Maxwell stress field induced biological cell deformation in an electric field stimulated medium

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Statement of Purpose: In the recent research by our group, we have demonstrated the influence of electric field (E-field) on cell functionality *in vitro*. Especially, cell morphological changes and enhanced proliferation are observed in a narrow range of E-field stimulation conditions (A. K. Dubey, J. Biomed. Mat.Res-B,98;1;2011 18-29). In an attempt to rationalize such observed experimental observations, we provide here a theoretical model proposing the development of Maxwell stress induced cell deformation in an electric field stimulated medium. The effect of other relevant factors like membrane surface charge density, substrate conductivity are considered in the model. Apart from the physical effects such as deformation, the current study also considers the electrohydrodynamic effects in the presence of external E-field in the vicinity of the cellular micro-environment and its biophysical significance in cell signaling and communication *in vitro*.

Methods: The cell is modeled as a double layered membrane separating intracellular region and extracellular regions with different dielectric properties. The direction of electric field is considered such that the system axisymmetric. To simplify the physical situation, a few assumptions are made: (i) The cell is assumed to be spherical and in a metabolically active state, (ii) The cell is exposed to homogenous E-field, (iii) The dynamic ion-transport mechanism due to the E-field are not considered, (iv) The effect of cell fate processes like division, necrosis and apoptosis are neglected and (v) Cell adhesion on the substrate is not considered. The electric potential in this system is described by the Poisson-Boltzmann equation and subsequently linearized by using Debye Huckel approximation. With the application of appropriate boundary conditions, the potential and electric field in the intracellular and extracellular regions are determined. The Maxwell stress tensor is calculated based on the electric field distribution in the respective regions as a function of multiple parameters like cell size, intracellular and extracellular permittivity and electric field strength,

$$\sigma_{kl} = \varepsilon\left(E_k E_l - \frac{1}{2}\delta_{kl}\|E\|^2\right)$$

where σ is the component of stress tensor, ϵ is the permittivity of the medium, E is the electric field and δ is the Kronecker delta.

Results: The system is solved for a cell with and without membrane surface charge density. In addition to this, the cell is considered to be in a suspension/on a conducting substrate and on an insulating substrate, to determine the effect of substrate conductivity. To obtain results relevant to the existing experiments, values for electric field (100V/m) typically observed to enhance cell functionality *in vitro* (A. K. Dubey; J. Mat. Sci.; 2013;1-10) and typical values for permittivity in the intracellular region, $50\epsilon_o$ and extracellular region $80\epsilon_o$ have been used. The stress experienced by a cell of size 25μm with a membrane surface charge density of 10^{-5} C/m^2 is determined of the order of 100mPa, a value much higher (5 orders) than for a membrane without surface charges. Qualitatively, based on the stress moments, it has been determined that when a cell is considered to be in a suspension/conducting substrate, it tends to deform parallel to the direction of electric field, resulting in a prolate shape. Whereas, when an insulating substrate is considered, the deformation is found to be in the direction perpendicular to the electric field, resulting in an oblate shape (Fig.1). Though the distribution of stresses is different when an insulating substrate is considered, the values of the stresses are found to be of the same order of magnitude. Electrohydrodynamic effects which manifest as convection flows have been determined through Oseen tensor formulation and flow velocities of 1μm/s have been determined in both cases (conducting and insulating substrate).

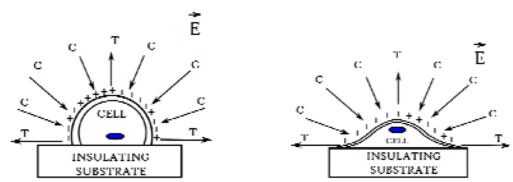

Fig.1: Schematic illustrating deformation of cell to an oblate shape

Conclusions: The presences of surface charges are found to significantly alter the stresses at the membrane, highlighting the importance of the surface charges in a biological cell system. Depending on the substrate and the direction of the E-field, the deformation of the cell is qualitatively different, which is justified by recent experimental observation of enhanced cell functionality on conducting biomaterial substrates under the influence of E-field G. Thrivikraman, Biomaterials; 34;2013). Another aspect that has to be highlighted is the secondary effects such as the convective flows due to the stresses which are found to result in a greater flux of molecules/ions than when diffusion is the only mechanism in action. This phenomenon, called Electrokinectic flow would result in enhanced transport of signaling molecules compared to diffusion.