NUMERICAL STUDY OF THE ELECTRIC POLARIZATION OF SPHERICAL CELLS SUSPENDED IN ELECTROLYTIC SOLUTION

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Abstract: The equivalent circuit method (ECM) was applied in the analysis of the membrane potential distribution in spherical membranes suspended in electrolytic solution. Numerical results are in agreement with the analytical cosine distribution for a single membrane in an uniform electric field. However, for a suspension of membranes, the numerical results show that the potential is distorted from the cosine distribution, with the major reduction occurring around the poles. The pole membrane potential was observed to decrease linearly with the increase of the volumetric fraction occupied by the cells. Furthermore, the conductivity of the suspension also was obtained as a function of the volumetric fraction and the results are in good agreement with the Maxwell model for spherical particles suspended in conductor liquid.

Key words: field calculation, numerical modeling, biological membranes, bioelectromagnetism.

Introduction

Cell membranes are very thin structures constituted basically by a bi-layer of lipidic molecules. Because the non-polar tails of these molecules fill the inner volume of the membrane, the energy barrier for ions crossing it is very higher than the averaged thermal energy in living systems [1], and the electrical conductance of the cell membrane is usually very low.

When biological tissues or suspensions of cells are excited by electric fields, ionic currents are established and ions coming from the electrolyte accumulate on the both sides of the membranes. Therefore, membranes are polarized and the potential distribution depends from the strength of the applied field and geometry of the cells. For a single spherical cell with radius ‘a’ immersed in a conductor liquid under an uniform electric field with strength ‘E_o’ applied in t=0, the membrane potential is given by [2]:

\[ V_m = 1.5\ a\ E_o\ \cos\ \theta\ \left(1-e^{-1/\tau}\right) \]  

(1)

where \( \theta \) is the angle between the direction of the field and the position vector of the point on the membrane relative to the centre of the cell. The time constant is given by [2]:

\[ \tau = a\ C_m\ \left(\frac{1}{\sigma_i} + \frac{1}{2\ \sigma_o}\right) \]  

(2)

where \( \sigma_i \) and \( \sigma_o \) are the conductivities of the electrolyte inside and outside the cell, respectively, and \( C_m \) is the capacitance per unit area of the membrane.

For cells suspended in an electrolytic solution, the membrane potential is different from the cosine distribution given by (1) because the proximity between cells distorts the current distribution in the interstitial space close to the membranes. The membrane potential is also a function of the volumetric fraction occupied by the cells and it is very hard to obtain it by any analytical method. Numerical approaches are better to do it.

Electrical stimulation of the plasmatic membrane can have important effects on the morphology and physiology of the cell. One of the most studied and utilized is the electroporation, which is the pore opening process that occur in the lipidic matrix of the membrane when an enough membrane potential is induced by the external field [3].

Method

The equivalent circuit method (ECM) [4,5] is a numerical approach suitable for field calculation in inhomogeneous and anisotropic media. It is based on the modeling of the transport properties of the media by means of an electric circuit whose elements are associated to a discrete mesh of regular blocks that fill the analyzed space (Figure 1a). Each block is modeled as a node of the equivalent circuit. In the cell scale model (Figure 1b), which is suitable for analysis around cells, the total current between two adjacent blocks in the mesh is described as having three components: conduction, diffusion and shift currents, and it is given by the equation [5]:

\[ I_{on} = \sum_k [g_k \left(V_o - V_n\right) + k_{diff} \rho + \nabla]\frac{\delta}{\delta t} \left(V_o - V_n\right) \]  

(3)

Where the nodes are identified by ‘o’ and ‘x’ and \( n \) indicate summation over all types of ions in the media surrounding the cells. \( V \) and \( \rho \) are respectively the voltage and charge density in the node while \( g \), \( k \) and \( c \) are the conductance, diffusion coefficient and capacitance of the connection, respectively. These parameters are given by [5].
\[ g_n = \mu_n \rho_n A/L \]
\[ k_n = f_n \cdot D_n A/L \]
\[ c = \varepsilon A/L \]  

Figure 1 – (a) Discretization scheme used in the MCE. Each block is represented by a node in the equivalent circuit. (b) Equivalent circuit with the lumped elements modeling the transport process in the media.

where \( \mu_n \) and \( D_n \) are the mobility and diffusion coefficient of the ion ‘n’, respectively, and \( \varepsilon \) are the electrical permittivity of the media. \( A \) and \( L \) are, respectively, the area and length of the connection between two adjacent nodes. \( f_n \) is a function of the voltage difference between the nodes. It is obtained from the spatial averaging of the Nernst-Planck equation supposing that the current density is uniform in the area \( A \) and the voltage varies linearly along the length \( L \). Its value is given by [5]:

\[ f_n = \frac{\Delta V}{v_n} \exp \left( \frac{\Delta V}{v_n} \right) + \frac{1}{2} \frac{v_n}{v_n} \exp \left( \frac{\Delta V}{v_n} \right) - 1 \]  

Where \( v_n = K^T/e \rho_n \) is a constant for each type of ion in the media.

The ECM consists in obtaining and analyzing the equivalent circuit of the media aiming to obtain the electric potential and charge density distribution in the space, in time steps, from specified initial and boundary conditions. The potential distribution is obtained from the computation of the node equations system and the charge distribution is obtained by finite integration of the continuity equation in each block of the mesh.

A schematic view of the cells suspended in the electrolytic solution is shown in the Figure 2. The discretization mesh was built having two levels of resolution. A big block regular mesh was defined using a cubic block with edge equal \( r_c/12 \) as the unit of discretization, where \( r_c \) is the cell radius. Around the membranes a high resolution mesh was defined dividing each big block in eight small one. This procedure is necessary for a good definition of the geometry of the membranes and the interstitial spaces. The distance between neighbor cells was varied in a set of 10 simulations in order to obtain several values of the volume fraction from 0 to 0,66. The volume fraction is the ratio between the internal volume of the cell and the specific volume occupied by the cell in the suspension. The final number of blocks varied from about 23,740 to 35,570. Table 1 summarizes the geometry, composition and electrical properties of the media.

The electrolyte is an aqueous solution of five types of ions: Na, Cl, K, HCO\(_3\) and proteins. Their concentrations are given in Table 1. Proteins are considered as having mobility zero, and they are included only for equilibrating the total charge of the electrolyte.

![Figure 2 – Schematic structure for simulation. A, B and C are three spherical cells. Other cells are not shown because the symmetry permits to limit the analyzed space to the volume defined by the rectangles. The above figure is on the plane z=0 and that below is on the plane y=0. A difference of potential is applied between the faces in x=0 and x=L.](image-url)
(y=0, z=0, y=W, z=W) the normal components of field and current vanish.

The time step for the iterative process was specified in 3 ns according to the rule for convergence given in [5]. The simulation time was 1.2 µs divided in 400 steps. This time is enough higher than 78 ns given by (2), so that, the membrane potential distribution can be consider as reaching the steady state.

Because of the cell A in the Figure 2 has the highest number of neighbors in that scheme (due to the symmetry only two neighbor cells are shown but, there are six), we choice it as the target cell for doing all calculation of the membrane potential and conductivity.

Table 1: Geometric and electric properties of the media

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell radius (µm)</td>
<td>7</td>
</tr>
<tr>
<td>Membrane thickness (nm)</td>
<td>7</td>
</tr>
<tr>
<td>Ionic concentration inside the cells (x10^{-3} M)</td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>10</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>4</td>
</tr>
<tr>
<td>K⁺</td>
<td>140</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>10</td>
</tr>
<tr>
<td>Ionic concentration outside the cells (x10^{-3} M)</td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>143</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>123</td>
</tr>
<tr>
<td>K⁺</td>
<td>5</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>25</td>
</tr>
<tr>
<td>Ionic mobility (x10^{-4} cm² V^{-1} s^{-1})</td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>5,19</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>7,91</td>
</tr>
<tr>
<td>K⁺</td>
<td>7,62</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>7,40</td>
</tr>
<tr>
<td>Dielectric constant of water</td>
<td>81</td>
</tr>
<tr>
<td>Membrane capacitance (µF cm⁻²)</td>
<td>1</td>
</tr>
</tbody>
</table>

Results

Figure 3 shows the potential distributions on the membrane of the target cell as functions of the angle between the direction of the field and the position on the membrane, for three values of the volumetric fraction, and the theoretical curve for an isolated cell according equation (1). The curves are normalized to the highest potential on the pole of the cell (V_{m0}=1.5 a E_o). (*) p=0.66; (O) p=0.44; (□) p=0.31; (—) equation (1).

Figure 4 shows the normalized potential on the pole of the target cell in function of the volumetric fraction of the suspension.

Using the obtained spatial distributions of charge and potential we calculate the averaged value of the current density and electric field in the specific volume of the target cell. With these values we can obtain the conductivity of the suspension. Figure 5 shows the obtained dependence of the conductivity to the volume fraction.

Analysis

In the Figure 3 we see that as the suspension becomes more concentrate, the membrane potential is reduced on the pole and distorted from the cosine distribution. This happens because ionic currents arriving to the pole of the cells are reduced as they are closer to each other.

In the Figure 4 is observed a linear decrease of the potential as the volumetric fraction increase. This trend of the membrane potential is not possible to account analytically, mainly for a volumetric fraction as high as 0.50 or more. This relation between V_{m} and p can be useful for obtaining the threshold of electroporation in suspension of different concentrations of cells. According to the Figure 4, the potential on the pole of the cell can be given by:

\[ V_m = 1.5 a E_o (1 - 0.38 p) \]  

(6)

If the threshold electric field E_{p1} for electroporation is measured for a known value of the volumetric fraction (p_1), the threshold E_{p2} for another value (p_2) can be given by:

\[ E_{p2} = \frac{E_{p1}}{\frac{C_{p2}}{C_{p1}}} \]

Figure 3 – Normalized potential distributions on the membrane of the target cell as functions of the angle between the field direction and the position on the membrane. V_{mo} is the potential on the pole of a single cell (V_{mo}=1.5aE_o). (*) p=0.66; (O) p=0.44; (□) p=0.31; (—) equation (1).

Figure 4 – Normalized potential on the pole of the target cell in function of the volumetric fraction of the suspension. V_{mo} is the potential on the pole of a single cell (V_{mo}=1.5aE_o). The circles are the numerical results. The continuous line is the trend of the results.
\[
\frac{E_{p2}}{E_{p1}} = 1 - 0.38 \frac{p_1}{p_2}, \quad (7)
\]

The continuous line in the Figure 5 is the theoretical model from Maxwell for dielectric spherical particles suspended in liquid conductor, which is given by [6]:

\[
\frac{\sigma}{\sigma_o} = 1 - p_1 \frac{p}{1 + p/2}, \quad (8)
\]

This excellent agreement between analytical model and numerical results corroborates the reliability of the numerical method. The equation (8) can be used to estimate the volume fraction of the suspension from a measured conductivity.

\[\text{Figure 5} \quad \text{Dependence of the conductivity to the volume fraction of the suspension.} \quad \text{\sigma}_o \text{ is the conductivity of the electrolyte outside the cells. The circles are the numerical results. The continuous line is related to the model proposed by Maxwell for dielectric spherical particles suspended in conductor liquid [6].}\]

**Conclusion**

The ECM was applied to solve the relatively complex problem of the polarization of spherical membranes suspended in an electrolyte. The numerical results revealed an important and simple relation between membrane potential and volumetric fraction. That relation can be useful when a good estimate of the membrane potential is necessary as in electroporation studies of suspended cells.

The agreement between numerical calculated conductivity and the equation (8) from Maxwell model is a warranty of reliability of the method. Another important agreement happens between the numerically obtained membrane potential for a single cell and the equation (1) [7].

Future works will be dealing with the electroporation modeling using ECM and the application on living tissues.

**References**


