1 The Foundations of Biochemistry

Life Arose on Earth around 4 Billion Years Ago

- simple microorganisms:
  - extracted energy from chemical compounds and sunlight
  - used energy to make **biomolecules** from the simple elements and compounds on the Earth's surface

P1 Principle 1 (1 of 2)

Cells are the fundamental unit of life. Although they vary in complexity and can be highly specialized for their environment or function within a multicellular organism, they share remarkable similarities.

P2 Principle 2 (1 of 6)

Cells use a relatively small set of carbon-based metabolites to create polymeric machines, supramolecular structures, and information repositories. The chemical structure of these components defines their cellular function. The collection of molecules carries out a program, the end result of which is reproduction of the program and self-perpetuation of that collection of molecules—in short, life.

P3 Principle 3 (1 of 5)

Living organisms exist in a dynamic steady state, never at equilibrium with their surroundings. Following the laws of thermodynamics, living organisms extract energy from their surroundings and employ it to maintain homeostasis and do useful work. Essentially all of the energy obtained by a cell comes from the flow of electrons, driven by sunlight or by metabolic redox reactions.

P4 Principle 4 (1 of 5)

Cells have the capacity for precise self-replication and self-assembly using chemical information stored in the genome. A single bacterial cell placed in a sterile nutrient medium can give rise to a billion identical “daughter” cells in 24 hours. Each cell is a faithful copy of the original, its construction directed entirely by information contained in the genetic material of the original cell. On a larger scale, the progeny of vertebrate animals share a striking resemblance to their parents, also the result of their inheritance of parental genes.

P5 Principle 5 (1 of 3)

Living organisms change over time by gradual evolution. The result of eons of evolution is an enormous diversity of life forms, fundamentally related through their shared ancestry, which can be seen at the molecular level in the similarity of gene sequences and protein structures.

What Is Biochemistry?

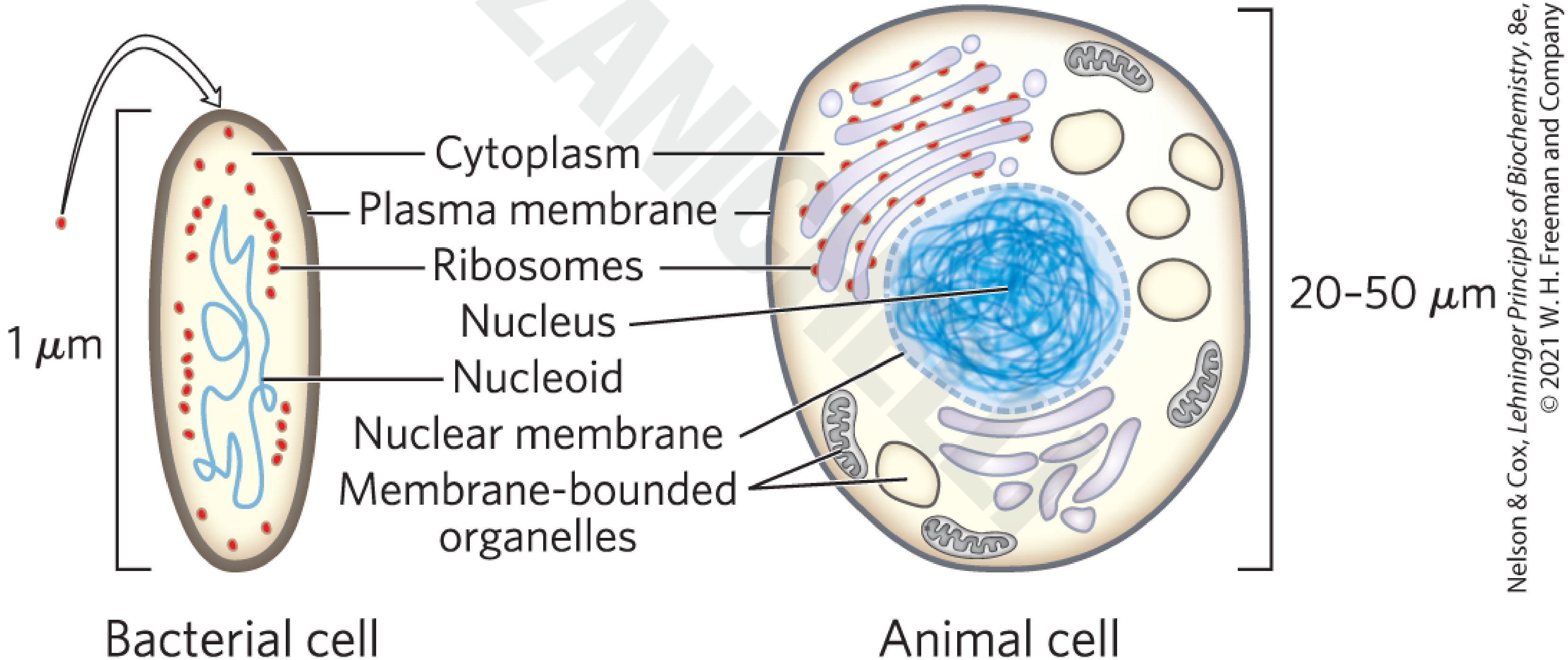
- **biochemistry** = describes the structures, mechanisms, and chemical processes shared by all organisms

1.1 Cellular Foundations

P1 Principle 1 (2 of 2)

Cells are the fundamental unit of life. Although they vary in complexity and can be highly specialized for their environment or function within a multicellular organism, they share remarkable similarities.

Cells Are the Structural and Functional Units of All Living Organisms



The Plasma Membrane

- **plasma membrane** = defines the periphery of the cell
  - composed of lipid and protein molecules
  - thin, flexible, hydrophobic barrier around the cell
  - contains embedded transport proteins, receptor proteins, and membrane enzymes

Cytoplasm Contains Cytosol and Suspended Particles

- **cytoplasm** = internal volume enclosed by the plasma membrane
  - composed of the **cytosol** (an aqueous solution) and a variety of suspended particles (such as mitochondria, chloroplasts, **ribosomes**, and **proteasomes**)

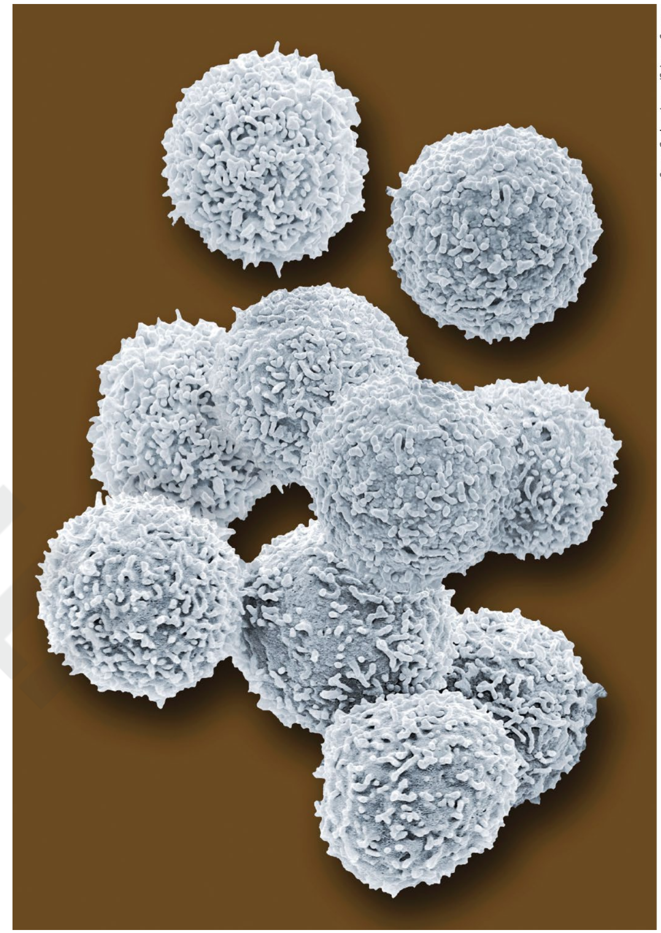
- **cytosol** = highly concentrated solution
  - contains enzymes, RNA, amino acids, nucleotides, **metabolites**, **coenzymes**, and inorganic ions

The Nucleoid or Nucleus of a Cell Stores the Genome

- **genome** = complete set of genes, composed of DNA
  - bacteria and archaea (formally grouped as **prokaryotes**) store their genome in a **nucleoid**
  - **eukaryotes** store their genome in a membrane-enclosed **nucleus**

Cellular Dimensions Are Limited by Diffusion

- cells are microscopic:
  - animal and plant cells: 5 to 100 μm in diameter
  - unicellular microorganisms: 1 to 2 μm long
- upper limit of cell size is likely set by the rate of transport and the need to deliver O_2 to all parts of the cell
  - as size increases, surface-to-volume ratio decreases



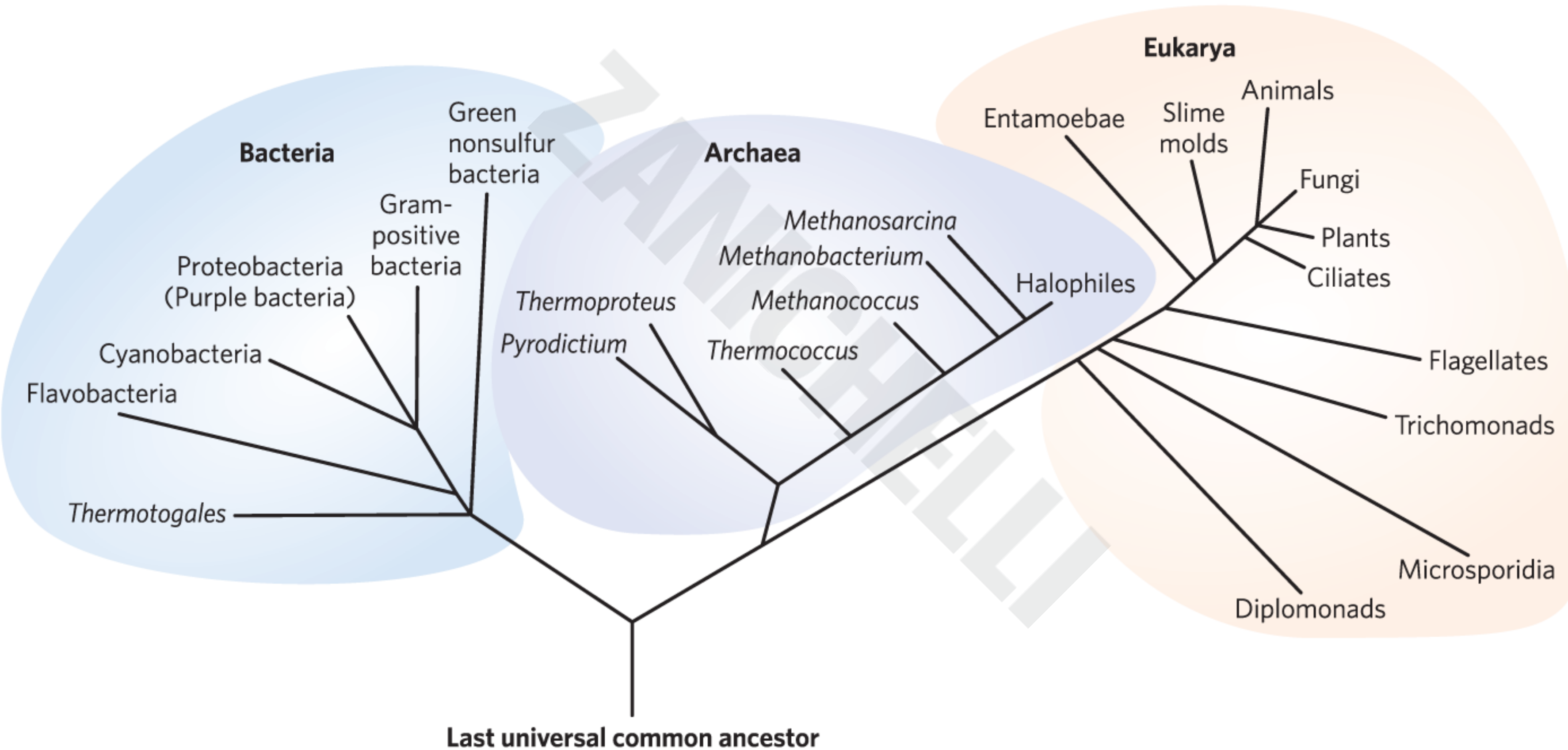
Steve Gschmeissner/Science Source.

human lymphocytes

Organisms Belong to Three Distinct Domains of Life

- **Bacteria** = inhabit soils, surface waters, and the tissues of other living or decaying organisms
- **Archaea** = inhabit extreme environments
- **Eukarya** = all eukaryotic organisms
  - more closely related to archaea than bacteria

Phylogeny of the Three Domains of Life



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Archaea and Bacteria Subgroups Are Distinguished by Their Habitats

- **aerobic** = plentiful supply of O_2; organisms transfer electrons from fuel to O_2 for energy

- **anaerobic** = devoid of O_2; organisms transfer electrons to nitrate, sulfate or CO_2 for energy
  - *obligate* anaerobes = die when exposed to O_2
  - *facultative* anaerobes = can live with or without O_2

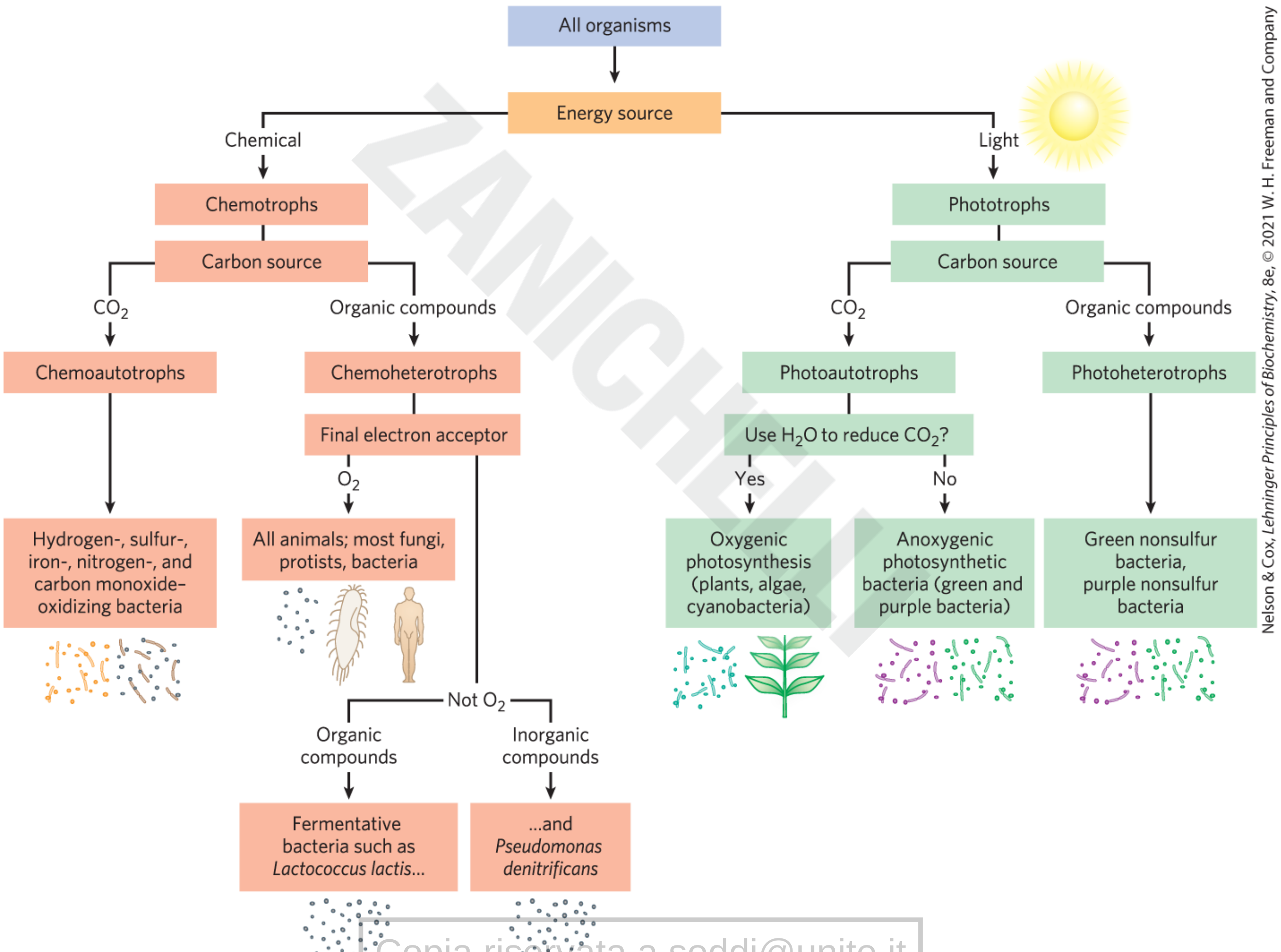
P3 Principle 3 (2 of 5)

Living organisms exist in a dynamic steady state, never at equilibrium with their surroundings. Following the laws of thermodynamics, living organisms extract energy from their surroundings and employ it to maintain homeostasis and do useful work. Essentially all of the energy obtained by a cell comes from the flow of electrons, driven by sunlight or by metabolic redox reactions.

Organisms Differ Widely in Their Sources of Energy and Biosynthetic Precursors

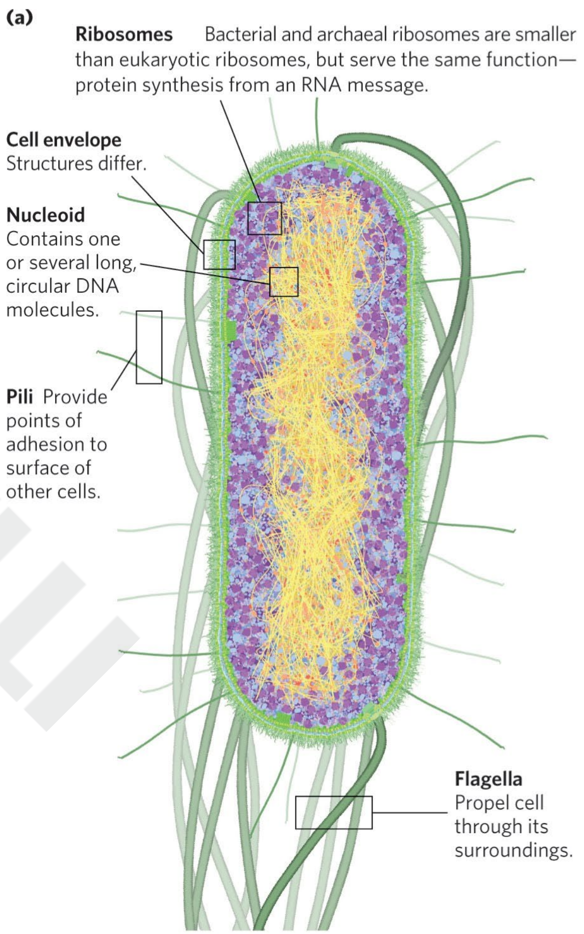
- **phototrophs** = trap and use sunlight
- **chemotrophs** = derive energy from oxidation of a chemical fuel
- **autotrophs** = can synthesize all their biomolecules directly from CO_2
- **heterotrophs** = require some preformed organic nutrients made by other organisms

Classifying Organisms According to Their Source of Energy



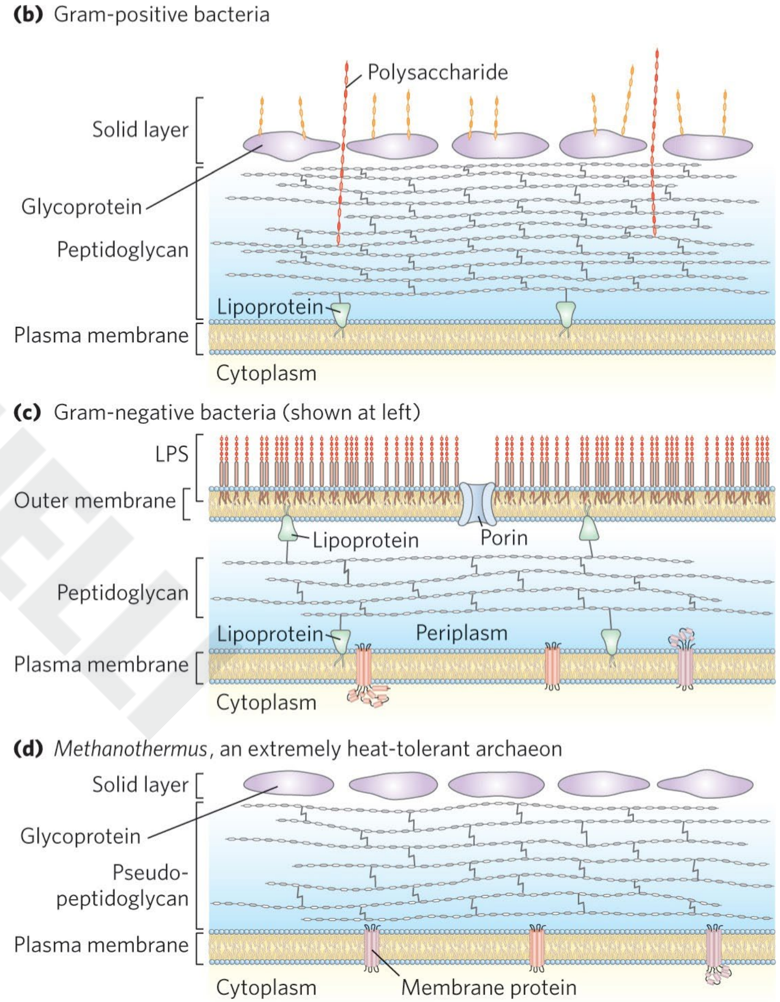
Bacteria and Archaeal Cells Share Common Features but Differ in Important Ways

- **cell envelope** = composed of plasma membrane, outer membrane, and peptidoglycan (high molecular weight polymer)



Bacterial and Archaeal Cell Envelopes

- gram-positive bacteria:
  - colored by Gram's stain
  - thick peptidoglycan layer outside plasma membrane
  - lack an outer membrane
- gram-negative bacteria:
  - outer membrane composed of a lipid bilayer
- archaea:
  - layer of peptidoglycan or protein confers rigidity on their cell envelopes



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P2 Principle 2 (2 of 6)

Cells use a relatively small set of carbon-based metabolites to create polymeric machines, supramolecular structures, and information repositories. The chemical structure of these components defines their cellular function. The collection of molecules carries out a program, the end result of which is reproduction of the program and self-perpetuation of that collection of molecules—in short, life.

The *E. coli* Cytoplasm

- contains ribosomes, enzymes, metabolites, cofactors, and inorganic ions.

- the nucleoid contains a single, circular molecule of DNA

- **plasmids** = smaller, circular segments of DNA that confer resistance to toxins and antibiotics in the environment

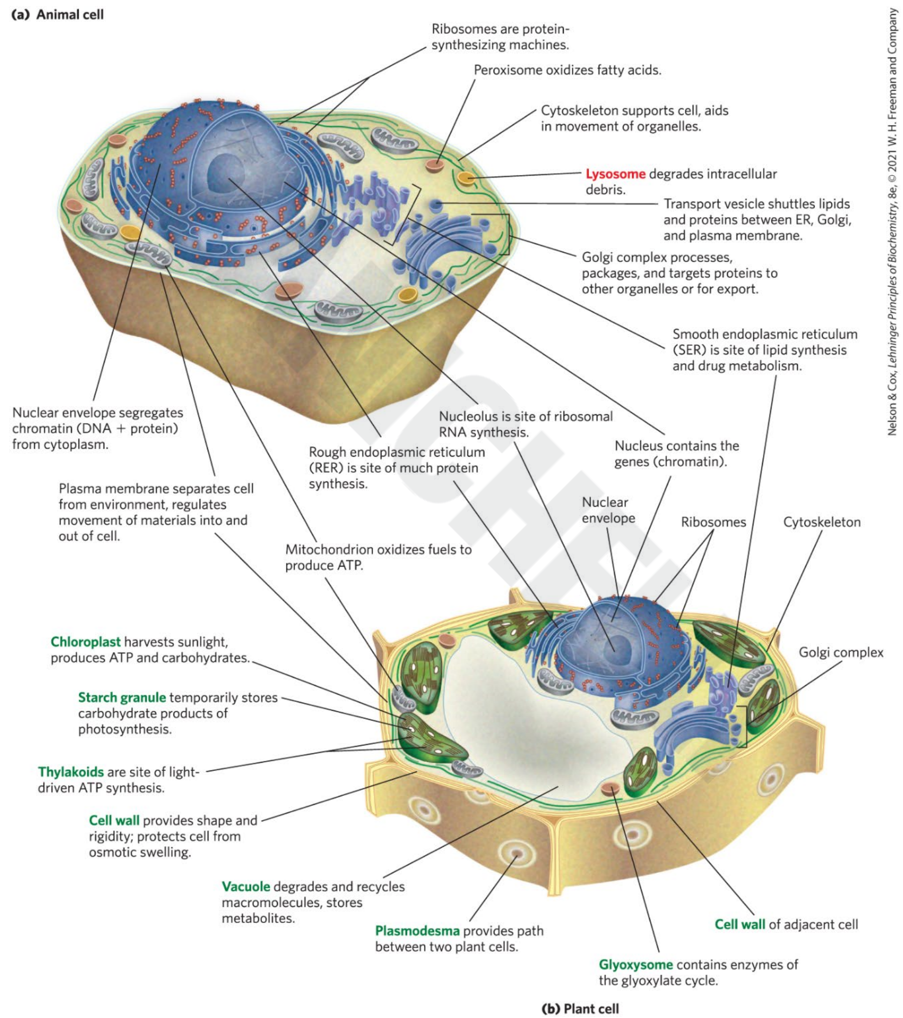
Eukaryotic Cells Have a Variety of Membranous Organelles, Which Can Be Isolated for Study

- **mitochondria** = the site of most of the energy-extracting reactions of the cell
- **endoplasmic reticulum** and **Golgi complexes** = play central roles in the synthesis and processing of lipids and membrane proteins
- **peroxisomes** = site of the oxidation of very-long-chain fatty acids and detoxification of reactive oxygen species
- **lysosomes** = filled with digestive enzymes
- granules or droplets containing stored nutrients, such as starch and fat

Plant Cell Organelles

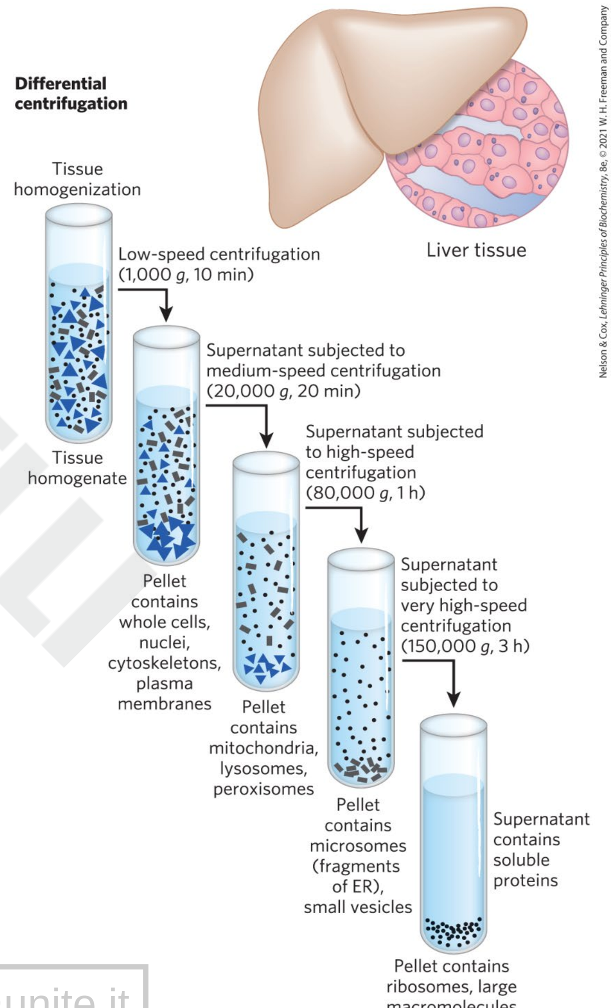
- **vacuoles** = store large quantities of organic acids
- **chloroplasts** = where sunlight drives the synthesis of ATP (adenosine triphosphate) in the process of photosynthesis

Eukaryotic Cell Structure



Subcellular Fractionation of Tissue

- first step = gently disrupt cells or tissues by physical shear to rupture the plasma membrane
- second step = centrifuge the homogenate
- organelles differ in size and sediment at different rates

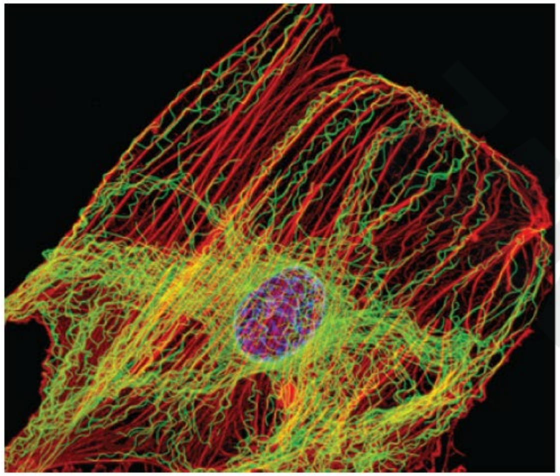


The Cytoplasm Is Organized by the Cytoskeleton and Is Highly Dynamic

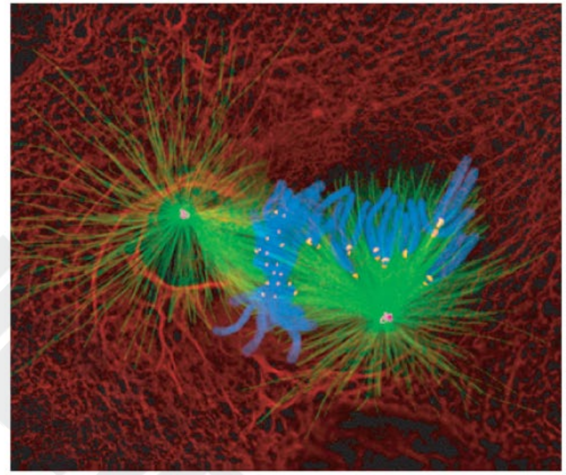
- **cytoskeleton** = three-dimensional network of protein filaments in eukaryotic cells
  - actin filaments
  - microtubules
  - intermediate filaments

- filaments undergo constant disassembly into their protein subunits and reassembly into filaments

Cytoskeletal Filaments



(a)



(b)

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actin filaments
microtubules
chromosomes

microtubules
kinetochores
chromosomes
centrosomes
intermediate filaments

The Structural Organization of the Cytoplasm

- **endomembrane system** = segregates specific metabolic processes and provides surfaces on which certain enzyme-catalyzed reactions occur

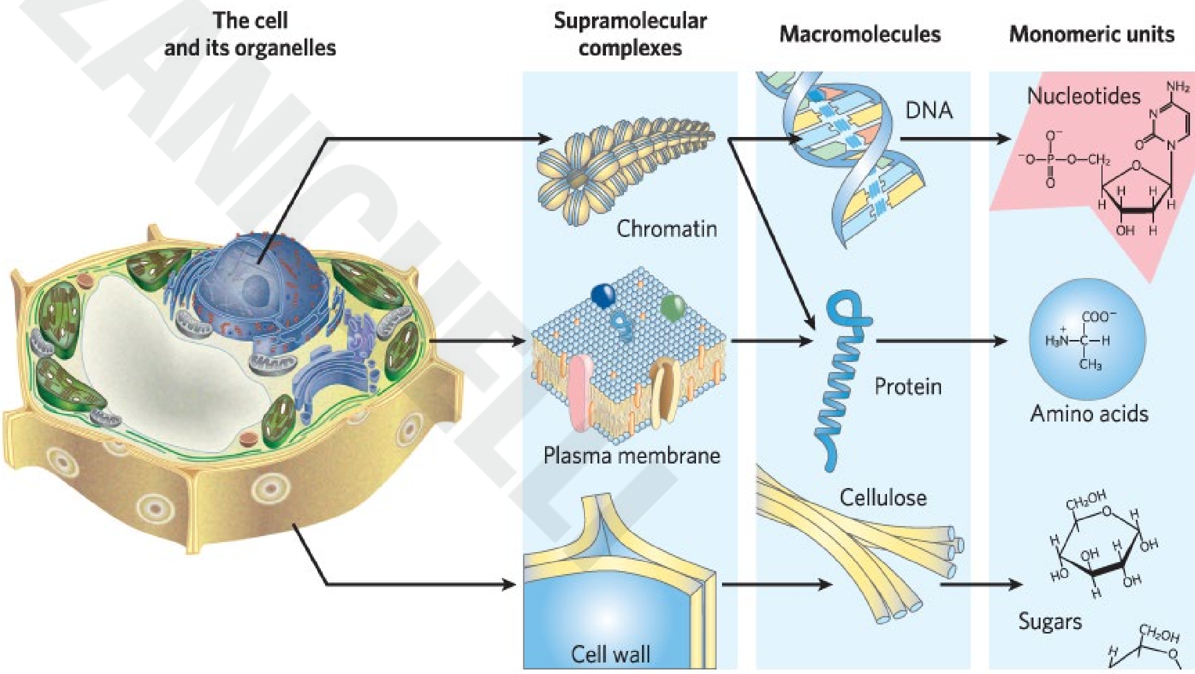
- **exocytosis** and **endocytosis** = mechanisms of transport (out of and into cells, respectively)
  - involve membrane fusion and fission
  - provide paths between the cytoplasm and the surrounding medium

P2 Principle 2 (3 of 6)

Cells use a relatively small set of carbon-based metabolites to create polymeric machines, supramolecular structures, and information repositories. The chemical structure of these components defines their cellular function. The collection of molecules carries out a program, the end result of which is reproduction of the program and self-perpetuation of that collection of molecules—in short, life.

Cells Build Supramolecular Structures

- held together by noncovalent interactions (hydrogen bonds, ionic interactions, van der Waals interactions, and the hydrophobic effect)



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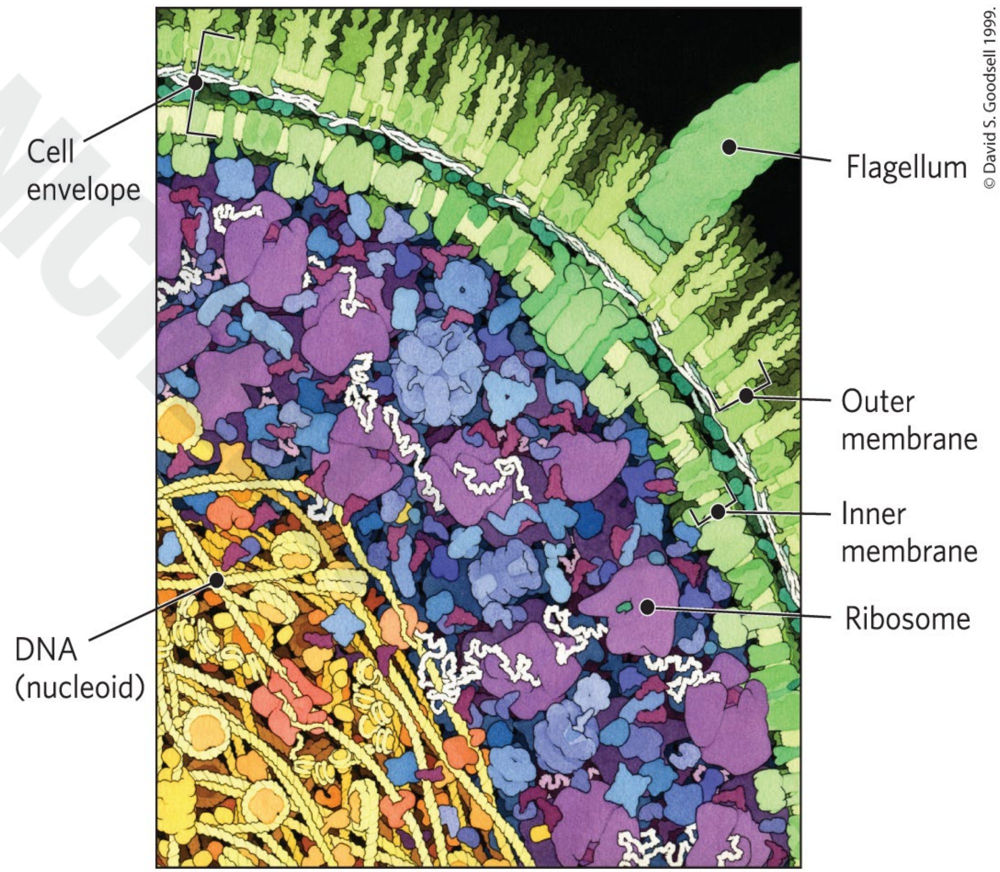
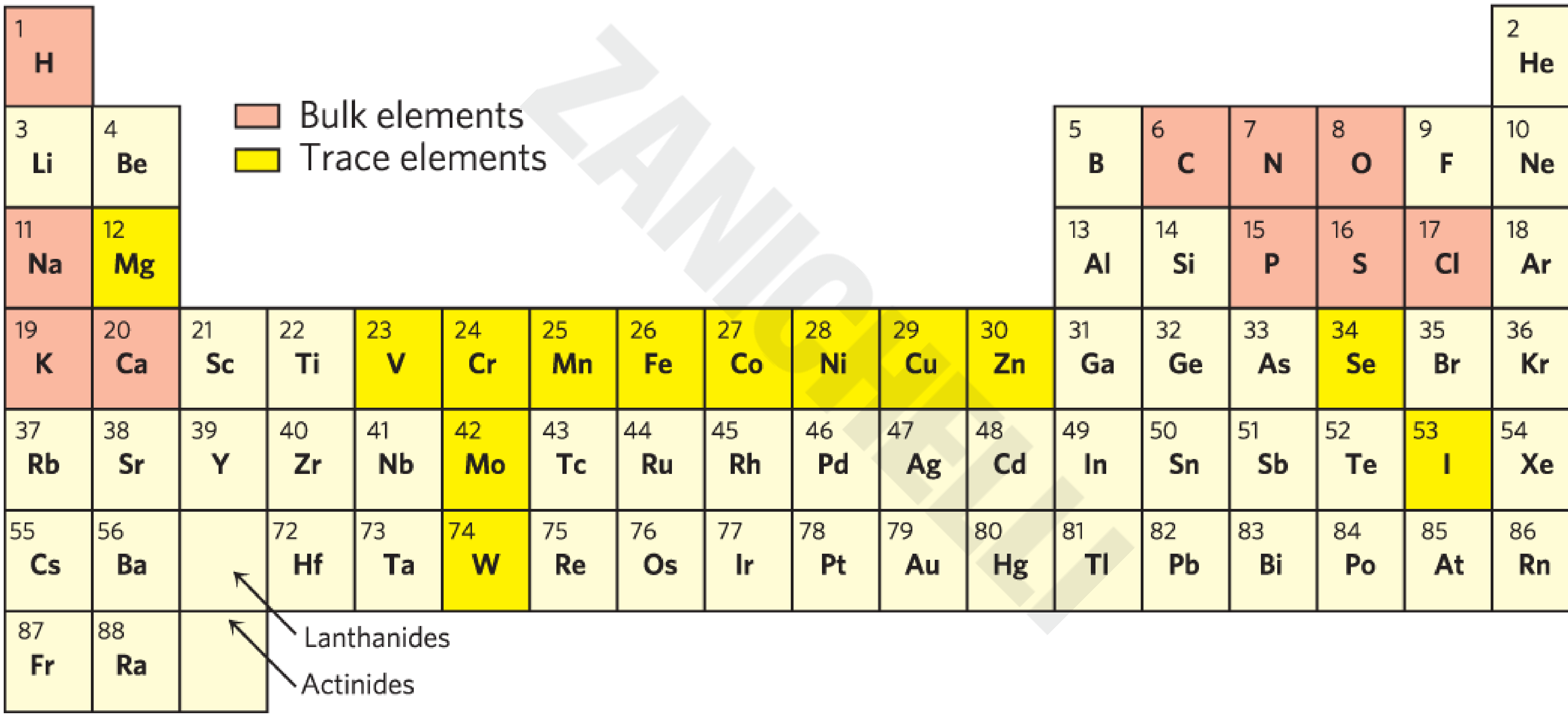
In Vitro Studies May Overlook Important Interactions among Molecules

- in vitro = “in glass”
- in vivo = “in the living”
- molecules may behave differently in vivo and in vitro

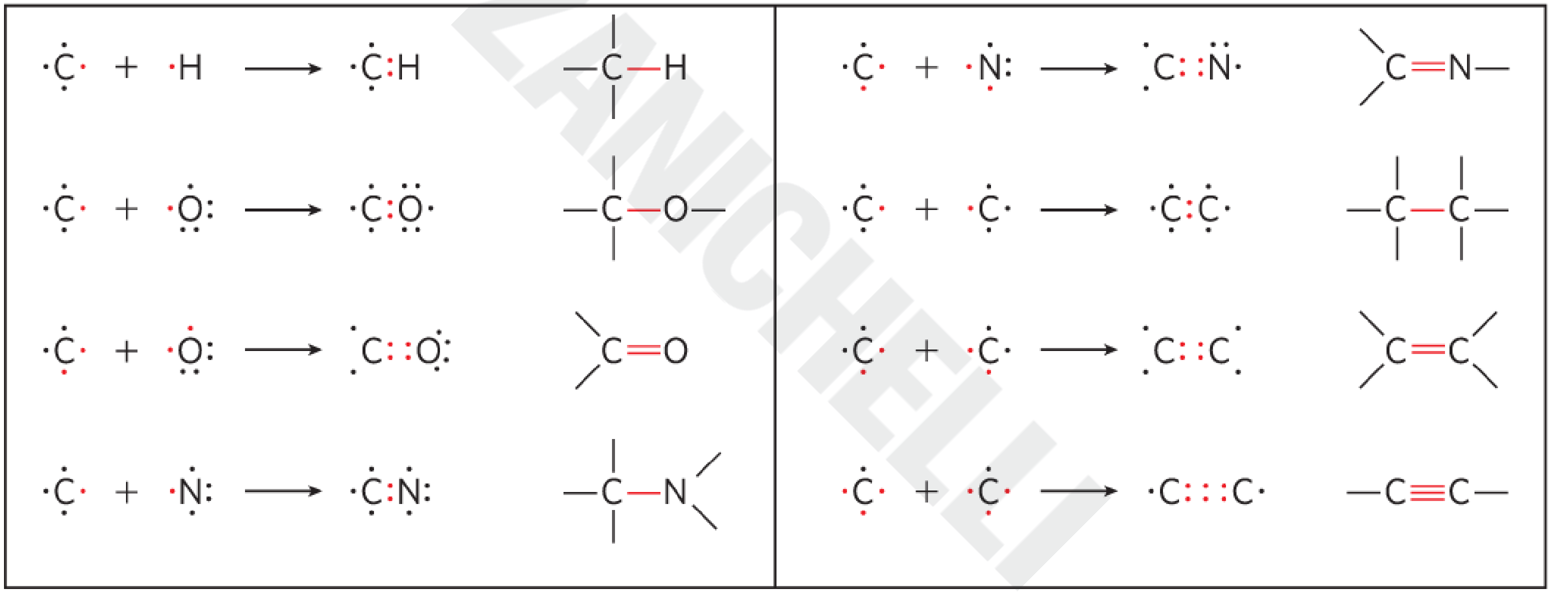


1.2 Chemical Foundations

Elements Essential to Animal Life and Health

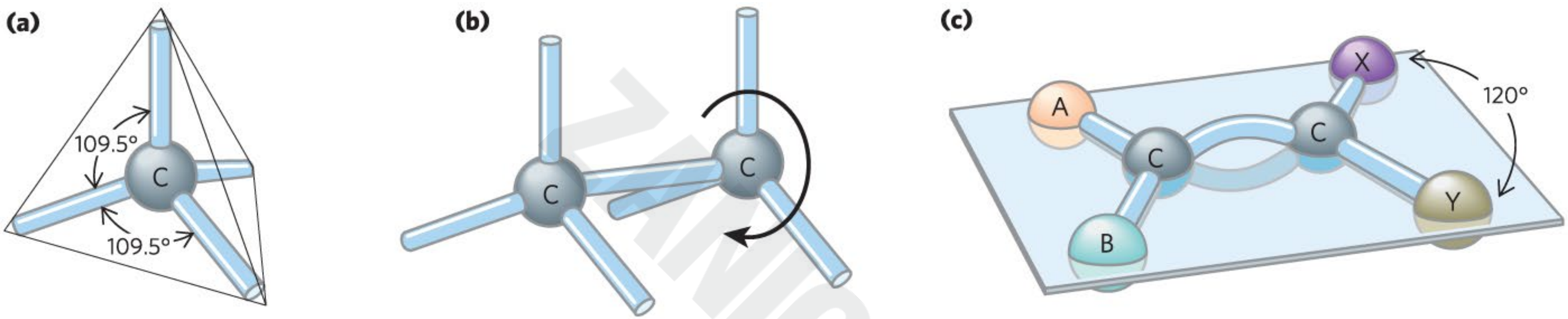


Biomolecules Are Compounds of Carbon with a Variety of Functional Groups



carbon can form covalent single, double, and triple bonds

Geometry of Carbon Bonding



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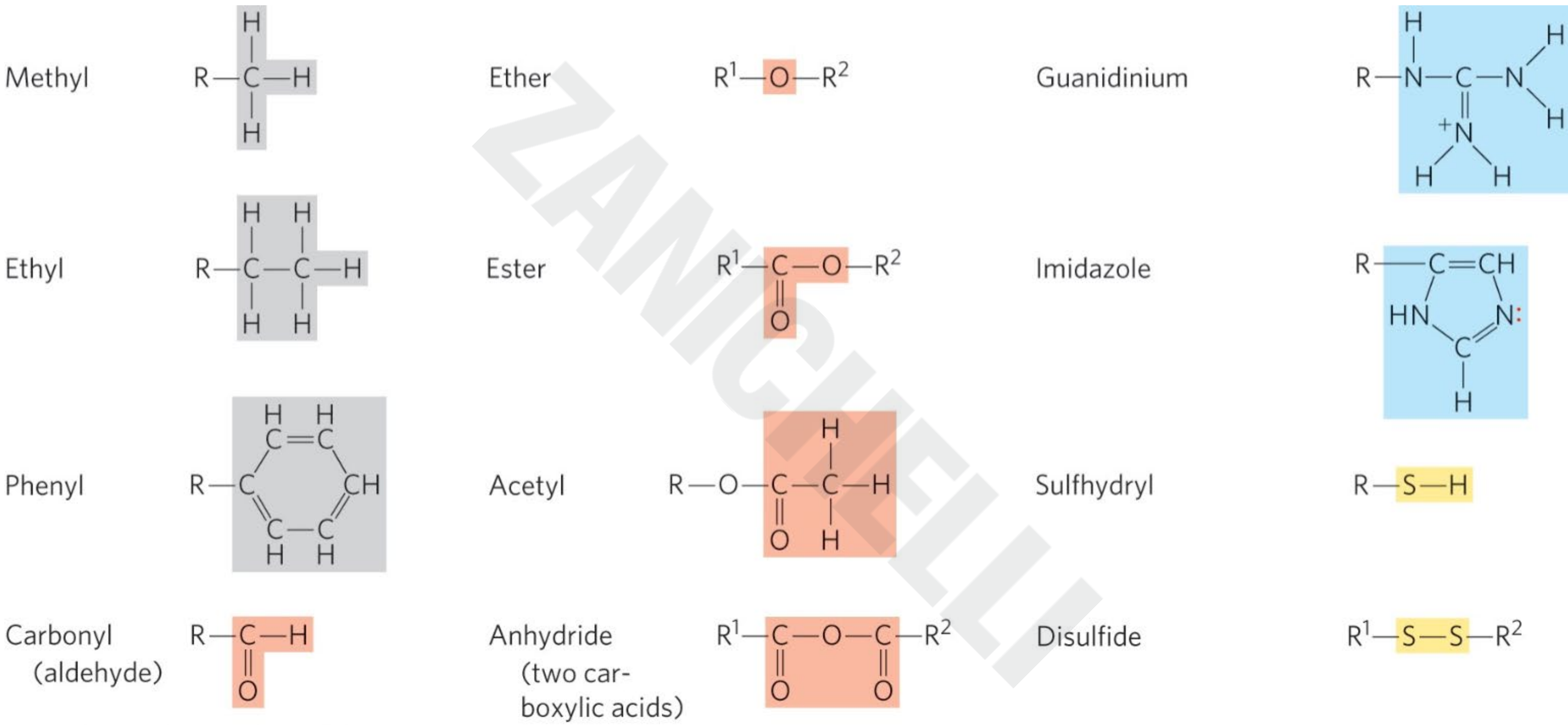
- carbon atoms have a characteristic tetrahedral arrangement of their four single bonds
- free rotation around each single bond
- limited rotation about the axis of a double bond

Common Functional Groups of Biomolecules



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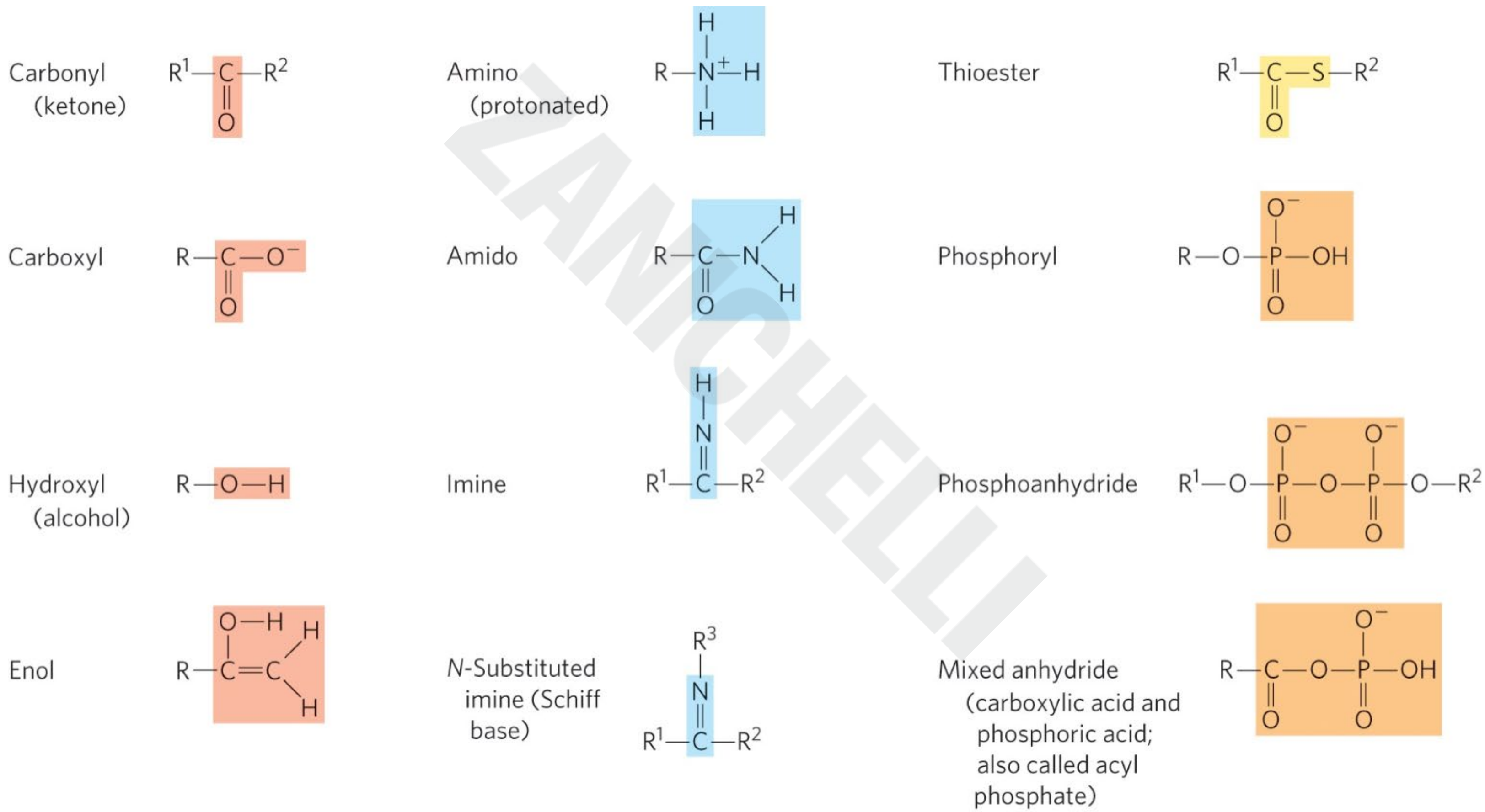
Additional Functional Groups of Biomolecules



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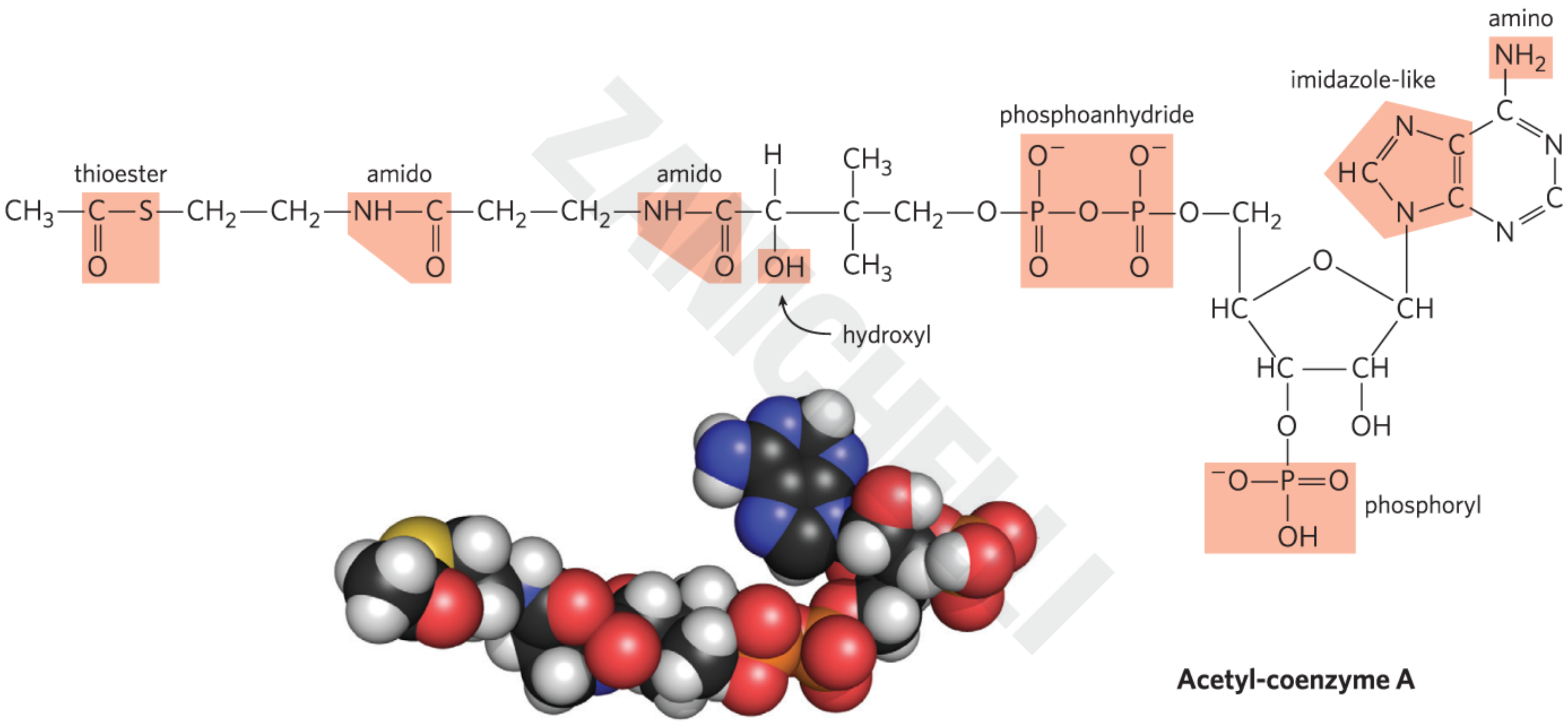
Many Biomolecules Are Polyfunctional



Acetyl-coenzyme A

Cells Contain a Universal Set of Small Molecules

- central metabolites:
  - common amino acids
  - nucleotides
  - sugars and their phosphorylated derivatives
  - mono-, di-, and tricarboxylic acids

- **secondary metabolites** = specific to the organism

- **metabolome** = entire collection of small molecules in a given cell under a specific set of conditions
  - **metabolomics** = the systematic characterization of the metabolome under very specific conditions

Macromolecules Are the Major Constituents of Cells

- **macromolecules** = polymers with molecular weights above ~5,000 that are assembled from relatively simple precursors
  - proteins
  - nucleic acids
  - polysaccharides

- **oligomers** = shorter polymers

- **informational macromolecules** = name for proteins, nucleic acids, and some oligosaccharides, given their information-rich subunit sequences

Protein Macromolecules

- **proteins** = long polymers of amino acids
  - can function as enzymes, structural elements, signal receptors, transporters

- **proteome** = sum of all the proteins functioning in a cell

- **proteomics** = the systematic characterization of this protein complement under a specific set of conditions

Nucleic Acid Macromolecules

- **nucleic acids** = DNA and RNA = polymers of nucleotides
  - store and transmit genetic information
  - some RNA molecules have structural and catalytic roles in supramolecular complexes

- **genome** = entire sequence of a cell’s DNA or RNA

- **genomics** = the characterization of the structure, function, evolution, and mapping of genomes

Polysaccharide Macromolecules

- **polysaccharides** = polymers of simple sugars
  - energy-rich fuel stores
  - rigid structural components of cell walls (in plants and bacteria)
  - extracellular recognition elements that bind to proteins on other cells

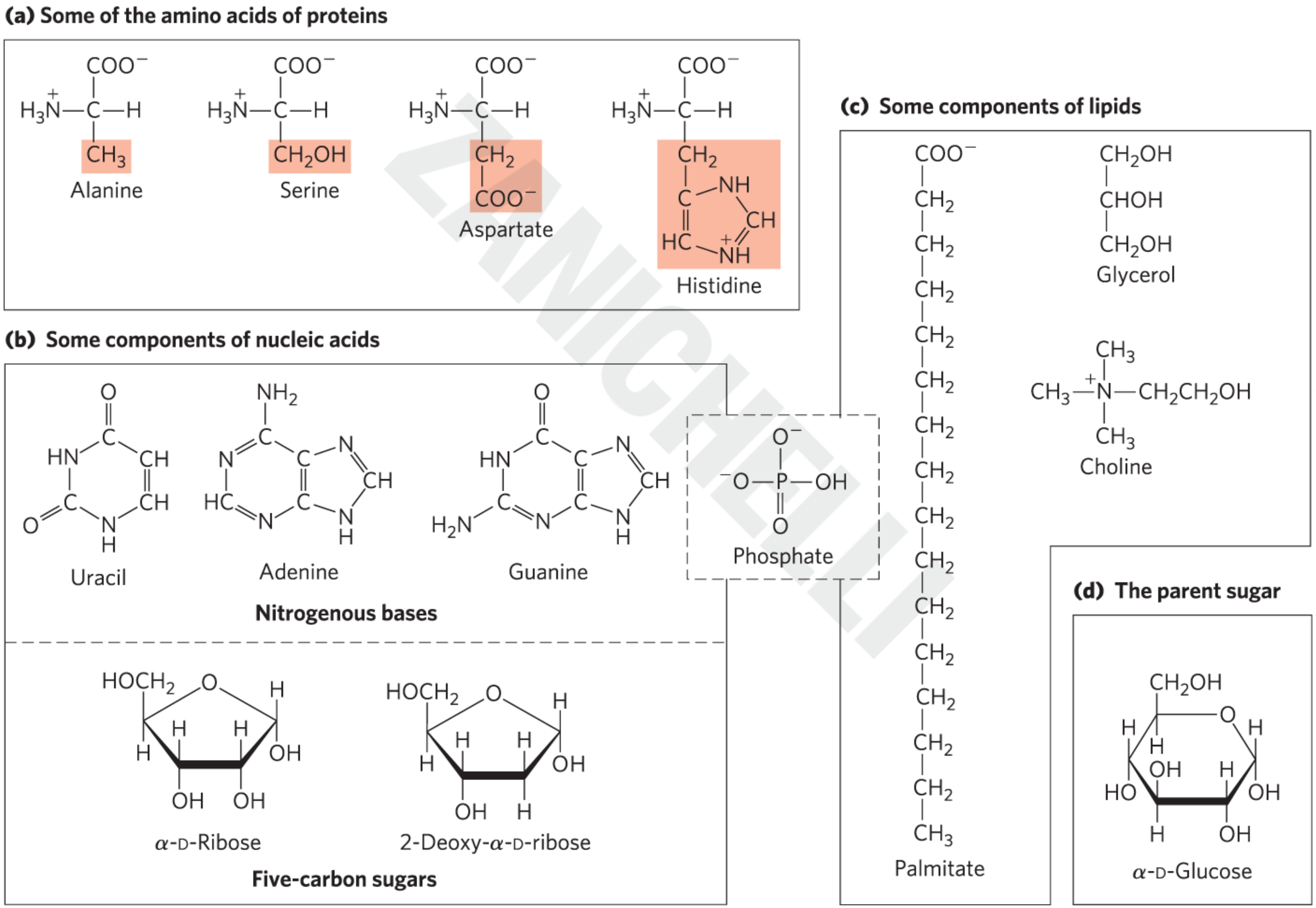
- **glycome** = entire complement of carbohydrate-containing molecules

Lipid Molecules

- **lipids** = water-insoluble hydrocarbon derivatives
  - structural components of membranes
  - energy-rich fuel stores
  - pigments
  - intracellular signals

- **lipidome** = the lipid containing molecules in a cell

Building Blocks of Biochemistry



Major Classes of Biomolecules in *E. coli* Cells

Table 1-1 Molecular Components of an *E. coli* Cell

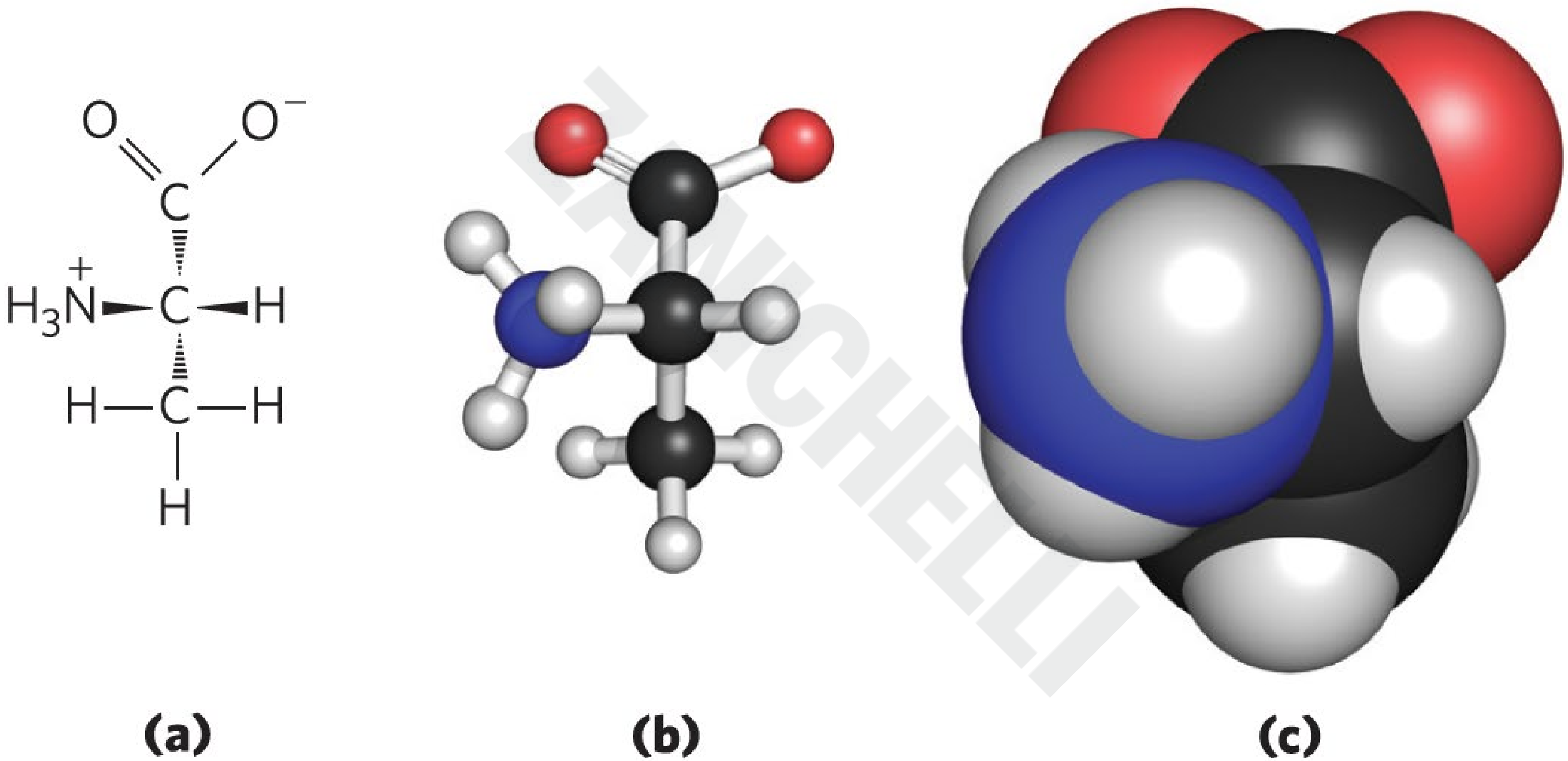
	Percentage of total weight of cell	Approximate number of different molecular species
Water	70	1
Proteins	15	3,000
Nucleic acids: DNA	1	1–4
Nucleic acids: RNA	6	>3,000
Polysaccharides	3	20
Lipids	2	50[a]
Monomeric subunits and intermediates	2	2,600
Inorganic ions	1	20

Source: A. C. Guo et al., *Nucleic Acids Res.* 41:D625, 2013.
[a]If all permutations and combinations of fatty acid substitutions are considered, this number is much larger.

Three-Dimensional Structure Is Described by Configuration and Conformation

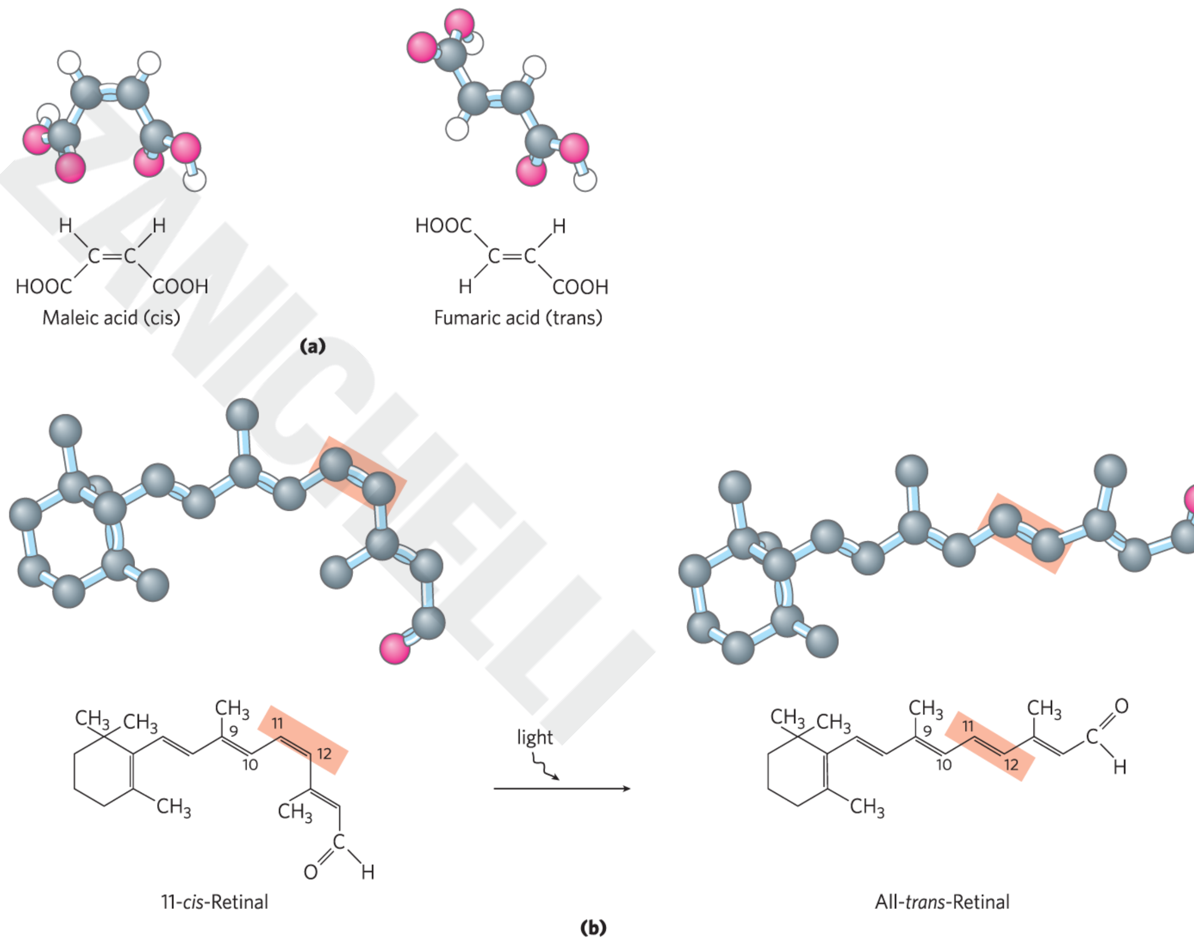
- **configuration** = the fixed spatial arrangement of atoms
- **stereoisomers** = molecules with the same chemical bonds and same chemical formula
- **stereospecific** = requiring specific conformations in the interacting molecules
  - describes typical interactions between biomolecules

Illustrating Stereochemistry



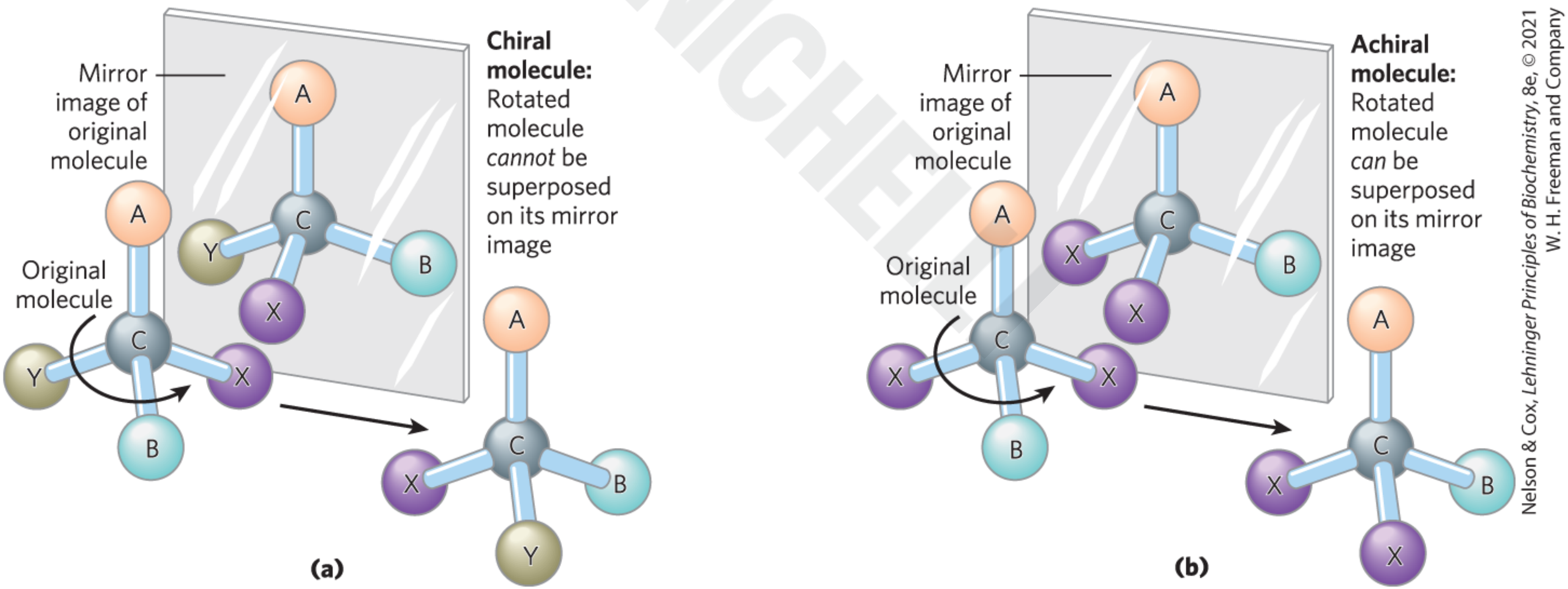
Configurations of Geometric Isomers

- **geometric isomers**, or **cis-trans isomers** = differ in the arrangement of substituent groups with respect to the double bond



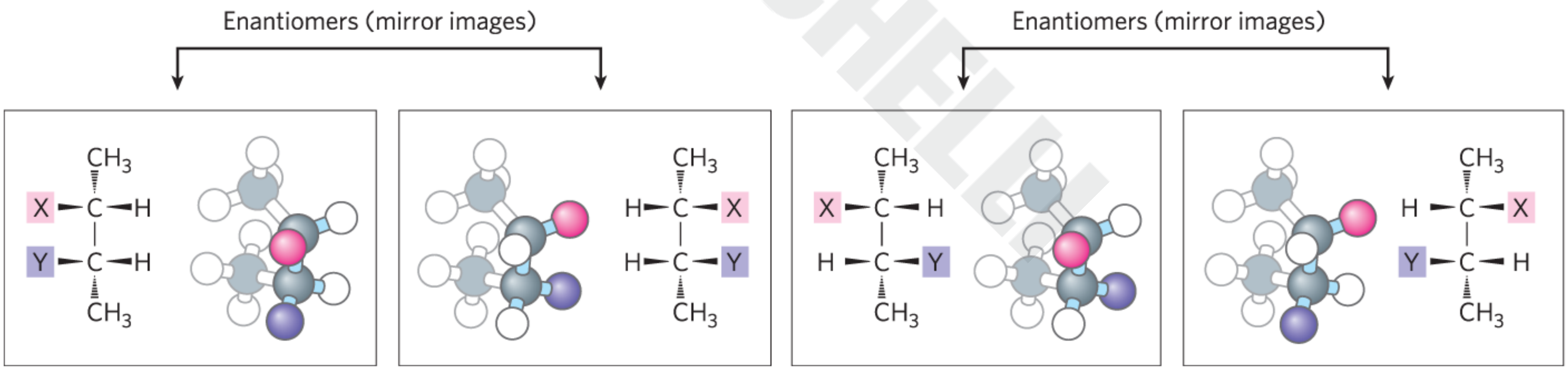
Chiral and Achiral Molecules

- **chiral centers** = asymmetric carbons
- a molecule can have 2^n stereoisomers, where n is the number of chiral carbons



Enantiomers and Diastereomers

- **enantiomers** = stereoisomers that are mirror images of each other
- **diastereomers** = stereoisomers that are not mirror images of each other



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Optical Activity of Enantiomers

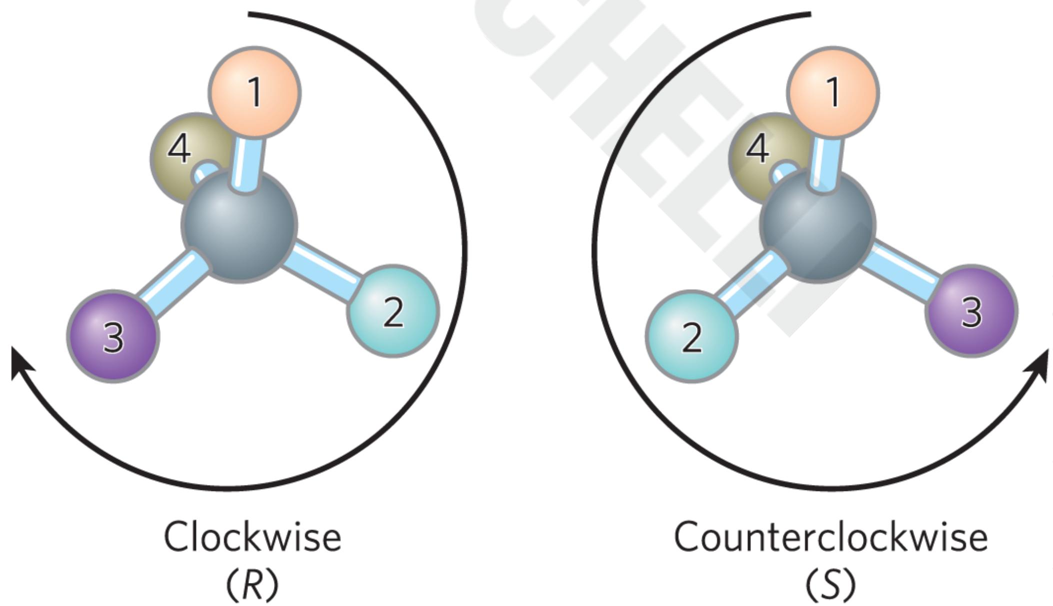
- **enantiomers** have nearly identical chemical reactivities, but differ in **optical activity**

- a **racemic mixture** (equimolar solution of two enantiomers) shows no optical rotation

Naming Stereoisomers Using the RS System

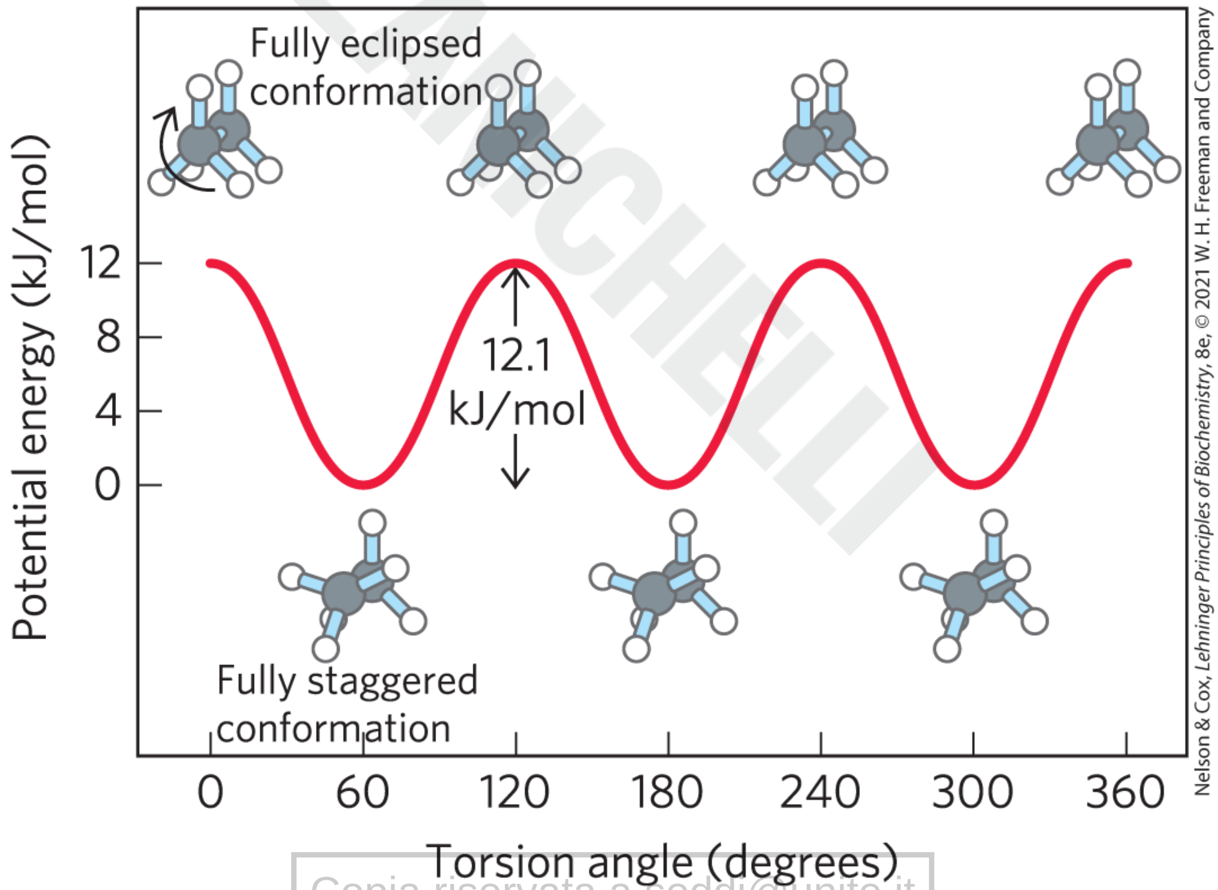
- each group attached to a chiral carbon is assigned a *priority,* where:

$$—OCH_3 > —OH > —NH_2 > —COOH > —CHO > —CH_2OH > —CH_3 > —H$$



Molecular Conformation

- **conformation** = the spatial arrangement of substituent groups that are free to assume different positions in space



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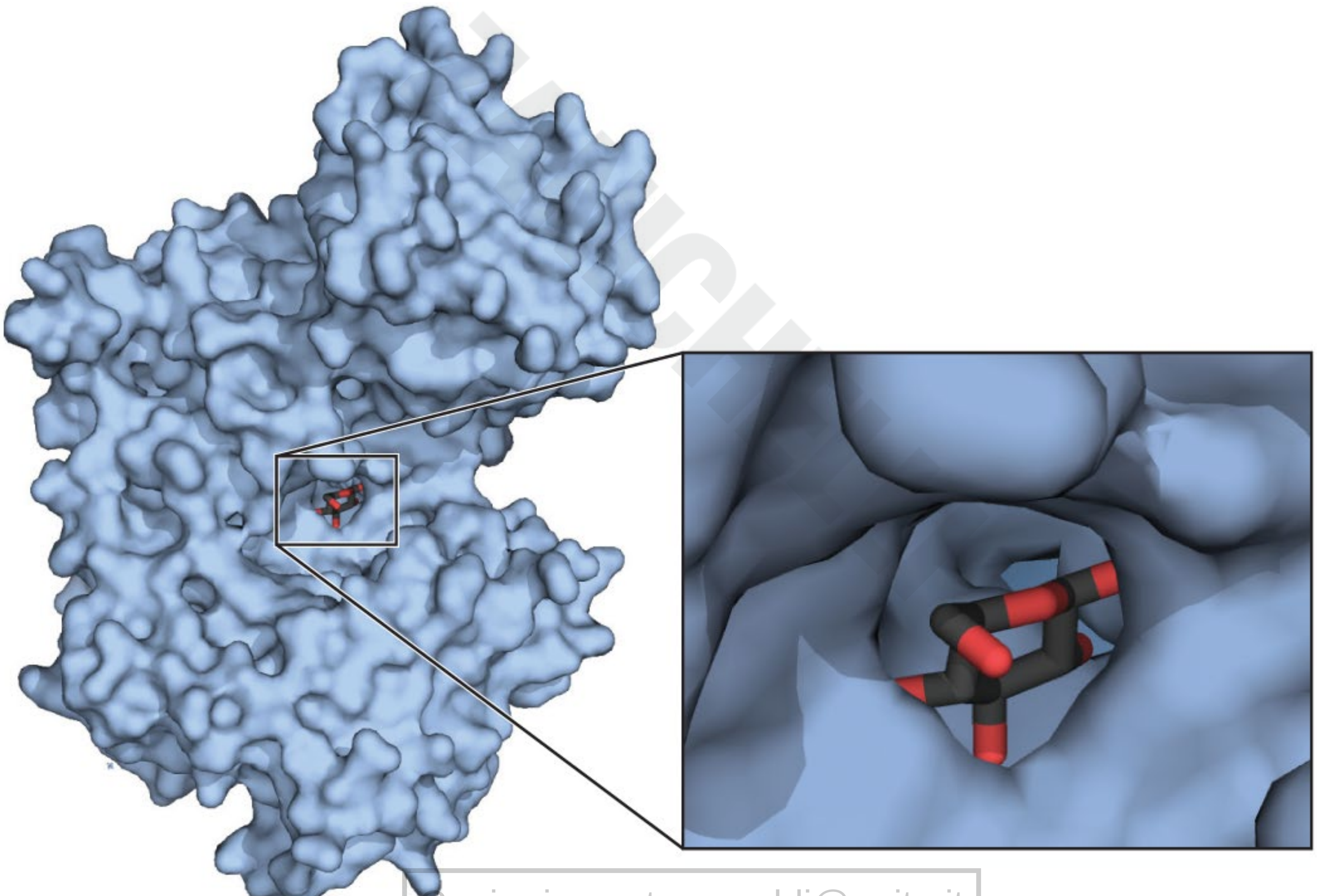
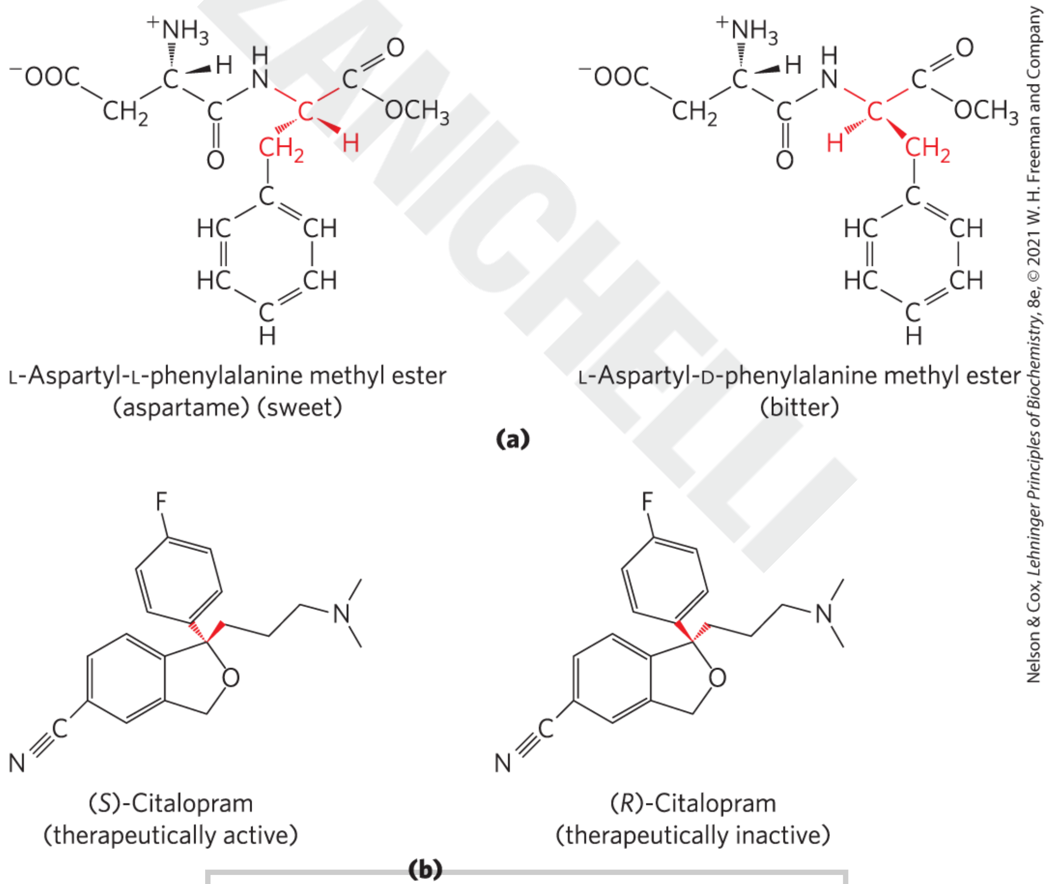
Interactions between Biomolecules Are Stereospecific



Biological Systems Can Distinguish Stereoisomers

- **stereospecificity** = the ability to distinguish between stereoisomers



1.3 Physical Foundations

Living Organisms Exist in a Dynamic Steady State, Never at Equilibrium with Their Surroundings

- small molecules, macromolecules, and supramolecular complexes are continuously synthesized and broken down
- living cells maintain themselves in a *dynamic steady state* distant from equilibrium
- maintaining steady state requires the constant investment of energy

Organisms Transform Energy and Matter from Their Surroundings

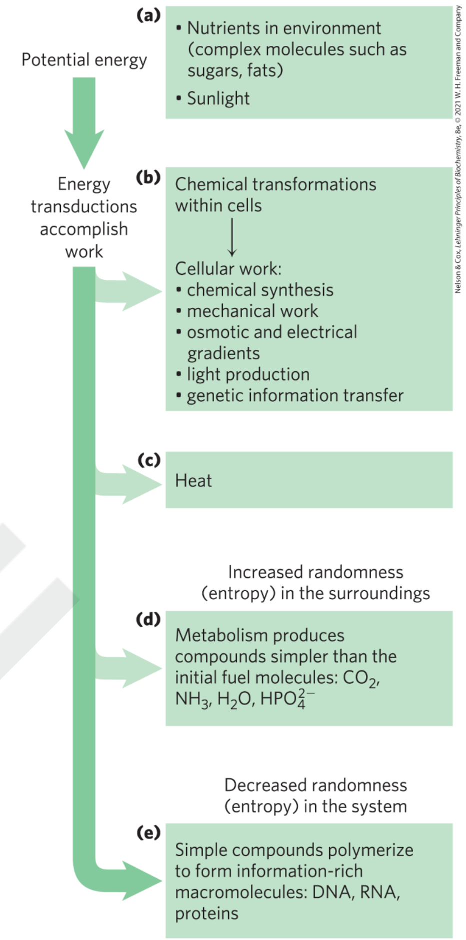
- **system** = all the constituent reactants and products, the solvent that contains them, and the immediate atmosphere

- **universe** = system and its surroundings

- types of systems:
  - **isolated** = system exchanges neither matter nor energy with its surroundings
  - **closed system** = system exchanges energy but not matter with its surroundings
  - **open system** = system exchanges both energy and matter with its surroundings

Energy Transformation in Living Organisms

- first law of thermodynamics:
  in any physical or chemical change, the total amount of energy in the universe remains constant, although the form of the energy may change



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Extracting Energy from the Surroundings

- photoautotrophs:

$$6CO_2 + 6H_2O \xrightarrow{\text{light}} C_6H_{12}O_6 + 6O_2$$

(light-driven reduction of CO_2)

- chemotrophs:

$$C_6H_{12}O_6 + 6O \rightarrow 6CO_2 + 6H_2O + \text{energy}$$

(energy-yielding oxidation of glucose)

Oxidation-Reduction Reactions

- autotrophs and heterotrophs participate in global cycles of O_2 and CO_2, driven by sunlight, making these two groups interdependent

- **oxidation-reduction reactions** = one reactant is oxidized (loses electrons) as another is reduced (gains electrons)
  - describes reactions involved in electron flow

Creating and Maintaining Order Requires Work and Energy

- second law of thermodynamics: *randomness in the universe is constantly increasing*

- **entropy, *S*** = represents the randomness or disorder of the components of a chemical system

Free Energy, *G*

- **enthalpy, *H*** = heat content, roughly reflecting the number and kinds of bonds

- **free energy, *G*,** of a closed system = $H - TS$,
  where H represents enthalpy, T represents absolute temperature, and S represents entropy

Free-Energy Change, ΔG

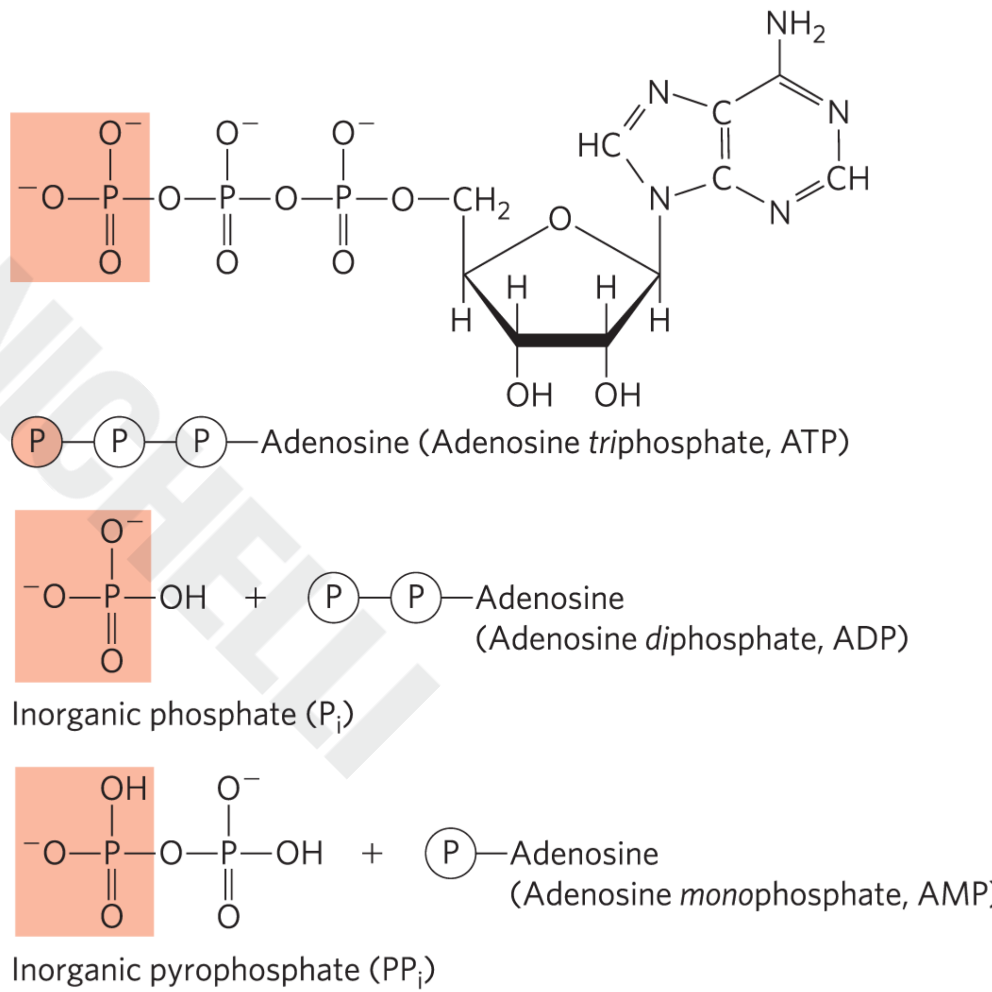
- **free-energy change, ΔG** $= \Delta H - T\Delta S$

  where ΔH is negative for a reaction that releases heat, and ΔS is positive for a reaction that increases the system's randomness

- spontaneous reactions occur when ΔG is negative

Coupling Reactions

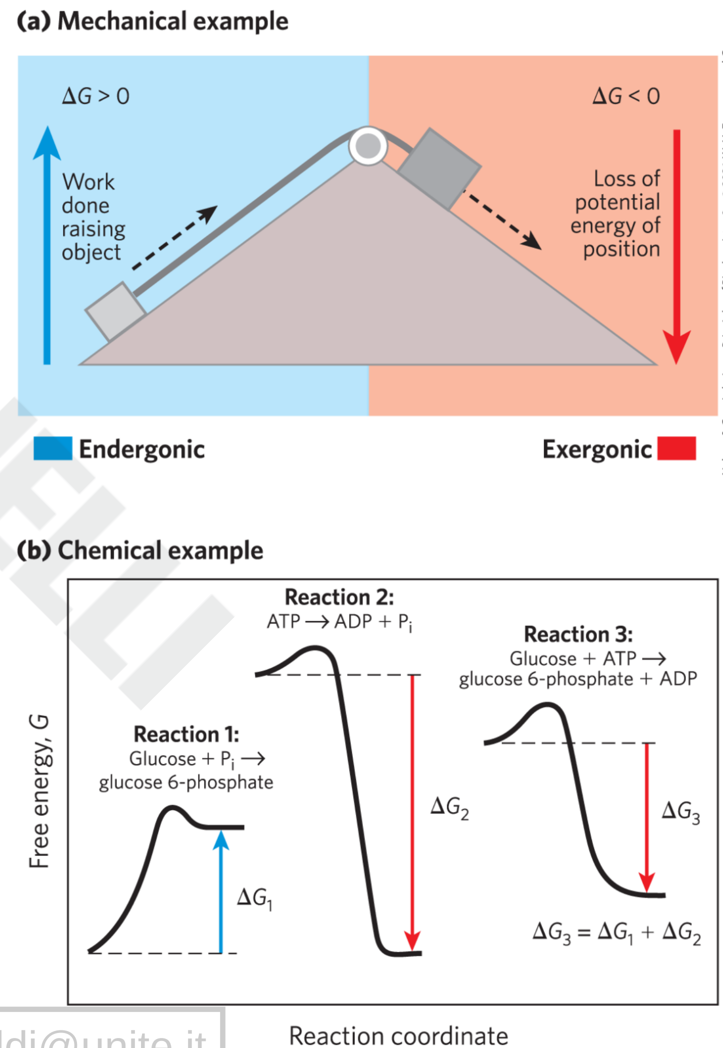
- energy-requiring (**endergonic**) reactions are often coupled to reactions that release free energy (**exergonic**)
- the breakage of phosphoanhydride bonds in ATP is highly exergonic



Energy Coupling Links Reactions in Biology

- **free-energy change, Δ*G*** = amount of energy available to do work
  - always less than the theoretical amount of energy released

- in closed systems, chemical reactions proceed spontaneously until **equilibrium** is reached



K_{eq} and $\Delta G°$ Are Measures of a Reaction's Tendency to Proceed Spontaneously

For the reaction,

$$aA + bB \longrightarrow cC + dD$$

The equilibrium constant, K_{eq}, is given by

$$K_{eq} = \frac{[C]_{eq}^{c}\,[D]_{eq}^{d}}{[A]_{eq}^{a}\,[B]_{eq}^{b}}$$

Where $[A]_{eq}$ is the concentration of A, $[B]_{eq}$ the concentration of B, and so on, when the system has reached equilibrium.

Mass-Action Ratio, *Q*

- **mass-action ratio, *Q*** = ratio of product concentrations to reactant concentrations at a given time
  – can be calculated to determine how far the reaction is from equilibrium

Standard Free-Energy Change, ΔG°

- ΔG (the actual free-energy change) for any chemical reaction is a function of the **standard free-energy change, ΔG°**

$$\Delta G = \Delta G^\circ + RT \ln \frac{[\mathrm{C}]_i^c [\mathrm{D}]_i^d}{[\mathrm{A}]_i^a [\mathrm{B}]_i^b} \quad \text{(Eqn 1-1)}$$

where $[A]_i$ is the initial concentration of A, and so forth; R is the gas constant; and T is the absolute temperature

Reactions Can Do No Work at Equilibrium

at equilibrium, ΔG = 0 and $$\frac{[\mathrm{C}]_\mathrm{i}^c\,[\mathrm{D}]_\mathrm{i}^d}{[\mathrm{A}]_\mathrm{i}^a\,[\mathrm{B}]_\mathrm{i}^b} = \frac{[\mathrm{C}]_\mathrm{eq}^c\,[\mathrm{D}]_\mathrm{eq}^d}{[\mathrm{A}]_\mathrm{eq}^a\,[\mathrm{B}]_\mathrm{eq}^b}$$

thus,

$$\Delta G = \Delta G^\circ + RT\ln\frac{[\mathrm{C}]_\mathrm{i}^c\,[\mathrm{D}]_\mathrm{i}^d}{[\mathrm{A}]_\mathrm{i}^a\,[\mathrm{B}]_\mathrm{i}^b}$$

$$\Delta G^\circ = -RT\ln K_\mathrm{eq}$$

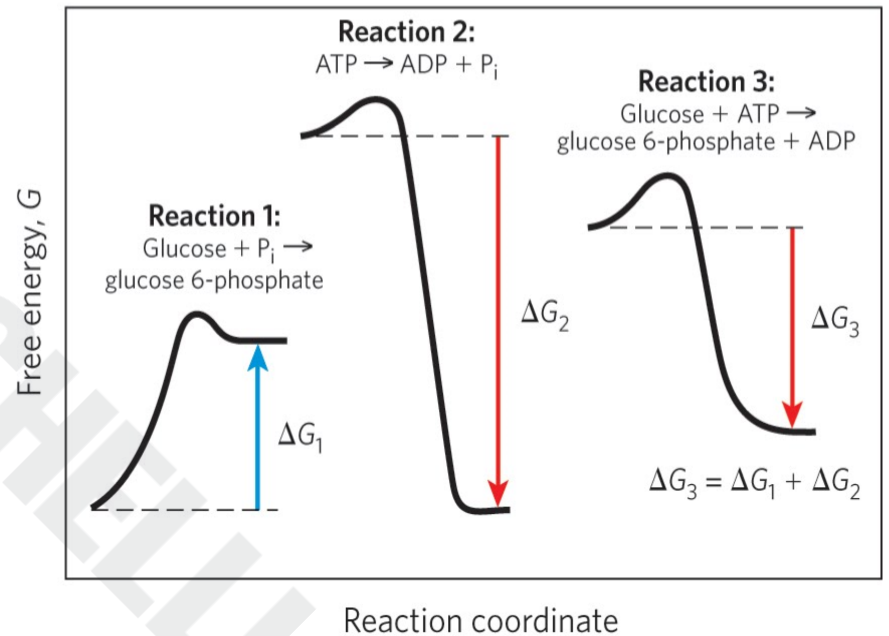
P3 Principle 3 (4 of 5)

Living organisms exist in a dynamic steady state, never at equilibrium with their surroundings. Following the laws of thermodynamics, living organisms extract energy from their surroundings and employ it to maintain homeostasis and do useful work. Essentially all of the energy obtained by a cell comes from the flow of electrons, driven by sunlight or by metabolic redox reactions.

Reaction Coordinate Diagrams

- **reaction coordinate diagrams** = illustrates how exergonic reactions can be coupled to endergonic reactions
- reaction 1: endergonic; ΔG_1 is positive
- reaction 2: exergonic; ΔG_2 is negative
- reaction 3: ΔG_3 is negative

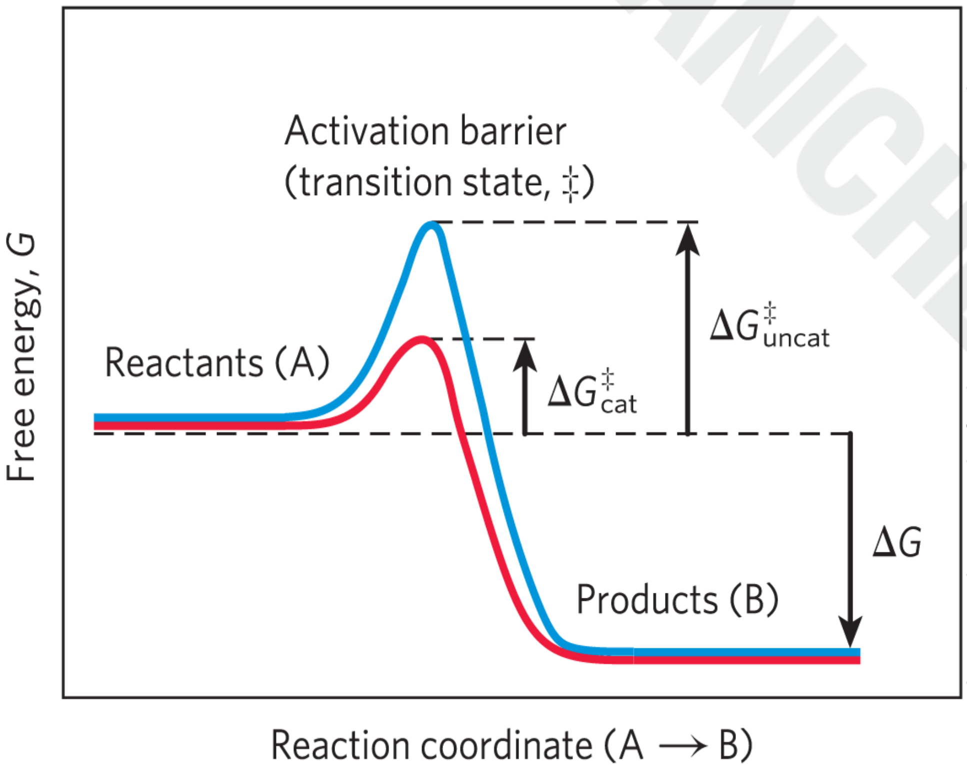
(b) Chemical example



Nelson & Cox, Lehninger Principles of Biochemistry, 8e, © 2021 W. H. Freeman and Company

Enzymes Promote Sequences of Chemical Reactions

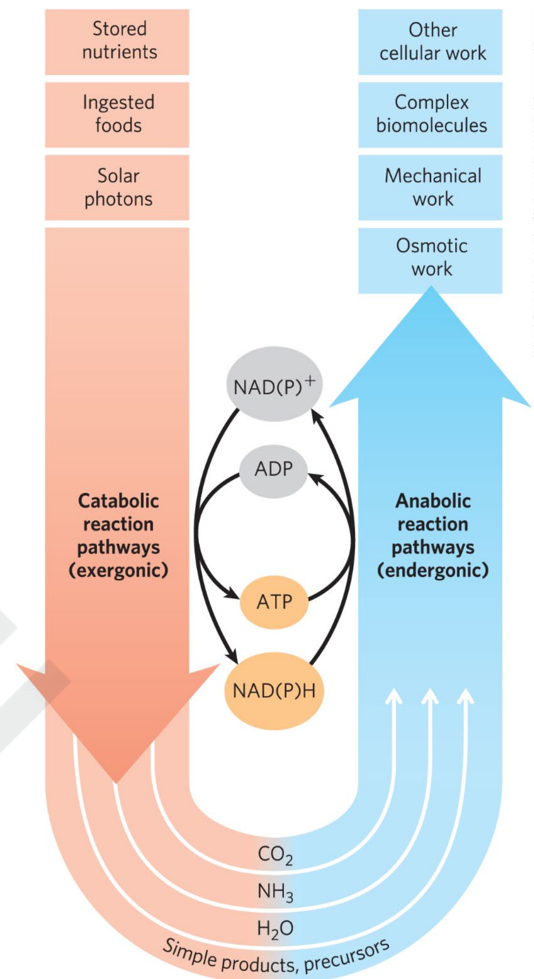
- **enzymes** = greatly enhance reaction rates of specific chemical reactions without being consumed in the process



- **transition state** = higher free energy than reactant or product
- **activation energy, $\Delta G^{\ddagger}$** = difference in energy between the reactant in its ground state and its transition state

Catabolism and Anabolism

- **pathways** = sequences of consecutive reactions in which the product of one reaction becomes the reactant in the next
- **catabolism** = degradative, free-energy-yielding reactions
  - drives ATP synthesis
  - produces the reduced electron carriers NAD(P)H
- **anabolism** = synthetic pathways that require the input of energy



P2 Principle 2 (5 of 6)

Cells use a relatively small set of carbon-based metabolites to create polymeric machines, supramolecular structures, and information repositories. The chemical structure of these components defines their cellular function. The collection of molecules carries out a program, the end result of which is reproduction of the program and self-perpetuation of that collection of molecules—in short, life.

Metabolism

- **metabolism** = overall network of enzyme-catalyzed pathways, both catabolic and anabolic

- **unity of life** = pathways of enzyme-catalyzed reactions that act on the main constituents of cells—proteins, fats, sugars, and nucleic acids—are nearly identical in all living organisms

P3 Principle 3 (5 of 5)

Living organisms exist in a dynamic steady state, never at equilibrium with their surroundings. Following the laws of thermodynamics, living organisms extract energy from their surroundings and employ it to maintain homeostasis and do useful work. Essentially all of the energy obtained by a cell comes from the flow of electrons, driven by sunlight or by metabolic redox reactions.

Metabolism Is Regulated to Achieve Balance and Economy

- **feedback inhibition** = keeps the production and utilization of each metabolic intermediate in balance

- **systems biology** = tasked with understanding complex interactions among intermediates and pathways in quantitative terms

1.4 Genetic Foundations

P4 Principle 4 (2 of 5)

Cells have the capacity for precise self-replication and self-assembly using chemical information stored in the genome. A single bacterial cell placed in a sterile nutrient medium can give rise to a billion identical "daughter" cells in 24 hours. Each cell is a faithful copy of the original, its construction directed entirely by information contained in the genetic material of the original cell. On a larger scale, the progeny of vertebrate animals share a striking resemblance to their parents, also the result of their inheritance of parental genes.

P2 Principle 2 (6 of 6)

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Genetic Information Is Encoded in DNA

- **deoxyribonucleic acid, DNA** = sequence of the monomeric subunits (deoxyribonucleotides)
  - encode the instructions for forming all other cellular components
  - provide a template to produce identical DNA molecules

Dr. Gopal Murti/Science Source.

(b)

P4 Principle 4 (3 of 5)

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Genetic Continuity Is Vested in Single DNA Molecules

- DNA of an *E. coli* cell is a *single molecule* containing 4.64 million nucleotide pairs
  - must be replicated perfectly to give rise to identical progeny by cell division

P4 Principle 4 (4 of 5)

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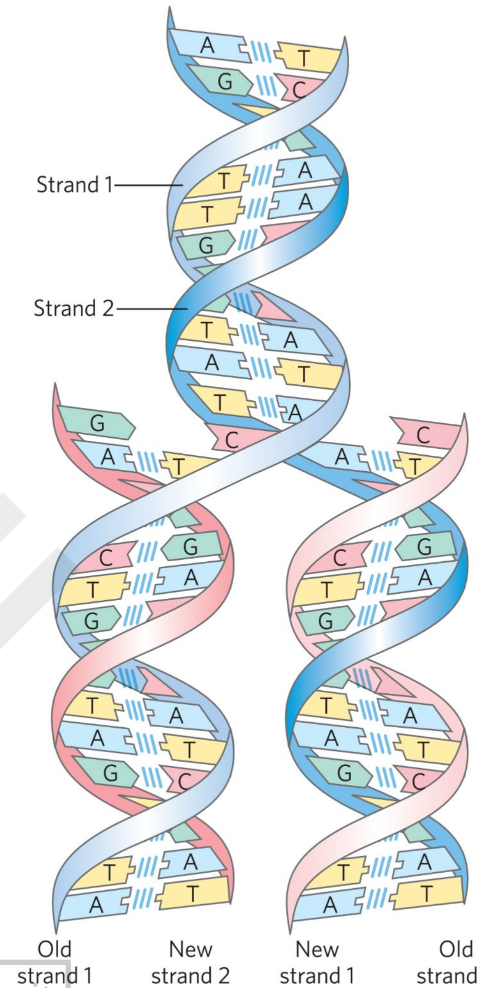
The Structure of DNA Allows Its Replication and Repair with Near-Perfect Fidelity

- **deoxyribonucleotides** = monomeric subunit that make up the DNA polymer
  - each deoxyribonucleotide in one strand pairs specifically with a complementary deoxyribonucleotide in the opposite strand
  - strands are held together by hydrogen bonds



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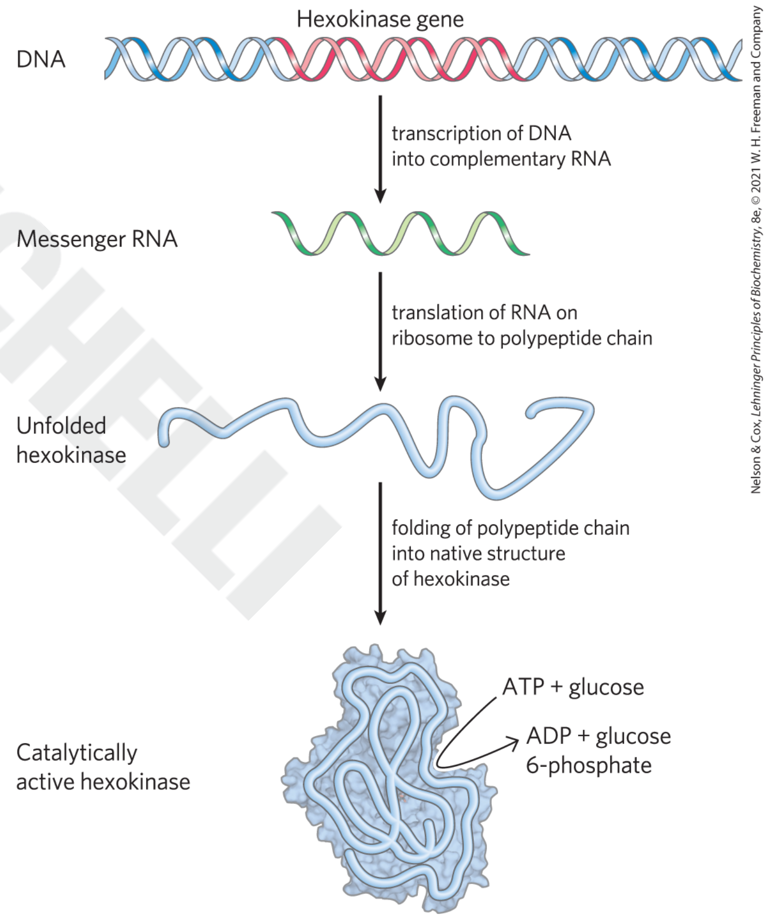
The Linear Sequence in DNA Encodes Proteins with Three-Dimensional Structures

- **native conformation** = precise three-dimensional structure of a protein
  - crucial to protein function



1.5 Evolutionary Foundations

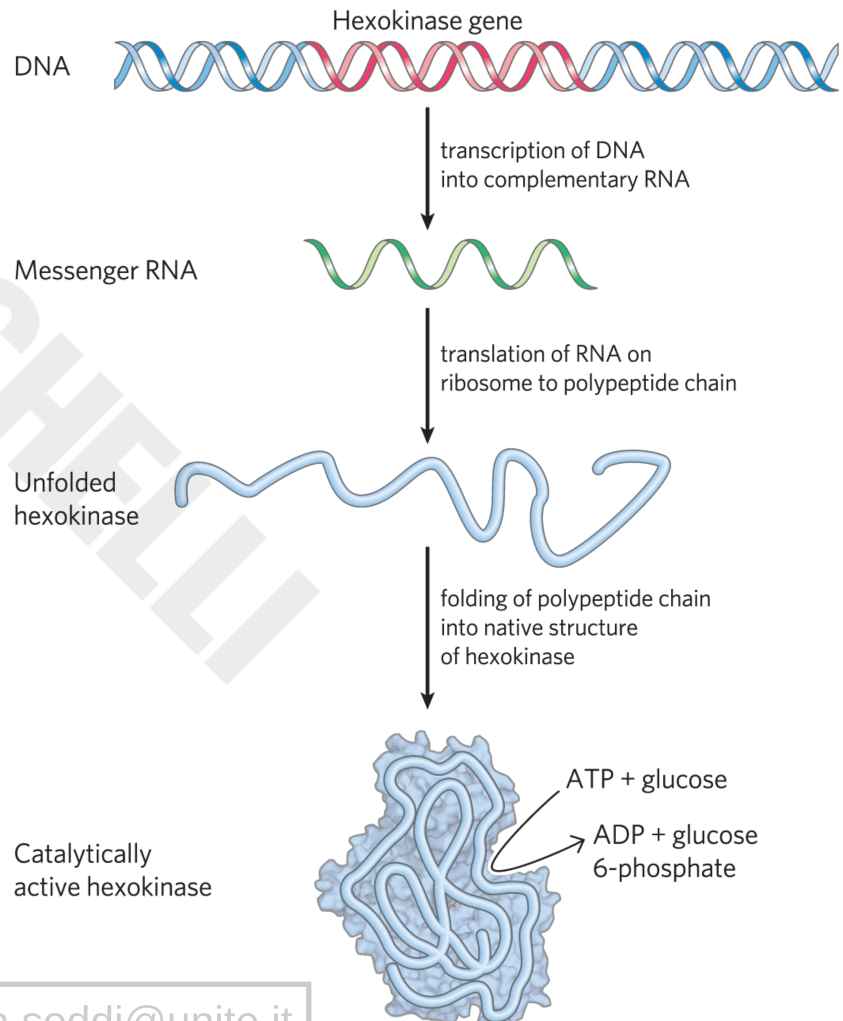
P5 Principle 5 (2 of 3)

Living organisms change over time by gradual evolution. The result of eons of evolution is an enormous diversity of life forms, fundamentally related through their shared ancestry, which can be seen at the molecular level in the similarity of gene sequences and protein structures.

Changes in the Hereditary Instructions Allow Evolution

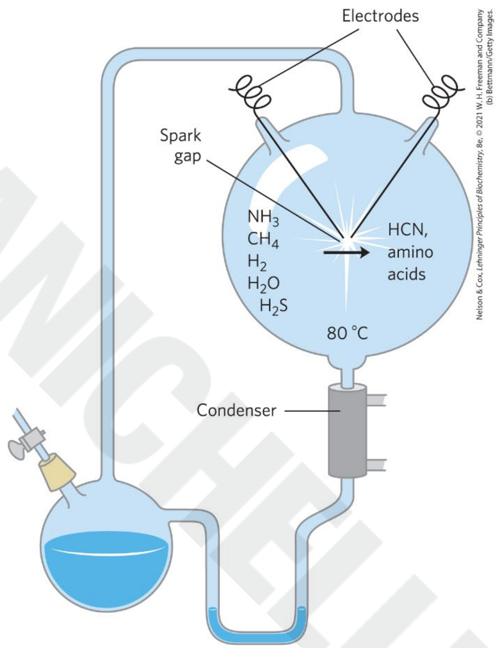
- **mutation** = changes in the nucleotide sequence of DNA
  - changes the instructions for a cellular component
  - can be beneficial

- **wild type** = unmutated cells



Biomolecules First Arose by Chemical Evolution

- Miller and Urey experiments found that biomolecules may have been produced near hydrothermal vents at the bottom of the sea or by the action of lightning and high temperature on gaseous mixtures



(a)

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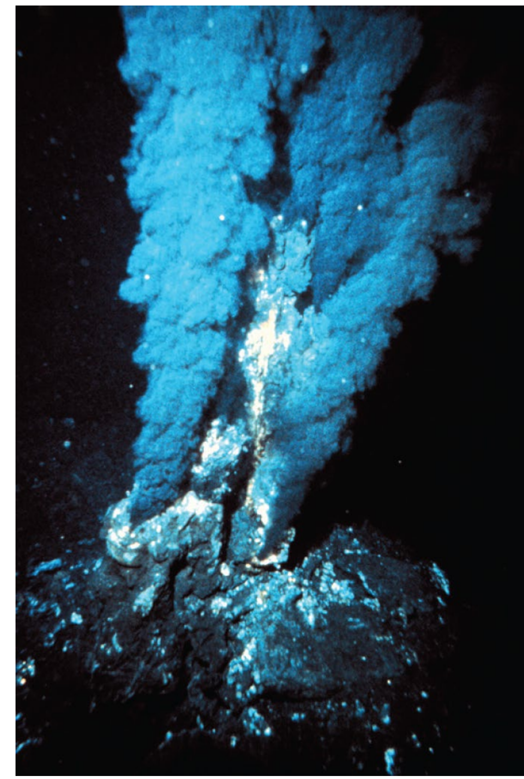


NOAA/Science Source

The Role of RNA in Prebiotic Evolution

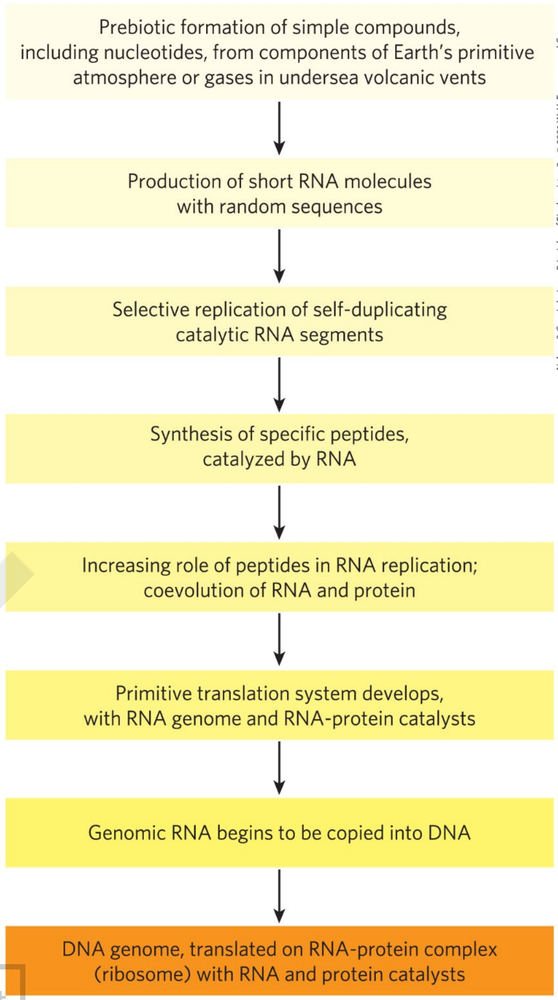
- **RNA (ribonucleic acid)** = can act as catalysts in biologically significant reactions

- likely played a crucial role in prebiotic evolution, both as catalyst and as information repository

RNA or Related Precursors May Have Been the First Genes and Catalysts

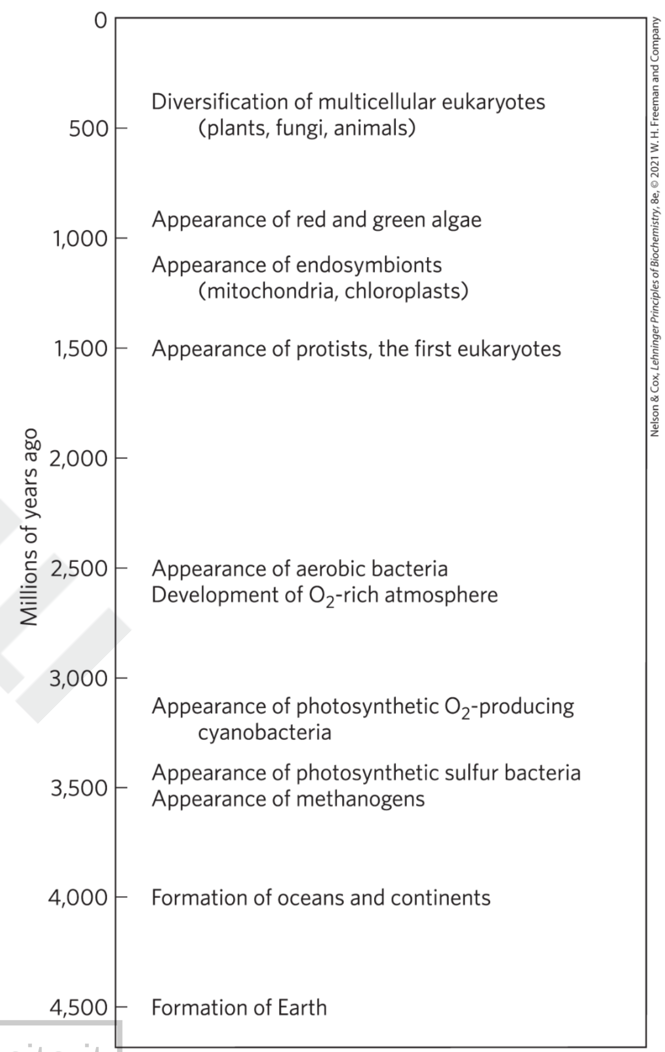
- RNA or similar molecule may have been the first gene and the first catalyst

- alternatively, simple metabolic pathways may have evolved first, perhaps at the hot vents in the ocean floor



Biological Evolution Began More Than Three and a Half Billion Years Ago

- lipid vesicles containing organic compounds and self-replicating RNA gave rise to protocells
- protocells with the greatest capacity for self-replication became more numerous



The First Cell Probably Used Inorganic Fuels

- earliest cells probably obtained energy from inorganic fuels, such as ferrous sulfide and ferrous carbonate

- **photosynthetic** processes:
  - arose from evolution
  - pigments capture energy of light from the sun and reduce CO_2 to organic compounds

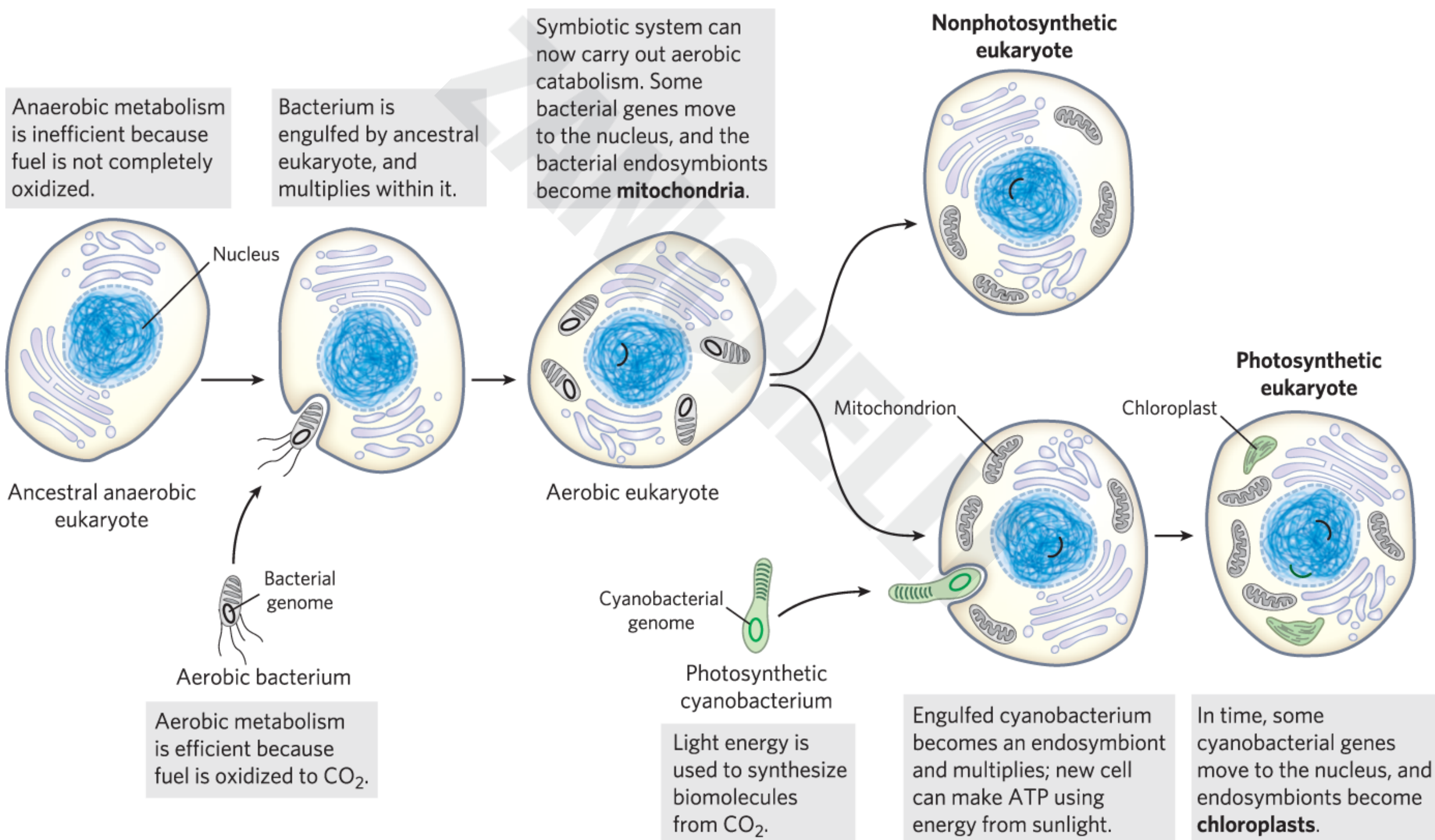
- atmosphere became richer in O_2 with the rise of O_2-producing photosynthetic bacteria

Eukaryotic Cells Evolved from Simpler Precursors in Several Stages

- three major changes led to the evolution of eukaryotes:
  – evolution of the chromosome
  – evolution of the nucleus
  – formation of **endosymbiotic** associations between early eukaryotic cells and aerobic or photosynthetic bacteria

- in multicellular organisms, differentiated cell types specialize in functions essential to the organism's survival

Evolution of Eukaryotes through Endosymbiosis



P5 Principle 5 (3 of 3)

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Molecular Anatomy Reveals Evolutionary Relationships

- **homologs** = proteins encoded by genes that share ready detectable sequence similarities

- gene or protein sequence similarities between organisms can determine phylogenetic relationships

Functional Genomics Shows the Allocations of Genes to Specific Cellular Processes

- genes can be grouped according to the specific process in which they function
  - can approximate the proportion of the genome dedicated to a specific process
  - genes involved in regulation of cellular processes tend to increase with organism complexity
- **housekeeping genes** = expressed under all conditions, not subject to much regulation

Genomic Comparisons Have Increasing Importance in Medicine

- large-scale sequencing studies have identified many genes in which mutations correlate with a medical condition

- the proteins these genes encode might become the target for drugs to treat a given condition