

Thermodynamics

All biochemical and cellular processes obey the laws of chemistry and physics

Biochemistry is not a special case. Therefore, in studying biochemistry, it is necessary to consider the relevant laws that control possible reactions.

The three laws of thermodynamics

First law: Energy is conserved

The overall energy of the universe is constant. Mathematically this can be stated as $\Delta E_{\text{universe}} = 0$. *Within* the universe, however, energy can be exchanged between systems. The overall amount of energy may not change, but the energy of one system can increase, as long as the energy of the surroundings decreases by the same amount.¹

The energy of a system is a **state function**. This means that the energy of any given system is the same regardless of the nature of the process used to reach this state. For example, all glucose molecules contain the same energy, regardless of their synthesis pathway.

The energy of a system can be difficult to measure. A more useful term is **enthalpy**, which is usually abbreviated **H**. The change in enthalpy for a process is given by the equation:

$$\Delta H = \Delta E + P\Delta V$$

In biological processes, the pressure and volume are nearly always constant. If the volume is constant, then the change in volume $\Delta V = 0$, and therefore $\Delta H = \Delta E$. This means that the heat transferred between system and surroundings is equal to the energy change in the system.

Exothermic processes are processes in which heat is transferred from a system to its surroundings. For an exothermic process, the enthalpy (H) of the system decreases, and therefore ΔH is negative. **Endothermic** processes are processes in which heat is transferred from the surroundings to a system. In an endothermic process, the enthalpy of the system increases, and therefore ΔH is positive. A negative value for ΔH acts as a driving force for a process.

Heat can be measured, which is useful. Even more useful is the fact that, as for energy change, enthalpy change is a state function. If you know the starting and ending points, a measurement of the heat change can be performed using **any** process that is convenient to measure. For example, biological processes convert each molecule of glucose to $6 \text{ CO}_2 + 6 \text{ H}_2\text{O}$. The ΔH for the conversion of glucose to

¹Note that Einstein's most famous equation, $E = mc^2$, relates mass and energy. It is more strictly correct to state that, for any process, the overall mass-energy does not change, although mass and energy can be interconverted. While the conversion of glucose to the corresponding number of water and carbon dioxide molecules does result in a mass change, the change in mass is too small to be readily measured except in terms of the energy released in the process. This is the source of the concept that molecules such as glucose contain "potential energy".

the $\text{CO}_2 + \text{H}_2\text{O}$ products is always the same, whether this is done by burning the glucose or by using the much more complex multistep biological processes actually employed by organisms.

For chemical processes, enthalpy change reflects the disruption and formation of bonds. **Bond disruption is always associated with a positive ΔH , while bond formation is associated with a negative ΔH** ; for reactions with an overall negative ΔH , the bond formation term has a larger magnitude than the bond disruption term.

Second Law: Entropy increases

In principle, it is possible for a cold object to release heat to a warm one (this does not violate the First Law). Such a process turns out to be extremely unlikely: it is a low probability event. Unlike energy, the entropy of the universe can change.

Entropy (abbreviated S) is a measure of the amount of order in a system. For any given process, the $\Delta S_{\text{system}} + \Delta S_{\text{surroundings}} = \Delta S_{\text{universe}}$. The Second Law states that $\Delta S_{\text{universe}}$ increases for all processes; in other words, $\Delta S_{\text{universe}}$ is always positive.

Note that it is possible for the entropy of a system to decrease (by increasing the disorder of the surroundings). Reducing the entropy of a system requires energy obtained from the environment, or from a negative enthalpy change in the process.

The overall entropy change is usually difficult to measure directly. It is rarely possible to monitor the entropy of the universe.

Third Law: Entropy is zero at 0 K, but reaching 0 K is impossible

The Third Law is not really relevant to biology. All known biological processes occur at temperatures far above absolute zero.

Will a process occur?

Many chemical reactions occur spontaneously. The spontaneity of a reaction cannot be predicted based simply on entropic considerations. (For example, the reaction $2 \text{H}_2 + \text{O}_2 \rightarrow 2 \text{H}_2\text{O}$ is usually spontaneous, in spite of the lower entropy associated with fewer products than reactants. Note, however, that if the heat released by the reaction is taken into account the *overall* entropy change is positive.)

The **free energy change** (ΔG) is a measure of the spontaneity of a process under conditions of constant temperature and pressure. Negative values of ΔG are indicative of spontaneous processes. The free energy change can be stated as:

$$\Delta G = \Delta H - T\Delta S$$

This means that any process has two possible driving forces: decreases in enthalpy (*i.e.* negative values of ΔH) and increases in entropy (*i.e.* positive values of ΔS). A process with a negative ΔG is spontaneous, and is termed **exergonic**. A process with a positive ΔG is non-spontaneous, and is termed **endergonic**.

At equilibrium $\Delta G = 0$. Note that this means that entropy is at a maximum. Equilibrium is the state that all processes tend to approach. Life is (among other things), an ultimately futile attempt to avoid equilibrium.

For biological systems (where pressure and volume changes are negligible), ΔG represents the maximum possible work resulting from a reaction. In other words, **the ΔG represents the maximum possible amount of useful energy obtainable from a reaction.** This is a critically important concept.

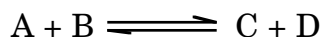
An understanding of thermodynamics, and in particular, of the ΔG of the system, is important for analyzing any chemical or biological system. However, the ΔG only determines the direction in which a process will occur, and does not include the time required for a process to occur. ΔG is a measure of spontaneity, but **ΔG is totally unrelated to rate.** A reaction may have a very large negative ΔG and still require the lifetime of the universe to occur. Another reaction may have a very small negative ΔG , and occur in nanoseconds. Determining how long a process will take requires an analysis of the kinetics of the process.

Reference point – Standard free energy (ΔG°)

In comparing reactions, it is useful to have a standard condition to which to refer, known as the “reference state” or the “standard state”. The standard state most widely used in chemistry is: 298 K (corresponding to 25°C), 1 atmosphere pressure, and 1 molar concentrations of all products and reactants. Note, however, that the “standard state” is intended to make experimental analysis easier, and that it is possible to have a standard state in which, for example, pressure is a variable rather than the constant 1 atmosphere.

Although the standard-condition ΔG (abbreviated as ΔG°) usually cannot be measured directly, ΔG° can be calculated for any process based on the equilibrium constant for the process under those conditions.

Consider a reaction:



The equilibrium constant, K_{eq} is given by the product of the different product concentrations divided by the product of the different reactant concentrations:

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

If the reaction is allowed to reach equilibrium, the measured ratio of the products and reactants can then be used to calculate ΔG° .

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

Although temperature appears as a variable in the equation, this is not quite true (unless made explicit in the experiment), because K_{eq} is somewhat temperature

dependent. (In doing calculations regarding biological processes, the difference between K_{eq} at 298 K (25°C) and K_{eq} at 310 K (37°C) is usually assumed to be negligible, or is explicitly measured.)

In order to determine whether the process is spontaneous under the actual experimental conditions, the ΔG° needs to be modified to take the actual conditions into account. The actual ***measure of spontaneity is ΔG*** , not ΔG° .

$$\Delta G = \Delta G^\circ + RT \ln \left(\frac{[C][D]}{[A][B]} \right)$$

or, more generally:
$$\Delta G = \Delta G^\circ + RT \ln \left(\frac{[\text{Products}]}{[\text{Reactants}]} \right)$$

where [Products] = product of different product concentrations ([C][D]...), and [Reactants] = product of different reactant concentrations ([A][B]...). If [Products] = [Reactants], then $\Delta G = \Delta G^\circ$ (because $\ln(1) = 0$). Note that, if the number of products and reactants differ, the ***concentration units used must be molar***.

In biochemistry, the standard condition values of ΔG° nearly always modified to $\Delta G'^\circ$. The difference between $\Delta G'^\circ$ and ΔG° are generally those in which $\Delta G'^\circ$ assumes a pH of 7.0 instead of a pH of 0, and includes concentration of H_2O molecules in the $\Delta G'^\circ$, and stipulates a Mg^{2+} concentration of 1 mM for reactions that require Mg^{2+} as a counterion. For reactions in which water and H^+ , and Mg^{2+} are not directly involved, $\Delta G'^\circ = \Delta G^\circ$.

Summary

The laws of thermodynamics apply to biochemistry as well as to all other branches of chemistry and physics.

For any reaction, the overall energy of the universe remains constant; however, the overall entropy of the universe increases.

Two driving forces are relevant to any process: the increase in entropy and the decrease in enthalpy of the system. Neither of these driving forces alone determines whether a process will be spontaneous; instead, the free energy change determines spontaneity based on the relative magnitudes of entropy and enthalpy contributions.

ΔG° (or $\Delta G'^\circ$) is the free energy change under the chosen definition of standard conditions. However, standard conditions are rarely encountered experimentally.

ΔG° (or $\Delta G'^\circ$) reflects the difference in stability between reactant and product molecules.

ΔG depends on the stability difference and on the actual conditions of reactant and

product concentrations. ΔG , not ΔG° , determines the spontaneity of the process, with a negative value for ΔG meaning that the reaction will proceed in net amounts in the direction written.

ΔG is the amount of usable energy that may be extracted from a process.

The value of ΔG is **not** related to the rate of a process (except in that processes with positive values of ΔG tend not to occur).²

² Note, however, that it is possible to evaluate kinetic factors based on ΔG values for coupled reactions (which is relevant to understanding biochemical pathways involving multiple enzymatic reactions). In addition, any system for which ΔG is not zero is at least partially kinetically controlled until the ΔG is zero.