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Kybernetika, Vol. 15 (1979), No. 6, (488)--496

Persistent URL: <http://dml.cz/dmlcz/125240>

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The Electrokinetic Model of Matter Transport through Biological Barriers

JOZEF MICHALOV

In the present paper a group of mathematical relations is given as a mathematical model, which allows to describe the permeable and conductive properties of biological barriers. The input quantities for the model are changes of the electric and concentration gradient in the live system, as well as the ionic current, which can be measured by up-to-date experimental devices. Thus it is possible to obtain important dates on fundamental properties of biological barriers.

INTRODUCTION

The work of sophisticated biological systems may be analysed from the point of view of metabolism and energy and information exchange. In live systems biochemical reactions produce a rigorous self-organisation. If a metabolite is piled up, its synthesis is inhibited and its flow-off from the system is quickened until the needed concentration steadies. The work of each portion of the live system is determined by a sophisticated entanglement of feedbacks.

There is an incessant flow of information in the live system, emitted and transferred by biopotentials and bioelectric currents from organs to others. This information is being worked through by the system cells to select a way allowing, in the best possible manner, to implement the vital functions under given conditions.

Under the present conditions of technical development, it is difficult to observe this activity of the system directly. At present, mathematical models are used for this purpose, which have to indicate, or even to contribute for proving a certain general result in studying activities of a living system.

Aim of the present work is, to point at the necessity of the complex use of mathematical equations of physical chemistry, when studying electrokinetical phenomena in living objects, instead of hitherto separate studies. This would be the only way to obtain a more complete system of informations on them.

In the part of this article, dealing with the theoretical base of the model, we intend to give a complex view on these well known equations, which are, however, only seldom used in connection the ones with the others, as it is given in our contribution. In the part concerning the application of our model, examples are given for using it in obtaining important quantities (*coefficient of permeability, relative coefficient of permeability, conductivity, relative conductivity* and others) for characterizing the permeable and conductive properties of membranes, cell walls and single-cell layers of living systems.

THE THEORETICAL BASIS OF THE MODEL

Ion translocation in the live system leads to the formation of a concentration gradient along the walls of biological barriers (*membranes, walls, tissue segments* etc.) manifesting itself in the change of electro-chemical potentials and hence also in the change of the electromotric voltage of the biological barrier. This process is also practicable in the converse direction and suitable for investigating the biophysical aspects of the transport phenomenon through biological barriers.

Electromotric voltage E , originating between two solutions according to Nernst and Donnan, is given by the relations:

$$(1) \quad E_{x_{j+}} = \frac{RT}{F} \ln \frac{[a_{x_{j+}}]_1}{[a_{x_{j+}}]_2} = -\frac{RT}{F} \ln \frac{[a_{y_{j-}}]_2}{[a_{y_{j-}}]_1} = E_{y_{j-}},$$

where R is the gas constant ($R = 8.314 \text{ Joule} \times \text{deg}^{-1}$); F is the Faraday charge ($F = 96494 \text{ C}$), T the absolute temperature on the Kelvin scale; $a_{x_{j+}}$ the electrochemical activity of x_{j+} ions, $a_{y_{j-}}$ the electrochemical activity of y_{j-} ions; numbers 1 and 2 designate compartments.

Since salts are to be solved in a solvent and the natural solvent is H_2O , an electrolyte, electromotric voltage must be expressed with respect to H^+ and OH^- ions by the relation:

$$(2) \quad E_{x_{j+}(y_{j-})} = \frac{RT}{F} \ln \frac{[x_{j+}]_1}{[x_{j+}]_2} = \frac{RT}{F} \ln \frac{[y_{j-}]_2}{[y_{j-}]_1} = \frac{RT}{F} \ln \frac{RT}{F} \ln \frac{[H^+]_1}{[H^+]_2} = \\ = \frac{RT}{F} \ln \frac{[OH^-]_2}{[OH^-]_1}.$$

Electromotric voltage is essentially the difference of electric potentials, occurring between two environments, either in the structure proper of the permeable barrier, or between the barrier and the surrounding environment.

The availability of electric potentials is conditioned by the presence of electric charges, fixly bound in the structure of the barriers (*membranes or walls*) of the live system. The barriers are porous. At the pore wall-solution interface an electric double-

layer is developing. Charges constituting the unmoved portion of the electric double-layer at the interface of the pore walls and the solution, are steadily bound to the pore walls and determine the electric charge of the barrier. In the solution surrounding the pore walls from one side, particles are moving with an electric charge of a polarity converse to the charge of the pore walls.

It ensues from the above-said that ion transport through barriers is passing off in consequence of the existence of natural electric and concentration gradients between two environments. Measurable electric potentials, however, or, to put it more precisely, voltages or potential differences through porous barriers, consist, as a rule, of three portions, namely of two phase functional potentials at two barrier-solution interfaces and of a diffuse potential inside the barrier. According to Wilbrant [10] and Sollner [9], the magnitudes of the potentials arising at the barrier-solution interfaces, may be determined with the aid of the concentration gradient between the solutions washing the barriers and the presumed corresponding equilibrium distribution of the concentration in the solution, of the immediately adjacent layers of water in the pore space.

The complete formulation for the total electric voltage of the barrier may be described by the relation:

$$(3) \quad E_{x_j} = 58 \left[\log \frac{a_1 x_{j2}}{a_2 x_{j1}} + \frac{u-v}{u+v} \log \frac{x_{j1}(u+v) - x \cdot v}{x_{j2}(u-v) - x \cdot v} \right],$$

where a_1, a_2 are the total concentrations $x_j \cdot y_j$; x_{j1} and x_{j2} are concentration limits conditioned by Donnan's distribution; u and v designate the motivity of ions x_j and y_j ; x the barrier concentration of the corresponding x_j ion.

Concentration limits $x_{j1}(x_{j2})$ may be calculated with the help of the Donnan equation $a_1 \cdot a_2 = x_{j1} \cdot y_{j1}$. By substitution $a_1 = (x_{j1} - x)$ we get for $x_{j1} = \sqrt{(a_1^2 + 0.25x^2)} + 0.5x$; x_{j2} may be expressed similarly.

The mechanism of the differential uptake of diverse ions of substances of the same charge by live cells of the surrounding environment is tied up with the unbalanced state leveled at the Gibbs-Donnan equilibrium, and the number of mechanisms may be explained by the different intrusion speeds of ions of the same charge through the semipermeable barrier. Moreover, differences in the diffuse speeds of diverse ions in water may be a determinant factor.

THE DENSITY OF THE ION FLOW THROUGH THE BARRIER

Two electro-chemical parameters — *electric voltage* of the barrier and the *speed of electroosmosis* — serve to characterize the permeable properties of a barrier of high porosity. The magnitude of the electric barrier voltage may be measured, as already mentioned, by the principle of the Nernst law, by the improved Nernst-Planck law or by the Donnan-Henderson relation.

By applying the electric field to the *solution-barrier-solution system*, gradients of the electrostatic field and concentrations come into being. In such case begins the ion flow Φ_j from one environment into another, through a permeable barrier. The size of ion flow may be derived from known laws of physical chemistry.

The density of ion flow in the electrolyte under the influence of the electric field is given e.g. for cations by the relation:

$$(4) \quad \Phi_{E_{j^+}} = -\mu_{j^+} c_{j^+} \frac{dE}{dl},$$

where μ_{j^+} is the mobility of the cation, c_{j^+} the concentration of cations and dE/dl the difference of electric potential on the one and other side of the permeable barrier, falling upon a length unit of the barrier. In terms of Fick's law, the diffuse flux ions through the permeable barrier is given by the relation:

$$(5) \quad \Phi_{D_{j^+}} = -D_{j^+} \frac{dc_{j^+}}{dl},$$

where D_{j^+} is the *diffusion coefficient* depending on the permeable properties of the barrier; dc_{j^+}/dl is the change of ion concentration falling upon the length unit of barrier dl .

Provided that only the forces of the electric field and diffusion will be acting upon the ion, the overall flow of transported ions (cations in our case) through the barrier is:

$$(6) \quad \Phi_{j^+} = -D_{j^+} \frac{dc_{j^+}}{dl} - \mu_{j^+} c_{j^+} \frac{dE}{dl}.$$

Presuming that $dE/dl = -E/d$, where E is the magnitude of the electric potential difference of the barrier and d the thickness of the barrier, equation (6) assumes the form

$$(7) \quad \Phi_{j^+} = -D_{j^+} \frac{dc_{j^+}}{dl} + \mu_{j^+} c_{j^+} \frac{E}{d},$$

the solution of which is:

$$(8) \quad \Phi_{j^+} = -\frac{\mu_{j^+} E}{d} \cdot \frac{[c_{j^+}]_o - [c_{j^+}]_i \exp[-\mu_{j^+} E/D_{j^+}]}{\exp[-\mu_{j^+} E/D_{j^+}] - 1}.$$

By respecting condition $\mu_{j^+}/D_{j^+} = Fz_{j^+}/RT$ and taking into account that the charge of one mole is represented by the product Fz_{j^+} , and by introducing the *coefficient of permeability* $P_{j^+} = D_{j^+}/d$, the electric flow density of cations through the permeable barrier is given by the relation

$$(9) \quad I_{j^+} = -\frac{z_{j^+}^2 \cdot F^2 E}{RT} P_{j^+} \frac{[c_{j^+}]_o - [c_{j^+}]_i \exp[-z_{j^+} \cdot FE/RT]}{\exp[-z_{j^+} \cdot FE/RT] - 1}.$$

For anions the same relations holds, only with a converse sign. *The permeability coefficient introduced into relation (9) characterizes the permeable properties of the permeable barrier.* Its dimension amounts to $10^{-2} [\text{ms}^{-1}]$.

If the density of the electric current flowing in the electric circuit is unknown but the conditions of the experiment warrant the constancy of that current, it is suitable to characterize the permeable properties by *relative permeabilities* P_{x_j+}/P_{y_j+} .

$$(10) \quad \frac{P_{x_{j+}}}{P_{y_{j+}}} = \frac{[y_{j+}]_o - [y_{j+}]_i \exp \left[\frac{-z_{j+} \cdot FE_{y_{j+}}}{RT} \right]}{[x_{j+}]_o - [x_{j+}]_i \exp \left[\frac{-z_{j+} \cdot FE_{x_{j+}}}{RT} \right]}$$

where $P_{x_{j+}}$ is the permeability coefficient of the barrier for x_{j+} ions; $P_{y_{j+}}$ the permeability coefficient of the barrier for y_{j+} ions; $[y_{j+}]_o$ the concentration of y_{j+} ions in external environment; $[y_{j+}]_i$ the concentration of y_{j+} ions in internal environment; $[x_{j+}]_o$ the concentration of x_{j+} ions in external environment; $[x_{j+}]_i$ the concentration of x_{j+} ions in interval environment; F , R , T are already known constants. $E_{y_{j+}}$ is the electromotric voltage of y_{j+} ions; $E_{x_{j+}}$ the electromotric voltage of the corresponding x_{j+} ions on the permeable barrier.

Dependencies of electric voltage of barrier E_m on the concentration change of x_{j+} ions and y_{j+} ions in external environment, as obtained by calculation, may serve for checking the measurements. The E_m values may be calculated according to the adapted Goldman equation

$$(11) \quad E_m = - \frac{RT}{F} \ln \frac{(P_{x_j}/P_{y_j}) [x_j]_i + [y_j]_i}{(P_{x_j}/P_{y_j}) [x_j]_o + [y_j]_o}$$

By calculating E_m the way is open to calculate conductivity g_m of the permeable barrier in terms of the equation obtainable by partially differentiating the Goldman equation for ion flow I with respect to E :

$$(12) \quad g_m = - \frac{z_j^2 F^3 E_m (P_{x_j}/P_{y_j}) ([x_j]_o + [x_j]_i) + ([y_j]_o + [y_j]_i)}{(RT)^2 (P_{x_j}/P_{y_j}) ([x_j]_o - [x_j]_i) + ([y_j]_o - [y_j]_i)}$$

where $[x_j]_o$ and $[y_j]_o$ are external concentrations of x_j ions and y_j ions; $[x_j]_i$ and $[y_j]_i$ are internal concentrations of x_j and y_j ions; F is the Faraday number; E_m the electric voltage calculated according to relation (11); R is the gas constant and T absolute temperature.

By combining relations (8) up to (12) we get an equation system describing the ion and current flow as well as the permeable and conductive properties of permeable barriers (*biological and artificial membranes, walls, tissue segments etc.*).

The input quantity for studying the permeable and conductive properties of the permeable barrier is its electromotoric voltage. By applying available electrometric devices and suitable large-area Ag-AgCl electrodes or calomel electrodes, it is possible

Tab. 1.

Concentrat. gradient [mM]	E [mV]	P_{xj+} [ms ⁻¹] · 10 ⁻¹⁰	P_{yj+} [ms ⁻¹] · 10 ⁻¹⁰	P_{xj+}, P_{yj+}	g [mS] · 10 ⁸
Potassium					
10:28	-31:80	47:80	—	1:21	93:38
23:07	-52:00	57:86	—	2:93	108:19
48:65	-70:00	50:43	—	4:01	126:96
74:23	-78:00	32:31	—	3:34	139:42
99:80	-85:54	30:89	—	3:45	148:71
125:37	-92:30	34:48	—	4:05	156:10
Natrium					
17:40	-33:90	—	42:97	—	90:78
39:15	-45:20	—	16:56	—	107:89
82:65	-57:50	—	8:56	—	126:21
126:13	-63:80	—	6:21	—	139:98
169:63	-72:28	—	6:12	—	148:76
213:12	-77:03	—	5:44	—	155:99
Calcium					
9:97	-18:13	58:35	—	2:98	44:22
22:45	-28:29	138:37	—	0:15	53:26
46:40	-36:73	75:31	—	2:96	63:01
72:30	-47:33	—18:33	—	-1:45	69:89
97:30	-50:40	-19:38	—	-0:54	73:59
122:25	-53:69	-16:45	—	-0:33	77:64
Magnesium					
16:45	-16:07	—	17:39	—	72:70
37:01	-29:05	—	870:80	—	85:86
78:13	-35:73	—	24:17	—	100:40
119:25	-38:58	—	13:80	—	110:05
160:36	-44:89	—	25:95	—	117:14
201:48	-48:27	—	36:26	—	123:54

to measure, with a relatively high accuracy, the electromotoric voltage of the permeable barrier, mounted as a parting wall in the concentration element (Fig. 1).

A large number of measurements was carried out by this method on the walls of monocellular plants (*algae*), erythrocytes, nervous fibres, nervous cells and on objects composed of several cell layers (e.g. *the epidermis of the primary root, bark, cuticle, wall of the abdominal tract etc.*).

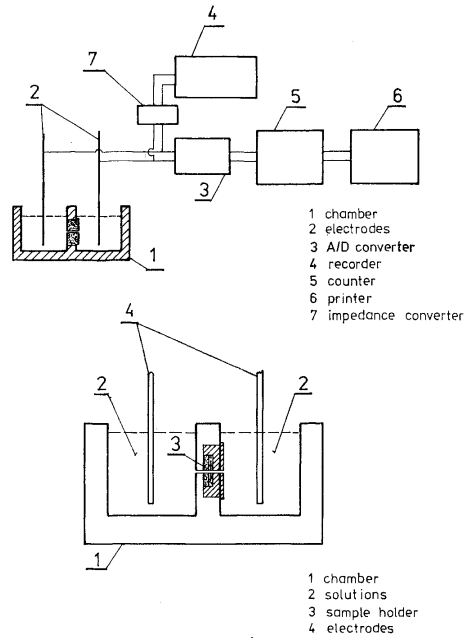


Fig. 1. Diagram of the electric registration circuit.

The measured E and I values, under diverse gradient concentrations along the walls of the permeable barrier, allow to establish, on substitution in equations (9)–(12), important physical quantities characterizing permeable, conductive and regulating properties of the investigated barriers. Important characteristics of the epidermis of the primary root of maize, an important agricultural product, were obtained in this way.

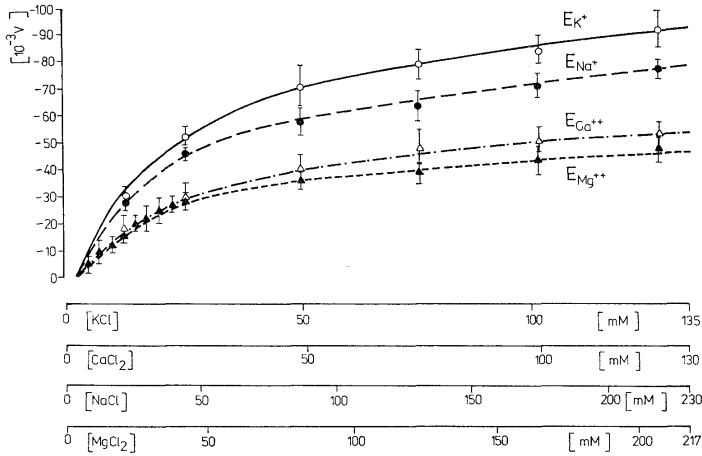


Fig. 2. Comparison of measured electromotric voltages of the epidermis of the maize primary root for K^+ , Na^+ , Ca^{++} and Mg^{++} (according to the percentage composition of the respective external solution) in dependence on the change of external concentration of KCl, NaCl, $CaCl_2$ and $MgCl_2$.

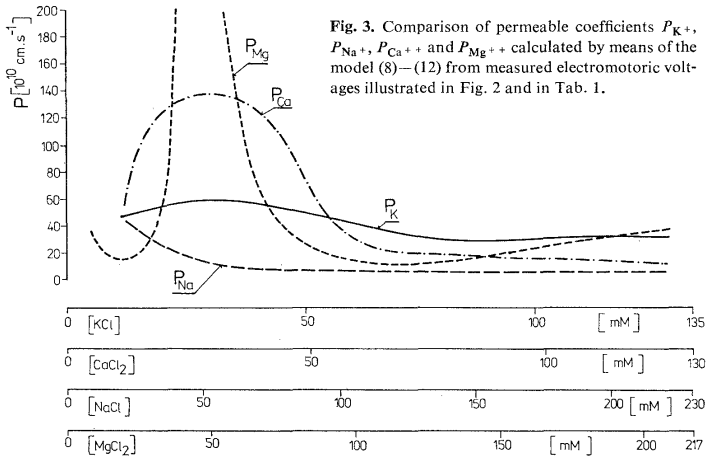


Fig. 3. Comparison of permeable coefficients P_{K^+} , P_{Na^+} , $P_{Ca^{++}}$ and $P_{Mg^{++}}$ calculated by means of the model (8)–(12) from measured electromotric voltages illustrated in Fig. 2 and in Tab. 1.

One part of the results is given on Table 1 and on the Figures 2 and 3. On Fig. 2 changes of the transepidermal potential can be seen for the cations of potassium, sodium, calcium and magnesium, in dependence on the concentration changes of the external solution washing the epidermis from the outer part. The measured values of the transepidermal potential and epidermal current allow computing the coefficients of permeability for the single ions (Fig. 3) and characterizing the permeable abilities of the root epidermis at certain concentration gradients. Moreover, it is possible to determine the conductivity of the epidermis at the given concentration gradients, by help of the equations (11) and (12). A more detailed explanation of the significance of this model can be found in former works [2], [3], [4], [5], [6], [7], [8].

The importance of this model is also underlined by the results, which can be used in applied agricultural research, when studying question of nutrition and protection of agricultural plants and animals [2], [3], [4].

(Received February 4, 1976.)

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