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Computational 3D Model of in-vitro Cell Stimulated by Electric and Magnetic Fields

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Abstract - **This work presents the development of 3D computational models that represent two studies about in-vitro cellular experimentation of cell stimulated by magnetic and electric field. The development considered the construction of the stimulation devices, the cell seeding, and the creation of the 3D computational models representing the arrangements. The models and their electromagnetic analysis were done in the ANSYS program. The volumes considered were: source of stimulation, Falcon cell culture plate, cell content, and space for zero potential. The electric field stimulation model considered an applied electric field between 250 V/m and 1 kV/m. While the magnetic field stimulation model considered an applied magnetic field between 0.5 mT and 2.0 mT. For both models, the frequency range was between 5 Hz and 105 Hz. As a result, the error between the stimulation devices and the created models was lower than 5%. The homogeneous area of the magnetic and electric field was established and the behavior of field strength produced by the stimulation devices was the expected one. In both models, the induced current density was the variable evaluated in the cellular material. The current density induced by the applied magnetic field was greater than by the applied electric field.**

I. Introduction

The use of therapy with electromagnetic fields (EMF) continues to be presented as one alternative to pharmacological treatments without the side or toxic effects. The EMF are used in different treatments against skin ulcers generated by pressure [1], vascular insufficiency, trauma, diabetes or surgery [2,3], and cancer [4]. The cellular response to electromagnetic stimuli seems to be associated with: an increase in circulation; decrease in edema; increase in epithelial cells migration, neutrophils and macrophages; mast cells inhibition; DNA synthesis stimulation; and increase in growth factors [5]. Also, the EMF increase the fibroblasts production, bacterial inhibition, debridement, and restoration of bioelectric potential of healing [3,5].

The experimental evidence found in EMF application at cellular level indicates that is necessary the development of computational models to estimate the induced variables in cell cultures and associate the applied signals with the biological behavior. This will allow to find relationship patterns to obtain reduction of time, money, and procedures. The authors have conducted research in *in-vitro* computational models and experimentation, [6] and clinical studies and computational models [7-9].

This work presents the development of 3D computational models that represent an in-vitro cell culture stimulated by magnetic and electric field. The development considered the construction of stimulation devices, cell seeding, and creation of the 3D computational models representing the arrangements which the induced variables were studied. The models and their electromagnetic analysis were done in Ansys. The considered volumes were the source, the Falcon cell culture plate, the cell contents, and space for zero potential. The model for stimulation with electric field considered field strength between 250 V/m and 1 kV/m, and between 0.5 mT and 2.0 mT for magnetic field model. For both models, the frequency range was between 5 Hz and 105 Hz. The induced current density was the variable evaluated for both cases. As a result, the error between the stimulation devices and the created models was lower than 5%. The homogeneous area of the magnetic and electric field was established and the behavior of field strength produced by the stimulation devices was the expected one.

II. Methodology

The *Instituto Tecnológico Metropolitano (ITM)*, and the *Universidad del Valle* developed two in-vitro studies of epithelial cells stimulated by electric and magnetic fields. The experimental design included the design and construction of stimulation equipments, cell stimulation, and development of a computational model for each type of stimulation. Fig. 1 shows the experimental design.

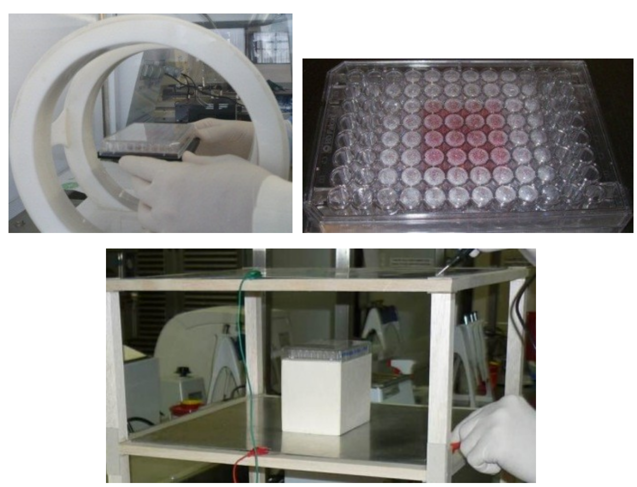

Figure 1. Cellular stimulation with magnetic and electric field

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The computational models were developed in the Ansys program to validate the stimulation devices built. Later, representative geometries of the Falcon cell culture plate and the stimulated cell material were included. The simulations were done for different intensities and frequencies of electric and magnetic field. The electric field (for the electric field model), magnetic field (for the magnetic field model), and induced current density (for both, electric and magnetic field) were the variables estimated in the cellular material.

A. Computational model of cell stimulated by magnetic field

The magnetic field source was a 12.5 cm radius Helmholtz coil (stimulator device) to guarantee a homogeneous area of magnetic field. The magnetic field stimulator device model can modify the coil radius, applied magnetic field, and frequency. The used properties were electrical resistivity, magnetic permeability, and relative permeability, this last one with a value of 1. The properties were considered isotropic and it was not considered the permittivity. The properties were taken from literature. The magnetic field applied was between 0.5 and 2.0 mT in the frequency range of 5 Hz to 105 Hz. The simulation data were compared with the obtained values from the technical proof to the equipment.

The computational model of the coil-cell system was formed by four parts: the Helmholtz coil (source), the Falcon cell culture plate, solid cylinders representing the cellular content, and a large enough cylinder for the assignment of the zero potential. Due to computational limitation, only 36 of the 96 wells were constructed. Sixteen wells containing cellular material (Fig. 1). The magnetic field generated by the source was unidirectional to the Z axis (perpendicular to the cellular monolayer). The induced variables evaluated in the cellular material were the magnetic field and current density.

B. Computational model of cell stimulated by electric field

A pair of parallel electrodes was the electric field source. It was designed and built according to the IEEE Std 1308-1994 [10], in order to guarantee the homogeneous electric field in the same area of homogeneous magnetic field. The electrodes dimension was 40 cm x 40 cm (representing the electric field stimulator). The electric field stimulator device model can modify the electrodes dimension, electric field intensity, and frequency. The considered properties were: the dielectric permeability, the electrical resistivity, and the relative permeability. The properties were taken from literature. The electric field applied was between 250 V/m to 1 kV/m in the frequency range of 5 Hz to 105 Hz. The simulation data were compared with the expected values of the equipment.

The geometry of the cell-electrode full system was compound by four parts: the parallel electrodes (source), the Falcon cell culture plate, solid cylinders representing the cellular content, and a big enough sphere for the assignation of zero potential. The model of electric field stimulator was analyzed in three ways: a) only electrodes, b) electrodes with Falcon cell culture plate in their center, without cellular content, and c) complete set of electrodes with Falcon cell plate and cellular contents. This was done to evaluate the behavior of electric field even with the presence of the Falcon cell culture plate. In the model, only 36 of the 96 wells were considered. Sixteen wells containing cellular material were located in the homogeneous area electric field, in order to establish the same conditions of the magnetic field stimulation. As for the magnetic field, the applied electric field was unidirectional to the z axis (perpendicular to the cellular monolayer). The induced variables evaluated in the cellular material were the electric field and current density.

III. Results

A. Computational model of cell stimulated by magnetic field

Fig. 2 shows the magnetic field stimulator and its representation in the computational 3D model. The maximum error found between the measured and calculated values was 4.4%. The built equipment presented stability in the signal with changes of frequency.

Figure 2. a) Magnetic field stimulator and b) computational 3D model

Fig. 3 shows the homogeneous area of magnetic field of the equipment (calculated) and the magnetic field strength along the line A, for an expected value of 2 mT. Fig. 4 shows the built mesh of the cell-coil system and the contour map of induced magnetic field in the cellular material. Fig. 5 compares the induced current density at different frequencies for two values of applied magnetic field.

B. Computational model of cell stimulated by electric field

Fig. 6 shows the electric field stimulator and its representation in the computational 3D model. The maximum error found between the measured and calculated values was 0.22%. The built equipment presented stability in the signal with changes of frequency.

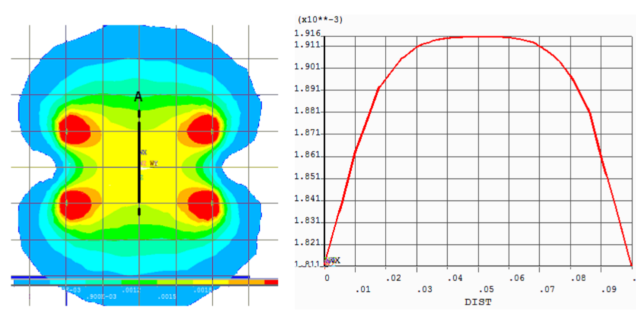

Figure 3. Magnetic field contour map and field strength along the line A

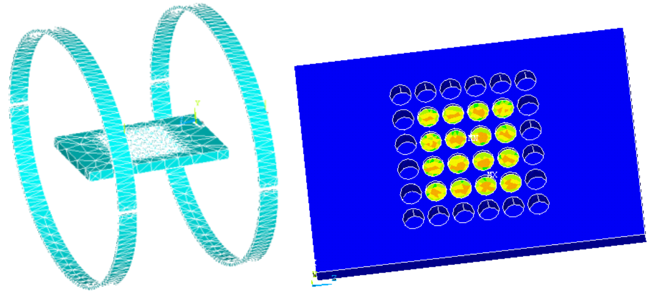

Figure 4. Computational model of the cell-coil system, a) meshing creation; b) induced magnetic field in the cellular material

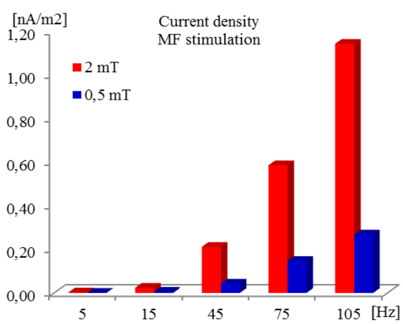

Figure 5. Induced current density for two values of applied magnetic field vs. frequency

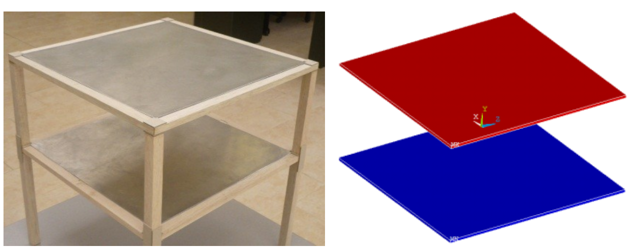

Figure 6. a) Electric field stimulator and b) computational 3D model

The electric field stimulator model was analyzed in three ways: a) only electrodes, b) electrodes with Falcon cell culture plate in their center, without cellular content, and c) complete set of electrodes with Falcon cell plate and cellular contents. Fig. 7 shows the homogeneous area of electric field and the field strength along the dotted line for a) condition. Fig. 8 and 9 show the electric field contour map and field strength along the lines A and B for b) condition and c) condition, respectively. Fig. 10 compares the induced current density at different frequencies for two values of applied electric field.

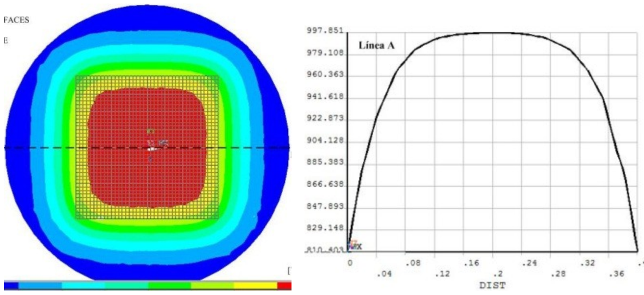

Figure 7. Electric field contour map and field strength along the dotted line

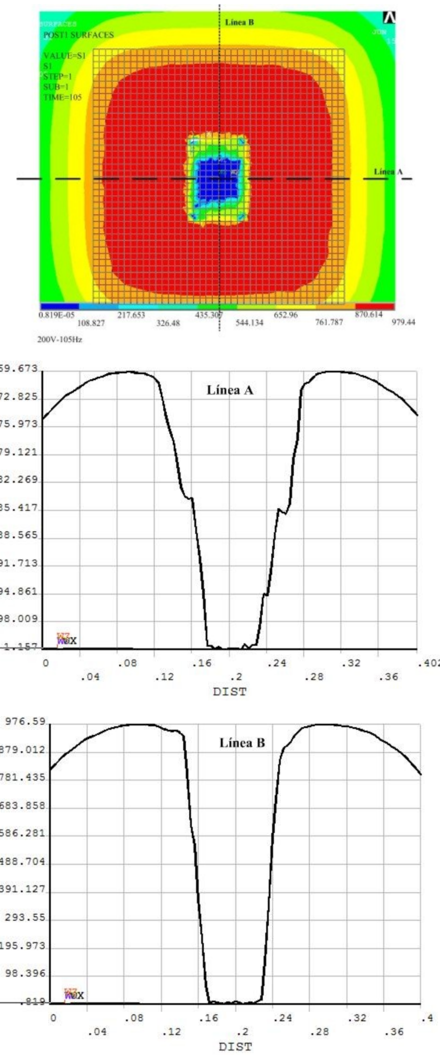

Figure 8. Homogeneous area of electric field and field strength along the dotted line (electrodes and Falcon cell plate)

We can observe that the induced current density was higher for the applied magnetic field than for applied electric field. The induced current density presented more significant changes from 5 Hz to 105 Hz for the stimulation with electric field with increases between 600 times for the different voltages values, while when it was stimulated by magnetic field, the increase was found about 450 times to 105 Hz over 5 Hz.

IV. Conclusions

The 3D stimulation model of electric field allowed to observe the proximity and non-uniformity phenomena. Although induced current density by magnetic stimulation was up to 103 times superior than the induced one by stimulation with electric field (for the study values), for stimulation with electric field it was presented a superior growth rate when the frequency increases.

The aim of building a computational model was that it allowed the representation of an in-vitro experimental study. It was the beginning of studies in which the behavior of induced signals in cells submitted to electromagnetic fields could be estimated. In order to give continuity to the validity of the created model is now necessary to detect better ways to measure electrical and magnetic properties of cellular systems. With a better model, it can be computationally determined the induced electrical variables of interest, before the experimental developments, saving research time, and money.

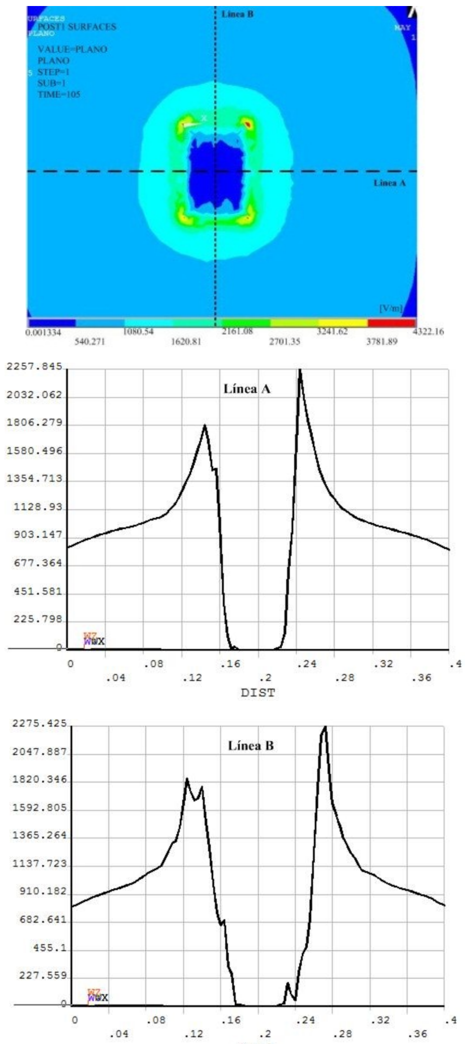

Figure 9. Homogeneous area of electric field and field strength along the dotted line (electrodes and Falcon cell plate with cellular content)

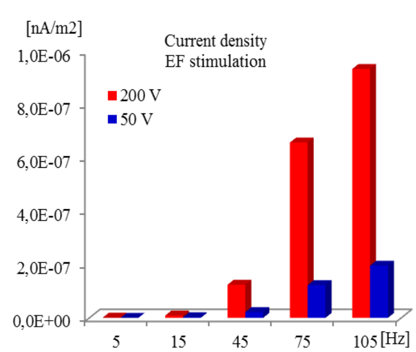

Figure 10. Induced current density for two values of applied electric field vs. frequency

Acknowledgment

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