A novel multiple objective optimization framework for constraining conductance-based neuron models by experimental data

By segev
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By segev January 21, 2011


Abstract:

We present a novel framework for automatically constraining parameters of compartmental models of neurons, given a large set of experimentally measured responses of these neurons. In experiments, intrinsic noise gives rise to a large variability (e.g., in firing pattern) in the voltage responses to repetitions of the exact same input. Thus, the common approach of fitting models by attempting to perfectly replicate, point by point, a single chosen trace out of the spectrum of variable responses does not seem to do justice to the data. In addition, finding a single error function that faithfully characterizes the distance between two spiking traces is not a trivial pursuit. To address these issues, one can adopt a multiple objective optimization approach that allows the use of several error functions jointly. When more than one error function is available, the comparison between experimental voltage traces and model response can be performed on the basis of individual features of interest (e.g., spike rate, spike width). Each feature can be compared between model and experimental mean, in units of its experimental variability, thereby incorporating into the fitting this variability. We demonstrate the success of this approach, when used in conjunction with genetic algorithm optimization, in generating an excellent fit between model behavior and the firing pattern of two distinct electrical classes of cortical interneurons, accommodating and fast-spiking. We argue that the multiple, diverse models generated by this method could serve as the building blocks for the realistic simulation of large neuronal networks.

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