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Appendix A: Physical Constants and Conversion of Units

Values of physical constants

Physical constant	Symbol	Value
Atomic mass unit (dalton)	amu	1.660×10^{-24} g
Avogadro's number	*N*	6.022×10^{23} mol^{-1}
Boltzmann's constant	*k*	1.381×10^{-23} J K^{-1}
		3.298×10^{-24} cal K^{-1}
Electron volt	eV	1.602×10^{-19} J
		3.828×10^{-20} cal
Faraday constant	F	9.649×10^{4} C mol^{-1}
		2.306×10^{4} cal volt^{-1} eq^{-1}
Curie	Ci	3.70×10^{10} disintegrations s^{-1}
Gas constant	*R*	8.315 J mol^{-1} K^{-1}
		1.987 cal mol^{-1} K^{-1}
Planck's constant	*h*	6.626×10^{-34} J s
		1.584×10^{-34} cal s
Speed of light in a vacuum	*c*	2.998×10^{10} cm s^{-1}

Abbreviations: C, coulomb; cal, calorie; cm, centimeter; K, Kelvin;eq, equivalent; g, gram; J, joule; mol, mole; s, second.

Mathematical constants

$\pi = 3.14159$

$e = 2.71828$

$\log_e x = 2.303 \log_{10} x$

Conversion factors

Physical quantity	Equivalent
Length	1 cm = 10^{-2} m = 10 mm = 10^{4} μm = 10^{7} nm
	1 cm = 10^{8} Å = 0.3937 inch
Mass	1 g = 10^{-3} kg = 10^{-3} mg = 10^{6} μg
	1 g = 3.527×10^{-2} ounce (avoirdupois)

Volume	$1\ cm^3 = 10^{-6}\ m^3 = 10^3\ mm^3$
	$1\ ml = 1\ cm^3 = 10^{-3}\ liter = 10^3\ \mu l$
	$1\ cm^3 = 6.1 \times 10^{-2}\ in^3 = 3.53 \times 10^{-5}\ ft^3$
Temperature	$K = °C + 273.15$
	$°C = (5/9)(°F - 32)$
Energy	$1\ J = 10^7\ erg = 0.239\ cal = 1\ watt\ s -$
Pressure	1 torr = 1 mm Hg (0°C)
	$= 1.333 \times 10^2\ newtons\ m^{-2}$
	$= 1.333 \times 10^2\ pascal$
	$= 1.316 \times 10^{-3}\ atmospheres$

Standard prefixes

Prefix	Symbol	Factor
kilo	k	10^3
hecto	h	10^2
deca	da	10^1
deci	d	10^{-1}
centi	c	10^{-2}
milli	m	10^{-3}
micro	μ	10^{-6}
nano	n	10^{-9}
pico	p	10^{-12}

Appendix B: Acidity Constants

pK_a Values of Some Acids

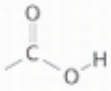
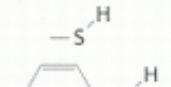
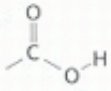
Acid	pK' (at 25°C)	Acid	pK' (at 25°C)
Acetic acid	4.76	Lactic acid	3.86
Acetoacetic acid	3.58	Maleic acid, pK_1	1.83
Ammonium ion	9.25	pK_2	6.07
Ascorbic acid, pK_1	4.10	Malic acid, pK_1	3.40

	pK_2	11.79	pK_2 5.11
Benzoic acid		4.20	Phenol 9.89
n-Butyric acid		4.81	Phosphoric acid, pK_1 2.12
Cacodylic acid		6.19	pK_2 7.21
Carbonic acid, pK_1		6.35	pK_3 12.67
	pK_2	10.33	Pyridinium ion 5.25
Citric acid, pK_1		3.14	Pyrophosphoric acid, pK_1 0.85
	pK_2	4.77	pK_2 1.49
	pK_3	6.39	pK_3 5.77
Ethylammonium ion		10.81	pK_4 8.22
Formic acid		3.75	Succinic acid, pK_1 4.21
Glycine, pK_1		2.35	pK_2 5.64
	pK_2	9.78	Trimethylammonium ion 9.79
Imidazolium ion		6.95	Tris (hydroxymethyl) aminomethane 8.08
			Water* 15.74

* $[H^+]\,[OH^-] = 10^{-14}$; $[H_2O] = 55.5$ M.

Typical pK_a values of ionizable groups in proteins

Typical pK_a values of ionizable groups in proteins

Group	Acid ⇌ Base	Typical pK_a	Group	Acid ⇌ Base	Typical pK_a
Terminal α-carboxyl group		3.1	Cysteine		8.3
Aspartic acid		4.1	Tyrosine		10.4
Glutamic acid			Lysine		10.0
Histidine		6.0	Arginine		12.5
Terminal α-amino group		8.0			

Note: pK_a values depend on temperature, ionic strength, and the microenvironment of the ionizable group.

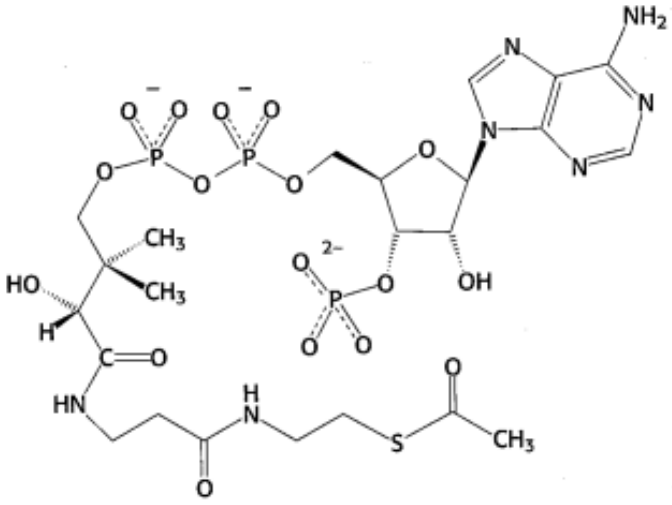
Appendix C: Standard Bond Lengths

Standard Bond Lengths

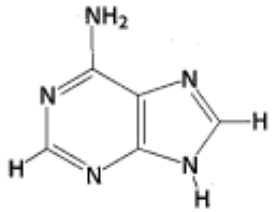
Bond	Structure	Length (Å)
C—H	R_2CH_2	1.07
	Aromatic	1.08
	RCH_3	1.10
C—C	Hydrocarbon	1.54
	Aromatic	1.40
C=C	Ethylene	1.33
C≡C	Acetylene	1.20
C—O	RNH_2	1.47
	O=C—N	1.34
C—O	Alcohol	1.43
	Ester	1.36
C=O	Aldehyde	1.22
	Amide	1.24
C—S	R_2S	1.82
N—H	Amide	0.99
O—H	Alcohol	0.97
O—O	O_2	1.21
P—O	Ester	1.56
S—H	Thiol	1.33
S—S	Disulfide	2.05

Glossary of Compounds

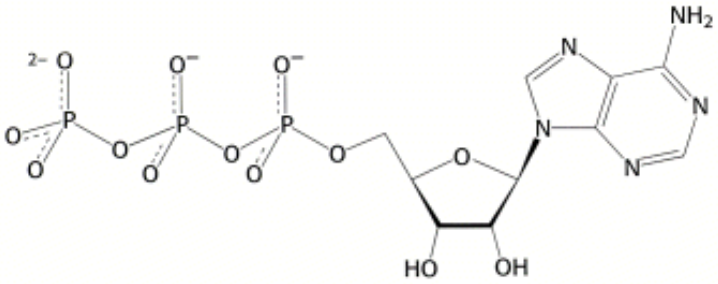
The following pages contain the structures of amino acids, common metabolic intermediates, nucleotide bases, and important cofactors. In many cases, two versions of the structure are shown: the Fisher structure (bottom) and a more stereochemically accurate version (top).

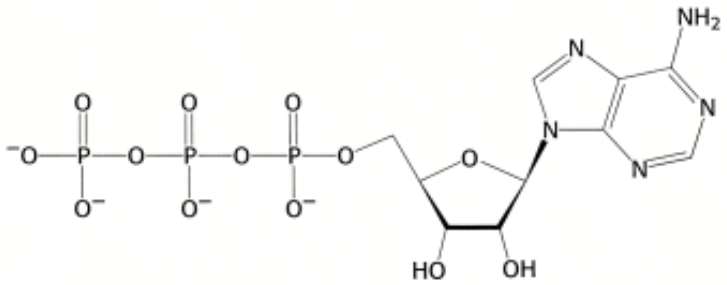


Acetyl coenzyme A (acetyl CoA)

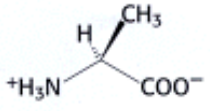


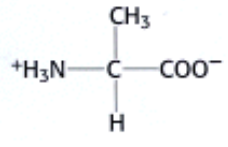
Adenine



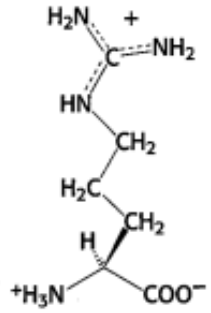


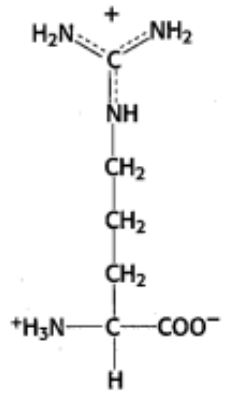
Adenosine triphosphate (ATP)



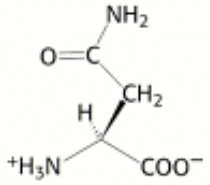


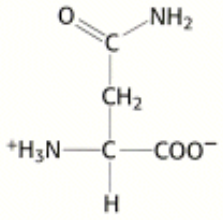
Alanine



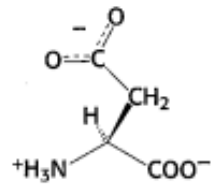


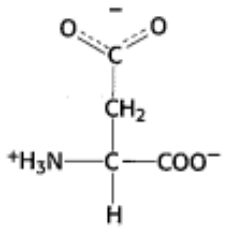
Arginine



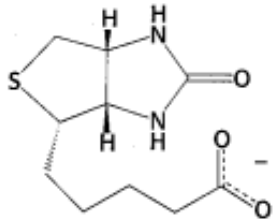


Asparagine

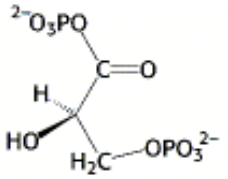


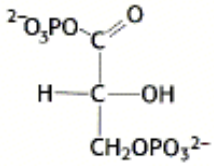


Aspartate

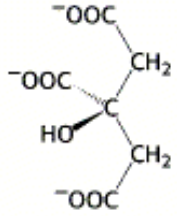


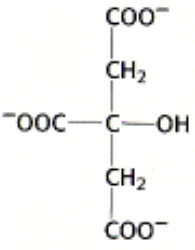
Biotin



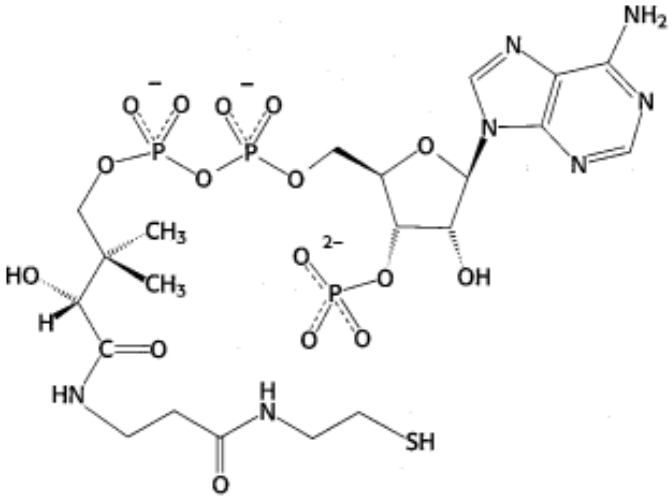


1,3-Bisphosphoglycerate

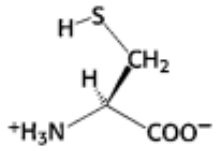


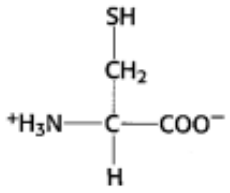


Citrate

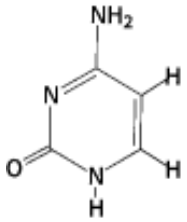


Coenzyme A

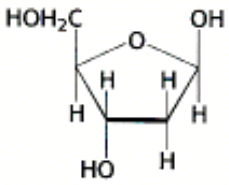




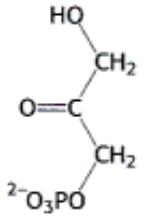
Cysteine

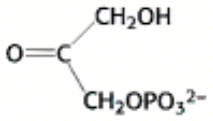


Cytosine

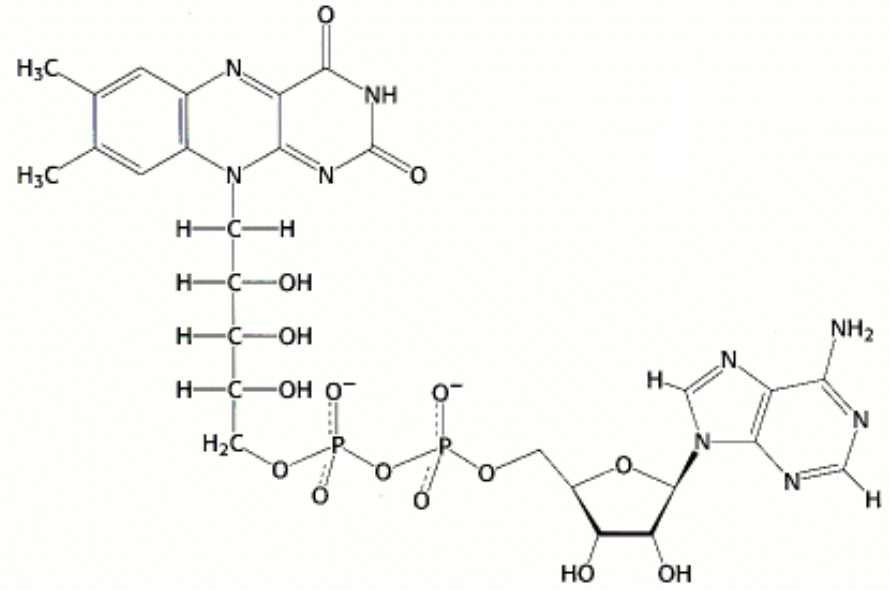


Deoxyribose

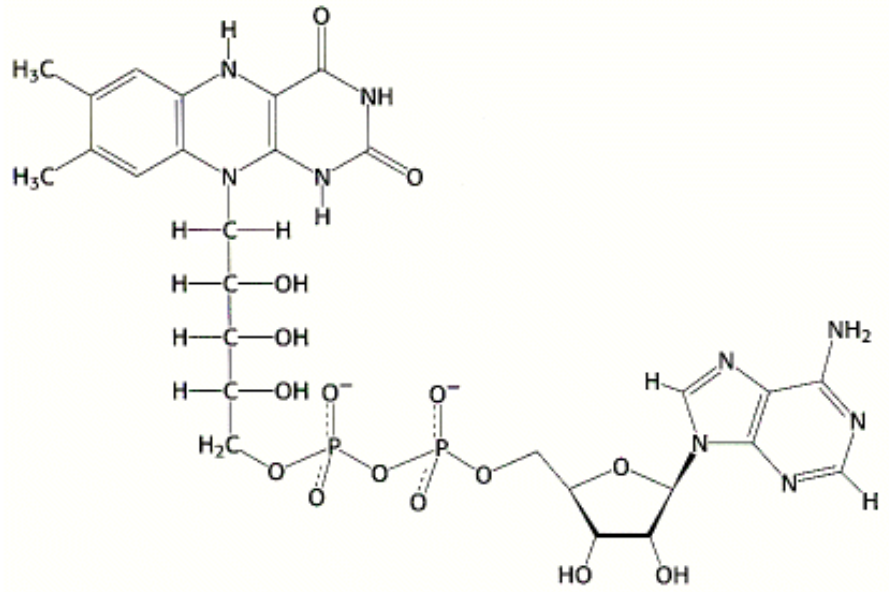




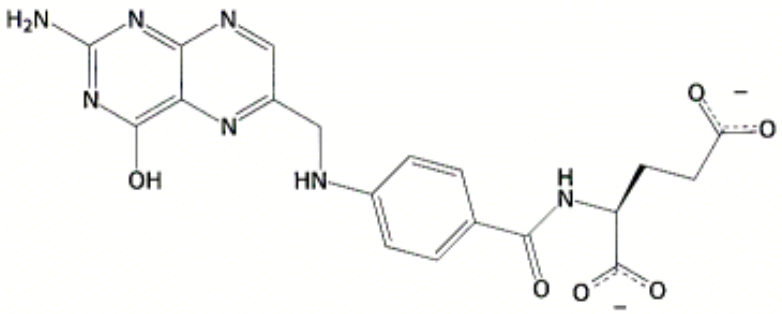
Dihydroxyacetone phosphate



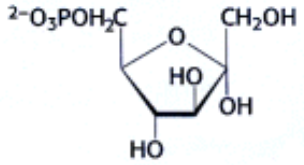
Flavin adenine dinucleotide (FAD)



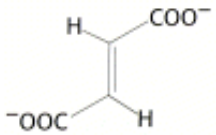
Flavin adenine dinucleotide (reduced) ($FADH_2$)



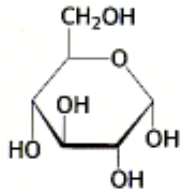
Folic acid



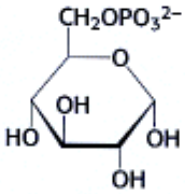
Fructose-6-phosphate



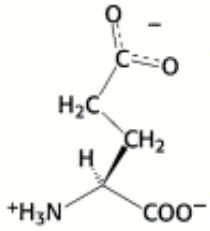
Fumarate

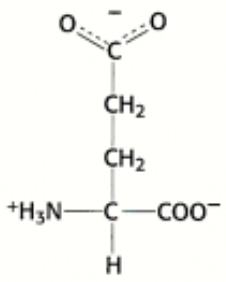


Glucose
(α-D-glucose)

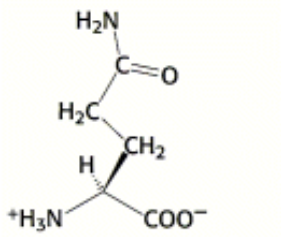


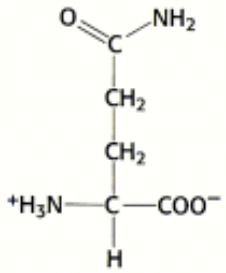
Glucose-6-phosphate



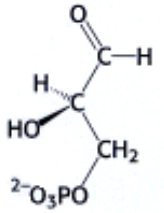


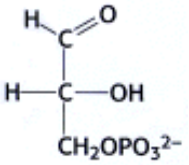
Glutamate



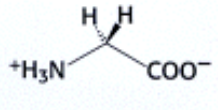


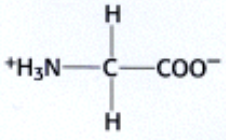
Glutamine



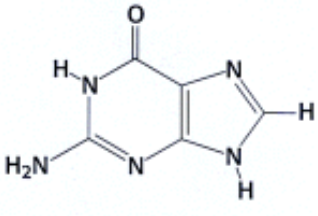


Glyceraldehyde 3-phosphate

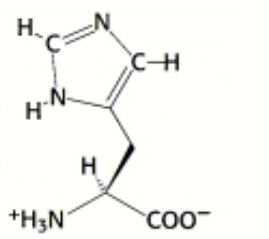


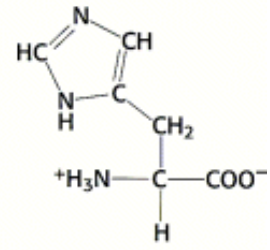


Glycine

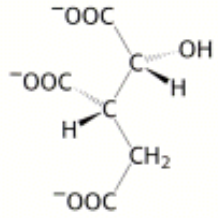


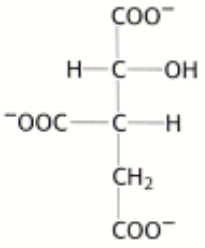
Guanine



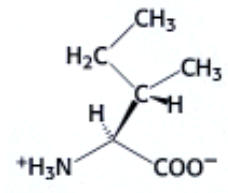


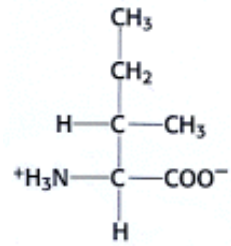
Histidine



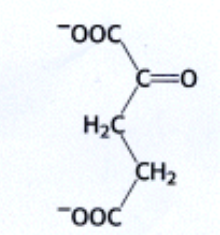


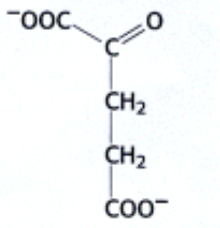
Isocitrate



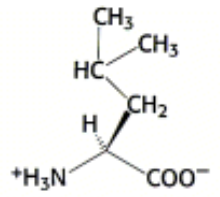


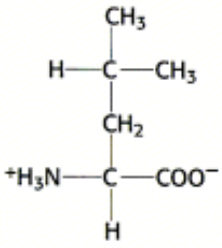
Isoleucine



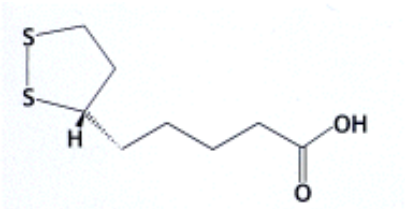


α-Ketoglutarate

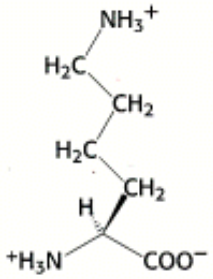


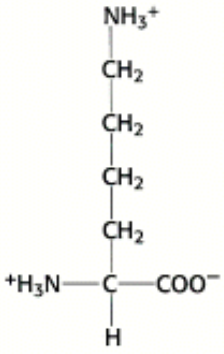


Leucine

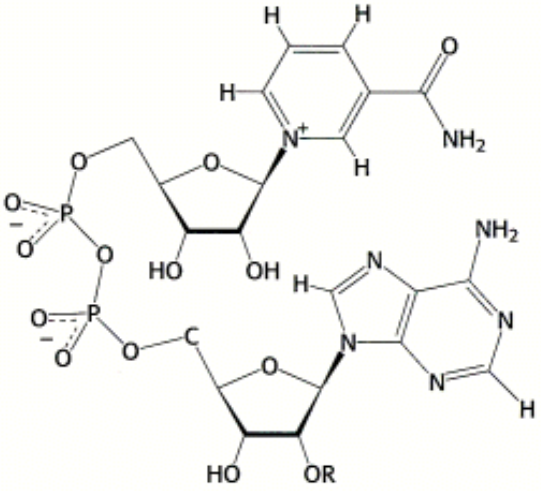


Lipoic acid



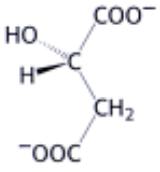


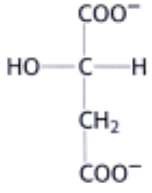
Lysine



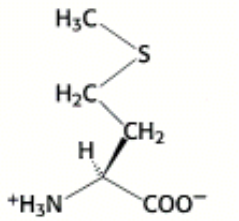
Nicotinamide adenine dinucleotide (R = H), (NAD^+)

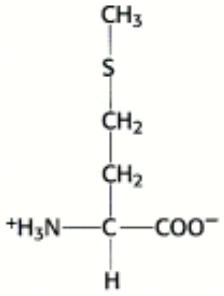
Nicotinamide adenine dinucleotide phosphate (R = PO_3^{2-}) ($NADP^+$)



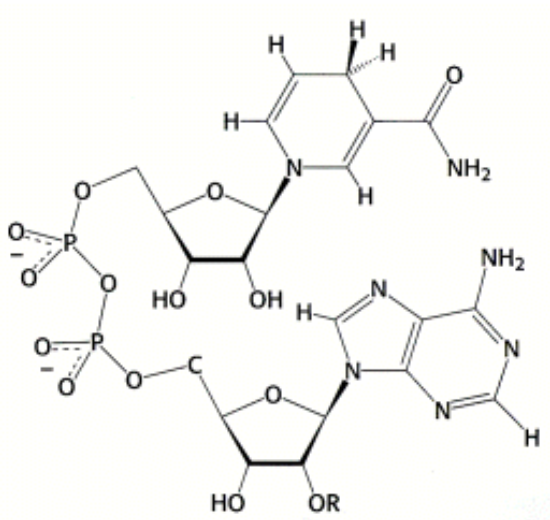


Malate

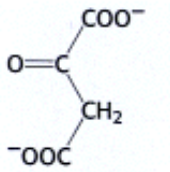


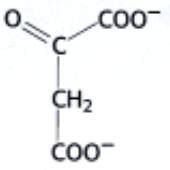


Methionine

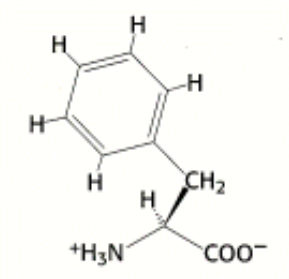


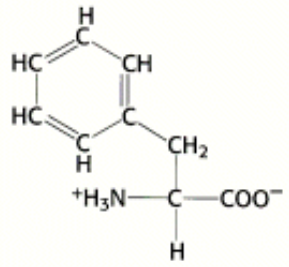
NADH (R = H), NADPH (R = PO_3^{2-})



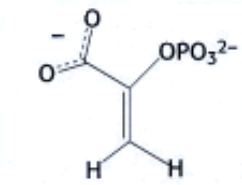


Oxaloacetate

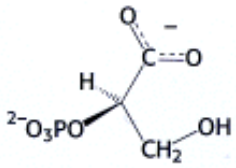


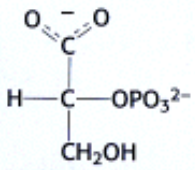


Phenylalanine

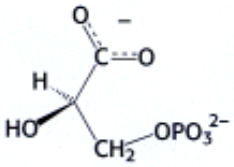


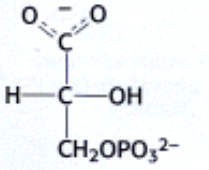
Phosphoenolpyruvate



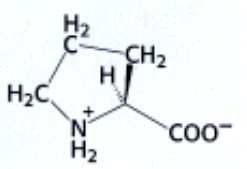


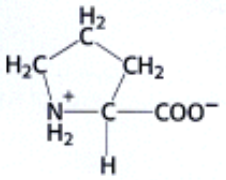
2-Phosphoglycerate



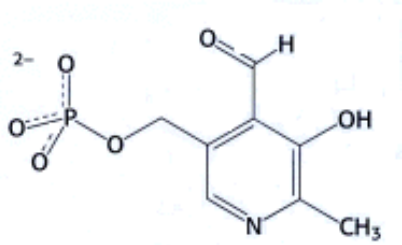


3-Phosphoglycerate

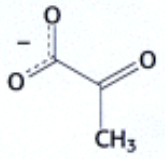




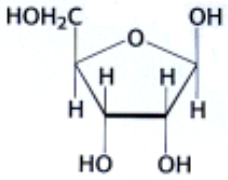
Proline



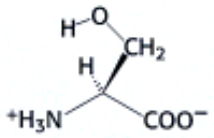
Pyridoxal phosphate

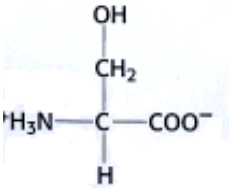


Pyruvate

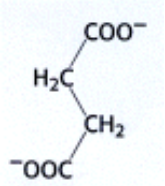


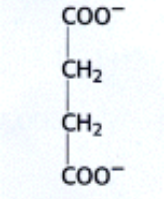
Ribose



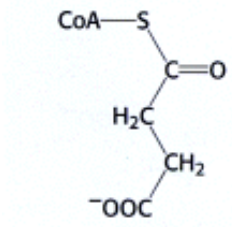


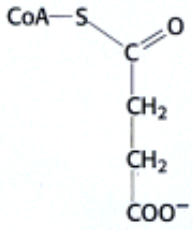
Serine



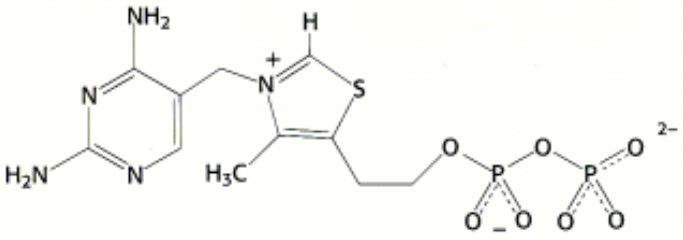


Succinate

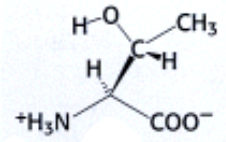


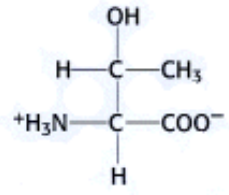


Succinyl CoA

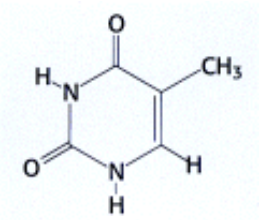


Thiamine pyrophosphate (TPP)

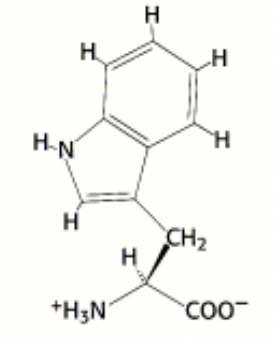


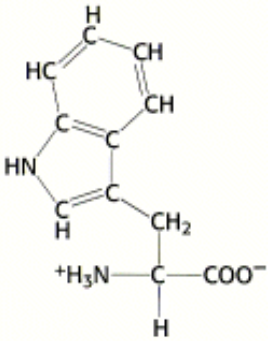


Threonine

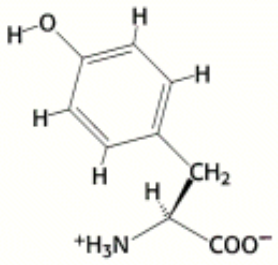


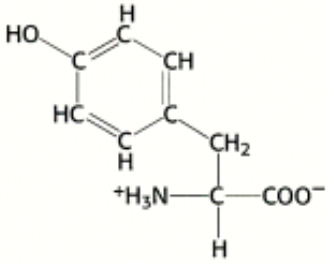
Thymine



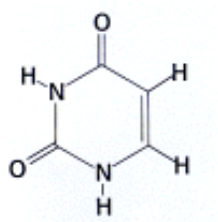


Tryptophan

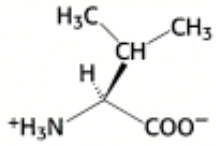


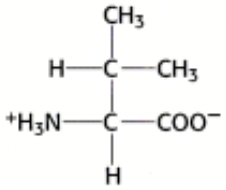


Tyrosine

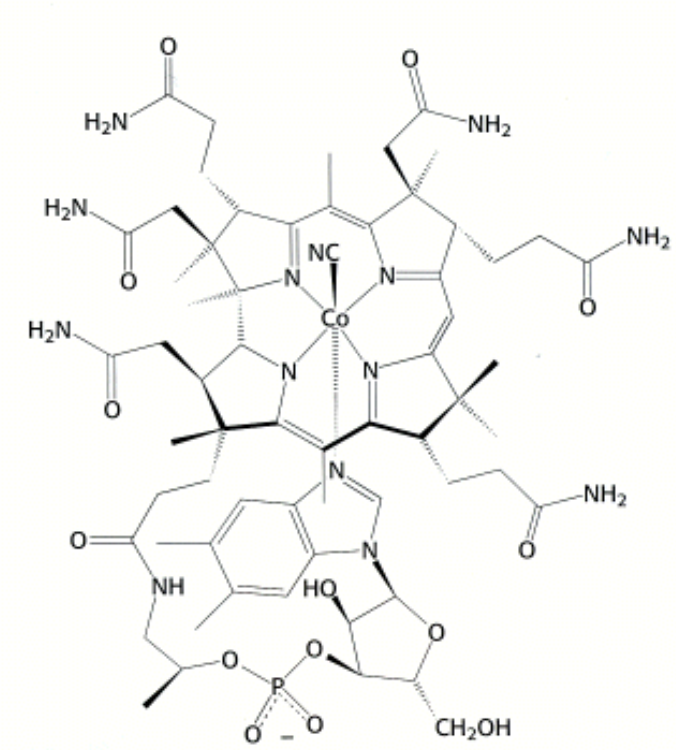


Uracil





Valine



Vitamin B_{12} (cyanocobalamin)

Answers to Problems

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Chapter 2

1. The amino group comes from ammonia. All of the carbon atoms are derived from methane. The hydrogen atoms bonded to the carbon atoms remain with the methane during bond formation or they may come from hydrogen gas. The oxygen atoms of the carboxyl group are from water.

   See question

2. We start with 99 identical RNA molecules (which we will call L) that replicate in 15 minutes and 1 variant molecule (which we will call S) that replicates in 5 minutes. After 15 minutes, we will have $2 \times 99 = 198$ molecules of L and $2^3 \times 1 = 8$ molecules of S since it replicates 3 times in 15 minutes. Thus, the population now contains $8/(8 + 198) = 3.9\%$ S. After 10 generations, each molecule of L will have replicated 10 times while each molecule of S will have replicated 30 times. The population will contain $1 \times 2^{30}/(1 \times 2^{30} + 99 \times 2^{10}) = 99.991\%$ S. After 25 generations, the population will contain essentially all S and no L.

   See question

3. The mutation permits more efficient use of substrates and thus would be most beneficial when substrate is present in low concentrations.

   See question

4. The formation of an ion gradient requires a reduction in entropy, which requires an input of free energy.

   See question

5. The decrease in free energy that results when the protons run down the ion gradient could be used to pump ions out of the cell against a concentration gradient, an energy-requiring process.

   See question

6. Two protons per electron, or eight. The generation of four hydroxyl ions (OH^-) is equivalent to the generation of four protons (H^+) on the other side of the membrane from which the reaction is taking place. The oxidation of water produces four more protons.

   See question

7. Only the gene-control protein is necessary. The hydrophobic molecule can pass through the membrane on its own.

   See question

8. Approximately eight times.

   See question

Chapter 3

1. (a) Each strand is 35 kd and hence has about 318 residues (the mean residue mass is 110 daltons). Because the rise per residue in an α helix is 1.5 Å, the length is 477 Å. More precisely, for an α-helical coiled coil the rise per residue is 1.46 Å so that the length will be 464 Å.

(b) Eighteen residues in each strand (40 minus 4 divided by 2) are in a β-sheet conformation. Because the rise per residue is 3.5 Å, the length is 63 Å.

See question

2. The methyl group attached to the β-carbon atom of isoleucine sterically interferes with α-helix formation. In leucine, this methyl group is attached to the γ-carbon atom, which is farther from the main chain and hence does not interfere.

See question

3. The first mutation destroys activity because valine occupies more space than alanine does, and so the protein must take a different shape, assuming that this residue lies in the closely packed interior. The second mutation restores activity because of a compensatory reduction of volume; glycine is smaller than isoleucine.

See question

4. The native conformation of insulin is not the thermodynamically most stable form since it contains two separate chains linked by disulfide bonds. Insulin is formed from proinsulin, a single-chain precursor, that is cleaved to form insulin with 33 residues once the disulfide bonds have formed.

See question

5. A segment of the main chain of the protease could hydrogen bond to the main chain of the substrate to form an extended parallel or antiparallel pair of β strands.

See question

6. Glycine has the smallest side chain of any amino acid. Its size often is critical in allowing polypeptide chains to make tight turns or to approach one another closely.

See question

7. Glutamate, aspartate, and the terminal carboxylate can form salt bridges with the guanidinium group of arginine. In addition, this group can be a hydrogen-bond donor to the side chains of glutamine, asparagine, serine, threonine, aspartate, and glutamate, and to the main-chain carbonyl group.

See question

8. Disulfide bonds in hair are broken by adding a thiol and applying gentle heat. The hair is curled, and an oxidizing agent is added to re-form disulfide bonds to stabilize the desired shape.

See question

9. The amino acids would be hydrophobic in nature. An α helix is especially suited to cross a membrane because all of the amide hydrogen atoms and carbonyl oxygen atoms of the peptide backbone take part in intrachain hydrogen bonds, thus stabilizing these polar atoms in a hydrophobic environment.

See question

10. The energy barrier that must be crossed to go from the polymerized state to the hydrolyzed state is large even though the reaction is thermodynamically favorable.

See question

11. Using the Henderson-Hasselbach equation, we find the ratio of alanine-COOH to alanine-COO^- at pH 7 to be 10^{-4}. The ratio of alanine-NH_2 to alanine-NH_3^+, determined in the same fashion, is 10^{-1}. Thus, the ratio of neutral alanine to zwitterionic species is $10^{-4} \times 10^{-1} = 10^{-5}$.

See question

12. The assignment of absolute configuration requires the assignment of priorities to the four groups connected to a tetrahedral carbon. For all amino acids except cysteine, the priorities are: (1) amino group; (2) carbonyl group; (3) side chain; (4) hydrogen. For cysteine, because of the sulfur atom in its side chain, the side chain has a greater priority than does the carbonyl group, leading to the assignment of an R rather than S configuration.

See question

13. LEARNINGSCIENCEISGREAT.

See question

14. No, Pro-X would have the characteristics of any other peptide bond. The steric hindrance in X-Pro arises because the R group of Pro is bonded to the amino group. Hence, in X-Pro, the proline R group is near the R group of X. This would not be the case in Pro-X.

See question

15. A, c; B, e; C, d; D, a; E, b.

See question

16. With the use of Beer's law and the value of ε obtained from Section 3.1 ($\varepsilon = 3400\ M^{-1}\ cm^{-1}$), the concentration of tryptophan is found to be ≈30 μM. Because there are three molecules of tryptophan per molecule of protein, the concentration of protein is ≈10 μM. There is 1 mg of protein per milliliter of solution.

See question

Chapter 4

1. (a) Phenyl isothiocyanate; (b) dansyl chloride or dabsyl chloride; (c) urea; β-mercaptoethanol to reduce disulfides; (d) chymotrypsin; (e) CNBr; (f) trypsin

See question

2. Each amino acid residue, except the carboxyl-terminal residue, gives rise to a hydrazide on reacting with hydrazine. The carboxyl-terminal residue can be identified because it yields a free amino acid.

See question

3. The *S*-aminoethylcysteine side chain resembles that of lysine. The only difference is a sulfur atom in place of a methylene group.

See question

4. A 1 mg/ml solution of myoglobin (17.8 kd) corresponds to 5.62×10^{-5} M. The absorbance of a 1-cm path length is 0.84, which corresponds to an I_0/I ratio of 6.96. Hence 14.4% of the incident light is transmitted.

See question

5. Tropomyosin is rod shaped, whereas hemoglobin is approximately spherical.

See question

6. The frictional coefficient f and the mass m determine S. Specifically, f is proportional to r (see equation 2 on p. 83). Hence, f is proportional to $m^{1/3}$, and so S is proportional to $m^{2/3}$ (see the equation on p. 88). An 80-kd spherical protein sediments 1.59 times as rapidly as a 40-kd spherical protein.

See question

7. 50 kd.

See question

8. The positions of disulfide bonds can be determined by diagonal electrophoresis (p. 96). The disulfide pairing is unaltered by the mutation if the off-diagonal peptides formed from the native and mutant proteins are the same.

See question

9. A fluorescent-labeled derivative of a bacterial degradation product (e.g., a formylmethionyl peptide) would bind to cells containing the receptor of interest.

See question

10. (a) Trypsin cleaves after arginine (R) and lysine (K), generating AVGWR, VK, and S. Because they differ in size, these products could be separated by molecular exclusion chromatography.

(b) Chymotrypsin, which cleaves after large aliphatic or aromatic R groups, generates two peptides of equal size (AVGW) and (RVKS). Separation based on size would not be effective. The peptide RVKS has two positive charges (R and K), whereas the other peptide is neutral. Therefore, the two products could be separated by ion-exchange chromatography.

See question

11. An inhibitor of the enzyme being purified might have been present and subsequently removed by a purification step. This would lead to an apparent increase in the total amount of enzyme present.

See question

12. See table below.

Purification procedure	Total protein (mg)	Total activity (units)	Specific activity (units/mg)	Purification level	Yield (%)
Crude extract	20,000	4,000,000	200	1	100
$(NH_4)_2SO_4$ precipitation	5,000	3,000,000	600	3	75
DEAE–cellulose chromatography	1,500	1,000,000	667	3.3	25
Size-exclusion chromatography	500	750,000	1,500	7.5	19
Affinity chromatography	45	675,000	15,000	75	17

See question

13. Treatment with urea will disrupt noncovalent bonds. Thus the original 60-kd protein must be made of two 30-kd subunits. When these subunits are treated with urea and mercaptoethanol, a single 15-kd species results, suggesting that disulfide bonds link the 30-kd subunits.

See question

14. (a) Electrostatic repulsion between positively charged ε-amino groups hinders α-helix formation at pH 7. At pH 10, the side chains become deprotonated, allowing α-helix formation.

(b) Poly-l-glutamate is a random coil at pH 7 and becomes α helical below pH 4.5 because the γ-carboxylate groups become protonated.

See question

15. Light was used to direct the synthesis of these peptides. Each amino acid added to the solid support contained a photolabile protecting group instead of a *t*-Boc protecting group at its α-amino group. Illumination of selected regions of the solid support led to the release of the protecting group, which exposed the amino groups in these sites to make them reactive. The pattern of masks used in these illuminations and the sequence of reactants define the ultimate products and their locations.

See question

16. AVRYSR

See question

17. First amino acid: S

Last amino acid: L

Cyanogen bromide cleavage: M is 10th position, C-terminal residues are: (2S,L,W)

Amino-terminal residues: (G,K,S,Y), tryptic peptide, ends in K

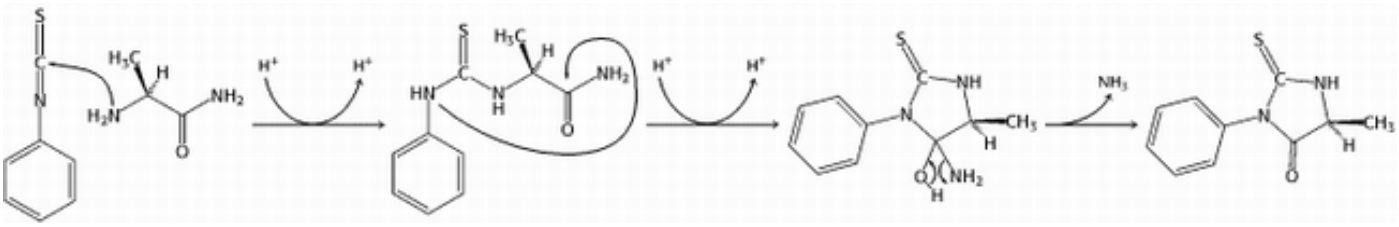
Amino-terminal sequence: SYGK

Chymotryptic peptide order: (S,Y), (G,K,L), (F,I,S), (M,T), (S,W), (S,L)

Sequence: SYGKLSIFTMSWSL

See question

18. See equation below.



See question

Chapter 5

1. (a) TTGATC; (b) GTTCGA; (c) ACGCGT; (d) ATGGTA.

See question

2. (a) [T] + [C] = 0.46. (b) [T] = 0.30, [C] = 0.24, and [A] + [G] = 0.46.

See question

3. 5.7×10^3 base pairs.

See question

4. In conservative replication, after 1.0 generation, half of the molecules would be ^{15}N-^{15}N, the other half ^{14}N-^{14}N. After 2.0 generations, one-quarter of the molecules would be ^{15}N-^{15}N, the other three-quarters ^{14}N-^{14}N. Hybrid ^{14}N-^{15}N molecules would not be observed in conservative replication.

See question

5. (a) Tritiated thymine or tritiated thymidine. (b) dATP, dGTP, dCTP, and dTTP labeled with ^{32}P in the innermost (α) phosphorus atom.

See question

6. Molecules in parts *a* and *b* would not lead to DNA synthesis because they lack a 3′-OH group (a primer). The molecule in part *d* has a free 3′-OH at one end of each strand but no template strand beyond. Only the molecule in part *c* would lead to DNA synthesis.

See question

7. A thymidylate oligonucleotide should be used as the primer. The poly(rA) template specifies the incorporation of T; hence, radioactive TTP (labeled in the α-phosphate) should be used in the assay.

See question

8. The ribonuclease serves to degrade the RNA strand, a necessary step in forming duplex DNA from the RNA-DNA hybrid.

See question

9. Treat one aliquot of the sample with ribonuclease and another with deoxyribonuclease. Test these nuclease-treated samples for infectivity.

See question

10. Deamination changes the original G · C base pair into a G · U pair. After one round of replication, one daughter duplex will contain a G · C pair, and the other duplex an A · U pair. After two rounds of replication, there would be two G · C pairs, one A · U pair, and one A · T pair.

See question

11. (a) $4^8 = 65{,}536$. In computer terminology, there are 64K 8-mers of DNA.

(b) A bit specifies two bases (say, A and C) and a second bit specifies the other two (G and T). Hence, two bits are needed to specify a single nucleotide (base pair) in DNA. For example, 00, 01, 10, and 11 could encode A, C, G, and T. An 8-mer stores 16 bits ($2^{16} = 65{,}536$), the *E. coli* genome (4×10^6 bp) stores 8×10^6 bits, and the human genome (2.9×10^9 bases) stores 5.8×10^9 bits of genetic information.

(c) A floppy diskette stores about 1.5 megabytes, which is equal to 1.2×10^7 bits. A large number of 8-mer sequences could be stored on such a diskette. The DNA sequence of *E. coli*, could be written on a single diskette. Nearly 500 diskettes would be needed to record the human DNA sequence.

See question

12. (a) Deoxyribonucleoside triphosphates versus ribonucleoside triphosphates.

(b) $5' \rightarrow 3'$ for both.

(c) Semiconserved for DNA polymerase I; conserved for RNA polymerase.

(d) DNA polymerase I needs a primer, whereas RNA polymerase does not.

See question

13. (a) 5′-UAACGGUACGAU-3′.

(b) Leu-Pro-Ser-Asp-Trp-Met.

(c) Poly(Leu-Leu-Thr-Tyr).

See question

14. The 2′-OH group in RNA acts as an intramolecular nucleophil. In the alkaline hydrolysis of RNA, it forms a 2′-3′ cyclic intermediate.

See question

15. Cordycepin terminates RNA synthesis. An RNA chain containing cordycepin lacks a 3′-OH group.

See question

16. Only single-stranded RNA can serve as a template for protein synthesis.

See question

17. Incubation with RNA polymerase and only UTP, ATP, and CTP led to the synthesis of only poly(UAC). Only poly (GUA) was formed when GTP was used in place of CTP.

See question

18. These alternatives were distinguished by the results of studies of the sequence of amino acids in mutants. Suppose that the base C is mutated to C′. In a nonoverlapping code, only amino acid 1 will be changed. In a completely overlapping code, amino acids 1, 2, and 3 will all be altered by a mutation of C to C′. The results of amino acid sequence studies of tobacco mosaic virus mutants and abnormal hemoglobins showed that alterations usually affected only a single amino acid. Hence, it was concluded that the *genetic code is nonoverlapping.*

See question

19. A peptide terminating with Lys (UGA is a stop codon), -Asn-Glu-, and -Met-Arg-.

See question

20. Highly abundant amino acid residues have the most codons (e.g., Leu and Ser each have six), whereas the least-abundant amino acids have the fewest (Met and Trp each have only one). Degeneracy (a) allows variation in base composition and (b) decreases the likelihood that a substitution for a base will change the encoded amino acid. If the degeneracy were equally distributed, each of the 20 amino acids would have three codons. Both benefits (a and b) are maximized by the assignment of more codons to prevalent amino acids than to less frequently used ones.

See question

21. Phe-Cys-His-Val-Ala-Ala.

See question

22. Hydrogen cyanide. Adenine can be viewed as a pentamer of HCN.

See question

23. (a) A codon for lysine cannot be changed to one for aspartate by the mutation of a single nucleotide.

(b) Arg, Asn, Gln, Glu, Ile, Met, or Thr.

See question

24. The genetic code is degenerate. Of the 20 amino acids, 18 are specified by more than one codon. Hence, many nucleotide changes (especially in the third base of a codon) do not alter the nature of the encoded amino acid. Mutations leading to an altered amino acid are usually more deleterious than those that do not and hence are subject to more stringent selection.

See question

Chapter 12

1. 2.86×10^6 molecules, because each leaflet of the bilayer contains 1.43×10^6 molecules.

See question

2. 2×10^{-7} cm, 6×10^{-6} cm, and 2×10^{-4} cm.

See question

3. The radius of this molecule is 3.1×10^{-7} cm, and its diffusion coefficient is 7.4×10^{-9} cm^2 s^{-1}. The average distances traversed are 1.7×10^{-7} cm in 1 μs, 5.4×10^{-6} in 1 ms, and 1.7×10^{-4} cm in 1 s.

See question

4. The membrane underwent a phase transition from a highly fluid to a nearly frozen state when the temperature was lowered. A carrier can shuttle ions across a membrane only when the bilayer is highly fluid. A channel former, in contrast, allows ions to traverse its pore even when the bilayer is quite rigid.

See question

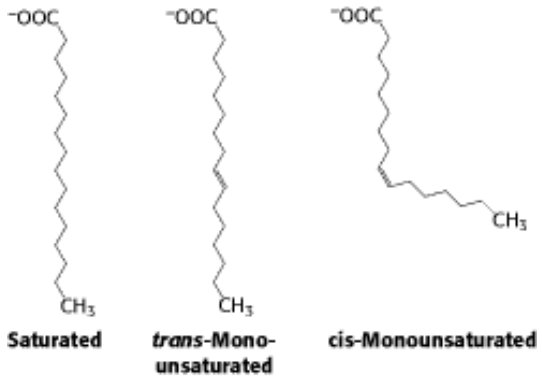
5. The initial decrease in the amplitude of the paramagnetic resonance spectrum results from the reduction of spinlabeled phosphatidyl choline molecules in the outer leaflet of the bilayer. Ascorbate does not traverse the membrane under these experimental conditions; hence, it does not reduce the phospholipids in the inner leaflet. The slow decay of the residual spectrum is due to the reduction of phospholipids that have flipped over to the outer leaflet of the bilayer.

See question

6. The addition of the carbohydrate introduces a significant energy barrier to the flip-flop because a hydrophilic carbohydrate moiety would need to be moved through a hydrophobic environment. This energetic barrier enhances membrane asymmetry.

See question

7. The presence of a cis double bond introduces a kink that prevents packing of the fatty acid chains. Cis double bonds maintain fluidity. Trans fatty acids have no structural effect, relative to saturated fatty acids, and so they are rare.



See question

8. In a hydrophobic environment, the formation of intrachain hydrogen bonds would stabilize the amide hydrogen atom and carbonyl oxygen atoms of the polypeptide chain; so an α helix would form. In an aqueous environment, these groups would be stabilized by interaction with water, so there would be no energetic reason to form an α helix. Thus, the α helix would be most likely to form in an hydrophobic environment.

See question

9. The shift to the lower temperature would decrease fluidity by enhancing packing of the hydrophobic chains by van der Waals interaction. To prevent this, new phospholipids would be synthesized having shorter chains and a greater number of cis double bonds. The shorter chains would reduce the amount of van der Waals interaction, and the cis double bonds, causing the kink in structure, would prevent packing of the fatty acid tails of the phospholipids.

See question

10. (a) The graph shows that, as temperature increases, the phospholipid bilayer becomes more fluid. T_m is the temperature of the transition from the predominantly less fluid state to the predominantly more fluid state. Cholesterol broadens the transition from the less-fluid to the more-fluid state. In essence, cholesterol makes membrane fluidity less sensitive to temperature changes.

(b) This effect is important because the presence of cholesterol tends to stabilize membrane fluidity by preventing sharp transitions. Because protein function depends on the proper fluidity of the membrane, cholesterol maintains the proper environment for membrane-protein function.

See question

11. Protein C is a transmembrane protein from *C. elegans.* It spans the membrane with four α helices that are prominently displayed as hydrophobic peaks in the hydropathy plot. Interestingly, protein A also is a membrane protein, a porin. This protein is made primarily of β strands, which lack the prominent hydrophobic window of membrane helices. This example shows that, although hydropathy plots are useful, they are not infallible.

See question

12. To purify any protein, the protein must first be solubilized. For a membrane protein, solubilization usually requires a detergent—hydrophobic molecules that bind to the protein and thus replace the lipid environment of the membrane. If the detergent is removed, the protein aggregates and precipitates from solution. Often, performing purification steps, such as ion-exchange chromatography, in the presence of sufficient detergent to solubilize the protein is difficult. Crystals must be generated of appropriate protein-detergent complexes.

See question

Chapter 14

1. Reactions in parts *a* and *c,* to the left; reactions in parts *b* and *d,* to the right.

See question

2. None whatsoever.

See question

3. (a) $\Delta G^{\circ\prime} = +7.5$ kcal mol^{-1} (+31.4 kJ mol^{-1}) and $K'_{eq} = 3.2 \times 10^{-6}$. (b) 3.28×10^{4}.

See question

4. $\Delta G^{\circ\prime} = -1.7$ kcal mol^{-1} (-7.1 kJ mol^{-1}). The equilibrium ratio is 17.8.

See question

5. (a) Acetate + CoA + H^+ goes to acetyl CoA + H_2O, $\Delta G^{\circ\prime} = +7.5$ kcal mol^{-1} (+31.4 kJ mol^{-1}). ATP hydrolysis, $\Delta G^{\circ\prime} = -10.9$ kcal mol^{-1} (-45.6 kJ mol^{-1}). Overall reaction, $\Delta G^{\circ\prime} = -3.4$ kcal mol^{-1} (-14.2 kJ mol^{-1}).

(b) With pyrophosphate hydrolysis, $\Delta G^{\circ\prime} = -8.0$ kcal mol^{-1} (-33.4 kJ mol^{-1}).

See question

6. (a)

$$\text{For an acid AH, } AH \rightleftharpoons A^- + H^+, \; K = \frac{[A^-][H^+]}{[AH]}$$

The pK is defined as pK = $-\log_{10} K$. $\Delta G^{\circ\prime}$ is the standard free energy change at pH 7. Thus, $\Delta G^{\circ\prime} = -RT \ln K = -2.303 \log_{10} K = -2.303$ (pK - 7) kcal mol^{-1} since $[H^+] = 10^{-7}$ M.

(b) $\Delta G^{\circ\prime} = -2.303$ (4.8 - 7) = -5.1 kcal mol^{-1} (-21.3 kJ mol^{-1}).

See question

7. Arginine phosphate in invertebrate muscle, like creatine phosphate in vertebrate muscle, serves as a reservoir of high-potential phosphoryl groups. Arginine phosphate maintains a high level of ATP in muscular exertion.

See question

8. An ADP unit.

See question

9. (a) The rationale behind creatine supplementation is that it would be converted into creatine phosphate and thus serves as a rapid means of replenishing ATP after muscle contraction.

(b) If it is beneficial, it would affect activities that depend on short bursts of activity; any sustained activity would require ATP generation by fuel metabolism, which, as Figure 14.7 shows, requires more time.

See question

10. Under standard conditions, $\Delta G^{\circ\prime} = -RT \ln$ [product]/[reactants]. Substituting +5.7 kcal mol^{-1} for $\Delta G^{\circ\prime}$ and solving for [products]/[reactants] yields 7×10^{-5}. In other words, the forward reaction does not take place to a significant extent. Under intracellular conditions, ΔG is 0.3 kcal mol^{-1}. If one uses the equation $\Delta G = \Delta G^{\circ\prime} + RT \ln$ [product]/ [reactants] and solves for [products]/[reactants], the ratio is 3.7×10^{-5}. Thus, a reaction that is endergonic under standard conditions can be converted into an exergonic reaction by maintaining the [products]/[reactants] ratio below the equilibrium value. This conversion is usually attained by using the products in another coupled reaction as soon as they are formed.

See question

11. Liver: -10.8 kcal mol^{-1} (-45.2 kJ mol^{-1}); muscle: -11.5 kcal mol^{-1} (-47.8 kJ mol^{-1}); brain: -11.6 kcal mol^{-1}(-48.4 kJ mol^{-1}).

See question

12. Recall that $\Delta G = \Delta G^{\circ'} + RT \ln$ [products/reactants]. Altering the ratio of products to reactants will cause ΔG to vary. In glycolysis, the concentrations of the components of the pathway result in a value of ΔG greater than that of $\Delta G^{\circ'}$.

See question

13. The activated form of sulfate in most organisms is 3′-phosphoadenosine 5′-phosphosulfate.

See question

14. (a) As the Mg^{2+} concentration falls, the ΔG of hydrolysis rises. Note that pMg is a logarithmic plot, and so each number on the *x*-axis represents a 10-fold change in [Mg^{2+}].

(b) Mg^{2+} would bind to the phosphates of ATP and help to mitigate charge repulsion. As the [Mg^{2+}] falls, charge stabilization of ATP would be less, leading to greater charge repulsion and an increase in ΔG on hydrolysis.

See question

Chapter 15

1. Each activated β-adrenergic receptor activates many G proteins. Each G protein activates one molecule of adenylate cyclase, which generates many molecules of cAMP. Each activated human growth-factor receptor can activate more than one molecule of JAK2. Each JAK2 molecule can phosphorylate many STAT5 molecules. Each activated EGF receptor can activate Grb-2 and Sos. Each molecule of Sos can activate many molecules of Ras.

See question

2. The negatively charged glutamate residues mimic the negatively charged phosphoserine or phosphothreonine residues and stabilize the active conformation of the enzyme.

See question

3. No. Phosphoserine and phosphothreonine are considerably shorter than phosphotyrosine.

See question

4. Removal of the regulatory subunit from PKA with the binding of cAMP. Removal of the pseudosubstrate from PKC by diacylglycerol binding. Removal of the amphipathic helix from the active site of CaM kinase by calmodulin.

See question

5. The mutant should always be active because the pseudosubstrate will not bind in the active site.

See question

6. Growth-factor receptors can be activated by dimerization. If an antibody causes a receptor to dimerize, the signal-transduction pathway in a cell will be activated.

See question

7. The α subunit will always be in the GTP form and, hence, should always be in the active form, stimulating its signaling pathway.

See question

8. The mutated hormone would bind to the growth-hormone receptor but would not favor receptor dimerization. Thus, it would not stimulate the JAK-STAT signaling pathway. Such a mutated hormone might be useful as a competitive inhibitor for growth hormone. It would block the activity of native growth hormone.

See question

9. Calcium ions diffuse slowly because they bind to many protein surfaces within a cell, impeding their free motion. cAMP does not bind as frequently, and so it diffuses more rapidly.

See question

10. G_{α^s} stimulates adenylate cyclase, leading to the generation of cAMP. This signal then leads to glucose mobilization (see Chapter 21). If cAMP phosphodiesterase were inhibited, then cAMP levels would remain high even after the termination of the epinephrine signal, and glucose mobilization would continue.

See question

11. The formation of diacylglycerol implies the participation of phospholipase C. A simple pathway would entail receptor activation by cross-phosphorylation, followed by the binding of phospholipase C γ (through its SH2 domains). The participation of phospholipase C indicates that IP_3 should be formed and, hence, calcium concentrations should increase.

See question

12. In the reaction catalyzed by adenylate cyclase, the 3′-OH group nucleophilically attacks the α-phosphorus atom attached to the 5′-OH group, leading to displacement of pyrophosphate. The reaction catalyzed by DNA polymerase is similar except that the 3′-OH group is on a different nucleotide.

See question

13. (a) X ≈ 10^{-7} M; Y ≈ 5 × 10^{-6} M; Z ≈ 10^{-3} M. (b) Because much less X is required to fill half of the sites, X displays the highest affinity. (c) The binding affinity almost perfectly matches the ability to stimulate adenylate cyclase, suggesting that the hormone-receptor complex leads to the stimulation of adenylate cyclase. (d) Try performing the experiment in the presence of antibodies to $G_{\alpha s}$.

See question

14. (a) The total binding does not distinguish between binding to a specific receptor, binding to different receptors, and nonspecific binding to the membrane.

(b) The rationale is that the receptor will have a high affinity for the ligand. Thus, in the presence of excess nonradioactive ligand, the receptor will bind to nonradioactive ligand. Therefore, any binding of the radioactive ligand must be nonspecific.

(c) The plateau suggests that the number of receptor-binding sites in the cell membrane is limited.

See question

15. Number of receptors per cell =

$$\frac{10^4 \text{ cpm}}{\text{mg of membrane protein}} \times \frac{\text{mg of membrane protein}}{10^{10} \text{ cells}} \times \frac{\text{mmol}}{10^{12} \text{ cpm}} \times \frac{6.023 \times 10^{20} \text{ molecules}}{\text{mmol}} = 600$$

See question

Chapter 16

1. Glucose is reactive because its open-chain form contains an aldehyde group.

See question

2. (a) The label is in the methyl carbon atom of pyruvate.

(b) 5 mCi/mM. The specific activity is halved because the number of moles of product (pyruvate) is twice that of the labeled substrate (glucose).

See question

3. (a) Glucose + 2 P_i + 2 ADP ⟶ 2 lactate + 2 ATP

(b) $\Delta G'$ = -27.2 kcal mol^{-1} (-114 kJ mol^{-1}).

See question

4. 3.06×10^{-5}.

See question

5. The equilibrium concentrations of fructose 1,6-bisphosphate, dihydroxyacetone phosphate, and glyceraldehyde 3-phosphate are 7.8×10^{-4} M, 2.2×10^{-4} M, and 2.2×10^{-4} M, respectively.

See question

6. All three carbon atoms of 2,3-BPG are ^{14}C labeled. The phosphorus atom attached to the C-2 hydroxyl group is ^{32}P labeled.

See question

7. Hexokinase has a low ATPase activity in the absence of a sugar because it is in a catalytically inactive conformation. The addition of xylose closes the cleft between the two lobes of the enzyme. However, xylose lacks a hydroxymethyl group, and so it cannot be phosphorylated. Instead, a water molecule at the site normally occupied by the C-6 hydroxymethyl group acts as the acceptor of the phosphoryl group from ATP.

See question

8. (a) The fructose 1-phosphate pathway forms glyceraldehyde 3-phosphate.

(b) Phosphofructokinase, a key control enzyme, is bypassed. Furthermore, fructose 1-phosphate stimulates pyruvate kinase.

See question

9. (a) Increased; (b) increased; (c) increased; (d) decreased.

See question

10. Fructose 2,6-bisphosphate, present at high concentration when glucose is abundant, normally inhibits gluconeogenesis by blocking fructose 1,6-bisphosphatase. In this genetic disorder, the phosphatase is active irrespective of the glucose level. Hence, substrate cycling is increased. The level of fructose 1,6-bisphosphate is consequently lower than normal. Less pyruvate is formed and thus less ATP is generated.

See question

11. Reactions in parts *b* and *e* would be blocked.

See question

12. There will be no labeled carbons. The CO_2 added to pyruvate (formed from the lactate) to form oxaloacetate is lost with the conversion of oxaloacetate into phosphoenolpyruvate.

See question

13. The net reaction in the presence of arsenate is

$$\text{Glyceraldehyde 3-phosphate} + NAD^+ + H_2O \longrightarrow \text{3-phosphoglycerate} + NADH + 2\,H^+$$

Glycolysis proceeds in the presence of arsenate, but the ATP normally formed in the conversion of 1,3-bisphosphoglycerate into 3-phosphoglycerate is lost. Thus, arsenate uncouples oxidation and phosphorylation by forming a highly labile acyl arsenate.

See question

14. This example illustrates the difference between *stoichio-metric* and *catalytic* utilization of a molecule. If cells used NAD^+ stoichiometrically, a new molecule of NAD^+ would be required each time a lactate is produced. As we will see, the synthesis of NAD^+ requires ATP. On the other hand, if the NAD^+ that is converted into NADH could be recycled and reused, a small amount of the molecule could regenerate a vast amount of lactate. This is the case in the cell. NAD^+ is regenerated by the oxidation of NADH and reused. NAD^+ is thus used catalytically.

See question

15. Consider the equilibrium equation of adenylate kinase.

$$K_{eq} = [ATP][AMP]/[ADP]^2 \qquad (1)$$

or

$$[AMP] = K_{eq}[ADP]^2/[ATP] \qquad (2)$$

Recall that [ATP] > [ADP] > [AMP] in the cell. As ATP is utilized, a small decrease in its concentration will result in a larger percentage increase in [ADP] because its concentration is greater than that of ADP. This larger percentage increase in [ADP] will result in an even greater percentage increase in [AMP] because its concentration is related to the square of [ADP]. In essence, equation 2 shows that monitoring the energy status with AMP magnifies small changes in [ATP], leading to tighter control.

See question

16. The synthesis of glucose during intense exercise provides a good example of interorgan cooperation in higher organisms. When muscle is actively contracting, lactate is produced from glucose by glycolysis. The lactate is released into the blood and absorbed by the liver, where it is converted by gluconeogenesis into glucose. The newly synthesized glucose is then released and taken up by the muscle for energy generation.

See question

17. The input of four additional high-phosphoryl-transfer potential molecules in gluconeogenesis changes the equilibrium constant by a factor of 10^{32}, which makes the conversion of pyruvate into glucose thermodynamically feasible. Without this energetic input, gluconeogenesis would not take place.

See question

18. The mechanism is analogous to that for triose phosphate isomerase (Figure 16.6). It proceeds through an enediol intermediate. The active site would be expected to have a general base (analogous to Glu 165 in TIM) and a general acid (analogous to His 95 in TIM).

See question

19. Galactose is a component of glycoproteins. Possibly, the absence of galactose leads to the improper formation or function of glycoproteins required in the central nervous system. More generally, the fact that the symptoms arise in the absence of galactose suggests that galactose is required in some fashion.

See question

20. (a) Curiously, the enzyme uses ADP as the phosphoryl donor rather than ATP.

(b) Both AMP and ATP behave as competitive inhibitors of ADP, the phosphoryl donor. Apparently, the *P. furiosus* enzyme is not allosterically inhibited by ATP.

See question

Chapter 17

1. (a) After one round of the citric acid cycle, the label emerges in C-2 and C-3 of oxaloacetate. (b) The label emerges in CO_2 in the formation of acetyl CoA from pyruvate. (c) After one round of the citric acid cycle, the label emerges in C-1 and C-4 of oxaloacetate. (d and e) Same fate as that in part *a*.

See question

2. (a) Isocitrate lyase and malate synthase are required in addition to the enzymes of the citric acid cycle.

(b) 2 Acetyl CoA + 2 NAD^+ + FAD + 3 $H_2O \rightarrow$ oxaloacetate + 2 CoA + 2 NADH + $FADH_2$ + 3 H^+

(c) No. Hence, mammals cannot carry out the net synthesis of oxaloacetate from acetyl CoA.

See question

3. -9.8 kcal mol^{-1} (-41.0 kJ mol^{-1}).

See question

4. Enzymes or enzyme complexes are biological catalysts. Recall that a catalyst facilitates a chemical reaction without the catalyst itself being permanently altered. Oxaloacetate can be thought of as a catalyst because it binds to an acetyl group, leads to the oxidative decarboxylation of the two carbon atoms, and is regenerated at the completion of a cycle. In essence, oxaloacetate (and any cycle intermediate) acts as a catalyst.

See question

5. The coenzyme stereospecificity of glyceraldehyde 3-phosphate dehydrogenase is the opposite of that of alcohol dehydrogenase

See question

6. Thiamine thiazolone pyrophosphate is a transition-state analog. The sulfur-containing ring of this analog is uncharged, and so it closely resembles the transition state of the normal coenzyme in thiamine-catalyzed reactions (e. g., the uncharged resonance form of hydroxyethyl-TPP).

See question

7. A decrease in the amount of O_2 will necessitate an increase in anaerobic glycolysis for energy production, leading to the generation of a large amount of lactic acid. Under conditions of shock, the kinase inhibitor is administered to ensure that pyruvate dehydrogenase is operating maximally.

See question

8. (a) The steady-state concentrations of the products are low compared with those of the substrates. (b) The ratio of malate to oxaloacetate must be greater than 1.75×10^4 for oxaloacetate to be formed.

See question

9.

$$\text{Pyruvate} + \text{CoA} + \text{NAD}^+ \xrightarrow{\text{Pyruvate dehydrogenase complex}} \text{acetyl CoA} + \text{CO}_2 + \text{NADH}$$

$$\text{Pyruvate} + \text{CO}_2 + \text{ATP} + \text{H}_2\text{O} \xrightarrow{\text{Pyruvate carboxylase}} \text{oxaloacetate} + \text{ADP} + \text{P}_i$$

$$\text{Oxaloacetate} + \text{acetyl CoA} + \text{H}_2\text{O} \xrightarrow{\text{Citrate synthase}} \text{citrate} + \text{CoA} + \text{H}^+$$

$$\text{Citrate} \xrightarrow{\text{Aconitase}} \text{isocitrate}$$

$$\text{Isocitrate} + \text{NAD}^+ \xrightarrow{\text{Isocitrate dehydrogenase}} \alpha\text{-ketoglutarate} + \text{CO}_2 + \text{NADH}$$

Net:

$$2 \text{ pyruvate} + 2 \text{ NAD}^+ + \text{ATP} + \text{H}_2\text{O} \longrightarrow \alpha\text{-ketoglutarate} + \text{CO}_2 + \text{ADP} + \text{P}_i + 2 \text{ NADH} + 2 \text{ H}^+$$

See question

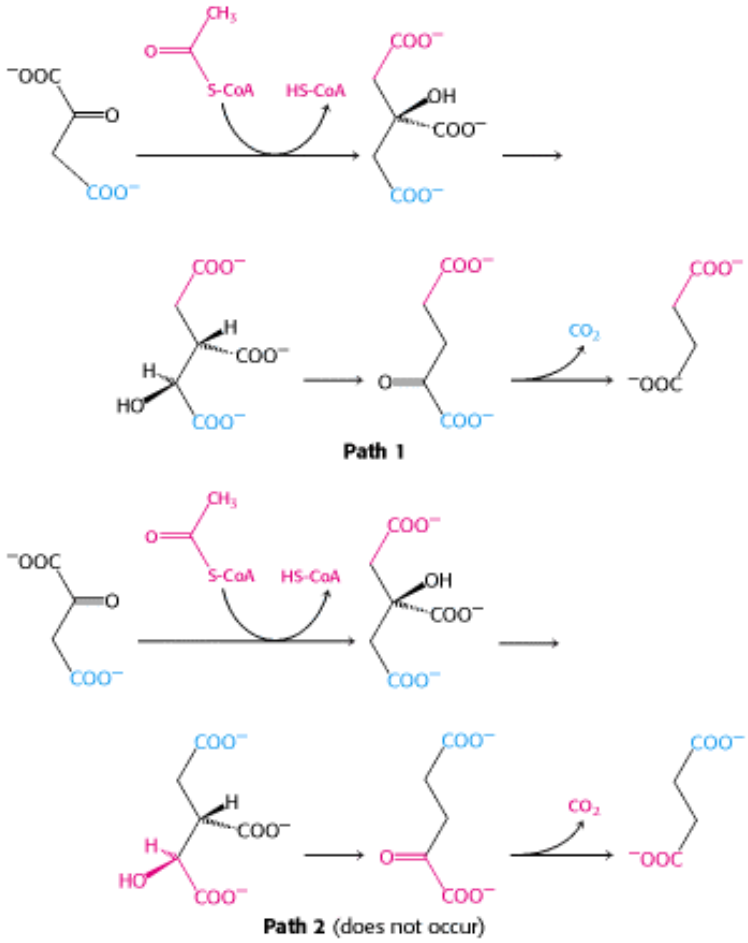
10. We cannot get the net conversion of fats into glucose because the only means to get the carbons from fats into oxaloace-tate, the precursor to glucose, is through the citric acid cycle. However, although two carbon atoms enter the cycle as acetyl CoA, two carbon atoms are lost as CO_2 before oxaloacetate is formed. Thus, although some carbon atoms from fats may end up as carbon atoms in glucose, we cannot obtain a *net* synthesis of glucose from fats.

See question

11. The enol intermediate of acetyl CoA attacks the carbonyl carbon atom of glyoxylate to form a C-C bond. This reaction is like the condensation of oxaloacetate with the enol intermediate of acetyl CoA in the reaction catalyzed by citrate synthase. Glyoxylate contains a hydrogen atom in place of the $-CH_2COO^-$ group of oxaloacetate; the reactions are otherwise nearly identical.

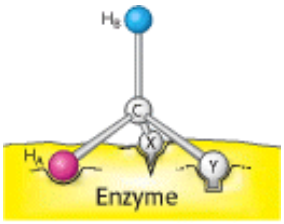
See question

12. Citrate is a symmetric molecule. Consequently, it was assumed that the two $-CH_2COO^-$ groups in it would react identically. Thus, for every citrate molecule undergoing the reactions shown in path 1, it was thought that another citrate molecule would react as shown in path 2. If so, then only *half* the label should have emerged in the CO_2.



See question

13. Call one hydrogen atom A and the other B. Now suppose that an enzyme binds three groups of this substrate—X, Y, and H—at three complementary sites. The adjoining diagram shows X, Y, and H_A bound to three points on the enzyme. In contrast, X, Y, and H_B cannot be bound to this active site; two of these three groups can be bound, but not all three. Thus, H_A and H_B will have different fates.



Sterically nonequivalent groups such as H_A and H_B will almost always be distinguished in enzymatic reactions. The essence of the differentiation of these groups is that the enzyme holds the substrate in a specific orientation. Attachment at three points, as depicted in the diagram, is a readily visualized way of achieving a particular orientation of the substrate, but it is not the only means of doing so.

See question

14. (a) The complete oxidation of citrate requires 4.5 μmol of O_2 for every μ mol of citrate.

$$C_6H_8O_7 + 4.5\ O_2 \longrightarrow 6\ CO_2 + 4\ H_2O$$

Thus, 13.5 μmol of O_2 would be consumed by 3 μmol of citrate.

(b) Citrate led to the consumption of far more O_2 than can be accounted for simply by the oxidation of citrate itself. Citrate thus facilitated O_2 consumption.

See question

15. (a) In the absence of arsenite, the amount of citrate remained constant. In its presence, the concentration of citrate fell, suggesting that it was being metabolized.

(b) It is not altered. Citrate still disappears.

(c) Arsenite is preventing the regeneration of citrate. Recall (Section 17.3.2) that arsenite inhibits the pyruvate dehydrogenase complex.

See question

16. (a) The initial infection is unaffected by the absence of isocitrate lyase, but the absence of this enzyme inhibits the latent phase of the infection.

(b) Yes.

(c) A critic could say that, in the process of deleting the isocitrate lyase gene, some other gene was damaged, and it is the absence of this other gene that prevents latent infection. Reinserting the isocitrate lyase gene into the bacteria from which it had been removed renders the criticism less valid.

(d) Isocitrate lyase enables the bacteria to synthesize carbohydrates that are necessary for survival, including carbohydrate components of the cell membrane.

See question

Chapter 18

1. (a) 12.5; (b) 14; (c) 32; (d) 13.5; (e) 30; (f) 16.

See question

2. Biochemists use E_0', the value at pH 7, whereas chemists use E_0, the value in 1 M H^+. The prime denotes that pH 7 is the standard state.

See question

3. (a) Blocks electron transport and proton pumping at Complex III. (b) Blocks electron transport and ATP synthesis by inhibiting the exchange of ATP and ADP across the inner mitochondrial membrane. (c) Blocks electron transport and proton pumping at Complex I. (d) Blocks ATP synthesis without inhibiting electron transport by dissipating the proton gradient. (e) Blocks electron transport and proton pumping at Complex III. (f) Blocks electron transport and proton pumping at Complex II.

See question

4. If the proton gradient is not dissipated by the influx of protons into a mitochondrion with the generation of ATP, eventually the outside of the mitochondrion develops such a large positive charge that the electron-transport chain can no longer pump protons against the gradient.

See question

5. (a) No effect. Mitochondria cannot metabolize glucose.

(b) No effect. No fuel is present to power the synthesis of ATP.

(c) The [O_2] falls because citrate is a fuel and ATP can be formed from ADP and P_i.

(d) Oxygen consumption stops because oligomycin inhibits ATP synthesis, which is coupled to the activity of the electron-transport chain.

(e) No effect for the reasons given in part *d.*

(f) [O_2] falls rapidly because the system is uncoupled and does not require ATP synthesis to lower the proton-motive force.

(g) [O_2] falls at a lower rate but still falls. Rotenone inhibits Complex I, but the presence of succinate will enable electrons to enter at Complex II.

(h) Oxygen consumption ceases because Complex IV is inhibited and the entire chain backs up.

See question

6. (a) The P:O ratio is equal to the product of (H^+/2 e^-) and (~P/H^+). Note that the P:O ratio is identical with the (P:2 e^-) ratio. (b) 2.5 and 1.5, respectively.

See question

7. $\Delta G^{\circ\prime}$ is +16.1 kcal mol^{-1} (67 kJ mol^{-1}) for oxidation by NAD^+ and +1.4 kcal/mol^{-1} (5.9 kJ mol^{-1}) for oxidation by FAD. The oxidation of succinate by NAD^+ is not thermodynamically feasible.

See question

8. Cyanide can be lethal because it binds to the ferric form of cytochrome oxidase and thereby inhibits oxidative phosphorylation. Nitrite converts ferrohemoglobin into ferrihemoglobin, which also binds cyanide. Thus, ferrihemoglobin competes with cytochrome oxidase for cyanide. This competition is therapeutically effective because the amount of ferrihemoglobin that can be formed without impairing oxygen transport is much greater than the amount of cytochrome oxidase.

See question

9. The available free energy from the translocation of two, three, and four protons is -9.2, -13.8, and -18.5 kcal mol^{-1} (-38.5, -57.7, and -77.4 kJ mol^{-1}), respectively. The free energy consumed in synthesizing a mole of ATP under standard conditions is 7.3 kcal. Hence, the residual free energy of -1.93, -6.5, and -11.2 kcal (-8.1, -27.2, and -46.7 kJ mol^{-1}) can drive the synthesis of ATP until the [ATP]/[ADP][P_i] ratio is 26.2, 6.5×10^4, and 1.6×10^8, respectively. Suspensions of isolated mitochondria synthesize ATP until this ratio is greater than 10^4, which shows that the number of protons translocated per ATP synthesized is at least three.

See question

10. Such a defect (called Luft syndrome) was found in a 38-year-old woman who was incapable of performing prolonged physical work. Her basal metabolic rate was more than twice normal, but her thyroid function was normal. A muscle biopsy showed that her mitochondria were highly variable and atypical in structure. Biochemical studies then revealed that oxidation and phosphorylation were not tightly coupled in these mitochondria. In this patient, much of the energy of fuel molecules was converted into heat rather than ATP.

See question

11. Dicyclohexylcarbodiimide reacts readily with carboxyl groups, as discussed earlier in regard to its use in peptide synthesis (Section 4.4). Hence, the most likely targets are aspartate and glutamate side chains. In fact, aspartate 61 of subunit **c** of *E. coli* F_0 is specifically modified by this reagent. Conversion of this aspartate into asparagine by site-specific mutagenesis also eliminated proton conduction.

See question

12. Triose phosphate isomerase converts dihydroxyacetone phosphate (a potential dead end) into glyceraldehyde 3-phosphate (a mainstream glycolytic intermediate).

See question

13. This inhibitor (like antimycin A) blocks the reduction of cytochrome c_1 by QH_2, the crossover point.

See question

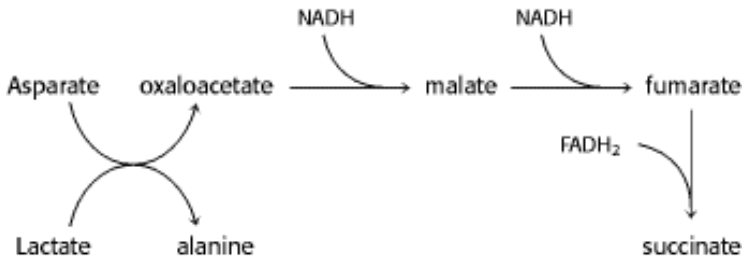
14. If oxidative phosphorylation were uncoupled, no ATP could be produced. In a futile attempt to generate ATP, much fuel would be consumed. The danger lies in the dose. Too much uncoupling would lead to tissue damage in highly aerobic organs such as the brain and heart, which would have severe consequences for the organism as a whole. The energy that is normally transformed into ATP would be released as heat. To maintain body temperature, sweating might increase, although the very process of sweating itself depends on ATP.

See question

15. Add the inhibitor with and without an uncoupler, and monitor the rate of O_2 consumption. If the O_2 consumption increases again in the presence of inhibitor and uncoupler, the inhibitor must be inhibiting ATP synthase. If the uncoupler has no effect on the inhibition, the inhibitor is inhibiting the electron-transport chain.

See question

16. The organic acids in the blood are indications that the mice are deriving a large part of their energy needs through anaerobic glycolysis. Lactate is the end product of anaerobic glycolysis. Alanine is an aminated transport form of lactate. Alanine formation plays a role in succinate formation, which is caused by the reduced state of the mitochondria.



The electron-transport chain is slowed because the inner mitochondrial membrane is hyperpolarized. Without ADP to accept the energy of the proton-motive force, the membrane becomes polarized to such an extent that protons can no longer be pumped. The excess H_2O_2 is probably due to the fact the superoxide radical is present in higher concentration because the oxygen can no longer be effectively reduced.

$$O_2^{\cdot-} + O_2^{\cdot-} \longrightarrow H_2O_2$$

Indeed, these mice display evidence of such oxidative damage.

See question

17. (a) Succinate is oxidized by Complex II, and the electrons are used to establish a proton-motive force that powers ATP synthesis.

(b) The ability to synthesize ATP is greatly reduced.

(c) Because the goal was to measure ATP hydrolysis. If succinate had been added in the presence of ATP, no reaction would have taken place, because of respiratory control.

(d) The mutation has little effect on the ability of the enzyme to catalyze the hydrolysis of ATP.

(e) They suggest two things: (1) the mutation did not affect the catalytic site on the enzyme, because the ATP synthase is still capable of catalyzing the reverse reaction; (2) the mutation did not affect the amount of enzyme present, given that the controls and patients had similar amounts of activity.

See question

18. The absolute configuration of thiophosphate indicates that inversion at phosphorus has occurred in the reaction catalyzed by ATP synthase. This result is consistent with an in-line phosphoryl transfer reaction taking place in a single step. The retention of configuration in the Ca^{2+}-ATPase reaction points to two phosphoryl transfer reactions—inversion by the first and a return to the starting configuration by the second. The Ca^{2+}-ATPase reaction proceeds by a phosphorylated enzyme intermediate.

See question

Chapter 19

1. $\Delta E'_0 = +0.11$ V and $\Delta G^{\circ\prime} = -5.1$ kcal mol^{-1} (-21.3 kJ mol^{-1}).

See question

2. (a) All ecosystems require an energy source from outside the system, because the chemical-energy sources will ultimately be limited. The photosynthetic conversion of sunlight is one example of such a conversion.

(b) Not at all. Spock would point out that chemicals other than water can donate electrons and protons.

See question

3. DCMU inhibits electron transfer in the link between photosystems II and I. O_2 can evolve in the presence of DCMU if an artificial electron acceptor such as ferricyanide can accept electrons from Q.

See question

4. DCMU will have no effect, because it blocks photosystem II, and cyclic photophosphorylation uses photosystem I and the cytochrome *bf* complex.

See question

5. (a) 28.7 kcal einstein^{-1} (120 kJ einstein^{-1}).

(b) 1.24 V.

(c) One 1000-nm photon has the free energy content of 2.4 molecules of ATP. A minimum of 0.42 photon is needed to drive the synthesis of a molecule of ATP.

See question

6. At this distance, the expected rate is one electron per second.

See question

7. Phycoerythrin, the most peripheral protein in the phycobilisome.

See question

8. The distance doubles, and so the rate should decrease by a factor of 64 to 640 ps.

See question

9. The electrons flow through photosystem II directly to ferricyanide. No other steps are required.

See question

10. (a) Thioredoxin.

(b) The control enzyme is unaffected, but the mitochondrial enzyme with part of the chloroplast γ subunit increases activity as the concentration of DTT increases.

(c) The increase was even larger when thioredoxin was present. Thioredoxin is the natural reductant for the chloroplast enzyme, so presumably it operates more efficiently than would DTT, which probably functions to keep the thioredoxin reduced.

(d) It seems that they did.

(e) The enzyme is susceptible to control by the redox state. In plant cells, reduced thioredoxin is generated by photosystem I. Thus, the enzyme is active when photosynthesis is taking place.

(f) Cysteine.

(g) Group-specific modification or site-specific mutagenesis.

See question

Chapter 20

1. Aldolase participates in the Calvin cycle, whereas transaldolase participates in the pentose phosphate pathway.

   See question

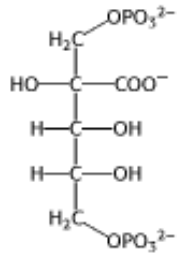
2. The concentration of 3-phosphoglycerate would increase, whereas that of ribulose 1,5-bisphosphate would decrease.

   See question

3. The concentration of 3-phosphoglycerate would decrease, whereas that of ribulose 1,5-bisphosphate would increase.

   See question

4. (a)



2-Carboxyarabinitol 1,5-bisphosphate (CABP)

   (b) CABP resembles the addition compound formed in the reaction of CO_2 and ribulose 1,5-bisphosphate.

   (c) CABP is predicted to be a potent inhibitor of rubisco.

   See question

5. Aspartate + glyoxylate $\rightarrow$ oxaloacetate + glycine

   See question

6. ATP is converted into AMP. To convert this AMP back into ATP, two molecules of ATP are required: one to form ADP and another to form ATP from the ADP.

   See question

7. The oxygenase activity of rubisco increases with temperature. Crabgrass is a C_4 plant, whereas most grasses lack this capability. Consequently, the crabgrass will thrive at the hottest part of the summer because the C_4 pathway provides an ample supply of CO_2.

See question

8. As global warming progresses, C_4 plants will invade the higher latitudes, whereas C_3 plants will retreat to cooler regions.

See question

9. The label emerges at C-5 of ribulose 5-phosphate.

See question

10. Oxidative decarboxylation of isocitrate to α-ketoglutarate. A β-ketoacid intermediate is formed in both reactions.

See question

11. C-1 and C-3 of fructose 6-phosphate are labeled, whereas erythrose 4-phosphate is not labeled.

See question

12. (a) 5 Glucose 6-phosphate + ATP $\longrightarrow$ 6 ribose 5-phosphate + ADP + H^+

(b) Glucose 6-phosphate + 12 $NADP^+$ + 7 H_2O $\longrightarrow$ 6 CO_2 + 12 NADPH + 12 H^+ + P_i

See question

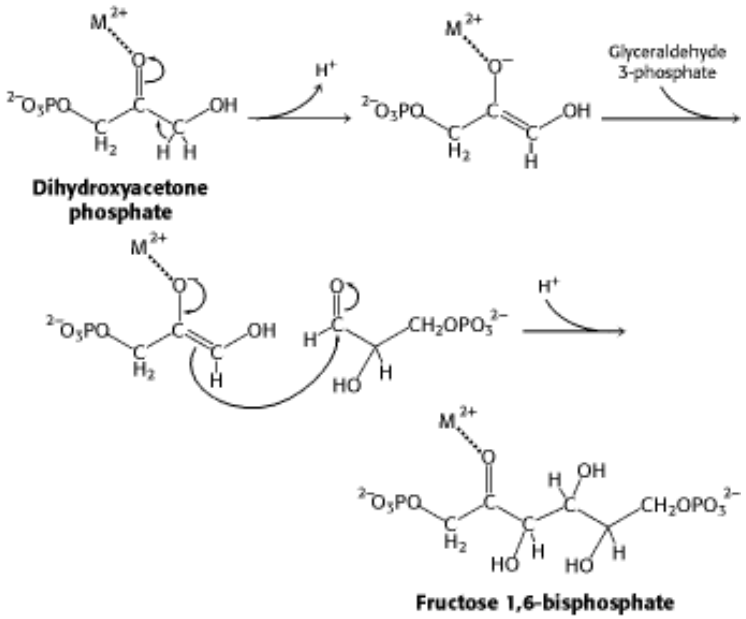
13. Form a Schiff base between a ketose substrate and transaldolase, reduce it with tritiated $NaBH_4$, and fingerprint the labeled enzyme.

See question

14. $\Delta E_0'$ for the reduction of glutathione by NADPH is +0.09 V. Hence, $\Delta G^{\circ\prime}$ is -4.2 kcal mol^{-1} (-17.5 kJ mol^{-1}), which corresponds to an equilibrium constant of 1126. The required [NADPH]/[$NADP^+$] ratio is 8.9×10^{-2}.

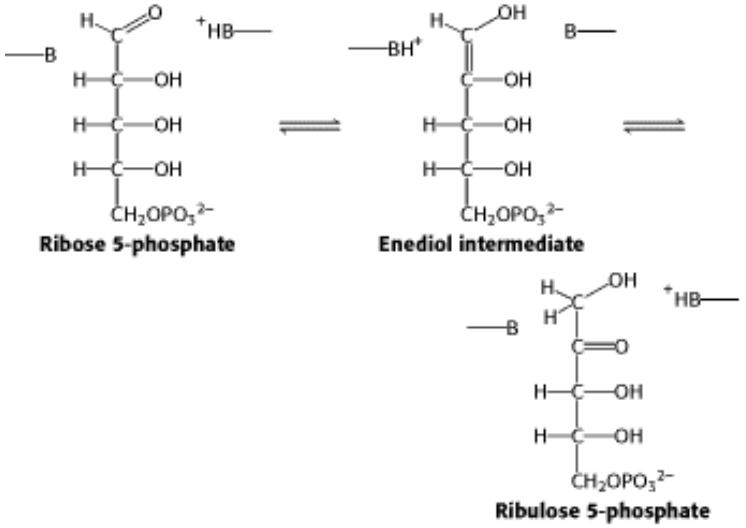
See question

15.



See question

16.



See question

17. An aliquot of a tissue homogenate is incubated with glucose labeled with ^{14}C at C-1, and another is incubated with glucose labeled with ^{14}C at C-6. The radioactivity of the CO_2 produced by the two samples is then compared. The rationale of this experiment is that only C-1 is decarboxylated by the pentose phosphate pathway, whereas C-1 and C-6 are decarboxylated equally when glucose is metabolized by the glycolytic pathway, the pyruvate dehydrogenase complex, and the citric acid cycle. The reason for the equivalence of C-1 and C-6 in the latter set of reactions is that glyceraldehyde 3-phosphate and dihydroxyacetone phosphate are rapidly interconverted by triose phosphate isomerase.

See question

18. The reduction of each CO_2 to the level of a hexose requires 2 moles of NADPH. The reduction of $NADP^+$ is a two-electron process. Hence, the formation of 2 moles of NADPH requires the pumping of four photons by photosystem I. The electrons given up by photosystem I are replenished by photosystem II, which needs to absorb an equal number of photons. Hence, eight photons are needed to generate the required NADPH. The energy input of 8 moles of photons is 381 kcal. Thus, the overall efficiency of photosynthesis under standard conditions is at least 114/381, or 30%.

See question

19. (a) The curve on the right was generated by the C_4 plant. Recall that the oxygenase activity of rubisco increases with temperature more rapidly than does the carboxylase activity. Consequently, at higher temperatures, the C_3 plants would fix less carbon. Because C_4 plants can maintain a higher CO_2 concentration, the rise in temperature is less deleterious.

(b) The oxygenase activity will predominate. Additionally, when the temperature rise is very high, evaporation of water might become a problem. The higher temperatures can begin to damage protein structures as well.

(c) The C_4 pathway is a very effective active-transport system for concentrating CO_2, even when environmental concentrations are very low.

(d) With the assumption that the plants have approximately the same capability to fix CO_2, the C_4 pathway is apparently the rate-limiting step in C_4 plants.

See question

Chapter 21

1. Galactose + ATP + UTP + H_2O + glycogen $_n \rightarrow$ glycogen $_{n+1}$ + ADP + UDP + 2 P_i + H^+

See question

2. As an unbranched polymer, α-amylose has only one nonreducing end. Therefore, only one glycogen phosphorylase molecule could degrade each α-amylose molecule. Because glycogen is highly branched, there are many nonreducing ends per molecule. Consequently, many phosphorylase molecules can release many glucose molecules per glycogen molecule.

See question

3. The patient has a deficiency of the branching enzyme.

See question

4. The high level of glucose 6-phosphate in von Gierke disease, resulting from the absence of glucose 6-phosphatase or the transporter, shifts the allosteric equilibrium of phosphorylated glycogen synthase toward the active form.

See question

5. Glucose is an allosteric inhibitor of phosphorylase *a*. Hence, crystals grown in its presence are in the T state. The addition of glucose 1-phosphate, a substrate, shifts the R ⇌ T equilibrium toward the R state. The conformational differences between these states are sufficiently large that the crystal shatters unless it is stabilized by chemical cross-links.

See question

6. The phosphoryl donor is glucose 1,6-bisphosphate, which is formed from glucose 1-phosphate and ATP in a reaction catalyzed by phosphoglucokinase.

See question

7. Water is excluded from the active site to prevent hydrolysis. The entry of water could lead to the formation of glucose rather than glucose 1-phosphate. A site-specific mutagenesis experiment is revealing in this regard. In phosphorylase, Tyr 573 is hydrogen bonded to the 2′-OH of a glucose residue. The ratio of glucose 1-phosphate to glucose product is 9000:1 for the wild-type enzyme, and 500:1 for the Phe 573 mutant. Model building suggests that a water molecule occupies the site normally filled by the phenolic OH of tyrosine and occasionally attacks the oxocarbonium ion intermediate to form glucose.

See question

8. The amylase activity was necessary to remove all of the glycogen from the glycogenin. Recall that glycogenin synthesizes oligosaccharides of about eight glucose units, and then activity stops. Consequently, if the glucose residues are not removed by extensive amylase treatment, glycogenin would not function.

See question

9. The substrate can be handed directly from the transferase site to the debranching site.

See question

10. During exercise, [ATP] falls and [AMP] rises. Recall that AMP is an allosteric activator of glycogen phosphorylase *b*. Thus, even in the absence of covalent modification by phosphorylase kinase, glycogen is degraded.

See question

11. (a) Muscle phosphorylase *b* will be inactive even when the AMP level is high. Hence, glycogen will not be degraded unless phosphorylase is converted into the *a* form by hormone-induced or Ca^{2+}-induced phosphorylation.

(b) Phosphorylase *b* cannot be converted into the much more active *a* form. Hence, the mobilization of liver glycogen will be markedly impaired.

(c) The elevated level of the kinase will lead to the phosphorylation and activation of glycogen phosphorylase. Because glycogen will be persistently degraded, little glycogen will be present in the liver.

(d) Protein phosphatase 1 will be continually active. Hence, the level of phosphorylase *b* will be higher than normal, and glycogen will be less readily degraded.

(e) Protein phosphatase 1 will be much less effective in dephosphorylating glycogen synthase and glycogen phosphorylase. Consequently, the synthase will stay in the less active *b* form, and the phosphorylase will stay in the more active *a* form. Both changes will lead to increased degradation of glycogen.

(f) The absence of glycogenin will block the initiation of glycogen synthesis. Very little glycogen will be synthesized in its absence.

See question

12. (a) The α subunit is thus always active. cAMP is always produced. Glycogen degradation always occurs, and glycogen synthesis is always inhibited.

(b) Glycogen phosphorylase cannot be covalently activated. Glycogen degradation is always inhibited; nothing can remain phosphorylated. Glycogen synthesis is always active; nothing can remain phosphorylated.

(c) Phosphodiesterase destroys cAMP. Therefore, glycogen degradation would always be active and glycogen synthesis would always be inhibited.

See question

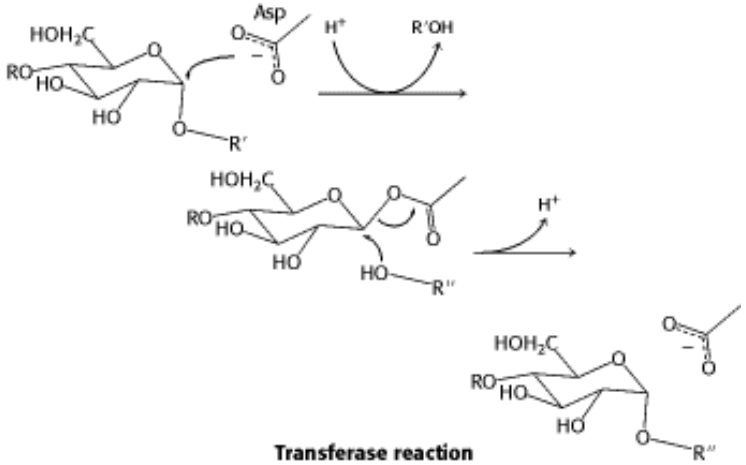
13. The slow phosphorylation of the α subunits of phosphor-ylase kinase serves to prolong the degradation of glycogen. The kinase cannot be deactivated until its α subunits are phosphorylated. The slow phosphorylation of α subunits ensures that the kinase and, in turn, phosphorylase stay active for an extended interval.

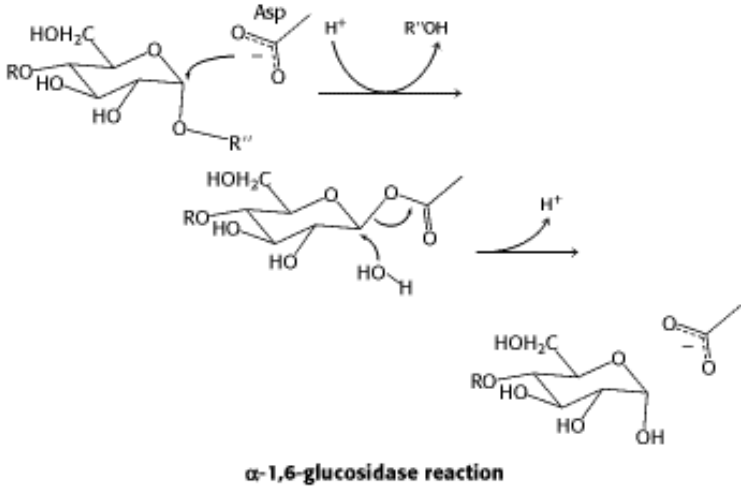
See question

14. Phosphorylation of the β subunit activates the kinase and leads to glycogen degradation. Subsequent phosphorylation of the α subunit make the β subunit and the α subunit substrates for protein phosphatase. Thus, if the α subunit were modified before the β subunit, the enzyme would be primed for shutdown before it was activated and little glycogen degradation would take place.

See question

15.





See question

16. (a) The glycogen was too large to enter the gel and, because analysis was by Western blot with the use of an antibody specific to glycogenin, one would not expect to see background proteins.

(b) α-Amylase degrades glycogen, releasing the protein glycogenin so that it can be visualized by the Western blot.

(c) Glycogen phosphorylase, glycogen synthase, and protein phosphatase 1. These proteins might be visible if the gel were stained for protein, but a Western analysis reveals the presence of glycogenin only.

See question

17. (a) The smear was due to molecules of glycogenin with increasingly large amounts of glycogen attached to them.

(b) In the absence of glucose in the medium, glycogen is metabolized, resulting in a loss of the high-molecular-weight material.

(c) Glycogen could be resynthesized and added to the glycogenin when the cells were fed glucose again.

(d) No difference between lanes 3 and 4 suggests that, by 1 hour, the glycogen molecules had attained maximum size in this cell line. Prolonged incubation does not apparently increase the amount of glycogen.

(e) α-Amylase removes essentially all of the glycogen, and so only the glycogenin remains.

Chapter 22

1. Glycerol + 2 NAD^+ + P_i + ADP $\rightarrow$ pyruvate + ATP + H_2O + 2 NADH + H^+ Glycerol kinase and glycerol phosphate dehydrogenase.

See question

2. Stearate + ATP + 13 $^1/_2$ H_2O + 8 FAD + 8 NAD^+ $\rightarrow$ 4 $^1/_2$ acetoacetate + 14 $^1/_2$ H^+ + 8 $FADH_2$ + 8 NADH + AMP + 2 P_i

See question

3. (a) Oxidation in mitochondria; synthesis in the cytosol. (b) Acetyl CoA in oxidation; acyl carrier protein for synthesis. (c) FAD and NAD^+ in oxidation; NADPH for synthesis. (d) l isomer of 3-hydroxyacyl CoA in oxidation; d isomer in synthesis. (e) From carboxyl to methyl in oxidation; from methyl to carboxyl in synthesis. (f) The enzymes of fatty acid synthesis, but not those of oxidation, are organized in a multienzyme complex.

See question

4. (a) Palmitoleate; (b) linoleate; (c) linoleate; (d) oleate; (e) oleate; (f) linolenate.

See question

5. C-1 is more radioactive.

See question

6. Decarboxylation drives the condensation of malonyl ACP and acetyl ACP. In contrast, the condensation of two molecules of acetyl ACP is energetically unfavorable. In gluconeogenesis, decarboxylation drives the formation of phosphoenolpyruvate from oxaloacetate.

See question

7. Adipose-cell lipase is activated by phosphorylation. Hence, overproduction of the cAMP-activated kinase will lead to an accelerated breakdown of triacylglycerols and a depletion of fat stores.

See question

8. The mutant enzyme would be persistently active because it could not be inhibited by phosphorylation. Fatty acid synthesis would be abnormally active. Such a mutation might lead to obesity.

See question

9. Carnitine translocase deficiency and glucose 6-phosphate transporter deficiency.

See question

10. In the fifth round of β oxidation, *cis*-Δ^2-enoyl CoA is formed. Dehydration by the classic hydratase yields d-3-hydroxyacyl CoA, the wrong isomer for the next enzyme in β oxidation. This dead end is circumvented by a second hydratase that removes water to give *trans*-Δ^2-enoyl CoA. The addition of water by the classic hydratase then yields l-3- hydroxyacyl CoA, the appropriate isomer. Thus, hydratases of opposite stereospecificities serve to *epimerize* (invert the configuration of) the 3-hydroxyl group of the acyl CoA intermediate.

See question

11. The probability of synthesizing an error-free polypeptide chain decreases as the length of the chain increases. A single mistake can make the entire polypeptide ineffective. In contrast, a defective subunit can be spurned in forming a noncovalent multienzyme complex; the good subunits are not wasted.

See question

12. The absence of ketone bodies is due to the fact that the liver, the source of blood-ketone bodies, cannot oxidize fatty acids to produce acetyl CoA. Moreover, because of the impaired fatty acid oxidation, the liver becomes more dependent on glucose as an energy source. This dependency results in a decrease in gluconeogenesis and a drop in blood-glucose levels, which is exacerbated by the lack of fatty acid oxidation in muscle and a subsequent increase in glucose uptake from the blood.

See question

13. Peroxisomes enhance the degradation of fatty acids. Consequently, increasing the activity of peroxisomes could help to lower levels of blood triacylglycerides. In fact, clofibrate is rarely used because of serious side effects.

See question

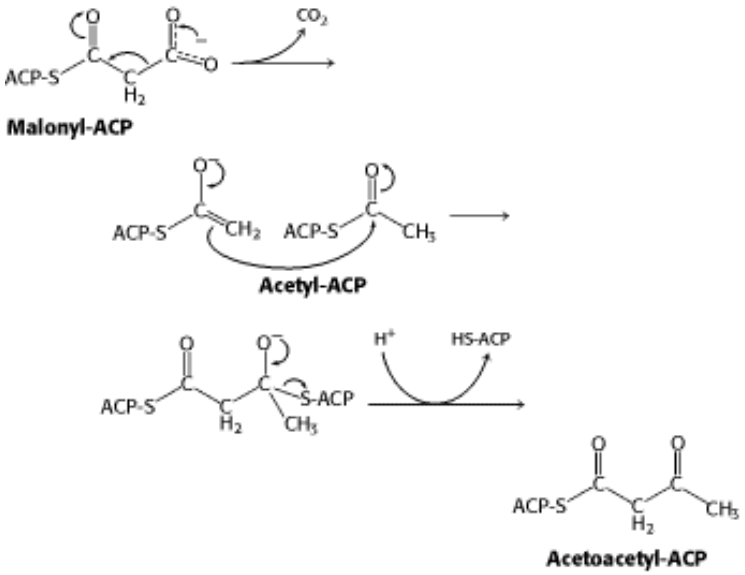
14. Citrate works by facilitating the formation of active filaments from inactive monomers. In essence, it increases the number of active sites available, or the concentration of enzyme. Consequently, its effect is visible as an increase in the value of V_{max}. Allosteric enzymes that alter their V_{max} values in response to regulators are sometimes called V-class enzymes. The more common type of allosteric enzyme, in which K_m is altered, comprises K-class enzymes. Palmitoyl CoA causes depolymerization and thus inactivation.

See question

15. The thiolate anion of CoA attacks the 3-keto group to form a tetrahedral intermediate. This collapses to form acyl CoA and the enolate anion of acetyl CoA. Protonation of the enolate yields acetyl CoA.

See question

16.



See question

17. (a) Fats burn in the flame of carbohydrates. Without carbohydrates, there would be no anapleurotic reactions to replenish the TCA-cycle components. With a diet of fats only, the acetyl CoA from fatty acid degradation would build up.

(b) Acetone from ketone bodies.

(c) Yes. Odd-chain fatty acids would lead to the production of propionyl CoA, which can be converted into succinyl CoA, a TCA-cycle component. It would serve to replenish the TCA cycle and mitigate the halitosis.

See question

18. A labeled fat can enter the citric acid cycle as acetyl CoA and yield labeled oxaloacetate, but only after two carbon atoms have been lost as CO_2. Consequently, even though oxaloacetate may be labeled, there can be no net synthesis in the amount of oxaloacetate and hence no net synthesis of glucose or glycogen.

See question

19. (a) The V_{max} is decreased and the K_m is increased. V_{max} (wild type) = 13 nmol minute^{-1} mg^{-1}; K_m (wild type) = 45 μM; V_{max} (mutant) = 8.3 nmol minute^{-1} mg^{-1}; K_m (mutant) = 74 μM.

(b) Both the V_{max} and the K_m are decreased. V_{max} (wild type) = 41 nmol minute^{-1} mg^{-1}; K_m (wild type) = 104 μM; V_{max} (mutant) = 23 nmol minute^{-1} mg^{-1}; K_m (mutant) = 69 μM.

(c) The wild type is significantly more sensitive to malonyl CoA.

(d) With respect to carnitine, the mutant displays approximately 65% of the activity of the wild type; with respect to palmitoyl CoA, approximately 50% activity. On the other hand, 10 μM of malonyl CoA inhibits approximately 80% of the wild type but has essentially no effect on the mutant enzyme.

(e) The glutamate appears to play a more prominent role in regulation by malonyl CoA than in catalysis.

See question

Chapter 23

1. (a) The ATPase activity of the 26S proteasome resides in the 19S subunit. The energy of ATP hydrolysis could be used to unfold the substrate, which is too large to enter the catalytic barrel. ATP may also be required for translocation of the substrate into the barrel.

(b) Substantiates the answer in part *a*. Because they are small, the peptides do not need to be unfolded. Moreover, small peptides could probably enter all at once and not require translocation.

See question

2. (a) Pyruvate; (b) oxaloacetate; (c) α-ketoglutarate; (d) α-ketoisocaproate; (e) phenylpyruvate; (f) hydroxyphenyl-pyruvate.

See question

3. (a) Aspartate + α-ketoglutarate + GTP + ATP + 2 H_2O + NADH + H^+ $\longrightarrow$ $^1/_2$ glucose + glutamate + CO_2 + ADP + GDP + NAD^+ + 2 P_i

The required coenzymes are pyridoxal phosphate in the transamination reaction and NAD^+/NADH in the redox reactions.

(b) Aspartate + CO_2 + NH_4^+ + 3 ATP + NAD^+ + 4 H_2O $\longrightarrow$ oxaloacetate + urea + 2 ADP + 4 P_i + AMP + NADH + H^+

See question

4. In the eukaryotic proteasome, the distinct β subunits have different substrate specificities, allowing proteins to be more thoroughly degraded.

See question

5. The six subunits probably exist as a heterohexamer. Cross-linking experiments could test the model and help determine which subunits are adjacent to one another.

See question

6. Thiamine pyrophosphate.

See question

7. It acts as an electron sink.

See question

8. $CO_2 + NH_4^+ + 3\ ATP + NAD^+ + aspartate + 3\ H_2O \rightarrow urea + 2\ ADP + 2\ P_i + AMP + PP_i + NADH + H^+ +$ oxaloacetate

Four high-transfer-potential groups are spent.

See question

9. Ornithine transcarbamoylase (analogous to PALA; see Chapter 10).

See question

10. Ammonia could lead to the amination of α-ketoglutarate, producing a high concentration of glutamate in an unregulated fashion. α-Ketoglutarate for glutamate synthesis could be removed from the citric acid cycle, thereby diminishing the cell's respiration capacity.

See question

11. The mass spectrometric analysis strongly suggests that three enzymes—pyruvate dehydrogenase, α-ketoglutarate dehydrogenase, and the branched-chain α-keto dehydrogenase—are deficient. Most likely, the common E_3 component of these enzymes is missing or defective. This proposal could be tested by purifying these three enzymes and assaying their ability to catalyze the regeneration of lipoamide.

See question

12. Benzoate, phenylacetate, and arginine would be given to supply a protein-restricted diet. Nitrogen would emerge in hippurate, phenylacetylglutamine, and citrulline.

See question

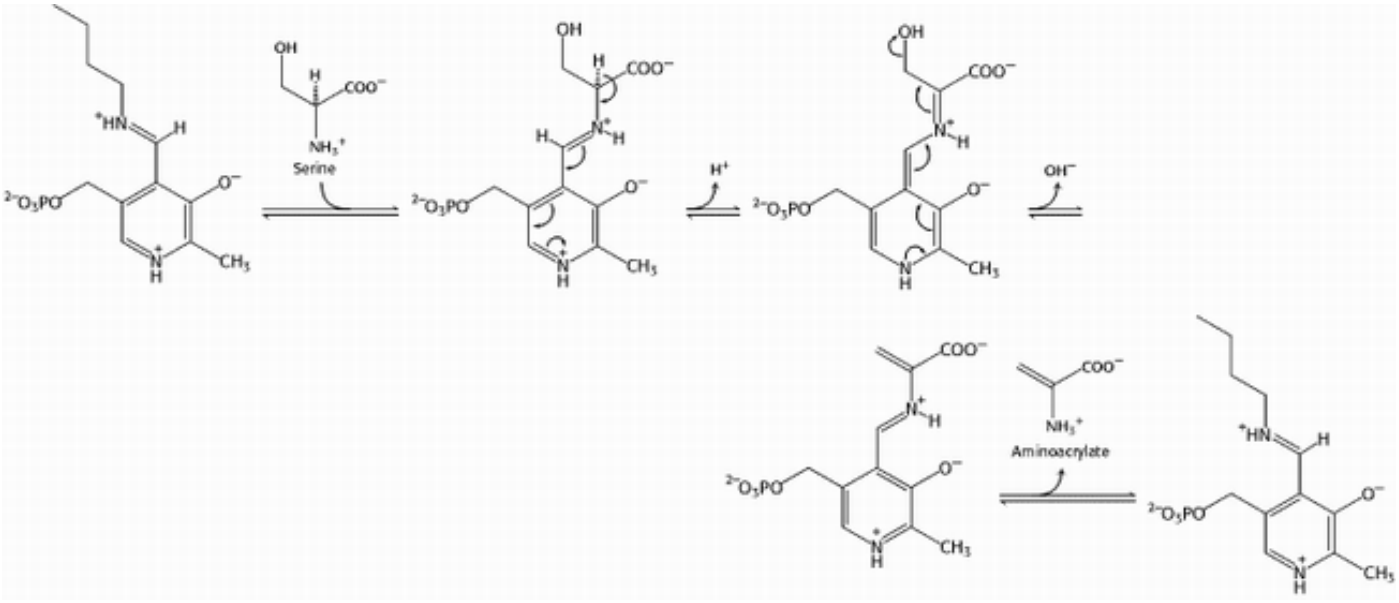
13. Aspartame, a dipeptide ester (l-aspartyl-l-phenylalanine methyl ester), is hydrolyzed to l-aspartate and l-phenylalanine. High levels of phenylalanine are harmful in phenylketonurics.

See question

14. *N*-Acetylglutamate is synthesized from acetyl CoA and glutamate. Once again, acetyl CoA serves as an activated acetyl donor. This reaction is catalyzed by *N*-acetylglutamate synthase.

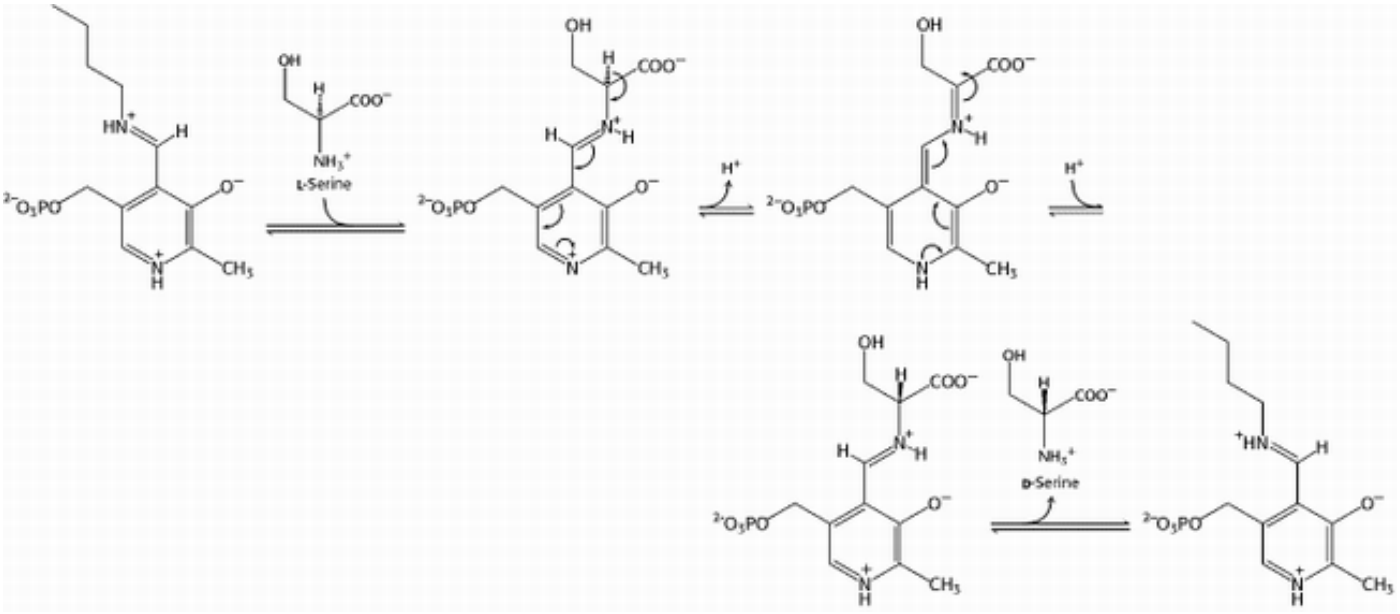
See question

15. See equation below.



See question

16.



The equilibrium constant for the interconversion of l-serine and d-serine is exactly 1.

See question

17. Exposure of such a domain would suggest that a component of a multiprotein complex has failed to form properly, or that one component has been synthesized in excess. This will lead to rapid degradation and restoration of appropriate stoichiometries.

See question

18. (a) Depletion of glycogen stores. When they are gone, proteins must be degraded to meet the glucose needs of the brain. The resulting amino acids are deaminated, and the nitrogen atoms are excreted as urea.

(b) The brain has adapted to the use of ketone bodies, which are derived from fatty acid catabolism. In other words, the brain is being powered by fatty acid breakdown.

(c) When the glycogen and lipid stores are gone, the only available energy source is protein.

See question

19. Deamination to α-keto-β-methylvalerate; oxidative decarboxylation to α-methylbutyryl CoA; oxidation to tiglyl CoA; hydration, oxidation and thiolysis yields acetyl CoA and propionyl CoA; propionyl CoA to succinyl CoA.

See question

20. (a) Virtually no digestion in the absence of nucleotides. (b) Protein digestion is greatly stimulated by the presence of ATP. (c) AMP-PNP, a nonhydrolyzable analog of ATP, is no more effective than ADP. (d) The proteasome requires neither ATP nor PAN to digest small substrates. (e) PAN and ATP hydrolysis may be required to unfold the peptide and translocate it into the proteasome. (f) Although *Thermoplasma* PAN is not as effective with the other proteasomes, it nonetheless results in threefold to fourfold stimulation of digestion. (g) In light of the fact that the archaea and eukarya diverged several billion years ago, the fact that *Thermoplasma* PAN can stimulate rabbit muscle suggests homology not only between the proteasomes, but also between PAN and the 19S subunit (most likely the ATPases) of the mammalian 26S proteasome.

See question

Chapter 24

1. Glucose + 2 ADP + 2 P_i + 2 NAD^+ + 2 glutamate $\rightarrow$ 2 alanine + 2 α-ketoglutarate + 2 ATP + 2 NADH + 2 H_2O + 2 H^+

See question

2. $N_2 \rightarrow NH_4^+ \rightarrow$ glutamate $\rightarrow$ serine $\rightarrow$ glycine $\rightarrow$ δ-aminolevulinate $\rightarrow$ porphobilinogen $\rightarrow$ heme

See question

3. (a) N^5, N^{10}-Methylenetetrahydrofolate; (b) N^5-methyltetra-hydrofolate.

See question

4. γ-Glutamyl phosphate is a likely reaction intermediate.

See question

5. The administration of glycine leads to the formation of isovalerylglycine. This water-soluble conjugate, in contrast with isovaleric acid, is excreted very rapidly by the kidneys.

See question

6. They carry out nitrogen fixation. The absence of photosystem II provides an environment in which O_2 is not produced. Recall that the nitrogenase is very rapidly inactivated by O_2.

See question

7. The cytosol is a reducing environment, whereas the extracellular milieu is an oxidizing environment.

See question

8. Succinyl CoA is formed in the mitochondrial matrix.

See question

9. Alanine from pyruvate; aspartate from oxaloacetate; glutamate from α-ketoglutarate.

See question

10. Y could inhibit the C $\rightarrow$ D step, Z could inhibit the C $\rightarrow$ F step, and C could inhibit A $\rightarrow$ B. This scheme is an example of sequential feedback inhibition. Alternatively, Y could inhibit the C $\rightarrow$ D step, Z could inhibit the C $\rightarrow$ F step, and the A $\rightarrow$ B step would be inhibited only in the presence of both Y and Z. This scheme is called concerted feedback inhibition.

See question

11. The rate of the A $\rightarrow$ B step in the presence of high levels of Y and Z would be 24 s^{-1} ($0.6 \times 0.4 \times 100\ s^{-1}$).

See question

12. An external aldimine forms with SAM, which is deprotonated to form the quinonoid intermediate. The deprotonated carbon atom attacks the carbon atom adjacent to the sulfur atom to form the cyclopropane ring and release methyl thio-adenosine, the other product.

See question

13. An external aldimine forms with l-serine, which is deprotonated to form the quinonoid intermediate. This intermediate is reprotonated on its opposite face to form an aldimine with d-serine. This compound is cleaved to release d-serine. The equilibrium constant for a racemization reaction is 1 because the reactant and product are exact mirror images of each other.

See question

14. Synthesis from oxaloacetate and α-ketoglutarate would deplete the citric acid cycle, which would decrease ATP production. Anapleurotic reactions would be required to replenish the citric acid cycle.

See question

15. SAM is the donor for DNA methylation reactions that protect a host from digestion by its own restriction enzymes. A lack of SAM would render the bacterial DNA susceptible to digestion by the cell's own restriction enzymes.

See question

16. (a) Asparagine is much more abundant in the dark. More glutamine is present in the light. These amino acids show the most dramatic effects. Glycine also is more abundant in the light.

(b) Glutamine is a more metabolically reactive amino acid, used in the synthesis of many other compounds. Consequently, when energy is available as light, glutamine will be preferentially synthesized. Asparagine, which carries more nitrogen per carbon atom and is thus a more efficient means of storing nitrogen when energy is short, is synthesized in the dark. Glycine is more prevalent in the light because of photorespiration.

(c) White asparagus has an especially high concentration of asparagine, which accounts for its intense taste. All asparagus has a large amount of asparagine. In fact, as suggested by its name, asparagine was first isolated from asparagus.

See question

Chapter 25

1. $\text{Glucose} + 2\ \text{ATP} + 2\ \text{NADP}^+ + \text{H}_2\text{O} \rightarrow \text{PRPP} + \text{CO}_2 + \text{ADP} + \text{AMP} + 2\ \text{NADPH} + 3\ \text{H}^+$

See question

2. $\text{Glutamine} + \text{aspartate} + \text{CO}_2 + 2\ \text{ATP} + \text{NAD}^+ \rightarrow \text{orotate} + 2\ \text{ADP} + 2\ \text{P}_\text{i} + \text{glutamate} + \text{NADH} + \text{H}^+$

See question

3. (a, c, d, and e) PRPP; (b) carbamoyl phosphate.

See question

4. PRPP and formylglycinamide ribonucleotide.

See question

5. $\text{dUMP} + \text{serine} + \text{NADPH} + \text{H}^+ \rightarrow \text{dTMP} + \text{NADP}^+ + \text{glycine}$

See question

6. There is a deficiency of N^{10}-formyltetrahydrofolate. Sulfanilamide inhibits the synthesis of folate by acting as an analog of *p*-aminobenzoate, one of the precursors of folate.

See question

7. PRPP is the activated intermediate in the synthesis of phosphoribosylamine in the de novo pathway of purine formation; of purine nucleotides from free bases by the salvage pathway; of orotidylate in the formation of pyrimidines; of nicotinate ribonucleotide; of phosphoribosyl ATP in the pathway leading to histidine; and of phosphoribosylanthranilate in the pathway leading to tryptophan.

See question

8. (a) Cell A cannot grow in a HAT medium, because it cannot synthesize TMP either from thymidine or from dUMP. Cell B cannot grow in this medium, because it cannot synthesize purines by either the de novo pathway or the salvage pathway. Cell C can grow in a HAT medium because it contains active thymidine kinase from cell B (enabling it to phosphorylate thymidine to TMP) and hypoxanthine-guanine phosphoribosyl transferase from cell A (enabling it to synthesize purines from hypoxanthine by the salvage pathway).

(b) Transform cell A with a plasmid containing foreign genes of interest and a functional thymidine kinase gene. The only cells that will grow in a HAT medium are those that have acquired a thymidylate kinase gene; nearly all of these transformed cells will also contain the other genes on the plasmid.

See question

9. These patients have a high level of urate because of the breakdown of nucleic acids. Allopurinol prevents the formation of kidney stones and blocks other deleterious consequences of hyperuricemia by preventing the formation of urate (Section 25.6.1).

See question

10. The free energies of binding are -13.8 (wild type), -11.9 (Asn 27), and -9.1 (Ser 27) kcal mol^{-1} (-57.7, -49.8, and -38.1 kJ mol^{-1}, respectively). The loss in binding energy is 1.9 kcal mol^{-1} (7.9 kJ mol^{-1}) and 4.7 kcal mol^{-1} (19.7 kJ mol^{-1}).

See question

11. Inosine or hypoxanthine could be administered.

See question

12. N-1 in both cases, and the amine group linked to C-6 in ATP.

See question

13. An oxygen atom is added to allopurinol to form alloxanthine.

See question

14. The first reaction proceeds by phosphorylation of glycine to form an acyl phosphate followed by nucleophilic attack by the amine of phosphoribosylamine to displace orthophosphate. The second reaction consists of adenylation of the carbonyl group of xanthylate followed by nucleophilic attack by ammonia to displace AMP.

See question

15. The -NH_2 group attacks the carbonyl carbon atom to form a tetrahedral intermediate. Removal of a proton leads to the elimination of water to form inosinate.

See question

16. (a) cAMP; (b) ATP; (c) UDP-glucose; (d) acetyl CoA; (e) NAD^+, FAD; (f) dideoxynucleotides; (g) fluorouracil; (h) CTP inhibits ATCase.

See question

17. In vitamin B_{12} deficiency, methyltetrahydrofolate cannot donate its methyl group to homocysteine to regenerate methionine. Because the synthesis of methyltetrahydrofolate is irreversible, the cell's tetrahydrofolate will ultimately be converted into this form. No formyl or methylene tetrahydrofolate will be left for nucleotide synthesis. Pernicious anemia illustrates the intimate connection between amino acid and nucleotide metabolism.

See question

18. The cytosolic level of ATP in the liver falls and that of AMP rises above normal in all three conditions. The excess AMP is degraded to urate.

See question

19. Succinate $\rightarrow$ malate $\rightarrow$ oxaloacetate by the citric acid cycle. Oxaloacetate $\rightarrow$ aspartate by transamination, followed by pyrimidine synthesis. Carbons 4, 5, and 6.

See question

20. (a) Some ATP can be salvaged from the ADP that is being generated. (b) There are equal numbers of high phosphoryl transfer potential groups on each side of the equation. (c) Because the adenylate kinase reaction is at equilibrium, removing AMP would lead to the formation of more ATP. (d) Essentially, the cycle serves as an anapleurotic reaction for the generation of the citric acid cycle intermediate fumarate.

See question

Chapter 26

1. Glycerol + 4 ATP + 3 fatty acids + 4 $H_2O \rightarrow$ triacyl-glycerol + ADP + 3 AMP + 7 P_i + 4 H^+

See question

2. Glycerol + 3 ATP + 2 fatty acids + 2 H_2O + CTP + serine $\rightarrow$ phosphatidyl serine + CMP + ADP + 2 AMP + 6 P_i + 3 H^+

See question

3. (a) CDP-diacylglycerol; (b) CDP-ethanolamine; (c) acyl CoA; (d) CDP-choline; (e) UDP-glucose or UDP-galactose; (f) UDP-galactose; (g) geranyl pyrophosphate.

See question

4. (a and b) None, because the label is lost as CO_2.

See question

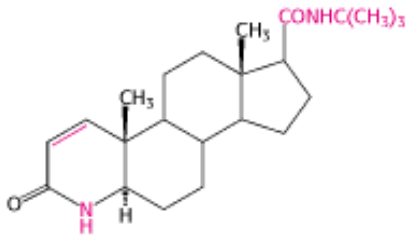
5. The categories of mutations are: (1) no receptor is synthesized; (2) receptors are synthesized but do not reach the plasma membrane, because they lack signals for intracellular transport or do not fold properly; (3) receptors reach the cell surface, but they fail to bind LDL normally because of a defect in the LDL-binding domain; (4) receptors reach the cell surface and bind LDL, but they fail to cluster in coated pits because of a defect in their carboxyl-terminal regions.

See question

6. Deamination of cytidine to uridine changes CAA (Gln) into UAA (stop).

See question

7. Benign prostatic hypertrophy can be treated by inhibiting 5α-reductase. Finasteride, the 4-aza steroid analog of dihydrotestosterone, competitively inhibits the reductase but does not act on androgen receptors. Patients taking finasteride have a markedly lower plasma level of dihydrotestosterone and a nearly normal level of testosterone. The prostate gland becomes smaller, whereas testosterone-dependent processes such as fertility, libido, and muscle strength appear to be unaffected.



Finasteride

See question

8. Patients who are most sensitive to debrisoquine have a deficiency of a liver P450 enzyme encoded by a member of the *CYP*2 subfamily. This characteristic is inherited as an autosomal recessive trait. The capacity to degrade other drugs may be impaired in people who hydroxylate debrisoquine at a slow rate, because a single P450 enzyme usually handles a broad range of substrates.

See question

9. Many hydrophobic odorants are deactivated by hydroxylation. Molecular oxygen is activated by a cytochrome P450 monooxygenase. NADPH serves as the reductant. One oxygen atom of O_2 goes into the odorant substrate, whereas the other is reduced to water.

See question

10. Recall that dihydrotestosterone is crucial for the development of male characteristics in the embryo. If a pregnant woman were to be exposed to Propecia, the 5α-reductase of the male embryo would be inhibited, which could result in severe developmental abnormalities.

See question

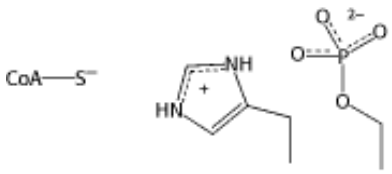
11. The oxygenation reactions catalyzed by the cytochrome P450 family permit greater flexibility in biosynthesis. Because plants are not mobile, they must rely on physical defenses, such as thorns, and chemical defenses, such as toxic alkaloids. The larger P450 array might permit greater biosynthetic versatility.

See question

12. This knowledge would enable clinicians to characterize the likelihood of a patient's having an adverse drug reaction or being susceptible to chemical-induced illnesses. It would also permit a personalized and especially effective drug-treatment regime for diseases such as cancer.

See question

13. The negatively charged phosphoserine residue interacts with the positively charged protonated histidine residue and decreases its ability to transfer a proton to the thiolate.



His

See question

14. The methyl group is first hydroxylated. The hydroxy-methylamine eliminated formaldehyde to form methylamine.

See question

15. (a) There is no effect.

(b) Because actin is not controlled by cholesterol, the amount isolated should be the same in both experimental groups. A difference would suggest a problem in the RNA isolation.

(c) The presence of cholesterol in the diet dramatically reduces the amount of HMG-CoA reductase protein.

(d) A common means of regulating the amount of a protein present is to regulate transcription, which is clearly not the case here.

(e) Translation of mRNA could be inhibited. The protein could be rapidly degraded.

See question

Chapter 27

1. DNA polymerase I uses deoxyribonucleoside triphosphates; pyrophosphate is the leaving group. DNA ligase uses a DNA-adenylate (AMP joined to the 5′-phosphate) as a reaction partner; AMP is the leaving group. Topoisomerase I uses a DNA-tyrosyl intermediate (5′-phosphate linked to the phenolic OH group); the tyrosine residue of the enzyme is the leaving group.

   See question

2. FAD, CoA, and $NADP^+$ are plausible alternatives.

   See question

3. Positive supercoiling resists the unwinding of DNA. The melting temperature of DNA increases in proceeding from negatively supercoiled to relaxed to positively supercoiled DNA. Positive supercoiling is probably an adaptation to high temperature.

   See question

4. (a) There are long stretches of each because the transition is highly cooperative. (b) B-Z junctions are energetically highly unfavorable. (c) A-B transitions are less cooperative than B-Z transitions because the helix stays right-handed at an A-B junction but not at a B-Z junction.

   See question

5. (a) 96.2 revolutions per second (1000 nucleotides per second divided by 10.4 nucleotides per turn for B-DNA gives 96.2 rps).

   (b) 0.34 μm/s (1000 nucleotides per second corresponds to 3400 Å/s because the axial distance between nucleotides in B-DNA is 3.4 Å).

   See question

6. Eventually, the DNA would become so tightly wound that movement of the replication complex would be energetically impossible.

   See question

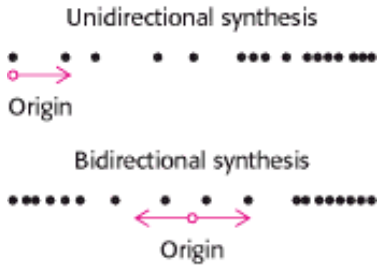
7. A hallmark of most cancer cells is prolific cell division, which requires DNA replication. If the telomerase were not activated, the chromosomes would shorten until they became nonfunctional, leading to cell death. Interestingly, telomerase is often, but not always, found to be activated in cancer cells.

   See question

8. Treat the DNA briefly with endonuclease to occasionally nick each strand. Add the polymerase with the radioactive dNTPs. At the broken bond, or nick, the polymerase will degrade the existing strand with its $5' \rightarrow 3'$ exonuclease activity and replace it with a radioactive complementary copy by using its polymerase activity. This reaction scheme is referred to as nick translation, because the nick is moved, or translated, along the DNA molecule without ever becoming sealed.

See question

9. If replication were unidirectional, tracks with a low grain density at one end and a high grain density at the other end would be seen. On the other hand, if replication were bidirectional, the middle of a track would have a low density, as shown in the adjoining diagram. For *E. coli*, the grain tracks are denser on both ends than in the middle, indicating that replication is bidirectional.



See question

10. (a) Pro (CCC), Ser (UCC), Leu (CUC), and Phe (UUC). Alternatively, the last base of each of these codons could be U.

(b) These C $\rightarrow$ U mutations were produced by nitrous acid.

See question

11. Potentially deleterious side reactions are prevented. The enzyme itself might be damaged by light if it could be activated by light in the absence of bound DNA harboring a pyrimidine dimer.

See question

12. DNA ligase relaxes supercoiled DNA by catalyzing the cleavage of a phosphodiester bond in a DNA strand. The attacking group is AMP, which becomes attached to the 5′-phos- phoryl group at the site of scission. AMP is required because this reaction is the reverse of the final step in the joining of pieces of DNA (see Figure 27.28).

See question

13. ATP hydrolysis is required to release DNA topoisomerase II after the enzyme has acted on its DNA substrate. Negative supercoiling requires only the binding of ATP, not its hydrolysis.

See question

14. (a) Size; the top is relaxed and the bottom is supercoiled DNA. (b) Topoisomers. (c) The DNA is becoming progressively more unwound, or relaxed, and thus slower moving.

See question

15. (a) It was used to determine the number of spontaneous revertants—that is, the background mutation rate.

(b) To firmly establish that the system was working. A known mutagen's failure to produce revertants would indicate that something was wrong with the experimental system.

(c) The chemical itself has little mutagenic ability but is apparently activated into a mutagen by the liver homogenate.

(d) Cytochrome P450 system.

See question

Chapter 29

1. (a) No; (b) no; (c) yes.

See question

2. Four bands: light, heavy, a hybrid of light 30S and heavy 50S, and a hybrid of heavy 30S and light 50S.

See question

3. Two hundred molecules of ATP are converted into AMP + 400 P_i to activate the 200 amino acids, which is equivalent to 400 molecules of ATP. One molecule of GTP is required for initiation, and 398 molecules of GTP are needed to form 199 peptide bonds.

See question

4. (a, d, and e) Type 2; (b, c, and f) type 1.

See question

5. A mutation caused by the insertion of an extra base can be suppressed by a tRNA that contains a fourth base in its anticodon. For example, UUUC rather than UUU is read as the codon for phenylalanine by a tRNA that contains 3′-AAAG-5′ as its anticodon.

See question

6. One approach is to synthesize a tRNA that is acylated with a reactive amino acid analog. For example, bromoacetylphenylalanyl-tRNA is an affinity-labeling reagent for the P site of *E. coli* ribosomes.

See question

7. The sequence GAGGU is complementary to a sequence of five bases at the $3'$ end of 16S rRNA and is located several bases on the $5'$ side of an AUG codon. Hence this region is a start signal for protein synthesis. The replacement of G by A would be expected to weaken the interaction of this mRNA with the 16S rRNA and thereby diminish its effectiveness as an initiation signal. In fact, this mutation results in a tenfold decrease in the rate of synthesis of the protein specified by this mRNA.

See question

8. Proteins are synthesized from the amino to the carboxyl end on ribosomes, whereas they are synthesized in the reverse direction in the solid-phase method. The activated intermediate in ribosomal synthesis is an aminoacyl-tRNA; in the solid-phase method, it is the adduct of the amino acid and dicyclohexylcarbodiimide.

See question

9. The error rates of DNA, RNA, and protein synthesis are of the order of 10^{-10}, 10^{-5}, and 10^{-4}, respectively, per nucleotide (or amino acid) incorporated. The fidelity of all three processes depends on the precision of base pairing to the DNA or mRNA template. No errors are corrected in RNA synthesis. In contrast, the fidelity of DNA synthesis is markedly increased by the $3' \rightarrow 5'$ proofreading nuclease activity and by postreplicative repair. In protein synthesis, the mischarging of some tRNAs is corrected by the hydrolytic action of aminoacyl-tRNA synthetase. Proofreading also takes place when aminoacyl-tRNA occupies the A site on the ribosome; the GTPase activity of EF-Tu sets the pace of this final stage of editing.

See question

10. GTP is not hydrolyzed until aminoacyl-tRNA is delivered to the A site of the ribosome. An earlier hydrolysis of GTP would be wasteful because EF-Tu-GDP has little affinity for aminoacyl-tRNA.

See question

11. The translation of an mRNA molecule can be blocked by antisense RNA, an RNA molecule with the complementary sequence. The antisense-sense RNA duplex cannot serve as a template for translation; single-stranded mRNA is required. Furthermore, the antisense-sense duplex is degraded by nucleases. Antisense RNA added to the external medium is spontaneously taken up by many cells. A precise quantity can be delivered by microinjection. Alternatively, a plasmid encoding the antisense RNA can be introduced into target cells.

See question

12. (a) A_5. (b) $A_5 > A_4 > A_3 > A_2$, (c) Synthesis is from the amino terminus to the carboxyl terminus.

See question

13. These enzymes convert nucleic acid information into protein information by interpreting the tRNA and linking it to the proper amino acid.

See question

14. The rate would fall because the elongation step requires that the GTP be hydrolyzed before any further elongation can take place.

See question

15. The nucleophile is the amino group of the aminoacyl-tRNA. This amino group attacks the carbonyl group of the ester of peptidyl-tRNA to form a tetrahedral intermediate, which eliminates the tRNA alcohol to form a new peptide bond.

See question

16. The aminoacyl-tRNA can be initially synthesized. However, the side-chain amino group attacks the ester linkage to form a six-membered amide, releasing the tRNA.

See question

17. EF-Ts catalyzes the exchange of GTP for GDP bound to EF-Tu. In G-protein cascades, an activated 7TM receptor catalyzes GTP-GDP exchange in a G protein.

See question

18. The α subunits of G proteins are inhibited by a similar mechanism in cholera and whooping cough (Section 15.5.2).

See question

19. (a) eIF4H had two effects: (1) the extent of unwinding was increased and (2) the rate of unwinding was increased, as indicated by the increased rise in activity at early reaction times.

(b) To firmly establish that the effect of eIFH4 was not due to any inherent helicase activity.

(c) Half-maximal activity was achieved at 0.11 μM of eIF4H. Therefore, maximal stimulation would be achieved at a ratio of 1:1.

(d) eIF4H enhances the rate of unwinding of all helices, but the effect is greater as the helices increase in stability.

(e) The results in graph C suggest that it increases the processivity.

See question

Chapter 30

1. The liver and to a lesser extent the kidneys, contain glucose 6-phosphatase, whereas muscle and the brain do not. Hence, muscle and the brain, in contrast with the liver, do not release glucose. Another key enzymatic difference is that the liver has little of the transferase needed to activate acetoacetate to acetoacetyl CoA. Consequently, acetoacetate and 3-hydroxybutyrate are exported by the liver for use by heart muscle, skeletal muscle, and the brain.

See question

2. (a) Adipose cells normally convert glucose into glycerol 3-phosphate for the formation of triacylglycerols. A deficiency of hexokinase would interfere with the synthesis of triacyl-glycerols.

(b) A deficiency of glucose 6-phosphatase would block the export of glucose from the liver after glycogenolysis. This disorder (called von Gierke disease) is characterized by an abnormally high content of glycogen in the liver and a low bloodglucose level.

(c) A deficiency of carnitine acyltransferase I impairs the oxidation of long-chain fatty acids. Fasting and exercise precipitate muscle cramps.

(d) Glucokinase enables the liver to phosphorylate glucose even in the presence of a high level of glucose 6-phosphate. A deficiency of glucokinase would interfere with the synthesis of glycogen.

(e) Thiolase catalyzes the formation of two molecules of acetyl CoA from acetoacetyl CoA and CoA. A deficiency of thiolase would interfere with the utilization of acetoacetate as a fuel when the blood-sugar level is low.

(f) Phosphofructokinase will be less active than normal because of the lowered level of F-2,6-BP. Hence, glycolysis will be much slower than normal.

See question

3. (a) A high proportion of fatty acids in the blood are bound to albumin. Cerebrospinal fluid has a low content of fatty acids because it has little albumin.

(b) Glucose is highly hydrophilic and soluble in aqueous media, in contrast with fatty acids, which must be carried by transport proteins such as albumin. Micelles of fatty acids would disrupt membrane structure.

(c) Fatty acids, not glucose, are the major fuel of resting muscle.

See question

4. (a) A watt is equal to 1 joule (J) per second (0.239 calorie per second). Hence, 70 W is equivalent to 0.07 kJ s^{-1}, or 0.017 kcal s^{-1}.

(b) A watt is a current of 1 ampere (A) across a potential of 1 volt (V). For simplicity, let us assume that all the electron flow is from NADH to O_2 (a potential drop of 1.14 V).

Hence, the current is 61.4 A, which corresponds to 3.86×10^{20} electrons per second (1 A = 1 coulomb s^{-1} = 6.28×10^{18} charge s^{-1}).

(c) Three molecules of ATP are formed per molecule of NADH oxidized (two electrons). Hence, one molecule of ATP is formed per 0.67 electron transferred. A flow of 3.86×10^{20} electrons per second therefore leads to the generation of 5.8×10^{20} molecules of ATP per second, or 0.96 mmol s^{-1}.

(d) The molecular weight of ATP is 507. The total body content of ATP of 50 g is equal to 0.099 mol. Hence, ATP turns over about once per 100 seconds when the body is at rest.

See question

5. (a) The stoichiometry of the complete oxidation of glucose is

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O$$

and that of tripalmitoylglycerol is

$$C_{51}H_{98}O_2 + 72.5\,O_2 \longrightarrow 51\,CO_2 + 49\,H_2O$$

Hence, the RQ values are 1.0 and 0.703, respectively.

(b) An RQ value reveals the relative usage of carbohydrate and fats as fuels. The RQ of a marathon runner typically decreases from 0.97 to 0.77 during a race. The lowering of the RQ indicates the shift in fuel from carbohydrate to fat.

See question

6. One gram of glucose (molecular weight 180.2) is equal to 5.55 mmol, and one gram of tripalmitoylglycerol (molecular weight 807.3) is equal to 1.24 mmol. The reaction stoichiometries (see problem 5) indicate that 6 mol of H_2O are produced per mole of glucose oxidized, and 49 mol of H_2O per mole of tripalmitoylglycerol oxidized. Hence, the H_2O yields per gram of fuel are 33.3 mmol (0.6 g) for glucose, and 60.8 mmol (1.09 g) for tripalmitoylglycerol. Thus, complete oxidation of this fat gives 1.82 times as much water as does glucose. Another advantage of triacylglycerols is that they can be stored in essentially anhydrous form, whereas glucose is stored as glycogen, a highly hydrated polymer. A hump consisting mainly of glycogen would be an intolerable burden—far more than the straw that broke the camel's back.

See question

7. A typical macadamia nut has a mass of about 2 g. Because it consists mainly of fats (~9 kcal/g, ~37 kJ/g), a nut has a value of about 18 kcal (75 kJ). The ingestion of 10 nuts results in an intake of about 180 kcal (753 kJ). As stated in the answer to problem 4, a power consumption of 1 W corresponds to 0.239 cal s^{-1} (1 J s^{-1}), and so 400-W running requires 95.6 cal s^{-1}, or .0956 kcal s^{-1} (0.4 kJ s^{-1}). Hence, one would have to run 1882 s, or about 31 minutes, to spend the calories provided by 10 nuts.

See question

8. A high blood-glucose level would trigger the secretion of insulin, which would stimulate the synthesis of glycogen and triacylglycerols. A high insulin level would impede the mobilization of fuel reserves during the marathon.

See question

9. Lipid mobilization can occur so rapidly that it exceeds the ability of the liver to oxidize the lipids or convert them into ketone bodies. The excess is reesterified and released into the blood as VLDL.

See question

10. A role of the liver is to provide glucose for other tissues. In the liver, glycolysis is used not for energy production but for biosynthetic purposes. Consequently, in the presence of glucagon, liver glycolysis stops so that the glucose can be released into the blood.

See question

11. Urea cycle and gluconeogenesis.

See question

12. (a) Insulin inhibits lipid utilization.

(b) Insulin stimulates protein synthesis, but there are no amino acids in the children's diet. Moreover, insulin inhibits protein breakdown. Consequently, muscle proteins cannot be broken down and used for the synthesis of essential proteins.

(c) Because proteins cannot be synthesized, blood osmolarity is too low. Consequently, fluid leaves the blood. An especially im- portant protein for maintaining blood osmolarity is albumin.

See question

13. The oxygen consumption at the end of exercise is used to replenish ATP and creatine phosphate and to oxidize any lactate produced.

See question

14. Oxygen is used in oxidative phosphorylation to resynthesize ATP and creatine phosphate. The liver converts lactate released by the muscle into glucose. Blood must be circulated to return the body temperature to normal, and so the heart cannot return to its resting rate immediately. Hemoglobin must be reoxygenated to replace the oxygen used in exercise. The muscles that power breathing must continue working at the same time that the exercised muscles are returning to resting states. In essence, all the biochemical systems activated in intense exercise need increased oxygen to return to the resting state.

See question

15. Ethanol may replace water that is hydrogen bonded to proteins and membrane surfaces. This alteration of the hydration state of the protein would alter its conformation and hence function. Ethanol may also alter phospholipid packing in membranes. The two effects suggest that integral membrane proteins would be most sensitive to ethanol, as indeed seems to be the case.

See question

16. Cells from the type I fiber would be rich in mitochondria, whereas those of the type II fiber would have few mitochondria.

See question

17. (a) The ATP expended during this race amounts to about 8380 kg, or 18,400 pounds.

(b) The cyclist would need about $1,260,000 to complete the race.

See question

Chapter 31

1. (a) Cells will express β-galactosidase, *lac* permease, and thiogalactoside transacetylase even in the absence of lactose.

(b) Cells will express β-galactosidase, *lac* permease, and thiogalactoside transacetylase even in the absence of lactose.

(c) The levels of catabolic enzymes such as β-galactosidase and arabinose isomerase will remain low even at low levels of glucose.

See question

2. The concentration is $1/(6 \times 10^{23})$ moles per 10^{-15} liter = 1.7×10^{-9} M. Because $K_d = 10^{-13}$ M, the single molecule should be bound to its specific binding site.

See question

3. The number of possible 8-bp sites is $4^8 = 65{,}536$. In a genome of 4.6×10^6 base pairs, the average site should appear $4.6 \times 10^6/65{,}536 = 70$ times. Each 10-bp site should appear 4 times. Each 12-bp site should appear 0.27 times (many 12-bp sites will not appear at all).

See question

4. The distribution of charged amino acids is H2A (13K, 13R, 2D, 7E, charge = +15), H2B (20K, 8R, 3D, 7E, charge = +18), H3 (13K, 18R, 4D, 7E, charge = +20), H4 (11K, 14R, 3D, 4E, charge = +18). The total charge of the histone octamer is estimated to be $2 \times (15 + 18 + 20 + 18) = +142$. The total charge on 150 base pairs of DNA is -300. Thus, the histone octamer neutralizes approximately one-half of the charge.

See question

5. The presence of a particular DNA fragment could be detected by hybridization or by PCR. For *lac* repressor, a single fragment should be isolated. For *pur* repressor, approximately 20 distinct fragments should be isolated.

See question

6. 5-Azacytidine cannot be methylated. Some genes, normally repressed by methylation, will be active.

See question

7. Proteins containing these domains will be targeted to methylated DNA in repressed promoter regions. They would likely bind in the major groove because that is where the methyl group is.

See question

8. The *lac* repressor does not bind DNA when the repressor is bound to a small molecule (the inducer), whereas *pur* repressor binds DNA only when the repressor is bound to a small molecule (the corepressor). The *E. coli* genome contains only a single *lac* repressor-binding region, whereas it has many sites for the *pur* repressor.

See question

9. Anti-inducers bind to the conformation of repressors, such as the *lac* repressor, that are capable of binding DNA. They occupy a site that overlaps that for the inducer and, therefore, compete for binding to the repressor.

See question

10. The inverted repeat may be a binding site for a dimeric DNA-binding protein or it may correspond to a stem-loop structure in the encoded RNA.

See question

11. The amino group of the lysine residue, formed from the protonated form by a base, attacks the carbonyl group of acetyl CoA to generate a tetrahedral intermediate. This intermediate collapses to form the amide bond and release CoA.

See question

12. Long-term memory requires gene expression stimulated by CREB. The injection of many binding sites for this protein prevents CREB from binding to the necessary sites in chromatin and, hence, blocks the activation of gene expression. A possible pathway begins with serotonin binding to a 7TM receptor, which activates a G protein which in turn activates adenylate cyclase. This activation increases the concentration of cAMP-activiated protein kinase A, which phosphorylates CREB, thus activating gene expression necessary for memory storage.

See question

13. In mouse DNA, most of the HpaII sites are methylated and therefore not cut by the enzyme, resulting in large fragments. Some small fragments are produced from CpG islands that are unmethylated. For *Drosophila* and *E. coli* DNA, there is no methylation and all sites are cut.

See question

Chapter 33

1. (a) $\Delta G^{\circ\prime} = -8.9$ kcal mol^{-1} (-37 kJ mol^{-1}).

(b) $K_a = 3.3 \times 10^6$ M^{-1}

(c)$k_{on} = 4 \times 10^8$ M^{-1} s^{-1}. This value is close to the diffusion- controlled limit for the combination of a small molecule with a protein (Section 8.4.2). Hence, the extent of structural change is likely to be small; extensive conformational transitions take time.

See question

2. Each glucose residue is approximately 5-Å long; so an extended chain of six residues is 6 × 5 Å = 30 Å long. This length is comparable to the size of an antibody combining site.

See question

3. The fluorescence enhancement and the shift to blue indicate that water is largely excluded from the combining site when the hapten is bound. Hydrophobic interactions contribute significantly to the formation of most antigen-antibody complexes.

See question

4. (a) 7.1 μM.

(b) $\Delta G^{\circ\prime}$ is equal to 2 × -7 + 3 kcal mol^{-1}, or -11 kcal mol^{-1} (-46 kJ mol^{-1}), which corresponds to an apparent dissociation constant of 8 nM. The avidity (apparent affinity) of bivalent binding in this case is 888 times as much as the affinity of the univalent interaction.

See question

5. (a) An antibody combining site is formed by CDRs from both the H and the L chains. The V_H and V_L domains are essential. A small proportion of F_{ab} fragments can be further digested to produce F_v, a fragment that contains just these two domains. C_H1 and C_L contribute to the stability of F_{ab} but not to antigen binding.

(b) A synthetic F_v analog 248 residues long was prepared by expressing a synthetic gene consisting of a V_H gene joined to a V_L gene through a linker. See J. S. Huston et al., *Proc. Natl. Acad. Sci. U.S.A.* 85(1988):5879.

See question

6. (a) Multivalent antigens lead to the dimerization or oligomerization of transmembrane immunoglobulins, an essential step in their activation. This mode of activation is reminiscent of that of receptor tyrosine kinases (Section 15.4.1).

(b) An antibody specific for a transmembrane immunoglobulin will activate a B cell by cross-linking these receptors. This experiment can be carried out by using, for example, a goat antibody to cross-link receptors on a mouse B cell.

See question

7. B cells do not express T-cell receptors. Hybridization of T-cell cDNAs with B-cell mRNAs removes cDNAs that are expressed in both cells. Hence, the mixture of cDNAs subsequent to this hybridization are enriched in those encoding T-cell receptors. This procedure, called subtractive hybridization, is generally useful in isolating low-abundance cDNAs. Hybridization should be carried out by using mRNAs from a closely related cell that does not express the gene of interest. See S. M. Hedrick, M. M. Davis, D. I. Cohen, E. A. Nielsen, and M. M. Davis, *Nature* 308(1984):149, for an interesting account of how this method was used to obtain genes for T-cell receptors.

See question

8. Purify an antibody with a specificity to one antigen. Unfold the antibody and allow it to refold either in the presence of the antigen or in the absence of the antigen. Test the refolded antibodies for antigen-binding ability.

See question

9. In some cases, V-D-J rearrangement will result in combining V, D, and J segments out of frame. mRNA molecules produced from such rearranged genes will produce truncated molecules if translated. This possibility is excluded by degrading the mRNA.

See question

10. F_c fragments are much more uniform than F_{ab} fragments because F_c fragments are composed of constant regions. Such homogeneity is important for crystallization.

See question

11. The peptide is LLQATYSAV (L in second position, V in last).

See question

12. Catalysis is likely to require a base for removing a proton from a water molecule. A histidine, glutamate, or aspartate residue is most likely. In addition, potential hydrogen-bond donors may be present and will interact with the negatively charged oxygen atom that forms in the transition state.

See question

13. A phosphotyrosine residue in the carboxyl terminus of Src and related protein tyrosine kinases binds to its own SH2 domain to generate the inhibited from of Src (Section 15.5). Removal of the phosphate from this residue will activate the kinase.

See question

14. (a) $K_d = 10^{-7}$ M; (b) $K_d = 10^{-9}$ M. The gene was probably generated by a point mutation in the gene for antibody A rather than by de novo rearrangement.

See question

Chapter 34

1. (a) Skeletal muscle and eukaryotic cilia derive their free energy from ATP hydrolysis; the bacterial flagellar motor uses a protonmotive force. (b) Skeletal muscle requires myosin and actin. Eukaryotic cilia require microtubules and dynein. The bacterial flagellar motor requires MotA, MotB, and FliG, as well as many ancillary components.

See question

2. 6400Å/80Å = 80 body lengths per second. For a 10-foot automobile, this body-length speed corresponds to a speed of 80 × 10 feet = 800 feet per second, or 545 miles per hour.

See question

3. 4 pN = 8.8×10^{-13} pounds. The weight of a single motor domain is 100,000 g mol^{-1}(6.023×10^{23} molecules mol^{-1}) = 1.7×10^{-19} g = 7.6×10^{-23} pounds. Thus, a motor domain can lift ($8.8 \times 10^{-13}/7.6 \times 10^{-23}$) = 1.2×10^{10} times its weight.

See question

4. After death, the ratio of ADP to ATP increases rapidly. In the ADP form, myosin motor domains bind tightly to actin. Myosin-actin interactions are possible because the drop in ATP concentration also allows the calcium concentration to rise, clearing the blockage of actin by tropomyosin through the action of the troponin complex.

See question

5. Above its critical concentration, ATP-actin will polymerize. The ATP will hydrolyze through time to form ADP-actin, which has a higher critical concentration. Thus, if the initial subunit concentration is between the critical concentrations of ATP-actin and ADP-actin, filaments will form initially and then disappear on ATP hydrolysis.

See question

6. Actin monomers bind and hydrolyze ATP and are in somewhat different conformations, depending on the identity of the bound nucleotide. Thus, nucleotide binding and then hydrolysis by actin filaments might change actin's length, shape, or rigidity.

See question

7. The first (a) should behave like conventional kinesin and move toward the plus end of microtubules, whereas the second (b) should behave like ncd and move toward the minus end.

See question

8. A one-base step is approximately 3.4 Å = 3.4×10^{-4} μm. If a stoichiometry of one molecule of ATP per step is assumed, this distance corresponds to a velocity of 0.017 μm s^{-1}. Kinesin moves at a velocity of 6400 Å per second, or 0.64 μm s^{-1}.

See question

9. A protonmotive force across the plasma membrane is necessary to drive the flagellar motor. Under conditions of starvation, this protonmotive force is depleted. In acidic solution, the pH difference across the membrane is sufficient to power the motor.

See question

10. (a) The force is 6π(0.01 g cm^{-1} s^{-1})(0.0002 cm)(0.00006 cm s^{-1}) = 2.3×10^{-9} dyne. (b) The work performed is (2.3×10^{-9} dyne)(0.00006 cm) = 1.4×10^{-13} erg. (c) On the basis of a ΔG value of -12 kcal mol^{-1} (50 kJ mol^{-1}) under typical cellular conditions, the energy available is 8.3×10^{-13} erg per molecule. In 1 second, 80 molecules of ATP are hydrolyzed, corresponding to 6.6×10^{-11} erg. Thus, a single kinesin motor provides more than enough free energy to power the transport of micrometer-size cargoes at micrometer-per-second velocities.

See question

11. The spacing between identical subunits on microtubules is 8 nm. Thus, a kinesin with a step size that is not a multiple of 8 nm would have to be able to bind on more than one type of site on the microtubule surface.

See question

12. KIF1A must be tethered to an additional microtubule-binding element that retains an attachment to the microtubule when the motor domain releases.

See question

13. Protons still flow from outside to inside the cell. Each proton might pass into the outer half-channel of one MotA-MotB complex, bind to the MS ring, rotate clockwise, and pass into the inner half-channel of the neighboring MotA-MotB complex.

See question

14. At a high concentration of calcium ion, calcium binds to calmodulin. In turn, calmodulin binds to and activates a protein kinase that phosphorylates myosin light chains. At low calcium concentration, the light chains are dephosphorylated by a calcium-independent phosphatase.

See question

15. (a) The value of k_{cat} is approximately 13 molecules per second, whereas the K_M value for ATP is approximately 12 μM. (b) The step size is approximately (380 - 120)/7 = 37 nm. (c) The step size is very large, which is consistent with the presence of six light-chain-binding sites and, hence, very long lever arms. The rate of ADP release is essentially identical with the overall k_{cat}; so ADP release is rate limiting, which suggests that both motor domains can bind to sites 37 nm apart simultaneously. ADP release from the hindmost domain allows ATP to bind, leading to actin release and lever-arm motion.

See question

Common Abbreviations in Biochemistry

A adenine

ACP acyl carrier protein

ADP adenosine diphosphate

Ala alanine

AMP adenosine monophosphate

cAMP cyclic AMP

Arg arginine

Asn asparagine

Asp aspartate

ATP adenosine triphosphate

ATPase adenosine triphosphatase

C cytosine

CDP cytidine diphosphate

CMP cytidine monophosphate

CoA coenzyme A

CoQ coenzyme Q (ubiquinone)

CTP cytidine triphosphate

cAMP adenosine 3′,5′-cyclic monophosphate

cGMP guanosine 3′,5′-cyclic monophosphate

Cys cysteine

Cyt cytochrome

d 2′-deoxyribo-

DNA deoxyribonucleic acid

cDNA complementary DNA

DNAse deoxyribonuclease

EcoRI *Eco*RI restriction endonuclease

EF elongation factor

FAD flavin adenine dinucleotide (oxidized form)

$FADH_2$ flavin adenine dinucleotide (reduced form)

fMet formylmethionine

FMN flavin mononucleotide (oxidized form)

$FMNH_2$ flavin mononucleotide (reduced form)

G guanine

GDP guanosine diphosphate

Gln glutamine

Glu glutamate

Gly glycine

GMP guanosine monophosphate

cGMP cyclic GMP

GSH reduced glutathione

GSSG oxidized glutathione

GTP guanosine triphosphate

GTPase guanosine triphosphatase

Hb hemoglobin

HDL high-density lipoprotein

HGPRT hypoxanthine-guanine phosphoribosyl-transferase

His histidine

Hyp hydroxyproline

IgG immunoglobulin G

Ile isoleucine

IP_3 inositol 1,4,5,-trisphosphate

ITP inosine triphosphate

LDL low-density lipoprotein

Leu leucine

Lys lysine

Met methionine

NAD^+ nicotinamide adenine dinucleotide (oxidized form)

NADH nicotinamide adenine dinucleotide (reduced form)

$NADP^+$ nicotinamide adenine dinucleotide phosphate (oxidized form)

NADPH nicotinamide adenine dinucleotide phosphate (reduced form)

PFK phosphofructokinase

Phe phenylalanine

P_i inorganic orthophosphate

PLP pyridoxal phosphate

PP_i inorganic pyrophosphate

Pro proline

PRPP 5-phosphoribosyl-1-pyrophosphate

Q ubiquinone (or plastoquinone)

QH_2 ubiquinol (or plastoquinol)

RNA ribonucleic acid

mRNA messenger RNA

rRNA ribosomal RNA

scRNA small cytoplasmic RNA

snRNA small nuclear RNA

tRNA transfer RNA

RNAse ribonuclease

Ser serine

T thymine

Thr threonine

TPP thiamine pyrophosphate

Trp tryptophan

TTP thymidine triphosphate

Tyr tyrosine

U uracil

UDP uridine diphosphate

UDP-galactose uridine diphosphate galactose

UDP-glucose uridine diphosphate glucose

UMP uridine monophosphate

UTP uridine triphosphate

Val valine

VLDL very low density lipoprotein