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THE ELECTROROTATION OF AXISYMMETRICAL CELL

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The phenomenon of electrorotation of cells with a more complicated shape than the spherical one has been theoretically investigated. The cell membrane was assumed to consist of several layers differing by their electrical characteristics while all boundaries to be cofocal ellipsoids of revolution (elongated or flattened). Even for rather strongly deformed cells the speed of rotation was shown to equal (to the accuracy of about tens of percent) that of the spherical cell of the same volume.

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A number of works [1-8] studied theoretically the movement of cells in an external alternating electric field. In study [1] an integral theory of dielectrophoresis and electrorotation has been developed for the spherically symmetrical cells with an arbitrary membrane structure.

However, most cells and vesicles may be regarded as ball-shaped only with a certain approximation. In reality, they are either stretched in one direction or are relatively thick discs. Calculation of the movement of such cells using the formula for the spherical cells may lead to noticeable errors due to an incorrect choice of their effective sizes. Furthermore, it should be taken into account that for the movement of the cells having no spherical symmetry it is much more complicated to determine the distribution of the rates of hydrodynamic fluxes in a viscous liquid surrounding them. The present study was concerned with the solution of such problems.

FORMULATION OF THE PROBLEM OF FINDING THE MOMENTS OF ELECTRIC FORCES

To calculate the electric force acting on the cell surface and describe the cell movement, in the first place it is necessary to solve the Laplace equation for potential ϕ:

$$\Delta\phi = 0. \tag{1}$$

Since the analytical solution of eq. (1) is possible only for certain types of boundary conditions, let us impose definite restrictions on the form of the cell surface by replacing the real cell form by a simpler one so that the interface may coincide with the surface coordinates in one of the orthogonal system of coordinates. In our problem it is convenient to approximate the cell surface by an ellipsoid of revolution and to use the ellipsoidal coordinates. In the stretched cells the inner and outer surfaces of the membrane are formed by cofocal elongated ellipsoids of revolution, whereas for the disc-shaped cells these are formed by flattened spheroids. As a particular case, spheroids also describe the spherically symmetrical cells.

We will consider below a detailed solution solely for the case of elongated ellipsoids. Such a problem for the flattened ellipsoids is solved in an analogous manner.

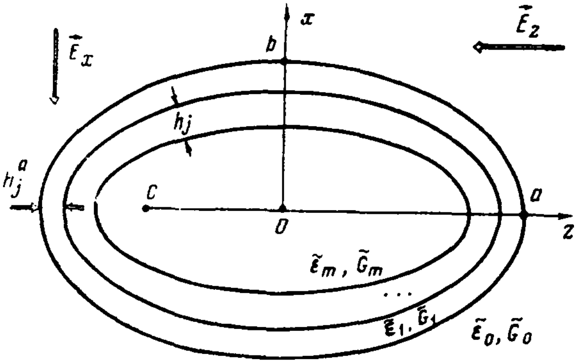

FIGURE 1. Diagram of the structure of the cellular shell and designations of geometric and electrical characteristics: a and b are the semiaxes (a > b for elongated ellipsoids); c, the half-distance between the foci; h_j, the shell thickness; $\tilde{\varepsilon}$ and $\tilde{Q}_j$, relative dielectric constant and conductivity, respectively.

Let us characterize the cell form by a ratio of two linear sizes a/b - the largest and the smallest one and by its volume $V = 4/3\pi ab^2 = 4/3\pi r_0{}^3$. The value of r_0 corresponds to a ball of the same volume. For an elongated ellipsoid of revolution a and b mean the large and small semiaxes of an ellipse

$$\frac{r^2}{b^2} + \frac{z^2}{a^2} = 1 \tag{2}$$

whose rotation around axis OZ provided the given ellipsoid, $r = (x^2 + y^2)^{1/2}$ (see Fig. 1). The extent of ellipsoid stretching may also be characterized by eccentricity

$$e = [1 - (b/a)^2]^{1/2}, \tag{3}$$

which is uniquely related to the ratio of semi-axes, and as a linear size it is more convenient to use c - the half-distance between the ellipsoid foci

$$c = \frac{r_0 e}{(1 - e^2)^{1/3}} \tag{4}$$

Transformation to the ellipsoidal coordinates is done in accordance with following formulas [9]:

$$x^2 = c^2(\sigma^2 - 1)(1 - \tau^2)\cos^2\varphi, \tag{5}$$

$$y^2 = c^2(\sigma^2 - 1)(1 - \tau^2)\sin^2\varphi, \tag{6}$$

$$z = c\sigma\tau, \tag{7}$$

where $\sigma \geq 1$, $0 \leq \tau \leq 1$. The coordinate surface σ = const is a cofocal ellipsoid of revolution; τ = const, cofocal hyperboloids; $0 \leq \varphi \leq 2\pi$, an angle in the cylindric system of coordinates r, φ, z. Since the membranes of the cells under study can have a rather complicated structure, let us use the multilayer membrane model [2]. This model assumes that the regions with invariable physical parameters are located between the cofocal ellipsoids $\sigma = \sigma_j$:

$$\sigma_m < \sigma_{m-1} < \ldots < \sigma_1.$$

An ellipsoid with coordinate σ_m corresponds to the innermost surface and and ellipsoid with $\sigma = \sigma_1$, to the outer surface, $\sigma_1 \equiv 1/e$.

While deducing the expressions for other σ_j, one should bear in mind that the distance between the surface of two cofocal ellipsoids is not constant and, in contrast to the spherical shell, changes from point to point. If as the thickness of layers we assume their values h_j^0 $(1 \leq j \leq m)$ at the 'equator' (at $z = 0$), then in the remaining points it will be calculated from the relation $h_j = h_j^0(1 - e^2\tau^2)^{1/2}$ and

$$\sigma_{j+1} = (1 - [-h_j^0/c + [(\sigma_j)^2 - 1]^{1/2})^2)^{1/2} \tag{8}$$

If we assume the effective thickness of layers to be their values h_j^a at the 'poles' (at $z = \pm a$), then we have for it the relation $h_j = h_j^a(1 - e^2\tau^2)^{1/2}/(1 - e^2)^{1/2}$, from where

$$\sigma_{j+1} = \sigma_j - h_j^a/c. \tag{9}$$

The approximation of a variable thickness of the shell ought to lead to changes in the specific membrane capacity. Since a basically capacitive current passes through the cell regions close to the poles, it is more rational to call the layer thickness the magnitude h_J^a, and, respectively, use eq. (9).

To calculate the time-dependent magnitudes appearing in the problem, it is convenient to use the complex formalism, i.e., to record the time dependence of any variable in the form

$$\mathcal{K} = \mathrm{Re}\ X, \tag{10}$$

where X is the complex value expressed as

$$X = X_0 \exp(i\omega t),$$

where w is the angular frequency; t, time; $i^2 = -1$; complex number X_0, which in a general case is the function of coordinates, is the amplitude of X [1]. Thus an electric field rotating around axis y may be written in the real part of the complex field E_{EXT}:

$$\mathbf{E}_{EXT} = (\mathbf{k}_x - i\mathbf{k}_z)E_0 \exp(i\omega t), \tag{11}$$

where E_0 is the absolute value of the amplitude of a rotating field, k_x and k are unit vectors of the axes. The field rotating around axis z is derived from (11) by substituting $z \to y$.

As known, during polarization of an ellipsoid by an external homogeneous electric field the ellipsoid acquires only a dipolar moment and multipoles of higher orders are absent [10]. As it will be shown for the case when the interface is cofocal ellipsoids, this property is preserved. General reasoning gives that the induced complex dipolar moment **d** is linearly related to the complex amplitude of external field $\mathbf{E}_0$

$$\mathbf{d} = \sum_{m=x,y,z} \chi_m(\mathbf{E}_0\mathbf{k}_m)\mathbf{k}_m \exp(i\omega t), \tag{12}$$

where χ_m is the complex polarizability along the relevant axis ($\chi = \chi_Y$). The moment of forces N created by the electric field is calculated by the formula N = [Re d, Re $\mathbf{E}_{ext}$]. For field $\mathbf{E}_{EXT}$ revolving around the symmetry axis of an ellipsoid, the moment is time-independent and is expressed as [1]

$$\mathbf{N} = -\mathrm{Im}\ \chi_x E_0^2 \mathbf{k}_z, \tag{13}$$

and the time-averaged value of the moment induced by the electric field rotating around axis y:

$$\mathbf{N} = -\mathrm{Im}\ \frac{\chi_x + \chi_z}{2} E_0^2 \mathbf{k}_y. \tag{14}$$

Thus, to find the induced electric field it is sufficient to calculate two complex magnitudes χ_x and χ_z.

CALCULATION OF THE COMPLEX POLARIZABILITY

In the stretched ellipsoidal coordinates eq. (1) is written in the following form [9]:

$$\frac{\partial}{\partial\sigma}\left[(\sigma^2 - 1)\frac{\partial\phi}{\partial\sigma}\right] + \frac{\partial}{\partial\tau}\left[(1 - \tau^2)\frac{\partial\phi}{\partial\tau}\right] + \frac{\sigma^2 - \tau^2}{(\sigma^2 - 1)(1 - \tau^2)}\frac{\partial^2\phi}{\partial\varphi^2} = 0 \tag{15}$$

At the boundaries of the neighbouring regions the conditions of continuity of potential and complex current density, which express the law of charge conservation [5], are written as follows:

$$\phi_{j=1}\Big|_{\sigma=\sigma_j} = \phi_j\Big|_{\sigma=\sigma_j}, \tag{16}$$

$$\varepsilon_{j-1}\frac{\partial\phi_{j-1}}{\partial\sigma}\Big|_{\sigma=\sigma_j} = \varepsilon_j\frac{\partial\phi_j}{\partial\sigma}\Big|_{\sigma=\sigma_j}^{j=1,\dots,m} \tag{17}$$

Here, the complex dielectric constant is introduced

$$\varepsilon_j = \varepsilon_0\bar{\varepsilon}_j - iG_j/\omega \qquad j = 0,\dots, \tag{18}$$

where ε_J and C_J are the specific dielectric constant and conductivity of layers, respectively; ε_0 is the electric constant. While writing conditions (17) we used the orthogonality of ellipsoidal coordinates which enabled us to replace the normal derivative to the surface $\sigma = \sigma_J$ by the σ derivative.

The boundary conditions for this system of equations look as a condition of potential limitedness inside the cell, and an asymptotically homogeneous field at large distances from the cell:

$$\phi_1 \longrightarrow E_0 x \quad \text{at } x \longrightarrow \infty \tag{19}$$

– to calculate complex magnitude χ :

$$\phi_1 \longrightarrow E_0 z \quad \text{at } z \longrightarrow \infty \tag{20}$$

– to calculate complex magnitude χ (the electric field is implied to be couterdirectional to the respective axis).

In the case when the field is directed along the symmetry axis of the ellipsoid, the potential is evidently independent of variable φ: $\partial\phi/\partial\varphi = 0$, and the general solution of eq. (15) should be sought in the form

$$\phi_j = E_0 c\tau[A_j P(\sigma + B_J Q(\sigma)], \tag{21}$$

where P and Q are the first Legendre functions of the first and second type, respectively:

$$P(\sigma) = \sigma, \qquad Q(\sigma) = \frac{\sigma}{2} \ln \frac{\sigma + 1}{\sigma - 1}, \tag{22}$$

$A_{J'}$ B_J are the arbitrary constants. From the condition of limitedness (20) one can directly find two constants included in condition (21):

$$A_1 = 1, \qquad B_m = 0, \tag{23}$$

whereas for the other constants recurrent relations are obtained from conditions (16) and (17):

$$A_{j-1} = \frac{[A_j P(\sigma_j) + B_j Q(\sigma_j)]Q'(\sigma_j) - (\varepsilon_{j-1})\varepsilon_j^{-1}[A_j P'(\sigma_j) + B_j Q'(\sigma_j)]Q(\sigma_j)}{P(\sigma_j)Q'(\sigma_j) - P'(\sigma_j)Q(\sigma_j)} \tag{24}$$

$$B_{j-1} = [A_j - A_{j-1}]\frac{P(\sigma_j)}{Q(\sigma_j)} + B_j , \tag{25}$$

where the prim designates the derivative of the corresponding function.

From eqs. (23)-(25) one can easily find all coefficients $A_{J'}$ B_J using the method following from the proportionality of all $A_{J'}$ B_J $(j < m)$ to coefficient A_m. Assuming conditionally that $A_m^1 = 1$, it is possible to find all coefficients A_j^1, B_j^1 from (24) and (25). The superscript «1» means that all coefficients are calculated at $A_m = 1$. Naturally, in this case A_0^1 differs from unity, therefore, the real values of coefficients are smaller than the calculated ones A_0^1 times:

$$A_j = A_j^1/A_0^1, \quad B_j = B_j^1/A_0^1 \tag{26}$$

Let us consider now the expression for ϕ_0 in more detail. The first term proportional to $P(\sigma)$ increases with increasing σ and is exactly equal to the right part of (20). The second term corresponds to the dipolar member and at sufficiently large $\rho = (x^2 + y^2 + z^2)^{1/2} \gg 1$ may be presented as follows:

$$E_0 c\tau B_0 Q(\sigma) \approx -\frac{\chi_z E_0 \cos\theta}{4\pi\varepsilon_1\varepsilon_0\rho^2} , \tag{27}$$

where θ is the angle between the radius–vector of a point and axis z. Considering the type of asymptotic decomposition for function $Q(\sigma)$ [12] and eqs. (5)-(7) we obtain:

$$\chi_z = -B_0[\frac{4}{3}\pi\varepsilon_1\varepsilon_0 c^3]. \tag{28}$$

The magnitude $-B_0$ in eq. (28) may be regarded as a dimensionless value of polarizability along axis z.

While calculating values of complex polarizability χ_x along axis x, one should take into account that potential ϕ is a function of all spatial variables: σ, r, φ. Therefore, when one uses condition *(19)* instead of boundary condition (20),the solution of equation (15) may be sought in the form:

$$\phi_j = E_0 c(1 - \tau^2)^{1/2}[a_j p(\sigma) + b_j q(\sigma)] \cos\varphi, \quad j = 0,\ldots,m, \tag{29}$$

where a_j, b_j are the arbitrary constants, $p(\sigma)$ and $q(\sigma)$ are the joint Legendre functions of the first and second type (with the subscripts and superscripts equal to unity [11]):

$$p(\sigma) = (\sigma^2 - 1)^{1/2}, \qquad q(\sigma) = (\sigma^2 - 1)^{1/2}\left(\frac{1}{2}\ln\frac{\sigma+1}{\sigma-1} - \frac{\sigma}{\sigma^2 - 1}\right). \tag{30}$$

Further solution steps are performed similarly. The expressions for coefficients a_j, b_j are obtained from eqs, (24), (25) by substituting the joint functions for the Legendre functions. Considering the asymptotics $q(\sigma)$ at high σ values [11], one can write the expression for polarization along axis x for the case of a cell stretched along axis z.

$$\chi_x = 2b_0[\tfrac{4}{3}\pi\varepsilon_1\varepsilon_0 c^3]. \tag{31}$$

Thus, we have calculated the values of complex polarizability χ_x and χ_z included in expressions (13), (14) for the moments of forces acting upon the cell.

In the case of disc-shaped cells (flattened ellipsoids of revolution, a < b) a number of changes may be brought into the above formulas:

$$e = [(b/a)^2 - 1]^{1/2} \tag{3'}$$

$$c = \frac{r_0 e}{(1 + e^2)^{1/3}} \tag{4'}$$

$$x^2 = c^2(\sigma^2 + 1)(1 - \tau^2)\cos^2\varphi\ , \tag{5'}$$

$$y^2 = c^2(\sigma^2 + 1)(1 - \tau^2)\sin^2\varphi \tag{6'}$$

The Laplace equation (1) in the flattened ellipsoidal system of coordinates is written as follows:

$$\frac{\partial}{\partial\sigma}\left[(\sigma^2 + 1)\frac{\partial\phi}{\partial\sigma}\right] + \frac{\partial}{\partial\tau}\left[(1 - \tau^2)\frac{\partial\phi}{\partial\tau}\right] + \frac{\sigma^2 + \tau^2}{(\sigma^2 + 1)(1 - \tau^2)}\frac{\partial^2\phi}{\partial\varphi^2} = 0 \tag{15'}$$

Its solution may always be sought in the form of (21) and (29) for the fields of respective orientations; however, instead of Legendre functions $P(\sigma)$ and $p(\sigma)$ one should use the corresponding functions of a purely imaginary argument $i\sigma$ divided by i, whereas functions $Q(\sigma)$ and $q(\sigma)$ should be replaced by $Q(i\sigma)$ and $q(i\sigma)$:

$$P(\sigma) = \sigma, \qquad Q(\sigma) = \sigma \operatorname{arctg} \sigma - 1, \tag{22'}$$

$$p(\sigma) = (\sigma^2 + 1)^{1/2}, \qquad q(\sigma) = (\sigma^2 + 1)^{1/2}(\operatorname{arctg} \sigma - \frac{\sigma}{\sigma^2 + 1}). \tag{30'}$$

All other formulas remain unchanged.

Thus, at the orientation of the cell symmetry axis along the axis of electric field rotation or normally to this axis we have found the rotatory moment of electrical forces acting on the cell.

Note that when the axis of cell symmetry forms with the rotation axis an angle ψ: $0 < \psi < \pi/2$, the dipolar moment of the cell will not lie in the plane of electric field rotation which, after some time, will inevitably lead after some time to a turn of dipolar moment and, consequently, of the cell itself [12].

THE FORCE OF VISCOUS FRICTION ACTING ON A ROTATING AXISYMMETRIC CELL

In works [13,14] an expression was deduced for the moment N of friction forces acting on the surface of an elongated ellipsoid rotating around its axis:

$$N = \frac{16\pi}{3} \eta\Omega c^3 \frac{1}{Q'(1/e)}, \tag{32}$$

where η is the viscosity of a liquid, Ω is the angular velocity of rotation. Using (4) one can express the angular velocity from (32):

$$\Omega = \frac{N}{8\pi\eta(r_0)^3} \{\frac{3(1 - e^2)Q'(1/e)}{2e^3}\}. \tag{33}$$

The expression in the braces is independent of characteristic size r_0 but is determined solely by the cell eccentricity e. If the cell form is close to the spherical one ($e \longrightarrow 0$), the expression enclosed in the braces tends to 1 and formula (33) is transformed into a simple relation for the sphere [15].

For the flattened ellipsoids of revolution it is also possible to use (32) in which ***e***, c and functions $Q(\sigma)$ should be determined by formulas (3'), (4') and (22'), respectively.

Hence, having found the total moment of electric field forces acting on the cell from the formulas of the section **Calculation of the Complex Polarizability,** using eq. (33) one can calculate the angular velocity of its rotation. Let us emphasize that within the framework of the above suggestions about the cell form these formulas give evident analytical relations.

DISCUSSION

Figure 2 shows the dependence of dimensionless rate of cell rotation Ω on the logarithm of frequency of external electric field rotation *w* for various ratios *a/b*. In the first place it should be noted that in fact the rotation rate is rather weakly dependent on the cell form. Variation of ***a/b*** ratio from 1 to 8 leads to the change in the rotation rate by no more than tens of percent. Note that this result is not trivial because at such an elongation of the ellipsoid its polarization in the direction normal to the symmetry axis decreases several times and, consequently, the moment of electrical forces also decreases. However, the viscous friction diminishes too which results in an unchanged rate of cell rotation.

Let us discuss now the dependences $\Omega(\omega)$ for the monolayer membrane. (Multilayer membranes have a more complicated form of $\Omega(\omega)$ which will be discussed against the background of experimental results in subsequent papers). At sufficiently low frequencies *w* electric current does not cross the dielectric shell of the cell but symmetrically passes round it. Therefore, no electrical moments arise in the system. Coming nearer to the frequency of the first peak *w*, the capacitive current

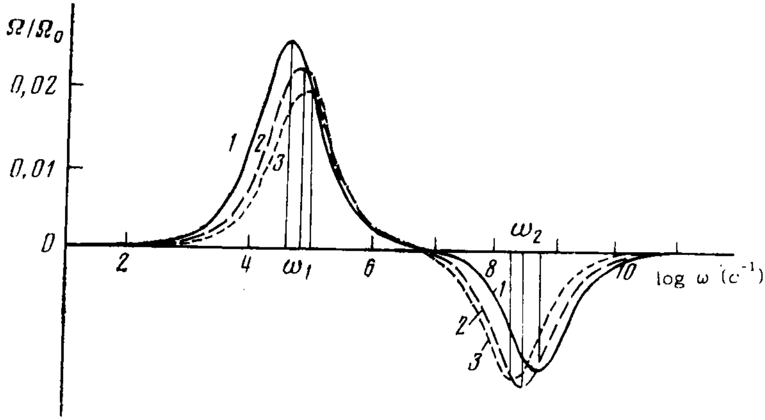

FIGURE 2. Dependence of dimensionless rate of cell rotation on frequency of external electric field. The ratio of cell shell thickness to cell size $h^a/r = 10^{-4}$, specific conductivities of the shell, the medium inside and outside the cell are 10^{-12}, 1 and 10^{-4} S/m, respectively; relative dielectric constant of the the shell $\tilde{\varepsilon} = 2$. $a/b = 1$ *(1)*, 4 *(2)* and 8 *(3)*.

across membrane increases which leads to the appearance of a substantial imaginary part in complex polarizability χ. Thus, the position of the first peak is basically determined by the capacity of the cell membrane. Therefore, the shift of the peak, corresponding to ω_1, towards higher frequencies is not strictly substantiated, since in the solution of our problem the specific membrane capacitance was not assumed to be a strictly constant magnitude.

More interesting is the shift of ω_2 corresponding to the second (negative) peak. In the course of the development of the theory of electrorotation for the ball-shaped cells 11 ω_2 was estimated as follows:

$$\omega_2 \sim \frac{\sigma_2}{\varepsilon_0 \tilde{\varepsilon}_2}, \tag{34}$$

i.e., it was suggested that the real and imaginary parts of the complex dielectric constant of the medium inside the cell are approximately equal to each other. Since $\tilde{\varepsilon}_2$ is little different from the dielectric constant of water, formula (34) makes it possible to estimate the conductivity inside the cell. However, as seen in Fig. 2, the position of

ω_2 is dependent on the cell form. This does not disprove estimate (34) because the dimensionless form factor can be contained in the right part of (34). Interestingly, the peak of curve 2 goes down lower than the peaks of curve *1* and **3** which is indicative of a nonmonotonous character of the curve expressing the dependence of $(\Omega(\omega)_2)$ on a/b ratio.

In conclusion it is noteworthy that the relations for polarizability χ of elongated and flattened cells may also be used to describe electrophoretic phenomena in an alternating electric field [l1, 12].

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