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ENTROPY CHANGE OF OPEN THERMODYNAMIC SYSTEMS IN SELF-ORGANIZING PROCESSES

by

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The thermodynamic models available in the literature predict that during self-organizing processes the entropy of a cell considered as an open thermodynamic system decreases. This prediction leads to conclusion that cell imports a certain amount of negative entropy and generates entropy during irreversible metabolic processes. The controversial concept of negentropy was criticized recently. In this research a new model was proposed that is not based on the steady-state approximation and describes living systems more realistically. The analysis of the suggested model of an open thermodynamic system far from equilibrium, led to the conclusion that the entropy during self-organizing processes increases during growth (of a molecule or a cell). Using as models the synthesis of an oligopeptide and a growing hydrocarbon chain, it was shown that entropy of an open thermodynamic system increases during addition of monomers (a self-organizing process). A derived equation confirms the results obtained by calculations with literature experimental values of molar entropy. The decrease of entropy observed in self-organizing processes occurred only during phase transition.

Key words: *entropy, open system, non-equilibrium thermodynamics, rate of entropy change*

Introduction

Schrodinger [1] suggested that the behavior of living organisms should be described by the basic laws of physics and chemistry. Boltzmann [2] claimed earlier, that living organisms reduce their entropy while increasing the entropy of their surroundings. Prigogine [3, 4] suggested a model of a cell considered as an open thermodynamic system using the steady-state approximation, developed non-equilibrium thermodynamics and applied it to biological cells. Von Bertalanffy [5, 6] suggested a theory of open systems in biology.

The idea that biological systems decrease their entropy resulted with the controversial concept of negentropy. This idea itself came from Schrodinger [1] and Boltzmann [2]. Mahulikar [7], and Ho [8, 9] gave their contribution to development of this concept. However, the concept of negentropy and the idea that a cell decreases its entropy during self-organizing processes was criticized from the start [10] and is being criticized even more lately [11-13].

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Prigogine's model demands a real life version of Maxwell demon to play its role in entropy reduction of the cell. Maxwell's demon has an ability to decrease entropy of a thermodynamic system, thus violating the second law of thermodynamics. Real life version of Maxwell's demon is believed to play a role in evolution [14, 15], and possibly in abiogenesis [14-17]. This presents a problem for the RNA world abiogenesis theory. Living cells are for Davies, dissipative, open, and far-from-equilibrium systems that lower their entropy utilizing an influx of energy and molecular material in a multi-compartment structure with specific functional characteristics [18].

Oppositely, Silva [19] reported that entropy of the organism increases in time. Gems and Doonan [20] published similar results that the entropy of the *C. elegans* pharynx tissues increases as the animal ages (and organizes itself). Hansen [11-13], Frenkel [21], Schneider and Key [22], and Michaelian [23] reported that change of entropy of an open thermodynamic system during self-organizing processes does not have to decrease. Toussaint [24-26] reported that rate of the entropy production ($\mathrm{d}S/\mathrm{d}t$) decreases during aging (in time). So the entropy itself increases, but the rate of its production decreases during life. Hayflick [27-29] describes the role of entropy increase in aging process.

The aim of this research is to consider the general behavior of an open thermodynamic system out of equilibrium, and then to analyze the behavior of a cell as a real-life example of an open thermodynamic system. Having in mind the growth of real organisms it seems reasonable to develop a model that is not based on the steady state approximation.

Theoretical analysis

Prigogine modeled living organisms as open thermodynamic systems [3, 4]. Into his model he introduced the steady-state approximation. Von Bertalanffy [5, 6] and others [7-9], followed his lead. This approximation neglects growth. However, growth is one of the most fundamental characteristics of living structures. So, living organisms will be considered in this paper as open thermodynamic systems with the property of growth. Homeostatic mechanisms maintain internal compositional balance in cells, but the number of cells increases during cell division. So, the whole organism grows trough cell division keeping the inner space of the each cell constant. In that case because of growth it is not possible to use steady state approximation for the whole organism. This approximation is even less justified in case of organisms exhibiting intensive growth. Cell is an open thermodynamic system in steady-state but the whole organism is open thermodynamic system far from equilibrium (out of steady-state). A real organism changes its volume, mass and entropy during growth. Introduction of the steady-state approximation neglects growth and also sets all the thermodynamic properties of the cell model constant, including its entropy. That is opposite to observation reported by many researchers [11-13, 20-27, 30, 31].

Steady-state conditions [3, 4] imply that the entropy generated in irreversible processes in the organism must be fully compensated by import of negative entropy from the surroundings, so that the total change of entropy of the system in steady-state is zero. This is the root of the negentropy concept.

Living cells synthesize complex molecules from simple substances. Therefore they perform self-organizing processes. Models found in the literature assumed that entropy of cells decreases as a consequence of these processes [32-34]. This conclusion diverges these models from the initial steady-state assumption. The properties of cells, including entropy, are no longer constant. If cells are open thermodynamic systems far from equilibrium, they can change their entropy.

In order for the thermodynamic system to be open, it must possess its contents, border, and surroundings. An open thermodynamic system must exchange substance and energy with its surroundings. If the input of substance is balanced by the output, then the system is in steady state and doesn't exhibit growth. This does not correspond to a living organism. Because of that it is necessary to develop a model without the steady state approximation.

Figure 1 shows a thermodynamic system, taken from state A to state B by self organizing processes. The system on fig. 1(a), can be analyzed as an open or a closed system.

If we assume that it's closed, then all the particles in the figure make that system. In that case the surroundings are located outside the rectangle, and there is no exchange of substance. Therefore the surroundings are not shown. Then during its transition into state B through a self organizing process it decreases its entropy. The entropy of the system decreases because the system loose degrees of freedom, as the chaotically distributed monomers are organized into a more ordered polymer. So the system changes from state of maximum entropy (A) into a state characterized by lower entropy (B).

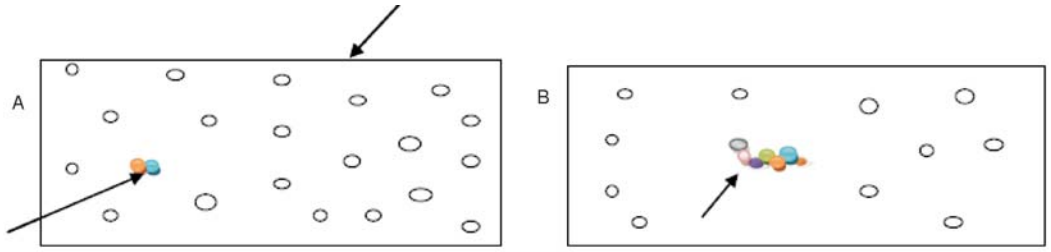


Figure 1. Schrodinger's model of an open thermodynamic system in a self-organizing process. The system shifts from state (A) characterized by randomly organized matter, into state (B) with a higher level of organization. Schrodinger concluded that the entropy of this system decreases. However, he failed to define the border of the open system with its surroundings. If he considered the open system to be all matter on (A), then its transition into state (B) is a process performed by an isolated system, because it lacks surroundings

If we assume that the system is open, then its content is made of a two-monomer chain, while the surroundings are consisted of the other monomers. The system grows with the addition of monomers. The entropy of the growing chain increases during the addition of monomers.

From the above consideration we can conclude that despite the starting assumption that a cell is an open thermodynamic system, only an analysis a closed system could lead us to conclude that its entropy decreases. Confusions of this type are not rare. Davies assumes the cell to be an open thermodynamic system far from equilibrium, and then uses an inappropriate form of the first law of thermodynamics for closed systems. The failure to define what is exactly considered as the open thermodynamic system (its elements, borders and surroundings) is the cause of such confusions.

In order to avoid possible mistakes, let us try to define the thermodynamic system, its border and surroundings. As an open thermodynamic system we'll consider here a growing polymer molecule. Its surroundings will be the particles of monomers that surround it. On fig. 2 an open thermodynamic system clearly separated from its surroundings by permeable borders is presented. Such a system exhibits growth, and is therefore more appropriate for a living organism model.

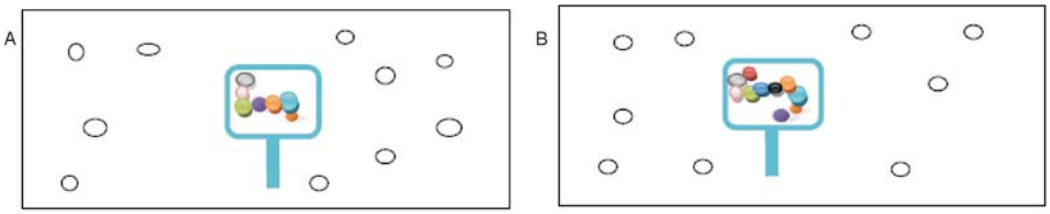
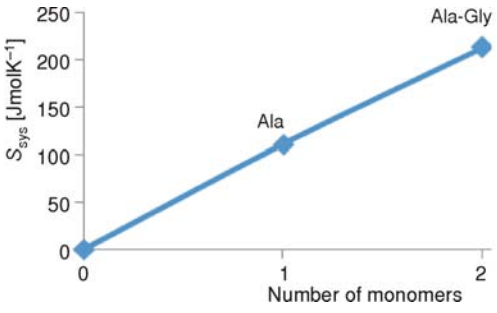


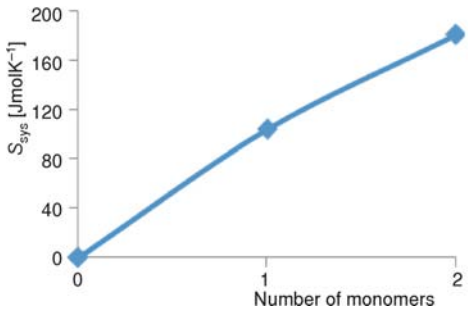
Figure 2. An open thermodynamic system far from equilibrium with the property of growth clearly separated from its surroundings: The magnifying glass marks the border of the open thermodynamic system. The particles outside of the magnifying glass are the surroundings. Notice that the number of monomers that make a polymer on the right side is greater than it is on the left side. This causes a decrease of the number of free monomers in the surroundings

As can be seen from fig. 2, our model includes an open thermodynamic system, a defined border, and defined surroundings. The system imports monomers from its surroundings, incorporates them into itself and therefore grows. The steady state approximation isn't made in this model. From fig. 2 we also see that the number microstates (and therefore the entropy) in a distribution of the polymer molecule increases as a consequence of the increase in the number of monomers that make it.

Synthesis of a polypeptide is certainly a self-organizing process. By analysis of the data available from the literature [32] we conclude that entropy of a polymer or aggregate increases with the increase of the number of monomer units. Graph 1 shows the entropy of a growing peptide as a function of the number of monomers that form it. Notice that the correlation is almost linear.



Graph 1. Dependence of entropy of an oligopeptide Ala-Gly on the number of monomers that form it



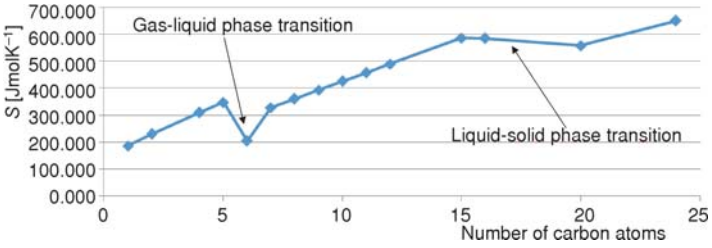
Graph 2. Dependence of entropy of an oligopeptide Gly-Gly on the number of monomers that form it

The thermodynamic system in state 1 is consisted of one molecule of aminoacid alanine, and is characterized by entropy S_1. In the thermodynamic process (the chemical reaction of binding of glycine to alanine) the system transits to state 2 which is characterized by S_2 that is larger than S_1. We can conclude that the entropy of the system increased by $\Delta S = S_2 - S_1$. The increase of entropy is almost (but never) linear. The correlation is not linear because a part of the entropy left the system as heat, and the entropy carried by the water that left the system.

Graph 2 shows the entropy of another growing peptide as a function of the number of monomers that form it. From both graphs we can conclude that the entropy of the system increases, almost linearly, trough self organizing process as a consequence of incorporation of

new monomers into a system during polymerization. Aggregation of monomers shows a similar effect.

However, oppositely to Prigogine's model from the graphs 1 and 2 we can clearly see the increase of entropy during synthesis of an oligopeptide. The synthesis of oligopeptides and polypeptides is an everyday process in a cells life.



Graph 3. Entropy of a growing hydrocarbon chain. An increase of molar entropy of a growing hydrocarbon is clearly visible. Addition of each CH_2 group increases the entropy of the thermodynamic system consisted of a hydrocarbon. Decrease of entropy appears only in case of a phase transition. The data was taken from [32]

We can also observe an increase in entropy of an n-alkane chain with the increase of its length in a self-organizing process (graph 3).

Oppositely to the prediction of Prigogine's model, graph 3 shows that during addition of each CH_2 group to the chain the entropy of the chain increases. Decrease in entropy appears only in case of a phase transition from gaseous to liquid state (C_5-C_6) and from liquid to solid state (C_{15}-C_{20}) at 298 K. After C_{20} the entropy continues to increase. Notice that the values of entropy on the graph are related only for the molecule considered as the system, and are not related to the entropy of the surroundings. The n-alkane molecule is an open thermodynamic system which adds one by one CH_2 group from the surroundings. Notice that this model doesn't require the existence of negentropy, nor the Maxwell's demon. Actually, this model is related to the Third law of thermodynamics and it shows that the concept of negentropy becomes pointless. A part of imported entropy escapes into the surroundings in form of heat, and entropy that the molecules that are products of chemical reactions carry out of the system. This contributes positively to the entropy change of the surroundings.

Equation of entropy change for a growing open thermodynamic system far from equilibrium, valid for a cell and systems such as a polypeptide, or a growing hydrocarbon chain, according to Popovic and Juranic [30], is given as:

$$\mathrm{d}S_{\alpha\beta} = \mathrm{d}S_{\mathrm{in},\alpha} + \mathrm{d}S_{\mathrm{in},\beta} - 2\frac{dw_{\mathrm{exp}}}{T} + \sum_{i=1}^{4}\Delta_{\mathrm{r}}S_i\ \mathrm{d}n_{i,\alpha} + \sum_{j=8}^{9}\Delta_{\mathrm{r}}S_j\ \mathrm{d}n_{j,\alpha} +$$
$$+\sum_{i=1}^{7}\Delta_{\mathrm{r}}S_i\ \mathrm{d}n_{i,\beta} + \frac{\mathrm{d}H_{\mathrm{disp},5} - \gamma\mathrm{d}\sigma_{5,\beta}}{T} + \sum_{j=8}^{10}\Delta_{r}S_j\ \mathrm{d}n_{j,\beta}$$

where $\mathrm{d}n_{\mathrm{i},\alpha}$ is the change of extent of reaction i the α subunit, $\mathrm{d}n_{\mathrm{j},\alpha}$ – the change of extent of reaction j in the α subunit, $\mathrm{d}n_{\mathrm{i},\beta}$ – the change of extent of reaction i in the β subunit, and $\mathrm{d}n_{\mathrm{j},\beta}$ – the change of extent of reaction j in the β subunit.

We can generalize this equation to any living system, containing M subsystems (cells) and N (metabolic) reactions in them:

$$\mathrm{d}S = \sum_{i=1}^{M}\left(\mathrm{d}S_{\mathrm{in},j} + \frac{\mathrm{d}w_{\mathrm{exp},j}}{T} + \sum_{j=1}^{N_i}\Delta_{\mathrm{r}}S_{i,j}\mathrm{d}n_{i,j}\right)$$

Where $\mathrm{d}S$ is the entropy change of an open system and M – the number of subunits that make the thermodynamic system (if any). If the system is not divided into subunits then $M = 1$. $\mathrm{d}S_{\mathrm{in},i}$ is the change of entropy caused by the input of substance into the subunit i, $\mathrm{d}w_{\mathrm{exp,i}}$ – the work done by

the subunit i on its surroundings during growth, T – the temperature, N_i – the number of chemical reactions occurring in subunit i, $\Delta_r S_{i,j}$ – the molar reaction entropy of reaction j occurring in subunit i, and $dn_{i,j}$ – the change of extent of reaction j occurring in subunit i.

The change of entropy of the system depends on the entropy of the substance that is added to the growing molecule or cell, the work done by the growing molecule on its surroundings, and the entropy created in irreversible processes in the system. Since first and third factors can be only positive, then the change of entropy of the growing open thermodynamic system must be positive, so the entropy of the system increases during synthesis reactions (growth of a molecule). The equation given above gives a theoretical explanation for graphs 1, 2, and 3.

A cell is a hierarchically higher structure then a macromolecule. However, its higher hierarchical structure is a consequence of integrated self-organization processes of many macromolecules in many structures of the cell. Because of that the trend noticed in macromolecules is reflected to cells. Consequently, the entropy of an organism increases during its growth as [11-13, 19-23, 31] noticed. The increase of entropy of living systems during aging was reported theoretically and determined experimentally by Hayflick [27-29], Toussaint [35, 36], Silva [19], and others [37]. However the equation presented in this paper leads us to conclude that thermodynamic processes of life express two opposite tendencies. One is to increase the cell's entropy by import and degradation. The second tendency is to decrease its entropy by export and synthesis. These two opposite tendencies aren't fully balanced. We can consider the self-organizing processes as an act of the organized biological machine. Efficiency of any, including biological, machine responsible for synthesis and reparation never reaches 100%. This leads to the dominance of the positive contribution to the total change of entropy. As a consequence of the difference between the generated and imported entropy, on one hand, and the decrease of entropy by an organized biological machine, on the other, a change of state of thermodynamic system appears. This irreversible and unavoidable change of state we macroscopically observe as aging. Toussaint [25] described aging as a multi-step process. If aging is a consequence of entropy accumulation then the change of state of the cell is continuous and irreversible. In that case aging is a continuous transition from one state to the next state of a biothermodynamic system. The frequency of the change of state is in some phases higher, so the changes are macroscopically observable, and those are the seven phases described by Toussaint.

Conclusions

A model was developed that is not based on the steady-state approximation. This allows it to describe growing organisms. The developed model is more realistic in describing the behavior of living organisms than models found in the literature.

The entropy of an open thermodynamic system (composed of a polymer) increases with addition of each monomer unit into it. Increase of entropy is almost linear. However, a part of imported entropy escapes into the surroundings in form of heat, and with molecules that are products of chemical reactions and leave the system. Entropy of open thermodynamic systems was found to decrease only in case if a phase transition occurs during growth.

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