Big Idea 4: Biological systems interact, and these systems and their interactions possess complex properties.

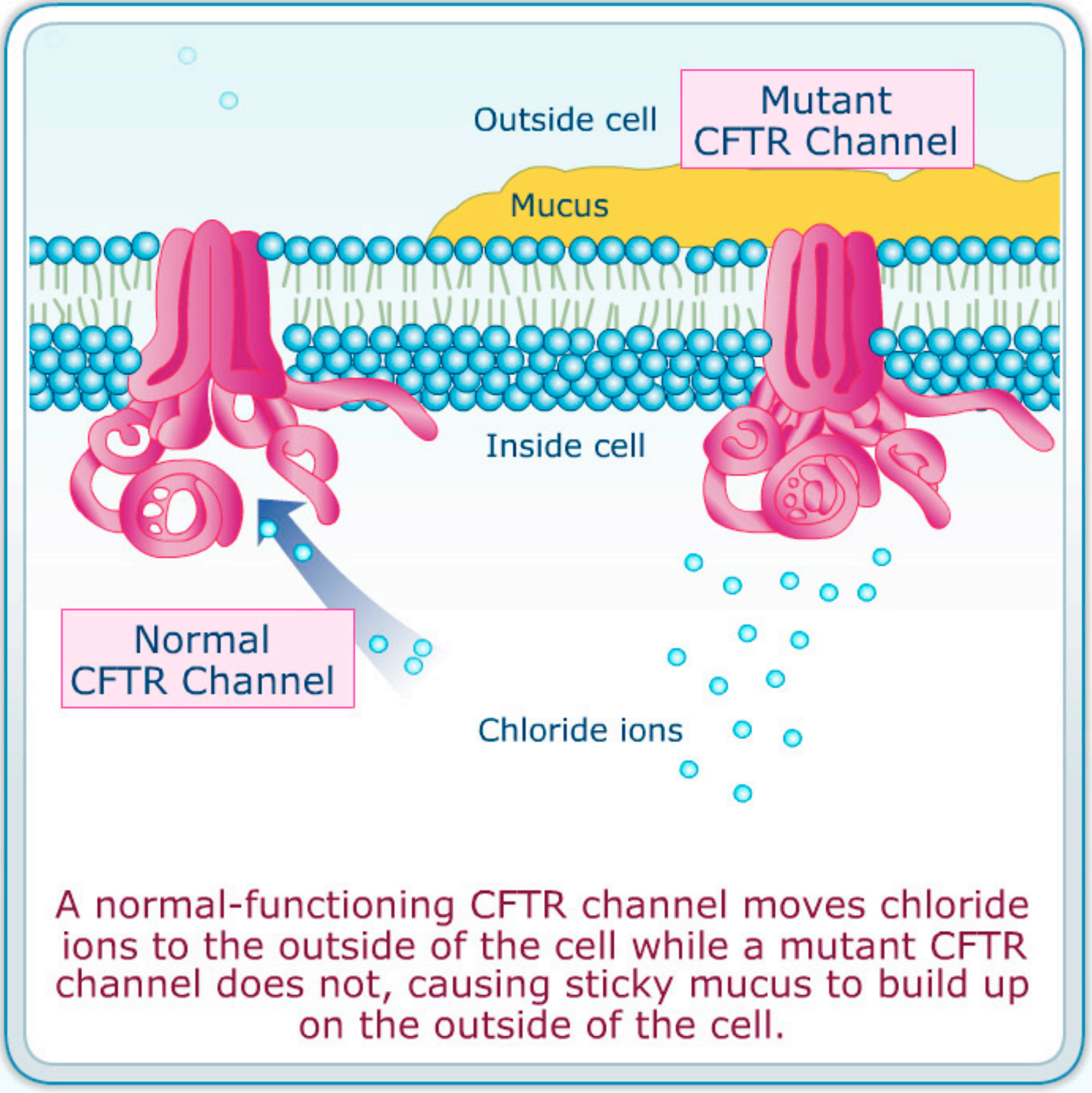
Enduring understanding 4.B: Competition and cooperation are important aspects of biological systems.

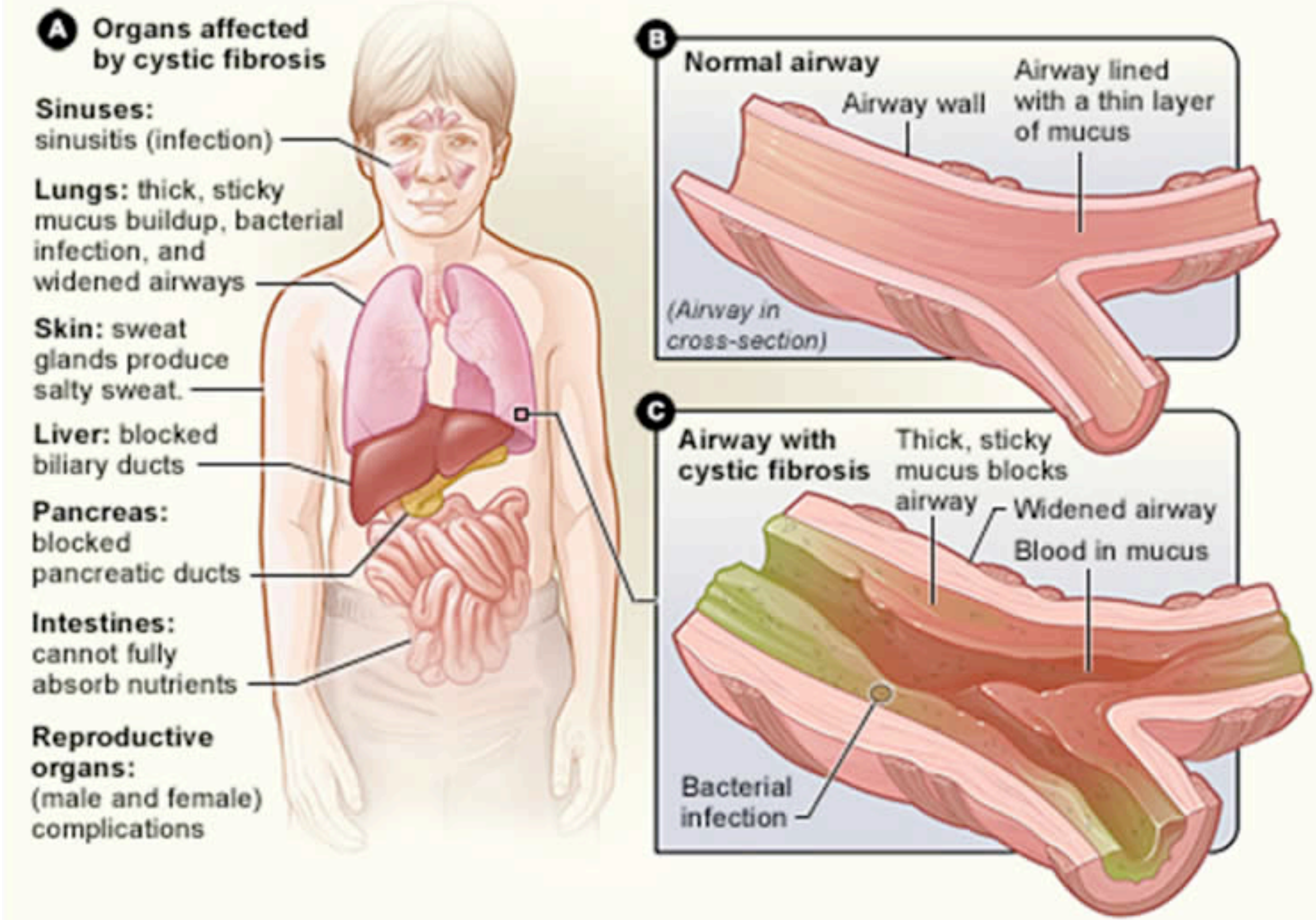
Essential knowledge 4.B.1: Interactions between molecules affect their structure and function.

a. Change in the structure of a molecular system may result in a change of the function of the system. [See also 3.D.3]

Cystic Fibrosis

- The most common lethal genetic disease in the United States, strikes 1in 2500 people of European descent.
- 4% of people with European descent are carriers for the trait.
- If untreated most children die before the age of 5.
- With treatment, more than 50% of those in the U.S. live into their 20's or 30's.
    - Treatment includes: antibiotics, daily pounding on the chest to clear mucous and other preventive treatments


Outside cell
Mutant
CFTR Channel
Mucus
Inside cell
Normal
CFTR Channel
Chloride ions
A normal-functioning CFTR channel moves chloride ions to the outside of the cell while a mutant CFTR channel does not, causing sticky mucus to build up on the outside of the cell.


A Organs affected by cystic fibrosis
Sinuses: sinusitis (infection)
Lungs: thick, sticky mucus buildup, bacterial infection, and widened airways
Skin: sweat glands produce salty sweat.
Liver: blocked biliary ducts
Pancreas: blocked pancreatic ducts
Intestines: cannot fully absorb nutrients
Reproductive organs: (male and female) complications
B Normal airway
Airway wall
Airway lined with a thin layer of mucus
(Airway in cross-section)
C Airway with cystic fibrosis
Thick, sticky mucus blocks airway
Widened airway
Blood in mucus
Bacterial infection

Sickle Cell Anemia

- The most common genetic disease in people of African descent, strikes 1 in 400 people.
- About 1 in 10 African-Americans carry the trait.
- The high incidence stems from the partial resistance to malaria conferred by carrying the sickle cell trait thus being selected for in Africa where malaria is common.
- Regular blood transfusions can ward off brain damage in children and new drugs can help prevent and treat the disease other related problems but there is no cure.

Two copies of the sickle-cell allele

↓

All hemoglobin is the sickle-cell (abnormal) variety

↓

Abnormal hemoglobin crystallizes when oxygen content of blood is low, causing red blood cells to become sickle-shaped

Normal cells

Sickled cells

Breakdown of red blood cells

Clumping of cells and clogging of small blood vessels

Accumulation of sickled cells in spleen

Physical weakness

Anemia

Heart failure

Pain and fever

Brain damage

Damage to other organs

Spleen damage

Impaired mental function

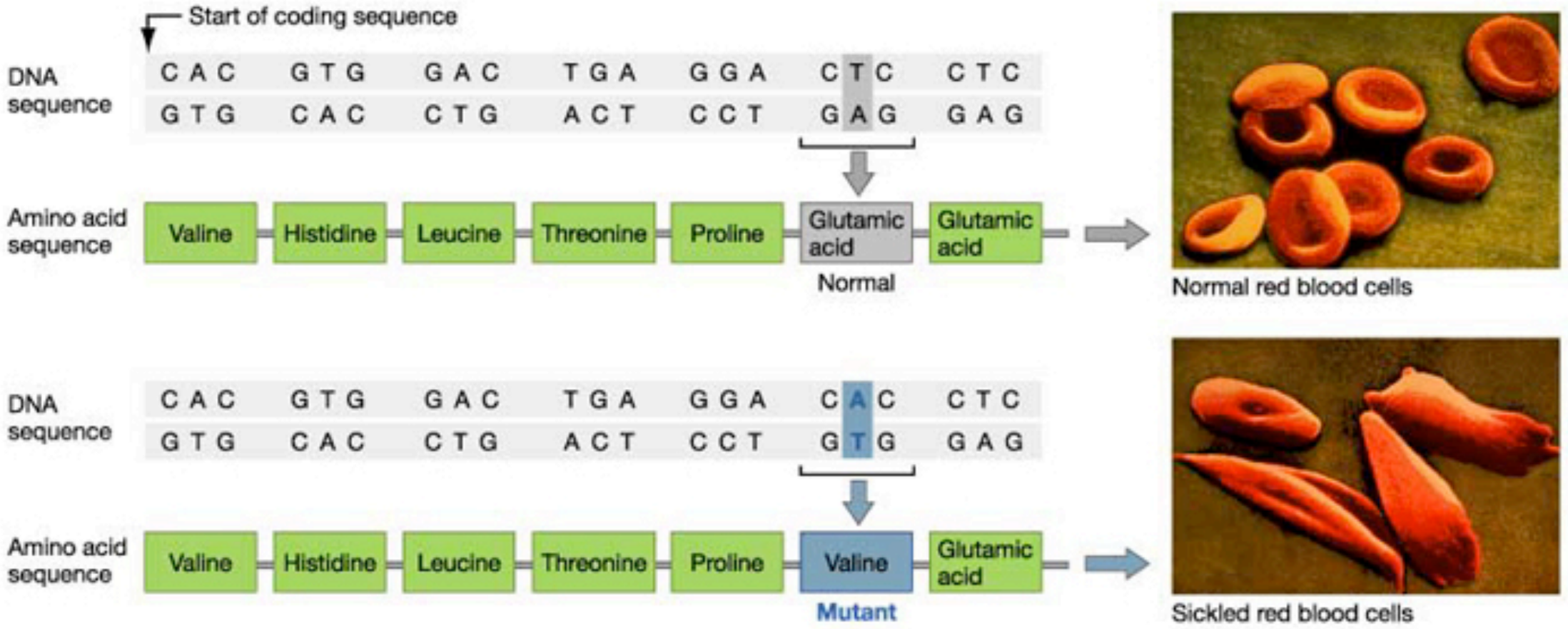
Paralysis

Pneumonia and other infections

Rheumatism

Kidney failure

Sickle Cell Trait & Malaria



The change in amino acid sequence causes hemoglobin molecules to crystallize when oxygen levels in the blood are low. As a result, red blood cells sickle and get stuck in small blood vessels.

This is a "substitution" mutation notice the thymine was switched with alanine.

The normal beta subunit consists of 438 nucleotides and 146 amino acids.

A change in 1 nucleotide, changes 1 amino acid resulting in sickle cell disease

Essential knowledge 4.B.1: Interactions between molecules affect their structure and function.

b. The shape of enzymes, active sites and interaction with specific molecules are essential for basic functioning of the enzyme.

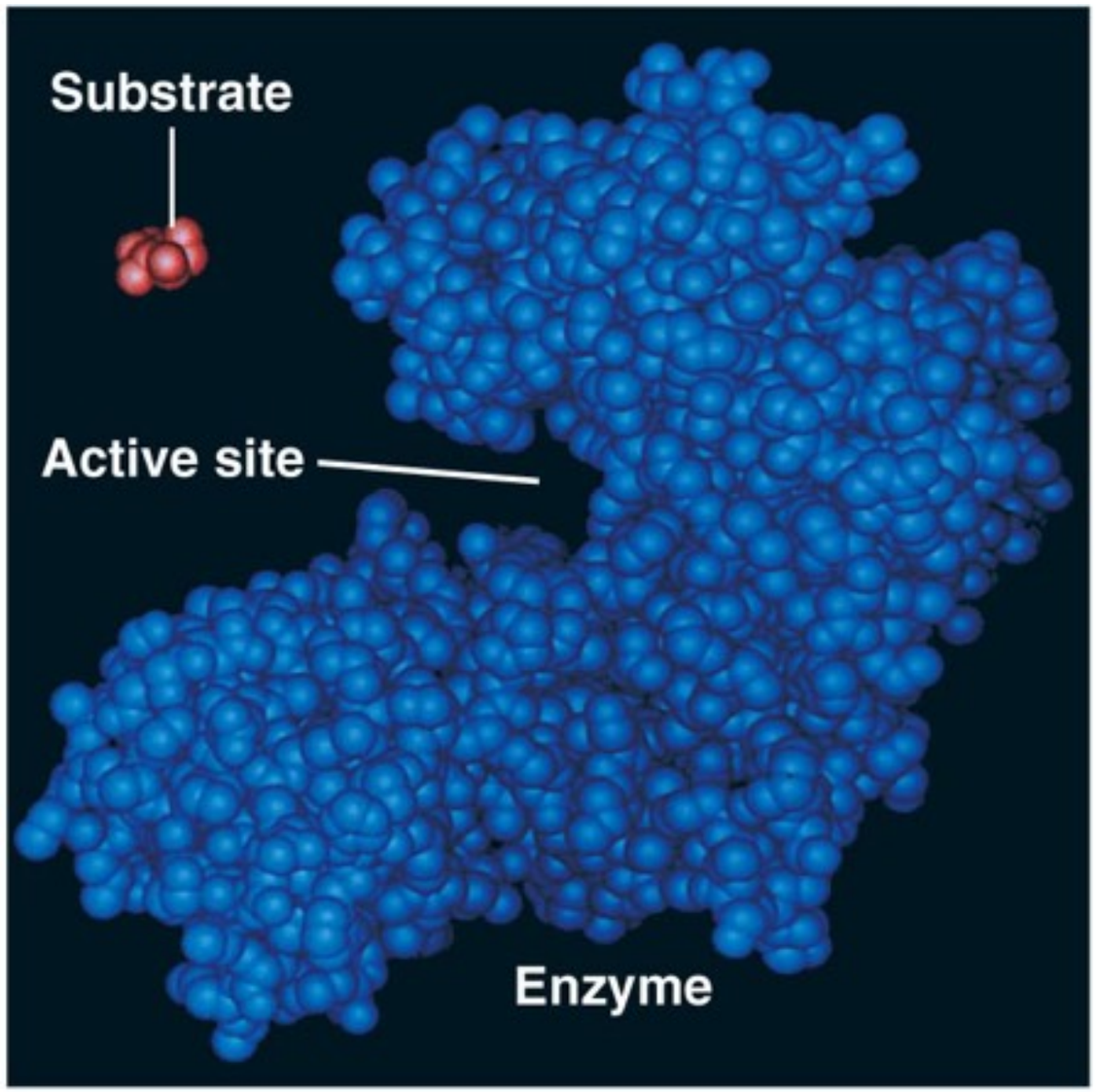
Evidence of student learning is a demonstrated understanding of each of the following:

1. For an enzyme-mediated chemical reaction to occur, the substrate must be complementary to the surface properties (shape and charge) of the active site. In other words, the substrate must fit into the enzyme's active site.
2. Cofactors and coenzymes affect enzyme function; this interaction relates to a structural change that alters the activity rate of the enzyme. The enzyme may only become active when all the appropriate cofactors or coenzymes are present and bind to the appropriate sites on the enzyme.

✘ *No specific cofactors or coenzymes are within the scope of the course and the AP Exam.*

Substrate Specificity of Enzymes

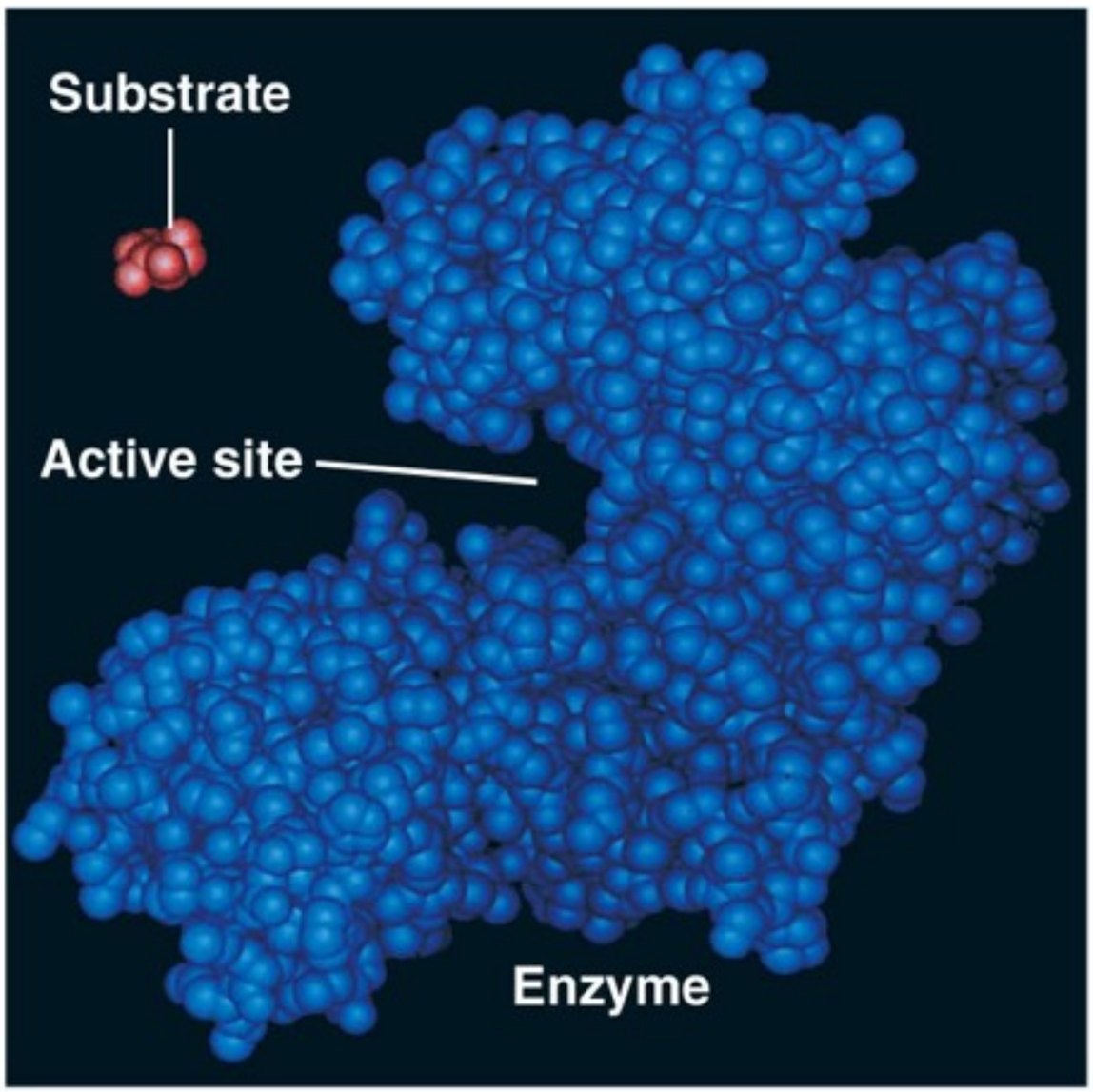
- **Substrate:** the reactant an enzyme acts upon.
  - Most enzymes are proteins
  - Most enzymes end in *-ase*
- **Active site:** is typically a pocket or groove on the surface of the enzyme where catalysis occurs.

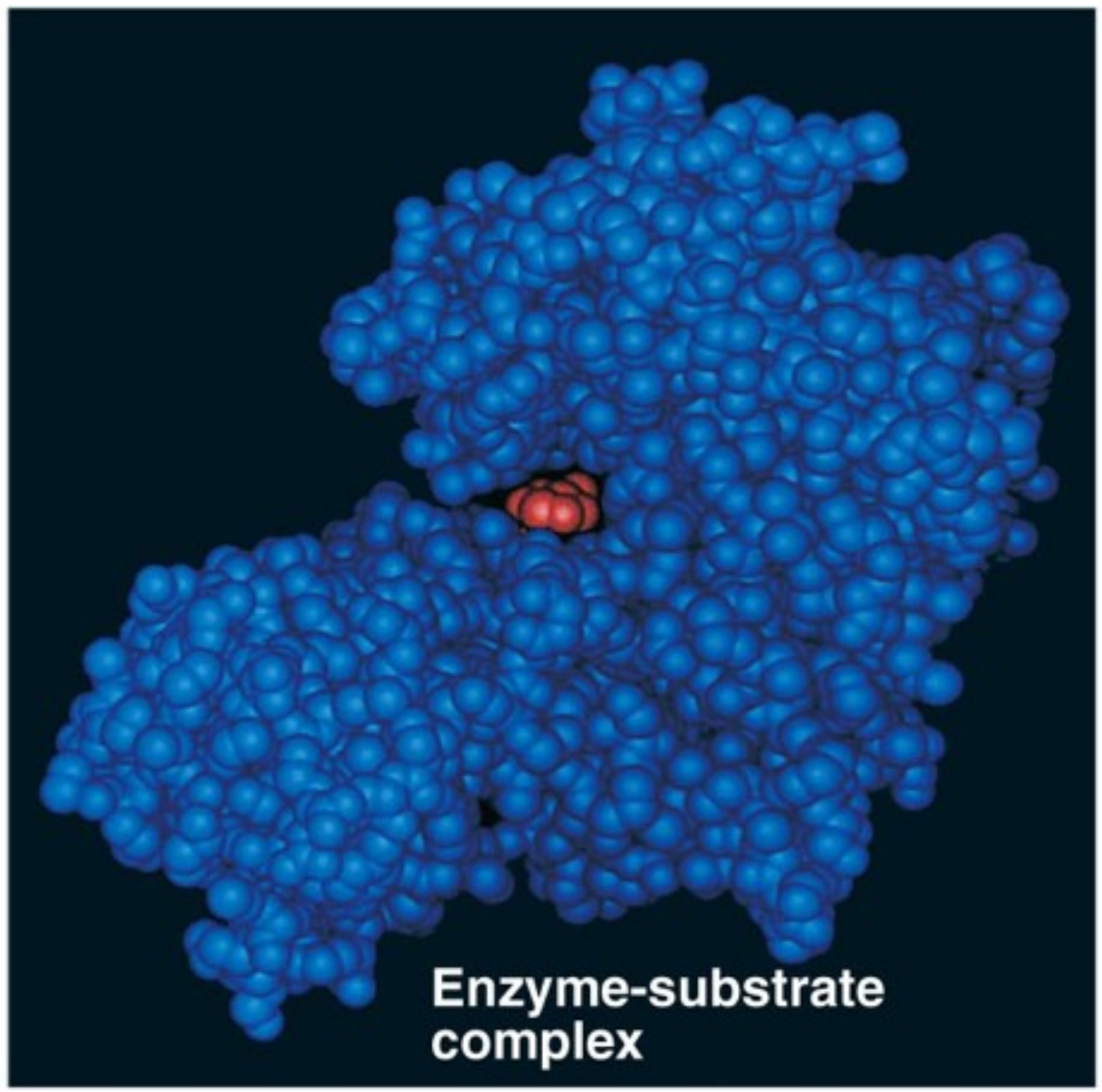


Substrate Specificity of Enzymes

- Enzymes are not stiff, they alternate between continually between subtly different shapes

- **Induced fit**: as the substrate moves into the active site, the enzyme moves into another conformation that snugly fits the substrate





Cofactors

- Many enzymes require nonprotein helpers for catalytic activity.

- **Cofactors:**
  - Inorganic
  - Minerals (metal ions)
  - Can bind tightly as permanent residents
  - Can bind loosely and reversibly

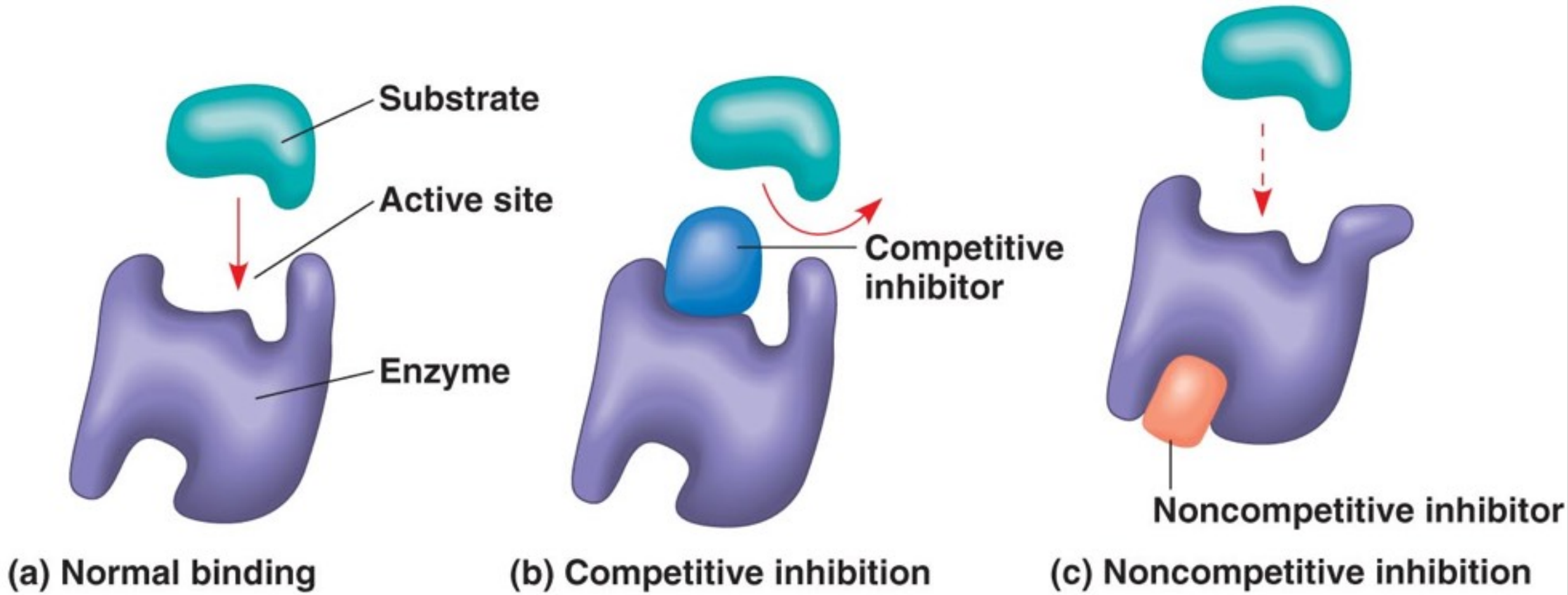
- **Coenzymes:**
  - Organic
  - Vitamins
  - Can bind tightly as permanent residents
  - Can bind loosely and reversibly

Enzyme Inhibitors

- Certain chemicals selectively inhibit the action of specific enzymes...**inhibitors**
- If the inhibitor binds covalently the inhibition is irreversible.
- If the inhibitor binds with weak interactions the inhibition is reversible.

- Some reversible inhibitors compete with the substrate for the active site, these mimics called **Competitive Inhibitors** decrease the productivity of the enzyme.
  - *The inhibition can be overcome by adding more substrate!*

- **NonCompetitive Inhibitors** decrease the productivity of the enzyme but they do not compete with substrates for the active site, instead they bind to another part of enzyme which results in a change of in the shape of the active site.



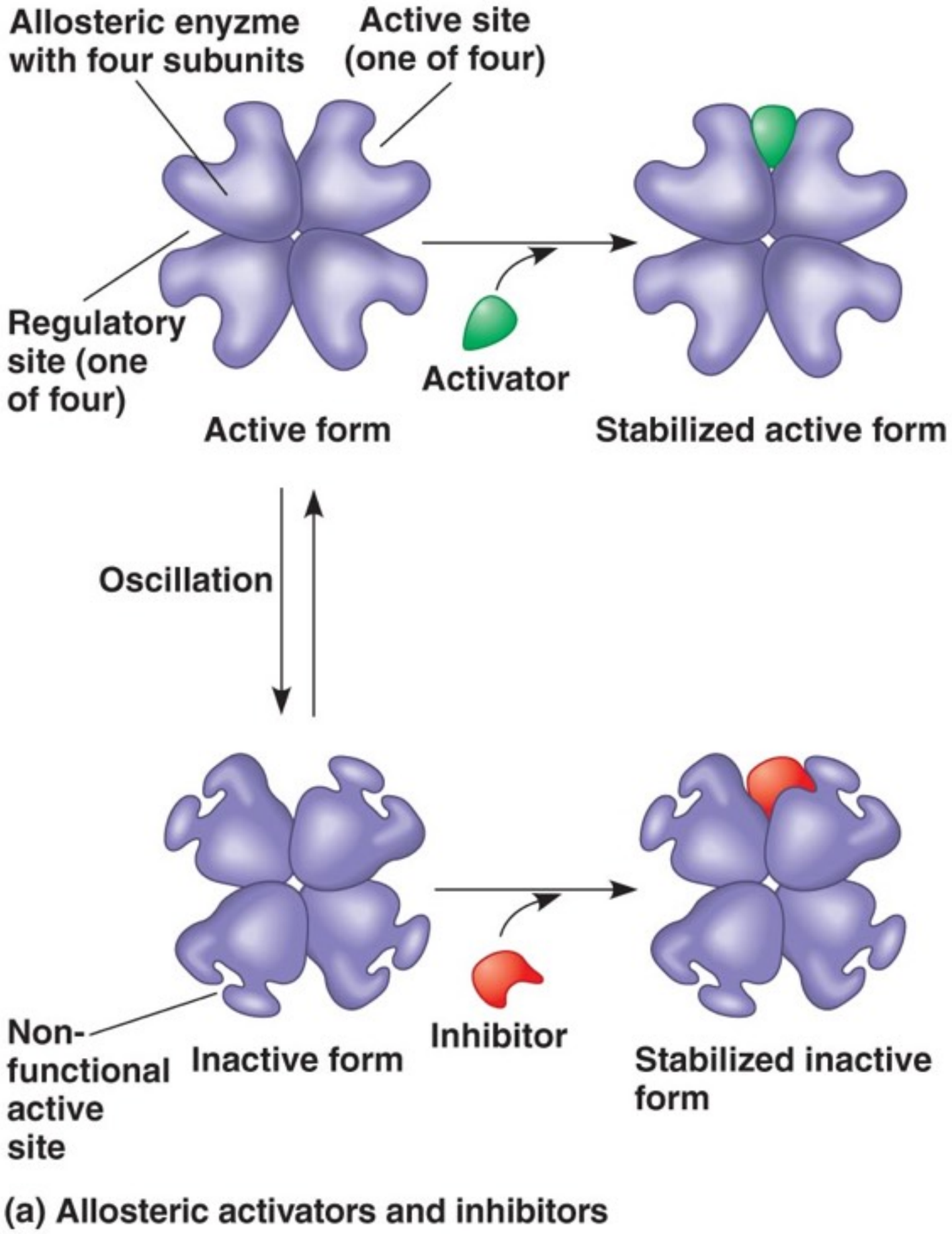
REGULATION OF ENZYME ACTIVITY HELPS CONTROL METABOLISM

Allosteric Regulation of Enzymes

- Allosteric Regulation involves molecules that naturally regulate enzyme activity, by behaving like reversible noncompetitive inhibitors.
- These molecules bind to the enzyme, alter its active site and therefore its activity.

Allosteric Activation & Inhibition

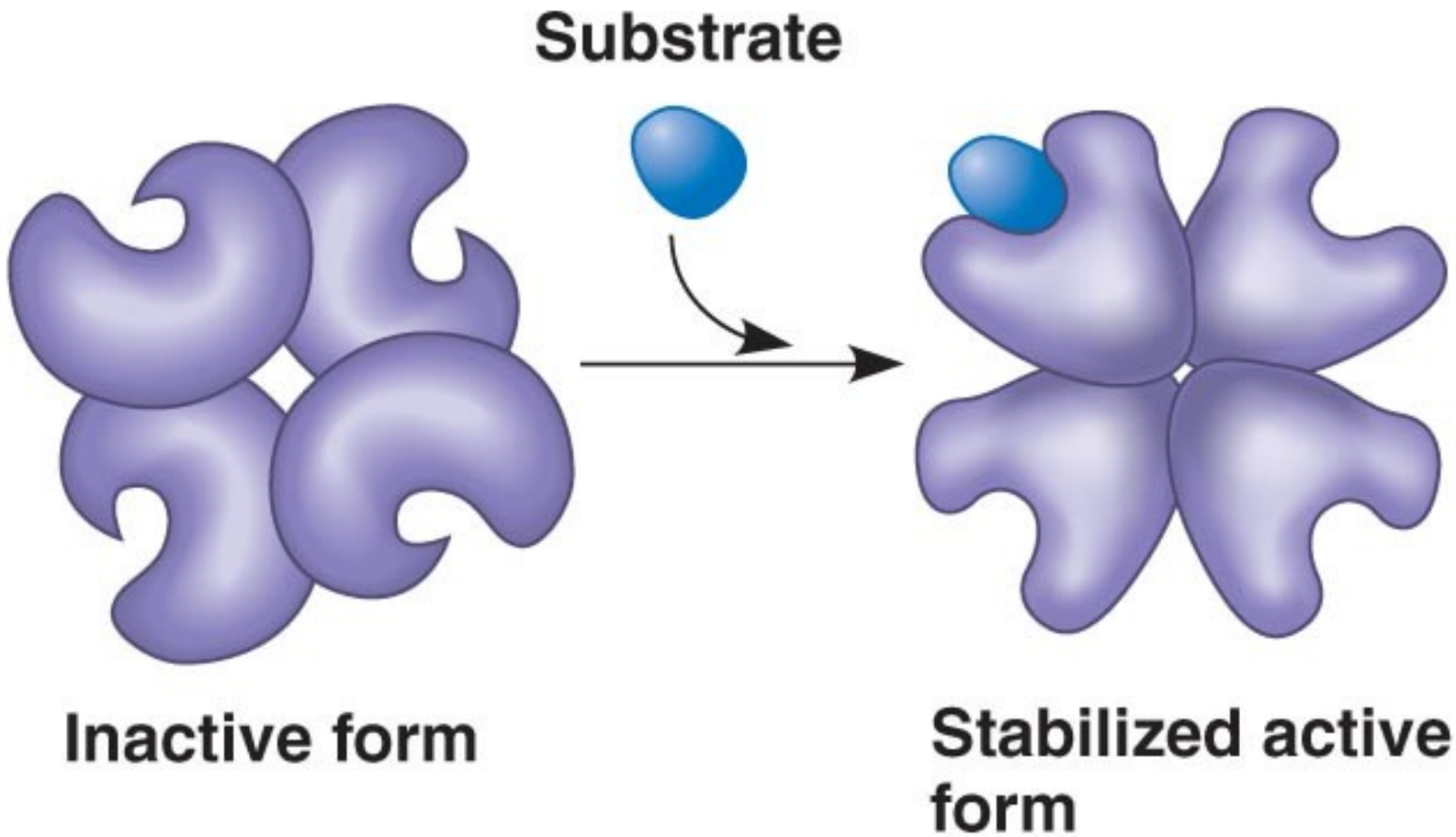
- Most enzymes allosterically regulated have multiple subunits.
- The simplest kind of regulation involves activation or inhibition by binding a molecule to a *regulatory site*.
  - *Activators* stabilize shape and keeps the enzyme functioning
  - *Inhibitors* stabilize the inactive form and prevents the enzyme from functioning
- Fluctuating concentrations of these regulators can result in a sophisticated pattern of response in the activity of enzymes.



(a) Allosteric activators and inhibitors

Allosteric Activation & Inhibition

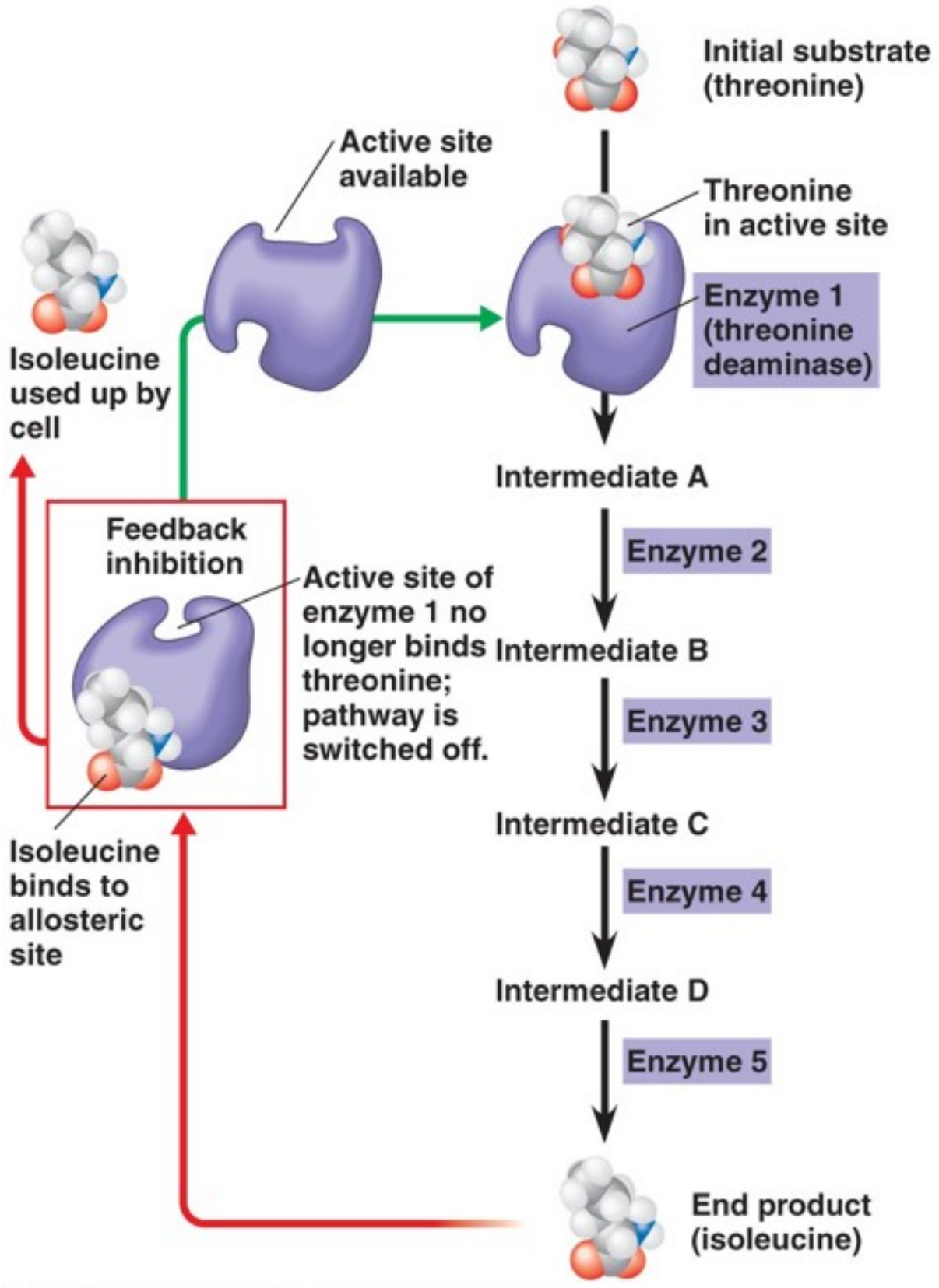
- **Cooperativity**, is another kind of allosteric activation where a substrate binds to one active site in a multisubunit enzyme triggering a shape change in other active sites that are more receptive to binding thereby increasing the catalytic activity.



(b) Cooperativity: another type of allosteric activation

Feedback Inhibition

- **Feedback Inhibition**, a metabolic pathway is switched off by the inhibitory binding of its end product to an enzyme that acts early in the pathway



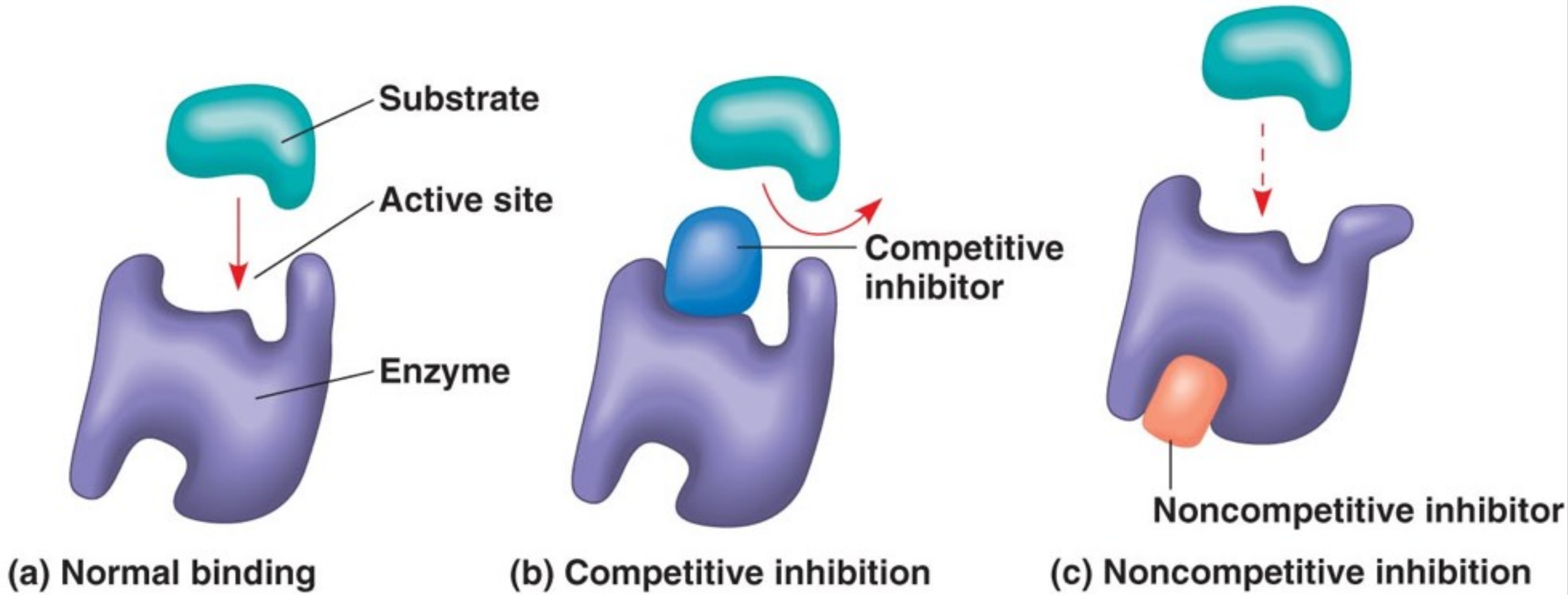
Essential knowledge 4.B.1: Interactions between molecules affect their structure and function.

c. Other molecules and the environment in which the enzyme acts can enhance or inhibit enzyme activity. Molecules can bind reversibly or irreversibly to the active or allosteric sites, changing the activity of the enzyme.

"Other Molecules" Poisons & Toxins

- **Poisons and toxins are often irreversible inhibitors**
- *Sarin a nerve gas.*
- *DDT a pesticide.*
- *Penicillin an antibiotic*
- Keep this in mind...molecules naturally present in the cell often regulate enzyme activity by acting as inhibitors. Such regulation is essential to cellular metabolism.

- **NonCompetitive Inhibitors** decrease the productivity of the enzyme but they do not compete with substrates for the active site, instead they bind to another part of enzyme which results in a change of in the shape of the active site.



Effects of Local Conditions on Enzyme activity

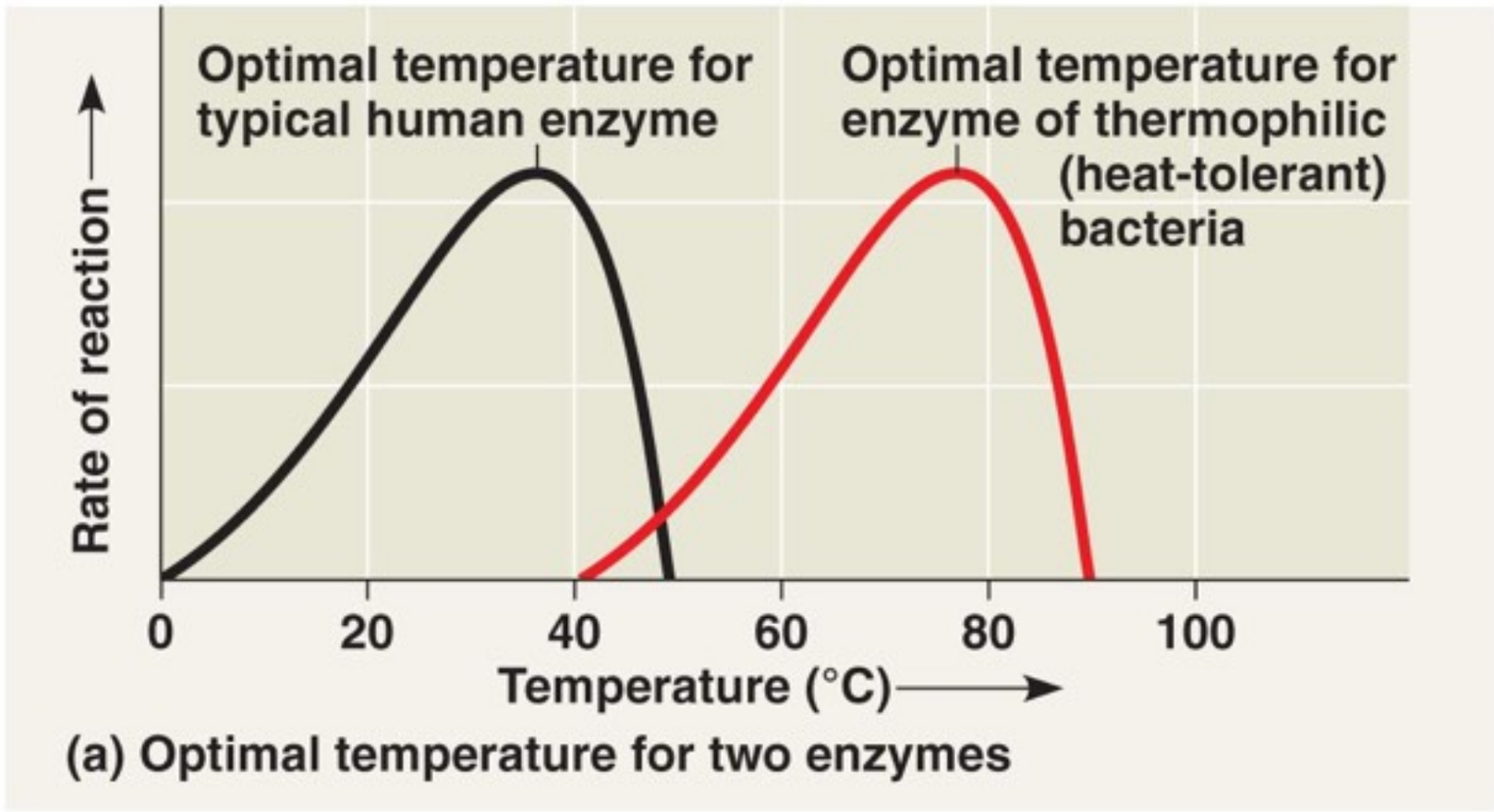
- The activity of an enzyme is affected by general environmental factors such as temperature, pH, chemicals, etc.
- Enzymes work better under some conditions than under other conditions.

Effects of Temperature and pH

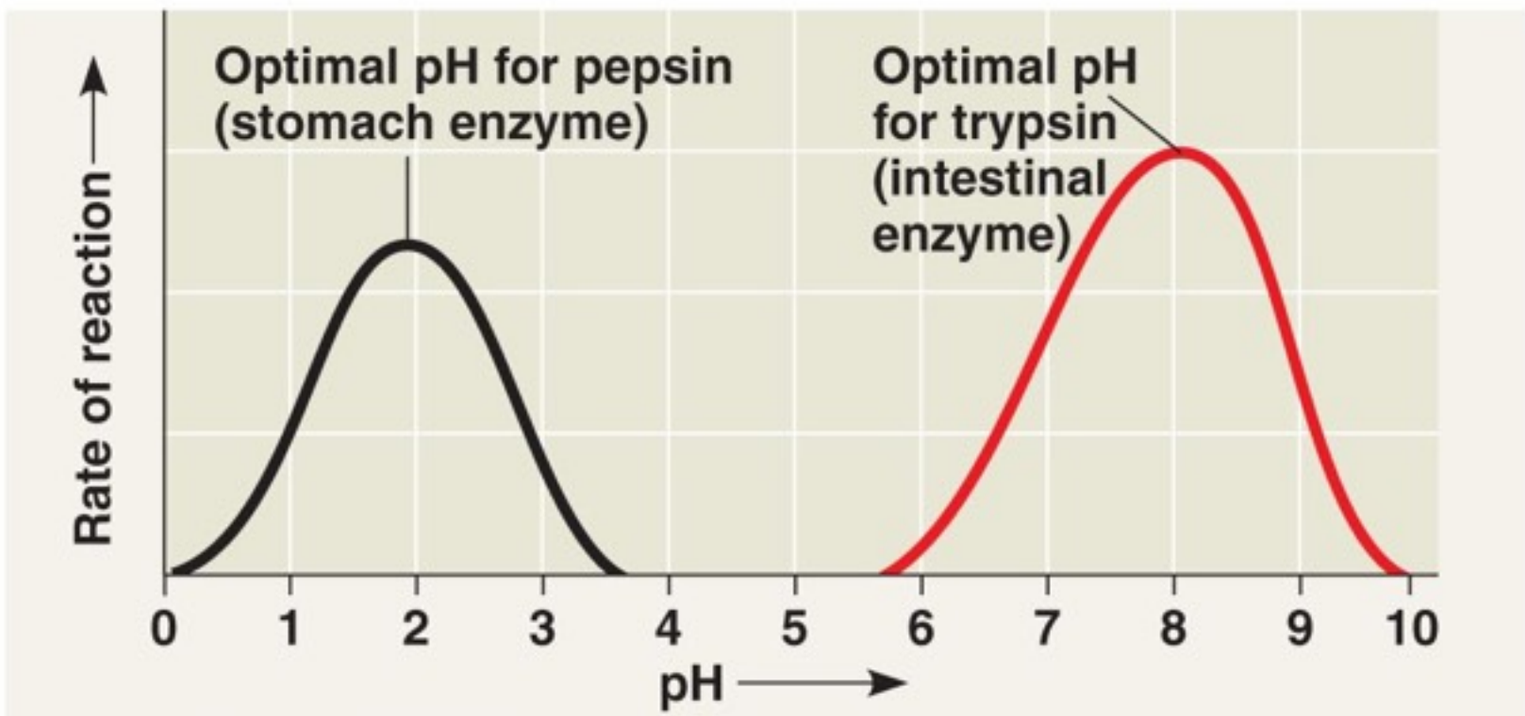
- The rate of enzyme activity is directly correlated with temperature, up to a point.
  - *Each enzyme has an optimum temperature*
  - *Most enzymes work best around the normal body temperature*

Effects of Temperature and pH

- The rate of enzyme activity is dependent upon pH, like temperature enzymes have optimum pH's.
- *Acidic environments can denature proteins!*



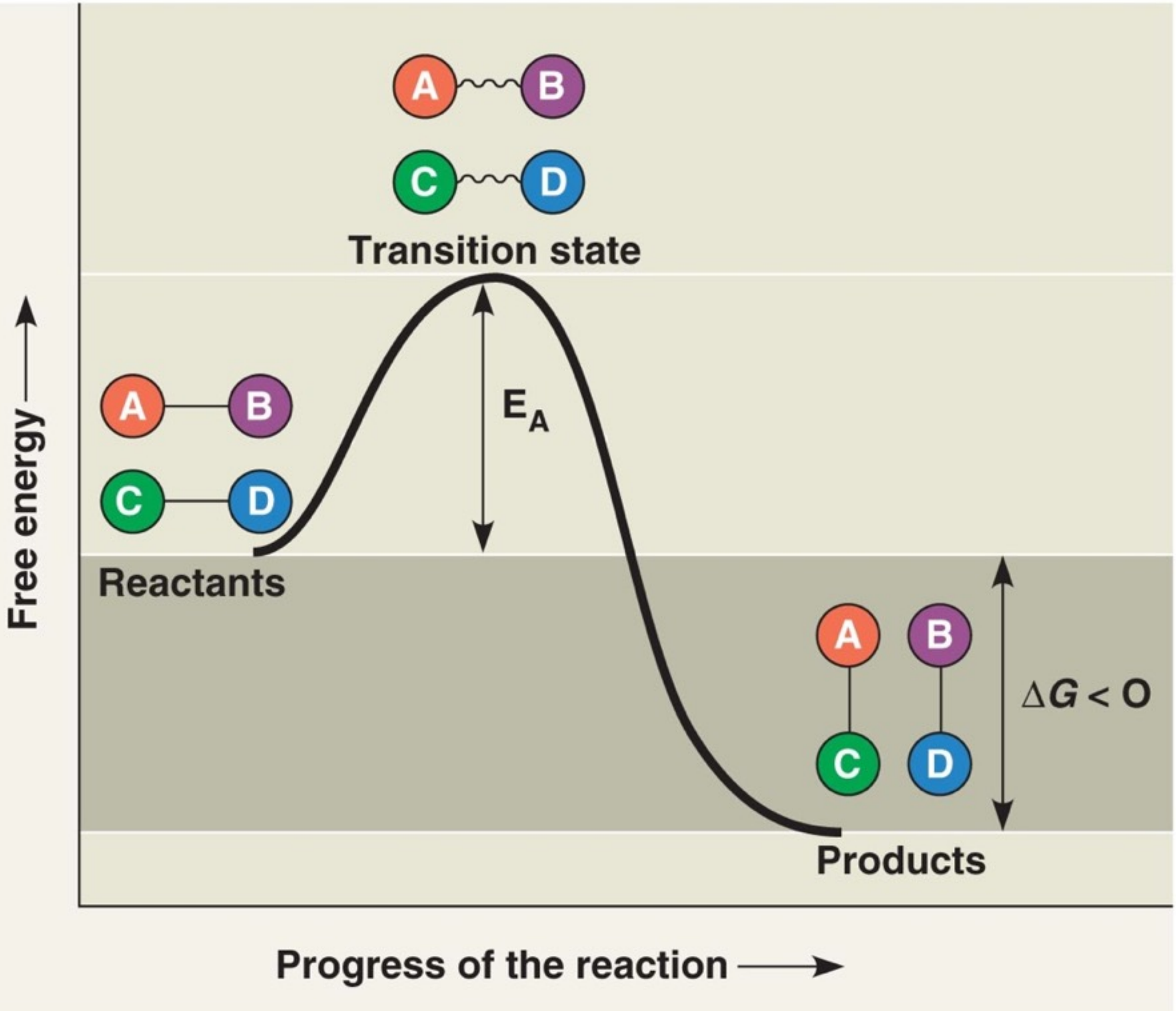
(a) Optimal temperature for two enzymes

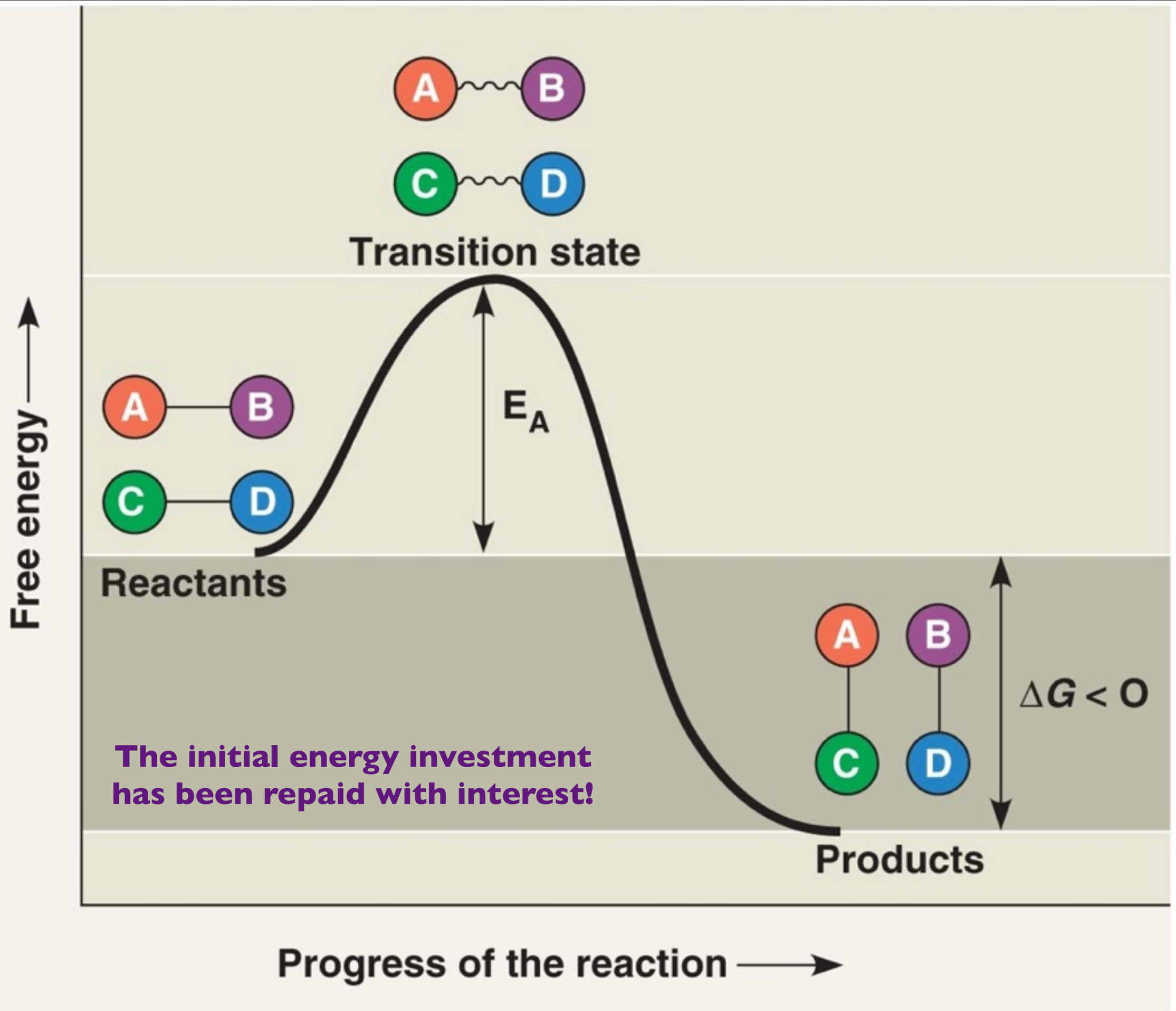


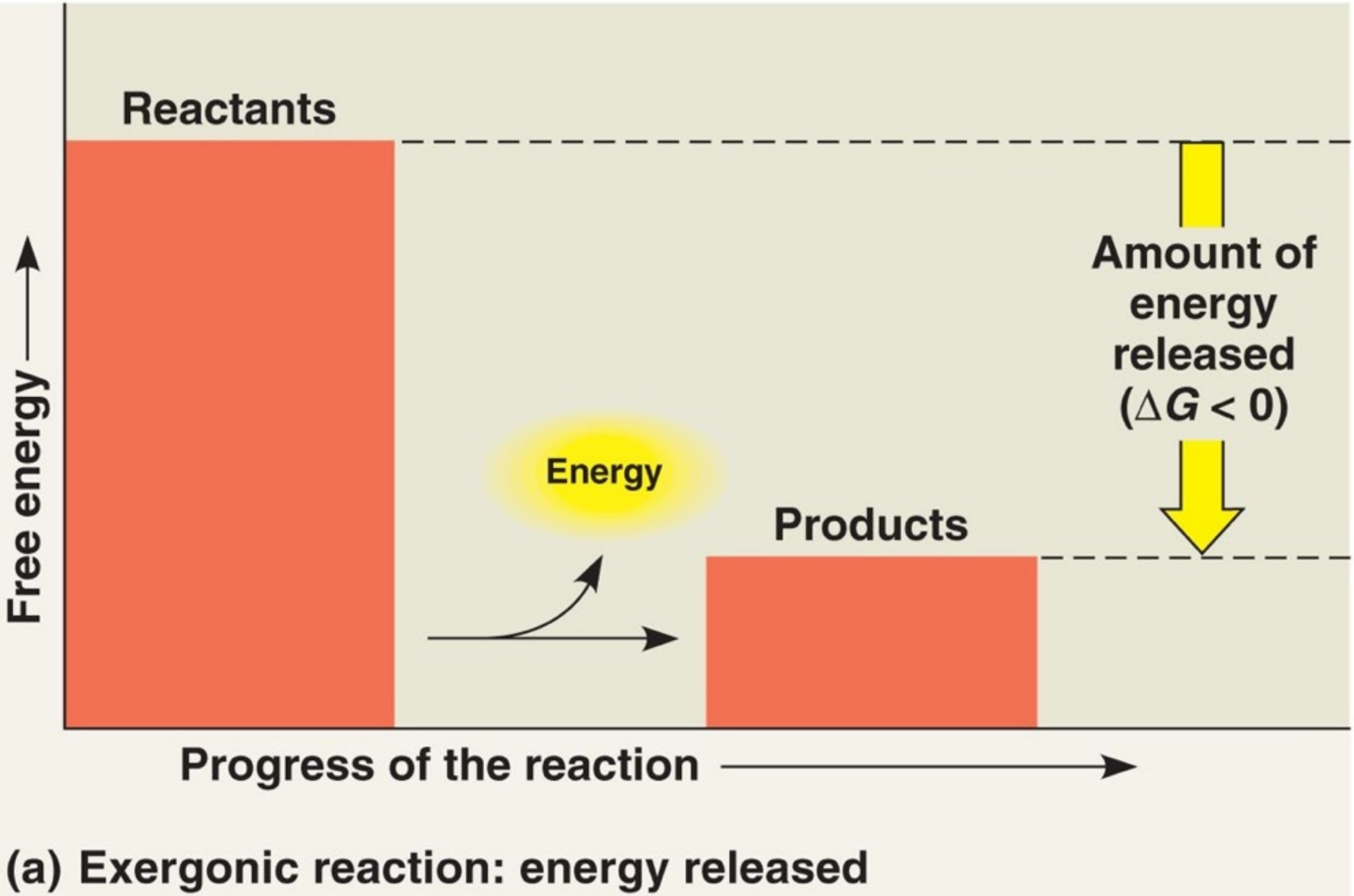
(b) Optimal pH for two enzymes

Essential knowledge 4.B.1: Interactions between molecules affect their structure and function.

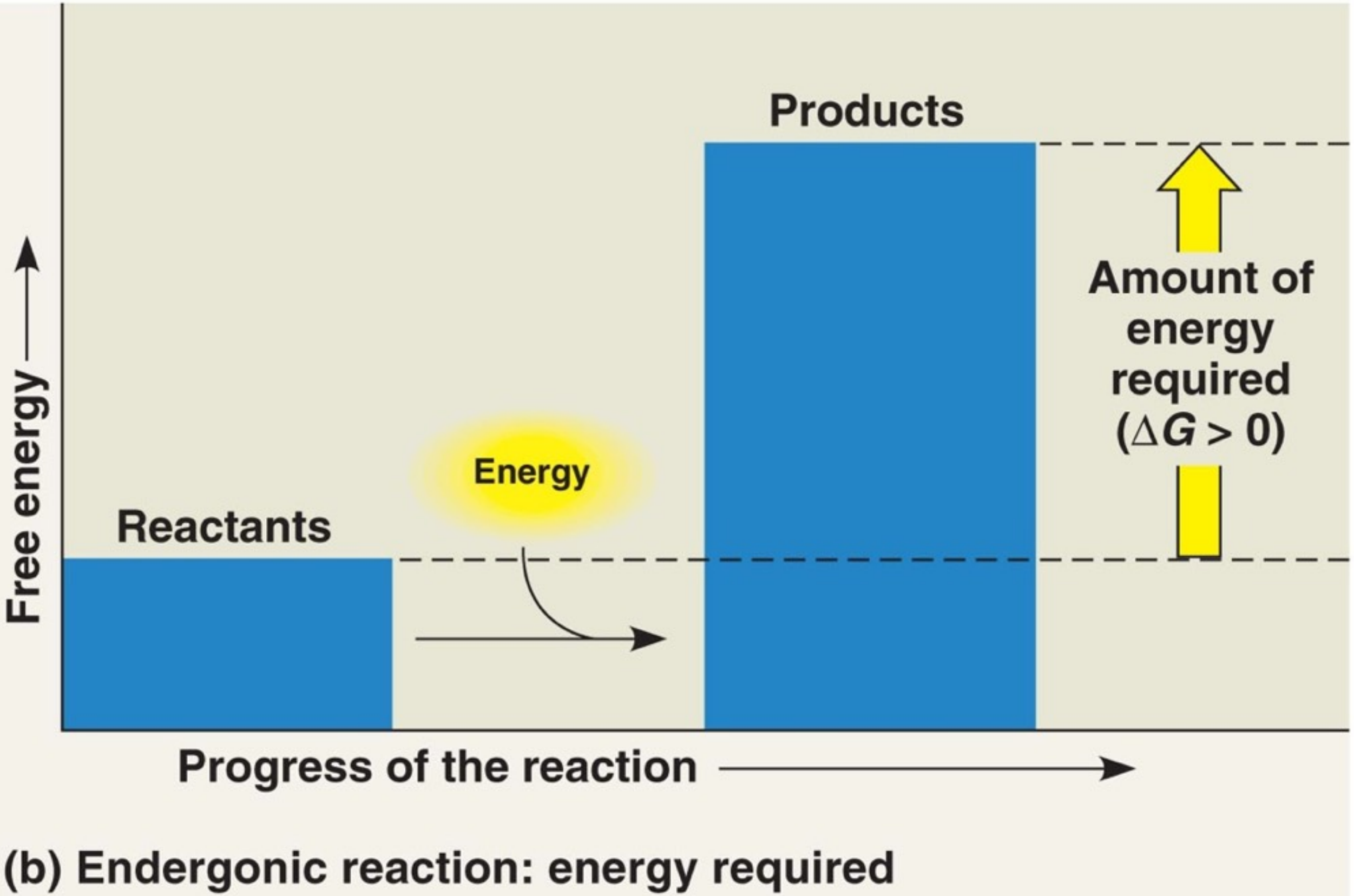
d. The change in function of an enzyme can be interpreted from data regarding the concentrations of product or substrate as a function of time. These representations demonstrate the relationship between an enzyme's activity, the disappearance of substrate, and/ or presence of a competitive inhibitor.


A
B
C
D
Transition state
E_A
Reactants
A
B
C
D
$\Delta G < 0$
Products
Free energy
Progress of the reaction


A
B
C
D
Transition state
E_A
Reactants
Products
$\Delta G < 0$
The initial energy investment has been repaid with interest!
Free energy
Progress of the reaction



(a) Exergonic reaction: energy released



(b) Endergonic reaction: energy required

Learning Objectives:

LO 4.17 The student is able to analyze data to identify how molecular interactions affect structure and function. [See SP 5.1]