Circuit Simulation Approaches to Extending Neuronal System Simulation and Design.

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Introduction
Simulation of neural systems opens many avenues of discovery. Through detailed, neural-circuit simulation, we are investigating:
• extraction of governing parameters from large experimental data sets
• understand the dynamics and stability of natural systems
• constraining the design of new, experimental systems.

Approach
• Circuit Simulation: Xyce
  To model a system of interacting neurons, we use Sandia’s parallel, electrical circuit simulator, Xyce. Without any loss of generality, Xyce allows us to solve detailed, ordinary differential equation models for neuron membrane potentials, ion concentrations and channel currents as well as pre and post synapse dynamics. Because Xyce is a parallel code, the simulation of very large systems (i.e. over 10⁶ neurons) is possible.
• Uncertainty Quantification: Dakota
  However, direct simulation alone provides only part of the dynamical picture of how neuronal systems work. We employ Sandia’s optimization and uncertainty quantification package, Dakota, to constrain and control the model parameters and topology of our neural systems.
  Using Xyce and Dakota together allows one to not only optimize the fit of a simulation to some standard, but also discover system stability and sensitivity of modeling parameters.
• Experimental Benefits
  Simulations designed to mimic experiments and extract modeling parameters or examine stability can illuminate the information content of an experiment. This analysis has been applied to in vitro cultures and soon will be applied to in vivo measurements with quantum dots.

Using Fourier analysis for parameter extraction

By coupling simulation with fitting to experimental data, we can find not only an optimal fit, but the range within which the simulations dynamically behave the same as the experiments.

Understanding the egg-laying motor circuit in C. elegans

• Common microcircuit motif
• Feed-forward excitation, feedback inhibition
• Understanding its functional properties may aid understanding of more complex systems that include this microcircuit
• From simulations we can find a set of conductance parameters which produce experimentally observed calcium oscillations.

Design of neural systems

• Aid the design of neural circuits with desired properties
• Start with simplest single-neuron circuit – autapse
• Calibration: measure and model spontaneous firing rate.
• How does cell morphology and circuit topology affect firing rate and signal transmission?