



# THE FRONTIERS COLLECTION

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## THE FRONTIERS COLLECTION

### *Series Editors*

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Alexander S. Mikhailov · Gerhard Ertl

# Chemical Complexity

Self-Organization Processes in Molecular  
Systems

 Springer

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# Preface

A concise definition of *complexity* might be: “The whole is more than the sum of its constituents”. Usually, chemistry is concerned with the interactions between individual atoms or molecules, and such interactions can lead to the formation of condensed matter with a high degree of the “dead” order at equilibrium. But the experience tells us that, in biological systems, quite different other processes of order formation may take place, prompting in the beginning of the twentieth century even to ask whether new physical laws had to be found in order to explain such “living” order. Since the lectures on “What is Life?” held by E. Schrödinger in 1943, one knows that this is not needed and that self-organization phenomena can also be observed in rather simple inorganic systems with only small reacting molecules if these systems are out of thermal equilibrium.

Our book intends to provide an outline of underlying theoretical concepts and their experimental verification, as they emerged in the middle of the twentieth century and evolved afterwards. In its style, the book can be regarded as a series of essays on selected topics. Their choice is determined by personal preferences of the authors and reflects their research interests. We do not aim to present a systematic introduction and to review the entire discipline. Particularly, the list of literature references is far from being complete. Since our focus is on the concepts, not methods, mathematical aspects are moreover only briefly touched.

Today, the field is in the state of intense research and much attention is paid to it, as evidenced, for instance, by the Nobel Prize in Chemistry of 2016 for studies of molecular machines. Some of the topics are rapidly developing and are vividly discussed. Nonetheless, we tried not to be biased towards them. In our opinion, it became important to look back and to analyze what has been done since E. Schrödinger has posed his question, and whether we already have an ultimate answer to it.

While finishing the book, we want to emphasize how much we owe to discussions and collaborations with our colleagues, and we would like to express our deep gratitude to all of them. The series of conferences on “Engineering of Chemical Complexity”, organized by the Berlin Center for Studies of Complex Chemical Systems, has contributed much to the present work.

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# Contents

<b>1</b>	<b>From Structure to Function: An Introduction</b> . . . . .	1
<b>2</b>	<b>Thermodynamics of Open Systems</b> . . . . .	5
	References . . . . .	14
<b>3</b>	<b>Self-assembly Phenomena</b> . . . . .	17
	References . . . . .	28
<b>4</b>	<b>Self-organized Stationary Structures</b> . . . . .	31
	References . . . . .	45
<b>5</b>	<b>Chemical Oscillations</b> . . . . .	47
	References . . . . .	67
<b>6</b>	<b>Propagating Waves</b> . . . . .	69
	References . . . . .	86
<b>7</b>	<b>The Belousov–Zhabotinsky Reaction</b> . . . . .	89
	References . . . . .	102
<b>8</b>	<b>Catalytic Reactions at Solid Surfaces</b> . . . . .	105
	References . . . . .	123
<b>9</b>	<b>Electrochemical Reactions</b> . . . . .	125
	References . . . . .	134
<b>10</b>	<b>Design and Control of Self-organizing Chemical Systems</b> . . . . .	137
	References . . . . .	157
<b>11</b>	<b>Systems with Interacting Particles and Soft Matter</b> . . . . .	159
	References . . . . .	179
<b>12</b>	<b>Molecular Machines</b> . . . . .	181
	References . . . . .	201
	<b>Titles in this Series</b> . . . . .	203



# Chapter 1

## From Structure to Function: An Introduction

Atoms and molecules build all matter around us. Through interactions between them, condensed materials—fluids or solids—are formed. Through reactions, molecules can be transformed one into another and new kinds of molecules can be produced. It is therefore quite natural that first the properties of molecular structures and condensed matter have to be investigated and understood. Traditionally, studies of individual molecules, as well as of interactions and reactions between them, were the subject of physical chemistry as a separate scientific discipline. Over the years, an impressive progress has been made in this field. Structures of most molecules, including such macromolecules as proteins or DNA, have been determined and complex reaction mechanisms have been revealed. Nonetheless, it becomes also clear that even such broad structural knowledge does not straightforwardly lead to the understanding of essential processes in the inorganic nature and in biological cells.

In a major international effort, the complete structure of the human genome has been deciphered within the last decades. But, as this was done, it also became evident that understanding of the genetic system is still far from reached. While all cells in an organism contain the same set of genes, their expression is different and the actual difference is determined by patterns of cross-regulation processes in a genetic network. This situation is not a special property of biological systems, as it may seem at the first glance. Through experimental investigations of heterogeneous catalysis, the mechanisms of many surface reactions became understood. However, it became also clear that there is no straightforward connection between such mechanisms and the reaction course. Due to an interplay between elementary reaction steps, complex spatiotemporal patterns of catalytic activity on metal surfaces can develop and they can change sensitively when environmental conditions are modified.

The task of an architect is to design a house as a static structure and, for this, material properties of construction components should be examined and employed. In contrast to this, a mechanical engineer wants to design a functional device, i.e. a dynamical structure where a set of mechanical parts would be interacting in such a way that desired concerted action takes place. In a similar manner, the task of

industrial engineers would be to design the entire factory as a manufacturing system that incorporates various machines. These machines, often forming production lines and conveyor belts, need to operate in a coordinated and predictable way. Of course, construction of a house would also involve a sequence of processes and operation steps. However, such processes are only of transient nature; they are terminated when the final structure is raised. But the operation of a manufacturing factory is persistent—certain processes are repeatedly and indefinitely performed, as long as the factory works. It is such persistent coherent operation that defines a manufacturing system or a mechanical machine.

Persistent functioning can also be characteristic for chemical systems, both natural or synthetic, and artificially designed. Obviously, biological cells are the best example of such a natural system. As long as the cell is alive, many interwoven chemical processes run inside it. In molecular biology, a shift from the structure to the function in the research attitude has already taken place. To understand how a cell works, the knowledge of structures of various molecular components is not enough. Dynamic interactions between these components are essential for their specific functions and such interactions need to be understood in detail. Moreover, patterns of collective operation determined by such interactions should be explored.

Comparing the operation of an industrial factory and a living cell, an important difference can also be observed. In a factory, coordination of various manufacturing processes and operations by machines is to a large extent due to the supervision and control by a human manager or, more recently, by a central digital computer. In the cells, such central control is however absent. It is not possible to find, within a cell, an entity that collects information from various dynamical subsystems, processes such information and interferes into such subsystems, ensuring that they evolve in the required coordinated form. Instead, the coordination of various molecular processes comes as a result of autonomous interactions between them or, in other words, it is *self-organised*.

While biological cells and organisms are naturally available, they can also be seen as designed—not by an engineer, but by the process of biological evolution. Some basic underlying aspects of their operation could be already found in the original inanimate nature. However, through a long evolution history, extremely intricate self-organised systems of interacting chemical processes have emerged. A biological cell is a chemical micrometer-size reactor where thousands of different chemical reactions, sometimes involving only small numbers of molecules, proceed in a coordinated way. Such reactions are interconnected, when this is required by a function. Remarkably, however, they may be also non-interfering, even though confined to the same microvolume. On top of that, the entire system is accurately reproducing itself after every replication of the cell.

Definitely, this extreme level of molecular self-organisation comes at a high price. Because so many processes need to be packed into a tiny volume, some molecular components become shared by different mechanisms, so that they are optimised with respect to various functions. This presents a difficulty when biological systems are analysed. Another complication is that the actual living cells and organisms are the product of a unique and singular biological evolution, making it often difficult to

say whether some property is essential for a specific function or it is accidental and results from a particular evolutionary path.

For those not involved in biology research, molecular biosystems may look very special—almost esoteric—and well outside their field. In a fact, they share the same basic physical principles with the systems of other origins and, in a more primitive form, the analogs of biological molecular processes can be identified in the inorganic nature too. Furthermore, artificial systems with similar functional properties can be designed.

Note that the development of new kinds of materials and physical systems already represents a major part of scientific research. Many physical processes that are broadly employed in modern technology can be found only in the rudimentary form, if at all, in the nature, so that the respective materials and devices need to be intentionally designed and produced. The semiconductors used in the electronics and computer chips are carefully fabricated and their performance is superficial as compared to those of naturally available materials where the phenomenon of semiconductivity is observed. Optical lasers are all artificially designed and manufactured, with no analogs found in the nature itself. In the chemistry field, most of the broadly used polymer materials are the products of intentional development and design.

One of the aims of our book is to emphasize that molecular processes with special functional properties, resembling to some extent biological organisation, need to be systematically developed and designed on a broad scale. In terms of future applications, introduction of such molecular processes into technology may well have an effect comparable to that of the invention of semiconductor circuits and laser devices. Noticing how much public attention and financial investment has been invested in the last decades to nanoscience and nanotechnology, it is surprising how little, in comparison, has been here done. Partly, this is explained by the fact that, in contrast to nanotechnology, the research on molecular self-organising systems has been historically fragmented and proceeding along several loosely connected lines.

Theoretical foundations have been laid, in terms of the thermodynamics of open systems, already by L. von Bertalanffy, E. Schrödinger and I. Prigogine. However, their contributions have only elucidated the governing principles of molecular self-organisation, without proposing specific design schemes. Taking optical lasers as a comparative example, one can notice that quantum statistical mechanics provides the basis for the design of such devices, but does not yet tell how to develop them. Subsequently, this theoretical approach has been explored using abstract reaction-diffusion models by A. Turing and I. Prigogine.

Experiments on self-organisation in molecular systems have been for a long time focused on the inorganic Belousov–Zhabotinsky reaction where persistent oscillations and various kinds of non-equilibrium wave patterns can readily be observed. This chemical system has however a model character. While it allowed one to demonstrate a rich spectrum of self-organisation phenomena, no practical applications could have been designed. More recently, oscillations and self-organised wave patterns could also be observed in catalytic reactions on solid surfaces. Nonetheless, such observations were mostly made in the context of understanding the mechanisms of heterogeneous catalysis.

Meanwhile, the attention had also become diverted from physical chemistry. Proceeding from his studies on quantum laser generation, H. Haken has noticed that spontaneous development of coherence and order can be a property of many different systems, including those of social origin. Hence, the term “synergetics” (from Greek: working together) has been coined for the new interdisciplinary field. In the US, a group of scientists in the Santa Fe institute was pushing forward the idea of artificial life; their theoretical studies were primarily focused on deeper understanding of evolution processes, but also contributed to the field of machine intelligence and networks science. At the same time, the concept of complex systems has emerged and became wide-spread in the context of interdisciplinary research.

While the suggestion of a molecular mechanism of heredity by E. Schrödinger has played a decisive role in the subsequent discovery of the genetic code by J. Watson and F. Crick and thus had a profound effect, his ideas on physical mechanisms of self-organisation remained for a long time discussed by physicists, rather than by biologists themselves. Despite its impressive experimental achievements, molecular biology continued to rely, in its theoretical interpretations, on the concepts of classical chemical kinetics. It was not, until recently, much affected by the developments in the theory of complex systems that became gradually dominating the interdisciplinary research. The situation in molecular and cell biology has however changed within the last decade. High-resolution microscopy methods for *in vivo* monitoring of chemical processes in biological cells have become available. Thus, various self-organisation processes in living cells could be observed and this has stimulated the respective modeling and theoretical research.

Perhaps, the time has come to summarise, in a historical perspective and from the viewpoint of physical chemistry, what has been done in the studies of self-organisation processes in molecular systems. It needs also to be discussed in what directions the future studies can proceed and what applications become feasible. The present book does not however intend to systematically cover all relevant aspects—our attention is only paid to selected topics whose choice reflects largely the personal interests of the authors. Nonetheless we hope that this work can contribute to the broad survey of the history and the current status of the research on self-organization in molecular systems.

## Chapter 2

# Thermodynamics of Open Systems

In his speech at the Prussian Academy of Sciences in 1882, the scientist Emil du Bois-Reymond, well-known at that time, has concluded: “Chemistry is not a science in the sense of the mathematical description of Nature. Chemistry will be the science in this highest human sense only if we would understand the forces, velocities, stable and unstable equilibria of particles in a similar manner as the motion of stars” [1]. The thermodynamic theory for “stable equilibria” in closed systems was essentially developed during the second half of the 19th century and completed in 1905 by W. Nernst through the formulation of the Third Law of thermodynamics, while the basis for “forces and velocities” had to wait for the advent of quantum mechanics during the first decades of the 20th century. The description of “unstable equilibria” (which among other underlies all phenomena of structure formation in biological systems) became however only accessible in the middle of the 20th century in the framework of thermodynamics of open systems.

According to the Second Law of thermodynamics, all closed physical systems tend to reach the state of thermal equilibrium characterized by the minimum of free energy. But this is obviously not the case in biology. A living biological organism is not in the state of thermal equilibrium which can only be reached when the organism is dead. Quite in contrast, the degree of organisation, i.e. the order, of a bio-organism increases over time in the process of its development from the initial cell.

At the beginning of the 20th century, many have suspected that peculiar “vitalistic” forces, valid only in biology, exist. If such forces were indeed found, this would have however made thermodynamics and statistical physics not universally applicable, thus undermining the unique physical picture of the world. Therefore, efforts have been started to reconcile biology to the physical laws. Ludwig von Bertalanffy, an Austrian philosopher, biologist, system scientist and psychologist, was the first to address this paradox. In 1926, von Bertalanffy had finished his study of philosophy and art history with a doctoral degree at the University of Vienna and, 2 years later, published his first book on theoretical biology, *Kritische Theorie der Formbildung* (Critical Theory of Form Development), soon followed by

two volumes of *Theoretische Biologie*. In his article [2] with the title “Der Organismus als Physikalisches System Betrachtet” (The Organism Considered as a Physical System), von Bertalanffy offered in 1940 deep insights in the physical nature of biological phenomena.

As he noted, a biological organism shows properties similar to those of equilibrium systems. Indeed, the composition of a cell or of a multi-cellular organism is maintained over time and recovered after perturbations. But, although equilibrium of elementary subsystems can be found within it, the organism as a whole cannot be considered as being in the state of equilibrium. This is because we deal here not with a closed, but with an open system. A system should be called “closed” if there is no material entering it from outside and leaving it. In an open system, on the other hand, supply and release of materials take place. Thus, he wrote:

The organism is not a static, isolated from the exterior, system that always contains identical components. Rather, it is an open system in a (quasi) stationary, or steady, state that retains its mass relations under permanent exchange of substances and energies building it, the state where some components persistently arrive from outside while other components are persistently leaving.

At that time, physical chemistry was essentially limited to the analysis of reaction processes in closed systems. As von Bertalanffy remarked, open systems are not of much theoretical interest in the field of pure physics. One can however easily imagine that, for example, in the reaction  $a \rightleftharpoons b$  the product  $b$  of the reaction running from the left to the right is permanently removed, whereas the substrate  $a$  is permanently supplied. This is exactly so with a chemical flow reactor working under steady-state conditions, and such systems also play a fundamental role in biology.

L. von Bertalanffy stressed that, while there are similarities between stationary states (“unstable equilibria”) in open systems and the equilibrium in closed systems, the physical situation is principally different in these two cases:

True chemical equilibria in closed systems rely on reversible reactions [...]; they are furthermore a consequence of the Second Law [of thermodynamics] and are defined through the minimum of free energy. In open systems, the steady state as a whole and, eventually, also many elementary reactions are not however reversible. Moreover, the Second law is applicable only to closed systems, it does not determine the steady states. A closed system *must*, on the basis of the Second Law, finally go into a time-independent state of equilibrium [...] where the relationship between phases stays constant. An open chemical system *can* (when certain conditions are satisfied) finally go to a time-independent steady state. The characteristic property of this state is that the system, as a whole and also in view of its (macroscopic) phases, keeps itself constant through an exchange of elements (the so-called dynamic equilibrium).

Thus, according to von Bertalanffy, the paradox is only superficial. All laws of physics are in principle applicable to biological systems, provided that their necessary conditions are satisfied. The Second Law of thermodynamics is not violated in biology—it does not hold for biological organisms because they represent open systems and thus the applicability conditions are not satisfied. The steady state of an open system can change when flows passing through it are modified.

There is one further important consequence of this analysis. To maintain a closed system at equilibrium, no work is needed, but work cannot be also performed by a system in such a state. As von Bertalanffy remarks, a dammed mountain lake contains much potential energy, but, in absence of the outgoing flow, it cannot power a motor or a turbine. To generate work, the system needs to be under transition to an equilibrium state. To keep the system over a long time under a transition, one has to engineer it like a water power station, supplying new material whose energy is used to produce work. Furthermore,

Persistent work generation is therefore not possible in a closed system that rapidly transits to the equilibrium state, but only in an open system. The apparent “equilibrium”, in which an organism finds itself, is therefore not a true - and hence not capable of work - equilibrium state, but rather a dynamic pseudo-equilibrium. It is held at a certain separation from the true one and is therefore able to produce work. On the other hand, it also permanently needs new energy supply to ensure that a distance from the true equilibrium state remains maintained.

After the second world war, von Bertalanffy has moved to the US where his interests became shifted from theoretical biology to other fields. He has founded the general systems theory, analysing organization principles in systems of various origins, and was also involved in cancer studies and psychology research. Although his analysis of physical principles in biological organisms was brilliant, it was mostly confined to the conceptual level. Being not a mathematician or a theoretical physicist, von Bertalanffy could not further cast his ideas into an adequate mathematical form.

At about the same time, biology problems attracted attention of Erwin Schrödinger, famous for his discovery of quantum mechanics together with Werner Heisenberg. In emigration in Ireland, he had given in 1943 several lectures in the Dublin Institute for Advanced Studies which were published one year later as a book with the title *What is Life? The Physical Aspect of a Living Cell* [3]. The lectures were attended by an audience of about four hundred, both physicists and biologists. Despite his brilliant command of mathematics, Schrödinger almost did not use it during these lectures.

The lectures were focused on unveiling possible mechanisms of genetic inheritance in biological organisms. The puzzle was to explain how genetic information is reliably transferred in large amounts from one generation to another, despite the apparent frailty of biological organisms. His conclusion was that the information should be stored at the molecular level, in large molecules that may resemble an “aperiodic crystal”. Somewhat later, this conjecture became indeed confirmed when the genetic DNA code was discovered by J. Watson and F. Crick. However, one of the lectures was devoted to thermodynamic aspects of the living cell.

Schrödinger begins by noting that biological organisms are open systems and therefore the Second Law of thermodynamics is not applicable to them. It is not clear whether he was familiar at that time with the work by von Bertalanffy; the book contains no reference to it. During the war, Schrödinger was in relative isolation in Ireland and did not also know about some contemporary experimental developments in biophysics. Similar to von Bertalanffy, he asks a question whether the laws of physics hold in biology. His answer is that “the living matter, while not eluding the “laws of physics” as established up to date, is likely to involve “other laws of

physics” hitherto unknown, which, however, once they have been revealed, will form just integral a part of this science as the former.”

How does a biological organism avoid decay?—By eating, drinking and breathing (or assimilating in the case of plants). Indeed, one of the fundamental concepts in biology is that of metabolism. This word, translated from Greek, means change or exchange. In German literature, the term *Stoffwechsel*, i.e. exchange of material, is used as a synonym of metabolism. Obviously, the metabolism is essential for keeping the cell alive, but this does not simply mean the exchange of molecules.

The characteristic feature of a biological organism is a high degree of order within it. This order is maintained despite large variations in the environment. It can also increase with time, as, for example, in the process of development of a multi-cellular organism from a single initial cell. In thermodynamics, entropy serves as the measure of disorder and this means that, when order of an organism is increased, its entropy content must become lower.

Assume that  $S$  is the entropy contained within a system. Then, its rate of change is given by the sum of two terms

$$\frac{dS}{dt} = \sigma + j^s. \quad (2.1)$$

The first of them,  $\sigma$ , is the rate of entropy generation within the system. The Second Law of thermodynamics implies that this term is always non-negative and vanishes in the state of thermal equilibrium. The second term,  $j^s$ , is the rate of exchange of entropy between the system and its environment. It is given by the difference  $j^s = j_{in}^s - j_{out}^s$  of incoming and outgoing entropy fluxes. Note that this second term should also include the exchange of entropy between the system and the thermal bath.

If the amount of entropy arriving per unit time to an open system is smaller than the amount exported by it per unit time, the total entropy flux  $j^s$  in Eq. (2.1) becomes negative. Furthermore, if this negative flux is sufficiently strong, it can prevail over the entropy production rate, so that we would have  $\sigma + j^s < 0$ . But this means that, under such conditions,  $dS/dt < 0$  and thus the entropy content of the system *decreases* with time.

Moreover, if the two terms exactly balance one another,  $j^s = -\sigma$ , the entropy content of the system remains constant with time. However, this is obviously not the state of thermal equilibrium, since entropy continues to be produced. Instead, the open system will find itself in this case in the steady state of flow equilibrium that we have already discussed above.

In his book, Schrödinger suggests that, instead of the entropy, its reverse  $\Psi = -S$  should be rather used in such arguments. The “negative entropy”  $\Psi$  characterizes the degree of order in the system and, for it, an analog of Eq. (2.1) holds,

$$\frac{d\Psi}{dt} = -\sigma + j_{in}^{\psi} - j_{out}^{\psi}. \quad (2.2)$$



The order of an organism would increase if the amount  $j_{in}^{\psi}$  of negative entropy consumed by it per unit time exceeds the amount  $j_{out}^{\psi}$  of negative entropy exported within the same time. To maintain an organism in the non-equilibrium steady state, the flow of incoming negative entropy has at least to overcome entropy production within it,

$$j_{in}^{\psi} = \sigma + j_{out}^{\psi} \geq \sigma. \quad (2.3)$$

Thus, to keep itself alive, a biological organism needs to “feed on negative entropy” or, in other words, it should continuously import “order” from an external source. The rate of such import should be high enough, so that the internal entropy production is counter-balanced. The conclusion by Schrödinger was that, in biological organisms, order is not created—it is only imported from outside. Indeed, “Order from Order” was the title of the section where such questions were discussed.

However, the concept of “negative entropy” has not become popular, partly because this is just the common entropy taken with the opposite sign. In the *Notion* to the respective chapter of the book, Schrödinger admitted that his remarks on negative entropy were met with doubt and opposition from his physicist colleagues. He said that he had chosen to talk about negative entropy in his lecture only to explain the situation in a simpler way for a broad audience. Instead, he should have talked about the free energy of a biological organism.

Indeed, thermodynamic free energy is defined as  $F = E - TS$  where  $E$  is the energy and  $T$  is the temperature of a system. Assuming that (internal) energy  $E$  is not consumed or released inside a system, the balance equation for free energy can be written as

$$\frac{dF}{dt} = -T\sigma + j_{in}^F - j_{out}^F. \quad (2.4)$$

Hence, in the steady state of an open system, the influx of free energy should be sufficiently high,

$$j_{in}^F \geq T\sigma. \quad (2.5)$$

It has to overcome the effect of persistent entropy production in the steady state.

Hence, there is indeed something essential that should be received by all of us with food. This is not however the simple energy, but rather the thermodynamic free energy contained in it. A minimum amount of free energy has to be consumed every day in order that a biological organism survives.

After the war, Schrödinger returned to Austria where his research was again focused on physics. The book *What is Life?* was his only major publication where problems of biology were discussed.

The third main contribution to studies in thermodynamics of open systems came from Ilya Prigogine. He was born in Russia and emigrated as a child with his parents first to Germany and then to Belgium. In 1941 he has received a doctoral degree

from Université Libre de Bruxelles and, in 1947, published his first book *Étude Thermodynamique des Phénomènes Irreversibles* [4]. In contrast to von Bertalanffy, a theoretical biologist, or to the physicist Schrödinger, he was a physical chemist. Apparently without being aware of previous work, Prigogine has not only reinvented the principles of thermodynamics of open systems, but also systematically built up this theory as applied to specific chemical systems.

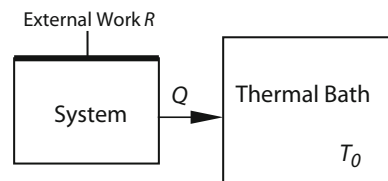
Reviewing in 1949 the book [4] by Prigogine for the *Nature* magazine [5], von Bertalanffy wrote: “Since 1932, the present reviewer has advanced the conception of an organism as an “open system”. So far, physical chemistry was concerned almost exclusively with reactions and equilibria in closed systems, while living organisms are open systems, maintaining themselves in a continuous exchange of materials with environment. [...] Prigogine’s work, devoted to the extension and generalization of the thermodynamic theory, is of outstanding importance for physics, as well as for biology. As the author states, “classical thermodynamics is an admirable, but *fragmentary* doctrine; this fragmentary character results from the fact that it is applicable only to states of equilibria in closed systems. *Therefore, it is necessary to establish a broader theory, comprising states of non-equilibrium as well as those of equilibrium.*” Starting, on one hand from, from the concept of open systems and, on the other, from thermodynamics of irreversible processes [...], Prigogine derives the generalized thermodynamics for the whole realm of physical chemistry, including chemical reactions, electrochemistry, polythermic systems, diffusion, thermoelectricity, etc. [...] The new thermodynamics shows that it is necessary not only for biological theory to be based upon physics, but also that biological points of view can open new pathways in physical theory as well.”

Over his long life in science, Prigogine has worked on a broad spectrum of topics, including not only thermodynamics of open systems, but also various aspects of non-equilibrium pattern formation, foundations of physical kinetics and quantum statistics, and interdisciplinary applications to social and technological problems. He was a prolific writer and has left a series of excellent books. In 1977, Prigogine was awarded with the Nobel prize in chemistry “for his contributions to non-equilibrium thermodynamics, particularly the theory of dissipative structures”.

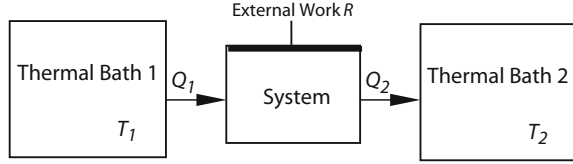
Below we show, following [6], how thermodynamics of open systems can be applied to specific examples.

Suppose that a system is connected to just one other system that is large and plays a role of the thermal bath (Fig. 2.1). Such a system is closed in the thermodynamic sense and can only undergo a transition to the equilibrium state. Note that, during

**Fig. 2.1** A system in contact with the thermal bath



**Fig. 2.2** A system in contact with two thermal baths at different temperatures



the transient, the system can still exchange heat with the thermal bath, so that the internally produced entropy is exported and the entropy content of the system is decreased. This indeed takes place if, for example, the initial temperature of a closed system is higher than that of the thermal bath, so that it gets cooled.

The situation is however different if a system is connected to two (or more) thermal baths with different temperatures, as shown in Fig. 2.2. Now, the system cannot settle down to any definite equilibrium state. Even if its state is stationary (steady), heat would continue to arrive from the bath with the higher temperature  $T_1$  and become released into the colder bath at the temperature  $T_2$ . To estimate the amounts of entropy transported with the heat flows, a simple argument can be used. If the heat  $dQ_1$  flows into the system from the thermal bath at temperature  $T_1$ , the same amount is leaving that bath. Thus, the bath entropy becomes decreased by  $dS_1 = dQ_1/T_1$  and the same amount of entropy arrives with the heat flow into the considered middle system. On the other hand, if an amount of heat  $dQ_2$  enters the second thermal bath which is at temperature  $T_2$ , it brings with it the entropy  $dS_2 = dQ_2/T_2$  and, therefore, the same amount of entropy is leaving the system connected to that bath.

Thus, the Second Law of thermodynamics takes here the form

$$\frac{dS}{dt} = \sigma + \frac{1}{T_1} \frac{dQ_1}{dt} - \frac{1}{T_2} \frac{dQ_2}{dt} \quad (2.6)$$

Moreover, the First Law of thermodynamics implies that the balance equation for the internal energy  $E$  of the system should hold,

$$\frac{dE}{dt} = \frac{dQ_1}{dt} - \frac{dQ_2}{dt} + \frac{dR}{dt}. \quad (2.7)$$

where  $R$  is the work produced by the system. If the system is changing its volume  $V$ , the rate of work generation (or the generated power) is given by  $dR/dt = -p(dV/dt)$  where  $p$  is pressure.

Because the system is away from equilibrium, it does not generally need to approach a steady state and can, as well, perform periodic oscillations or even show more complex dynamics. Suppose however that such a stationary state exists. Then,  $dE/dt = dS/dt = 0$  and, from Eq. (2.6) we find

$$\frac{dQ_2}{dt} = T_2\sigma + \frac{T_2}{T_1} \frac{dQ_1}{dt} \quad (2.8)$$

This expression can be further substituted into Eq. (2.7) and the rate of work generation can be determined,

$$\frac{dR}{dt} = -T_2\sigma + \left(\frac{T_2}{T_1} - 1\right)\frac{dQ_1}{dt}. \quad (2.9)$$

As we see, this open system can operate as a *heat engine* and perform work. Because the entropy production rate  $\sigma$  is positive, the maximum efficiency is reached when  $\sigma \rightarrow 0$ , i.e. if the system approaches equilibrium. Then, the efficiency coefficient is

$$\eta = \frac{dR/dt}{dQ_1/dt} = \frac{T_2}{T_1} - 1. \quad (2.10)$$

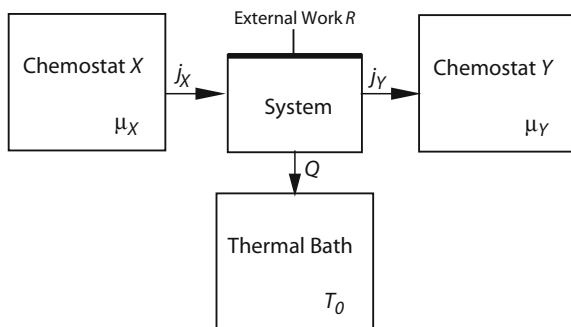
Remarkably, this is indeed the maximum energetic efficiency of the Carnot cycle.

In the above arguments, we have assumed that only heat could be exchanged, but the material composition of the system remained fixed. In chemistry and biology, a situation would however often be found where material flows are taking place, whereas temperatures are not different for different parts. Typically, a chemical reaction is taking place inside a system (the *reactor*) where molecules  $X$  are reversibly converted into some other molecules  $Y$ . Again, if the system is closed, an equilibrium state with certain stationary concentration of species  $X$  and  $Y$  is eventually reached. Now we assume that the considered chemical reactor is connected to two large external systems (or *chemostats*) where molecules  $X$  or  $Y$  are contained and their concentrations are maintained constant (Fig. 2.3). Moreover, chemical potentials  $\mu_X$  and  $\mu_Y$  in the chemostats are different and  $\mu_X > \mu_Y$ . The chemostats and the system are kept at a constant pressure, so that the Gibbs free energy should be employed. The system is also connected to a thermal bath at temperature  $T_0$ .

The First Law of thermodynamics then reads

$$\frac{dE}{dt} = \mu_X j_X - \mu_Y j_Y + \frac{dR}{dt} - \frac{dQ}{dt} \quad (2.11)$$

**Fig. 2.3** Open system connected to two chemostats



where  $j_X$  is the number of molecules  $X$  arriving per unit time into the system and  $j_Y$  the number of molecules  $Y$  leaving it per unit time, and the last term takes into account the heat flow into the thermal bath.

The Second Law implies that

$$\frac{dS}{dt} = \sigma + s_X j_X - s_Y j_Y - \frac{1}{T_0} \frac{dQ}{dt} \quad (2.12)$$

where  $s_X$  and  $s_Y$  are amounts of entropy per molecule  $X$  or  $Y$  in the respective chemostats; they are given by  $s_X = -\partial\mu_X/\partial T$  and  $s_Y = -\partial\mu_Y/\partial T$ .

Additionally, mass balance equation needs to be written. Assuming that, in the considered chemical reaction, one molecule  $X$  is converted into one molecule  $Y$ , that is we have  $X \rightleftharpoons Y$ , the mass balance implies that the number of molecules entering the reactor per unit time is equal to the number of molecules leaving it, i.e.  $j_X = j_Y = j$ .

Such a flow reactor will be maintained away from thermal equilibrium as long as there is a flow of molecules passing through it. Generally, oscillations and various wave patterns can develop inside it. It may happen however also that a stationary (steady) state becomes formed, so that  $dE/dt = dS/dt = 0$ . In contrast to thermal equilibrium state, entropy continues to be produced under stationary non-equilibrium conditions. Additionally, some entropy arrives together with substrate molecules  $X$ . All such entropy has to be exported away from the reactor. According to Eq. (2.12), it is exported together with the heat flow into the thermal bath and together with the product molecules into the respective chemostat.

From Eq. (2.12), we find that, in the steady state, the heat flow into the thermal bath is

$$\frac{dQ}{dt} = T_0\sigma + T_0(s_X - s_Y)j. \quad (2.13)$$

Substituting this, in the steady state, into Eq. (2.11), mechanical work performed per unit time by such chemical engine can be determined,

$$\frac{dR}{dt} = -T_0\sigma + [T_0(s_X - s_Y) - (\mu_X - \mu_Y)]j. \quad (2.14)$$

As in the case of the heat engine, the work is maximal when approaching equilibrium, i.e. for  $\sigma \rightarrow 0$ . The maximum possible efficiency of the chemical engine is

$$\eta = \frac{dR/dt}{(\mu_X - \mu_Y)j} = \frac{T_0}{\mu_X - \mu_Y} \frac{\partial}{\partial T} (\mu_X - \mu_Y) - 1. \quad (2.15)$$

The possibility to operate as an engine, persistently producing mechanical work, is a remarkable property of open flow systems, both thermal and chemical. There is however also another important property of such systems revealed by this analysis. Their entropy content is controlled by a balance between the entropy production