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Electric field modulation of theta and gamma rhythms: probe into network connectivity

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Introduction and background

Subthreshold electric fields are effective in suppressing epilepsy [1], modulating the state of single neurons via polarization [2], and affecting neuronal synchronization [3]. Here we employ detailed computational modeling to test the use of global and local electric fields as a tool for dissecting neural population dynamics and connectivity. For example, modulation of cellular firing by theta rhythms plays an important role in hippocampal cognitive functions. It has been proposed that theta modulation can synchronize cell assemblies across the hippocampus; that place cell firing phase can code for the animal position; and that different phases of theta correlate with learning vs. recall. To demonstrate control of theta and gamma rhythms by electric field (EF), we developed a simplified 2-dimensional CA1 network based on [4] showing theta-modulated high frequency activity of pyramidal neurons [5]. Application of EF alone was able to shift the firing mode of the simplified network in the theta-gamma range.

Methods and results

Current implementation of this model (NEURON) includes morphologically realistic pyramidal cells (P) with detailed passive, active, and synaptic properties [6] as well as simplified 3-compartment basket (B) and oriens (O) cells. O and B simplification reduces simulation time but still captures key determinants of the single cell response to EF (cell orientation with respect to the direction of the EF and the asymmetry of its dendritic tree). EF effects at the level of single cells in the model are consistent with previous experimental observations [2,7]. Results obtained in our previous model [5] are reproduced.

We analyze two alternative network configurations: OPb, strong O-P connections and weak O-B connections; and OBp, strong O-B but weak O-P connections. OPb model predicts a critical role of oriens-bistratified cells in theta-oscillations. In the OBp configuration, two different populations of B cells appear necessary to maintain a realistic firing rate of P cells. Both basket and oriens cell populations are diverse in their morphological and electrophysiological properties and specific cellular subtypes participating in the genesis of theta and gamma rhythms are unknown. By varying composition of "unknown" populations from cells with mostly horizontal dendrites (not affected by electric field) to cells with mostly vertical asymmetric dendrites (most strongly affected by EF) we analyze EF effect on rhythm generation.

Conclusion

While the exact architecture underlying CA3-CA1 rhythmic activity is unknown, it might be possible to distinguish between alternative mechanisms by subthreshold electric field application.

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