helix, adjacent base pairs are stacked nearly on top of one another, and so many atoms in each base pair are separated by their van der Waals contact distance. The central base pair is shown in dark blue and the two adjacent base pairs in light blue. Several van der Waals contacts are shown in red.

- *The hydrophobic effect also contributes to the favorability of base stacking.* More-complete base stacking moves the nonpolar surfaces of the bases away from water molecules and into contact with each other.

The principles of double-helix formation between two strands of DNA apply to many other biochemical processes. Many weak interactions contribute to the overall energetics of the process, some favorably and some unfavorably. Furthermore, **surface complementarity** is a key feature: when complementary surfaces meet, hydrogen-bond donors align with hydrogen-bond acceptors, and nonpolar surfaces come together to maximize van der Waals interactions and minimize nonpolar surface area exposed to the aqueous environment. The properties of water play a major role in determining the importance of these interactions. Interactions between complementary surfaces play central roles in a great many biochemical processes, and we will encounter them repeatedly throughout the book.

## The laws of thermodynamics govern the behavior of biochemical systems

We can look at the formation of the double helix from a different perspective by examining the laws of thermodynamics, general principles that apply to all physical (and biological) processes. The laws distinguish between a system and its surroundings; a *system* refers to the matter and energy within a defined region of space, and the matter and energy in the rest of the universe is called the *surroundings.*

The laws of thermodynamics are of great importance because they determine the conditions under which specific processes can or cannot take place. We will consider these laws from a general perspective first and then apply the principles that we have developed to the formation of the double helix.

- *The First Law of Thermodynamics states that the total energy of a system and its surroundings is constant.* In other words, the energy content of the universe is constant; energy can be neither created nor destroyed. Energy can take different forms, however. Heat, for example, is one form of energy. Heat is a manifestation of the *kinetic energy* associated with the random motion of molecules. Alternatively, energy can be present as *potential energy* — energy of position that will be released on the occurrence of some process. Consider, for example, a ball held at the top of a tower. In this position the ball has considerable gravitational potential energy because, when it is released, the ball will develop kinetic energy associated with its motion as it falls. Chemical potential energy is related to the plausible ways that atoms might react with one another. For instance, a mixture of gasoline and oxygen has a large potential energy because these molecules can react to form carbon dioxide and water and release energy as heat.

  Energy is always required to break chemical bonds and is released when new bonds form. The First Law requires that any energy released in the formation of chemical bonds must be used to break other bonds, released as heat or light, or stored in some other form.

- *The Second Law of Thermodynamics states that the total entropy of a system plus that of its surroundings always increases.* **Entropy** is a measure of the degree of randomness or disorder in a system. For example, the hydrophobic effect — the release of water from nonpolar surfaces — is favorable because water molecules that are

> free in solution are more disordered than they are when they are associated with nonpolar surfaces.

At first glance, the Second Law appears to contradict much common experience, particularly about biological systems. Many biological processes, such as the generation of a leaf from carbon dioxide gas and other nutrients, clearly increase the level of order and hence decrease entropy. Entropy may be decreased locally in the formation of such ordered structures only if the entropy of other parts of the universe is increased by an equal or greater amount. The local decrease in entropy is usually accomplished by a release of heat, which increases the entropy of the surroundings.

We can analyze this process in quantitative terms. First, consider the system. The entropy (*S*) of the system may change in the course of a chemical reaction by an amount $\Delta S_{\text{system}}$. If heat flows from the system to its surroundings, then the heat content, often referred to as the **enthalpy** (*H*), of the system will be reduced by an amount $\Delta H_{\text{system}}$. To apply the Second Law, we must determine the change in entropy of the surroundings. If heat flows from the system to the surroundings, then the entropy of the surroundings will increase.

The precise change in the entropy of the surroundings depends on the temperature; the change in entropy is greater when heat is added to relatively cold surroundings than when heat is added to surroundings at high temperatures; these surroundings are already in a high degree of disorder. To be even more specific, the change in the entropy of the surroundings will be proportional to the amount of heat transferred from the system and inversely proportional to the temperature (*T*) of the surroundings. In biological systems, *T*, absolute temperature in kelvins (K), is usually assumed to be constant. Thus, a change in the entropy of the surroundings is given by

$$\Delta S_{\text{surroundings}} = -\Delta H_{\text{system}} / T$$

**(1)**

The total entropy change is given by the expression

$$\Delta S_{\text{total}} = \Delta S_{\text{system}} + \Delta S_{\text{surroundings}}$$

**(2)**

Substituting equation 1 into equation 2 yields

$$\Delta S_{\text{total}} = \Delta S_{\text{system}} - \Delta H_{\text{system}} / T$$

**(3)**

Multiplying by $-T$ gives

$$-T\Delta S_{\text{total}} = \Delta H_{\text{system}} - T\Delta S_{\text{system}}$$

The function $-T\Delta S$ has units of energy and is referred to as **free energy** or **Gibbs free energy**, after Josiah Willard Gibbs, who developed this function in 1878:

$$\Delta G = \Delta H_{\text{system}} - T\Delta S_{\text{system}}$$

The free-energy change, $\Delta G$, will be used throughout this book to describe the energetics of biochemical reactions. The Gibbs free energy can also be considered the energy available to do useful work; it is essentially an accounting tool that keeps track of both the entropy of the system (directly) and the entropy of the surroundings (in the form of heat released from the system).

Recall that the Second Law of Thermodynamics states that, for a process to take place, the entropy of the universe must increase. Examination of equation 3 shows that the total entropy will increase if and only if

$$\Delta S_{\text{system}} > \Delta H_{\text{system}} / T$$

Rearranging gives $T\Delta S_{\text{system}} > \Delta H_{\text{system}}$ or, in other words, entropy will increase if and only if

$$\Delta G = \Delta H_{\text{system}} - T\Delta S_{\text{system}} < 0$$

Thus, the free-energy change must be negative for a process to take place spontaneously. There is negative free-energy change when and only when the overall entropy of the universe is increased.

## SELF-CHECK QUESTION

The free energy can be calculated based on the system only. Why don’t the surroundings need to be considered separately?

## By releasing heat, the formation of the double helix obeys the Second Law of Thermodynamics

Let's see how the principles of thermodynamics apply to the formation of the double helix (**Figure 1.16**). Suppose solutions containing each of the two single strands are mixed. Before the double helix forms, each of the single strands is free to translate (change position) and rotate in solution, whereas each matched pair of strands in the double helix must move together. Additionally, the free single strands exist in more conformations than possible when bound together in a double helix. Thus, the formation of a double helix from two single strands appears to result in a decrease rather than an increase in disorder, and therefore entropy, of the system.