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Title: Computational Simulation of Electrical Temporal Interference Stimulation of a Myelinated and Unmyelinated Neurons

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Abstract

Temporal Interference Stimulation (TIS) is a promising non-invasive neuromodulation technique that allows targeted deep brain stimulation by generating low-frequency amplitude envelopes from the interference of high-frequency electric fields. Whereas its potential is promising, the mechanisms by which TIS interacts with neuronal cells are not fully understood, including the role of axonal myelination. This study aimed to clarify how myelination shapes neuronal responses to TIS.

We conducted computational simulations using modified Hodgkin–Huxley multicompartment neuron models from the Blue Brain Project. These models incorporated realistic morphologies and ion channel dynamics and were adapted to include both myelinated and unmyelinated axons. Simulations were performed with uniform electric fields produced by the interference of two high-frequency fields, and activation thresholds were measured across field strengths and orientations.

Results showed that myelinated pyramidal neuron models exhibited lower activation thresholds than unmyelinated counterparts, indicating a heightened susceptibility to TIS. As deep brain networks comprise both myelinated and unmyelinated neurons, these findings reveal that axonal properties influence stimulation outcomes.

In conclusion, our simulations demonstrate that myelination significantly modulates TIS effects at the single-neuron level. These results draw attention to the importance of considering cellular composition when developing stimulation protocols and calls for further investigations into cell-type-specific and network-level responses. The results of this study will be essential to optimize the efficacy and safety of TIS for clinical applications.