CNS2007 Workshops (July 11 and 12, 2007)

Summary Descriptions can be found in the program booklet.

Feedback summaries provided by the workshop organizers are included here.

In addition to a short NEURON course (organizers: Hines, Carnevale, Calin-Jageman, Schürmann), workshops included:

Title: *Cortical Microcircuits: Structure, Function and Theory*

Title: *Modeling of anaesthesia and sleep by neuronal networks*
(see feedback summary below)

Title: *Synchronization of brain signals: what is real, what is not*

Title: *Developing Database and Analysis Software for Electrophysiology: Design, Application, and Visualization*
(see feedback summary below)

Title: *Availability of published computational models for testing and attributed reuse*

Title: *Methods of Information Theory in Computational Neuroscience*

Title: *Neuro-Machine Interfaces: Integrating Biology and Technology to Develop Functionally Relevant Devices*
(see feedback summary below)

Title: *Reconstructing neuronal morphology from serial image stacks*

Workshop "Modeling of anaesthesia and sleep by neuronal networks"

The aim of the workshop was the neural mechanisms present during the lack of consciousness of subjects, i.e. the inability to respond to external stimuli. In this context, the theoretical and experimental study of aneasthesia and sleep are important research fields. The workshop brought together researchers, who apply different network modeling approaches, in order to gain an overview on current research in aneasthesia and sleep. The specific focus of the presented research was the combination of theoretical network models and experimental results. Topics were the effects of anaesthetic agents, the modelling of sleep rhythms, and the interaction of the thalamus and hippocampus during sleep.

1) Dr. Alistair Steyn-Ross, The University of Waikato, Hamilton, New Zealand
Title of talk: Phase transitions in single neurons and in neural populations: Critical slowing, anaesthesia, and sleep cycles
Authors: D. A. Steyn-Ross, Moira L. Steyn-Ross, M. T. Wilson, J. W. Sleigh
The firing of an action potential by a biological neuron represents a dramatic transition from small-scale linear stochastics (subthreshold voltage fluctuations) to gross-scale nonlinear dynamics (birth of a 1- ms voltage spike). In populations of neurons we see similar, but slower, switch-like there-and-back transitions between low-firing background states and high-firing activated states. These state transitions are controlled by varying levels of input current (single neuron), varying amounts of GABAergic drug (anaesthesia), or varying concentrations of neuromodulators and neurotransmitters (natural sleep), and all occur within a milieu of unrelenting biological noise. By tracking the altering responsiveness of the excitable membrane to noisy stimulus, we can infer how close the neuronal system (single unit or entire population) is to switching threshold. We can quantify this "nearness to switching" in terms of the altering eigenvalue structure: the dominant eigenvalue approaches zero, leading to a growth in correlated, low-frequency power, with exaggerated responsiveness to small perturbations, the responses becoming larger and slower as the neural population approaches its critical point---this is critical slowing. In this talk we will discuss phase-transition predictions for both single-neuron and neural-populations models, comparing theory with laboratory and clinical measurement.

2) Dr. Lennaert van Veen, Department of Mathematics and Statistics, Concordia University, Canada
Titel of talk: Modelling the effects of anaesthesia on human brain electrical activity
Despite many decades of research into the mechanisms underlying general anaesthesia there are surprisingly few integrated theories attempting to explain this remarkable phenomenon. This has been largely due to the fact that there has been no real agreement on what macroscopic observable or observables of anaesthetic action are to be modelled that quantitatively reflect the hypnotic (unconsciousness) state. However the recent development of a number of

successful clinical depth-of-anaesthesia monitoring approaches clearly indicate that the macroscopic consequences of general anaesthesia correlate well with electroencephalographic (EEG) activity. Here we outline an integrated theory of general anaesthetic (GA) action based on a physiologically motivated continuum theory of cortical electrorhythmogenesis. This theory establishes a mesoscopic link between the well characterised effects of GAs on the subcellular and molecular machinery of inter-neuronal communication with the GA induced electroencephalographic changes. Further the theory is able to explain a number of paradoxical phenomena associated with anaesthetic action which include the low dose acceleration of the EEG and the anomolous generation of ictal activity.

3) Dr. Sean Hill, Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne, Switzerland & IBM T.J. Watson Research Center, New York, USA
Titel of talk: Modeling Wakefulness and Sleep in the Thalamocortical System
When the brain goes from wakefulness to sleep, cortical neurons begin to undergo slow oscillations in their membrane potential that are synchronized by thalamocortical circuits and reflected in EEG slow waves. In order to provide a self-consistent account of the transition from wakefulness to sleep and of the generation of sleep slow waves, we have constructed a large-scale computer model that encompasses portions of two visual areas and associated thalamic and reticular thalamic nuclei. Thousands of model neurons, incorporating several intrinsic currents, are interconnected with millions of thalamocortical, corticothalamic, intra- and inter-areal corticocortical connections. In the waking mode, the model exhibits irregular spontaneous firing and selective responses to visual stimuli. In the sleep mode, neuromodulatory changes lead to slow oscillations that closely resemble those observed in vivo and in vitro. The model is the first to integrate intrinsic neuronal properties with detailed thalamocortical anatomy and reproduce neural activity patterns of waking, slow wave sleep and anesthetized states.

Neuro-Machine Interfaces: Integrating Biology and Technology to Develop Functionally Relevant Devices

Workshop Objective

Neuroprostheses are medical devices that replace the function of an impaired nervous system. Successful development of functional neuroprostheses requires an interdisciplinary approach, involving experimentalists to understand the physiology and behavior of the nervous system, engineers to develop adaptive biocompatible devices, clinicians to implement and study the interaction between the device and the patient, and computational modelers to integrate the diverse approaches. The workshop aims at developing strategies to deal with the most important issue in NMI development - optimizing the behavior of the combined system (biological and technological) by fully utilizing the plasticity of the nervous system

Thursday July 12, 2007, Bahen Building, University of Toronto

08:30 - 08:45 Introduction & ANS Presentation
Prof. Ranu Jung
Co-Director, Center for Adaptive Neural Systems
Associate Professor of Bioengineering, Arizona State University
http://www.fulton.asu.edu/~bme/faculty/core/jung.php

08:45 - 09:35 Prof. Don H. Johnson & Ilan N. Goodman
"Information theoretic analysis of the effectiveness of neural prosthetics"
J.S. Abercrombie Professor of Electrical & Computer Engineering and of Statistics, Rice University
http://www.ece.rice.edu/~dhj

09:40 - 10:00 Dr. Dongchul C. Lee
"Field Sculpting to correct electric field distortion by percutaneous lead migration"
Senior System Engineer, Advanced Bionics

10:00 - 10:20 Coffee Break

10:20 - 11:10 Prof. Astrid Prinz
"Neuronal network plasticity and homeostasis - implications for neuroprosthetics"
Assistant Professor of Biology, Emory University
http://www.biology.emory.edu/research/Prinz

11:15 - 12:30 Panel Discussion

TITLES & ABSTRACTS

1. Ranu Jung

TITLE: "Adaptation and Learning in Neuro-Biomechatronic Systems"

ABSTRACT: Center for Adaptive Neural Systems at Arizona State University was established to explore key issues regarding co-adaptation of engineered systems with biological systems.

Applying a multifaceted approach, the center seeks to investigate the effects of trauma and disorders of the nervous system, to replace damaged or lost functionality, to repair the system using advanced adaptive devices and therapeutic techniques. The center brings together life scientists, engineers, mathematicians, and clinician-scientists to identify key limitations and opportunities in integration of adaptive engineered systems with the inherent learning and plastic capabilities of living systems. The scope of activities include experimental biological investigation, design and development of new technology to maximize learning outcomes, the evaluation of the effects of the technology on biological learning processes, and the transfer of these techniques to biomedical industry and clinical practice.

2. Don H. Johnson

TITLE: “Information theoretic analysis of the effectiveness of neural prosthetics”

ABSTRACT: Information capacity determines how well any system can extract information from a signal or set of signals that encodes the information. We extend our recent capacity calculations for neural populations to situations relevant to neural prosthetics. For neural stimulation scenarios, capacity calculations suggest no fundamental barriers prohibit obtaining high-fidelity prosthetics. In contrast, capacity results for neural control situations using few, unsorted recordings suggest that severe degradations in extracting information must occur. More detailed analysis shows that either increasing the number of simultaneous recordings (even if the recording fields overlap) or using even primitive spike sorting algorithms will greatly boost capacity, allowing more detailed information extraction.

3. Dongchul C. Lee

TITLE: "Field Sculpting to correct electric field distortion by percutaneous lead migration"

ABSTRACT:
Introduction: Technical advancement in computational models can provide not only theoretical tools to improve understanding of the mechanism of electrical stimulation, but also evaluations of new stimulation technologies, such as current fractionalization to correct electric field distortion by lead migration. We report on our development and use of a new computer model to study (1) the effect of lead migration on activation of dorsal column (DC) and dorsal root (DR) neurons in spinal cord stimulation (SCS), and (2) correction by current fractionalization using independent multiple current sources.

Method: A volume conductor model of a low-thoracic spinal cord with three epidurally-positioned cylindrical percutaneous leads with medio-lateral, rostro-caudal and dorso-lateral migration were created using the finite element model tool ANSYS from which the electric field was calculated. The electric field results were then coupled with the NEURON simulator to determine the activated region of spinal cord DC and DR fibers. DC and DR fiber models were adopted from double-cable axon model (McIntyre et al., 2002) with various fiber sizes (5.7-15 um diameter).

Results: Three leads placed in a symmetric, parallel mediolateral arrangement with medio-lateral tripolar configuration, has deeper penetration than a single lead or dual leads. However, the shape and depth of the activated region of spinal cord fibers is compromised by lead migration for any direction. The model predicts that properly adjusted current-fractionalization from independent multiple current sources can re-orient current flow to correct the electric field and potentially restore therapeutic benefits.

Conclusion: Our computational model was able (1) to predict the sensitivity of the region of activated spinal cord fibers due to variability in lead and spinal cord positions while using medio-lateral tripolar stimulation, and (2) to predict a candidate approach to compensate for variability in relative lead and spinal cord positions (namely, fractionalization of current using independent sources) that may yield improved therapy. Follow-up clinical investigation of the model-predicted solution is the appropriate next step.

4. Astrid A. Prinz

TITLE:"Neuronal network plasticity and homeostasis - implications for neuroprosthetics"

ABSTRACT: Interfaces between brains and machines are facing a challenge, because neural circuits can undergo changes on multiple timescales. Neuronal networks show both plasticity and stability, the former in order to encode information and store memories, and the latter in order to maintain network activity in a functional range. Both plasticity and stability mechanisms operate at the cellular, synaptic, and network levels. I will describe recent findings on the mechanisms of network stability and homeostasis, and will speculate on the implications of these findings for the design and function of neural prostheses.

SUMMARY

The Neuro Machine Interfaces (NMI) workshop addressed crucial issues in developing successful neuro-machine interfaces from theoretical and experimental perspectives. The focus of the workshop was on information theory and use of computational neuroscience models for guiding the development of soft- and hardware devices. After an introduction to the topic by the workshop organizers and general overview of the potential role of the use of neuro-machine interfaces to promote neural plasticity, three invited speakers gave lectures. In the first lecture use of information theoretic approaches to measure the efficiency of neuroprosthetic devices was discussed. The discussions led to the suggestions that capacity calculations could be used to find if single unit or multi-unit electrodes are more optimal in a neural stimulator. Rate distortion theory could be applied to give performance bounds on any signal processing or control system. The second lecture discussed how computational neuroscience models could prove to be effective tools for optimizing neuroprostheses applications. As an example the role of such models to study the effects of lead migration and sub-optimal placements of spinal cord stimulating leads for therapeutic targets was discussed. The third lecture addressed the importance of understanding the mechanisms of neural plasticity. The discussions suggested that an understanding of mechanisms of neuronal plasticity and activity dependent homeostatic regulations at cellular, synaptic and network level would enhance the ability to design neural prostheses that adapt to dynamic biological systems. The overall conclusion was that a neuroprosthetic device will be effective only if it is able to integrate with the adaptive biological mechanisms. Interdisciplinary efforts are needed to elucidate how adaptive technology should interact with adaptive biological systems.

Organizers:
Mini Kurian[1, 4], Joe Graham [2, 4], Sharon Crook[1, 3, 4], Ranu Jung[2, 4]
[1]Department of Mathematics and Statistics
[2]Harrington Department of Bioengineering

[3]School of Life Science
[4]Center for Adaptive Neural Systems
Arizona State University

Workshop Webpage:
http://www.public.asu.edu/~mputhaya/CNS2007Workshop/

CNS*07 Electrophysiology Database and Analysis Software Post-Workshop Summary

Following the introduction by workshop organizer Cengiz Gunay, Padraig Gleeson's talked about the use of the neuroConstruct tool to build neuronal network models for multiple simulators. Dr. Gleeson's work aimed at unifying different approaches to neural simulation under a flexible neural model description language, NeuroML. The Neural Open Markup Language project, NeuroML [1, 2] [http://www.neuroml.org], is an international, collaborative initiative to create standards for the description and interchange of models of neuronal systems. MorphML and ChannelML are standards under the NeuroML framework, and they are designed to model morphology and ion channels, respectively. These languages take their strength from the XML language which already changed many other fields, such as e-commerce, by standardizing the way computers and software communicate. Dr. Gleeson's neuroConstruct software is a Java application that can read model descriptions and visualize neuron and network topologies [3]. It can delegate simulations to Neuron and Genesis neural simulators, collect and visualize their outputs. To do this, it creates Neuron and Genesis input files from the model's description in NeuroML. It can load morphology files from a number of formats and convert between them, as well. NeuroConstruct's major advantage is its flexibility to attach its models to new simulators, and understand new input formats. This was made possible by employing modern computer science concepts such as XML style-sheets (XSLT). These recipes allow transforming, for example a channel description in ChannelML, to a web page, a kinetics plot, or transforming a neural model to a Genesis input script. This makes adding new target simulators as easy as defining a new XSLT transformation. In fairness, neuroConstruct cannot yet support all Genesis and Neuron model descriptions. Given the limitless programming options available in a full simulator, NeuroML cannot convert an arbitrary Genesis or Neuron script into NeuroML. Dr. Gleeson recommended that researchers starting new models would choose an existing simulator, and transfer the model to NeuroML only after its maturation. The CNS audience appreciated Dr. Gleeson's software and several people showed interest in using it. The consensus was that neuroConstruct could provide a useful medium for collaboration between modelers and for testing and validations of available models.

Tom Morse talked about the use of computational intellligence for electrophysiological databases (EPDBs). This subject was changed from his proposed title on data sharing methods with NeuronDB and ModelDB, because these has already been discussed in a spontenously-formed workshop the previous day. Dr. Morse made a comprehensive effort to justify the need for making EPDBs widely available and feasible. He suggested that software utilities, such as spike sorting methods, should be collected in a central repository, similar to the SimToolDB repository [http://senselab.med.yale.edu/simtooldb/]. He identified several reasons that require EPDBs. One was parameter extraction approaches which required a seed of single cell data to verify the models found. The major obstacle to creating public EPDBs was that each researcher keeps their own specialized EPDBs. Many people agreed that this is most simple for many research projects, and maintaining a large common database requires a lot of time that experimentalists in the field cannot afford. A solution was offered to prepare EPDB support into existing data acquisition systems such that the experimentalist did not spend extra time for entering data. Another question that was raised was how the experimenter can be credited if his/her data was used. Unfortunately, the alternative to EPDBs is the use of "data thief" software to get data from published papers. Many people agreed from their own experience that this is tedious and inadequate solution, but may be the last resort in certain cases. Dr. Morse's conclusion was that the much-hyped semantic web failed to bring its promise so far, and there is still a dire need for data sharing among modelers and electrophysiologists.

Workshop organizer Tomasz Smolinski introduced the next session on special data analysis methods. As first speaker, Bill Lytton focused on data-mining algorithms in spike-wave detection and seizure classification. He reviewed the need for data-mining in biological projects. He pointed to the Structured Query Language (SQL) as one of the widely adopted and easy-to-use database software for data-mining. His Neural Query System (NQS) is a software package that allows making similar queries from within the Neuron simulator, as well as connecting to an SQL engine. He applied this method to seizure prediction

from recorded traces by analyzing "bumps" in the data. In this process, he introduced a graph that can convey information in five-dimensions using various parameters of circles to represent the different aspects of the data. His method involved using K-means clustering of bump intervals.

Jean-Marc Fellous talked about a method for discovering spatio-temporal spike patterns in multi-unit recordings. Timing and reliability of timing from multiple trials or animals has been an interesting question [5]. He introduced a method that involved sorting spike rasters for finding order among them. This method used the similarity matrix obtained by comparing spike rasterograms after convolving with a Gaussian kernel. Then, fuzzy-clustering was used to organize the matrix into distinct regions, which was used to sort the raster plots. In the discussion, a method based on random shuffling was proposed to replace the fuzzy clustering.

Workshop organizer Bill Lytton introduced the next session on community software projects. Cengiz Gunay presented his PANDORA Matlab toolbox for analyzing simulated or recorded intracellular traces. He demonstrated databases can be created from recorded or simulated data alike, and complex analysis can be performed to result in descriptive plots. The toolbox's features produced substantial interest but there was some concern that its dependency on a commercial package (Matlab) rather than a free software variant (such as GNU Octave or Python) could limit its adaptation. A request was made to have more database templates suitable for researchers using different experimental and model setups. During the discussion, the need for common data to test new algorithms was voiced again. Dr. Gunay's toolbox can be downloaded for free [http://userwww.service.emory.edu/~cgunay/pandora].

Horatiu Voicu demonstrated a very low-maintenance method to feed parameter values into custom simulation software as an alternative to creating sophisticated graphical user interfaces. He demonstrated this method using a free text editor software, GWD [http://www.gwdsoft.com/], and the message-passing capabilities of the Windows operating system to drive a hippocampal simulation system. He was able to change arbitrary parameter values of the simulator on-the-fly. His software can be downloaded from [http://www.voicu.us/software.zip].

Workshop organizer Cengiz Gunay introduced the final session on parameter search and other analysis methods. Adam Taylor talked about mapping from model neuron parameters to functional output. He demonstrated methods for correlating variability of channels with other measurements. He aimed to model the results of mRNA measurements predicting channel densities [4]. He created a model database with 80k models and found 100 models matching target data within 1 STD. He used a scatter plot matrix to explain these matches. From this database he concluded that real cells are more constrained in changing their conductance densities than the models he found. To find such constraints in real neuron data he used linear and quadratic fits to channel dependencies from recorded data.

Gloster Aaron presented a method for finding repeating synaptic inputs on a single neuron. He used Matlab programs for finding repeating synaptic inputs in intracellular voltage data from recordings [6]. However, he showed that his method did not work with new data. There was a discussion on the non-stationarity of the recorded data affecting method results. The resolution was to adjust the window of comparison to have sufficiently good estimate of the mean and variance of the data.

The workshop closed with the audience's wishes for its repeat in the next year's CNS meeting.

References

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