Lecture Series 6

Energy, Enzymes, and Metabolism

Energy, Enzymes, and Metabolism

A. Energy and Energy Conversions

B. ATP: Transferring Energy in Cells

C. Enzymes: Biological Catalysts

D. Molecular Structure Determines Enzyme Fxn

E. Metabolism and the Regulation of Enzymes

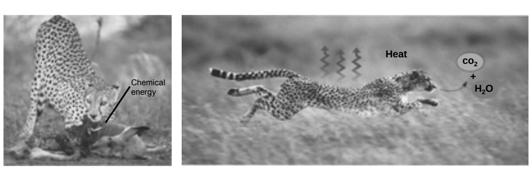
A. Energy and Energy Conversions

- Energy is the capacity to do work (cause change).
- Potential energy is the energy of state or position; it includes energy stored in chemical bonds. Examples are chemical (candy bar or gasoline) or elevated mass.
- Kinetic energy is the energy of motion. Examples are heat, light and electricity.
- Potential energy can be converted to kinetic energy and vice versa.

A. Energy and Energy Conversions

- The first law of thermodynamics tells us energy cannot be created or destroyed. [Except when mass is converted to energy, as in the sun where hydrogen is converted to helium with some mass converted to energy.]
- The second tells us that, in a closed system, the quantity of energy available to do work decreases and unusable energy increases. **Entropic doom** = the disorder or entropy of the universe is increasing.

The two laws of thermodynamics

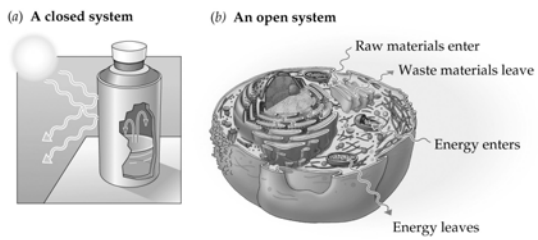


(a) **First law of thermodynamics:** Energy can be transferred or transformed but neither created nor destroyed. For example, the chemical (potential) energy in food will be converted to the kinetic energy of the cheetah's movement in (b).

(b) **Second law of thermodynamics:** Every energy transfer or transformation increases the disorder (entropy) of the universe. For example, disorder is added to the cheetah's surroundings in the form of heat and the small molecules that are the by-products of metabolism.

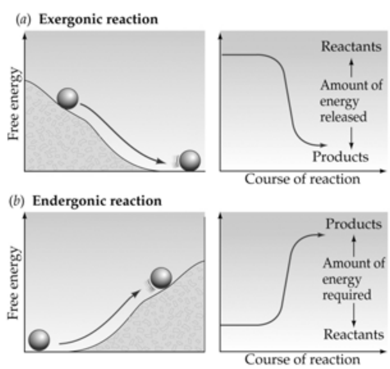
A. Energy and Energy Conversions

- Living things obey the laws of thermodynamics. Organisms are open systems that are part of a larger closed system.



A. Energy and Energy Conversions

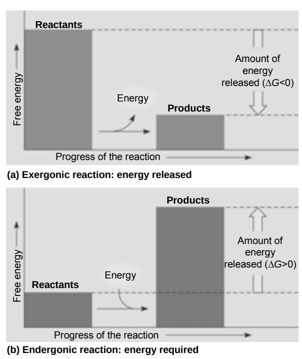
- Changes in free energy, total energy (enthalpy), temperature, and entropy are related by the equation $\Delta G = \Delta H - T\Delta S$.
- Spontaneous, exergonic reactions release free energy and have a negative ΔG. Non-spontaneous, endergonic reactions take up free energy, have a positive ΔG, and proceed only if free energy is provided.



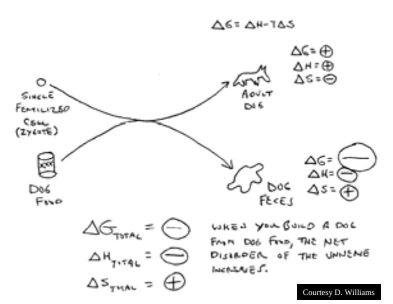
A. Energy and Energy Conversions

- The change in free energy of a reaction determines its point of chemical equilibrium, at which forward and reverse reactions proceed at the same rate. For spontaneous, exergonic reactions, the equilibrium point lies toward completion.

Free energy changes (ΔG) in exergonic and endergonic reactions

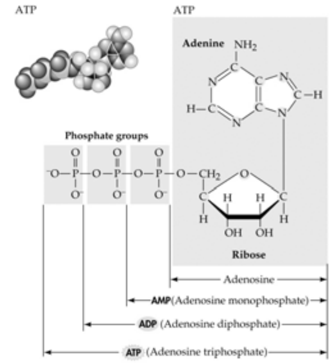


Ordered (living) systems can be built as long as the net disorder of the universe is increased in the process of building that order. Thus living systems adhere to the second law of thermodynamics. If living systems did not adhere, then it wouldn't be a "law". Laws are observations or rules that have been found over hundreds of years of experimentation not to be violated.



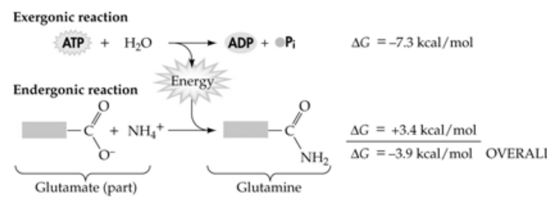
B. ATP: Transferring Energy in Cells

- ATP serves as an energy currency in cells.
- Hydrolysis of ATP releases a relatively large amount of free energy.



B. ATP: Transferring Energy in Cells

- The ATP cycle couples exergonic and endergonic reactions, transferring free energy from the exergonic to the endergonic reaction.

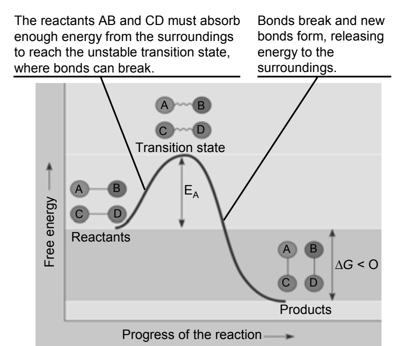


The way energy is supplied for the formation of glutamine is the following: Glutamate is converted to a phosphate derivative, which makes the molecule electrophilic. Ammonia, because it is nucleophilic, can now attack the phosphate derivative, forming glutamine (GLN).

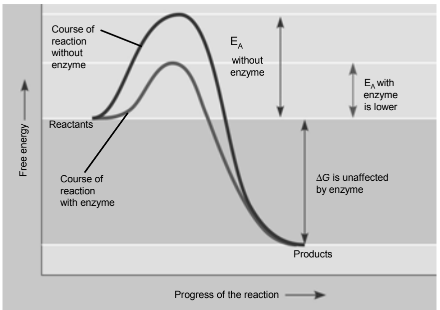
C. Enzymes: Biological Catalysts

- The rate of a chemical reaction is independent of ΔG but is determined by the size of the activation energy barrier.
- Catalysts speed reactions by lowering the activation energy barrier.

Energy profile of an exergonic reaction



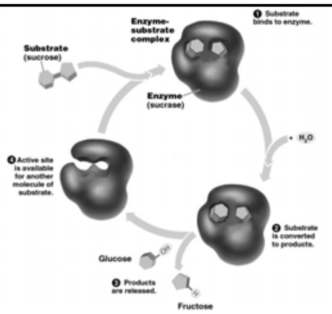
The effect of enzymes (catalysts) on reaction rate.

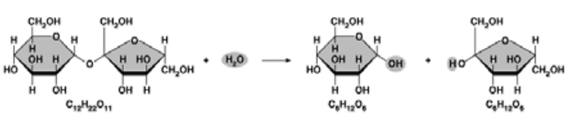


C. Enzymes: Biological Catalysts

- Enzymes are biological catalysts, highly specific for their substrates. Substrates bind to the active site, where catalysis takes place, forming an enzyme–substrate complex.

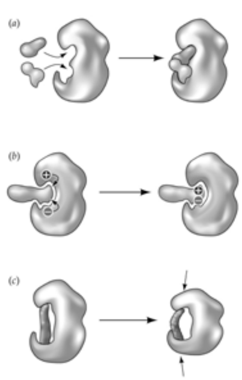
Chemical reactions must be accelerated in biological systems because the intrinsic rate is two slow to be useful. Processes such as thought or movement would be hundreds-of-thousands of times slower than they are now. Reactions are accelerated in biological systems by enzymes. Enzymes are usually protein molecules (there are a few enzymes which are constructed of RNA) with specific regions (active sites) which bind with reactants in such a way that they perform some chemistry upon them and convert them to products.





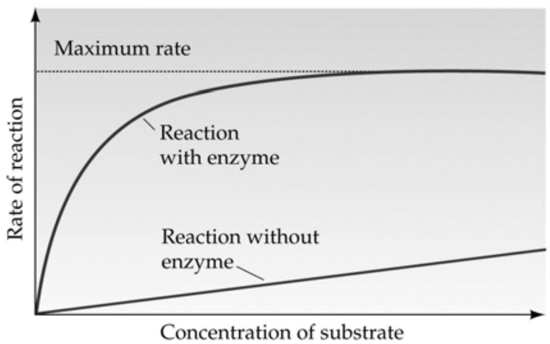
C. Enzymes: Biological Catalysts

- At the active site, a substrate can be oriented correctly, chemically modified, or strained. As a result, the substrate readily forms its transition state, and the reaction proceeds.



C. Enzymes: Biological Catalysts

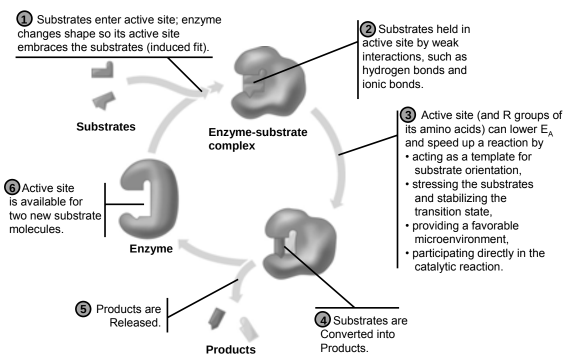
- Substrate concentration affects the rate of an enzyme-catalyzed reaction.



D. Molecular Structure Determines Enzyme Function

- The active site where substrate binds determines the specificity of an enzyme.
- Upon binding to substrate, some enzymes change shape, facilitating catalysis.

The active site and catalytic cycle of an enzyme



D. Molecular Structure Determines Enzyme Function

- Some enzymes require **cofactors** for catalysis (non-protein parts).
  - **Prosthetic groups** are permanently bound to the enzyme.
  - **Coenzymes** usually are not. They enter into the reaction as a "cosubstrate," as they are changed by the reaction and released from the enzyme.

6.1 A Few Examples of Nonprotein Molecular "Partners" of Enzymes

TYPE OF MOLECULE	ROLE IN CATALYZED REACTIONS
Cofactors	
Iron	Oxidation/reduction
Copper	Oxidation/reduction
Zinc	Helps bind NAD
Coenzymes	
Biotin	Carries —COO^-
Coenzyme A	Carries —CH_2—CH_3
NAD	Carries electrons
FAD	Carries electrons
Prosthetic groups	
Heme	Binds ions, O_2, and electrons; contains iron cofactor
Flavin	Binds electrons
Retinal	Converts light energy

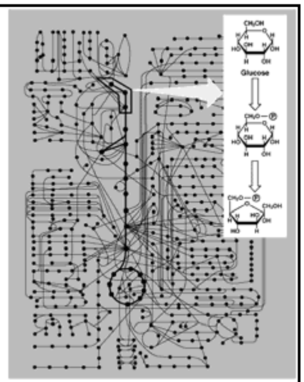
E. Metabolism and the Regulation of Enzymes

- Metabolism is organized into pathways: the product of one reaction is a reactant for the next. Each reaction is catalyzed by an enzyme.

Living systems produce energy and a great variety of chemical molecules (amino acids, nucleotides, sugars, steroids, etc.) by series of enzyme-catalyzed chemical reactions. These pathways are collectively called **metabolism**.

Catabolic: breakdown or hydrolysis reactions

Anabolic: biosynthetic or condensation reactions



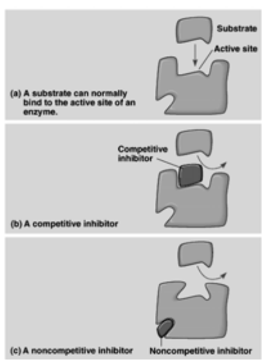
E. Metabolism and the Regulation of Enzymes

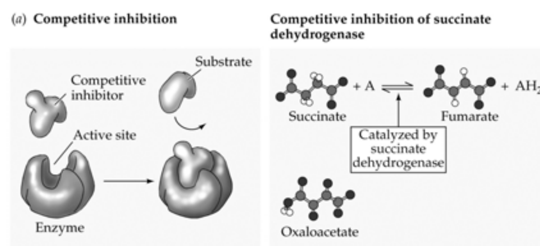
- Enzyme activity is subject to regulation.
- Some compounds react irreversibly with them and reduce their catalytic activity. Others react reversibly, inhibiting enzyme action temporarily.
- A compound structurally similar to an enzyme's normal substrate may also inhibit enzyme action through competitive inhibition.

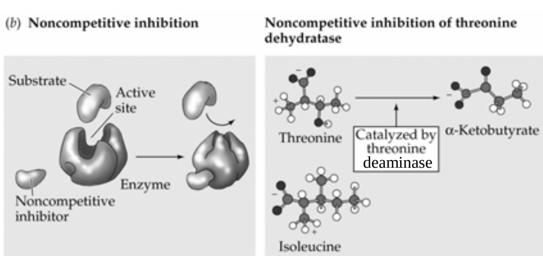
Enzymes are sensitive to both competitive and noncompetitive inhibitors.

Competitive inhibitors resemble the substrate and thus bind to the active site (which prevents or reduces the binding of the substrate).

Noncompetitive binding arises when a particular substance binds at an area outside of the active site and alters the conformation of the enzyme (which also alters the structure of the active site).



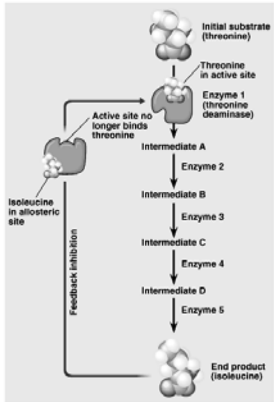




E. Metabolism and the Regulation of Enzymes

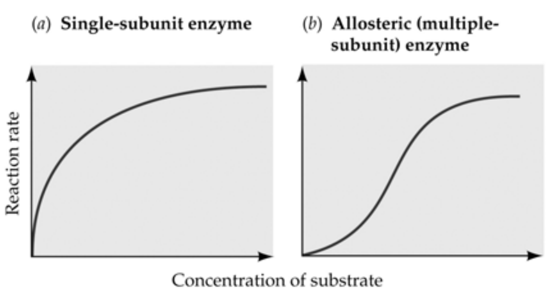
- The end product of a metabolic pathway may inhibit an allosteric enzyme that catalyzes the commitment step of the pathway.
- An allosteric enzyme is one where the enzyme function is affected by the binding of a small regulatory molecule at a site other than the active site. Most have two or more subunits.

The end product often inhibits (allosterically) a key enzyme in the pathway, thus shutting down the pathway when there is a sufficiency of the isoleucine amino acid.



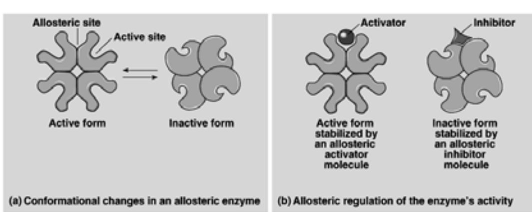
E. Metabolism and the Regulation of Enzymes

- For allosteric enzymes with multiple subunits, plots of reaction rate versus substrate concentration are sigmoidal, in contrast to plots of the same variables for non-allosteric enzymes with a single subunit.

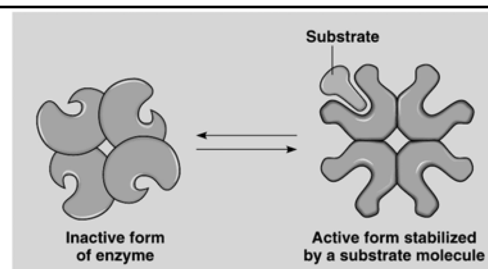


E. Metabolism and the Regulation of Enzymes

- Allosteric inhibitors (or enhancers) bind to a site different from the active site and stabilize the inactive (or active) form of the enzyme.
- The multiple catalytic subunits of many allosteric enzymes can interact cooperatively.



Many enzymes display quaternary structure (they are made up of subunits). If each subunits possesses an active site, then a substance which binds with the enzyme (protein) and alters its conformation, can influence a larger number of active sites than would be the case if the enzyme were a single subunit. This represents a key regulatory process in living systems.

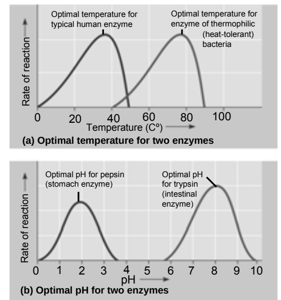


Cooperativity: When the protein hemoglobin (which displays quaternary structure) binds with oxygen, binding of the first oxygen molecule alters the conformation of the protein and locks it in a more active form. Successive oxygen molecules (there are 3 of them) bind more easily. Thus hemoglobin is oxygenated in the lungs more rapidly than it would be were it simply a single subunit.

E. Metabolism and the Regulation of Enzymes

- Enzymes are sensitive to their environment. Both pH and temperature affect enzyme activity.

Environmental factors affecting enzyme activity



(a) Optimal temperature for two enzymes

(b) Optimal pH for two enzymes