

# **Bioenergetics**

# **I. OVERVIEW**

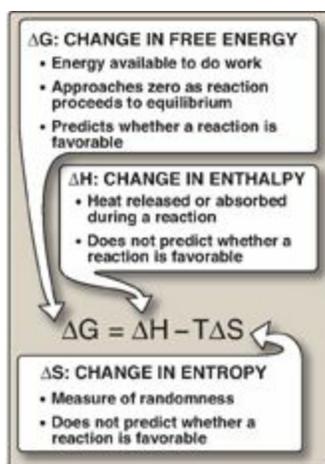
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Bioenergetics describes the transfer and utilization of energy in biologic systems. It makes use of a few basic ideas from the field of thermodynamics, particularly the concept of free energy. Changes in free energy provide a measure of the energetic feasibility of a chemical reaction and can, therefore, allow prediction of whether a reaction or process can take place. Bioenergetics concerns only the initial and final energy states of reaction components, not the mechanism or how much time is needed for the chemical change to take place (the rate). In short, bioenergetics predicts if a process is possible, whereas kinetics measures how fast the reaction occurs (see p. 54).

## II. FREE ENERGY

The direction and extent to which a chemical reaction proceeds is determined by the degree to which two factors change during the reaction. These are enthalpy ( $\Delta H$ , a measure of the change in heat content of the reactants and products) and entropy ( $\Delta S$ , a measure of the change in randomness or disorder of reactants and products; [Figure 6.1](#)). Neither of these thermodynamic quantities by itself is sufficient to determine whether a chemical reaction will proceed spontaneously in the direction it is written. However, when combined mathematically (see [Figure 6.1](#)), enthalpy and entropy can be used to define a third quantity, free energy ( $G$ ), which predicts the direction in which a reaction will spontaneously proceed.

**Figure 6.1** Relationship between changes in free energy ( $G$ ), enthalpy ( $H$ ), and entropy ( $S$ ).  $T$  is the absolute temperature in Kelvin ( $K$ ):  $K = ^\circ C + 273$ .



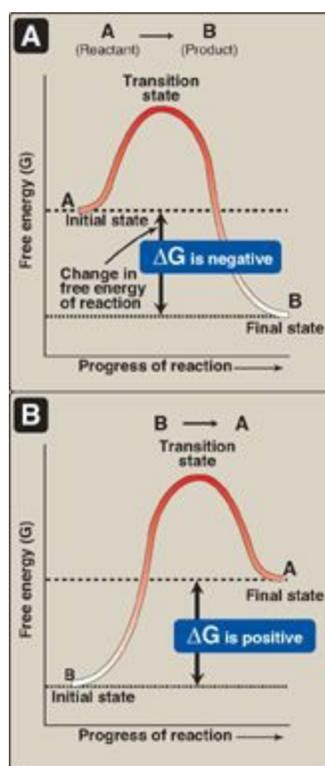
### III. FREE ENERGY CHANGE

The change in free energy is represented in two ways,  $\Delta G$  and  $\Delta G^\circ$ . The first,  $\Delta G$  (without the superscript "o"), represents the change in free energy and, thus, the direction of a reaction at any specified concentration of products and reactants.  $\Delta G$ , then, is a variable. This contrasts with the standard free energy change,  $\Delta G^\circ$  (with the superscript "o"), which is the energy change when reactants and products are at a concentration of 1 mol/l. [Note: The concentration of protons is assumed to be  $10^{-7}$  mol/l (that is, pH = 7). This may be shown by a prime sign (I), for example,  $\Delta G^{\circ I}$ .] Although  $\Delta G^\circ$ , a constant, represents energy changes at these nonphysiologic concentrations of reactants and products, it is nonetheless useful in comparing the energy changes of different reactions. Furthermore,  $\Delta G^\circ$  can readily be determined from measurement of the equilibrium constant (see p. 72). This section outlines the uses of  $\Delta G$ , and  $\Delta G^\circ$  is described on p. 71.

#### A. Sign of $\Delta G$ and the direction of a reaction

$\Delta G$  can be used to predict the direction of a reaction at constant temperature and pressure. Consider the reaction:

**Figure 6.2** Change in free energy ( $\Delta G$ ) during a reaction. **A** The product has a lower free energy (G) than the reactant. **B** The product has a higher free energy than the reactant.



**1. Negative  $\Delta G$ :** If  $\Delta G$  is negative, there is a net loss of energy, and the reaction goes spontaneously as written (that is, A is converted into B) as shown in Figure 6.2A. The reaction is said to be exergonic.

**2. Positive  $\Delta G$ :** If  $\Delta G$  is positive, there is a net gain of energy, and the reaction does not go spontaneously from B to A (see [Figure 6.2B](#)). Energy must be added to the system to make the reaction go from B to A. The reaction is said to be endergonic.

**3.  $\Delta G$  is zero:** If  $\Delta G = 0$ , the reactants are in equilibrium. [Note: When a reaction is proceeding spontaneously (that is, free energy is being lost) then the reaction continues until  $\Delta G$  reaches zero and equilibrium is established.]

## B. $\Delta G$ of the forward and back reactions

The free energy of the forward reaction ( $A \rightarrow B$ ) is equal in magnitude but opposite in sign to that of the back reaction ( $B \rightarrow A$ ). For example, if  $\Delta G$  of the forward reaction is  $-5$  kcal/mol, then that of the back reaction is  $+5$  kcal/mol. [Note:  $\Delta G$  can also be expressed in kilojoules per mole or kJ/mol ( $1$  kcal =  $4.2$  kJ).]

## C. $\Delta G$ and the concentration of reactants and products

The  $\Delta G$  of the reaction  $A \rightarrow B$  depends on the concentration of the reactant and product. At constant temperature and pressure, the following relationship can be derived:

$$\Delta G = \Delta G^\circ + RT \ln \frac{[B]}{[A]}$$

where

where  $\Delta G^\circ$  is the standard free energy change (see below)

R is the gas constant ( $1.987$  cal/mol K)

T is the absolute temperature (K)

[A] and [B] are the actual concentrations of the reactant and product

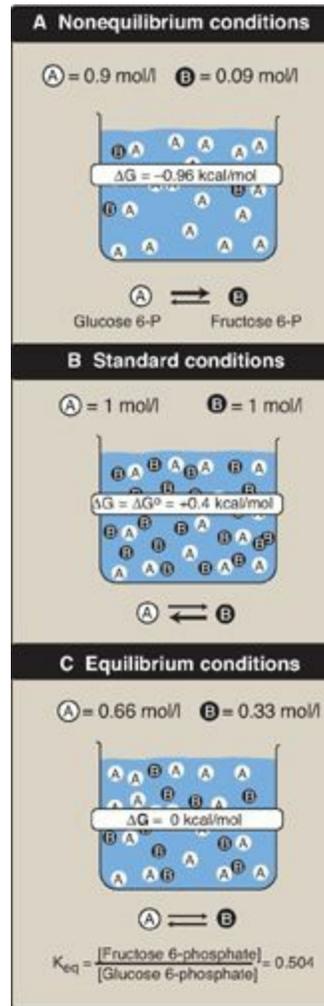
ln represents the natural logarithm

A reaction with a positive  $\Delta G^\circ$  can proceed in the forward direction (have a negative overall  $\Delta G$ ) if the ratio of products to reactants ( $[B]/[A]$ ) is sufficiently small (that is, the ratio of reactants to products is large). For example, consider the reaction:



Figure 6.3A shows reaction conditions in which the concentration of reactant, glucose 6-phosphate, is high compared with the concentration of product, fructose 6-phosphate. This means that the ratio of the product to reactant is small, and  $RT \ln([ \text{fructose 6-phosphate} ] / [ \text{glucose 6-phosphate} ])$  is large and negative, causing  $\Delta G$  to be negative despite  $\Delta G^\circ$  being positive. Thus, the reaction can proceed in the forward direction.

**Figure 6.3** Free energy change ( $\Delta G$ ) of a reaction depends on the concentration of reactant and product  $B$ . For the conversion of glucose 6-phosphate to fructose 6-phosphate,  $\Delta G$  is negative when the ratio of reactant  $A$  to product  $B$  is large (top, panel A), is positive under standard conditions (middle, panel B), and is zero at equilibrium (bottom, panel C).  $\Delta G^0$  = standard free energy change.



## D. Standard free energy change

The standard free energy change,  $\Delta G^0$ , is so called because it is equal to the free energy change,  $\Delta G$ , under standard conditions (that is, when reactants and products are at 1 mol/l concentrations; see [Figure 6.3B](#)). Under these conditions, the natural logarithm of the ratio of products to reactants is zero ( $\ln 1 = 0$ ), and, therefore, the equation shown at the bottom of the previous page becomes:

$$\Delta G = \Delta G^0 + 0$$

**1.  $\Delta G^0$  and the direction of a reaction:** Under standard conditions,  $\Delta G^0$  can be used to predict the direction a reaction proceeds because, under these conditions,  $\Delta G^0$  is equal to  $\Delta G$ . However,  $\Delta G^0$  cannot predict the direction of a reaction under physiologic conditions, because it is composed solely of constants ( $R$ ,  $T$ , and  $K_{eq}$  [see below]) and is not, therefore, altered by changes in product or substrate concentrations.

**2. Relationship between  $\Delta G^\circ$  and  $K_{eq}$ :** In a reaction  $A \rightleftharpoons B$ , a point of equilibrium is reached at which no further net chemical change takes place (that is, when A is being converted to B as fast as B is being converted to A). In this state, the ratio of [B] to [A] is constant, regardless of the actual concentrations of the two compounds:

$$K_{eq} = \frac{[B]_{eq}}{[A]_{eq}}$$

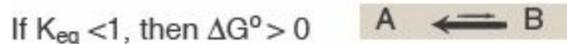
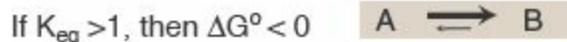
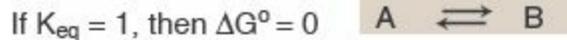
where  $K_{eq}$  is the equilibrium constant, and  $[A]_{eq}$  and  $[B]_{eq}$  are the concentrations of A and B at equilibrium. If the reaction  $A \rightleftharpoons B$  is allowed to go to equilibrium at constant temperature and pressure, then, at equilibrium, the overall  $\Delta G$  is zero. Therefore,

$$\Delta G = 0 = \Delta G^\circ + RT \ln \frac{[B]_{eq}}{[A]_{eq}}$$

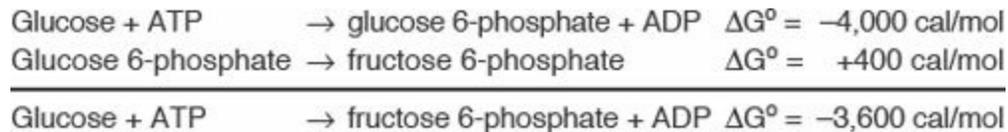
where the actual concentrations of A and B are equal to the equilibrium concentrations of reactant and product  $[A]_{eq}$  and  $[B]_{eq}$ , and their ratio is equal to the  $K_{eq}$ . Thus,

$$\Delta G^\circ = -RT \ln K_{eq}$$

This equation allows some simple predictions:

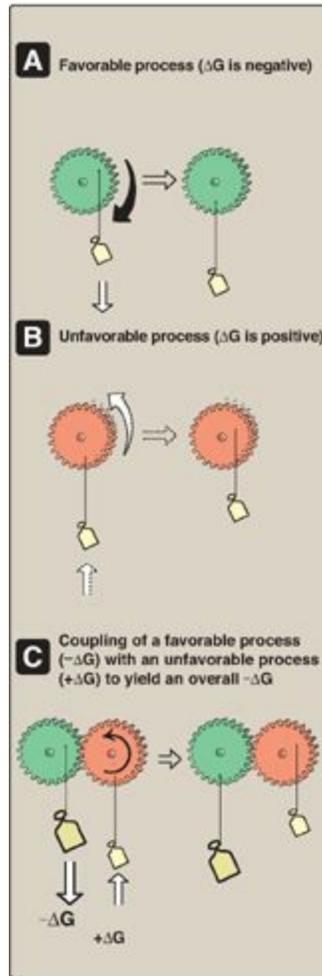


**3.  $\Delta G^\circ$  of two consecutive reactions:** The  $\Delta G^\circ$ s are additive in any sequence of consecutive reactions, as are the  $\Delta G$ s. For example:



**4.  $\Delta G$ s of a pathway:** The additive property of free energy changes is very important in biochemical pathways through which substrates must pass in a particular direction (for example,  $A \rightarrow B \rightarrow C \rightarrow D \rightarrow \dots$ ). As long as the sum of the  $\Delta G$ s of the individual reactions is negative, the pathway can potentially proceed as written, even if some of the individual reactions of the pathway have a positive  $\Delta G$ . The actual rate of the reactions does, of course, depend on the lowering of activation energies by the enzymes that catalyze the reactions (see p. 55).

**Figure 6.4** Mechanical model of coupling of favorable and unfavorable processes. **A** Gear with weight attached spontaneously turns in the direction that achieves the lowest energy state. **B** The reverse movement is energetically unfavorable (not spontaneous). **C** The energetically favorable movement can drive the unfavorable one.

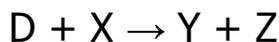
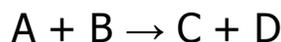


## IV. ADENOSINE TRIPHOSPHATE AS AN ENERGY CARRIER

Reactions or processes that have a large positive  $\Delta G$ , such as moving ions against a concentration gradient across a cell membrane, are made possible by coupling the endergonic movement of ions with a second, spontaneous process with a large negative  $\Delta G$  such as the exergonic hydrolysis of adenosine triphosphate (ATP). [Note: In the absence of enzymes, ATP is a stable molecule because its hydrolysis has a high activation energy (see p. 55).] [Figure 6.4](#) shows a mechanical model of energy coupling. The simplest example of energy coupling in biologic reactions occurs when the energy-requiring and the energy-yielding reactions share a common intermediate.

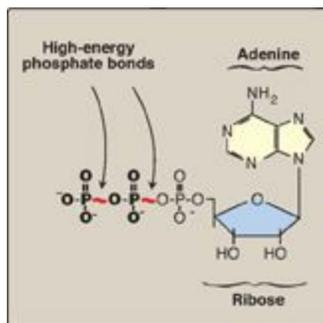
### A. Common intermediates

Two chemical reactions have a common intermediate when they occur sequentially so that the product of the first reaction is a substrate for the second. For example, given the reactions



D is the common intermediate and can serve as a carrier of chemical energy between the two reactions. Many coupled reactions use ATP to generate a common intermediate. These reactions may involve the transfer of a phosphate group from ATP to another molecule. Other reactions involve the transfer of phosphate from an energy-rich intermediate to adenosine diphosphate (ADP), forming ATP.

**Figure 6.5** Adenosine triphosphate.



### B. Energy carried by adenosine triphosphate

ATP consists of a molecule of adenosine (adenine + ribose) to which three phosphate groups are attached ([Figure 6.5](#)). If one phosphate is removed, ADP is produced. If two phosphates are removed, adenosine monophosphate (AMP) results. The standard free energy of hydrolysis of ATP,  $\Delta G^\circ$ , is approximately  $-7.3$  kcal/mol for each of the two terminal phosphate groups. Because of this large negative  $\Delta G^\circ$ , ATP is called a high-energy phosphate compound.