CHAPTER 2

Cell Chemistry and Biosynthesis

Molecular Biology of the Cell, Fifth Edition

Questions

2-1 A major goal of interplanetary research is to find evidence of water on other planets, in the search for extraterrestrial life. All known life requires water.

A. Describe three properties of water that make it uniquely suited for life. In one or two sentences, describe each property and a consequence of that property for cells or organisms.

B. Both C–H bonds and O–H bonds have special properties that make life possible. What is the most notable difference between a C–H bond and an O–H bond? Why is this difference important? Is an N–H bond more like an O–H bond or a C–H bond?

C. In the search for interplanetary life, scientists are designing detection methods for an unmanned rover that can be used to identify five kinds of biomolecules. Name four of these five critical biomolecules.

2-2 Your friend learns about Avogadro's number and thinks it is so huge that there may not even be a mole of living cells on Earth. You have recently heard that there are about 50 trillion (50×10^{12}) human cells in each adult human body, so you bet your friend $5 that there is more than a mole of cells on Earth. Once you learn that each human contains more bacterial cells (in the digestive system) than human cells, you are sure that you have won the bet. In the year 2000, the human population surpassed 6 billion (6×10^{9}). What calculation can you show your friend to convince him you are right?

2-3 Your friend challenges you to a bet. He says that cola is so sweet that the sugar molecules in cola are more crowded than people packed into a 747 airplane. After an uncomfortable cross-country airplane trip, you think this cannot be true. Cola has 39 grams of sugar in 240 ml (0.9 M sugar). A person is roughly 2×10^{26} times larger than a sugar molecule, so scaling a person down to the size of a sugar molecule would correspondingly scale down the cabin volume of a 747 from about a million liters to 4×10^{-21} liters. The maximum capacity of a 747 is 568 people. Which is more crowded, the sugar molecules in soda or the passengers on a 747? What is the molarity of people on a 747, using the scaling described?

2-4 The yeast species *Saccharomyces cerevisiae* is commonly used to brew beer and leaven bread (the Latin words of the species name mean "sugar fungus" and "beer"). In making bread and beer, the yeast converts sugars to carbon dioxide, which forms bubbles that cause dough to rise, and ethanol, which gives beer its alcoholic punch. From the facts about sugar metabolism, you can explain to your friends how the alcohol and carbon dioxide arise. In glycolysis, a glucose molecule is converted into two pyruvate molecules (see Figure Q2-4).

A. Yeast can grow in the presence or absence of oxygen (aerobically or anaerobically, respectively). Does glycolysis oxidize glucose? Can cells growing anaerobically perform glycolysis? Explain.

B. Pyruvate can be converted to acetyl CoA or ethanol. Acetyl CoA then enters the citric acid cycle; ethanol is not metabolized further. Use chemical formulas to show what happens to the three carbon molecules in pyruvate in each case when both reactions are complete (drawn as in Figure Q2-4).

C. Is more ethanol made if yeast grows aerobically or anaerobically? Is more CO_2 made if yeast grows aerobically or anaerobically? Explain.

D. Bread yeast strains have been optimized for their task. What do you think would happen if you brewed beer using bread yeast?

E. Some yeast (called rho$^-$) have defective mitochondria, unlike the functional wild-type rho$^+$ yeast. A friend gave you a rho$^-$ strain and a rho$^+$ strain, but forgot to label the strains. What carbon source would you use to determine the identities of the strains? Name a carbon source that will allow both strains to grow and one that will allow only one to grow (and indicate which will grow).

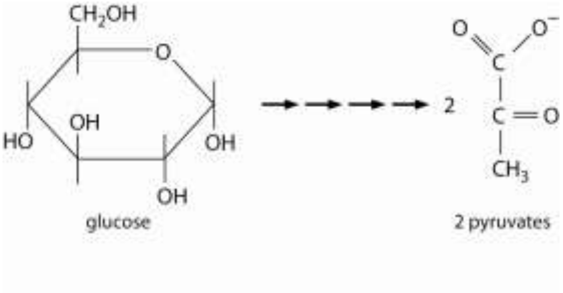

Figure Q2-4

2-5 Lysine and glutamate are amino acids that are often positively and negatively charged, respectively, in proteins in the cell.

A. The neutral forms are shown in Figure Q2-5. Write the charged forms of the amino acids.

B. Consider a protein that has eight lysines and five glutamates, and no other potentially charged amino acids. What will be the net charge on the protein when it is dissolved in a solution at pH 3? At pH 7? At pH 13?

C. Histidine is usually neutral at high pH and charged at low pH when incorporated in a protein. Its pK_a is about 6.5. Roughly what percentage of histidines will be charged in a solution at pH 6.5? At pH 5.5? At pH 8.5?

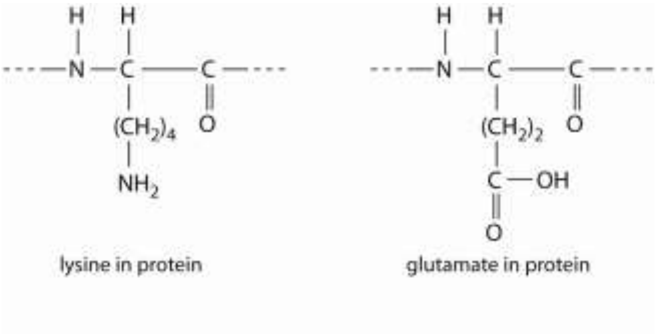

Figure Q2-5

2-6 Consider the reaction X → Y in a cell at 37°C. At equilibrium, the concentrations of X and Y are 80 µM and 16 µM, respectively.

$\Delta G° = –0.616 \ln K_{eq}$

$\Delta G = \Delta G° + 0.616 \ln [Y]/[X]$

The natural log of a number z will be negative when $z < 1$, positive when $z > 1$, and 0 when $z = 1$.

A. What is the value of K_{eq} for this reaction?

B. Is the standard free-energy change of this reaction positive or negative? Is the reaction X → Y an energetically favorable or unfavorable reaction under standard conditions?

C. Imagine circumstances in which the concentration of X is 1000 µM and Y is 1 µM. Is a net conversion of X to Y favorable? For a given X molecule, will it be converted to a Y molecule quickly? Explain.

D. Consider 20 µM of Y added to a test tube with 80 µM of X that contains a radioactive atom to allow tracing of the individual atoms. The mixture is incubated for 2 hours before separating Y from X and measuring the radioactivity of Y. Does the information provided allow you to determine whether the Y molecules contain any radioactivity? If the reaction also contained an enzyme that catalyzes the interconversion of X and Y, would the Y molecules be radioactive? Explain.

E. Imagine starting conditions in which the reaction X → Y is unfavorable, yet the cell needs to produce more Y. Describe two ways in which this may be accomplished.

2-7 Many critical molecules in cells are polymers. Which is more disordered, a polymer or a collection of monomers? On the basis of your answer, is the $\Delta G°$ of a condensation reaction positive, negative, or zero? What about the $\Delta G°$ of a hydrolysis reaction? Is a condensation or a hydrolysis reaction usually coupled to a reaction involving ATP or another activated carrier molecule?

2-8 The energetic trajectory of a series of reactions in a catabolic pathway can be plotted on a graph like that in Figure Q2-8. The graph shows a hypothetical pathway similar to glycolysis, in which the catabolic intermediates are designated

A, B, C, etc. The energetic contributions of activated carrier molecules have been omitted from this energy plot. Which reaction is most likely to occur without an enzyme? Which reaction is most likely to be catalyzed by an enzyme that simultaneously uses ATP as a substrate? Which reaction is most likely to be catalyzed by an enzyme that simultaneously uses ADP as a substrate and produces ATP? Which reaction can most readily be driven by a subsequent reaction that acts as a siphon on the product? For each of the four answers, explain your reasoning.

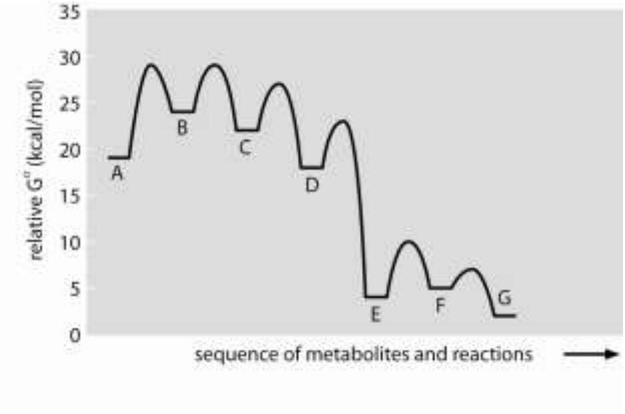

Figure Q2-8

Answers

2-1

A. Your answer should include three of the following six partly overlapping properties of water. (1) Water forms hydrogen bonds with itself and with other molecules that have polar N–H or O–H bonds, which is critical for the solubility and reactivity of DNA, proteins, polysaccharides, and fatty acids. (2) Water is a polar molecule with partial positive charges on the hydrogen atoms and a partial negative charge on the oxygen atom; thus it engages in charged interactions that help dissolve ions and solubilize molecules with partial or complete ionic charges (thus these molecules are "hydrophilic" or water-loving). Water also helps shield charges on ions so that, for example, two highly negatively charged strands of DNA can bind each other. (3) Water is a liquid with a high surface tension due to its hydrogen bonding. The high surface tension allows capillary action, which is important for the uptake of water through vessels in plants. (4) Water is a liquid with a high heat capacity and a high boiling point. This is caused by the dissipation of heat into breakage of the hydrogen bonds between water molecules, in addition to dissipation into kinetic energy of the molecules. If water did not have such a high heat capacity, then the substantial heat released by metabolic reactions might cause water to boil and organisms to die. (5) Water forces nonpolar hydrocarbons to aggregate, promoting hydrophobic interactions (thus these molecules are "hydrophobic" or water-hating); water aids in protein folding and lipid bilayer formation. (6) Frozen water (ice) is less dense than liquid water, and thus large bodies of water freeze on top, which insulates the water underneath and allows living things to survive in oceans even in extremely cold weather.

B. The most notable difference is that C–H bonds are largely non-polar, whereas O–H bonds are polar. This means that C and H share electrons almost equally, and regions of a molecule with many C–H bonds tend to avoid interactions with charged ions and cluster together in a polar solvent like water. In contrast, O atoms have a higher affinity for electrons (electronegativity) than H atoms, and thus the O–H bond creates a permanent dipole that allows molecules to interact with other polar or charged regions of molecules through electrical forces, similar to but weaker than ionic bonds. An N–H bond is more like an O–H bond, because it is polar and can participate in hydrogen bonding.

C. The five molecules are (1) chlorophyll (for photosynthesis and harvesting light energy from the Sun), (2) nucleic acids, including RNA and DNA, (3) proteins or polypeptides, (4) lipids or fatty acids, and (5) carbohydrates or polysaccharides.

2-2 Avogadro's number, about 6×10^{23}, is the number of atoms (or units) in a mole. If you multiply the number of people on Earth by the number of cells in the human body, then double it to approximate the number of bacterial cells contained in the human body, you will calculate: $(6 \times 10^9) \times (50 \times 10^{12}) \times 2 = 6 \times 10^{23}$. Thus, there must be much more than a mole of living cells on Earth, and you win $5.

2-3 The sugar molecules in soda are about four times more crowded than the passengers on a 747. Whereas sugar molecules in soda are present at about 0.9 M, people on a 747 are about 0.24 molar. The people on a 747, when scaled appropriately, are present at about (568 people)/[$(6 \times 10^{23}$ people/mole) $(4 \times 10^{-21}$ liter)] = 0.236 mole/liter. Thus, your friend is right and cola is crowded with sugar molecules.

2-4

A. Yes, glycolysis oxidizes glucose. Yes, cells growing anaerobically can perform glycolysis. No oxygen is required for glycolysis because other compounds (NAD^+) are reduced. If the products of glycolysis enter the citric acid cycle and oxidative phosphorylation, then the subsequent oxidation of NADH is coupled to the reduction of oxygen.

B. See Figure A2-4. At the top is fermentation, the conversion of pyruvate to ethanol (with two carbons) and one CO_2. At the bottom is the result of respiration, the conversion of all three carbons in pyruvate to CO_2, which requires oxygen to regenerate oxidizing agents needed for the citric acid cycle.

C. More ethanol is made if yeast grows anaerobically. More CO_2 is made if yeast grows aerobically. The production of ethanol is a kind of fermentation, an anaerobic process needed in the absence of oxygen to regenerate NAD^+ and allow glycolysis to continue. If oxygen is plentiful, the cell will convert pyruvate into acetyl CoA and not ethanol, thereby allowing the remaining carbons to enter the citric acid cycle. The citric acid cycle will then release the last two carbons as CO_2 and, coupled with oxidative phosphorylation, will generate about 15 times more energy than glycolysis and fermentation alone. So the aerobic metabolism of sugar will produce more CO_2 and will thus be better for making bread, whereas anaerobic metabolism will produce more ethanol for beer and wine.

D. The beer would be less alcoholic and more bubbly than usual.

E. Any non-fermentable carbon source will allow the rho^+ strain to grow but will not allow the rho^- strain to grow. These carbon sources must be metabolized in the mitochondria by the citric acid cycle and oxidative phosphorylation, which requires oxygen: for example, ethanol, lactate, pyruvate, glycerol, acetate, some amino acids, and fatty acids. Both strains can grow on glucose.

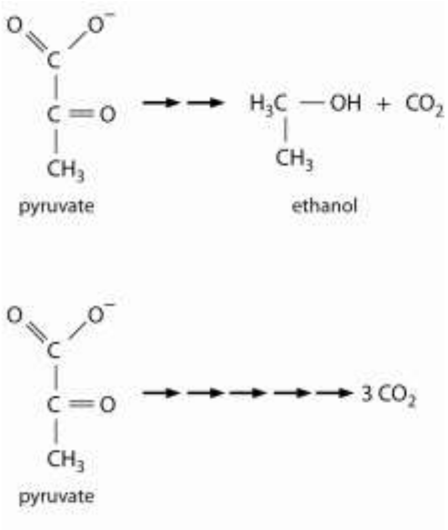

Figure A2-4

2-5

A. See Figure A2-5.

B. The net charge on the protein at pH 3 is likely to be +8, because the glutamates will be neutral and the lysines will be charged. The net charge at pH 7 will be +3, because the glutamates and the lysines will be charged. The net charge at pH 13 will be about –5, because the lysines will be neutral and the glutamates will be charged.

C. Exactly 50% of the histidines will be charged when the pH is equal to the pK_a of 6.5. When the pH is 5.5, one unit lower than the pKa, the proportion of charged histidines is about 90%. When the pH is 8.5, two units higher than the pK_a, the proportion of charged histidines is about 1%.

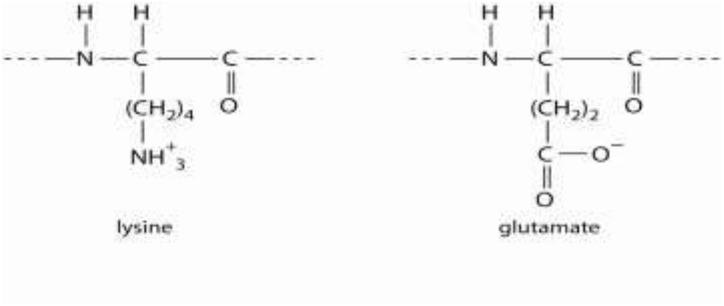

Figure A2-5

2-6

A. $K_{eq} = [Y]/[X] = 16\ \mu M/80\ \mu M = 0.2$.

B. The standard free-energy change, $\Delta G°$, is positive because K_{eq} is less than 1. Under standard conditions (equal concentrations of X and Y), the reaction X → Y is unfavorable.

C. Yes, the conversion is favorable because the value of [Y]/[X] is less than the equilibrium value. However, the speed of the reaction cannot be determined from the free-energy difference. For example, combustion of this piece of paper is a highly favorable reaction, yet it will not happen in our lifetime without a catalyst.

D. The information is not sufficient to determine whether the interconversion between X and Y will proceed in a test tube without an enzyme. Yes, the addition of an enzyme will yield some radioactive molecules of Y. The net conversion of X to Y is not favorable under these conditions, yet given an appropriate boost in the reaction rates from a catalyst, some molecules of X will be converted into Y although more molecules of Y will be converted into X.

E. The cell may directly couple the unfavorable reaction to a second, energetically favorable reaction whose negative ΔG has a value larger than the positive ΔG of the X → Y reaction; the coupled reaction will have a ΔG equal to the sum of the component reactions. Alternatively, more X will be converted to Y if the concentration of Y drops; this may happen if Y is converted to Z in a second reaction or if Y is exported from the cell or compartment where the X → Y reaction occurs.

2-7 A collection of monomers is more disordered than a polymer of those monomers. Thus, the $\Delta G°$ of a condensation reaction is positive; condensation to make a polymer is energetically unfavorable. The $\Delta G°$ of a hydrolysis reaction is negative, or energetically favorable. For them to be made favorable and to occur, condensation reactions are usually coupled to the hydrolysis of ATP or another activated carrier molecule.

2-8 Reaction F to G is most likely to occur without an enzyme, because it has the lowest activation energy barrier. Reaction A to B is most likely to be catalyzed by an enzyme that simultaneously uses ATP as a substrate, because it has the most positive or unfavorable $\Delta G°$ and thus probably needs to be coupled to a highly favorable reaction such as ATP hydrolysis. Reaction D to E is most likely to be catalyzed by an enzyme that simultaneously uses ADP as a substrate to make ATP, because it has the most negative or favorable $\Delta G°$, with a value of more than 8 kcal/mol and thus can potentially be used to drive an energetically unfavorable ATP synthesis reaction. Reaction E to F can most readily be driven by a subsequent reaction that acts as a siphon on the product, because it is slightly unfavorable so a relative excess of substrate and paucity of product (due to a subsequent reaction) can readily drive the reaction forward.