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**Abstract 1962**

A hybrid computational model of the hippocampal formation to replicate theta-nested gamma oscillations and theta phase reset during neurostimulation

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**Abstract Body**

Theta and gamma oscillations in the hippocampal formation play a crucial role in memory processes and are disrupted in several neurological disorders. Recently, electrical neurostimulation of the human entorhinal area has been shown to enhance memory encoding, but the underlying mechanisms need to be investigated. Here, we aimed to validate the hypothesis that neurostimulation entrains theta-gamma oscillations and induces phase reset of theta oscillations, through a novel hybrid computational model that replicates both theta-gamma hippocampal oscillations and theta phase reset.

Specifically, we used an existing biophysically realistic model of the hippocampal formation able to generate theta-nested gamma oscillations, and interfaced it with abstract Kuramoto oscillators that dynamically generate theta oscillations and theta phase reset. Biophysically realistic neurons were modeled using the Hodgkin-Huxley formalism and connected based on anatomical data from the literature. The set of Kuramoto oscillators had reciprocal connections with the CA1 field of the hippocampus and was meant as an abstract representation of the generation of hippocampal theta, which is thought to originate mainly from the medial septum.

Our model replicates both theta-nested gamma oscillations and theta phase reset, and can be used to probe the effects of different neurostimulation protocols on theta and gamma oscillations and their couplings. In particular, we show that neurostimulation pulses delivered in-phase with the underlying theta rhythm can rescue impaired oscillations caused by changes in the model parameters that reflect pathophysiological circuit alterations.

Overall, our novel computational framework opens new avenues for studying the effects of neurostimulation on hippocampal circuits

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