CAMPBELL BIOLOGY IN FOCUS

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6

An Introduction to Metabolism

Lecture Presentations by
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SECOND EDITION

The Energy of Life

- The living cell is a miniature chemical factory where thousands of reactions occur
- The cell extracts energy and applies energy to perform work
- Some organisms even convert energy to light, as in bioluminescence

Figure 6.1 What Causes These Breaking Waves to Glow?

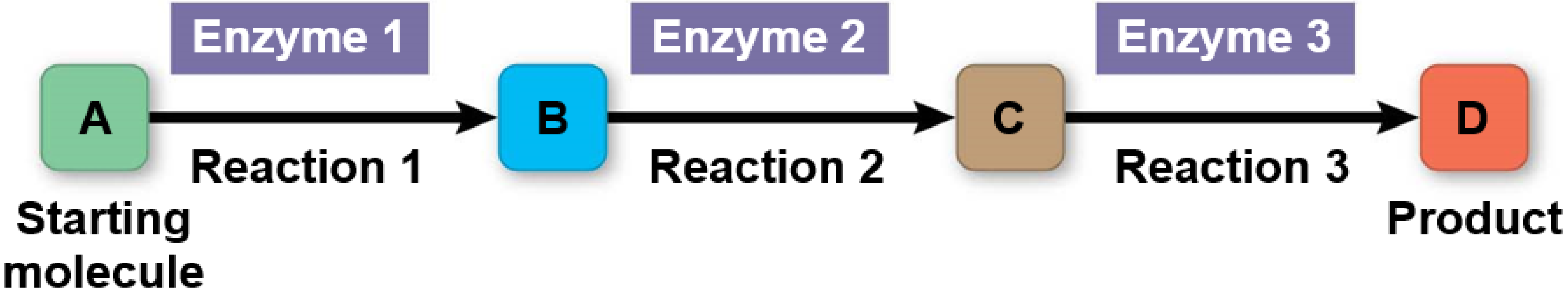
Concept 6.1: An organism’s metabolism transforms matter and energy

- **Metabolism** is the totality of an organism’s chemical reactions
- Metabolism is an emergent property of life that arises from interactions between molecules within the cell

Metabolic Pathways

- A **metabolic pathway** begins with a specific molecule and ends with a product
- Each step is catalyzed by a specific enzyme

Figure 6.UN01 In-Text Figure, Metabolic Pathway, p. 122



Metabolic Pathways, Continued

- **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds
- One example of catabolism is cellular respiration, the breakdown of glucose and other organic fuels to carbon dioxide and water

Metabolic Pathways, Continued-1

- **Anabolic pathways** consume energy to build complex molecules from simpler ones
- The synthesis of proteins from amino acids is an example of anabolism
- **Bioenergetics** is the study of how energy flows through living organisms

Forms of Energy

- **Energy** is the capacity to cause change
- Energy exists in various forms, some of which can perform work

Forms of Energy, Continued

- **Kinetic energy** is energy associated with motion
- **Thermal energy** is kinetic energy associated with random movement of atoms or molecules
- **Heat** is thermal energy in transfer from one object to another
- Light is another type of energy that can be harnessed to perform work

Forms of Energy, Continued-1

- **Potential energy** is energy that matter possesses because of its location or structure
- **Chemical energy** is potential energy available for release in a chemical reaction
- Energy can be converted from one form to another

Animation: Energy Concepts

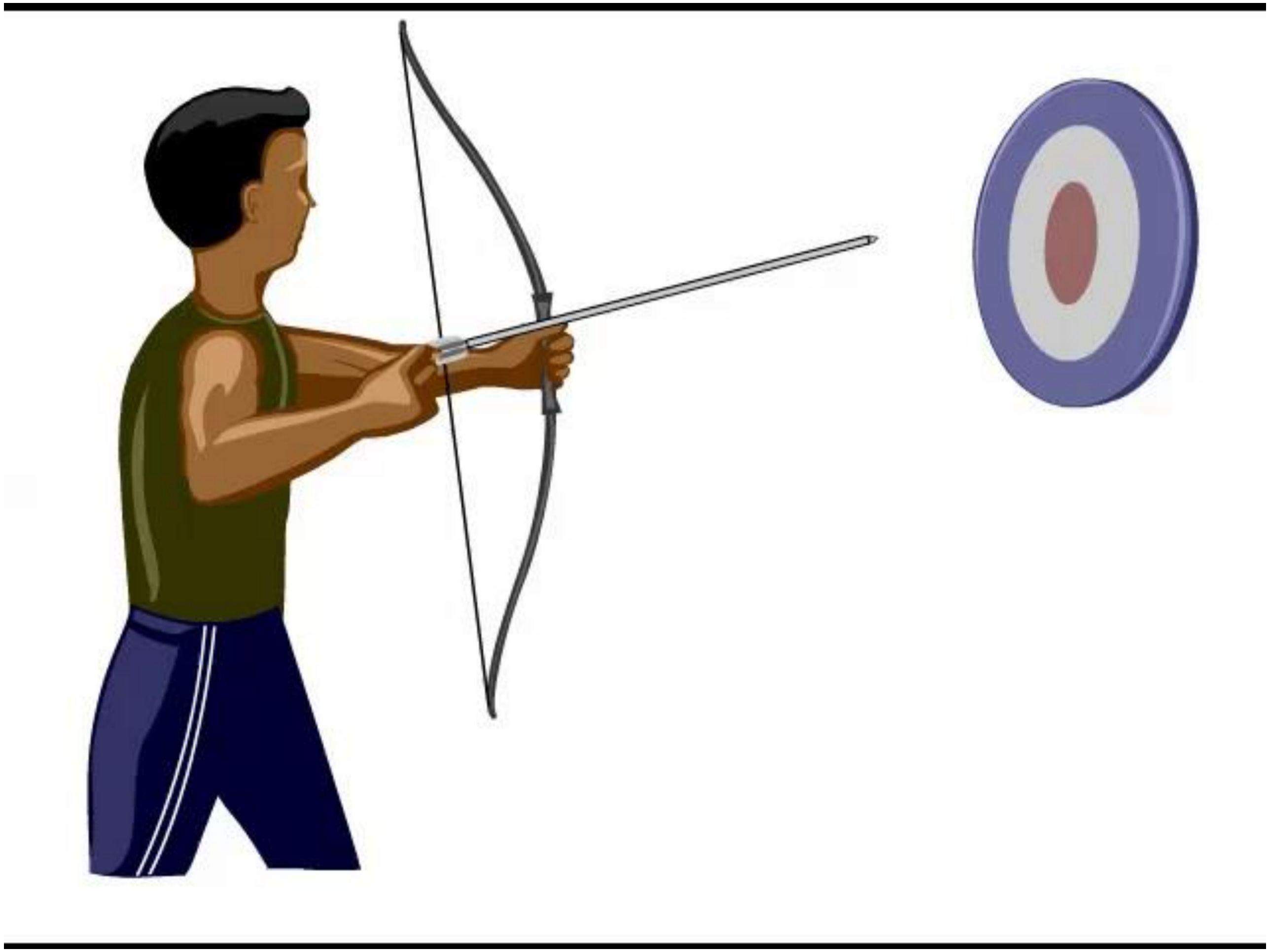


Figure 6.2 Transformations Between Potential and Kinetic Energy

A diver has more potential energy on the platform.

Diving converts potential energy to kinetic energy.

Climbing up converts the kinetic energy of muscle movement to potential energy.

A diver has less potential energy in the water.

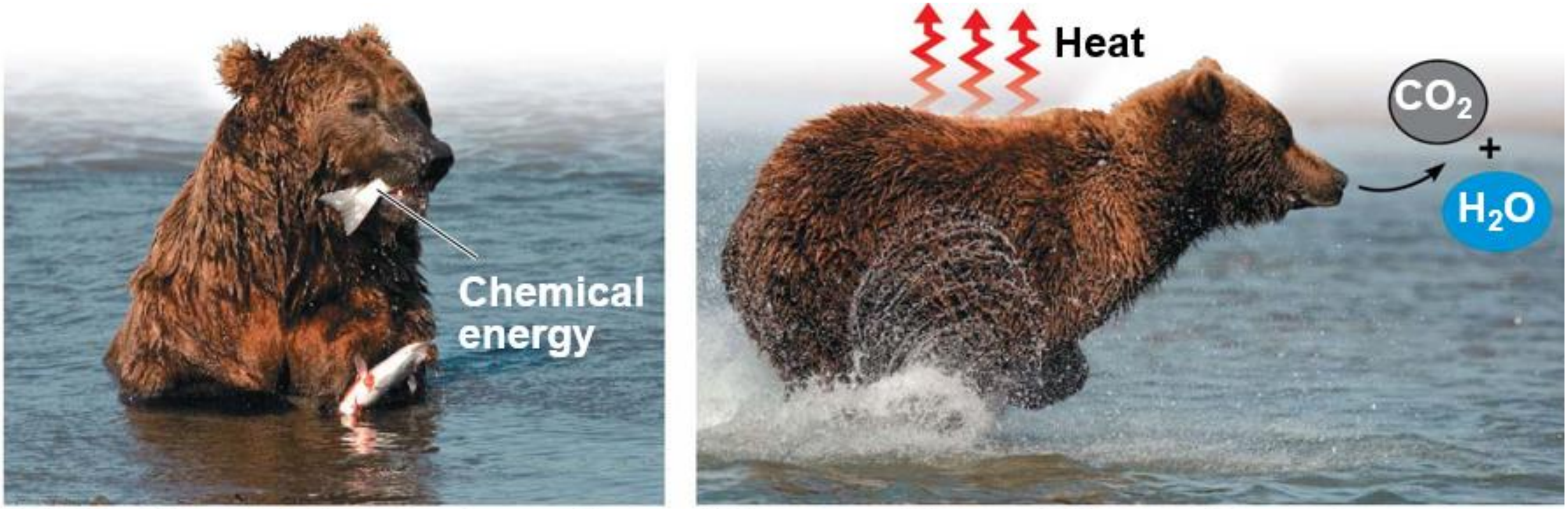
The Laws of Energy Transformation

- **Thermodynamics** is the study of energy transformations
- In an open system, energy and matter can be transferred between the system and its surroundings
- In an isolated system, exchange with the surroundings cannot occur
- Organisms are open systems

The First Law of Thermodynamics

- According to the **first law of thermodynamics**, the energy of the universe is constant
    - *Energy can be transferred and or transformed, but it cannot be created or destroyed*
- The first law is also called the *principle of conservation of energy*

Figure 6.3 The Two Laws of Thermodynamics



(a) First law of thermodynamics

(b) Second law of thermodynamics

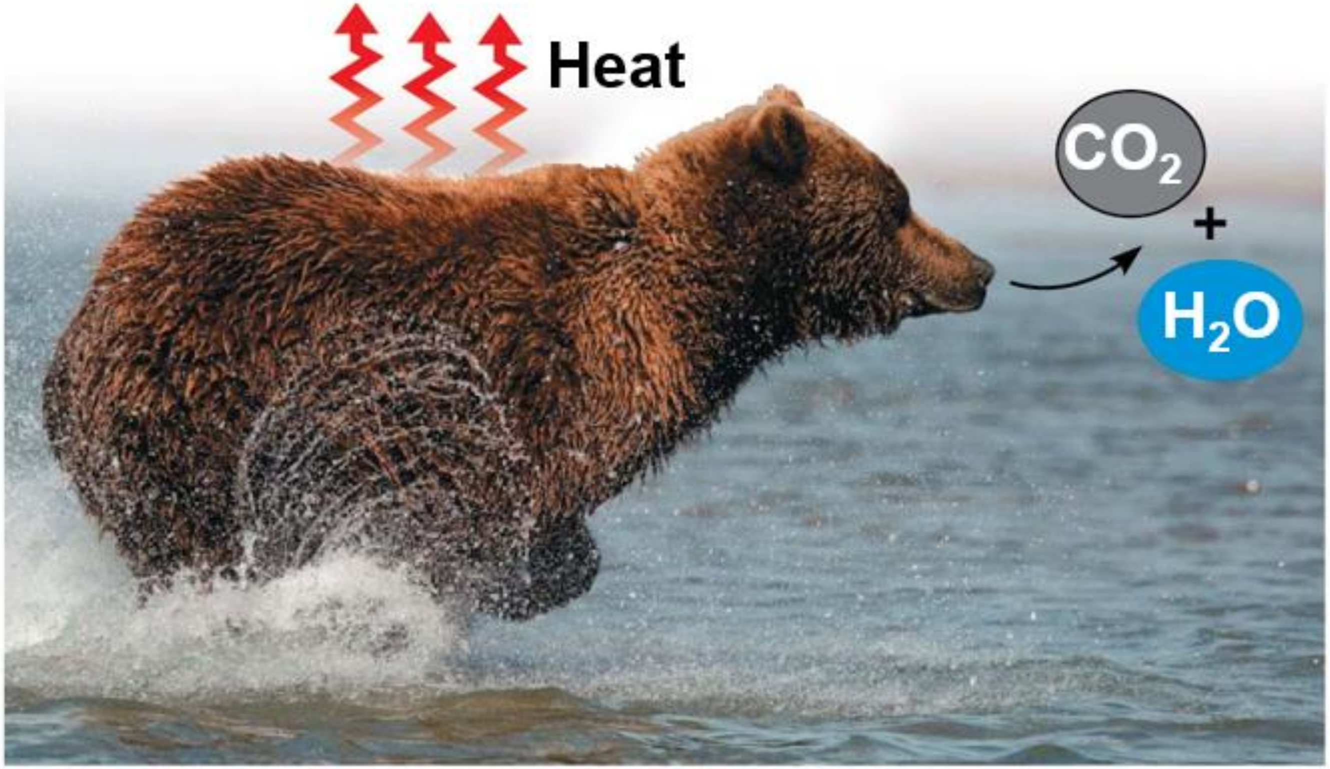
Figure 6.3-1 The Two Laws of Thermodynamics (Part 1: Conservation of Energy)

(a) First law of thermodynamics

The Second Law of Thermodynamics

- During every energy transfer or transformation, some energy is lost as heat
- According to the **second law of thermodynamics**
  - *Every energy transfer or transformation increases the entropy of the universe*
- **Entropy** is a measure of disorder, or randomness

Figure 6.3-2 The Two Laws of Thermodynamics (Part 2: Entropy)



(b) Second law of thermodynamics

The Second Law of Thermodynamics, Continued

- Living cells unavoidably convert organized forms of energy to heat
- **Spontaneous processes** occur without energy input; they can happen quickly or slowly
    - *For a process to occur spontaneously, it must increase the entropy of the universe*

Biological Order and Disorder

- Cells create ordered structures from less ordered materials
- Organisms also replace ordered forms of matter and energy with less ordered forms
- Energy flows into an ecosystem in the form of light and exits in the form of heat

Figure 6.4 Order as a Characteristic of Life

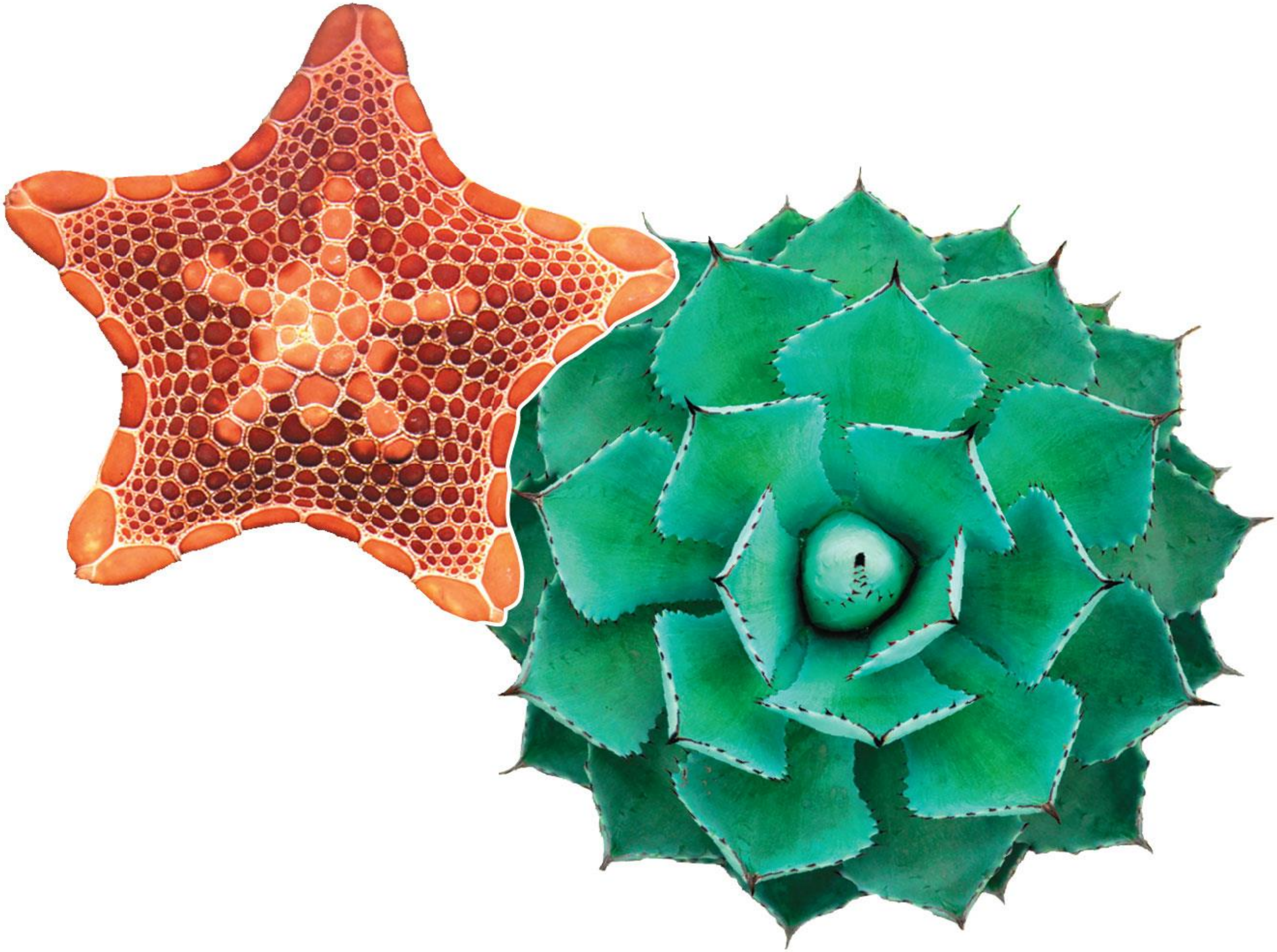


Figure 6.4-1 Order as a Characteristic of Life (Part 1: Biscuit Star)

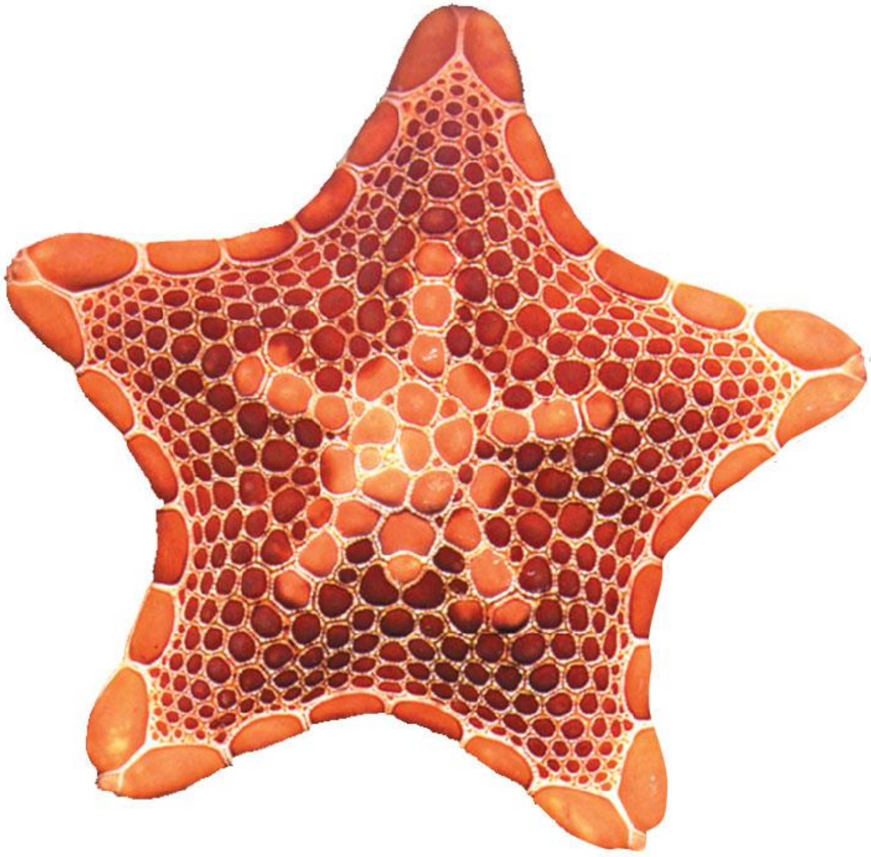


Figure 6.4-2 Order as a Characteristic of Life (Part 2: Agave Plant)

Biological Order and Disorder, Continued

- The evolution of more complex organisms does not violate the second law of thermodynamics
- Entropy (disorder) may decrease in a system, but the universe’s total entropy increases
- Organisms are islands of low entropy in an increasingly random universe

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

- Biologists measure changes in free energy to help them understand the chemical reactions of life

Free-Energy Change (ΔG), Stability, and Equilibrium

- A living system's **free energy** is energy that can do work when temperature and pressure are uniform, as in a living cell

Free-Energy Change (ΔG), Stability, and Equilibrium, Continued

- The change in free energy (ΔG) during a chemical reaction is the difference between the free energy of the final state and the free energy of the initial state

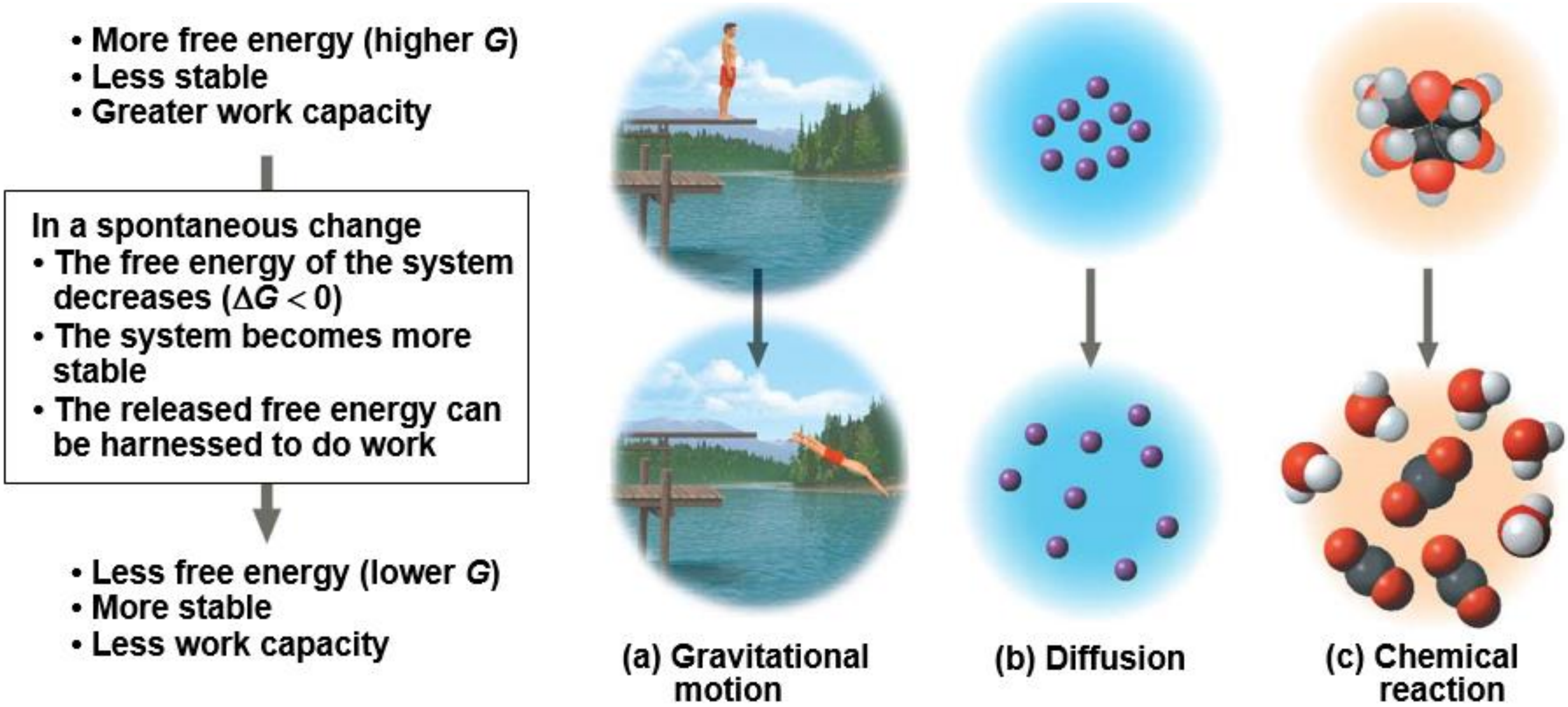
$$\Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

- Only processes with a negative ΔG are spontaneous
- Spontaneous processes can be harnessed to perform work

Free-Energy Change (ΔG), Stability, and Equilibrium, Continued-1

- Free energy is a measure of a system's instability, its tendency to change to a more stable state
- During a spontaneous change, free energy decreases and the stability of a system increases

Figure 6.5 The Relationship of Free Energy to Stability, Work Capacity, and Spontaneous Change



- More free energy (higher *G*)
- Less stable
- Greater work capacity

In a spontaneous change
- The free energy of the system decreases ($\Delta G < 0$)
- The system becomes more stable
- The released free energy can be harnessed to do work

- Less free energy (lower *G*)
- More stable
- Less work capacity

(a) Gravitational motion

(b) Diffusion

(c) Chemical reaction

Figure 6.5-1 The Relationship of Free Energy to Stability, Work Capacity, and Spontaneous Change (Part 1: Free Energy and Spontaneity)

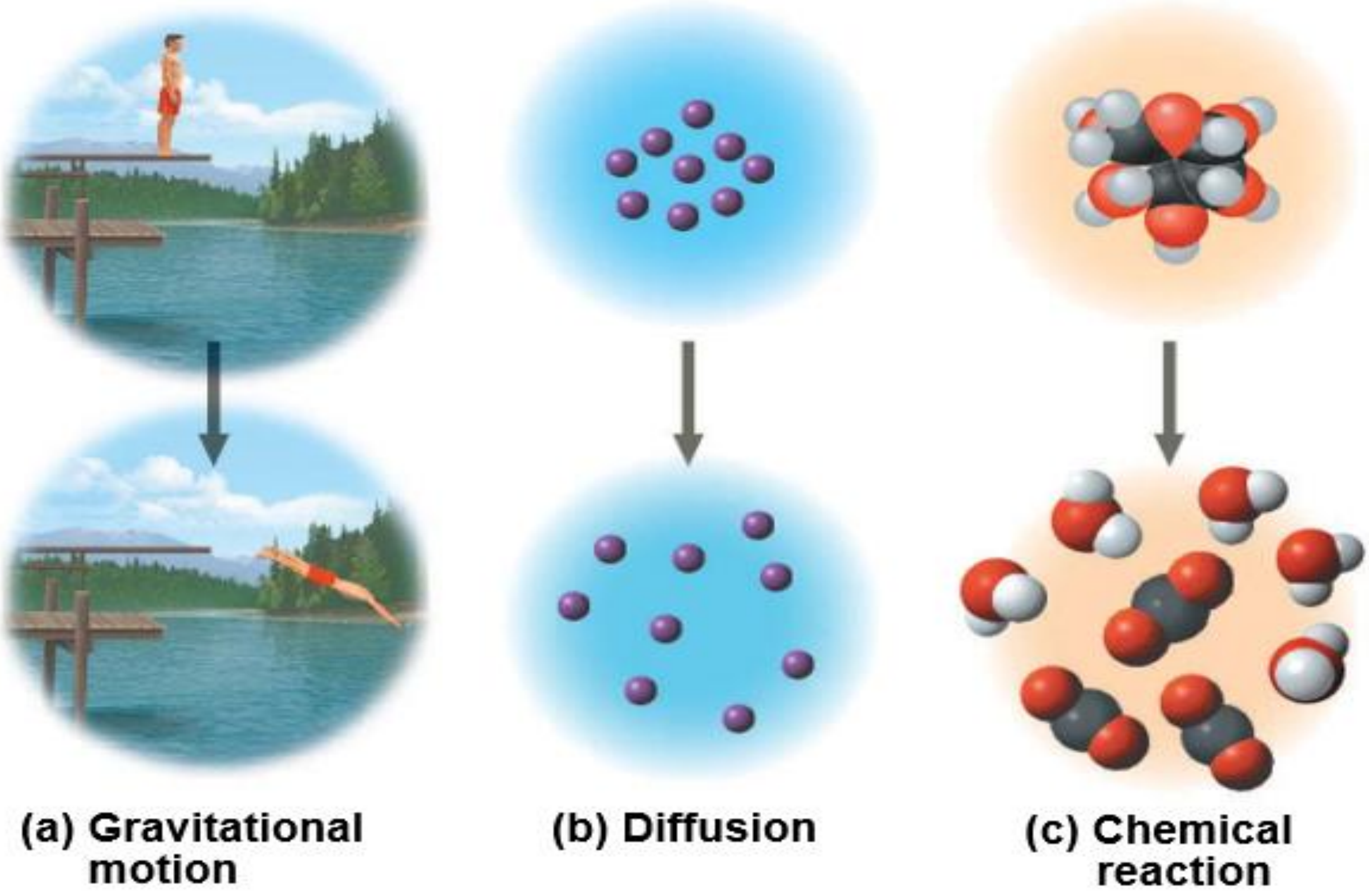
- More free energy (higher *G*)
- Less stable
- Greater work capacity

In a spontaneous change

- The free energy of the system decreases ($\Delta G < 0$)
- The system becomes more stable
- The released free energy can be harnessed to do work

- Less free energy (lower *G*)
- More stable
- Less work capacity

Figure 6.5-2 The Relationship of Free Energy to Stability, Work Capacity, and Spontaneous Change (Part 2: Gravitational Motion, Diffusion, and Chemical Reaction)



Free-Energy Change (ΔG), Stability, and Equilibrium, Continued-2

- At equilibrium, forward and reverse reactions occur at the same rate; it is a state of maximum stability
    - *A process is spontaneous and can perform work only when it is moving toward equilibrium*

Free Energy and Metabolism

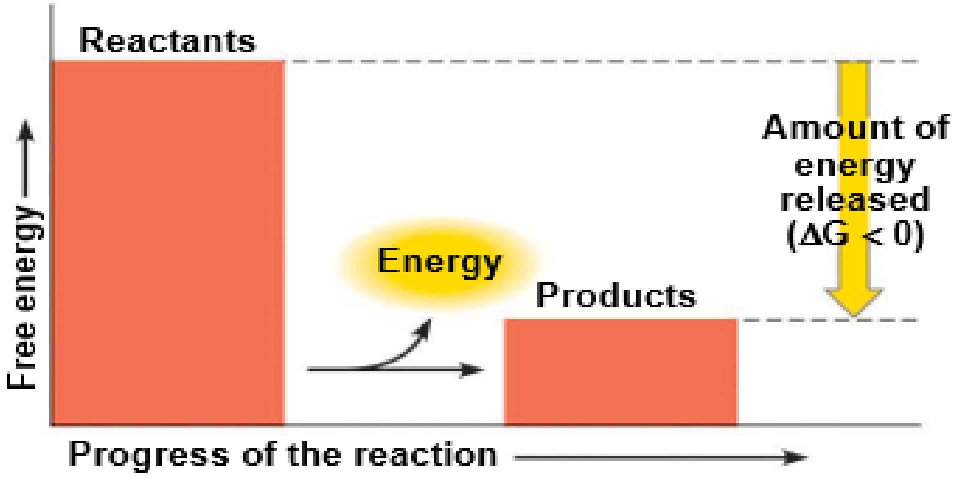
- The concept of free energy can be applied to the chemistry of life’s processes

Exergonic and Endergonic Reactions in Metabolism

- An **exergonic reaction** proceeds with a net release of free energy and is spontaneous; Δ*G* is negative
- The magnitude of Δ*G* represents the maximum amount of work the reaction can perform

Figure 6.6 Free Energy Changes (ΔG) in Exergonic and Endergonic Reactions

(a) Exergonic reaction: energy released, spontaneous



(b) Endergonic reaction: energy required, nonspontaneous

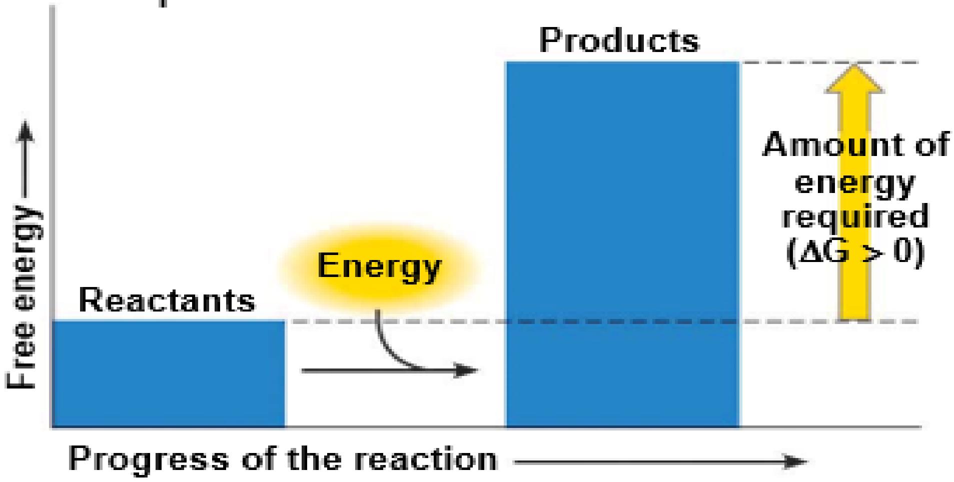
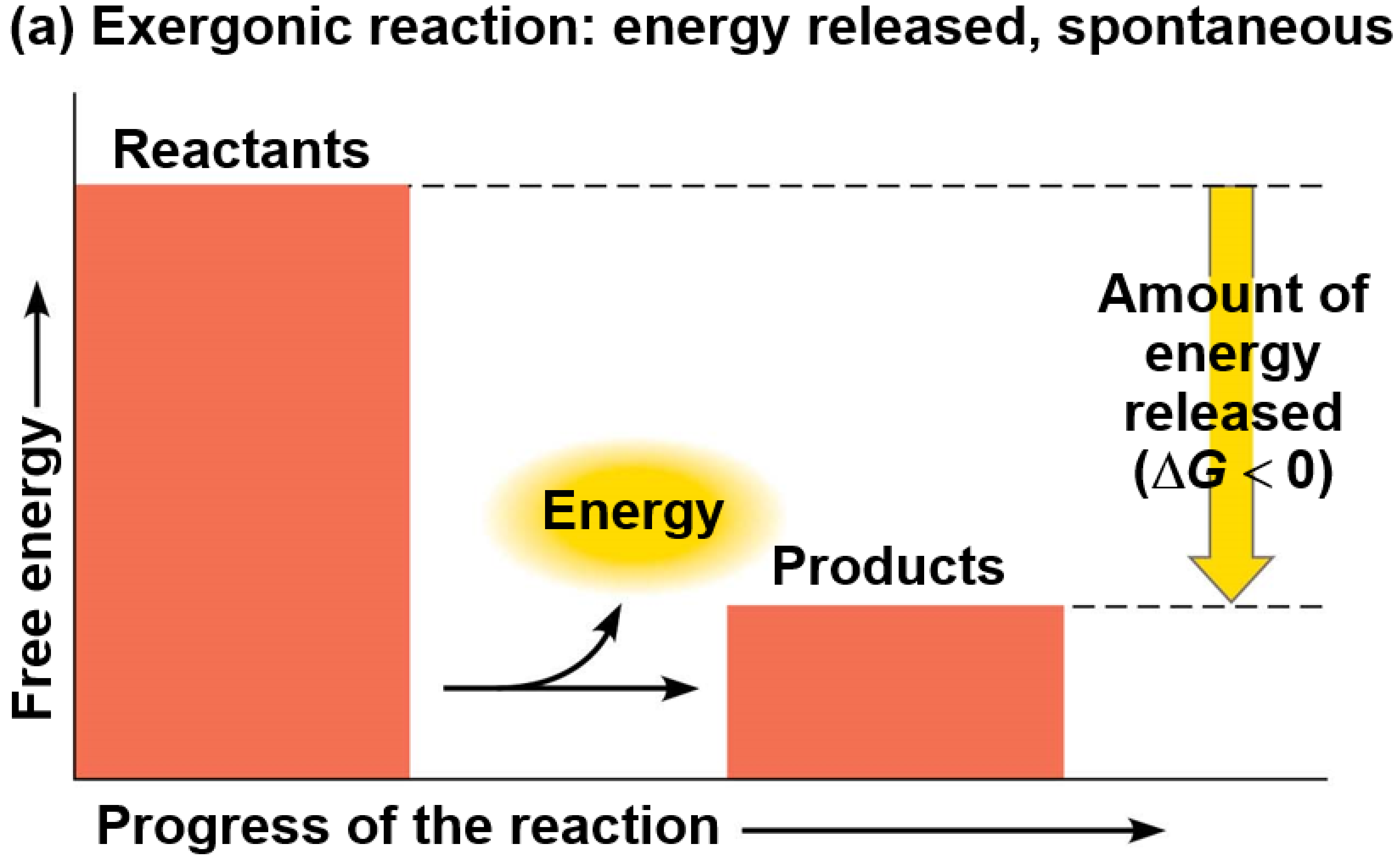


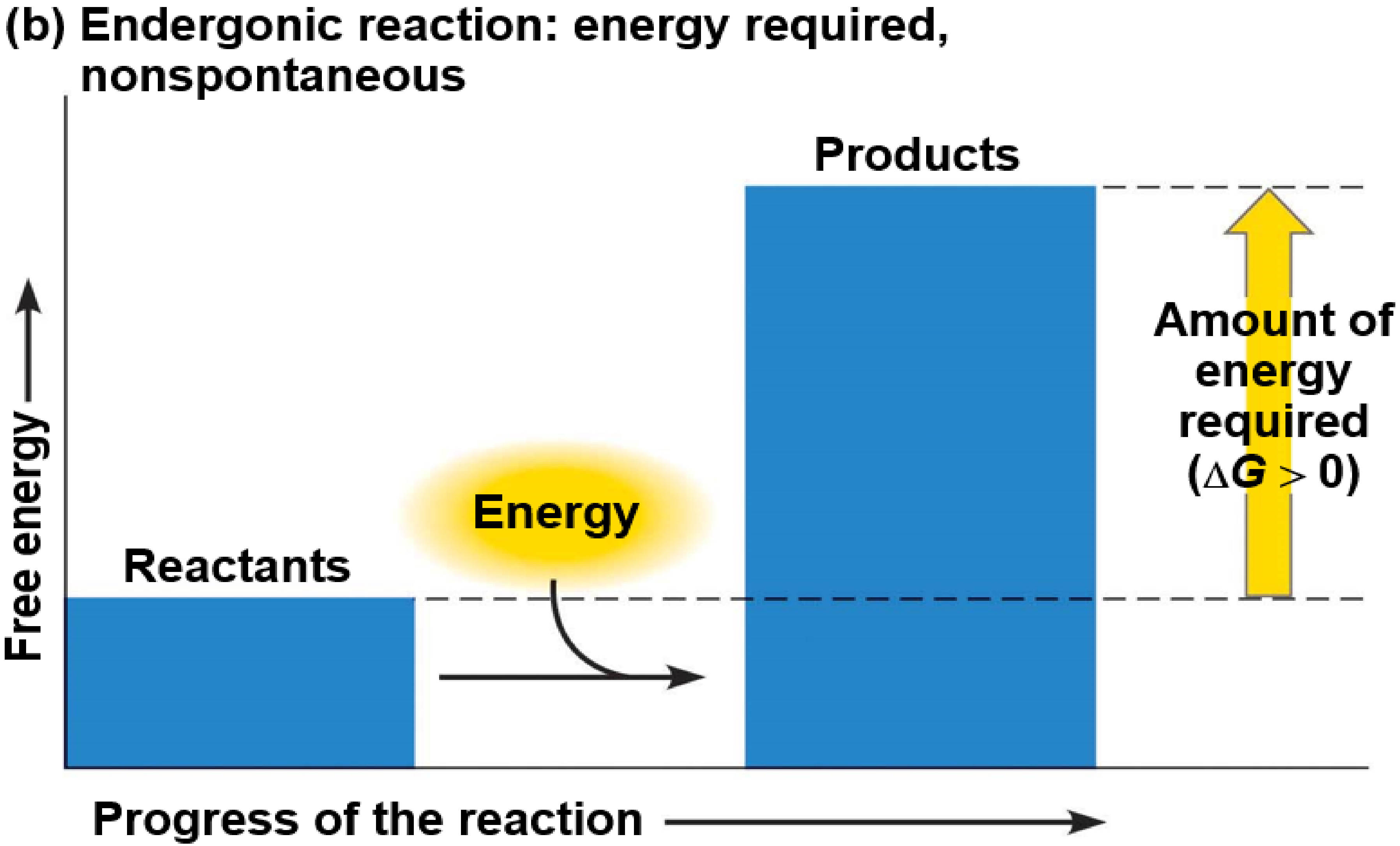
Figure 6.6-1 Free Energy Changes (ΔG) in Exergonic and Endergonic Reactions (Part 1: Exergonic)



Exergonic and Endergonic Reactions in Metabolism, Continued

- An **endergonic reaction** absorbs free energy from its surroundings and is nonspontaneous; ΔG is positive
- The magnitude of ΔG is the quantity of energy required to drive the reaction

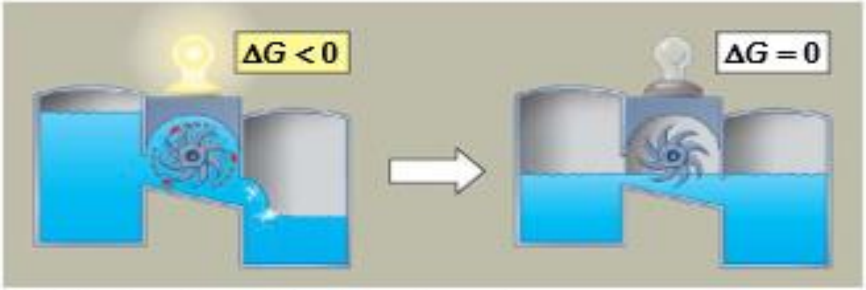
Figure 6.6-2 Free Energy Changes (ΔG) in Exergonic and Endergonic Reactions (Part 2: Endergonic)



Equilibrium and Metabolism

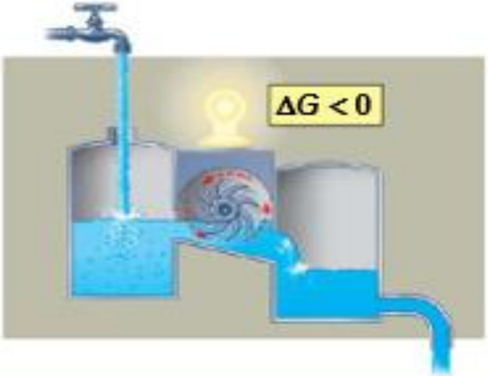
- Hydroelectric systems can serve as analogies for chemical reactions in living systems
- Reactions in an isolated system eventually reach equilibrium and can then do no work

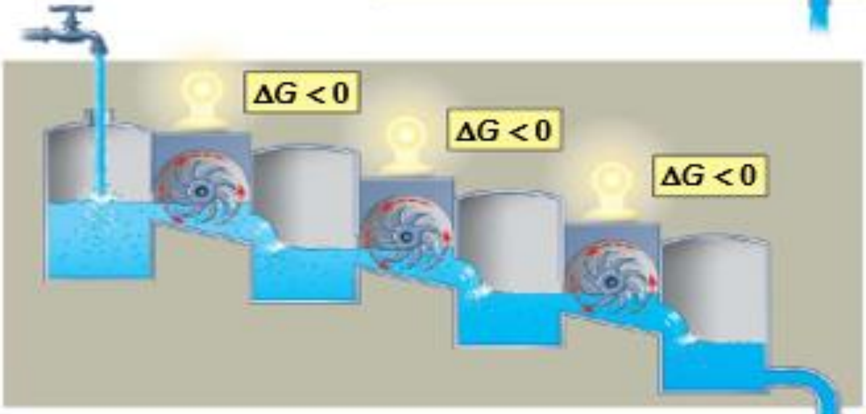
Figure 6.7 Equilibrium and Work in Isolated and Open Systems



(a) An isolated hydroelectric system

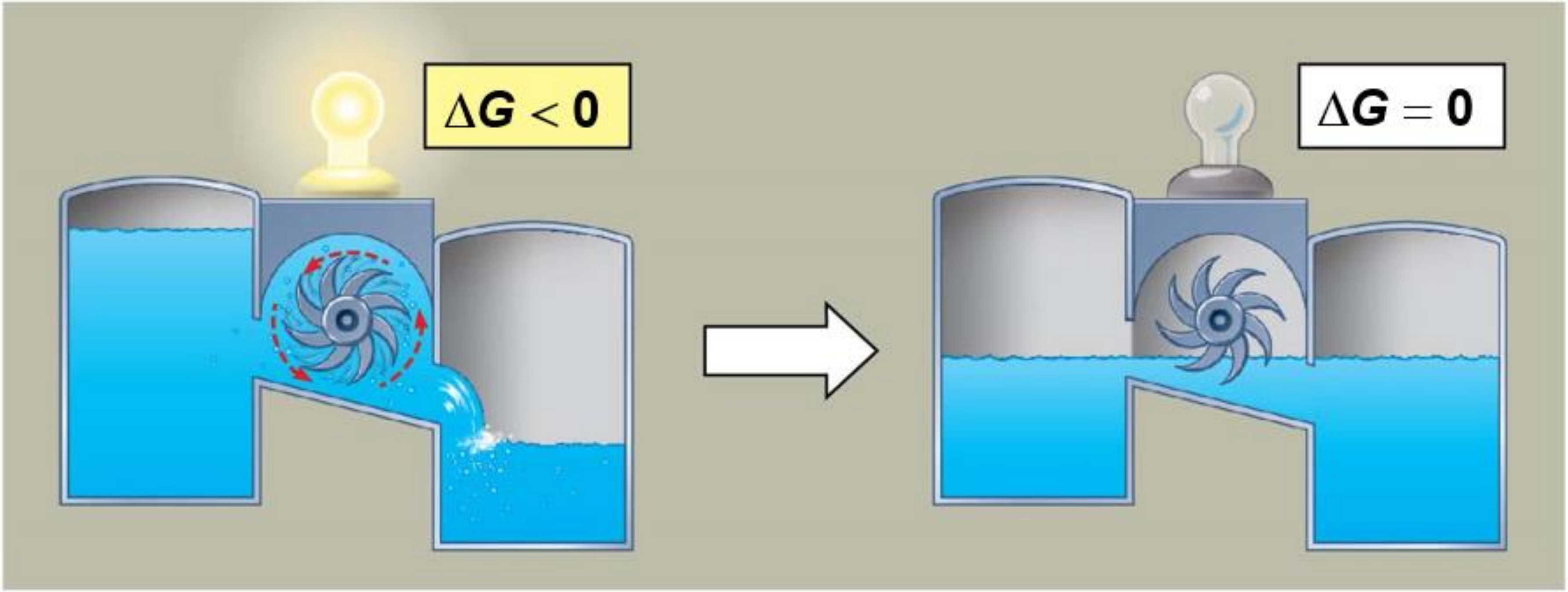
(b) An open hydroelectric system





(c) A multistep open hydroelectric system

Figure 6.7-1 Equilibrium and Work in Isolated and Open Systems (Part 1: Isolated System)



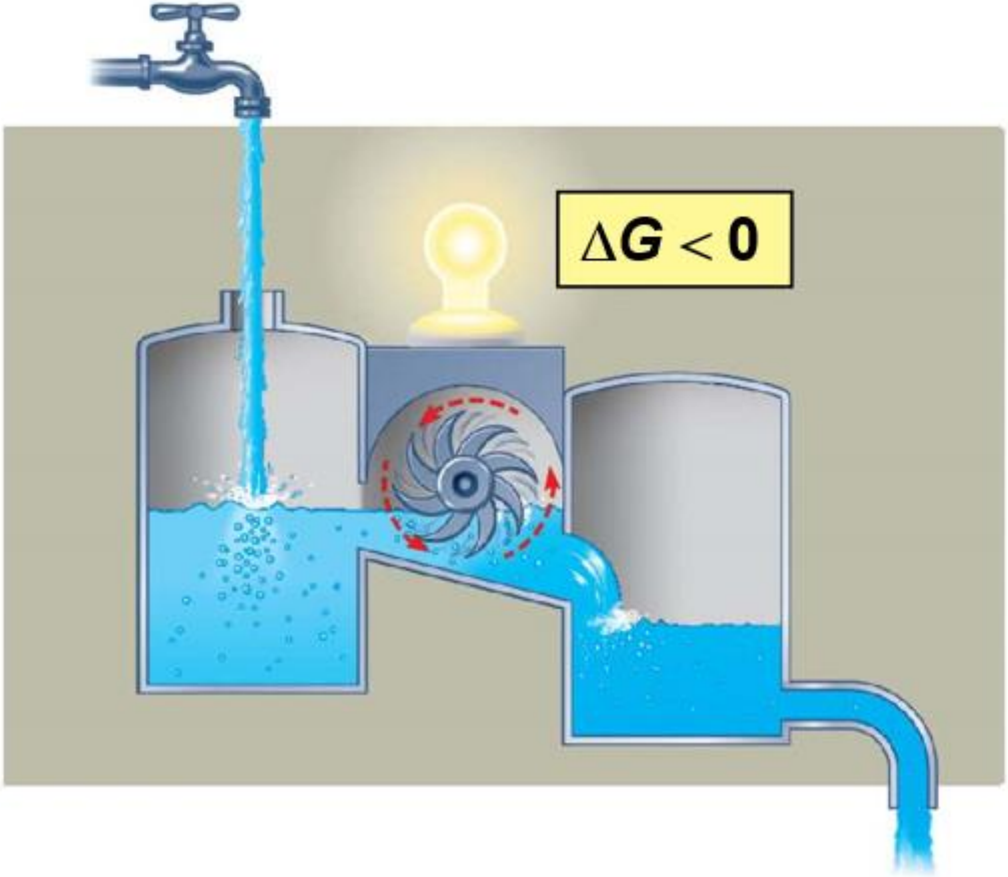
(a) An isolated hydroelectric system

Equilibrium and Metabolism, Continued

- Cells are not in equilibrium; they are open systems experiencing a constant flow of materials

Figure 6.7-2 Equilibrium and Work in Isolated and Open Systems (Part 2: Open System)

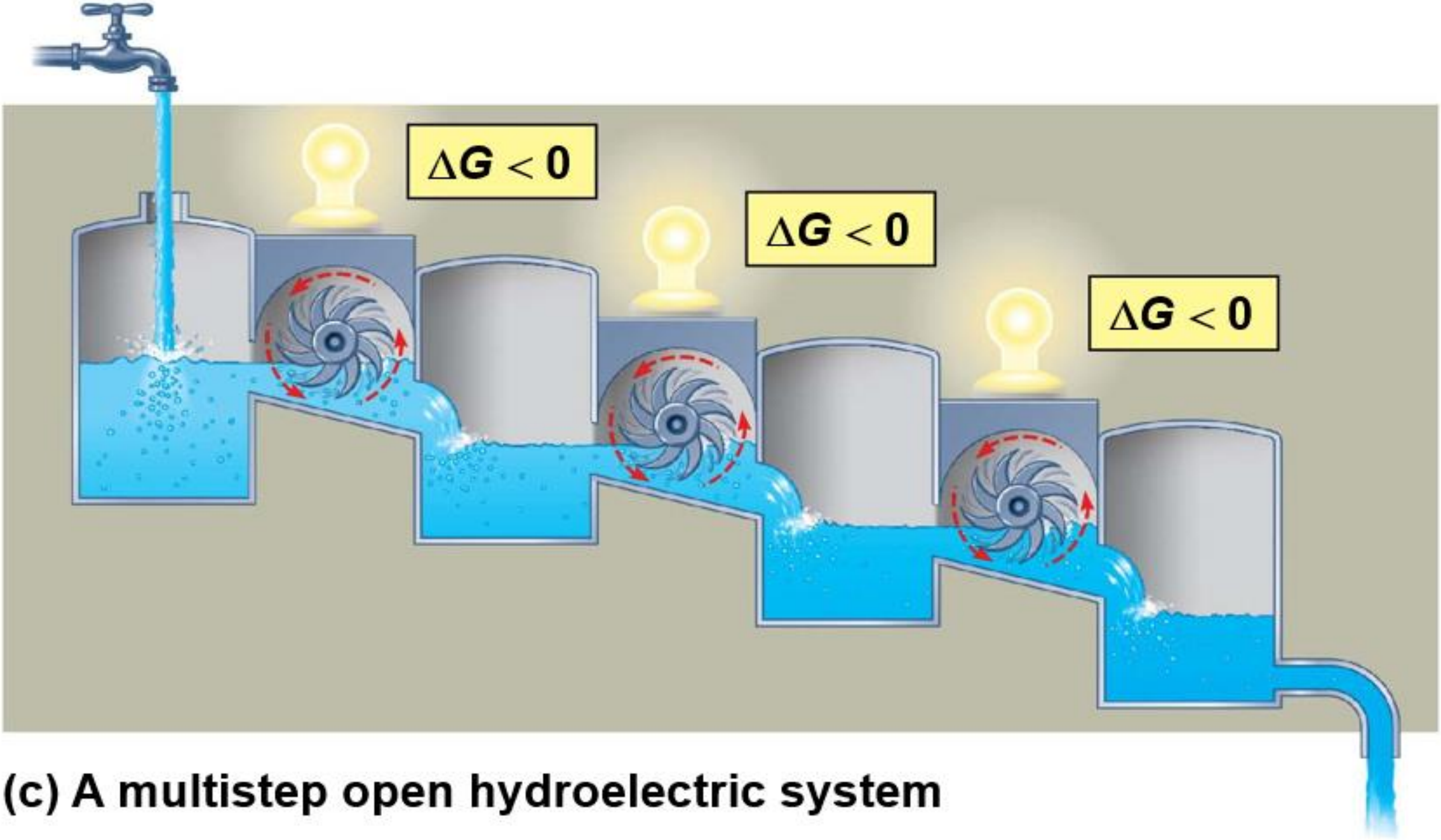
(b) An open hydroelectric system



Equilibrium and Metabolism, Continued-1

- A catabolic pathway in a cell releases free energy in a series of reactions
- The product of each reaction is the reactant for the next, preventing the system from reaching equilibrium

Figure 6.7-3 Equilibrium and Work in Isolated and Open Systems (Part 3: Multistep Open System)



(c) A multistep open hydroelectric system

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

- A cell does three main kinds of work
  - Chemical
  - Transport
  - Mechanical

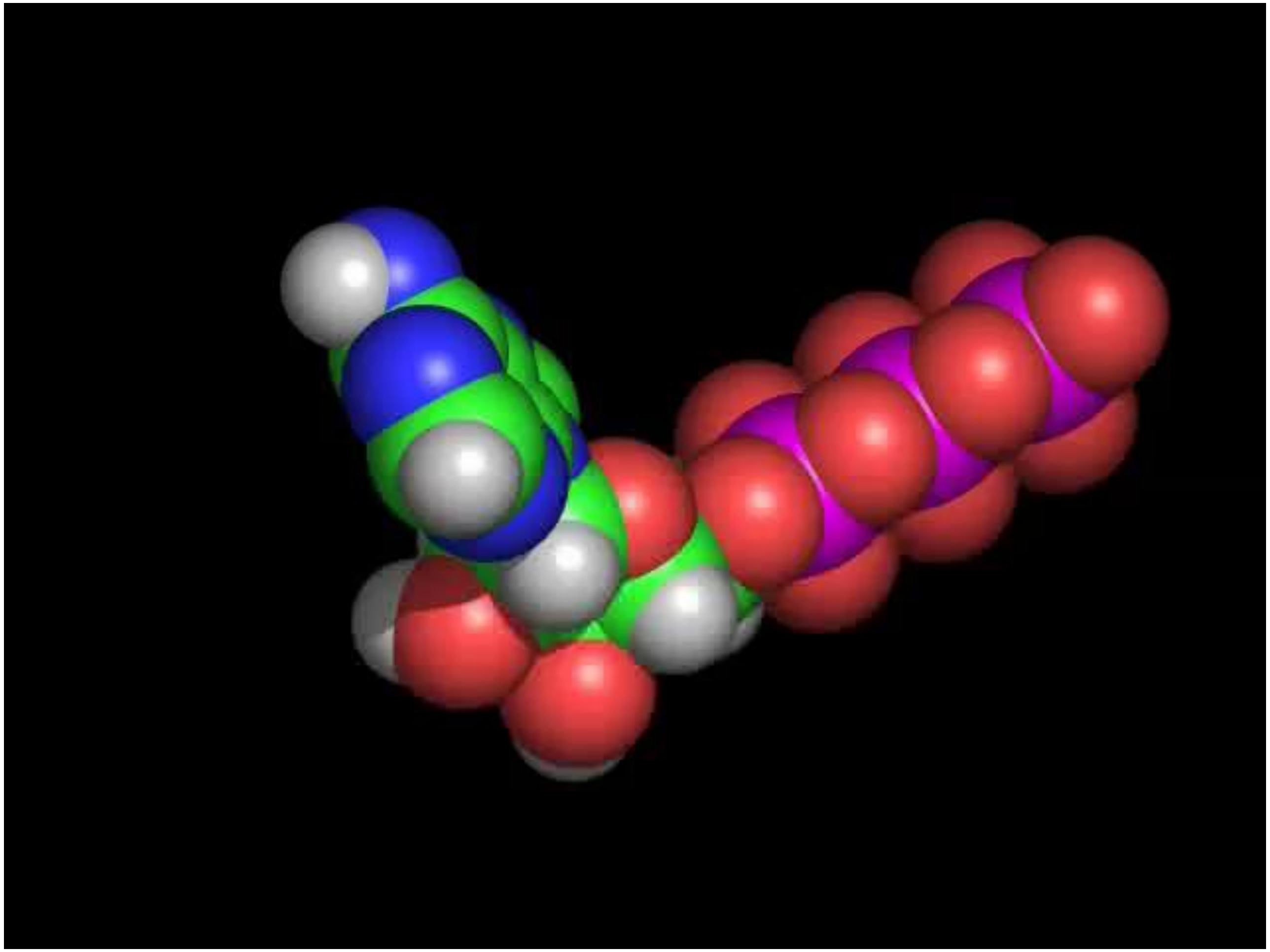
Concept 6.3: ATP powers cellular work by coupling exergonic reactions to endergonic reactions, Continued

- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP

The Structure and Hydrolysis of ATP

- **ATP (adenosine triphosphate)** is composed of ribose (a sugar), adenine (a nitrogenous base), and three phosphate groups
- In addition to its role in energy coupling, ATP is also used to make RNA

Video: ATP Space-filling Model



Video: ATP Stick Model

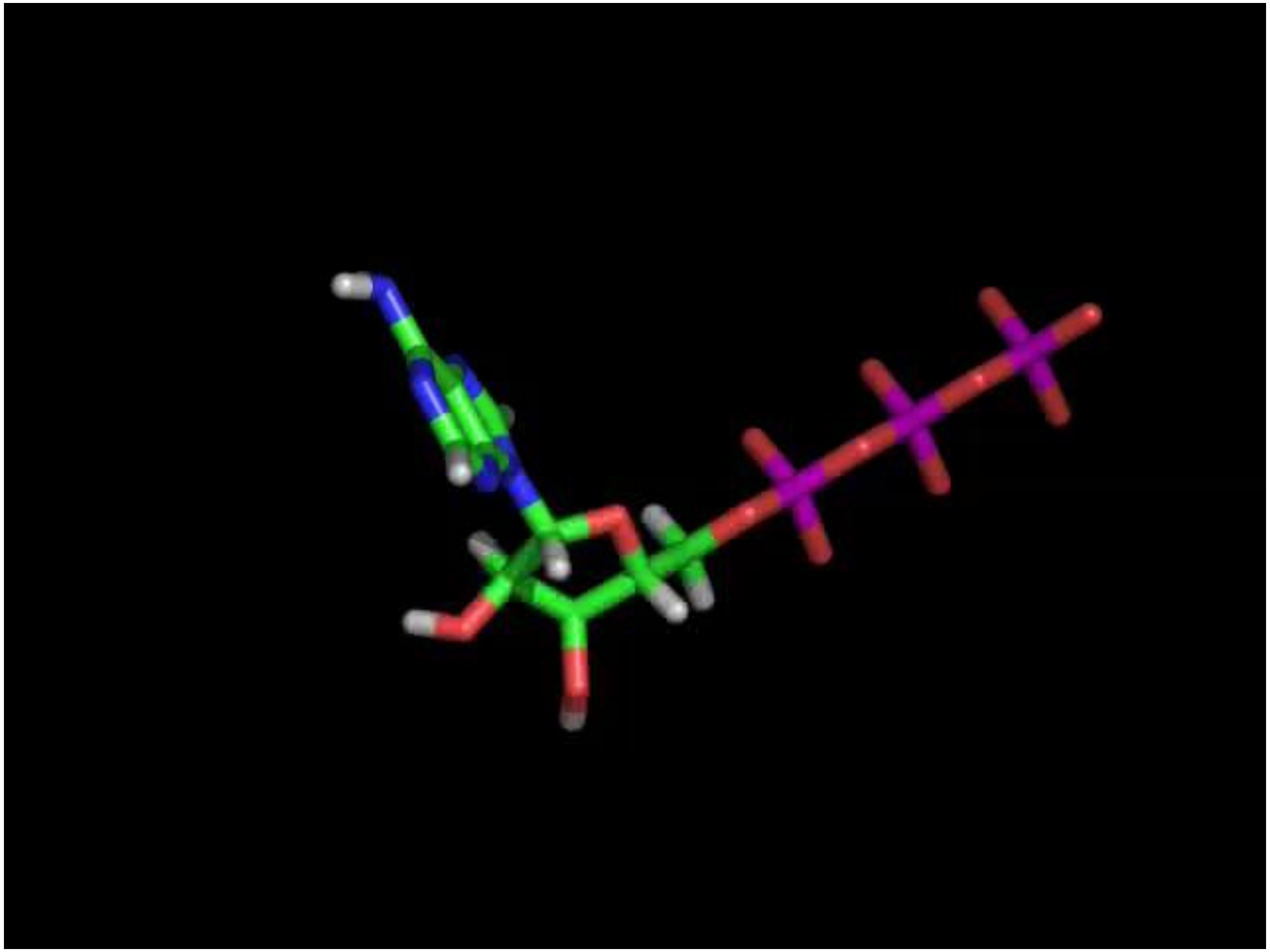
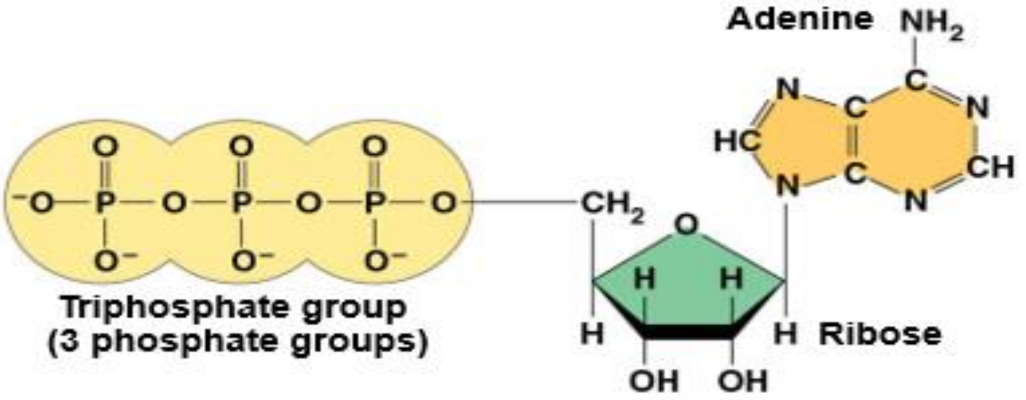
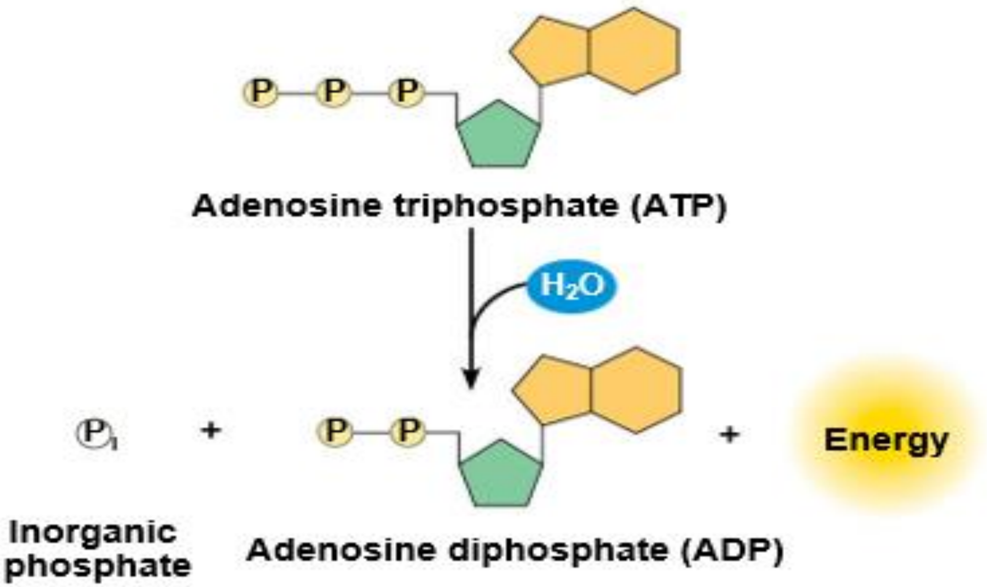


Figure 6.8 The Structure and Hydrolysis of Adenosine Triphosphate (ATP)

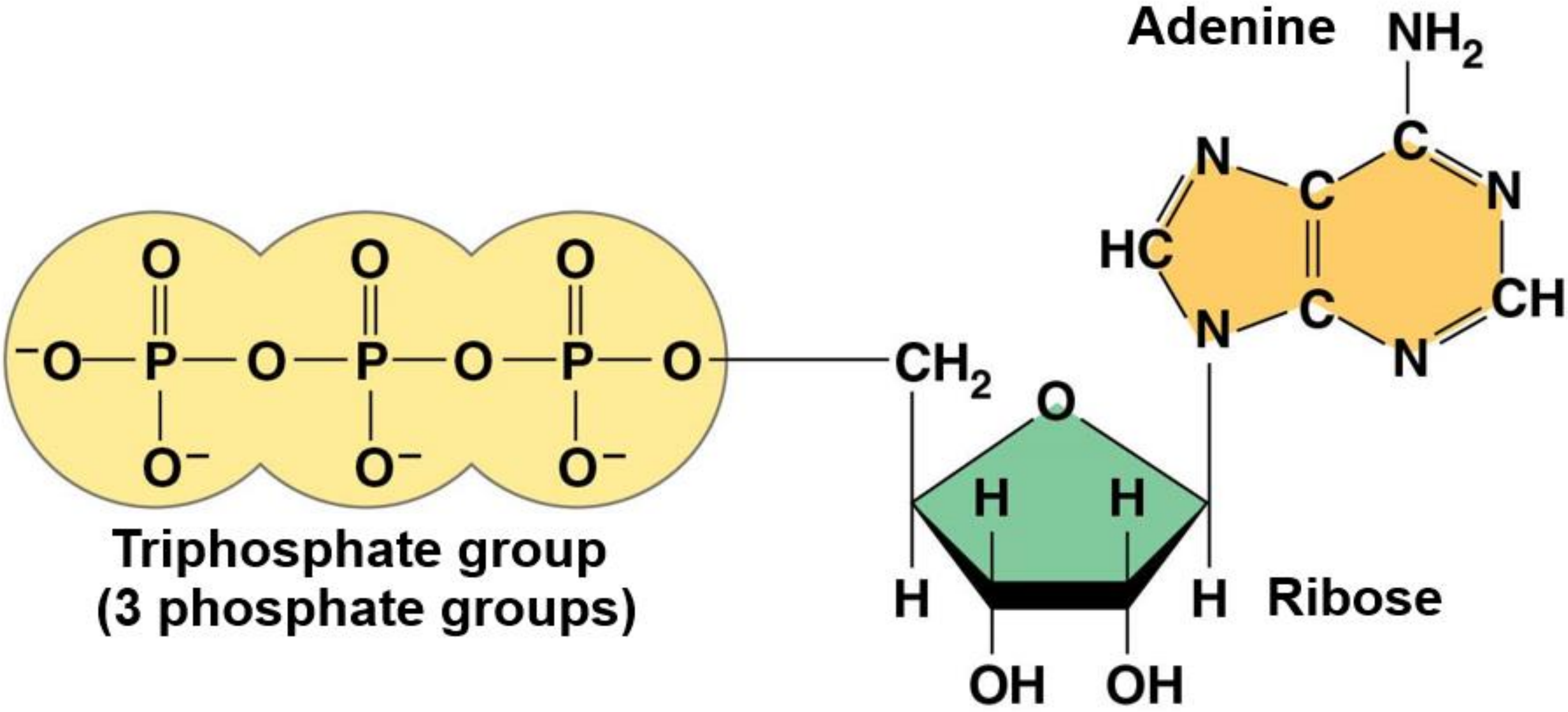


(a) The structure of ATP



(b) The hydrolysis of ATP

Figure 6.8-1 The Structure and Hydrolysis of Adenosine Triphosphate (ATP) (Part 1: Structure)

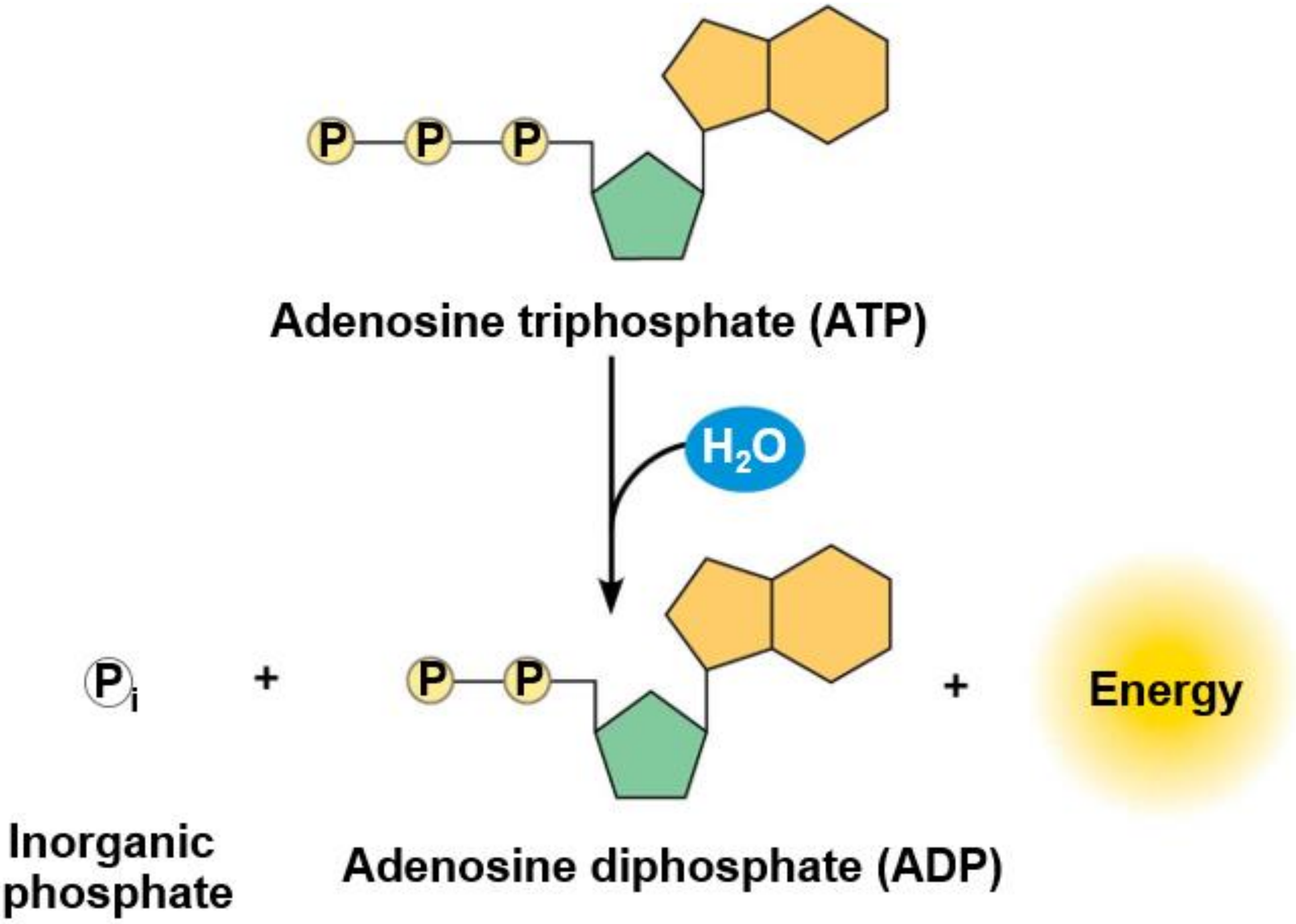


(a) The structure of ATP

The Structure and Hydrolysis of ATP, Continued

- The bonds between the phosphate groups of ATP can be broken by hydrolysis
- Energy is released from ATP when the terminal phosphate bond is broken
- This release of energy comes from the chemical change to a state of lower free energy, not from the phosphate bonds themselves

Figure 6.8-2 The Structure and Hydrolysis of Adenosine Triphosphate (ATP) (Part 2: Hydrolysis)



(b) The hydrolysis of ATP

The Structure and Hydrolysis of ATP, Continued-1

- ATP hydrolysis releases a lot of energy due to the repulsive force of the three negatively charged phosphate groups
- The triphosphate tail of ATP is the chemical equivalent of a compressed spring

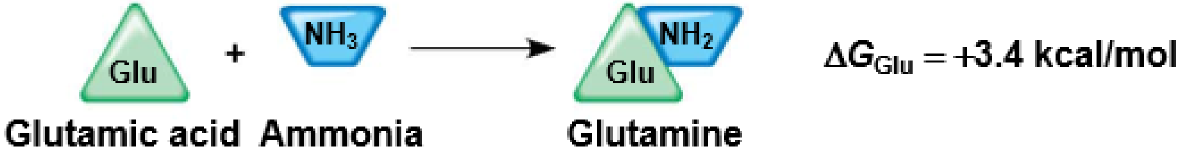
How the Hydrolysis of ATP Performs Work

- The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP
- In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive endergonic reactions

How the Hydrolysis of ATP Performs Work, Continued

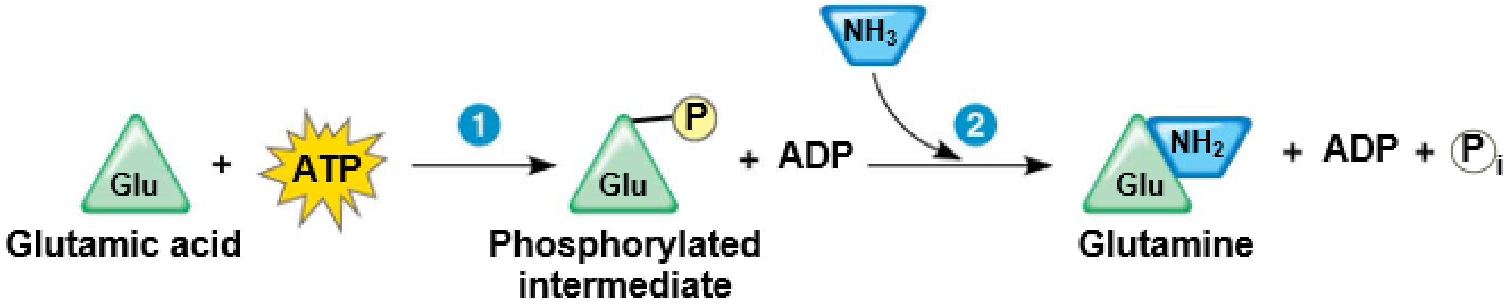
- ATP drives endergonic reactions by phosphorylation, transferring a phosphate group to some other molecule, such as a reactant
- The recipient molecule is now called a **phosphorylated intermediate**
- Overall, the coupled reactions are exergonic

Figure 6.9 How ATP Drives Chemical Work: Energy Coupling Using ATP Hydrolysis

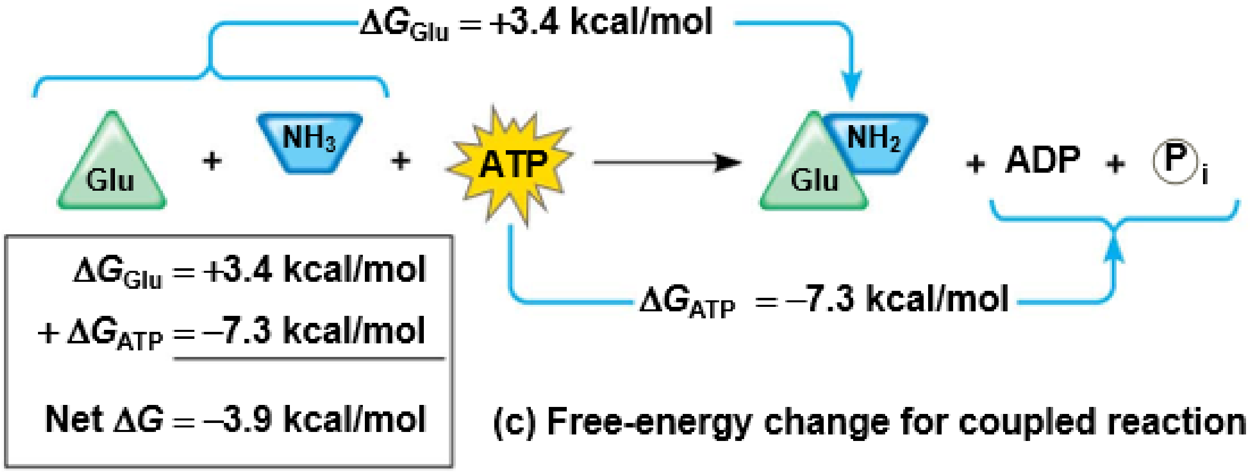


$\Delta G_{Glu} = +3.4$ kcal/mol

(a) Glutamic acid conversion to glutamine



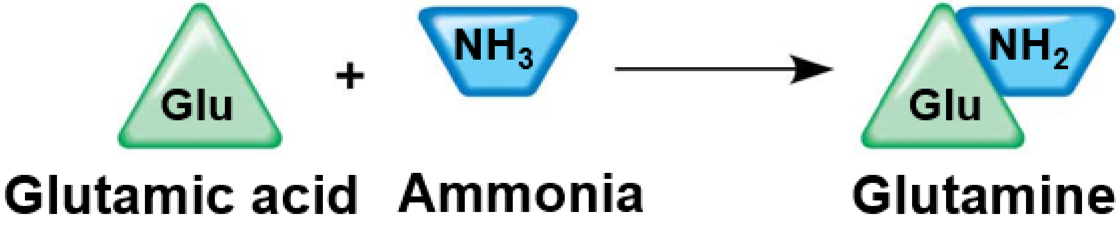
(b) Conversion reaction coupled with ATP hydrolysis



$$\begin{array}{rl} \Delta G_{Glu} = & +3.4 \text{ kcal/mol} \\ + \Delta G_{ATP} = & \underline{-7.3 \text{ kcal/mol}} \\ \text{Net } \Delta G = & -3.9 \text{ kcal/mol} \end{array}$$

(c) Free-energy change for coupled reaction

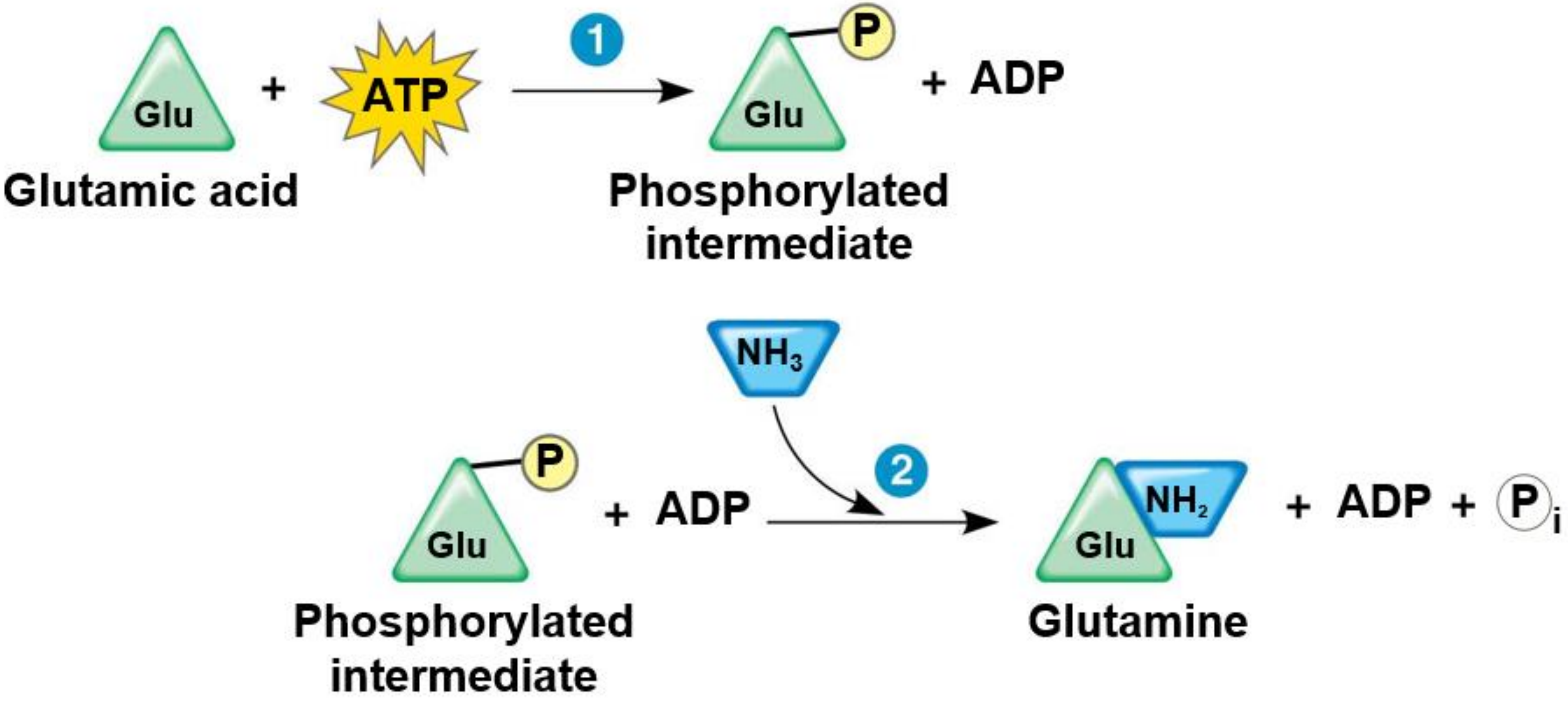
Figure 6.9-1 How ATP Drives Chemical Work: Energy Coupling Using ATP Hydrolysis (Part 1: A Nonspontaneous Reaction)



$\Delta G_{\mathrm{Glu}} = +3.4$ kcal/mol

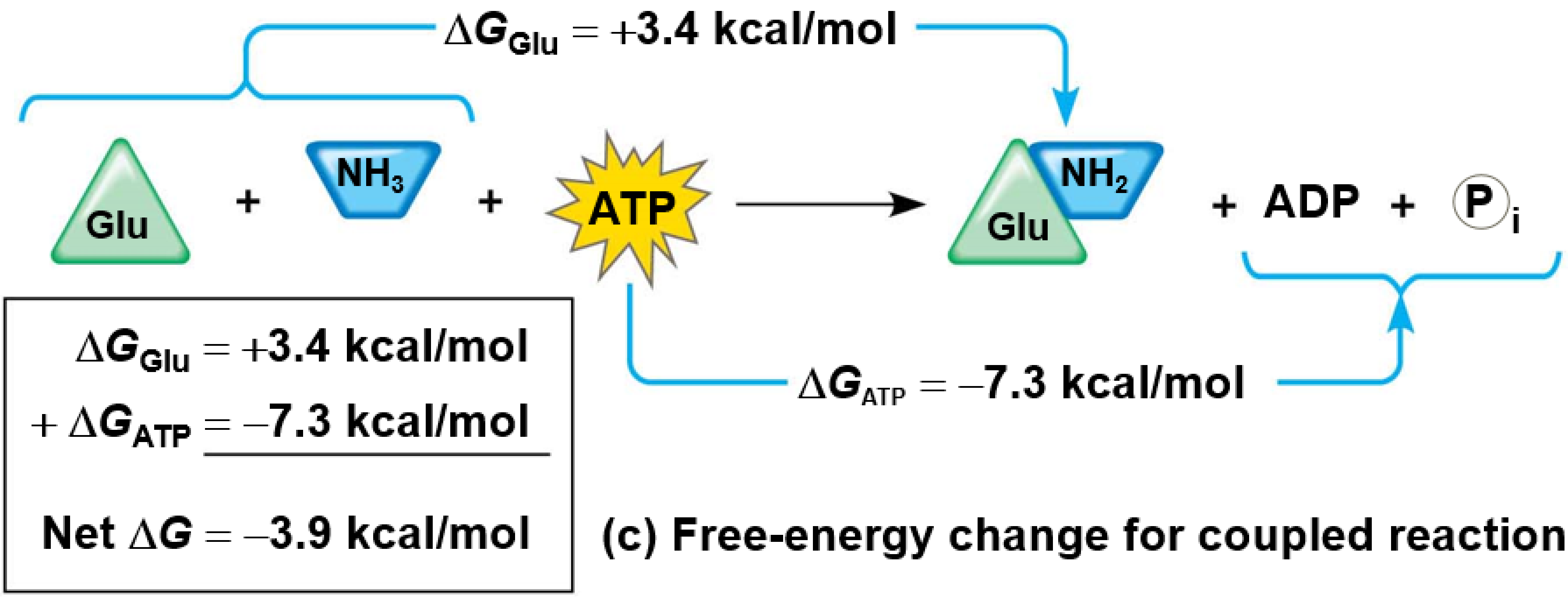
(a) Glutamic acid conversion to glutamine

Figure 6.9-2 How ATP Drives Chemical Work: Energy Coupling Using ATP Hydrolysis (Part 2: Phosphorylation)



(b) Conversion reaction coupled with ATP hydrolysis

Figure 6.9-3 How ATP Drives Chemical Work: Energy Coupling Using ATP Hydrolysis (Part 3: Coupled Free Energy Change)



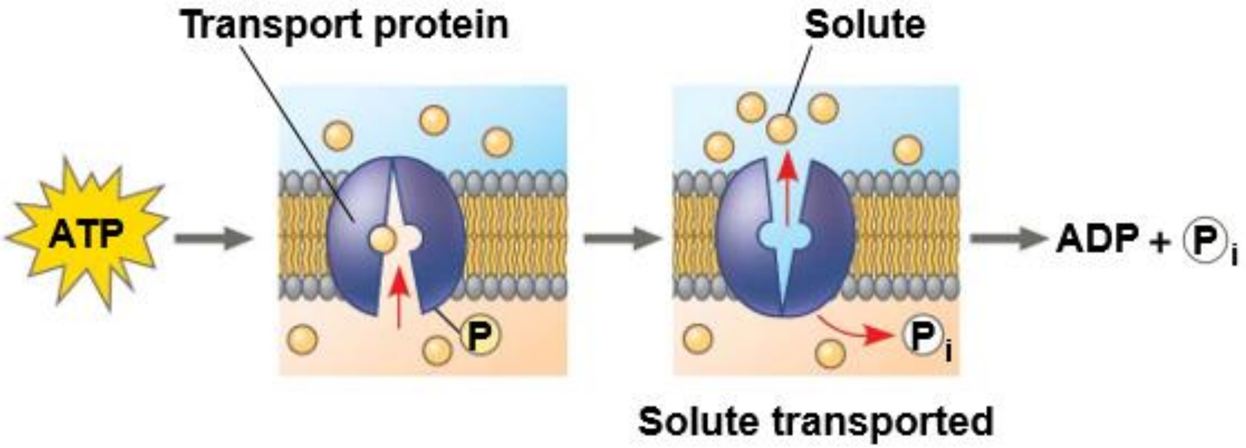
$$\begin{array}{rl} \Delta G_{Glu} & = +3.4 \text{ kcal/mol} \\ + \Delta G_{ATP} & = \underline{-7.3 \text{ kcal/mol}} \\ \text{Net } \Delta G & = -3.9 \text{ kcal/mol} \end{array}$$

(c) Free-energy change for coupled reaction

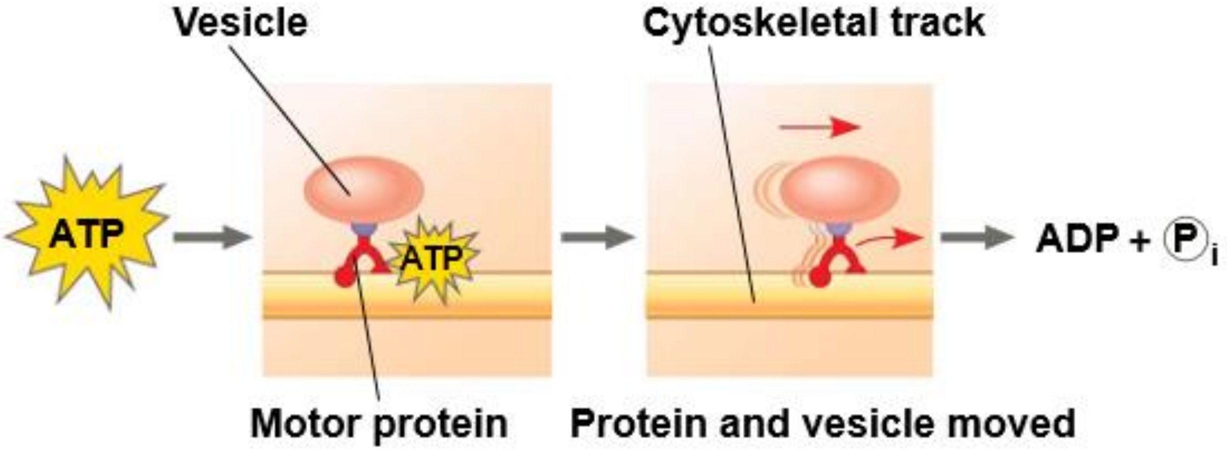
How the Hydrolysis of ATP Performs Work, Continued-1

- Transport and mechanical work in the cell are powered by ATP hydrolysis
- ATP hydrolysis leads to a change in a protein’s shape and often its ability to bind to another molecule

Figure 6.10 How ATP Drives Transport and Mechanical Work



(a) Transport work: ATP phosphorylates transport proteins.

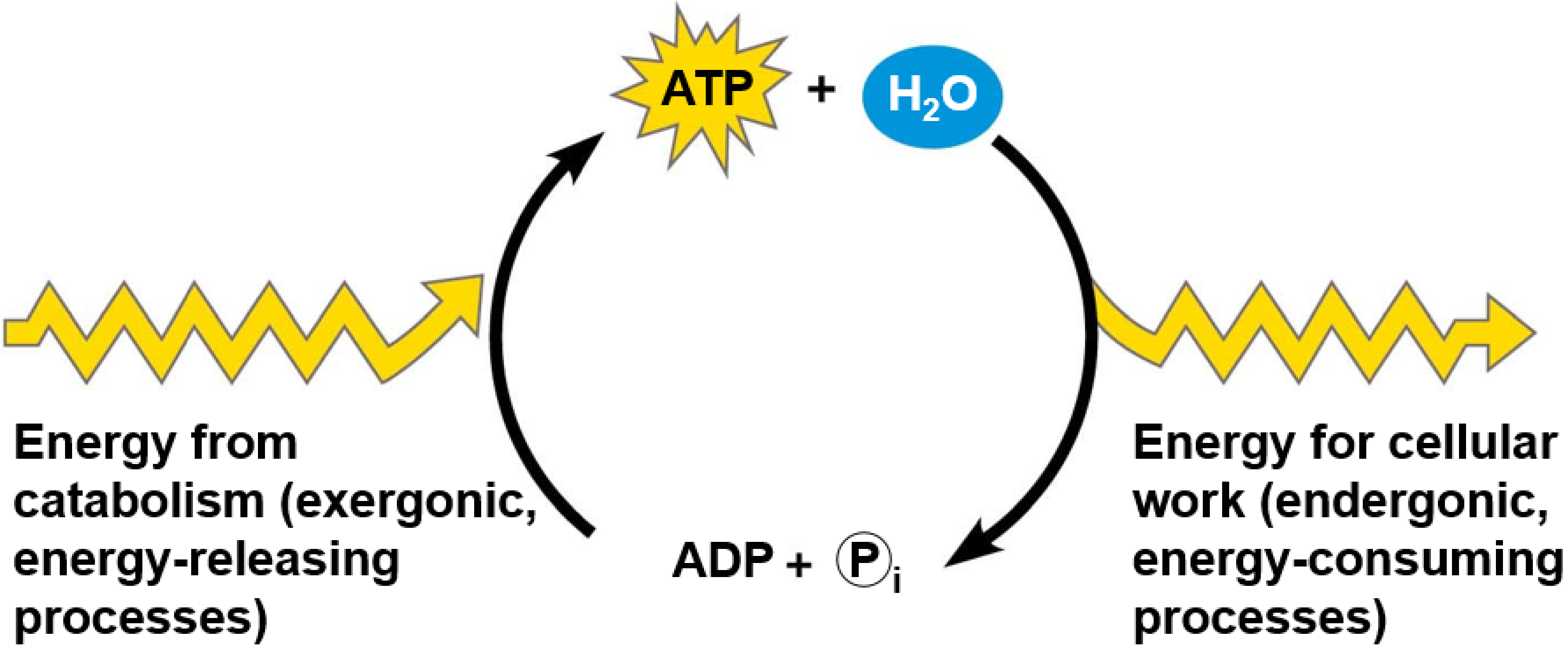


(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed.

The Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP)
- The energy to phosphorylate ADP comes from catabolic reactions in the cell
- The ATP cycle is a revolving door through which energy passes during its transfer from catabolic to anabolic pathways

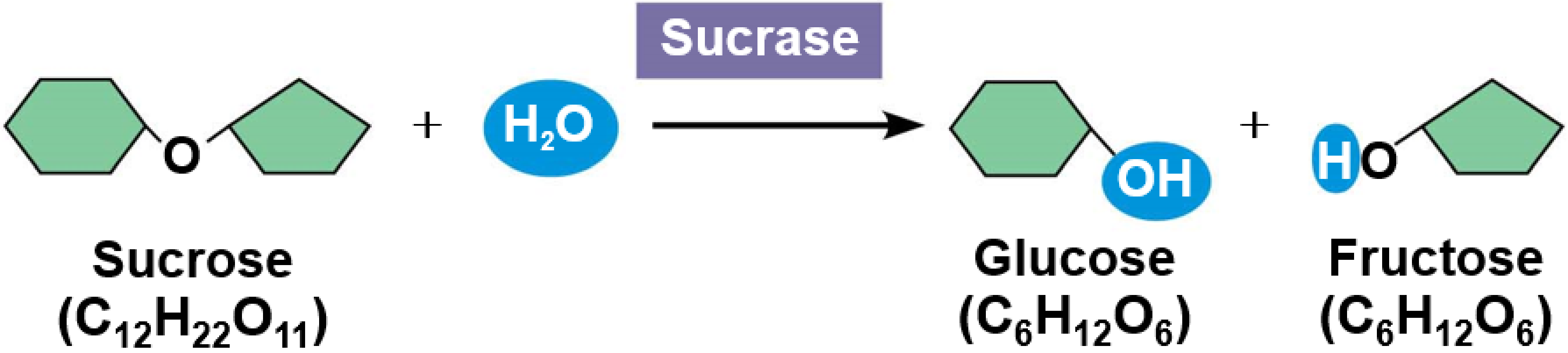
Figure 6.11 The ATP Cycle



Concept 6.4: Enzymes speed up metabolic reactions by lowering energy barriers

- A **catalyst** is a chemical agent that speeds up a reaction without being consumed by the reaction
- An **enzyme** is a catalytic protein
- Hydrolysis of sucrose by the enzyme sucrose is an example of an enzyme-catalyzed reaction

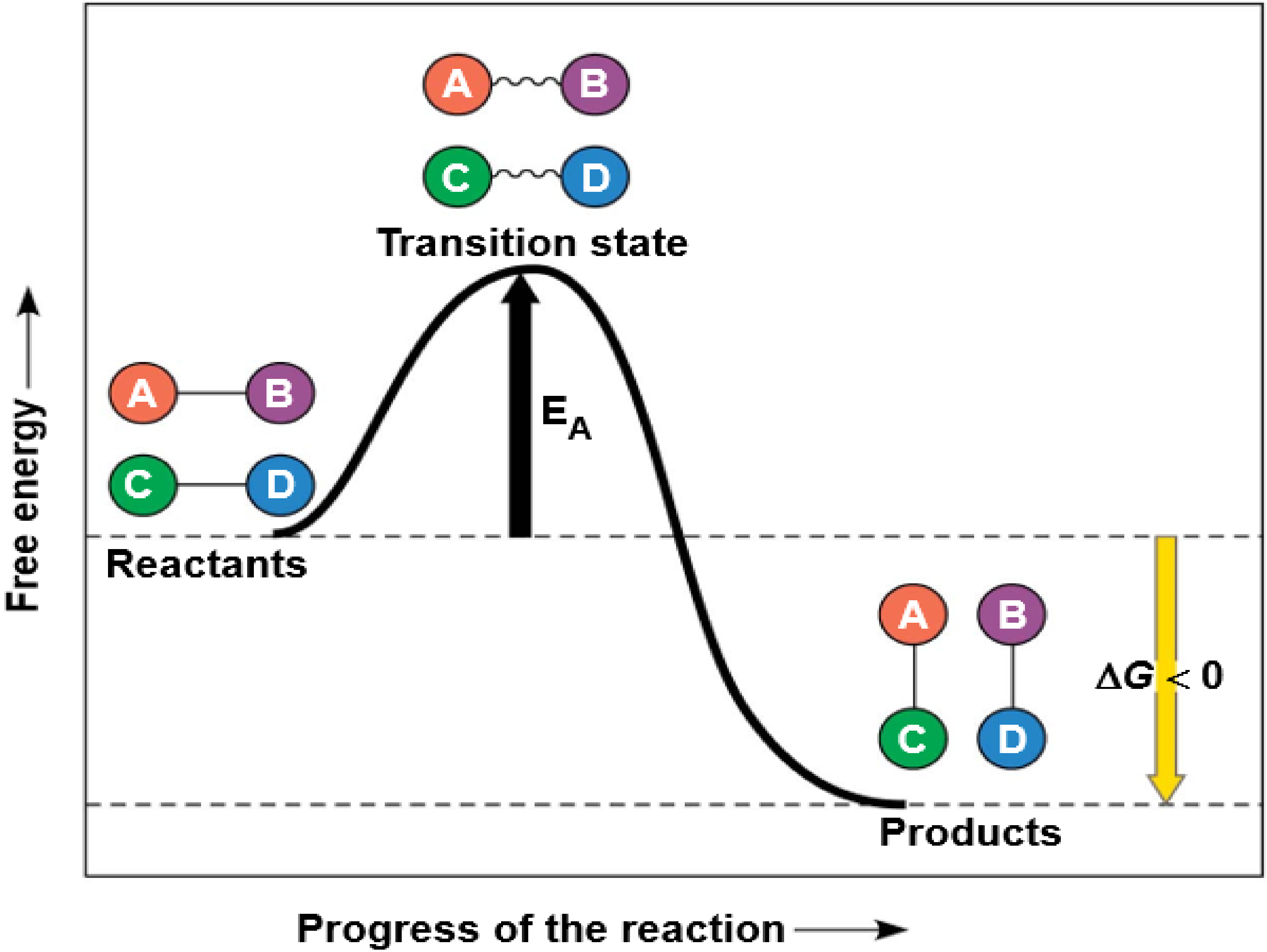
Figure 6.UN02 In-Text Figure, Sucrose Hydrolysis, p. 131



The Activation Energy Barrier

- Every chemical reaction between molecules involves bond breaking and bond forming
- The initial energy needed to start a chemical reaction is called the free energy of activation, or **activation energy** (E_A)
- Activation energy often occurs in the form of heat that reactant molecules absorb from the surroundings

Figure 6.12 Energy Profile of an Exergonic Reaction



How Enzymes Speed Up Reactions

- Instead of relying on heat, organisms carry out **catalysis** to speed up reactions
- A catalyst (for example, an enzyme) can speed up a reaction by lowering the E_A barrier without itself being consumed
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually

Animation: How Enzymes Work

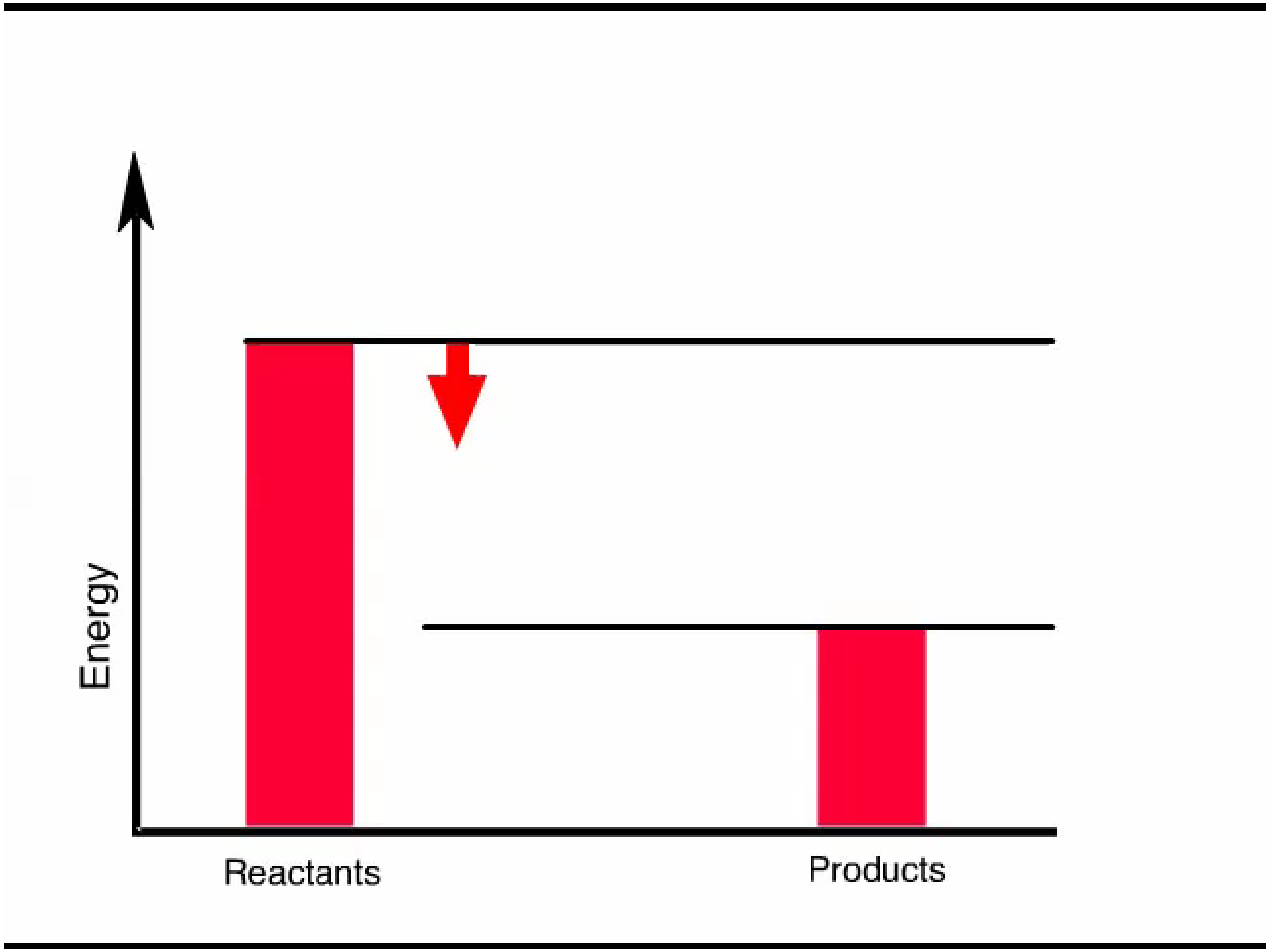
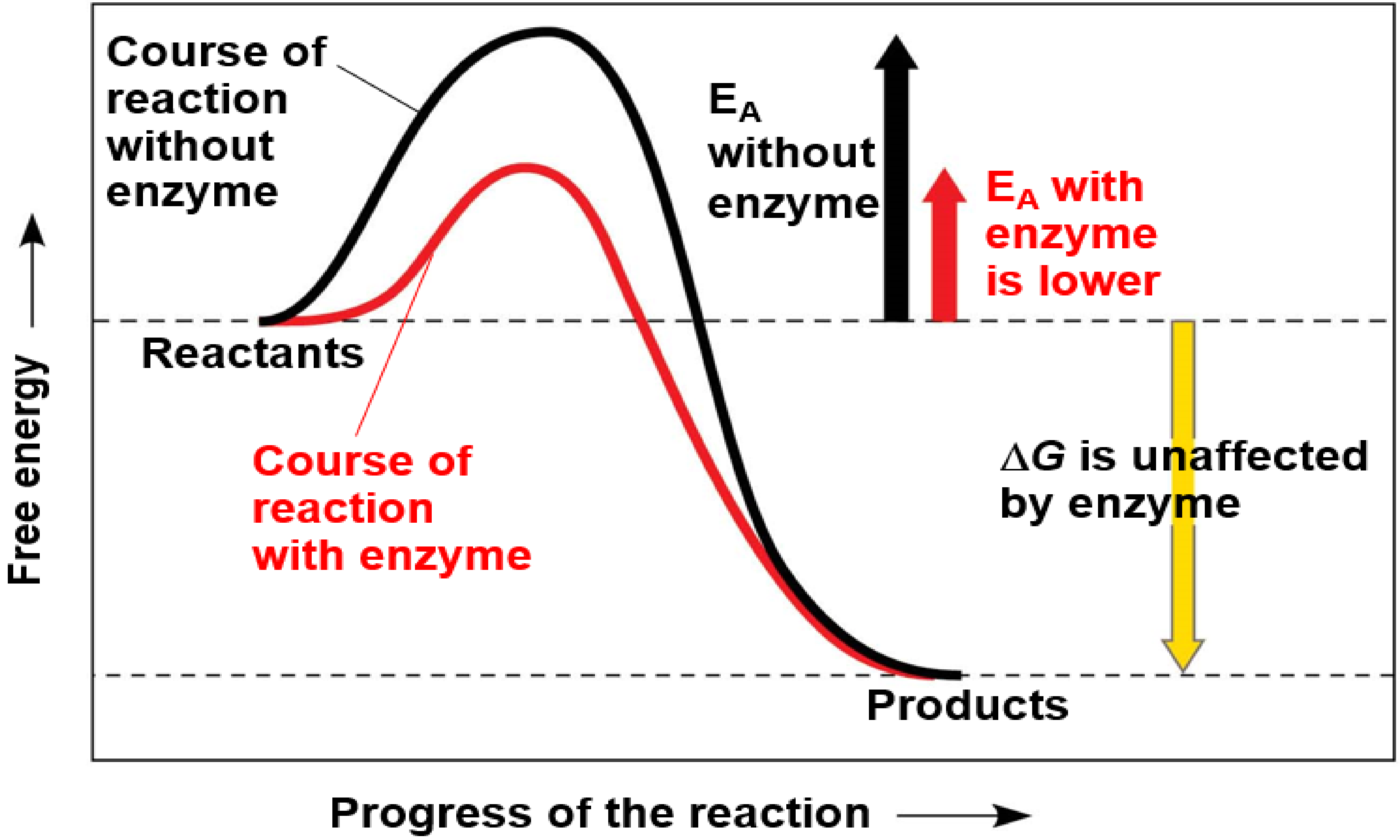


Figure 6.13 The Effect of an Enzyme on Activation Energy



Substrate Specificity of Enzymes

- Enzymes are very specific for the reactions they catalyze
- The reactant that an enzyme acts on is called the enzyme's **substrate**
- The enzyme binds to its substrate, forming an **enzyme-substrate complex**
- The **active site** is the region on the enzyme where the substrate binds

Substrate Specificity of Enzymes, Continued

- Enzyme specificity results from the complementary fit between the shape of the enzyme’s active site and the shape of the substrate
- Enzymes change shape due to chemical interactions with the substrate
- This **induced fit** of the enzyme to the substrate brings chemical groups of the active site together

Video: Enzyme Induced Fit

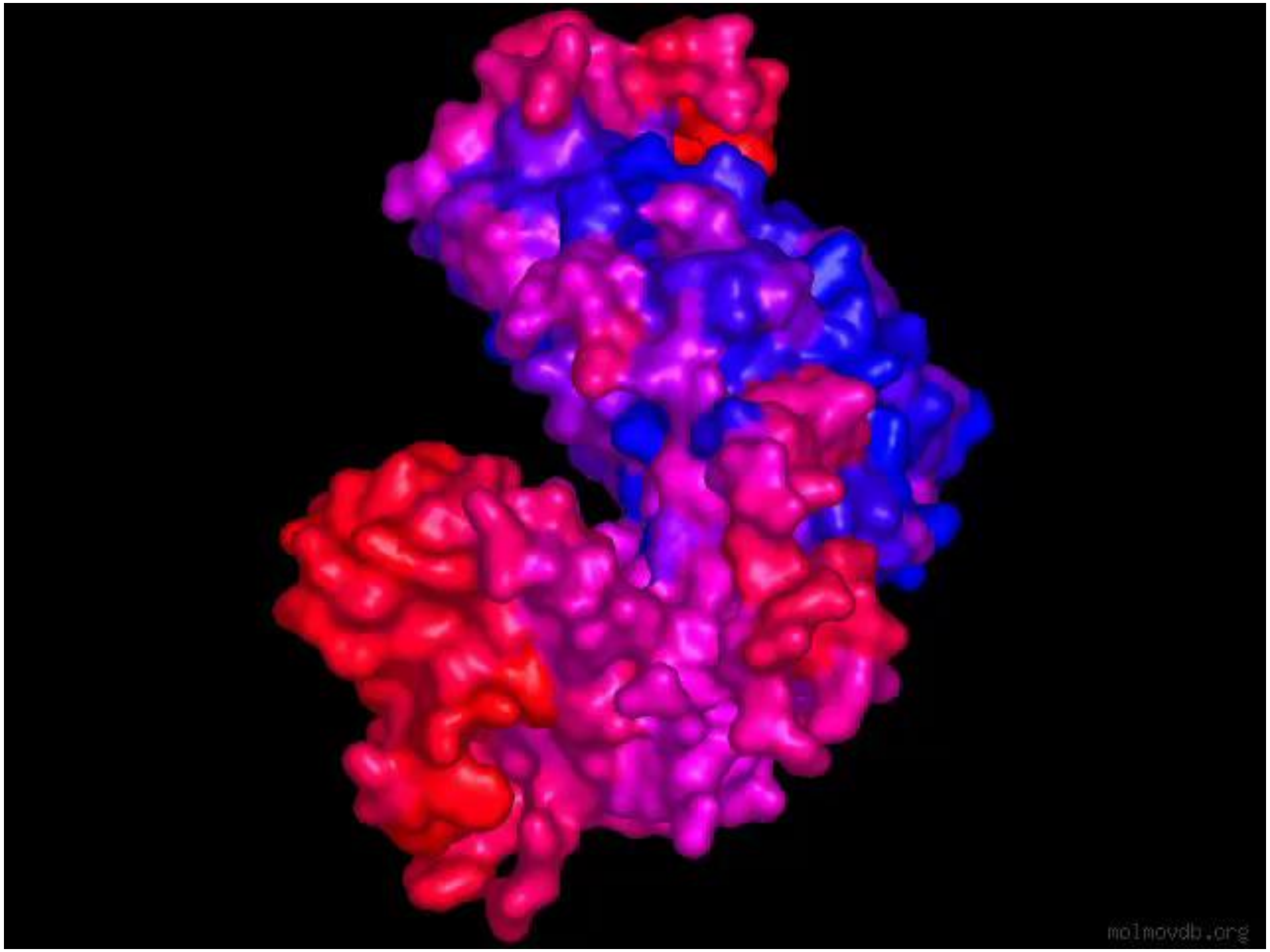
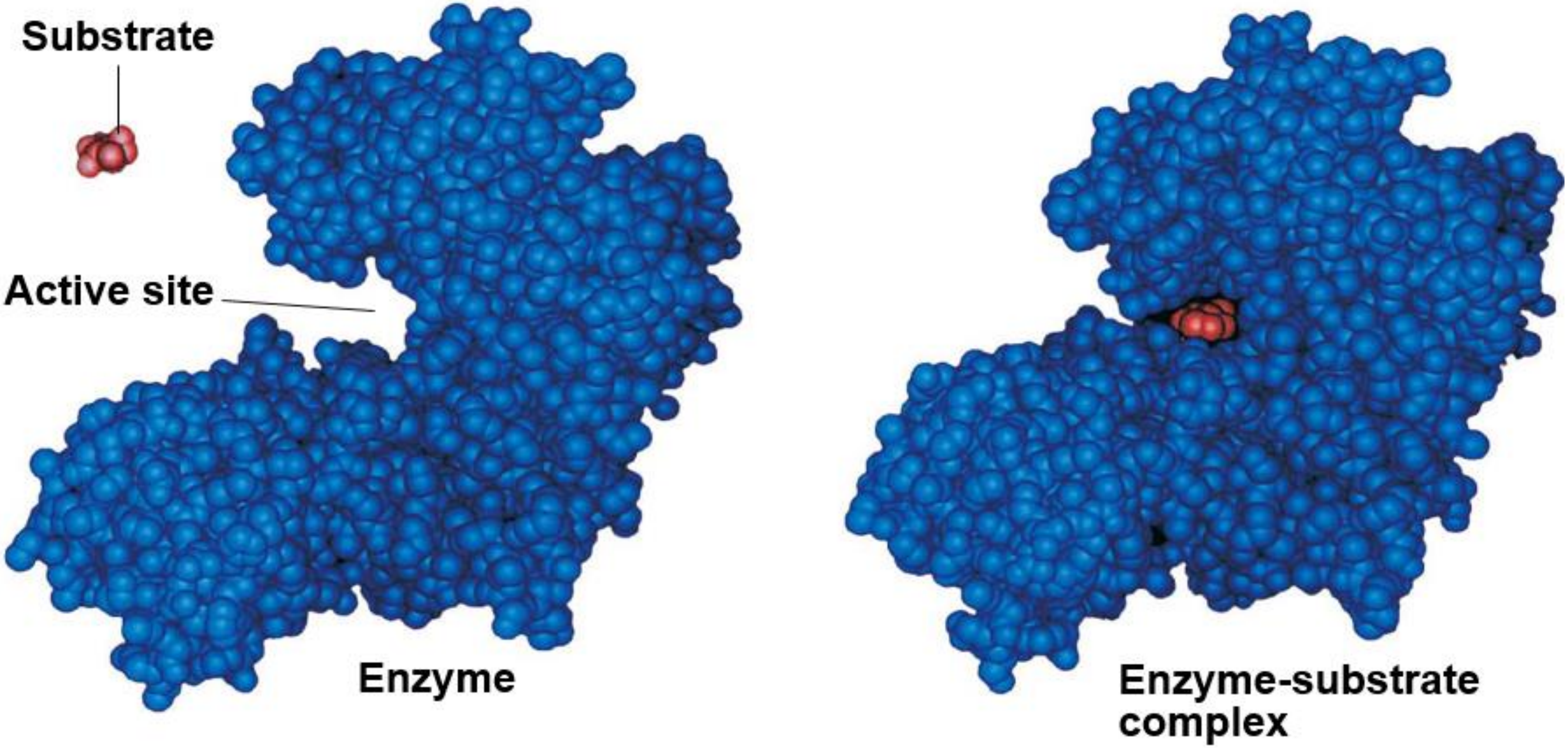


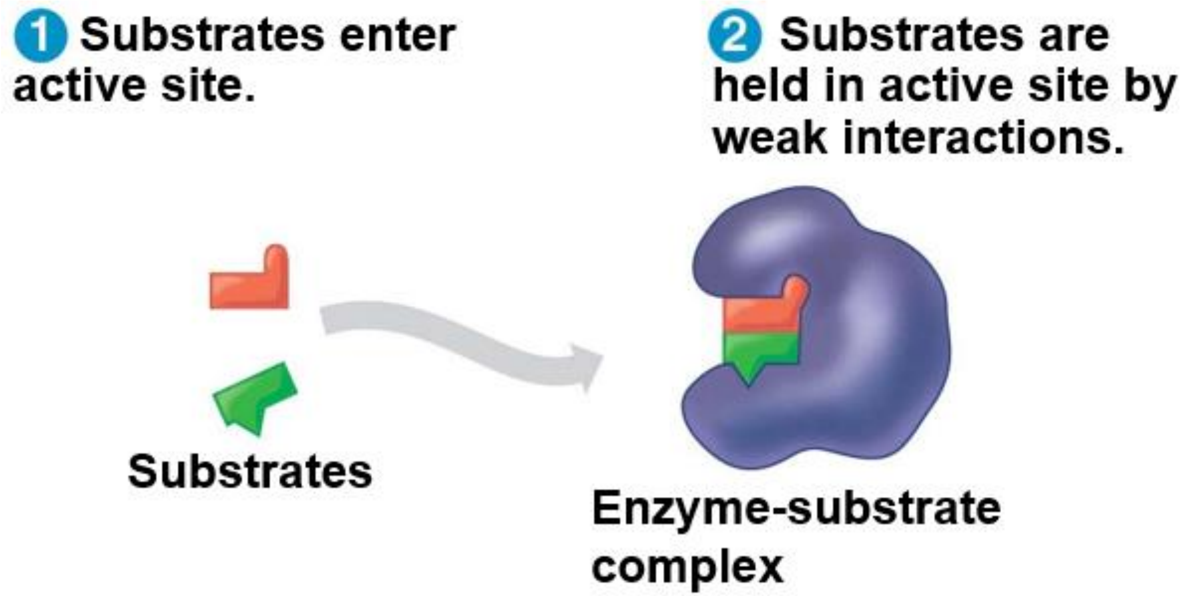
Figure 6.14 Induced Fit Between an Enzyme and its Substrate



Catalysis in the Enzyme's Active Site

- In an enzymatic reaction, the substrate binds to the active site of the enzyme
- The active site can lower an E_A barrier by
    - Orienting substrates correctly
    - Straining substrate bonds
    - Providing a favorable microenvironment
    - Covalently bonding to the substrate

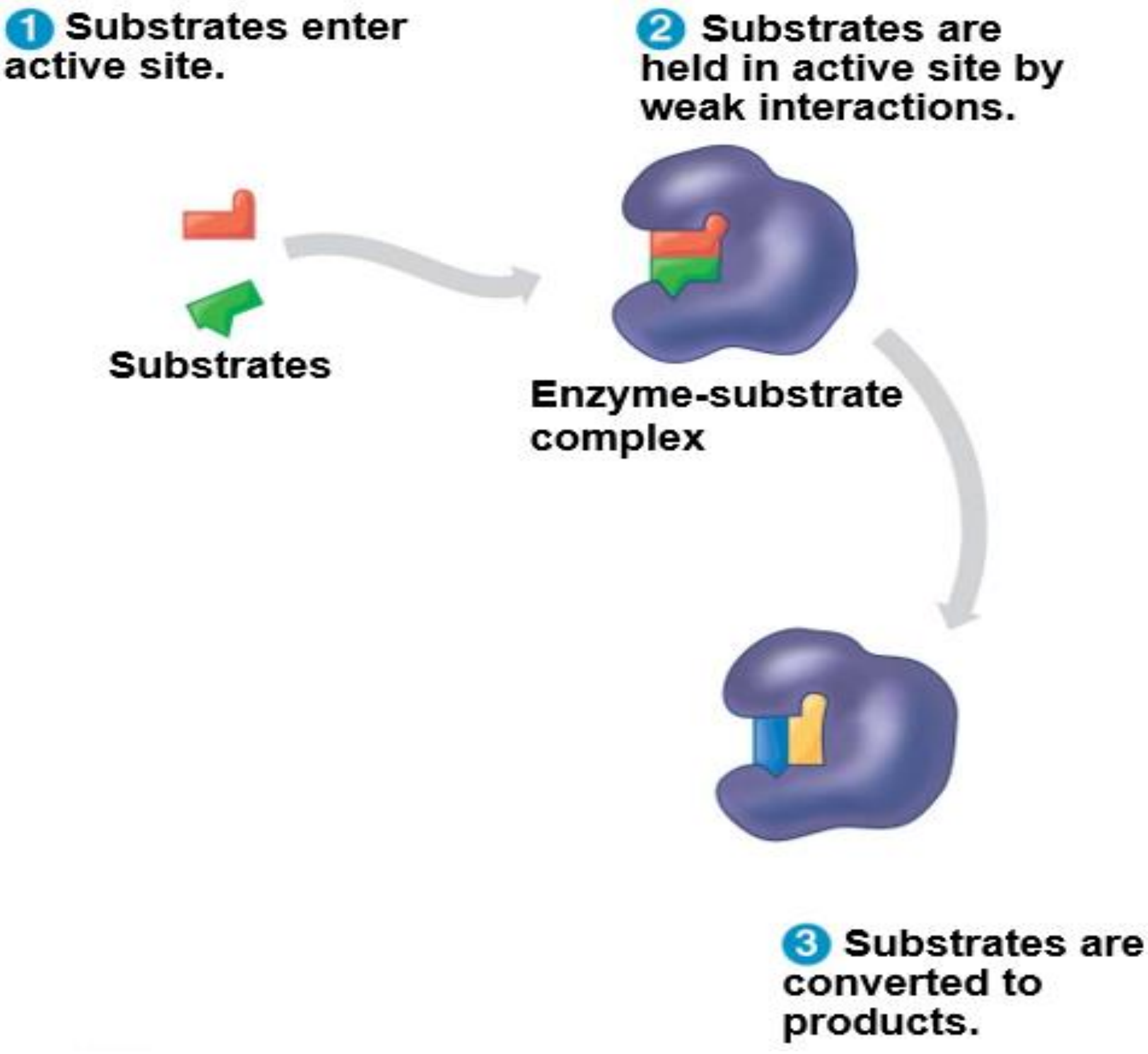
Figure 6.15-s1 The Active Site and Catalytic Cycle of An Enzyme (Step 1)



① Substrates enter active site.

② Substrates are held in active site by weak interactions.

Figure 6.15-s2 The Active Site and Catalytic Cycle of An Enzyme (Step 2)



① Substrates enter active site.

② Substrates are held in active site by weak interactions.

③ Substrates are converted to products.

Figure 6.15-s3 The Active Site and Catalytic Cycle of An Enzyme (Step 3)

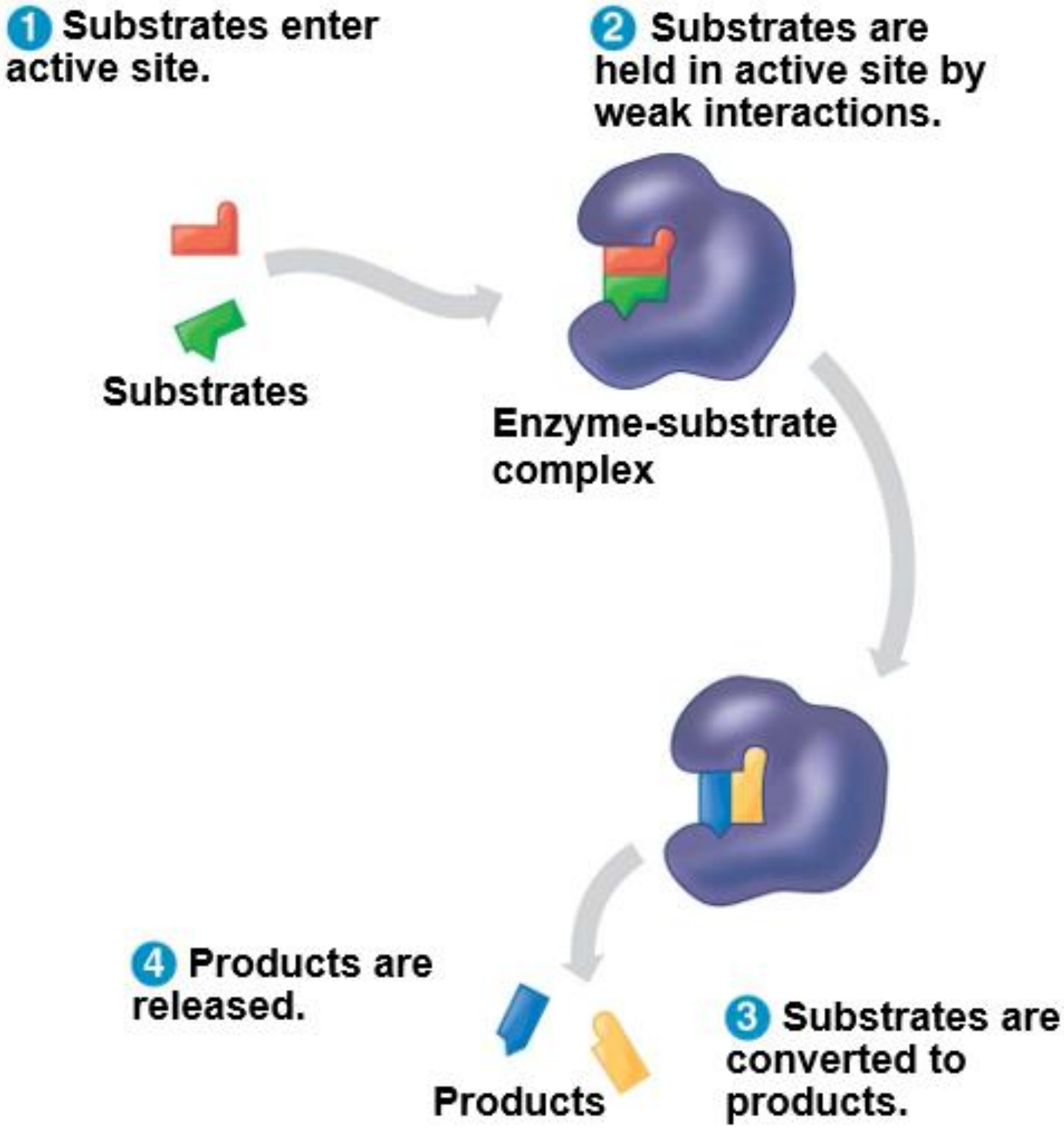
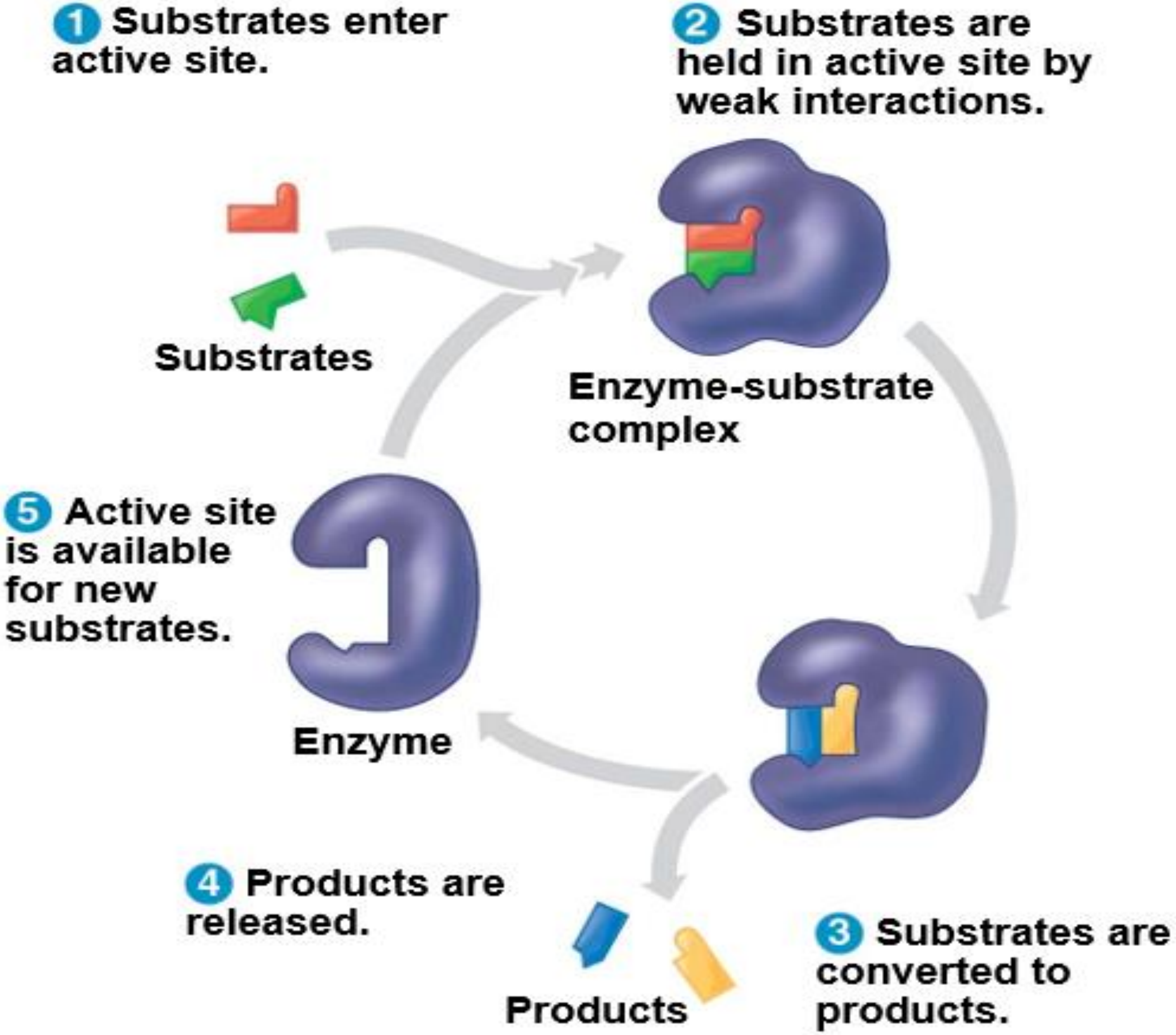


Figure 6.15-s4 The Active Site and Catalytic Cycle of An Enzyme (Step 4)



① Substrates enter active site.

② Substrates are held in active site by weak interactions.

③ Substrates are converted to products.

④ Products are released.

⑤ Active site is available for new substrates.

Catalysis in the Enzyme's Active Site, Continued

- The rate of enzyme catalysis can usually be sped up by increasing the substrate concentration in a solution
- When all enzyme molecules in a solution are bonded with substrate, the enzyme is saturated
- At enzyme saturation, reaction speed can only be increased by adding more enzyme

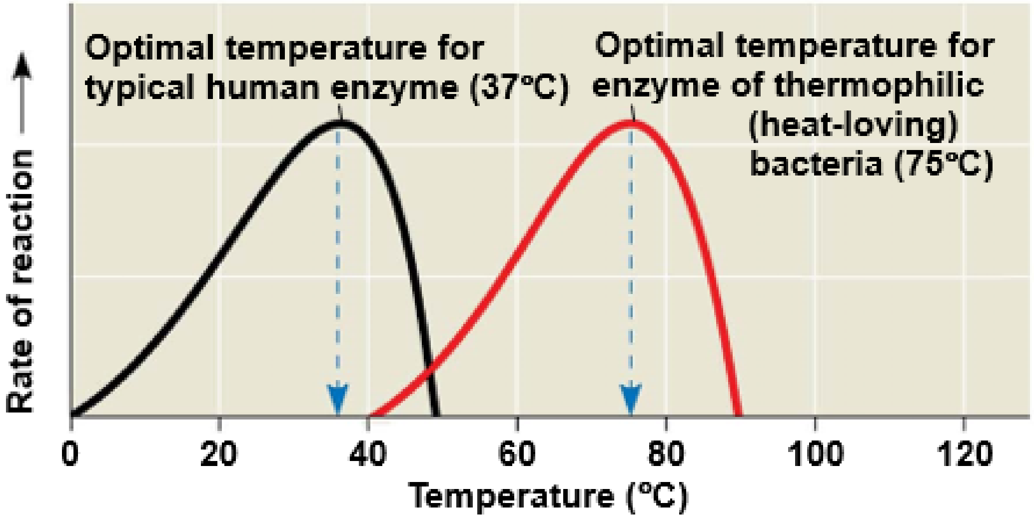
Effects of Local Conditions on Enzyme Activity

- An enzyme’s activity can be affected by
  - General environmental factors, such as temperature and pH
  - Chemicals that specifically influence the enzyme

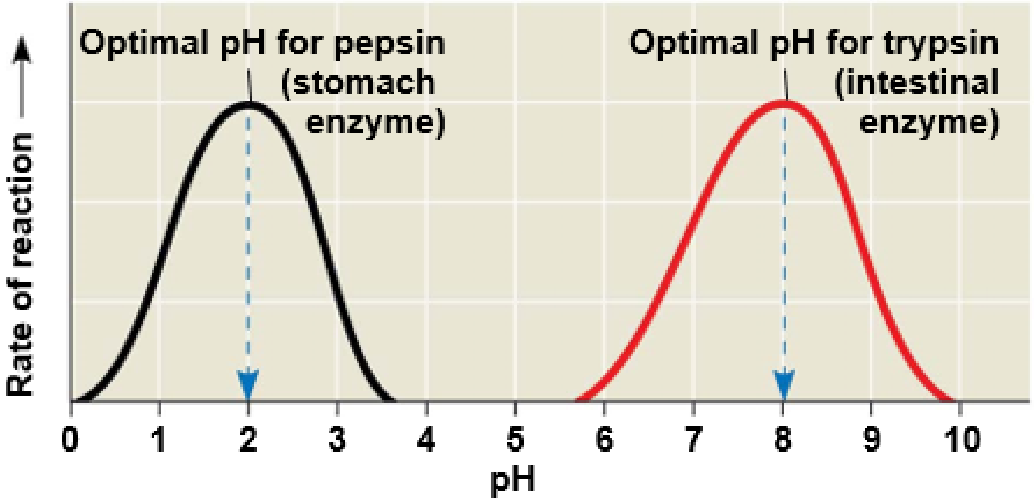
Effects of Temperature and pH

- Each enzyme has an optimal temperature and pH at which its reaction rate is the greatest

Figure 6.16 Environmental Factors Affecting Enzyme Activity

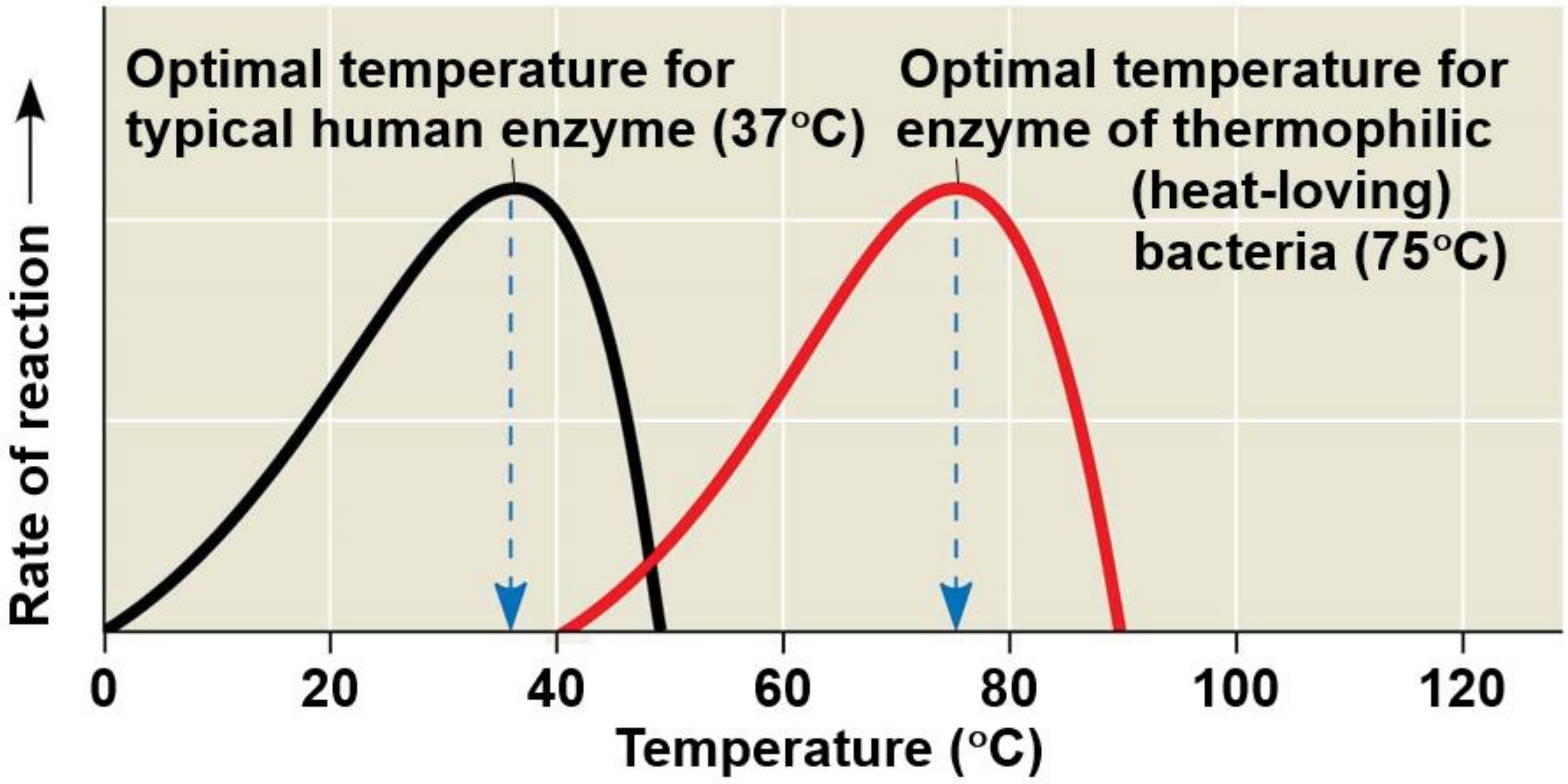


(a) Optimal temperature for two enzymes



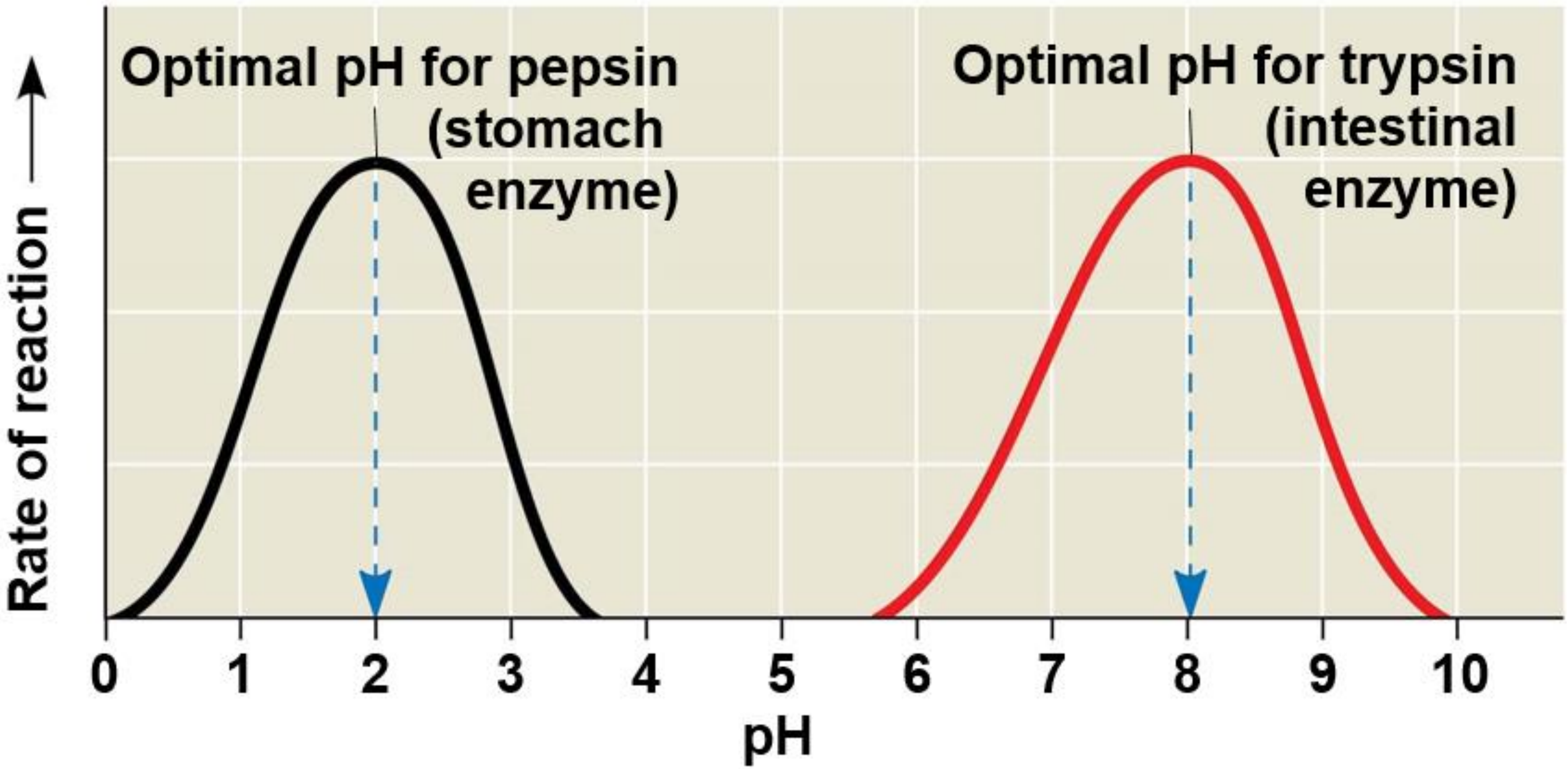
(b) Optimal pH for two enzymes

Figure 6.16-1 Environmental Factors Affecting Enzyme Activity (Part 1: Temperature)



(a) Optimal temperature for two enzymes

Figure 6.16-2 Environmental Factors Affecting Enzyme Activity (Part 2: pH)



(b) Optimal pH for two enzymes

Figure 6.16-3 Environmental Factors Affecting Enzyme Activity (Part 3: Cyanobacteria)

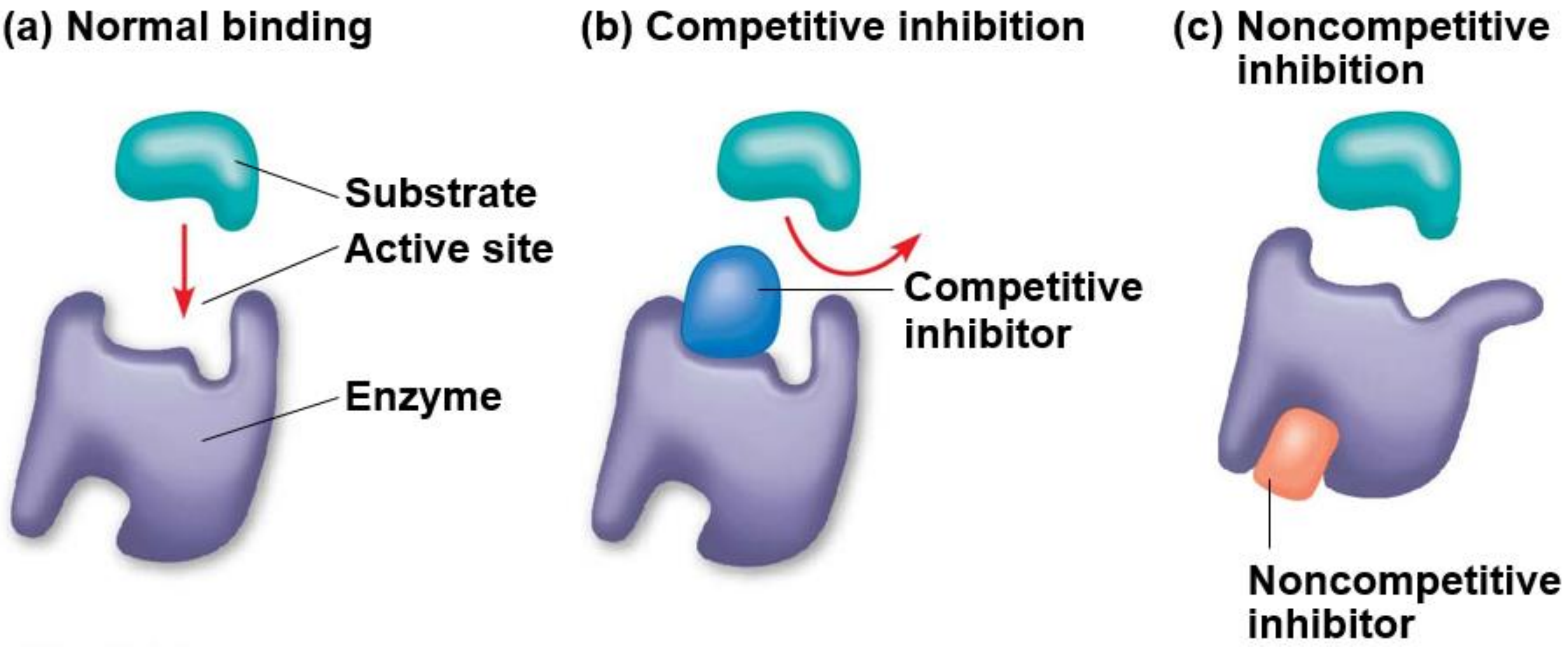
Cofactors

- **Cofactors** are nonprotein enzyme helpers
- Cofactors may be inorganic (such as a metal in ionic form) or organic
- An organic cofactor is called a **coenzyme**
- Most vitamins act as coenzymes or as the raw materials from which coenzymes are made

Enzyme Inhibitors

- **Competitive inhibitors** bind to the active site of an enzyme, competing with the substrate
- **Noncompetitive inhibitors** bind to another part of an enzyme, causing the enzyme to change shape and making the active site less effective
- Examples of inhibitors include toxins, poisons, pesticides, and antibiotics

Figure 6.17 Inhibition of Enzyme Activity



The Evolution of Enzymes

- Most enzymes are proteins encoded by genes
- Changes (mutations) in genes lead to changes in amino acid composition of an enzyme
- Altered amino acids in enzymes may alter their activity or substrate specificity
- Under new environmental conditions a novel form of an enzyme might be favored

Concept 6.5: Regulation of enzyme activity helps control metabolism

- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated
- A cell does this by switching on or off the genes that encode specific enzymes or by regulating the activity of enzymes

Allosteric Regulation of Enzymes

- **Allosteric regulation** may either inhibit or stimulate an enzyme's activity
- Allosteric regulation occurs when a regulatory molecule binds to a protein at one site and affects the protein's function at another site

Allosteric Activation and Inhibition

- Most allosterically regulated enzymes are made from polypeptide subunits
- Each enzyme has active and inactive forms
- The binding of an activator stabilizes the active form of the enzyme
- The binding of an inhibitor stabilizes the inactive form of the enzyme

Figure 6.18 Allosteric Regulation of Enzyme Activity

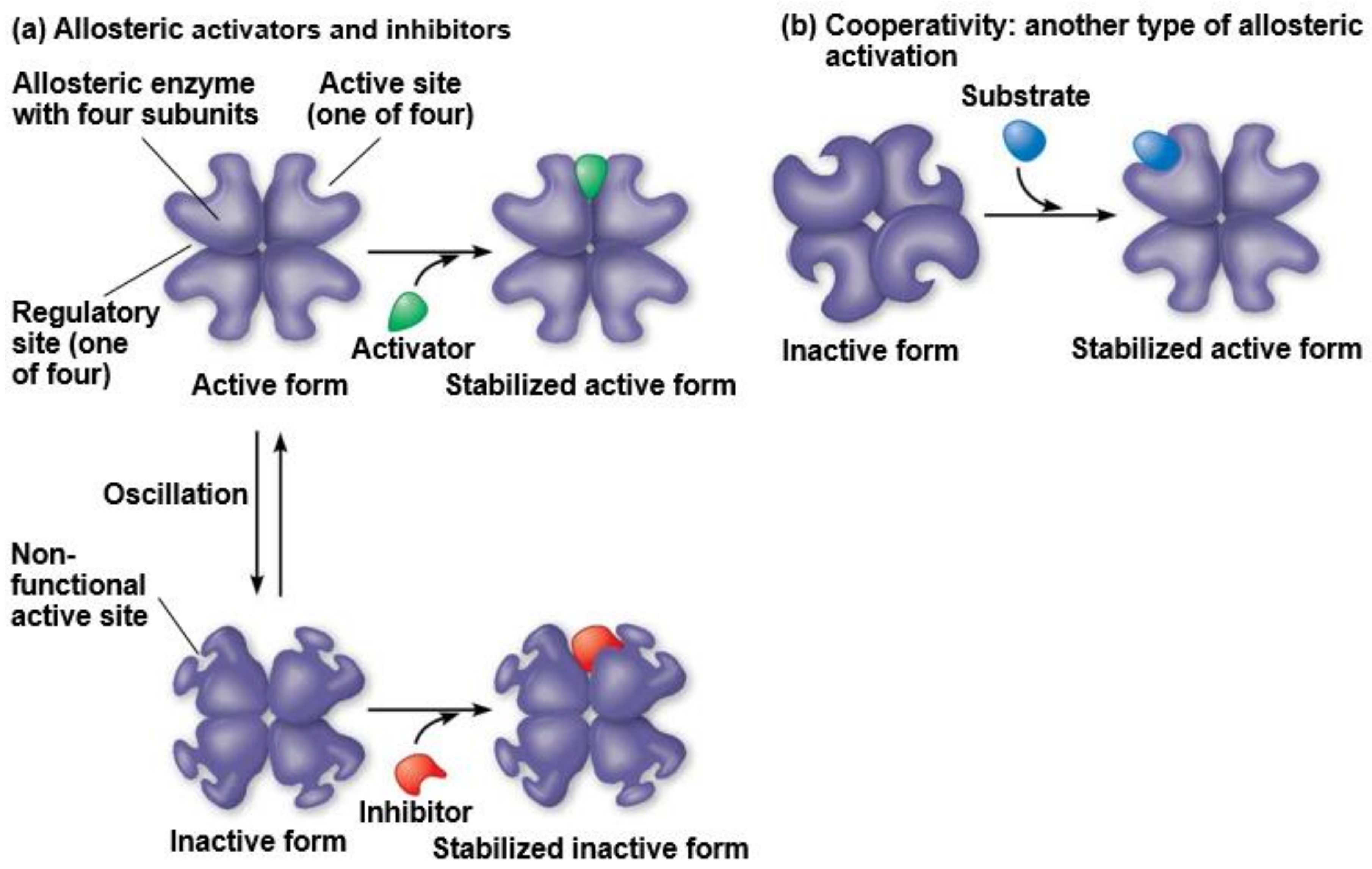
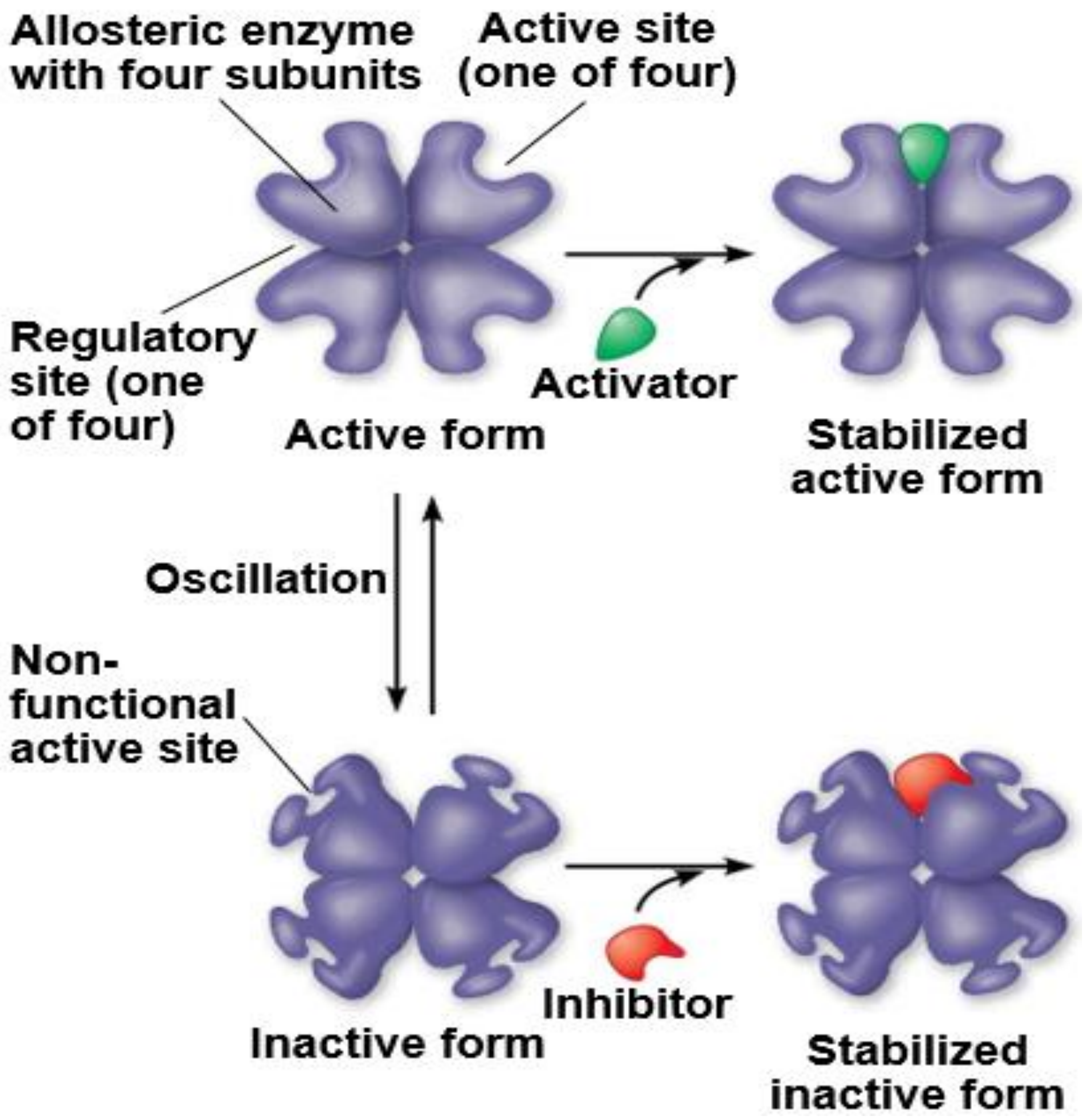


Figure 6.18-1 Allosteric Regulation of Enzyme Activity (Part 1: Activation and Inhibition)

(a) Allosteric activators and inhibitors

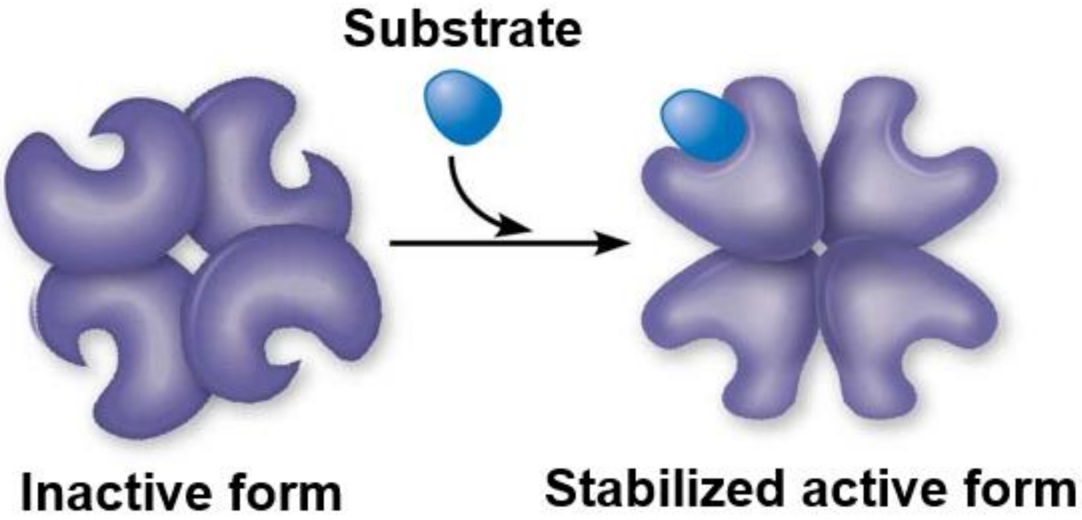


Allosteric Activation and Inhibition, Continued

- **Cooperativity** is a form of allosteric regulation that can amplify enzyme activity
- One substrate molecule primes an enzyme to act on additional substrate molecules more readily
- Cooperativity is allosteric because binding by a substrate to one active site affects catalysis in a different active site

Figure 6.18-2 Allosteric Regulation of Enzyme Activity (Part 2: Cooperativity)

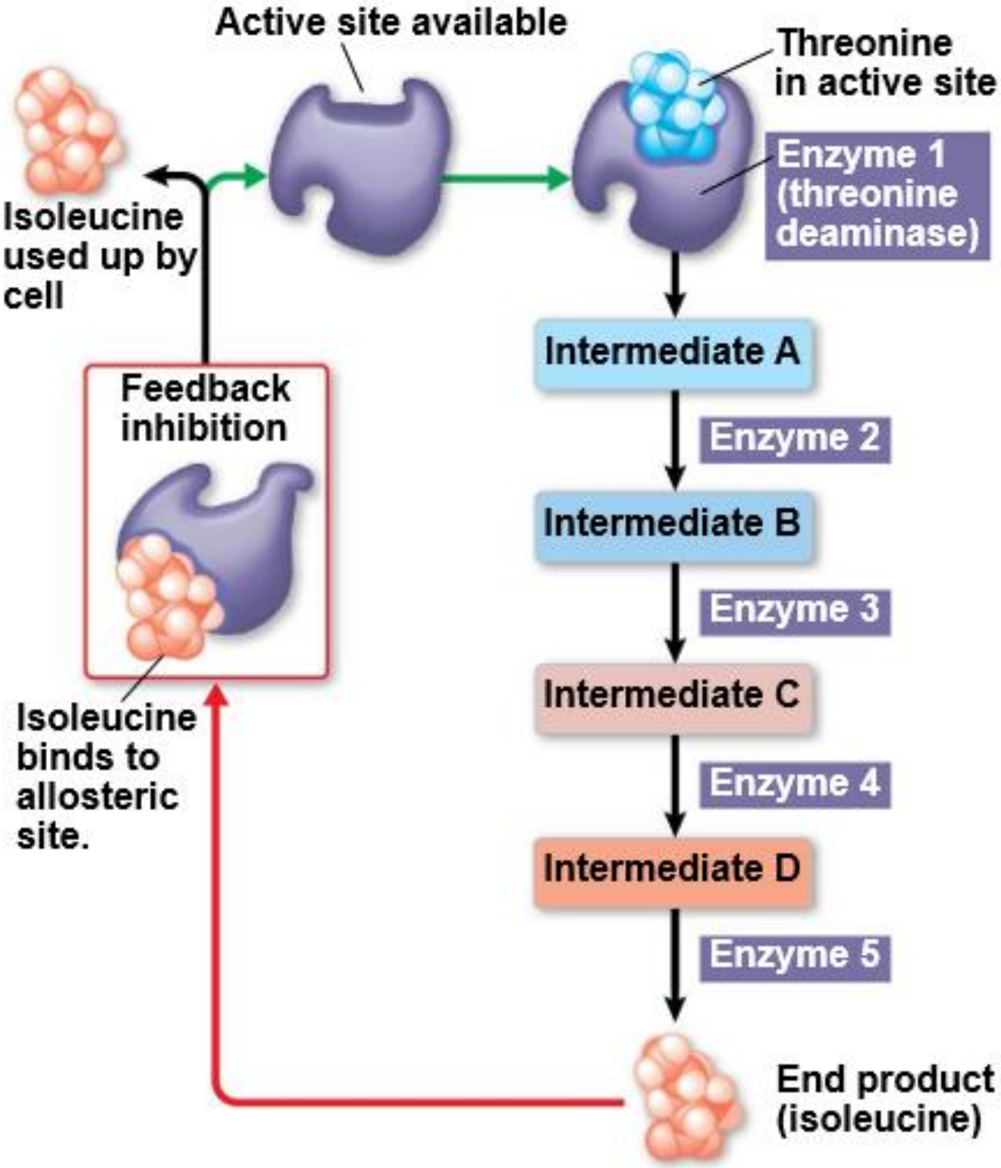
(b) Cooperativity: another type of allosteric activation



Feedback Inhibition

- In **feedback inhibition**, the end product of a metabolic pathway shuts down the pathway
- Feedback inhibition prevents a cell from wasting chemical resources by synthesizing more product than is needed

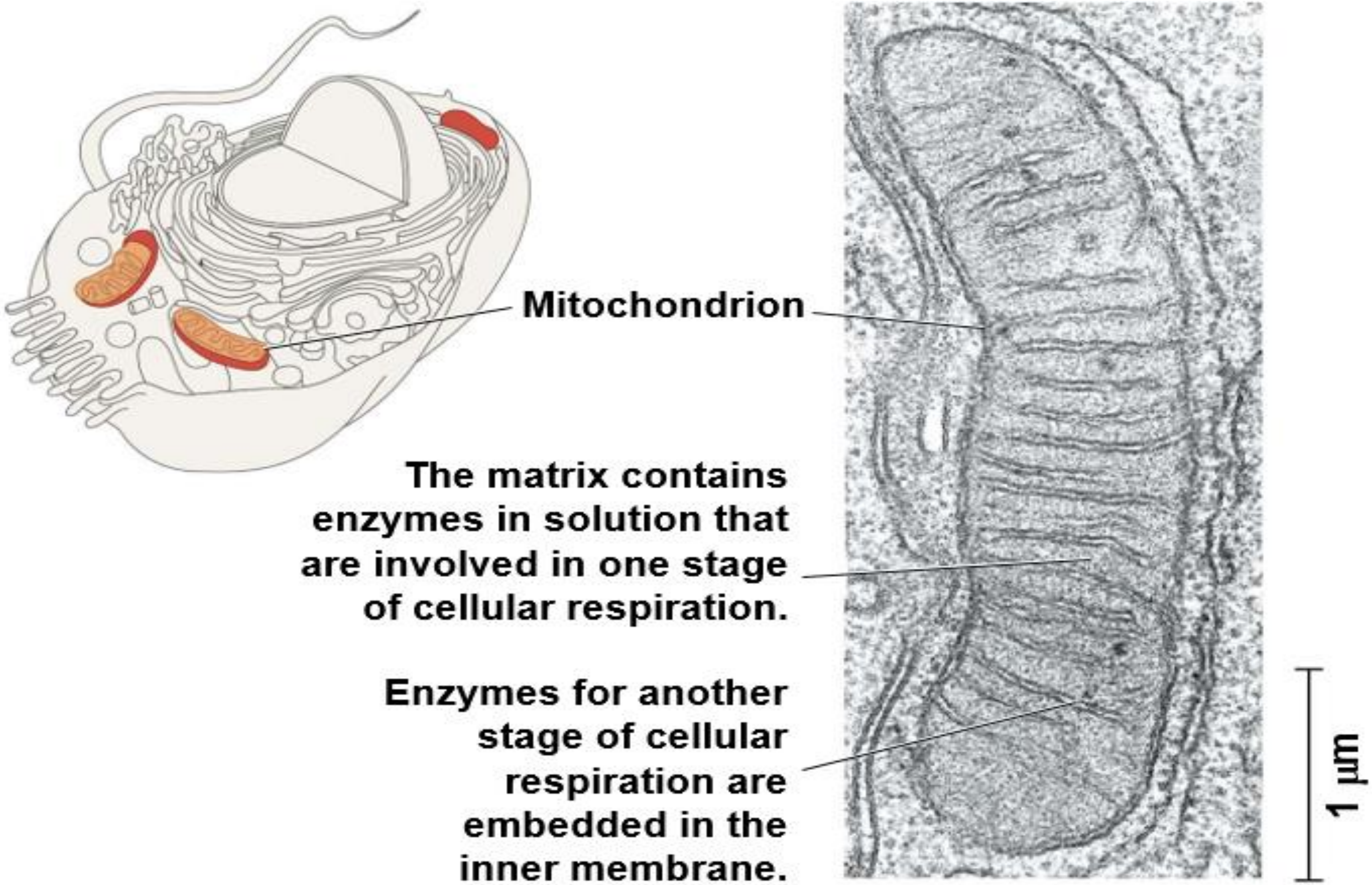
Figure 6.19 Feedback Inhibition in Isoleucine Synthesis



Organization of Enzymes Within the Cell

- Structures within the cell help bring order to metabolic pathways
- Some enzymes act as structural components of membranes
- In eukaryotic cells, some enzymes reside in specific organelles; for example, enzymes for cellular respiration are located in mitochondria

Figure 6.20 Organelles and Structural Order in Metabolism

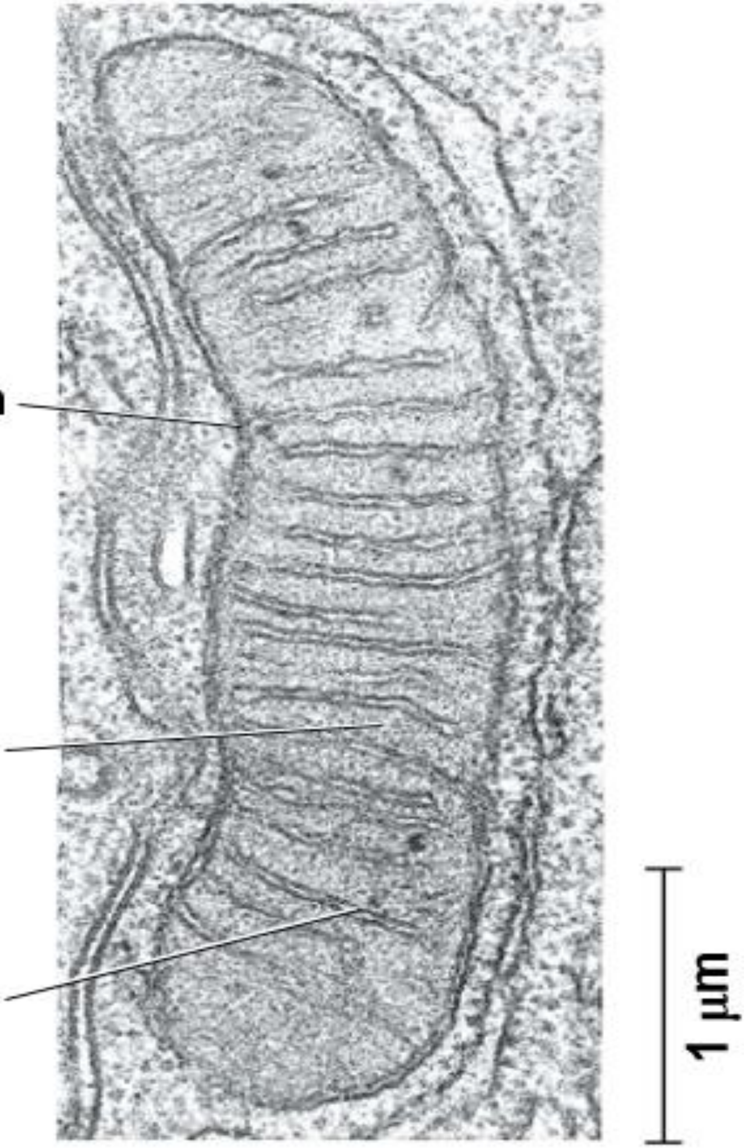


Mitochondrion

The matrix contains enzymes in solution that are involved in one stage of cellular respiration.

Enzymes for another stage of cellular respiration are embedded in the inner membrane.

Figure 6.20-1 Organelles and Structural Order in Metabolism (Part 1: TEM)



The matrix contains enzymes in solution that are involved in one stage of cellular respiration.

Enzymes for another stage of cellular respiration are embedded in the inner membrane.

Figure 6.UN03a Skills Exercise: Making a Line Graph and Calculating a Slope (Part 1)

Time (min)	Concentration of Ⓟ$_i$ (µmol/mL)
0	0
5	10
10	90
15	180
20	270
25	330
30	355
35	355
40	355

Data from S. R. Commerford et al., Diets enriched in sucrose or fat increase gluconeogenesis and G-6-Pase but not basal glucose production in rats, *American Journal of Physiology—Endocrinology and Metabolism* 283:E545–E555 (2002).

Figure 6.UN03b Skills Exercise: Making a Line Graph and Calculating a Slope (Part 2)

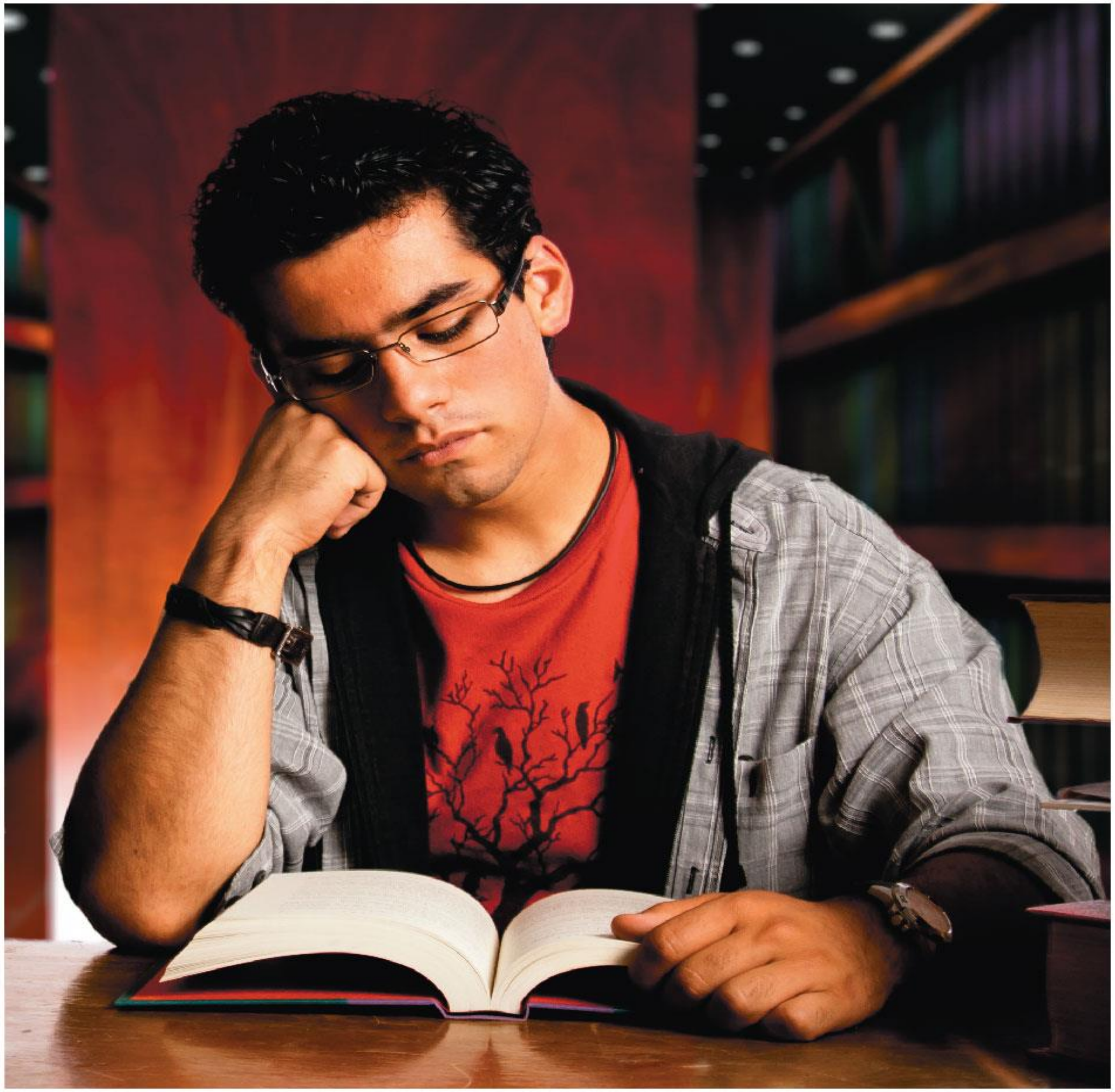


Figure 6.UN04 Summary of Key Concepts: Enzymes and Activation Energy

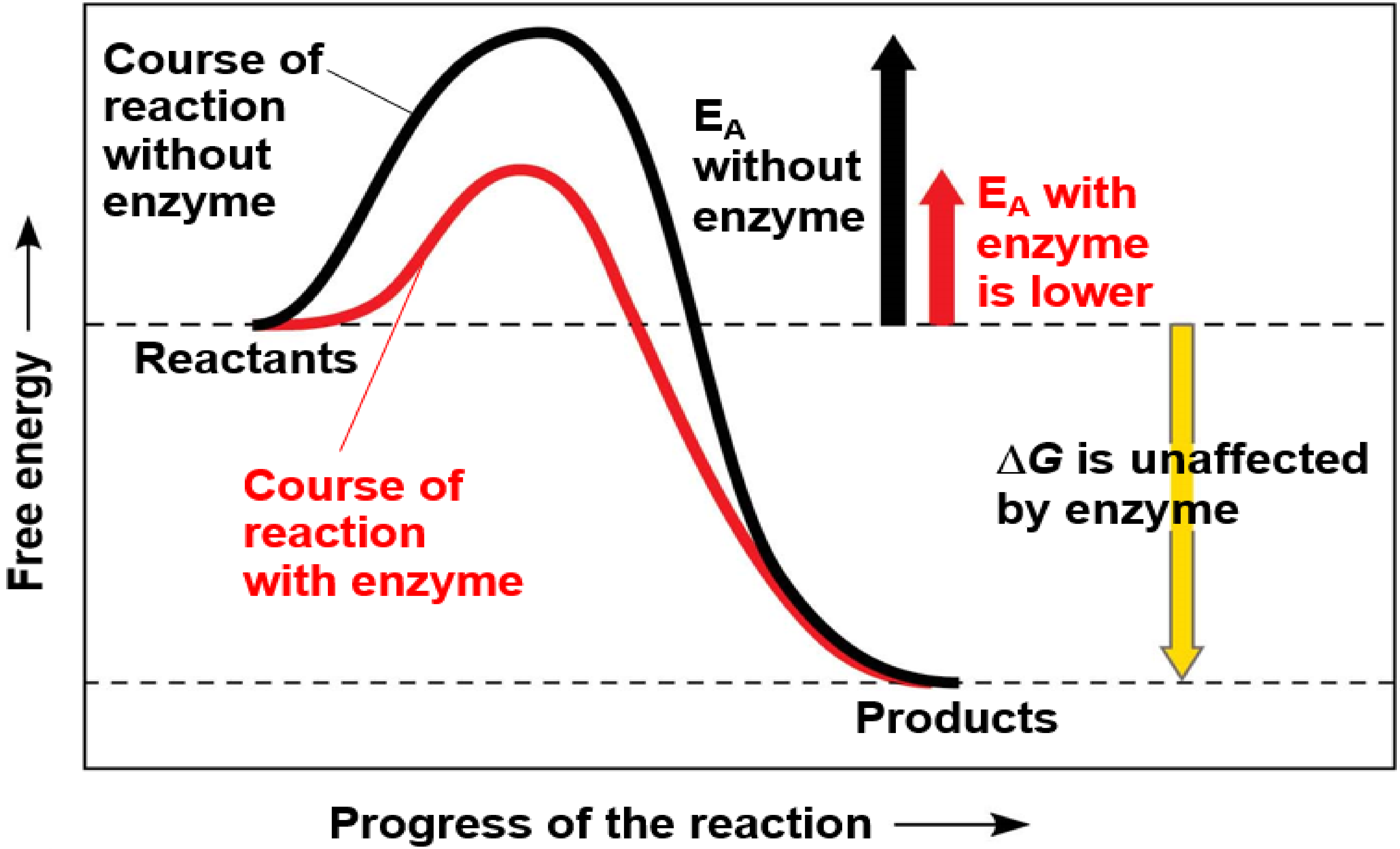


Figure 6.UN05 Test Your Understanding, Question 12 (Kinetic and Potential Energy)