Chapter 8

An Introduction to Metabolism

Key Concepts

8.1 An organism's metabolism transforms matter and energy, subject to the laws of thermodynamics

8.2 The free-energy change of a reaction tells us whether the reaction occurs spontaneously

8.3 ATP powers cellular work by coupling exergonic reactions to endergonic reactions

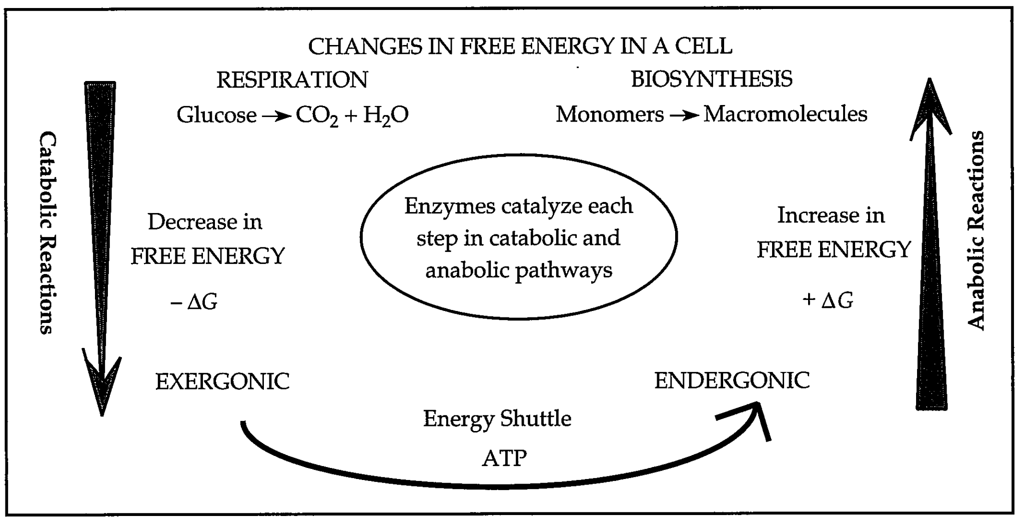
8.4 Enzymes speed up metabolic reactions by lowering energy barriers

8.5 Regulation of enzyme activity helps control metabolism

Framework

This chapter considers metabolism, the totality of the chemical reactions that take place in living organisms. Two key topics are emphasized: the energy transformations that underlie all chemical reactions and the role of enzymes in the "cold chemistry" of the cell. Enzymes are biological catalysts that lower the activation energy of a reaction and thus greatly speed up metabolic processes. An enzyme is a three-dimensional protein molecule with an active site specific for its substrate. Intricate control and feedback mechanisms produce the metabolic integration necessary for life.

The reactions in a cell either release or consume energy. The following illustration summarizes some of the components of the energy changes within a cell.



Chapter Review

8.1 An organism's metabolism transforms matter and energy, subject to the laws of thermodynamics

Organization of the Chemistry of Life into Metabolic Pathways **Metabolism** includes all of the chemical reactions in an organism. These reactions are ordered into **metabolic pathways,** a sequence of steps, each controlled by an enzyme, that convert a specific molecule to a product. Through these pathways the cell transforms and creates the organic molecules that provide the energy and material for life.

Catabolic pathways release the energy stored in complex molecules through the breaking down of these molecules into simpler compounds. **Anabolic pathways,** sometimes called biosynthetic pathways, require energy to combine simpler molecules into more complicated ones. The energy released from catabolic pathways drives the anabolic pathways in a cell. The study of how organisms transform energy, called **bioenergetics,** is central to understanding metabolism.

Forms of Energy **Energy** has been defined as the capacity to cause change. Some forms of energy can do work, such as moving matter against an opposing force. **Kinetic energy** is the energy of motion, of matter that is moving. This matter does its work by transferring its motion to other matter. The kinetic energy of randomly moving molecules is **heat,** or **thermal energy. Potential energy** is the capacity of matter to cause change as a consequence of its location or arrangement. **Chemical energy** is a form of potential energy stored in the arrangement of atoms in molecules and available for release in chemical reactions.

Energy can be converted from one form to another. Plants convert light energy to the chemical energy in sugar, and cells release this potential energy to drive cellular processes.

The Laws of Energy Transformation **Thermodynamics** is the study of energy transformations. In an open system, energy (and matter) may be exchanged between the system and the surroundings.

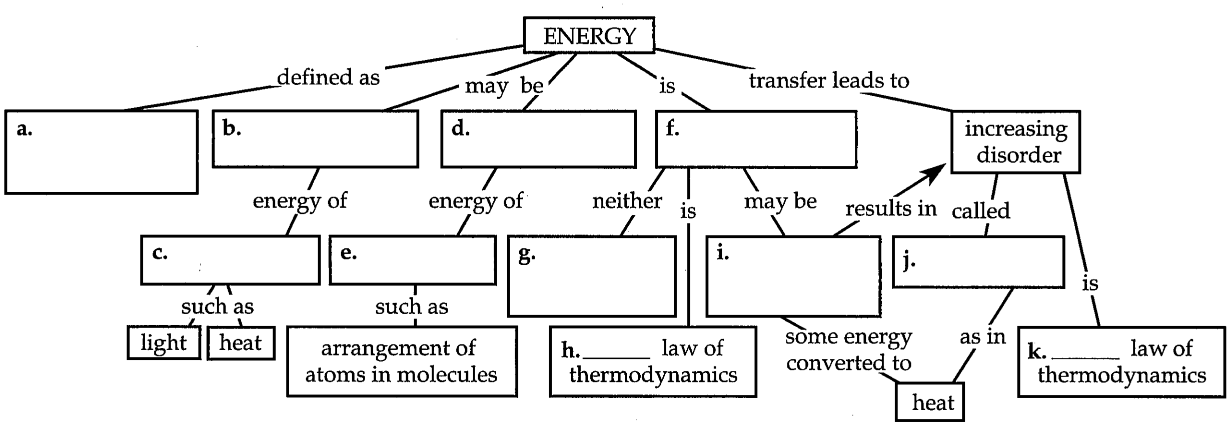
The **first law of thermodynamics** states that energy can be neither created nor destroyed. According to this *principle of conservation of energy,* energy can be transferred between matter and transformed from one kind to another, but the total energy of the universe is constant.

The **second law of thermodynamics** states that every energy transformation or transfer results in an increasing disorder within the universe. **Entropy** is used as a measure of disorder or randomness. In every energy transfer or transformation, some of the energy is converted to heat, the least ordered form of energy. For a process to occur spontaneously, without the input of external energy, it must result in an increase in entropy. A nonspontaneous process will occur only if energy is added to the system.

A cell may become more ordered, but it does so with an attendant increase in the entropy of its surroundings. An organism takes in and uses highly ordered organic molecules as a source of the energy needed to create and maintain its own organized structure, but it returns heat and the simple molecules of carbon dioxide and water to the environment.

Fill in the concept map in Interactive Question 8.1 to review the key concepts of energy.

■ INTERACTIVE QUESTION 8.1



8.2 The free-energy change of a reaction tells us whether the reaction occurs spontaneously

Free-Energy Change, ΔG Free energy can be defined as the portion of a system's energy available to perform work when the system's temperature and pressure are uniform. The change in free energy during a reaction is represented by $\Delta G = \Delta H - T\Delta S$. Enthalpy ($H$) is the total energy of a system; entropy (S) is a measure of its disorder, and T is absolute temperature (°Kelvin, or °C + 273). For a reaction to be spontaneous, the free energy of the system must decrease ($-\Delta G$): the system must lose energy (H must decrease), become more disordered (S must increase), or both.

Free Energy, Stability, and Equilibrium When ΔG is negative, the final state has less free energy than the initial state; thus the final state is less likely to change and is more stable. A system rich in free energy has a tendency to change spontaneously to a more stable state. At equilibrium in a chemical reaction, the forward and backward reactions are proceeding at the same rate and the relative concentration of products and reactants stays the same. Moving toward equilibrium is spontaneous; the ΔG of the reaction is negative. Once at equilibrium, a system is at a minimum of free energy and will not spontaneously change.

■ INTERACTIVE QUESTION 8.2

Complete the table to show how the free energy of a system or reaction relates to its stability, tendency for spontaneous change, equilibrium, and capacity to do work.

	System with high free energy	System with low free energy
Stability		
Spontaneous		
Equilibrium		
Work capacity		

Free Energy and Metabolism An **exergonic reaction** ($-\Delta G$) proceeds with a net release of free energy and is spontaneous. The magnitude of ΔG indicates the maximum amount of work the reaction can do. **Endergonic reactions** ($+\Delta G$) are nonspontaneous; they must absorb free energy from the surroundings. The energy released by an exergonic reaction ($-\Delta G$) is equal to the energy required by the reverse reaction ($+\Delta G$).

Metabolic disequilibrium is essential to life. Metabolic reactions are reversible and could reach equilibrium if the cell did not maintain a steady supply of reactants and siphon off the products (as reactants for new processes or as waste products to be expelled).

■ INTERACTIVE QUESTION 8.3

Develop a concept map on free energy and ΔG. The value in this exercise is for you to wrestle with and organize these concepts for yourself. Do not turn to the suggested concept map until you have worked on your own understanding. Remember that the concept map in the answer section is only one way of structuring these ideas—have confidence in your own organization.

8.3 ATP powers cellular work by coupling exergonic reactions to endergonic reactions

Central to a cell's bioenergetics is **energy coupling**, using exergonic processes to power endergonic ones.

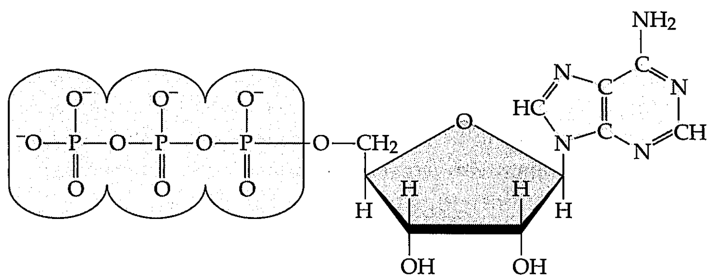
A cell usually uses ATP as the immediate source of energy for its mechanical, transport, and chemical work.

The Structure and Hydrolysis of ATP **ATP (adenosine triphosphate)** consists of the nitrogenous base adenine bonded to the sugar ribose, which is connected to a chain of three phosphate groups. ATP can be hydrolyzed to ADP (adenosine diphosphate) and an inorganic phosphate molecule (Ⓟ$_i$), releasing 7.3 kcal (30.5 kJ) of energy per mole of ATP when measured under standard conditions. The ΔG of the reaction in the cell is estimated to be closer to -13 kcal/mol.

■ INTERACTIVE QUESTION 8.4

Label the three components (a through c) of the ATP molecule shown below.

a. ____________



c. ____________ b. ____________

d. Indicate which bond is likely to break. By what chemical mechanism is the bond broken?

e. Explain why this reaction releases so much energy?

How ATP Performs Work In a cell, the free energy released from the hydrolysis of ATP is used to transfer the phosphate group to another molecule, producing a **phosphorylated** molecule that is more reactive (less stable). The phosphorylation of other molecules by ATP forms the basis for almost all cellular work.

The Regeneration of ATP A cell regenerates ATP at a phenomenal rate. The formation of ATP from ADP and

Ⓟi is endergonic, with a ΔG of +7.3 kcal/mol (standard conditions). Cellular respiration (the catabolic processing of glucose and other organic molecules) provides the energy for the regeneration of ATP. Plants can also produce ATP using light energy.

8.4 Enzymes speed up metabolic reactions by lowering energy barriers

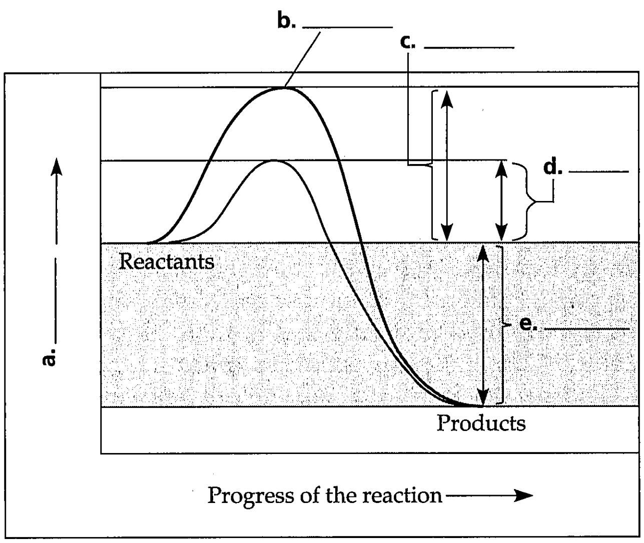
Enzymes are biological **catalysts**—agents that speed the rate of a reaction but are unchanged by the reaction.

The Activation Energy Barrier Chemical reactions involve both the breaking and forming of chemical bonds. Energy must be absorbed to make bonds unstable enough that they will break, and energy is released when bonds form and molecules return to stable, lower energy states. **Activation energy,** or the **free energy of activation** (E_A), is the energy that must be absorbed by reactants to reach the unstable *transition state,* in which bonds are likely to break, and from which the reaction can proceed.

How Enzymes Lower the E_A Barrier The E_A barrier is essential to life because it prevents the energy-rich macromolecules of the cell from decomposing spontaneously. For metabolism to proceed in a cell, however, E_A must be reached. Heat, a possible source of activation energy in reactions, would be harmful to the cell and would also speed metabolic reactions indiscriminately. Enzymes are able to lower E_A for specific reactions so that metabolism can proceed at cellular tem- peratures. Enzymes do not change the ΔG for a reaction.

■ INTERACTIVE QUESTION 8.5

In this graph of an exergonic reaction with and without an enzyme catalyst, label the parts a through e.



Substrate Specificity of Enzymes Protein enzymes are macromolecules with characteristic three-dimensional shapes. The specificity of an enzyme for a particular **substrate** is determined by this shape. The substrate attaches at the enzyme's **active site,** a pocket or groove found on the surface of the enzyme that has a shape complementary to the substrate. The substrate is temporarily bound to its enzyme, forming an **enzyme-substrate complex.** Interactions between substrate and active site cause the enzyme to change shape slightly, creating what is called an **induced fit** that enhances the ability of the enzyme to catalyze the chemical reaction.

Catalysis in the Enzyme's Active Site The substrate is often held in the active site by hydrogen or ionic bonds. The side chains (R groups) of some of the surrounding amino acids in the active site facilitate the conversion of substrate to product. The product then leaves the active site, and the catalytic cycle repeats, often at astonishing speed.

Whether an enzyme catalyzes the forward or backward reaction is influenced by the relative concentrations of reactants and products and the ΔG of the reactions. Enzymes catalyze reactions moving toward equilibrium.

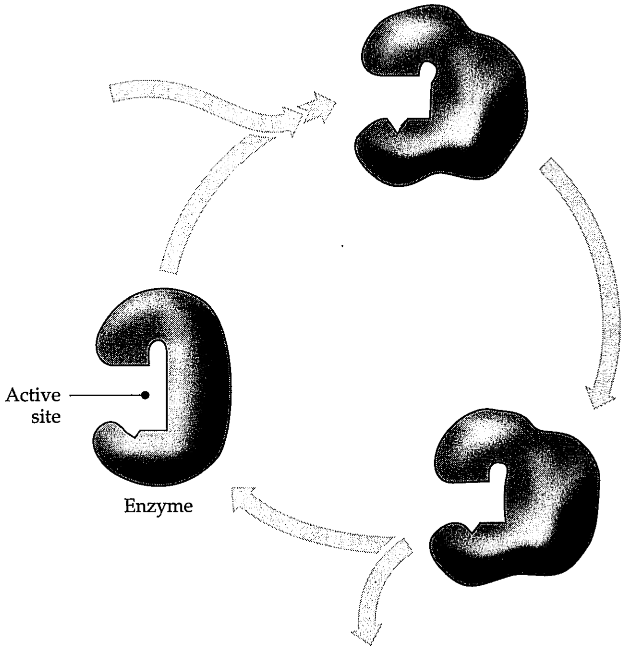
Enzymes catalyze reactions involving the joining of two reactants by binding the substrates closely together and properly oriented. An induced fit can stretch critical bonds in the substrate molecule and make them easier to break. An active site may provide a microenvironment, such as a lower pH, that is necessary for a particular reaction. Enzymes may also actually participate in a reaction by forming brief covalent bonds with the substrate.

The rate of a reaction will increase with increasing substrate concentration up to the point at which all enzyme molecules are saturated with substrate molecules and working at full speed. Only adding more enzyme molecules will increase the rate of the reaction at that point.

Effects of Local Conditions on Enzyme Activity The velocity of an enzyme-catalyzed reaction may increase with rising temperature up to the point at which increased thermal agitation begins to disrupt the hydrogen and ionic bonds and other interactions that stabilize protein conformation. A change in pH may also affect protein shape and enzyme function. Each enzyme has a temperature and pH optimum at which it is most active.

■ **INTERACTIVE QUESTION 8.6**

Outline a catalytic cycle using the diagrammatic enzyme below. Sketch two appropriate substrate molecules and two products, identify the enzyme-substrate complex, and describe the key steps of the cycle.



Cofactors are small molecules that bind either permanently or reversibly with enzymes and are necessary for enzyme catalytic function. They may be inorganic, such as various metal ions, or organic molecules called **coenzymes.** Most vitamins are coenzymes or precursors of coenzymes.

Enzyme inhibitors selectively disrupt the action of enzymes, either reversibly by binding with the enzyme with weak bonds or irreversibly by attaching with covalent bonds. **Competitive inhibitors** compete with the substrate for the active site of the enzyme. Increasing the concentration of substrate molecules may overcome this type of inhibition. **Noncompetitive inhibitors** bind to a part of the enzyme separate from the active site and change the conformation of the enzyme, thus impeding enzyme action.

■ **INTERACTIVE QUESTION 8.7**

Return to your diagram in Interactive Question 8.6. Draw a competitive and a noncompetitive inhibitor, and indicate where each would bind to the enzyme molecule.

8.5 Regulation of enzyme activity helps control metabolism

Allosteric Regulation of Enzymes In **allosteric regulation** molecules may inhibit or activate enzyme activity when they bind to a site separate from the active site. Enzymes made of two or more polypeptides, each with its own active site, may have binding sites (sometimes called allosteric sites) located where subunits join. The entire unit may oscillate between two conformational states. The binding of an activator stabilizes the catalytically active conformation, whereas an inhibitor reinforces the inactive form of the enzyme. Allosteric enzymes may be critical regulators of metabolic pathways.

Through a phenomenon called **cooperativity,** the induced-fit binding of a substrate molecule to one subunit can change the conformation such that the active sites of all subunits are more active.

Metabolic pathways are commonly regulated by **feedback inhibition,** in which the product of a pathway acts as an allosteric inhibitor of an enzyme early in the pathway.

■ **INTERACTIVE QUESTION 8.8**

Both ATP and ADP serve as regulators of enzyme activity. In catabolic pathways, which of these molecules would you predict would act as an inhibitor?

Which molecule would you expect to act as an activator of anabolic pathways?

Specific Localization of Enzymes within the Cell Enzymes for several steps of a metabolic pathway may be associated in a multienzyme complex, facilitating the sequence of reactions. Specialized cellular compartments may contain high concentrations of the enzymes and substrates needed for a particular pathway. Enzymes are often incorporated into the membranes of cellular compartments. The complex internal structures of the cell facilitate metabolic order.

Word Roots

cata- = down (*catabolic pathway:* a metabolic pathway that releases energy by breaking down complex molecules into simpler ones)

ana- = up (*anabolic pathway:* a metabolic pathway that consumes energy to build complex molecules from simpler ones)

bio- = life (*bioenergetics:* the study of how organisms manage their energy resources)
kinet- = movement (*kinetic energy:* the energy of motion)
therm- = heat (*thermodynamics:* the study of the energy transformations that occur in a collection of matter)
ex- = out (*exergonic reaction:* a reaction that proceeds with a net release of free energy)
endo- = within (*endergonic reaction:* a reaction that absorbs free energy from its surroundings)
allo- = different (*allosteric site:* a specific receptor site on some part of an enzyme molecule remote from the active site)

Structure Your Knowledge

This chapter introduced many new and complex concepts. See if you can step back from the details and answer the following general questions.

1. Relate the concept of free energy to metabolism.
2. What role do enzymes play in metabolism?

Test Your Knowledge

MULTIPLE CHOICE: *Choose the one best answer.*

1. Catabolic and anabolic pathways are often coupled in a cell because
   a. the intermediates of a catabolic pathway are used in the anabolic pathway.
   b. both pathways use the same enzymes.
   c. the free energy released from one pathway is used to drive the other.
   d. the activation energy of the catabolic pathway can be used in the anabolic pathway.
   e. their enzymes are controlled by the same activators and inhibitors.
2. When glucose is converted to CO_2 and H_2O, changes in total energy, entropy, and free energy are as follows:
   a. $-\Delta H, -\Delta S, -\Delta G$
   b. $-\Delta H, +\Delta S, -\Delta G$
   c. $-\Delta H, +\Delta S, +\Delta G$
   d. $+\Delta H, +\Delta S, +\Delta G$
   e. $+\Delta H, -\Delta S, +\Delta G$
3. When a protein forms from amino acids, the following energy and entropy changes apply:
   a. $+\Delta H, -\Delta S, +\Delta G$
   b. $+\Delta H, +\Delta S, -\Delta G$
   c. $+\Delta H, +\Delta S, +\Delta G$
   d. $-\Delta H, +\Delta S, +\Delta G$
   e. $-\Delta H, -\Delta S, +\Delta G$
4. A negative ΔG means that
   a. the quantity G of energy is available to do work.
   b. the reaction is spontaneous.
   c. the reactants have more free energy than the products.
   d. the reaction is exergonic.
   e. all of the above are true.
5. According to the first law of thermodynamics,
   a. for every action there is an equal and opposite reaction.
   b. every energy transfer results in an increase in disorder or entropy.
   c. the total amount of energy in the universe is conserved or constant.
   d. energy can be transferred or transformed, but disorder always increases.
   e. potential energy is converted to kinetic energy, and kinetic energy is converted to heat.
6. What is meant by an induced fit?
   a. The binding of the substrate is an energy-requiring process.
   b. A competitive inhibitor can outcompete the substrate for the active site.
   c. The binding of the substrate changes the shape of the active site, which can stress or bend substrate bonds.
   d. The active site creates a microenvironment ideal for the reaction.
   e. Substrates are held in the active site by hydrogen and ionic bonds.
7. One way in which a cell maintains metabolic disequilibrium is to
   a. siphon products of a reaction off to the next step in a metabolic pathway.
   b. provide a constant supply of enzymes for critical reactions.
   c. use feedback inhibition to turn off pathways.
   d. use allosteric enzymes that can bind to activators or inhibitors.
   e. use the energy from anabolic pathways to drive catabolic pathways.

8. In an experiment, changing the pH from 7 to 6 resulted in an increase in product formation. From this we could conclude that
   a. the enzyme became saturated at pH 6.
   b. the enzyme's optimal pH is 6.
   c. this enzyme works best in a neutral pH.
   d. the temperature must have increased when the pH was changed to 6.
   e. the enzyme was in a more active conformation at pH 6.

9. When substance A was added to an enzyme reaction, product formation decreased. The addition of more substrate did not increase product formation. From this we conclude that substance A could be
   a. product molecules.
   b. a cofactor.
   c. an allosteric enzyme.
   d. a competitive inhibitor.
   e. a noncompetitive inhibitor.

10. The formation of ATP from ADP and inorganic phosphate
    a. is an exergonic process.
    b. transfers the phosphate to another intermediate that becomes more reactive.
    c. produces an unstable energy compound that can drive cellular work.
    d. has a ΔG of -7.3 kcal/mol under standard conditions.
    e. involves the hydrolysis of a phosphate bond.

11. At equilibrium,
    a. no enzymes are functioning.
    b. free energy is at a minimum.
    c. the forward and backward reactions have stopped.
    d. the products and reactants have equal values of H.
    e. a reaction has a $+\Delta G$.

12. In cooperativity,
    a. a cellular organelle contains all the enzymes needed for a metabolic pathway.
    b. a product of a pathway serves as a competitive inhibitor of an early enzyme in the pathway.
    c. a molecule bound to the active site of one subunit of an enzyme affects the active site of other subunits.
    d. the allosteric site is filled with an activator molecule.
    e. the product of one reaction serves as the substrate for the next in intricately ordered metabolic pathways.

13. When a cell breaks down glucose, only about 40% of the energy is captured in ATP molecules. The remaining 60% of the energy is
    a. used to increase the order necessary for life to exist.
    b. lost as heat because of the second law of thermodynamics.
    c. used to increase the entropy of the system by converting kinetic energy into potential energy.
    d. stored in starch or glycogen for use later by the cell.
    e. released when the ATP molecules are hydrolyzed.

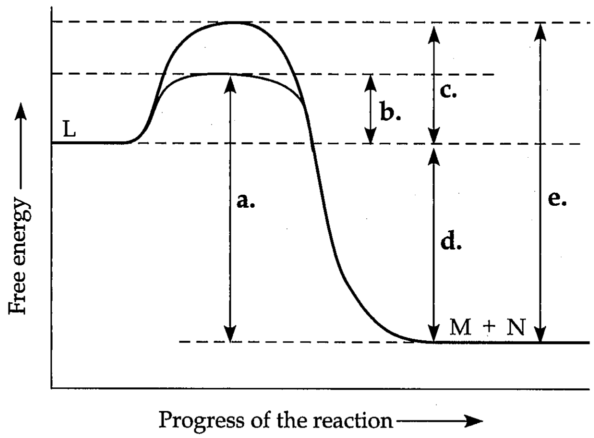
14. An endergonic reaction could be described as one that will
    a. proceed spontaneously with the addition of activation energy.
    b. produce products with more free energy than the reactants.
    c. not be able to be catalyzed by enzymes.
    d. release energy.
    e. produce ATP for energy coupling.

15. What is most directly responsible for the specificity of a protein enzyme?
    a. its primary structure
    b. its secondary and tertiary structure
    c. the conformation of its allosteric site
    d. its cofactors
    e. the R groups of the amino acids in its active site

16. Which of the following parameters does an enzyme raise?
    a. ΔG
    b. ΔH
    c. equilibrium of a reaction
    d. speed of a reaction
    e. free energy of activation

17. Zinc, an essential trace element, may be found bound to the active site of some enzymes. What would be the most likely function of such zinc ions?
    a. coenzyme derived from a vitamin
    b. a cofactor necessary for catalysis
    c. a substrate of the enzyme
    d. a competitive inhibitor of the enzyme
    e. an allosteric activator of the enzyme

Use this diagram to answer questions 18 through 20.



18. Which line in the diagram above indicates the ΔG of the enzyme-catalyzed reaction of L $\rightarrow$ M + N?

19. Which line in the diagram indicates the activation energy of the noncatalyzed reaction?

20. Which of the following terms would best describe this reaction?
- **a.** nonspontaneous
- **b.** $-\Delta G$
- **c.** endergonic
- **d.** coupled reaction
- **e.** anabolic reaction

21. A reaction that is spontaneous
- **a.** has a $+\Delta G$.
- **b.** occurs very rapidly.
- **c.** does not require enzyme catalysis in a cell.
- **d.** will decrease the entropy of a system.
- **e.** is exergonic.

22. In the metabolic pathway, A $\rightarrow$ B $\rightarrow$ C $\rightarrow$ D $\rightarrow$ E, what effect would molecule E likely have on the enzyme that catalyzes A $\rightarrow$ B?
- **a.** allosteric inhibitor
- **b.** allosteric activator
- **c.** competitive inhibitor
- **d.** feedback activator
- **e.** coenzyme

FILL IN THE BLANKS

________ **1.** the totality of an organism's chemical processes

________ **2.** pathways that require energy to combine molecules together

________ **3.** the energy of motion

________ **4.** enzymes that change between two conformations, depending on whether an activator or inhibitor is bound to them

________ **5.** term for the measure of disorder or randomness

________ **6.** the energy that must be absorbed by molecules to reach the transition state

________ **7.** inhibitors that decrease an enzyme's activity by binding to the active site

________ **8.** organic molecules that bind to enzymes and are necessary for their functioning

________ **9.** regulatory device in which the product of a pathway binds to an enzyme early in the pathway

________ **10.** more reactive molecules created by the transfer of a phosphate group from ATP