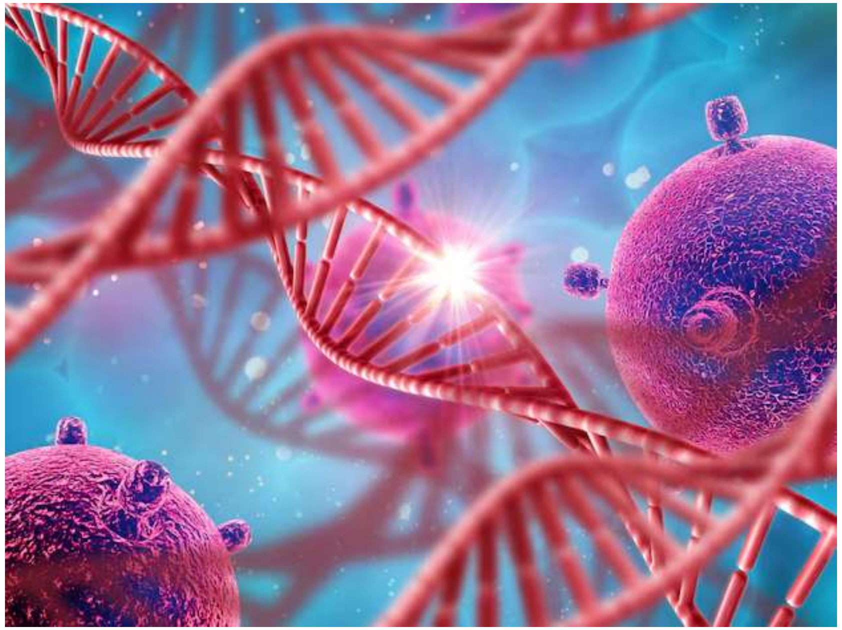
Lecture 13

General Biology & Cytology Course
2301130



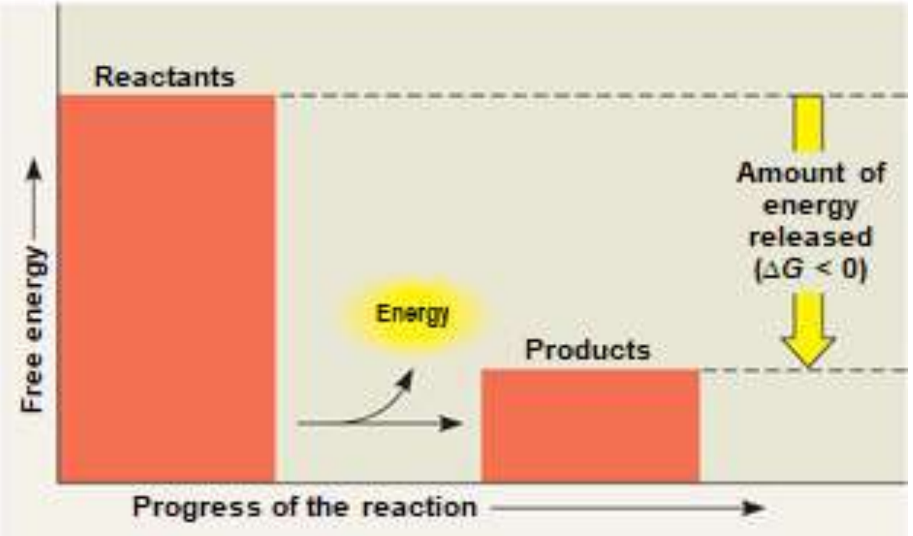
Faculty of Dentistry, Mutah University

Dr. Samer Yousef Alqaraleh

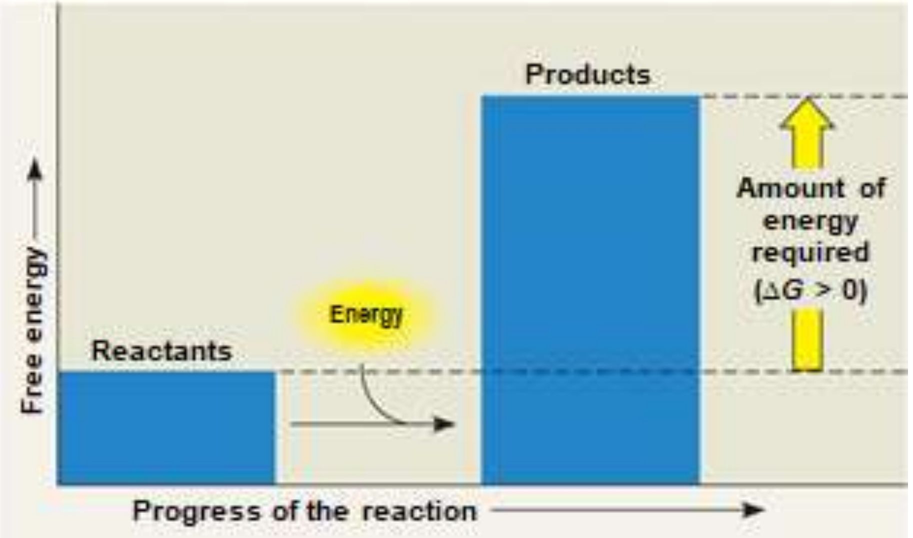
Metabolism Part 2

Exergonic and Endergonic Reactions in Metabolism

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



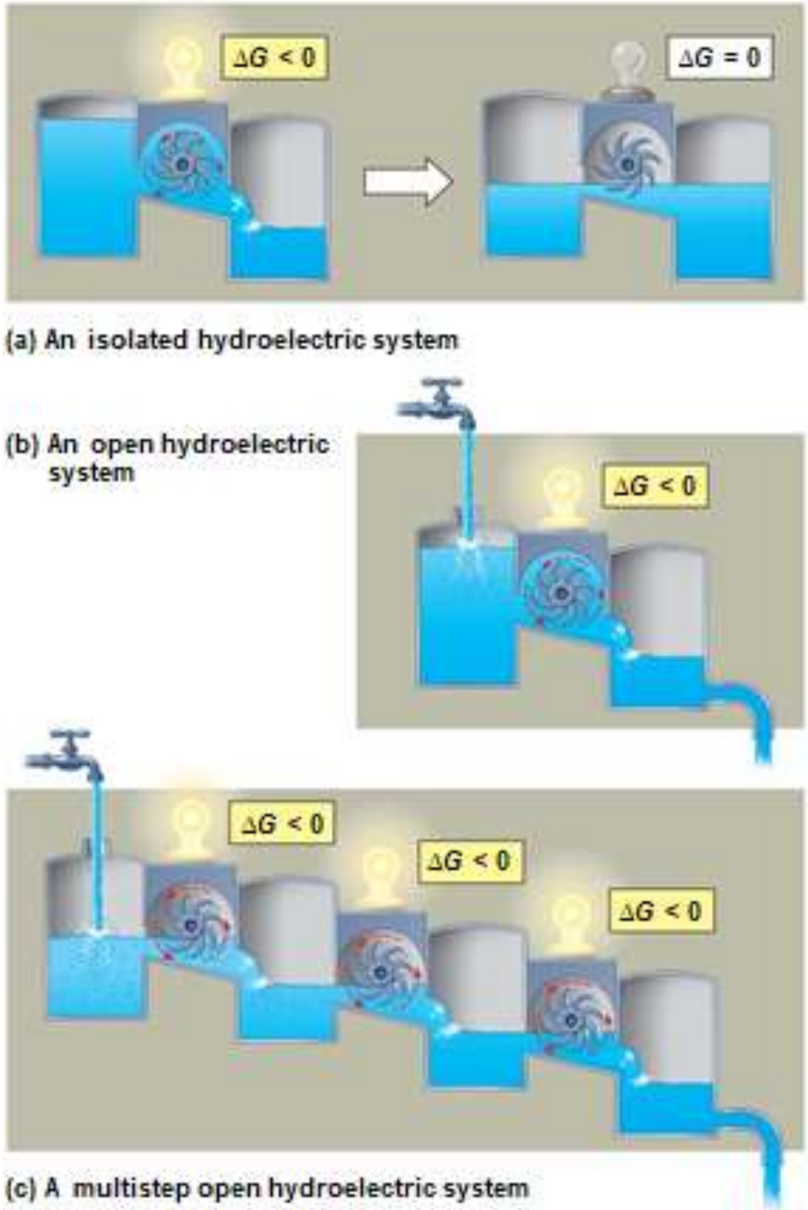
(a) Exergonic reaction: energy released



(b) Endergonic reaction: energy required

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



(a) An isolated hydroelectric system

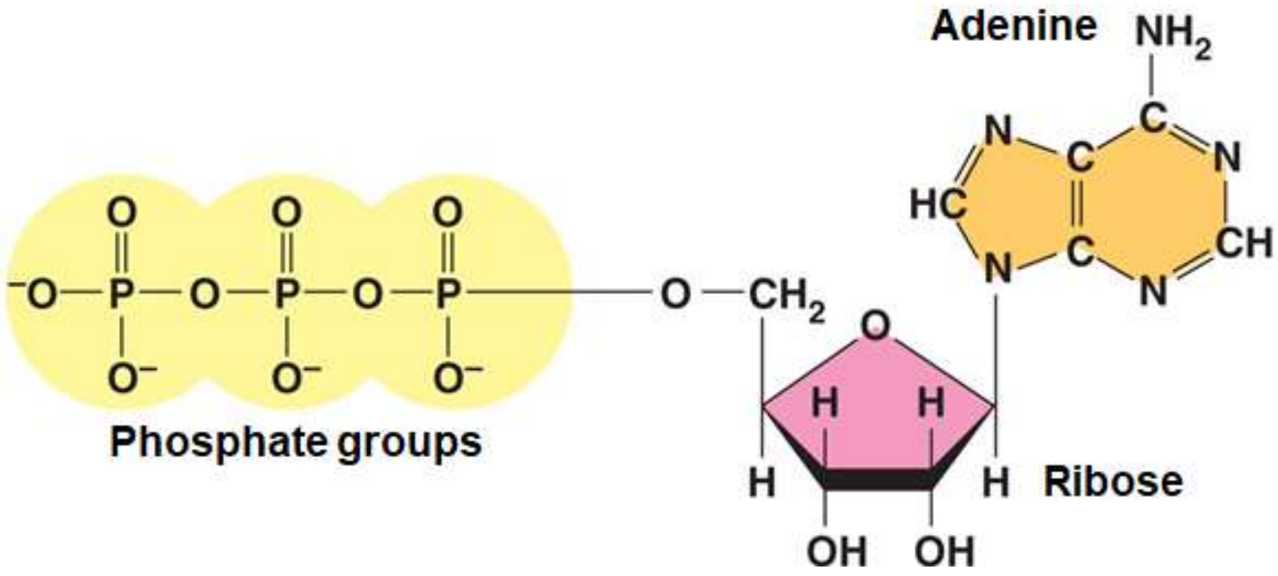
(c) A multistep open hydroelectric system

ATP powers cellular work by coupling exergonic reactions to endergonic reactions

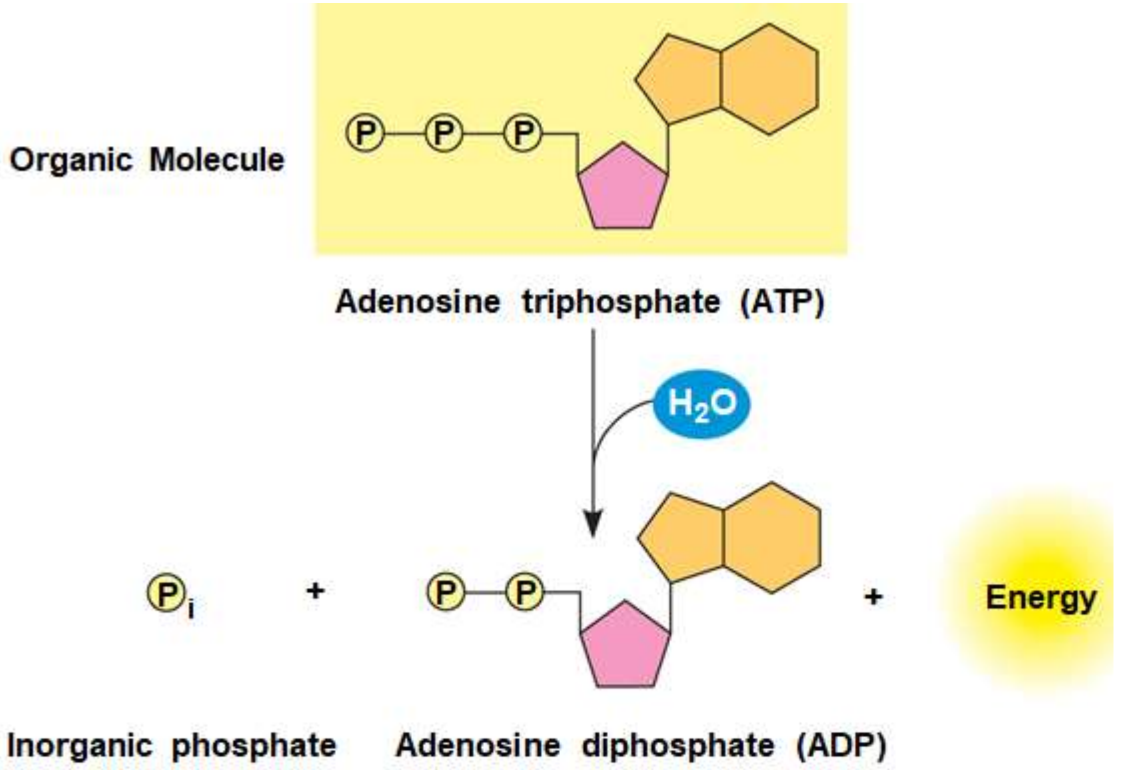
- A cell does three main kinds of work:
  - Chemical work, pushing endergonic reactions
  - Transport work, pump substance across membrane.
  - Mechanical work, contacting muscle cells
- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic 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
- Other function of ATP as one of the nucleoside triphosphate used to **make RNA**
- ATP is a chemical Energy form.
- The potential Energy is high based on the structure



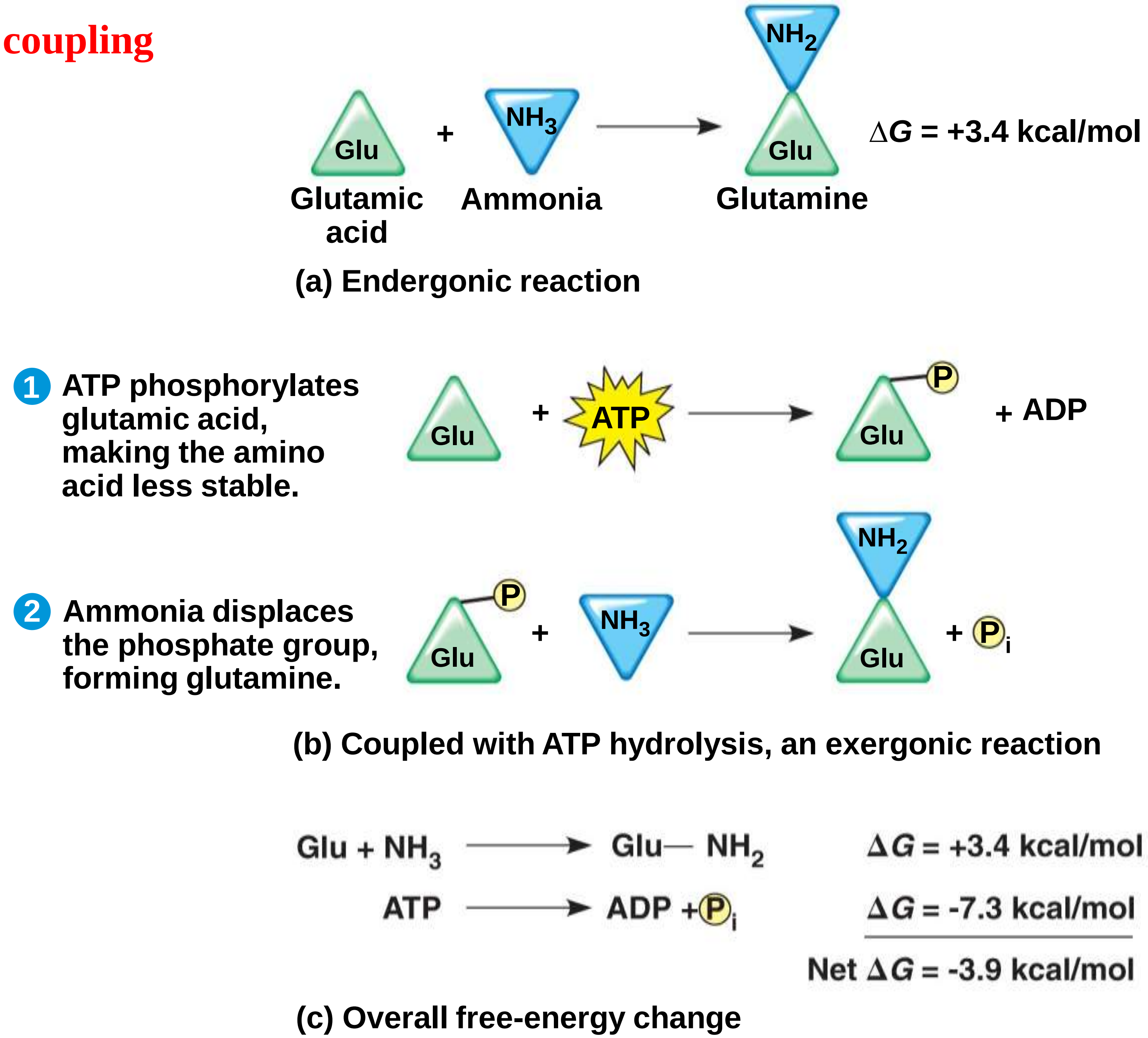
- The bonds between the phosphate groups of ATP’s tail can be broken by hydrolysis (added water).
- Energy is released from ATP when the terminal phosphate bond is broken
- This release of energy comes from the chemical change to a state of lower free energy in the products, not from the phosphate bonds themselves.



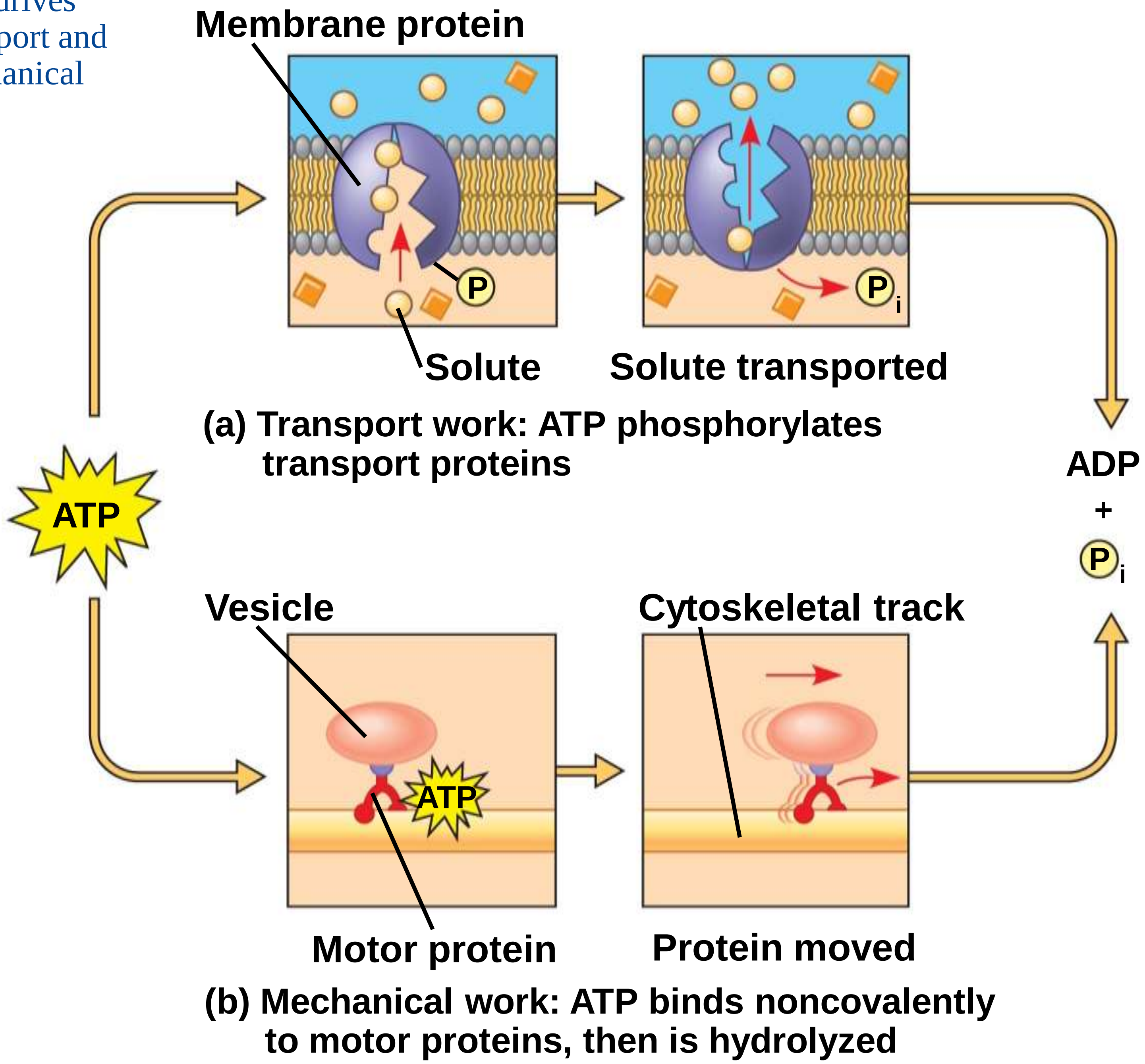
How ATP Performs Work

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

Energy coupling

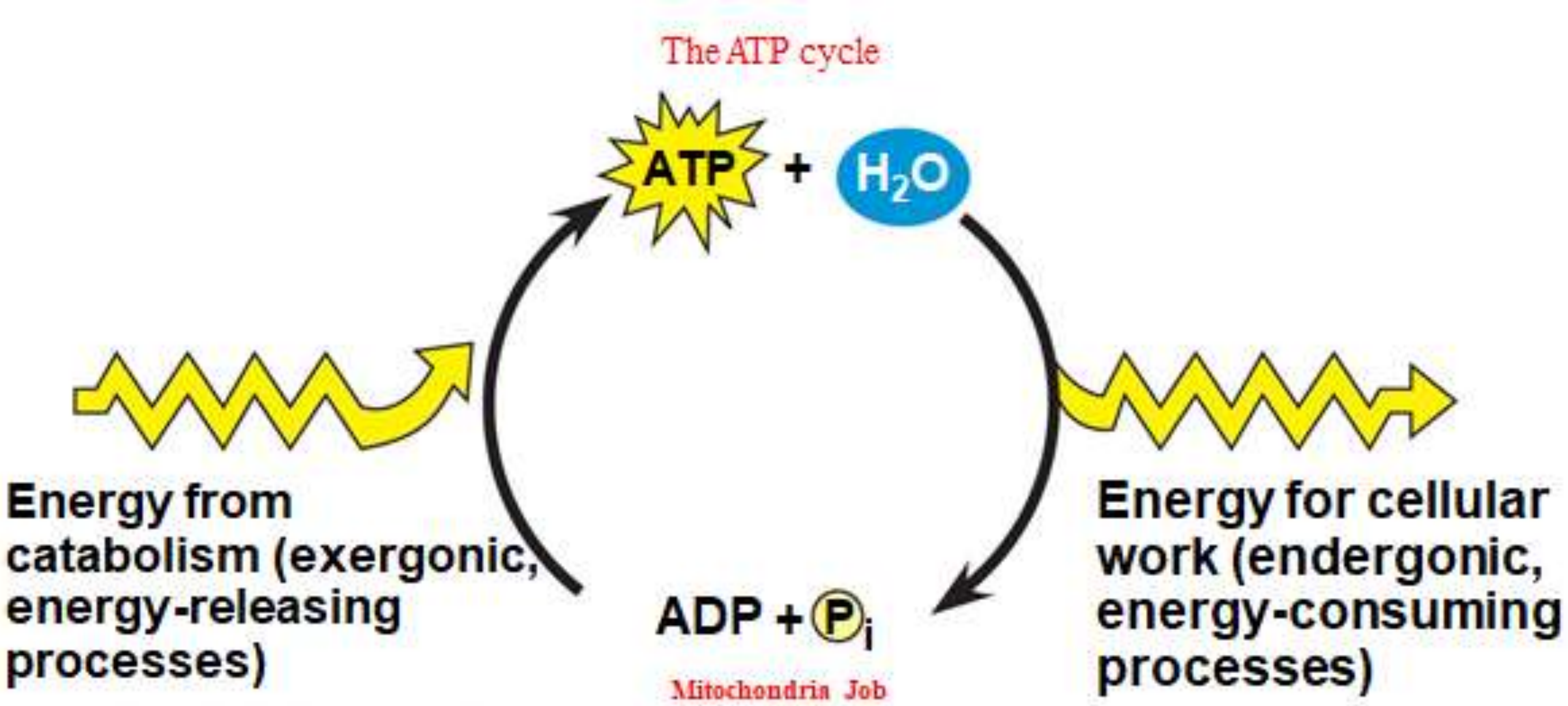


How ATP drives transport and mechanical work



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 exergonic reaction (catabolic reactions) in the cell
- The chemical potential energy temporarily stored in ATP drives most cellular work



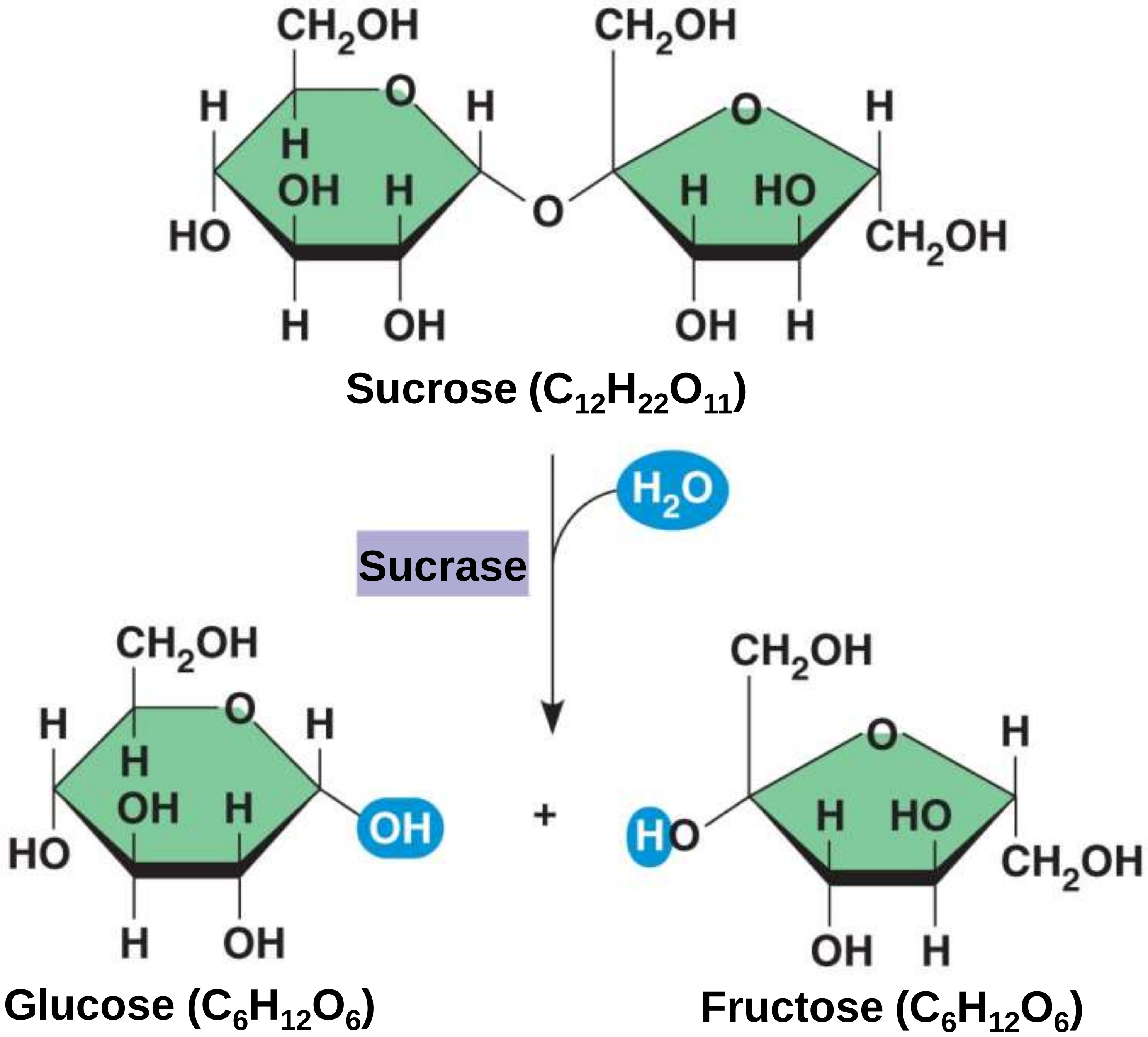
Enzymes speed up metabolic reactions by lowering energy barrier

- Spontaneous reactions no need E, but they can slow enough.

  -Hydrolysis of sucrose to G+F is spont-

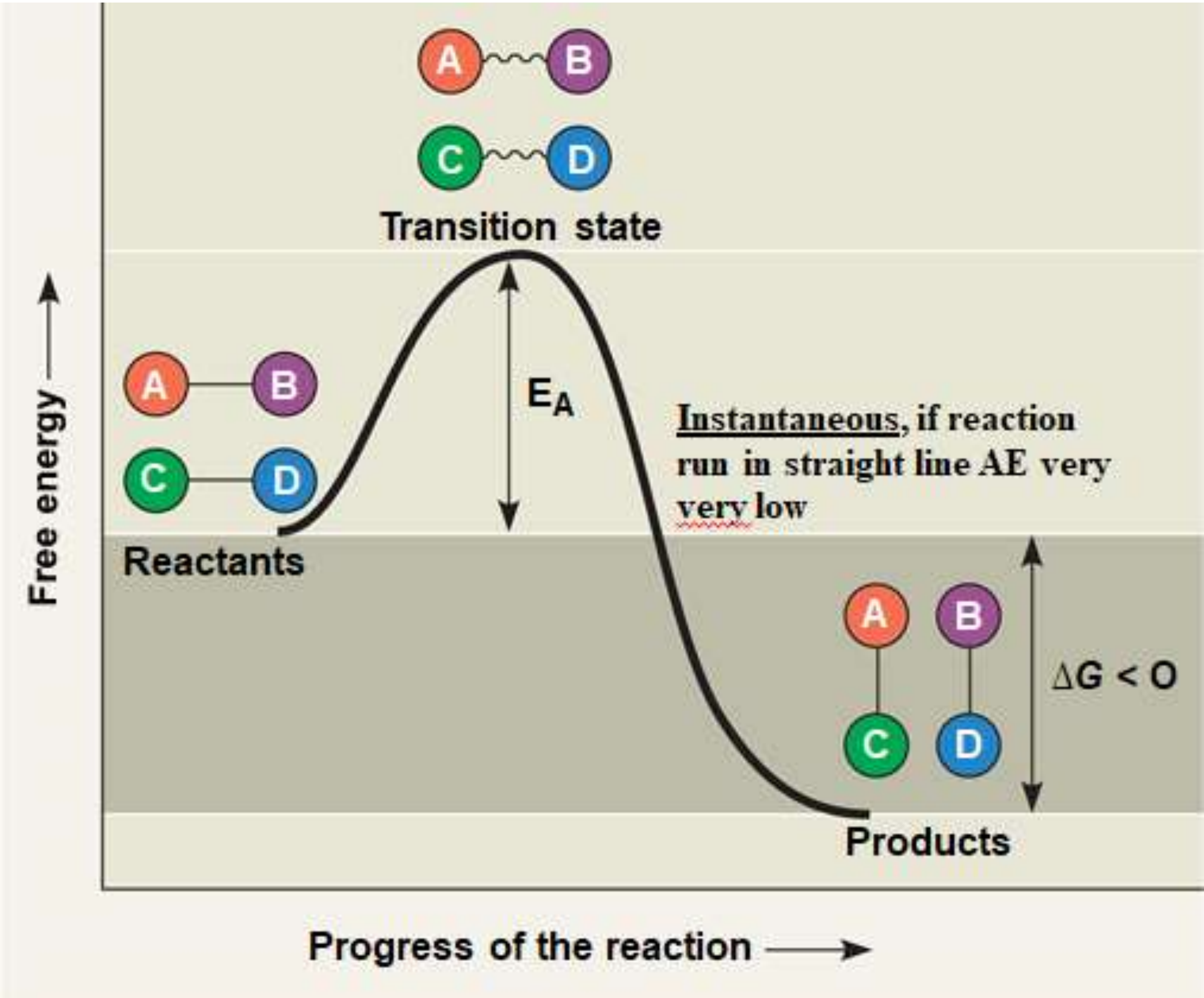
  - At room Temp, sucrose solution to be hydrolysis in water to G+F need set of years.

- 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 solution by the enzyme sucrase is an example of an enzyme-catalyzed reaction, within seconds


Sucrose ($C_{12}H_{22}O_{11}$)
H_2O
Sucrase
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
- Molecules becomes unstable when enough energy absorbed to break bonds this is transition state.



Activation Energy barrier

- The activation E provides a barrier that determines the rate of spontaneous reactions.

- Some of reactions, **E_A** is low enough that thermal E at room temp. is sufficient to overcome the activation E barrier.

- Most reactions have high **E_A**, and need addition energy as heat (thermal energy) to reach the transition state.

- But adding heat is not useful way to speed the reactions in cells because it can cause denaturation of proteins.

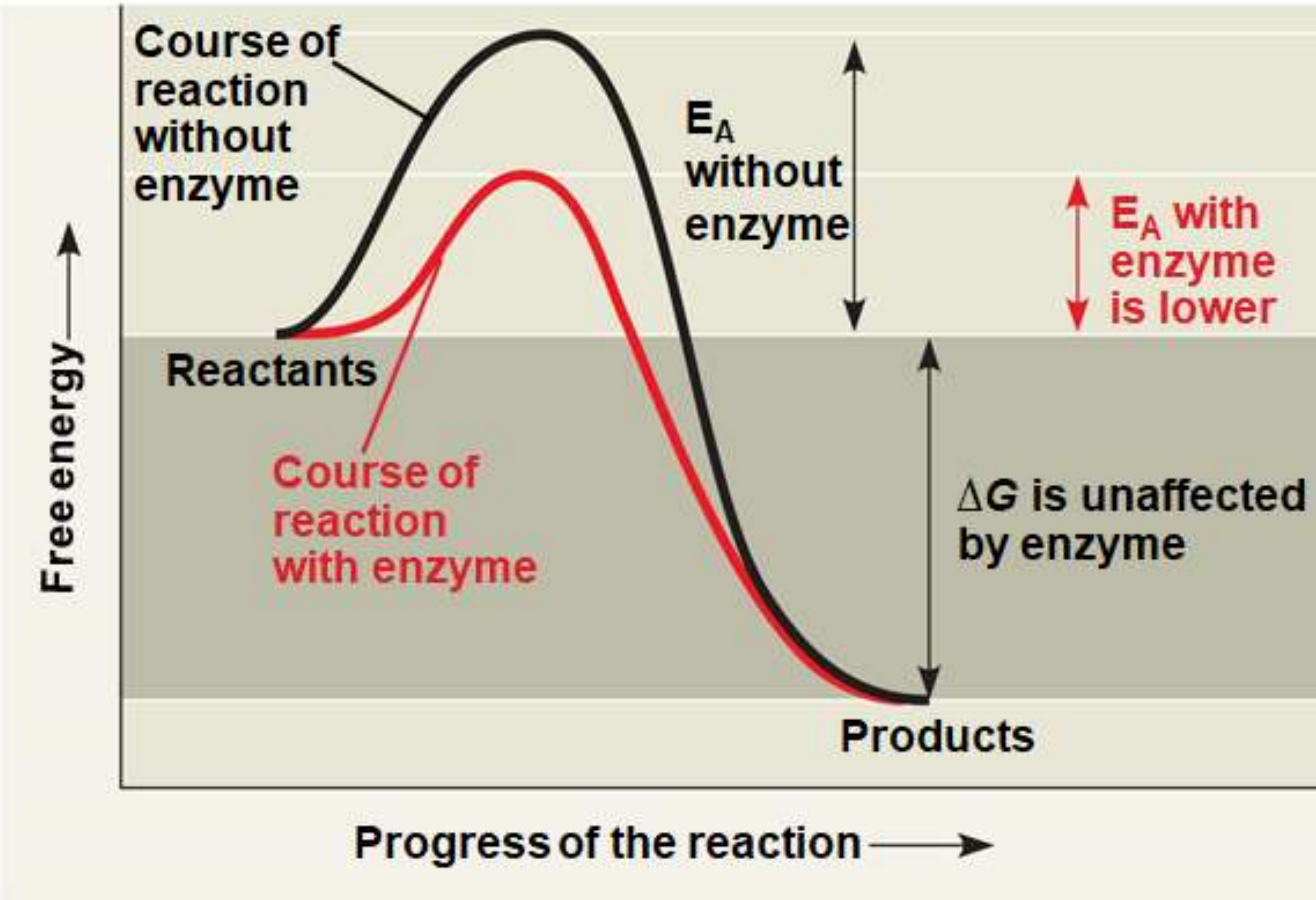
- Heat is also impractical because it would speed up all reactions, not those needed.

- So, living cells used catalysts to overcome these obstacles.

How Enzymes Lower the E_A Barrier

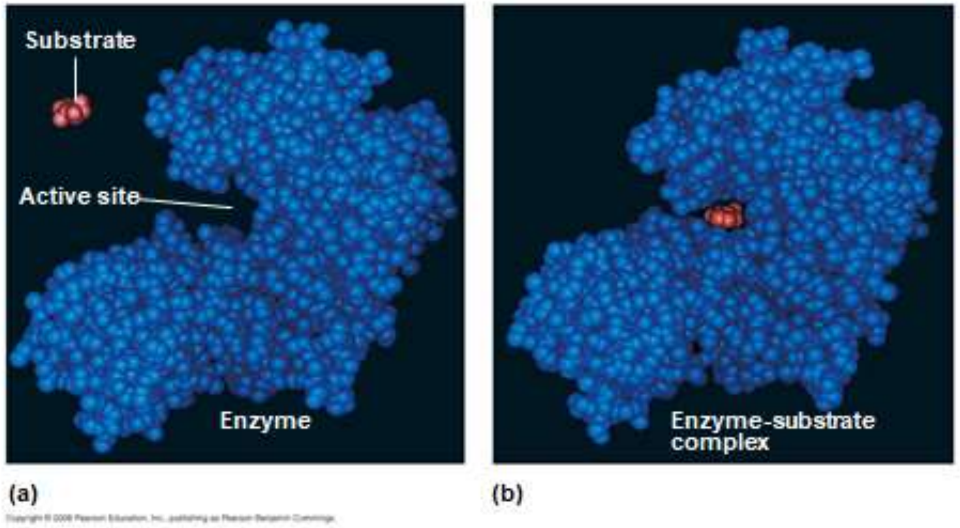
- Enzymes catalyze reactions by lowering the E_A barrier
- Enzymes do not affect the change in free energy (ΔG); instead, they hasten reactions that would occur eventually.

The effect of an enzyme on activation energy



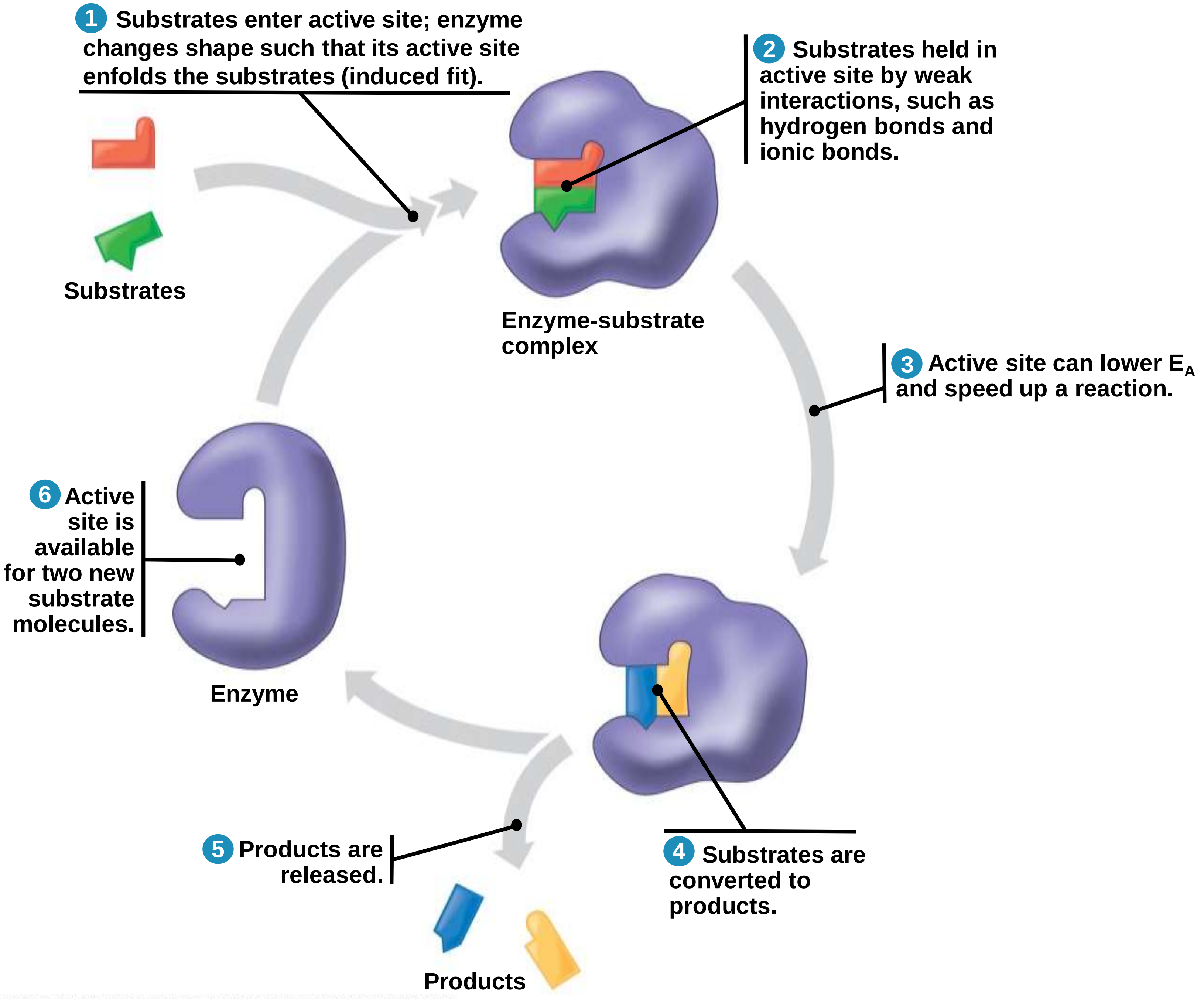
Substrate Specificity of Enzymes

- 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



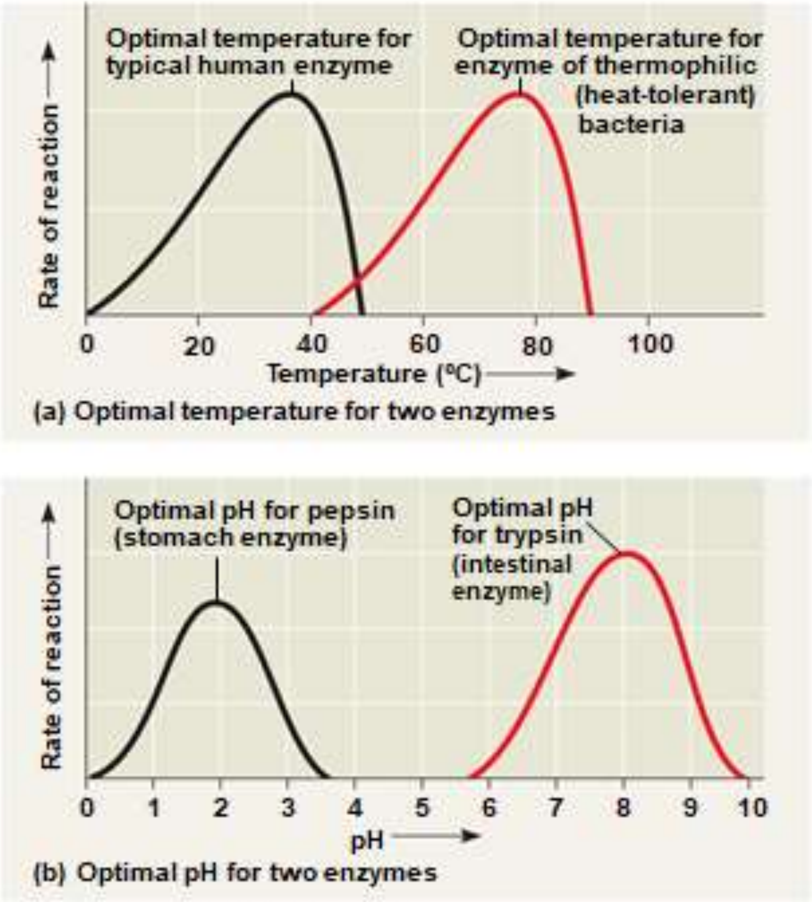
Catalysis in the Enzyme's Active Site

- 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


1 Substrates enter active site; enzyme changes shape such that its active site enfolds the substrates (induced fit).
2 Substrates held in active site by weak interactions, such as hydrogen bonds and ionic bonds.
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

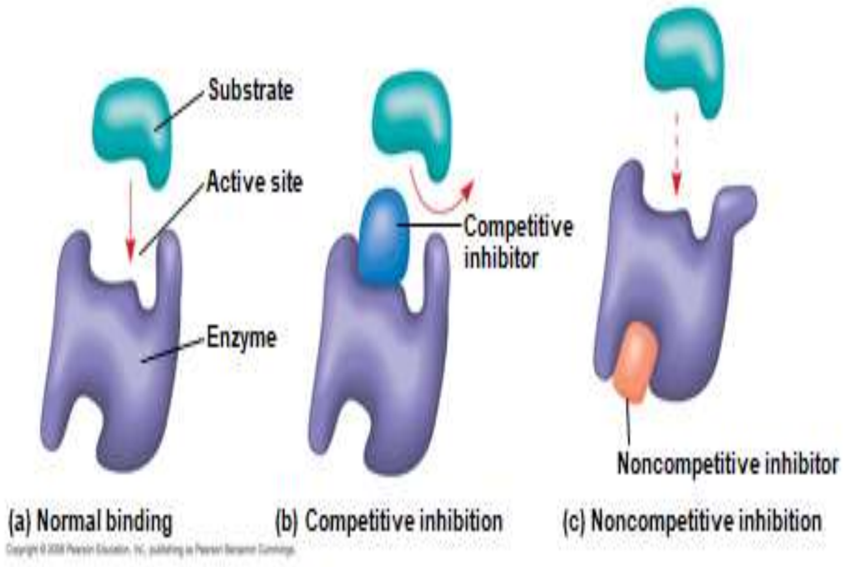
- An enzyme's activity can be affected by
  - General environmental factors, such as temperature and pH
  - Chemicals that specifically influence the enzyme



(a) Optimal temperature for two enzymes
(b) Optimal pH for two enzymes

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.



Regulation of enzyme activity helps control metabolism

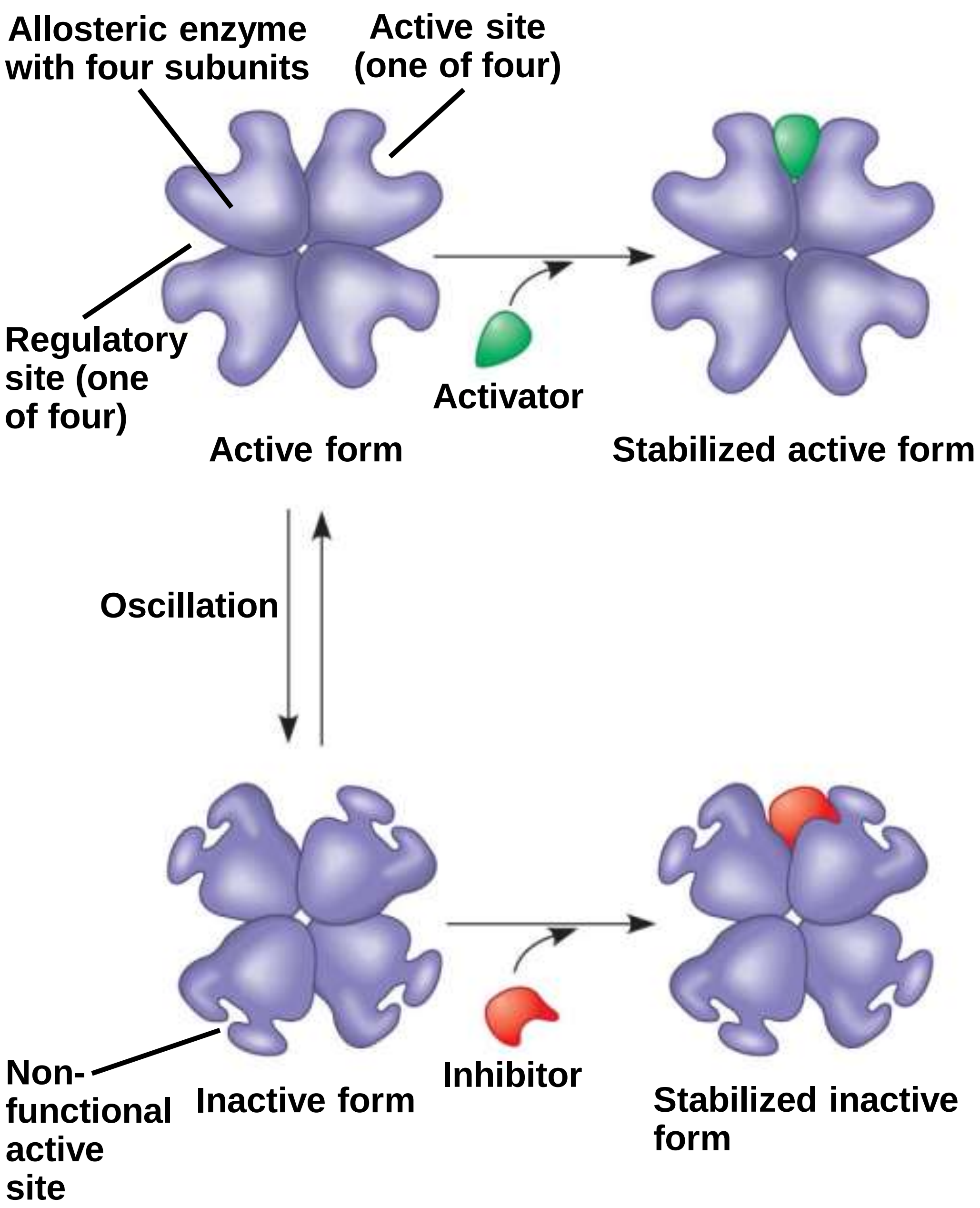
- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated

- 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** may either inhibit or stimulate an enzyme's activity

- Allosteric regulation occurs when a regulatory molecule (**activator** or **inhibitor**) binds to a protein at one site and affects the protein's function at another site

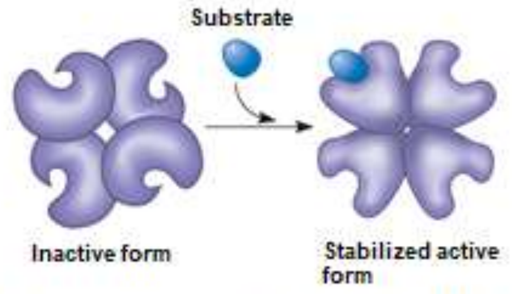
- Each enzyme has active and inactive form



(a) Allosteric activators and inhibitors

- **Cooperativity** is a form of allosteric regulation that can amplify enzyme activity

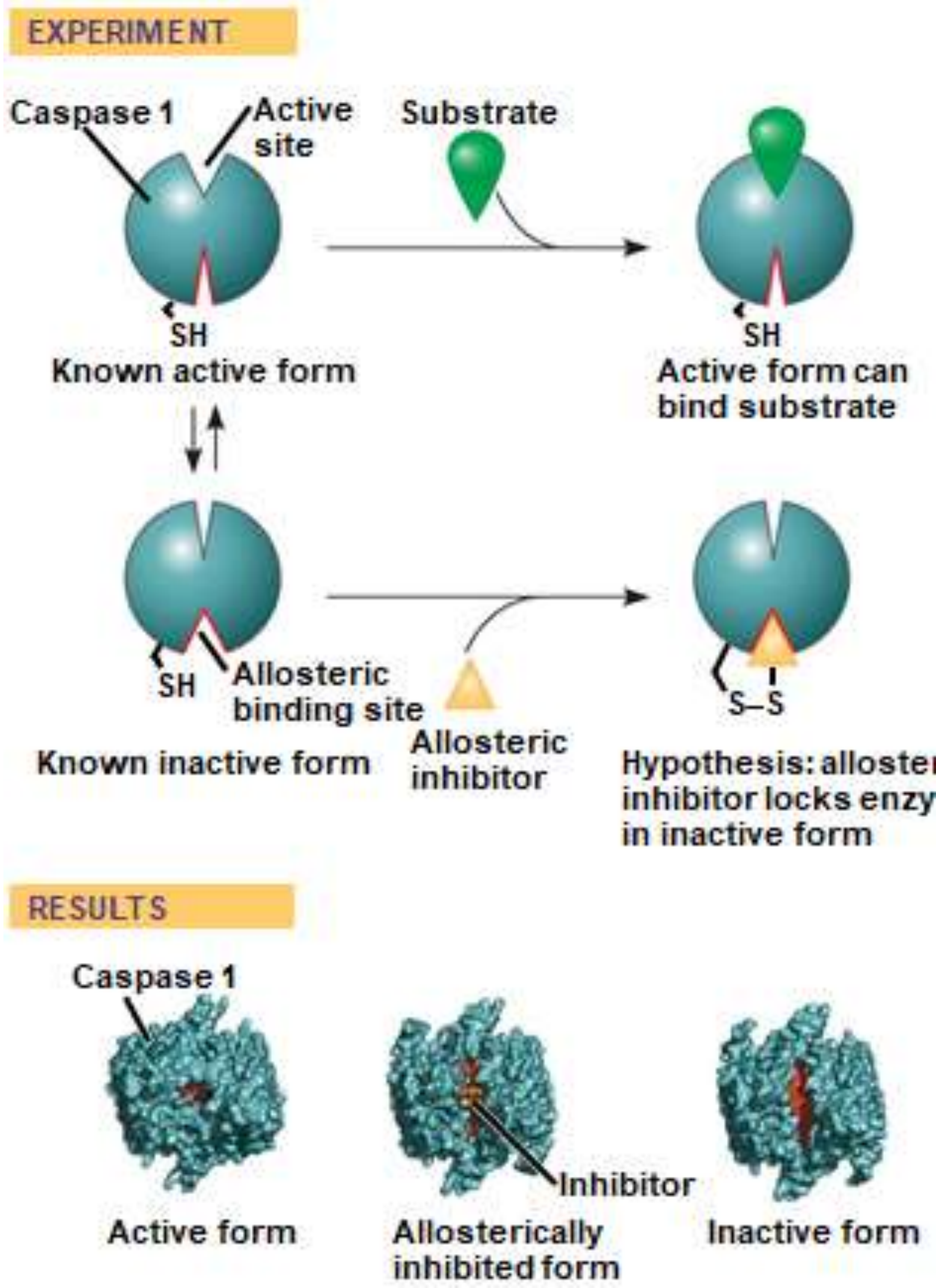
- In cooperativity, binding by a substrate to one active site stabilizes favorable conformational changes at all other subunits



(b) Cooperativity: another type of allosteric activation

Identification of Allosteric Regulators

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



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