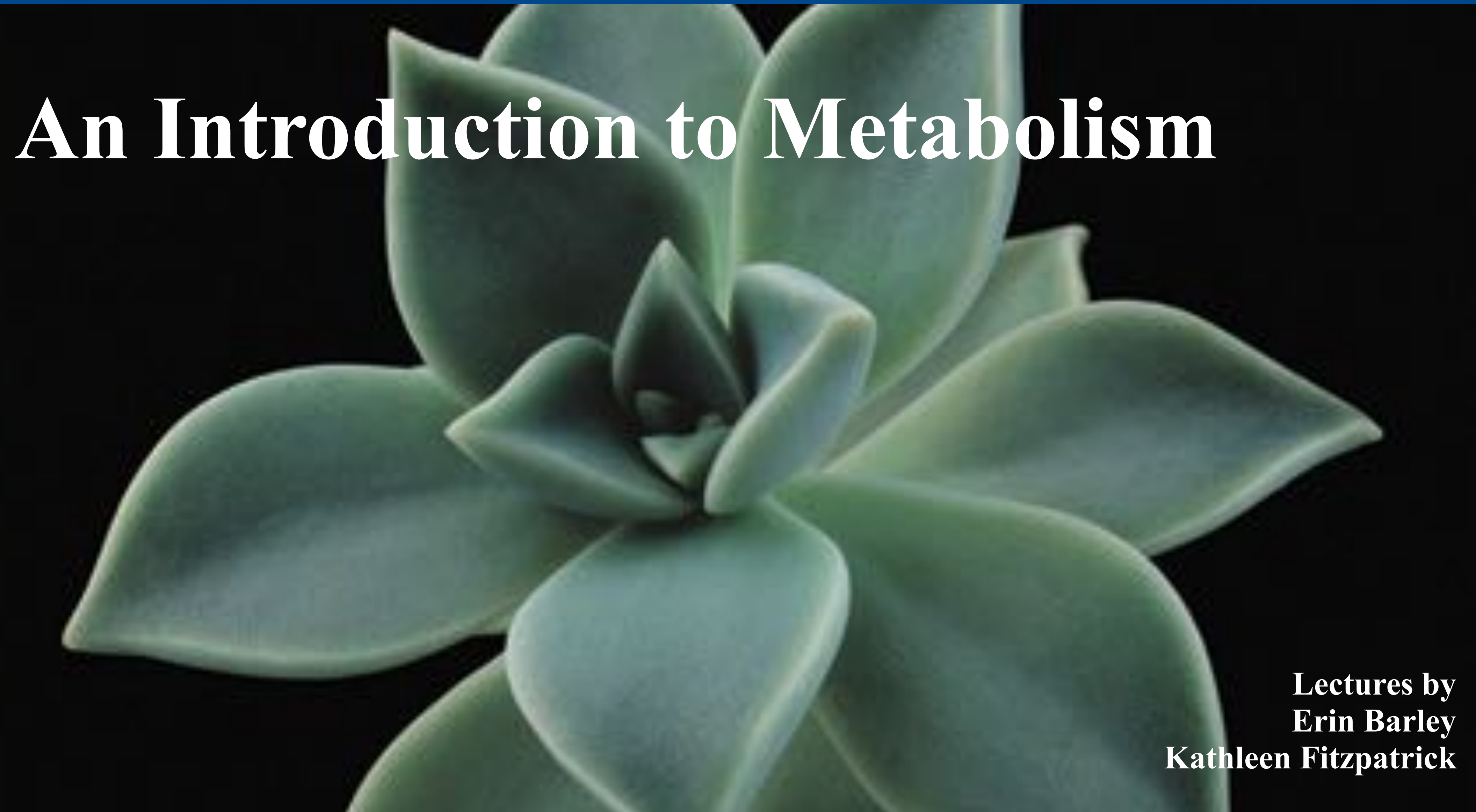
LECTURE PRESENTATIONS
For CAMPBELL BIOLOGY, NINTH EDITION
Jane B. Reece, Lisa A. Urry, Michael L. Cain, Steven A. Wasserman, Peter V. Minorsky, Robert B. Jackson

Chapter 8



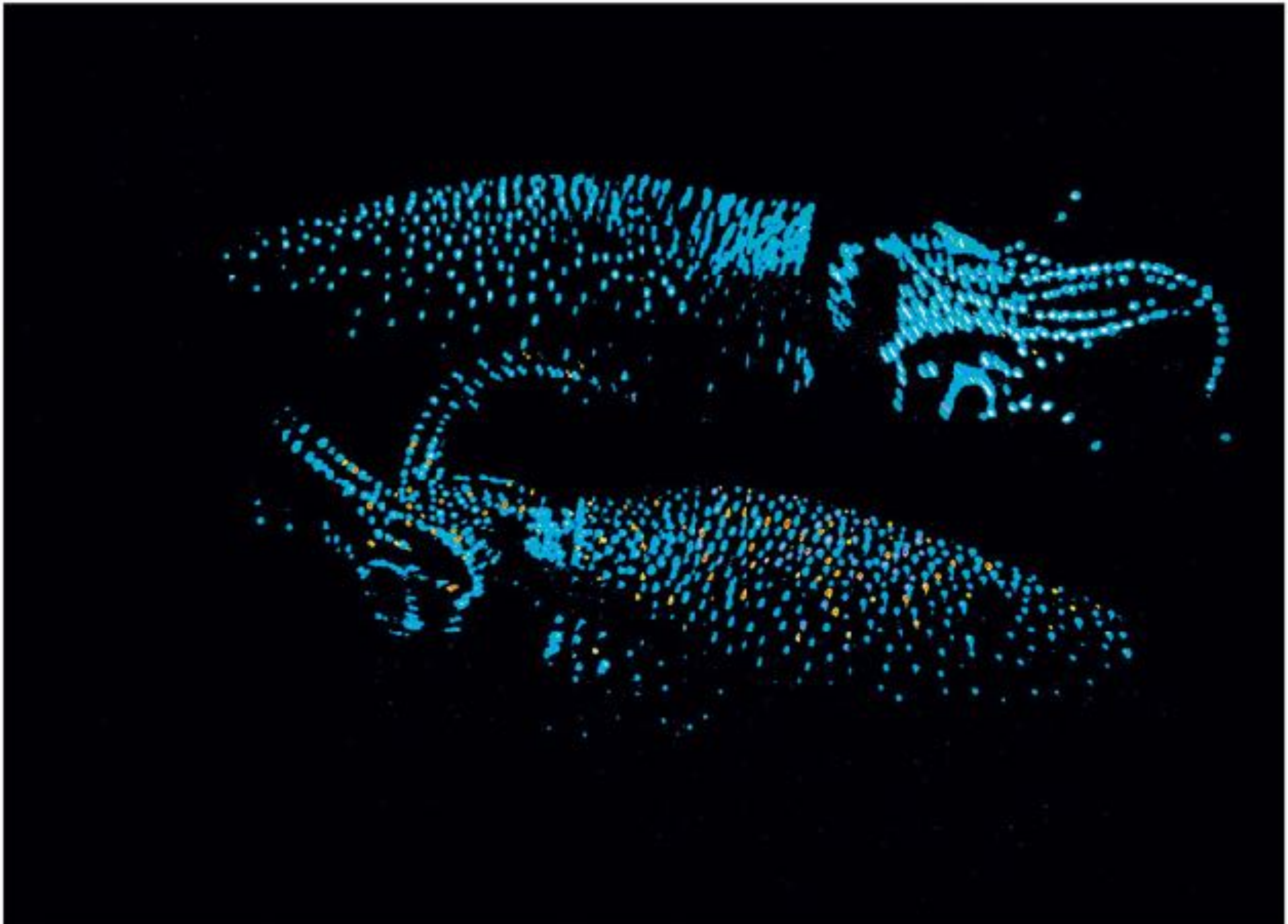
An Introduction to Metabolism

Lectures by
Erin Barley
Kathleen Fitzpatrick

Overview: 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 8.1



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

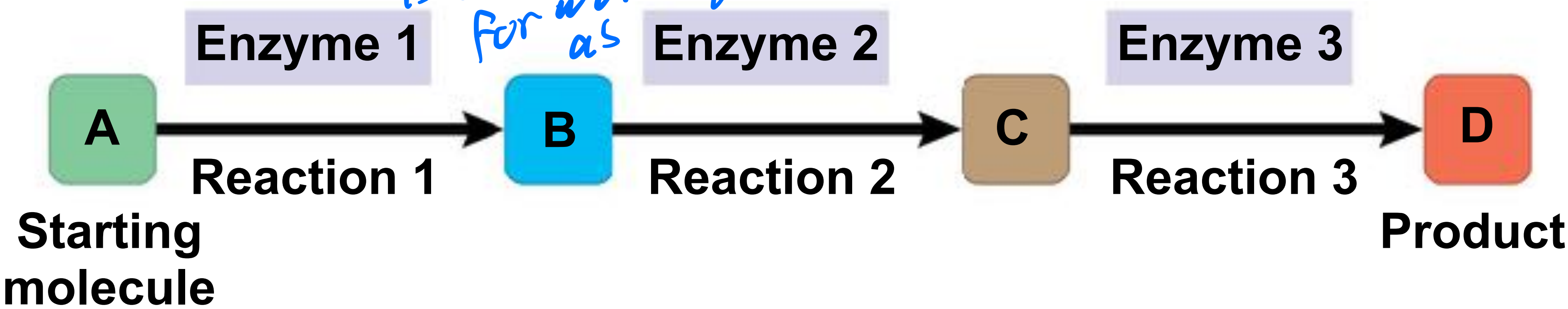
- **Metabolism** is the totality of an organism's chemical reactions
- Metabolism is an emergent property of life that arises from interactions between molecules within the cell

Organization of the Chemistry of Life into Metabolic Pathways

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

Figure 8.UN01

Suppose ΔG is positive
reaction can be "drawn" forward as $B \to C$



- **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds
- Cellular respiration, the breakdown of glucose in the presence of oxygen, is an example of a pathway of catabolism

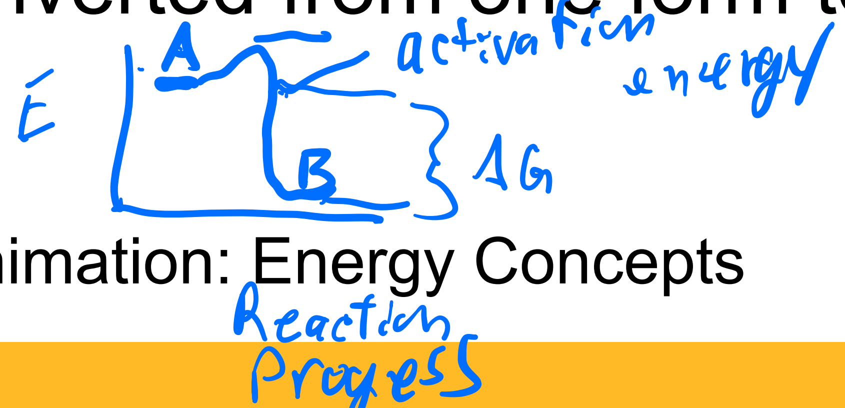
- **Anabolic pathways** consume energy to build complex molecules from simpler ones
- The synthesis of protein from amino acids is an example of anabolism
- **Bioenergetics** is the study of how organisms manage their energy resources

Forms of Energy

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

- **Kinetic energy** is energy associated with motion
- **Heat (thermal energy)** is kinetic energy associated with random movement of atoms or molecules
- **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

A → B



PLAY Animation: Energy Concepts

Figure 8.2


A diver has more potential energy on the platform than in the water.
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 than on the platform.

The Laws of Energy Transformation

- **Thermodynamics** is the study of energy transformations
- A isolated system, such as that approximated by liquid in a thermos, is isolated from its surroundings
- In an open system, energy and matter can be transferred between the system and its surroundings
- 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 transformed, but it cannot be created or destroyed*
- The first law is also called the principle of conservation of energy

$E = mc^2$

The Second Law of Thermodynamics

- During every energy transfer or transformation, some energy is unusable, and is often lost as heat
- According to the **second law of thermodynamics**
  - *Every energy transfer or transformation increases the **entropy** (disorder) of the universe*

Figure 8.3

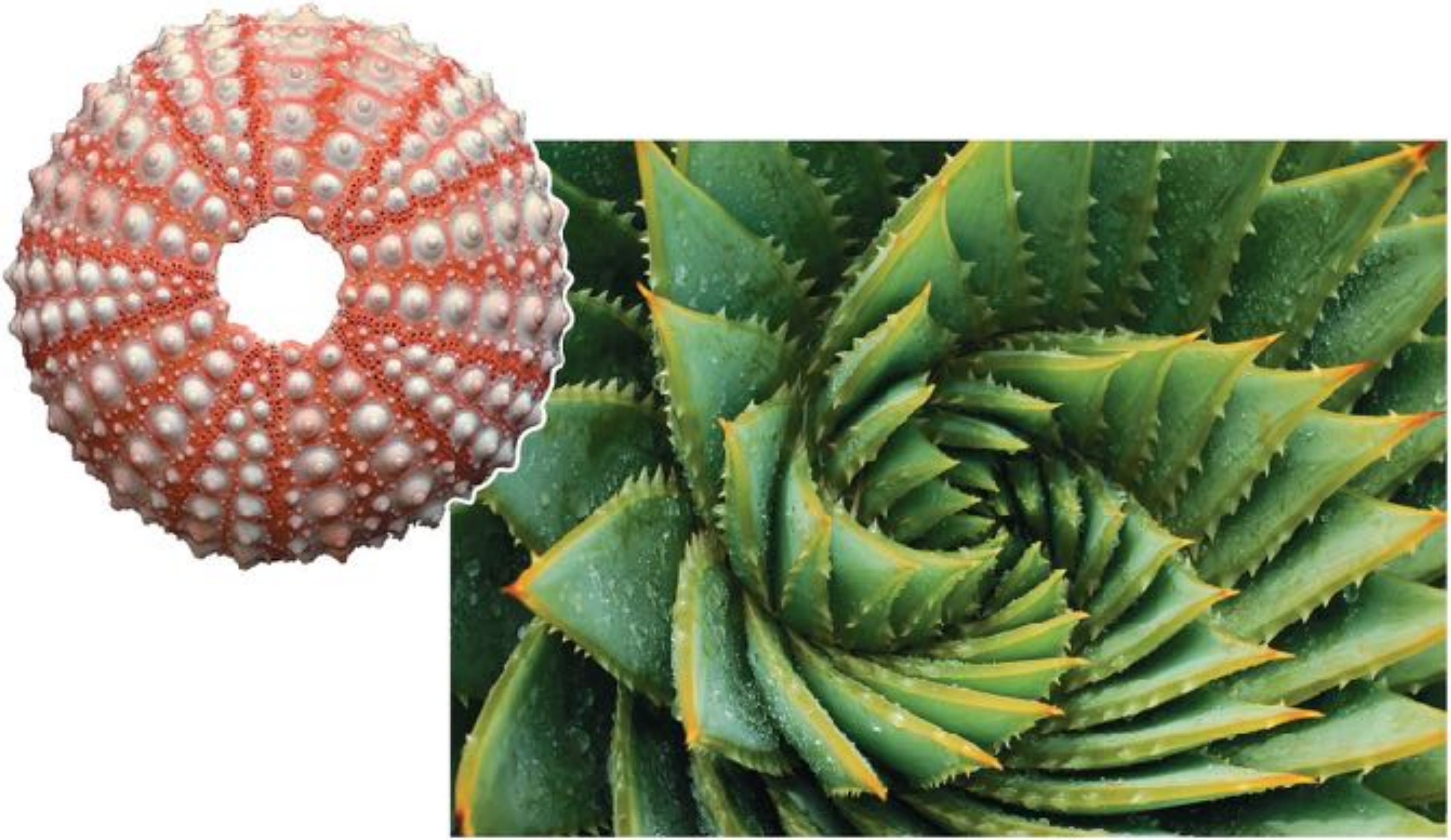
(a) First law of thermodynamics **(b) Second law of thermodynamics**

- 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 without energy input, 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 8.4



- The evolution of more complex organisms does not violate the second law of thermodynamics
- Entropy (disorder) may decrease in an organism, but the universe’s total entropy increases

Concept 8.2: The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously

- Biologists want to know which reactions occur spontaneously and which require input of energy
- To do so, they need to determine energy changes that occur in chemical reactions

Free-Energy Change, ΔG

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

- The change in free energy (ΔG) during a process is related to the change in enthalpy, or change in total energy (ΔH), change in entropy (ΔS), and temperature in Kelvin *(T)*

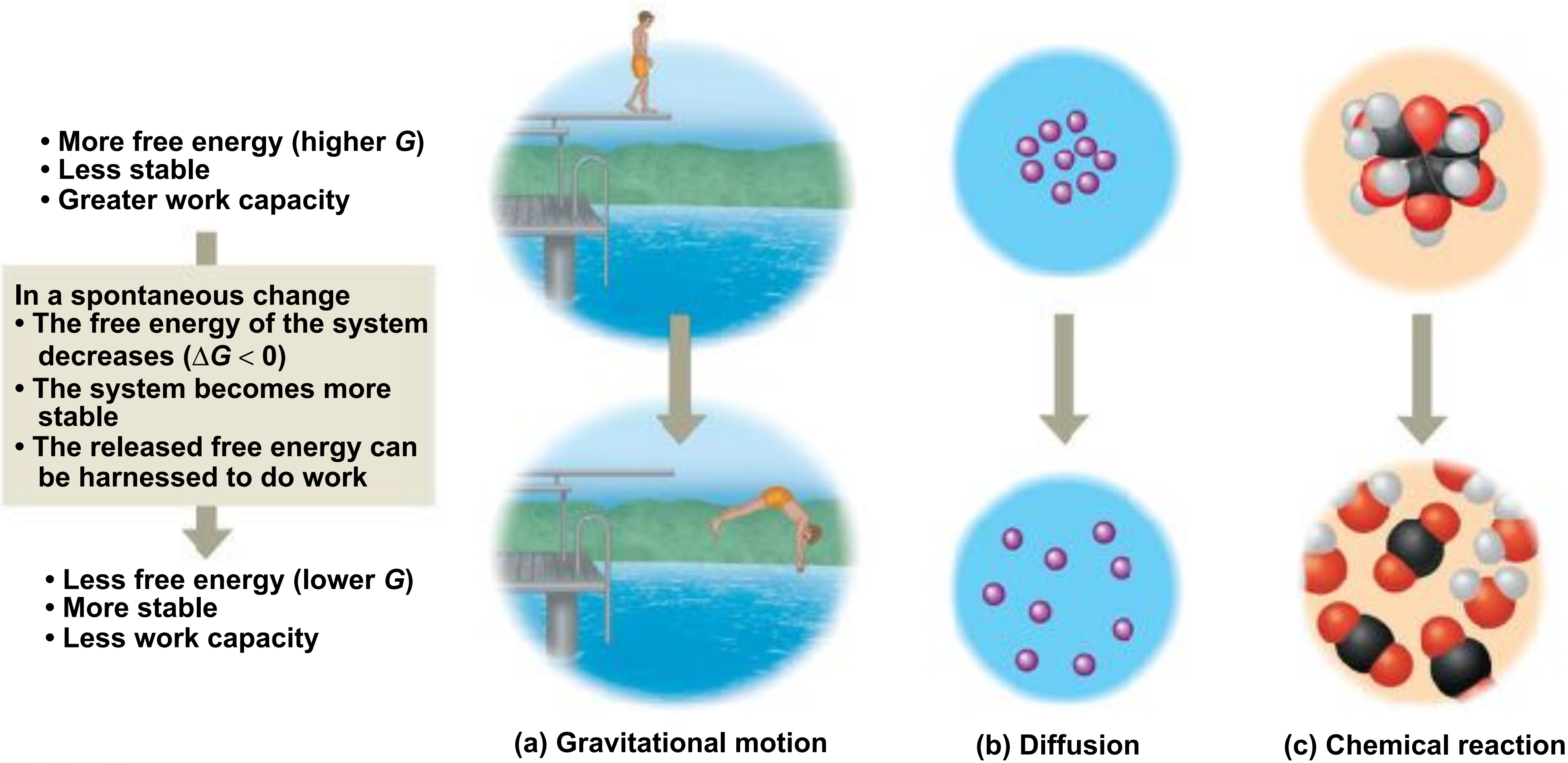
$$\Delta G = \Delta H - T\Delta S$$

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

Free Energy, Stability, and Equilibrium

- 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
- Equilibrium is a state of maximum stability
- A process is spontaneous and can perform work only when it is moving toward equilibrium

Figure 8.5



• More free energy (higher G)
• Less stable
• Greater work capacity
In a spontaneous change
• The free energy of the system decreases (ΔG < 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

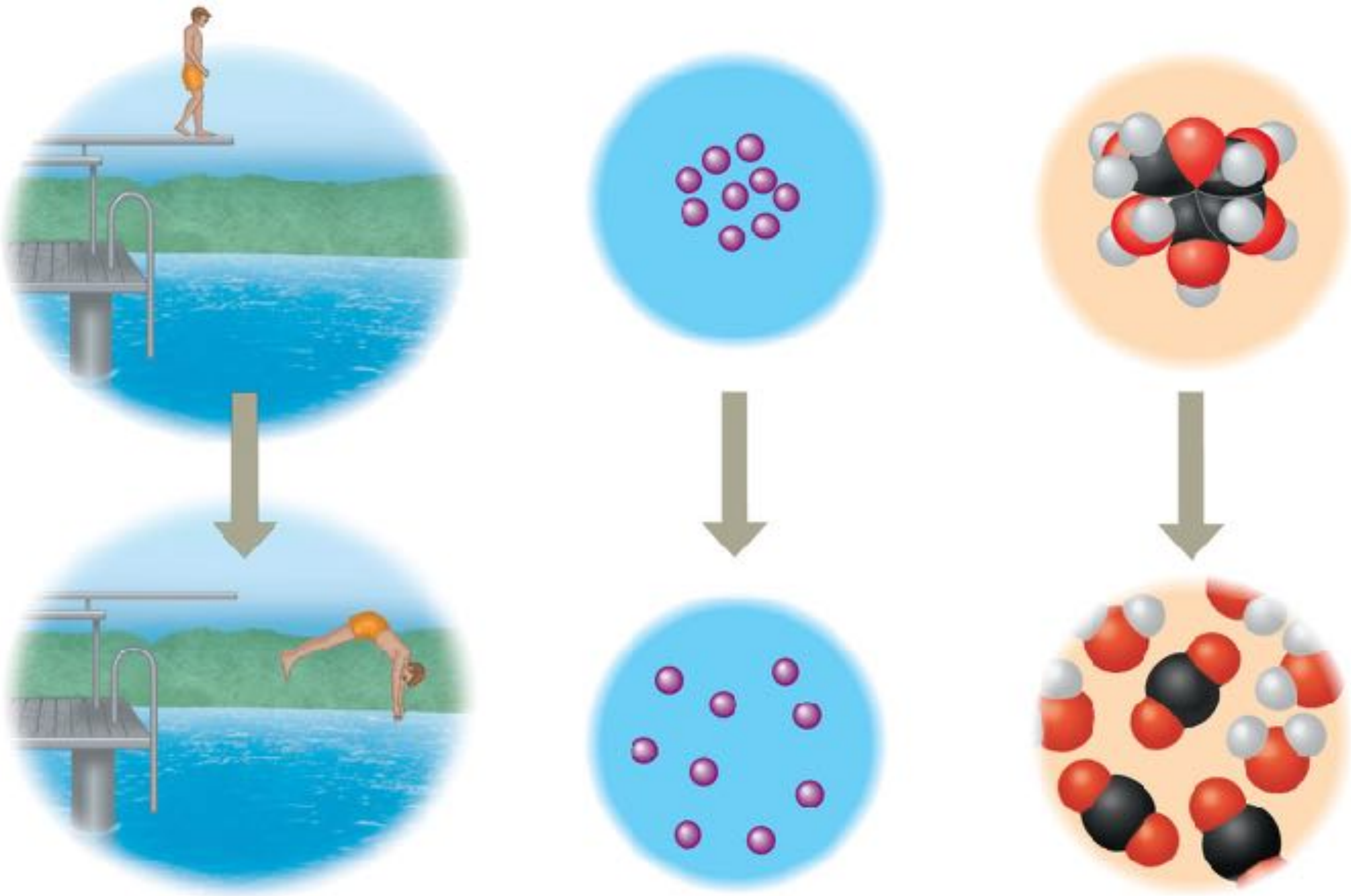
Figure 8.5a

- 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 8.5b



(a) Gravitational motion (b) Diffusion (c) Chemical reaction

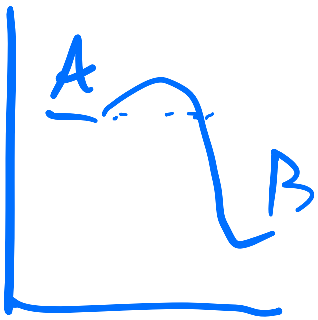
Free Energy and Metabolism

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

Exergonic and Endergonic Reactions in Metabolism

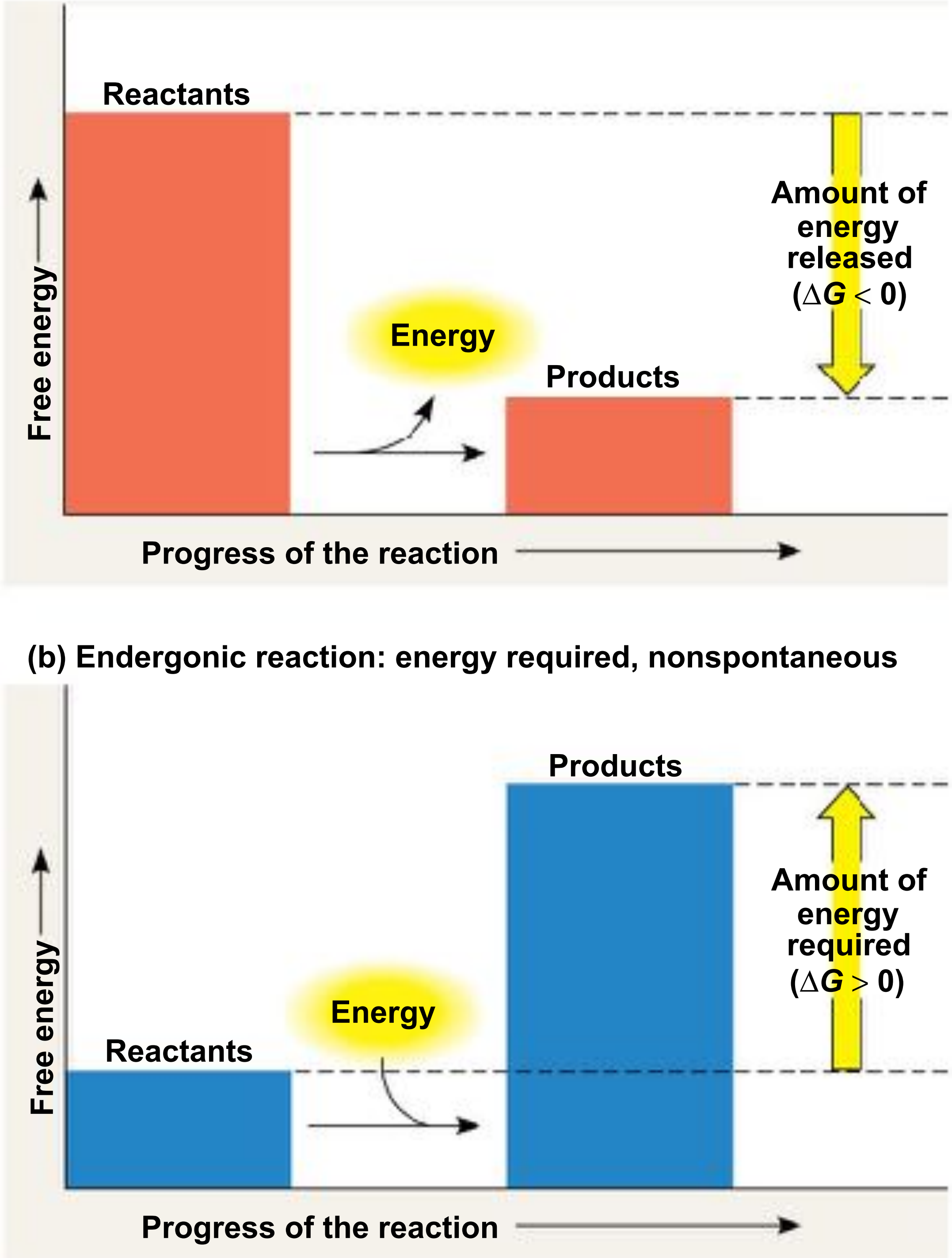
- An **exergonic reaction** proceeds with a net release of free energy and is spontaneous
- An **endergonic reaction** absorbs free energy from its surroundings and is nonspontaneous

Figure 8.6



(a) Exergonic reaction: energy released, spontaneous

(b) Endergonic reaction: energy required, nonspontaneous



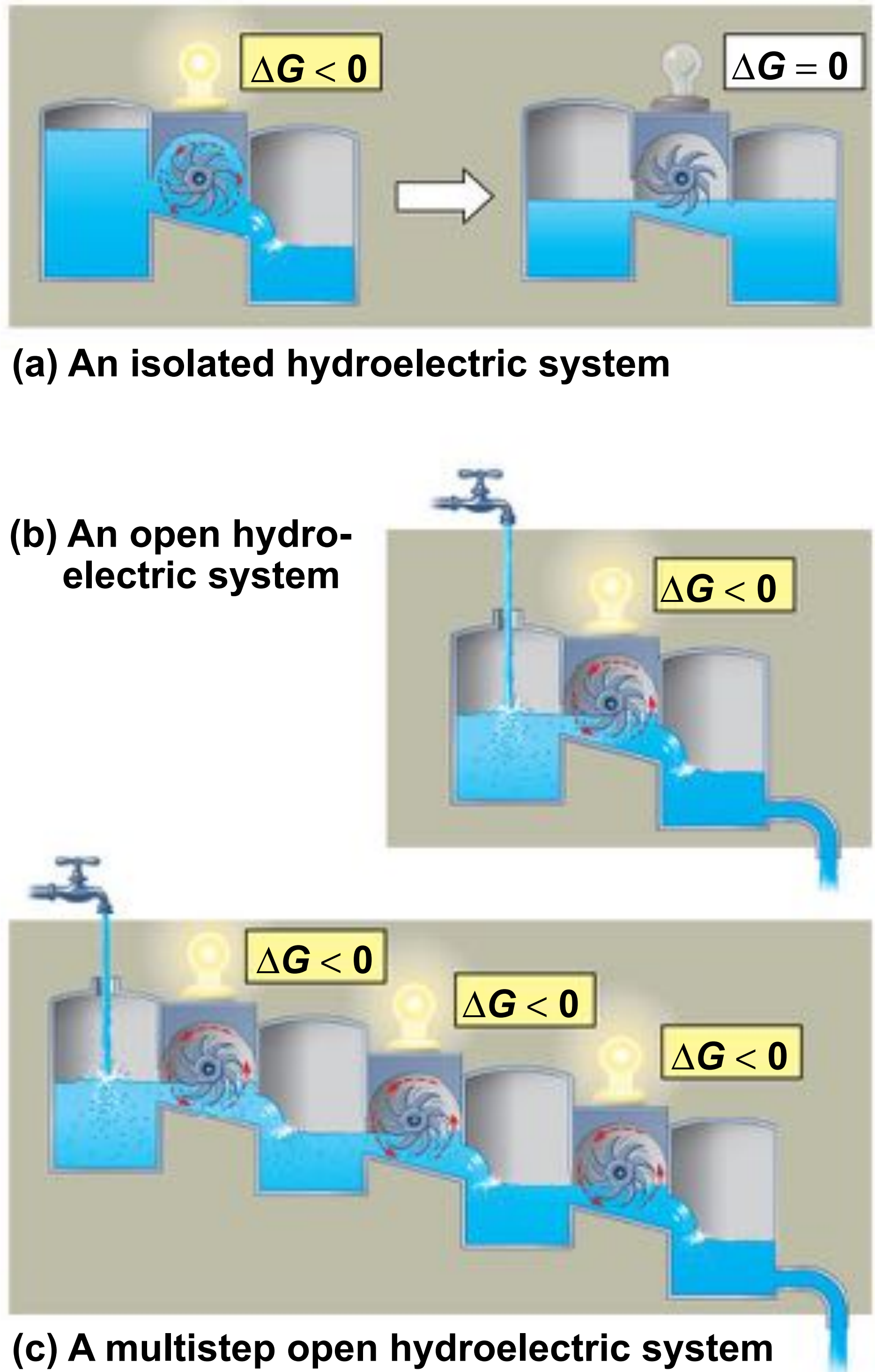
ΔG is −

ΔG is positive

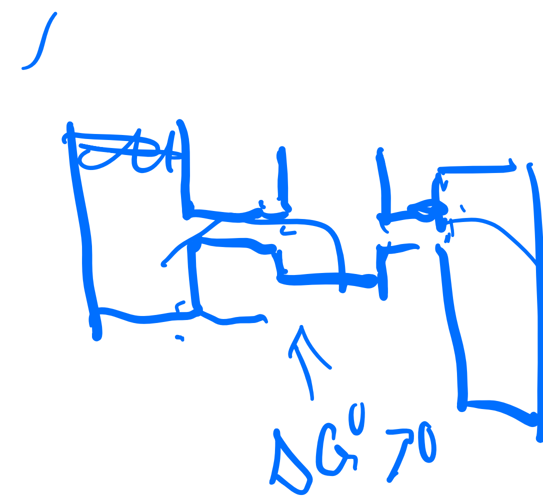
Equilibrium and Metabolism

- Reactions in a closed system eventually reach equilibrium and then do no work
- Cells are not in equilibrium; they are open systems experiencing a constant flow of materials
- A defining feature of life is that metabolism is never at equilibrium
- A catabolic pathway in a cell releases free energy in a series of reactions
- Closed and open hydroelectric systems can serve as analogies

Figure 8.7



ΔG < 0
ΔG = 0
(a) An isolated hydroelectric system
(b) An open hydro-electric system
ΔG < 0
ΔG < 0
ΔG < 0
ΔG < 0
(c) A multistep open hydroelectric system



ΔG° > 0

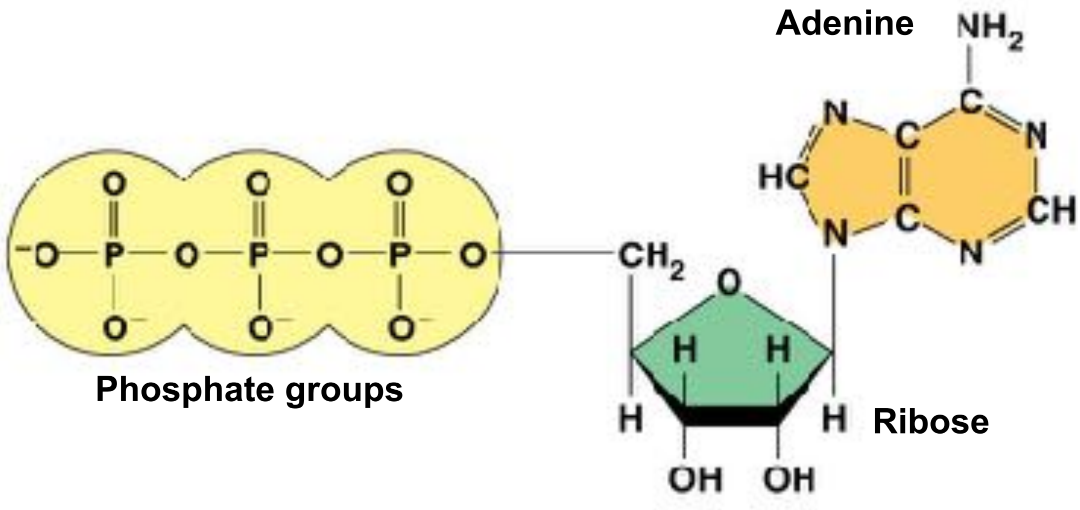
Concept 8.3: ATP powers cellular work by coupling exergonic reactions to endergonic reactions

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

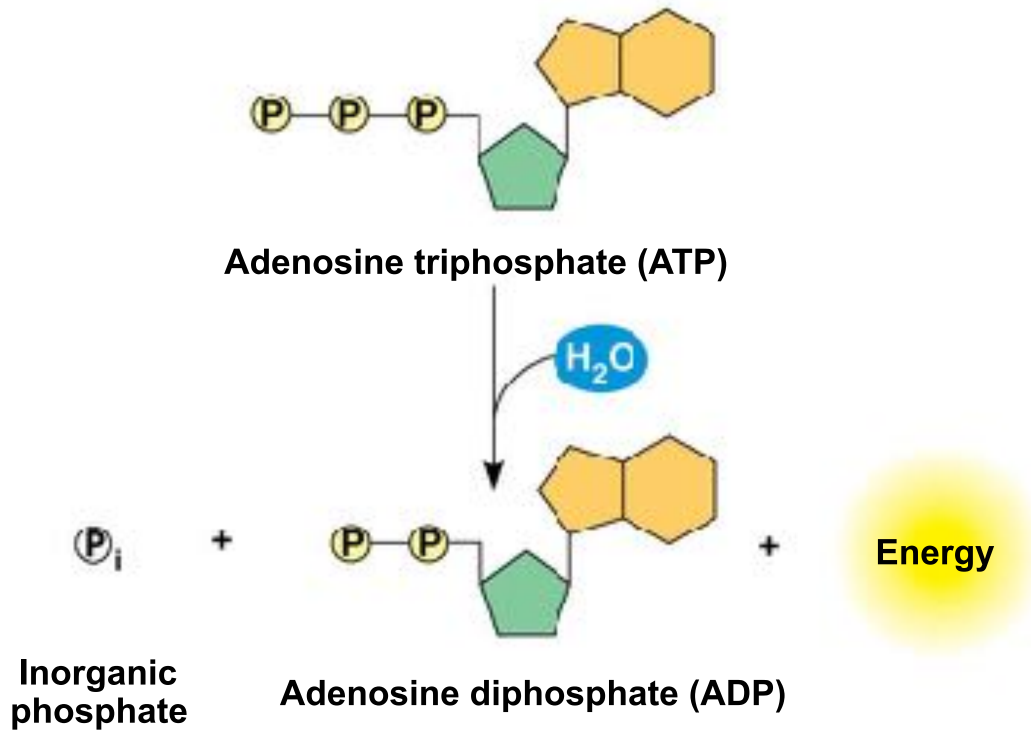
The Structure and Hydrolysis of ATP

- **ATP (adenosine triphosphate)** is the cell's energy shuttle
- ATP is composed of ribose (a sugar), adenine (a nitrogenous base), and three phosphate groups

Figure 8.8

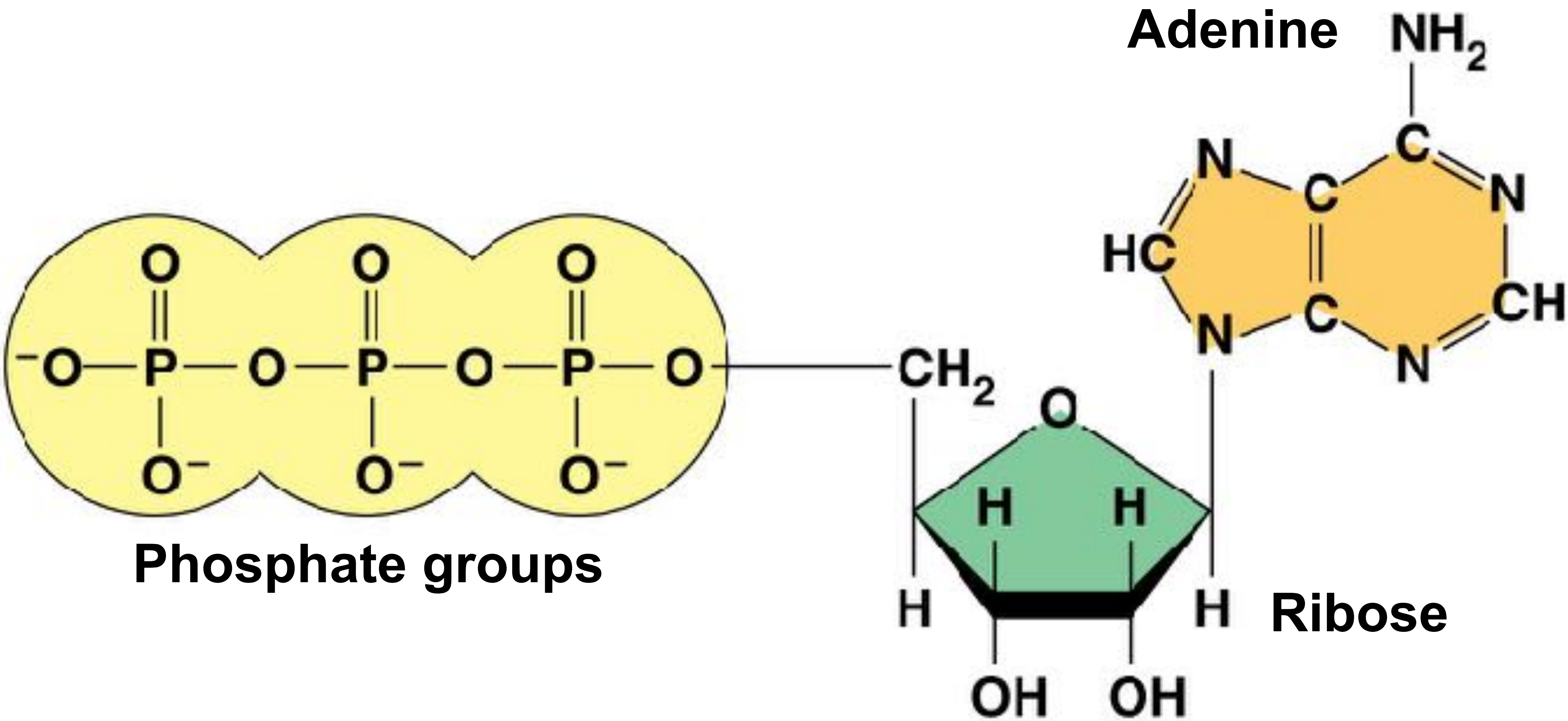


(a) The structure of ATP



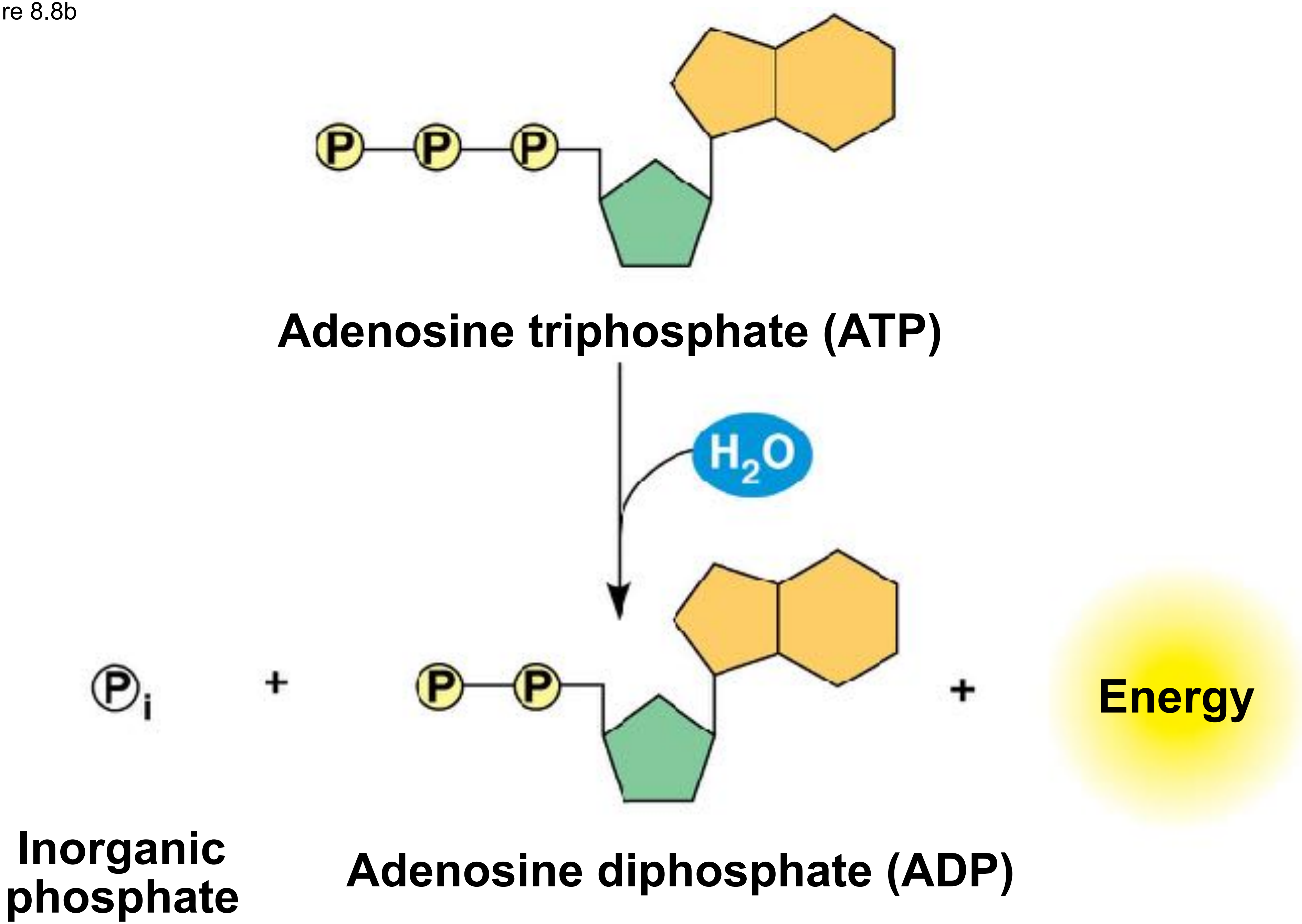
(b) The hydrolysis of ATP

Figure 8.8a



(a) The structure of ATP

Figure 8.8b



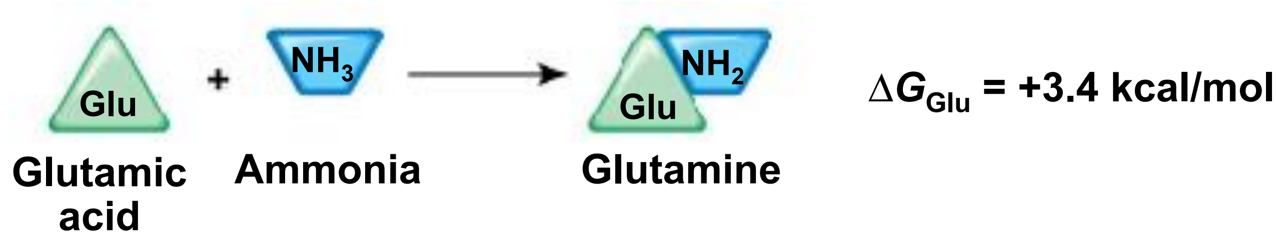
(b) The hydrolysis of ATP

- The bonds between the phosphate groups of ATP's tail 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

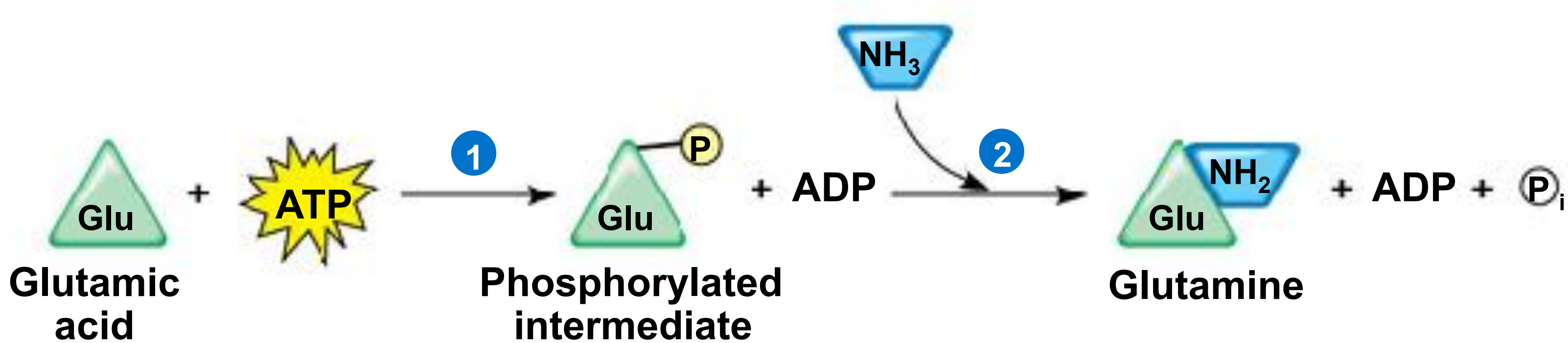
How the Hydrolysis of ATP Performs Work

- 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 an endergonic reaction
- Overall, the coupled reactions are exergonic

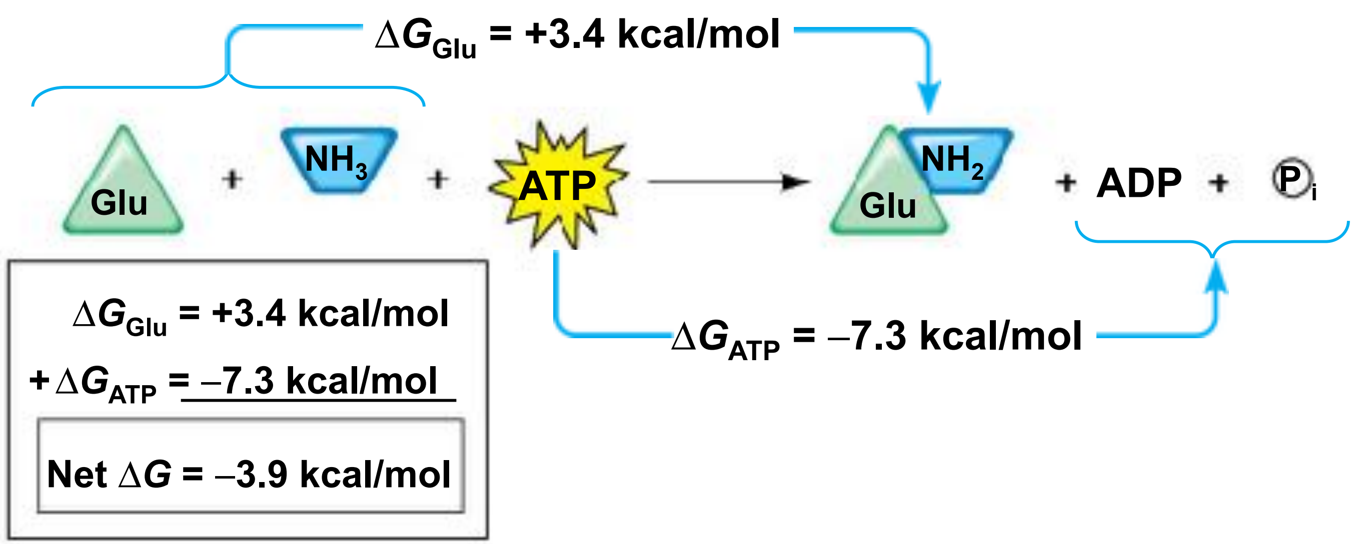
(a) Glutamic acid conversion to glutamine



(b) Conversion reaction coupled with ATP hydrolysis

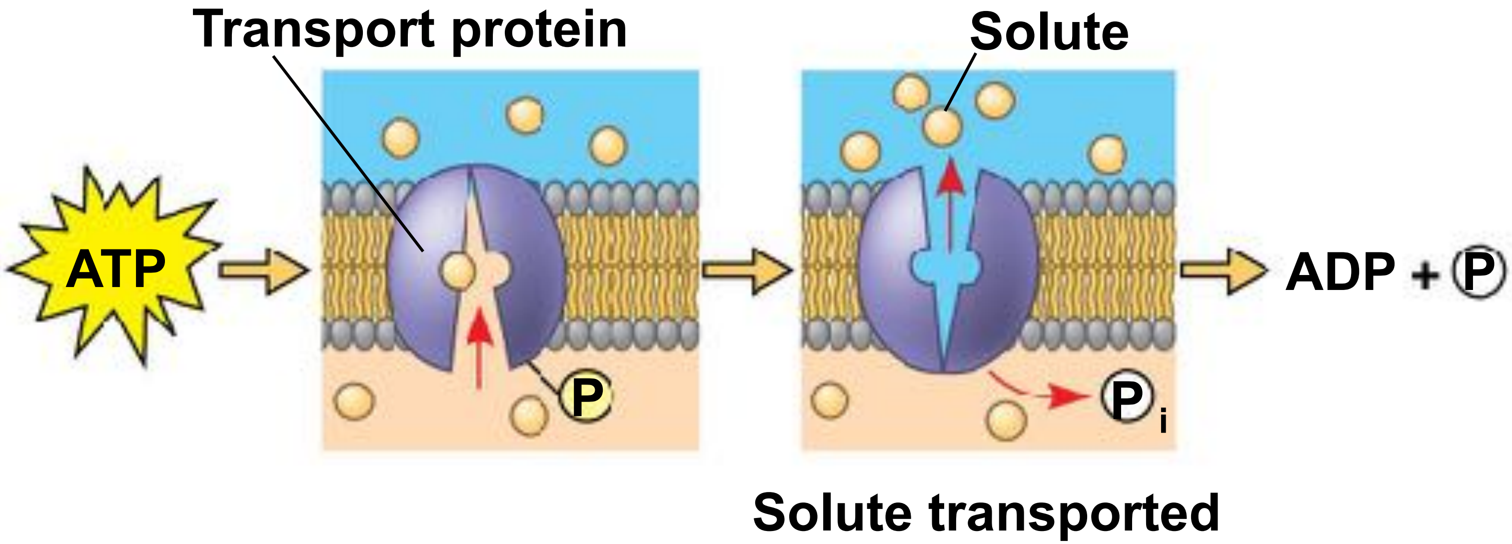


(c) Free-energy change for coupled reaction

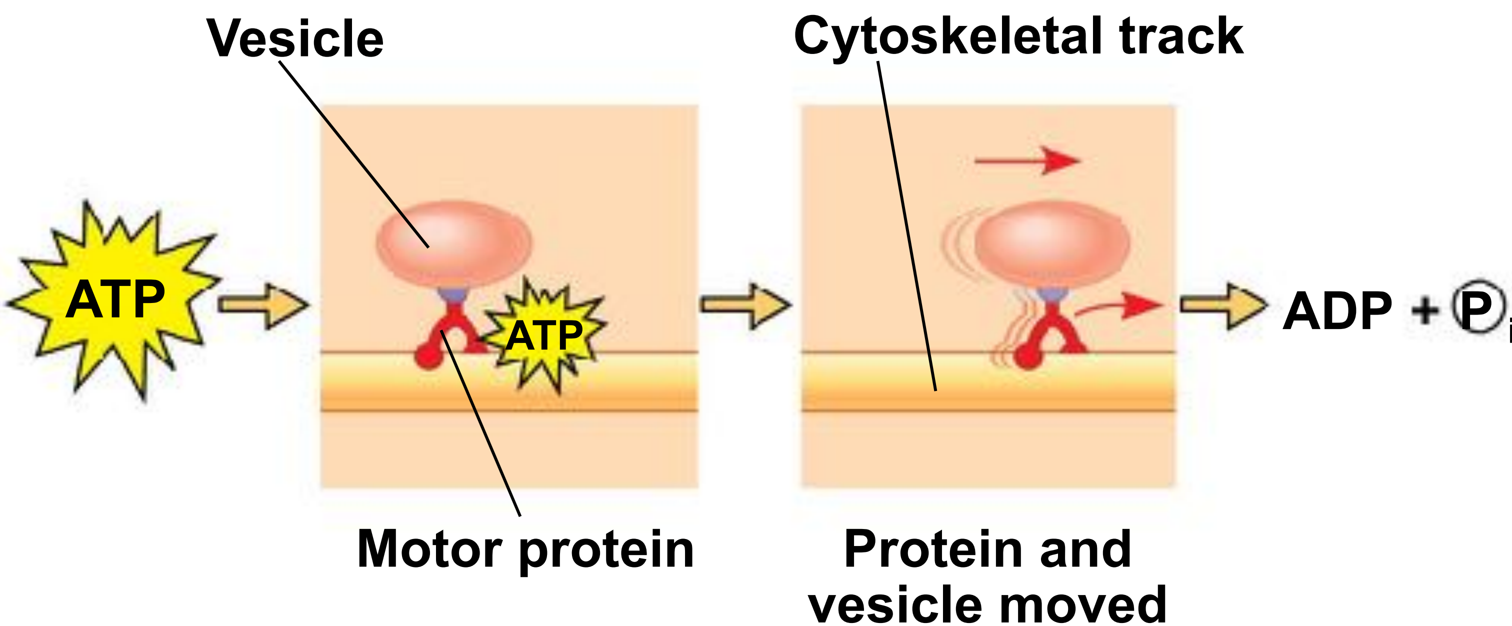


- ATP drives endergonic reactions by phosphorylation, transferring a phosphate group to some other molecule, such as a reactant
- The recipient molecule is now called a **phosphorylated intermediate**

Figure 8.10



(a) Transport work: ATP phosphorylates transport proteins.

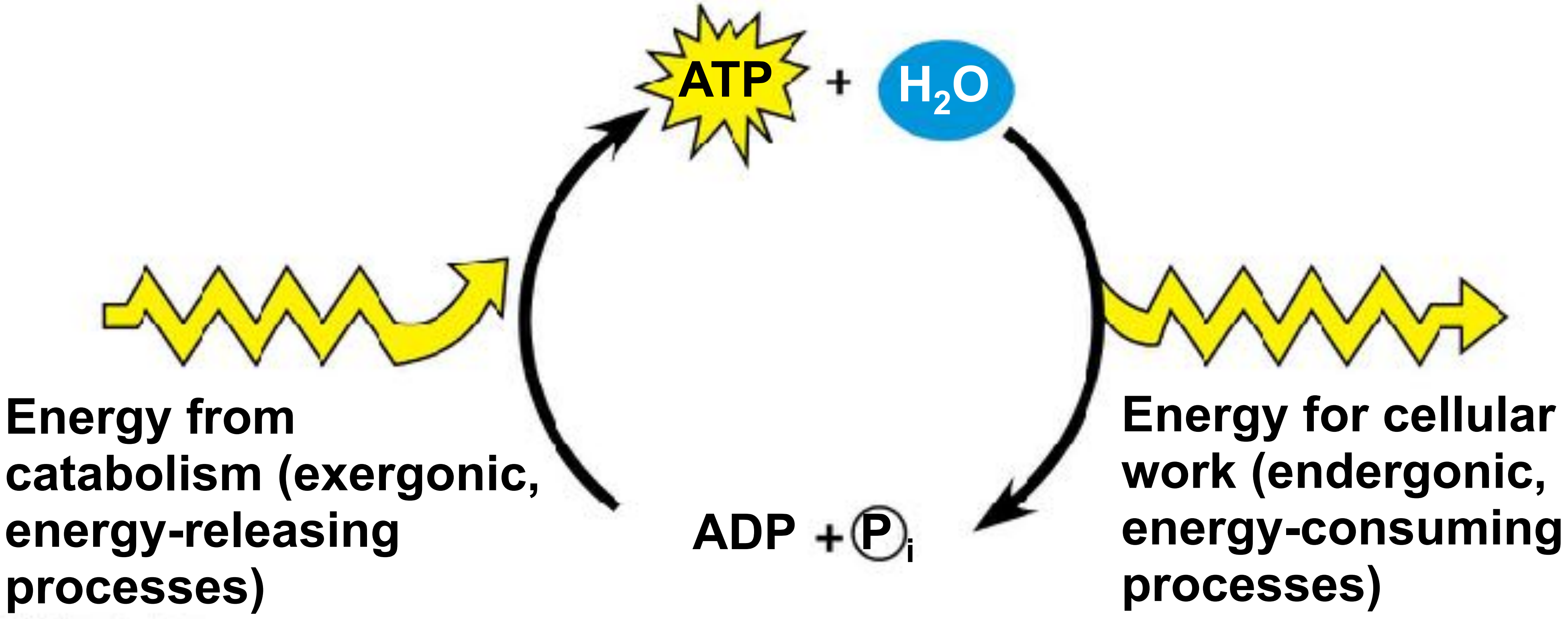


(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed.

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 8.11

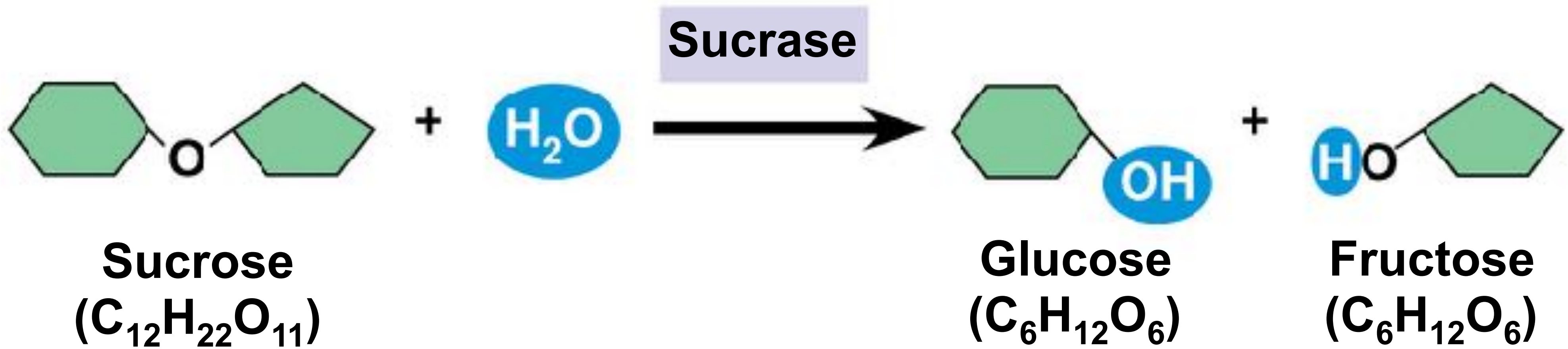


ATP
+
H_2O
Energy from catabolism (exergonic, energy-releasing processes)
ADP + Ⓟi
Energy for cellular work (endergonic, energy-consuming processes)

Concept 8.4: 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 sucrase is an example of an enzyme-catalyzed reaction

Figure 8.UN02



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 is often supplied in the form of thermal energy that the reactant molecules absorb from their surroundings

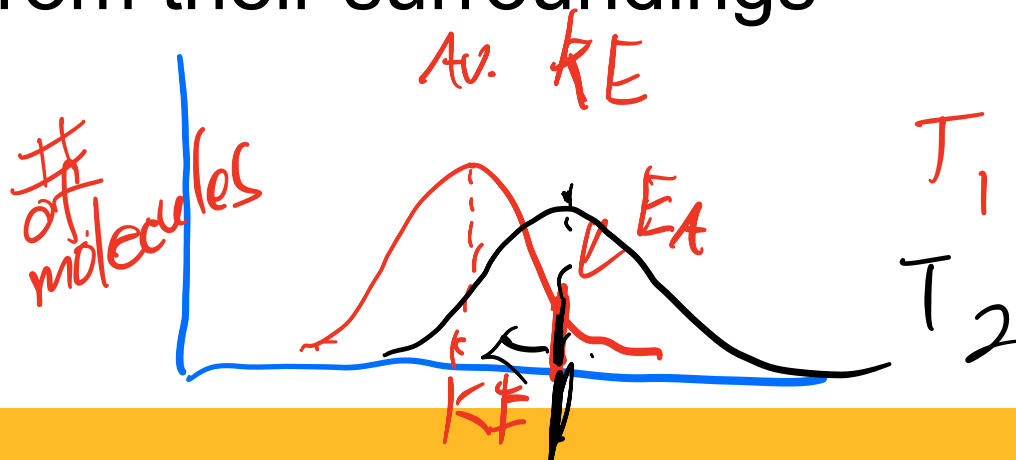
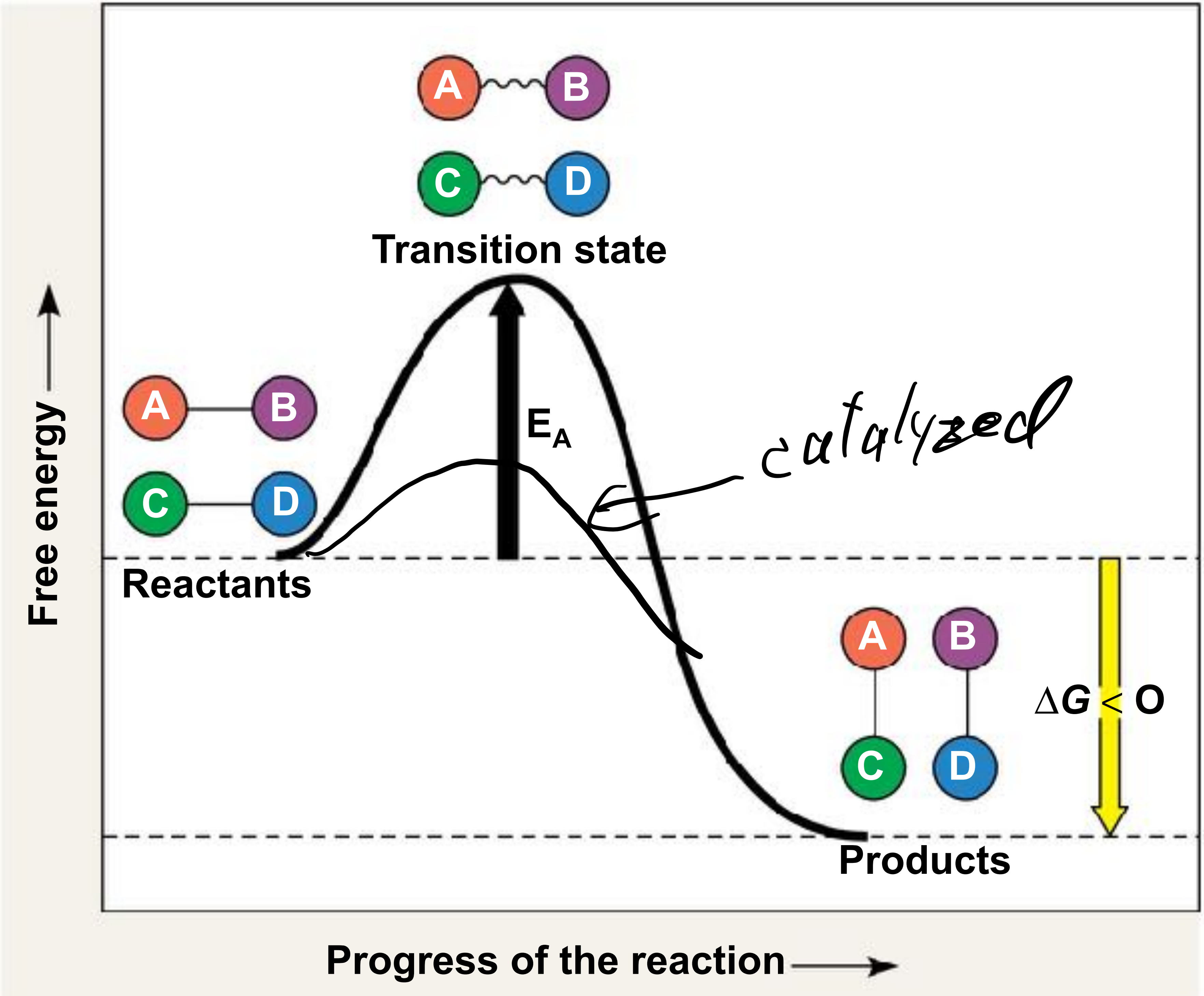


Figure 8.12

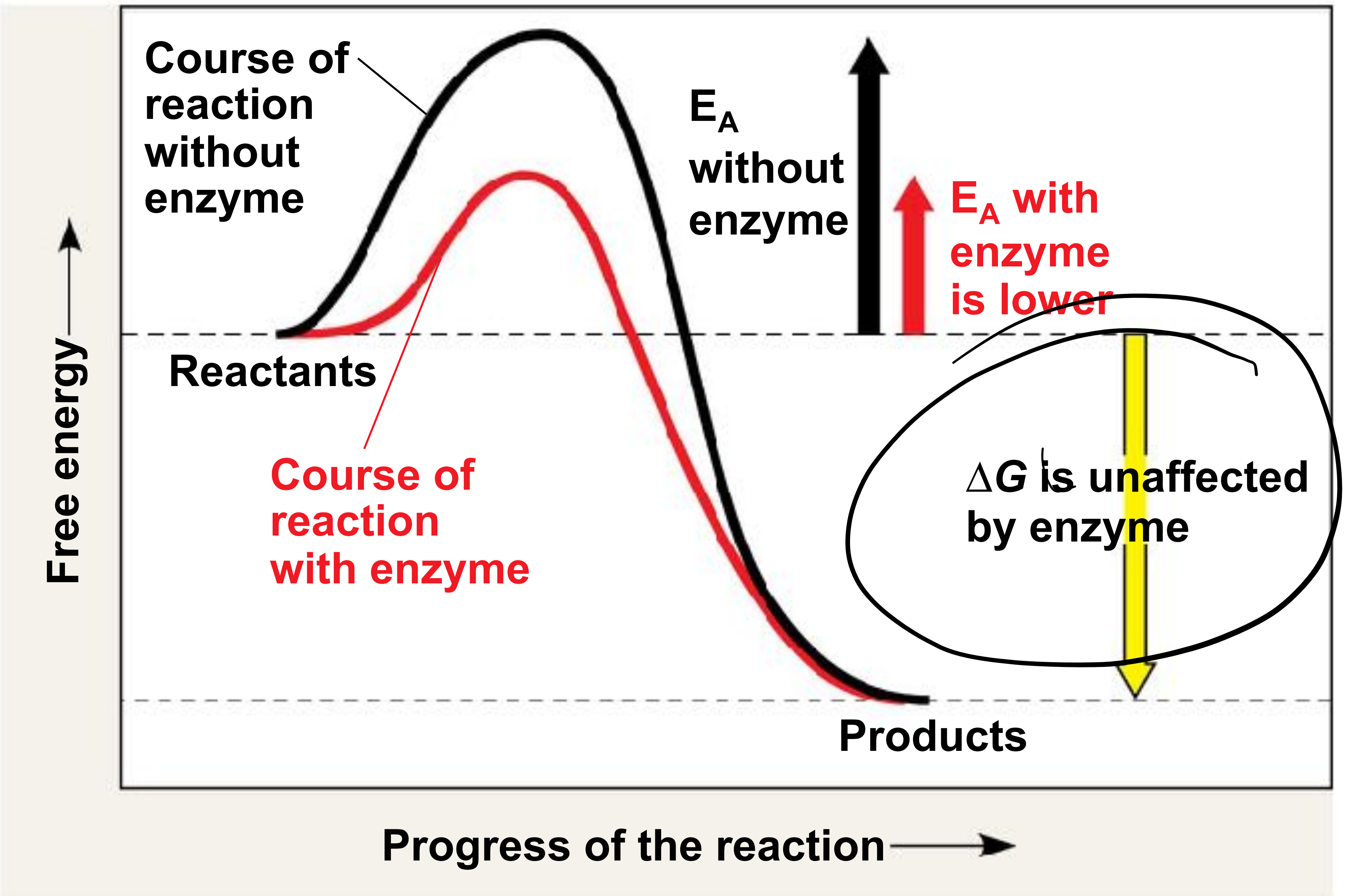

A
B
C
D
Transition state
A
B
C
D
Reactants
E$_A$
catalyzed
A
B
C
D
ΔG < O
Products
Free energy
Progress of the reaction

How Enzymes Lower the E_A Barrier

- Enzymes catalyze reactions by lowering the E_A barrier
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually

PLAY Animation: How Enzymes Work

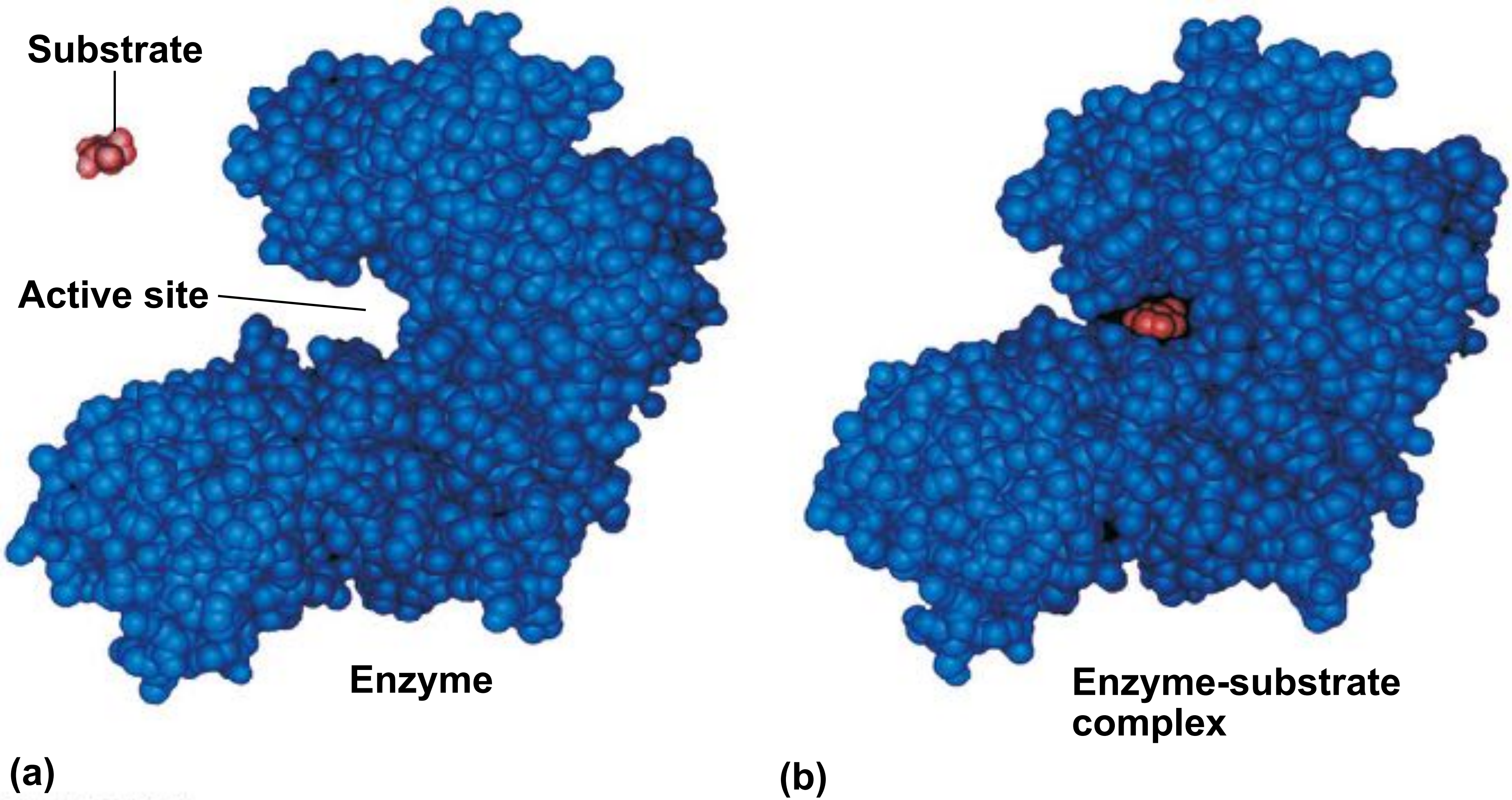
Figure 8.13


Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Reactants
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Free energy
Progress of the reaction

Substrate Specificity of Enzymes

- 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
- **Induced fit** of a substrate brings chemical groups of the active site into positions that enhance their ability to catalyze the reaction

Figure 8.14



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 8.15-1

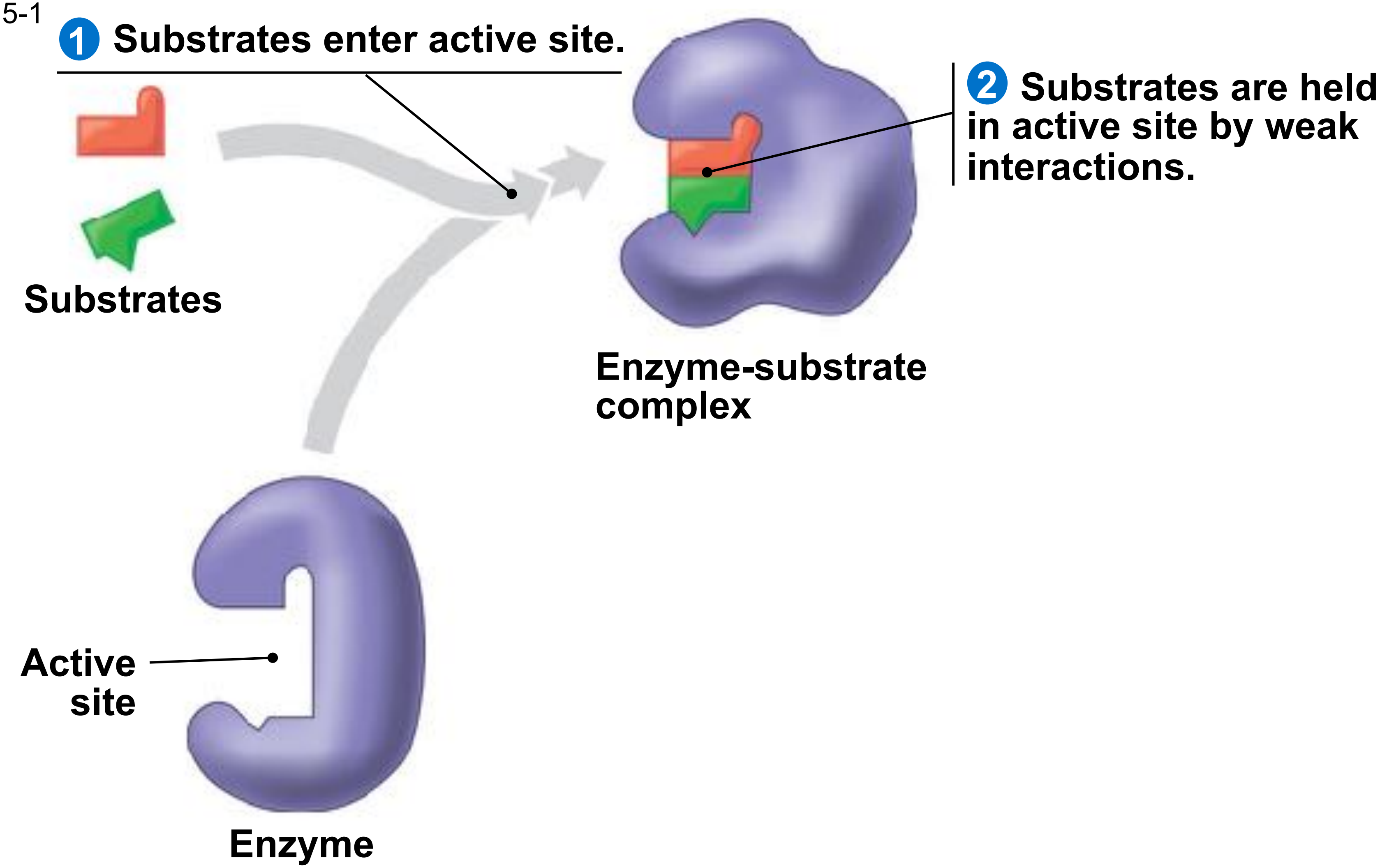
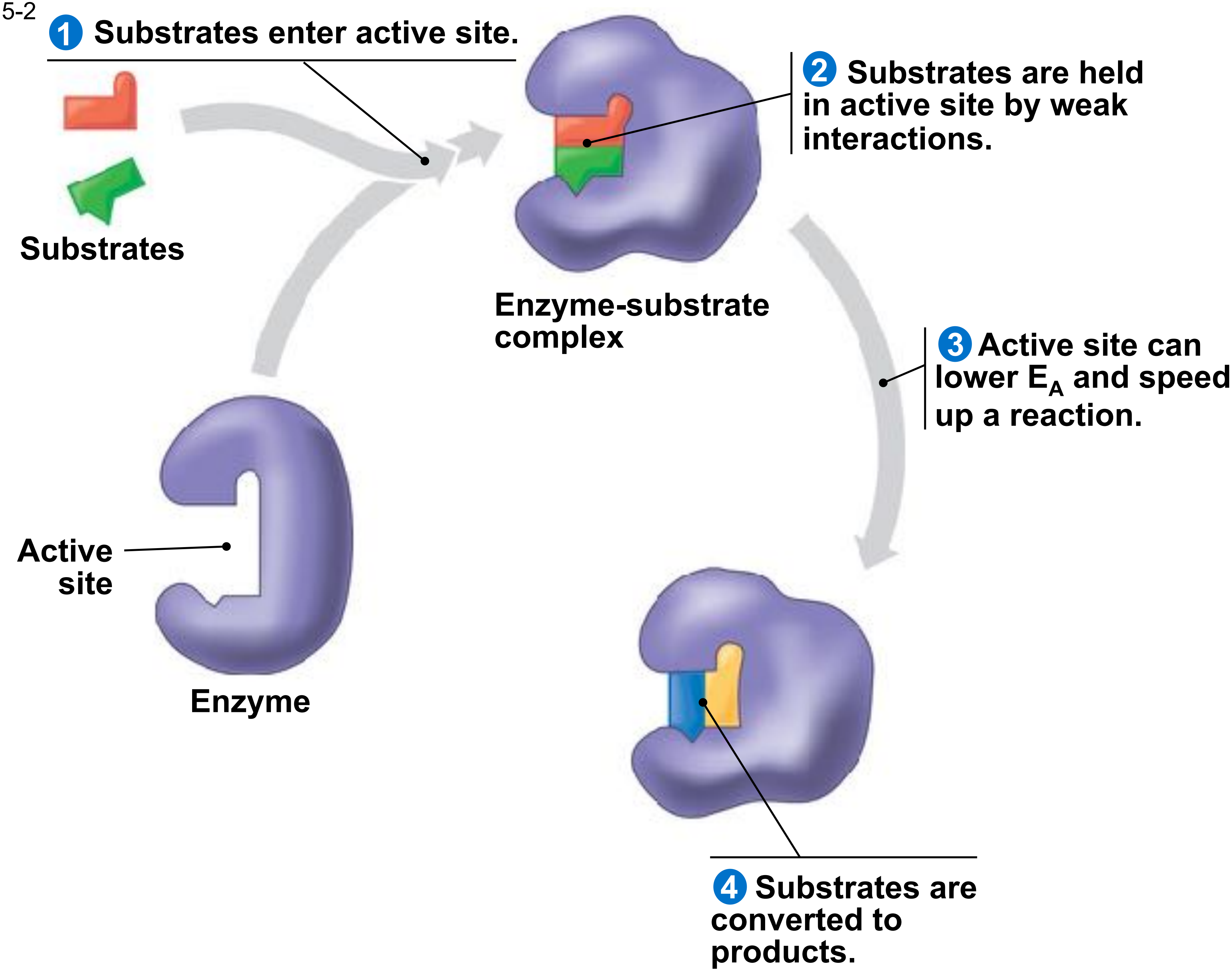
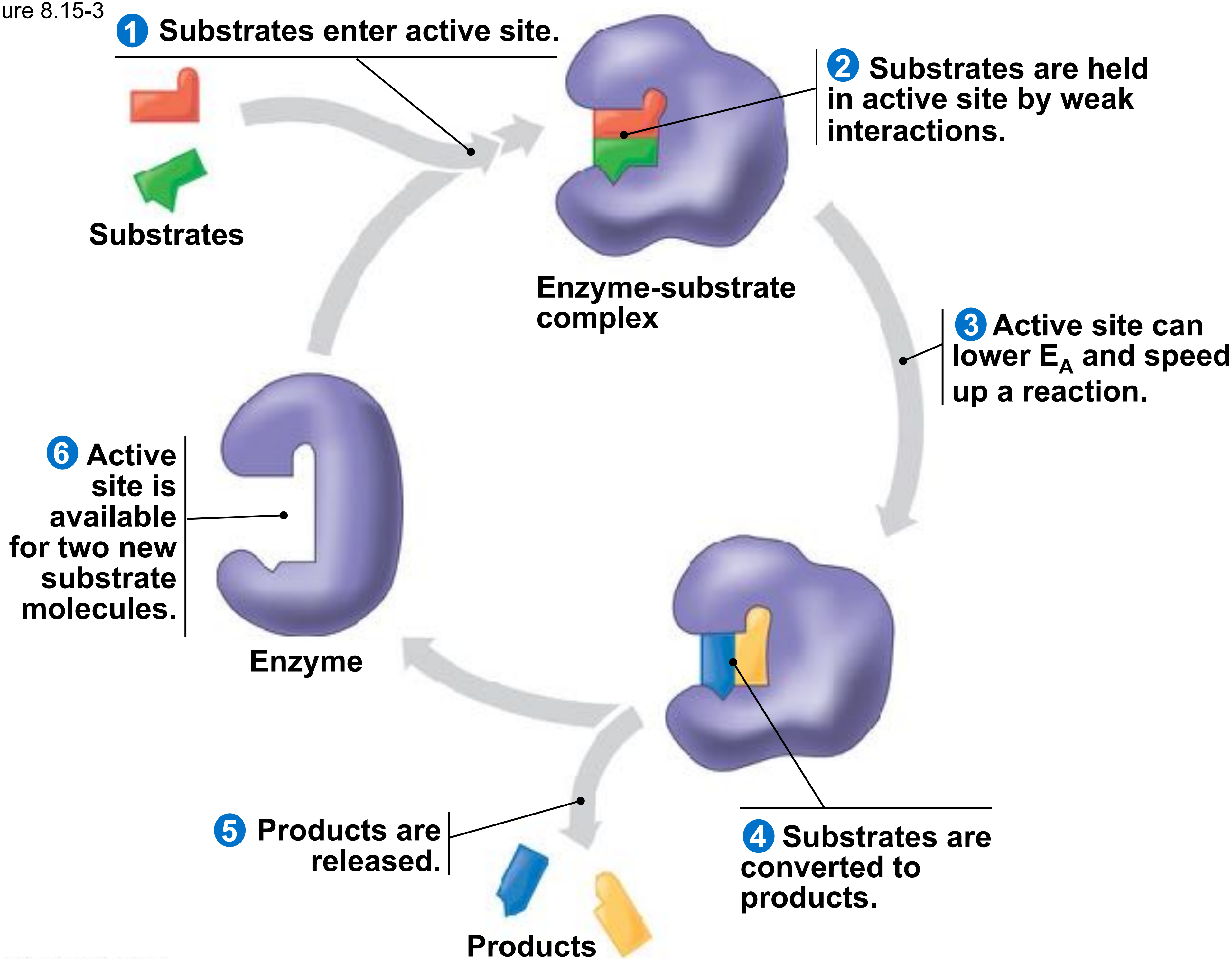

1 Substrates enter active site.
Substrates
2 Substrates are held in active site by weak interactions.
Enzyme-substrate complex
Active site
Enzyme

Figure 8.15-2



1 Substrates enter active site.
Substrates
2 Substrates are held in active site by weak interactions.
Enzyme-substrate complex
3 Active site can lower E_A and speed up a reaction.
Active site
Enzyme
4 Substrates are converted to products.

Figure 8.15-3



1 Substrates enter active site.
2 Substrates are held in active site by weak interactions.
Substrates
Enzyme-substrate complex
3 Active site can lower E_A and speed up a reaction.
6 Active site is available for two new substrate molecules.
Enzyme
5 Products are released.
4 Substrates are converted to products.
Products

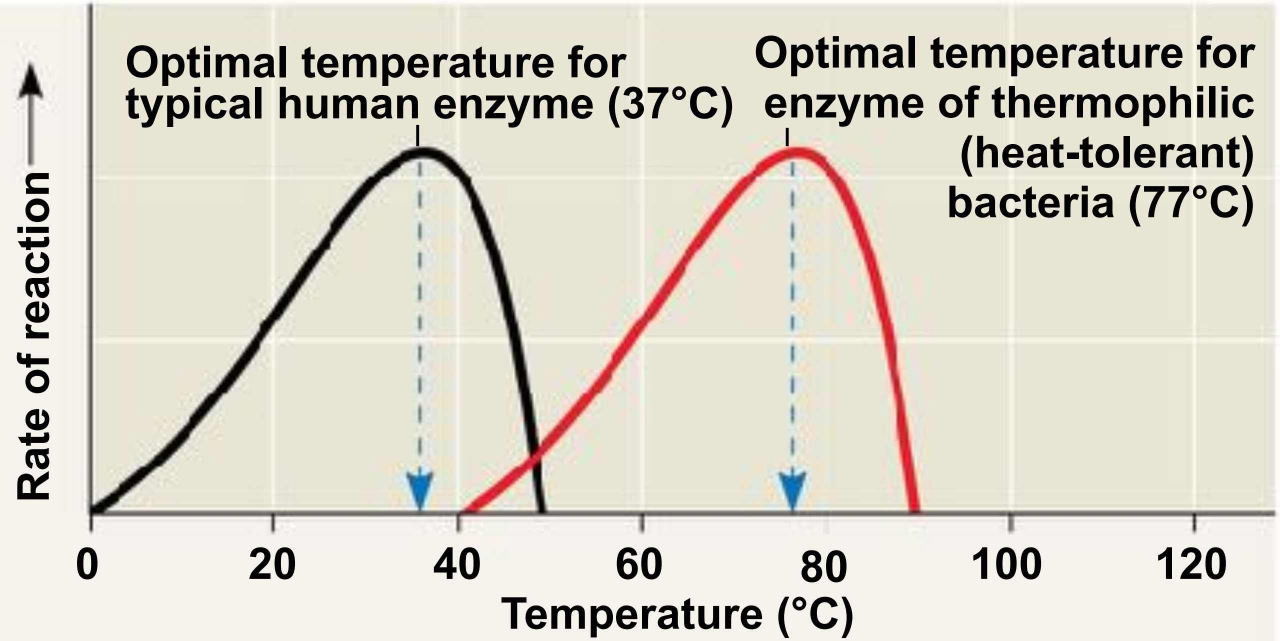
Effects of Local Conditions on Enzyme Activity

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

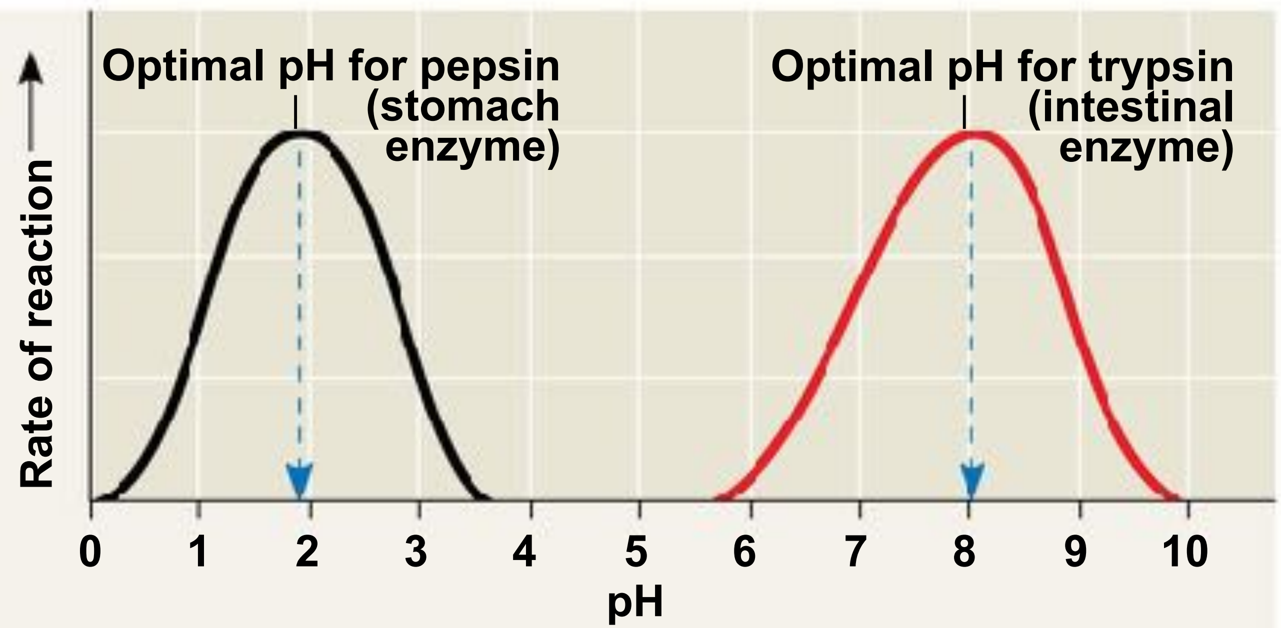
Effects of Temperature and pH

- Each enzyme has an optimal temperature in which it can function
- Each enzyme has an optimal pH in which it can function
- Optimal conditions favor the most active shape for the enzyme molecule

Figure 8.16

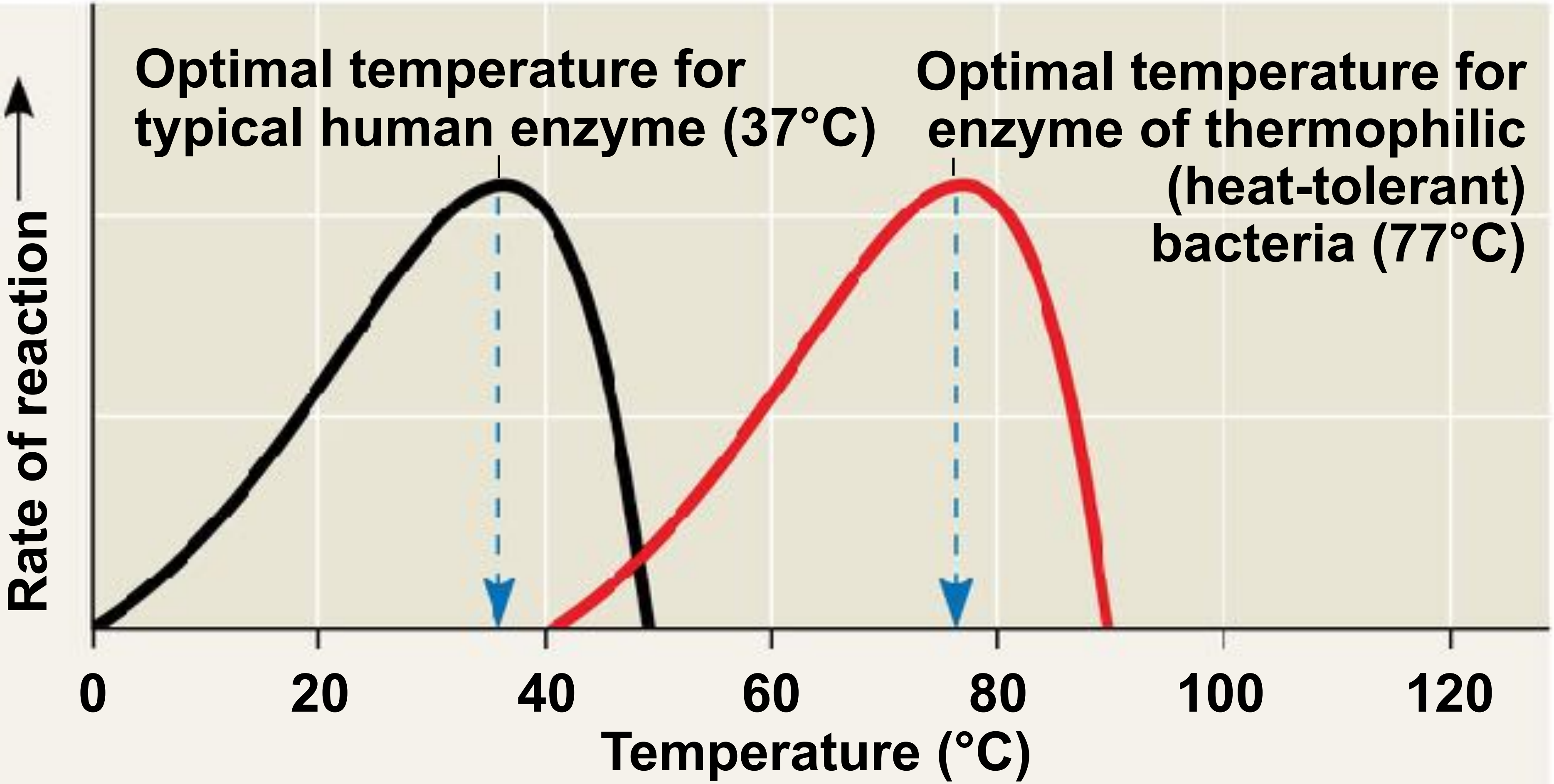


(a) Optimal temperature for two enzymes



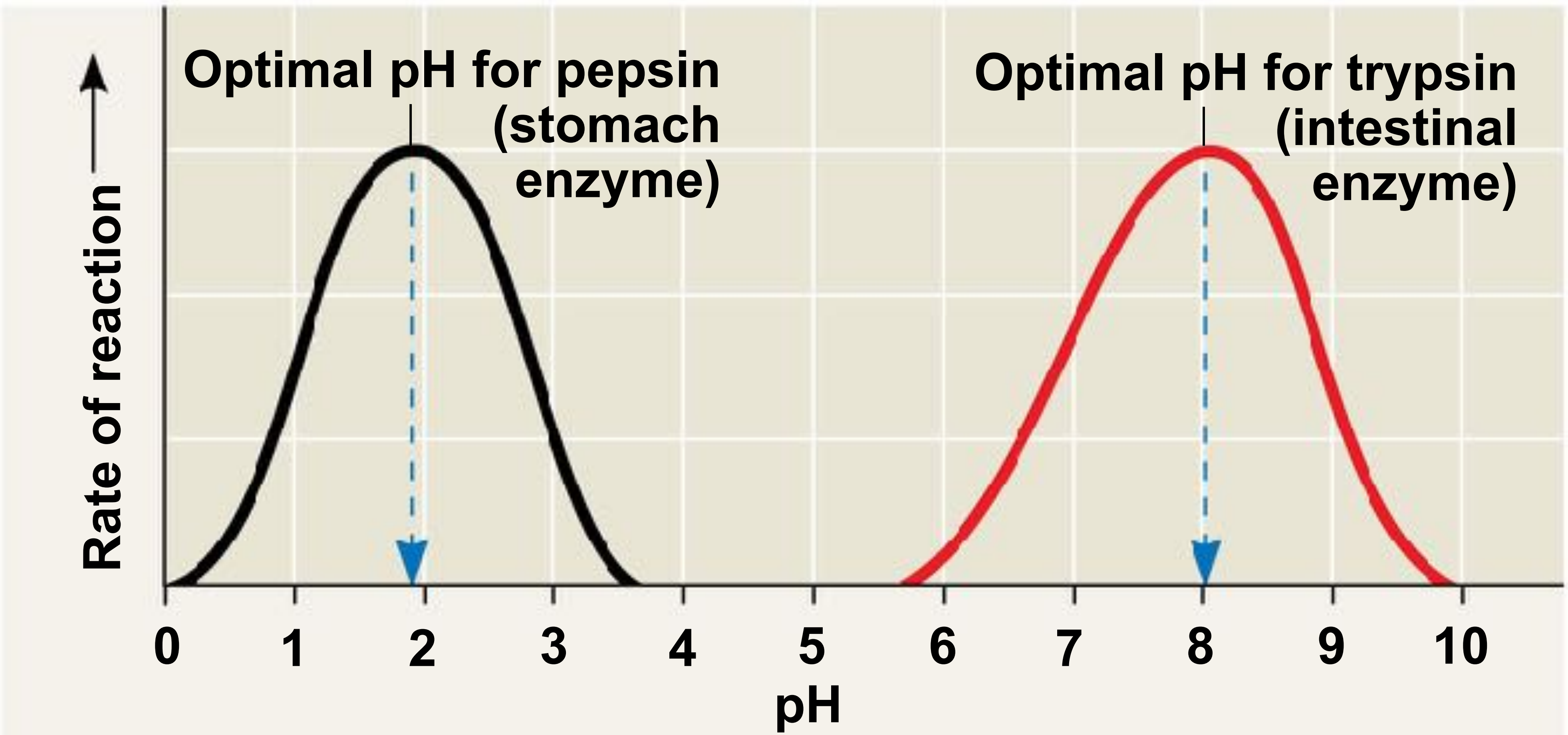
(b) Optimal pH for two enzymes

Figure 8.16a



(a) Optimal temperature for two enzymes

Figure 8.16b



(b) Optimal pH for two enzymes

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**
- Coenzymes include vitamins

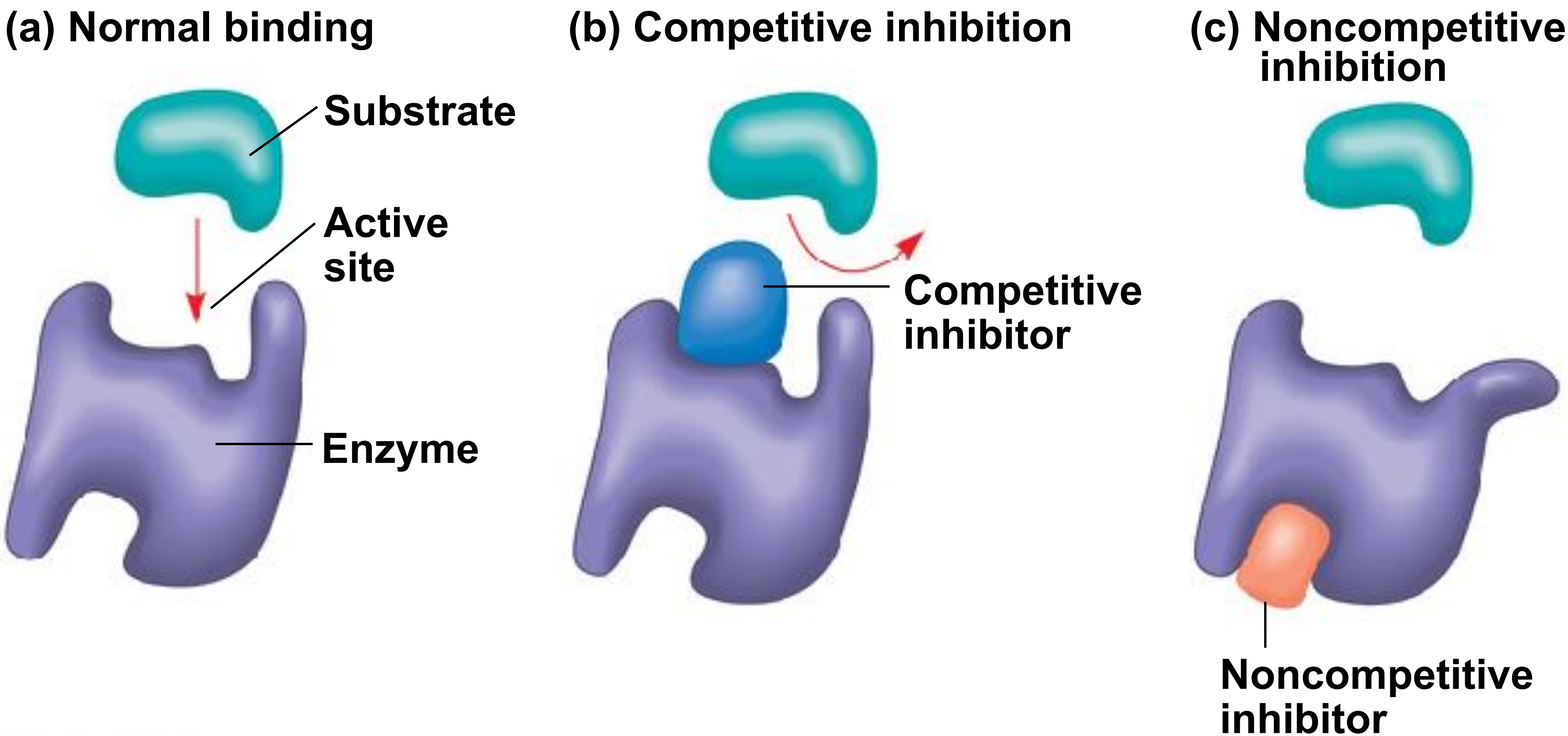
Enzyme Inhibitors

- **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

stimulation by binding
+ changing shape

Allosteric → inhibitors
→ stimulators

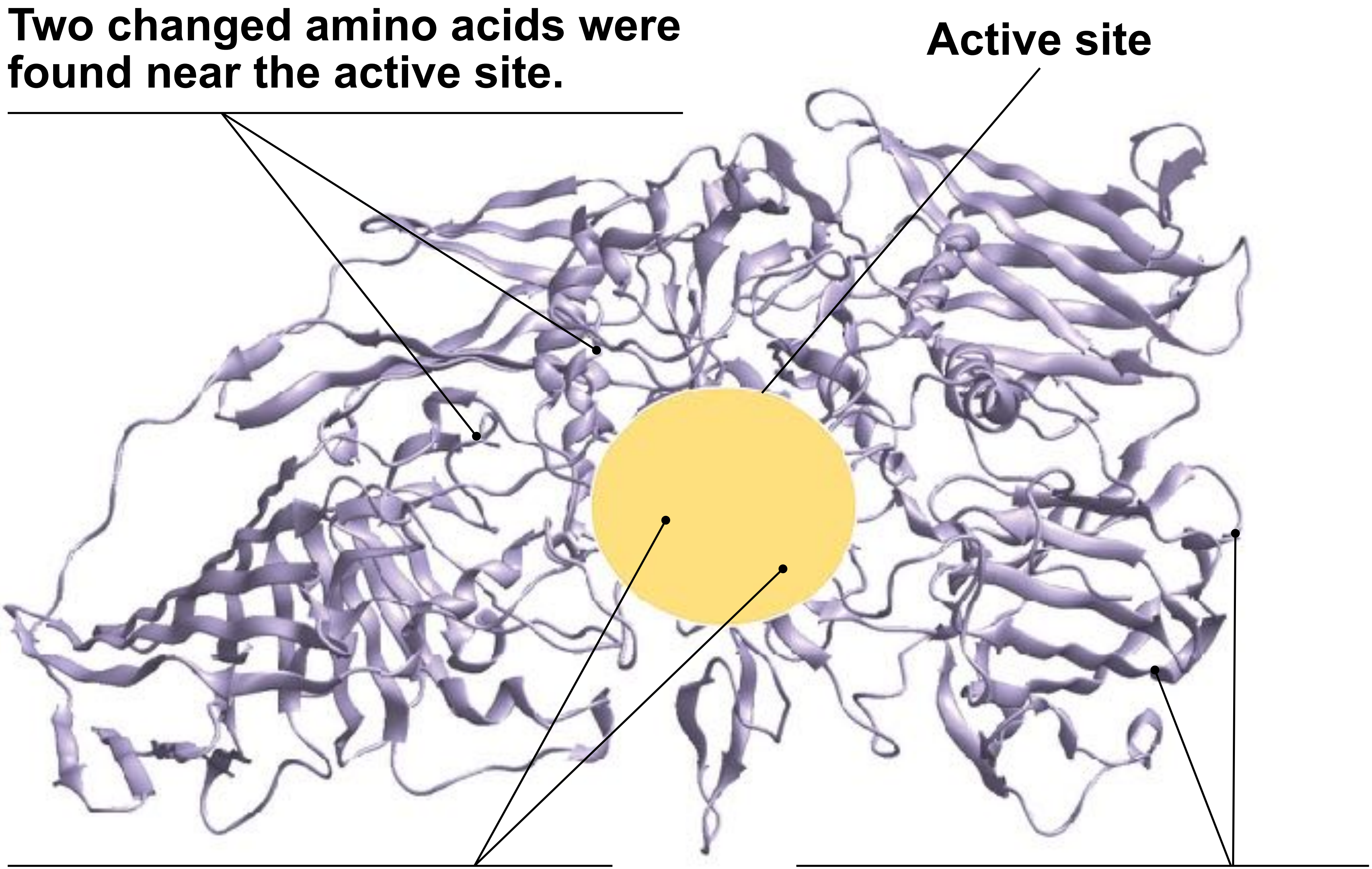
Figure 8.17


(a) Normal binding
Substrate
Active site
Enzyme
(b) Competitive inhibition
Competitive inhibitor
(c) Noncompetitive inhibition
Noncompetitive inhibitor

The Evolution of Enzymes

- 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 substrate specificity
- Under new environmental conditions a novel form of an enzyme might be favored

Figure 8.18


Two changed amino acids were found near the active site.
Active site
Two changed amino acids were found in the active site.
Two changed amino acids were found on the surface.

Concept 8.5: 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 8.19

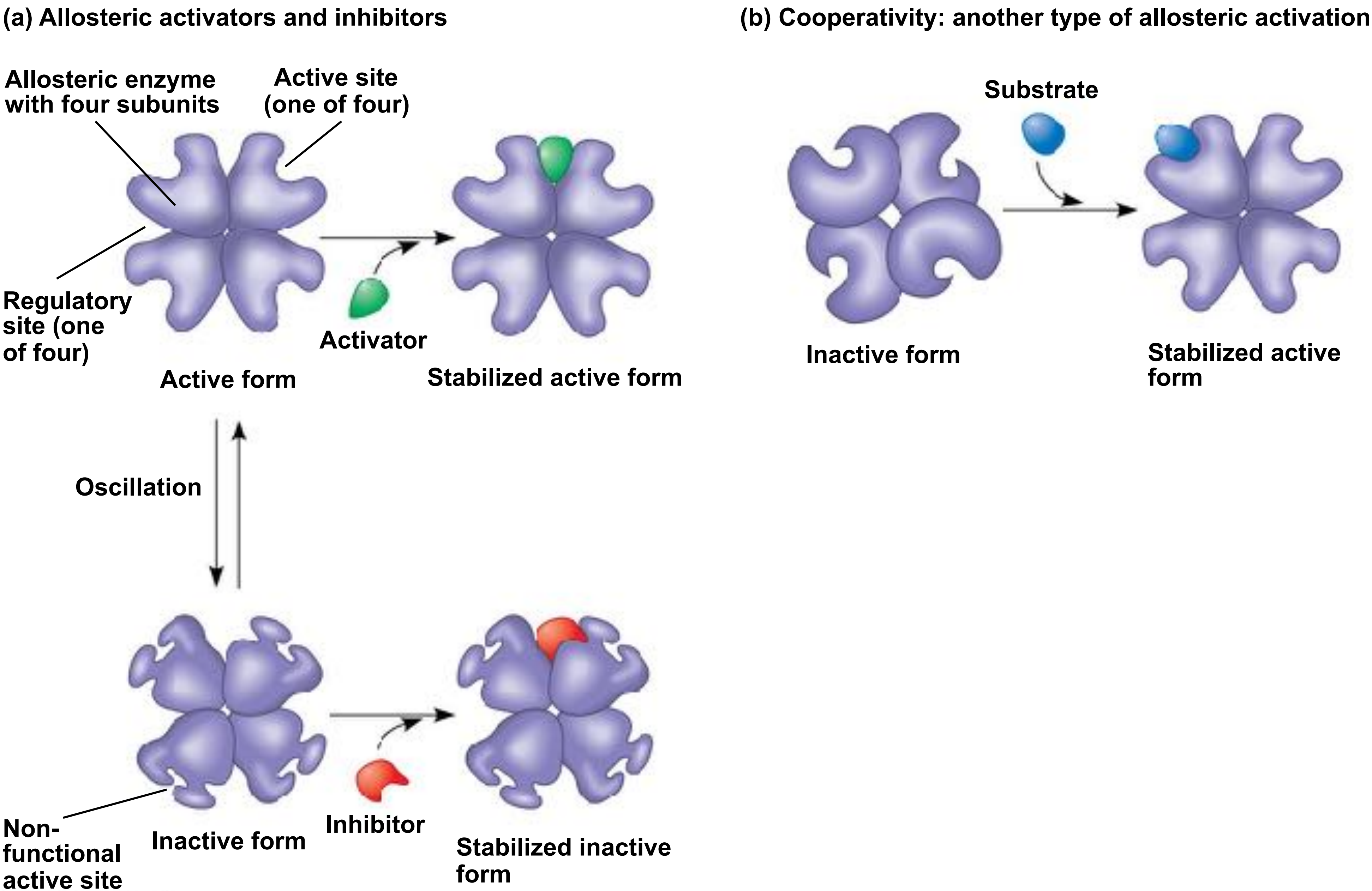

(a) Allosteric activators and inhibitors
Allosteric enzyme with four subunits
Active site (one of four)
Regulatory site (one of four)
Active form
Activator
Stabilized active form
Oscillation
Non-functional active site
Inactive form
Inhibitor
Stabilized inactive form
(b) Cooperativity: another type of allosteric activation
Substrate
Inactive form
Stabilized active form

Figure 8.19a

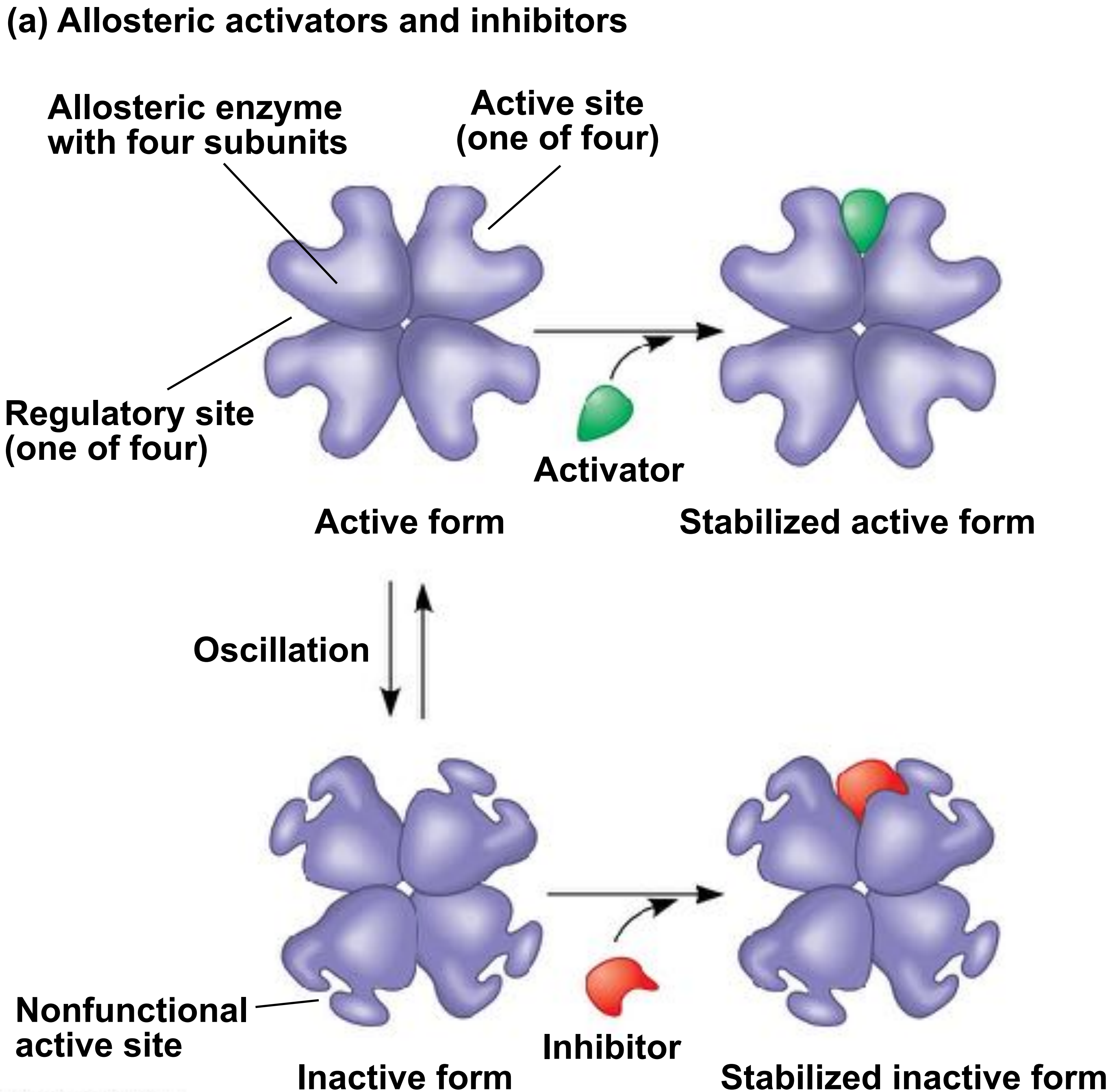
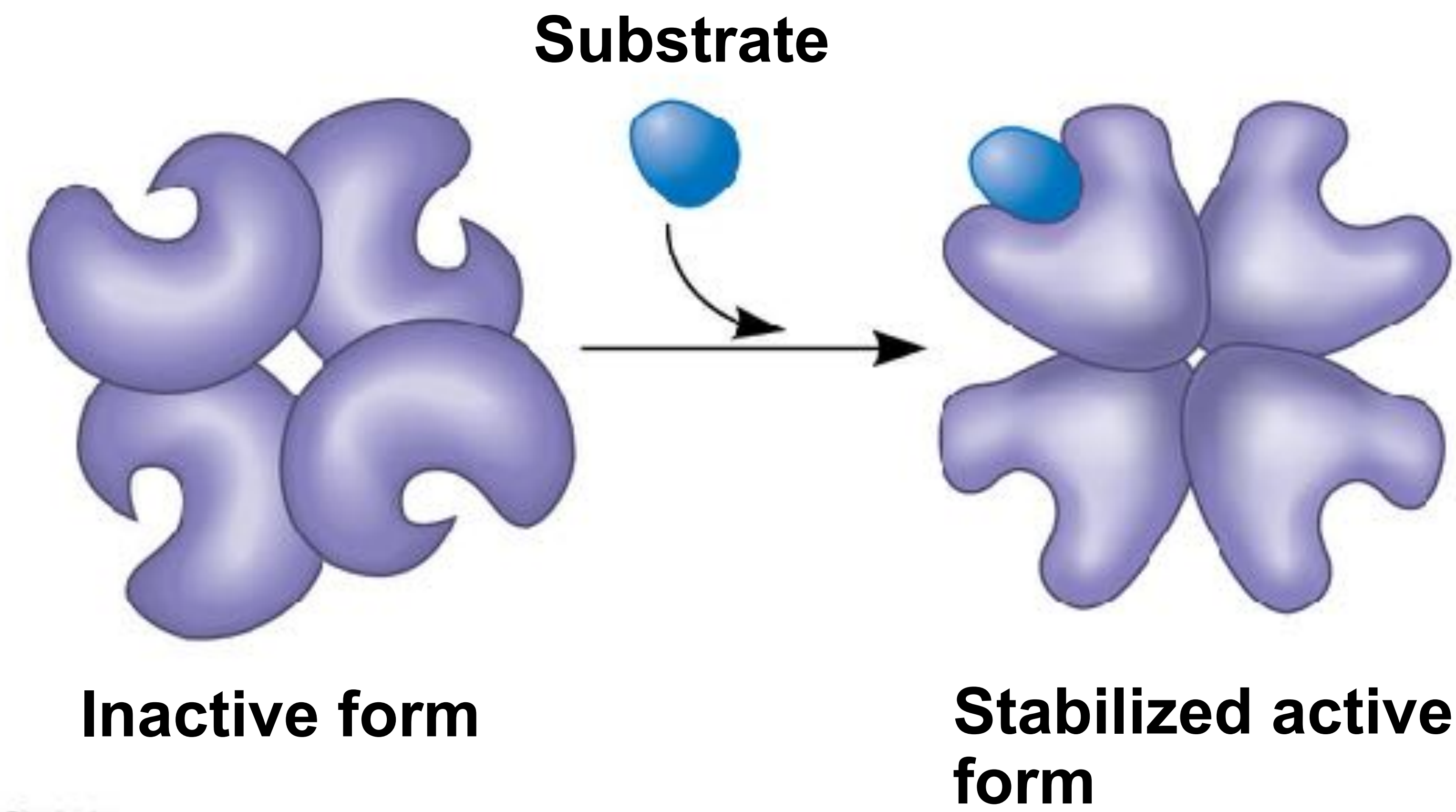

(a) Allosteric activators and inhibitors
Allosteric enzyme
with four subunits
Active site
(one of four)
Regulatory site
(one of four)
Activator
Active form
Stabilized active form
Oscillation
Nonfunctional
active site
Inhibitor
Inactive form
Stabilized inactive form

Figure 8.19b

(b) Cooperativity: another type of allosteric activation



- **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

Identification of Allosteric Regulators

- Allosteric regulators are attractive drug candidates for enzyme regulation because of their specificity
- Inhibition of proteolytic enzymes called *caspases* may help management of inappropriate inflammatory responses

Figure 8.20

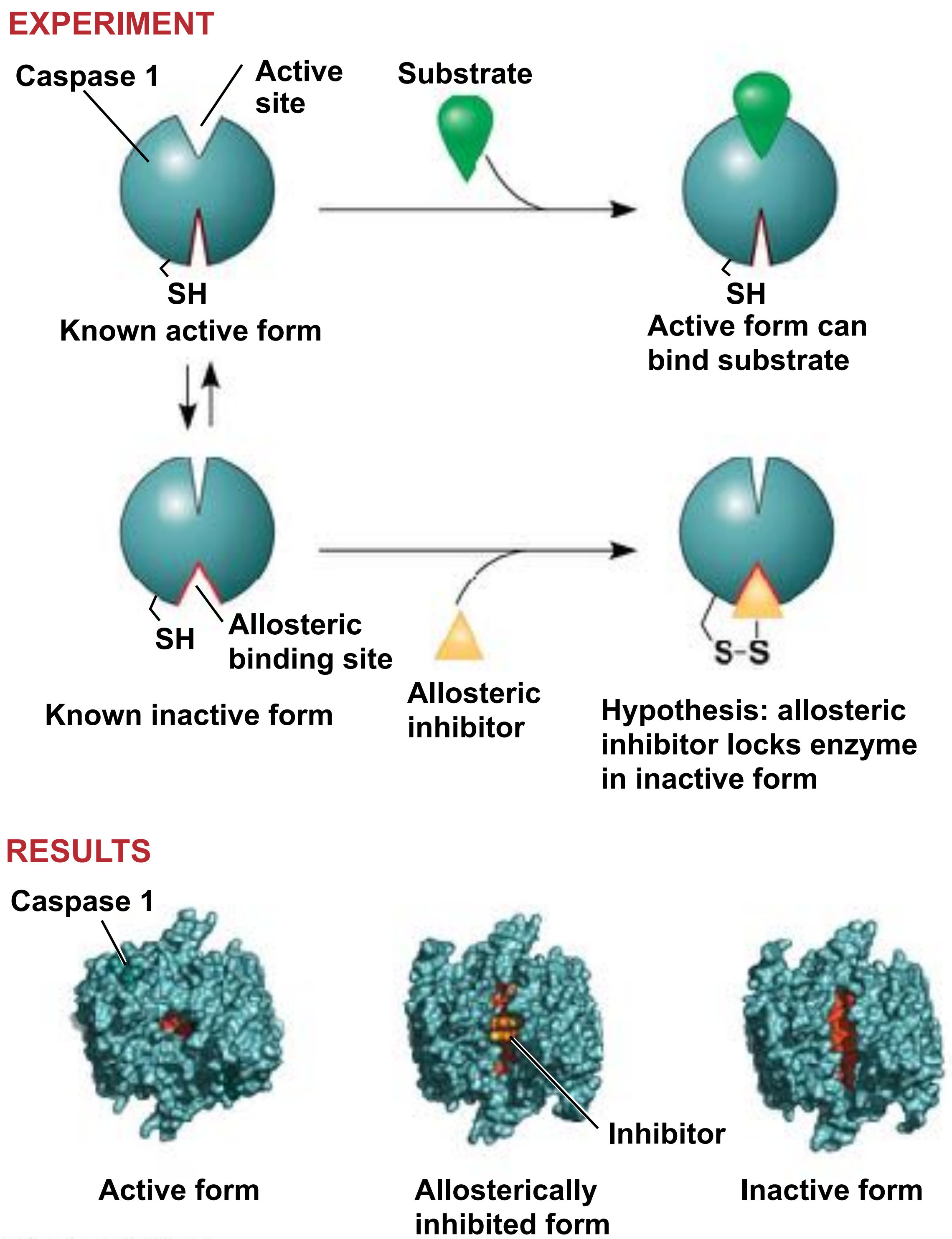
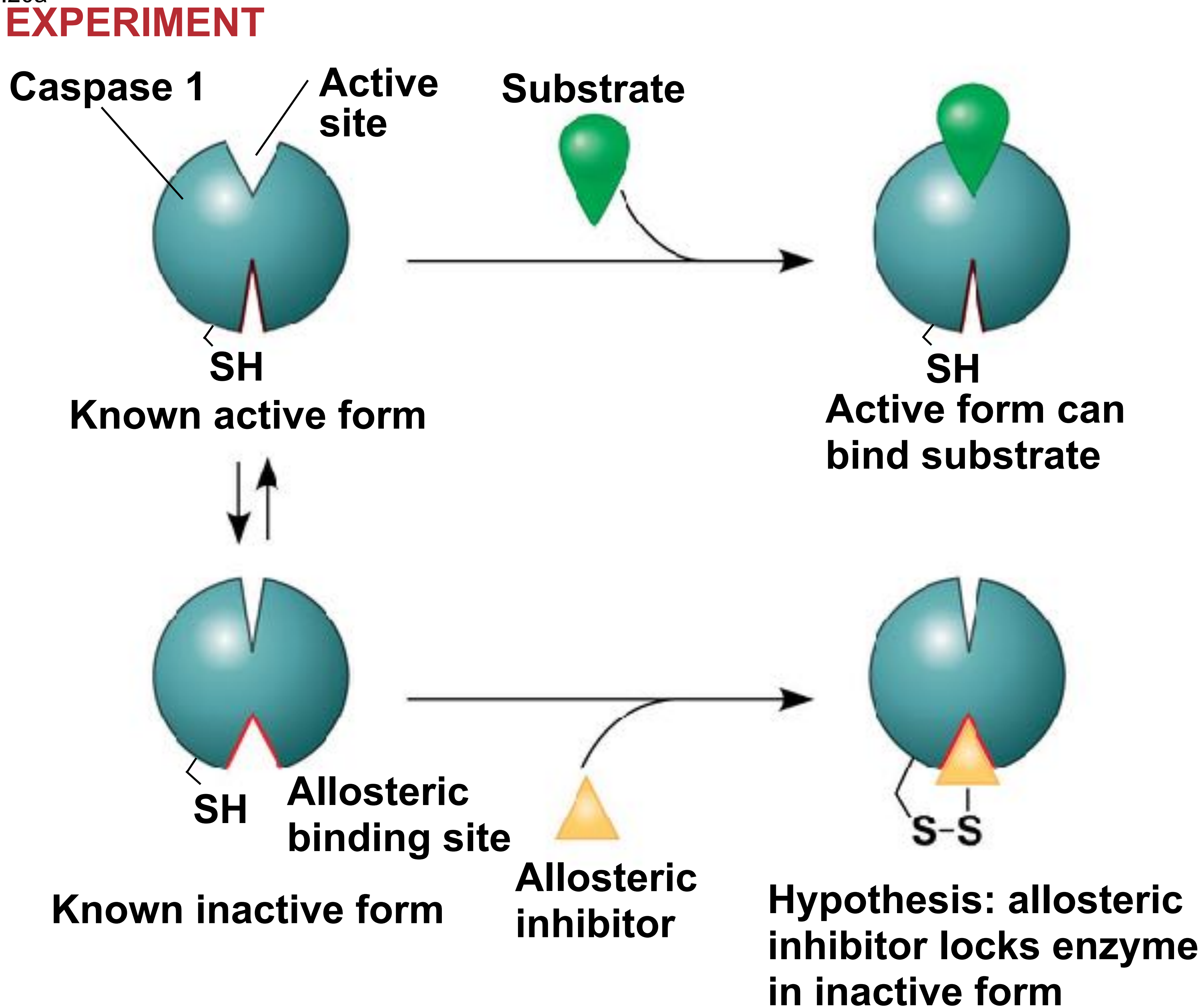
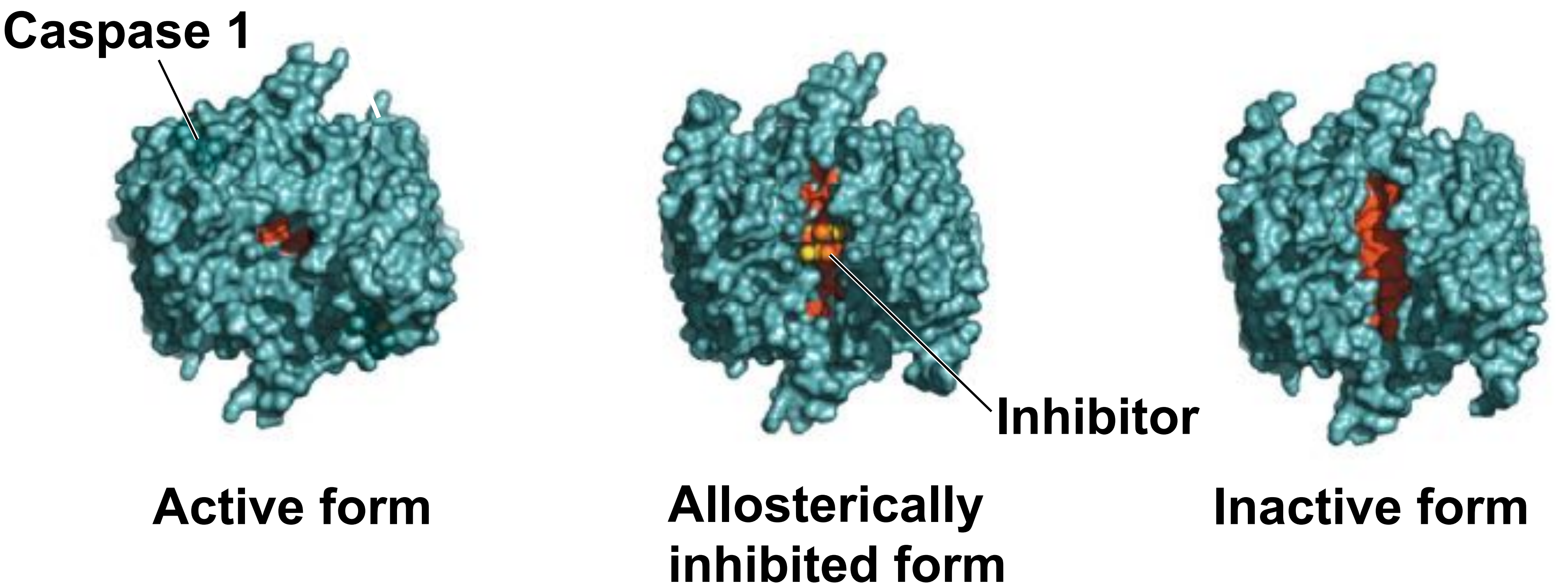

EXPERIMENT
Caspase 1
Active site
Substrate
SH
Known active form
SH
Active form can bind substrate
SH
Allosteric binding site
Known inactive form
Allosteric inhibitor
S–S
Hypothesis: allosteric inhibitor locks enzyme in inactive form
RESULTS
Caspase 1
Inhibitor
Active form
Allosterically inhibited form
Inactive form

Figure 8.20a


EXPERIMENT
Caspase 1
Active site
Substrate
SH
Known active form
SH
Active form can bind substrate
SH
Allosteric binding site
Allosteric inhibitor
S–S
Known inactive form
Hypothesis: allosteric inhibitor locks enzyme in inactive form

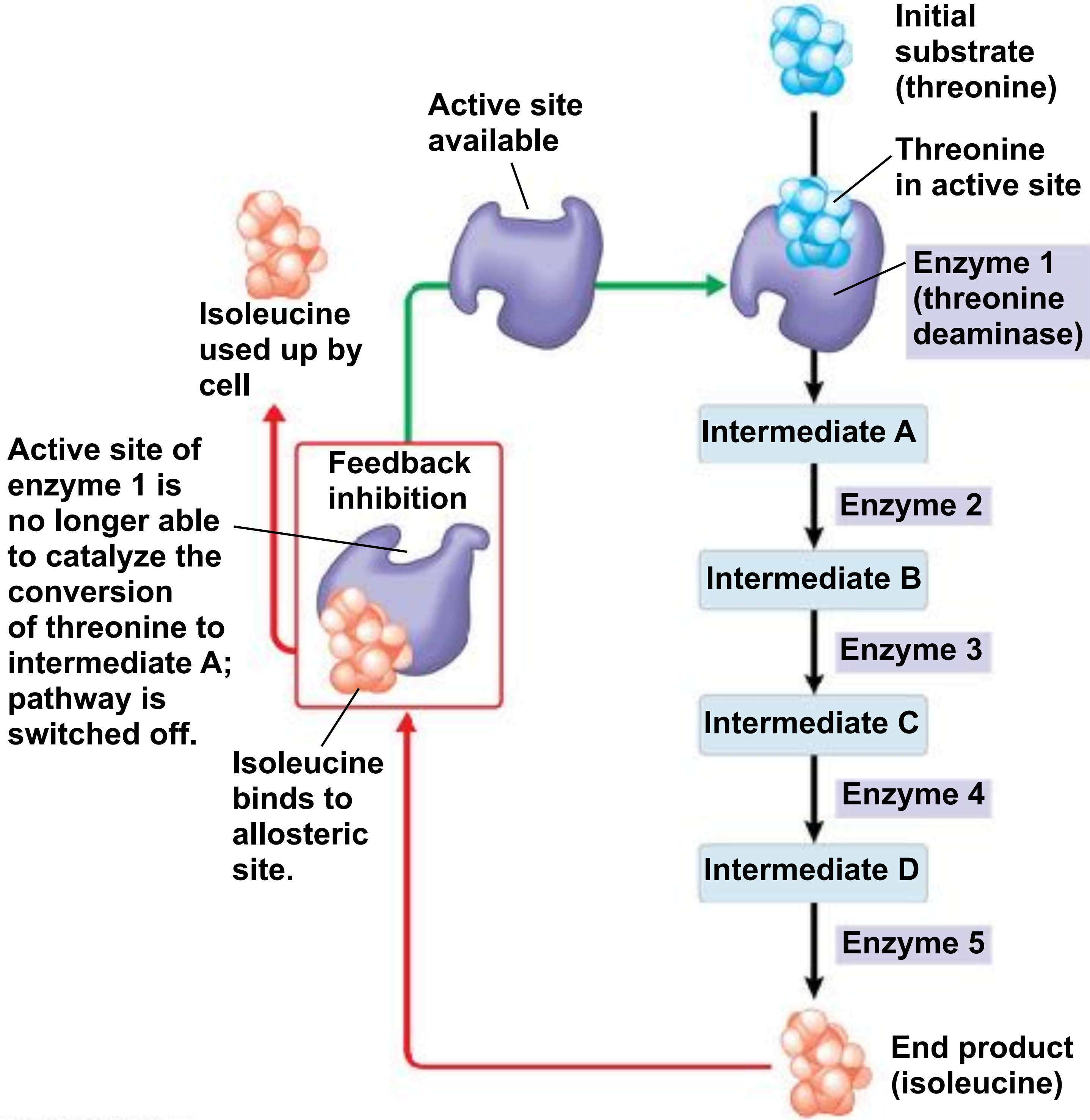
RESULTS


Caspase 1
Inhibitor
Active form
Allosterically inhibited form
Inactive form

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 8.21


Initial substrate (threonine)
Active site available
Threonine in active site
Enzyme 1 (threonine deaminase)
Isoleucine used up by cell
Active site of enzyme 1 is no longer able to catalyze the conversion of threonine to intermediate A; pathway is switched off.
Feedback inhibition
Intermediate A
Enzyme 2
Intermediate B
Enzyme 3
Intermediate C
Enzyme 4
Intermediate D
Enzyme 5
Isoleucine binds to allosteric site.
End product (isoleucine)

Specific Localization 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 8.22

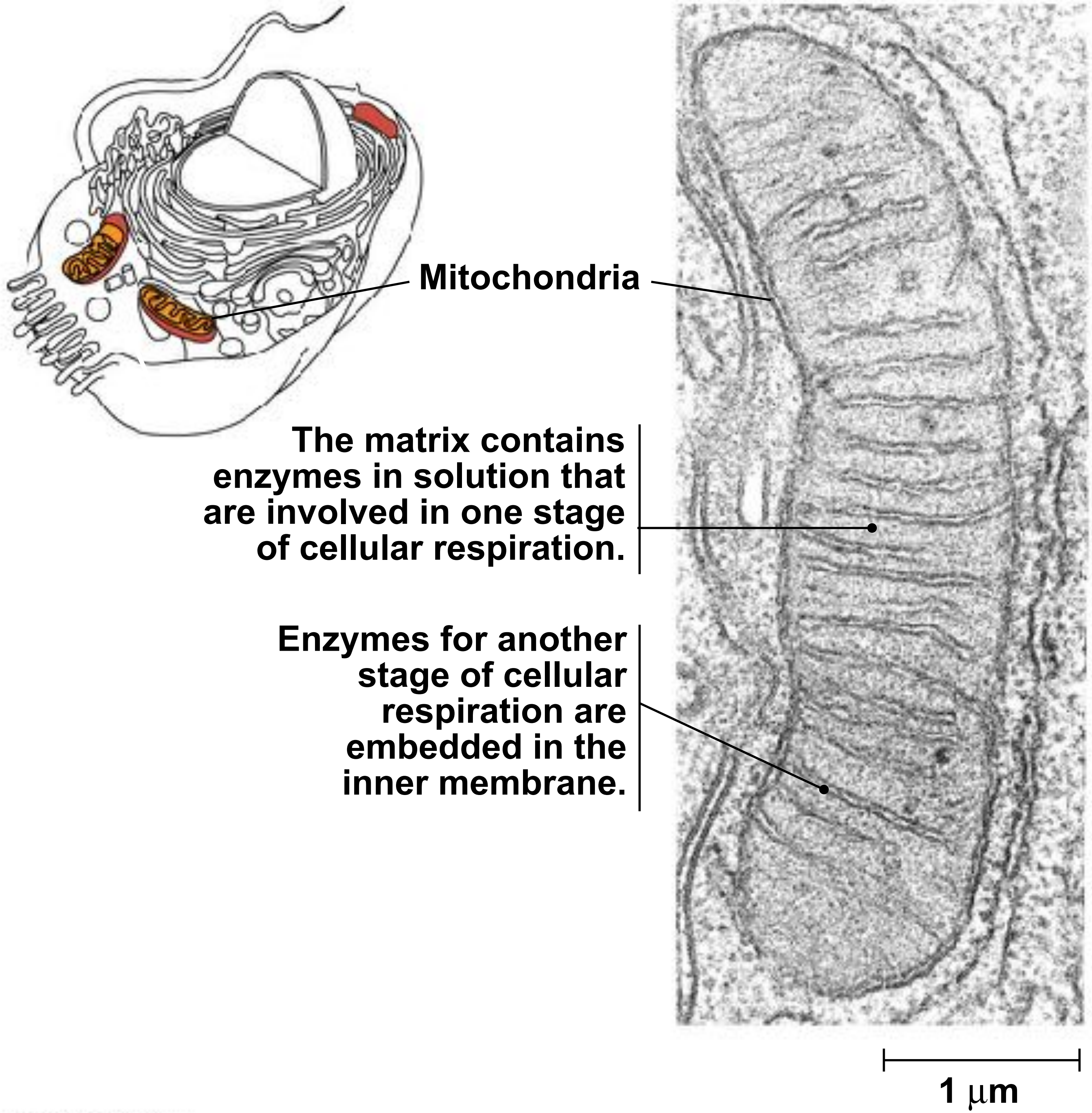
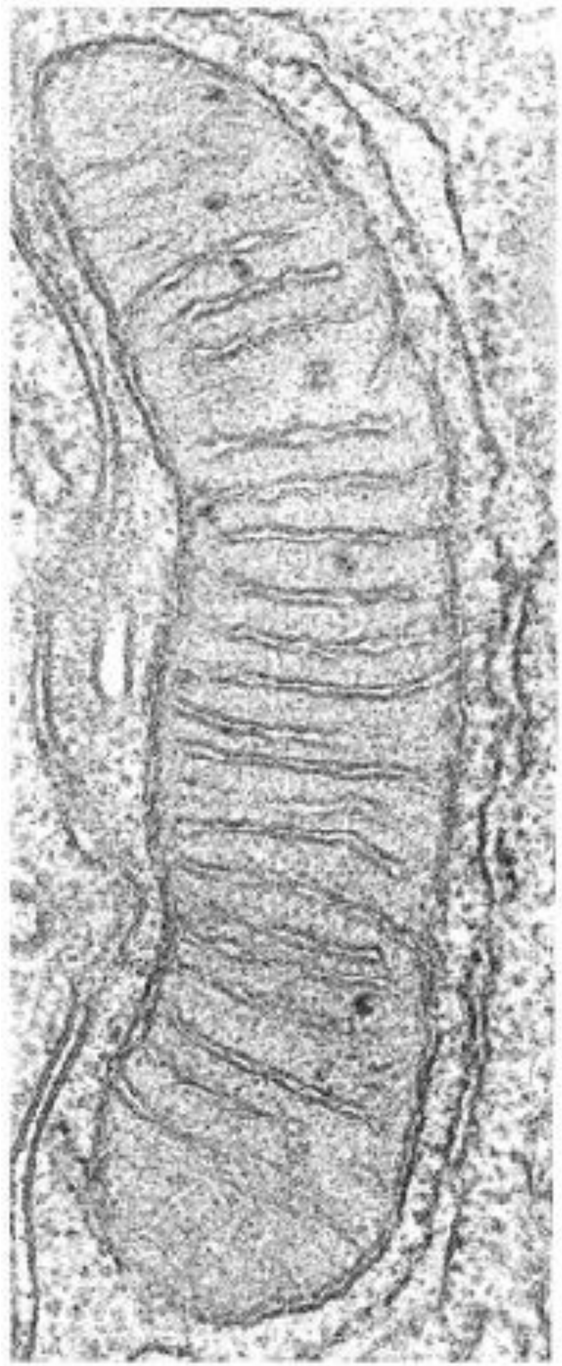

Mitochondria
The matrix contains enzymes in solution that are involved in one stage of cellular respiration.
Enzymes for another stage of cellular respiration are embedded in the inner membrane.
1 μm

Figure 8.22a



1 μm

Figure 8.UN03

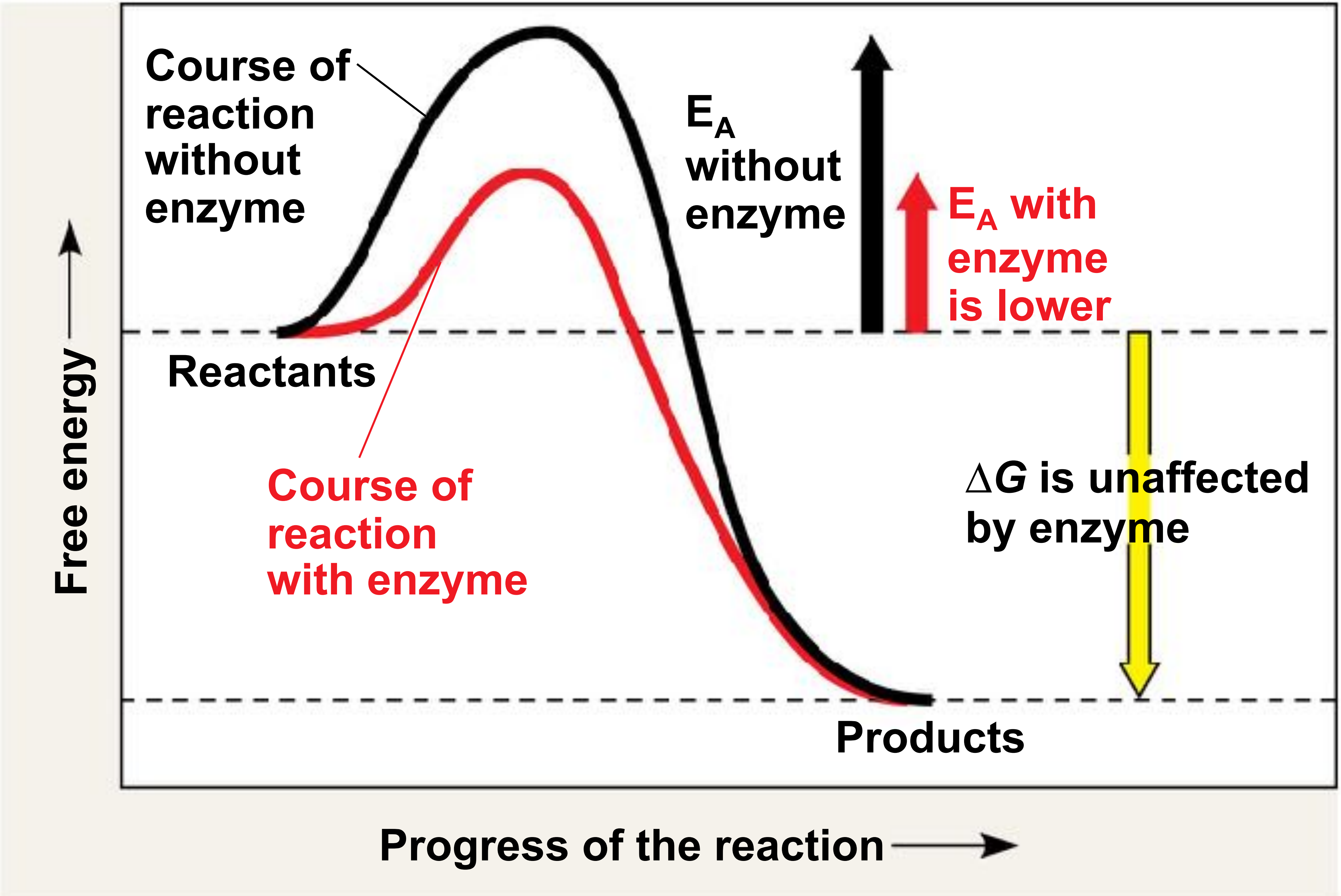


Figure 8.UN04

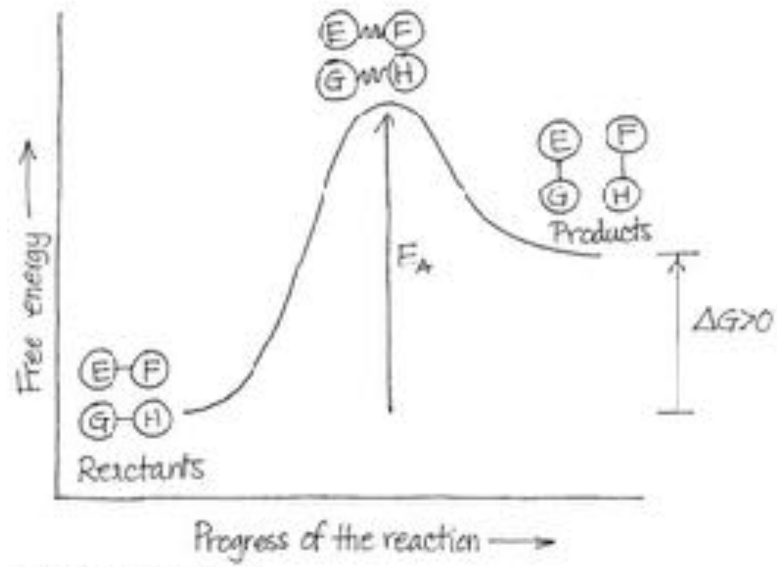


Figure 8.UN05

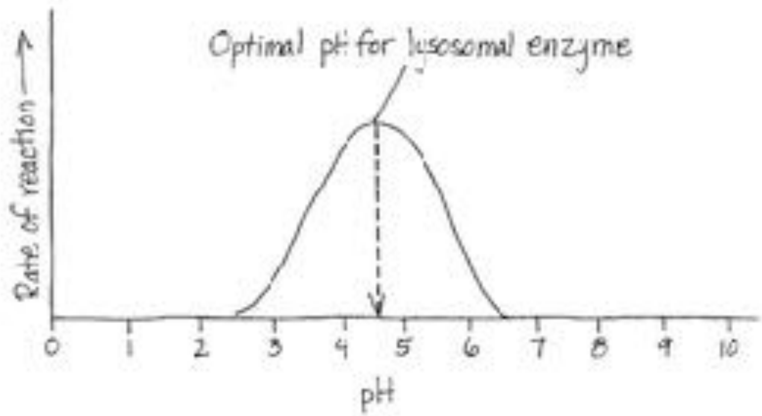


Figure 8.UN06

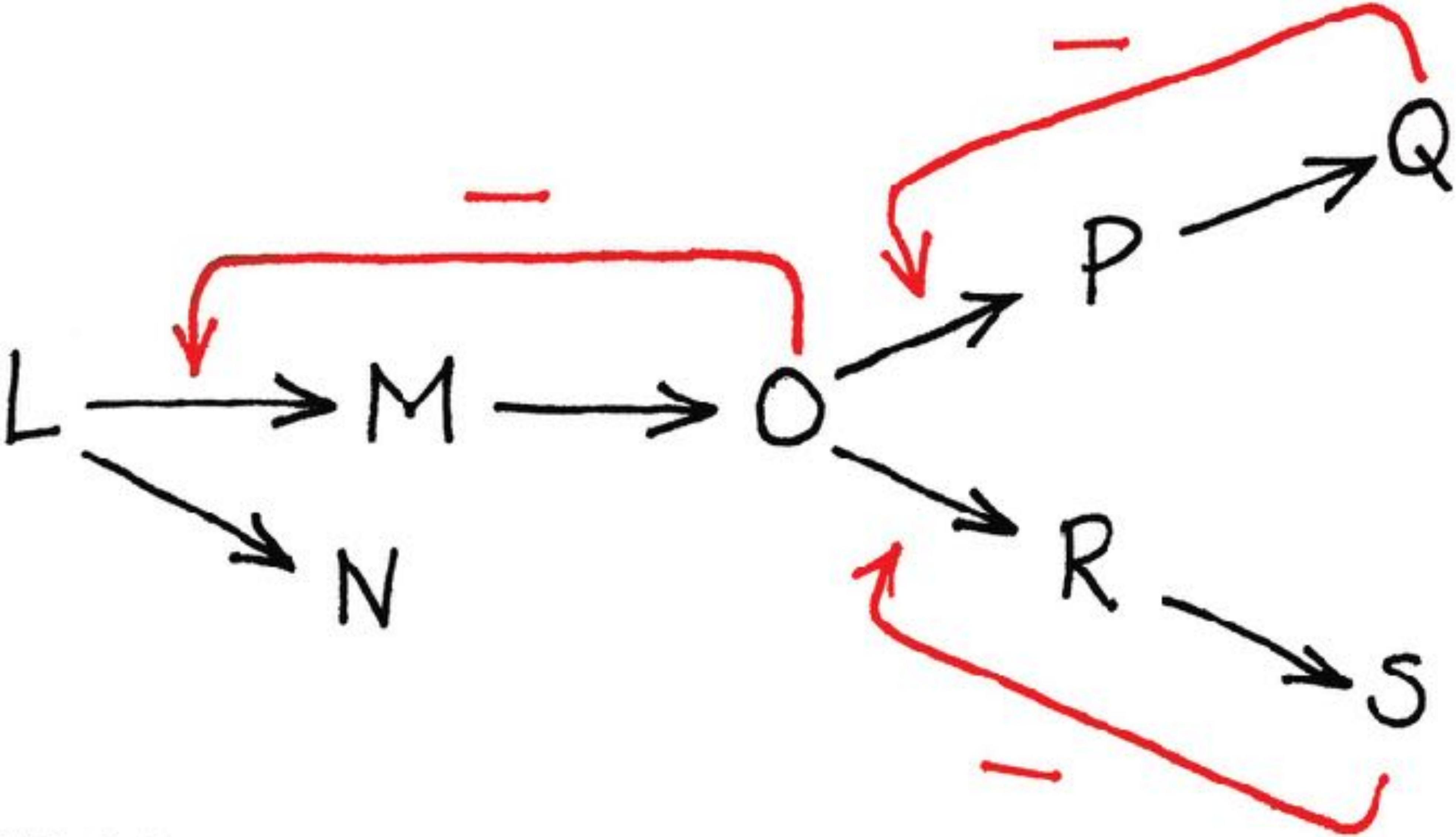


Figure 8.UN07