

CHAPTER SCOPE

In the last chapter we learned about the amino acid composition and the structure of proteins. We also studied the process by which proteins are synthesized from information coded in the genes of the chromosomes. Perhaps the most important group of body proteins is that of **enzymes** — the subject of this chapter. These vital molecules act as biological catalysts, speeding up chemical reactions in such diverse regions of the body as in the stomach or in the intestine where powerful enzymes digest foods by hydrolysis (chapter 17), in the blood and kidney where the enzyme **carbonic anhydrase** helps maintain *acid-base balance* (chapter 15), and within target cells where various enzymes activate *second messenger systems* in response to visiting hormones (chapter 11). Enzymes also serve as critical facilitators of *cell respiration* and other important metabolic pathways that take place in the cytoplasm and within the mitochondria of all cells to combust fuel molecules and provide energy for the cell's many activities (chapters 5, 18).

In the next chapter on cell metabolism, the enzymes introduced here will be appreciated as a specific enzyme catalyzes each step in the breakdown of fuel food molecules and the transfer of energy to **adenosine triphosphate (ATP)**. Since enzymes are protein molecules assembled under the direction of the cell's DNA, a single defective gene will result in the synthesis of a defective enzyme. Such defective enzymes can cause *inborn errors of metabolism*, which in severe cases may cause nervous system disorders or even death. Furthermore, the delicate tertiary structure of enzymes must be maintained so that the active site can receive substrate molecules during normal catalysis. Changes in acid-base balance (such as *acidosis* or *alkalosis*) or variations in body temperature (such as *hyperthermia* or *hypothermia*) can disturb this precise protein architecture and interfere with the ability of enzymes to regulate metabolism.

With a job this vital to life, it is no wonder that enzymes recruit help from other molecules — namely, **coenzymes** and **cofactors**. In this chapter, we will be introduced to two important coenzymes, *NAD* and *FAD*, both derived from water-soluble B vitamins. In similar fashion, these coenzymes function as carriers of hydrogen atoms, shuttling these atoms from place to place along metabolic pathways of the cell. In the next chapter on cell respiration, a third coenzyme (*coenzyme A*) is introduced that will join *NAD* and *FAD* in assisting the many metabolic enzymes working to extract and transfer energy from fuel foods to high-energy ATP molecules.

I. ENZYMES AS CATALYSTS

Enzymes are biological catalysts that function to increase the rate of chemical reactions. Most enzymes are proteins, and their catalytic action results from their complex structure. The great diversity of protein structure allows different enzymes to be specialized in their action.

A. Multiple Choice

- ___ 1. A *catalyst* is a chemical substance that
 - a. increases the rate of a reaction.
 - b. is not itself changed by the reaction.
 - c. does not change the nature of the reaction.
 - d. does not change the final result of the reaction.
 - e. All of these describe a catalyst.
- ___ 2. Catalysts make reactions go faster by
 - a. increasing the energy level of the reactants.
 - b. lowering the activation energy.
 - c. raising the temperature of the reaction.
 - d. reducing the repulsion between ions within the reactants.
- ___ 3. In enzyme-catalyzed reactions, the reactant molecules are better known as
 - a. active sites.
 - b. substrates.
 - c. enzyme-substrate complexes.
 - d. products.

- ___ 4. Enzymes that rearrange atoms within their substrate molecules to form products with the same composition but with a different structure, are called
 - a. hydrolases.
 - b. phosphatases.
 - c. synthetases.
 - d. isomerases.
- ___ 5. Different models of the same enzyme (they must have the same active site and catalyze the same reaction) made by different tissues are called
 - a. isomers.
 - b. isomerases.
 - c. isoenzymes.
 - d. isomodels.
- ___ 6. Which of the following statements about enzymes is *false*?
 - a. Enzymes are biological catalysts.
 - b. Enzymes speed up chemical reactions by raising the activation energy.
 - c. Enzymes work faster at higher temperatures.
 - d. Enzymes are not changed by the reaction they catalyze.
 - e. Enzymes often require the presence of minerals or other “helper” molecules.
- ___ 7. Which of the following molecules is the correct substrate molecule for the enzyme carbonic anhydrase? (Hint: see Table 4.2)
 - a. H₂O
 - b. starch
 - c. lactic acid
 - d. H₂CO₃

B. True or False/Edit

- ___ 8. Most proteins are enzymes.
- ___ 9. Without enzymes all chemical reactions simply will not run.
- ___ 10. Energy of activation is the amount of energy required for a reaction to proceed.
- ___ 11. There are enzymes whose names do *not* have the characteristic “-ase” ending, or suffix.
- ___ 12. Isoenzymes display the same active site and catalyze the same chemical reaction but will differ in composition and structure elsewhere in the molecules.
- ___ 13. Ribozymes are unique molecules of RNA that function as enzymes in reactions involving the remodeling of other RNA molecules and in the formation of a growing polypeptide during protein synthesis at the ribosome.
- ___ 14. Enzymes known as synthases or synthetases catalyze reactions that involve removing water (dehydration) from smaller molecules to form bonds that result in a larger product molecule.
- ___ 15. The term substrate always refers to the reactant molecule in an enzyme-catalyzed reaction.

II. CONTROL OF ENZYME ACTIVITY

The rate of an enzyme-catalyzed reaction depends on numerous factors, including the concentration of the enzyme and the pH and temperature of the solution. Genetic control of enzyme concentration, for example, affects the rate of progress along particular metabolic pathways and thus regulates cellular metabolism.

A. Multiple Choice

- ___ 16. Which of the following does *not* alter enzyme activity?
 - a. the temperature and pH of the solution
 - b. the concentration of cofactors and coenzymes present
 - c. the concentration of oxygen present
 - d. the concentration of enzyme and substrate molecules present

- ___ 17. Pepsin, an enzyme secreted by the stomach lining, would be expected to have an *optimal* pH of
- 2.
 - 4.
 - 7.4.
 - 9.
 - 14.
- ___ 18. Which of the following is *least* likely to act as a cofactor?
- calcium
 - magnesium
 - copper
 - oxygen
 - zinc
- ___ 19. In enzyme-catalyzed reactions, cofactors bind directly to the
- enzyme.
 - active site.
 - substrate.
 - Cofactors bind to all of these locations.
 - Cofactors bind to none of these locations.
- ___ 20. Coenzymes participate in enzyme-catalyzed reactions by
- lowering the activation energy required.
 - transporting hydrogen atoms and small molecules from one enzyme to another
 - binding to the enzyme, causing conformational changes.
 - providing the pH and temperature optima for the reactions.
- ___ 21. Which statement about *zymogens* is *false*?
- Zymogens are extremely active, hydrolytic enzymes.
 - Examples of zymogens include the protein kinase enzymes in cytoplasm.
 - Examples of zymogens include the digestive enzymes from the pancreas.
 - Zymogens must first be activated by another enzyme or ligand molecule.
 - Attachment of a phosphate group can inactivate certain zymogens.
- ___ 22. Cyclic AMP (cAMP), is
- an intracellular regulator molecule directing activities within the cell.
 - a particular ligand for activating enzymes such as protein kinase.
 - a molecule known also as a second messenger.
 - often controlled by extracellular regulatory molecules such as hormones and neurotransmitter molecules.
 - All of these statements are true.
- ___ 23. "Saturation" in an enzyme-catalyzed reaction means that the _____ are saturated with _____.
- products; enzymes
 - substrates; products
 - enzymes; substrates
 - products; substrates
- ___ 24. Allosteric inhibition is a mechanism along metabolic pathways by which
- inhibition of an earlier step at a branch point along that pathway occurs.
 - structural changes at the active site occurs to interfere with the enzyme.
 - the final product inhibits an earlier enzymatic step (end-product inhibition).
 - All of these statements describe allosteric inhibition.
- ___ 25. Inborn errors of metabolism that cause disease result in a (an) _____ (increase/decrease) in the amount of intermediates formed prior to the defective step, and a (an) _____ (increase/decrease) in the number of final products formed along alternate pathways.
- increase; increase
 - increase; decrease
 - decrease; increase
 - decrease; decrease

- ___ 26. The inborn error of metabolism that all newborn babies are tested for and that, once detected, can be controlled by a diet low in one specific amino acid, is known as
- albinism.
 - phenylketonuria (PKU).
 - Gaucher's disease.
 - Tay-Sachs disease.
 - lactose intolerance.

B. True or False/Edit

- ___ 27. Higher temperatures decrease the rate of enzyme activity by altering the tertiary structure of the enzyme.
- ___ 28. The rate of enzyme activity is decreased by concentrations of hydrogen ion (pH), which are either too high or too low.
- ___ 29. Alkaline phosphatase is an enzyme with a pH optimum having a lower number than that of acid phosphatase enzymes.
- ___ 30. Cofactors are organic molecules derived from water-soluble vitamins such as niacin and riboflavin.
- ___ 31. Powerful digestive enzymes destined to digest food in the intestine must be secreted in an inactive zymogen form by the pancreas to prevent local damage to cells of the pancreas.
- ___ 32. The activation or inactivation of zymogen molecules can be as simple as adding (phosphorylation) or removing (dephosphorylation) of a phosphate group from the molecule.
- ___ 33. Cyclic AMP (cAMP) is an important neurotransmitter molecule released from the axon terminal of neurons.
- ___ 34. Circulating hormones from the blood and neurotransmitters from neurons can regulate the activities of intracellular enzymes, and thereby regulate many aspects of metabolism in those cells.
- ___ 35. Given a certain number of enzymes, increasing the number of substrate molecules will increase the number of products formed.
- ___ 36. Two different enzymes often catalyze reversible reactions, one for each direction in the reaction.
- ___ 37. During metabolism, the product formed by one enzyme can become the substrate for the next enzyme in the pathway.
- ___ 38. During metabolism, one intermediate can serve as a substrate for two different enzymes, thus ultimately forming two different products.
- ___ 39. In end-product inhibition, the function of the last product formed is inhibited.
- ___ 40. In diseases known as inborn errors of metabolism, the quantity of intermediates formed prior to the defective enzyme step decreases, and the quantity of intermediates and final products formed after the defective step increases.
- ___ 41. Phenylketonuria (PKU) is an inborn error of phenylalanine metabolism due to an inherited defect in the enzyme that catalyzes the formation of melanin from dihydroxyphenylalanine (DOPA).

III. BIOENERGETICS

Living organisms require the constant expenditure of energy to maintain their complex structures and processes. Central to life processes are chemical reactions that are coupled, so that the energy released by one reaction is incorporated into the products of another reaction.

A. Multiple Choice

- ___ 42. Which of the following statements about *entropy* is *false*?
- It describes the degree of disorganization of a system.
 - It is increased as energy is changed to another form.
 - As it increases the amount of free energy available to do work is reduced.
 - It is defined by the first law of thermodynamics.
 - All of these statements regarding entropy are true.
- ___ 43. Which of the following statements about *exergonic* reactions is *false*?
- They can release energy in the form of heat.
 - They convert molecules with less free energy to molecules with more free energy.
 - The combustion of glucose to CO₂ and H₂O is an example.
 - They convert molecules with less entropy to molecules with more entropy.
 - All of these statements regarding exergonic reactions are true.

- ___ 44. Which of the following statements about *oxidation-reduction* reactions is *false*?
- Reducing agents donate electrons to another atom or molecule.
 - Oxidizing agents accept electrons from another atom or molecule.
 - An atom or molecule cannot be both an oxidizing and reducing agent.
 - Oxidation and reduction are always coupled reactions.
 - All of these statements regarding oxidation-reduction reactions are true.
- ___ 45. The final electron acceptor in a chain of oxidation-reduction reactions that provides energy for ATP production in the cell is
- oxygen.
 - proton (H^+).
 - electron (e^-).
 - water.
 - ATP.

B. True or False/Edit

- ___ 46. The first law of thermodynamics states that entropy can be neither created nor destroyed.
- ___ 47. Only organized or free energy can be used to perform work.
- ___ 48. Photosynthesis is an example of an endergonic reaction.
- ___ 49. A *calorie* is a unit of free energy.
- ___ 50. Living cells are able to use heat energy to drive most chemical reactions.
- ___ 51. The breakdown of $ATP \rightarrow ADP + P_i$ is an exergonic reaction.
- ___ 52. Oxygen is a very strong oxidizing agent and thus, a strong electron acceptor in oxidation-reduction reactions.
- ___ 53. NAD is a coenzyme derived from vitamin B_2 .
- ___ 54. A molecule such as NAD or FAD can be an electron acceptor in one reaction and an electron donor in another reaction.

CHAPTER REVIEW

A. Completion

Assume you have recently consumed a delicious cheeseburger as a source of body fuel. Also, assume that digestion and absorption into the body was successful such that simple sugars (like glucose) from carbohydrates, triglycerides from lipids, and amino acids from proteins are now present in your body cells. Here, the amino acids floating in the cytoplasm are used to make biological catalysts, or 55. _____, as instructed by DNA. The various metal ions assist enzymes by working as 56. _____, while the water-soluble vitamins work primarily as 57. _____. Under optimal conditions of 58. _____ and 59. _____, enzymes can speed up the metabolism of your cheeseburger fuels, releasing 60. _____ from chemical bonds. Therefore, these reactions are 61. _____ (endergonic/exergonic). The combustion of glucose as fuel in the cell results in the formation of 62. _____ and water; while some of the chemical-bond energy is transferred to “high-energy” bonds of 63. _____ or (_____), and the rest of the energy is lost as 64. _____. The formation of this “universal energy carrier” is 65. _____ (endergonic/exergonic), providing the cell with a usable form of energy.

In a similar fashion, triglycerides and amino acids can be combusted in the cell, transferring energy to power the cell's many energy-requiring processes. Complete combustion of these fuels requires that we breathe so that blood can deliver the gas 66. _____, which is the final electron 67. _____ (acceptor/donor) in the cell. In the final step of metabolism, this gas is ultimately 68. _____ (oxidized/reduced) to form 69. _____.

B. Crossword Puzzle — Enzymes and Energy

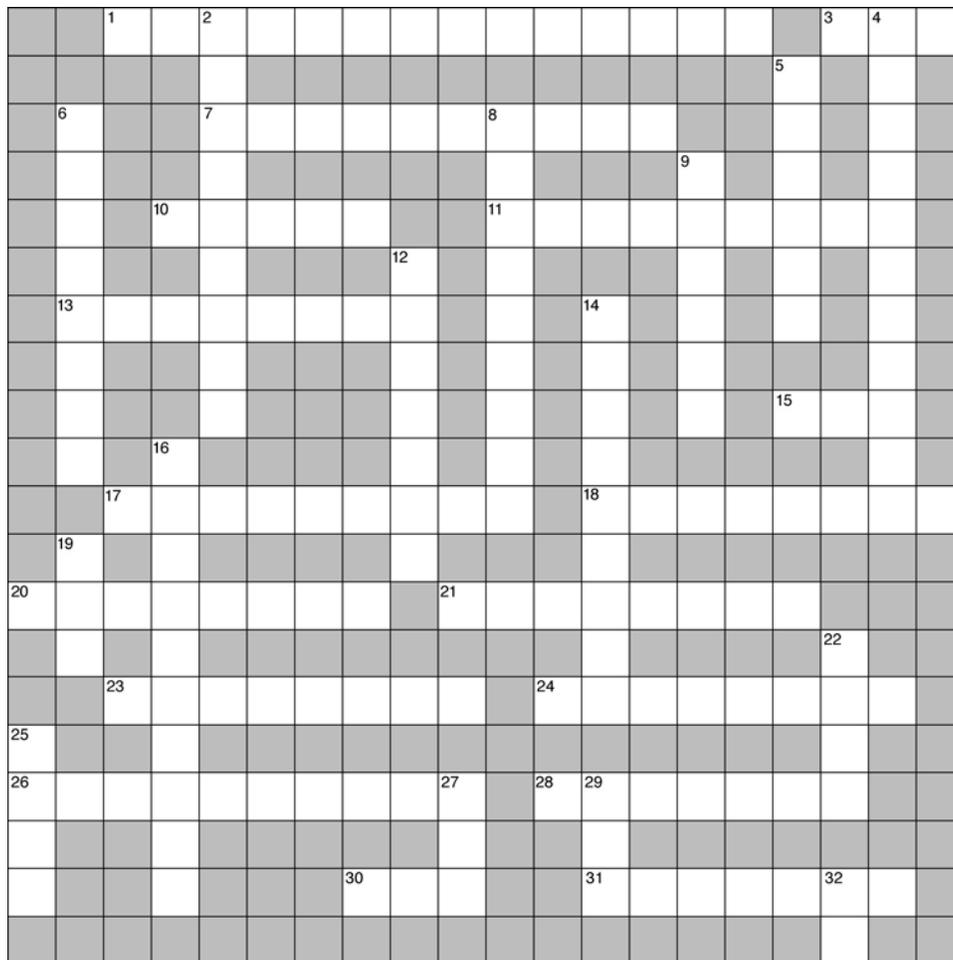
Across

1. bioenergetics incorporates these first and second laws
3. the cell's "universal energy carrier"
7. reactions that require energy input
10. oxidizing or reducing _____
11. different model of the same enzyme
13. compounds mainly derived from water-soluble vitamins
15. inborn error of phenylalanine (amino acid) metabolism
17. when an atom or molecule gains electrons
18. a new term, or number used to measure the ability of enzymes to convert substrates into products
20. an enzyme acts as a biological _____
21. an enzyme in blood/liver that breaks down hydrogen peroxide
23. a metal ion such as Ca^{2+} , Mg^{2+} , Mn^{2+} , Cu^{2+} , or Zn^{2+}
24. the precise protein structure altered by pH and temperature
26. enzymes work by lowering the energy of _____
28. a unit of heat measurement
30. _____-product inhibition

31. degree of disorganization or less free energy
(*hint*: second law of thermodynamics)

Down

2. reactions that release energy
4. enzymes are most affected by pH and _____
5. biological catalyst described in this chapter
6. most metabolic pathways are not linear; rather they are _____
8. loss of electrons from an atom or molecule
9. the first law of thermodynamics conserves _____
12. the pigment missing in the albino due to a defective gene in DNA
14. also known as the *reactant* for enzyme-catalyzed reactions
16. inborn errors of _____
19. a coenzyme derived from vitamin B₂ (riboflavin)
22. energy that is organized and can be used to perform work
25. reversible chemical reactions must obey the law of _____ action
27. a hydrogen-carrying coenzyme derived from niacin
29. the universal suffix for enzymes
32. all enzymes work best at their optimal _____



C. Essay

Essay Tutorial

This essay tutorial will answer the first essay question found in the “**Review Activities,**” section of your *Human Physiology* textbook. Read question 1 in the “**Test Your Understanding of Concepts and Principles**” section located at the end of chapter 4 and let me guide you through one possible answer. Watch for key terms in boldface type, helpful tips and general suggestions on writing the essay or short-answer questions. Go ahead try this one, and a few of mine that follow!

70. Explain the relationship between an enzyme’s chemical **structure** and the **function** of the enzyme, and describe how both structure and function may be altered in various ways.

Answer. Most enzymes are proteins. Therefore enzymes exhibit primary, secondary, tertiary, and even quaternary structure. Since enzymes must bind to substrates with the three-dimensional precision of a lock-and-key, any change in the enzyme (the lock) structure can interfere with binding by the substrate (the key).

Inborn errors of metabolism are inherited defects in the gene (DNA) which direct alterations of the enzyme’s primary structure (amino acid sequence) and, thus, can cause disease by reducing the activity or the “fit” between the substrate and the enzyme active site. In this way the tertiary structure (bending and folding) of the active site region of the enzyme determines its efficiency. Variation in both pH and temperature from some optimal value can distort or “warp” the delicate active site, reducing the “activity” of the enzyme and decreasing the number of products formed. Finally, the normal function of many enzymes requires the help of coenzymes and/or cofactors obtained from raw material such as vitamins and minerals, respectively. Consequently, a diet deficient in these raw materials can result in less productive enzyme-catalyzed reactions.

71. Describe what is meant by the term “isoenzyme,” and include one example of an isoenzyme whose various forms rise abnormally high in the blood, thus aiding in the diagnosis of certain diseases. [*Hint*: see Table 4.1.]

72. Describe the variation in the pH experienced by your cheeseburger (from the Completion section) as it travels along the mouth, stomach, and small intestine (pancreas). From each of these locations, name one enzyme, state its optimal pH, and describe a reaction catalyzed by each enzyme.
[*Hint*: see Table 4.3.]

Note: These last two essay questions were written from information provided by tables — then, would it not make sense to answer each question using a similar table format? Try it!

73. Using phenylketonuria (PKU) as an example, explain how inborn errors of metabolism are inherited and describe how these errors can alter metabolism.

74. Explain the step-by-step processes that occur in the cytoplasm as the chemical-bond energy in glucose is transferred to the “high-energy” bonds of adenosine triphosphate (ATP).

Answers — Chapter 4

I. Enzymes as Catalysts

- A. 1. e, 2. b, 3. b, 4. d,
5. c, 6. b, 7. d
- B. 8. F—Most enzymes are proteins, 9. F—Without enzymes reactions *will* run, but much more slowly, 10. T, 11. T, 12. T, 13. T, 14. T, 15. T

II. Control of Enzyme Activity

- A. 16. c, 17. a, 18. d, 19. d, 20. b, 21. a, 22. e, 23. c, 24. d, 25. a, 26. b
- B. 27. T, 28. T, 29. F—Replace “lower” with “higher,” 30. F—Replace “cofactors” with “coenzymes,” 31. T, 32. T, 33. F—cAMP is an intracellular

regulator, **not** a neurotransmitter, 34. T, 35. T, 36. T, 37. T, 38. T, 39. F—End-product inhibition features inhibition of earlier steps by the last product, 40. F—Switch “decreases” with “increases”, 41. F—Replace “phenylketonuria (PKU)” with “Albinism”

III. Bioenergetics

- A. 42. d, 43. b, 44. c, 45. a
- B. 46. F—Replace “entropy” with “energy,” 47. T, 48. T, 49. F—Replace “free” with “heat,”

50. F—Heat energy is lost from the cell and can't be used, 51. T, 52. T, 53. F—Replace “B₂” with “B₃,” 54. T

Chapter Review

- A. 55. enzymes, 56. cofactors, 57. coenzymes, 58. pH, 59. temperature, 60. energy, 61. exergonic, 62. CO₂, 63. adenosine triphosphate; ATP, 64. heat, 65. endergonic, 66. O₂, 67. acceptor, 68. reduced, 69. water

B. Crossword Puzzle

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			X														⁵ E		E	
	⁶ B			⁷ E	N	D	E	R	G	⁸ O	N	I	C				N		M	
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	¹³ C	O	E	N	Z	Y	M	E		A		¹⁴ S	R	E		A				
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	E			C				A	I	B	Y				¹⁵ P	K	U			
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	¹⁹ F		T					N					R							
²⁰ C	A	T	A	L	Y	S	T			²¹ C	A	T	A	L	A	S	E			
	D		B										T						²² F	
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