RESPONSE OF NONSPHERICAL BIOLOGICAL PARTICLES TO ALTERNATING ELECTRIC FIELDS

M. SAITO, H. P. SCHWAN, *and* G. SCHWARZ

From the Department of Biomedical Engineering, The Moore School, University of Pennsylvania, Philadelphia

ABSTRACT The stable orientation evoked by an alternating electric field is discussed for biological particles of arbitrary shapes and compositions. Ellipsoidal particles with and without shells are treated as special cases. It is shown that as the frequency of the electric field changes there may be sudden jumps in the stable direction as well as gradual changes.

INTRODUCTION

The phenomenon called pearl chain formation (1), the lining up of particles in suspension along the direction of the impressed electric field, is one of the nonthermal effects of electric fields that have attracted the attention of investigators in biophysical science. Some quantitative investigations on this phenomenon are given elsewhere (2). While this phenomenon can occur in a suspension of spherical particles, little has been known about other nonthermal phenomena which are inherent to the nonspherical shape of the particles.

A phenomenon pointed out first by Heller (3) and confirmed by others (4–6) belongs to the latter category. It was observed that, under an electric field, living cells such as bacteria or protozoa may move in a particular direction in relation to that of the field. A possible explanation for this phenomenon is that, since such a dielectric particle has a most stable orientation in relation to the field, the living particles are forced to move in the direction thus determined.

This paper attempts to explain this orientation phenomenon simply as a result of the electrostatic forces acting on nonspherical particles of dielectric properties different from those of the suspending material. A number of examples are presented. A general investigation of the orientation effect from a theoretical point of view can be found elsewhere (7).

ELECTRICAL PROPERTIES OF LIVING MATERIALS

Dielectric properties of the living tissues and cell suspensions change with the frequency as illustrated in Fig. 1. There are three remarkable changes, termed α-, β-, and γ-dispersions, in the range of our interest. Conductivities also show changes corresponding to these three dispersions, the conductivity increasing with increasing frequency. The absolute values of conductivity depend on the material, but are usually of the order of 10 mmho/cm for soft tissues at the frequencies below the γ-dispersion region.

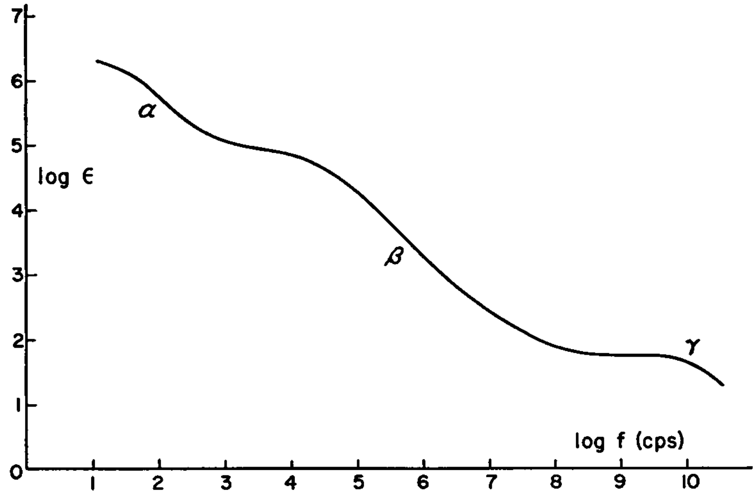

FIGURE 1 Dielectric constant of biological substances. The illustrated case pertains to tissues.

These electrical properties are the direct result of the structural form and composition of the biological material. The sizes of the particles constituting the bulk of the material are usually of the order of 1 to 10 μ, although the calculations in this paper apply also to particles of larger sizes. The shapes of the particles are different for different cases, some being nearly spherical and some nearly ellipsoidal.

Another remarkable property of these biological particles is their shell, composed of lipid and proteins. The capacitance and the conductance across the membrane of this shell are near 1 $\mu f/cm^2$ and very roughly 10 $mmho/cm^2$ respectively, and the thickness of the membrane is considered to be of the order of 100 A. The β-dispersion, which plays a role in determining the stable directions of the particles as will be shown in later sections, is due to the presence of this membrane. But at higher frequencies the membrane capacitance effectively short-circuits the membrane, and the particle behaves as though it is a particle of a uniform dielectric constant and conductivity, as a first approximation.

For the details of these properties of living materials, refer to Schwan (8, 9).

THE STATIC STABILITY IN GENERAL

A brief review of the general theory, given elsewhere (7), will be presented first. The model to be considered is a rigid particle of arbitrary shape and composition imbedded in a uniform fluid medium. The complex dielectric constants of the particles and the medium are ϵ^* and ϵ_0^* respectively; ϵ^* may be a function of position in the particle, while ϵ_0^* is a constant. A uniform AC field of field strength E is impressed on the model, and forces other than the electrostatic ones are neglected. Moreover, in the following several sections only the static stability is considered; that is, mechanical vibrations are assumed not to be excited to an extent that may influence the conclusions.

Let a rectangular coordinate axis be fixed to the particle. The direction of the impressed field is indicated by a unit vector $\mathbf{n}$:

$$\mathbf{E} = E\mathbf{n} \tag{1}$$

The field $\mathbf{F}$ at any point inside of the particle is, from the linear property of the material,

$$\mathbf{F} = A\mathbf{E} \tag{2}$$

where A is a 3×3 tensor which is a function of the shape and the size of the particle, the dielectric properties inside and outside the particle, and the position of the point being considered.

The time mean of the potential energy $\overline{\mathbf{W}}$ stored inside and outside of the particle is given by Schwarz (10) as:

$$\overline{\mathbf{W}} = \tfrac{1}{2}\ \mathrm{Re}\left\{\int_{V_B} \tilde{\epsilon}_0{}^*\left(1 - \frac{\epsilon^*}{\epsilon_0{}^*}\right)\mathbf{F}\cdot\mathbf{E}\ dV\right\} \tag{3}$$

(where $\sim$ indicates the complex conjugate, $\mathbf{E}$ is taken as real, and V_B denotes the volume of the particle). Using relation (2), this expression can be rewritten as

$$\overline{\mathbf{W}} = \tfrac{1}{2}E^2[(B\mathbf{n})\cdot\mathbf{n}] \tag{4}$$

where

$$B = Re\left\{\int_{V_B} \tilde{\epsilon}_0{}^*\left(1 - \frac{\epsilon^*}{\epsilon_0{}^*}\right)A\ dV\right\} \tag{5}$$

(in the sense that

$$B_{ij} = Re\left\{\int_{V_B} \tilde{\epsilon}_0{}^*\left(1 - \frac{\epsilon^*}{\epsilon_0{}^*}\right)A_{ij}\ dV\right\}\Bigg).$$

Equation (4) shows that the potential energy can be expressed by a quadratic form of the components of the unit vector representing the direction of the field.

Using a theorem in linear algebra, the symmetric part of B can be diagonalized by a rotation of the coordinate system:

$$\mathbf{n} = C\mathbf{n}' \tag{6}$$

and B_s, the symmetric part of B, is transformed into:

$$C^{-1}B_sC = \text{Diag. }(\lambda_1, \lambda_2, \lambda_3) \tag{7}$$

or,

$$\overline{\mathbf{W}} = \tfrac{1}{2}E^2(\lambda_1 n_1'^2 + \lambda_2 n_2'^2 + \lambda_3 n_3'^2) \tag{8}$$

This last expression shows that $\overline{\mathbf{W}}$ can be represented by an ellipsoid as shown in Fig. 2. The potential energy is stationary, (i.e. $\delta\overline{\mathbf{W}} = 0$ upon rotating the particle by

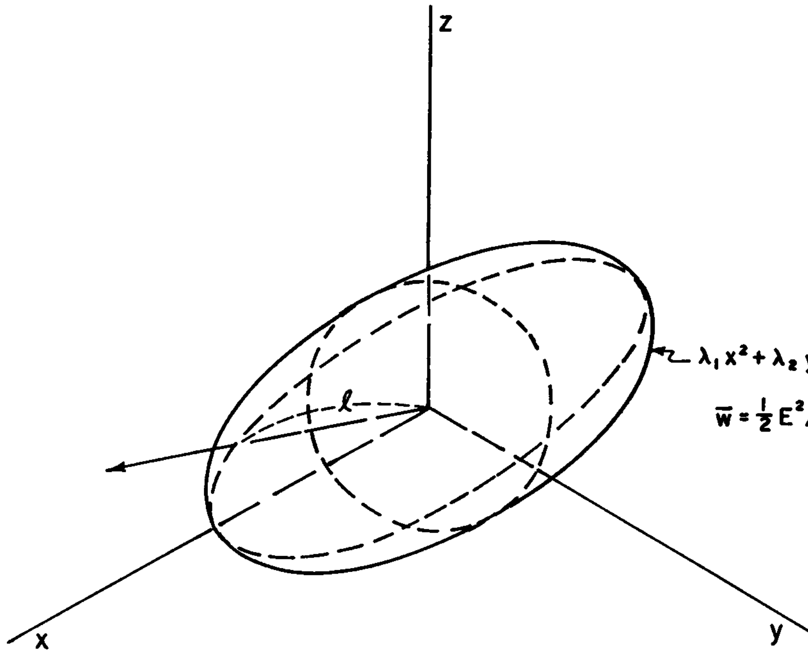

FIGURE 2 An ellipsoid representing the potential energy.

a small angle) when $n_i' = 1$, $n_j' = 0 (j \neq i = 1, 2, 3)$, corresponding to three directions, which Fig. 2 shows to be mutually orthogonal. The stable direction is determined by the minimum of these λ_i's. It does not depend on the actual orientation of the body.

The behavior of the particle in general under the influence of a uniform impressed electric field can easily be concluded from these considerations: (*a*) There are three directions of stationary potential energy which are mutually orthogonal (except degenerate cases). (*b*) Of these three directions, one is stable and the other two are unstable (except degenerate cases). (*c*) These three directions are in general functions of the frequency of the impressed field. When the frequency of the impressed field changes continuously, the stable direction may change continuously. Moreover, there might occur a sudden jump of 90° in the direction of the stable equilibrium. (The latter phenomenon will be called a "turnover.")

An ellipsoid with or without a shell is a good approximation for many biological particles. An ellipsoid with uniform dielectric properties is considered in this section, while an ellipsoid with a shell will be considered in a later section.

The considerations in the preceding section reveal that it is necessary only to calculate A, B, and the λ_i's. From the symmetry of the ellipsoid, it is obvious that the coordinate axes which give a diagonal form to B_s coincide for all frequencies, with the principal axes of the ellipsoid. In that case, the field distribution inside of the particle can be calculated to show that (7)

$$\lambda_i = \tfrac{4}{3}\pi abc \cdot Re \left\{ \bar{\epsilon}_0^* \left(1 - \frac{\epsilon^*}{\epsilon_0^*}\right) \frac{1}{1 + L_i \dfrac{\epsilon^* - \epsilon_0^*}{\epsilon_0^*}} \right\} \tag{9}$$

where

$$L_1 = \frac{abc}{2} \int_0^\infty \frac{ds}{(s + a^2)\, R(s)} \tag{10}$$

$$L_2 = \frac{abc}{2} \int_0^\infty \frac{ds}{(s + b^2) R(s)} \tag{11}$$

$$L_3 = \frac{abc}{2} \int_0^\infty \frac{ds}{(s + c^2) R(s)} \tag{12}$$

$$R(s) = \{(s + a^2)(s + b^2)(s + c^2)\}^{1/2} \tag{13}$$

and a, b, and c are half of the lengths of the principal axes of the ellipsoid. In the following it is assumed, without losing generality, that $a \geq b \geq c$ which leads to:

$$L_1 \leq L_2 \leq L_3 \tag{14}$$

With the following expressions for the complex dielectric constants

$$\epsilon_0^* = \epsilon_0 + \frac{\kappa_0}{i\omega} \tag{15}$$

$$\epsilon^* = \epsilon + \frac{\kappa}{i\omega} \tag{16}$$

the dimensionless quantity

$$u_i = \lambda_i / (\tfrac{4}{3}\pi abc \cdot \epsilon_0) \tag{17}$$

will be used as a measure of the energy of the ellipsoid when oriented along one of the axes. Using partial fraction expansion, u_i can be rewritten as

$$u_i = A_i + \frac{B_i}{k_i^2 + e_i^2 \omega^2} \tag{18}$$

where

$$A_i = \frac{\epsilon_0 - \epsilon}{\epsilon_0 - (\epsilon_0 - \epsilon) L_i} \tag{19}$$

$$B_i = \frac{\kappa_0\epsilon - \kappa\epsilon_0}{\epsilon_0\{\epsilon_0 - (\epsilon_0 - \epsilon)L_i\}}\{2\kappa_0\epsilon_0(1 - L_i) + (\kappa_0\epsilon + \kappa\epsilon_0)L_i\} \tag{20}$$

$$k_i = \kappa_0 - (\kappa_0 - \kappa)L_i \tag{21}$$

$$e_i = \epsilon_0 - (\epsilon_0 - \epsilon)L_i \tag{22}$$

In other words, the behavior of the u_i with changing frequency is characterized by a single time constant. The u-values at zero and infinite frequencies are given by:

$$u_i(0) = \frac{\kappa_0(\kappa_0\epsilon - \kappa\epsilon_0) + \epsilon_0\kappa_0(\kappa_0 - \kappa) - \epsilon_0(\kappa_0 - \kappa)^2 L_i}{\epsilon_0 k_i^2} \tag{23}$$

and

$$u_i(\infty) = \frac{\epsilon_0 - \epsilon}{\epsilon_0 - (\epsilon_0 - \epsilon)L_i} \tag{24}$$

The transition between these two values occurs in the range around the dispersion which is given by:

$$\omega_i = \frac{k_i}{e_i} \tag{25}$$

The behavior of u_i with the change in frequency is shown in Fig. 3. As can be easily seen we have in general

$$u_1(\infty) < u_2(\infty) < u_3(\infty) \tag{26}$$

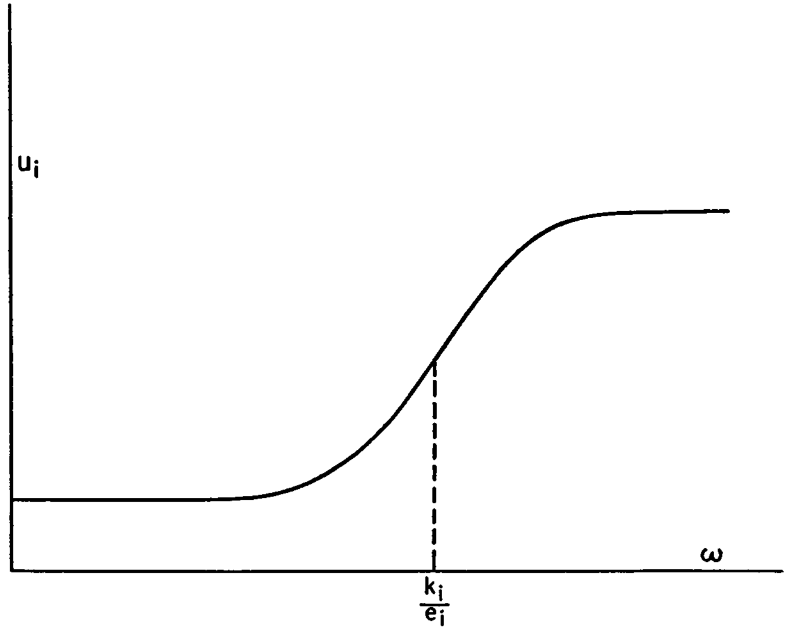

FIGURE 3 Behavior of potential energy in u_i.

In other words, the stable position of equilibrium at sufficiently high frequencies is always with the longest axis along the direction of the impressed field. On the other hand, for the values of u_i, and consequently for the stable position of equilibrium at lower frequencies, there does not exist such a simple formula as formula (26), and these values have to be computed and compared numerically.

The transition of the stable direction from one direction to another occurs at the intersecting point of the curve representing the minimum of one u_i with that of another u_i. Let us now consider the curves for u_1 and u_2 as an example. Since the equation which determines the intersection point of the curves for u_1 and u_2 is of second degree, and since $u_1(\infty) < u_2(\infty)$, it can be shown in general that the number of the intersecting points is (Fig. 4)

$$1, \text{ if } \quad u_1(0) > u_2(0) \quad \text{and; } 2 \quad \text{or} \quad 0, \text{ if } \quad u_1(0) < u_2(0)$$

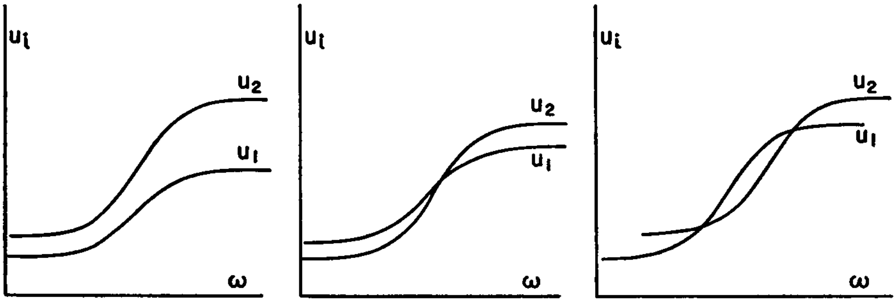

FIGURE 4 Curves representing u_i's.

The alternatives in the latter case are rather difficult to discriminate in general, though it is easy to do so by numerical computations. Many sufficient conditions for the existence of turnover frequencies can easily de derived from these considerations but will not be mentioned further in this paper.

Example 1–An Ellipsoid with a Uniform Composition.

The parameters L_i are given by (11):

$$L_1 = \frac{bc}{a^2k^2e^3}(F - E) \tag{27}$$

$$L_2 = \frac{bc}{a^2k^2h^2e^3}\left(E - h^2F - k^2\frac{\sin\varphi\cos\varphi}{\sqrt{1 - k^2\sin^2\varphi}}\right) \tag{28}$$

$$L_3 = \frac{bc}{a^2h^2e^3}(\tan\varphi\sqrt{1 - k^2\sin^2\varphi} - E) \tag{29}$$

where

$$\sin\varphi = e = \sqrt{1 - (c^2/a^2)} \tag{30}$$

$$k = \sqrt{1 - (b/a)^2} / \sqrt{1 - (c/a)^2} \quad (31)$$

$$h = \sqrt{1 - k^2} \quad (32)$$

and where

$$F = F(\varphi, k) \quad (33)$$

$$E = E(\varphi, k) \quad (34)$$

are the elliptic integrals of the first and the second kind.

Let the axial ratio be

$$a : b : c = 4 : 2 : 1$$

For this example, the L_i are calculated to be:

$$L_1 = 0.113$$

$$L_2 = 0.285$$

$$L_3 = 0.602$$

Case 1. The electrical properties of the media are assumed as:

$$\kappa = 5 \text{ m mho/cm} \qquad \epsilon = 60\epsilon r$$

$$\kappa_0 = 2.5 \text{ m mho/cm} \quad \epsilon_0 = 75\epsilon r$$

$$(\epsilon r = 8.85 \times 10^{-14} \text{ farad/cm})$$

These data (and those of case 2) are quite typical for many biological cells and their suspending medium at frequencies between 30 and 100 mc (8, 9). The result of the calculations for the change of the u_i with the change in frequency is shown in Fig. 5, with the result that turnovers occur at the frequencies of 80, 90, and

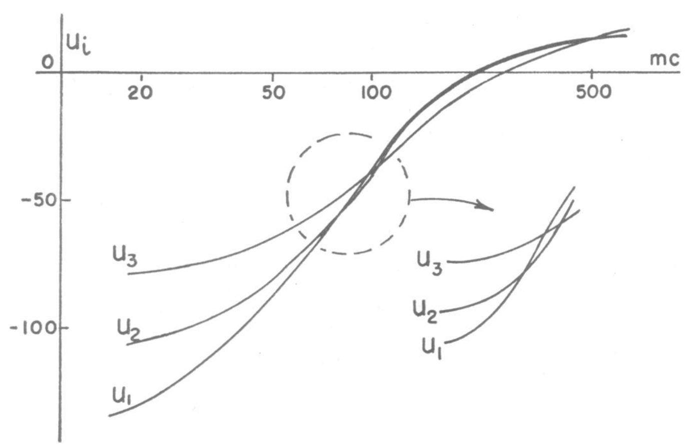

FIGURE 5 Stable direction of ellipsoid (case 1).

500 mc. The direction of the stable equilibrium changes as follows:

$$a \rightarrow b \rightarrow c \rightarrow a$$

Case 2. The electrical properties of the media are assumed as:

$$\kappa = 5 \text{ m mho/cm} \qquad \epsilon = 60\epsilon r$$
$$\kappa_0 = 10 \text{ m mho/cm} \qquad \epsilon_0 = 50\epsilon r$$

The result is shown in Fig. 6, with the turnovers occurring at 190, 850, and 910 mc in the order of

$$a \rightarrow c \rightarrow b \rightarrow a$$

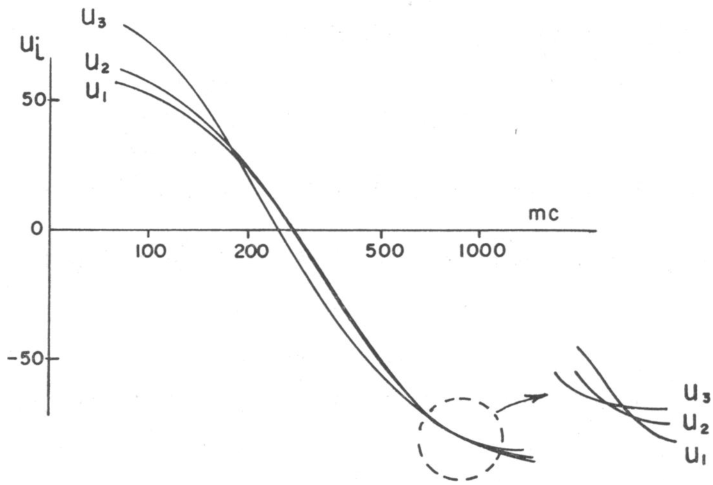

FIGURE 6 Stable direction of ellipsoid (case 2).

Case 3. As an example of a more definite occurrence of the turnovers, where the order of u_i are different for zero and infinite frequencies, the electrical properties are assumed as:

$$\kappa = 10 \text{ m mho/cm} \qquad \epsilon = 60\epsilon r$$
$$\kappa_0 = 9 \text{ m mho/cm} \qquad \epsilon_0 = 30\epsilon r$$

The result is shown in Fig. 7, turnovers occurring at 450 and 520 mc in the order of

$$c \rightarrow b \rightarrow a$$

Example 2–A Prolate Spheroid with a Uniform Composition

For a prolate spheroid ($a > b = c$), the parameters L_i are given by

$$L_1 = \frac{b^2}{2a^2e^3}\left(-2e + \ln\frac{1+e}{1-e}\right) \tag{35}$$

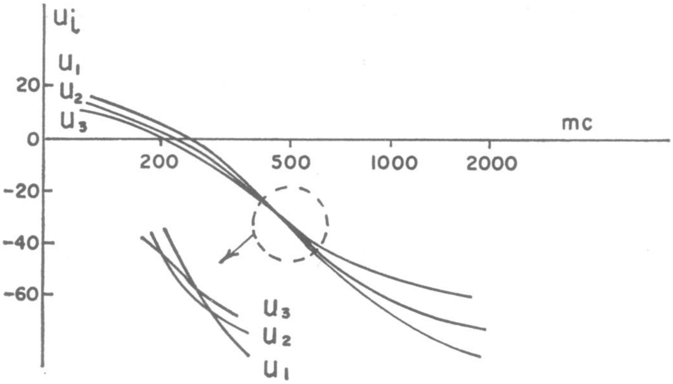

FIGURE 7 Stable direction of ellipsoid (case 3).

$$L_2 = L_3 = \frac{b^2}{2a^2e^3}\left(\frac{e}{1 - e^2} - \frac{1}{2}\ln\frac{1 + e}{1 - e}\right) \tag{36}$$

where e is given by equation (30). In the following cases $e = 0.8$ is assumed; i.e., $c/a = 0.6$.

Case 1. The electrical properties of the media are assumed as:

$$\kappa = 5 \text{ m mho/cm} \quad \epsilon = 60\epsilon r$$

$$\kappa_0 = 0 - 10 \text{ m mho/cm} \quad \epsilon_0 = 75\epsilon r$$

The turnover frequencies are calculated with κ_0 as the variable. The result is shown in Fig. 8, with the direction of the stable equilibrium shown in the diagram.

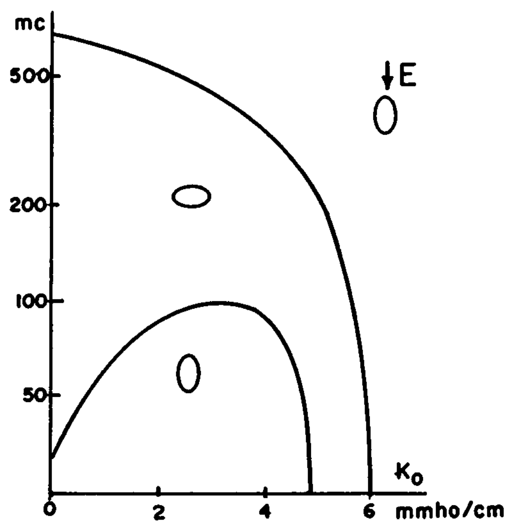

FIGURE 8 Stable direction of spheroid (case 1).

Case 2. The electrical properties of the media are assumed as:

$$\kappa = 5 \text{ m mho/cm} \quad \epsilon = 60\epsilon r$$

$$\kappa_0 = 0 - 10 \text{ m mho/cm} \quad \epsilon_0 = 50\epsilon r$$

The turnover frequencies are calculated with κ_0 as the variable. The result is shown in Fig. 9, with the direction of the stable equilibrium shown in the diagram. Both of these calculations reveal that the situation is fairly complicated, particularly since only a minor change in ϵ_0 results in completely different data.

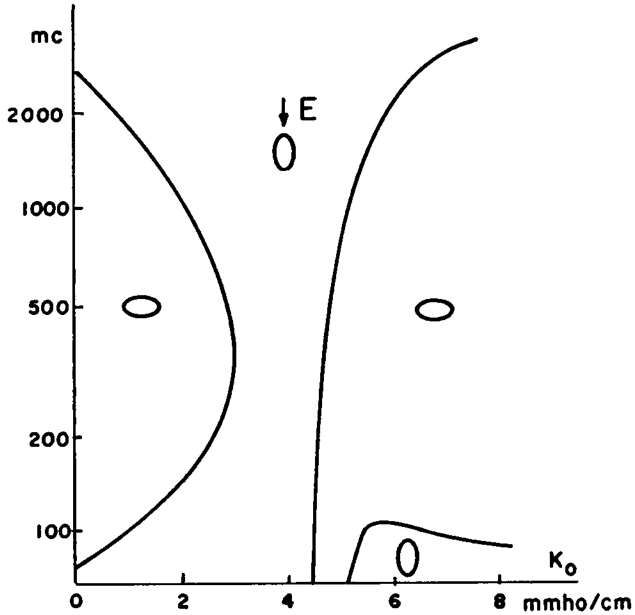

FIGURE 9 Stable direction of spheroid (case 2).

STABLE DIRECTION OF AN ELLIPSOID WITH A SHELL

The ellipsoidal particle with a shell is of a particular biological interest. An interesting relationship derived by Shen can be used in the computation of the stable direction of an ellipsoid under the influence of an electric field (12).

When a uniform electric field is impressed, the field distributions outside the two ellipsoids shown in Fig. 10 are the same if the following conditions are fulfilled: (*a*) The two ellipsoidal surfaces in Fig. 10*a* are confocal. (*b*) The outer surface of the ellipsoid of Fig. 10*a* is congruent with the homogeneous ellipsoid of Fig. 10*b*. (*c*) The external media for the two cases are identical homogeneous, isotropic materials. (*d*) The complex dielectric constant of the ellipsoid in Fig. 10*b*, ϵ_a^* is related to the properties of the shell-covered ellipsoid in the following way (9):

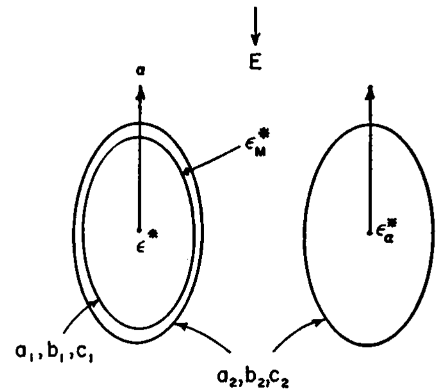

FIGURE 10 Ellipsoids with and without shell.

$$\epsilon_\alpha^* = \frac{2\epsilon_M^* + (\epsilon^* - \epsilon_M^*)a_1b_1c_1\left[\int_0^\sigma \frac{ds}{(s+\alpha_1^2)R_1(s)} + \frac{2}{a_2b_2c_2}\right]}{2\epsilon_M^* + (\epsilon^* - \epsilon_M^*)a_1b_1c_1 \int_0^\sigma \frac{ds}{(s+\alpha_1^2)R_1(s)}}\,\epsilon_M^* \tag{37}$$

where

$$R_1(s) = \{(s + a_1^2)(s + b_1^2)(s + c_1^2)\}^{1/2} \tag{38}$$

$$\alpha_1 = a_1,\ b_1,\ c_1 \quad \text{depending on the direction of the impressed field} \tag{39}$$

$$\sigma = a_2^2 - a_1^2 = b_2^2 - b_1^2 = c_2^2 - c_1^2 \tag{40}$$

The two particles in Fig. 10*a* and *b* are identical in the sense that they give the same disturbances to the uniform field which is impressed along the α-axis. Hence, they are also equivalent in the sense that the energy stored inside and outside of the particle is equal. Using the relations, (37) to (40), the u_i's can be calculated from the formulas for the ellipsoid without a shell.

For biological cells,

$$\sigma \ll c_1^2$$

Hence equation (37) reduces to

$$\epsilon_\alpha^* = \frac{(2 - \sigma M_\alpha)\epsilon_1^* + \sigma M_\alpha \epsilon_M^*}{\sigma L_\alpha \epsilon^* + (2 - \sigma N_\alpha)\epsilon_M^*}\,\epsilon_M^* \tag{41}$$

where

$$M_\alpha = \frac{1}{a_1^2} + \frac{1}{b_1^2} + \frac{1}{c_1^2} - \frac{1}{\alpha_1^2} \tag{42}$$

$$N_\alpha = \frac{1}{\alpha_1^2} \tag{43}$$

Examinations of the above formula reveal that in this case there are two frequencies at which the magnitude of u_i changes from one value to another (Fig. 11), instead of only one as in the case of an ellipsoid of uniform composition. Clearly, at very high frequencies, at which the shell is effectively short-circuited, the ellipsoid behaves as an ellipsoid of uniform composition and thus displays one turnover frequency. The new frequency appears roughly in the region where the cells undergo their β-dispersion.

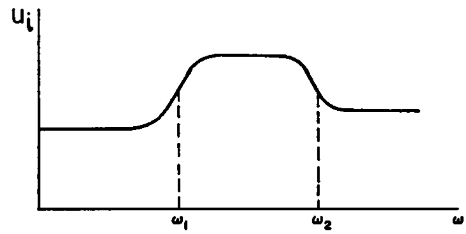

FIGURE 11 Behavior of u_i

Example 3–An Ellipsoid with a Shell

The following parameters are assumed for the electrical properties:

$$\kappa = 5 \text{ m mho/cm} \qquad \epsilon = 60\epsilon r$$

$$\kappa_0 = 2.5 \text{ m mho/cm} \qquad \epsilon_0 = 75\epsilon r$$

The capacitance of the membrane on the b axis is 1 μf/cm^2, the conductance of the membrane on the b axis is 10 m mho/cm^2, a negligibly small value.
Dimensions:

$$a = 20\mu, \quad b = 10\mu, \quad c = 5\mu, \quad b_2 - b_1 = 0.01\mu$$

The result of the calculation is shown in Fig. 12. It is seen that the direction of stable equilibrium changes in the following way

$$c \rightarrow a \rightarrow b \rightarrow c \rightarrow a$$

with the turnovers at 1.5, 20, 60, and 700 mc.

DISCUSSIONS AND CONCLUSIONS

It has been shown in the preceding sections that it is possible to predict, at least to some extent, the behavior of a particle under the influence of an electric field from a knowledge of its dielectric properties and vice versa.

In general there can be only one stable direction of equilibrium. The change in the stable direction with the change in frequency can occur either as a gradual change or as a sudden jump of 90°.

For ellipsoidal particles of symmetrical composition with or without a shell and with parameters of biological interest, only the latter (turnover) can occur. It takes

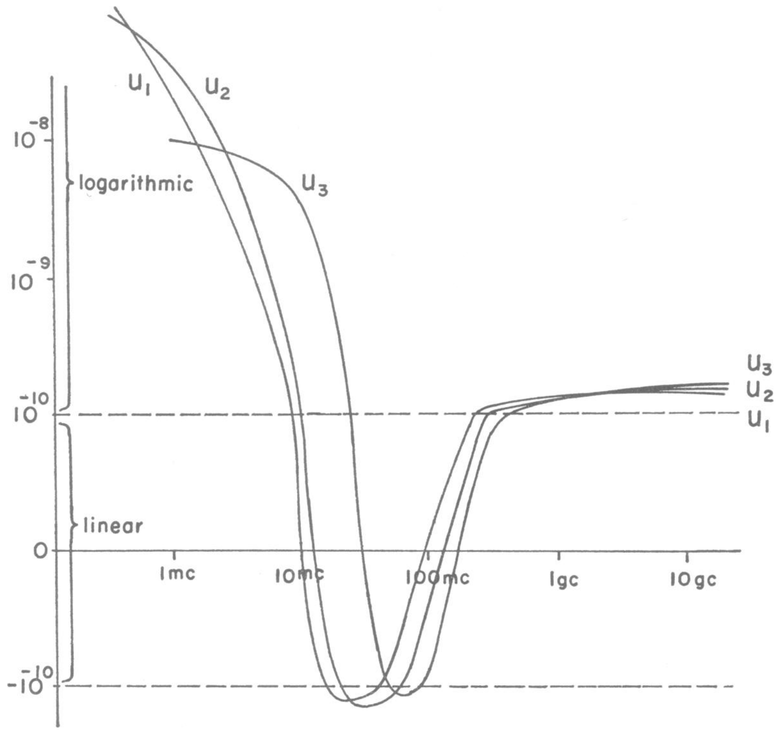

FIGURE 12 Stable direction of an ellipsoid with a shell.

place usually in the frequency range of several megacycles to several thousand megacycles.

In actual situations where the field intensity is not sufficiently high, this sudden jump may be blurred by the Brownian motion of the particle. The field intensity to overcome this effect can be calculated from the formula for the stored energy. Typical threshold field strength values are in the 100v/cm range but depend on all parameters involved.

The analysis made in this paper may be an explanation of the phenomena which Heller has described (3–6). Though no practical application of these phenomena has been tried yet, the fact that the turnover frequencies are sensitive to the geometric and electric parameters of the particles may suggest some applications.

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