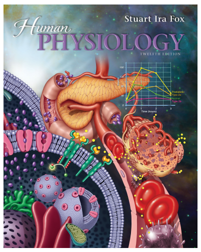
Connect Learn Succeed



Chapter 4

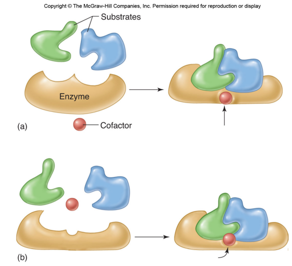
Enzymes and Energy

Lecture PowerPoint

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

I. Enzymes as Catalysts

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display



Enzymes

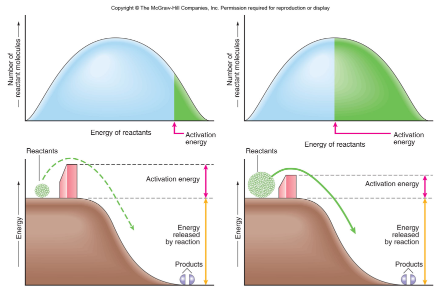
- A class of proteins that serve as catalysts. Catalysts are chemicals that:
  - Increase the rate of a reaction
  - Are not changed by the reaction (so can be used again)
  - Do not change the nature of the reaction--the reaction could have occurred without the enzyme, just much slower

Activation Energy

- The energy required for the reactants to engage in a reaction
- Most molecules lack the activation energy for a reaction.
  - Adding heat increases the likelihood of a reaction occurring. This increases the rate of reactions.
  - Heat has some negative effects on cells. Catalysts help the reaction occur at lower temperatures.

Catalyzed vs. Noncatalyzed Reactions

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display



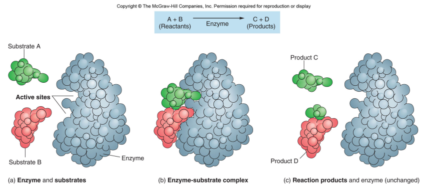
Mechanisms of Enzyme Activity

- 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.

Mechanisms of Enzyme Activity

- When a substrate binds to the active site of an enzyme, it forms temporary bonds, weakening the original bonds of the substrate and allowing them to break easily.

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display



Mechanisms of Enzyme Activity

- New bonds are formed between substrates as they are brought close together by the enzyme.
  - Bonding of enzyme to substrates forms a temporary enzyme-substrate complex.
  - This breaks to yield the products of the reaction.
  - The amount of enzyme in a sample of fluid can be measured based on the rate of product synthesis.

Naming Enzymes

- The first enzymes discovered were given arbitrary names. An international committee later decided to end all enzymes with the suffix –ase.
- They also decided to make the first part of the name apply to the function of the enzyme.
  - Phosphatases remove phosphate groups.
  - Synthetases catalyze dehydration synthesis.

Isoenzymes

- Because names are given to enzymes based on function, an enzyme that does the same job in two different organs has the same name.

- However, the molecules may be slightly different (in areas outside the active site) and are called isoenzymes.

Diagnostic Value of Measuring Enzymes in Blood

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display

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

II. Control of Enzyme Activity

Enzyme Activity

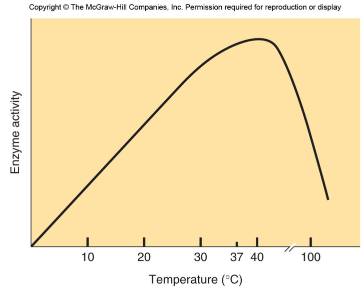
- Measured by the rate at which substrate is converted to product
- Influenced by:
  - Temperature
  - pH
  - Concentration of cofactors and coenzymes
  - Concentration of enzyme and substrate
  - Possible stimulatory or inhibitory effects of products on enzyme function

Effects of Temperature

- An increase in temperature will increase the rate of reactions until the temperature reaches a few degrees above body temperature. At this point, the enzyme is denatured.

Effects of Temperature

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display

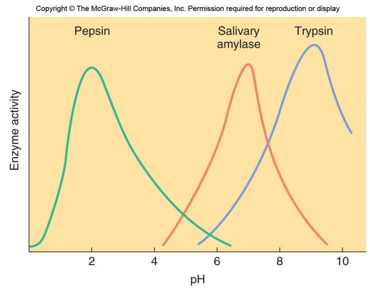


Effects of pH

- Enzymes exhibit peak activity within a narrow pH range = pH optimum.
  - Due to changes in enzyme conformation
  - Optimum pH reflects the pH of the fluid the enzyme is found in:
    - Stomach vs. saliva vs. small intestine

Effects of pH

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display



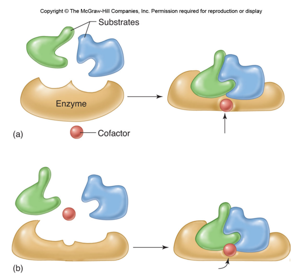
Coenzymes

- Most enzymes need additional small molecules to aid in a reaction.
- Coenzymes transport hydrogen atoms and other small molecules between enzymes.
  - Coenzymes are organic molecules derived from water-soluble vitamins.

Cofactors

- Cofactors help form the active site through a conformational change of the enzyme or help in enzyme-substrate binding.
- Cofactors are metal ions (Ca^{2+}, Mg^{2+}, Mn^{2+}, Cu^{2+}, Zn^{2+}).

Cofactors



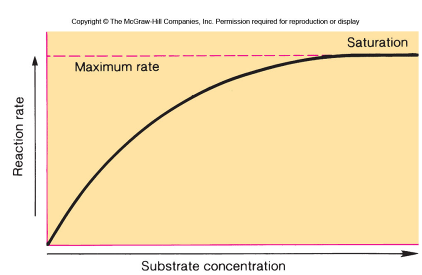
Enzyme Activation

- Enzymes are often produced in an inactive form and activated when needed (pepsinogen → pepsin).
- It often requires additional enzymes to phosphorylate or dephosphorylate the molecule.
- Enzyme inhibition can be controlled through turnover, by which enzymes are degraded.

Substrate Concentrations

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

Substrate Concentrations



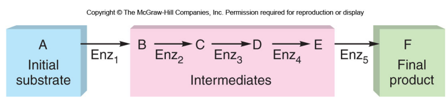
Reversible Reactions

- Sometimes a single enzyme can drive a reaction in two directions, depending on the concentration of substrate/product. When one side gets higher, the other reaction reverses.
  - This is called the law of mass action.
  - Example: the enzyme carbonic anhydrase

$$H_2O + CO_2 \leftrightarrow H_2CO_3$$

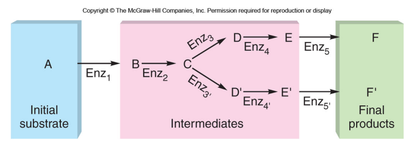
Metabolic Pathways

- Most reactions are linked together in a chain (or web) called a *metabolic pathway.*
  - These begin with an initial substrate and end with a final product, with many enzymatic steps along the way.



Branched Metabolic Pathways

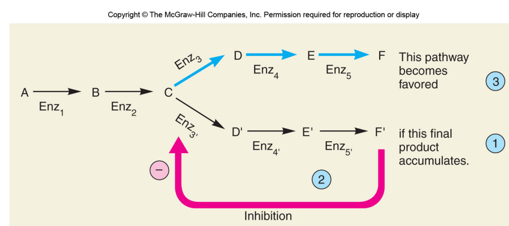
- Few metabolic pathways are linear. Most include branches where several products can be produced.



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

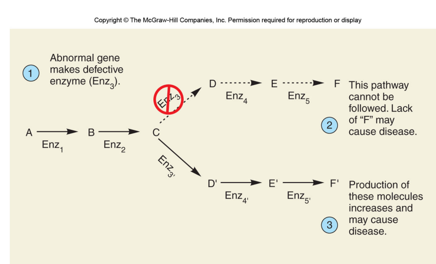
End Product Inhibition



Inborn Errors of Metabolism

- Occur when there is a mutation in a single gene that codes for an enzyme in a metabolic pathway
  - Products to be formed after this enzyme in the chain are not formed.
  - Diseases occur due to loss of end product or accumulation of intermediary products (those before the bad enzyme) or alternative products in a branch.

Inborn Errors of Metabolism



Examples of Diseases Caused by Inborn Errors of Metabolism

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display

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

III. Bioenergetics

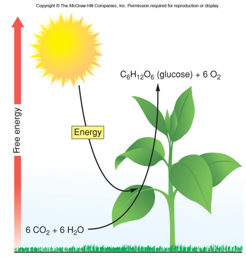
Bioenergetics

- The flow of energy in living systems
- Obeys the laws of thermodynamics:
  1. *First Law of Thermodynamics:* Energy can not be destroyed or created, only transformed.

First Law of Thermodynamics

Conversion of light energy into glucose by plants

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display



Second Law of Thermodynamics

- Energy is lost with each transformation as heat, so the available "organized" energy (free energy) decreases.
  - Entropy = degree of disorganization
  - Entropy increases at each step of energy transformation.
- This law relates to endergonic and exergonic reactions.

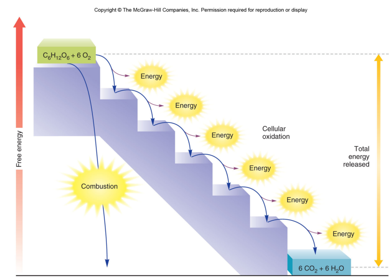
Endergonic Reactions

- Chemical reactions that require an input of energy. Products contain more free energy than the reactants.
  - Occur in reactions where the reactants are at a greater state of entropy and the products are at a lesser state of entropy
  - Plants need the energy from light to turn carbon dioxide and water into glucose.

Exergonic Reactions

- Chemical reactions that produce energy. Products will have less free energy than the reactants.
  - Breaking glucose down into carbon dioxide and water produces energy.
  - Energy is used to make ATP for use in other endergonic reactions in the body.

Energy Obtained from Glucose



Calories

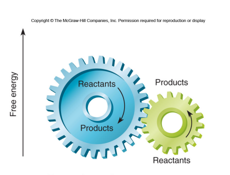
- The amount of energy in a molecule can be measured in calories.
- One calorie = amount of heat required to raise the temperature of 1 cubic centimeter of water 1 degree Celsius.
- Calories in food are actually reported in kilocalories (= 1,000 calories).

Coupled Reactions

- Energy from the environment (food) is broken down in exergonic reactions to drive the endergonic reactions in our bodies.
- Energy must be stored in a usable form:
  - The production of ATP is actually an endergonic reaction that is coupled to an exergonic reaction to drive it.
  - The ATP molecule stores energy in its bonds to be used elsewhere.
  - ATP is called the *universal energy carrier.*

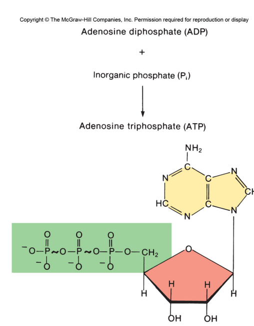
Coupled Reactions

- How coupled reactions work.

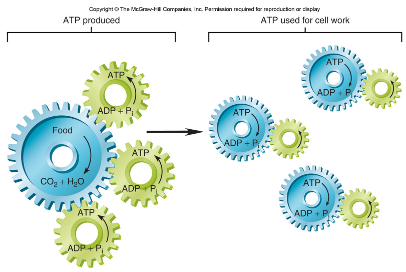


- The formation of ATP

Coupled Reactions



ATP as the Universal Energy Carrier



Oxidation-Reduction

- Reduction: when an atom or molecule gains electrons (is reduced)
  - It is reduced in charge (electrons are negative).
- Oxidation: when an atom or molecule loses electrons (is oxidized)
- These reactions are always coupled. For one molecule to lose an electron, it has to give it to another molecule.
  - Reducing agent: electron donor
  - Oxidizing agent: electron receiver

Oxidation - Reduction

- Many molecules can be both oxidizers and reducers in a chain reaction where electrons are passed along.
  - Oxygen is a great electron acceptor, which is why the process is called oxidation. Oxygen is not the *only* oxidizer, however.

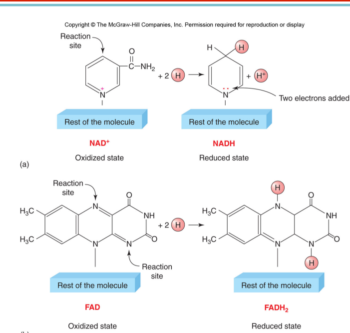
Oxidation-Reduction

- Usually, free electrons are not passed along, but hydrogen atoms carrying the electrons are.
  - A molecule that loses hydrogen is oxidized.
  - A molecule that gains hydrogen is reduced.

NAD and FAD

- NAD = nicotinamide adenine dinucleotide
  - From the vitamin niacin (B_3)
- FAD = flavin adenine dinucleotide
  - From the vitamin riboflavin (B_2)
- NAD and FAD are coenzymes that play an important role in hydrogen transfer.

Oxidation and Reduction of NAD and FAD



NAD and FAD

- Each FAD can accept 2 electrons and bind to 2 protons, thus reduced FAD = $FADH_2$.
- Each NAD can accept 2 electrons and bind to 1 proton, thus reduced NAD = NADH + H^+.

NAD and FAD

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display