

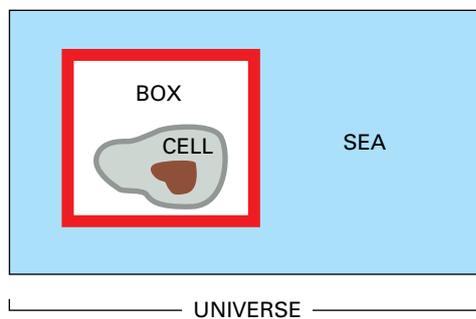
## PANEL 2-7 Free Energy and Biological Reactions

### THE IMPORTANCE OF FREE ENERGY FOR CELLS

Life is possible because of the complex network of interacting chemical reactions occurring in every cell. In viewing the metabolic pathways that comprise this network, one might suspect that the cell has had the ability to evolve an enzyme to carry out any reaction that it needs. But this is not so. Although enzymes are powerful catalysts, they can speed up only those reactions that are thermodynamically possible; other reactions proceed in cells only because they are *coupled* to very favorable reactions that drive them. The question of whether a reaction

can occur spontaneously, or instead needs to be coupled to another reaction, is central to cell biology. The answer is obtained by reference to a quantity called the *free energy*: the total change in free energy during a set of reactions determines whether or not the entire reaction sequence can occur. In this panel we shall explain some of the fundamental ideas—derived from a special branch of chemistry and physics called *thermodynamics*—that are required for understanding what free energy is and why it is so important to cells.

### ENERGY RELEASED BY CHANGES IN CHEMICAL BONDING IS CONVERTED INTO HEAT



An *enclosed system* is defined as a collection of molecules that does not exchange matter with the rest of the universe (for example, the “cell in a box” shown above). Any such system will contain molecules with a total energy  $E$ . This energy will be distributed in a variety of ways: some as the translational energy of the molecules, some as their vibrational and rotational energies, but most as the bonding energies between the individual atoms that make up the molecules. Suppose that a reaction occurs in the system. The **first law of thermodynamics** places a constraint on what types of reactions are possible: it states that “**in any process, the total energy of the universe remains constant.**” For example, suppose that reaction  $A \rightarrow B$  occurs somewhere in the box and releases a great deal of chemical bond energy. This energy will initially increase the intensity of molecular motions (translational, vibrational, and rotational) in the system, which is equivalent to raising its temperature. However, these increased motions will soon be transferred out of the system by a series

of molecular collisions that heat up first the walls of the box and then the outside world (represented by the sea in our example). In the end, the system returns to its initial temperature, by which time all the chemical bond energy released in the box has been converted into heat energy and transferred out of the box to the surroundings. According to the first law, the change in the energy in the box ( $\Delta E_{\text{box}}$ , which we shall denote as  $\Delta E$ ) must be equal and opposite to the amount of heat energy transferred, which we shall designate as  $h$ : that is,  $\Delta E = -h$ . Thus, the energy in the box ( $E$ ) decreases when heat leaves the system.

$E$  also can change during a reaction due to work being done on the outside world. For example, suppose that there is a small increase in the volume ( $\Delta V$ ) of the box during a reaction. Since the walls of the box must push against the constant pressure ( $P$ ) in the surroundings in order to expand, this does work on the outside world and requires energy. The energy used is  $P(\Delta V)$ , which according to the first law must decrease the energy in the box ( $E$ ) by the same amount. In most reactions chemical bond energy is converted into both work and heat. *Enthalpy* ( $H$ ) is a composite function that includes both of these ( $H = E + PV$ ). To be rigorous, it is the change in enthalpy ( $\Delta H$ ) in an enclosed system and not the change in energy that is equal to the heat transferred to the outside world during a reaction. Reactions in which  $H$  decreases release heat to the surroundings and are said to be “exothermic,” while reactions in which  $H$  increases absorb heat from the surroundings and are said to be “endothermic.” Thus,  $-h = \Delta H$ . However, the volume change is negligible in most biological reactions, so to a good approximation

$$-h = \Delta H \cong \Delta E$$

### THE SECOND LAW OF THERMODYNAMICS

Consider a container in which 1000 coins are all lying heads up. If the container is shaken vigorously, subjecting the coins to the types of random motions that all molecules experience due to their frequent collisions with other molecules, one will end up with about half the coins oriented heads down. The reason for this reorientation is that there is only a single way in which the original orderly state of the coins can be reinstated (every coin must lie heads up), whereas there are many different ways (about  $10^{298}$ ) to achieve a disorderly state in which there is an equal mixture of heads and tails; in fact, there are more ways to

achieve a 50-50 state than to achieve any other state. Each state has a probability of occurrence that is proportional to the number of ways it can be realized. The **second law of thermodynamics** states that “**systems will change spontaneously from states of lower probability to states of higher probability.**” Since states of lower probability are more “ordered” than states of high probability, the second law can be restated: “the universe constantly changes so as to become more disordered.”