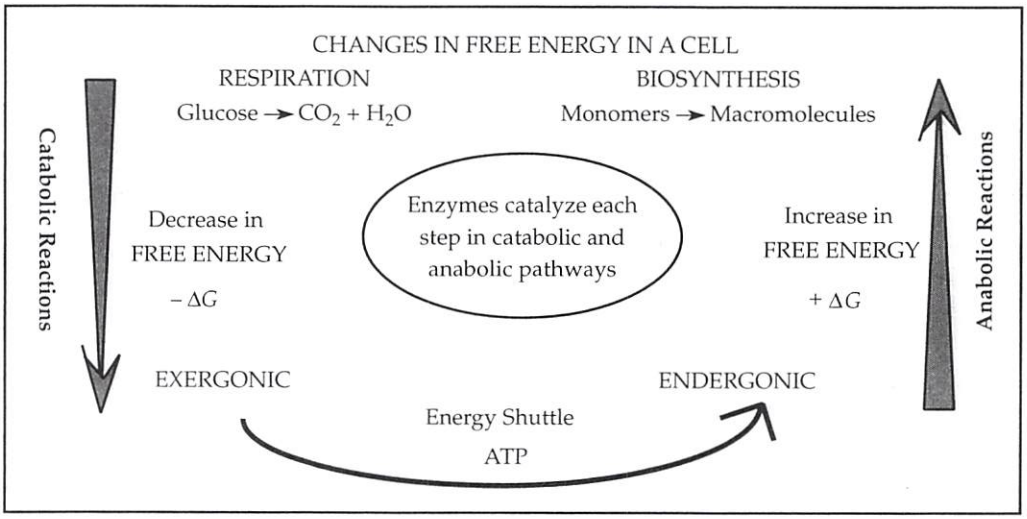
Chapter 6

An Introduction to Metabolism

Chapter Focus



Chapter Review

6.1 An organism's metabolism transforms matter and energy

Metabolic Pathways **Metabolism** includes all the chemical reactions in an organism. These reactions are ordered into **metabolic pathways**, a sequence of steps, each controlled by an enzyme, that converts specific molecules to products.

Catabolic pathways release the energy stored in complex molecules through the breakdown 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 energy transformations in organisms, called **bioenergetics**, is central to understanding metabolism.

Forms of Energy **Energy** can be 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 atoms or molecules is **thermal energy**. Thermal energy transferring from one body of matter to another is called **heat**.

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 that is 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 a collection of matter. In an *open system*, energy and matter may be exchanged between the *system* and its *surroundings*. (In an *isolated system*, such exchange does not occur.) Organisms are open systems.

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 and transformed from one kind to another, but the total energy of the universe is constant.

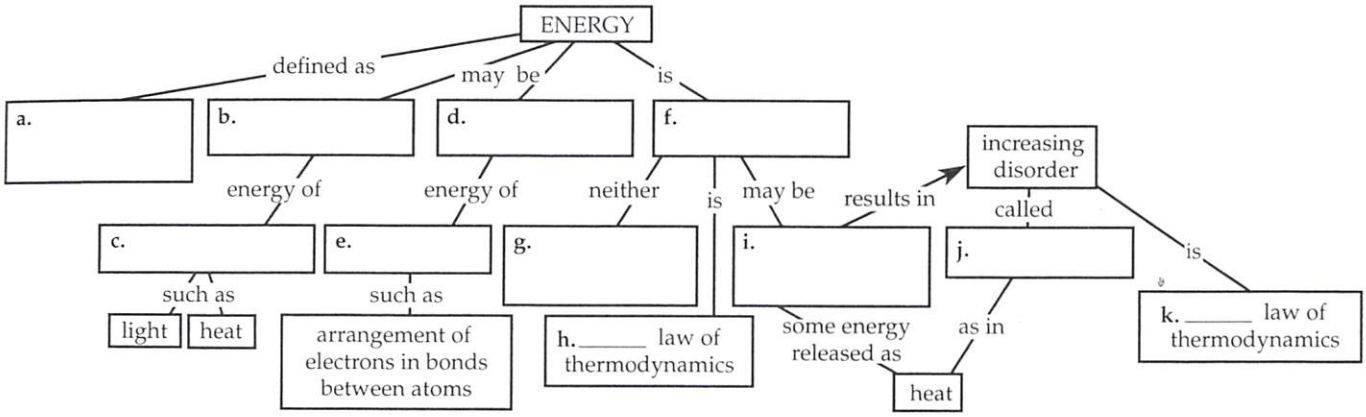
The **second law of thermodynamics** states that every energy transfer or transformation results in increasing disorder within the universe. **Entropy** is used as a measure of disorder or randomness. In every energy transfer or transformation, some of the energy is converted to thermal energy, a disordered form of energy, and released as heat.

A **spontaneous process** is one that is "energetically favorable"; in other words, it occurs without an input of energy. For a process to occur spontaneously, 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. For example, an animal takes in and uses highly ordered organic molecules as a source of the matter and 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.

FOCUS QUESTION 6.1

Complete the following concept map that summarizes some of the key ideas about energy.



6.2 The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously

Free-Energy Change (ΔG), Stability, and Equilibrium The portion of a system's energy available to perform work when the system's temperature and pressure are uniform is defined as **free energy** (symbolized by G). The *change* in free energy during a chemical reaction is represented by ΔG and is equal to $G_{\text{final state}} - G_{\text{initial state}}$. The free energy of the system must decrease ($-\Delta G$) for a reaction to be spontaneous.

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. This change may be harnessed to perform work. A state of maximum stability is called *equilibrium*. At equilibrium in a chemical reaction, the forward and backward reactions occur at the same rate, and the relative concentrations of products and reactants stay the same. Moving toward equilibrium is spontaneous; the ΔG of the reaction is negative. Once at equilibrium, a system is at its minimum of free energy; it will not spontaneously change, and it can do no work.

FOCUS QUESTION 6.2

Complete the following table to indicate how the free energy of a system (or a chemical reaction) relates to the system's stability, capacity to do work, tendency for spontaneous change, and equilibrium.

	Stability	Work Capacity	Spontaneous Change?	Equilibrium
System with High Free Energy				
System with Low Free Energy				

Free Energy and Metabolism Now let's see how these energy concepts apply to metabolism. An **exergonic reaction** ($-\Delta G$) proceeds with a net release of free energy and is spontaneous (energetically favorable). The magnitude of ΔG indicates the maximum amount of work an exergonic reaction can perform. **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 ($+\Delta G$).

FOCUS QUESTION 6.3

Metabolic disequilibrium is essential to life—a cell whose metabolic reactions reached equilibrium would be dead. What mechanisms prevent a cell's reactions from reaching equilibrium?

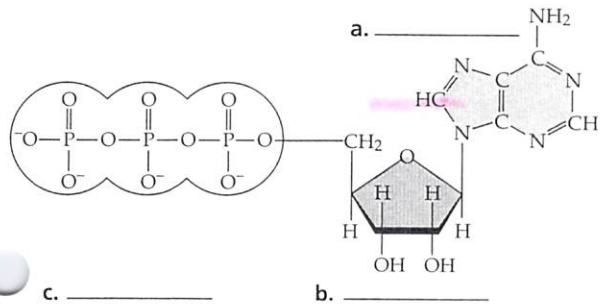
6.3 ATP powers cellular work by coupling exergonic reactions to endergonic reactions

Central to a cell's bioenergetics is **energy coupling**, the use of exergonic processes to drive endergonic ones. A cell usually uses ATP as the immediate source of energy for its *chemical, transport,* and *mechanical 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.

FOCUS QUESTION 6.4

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



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

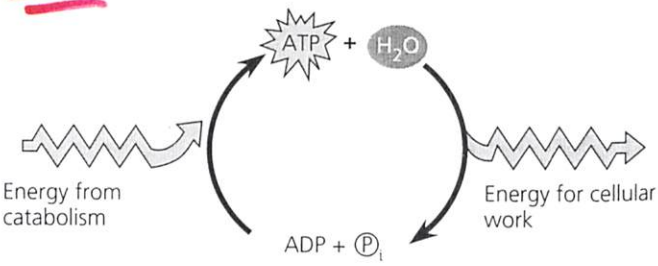
e. Explain why this reaction releases so much energy.

How the Hydrolysis of ATP Performs Work ATP is used to couple exergonic and endergonic reactions in a cell. The free energy released from the hydrolysis of ATP is used to transfer the phosphate group to a reactant molecule, producing a **phosphorylated intermediate** that is more reactive (less stable). The hydrolysis of ATP also forms the basis for almost all transport and mechanical work in a cell by changing the shapes and binding affinities of proteins.

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.

FOCUS QUESTION 6.5

Look at the following ATP cycle and explain why both the left and right sides of the cycle are examples of energy coupling.



6.4 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.

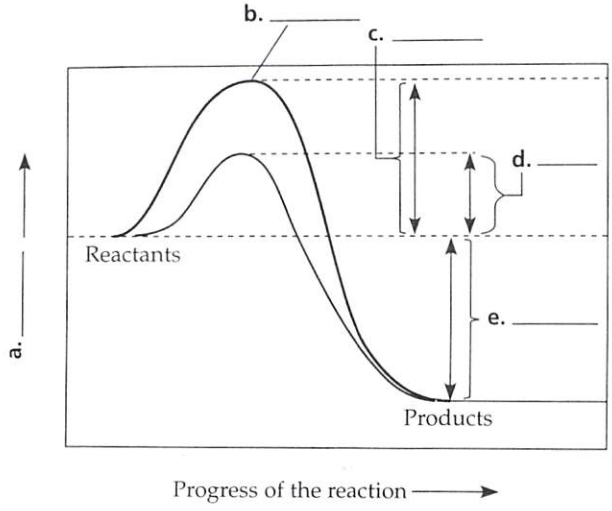
The Activation Energy Barrier Chemical reactions involve both the breaking and forming of chemical bonds. Energy must be absorbed to contort molecules to an unstable state in which bonds can break. Energy

is released when new 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 Speed Up Reactions 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. Enzymes are able to lower E_A so that specific reactions can proceed at cellular temperatures. Enzymes do not change the ΔG for a reaction.

FOCUS QUESTION 6.6

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



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

Catalysis in the Enzyme's Active Site What happens in an enzyme's active site? The substrate is often held in the active site by hydrogen bonds 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.

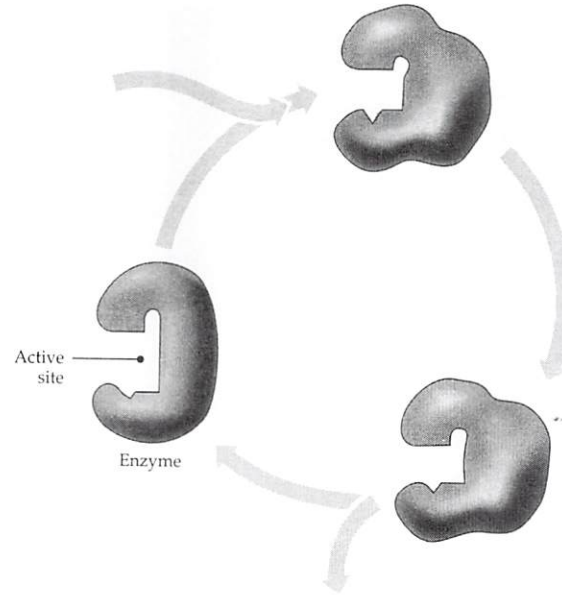
Whether an enzyme catalyzes the forward or backward reaction is influenced by the relative concentrations of reactants and products and the ΔG of the reactions. Enzymes catalyze reactions moving toward equilibrium.

Enzymes may catalyze reactions involving the joining of two reactants by properly orienting the substrates closely together. 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. At that point, only adding more enzyme molecules will increase the rate of the reaction.

FOCUS QUESTION 6.7

In the following diagram of a catalytic cycle, sketch two appropriate substrate molecules and two products, and identify the key steps of the cycle.



Effects of Local Conditions on Enzyme Activity The speed of an enzyme-catalyzed reaction may increase with rising temperature up to the point at which

increased thermal agitation begins to disrupt the weak bonds and interactions that stabilize protein shape. Each enzyme has *optimal conditions* that include a temperature and pH that favor its most active shape.

Cofactors are small molecules that bind either permanently or reversibly with enzymes and are necessary for enzyme 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 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 impede enzyme action by changing the shape of the enzyme.

FOCUS QUESTION 6.8

Return to the diagram in Focus Question 6.7. Draw a competitive inhibitor and a noncompetitive inhibitor, and indicate where each would bind to the enzyme molecule.

The Evolution of Enzymes *Mutations* in genes may alter the amino acid sequence and thus change the substrate specificity or activity of an enzyme. If this novel function is beneficial, natural selection would be expected to preserve the mutated gene in the population.

6.5 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 regulatory sites (sometimes called allosteric sites) located where subunits join. The entire unit may oscillate between two forms. The binding of an *activator* stabilizes the catalytically active shape, whereas an *inhibitor* reinforces the inactive form of the enzyme. Allosteric enzymes may be critical regulators of both catabolic and anabolic pathways.

Through a phenomenon called **cooperativity**, the binding of a substrate molecule to one subunit changes the shape of all subunits such that their active sites are stabilized in the active form.

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

FOCUS QUESTION 6.9

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

Which would you predict would act as an activator?

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 eukaryotic 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

allo- = different (*allosteric regulation:* the binding of a regulatory molecule to a protein at one site that affects the function of the protein at a different site)

ana- = up (*anabolic pathway:* a metabolic pathway that consumes energy to synthesize a complex molecule from simpler compounds)

bio- = life (*bioenergetics:* the overall flow and transformation of energy in an organism)

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

endo- = within (*endergonic reaction:* a nonspontaneous chemical reaction in which free energy is absorbed from the surroundings)

ex- = out (*exergonic reaction:* a spontaneous reaction, in which there is a net release of free energy)

kinet- = movement (*kinetic energy:* the energy associated with the relative motion of objects)

therm- = heat (*thermodynamics:* the study of the energy transformations that occur in a collection of matter)

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. What is the relationship between the concept of free energy and metabolism?
2. What role do enzymes play in metabolism?

Test Your Knowledge

FILL IN THE BLANKS

metabolism 1. the totality of an organism's chemical processes

Anabolic 2. pathways that use energy to synthesize complex molecules

potential 3. the form of energy resulting from location or structure

thermal 4. the most random form of energy

entropy 5. term for the measure of disorder or randomness

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

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

coenzyme 8. nonprotein organic molecules that bind to enzymes and are necessary for their functioning

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

phosphorylated intermediate 10. more reactive molecules created by the transfer of a phosphate group from ATP

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 pathway.
   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. 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 released as heat.
3. When a cell breaks down glucose, only about 34% of the energy is captured in ATP molecules. The remaining 66% of the energy is
   a. used to increase the order necessary for life to exist.
   b. lost as heat, in accordance with 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 later use by the cell.
   e. released when the ATP molecules are hydrolyzed.
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. 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.
6. An endergonic reaction could be described as one that
   a. proceeds spontaneously with the addition of activation energy.
   b. produces products with more free energy than the reactants.
   c. is not able to be catalyzed by enzymes.
   d. releases energy.
   e. produces ATP for energy coupling.
7. The formation of ATP from ADP and inorganic phosphate
   a. is an exergonic process.
   b. transfers the phosphate to an 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.

8. 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. The binding of an activator to an allosteric site induces a more active form of the subunits of an enzyme.

9. 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 at a neutral pH.
   d. the temperature must have increased when the pH was changed to 6.
   e. the enzyme was in a more active shape at pH 6.

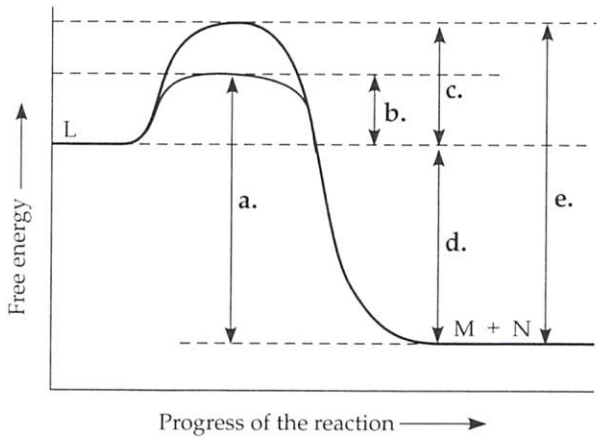
10. When substance A was added to an enzyme reaction, product formation decreased. The addition of more substrate did not increase product formation. From this we conclude that substance A could be
    a. product molecules.
    b. a cofactor.
    c. an allosteric enzyme.
    d. a competitive inhibitor.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

11. Which of the following characteristics is most directly responsible for the specificity of a protein enzyme for its substrate?
    a. its primary structure
    b. its secondary and tertiary structures
    c. the shape and characteristics of its allosteric site
    d. its cofactors
    e. the R groups of the amino acids in its active site

12. An enzyme raises which of the following parameters?
    a. ΔG
    b. the free energy of the products
    c. the free energy of activation
    d. the speed of a reaction
    e. the equilibrium of a reaction

13. Zinc, an essential trace element, may be found bound to the active site of some enzymes. Such zinc ions most likely function as
    a. 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 the following diagram to answer questions 14 through 16.



14. Which line in the diagram indicates the ΔG of the enzyme-catalyzed reaction L → M + N?

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

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

17. 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 enzyme early 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 reaction in intricately ordered metabolic pathways.

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

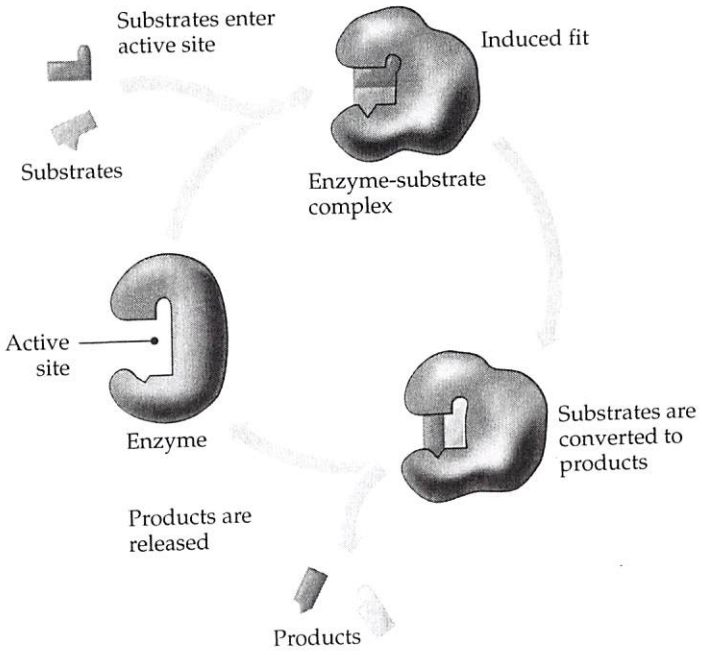
6.3. A cell is provided with a steady supply of reactants, and the products of each reaction are siphoned off (as reactants for the next reaction or as waste products to be expelled).

6.4. **a.** adenine
b. ribose
c. three phosphate groups
d. A hydrolysis reaction breaks the terminal phosphate bond and releases a molecule of inorganic phosphate: ATP + $H_2O \rightarrow$ ADP + Ⓟ$_i$ + energy
e. The negatively charged phosphate groups are crowded together, and their mutual repulsion makes this area unstable. The chemical change to a more stable state of lower free energy accounts for the relatively high release of energy.

6.5. Energy coupling is the use of an exergonic process to drive an endergonic one. The ATP cycle itself illustrates this coupling in that energy-releasing processes of catabolism are coupled with the energy-consuming process of cellular work. But each side is also an example: The endergonic synthesis of ATP from ADP and Ⓟ$_i$ is coupled to the exergonic reactions of catabolism (left side), and the exergonic hydrolysis of ATP to ADP and Ⓟ$_i$ provides the immediate energy source for cellular work (right side).

6.6. **a.** free energy
b. transition state
c. E_A (free energy of activation) without enzyme
d. E_A with enzyme
e. ΔG of reaction

6.7.



6.8. A competitive inhibitor would mimic the shape of the substrates and compete with them for the active site. A noncompetitive inhibitor would be a shape that could bind to another site on the enzyme molecule and would change the shape of the enzyme such that the active site functions less effectively.

6.9. ATP would act as an inhibitor to catabolic pathways, slowing the breakdown of fuel molecules if the supply of ATP exceeds demand. If ATP supplies drop, ADP (or its breakdown product AMP) would act as an activator of these catabolic enzymes, and more ATP would be produced.

SUGGESTED ANSWERS TO STRUCTURE YOUR KNOWLEDGE

1. Metabolism is the totality of chemical reactions that take place in living organisms. To create and maintain the structural order required for life requires an input of free energy—from sunlight for photosynthetic organisms and from energy-rich food molecules for other organisms. A cell couples catabolic, exergonic reactions ($-\Delta G$) with anabolic, endergonic reactions ($+\Delta G$), using ATP as the primary energy shuttle between the two.

2. Enzymes are essential for metabolism because they lower the activation energy of the specific reactions they catalyze and allow those reactions to occur extremely rapidly at a temperature conducive to life. By regulating the enzymes it produces, a cell can regulate which of the myriad of possible chemical reactions take place at any given time. Metabolic control also occurs through allosteric regulation and feedback inhibition. The compartmental organization of a cell facilitates a cell's metabolism.

ANSWERS TO TEST YOUR KNOWLEDGE

Fill in the Blanks:

1. metabolism
2. anabolic
3. potential
4. thermal energy
5. entropy
6. activation energy
7. competitive inhibitors
8. coenzymes
9. feedback inhibition
10. phosphorylated intermediate

Multiple Choice:

1. c	6. b	11. e	16. b
2. c	7. c	12. d	17. c
3. b	8. c	13. b	18. a
4. e	9. e	14. d	
5. a	10. e	15. c	

2. **a.** II represents facilitated diffusion. The solute is moving through a transport protein and down its concentration gradient. The cell does not expend energy in this transport. Polar molecules and ions may move by facilitated diffusion.
b. III represents active transport because the solute is clearly moving against its concentration gradient and the cell is expending ATP to drive this transport against the gradient.
c. In order to diffuse through the lipid bilayer, solute molecules must be hydrophobic (nonpolar) or very small polar molecules.
d. I and II. Both diffusion through the lipid bilayer and facilitated diffusion are considered passive transport because the solute moves down its concentration gradient and the cell does not expend energy in the process.
3. Cell signaling occurs through signal transduction pathways that include reception, transduction, and response. First, a signaling molecule binds to a specific receptor. The message is transduced as the receptor activates a protein that may relay the message through a sequence of activations, finally leading to the specific cellular response.
4. A signal transduction pathway often results in the activation of cellular proteins. When the signal is transduced to activate a transcription factor, however, the cellular response is a change in gene expression and the production of new proteins.

ANSWERS TO TEST YOUR KNOWLEDGE

Multiple Choice:

1. b	**4.** b	**7.** e	**10.** d**	**13.** d	**16.** b	**19.** b	**22.** d
2. c	**5.** d	**8.** a*	**11.** a	**14.** a	**17.** d	**20.** a	**23.** c
3. e	**6.** c	**9.** c	**12.** b	**15.** e	**18.** a	**21.** b	**24.** c

*Explanation for answer to question 8: This problem involves both osmosis and diffusion. Although the solutions are initially equal in molarity, glucose will diffuse down its concentration gradient until it reaches dynamic equilibrium with a 1.5 *M* concentration on both sides. The increasing solute concentration on side A will cause water to move into this side, and the water level will rise.

**Explanation for answer to question 10: As the solute in the solution crosses the cell membrane, it increases the concentration of solutes within the cell, reducing the hypertonicity of the solution. As the solute reaches an equal concentration inside and outside the cell, it no longer causes osmotic changes in the cell.

CHAPTER 6: AN INTRODUCTION TO METABOLISM

FOCUS QUESTIONS

6.1. **a.** capacity to cause change
b. kinetic
c. motion
d. potential
e. position
f. conserved or constant
g. created nor destroyed
h. first
i. transformed or transferred
j. entropy
k. second

6.2.

	Stability	Work Capacity	Spontaneous Change?	Equilibrium
System with High Free Energy	low	high	yes	moves toward
System with Low Free Energy	high	low	no	is at or near