Simulation of Electrode-Tissue Interface with Biphasic Pulse Train for Epiretinal Prosthesis

S. Biswas[*1], S. Das[1,2], and M. Mahadevappa[2]
[1]Advaced Technology Development Center, Indian Institute of Technology, Kharagpur, India,
[2]School of Medical Science and Technology, Indian Institute of Technology, Kharagpur, India.
*Corresponding author: satarupa.biomed@gmail.com

Abstract: Retinitis Pigmentosa (RP) and Age-related Macular Degeneration (AMD) are diseases causing blindness in a large number of people. In this type of degenerative disease, mostly the photoreceptors are damaged, and thus attempts have been made to electrically stimulate the surviving inner retinal neurons and retinal ganglion cells (RGC) in order to restore vision. In this paper, the electrode-tissue interface is modeled to study the effect of electrode size and distance between the electrode and retina by applying biphasic pulse trains similar to in-vitro experiments and in-vivo trials. Simulations were carried out using the AC/DC module of COMSOL v4.3a with planer electrodes placed over the constitutive layers of retina. Biphasic pulses with varying pulse width, inter pulse interval and amplitude were applied to the stimulating electrode. The model is solved for time and frequency domain. Electric potential in the RGC layer was found to vary both as a function of electrode diameter and distance of the electrode.

Keywords: Epiretinal prosthesis, biphasic pulsetrain, tissue impedance, electrode.

1. Introduction

Retinitis Pigmentosa (RP) is the name given to a group of inherited eye diseases that causes breakdown of the photoreceptor cells of the retina. The other common disease affecting the photoreceptors over the age of 50 is age related macular degeneration (AMD). Since both the diseases are degenerative in nature, with treatment they can be slowed down but never cured; rather it progresses to complete blindness. Millions of people all over the world lose vision due to these diseases. But Stone et al. [1] showed that between 30% and 80% of the retinal ganglion cells (RGC) and neurons of the inner nuclear layer remains intact and functional in AMD and RP respectively. Thus attempts have been made to bypass the natural photoreceptor process and stimulate all or some of the ganglion cells in order to restore vision to some extent. Visual perception, called "phosphenes" could be elicited in human trials by electrically stimulating the inner surviving RGC layers first shown by Brindley and Lewin [2]. This type of prosthesis attached close to the RGCs was termed as epi-retinal prosthesis. Humayun and his co-workers [3,4,5] and Rizzo et al [6] are among the few groups working with Multi-electrode arrays (MEA) for improving the quality of perception. Starting with four electrodes, currently researchers use a sixty electrode array for better temporal and spatial resolution. This, on human trial, was able to differentiate basic forms of motion, perceive light and dark and even shoot baskets. [7]

In-vitro studies are being carried out with isolated animal retina in order to record the responses from the ganglion cells while experimenting with the input pulses for better spatial and temporal resolution. Threshold current and charge densities could be obtained directly from the tissues [8]. Further, finite element modeling of the electrical response is also attempted by a few groups of researchers mostly to optimize the electrode design [9,10]. The issues under consideration were mainly the electrode size which will produce a better threshold maintaining the safe charge density limits, impedance between the electrode and retina and also the distance between the electrodes to reduce interference of the signals.

In this study, the electrode-tissue interface is modeled with varying electrode diameters. The input pulse train produced an electric field across the tissue layers. These retinal tissue layers are modeled with dimensions close to the human retinal tissue structured layers. The biphasic pulse train also resembles the pulses actually used in clinical trials. Recent studies have found both amplitude and frequency have effects on percept size [11]. Therefore, this study can elucidate on the electric field and charge distribution due to the application of such

modulated bi-phasic pulses across the tissue layers. This along with impedance measurement across the layers can throws light to the proper positioning of the electrodes during implantation so that either single cells or a group of cells can be targeted with necessary threshold values as required for stimulation.

2. Methodology

The simulation was done considering the retinal layers having inhomogeneous characteristics with the total thickness of 605µm. The different layers include RGC layer (22µm), inner plexiform layer (23µm), inner nuclear layer (27µm), outer plexiform layer (16µm), outer nuclear layer (31µm), sub-retinal space (40µm), retinal pigment epithelium (20µm) and choroid (426µm)[9]. Each layer has different resistivity values obtained from C. Karwoski et al [12]. The electrodes were separated from the retina by the vitreous layer (10-50micron). The parametric sweep function was used to vary the diameter of the electrode from 10µm to 50µm, 50µm to 100µm and then from 100µm to 500µm with the center-to-center spacing of 100µm for 10µm diameter and increasing proportionally with increase in diameter. The height of the electrode was taken as 1 micron in 2D model. The electrode material properties were selected assuming them to be platinum electrodes and the substrate as polymide.

2.1 Time domain study

The biphasic pulse train was generated using piecewise function which was made periodic and continuous within a time limit. The pulse width, amplitude and inter-pulse delay was varied accordingly to vary the amplitude and frequency of the pulse train. This pulse was given at the terminal of the electrode-tissue model as a current input. The output response was evaluated at a point on the RGC layer below the stimulating electrode.

2.2 Frequency domain study

The impedance between the electrode and the retinal tissue was obtained at different frequency values varying from 1 to 10^5 Hz. For impedance study a constant current input of 100uA was used. Dependence of electrode size was considered in this study also.

3. Use of COMSOL Multiphysics

The Electric Current physics of AC/DC module is used for solving the 2D model of electrode tissue interface. The inhomogeneous nature of the tissue layers is incorporated by selecting the material properties like electrical conductivity and relative permittivity according to the experimentally obtained values [12].

3.1 Equations involved

Considering electric current in a conductive media, the model solves the continuity equation with a current source Q_j given in equation 1.

$$\Delta . J = Q_j \quad (1)$$

where, J is the current density. For the time dependent study, it solves for equation 2

$$J = \sigma E + \frac{\partial D}{\partial t} + J_e \quad (2)$$

Where, σ is the conductivity of the medium, D being electric displacement, J_e is the external current density.

3.2 Boundary conditions

The relevant interface condition at interfaces between different media and interior boundaries is continuity; that is,

$$n_2 . (J_1 - J_2) = 0 \quad (3)$$

which is the natural boundary condition.
Apart from that there is an electric insulation of the model from the external environment which means that no electric current flows into the boundary.

$$n . J = 0 \quad (4)$$

The initial value taken to solve the problem was potential V2=0
At the electrode surfaces, one was marked as ground electrode with V=0 and the other

stimulating electrode where the biphasic current pulse was given as stimulus input.

4. Results and Discussions

The activation criterion for the retinal ganglion cells in this study was considered to be around 1500V/m above which the neurons will be able to generate action potentials. Charge density was well below the safe limit of 0.35mC/cm2 for platinum electrodes.

4.1 Electric potential distribution

From the literatures available, it could be seen that electrodes with very small diameters are not often used due to excessive charge density which can damage the tissues. Also, they are used for targeting single neuron. Most of the in vivo experiments were performed with diameters above 150µm. In this simulation study, a wide range of diameters was considered keeping other factors constant to observe the effect of electrode size on the electric field created in the retinal tissue layer, mostly over the RGC layer. Figure 1 shows the distribution of electric potential across the retinal layers for the applied biphasic pulse with 200µm diameter electrodes. This distribution is at a time when the pulse reaches positive potential. A point below the stimulating electrode was selected to evaluate the potential reaching that point through the vitreous layer. For electrode diameters 10µm to 50µm, there was a decrease in electric potential at the point of evaluation on the RGC layer. Upto 100µm, the variation was visible. But beyond 100µm the change was not distinguishable. In other words, there was an exponential decrease of potential with increasing diameter. Figure 2 shows the variation of potential with electrode diameters varying from 10µm to 50µm. Results also showed that the potential increased with decrease in distance from the electrode i.e., higher potential will be developed as the electrodes are moved towards the retina.

4.2. Variation of Pulse train

The pulse duration or pulse width, amplitude of the pulse or applied current, the interpulse interval and the frequency were modified for the input pulse at the terminal.

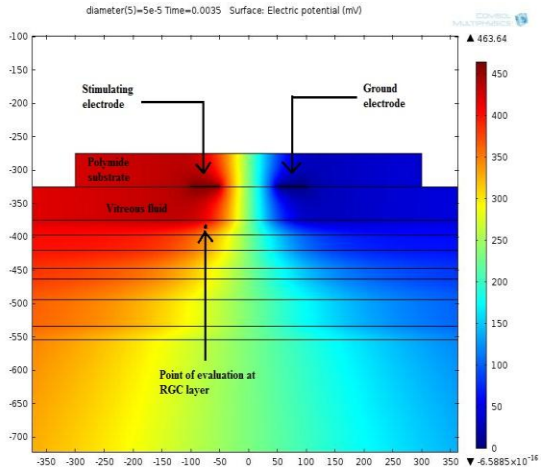

Figure 1. Electric potential distribution across the retinal layers at the onset of positive cycle of the biphasic pulse

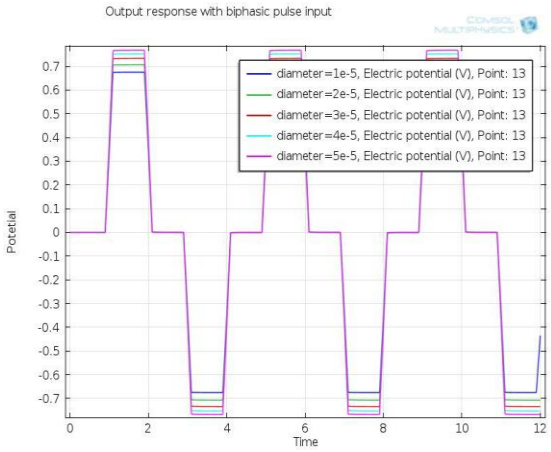

Figure 2. Variation of electric potential with diameter of electrodes ranging from 10 to 50 µm at the point of evaluation on the RGC layer.

With increasing amplitude, a proportional increase in output voltage was observed. Figure 3 shows the effect of increasing the interpulse delay. The duration of delivering maximum charge decreased with increase in interpulse delay. When the interpulse delay is small, during changing of phase, it tends to zero but never reaches a zero. With little variation in frequency, no major change could be observed. Due to certain computational limitations, very high frequency pulses could not be studied yet.

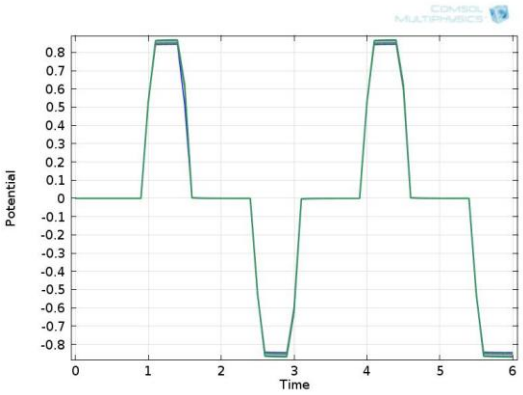

Figure 3. Output response at the point of evaluation with increased delay in the input pulse

4.3. Impedance Study

The electrode tissue impedance was observed with varying frequency (1-10^5 Hz). The impedance varied to a large extent with the variation of vitreous thickness below 1 kHz whereas dependence was found to be at minimum above 10 kHz shown in figure 4. In-vivo experiments with rat retina using OCT for measuring impedance have shown similar trends. Aditi et al used 75µm diameter inner pole of a concentric bipolar Pt/Ir electrode as stimulating electrode and the 300µm diameter stainless steel outer pole of the electrode was used as the return electrode [13]. There was a steep gradient till around 10 kHz and a flat zone after that. As shown in figure 4, below 1 kHz, impedance value was maximum for the least distance of 10µm.

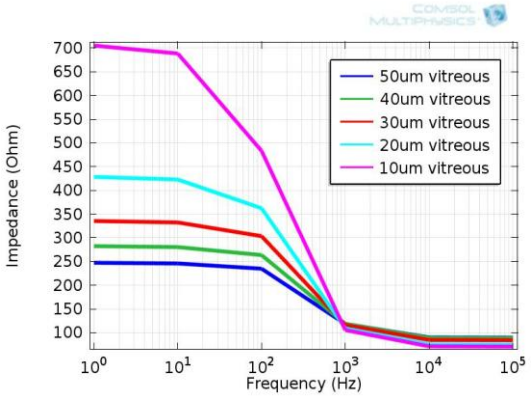

Figure 4. Impedance within the retinal layer with varying distance from electrode.

But with 20 µm distance and above, there was a gradual decrease in impedance. There is a sharp decrease in impedance with frequency over 1 kHz. Impedance varying as a function of distance between the electrode and the retina is also in accordance with the experimental results [13].

5. Conclusions

A theoretical study of simulations on electrodes for epi-retinal prosthesis is presented in this paper. The various parameters for stimulating retinal tissues are taken into consideration. The effect of electrode size on stimulation current was observed. For electrode diameters 10µm to 50µm, there was a sharp decrease in electric potential up to about 35% while beyond 200µm the change was not quite distinguishable due to exponential decrease. The impedance within the retinal tissue, which can serve to determine proximity of electrode, was also studied. Impedance was found to be a function of frequency as well as distance from the electrode. The input biphasic pulse, similar to those used in clinical trials, was varied to observe their effect. Input current amplitude variation caused proportional variation in output voltage. Increased interpulse delay caused decreased peak stimulation time. Experimental studies have suggested variations percept size due to both amplitude and frequency. Therefore, it is expected to reflect in simulations as well. This study thus throws light on the electric field and charge distribution due to the application of bi-phasic pulses across the tissue layers. The variation in frequency will be taken up in future studies. With further extension to 3D geometry, it will be possible to optimize the electrode geometry for better performances of the retinal implant.

6. References

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7. Acknowledgements

Satarupa Biswas thanks Debashis Maji and Debanjan Das, research scholars of BIOMEMS Lab, SMST, Indian Institute of Technology, Kharagpur for extending their help in solving the model with COMOL Multiphysics.