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Book Review

The Book of GENESIS: Exploring Realistic Neural Models with the GEneral NEural SImulation System by J. M. Bower and D. Beeman

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The field of computational neuroscience has grown rapidly in recent years. Neuroscientists are turning to realistic computational modeling as a means for exploring new hypotheses and generating experimentally testable predictions. However, the development of detailed biophysical models is a laborious process unless researchers start with the appropriate modeling tools.

Scientists interested in computational neuroscience will find a useful set of tools described in *The Book of GENESIS.* GENESIS is a free software package (GEneral NEural SImulation System) available through the California Institute of Technology and developed under the leadership of Jim Bower. The software package provides an excellent programming environment with script commands specifically designed to ease the construction of detailed compartmental biophysical simulations of neurons and neural systems. Researchers in the field have already used GENESIS to develop simulations ranging from complex single cell compartmental simulations of Purkinje cells (e.g., work by Erik DeSchutter) to invertebrate central pattern generators (work by Avis Cohen) to large scale biophysical simulations of the piriform cortex (the first use of GENESIS when it was initially written by Matthew Wilson).

The Book of GENESIS can be used both as a study guide and a research tool. As a study guide, the first half of the book presents a series of detailed tutorial programs demonstrating basic principles of neural systems. For example, in chapter 4, Mark Nelson and John Rinzel present a GENESIS tutorial on the computational model of action potential generation developed by Hodgkin and Huxley. The description of the historical background and computational structure of the Hodgkin-Huxley equations is exceptionally clear, and the tutorial program allows the reader to observe the time course of action potential dynamics and interactively explore the role of different parameters in action potential generation. As a research tool, the second half of the book describes the step-by-step construction of custom simulations of interacting populations of neurons. For example, the Hodgkin-Huxley currents are incorporated into multicompartmental neurons interacting with realistic synaptic potentials.

In the first half of the book, readers are guided through a series of GENESIS tutorials with clear and accessible prose, which progresses patiently through the steps involved in starting individual simulations, observing the changes in different experimental variables (ranging from membrane potential to synaptic currents to field potentials) and changing parameters to observe how they affect network function. In all tutorials, the graphics program, XODUS (written by Upi Bhalla), creates easily used windows for displaying variables and resetting parameters. Exercises at the end of each chapter provide useful guides for self-study, or projects which could be assigned in a course. Cross-references in the first chapter will aid the use of this book as a supplement to textbooks including *Neurobiology* and *Principles of Neural Science* for an advanced undergraduate or graduate level course. In addition to the description of Hodgkin-Huxley dynamics, chapters by Idan Segev introduce the theoretical basis for compartmental models of dendritic trees—work pioneered by researchers such as Wilfrid Rall and Gordon Shepherd—and for simplified representations of interactions between postsynaptic potentials. An important chapter reviews the voltage and calcium-dependent ionic currents that give most neurons complex behavior beyond that of the squid giant axon, and provides a valuable overview of Roger Traub's model of hippocampal region CA3 pyramidal cells that has been implemented in GENESIS by David Beeman. GENESIS could prove vital to computational neuroscience as a common program in which a wide range of computational models can be implemented and distributed. For those interested in the interaction of neurons, the last two chapters of the first half describe GENESIS models of the dynamics of central pattern generators and of the rat piriform cortex.

In the second half of the book, the easy tone of the writing does not change, but it is assumed that readers are interested in developing their own custom simulation script. In a very useful sequence of tutorials written by David Beeman, the essentials of GENESIS script programming are set out step by step, with descriptions of basic commands and syntax, common errors in programming, and methods for debugging programs. These tutorials progress from the passive membrane potential dynamics of a single compartment to include multiple dendritic compartments, action potential generation, and synaptic potentials. Additional chapters introduce commands for establishing synaptic connectivity in a network of neurons. Methods for simulating synaptic modification (e.g., long-term potentiation) are not described in the book, but the GENESIS software includes objects that can implement Hebbian synaptic modification. Researchers are expected to start with one of the GENESIS tutorials from the first or second half, which can then be modified and elaborated to incorporate experimental data on a range of membrane conductances and synaptic interactions. A chapter describes how the tabchannel object can be used in place of the Hodgkin-Huxley formalism to directly implement new channels based on collected data about channel kinetics. In addition, an excellent chapter reviews methods for increasing the speed of individual simulations, and includes a useful summary of the many different techniques available in GENESIS for performing numerical solutions to differential equations. For researchers implementing properties outside the current command structure of GENESIS, additional objects can be programmed in C and compiled with GENESIS.

For a researcher interested in using an easily accessible program directly designed for the task of neural modeling, GENESIS is an appropriate software package. With publication of the Book of GENESIS, the documentation for GENESIS is extensive, and the program has been designed with a focus on incorporating synaptic interactions between neurons. GENESIS also includes the specialized algorithm developed by Michael Hines for rapidly solving differential equations representing large numbers of interacting dendritic compartments. GENESIS runs on most computers that use the UNIX operating system. The appendix describes the steps for copying, compiling and installing the program.

Currently, many neuroscientists focus on amassing a wealth of data on the molecular structure of brain proteins. However, sophisticated techniques will be necessary for linking the dynamics of protein function to the behavior of an organism. At the other extreme, in the new field of cognitive neuroscience, psychologists have begun to use brain imaging techniques to link cognitive function to specific brain regions—but this work can only move beyond drawing flow charts in the brain when imaging results have been linked to cellular and circuit properties of these regions. Between behavior and molecules lie numerous levels of physiological and anatomical complexity. The techniques of computational neuroscience, as described in the book of GENESIS, will prove necessary for understanding these multiple levels.