BMC Neuroscience



Poster presentation

Open Access

Simulated-annealing as a tool to identify parameter values associated with epileptiform activity in single-neuron and network compartmental models

Marc Benayoun*1, Jennifer Dwyer1, Hyong C Lee1, Mark Herald2, Rick L Stevens2 and Wim van Drongelen1

Address: ¹Department of Pediatrics, University of Chicago Hospitals, The University of Chicago, Chicago, IL USA and ²Mathematics and Computer Science Division, Argonne National Laboratory, Argonne, IL USA

Email: Marc Benayoun* - marcb@uchicago.edu

from Sixteenth Annual Computational Neuroscience Meeting: CNS*2007 Toronto, Canada. 7–12 July 2007

Published: 6 July 2007

BMC Neuroscience 2007, 8(Suppl 2):P23 doi:10.1186/1471-2202-8-S2-P23

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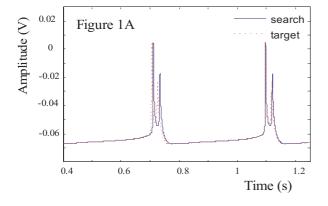
Background

Automated parameter search algorithms, such as simulated annealing, seek to tune a model's parameters to reproduce important features of a target data set. A match function compares the model and target data to generate a goodness of fit and is crucial because it reflects which target features are considered of interest. Previous work has shown the effectiveness of combining simulated

annealing with time-domain match functions (e.g., spike timing and least mean square (LMS) of membrane potentials) to tune a compartmental model of a cortical pyramidal cell [1].

Methods

Here, we assessed the applicability of LMS and spike timing match functions to single-cell and cortical network tar-



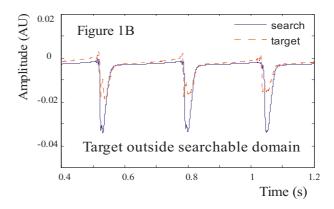


Figure I LMS match function results.

^{*} Corresponding author

gets displaying epileptiform activity. To accommodate the more time-variable nature of network activity, we also included frequency-domain (e.g., raw and banded power spectra) match functions with the goal of determining their relative efficacy in identifying and constraining the model parameters important for generating epileptiform discharges.

Results

The results of two representative cases are depicted in Figure 1. Figure 1a shows a bursting single-cell model target and a representative best-match found using an LMS match function; the parameter domain subject to search varied over a factor of 2 about the target value. Runs using larger domains, more parameters, and other match functions, such as spike timing, indicate that, for this target, the fraction of reasonable matches as a function of search domain scales most poorly for LMS. Figure 1b shows the LMS match function applied to a network model. This search restricted the domain to exclude the correct value of one of the parameters to simulate a real target in which parameters are not known a priori and may be situated outside the searchable domain. Encouragingly, the search found the value at the boundary of the allowable space, closest to the excluded target value.

Conclusion

Both our single-cell and network search results demonstrate the feasibility of using simulated annealing to identify parameters underlying behaviors related epileptiform bursting activity. In real intracellular target traces, lack of knowledge about target parameter values may necessitate larger searchable spaces, for which LMS appears to be suboptimal compared to other match functions such as spike timing. If the searchable space is poorly chosen, so that the true parameters are excluded, then the search algorithm often indicates the situation by finding parameters at the edge of the searchable space, even for relatively complex network models as illustrated by Figure 1b. We note anecdotally that, at least in our models, it is easy to determine by inspection whether the automated searches have settled on a reasonable match, which makes them useful tools for selecting interesting areas of parameter space even when they do not provide exact matches to the targets.

Acknowledgements

This work was supported in part by the Falk Foundation, the Linn family, and the U.S. Department of Energy under Contract DE-AC02-06CH11357.

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