Designing Electrical Stimulation in Hippocampal Prosthetic Devices Using a Closed-Loop Multi-Scale Simulation Strategy

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A hippocampus prosthetic is currently under development for enhancing or restoring memory for subjects with memory disorders such as Alzheimer's disease or dementia. In this device, neural recordings in the hippocampus are used to predict the accuracy of memory creation. When a 'weak' memory recollection is detected, stimulating electrodes are used to induce neural activity appropriately. Encouraging results have been presented in non-human primate and mice experiments (Berger et al., Journal Neur Eng, 8, 2011). To improve implementation towards clinical trials and identify the most advantageous stimulation parameters, we propose a multi-scale computational model of electrical stimulation of hippocampal tissue, coupling a bulk-tissue level model of heterogeneous tissue and electronics with a model of a hippocampal pyramidal cell.

One commonality amongst previous attempts at such coupled multi-scale methodologies is an open-loop simulation setup. Typically, the electric field in bulk tissue is first computed using techniques in electromagnetics, such as finite element method or the impedance method. This is then applied as the extracellular electric field to a model of a neuron or neural network to approximate the neural tissue's response to the stimulation. It is assumed that the extracellular electric field is solely due to the stimulating electronics, or that any changes to the extracellular space due to neural activity is negligible. However, this is not necessarily the case. There is constant electrical activity in neural tissue, all contributing to changes to the extracellular electric field, providing feedback to the cells themselves, as well as influencing their neighbors. Coupling between adjacent neurons due to their influence on the extracellular electric field has been observed experimentally, described with the term ephaptic coupling. In neural tissue with high cellular density like the hippocampus, such behavior is even more likely.

The authors have proposed a closed-loop simulation strategy for dynamically updating the extracellular electric field based on both electrical stimulation and neural electrical activity, showing that neural activity does in fact alter the neural network response to electrical stimulation. This methodology is applied to the design of hippocampus prosthetic electrical stimulation in this work, considering complex pyramidal cells with high cellular density, along with heterogeneous hippocampal anatomy and stimulating electrodes. Results to be presented include stimulation thresholds for existing prosthetic electrodes with and without the proposed closed-loop simulation strategy, illustrating the functionality of ephaptic coupling in inducing neural population response and providing recommendation for future stimulation parameters.