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Fast and accurate optimization of targeted neurostimulation using a generalized activating function

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Electrical stimulation of nerve fibers is the cornerstone of electroceutical and neuroprosthetic therapies. However, stimulation protocols are typically informed by clinical experience, and therefore do not account for important individual differences in anatomy and physiology. Furthermore, labor-intensive hand-tuning is required post-implantation, severely constraining the search space for parameter optimization. Recently, hybrid electromagnetic (EM) – electrophysiological simulations have emerged as a tool to evaluate the effects of stimulation in personalized patient models [1]. However, the nonlinearity of neural activation dynamics means that configurations are not superposable, and each possible stimulation configuration must be considered individually. The attendant computational costs limit comprehensive optimization (e.g. electrode design, pulse shape optimization, multipolar electrode configurations), and prohibit metamodeling (e.g. sensitivity analysis, uncertainty propagation, surrogate modeling, model-based control). Thus, a technique for reducing computational complexity is required to unlock the full potential of simulations for personalized neurostimulation.

The classical activating function (AF) is a mathematical formalism developed to approximate the influence of applied neuromodulatory fields on target axons [2]. Here, we propose a Green's function-based extension, the generalized activating function (GAF), which includes leakage currents and conductive diffusion along the fiber. The GAF improves stimulation predictive accuracy while retaining computational efficiency and linearity. Optimization of electrode amplitudes for the selective recruitment of target fibers was carried out using: i) classical differential evolution, and ii) backpropagation. In combination with the GAF, both optimization approaches permit a significantly broader exploration of the parameter space in comparison with compartment-based simulations, and more accurate results than the classical AF.

To test our GAF-based approach, we performed simulations of a complex, anatomically realistic computational model of a spinal cord (SC) injury patient originally developed for planning neuroprosthetic therapies in paraplegics [3], as well as in a multifascular nerve model to analyse how current could be steered to stimulate target fascicles, identifying optimal electrode locations that produce maximal selectivity.

GAF-based predictions of optimal stimulation parameters for individual spinal roots in the SC model were validated against detailed, compartment-based electrophysiological simulations (NEURON [4]). Moreover, GAF-based optimizations in the multifascicular nerve model resulted in superior electrode designs with a minimal set of independent electrode contacts. In both cases, the GAF permitted an investigation of the trade-off between target selectivity and robustness of nerve recruitment. The GAF offers a significant reduction in computational complexity with respect to full electrophysiological models while improving on the accuracy of the classical AF. Moreover, its linearity enables the use of the superposition principle for metamodeling applications. This approach produced accurate results for two different, anatomically complex models, showcasing its practical relevance for neuroprosthetic and electroceutical applications.

References

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