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Analytical model for power dissipation in cell membranes in suspensions exposed to electric fields

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Abstract: Due to interaction among cells, it is too complex to build an exact analytical model for the power dissipation within the cell membrane in suspensions exposed to external fields. An approximate equivalence method is proposed to resolve this problem. Based on the effective medium theory, the transmembrane voltage on cells in suspensions was investigated by the equivalence principle. Then the electric field in the cell membrane was determined. Finally, analytical solutions for the power dissipation within the cell membrane in suspensions exposed to external fields were derived according to the Joule principle. The equations show that the conductive power dissipation is predominant within the cell membrane in suspensions exposed to direct current or lower frequencies, and dielectric power dissipation prevails at high frequencies exceeding the relaxation frequency of the exposed membrane.

Key words: power dissipation; analytical model; cell suspension; external electric fields

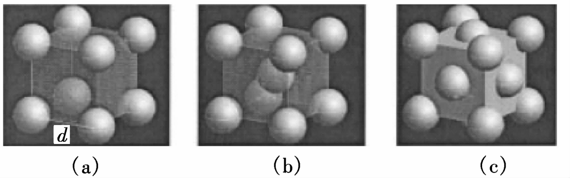
Biological cells are responsive to electromagnetic irradiation. In general, evaluation of these bioeffects is based on the power dissipation caused by the exposure. While an electric field is applied to biological cells, the motion ions in the medium surrounding the membrane, accumulation of the charges at the membrane surfaces and membrane polarization will result in a transmembrane voltage, leading to a variety of biochemical and biophysical changes in cells. For an exposure at frequencies in the range of direct current (DC) and millimeter waves, the power dissipation in the cytoplasm is far less than that within the cell membrane[1]. Thus, it is very significant to study the power dissipation in a cell membrane exposed to an external field.

Due to interaction among cells, it is an especially complex theoretical problem to build an exact analytical model for the power dissipation within the cell membrane in suspensions exposed to external fields. Therefore, based on the Maxwell-Wagner equation, several equations were derived in this paper for power dissipation in the cell membrane in suspensions exposed to external fields of various frequencies by the equivalence principle.

1 Derivation of Equations for $\Delta\Psi$ Induced on Cells in Suspensions Exposed to AC Fields

For spherical cells in suspensions arranged orderly in an sc, bcc or fcc lattice[2] (see Fig. 1), the transmembrane voltage $\Delta\psi$ induced on the cells in suspensions exposed to a DC field on the cells is[3]

$$\Delta\psi_{\mathrm{d}} = \frac{3}{2}\frac{(1+0.5f_{\mathrm{o}})}{1+\left(\dfrac{3f_{\mathrm{o}}}{4N\pi}\right)^{\frac{1}{3}}}E_{\mathrm{o}}R\cos\theta \tag{1}$$



(a) (b) (c)

Fig. 1 Unit cells arranged orderly in different lattices. (a) sc; (b) bcc; (c) fcc

where E_{o} is the amplitude of the external electric fields, θ is the angle between the field line and a normal drawn from the coordinate origin to a point of intersection on the cell membrane, R is the cell radius, f_{o} is the volume fraction of the cells, and N is the number of the cells in the unit lattice.

As a suspension is exposed to an AC field, the Maxwell-Wagner equation can be used to calculate the effective complex conductivity σ^* of the equivalent body of the dilute suspensions[2,4].

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$$\frac{\sigma_e^* - \sigma^*}{2\sigma_e^* + \sigma^*} = f_o \frac{\sigma_e^* - \sigma_p^*}{2\sigma_e^* + \sigma_p^*} \tag{2}$$

$$\sigma_p^* = \sigma_m^* \frac{2(1-v)\sigma_m^* + (1+2v)\sigma_i^*}{(2+v)\sigma_m^* + (1-v)\sigma_i^*} \qquad v = \left(\frac{1-d_o}{R}\right)^3 \tag{3}$$

where $\sigma_e^* = \sigma_e + j\omega\varepsilon_e$ is the complex conductivity of the external medium; $\sigma_p^* = \sigma_p + j\omega\varepsilon_p$ is the equivalent complex conductivity of a biological cell, which has a heterogeneous structure having complex conductivity of membrane $\sigma_m^* = \sigma_m + j\omega\varepsilon_m$ and cytoplasm $\sigma_i^* = \sigma_i + j\omega\varepsilon_i$; $\sigma_m(\varepsilon_m)$, $\sigma_i(\varepsilon_i)$ and $\sigma_e(\varepsilon_e)$ are the conductivity (permittivity) of the membrane, cytoplasm and external medium, respectively; d_o is the membrane thickness.

A physiological cell has a zero value of membrane conductivity. Thus $\sigma_p^* = 0$. Written in the frequency plane, the effective field inside the equivalent sphere can be obtained according to the Laplace equation:

$$E(j\omega) = \frac{3\sigma_e^*}{\sigma^* + 2\sigma_e^*} E_o(j\omega) = (1 + 0.5f_o) E_o(j\omega) \tag{4}$$

Under the same conditions of the exposure to $E_o(j\omega)$, the value of the potential of the unit cell in suspensions is different from that of a single cell. The shape of the equipotential plane in the internal medium and in the external medium close to the membrane of both cells, however, is similar (for details of the discussion see Ref. [3]). Assume that when a cell suspension is exposed to an alternating field $E_o(j\omega)$ and a single cell to $E'_o(j\omega)$, the distribution of the local field of the cell in suspensions is the same as that of the single cell. We proceed as the derivation of the transmembrane voltage on the cells in suspensions exposed to a DC field[3], but with complex conductivity and electric field written in the frequency plane, we obtain

$$E'_o(j\omega) = \frac{1 + 0.5f_o}{1 + \left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}} E_o(j\omega) \tag{5}$$

If $f \leqslant 100$ kHz, the transmembrane voltage on a single cell exposed to $E'_o(j\omega)$ is[5]

$$\Delta\psi_{1s}(j\omega) = \frac{3}{2}\frac{1}{(1 + j\omega\tau_m)} E'_o(j\omega) R\cos\theta \tag{6}$$

where $\tau_m = RC_m\left(\frac{1}{\sigma_i} + \frac{1}{2\sigma_e}\right)$ is the time constant of the membrane charging process, and $C_m = \varepsilon_m / d_o$ is the membrane capacitance.

Inserting Eq. (5) into Eq. (6), $\Delta\psi$ on the cells in suspensions exposed to $E_o(j\omega)$ should be

$$\Delta\psi_1(j\omega) = \frac{3}{2}\frac{(1 + 0.5f_o)}{1 + \left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}} \frac{1}{1 + j\omega\tau_m} E_o(j\omega) R\cos\theta \tag{7}$$

For 100 kHz $\leqslant f \leqslant$ 100 MHz, $\Delta\psi$ on a single cell exposed to $E'_o(j\omega)$ is[1]

$$\Delta\psi_{2s}(j\omega) = \frac{3}{2}\frac{(1 + j\omega\tau_{m2})}{(1 + j\omega\tau_{m1})} E'_o(j\omega) R\cos\theta \tag{8}$$

$$\tau_{m1} = RC_m\left(\frac{1}{\sigma_i} + \frac{1}{2\sigma_e}\right), \quad \tau_{m2} = \frac{\varepsilon_i + 2\varepsilon_e}{\sigma_i + 2\varepsilon_e} \tag{9}$$

where τ_{m1} and τ_{m2} are the first and second time constants of the membrane charging process.

As the derivation of Eq. (7), $\Delta\psi$ induced on the cells in suspensions exposed to $E_o(j\omega)$ is

$$\Delta\psi_2(j\omega) = \frac{3}{2}\frac{(1 + 0.5f_o)}{1 + \left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}} \frac{1 + j\omega\tau_{m2}}{1 + j\omega\tau_{m1}} E_o(j\omega) R\cos\theta \tag{10}$$

If $f \geqslant 100$ MHz, $\Delta\psi$ induced on a single cell exposed to $E'_o(j\omega)$ is[1]

$$\Delta\psi_{s(2+DR)}(j\omega) = f_{s(2+DR)}(\omega)\frac{1 + j\omega\tau_{m2}(\omega)}{1 + j\omega\tau_{m1}(\omega)} E'_o(j\omega) R\cos\theta \tag{11}$$

where

$$f_{s(2+DR)}(\omega) = \frac{3\sigma_e^*(\omega)[3R^3\sigma_i^*(\omega) + (3d_oR^2 - d_o^2R)][\sigma_m^*(\omega) - \sigma_i^*(\omega)]}{2R^3[\sigma_m^*(\omega) + 2\sigma_e^*(\omega)][\sigma_m^*(\omega) + \frac{1}{2}\sigma_i^*(\omega)] - 2(R - d_o)^3[\sigma_e^*(\omega) - \sigma_m^*(\omega)][\sigma_i^*(\omega) - \sigma_m^*(\omega)]} \tag{12}$$

$$\sigma(\omega) = \sigma(0) + \omega \sum_{k=1}^{n} \frac{\Delta\varepsilon_k \omega \tau_k}{1 + \omega^2 \tau_k^2} \tag{13}$$

$$\varepsilon(\omega) = \varepsilon(0) - \sum_{k=1}^{n} \frac{\Delta\varepsilon_k \omega^2 \tau_k^2}{1 + \omega^2 \tau_k^2} \tag{14}$$

where n is the number of steps of dielectric relaxation of the material, $\Delta\varepsilon_k$ is the magnitude of the k-th relaxation step, τ_k is the time constant of the k-th step, while $\sigma(0)$ and $\sigma(\omega)$ are respectively the conductivity and dielectric permittivity of the material $\left(\text{values measured at } f \ll \frac{1}{2\pi\tau_1}\right)$[1].

Analogously, we can derive $\Delta\psi$ on the cells in suspensions exposed to $E_o(j\omega)$:

$$\Delta\psi_{(2+DR)}(j\omega) = f_{s(2+DR)}(\omega) \frac{(1+0.5f_o)}{1+\left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}} \frac{1+j\omega\tau_{m2}(\omega)}{1+j\omega\tau_{m1}(\omega)} E_o(j\omega) R\cos\theta \tag{15}$$

2 Derivation of Equations for Power Dissipation within Cell Membrane in Suspensions

The power dissipation per unit volume P_m in membrane in suspensions is given by[1]

$$P_m = \frac{1}{2}\sigma_m \frac{\Delta^2\psi}{d_o^2} \tag{16}$$

According to Eqs. (1), (7), (10) and (12), P_m within the cells in suspensions exposed to various frequencies can be determined as follows:

For DC field,

$$P_{md} = \frac{9}{8}\sigma_m \frac{(1+0.5f_o)^2}{\left[1+\left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}\right]^2} \frac{E_o^2 R^2 \cos^2\theta}{d_o^2} \tag{17}$$

For $f \leqslant 100$ kHz,

$$P_{m1} = \frac{9}{8}\sigma_m \frac{(1+0.5f_o)^2}{\left[1+\left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}\right]^2} \frac{1}{1+(\omega\tau_m)^2} \frac{E_o^2 R^2 \cos^2\theta}{d_o^2} \tag{18}$$

For 100 kHz $\leqslant f \leqslant$ 100 MHz,

$$P_{m2} = \frac{9}{8}\sigma_m \frac{(1+0.5f_o)^2}{\left[1+\left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}\right]^2} \frac{1+(\omega\tau_{m2})^2}{1+(\omega\tau_{m1})^2} \frac{E_o^2 R^2 \cos^2\theta}{{d_o}^2} \tag{19}$$

For $f \geqslant 100$ MHz (relaxation frequency of the exposed membrane),

$$P_{m(2+DR)} = \frac{1}{2}F^2_{s(2+DR)}\sigma_m \frac{(1+0.5f_o)^2}{\left[1+\left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}\right]^2} \frac{1+(\omega\tau_{m2})^2}{1+(\omega\tau_{m1})^2} \frac{E_o^2 R^2 \cos^2\theta}{{d_o}^2} \tag{20}$$

where $F_{s(2+DR)}$ is the magnitude of $f_{s(2+DR)}(j\omega)$. For $f \geqslant 20$ GHz, the conductivity of the membrane σ_m is far less than that of the cytoplasm and external medium and can be ignored. Thus one can get $F_{s(2+DR)} = 3/2$. But for 100 MHz $\leqslant f \leqslant$ 20 GHz, σ_m increases dramatically. In this case, it cannot be assumed to be zero value[1].

3 Conclusion

Eqs. (17) to (20) show that the power dissipation in membrane of cells in orderly cell suspensions exposed to external fields depends on the intension of external fields, the conductivity of the cytoplasm and external medium, the cell arrangement and cell volume fraction. Moreover, for AC fields, the frequency of external fields, the permittivity of the cytoplasm, membrane and external medium also have an influence on the value of the power dissipation.

Compared with the analytical solution for the power dissipation within the membrane of a single cell[1], there is an added function of $(1+0.5f_o)^2 \Big/ \left[1+\left(\frac{3f_o}{4N\pi}\right)^{\frac{1}{3}}\right]^2$ which only varies with f_o in Eq. (19). Thus, the distributed power dissipation within the membrane in suspensions has the same characteristics as for a single cell[1]: At DC and lower frequencies below 100 kHz, the dielectric power dissipation can be ignored. The conductive component is predominant. If the frequency exceeds the relaxation frequency of the cell membrane, dielectric power dissipation prevails. However, for frequencies above 20 GHz, dielectric power dissipation starts decreasing, and the power dissipation of the aqueous media inside and outside the membrane are predominant.

Since the Maxwell-Wagner equation is the best valid for deriving the analytical solutions of power dissipation volume fractions in the range of 0 and 0.6[2], the equations obtained in this study are very significant for studying in vitro the electromagnetic bioeffects on cells in suspensions which are usually used at a density between about 10^3 and 10^8 cells/mL ($0 < f_o \leqslant 0.6$).

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外电场作用下悬液中细胞膜损耗功率计算模型

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摘要: 由于细胞间相互作用的复杂性使得建立外电场作用下悬液细胞膜损耗功率计算模型非常困难, 提出了用场近似等效方法解决该建模难题. 基于有效介质理论, 用等效原理, 研究了外电场作用下悬液细胞跨膜电压变化规律, 然后确定细胞膜内电场分布. 最后根据焦耳定律, 建立了外电场作用下悬液细胞膜损耗功率计算模型. 模型表明: 对直流和低频场, 悬液细胞膜的能量损耗主要为导电损耗; 当外加频率超过细胞膜的弛豫频率时, 介质损耗占主导部分.

关键词: 损耗功率; 计算模型; 细胞悬液; 外加电场

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