

## Chapter 2

# Molecular Structure of Biological Systems

It is the intention of this section to familiarize the reader with some specific physical properties of biological systems on the molecular level. The overriding theme of this section is the controversy of thermal fluctuation against the forces of molecular orientation and organization.

Two kinds of physical behavior meet on the molecular level of biological structures: On the one hand, there are the characteristic properties of *microphysical* processes, based on the individual behavior of single small particles like atoms, molecules, or supramolecular structures. These processes are mostly stochastic. On the other hand, there are reactions which resemble *macrophysical* properties, the kind of behavior of “large” bodies. *Macrophysics* is ruled by the laws of classical physics, as for the example of classical mechanics. Our daily experiences with macrophysical systems teach us that their behavior is generally deterministic.

To explain this difference, let us consider a simple mechanical wheelwork. The knowledge of its design and construction allows a precise prediction of the behavior of the system. This prediction is based on the laws of classical mechanics. In contrast to this, a chemical reaction with a small number of molecules in a homogeneous phase depends on stochastic collisions of the individual molecules with each other. Since this process is stochastic, it is predictable only in a statistical way.

This stochastic behavior of molecular systems can be transformed into a deterministic one, if the number of participating stochastic events is large, or if the degrees of freedom of the single reactions are extremely limited. The increase of stochastic events can be realized either by an increasing number of participating molecules, by enlarging the volume for example, where the reaction takes place, or by an increase of the time interval of observation. This consideration indicates an interesting interplay between volume, time constants, and reliability of a biochemical reaction.

The limitation of the degree of freedom of a biochemical reaction is realized by a property of the system which is called *anisotropy*. In contrast to *isotropic* systems, like simple solutions, in anisotropic systems the mobility of molecules in various directions is not identical, but is restricted in some directions, and promoted in

others. This, for example, is the case for enzymatic reactions, where the participating enzymes are oriented in membranes, or if the reactions of charged or polar reactants occur in strong electric fields of electrical double layers.

In many fields the biological organism works as an amplifier of microphysical stochastics. A molecular mutation, for example, leads to a reaction chain, which finally ends with a phenomenological alteration of the organism. Or, as another example: a few molecular events in the pigments of an optical receptor can lead to perception and to reaction in behavior.

During the first steps in considering molecular mechanisms of biological systems, a further aspect is taken into consideration. Unfortunately, biologists often ignore that a qualitative jump has to be considered in the transition from the “visible” macrophysical structures, to the microphysical systems such as atoms or molecules. This includes not only the above-mentioned transition from the deterministic behavior of macroscopic systems to the stochastic behavior of single molecules, but many further aspects as well.

The biologists, for example, must acknowledge that the term “structure” now receives a new meaning. The visible “biological structure,” as known in the fields of anatomy, morphology, and histology, now appears as concentration profiles, or as systems of electric charges, or electromagnetic fields. Instead of visible and measurable lengths, diameters, or distances, as common in the visible world, in the microphysical world so-called *effective parameters* are used. These sorts of parameters are exactly defined, and they can be measured with arbitrary exactness, but they do not correspond to some visible boundaries. A single ion, for example, has no diameter in the sense of the diameter of a cell, or a cell nucleus, which can be measured by a microscopic scale. In the following sections we will define effective parameters like crystal radius, hydration radius, and Debye–Hückel radius, which are very important parameters for functional explanations. We will consider this aspect in detail in Sect. 2.1.3.

It is not the intention of this book to describe the topics of molecular biology. However, the theoretical foundations and principles will be explained to make possible a link between structure and function at the molecular level and current biological thinking in these dimensions.

## 2.1 Thermal Molecular Movement, Order and Probability

In this section, the biophysics of molecular organization of biological systems will be discussed in the context of processes of thermal movements where a statistical mechanics approach can be applied. Stochastic phenomena are of great importance in molecular biophysics. Here, we are immediately confronted with the dialectics of arbitrary distribution on the one hand, and organized order on the other hand. This also touches upon problems of biological self-organization and stability of the resulting structures.

### 2.1.1 Thermodynamic Probability and Entropy

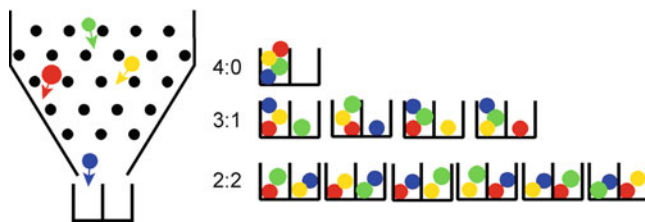
In 1854, Rudolf J. E. Clausius introduced the *entropy* ( $S$ ) as a parameter of phenomenological thermodynamics, and defined it as the heat, added to a system in a reversible way in relation to the temperature (see Eq. 3.10). Later, in 1894, Ludwig Boltzmann used this parameter in the framework of statistical thermodynamics. In these circumstances, the entropy, and in context to this, the second principle of thermodynamics becomes more imaginable. Entropy appears as a kind of measure of disorder, or as a degree of random distribution, i.e., of missing order. The correlation between order and probability and, as will be explained later – information – is of great importance for the understanding of the principles of biological organization.

Let us start with the assumption that the entropy is a measure indicating the degree of randomization of a given distribution. We will consider a system of maximal entropy as a system in maximal disorder. Furthermore, let us demand that the entropy be an *extensive* parameter. Therefore, like volume, or mass, but in contrast to the *intensive* parameters such as for example temperature or density, the entropies  $S_1$  and  $S_2$  of two systems can be added, if these systems come together:

$$S_1 + S_2 = S \quad (2.1)$$

How can we now define a parameter, which indicates the degree of randomization or, on the contrary, a degree of disorder? What does order of organization mean? Of course, our daily experience shows that an ordered system spontaneously transforms into a disordered one, but not vice versa. This, actually, is the consequence of the second principle of thermodynamics.

Let us consider a very simple structure, just the distribution of four distinguishable spheres on two compartments of a box (Fig. 2.1). Let each of these spheres, independently of the three others, just by chance fall into one or the other compartment of the box. All of the 11 possibilities of the distribution, as indicated in Fig. 2.1, therefore, have the same degree of probability, because the probability of each sphere individually, to fall into compartment 1 or into compartment 2 is equal. Summarizing the patterns of distribution shows that there is only one way to



**Fig. 2.1** All possibilities of the statistical distribution of four distinguishable spheres in two compartments of a box

realize the distributions 0:4 and 4:0. In contrast, there are four ways to realize the distributions 3:1 and 1:3, and, finally, six ways for equal distribution: 2:2.

Let us now ignore the fact that the spheres are distinguishable. Let us simply ask: How large is the probability that just by stochastic distributions one of the relations 4:0, 3:1, 2:2, 1:3, or 0:4 occur? Apparently, the probability of any kind of distribution will be larger, if it can be realized by a larger number of ways. The distribution mode 2:2, for example, is 6 times more likely, than the distribution 4:0, or 0:4. The number of ways which lead to the realization of a definite situation, in fact, seems to be a measure of the probability of the occurrence of it. We will designate this number of ways by the parameter  $W$  which we will call *thermodynamic probability*. The amount of  $W$  can be at least 1 and at maximum  $\infty$ , in contrast to the mathematical probability ( $P$ ), which we will use in Sect. 2.1.2, and which ranges between 0 and 1.

Now, we come to the following sequence of conclusions: If  $W$  really is a measure of the probability of getting a definite distribution, and if an increase of the degree of order is the most uncertain result of a stochastic distribution and finally, if the entropy ( $S$ ) is a parameter, indicating the degree of disorder – than  $S$  should be a function of  $W$ . If two situations with relative probabilities  $W_1$  and  $W_2$  are connected together, then the probability of this combined situation results from the product ( $W_1 \cdot W_2$ ). Using Eq. 2.1, this means:

$$S = f(W) = S_1 + S_2 = f(W_1) + f(W_2) = f(W_1 \cdot W_2) \quad (2.2)$$

This demand is met by the logarithmic function:

$$\ln A + \ln B = \ln(A \cdot B) \quad (2.3)$$

Hence entropy is proportional to the logarithm of  $W$ :

$$S = k \ln W \quad (2.4)$$

This is the Boltzmann equation of entropy. Boltzmann's constant  $k$  was defined as a universal constant later by Max Planck. It must have the same unit of measurement as entropy, and is as follows:

$$k = 1.380658 \cdot 10^{-23} \text{ J K}^{-1} = 8.6174 \cdot 10^{-5} \text{ eV K}^{-1}$$

This explanation was just based on the simplest experiment where four spheres were distributed randomly over two compartments. One step toward serious thermodynamics can be taken, considering for example the compartments of this box as molecules of a system, and the spheres, as quanta of energy, distributed among them. This complication, of course, means a transition of handling with larger numbers. If the number of elements and classes are increased,  $W$  cannot be

evaluated just by simple trial. It is possible to calculate this value using the following equation:

$$W = \frac{n!}{n_1! \cdot n_2! \cdot n_3! \cdot \dots \cdot n_m!} \quad (2.5)$$

where  $n$  is the total number of all elements in the system (in case of Fig. 2.1 – the total number of spheres:  $n = 4$ );  $n_i$  (for  $i = 1 \dots m$ ) is the number of elements in each class of state (this means, the number  $n_1$  in compartment 1 and  $n_2$  in compartment 2); and  $m$  is the number of classes of state (namely: number of compartments in the box).

### 2.1.2 Information and Entropy

In 1948, C. E. Shannon introduced a parameter which in technical information theory has been proved as a useful measure of information content of a message. The information ( $I$ ) of a message depends on the effort required to guess it by a highly systematic system of questions. Hence, information is some sort of degree of the actuality of a message.

It is not difficult to guess the result of the toss of a coin, since there are only two possibilities of equal probability. To guess a certain card in a full deck of playing cards is much more difficult. In this case, a much greater uncertainty factor has to be taken into account. Using a more systematic approach, a large number of yes-no questions have to be answered. Hence, the information content of a particular playing card is higher than that of a tossed coin. Should a deck consist of cards which are all the same, and should this be known to the challenged person, guessing will not make sense at all. The information content of each of these cards is zero. The probability by which possibilities are turned into reality, consequently, seems to become a measure of information.

In contrast to thermodynamics, in the information theory the mathematical term of probability ( $P$ ) is used which is defined as follows:

$$P = \frac{\text{number of favorable cases}}{\text{greatest possible number of cases}}$$

On average, coins tossed a 100 times will land with heads up in 50 instances. Hence, the probability of heads facing up may be expressed by:

$$P = \frac{50}{100} = \frac{1}{2}$$

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