

BASIC PRINCIPLES OF BIOENERGETICS

A living cell undergoes several metabolic activity and to maintain such a high level of activity, a cell must acquire and expend energy. The study of the various types of energy transformations that occur in living organisms is referred to as **bioenergetics**. **Energy** is defined as the capacity to do work, that is, the capacity to change or move something.

The First Law of Thermodynamics

The first law of thermodynamics is the law of conservation of energy. It states that energy can neither be created nor destroyed. Energy can, however, be converted (*transduced*) from one form to another. Such as The **transduction** of electric energy to mechanical energy; chemical energy to thermal energy etc. ATP, is converted to mechanical energy when organelles are moved from place to place in a cell. the first law of thermodynamics indicates that the loss or gain must be balanced by a corresponding gain or loss in the surroundings, so that the amount in the universe as a whole remains constant.

The energy of the system is termed the *internal energy* (E), and its change during a transformation is δE (delta E). One way to describe the first law of thermodynamics is that $\delta E = Q - W$, where Q is the heat energy and W is the work energy.

Depending on the process, the internal energy of the system at the end can be greater than, equal to, or less than its internal energy at the start, depending on its relationship to its surroundings. In other words, dE can be positive, zero, or negative. Consider a system to be the contents of a reaction vessel. As the change in pressure or volume remains contents, there is no work being done by the system on its surroundings, or vice versa. In that case, the internal energy at the end of the transformation will be greater than that at the beginning if heat is absorbed and less if heat is released. Reactions that lose heat are termed **exothermic**, and ones that gain heat are **endothermic**, and if E remains same at the start and at the end of the reaction the system called **isothermic**.

The Second Law of Thermodynamics: it expresses that energy flow from a state of higher energy to a state of lower energy or heat flows from a warmer to a cooler body, not the reverse. Such events are said to be **spontaneous**, a term that indicates they are thermodynamically favorable and can occur *without the input of external energy*. however the reverse could not be possible without the input of external energy. It is impossible for a machine to be 100 percent efficient. Some of the energy is inevitably lost as the machine carries out its activity. Because a few amount of energy are dissipated in the surrounding as waste. The loss of available energy during a reaction/process is a result of a tendency for the randomness, or disorder, of the universe to increase every time there is a transfer of energy. This gain in disorder is measured by the term **entropy**, and the loss of available energy is equal to $T\delta S$, where δS is the change in entropy between the initial and final states. Entropy is associated with the *random* movements of particles of matter, which, because they are random, cannot be made to accomplish a *directed* work process. According to the second law of thermodynamics, every event is accompanied by an increase in the entropy of the universe.

When a sugar cube is dropped into a cup of hot water, for example, there is a spontaneous shift of the molecules from an ordered state in the crystal to a much more disordered condition when the sugar molecules are spread throughout the solution. As the molecules of the sugar cube dissolve into solution, their freedom of movement increases, as does the entropy of the system. The change from a concentrated to a dispersed state results from the random movements of the molecules. The sugar molecules eventually spread themselves equally through the available volume because the state of uniform distribution is the most probable state. The release of heat, for example, from the oxidation of glucose within a cell or from the friction generated as blood flows through a vessel, is another example of an increase in entropy. The release of thermal energy by living organisms increases the rate of random movements of atoms and molecules; it cannot be redirected to accomplish additional work. Since the energy of molecular and atomic movements increases with temperature, so too does

the entropy. It is only at absolute zero (0 K), when all movements cease, that the entropy is zero. As with other spontaneous events, we must distinguish between the system and its surroundings. The second law of thermodynamics indicates only that the total entropy in the universe must increase; the disorder within one part of the universe (the system) can decrease at the greater expense of its surroundings. The dissolved sugar in can decrease in entropy; it can be recrystallized by evaporating off the water. The consequence of this process, however, is an even greater increase in the entropy of the surroundings. The increased freedom of movement of the water molecules in the gaseous phase more than balances the decrease in freedom of the molecules of the sugar crystals. Life operates on a similar principle. Living organisms are able to decrease their own entropy by increasing the entropy of their environment. Entropy is decreased in an organism when relatively simple molecules, such as amino acids, are ordered into more complex molecules, such as the protein myoglobin in a muscle cell. For this to occur, however, the entropy of the environment must increase, which is accomplished as complex, ordered molecules such as glycogen stored in liver or muscle tissue are converted into heat and smaller, less ordered compounds (such as CO₂ and H₂O) are released to the environment. It is this feature of metabolism that allows living organisms to maintain such a highly ordered and improbable state—at least for a while. Another measure of the energy state of a living organism is provided by the information content of its macromolecules. Information is a subject that is difficult to define but easy to recognize. Information can be measured in terms of the ordered arrangement of a structure's subunits. For example, proteins and nucleic acids, in which the specific linear sequence of the subunits is highly ordered, are low in entropy and high in information content. Maintaining a state of high information content (low entropy) requires the input of energy. Consider just one molecule of DNA located in one cell in your liver. That cell has dozens of different proteins whose sole job is to patrol the DNA, looking for damage and repairing it. Nucleotide damage in an active cell can be so great that, without this expenditure of energy, the information content of DNA would rapidly deteriorate.

Free Energy

Together, the first and second laws of thermodynamics indicate that the energy of the universe is constant, but the entropy continues to increase toward a maximum. The concepts inherent in the first two laws were combined into the expression $\delta H = \delta G + T\delta S$, where δG (delta G) is the change in free energy, that is, the change during a process in the energy available to do work; δH is the change in *enthalpy* or total energy content of the system (equivalent to δE for our purposes), T is the absolute temperature (K = °C + 273), and δS is the change in the entropy of the system. The equation states that the total energy change is equal to the sum of the changes in useful energy (δG) and energy that is unavailable to do further work ($T\delta S$). When rearranged and written as $\delta G = \delta H - T\delta S$, the above equation provides a measure of the spontaneity of a particular process. It allows one to predict the direction in which a process will proceed and the extent to which that process will occur. All *spontaneous* energy transformations must have a negative δG ; that is, the process must proceed toward a state of lower free energy. The magnitude of δG indicates the maximum amount of energy that can be passed on for use in another process but tells us nothing about how rapidly the process will occur.

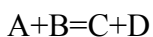
Processes that can occur spontaneously, is, processes that are thermodynamically favored (have a δG), are described as **exergonic**.

In contrast, if the δG for a given process is positive, then it cannot occur spontaneously. Such processes are thermodynamically unfavorable and are described as **endergonic**.

As we will see, reactions that are normally endergonic can be made to occur by coupling them to energy-releasing processes. The signs of δH and δS for a given transformation can be positive or negative, depending on the relation between the system and its surroundings. (Hence, δH will be positive if heat is gained by the system and negative if heat is lost; δS will be positive if the system becomes more disordered and negative if it becomes more ordered.) The counterplay between δH and δS is illustrated by the ice–water transformation. The conversion of water from the liquid to the solid state is accompanied by a decrease in entropy (δS is negative) and a decrease in enthalpy (δH is negative). In order for this transformation to occur (i.e., for δG to be negative), δH must be more negative than $T\delta S$, a condition that occurs only below 0°C. at 0°C,

10°C and -10°C of ice water conversion. In all cases, regardless of the temperature, the energy level of the ice is less than that of the liquid (the δH is negative). However, at the higher temperature, the entropy term of the equation ($T\delta S$) is more negative than the enthalpy term; therefore, the free energy change is positive, and the process cannot occur spontaneously. At 0°C, the system is in equilibrium; at -10°C, the solidification process is favored, that is, the δG is negative.

Free-Energy Changes in Chemical Reactions Now that we have discussed the concept of free energy in general terms, we can apply the information to chemical reactions within the cell. All chemical reactions within the cell are reversible, and therefore we must consider two reactions occurring simultaneously, one forward and the other in reverse. **According to the law of mass action, the rate of a reaction is proportional to the concentration of the reactants. The rate of the forward reaction is directly proportional to the product of the molar concentrations of A and B. The rate of the forward reaction can be expressed as $k_1[A][B]$, where k_1 is a rate constant for the forward reaction.** The rate of the backward reaction equals $k_2[C][D]$. All chemical reactions proceed, however slowly, toward a state of equilibrium, that is, toward a point at which the rates of the forward and backward reactions are equal. At equilibrium, the same number of A and B molecules are converted into C and D molecules per unit time as are formed from them. At equilibrium, therefore, which can be rearranged to In other words, at equilibrium there is a predictable ratio of the concentration of products to the concentration of reactants. This ratio, which is equal to k_1/k_2 , is termed the **equilibrium constant, K_{eq}** . The equilibrium constant allows one to predict the direction (forward or reverse) in which the reaction is favored under a given set of conditions. Suppose, for example, that we are studying the above reaction, and we have just mixed the four components (A, B, C, D) so that each is present at an initial concentration of 0.5 M. The direction in which this reaction will proceed depends on the equilibrium constant. **If the K_{eq} is greater than 1, the reaction will proceed at a greater rate toward the formation of the products C and D than in the reverse direction. For example, if the K_{eq} happens to be 9.0, then the concentration of the reactants and products at equilibrium in this particular reaction mixture will be 0.25 M and 0.75 M, respectively. If, on the other hand, the K_{eq} is less than 1, the reverse reaction will proceed at a greater rate than the forward reaction, so that the concentration of A and B will rise at the expense of C and D.** It follows from these points that the net direction in which the reaction is proceeding at any moment depends on the relative concentrations of all participating molecules and can be predicted from the K_{eq} .



$$K_1 [A][B]=K_2[C][D]$$

$$K_1/K_2=[C][D]/[A][B]$$

$$[C][D]/[A][B]=[0.5][0.5]/[0.5][0.5]=1$$

$$[C][D]/[A][B]=[0.75][0.75]/[0.25][0.25]=9$$

The ratio of reactants to products present at equilibrium is determined by the relative free-energy levels of the reactants and products. As long as the total free energy of the reactants is greater than the total free energy of the products, then δG has a negative value and the reaction proceeds in the direction of formation of products. The greater the δG , the farther the reaction is from equilibrium and the more work that can be performed by the system. As the reaction proceeds, the difference in free energy content between the reactants and products decreases (δG becomes less negative), until at equilibrium the difference is zero ($\delta G = 0$) and no further work can be obtained. The **standard free-energy change (δG°)** describes the free energy released when reactants are converted to products under these standard conditions. It must be kept in mind that standard conditions do not prevail in the cell, and therefore one must be cautious in the use of values for standard free-energy differences in calculations of cellular energetics.

The relationship between the equilibrium constant and standard free-energy change is given by the equation:

VKM

$$\Delta G^{\circ'} = -RT \ln K'_{\text{eq}}$$

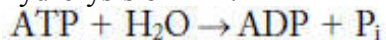
When the natural log (ln) is converted to log₁₀, the equation becomes

$$\Delta G^{\circ'} = -2.303RT \log K'_{\text{eq}}$$

where R is the gas constant (1.987 cal/mol K) and T is the absolute temperature (298 K).³ Recall that the log of 1.0 is zero. Consequently, it follows from the above equation that reactions having equilibrium constants greater than 1.0 have negative δG° values, which indicates that they can occur spontaneously under *standard conditions*. Reactions having equilibrium constants of less than 1 have positive δG° values and cannot occur spontaneously under standard conditions.

In other words, given the reaction written as follows: $A+B = C + D$, if the δG is negative, the reaction will go to the right when reactants and products are all present at 1.0 M concentration at pH 7. The greater the negative value, the farther to the right the reaction will proceed before equilibrium is reached. Under the same conditions, if the δG° is positive, the reaction will proceed to the left; that is, the reverse reaction is favored.

Free-Energy Changes in Metabolic Reactions One of the most important chemical reactions in the cell is the hydrolysis of ATP.



In the reaction, the standard free-energy difference between the products and reactants is --7.3 kcal/mol. Based on this information, it is evident that the hydrolysis of ATP is a highly favorable (exergonic) reaction, that is, one that tends toward a large $[\text{ADP}]/[\text{ATP}]$ ratio at equilibrium. Because the electrostatic repulsion created by four closely spaced negative charges on ATP^{4-} is partially relieved by formation of ADP^{3-} it is important that the difference between δG and δG° be kept clearly in mind. The δG° is a fixed value for a given reaction and indicates the direction in which that reaction would proceed were the system at standard conditions. Since standard conditions do not prevail within a cell, δG° values cannot be used to predict the direction in which a particular reaction is proceeding at a given moment within a particular cellular compartment. To do this, one must know the δG , which is determined by the concentrations of the reactants and products that are present at the time. At 25°C

$$\Delta G = \Delta G^{\circ'} + 2.303RT \log \frac{[\text{C}][\text{D}]}{[\text{A}][\text{B}]}$$

$$\Delta G = \Delta G^{\circ'} + 2.303(1.987 \text{ cal/mol} \cdot \text{K})(298 \text{ K})$$

$$\log \frac{[\text{C}][\text{D}]}{[\text{A}][\text{B}]}$$

$$\Delta G = \Delta G^{\circ'} + (1.4 \text{ kcal/mol}) \log \frac{[\text{C}][\text{D}]}{[\text{A}][\text{B}]}$$

where $[\text{A}]$, $[\text{B}]$, $[\text{C}]$, and $[\text{D}]$ are the actual concentrations at the time. Calculation of the δG reveals the direction in which the reaction in the cell is proceeding and how close the particular reaction in question is to

equilibrium. For example, typical cellular concentrations of the reactants and products in the reaction for ATP hydrolysis might be $[ATP]=10\text{ mM}$; $[ADP]=1\text{ mM}$; $[P_i]=10\text{ mM}$. Substituting these values into the equation,

$$\Delta G = \Delta G^{\circ'} + 2.303RT \log \frac{[ADP][P_i]}{[ATP]}$$

$$\Delta G = -7.3\text{ kcal/mol} + (1.4\text{ kcal/mol}) \log \frac{[10^{-3}][10^{-2}]}{[10^{-2}]}$$

$$\Delta G = -7.3\text{ kcal/mol} + (1.4\text{ kcal/mol})(-3)$$

$$\Delta G = -11.5\text{ kcal/mol (or } -46.2\text{ kJ/mol)}$$

Thus, even though the δG^0 for the hydrolysis of ATP is -7.3 kcal/mol , the typical δG in the cell for this reaction is about -12 kcal/mol because a cell maintains a high $[ATP]/[ADP]$ ratio.

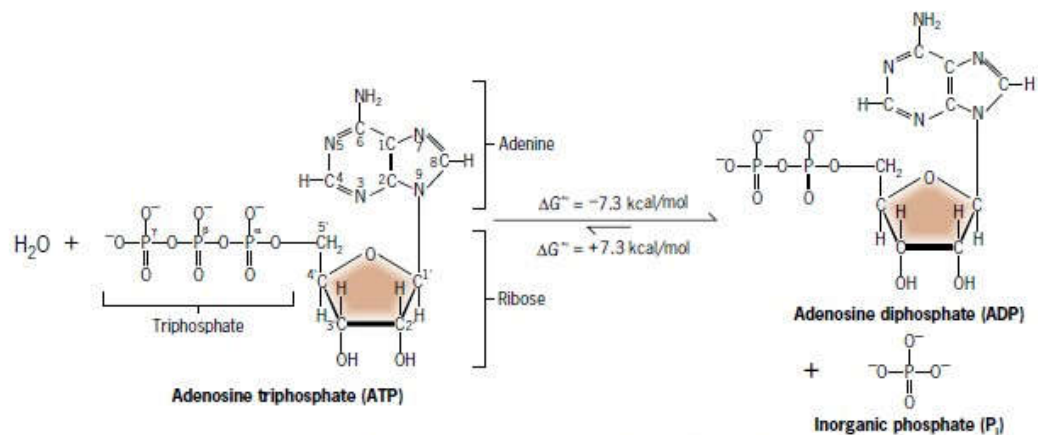


Figure 3.5 ATP hydrolysis. Adenosine triphosphate (ATP) is hydrolyzed as part of many biochemical processes. In most reactions, as shown here, ATP is hydrolyzed to ADP and inorganic phosphate (P_i), but in some cases (not shown) it is hydrolyzed to AMP, a compound

with only one phosphate group, and pyrophosphate (PP_i). Both of these reactions have essentially the same $\Delta G^{\circ'}$ of -7.3 kcal/mol (-30.5 kJ/mol).

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