**Lehninger**

**Principles of Biochemistry**

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**BIOCHEMISTRY 1**

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**Chapter 1** **The Foundations of Biochemistry**

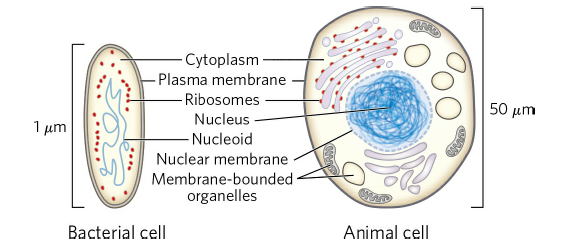
* We live on the earth.
* The earth has chemical elements and compounds.
* More complex biomolecules are made from them.
* Living organisms are composed of lifeless biomolecules.
* Each component of a living organism has a specific function.
* The collection of biomolecules carries out a program.
* A life is come into existence.
* The life itself is a wonder.
* Biochemistry asks how the remarkable properties of living organisms arise from the thousands of different biomolecules.
* Biochemistry describes the structures, mechanisms and chemical processes shared by all organisms.
* Biochemistry explains diverse forms of life in unifying chemical terms.
* Diverse living organisms share common chemical features.
* Birds, plants, microorganisms and humans share
* the same structural units (cells)
* the same kind of macromolecules (DNA, RNA, proteins)
* the same pathways for synthesis of cellular components.
* Biochemistry provides important insights and practical applications in medicine, agriculture, nutrition and industry.
* In this chapter, I will summarize
  + cellular, chemical, physical and genetic backgrounds to biochemistry
  + these backgrounds will help to understand the later discussions of biochemical structure and reactions.

**1.1 Cellular Foundations**

* The smallest organisms consist of single cells and are microscopic.
* Larger, multicellular organisms contain many different types of cells
  + vary in size, shape and function.

**Cells Are the Structural and Functional Units of All Living Organisms**

* Cells of all kinds share certain structural features **(Fig. 1-3).**





* The **plasma membrane** defines the periphery of the cell, separating its contents from the surroundings.
* it is composed of lipid and protein molecules that form a hydrophobic barrier to the free passage of inorganic ions and most other charged or polar compounds around the cell.
* in the plasma membrane
  + transport proteins allow the passage of certain ions and molecules
  + receptor proteins transmit signals into the cell
  + enzymes participate in some reaction pathways.
* The **cytoplasm** (the internal volume bounded by the plasma membrane) contains
* an aqueous solution (**cytosol**)
* ribosomes (protein-synthesizing machines)
* proteins
* RNA molecules (encodes proteins)
* amino acids and nucleotides (monomers of proteins and nucleic acids)
* metabolites (small organic molecules)
* coenzymes (complex organic molecules)
* inorganic ions
* All cells have either a **nucleoid** or a **nucleus** (the complete set of genes called **genome)**
  + the nucleoid (in bacteria) is not separated from the cytoplasm by a membrane.
  + the nucleus (in eukaryotes) is enclosed within a double membrane.

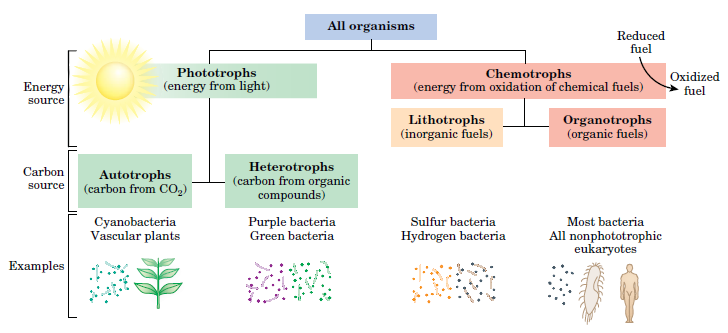
**Cellular Dimensions Are Limited by Diffusion**

* The human body contains at least 1014 cells.
* Most cells are microscopic and invisible. (1 m = 10 -6 m)
* animal and plant cells are typically 5 to 100 m in diameter.
* many microorganisms are only 1 to 2 m long and have a volume of about 10-14 mL.

**There Are Distinct Domains of Life**

* In **aerobic** cells,
* organisms derive energy from the transfer of electrons from fuel molecules to oxygen.
* In **anaerobic** cells,
* microorganisms carry out catabolism without oxygen.
* microorganisms obtain energy by transferring electrons to nitrate (forming N2), sulfate (forming H2S) or CO2 (forming methane, CH4).

**Organisms Differ in Their Sources of Energy and Biosynthetic Precursors**

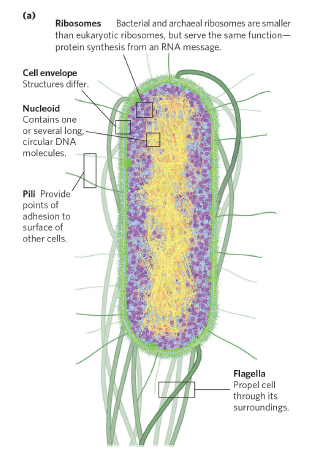




* Organisms can be classified according to their source of
* energy (sunlight or oxidizable chemical compounds)
* carbon for the synthesis of cellular material (**Fig. 1-5)**.

**Bacterial Cells Share Common Features**

* *Escherichia coli* is the best-studied bacterium
* The *E. coli* cell is about 2 m long and a little less than 1 m in diameter (**Fig. 1-7)**
* It has a protective **outer membrane** and an **inner plasma membrane**
* encloses the **cytoplasm** and the **nucleoid**
* between the inner and outer membranes is a thin but strong layer of a high molecular weight polymer called peptidoglycan (sugar polymers cross-linked by amino acids), which gives the cell its shape and rigidity.
* The plasma membrane and the layers outside it constitute the **cell envelope**.
* The plasma membranes of bacteria consist of a thin bilayer of lipid molecules penetrated by proteins.



**FIGURE 1-7 Some common structural features of bacterial cells.**

* Bacterial cells show group-specific specializations because of differences in cell envelope structure (called gram-positive bacteria, gram-negative bacteria).
* Outer membrane protrude hairlike structures

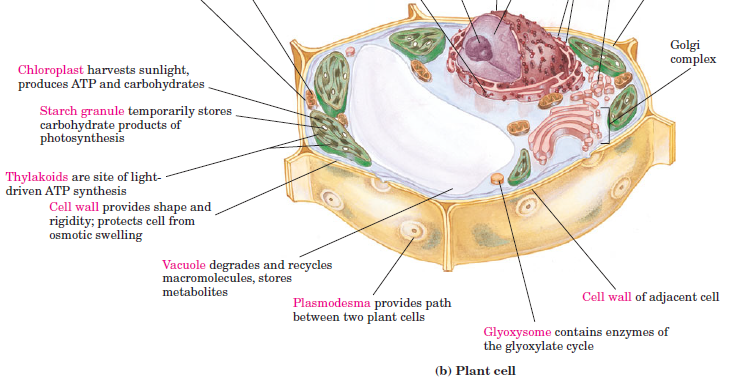
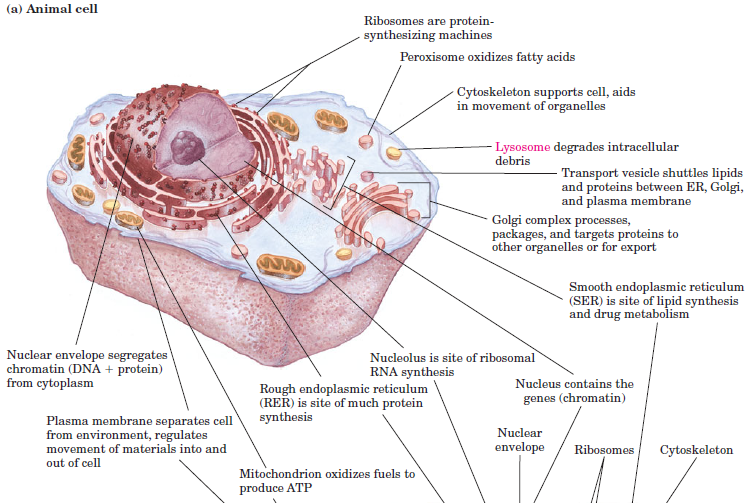
- short is called **pili** (pili provide points of adhesion to surface of other cells)

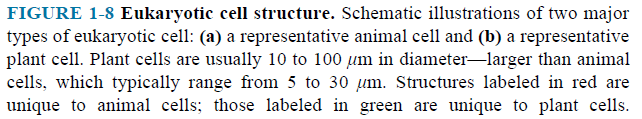
- long is called **flagella** (singular flagellum) (flagella propel cell through its surroundings).

* The cytoplasm of *E. coli* contains about
* 15,000 ribosomes (protein-synthesizing machines)
* 1,000 different enzymes
* 1,000 organic compounds (metabolites and cofactors)
* inorganic ions.
* The nucleoid contains a single, circular molecule of DNA.
* although the DNA molecule of an *E. coli* cell is 1,000 times longer than the cell itself, it is packaged which is less than 1 m (if it is linear 1 mm)
* as in all bacteria, no membrane surrounds the genetic material.

**Eukaryotic Cells Have a Variety of Membranous Organelles**

* Typical eukaryotic cells **(Fig. 1–8)** are much larger than bacteria—commonly 5 to 100 m in diameter.
* The distinguishing characteristics of eukaryotes are
  + the nucleus and
  + membrane-enclosed organelles with specific functions.
* **Nucleus** contains the genes (chromatin = DNA + Histone proteins)
* is surrounded by a **nuclear envelope**.
* has a specific region called **nucleolus** which is the site of ribosomal RNA synthesis
* Cells of each species have a characteristic number of chromosomes
* humans have 23 chromosomes and have two copies of each chromosome.
* the combined length of all 46 chromosomes is only about 200 m. (if all of them are linear total 2 m)
  + **Mitochondria** are the site of most of the energy-extracting reactions of the cell.
    - mitochondrian oxidizes fuels to produce ATP.
    - a small amount of DNA is also present in mitochondria.

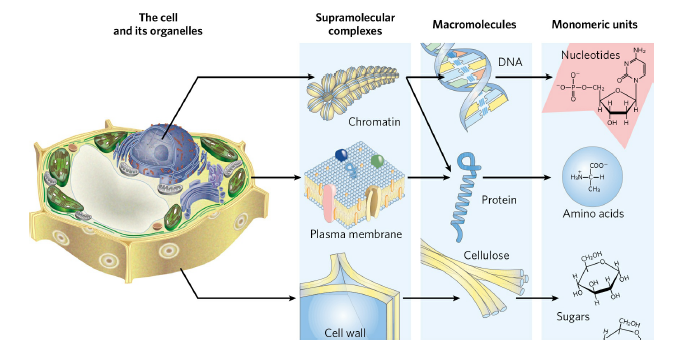




* **Smooth endoplasmic reticulum** (free of ribosomes) is the site of lipid synthesis and drug metabolism.
* **Rough endoplasmic reticulum** (attached of ribosomes) is the site of much protein synthesis.
* **Golgi complex** processes (by adding sulfate, carbohydrate, or lipid moieties to newly synthesized proteins), packages, and targets proteins to other organelles or for export.
* **Peroxisomes** oxidize very long-chain fatty acids.
* **Lysosome** (in animal cells) degrades unneeded cellular debris (proteins, polysaccharides, nucleic acids and lipids).
* **Vacuole** (in plant cells) degrades and recycles macromolecules, stores metabolites.
* **Chloroplast** (in plant cells) harvests sunlight, produces ATP and carbohydrates.
* a small amount of DNA is also present in chloroplast.
* **Glyoxysome** (in plant cells) converts stored fats to carbohydrates.
* **Ribosomes** are protein-synthesizing machines.
* **Plasma membrane** separates cell from environment, regulates movement of materials into and out of cell.
* **Cell wall** provides shape and rigidity; protects cell from osmotic swelling.
* **Cytoskeletons** provide structure and organization to the cytoplasm and shape to the cell. They also help to produce the motion of organelles or of the whole cell.
* these organizations are
  + far from random, dramatic, finely orchestrated reorganizations.

**Cells Build Supramolecular Structures**

* There is a structural hierarchy in the molecular organization of cells **(Fig. 1–12).**





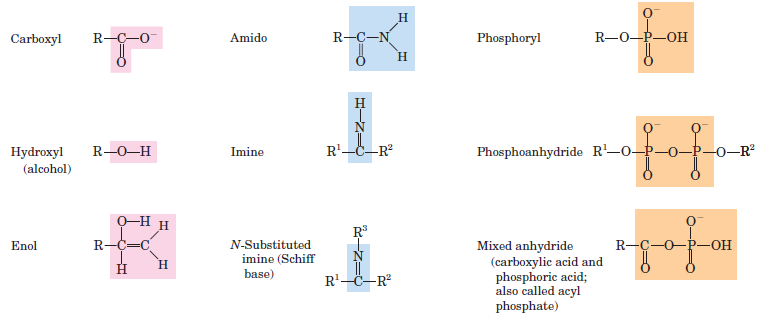
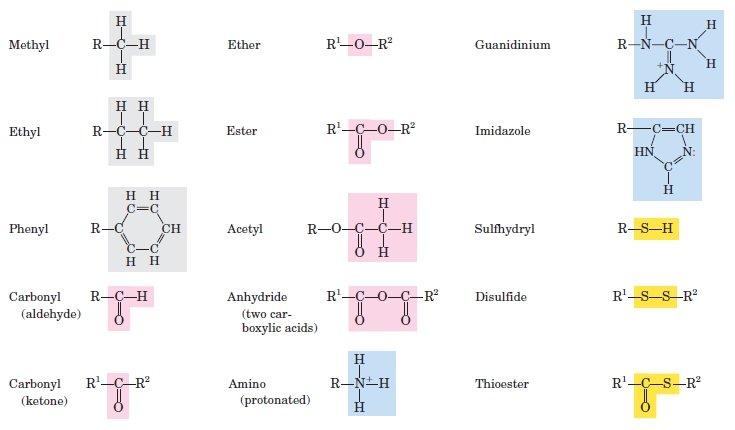
* The monomeric subunits of proteins, nucleic acids and polysaccharides are joined by covalent bonds.
* In supramolecular complexes, however, macromolecules are held together by noncovalent interactions—much weaker, individually, than covalent bonds.
* among these noncovalent interactions are
  + hydrogen bonds (between polar groups)
  + ionic interactions (between charged groups)
  + hydrophobic interactions (among nonpolar groups in aqueous solution)
  + van der Waals interactions (London forces).

**1.2 Chemical Foundations**

* Biochemistry aims to explain biological form and function in chemical terms.
* Fewer than 30 of the more than 90 naturally occurring chemical elements are essential to organisms.
* H, C, N, O, Na, P, S, Cl, K and Ca are bulk elements.
* Mg, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Se, Mo, I and W are trace elements.
* The four most abundant elements in living organisms
  + are H, O, N, and C
    - which together make up more than 99% of the mass of most cells.

**Biomolecules Are Compounds of Carbon with a Variety of Functional Groups**

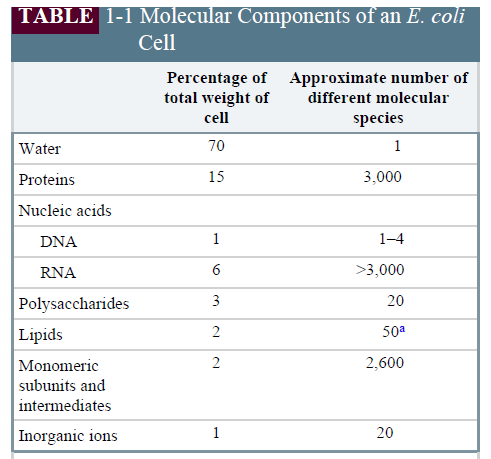
* The chemistry of living organisms is organized around carbon
  + which accounts for more than half the dry weight of cells.
* Carbon can form
  + single bonds with hydrogen atoms
  + both single and double bonds with oxygen and nitrogen atoms
  + single, double and triple bonds with carbon atoms.
* Most biomolecules can be regarded as derivatives of hydrocarbons.
* Functional groups of biomolecules determine chemical properties of biomolecules.
* Some common functional groups are given in **(Fig. 1–17)**.





**Macromolecules Are the Major Constituents of Cells**

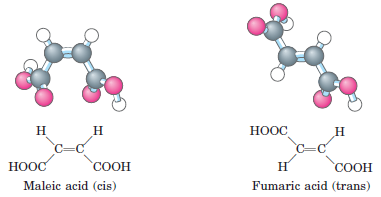
* Many biological molecules are **macromolecules**
* are assembled from relatively simple precursors.
* Shorter polymers are called **oligomers**.
* Proteins, nucleic acids, and polysaccharides are macromolecules composed of monomers.
* The molecular mass of a particle may be expressed in units of Daltons
* 1 dalton defines the mass of a H atom
* **Proteins** are composed of 20 different kinds of amino acids.
* **Deoxyribonucleic acids (DNA)** are constructed from only four different kinds of deoxyribonucleotides.
* **Ribonucleic acids (RNA)** are composed of just four types of ribonucleotides.
* **Polysaccharides** are polymers of simple sugars such as glucose.
* **Lipids** are water insoluble hydrocarbon derivatives.
* **(Table 1–1)** shows the major classes of biomolecules in an *E. coli* cell.



* Proteins, polynucleotides and polysaccharides have large numbers of monomeric subunits and thus high molecular weights — in the range of
  + 5,000 to more than 1 million for proteins
  + up to several billion for nucleic acids
  + in the millions for polysaccharides such as starch.
* Individual lipid molecules are much smaller (750 to 1,500) and are not classified as macromolecules.
* These monomeric subunits can be covalently linked in a limitless variety of sequences,
* just as the 26 letters of the English alphabet can be arranged into a limitless number of words, sentences and books.

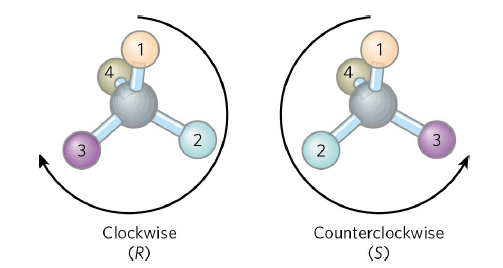
**Three-Dimensional Structure Is Described by Configuration and Conformation**

* The covalent bonds and functional groups of a biomolecule are central to its function
* the arrangement of atoms is also important.
* A carbon containing compound commonly exists as **stereoisomers**
* molecules with the same chemical bonds but different **configuration**
  + the fixed spatial arrangement of atoms.
* Interactions between biomolecules are **stereospecific**
* requiring specific configurations in the interacting molecules.
* **(Fig. 1.20)** shows the configurations of maleic acid and fumaric acid **(cis-trans isomers)**.





* the two compounds have distinct biological roles despite their similar chemistry.
* A carbon atom with four different substituents is said to be asymmetric
* asymmetric carbons are called **chrical** **centers.**
* Some stereoisomers are mirror images of each other
* they are called **enantiomers**.
* Some stereoisomers are not mirror images of each other
* they are called **diastereomers**.
* For compounds with more than one chiral center
* the most useful system of nomenclature is the RS system.



* Another naming system for stereoisomers, the D and L system, is described in Chapter 3.
* Distinct from configuration is molecular **conformation**
* the spatial arrangement of substituent groups
* are free to assume different positions in space because of the freedom of rotation about single bonds.

**Interactions between Biomolecules Are Stereospecific**

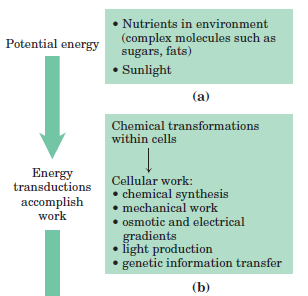
* The three-dimensional structure of biomolecules (the combination of configuration and conformation)
* is important in their biological interactions.
* When biomolecules interact
* the “fit” between them must be stereochemically correct.
* For example, molecular interactions between enzyme and substrate are stereospesific.
* In living organisms, chiral molecules are usually present in only one of their chiral forms.
* the amino acids occur only as their L isomers
* glucose occurs only as its D isomer.
* Stereospecificity (the ability to distinguish between stereoisomers) is
* a characteristic feature of the molecular logic of living cells.

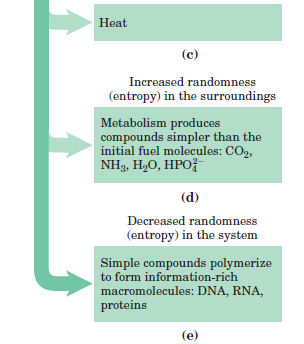
**1.3 Physical Foundations**

* Energy is central theme in biochemistry
* cells and organisms depends on a constant supply of energy.
* One goal of biochemistry is to understand the energy (in quantitative and chemical terms)
* the energy is extracted, stored and channeled into useful work in living cells.
* Cells have evolved highly efficient mechanisms
* for coupling the energy obtained from sunlight or fuels to the many energy-consuming processes.

**Organisms Transform Energy and Matter from Their Surroundings**

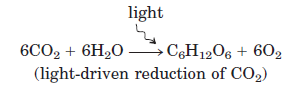
* For chemical reactions occurring in solution, we can define a **system**.
* If system exchanges both energy and matter with its surroundings, it is an **open** system.
* A living organism is an open system
* Organisms obtain energy from their surroundings in two ways:
* they take up chemical fuels (such as glucose) and extract energy by oxidizing them
* they absorb energy from sunlight.
* Cells are consummate transducers of energy
* capable of interconverting chemical, electromagnetic, mechanical and osmotic energy with great efficiency **(Fig. 1-24)**.
* Living cells are chemical engines.





**The Flow of Electrons Provides Energy for Organisms**

* Nearly all living organisms derive their energy, directly or indirectly, from the radiant energy of sunlight.
* Sunlight is transmitted to the earth and converted into chemical energy by plants and some algae and bacteria.
* Photosynthetic cells absorb light energy and use it to drive electrons from H2O to CO2
* forming energy-rich products such as starch and sucrose and releasing O2 into the atmosphere.



* Nonphotosynthetic organisms obtain the energy
* by oxidizing the energy-rich products of photosynthesis and then passing the electrons to atmospheric O2 to form H2O, CO2 and other products.



* All these reactions involving electron flow are **oxidation-reduction reactions**.

**Energy Coupling Links Reactions in Biology**

* The central issue in **bioenergetics** is the study of energy transformations in living systems.
* The amount of energy available to do work is the **free-energy change, G**.
* The energy change as the system moves from its initial state to equilibrium is given by the G.
* In spontaneously reactions, the products have less free energy than the reactants
* the reaction releases free energy
* is then available to do work.
* such reactions are **exergonic** and G is negative (G < 0).
* **Endergonic** reactions require an input of energy, G is positive (G > 0).
* In living organisms, an exergonic reaction can be coupled to an endergonic reaction or process to drive otherwise unfavorable reactions **(Fig. 1-26)**.

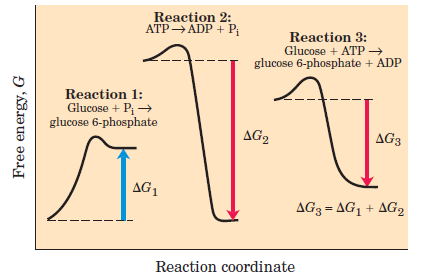
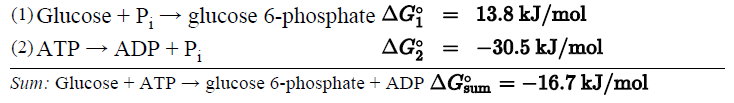
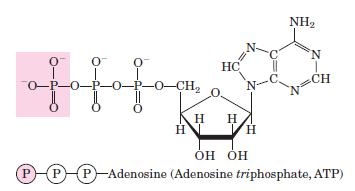


FIGURE 1–26 Energy coupling in chemical processes.

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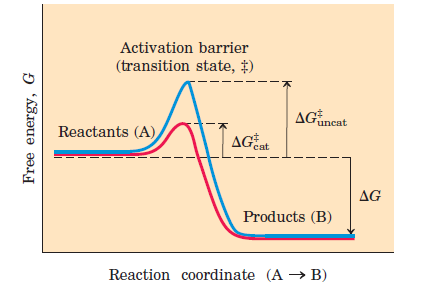
* Reaction 1: (endergonic, G1 is positive) (Pi : inorganic phosphate, HPO42-)
* Reaction 2: (exergonic, G2 is negative)
* The two chemical reactions share a common intermediate, Pi. The two reactions can be coupled in the form of a third reaction.
* Reaction 3: (exergonic, G3 is negative). The overall reaction proceeds spontaneously.
* The coupling of exergonic reactions with endergonic ones is absolutely central to the energy exchanges in living systems.
* **ATP** is the major carrier of chemical energy in all cells.



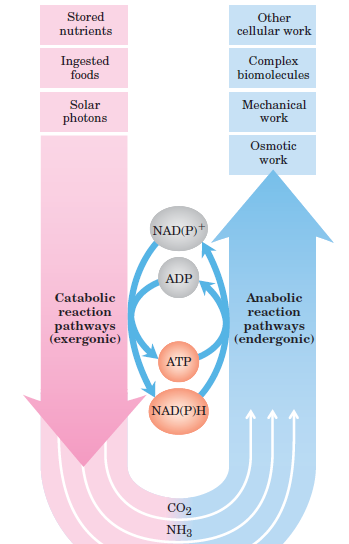
* The removal of the terminal phosphoryl group of ATP by breakage of a phosphoanhydride bond is highly exergonic.
* this reaction is coupled to many endergonic reactions in the cell.

**Enzymes Promote Sequences of Chemical Reactions**

* Every chemical reaction in a cell occurs at a significant rate only because of the presence of **enzymes**—biocatalysts
* increase the rate of specific chemical reactions without being consumed in the process.
* The path from reactant(s) to product(s) involves an energy barrier (**Fig. 1-27)**



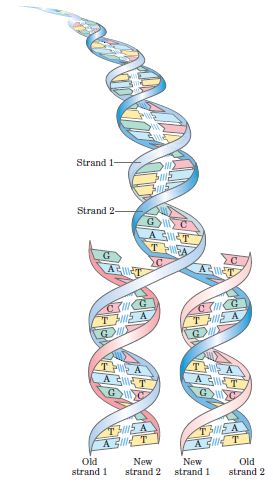
* it is called the activation barrier
* it must be surmounted.
* Enzymes lower the energy barrier between reactant and product.
* Enzyme catalyzed reactions commonly proceed at rates greater than 1012 times faster than uncatalyzed reactions.
* Cellular catalysts are generally proteins
* each enzyme catalyzes a specific reaction.
* thousands of different enzymes are required by each cell.
* The thousands of enzyme in cells are functionally organized into many sequences of consecutive reactions, called **pathways**,
* the product of one reaction becomes the reactant in the next.
* Degradative and free-energy-yielding reactions are designated **catabolism.**
* ATP is synthesized.
* the reduced electron carriers NADH and NADPH are produced.
* Small precursor molecules are converted to larger and more complex molecules, represent **anabolism** (requires the input of energy)
* The overall network of enzyme-catalyzed pathways, both catabolic and anabolic,
* constitutes cellular **metabolism** **(Fig. 1-28).**





**Metabolism is Regulated to Achieve Balance and Economy**

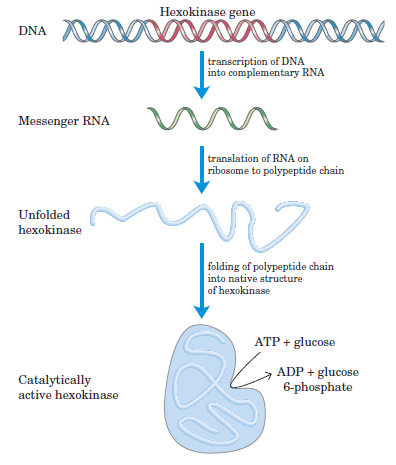
* Key enzymes in each metabolic pathway are regulated
* each type of precursor molecule is produced in a quantity appropriate to the current requirements of the cell.
* Living cells are self-regulating chemical engines
* continually adjusting for maximum economy.
  1. **Genetic Foundations**
* Continuity of structure and composition of living organisms is the result of continuity in the structure of the genetic material.
* Genetic material is called deoxyribonucleic acid (DNA).
* DNA is a long and thin organic polymer.
* Genetic information is encoded in the linear sequence of four kinds of **deoxyribonucleotides.**
* DNA is double-helical molecule (**Fig. 1-32).**



* Changes in the nucleotide sequence represent a genetic mutation.
* Mutations can change the instructions for producing cellular components.
* Many mutations are harmful or even lethal to the organism.

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

* Linear sequences of deoxyribonucleotides in DNA, known as genes,
* are transcribed into ribonucleic acid (RNA) molecules.
* The RNA sequence is translated into linear sequence of amino acids called protein.
* The protein is folded into a particular three-dimensional shape **(Fig. 1-33).**



* The entire genetic material of
* *E. coli* is 4.64 million nucleotide pairs ( ~3,000 different genes and proteins)
* a human is 3 billion nucleotide pairs ( ~20,000 different genes and proteins)
* These monomeric subunits of DNA and proteins can be covalently linked in a limitless variety of sequences,
* just as the 26 letters of the English alphabet can be arranged into a limitless number of words, sentences and books.
* An amazing chemical feat!