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The dielectric behaviour of suspensions of spherical cells: a unitary approach

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Abstract. The dielectric behaviour of a suspension of conducting spherical particles surrounded by low conducting shells, with fixed charges on the inner side, in respect of diffusive effects has been investigated. The results describe both α and β dispersion and reduce, in the corresponding limiting cases, to those previously presented by Garcia and co-workers, Pauly, Schwan and Schwarz. The α dispersion is shown to be strongly dependent on charge density, shell thickness and diffusion effects, as well.

1. Introduction

One of the most important problems of our times consists in finding out quantitative methods to characterize the living state.

Electrical (dielectric) properties of biological systems are assumed to lead to suitable parameters to describe the state of a living system and consequently, the contrivance of an appropriate model to describe the dielectric behaviour of biological systems has to be accomplished.

It was not our aim to work out a complete electrical model of a living cell, but to develop a simplified one to contain the major features known about a biological cell and to exhibit the same behaviour when applying an armonic, low intensity electric field (with frequency range: 1 Hz–10 MHz). Consequently, the dielectric behaviour of a suspension of diffusive, conducting spheres, surrounded by low conductive shells with negligible diffusion coefficient and regular surface distribution of fixed charges on the inner side, is presented.

Neglecting the effect of the active transport as well as of the cytoplasmic nonhomogeneities on the dielectric behaviour, this model is assumed to exhibit large similarities with spherical biological cell suspensions regarding α and β dispersion (that appear at 100 Hz–10 kHz and 100 kHz–10 MHz, respectively). The present study is an extension of the following treatments:

(i) The influence of diffusion on the β dispersion of the permittivity of a spherical particles suspension, with insulating shells, conceived by Garcia *et al* (1985).

(ii) The theory of the low-frequency dispersion of charged spherical particles in an electrolyte, developed by Schwarz (1962).

The equivalent permittivity of a suspension of spherical particles provided by our approach describes both α and β dispersion. It reduces in the case of zero fixed charge and null membrane (shell) conductivity, to the results of Garcia and co-workers and

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in the case of negligible shell thickness and no volume diffusion effects to those of Schwarz.

2. Charge density distribution and potential calculation

We shall consider (as in figure 1) a spherical particle (indicated by subscript 1) with complex permittivity and conductivity:

$$\varepsilon_{g1} = \varepsilon_1 + \frac{\sigma_1}{i\omega\varepsilon_0}$$
$$\sigma_{g1} = \sigma_1 + i\omega\varepsilon_0\varepsilon_1 \tag{1}$$

with radius R_1, surrounded by a low conducting, non-diffusive shell (subscript 2) of thickness d and complex permittivity and conductivity:

$$\varepsilon_{g2} = \varepsilon_2 + \frac{\sigma_2}{i\omega\varepsilon_0}$$
$$\sigma_{g2} = \sigma_2 + i\omega\varepsilon_0\varepsilon_2. \tag{2}$$

On the inner face of the shell there is a uniform distribution of fixed charges n_{01}. This system is embedded in an infinite medium (subscript 3) with complex permittivity and conductivity:

$$\varepsilon_{g3} = \varepsilon_3 + \frac{\sigma_3}{i\omega\varepsilon_0}$$
$$\sigma_{g3} = \sigma_3 + i\omega\varepsilon_0\varepsilon_3 \tag{3}$$

to which a uniform field is applied: $E(t) = E_0 \exp(i\omega t)$.

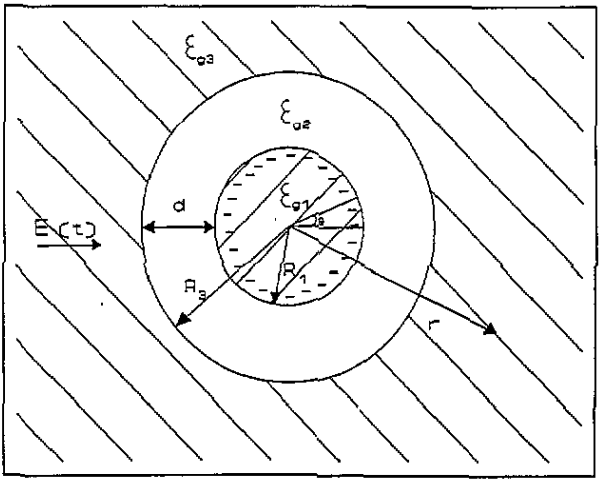

Figure 1. A spherical particle surrounded by a membrane with fixed negative charges on the inner side.

The external medium ($k=3$) is considered to be a charge reservoir that enables positive ions to migrate to the external side of the membrane balancing the fixed negative charges on the inner side when no field is applied:

$$n_{03}=n_{01}\left(\frac{R_1}{R_1+d}\right)^2. \tag{4}$$

In each diffusive media we consider the simple case of opposite sign monovalent ions that have in the same media k ($k=1, 3$) the same volume density N_{0k} (when no field is applied) and the same mobility u_k.

The conductivity σ_k is in this case:

$$\sigma_k=2N_{0k}u_k e \tag{5}$$

where e is the absolute value of the electron charge, and eN_{0k} is the volume charge density in medium k in the field absence.

The mobilities are related to the diffusion coefficient D_k according to Einstein's formula:

$$D_k=\frac{u_k}{e}KT. \tag{6}$$

When applying a field the ion density changes to (Garcia *et al* 1985):

$$N_k^{\pm}=N_{0k}+(\rho_k^{\pm}(r)/e)\exp(i\omega t). \tag{7}$$

In the weak field limit we have:

$$|\rho_k^{\pm}(r)|\leqslant N_{0k}e \tag{8}$$

consequently, we shall consider that relation (5) remains valid in this limit.

Taking into account the balance equation for charge we obtain for volume charge density:

$$\nabla^2\rho_k(r)=G_k^2\rho_k(r) \tag{9}$$

where:

$$G_k^2=\frac{\sigma_{gk}}{D_k\varepsilon_0\varepsilon_k}. \tag{10}$$

The general solution of (9) in spherical coordinates and with axial symmetry is:

$$\rho_k(r,\theta)=e\sum_{n=0}^{\infty}\frac{A_{nk}J_{n+1/2}(iG_kr)+(-1)^{n+1}B_{nk}J_{-n-1/2}(iG_kr)}{\sqrt{r}}P_n(\cos\theta) \tag{11}$$

where A_{nk} and B_{nk} are constants, $P_n(\cos\theta)$ represents Legendre Polynomials and $J_{\pm(n+1/2)}$ are Bessel Functions.

The equations for potential

$$\varphi_k(r,\theta,t)=\varphi_k(r,\theta)\exp(i\omega t) \tag{12}$$

are listed below in the quasistatic approximation (Poisson equation for media 1 and 3, and Laplace equation for the shell):

$$\nabla^2\varphi_1(r,\theta)=-\frac{1}{\varepsilon_0\varepsilon_1}\rho_1(r,\theta) \qquad (r\leqslant R_1) \tag{13}$$

$$\nabla^2\varphi_2(r,\theta)=0 \qquad (R_1<r<R_1+d=R_3) \tag{14}$$

$$\nabla^2\varphi_3(r,\theta)=-\frac{1}{\varepsilon_0\varepsilon_3}\rho_3(r,\theta) \qquad (r\geqslant R_3). \tag{15}$$

Using the regularity conditions, we find the particular solution of the following type:

$$\varphi_1=\sum_{n=0}^{\infty}\left[C_nr^n-\frac{e}{\varepsilon_0\varepsilon_1G_1^2}A_{n1}\frac{J_{n+1/2}(\mathrm{i}G_1r)}{\sqrt{r}}\right]P_n(\cos\theta) \tag{16}$$

$$\varphi_2=\sum_{n=0}^{\infty}\left(D_nr^n+\frac{F_n}{r^{n+1}}\right)P_n(\cos\theta) \tag{17}$$

$$\varphi_3=\sum_{n=0}^{\infty}\left[\frac{H_n}{r^{n+1}}-eA_{n3}\frac{J_{n+1/2}(\mathrm{i}G_3r)+\mathrm{i}(-1)^{n+1}J_{-n-1/2}(\mathrm{i}G_3r)}{\varepsilon_0\varepsilon_3G_3^2\sqrt{r}}\right]P_n(\cos\theta)-E_0r\cos\theta. \tag{18}$$

The boundary conditions used to determine the coefficients A_{n1}, A_{n3}, C_n, D_n, F_n, H_n are given in the appendix.

Non trivial solutions are derived for $n=0$ and $n=1$, that is:

(i) For charge density:

$$\rho_1(r,\theta)=eA_1\left(\frac{\cosh(G_1r)}{G_1r}-\frac{\sinh(G_1r)}{(G_1r)^2}\right)\cos\theta+eA_{10}\frac{\sinh(G_1r)}{G_1r} \qquad (r<R_1) \tag{19}$$

$$\rho_2(r,\theta)=0 \qquad (R_1<r<R_3) \tag{20}$$

$$\rho_3(r,\theta)=eA_3\exp(-G_3r)\left[\frac{1}{G_3r}+\frac{1}{(G_3r)^2}\right]\cos\theta+eA_{30}\frac{\exp(-G_3r)}{2G_3r} \qquad (r>R_3). \tag{21}$$

Figure 2 presents the radial distribution of the intracellular field induced charge density relative to volume charge density eN_{01}. The maximum value is achieved at $R_1=2\times10^{-6}$ m and is in agreement with relation (8), $\omega=10^6\,s^{-1}$, $E_0=100$ V/m.

(ii) For potential:

$$\varphi_1(r,\theta)=Cr\cos\theta-\frac{1}{\varepsilon_0\varepsilon_1G_1^2}\rho_1(r,\theta)+C_0 \qquad (R_1\leqslant r) \tag{22}$$

$$\varphi_2(r,\theta)=\left(Dr+\frac{F}{r^2}\right)\cos\theta+D_0+\frac{F_0}{r} \qquad (R_1\leqslant r\leqslant R_2) \tag{23}$$

$$\varphi_3(r,\theta)=-E_0r\cos\theta+\frac{H}{r^2}\cos\theta+\frac{H_0}{r}-\frac{1}{\varepsilon_0\varepsilon_3G_3^2}\rho_3(r,\theta) \qquad (R_3\leqslant r). \tag{24}$$

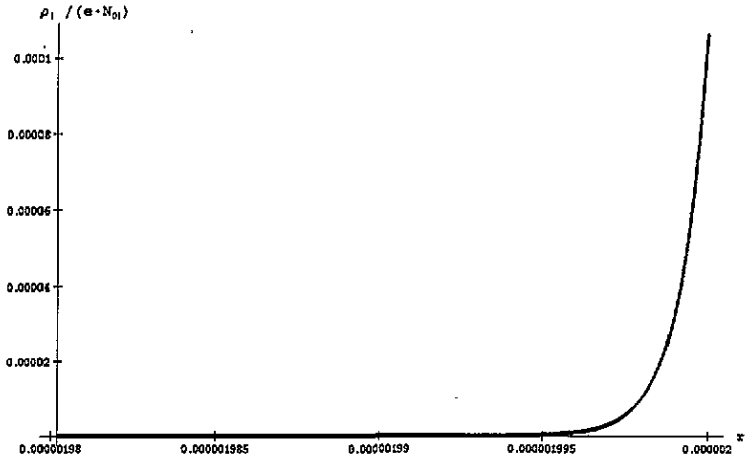

Figure 2. The radial distribution of volume charge density in the internal sphere, $r(m)$, $\omega = 10^6\ s^{-1}$, $\theta = 0$.

Only $\varphi_3(r, \theta)$ is needed to obtain the equivalent complex permittivity. For H and H_0 we subsequently have:

$$H = \frac{\dfrac{g}{h}\left[\sigma_2 + i\omega\varepsilon_2\varepsilon_0(1-Q) + i\omega\varepsilon_3\varepsilon_0 Q\dfrac{\sigma_2}{\sigma_3}\right] + i\omega eN(R_1+d)(1-Q) - \sigma_{g3}}{\dfrac{g}{h}\left[\sigma_2 + i\omega\varepsilon_2\varepsilon_0(1+2Q) - 2i\omega\varepsilon_1\varepsilon_0 Q\dfrac{\sigma_2}{\sigma_3}\right] + i\omega eN(R_1+d)(1+2Q) + 2\sigma_{g3}}(R_1+d)^3E_0$$

$H_0 = 0$.

If there is no surface charge density and negligible membrane conductivity, then H reduces to

$$\begin{aligned} H = {} & \{R_1^3[\varepsilon_0\varepsilon_{g1} - \varepsilon_0\varepsilon_2(1+S)][2\varepsilon_0\varepsilon_2(1-Q) + \varepsilon_0\varepsilon_{g3}] \\ & + (R_1+d)^3[\varepsilon_2\varepsilon_0 - \varepsilon_{g1} - 2\varepsilon_0\varepsilon_2(1+S)]\} \\ & \times \{2R_1^3[\varepsilon_{g1} - \varepsilon_0\varepsilon_2(1+S)][\varepsilon_0\varepsilon_2(1+2Q) - \varepsilon_{g3}] \\ & + (R_1+d)^3[\varepsilon_0\varepsilon_2 + 2(\varepsilon_{g3} + Q\varepsilon_0\varepsilon_3)][\varepsilon_{g1} + 2\varepsilon_0\varepsilon_2(1+S)]\} \\ & \times (R_1+d)^3E_0 \end{aligned} \tag{26}$$

in accordance with A_m obtained by Garcia *et al* (1985).

3. Equivalent complex permittivity

The complex permittivity ε_g of a homogeneous sphere is derived in the frame of Maxwell–Wagner formalism (Maxwell 1892, Wagner 1914) using the condition that the whole suspension has the same dielectric behaviour as an homogeneous sphere suspended in medium 3. In both cases the same expression of potential in medium 3 has to be derived. As $\exp(-G_3 r)$ drops sharply, only the second term in (24) is used to calculate ε_g.

Considering p the volume concentration of the spherical particles in suspension, neglecting the interactions between particles, the following expression for suspension equivalent complex permittivity is obtained:

$$\varepsilon_g = \varepsilon_{g3} \frac{1 + 2p \dfrac{H}{R_3^3 E_0}}{1 - p \dfrac{H}{R_3^3 E_0}} \qquad \varepsilon_g = \varepsilon + \frac{\sigma}{i\omega \varepsilon_0}. \tag{27}$$

4. Conclusions

The expression for ε_g enables the description of both α and β dispersions as might be noticed in figures 3 and 4. This approach emphasizes the relationship between α dispersion and the fixed charge on the inner face of the membrane. Consequently, α dispersion

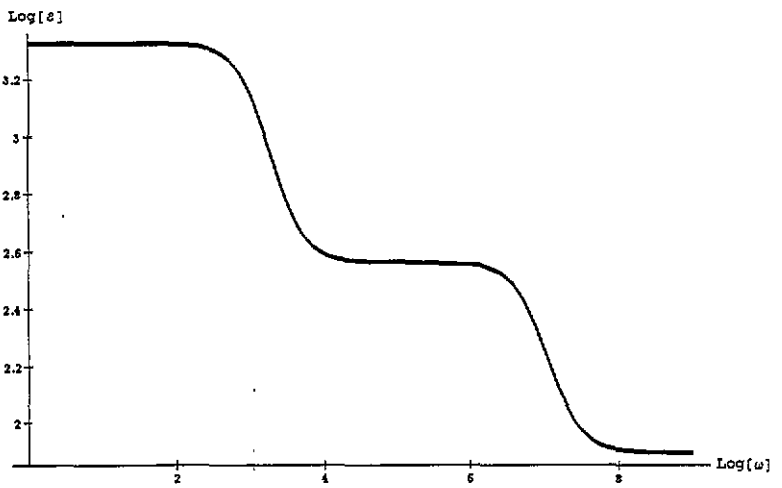

Figure 3. α and β dispersions of ε (relative units) $\varepsilon_1 = 80$, $\sigma_1 = 0.20\ \mathrm{S\,m^{-1}}$, $\varepsilon_2 = 12$, $\sigma_2 = 10^{-6}\ \mathrm{S\,m^{-1}}$, $\varepsilon_3 = 78$, $\sigma_3 = 0.377\ \mathrm{S\,m^{-1}}$, $R_1 = 2\,10^{-6}\ \mathrm{m}$, $d = 10^{-8}\ \mathrm{m}$, $n_{01} = 10^{16}\ \mathrm{m^{-2}}$, $p = 0.06$, $D_1 = 2.07 \times 10^{-10}\ \mathrm{m^2\,s^{-1}}$, $D_3 = 2.07 \times 10^{-9}\ \mathrm{m^2\,s^{-1}}$.

is related to the field induced displacement of the charges on the external side of the membrane that are connected with the fixed charge density n_{01} through relations (4) and (A15). That is why information regarding this dispersion enables the determination of the biological cell resting potential (Gheorghiu 1993).

Our results reduce:

- to those of Garcia *et al* (1985) in the case of zero fixed charge density ($n_{01} = 0$) and zero membrane conductivity ($\sigma_2 = 0$), relation (26) and (27);
- to those of Pauly and Schwan (1959) in the case of zero fixed charge density and zero diffusion ($N = 0$, $S = 0$, $Q = 0$), figure 5;
- to those of Schwarz (1962) in the case of diffusion, only on the external side of the membrane and for zero thickness of membrane ($S = 0$, $Q = 0$, $d = 0$), figure 6.

Figures 6 and 7 reveal the dependence of α dispersion on membrane thickness and on diffusion in the external medium and on fixed charge density, respectively.

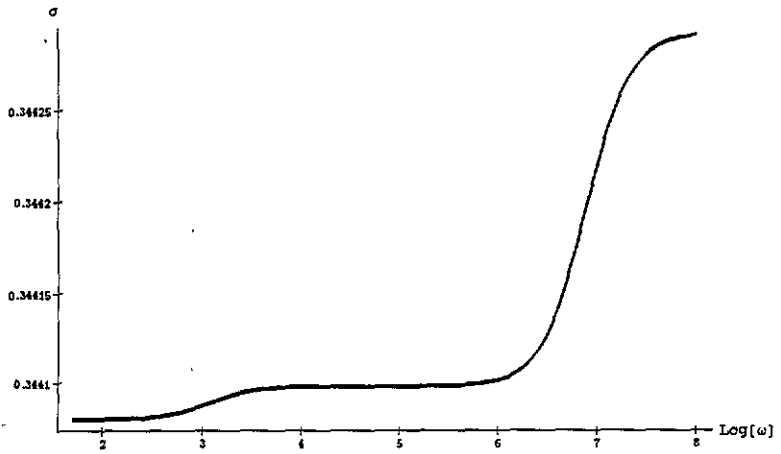

Figure 4. α and β dispersions of equivalent conductivity σ (S m^{-1}). $\varepsilon_1=80$, $\sigma_1=0.200$ S m^{-1}, $\varepsilon_2=12$, $\sigma_2=10^{-6}$ S m^{-1}, $\varepsilon_3=78$, $\sigma_3=0.377$ S m^{-1}, $R_1=2\times10^{-6}$ m, $d=10^{-8}$ m, $n_{01}=10^{16}$ m^{-2}, $p=0.06$, $D_1=2.07\times10^{-10}$ m^2 s^{-1}, $D_3=2.07\times10^{-9}$ m^2 s^{-1}. In β dispersion range the conductivity increment is reduced by a factor 100.

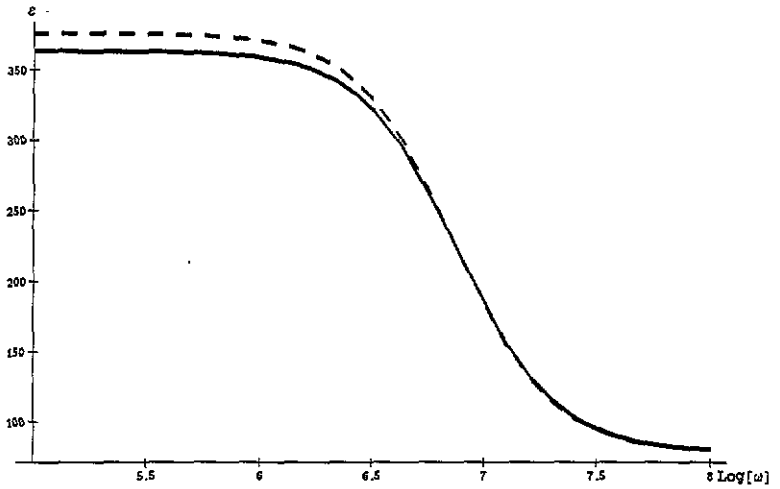

Figure 5. β dispersion of equivalent permittivity ε (relative units), in the case of zero fixed charge density and no diffusion (----) and β dispersion according to (27) in the same conditions as in figure 3 (——).

The strong dependence of the equivalent permittivity in α dispersion range (e.g. $\omega=100$ s^{-1}) on diffusion effects in medium 3 is pointed out in figure 8.

By taking into consideration the diffusive phenomena as well as the presence of the membrane charge densities, one may notice important effects in the α dispersion range, whereas in the β one the related effects are rather small. As shown in figure 9, β dispersion exhibits a weak dependence on membrane charge distribution in this frequency range, our results being similar to those obtained by Garcia *et al* (1985). Consequently, in β dispersion range the validity of our model is implicit (as shown in figures 5 and 9, the differences between our results and those of Pauly and Schwan (1959), or Garcia *et al* (1985) are in the range of the experimental errors). The lack of data on α

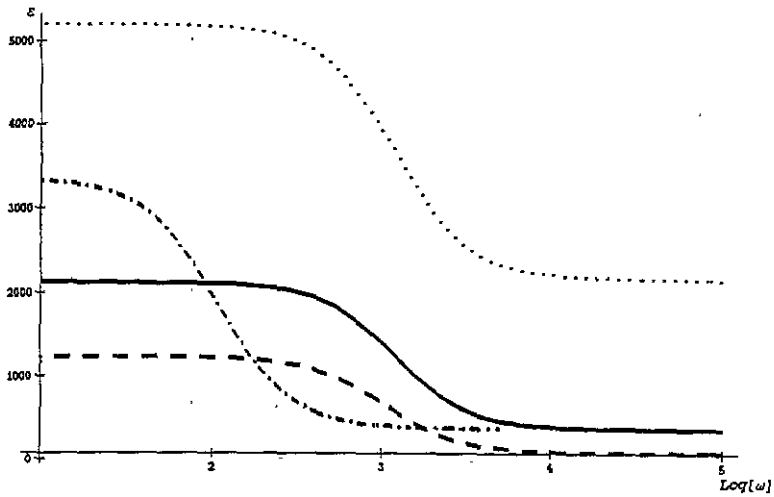

Figure 6. α dispersion of equivalent permittivity ε (relative units) $\varepsilon_1 = 80$, $\sigma_1 = 0.200\ \mathrm{S\ m^{-1}}$, $\varepsilon_2 = 12$, $s_2 = 10^{-6}\ \mathrm{S\ m^{-1}}$, $\varepsilon_3 = 78$, $\sigma_3 = 0.377\ \mathrm{S\ m^{-1}}$, $R_1 = 2 \times 10^{-6}$ m, $d = 10^{-8}$ m, $n_{01} = 10^{16}\ \mathrm{m^{-2}}$, $p = 0.06$, $D_1 = 2.07 \times 10^{-10}\ \mathrm{m^2\ s^{-1}}$, $D_3 = 2.07 \times 10^{-9}\ \mathrm{m^2\ s^{-1}}$ according to (27) (——), in the case of zero membrane thickness, no diffusion in medium 1 and 3 but on the external face of the membrane (– – –), for a different ion diffusion coefficient in the external medium $D_3 = 2 \times 10^{-10}\ \mathrm{m^2\ s^{-1}}$ (–·–) and for a different membrane thickness, $d = 10^{-9}$ m (· · · ·).

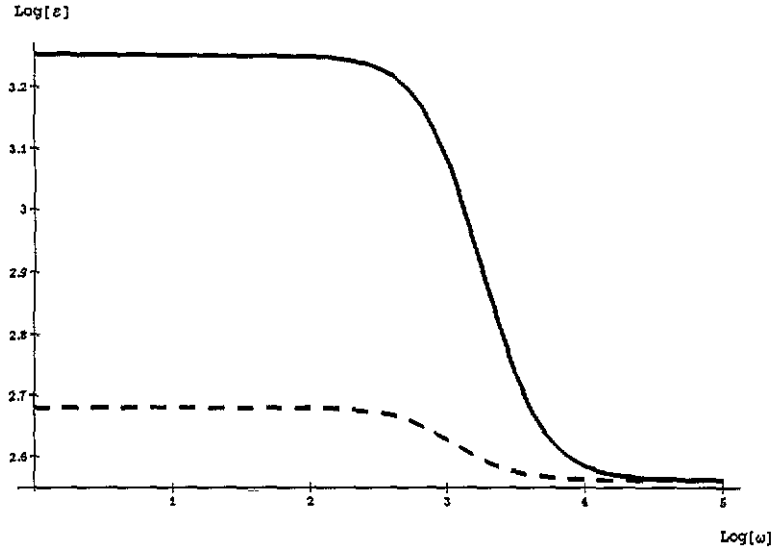

Figure 7. α dispersion of equivalent permittivity (relative units) for different values of negative fixed charge surface density $n_{01} = 10^{16}\ \mathrm{m^{-2}}$ (——), $n_{01} = 10^{15}\ \mathrm{m^{-2}}$ (– – –).

dispersion exhibited by cell suspensions under physiological conditions, prevent us fitting our model at lower frequencies too. Having in view the possibility of determining the electrical parameters of biological cells (including resting potential) by *in vivo* dielectric spectroscopy on synchronized, spherical cell suspensions, emphasized by our

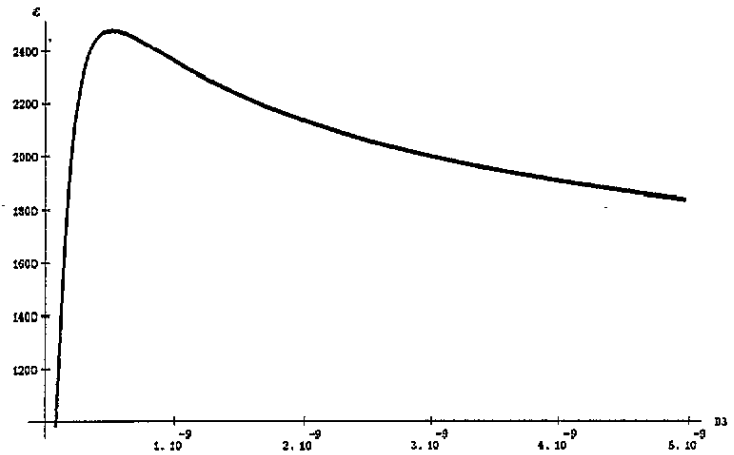

Figure 8. The dependence of the equivalent permittivity ε (relative units) at α dispersion, on the diffusion coefficient of medium 3, $D_3(m^2/s)$ at $\omega = 100\ s^{-1}$.

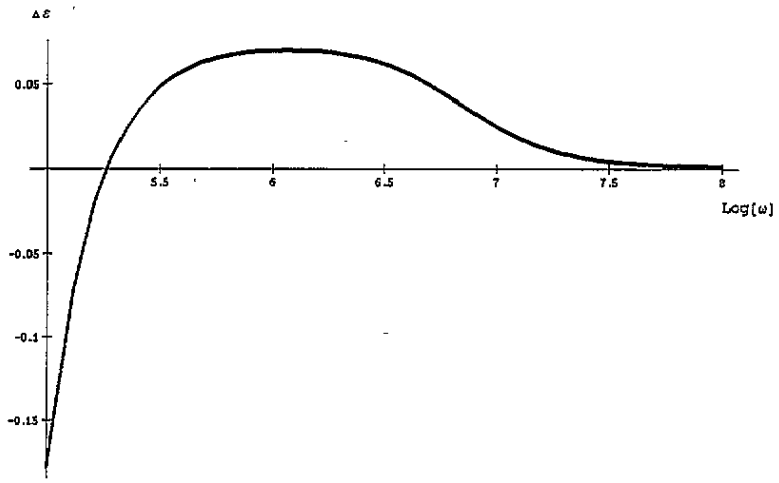

Figure 9. The plot of the difference between the equivalent permittivities (relative units) corresponding to $DV_0 = 0$ V and $DV_0 = -150$ mV respectively, in β dispersion range.

approach, we hope that, in spite of the experimental difficulties, α dispersion measurements will soon be available. Then, the validity of our model could be tested on the entire range of α and β dispersions, and further improvements of this study would become possible.

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Appendix

The boundary conditions used to determine the coefficients A_{n1}, A_{n3}, C_n, D_n, F_n, H_n are as below.

The potential must be continuous at the interfaces:

$$\varphi_3(r=R_3)=\varphi_2(r=R_3) \tag{A1}$$

$$\varphi_1(r=R_1)=\varphi_2(r=R_1). \tag{A2}$$

The normal components of the displacement must be related to the charges at the interfaces:

$$\varepsilon_2\frac{\partial\varphi_2}{\partial r}-\varepsilon_1\frac{\partial\varphi_1}{\partial r}=-en_{01} \qquad (r=R_1) \tag{A3}$$

$$\varepsilon_3\frac{\partial\varphi_3}{\partial r}-\varepsilon_2\frac{\partial\varphi_2}{\partial r}=en_3(\theta) \qquad (r=R_3) \tag{A4}$$

$$n_3(\theta)=\sum_{n=0}^{\infty}N_nP_n(\cos\theta) \qquad N_0=n_{03} \tag{A5}$$

where en_{01}, en_3 is the surface charge density on the inner, respectively, the external, side of the membrane.

N_n is obtained by considering the balance equation for the charge on the external interface (Schwarz 1962).

The normal component of the total current density must vanish at the interfaces (in the case of the insulating membrane):

$$\sigma_3\frac{\partial\varphi_3}{\partial r}+D_3\frac{\partial\rho_3}{\partial r}=0 \qquad r=R_3 \tag{A6}$$

$$\sigma_1\frac{\partial\varphi_1}{\partial r}+D_1\frac{\partial\rho_1}{\partial r}=0 \qquad r=R_1. \tag{A7}$$

For low conductive membrane the normal component of the total current density must be continuous. For non-negligible shell conductivity, we have instead of (A6) and (A7):

$$\sigma_3\frac{\partial\varphi_3}{\partial r}+D_3\frac{\partial\rho_3}{\partial r}=\sigma_2\frac{\partial\varphi_2}{\partial r} \qquad (r=R_3) \tag{A8}$$

$$\sigma_1\frac{\partial\varphi_1}{\partial r}+D_1\frac{\partial\rho_1}{\partial r}=\sigma_2\frac{\partial\varphi_2}{\partial r} \qquad (r=R_1). \tag{A9}$$

A_3 and A_{30} are needed for the calculation of potential in medium $k=3$:

$$A_3=-3E_0\frac{G_3^2}{e}\frac{G_3^2(R_1+d)^3\exp[G_3(R_1+d)]}{G_3^2(R_1+d)^2+2[1+G_3(R_1+d)]}$$
$$\times\frac{\frac{g}{h}(\sigma_3\varepsilon_2-\sigma_2\varepsilon_3)+eN(R_1+d)\sigma_3}{\frac{g}{h}\left[\sigma_2+i\omega\varepsilon_2(1+2Q)-2i\omega\varepsilon_3Q\frac{\sigma_2}{\sigma_3}\right]+i\omega eN(R_1+d)(1+2Q)+2\sigma_{g3}} \tag{A10}$$

$$A_{30}=-\frac{2G_3R_1^2\exp[G_3(R_1+d)]n_{01}\sigma_2\sigma_{g3}}{e[1+G_3(R_1+d)]D_3\varepsilon_3\sigma_{g2}}$$

where:

$$g=(1+2\delta)\sigma_1\sigma_{g1}+2(1-\delta)[i\omega\sigma_1\varepsilon_2(1+S)+\sigma_2(\sigma_1-i\omega\varepsilon_1S)] \tag{A11}$$

$$h=(1-\delta)\sigma_1\sigma_{g1}+(2+\delta)[i\omega\sigma_1\varepsilon_2(1+S)+\sigma_2(\sigma_1-i\omega\varepsilon_1S)] \tag{A12}$$

$$S=\frac{\sigma_1}{i\omega\varepsilon_1}\frac{G_1R_1-\tanh(G_1R_1)}{(G_1R_1)^2\tanh(G_1R_1)-2[G_1R_1-\tanh(G_1R_1)]} \tag{A13}$$

$$Q=\frac{\sigma_3}{i\omega\varepsilon_3}\frac{1+G_3(R_1+d)}{G_3^2(R_1+d)^2+2[1+G_3(R_1+d)]} \tag{A14}$$

$$n_3(\theta)=n_{03}-N\cos\theta$$

$$N=\frac{n_{03}}{KT}\frac{1}{1+i\omega\dfrac{(R_1+d)^2}{2u_3KT}} \tag{A15}$$

$$\delta=\left(\frac{R_1}{R_1+d}\right)^3. \tag{A16}$$

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