

BIOENERGETICS

Human locomotion and other physical activities in daily life and athletics are energetic events. Understanding what energy is and how the body acquires, converts, stores, and utilizes it is the key to understanding how the body performs in sports, recreational, and occupational activities. The science that studies the principles limiting energy exchange is known by two names: *thermodynamics* and *energetics*. With some limitations, the same principles that govern energetic events in the physical world—for example, the explosion of dynamite—also govern events in the biological world—for example, a sprinter's first step out of the starting blocks. The science that involves studies of energetic events in the biological world is called *bioenergetics*. In describing energy in the body there are two things to keep in mind. First, energy is not created; rather, it is acquired in one form and converted to another. Second, the conversion process is fairly inefficient, and much of the energy released is in a nonusable form: heat. In this chapter, we discuss energy and begin to describe three energy systems that power and sustain muscular activities. These energy systems can function under different conditions, at different speeds, and for different durations. Together, these three energy systems determine our capacities for power events (e.g., shot putting), speed events (e.g., 100-m sprint running), and endurance events (e.g., marathon running).

To beginning students of biology, the study of energetics seems abstract, especially when they



Figure 2-1 Bob Beamon soars to a new world and Olympic record during the 1968 games in Mexico City. Long jumping is one of the classic events in human bioenergetics. SOURCE: © Corbis/Bettman.

learn that thermodynamics does not tell them much about the specific steps in a process or the time it takes to complete a biological process. However, if one understands that the ability to do work, or exercise, depends on the conversion of one form of energy to another, then the importance of studying energetics becomes apparent.

■ Terminology

Before starting the formal presentation of bioenergetics, we need to define some important terms.

Energy The capacity to do work.

Work The product of a given force acting through a given distance.

Power The rate of work production.

System An organized, functional unit. The boundaries of systems vary from situation to situation and depend on the process under consideration. Systems can vary from sublight microscopic cellular organelles such as mitochondria, to muscles, to whole individuals.

Surroundings Exchanges of energy and matter frequently occur between systems and their environments. Once we have defined a system, all else comprises the surroundings.

Universe Together, the system and its surroundings make up the universe (Figure 2-2).

Turnover In our bodies, molecules of energy exchange are constantly used and restored. Turnover refers to the rate of renewal which in a steady state of metabolism means that the rate of use equals the rate of restoration (renewal).

The definition of *work* is a Newtonian or mechanical definition. In actuality, cells more commonly perform chemical and electrical work than mechanical work. However, it is possible to exchange and convert energy from one form to another. The physical science dealing with energy exchange is called *thermodynamics*.

The study of thermodynamics began in the nineteenth century, with the desire to predict the work output of machines such as steam engines. It was so called because heat was the most common form of energy used. However, as there are six primary forms of energy (thermal, chemical, mechanical, electrical, radiant, and atomic), a more appropriate term—and one that is used more often today—is *energetics*. Again, the branch of science that deals with energy exchanges in living things is called *bioenergetics*. Although a few limitations and

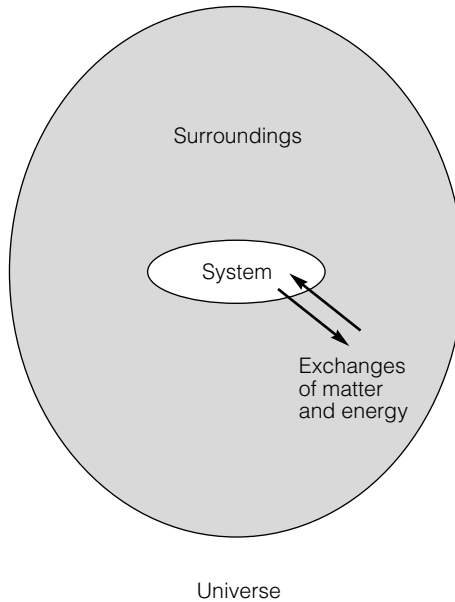


Figure 2-2 The universe consists of the system(s) plus the surroundings. At any one time, a reaction taking place in the system results in a decrease in the energy (free energy) available to do the work of the system. Consequently, over the long term, an input of energy from the surroundings is required to maintain the system. The energy content of the universe is always constant.

properties involving heat and temperature are unique to biological systems, these systems and other types of machines follow the same general principles of energetics.

■ Heat, Temperature, and the Biological Apparatus

Steam and internal combustion engines are examples of machines that convert chemical energy (coal and gasoline) to heat. That heat energy is then converted to mechanical energy. Generally, the higher the heat, the more the power produced. Biological engines differ from mechanical engines with respect to their ability to use heat. Biological engines *cannot* convert heat energy to other forms, such as me-

chanical energy. In biological systems, heat is released as an essential but useless component of reactions in which other forms of work are accomplished. This is a fundamental difference between biological and mechanical engines.

Another characteristic of biological systems is their temperature dependence. Two factors merit consideration here. First, biological systems are sensitive to small increments in temperature. Above 45° C, and certainly above 60° C, tissue proteins become denatured, or degraded. Consequently, although a muscle might theoretically contract faster at 50° C than at 35° C, increasing the temperature that much would literally cook the muscle.

Second, the rates of biological or enzymatic reactions are also sensitive to temperature. Usually, the effect of temperature on reaction rates is studied by changing the temperature in multiples of 10° C. The result of such a change is called a “ Q_{10} effect.” Increasing the temperature 10° C, for example, doubles the rate of an enzymatic reaction, and the Q_{10} is 2. Figure 2-3 illustrates the Q_{10} effect. In that figure, note the large effect of temperature changes within the normal range of muscle temperature.

Changes in temperature can be advantageous as well as deleterious to individuals. For instance, even though a lizard cannot capture heat to do cellular work, it can sit in the sun to warm itself, and in this way it takes advantage of the Q_{10} effect. Some rodents can adapt biochemically when they are exposed to extreme cold; these adaptations allow them to consume extra oxygen and generate heat without shivering, which would endanger their survival. Also, many athletes have found that preliminary exercise (“warming up”) makes for better performance. We shall see (in Chapter 21) that preliminary exercise has several beneficial effects, one of which is to warm up muscle, thus taking advantage of the local Q_{10} effect.

Excessively high as well as low temperatures can be harmful. Although warming up can increase the speed of particular enzymatic processes in muscles through the Q_{10} effect, temperatures of over 40° C have been observed to decrease the efficiency of oxygen use in muscle. This can negatively affect endurance. It has also been noted that cooling brain

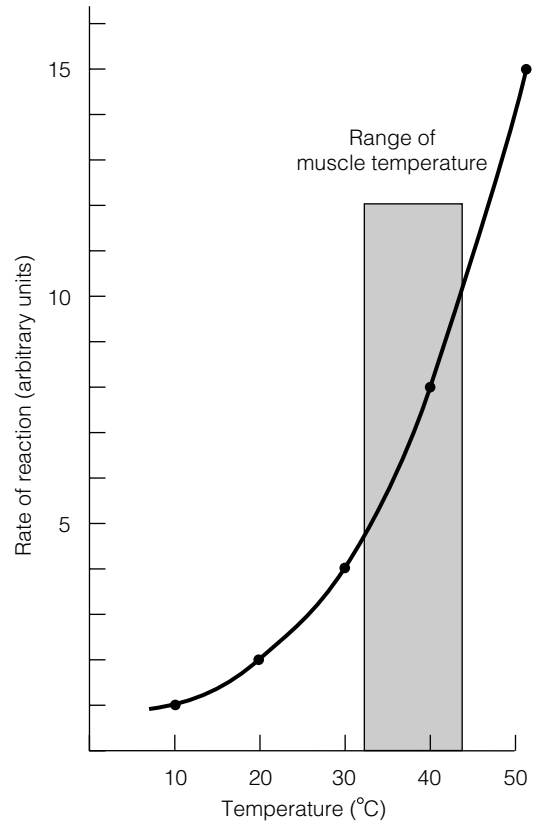


Figure 2-3 Illustration of a Q_{10} effect, where each 10° C increase in temperature doubles the rate of reaction. In the physiological range (shaded area) the curve is very steep.

temperature by only a few degrees below the norm of 37° C can affect thinking and cause disorientation. This can be especially serious for campers, swimmers, or divers, whose survival in a hostile environment often depends on their behavior.

■ Laws of Thermodynamics

Repeated observations of events in the physical world reveal that two fundamental principles, or laws, always hold. The *first law of thermodynamics* states that energy can be neither created nor destroyed. Whenever there is an exchange of energy or matter between a system and its surroundings, the

total energy content in the universe remains constant. The expression “We get a burst of energy” is not quite correct. Rather, humans consume food (parcels of chemical energy) and degrade the food-stuffs, converting some of the chemical energy to heat and cell work, and releasing the remaining chemical energy unused in body excrements.

Equation 2-1, which describes weight loss or gain in healthy human bodies, is not a statement of the first law but does conform to the first law. According to this equation, the only way obese people can lose fat is to eat less and exercise more. If the energy input (food) is less than that expended as work and heat resulting from exercise, then the amount stored (as fat) will be reduced.

$$\text{Energy in (food)} = \text{Energy out (work)} + \text{Energy out (heat)} \pm \text{Energy stored (fat)} \quad (2-1)$$

In addition to telling us that energy is not created or destroyed, but rather interconverted among forms, the first law tells us to be careful to account for all the energy.

The first law of thermodynamics implies that energy forms can be exchanged, but it does not tell us in what direction the exchanges will occur. The second law of thermodynamics tells us that processes always go in the direction of randomness, or disorder. A quantitative measure of this disorder is termed *entropy*. As the result of the second law, entropy always increases. In biology, the second law tells us that whenever energy is exchanged, the efficiency of the exchange will be imperfect and some energy will escape—usually in the form of heat—thus increasing entropy in the universe. Now consider a system that is increasing in organization, such as a child growing. Is this increasing organization of matter contrary to the second law? The answer is no. The process of growth requires a tremendous input of energy from the environment, and for a little growth—a little increase in order—a lot of heat (random energy) is released. In general, when one biological process moves some product toward a higher level of organization, it is driven by at least one “linked” or “coupled” entropic reaction.

There are many examples of concentrated units of energy being dispersed into random energy—

the cooling of the sun, for example—and increasing entropy. What are the consequences of this increasing entropy for the biological and physical world? Ultimately, the universe will be complete randomness and disorder, which means that life is ultimately doomed. In the meantime, however, the energetic trend toward entropy allows us to capture energy in useful forms and perform biological reactions that require energy input. In this sense, then, for now, the trend toward entropy is necessary, and therefore, good.

■ Exergonic and Endergonic Reactions

An *exergonic* reaction is one that gives up energy. If heat is the form of energy given off, another term used is *exothermic*. *Spontaneous reaction* is another synonymous term. An *endergonic* reaction is one that absorbs energy from its surroundings. If heat is the energy form absorbed, the reaction is *endothermic*. In these terms, *erg* refers to work or energy, and *therm* refers to heat.

An example of a spontaneous reaction ($A \rightarrow B$) is diagrammed in Figure 2-4. The energy content of the product B is less than that of the reactant A. The difference or change in energy is ΔE_1 . In this example, ΔE is negative because the energy content of B (the product) is less than that of A (the reactant).

Reaction ($C \rightarrow D$) is an example of an endergonic, nonspontaneous, energetically uphill reaction. Here, the energy level of the product is greater than that of the reactant. This reaction will not occur unless there is an energy input. Here, ΔE_2 is positive in sign because the energy content of D (product) is greater than that of C (reactant). Many important reactions and processes in the physical and biological world are endergonic—that is, require energy inputs. In the biological world, endergonic reactions such as $C \rightarrow D$ are linked or coupled to, and driven by, exergonic reactions such as $A \rightarrow B$. In the example given, the overall process is $A \rightarrow D$. Note that the energy level of D, the final product, is less than that of A, the initial reactant.

Although chemical reactions and processes in biological systems are governed by laws of ener-

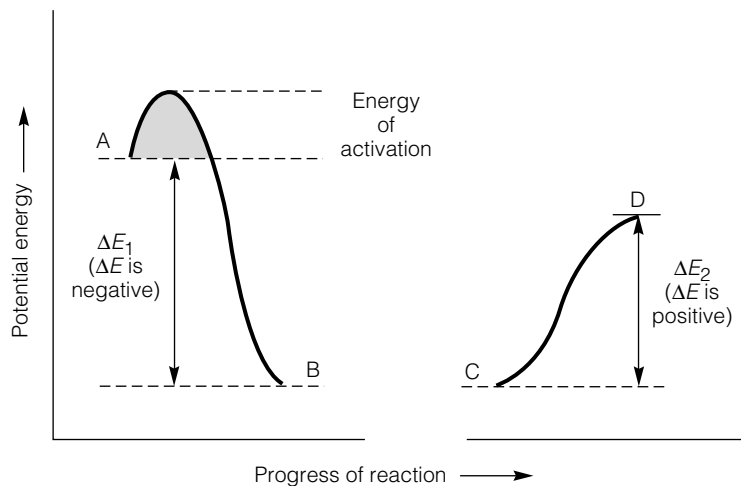


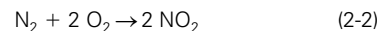
Figure 2-4 Examples of spontaneous ($A \rightarrow B$) and nonspontaneous ($C \rightarrow D$) reactions. Even though $A \rightarrow B$ is energetically downhill, the impediment imposed by the energy of activation may prohibit $A \rightarrow B$ unless energy is put in to overcome the energy of activation. Note that if $C \rightarrow D$ is driven by $A \rightarrow B$, then the absolute value of ΔE_2 is less than ΔE_1 .

getics, the linkages between exergonic (energy-yielding) and endergonic (energy-consuming) reactions is usually indirect. As we shall see in the following sections, part of the energy available from exergonic processes is captured in the form of a high-energy intermediate compound, adenosine triphosphate (ATP). In a complementary way, most endergonic reactions in mammalian systems are catalyzed by an enzyme that uses the energy of ATP.

Even though reaction $A \rightarrow B$ is downhill and “spontaneous,” it is not likely to happen because an energy barrier, called the *energy of activation*, must first be overcome. In other words, even though the reaction $A \rightarrow B$ is classified as spontaneous, some energy has to be put in to activate the system and “prime the pump.” As we shall see, several important biochemical pathways, such as the conversion of glucose to glucose 6-phosphate in glycolysis (Chapter 5), begin with such activating steps. We will also see that enzymes are important because they lower the energy of activation.

Although the energy of activation impedes some processes, the world as we know it depends on other processes having very high energies of activation. For example, oxides of nitrogen and other automobile exhaust emissions are currently very much in the news. Oxides of nitrogen are formed

from nitrogen and oxygen according to the following reactions:



These are spontaneous reactions with high energies of activation. In the automobile combustion chamber, extremes of temperature and pressure activate the reaction and produce noxious products. Without very high energies of activation, these reactions might well cause the atmosphere to catch fire.

In metabolic processes, initial reactants must first be activated. Because enzymes can lower the energy of activation, there is enzymatic control over these processes.

■ Enthalpy

In the example of a spontaneous reaction just cited ($A \rightarrow B$ in Figure 2-4), we saw that energy was released (ΔE_1) because the energy content of the products was less than that of the reactants. More specifically,

$$\Sigma(EA) = \Sigma(EB) + \Delta E_1 \quad (2-4)$$

Here, Σ means “sum of” or “content of.” Accordingly, $\Sigma(EA)$ means the content of all the energy in A.

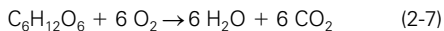
In natural events, however, it is difficult to determine the change in energy (ΔE) because some work is done in the atmosphere. *Enthalpy* (symbolized by H) takes into account this work done in the atmosphere by adjusting ΔE for changes in pressure and volume.

$$\Delta H = \Delta E + P\Delta V \quad (2-5)$$

Fortunately, volume changes at constant pressures are extremely small, and for most biological reactions, $P\Delta V = 0$. Therefore,

$$\Delta E = \Delta H \quad (2-6)$$

An example of this is the important reaction of carbohydrate oxidation:



In the aqueous medium of a cell, the volume of O_2 consumed is equal to the volume of CO_2 formed, so the net volume change is zero.

Note: The trend of biologists to use the terms *energy* and *enthalpy* interchangeably is somewhat confusing. In addition, early theorists used the terms *enthalpy* and *entropy*, which sound alike but are very different. Be aware of this possible confusion in terminology and take care to avoid it.

■ Free Energy

Although the second law of thermodynamics states that the entropy of the universe always increases, and it is the drive toward the entropic condition that allows physical and chemical reactions to occur, the random energy of entropy is not directly useful in the performance of cell work. As implied by the first and second laws of thermodynamics, there exists another component to the total energy of a system. The term *free energy* is used because

this energy is available, or free, to do work. In biological reactions, such as those involved in muscle contraction, free energy changes are of primary importance.

The following equations summarize what has been covered so far:

$$\begin{aligned} \text{Energy change} &= \text{Change in energy available} \\ \text{(enthalpy)} &\quad \text{to do work} + \quad (2-8) \\ &\quad \text{Change in unavailable energy} \end{aligned}$$

For energy change let us substitute ΔH , and for unavailable energy let us substitute entropy. Therefore,

$$\begin{aligned} \Delta H &= \text{Change in available energy} \\ &\quad + \text{Change in entropy} \end{aligned} \quad (2-9)$$

Recall that the energy available to do work was termed free energy. Therefore, we now have

$$\begin{aligned} \Delta H &= \text{Change in free energy} \\ &\quad + \text{Change in entropy} \end{aligned} \quad (2-10)$$

Formally, free energy is symbolized by G , after the scientist Willard Gibbs, and entropy is symbolized by S . With substitution, we then obtain

$$\Delta H = \Delta G + T\Delta S \quad (2-11)$$

where Δ means change and T is absolute temperature. The temperature term is necessary to get entropy in appropriate units. Because of the second law, and by convention, as any real process proceeds, the free energy carries a negative sign. Another way to remember that free energy (the useful component) carries a negative sign is to reason that a negative free energy term means that energy is given up by a reaction and is available to do work. Typically, in working human muscle 25% of the enthalpy change is available to do work and 75% appears as heat; rephrased, muscle efficiency during locomotion approximates 25%. Figure 2-5 summarizes the various components of chemical energy.

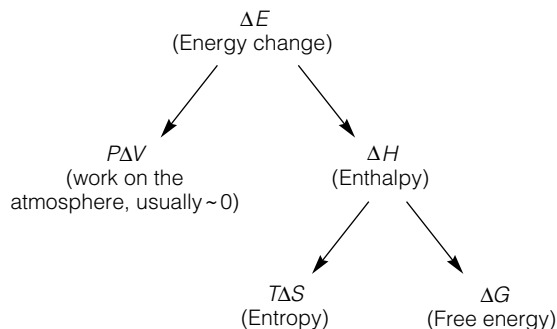


Figure 2-5 Enthalpy, free energy, and entropy. Only part of the energy change of a spontaneous reaction results in work. For a muscle, work may be only 25% of energy release.

■ The Equilibrium Constant and Free Energy

The second law of thermodynamics states that entropy is always increasing in the universe. Entropy was defined as a random, disordered condition. When a reaction has reached the end of the road and entropy is at a maximum, the reaction has reached equilibrium. At chemical equilibrium there is no longer any net change from reactant to product. At equilibrium, then, there is no further potential to do work. In other words, the further from equilibrium the reactants of a process are, the more potential use the reaction has.

The importance of the equilibrium constant in determining the free energy change for a reaction is illustrated in Figure 2-6, where A is the reactant, B is

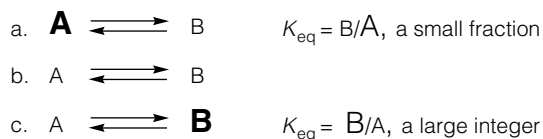


Figure 2-6 Reactant and product levels as related to K_{eq} . At time zero, when the reaction begins, only the reactant A is present. Given enough time (a), A changes to B and reaches equilibrium with B. At equilibrium (b), the net amount of $\text{A} \rightarrow \text{B}$ equals the net amount of $\text{B} \rightarrow \text{A}$. Useful reactions, therefore, are those in which a large fraction of A changes to B and the K_{eq} is large (c).

the product, and each of the reactions proceeds to equilibrium. In reaction (a), where very little or no product is formed, it is obvious that little has happened, so there is little opportunity for energy to be exchanged. At the other end, in reaction (c), almost all the reactant has become product. In this reaction, much has happened chemically, and there has been opportunity to capture some of the energy given off.

The equilibrium constant K_{eq} is used to denote the ratio of concentrations of products to reactants at equilibrium:

$$K_{\text{eq}} = \frac{[\text{B}]}{[\text{A}]} = \frac{[\text{products}]}{[\text{reactants}]} \quad (2-12)$$

Here the brackets indicate “concentration of.” The K_{eq} of a reaction is an immutable constant at specified conditions of temperature and pressure.

In examining K_{eq} and looking at the reactions in Figure 2-6, we can see that if the quotient is large, the reaction has potential use in driving a biological system.

Empirically, it has been determined that the change in free energy in a reaction is simply related to its equilibrium constant:

$$\Delta G^{\circ'} = -RT \ln K'_{\text{eq}} \quad (2-13)$$

where R is the gas constant ($1.99 \text{ cal} \cdot \text{mol}^{-1} \text{ deg}^{-1}$), T is absolute temperature, and $\ln K'_{\text{eq}}$ is the natural logarithm of the equilibrium constant determined under standard laboratory conditions.

The symbol $\Delta G^{\circ'}$ thus refers to the standard free energy change determined in the laboratory when a reaction takes place at 25°C , at 1 atmosphere of pressure, and where the concentrations are maintained at 1 molal and in an aqueous medium at pH 7. In the notation the superscript ' refers to pH 7; the $^{\circ}$ refers to the other standard conditions. Although these “standard conditions” seem to be far removed from those in the body, categorizing reactions by this system allows us to compare free energy potentials of various reactions.

The relationship between K'_{eq} and $\Delta G^{\circ'}$ is further illustrated in Table 2-1.

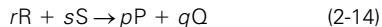
TABLE 2-1

Relationship Between Equilibrium Constant K'_{eq} and Free Energy Change $\Delta G^{\circ'}$ Determined Under Standard Conditions (25° C, or 298 K, and pH 7)

K'_{eq}	$\Delta G^{\circ'}$ (kcal · mol ⁻¹)	
0.001	+4.09	} Endergonic reactions
0.010	+2.73	
0.100	+1.36	
1.000	0.00	} Exergonic reactions
10.000	-1.36	
100.000	-2.73	
1000.000	-4.09	

■ The Actual Free Energy Change

In order to consider a more realistic evaluation of free energy change, let us consider the reaction



By convention, for this reaction at equilibrium,

$$K'_{eq} = \frac{[P]^p [Q]^q}{[R]^r [S]^s} \quad (2-15)$$

For the same reaction in a living cell, a determination of the actual, not equilibrium, concentrations gives the mass action ratio (MAR):

$$MAR = \frac{[P]^p [Q]^q}{[R]^r [S]^s} \quad (2-16)$$

The formulas for the K'_{eq} and the MAR may look alike, but their values may be far apart. In fact, a key to having a flux of energy in living organisms is having MARs removed from the K'_{eq} in various reactions, or steps, of a process. It has been found that the actual (ΔG) and standard free energy changes ($\Delta G^{\circ'}$) are related by the equation

$$\Delta G = \Delta G^{\circ'} + RT \ln MAR \quad (2-17)$$

Here we can clearly see what the effect of concentration change is on the actual free energy change of a reaction. Also, we can see that temperature has a direct effect on the free energy change. Although it is not directly shown, a change in pH would also affect the actual free energy. Some things to consider are the effects of exercise on muscle metabolite concentrations, pH, and temperature. These factors can affect exercise performance.

■ ATP: The Common Chemical Intermediate

The mechanisms of energy conversion are contained within each cell; therefore, cells require the presence of a substance that can receive energy input from energy-yielding reactions. Equally important, that substance must be able to yield energy to reactions requiring an energy input. In our cells, that substance is almost always adenosine triphosphate (ATP).

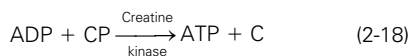
In Chapter 4, we will discuss in some detail the processes of cell respiration and cell work. In the cell, respiration represents the conversion of the chemical energy of foodstuffs into useful chemical form. Cell work represents the conversion of that useful form to other forms of energy. In order to function, this coupled system of energy-yielding and energy-utilizing reactions depends on having a substance that can act both as an energy receiver and as an energy resource, or donor. In most cells of most organisms, ATP is that substance. Because of its central role in metabolism, ATP is frequently referred to as the "common chemical intermediate." If most species had not evolved to use ATP, they would have evolved to use a related compound.

The history of the study of ATP is marked by several notable discoveries. In the 1920s, the work of Fletcher, Hopkins, and Hill led to the belief that the release of lactic acid in muscles was the stimulus for contraction. Subsequently, after Embden showed that rapid freezing of small isolated muscles after a contraction prevented the formation of lactic acid, it was concluded that lactate was not the cause of contraction. In the early 1930s, Lundsgaard showed

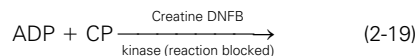
that poisoning glucose metabolism in muscles with iodoacetic acid hastened fatigue and prevented lactate formation. Instead, there was a decrease in a phosphorylated compound (later shown to be creatine phosphate) and an increase in inorganic phosphate. In 1929, Fiske and Subbarow isolated and deduced the structure of ATP. Embden and Meyerhof independently found that ATP is formed by joining inorganic phosphate (P_i) to adenosine diphosphate (ADP) during the catabolism of glucose. Englehardt discovered that ATP was split to ADP by myosin, one of the two major contractile proteins of muscle. Szent Gyorgi found that injections of ATP into muscle fibers that had been soaked in glycerin to remove metabolites had two effects: An initial infusion of ATP caused the muscles to contract; a second injection frequently caused relaxation. Cori and Cori observed that ATP had a biosynthetic function and could stimulate the aggregation of glucose (a simple sugar) into glycogen (a polymeric form of glucose).

In 1940, Lipman deduced from these various bits of information that ATP was the substance that linked energy-yielding and energy-using functions in the cell. This hypothesis was confirmed and generally accepted when Cain and Davies used the poison dinitrofluorobenzene (DNFB) on small isolated muscles to show that contractions resulted in a utilization of ATP. In the normal muscle cell, little ATP is present. This rather low concentration of ATP is probably more advantageous than not. As will be shown, the energy-yielding processes of metabolism are finely tuned to comparative levels of ATP, ADP, P_i , and AMP. By keeping the normal level of ATP low, any small utilization immediately changes the level markedly and stimulates the processes that generate ATP.

More cellular energy is stored in the form of creatine phosphate (CP) than in the form of ATP. The metabolisms of ATP and CP are linked by the reaction governed by the enzyme creatine kinase.



The poison DNFB blocks the action of creatine kinase.



In most cells, such as muscle, there is enough CP and the action of creatine kinase is so rapid that it is difficult to determine an overall decrease in ATP level after a twitch or contraction. Therefore, although the muscle uses ATP as an immediate energy source for contraction, the ATP is replenished almost immediately by CP. Hence, as emphasized by Kushmerick and Conley, CP acts as a “chemical capacitor” for ATP, thus buffering the effects of cell events on the concentration of ATP. By using DNFB, Cain and Davies demonstrated that muscle contractions are powered directly by ATP.

Structure of ATP

The structure of ATP is shown in Figure 2-7. One of the group of compounds called nucleotides, ATP contains a nitrogenous base (adenine), a five-carbon sugar (ribose), and three phosphates. Removal of

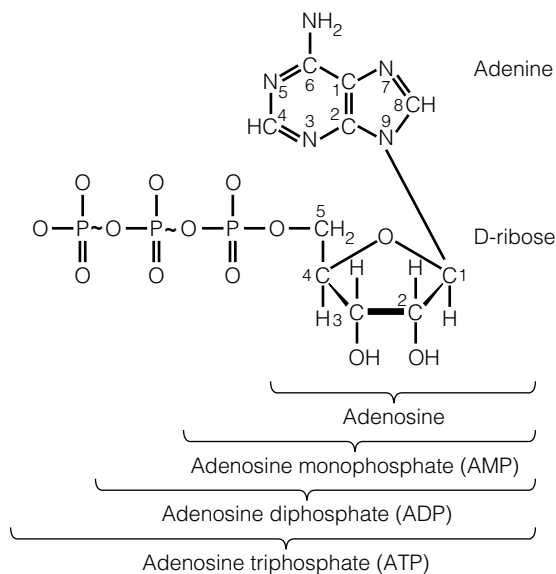


Figure 2-7 The structure of adenosine triphosphate (ATP). At pH 7 the molecule is ionized. Usually, the terminal phosphate (~bond) is hydrolyzed to provide energy. Atoms in the ring structures are numbered.

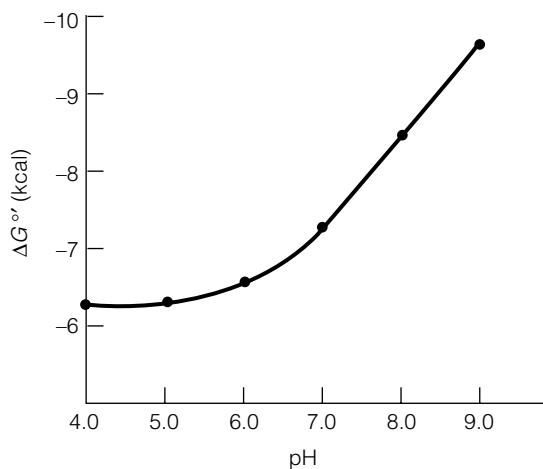


Figure 2-8 Effect of pH on ΔG° of ATP at 25° C (298 K).

the terminal phosphate results in adenosine diphosphate (ADP); cleaving two phosphates gives adenosine monophosphate (AMP). With no phosphates, the compound is simply the nucleotide, adenosine. In the cell, ATP is negatively charged, and the terminal phosphates of each ATP molecule often associate with a magnesium (Mg^{2+}). The Mg^{2+} is usually required for enzymatic activity.

The reactions in which ATP is split to ADP to liberate energy involve water. Accordingly these reactions are called *hydrolyses*, meaning “split by water.”



The standard free energy of ATP hydrolysis (ΔG°) is $-7.3 \text{ kcal} \cdot \text{mol}^{-1}$. As pointed out earlier, the factors of metabolite concentration, temperature, and pH affect the actual free energy of hydrolysis (ΔG) in the cell. The effect of pH on the ΔG° of ATP is given in Figure 2-8. In the working muscle, ΔG for ATP is probably close to $-11 \text{ kcal} \cdot \text{mol}^{-1}$.

Three factors operate to give ATP a relatively high free energy of hydrolysis. First, the negative charges of the phosphates repel each other. Second, the products ADP and P_i form “resonance hybrids,”

which means that they can share electrons in ways to reduce the energy state. Third, ADP and ATP have the proper configurations to be accepted by enzymes that regulate energy-yielding and energy-requiring reactions, respectively.

The hydrolysis of ATP almost always involves splitting the terminal phosphate group. Therefore, it is possible to write ATP as $ADP \sim P$, where the $\sim P$ is the “high-energy” phosphate. Similarly, creatine phosphate can be abbreviated as $C \sim P$. Exergonic reactions of metabolism that hydrolyze the second phosphate group of ATP are infrequent; the myokinase (adenylate kinase) reaction that produces AMP is a notable exception (Equation 3-4).

As we shall see, Equations 2-20 and 3-4, which produce P_i and AMP, respectively, are extremely important in the regulation of intermediary metabolism. As already noted, in working muscle and other metabolically active cells the use of ATP is so well buffered by $C \sim P$ degradation that the concentration of ATP changes little, even during maximum effort. Hence, changes (decrements) in ATP concentration $[ATP]$ are poor signals to increase metabolic rate, whereas changes (increments) in $[AMP]$ and $[P_i]$ are powerful signals in metabolic control (see Chapters 3 and 5).

ATP: The High-Energy Chemical Intermediate

The potential chemical energy of hydrolyzing the terminal phosphate of ATP is intermediate with regard to the hydrolysis of other phosphorylated biological compounds (Figure 2-9). The term *high energy*, when applied to ATP, more properly refers to the fact that the probability is high of hydrolysis transferring energy.

Figure 2-9 illustrates several aspects of the role of ATP in cellular energy transfer. First, the intermediate level of ATP in the scale of phosphate metabolites means that the phosphorylation of ADP to ATP can be driven by phosphorylated compounds of higher energy. These are energy-conserving reactions. The hydrolysis of ATP to ADP and P_i can transfer energy to other compounds or do cell work. These are energy-yielding reactions.

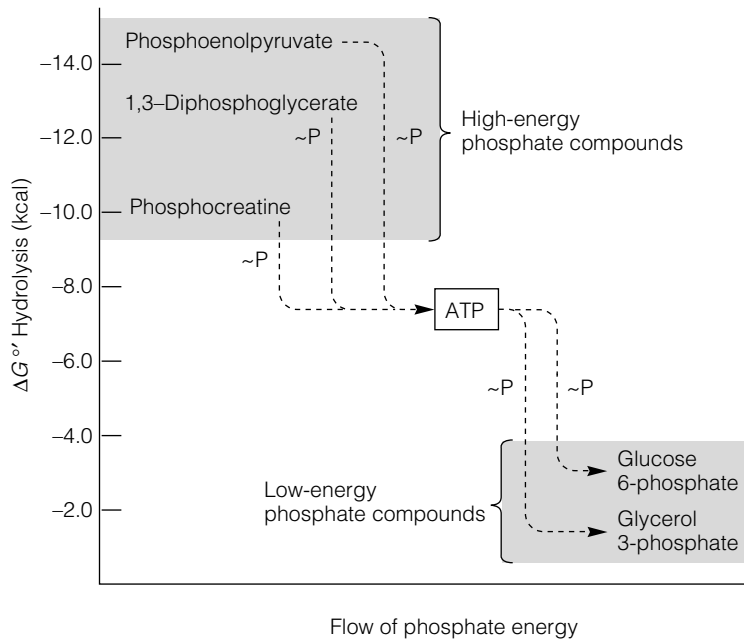


Figure 2-9 Standard free energies of hydrolysis of ATP compared to those of related physiological compounds. Because of its intermediate position, ATP can transfer phosphate group energy to “low-energy” phosphate compounds, whereas ADP can accept phosphate group energy from “high-energy” compounds.

Second, it should be noted that many biological reactions of energy transfer involve phosphate exchange. The $\text{ATP} \rightleftharpoons \text{ADP} + \text{P}_i$ system functions as a

shuttle, or energy bridge, for exchanging phosphate energy.

SUMMARY

Performance in muscular activity depends on energetics. The utilization of energy by machines, both mechanical and biological, can be precisely defined. Basically, two considerations govern physical and biological reactions involving energy exchanges: (1) Energy is not created but is acquired in one form and converted to another; and (2) the interconversion of energy among forms is inefficient, and a large fraction of the energy released appears in an unusable form, usually heat. In the cell, the transduction of chemical energy to other forms of energy depends on the metabolism of adenosine triphosphate (ATP). Elaborate enzymatic pathways exist to

capture the energy content of foodstuffs in the form of ATP. Similarly, complex enzymatic pathways are evolved to utilize the potential energy in ATP to do cell work. Indeed, the overall processes sustaining working muscle during exercise can be considered as a balance between those processes that degrade ATP to its products ADP, AMP, and P_i , and those processes that restore and maintain the level of ATP. As we shall see, ATP use and restoration (turnover) rates can vary widely, but these variations occur around a setpoint of ATP homeostasis. In coming chapters, we shall describe these processes in detail.

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