Thermodynamics of Biological Processes

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with 69 Figures

This collection surveys current problems in the thermodynamics of non-linear irreversible processes and the applications of thermodynamics in biology. Problems concerning the theoretical and experimental substantiation of the phenomenological theory of development, growth and aging of organisms are discussed, and experimental data are presented on oogenesis, animal development and growth, and on heat production and energy metabolism during the growth of microorganisms in culture. The concluding chapters treat modern theories of dissipation structures, problems of progressive evolution and the classification of animals.

This monograph will be useful to biophysicists, physiologists and embryologists as well as to physicists and mathematicians interested in modern problems in thermodynamics and the application of this field to biology.

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Preface

The main difficulty, as we see it, is that thermodynamics, as
a general phenomenological theory of all processes that are
accompanied by a dissipation of energy, is far from complete.
True, two large divisions of thermodynamics (the theories of
reversible and linear irreversible processes) are now well
established; but the theory of non-linear irreversible proces-
ses is still at the onset of its development. Among the main
approaches under consideration are the creation of variational
principles of thermodynamics, the application of the basic
concepts of Prigogine's local thermodynamics theory to non-
linear processes, using the theory of graph, the generalized
reciprocal relations and global characteristics, and stochastic
considerations of thermodynamics processes. At present it is
rather difficult to say which of these trends will take hold as
a basis for the thermodynamics of non-linear irreversible pro-
cesses. Yet it is quite obvious that work of this kind is es-
sential to our understanding of phenomena occurring in systems
far from equilibrium, particularly in living systems. Some data
in biology suggest that the thermodynamics of irreversible pro-
cesses could be used as a tool for solving the most important
problems in physiology, biochemistry and developmental biology.

It should be noted that the introduction of thermodynamics
into biology was long delayed because no satistactory methods
were available for measuring slow heat flows. It was not until
recent decades that sensitive microcalorimeters were designed
and came into common use. It is hoped that their wide distri-
bution and extensive deployment will help create a reliable
experimental basis for the thermodynamics of biological pro-
cesses.

This monograph resulted from a cooperative effort between two
laboratories: the Biophysical Laboratory of the Central Insti-
tute for Biochemistry and Biophysics at the Free University,

West Berlin, and the Laboratory of Developmental Biology of
the Academy of Sciences of the USSR. Each contributor to this
volume is in some way connected with one of these two labora-
tories. As we could hardly embrace all the fields of biology
in which thermodynamics of irreversible processes may be
applied, we confined ourselves to the problems which are being
studied in our laboratories. Accordingly it should be empha-
sized that the main theories discussed in the book are based
on the global approach to non-linear irreversible processes,
most of the authors being adherents of this approach which is
discussed in considerable detail and substantiated in the first
chapters.

The material presented was thoroughly discussed beforehand
at the theoretical physics seminars of the Physical Institute
of the Academy of Sciences of the USSR, at various seminars
and colloquia in the same academy's Institute of Developmental
Biology, in the Society of Mathematical and Physical Biology
of the German Democratic Republic, and in the Central Institute
of Biochemistry and Biophysics of the Free University, West
Berlin. We are most grateful to a number of colleagues for
these fruitful discussions.

Doubtless a book such as this, being devoted to a science at
the very beginning of its development, will contain inaccura-
cies or even outright mistakes. The authors will be very grate-
ful for all critical remarks aimed at removing these unavoi-
dable defects of their work.

I. Lamprecht, A.I. Zotin

I. General Problems of Biological Thermodynamics

None of the fields of theoretical physics is so closely connected with biology or gives such an effective description of the life processes as thermodynamics. Although mechanics, hydrodynamics, electrodynamics and optics are widely applied in biology, they describe phenomena which are not as characteristic of the living systems as heat production and the process of metabolism concerned with it.

Modern thermodynamics also includes other concepts extremely important for biology such as "time arrows" (see Popper, 1965, 1967 a, b) or various evolution criteria specifying the direction of the changes of thermodynamic systems (Glansdorff, Prigogine, 1964, 1971; Prigogine, 1966; Nicolis, 1971; Zotin, 1972, 1974; Presnov, 1973). In spite of this, the problems of applying individual fields of thermodynamics in biology are still open to discussion (Lazarev, 1945; Schrödinger, 1945; Ubbe-lohde, 1947; Brillouin, 1949, 1955; Raymond, 1950; Pasynsky, 1953, 1963; Touloukian, 1956; Volkenstein, 1958, 1965, 1973; Wilkie, 1960; Bernhard, 1964; Morrison, 1964; Riegel, 1965; Calloway, 1966; Blum, 1967; Molchanov, 1967; Trintscher, 1967; Antonov, 1968; Morowitz, 1968, 1970; Kobozev, 1971; Rebane, 1972; Zotin, 1971, 1972, 1974; Blumenfeld, 1974; Pritz, 1974; Chernavsky, 1975; Nikolaev, 1976).

The applicability of the concepts of classical thermodynamics and thermodynamics of linear irreversible processes to some biological phenomena are reviewed below, and basic concepts of the so-called global theory of non-linear irreversible processes are presented. Much of the theoretical and experimental work presented in this book rest upon this global theory.

Application of the Concepts of Classical Thermodynamics in Biology

I. Lamprecht

Thermodynamics was born 200 years ago when Lavoisier's experiments on the oxidation broke with Stahl's theory of phlogiston. At the very beginning of this development, there were calorimetric measurements on the heat production of small animals in an ice calorimeter of the Lavoisier-Laplace-type. This strong connection between biology and thermodynamics was never broken, and two physicians made the first steps toward a modern theory of energy: Mayer and Helmholtz with their formulation of the first law of thermodynamics. Half a century later, Rubner in Berlin demonstrated the validity of the first law in biology with his experiments on the metabolism of microorganisms - and nowadays living matter is one of the favoured topics of both classical thermodynamics and (more recently) the thermodynamics of irreversible processes. There is no question that just this theory leads to deeper understanding of living matter and predicts developments which are not comprehensible in other ways. In this chapter we shall introduce the characteristic thermodynamical quantities and explain their connection with biological processes.

Internal Energy U

Although there exists a mathematical, axiomatic deduction of thermodynamics which postulates the existence of variables of state as consequence of the different laws, we shall follow a more empirical approach, and define the quantities and regard the first and second laws as prooved by experience.[+]

[+] M. Planck formulated that the sad fate of the would-be inventors of the perpetuum mobile is the strongest proof for the truth of the first law.

If a system, separated by fixed or movable walls from its environ-
ment, undergoes a change of state, this might involve a flow of heat to or
from the system and work done by or on the system. If a negative sign is
assigned to energy which is delivered to the surroundings, the influx of
heat is Q, while the work on or produced by the system is A. There
exists a variable of state, the internal energy U, which combines these
two parameters in the equation:

$$\Delta U = \Delta Q + \Delta A \tag{1.1}$$

Very often the work done is an expansion of a gas against an outside
pressure. Following the Boyle-Mariotte law we find:

$$\Delta A = -p\Delta V$$

and inserting this value in (1.1):

$$\Delta U = \Delta Q - p\Delta V \tag{1.2}$$

By integrating (1.2) we could obtain the value of the internal
energy U, but in the most experiments we are only interested in the
change ΔU, when the system passes from a state 1 to a state 2. The
value of ΔQ is measured calorimetrically, while the following term
may be obtained by calculation for a known reaction or by manometric
experiments. Therfore, we have to distinguish three different cases:
a) The calorimetric vessel is open to the surrounding, so that no change
   in pressure can occur, i. e. $\Delta p = 0$.
b) The calorimetric vessel is closed, the pressure changes ($\Delta p \neq 0$),
   but the volume stays constant, i. e. $\Delta V = 0$.
c) Although one of the two cases a) and b) must be fullfilled, we have
   $\Delta V = \Delta p = 0$, if no gaseous parts are involved in the observed re-
   action.

Let us explain these differences with a simple example of great
importance in biology. During glycolysis the sugar glucose is decom-
posed by a chain of enzymes to ethanol or to lactic acid. In the first

case, the reaction follows the equation:

$$C_6H_{12}O_6 \longrightarrow 2C_2H_5OH + 2\ CO_2.$$

For simplicity, we take one mole of sugar dissolved in one liter of water which is contained in a two liter vessel. If it is open to air ($\Delta p = 0$), we have to calculate ΔV, which for two moles of the gas is 2 x 22.4 liter = 44,800 cm^3. With a normal pressure of 760 mm Hg we get:

$$-p\ \Delta V = 1,013\ kp/cm^2 \cdot 44,800\ cm^3 = 454\ mkp = 4,450\ J = 1060\ cal.$$

The heat exchanged in this process is ΔQ = -17 kcal/mole, so that the total change in internal energy is:

$$\Delta u = \Delta Q - p\Delta V = 67\ kJ/mole\ .$$

It was assumed in our calculation that the water was saturated by carbon dioxide so that none of the gas generated went into solution. The role of work is small and negligible in most biological experiments.

When glucose is metabolized to lactic acid the reaction is:

$$C_6H_{12}O_6 \longrightarrow 2CHOHCOOH$$

with no production of gas. The change of the internal energy equals the production of heat, which amounts to -151 kJ/mole = -36 kcal/mole.

The error due to neglecting work in the energy calculation increases with the amount of gas produced. In the case of respiration of glucose, 6 moles of carbon dioxide are formed for each mole of glucose. The effect of work is thus threetimes as high as when ethanol is produced, but as the change in internal energy ΔU = -678 kcal/mole, the energy contribution from work is negligible.

Equation (1.1) is one formulation of the first law of thermodynamics: that all energy added to the system is to be found in the internal energy. More impressively, energy is neither created nor destroyed. This law, first formulated for physical (e. g. gaseous) systems, was successfully checked for biological entities as well. Rubner showed at the beginning of this century, in a series of papers for microbial cultures, that the energy content of the nutrient was completely divided into three parts, the sum of which remains constant: the energy wasted as heat and trans-

mitted to the surroundings, the energy stored as cell material (measured by bomb calorimetry) and the energy left in the medium as metabolites.

Lateron Sedlaczek (1964) repeated this measurement with higher accuracy for various bacteria, such as E. coli, P. vulgaris, S. aureus and P. fluorescens. He compared the decrease in heat content (measured as heat of combustion) between the initial and the final medium with the sum of energy converted to heat and the heat of combustion of the bacterial crop. Let us consider one example, the growth of E. coli:

heat of combustion of the initial medium	- 17,338 cal
heat of combustion of the final medium	- 16,264 "
difference	1,074 "
heat of combustion of bacterial crop	- 528 "
energy converted to heat during growth	- 468 "
	- 996 cal

There is a discrepancy of 1,074 - 996 = 78 cal or 7.3 % of the calculated heat, but when we take into account that the decrease in energy content is found as a small difference between two large figures, the discrepancy is negligible (78 cal of 17,338 cal are just 0.4 %). The experiments are in full agreement with the first law.

Enthalpy H

As shown above, the change in internal energy might be due to a heat flux and an expansion of gas against an outside pressure. This energy is called the work of volume. As it is essential in all reactions combined with a production of gas, a new function is defined by:

$$H = U + p.V \tag{1.3}$$

which is called the enthalpy of the system. In differential form we may write:

$$\Delta H = \Delta U + \Delta(p.V) = \Delta U + V\Delta p + p\Delta V$$

and together with (1.2)

$$\Delta H = \Delta Q - p\Delta V + V\Delta p + p\Delta V = \Delta Q + V\Delta p . \qquad (1.4)$$

In the case that the pressure does not change during the experiment (i. e. that the vessel is open in a biological calorimeter), Δp equals zero and the change in enthalpy is the heat consumed or produced in the reaction. As in most reactions, the pressure stays constant, the increase in enthalpy is the heat of reaction of the process.

We have pointed out above that the amount of work energy is small compared with the heat. Therefore, the values obtained for the internal energy are nearly the same as for the enthalpy; or put another way, although calorimetry evaluates heat exchanges, these values can be taken for the enthalpy, too.

Temperature T

Before we explain the next thermodynamic variable of state, the entropy, we have first to introduce the temperature, well known from the daily life. In contrast to internal energy, enthalpy and entropy, temperature is an intensive quantity which characterizes the state of a system. By definition two bodies in contact have the same temperature (independently of the scale used) if there is no heat exchange between them.

Normally two different scales for temperature are used: the Celsius scale with 100 centigrade between the two fixed points of water and the Kelvin scale with only one fixed point (triple point of water) set equal to 273.15 K above absolute zero. It has recently been recommended that only this scale should be used.

Temperature is a very important parameter for living systems. Although one is usually interested only in changes in internal energy and enthalpy, one needs to know the absolute value of the temperature rather than the change in temperature.

Normal life is bound to a very small region of temperature, per-

haps (let us say) between 10 and 40 degrees centigrade. Some higher organisms have developed special systems to withstand extreme temperatures, i. e. between -100° C and perhaps +55° C at the upper end. However, thermophilic organisms are known, especially bacteria and algae, which are so well adapted to their biotops that they even grow near +100° C, and one believes that life may exist as long as liquid water is present. On the other hand, the freezing of water at lower temperatures limits life at the lower limit, although the freezing point may be shifted by high concentrations of salts or organic substances.

Entropy S

A very essential but often misused and misinterpreted thermodynamic value of state is the entropy of the system, an extensive figure like internal energy, enthalpy and volume. If at a given temperature T an amount Q of heat is exchanged with the surroundings, it is accompanied by a reversible change in entropy:

$$\Delta S = \Delta Q / T.$$

According to the second law of thermodynamics, total entropy can not diminish in an isolated system. In the ideal reversible experiment it stays constant (being a function of state!), but in all real isolated systems, the entropy tends to reach a maximum. In this way, the increase in entropy is closely connected to the passage of time; it is "time's arrow".

Boltzmann was able to explain this tendency of entropy to attain a maximal value by his statistical theory. He showed that entropy is combined with the probability P_T of a state by the equation:

$$S = k \ln P_T \tag{1.5}$$