NEURAL SIGNALLING MODELLED WITH FINITE ELEMENT METHOD

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INTRODUCTION

Neural implants like visual prosthesis or cochlea implants are based on electrical stimulation of excitable neurons. To investigate the effects of extracellular stimulation of practical devices or to reproduce experimental results, mathematical models simulate the physiological neuronal behaviour. A common approach are Hodgkin-Huxley (HH) like cell models[1], which take the electrical properties of the cell membrane as well as ion channel kinetics in form of probability functions into account. Multi-Compartment model designs are used to implement geometric aspects of neuronal structures. However, besides the physiological cell behaviour, also the consideration of other physical effects might be crucial for a correct reproduction of cellular responses, i.e. geometric relations between neurons and electrodes, generated heat, or influences between the electrode neural tissue. These effects essentially depend on geometry of the neuron and its environment. The finite element method (FEM) provides solutions to solve complex physical interactions in space and time. Therefore, to couple cellular membrane properties with other physical phenomena, a HH cell membrane was realized in the FEM software COMSOL (www.comsol.com). This implementation is used to simulate situations where cellular responses strongly depend on the distribution of the electric field caused by stimulating electrodes, which is not only influenced by the electrodes itself but also by the neurons and their electrical activities (Figure 1).

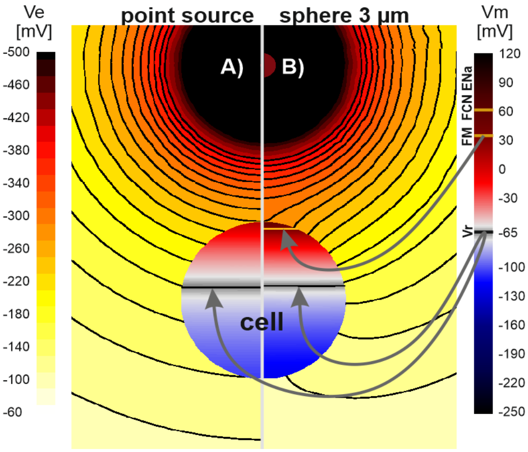

Figure 1: Difference in polarization of a spherical cell and the electrical field between idealized point source current approach (A) and FEM simulation which considers the influence of the cell itself on the electrical field (B)[2].

FUNDAMENTAL OF THE PROBLEM

Many physical phenomena addressed in neuroscience are multidimensional problems which can be described by partial differential equations (PDEs). Classical multi-compartment models are an easy and effective way to solve cellular responses of excitable cells. By utilizing symmetries in space and simplified physics for voltage distribution caused by electrodes, such models are also suitable to simulate complex extracellular stimulation situations. But, depending on the scientific question, there are electrode-neuron geometries which cannot be reproduced by multi-compartment models or assumed simplifications in physics might produce skewed results. This is in contrast to the FEM which allows to couple different physical aspects in a spatial discretized geometry which influence each other. While general electrical behaviour in and outside of a neuron is completely realized by AC/DC physics modules provided by COMSOL, the cellular kinetics were implemented as PDEs using COMSOL mathematical modules an then set as boundary conditions[3,4] at the cell membrane.

RESULTS AND DISCUSSION

Together with other necessary electrical parameters, the transmembrane current density is calculated and induced in the AC/DC physic modules of COMSOL to simulate intra- and extracellular potentials. This approach not only returns the relevant output of a nerve cell model like polarization of the surface or respective ionic currents, it also correctly reproduces the electrical effects of the electrodes and the influence of electrical neural activity on the cellular environment.

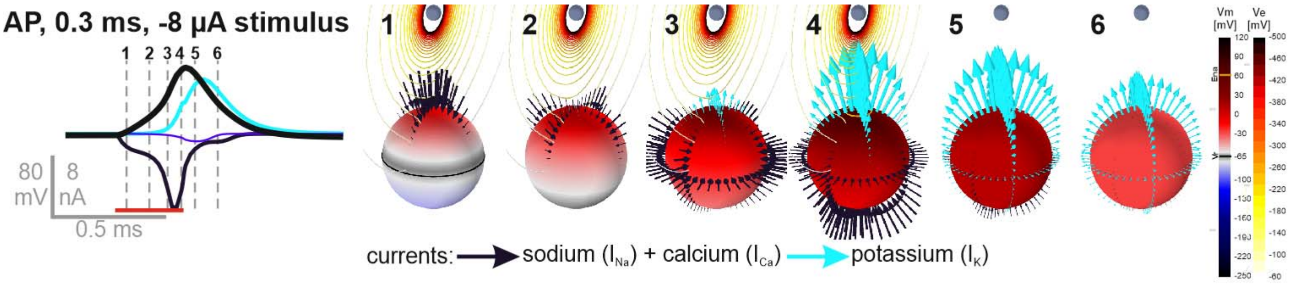

Figure 2: Polarization and ionic currents during an action potential of an extracellularly stimulated spherical cell[2]. Animated videos at: https://figshare.com/articles/Figure_9_Supplement/7624373

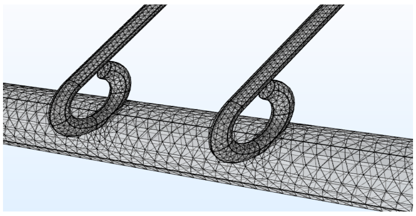

Figure 3: Example mesh of electrode configuration of a stimulated nerve.

Among other model concepts, this method is used to investigate the upper threshold phenomenon and its causes especially for very close electrodes (Figure 2). It has been shown, that for large spherical neurons and/or a very close electrode, the influence of the neuron on the electrical field becomes a non-neglectable factor on the cell behaviour for the investigated phenomenon[2]. In an ongoing study, this model approach is being used to answer actual questions in muscle activation of in-vivo experiments done at the Liverpool John Moores University. Here, the common peroneal nerve is stimulated with two ring electrodes placed as shown in Figure 3. Due to the kind of electrode configuration and the influence of neurons on the electrical field inside the tightly packed nerve, a FEM simulation was chosen to get as meaningful results as possible.

CONCLUSION

The possibility to consider complex 3D geometries of neurons, their environment, and the actual electrode setup in combination with realistic space- and time-dependent physics, allows a precise reproduction of in-vitro or in-vivo experiments. Additional physics as provided by COMSOL are usable together with the implemented membrane kinetics. Disadvantages of this approach are the extremely high computational costs and the complexity of the models.

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