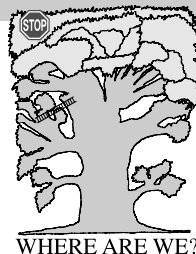


Chapter 15

INFORMATION PROCESSING – THE MISSION OF CHEMISTRY



Where are we?

We have now explored almost the whole TREE.

An example

Chemistry has played, and continues to play, a prominent role in human civilization. If you doubt it, just touch *any* surface around you – most probably it represents a product of the chemical industry.¹ Pharmaceutical chemistry may be seen as a real benefactor, for it makes our lives longer and more comfortable. Is the mission of chemistry therefore to produce better dyes, polymers, semi-conductors, drugs? *No, its true mission is much, much more exciting.*

What is it all about

MOLECULAR STRUCTURES (STATICS)	p. 852
Complex systems (⊢□)	p. 852
Self-organizing complex systems (⊢□)	p. 853
Cooperative interactions (⊢□)	p. 854
Sensitivity analysis (⊢)	p. 855
Combinatorial chemistry – molecular libraries (⊢□)	p. 855
DYNAMICS	p. 857
Non-linearity (⊢)	p. 857
Attractors (⊢)	p. 858
Limit cycles (⊢)	p. 859
Bifurcations and chaos (⊢)	p. 860
Catastrophes (⊢)	p. 862
Collective phenomena (⊢)	p. 863
• Scale symmetry (renormalization)	
• Fractals	

¹Just a quick test around myself (random choice of surfaces): laptop (polymers), marble table (holes filled with a polymer), pencil (wood, but coated by a polymer), box of paper tissue (dyes and polymer coat), etc.

Chemical feedback – non-linear chemical dynamics (㊦㊧㊨)	p. 866
• Brusselator – dissipative structures	
• Hypercycles	
CHEMICAL INFORMATION PROCESSING	p. 875
Functions and their space-time organization (㊦㊧)	p. 875
The measure of information	p. 875
The mission of chemistry	p. 877
Molecular computers based on synthon interactions	p. 878

Why is this important?

In this book we have dealt with many problems in quantum chemistry. If this book were only about quantum chemistry, I would not write it. My goal was to focus on perspectives and images, rather than on pixel-like separate problems. Before we are quantum chemists we are scientists, happy eye-witnesses of miracles going on around us. We are also human beings, and have the right to ask ourselves, just what are we aiming for? *Why* is the Schrödinger equation to be solved? *Why* do we want to understand the chemical foundations of the world? Just for curiosity? Well, should curiosity legitimize *any* investigation?² What will the future role of chemistry be?

Chemistry is on the threshold of a big leap forward. Students of today will participate in this revolution. The limits will be set by our imagination, maybe by our responsibility as well. The direction we choose for the future progress in chemistry and biochemistry will determine the fate of human civilization. This *is* important...

What is needed?

- Elements of chemical kinetics.
- Elements of differential equations.
- Let us leave the traditional topics of chemistry, let us look around, let us look at how Nature operates.

Classical works

The classic papers pertain to three, at first sight unrelated, topics: molecular recognition, oscillatory solutions in mathematics and information flow. These topics evolved virtually separately within chemistry, mathematics and radio-communication, and only now³ are beginning to converge. ★ Emil Hermann Fischer was the first to stress the importance of molecular recognition. In *“Einfluss der Konfiguration auf die Wirkung der Enzyme”* published in *Berichte*, 27 (1894) 2985 Fischer used the self-explanatory words “key-lock” for the perfect fit of an enzyme and its ligand. ★ In 1903 Jules Henri Poincaré published in *Journal de Mathématiques Pures et Appliquées*, 7 (1881) 251 an article *“Mémoire sur les courbes définies par une équation différentielle”*, where he showed that a wide class of two coupled non-linear differential equations leads to oscillating solutions that tend

Jules Henri Poincaré (1854–1912), French mathematician and physicist, professor at the Sorbonne, made important contributions to the theory of differential equations, topology, celestial mechanics, probability theory, and the theory of functions.



²Do not answer “yes” too easily, for it gives people the right to any experiments on you and me.

³The aim of the present chapter is to highlight these connections.

Boris Pavlovich Belousov (1893–1970) looked for an inorganic analogue of the biochemical Krebs cycle. The investigations began in 1950 in a Soviet secret military institute. Belousov studied mixtures of potassium bromate with citric acid, and a small admixture of a catalyst: a salt of cerium ions. He expected a monotonic transformation of the yellow Ce^{4+} ions into the colourless Ce^{3+} . Instead, he found oscillations of the colour of the solvent (colourless-yellow-colourless... etc., also called by Russians “vodka-cognac-vodka...”).

He wrote a paper and sent it to a Soviet journal, but the paper was rejected with a referee’s remark that what the author had described was simply impossible. His involvement in classified research caused him to limit himself to bringing (by intermediacy of somebody) a piece of paper with reactants and his phone number written on it. He refused to meet anybody. Finally, Simon Schnoll per-



suaded him to publish his results. Neither Schnoll nor his PhD student Zhabotinsky ever met Belousov, though all they lived in Moscow.

Belousov’s first chemistry experience was at the age of 12, while engaged in making bombs in the Marxist underground. Stalin thought of everything. When, formally underqualified, Belousov had problems as head of the lab, Stalin’s handwriting in ordinary blue-pencil on a piece of paper: “*Has to be paid as a head of laboratory as long as he has this position*” worked miracles.

After S.E. Schnoll “*Geroi i zladiei rossiyskoi nauki*”, Kron-Press, Moscow, 1997.

to a particular behaviour *independently of the initial conditions* (called the *limit cycle*). ★ It seems that the first experiment with an oscillatory chemical reaction was reported by Robert Boyle in the XVII century (oxidation of phosphorus). Then several new reports on chemical oscillations were published (including books). *All these results did not attract any significant interest in the scientific community, because they contradicted the widely known, all important, and successful equilibrium thermodynamics.* ★ The Soviet general Boris Belousov finally agreed to publish his only unclassified paper “*Periodichesky deystvuyushchaya reaktsiya i yeyo mekhanizm*” in an obscure Soviet medical journal *Sbornik Riefieratow Radiacjonnoj Mediciny, Medgiz, Moskwa*, 1 (1959) 145 reporting spectacular colour oscillations in his test tube: yellow Ce^{4+} and then colourless Ce^{3+} , and again yellow, etc. (nowadays called the Belousov–Zhabotinsky reaction). ★ Independently, there was a continuing parallel progress in oscillatory solutions in mathematics. In 1910 Alfred J. Lotka in “*Contributions to the theory of chemical reactions*” published in the *Journal of Physical Chemistry*, 14 (1910) 271 proposed some differential equations that corresponded to the kinetics of an autocatalytic chemical reaction, and then with Vito Volterra gave a differential equation that describes a prey-predator *feedback* (oscillation) known as Lotka–Volterra model. ★ In February 1943, at the Dublin Institute for Advanced Studies,⁴ Erwin Schrödinger gave several lectures trying to reconcile thermodynamics and biology. He stressed that biological systems are open: there is a flow of matter and energy. Independently of all these investigations there were attempts in radio-communication to look quantitatively at information flow. ★ Ralph V.L. Hartley, published the first article on measuring informa-

Ilya Prigogine (1917–2003) Belgian physicist, professor at the Université Libre de Bruxelles. In 1977 he received the Nobel prize “*for his contributions to non-equilibrium thermodynamics, particularly the theory of dissipative structures*”.



tion entitled “*Transmission of Information*” in *The Bell Systems Technical Journal*, 7 (1928) 535. ★ Twenty years later, the same topic was developed by Claude E. Shannon in “*A Math-*

⁴In that period of the war certainly looking like a tiny nucleus of civilization beyond the reach of barbarians. The lecture notes were published in 1944 by Cambridge University Press under the title “*What is Life?*”

ematical Theory of Communication” also published in *The Bell Systems Technical Journal*, 27 (1948) 379, 623, in which he related the notion of information and that of entropy. ★ The Belgian scientists Paul Glansdorff and Ilya Prigogine published a paper “*Sur les propriétés différentielles de la production d’entropie*” in *Physica*, 20 (1954) 773, that became the basis of irreversible thermodynamics. Ilya Prigogine and Gregoire Nicolis in an article “*On Symmetry-Breaking Instabilities in Dissipative Systems*”, *Journal of Chemical Physics* 46 (1967) 3542 introduced the notion of dissipative structures. ★ Charles John Pedersen reopened (after the pioneering work of Emil Fischer) the field of supramolecular chemistry, publishing an article “*Cyclic Polyethers and their Complexes with Metal Salts*”, which appeared in the *Journal of the American Chemical Society*, 89 (1967) 7017 and dealt with molecular recognition (cf. Chapter 13). ★ Manfred Eigen and Peter Schuster, in three articles “*The Hypercycle. A Principle of Natural Self-Organization*” in *Naturwissenschaften* 11 (1977), 1 (1978) and 7 (1978) introduced the idea of a hypercycle and of the natural selection of molecules to chemistry. ★ The mathematician Leonard Adleman published in *Science*, 266 (1994) 1021 “*Molecular Computation of Solutions to Combinatorial Problems*”, in which he described his own chemical experiments that shed new light on the role molecules can play in processing information.

What are the most important problems in chemistry? Usually we have no time to compose such a list, not even to speak of presenting it to our students. The choice made reflects the author’s personal point of view. The author tried to keep in mind that he is writing for mainly young (undergraduate and graduate) students, who are seeking not only for detailed research reports, but also for new *guidelines* in chemistry, for some general *trends* in it, and who want to establish strong and general *links* between mathematics, physics, chemistry and biology. An effort was made to expose the ideas, not only to students’ minds but also to their hearts.

It is good to recall from time to time that all of us: physicists, chemists and biologists share the same electrons and nuclei as the objects of our investigation. It sounds trivial, but sometimes there is the impression that these disciplines investigate three different worlds. In the triad physics–chemistry–biology, chemistry plays a bridging role. By the middle of the twentieth century, chemistry had closed the

Kurt Gödel (1906–1978), German mathematician (then American, he was hardly persuaded in a taxi going to the ceremony of his naturalisation not to present inconsistencies in the US Constitution he had found). This mathematical genius proved a theorem now called Gödel’s Undecidability Theorem that has shaken the foundations of mathematics (K. Gödel, *Monatshefte Math. Phys.*, 38 (1931) 173). Roughly speaking, the theorem says that any system of axioms leads to theorems neither true nor false. Gödel was probably inspired by old Greek paradoxes, like “*all Creteans lie* – said a Cretean”.



Kurt Gödel was permanently afraid of being poisoned. After his wife’s death, when nobody could persuade him that his food was safe, he died of hunger. . .

period of the exploration of its basic building blocks: elements, chemical bonds and their typical lengths, typical values of angles between chemical bonds, etc. Future discoveries in this field are not expected to change our ideas fundamentally. Now we are in a period of using this knowledge for the construction of what we only could dream of. In this Chapter I will refer now and then to mathematicians and mathematics, who deal with ideal worlds. For some strange reason at the foundation of (almost⁵) everything there is logic and mathematics. We have to notice, however, that after Kurt Gödel's proof of the incompleteness of *any* axiomatic system mathematics has become more like natural sciences. Physics, while describing the real rather than the ideal world, more than other natural sciences is symbiotic with mathematics.

Important cornerstones of this frontier region are given in brief below in three sections: Molecular Structures, Dynamics and Chemical Information Processing.

MOLECULAR STRUCTURES (STATICS)

15.1 COMPLEX SYSTEMS

Even a relatively simple system (e.g., an atom) often exhibits strange properties. Understanding simple objects seemed to represent a key for description of complex systems (e.g., molecules). Complexity *can* be explained using the first principles.⁶ However, the complexity itself may add some important features. In a complex system some phenomena may occur, which would be extremely difficult to foresee from a knowledge of their component parts. Most importantly, sometimes the behaviour of a complex system is universal, i.e. independent of the properties of the parts of which it is composed (some of them will be mentioned in the present chapter) and related to the very fact that the system is composed of many small parts interacting in a simple way.

The behaviour of a large number of argon atoms represents a difficult task for theoretical description, but is still quite predictable. When the number of atoms increases, they pack together in compact clusters similar to those we would have with the densest packing of tennis balls (the maximum number of contacts). We may have to do here with complicated phenomena (similar to chemical reactions) and connected to the different stability of the clusters (e.g., “magic numbers” related to particularly robust closed shells⁷). Yet, the interaction of the argon atoms, however difficult for quantum mechanical description, comes from the quite primitive two-body, three-body etc. interactions (Chapter 13).

⁵Yes, almost: e.g., generosity is not included here.

⁶In the 20-ties of the twentieth century, after presenting his equation (see Chapter 3), Paul Dirac said that now chemistry is explained. Yet, from the equation to foreseeing the properties of complex organic molecules is a long, long way.

⁷Similar closed shells are observed in nuclear matter, where the “tennis balls” correspond to nucleons.

15.2 SELF-ORGANIZING COMPLEX SYSTEMS

Chemistry offers a plethora of intermolecular interactions.

Some intermolecular interactions are specific, i.e. a substrate A interacts with a particular molecule B_i from a set B_1, B_2, \dots, B_N (N is large) much more strongly than with others. The reasons for this are their shape, the electric field⁸ compatibility, a favourable hydrophobic interaction etc. resulting either in the “key-lock” or “hand-glove” types of interaction, cf. Chapter 13. A molecule may provide a set of potential contacts localized in space (synthon, p. 744), which may fit to another synthon of another molecule. Two of nature’s most important pairs of synthons are the hydrogen bond system of guanine and cytosine (GC) and of adenine and thymine (AT)⁹ (see Fig. 13.17): in the case of *extended* synthons exhibiting an internal structure (“polysynthons” like, e.g., GAATC and CTTAG being sections of a DNA strand) finding in solution the first two matching synthons, e.g., in our case G and C, makes the next ones much easier, i.e. A and T etc., to fit, since they are already close in space and the entropy barrier is much easier to overcome.¹⁰

This idea is used in supramolecular chemistry. Suppose a particular reaction does not proceed with sufficient yield. Usually the reason is that, to run just this reaction the molecules have to find themselves in a very specific position in space (a huge entropy barrier to overcome), but before this happens they undergo some unwanted reactions. We may however “instruct” the reactants by substituting them with such synthons that the latter lock the reactants in the right position in space. The reaction we want to happen becomes inevitable. The driving force for all this is the particularly high interaction energy of the reactants. Very often however, the interaction energy has to be high, but not too high, in order to enable the reaction products to separate. This reversibility is one of the critically important features for “intelligent” molecules, which could adapt to external conditions in a flexible way. If a system with synthons is not flexible enough, we will still have to do with a relatively primitive structure.

If the system under consideration is relatively simple, even if the matching of corresponding synthons is completed, we would still have a relatively primitive spatial structure. However, we may imagine far more interesting situation, when:

- The molecules were *chosen* in such a way as to ensure that some intermolecular interaction is particularly attractive. A specific matching is known as molecular recognition.
- The molecular complexes formed this way may recognize themselves again by using synthons previously existing or created *in situ*. In this way a multilevel structure can be formed, each level characterized by its own stability (cf. p. 744).

molecular
recognition

⁸Both molecules carry their charge distributions, their interaction at a certain geometry may considerably lower the Coulombic energy.

⁹G, C, A, T are four letters used by nature to compose the words, sentences, chapters, essays and poems of the Book of Life (the DNA code). The complementarity of the related synthons is of prime importance.

¹⁰The entropy barrier for A and B to make a complex AB is large when there are a lot of non-reactive A and B positions, and only a few that lead to formation of the complex.

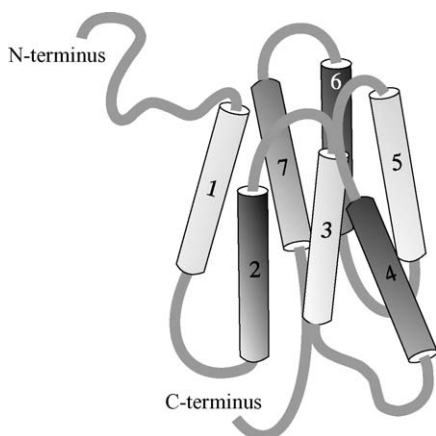


Fig. 15.1. A “universal” biological sensor based on rhodopsin. The sensor consists of seven α -helices connected by some oligopeptide links (a schematic view), the α -helices are shown as cylinders. The helices form a cavity, in which (in one of version of the sensor) there is a cis-retinal molecule (a chain of alternating single and double bonds), not shown in the figure, stretching between two helices. The cis-retinal is able to absorb a photon and change its conformation to trans. This triggers the cascade of processes responsible for our vision. The total system is hydrophobic outside, which makes it spontaneously anchor inside the cell walls composed of a lipid bilayer. The protruding protein loops exhibit specific interactions with some drugs. Such a system is at the basis of interaction with about 70% of drugs.

- The multilevel molecular structure may depend very strongly on its environment. When this changes, the structure may decompose, and eventually another structure may emerge.

A *hierarchical* multilevel structure may be formed, where the levels exhibit different stability with regard to external perturbations. The stability differs due to the different binding energies of the synthons involved and/or on the steric constraints.

The coiled-coil structure of oligopeptides described on p. 748 may serve as an example of such a multilevel structure, or the spontaneous folding of enzymes to their native structure, e.g., rhodopsin is composed of seven α -helices linked by some oligopeptide links (Fig. 15.1).

There is nothing accidental in this system. The helices are composed of such amino acids, that ensure that the external surface of the helices is hydrophobic, and therefore enter the hydrophobic lipid bilayer of the cell walls. The peptide links serve to *recognize* and dock some particular signalling molecules. The 7-helix systems serve in biology as a universal sensor, with variations to make it specific for some particular molecular recognition and the processes that occur afterwards. After docking with a ligand or by undergoing photochemical isomerization of the retinal, some conformational changes take place, which after involving several intermediates, finally resulting in a signal arriving at a nerve cell. We see how wonderful things this sophisticated structure is able to do in a dynamic way.

15.3 COOPERATIVE INTERACTIONS

Some events may cooperate. Suppose we have an extended object, which may undergo a set of events: A, B, C, ..., each taking place separately and locally with a small probability. However, it may happen that for a less extended object the events cooperate, i.e. event A makes it easier for event B to occur, and when A and then B happens this makes it easier for event C to happen, etc.

Self-organization is possible without cooperativity, but cooperativity may greatly increase the effectiveness of self-organization. The hemoglobin molecule may serve as an example of cooperativity in intermolecular interactions, where its interaction with the first oxygen molecule makes its interaction with the second easier despite a considerable separation of the two binding events in space.

15.4 SENSITIVITY ANALYSIS

Sensitivity analysis represents a fast developing branch of applied mathematics. The essence of this approach is determining the response of a structure to a perturbation. The structure may represent a building or a molecule, and the perturbations may be of different kinds.¹¹ Experimental chemists very often introduce some substitutions, exchanging one functional group for another, and then observing the changes in the structure and properties of the system. Similarly, in biochemistry, both in experiment and theory (e.g., in molecular mechanics or dynamics), we make some artificial mutations. However, the current limitations of theory do not enable us to perform global molecular mechanics (cf. Chapter 7) and carry out sensitivity analysis when large responses of the system are admitted. It is very probable that this type of analysis will be of great importance in the future, because we will try to control the system globally, e.g., to foresee what will be the most stable structure after a perturbation is switched on.

15.5 COMBINATORIAL CHEMISTRY – MOLECULAR LIBRARIES

Chemistry is often regarded as dealing with pure substances,¹² which is obviously too demanding. This is difficult to achieve even for a pure compound, because of isomerization. In most cases we are interested in having a single isomer in the specimen. However, there are cases when the chemist is interested in a *mixture* of all possible isomers instead of a single isomer. Such a mixture is called a chemical library, and the chemistry that uses such libraries is called combinatorial chemistry. Thanks to the libraries we can search and find a given isomer. This is particularly spectacular in cases in which we have a labile equilibrium (i.e. easily shiftable) among the isomers.

A complex system may adjust itself to an external stimulus by changing its molecular structure. A good example is liquid water, which may be regarded as a “library” of different clusters, all of them being in an easy-to-shift equilibrium with others. This is why water is able to hydrate a nearly infinite variety of molecules, shifting the equilibrium towards the clusters that are needed to “wrap the solute by a water coat”.

¹¹Sensitivity analysis is *universal*. We apply it in everyday life (we see how our organism reacts to a perturbation by drug A, drug B, ...).

¹²This is stressed by the Dutch name for chemistry: “*scheikunde*” – i.e. the art of separation.

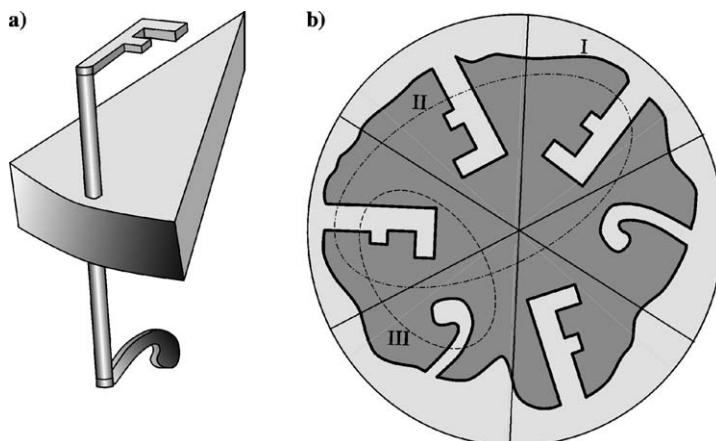


Fig. 15.2. A model of the immune system. (a) The figure shows schematically some monomers in a solvent. They have the shape of a slice of pie with two synthons: protruding up and protruding down, differing in shape. The monomers form some side-by-side aggregates containing from two to six monomers, each aggregate resulting in some pattern of synthons on one face and the complementary pattern on the other face. We have then a library of all possible associates in thermodynamical equilibrium. Say, there are plenty of monomers, a smaller number of dimers, even fewer trimers, etc. up to a tiny concentration of hexamers. (b) The attacking factor I (the irregular body shown) is best recognized and bound by one of the hexamers. If the concentration of I is sufficiently high, the *equilibrium among the aggregates shifts towards the hexamer mentioned above, which therefore binds all the molecules of I, making them harmless*. If the attacking factor was II and III, binding could be accomplished with some trimers or dimers (as well as some higher aggregates). The defence is highly specific and at the same time highly flexible (adjustable).

The immune system in our body is able to fight and win against practically any enemy, irrespective of its shape and molecular properties (charge distribution). How is it possible? Would the organism be prepared for everything? Well, yes and no.

Let us imagine a system of molecules (building blocks) having some synthons and able to create some van der Waals complexes, Fig. 15.2. Since the van der Waals forces are quite weak, the complexes are in dynamic equilibrium. All possible complexes are present in the solution, none of the complexes dominates.

Now, let us introduce some “enemy-molecules”. The building blocks use part of their synthons for binding the enemies (that have complementary synthons), and at the same time bind among themselves in order to strengthen the interaction. Some of the complexes are especially effective in this binding. Now, the Le Chatelier rule comes into play and the equilibrium shifts to produce as many of the most effective binders as possible. On top of this, the most effective binder may undergo a chemical reaction that replaces the weak van der Waals forces by strong chemical forces (the reaction rate is enhanced by the supramolecular interaction). The enemy was tightly secured, the invasion is over.¹³

¹³A simple model of immunological defence, similar to that described above, was proposed by F. Cardullo, M. Crego Calama, B.H.M. Snelling-Ruël, J.-L. Weidmann, A. Bielejewska, R. Fokkens, N.M.M. Nibbering, P. Timmerman, D.N. Reinhoudt, *J. Chem. Soc. Chem. Commun.* 367 (2000).

DYNAMICS

15.6 NON-LINEARITY

Its origin is mathematical, where non-linearity is defined as opposed to linearity. Linearity, in the sense of the proportionality between a cause and an effect, is widely used in physics and technical sciences. There is common sense in this, since when a cause is small, the result is in most cases also small.¹⁴ For instance, when a light object is hanging on a spring, the spring elongates in proportion to its weight (to high accuracy).¹⁵ Similarly, when a homogeneous weak electric field is applied to the helium atom, its electrons will shift slightly towards the anode, while the nucleus will be displaced a little in the direction of the cathode, cf. Chapter 12. This results in an induced dipole moment, which to a high degree of accuracy is proportional to the electric field intensity, and the proportionality coefficient is the polarizability of the helium atom. Evidently, reversing the direction of the electric field would produce exactly the same magnitude of induced dipole moment, but its direction will be opposite. We can perform such an experiment with the HCl molecule (the molecule is fixed in space, the electric field directed along the H...Cl axis, from H to Cl).¹⁶ When an electric field is applied, the dipole moment of the molecule will change slightly, and the change (an induced dipole moment) is to a good accuracy proportional to the field with the proportionality coefficient being the longitudinal polarizability of HCl. However, when the direction of the field is reversed, the absolute value of the induced dipole moment will be the same as before. Wait a minute! This is pure nonsense. The electrons move with the same facility towards the electron acceptor (chlorine) as to the electron donor (hydrogen)? Yes, as far as the polarizability (i.e. linearity) decides, this is true indeed. Only, when going beyond the linearity, i.e. when the induced dipole moment depends on higher powers of the electric field intensity, we recover common sense: electrons move more easily towards an electron acceptor than towards an electron donor... Thus, the non-linearity is there and is important.

Non-linearity was an unwanted child of physics. It sharply interfered with making equations easy to solve. Without it, the solutions often represent beautiful, concise expressions, with great interpretative value, whereas with it everything gets difficult, clumsy and most often impossible to treat. We are eventually left with numerical solutions, which have to be treated case by case with no hope of a nice generalization. Sometimes the non-linearity could be treated by perturbation theories,

¹⁴“Most” is a dangerous word. What about such things dice, roulette, etc.? There is a kind of “historical” dependence of the result from the initial conditions. The same is true for the solution of the equation... $x^3 = -1$. Until the nineteen-eighties mathematicians thought that nothing new would be added to this solution. However, when they applied Newton’s method to solve it numerically, a fractal dependence on the initial conditions appeared.

¹⁵Non-linearity is, however, entering into play if the object is heavy and/or if the spring is compressed with the same force instead of elongated.

¹⁶In this molecule, without any external electric field applied, the electrons are slightly shifted from the hydrogen (electron donor) to the chlorine atom (electron acceptor), which results in a permanent dipole moment.

where the linear case is considered as a reference and the non-linear corrections are taken into account and calculated. Nothing particularly important emerged from this. Now we know why. Perturbation theory requires a small perturbation (a weak non-linearity), while the most interesting phenomena discovered in the 1970-ties by Prigogine, emerged when non-linearity is large (large fluctuations exploring new possibilities of the system).

With the advent of computers that which was difficult to solve (numerically) before, often became easy. Without computers, we would understand much less about dissipative structures, chaos theory, attractors, etc. These subjects are of a mathematical nature, but have a direct relation to physics and chemistry, and most of all to biology. The relation happens on remarkably different scales and in remarkably different circumstances:¹⁷ from chemical waves *in space* rationalizing the extraordinary pattern of the zebra skin to population waves of lynxes and rabbits as functions of time. In all these phenomena non-linearity plays a prominent role.

Quite surprisingly, it turns out that a few non-linear equations have analytical and simple solutions. One of such cases is a soliton, i.e. a solitary wave (a kind of hump). Today solitons already serve to process information, thanks to the *non-linear* change of the refractive index in a strong laser electric field. Conducting polymers turn out to be channels for another kind of solitons¹⁸ (cf. Chapter 9).

15.7 ATTRACTORS

Mitchell Feigenbaum (b. 1944), American physicist, employee of the Los Alamos National Laboratory, then professor at the Cornell University and at the Rockefeller University. Feigenbaum discovered attractors after making some observations just playing with a pocket calculator.



Non-linearity in mathematics is connected to the notion of attractors.

The theory of attractors was created by Mitchell Feigenbaum. When applying an iterative method of finding a solution,¹⁹ we first decide which operation is supposed to bring us closer to the solution as well as what represents a reasonable zero-order guess (starting point: a number, a function, a sequence of functions).

Then we force an evolution (“dynamics”) of the approximate solutions by applying the operation first to the starting point, then to the result obtained by the operation on the starting point, and then again and again until convergence is achieved.

Let us take an example and choose as the operation on a number x the following $x_{n+1} = \sin(x_n^2 + 1)$, where n stands for the iteration number. The iterative scheme therefore means choosing any x_0 , and then applying many times a sequence of

¹⁷This witnesses the universality of Nature’s strategy.

¹⁸The word “channel” has been used on purpose to allude to the first soliton wave observed in an irrigation channel.

¹⁹Cf. the SCF LCAO MO method, p. 364, or the iterative version of perturbational theory, p. 717.

four keys on the calculator keyboard. Here are the results of two different starting points: $x_0 = 1410$ and -2000 .

1410	-2000
-0.0174524	0.656059
0.0174577	0.0249628
0.0174577	0.0174633
0.0174577	0.0174577

The *result is independent of the starting point chosen*. The number 0.0174577 represents an attractor or a *fixed point* for the operation. In the SCF method the fixed point is identical with the single Slater-determinant function (a point in the Hilbert space, cf. Appendix B) – a result of the SCF iterative procedure.

fixed point

Let us consider some other attractors. If we take the clamped-nuclei electronic energy $V(\mathbf{R})$ as a function of the nuclear configuration \mathbf{R} ($V(\mathbf{R})$ represents a generalization of $E_0^0(R)$ from eq. (6.18), p. 227, that pertains to a diatomic molecule). The forces acting on atoms can be computed as the components of the vector $\mathbf{F} = -\nabla V$. Imagine we are looking for the most stable configurations of the nuclei, i.e. for the minima of $V(\mathbf{R})$. We know that when such a configuration is achieved, the forces acting on all the atoms are zero. When we start from an initial guess \mathbf{R}_0 and follow the computed force $\mathbf{F} = -\nabla V$ (this defines the operation in question), then it is hoped that we end up at a local minimum of V independent of the starting point, provided the point belongs to the basin corresponding to the minimum (cf. p. 769). If, however, the starting point were outside the basin, we would find another minimum (having its own basin, where the starts would all lead to the same result). Thus, we may have to do with many attractors at the same time. The positions of the *maxima* of V may be called *repellers* to stress their action opposite to the attractors. For a repeller the procedure of following the direction of $-\nabla V$ gets us further and further away from the repeller.

repellers

In thermodynamics, the equilibrium state of an isolated system (at some fixed external parameters) may be regarded as an attractor, that *any* non-equilibrium state attains after a sufficiently long time.

15.8 LIMIT CYCLES

Sometimes an attractor represents something other than just a point at which the evolution of the system definitely ends up.

Consider a set of two differential equations with time t as variable. Usually their solution $[x(t)$ and $y(t)]$ depends on the initial conditions assumed, Fig. 15.3.a.

Now let us take a particular set of two *non-linear* differential equations. As seen from Fig. 15.3.b, this time the behaviour of the solution as a function of time is completely different: for high values of t the solution does not depend on the ini-

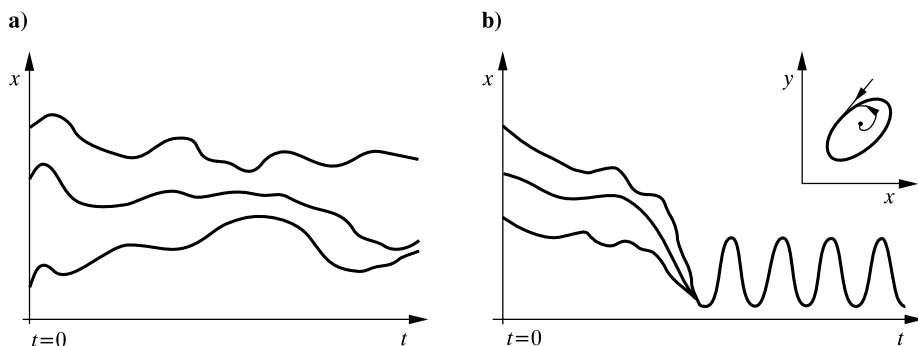


Fig. 15.3. Two different behaviours of solutions of differential equations, depending on initial conditions. (a) The plots represent $x(t)$ for three sets of initial conditions. As seen, the trajectories differ widely, i.e. the fate of the system depends very much on the initial conditions. Fig. (b) shows the idea of the limit cycle for a set of hypothetical non-linear differential equations. For large values of t , the three sets of initial conditions lead to *the same* trajectory.

tial conditions chosen. We obtain the $y(x)$ dependence in a form called the *limit cycle*, and the functions $x(t)$ and $y(t)$ exhibit periodic oscillations. The system is condemned to repeat forever the same sequence of positions – the limit cycle.

In chemistry x and y may correspond to the concentrations of two substances. The limit cycles play a prominent role in new chemistry, since they ensure that the system evolves to the same periodic oscillations independent of the initial conditions of some chemical reactions (with the non-linear dependence of their velocity on concentrations, cf. p. 872). Such reactions could, therefore,

chemical clock

- provide a stimulus for the periodic triggering of some chemical processes (*chemical clock*),
- provide chemical counting, which (similar to today's computers) could be related to chemical programming in the future.

15.9 BIFURCATIONS²⁰ AND CHAOS

Non-linear dynamics turned out to be extremely sensitive to coupling with some external parameters (representing the “neighbourhood”).

logistic equation

Let us take what is called the *logistic equation*

$$x = Kx(1 - x),$$

where $K > 0$ is a constant. The Oxford biologist, Sir Robert May, gave a numerical exercise to his Australian graduate students. They had to calculate how a rabbit

²⁰A bifurcation (corresponding to a parameter p) denotes in mathematics a doubling of an object when the parameter exceeds a value p_0 . For example, when the object corresponds to the number of solutions of equation $x^2 + px + 1 = 0$, then the bifurcation point $p_0 = 2$. Another example of bifurcation is branching of roads, valleys, etc.

population evolves when we let it grow according to the rule

$$x_{n+1} = Kx_n(1 - x_n),$$

which is obviously related to the logistic equation. The natural number n denotes the current year, while x_n stands for the (relative) population of, say, rabbits in a field, $0 \leq x_n \leq 1$. The number of the rabbits in year $(n + 1)$ is proportional to their population in the preceding year (x_n), because they reproduce very fast, but the rabbits eat grass and the field has a finite size. The larger x_n the less the amount of grass to eat, which makes the rabbits a bit weaker and less able to reproduce (this effect corresponds to $1 - x_n$).

The logistic equation contains a feed back mechanism.

The constant K measures the population–grass coupling strength (low-quality grass means a small K). What interests us is the fixed point of this operation, i.e. the final population the rabbits develop after many years at a given coupling constant K . For example, for $K = 1$ the evolution leads to a steady self-reproducing population x_0 , and x_0 depends on K (the larger K the larger x_0). The graduate students took various values of K . *Nobody* imagined this quadratic equation could hide a mystery.

If K were small ($0 \leq K < 1$, extremely poor grass), the rabbit population would simply vanish (the first part of Fig. 15.4). If K increased (the second part of the plot, $1 \leq K < 3$), the population would flourish. When K exceeded 3 this flourishing would give, however, a unexpected twist: instead of reaching a fixed point, the system would oscillate between two sizes of the population (every second year the population was the same, but two consecutive years have different populations). This resembles the limit cycle described above – the system just repeats the same cycle all the time.

This mathematical phenomenon was carefully investigated and the results were really amazing. Further increase in K introduces further qualitative changes. First, for $3 \leq K < 3.44948$ the oscillations have period two (*bifurcation*), then at $3.44948 \leq K < 3.5441$ the oscillations have period four (next bifurcation, the four-member limit cycle), then for $3.5441 \leq K < 3.5644$ the period is eight (next bifurcation).²¹

bifurcation

Then, the next surprise: exceeding $K = 3.56994$ we obtain populations that do not exhibit any regularity (no limit cycle, just *chaos*). A further surprise is that this is not the end of the surprises. Some sections of K began to exhibit *odd*-period behaviour, separated by some sections of chaotic behaviour.

chaos

²¹Mitchell Feigenbaum was interested to see at which value $K(n)$ the next bifurcation into 2^n branches occurs. It turned out that there is a certain regularity, namely, $\lim_{n \rightarrow \infty} \frac{K_{n+1} - K_n}{K_{n+2} - K_{n+1}} = 4.669201609 \dots \equiv \delta$. To the astonishment of scientists, the value of δ turned out to be “universal”, i.e. characteristic for many *very different* mathematical problems and, therefore, reached a status similar to that of the numbers π and e . The numbers π and e satisfy the exact relation $e^{i\pi} = -1$, but so far no similar relation was found for the Feigenbaum constant. There is an *approximate* relation (used by physicists in phase transition theory) which is satisfied: $\pi + \tan^{-1} e^\pi = 4.669201932 \approx \delta$.

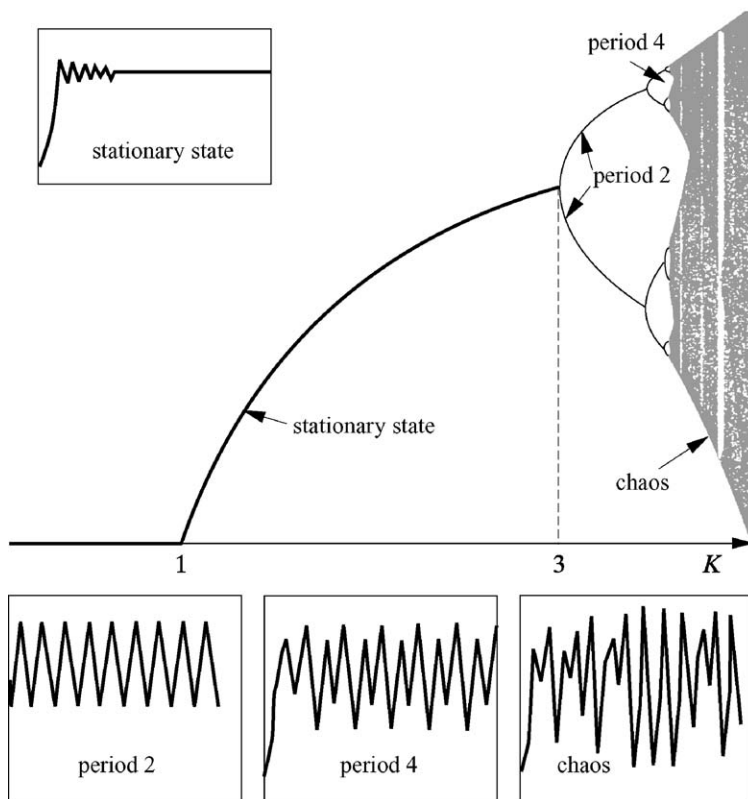


Fig. 15.4. The diagram of the fixed points and the limit cycles for the logistic equation as a function of the coupling constant K . From J. Gleick, “*Chaos*”, Viking, New York, 1988, reproduced with permission of the author.

15.10 CATASTROPHES

The problems described above have to do with another important mathematical theory.

As has been shown for electronic energy $V(\mathbf{R})$, we may have several minima. Having a deterministic procedure that leads from a given point to a minimum means creating the dynamics of the system (along a trajectory), in which any minimum may be treated as an attractor (Chapter 6), with its basin meaning those points that, following the dynamics, produce trajectories that end up at the minimum. We can also imagine trajectories that do not end up at a point, but in a closed loop (limit cycle).

Imagine $V(\mathbf{R})$ depends on a parameter t . What would happen to the attractors and limit cycles if we changed the value of the parameter? When a change has a qualitative character (e.g., the number of basins changes), the founder of the theory, René Thom, called it a catastrophe.

15.11 COLLECTIVE PHENOMENA

Imagine some subunits cooperate so strongly that many events require less energy than a single one or a few. In such a case, a few events may trigger an avalanche of other events (*domino effect*). Numerous examples of this are phase transitions, where a change of the position, orientation or conformation of a few molecules requires energy, whereas when a barrier is overcome the changes occur spontaneously for all the molecules. Imagine a photoisomerization (such as that of azabenzene) in the solid state. If a *single* molecule in a crystal were to undergo the change, such an excitation might cost a lot of energy, because there might not be enough space to perform the trans to cis transition.²² When, however, a lot of molecules undergo such a change in a concerted motion, the atomic collision would not necessarily take place and the cost in energy would be much smaller than the sum of all the single excitations.

domino effect

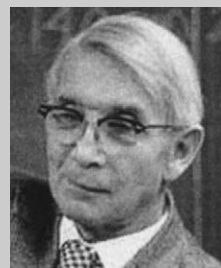
An example of electronic collectivity may also be the electronic bistability effect expected to occur in a rigid donor–acceptor oligomer; (DA)_N, composed of suitable electron donors (D) and acceptors (A) at a proper DA distance and orientation, Fig. 15.5.

15.11.1 SCALE SYMMETRY (RENORMALIZATION)

It turns out that different substances, when subject to phase transition, behave in exactly the same way exhibiting therefore a universal behaviour.

Imagine a system of N identical equidistant spin magnetic moments located on the z axis, each spin parallel or antiparallel to the axis.²³ The j -th spin has two components (cf. p. 28) $\sigma_j = 1, -1$. Often the Hamiltonian H of a system is approximated by taking into account nearest-neighbour interactions only (*Ising model*) in the following way (the constants K, h, C fully determine the Hamiltonian)

Ernst Ising (1900–1998), German mathematician and physicist. In 1939, after interrogation by the gestapo in Berlin, Ising emigrated to Luxembourg, and there in a German labour camp he held out until liberation by the Allies. From 1948 he became a professor at Bradley University (USA). His two-state chain model is very often used in mathematical physics.



$$H = K \sum_j \sigma_j \sigma_{j+1} + h \sum_j \sigma_j + C, \quad (15.1)$$

where the first term corresponds to dipole-dipole magnetic interactions like those described on p. 655, the second term takes care of the interactions with an external magnetic field (Zeeman effect, p. 659), and C is a constant.

²²Some atoms would simply hit others, causing an enormous increase in energy resulting in an energy barrier.

²³The objects need not be spins, they may represent two possible orientations of the molecules, etc.

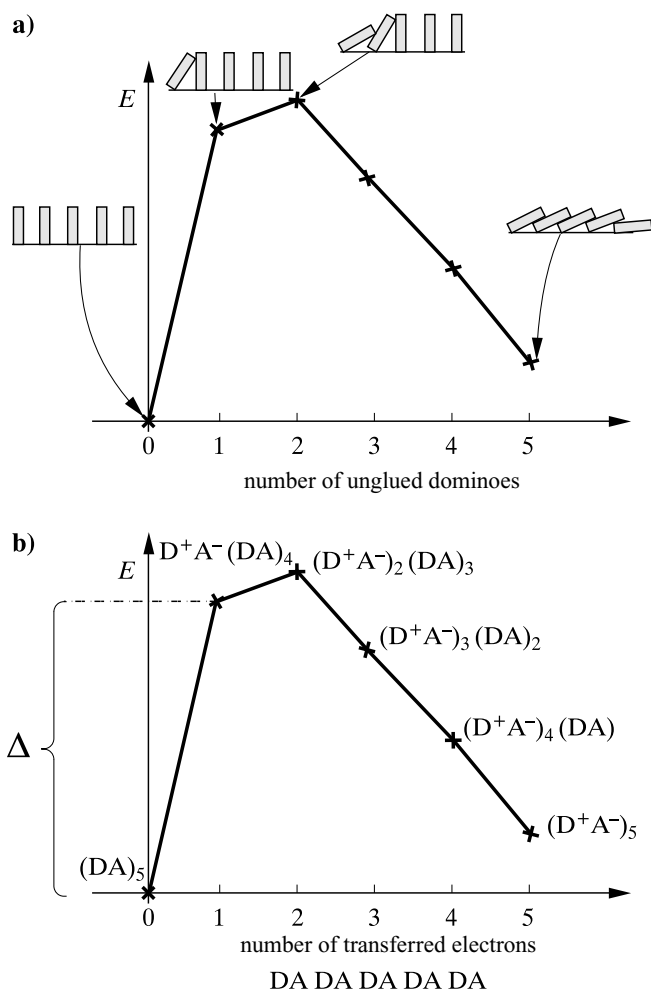


Fig. 15.5. Collective phenomena. (a) The domino principle. An energy cost corresponding to ungluing and knocking down the dominoes. (b) Hypothetical electronic domino (or “mnemon” – an element of molecular memory) composed of electron donors (D) and electron acceptors (A). In order to transfer the first electron we have to pay energy Δ . The second electron transfer (when the first is already transferred) needs less energy, because it is facilitated by the dipole created. The transfer of the third and further electrons does not need any energy at all (the energy actually decreases). The hypothetical electronic domino starts running (L.Z. Stolarczyk, L. Piela, *Chem. Phys.* 85 (1984) 451).

The partition function (which all the thermodynamic properties can be computed from) is defined as:

$$Z(T) = \frac{1}{2^N} \sum_{\sigma_1} \sum_{\sigma_2} \dots \sum_{\sigma_N} \exp\left(-\frac{H(K, h, C)}{k_B T}\right). \quad (15.2)$$

Each of the N sums in eq. (15.2) pertains to a single spin. A trivial observation that the summation in eq. (15.2) *can* be carried out in (two) steps, leads to something extraordinary. We may first *sum over every other object*.²⁴ Then, the spins of the objects we have summed formally disappear from the formula, we have the summation over spins of the *remaining* objects only. Such a procedure is called *decimation*²⁵ from a form of collective capital punishment in the regulations of the Roman legions (very unpleasant for every tenth legionary). As a result of the procedure, the Hamiltonian H is changed and now corresponds to the interaction of the spins of the remaining objects. These spins, however, are “dressed” in the interaction with the other spins, which have been killed in the decimation procedure. What purpose may such a decimation serve? Well,

decimation

after this is done, the expression $Z(T)$ from formula (15.2) will look *similar* to that before the transformation (*self-similarity*). Only the constants $K \rightarrow K'$, $h \rightarrow h'$, $C \rightarrow C'$ change.²⁶

self-similarity

The two Hamiltonians are related by a self-similarity. The decimation may then be repeated again and again, leading to a trajectory in the space of the parameters K, h, C . It turns out that a system undergoing a phase transition is located on such a trajectory. By repeating the decimation, we may reach a fixed point (cf. p. 858), i.e. further decimations do not change the parameters, the system attains *self-similarity on all scales*. The *fixed point may be common for a series of substances*, because the trajectories (each for a given substance) may converge to a common fixed point. The substances may be different, may interact differently, may undergo different phase transitions, but since they share the fixed point, some features of their phase transitions are nevertheless identical.

This section links together several topics: attractors, self-similarity (renormalization group theory), catastrophe theory.

15.11.2 FRACTALS

Self-similarity, highlighted by renormalization, represents the essence of fractals. Let us consider what is called the *Sierpiński carpet* (Fig. 15.6.a).

Sierpiński carpet

²⁴Here we follow D.R. Nelson and M.E. Fisher, *Ann. Phys. (N.Y.)* 91 (1975) 226.

²⁵Although in this situation the name does not fit quite so well.

²⁶It is a matter of fifteen minutes to show (e.g., M. Fisher, *Lecture Notes in Physics* 186 (1983)), that the new constants are expressed by the old ones as follows:

$$\begin{aligned}\exp(4K') &= \frac{\cosh(2K+h)\cosh(2K-h)}{\cosh^2 h}, \\ \exp(2h') &= \exp(2h) \frac{\cosh(2K+h)}{\cosh(2K-h)}, \\ \exp(4C') &= \exp(8C) \cosh(2K+h)\cosh(2K-h)\cosh^2 h.\end{aligned}$$

The self-similarity of this mathematical object (when we decide to use more and more magnifying glasses) is evident.

Wacław Sierpiński (1882–1969), Polish mathematician, from 1910 professor at the Jan Casimir University in Lwów, and from 1918 at the University of Warsaw. One of the founders of the famous Polish school of mathematics. His most important achievements are related to set theory, number theory, theory of real functions and topology



(there is the carpet in question).

Benoit Mandelbrot, French mathematician, born in 1924 in Warsaw, first worked at the Centre National de la Recherche Scientifique in Paris, then at the Université de Lille, from 1974 an employee of the IBM Research Center in New York. When playing with a computer, Mandelbrot discovered the world of fractals.



On the other hand, it is striking that fractals of fantastic complexity and shape may be constructed in an amazingly simple way by using the dynamics of the iteration processes described on p. 858. Let us take, for example, the following operation defined on the complex plane: let us choose a complex number C , and then let us carry out the iterations

$$z_{n+1} = z_n^2 + C$$

for $n = 0, 1, 2, 3, \dots$ starting from $z_0 = 0$. The point C will be counted as belonging to what is called the Mandelbrot set, if the points z_n do not exceed a circle of radius 1. The points of the Mandelbrot set will be denoted by black, the other points will be coloured depending on the velocity at which they flee the circle. Could anybody ever think that we would get the incredibly rich pattern shown in Fig. 15.6.b?

15.12 CHEMICAL FEEDBACK – NON-LINEAR CHEMICAL DYNAMICS

Could we construct chemical feedback? What for? Those who have ever seen feedback working know the answer²⁷ – this is the very basis of control. Such control of chemical concentrations is at the heart of how biological systems operate.

The first idea is to prepare such a system in which an increase in the concentration of species X triggers the process of its decreasing. The decreasing occurs by replacing X by a very special substance Y , each molecule of which, when disintegrating, produces several X molecules. Thus we would have a scheme (X denotes a large concentration of X , x denotes a small concentration of X ; similarly for the species Y): $(X, y) \rightarrow (x, Y) \rightarrow (X, y)$ or *oscillations of the concentration of X and Y in time*.²⁸

²⁷For example, an oven heats until the temperature exceeds an upper bound, then it switches off. When the temperature reaches a lower bound, the oven switches *itself* on (therefore, we have temperature oscillations).

²⁸Similar to the temperature oscillations in the feedback of the oven.

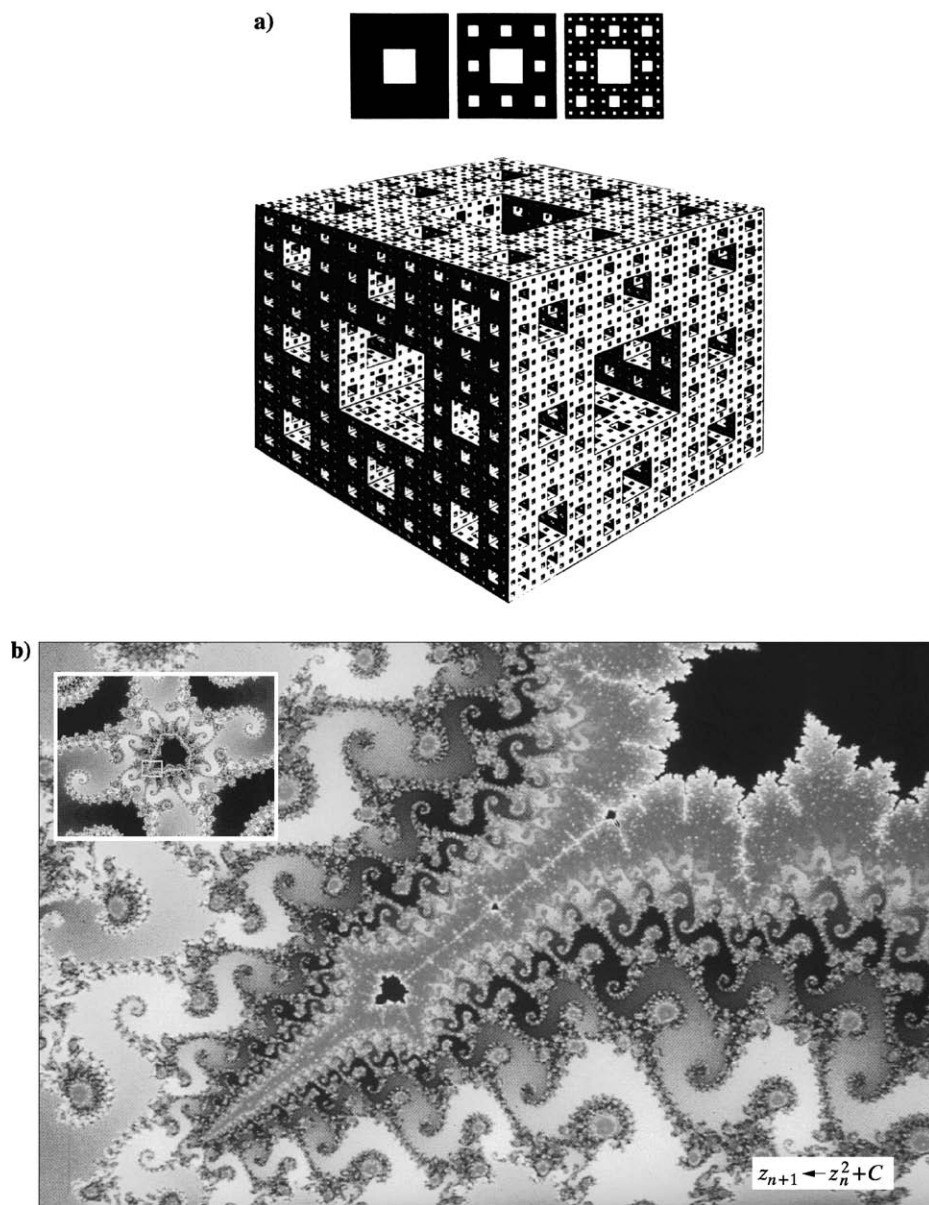


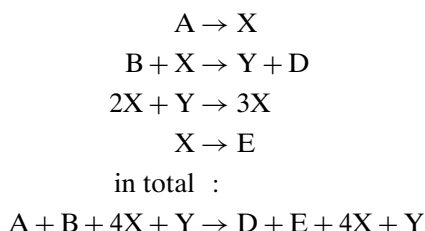
Fig. 15.6. Fractals. (a) Sierpiński carpet. (b) Mandelbrot set. Note that the incredibly complex (and beautiful) set exhibits some features of self-similarity, e.g., the central “turtle” is repeated many times in different scales and variations, as does the fantasy creature in the form of an S. On top of this, the system resembles the complexity of the Universe: using more and more powerful magnifying glasses, we encounter ever new elements that resemble (but not just copy) those we have already seen. From J. Gleick, “*Chaos*”, Viking, New York, 1988, reproduced by permission of the author.

15.12.1 BRUSSELATOR – DISSIPATIVE STRUCTURES

Brusselator without diffusion

Imagine we carry out a complex chemical reaction in flow conditions,²⁹ i.e. the reactants A and B are pumped with a constant speed into a long narrow tube reactor, there is intensive stirring in the reactor, then the products flow out to the sink (Fig. 15.7). After a while a steady state is established.³⁰

After the A and B are supplied, the substances³¹ X and Y appear, which play the role of catalysts, i.e. they participate in the reaction, but in total their amounts do not change. To model such a situation let us assume the following chain of chemical reactions:



This chain of reactions satisfies our feedback postulates. In step 1 the concentration of X increases, in step 2 Y is produced at the expense of X, in step 3 substance Y enhances the production of X (at the expense of itself, this is an *autocatalytic step*), then again X transforms to Y (step 2), etc.

If we shut down the fluxes in and out, after a while a thermodynamic equilibrium is attained with all the concentrations of the six substances (A, B, D, E, X, Y; their concentrations will be denoted as A, B, D, E, X, Y , respectively) being constant

autocatalysis

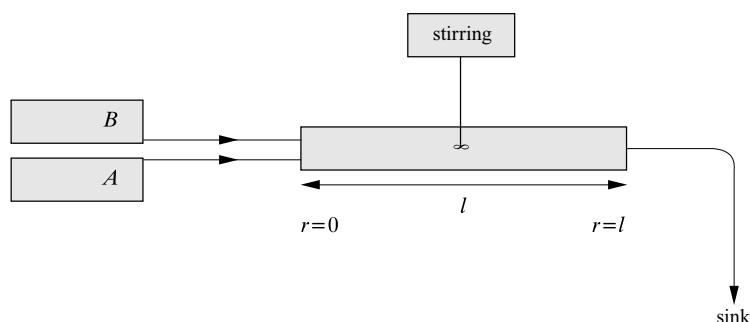


Fig. 15.7. A flow reactor (a narrow tube – in order to make a 1D description possible) with stirring (no space oscillations in the concentrations). The concentrations of A and B are kept constant at all times (the corresponding fluxes are constant).

²⁹Such reaction conditions are typical for industry.

³⁰To be distinguished from the thermodynamic equilibrium state, where the system is isolated (no energy or matter flows).

³¹Due to the chemical reactions running.

in space (along the reactor) and time. On the other hand, when we fix the in and out fluxes to be constant (but non-zero) for a long time, we force the system to be in a steady state and as far from thermodynamic equilibrium as we wish. In order to simplify the kinetic equations, let us assume the irreversibility of all the reactions considered (as shown in the reaction equations above) and put all the velocity constants equal to 1. This gives the kinetic equations for what is called the *Brusselator model* (of the reactor)

brusselator

$$\begin{aligned}\frac{dX}{dt} &= A - (B + 1)X + X^2Y, \\ \frac{dY}{dt} &= BX - X^2Y.\end{aligned}\tag{15.3}$$

These two equations, plus the initial concentrations of X and Y, totally determine the concentrations of all the species as functions of time (due to the stirring there will be no dependence on position in the reaction tube).

Steady state

A steady state (at constant fluxes of A and B) means $\frac{dX}{dt} = \frac{dY}{dt} = 0$ and therefore we easily obtain the corresponding steady-state concentrations X_s, Y_s by solving eq. (15.3)

$$\begin{aligned}0 &= A - (B + 1)X_s + X_s^2Y_s, \\ 0 &= BX_s - X_s^2Y_s.\end{aligned}$$

Please check that these equations are satisfied by

$$\begin{aligned}X_s &= A, \\ Y_s &= \frac{B}{A}.\end{aligned}$$

Evolution of fluctuations from the steady state

Any system undergoes some spontaneous concentration fluctuations, or we may perturb the system by injecting a small amount of X and/or Y. *What will happen to the stationary state found a while before, if such a fluctuation happens?*

Let us see. We have fluctuations x and y from the steady state

$$\begin{aligned}X(t) &= X_s + x(t), \\ Y(t) &= Y_s + y(t).\end{aligned}\tag{15.4}$$

What will happen next?

After inserting (15.4) in eqs. (15.3) we obtain the equations describing how the fluctuations evolve in time

$$\begin{aligned}\frac{dx}{dt} &= -(B+1)x + Y_s(2X_sx + x^2) + y(X_s^2 + 2xX_s + x^2), \\ \frac{dy}{dt} &= Bx - Y_s(2X_sx + x^2) - y(X_s^2 + 2xX_s + x^2).\end{aligned}\quad (15.5)$$

linearization

Since a mathematical theory for arbitrarily large fluctuations does not exist, we will limit ourselves to small x and y . Then, all the quadratic terms of these fluctuations can be neglected (*linearization* of (15.5)). We obtain

$$\begin{aligned}\frac{dx}{dt} &= -(B+1)x + Y_s(2X_sx) + yX_s^2, \\ \frac{dy}{dt} &= Bx - Y_s(2X_sx) - yX_s^2.\end{aligned}\quad (15.6)$$

Let us assume fluctuations of the form³²

$$\begin{aligned}x &= x_0 \exp(\omega t), \\ y &= y_0 \exp(\omega t)\end{aligned}\quad (15.7)$$

and represent particular solutions to eqs. (15.6) provided the proper values of ω , x_0 and y_0 are chosen. After inserting (15.7) in eqs. (15.6) we obtain the following set of equations for the unknowns ω , x_0 and y_0

$$\begin{aligned}\omega x_0 &= (B-1)x_0 + A^2 y_0, \\ \omega y_0 &= -Bx_0 - A^2 y_0.\end{aligned}\quad (15.8)$$

This represents a set of homogeneous linear equations with respect to x_0 and y_0 , and this means we have to ensure that the determinant, composed of the coefficients multiplying the unknowns x_0 and y_0 , vanishes (*characteristic equation*, cf. secular equation, p. 202)

$$\begin{vmatrix} \omega - B + 1 & -A^2 \\ B & \omega + A^2 \end{vmatrix} = 0.$$

This equation is satisfied by some special values of³³ ω :

$$\omega_{1,2} = \frac{T \pm \sqrt{T^2 - 4\Delta}}{2}, \quad (15.9)$$

where

³²Such a form allows for exponential growth ($\omega > 0$), decaying ($\omega < 0$) or staying constant ($\omega = 0$), as well as for periodic behaviour ($\text{Re } \omega = 0, \text{Im } \omega \neq 0$), quasiperiodic growth ($\text{Re } \omega > 0, \text{Im } \omega \neq 0$) or decay ($\text{Re } \omega < 0, \text{Im } \omega \neq 0$).

³³They represent an analogue of the normal mode frequencies from Chapter 7.

$$T = -(A^2 - B + 1), \quad (15.10)$$

$$\Delta = A^2. \quad (15.11)$$

Fluctuation stability analysis

Now it is time to pick the fruits of our hard work.

How the fluctuations depend on time is characterized by the roots $\omega_1(t)$ and $\omega_2(t)$ of eq. (15.9), because x_0 and y_0 are nothing but some constant amplitudes of the changes. We have the following possibilities (Fig. 15.8, Table 15.1.):

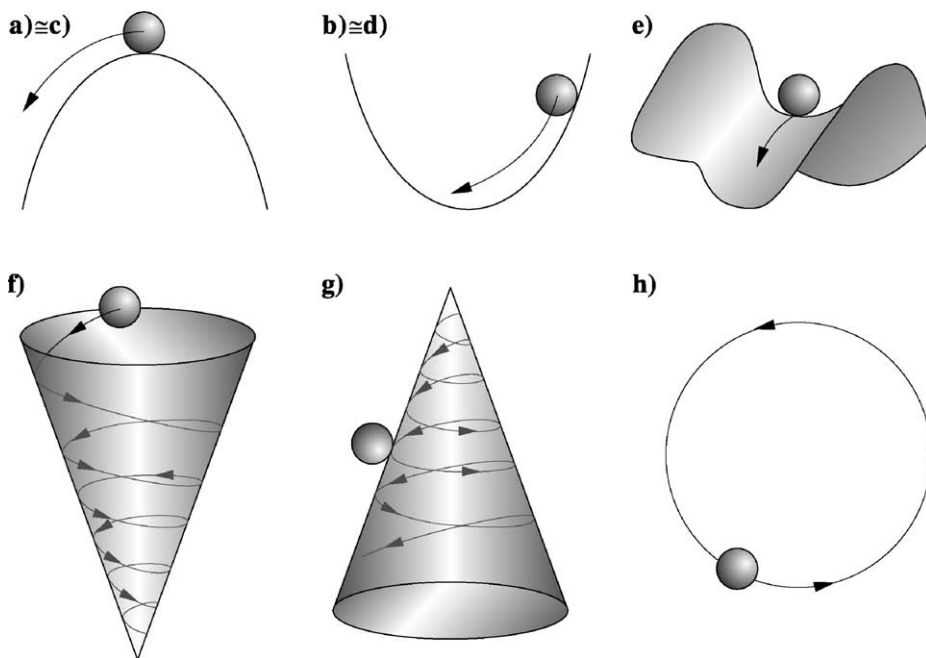


Fig. 15.8. Evolution types of fluctuations from the reaction steady state. The classification is based on the numbers ω_1 and ω_2 of eq. (15.9). The individual figures correspond to the rows of Table 15.1. The behaviour of the system (in the space of chemical concentrations) resembles sliding of a point or rolling a ball over certain surfaces in a gravitational field directed downward:

- (a) unstable node resembles sliding from the top of a mountain;
- (b) stable node resembles moving inside a bowl-like shape;
- (c) the unstable stellar node is similar to case (a), with a slightly different mathematical reason behind it;
- (d) similarly for the stable stellar node [resembles case (b)];
- (e) saddle – the corresponding motion is similar to a ball rolling over a cavalry saddle (applicable for a more general model than the one considered so far);
- (f) stable focus – the motion resembles rolling a ball over the interior surface of a cone pointing downward;
- (g) unstable focus – a similar rolling but on the external surface of a cone that points up;
- (h) centre marginal stability corresponds to a circular motion.

Table 15.1. Fluctuation stability analysis, i.e. what happens if the concentrations undergo a fluctuation from the steady state values. The analysis is based on the values of ω_1 and ω_2 from eq. (15.9); they may have real (subscript r) as well as imaginary (subscript i) parts, hence: $\omega_{r,1}, \omega_{i,1}, \omega_{r,2}, \omega_{i,2}$

T	Δ	$T^2 - 4\Delta$	$\omega_{r,1}$	$\omega_{i,1}$	$\omega_{r,2}$	$\omega_{i,2}$	Stability
+	+	+	+	0	+	0	unstable node
−	+	+	−	0	−	0	stable node
−	+	0	−	0	−	0	stable stellar node
+	+	0	+	0	+	0	unstable stellar node
−	+	−	−	$i\omega$	−	$-i\omega$	stable focus
+	+	−	+	$i\omega$	+	$-i\omega$	unstable focus
0	+	−	0	$i\omega$	0	$-i\omega$	centre marginal stability

- Both roots are real, which happens only if $T^2 - 4\Delta \geq 0$. Since $\Delta > 0$, the two roots are of the same sign (sign of T). If $T > 0$, then both roots are positive, which means that the fluctuations $x = x_0 \exp(\omega t)$, $y = y_0 \exp(\omega t)$ *increase over time and the system will never return to the steady state* (“*unstable node*”). Thus the steady state represents a *repeller* of the concentrations X and Y.
unstable node
- If, as in the previous case at $T^2 - 4\Delta \geq 0$, but this time $T < 0$, then both roots are negative, and this means that the fluctuations from the steady state will vanish (“*stable node*”). It looks as if we had in the steady state an *attractor* of the concentrations X and Y.
stable node
- Now let us take $T^2 - 4\Delta = 0$, which means that the two roots are equal (“degeneracy”). This case is similar to the two previous ones. If the two roots are positive then the point is called the *stable stellar node* (attractor), if they are negative it is called the *unstable stellar node* (repeller).
stable and unstable stellar nodes
- If $T^2 - 4\Delta < 0$, we have an interesting situation: both roots are complex conjugate $\omega_1 = \omega_r + i\omega_i$, $\omega_2 = \omega_r - i\omega_i$, or $\exp \omega_{1,2}t = \exp \omega_r t \exp(\pm i\omega_i t) = \exp \omega_r (\cos \omega_i t \pm i \sin \omega_i t)$. Note that $\omega_r = \frac{T}{2}$. We have therefore three special cases:
 - $T > 0$. Because of $\exp \omega_r t$ we have, therefore, a monotonic increase in the *fluctuations*, and at the same time because of $\cos \omega_i t \pm i \sin \omega_i t$ the two concentrations oscillate. Such a point is called the *unstable focus* (and represents a repeller).
stable and unstable focuses
 - $T < 0$. In a similar way we obtain the *stable focus*, which means some damped vanishing concentration oscillations (attractor).
 - $T = 0$. In this case $\exp \omega_{1,2}t = \exp(\pm i\omega_i t)$, i.e. we have the *undamped oscillations* of X and Y about the stationary point X_s, Y_s , which is called, in this case, the *centre marginal stability*.
centre marginal stability

Qualitative change

Can we qualitatively change the behaviour of the reaction? Yes. It is sufficient just to change the concentrations of A or B (i.e. to rotate the reactor taps). For example, let us gradually change B. Then, from eqs. (15.10), it follows that the key parameter T begins to change, which leads to an *abrupt qualitative change* in

the behaviour (a catastrophe in the mathematical sense, p. 862). Such changes may be of great importance, and as the control switch may serve to regulate the concentrations of some substances in the reaction mixture.

Note that the reaction is autocatalytic, because in step 3 the species X catalyzes the production of itself.³⁴

Brusselator with diffusion

If the stirrer were removed from the reactor, eqs. (15.3) have to be modified by adding diffusion terms

$$\frac{dX}{dt} = A - (B + 1)X + X^2Y + D_X \frac{\partial^2 X}{\partial r^2}, \quad (15.12)$$

$$\frac{dY}{dt} = BX - X^2Y + D_Y \frac{\partial^2 Y}{\partial r^2}. \quad (15.13)$$

A stability analysis similar to that carried out a moment before results *not only in oscillations in time, but also in space, i.e. in the reaction tube there are waves of the concentrations of X and Y moving in space (dissipative structures)*. Now, look at the photo of a zebra (Fig. 15.9) and at the bifurcation diagram in the logistic equation, Fig. 15.4.

dissipative
structures

15.12.2 HYPERCYCLES

Let us imagine a system with a chain of consecutive chemical reactions. There are a lot of such reaction chains around, it is difficult to single out an elementary reaction without such a chain being involved. They end up with a final product and everything stops. What would happen however, if at a given point of the reaction chain, a substance X were created, the same as one of the reactants at a previous stage of the reaction chain? The X would take control over its own fate, by the Le Chatelier rule. In such a way, feedback would have been established, and instead of the chain, we would have a catalytic cycle. A system with feedback may adapt to changing external conditions, reaching a steady or oscillatory state. Moreover, in our system a number of such independent cycles may be present. However, when two of them share a common reactant X , both cycles would begin to cooperate, usually exhibiting a very complicated stability/instability pattern or an oscillatory character. We may think of coupling many such cycles in a *hypercycle*, etc.

hypercycle

Cooperating hypercycles based on multilevel supramolecular structures could behave in an extremely complex way when subject to variable fluxes of energy and matter.³⁵ No wonder, then, that a single photon produced by the prey hidden in the dark and absorbed by the retinal in the lynx's eye may trigger an enormous

³⁴If autocatalysis were absent, our goal, i.e. concentration oscillations (dissipative structures), would not be achieved.

³⁵Note that similar hypercycles function in economics...

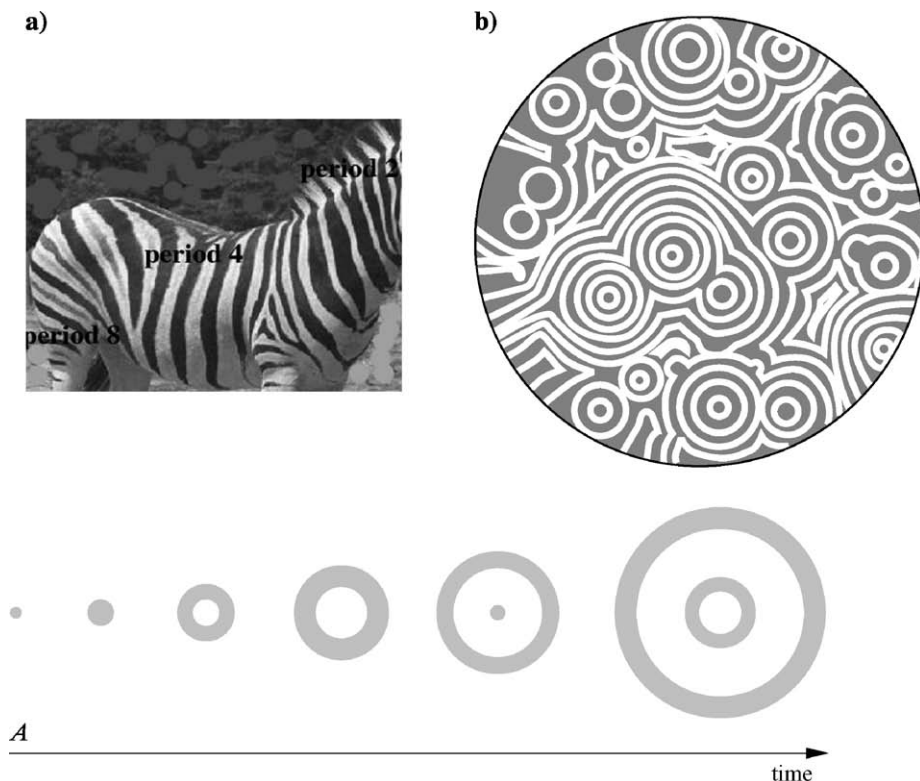


Fig. 15.9. (a) Such an animal “should not exist”. Indeed, how did the *molecules* know that they have to make a beautiful pattern. I looked many times on zebras, but only recently I was struck by the observation that what I see on the zebra’s skin is described by the logistic equation. The skin on the zebra’s neck exhibits quasiperiodic oscillations of the black and white colour (period 2), in the middle of the zebra’s body we have a *period doubling* (period 4), the zebra’s back has period 8. Fig. (b) shows the waves of the chemical information (concentration oscillations in space and time) in the Belousov–Zhabotinski reaction from several sources in space. A “freezing” (for any reason) of the chemical waves leads to a striking similarity with the zebra’s skin, from A. Babloyantz, “*Molecules, Dynamics and Life*”, Wiley-Interscience Publ., New York, 1986, reproduced with permission from John Wiley and Sons, Inc. Fig. (c) shows similar waves of an epidemic in a rather immobile society. The epidemic broke out in centre A. Those who have contact with the sick person get sick, but after some time they regain their health, and *for some time* become immune. After the immune period is over these people get sick again, because there are a lot of microbes around. This is how the epidemic waves may propagate.

variety of hunting behaviours. Or, maybe from another domain: a single glimpse of a girl may change the fates of many people,³⁶ and sometimes the fate of the world. This is the retinal in the eye hit by the photon of a certain energy changes its conformation from *cis* to *trans*. This triggers a cascade of further processes, which end up as a nerve impulse travelling to the brain, and it is over.

³⁶Well, think of a husband, children, grandchildren, etc.

CHEMICAL INFORMATION PROCESSING

15.13 FUNCTIONS AND THEIR SPACE-TIME ORGANIZATION

Using multi-level supramolecular architectures we may tailor new materials exhibiting desired properties, e.g., adapting themselves to changes in the neighbourhood (“smart materials”). Such materials have a function to perform, i.e. an action in time like ligand binding and/or releasing, transport of a ligand, an electron, a photon.³⁷

A molecule may perform *several* functions. Sometimes these functions may be *coupled*, giving functional cooperation. The cooperation is most interesting when the system is far from thermodynamic equilibrium, and the equilibrium is most important when it is complex. In such a case the energy and matter fluxes result in structures with unique features.

Biology teaches us that an unbelievable effect is possible: molecules may spontaneously form some large aggregates with very complex dynamics and the whole system searches for energy-rich substances to keep itself running. However, one question evades answer: what is the goal of the system?

The molecular functions of very many molecules may be coupled in a complex space-time relationship on many time and space scales involving enormous transport problems at huge distances of the size of our body, engaging many structural levels, at the upper level the internal organs (heart, liver, etc.), which themselves have to cooperate³⁸ by exchanging *information*.

Chemists of the future will deal with molecular functions and their interactions. The achievements of today, such as molecular switches, molecular wires, etc. represent just simple elements of the big machinery of tomorrow.

15.14 THE MEASURE OF INFORMATION

The TV News service presents a series of information items each evening. What kind of selection criteria are used by the TV managers? One of possible answers is that, for a given time period, they maximize the amount information given. A particular news bulletin contains a large amount of information, if it does not represent trivial common knowledge, but instead reports some unexpected facts. Claude Shannon defined the amount of information in a news bulletin as

$$I = -\log_2 p, \quad (15.14)$$

³⁷For example, a molecular antenna on one side of the molecule absorbs a photon, another antenna at the opposite end of the molecule emits another photon.

³⁸This recalls the renormalization group or self-similarity problem in mathematics and physics.

Claude Elwood Shannon (1916–2001), American mathematician, professor at the Massachusetts Institute of Technology, his professional life was associated with the Bell Laboratories. His idea, now so obvious, that information may be transmitted as a sequence of “0” and “1” was shocking in 1948. It was said that Shannon used to understand problems ‘in zero time’.



where p stands for the probability of the event the information reports. How much information is contained in the news that in a single trial coin came down tails? Well, it is $I = -\log_2 \frac{1}{2} = 1$ bit. The news “*there is air in Paris*” is of no use in a TV news service,³⁹ because in this case $I = -\log_2 1 = 0$.

Claude Shannon introduced the notion of the average information associated with all possible N results of an event in the usual way

$$H = \sum_{i=1}^N p_i I_i = - \sum_{i=1}^N p_i \log_2 p_i, \quad (15.15)$$

information
entropy

where H is called the *entropy of information*, because a similar formula works in thermodynamics for entropy.

The quantity H (a measure of our ignorance) is largest, if all p_i are equal.

At a given instant we estimate the probabilities of all possible results of an event (we compute H_o), then reliable information arrives and the estimation changes (we compute the information entropy in the new situation H_f). Then, according to Shannon the measure of the information received is

$$I = H_o - H_f. \quad (15.16)$$

codon

Example 1. Information flow in transcription. The sequence of three DNA bases (there are four bases possible: A, T, G, C), or a *codon*, codes for a single amino acid (there are 20 possible amino acids) in protein. Why three? Maybe three is too many? Let us see, what the problem looks like from the point of view of information flow.

A single codon carries the following information (in bits)

$$I_{\text{codon3}} = -\log_2 \left(\frac{1}{4} \cdot \frac{1}{4} \cdot \frac{1}{4} \right) = 6,$$

³⁹Now we know why the everyday TV news is full of thefts, catastrophes and unbridled crimes... Although it apparently looks upsetting, in fact it represents an optimistic signal: this is just incredibly rare.

while a single amino acid in a protein

$$I_{\text{aa}} = -\log_2 \left(\frac{1}{20} \right) = 4.23.$$

Thus, the codon information is sufficient to choose a particular amino acid from 20 possibilities.

If nature designed the two-base codons, then such a codon would contain only $I_{\text{codon2}} = -\log_2(\frac{1}{4} \cdot \frac{1}{4}) = 4$ bits, which would be insufficient to code the amino acid.

Thus, the protein coding that uses the information from the DNA sequence, takes place with the information excess of $6 - 4.23 = 1.77$ bits per amino acid.

15.15 THE MISSION OF CHEMISTRY

There is an impression that chemistry in biology is only a kind of substitute, a pre-text, no more than a material carrier of the mission of the whole organism. Text-books of biochemistry do not say much about chemistry, they talk about molecular functions to perform, in a sense about metachemistry. A particular molecule seems not to be so important. What counts is its function. A good example are enzymes. One *type* of enzyme may perform the same or similar functions in many different organisms (from fungi to man). The function is the same, but the composition of the enzyme changes from species to species: two species may differ by as much as 70% of the amino acids. However, those amino acids that are crucial for the enzyme function are preserved in all species.

We may perceive chemistry as a potential medium for information processing. This unbelievable chemical task would be collecting, transporting, changing, dispatching and transferring of information.

Chemistry, as we develop it, is far from such a masterpiece. What we are doing currently might be compared to chemical research by a Martian with a beautifully edited “Auguries of Innocence” by William Blake. The little green guy would perform a chemical analysis of the paper (he probably would even make a whole branch of science of that), examine the chemical composition of the printing dye; with other Martian Professors he would make some crazy hypotheses on the possible source of the leather cover, list the 26 different black signs as well as their perpendicular and horizontal clusters, analyze their frequencies, etc. He would, however, be very far from the *information* the book contains, including the boring matrix of black marks:

*To see a world in a grain of sand
And heaven in a wild flower
Hold infinity in the palm of your hand
And eternity in an hour*

and most importantly he could not even imagine his heart⁴⁰ beating any faster

⁴⁰If any...

after reading this passage, because of thousands of associations *he could never have had*... We are close to what the Martian Professor would do. We have wonderful matter in our hands from which we could make chemical poems, but so far we are able to do only very little.

Molecules *could* play much more demanding roles than those, we have foreseen for them: *they can process information*. The first achievement in this direction came from Leonard Adleman – a mathematician.

15.16 MOLECULAR COMPUTERS BASED ON SYNTHON INTERACTIONS

Computers have changed human civilization. Their speed doubles every year or so, but the expectations are even greater. A possible solution is parallel processing, or making lots of computations at the same time, another is miniaturization. As will be seen in a moment, both these possibilities could be offered by molecular computers, in which the elementary devices would be the individual molecules chemists work with all the time. This stage of technology is not yet achieved. The highly elaborated silicon lithographic technology makes it possible to create

Leonard M. Adleman (b. 1945), American mathematician, professor of computer science and of molecular biology at the University of California, Los Angeles. As a young boy he dreamed of becoming a chemist, then a medical doctor. These dreams led him to the discovery described here.



electronic devices of size of the order of 1000 Å. Chemists would be able to go down to the hundreds or even tens of Å. Besides, the new technology would be based on self-organization (supramolecular chemistry) and self-assembling. In 1 cm³ we could store the information of a huge number of today's CD-ROMs. People thought a computer had to have the form of a box with metallic and non-

metallic tools inside, as it is now. However,...

In 1994 mathematician Leonard M. Adleman⁴¹ began his experiments in one of the American genetics labs, while learning the biological stuff in the evenings. Once, reading in bed Watson's textbook "*The Molecular Biology of the Gene*", he recognized that the features of the polymerase molecule interacting with the DNA strand described in the textbook perfectly match the features of what is called Turing machine, or, an *abstract representation of a computing device*, made just before the Second World War by Alan Turing.

Therefore, it was *certain* that the polymerase and the DNA (and certainly some other molecules) could be used as computers. If we think about it *now*, the computer in our head is more similar to *excusez le mot* water, than to a box with hard disks, etc. The achievement of Adleman was that he was able to translate a known and important mathematical problem into the language of laboratory recipes, and then using a chemical procedure he was able to solve the mathematical problem.

⁴¹L. Adleman, *Science* 266 (1994) 1021.

polymerase

Turing machine

Alan Mathison Turing (1912–1954), British mathematical genius, in a paper in *Proc. London Math. Soc.* 42 (1937) 230, defined a simple device (known now as the Turing machine). The machine consists of a read/write head that scans a 1D tape divided into squares, each of which contains a “0” or “1”. The behaviour of the machine is completely characterized by the current state of the machine, the content of the square it is just reading, and a table of instructions. Such a theoretical concept was of importance in considering the feasibility of any program coded on the tape. During the Second World War Turing continued Polish achievements by decoding further versions of the German Enigma code at Bletchley Park, the British wartime cryptanalytic headquarter. He was re-



membered for his eccentric habits. People saw him riding his bicycle with a gas mask on (he claimed it relieved his allergies). Alan Turing was found dead in his bed with a half eaten poisoned apple.

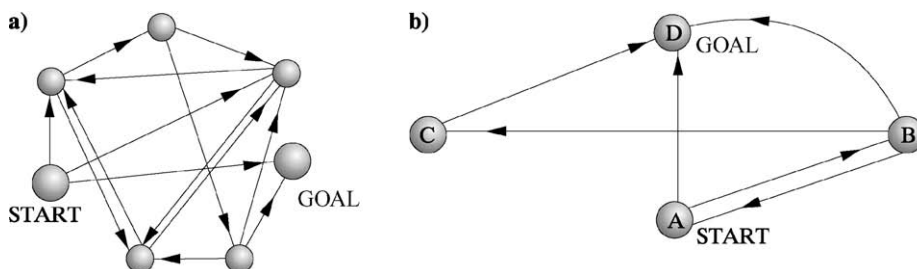


Fig. 15.10. A graph of airplane flights. Is the graph of the Hamilton type? This was a question for the molecular computer. (a) The graph from the Adleman's experiment. (b) A simplified graph described in this book.

Fig. 15.10 shows the original problem of Adleman: a graph with 14 airplane flights involving seven cities.

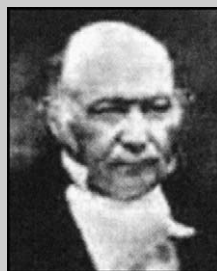
The task is called the *travelling salesman* problem, notorious in mathematics as extremely difficult.⁴² The salesman begins his journey from the city START and wants to go to the city GOAL, visiting every other city precisely once. This is feasible only for some flight patterns. Those graphs for which it is feasible are called the *Hamilton graphs*. When the number of cities is small, such a problem may be quite effectively solved by the computer in our head. For seven cities it takes on average 56 s, as stated by Adleman, for a little larger number we need a desk computer, but *for a hundred cities all the computers of the world would be unable to provide the answer*. But, ... a molecular computer would have the answer within a second.

travelling
salesman
problem

Hamilton graphs

⁴²The problem belongs to what is called NP-hard (NP from *non-polynomial*), in which the difficulties increase faster than any polynomial with the size of the problem.

William Rowan Hamilton (1805–1865) was a Astronomer Royal in Ireland. At the age of 17 he found an error in the famous “Celestial Mechanics” by Laplace. This drew the attention of scientists and was the beginning of the Hamilton’s scientific career. In the present book his name is repeated many times (because of Hamiltonian).



How does a molecular computer work?

Let us recall two important examples of complementary synthons: guanine and cytosine (GC) and adenine with thymine, see p. 751.

Let us repeat Adleman’s algorithm for a much simpler graph (Fig. 15.10.b). What Adleman did was the following.

1. He assigned for every city some particular piece of DNA (sequence) composed of eight nucleic bases:

City A	A	C	T	T	G	C	A	G
City B	T	C	G	G	A	C	T	G
City C	G	G	C	T	A	T	G	T
City D	C	C	G	A	G	C	A	A

2. Then to each existing flight $X \rightarrow Y$, another eight-base DNA sequence was assigned: composed of the second half of the sequence of X and the first part of the sequence of Y:

Flight A \rightarrow B	G	C	A	G	T	C	G	G
Flight A \rightarrow D	G	C	A	G	C	C	G	A
Flight B \rightarrow C	A	C	T	G	G	G	C	T
Flight B \rightarrow D	A	C	T	G	C	C	G	A
Flight B \rightarrow A	A	C	T	G	A	C	T	T
Flight C \rightarrow D	A	T	G	T	C	C	G	A

3. Then, Adleman ordered the synthesis of the DNA sequences of the flights and the DNA sequences complementary to the cities, i.e.

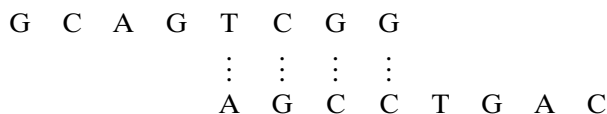
co-City A	T	G	A	A	C	G	T	C
co-City B	A	G	C	C	T	G	A	C
co-City C	C	C	G	A	T	A	C	A
co-City D	G	G	C	T	C	G	T	T

4. All these substances are to be mixed together, dissolved in water, add a bit of salt and an enzyme called ligase.⁴³

⁴³To be as effective as Nature, we want to have conditions similar to those in living cells.

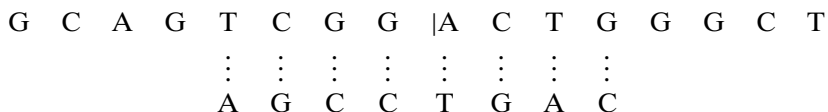
How to read the solution

What happened in the test tube? First of all matching and pairing of the corresponding synthons took place. For example, the DNA strand that codes the AB-flight (i.e. GCAGTCGG) found in the solution the complementary synthon of city B (i.e. the co-City AGCCTGAC) and because of the molecular recognition mechanism made a strong intermolecular complex:



where the upper part is flights, and the lower part is co-Cities. Note that the flights are the only feasible ones, because only feasible flights' DNA sequences were synthesized. The role of a co-City's DNA is to provide the information that there is the possibility to land and take-off in this particular city.

In the example just given, the complex will also find the synthon that corresponds to flight $B \rightarrow C$, i.e. ACTGGGCT, and we obtain a more extended strand



In this way from the upper part⁴⁴ of the intermolecular complexes we can read a particular itinerary. The ligase was needed, because this enzyme binds the loose ends of the DNA strands (thus removing the perpendicular separators above). *Therefore, every possible itinerary is represented by a DNA oligomer. If the graph were Hamiltonian, then in the solution there would be the DNA molecule composed of 24 nucleotides that codes the proper itinerary:*



Eliminating wrong trajectories...

Practically, independent of how large N is, after a second the solution to the travelling salesman problem is ready. The only problem now is to be able to read the solution. This will currently take much more than a second, but in principle only depends linearly on the number of cities.

To get the solution we use three techniques: polymerase chain reaction (PCR), electrophoresis and separation through affinity. The machinery behind all this is recognition of synthons and co-synthons (known in biochemistry as hybridization, it has nothing to do with hybridization described in Chapter 8).

⁴⁴From the lower part as well.

The itineraries coded by the hybridization are mostly wrong. *One* of the reasons is that they do not start from the START CITY (A) and do not end up at the GOAL CITY (D). Using the PCR technique⁴⁵ it is possible to increase the concentration of only those itineraries, which start from START and end at GOAL to such an extent that all other concentrations may be treated as marginal.

Still there are a lot of wrong itineraries. First of all there are a lot of itineraries that are too long or too short. This problem may be fixed by electrophoresis,⁴⁶ which allows the separation of DNA strands of a given length, in our case the 24-city itineraries. In this way we have itineraries starting from START and ending at GOAL and having 24 cities. They can be copied again by PCR.

Now we have to eliminate more wrong itineraries: those which repeat some transit cities and leave others unvisited. This is done by the affinity separation method.⁴⁷ First, the co-synthon for the first transit city (in our case: C) on the list of transit cities (in our case: C and D) is prepared and attached to the surface of iron balls. The iron balls are then added to the solution and after allowing a second to bind to those itineraries that contain the city, they are picked out using a magnet. The balls are then placed in another test tube, the attached “itineraries” released from the surface of the iron balls and the empty iron balls are separated. Thus, we have in a test tube the “itineraries” that begin and end correctly, have the correct number of 24 nucleotides and certainly go through the first transit city (C) on our list of transit cities.

The process is repeated for the second etc. transit cities. If, in the last test tube, there is an “itinerary”, the answer to the salesman problem is positive and the corresponding “itinerary” is identified (after copying by PCR and sequencing). Otherwise the answer is negative.

Thus, a mathematical problem was solved using a kind of molecular biocomputer. From the information processing point of view, this was possible because parallel processing was under way – a lot of DNA oligomers interacted with themselves at the same time. The number of such molecular processors was of the order of 10^{23} . This number is so huge, that such a biocomputer is able to check (virtually) all possibilities and to find the solution.

⁴⁵The PCR technique is able to copy a chosen DNA sequence and to grow its population even from a single molecule to a high concentration by using the repeated action of an enzyme, a polymerase.

The reaction was invented by Kary B. Mullis (b. 1944), American technical chemist in an industrial company. In 1983 Mullis was driving to his favourite California surfing area, when the idea of a DNA copying molecular machine struck him suddenly. He stopped the car and made a note of the reaction. His company gave him a prize of \$10 000 and sold the patent to another company for \$300 000 000. In 1993 Kary Mullis received the Nobel Prize in chemistry “for his invention of the polymerase chain reaction (PCTR) method”.

⁴⁶Electrophoresis is able to physically separate DNA sequences according to their length. It is based on the electrolysis of a gel. Since DNA is an anion, it will travel through the gel to anode. The shorter the molecule, the longer distance it will reach. The DNA molecules of a given length can then be picked out by cutting the particular piece of gel and then they can be multiplied by PCR.

⁴⁷Affinity separation method makes possible to separate particular sequences from a mixture of DNA sequences. This is achieved by providing its co-synthon attached to iron spheres. The particular sequence we are looking for binds to the surface of the iron ball, which may afterwards be separated from the solution using a magnet.

Summary

Chemistry has attained such a stage that soon a new quality can be achieved:

- chemistry entered the second half of the twentieth century with detailed knowledge of the main building blocks of molecular structures: atoms, chemical bonds, bond angles and intermolecular interactions;
- the accumulated knowledge now serves to build more and more complex molecular architectures;
- in these architectures we may use *chemical bonds* (with energy of the order of 50–150 kcal/mol) to build the molecules as well as *intermolecular interactions* (with energy of about 1–20 kcal/mol) to construct supramolecular structures from them;
- in supramolecular chemistry we operate with synthons, i.e. some special systems of functional groups that fit together perfectly when rigid (“key-lock” mechanism) or flexible (“hand-glove” mechanism), giving rise to molecular recognition;
- the interaction leads to a molecular complex that facilitates further evolution of the system: either by a chemical reaction going on selectively at such a configuration of the molecules, or by further self-organization due to next-step molecular recognition of the newly formed synthons;
- this may result in forming complex systems of multilevel architecture, each level characterized by its own stability;
- the self-organization may take place with significant interaction non-additivity effects (“non-linearity” in mathematical terms) that may lead to cooperation in forming the multilevel structure;
- high cooperation may lead to spontaneous transformation of the structure, called collective transformation, to another state (“domino effect”);
- the self-organized structures may interact with other such structures (chemical reactions or association);
- in particular they may create the autocatalytic cycle which represents chemical feed back;
- such cycles may couple in a higher-order cycle forming hypercycles;
- a dynamic system with hypercycles, when perturbed by an external stimulus, reacts in a complex and non-linear way;
- one of the possibilities in non-equilibrium conditions are the limit cycles, which lead to dissipative structures, which may exhibit periodicity (in space and time) as well as chaotic behaviour;
- some dynamic systems may represent molecular libraries with the proportions of species strongly depending on external conditions (cf. the immune system);
- molecules may act (e.g., transfer photon, electron, proton, ion, conformational change, etc.) thus performing a function;
- several functions may cooperate exhibiting a space/time organization of the individual functions;
- some molecules may serve for effective information processing;
- information processing seems to represent the ultimate goal of the future chemistry.

Main concepts, new terms

complex systems (p. 852)
self-organization (p. 853)
cooperativity (p. 854)
combinatorial chemistry (p. 855)

molecular libraries (p. 855)
non-linearity (p. 857)
attractors (p. 858)
repellers (p. 858)

fixed point (p. 858)	stellar nodes (stable and unstable, p. 872)
limit cycle (p. 858)	focus (stable and unstable, p. 872)
logistic equation (p. 860)	reaction centre (p. 872)
chaos (p. 860)	dissipative structures (p. 873)
bifurcation (p. 861)	hypercycles (p. 873)
catastrophe (p. 862)	molecular function (p. 875)
domino (p. 863)	information (p. 876)
renormalization (p. 863)	information entropy (p. 876)
collectivity (p. 863)	DNA computing (p. 878)
decimation (p. 865)	Turing machine (p. 878)
self-similarity (p. 865)	Hamilton graph (p. 879)
fractals (p. 865)	travelling salesman problem (p. 879)
feed-back (p. 866)	NP-hard problem (p. 879)
autocatalysis (p. 868)	DNA hybridization (p. 881)
brusselator (p. 868)	PCR (p. 882)
nodes (stable and unstable, p. 872)	separation by affinity (p. 882)
saddle point of reaction (p. 872)	

From the research front

To say that organic chemists are able to synthesize almost any molecule one may think of is certainly an exaggeration, but the statement seems sometimes to be very close to reality. Chemists were able to synthesize the five-olympic-ring molecule, the three interlocked Borromean rings, the football made of carbon atoms, the “cuban” – a hydrocarbon cube, “basketan” – in the form of an apple basket, the rotaxans shown in Fig. 13.2, a molecular in the form of Möbius band, etc. Now we may ask *why* the enormous synthetic effort was undertaken and what these molecules were synthesized for. Well, the answer seems to be that contemporary chemists are fascinated by their art of making complex and yet perfect and beautiful molecular objects. The main goal apparently was to demonstrate the mastery of modern chemistry. However, high symmetry does not necessarily mean a particular usefulness. The synthetic targets should be identified by the careful planning of molecular *functions*, rather than molecular beauty.

Ad futurum...

We may expect that more and more often chemical research will focus on molecular function, and (later) on the space/time cooperation of the functions. Research projects will be formulated in a way that will highlight the role of the molecular function, and will consist of several (interrelated) steps:

- first, the technical goal will be defined,
- the molecular functions will be identified which will make this goal achievable,
- theoreticians will design and test in computers (“in silico”) the molecules which will exhibit the above functions,
- synthetic chemists will synthesize the molecules designed,
- physicochemists will check whether the molecular functions are there,
- finally, the material will be checked against the technical goal.

We will be able to produce “smart” materials which will respond to external conditions in a previously designed, complex, yet we hope, predictable way. The materials that will be created this way will not resemble the materials of today, which are mostly carrying out

one primitive function. The drugs of today are usually quite simple molecules, which enter the extremely complex system of our body. The drugs of tomorrow will involve much larger molecules (like proteins). Will we be clever enough to avoid unpredictable interactions with our body? What in principle do we want to achieve?

What will the motivation of our work be? Will we take into account the psychological needs of the human being, equilibrium of their minds?

What will the future of the human family be, which was able in the past to create such wonderful music, Chartres cathedral, breathtaking painting, moving poetry, abstract mathematics, proudly landed on other celestial bodies? In the past nothing could stop their curiosity and ingeniousness, they were able to resist the harshest conditions on their planet. Humans have reached nowadays the technical level that probably will assure avoiding the next glaciation,⁴⁸ maybe allow a *small* asteroid be pushed off the target by nuclear warheads if it were aimed dangerously at the Earth, also ... erasing in nuclear war most of its own population together with the wonders of our civilization.

What is the goal of these beings and what will be the final limit of their existence? What are they aiming at? Do we want to know the smell of fresh bread, to be charmed by Chartres cathedral with all it has in it, to use our knowledge to cherish the friendship of the human family, or will it be sufficient to pack a newborn into a personal container and make computers inject substances that will make his neural system as happy as in Seventh Heaven?

Which of the goals we do want, as chemists, to participate in?

Additional literature

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A book written by the most prominent specialist in the field.

A. Babloyantz, "Molecules, Dynamics and Life", Wiley, New York, 1987.

The author describes the scientific achievements of Prigogine and his group, which she participated in. An excellent, competent book, the most comprehensible among the first three recommended books.

J.-M. Lehn, "Supramolecular chemistry: Concept and Perspectives", VCH, 1995.

A vision of supramolecular chemistry given by one of its founders.

Questions

1. Decimation means:
 - a) bifurcation; b) renormalization of the Hamiltonian and reaching self-similarity;
 - c) scaling all the distances by a factor of ten; d) taking explicitly every tenth electron in a wave function.
2. A dissipative structure in a complex system:
 - a) appears in a system far from equilibrium;
 - b) means the largest molecular complex in the system;

⁴⁸Well, it is expected within the next 500 years.

- c) is independent of external conditions;
d) is the least stable structure appearing in equilibrium conditions.
3. A molecular library composed of the associates of the molecules A and B represents:
a) a mixture of the complexes AB; b) a mixture of all possible complexes of the A and B species; c) the complete physicochemical characterization of A and B; d) a mixture of all A_nB_n .
4. The self-organization of molecules is the spontaneous formation of:
a) molecular complexes only in equilibrium conditions; b) a structure with minimum entropy; c) a structure with maximum entropy; d) complexes of molecules with synthons.
5. In the iterative solution of the logistic equation $x_{n+1} = Kx_n(1 - x_n)$:
a) there is a fixed point at any K ; b) at any attempt to increase of K we obtain a bifurcation; c) some values of K lead to chaotic behaviour; d) at no value of K do we have extinction of the population.
6. In the Brusselator without diffusion the stable focus means:
a) monotonic decreasing of the fluctuations x and y ; b) damped oscillations of the fluctuations x and y ; c) non-vanishing oscillations of the fluctuations x and y ; d) a limit circle.
7. In the thermodynamic equilibrium of an isolated system:
a) the entropy increases; b) we may have a non-zero gradient of temperature; c) we may have a non-zero gradient of concentration; d) no dissipative structures are possible.
8. The bifurcation point for the number of solutions of $x^2 - px + 2 = 0$ corresponds to:
a) $p = 2\sqrt{2}$; b) $p = 1$; c) $p = -1$; d) $p = \sqrt{2}$.
9. An event has only four possible outputs with *a priori* probabilities $p_1 = p_2 = p_3 = p_4 = \frac{1}{4}$. Reliable information comes that in fact the probabilities are different: $p_1 = \frac{1}{2}$, $p_2 = \frac{1}{4}$, $p_3 = \frac{1}{8}$, $p_4 = \frac{1}{8}$. The information had I_1 bits and I_1 is equal to:
a) 1 bit; b) 0.5 bit; c) 2 bits; d) 0.25 bit.
10. The situation corresponds to Question 9, but a second piece of reliable information coming says that the situation has changed once more and now: $p_1 = \frac{1}{2}$, $p_2 = 0$, $p_3 = 0$, $p_4 = \frac{1}{2}$. The second piece of information had I_2 bits. We pay for information in proportion to its quantity. Therefore, for the second piece of information we have to pay:
a) the same as for the first piece of information; b) twice as much as for the first piece of information; c) half of the prize for the first piece of information; d) three times more than for the first piece of information.

Answers

1b, 2a, 3b, 4d, 5c, 6b, 7d, 8a, 9d, 10d