

Electrochemical Potential and Free Energy 1.7

Learning Objectives

- Write Fick's First Law of Diffusion and explain how a concentration gradient makes a flux
- Describe how an external force such as electrostatic force can make a flux of charged solute
- Write the formula for the electrochemical potential
- Explain the formula for electrochemical potential in terms of the component driving forces
- Explain how the driving forces that produce a flux equal the negative gradient of the electrochemical potential
- Define the term **free energy**
- Describe the relationship between the free energy and the direction of any process
- Be able to calculate the free energy of ATP hydrolysis under specified conditions of temperature and concentrations of reactants ATP, ADP, and Pi
- Write the relationship between the standard free energy change and the equilibrium constant
- Know the approximate value for the free energy of ATP hydrolysis under cellular conditions

DIFFUSIVE AND ELECTRICAL FORCES CAN BE UNIFIED IN THE ELECTROCHEMICAL POTENTIAL

Let us recapitulate what we learned in Chapters 1.3 and 1.6 about the movement of charged particles in solution. First, the relationship between the flux and the concentration defines an average velocity, given as

$$[1.7.1] \quad J = vC$$

where J is the one-dimensional flux, v is the velocity, and C is the concentration. Second, the presence of a concentration gradient, in the absence of any other forces, produces a flux given by Fick's First Law of Diffusion:

$$[1.7.2] \quad J = -D \frac{\partial C}{\partial x}$$

where D is the diffusion coefficient. Here we drop the vector notation because the equation used here is one dimensional and the direction is assumed to be along the x -axis. If we use the gradient of C , instead of the

derivative, we retain the three-dimensional vector that describes diffusive flux in three dimensions.

Third, in the absence of a concentration gradient, any external force acting on solute particles causes them to be accelerated until they reach a terminal velocity. At this terminal velocity, the external force is balanced by the drag force on the particle by the solvent. This drag force is proportional to the velocity. Because of this, there is a relationship between the flux and the external force, given as

$$[1.7.3] \quad J = \frac{D}{kT} Cf$$

where f is the force acting on the solute particles, per particle. The concentration gradient has some of the appearances of a force in that it causes a flux. So does an externally applied force. What we seek to do is to combine diffusion and other forces into a single equivalent force. When both are operating, the flux is given as

$$[1.7.4] \quad J = -D \frac{\partial C}{\partial x} + \frac{D}{kT} Cf$$

If the force is an electrical force, its magnitude is given by

$$[1.7.5] \quad F = F_E = zeE$$

where z is the valence of the particle (\pm integer), e is the charge on the electron, and E is the electric field. Assuming one dimension, we drop the vector notation for force and insert Eqn [1.7.5] into Eqn [1.7.4] to give

$$[1.7.6] \quad J = -D \frac{\partial C}{\partial x} + \frac{D}{kT} CzeE$$

Thus we have these two equations:

$$[1.7.7] \quad J = \frac{D}{kT} Cf$$

$$J = -D \frac{\partial C}{\partial x} + \frac{D}{kT} CzeE$$

The top equation says that there is a flux produced by some unknown force. The bottom equation says that now we know what these forces are and we have parceled them out. Part of the flux is caused by diffusion and part of the flux is caused by an electrical force. What we desire is an expression for the total force in the top equation that will produce the flux in the bottom equation. To unite the diffusive force and

the electrical force, we solve these two equations for the unknown force, f , and find that

$$[1.7.8] \quad f = -\frac{kT}{C} \frac{\partial C}{\partial x} + zeE$$

The electric field, E , is the electric force per unit charge. This electric force is the negative gradient of its potential (see Chapter 1.3 for a definition of potential, gradients, and conservative forces). In a three-dimensional model, the electric field is a vector and the potential is a scalar. We will ignore these realities in this one-dimensional model because in one dimension the force and gradient have a single direction. Using Ψ as the symbol for electrical potential energy, we can rewrite Eqn [1.7.8] as

$$[1.7.9] \quad f = -\frac{kT}{C} \frac{\partial C}{\partial x} - ze \frac{\partial \Psi}{\partial x}$$

The units of Ψ are volts. The force in this equation is the force per particle. It is customary to convert this to the force per mole of particles by multiplying by Avogadro's number:

$$[1.7.10] \quad \begin{aligned} F = N_0 f &= -\frac{N_0 kT}{C} \frac{\partial C}{\partial x} - zN_0 e \frac{\partial \Psi}{\partial x} \\ F &= -\frac{RT}{C} \frac{\partial C}{\partial x} - z\mathfrak{F} \frac{\partial \Psi}{\partial x} \end{aligned}$$

where R is the gas constant ($=8.314 \text{ J mol}^{-1} \text{ K}^{-1}$) and \mathfrak{F} is the Faraday ($9.649 \times 10^4 \text{ C mol}^{-1} = 6.02 \times 10^{23} \text{ electrons mol}^{-1} \times 1.6 \times 10^{-19} \text{ C electron}^{-1}$). We define an **electrochemical potential** so that the overall force (produced by both diffusion and electrical forces, in this case) is the negative derivative of the electrochemical potential:

$$[1.7.11] \quad F = -\frac{\partial \mu}{\partial x}$$

Combining Eqns [1.7.10] and [1.7.11], we get

$$[1.7.12] \quad -\frac{\partial \mu}{\partial x} = -\frac{RT}{C} \frac{\partial C}{\partial x} - z\mathfrak{F} \frac{\partial \Psi}{\partial x}$$

Integrating, we obtain

$$[1.7.13] \quad \mu = \mu^0 + RT \ln C + z\mathfrak{F}\Psi$$

This is the **electrochemical potential**. We will use it to make calculations about membrane potential and the energetics involved in physiological processes. It is a potential in the same sense as the electrical potential. It has the units of energy per mole. The electrical potential, in volts, is equivalent to joules per coulomb, which can be converted to units of energy per mole. Similarly, the electrochemical potential can be converted into volts.

As can be seen from Eqn [1.7.13], the electrochemical potential has three components. The first component, μ^0 , has the sense of a constant of integration. It sets the zero of the electrochemical potential and its reference is a standard state. For solutions, μ^0 refers to the chemical potential of a hypothetical solution of unit molarity and no potential. That is, when $C = 1$ and $\Psi = 0$, $\mu = \mu^0$

by Eqn [1.7.13]. The second term, $RT \ln C$, refers to the work necessary to concentrate the solute, per mole; the third term, $z\mathfrak{F}\Psi$, is an electrical work term. It is the work necessary to bring one mole of particles from zero potential to Ψ . If other kinds of work are involved, we would need to expand Eqn [1.7.13] to include the other work terms.

In a typical physiological solution, several kinds of particles are dissolved. Since their concentrations are nearly independent of one another, they each have an identifiable electrochemical potential. Each solute within a local region, on the other hand, experiences the same electrical potential. Therefore, we can write an electrochemical potential for each material in the solution:

$$[1.7.14] \quad \mu_i = \mu_i^0 + RT \ln C_i + z_i \mathfrak{F}\Psi$$

THE OVERALL FORCE THAT DRIVES FLUX IS THE NEGATIVE GRADIENT OF THE ELECTROCHEMICAL POTENTIAL

The flux produced by a concentration difference and electric potential difference is given by

$$[1.7.3] \quad \mathbf{J} = \frac{D}{kT} \mathbf{C} \mathbf{f}$$

where \mathbf{J} and \mathbf{f} are both vectors. \mathbf{f} is the force per molecule. We convert to molar dimensions by multiplying and dividing by Avogadro's number:

$$[1.7.15] \quad \begin{aligned} \mathbf{J} &= \frac{D}{N_0 kT} \mathbf{C} N_0 \mathbf{f} \\ \mathbf{J} &= \frac{D}{RT} \mathbf{C} \mathbf{F} \end{aligned}$$

This emphasizes that \mathbf{J} is a vector in the same direction as \mathbf{F} , the force on the solute particles per mole. The force per mole is, in turn, given by the negative gradient of the electrochemical potential:

$$[1.7.16] \quad \mathbf{F} = -\nabla \mu = \left[\mathbf{i} \frac{\partial \mu}{\partial x} + \mathbf{j} \frac{\partial \mu}{\partial y} + \mathbf{k} \frac{\partial \mu}{\partial z} \right]$$

Inserting in μ from Eqn [1.7.13] and \mathbf{F} into Eqn [1.7.15], we get

$$[1.7.17] \quad \begin{aligned} \mathbf{J} &= \frac{D}{RT} \mathbf{C} \left[-\frac{RT}{C} \left(\mathbf{i} \frac{\partial C}{\partial x} + \mathbf{j} \frac{\partial C}{\partial y} + \mathbf{k} \frac{\partial C}{\partial z} \right) \right. \\ &\quad \left. - z\mathfrak{F} \left(\mathbf{i} \frac{\partial \Psi}{\partial x} + \mathbf{j} \frac{\partial \Psi}{\partial y} + \mathbf{k} \frac{\partial \Psi}{\partial z} \right) \right] \end{aligned}$$

which is simplified to

$$[1.7.18] \quad \mathbf{J} = -D \left[\nabla C + \frac{z\mathfrak{F}}{RT} C \nabla \Psi \right]$$

The one-dimensional version of this equation is

$$[1.7.19] \quad J = -D \frac{\partial C}{\partial x} - \frac{D}{RT} z\mathfrak{F} C \frac{\partial \Psi}{\partial x}$$

THE ELECTROCHEMICAL POTENTIAL IS THE GIBBS FREE ENERGY PER MOLE

Throughout the derivation of Fick's Laws of Diffusion, we made an unstated assumption that the pressure and temperature of the diffusing particles were constant. Under these conditions, we could derive the electrochemical potential. The constraints of constant temperature and pressure are useful when applied to problems in mammalian physiology, where these conditions are usually met. Under these conditions, it is useful to define a thermodynamic variable called the **Gibbs free energy**:

$$[1.7.20] \quad G = E + PV - TS$$

where E is the internal energy, P is the pressure, V is the volume, T is the temperature, and S is the **entropy**. The internal energy consists of all of the myriads of movements of the particles, including their internal motions. This is the part of the free energy where chemical bonding energy is stored. When compounds undergo chemical transformations, energy is either released or stored, depending on whether the reaction is exothermic or endothermic, respectively. The entropy has a specific thermodynamic definition which has been shown to be related to the number of ways that the particles can be arranged in the system which are consistent with the state of the system (its temperature, pressure, volume, and number of particles). This is related to the probability of finding the state for randomly arranged particles. Thus states with high probabilities have high entropy. Highly organized states, which can be accomplished in only a few ways, have a low probability and a low entropy. For example, a concentrated solution has only a few ways to crowd all the solute particles together compared to a dilute solution, so a concentrated solution has less entropy than a dilute solution.

As mentioned above, the Gibbs free energy is used to describe transformations that occur at constant temperature and under constant pressure. It is a **state variable**, meaning that it depends only on the state of the system and not on the path required to get there. Thus there is a defined difference in the free energy between an initial state and a final state:

$$[1.7.21] \quad \Delta G = G_{\text{final}} - G_{\text{initial}}$$

The energy involved in a chemical transformation can be harnessed to do useful work. For example, a reaction that gives off heat can be used to expand a gas to move a piston, producing work. The relationship between the free energy and the work that can be accomplished by a chemical transformation is

$$[1.7.22] \quad -\Delta G \geq W$$

where W is the work energy. That is the decrease in free energy in any transformation at constant T and P is equal to the maximum amount of work that can be performed by that transformation. It is for this reason that the function G is called the "free energy"; it is the energy which is available to perform work. The work that can be performed could be mechanical or electrical or chemical or concentration work.

Another variable determining the state of a system is its composition. Suppose that the system is composed of a number of substances, i, j, k, \dots of mole amounts n_i, n_j, n_k, \dots . If a small amount of substance i is added, then the system will experience a change in its free energy, G . The chemical potential is

$$[1.7.23] \quad \mu_i = \left(\frac{\partial G}{\partial n_i} \right)_{T, P, n_{j \neq i}}$$

Thus the chemical potential is the free energy per mole. The Gibbs free energy is an extensive variable that increases with the volume of the system or the number of moles of materials in the system. The chemical potential is an intensive variable, meaning that it depends on the state of the system and not its extent. However, usually ΔG values are calculated per mole so that G and μ are often used interchangeably. Equation [1.7.23] can be integrated to give

$$[1.7.24] \quad G = \sum_i \mu_i n_i$$

THE SIGN OF ΔG DETERMINES THE DIRECTION OF A REACTION

One of the conclusions of thermodynamics is that natural processes always occur in such a way that the free energy of the universe decreases. That is, in all natural processes, ΔG in Eqn [1.7.21] is negative. A corollary of this conclusion is the condition of equilibrium. Equilibrium occurs when no further change can occur. In this case, the free energy has reached a minimum, and the free energy change is zero with respect to this process. On the other hand, if ΔG is positive, then the reverse reaction will occur spontaneously:

$$\Delta G < 0 \Rightarrow \text{spontaneous reaction}$$

$$\Delta G = 0 \Rightarrow \text{reaction is at equilibrium}$$

$$\Delta G > 0 \Rightarrow \text{opposite reaction occurs spontaneously}$$

$$[1.7.25]$$

PROCESSES WITH $\Delta G > 0$ CAN PROCEED ONLY BY LINKING THEM WITH ANOTHER PROCESS WITH $\Delta G < 0$

As described earlier, a natural process can proceed only if $\Delta G < 0$ for that process. Many processes that occur in biological systems require energy, meaning that $\Delta G > 0$. These processes cannot proceed on their own. They can be made to proceed, however, by linking the process for which $\Delta G > 0$ with another process for which $\Delta G < 0$. The combined processes will proceed spontaneously only if the global ΔG for both of them is less than zero. We will consider these kinds of processes in detail when we consider active transport in Chapter 2.6. "Proceed spontaneously" here means that the linked processes will occur with no further input of energy outside the combined processes. It does not mean that the processes will occur rapidly or slowly. Thermodynamics tells us whether or not a process will occur, and with what energy changes, but it does not speak of the kinetics of the processes. In this sense, the term "thermodynamics"

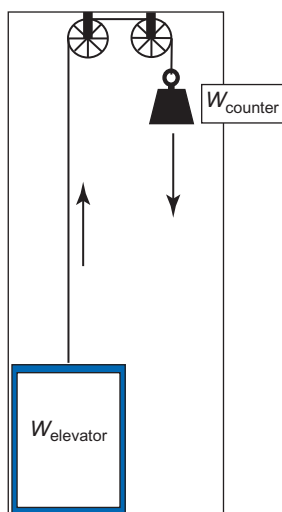


FIGURE 1.7.1 Coupling of a spontaneous process to a nonspontaneous process. An elevator sits on the ground floor. It will not rise spontaneously because the free energy for that process is positive: $\Delta G_{\text{elevator}} > 0$. A large counterweight at the top floor will fall spontaneously; the free energy change for this process is negative: $\Delta G_{\text{counter}} < 0$. The elevator can be raised if it is coupled to the larger negative free energy of the counterweight's fall: $\Delta G_{\text{elevator}} + \Delta G_{\text{counter}} < 0$. In this case, the elevator can be raised only once. Repetition of the process would require coupling to yet another process that provides the free energy to raise the counterweight back up again. In a real process, some of the free energy for the counterweight's fall would be dissipated. One can never recover 100% of the energy as useful work.

is something of a misnomer, as really it is about the statics of energy transformation.

An example of coupling is lifting a weight against gravity by using another weight, as shown in Figure 1.7.1.

The coupling of biological process can be visualized using the energy diagrams for chemical reactions such as those shown in Chapter 1.5. Reactions that involve a decrease in free energy ($G_{\text{final}} - G_{\text{initial}} < 0$ and thus $G_{\text{final}} < G_{\text{initial}}$) are called **exergonic** reactions, and they proceed spontaneously. A schematic example of an exergonic reaction is shown in Figure 1.7.2A. Reactions that involve an increase in free energy ($G_{\text{final}} - G_{\text{initial}} > 0$ and thus $G_{\text{final}} > G_{\text{initial}}$) are called **endergonic** reactions, and they do not proceed spontaneously (see Figure 1.7.2B). If an exergonic reaction can be coupled to an endergonic reaction, and the sum of the ΔG for the two reactions is less than zero, then the combined processes will both proceed spontaneously (see Figure 1.7.2C).

THE LARGE NEGATIVE FREE ENERGY OF ATP HYDROLYSIS POWERS MANY BIOLOGICAL PROCESSES

ATP is adenosine triphosphate and its structure is shown in Figure 1.7.3. It occupies a special position in the cellular flow of energy because of the energy stored in its terminal phosphate bond. It takes a lot of energy to add a phosphate to ADP to form ATP, and that chemical energy becomes available to do work when the bond is split. The cell uses ATP as its energy

currency. Energy derived from the oxidation of food-stuffs is stored in this terminal phosphate bond, and it is used in myriad reactions involving synthesis of materials, transport of materials, and the performance of mechanical work. The hydrolysis reaction of ATP to ADP and Pi is shown in Figure 1.7.3.

The free energy change for the ATP hydrolysis reaction is given by a combination of Eqns [1.7.21] and [1.7.24]:

$$\begin{aligned}\Delta G &= G_{\text{final}} - G_{\text{initial}} \\ &= n_{\text{final ATP}} \mu_{\text{ATP}} + n_{\text{final ADP}} \mu_{\text{ADP}} + n_{\text{final Pi}} \mu_{\text{Pi}} \\ &= -n_{\text{initial ATP}} \mu_{\text{ATP}} - n_{\text{initial ADP}} \mu_{\text{ADP}} - n_{\text{initial Pi}} \mu_{\text{Pi}} \\ &= \Delta n_{\text{ATP}} \mu_{\text{ATP}} + \Delta n_{\text{ADP}} \mu_{\text{ADP}} + \Delta n_{\text{Pi}} \mu_{\text{Pi}} \\ &= \Delta n_{\text{rxn}} \mu_{\text{ADP}} + \Delta n_{\text{rxn}} \mu_{\text{Pi}} - \Delta n_{\text{rxn}} \mu_{\text{ATP}}\end{aligned}$$

[1.7.26]

where the subscripts denote the chemical species, μ is the chemical potential, and Δn is the number of moles of each material that participates in the reaction. The last line in Eqn [1.7.26] relates the change in the number of moles of participating reactants to the number of completed reactions. This is just the stoichiometry of the reaction. We may write it as follows:

$$\begin{aligned}[1.7.27] \quad &1 \text{ ATP} = 1 \text{ ADP} + 1 \text{ Pi} \\ &- 1 \text{ ATP} + 1 \text{ ADP} + 1 \text{ Pi} = 0\end{aligned}$$

The coefficients here are the stoichiometry. Here they indicate that, for every completed reaction, the number of molecules of ATP decreases by one and the number of molecules of ADP and Pi increases by one. Thus the last line in Eqn [1.7.26] relates the change in free energy upon completion of a Δn number of reactions.

This number can be specified in moles because, as described in Chapter 1.5, using moles is just another way of counting a large number of things.

We divide the last line of Eqn [1.7.26] by the number of completed reactions to obtain

$$[1.7.28] \quad \frac{\Delta G}{\Delta n_{\text{rxn}}} = \mu_{\text{ADP}} + \mu_{\text{Pi}} - \mu_{\text{ATP}}$$

Substituting in for the chemical potentials, we get

$$[1.7.29a] \quad \frac{\Delta G}{\Delta n} = \mu_{\text{ADP}}^0 + RT \ln[\text{ADP}] + \mu_{\text{Pi}}^0 + RT \ln[\text{Pi}] - \mu_{\text{ATP}}^0 - RT \ln[\text{ATP}]$$

$$[1.7.29b] \quad \frac{\Delta G}{\Delta n} = \Delta \mu^0 + RT \ln \left(\frac{[\text{ADP}][\text{Pi}]}{[\text{ATP}]} \right)$$

If we will let $\Delta n = 1.0$ to indicate that we are speaking of the free energy change for Avogadro's number of completed reactions, then we have

$$[1.7.30] \quad \Delta G = \Delta G^0 + RT \ln \left(\frac{[\text{ADP}][\text{Pi}]}{[\text{ATP}]} \right)$$

where ΔG^0 is the **standard free energy change**. It refers to the **free energy change per mole** under standard

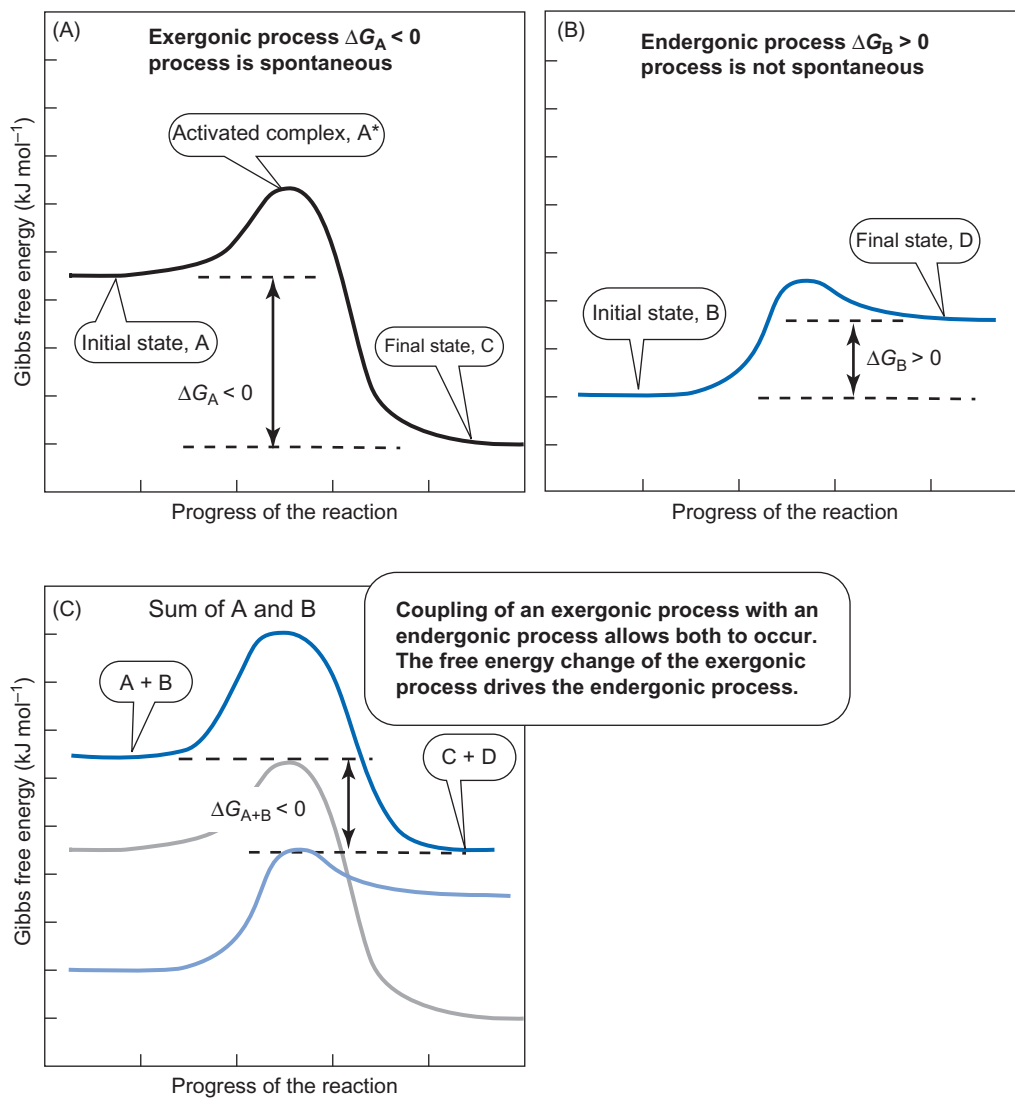


FIGURE 1.7.2 Coupling of an endergonic reaction with an exergonic reaction. Exergonic reactions are those for which $\Delta G_A = G_{\text{final}} - G_{\text{initial}} < 0$, and so these reactions proceed spontaneously (panel A). Endergonic reactions are those for which $\Delta G_B = G_{\text{final}} - G_{\text{initial}} > 0$, and these reactions do not proceed spontaneously (panel B). However, an endergonic reaction can be made to proceed if it can obtain a decrease in free energy by linking it to the exergonic reaction. In essence, a coupled reaction involves a completion of both the exergonic and endergonic reactions. If the combined $\Delta G_{A+B} = \Delta G_A + \Delta G_B < 0$, then the combined reaction will occur spontaneously (panel C).

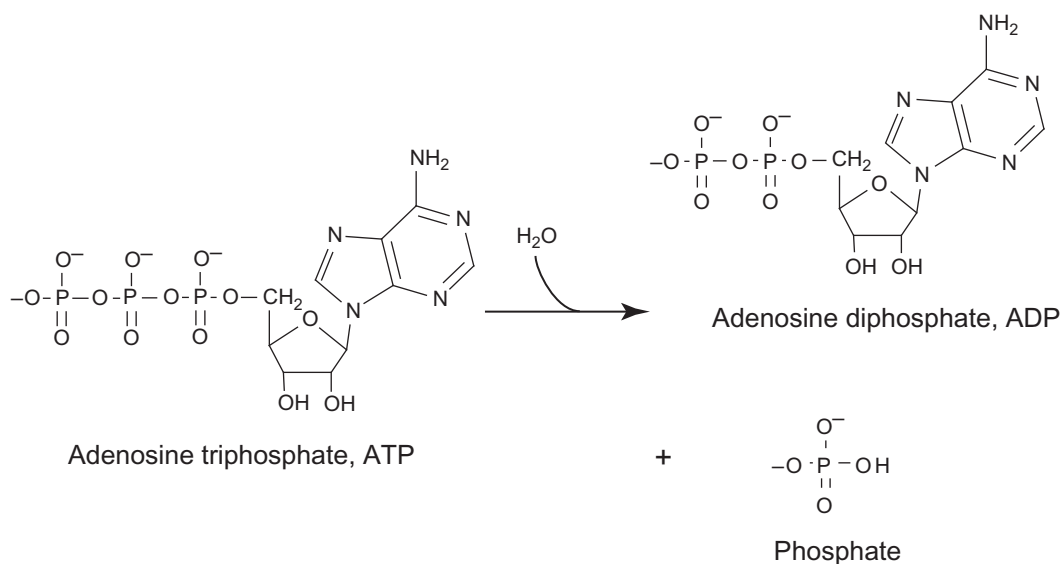


FIGURE 1.7.3 ATP and its hydrolysis to ADP and P_i . Chemical energy is stored in each of the phosphate bonds of ATP. The last one, the γ -phosphate, is typically used to power mechanical, electrical, and chemical energy needs of the cell.

EXAMPLE 1.7.1 Free Energy of ATP Hydrolysis Under “Typical” Cell Conditions

“Typical” values for the concentrations of ATP, ADP, and Pi are about 5 mM for ATP, 5 mM for Pi, and 40 μ M for ADP. Calculate the free energy of ATP hydrolysis under these conditions.

Here we use Eqn [1.7.33]. The value of ΔG^0 is given in the text as $-7.4 \text{ kcal mol}^{-1}$ or $-30.9 \text{ kJ mol}^{-1}$. The value of R we use is $8.314 \text{ J mol}^{-1} \text{ K}^{-1}$ and $T = 37^\circ\text{C} = 310 \text{ K}$. **In the calculation, all concentrations must be expressed in M.** We insert these values and calculate:

$$\Delta G = -31.0 \text{ kJ mol}^{-1} + 8.314 \text{ J mol}^{-1} \text{ K}^{-1} \times 310 \text{ K} \\ \times \ln[40 \times 10^{-6} \text{ M} \times 5 \times 10^{-3} \text{ M} / 5 \times 10^{-3} \text{ M}]$$

$$= -31.0 \text{ kJ mol}^{-1} + 2.58 \text{ kJ mol}^{-1} \times (-10.12) \\ = -57.1 \text{ kJ mol}^{-1} = -13.6 \text{ kcal mol}^{-1}$$

This free energy of ATP hydrolysis under cell conditions is the energy available for the various kinds of work undertaken by the cell, including chemical work (synthesis), mechanical work (movement and transport), and electrical work. In the final analysis, nearly all of the work produced by the cells is eventually degraded and appears as heat.

conditions of 25°C , 1 atmosphere pressure and unit concentration. Note that we have said all along that ΔG is an extensive variable, and now it seems that we have transformed it into an intensive variable. Tabulated values of ΔG^0 necessarily report it in units of energy per mole, so these values are actually values of $\Delta \mu^0$.

You can see that if all species were at unit concentration, the second term on the right-hand side of Eqn [1.7.25] would be zero. Under these conditions, $\Delta G = \Delta G^0$. Experimental determination of ΔG^0 takes advantage of the fact that at equilibrium $\Delta G = 0$ (see Eqn [1.7.25]) and the fact that the second term in Eqn [1.7.30] incorporates the equilibrium constant for the reaction:

$$[1.7.31] \quad K_{\text{eq}} = \left(\frac{[\text{ADP}][\text{Pi}]}{[\text{ATP}]} \right)$$

So that at equilibrium ($\Delta G = 0$), Eqn [1.7.30] becomes

$$[1.7.32] \quad \Delta G^0 = -RT \ln K_{\text{eq}}$$

MEASUREMENT OF THE EQUILIBRIUM CONCENTRATIONS OF ADP, ATP, AND PI ALLOWS US TO CALCULATE ΔG^0

It turns out that the free energy of ATP hydrolysis is a bit more complicated than we have let on here. The chemical species produced have different ionizations at different pH values, and ATP and ADP both bind Mg^{2+} ions. The energy of binding of H^+ and Mg^{2+} ions should be incorporated into the reaction. In addition, we are interested in the hydrolysis of ATP under physiological conditions of 37°C . The free energy of ATP hydrolysis has been determined for these different conditions. Since the details of these conditions differ from cell to cell, no one value can be used. However, a “typical” value is given a special symbol, ΔG^0 , and signifies the free energy of ATP hydrolysis under the “typical” cell conditions. **Its value is about $-7.4 \text{ kcal mol}^{-1}$ or $-31.0 \text{ kJ mol}^{-1}$.**

The units of ΔG are those of RT . Values of R usually used here are $1.987 \text{ cal mol}^{-1} \text{ K}^{-1} = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}$.

The conversion between joule and calorie is $1 \text{ J} = 0.239 \text{ cal}$.

Under cellular conditions, [ATP], [ADP], and [Pi] are not at their equilibrium values, nor are they unit concentrations. The free energy under these conditions is given by

$$[1.7.33] \quad \Delta G = \Delta G^0 + RT \ln \left(\frac{[\text{ADP}][\text{Pi}]}{[\text{ATP}]} \right)$$

It is important to realize that the argument of the logarithm ($[\text{ADP}][\text{Pi}]/[\text{ATP}]$) is generally not equal to the equilibrium constant, but only when the reaction is at equilibrium.

SUMMARY

A difference of concentration produces a flow of material in solution. Application of an electric force to charged particles also produces a flow of material in solution. These two forces can be united in the definition of a single force that is proportional to the negative gradient of a potential. This potential is the electrochemical potential written as

$$\mu = \mu^0 + RT \ln C + z\mathfrak{I}\Psi$$

This electrochemical potential is the Gibbs free energy per mole. The Gibbs free energy, G , is an extensive variable, whereas μ is an intensive variable. G is also a state variable, depending only on the state of a system and not on the path it took to reach that state. The free energy is the maximum energy that can be extracted to do useful work. For all spontaneous reactions, the change in free energy, $\Delta G = G_{\text{final}} - G_{\text{initial}}$, is negative. Processes that require work occur spontaneously only if they are linked to other processes that lose free energy, so that for the overall process $\Delta G < 0$. For any process at equilibrium, $\Delta G = 0$.

Many cellular processes require energy for the synthesis of materials, transport, or mechanical or electrical work. These occur because energy is supplied by the hydrolysis of ATP. ATP hydrolysis to ADP and Pi has a large

negative ΔG under cellular conditions. The free energy of ATP hydrolysis per mole is given as

$$\Delta G_{\text{ATP hydrolysis}} = \Delta G^{\circ'} + RT \ln \left(\frac{[\text{ADP}][\text{Pi}]}{[\text{ATP}]} \right)$$

Under "typical" cellular conditions, $\Delta G_{\text{ATP hydrolysis}} = -13.6 \text{ kcal mol}^{-1} = -57.1 \text{ kJ mol}^{-1}$.

REVIEW QUESTIONS

1. In the formula for the electrochemical potential, what is R ? What is T ? What are the units of $RT \ln C$? What units must C be in? What is z ? What is the Faraday? What is Ψ ?
2. What is the Gibbs free energy?
3. What is the relationship between the electrochemical potential and the Gibbs free energy?
4. How does the sign of ΔG determine the direction of a process?
5. Describe thermodynamic coupling.
6. What is the relationship between the free energy change and the equilibrium constant?
7. How would you determine the free energy change for ATP hydrolysis under cellular conditions?
8. What is the approximate free energy change of ATP hydrolysis in cells?