and some macromolecules are synthesized, interconverted, and metabolized for energy production are described.

Part 3 is Genes, Gene Expression, and the Metabolism of Informational Macromolecules. The genetic control of the cell, as it is mediated by the synthesis of biological macromolecules, is the primary topic.

As an introduction to Part 1, we point out that most of the organic molecules of living systems fall into one of four general classes: carbohydrates, proteins, nucleic acids, and lipids. Only six elements account for almost the entire mass of these organic molecules: carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur. The carbohydrates, compounds principally of carbon, hydrogen, and oxygen, serve mainly as sources of energy and structural materials. However, they also control the polarity of proteins and lipids to which they may be attached and often serve as recognition sites. As such, the carbohydrate portions of biological macromolecules may control their subcellular location and other important characteristics. We consider carbohydrates as the first of the four classes because they illustrate simply and directly certain important chemical characteristics of biological molecules, such as molecular asymmetry.

Proteins are polymers of amino acids and are the biological macromolecules that show the greatest diversity of function, including serving as structures and structural components, catalysts, and hormones.

Nucleic acids, the informational macromolecules, are essential contributors to that most characteristic properties of living systems: reproduction and genetic control. Low molecular weight forms of nucleic acids participate in energy metabolism and biosynthesis.

Lipids serve as energy stores and the principal building blocks of cell membranes. Certain lipids serve as hormones and other types of biological signals; others are key metabolic intermediates.

The organic and most of the inorganic constituents of the cell, as crucial as they are to the structure and functioning of the cell, constitute only a small fraction of the mass of a typical cell. The most abundant compound of the cell is, of course, water.

1.4 SOME IMPORTANT PROPERTIES OF WATER

Undoubtedly, no factor has had more influence on the development of life on earth than the peculiar properties of water and its abundance on our planet. Consider the group of compounds listed in Table 1.1. These compounds may be compared with H_2O because they all have protons bound to oxygen or some other electronegative atom. As can be seen, H_2O has the highest boiling point, the highest specific heat of vaporization, and, by far, the highest melting point of all these compounds. Pauling has expressed the anomalous behavior of H_2O in another way by comparing it with the hydrides of other elements in Group VI of the periodic table: H_2S, H_2Se, and H_2Te. When this is done, we would predict that H_2O should have boiling point of $-100°C$, instead of its $+100°C$ boiling point!

The water molecule is highly polarized. That is, its electrons are not evenly distributed over it. The electronegative oxygen atom tends to draw electrons away from the hydrogen atoms, leaving a net positive charge surrounding the

TABLE 1.1 Some Physical Properties of Water and Other Compounds

SUBSTANCE	MELTING POINT (°C)	BOILING POINT (°C)	HEAT OF VAPORIZATION (cal/g)	HEAT CAPACITY (cal/g)	HEAT OF FUSION (cal/g)
Water	0	100	540	1.00	80
Ethanol	−114	78	204	0.58	25
Methanol	−98	65	263	0.60	22
NH_3	−78	−33	327	1.12	84
H_2S	−83	−60	132	—	17
HF	−92	19	360	—	55

proton. Because of this polarization, water molecules behave like dipoles and can be oriented toward both positive and negative ions. This property, in turn, accounts for the unusual ability of water to act as a solvent for polar compounds. Positive or negative ions in a crystal lattice can be approached by dipolar water molecules and brought into solution. Once in solution, ions of both positive and negative charge will be surrounded by protective layers of water molecules, and further interaction between those ions of opposite charge subsequently will be decreased.

The high boiling and melting points of H_2O and its high heat of vaporization are the result of an interaction between adjacent water molecules known as hydrogen bonding. Briefly put, the term **hydrogen bond** refers to the interaction of a hydrogen atom that is covalently bonded to one electronegative atom with the electrons of a second electronegative atom to which it is not directly covalently bonded. There is a tendency for the hydrogen atom to associate with the second electronegative atom by sharing the nonbonded electron pair of that atom, and a weak bond of approximately 4.5 kcal/mole can exist. In biological material, the two atoms most commonly involved in hydrogen bonding are nitrogen and oxygen. In ice, the water molecules are nearly completely hydrogen-bonded. Even in liquid water, small transient chains of water molecules will occur due to this interaction.
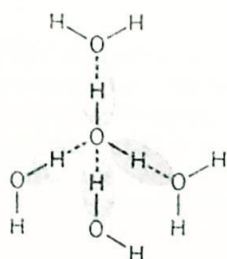
The energy necessary to disrupt even the most stable hydrogen bonds (4 – 10 kcal/mole) is much less than that required to break most covalent bonds. In an aqueous solution, hydrogen bonds are broken and formed readily. The cumulative effect of hydrogen bonding in water is a major factor in explaining many of the unusual properties of H_2O. Thus, the extra energy required to boil water and melt ice may be attributed largely to extensive hydrogen bonding.

Other unusual properties of water make it an ideal medium for living orga-

nisms. The specific heat capacity of H_2O — the number of calories required to raise the temperature of 1 g of water from 15 to 16°C — is 1.0 and is unusually high among several of the hydrogen bonding solvents considered in Table 1.1. Only a few solvents, such as liquid ammonia, have greater heat capacities than water. The greater the specific heat of a substance, the less the change in temperature that results when a given amount of heat is absorbed by that substance. Thus, H_2O is well-designed for keeping the temperature of a living organism relatively constant.

The heat of vaporization of water, as already mentioned, is unusually high. Expressed as the specific heat of vaporization (calories absorbed per gram vaporized), the value for water is 540 at its boiling point and even greater at lower temperatures. This high value is very useful in helping the living organism keep its temperature constant, since a large amount of heat can be dissipated by vaporization of H_2O.

The high heat of fusion of water (Table 1.1) is also of significance in stabilizing the biological environment. Although cellular water rarely freezes in higher living forms, the heat released by H_2O on freezing is a major factor in slowing the temperature drop of a body of water during the winter. Thus, a gram of H_2O must give up 80 times as much heat in freezing at 0°C as it does in being lowered from 1 to 0°C just before freezing.

One final example of a property of H_2O that is of biological significance must be cited: H_2O expands on solidifying, and ice is less dense than water. Only a few other substances expand on freezing. The importance of this property for biology has long been recognized. If ice were heavier than liquid water, it would sink to the bottom of its container on freezing. This would mean that oceans, lakes, and streams would freeze from the bottom to the top and, once frozen, would be extremely difficult to melt. Such a situation would obviously be incompatible with those bodies of water serving as the habitat of many living forms, as they do. As it is, however, the warmer, liquid water falls to the bottom of any lake and the ice floats on top where heat from the external environment can reach and melt it.

Additional properties of water such as high surface tension and a high dielectric constant have significance in biology. However, we refer the student to the classical publication by Henderson, *The Fitness of the Environment,* in which this subject is discussed in more detail. Instead, in the next section, we consider the ability of water to dissociate into hydrogen (H^+) and hydroxyl (OH^-) ions and the mechanisms by which the concentrations of hydrogen and hydroxyl ions in aqueous solutions are controlled, both experimentally and in the living organism. To do this, we review first the *law of mass action* and the *ion product of water.*

1.5 THE LAW OF MASS ACTION

For the reaction

$$A + B \rightleftharpoons C + D \tag{1.1}$$

in which two reactants A and B interact to form two products C and D, we may write the expression

$$K_{eq} = \frac{C_C \cdot C_D}{C_A \cdot C_B} \tag{1.2}$$

This is an expression of the **law of mass action,** applied to Reaction 1.1, which states that *at equilibrium, the product of the concentrations of the product divided by the product of the concentrations of the reactants is a constant known as the equilibrium constant, K_{eq}.* This constant is fixed for any given temperature. If the concentration of any single component of the reaction is varied, it follows that the concentration of at least one other component must also change in order to meet the conditions of the equilibrium as defined by K_{eq}.

To be precise, we should distinguish between the concentration of the reactants and products in this reaction and the **activity** or **effective concentration** of these reactants and products. It has long been recognized that the concentration of a substance does not precisely reflect its reactivity in a chemical reaction. Moreover, these discrepancies in behavior are appreciable when the concentration of reactant is large. At high concentrations, the individual reactant molecules may exert a mutual attraction on each other or exhibit alterations in their interactions with the solvent in which the reaction occurs. On the other hand, in dilute solutions, chemical reactivity may be proportional to reactant concentration, indicating that such interactions are negligible. In order to correct for the difference between concentration and effective concentration, the activity coefficient γ was introduced. Thus,

$$a_A = C_A \times \gamma \tag{1.3}$$

where a_A refers to the activity and C_A to the concentration of the substance. The activity coefficient is not a fixed quantity but varies in value depending on the solution composition. At very dilute concentrations, the activity coefficient of the solute approaches unity, because there is little if any solute-solute interaction. At infinite dilution, the activity and the concentration are the same. For the purpose of this book, we usually will not distinguish between activities and concentrations; rather, we use the latter term. Often, this does not cause serious error, since the reactants in many biochemical reactions are quite low in concentration, including the H^+ ion concentration, the subject of the next subsection.

1.6   DISSOCIATION OF WATER AND ITS ION PRODUCT, K_w

Water is far from inert in its service as a solvent for biochemical reactions. In addition to its abilities as a solvent, water is chemically reactive. It is a weak electrolyte that dissociates only slightly to form H^+ and OH^- ions.

$$H_2O \rightleftharpoons H^+ + OH^- \tag{1.4}$$

The equilibrium constant for this dissociation reaction has been accurately measured, and at 25°C, it has the value 1.8×10^{-16} mole/liter. That is,

$$K_{eq} = \frac{C_{H^+} C_{OH^-}}{C_{H_2O}} = 1.8 \times 10^{-16}$$

The concentration of H_2O (C_{H_2O}) in pure water may be calculated to be 1000 g/liter divided by 18 g/mole, giving 55.5 moles/liter. Since the concentration of H_2O in dilute aqueous solutions is essentially unchanged from that in pure H_2O, this figure may be taken as a constant. It is, in fact, usually incorporated into the expression for the dissociation of water, to give