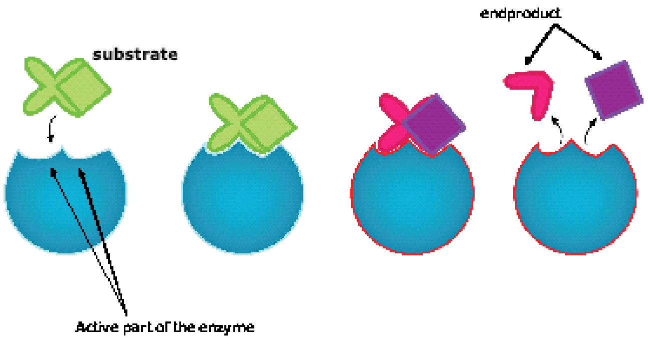
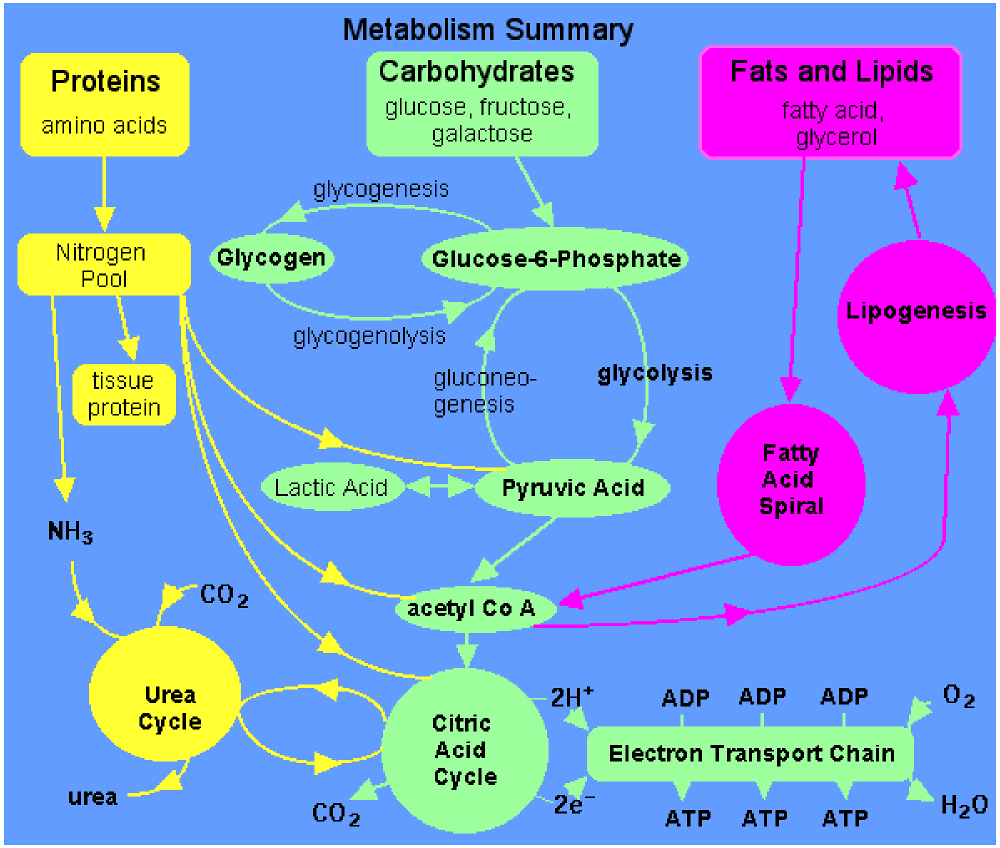
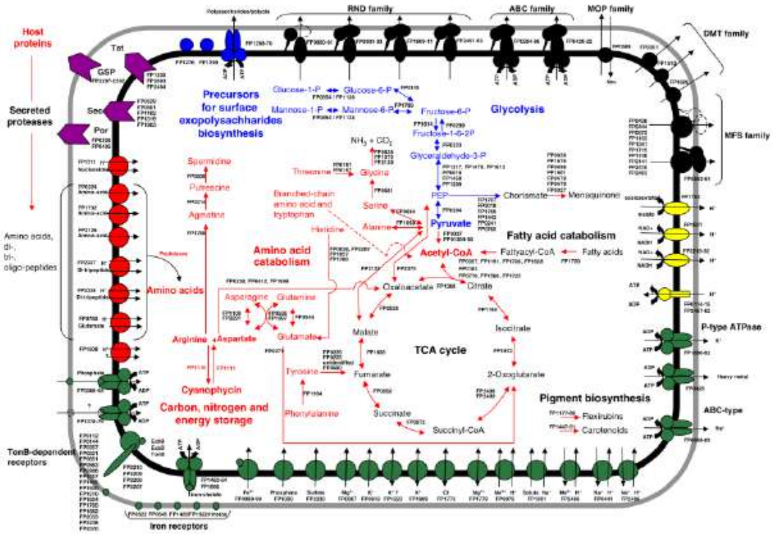
<u>NOTES: Ch 8</u> – Metabolism and Enzymes





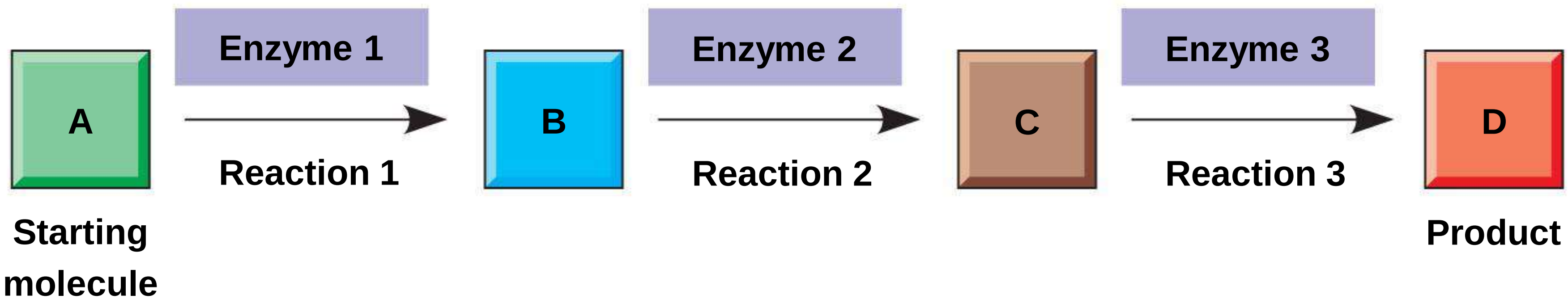
8.1 - METABOLISM

- Metabolism is the <u>totality of an organism's chemical reactions</u>
- Metabolism 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



Metabolism includes reactions that are:

- **CATABOLIC** pathways release energy by breaking down complex molecules into simpler compounds
- **ANABOLIC** pathways consume energy to build complex molecules from simpler ones

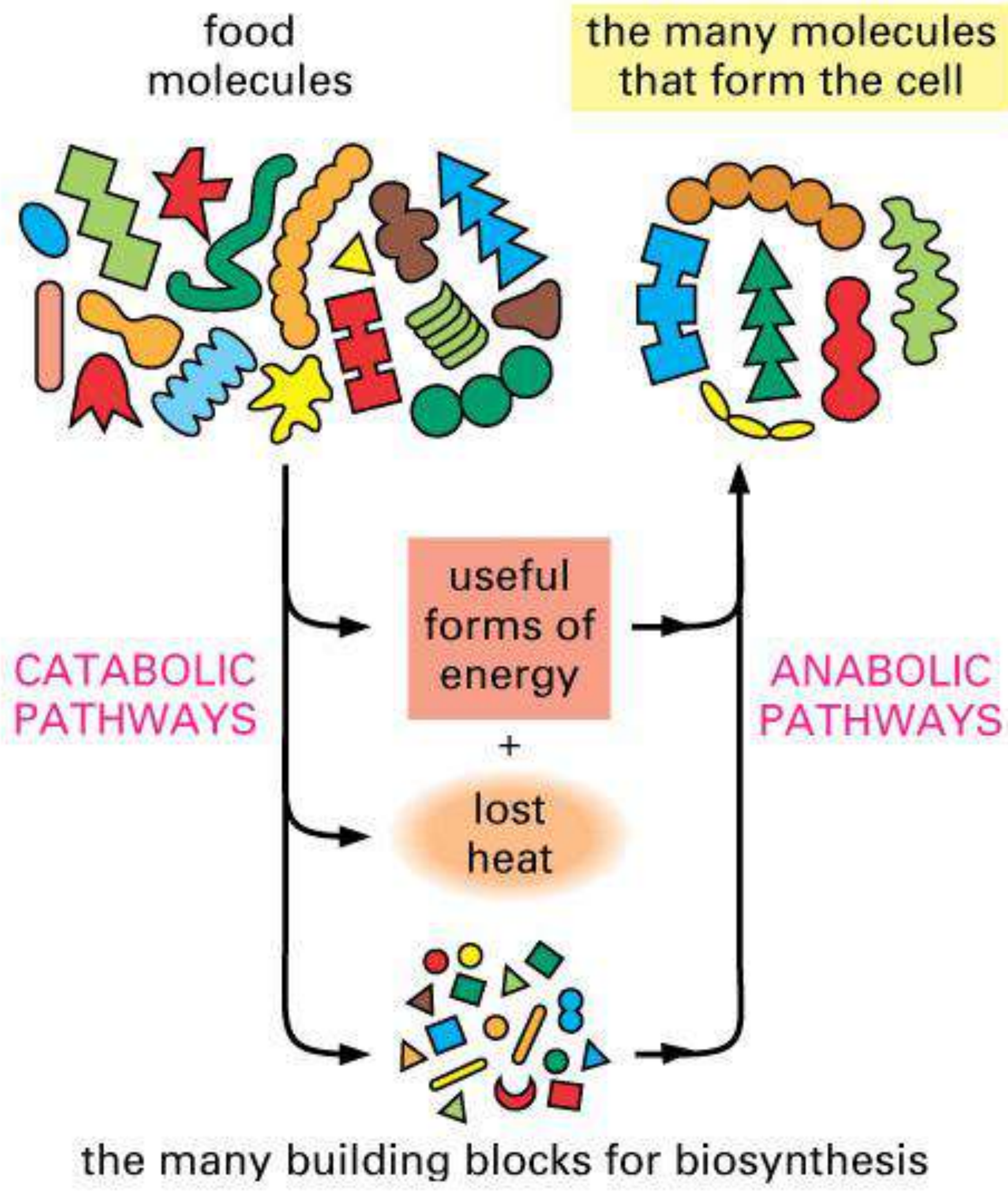
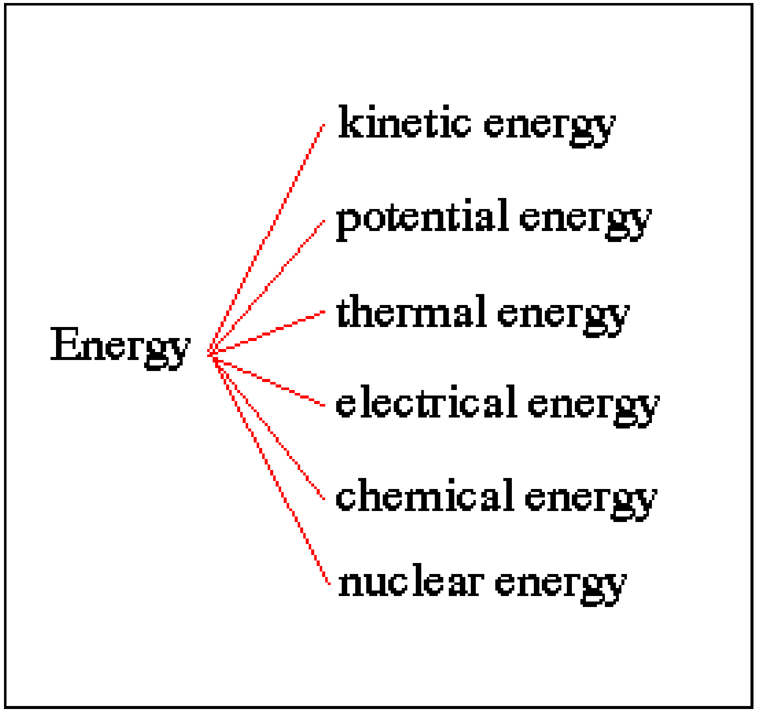


Figure 3-3 Essential Cell Biology, 2/e. (© 2004 Garland Science)

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 <u>motion</u>

  -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

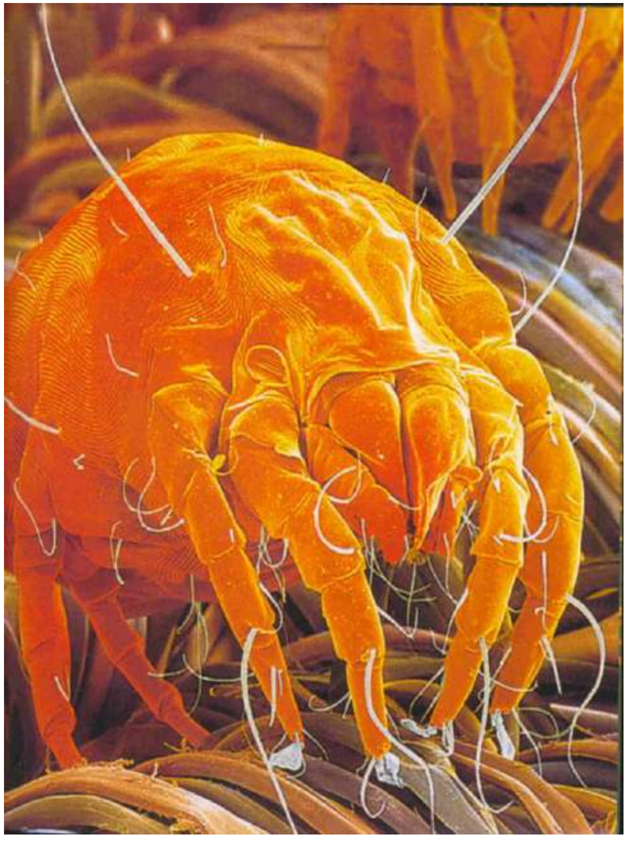
  -Chemical energy is <u>potential (stored) energy</u> available for release in a chemical reaction

- <u>**Energy can be converted from one form to another**</u>

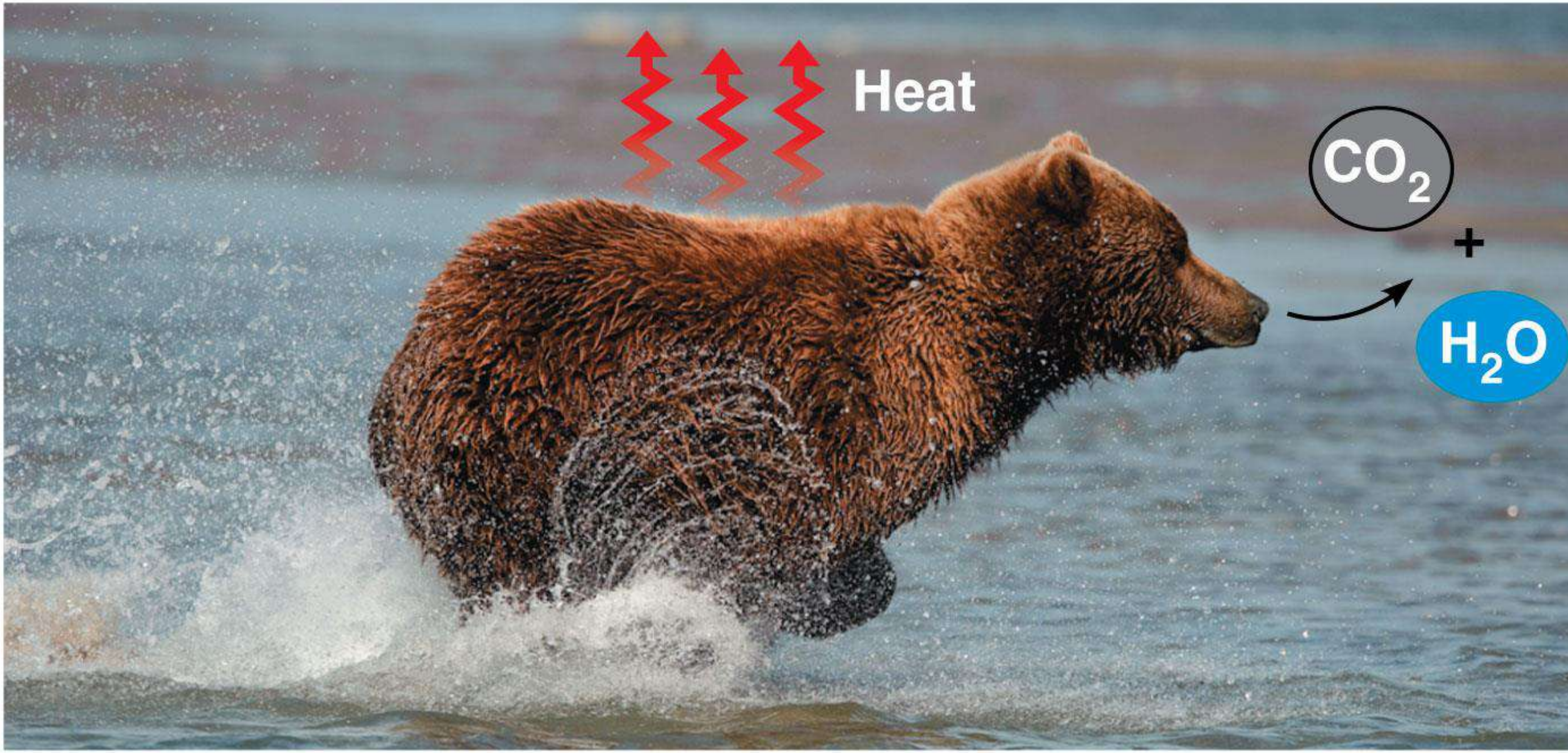

On the platform, the diver has more potential energy.
Diving converts potential energy to kinetic energy.
Climbing up converts kinetic energy of muscle movement to potential energy.
In the water, the diver has less potential energy.

Energy Transformations:

- A closed system 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!**

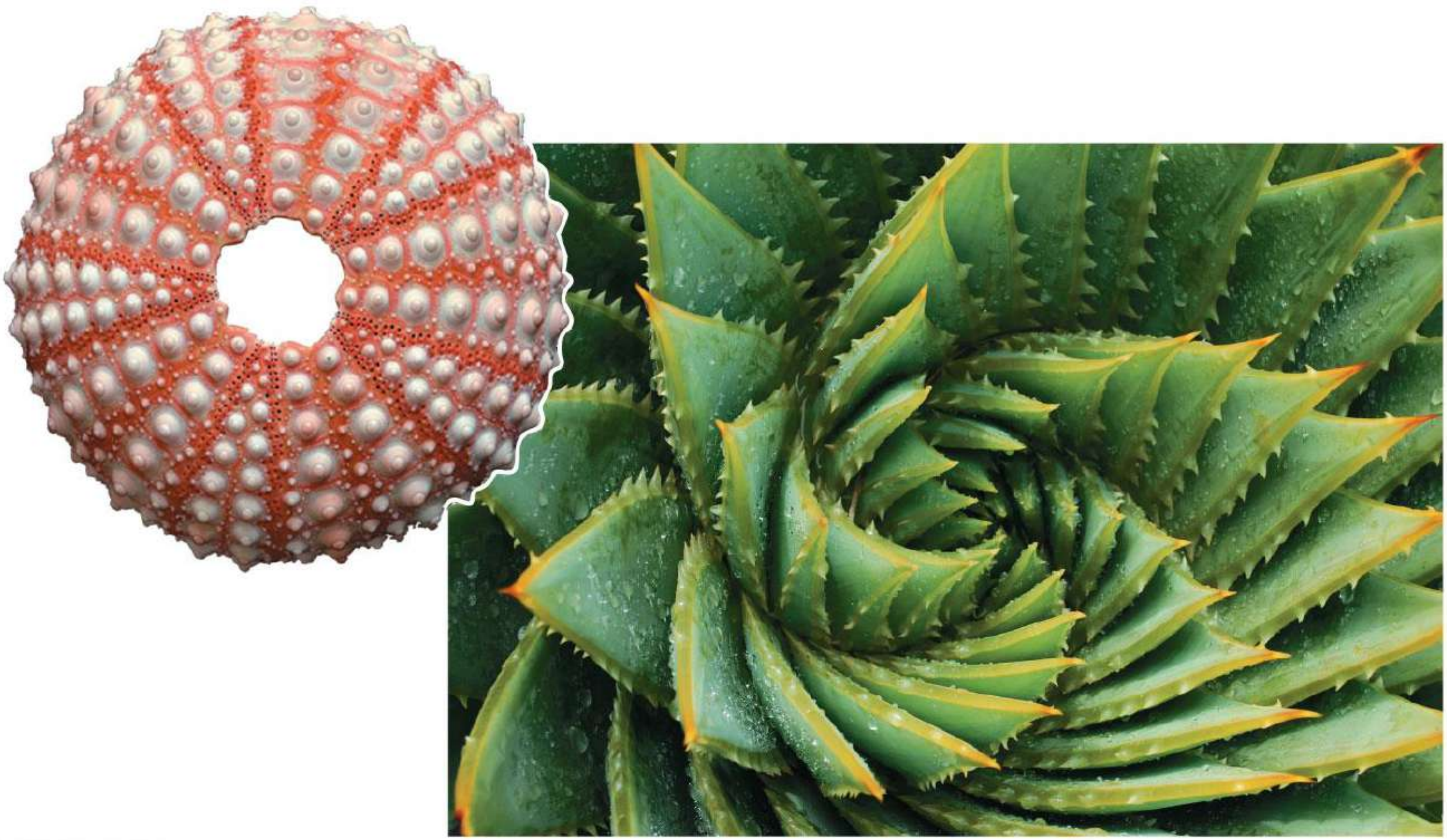


(a) First law of thermodynamics



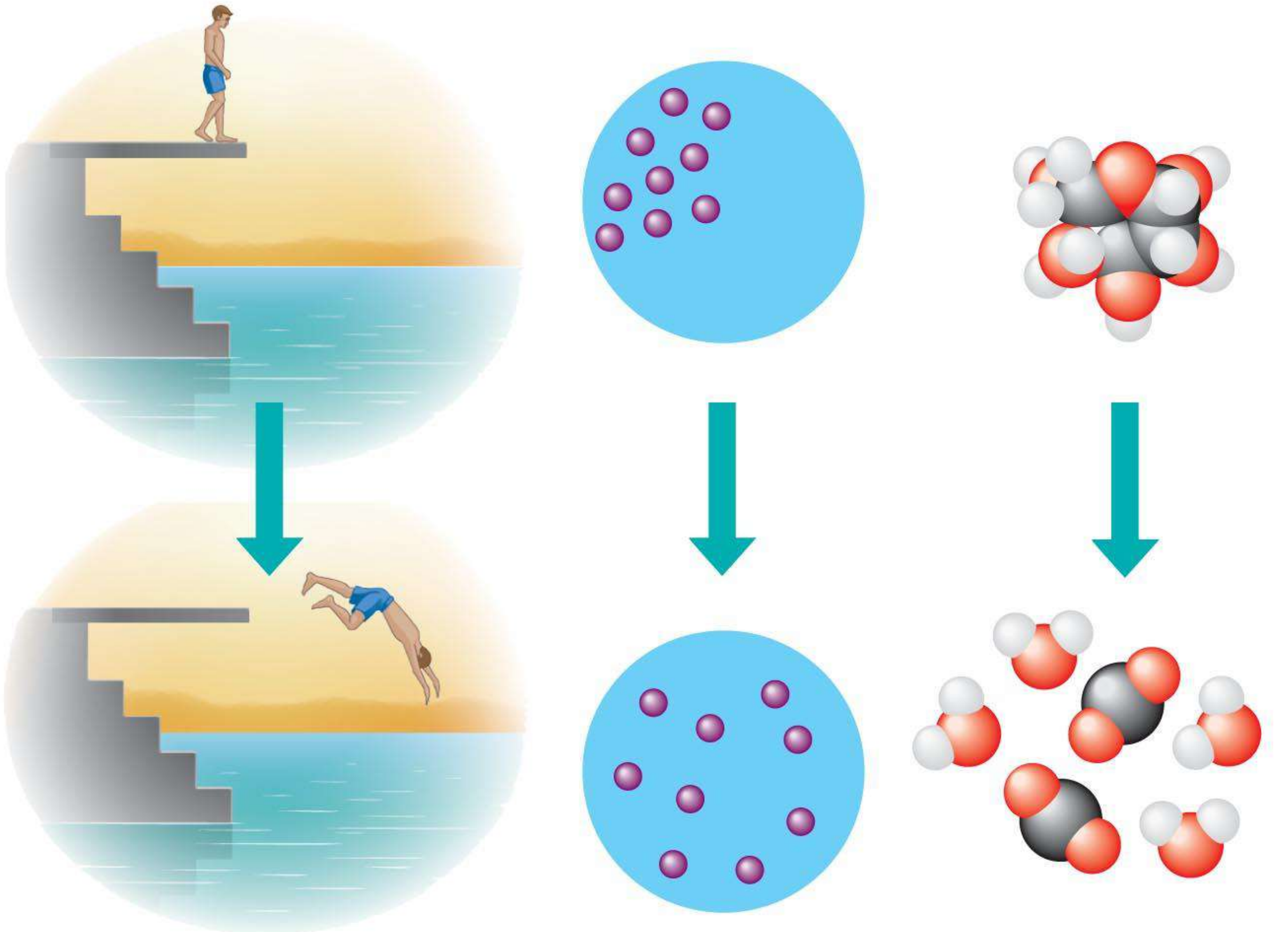
(b) Second law of thermodynamics

Living things have order!...this takes energy to achieve!



8.2 – Free Energy

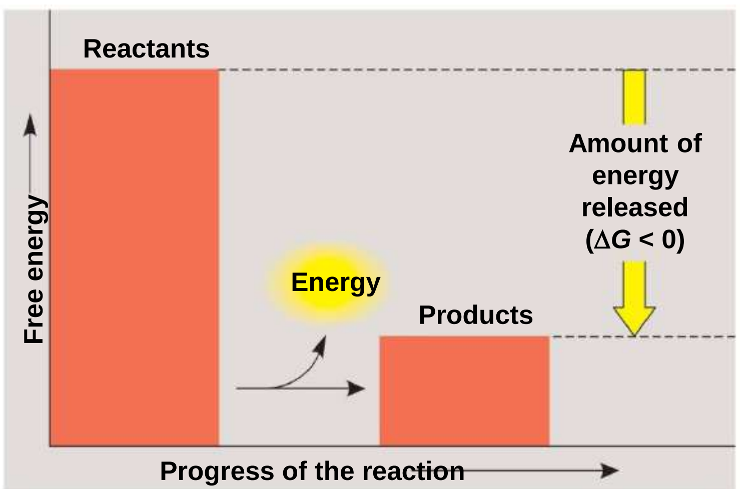
- **FREE ENERGY**: the portion of a system's energy that is available to do work
- Systems tend to change spontaneously to a more stable state **(so, $\Delta G < 0$)**



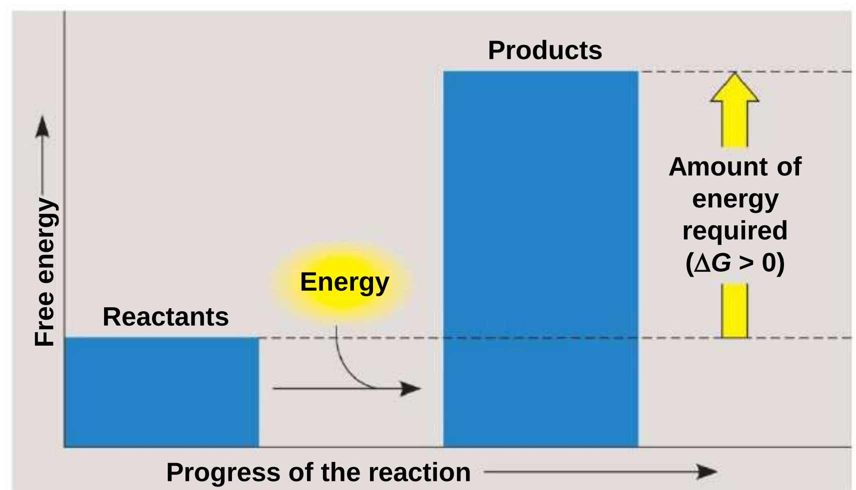
(a) Gravitational motion **(b) Diffusion** **(c) Chemical reaction**

Exergonic and Endergonic Reactions in Metabolism

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



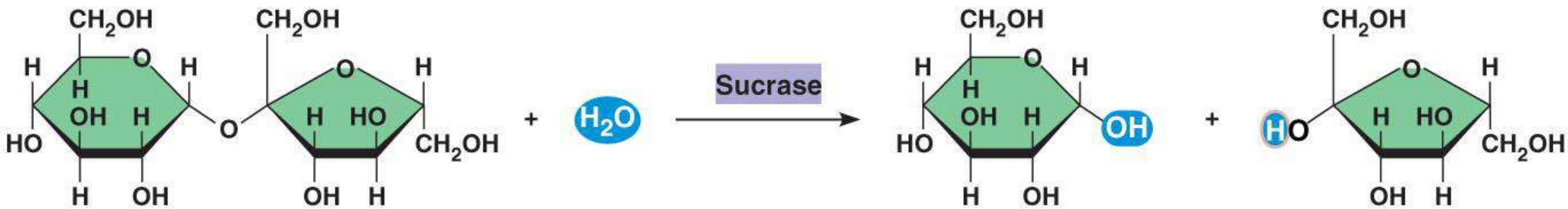
(a) Exergonic reaction: energy released



(b) Endergonic reaction: energy required

8.4 - Enzymes speed up metabolic reactions by lowering energy barriers

- A catalyst is a chemical agent that speeds up a reaction <u>**without being consumed by the reaction**</u>
- An enzyme is a <u>catalytic protein</u>
- Hydrolysis of <u>**SUCROSE**</u> by the enzyme <u>**SUCRASE**</u> is an example of an enzyme-catalyzed reaction



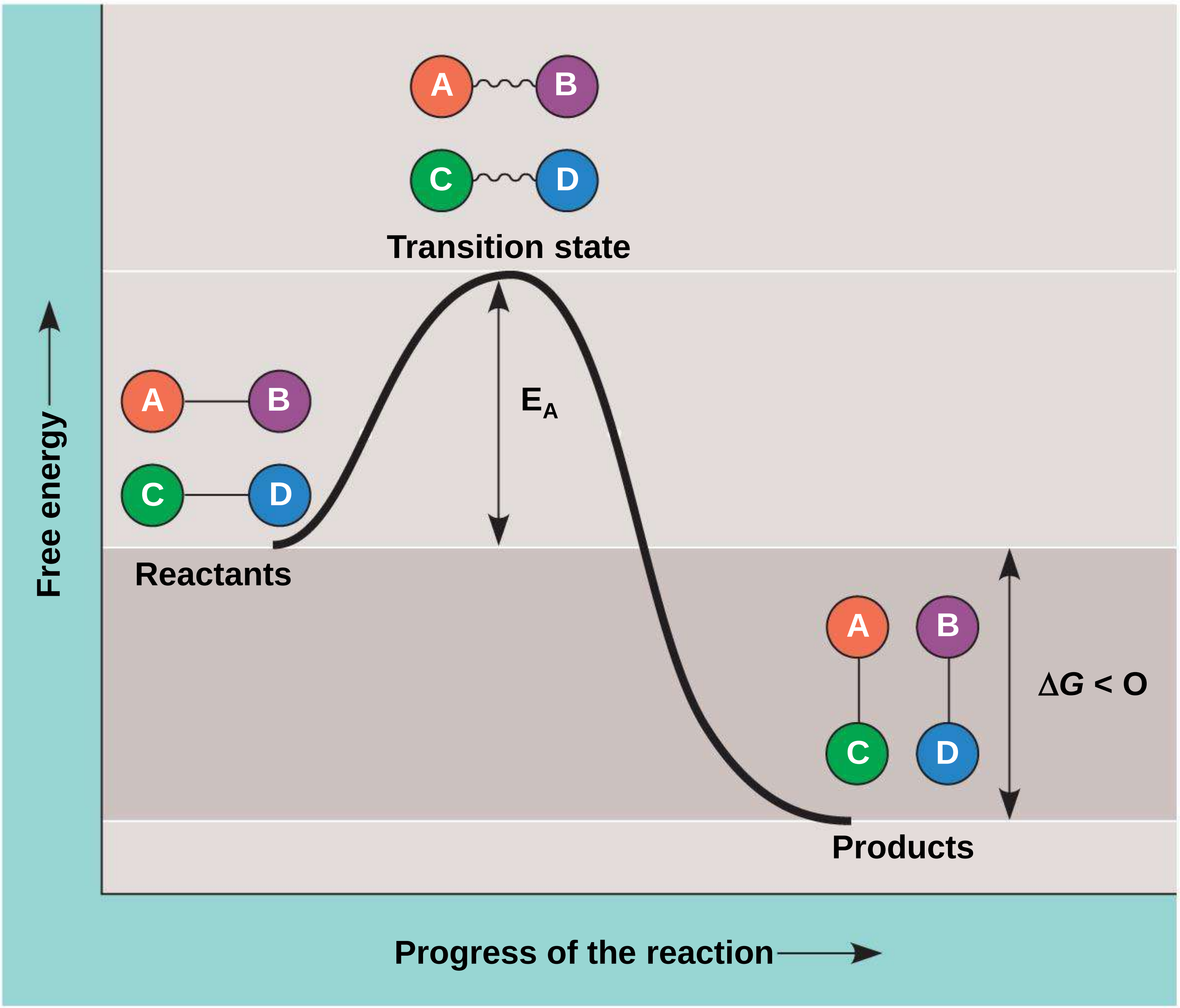
Sucrose $C_{12}H_{22}O_{11}$

Glucose $C_6H_{12}O_6$

Fructose $C_6H_{12}O_6$

The Activation Energy Barrier

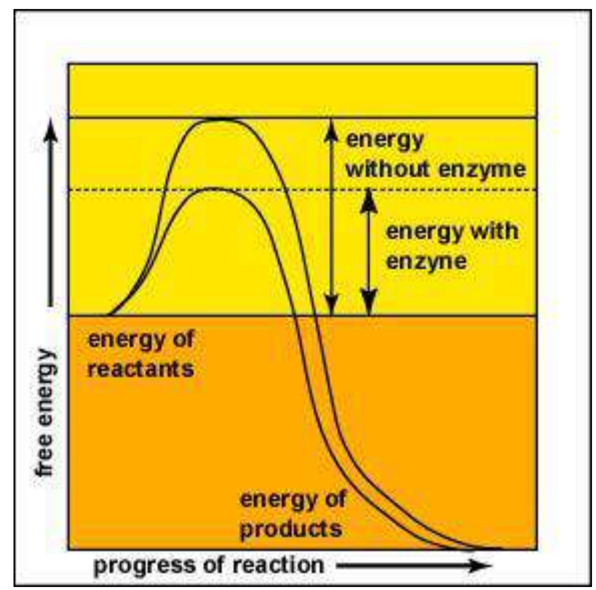
- Every chemical reaction between molecules involves bond breaking and bond forming
- **The initial energy needed to start a chemical reaction** is called the free energy of activation, or **activation energy (E_A)**
- Activation energy is often supplied in the form of heat from the surroundings

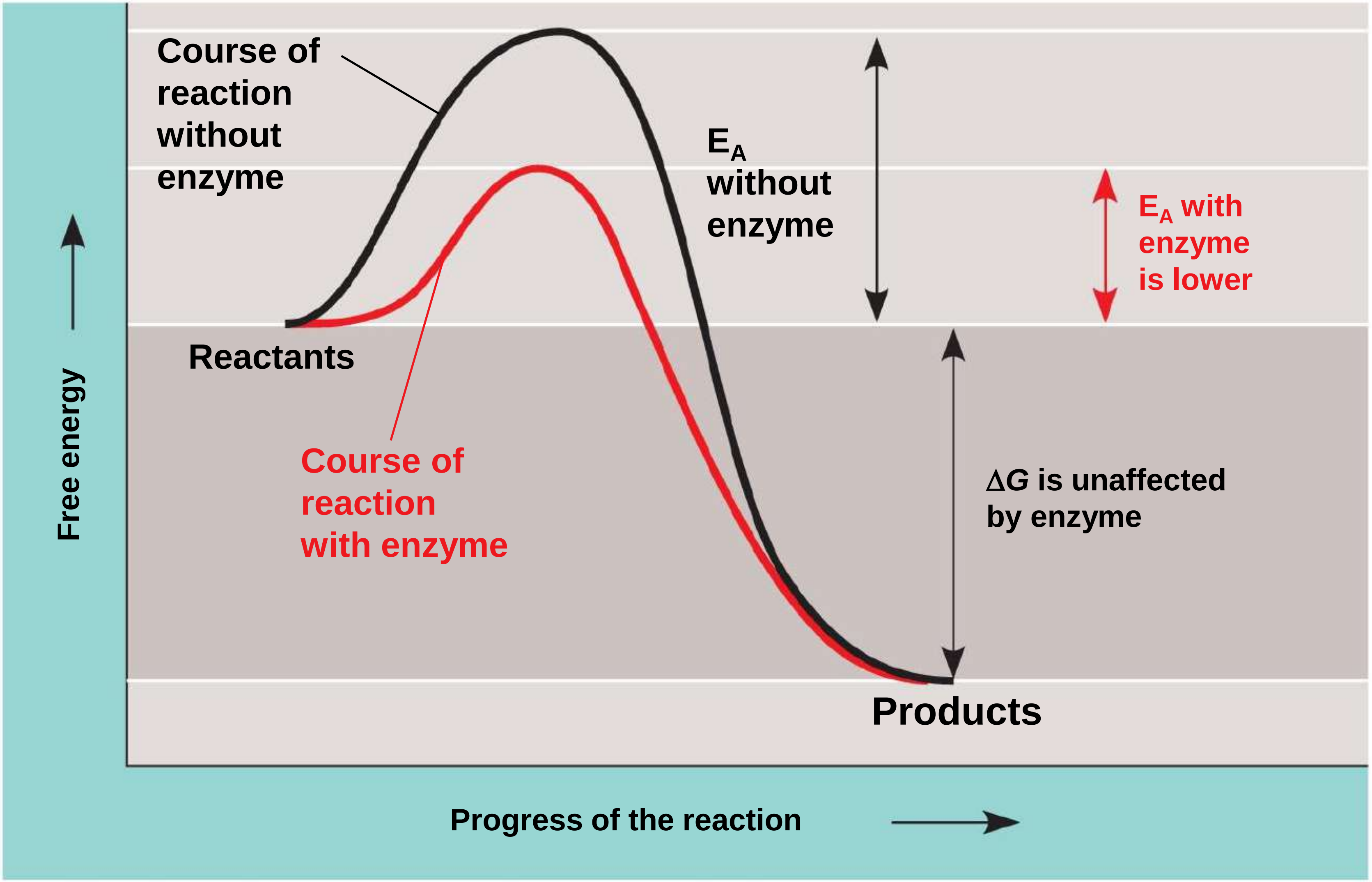


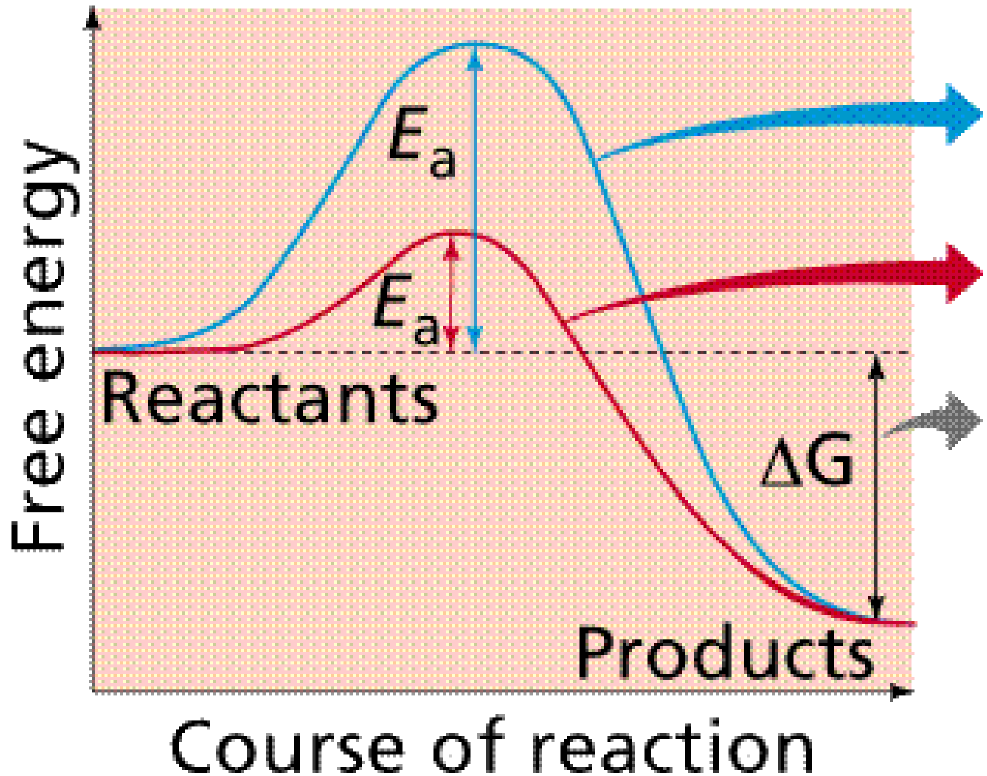
A
B
C
D
Transition state
E_A
A
B
C
D
Reactants
A
B
C
D
ΔG < O
Products
Free energy
Progress of the reaction

How Enzymes Lower the E_A Barrier:

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




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

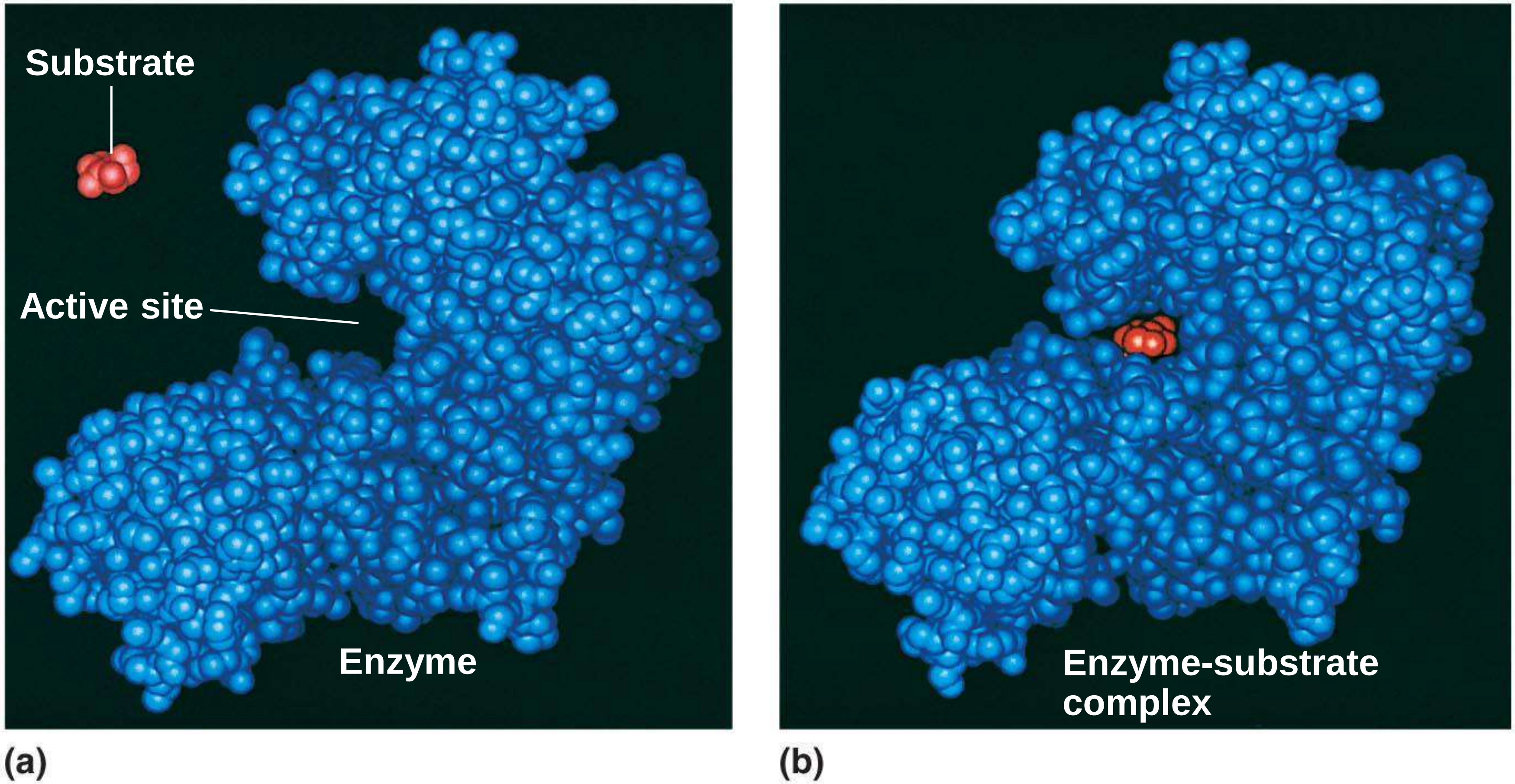


An uncatalyzed reaction requires a higher activation energy than does a catalyzed reaction

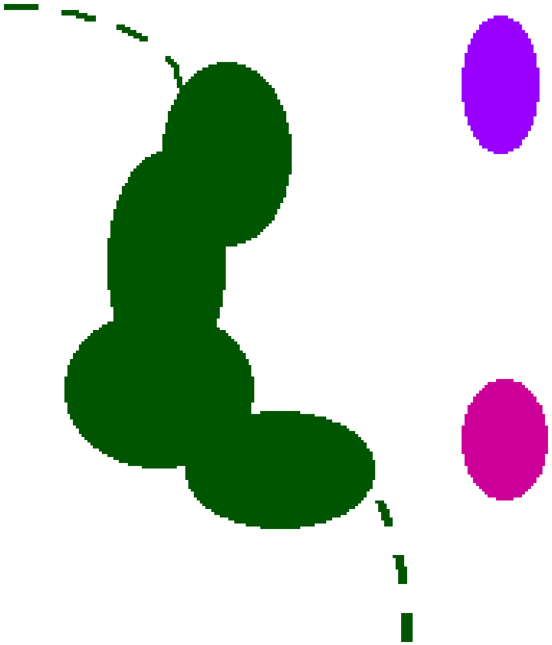
There is no difference in free energy between catalyzed and uncatalyzed reactions

Substrate Specificity of Enzymes

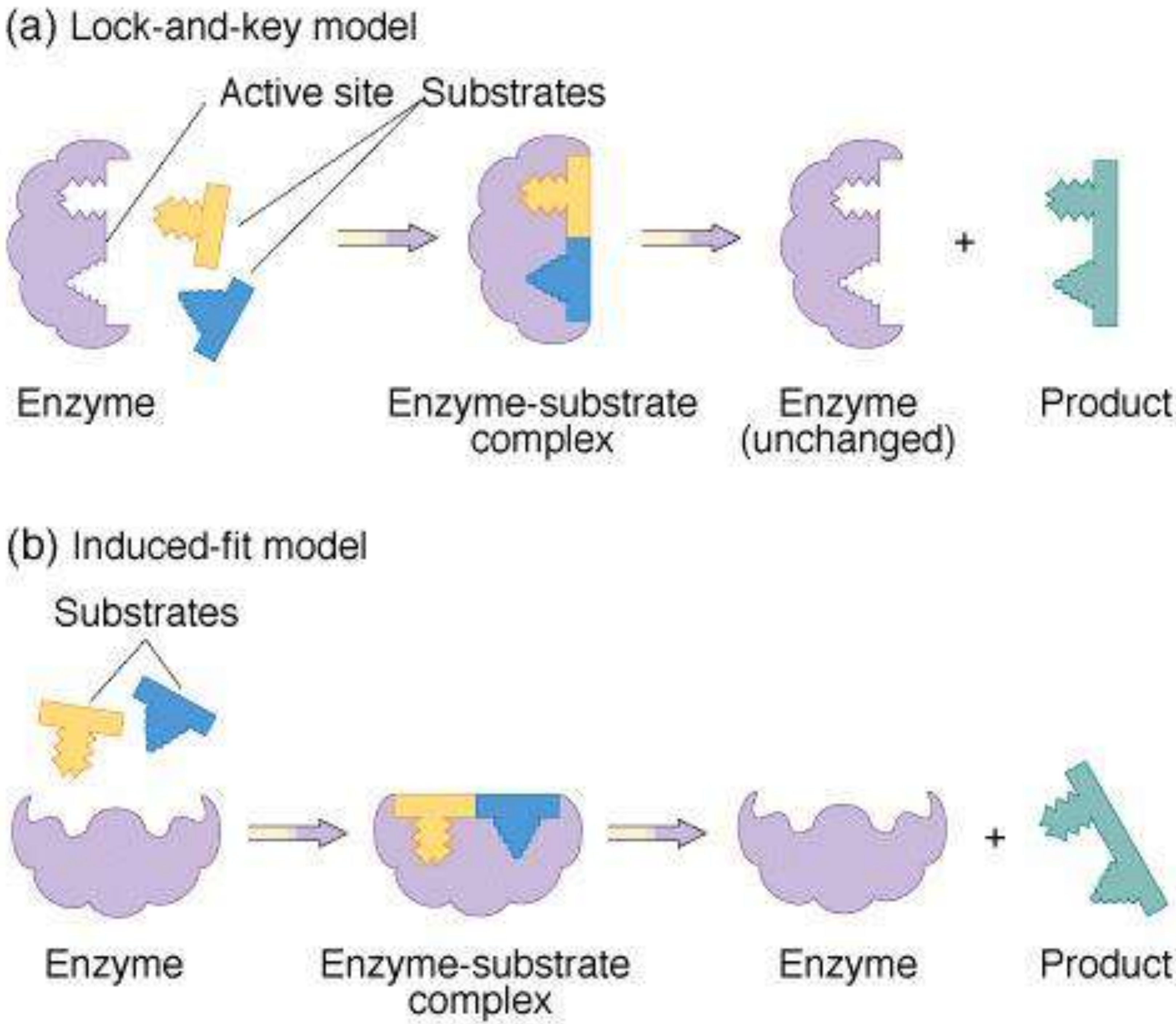
- The reactant that an enzyme acts on is called the enzyme's **SUBSTRATE**
- The enzyme binds to its substrate, forming an **enzyme-substrate complex**
- The **ACTIVE SITE** is the region on the enzyme where the substrate binds

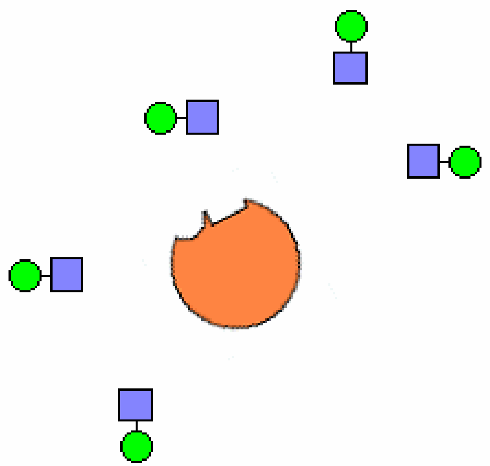

Substrate
Active site
Enzyme
(a)
Enzyme-substrate
complex
(b)

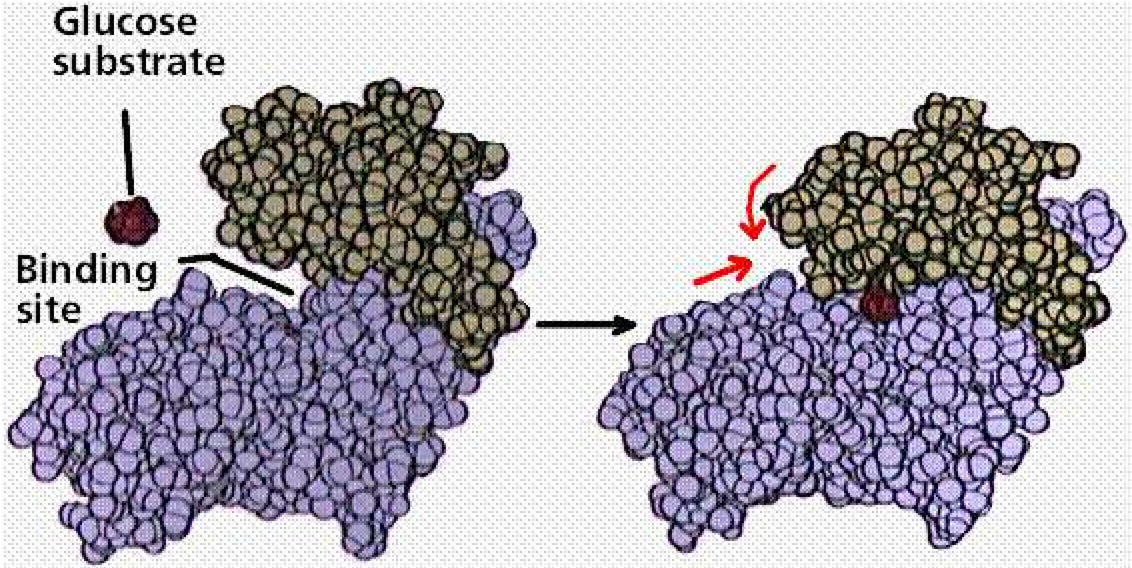
- **ENZYMES** are very selective for which reaction they will catalyze
- **ENZYMES** are not changed or "used up" by a reaction; <u>can be used over and over</u>

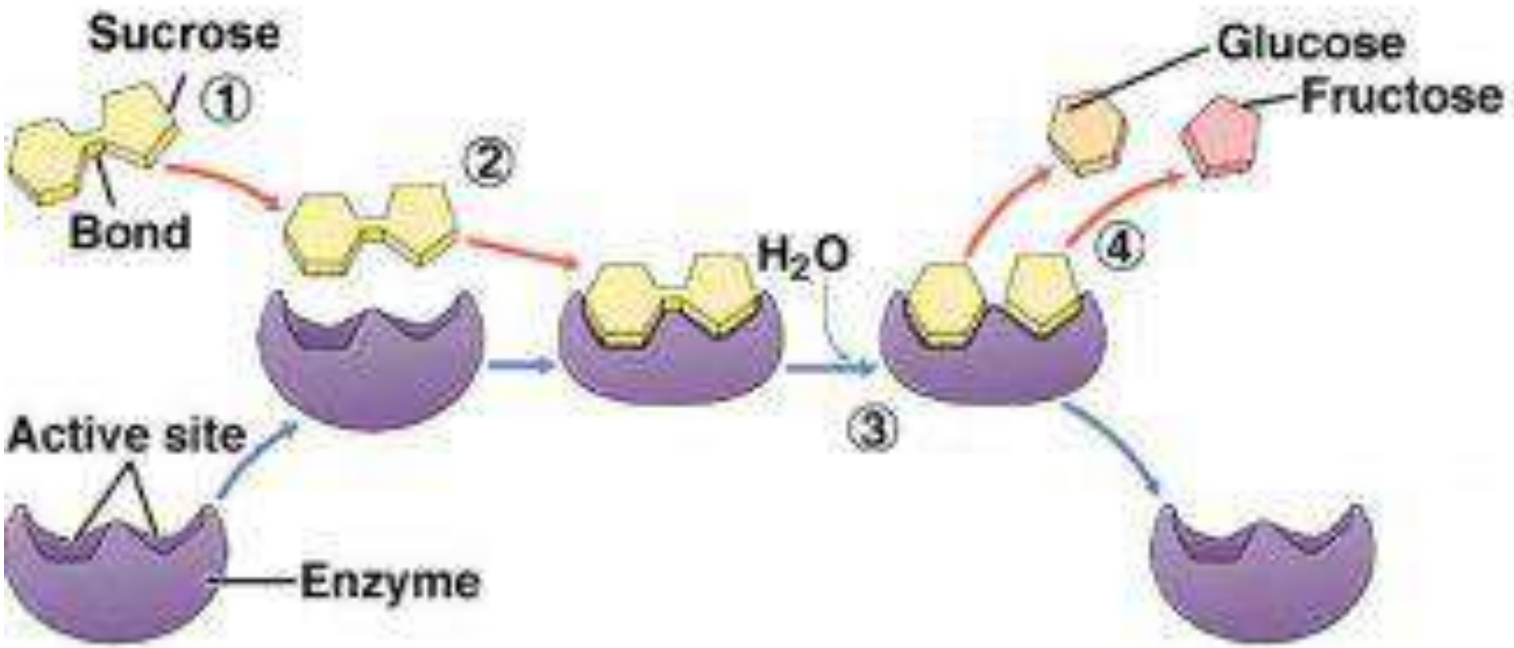


- <u>**ACTIVE SITE**</u> = region of an enzyme which binds to the substrate
  - is usually a <u>pocket or groove on surface</u>
  - determines enzyme’s specificity
  - <u>compatible “fit”</u> between shape of enzyme’s active site and shape of substrate (“Lock-and-Key” analogy)

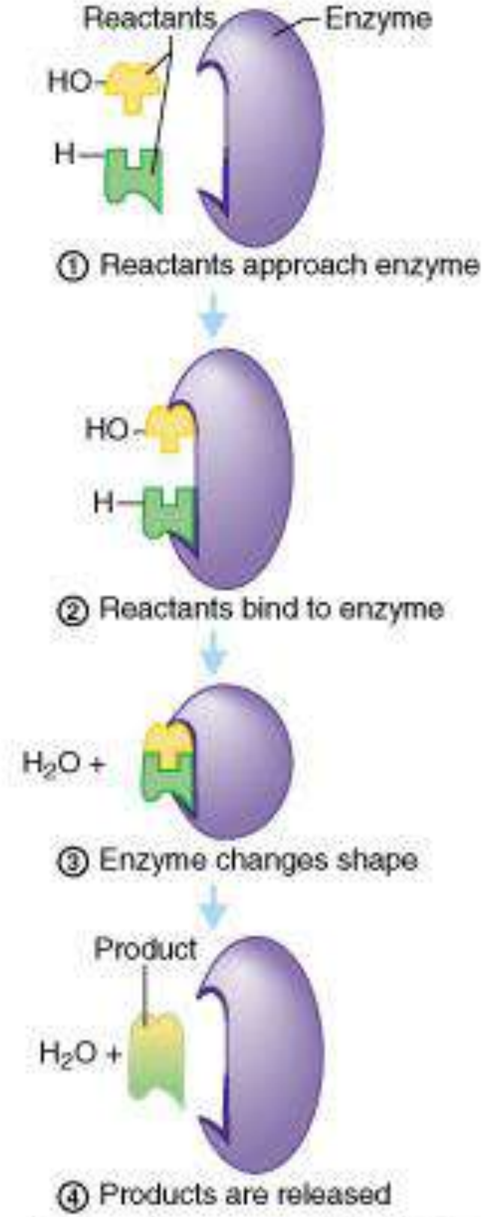

(a) Lock-and-key model
Active site
Substrates
Enzyme
Enzyme-substrate complex
Enzyme (unchanged)
+
Product
(b) Induced-fit model
Substrates
Enzyme
Enzyme-substrate complex
Enzyme
+
Product




Glucose
substrate
Binding
site


Sucrose
①
Bond
②
H_2O
③
Glucose
Fructose
④
Active site
Enzyme

- **<u>INDUCED FIT</u>**: a change in the shape of an enzyme's active site, which is induced by the substrate
- Induced fit of a substrate brings chemical groups of the active site into positions that enhance their ability to catalyze the reaction



Catalysis in the Enzyme's Active Site:

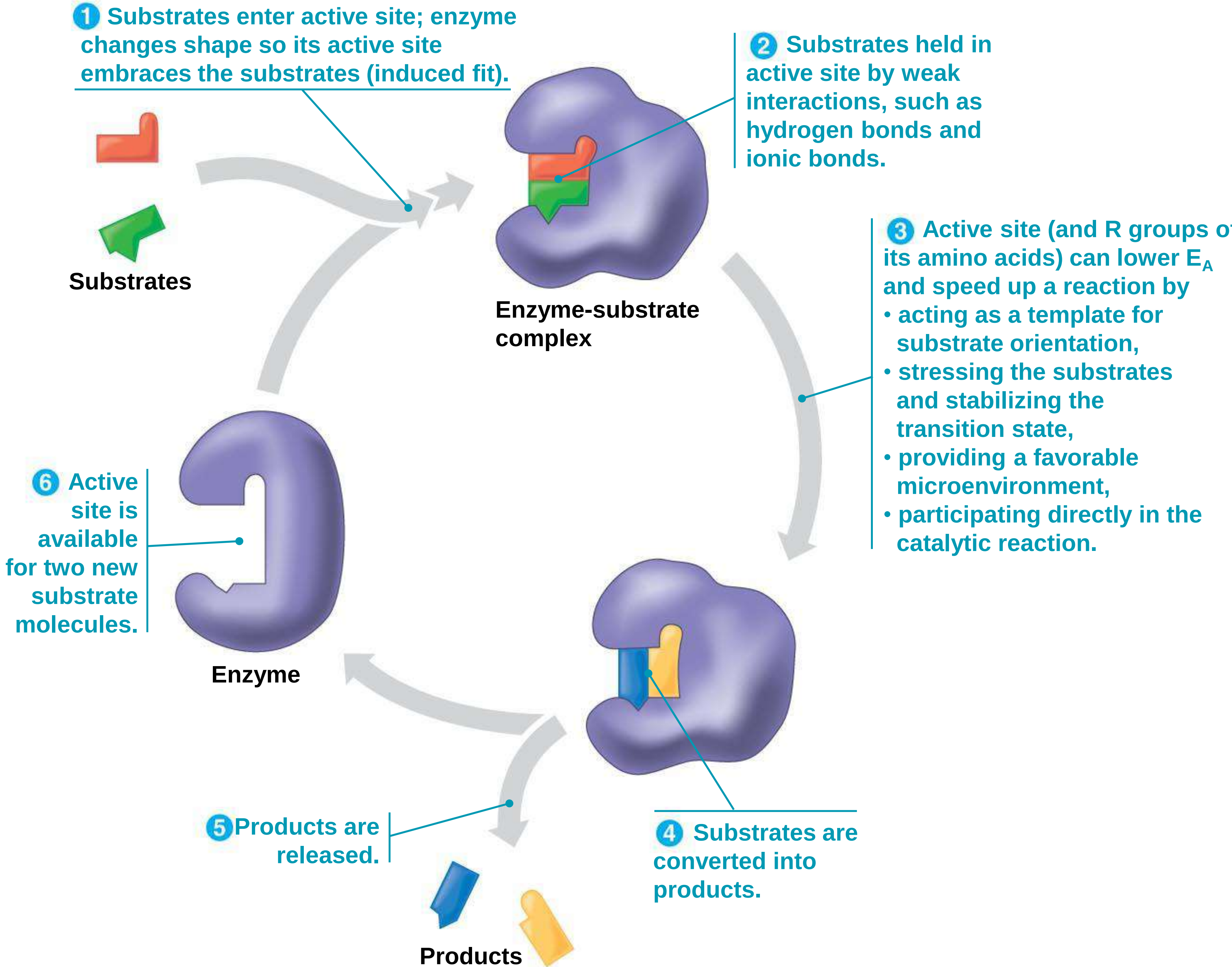
- In an enzymatic reaction, the substrate binds to the active site
- The active site can lower an E_A barrier by

-Orienting substrates correctly

-Straining substrate bonds

-Providing a favorable microenvironment

-Covalently bonding to the substrate


1 Substrates enter active site; enzyme changes shape so its active site embraces the substrates (induced fit).
2 Substrates held in active site by weak interactions, such as hydrogen bonds and ionic bonds.
3 Active site (and R groups of its amino acids) can lower E_A and speed up a reaction by
• acting as a template for substrate orientation,
• stressing the substrates and stabilizing the transition state,
• providing a favorable microenvironment,
• participating directly in the catalytic reaction.
4 Substrates are converted into products.
5 Products are released.
6 Active site is available for two new substrate molecules.
Substrates
Enzyme-substrate complex
Enzyme
Products

Enzyme Reaction Rate:

Substrate Concentration:

-the higher the substrate concentration, the faster the reaction

-if the substrate concentration is high enough, the enzyme is saturated; in this case, the reaction rate can be increased by adding more enzyme

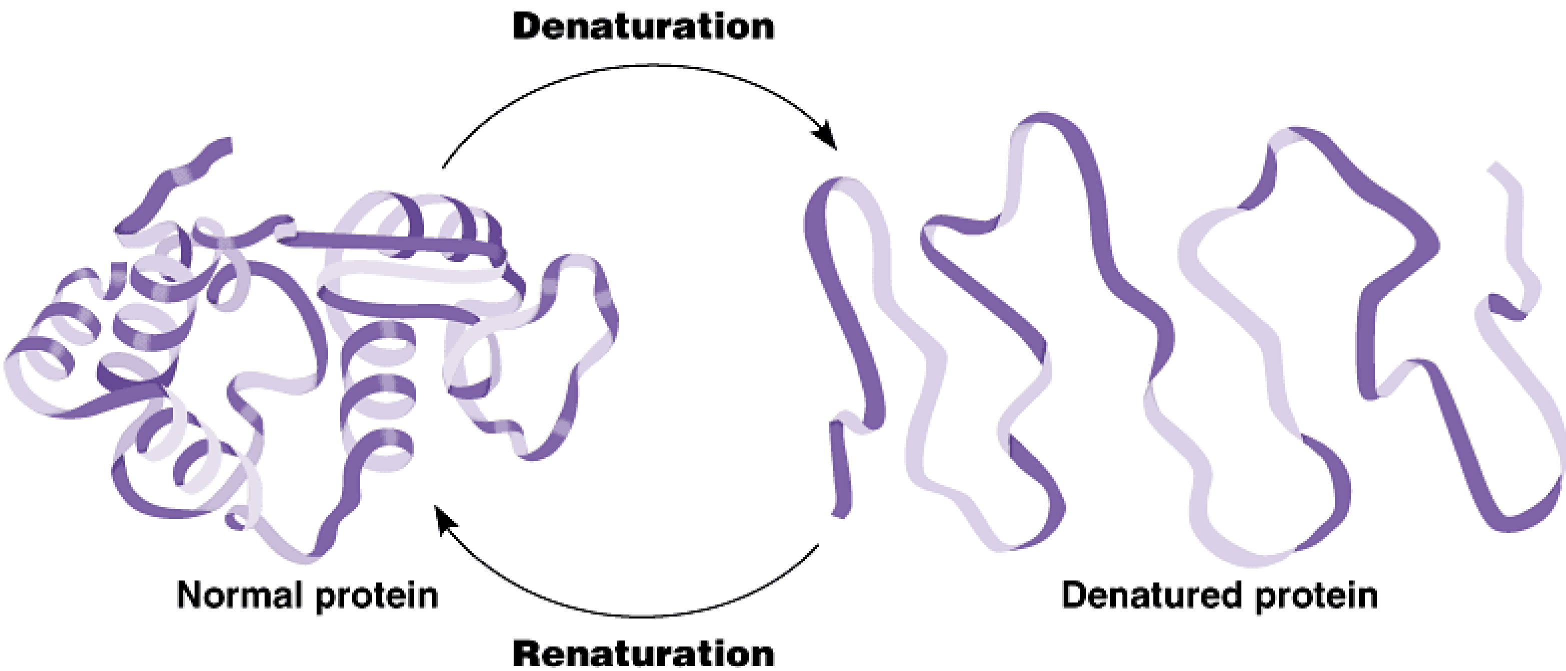
Factors Affecting Enzyme Activity:

1) Temperature:

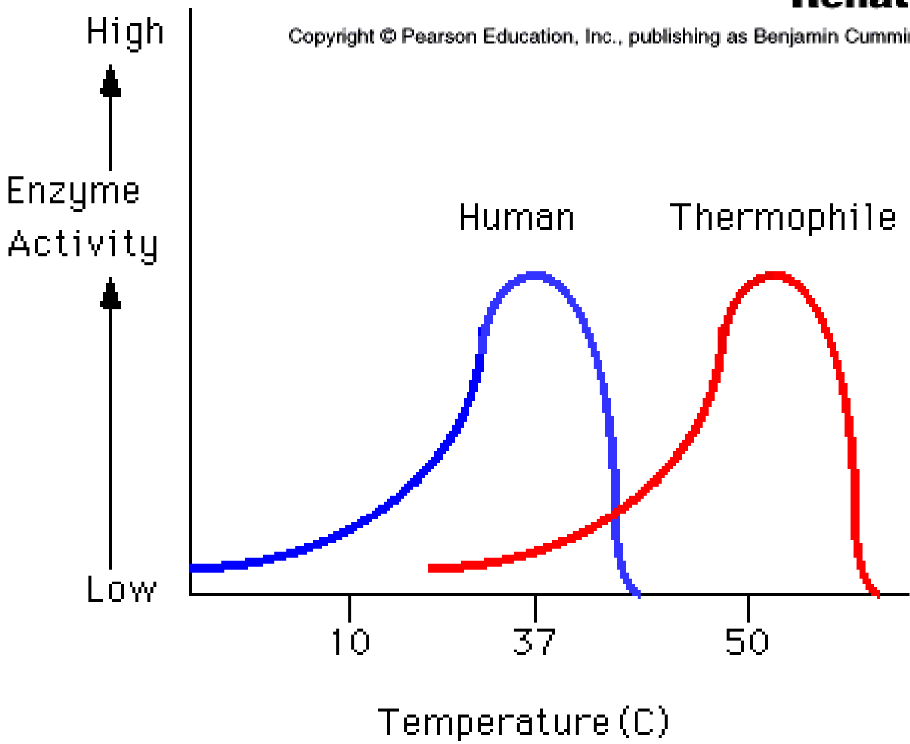
-as temp increases, reaction rate increases

-if temp gets too high, enzyme denatures and loses shape and function

-optimal range for human enzymes: 35-40°C



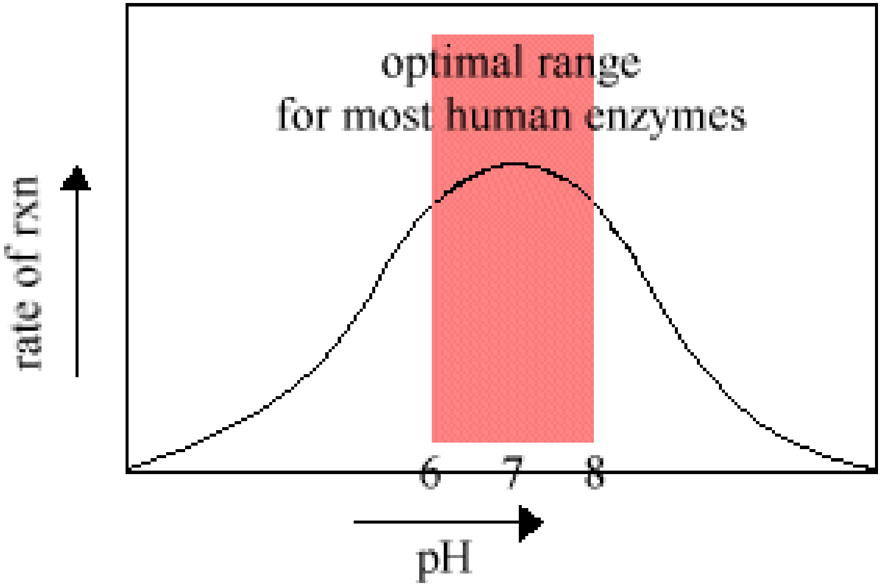
Denaturation
Normal protein
Denatured protein
Renaturation



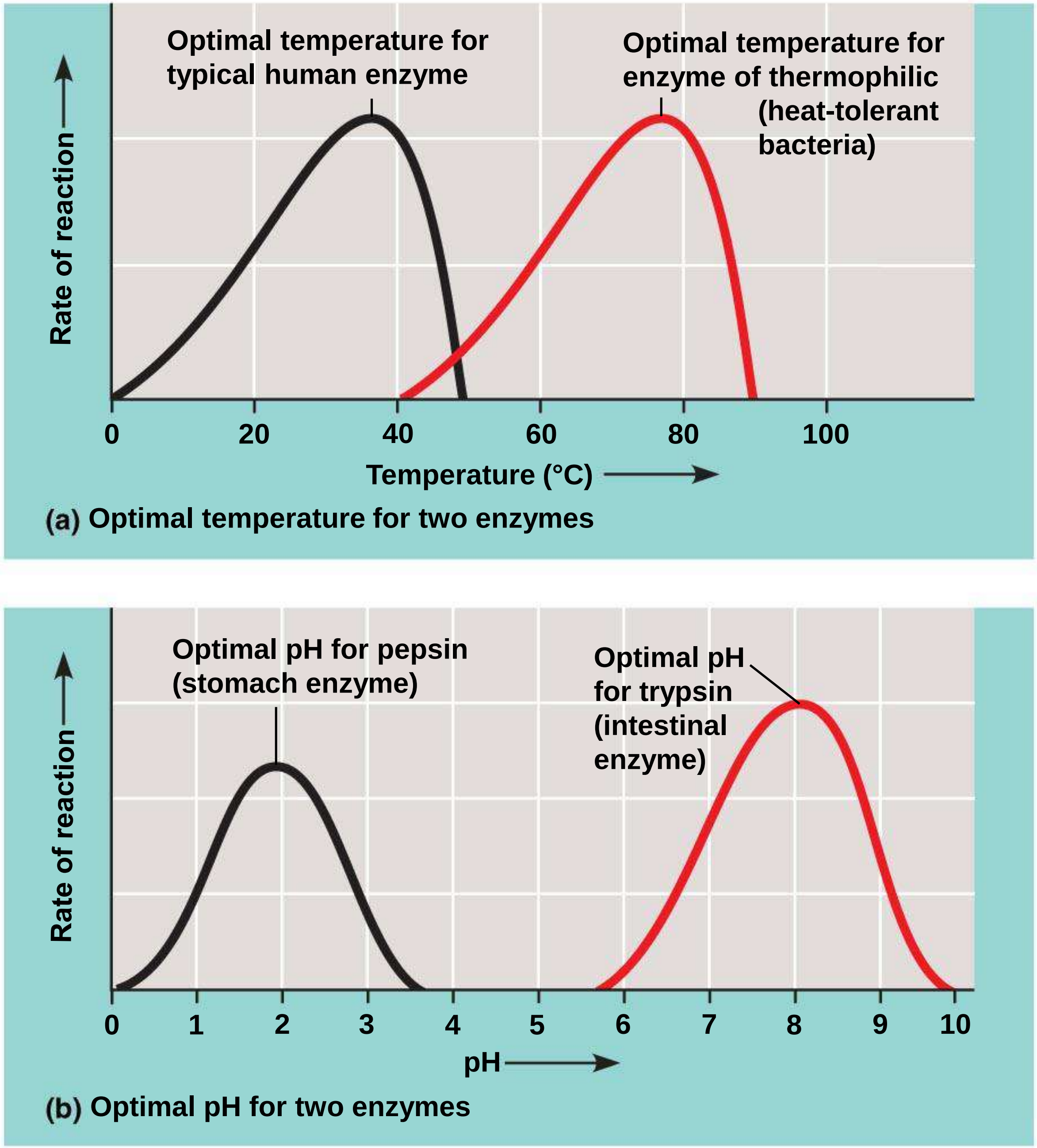
High
Enzyme
Activity
Low
Human
Thermophile
10
37
50
Temperature (C)

2) pH:

-optimal range for most enzymes: **pH 6-8**



-some enzymes operate best at extremes of pH (e.g. digestive enzyme pepsin, found in the acidic environment of the stomach, works best at pH 2)



(a) Optimal temperature for two enzymes

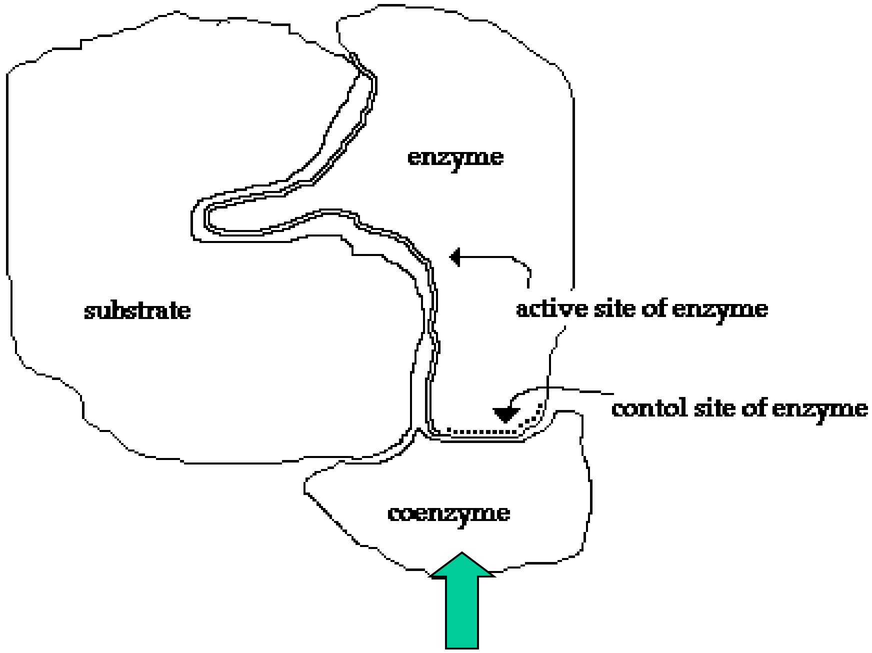
(b) Optimal pH for two enzymes

<u>3) Cofactors</u>: small non-protein molecules <u>required for proper enzyme function</u>

-may bind to active site or substrate

-some are inorganic (e.g. Zn, Fe, Cu)

-some are organic and are called **coenzymes** (e.g. vitamins)



Coenzymes may assist the functioning of enzymes. They work with the enzyme and may help to position the substrate molecules in ways that facilitate the initiation of reactions.

4) Enzyme inhibitors:

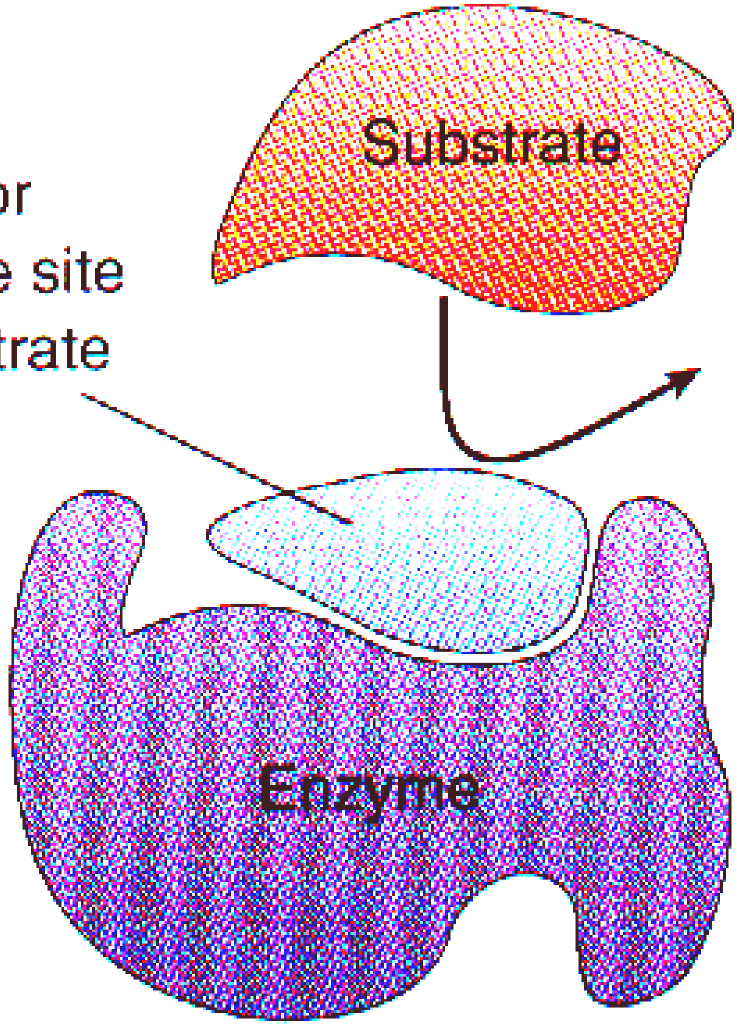
-COMPETITIVE INHIBITORS: chemicals that resemble an enzyme's normal substrate and compete with it for the active site

➔ block active site from substrate

(example: penicillin)

Competitive inhibition

Competitive inhibitor inteferes with active site of enzyme so substrate cannot bind

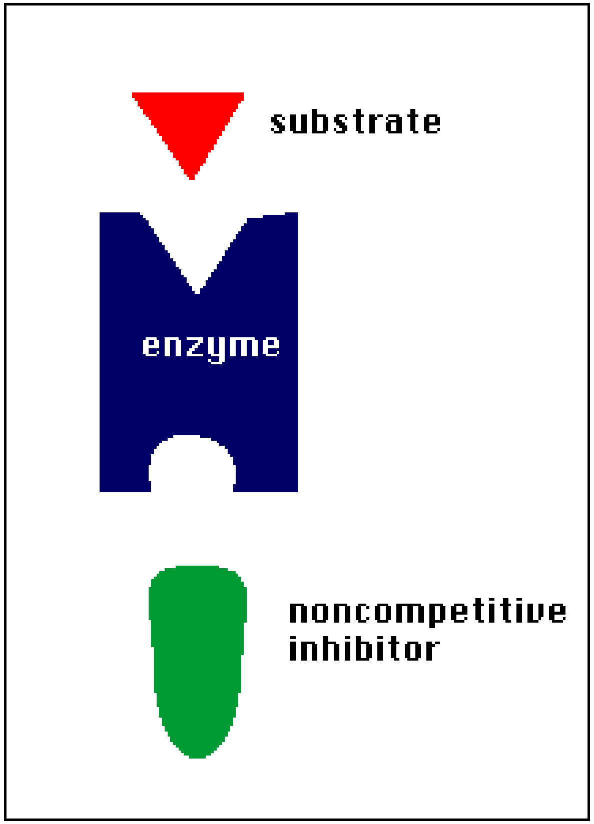


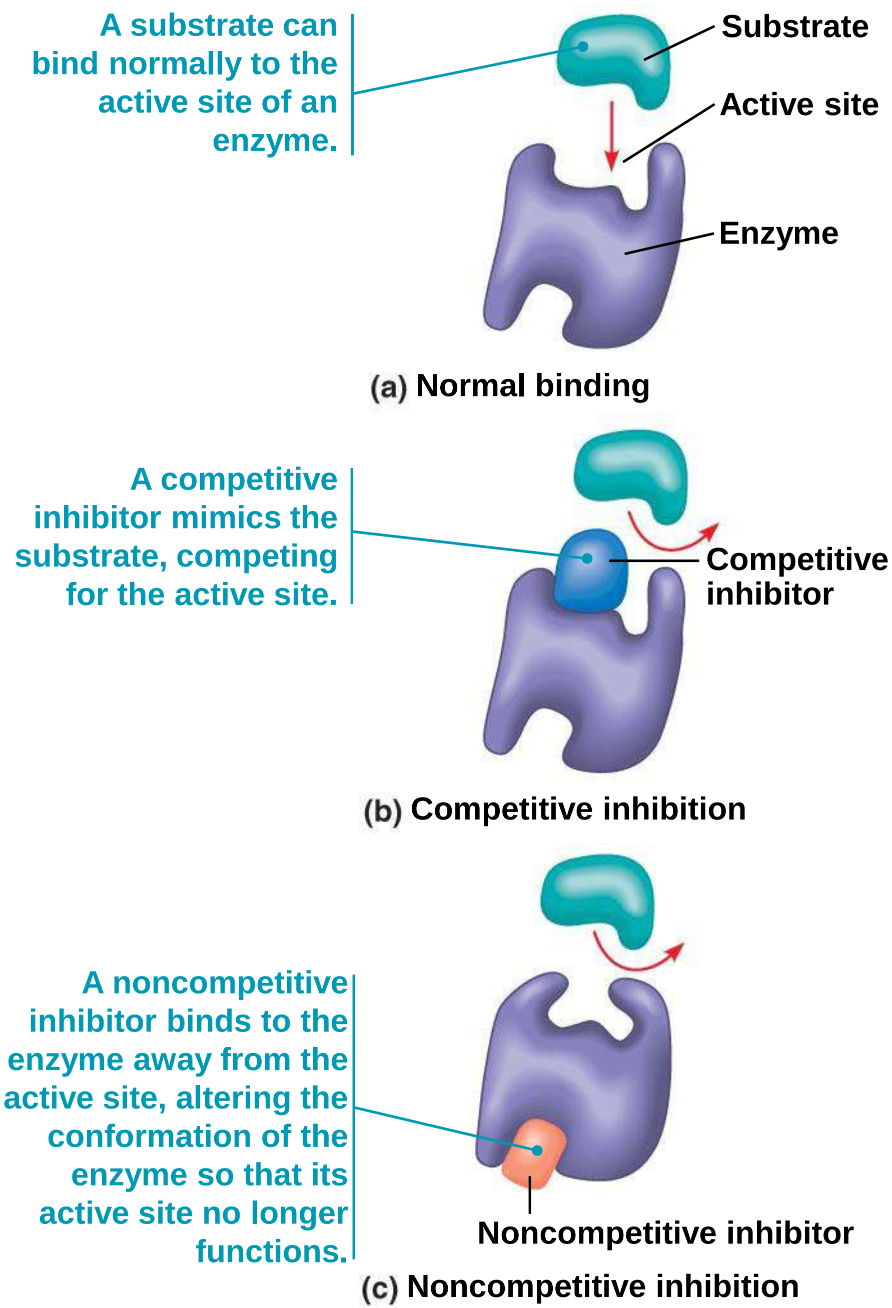
-NONCOMPETITIVE INHIBITORS:

enzyme inhibitors that do not enter the active site, <u>but bind to another part of the enzyme</u> molecule

→ cause enzyme to change its shape so active site cannot bind substrate (less effective!)

→ may act as metabolic poisons (e.g. DDT, some antibiotics)




A substrate can bind normally to the active site of an enzyme.
Substrate
Active site
Enzyme
(a) Normal binding
A competitive inhibitor mimics the substrate, competing for the active site.
Competitive inhibitor
(b) Competitive inhibition
A noncompetitive inhibitor binds to the enzyme away from the active site, altering the conformation of the enzyme so that its active site no longer functions.
Noncompetitive inhibitor
(c) Noncompetitive inhibition

8.5 - Regulation of enzyme activity helps control metabolism

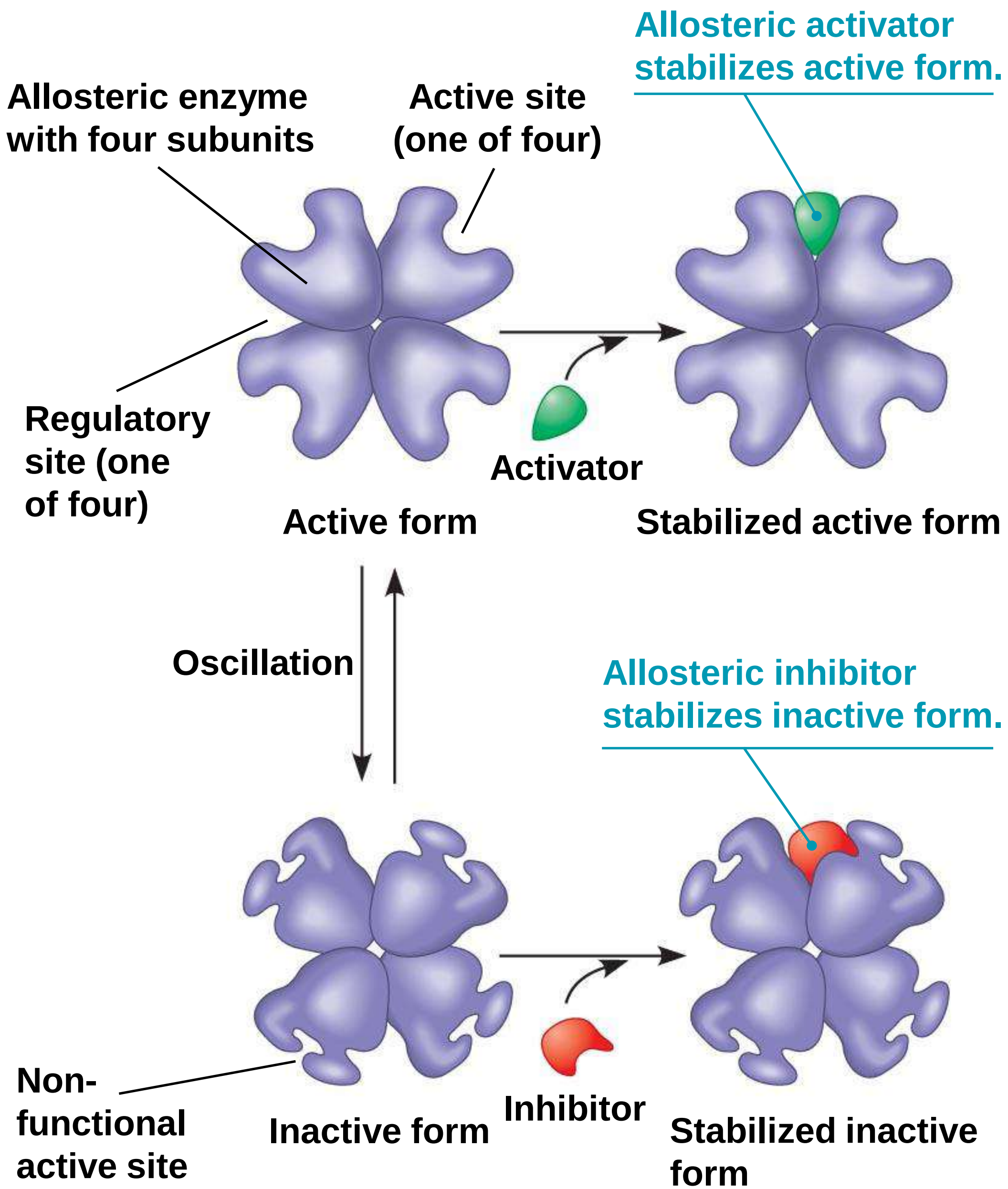
- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated
- To regulate metabolic pathways, the cell switches on or off the genes that encode specific enzymes

Allosteric Regulation of Enzymes

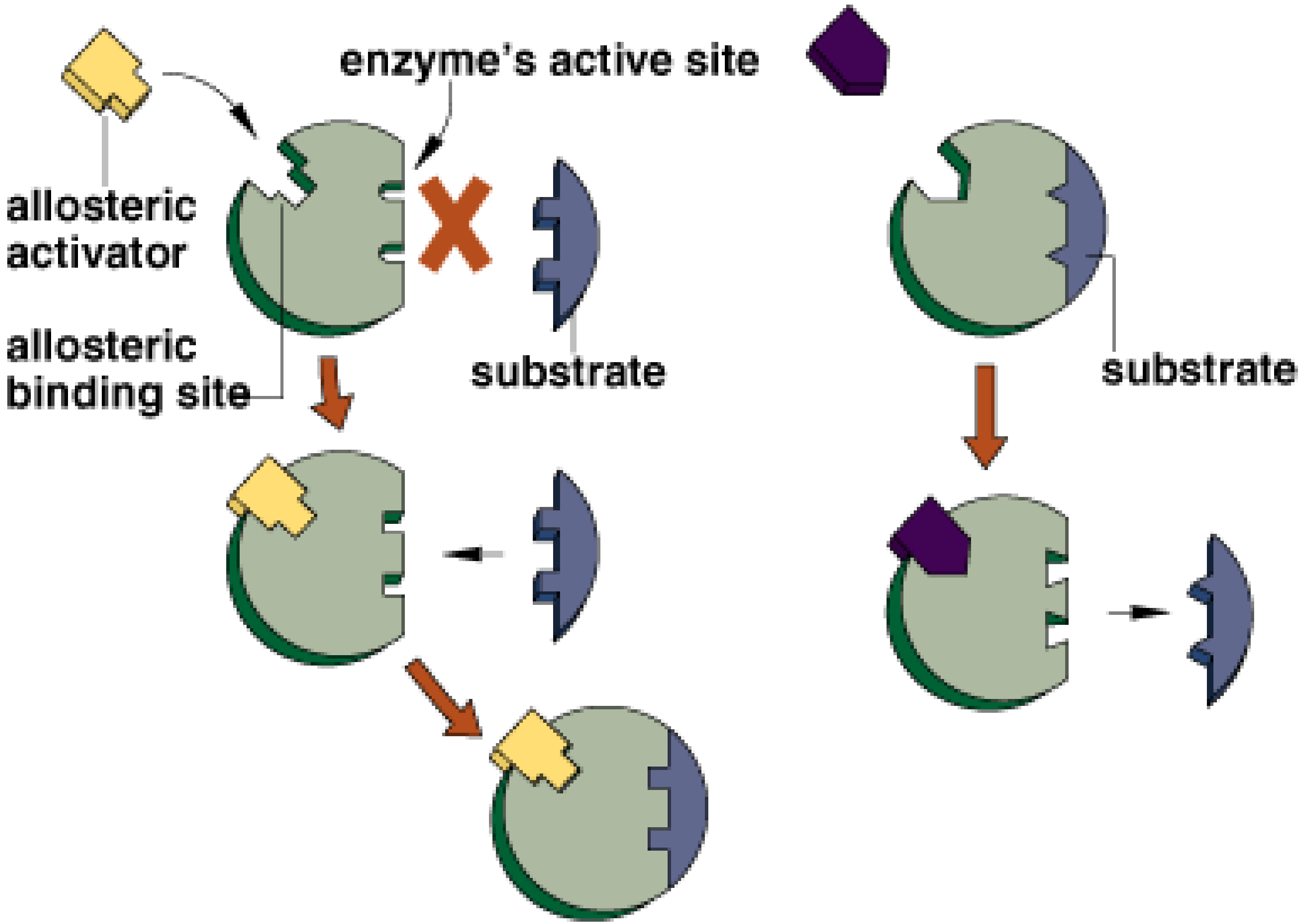
- Allosteric regulation is the term used to describe cases where a protein's function at one site is affected by binding of a regulatory molecule at another site
- Allosteric regulation may either inhibit or stimulate an enzyme's activity

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

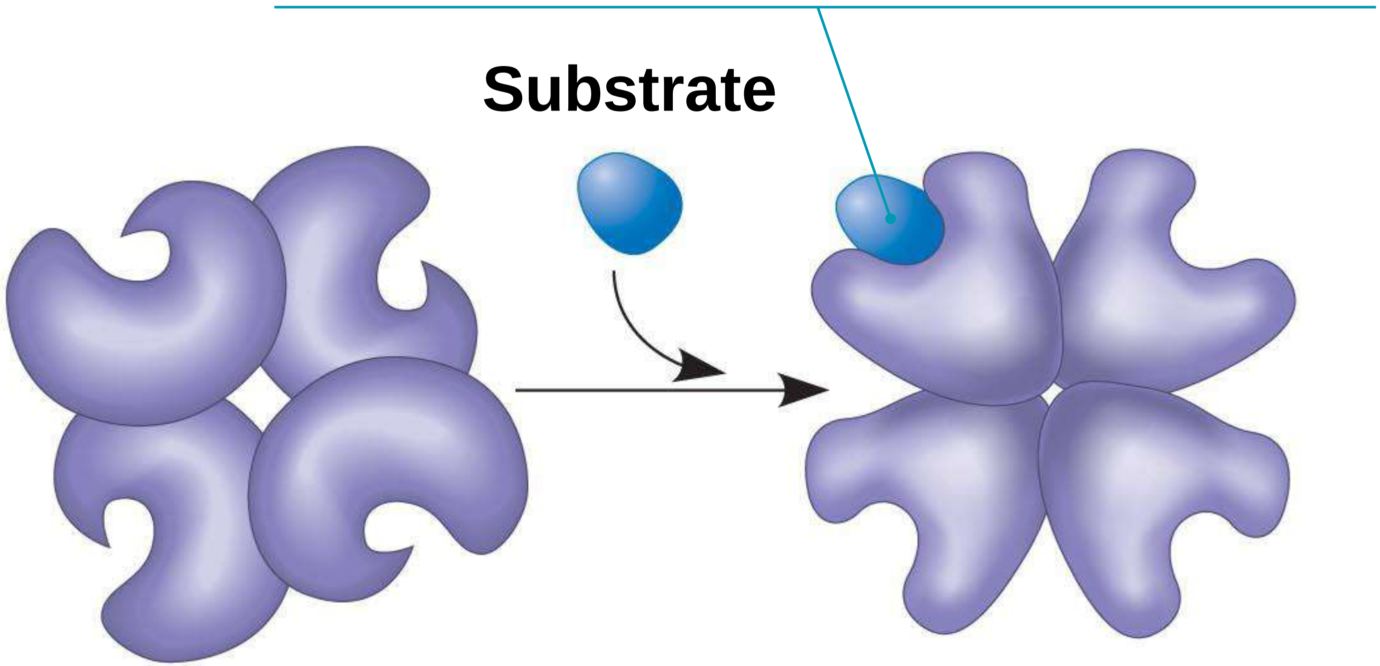


(a) Allosteric activators and inhibitors


enzyme's active site
allosteric activator
allosteric binding site
substrate
substrate

Allosteric Activation and Inhibition

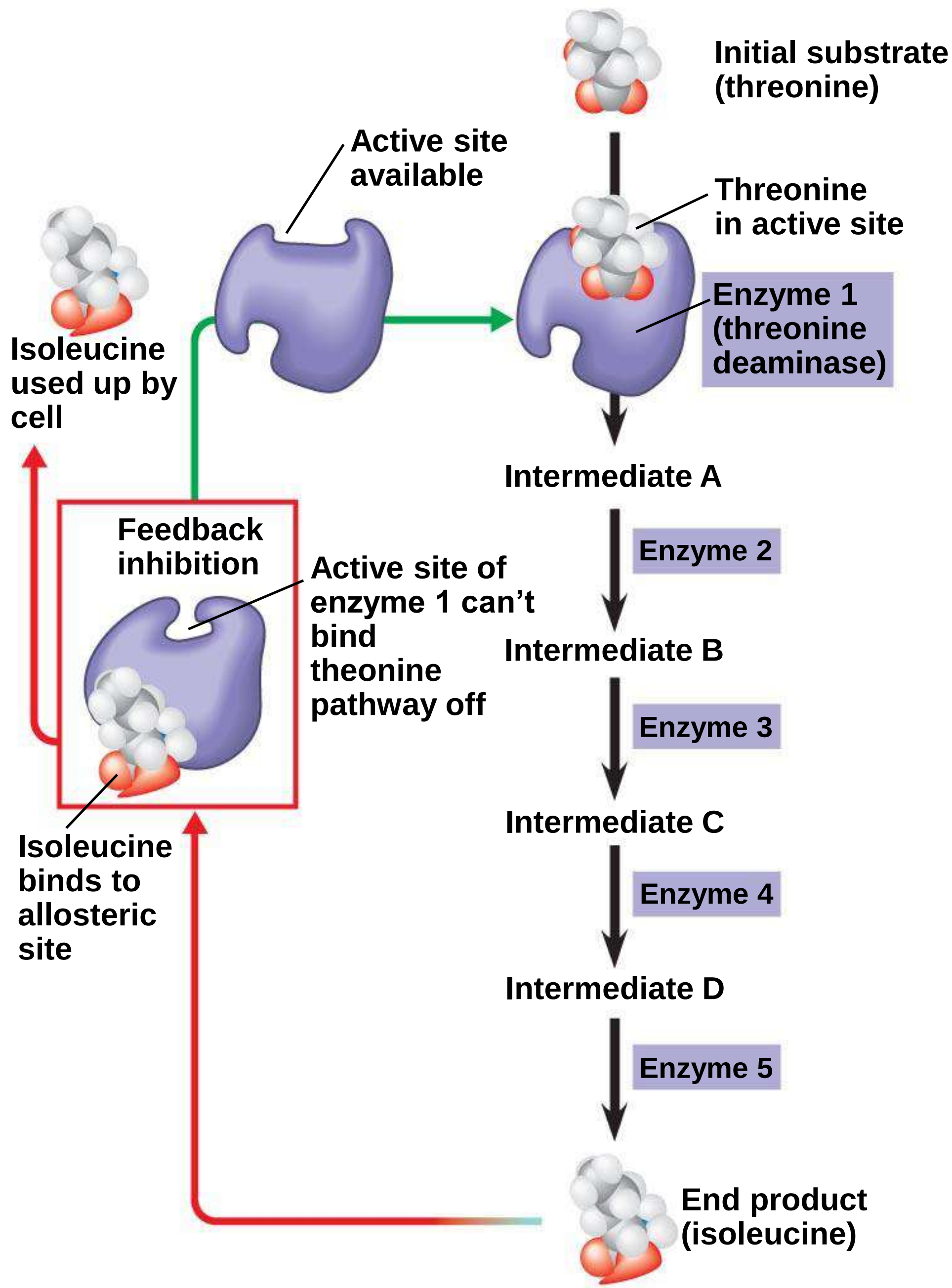
- **Cooperativity** is a form of allosteric regulation that can amplify enzyme activity
- In cooperativity, binding by a substrate to one active site stabilizes favorable conformational changes at all other subunits

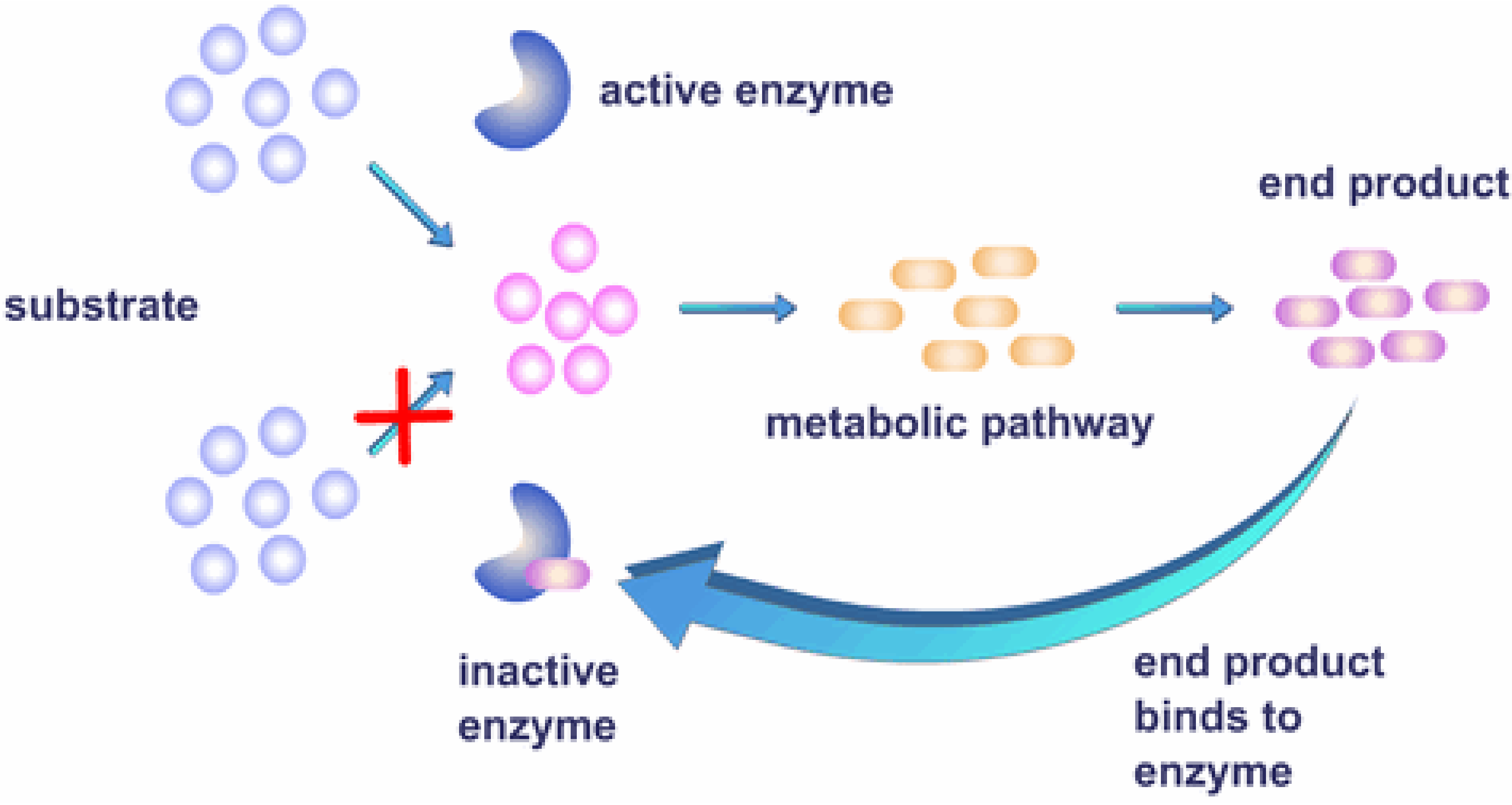


(b) Cooperativity another type of allosteric activation

Feedback Inhibition

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


Initial substrate
(threonine)
Active site
available
Threonine
in active site
Isoleucine
used up by
cell
Enzyme 1
(threonine
deaminase)
Intermediate A
Feedback
inhibition
Active site of
enzyme 1 can’t
bind
theonine
pathway off
Enzyme 2
Intermediate B
Enzyme 3
Intermediate C
Isoleucine
binds to
allosteric
site
Enzyme 4
Intermediate D
Enzyme 5
End product
(isoleucine)


active enzyme
end product
substrate
metabolic pathway
inactive
enzyme
end product
binds to
enzyme

Specific Localization of Enzymes Within the Cell:

- Structures within the cell help bring order to metabolic pathways
- Some enzymes reside in specific organelles, such as: enzymes for cellular respiration being located in mitochondria