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Introduction to the Chemistry of Life

This chapter introduces you to life at the biochemical and cellular level. It begins with a discussion of the chemical origins of life and its early evolution. This discussion continues into ideas and theories about the evolution of organisms, followed by a brief introduction to taxonomy and phylogeny viewed from a molecular perspective. The chapter concludes with an introduction to the basic concepts of thermodynamics and its application to living systems. Biochemistry, like all other sciences, is a based on the measurement of observable phenomena. Hence, it is important to become familiar with the conventions used to measure energy and mass. Box 1-1 presents the essential biochemical conventions that we will encounter throughout *Fundamentals of Biochemistry*.

Essential Concepts

The Origin of Life

1. Living matter consists of a relatively small number of elements, of which C, N, O, H, Ca, P, K, and S account for ~98% of the dry weight of most organisms (which are 70% water). These elements form a variety of reactive functional groups that participate in biological structure and biochemical reactions.

2. The current model for the origin of life proposes that organisms arose from the polymerization of simple organic molecules to form more complex molecules, some of which were capable of self-replication.

3. Most polymerization reactions involving the building of small organic molecules into larger more complex ones occur by the formation of water. This is called a condensation reaction.

Cellular Architecture

4. A key development in the origin of life was the formation of a membrane that could separate the critical molecules required for replication and energy capture from a potentially degradative environment.

5. Complementary surfaces of molecules and macromolecules provide a template for biological specificity (e.g., macromolecular assembly, enzyme activity, and expression and replication of the genome).

6. Modern cells can be classified as either prokaryotic or eukaryotic. Eukaryotic cells are distinguished by a variety of membrane-bounded organelles and an extensive cytoskeleton.

Organismal Evolution

7. Prokaryotes show a limited range of morphologies but very diverse metabolic capabilities.

8. Phylogenetic evidence based on comparisons of ribosomal RNA genes have been used by Woese and colleagues to group all organisms into three domains: archaea, bacteria, and eukarya.

9. The evolution of sexual reproduction marks an important step of the evolution of organisms, because it allows for genetic exchanges that lead to an increase in the adaptability of a population of organisms to changing environments.

10. Eukaryotes contain several membrane-bounded structures, such as mitochondria and chloroplasts, that may be descended from ancient symbionts.

11. Archaea represent a third domain or branch of life in the three-domain system of classification. While they outwardly resemble bacteria, their genomes and the proteins encoded in them more closely resemble those of eukaryotes.

12. Biological evolution is not goal-directed, requires some built-in sloppiness, is constrained by its past, and is ongoing.

13. Natural selection directs the evolution of species.

Thermodynamics

14. The first law of thermodynamics states that energy (U) is conserved; it can neither be created nor destroyed.

15. Enthalpy is a thermodynamic function that is a sum of the energy of the system and the product of the pressure and the volume (PV). Since biochemical processes occur at constant pressure and have negligible changes in volume, the change of energy of the system is nearly equivalent to the change in enthalpy ($\Delta U = \Delta H$).

16. The second law of thermodynamics states that spontaneous processes are characterized by an increase in the entropy of the universe, that is, by the conversion of order to disorder.

17. The spontaneity of a process i*s determined by its free energy change* ($\Delta G = \Delta H - T\Delta S$). Spontaneous reactions have $\Delta G < 0$ (exergonic) and nonspontaneous reactions have $\Delta G > 0$ (endergonic).

15. For any process at equilibrium, the rate of the forward reaction is equal to the rate of the reverse reaction, and $\Delta G = 0$.

18. Energy, enthalpy, entropy, and free energy are state functions; that is, they depend only on the state of the system, not its history. Hence, they can be measured by considering only the initial and final states of the system and ignoring the path by which the system reached its final state.

19. The entropy of a solute varies with concentration; therefore, so does its free energy. The free energy change of a chemical reaction depends on the concentration of both its reactants and its products.

20. For the general reaction

$$a\text{A} + b\text{B} \rightleftharpoons c\text{C} + d\text{D}$$

the free energy change is given by the following relationship:

$$\Delta G = \Delta G^\circ + RTln\left(\frac{[C]c[D]d}{[A]a[B]b}\right)$$

21. The equilibrium constant of a chemical reaction is related to the standard free energy of the reaction when the reaction is at equilibrium ($\Delta G = 0$), so that we have

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

where K_{eq} is the equilibrium constant of the reaction:

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

The equilibrium constant can therefore be calculated from standard free energy data and *vice versa*.

22. The equilibrium constant varies with temperature by the relation

$$lnKeq = \frac{\Delta H^\circ}{R}\left(\frac{1}{T}\right) + \frac{\Delta S^\circ}{R}$$

where ΔH° and ΔS° represent enthalpy and entropy in the standard state. A plot of K_{eq} versus $1/T$, known as a van't Hoff plot, permits the values of ΔH° and ΔS° (and therefore ΔG° at any temperature) to be determined from measurements of K_{eq} at two (or more) temperatures.

23. The biochemical standard state is defined as follows: The temperature is 25°C, the pH is 7.0, and the pressure is 1 atm. The activities of reactants and products are taken to be the total activities of all their ionic species, except for water, which is assigned an activity of 1. $[H^+]$ is also assigned an activity of 1 at the physiologically relevant pH of 7. These

conditions are different than the chemical standard state, so that the biochemical standard free energy is designated as $\Delta G^{\circ\prime}$ and in the chemical standard state is ΔG°. We assume that activity equals molarity for dilute solutions.

24. An isolated system cannot exchange matter or energy with its surroundings. A closed system can exchange only energy with its surroundings. A closed system inevitably reaches equilibrium. Open systems exchange both matter and energy with their surroundings and therefore cannot be at equilibrium. Living organisms must exchange both matter and energy with their surroundings and are thus open systems. Living organisms tend to maintain a constant flow of matter and energy, referred to as the steady state.

25. Living systems can respond to slight perturbations from the steady state to restore the system back to the steady state. This process underlies the physiological concept of homeostasis.

26. The recovery of free energy from a biochemical process is never total, and some energy is lost to the surroundings as heat. Hence, while the system becomes more ordered, the surroundings experience an increase in entropy.

27. Enzymes accelerate the rate at which a biochemical process reaches equilibrium. They accomplish this by interacting with reactants and products to provide a more energetically favorable pathway for the biochemical process to take place.

Key Equations

Be sure to know the conditions for which the following thermodynamics equations apply and be able to interpret their meaning.

1. $\Delta U = q - \mathrm{w}$

2. $H = U + PV$

3. $\Delta H = q_{\mathrm{P}} - w + P\Delta V$

4. $S = k_{\mathrm{B}} \ln W$

5. $\Delta S \geq \dfrac{q}{T} = \dfrac{\Delta H}{T}$

6. $\Delta G = \Delta H - T\Delta S$

7. $\Delta G = \Delta G^{\circ} + RTln\left(\dfrac{[C]c[D]d}{[A]a[B]b}\right)$

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

9. $$K_{eq} = \frac{[C]^c_{eq}\,[D]^d_{eq}}{[A]^a_{eq}\,[B]^b_{eq}}$$

10. $$lnKeq = \frac{\Delta H^\circ}{R}\left(\frac{1}{T}\right) + \frac{\Delta S^\circ}{R}$$

Guide to Study Exercises (Text p. 20)

1. The major stages of chemical and organismal evolution are:
Formation of simple organic compounds.
Polymerization of small molecules to form more complex molecules.
Replication, the self-directed synthesis of additional molecules.
Concentration of molecules and compartmentation of chemical reactions.
Development of systems for synthesizing precursors and generating energy.
Organization of simple cells.
Emergence of sexual reproduction.
Cooperation among cells in multicellular organisms. (Sections 1-1 to 1-3)

2. Evolution occurs when the makeup of a population is altered as specific variants are passed from individuals to their offspring. The variants that come to predominate are those that increase the ability of individuals to survive and reproduce under the prevailing conditions; that is, those that are "selected" by nature. These principles of evolution by natural selection apply to living organisms or any self-replicating system. (Sections 1-1B and 1-3C)

3. The archaea include methanogens, halobacteria, and some thermophiles. The bacteria include organisms such as *E. coli* and cyanobacteria. The eukarya include protozoans, fungi, plants, and animals. (Section 1-3A)

4. The first law of thermodynamics states that energy is conserved and can be neither created nor destroyed. It may, however, be transferred, for example, in the form of heat or work, between a closed or open system and its surroundings. The second law of thermodynamics states that spontaneous processes are characterized by increasing disorder (increasing entropy). These laws are sometimes restated as "You can't win" and "You can't even break even." (Sections 1-4A and B)

5. The overall free energy change of a process (ΔG) varies with the difference between the enthalpy change (ΔH) and the product of the temperature and the entropy change ($T\Delta S$): $\Delta G = \Delta H - T\Delta S$. Therefore, ΔG varies not only with the relative magnitudes of ΔH and ΔS but also with the temperature. (Section 1-4C)

6. In the biochemical standard state (which is indicated by a degree symbol and a prime following the symbol for the state function, e.g., $\Delta G^{\circ\prime}$), the temperature is 25°C, the pressure is 1 atm, the activity of each solute is equivalent to its total molar activity (assumed to equal molarity for dilute solutions; water has an activity of 1), and the pH is 7.0 ($[H^+] = 10^{-7}$ M). (Section 1-4D)

7. While they are alive, organisms resist the second law of thermodynamics by maintaining a steady state in which energy and matter constantly flow through the organism, far from equilibrium. The high degree of organization of a living thing requires free energy; without this free energy (i.e., when $\Delta G = 0$), the organism dies and, thermodynamically speaking, comes to equilibrium. (Section 1-4E)

Questions

The Origin of Life

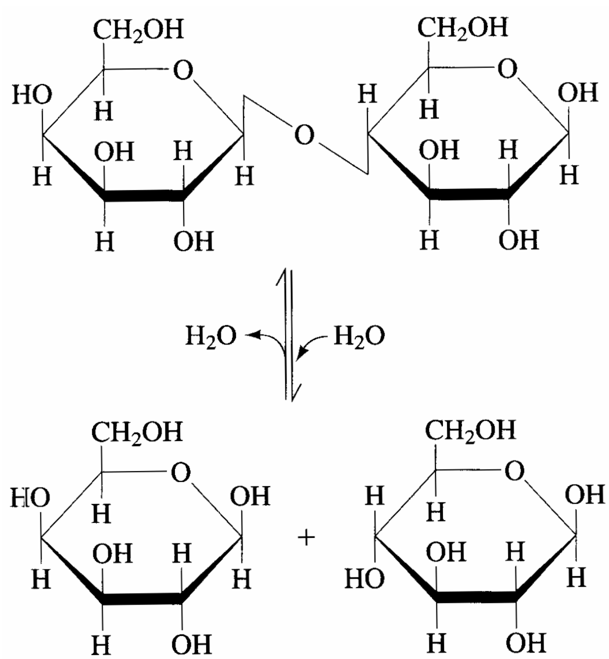
1. What are the elements that account for 98% of the dry weight of living cells?

2. In what critical ways was the atmosphere of the primitive earth different than the earth's current atmosphere?

3. What is the rationale and significance of the Miller and Urey experiments?

4. What was, and continues to be, the source of atmospheric oxygen?

5. Examine the reaction shown below for the condensation and hydrolysis of lactose (two covalently linked sugars, a disaccharide). Circle the functional groups that will form water during the condensation.



6. The condensation of two functional groups can result in the formation of another common functional group, which can be referred to as a compound functional group. Examine the functional groups in Table 1-2. Which compound functional groups are the combination of two other functional groups found in that figure? Show how these compound functional groups form.

Cellular Architecture

7. Draw a schematic diagram of an eukaryotic cell showing its principal organelles.

8. Give the principal distinguishing feature(s) of each pair of terms:

   (a) Prokaryote and eukaryote
   (b) Cytosol and cytoplasm
   (c) Endoplasmic reticulum and cytoskeleton

Organismal Evolution

9. Living organisms are classified into three domains: _________________,

   __________________, and __________________.

10. What is the most compelling evidence that mitochondria and chloroplasts represent descendents of symbiotic bacteria that lived inside of ancient eukaryotic cells?

11. What is the relationship between mutation and genetic variation in a population of organisms? Of what significance is it to evolution?

Thermodynamics

12. Distinguish between enthalpy and total energy. Under what conditions are they equivalent?

13. What does it mean when q and w are positive?

14. When crystalline urea is dissolved in water, the temperature of the solution drops precipitously. Does the enthalpy of the system increase or decrease? Explain.

15. List and define the four major thermodynamic state functions.

16. Which of the following pairs of states has higher entropy?

    (a) Two separate beakers of NaCl and KCH_3COO in solution and a beaker containing a solution of both salts.
    (b) A set of dice in which all the dice show 6 dots on the top side and a set of dice in which the 6's show up on one of the side faces.
    (c) A small symmetric molecule that can form a polymer through reaction at either end and a small asymmetric molecule that can polymerize from only one end.

17. Rationalize the temperature dependence of Gibbs free energy changes when both the enthalpy and entropy terms are positive values or when they are both negative values.

18. Hydrogen gas combines spontaneously with oxygen gas to form water

$$2\ H_2 + O_2 \rightarrow 2\ H_2O$$

Which term, enthalpy or entropy, predominates in the equation for the Gibbs free energy? How are the surroundings affected by this reaction?

19. Evaluate the following statement: Enzymes accelerate the rate of a reaction by increasing the spontaneity of the reaction.

20. Based on your reading in this chapter, suggest simple criteria for a reasonable definition of life.

Answers to Questions

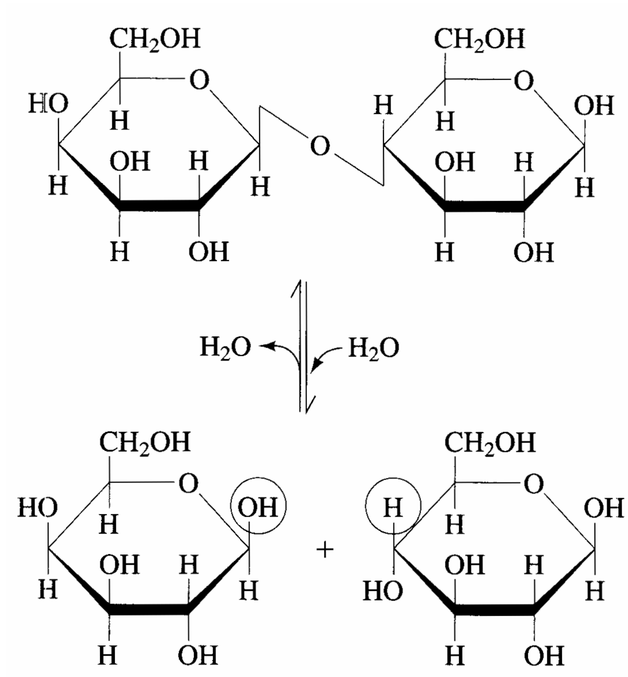
1. Carbon, nitrogen, oxygen, hydrogen, phosphorus, calcium, potassium, and sulfur account for 98% of the dry weight of living cells.

2. The primitive earth's atmosphere was a relatively reducing atmosphere lacking appreciable amounts of O_2. Much recent controversy revolves around just how much NH_3 and CH_4 existed in the young earth's atmosphere. Relatively low amounts would indicate that the atmosphere was both nonreducing and nonoxidizing. In either case, the absence of significant levels of O_2 indicate that the atmosphere was nonoxidizing compared to the present atmosphere.

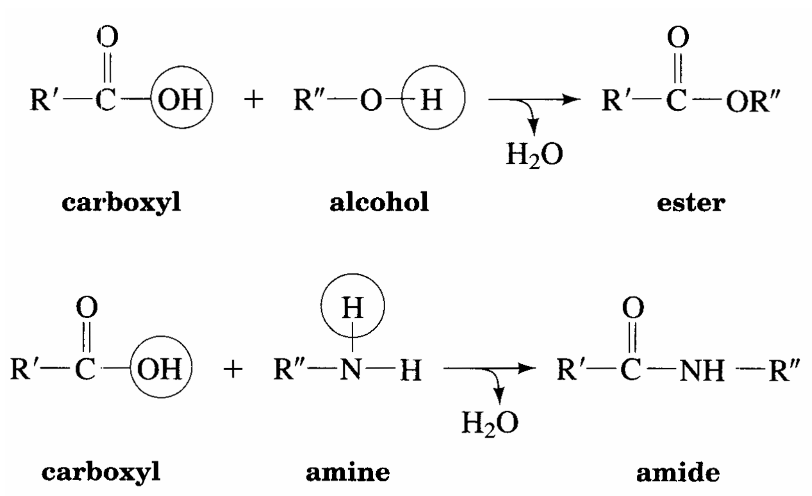
3. The Miller and Urey experiments were designed to ask whether biological molecules could be generated by mimicking the atmospheric conditions of the early earth. The early atmosphere was thought then to consist of H_2O, CH_4, NH_3, SO_2, and possibly H_2. Miller and Urey subjected these molecules, except for SO_2, to electrical discharges that were meant to simulate discharges believed to be prevalent in the earth's early atmosphere. The generation of diverse organic acids showed that the precursors for larger biological molecules could be spontaneously produced in the early atmosphere, paving the way for subsequent chemical evolution.

4. Photosynthesis.

5. Shown below is the condensation of galactose and glucose to form lactose. The atoms involved in the elimination of water are circled.



6. Shown below are condensation reactions of two pairs of functional groups found in Table 1-2. The atoms involved in the elimination of water are circled.



7. See Figure 1-8.

8. (a) Eukaryotes are defined by their elaborate internal membrane system and the enclosure of genomic DNA inside a double-membrane compartment, the nucleus, which is lacking in prokaryotes.
   (b) The cytoplasm is the contents of a prokaryotic cell and also refers to the cellular contents outside of the nucleus in eukaryotes. The cytosol is the cellular contents minus all of the membranous compartments of the cell (e.g., mitochondria, endoplasmic reticulum, Golgi apparatus, chloroplasts, and vacuoles).
   (c) The endoplasmic reticulum is the extensive network of internal membranes in eukaryotic cells, which is topologically continuous with the nuclear membrane. The cytoskeleton is the extensive network of protein filaments in the cytosol of eukaryotic cells.

9. All living organisms can be classified into three domains: archaea (archaebacteria), bacteria (eubacteria), and eukarya (eukaryotes).

10. The most compelling evidence that these organelles were once symbiotic bacteria is the presence of distinct genetic material and protein synthesis machinery inside of these organelles. The RNA and proteins that make up the protein synthesis machinery of these organelles is much more similar to that of bacteria than that of eukaryotes (see Chapter 26).

11. Genetic variation results from mutations that persist in a population and have not been eliminated by natural selection because they did not significantly decrease fitness. Evolution of a population occurs when variations that increase an individual's chances for survival and reproduction spread throughout the population.

12. Enthalpy is defined as $H = U + PV$. Hence $\Delta H = \Delta U + \Delta(PV)$. The enthalpy of a system is equal to its energy change when $\Delta(PV) = 0$, which occurs at the constant pressure and volume conditions typical of living things.

13. If q is positive, then heat has been transferred *to* the system, increasing its internal energy. If w is positive, then work has been done *by* the system, decreasing its internal energy.

14. In this example, urea and the water are the system, and the vessel and beyond are the surroundings. As urea dissolves, the enthalpy increases (an endothermic process). Heat is absorbed into the interactions between the urea and water, making the solution cooler.

15. **Energy** is measured as the heat absorbed by a system minus the work done by the system on its surroundings. **Enthalpy**, or heat content, is the amount of heat generated or absorbed by a system when a process occurs at constant pressure, as in biological systems, and no work is done other than the work of expansion or contraction (ΔV) of the system. **Entropy** is a measure of the heat absorbed or generated by a system at constant temperature and reflects the number of equivalent ways of arranging a system with no change in its internal energy. **Gibbs free energy** is the energy available to do work; it is a combination of

enthalpy and entropy ($\Delta H - T\Delta S$) and an indicator of the spontaneity of a process at constant pressure and temperature.

16. (a) The beaker containing the solution with both salts has higher entropy. The molecules in this solution can be arranged in many more orientations with respect to each other than each salt solution alone.
    (b) The set of dice with the 6's showing on the side faces has more entropy since there are many more ways to obtain this configuration.
    (c) The symmetric molecule has greater entropy, since it can polymerize by joining reactions involving either end. Note that the information content of the asymmetric molecule is higher, however. All biological polymers are formed from asymmetric subunits.

17. When enthalpy and entropy are both positive, ΔG decreases with increasing temperature, and the temperature at which the reaction occurs spontaneously must be high enough that the $T\Delta S$ term is larger than the ΔH term in the equation $\Delta G = \Delta H - T\Delta S$. For instance, dissolving crystalline urea in water is endothermic, however the process is spontaneous when it is carried out at room temperature. When enthalpy and entropy are both negative, ΔG decreases with decreasing temperature, and for the reaction to be spontaneous, the temperature must be low enough that the $T\Delta$S term is not more negative than the ΔH term.

18. The expression for the Gibbs free energy is $\Delta G = \Delta H - T\Delta S$. In this reaction, the entropy decreases since the number of molecules decreases and the product is therefore more ordered than the reactants. Hence, in order for this reaction to be spontaneous the enthalpy term (ΔH) must be more negative than the entropy term ($T\Delta S$). In many cases such as this, the enthalpy of the reaction is negative and the reaction releases heat to the surroundings.

19. This statement is incorrect. An enzymes does not alter the spontaneity of a reaction; rather, it increases the rate at which a reaction reaches equilibrium.

20. Catalysis, replication, and mutability have been argued to be the minimum criteria for life. In addition, an organisms must be able to maintain a novel chemical environment that is not in equilibrium with its surroundings and to resist the environmental fluctuations that might disturb its ability to carry out the other three essential functions of living systems—this steady state condition is called homeostasis.