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Shape dependence of the neuronal response to alternating electrical fields

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Neuronal interactions with electric fields depend on the biophysical properties of the neuronal membrane as well as the geometry of the cell relative to the field vector. Biophysically detailed modeling of these spatial effects is central to understanding neuron-to-neuron electrical (ephaptic) interactions as well as how externally applied electrical fields, such as radio-frequency radiation from wireless devices or therapeutic Deep Brain Stimulation (DBS), interact with neurons. Here we examine in detail the shape-dependent response properties of cells in oscillating electrical fields by solving Maxwell's equations for a geometrically extended neuron of various radii-to-length ratios.

Early modeling [1] for compact (spherical) cells in alternating fields predicts a smaller effective membrane time constant for the field-cell system compared to direct current injection via whole-cell patch clamp. This result, predicting that cells should respond strongly to field oscillations in the kHz range, was verified later [2] in vitro for murine myeloma cells. However, recent experiments [3] on CA3 pyramidal cells (highly elongated neurons) in the hippocampus do not exhibit this high frequency response.

Our modeling demonstrates that the radius-length ratio and orientation of the cell to the field are key determinants of the neuronal response to oscillating fields. This explains the experimentally observed absence of the high frequency response for pyramidal neurons when the applied field direction is oriented along their dendritic axis. Additionally, we developed biophysically detailed models of neuronal membranes with quasi-active electrical properties stemming from voltage-gated currents. These are known to lead to resonances at characteristic frequencies in the case of current injection via whole-cell patch clamp. Interestingly, in the field-cell system, the resonance was masked in compact, spherical neurons but recovered in elongated neurons.

These findings delineate the relationship between neuron shape, orientation and susceptibility to high frequency electric fields, with implications for DBS efficacy, ephaptic coupling in networks and the filtering properties of cortical tissue.

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