Microconnectomics of primary motor cortex: a multiscale computer model

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Introduction

Multiple scales in motor cortex

Stage 1: optimize model using PRAXIS for subthreshold fits, then tune manually to get right spike times, AHPs, and AP durations.

Stage 2: add Ca,KCa channels, re-optimization required

Methods

The thick tufted corticospinal cells (SPI) in layer 5 of motor cortex gate information flow out of motor cortex, thereby contributing to movement. We have developed computer models of SPI neurons to understand their complex dynamics.

Cell Level

We used SPI somatic whole-cell recordings to optimize multiple types of neuronal models to match in silico to in vitro dynamics.

Model Complexity

Our most detailed SPI model had dendritic and axonal geometry from Neurolucida reconstruction.

Results

Select for subthreshold voltage

Select for firing rates (FI)

Select for spike timing

Select for spike shape

Select for interspike voltage shape

Conclusions

1. Our SPI neuron models replicated important dynamical features of SPI neurons observed in vitro, including subthreshold voltage, firing rate, spike timing, and interspike-interval voltage.

2. Sequential optimization produced better models:
a. optimize passive parameters (capacitance, leak, Ra) and density of channels contributing to sub-threshold responses (HCN, Kd).
b. optimize density of channels contributing to super-threshold responses (Na, Kdr, Ka, Ca, KCa).

3. Evolution created a set of models optimized in multidimensional fitness space; searching allowed selecting the quality-of-fit of specific fitness functions.