

BIOENERGITIKA MIKROBA

Metabolism: Energy, Enzymes, and The Generation of Energy

Chapter Overview

This chapter discusses energy and the laws of thermodynamics. The participation of energy in cellular metabolic processes and the role of adenosine-5'-triphosphate (ATP) as the energy currency of cells are examined. The chapter concludes with a discussion of enzymes as biological catalysts: how they work, how they are affected by their environment, and how they are regulated.

Chapter Objectives

After reading this chapter you should be able to:

- discuss the first and second laws of thermodynamics and show how they apply to biological systems
- discuss enthalpy, entropy, and free energy and their application to biological reactions
- discuss the use of ATP as the energy currency of the cell and show how it is used to couple energy-yielding exergonic reactions with energy-requiring endergonic reactions
- discuss reduction potential and its relationship to exergonic and endergonic processes
- describe the role of enzymes in the catalysis of biological reactions, and discuss the ways in which enzymes are influenced by their environment
- discuss the need for metabolic regulation
- describe metabolic channeling
- describe how enzyme activity can be controlled by allosteric regulation and covalent modification
- describe how feedback inhibition can be used to control the activity of a metabolic pathway

These are the most important concepts you are learning in this chapter:

1. Energy is the capacity to do work. Living organisms can perform three major types of work: chemical work, transport work, and mechanical work.
2. Most energy used by living organisms originally comes from sunlight trapped during photosynthesis by photoautotrophs. Chemoheterotrophs then consume autotrophic organic materials and use them as sources of energy and as building blocks.
3. An energy currency is needed to connect energy-yielding exergonic reactions with energy-requiring endergonic reactions. The most commonly used currency is ATP.
4. All living systems obey the laws of thermodynamics.
5. When electrons are transferred from a reductant with a more negative reduction potential to an oxidant with a more positive potential, energy is made available. A reversal of the direction of electron transfer — for example, during photosynthesis — requires energy input.

6. Enzymes are protein catalysts that make life possible by increasing the rate of reactions at ambient temperatures.
7. Enzymes do not change chemical equilibria or violate the laws of thermodynamics but accelerate reactions by lowering their activation energy.

Study Outline

I. Energy and Work

- A. Energy is the capacity to do work
- B. Living cells carry out three major types of work
 1. Chemical work--synthesis of complex molecules
 2. Transport work nutrient uptake, waste elimination, ion balance
 3. Mechanical work internal and external movement
- C. In ecosystems, photoautotrophs and chemolithoautotrophs trap energy and use some of it to transform carbon dioxide into organic molecules; the organic molecules then serve as sources of carbon and energy for chemoheterotrophs, which in turn oxidize the organic molecule by processes such as aerobic respiration, releasing carbon dioxide
- D. The major energy currency in a living cell is adenosine-5'-triphosphate (ATP)

II. The Laws of Thermodynamics

- A. The science of thermodynamics analyzes energy changes in a collection of matter called a system; all other matter in the universe is called the surroundings
- B. First law energy can be neither created nor destroyed
 1. The total energy in the universe remains constant
 2. Energy may be redistributed either within a system or between the system and its surroundings
 3. Energy is measured in calories where 1 calorie is the amount of heat energy needed to raise 1 gram of water from 14.5° C to 15.5°C
- C. Second law physical and chemical processes proceed in such a way that the disorder of the universe increases to the maximum possible

III. Free Energy and Reactions

- A. The changes in energy that can occur in chemical reactions is expressed by the equation for free energy change ($\Delta G = \Delta H - T \Delta S$); free energy change (ΔG) is the amount of energy in a system that is available to do work
- B. The change in free energy of a chemical reaction is directly related to the equilibrium constant of the reaction
 1. The standard free energy change (ΔG°) is the change in free energy under standard conditions of concentration, pH, pressure, and temperature
 2. When ΔG° is negative, the equilibrium constant is greater than one and the reaction goes to completion as written; the reaction is said to be exergonic
 3. When ΔG° is positive, the equilibrium constant is less than one and little product will be formed at equilibrium; the reaction is said to be endergonic

IV. The Role of ATP in Metabolism

- A. ATP is a high-energy molecule; removal of the terminal phosphate by hydrolysis goes almost to completion with a large negative standard free energy change (i.e., the reaction is strongly exergonic); ATP also has high phosphate group transfer potential
- B. These characteristics make ATP well suited for its role as an energy currency; ATP is formed from ADP and P_i by energy-trapping processes; exergonic breakdown of ATP can be coupled with various endergonic reactions to facilitate their completion

V. Oxidation-Reduction Reactions and Electron Carriers

- A. The release of energy during metabolic processes normally involves oxidation-reduction reactions
 - 1. Oxidation-reduction (redox) reactions involve the transfer of electrons from a donor (reducing agent or reductant) to an acceptor (oxidizing agent or oxidant)
 - 2. The equilibrium constant for an oxidation-reduction reaction is called the standard reduction potential (E_0) and is a measure of the tendency of the reducing agent to lose electrons; the more negative the reduction potential, the better the reducing agent is as an electron donor
- B. When electrons are transferred from an electron donor to an electron acceptor with a more positive reduction potential, free energy is released and can be used to form ATP
- C. Electron transport is important in a variety of metabolic processes (e.g., respiration and photosynthesis); cells use a variety of electron carriers organized into a chain to move electrons; electron carriers include NAD^+ , $NADP^+$, flavoproteins, coenzymes, and cytochromes; these carriers differ in terms of how they carry electrons, and this impacts how they function in electron transport chains

VI. Enzymes

- A. Structure and classification of enzymes
 - 1. Enzymes are protein catalysts with great specificity for the reaction catalyzed and the molecules acted upon
 - a. A catalyst is a substance that increases the rate of a reaction without being permanently altered
 - b. The reacting molecules are called substrates and the substances formed are the products
 - 2. An enzyme may be composed only of protein or it may be a holoenzyme, consisting of a protein component (apoenzyme) and a nonprotein component (cofactor)
 - a. Prosthetic group a cofactor that is firmly attached to the apoenzyme
 - b. Coenzyme a cofactor that is loosely attached to the apoenzyme; it may dissociate from the apoenzyme and carry one or more of the products of the reaction to another enzyme
- B. The mechanism of enzyme reactions
 - 1. Enzymes increase the rate of a reaction, but do not alter the equilibrium constant (or the standard free energy change) of the reaction
 - 2. Enzymes lower the activation energy required to bring the reacting molecules together correctly to form the transition-state complex; once the transition state has been reached the reaction can proceed rapidly

3. Enzymes bring substrates together at the active site to form an enzyme-substrate complex; this can lower activation energy in several ways:
 - a. Local concentrations of the substrates are increased at the active (catalytic) site of the enzyme
 - b. Molecules at the active site are oriented properly for the reaction to take place
- C. The effect of environment on enzyme activity
1. The amount of substrate present affects the reaction rate, which increases as the substrate concentration increases until all available enzyme molecules are binding substrate and converting it to products as rapidly as possible
 - a. No further increase in rate occurs with subsequent increases in substrate concentration, and the reaction is said to be proceeding at maximal velocity (V_{\max})
 - b. The Michaelis constant (K_m) of an enzyme is the substrate concentration required for the reaction to reach half maximal velocity and is used as a measure for the apparent affinity of an enzyme for its substrate
 2. Enzyme activity is affected by alterations in pH and temperature; each enzyme has specific pH and temperature optima; extremes of pH, temperature, and other factors can cause denaturation (loss of activity due to disruption of enzyme structure)
- D. Enzyme inhibition
1. Competitive inhibition occurs when the inhibitor binds at the active site and thereby competes with the substrate (if the inhibitor binds, then the substrate cannot, and no reaction occurs); this type of inhibition can be overcome by adding excess substrate
 2. Noncompetitive inhibition occurs when the inhibitor binds to the enzyme at some location other than the active site and changes the enzyme's shape so that it is inactive or less active; this type of inhibition cannot be overcome by the addition of excess substrate

VII. The Nature and Significance of Metabolic Regulation

- A. Regulation is essential for microorganisms to conserve energy and material and to maintain metabolic balance despite frequent changes in their environment
- B. Metabolic processes can be regulated in three major ways:
 1. Metabolic channeling the localization of metabolites and enzymes in different parts of a cell
 2. Stimulation or inhibition of critical enzymes in a pathway
 3. Increasing or decreasing the number of enzyme molecules present (regulation of gene expression)

VIII. Metabolic Channeling

- A. Compartmentation is a common mechanism for metabolic channeling; enzymes and metabolites are distributed in separate cell structures or organelles
- B. Channeling can generate marked variations in metabolite concentrations and therefore directly affect enzyme activity

IX. Control of Enzyme Activity

- A. Allosteric regulation of enzyme activity by an effector or modulator, which binds reversibly and noncovalently to a regulatory site on the enzyme; the regulatory site is distinct from the catalytic site
- B. Covalent modification of enzymes regulation of enzyme activity by the covalent addition or removal of a chemical group (e.g., phosphate, methyl group, adenylic acid)
- C. Feedback Inhibition
 1. Every pathway has at least one pacemaker enzyme that catalyzes the slowest (rate-limiting) reaction in the pathway; often this is the first reaction in a pathway
 2. In feedback inhibition (end product inhibition), the end product of the pathway inhibits the pacemaker enzyme
 3. In branched pathways, balance between end products is maintained through the use of regulatory enzymes at branch points; multiply branched pathways often use isoenzymes, each under separate and independent control

Chapter Web Links

Mechanism of Non-Competitive Inhibition (animation)

(<http://bio.winona.msus.edu/berg/ANIMTNS/n-c-inan.htm>)

Energy, Enzymes, and Catalysis Problem Set

(http://www.biology.arizona.edu/biochemistry/problem_sets/energy_enzymes_catalysis/energy_...)

Metabolism: The Generation of Energy

Chapter Overview

This chapter presents an overview of energy release and conservation mechanisms beginning with glucose degradation to pyruvate. Fermentation, aerobic respiration, and anaerobic respiration are then examined. The consideration of chemoorganoheterotrophic metabolism concludes with a discussion of the catabolism of lipids, proteins, and amino acids. Chemolithotrophic metabolism follows and the chapter concludes with a discussion of the trapping of energy by photosynthesis.

Chapter Objectives

After reading this chapter you should be able to:

1. discuss the difference between catabolism and anabolism
2. describe the various pathways for the catabolism of glucose to pyruvate
3. list the various types of fermentations and give examples of their practical importance
4. discuss the tricarboxylic acid (TCA) cycle and its central role in aerobic metabolism
5. describe the electron transport process, and compare and contrast the electron transport systems of eucaryotes with those of procaryotes
6. describe oxidative phosphorylation and the chemiosmotic hypothesis
7. compare and contrast aerobic respiration, fermentation, and anaerobic respiration of organic molecules
8. describe in general terms the catabolism of molecules other than carbohydrates
9. discuss the photosynthetic light reactions
10. compare and contrast the light reactions of eucaryotes (and cyanobacteria) with those of green (or purple) photosynthetic bacteria

These are the most important concepts you are learning in this chapter:

1. Metabolism, the sum total of all chemical reactions occurring in the cell, can be divided into catabolism and anabolism. In catabolism, molecules are reduced in complexity and free energy is made available. Anabolism involves the use of free energy to increase the complexity of molecules.
2. During catabolism, nutrients are funneled into a few common pathways for more efficient use of enzymes (a few pathways process a wide variety of nutrients).
3. The tricarboxylic acid cycle is the final pathway for the aerobic oxidation of nutrients to CO₂.
4. The majority of energy released in catabolism is generated by the movement of electrons from electron transport carriers with more negative reduction potentials to ones with more positive reduction potentials. Thus aerobic respiration is much more efficient than anaerobic catabolism.
5. A wide variety of electron acceptors can be used in catabolism: O₂ (aerobic respiration), organic molecules (fermentation), and oxidized inorganic molecules other than O₂ (anaerobic respiration). Furthermore, reduced inorganic molecules as well as organic molecules can serve as electron donors for electron transport and

ATP synthesis. Microbial catabolism is unique in the diversity of nutrients and mechanisms employed to make energy available.

6. In photosynthesis trapped light energy boosts electrons to more negative reduction potentials or higher energy levels. These energized electrons are then used to make ATP and NADPH or NADH during electron transport.

Study Outline

- I. An Overview of Metabolism
 - A. Metabolism (the total of all chemical reactions occurring in a cell) can be divided into two major parts: catabolism and anabolism
 1. Catabolism-the breakdown of larger, more complex molecules into smaller, simpler ones, during which energy is released, trapped, and made available for work
 2. Anabolism-the synthesis of complex molecules from simpler ones during which energy is added as input
 3. Chemolithotrophy and photosynthesis are included as energy-yielding catabolic processes, even though they do not involve degradation of complex molecules
 - B. Chemotrophic microorganisms not only vary in terms of their energy source, but also in terms of their electron acceptors
 1. If an organic energy source is oxidized and degraded without the use of an exogenous electron acceptor, the process is called fermentation
 2. If the energy source is oxidized and degraded with the use of an exogenous electron acceptor, the process is called respiration; in aerobic respiration the final electron acceptor is oxygen, whereas in anaerobic respiration the final electron acceptor is a molecule other than oxygen
 - C. For chemoorganoheterotrophic organisms, catabolism is often a three stage process during which nutrients are fed into common degradative pathways; these common pathways function both catabolically and anabolically and are said to be amphibolic
- II. The Breakdown of Glucose to Pyruvate
 - A. The glycolytic pathway
 1. Also known as the Embden-Meyerhof pathway, it is the most common pathway and is found in all major groups of microorganisms
 2. It functions in the presence or absence of oxygen and is divided into two parts:
 - a. The 6-carbon sugar stage glucose is phosphorylated twice to yield fructose 1,6-bisphosphate; this requires the expenditure of two molecules of ATP
 - b. The 3-carbon sugar stage cleaves fructose 1,6-bisphosphate into two 3-carbon molecules, which are each processed to pyruvate; two molecules of ATP are produced by substrate-level phosphorylation from each of the 3-carbon molecules for a net yield of two molecules of ATP; 2 molecules of NADH are also produced per glucose molecule
 - B. The pentose phosphate pathway

1. Also known as the hexose monophosphate pathway, this pathway uses a different set of reactions to produce a variety of 3-, 4-, 5-, 6-, and 7-carbon sugar phosphates
 2. Has several catabolic and anabolic functions
 - a. Production of NADPH, which serves as a source of electrons for biosynthetic processes
 - b. A source of four and five carbon skeletons that can be used for the synthesis of amino acids, nucleic acids, and other macromolecules
 - c. The complete catabolism of hexoses and pentoses, yielding ATP and NADH (made by converting NADPH to NADH)
 - C. The Entner-Doudoroff pathway
 1. This pathway links reactions of the pentose phosphate pathway and the glycolytic pathway with unique reactions
 2. This pathway produces ATP, NADPH, and NADH
- III. Fermentations
- A. Fermentation-a process in which an organism oxidizes the NADH produced by one of the pathways above by using pyruvate or one of its derivatives as an electron and hydrogen acceptor; thus the process involves the use of an endogenous electron acceptor
 - B. Many different types of fermentations are known
 1. Alcoholic fermentations produce ethanol and CO₂
 2. Lactic acid fermentations produce lactic acid (lactate)
 - a. Homolactic fermenters reduce almost all pyruvate to lactate
 - b. Heterolactic fermenters form substantial amounts of products other than lactate
 3. Formic acid fermentation produces either mixed acids or butanediol
 - C. Microorganisms can ferment substances other than sugars (e.g., amino acids)
- IV. The Tricarboxylic Acid Cycle
- A. Pyruvate can be degraded to carbon dioxide by the tricarboxylic acid (TCA) cycle after first being converted to acetyl CoA; this reaction is accompanied by the loss of one carbon atom as carbon dioxide
 - B. Acetyl-CoA reacts with oxaloacetate (a 4-carbon molecule) to produce a 6-carbon molecule, which is subsequently broken down to two molecules of carbon dioxide, regenerating the oxaloacetate; during this process, the following occurs:
 1. ATP is produced by substrate-level phosphorylation
 2. Three molecules of NADH and one molecule of FADH₂ are produced
 - C. Even those organisms that lack the complete TCA cycle usually have most of the cycle enzymes because one of the TCA cycle's major functions is to provide carbon skeletons for use in biosynthesis
- V. Electron Transport and Oxidative Phosphorylation
- A. The Electron Transport Chain
 1. The mitochondrial electron transport chain uses a series of electron carriers to transfer electrons from NADH and FADH₂ to O₂
 - a. Electron carriers are located within the inner membrane of the mitochondrion

- b. During oxidative phosphorylation, three ATP molecules may be synthesized when a pair of electrons passes from NADH to O₂; two ATP molecules may be synthesized when electrons from FADH₂ pass to O₂
 - 2. Although they operate according to the same fundamental principles, bacterial electron transport chains usually differ in structure: they may be branched, be composed of different electron carriers, or may be shorter than mitochondrial electron transport chains; bacterial electron transport chains are located in the plasma membrane
 - B. Oxidative Phosphorylation
 - 1. The chemiosmotic hypothesis of oxidative phosphorylation postulates that the energy released during electron transport is used to establish a protonmotive force (potential energy due to the difference in proton concentration and charge on either side of the membrane), which can be used to drive ATP synthesis, flagellar rotation, and transport of molecules across the membrane
 - 2. ATP synthesis is catalyzed by the ATP synthase complex, which is thought to behave like a small rotary motor
 - 3. Inhibitors of ATP synthesis fall into two main categories:
 - a. Blockers that inhibit the flow of electrons through the system
 - b. Uncouplers that allow electron flow, but disconnect it from oxidative phosphorylation
 - C. The Yield of ATP in Glycolysis and Aerobic Respiration
 - 1. The yield of ATP by glycolysis during fermentation is 2 ATP
 - 2. Aerobic respiration yields between 2 and 38 ATP molecules per glucose molecule, depending on the precise nature of the electron transport system
 - 3. The Pasteur effect is a regulatory phenomenon by which organisms lower their rate of sugar catabolism when conditions cause a shift from fermentation to aerobic respiration; this occurs because aerobic respiration is more efficient and generates greater energy per glucose molecule
- VI. Anaerobic Respiration
 - A. Uses molecules other than oxygen as terminal electron acceptors; the most commonly used alternative electron acceptors are nitrate, sulfate, and CO₂
 - B. Dissimilatory nitrate reduction occurs when nitrate is used as the terminal electron acceptor; if the nitrate is reduced to nitrogen gas, the process is called denitrification
 - C. Anaerobic respiration is not as efficient in ATP synthesis as aerobic respiration because the alternative electron acceptors do not have as positive a reduction potential as O₂; despite this, anaerobic respiration is useful because it is more efficient than fermentation
- VII. Catabolism of Carbohydrates and Intracellular Reserve Polymers
 - A. Carbohydrates
 - 1. Most monosaccharides feed easily into the glycolytic pathway
 - 2. Disaccharides are cleaved into monosaccharides either by hydrolysis or phosphorolysis

3. Polysaccharides are cleaved into smaller molecules either by hydrolysis or phosphorolysis; many, however, are not easily degraded (e.g., cellulose, agar)
 4. Microorganisms are also capable of degrading xenobiotic molecules (foreign substances not formed by natural biosynthetic processes) such as pesticides
- B. Reserve polymers-when exogenous nutrients are absent, microorganisms catabolize internal stores of glycogen, starch, etc.
- VIII. Lipid Catabolism
- A. Triglycerides are common energy sources; they are hydrolyzed to glycerol and fatty acids
 - B. Fatty acids are catalyzed by the β -oxidation pathway, which produces acetyl-CoA, NADH, and FADH₂; NADH and FADH₂ can be oxidized by an electron transport chain to produce ATP
- IX. Protein and Amino Acid Catabolism
- A. Proteins are degraded by proteases to their component amino acids
 - B. Amino acids are first deaminated and then the remaining carbon skeletons are converted to pyruvate, acetyl-CoA, or a TCA-cycle intermediate
- X. Oxidation of Inorganic Molecules
- A. Chemolithotrophy-a metabolic process that uses inorganic molecules as a source of energy; the energy source is oxidized; the electron acceptor is usually O₂, but sulfate and nitrate are also used; the most common electron donors (energy sources) are hydrogen, reduced nitrogen compounds, reduced sulfur compounds, and ferrous iron (Fe²⁺)
 - B. Chemolithotrophs are usually autotrophs; they use the Calvin Cycle to fix carbon dioxide
- XI. Photosynthesis
- A. During photosynthesis, energy from light is trapped and used to produce ATP and NADPH (light reactions), which are used to reduce carbon dioxide to form carbohydrates (dark reactions)
 - B. The light reactions of eucaryotes and cyanobacteria
 1. Chlorophyll molecules and a variety of accessory pigments are used to form antennas; the antennas trap photons and transfer them to a reaction-center chlorophyll; this special chlorophyll is directly involved in photosynthetic electron transport
 2. Eucaryotes and cyanobacteria have two photosystems; in each, electrons from the light energized reaction-center chlorophyll are transferred to the associated electron transport chain
 - a. Photosystem I can carry out cyclic photophosphorylation, producing ATP
 - b. Photosystems I and II, working together, can carry out noncyclic photophosphorylation, producing ATP and NADPH; the electrons for noncyclic photophosphorylation are obtained from water, which is oxidized to O₂ (oxygenic photosynthesis)
 3. Photosynthetic electron transport takes place in membranes
 - C. The light reactions of green and purple bacteria
 1. Green and purple bacteria carry out anoxygenic photosynthesis (they do not use water as a source of electrons, so do not produce O₂), and

- they have different photosynthetic pigments called bacteriochlorophylls
2. Many of the differences in the light reactions of the green and purple bacteria are due to the fact that they only have a single photosystem
 3. Green and purple bacteria are usually autotrophs that used NADH or NADPH for carbon dioxide fixation; three methods for making NADH are known:
 - a. Reduction of NAD⁺ directly by hydrogen gas
 - b. Reverse electron flow
 - c. A simplified form of noncyclic electron flow

Chapter Web Links

Simplified Diagram of Cellular Metabolism

(<http://www.accessexcellence.org/AB/GG/>)

Gallery (Scroll down to "Cell Processes")

(<http://www.gene.com/ae/AB/GG/Graphics>)

Metabolism: The Use of Energy

Chapter Overview

This chapter presents an overview of anabolism starting with the fixation of carbon dioxide. It then focuses on the synthesis of carbohydrates; the assimilation of phosphorus, sulfur, and nitrogen; and then the synthesis of amino acids, purines and pyrimidines, and lipids. The chapter concludes with a discussion of the synthesis of peptidoglycan and bacterial cell walls.

Chapter Objectives

After reading this chapter you should be able to:

1. discuss the use of energy to construct more complex molecules and structures from smaller, simpler precursors
2. discuss the way that biosynthetic pathways are organized to conserve genetic storage space, biosynthetic raw materials, and energy
3. discuss the way that autotrophs use ATP and NADPH (or NADH) to reduce carbon dioxide and incorporate it into organic material
4. describe the assimilation of phosphorus, sulfur, and nitrogen
5. discuss the use of the TCA cycle as an amphibolic pathway and the need for anaplerotic reactions to maintain adequate levels of TCA cycle intermediates
6. discuss the synthesis of glucose (gluconeogenesis) and the synthesis of fatty acids
7. describe in general terms the synthesis of peptidoglycan and the construction of new cell walls

These are the most important concepts you are learning in this chapter:

1. In anabolism or biosynthesis, cells use free energy to construct more complex molecules and structures from smaller, simpler precursors.
2. Biosynthetic pathways are organized to optimize efficiently by conserving biosynthetic raw materials and energy.
3. Autotrophs use ATP and NADPH from photosynthesis or from oxidation of inorganic molecules to reduce CO₂ and incorporate it into organic material.
4. Catabolic and anabolic pathways may differ in enzymes, regulation, intracellular location, and use of cofactors and nucleoside diphosphate carriers. Although many enzymes of amphibolic pathways participate in both catabolism and anabolism, some pathway enzymes are involved only in one of the two processes.
5. Phosphorus, in the form of phosphate, can be directly assimilated, whereas inorganic sulfur and nitrogen compounds must often be reduced before incorporation into organic material.
6. The tricarboxylic acid (TCA) cycle acts as an amphibolic pathway and requires anaplerotic reactions to maintain adequate levels of cycle intermediates.
7. Most glycolytic enzymes participate in both the synthesis and catabolism of glucose. In contrast, fatty acids are synthesized from acetyl-CoA and malonyl-CoA by a pathway quite different from fatty acid β -oxidation.
8. Peptidoglycan synthesis is a complex, multistep process that is begun in the cytoplasm and completed at the cell wall after the peptidoglycan repeat unit has been transported across the plasma membrane.

Study Outline

- I. Introduction
 - A. Anabolism-the creation of order by the synthesis of complex molecules from simpler ones; it requires the input of energy
 - B. Turnover-the continual degradation and resynthesis of cellular constituents
 - C. The rate of biosynthesis is approximately balanced by that of catabolism, due to careful regulation of metabolic processes
- II. Principles Governing Biosynthesis
 - A. Biosynthetic metabolism follows a few general principles:
 1. The synthesis of large complex molecules (macromolecules) from a limited number of simple structural units (monomers) saves much genetic storage capacity, biosynthetic raw material, and energy
 2. The use of many of the same enzymes for both catabolism and anabolism saves additional materials and energy
 3. Many biosynthetic pathways are reversals of catabolic pathways; many steps of the pathway are catalyzed by enzymes that participate in both catabolic and anabolic activities; however, some steps are catalyzed by two different enzymes: one that functions in the catabolic direction and second that functions in the biosynthetic direction; this permits independent regulation of catabolism and anabolism
 4. Coupling some biosynthetic reactions with the breakdown of ATP (or other nucleoside triphosphates) drives the anabolic pathways irreversibly in the direction of biosynthesis
 5. In eucaryotic cells, anabolic and catabolic reactions involving the same constituents are frequently located in separate compartments for simultaneous but independent operation
 6. Catabolic and anabolic pathways use different cofactors: catabolic oxidations produce NADH, which is a substrate for electron transport, while NADPH acts as a reductant for anabolic pathways
 - B. Once macromolecules have been made from simpler precursors, cell structures (e.g., ribosomes) form spontaneously from the macromolecules by a process known as self-assembly
- III. The Photosynthetic Fixation of Carbon Dioxide
 - A. Three different processes for converting carbon dioxide into organic carbon are known
 1. Calvin cycle (reductive pentose phosphate cycle)-observed in photosynthetic eucaryotes and many photosynthetic bacteria
 2. Reductive TCA cycle-used by some archaea and bacteria
 3. Acetyl-CoA pathway-used by methanogens, sulfate reducers, and acetogens
 - B. Calvin cycle
 1. Consists of three phases
 - a. The carboxylation phase-the enzyme ribulose 1,5-bisphosphate carboxylase catalyzes the addition of carbon dioxide to ribulose 1,5-bisphosphate, forming two molecules of 3-phosphoglycerate

- b. The reduction phase-3-phosphoglycerate is reduced to glyceraldehyde 3-phosphate
 - c. The regeneration phase-a series of reactions is used to regenerate ribulose 1,5-bisphosphate and to produce carbohydrates such as fructose and glucose; this phase is similar to the pentose phosphate pathway and involves transketolase and transaldolase reactions
 - 2. Each carbon dioxide takes three ATP molecules and two NADPH molecules, thus the formation of a single glucose molecule requires six turns through the cycle with an expenditure of 18 ATP molecules and 12 NADPH molecules; sugars formed in the Calvin cycle can then be used to synthesize other essential molecules
- IV. Synthesis of Sugars and Polysaccharides
 - A. Heterotrophs synthesize glucose from noncarbohydrate precursors in a process called gluconeogenesis; the gluconeogenic pathway is a functional reversal of glycolysis-it shares seven enzymes with the glycolytic pathway, reversing their catabolic direction, and uses several distinct enzymes or multi-enzyme systems to catalyze steps that cannot be directly reversed
 - B. Once glucose and fructose are synthesized by gluconeogenesis, other sugars are manufactured; several of these other sugars are synthesized while attached to a nucleoside diphosphate
 - C. Polysaccharide production also requires the use of nucleoside diphosphate sugars as precursors
- V. The Assimilation of Inorganic Phosphorus, Sulfur, and Nitrogen
 - A. Phosphorus assimilation
 - 1. Inorganic phosphates are incorporated through the formation of ATP by photophosphorylation, oxidative phosphorylation, and substrate-level phosphorylation
 - 2. Organic phosphates obtained from the surroundings are hydrolyzed to release inorganic phosphates by enzymes called phosphatases
 - B. Sulfur assimilation
 - 1. Organic sulfur in the form of cysteine and methionine can be obtained from external sources
 - 2. Assimilatory sulfate reduction is used to reduce inorganic sulfate before it is incorporated into cysteine
 - C. Nitrogen assimilation
 - 1. Ammonia incorporation
 - a. Many microorganisms use reductive amination to make alanine and glutamate, which are then used as sources of amino groups; the amino groups are transferred from alanine or glutamate to other carbon skeletons by transamination reactions
 - b. Other microorganisms use the enzymes glutamine synthetase and glutamate synthase to synthesize glutamate, which then acts as an amino group donor in transaminase reactions
 - 2. Assimilatory nitrate reduction-involves the reduction of nitrate to nitrite, then to hydroxylamine, and finally to ammonia, which can then be incorporated by the routes described above
 - 3. Nitrogen fixation-the reduction of atmospheric nitrogen to ammonia; this is catalyzed by the enzyme nitrogenase, which is found in only a

few species of bacteria; nitrogen fixation requires an expenditure of 16 ATP molecules; the ammonia produced can be incorporated into organic molecules by the processes described above

- VI. The Synthesis of Amino Acids
 - A. Involves attachment of an amino group to a carbon skeleton
 - B. Carbon skeletons are derived from acetyl-CoA and from intermediates of the TCA cycle, glycolysis, and the pentose phosphate pathway
- VII. Anaplerotic Reactions
 - A. Biosynthetic functions of the TCA cycle are so important that many of its intermediates must be synthesized even when the TCA cycle is not functioning to catabolize pyruvate or to provide NADH for electron transport
 - B. Anaplerotic reactions replenish TCA cycle intermediates so that biosynthesis can occur; two major types of anaplerotic reactions have been observed
 - 1. Anaplerotic carbon dioxide fixation (e.g., pyruvate carboxylase reaction)
 - 2. Glyoxylate cycle-used by microorganisms that can grow on acetate as a sole carbon source; is a modified TCA cycle
- VIII. The Synthesis of Purines, Pyrimidines, and Nucleotides
 - A. These molecules are critical for all cells because they are used in the synthesis of ATP, several cofactors, RNA, and DNA
 - B. Purine biosynthesis-very complex pathway in which seven different molecules (including folic acid) contribute parts to the final purine skeleton; the first purine product is the nucleotide inosinic acid, from which all other purine nucleotides can be made
 - C. Pyrimidine biosynthesis-aspartic acid and carbamoyl phosphate form the initial pyrimidine product (orotic acid), which can then be converted to pyrimidine nucleotides
- IX. Lipid Synthesis
 - A. Fatty acid synthesis is catalyzed by fatty acid synthetase using the substrates acetyl-CoA and malonyl-CoA, the reductant NADPH, and a small protein called acyl carrier protein, which carries the growing fatty acid chain; the fatty acid is lengthened by adding two carbons at a time to its carboxyl end
 - B. Triacylglycerols are formed from the reduction of dihydroxyacetone phosphate (a glycolytic pathway intermediate) to glycerol 3-phosphate, which then undergoes esterification with two fatty acids to form phosphatidic acid; this can then be used to produce triacylglycerol
 - C. Phospholipids are also produced from phosphatidic acid using a cytidine diphosphate (CDP) carrier
- X. Peptidoglycan Synthesis
 - A. A multistep process that involves two carriers: uridine diphosphate and bactoprenol; during the process a peptidoglycan repeat unit is formed and is attached to the growing peptidoglycan chain after being transported across the cytoplasmic membrane; crosslinks are then formed by transpeptidation
 - B. Peptidoglycan synthesis is very vulnerable to disruption by antimicrobial agents, including antibiotics such as penicillin; inhibition of any step in the process weakens the cell wall and can cause lysis
- XI. Patterns of Cell Wall Formation

- A. Autolysins carry out limited digestion of peptidoglycan, and provide acceptor ends for the addition of new peptidoglycan units
- B. Two general patterns of cell wall synthetic activity have been observed
 - 1. Many gram-positive cocci have only one or a few growth zones, usually at the site of septum formation
 - 2. Rod-shaped bacteria usually have growth sites scattered along the cylindrical portion of the cell as well as at the site of septum formation

Chapter Web Links

Graphics Gallery

(<http://www.accessexcellence.org/AB/GG/#Anchor-Genetics-35326>)

Graphics Gallery - click on Cell Processes for a series of labeled diagrams with explanations.

The Diversity of Metabolism in Prokaryotes.

(<http://www.bact.wisc.edu/Bact303/bact303metabolism>)

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