https://doi.org/10.15407/ujpe66.8.714

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ENTROPY PRODUCTION IN A MODEL BIOLOGICAL SYSTEM WITH FACILITATED DIFFUSION

Expressions for the calculation of the diffusion flow and the entropy production in a model biological system, an ideal binary solution in a plane-parallel layer under osmotic boundary conditions and the facilitated diffusion, have been derived in the framework of the linear thermodynamics of irreversible processes. It is shown that the consistent consideration of the dependence of the diffusion coefficient on the field variables leads to a substantial difference of the values obtained for the substance flow and the entropy production in biological systems from the values obtained in the framework of standard approach with a constant diffusion coefficient.

K e y w o r d s: entropy production, facilitated diffusion, biological system, ideal solution, osmotic boundary conditions.

1. Introduction. Entropy Production in Systems with Diffusion

Diffusion is a process that remains extremely important for a large variety of natural phenomena and technologies, so nowadays it is continued to be studied both experimentally and theoretically. The most general equations describing diffusion processes can be obtained by applying the basic principles of the thermodynamics of nonequilibrium processes [1, 2]. However, some approaches applied to the description of diffusion phenomena are based on specific ideas concerning the internal microscopic structure of the medium. It is important to emphasize that there is no theory at present that, on the one hand, would be rather convenient when describing the behavior of real systems and, on the other hand, would not possess substantial restrictions on its application [3].

Various physical approaches can be used to describe diffusion processes. There are phenomenological theories that describe this phenomenon in the most general form. In the general case, the mass conservation law written in the local form serves as a basis for phenomenological theories taking chemical reactions and convection into account. But the conservation laws form an open set of equations. So, for the researched system to be described completely, the set of equations has to be closed. For this purpose, the equations of state for a multicomponent system and the relationships between the substance flows and the generating thermodynamic forces are used. The linear thermodynamics of irreversible processes is based on the assumption that, in the case of a nonequilibrium system that is close to its equilibrium state, any flows are linearly related to independent thermodynamic forces that drive the system to the equilibrium state [4]. Therefore, the equations for the flows are written as linear combinations of thermodynamic forces with the coefficients that must be determined empirically.

In recent decades, a general statistical theory has been developed that substantiates the basic relationships in the thermodynamics of irreversible processes and can provide theoretical methods for the determination of the Onsager coefficients (which are phenomenological by their nature). Besides that, this can establish the application limits for the linear theory. The theory is based on the quantum-mechanical description of an isolated many-particle system [5, 6]. In addition, rather wide-spread are theories that describe the diffusion with the help of kinetic equations and making use of certain model concepts concerning the structure of the matter and the interaction between the particles. It is clear that this approach is

associated with the solution of a dynamic many-body problem [7–9]. As a result, the most significant results in the framework of this approach can be achieved using computer simulation methods [10, 11].

It should be emphasized that the results currently obtained in the framework of the described approaches (both experimental and theoretical) testify that the diffusion coefficient may substantially depend on the concentration, which cannot be taken into account when solving the classical diffusion equation in the form of Fick's law.

In many real systems – in particular, biological membranes – there is the so-called facilitated diffusion. This process can arise in a system with a reversible chemical reaction, when the diffusing substance (the so-called substrate) joins the carrier (the macromolecules that are contained within the membrane), so that there emerge the flows of both the substrate and the substrate-carrier complex in the system. Among the processes associated with the facilitated diffusion, we distinguish the transfer of oxygen (the substrate) through the membrane by hemoglobin (the carrier) and the effect of antibiotics on biological membranes [12, 13]. Note that, owing to the facilitated diffusion mechanism, the transfer rates of oxygen, alkali metal ions, and glucose can be higher by two orders of magnitude [14].

One of the most striking examples illustrating the process of facilitated diffusion is the diffusion of oxygen (O_2) in living organisms. It was experimentally found that myoglobin (Mb) facilitates the diffusion of O_2 in the cell [15, 16]. A large number of works (see, e.g., works [17, 18]) were devoted to the theoretical modeling and experimental study of the reversible binding of O_2 by myoglobin and its translational diffusion in the cell. The facilitated diffusion of oxygen by means of myoglobin is especially efficient at low partial pressures of the substrate, and its contribution to the diffusion flow depends on the concentration gradient of the carrier-substrate complex.

In the field of theoretical modeling of the diffusion in membrane biological systems with reversible chemical reactions, the pioneering results were obtained by Murray in works [19,20]. In particular, several models of membrane systems were considered, e.g., a model with a plane-parallel membrane containing a solution of hemoglobin or myoglobin through which the diffusion occurs. The protein available in the solution can reversibly join the substrate, for example, oxygen. The developed mathematical model allows one to find the spatial distributions of the oxygen concentration and the saturation function over the membrane volume, as well as the concentration dependences of the corresponding flows. The analysis of the obtained results points to a substantial nonlinearity in the concentration dependences of the substrate flows through such systems. It is important to note that there is a lack of calculations for the entropy production and flows in a wide class of such biological systems with a correct consideration of chemical reactions in them.

Let us introduce the entropy source intensity σ, i.e. the entropy production per unit time per unit volume of the system, with the help of the following expression for the rate of entropy production in the system [1]:

$$\frac{d_i S}{dt} = \int\limits_V d\mathbf{r}\,\sigma. \tag{1}$$

Now, let us consider a liquid or gaseous n-component system in which diffusion processes and chemical reactions can take place. We assume that the system is far from the stability thresholds (the critical points of various origins). Furthermore, we assume that the system is not undergone the action of external fields. In this case, for the intensity σ of the entropy production source, we may write [1]

$$\sigma = -\frac{1}{T^2}\mathbf{J}_q \boldsymbol{\nabla} T - \frac{1}{T}\sum_{k=1}^{n} \mathbf{J}_k T \boldsymbol{\nabla}\frac{\mu_k}{T} - \frac{1}{T}\sum_{i=1}^{r}\sum_{k=1}^{n} J_i \nu_{ki}\mu_k, \tag{2}$$

where $\mathbf{J}_q$ is the heat flux, T the temperature, $\mathbf{J}_k = \rho_k(\mathbf{v}_k - \mathbf{v})$ is the diffusion flux relative to the center of mass, $\mathbf{v}$ is the mass velocity, $\mathbf{v}_k$ the mass velocity of the k-th component, J_i the local rate of the i-th chemical reaction, ν_{ki} the stoichiometric coefficient, r the number of chemical reactions, and μ_k the chemical potential of the k-th component (it is a function of the pressure, temperature, and substance concentrations expressed in molar fractions x_k).

It is obvious that, in order to calculate the rate of entropy production σ making use of Eq. (2), it is necessary to have an expression for $\mathbf{J}_k$. For the diffusion

flows $\mathbf{J}_k$, we can use the law

$$\mathbf{J}_k = -D_k \boldsymbol{\nabla} x_k - \sum_{i=1}^{n} \sum_{\substack{j=1 \\ j \neq k}}^{n} L_{ki} \left[v_i \frac{\partial p}{\partial x_j} + kT \left(\frac{\delta_{ij}}{c_i} + \right.\right.$$
$$\left.\left. + \frac{1}{\gamma_i} \frac{\partial \gamma_i}{\partial x_j} \right) \right] \boldsymbol{\nabla} x_j - \sum_{i=1}^{n} L_{ki} v_i \frac{K_T}{\rho} \boldsymbol{\nabla} \rho - D_T \boldsymbol{\nabla} T, \qquad (3)$$

where v_i is the partial molar volume of the i-th component, K_T the isothermal compression modulus,

$$D_k = \sum_{i=1}^{n} L_{ki} \left[v_i \frac{\partial p}{\partial x_k} + kT \left(\frac{\delta_{ik}}{c_i} + \frac{1}{\gamma_i} \frac{\partial \gamma_i}{\partial x_k} \right) \right]$$

is the diffusion coefficient of the k-th component,

$$D_T = \sum_{i=1}^{n} L_{ki} \left(p v_i \gamma_V - s_i \right) + L_{kq}$$

is the Soret coefficient, γ_V is the thermal pressure coefficient, and s_i the partial molar entropy of the i-th component. For the chemical potential of the i-th component, μ_i, the following expression was used:

$$\mu_i \left(T, \rho, x_1, ..., x_n \right) =$$
$$= \mu_{i0} \left(T, \rho \right) + kT \ln x_i \gamma_i \left(T, \rho, x_1, ..., x_n \right), \qquad (4)$$

where μ_{i0} is the chemical potential of the pure substance, and γ_i the coefficient of activity of the i-th component. The account for only the entropy contribution to the change in the chemical potential of the i-th component (the term $\ln x_i$) corresponds to the ideal solution approximation. For the theoretical determination of the other term (the case of non-ideal solutions), the known approximations of the regular solution are used, such as the Margules, van Laar, Scatchard–Hamer, and other approximations [21, 22]. Then, the general expression for the entropy production can be written in the form

$$\sigma \left(T, \rho, c_i \right) = -\frac{1}{T^2} \mathbf{J}_q \boldsymbol{\nabla} T - \frac{1}{T} \sum_{i=1}^{r} \sum_{k=1}^{n} J_i \nu_{ki} \mu_k +$$
$$+ \left\{ \sum_{k=1}^{n} D_k \boldsymbol{\nabla} x_k + \sum_{k=1}^{n} \sum_{i=1}^{n} \sum_{\substack{j=1 \\ j \neq k}}^{n} L_{ki} \left[v_i \frac{\partial p}{\partial c_j} + \right.\right.$$
$$\left.\left. + kT \left(\frac{\delta_{ij}}{c_i} + \frac{1}{\gamma_i} \frac{\partial \gamma_i}{\partial c_j} \right) \right] \boldsymbol{\nabla} x_j +$$
$$+ \sum_{k=1}^{n} \sum_{i=1}^{n} L_{ki} v_i \frac{K_T}{\rho} \boldsymbol{\nabla} \rho + D_T \boldsymbol{\nabla} T \right\} \times$$
$$\times \left\{ \frac{1}{T} \sum_{j=1}^{n} \left(v_k \frac{\partial p}{\partial c_j} + kT \left(\frac{1}{\gamma_k} \frac{\partial \gamma_k}{\partial c_j} + \frac{\delta_{kj}}{c_k} \right) \frac{\partial \mu_k}{\partial c_j} \right) \boldsymbol{\nabla} x_j + \right.$$
$$\left. + \frac{v_k K_T}{T \rho} \boldsymbol{\nabla} \rho + \left(\frac{p v_k \gamma_T + s_k}{T} - \frac{\mu_k}{T^2} \right) \boldsymbol{\nabla} T \right\}. \qquad (5)$$

The obtained expression makes it possible to calculate the entropy production in systems with chemical reactions and the diffusion, including the facilitated one.

2. Stationary Diffusion and Entropy Production in a Plane-Parallel Pore

Let us apply the obtained general equation (5) to describe the process of entropy production in a membrane biological system. By a membrane, we mean a plane-parallel layer of a substance confined in between two semipermeable walls. Note that when constructing the membrane model, the Murray model for the diffusion of oxygen in the hemoglobin and myoglobin solutions [15, 19] was taken as a basis. Reversible chemical reactions are possible in the system. However, unlike the approach developed by Murray and Wittenberg [23], information about those reactions is taken into account via the activity coefficient γ. Such a consideration of chemical reactions allows the term $\frac{1}{T} \sum_{i=1}^{r} \sum_{k=1}^{n} J_i \nu_{ki} \mu_k$ to be not considered in the explicit form [24].

Let us consider the process of stationary diffusion in a two-component solution located in a plane-parallel membrane with the distance l confined between two semipermeable walls. It is evident that

$$\frac{dJ_1}{dt} = 0 \qquad (6)$$

in this case. We also assume that the system is not affected by external forces. The temperature gradients are absent as well. Such a model adequately describes the behavior of a large number of biological systems [19]. In this case, the membrane only contains the substrate (component 1) diffusing through it and the carrier (component 2) responsible for the realization of the facilitated diffusion regime [16].

Let us introduce such a coordinate system that its axis $0z$ be perpendicular to the surfaces that confine the system and are located at the coordinates $z = 0$

and $z = l$. Since substance 2 (carriers) always remains within the membrane, we have

$$J_2(0) = J_2(l) = 0. \tag{7}$$

Besides that, we assume that a gradient of the concentration of substance 1 is maintained in the system. Namely, the substrate concentrations are constant at the system boundaries, so that the boundary conditions look like

$$\begin{cases} x_1(z=0) = x_0, \\ x_1(x=l) = x_l, \end{cases} \tag{8}$$

where $x_0 > x_l > 0$.

The stationary character of the diffusion process allows the order of the differential equation describing the diffusion process to be correctly reduced by one. At the same time, this condition fits well to plenty of physical phenomena. Note that the processes of entropy production in native wildlife are stationary.

Furthermore, in the framework of the proposed model, we may neglect crossed processes, such as the thermodiffusion, because their contributions are several orders of magnitude smaller than those of direct processes in liquid systems [25]. In this case, the diffusion is driven exclusively by the chemical potential gradients of the components. Therefore, all nondiagonal elements in the matrix of phenomenological coefficients L_{ik} can be put equal to zero. The diagonal elements will be denoted as L_i.

Since the diffusion is considered in a membrane with semipermeable walls, osmotic phenomena must appear in such a system. In other words, the dependence of chemical potentials on the pressure must be taken into consideration, which was marked for the first time in work [26]. Those osmotic phenomena (namely, the pressure gradient that arises in the system) make it possible to explain the mechanism giving rise to the absence of substance diffusion between the semipermeable walls of the membrane, although the concentration gradient does exist. In this case, we obtain the following expression for the substrate flux:

$$J_1 = -2kL_1 \frac{dx_1}{dz} \left\{ \left[\frac{1}{x_1} + \frac{\partial}{\partial x_1} \ln \gamma_1 \right] + \right.$$
$$\left. + \frac{v_{10} + kT \frac{\partial}{\partial p} \ln \gamma_1}{v_{20} + kT \frac{\partial}{\partial p} \ln \gamma_2} \left[\frac{1}{1 - x_1} - \frac{\partial}{\partial x_1} \ln \gamma_2 \right] \right\}. \tag{9}$$

By comparing the obtained expression for the substrate flux with Fick's law, we can write the following expression for the diffusion coefficient $D\,(T, p, x_1)$:

$$D(T, p, x_1) = 2\frac{L_1}{T} \left\{ \left(\frac{\partial \mu_1}{\partial x_1} \right) - \frac{\left(\frac{\partial \mu_1}{\partial p} \right)}{\left(\frac{\partial \mu_2}{\partial p} \right)} \left(\frac{\partial \mu_2}{\partial x_1} \right) \right\} =$$
$$= 2kL_1 \left\{ \left[\frac{1}{x_1} + \frac{\partial}{\partial x_1} \ln \gamma_1 \right] + \right.$$
$$\left. + \frac{v_{10} + kT \frac{\partial}{\partial p} \ln \gamma_1}{v_{20} + kT \frac{\partial}{\partial p} \ln \gamma_2} \left[\frac{1}{1 - x_1} - \frac{\partial}{\partial x_1} \ln \gamma_2 \right] \right\}. \tag{10}$$

This formula demonstrates an essential dependence of the diffusion coefficient on the thermodynamic parameters of the system and the thermal equation of state. It is evident that, in the case of stationary diffusion in a binary solution, we can write the following ultimate expression for the entropy production:

$$\sigma = L_1 (2k)^2 \left(\frac{dx_1}{dz} \right)^2 \left\{ \left[\frac{1}{x_1} + \frac{\partial}{\partial x_1} \ln \gamma_1 \right] - \right.$$
$$\left. - \frac{v_{10} + kT \frac{\partial}{\partial p} \ln \gamma_1}{v_{20} + kT \frac{\partial}{\partial p} \ln \gamma_2} \left[\frac{\partial}{\partial x_1} \ln \gamma_2 - \frac{1}{1 - x_1} \right] \right\}^2. \tag{11}$$

In order to calculate the substance flow and the entropy production with the help of expression (9), it is necessary to know the dependence of the activity coefficients on the pressure and concentration. It is known that the activity coefficient is associated with the peculiarities in the equation of state. Therefore, in accordance with Shakhparonov's ideas [27], we may assume that its account will enable us to model possible reversible chemical reactions as a specific kind of intermolecular interaction [28]. In particular, as was shown in works [28, 29], there is a possibility to simulate chemical reactions by considering the changes of thermodynamic parameters.

In work [30], it was demonstrated that, in the general case, the results obtained with the help of the perturbation theory applied to an isobaric-isothermal ensemble can be used to determine the dependence of the activity coefficients on the pressure and concentration. The explicit form of this dependence is often determined by the model of regular solutions and the Margules, van Laar, and Scatchard–Hamer empirical equations.

Thus, making use of Eqs. (9) and (11), it is possible to calculate the substance flow and the entropy production in a binary solution located in a plane-parallel

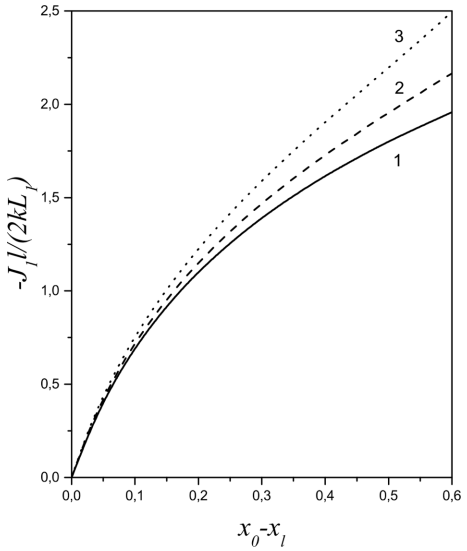

Fig. 1. Dependences of the normalized flow $-\frac{l}{2kL_1}J_1$ on the quantity $x_0 - x_l$ in the ideal solution model for various values of the ratio $v_{10}/v_{20} = 0.01$ (*1*), 0.2 (*2*), and 0.5 (*3*). The concentration at the right boundary of the membrane $x_l = 10^{-1}$

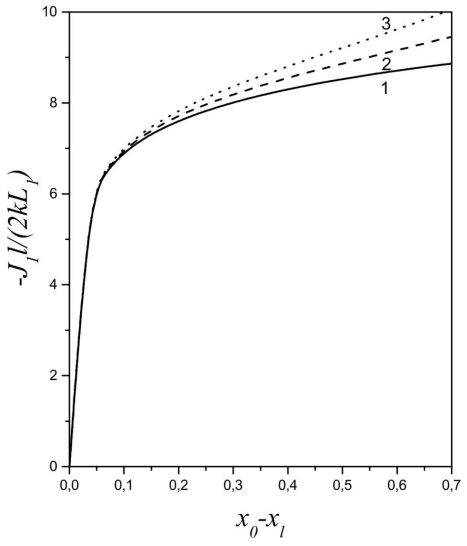

Fig. 2. Dependences of the normalized flow $-\frac{l}{2kL_1}J_1$ on the quantity $x_0 - x_l$ in the ideal solution model for various values of the ratio $v_{10}/v_{20} = 0.01$ (*1*), 0.5 (*2*), and 1.0 (*3*). The concentration at the right boundary of the membrane $x_l = 10^{-4}$

pore, if we specify the interaction between the particles in the solution (i.e. the solution type) and the character of possible chemical reactions making use of the activity coefficient.

3. Entropy Production in a Plane-Parallel Pore in the Case of Ideal Solution

Let us consider the case of ideal solution. In this model, the contribution of the entropy factors given to thermodynamic potentials at the mixing dominates over that of energy ones, so that the latter can be neglected. Then, the activity coefficient is identically equal to unity and, after the integration, the expression for the substrate flow takes the form

$$J_1 = -\frac{2kL_1}{l}\left(\ln\frac{x_l}{x_0} - \frac{v_{10}}{v_{20}}\ln\frac{1-x_l}{1-x_0}\right). \tag{12}$$

In Figs. 1 and 2, the dependences of the normalized flow of the substance diffusing through the membrane on the concentration difference between the boundaries, $x_0 - x_l$, are shown for various ratios between the partial volumes of the solution components and for two values of x_l. The presented results demonstrate a substantial nonlinear dependence of the flow on the value of the difference $x_0 - x_l$. Recall that they were obtained in the case of ideal solution, i.e. considering only the entropy contribution to the variation of the thermodynamic potential at the mixing.

The analysis of the presented results testifies that, for small values of the difference $x_0 - x_l$ (in particular, $x_0 - x_l < 0.1$ for the data shown in Fig. 1 and $x_0 - x_l < 0.01$ for the data shown in Fig. 2), the observed dependence of the flow is almost linear. However, as the difference $x_0 - x_l$ grows, the dependence $J_1(x_0 - x_l)$ considerably deviates from the linear one, and the stabilizing effect takes place, i.e. the flow begins to depend weakly on the concentration difference between system's boundaries. The presented data also demonstrate that if the ratio between the partial molar volumes of the substance diffusing through the membrane and the solvent decreases, an essential enhancement of the stabilizing effect is observed with the growth of the concentration difference between the membrane boundaries.

In the case of facilitated diffusion of a biologically active substance through membranes (e.g., the hemoglobin-assisted diffusion of oxygen), the ratio v_{10}/v_{20} is extremely small. Furthermore, the concentration of the transferred substance at the right boundary of the system is maintained at a rather low level in most cases, so the biological transport is described by curve *1* in Fig. 2. In this case, the

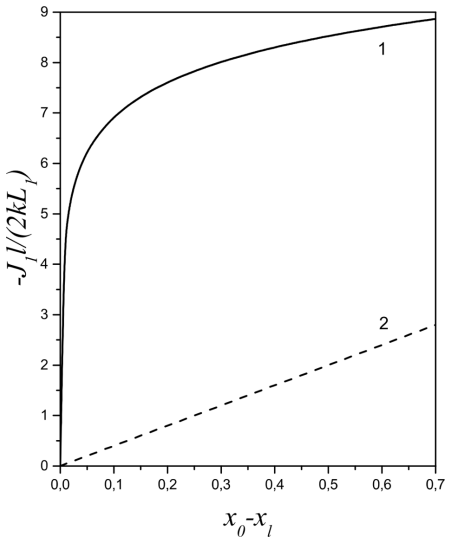

Fig. 3. Dependences of the normalized diffusion flow on the quantity $x_0 - x_l$ calculated for $v_{10}/v_{20} = 0.01$: in the ideal solution model (*1*) and at $D = \text{const}$ (*2*). The concentration at the right boundary of the membrane $x_l = 10^{-4}$

flow remains almost constant within the physiologically relevant variation interval of the concentration difference $x_0 - x_l$. Such behavior corresponds to the specific features of the facilitated diffusion in biological systems.

Figure 3 exhibits the dependences of the normalized diffusion flow on the $x_0 - x_l$ value calculated for $v_{10}/v_{20} = 0.01$ and in the case of the constant diffusion coefficient. One can see that at small $x_0 - x_l$ values, a substantial increase of the facilitated diffusion flow is observed: the flow ratio reaches a value of about 110 at $x_0 - x_l = 10^{-2}$, being of about 15 at $x_0 - x_l = 10^{-1}$. The stabilizing effect manifests itself well with the further increase of the difference $x_0 - x_l$: when $x_0 - x_l$ changes from 0.2 to 0.7, the facilitated flow grows by about 17%, whereas the flow with the constant diffusion coefficient, expectedly, by about 250%.

The obtained expression (12) for the diffusion flow makes it possible, using formula (11), to find an expression for the entropy production in the case concerned:

$$\sigma = \frac{(2k)^2 L_1}{l^2}\left(\ln\frac{x_l}{x_0} - \frac{v_{10}}{v_{20}}\ln\frac{1-x_l}{1-x_0}\right)^2. \qquad (13)$$

In Figs. 4 and 5, the dependence of the entropy production on the concentration difference between the

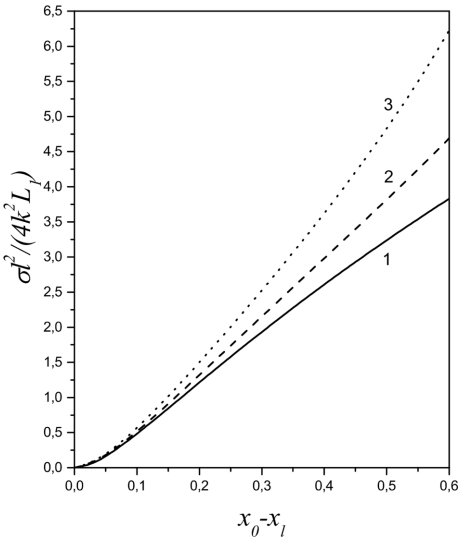

Fig. 4. Dependences of the normalized entropy production $\frac{l^2}{(2k)^2 L_1}\sigma$ on the quantity $x_0 - x_l$ in the ideal solution model for various values of the ratio $v_{10}/v_{20} = 0.01$ (*1*), 0.2 (*2*), and 0.5 (*3*). The concentration at the right boundary of the membrane $x_l = 10^{-1}$

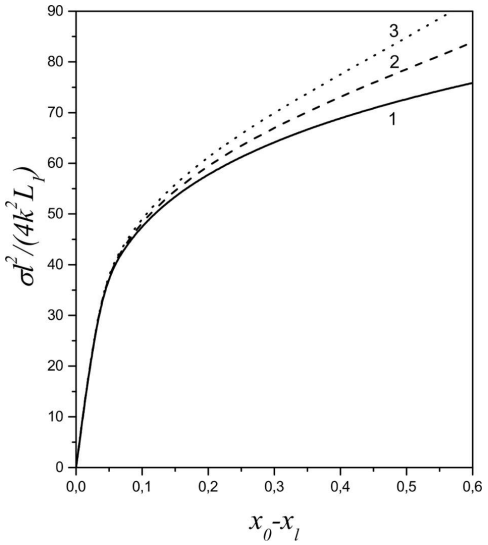

Fig. 5. Dependences of the normalized entropy production $\frac{l^2}{(2k)^2 L_1}\sigma$ on the quantity $x_0 - x_l$ in the ideal solution model for various values of the ratio $v_{10}/v_{20} = 0.01$ (*1*), 0.5 (*2*), and 1.0 (*3*). The concentration at the right boundary of the membrane $x_l = 10^{-4}$

boundaries, $x_0 - x_l$, is shown for various ratios between the partial volumes of the solution components and for two x_l-values. The presented results point to a substantial deviation of the entropy production be-

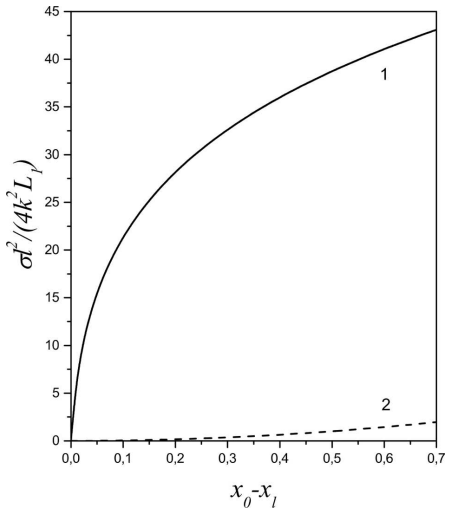

Fig. 6. Dependences of the normalized entropy production $\frac{l^2}{(2k)^2 L_1}\sigma$ on the quantity $x_0 - x_l$ calculated for $v_{10}/v_{20} = 0.01$: (1) in the ideal solution model and (*2*) at $D = \text{const}$. The concentration at the right boundary of the membrane $x_l = 10^{-4}$

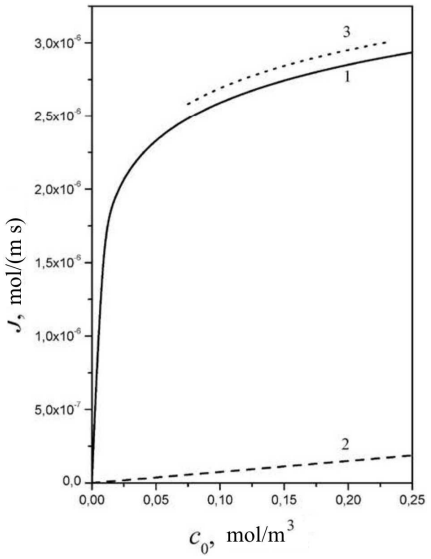

Fig. 7. Oxygen flow in the aqueous hemoglobin solution as a function of the oxygen concentration at the left membrane boundary: (*1*) facilitated diffusion according to the results of Murray's calculations [19], (*2*) diffusion flow, (*3*) Wittenberg's experimental results [16]

havior from the quadratic dependence on the quantity $x_0 - x_l$ (the latter should have been expected according to the general expressions).

The analysis of the presented results testifies that, for small values of the quantity $x_0 - x_l$ ($x_0 - x_l < 0.1$ for the data shown in Fig. 4 and $x_0 - x_l < 0.01$ for the data shown in Fig. 5), an almost quadratic dependence of the entropy production is observed. However, as the difference $x_0 - x_l$ grows, the dependence $\sigma(x_0 - x_l)$ starts to deviate substantially from the quadratic one, and the stabilizing effect takes place, i.e. the entropy production begins to depend weakly on the concentration difference between the boundaries of the system. As one may expect from the analysis of the results obtained for the flows, the presented data testify that the decrease of the ratio between the partial molar volumes of the substance diffusing through the membrane and the solvent brings about a substantial enhancement of the stabilizing effect, when the concentration difference between the membrane boundaries increases.

As was said above, in the case of facilitated diffusion of a biologically active substance through membranes, the ratio v_{10}/v_{20} is extremely small. As a result, the entropy production remains almost constant within the physiologically relevant variation interval of the concentration difference $x_0 - x_l$. Such a behavior also corresponds to the specific features of the facilitated diffusion in biological systems.

In Fig. 6, the dependences of the normalized entropy production on the difference $x_0 - x_l$ are shown for $v_{10}/v_{20} = 0.01$ and the case of the constant diffusion coefficient. One can see that at small $x_0 - x_l$ values, a substantial increase of the entropy production is observed in the facilitated diffusion case: the entropy production ratio reaches a value of about 1.1×10^4 at $x_0 - x_l = 10^{-2}$, whereas it is of about 5×10^2 at $x_0 - x_l = 10^{-1}$. The stabilizing effect manifests itself well with the further increase of the difference $x_0 - x_l$: when $x_0 - x_l$ changes from 0.2 to 0.7, the entropy production grows by about 50% at the facilitated diffusion, whereas the entropy production at the constant diffusion coefficient expectedly increases by about 1100%.

Figure 7 demonstrates the dependences of the total oxygen flux in the aqueous hemoglobin solution as a function of the oxygen concentration at the left membrane boundary provided that the oxygen concentration at the right boundary is constant (i.e., actually as a function of the oxygen concentration gradient), which were obtained theoretically by Murray [19] and experimentally by Wittenberg [16]. Murray's results were obtained by explicitly accounting for the presence of reversible chemical reactions in the system,

namely, by constructing a solution for the asymptotic expansion of a singularly perturbed equation of the diffusion type in the zeroth-order approximation. A comparison of our results (Fig. 2) with the data presented in Fig. 7 testifies that the approach with the account for reversible chemical reactions with regard for the physicochemical characteristics of the solution, where the diffusion process takes place, brings about results that are in good qualitative and quantitative agreement with the literature data obtained both experimentally and theoretically. In particular, a substantial growth of the facilitated diffusion flow is observed at small c_0-values, whereas a considerable stabilizing effect is well-pronounced at larger c_0-values.

4. Conclusions

1. The formula obtained for the diffusion coefficient demonstrates its strong dependence on the solution concentration, which is mainly determined by the thermal equation of state of the system.

2. While describing the process of facilitated diffusion in biological systems, there is no need to explicitly consider the presence of reversible chemical reactions. The correct account for the concentration dependence of the diffusion coefficient leads to results that are qualitatively similar to those obtained, when the chemical reactions are considered explicitly.

3. The results obtained for the entropy production testify to the existence of a stabilizing effect in biological systems. If the concentration gradient of the diffusing substance changes, the entropy production changes within narrower limits as compared with the results obtained for a constant diffusion coefficient.

4. The entropy contributions to the variation of thermodynamic potentials at the mixing play an important role in the change of the character of entropy production in biological systems.

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Received 29.08.20.
Translated from Ukrainian by O.I. Voitenko

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ПРОДУКУВАННЯ ЕНТРОПІЇ
В МОДЕЛЬНІЙ БІОЛОГІЧНІЙ СИСТЕМІ
В ПРОЦЕСІ ПОЛЕГШЕНОЇ ДИФУЗІЇ

Отримано вирази для визначення потоку речовини, що дифундує, та продукування ентропії в модельній біологічній системі – плоскопаралельному шарі з осмотичними граничними умовами за наявності процесів дифузії для бінарного ідеального розчину в рамках лінійної термодинаміки незворотних процесів. Показано, що послідовне врахування залежності коефіцієнта дифузії від польових змінних призводить до суттєвої відмінності залежності потоку речовини та продукування ентропії в біологічній системі від значень, отриманих в рамках загальновживаного підходу зі сталим коефіцієнтом дифузії.

Ключові слова: продукування ентропії, полегшена дифузія, біологічна система, ідеальний розчин, осмотичні граничні умови.