BMC Neuroscience

Poster presentation

Efficient current-based optimization techniques for parameter estimation in multi-compartment neuronal models

Nathan F Lepora*, Paul G Overton and Kevin Gurney

Address: Department of Psychology, University of Sheffield, Sheffield, S10 2TN, UK

Email: Nathan F Lepora* - n.lepora@sheffield.ac.uk

* Corresponding author

from Eighteenth Annual Computational Neuroscience Meeting: CNS*2009
Berlin, Germany. 18–23 July 2009

Published: 13 July 2009

BMC Neuroscience 2009, **10**(Suppl 1):P347 doi:10.1186/1471-2202-10-S1-P347

This abstract is available from: http://www.biomedcentral.com/1471-2202/10/S1/P347

Introduction

Estimation of the maximal ion channel conductances in Hodgkin-Huxley models from patch clamp data is a difficult optimization problem. Automating this process promises *high-throughput computational modeling* of use to both experimenters (for rapid feedback on their experimental preparations) and modelers (for investigating the details of neuronal function). Hitherto, attempts to do this have focused on stochastic searches such as genetic algorithms and simulated annealing [1-3]. Such methods give robust estimates of model parameters but converge slowly or need to sample a large population of test cases in parallel, and therefore require substantial computing resources. Meanwhile, deterministic searches (*e.g.* the simplex search and conjugate gradient descent) are far more computationally efficient but are hampered by the complex fitting landscape of the optimization problem. As such, there is no general neuronal parameter-fitting algorithm that is both computationally efficient and robust.

Methods

Almost all methods for neuronal parameter estimation have been based on minimizing the error between model and target membrane potentials. However, many of the neuronal parameters are linear in a residual current error I_{res} between model and data [4], which simplifies the optimization problem. Building on this observation, we present a novel deterministic technique for estimating the maximal conductances G, of multi-compartment neurons with active dendrites. Mathematically, our method iteratively looks for roots of $I_{res}(G) = 0$, at which the residual current is zero using methods including Newton-Raphson.

Results

Two types of simulated current-clamp data were used for method validation: (i) spiking data from simple (few channels) neuronal models; and (ii) subthreshold data from complicated (many channels) neuronal models. The search typically converged in relatively few iterations ($\sim 10^2$ compared to $>10^4$ for stochastic methods) and was more robust than searches such as the simplex algorithm, which require a localized search space near to the target values.

Discussion and conclusion

Our novel search technique has been validated against a variety of model-derived data and, on the examples we have considered, shows efficient and robust neuronal parameter fitting. Work is underway to examine performance on more complex spiking models and preliminary findings indicate that phase plane methods [2,5] may be helpful in this respect. Our aim is to incorporate this work into the CARMEN neuroinformatics infrastructure as a research tool for use by the general neuroscience community.

Acknowledgements

N. Lepora was supported by EPSRC through the CARMEN e-Science Project.

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