phosphoglycerate] falls. The rate-limiting step in sucrose synthesis is the formation of ADP-glucose from glucose 1-phosphate and ATP, and this step is inhibited by P_i and activated by 3-phosphoglycerate (see Fig. 20–28). Sucrose synthesis therefore occurs at a high rate when photosynthesis is occurring, [P_i] is low, and [3-phosphoglycerate] is high.

17. Sucrose and Dental Caries The most prevalent infection in humans worldwide is dental caries, which stems from the colonization and destruction of tooth enamel by a variety of acidifying microorganisms. These organisms synthesize and live within a water-insoluble network of dextrans, called dental plaque, composed of ($\alpha 1 \rightarrow 6$)-linked polymers of glucose with many ($\alpha 1 \rightarrow 3$) branch points. Polymerization of dextran requires dietary sucrose, and the reaction is catalyzed by a bacterial enzyme, dextran-sucrose glucosyltransferase.

(a) Write the overall reaction for dextran polymerization.

(b) In addition to providing a substrate for the formation of dental plaque, how does dietary sucrose also provide oral bacteria with an abundant source of metabolic energy?

Answer

(a) $$\text{Sucrose} + \underset{\text{dextran}_n}{(\text{glucose})_n} \longrightarrow \underset{\text{dextran}_{n+1}}{(\text{glucose})_{n+1}} + \text{fructose}$$

(b) Fructose generated in the synthesis of dextran is readily taken up by the bacteria and metabolized to acidic compounds.

18. Differences between C_3 and C_4 Plants The plant genus *Atriplex* includes some C_3 and some C_4 species. From the data in the plots below (species 1, upper curve; species 2, lower curve), identify which is a C_3 plant and which is a C_4 plant. Justify your answer in molecular terms that account for the data in all three plots.