Steady-state changes induced by external electric fields in different neocortical neuron types

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Transcranial electrical stimulation (tES) is a non-invasive method to generate weak electric fields inside the brain via the injection of small currents (~1 mA) through the scalp. Transcranial direct current stimulation (tDCS) generates a constant electric field in the different tissues that can be estimated through computational head models that represent the brain geometry and its passive electrical properties based on neuroimaging structural data. We set out to model the effect that these weak fields have on resting neurons in terms of changes in their steady-state condition. We define the *response function* of a neuron model as the steady-state change of the membrane potential induced by a canonical external field of 1 V/m as a function of its orientation. We estimate the response function employing reconstructions of the rat somatosensory cortex from the Blue Brain Project [1] to simulate the response of different neocortical cells using the NEURON simulation environment [2]. We analyze the estimates in terms of a spherical harmonic expansion. Each coefficient provides a meaningful quantification of different effects and constitutes a simplified approximation that allows to accurately predict the effect in any direction in space. The azimuthal orientation of a specific cell type is not readily accessible in realistic settings. The expansion naturally provides an azimuth-independent version of the model (m=0 terms) that can be used for realistic non-invasive stimulation simulations, providing an averaged response that only depends on the angle between the electric field vector and the cortical surface. From the dipole terms of the expansion (l=1 terms) we validate that the effect of fields on resting neurons can be modeled as a dot product of a vector parallel to the orthodromic direction of cortical neurons with the electric field (as in the *lambda*-E model [3]). However, we show that the dipole effects captured by the l=1 term are state dependent, as assessed with the cell moved away from its natural resting condition via a somatic current clamp. Moreover, we observe asymmetries in the response can arise when the cell is not close to its resting state as reflected by l=0 and l=2 terms in the expansion. In this case, the pure dipolar approach is not valid anymore. We show as well that the most affected group of neocortical cells at the level of the soma are pyramidal cells. We observe that morphological features that impact on the effect perceived at the soma are the layer at which cells are located and whether they show an apical tuft or not. In terms of interneurons, while there is a large variety of generally smaller responses with characteristics that depend on their morphoelectrical typology, some interneurons produce a response of similar amplitude with pyramidal cells. We conclude that representing the response function in terms of spherical harmonics provides insightful qualitative and quantitative information of the changes induced in the steady-state condition of neurons and that these results can be used to better design stimulation protocols in the future.

References:

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