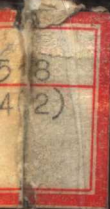# Principles of Animal Physiology

SECOND EDITION

Dennis W. Wood

CONTEMPORARY BIOLOGY

Principles of Animal Physiology

Second Edition

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Preface to the Second Edition

The welcome accorded to the first edition suggests that it filled a definite gap in the provision of textbooks in this field, and in revising it I have tried to resist the temptation to add too much material in such a way that its scope and content would be altered. At the same time, new work and the experience of using the book in the teaching of undergraduates have made it necessary to carry out some revision of most chapters; and more extensive revision of those parts that have been the subject of considerable advances in recent years, such as cell structure and function and the structure and function of muscle. Apart from the revision of existing material, some sections have been deleted and others added. The latter include material on enzyme kinetics, renal organs, air-breathing aquatic animals, hormones and cyclic AMP. There are several new figures, and some other figures have been revised.

With some reluctance all units have been changed to the Système International. The formulation of the SI system appears to have been dominated by physical scientists, and I regret the failure to retain the Ångstrom unit (or a named equivalent) and the calorie. I have taken advantage of the permission granted during the transitional phase of change to SI units to include in brackets the calorific equivalent of joules where this seemed appropriate.

I am grateful to all those who took the trouble to write and point out errors in the first edition, or to suggest improvements; and to my colleagues Drs Anstee, Bowler and Hyde, who read certain old or proposed new sections and gave me the benefit of their specialist knowledge and advice.

D.W.W.

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I

Introduction

Physiology is the analysis of function in living organisms. Because these are composed of chemical substances, the analysis involves the application of the laws of chemistry and physics, and there is no need to invoke a special 'vitalistic principle' to explain how living organisms work, although this does not mean that other ways of looking at life are either wrong or invalid.

Physiological processes are exceedingly complex, being the sum of many interrelated reactions. For this reason, animals have often been able to change some of the details of their physiology through the play of selection on genetic mutation, although there remains a striking uniformity of principle and often of detail in fundamental physiological phenomena. This has enabled some authors to make a distinction between *general* physiology—the study of fundamental processes in terms of chemistry and physics; and *comparative* physiology—the attempt to discern functional similarities and differences between gross systems of whole organisms. The distinction may sometimes be convenient, but it is artificial because it is impossible to understand the functioning of the whole organism without a thorough knowledge of fundamental processes, and this book makes no attempt to separate the two approaches.

Thus, the initial approach of the physiologist must be to analyse physiological processes in terms of the individual reactions which comprise them, and then to put them together to make an intelligible picture of the whole process. This approach has yielded valuable information, but it is necessary to remember that the integration of individual reactions into a complete process may involve their modification, and the development of properties that are peculiar to the overall process but which cannot

necessarily be deduced from a study of the individual reactions. A chemical parallel is the way in which molecules possess properties of their own which are not exhibited by the atoms they contain when these exist independently.

One way of trying to understand a complex system is to formulate a *model* that will exhibit the same properties. Thus we may describe an excitable membrane in terms of an equivalent electrical circuit or draw analogies between the contractile mechanism of a muscle and a damped spring. Such models may be misleading if the analogies are pressed too far but, properly used, they can help to clarify thought, and to suggest further experiments which will aid in the testing of the concepts on which they are based.

Physiology, like all natural sciences, lives and feeds on experiment. We begin the study of a system by accumulating descriptive information about it, and when there is a sufficient quantity of that we erect a hypothesis to explain it. This hypothesis must then be tested by experiment, and if the results of our experiments conform to our hypothesis, it will become a theory which gains a wide measure of acceptance, and which will stand unless and until some piece of information is obtained which does not seem to be in accordance with it. Then it must either be modified or a new theory formulated. In biological research we rarely know all the facts about a situation, and hypotheses are erected on the basis of the weight of the evidence, which may shift as more data is accumulated. The topics dealt with in this book are often in this exciting and stimulating state, and new information about many of them is published daily. Nevertheless, it is sometimes surprising to find how many of the basic ideas remain unchallenged over the years.

Physiological processes often possess an intrinsic interest of their own for anyone who enjoys the feel of precision and order, and may even be held to exhibit a kind of elegance and beauty for this reason. But the primary aim of physiologists must be to understand the relationship between the living organism and its environment. This book therefore begins with a consideration of the energy relationships between organisms and their environment, because it is their use of energy that distinguishes animate organisms from inanimate matter. This leads us naturally to the nutritional requirements of animals, which obtain their energy by ingesting solid food, from which we turn to the organization and functioning of the cells since it is their job to deal with the raw materials obtained through feeding. This involves a consideration of the cellular oxidation of metabolites, and thence of more general topics relating to metabolism such as respiration and excretion. With this basis, the relationship between animals and various environmental factors such as temperature, pH and the supply of water can be examined.

One feature that emerges from the consideration of such topics is that animals tend to be adapted to a particular kind of environment, and their behaviour is therefore directed towards remaining in this environment as far as possible. To do this they must be able to detect various environmental characteristics and to react to changes in them with appropriate responses. The final chapters are therefore concerned with the mechanisms of nervous integration and the various effector systems used by animals in responding to their environment. The last chapter seeks to look back in general terms over the ground covered and to find whether there are some features of the physiological processes through which animals maintain more or less constant living conditions which are common to them all.

2

Energy and Food

Animals need food for growth and for the energy to maintain their
bodies in the living state, and hence to behave in those ways that we con-
sider to be characteristic of living organisms. Since the processes re-
sponsible for growth also require a supply of energy to drive them, it is
evident that the fundamental requirement of the food intake of any ani-
mal is that it should contain foods which may be used as fuels, for the
liberation of energy. Elementary books of biology often attempt to define
'life' in descriptive terms, but the real difference between living organ-
isms and non-living matter lies in the way they utilize energy. Although
both obey the same physico-chemical laws, they differ in the way these
apply to them.

ENERGETICS OF MATTER

2.1 Energy

Energy is often defined as the capacity to do work, although this defini-
tion applies fully only to systems not encountered in practice. *Work* is
defined as the product of a given force acting through a given distance,
which implies that movement takes place when work is done. Two fac-
tors are involved in the production of this movement: an intensity factor
(the force), and a capacity factor (the distance). The intensity factors in,
for example, stretching, the passage of an electrical current, and expansion
are tension, voltage and pressure respectively. The corresponding capa-
city factors are length, charge and volume. These definitions apply equally
well to other forms of work, but not to heat, although this is also a form
of energy. Heat possesses no capacity factor to match its intensity factor,

temperature. Nor does the production of heat obviously result in the performance of work, although it can certainly be converted into mechanical energy, as in a steam engine, and thence into other forms of energy. The conversion, however, as we shall see below, is never 100% efficient. These preliminary considerations are sufficient to show that heat occupies a special position in energetics.

The energetics of systems is governed by the laws of *thermodynamics*. These are three in number, but the third is really an extension of the second, and being concerned with events at absolute zero temperature, will not concern us here. It should be emphasized that no special ability is required for an understanding of the basic concepts of thermodynamics, which exhibit the stark simplicity of most fundamental scientific laws.

2.2 First Law of Thermodynamics

This states that *the energy of the universe remains constant*. Thus, although one form of energy may be converted to another, none is lost in the process. This does not mean that a given system may not lose energy to its surroundings, for the law is concerned simply with the total energy of the universe. Nor does it imply that all forms of energy are equally useful, a subject covered by the Second Law. It is convenient to distinguish between *potential* energy, which is the inherent capacity of a system to do work, and the *kinetic* energy that is actually expended in the performance of work. The difference is well illustrated by a car at rest and in motion. When the car is at rest, and provided that it has petrol in its tank, it possesses potential energy although it is not doing work. When the car is moving, the potential energy is being converted into kinetic energy, and at the end of the journey there is less potential energy in the system than there was at the beginning, a loss largely represented by a decrease in the quantity of petrol in the tank. It should be noted that the potential energy of the system has been converted into heat as well as into kinetic energy. It is universally true that under normal conditions the conversion of potential energy into kinetic energy always involves the production of heat, which escapes into the surrounding medium and hence represents a waste of some of the potential energy.

2.3 Second Law of Thermodynamics

This law, which may be stated in a variety of forms, is concerned with the *probability* that a particular energy change will take place. It states that matter tends towards disorderliness rather than orderliness, because orderliness in matter is always accompanied by a high degree of potential energy; and there is a perpetual tendency for the potential energy of systems to become converted into kinetic energy and heat. The kinetic energy will be used to perform work, but in the course of this work, it will

become effectively lost to the system. If it is used to convert a compound into some other compound with some potential energy of its own, the conversion will have been accompanied by the loss of some of the original potential energy as heat, and so the potential energy of the new compound will always be less than that of the original compound. And the new compound, in turn, will follow the same trend as the one that produced it. The heat produced could, in theory, be used to provide more work, by means of a heat engine, of which the steam engine is one example. But this conversion can never be 100% efficient, because a heat engine functions by taking heat from a source and rejecting it to what is known as a 'sink', i.e. to an area of less heat. The very mechanism of conversion therefore depends on the loss of some of the heat. The trend is clear: unless heat is supplied to a system from an external source, its potential energy will be reduced through its conversion into other forms of energy which will be lost.

2.4 Entropy

The transformation of order into disorder involves the breakdown of an ordered-pattern into randomness. Translated into terms of the breakdown of molecules, it implies the tendency of large molecules to break down into smaller ones, until ultimately the original potential energy of the system has been converted into the random movement of small molecules. Energy in a random disorganized state in which it simply functions as the kinetic energy of the random movement of molecules is known as *entropy*; and a common way of stating the Second Law of Thermodynamics is that *all processes tend towards maximum entropy*. Any reaction that will increase entropy will therefore tend to be thermodynamically *spontaneous*. This does not mean that it will happen automatically and immediately, but that if the conditions are right it is this reaction that will proceed and not the opposite one. Thus, the Second Law tells us the *direction* in which a reaction will normally proceed.

Chemists normally deal with what is known as a *closed* system—one in which the amounts of the initial reactants is specific and fixed. In such a system, the result of an energy change in accordance with the Second Law is given by

$$\Delta E = Q + W \qquad (2.1)$$

where ΔE is the change in the energy of the system, Q represents the heat given off, and W the work done. The heat Q will exchange with its surroundings, since a closed system has fixed reactants but is not insulated from its environment. Equation *2.1* is sometimes written with a minus sign in front of W, an alternative which emphasizes that a change in energy may be positive or negative (gained or lost), depending on the con-

ditions in which the reaction takes place. The clear conclusion from equation 2.1 is that any flow of heat between a system and its surroundings must be accompanied by changes in the energy content of the system and in the work done by it on its surroundings.

2.5 Enthalpy

A change in heat between a system and its surroundings is called enthalpy, and given the symbol ΔH. In terms of enthalpy, equation 2.1 can therefore be rewritten

$$\Delta E = \Delta H + W \qquad (2.2)$$

The performance of work in a chemical system implies that changes in pressure and volume must be occurring. If the volume and pressure can be kept constant, however, then

$$\Delta E = \Delta H \qquad (2.3)$$

In fact, volume and pressure changes are negligible in living cells, and it is this equation which applies to them. It can also be arranged, by suitable techniques, to apply to the combustion of substances in the process of *direct calorimetry*, in which the potential energy of a substance is converted entirely into heat, which is measured. Thus, the energetics of living cells and the energy potential of individual compounds can both be considered in terms of heat changes. For this reason, it is customary to refer to changes in the energy content of a biological system as changes in heat. Formerly, the calorie was the unit of measurement (the amount of heat needed to raise 1 g of water by 1°C, between 14.5°C and 15.5°C), but this has now been superseded by the *Joule* (1 cal ≡ 4.19 J). Biological reactions usually involve large heat values, and these are dealt with in kiloJoules (kJ).

2.6 Free energy

It will now be appreciated that every physical and chemical event is dictated by its energy relationships, and that the Second Law gives guidance about the probability that a given change will take place. It is often difficult to work out the full energy relationships of such a change, and for this reason a further concept has been introduced, that of *free energy*, denoted by F. Free energy is the energy that can be obtained as useful work during a change in a system. In other words, it is the energy that can be 'freed' or liberated during the course of such a change. The useful energy obtained during a reaction will be equal to the total energy change less the entropy, i.e.

$$\Delta F = \Delta E - T\Delta S \qquad (2.4)$$

where ΔF is the change in the free energy of the system, or the extent of

the conversion of useful energy, and $T\Delta S$ represents the change in entropy (the energy degraded to heat). S is the symbol for entropy and T refers to the temperature of the reaction.

In practice, a modified concept of free energy is often used, known as *standard free energy* and denoted variously in textbooks by the symbol F°, ΔG and F'. In the generalized reaction

$$A \rightleftharpoons B \tag{2.5}$$

in which the reactant A is converted into the product B, the free energy change may be expressed by the equation

$$\Delta F = \Delta F^\circ + RT \log_e \frac{B}{A} \tag{2.6}$$

where R is the gas constant (8.3 J mole^{-1} degree^{-1}), T the absolute temperature and A, B, the molar concentrations of the reactant A and the product B. Let us now consider the special case when the system is at equilibrium. In this situation there is no conversion of A to B, and from this two consequences follow. The first is that the reactant A and the product B can be represented by an equilibrium constant, i.e.

$$\frac{B}{A} = K_{eq} \tag{2.7}$$

Secondly, since no conversion is taking place, there is no further change in free energy in the system, and $\Delta F = 0$. Thus, for the system at equilibrium, we may rewrite equation 2.6 as

$$0 = \Delta F^\circ + RT \log_e K_{eq}$$

which when re-arranged, becomes

$$\Delta F^\circ = -RT \log_e K_{eq}.$$

Since R is a constant, T is constant for a given temperature, and Napierian logarithms can be converted to base 10 logarithms by multiplying by 2.303, the equation can be further simplified:

$$\Delta F^\circ = -(8.3 \times 2.303)\ T \log_{10} K_{eq}$$
$$= -19.1\ T \log_{10} K_{eq} \tag{2.8}$$

It will be evident from equations 2.7 and 2.8 that if the concentrations of reactants and products in a system at equilibrium are known, K_{eq} and hence ΔF° can be calculated.

In the ideal case in which 1 mole reactant is converted to 1 mole of product, the K_{eq} would be unity, and since the logarithm of one is zero, in this situation $\Delta F^\circ = 0$. When K_{eq} is less than unity, since the logarithm

of a fraction is negative, ΔF° must be positive; and the smaller the value of K_{eq} the greater will be the positive value of ΔF°. Conversely, if the K_{eq} is greater than unity, ΔF° will be negative, increasing in negative value as K_{eq} increases. Tables showing the numerical relationship between ΔF° and K_{eq} can be found in many text-books of biochemistry.

Reference to equation 2.7 shows than when ΔF° is positive, more A is present than B, in other words the reaction is proceeding in the *backward* direction; when ΔF° is negative, the reaction is proceeding in the *forward* direction. Reactions in which ΔF° is positive (K_{eq} less than unity) are known as *endergonic*, because they will proceed spontaneously in the reverse direction, starting with unimolar concentrations of reactants and products. To make them proceed in the forward direction, energy must be supplied to the system from an external source. When ΔF° is negative (K_{eq} greater than unity) the reaction will proceed spontaneously in the forward direction, with liberation of energy, and is then termed *exergonic*.

A practical example will help to illustrate these concepts. One of the stages in the breakdown of glucose in the cell is the rearrangement of the phosphorylated glucose-1-phosphate configuration to the glucose-6-phosphate configuration, by the action of an enzyme *phosphoglucomutase*. For a substrate concentration of 0.02 M at 25°C, and provided excess enzyme is present, it is found that the final equilibrium mixture contains 0.001 M glucose-1-phosphate and 0.019 M glucose-6-phosphate. Exactly the same molar concentrations result if the substrate is glucose-6-phosphate and the reaction is allowed to proceed the other way round. Hence,

$$K_{eq} = \frac{0.019}{0.001} = 19$$

and since this is greater than unity, we shall expect ΔF° to be negative. Using equation 2.8,

$$\Delta F^\circ = -19.1 \times 298 \times \log_{10} 19$$
$$= -7305 \text{ J } (-1745 \text{ calories})$$

This is therefore a reaction that tends to proceed in the forward direction.

From the point of view of thermodynamics, then, reactions will tend to take place spontaneously in the direction indicated by the sign of ΔF°. It has already been pointed out that such reactions are not necessarily spontaneous in the literal sense. Some are, but it will be found that the value of ΔF° in these cases is relatively high. Many reactions which have a negative ΔF° nevertheless require some help to get them going. In the majority of cellular reactions, a catalyst is required for the change to occur, and in all living systems the necessary catalysts take the form of *enzymes*. The nature of enzymes, and the way they facilitate reactions, is discussed in §3.13. For the present, we need note only two facts about them. The