2004 NEURON Simulator Meeting

Schedule

Friday, May 14, 2004

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Abstracts in order of presentation

Friday, May 14, 2004
AM Session

Michael Hines: "NEURON open source development"

This presentation will be of interest to people who want to participate in NEURON's development. Topics that will be discussed include:

- How to use the CVS repository to obtain and contribute source code.
- How to build NEURON, using source code from the CVS repository, in the UNIX, MSWindows, and MacOS environments.

Fernanda Saraga: "From the slice to the model: problems, pitfalls and solutions to reconstructing multi-compartment models"

Multi-compartment models based on detailed morphological reconstructions of a cell can greatly enhance the understanding of signal generation, synaptic integration, coincidence detection and other issues which require the inclusion of processes such as axons and dendrites. The steps for creating a multi-compartment model from fixed slice preparations will be discussed. Topics explored during the talk will include tissue problems such as fixation, thickness and orientation of slices, the use of Neurolucida for 3-D morphology reconstruction, how to use/install CVAPP in order to convert Neurolucida files into a NEURON compatible file (.hoc) and issues with importing morphological files into NEURON. I will use several example morphology files from Neurolucida and explore them both in CVAPP and the consequent converted files in NEURON. Previously reconstructed morphologies from online databases will also be discussed in the context of using these morphologies in NEURON. This talk will be followed by a small panel discussion including myself and a representative from Neurolucida, Geoff Green.

Ruggero Scorcioni: "Quantitative morphometry of hippocampal pyramidal cells: differences between anatomical classes and reconstructing laboratories"

The dendritic trees of hippocampal pyramidal cells play important roles in the establishment and regulation of network connectivity, synaptic plasticity, and firing dynamics. Several laboratories routinely reconstruct CA3 and CA1 dendrites to correlate their three-dimensional structure with biophysical, electrophysiological, and anatomical observables. To integrate and assess the consistency of the quantitative data available to the scientific community, we exhaustively analyzed 143 completely reconstructed neurons intracellularly filled and digitized in 5 different laboratories from 10 experimental conditions. Thirty morphometric parameters, including the most common neuroanatomical measurements, were extracted from all neurons. A consistent fraction of parameters (11/30) was significantly different between CA3 and CA1 cells. A considerably large number of parameters was also found that discriminated among neurons within the same morphological class, but reconstructed in different laboratories. These interlaboratory differences (8/30 parameters) far outweighed the differences between experimental conditions within a single lab, such as aging or preparation method (at most two significant parameters). The set of morphometrics separating anatomical regions and that separating reconstructing laboratories were almost entirely non-overlapping. CA3 and CA1 neurons could be distinguished by global quantities such as branch order and Sholl distance. Differences among laboratories were largely due to local variables such as branch diameter and local bifurcation angles. Only one parameter (a ratio of branch diameters) separated both morphological classes and reconstructing laboratories. Compartmental simulations of electrophysiological activity showed that both differences between anatomical classes and reconstructing laboratories could dramatically affect the firing rate of these neurons under different experimental conditions.

Friday, May 14, 2004
PM Session

Workshop: "NEURON for education." Moderator: Bill Lytton

Bill Lytton: "NEURON for education"

Neuron boasts several advantages as a platform for neurophysiology and computational neuroscience education: 1) it is free; 2) it is available for all platforms and easy to install; 3) simple, user-friendly GUIs are easily implemented; 4) exercises can be readily incorporated in text for direct launch from a web page. Examples will be taken from 3 courses that have been implemented using Neuron. We will present a simple GUI framework that incorporates "Exercise" and "Help" buttons.

John W. Moore: "*Neurons in Action*: using NEURON as a learning tool"

The ability to launch a NEURON application (distinguished by a unique suffix) by clicking a link in an HTML document provides the possibility of a spectacularly powerful learning tool: coupling simulations with tutorials. From my experience in using NEURON simulations in the classroom for graduate and medical students, I began to develop tutorials and associated, customized NEURON application files. Topics ranged from membrane patches to impulse generation and propagation in a variety of axons and stylized nerve cells. My wife, Ann Stuart, a Professor of Physiology at UNC, soon joined me in writing 17 tutorials published as a CD/Book in 2000 by Sinauer Associates

The customized NEURON simulations offer the user relevant variables, where each may be individually controlled, an invaluable tool for learning neurophysiology in a dissection-free environment.

Recently we achieved the goal of creating an integrated package containing NEURON, the tutorials, and a customized browser, an important advance in permitting the user to install a fully functional Neurons in Action environment in a single drag-and-drop step.

Ann E. Stuart: "Extending *Neurons in Action*"

Portions of the Neurons in Action (NIA) tutorials may be used selectively by faculty in a myriad of ways. Here I provide examples from my own teaching. For a lecture on the action potential in an undergraduate course in physiology I use minimovies captured from the tutorials and inserted into my PowerPoint presentation. This lecture is followed by a laboratory where the students are asked to figure out what conditions, or types of drugs, would help a patient with multiple sclerosis, thereby deepening their understanding of the propagation of action potentials in bare and myelinated axons. In a graduate course in neurobiology I introduce current flow across the membrane with PowerPoint graphics keyed to the simulations of The Membrane Tutorial, then assign homework questions to guide the students as they work through the tutorials of Level I. A take-home exam using the Postsynaptic Membrane Tutorial tests their knowledge of current flow across membranes and voltage spread in a cell.

We encourage faculty who make customized extensions of the NIA tutorials for lecture, conference or review, or a computer lab to send them to the authors for posting at the NIA web site (www.neuronsinaction.com) under "Suggestions for Faculty."

Michele Migliore: "Running simulations on parallel systems: a user's perspective on the use of the ParallelContext class"

Using the ParallelContext class, many simulations can be launched at the same time on different processors. In principle, this could reduce the total simulation time, with respect to a single CPU machine, in several cases. However, the most useful and efficient way to exploit a parallel system is, by far, to explore the parameter's space. I'll discuss my experience in one of these cases. An actual simulation file, previously implemented for a single processor, was adapted in such a way to run in a 24-processors cluster. The conceptual reorganization of the program flow and the (arcane at first) details on passing variables and collecting simulations result will be described from a user's point of view.

Workshop: "Hacking NEURON." Moderators: Ted Carnevale and Bill Lytton

The aim of this event is to exchange "power programming" tips for getting the most out of NEURON. Discussion and specific practical examples will range over topics such as:

- essential idioms in hoc
- organizing programs for efficiency and clarity
- combining hoc code and the GUI to exploit the strengths of both
- discovering and exploiting the single largest collection of useful hoc code
- hacking session files
- hacking NEURON's run-time system
- custom initializations
- automating execution of simulations and analysis of results

The moderators will present many of their own tips and tricks, and audience participation is strongly encouraged.

Saturday, May 15, 2004
AM Session

Michael Hines: "Variable time step methods in NEURON"

This talk will address important topics related to using NEURON's built-in adaptive integrators (AKA "variable dt" methods or "CVODE"). These include the following:

- How does the local variable step method work?
- How does one choose absolute tolerance scale factors?
- How does one record and plot with the local variable step method?
- What is required for a model description (in NMODL) to be compatible with variable dt integration?

Carl Gold: "Simulating extracellular fields with NEURON and the Line Source Approximation"

The Line Source Approximation (LSA) is an efficient and accurate method for calculating the extra-cellular electric potential resulting from the currents distributed over the entire 3-D membrane surface of a neuron. The LSA consists of approximating the 3-D distribution of membrane currents on a cylindrical neurite surface as a line source of current down the center of the neurite. With this simplification the calculation of extra-cellular voltage simplifies to an analytic expression at the cost of a minimal loss of accuracy (Holt and Koch, 1998). To apply the Line Source Approximation, a precise 3-D neuron morphology is obtained from histological measurements, the neuron is simulated in the NEURON, and the currents for all compartments are written to a data file at discrete time steps. The data is then loaded into a Matlab program which efficiently performs the LSA calculation on matrix representations of the neuron geometry and membrane currents. The talk will review the theory of the LSA, and discuss practical aspects of the implementation in NEURON and Matlab. The talk will showcase the application of the technique in a theoretical comparison of extra- and intra-cellular recording action potentials from hippocampal neurons (Henze, et. al. 2000).

Seminar: "Extracellular stimulation." Moderator: Cameron McIntyre

Cameron McIntyre: "Modeling extracellular stimulation of 3D reconstruction neuron models"

Electrical stimulation of the central nervous system via extracellular electrodes is widely used for both experimental and clinical applications; however, understanding of the neural response to the stimulation is limited. The electric field generated by the electrode is a three-dimensionally complex phenomenon that is distributed throughout the brain. To further complicate matters, this field is applied to the equally complex three-dimensional geometry of the surrounding neural processes (i.e. axons and dendrites). The response of the neuron to the applied field is related to the second derivative of the extracellular potential distribution along each process. In turn, each neuron (or neural process) surrounding the electrode will be subject to both depolarizing and hyperpolarizing effects from the stimulation. The use of multi-compartment cable models of neurons coupled to extracellular electric fields has provided the opportunity to study the effects of stimulation on neural activity in a highly controlled environment, impossible to achieve experimentally. I will present a step-by-step account of the development of a 3D reconstruction NEURON model stimulated by an extracellular electrode. I will then use this model to demonstrate the effects of changes in the stimulation parameters on the neural response to the stimulation.

Dongchul Lee: "Fundamentals of extracellular stimulation and the application of different electric fields on neuron models"

Extracellular stimulation is a practical method to stimulate population of CNS neurons in the brain and the spinal cord. During the stimulation, neural elements (axon, dendrite and cell body) are exposed to the electric field generated by the stimulating electrode. The extracellular electric field along each neural element is primary source to active the neurons. Therefore, cable model under extracellular stimulation is more complicated than the model with intracellular stimulation such as injecting current directly to the cell. Understanding equivalent cable model will provide basic concept for using the extracellular mechanism in NEURON. I will introduce theoretical background of modeling in the extracellular stimulation and present practical coding technique for (1) creating extracellular electric field from different electrodes and (2) connecting extracellular mechanism with the electric field. The effect of electric fields on the response of neural elements to the stimulation will be demonstrated.

Roy Testerman: "Modeling clinical axonal stimulation via the NEURON extracellular mechanism"

Clinically useful models of axonal stimulation (peripheral nerve, spinal cord or brain) can mean that three different software applications have to be interfaced; an electric field simulation module, a NEURON module, and a third module to map data between the other modules. This presentation presents an overview of this interfacing process, including the mapping of NEURON model coordinates to the model coordinates of an external field simulation program. NEURON coding excerpts are given which (a) read in a spatial array of voltages from an external source, (b) apply a variable multiplier to these voltages, (c) apply these scaled voltages to an axon model and (d) determine the excitation threshold. This system was used to examine the effects of stimulus pulse width and electrode-axon distance on stimulus chronaxie and rheobase. Results are presented for two specific NEURON axon models.

Saturday, May 15, 2004
PM Session

Thomas M. Morse: "Retrieving and entering neuronal and network models in a web database, ModelDB"

The advantages of making model code electronically available will be briefly reviewed. One possible instance of a mechanism for code sharing, ModelDB, a publicly accessible database of neuronal models (http://senselab.med.yale.edu/senselab/modeldb) offers reliability and ease of use. We will demonstrate the different search mechanisms available to find public models in ModelDB. ModelDB also has the ability to store private models. Investigators use this feature to prepare model entries that will eventually be made public. Participants will be lead through the steps required to deposit private models, and be given guidelines for setting the attributes for a model in ModelDB. Participants can deposit their own model, or a provided "dummy" model into their private accounts during the workshop. We would like to give permanent ModelDB accounts, before the meeting, to those interested in gaining hands on experience in this workshop, so please let us know if you wish to attend.

Seminar: "Network modeling." Moderator: Bill Lytton

Johan Hake: "Efficient synaptic models for network simulations"

Effective and reliable models of synaptic transmissions are a prerequisite to model large neuronal networks. Today NEURON supplies us with a vast number of such models. I present an accelerated model of the synaptic conductances based on the dynamics of a beta-function. This is described by a system of two linear and time invariant differential equations. These are chosen so the second state variable contains the value of the beta-function. The integration can be done exact and very efficient. With fixed time steps it is done by a single matrix calculation, and with variable time steps the built in solver method can be used. Using the NetCon class several connections that use the same synaptic dynamics, can converge in the same synapse. A spike event is registered only by adding a single value to the first state variable, and we avoid any self events. The added value depends on the strength of the particular synapse, the weight, and the present value of the first state variable. The latter is done by an evaluation of an exponential function in the NET_RECEIVE block and this lets the synapse saturate. The acceleration compared to existing models, that do the same, lays in the registration of a presynaptic AP, without any self event, and in some concerns in the integration of the system. By using a beta-function we have the opportunity to alter the strength of the synaptic conductance as well as the rise and decay phase of it.

Alexander Roxin: "Large-scale synaptic stimulation of single cells in NEURON: how to model realistic synaptic input"

I will discuss how to construct a NEURON procedure that inserts synaptic point processes (intrinsic or user-defined) in a given morphology in order to model realistic synaptic input. Given best-available experimental data on the distribution of synapses in a particular cell, the procedure inserts synapses by cell region and allows the user to manipulate the synaptic drive via a graphical user interface. Synapses can then be activated in specific cell regions, modeling input from designated pathways, and noisy synaptic activity can be added to model in vivo conditions. I will explain how only minimal modifications need be made in order to add this procedure to any pre-existing code. I will illustrate the use of the procedure with a reconstructed CA1 pyramidal cell in which input via different pathways targets spatially distinct locations of the dendritic arbor.

Padraig Gleeson: "Automated development of large-scale realistic networks for NEURON using neuroConstruct"

Padraig Gleeson*, Volker Steuber and R. Angus Silver
Department of Physiology, University College London,
WC1E 6BT, UK.

Neuron has long been the industry standard simulator for single cell applications and has more recently been extended for network applications. However, development of large-scale neural networks with multiple cell types and anatomically realistic connectivity requires considerable low level programming or time consuming manual connection of individual cells. We have developed an application, neuroConstruct, that facilitates the creation, visualization and analysis of complex large-scale networks. It is built in Java and produces hoc files that can be automatically run in NEURON. NeuroConstruct allows the specification of positioning (e.g. randomly placed, optimally packed, etc.) and connectivity of neurons in 3D; visualization of generated network structure; simplified creation of new synapses/channel mechanisms via integrated mod file generation; recording of simulation data generated by NEURON and visualization/analysis of data in neuroConstruct. The tool can be used to simulate any neuronal system and is controlled through a GUI letting users concentrate on specifying biophysical and anatomical parameters. We intend to use it to investigate signal processing in the cerebellar cortex. The application is currently being tested in collaboration with the Institute for Adaptive and Neural Computation in Edinburgh and it will be made available to the community once developed.

Funded by the MRC.

Bill Lytton: "Large network simulations"

Large network simulations require substantial organization and planning in order to ensure that What You Get is What You Wanted (WYGIWYW). A strategy will be introduced that includes 1) the use of templates for defining cells; 2) localization of synapses on postsynaptic cells; 3) separate file definitions for cell geometries, network connectivity, parameter settings and simulator settings; 4) batch collection of spike times or other outputs. The use of a version storage system (such as SCCS, RCS, CVS or SIMCTRL) to organize simulation files will also be introduced.

Sunday, May 16, 2004
AM Session

Michael Hines: "Using NEURON's new ChannelBuilder"

A new GUI tool called the ChannelBuilder is being added to NEURON. The ChannelBuilder makes it very easy to construct new channel types (distributed mechanisms). It is launchable from the NEURON Main Menu toolbar, and its functionality is slightly extended compared to the Catacomb ChannelBuilder. However, the new ChannelBuilder is written in hoc and does _not_ require Java. It can specify channels that are voltage- and/or ligand-gated, with "gates" that are described by the HH formalism, kinetic schemes, or a combination of these approaches. These channels are computationally efficient, completely interoperable with NEURON's other GUI tools, and can be saved to a session file for subsequent re-use.

Michael Rempe: "Adaptive grids in neural simulations"

Current software packages used for simulating neural activity, including NEURON, are robust and accurate and have benefited from many improvements over the years including adaptive time steps and discrete event simulation. However, to accurately simulate a large network of complex cells or to search a large parameter space, the computations can be prohibitively time-consuming. One area where we see opportunity for performance improvement is in the simple case of an action potential propagating down an axon or a section of dendrite. Current schemes, including those used in NEURON, do not take advantage of the local nature of these disturbances and therefore make many more calculations than is necessary. We present two techniques to improve the speed of simulating action potential propagation: moving meshes and adaptive meshes. In the moving mesh scheme grid points move down the axon with the disturbance, so grid points are not used where there is no activity. With the adaptive mesh algorithm, local errors are measured and grid points are added or removed accordingly. In both schemes the strategy is to save memory and increase computing speed by minimizing the size of the matrix system that is solved at each time step. So far we have seen significant improvements in computing speed with both algorithms, but especially the moving mesh. With this scheme computing times for propagating an action potential down an axon are reduced by up to 90% compared to the same calculation done on a static grid. The adaptive mesh also shows much promise and a 60% reduction in computing time

Yann Le Franc: "Real-time NEURON for dynamic clamp and hybrid systems"

Yann Le Franc, Bruno Foutry, Frederic Nagy, Gwendal Le Masson
INSERM0358 and Université Bordeaux 2, Bordeaux FRANCE

Hybrid network and dynamic clamp methods are used for real time interactions between different neuronal models (from conductance to single neurons and networks) and biological neurons recorded intra-cellularly. These techniques allow the injection of artificial cellular or synaptic current to study dynamically the effect of an additional voltage dependent channel or extra synaptic connection. To achieve such experiments the technical requirement are (1) Real time computation to follow the natural dynamics of biological systems (2) Control of the current injection system according to a defined model.

To use the power of the NEURON packages as a standard environment, we develop a 'Real-Time' version of NEURON. Our system controls and acquires data through a plugged DSP board with build-in DAC and ADC (Innovative Integration). Specific libraries were developed to handle real time processing under Windows NT and 2000. The control of parameters (real time and acquisition) is fully accessible through hoc graphic interfaces. Several signal-processing tools are also available to handle on line analysis of data. This RT-NEURON version is fully compatible with standard model description and only require specific mod files for the dynamic clamp procedure.

This system is currently used to analyze electrophysiological aspects of spinal cord, thalamic and cortical networks.

Ted Carnevale: "Electrotonic analysis with NEURON"

The electrotonic structure of a neuron is the framework within which the signals generated by synaptic inputs and active currents spread and interact. It is also important to the design and interpretation of experimental studies of synaptic inputs and voltage-gated currents. This tutorial will show how to use NEURON's built-in tools for electrotonic analysis. These tools are helpful for gaining quick insights to the functional consequences of the anatomical and biophysical properties of neurons. This tutorial presents the theoretical background of these tools, and includes a hands-on component that shows how to use them via the graphical interface.

Round table discussion: "Planning for the next meeting"

The agenda is to plan for the next NEURON Simulator Meeting.