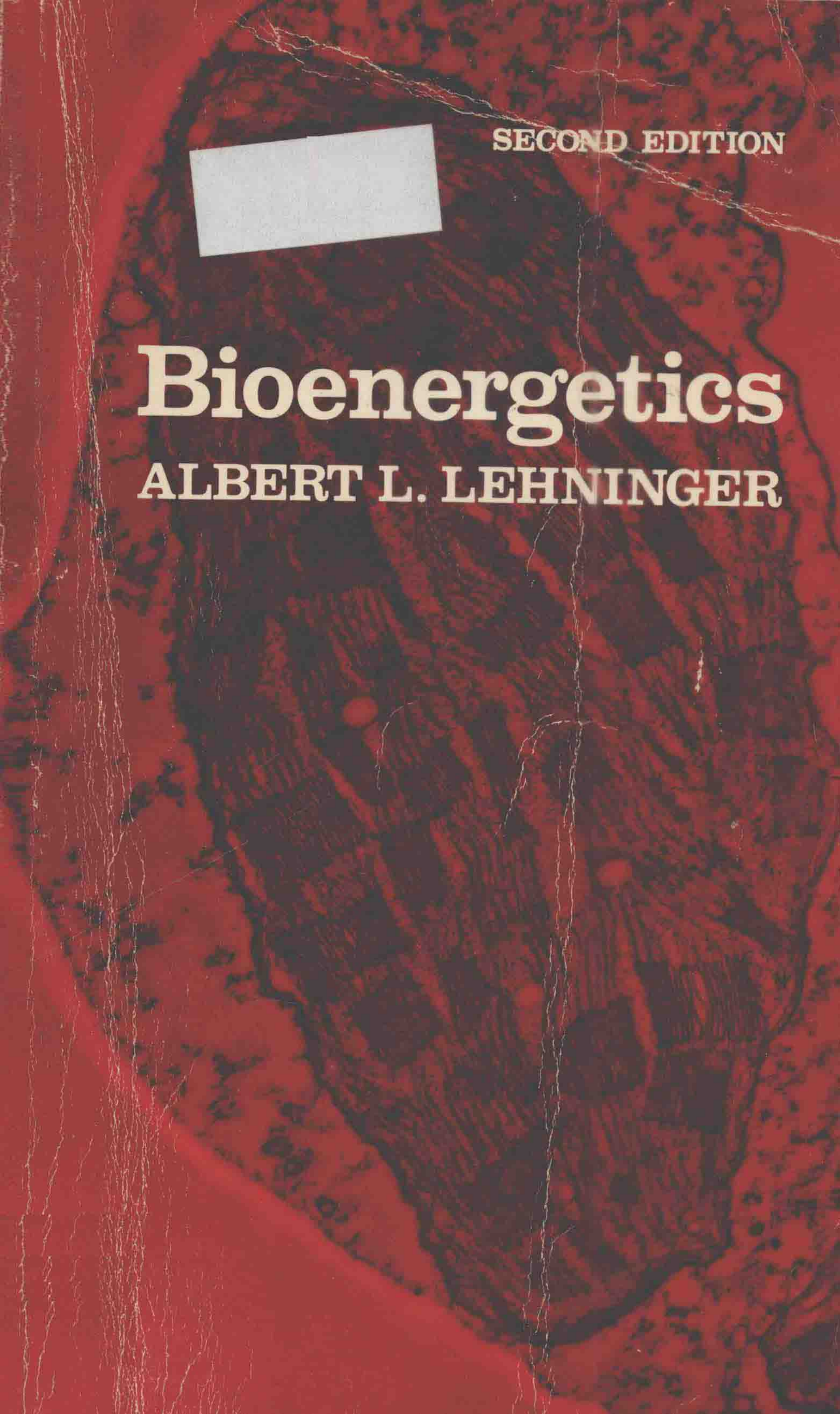

SECOND EDITION

Bioenergetics

ALBERT L. LEHNINGER

BIOENERGETICS
Second Edition

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The Molecular Basis of Biological Energy Transformations

Second Edition

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PREFACE

In this book I have attempted to sketch in brief form the molecular mechanisms by which living cells transform energy for their various activities and for their growth and replication. Because exchanges of energy are fundamental to all activities of cells, this book touches on most of the important areas of dynamic biochemistry and may indeed be regarded as an introduction to biochemistry.

I wrote this book for college undergraduates beginning the study of cell biology or molecular biology, to be used as a supplement to textbooks in general biology. However, I have tried to make this new edition rigorous enough in its fundamentals to be useful, at least as a review, for more advanced students of biology, including premedical and medical students. The book presupposes a course in general chemistry, as well as a concurrent biology course.

The book first outlines the basic principles governing energy exchanges in simple enzymatic reactions. These principles are then applied to the ATP-ADP system as the carrier of chemical energy in the cell. The enzymatic reactions which yield phosphate bond energy, such as photosynthesis, fermentation, and respiration, as well as the basic processes requiring phosphate bond energy, biosynthesis, active transport, and contractile processes, are then analyzed. The concept that information is related to energy is developed as a basis for considering the biosynthesis and role of DNA, RNA, and protein in the transmission and expression of genetic information.

This edition of *Bioenergetics* represents a substantial revision and updating, particularly of the chapters on thermodynamics, photosynthesis, active transport, and the biosynthesis of nucleic acids and proteins.

My sincere thanks go to the many students and teachers who have written helpful letters since the first edition appeared. As before, I will continue to welcome comments and criticisms from all.

Sparks, Maryland A. L. L.
June 1971

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THE FLOW OF ENERGY IN THE BIOLOGICAL WORLD

Energy is most simply defined as the capacity to do work. There are different kinds or states of energy: potential, kinetic, thermal, electrical, and radiant energy, among others. There are also different kinds of work, such as mechanical, electrical, and osmotic work. The transformation of energy from one type to another and the efficiency of the conversion of energy into work are of central importance in the study of physics and chemistry. When the physical scientist studies a physical or chemical change the first questions he asks are: What forces caused the change to occur? Why did the change come to a stop? Could the occurrence and nature of the change have been predicted? These are very basic questions because every physical or chemical process is the result of the action of an unbalanced force, and a force, in turn, is the product or result of the movement of energy. From these considerations we see that all physical and chemical processes are ultimately the result of the application, movement, or transformation of energy. That area of physical science which deals with the exchanges of energy in collections of matter is known as *thermodynamics*.

Today, all scientists agree that the laws of physics and chemistry, including the principles of thermodynamics, also hold in the biological world: there can be no vitalism or black magic by which living organisms sustain and perpetuate themselves. Just as thermodynamics is the first and most basic way of analyzing processes involving inanimate matter, so is it fundamental in analyzing the behavior of living organisms. *Bioenergetics* is the term we use to designate the study of energy transformations in living organisms. As an introduction to bioenergetics, let us now survey, in this first chapter, the major processes in which energy is transformed in the world of living organisms. First we shall sketch the successive stages in the flow of energy through the biological macrocosm, and contrast the magnitude of the flow of biological energy on the face of the earth with the energy flow taking place in man-made machines. Then we shall consider energy flow in the biological microcosm, the individual cell. In succeeding chapters we shall examine each aspect of biological energy transformations in much more detail.

1–1 FOOD WEBS AND ENERGY FLOW

If we should trace the ultimate source of the energy utilized by any given organism in its natural habitat, let us say a fox in a given domain of woodland, we would find that there is a hierarchy of organisms, called a *food chain*, that provides the fox with the energy and materials required to sustain his life. This food chain might begin with the photosynthetic cells of green plants, which convert carbon dioxide into new cell material. The plant may in turn be consumed by insect larvae, which may in turn be consumed by toads or birds, which may in turn be consumed by the fox. In any given ecological community of living organisms, many individual food chains are interlocked into a *food web*.

Such a food web consists of several layers of organisms. First we have the *producers*, those cells that can utilize the simplest forms of carbon from the surroundings, such as carbon dioxide; then we have a primary layer of *consumers*, which feed on the producers, followed by further layers of consumers. Finally, to complete the cycle, there are the *decomposers*, the bacteria and fungi, which cause decomposition and decay of dead consumers and thus return simple forms of carbon to the soil and atmosphere.

Living organisms can be classified into two great groups depending on their position in the food web: *autotrophic* and *heterotrophic*. Autotrophic organisms (the name means "self-feeding") are those that can use simple forms of carbon, such as carbon dioxide, from which to build all their cell components. The "producers" at the bottom of the food web are autotrophs; they include many bacteria and algae, as well as higher plants. Heterotrophic organisms ("feeding on others"), on the other hand, cannot utilize simple forms of carbon, such as carbon dioxide, and require more complex forms—organic molecules such as glucose. The consumers and decomposers in the food web are heterotrophs, and they ultimately depend on autotrophs to generate the complex nutrients they require.

Now let us examine this food web and trace the sources of energy for each layer of organism. We will find that the great majority of the producers or autotrophic organisms obtain their energy from sunlight, which they use to convert carbon dioxide into more complex cell materials in the process of *photosynthesis*. Thus most of the producers are *photosynthetic autotrophs*. But when we examine the successive layers of consumers we find that none of them have the capacity to use light energy. Rather most of them obtain the energy they need by the combustion of complex organic molecules, such as glucose, obtained from the producers they consume. In this process, which requires oxygen and is called *respiration*, the simple, small carbon dioxide molecule is the end product. Heterotrophic cells, therefore, obtain energy by degrading complex nutrient molecules to simpler forms.

At each level in the food web, energy is expended to perform various kinds of biological work, such as synthesis of new cell material from simple precursors, movement of materials against gradients, and the work of contraction or motion. However, at each level in the food web we find that there are "friction" losses, so that each time some chemical or physical process occurs there is incomplete conversion of one kind of energy into another. As a result, some of the energy made available to each layer of organisms becomes dissipated in the environment and thus unavailable to do work. Only a small fraction of the solar energy absorbed by the producers in the bottom layer of the food web ever reaches the top layer of ultimate consumers. As these ultimate consumers die, and their tissues are degraded to simple organic products by the decomposers, energy is again lost and dissipated in the environment. Ultimately, then, the flow of energy that begins from the sun and courses through the biological food web finally becomes randomized in the environment (Fig. 1–1).

Now let us examine the three major steps in the flow of biological energy: (1) photosynthesis, (2) respiration, and (3) the performance of biological work.

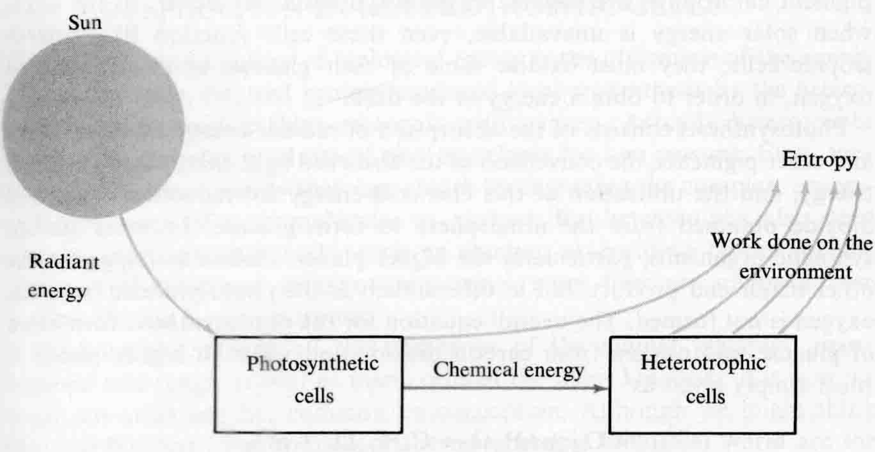

Figure 1–1. The flow of energy through the biosphere.

1–2 SOLAR ENERGY AND PHOTOSYNTHESIS

Visible sunlight, the source of all biological energy, is a form of electromagnetic or radiant energy, which ultimately arises from nuclear energy. In the immensely high temperature of the sun, which is believed to be several million degrees centigrade, a part of the enormous energy locked in the nucleus of hydrogen atoms is released as they are converted into helium atoms (He) and positrons ($_1e^0$) by thermonuclear fusion.

$$4\,{}^1H \rightarrow {}^4He + 2\,{}_1e^0 + h\nu$$

In this process a quantum of energy in the form of gamma radiation is released. The quantum is represented by the term $h\nu$, in which h is Planck's constant and ν is the frequency of the gamma radiation. After a complex series of reactions in which the gamma radiation is absorbed by the positrons much of the energy of the gamma radiation is emitted in the form of photons, or quanta of light energy. Ultimately then, nuclear fusion reactions in the sun are the source of all biological energy on the earth.

The term "photosynthesis" we tend to associate with the visible world of higher plants: grass, crop plants, and trees. But those macroscopic photosynthetic organisms actually make up but a small fraction of all the known organisms capable of photosynthesis. It has been estimated that some 90 per cent of all the photosynthesis on the earth is carried out in the seas by various kinds of microorganisms, including bacteria, algae, diatoms, and dinoflagellates.

There is another common misconception about photosynthesis in higher plants. Not all cells of a higher plant are capable of photosynthesis. The cells in the roots, stems, and fruits of plants are incapable of photosynthesis; they are heterotrophic and thus resemble animal cells. Only cells with the green pigment chlorophyll are capable of photosynthesis. Moreover, in the dark, when solar energy is unavailable, even these cells function like heterotrophic cells; they must oxidize some of their glucose, at the expense of oxygen, in order to obtain energy in the dark.

Photosynthesis consists of the absorption of radiant energy by chlorophyll and other pigments, the conversion of the absorbed light energy into chemical energy, and the utilization of this chemical energy for reduction of carbon dioxide obtained from the atmosphere to form glucose. In most photosynthetic organisms, particularly the higher plants, molecular oxygen is the other major end product, but in others, such as the photosynthetic bacteria, oxygen is not formed. The overall equation for the photosynthetic formation of glucose and oxygen from carbon dioxide and water in higher plants is most simply given as

$$6CO_2 + 6H_2O \rightarrow C_6H_{12}O_6 + 6O_2 \qquad \Delta G^{0\prime} = +686 \text{ kcal}$$

where the symbol $\Delta G^{0\prime}$ denotes the minimum amount of useful energy that must be furnished by absorbed sunlight to bring about the formation of 1 mole of glucose from one each of CO_2 and H_2O under standard conditions we shall describe later. In chemical thermodynamics the basic unit of energy is the *small* or *gram calorie*, the amount of energy required, in the form of heat, to raise the temperature of 1 g of water at 15.0°C by exactly 1.00°C. The *large calorie* or *kilocalorie* is equal to 1000 small calories.

The large amount of energy that is required to make photosynthesis occur is supplied by the light energy that is captured by the chlorophyll of the leaves. The photosynthetic equation may thus be rewritten to indicate that light quanta are the energy source, as follows.

$$6CO_2 + 6H_2O + n\,h\nu \rightarrow C_6H_{12}O_6 + 6O_2$$

This equation gives us only an overall statement of the photosynthetic process; it says nothing of the mechanism or pathway by which it occurs. Actually photosynthesis in plant cells is a far more complex process than this simple-looking equation might suggest. Although the complete molecular mechanism of photosynthesis is not yet known, there are probably more than a hundred sequential chemical steps in the photosynthetic production of glucose from carbon dioxide and water, each catalyzed by a specific kind of enzyme molecule.

Glucose is not the only product of photosynthesis. Other carbon-containing components of plant cells, such as cellulose, proteins, and lipids, are also produced during photosynthesis. All these substances, which are rich in chemical energy, are ultimately utilized as energy sources by heterotrophic organisms, that is, the consumers that feed on green plants.

1–3 RESPIRATION IN HETEROTROPHIC CELLS

The next stage in the flow of biological energy is the utilization of the energy of carbohydrate, fat, and protein produced in photosynthesis by the heterotrophs, which oxidize these materials with oxygen. Actually heterotrophs require the complex products of photosynthesis for two reasons. First, they need the chemical energy they can obtain by degrading the complex, energy-rich structures of such molecules as glucose. But heterotrophs also need complex carbon compounds, such as glucose, as building blocks for the synthesis of their own cellular components, since they are unable to use carbon dioxide for this purpose.

Heterotrophs include all the organisms of the animal kingdom, many bacteria and fungi, as well as many cells of the plant kingdom. But now we must put aside another common misconception. Although we might think that the familiar large animals of the macroscopic biological world are the predominant heterotrophs in the biosphere, nothing could be further from the truth. It is estimated that over 90 per cent of all the oxygen consumed by all heterotrophs is used by invisible microorganisms of the soil and seas.

Most heterotrophic cells use oxygen they take from the atmosphere to oxidize glucose and other nutrients to form the stable end products carbon dioxide and water. However, some heterotrophs are unable to use oxygen; they degrade glucose to simpler compounds, such as lactic acid, in the absence of oxygen, in the process called *fermentation*. Fermentation products such as lactic acid are ultimately oxidized to CO_2 and H_2O by still other heterotrophic organisms, particularly those that use oxygen. Ultimately, therefore, the cells of the heterotrophic world bring about the complete oxidation of organic nutrients produced by autotrophs, to the end product carbon dioxide. The total process by which foodstuff molecules are ultimately oxidized by heterotrophic cells at the expense of oxygen is referred to as *respiration*.

The chemical equation for oxidation of glucose during respiration is

$$\text{glucose} + 6O_2 \rightarrow 6CO_2 + 6H_2O$$

$$\Delta G^{0\prime} = -686 \text{ kcal}$$

We see immediately that this equation is the reverse of that for photosynthesis. Moreover, we note that the complete combustion of 1 mole of glucose can yield a maximum of 686 kcal of useful chemical energy. This is not necessarily the actual yield of work realized by the heterotrophic cell; it is only the theoretical maximum that can be obtained if we have a completely efficient, frictionless machine to harness the energy yielded from the combustion of a mole of glucose.

Although the chemical equation of respiration looks simple, it does not tell us anything of the mechanism or pathway of respiration in heterotrophic cells. Actually there are more than seventy sequential chemical reactions in the oxidation of glucose in heterotrophic cells.

1–4 BIOLOGICAL WORK

We come now to the last great stage in the flow of biological energy, the utilization of chemical energy to do different kinds of cellular work. All living organisms must do work of one kind or another merely to stay alive in an environment that is essentially hostile to them. Some organisms, such as higher vertebrates, may do work on their environment to make it less hostile, whereas others, such as bacteria, overcome the effects of a hostile environment by multiplying rapidly. There are basically three types of work done by living organisms: chemical work, concentration work, and mechanical work.

Chemical work is done by all cells, not only during active growth but also to maintain themselves. The macromolecular components of cells, such as the proteins, nucleic acids, lipids, and polysaccharides, are continuously synthesized from small building-block molecules by the action of enzymes. These processes are collectively called *biosynthesis*. Biosynthesis occurs not only during growth of an organism, when there is a net formation of new cellular material, but also in nongrowing, mature organisms. In the latter, the carbohydrates, proteins, and lipids are constantly being synthesized and degraded in such a way that the rate of formation of the new molecules is exactly balanced by the rate of degradation of the old. Most of the molecular components of living cells exist in such a dynamic steady state.

Whenever we put together a large, ordered structure from simple, randomly disposed units, whether it is a macromolecule or a brick wall, energy is required. To construct a protein molecule, hundreds of individual amino acid molecules must be assembled in the correct sequence and joined in peptide linkage by the action of specific enzymes. To construct a polysaccharide molecule, such as cellulose or starch, hundreds of glucose molecules must be joined in glycosidic linkage. The overall equation for biosynthesis of such macromolecules may be written in generalized form as

$$n(\text{building blocks}) \rightarrow \text{macromolecule} + nH_2O$$

Such biosynthetic reactions, which proceed with loss of water as the building blocks come together, are highly endergonic in the aqueous medium of the cell; they are "uphill" reactions. In Table 1–1 are shown the amounts of useful or free energy required in the biosynthesis of the major types of bonds linking the building blocks of various cell macromolecules.

The second type of cellular work is that required to transport and concentrate substances; it is often, but less accurately, called osmotic work. This kind of work is less conspicuous to us than the mechanical work of contraction or the biosynthetic work involved in cell growth, but it is of equal importance in cell function. All cells are capable of accumulating certain essential substances from the environment, either minerals such as potassium, or nutrients such as glucose, so that their intracellular concentration may be much higher than in the medium outside the cell. Conversely, unwanted or deleterious substances may be actively pumped out of the cell, or *secreted*, even when the external concentration of the substance is much higher than the internal. Such movements of molecules against gradients of concentration cannot occur spontaneously, since solute molecules normally tend to distribute themselves in all the space available to them, so that they are completely randomized in it. The term *active transport* is applied to the energy-dependent movement of solute molecules against their tendency to randomize. Through the action of active transport "pumps" in their membranes, cells can maintain