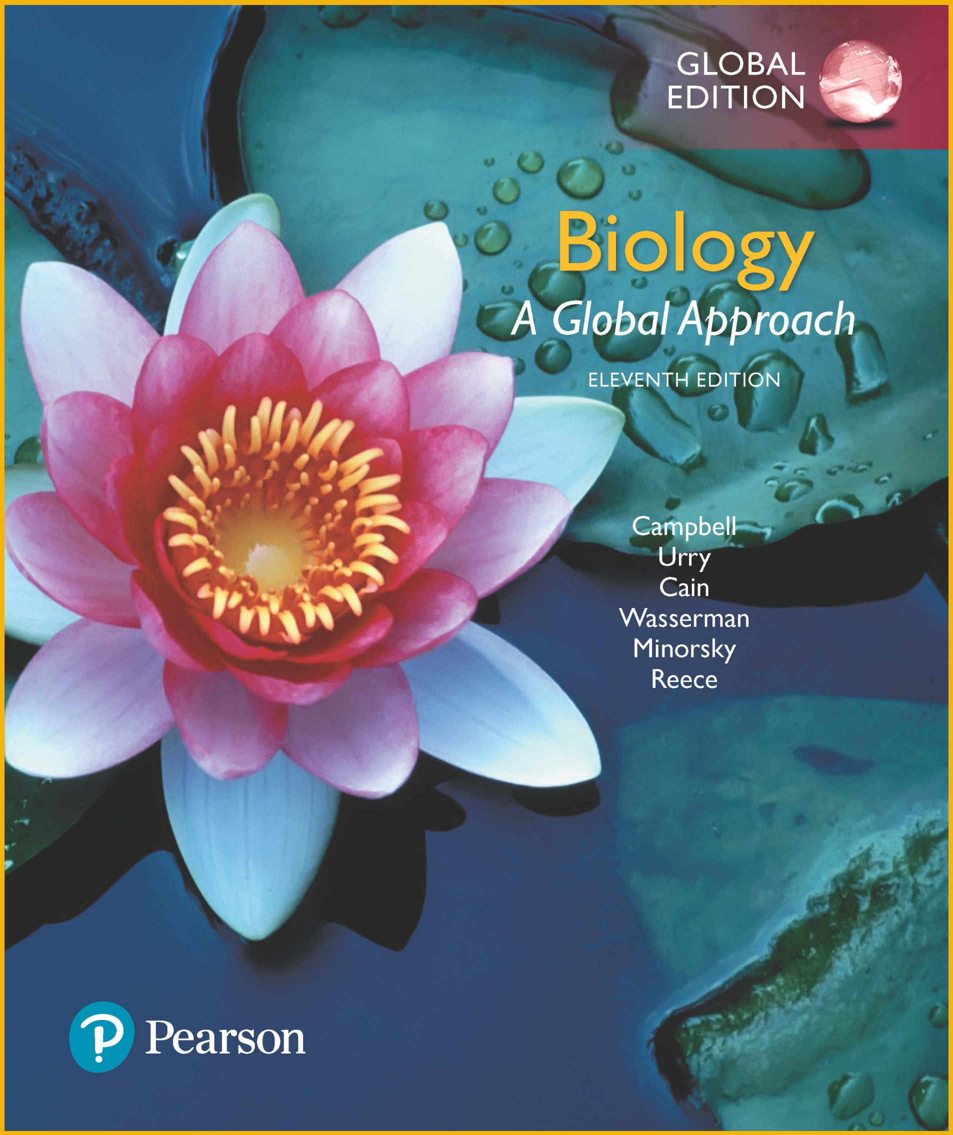


Chapter 6

Energy and Life

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

oncept 6.2: 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 the energy and entropy changes that occur in chemical reactions

ree-Energy Change, $\triangle G$

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

For a specific reactions, also depends on pH, concentrations, temperature ...

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

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

energy favorable

not literally spontaneous

not instantaneous

E_A barrier must be overcome.

- ΔG is negative for all spontaneous processes; processes with zero or positive ΔG are never spontaneous
- Spontaneous processes can be harnessed to perform work

ree 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

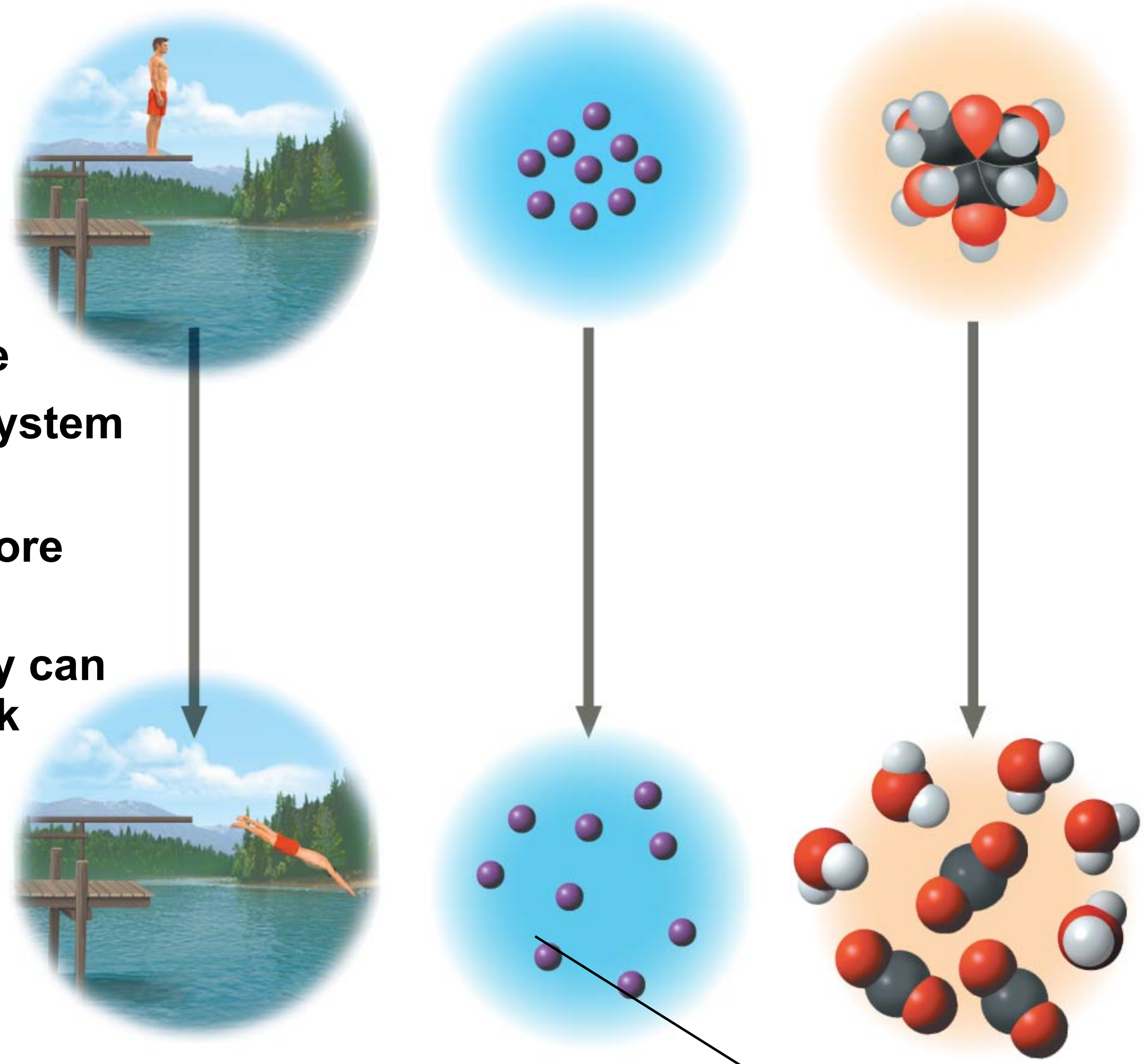
Figure 6.5

- **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**

ree Energy and Metabolism

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

unlike a cell.

[Closed systems will eventually reach equilibrium] doing no work

dead.

Equilibrium:

1. Forward and reverse reaction occur at equal rates.

2. No further net change in pr. & reac. conc.'s.

3. Free energy (G) is at its lowest possible value.

4. A system at equilibrium can not do work since free energy is at its minimum and ΔG is not negative.

Exergonic and Endergonic Reactions in Metabolism

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

For exergonic reactions, $|\Delta G|$ determines the amount of work a reaction can do.

→ endergonic ... the amount of work needed to drive the reaction

overall reaction for cellular respiration.

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6H_2O + 6CO_2$$

$\Delta G = -686$ kcal/mol $\equiv -2870$ kJ/mol.

Standard conditions: pH = 7, T = 25°C, [reac./prod.] = 1 M ≡ 1 mol/L

the reverse reaction "The assemble of $C_6H_{12}O_6$ from $6H_2O$ and $6H_2O$ needs $+686$ kcal/mol.

Figure 6.6a

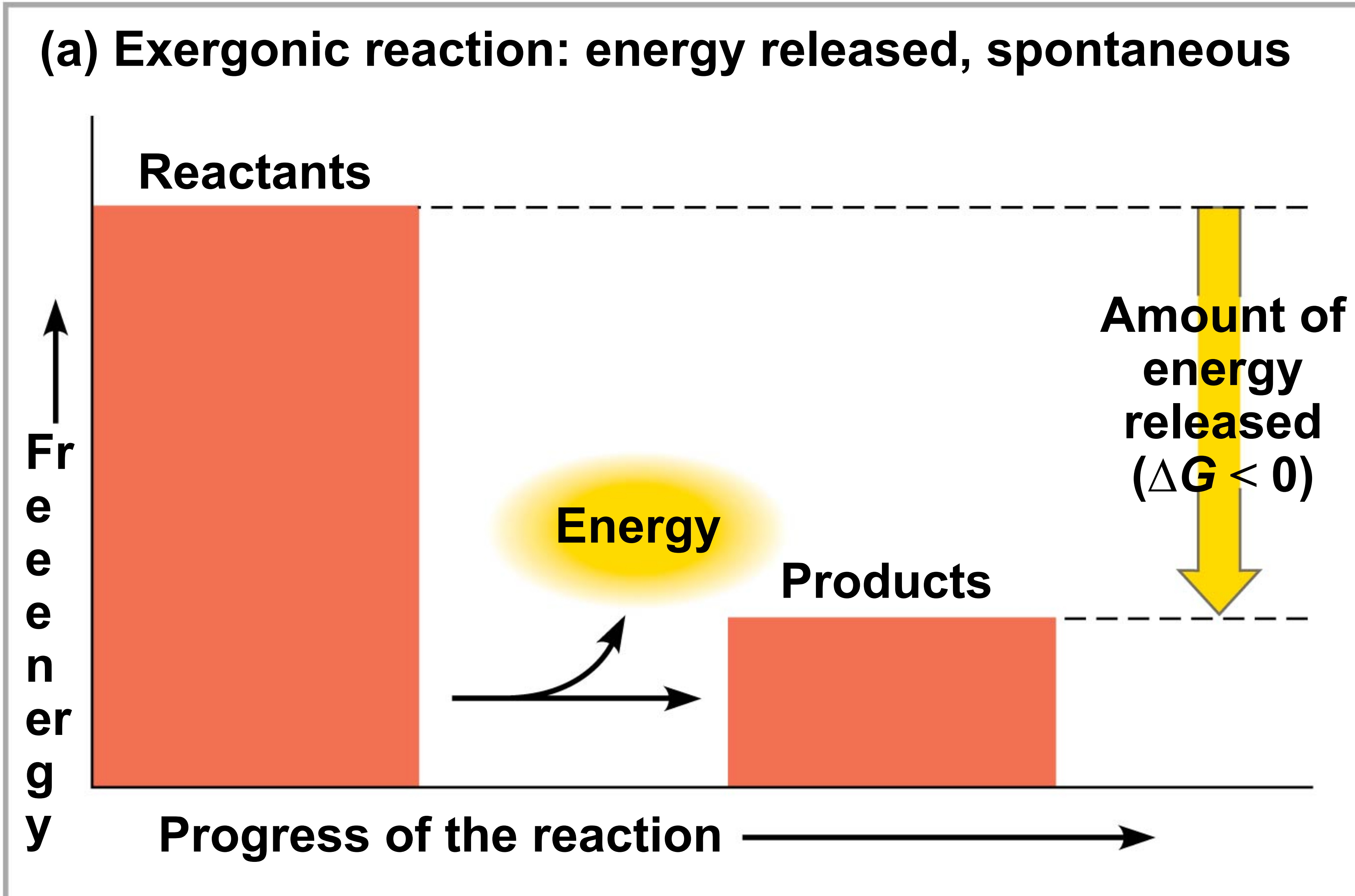
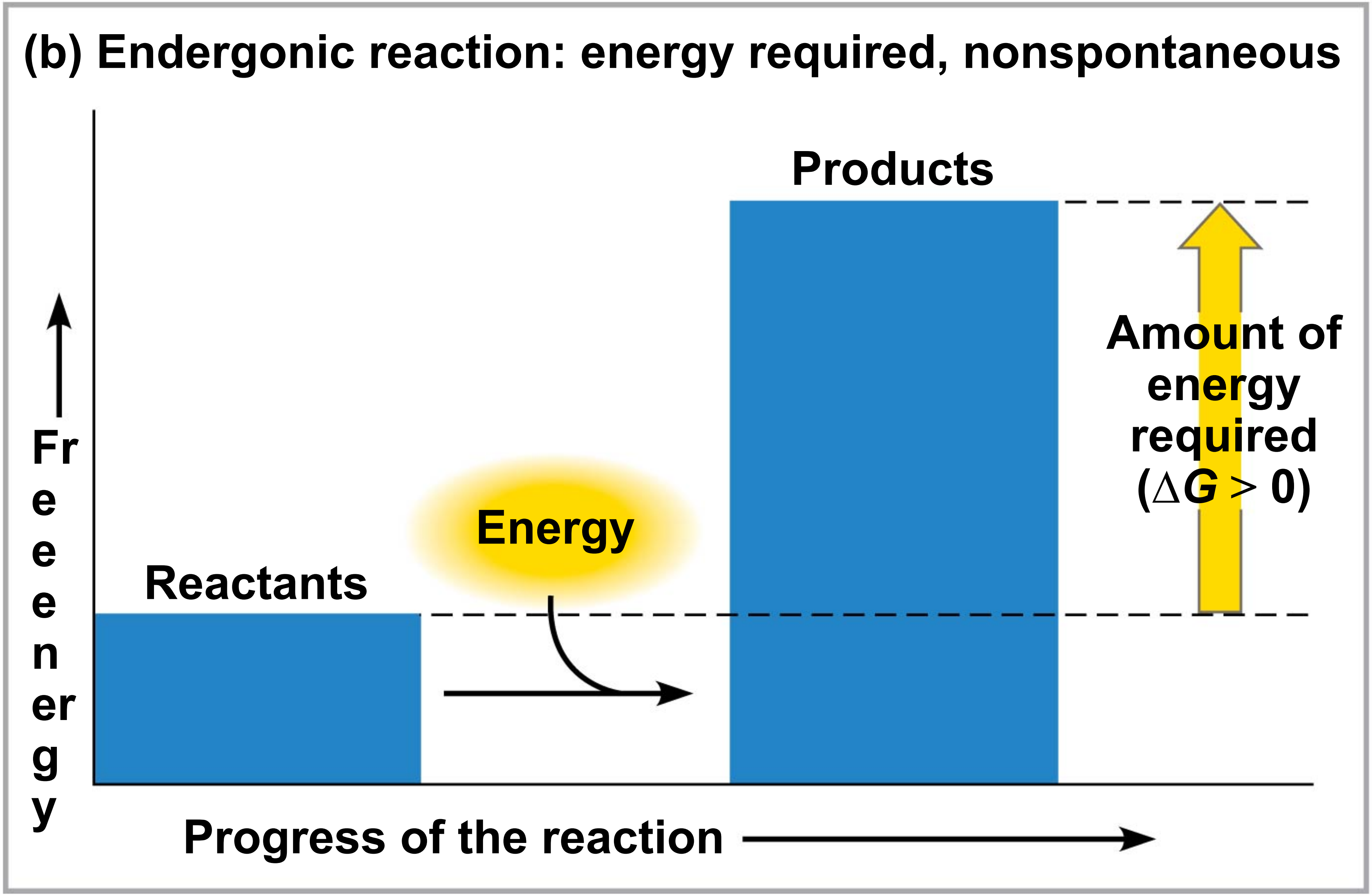

(a) Exergonic reaction: energy released, spontaneous
Reactants
Free energy
Energy
Products
Amount of energy released ($\Delta G < 0$)
Progress of the reaction

Figure 6.6b



(b) Endergonic reaction: energy required, nonspontaneous
Products
Amount of energy required ($\Delta G > 0$)
Energy
Reactants
Free energy
Progress of the reaction

Equilibrium and Metabolism

- Reactions in a closed system eventually reach equilibrium and can then do no work

The key in not reaching equilibrium is the decrease in concentrations of Products in a step as they become Reactants in a next step. [never accumulating].

Wastes are expelled out of the body

→ CO_2 & H_2O in cellular respiration

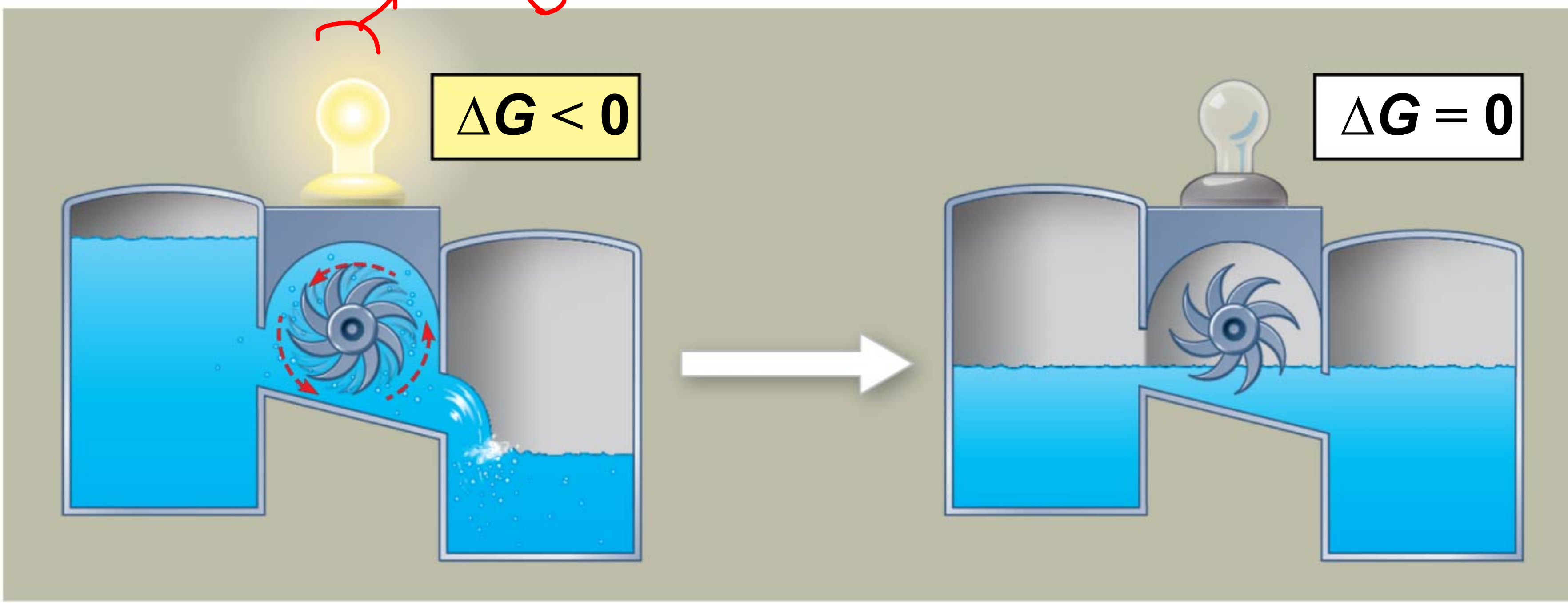
organisms are open systems.

→ Photosynthetic takes G from sunlight

→ non-Photosynthetic takes G from organic products of photosynthesis

Figure 6.7

Work Done.

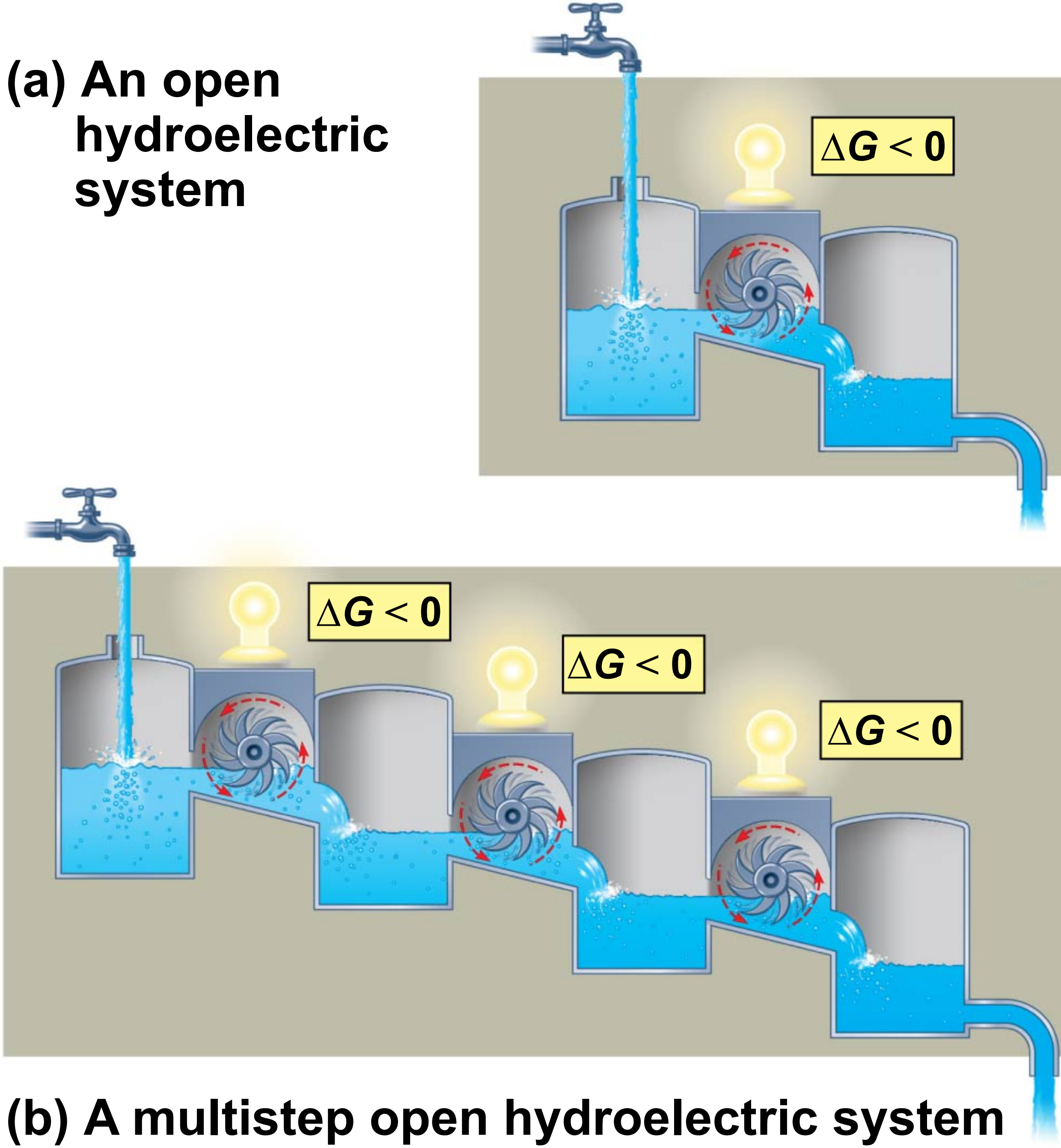


Equilibrium

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

Figure 6.8


(a) An open hydroelectric system
ΔG < 0
ΔG < 0
ΔG < 0
ΔG < 0
(b) A multistep open hydroelectric system

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

need energy

- A cell does three main kinds of work:
  - Chemical work—pushing endergonic reactions
  - Transport work—pumping substances against the direction of spontaneous movement
  - Mechanical work—such as contraction of muscle cells

e.g's

Synthesis of polymers from monomers.

Active transport, endocytosis or exocytosis.

Beating of cilia, contraction of muscles or movement of chromosomes during cell division.

- 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

acts as an immediate energy source.

he Structure and Hydrolysis of ATP

one of nucleoside triphospates used in making RNA.

- **ATP (adenosine triphosphate)** is the cell's energy shuttle

C2 has Oxygen

- ATP is composed of ribose (a sugar), adenine (a nitrogenous base), and three phosphate groups

For ATP hydrolysis:

$ATP + H_2O \longrightarrow ADP + P_i$ [exergonic]

$\Delta G = -7.3$ kcal/mol $\equiv -30.5$ kJ/mol

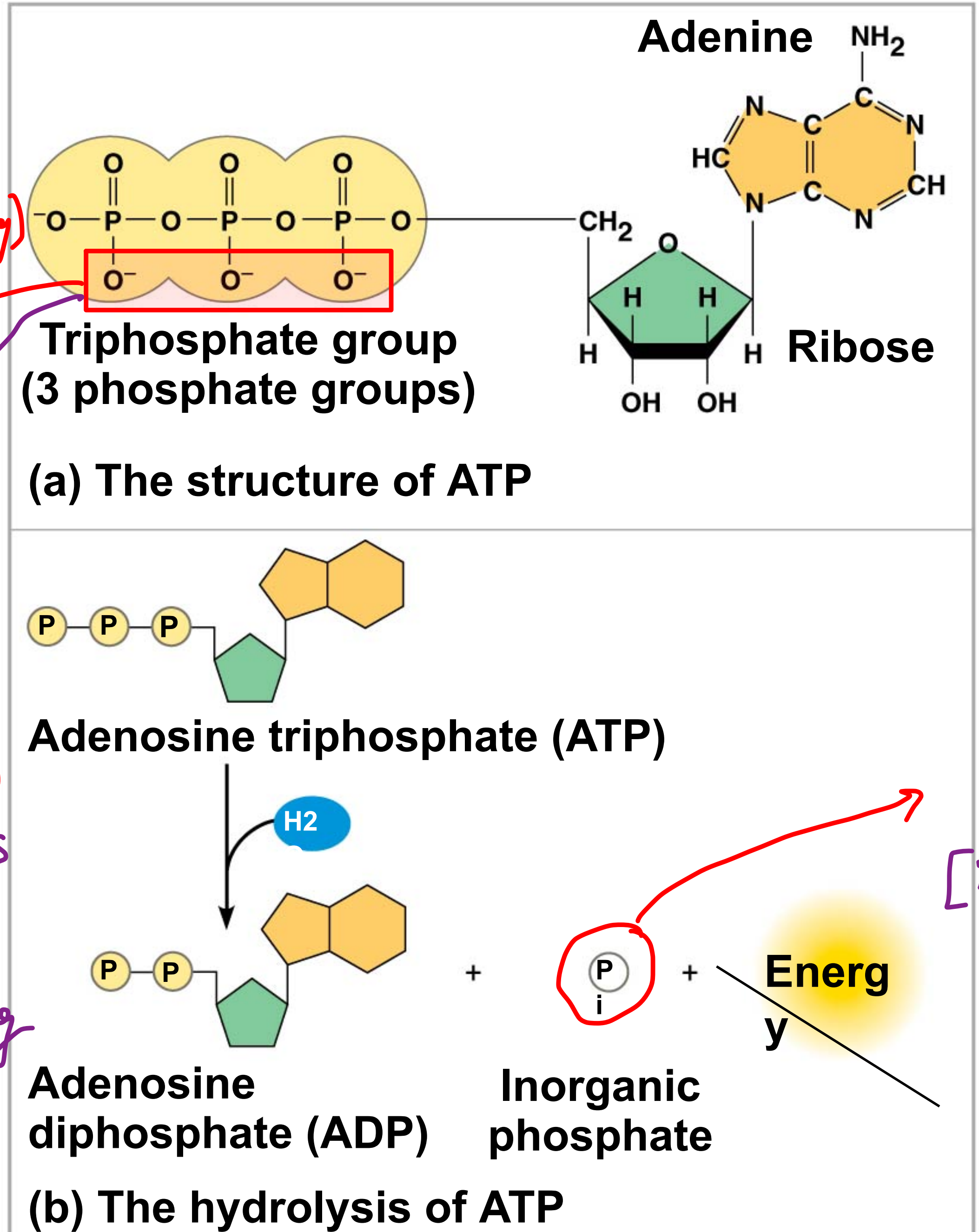
For Standard con. (1M, 25 °C, 7(pH)).

For Cellular conditions:

$\Delta G = -13$ kcal/mol $\cong 178\% * \Delta G^\circ$ [notation not rigid here].

Figure 6.9

(mostly occurring) ionized form of —OH



repulsive force between phosphate (−) groups acts as a compressed spring [high energy output].

$HOPO_3^{2-}$ [inorganic phosphate]

- 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 } → Important.

⊛ destroying of High energy bonds
&
formation of low energy bonds } $\Delta G < 0$

ow 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

For an endergonic reaction, ΔG_1

& an exergonic reaction, ΔG_2

if $\Delta G_1 + \Delta G_2 < 0 \Rightarrow$ they (the 2 reactions) can be coupled

[overall $\Rightarrow$ exergonic] [spontaneous]

- 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**

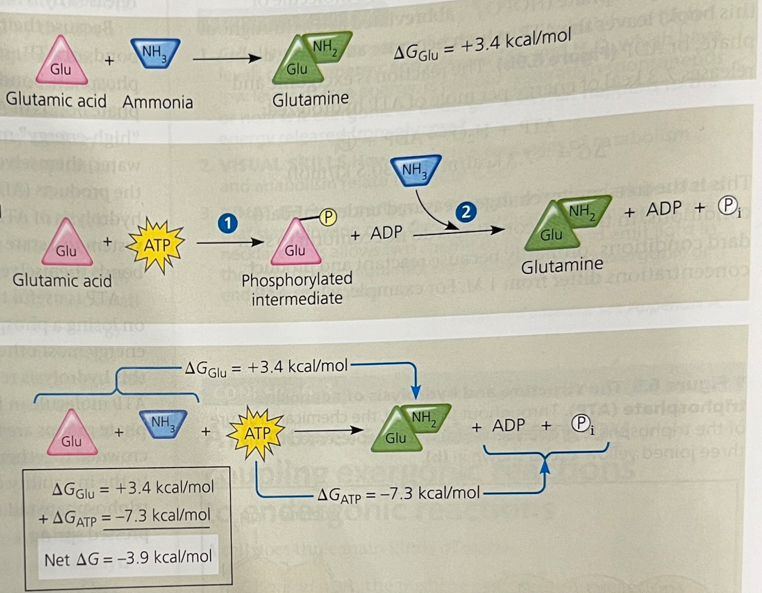
more reactive
higher free energy
less stable
than the original unphosporylated molecule.

▼ Figure 6.10 How ATP drives chemical work: energy coupling using ATP hydrolysis. In this example, the exergonic process of ATP hydrolysis drives an endergonic process—synthesis of the amino acid glutamine.

(a) Glutamic acid conversion to glutamine. Glutamine synthesis from glutamic acid (Glu) by itself is endergonic (ΔG is positive), so it is not spontaneous.

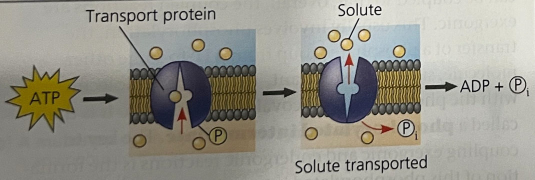
(b) Conversion reaction coupled with ATP hydrolysis. In the cell, glutamine synthesis occurs in two steps, coupled by a phosphorylated intermediate (Glu-Ⓟ). ❶ ATP phosphorylates glutamic acid, making it less stable, with more free energy. ❷ Ammonia displaces the phosphate group, forming glutamine.

(c) Free-energy change for coupled reaction. ΔG for the glutamic acid conversion to glutamine (+3.4 kcal/mol) plus ΔG for ATP hydrolysis (–7.3 kcal/mol) gives the free-energy change for the overall reaction (–3.9 kcal/mol). Because the overall process is exergonic (net ΔG is negative), it occurs spontaneously.

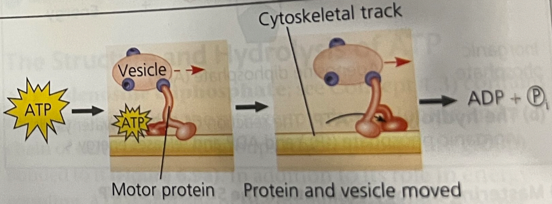


- Transport and mechanical work in the cell are also powered by ATP hydrolysis
- ATP hydrolysis leads to a change in protein shape and binding ability

▼ **Figure 6.11 How ATP drives transport and mechanical work.** ATP hydrolysis causes changes in the shapes and binding affinities of proteins. This can occur either **(a)** directly, by phosphorylation, as shown for a membrane protein carrying out active transport of a solute (see also Figure 8.16 and the proton pump in Figure 7.32, upper left), or **(b)** indirectly, via noncovalent binding of ATP and its hydrolytic products, as is the case for motor proteins that move vesicles (and other organelles) along cytoskeletal "tracks" in the cell (see also Figures 7.21 and 7.32, lower right).



(a) Transport work: ATP phosphorylates transport proteins, causing a shape change that allows transport of solutes.



(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed, causing a shape change that walks the motor protein forward.

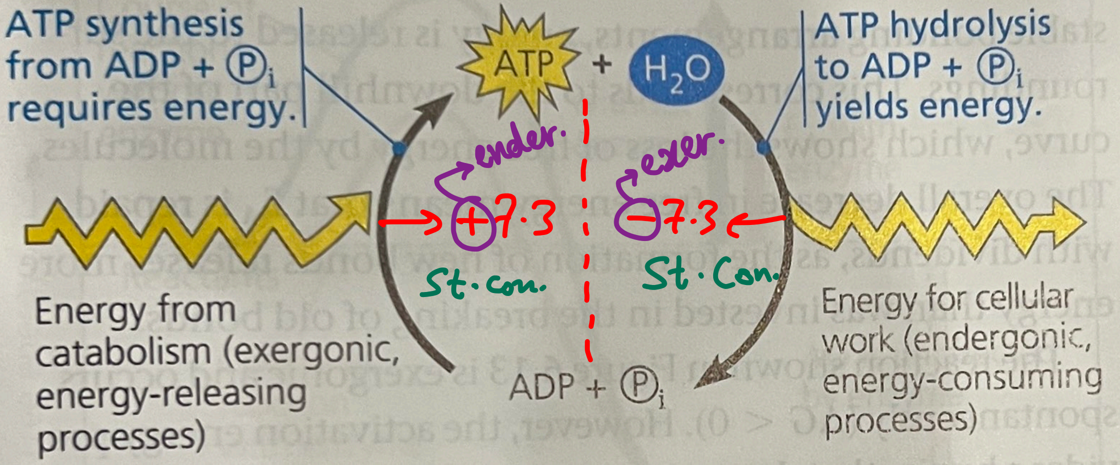
he Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP) needs energy [endergonic].
- 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

A muscle cell usually recycles its ATP pool in less than a minute.

10,000,000 ATP molecules per second per cell !!

▼ Figure 6.12 The ATP cycle. Energy released by breakdown reactions (catabolism) in the cell is used to phosphorylate ADP, regenerating ATP. Chemical potential energy stored in ATP drives most cellular work.



oncept 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

  Some RNA's [ribozymes] can act as catalysts

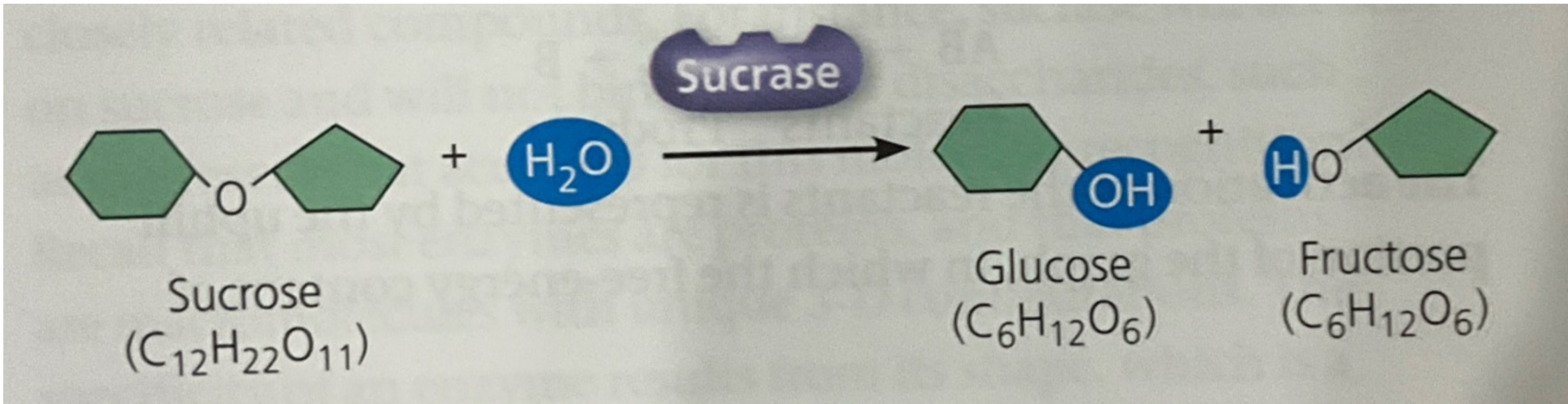
  - For example, sucrase is an enzyme that catalyzes the hydrolysis of sucrose + H_2O

    glucose + fructose

Figure 6.UN02

25°C, 1M, 7(pH).

→ exergonic $\Delta G^\circ = -7$ Kcal/mol.



without a catalyst (enzyme in this case), the reaction would take much longer time to be completed

he Activation Energy Barrier

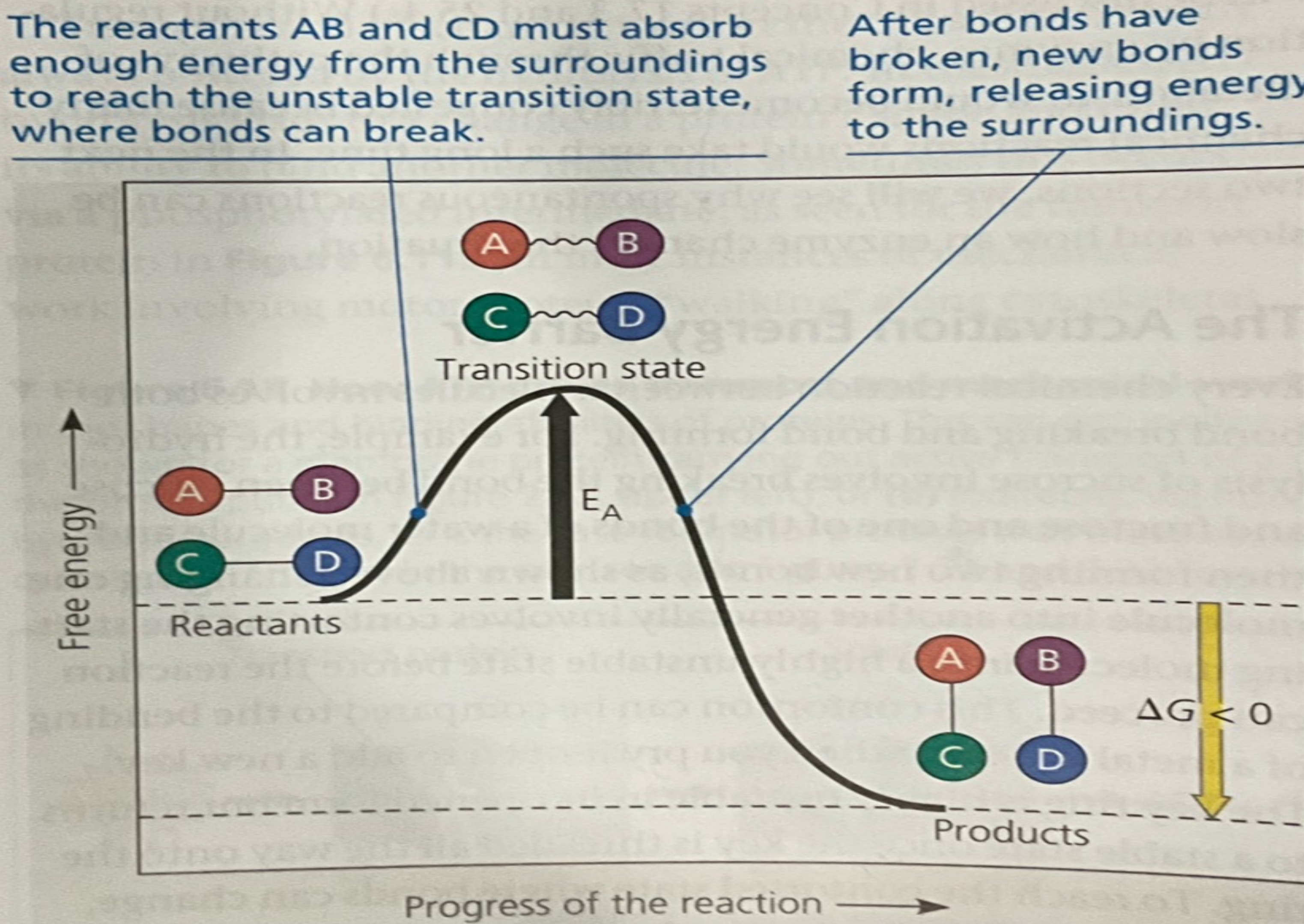
(*) The energy barrier determines the rate of the reaction.

- 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

- Chemical reactions involve breaking down of bonds and forming of new bonds with different (>, <) energy content [ΔG is dissipated as heat in spontaneous reactions]
  - heat ↳ transfer of thermal energy.

Figure 6

▼ Figure 6.13 Energy profile of an exergonic reaction. The "molecules" are hypothetical, with A, B, C, and D representing portions of the molecules. Thermodynamically, this is an exergonic reaction, with a negative ΔG, and the reaction occurs spontaneously. However, the activation energy (E_A) provides a barrier that determines the rate of the reaction.



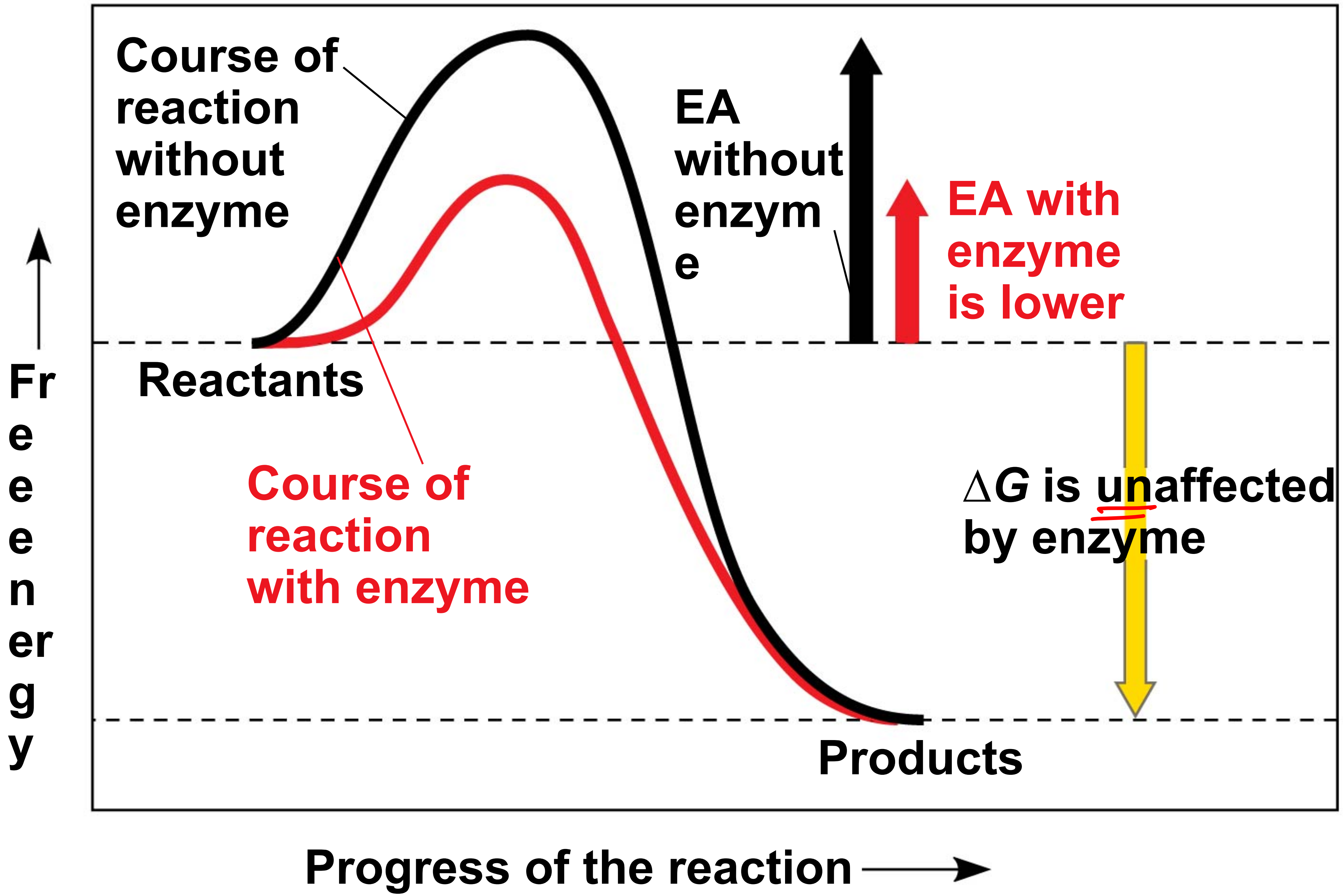
ow Enzymes Speed Up Reactions

- In **catalysis**, enzymes or other catalysts speed up specific reactions by lowering the EA barrier
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually

- Most macromolecules (DNA, Proteins, ...) have (−) ΔG of breaking down, but they exist (in high energy state) because their breakdown requires high E_A which is not present in biological cells [for good].

⊛ Enzymes can not change ΔG of a reaction.

Figure 6.14


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

ubstrate 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**
- While bound, the activity of the enzyme converts substrate to product

Enzymatic Activity

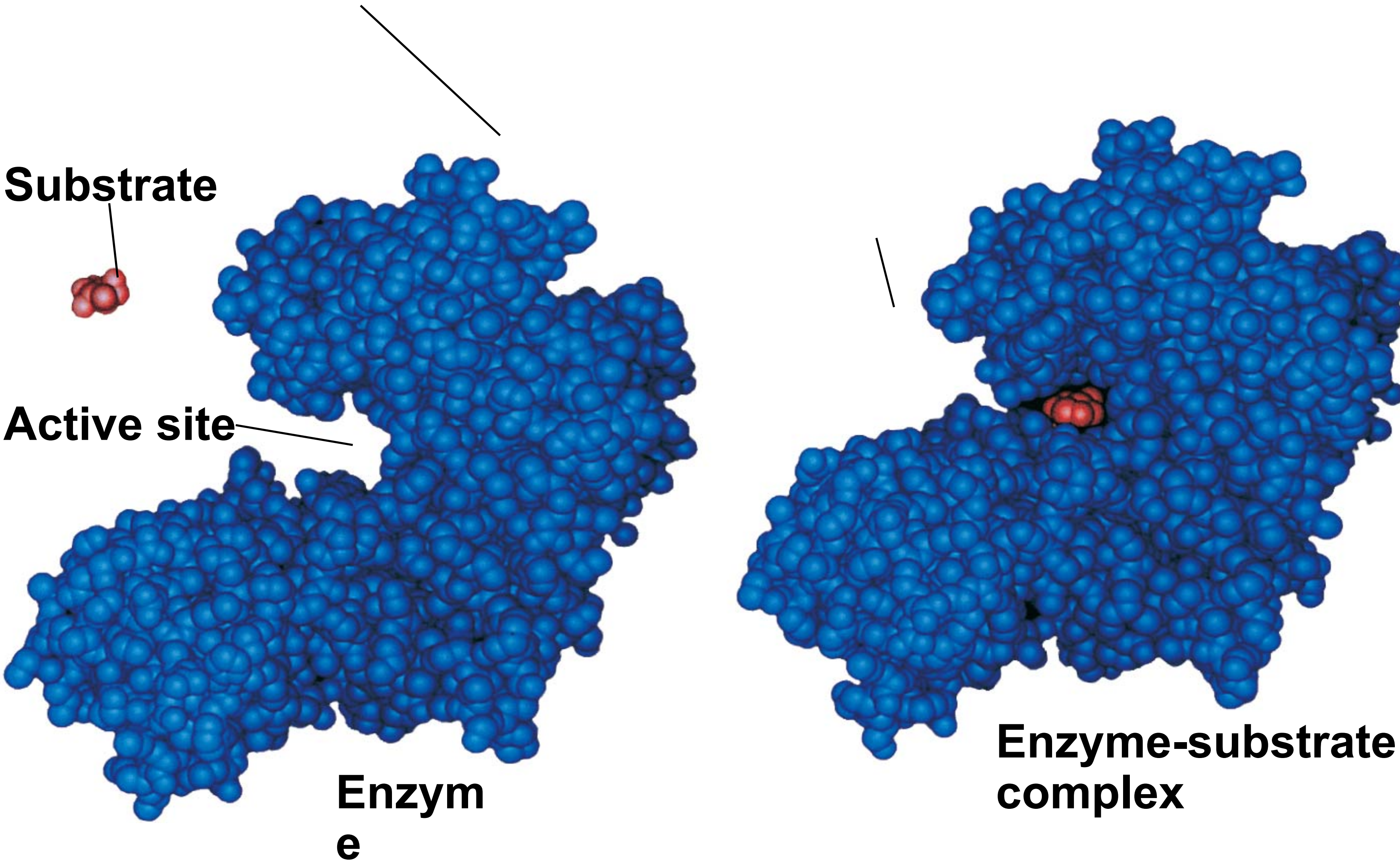
Enz. + substrate(s) ⇌ Enz–subs. comp. ⇌ Enz. + product(s)

* The Specificity of an enzyme comes from its unique 3-D shape [as a protein], a consequence of its A.acid sequence (Primary structure).

- The reaction catalyzed by each enzyme is very specific] → sucrase can not hydrolyze Maltose
- 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
- Enzymes are dynamic structures that keep oscillating between slightly different shapes.

* Non-Active Site A.acids make the framework of the enzyme to help the active site do its work.

Figure 6.15



atalysis in the Enzyme's Active Site

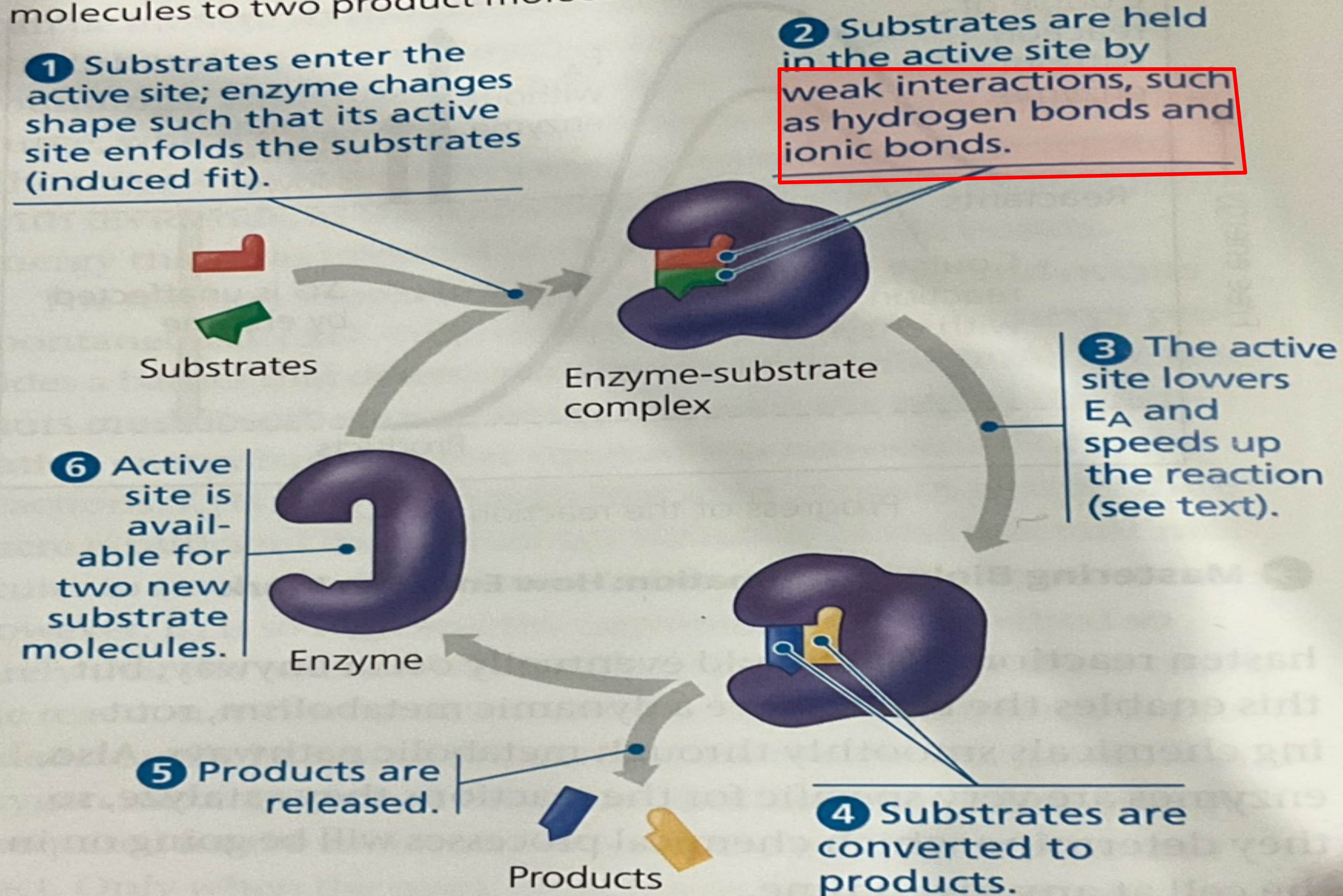
- In an enzymatic reaction, the substrate binds to the active site of the enzyme
- Enzymes are extremely fast acting and emerge from reactions in their original form
- Very small amounts of enzyme can have huge metabolic effects because they are used repeatedly in catalytic cycles

> 1000 Hz → bound with a distinct substrate molecule in one second.

(*) Most metabolic cycles are reversible and which of the 2 directions the enzyme catalyzes depends on ΔG (being (−)). and other factors such as the conc.'s.

Figure 6.16_4

▼ **Figure 6.16 The active site and catalytic cycle of an enzyme.** An enzyme can convert one or more reactant molecules to one or more product molecules. The enzyme shown here converts two substrate molecules to two product molecules.



- The active site can lower an EA barrier by
  - orienting substrates correctly] → provides a template for proper collisions
  - straining substrate bonds] → distorting substrate molecules to easily break them (less E_A) needed.
  - providing a favorable microenvironment → R-groups of active site — A.acids may contribute to pH conditions different from what a cell already has.
  - covalently bonding to the substrate

≡ direct participation

followed by steps to ensure that the active site returns to its original shape after the reaction is complete.

Acidic (R) → Low pH.
Glu [E]
Asp [D]
<7

- The rate of an enzyme-catalyzed reaction can be sped up by increasing substrate concentration
- When all enzyme molecules have their active sites engaged, the enzyme is saturated
- If the enzyme is saturated, the reaction rate can only be sped up by adding more enzyme

(A) for const. Enz. conc. $(n, m \in \mathbb{R}^+)$

Rate $\propto$ [subs.]^n · (speed of Enz. to convert subs.)^m

→ when "saturated" → only depends on (speed of Enz. ...). as [subs.] is excess.

(B) to increase Rate in "saturated"

→ add more enzyme ≡ change saturation status.

ffects 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

ffects 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

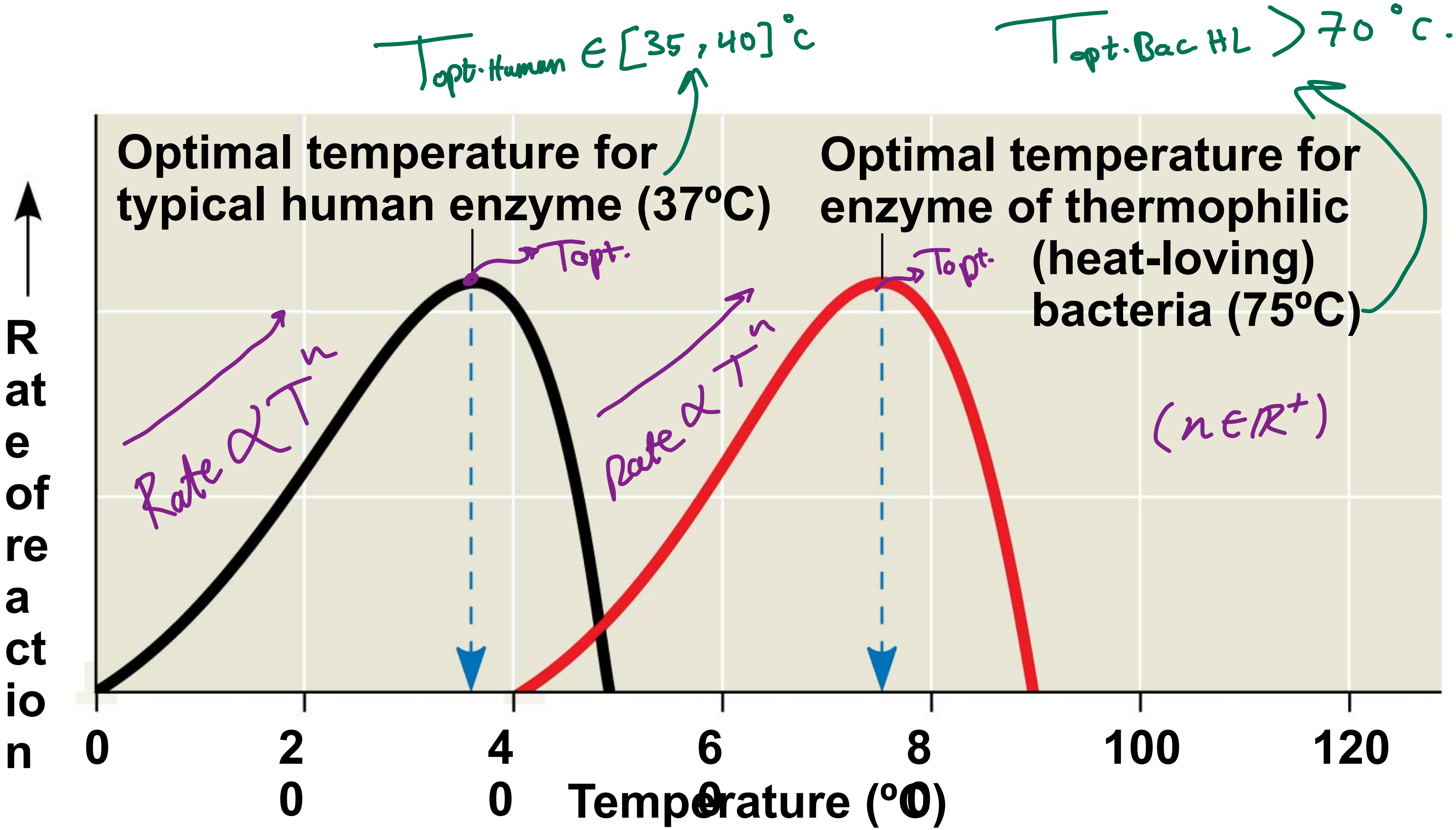
3-D structure suitable for catalysis.

(*) The enzyme (as a protein) denatures at "harsh" environmental conditions changing its shape and no longer suitable to work properly.

$Rate \propto T^n, n \in \mathbb{R}^+$ (usually)

$\equiv$ At $T < T_{opt}$. [see graph next].

Figure 6.17b

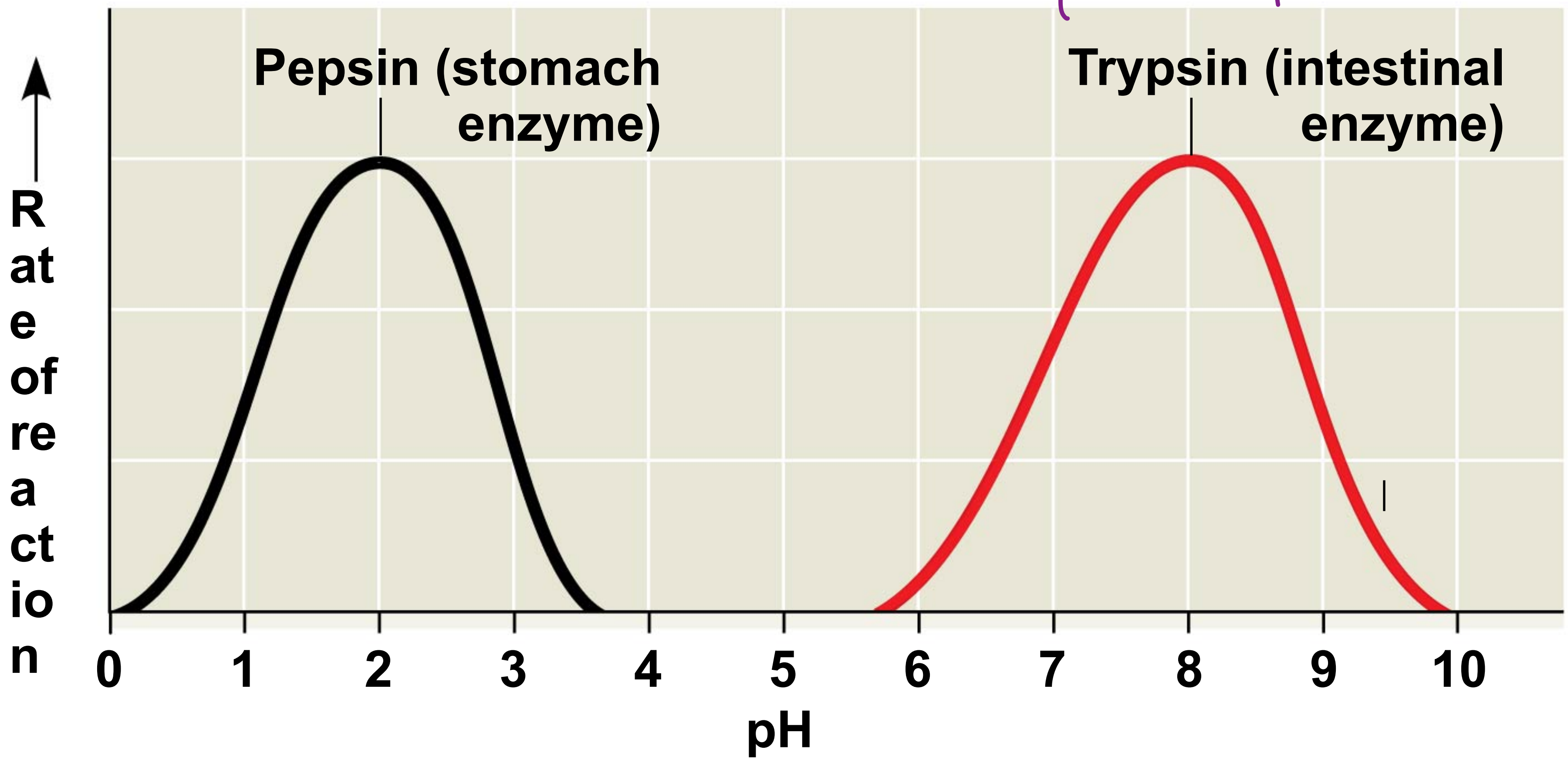


(a) Optimal temperature for two enzymes

Figure 6.17c

pH opt. most Enz. Human ∈ [6, 8] / {pepsin, ...}

would denature in stomach.



(b) Optimal pH for two enzymes

⊛ Pepsin adapts to low pH levels due to its unique 3-D structure.

Cofactors

- **Cofactors** are nonprotein enzyme helpers
- Cofactors may be inorganic (such as a metal in ionic form) or organic

  ↳ {Zn, Fe, Cu…}
- An organic cofactor is called a **coenzyme**
- Coenzymes include vitamins

Enzyme Inhibitors

can be overcome by increasing [subs.] unlike Noncomp.

- **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
- Some examples of inhibitors are toxins, poisons, pesticides, and antibiotics → usually irreversible

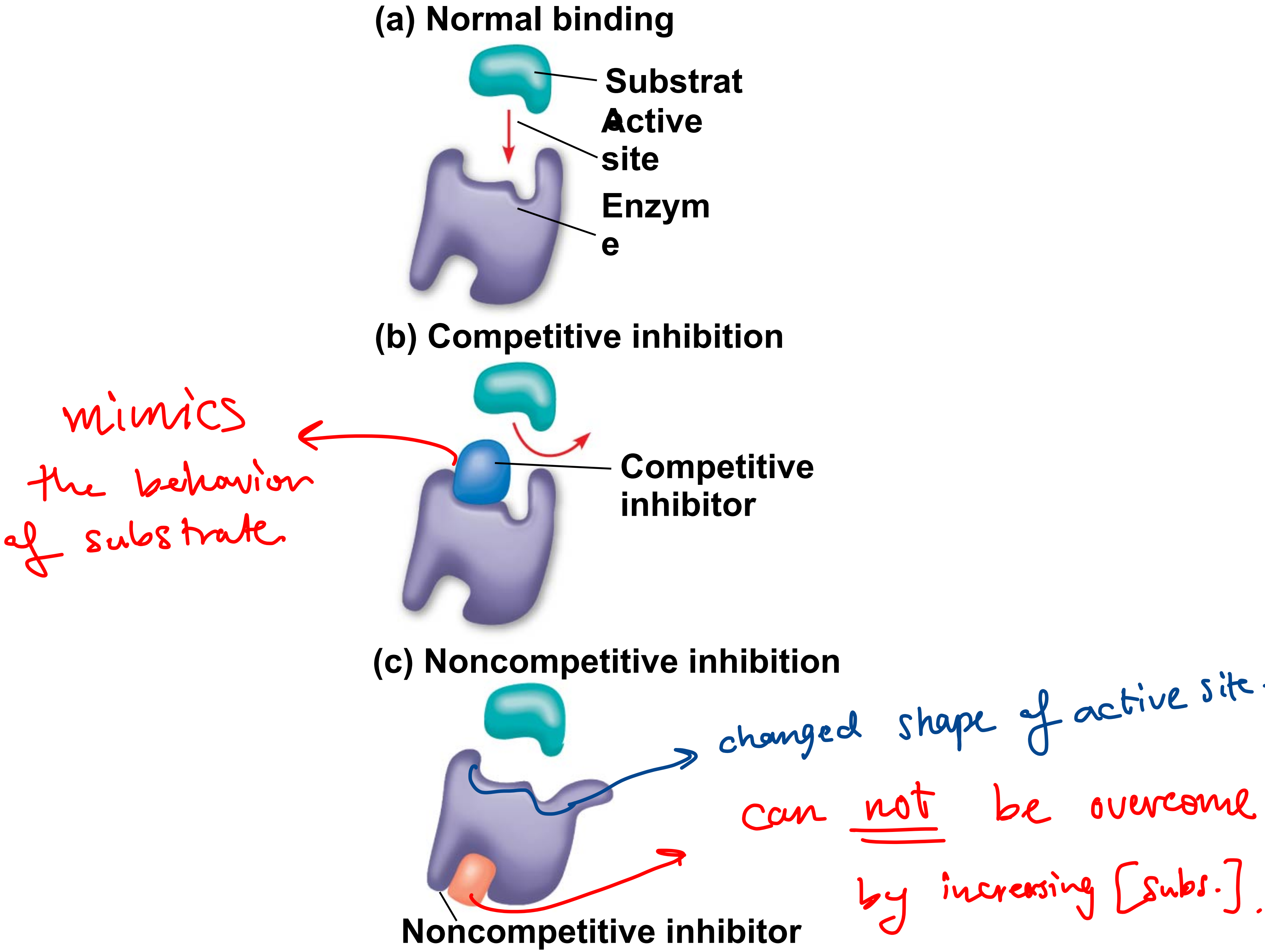
(*) If an inhibitor covalently bonds to an enzyme, it is most likely irreversible.

e.g. Sarin ↳ affects Nerv. Sys.
by cov. bond to $(CH_2OH)(R)$ in Serine in Acetyl-Cholinesterase.

DDT, Parathion

Penicillin ↳ affects Bac's ability to make cell walls.

Figure 6.18


(a) Normal binding
Substrat
Active site
Enzym e
(b) Competitive inhibition
Competitive inhibitor
mimics the behavior of substrate
(c) Noncompetitive inhibition
changed shape of active site.
can not be overcome by increasing [Subs.].
Noncompetitive inhibitor

he 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, particularly at the active site, can result in novel enzyme activity or altered substrate specificity

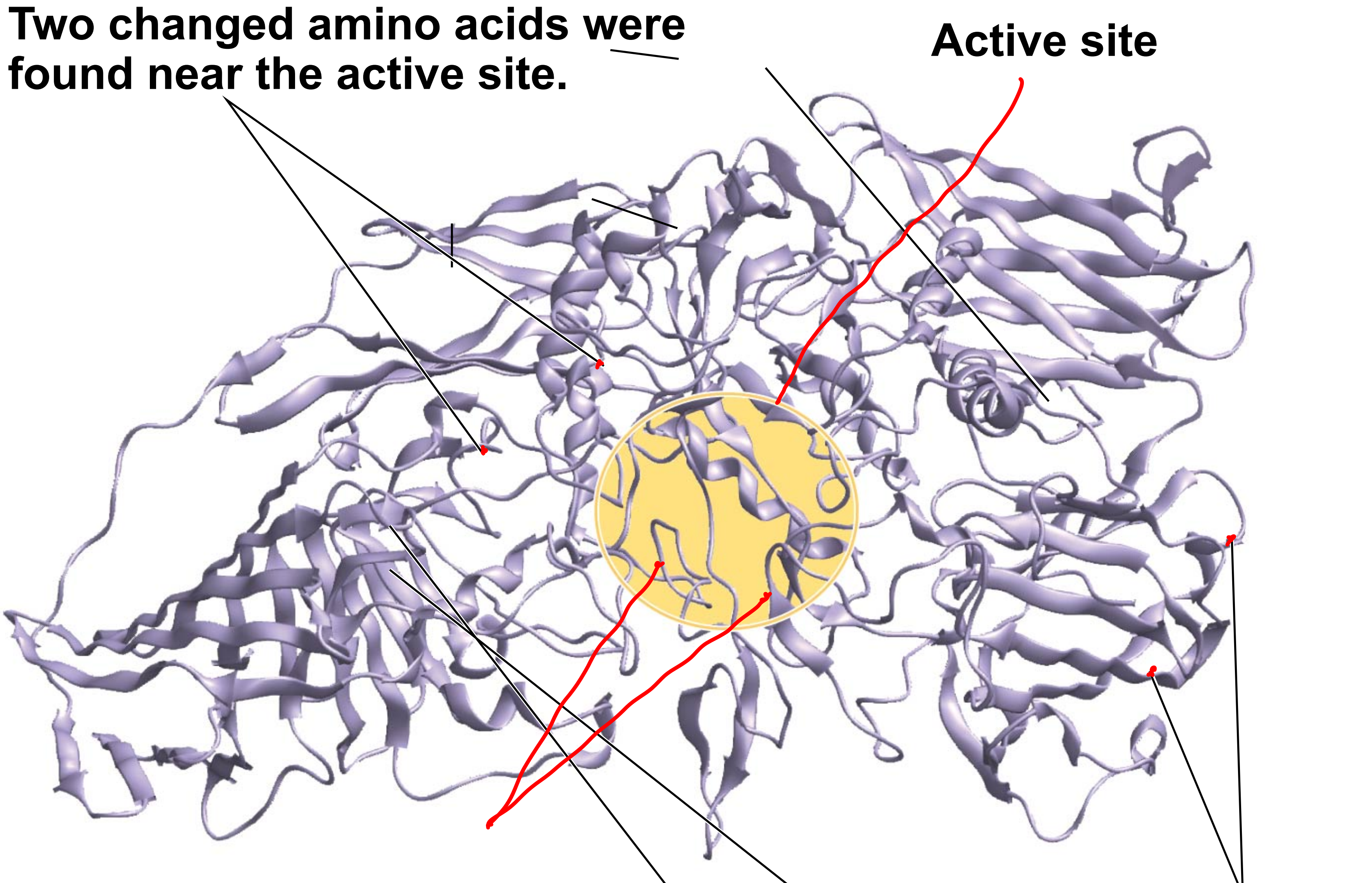
- Under environmental conditions where the new function is beneficial, natural selection would favor the mutated allele
  - For example, repeated mutation and selection on the β-galactosidase enzyme in *E. coli* resulted in a change of sugar substrate under lab conditions

breaks lactose (disaccharide). [usually]

breaks another sugar [after change].

[after being put in E.coli community].

Figure 6.19


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.

oncept 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 once they have been made

→ (our concern now).

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

llosteric Activation and Inhibition

- Most allosterically regulated enzymes are made from polypeptide subunits, each with its own active site

  Quaternary Structure

- The enzyme complex has active and inactive forms
- The binding of an activator stabilizes the active form of the enzyme

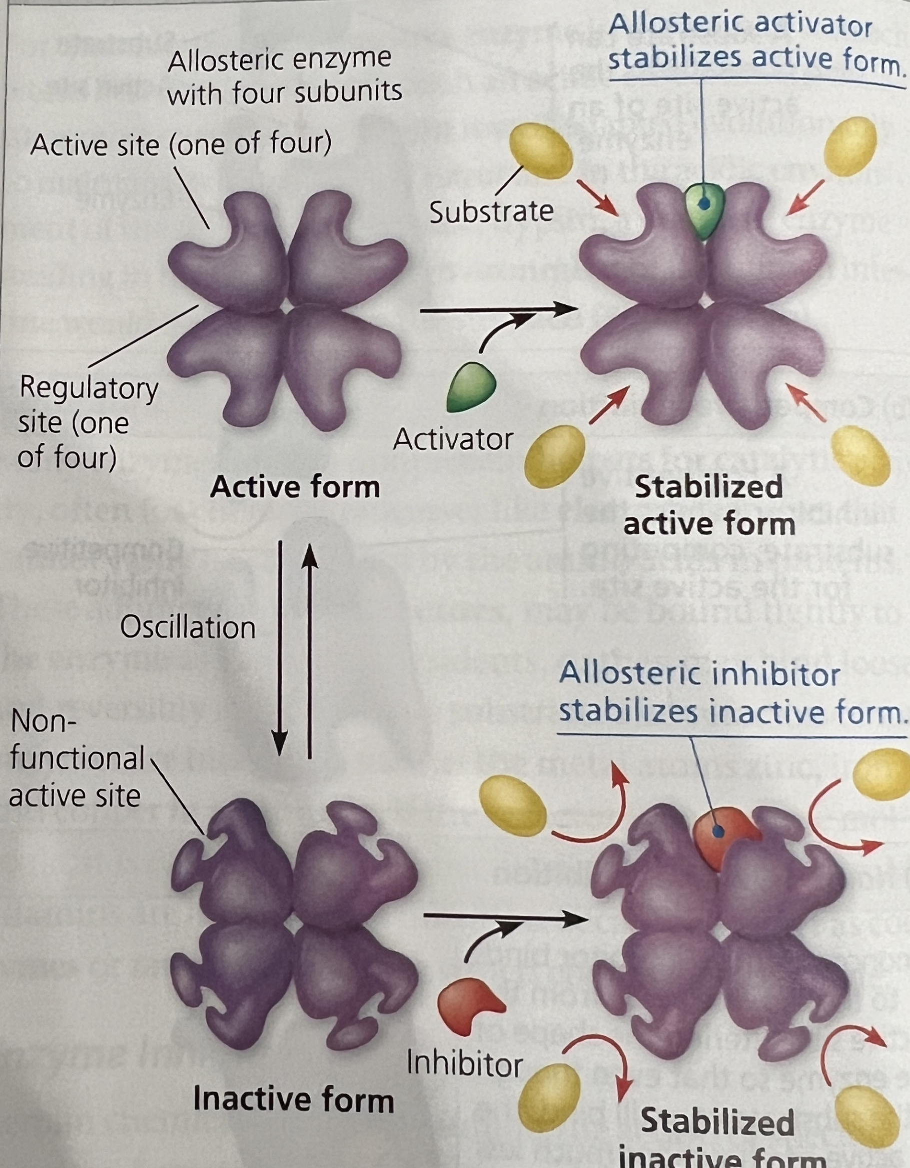
  usually binds in the place of connection between subunits.

- The binding of an inhibitor stabilizes the inactive form of the enzyme

⊛ Although the activator / inhibitor acts directly upon a specific subunit(s) ⟶ all subunits are affected.

▼ **Figure 6.20 Allosteric regulation of enzyme activity.**

(a) Allosteric activators and inhibitors



At low concentrations, activators and inhibitors dissociate from the enzyme. The enzyme can then oscillate again.

Fluctuating concentrations of regulators can cause a sophisticated pattern of response in the activity of cellular enzymes. The products of ATP hydrolysis (ADP and Ⓟ$_i$), for example, play a complex role in balancing the flow of traffic between anabolic and catabolic pathways by their effects on key enzymes. ATP binds to several catabolic enzymes allosterically, lowering their affinity for substrate and thus inhibiting their activity. ADP, however, functions as an activator of the same enzymes. This is logical because catabolism functions in regenerating ATP. If ATP production lags behind its use, ADP accumulates and activates the enzymes that speed up catabolism, producing more ATP. If the supply of ATP exceeds demand, then catabolism slows down as ATP molecules accumulate and bind to the same enzymes, inhibiting them. (You'll see specific examples of this type of regulation when you learn about cellular respiration in Chapter 10; see, for example, Figure 10.19.) ATP, ADP, and other related molecules also affect key enzymes in anabolic pathways. In this way, allosteric enzymes control the rates of important reactions in both sorts of metabolic pathways.

- **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

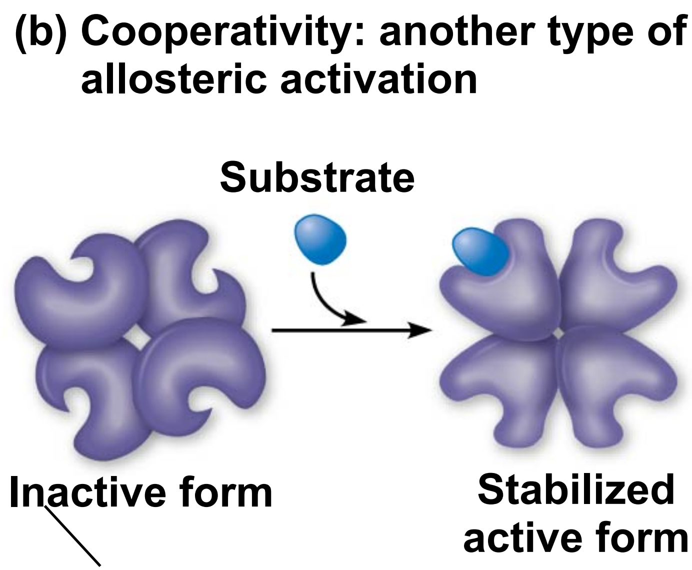
- Many multi-subunit enzymes perform cooperativity.

  Sim. e.g.

  Hemoglobin (not an enzyme)

  its affinity for O_2 increases when one O_2 molecule binds to one of its 4 subunits. Affinity $\propto [O_2]^n$; $n \in R^+$

Figure 6.20b


(b) Cooperativity: another type of allosteric activation
Substrate
Inactive form
Stabilized active form

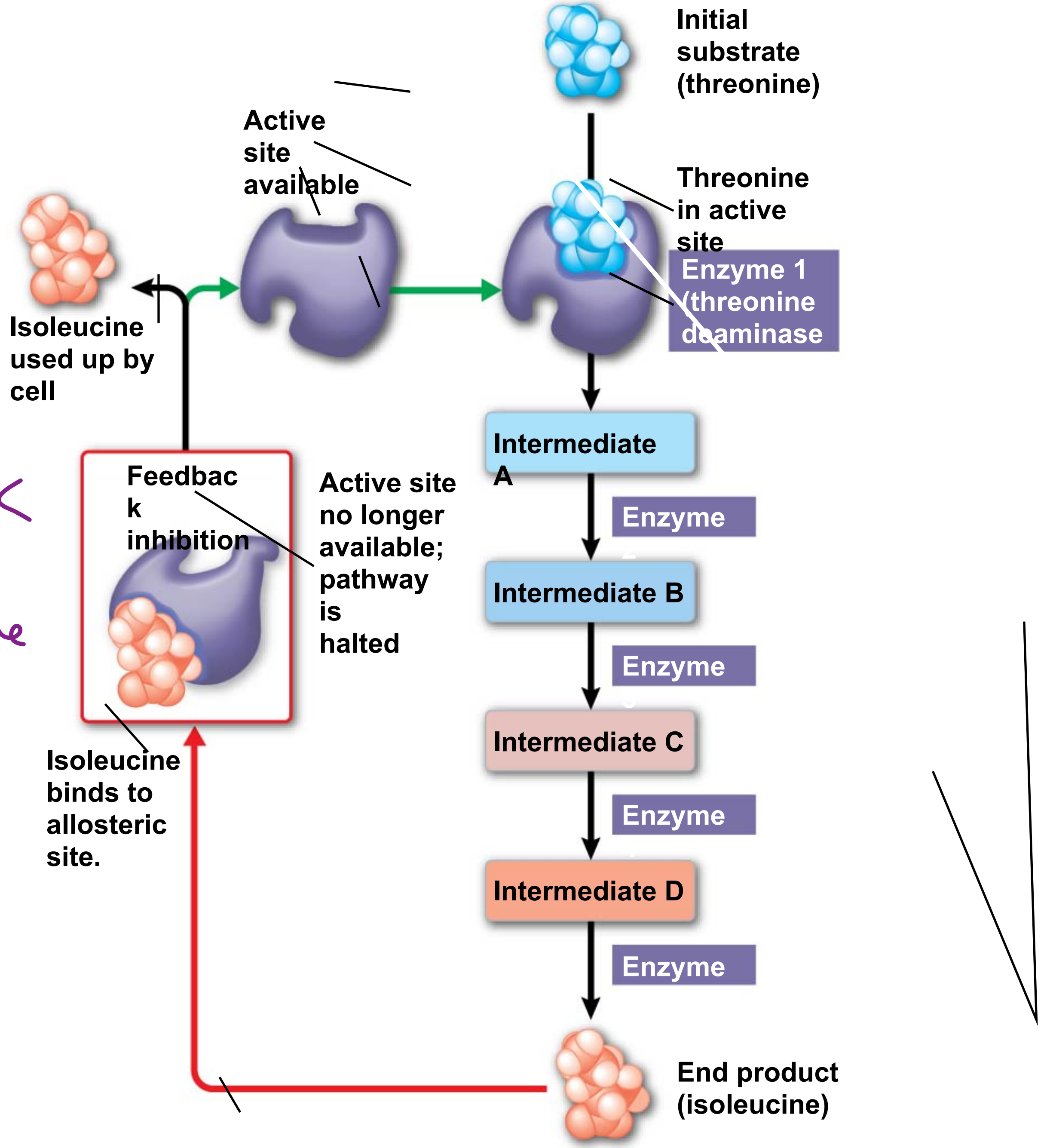
eedback Inhibition

- 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

e.g. ATP – synthesis pathway (N_s – = 3) [right].

e.g (2) see next.

Figure 6.21

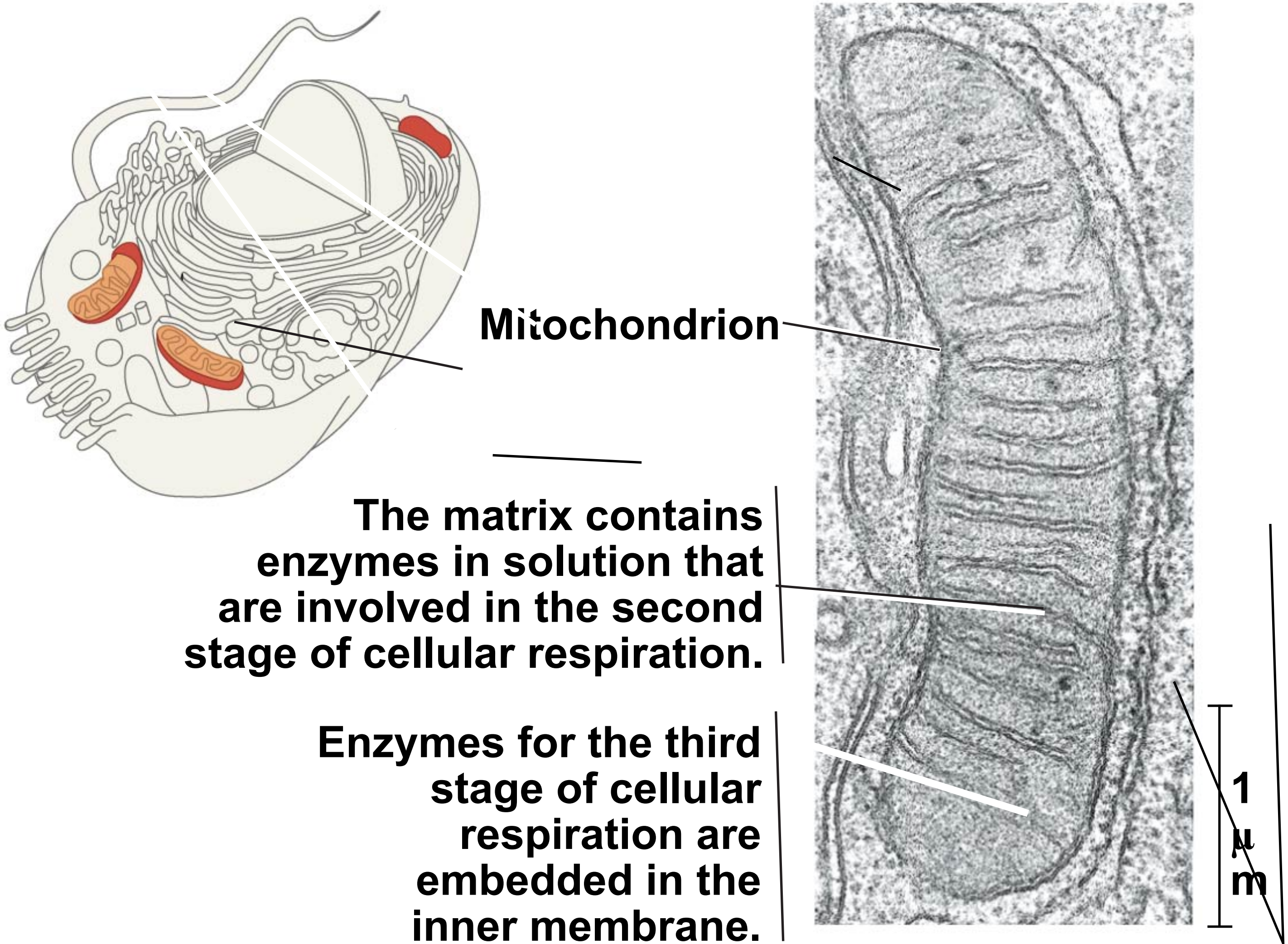


Feedback
⊕
noncompetitive
inhibition
+
Allosteric
regulation.

ocalization 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 6.22


Mitochondrion
The matrix contains enzymes in solution that are involved in the second stage of cellular respiration.
Enzymes for the third stage of cellular respiration are embedded in the inner membrane.
1 µm