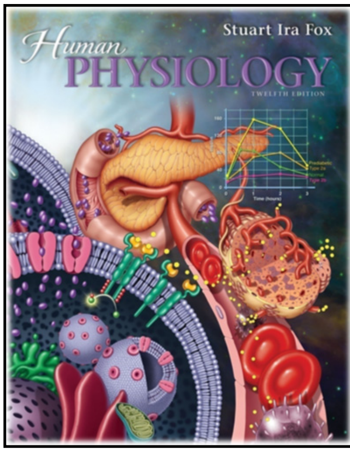
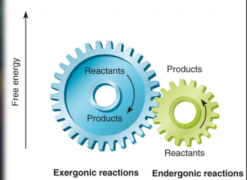


CHAPTER 4

Enzymes and Energy



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Chapter 4 Outline

- Enzymes as catalysts
- Control of enzyme activity
- Bioenergetics

2

Enzymes

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Enzymes

- **Catalyst** is a substance that increases the rate of a chemical reaction without itself undergoing any permanent chemical change.
- **Enzymes** are biological catalysts
  - Increase rate of chemical reactions
  - Is not changed at the end of the reaction
  - Does not change the result of the reaction
- Most are proteins (some are RNA)
- Act by lowering energy required for a reaction to proceed (lowering activation energy)

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Catalyzed vs. Noncatalyzed RxNs

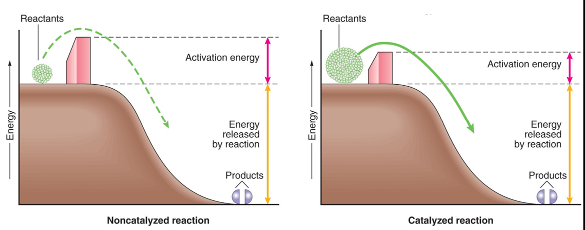

Figure 4.1

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Mechanisms of Enzyme Activity

- The function of an enzyme is dictated by its structure.
- Each enzyme has a characteristic 3D shape or **conformation**, with pockets that serve as **active sites** in the enzyme.
- The reactants are called **substrates**, and they fit into the active site like a key to a lock.

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Mechanisms of Enzyme Activity

- Substrates fit into active sites
- Enzyme-substrate complex formed
- Reaction occurs
- Products dissociate
- Enzyme is unaltered

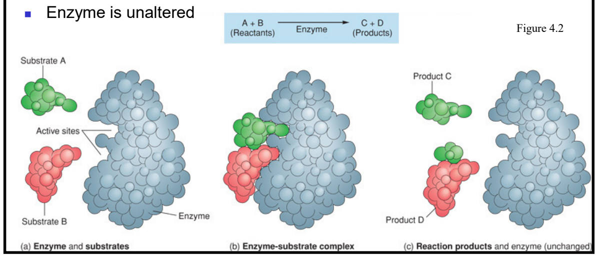

Figure 4.2

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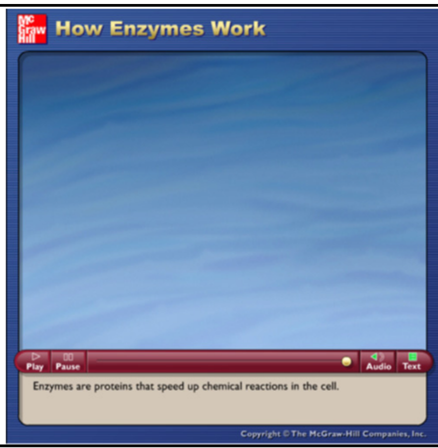

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Mechanisms of Enzyme Activity

- The amount of enzyme in a sample of fluid can be measured based on the rate of product synthesis.
- Such measurements are clinically useful because abnormally high plasma concentrations of particular enzymes are characteristic of certain diseases

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Table 4.1 | Examples of the Diagnostic Value of Some Enzymes Found in Plasma

Enzyme	Diseases Associated with Abnormal Plasma Enzyme Concentrations
Alkaline phosphatase	Obstructive jaundice, Paget's disease (osteitis deformans), carcinoma of bone
Acid phosphatase	Benign hypertrophy of prostate, cancer of prostate
Amylase	Pancreatitis, perforated peptic ulcer
Aldolase	Muscular dystrophy
Creatine kinase (or creatine phosphokinase-CPK)	Muscular dystrophy, myocardial infarction
Lactate dehydrogenase (LDH)	Myocardial infarction, liver disease, renal disease, pernicious anemia
Transaminases (AST and ALT)	Myocardial infarction, hepatitis, muscular dystrophy

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Naming of Enzymes

- Most enzyme names end with "-ase"
- Classes of enzymes named according to activity
  - Such as phosphatases that remove, or kinases that add, phosphate groups
- Name may specify substrate of enzyme and activity
  - Such as lactate dehydrogenase

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Table 4.2 | Selected Enzymes and the Reactions They Catalyze

Enzyme	Reaction Catalyzed
Catalase	$2\ H_2O_2 \rightarrow 2\ H_2O + O_2$
Carbonic anhydrase	$H_2CO_3 \rightarrow H_2O + CO_2$
Amylase	starch + $H_2O \rightarrow$ maltose
Lactate dehydrogenase	lactic acid $\rightarrow$ pyruvic acid + NADH + H^+
Ribonuclease	RNA + $H_2O \rightarrow$ ribonucleotides

- Enzyme activity = The rate its substrates are converted to products

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Enzyme Activity

- Measured by the rate at which substrate is converted to product
- Influenced by:
  - Temperature
  - pH
  - Concentration of cofactors and coenzymes
  - Concentration of enzyme and substrate
  - Possible stimulatory or inhibitory effects of products on enzyme function

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Enzyme Activity - Temperature and pH

- Enzymes have optimal temperature and pH ranges
  - Typically near normal physiological values
  - Because 3-D structure is affected outside range

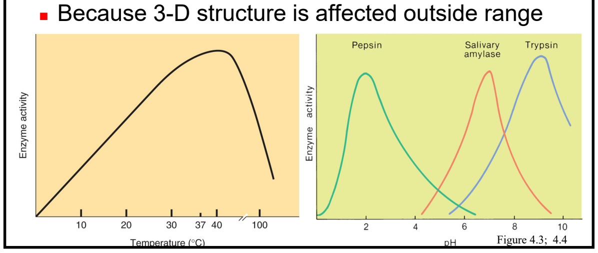

Figure 4.3; 4.4

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Table 4.3 | pH Optima of Selected Enzymes

Enzyme	Reaction Catalyzed	pH Optimum
Pepsin (stomach)	Digestion of protein	2.0
Acid phosphatase (prostate)	Removal of phosphate group	5.5
Salivary amylase (saliva)	Digestion of starch	6.8
Lipase (pancreatic juice)	Digestion of fat	7.0
Alkaline phosphatase (bone)	Removal of phosphate group	9.0
Trypsin (pancreatic juice)	Digestion of protein	9.5
Monoamine oxidase (nerve endings)	Removal of amine group from norepinephrine	9.8

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Cofactors and Coenzymes

- Are necessary for normal activity of enzymes
- Cofactors include metal ions such as Ca^{+2}, Mg^{+2}, Mn^{+2}, Cu^{+2}, Zn^{+2} and selenium
- Coenzymes are derived from vitamins; **transport** small molecules needed by enzymes

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Cofactors and Coenzymes

- Cofactor binding changes conformation of active site
- Aids in temporary bonding between enzyme and substrates

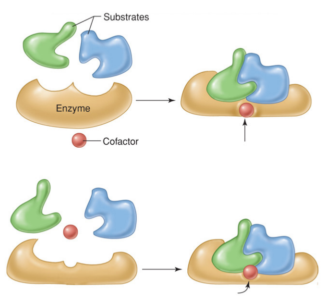

Figure 4.5

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Enzyme Activation

- **Many** enzymes are produced in an **inactive** form
  - e.g. pancreatic digestive enzymes are not activated until they reach the intestine
    - Protects pancreas against self-digestion
  - Many are activated by phosphorylation and inactivated by dephosphorylation
  - Others activated by 2nd messengers
  - Enzymes also regulated by turnover of enzyme (breakdown and re-synthesis of enzymes) therefore allowing genes to alter enzyme activity as conditions change

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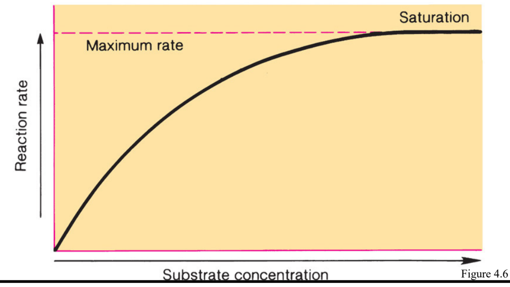
Effect of Substrate Concentration

- As the substrate concentration increases, so will the rate of the reaction until the enzyme becomes **saturated** = every enzyme in the solution is busy.



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Reversible Reactions

- Some enzymatic reactions are reversible
  - Both forward and backward reactions are catalyzed by same enzyme
  - **Law of mass action:** direction of reaction is from side of equation where concentration is higher to side where concentration is lower
  - e.g. carbonic anhydrase catalyzes
    - $H_2O + CO_2 \Leftrightarrow H_2CO_3$

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Metabolic Pathways

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Metabolic Pathways

Are sequences of enzymatic reactions that begin with initial substrate, progress through intermediates and end with a final product

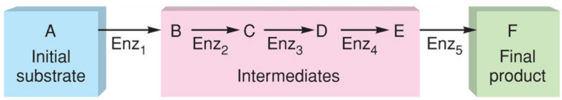

Figure 4.7

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Branched Metabolic Pathways

- Few metabolic pathways are linear. Most include branches where several products can be produced.

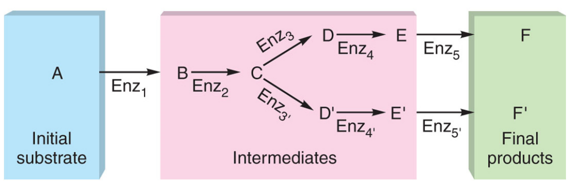

Figure 4.8

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End Product Inhibition

- Branch points are often inhibited by a form of negative feedback in which one of the final products inhibits the branch point enzyme.
- In the process called **allosteric inhibition**, the product binds to the enzyme at a location away from the active site and changes the 3D conformation of the enzyme.
  - Keeps the final product from accumulating

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End-Product Inhibition

- Occurs when 1 product in a divergent pathway inhibits activity of the branch-point enzyme
  - Prevents final product accumulation
  - Causes reaction to favor alternate pathway
  - Occurs by **allosteric inhibition** whereby product binds to enzyme causing it to change to an inactive shape

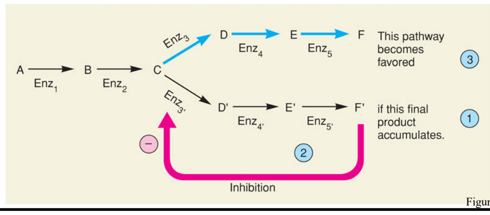

Figure 4.9

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Inborn Errors of Metabolism

- Are due to inherited defects in genes for enzymes in metabolic pathways
- Metabolic disease can result from either:
  - Increases in intermediates formed prior to the defective enzyme
  - Or decreases in products normally formed after the defective enzyme

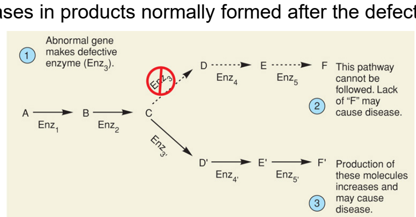

Figure 4.10

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Table 4.4 | Examples of Inborn Errors in the Metabolism of Amino Acids, Carbohydrates, and Lipids

Metabolic Defect	Disease	Abnormality	Clinical Result
Amino acid metabolism	Phenylketonuria (PKU)	Increase in phenylpyruvic acid	Mental retardation, epilepsy
	Albinism	Lack of melanin	Susceptibility to skin cancer
	Maple-syrup disease	Increase in leucine, isoleucine, and valine	Degeneration of brain, early death
	Homocystinuria	Accumulation of homocystine	Mental retardation, eye problems
Carbohydrate metabolism	Lactose intolerance	Lactose not utilized	Diarrhea
	Glucose 6-phosphatase deficiency (Gierke's disease)	Accumulation of glycogen in liver	Liver enlargement, hypoglycemia
	Glycogen phosphorylase deficiency	Accumulation of glycogen in muscle	Muscle fatigue and pain
Lipid metabolism	Gaucher's disease	Lipid accumulation (glucocerebroside)	Liver and spleen enlargement, brain degeneration
	Tay-Sachs disease	Lipid accumulation (ganglioside G_{M2})	Brain degeneration, death by age five
	Hypercholestremia	High blood cholesterol	Atherosclerosis of coronary and large arteries

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Bioenergetics

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Bioenergetics

- Flow of energy in living systems
- **1st law of thermodynamics** Energy can not be destroyed or created, only transformed.
- **2nd law of thermodynamics** Energy is lost with each transformation as heat. Energy transformations increase **entropy** (degree of disorganization)
- Only free energy (energy in organized state) can be used to do work
  - Systems tend to go from states of higher free energy to states of lower free energy

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Bioenergetics

- 2nd law dictates that all living organisms require continued input of energy
- Plants obtain this from sunlight
  - Use it to make high free energy glucose from CO_2 and H_2O that have less free energy (more entropy)
    - we use energy in glucose to combat entropy and power our bodies

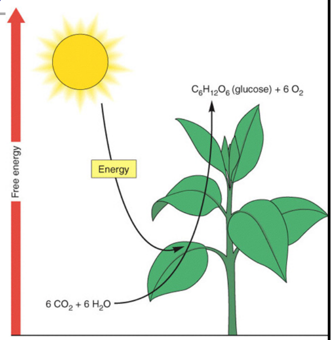

Figure 4.12

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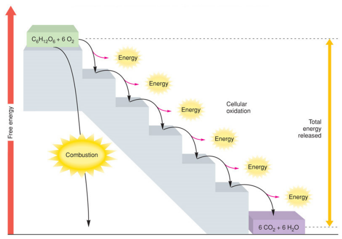
Endergonic and Exergonic Reactions

- **Endergonic reactions** require input of energy to proceed
  - Products contain more free energy than reactants
- **Exergonic reactions** release energy as they proceed
  - Products contain less free energy than reactants



Breaking glucose down into carbon dioxide and water produces energy (exergonic).

Energy is used to make ATP for use in other endergonic reactions in the body.

Figure 4.13

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Coupled Reactions: ATP

- Cells require constant inputs of free energy from environment to buck entropy and remain highly organized
  - Do this by coupling endergonic reactions to exergonic reactions
    - An exergonic reaction breaks down ATP - the universal energy carrier
  - Most endergonic reactions in body make ATP

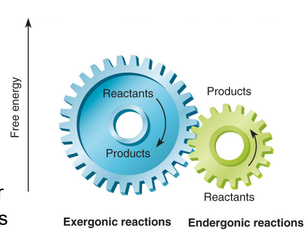

Figure 4.14

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ATP

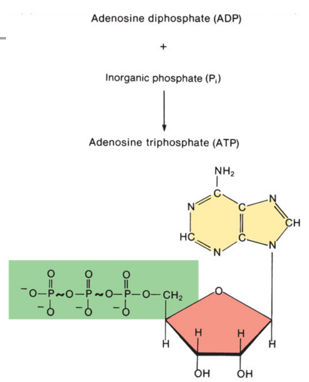

Figure 4.15

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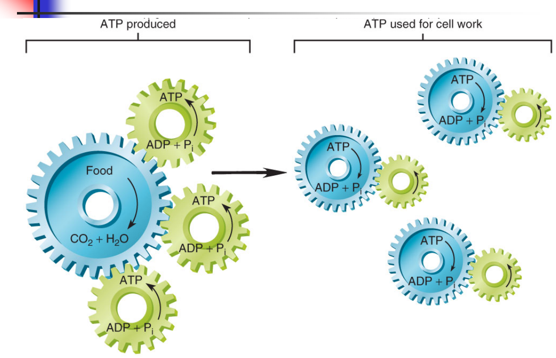

Figure 4.16

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Coupled Reactions: Oxidation-Reduction

- If a molecule gains electrons it is reduced
- If it loses electrons it is oxidized
- A reducing agent donates electrons
- An oxidizing agent accepts electrons
- Reduction and oxidation are always coupled reactions
  - Often involve transfer of Hs instead of electrons
  - Coenzymes that play important roles as H carriers are NAD and FAD
    - These are also vitamins

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Oxidation-Reduction

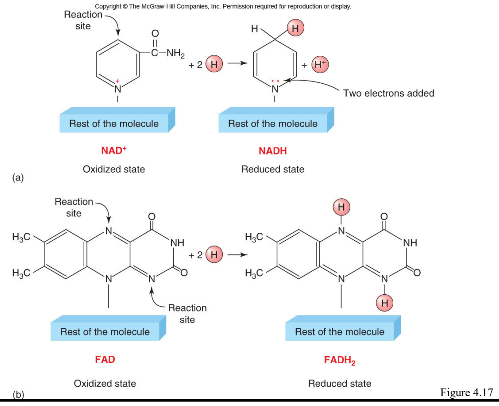

Figure 4.17

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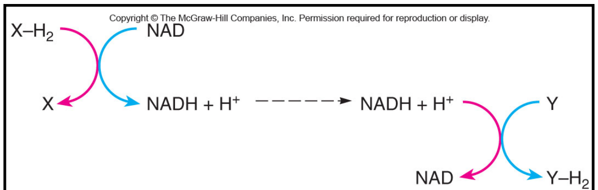

NAD is oxidizing agent (it becomes reduced)

NADH is reducing agent (it becomes oxidized)

Figure 4.18

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