

Thermodynamics of Ion and Electron Transport

CHAPTER

5

Measurements such as the ones we describe in this chapter lead to collections of data that are very useful for discussing the characteristics of electrolyte solutions and the migration of ions across biological membranes. They are used to discuss the details of the propagation of signals in neurons and of the synthesis of ATP.

We shall also see that such apparently unrelated processes as combustion, respiration, photosynthesis, and corrosion are actually all closely related, for in each of them an electron, sometimes accompanied by a group of atoms, is transferred from one species to another. Indeed, together with the proton transfer typical of acid-base reactions, processes in which electrons are transferred, the so-called **redox reactions**, account for many of the reactions encountered in chemistry and biology.

Before getting down to business, a word about notation. Throughout this chapter (and book) we use $\ln x$ for the natural logarithm of x (to the base e); this logarithm is sometimes written $\log_e x$. We use $\log x$ for the common logarithm of x (to the base 10); this logarithm is sometimes denoted $\log_{10} x$. The two logarithms are related by

$$\ln x = \ln 10 \times \log x \approx 2.303 \log x$$

Transport of ions across biological membranes

The cell membrane may be regarded as a barrier that slows down the transfer of material into or out of the cell. Here we focus on the transport of ions across biological membranes. We begin by developing some general ideas about solutions of electrolytes. Then we describe the thermodynamics of ion transport mediated by special membrane-spanning proteins. In Section 5.11 we shall see how electron transfer reactions during the later stages of aerobic metabolism of glucose couple to the movement of protons across biological membranes and contribute to the synthesis of ATP.

5.1 Ions in solution

To prepare for the discussion of biological redox reactions and the role of ions in physiological processes, we need to describe the factors that influence the activities of ions in aqueous solutions.

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The most significant difference between the solution of an electrolyte and a non-electrolyte is that there are long-range Coulombic interactions between the ions in the former. As a result, electrolyte solutions exhibit non-ideal behavior even at very low concentrations because the solute particles, the ions, do not move independently of one another. Some idea of the importance of ion-ion interactions is obtained by noting their average separations in solutions of different molar concentration c and, to appreciate the scale, the typical number of H_2O molecules that can fit between them:

$c/(\text{mol L}^{-1})$	0.001	0.01	0.1	1	10
Separation/nm	90	40	20	9	4
Number of H_2O molecules	30	14	6	3	1

To take the interactions into account—which become very serious for concentrations of 0.01 mol L^{-1} and more—we work with the activities of the charged solutes. We saw in Chapter 3 that the activity, a_j , is a kind of effective concentration and is related to concentrations by multiplication by an activity coefficient, γ_j . There are various ways of expressing concentration; in the first part of this chapter we use the molality, b_j , and write

$$a_j = \gamma_j b_j / b^\ominus \quad (5.1a)$$

with $b^\ominus = 1 \text{ mol kg}^{-1}$. For notational simplicity, we often replace b_j/b^\ominus by b_j , interpret b_j as the numerical value of the molality, and write

$$a_j = \gamma_j b_j \quad (5.1b)$$

Because the solution becomes more ideal as the molality approaches zero, we know that $\gamma_j \rightarrow 1$ as $b_j \rightarrow 0$. Once we know the activity of the species J , we can write its chemical potential by using

$$\mu_j = \mu_j^\ominus + RT \ln a_j \quad (5.2)$$

The thermodynamic properties of the solution—such as the equilibrium constants of reactions involving ions—can then be derived in the same way as for ideal solutions but with activities in place of concentrations. However, when we want to relate the results we derive, we need to know how to relate activities to concentrations. We ignored that problem when discussing acids and bases and simply assumed that all activity coefficients were 1. In this chapter, we see how to improve that approximation.

One problem that confronts us from the outset is that cations and anions always occur together in solution. As a result, there is no experimental procedure for distinguishing the deviations from ideal behavior due to the cations from those of the anions: we cannot measure the activity coefficients of cations and anions separately. The best we can do experimentally is to ascribe deviations from ideal behavior equally to each kind of ion and to talk in terms of a **mean activity coefficient**, γ_\pm . For a salt MX , such as NaCl , we show in the following *Derivation* that the mean activity coefficient is related to the activity coefficients of the individual ions as follows:

$$\gamma_\pm = (\gamma_+ \gamma_-)^{1/2} \quad (5.3a)$$

COMMENT 5.1 The Coulomb interaction between two charges q_1 and q_2 separated by a distance r is described by the *Coulombic potential energy*:

$$E_P = \frac{q_1 q_2}{4\pi\epsilon_0 r}$$

where $\epsilon_0 = 8.854 \times 10^{-12} \text{ J}^{-1} \text{ C}^2 \text{ m}^{-1}$ is the vacuum permittivity. Note that the interaction is attractive ($E_P < 0$) when q_1 and q_2 have opposite signs and repulsive ($E_P > 0$) when the charges have the same sign. The potential energy of a charge is zero when it is at an infinite distance from the other charge. Concepts related to electricity are reviewed in *Appendix 3*. ■

For a salt M_pX_q , the mean activity coefficient is related to the activity coefficients of the individual ions as follows:

$$\gamma_{\pm} = (\gamma_+^p \gamma_-^q)^{1/s} \quad s = p + q \quad (5.3b)$$

DERIVATION 5.1 Mean activity coefficients

In this *Derivation*, we use the relation $\ln xy = \ln x + \ln y$ several times (sometimes as $\ln x + \ln y = \ln xy$) and its implication (by setting $y = x$) that $\ln x^2 = 2 \ln x$. For a salt MX that dissociates completely in solution, the molar Gibbs energy of the ions is

$$G_m = \mu_+ + \mu_-$$

where μ_+ and μ_- are the chemical potentials of the cations and anions, respectively. Each chemical potential can be expressed in terms of a molality b and an activity coefficient γ by using eqn 5.2 ($\mu = \mu^\ominus + RT \ln a$) and then eqn 5.1 ($a = \gamma b$) together with $\ln \gamma b = \ln \gamma + \ln b$, which gives

$$\begin{aligned} G_m &= (\mu_+^\ominus + RT \ln \gamma_+ b_+) + (\mu_-^\ominus + RT \ln \gamma_- b_-) \\ &= (\mu_+^\ominus + RT \ln \gamma_+ + RT \ln b_+) + (\mu_-^\ominus + RT \ln \gamma_- + RT \ln b_-) \end{aligned}$$

We now use $\ln x + \ln y = \ln xy$ again to combine the two terms involving the activity coefficients as

$$RT \ln \gamma_+ + RT \ln \gamma_- = RT(\ln \gamma_+ + \ln \gamma_-) = RT \ln \gamma_+ \gamma_-$$

and write

$$G_m = (\mu_+^\ominus + RT \ln b_+) + (\mu_-^\ominus + RT \ln b_-) + RT \ln \gamma_+ \gamma_-$$

We now write the term inside the logarithm as γ_{\pm}^2 and use $\ln x^2 = 2 \ln x$ to obtain

$$\begin{aligned} G_m &= (\mu_+^\ominus + RT \ln b_+) + (\mu_-^\ominus + RT \ln b_-) + 2RT \ln \gamma_{\pm} \\ &= (\mu_+^\ominus + RT \ln b_+ + RT \ln \gamma_{\pm}) + (\mu_-^\ominus + RT \ln b_- + RT \ln \gamma_{\pm}) \\ &= (\mu_+^\ominus + RT \ln \gamma_{\pm} b_+) + (\mu_-^\ominus + RT \ln \gamma_{\pm} b_-) \end{aligned}$$

We see that, with the mean activity coefficient defined as in eqn 5.3a, the deviation from ideal behavior (as expressed by the activity coefficient) is now shared equally between the two types of ion. In exactly the same way, the Gibbs energy of a salt M_pX_q can be written

$$G_m = p(\mu_+^\ominus + RT \ln \gamma_{\pm} b_+) + q(\mu_-^\ominus + RT \ln \gamma_{\pm} b_-)$$

with the mean activity coefficient defined as in eqn 5.3b.¹

¹For the details of this general case, see our *Physical chemistry*, 7e (2002).

ILLUSTRATION 5.1 Using the mean activity coefficient

Suppose that we have devised a method for determining the activity coefficients of Na^+ and SO_4^{2-} ions in $0.010\text{ m Na}_2\text{SO}_4(\text{aq})$ and found them to be 0.98 and 0.84, respectively. It follows from eqn 5.3b that the mean activity coefficient is

$$\gamma_{\pm} = \{(0.98)^2 \times (0.84)\}^{1/3} = 0.93$$

because $p = 2$ and $q = 1$ and $s = 3$. From eqn 5.1b, the activities of the two ions are

$$a_+ = \gamma_{\pm} b_+ = 0.93 \times (2 \times 0.010) = 0.019$$

$$a_- = \gamma_{\pm} b_- = 0.93 \times (0.010) = 0.0093 \blacksquare$$

SELF-TEST 5.1 Write an expression for the mean activity coefficient of Mg^{2+} and PO_4^{3-} in an aqueous solution of $\text{Mg}_3(\text{PO}_4)_2$.

Answer: $\gamma_{\pm} = (\gamma_+^3 \gamma_-^2)^{1/5}$

The question still remains about how the mean activity coefficients can be estimated. A theory that accounts for their values in very dilute solutions was developed by Peter Debye and Erich Hückel in 1923. They supposed that each ion in solution is surrounded by an **ionic atmosphere** of counter-charge. This “atmosphere” is actually the slight imbalance of charge arising from the competition between the stirring effect of thermal motion, which tends to keep all the ions distributed uniformly throughout the solution, and the Coulombic interaction between ions, which tends to attract counter-ions (ions of opposite charge) into each other’s vicinity and repel ions of like charge (Fig. 5.1). As a result of this competition, there is a slight preponderance of cations near any anion, giving a positively charged ionic atmosphere around the anion, and a slight preponderance of anions near any cation, giving a negatively charged ionic atmosphere around the cation. Because each ion is in an atmosphere of opposite charge, its energy is lower than in a uniform, ideal solution, and therefore its chemical potential is lower than its ideal solution value. A lowering of the chemical potential of an ion below its ideal solution value is equivalent to the activity coefficient of the ion being less than 1 (because $\ln \gamma$ is negative when $\gamma < 1$). Debye and Hückel were able to derive an expression that is a limiting law in the sense that it becomes increasingly valid as the concentration of ions approaches zero. The **Debye-Hückel limiting law**² is

$$\log \gamma_{\pm} = -A|z_+ z_-| I^{1/2} \quad (5.4)$$

(Note the common logarithm.) In this expression, A is a constant that for water at 25°C works out as 0.509. The z_j are the charge numbers of the ions (so $z_+ = +1$ for Na^+ and $z_- = -2$ for SO_4^{2-}); the vertical bars mean that we ignore the sign of the product. The quantity I is the **ionic strength** of the solution, which is defined in terms of the numerical values of the molalities of the ions as

$$I = \frac{1}{2}(z_+^2 b_+ + z_-^2 b_-) \quad (5.5)$$

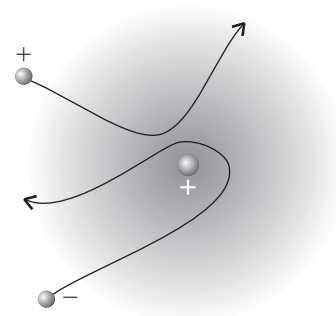


Fig. 5.1 The ionic atmosphere surrounding an ion consists of a slight excess of opposite charge as ions move through the vicinity of the central ion, with counter-ions lingering longer than ions of the same charge. The ionic atmosphere lowers the energy of the central ion.

²For a derivation of the Debye-Hückel limiting law, see our *Physical chemistry*, 7e (2002).

When using this expression, we must include all the ions present in the solution, not just those of interest. For instance, if you are calculating the ionic strength of a solution of silver chloride and potassium nitrate, there are contributions to the ionic strength from all four types of ion. When more than two ions contribute to the ionic strength, we write

$$I = \frac{1}{2} \sum_i z_i^2 b_i$$

where the symbol \sum denotes a sum (in this case of all terms of the form $z_i^2 b_i$), z_i is the charge number of an ion i (positive for cations and negative for anions), and b_i is its molality.

ILLUSTRATION 5.2 Estimating an activity coefficient

The sulfate ion, SO_4^{2-} , is an important source of sulfur used in the synthesis of the amino acids cysteine and methionine in plants and bacteria. To estimate the mean activity coefficient for the ions in $0.0010 \text{ m Na}_2\text{SO}_4(\text{aq})$ at 25°C , we begin by evaluating the ionic strength of the solution from eqn 5.5:

$$I = \frac{1}{2}\{(+1)^2 \times (2 \times 0.0010) + (-2)^2 \times (0.0010)\} = 0.0030$$

Then we use the Debye-Hückel limiting law (eqn 5.4), with $A = 0.509$, to calculate $\log \gamma_{\pm}$:

$$\log \gamma_{\pm} = -0.509 \times \{(+1)(-2)\} \times (0.0030)^{1/2} = -2 \times 0.509 \times (0.0030)^{1/2}$$

(This expression evaluates to -0.056 .) On taking the antilogarithm of $\log \gamma_{\pm}$ (by using $x = 10^{\log x}$), we conclude that $\gamma_{\pm} = 0.88$. ■

SELF-TEST 5.2 Estimate the mean activity coefficient of a solution that is $0.020 \text{ m NaCl}(\text{aq})$ and $0.035 \text{ m Ca}(\text{NO}_3)_2(\text{aq})$.

Answer: 0.661

As we have stressed, eqn 5.4 is a *limiting* law and is reliable only in very dilute solutions. For solutions more concentrated than about 10^{-3} M , it is better to use an empirical modification known as the **extended Debye-Hückel law**:

$$\log \gamma_{\pm} = -\frac{A|z_+z_-|I^{1/2}}{1 + BI^{1/2}} + CI \quad (5.6)$$

with B and C empirically determined constants (Fig. 5.2).

5.2 Passive and active transport of ions across biological membranes

Nature has devised complex strategies for controlling the flow of ions across cell membranes, some of which are thermodynamic and others kinetic. Here we consider thermodynamic aspects of ion transport.

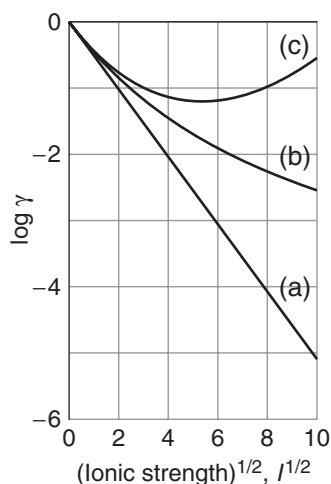


Fig. 5.2 The variation of the activity coefficient with ionic strength according to the extended Debye-Hückel theory. (a) The limiting law for a 1,1-electrolyte. (b) The extended law with $B = 0.5$. (c) The extended law, extended further by the addition of a term CI ; in this case with $C = 0.02$. The last form of the law reproduces the observed behavior reasonably well.

The thermodynamic tendency to transport a species A through a biological cell membrane is partially determined by an activity gradient across the membrane, which results in a difference in molar Gibbs energy between the inside and the outside of the cell

$$\Delta G_m = G_{m,\text{in}} - G_{m,\text{out}} = RT \ln \frac{a_{\text{in}}}{a_{\text{out}}} \quad (5.7)$$

The equation implies that transport into the cell of either neutral or charged species is thermodynamically favorable if $a_{\text{in}} < a_{\text{out}}$ or, if we set the activity coefficients to 1, if $[A]_{\text{in}} < [A]_{\text{out}}$. An ion also needs to cross a membrane potential difference $\Delta\phi = \phi_{\text{in}} - \phi_{\text{out}}$ that arises from differences in Coulomb repulsions on each side of the bilayer. This potential difference is measured in volts (V, where $1 \text{ V} = 1 \text{ J C}^{-1}$). We show in the following *Derivation* that the Gibbs energy of transfer of an ion of charge number z across a potential difference $\Delta\phi$ adds a term $zF\Delta\phi$ to eqn 5.7, where F is **Faraday's constant**, the magnitude of electric charge per mole of electrons:

$$F = eN_A = 96.485 \text{ kC mol}^{-1}$$

The final expression for ΔG_m is then

$$\Delta G_m = RT \ln \frac{[A]_{\text{in}}}{[A]_{\text{out}}} + zF\Delta\phi \quad (5.8)$$

DERIVATION 5.2 The Gibbs energy of transfer of an ion across a membrane potential gradient

The charge transferred per mole of ions of charge number z that cross a lipid bilayer is $N_A \times (ze)$, or zF , where $F = eN_A$. The work w' of transporting this charge is equal to the product of the charge and the potential difference $\Delta\phi$:

$$w' = zF \times \Delta\phi$$

Provided the work is done reversibly at constant temperature and pressure, we can equate this work to the molar Gibbs energy of transfer and write

$$\Delta G_m = zF\Delta\phi$$

Adding this term to eqn 5.7 gives eqn 5.8, the total Gibbs energy of transfer of an ion across both an activity and a membrane potential gradient.

EXAMPLE 5.1 Estimating a membrane potential

Estimate the equilibrium membrane potential of a cell at 298 K by using the fact that the concentration of K^+ inside the cell is about 20 times that on the outside. Repeat the calculation, this time using the fact that the concentration of Na^+ outside the cell is about 10 times that on the inside.

Strategy Because the cell is at equilibrium, set $\Delta G_m = 0$ in eqn 5.8 and, after rearrangement, write

$$\Delta\phi = -\frac{RT}{zF} \ln \frac{[A]_{\text{in}}}{[A]_{\text{out}}}$$

where $z = +1$ for both K^+ and Na^+ . Then calculate the equilibrium membrane potential from the given temperature and concentration ratios.

Solution When $[\text{K}^+]_{\text{in}}/[\text{K}^+]_{\text{out}} = 20$, we obtain

$$\begin{aligned} \Delta\phi &= -\frac{(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) \times (298 \text{ K})}{9.648 \times 10^4 \text{ C mol}^{-1}} \ln 20 \\ &= -7.69 \times 10^{-2} \text{ V} = -76.9 \text{ mV} \end{aligned}$$

where we have used $1 \text{ V} = 1 \text{ J C}^{-1}$. The negative sign denotes that the inside has the lower potential. When $[\text{Na}^+]_{\text{in}}/[\text{Na}^+]_{\text{out}} = 0.10$, we obtain

$$\begin{aligned} \Delta\phi &= -\frac{(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) \times (298 \text{ K})}{9.648 \times 10^4 \text{ C mol}^{-1}} \ln 0.10 \\ &= 5.91 \times 10^{-2} \text{ V} = 59.1 \text{ mV} \end{aligned}$$

and the positive sign denotes that the outside has the lower potential.

SELF-TEST 5.3 Is the transport of Na^+ ions across a cell membrane spontaneous when $[\text{Na}^+]_{\text{in}}/[\text{Na}^+]_{\text{out}} = 0.10$ and $\Delta\phi = +50 \text{ mV}$?

Answer: Yes, because $\Delta G_m < 0$ ■

Equation 5.8 implies that there is a tendency, called **passive transport**, for a species to move down concentration and membrane potential gradients. In **active transport**, a species moves against these gradients and the process is driven by its coupling to the exergonic hydrolysis of ATP. That is, when the sum of $RT \ln([A]_{\text{in}}/[A]_{\text{out}})$ and $zF\Delta\phi$ is positive, the overall Gibbs energy of transport can be made negative (and the process becomes spontaneous) by a large and negative Gibbs energy of ATP hydrolysis. It follows that the overall Gibbs energy of transport into a cell may be written as

$$\Delta G_m = RT \ln \frac{[A]_{\text{in}}}{[A]_{\text{out}}} + zF\Delta\phi + \Delta_r G^{\text{ATP}} \quad (5.9)$$

where $\Delta_r G^{\text{ATP}}$ is the Gibbs energy of hydrolysis of ATP at specific concentrations of ATP, ADP, P_i , and hydronium ion.

5.3 Ion channels and ion pumps

The mechanism of signal propagation along neurons in organisms is due to the migration of ions through membranes.

The transport of ions into or out of a cell needs to be mediated (that is, involve other species) because charged species do not partition well into the hydrophobic environment of the membrane. There are two mechanisms for ion transport: mediation by a carrier molecule or transport through a **channel former**, a protein that creates a hydrophilic pore through which the ion can pass. An example of a channel former is the polypeptide gramicidin A, which increases the membrane permeability to cations such as H^+ , K^+ , and Na^+ .

Ion channels are proteins that permit the movement of specific ions down a membrane potential gradient. They are highly selective, so there is a channel protein for Ca^{2+} , another for Cl^- , and so on. In a *voltage-gated channel*, the opening of the gate is triggered by a membrane potential, and in a *ligand-gated channel* the binding of an *effector* molecule to a specific receptor site on the channel initiates ion transport.

Ions such as H^+ , Na^+ , K^+ , and Ca^{2+} are often transported actively across membranes by integral proteins called **ion pumps**. Ion pumps are molecular machines that work by adopting conformations that are permeable to one type of ion but not others, depending on the state of phosphorylation of the protein. Because protein phosphorylation requires dephosphorylation of ATP, the conformational change that opens or closes the pump is endergonic and requires the use of energy stored during metabolism. In Sections 5.11 and 8.5 we discuss the ion pump H^+ -ATPase, which plays an important role in oxidative phosphorylation.

CASE STUDY 5.1 Action potentials

A striking example of the importance of ion channels is their role in the propagation of impulses by neurons, the fundamental units of the nervous system. Here we give a thermodynamic description of the process.

The cell membrane of a neuron is more permeable to K^+ ions than to either Na^+ or Cl^- ions. The key to the mechanism of action of a nerve cell is its use of Na^+ and K^+ channels to move ions across the membrane, modulating its potential. For example, the concentration of K^+ inside an inactive nerve cell is about 20 times that on the outside, whereas the concentration of Na^+ outside the cell is about 10 times that on the inside. The difference in concentrations of ions results in a transmembrane potential difference of about -62 mV. This potential difference is also called the **resting potential** of the cell membrane.

To estimate the resting potential, we need to understand that the cell is never at equilibrium, so the approach taken in *Example 5.1* is not appropriate. Ions continually cross the membrane, which is more permeable to some ions than others. To take into account membrane permeability, we use the **Goldman equation** to calculate the resting potential:

$$\Delta\phi = \frac{RT}{F} \ln \left(\frac{\sum_i P_i [M_i^+]_{out} + \sum_j P_j [X_j^-]_{in}}{\sum_i P_i [M_i^+]_{in} + \sum_j P_j [X_j^-]_{out}} \right)$$

where P_i and P_j are the relative permeabilities, respectively, for the cation M_i^+ and the anion X_j^- and the sum is over all ions. For example, taking the permeabilities of the K^+ , Na^+ , and Cl^- ions as $P_{K^+} = 1.0$, $P_{Na^+} = 0.04$, and $P_{Cl^-} = 0.45$, respectively, the temperature as 298 K, and the concentrations as

$[K^+]_{in} = 400 \text{ mmol L}^{-1}$, $[Na^+]_{in} = 50 \text{ mmol L}^{-1}$, $[Cl^-]_{in} = 50 \text{ mmol L}^{-1}$, $[K^+]_{out} = 20 \text{ mmol L}^{-1}$, $[Na^+]_{out} = 500 \text{ mmol L}^{-1}$, and $[Cl^-]_{out} = 560 \text{ mmol L}^{-1}$, we obtain

$$\begin{aligned}\Delta\phi &= \frac{(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) \times (298 \text{ K})}{9.648 \times 10^4 \text{ J mol}^{-1}} \\ &\quad \times \ln \left(\frac{(1.0 \times 20) + (0.04 \times 500) + (0.45 \times 50)}{(1.0 \times 400) + (0.04 \times 50) + (0.45 \times 560)} \right) \\ &= -6.0 \times 10^{-2} \text{ V} = -60 \text{ mV}\end{aligned}$$

(The concentration units in the logarithm all cancel.) We see that the Goldman equation leads to an estimate that agrees well with the experimental value of -62 mV .

The transmembrane potential difference plays a particularly interesting role in the transmission of nerve impulses. Upon receiving an impulse, which is called an **action potential**, a site in the nerve cell membrane becomes transiently permeable to Na^+ and the transmembrane potential changes. To propagate along a nerve cell, the action potential must change the transmembrane potential by at least 20 mV to values that are less negative than -40 mV . Propagation occurs when an action potential at one site of the membrane triggers an action potential at an adjacent site, with sites behind the moving action potential relaxing back to the resting potential. ■

Redox reactions

We now embark on an investigation of the thermodynamics of redox reactions. Our ultimate goal is a description of electron transfer in plant photosynthesis and in the last stages of the oxidative breakdown of glucose. However, before we can understand these complex processes, we must examine a very much simpler system with a more controllable environment where precise measurements can be made. That is, we must consider electron transfer in an **electrochemical cell**, a device that consists of two electronic conductors (metal or graphite, for instance) dipping into an electrolyte (an ionic conductor), which may be a solution, a liquid, or a solid.

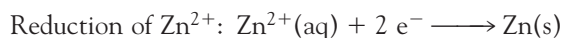
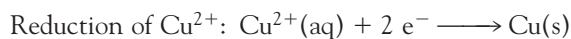
5.4 Half-reactions

A redox reaction, such as the breakdown of glucose by O_2 in biological cells, is the outcome of the loss of electrons, and perhaps atoms, from one species and their gain by another species; we need to be able to write chemical equations for redox reactions and the corresponding reaction quotients.

COMMENT 5.2 The oxidation number of a monatomic ion is equal to its charge. An oxidation number is assigned to an element in a compound by supposing that it is present as an ion with a characteristic charge; for instance, oxygen is supposed—for this purpose—to be present as O^{2-} in most of its compounds, and hydrogen is supposed to be present as H^+ . See *Appendix 4* for a more extensive review of oxidation numbers. ■

It will be familiar from introductory chemistry that we identify the loss of electrons (oxidation) by noting whether an element has undergone an increase in oxidation number. We identify the gain of electrons (reduction) by noting whether an element has undergone a decrease in oxidation number. The requirement to break and form covalent bonds in some redox reactions, as in the conversion of H_2O to O_2 (during plant photosynthesis) or of N_2 to NH_3 (during nitrogen fixation by certain microorganisms) is one of the reasons why redox reactions often achieve equilibrium quite slowly, often much more slowly than acid-base proton transfer reactions.

Any redox reaction may be expressed as the difference of two reduction **half-reactions**. Two examples are



A half-reaction in which atom transfer accompanies electron transfer is

Reduction of MnO_4^- :



where oxygen atoms are transferred from $\text{MnO}_4^-(\text{aq})$ to $\text{H}_2\text{O}(\text{l})$. In the discussion of redox reactions, the hydrogen ion is commonly denoted simply $\text{H}^+(\text{aq})$ rather than treated as a hydronium ion, $\text{H}_3\text{O}^+(\text{aq})$, as proton transfer is less of an issue and the chemical equations are simplified.

Half-reactions are *conceptual*. Redox reactions normally proceed by a much more complex mechanism in which the electron is never free. The electrons in these conceptual reactions are regarded as being “in transit” and are not ascribed a state. The oxidized and reduced species in a half-reaction form a **redox couple**, denoted Ox/Red. Thus, the redox couples mentioned so far are Cu^{2+}/Cu , Zn^{2+}/Zn , and $\text{MnO}_4^-/\text{H}^+/\text{Mn}^{2+}, \text{H}_2\text{O}$. In general, we adopt the notation

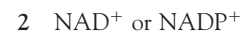
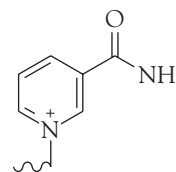
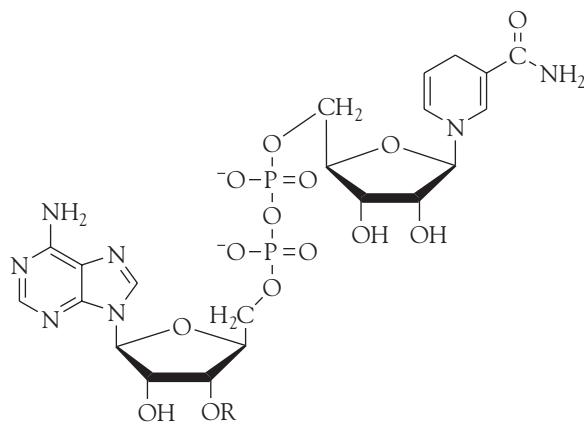
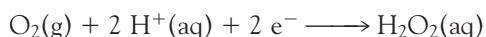


EXAMPLE 5.2 Expressing a reaction in terms of half-reactions

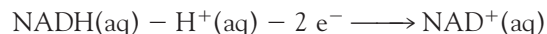
Express the oxidation of nicotinamide adenine dinucleotide (NADH, **1**), which participates in aerobic metabolism, to NAD^+ (**2**) by oxygen, when the latter is reduced to H_2O_2 , in aqueous solution as the difference of two reduction half-reactions. The overall reaction is $\text{NADH}(\text{aq}) + \text{O}_2(\text{g}) + \text{H}^+(\text{aq}) \longrightarrow \text{NAD}^+(\text{aq}) + \text{H}_2\text{O}_2(\text{aq})$.

Strategy To express a reaction as the difference of two reduction half-reactions, identify one reactant species that undergoes reduction and its corresponding reduction product, then write the half-reaction for this process. To find the second half-reaction, subtract the first half-reaction from the overall reaction and rearrange the species so that all the stoichiometric coefficients are positive and the equation is written as a reduction.

Solution Oxygen is reduced to H_2O_2 , so one half-reaction is



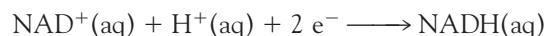
Subtraction of this half-reaction from the overall equation gives



Addition of $\text{H}^+(\text{aq}) + 2 \text{e}^-$ to both sides gives



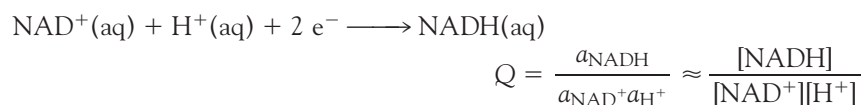
This is an oxidation half-reaction. We reverse it to find the corresponding reduction half-reaction:



SELF-TEST 5.4 Express the formation of H_2O from H_2 and O_2 in acidic solution as the difference of two reduction half-reactions.

Answer: $4 \text{H}^+(\text{aq}) + 4 \text{e}^- \longrightarrow 2 \text{H}_2(\text{g})$, $\text{O}_2(\text{g}) + 4 \text{H}^+(\text{aq}) + 4 \text{e}^- \longrightarrow 2 \text{H}_2\text{O}(\text{l})$

We saw in Chapter 4 that a natural way to express the composition of a system is in terms of the reaction quotient Q . The quotient for a half-reaction is defined like the quotient for the overall reaction, but with the electrons ignored. Thus, for the half-reaction of the NAD^+/NADH couple in Example 5.2 we would write



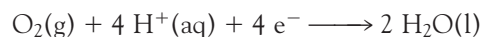
In elementary work, and provided the solution is very dilute, the activities are interpreted as the numerical values of the molar concentrations (see Table 3.3). The replacement of activities by molar concentrations is very hazardous for ionic solutions, as we have seen, so wherever possible we delay taking that final step.

EXAMPLE 5.3 Writing the reaction quotient for a half-reaction

During the last stage of oxidative phosphorylation in mitochondria, oxygen is reduced to water with the accompanying uptake of protons. Write the half-reaction and the reaction quotient for the reduction of oxygen to water in acidic solution.

Strategy Write the chemical equation for the half-reaction. Then express the reaction quotient in terms of the activities and the corresponding stoichiometric coefficients, with products in the numerator and reactants in the denominator. Pure (and nearly pure) solids and liquids do not appear in Q ; nor does the electron. The activity of a gas is set equal to the numerical value of its partial pressure in bar (more formally: $a_j = p_j/p^\ominus$).

Solution The equation for the reduction of O_2 in acidic solution is



The reaction quotient for the half-reaction is therefore

$$Q = \frac{1}{p_{\text{O}_2} a_{\text{H}^+}^4}$$

Note the very strong dependence of Q on the hydrogen ion activity.

SELF-TEST 5.5 Write the half-reaction and the reaction quotient for the reduction of chlorine gas to chloride ion.

Answer: $\text{Cl}_2(\text{g}) + 2 \text{e}^- \longrightarrow 2 \text{Cl}^-(\text{aq})$, $Q = a_{\text{Cl}^-}^2 / p_{\text{Cl}_2}$ ■

5.5 Reactions in electrochemical cells

Biological redox reactions take place in biological cells, not electrochemical cells. However, we shall see that the electron transfer processes that occur in respiration and photosynthesis can be modeled by electrochemical cells in which electrons are transferred between proteins.

In an electrochemical cell, the electronic conductor and its surrounding electrolyte is an **electrode**. The physical structure containing them is called an **electrode compartment**. The two electrodes may share the same compartment (Fig. 5.3). If the electrolytes are different, then the two compartments may be joined by a **salt bridge**, which is an electrolyte solution that completes the electrical circuit by permitting ions to move between the compartments (Fig. 5.4). Alternatively, the two solutions may be in direct physical contact (for example, through a porous membrane) and form a **liquid junction**. However, a liquid junction introduces complications into the interpretation of measurements, and we shall not consider it further.

A **galvanic cell** is an electrochemical cell that produces electricity as a result of the spontaneous reaction occurring inside it.³ An **electrolytic cell** is an electrochemical cell in which a nonspontaneous reaction is driven by an external source of direct current. The commercially available dry cells, mercury cells, nickel-cadmium (“nicad”), and lithium ion cells used to power electrical equipment are all galvanic cells and produce electricity as a result of the spontaneous chemical reaction between the substances built into them at manufacture. A **fuel cell** is a galvanic cell in which the reagents, such as hydrogen and oxygen or methane and oxygen, are supplied continuously from outside. Fuel cells are used on manned spacecraft, are beginning to be considered for use in automobiles, and gas supply companies hope that one day they may be used as a convenient, compact source of electricity in homes. Electric eels and electric catfish are biological versions of fuel cells in which the fuel is food and the cells are adaptations of muscle cells.

In an electrochemical cell, the **anode** is where oxidation takes place; the **cathode** is where reduction takes place. As the reaction proceeds in a galvanic cell, the electrons released at the anode travel through the external circuit (Fig. 5.5). They re-enter the cell at the cathode, where they bring about reduction. This flow of current in the external circuit, from anode to cathode, corresponds to the cathode having a higher potential than the anode and arises from the tendency of negatively charged electrons to travel to regions of higher potential. In an electrolytic

³The term *voltaic cell* is also used.

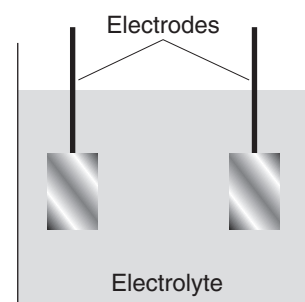


Fig. 5.3 The arrangement for an electrochemical cell in which the two electrodes share a common electrolyte.

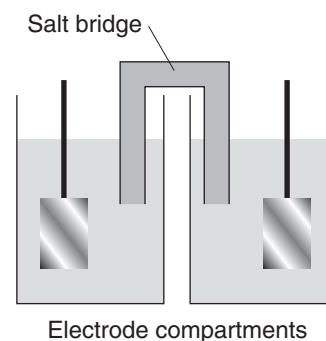


Fig. 5.4 When the electrolytes in the electrode compartments of a cell are different, they need to be joined so that ions can travel from one compartment to another. One device for joining the two compartments is a salt bridge.

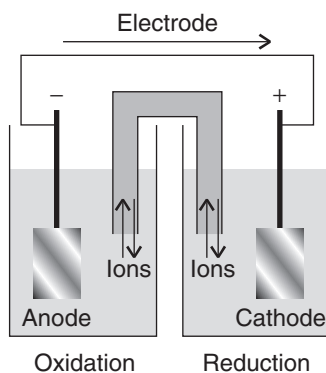
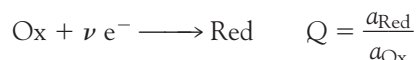


Fig. 5.5 The flow of electrons in the external circuit is from the anode of a galvanic cell, where they have been lost in the oxidation reaction, to the cathode, where they are used in the reduction reaction. Electrical neutrality is preserved in the electrolytes by the flow of cations and anions in opposite directions through the salt bridge.

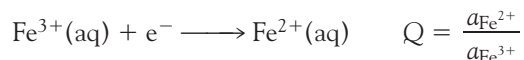
cell, the anode is also the location of oxidation (by definition). Now, though, electrons must be withdrawn from the species in the anode compartment, so the anode must be connected to the positive terminal of an external supply. Similarly, electrons must pass from the cathode to the species undergoing reduction, so the cathode must be connected to the negative terminal of a supply (Fig. 5.6).

In a **gas electrode** (Fig. 5.7), a gas is in equilibrium with a solution of its ions in the presence of an inert metal. The inert metal, which is often platinum, acts as a source or sink of electrons but takes no other part in the reaction except perhaps acting as a catalyst. One important example is the *hydrogen electrode*, in which hydrogen is bubbled through an aqueous solution of hydrogen ions and the redox couple is H^+/H_2 . This electrode is denoted $\text{Pt(s)}|\text{H}_2(\text{g})|\text{H}^+(\text{aq})$. The vertical bars denote junctions between phases. In this electrode, the junctions are between the platinum and the gas and between the gas and the liquid containing its ions.

The term **redox electrode** is normally reserved for an electrode in which the couple consists of the same element in two nonzero oxidation states (Fig. 5.8). An example is an electrode in which the couple is $\text{Fe}^{3+}/\text{Fe}^{2+}$. In general, the reaction is



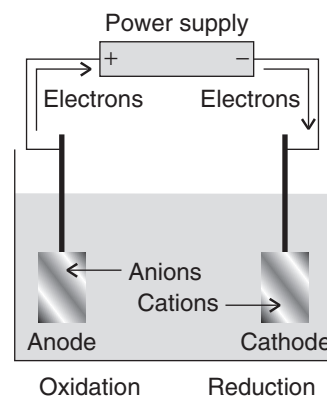
A redox electrode is denoted $\text{M}|\text{Red},\text{Ox}$, where M is an inert metal (typically platinum) making electrical contact with the solution. The electrode corresponding to the $\text{Fe}^{3+}/\text{Fe}^{2+}$ couple is therefore denoted $\text{Pt(s)}|\text{Fe}^{2+}(\text{aq}),\text{Fe}^{3+}(\text{aq})$ and the reduction half-reaction and reaction quotient are



Another example of a similar kind is the electrode $\text{Pt(s)}|\text{NADH}(\text{aq}),\text{NAD}^+(\text{aq}),\text{H}^+(\text{aq})$ used to study the NAD^+/NADH couple.

The simplest type of galvanic cell has a single electrolyte common to both electrodes (as in Fig. 5.3). In some cases it is necessary to immerse the electrodes in different electrolytes, as in the *Daniell cell* (Fig. 5.9), in which the redox couple at one electrode is Cu^{2+}/Cu and at the other is Zn^{2+}/Zn . In an **electrolyte concentration cell**, which would be constructed like the cell in Fig. 5.4, the electrode

Fig. 5.6 The flow of electrons and ions in an electrolytic cell. An external supply forces electrons into the cathode, where they are used to bring about a reduction, and withdraws them from the anode, which results in an oxidation reaction at that electrode. Cations migrate toward the negatively charged cathode and anions migrate toward the positively charged anode. An electrolytic cell usually consists of a single compartment, but a number of industrial versions have two compartments.



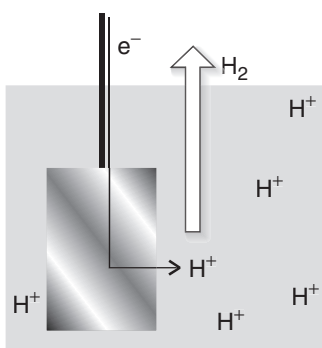


Fig. 5.7 The schematic structure of a hydrogen electrode, which is like other gas electrodes. Hydrogen is bubbled over a black (that is, finely divided) platinum surface that is in contact with a solution containing hydrogen ions. The platinum, as well as acting as a source or sink for electrons, speeds the electrode reaction because hydrogen attaches to (adsorbs on) the surface as atoms.

compartments are of identical composition except for the concentrations of the electrolytes. In an **electrode concentration cell** the electrodes themselves have different concentrations, either because they are gas electrodes operating at different pressures or because they are amalgams (solutions in mercury) with different concentrations.

In an electrochemical cell with two different electrolyte solutions in contact, as in the Daniell cell or an electrolyte concentration cell, the **liquid junction potential**, E_j , the potential difference across the interface of the two electrolytes, contributes to the overall potential difference generated by the cell. The contribution of the liquid junction to the potential can be decreased (to about 1 to 2 mV) by joining the electrolyte compartments through a salt bridge consisting of a saturated electrolyte solution (usually KCl) in agar jelly (as in Fig. 5.4). The reason for the success of the salt bridge is that the liquid junction potentials at either end are largely independent of the concentrations of the two more dilute solutions in the electrode compartments and so nearly cancel.

We have already seen that, in the notation for electrochemical cells, an interface between phases is denoted by a vertical bar, |. A double vertical line || denotes an interface for which the junction potential has been eliminated. Thus, an electrochemical cell in which the left-hand electrode, in an arrangement like that in Fig. 5.4, is zinc in contact with aqueous zinc sulfate and the right-hand electrode is copper in contact with aqueous copper(II) sulfate is denoted



SELF-TEST 5.6 Give the notation for an electrochemical cell in which the oxidation of NADH by oxygen could be studied (recall Example 5.2).

Answer: $\text{Pt(s)}|\text{NADH(aq),NAD}^+(\text{aq}),\text{H}^+(\text{aq})||\text{H}_2\text{O}_2(\text{aq}),\text{H}^+(\text{aq})|\text{O}_2(\text{g})|\text{Pt(s)}$

The current produced by a galvanic cell arises from the spontaneous reaction taking place inside it. The **cell reaction** is the reaction in the electrochemical cell written on the assumption that the right-hand electrode is the cathode and hence that reduction is taking place in the right-hand compartment. Later we see how to predict if the right-hand electrode is in fact the cathode; if it is, then the cell reaction is spontaneous as written. If the left-hand electrode turns out to be the cathode, then the reverse of the cell reaction is spontaneous.

To write the cell reaction corresponding to the electrochemical cell diagram, we first write the half-reactions at both electrodes as reductions and then subtract

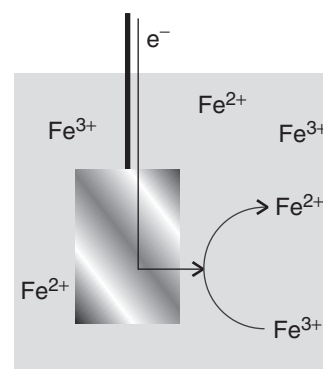


Fig. 5.8 The schematic structure of a redox electrode. The platinum metal acts as a source or sink for electrons required for the interconversion of (in this case) Fe^{2+} and Fe^{3+} ions in the surrounding solution.

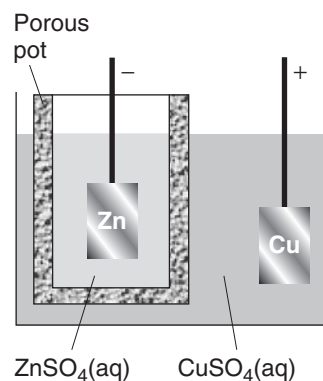
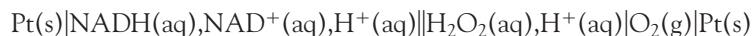
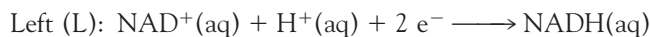
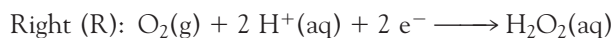


Fig. 5.9 A Daniell cell consists of copper in contact with copper(II) sulfate solution and zinc in contact with zinc sulfate solution; the two compartments are in contact through the porous pot that contains the zinc sulfate solution. The copper electrode is the cathode and the zinc electrode is the anode.

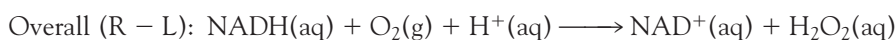
the equation for the left-hand electrode from the equation for the right-hand electrode. Thus, we saw in Example 5.2 that for the electrochemical cell used to study the reaction between NADH and O_2 ,



the two reduction half-reactions are



The equation for the cell reaction is the difference:



In other cases, it may be necessary to match the numbers of electrons in the two half-reactions by multiplying one of the equations through by a numerical factor: there should be no spare electrons showing in the overall equation.

5.6 The Nernst equation

The concentrations of electroactive species in biological systems do not normally have their standard values, so we need to be able to relate the potential difference of a cell to the actual concentrations.

A galvanic cell does electrical work as the reaction drives electrons through an external circuit. The work done by a given transfer of electrons depends on the potential difference between the two electrodes. When the potential difference is large (for instance, 2 V), a given number of electrons traveling between the electrodes can do a lot of electrical work. When the potential difference is small (such as 2 mV), the same number of electrons can do only a little work. An electrochemical cell in which the reaction is at equilibrium can do no work and the potential difference between its electrodes is zero.

According to the discussion in Section 2.13, we know that the maximum non-expansion work, w'_{\max} , that a system (in this context, the electrochemical cell) can do is given by the value of ΔG and in particular that

$$\text{At constant temperature and pressure: } w'_{\max} = \Delta G \quad (5.10)$$

Therefore, by measuring the potential difference and converting it to the electrical work done by the reaction, we have a means of determining a thermodynamic quantity, the reaction Gibbs energy. Conversely, if we know ΔG for a reaction, then we have a route to the prediction of the potential difference between the electrodes of an electrochemical cell. However, to use eqn 5.10, we need to recall that maximum work is achieved only when a process occurs reversibly. In the present context, reversibility means that the electrochemical cell should be connected to an external source of potential difference that opposes and exactly matches the potential difference generated by the cell. Then an infinitesimal change of the external potential difference will allow the reaction to proceed in its spontaneous direction and an opposite infinitesimal change will drive the reaction in its reverse

direction.⁴ The potential difference measured when an electrochemical cell is balanced against an external source of potential is called the **electromotive force** (emf) of the electrochemical cell and denoted E (Fig. 5.10). An alternative name for this quantity is the *zero-current cell potential*. In practice, to determine the emf of a cell, all we need do is to measure the potential difference with a voltmeter that draws negligible current.

As we show in the following *Derivation*, the relation between the emf and the Gibbs energy of the cell reaction is

$$-\nu FE = \Delta_r G \quad (5.11)$$

where F is Faraday's constant.

DERIVATION 5.3 The electromotive force

Suppose the cell reaction can be broken down into half-reactions of the form $A + \nu e^- \rightarrow B$. Then, when the reaction takes place, νN_A electrons are transferred from the reducing agent to the oxidizing agent per mole of reaction events, so the charge transferred between the electrodes is $\nu N_A \times (-e)$, or $-\nu F$. Now we proceed as in *Derivation 5.2* and write the electrical work w' done when this charge travels from the anode to the cathode as the product of the charge and the potential difference E :

$$w' = -\nu F \times E$$

Provided the work is done reversibly at constant temperature and pressure, we can equate this electrical work to the reaction Gibbs energy and obtain eqn 5.11.

Equation 5.11 shows that the sign of the emf is opposite to that of the reaction Gibbs energy, which we should recall is the slope of a graph of G plotted against the composition of the reaction mixture (Section 4.1). When the reaction is spontaneous in the forward direction, $\Delta_r G < 0$ and $E > 0$. When $\Delta_r G > 0$, the reverse reaction is spontaneous and $E < 0$. At equilibrium $\Delta_r G = 0$ and therefore $E = 0$ too.

Equation 5.11 provides an electrical method for measuring a reaction Gibbs energy at any composition of the reaction mixture: we simply measure the cell's emf and convert it to $\Delta_r G$. Conversely, if we know the value of $\Delta_r G$ at a particular composition, then we can predict the emf.

ILLUSTRATION 5.3 Estimating a typical emf

Suppose $\Delta_r G \approx -1 \times 10^2 \text{ kJ mol}^{-1}$ and $\nu = 1$; then

$$E = \frac{-\Delta_r G}{\nu F} = -\frac{(-1 \times 10^5 \text{ J mol}^{-1})}{1 \times (9.6485 \times 10^4 \text{ C mol}^{-1})} = 1 \text{ V}$$

Most electrochemical cells bought commercially are indeed rated at between 1 and 2 V. ■

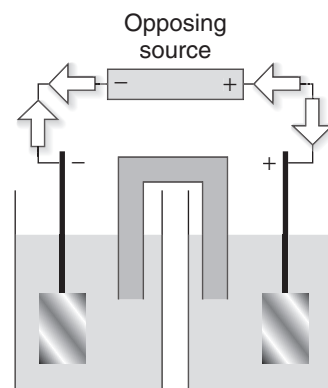


Fig. 5.10 The emf is measured by balancing the cell against an external potential that opposes the reaction in the cell. When there is no current flow, the external potential difference is equal to the emf of the cell.

⁴We saw in Chapter 1 that the criterion of thermodynamic reversibility is the reversal of a process by an infinitesimal change in the external conditions.

Our next step is to see how E varies with composition by combining eqn 5.11 and eqn 4.6, showing how the reaction Gibbs energy varies with composition:

$$\Delta_r G = \Delta_r G^\ominus + RT \ln Q$$

In this expression, $\Delta_r G^\ominus$ is the standard reaction Gibbs energy and Q is the reaction quotient for the cell reaction. When we substitute this relation into eqn 5.11 written as $E = -\Delta_r G/\nu F$, we obtain the **Nernst equation**:

$$E = E^\ominus - \frac{RT}{\nu F} \ln Q \quad (5.12)$$

E^\ominus is the **standard emf** of the electrochemical cell:

$$E^\ominus = -\frac{\Delta_r G^\ominus}{\nu F} \quad (5.13)$$

The standard emf is often interpreted as the emf of the electrochemical cell when all the reactants and products are in their standard states (unit activity for all solutes, pure gases, and solids, a pressure of 1 bar). However, because such an electrochemical cell is not in general attainable, it is better to regard E^\ominus simply as the standard Gibbs energy of the reaction expressed as a potential. Note that if all the stoichiometric coefficients in the equation for a cell reaction are multiplied by a factor, then $\Delta_r G^\ominus$ is increased by the same factor, but so too is ν , so the standard emf is unchanged. Likewise, Q is raised to a power equal to the factor (so if the factor is 2, Q is replaced by Q^2), and because $\ln Q^2 = 2 \ln Q$, and likewise for other factors, the second term on the right-hand side of the Nernst equation is also unchanged. That is, E is independent of how we write the balanced equation for the cell reaction.

At 25.00°C,

$$\frac{RT}{F} = \frac{(8.314 \text{ J K}^{-1} \text{ mol}^{-1}) \times (298.15 \text{ K})}{9.6485 \times 10^4 \text{ C mol}^{-1}} = 2.5693 \times 10^{-2} \text{ J C}^{-1}$$

Because $1 \text{ J} = 1 \text{ V C}$, $1 \text{ J C}^{-1} = 1 \text{ V}$, and $10^{-3} \text{ V} = 1 \text{ mV}$, we can write this result as

$$\frac{RT}{F} = 25.693 \text{ mV}$$

or approximately 25.7 mV. It follows from the Nernst equation that for a reaction in which $\nu = 1$, if Q is decreased by a factor of 10, then the emf of the electrochemical cell becomes more positive by $(25.7 \text{ mV}) \times \ln 10 = 59.2 \text{ mV}$. The reaction has a greater tendency to form products. If Q is increased by a factor of 10, then the emf falls by 59.2 mV and the reaction has a lower tendency to form products.

A special case of the Nernst equation has great importance in chemistry. Suppose the reaction has reached equilibrium; then $Q = K$, where K is the equilibrium constant of the cell reaction. However, because a chemical reaction at equilibrium cannot do work, it generates zero potential difference between the electrodes. Setting $Q = K$ and $E = 0$ in the Nernst equation gives

$$\ln K = \frac{\nu F E^\ominus}{RT} \quad (5.14)$$

This very important equation lets us predict equilibrium constants from the standard emf of an electrochemical cell.⁵ Note that

If $E^\ominus > 0$, then $K > 1$ and at equilibrium the cell reaction lies in favor of products.

If $E^\ominus < 0$, then $K < 1$ and at equilibrium the cell reaction lies in favor of reactants.

ILLUSTRATION 5.4 Calculating an equilibrium constant

Because the standard emf of the Daniell cell is +1.10 V, the equilibrium constant for the cell reaction (reaction A) is

$$\ln K = \frac{2 \times (9.6485 \times 10^4 \text{ C mol}^{-1}) \times (1.10 \text{ V})}{(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) \times (298.15 \text{ K})} = \frac{2 \times 9.6485 \times 1.10 \times 10^4}{8.3145 \times 298.15}$$

(we have used $1 \text{ C V} = 1 \text{ J}$ to cancel units) and therefore $K = 1.5 \times 10^{37}$. Hence, the displacement of copper by zinc goes virtually to completion in the sense that the ratio of concentrations of Zn^{2+} ions to Cu^{2+} ions at equilibrium is about 10^{37} . This value is far too large to be measured by classical analytical techniques, but its electrochemical measurement is straightforward. Note that a standard emf of +1 V corresponds to a very large equilibrium constant (and -1 V would correspond to a very small one). ■

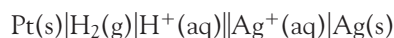
5.7 Standard potentials

To discuss the thermodynamics of biological processes, we need to be able to predict the standard reaction Gibbs energies of biological electron transfer reactions and their variation with pH.

Each electrode in a galvanic cell makes a characteristic contribution to the overall emf. Although it is not possible to measure the contribution of a single electrode, one electrode can be assigned a value zero and the others assigned relative values on that basis. The specially selected electrode is the **standard hydrogen electrode** (SHE):



The **standard potential**, $E^\ominus(\text{Ox/Red})$, of a couple Ox/Red is then measured by constructing an electrochemical cell in which the couple of interest forms the right-hand electrode and the standard hydrogen electrode is on the left.⁶ For example, the standard potential of the Ag^+/Ag couple is the standard emf of the cell



and is +0.80 V. Table 5.1 lists a selection of standard potentials; a longer list will be found in the *Data section*. However, we saw in Section 4.7 that in biochemical work, we adopt the biological standard state. To convert standard potentials to

⁵Equation 5.14, of course, is simply eqn 4.8 expressed electrochemically.

⁶Standard potentials are also called *standard electrode potentials* and *standard reduction potentials*. If in an older source of data you come across a “standard oxidation potential,” reverse its sign and use it as a standard reduction potential.

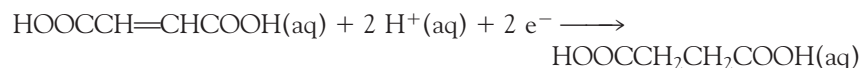
Table 5.1 Standard potentials at 25°C

Reduction half-reaction		E^\ominus/V
Oxidizing agent	Reducing agent	
<i>Strongly oxidizing</i>		
F_2	$+2 e^- \rightarrow 2 F^-$	+2.87
$S_2O_8^{2-}$	$+2 e^- \rightarrow 2 SO_4^{2-}$	+2.05
Au^+	$+e^- \rightarrow Au$	+1.69
Pb^{4+}	$+2 e^- \rightarrow Pb^{2+}$	+1.67
Ce^{4+}	$+e^- \rightarrow Ce^{3+}$	+1.61
$MnO_4^- + 8 H^+$	$+5 e^- \rightarrow Mn^{2+} + 4 H_2O$	+1.51
Cl_2	$+2 e^- \rightarrow 2 Cl^-$	+1.36
$Cr_2O_7^{2-} + 14 H^+$	$+6 e^- \rightarrow 2 Cr^{3+} + 7 H_2O$	+1.33
$O_2 + 4 H^+$	$+4 e^- \rightarrow 2 H_2O$	+1.23, +0.81 at pH = 7
Br_2	$+2 e^- \rightarrow 2 Br^-$	+1.09
Ag^+	$+e^- \rightarrow Ag$	+0.80
Hg_2^{2+}	$+2 e^- \rightarrow 2 Hg$	+0.79
Fe^{3+}	$+e^- \rightarrow Fe^{2+}$	+0.77
I_2	$+e^- \rightarrow 2 I^-$	+0.54
$O_2 + 2 H_2O$	$+4 e^- \rightarrow 4 OH^-$	+0.40, +0.81 at pH = 7
Cu^{2+}	$+2 e^- \rightarrow Cu$	+0.34
$AgCl$	$+e^- \rightarrow Ag + Cl^-$	+0.22
$2 H^+$	$+2 e^- \rightarrow H_2$	0, by definition
Fe^{3+}	$+3 e^- \rightarrow Fe$	-0.04
$O_2 + H_2O$	$+2 e^- \rightarrow HO_2^- + OH^-$	-0.08
Pb^{2+}	$+2 e^- \rightarrow Pb$	-0.13
Sn^{2+}	$+2 e^- \rightarrow Sn$	-0.14
Fe^{2+}	$+2 e^- \rightarrow Fe$	-0.44
Zn^{2+}	$+2 e^- \rightarrow Zn$	-0.76
$2 H_2O$	$+2 e^- \rightarrow H_2 + 2 OH^-$	-0.83, -0.42 at pH = 7
Al^{3+}	$+3 e^- \rightarrow Al$	-1.66
Mg^{2+}	$+2 e^- \rightarrow Mg$	-2.36
Na^+	$+e^- \rightarrow Na$	-2.71
Ca^{2+}	$+2 e^- \rightarrow Ca$	-2.87
K^+	$+e^- \rightarrow K$	-2.93
Li^+	$+e^- \rightarrow Li$	-3.05
<i>Strongly reducing</i>		

For a more extensive table, see the *Data section*.

biological standard potentials, E^\ominus , which correspond to neutral solution (pH = 7), we must first consider the variation of potential with pH.

The half-reactions of many redox couples involve hydrogen ions. For example, the fumaric acid/succinic acid couple ($HOOCCH=CHCOOH/HOOCCH_2CH_2COOH$), which plays a role in the citric acid cycle (Section 4.8), is



Half-reactions of this kind have potentials that depend on the pH of the medium. In this example, in which the hydrogen ions occur as reactants, an increase in pH, corresponding to a decrease in hydrogen ion activity, favors the formation of reactants, so the fumaric acid has a lower thermodynamic tendency to become reduced. We expect, therefore, that the potential of the fumaric/succinic acid couple should decrease as the pH is increased.

We can establish the quantitative variation of reduction potential with pH for a reaction by using the Nernst equation for the half-reaction and noting that (see the note in the introduction pointing out the relation between $\ln x$ and $\log x$)

$$\ln a_{\text{H}^+} = (\ln 10) \times \log a_{\text{H}^+} = -\ln 10 \times \text{pH}$$

with $\ln 10 = 2.303\dots$. If we suppose that fumaric acid and succinic acid have fixed concentrations, the potential of the fumaric/succinic redox couple is

$$E = E^\ominus - \frac{RT}{2F} \ln \frac{a_{\text{suc}}}{a_{\text{fum}} a_{\text{H}^+}^2} = \overbrace{E^\ominus - \frac{RT}{2F} \ln \frac{a_{\text{suc}}}{a_{\text{fum}}}}^{E'} + \frac{RT}{F} \ln a_{\text{H}^+}$$

which is easily rearranged into

$$E = E' - \frac{RT \ln 10}{F} \times \text{pH}$$

At 25°C,

$$E = E' - (59.2 \text{ mV}) \times \text{pH}$$

We see that an increase of 1 unit in pH decreases the potential by 59.2 mV, which is in agreement with the remark above, that the reduction of fumaric acid is discouraged by an increase in pH.

We use the same approach to convert standard potentials to biological standard potentials. If the hydrogen ions appear as reactants in the reduction half-reaction, then the potential is decreased below its standard value (for the fumaric/succinic couple, by $7 \times 59.2 \text{ mV} = 414 \text{ mV}$, or about 0.4 V). If the hydrogen ions appear as products, then the biological standard potential is higher than the thermodynamic standard potential. The precise change depends on the number of electrons and protons participating in the half-reaction. Biological standard potentials are important in the discussion of the electron transfer reactions of oxidative phosphorylation (Section 5.11). Table 5.2 is a partial list of biological standard potentials for redox couples that participate in important biochemical electron transfer reactions.

EXAMPLE 5.4 Converting a standard potential to a biological standard value

Estimate the biological standard potential of the NAD^+/NADH couple at 25°C (Example 5.2). The reduction half-reaction is



Strategy Write the Nernst equation for the potential, and express the reaction quotient in terms of the activities of the species. All species except H^+ are in

Table 5.2 Biological standard potentials at 25°C

Reduction half-reaction		E^\ominus/V
Oxidizing agent	Reducing agent	
<i>Strongly oxidizing</i>		
$O_2 + 4 H^+$	$+4 e^- \rightarrow 2 H_2O$	+0.81
$Fe^{3+}(\text{Cyt } f)$	$+e^- \rightarrow Fe^{2+}(\text{Cyt } f)$	+0.36
$O_2 + 2 H_2O$	$+4 e^- \rightarrow 2 H_2O_2$	+0.30
$Fe^{3+}(\text{Cyt } c)$	$+e^- \rightarrow Fe^{2+}(\text{Cyt } c)$	+0.25
$Fe^{3+}(\text{Cyt } b)$	$+e^- \rightarrow Fe^{2+}(\text{Cyt } b)$	+0.08
Dehydroascorbic acid + 2 H^+	$+2 e^- \rightarrow$ Ascorbic acid	+0.08
Coenzyme Q + 2 H^+	$+2 e^- \rightarrow$ Coenzyme QH_2	+0.04
Oxaloacetate ²⁻ + 2 H^+	$+2 e^- \rightarrow$ Malate ²⁻	-0.17
Pyruvate ⁻ + 2 H^+	$+2 e^- \rightarrow$ Lactate ⁻	-0.18
FAD + 2 H^+	$+2 e^- \rightarrow$ FADH ₂	-0.22
Glutathione (ox) + 2 H^+	$+2 e^- \rightarrow$ Glutathione (red)	-0.23
Lipoic acid (ox) + 2 H^+	$+2 e^- \rightarrow$ Lipoic acid (red)	-0.29
NAD ⁺ + H^+	$+2 e^- \rightarrow$ NADH	-0.32
2H ₂ O	$+2 e^- \rightarrow H_2 + 2 OH^-$	-0.42
Ferredoxin (ox)	$+e^- \rightarrow$ Ferredoxin (red)	-0.43
O ₂	$+e^- \rightarrow O_2^-$	-0.45
<i>Strongly reducing</i>		

For a more extensive table, see the *Data section*.

their standard states, so their activities are all equal to 1. The remaining task is to express the hydrogen ion activity in terms of the pH, exactly as was done in the text, and set $pH = 7$.

Solution The Nernst equation for the half-reaction, with $\nu = 2$, is

$$E = E^\ominus - \frac{RT}{2F} \ln \frac{\overbrace{a_{\text{NADH}}^1}}{a_{\text{H}^+} \underbrace{a_{\text{NAD}^+}}_1} = E^\ominus + \frac{RT}{2F} \ln a_{\text{H}^+}$$

We rearrange this expression to

$$\begin{aligned} E &= E^\ominus + \frac{RT}{2F} \ln a_{\text{H}^+} = E^\ominus - \frac{RT \ln 10}{2F} \times pH \\ &= E^\ominus - (29.58 \text{ mV}) \times pH \end{aligned}$$

The biological standard potential (at $pH = 7$) is therefore

$$E^\oplus = (-0.11 \text{ V}) - (29.58 \times 10^{-3} \text{ V}) \times 7 = -0.32 \text{ V}$$

A note on good practice: Whenever possible, avoid replacing activities by concentrations, especially when aiming to relate the electrode potential to pH, for the latter is defined in terms of the activity of hydrogen ions.

SELF-TEST 5.7 Calculate the biological standard potential of the half-reaction $\text{O}_2(\text{g}) + 4 \text{H}^+(\text{aq}) + 4 \text{e}^- \rightarrow 2 \text{H}_2\text{O}(\text{l})$ at 25°C given its value $+1.23 \text{ V}$ under thermodynamic standard conditions.

Answer: $+0.82 \text{ V}$ ■

To calculate the standard emf of an electrochemical cell formed from any pair of electrodes, we take the difference of their standard potentials:

$$E^\ominus = E_{\text{R}}^\ominus - E_{\text{L}}^\ominus \quad (5.15\text{a})$$

where E_{R}^\ominus is the standard potential of the right-hand electrode and E_{L}^\ominus is that of the left. The analogous expression for the biological standard state is

$$E^\oplus = E_{\text{R}}^\oplus - E_{\text{L}}^\oplus \quad (5.15\text{b})$$

When dealing with biological systems, the focus is not necessarily on reactions occurring at electrodes but on electron transfer processes in the cytosol or membranes of biological cells. We can still estimate the standard reaction Gibbs energy (and hence the equilibrium constant) of biological electron transfer reactions by using eqn 5.13 if we express the chemical equation for the redox reaction as the difference of two reduction half-reactions with known standard potentials. We then find E^\ominus or E^\oplus from eqn 5.15 and use eqn 5.13 for the calculation of the standard reaction Gibbs energy or eqn 5.14 for the calculation of the equilibrium constant. The approach is illustrated in the following example.

EXAMPLE 5.5 Calculating the equilibrium constant of a biological electron transfer reaction

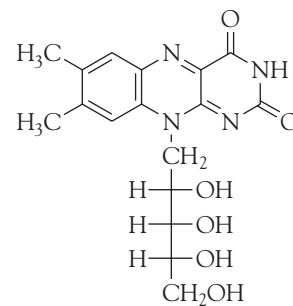
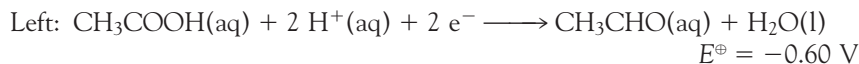
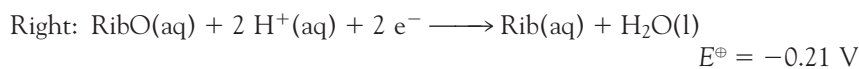
The reduced and oxidized forms of riboflavin (**3**) form a couple with $E^\oplus = -0.21 \text{ V}$ and the acetate/acetaldehyde couple has $E^\oplus = -0.60 \text{ V}$ under the same conditions. What is the equilibrium constant for the reduction of riboflavin (Rib) by acetaldehyde (ethanal) in neutral solution at 25°C ? The reaction is



where RibO is the oxidized form of riboflavin and Rib is the reduced form.

Strategy The aim is to find the values of E^\oplus and ν corresponding to the reaction, for then we can use eqn 5.14. To do so, we express the equation as the difference of two reduction half-reactions. The stoichiometric number of the electron in these matching half-reactions is the value of ν we require. We then look up the biological standard potentials for the couples corresponding to the half-reactions and calculate their difference to find E^\oplus .

Solution The two reduction half-reactions are



3 Riboflavin

and their difference is the redox reaction required. Note that $\nu = 2$. The corresponding standard emf is

$$E^\ominus = (-0.21 \text{ V}) - (-0.60 \text{ V}) = +0.39 \text{ V}$$

It follows that

$$\begin{aligned} \ln K &= \frac{2FE^\ominus}{RT} = \frac{2 \times (9.6485 \times 10^4 \text{ C mol}^{-1}) \times (0.39 \text{ V})}{(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) \times (298.15 \text{ K})} \\ &= \frac{2 \times 9.6485 \times 0.39 \times 10^4}{8.3145 \times 298.15} \end{aligned}$$

Therefore, because $K = e^{\ln K}$,

$$K = e^{(2 \times 9.6485 \times 0.39 \times 10^4) / (8.3145 \times 298.15)} = 1.5 \times 10^{13}$$

We conclude that riboflavin can be reduced by acetaldehyde in neutral solution. However, there may be mechanistic reasons—the energy required to break covalent bonds, for instance—that make the reduction too slow to be feasible in practice. Note that, because hydrogen ions do not appear in the chemical equation, the equilibrium constant is independent of pH.

SELF-TEST 5.8 What is the equilibrium constant for the reduction of riboflavin with rubredoxin, a bacterial iron-sulfur protein, in the reaction



given the biological standard potential of the rubredoxin couple is -0.06 V ?

Answer: 8.5×10^{-6} ; the reactants are favored ■

5.8 Toolbox: The measurement of pH

Biochemical reactions are sensitive to changes in hydronium ion concentration, so it is necessary to conduct experiments in solutions of known pH.

The potential of a hydrogen electrode is directly proportional to the pH of the solution. However, in practice, indirect methods are much more convenient to use than one based on the standard hydrogen electrode, and the hydrogen electrode is replaced by a *glass electrode* (Fig. 5.11). This electrode is sensitive to hydrogen ion activity and has a potential that depends linearly on the pH. It is filled with a phosphate buffer containing Cl^- ions and conveniently has $E \approx 0$ when the external medium is at $\text{pH} = 7$. The glass electrode is much more convenient to handle than the gas electrode itself and can be calibrated using solutions of known pH (for example, one of the buffer solutions described in Section 4.13).

SELF-TEST 5.9 What range should a voltmeter have (in volts) to display changes of pH from 1 to 14 at 25°C if it is arranged to give a reading of zero when $\text{pH} = 7$?

Answer: From -0.42 V to $+0.35 \text{ V}$, a range of 0.77 V

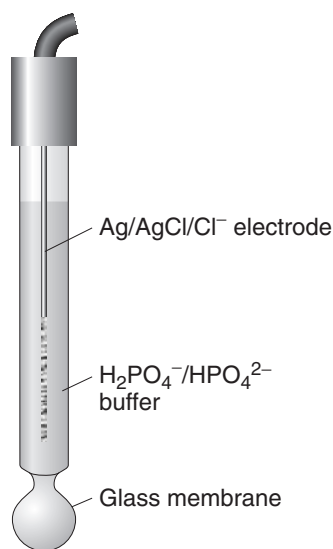


Fig. 5.11 A glass electrode has a potential that varies with the hydrogen ion concentration in the medium in which it is immersed. It consists of a thin glass membrane containing an electrolyte and a silver chloride electrode, $\text{Ag(s)}|\text{AgCl(s)}|\text{Cl}^-(\text{aq})$. The electrode is used in conjunction with a reference electrode, such as a calomel electrode, $\text{Hg(l)}|\text{Hg}_2\text{Cl}_2(\text{s})|\text{Cl}^-(\text{aq})$, that makes contact with the test solution through a salt bridge.

Finally, it should be noted that we now have a method for measuring the pK_a of an acid electrically. As we saw in Section 4.13, the pH of a solution containing equal amounts of the acid and its conjugate base is $pH = pK_a$. We now know how to determine pH and hence can determine pK_a in the same way.

Applications of standard potentials

The measurement of the emf of an electrochemical cell is a convenient source of data on the Gibbs energies, enthalpies, and entropies of reactions. In practice the standard values (and the biological standard values) of these quantities are the ones normally determined.

5.9 The electrochemical series

Some organic co-factors and metal centers in proteins act as electron transfer agents in a number of biological processes; we need to be able to predict which species is reduced or oxidized in a redox reaction.

We have seen that a cell reaction has $K > 1$ if $E^\ominus > 0$ and that $E > 0$ corresponds to reduction at the right-hand electrode. We have also seen that E^\ominus may be written as the difference of the standard potentials of the redox couples in the right and left electrodes (eqn 5.15, $E^\ominus = E_{R^\ominus} - E_{L^\ominus}$). A reaction corresponding to reduction at the right-hand electrode therefore has $K > 1$ if $E_{L^\ominus} < E_{R^\ominus}$, and we can conclude that

A couple with a low standard potential has a thermodynamic tendency to reduce a couple with a high standard potential.

More briefly: *low reduces high* and, equivalently, *high oxidizes low*. Of course, the same arguments apply to the biological standard values of the potentials. For example, consider the iron-containing protein ferredoxin, which participates in plant photosynthesis (Section 5.12), and cytochrome *c*, which participates in the last steps of respiration (Section 5.11). It follows from Table 5.2 that

$$E^\ominus(\text{ferredoxin}_{\text{ox}}, \text{ferredoxin}_{\text{red}}) = -0.43 \text{ V} < E^\ominus(\text{Cyt } c_{\text{ox}}, \text{Cyt } c_{\text{red}}) = +0.25 \text{ V}$$

and ferredoxin has a thermodynamic tendency to reduce cytochrome *c* at $pH = 7$. Hence, the reaction



can be expected to have $K > 1$.

SELF-TEST 5.10 Does NAD^+ have a thermodynamic tendency to oxidize the pyruvate ion at $pH = 7$?

Answer: No

5.10 The determination of thermodynamic functions

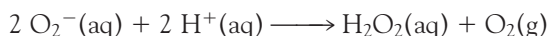
Calorimetry is not always practicable, especially for biochemically important reactions, but in some cases their thermodynamic properties can be measured electrochemically.

We have seen that the standard emf of an electrochemical cell is related to the standard reaction Gibbs energy by eqn 5.13 ($\Delta_r G^\ominus = -\nu F E^\ominus$). Therefore, by measuring the standard emf of a cell driven by the reaction of interest, we can obtain the standard reaction Gibbs energy. If we were interested in the biological standard state, then we would use the same expression but with the standard emf at pH = 7 ($\Delta_r G^\oplus = -\nu F E^\oplus$).

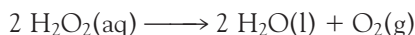
The relation between the standard emf and the standard reaction Gibbs energy is a convenient route for the calculation of the standard potential of a couple from two other standard potentials. We make use of the fact that G is a state function and that the Gibbs energy of an overall reaction is the sum of the Gibbs energies of the reactions into which it can be divided. In general, we cannot combine the E^\ominus values directly because they depend on the value of ν , which may be different for the two couples.

EXAMPLE 5.6 Calculating a standard potential from two other standard potentials

The superoxide ion (O_2^-) is an undesirable by-product of some enzyme-catalyzed reactions. It is metabolized by the enzyme superoxide dismutase (SOD) in a *disproportionation* (or *dismutation*), a reaction that both oxidizes and reduces a species. The reaction catalyzed by SOD is



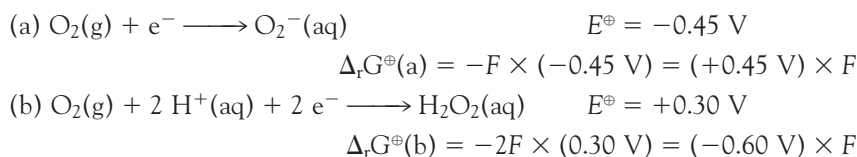
where O_2^- is oxidized to O_2 and reduced to O_2^{2-} (in H_2O_2). Hydrogen peroxide, H_2O_2 , is also produced by other biochemical reactions. It is a toxic substance that is metabolized by catalases and peroxidases. The disproportionation catalyzed by catalase is



Given the standard potentials $E^\ominus(O_2, O_2^-) = -0.45 \text{ V}$ and $E^\ominus(O_2, H_2O_2) = +0.30 \text{ V}$, calculate $E^\oplus(O_2^-, H_2O_2)$, the biological standard potential for the SOD-catalyzed reduction of O_2^- to H_2O_2 .

Strategy We need to convert the two E^\ominus to $\Delta_r G^\oplus$ by using eqn 5.13, add them appropriately, and then convert the overall $\Delta_r G^\oplus$ so obtained to the required E^\oplus by using eqn 5.13 again. Because the F s cancel at the end of the calculation, carry them through.

Solution The electrode reactions are as follows:



The required reaction is



Because (c) = (b) – (a), it follows that

$$\Delta_r G^\ominus(c) = \Delta_r G^\ominus(b) - \Delta_r G^\ominus(a)$$

Therefore, from eqn 5.13,

$$FE^\ominus(c) = -\{(-0.60 \text{ V})F - (+0.45 \text{ V})F\}$$

The F s cancel, and we are left with $E^\ominus(c) = +1.05 \text{ V}$.

A note on good practice: Whenever combining standard potentials to obtain the standard potential of a third couple, always work via the Gibbs energies because they are additive, whereas in general, standard potentials are not.

SELF-TEST 5.11 Given the standard potentials $E^\ominus(\text{Fe}^{3+}, \text{Fe}) = -0.04 \text{ V}$ and $E^\ominus(\text{Fe}^{2+}, \text{Fe}) = -0.44 \text{ V}$, calculate $E^\ominus(\text{Fe}^{3+}, \text{Fe}^{2+})$.

Answer: $+0.76 \text{ V}$ ■

Once $\Delta_r G^\ominus$ has been measured, we can use thermodynamic relations to determine other properties. For instance, the entropy of the cell reaction can be obtained from the change in the potential with temperature:

$$\Delta_r S^\ominus = \nu F \frac{dE^\ominus}{dT} \quad (5.16a)$$

DERIVATION 5.4 The reaction entropy from the electrochemical cell potential

In Section 3.3 we used the fact that, at constant pressure, when the temperature changes by dT , the Gibbs energy changes by $dG = -SdT$. Because this equation applies to the reactants and the products, it follows that

$$d(\Delta_r G^\ominus) = -\Delta_r S^\ominus \times dT$$

Substitution of $\Delta_r G^\ominus = -\nu FE^\ominus$ then gives

$$\nu F \times dE^\ominus = \Delta_r S^\ominus \times dT$$

which rearranges into eqn 5.16.

COMMENT 5.3 Infinitesimally small quantities may be treated like any other quantity in algebraic manipulations. Thus, the expression $dy = adx$ may be rewritten as $dy/dx = a$, $dx/dy = 1/a$, and so on. For instance, if $dy = 2dx$, then $dy/dx = 2$ and $dx/dy = 1/2$. ■

For macroscopic changes in temperature and cell potential, we replace dT by $\Delta T = T' - T$ and dE^\ominus by $\Delta E^\ominus = E^{\ominus'} - E^\ominus$ and write

$$\Delta_r S^\ominus = \frac{\nu F(E^\ominus - E^{\ominus'})}{T - T'} \quad (5.16b)$$

We see from eqn 5.16 that the standard emf of an electrochemical cell increases with temperature if the standard reaction entropy is positive and that the slope of a plot of potential against temperature is proportional to the reaction

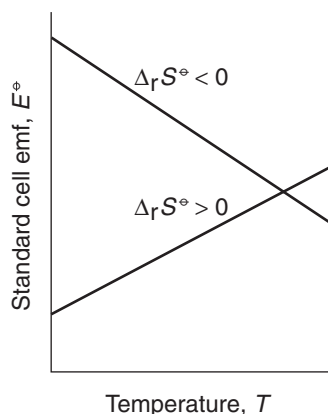


Fig. 5.12 The variation of the standard potential of a cell with temperature depends on the standard entropy of the cell reaction.

entropy (Fig. 5.12). An implication is that if the cell reaction produces a lot of gas, then its potential will increase with temperature. The opposite is true for a reaction that consumes gas.

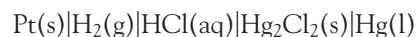
Finally, we can combine the results obtained so far by using $G = H - TS$ in the form $H = G + TS$ to obtain the standard reaction enthalpy:

$$\Delta_r H^\ominus = \Delta_r G^\ominus + T\Delta_r S^\ominus \quad (5.17)$$

with $\Delta_r G^\ominus$ determined from the cell potential and $\Delta_r S^\ominus$ from its temperature variation. Thus, we now have a non-calorimetric method of measuring a reaction enthalpy.

EXAMPLE 5.7 Using the temperature dependence of the cell potential

The pH of a solution can be measured by determining the emf of an electrochemical cell in which a hydrogen electrode is one component. For instance, consider the electrochemical cell



with the cell reaction



The Nernst equation gives

$$E = E^\ominus - \frac{RT}{2F} \ln Q \quad Q = \frac{a_{\text{H}^+}^2 a_{\text{Cl}^-}^2}{p_{\text{H}_2}}$$

The emf of this electrochemical cell was found to be +0.2699 V at 293 K and +0.2669 V at 303 K. Evaluate the standard Gibbs energy, enthalpy, and entropy at 298 K of the reaction.

Strategy We find the standard reaction Gibbs energy from the standard emf by using eqn 5.13 and making a linear interpolation between the two temperatures (in this case, we take the mean E^\ominus because 298 K lies midway between 293 K and 303 K). The standard reaction entropy is obtained by substituting the data into eqn 5.16. Then the standard reaction enthalpy is obtained by combining these two quantities by using eqn 5.17.

Solution Because the mean standard cell emf is +0.2684 V and $\nu = 2$ for the reaction,

$$\begin{aligned} \Delta_r G^\ominus &= -\nu F E^\ominus = -2 \times (9.6485 \times 10^4 \text{ C mol}^{-1}) \times (0.2684 \text{ V}) \\ &= -51.79 \text{ kJ mol}^{-1} \end{aligned}$$

Then, from eqn 5.16, the standard reaction entropy is

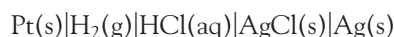
$$\begin{aligned} \Delta_r S^\ominus &= 2 \times (9.6485 \times 10^4 \text{ C mol}^{-1}) \times \left(\frac{0.2699 \text{ V} - 0.2669 \text{ V}}{293 \text{ K} - 303 \text{ K}} \right) \\ &= -57.9 \text{ J K}^{-1} \text{ mol}^{-1} \end{aligned}$$

For the next stage of the calculation it is convenient to write the last value as $-5.79 \times 10^{-2} \text{ kJ K}^{-1} \text{ mol}^{-1}$. Then, from eqn 5.17, we find

$$\begin{aligned}\Delta_r H^\ominus &= (-51.79 \text{ kJ mol}^{-1}) + (298 \text{ K}) \times (-5.79 \times 10^{-2} \text{ kJ K}^{-1} \text{ mol}^{-1}) \\ &= -69.0 \text{ kJ mol}^{-1}\end{aligned}$$

One difficulty with this procedure lies in the accurate measurement of small temperature variations of cell potential. Nevertheless, it is another example of the striking ability of thermodynamics to relate the apparently unrelated, in this case to relate electrical measurements to thermal properties.

SELF-TEST 5.12 Predict the standard potential of the *Harned cell*

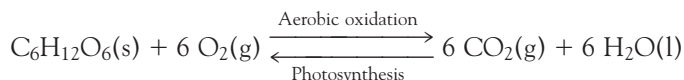


at 303 K from tables of thermodynamic data for 298 K.

Answer: +0.2168 V ■

Electron transfer in bioenergetics

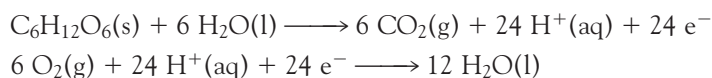
Electron transfer between protein-bound cofactors or between proteins plays a role in a number of biological processes, such as the oxidative breakdown of foods, photosynthesis, nitrogen fixation, the reduction of atmospheric N_2 to NH_3 by certain microorganisms, and the mechanisms of action of oxidoreductases, which are enzymes that catalyze redox reactions. Here, we examine the redox reactions associated with photosynthesis and the aerobic oxidation of glucose. These processes are related by the reactions



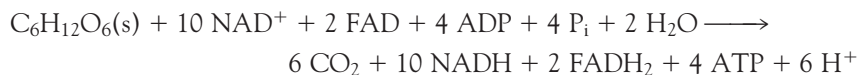
5.11 The respiratory chain

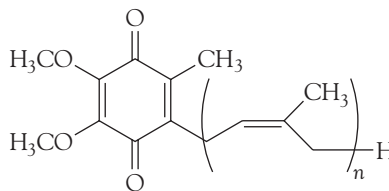
The centrally important processes of biochemistry include the electrochemical reactions between proteins in the mitochondrion of the cell, for they are responsible for delivering the electrons extracted from glucose to water.

The half-reactions for the oxidation of glucose and the reduction of O_2 are



We see that the exergonic oxidation of one $\text{C}_6\text{H}_{12}\text{O}_6$ molecule requires the transfer of 24 electrons to six O_2 molecules. However, the electrons do not flow directly from glucose to O_2 . In biological cells, glucose is oxidized to CO_2 by NAD^+ and FAD during glycolysis and the citric acid cycle (Section 4.8):

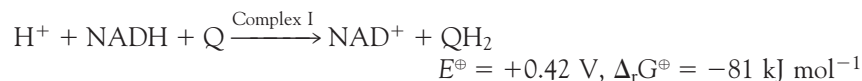




4 Coenzyme Q, Q

In the **respiratory chain**, electrons from the powerful reducing agents NADH and FADH_2 pass through four membrane-bound protein complexes and two mobile electron carriers before reducing O_2 to H_2O . We shall see that the electron transfer reactions drive the synthesis of ATP at three of the membrane protein complexes.

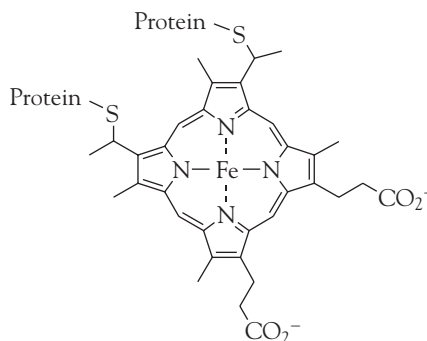
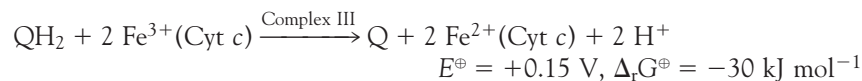
The respiratory chain begins in complex I (NADH-Q oxidoreductase), where NADH is oxidized by coenzyme Q (Q, 4) in a two-electron reaction:



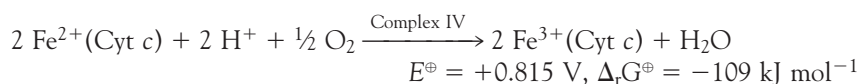
Additional Q molecules are reduced by FADH_2 in complex II (succinate-Q reductase):



Reduced Q migrates to complex III (Q-cytochrome *c* oxidoreductase), which catalyzes the reduction of the protein cytochrome *c* (Cyt *c*). Cytochrome *c* contains the heme *c* group (5), the central iron ion of which can exist in oxidation states +3 and +2. The net reaction catalyzed by complex III is

5 Heme *c*

Reduced cytochrome *c* carries electrons from complex III to complex IV (cytochrome *c* oxidase), where O_2 is reduced to H_2O :



The reactions that occur in complexes I, III, and IV are sufficiently exergonic to drive the synthesis of ATP in the process called **oxidative phosphorylation**:



We saw in Section 4.7 that the phosphorylation of ADP to ATP can be coupled to the exergonic dephosphorylation of other molecules. Indeed, this is the mechanism by which ATP is synthesized during glycolysis and the citric acid cycle (Section 4.8). However, oxidative phosphorylation operates by a different mechanism.

The structure of a mitochondrion is shown in Fig 5.13. The protein complexes associated with the electron transport chain span the inner membrane, and phosphorylation takes place in the intermembrane space. The Gibbs energy of the reactions in complexes I, III, and IV is first used to do the work of moving protons across the mitochondrial membrane. The complexes are oriented asymmetrically in the inner membrane so that the protons abstracted from one side of the membrane can be deposited on the other side. For example, the oxidation of NADH by Q in complex I is coupled to the transfer of four protons across the membrane. The coupling of electron transfer and proton pumping in complexes III and IV contribute further to a gradient of proton concentration across the membrane. Then the enzyme H^+ -ATPase uses the energy stored in the proton gradient to phosphorylate ADP to ATP. Experiments show that 11 molecules of ATP are made for every three molecules of NADH and one molecule of $FADH_2$ that are oxidized by the respiratory chain. The ATP is then hydrolyzed on demand to perform useful biochemical work throughout the cell.

The **chemiosmotic theory** proposed by Peter Mitchell explains how H^+ -ATPases use the energy stored in a transmembrane proton gradient to synthesize ATP from ADP. It follows from eqn 5.8 that we can estimate the Gibbs energy available for phosphorylation by writing

$$\Delta G_m = RT \ln \frac{[H^+]_{\text{in}}}{[H^+]_{\text{out}}} + F\Delta\phi \quad (5.18)$$

where $\Delta\phi = \phi_{\text{in}} - \phi_{\text{out}}$ is the membrane potential difference and we have used $z = +1$. After using $\ln [H^+] = (\ln 10) \log [H^+]$ and substituting $\Delta\text{pH} = \text{pH}_{\text{in}} - \text{pH}_{\text{out}} = -\log [H^+]_{\text{in}} + \log [H^+]_{\text{out}}$, it follows that

$$\Delta G_m = F\Delta\phi - (RT \ln 10)\Delta\text{pH} \quad (5.19)$$

ILLUSTRATION 5.5 Using the chemiosmotic theory

In the mitochondrion, $\Delta\text{pH} \approx -1.4$ and $\Delta\phi \approx 0.14 \text{ V}$, so it follows from eqn 5.19 that $\Delta G_m \approx +21.5 \text{ kJ mol}^{-1}$. Because 31 kJ mol^{-1} is needed for phosphorylation (Section 4.7), we conclude that at least 2 mol H^+ (and probably more) must flow through the membrane for the phosphorylation of 1 mol ADP. ■

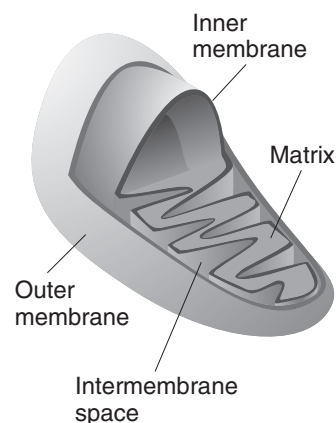
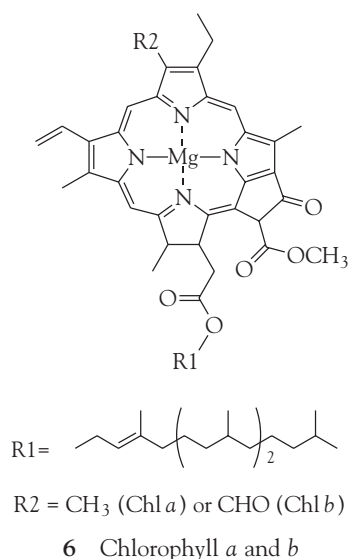


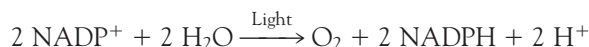
Fig. 5.13 The general structure of a mitochondrion.

5.12 Plant photosynthesis

We need to appreciate that the mechanism of formation of glucose from carbon dioxide and water in photosynthetic organisms is distinctly different from the mechanism of glucose breakdown.

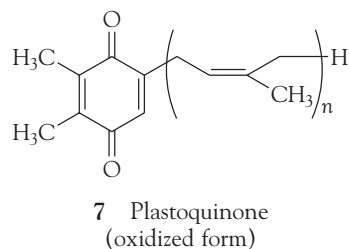
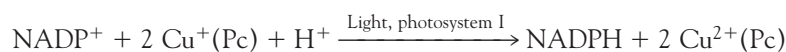


In plant photosynthesis, solar energy drives the endergonic reduction of CO₂ to glucose, with concomitant oxidation of water to O₂ ($\Delta_r G^\ominus = +2880 \text{ kJ mol}^{-1}$). The process takes place in the *chloroplast*, a special organelle of the plant cell. Electrons flow from reductant to oxidant via a series of electrochemical reactions that are coupled to the synthesis of ATP. First, the leaf absorbs solar energy and transfers it to membrane protein complexes known as photosystem I and photosystem II.⁷ The absorption of energy from light decreases the reduction potential of special dimers of chlorophyll *a* molecules (6) known as P700 (in photosystem I) and P680 (in photosystem II). In their high-energy or excited states, P680 and P700 initiate electron transfer reactions that culminate in the oxidation of water to O₂ and the reduction of NADP⁺ to NADPH (1):

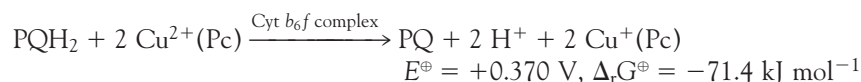


It is clear that energy from light is required to drive this reaction because, in the dark, $E^\ominus = -1.135 \text{ V}$ and $\Delta_r G^\ominus = +438.0 \text{ kJ mol}^{-1}$.

Working together, photosystem I and the enzyme ferredoxin:NADP⁺ oxidoreductase catalyze the light-induced oxidation of NADP⁺ to NADPH. The electrons required for this process come initially from P700 in its excited state. The resulting P700⁺ is then reduced by the mobile carrier plastocyanin (Pc), a protein in which the bound copper ion can exist in oxidation states +2 and +1. The net reaction is

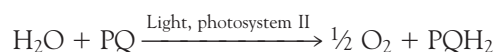


Oxidized plastocyanin accepts electrons from reduced plastoquinone (PQ, 7). The process is catalyzed by the cytochrome *b*₆*f* complex, a membrane protein complex that resembles complex III of mitochondria:



This reaction is sufficiently exergonic to drive the synthesis of ATP in the process known as **photophosphorylation**.

Plastoquinone is reduced by water in a process catalyzed by light and photosystem II. The electrons required for the reduction of plastoquinone come initially from P680 in its excited state. The resulting P680⁺ is then reduced ultimately by water. The net reaction is



⁷See Chapter 13 for details of the energy transfer process.

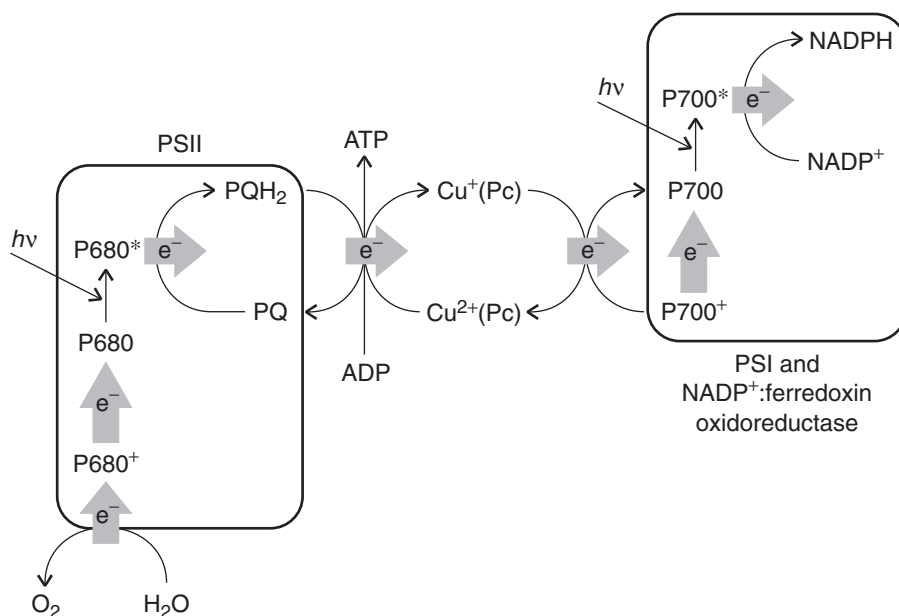
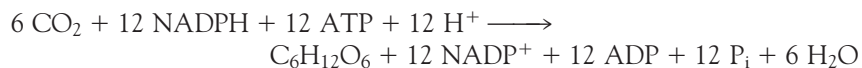


Fig. 5.14 In plant photosynthesis, light-induced electron transfer processes lead to the oxidation of water to O_2 and the reduction of $NADP^+$ to NADPH, with concomitant production of ATP. The energy stored in ATP and NADPH is used to reduce CO_2 to carbohydrate in a separate set of reactions. The scheme summarizes the general patterns of electron flow and does not show all the intermediate electron carriers in photosystems I and II, the cytochrome b_6f complex, and ferredoxin: $NADP^+$ oxidoreductase.

In this way, plant photosynthesis uses an abundant source of electrons (water) and of energy (the Sun) to drive the endergonic reduction of $NADP^+$, with concomitant synthesis of ATP (Fig. 5.14). Experiments show that for each molecule of NADPH formed in the chloroplast of green plants, one molecule of ATP is synthesized.

The ATP and NADPH molecules formed by the light-induced electron transfer reactions of plant photosynthesis participate directly in the reduction of CO_2 to glucose in the chloroplast:



In summary, electrochemical reactions mediated by membrane protein complexes harness energy in the form of ATP. Plant photosynthesis uses solar energy to transfer electrons from a poor reductant (water) to carbon dioxide. In the process, high-energy molecules (carbohydrates, such as glucose) are synthesized in the cell. Animals feed on the carbohydrates derived from photosynthesis. During aerobic metabolism, the O_2 released by photosynthesis as a waste product is used to oxidize carbohydrates to CO_2 , driving biological processes such as biosynthesis, muscle contraction, cell division, and nerve conduction. Hence, the sustenance of life on Earth depends on a tightly regulated carbon-oxygen cycle that is driven by solar energy.

Checklist of Key Ideas

You should now be familiar with the following concepts:

- 1. Deviations from ideal behavior in ionic solutions are ascribed to the interaction of an ion with its ionic atmosphere.
- 2. According to the Debye-Hückel limiting law, the mean activity of ions in a solution is related to the ionic strength, I , of the solution by $\log \gamma_{\pm} = -A|z_+z_-|I^{1/2}$.
- 3. The Gibbs energy of transfer of an ion across a cell membrane is determined by an activity gradient and a membrane potential difference, $\Delta\phi$, that arises from differences in Coulomb repulsions on each side of the bilayer: $\Delta G_m = RT \ln([A]_{in}/[A]_{out}) + zF\Delta\phi$.
- 4. A galvanic cell is an electrochemical cell in which a spontaneous chemical reaction produces a potential difference. An electrolytic cell is an electrochemical cell in which an external source of current is used to drive a non-spontaneous chemical reaction.
- 5. A redox reaction is expressed as the difference of two reduction half-reactions.
- 6. In an electrochemical cell, a cathode is the site of reduction; an anode is the site of oxidation.
- 7. The electromotive force of a cell is the potential difference it produces when operating reversibly: $E = -\Delta_r G/\nu F$.
- 8. The Nernst equation for the emf of a cell is $E = E^\ominus - (RT/\nu F) \ln Q$.
- 9. The standard potential of a couple is the standard emf of a cell in which it forms the right-hand electrode and a hydrogen electrode is on the left. Biological standard potentials are measured in neutral solution (pH = 7).
- 10. The standard emf of a cell is the difference of its standard electrode potentials: $E^\ominus = E_R^\ominus - E_L^\ominus$ or $E^\oplus = E_R^\oplus - E_L^\oplus$.
- 11. The equilibrium constant of a cell reaction is related to the standard emf of the cell by $\ln K = \nu FE^\ominus/RT$.
- 12. A couple with a low standard potential has a thermodynamic tendency (in the sense $K > 1$) to reduce a couple with a high standard potential.
- 13. The entropy and enthalpy of a cell reaction are measured from the temperature dependence of the cell's emf: $\Delta_r S^\ominus = \nu F(E^\ominus - E^{\ominus'})/(T - T')$, $\Delta H^\ominus = \Delta G^\ominus + T\Delta S^\ominus$.

Discussion questions

- 5.1 Describe the general features of the Debye-Hückel theory of electrolyte solutions.
- 5.2 The addition of a small amount of a salt, such as $(\text{NH}_4)_2\text{SO}_4$, to a solution containing a charged protein increases the solubility of the protein in water. This observation is called the *salting-in effect*. However, the addition of large amounts of salt can decrease the solubility of the protein to such an extent that the protein precipitates from solution. This observation is called the *salting-out effect* and is used widely by biochemists to isolate and purify proteins. Consider the equilibrium $\text{PX}_\nu(\text{s}) \rightleftharpoons \text{P}^{\nu+}(\text{aq}) + \nu \text{X}^-(\text{aq})$, where $\text{P}^{\nu+}$ is a polycationic protein of charge $+\nu$ and X^- is its counter-ion. Use Le Chatelier's principle and the physical principles behind the Debye-Hückel theory to provide a molecular interpretation for the salting-in and salting-out effects.
- 5.3 Discuss the mechanism of proton conduction in water.
- 5.4 Distinguish between galvanic, electrolytic, and fuel cells.
- 5.5 Describe a method for the determination of the standard emf of an electrochemical cell.
- 5.6 The photosynthetic oxidation of water to O_2 occurs in an enzyme that contains four manganese ions, each of which can exist in oxidation states ranging from +2 to +4. The electrochemical production of one molecule of O_2 requires the oxidation of two molecules of water by a total of four electrons. However, the excited state of P680 can donate only one electron at a time to plastoquinone. Explain how electron transfer mediated by P680 can lead to the formation of a molecule of O_2 in photosystem II. *Hint*: See V.A. Szalai and G.W. Brudvig, How plants produce dioxygen. *American Scientist* **86**, 542 (1998).
- 5.7 Review the concepts in Chapters 1 through 5 and prepare a summary of the experimental and calculational methods that can be used to measure or estimate the Gibbs energies of phase transitions and chemical reactions.

Exercises

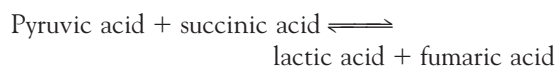
- 5.8 Relate the ionic strengths of (a) KCl, (b) FeCl₃, and (c) CuSO₄ solutions to their molalities, *b*.
- 5.9 Calculate the ionic strength of a solution that is 0.10 mol kg⁻¹ in KCl(aq) and 0.20 mol kg⁻¹ in CuSO₄(aq).
- 5.10 Calculate the masses of (a) Ca(NO₃)₂ and, separately, (b) NaCl to add to a 0.150 mol kg⁻¹ solution of KNO₃(aq) containing 500 g of solvent to raise its ionic strength to 0.250.
- 5.11 Express the mean activity coefficient of the ions in a solution of CaCl₂ in terms of the activity coefficients of the individual ions.
- 5.12 Estimate the mean ionic activity coefficient and activity of a solution that is 0.010 mol kg⁻¹ CaCl₂(aq) and 0.030 mol kg⁻¹ NaF(aq).
- 5.13 The mean activity coefficients of HBr in three dilute aqueous solutions at 25°C are 0.930 (at 5.0 mmol kg⁻¹), 0.907 (at 10.0 mmol kg⁻¹), and 0.879 (at 20.0 mmol kg⁻¹). Estimate the value of *B* in the extended Debye-Hückel law, with *C* = 0.
- 5.14 The overall reaction for the active transport of Na⁺ and K⁺ ions by the Na⁺/K⁺ pump is
- $$3 \text{Na}^+(\text{inside}) + 2 \text{K}^+(\text{outside}) + \text{ATP} \longrightarrow \text{ADP} + \text{P}_i + 3 \text{Na}^+(\text{outside}) + 2 \text{K}^+(\text{inside})$$
- At 310 K, Δ_rG[⊖] for the hydrolysis of ATP is -31.3 kJ mol⁻¹. Given that the [ATP]/[ADP] ratio is of the order of 100, is the hydrolysis of 1 mol ATP sufficient to provide the energy for the transport of Na⁺ and K⁺ according to the equation above? Take [P_i] = 1.0 mol L⁻¹.
- 5.15 Vision begins with the absorption of light by special cells in the retina. Ultimately, the energy is used to close ligand-gated ion channels, causing sizable changes in the transmembrane potential. The pulse of electric potential travels through the optical nerve and into the optical cortex, where it is interpreted as a signal and incorporated into the web of events we call visual perception (see Chapter 13). Taking the resting potential as -30 mV, the temperature as 310 K, permeabilities of the K⁺ and Cl⁻ ions as P_{K⁺} = 1.0 and P_{Cl⁻} = 0.45, respectively, and the concentrations as [K⁺]_{in} = 100 mmol L⁻¹, [Na⁺]_{in} = 10 mmol L⁻¹, [Cl⁻]_{in} = 10 mmol L⁻¹, [K⁺]_{out} = 5 mmol L⁻¹, [Na⁺]_{out} = 140 mmol L⁻¹, and [Cl⁻]_{out} = 100 mmol L⁻¹, calculate relative permeability of the Na⁺ ion.
- 5.16 Is the conversion of pyruvate ion to lactate ion in the reaction CH₃COCO₂⁻(aq) + NADH(aq) + H⁺(aq) → CH₃CH₂(OH)CO₂⁻(aq) + NAD⁺(aq) a redox reaction?
- 5.17 Express the reaction in Exercise 5.16 as the difference of two half-reactions.
- 5.18 Express the reaction in which ethanol is converted to acetaldehyde (propanal) by NAD⁺ in the presence of alcohol dehydrogenase as the difference of two half-reactions and write the corresponding reaction quotients for each half-reaction and the overall reaction.
- 5.19 Express the oxidation of cysteine (HSCH₂CH(NH₂)COOH) to cystine (HOOCCH(NH₂)CH₂SSCH₂CH(NH₂)COOH) as the difference of two half-reactions, one of which is O₂(g) + 4 H⁺(aq) + 4 e⁻ → 2 H₂O(l).
- 5.20 One of the steps in photosynthesis is the reduction of NADP⁺ by ferredoxin (fd) in the presence of ferredoxin:NADP oxidoreductase: 2 fd_{red}(aq) + NADP⁺(aq) + 2 H⁺(aq) → 2 fd_{ox}(aq) + NADPH(aq). Express this reaction as the difference of two half-reactions. How many electrons are transferred in the reaction event?
- 5.21 From the biological standard half-cell potentials E[⊖](O₂, H⁺, H₂O) = +0.82 V and E[⊖](NADH⁺, H⁺, NADH) = -0.32 V, calculate the standard potential arising from the reaction in which NADH is oxidized to NAD⁺ and the corresponding biological standard reaction Gibbs energy.
- 5.22 Cytochrome *c* oxidase receives electrons from reduced cytochrome *c* (Cyt *c*_{red}) and transmits them to molecular oxygen, with the formation of water. (a) Write a chemical equation for this process, which occurs in an acidic environment. (b) Estimate the values of E[⊖], Δ_rG[⊖], and *K* for the reaction at 25°C.
- 5.23 Consider a hydrogen electrode in HBr(aq) at 25°C operating at 1.45 bar. Estimate the change in the electrode potential when the solution is changed from 5.0 mmol L⁻¹ to 25.0 mmol L⁻¹.
- 5.24 A hydrogen electrode can, in principle, be used to monitor changes in the molar concentrations of weak acids in biologically active solutions. Consider a hydrogen electrode in a solution of lactic acid as part of an overall galvanic cell at 25°C and 1 bar. Estimate the change in the

electrode potential when the concentration of lactic acid in the solution is changed from 5.0 mmol L^{-1} to 25.0 mmol L^{-1} .

- 5.25 Write the cell reactions and electrode half-reactions for the following cells:
- $\text{Pt(s)}|\text{H}_2(\text{g}, p_L)|\text{HCl}(\text{aq})|\text{H}_2(\text{g}, p_R)|\text{Pt}(\text{s})$
 - $\text{Pt(s)}|\text{Cl}_2(\text{g})|\text{HCl}(\text{aq})||\text{HBr}(\text{aq})|\text{Br}_2(\text{l})|\text{Pt}(\text{s})$
 - $\text{Pt(s)}|\text{NAD}^+(\text{aq}), \text{H}^+(\text{aq}), \text{NADH}(\text{aq})||\text{oxaloacetate}^{2-}(\text{aq}), \text{H}^+(\text{aq}), \text{malate}^{2-}(\text{aq})|\text{Pt}(\text{s})$
 - $\text{Fe(s)}|\text{Fe}^{2+}(\text{aq})||\text{Mn}^{2+}(\text{aq}), \text{H}^+(\text{aq})|\text{MnO}_2(\text{s})|\text{Pt}(\text{s})$
- 5.26 Write the Nernst equations for the cells in the preceding exercise.
- 5.27 Devise cells to study the following biochemically important reactions. In each case state the value for ν to use in the Nernst equation.
- $\text{CH}_3\text{CH}_2\text{OH}(\text{aq}) + \text{NAD}^+(\text{aq}) \rightarrow \text{CH}_3\text{CHO}(\text{aq}) + \text{NADH}(\text{aq}) + \text{H}^+(\text{aq})$
 - $\text{ATP}^{4-}(\text{aq}) + \text{Mg}^{2+}(\text{aq}) \rightarrow \text{MgATP}^{2-}(\text{aq})$
 - $2 \text{Cyt-c}(\text{red}, \text{aq}) + \text{CH}_3\text{COCO}_2^-(\text{aq}) + 2 \text{H}^+(\text{aq}) \rightarrow 2 \text{Cyt-c}(\text{ox}, \text{aq}) + \text{CH}_3\text{CH}(\text{OH})\text{CO}_2^-(\text{aq})$
- 5.28 Use the standard potentials of the electrodes to calculate the standard potentials of the cells devised in *Exercise 5.27*.
- 5.29 The permanganate ion is a common oxidizing agent. What is the standard potential of the $\text{MnO}_4^-, \text{H}^+/\text{Mn}^{2+}$ couple at (a) $\text{pH} = 6.00$, (b) general pH ?
- 5.30 State what you would expect to happen to the cell potential when the following changes are made to the corresponding cells in *Exercise 5.25*. Confirm your prediction by using the Nernst equation in each case.
- The pressure of hydrogen in the left-hand compartment is increased.
 - The concentration of HCl is increased.
 - (d) Acid is added to both compartments.
- 5.31 State what you would expect to happen to the cell potential when the following changes are made to the corresponding cells devised in *Exercise 5.27*. Confirm your prediction by using the Nernst equation in each case.
- The pH of the solution is raised.
 - A solution of Epsom salts (magnesium sulfate) is added.
 - Sodium lactate is added to the solution.
- 5.32 (a) Calculate the standard potential of the cell $\text{Hg}(\text{l})|\text{HgCl}_2(\text{aq})||\text{TlNO}_3(\text{aq})|\text{Tl}(\text{s})$ at 25°C . (b) Calculate the cell potential when the molar concentration of the Hg^{2+} ion is 0.150 mol L^{-1} and that of the Tl^+ ion is 0.93 mol L^{-1} .
- 5.33 Calculate the biological standard Gibbs energies of reactions of the following reactions and half-reactions:
- $2 \text{NADH}(\text{aq}) + \text{O}_2(\text{g}) + 2 \text{H}^+(\text{aq}) \rightarrow 2 \text{NAD}^+(\text{aq}) + 2 \text{H}_2\text{O}(\text{l}) \quad E^\ominus = +1.14 \text{ V}$
 - $\text{Malate}^{2-}(\text{aq}) + \text{NAD}^+(\text{aq}) \rightarrow \text{oxaloacetate}^{2-}(\text{aq}) + \text{NADH}(\text{aq}) + \text{H}^+(\text{aq}) \quad E^\ominus = -0.154 \text{ V}$
 - $\text{O}_2(\text{g}) + 4 \text{H}^+(\text{aq}) + 4 \text{e}^- \rightarrow 2 \text{H}_2\text{O}(\text{l}) \quad E^\ominus = +0.81 \text{ V}$
- 5.34 The silver-silver chloride electrode, $\text{Ag}(\text{s})|\text{AgCl}(\text{s})|\text{Cl}^-(\text{aq})$, consists of metallic silver coated with a layer of silver chloride (which does not dissolve in water) in contact with a solution containing chloride ions. (a) Write the half-reaction for the silver-silver chloride half-electrode. (b) Estimate the emf of the cell
- $$\text{Ag}(\text{s})|\text{AgCl}(\text{s})|\text{KCl}(\text{aq}, 0.025 \text{ mol kg}^{-1})||\text{AgNO}_3(\text{aq}, 0.010 \text{ mol kg}^{-1})|\text{Ag}(\text{s})$$
- at 25°C .
- 5.35 (a) Calculate the standard emf of the cell $\text{Pt}(\text{s})|\text{cystine}(\text{aq}), \text{cysteine}(\text{aq})||\text{H}^+(\text{aq})|\text{O}_2(\text{g})|\text{Pt}(\text{s})$ and the standard Gibbs energy and enthalpy of the cell reaction at 25°C . (b) Estimate the value of $\Delta_r G^\ominus$ at 35°C . Use $E^\ominus = -0.34 \text{ V}$ for the cysteine/cystine couple.
- 5.36 The biological standard potential of the couple pyruvic acid/lactic acid is -0.19 V . What is the thermodynamic standard potential of the couple? Pyruvic acid is CH_3COCOOH and lactic acid is $\text{CH}_3\text{CH}(\text{OH})\text{COOH}$.
- 5.37 Calculate the biological standard values of the potentials (the two potentials and the cell potential) for the system in *Exercise 5.35* at 310 K .
- 5.38 (a) Does FADH_2 have a thermodynamic tendency to reduce coenzyme Q at $\text{pH} 7$? (b) Does oxidized cytochrome *b* have a thermodynamic tendency to oxidize reduced cytochrome *f* at $\text{pH} 7$?
- 5.39 Radicals, very reactive species containing one or more unpaired electrons, are among the

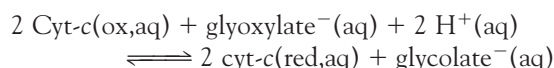
by-products of metabolism. Evidence is accumulating that radicals are involved in the mechanism of aging and in the development of a number of conditions, ranging from cardiovascular disease to cancer. *Antioxidants* are substances that reduce radicals readily. Which of the following known antioxidants is the most efficient (from a thermodynamic point of view): ascorbic acid (vitamin C), reduced glutathione, reduced lipoic acid, or reduced coenzyme Q?

- 5.40 The biological standard potential of the redox couple pyruvic acid/lactic acid is -0.19 V and that of the fumaric acid/succinic acid couple is $+0.03$ V at 298 K. What is the equilibrium constant for the reaction



at $\text{pH} = 7$?

- 5.41 Tabulated thermodynamic data can be used to predict the standard potential of a cell even if it cannot be measured directly. The presence of glyoxylate ion produced by the action of the enzyme glycolate oxidase on glycolate ion can be monitored by the following redox reaction:



The equilibrium constant for the reaction above is 2.14×10^{11} at $\text{pH} = 7.0$ and 298 K.

- (a) Calculate the biological standard potential of the corresponding galvanic cell and (b) the biological standard potential of the glyoxylate⁻/glycolate⁻ couple.

- 5.42 One ecologically important equilibrium is that between carbonate and hydrogencarbonate (bicarbonate) ions in natural water. (a) The standard Gibbs energies of formation of $\text{CO}_3^{2-}(\text{aq})$ and $\text{HCO}_3^-(\text{aq})$ are -527.81 kJ mol⁻¹ and -586.77 kJ mol⁻¹, respectively. What is the standard potential of the $\text{HCO}_3^-/\text{CO}_3^{2-}, \text{H}_2$ couple? (b) Calculate the standard potential of a cell in which the cell reaction is $\text{Na}_2\text{CO}_3(\text{aq}) + \text{H}_2\text{O}(\text{l}) \rightarrow \text{NaHCO}_3(\text{aq}) + \text{NaOH}(\text{aq})$. (c) Write the Nernst equation for the cell, and (d) predict and calculate the change in potential when the pH is

change to 7.0. (e) Calculate the value of pK_a for $\text{HCO}_3^-(\text{aq})$.

- 5.43 The dichromate ion in acidic solution is a common oxidizing agent for organic compounds. Derive an expression for the potential of an electrode for which the half-reaction is the reduction of $\text{Cr}_2\text{O}_7^{2-}$ ions to Cr^{3+} ions in acidic solution.
- 5.44 The emf of the cell $\text{Pt(s)}|\text{H}_2(\text{g})|\text{HCl}(\text{aq})|\text{AgCl(s)}|\text{Ag(s)}$ is 0.312 V at 25°C. What is the pH of the electrolyte solution?
- 5.45 If the mitochondrial electric potential between the matrix and the intermembrane space were 70 mV, as is common for other membranes, how much ATP could be synthesized from the transport of 4 mol H^+ , assuming the pH difference remains the same?
- 5.46 Under certain stress conditions, such as viral infection or hypoxia, plants have been shown to have an intercellular pH increase of about 0.1 pH. Suppose this pH change also occurs in the mitochondrial intermembrane space. How much ATP can now be synthesized for the transport of 2 mol H^+ assuming no other changes occur?
- 5.47 In anaerobic bacteria, the source of carbon may be a molecule other than glucose and the final electron acceptor some molecule other than O_2 . Could a bacterium evolve to use the ethanol/nitrate pair instead of the glucose/ O_2 pair as a source of metabolic energy?
- 5.48 The following reaction occurs in the cytochrome b_6f complex, a component of the electron transport chain of plant photosynthesis:



- (a) Calculate the biological standard Gibbs energy of this reaction. (b) The Gibbs energy for hydrolysis of ATP under conditions found in the chloroplast is -50 kJ mol⁻¹ and the synthesis of ATP by ATPase requires the transfer of four protons across the membrane. How many electrons must pass through the cytochrome b_6f complex to lead to the generation of a transmembrane proton gradient that is large enough to drive ATP synthesis in the chloroplast?

Project

5.49 The standard potentials of proteins are not commonly measured by the methods described in this chapter because proteins often lose their native structure and their function when they react on the surfaces of electrodes. In an alternative method, the oxidized protein is allowed to react with an appropriate electron donor in solution. The standard potential of the protein is then determined from the Nernst equation, the equilibrium concentrations of all species in solution, and the known standard potential of the electron donor. We shall illustrate this method with the protein cytochrome *c*.

(a) The one-electron reaction between cytochrome *c*, *cyt*, and 2,6-dichloroindophenol, *D*, can be written as



Consider E_{cyt}^{\ominus} and E_{D}^{\ominus} to be the standard potentials of cytochrome *c* and *D*, respectively. Show that, at equilibrium (eq), a plot of $\ln([\text{D}_{\text{ox}}]_{\text{eq}}/[\text{D}_{\text{red}}]_{\text{eq}})$ against $\ln([\text{cyt}_{\text{ox}}]_{\text{eq}}/[\text{cyt}_{\text{red}}]_{\text{eq}})$ is linear with a slope of 1 and *y*-intercept $F(E_{\text{cyt}}^{\ominus} - E_{\text{D}}^{\ominus})/RT$, where equilibrium activities are replaced by the numerical values of equilibrium molar concentrations.

(b) The following data were obtained for the reaction between oxidized cytochrome *c* and reduced *D* at pH = 6.5 buffer and 298 K. The ratios $[\text{D}_{\text{ox}}]_{\text{eq}}/[\text{D}_{\text{red}}]_{\text{eq}}$ and $[\text{cyt}_{\text{ox}}]_{\text{eq}}/[\text{cyt}_{\text{red}}]_{\text{eq}}$ were adjusted by adding known volumes of a solution of sodium ascorbate, a reducing agent, to a solution containing oxidized cytochrome *c* and reduced *D*. From the data and the standard potential of *D* of 0.237 V, determine the standard potential of cytochrome *c* at pH = 6.5 and 298 K.

$[\text{D}_{\text{ox}}]_{\text{eq}}/[\text{D}_{\text{red}}]_{\text{eq}}$	0.002 79	0.008 43	0.0257	0.0497	0.0748	0.238	0.534
$[\text{cyt}_{\text{ox}}]_{\text{eq}}/[\text{cyt}_{\text{red}}]_{\text{eq}}$	0.0106	0.0230	0.0894	0.197	0.335	0.809	1.39