A GENERALIZED MODEL OF ION TRANSPORT THROUGH ARTIFICIAL PHOSPHOLIPID MEMBRANES

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In previous papers on the theory of ion transport through artificial phospholipid membranes we investigated the carrier model [1] and the relay model [2]. In the carrier model it is assumed that the membrane contains certain mobile ions T with charge Z_T which can take up an ion A with charge Z_A from the solution of electrolyte surrounding the membrane and form an ion $L \equiv AT$ with charge $Z_L = Z_A + Z_T$. All the charges are expressed in units of proton charge. The ion L can then move under the action of the electrochemical gradient from one boundary of the membrane to the other, where the ion A is given up to the solution and the carrier T returns.

In the relay model it is assumed that passage of charge through the membrane is effected by transfer of the ion A between stationary particles T.

In both the carrier and relay models it is assumed that the ions T and L can pass through the boundary of the membrane, on which the following reactions take place:

$$(\mathrm{T}) \underset{k_2}{\overset{k_1}{\rightleftarrows}} [\mathrm{T}], \tag{1}$$

$$(\mathrm{A}) + [\mathrm{T}] \underset{k_4}{\overset{k_3}{\rightleftarrows}} [\mathrm{L}], \tag{2}$$

$$(\mathrm{L}) \underset{k_6}{\overset{k_5}{\rightleftarrows}} [\mathrm{L}], \tag{3}$$

where the round brackets denote the concentration of the corresponding substance in the solution, and the square brackets denote its concentration in the membrane.

In the present generalized model we regard the passage of an electric current through the membrane as due to direct passage of particles T, relay transfers of ions A, and the transport of A by the carrier mechanism. In the membrane the ions T and L can be located only in certain potential wells on the boundary. Each well can contain only one ion. Ions can only drop into a well if it is empty. In addition, the ions T and L can cross from the well on the left boundary to the opposite well on the right boundary, provided, of course, that the latter is empty, and vice versa. If two opposite wells contain an ion L and T, respectively, they can transfer a particle A. Transfers of ions T, L, and A proceed at rates ν_T, ν_L, and ν_A, respectively (Fig. 1). The number of wells on each boundary is limited and is equal to N per unit area of membrane.

The probability of occupation of one well by ions T and L is θ_T and θ_L, respectively. If a potential difference φ is imposed on the membrane there will be a redistribution of the charges in the wells in it. The charges of the left and right boundaries, referred to unit surface of membrane, will be

$$q^L = Ne[Z_T\theta_T{}^L + Z_L\theta_L{}^L], \tag{4}$$

$$q^R = Ne[Z_T\theta_T{}^R + Z_L\theta_L{}^R], \quad e \text{ is the proton charge}, \tag{5}$$

where the superscripts L and R denote that the quantity corresponds to the left or right boundary.

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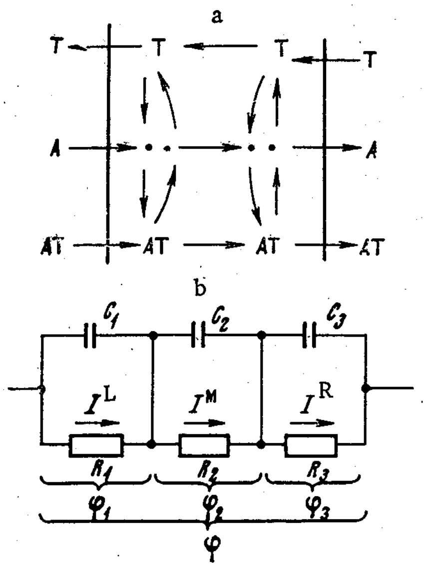

Fig. 1

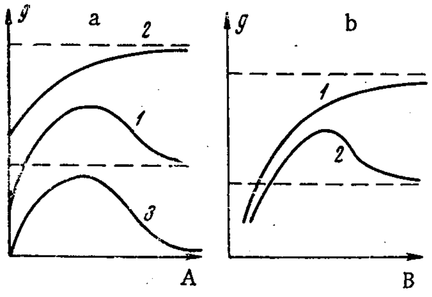

Fig. 2

Fig. 1. a) Generalized mechanism of ion transport through membrane; b) equivalent circuit.

Fig. 2. Case of absence of entrance channel L. a) Conductivity as function of concentration of ions A for $\nu_A \gg \nu_T$, ν_L (1), $\nu_A \ll \nu_T$, ν_L (2) and $C_1 \gg C_2$, $\nu_A \gg \nu_T$, ν_L (3); b) conductivity as function of total concentration of ions T for $\nu_A \gg \nu_T$, ν_L (1) and $\nu_A \ll \nu_T$, ν_L (2).

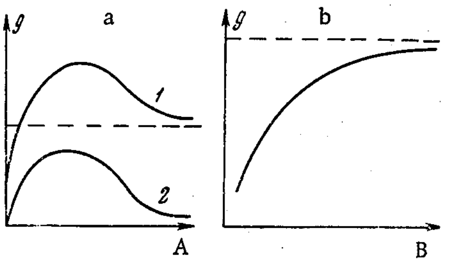

Fig. 3. Case of absence of entrance channel A and internal channels L and T. a) Conductivity as function of concentration of ions A: general case (1) and case $C_1 \gg C_2$ or $k_i \sim 0$ (2); b) conductivity as function of total concentration of ions T.

The external potential difference φ can be divided into three parts (Fig. 1). φ_1 and φ_3 are the potential falls in the double electric layers on the boundaries of the membrane, and φ_2 is the potential fall within the membrane. The potential falls φ_1, φ_2, and φ_3 occur on capacitances C_1, C_2, and C_3, respectively. C_1 and C_3 are the capacitances of the membrane-electrolyte interface boundaries, while C_2 is the capacitance of the membrane itself. These regions have resistance R_1, R_2, and R_3, respectively. Hence, the whole membrane can be represented by the equivalent circuit illustrated in Fig. 1.

We calculate the current through the membrane. We consider the symmetric case, i.e., $R_1 = R_3$, $C_1 = C_3$. The total current through unit surface of the membrane is

$$I = \frac{C_1 C_2}{C_1 + 2C_2} \frac{d\varphi}{dt} + (I^L + I^R) \frac{C_2}{C_1 + 2C_2} + I^M \frac{C_1}{C_1 + 2C_2}, \qquad (6)$$

where I^L, I^R, and I^M are the ion currents flowing through unit area of the left boundary, right boundary, and the membrane itself. The first term on the right side of Eq. (6) is the current responsible for charging the membrane as a whole. The other terms are the contributions of the corresponding parts of the membrane to the total current

$$\begin{aligned} I^L &= e[Z_T j_T^L + Z_L j_L^L + Z_A j_A^L], \\ I^R &= e[Z_T j_T^R + Z_L j_L^R + Z_A j_A^R], \\ I^M &= e[Z_T j_T^M + Z_L j_L^M + Z_A j_A^M], \end{aligned} \qquad (7)$$

where j_m^n denote the fluxes of the corresponding substance through the corresponding region of the membrane:

$$j_T^L = k_1(T) N (1 - \theta_T^L - \theta_L^L] \exp(1/2 Z_T \beta \varphi_1) - k_2 \theta_T^L N \exp(-1/2 Z_T \beta \varphi_1); \qquad (8)$$

$$j_A^L = k_3(A) \theta_T^L N \exp(1/2 Z_A \beta \varphi_1) - k_4 \theta_L^L N \exp(-1/2 Z_A \beta \varphi_1); \qquad (9)$$

$$j_T^M = \nu_T \theta_T^L N [1 - \theta_T^R - \theta_L^R] \exp(1/2 Z_T \beta \varphi_2) - \nu_T \theta_T^R N [1 - \theta_T^L - \theta_L^L] \cdot \exp(1/2 Z_T \beta \varphi_2); \qquad (10)$$

$$j_A^M = \nu_A \theta_L^L \theta_T^R N \exp(\tfrac{1}{2}\beta Z_A \varphi_2) - \nu_A \theta_L^R \theta_T^L N \exp(-\tfrac{1}{2}\beta Z_A \varphi_2), \tag{11}$$

where $\beta = e/kT$.

The other fluxes are expressed in a similar way. The division of the potential φ into parts depends on the redistribution of charges and on the electric parameters of the membrane and can be expressed in the following way:

$$\varphi_1 = \varphi C_2 / (C_1 + 2C_2) - q^L (C_1 + C_2) / C_1(C_1 + 2C_2) - q^R C_2 / C_1(C_1 + 2C_2); \tag{12}$$

$$\varphi_2 = \varphi C_1 / (C_1 + 2C_2) + q^L / (C_1 + 2C_2) - q^R / (C_1 + 2C_2); \tag{13}$$

$$\varphi_3 = \varphi C_2 / (C_1 + 2C_2) + q^L C_2 / C_1(C_1 + 2C_2) + q^R (C_1 + C_2) / C_1(C_1 + 2C_2). \tag{14}$$

The changes in the filling numbers of the wells in the membrane are given by the conservation laws:

$$N\, d\theta_T^L / dt = j_T^L - j_A^L - j_T^M + j_A^M; \tag{15}$$

$$N\, d\theta_L^L / dt = j_L^L + j_A^L - j_L^M - j_A^M; \tag{16}$$

$$N\, d\theta_T^R / dt = j_T^M - j_A^M - j_T^R + j_A^R; \tag{17}$$

$$N\, d\theta_L^R / dt = j_L^M + j_A^M - j_L^R - j_A^R. \tag{18}$$

Let the potential difference applied to the membrane change harmonically in time: $\varphi = \varphi_0 e^{i\omega t}$. Then in the steady state all the quantities vary according to the same harmonic law. Solving Eqs. (15)-(18) for the case of a small field we find the relationship between the current flowing through the membrane and the potential

$$I = B\varphi, \tag{19}$$

where B is the total admittance of the membrane. Since the general formula for the admittance in this model has a very complicated form we will not give it completely here and will investigate only high frequencies.

The case of low frequencies (direct current) was considered in Bruner's paper [3]. In addition, it is known from [1, 2] that for diagnosis of the transport mechanism the high-frequency limit is of the most interest.

The capacitance of the membrane, as is to be expected, is equal to the geometric capacitance

$$C = C_1 C_2 / (C_1 + 2C_2). \tag{20}$$

The conductivity of the membrane is written in the form

$$g = \beta \frac{C_1^2 e}{(C_1 + 2C_2)^2} [\nu_A Z_A^2 \theta_T^0 \theta_L^0 N + \nu_T Z_T^2 \theta N (1 - \theta_T^0 - \theta_L^0) + \nu_L z_L^2 \theta_L^0 N (1 - \theta_T^0 - \theta_L^0)] + 2\beta \frac{C_2 e}{(C_1 + 2C_2)^2} [z_T^2 k_2 \theta_T^0 N + z_A^2 k_4 \theta_L^0 N + z_L^2 k_6 \theta_L^0 N], \tag{21}$$

where θ_T^0 and θ_L^0 are the equilibrium filling numbers. The expressions for them have the form:

$$\theta_T^0 = k_1 k_4 \zeta b / [k_2 k_4 (\zeta + A) + k_1 k_4 \zeta b + k_1 k_3 \zeta b A, \tag{22}$$

$$\theta_L^0 = k_1 k_3 A \zeta b / [k_2 k_4 (\zeta + A) + k_1 k_4 \zeta b + k_1 k_3 \zeta b A], \tag{23}$$

$$k_2 k_4 k_5 / k_1 k_3 k_6 = \zeta, \tag{24}$$

where b is the total concentration of ions T in the solution of electrolyte enveloping the membrane, and ζ is the dissociation constant of the ion L.

I. We consider the case where the entrance channel L is absent, i.e., $k_5 = k_6 = 0$. We investigate the dependence of the conductivity on the concentration of ions A and the total concentration of ions T in the electrolyte solution. The investigation of this relationship shows that the behavior of the curve g depends considerably on the relationship between the transfer rates: ν_T, ν_L, ν_A (Fig. 2a). If the relay mechanism predominates, i.e., $\nu_T, \nu_L \ll \nu_A$, then with increase in concentration of A in the solution the conductivity begins to increase, but at higher concentration of A all the wells are occupied by ions L and the conductivity falls after passing through a maximum at some value of A (Fig. 2a, curve 1).* If $\nu_A \ll \nu_T$, ν_L, only the carriers will operate inside the membrane and the conductivity will depend monotonically on the concentration of A and have the form of curve 2 in Fig. 2a.

The relationship between g and the total concentration of ions T is shown in Fig. 2b. In fact, with increase in the total concentration of T in the relay case, i.e., $\nu_A \gg \nu_T$, ν_L (curve 1, Fig. 2b), the conductivity increases,

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*If $C_1 \gg C_2$, then curve 1 in Fig. 2a becomes curve 3 in Fig. 2a. This can be attributed to the fact that at low and high concentrations of A in the solution there will be no current through the membrane in this case, i.e., only relay transfer occurs.

since it depends significantly on the presence of ions T in the membrane, but, owing to the limited number of wells, when $b \to \infty$ the conductivity becomes constant. In the case of carriers, i.e., $\nu_A \ll \nu_T$, ν_L the dependence of the conductivity g on b has the form of curve 2, Fig. 2b. The conductivity increases at small b, passes through a maximum at a certain value of b, and then tends to a constant at large b.

II. We consider another special case, where the entrance channels T and L operate on the membrane boundary, i.e., carriers operate on the boundary, and at the internal stage the relay mechanism is the main channel. As before, we will consider high frequencies.

We investigate the conductivity in this case as a function of the concentration of ions A and the total concentration of ions T in the solution. Using expressions (22)-(24) and substituting the obtained expressions in (21) we find that the conductivity changes with increase in concentration of A, passing through a maximum (Fig. 3). If $Z_T^2 k_1 k_2 \zeta / (k_2 + k_1 b) > Z_L^2 k_5 k_6 / (k_6 + k_5 b)$, the conductivity at large A is smaller than at small A; if $Z_T^2 k_1 k_2 \zeta / (k_2 + k_1 b) < Z_L^2 k_5 k_6 / (k_6 + k_5 b)$, the opposite occurs. This is due to the fact that at low and high concentrations of A the internal relay stage makes no contribution to the total current. At low concentrations the most important role is due to transfer of ions T through the boundary, whereas at large L the transfer of ions L is most important. Hence, the conductivity has the form in Fig. 3a. If the contribution of the surface stage to the total current is neglected, which is equivalent to the assumption that $C_1 \gg C_2$ or $k_i \sim 0$, curve 1 in Fig. 3a will become curve 2 in the same figure.

We now consider the conductivity as a function of the total concentration of ions T in the solution. Using expressions (22)-(24) we find that this relationship has the form shown in Fig. 3b. This is understandable, since an increase in concentration b stimulates the carriers on the boundary and the relay mechanism within the membrane.

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