

The Second Law

Some things happen; some things don't. A gas expands to fill the vessel it occupies; a gas that already fills a vessel does not suddenly contract into a smaller volume. A hot object cools to the temperature of its surroundings; a cool object does not suddenly become hotter than its surroundings. Hydrogen and oxygen combine explosively (once their ability to do so has been liberated by a spark) and form water; water left standing in oceans and lakes does not gradually decompose into hydrogen and oxygen. These everyday observations suggest that changes can be divided into two classes. A **spontaneous change** is a change that has a tendency to occur without work having to be done to bring it about. A spontaneous change has a natural tendency to occur. A **non-spontaneous change** is a change that can be brought about only by doing work. A non-spontaneous change has no natural tendency to occur. Non-spontaneous changes can be *made* to occur by doing work: a gas can be compressed into a smaller volume by pushing in a piston, the temperature of a cool object can be raised by forcing an electric current through a heater attached to it, and water can be decomposed by the passage of an electric current. However, in each case we need to act in some way on the system to bring about the non-spontaneous change. There must be some feature of the world that accounts for the distinction between the two types of change.

Throughout the chapter we shall use the terms “spontaneous” and “non-spontaneous” in their thermodynamic sense. That is, we use them to signify that a change does or does not have a natural *tendency* to occur. In thermodynamics the term spontaneous has nothing to do with speed. Some spontaneous changes are very fast, such as the precipitation reaction that occurs when solutions of sodium chloride and silver nitrate are mixed. However, some spontaneous changes are so slow that there may be no observable change even after millions of years. For example, although the decomposition of benzene into carbon and hydrogen is spontaneous, it does not occur at a measurable rate under normal conditions, and benzene is a common laboratory commodity with a shelf life of (in principle) millions of years. Thermodynamics deals with the tendency to change; it is silent on the rate at which that tendency is realized.

We shall use the concepts introduced in this chapter to guide our study of bioenergetics and structure in biological systems. Our discussion of energy conversion in biological cells has focused on the chemical sources of energy that sustain life. We now begin an investigation—to be continued throughout the text—of the mechanisms by which energy in the form of radiation from the Sun or ingested as oxidizable molecules is converted to work of muscle contraction, neuronal activity, biosynthesis of essential molecules, and transport of material into and out of the cell. We shall also explain a remark made in Chapter 1, that only part of the energy of biological fuels leads to work, with the rest being dissipated in the surroundings as heat. Finally, we begin to describe some of the important thermodynamic and chemical factors that contribute to the formation and stability of proteins and biological membranes.

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Entropy

A few moments' thought is all that is needed to identify the reason why some changes are spontaneous and others are not. That reason is *not* the tendency of the system to move toward lower energy. This point is easily established by identifying an example of a spontaneous change in which there is no change in energy. The isothermal expansion of a perfect gas into a vacuum is spontaneous, but the total energy of the gas does not change because the molecules continue to travel at the same average speed and so keep their same total kinetic energy. Even in a process in which the energy of a system does decrease (as in the spontaneous cooling of a block of hot metal), the First Law requires the total energy to be constant. Therefore, in this case the energy of another part of the world must increase if the energy decreases in the part that interests us. For instance, a hot block of metal in contact with a cool block cools and loses energy; however, the second block becomes warmer and increases in energy. It is equally valid to say that the second block has a tendency to go to higher energy as it is to say that the first block has a tendency to go to lower energy!

In the next few sections we shall develop the thermodynamic criteria for spontaneity by using an approach similar to that adopted in Chapter 1. At first sight the ideas, models, and mathematical expressions in our discussion may appear to be of no immediate concern to a biochemist. But in due course we shall see how they are of the greatest importance for an understanding of the flow of energy in biological systems and the reactions that sustain them.

2.1 The direction of spontaneous change

To understand the spontaneous processes occurring in organisms, we need to identify the factors that drive any physical or chemical change.

We shall now show that *the apparent driving force of spontaneous change is the tendency of energy and matter to disperse*. For example, the molecules of a gas may all be in one region of a container initially, but their ceaseless disorderly motion ensures that they spread rapidly throughout the entire volume of the container (Fig. 2.1). Because their motion is so random, there is a negligibly small probability that all the molecules will find their way back simultaneously into the region of the container they occupied initially. In this instance, the natural direction of change corresponds to the dispersal of matter.

A similar explanation accounts for spontaneous cooling, but now we need to consider the dispersal of energy rather than that of matter. In a block of hot metal, the atoms are oscillating vigorously, and the hotter the block, the more vigorous their motion. The cooler surroundings also consist of oscillating atoms, but their motion is less vigorous. The vigorously oscillating atoms of the hot block jostle their neighbors in the surroundings, and the energy of the atoms in the block is handed on to the atoms in the surroundings (Fig. 2.2). The process continues until the vigor with which the atoms in the system are oscillating has fallen to that of the surroundings. The opposite flow of energy is very unlikely. It is highly improbable that there will be a net flow of energy into the system as a result of jostling from less vigorously oscillating molecules in the surroundings. In this case, the natural direction of change corresponds to the dispersal of energy.

The tendency toward dispersal of energy also explains the fact that, despite numerous attempts, it has proved impossible to construct an engine like that shown

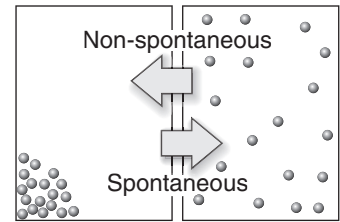


Fig. 2.1 One fundamental type of spontaneous process is the dispersal of matter. This tendency accounts for the spontaneous tendency of a gas to spread into and fill the container it occupies. It is extremely unlikely that all the particles will collect into one small region of the container. (In practice, the number of particles is of the order of 10^{23} .)

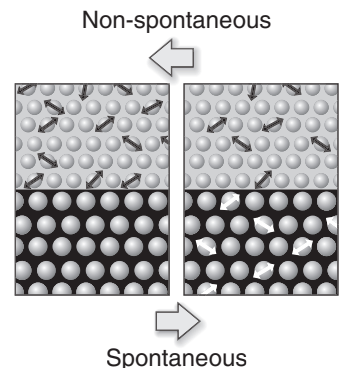


Fig. 2.2 Another fundamental type of spontaneous process is the dispersal of energy (represented by the small arrows). In these diagrams, the small spheres represent the system and the large spheres represent the surroundings. The double-headed arrows represent the thermal motion of the atoms.

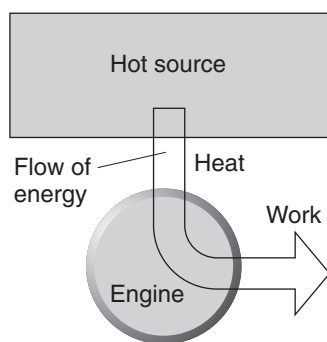


Fig. 2.3 The Second Law denies the possibility of the process illustrated here, in which heat is changed completely into work, there being no other change. The process is not in conflict with the First Law, because the energy is conserved.

in Fig 2.3, in which heat, perhaps from the combustion of a fuel, is drawn from a hot reservoir and completely converted into work, such as the work of moving an automobile. All actual heat engines have both a hot region, the “source,” and a cold region, the “sink,” and it has been found that some energy must be discarded into the cold sink as heat and not used to do work. In molecular terms, only some of the energy stored in the atoms and molecules of the hot source can be used to do work and transferred to the surroundings in an orderly way. For the engine to do work, some energy must be transferred to the cold sink as heat, to stimulate random motion of its atoms and molecules.

In summary, we have identified two basic types of spontaneous physical process:

1. Matter tends to become dispersed.
2. Energy tends to become dispersed.

Though it is convenient to regard the dispersal of matter and energy as two distinct processes, it is important to appreciate that they are sometimes related. To see why, consider the contraction and expansion of a gas. When a gas contracts isothermally, the kinetic energy of the atoms becomes localized. When it expands, the locations of the particles become more widely dispersed and so too does their kinetic energy.

Although it is easy to relate the spontaneous expansion of a perfect gas to the dispersal of matter and energy, we need to take the next step and see how these two fundamental processes result in some chemical reactions being spontaneous and others not. It may seem very puzzling that dispersal of matter can account for the formation of such organized systems as proteins and biological cells. Nevertheless, in due course we shall see that change in all its forms, including the formation of organized structures, can indeed emerge as energy and matter disperse.

2.2 Entropy and the Second Law

To make progress with our quantitative discussion of biological structure and reactivity, we need to associate the dispersal of energy and matter with the change in a state function.

The measure of the dispersal of energy or matter used in thermodynamics is called the **entropy**, S . We shall soon define entropy precisely and quantitatively, but for now all we need to know is that when matter and energy disperse, the entropy increases. That being so, we can combine the two remarks above into a single statement known as the **Second Law of thermodynamics**:

The entropy of an isolated system tends to increase.

The “isolated system” may consist of a system in which we have a special interest (a beaker containing reagents) and that system’s surroundings: the two components jointly form a little “universe” in the thermodynamic sense.

To make progress and turn the Second Law into a quantitatively useful statement, we need to define entropy precisely. We shall use the following definition of a *change* in entropy:

$$\Delta S = \frac{q_{\text{rev}}}{T} \quad (2.1)$$

That is, the change in entropy of a substance is equal to the energy transferred as heat to it *reversibly* divided by the temperature at which the transfer takes place. This definition can be justified thermodynamically, but we shall confine ourselves to showing that it is plausible and then show how to use it to obtain numerical values for a range of processes.

There are three points we need to understand about the definition in eqn 2.1: the significance of the term “reversible,” why heat (not work) appears in the numerator, and why temperature appears in the denominator.

We met the concept of reversibility in Section 1.4, where we saw that it refers to the ability of an infinitesimal change in a variable to change the direction of a process. Mechanical reversibility refers to the equality of pressure acting on either side of a movable wall. Thermal reversibility, the type involved in eqn 2.1, refers to the equality of temperature on either side of a thermally conducting wall. Reversible transfer of heat is smooth, careful, restrained transfer between two bodies at the same temperature. By making the transfer reversible, we ensure that there are no hot spots generated in the object that later disperse spontaneously and hence add to the entropy.

Now consider why heat and not work appears in eqn 2.1. Recall from Section 1.2 that to transfer energy as heat, we make use of the random motion of molecules, whereas to transfer energy as work, we make use of orderly motion. It should be plausible that the change in entropy—the change in the degree of dispersal of energy and matter—is proportional to the energy transfer that takes place by making use of random motion rather than orderly motion.

Finally, the presence of the temperature in the denominator in eqn 2.1 takes into account the randomness of motion that is already present. If a given quantity of energy is transferred as heat to a hot object (one in which the atoms already undergo a significant amount of thermal motion), then the additional randomness of motion generated is less significant than if the same quantity of energy is transferred as heat to a cold object in which the atoms have less thermal motion. The difference is like sneezing in a busy street (an environment analogous to a high temperature), which adds little to the disorder already present, and sneezing in a quiet library (an environment analogous to a low temperature), which can be very disruptive.

ILLUSTRATION 2.1 Calculating a change in entropy

The transfer of 100 kJ of heat to a large mass of water at 0°C (273 K) results in a change in entropy of

$$\Delta S = \frac{q_{\text{rev}}}{T} = \frac{100 \times 10^3 \text{ J}}{273 \text{ K}} = +366 \text{ J K}^{-1}$$

We use a large mass of water to ensure that the temperature of the sample does not change as heat is transferred. The same transfer at 100°C (373 K) results in

$$\Delta S = \frac{100 \times 10^3 \text{ J}}{373 \text{ K}} = +268 \text{ J K}^{-1}$$

The increase in entropy is greater at the lower temperature. Notice that the units of entropy are joules per kelvin (J K^{-1}). Entropy is an extensive property. When we deal with molar entropy, an intensive property, the units will be joules per kelvin per mole ($\text{J K}^{-1} \text{ mol}^{-1}$). ■

The entropy (it can be proved) is a state function, a property with a value that depends only on the present state of the system. The entropy is a measure of the current state of dispersal of energy and matter in the system, and how that change was achieved is not relevant to its current value. The implication of entropy being a state function is that a change in its value when a system undergoes a change of state is independent of how the change of state is brought about.

2.3 The entropy change accompanying heating

To calculate entropy changes associated with complex biological processes, we must first learn how to cope with simple physical changes, such as heating.

We can often rely on intuition to judge whether the entropy increases or decreases when a substance undergoes a physical change. For instance, the entropy of a sample of gas increases as it expands because the molecules are able to move in a greater volume and so are more widely dispersed. We should also expect the entropy of a sample to increase as the temperature is raised from T_i to T_f , because the thermal motion is greater at the higher temperature. To calculate the change in entropy, we go back to the definition in eqn 2.1 and find that, provided the heat capacity is constant over the range of temperatures of interest,

$$\Delta S = C \ln \frac{T_f}{T_i} \quad (2.2)$$

where C is the heat capacity of the system; if the pressure is held constant during the heating, we use the constant-pressure heat capacity, C_p , and if the volume is held constant, we use the constant-volume heat capacity, C_v .

DERIVATION 2.1 The variation of entropy with temperature

Equation 2.1 refers to the transfer of heat to a system at a temperature T . In general, the temperature changes as we heat a system, so we cannot use eqn 2.1 directly. Suppose, however, that we transfer only an infinitesimal energy, dq , to the system; then there is only an infinitesimal change in temperature and we introduce negligible error if we keep the temperature in the denominator of eqn 2.1 equal to T during that transfer. As a result, the entropy increases by an infinitesimal amount dS given by

$$dS = \frac{dq_{\text{rev}}}{T}$$

To calculate dq , we recall from Section 1.5 that the heat capacity C is

$$C = \frac{q}{\Delta T}$$

where ΔT is macroscopic change in temperature. For the case of an infinitesimal change dT , we write

$$C = \frac{dq}{dT}$$

This relation also applies when the transfer of energy is carried out reversibly. Because infinitesimally small quantities may be treated like any other quantity in algebraic manipulations (*Comment 1.8*), it follows that

$$dq_{\text{rev}} = CdT$$

and therefore that

$$dS = \frac{CdT}{T}$$

The total change in entropy, ΔS , when the temperature changes from T_i to T_f is the sum (integral) of all such infinitesimal terms:

$$\Delta S = \int_{T_i}^{T_f} \frac{CdT}{T}$$

For many substances and for small temperature ranges we may take C to be constant. (This is strictly true only for a monatomic perfect gas.) Then C may be taken outside the integral and the latter evaluated as follows:

$$\Delta S = \int_{T_i}^{T_f} \frac{CdT}{T} = \overset{\text{Constant heat capacity}}{C} \int_{T_i}^{T_f} \frac{dT}{T} = C \ln \frac{T_f}{T_i}$$

We have used the same standard integral from *Comment 1.3* and evaluated the limits similarly.

Equation 2.3 is in line with what we expect. When $T_f > T_i$, $T_f/T_i > 1$, which implies that the logarithm is positive, that $\Delta S > 0$, and therefore that the entropy increases (Fig. 2.4). Note that the relation also shows a less obvious point, that the higher the heat capacity of the substance, the greater the change in entropy for a given rise in temperature. A moment's thought shows this conclusion to be reasonable too: a high heat capacity implies that a lot of heat is required to produce a given change in temperature, so the “sneeze” must be more powerful than for when the heat capacity is low, and the entropy increase is correspondingly high.

SELF-TEST 2.1 Calculate the change in molar entropy when water vapor is heated from 160°C to 170°C at constant volume. ($C_{V,m} = 26.92 \text{ J K}^{-1} \text{ mol}^{-1}$.)

Answer: $+0.615 \text{ J K}^{-1} \text{ mol}^{-1}$

When we cannot assume that the heat capacity is constant over the temperature range of interest, which is the case for all solids at low temperatures, we have to allow for the variation of C with temperature. In *Derivation 2.1* we found, before making the assumption that the heat capacity is constant, that

$$\Delta S = \int_{T_i}^{T_f} \frac{CdT}{T}$$

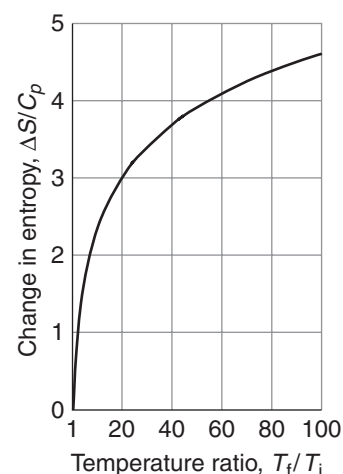


Fig. 2.4 The entropy of a sample with a heat capacity that is independent of temperature, such as a monatomic perfect gas, increases logarithmically (as $\ln T$) as the temperature is increased. The increase is proportional to the heat capacity of the sample.

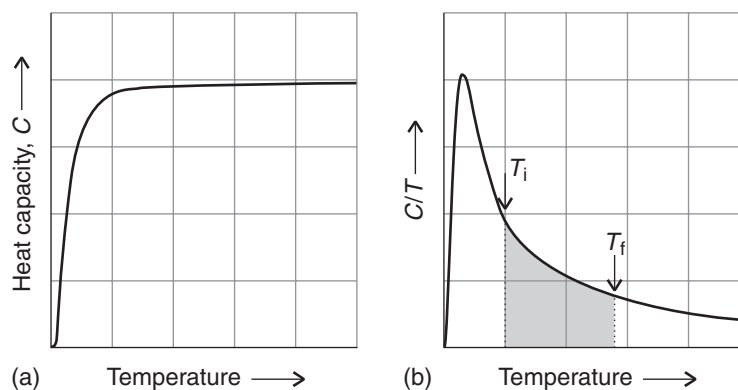


Fig. 2.5 The experimental determination of the change in entropy of a sample that has a heat capacity that varies with temperature, as shown in (a), involves measuring the heat capacity over the range of temperatures of interest, then plotting C_v/T against T and determining the area under the curve (the tinted area shown), as shown in (b). The heat capacity of all solids decreases toward zero as the temperature is reduced.

All we need to recognize is the standard result from calculus, illustrated in *Derivation 1.2*, that the integral of a function between two limits is the area under the graph of the function between the two limits. In this case, the function is C/T , the heat capacity at each temperature divided by that temperature, and it follows that

$$\Delta S = \text{area under the graph of } C/T \text{ plotted against } T, \text{ between } T_i \text{ and } T_f \quad (2.3)$$

This rule is illustrated in Fig. 2.5.

To use eqn 2.3, we measure the heat capacity throughout the range of temperatures of interest and make a list of values. Then we divide each one by the corresponding temperature to get C/T at each temperature, plot these C/T against T , and evaluate the area under the graph between the temperatures T_i and T_f .

2.4 The entropy change accompanying a phase transition

To prepare for being able to calculate the change in entropy associated with the unfolding of a biological macromolecule, we need to learn how to treat physical changes in general.

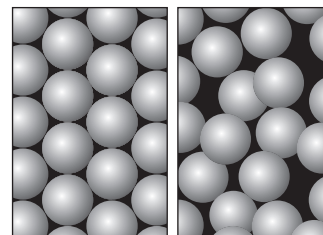
We can suspect that the entropy of a substance increases when it melts and when it vaporizes because its molecules become more dispersed as it changes from solid to liquid and from liquid to vapor. Likewise, we expect the unfolding of a protein from a compact, active three-dimensional conformation to a more flexible conformation, a process discussed in *Case study 1.1*, to be accompanied by an increase of entropy because the polypeptide chain becomes less organized.

The transfer of energy as heat occurs reversibly when a solid is at its melting temperature. If the temperature of the surroundings is infinitesimally lower than that of the system, then energy flows out of the system as heat and the substance freezes. If the temperature is infinitesimally higher, then energy flows into the system as heat and the substance melts. Moreover, because the transition occurs at constant pressure, we can identify the energy transferred by heating per mole of

substance with the enthalpy of fusion (melting). Therefore, the **entropy of fusion**, $\Delta_{\text{fus}}S$, the change of entropy per mole of substance, at the melting temperature, T_{fus} , is

$$\text{At the melting temperature: } \Delta_{\text{fus}}S = \frac{\Delta_{\text{fus}}H(T_{\text{fus}})}{T_{\text{fus}}} \quad (2.4)$$

Notice how we must use the enthalpy of fusion at the melting temperature. We get the standard entropy of fusion, $\Delta_{\text{fus}}S^\ominus$, if the solid and liquid are both at 1 bar; we use the melting temperature at 1 bar and the corresponding standard enthalpy of fusion at that temperature. All enthalpies of fusion are positive (melting is endothermic: it requires heat), so all entropies of fusion are positive too: disorder increases on melting. The entropy of water, for example, increases when it melts because the orderly structure of ice collapses as the liquid forms (Fig. 2.6).



(a) (b)

Fig. 2.6 When a solid, depicted by the orderly array of spheres (a), melts, the molecules form a liquid, the random array of spheres (b). As a result, the entropy of the sample increases.

ILLUSTRATION 2.2 The entropy change associated with unfolding of a protein

The protein lysozyme, an enzyme that breaks down bacterial cell walls, unfolds at a transition temperature of 75.5°C, and the standard enthalpy of transition is 509 kJ mol⁻¹. It follows that

$$\Delta_{\text{trs}}S^\ominus = \frac{\Delta_{\text{trs}}H^\ominus(T_{\text{trs}})}{T_{\text{trs}}} = \frac{+509 \text{ kJ mol}^{-1}}{(273.15 + 75.5) \text{ K}} = +1.46 \text{ kJ K}^{-1} \text{ mol}^{-1}$$

At the molecular level, the positive entropy change can be explained by the dispersal of matter and energy that accompanies the unraveling of the compact three-dimensional structure of lysozyme into a long, flexible chain that can adopt many different conformations as it writhes about in solution. ■

SELF-TEST 2.2 Calculate the standard entropy of fusion of ice at 0°C from the information in Table 1.2.

Answer: +22 J K⁻¹ mol⁻¹

The entropy of other types of transition may be discussed similarly. Thus, the entropy of vaporization, $\Delta_{\text{vap}}S$, at the boiling temperature, T_{b} , of a liquid is related to its enthalpy of vaporization at that temperature by

$$\text{At the boiling temperature: } \Delta_{\text{vap}}S = \frac{\Delta_{\text{vap}}H(T_{\text{b}})}{T_{\text{b}}} \quad (2.5)$$

Note that to use this formula, we use the enthalpy of vaporization at the boiling temperature. Table 2.1 lists the entropy of vaporization of several substances at 1 atm. For the standard value, $\Delta_{\text{vap}}S^\ominus$, we use data corresponding to 1 bar. Because vaporization is endothermic for all substances, all entropies of vaporization are positive. The increase in entropy accompanying vaporization is in line with what we should expect when a compact liquid turns into a gas. To calculate the entropy of phase transition at a temperature other than the transition temperature, we have to do additional calculations, as shown in the following *Illustration*.

Table 2.1 Entropies of vaporization at 1 atm and the normal boiling point

	$\Delta_{\text{vap}}S/(\text{J K}^{-1} \text{ mol}^{-1})$
Ammonia, NH_3	97.4
Benzene, C_6H_6	87.2
Bromine, Br_2	88.6
Carbon tetrachloride, CCl_4	85.9
Cyclohexane, C_6H_{12}	85.1
Ethanol, $\text{CH}_3\text{CH}_2\text{OH}$	104.1
Hydrogen sulfide, H_2S	87.9
Water, H_2O	109.1

ILLUSTRATION 2.3 The entropy of vaporization of water at 25°C

Suppose we want to calculate the entropy of vaporization of water at 25°C. The most convenient way to proceed is to perform three calculations. First, we calculate the entropy change for heating liquid water from 25°C to 100°C (using eqn 2.2 with data for the liquid from Table 1.1):

$$\begin{aligned}\Delta S_1 &= C_{p,m}(\text{H}_2\text{O, liquid}) \ln \frac{T_f}{T_i} = (75.29 \text{ J K}^{-1} \text{ mol}^{-1}) \times \ln \frac{373 \text{ K}}{298 \text{ K}} \\ &= +16.9 \text{ J K}^{-1} \text{ mol}^{-1}\end{aligned}$$

Then, we use eqn 2.5 and data from Table 1.2 to calculate the entropy of transition at 100°C:

$$\Delta S_2 = \frac{\Delta_{\text{vap}}H(T_b)}{T_b} = \frac{4.07 \times 10^4 \text{ J mol}^{-1}}{373 \text{ K}} = +1.09 \times 10^2 \text{ J K}^{-1} \text{ mol}^{-1}$$

Finally, we calculate the change in entropy for cooling the vapor from 100°C to 25°C (using eqn 2.2 again, but now with data for the vapor from Table 1.1):

$$\begin{aligned}\Delta S_3 &= C_{p,m}(\text{H}_2\text{O, vapor}) \ln \frac{T_f}{T_i} = (33.58 \text{ J K}^{-1} \text{ mol}^{-1}) \times \ln \frac{298 \text{ K}}{373 \text{ K}} \\ &= -7.54 \text{ J K}^{-1} \text{ mol}^{-1}\end{aligned}$$

The sum of the three entropy changes is the entropy of transition at 25°C:

$$\Delta_{\text{vap}}S(298 \text{ K}) = \Delta S_1 + \Delta S_2 + \Delta S_3 = +118 \text{ J K}^{-1} \text{ mol}^{-1} \blacksquare$$

2.5 Entropy changes in the surroundings

To develop a complete picture of entropy changes, we need to consider how a process occurring in an organism can affect the entropy of its surroundings.

We can use the definition of entropy in eqn 2.1 to calculate the entropy change of the surroundings in contact with the system at the temperature T :

$$\Delta S_{\text{sur}} = \frac{q_{\text{sur,rev}}}{T}$$

The surroundings are so extensive that they remain at constant pressure regardless of any events taking place in the system, so $q_{\text{sur,rev}} = \Delta H_{\text{sur}}$. The enthalpy is a state function, so a change in its value is independent of the path and we get the same value of ΔH_{sur} regardless of how the heat is transferred. Therefore, we can drop the label “rev” from q and write

$$\Delta S_{\text{sur}} = \frac{q_{\text{sur}}}{T} \quad (2.6)$$

We can use this formula to calculate the entropy change of the surroundings regardless of whether the change in the system is reversible or not.

EXAMPLE 2.1 Estimating the entropy change of the surroundings due to metabolism

The metabolic rate is the rate at which an organism expends energy from the oxidation of food. At rest, organisms still consume energy at the so-called *basal metabolic rate*. It follows from Section 1.3 that even a resting human being heats the surroundings, typically at a rate of 100 J s^{-1} . Estimate the entropy a resting person generates in the surroundings in the course of a day at 20°C .

Strategy We can estimate the approximate change in entropy from eqn 2.6 once we have calculated the energy transferred as heat. To find this quantity, we use the fact that there are 86 400 s in a day. Convert the temperature to kelvins.

Solution The energy transferred by heating the surroundings in the course of a day is

$$q_{\text{sur}} = (86\,400 \text{ s}) \times (100 \text{ J s}^{-1}) = 86\,400 \times 100 \text{ J}$$

The increase in entropy of the surroundings is therefore

$$\Delta S_{\text{sur}} = \frac{q_{\text{sur}}}{T} = \frac{86\,400 \times 100 \text{ J}}{293 \text{ K}} = +2.95 \times 10^4 \text{ J K}^{-1}$$

That is, the entropy production is about 30 kJ K^{-1} . Just to stay alive, each person on the planet contributes about 30 kJ K^{-1} each day to the entropy of their surroundings. The use of transport, machinery, and communications generates far more in addition.

SELF-TEST 2.3 Suppose a small reptile operates at 0.50 J s^{-1} . What entropy does it generate in the course of a day in the water in the lake that it inhabits, where the temperature is 15°C ?

Answer: $+150 \text{ J K}^{-1}$ ■

Equation 2.6 is expressed in terms of the energy supplied to the *surroundings* as heat, q_{sur} . Normally, we have information about the heat supplied to or escaping from the system, q . The two quantities are related by $q_{\text{sur}} = -q$. For instance, if $q = +100 \text{ J}$, an influx of 100 J , then $q_{\text{sur}} = -100 \text{ J}$, indicating that the surroundings

have lost that 100 J. Therefore, at this stage we can replace q_{sur} in eqn 2.6 by $-q$ and write

$$\Delta S_{\text{sur}} = -\frac{q}{T} \quad (2.7)$$

This expression is in terms of the properties of the system. Moreover, it applies whether or not the process taking place in the system is reversible.

If a chemical reaction or a phase transition takes place at constant pressure, we can identify q in eqn 2.7 with the change in enthalpy of the system and obtain

$$\text{For a process at constant pressure: } \Delta S_{\text{sur}} = -\frac{\Delta H}{T} \quad (2.8)$$

This enormously important expression will lie at the heart of our discussion of chemical equilibria. We see that it is consistent with common sense: if the process is exothermic, ΔH is negative and therefore ΔS_{sur} is positive. The entropy of the surroundings increases if heat is released into them. If the process is endothermic ($\Delta H > 0$), then the entropy of the surroundings decreases.

2.6 Absolute entropies and the Third Law of thermodynamics

To calculate entropy changes associated with biological processes, we need to see how to compile tables that list values of the entropies of substances.

The graphical procedure summarized by Fig. 2.5 and eqn 2.3 for the determination of the difference in entropy of a substance at two temperatures has a very important application. If $T_i = 0$, then the area under the graph between $T = 0$ and some temperature T gives us the value of $\Delta S = S(T) - S(0)$. However, at $T = 0$, all the motion of the atoms has been eliminated, and there is no thermal disorder. Moreover, if the substance is perfectly crystalline, with every atom in a well-defined location, then there is no spatial disorder either. We can therefore suspect that at $T = 0$, the entropy is zero.

The thermodynamic evidence for this conclusion is as follows. Sulfur undergoes a phase transition from its rhombic form to its monoclinic polymorph at 96°C (369 K) and the enthalpy of transition is $+402 \text{ J mol}^{-1}$. The entropy of transition is therefore $+1.09 \text{ J K}^{-1} \text{ mol}^{-1}$ at this temperature. We can also measure the molar entropy of each phase relative to its value at $T = 0$ by determining the heat capacity from $T = 0$ up to the transition temperature (Fig. 2.7). At this stage, we do not know the values of the entropies at $T = 0$. However, as we see from the illustration, to match the observed entropy of transition at 369 K, *the molar entropies of the two crystalline forms must be the same at $T = 0$* . We cannot say that the entropies are zero at $T = 0$, but from the experimental data we do know that they are the same. This observation is generalized into the **Third Law of thermodynamics**:

The entropies of all perfectly crystalline substances are the same at $T = 0$.

For convenience (and in accord with our understanding of entropy as a measure of dispersal of energy), we take this common value to be zero. Then, with this convention, according to the Third Law,

$$S(0) = 0 \text{ for all perfectly ordered crystalline materials.}$$

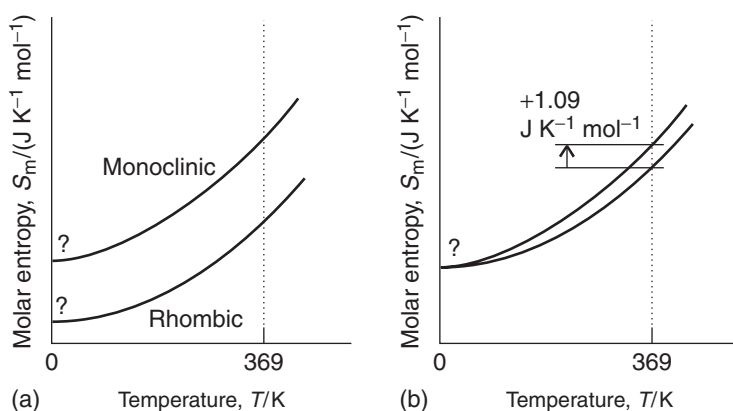


Fig. 2.7 (a) The molar entropies of monoclinic and rhombic sulfur vary with temperature as shown here. At this stage we do not know their values at $T = 0$. (b) When we slide the two curves together by matching their separation to the measured entropy of transition at the transition temperature, we find that the entropies of the two forms are the same at $T = 0$.

The **Third-Law entropy** at any temperature, $S(T)$, is equal to the area under the graph of C/T between $T = 0$ and the temperature T (Fig. 2.8). If there are any phase transitions (for example, melting) in the temperature range of interest, then the entropy of each transition at the transition temperature is calculated like that in eqn 2.4 and its contribution added to the contributions from each of the phases, as shown in Fig. 2.9. The Third-Law entropy, which is commonly called simply “the entropy,” of a substance depends on the pressure; we therefore select a standard pressure (1 bar) and report the **standard molar entropy**, S_m^\ominus , the molar entropy of a substance in its standard state at the temperature of interest. Some values at 298.15 K (the conventional temperature for reporting data) are given in Table 2.2.

It is worth spending a moment to look at the values in Table 2.2 to see that they are consistent with our understanding of entropy. All standard molar entropies

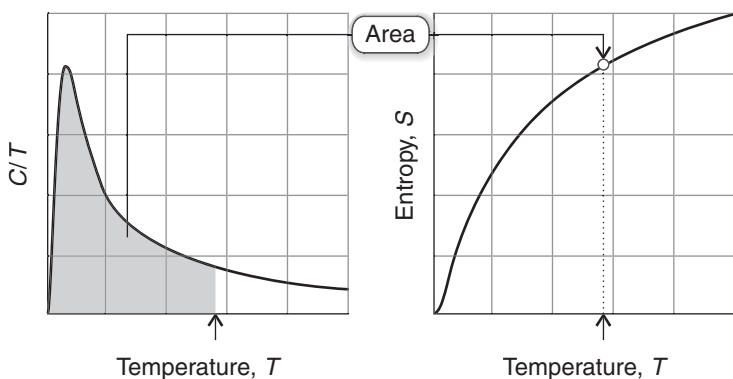


Fig. 2.8 The absolute entropy (or Third-Law entropy) of a substance is calculated by extending the measurement of heat capacities down to $T = 0$ (or as close to that value as possible) and then determining the area of the graph of C/T against T up to the temperature of interest. The area is equal to the absolute entropy at the temperature T .

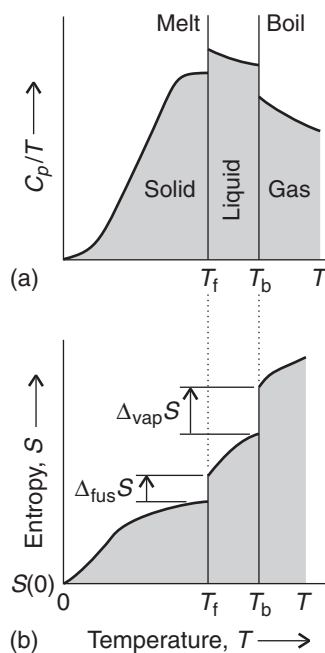


Fig. 2.9 The determination of entropy from heat capacity data. (a) Variation of C_p/T with the temperature of the sample. (b) The entropy, which is equal to the area beneath the upper curve up to the temperature of interest plus the entropy of each phase transition between $T = 0$ and the temperature of interest.

COMMENT 2.1 The text's web site contains links to online databases of thermochemical data, including tabulations of standard molar entropies. ■

Table 2.2 Standard molar entropies of some substances at 298.15 K*

Substance	$S_m^\ominus / (\text{J K}^{-1} \text{ mol}^{-1})$
<i>Gases</i>	
Ammonia, NH_3	192.5
Carbon dioxide, CO_2	213.7
Hydrogen, H_2	130.7
Nitrogen, N_2	191.6
Oxygen, O_2	205.1
Water vapor, H_2O	188.8
<i>Liquids</i>	
Acetic acid, CH_3COOH	159.8
Ethanol, $\text{CH}_3\text{CH}_2\text{OH}$	160.7
Water, H_2O	69.9
<i>Solids</i>	
Calcium carbonate, CaCO_3	92.9
Diamond, C	2.4
Glycine, $\text{CH}_2(\text{NH}_2)\text{COOH}$	103.5
Graphite, C	5.7
Sodium chloride, NaCl	72.1
Sucrose, $\text{C}_{12}\text{H}_{22}\text{O}_{11}$	360.2
Urea, $\text{CO}(\text{NH}_2)_2$	104.60

*See the *Data section* for more values.

are positive, because raising the temperature of a sample above $T = 0$ invariably increases its entropy above the value $S(0) = 0$. Another feature is that the standard molar entropy of diamond ($2.4 \text{ J K}^{-1} \text{ mol}^{-1}$) is lower than that of graphite ($5.7 \text{ J K}^{-1} \text{ mol}^{-1}$). This difference is consistent with the atoms being linked less rigidly in graphite than in diamond and their thermal motion being correspondingly greater. The standard molar entropies of ice, water, and water vapor at 25°C are, respectively, 45, 70, and $189 \text{ J K}^{-1} \text{ mol}^{-1}$, and the increase in values corresponds to the increasing dispersal of matter and energy on going from a solid to a liquid and then to a gas.

Heat capacities can be measured only with great difficulty at very low temperatures, particularly close to $T = 0$. However, it has been found that many non-metallic substances have a heat capacity that obeys the **Debye T^3 -law**:

$$\text{At temperatures close to } T = 0, C_{V,m} = aT^3 \quad (2.9a)$$

where a is a constant that depends on the substance and is found by fitting this equation to a series of measurements of the heat capacity close to $T = 0$. With a determined, it is easy to deduce the molar entropy at low temperatures, because

$$\text{At temperatures close to } T = 0, S_m(T) = \frac{1}{3}C_{V,m}(T) \quad (2.9b)$$

That is, the molar entropy at the low temperature T is equal to one-third of the constant-volume heat capacity at that temperature.

DERIVATION 2.2 Entropies close to $T = 0$

Once again, we use the general expression for the entropy change accompanying a change of temperature deduced in Section 2.3, with ΔS interpreted as $S(T_f) - S(T_i)$, taking molar values, and supposing that the heating takes place at constant volume:

$$S_m(T_f) - S_m(T_i) = \int_{T_i}^{T_f} \frac{C_{V,m}}{T} dT$$

If we set $T_i = 0$ and T_f some general temperature T , we can rearrange this expression into

$$S_m(T) - S_m(0) = \int_0^T \frac{C_{V,m}}{T} dT$$

According to the Third Law, $S(0) = 0$, and according to the Debye T^3 -law, $C_{V,m} = aT^3$, so

$$S_m(T) = \int_0^T \frac{aT^3}{T} dT = a \int_0^T T^2 dT$$

At this point we can use the standard integral

$$\int x^2 dx = \frac{1}{3}x^3 + \text{constant}$$

to write

$$\begin{aligned} \int_0^T T^2 dT &= \left(\frac{1}{3}T^3 + \text{constant} \right) \Big|_0^T \\ &= \left(\frac{1}{3}T^3 + \text{constant} \right) - \text{constant} \\ &= \frac{1}{3}T^3 \end{aligned}$$

We can conclude that

$$S_m(T) = \frac{1}{3}aT^3 = \frac{1}{3}C_{V,m}(T)$$

as in eqn 2.9b.

2.7 The standard reaction entropy

To move into the arena of biochemistry, where reactants are transformed into products, we need to establish procedures for using the tabulated values of absolute entropies to calculate entropy changes associated with chemical reactions.

Once again, we can use our intuition to predict the sign of the entropy change associated with a chemical reaction. When there is a net formation of a gas in a reaction, as in a combustion, we can usually anticipate that the entropy increases. When there is a net consumption of gas, as in the fixation of N_2 by certain

microorganisms, it is usually safe to predict that the entropy decreases. However, for a quantitative value of the change in entropy and to predict the sign of the change when no gases are involved, we need to do an explicit calculation.

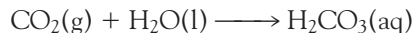
The difference in molar entropy between the products and the reactants in their standard states is called the **standard reaction entropy**, $\Delta_r S^\ominus$. It can be expressed in terms of the molar entropies of the substances in much the same way as we have already used for the standard reaction enthalpy:

$$\Delta_r S^\ominus = \sum \nu S_m^\ominus(\text{products}) - \sum \nu S_m^\ominus(\text{reactants}) \quad (2.10)$$

where the ν are the stoichiometric coefficients in the chemical equation.

ILLUSTRATION 2.4 Calculating a standard reaction entropy for an enzyme-catalyzed reaction

The enzyme carbonic anhydrase catalyzes the hydration of CO_2 gas in red blood cells:



We expect a negative entropy of reaction because a gas is consumed. To find the explicit value at 25°C , we use the information from the *Data section* to write

$$\begin{aligned} \Delta_r S^\ominus &= S_m^\ominus(\text{H}_2\text{CO}_3, \text{aq}) - \{S_m^\ominus(\text{CO}_2, \text{g}) + S_m^\ominus(\text{H}_2\text{O}, \text{l})\} \\ &= (187.4 \text{ J K}^{-1} \text{ mol}^{-1}) \\ &\quad - \{(213.74 \text{ J K}^{-1} \text{ mol}^{-1}) + (69.91 \text{ J K}^{-1} \text{ mol}^{-1})\} \\ &= -96.3 \text{ J K}^{-1} \text{ mol}^{-1} \blacksquare \end{aligned}$$

SELF-TEST 2.4 (a) Predict the sign of the entropy change associated with the complete oxidation of solid sucrose, $\text{C}_{12}\text{H}_{22}\text{O}_{11}(\text{s})$, by O_2 gas to CO_2 gas and liquid H_2O . (b) Calculate the standard reaction entropy at 25°C .

A note on good practice: Do not make the mistake of setting the standard molar entropies of elements equal to zero: they have nonzero values (provided $T > 0$), as we have already discussed.

Answer: (a) positive; (b) $+948.6 \text{ J K}^{-1} \text{ mol}^{-1}$

2.8 The spontaneity of chemical reactions

To assess the spontaneity of a biological process, we need to see how to take into account entropy changes in both the system and the surroundings.

A process may be spontaneous even though the entropy change that accompanies it is negative. Consider the binding of oxidized nicotinamide adenine dinucleotide (NAD^+), an important electron carrier in metabolism (Section 1.3), to the enzyme lactate dehydrogenase, which plays a role in catabolism and anabolism of carbohydrates. Experiments show that $\Delta_r S^\ominus = -16.8 \text{ J K}^{-1} \text{ mol}^{-1}$ for binding at 25°C and $\text{pH} = 7.0$. The negative sign of the entropy change is expected because the association of two reactants gives rise to a more compact structure. The reaction results in less dispersal of matter, yet it is spontaneous!

The resolution of this apparent paradox underscores a feature of entropy that recurs throughout chemistry and biology: *it is essential to consider the entropy of both the system and its surroundings when deciding whether a process is spontaneous or not.* The reduction in entropy by $16.8 \text{ J K}^{-1} \text{ mol}^{-1}$ relates only to the system, the reaction mixture. To apply the Second Law correctly, we need to calculate the *total* entropy, the sum of the changes in the system and the surroundings that jointly compose the “isolated system” referred to in the Second Law. It may well be the case that the entropy of the system decreases when a change takes place, but there may be a more than compensating increase in entropy of the surroundings, so that overall the entropy change is positive. The opposite may also be true: a large decrease in entropy of the surroundings may occur when the entropy of the system increases. In that case we would be wrong to conclude from the increase of the system alone that the change is spontaneous. *Whenever considering the implications of entropy, we must always consider the total change of the system and its surroundings.*

To calculate the entropy change in the surroundings when a reaction takes place at constant pressure, we use eqn 2.8, interpreting the ΔH in that expression as the reaction enthalpy. For example, for the formation of the NAD^+ -enzyme complex discussed above, with $\Delta_r H^\ominus = -24.2 \text{ kJ mol}^{-1}$, the change in entropy of the surroundings (which are maintained at 25°C , the same temperature as the reaction mixture) is

$$\Delta_r S_{\text{sur}} = -\frac{\Delta_r H}{T} = -\frac{(-24.2 \text{ kJ mol}^{-1})}{298 \text{ K}} = +81.2 \text{ J K}^{-1} \text{ mol}^{-1}$$

Now we can see that the total entropy change is positive:

$$\Delta_r S_{\text{total}} = (-16.8 \text{ J K}^{-1} \text{ mol}^{-1}) + (81.2 \text{ J K}^{-1} \text{ mol}^{-1}) = +64.4 \text{ J K}^{-1} \text{ mol}^{-1}$$

This calculation confirms that the reaction is spontaneous. In this case, the spontaneity is a result of the dispersal of energy that the reaction generates in the surroundings: the complex is dragged into existence, even though it has a lower entropy than the separated reactants, by the tendency of energy to disperse into the surroundings.

The Gibbs energy

One of the problems with entropy calculations is already apparent: we have to work out two entropy changes, the change in the system and the change in the surroundings, and then consider the sign of their sum. The great American theoretician J.W. Gibbs (1839–1903), who laid the foundations of chemical thermodynamics toward the end of the nineteenth century, discovered how to combine the two calculations into one. The combination of the two procedures in fact turns out to be of much greater relevance than just saving a little labor, and throughout this text we shall see consequences of the procedure he developed.

2.9 Focusing on the system

To simplify the discussion of the role of the total change in the entropy, we need to introduce a new state function, the Gibbs energy, which will be used extensively in our study of bioenergetics and biological structure.

The total entropy change that accompanies a process is

$$\Delta S_{\text{total}} = \Delta S + \Delta S_{\text{sur}}$$

where ΔS is the entropy change for the system; for a spontaneous change, $\Delta S_{\text{total}} > 0$. If the process occurs at constant pressure and temperature, we can use eqn 2.8 to express the change in entropy of the surroundings in terms of the enthalpy change of the system, ΔH . When the resulting expression is inserted into this one, we obtain

$$\text{At constant temperature and pressure: } \Delta S_{\text{total}} = \Delta S - \frac{\Delta H}{T} \quad (2.11)$$

The great advantage of this formula is that it expresses the total entropy change of the system and its surroundings in terms of properties of the system alone. The only restriction is to changes at constant pressure and temperature.

Now we take a very important step. First, we introduce the **Gibbs energy**, G , which is defined as¹

$$G = H - TS \quad (2.12)$$

Because H , T , and S are state functions, G is a state function too. A change in Gibbs energy, ΔG , at constant temperature arises from changes in enthalpy and entropy and is

$$\text{At constant temperature: } \Delta G = \Delta H - T\Delta S \quad (2.13)$$

By comparing eqns 2.11 and 2.13, we obtain

$$\text{At constant temperature and pressure: } \Delta G = -T\Delta S_{\text{total}} \quad (2.14)$$

We see that at constant temperature and pressure, the change in Gibbs energy of a system is proportional to the overall change in entropy of the system plus its surroundings.

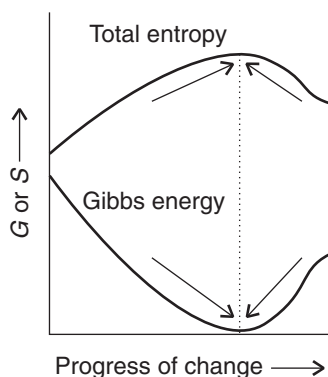


Fig. 2.10 The criterion of spontaneous change is the increase in total entropy of the system and its surroundings. Provided we accept the limitation of working at constant pressure and temperature, we can focus entirely on properties of the system and express the criterion as a tendency to move to lower Gibbs energy.

2.10 Spontaneity and the Gibbs energy

To see the basis of the central role of the Gibbs energy in the discussion of bioenergetics and biochemistry, we need to relate it to the spontaneity of processes.

The difference in sign between ΔG and ΔS_{total} implies that the condition for a process being spontaneous changes from $\Delta S_{\text{total}} > 0$ in terms of the total entropy (which is universally true) to $\Delta G < 0$ in terms of the Gibbs energy (for processes occurring at constant temperature and pressure). That is, *in a spontaneous change at constant temperature and pressure, the Gibbs energy decreases* (Fig. 2.10).

It may seem more natural to think of a system as falling to a lower value of some property. However, it must never be forgotten that to say that a system tends to fall toward lower Gibbs energy is only a modified way of saying that a system

¹The Gibbs energy is still commonly referred to by its older name, the “free energy.”

and its surroundings jointly tend toward a greater total entropy. The *only* criterion of spontaneous change is the total entropy of the system and its surroundings; the Gibbs energy merely contrives a way of expressing that total change in terms of the properties of the system alone and is valid only for processes that occur at constant temperature and pressure.

CASE STUDY 2.1 Life and the Second Law of thermodynamics

Every chemical reaction that is spontaneous under conditions of constant temperature and pressure, including those that drive the processes of growth, learning, and reproduction, is a reaction that changes in the direction of lower Gibbs energy, or—another way of expressing the same thing—results in the overall entropy of the system and its surroundings becoming greater. With these ideas in mind, it is easy to explain why life, which can be regarded as a collection of biological processes, proceeds in accord with the Second Law of thermodynamics.

It is not difficult to imagine conditions in the cell that may render spontaneous many of the reactions of catabolism described briefly in Section 1.3. After all, the breakdown of large molecules, such as sugars and lipids, into smaller molecules leads to the dispersal of matter in the cell. Energy is also dispersed, as it is released upon reorganization of bonds in foods. More difficult to rationalize is life's requirement of organization of a very large number of molecules into biological cells, which in turn assemble into organisms. To be sure, the entropy of the system—the organism—is very low because matter becomes less dispersed when molecules assemble to form cells, tissues, organs, and so on. However, the lowering of the system's entropy comes at the expense of an increase in the entropy of the surroundings. To understand this point, recall from Sections 1.3 and 2.1 that cells grow by converting energy from the Sun or oxidation of foods partially into work. The remaining energy is released as heat into the surroundings, so $q_{\text{sur}} > 0$ and $\Delta S_{\text{sur}} > 0$. As with any process, life is spontaneous and organisms thrive as long as the increase in the entropy of the organism's environment compensates for decreases in the entropy arising from the assembly of the organism. Alternatively, we may say that $\Delta G < 0$ for the overall sum of physical and chemical changes that we call life. ■

2.11 The Gibbs energy of assembly of proteins and biological membranes

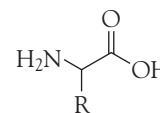
To gain insight into the thermodynamic factors that contribute to the spontaneous assembly of biological macromolecules, we need to examine in detail some of the interactions that bring molecular building blocks together.

Throughout the text we shall see how concepts of physical chemistry can be used to establish some of the known “rules” for the assembly of complex biological structures. Here, we describe how the Second Law can account for the formation of such organized assemblies as proteins and biological cell membranes.

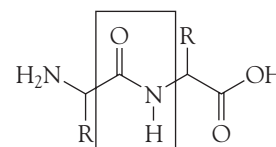
(a) The structures of proteins and biological membranes

Recall from your study of biochemistry that proteins are **polypeptides** formed from different α -amino acids of general form $\text{NH}_2\text{CHRCOOH}$ (1) strung together by the **peptide link**, $-\text{CONH}-$ (2), formed in a condensation reaction. Each monomer unit in the chain is referred to as a peptide **residue**. About twenty amino acids

COMMENT 2.2 Recall that a hydrogen bond is an attractive interaction between two species that arises from a link of the form $\text{A}-\text{H}\cdots\text{B}$, where A and B are highly electronegative elements and B possesses a lone pair of electrons. See Chapter 11 for a more detailed description of the molecular interactions that determine the three-dimensional structures of biological macromolecules. ■



1 General form of α -amino acids



2 The peptide link

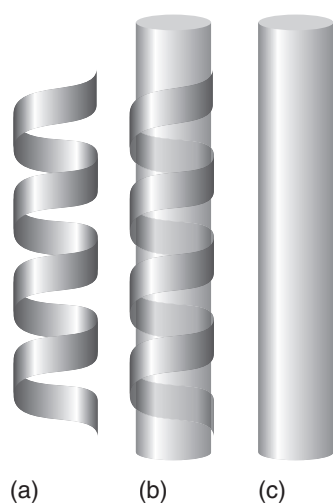


Fig. 2.11 (a) A polypeptide adopts a highly organized helical conformation, an example of a secondary structure. (b) The formation of a helix may be visualized as the winding of the polypeptide chain around a cylinder. (c) A helical polypeptide is often represented as a cylinder.

occur naturally and differ in the nature of the group R, as summarized in the *Data section*.

The concept of the “structure” of a protein takes on different meanings for the different levels at which we think about the spatial arrangement of the polypeptide chain. The **primary structure** of a protein is the sequence in which the amino acids are linked in the polymer. The **secondary structure** of a protein is the (often local) spatial arrangement of the chain. Examples of secondary structure motifs are random coils, in which the amino acid residues do not interact with each other by hydrogen bonds or any other type of bond, and ordered structures, such as helices and sheets, held together primarily by hydrogen bonds (Fig 2.11). The **tertiary structure** is the overall three-dimensional structure of a macromolecule. For instance, the hypothetical protein shown in Fig 2.12 has helical regions connected by short random-coil sections. The helices interact to form a compact tertiary structure. The **quaternary structure** of a macromolecule is the manner in which large molecules are formed by the aggregation of others. Figure 2.13 shows how four molecular subunits, each with a specific tertiary structure, aggregate together.

As remarked in the *Prologue*, we do not know all the rules that govern the folding of proteins into well-defined three-dimensional structures. However, a number of general conclusions from experimental studies give some insight into the origin of tertiary and quaternary structure in proteins. Here we focus on the observation that, in an aqueous environment (including the interior of biological cells), the chains of a protein fold in such a way as to place hydrophobic groups (water-repelling, non-polar groups such as $-\text{CHCH}_2(\text{CH}_3)_2$) in the interior, which is often not very accessible to solvent, and hydrophilic groups (water-loving, polar or charged groups such as $-\text{NH}_3^+$) on the surface, which is in direct contact with the polar solvent.

The tendency of nonpolar groups to cluster together in aqueous environments is also responsible for the assembly of complex systems in solution and in biological cells. An **amphipathic** species² has both hydrophobic and hydrophilic regions. An example is a molecule consisting of a long hydrocarbon tail that dissolves in hydrocarbon and other nonpolar materials and a hydrophilic **head group**, such as a carboxylate group, $-\text{CO}_2^-$, that dissolves in a polar solvent (typically water). Soaps, for example, consist of the alkali metal salts of long-chain carboxylic acids, and the surfactant in detergents is typically a long-chain benzenesulfonic acid ($\text{R}-\text{C}_6\text{H}_4\text{SO}_3\text{H}$). The mode of action of soap is to dissolve in both the aqueous phase and the hydrocarbon phase where their surfaces are in contact and hence to solubilize the hydrocarbon phase so that it can be washed away (Fig. 2.14).

Amphipathic molecules can group together as **micelles** even in the absence of grease droplets, for their hydrophobic tails tend to congregate, and their hydrophilic heads provide protection (Fig. 2.15). Micelles form only above the **critical micelle concentration** (CMC) and above the **Krafft temperature**. The shapes of the individual micelles vary with concentration. Although spherical micelles do occur, they are more commonly flattened spheres close to the CMC and are rodlike at higher concentrations. The interior of a micelle is like a droplet of oil, and experiments show that the hydrocarbon tails are mobile, but slightly more restricted than in the bulk.

Micelles are important in industry and biology on account of their solubilizing function: matter can be transported by water after it has been dissolved in their hy-

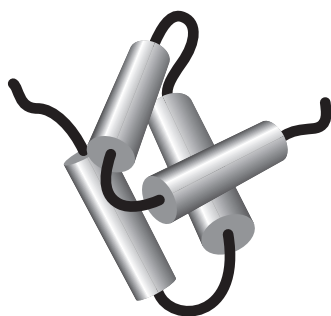


Fig. 2.12 Several helical segments connected by short random coils pack together, providing an example of tertiary structure.

²The *amphi-* part of the name is from the Greek word for “both,” and the *-pathic* part is from the same root (meaning “feeling”) as *sympathetic*.

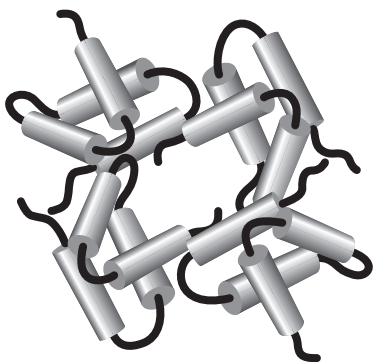


Fig. 2.13 Several subunits with specific structures pack together, providing an example of quaternary structure.

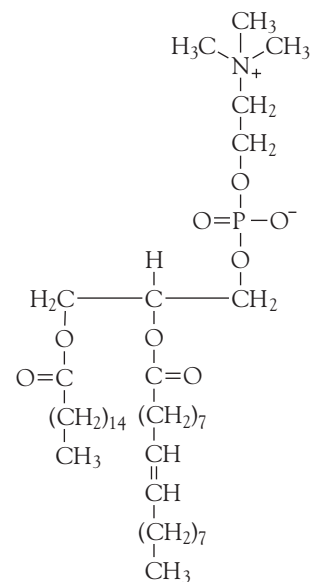
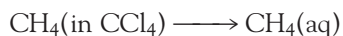
drocarbon interiors. For this reason, micellar systems are used as detergents and drug carriers and for organic synthesis and petroleum recovery. They can be perceived as a part of a family of similar structures formed when amphipathic substances are present in water (Fig. 2.16). A **monolayer** forms at the air-water interface, with the hydrophilic head groups facing the water. Micelles are like monolayers that enclose a region. A **bilayer vesicle** is like a double micelle, with an inward-pointing inner surface of molecules surrounded by an outward-pointing outer layer. The “flat” version of a bilayer vesicle is the analog of a biological cell membrane. The basic structural element of a membrane is a phospholipid, such as phosphatidyl choline (3), which contains long hydrocarbon chains (typically in the range C_{14} – C_{24}) and a variety of polar groups, such as $-\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_3^+$. The hydrophobic chains stack together to form an extensive bilayer about 5 nm across (Fig 2.17), leaving the polar groups exposed to the aqueous environment on either side of the membrane.

We see that important biological structures arise from the tendency of certain groups to avoid water in their immediate environment and to cluster together. Now we shall develop a molecular explanation for this effect in terms of the Second Law of thermodynamics.

(b) The hydrophobic interaction

Whenever we think about a tendency for an event to occur, we have to consider the total change in entropy of the system and its surroundings, not the system alone. The clustering together of hydrophobic groups results in a negative contribution to the change in entropy of the system because the clustering corresponds to a decrease in the disorder of the system. At first sight, therefore, we would not expect the hydrophobic groups to cluster together. However, we must not forget the role of the solvent.

Nonpolar molecules do dissolve slightly in polar solvents, but strong interactions between solute and solvent are not possible, and as a result it is found that each individual solute molecule is surrounded by a solvent cage (Fig 2.18). To understand the consequences of this effect, consider the thermodynamics of transfer of a nonpolar hydrocarbon solute from a nonpolar solvent to water, a polar solvent. Experiments indicate that the change in Gibbs energy for the transfer process is positive ($\Delta_{\text{transfer}}G > 0$), as expected on the basis of the increase in polarity of the solvent, but the enthalpy change is negative ($\Delta_{\text{transfer}}H < 0$). Therefore, it is a large decrease in the entropy of the system ($\Delta_{\text{transfer}}S < 0$) that accounts for the positive change in Gibbs energy. For example, the process



3 Phosphatidyl choline

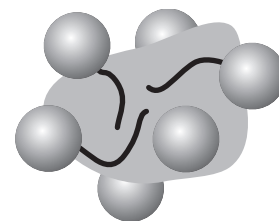


Fig. 2.14 An amphipathic molecule in a detergent or soap acts by sinking its hydrophobic hydrocarbon tail into the grease, so leaving its hydrophilic head groups on the surface of the grease where they can interact attractively with the surrounding water.

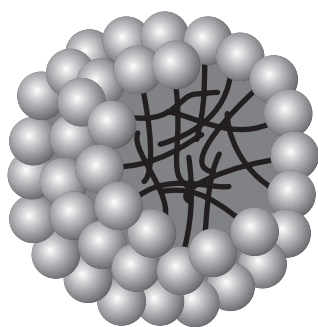


Fig. 2.15 A representation of a spherical micelle. The hydrophilic groups are represented by spheres and the hydrophobic hydrocarbon chains are represented by the stalks. The latter are mobile.

has $\Delta_{\text{transfer}}G = +12 \text{ kJ mol}^{-1}$, $\Delta_{\text{transfer}}H = -10 \text{ kJ mol}^{-1}$, and $\Delta_{\text{transfer}}S = -75 \text{ J K}^{-1} \text{ mol}^{-1}$ at 298 K.

The hydrophobicity of a small molecular group R is reported by defining the **hydrophobicity constant**, π , as

$$\pi = \log \frac{S(\text{RX})}{S(\text{HX})} \quad (2.15)$$

where $S(\text{RX})$ is the ratio of the molar solubility (the maximum chemical amount that can be dissolved to form 1 L of solution) of the compound R–X in octan-1-ol, a nonpolar solvent, to that in water, and $S(\text{HX})$ is the ratio of the molar solubility of the compound H–X in octan-1-ol to that in water. Therefore, positive values of π indicate hydrophobicity and negative values indicate hydrophilicity, the thermodynamic preference for water as a solvent. It is observed experimentally that the π values of most groups do not depend on the nature of X. However, measurements do suggest group additivity of π values:

–R	–CH ₃	–CH ₂ CH ₃	–(CH ₂) ₂ CH ₃	–(CH ₂) ₃ CH ₃	–(CH ₂) ₄ CH ₃
π	0.5	1	1.5	2	2.5

We see that acyclic saturated hydrocarbons become more hydrophobic as the carbon chain length increases. This trend can be rationalized by $\Delta_{\text{transfer}}H$ becoming more positive and $\Delta_{\text{transfer}}S$ more negative as the number of carbon atoms in the chain increases.

At the molecular level, formation of a cage of water around a hydrophobic molecule involves the formation of new hydrogen bonds among solvent molecules. This process is exothermic and accounts for the negative values of $\Delta_{\text{transfer}}H$. On the other hand, when a very large number of solvent cages must form, fewer molecules are free to disperse, and the result is a decrease in the entropy of the system that accounts for the negative values of $\Delta_{\text{transfer}}S$. However, when many solute molecules cluster together, fewer (albeit larger) cages are required, and more solvent molecules are free to move. The net effect of formation of large clusters of hydrophobic molecules is then a decrease in the organization of the solvent and therefore a net *increase* in entropy of the system. This increase in entropy of the solvent is large enough to result in the spontaneous association of hydrophobic molecules in a polar solvent.

The increase in entropy that results from putting fewer structural demands on the solvent by the clustering of non-polar molecules is the origin of the **hydrophobic interaction**, the favoring of the clustering of non-polar groups in an aqueous environment. The hydrophobic interaction is an example of a process that leads to the organization of solute molecules and is stabilized by a tendency toward greater dispersal of solvent molecules.

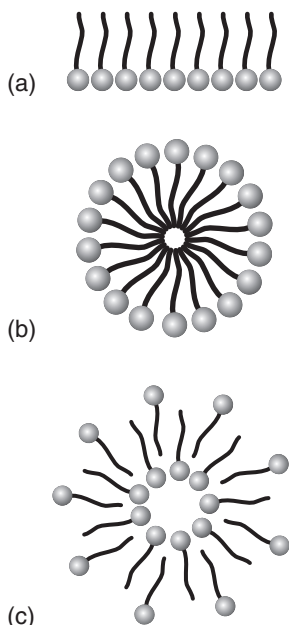


Fig. 2.16 Amphipathic molecules form a variety of related structures in water: (a) a monolayer, (b) a spherical micelle, (c) a bilayer vesicle.

SELF-TEST 2.5 Two long-chain hydrophobic polypeptides can associate end-to-end so that only the ends meet or side-by-side so that the entire chains are in contact. Which arrangement would produce a larger entropy change when they come together?

Answer: The side-by-side arrangement

One consequence of the hydrophobic interaction is that lower temperatures favor a more disorganized arrangement. To see why, we have to think about the entropy change in the surroundings. For a given transfer of heat into them, the change in their entropy increases as the temperature is decreased (eqn 2.1). Therefore, the entropy changes in the system become relatively less important, the system tends to change in its exothermic direction (the direction corresponding to an increase in entropy of the surroundings), and hydrophobic interactions become less important. This is the reason why some proteins dissociate into their individual subunits as the temperature is lowered to 0°C.

2.13 Work and the Gibbs energy change

To understand how biochemical reactions can be used to release energy as work in the cell, we need to gain deeper insight into the Gibbs energy.

An important feature of the Gibbs energy is that *the value of ΔG for a process gives the maximum non-expansion work that can be extracted from the process at constant temperature and pressure*. By **non-expansion work**, w' , we mean any work other than that arising from the expansion of the system. It may include electrical work, if the process takes place inside an electrochemical or biological cell, or other kinds of mechanical work, such as the winding of a spring or the contraction of a muscle (we saw an example in Exercise 1.41). To demonstrate this property, we need to combine the First and Second Laws, and then we find

$$\text{At constant temperature and pressure: } \Delta G = w_{\max}' \quad (2.16)$$

DERIVATION 2.3 Maximum non-expansion work

We need to consider infinitesimal changes because dealing with reversible processes is then much easier. Our aim is to derive the relation between the infinitesimal change in Gibbs energy, dG , accompanying a process and the maximum amount of non-expansion work that the process can do, dw' . We start with the infinitesimal form of eqn 2.13,

$$\text{At constant temperature: } dG = dH - TdS$$

where, as usual, d denotes an infinitesimal difference. A good rule in the manipulation of thermodynamic expressions is to feed in definitions of the terms that appear. We do this twice. First, we use the expression for the change in enthalpy at constant pressure (eqn 1.11, written as $dH = dU + pdV$) and obtain

$$\text{At constant temperature and pressure: } dG = dU + pdV - TdS$$

Then we replace dU in terms of infinitesimal contributions from work and heat ($dU = dw + dq$):

$$dG = dw + dq + pdV - TdS$$

The work done on the system consists of expansion work, $-p_{\text{ex}}dV$, and non-expansion work, dw' . Therefore,

$$dG = -p_{\text{ex}}dV + dw' + dq + pdV - TdS$$

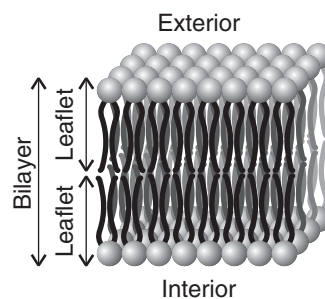


Fig. 2.17 The long hydrocarbon chains of a phospholipid can stack together to form a bilayer structure, with the polar groups (represented by the spheres) exposed to the aqueous environment.

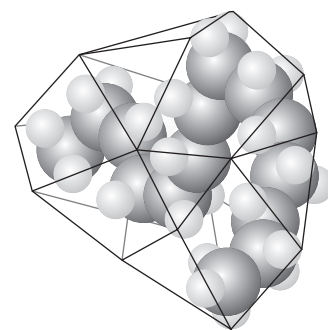


Fig. 2.18 When a hydrocarbon molecule is surrounded by water, the H_2O molecules form a cage. As a result of this acquisition of structure, the entropy of water decreases, so the dispersal of the hydrocarbon into the water is entropy opposed; its coalescence is entropy favored.

This derivation is valid for any process taking place at constant temperature and pressure.

Now we specialize to a reversible change. For expansion work to be reversible, we need to match p and p_{ex} , in which case the first and fourth terms on the right cancel. Moreover, because the transfer of energy as heat is also reversible, we can replace dq by TdS , in which case the third and fifth terms also cancel. We are left with

$$\text{At constant temperature and pressure, for a reversible process: } dG = dw_{\text{rev}}'$$

Maximum work is done during a reversible change (Section 1.4), so another way of writing this expression is

$$\text{At constant temperature and pressure: } dG = dw_{\text{max}}'$$

Because this relation holds for each infinitesimal step between the specified initial and final states, it applies to the overall change too. Therefore, we obtain eqn 2.16.

EXAMPLE 2.2 Estimating a change in Gibbs energy for a metabolic process

Suppose a certain small bird has a mass of 30 g. What is the minimum mass of glucose that it must consume to fly up to a branch 10 m above the ground? The change in Gibbs energy that accompanies the oxidation of 1.0 mol $\text{C}_6\text{H}_{12}\text{O}_6(\text{s})$ to carbon dioxide gas and liquid water at 25°C is -2828 kJ.

Strategy First, we need to calculate the work needed to raise a mass m through a height h on the surface of the Earth. As we saw in eqn 1.1, this work is equal to mgh , where g is the acceleration of free fall. This work, which is non-expansion work, can be identified with ΔG . We need to determine the amount of substance that corresponds to the required change in Gibbs energy and then convert that amount to a mass by using the molar mass of glucose.

Solution The non-expansion work to be done is

$$w' = (30 \times 10^{-3} \text{ kg}) \times (9.81 \text{ m s}^{-2}) \times (10 \text{ m}) = 3.0 \times 9.81 \times 1.0 \times 10^{-1} \text{ J}$$

(because $1 \text{ kg m}^2 \text{ s}^{-2} = 1 \text{ J}$). The amount, n , of glucose molecules required for oxidation to give a change in Gibbs energy of this value given that 1 mol provides 2828 kJ is

$$n = \frac{3.0 \times 9.81 \times 1.0 \times 10^{-1} \text{ J}}{2.828 \times 10^6 \text{ J mol}^{-1}} = \frac{3.0 \times 9.81 \times 1.0 \times 10^{-7}}{2.828} \text{ mol}$$

Therefore, because the molar mass, M , of glucose is 180 g mol^{-1} , the mass, m , of glucose that must be oxidized is

$$\begin{aligned} m &= nM = \left(\frac{3.0 \times 9.81 \times 1.0 \times 10^{-7}}{2.828} \text{ mol} \right) \times (180 \text{ g mol}^{-1}) \\ &= 1.9 \times 10^{-4} \text{ g} \end{aligned}$$

That is, the bird must consume at least 0.19 mg of glucose for the mechanical effort (and more if it thinks about it).

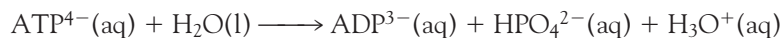
SELF-TEST 2.6 A hardworking human brain, perhaps one that is grappling with physical chemistry, operates at about 25 J s^{-1} . What mass of glucose must be consumed to sustain that metabolic rate for an hour?

Answer: 5.7 g ■

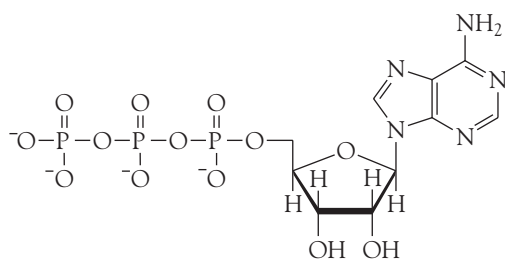
The great importance of the Gibbs energy in chemistry is becoming apparent. At this stage, we see that it is a measure of the non-expansion work resources of chemical reactions: if we know ΔG , then we know the maximum non-expansion work that we can obtain by harnessing the reaction in some way. In some cases, the non-expansion work is extracted as electrical energy. This is the case when electrons are transferred across cell membranes in some key reactions of photosynthesis and respiration (see Chapter 5).

CASE STUDY 2.2 The action of adenosine triphosphate

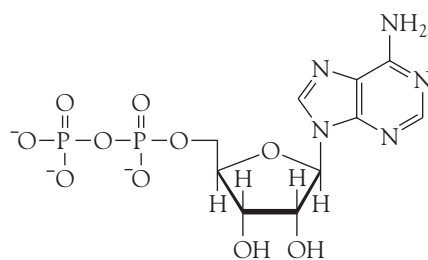
In biological cells, the energy released by the oxidation of foods (Section 1.3) is stored in adenosine triphosphate (ATP or ATP^{4-} , **4**). The essence of ATP's action is its ability to lose its terminal phosphate group by hydrolysis and to form adenosine diphosphate (ADP or ADP^{3-} , **5**):



At $\text{pH} = 7.0$ and 37°C (310 K, blood temperature) the enthalpy and Gibbs energy of hydrolysis are $\Delta_r H = -20 \text{ kJ mol}^{-1}$ and $\Delta_r G = -31 \text{ kJ mol}^{-1}$, respectively. Under these conditions, the hydrolysis of 1 mol $\text{ATP}^{4-}(\text{aq})$ results in the extraction of up to 31 kJ of energy that can be used to do non-expansion work,



4 ATP



5 ADP

such as the synthesis of proteins from amino acids, muscular contraction, and the activation of neuronal circuits in our brains, as we shall see in Chapter 5. If no attempt is made to extract any energy as work, then 20 kJ (in general, ΔH) of heat will be produced. ■

Some insight into the physical significance of G itself comes from its definition as $H - TS$. The enthalpy is a measure of the energy that can be obtained from the system as heat. The term TS is a measure of the quantity of energy stored in the *random* motion of the molecules making up the sample. Work, as we have seen, is energy transferred in an orderly way, so we cannot expect to obtain work from the energy stored randomly. The difference between the total stored energy and the energy stored randomly, $H - TS$, is available for doing work, and we recognize that difference as the Gibbs energy. In other words, the Gibbs energy is the energy stored in the uniform motion and arrangement of the molecules in the system.

Checklist of Key Ideas

You should now be familiar with the following concepts:

- 1. A spontaneous change is a change that has a tendency to occur without work having to be done to bring it about.
- 2. Matter and energy tend to disperse.
- 3. The Second Law states that the entropy of an isolated system tends to increase.
- 4. A change in entropy is defined as $\Delta S = q_{\text{rev}}/T$.
- 5. The entropy change accompanying heating a system of constant heat capacity is $\Delta S = C \ln(T_f/T_i)$.
- 6. In general, the entropy change accompanying the heating of a system is equal to the area under the graph of C/T against T between the two temperatures of interest.
- 7. The entropy of transition at the transition temperature is given by $\Delta_{\text{trs}}S = \Delta_{\text{trs}}H(T_{\text{trs}})/T_{\text{trs}}$.
- 8. The change in entropy of the surroundings is given by $\Delta S_{\text{sur}} = -q/T$.
- 9. The Third Law of thermodynamics states that the entropies of all perfectly crystalline substances are the same at $T = 0$ (and may be taken to be zero).
- 10. The standard reaction entropy is the difference in standard molar entropies of the products and reactants weighted by their stoichiometric coefficients, $\Delta_r S^\ominus = \sum \nu S_m^\ominus(\text{products}) - \sum \nu S_m^\ominus(\text{reactants})$.
- 11. The Gibbs energy is defined as $G = H - TS$ and is a state function.
- 12. At constant temperature, the change in Gibbs energy is $\Delta G = \Delta H - T\Delta S$.
- 13. At constant temperature and pressure, a system tends to change in the direction of decreasing Gibbs energy.
- 14. The hydrophobic interaction is a process that leads to the organization of solute molecules and is driven by a tendency toward greater dispersal of solvent molecules.
- 15. At constant temperature and pressure, the change in Gibbs energy accompanying a process is equal to the maximum non-expansion work the process can do, $\Delta G = w_{\text{max}}'$.

Discussion questions

- 2.1 The following expressions have been used to establish criteria for spontaneous change: $\Delta S_{\text{isolated system}} > 0$ and $\Delta G < 0$. Discuss the origin, significance, and applicability of each criterion.
- 2.2 Explain the limitations of the following expressions: (a) $\Delta S = C \ln(T_f/T_i)$, (b) $\Delta G = \Delta H - T\Delta S$, (c) $\Delta G = w_{\text{max}}'$.
- 2.3 Suggest a procedure for the measurement of the entropy of unfolding of a protein with differential scanning calorimetry, a technique discussed in Section 1.10.

- 2.4 Without performing a calculation, predict whether the standard entropies of the following reactions are positive or negative:
- (a) Ala-Ser-Thr-Lys-Gly-Arg-Ser $\xrightarrow{\text{Trypsin}}$ Ala-Ser-Thr-Lys + Gly-Arg
- (b) $\text{N}_2(\text{g}) + 3 \text{H}_2(\text{g}) \longrightarrow 2 \text{NH}_3(\text{g})$
- (c) $\text{ATP}^{4-}(\text{aq}) + \text{H}_2\text{O}(\text{l}) \longrightarrow \text{ADP}^{3-}(\text{aq}) + \text{HPO}_4^{2-}(\text{aq}) + \text{H}_3\text{O}^+(\text{aq})$
- 2.5 Provide a molecular interpretation of the hydrophobic interaction.

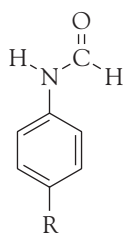
Exercises

- 2.6 A goldfish swims in a bowl of water at 20°C. Over a period of time, the fish transfers 120 J to the water as a result of its metabolism. What is the change in entropy of the water?
- 2.7 Suppose that when you exercise, you consume 100 g of glucose and that all the energy released as heat remains in your body at 37°C. What is the change in entropy of your body?
- 2.8 Whenever a gas expands—when we exhale, when a flask is opened, and so on—the gas undergoes an increase in entropy. Conversely, when a gas contracts, its entropy decreases. (a) Show that the entropy change due to reversible isothermal expansion or contraction of a perfect gas is $\Delta S = nR \ln(V_f/V_i)$, where V_i and V_f are the initial and final volumes, respectively. (b) Calculate the change in molar entropy when carbon dioxide expands isothermally from 1.5 L to 4.5 L. (c) A sample of carbon dioxide that initially occupies 15.0 L at 250 K and 1.00 atm is compressed isothermally. Into what volume must the gas be compressed to reduce its entropy by 10.0 J K⁻¹?
- 2.9 Suppose you put a cube of ice of mass 100 g into a glass of water at just above 0°C. When the ice melts, about 33 kJ of energy is absorbed from the surroundings as heat. What is the change in entropy of (a) the sample (the ice), (b) the surroundings (the glass of water)?
- 2.10 Calculate the change in entropy of 100 g of ice at 0°C as it is melted, heated to 100°C, and then vaporized at that temperature. Suppose that the changes are brought about by a heater that supplies energy at a constant rate, and sketch a graph showing (a) the change in temperature of the system, (b) the enthalpy of the system, (c) the entropy of the system as a function of time.
- 2.11 What is the change in entropy of 100 g of water when it is heated from room temperature (20°C) to body temperature (37°C)? Use $C_{p,m} = 75.5 \text{ J K}^{-1} \text{ mol}^{-1}$.
- 2.12 Estimate the molar entropy of potassium chloride at 5.0 K given that its molar heat capacity at that temperature is 1.2 mJ K⁻¹ mol⁻¹.
- 2.13 Equation 2.2 is based on the assumption that the heat capacity is independent of temperature. Suppose, instead, that the heat capacity depends on temperature as $C = a + bT + a/T^2$. Find an expression for the change of entropy accompanying heating from T_i to T_f . *Hint:* See *Derivation 2.1*.
- 2.14 Calculate the change in entropy when 100 g of water at 80°C is poured into 100 g of water at 10°C in an insulated vessel given that $C_{p,m} = 75.5 \text{ J K}^{-1} \text{ mol}^{-1}$.
- 2.15 The protein lysozyme unfolds at a transition temperature of 75.5°C, and the standard enthalpy of transition is 509 kJ mol⁻¹. Calculate the entropy of unfolding of lysozyme at 25.0°C, given that the difference in the constant-pressure heat capacities upon unfolding is 6.28 kJ K⁻¹ mol⁻¹ and can be assumed to be independent of temperature. *Hint:* Imagine that the transition at 25.0°C occurs in three steps: (i) heating of the folded protein from 25.0°C to the transition temperature, (ii) unfolding at the transition temperature, and (iii) cooling of the unfolded protein to 25.0°C. Because the entropy is a state function, the entropy change at 25.0°C is equal to the sum of the entropy changes of the steps.
- 2.16 The enthalpy of the graphite \rightarrow diamond phase transition, which under 100 kbar occurs at 2000 K, is +1.9 kJ mol⁻¹. Calculate the entropy of transition at that temperature.
- 2.17 The enthalpy of vaporization of methanol is 35.27 kJ mol⁻¹ at its normal boiling point of 64.1°C. Calculate (a) the entropy of vaporization of methanol at this temperature and (b) the entropy change of the surroundings.

- 2.18** Trouton's rule summarizes the results of experiments showing that the entropy of vaporization measured at the boiling point, $\Delta_{\text{vap}}S = \Delta_{\text{vap}}H(T_b)/T_b$, is approximately the same and equal to about $85 \text{ J K}^{-1} \text{ mol}^{-1}$ for all liquids except when hydrogen bonding or some other kind of specific molecular interaction is present. **(a)** Provide a molecular interpretation for Trouton's rule. **(b)** Estimate the entropy of vaporization and the enthalpy of vaporization of octane, which boils at 126°C . **(c)** Trouton's rule does not apply to water because in the liquid, water molecules are held together by an extensive network of hydrogen bonds. Provide a molecular interpretation for the observation that Trouton's rule underestimates the value of the entropy of vaporization of water.
- 2.19** Calculate the entropy of fusion of a compound at 25°C given that its enthalpy of fusion is 32 kJ mol^{-1} at its melting point of 146°C and the molar heat capacities (at constant pressure) of the liquid and solid forms are $28 \text{ J K}^{-1} \text{ mol}^{-1}$ and $19 \text{ J K}^{-1} \text{ mol}^{-1}$, respectively.
- 2.20** Calculate the standard reaction entropy at 298 K of the fermentation of glucose to ethanol:
 $\text{C}_6\text{H}_{12}\text{O}_6(\text{s}) \rightarrow 2 \text{ C}_2\text{H}_5\text{OH}(\text{l}) + 2 \text{ CO}_2(\text{g})$
- 2.21** In a particular biological reaction taking place in the body at 37°C , the change in enthalpy was -125 kJ mol^{-1} and the change in entropy was $-126 \text{ J K}^{-1} \text{ mol}^{-1}$. **(a)** Calculate the change in Gibbs energy. **(b)** Is the reaction spontaneous? **(c)** Calculate the total change in entropy of the system and the surroundings.
- 2.22** The change in Gibbs energy that accompanies the oxidation of $\text{C}_6\text{H}_{12}\text{O}_6(\text{s})$ to carbon dioxide and water vapor at 25°C is $-2828 \text{ kJ mol}^{-1}$. How much glucose does a person of mass 65 kg need to consume to climb through 10 m ?
- 2.23** A non-spontaneous reaction may be driven by coupling it to a reaction that is spontaneous. The formation of glutamine from glutamate and ammonium ions requires 14.2 kJ mol^{-1} of energy input. It is driven by the hydrolysis of ATP to ADP mediated by the enzyme glutamine synthetase. **(a)** Given that the change in Gibbs energy for the hydrolysis of ATP corresponds to $\Delta G = -31 \text{ kJ mol}^{-1}$ under the conditions prevailing in a typical cell, can the hydrolysis drive the formation of glutamine? **(b)** How many moles of ATP must be hydrolyzed to form 1 mol glutamine?
- 2.24** The hydrolysis of acetyl phosphate has $\Delta G = -42 \text{ kJ mol}^{-1}$ under typical biological conditions. If acetyl phosphate were to be synthesized by coupling to the hydrolysis of ATP, what is the minimum number of ATP molecules that would need to be involved?
- 2.25** Suppose that the radius of a typical cell is $10 \mu\text{m}$ and that inside it 10^6 ATP molecules are hydrolyzed each second. What is the power density of the cell in watts per cubic meter ($1 \text{ W} = 1 \text{ J s}^{-1}$)? A computer battery delivers about 15 W and has a volume of 100 cm^3 . Which has the greater power density, the cell or the battery? (For data, see *Exercise 2.23*.)

Projects

- 2.26** The following is an example of a structure-activity relation (SAR), in which it is possible to correlate the effect of a structural change in a compound with its biological function. The use of SARs can improve the design of drugs for the treatment of disease because it facilitates the prediction of the biological activity of a compound before it is synthesized. The binding of non-polar groups of amino acid to hydrophobic sites in the interior of proteins is governed largely by hydrophobic interactions.
- (a)** Consider a family of hydrocarbons R-H. The hydrophobicity constants, π , for R = CH₃, CH₂CH₃, (CH₂)₂CH₃, (CH₂)₃CH₃, and (CH₂)₄CH₃ are, respectively, 0.5, 1.0, 1.5, 2.0, and 2.5. Use these data to predict the π value for (CH₂)₆CH₃.
- (b)** The equilibrium constants K_I for the dissociation of inhibitors (**6**) from the enzyme chymotrypsin were measured for different substituents R:
- | | | | | | |
|------------|--------------------|--------|-----------------|-----------------|-------|
| R | CH ₃ CO | CN | NO ₂ | CH ₃ | Cl |
| π | -0.20 | -0.025 | 0.33 | 0.50 | 0.90 |
| $\log K_I$ | -1.73 | -1.90 | -2.43 | -2.55 | -3.40 |

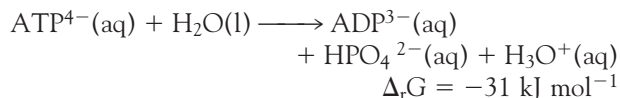


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Plot $\log K_I$ against π . Does the plot suggest a linear relationship? If so, what are the slope and intercept to the $\log K_I$ axis of the line that best fits the data?

(c) Predict the value of K_I for the case $R = H$.

2.27 An *exergonic reaction* is a reaction for which $\Delta G < 0$, and an *endergonic reaction* is a reaction for which $\Delta G > 0$. Here we investigate the molecular basis for the observation first discussed in *Case study 2.2* that the hydrolysis of ATP is exergonic at $\text{pH} = 7.0$ and 310 K :



(a) It is thought that the exergonicity of ATP hydrolysis is due in part to the fact that the standard entropies of hydrolysis of polyphosphates are positive.

Why would an increase in entropy accompany the hydrolysis of a triphosphate group into a diphosphate and a phosphate group?

(b) Under identical conditions, the Gibbs energies of hydrolysis of H_4ATP and MgATP^{2-} , a complex between the Mg^{2+} ion and ATP^{4-} , are less negative than the Gibbs energy of hydrolysis of ATP^{4-} . This observation has been used to support the hypothesis that electrostatic repulsion between adjacent phosphate groups is a factor that controls the exergonicity of ATP hydrolysis. Provide a rationale for the hypothesis and discuss how the experimental evidence supports it. Do these electrostatic effects contribute to the $\Delta_r H$ or $\Delta_r S$ terms that determine the exergonicity of the reaction? *Hint:* In the MgATP^{2-} complex, the Mg^{2+} ion and ATP^{4-} anion form two bonds: one that involves a negatively charged oxygen belonging to the terminal phosphate group of ATP^{4-} and another that involves a negatively charged oxygen belonging to the phosphate group adjacent to the terminal phosphate group of ATP^{4-} .

(c) Stabilization due to resonance in ATP^{4-} and the HPO_4^{2-} ion is thought to be one of the factors that controls the exergonicity of ATP hydrolysis. Provide a rationale for the hypothesis. Does stabilization through resonance contribute to the $\Delta_r H$ or $\Delta_r S$ terms that determine the exergonicity of the reaction?