Modeling Microcircuits of Realistic Hippocampal Neurons
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This project is a collaborative research program between an experimental cellular neurophysiologist and two applied mathematicians. The central aim of the project is to develop detailed computational models of microcircuits composed of principal neurons and interneurons in the CA1 region hippocampus. In particular, these computational models will: 1) Be based on the latest data available from patch-clamp experiments dealing with ionic conductances, calcium and two-photon imaging, and cell morphology. 2) Use ionic channel models specifically designed to accurately reproduce the experimentally determined behavior. 3) Use full-cell morphologies; in particular, the same individual cells from which electrophysiology data have been taken will be digitized for the computational studies. 4) Develop new adaptive computational methods that can be used to speed up the computational simulations. A long-term goal of the project is to develop sufficiently accurate models of excitatory and inhibitory cell types in the hippocampus so that realistic simulations of small networks present in the hippocampus can be performed. These computational simulations are intended to be a tool to guide the development of new patch-clamp experiments that further explore the functional behavior of the hippocampal region.

Accomplishments to date include: 1) The training of two applied mathematics faculty and three applied mathematics graduate students in neuroscience. 2) A new computational method capable of more efficiently simulating dendritic branching structures. 3) A morphological and electrophysiological database of principle interneurons from the CA1 region of the hippocampus. 4) Combined simulation and experimental studies demonstrating that dendritic spikes generated distally by perforant path inputs in CA1 pyramidal cells can be gated as they propagate toward the soma by more proximal Schaeffer collateral inputs.

PI Website

http://www.northwestern.edu/neurobiology/faculty/spruston/index.htm

Publications

N. Spruston and W.L. Kath. Dendritic arithmetic. Nat. Neuroscience 7:567-569, 2004.

N. Spruston. Branching out: a new idea for dendritic function. J. Neurophysiology, 90:2887-2888, 2003

A. Roxin, T. Jarsky, W.L. Kath and N. Spruston. Gating of dendritic spikes propagating toward the soma of CA1 pyramidal neurons, COSYNE 2005 abstract; to be submitted to Nature Neuroscience.

N.L. Golding, T. J. Mickus, Y. Katz, W.L. Kath and N. Spruston. Factors mediating powerful voltage attenuation along CA1 dendrites, submitted to J. Physiology.

W.L. Kath, The computational modeling of dendrites, J. Neurobiology, to appear.

T. Jarsky, Y. Katz, A.Roxin, W. Kath and N. Spruston. Powerful dendritic attenuation of distally generated EPSPs suggests an important role for dendritic spike initiation in the distal dendrites of CA1 pyramidal neurons, Society for Neuroscience Abstract, 2004.

R.E. Trana, Y. Katz, W.L. Kath and N. Spruston. Computational modeling of scaled synaptic inputs on CA1 dendritic shafts and spines, Society for Neuroscience Abstract, 2004.

M.J. Rempe, N. Spruston, W.L. Kath and D.L. Chopp. Efficient computational strategies for simulating neural activity, Society for Neuroscience Abstract, 2004

J. A. Varela, W. L. Kath and N. Spruston. Effects of metabotropic glutamate receptor agonists on horizontal inhibitory neurons in stratum oriens of hippocampal area CA1, Society for Neuroscience Abstract, 2003.

A. Roxin, W.L. Kath and N. Spruston. Propagation of distally generated dendritic spikes toward the soma is facilitated by Schaffer collateral inputs in CA1 pyramidal neurons of hippocampus: a simulation study, Society for Neuroscience Abstract, 2003.