8.2 The free–energy change of a reaction tells us whether the reaction occurs spontaneously

Section Vocabulary

Exergonic reaction - A spontaneous chemical reaction, in which there is a net release of free energy.
Endergonic reaction - A non–spontaneous chemical reaction, in which free energy is absorbed from the surroundings.

Free–Energy Change, ΔG

Recall that the universe is really equivalent to "the system" plus "the surroundings." In 1878, J. Willard Gibbs, a professor at Yale, defined a very useful function called the Gibbs free energy of a system (without considering its surroundings), symbolized by the letter G . We'll refer to the Gibbs free energy simply as free energy. Free energy measures the portion of a system's energy that can perform work when temperature and pressure are uniform throughout the system, as in a living cell. Let's consider how we determine the free energy change that occurs when a system changes—for example, during a chemical reaction.
The change in free energy, ΔG, can be calculated for any specific chemical reaction with the following formula:

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

This formula uses only properties of the system (the reaction) itself: ΔH symbolizes the change in the system's enthalpy (in biological systems, equivalent to total energy); ΔS is the change in the system's entropy; and T is the absolute temperature in Kelvin (K) units (K = °C + 273; see Appendix B).
Once we know the value of ΔG for a process, we can use it to predict whether the process will be spontaneous (that is, whether it will run without an outside input of energy). A century of experiments has shown that only processes with a negative ΔG are spontaneous. **For a process to occur spontaneously, therefore, the system must either give up enthalpy (H must decrease), give up order (TS must increase), or both**: When the changes in H and TS are tallied, ΔG must have a negative value ($\Delta G < 0$). This means that every spontaneous process decreases the system's free energy. **Processes that have a positive or zero ΔG are never spontaneous.**
This information is immensely interesting to biologists, for it gives us the power to predict which kinds of change can happen without help. Such spontaneous changes can be harnessed to perform work. This principle is very important in the study of metabolism, where a major goal is to determine which reactions can supply energy to do work in the living cell.

Free Energy, Stability, and Equilibrium

As we saw in the previous section, when a process occurs spontaneously in a system, we can be sure that ΔG is negative. Another way to think of ΔG is to realize that it represents the difference between the free energy of the final state and the free energy of the initial state:

$$\Delta G = \Delta G_{\textit{final state}} - \Delta G_{\textit{initial state}}$$

Thus, ΔG can only be negative when the process involves a loss of free energy during the change from initial state to final state. Because it has less free energy, the system in its final state is less likely to change and is therefore more stable than it was previously.
We can think of free energy as a measure of a system's instability—its tendency to change to a more stable state. Unstable systems (higher G) tend to change in such a way that they become more stable (lower G). For example, a diver on top of a platform is less stable than when floating in the water, a drop of concentrated dye is less stable

than when the dye is spread randomly through the liquid, and a sugar molecule is less stable than the simpler molecules into which it can be broken. Unless something prevents it, each of these systems will move toward greater stability: The diver falls, the solution becomes uniformly colored, and the sugar molecule is broken down.
Another term for a state of maximum stability is equilibrium. There is an important relationship between free energy and equilibrium, including chemical equilibrium. Recall that most chemical reactions are reversible and proceed to a point at which the forward and backward reactions occur at the same rate. The reaction is then said to be at chemical equilibrium, and there is no further net change in the relative concentration of products and reactants.
As a reaction proceeds toward equilibrium, the free energy of the mixture of reactants and products decreases. Free energy increases when a reaction is somehow pushed away from equilibrium, perhaps by removing some of the products (and thus changing their concentration relative to that of the reactants). For a system at equilibrium, G is at its lowest possible value in that system. We can think of the equilibrium state as an energy valley. Any small change from the equilibrium position will have a positive ΔG and will not be spontaneous. For this reason, systems never spontaneously move away from equilibrium. Because a system at equilibrium cannot spontaneously change, it can do no work. A process is spontaneous and can perform work only when it is moving toward equilibrium.

Exergonic and Endergonic Reactions in Metabolism

Based on their free–energy changes, chemical reactions can be classified as either exergonic ("energy outward") or endergonic ("energy inward"). An **exergonic reaction** proceeds with a net release of free energy (**Figure 8.6a**). Because the chemical mixture loses free energy (G decreases), **ΔG is negative for an exergonic reaction**. Using ΔG as a standard for spontaneity, **exergonic reactions are those that occur spontaneously**. (Remember, the word spontaneous does not imply that a reaction will occur instantaneously, or even rapidly.) The magnitude of ΔG for an exergonic reaction represents the maximum amount of work the reaction can perform.*The word maximum qualifies this statement, because some of the free energy is released as heat and cannot do work. Therefore, ΔG represents a theoretical upper limit of available energy.

Comment [b1]: Think Exergonic – Energy EXITS.

The greater the decrease in free energy, the greater the amount of work that can be done.
We can use the overall reaction for cellular respiration as an example:

$$C_6H_{12}O_6 + O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$

$$\Delta G = -686\ \text{kcal/mol}\ (-2{,}870\ \text{kJ/mol})$$

For each mole (180 g) of glucose broken down by respiration under what are called "standard conditions" (1 M of each reactant and product, 25°C, pH 7), 686 kcal (2,870 kJ) of energy are made available for work. Because energy must be conserved, the chemical products of respiration store 686 kcal less free energy per mole than the reactants. The products are, in a sense, the spent exhaust of a process that tapped the free energy stored in the sugar molecules.

Comment [b2]: This is how we can say that 1 gram of carbohydrate has 4 cal / gram!

An **endergonic reaction** is one that absorbs free energy from its surroundings (**Figure 8.6b**). Because this kind of reaction essentially stores free energy in molecules (G increases), ΔG is positive. Such reactions are nonspontaneous, and the magnitude of ΔG is the quantity of energy required to drive the reaction. If a chemical process is

Comment [b3]: Think Endergonic – Energy Enters.

8.2 The free–energy change of a reaction tells us whether the reaction occurs spontaneously

exergonic (downhill) in one direction, then the reverse process must be endergonic (uphill). A reversible process cannot be downhill in both directions. If ΔG = −686 kcal/mol for respiration, which converts sugar to carbon dioxide and water, then the reverse process—the conversion of carbon dioxide and water to sugar—must be strongly endergonic, with ΔG = +686 kcal/mol. Such a reaction would never happen by itself.

How, then, do plants make the sugar that the entire living world consumes for energy? They get the required energy—686 kcal to make a mole of sugar—from the environment by capturing light and converting its energy to chemical energy. Next, in a long series of exergonic steps, they gradually spend that chemical energy to assemble sugar molecules.

Equilibrium and Metabolism

Reactions in a closed system eventually reach equilibrium and can then do no work, as illustrated by the closed hydroelectric system in **Figure 8.7a** . The chemical reactions of metabolism are reversible, and they, too, would reach equilibrium if they occurred in the isolation of a test tube. Because systems at equilibrium are at a minimum of G and can do no work, a cell that has reached metabolic equilibrium is dead! The fact that metabolism as a whole is never at equilibrium is one of the defining features of life.

Like most systems, a cell in our body is not in equilibrium. The constant flow of materials in and out of the cell keeps the metabolic pathways from ever reaching equilibrium, and the cell continues to do work throughout its life. This principle is illustrated by the open (and more realistic) hydroelectric system in **Figure 8.7b** . However, unlike this simple single–step system, a catabolic pathway in a cell releases free energy in a series of reactions. An example is cellular respiration, illustrated by analogy in **Figure 8.7c** . Some of the reversible reactions of respiration are constantly "pulled" in one direction—that is, they are kept out of equilibrium. The key to maintaining this lack of equilibrium is that the product of one reaction does not accumulate, but instead becomes a reactant in the next step; finally, waste products are expelled from the cell. The overall sequence of reactions is kept going by the huge free–energy difference between glucose at the top of the energy "hill" and carbon dioxide and water at the "downhill" end. As long as our cells have a steady supply of glucose or other fuels and oxygen and are able to expel waste products to the surroundings, their metabolic pathways never reach equilibrium and can continue to do the work of life.

We see once again how important it is to think of organisms as open systems. Sunlight provides a daily source of free energy for an ecosystem's plants and other photosynthetic organisms. Animals and other nonphotosynthetic organisms in an ecosystem must have a source of free energy in the form of the organic products of photosynthesis.

1. Cellular respiration uses glucose, which has a high level of free energy, and releases CO_2 and water, which have low levels of free energy. Is respiration spontaneous or not? Is it exergonic or endergonic? What happens to the energy released from glucose?
    a. *Cellular respiration is a spontaneous and exergonic process. The energy released from glucose is used to do work in the cell, or is lost as heat.*
2. A key process in metabolism is the transport of H^+ ions across a membrane to create a concentration gradient. In some conditions, H^+ ions flow back across the membrane and come to equal concentrations on each side. In which conditions can the H^+ ions perform work in this system?
    a. *H^+ ions can perform work only if their concentrations on each side of a membrane differ. When the H^+ concentrations are the same, the system is at equilibrium and can do no work.*