Mathematical Neuroscience 2002-2003

The MBI receives major funding from the National Science Foundation Division of Mathematical Sciences and is supported by The Ohio State University. The Mathematical Biosciences Institute adheres to the AA/EOE guidelines.

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Director's Letter

In recent years we have witnessed unprecedented progress in the biosciences. Perhaps the most visible event is the announced completion of the Human Genome Project – the first step toward a molecular genetic understanding of the human organism. Advances are reported continually in the fights against cancer and degenerative diseases of the brain, such as Alzheimer's, Parkinson's and ALS, as well as in the management of health threats, such as AIDS, insect disease vectors, and antibiotic resistance. Society is eager to see basic research quickly translated into a longer and better quality of life through deeper understanding of disease mechanisms and better medical treatment. Accordingly, many topics from bioscience have been given high priority on the national agenda.

Behind headlines lie astonishing advances in basic science and technology including medical imaging, nanoscale bioengineering, and gene expression arrays. These technologies have rapidly generated massive sets of loosely structured data. This explosion of experimental results has challenged researchers' abilities to synthesize the data and draw knowledge from them. This can be achieved via mathematical and statistical modeling. Indeed, examples of recently developed models of this kind include thalamo-cortical interactions underlying sleep rhythms; 3-D modeling of the heart, heart rhythms, and pacemakers; gene sequencing algorithms; and the design and assessment of medical prosthetic devices, such as artificial hip and knee joints.

In order to fully utilize the potential opportunities for the mathematical sciences to accelerate progress in the biosciences, the following challenges must be met:

1. Learn the scientist's language;
2. Develop new mathematical/statistical models and techniques; and
3. Increase the community's size.

The Mathematical Biosciences Institute, funded by the National Science Foundation (NSF), was created in order to provide a national forum for mathematical bioscience which can address these challenges. The MBI will reinforce and build upon existing research efforts in mathematical bioscience, and quicken human and intellectual growth in this area.

The MBI runs "Emphasis Year" programs each year, concentrating on a broad range of topics in one area of bioscience, with approximately six 1-week workshops preceded by tutorials. In the summer, the MBI runs an educational program based on tutorials and team projects. Occasional "current topics" workshops introduce mathematical scientists to new opportunities for research. In this first year, the program focused on Mathematical Neuroscience. This document provides a summary of events and talks that took place in the first year of the MBI.

Avner Friedman
Director

Corporate Members

The MBI encourages involvement from those in private industry. The institute offers incentives to pharmaceutical and bioengineering companies interested in becoming a Corporate Member.

Membership benefits include:

- Regular visits by MBI Directors to identify problems and topics of interest, where mathematical sciences could be helpful;
- Follow-up to these problems by Institute Researchers;
- Membership on Industrial Advisory Committee.

Invitation to present industrial challenges and problems to MBI audiences and to participate in MBI programs and workshops

Current Corporate Members:

Pfizer

Institute Partners

The MBI Institute Partner Program subsidizes the travel and local expenses of IP member and faculty, postdoctoral fellows, and students to allow their participation in research and education programs at the MBI; for details see the MBI website: http://mbi.osu.edu.

Current Institute Partners

Case Western Reserve University
University of Maryland, Baltimore County
Iowa State University
University of Minnesota
Ohio University
University of Pittsburgh
University of Cincinnati
Vanderbilt University
University of Iowa

MBI Postdoctoral Fellows

Postdoctoral fellows fall into two support categories: Supported at 100 percent by the MBI or split 50/50 percent by the MBI and another specific program. Postdoctoral fellows sponsored by a specific organization spend 50 percent of their time on research suggested by the sponsor. All postdocs are provided with two mentors: one from the mathematical and statistical sciences, and another from one of the biosciences departments at The Ohio State University. Long-term visitors may also serve as mentors. More details are available in the Handbook for Postdocs on the MBI website.

A Brief Summary of the Year in Mathematical Neuroscience September 2002-2003

(Detailed description on page 8)

The use of mathematics to study the brain has had great impact on the field of neuroscience and simultaneously motivated important research in mathematics. Research aimed at understanding the nervous system has two major lines of inquiry: How is a signal from the external world represented in the brain, and what are the mechanistic models at the circuit and system levels? The MBI first-year program in Mathematical Neuroscience addressed both questions. Each quarter featured tutorial sessions to provide important background information as well as in-depth workshops examining the issues as described below. Postdocs and faculty members interested in learning more about neuronal systems and potential mathematical applications in this research were encouraged to attend.

Workshop 1
Neuronal Dynamics

The workshop attracted mathematicians, biologists, and other scientists to discuss the role of nonlinear dynamics in neural systems. The 2-week workshop consisted of four major themes,

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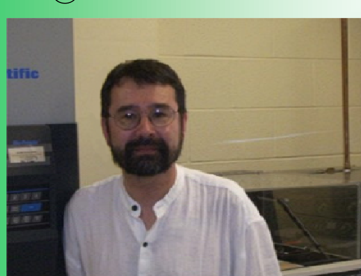

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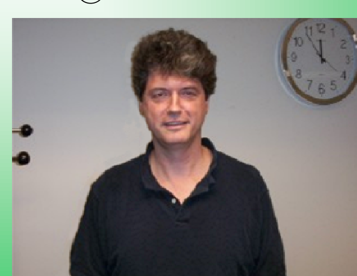

which included: (1) oscillations; (2) waves; (3) synaptic plasticity; and (4) vision. There were typically composed of two 1-hour lectures each morning and one or two 1-hour lectures each afternoon. There were also a small number of half-hour lectures each afternoon. The speakers included neuroscientists who discussed recent experiments in which nonlinear properties of neural systems play an important role in the system's behavior, and theoreticians who discussed recent modeling efforts and theoretical tools to analyze the models. The speakers were chosen for both their expertise in a particular area and their ability to speak to a multidisciplinary audience. There was significant free time in which no lectures were scheduled, which provided opportunities for the participants to have informal discussions. There was a formally scheduled meeting in which the participants discussed past successes of computational neuroscience and the major challenges for future research.

Organizing Committee for 2002-2003

- Catherine Carr – Department of Zoology, University of Maryland, College Park
- Bard Ermentrout – Department of Mathematics, University of Pittsburgh
- John Miller – Center for Computational Biology, Montana State University
- John Rinzel – Courant Institute and Center for Neural Science, New York University
- David Tank – Department of Molecular Biology, Princeton University
- David Terman – Department of Mathematics, The Ohio State University

Workshop 2
System Level Modeling

This workshop focused on the use of neural modeling to understand how populations of neurons interact to mediate complex behaviors. It attracted mathematicians, physicists, neurobiologists, psychologists, and other scientists interested in higher-level neural function. The 5-day workshop centered on several themes: (1) levels of investigation; (2) motor/sensory-motor integration; (3) cognitive function; and (4) modeling strategies for multilevel descriptions. Each session consisted of a few 1-hour talks that were generally introductory in tone, accompanied by several half-hour talks that focused on presenting specific examples of a modeling strategy. All the presentations considered vertebrates, with most focused on the mammalian central nervous system.

Because the levels of investigation varied so widely, from relatively small ensembles of neurons to essentially a large portion of the human brain, multiple modeling approaches were presented, and multiple kinds of neural data were considered. What became clear as the workshop progressed was that there were a variety of different neural modeling styles, such as: (1) bottom-up approaches; (2) top-down approaches; (3) approaches that stayed within one level of description; and (4) approaches that integrated data from several levels of investigation. These different approaches are required because there are a variety of questions that are being dealt with, and each approach is limited in what it can address.

Workshop 3
Neural Coding

How is information about the external world and about an animal's internal states represented within its nervous system? Although much is known about the relation between the stimulus/ response properties of neurons in a variety of systems, we are in many cases far from having a detailed understanding of the correspondence between neural activity patterns and the information represented by those patterns. We will not be able to understand the operation of any nervous system rigorously until we decipher the neural code, i.e., the collection of symbols and modes of communication used to represent and convey information within the nervous system. A rigorous understanding of neural coding is also essential for developing accurate, detailed models of neurons and the nervous systems.

This workshop brought together experimental neuroscientists and theoreticians (statisticians, computer scientists, physicists, and applied mathematicians) who are interested in quantitative analysis of neural data. The presentations covered experimental research, data analysis problems, and methodology development for data analysis. The experimental systems discussed included the rat hippocampus, cricket cercal system, rat barrel cortex, locust auditory system, rat auditory system, monkey primary visual cortex, monkey motor cortex, and monkey LIP. The presentations fell approximately into four methodological topic areas: information theory, Bayesian and dynamic estimation methods, stochastic modeling and simulation methods, and stimulus response and correlation methods. A wide range of methods were applied in each topic area.

" MBI serves as a visionary symbol and example to the larger community where scientific research often remains a solitary experience and where researchers are frequently reluctant to venture beyond their own disciplines."

-Dr. Rita Colwell, Director of the National Science Foundation, during the

The MBI provided an ideal environment for this workshop. The logistical, secretarial/ administrative, and audio-visual support were outstanding. At the workshop, there was ample time for extended discussions between lectures. Indeed, many of the discussions continued over dinner and beyond. Moreover, the ready availability of office space, chalk-boards, and workstations was highly conducive to further in-depth discussions as well as collaborative undertakings. Several of the latter were initiated during the meeting.

Workshop 4
Olfaction System

Olfaction provides an ideal model for a distributed neural code. Unlike other sensory systems, from the receptor level onward, there is no simple spatial organization of the inputs. The output from receptors terminates on the olfactory bulb (or its analogues, the antennal lobe in insects) where it is processed and sent on to the olfactory cortex (mushroom body, in insects). Thus, complex processing occurs at the earliest levels of input.

At the first level of processing, the olfactory bulb, and the analogue regions, is characterized by complex oscillations. These oscillations appear to be crucial in order for the animal to discriminate between odors, particularly those which are closely related. Furthermore, animals can learn a new odor with only a single presentation. Thus, part of this workshop focused on models and experiments for olfactory oscillations and learning.

Workshop 5
Auditory System

This 1-week workshop brought together an interdisciplinary group of about 40 theoreticians and experimentalists to discuss different approaches to understanding neural coding and infrastructure (cell/circuit correlates) that relate to sound localization, to processing of complex sounds, and spatio-temporal aspects of auditory environment. The discussions were lively and extensive. A number of participants commented that the workshop was outstanding, well-organized, and well-balanced between theory and experiment. One outstanding feature of this workshop is that it included an evening poster session, enabling non-speaker attendees the opportunity for presentation; the event was viewed as a success.

The presentations described research that involved investigation at multiple levels, including molecular, cellular, developmental, systems level, and with in vitro and in vivo experimental preparations. There were some human studies with imaging techniques. The modeling included biophysically-motivated mechanistic models as well as statistical models.

Issues related to sound localization were addressed with electrophysiology at early and higher stages in the auditory system from the first convergence site of binaural input to auditory cortex where the cues are less well understood. In mammals, neural input from the two ears first meets in the medial superior olive (MSO) where, for localization of low frequency tones, the relative timing of inputs is discriminated at sub-millisecond scales; in birds (including the well studied barn owl) this occurs in the nucleus laminaris (NL). Phase-locking and timing precision is crucial at this stage. At succeeding stations, including the inferior colliculus (IC) and thalamus (MGN) and into the primary auditory cortex (AI), different time scales of integration and discrimination are involved. Factors that influence timing and throughput even preceding the MSO/NL on the auditory nerve (AN) and the pre-superior olive relay stations (the cochlear nucleus, CN) were also discussed.

Emphasis Year Scientific Advisory
Committee 2002-2003

The Emphasis Year Scientific Advisory Committee reviews the Emphasis Year Proposals as they evolve and offers suggestions throughout the development of the Emphasis Year. A new Emphasis Year Scientific Advisory Committee is appointed for each Emphasis Year Program.

- Emery N. Brown – Massachusetts General Hospital
- Barry W. Conners – BioMed Neuroscience, Brown University
- David Kleinfeld – Physics Department, University of California, San Diego
- Nancy Kopell – Mathematics Department, Boston University
- Gilles Laurent – Biology Department, CalTech
- Steve Lisberger – Physiology Department, University of California, San Francisco
- Miguel Nicolelis – Neurobiology Department, Duke University
- Shihab A. Shermma – Electrical Engineering Department, University of Maryland, College Park
- Jeff Smith – Laboratory of Neural Control, National Institutes of Health
- Jonathan Victor – Weill Medical College, Neurology and Neuroscience Department, Cornell University
- Charles Wilson – Biology Department, University of Texas, San Antonio

Workshop 6
Sensory Motor Systems

This workshop focused on modeling the basal ganglia in both mammals and birds. In mammals, the basal ganglia are a group of forebrain nuclei that play an important role in the control of movement. They also appear to be involved in cognition, motivation, and emotion. Dysfunction of the basal ganglia is associated with movement disorders, such as Parkinson's disease and Huntington's chorea. Structures within the basal ganglia have been the target of therapeutic surgical procedures, including pallidotomy and deep brain stimulation. Recent work has shown just how similar the organization and function of the basal ganglia is in both birds and mammals. Experiments on the song system have provided a window into mammalian basal ganglion function.

The 5-day workshop brought together mathematicians, neurobiologists, physicians, and other scientists. The workshop centered on several major themes: (1) modeling neuronal activity at both the single cell and network level; (2) understanding the role of the basal ganglia in both normal and pathological states; and (3) understanding mechanisms underlying recent surgical procedures such as deep brain stimulation. Each session typically consisted of one or two 45-minute lectures that were somewhat introductory and several half-hour lectures that focused on presenting the results of a specific theoretical or experimental study.

Current Topics Workshop
Non-local Integro-Differential Equations in Mathematics and Biology

This workshop focused on surveying the mathematical techniques used to model and analyze nonlocal interactions that arise in biology, with special emphasis on concrete applications in neuroscience. It attracted mathematicians, physicists, neurobiologists, and other scientists interested in the analysis of neuronal and other biological models. The 3-day workshop centered on several major themes: (1) modeling the neuronal networks; (2) analysis of related mathematical models; and (3) general mathematical techniques for integro-differential equations. Each session typically consisted of two 1-hour lectures that were somewhat introductory and several half-hour lectures that focused on presenting specific examples of modeling strategy and analytic technique.

Program Details

Workshop 1
***Neuronal Dynamics*: October 7-18, 2002**
Organizers:
Bard Ermentrout - Department of Mathematics, University of Pittsburgh; David Terman – Department of Mathematics, The Ohio State University

Summary of Speakers:

Some of the experimentalists who spoke during the oscillations portion of the workshop were Barry Connors, Roger Traub, and Jeffery Smith. Connors described recent experiments that suggest electrical synapses are far more widespread in the nervous system than suspected just a few years ago. He presented evidence that electrical synapses now seem to play a major feature of the neural circuitry in the neocortex, hippocampus, thalamus, striatum, and many other brain structures. Traub also discussed electrical synapses. He emphasized the role of gap junctions between the axons of principal neurons and the generation of fast oscillations in neuronal populations. He also described modeling projects related to these issues. Smith described experimental and modeling studies related to the dynamics of the mammalian respiratory system. The studies have revealed how networks of heterogeneous neurons can produce synchronized activities that are believed to play an important role in breathing rhythms.

Theoreticians who spoke during the oscillations portion of the program were Tim Lewis, XJ Wang, and Carl van Vreeswijk. Lewis discussed modeling and analytical work to understand the possible roles of electrical coupling in generating synchronous and asynchronous rhythms. This was very closely related to the experimental studies of Connors. XJ Wang described recent results related to the role of noise in generating network oscillations, and van Vreeswijk presented interesting techniques for studying large populations of reduced neuronal models.

Experimentalists who spoke during the wave's portion of the program included Philip Ulinski, David Kleinfeld, and Marla Feller. Ulinski described experiments on waves of activity that propagate throughout the visual cortex of freshwater turtles. He went on to describe recent mathematical models of turtle visual cortex used to study the cellular mechanisms underlying the propagation of waves and to suggest that information about visual stimuli is encoded in the temporal dynamics of the waves. Feller described her work on the mechanisms underlying spontaneous propagating activity in the developing mammalian retina.

Theoreticians speaking during the wave portion of the program included David Hansel and David Golomb. Both described mathematical techniques to analyze large populations of model neurons. These techniques were used to understand mechanisms underlying propagating waves and other patterns in a variety of neural systems.

Speakers during the synaptic plasticity portion included Larry Abbott, Guoqiang Bi, Dan Johnston, and Carson Chow. Bi summarized experimental studies on so-called spike timing-dependent plasticity. This represents a quantitative extension of the famous Hebb's rule and may have profound implications in the development and function of neuronal circuits. Johnston described experiments and modeling studies on information processing and storage by neuronal dendrites. Abbott and Chow presented the results of theoretical and modeling studies on issues related to synaptic plasticity. Chow presented a model of neuronal ionic and molecular dynamics that seems to account for the experimental results described by Bi.

Some of the speakers during the vision portion were Robert Shapley, David McLaughlin, and Paul Bressloff. Shapley is an experimentalist and McLaughlin a mathematician who are working together on constructing a computational model for neurons within the primary visual cortex. These speakers described their model, the relevant experiments and recent results on how the model can be used to better understand time-dependent sensitivity and selectivity for orientation and spatial frequency in the visual cortex. Bressloff presented another approach for modeling dynamics within the visual cortex. He presented recent analytical results regarding the large-scale dynamics of cortex in the presence of periodically modulated long-range interactions.

There was a very interesting discussion at the end of the first week. The discussion began with listing major successes of mathematical methods in neuroscience. The list included the Hodgkin-Huxley model for the action potential and the works of Donald Hebb, David Marr, and William Rall. The discussion then turned to listing major developments within mathematics that were motivated by problems originating in neuroscience. This list included the development of the Evans function for determining the stability of propagating waves, many aspects of geometric singular perturbation theory, and biologically inspired machine learning. Major new challenges and open problems were then discussed. They included dynamic reorganization and homeostasis, modeling of diseases and degenerative disorders, and issues related to the spanning of many scales from the molecular to behavioral. Some participants questioned whether genetics or molecular research could help address these issues. Finally, there was a long discussion of how to get mathematicians more involved in neuroscience research.

Conclusion:

What was remarkable about this workshop was that scientists from numerous disciplines were speaking a common language. These disciplines include mathematics, biology, neuroscience, physics, and computer science. We expect that this development of multidisciplinary communication will allow for significant advances in our understanding of neuronal processes and the development of new and exciting mathematical theories to address new models in this area.

Workshop 2
***System Level Modeling*:**
November 18-22, 2002
Organizers:
John Rinzel – Center for Neural Science, New York University; Barry Horwitz – National Institutes of Health

Levels of Investigation:

This session included presentations of the types of data available to computational modelers, and the kinds of questions that these data generate that modeling can help address. Included were experimental data obtained at the single unit level of investigation (Wyeth Bair), at the mesoscopic (ensemble) level of investigation (Miguel Nicolelis), and at the whole-brain level (Barry Horwitz and John George). Electrical (spiking) activity is what is generally measured at the neuronal level of investigation, and Bair presented an overview of this approach. His talk, which focused on data obtained from visual cortex, touched on several issues that were to be brought up several times by other speakers: (1) the role of context in altering the signals measured; (2) the fact that one type of signal (e.g., single unit activity) may appear to be inconsistent with data obtained by other types of signals (e.g., optical imaging data); and (3) the crucial role that feedback connections play. Nicolelis gave an overview of his work employing multiunit recordings to obtain population activity from multiple brain regions simultaneously. By combining such data with a computational model, researchers seek to use the measured activity in one or more parts of the brain to predict activity in another part of the brain. A stunning example showed that the prediction and manipulation motor output by identifying preparatory neural activity in motor, pre-motor, and parietal cortex. Both Horwitz and George discussed the role computational modeling can play in understanding data obtained primarily from human subjects by fMRI (Horwitz) and MEG (George). It was emphasized that fMRI and MEG data are particularly complex, and that computational modeling will be essential for understanding how such data are to be interpreted in terms of neural activity. This is particularly the case for fMRI data, which reflects changes in local hemodynamic activity and are only indirectly related to neural activity. It was emphasized that functional brain imaging data have not, until recently, been the focus of computational neuromodeling.

Several of the subsequent talks reinforced the points expressed in the first three presentations. Detlef Heck demonstrated, using intra and extra cellular data from the frontal cortex of the rat, how integration of synaptic inputs is effected by the background network activity. Gustavo Deco, Martin Stetter, and Malle Tagamets presented fairly detailed network models (spatially distributed, cell, and local-circuit based) that simul-taneously generated both simulated single unit activity and simulated fMRI/PET data corresponding to specific cognitive tasks.

Sensorimotor Processing:

Steve Lisberger discussed the neural system mediating smooth pursuit eye movement. He introduced a type of control model for smooth pursuit, in which different modules perform such tasks as sensorimotor transformations and gain control, and then used single unit recordings from monkeys to identify neuroanatomical circuits that correspond to the modules in the model (e.g., frontal motor cortex associated with gain control - - part of a parieto-frontal circuit). The

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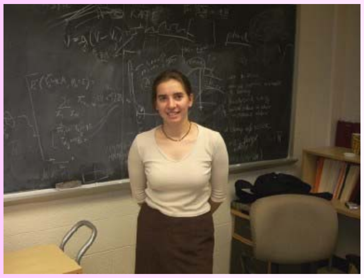

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remaining talks during this session focused primarily on the role of basal ganglia and cerebellar circuits in motor control. Jim Houk presented two models: one involved a cortical-basal ganglia circuit encoding the serial order of sensory events, and the second concerned how a cortical-cerebellar circuit can be used to regulate movement commands. Jose (Pepe) Contreras-Vidal, Dan Bullock and David Hansel all presented models that hypothesized that frontal-basal ganglia circuits function primarily to select internal models that had become established by prior learning. David Terman also focused on the basal ganglia, demonstrating with a computational model of spiking neurons the important role of the indirect pathway of the cortical-basal ganglia loops in Parkinson's disease, and in how deep brain stimulation may act in helping alleviate some of its symptoms by changing dynamic activity patterns.

Two Sessions on Cognitive Function:

A group of presentations by Jonathan Cohen, Marius Usher, Phil Holmes, and Todd Braver were related to the issue of cognitive control. Like the Lisberger presentation mentioned above, Cohen, Usher, and Braver started with a set of phenomena (e.g., tasks where the stronger, or more likely, of two responses must sometimes be inhibited), and a model - a connectionist model in this case - that is able to account for the behavioral performance of human subjects on such tasks. Lesion and fMRI data were then introduced that enabled different parts of the connectionist model to be associated with different parts of the brain (e.g., the anterior cingulate was proposed to play a critical role in conflict mediation). Holmes presented a model of the response of locus coeruleus neurons to target detection, which is a central component of the cognitive control hypothesis.

A variety of additional approaches to neural modeling of cognitive function were presented by other speakers. Steve Grossberg reviewed a large body of research centered on his Adaptive Resonance Theory of cognitive function that emphasizes the importance of matching bottom-up sensory data against top-down expectations. In a similar vein, Randy McIntosh discussed the way context affects how sensory stimuli are handled by the brain. In particular, he showed how this could be detected by applying techniques such as structural equation modeling to PET/fMRI data. Dana Ballard presented a model that enables synchronous spike codes on both feed forward and feedback connections between the Lateral Geniculate Nucleus (LGN) and visual cortex to form oriented receptive fields given natural images as input. This model incorporates both spiking synchrony and a rate code. In an effort to account for the fact that many human psychophysical results have been explained using Bayesian models, Rajesh Rao presented a neural model of the cortex that can perform Bayesian inferences. The model was applied to a visual motion detection task. David Horn's presentation addressed the question of how is it possible to learn what the perceptual features of importance are. He used a PDP model to suggest how internal representations of new perceptual features are created through repeated exposure.

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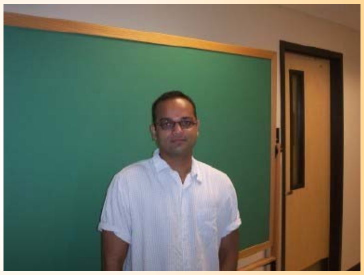

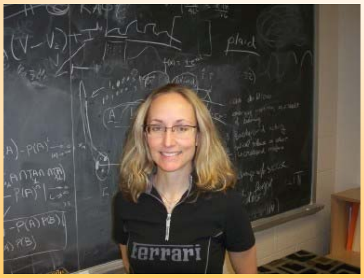

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Working Memory:

Neural models that enable a short-term memory of a presented stimulus to be maintained were included in the presentations by Gustavo Deco and Malle Tagamets. Tagamets reviewed a large-scale neural model of the ventral visual processing pathway that uses, at each stage, an ensemble of Wilson-Cowan units, each representing a basic local computational element. The model mimics perfor-mance of a delayed match-to-sample task for simple shapes, and is able to reproduce the electrical activities of monkey neurons in multiple brain regions (including pre-frontal cortex) and as well, the PET/fMRI activities observed in humans performing this type of task. The Deco model, which focuses primarily on prefrontal cortex, uses a network model of spiking neurons (developed by Nicholas Brunel and Xiao-Jing Wang). This model can account for both prefrontal electrical activity and prefrontal fMRI results in a delayed matching task incorporating both object and spatial components. XJ Wang showed how to account for performance measures (e.g., reaction times) by incorporating a simple decision rule in such a modeling framework. Brunel elaborated on the mean field approach, embedded in the Wilson-Cowan formulation, by showing how it could be extended so that the synaptic input could be described by both a mean and a variance. This will permit one to have a network of irregularly firing neurons modeled using a mean field theory type of formalism.

Program Participation	# Participants
Tutorial on Neural Dynamics: *August 26-30, 2002*	18
Neuronal Dynamics: *October 7-18, 2002*	86
System Level Modeling: *November 18-22, 2002*	60
Tutorial on Neural Coding: *January 9-10, 2003*	12
Neural Coding: *February 10-14, 2003*	54
Period of Concentration: *February 17-28, 2003*	15
Current Topics: *March 6-8, 2003*	36
Tutorial on Olfaction, Auditory System, and Sensory-Motor Systems: *March 31-April 2, 2003*	16
Olfaction System: *April 3-5, 2003*	39
Auditory System: *May 5-9, 2003*	64
Post-Workshop 5: *May 10-23, 2003*	22
Sensory-Motor System: *June 9-13, 2003*	61
Summer Program	24
Total	507
Long Term Visitors for 2002-2003	18

Lists of participants available at http://mbi.osu.edu

Modeling Strategies for Multi-Scale Integration:

Included here was a talk by Martin Stetter, who focused on the use of mean field theory at multiple scales in the mammalian primary visual cortex area V1. Among the topics he discussed was the importance of contextual information in modulating the response properties of visual orientation selective cells. Carson Chow presented models, both spiking and rate-based, to account for a number of experimental observations of visual binocular rivalry. John Rinzel also discussed both spiking and rate models, but in a non-cognitive setting with models that attempt to account for the slow episodic population rhythms (with a time scale on the order of minutes) that are seen in chick embryonic spinal cords. This structure is of great interest, since all the synaptic currents, including those associated with GABA, are excitatory, yet oscillations in activity still occur. Synaptic depression plays a critical role in generating these oscillations.

Conclusion:

Among the key conclusions from the multiple presentations at this workshop were the following: (1) much of importance in the way neurons affect behavior is based on their interaction with other neural populations, and to gain insights into these interactions require computational approaches; (2) increasingly, top-down effects (which come under a variety of names such as context, recurrent inputs, attention, and feedback) are being shown to play a central role in neural processing; (3) integration of multiple levels of data will become important for understanding neural systems, and such integration will be based on computational modeling; and (4) a variety of computational frameworks will be needed that range from, and bridge between, biophysically-based network models to high-level descriptions that employ cognitive/psychological-based state variables, and statistically-based formulations for discrimination and decision-making.

Workshop 3
***Neural Coding*: February 10-14, 2003**
Organizers:
John Miller – Computational Biology Center, Montana State University; Emery Brown – Department of Anesthesia, Massachusetts General Hospital

Information Theory:

Shun-ichi Amari used information-geometric measures to construct orthogonal decompositions of firing patterns into rates, pairwise correlations, and higher order interactions. He used this decomposition to analyze synfire chain properties and Fisher information in models of neural activity. Alexander Borst showed how the information rate for fly H1 interneurons did not increase with increasing stimulus entropy but that it did increase steeply with increases in the contrast of the stimulus. Alex Dimitrov studied information processing in the cricket cercal systems using rate distortion theory and quantization analyses from information theory. Don

Johnson used information theory methods to measure the degree to which neurons in an ensemble work in concert to encode information. Peter Latham demonstrated that for retinal neurons it is possible to extract nearly all the information in the ensemble without taking account of the correlations among the neurons. This suggests that correlated spiking activity may be less relevant for information encoding by ensembles of these neurons. Christian Machen used an algorithm to maximize the mutual information between stimulus and neural response, and used it to demonstrate the feasibility of extracting, on-line, the stimulus statistics auditory receptor neurons “expect.” Stefano Panzieri pre-sented a new information method that computes exactly the effects of higher order spike train statistics and used it to quantify the impact of correlated firing on the information transmitted by a neuronal population. Simon Schultz used information theory measures, developed with Panzieri, to study how spikes from the same or different cells affect information in encoding. P.K. Roy offered a new approach to analyzing a neuronal system using non-equilibrium information theory. He presented a model for a simple sensory-motor system to illustrate the ideas. Tatyana Sharpee described information theory measures appropriate for low spike count experiments.

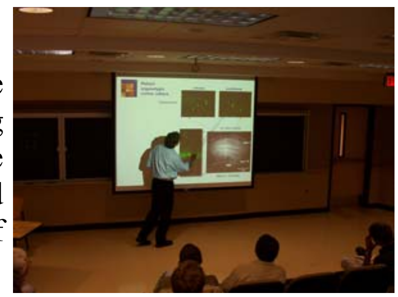
Stochastic Simulations and Modeling:

Charles Anderson and Chris Eliasmith presented their new systems analysis framework for modeling large-scale neural systems. David Arathorn used a simple ordering property of superpositions to define a class of simple circuits that can concurrently discover a correct memory match and a correct composition of transformations to parts of an input image in the midst of clutter or distractors. Sharon Crook studied how different aspects of temporal patterns play a role in evoking a response to a post-synaptic cell and described conditions under which this patterning allows the post-synaptic cell to be frequency selective. Michael Deweese explored binary spiking in auditory cortex in response to brief tone pips and showed that the activity of these neurons is most consistent with a cortical processing model in which synchronous packets of spikes are propogated stably from one neuronal population to another. David Field discussed the extent to which understanding repre-sentations by visual neurons of redundant structure in stimuli, such as natural scenes, can offer insight into the higher level coding strategies of this system. Thomas Gedeon described annealing methods for computing the information distortion function in order to find approximations to neural coding schemes. Bijoy Ghosh focused on wave propogation and their encoding properties in a large-scale model of interacting neurons in the turtle cortex. Sonja Gruen looked at the effects of non-stationarity spike rate across trials on estimates of correlations among neurons and showed that these non-stationarities induce apparent covariation of spike rates that can lead to false positive correlations. John Hertz developed a model network of neurons with dynamically balanced excitation and inhibition, and showed that it could describe the power law relation often seen between variance and the mean of spiking cortical neurons. Martin Stetter discussed the hypothesis that human-like cognitive processes might arise as emergent phenomena from the recurrent dynamics by which different aspects of a large-scale distributed code mutually interact and mutually guide each other’s local dynamics in order to form a coherent brain state.

Bayesian Analysis, Dynamic Estimation Methods, and Neural Spiking Train Decoding:

Michael Black developed a family of neural spike train decoding algorithms using encoding models constructed from the generalized linear model and the generalized additive model, and used the Kalman filter and particle filters to carry out the decoding computations. He applied the algorithms to the analysis of movement encoding by M1 neurons.

Emery Brown presented neural spike train decoding algorithms based on Gaussian approximations to the posterior distribution of the signal given the observations. He applied the paradigm to the analysis of position decoding from ensemble hippocampal activity. Rajesh Rao demonstrated how a network architecture commonly used to model the cerebral cortex can implement a probabilistic, Bayesian inference for an arbitrary Markov model and showed how this architecture may be applied in the analysis of a visual motion detection task. Barry Richmond presented a mixture of Poisson processes model to describe V1 spiking activity and showed that this encoding model used in a Bayesian decoder outperformed a decoder based on spike count alone.



For the topic of spectral analysis, Hemant Bokill compared the accuracy of local field potentials and spikes from LIP in decoding movement direction for a monkey performing a memory saccade task. Nandini Chatterjee-Singh used the modulation spectrum and temporal dynamics measures to characterize the properties of natural sounds.

Stimulus-Neural Spike Train Response Relations and Cross-Correlation Analyses:

Naama Brenner used information theory measures to study the functional aspects of adaptive coding in sensory systems. Yang Dan applied artificial neural networks with back-propogation and second-order Wiener kernels to study the coding properties of neurons in the visual system. Rob Kass developed parametric and nonparametric statistical models of neurons in a stimulus response experiment, and illustrated the potential advantages of using a model- based approach in neural data analysis. Tai Sing Lee demonstrated that signals with naturalistic power spectra have efficient representations and easily identifiable kernels (receptive fields) for V1 neurons. He also showed that different stages of the neural responses in V1 encode different aspects of the visual scene. Bruno Olhausen showed how the statistical regularities over time and space of the images that fall on the retinae can be efficiently represented by modeling this structure using sparse coding in time. Liam Paninski developed a stimulus response model that describes the firing rate of an M1 neuron as a nonlinear function of dynamic hand position and the state of the M1 ensemble neural spiking activity. Garrett Stanley described a point process theory cross-intensity analysis paradigm to study correlations between neurons in the rat barrel cortex. Jonathan Victor analyzed the extent to which individual spikes from V1 of a macaque monkey induced by either M-sequences or spatial grating patterns can be are accurately described by a rate function alone. He concluded that the detailed pattern of neural activity within individual spike trains and across neurons cannot be ignored.

Areas for Future Research:

The fact that the talks could be approximately divided into topic areas suggests that specific types of methodologies for the study of neural encoding from experimental data are beginning to be defined. This characterization may be helpful for students and young investigators wishing to know what methods are being applied and, which ones have been successful in analyzing neural data. Despite being able to identify these topic areas, there were several research themes that surfaced repeatedly during the workshop. They represent the following topics for future research:

1. Development of multivariate statistical models of neural ensembles that take account of history and interactions between neurons.
2. Development of time-dependent measures of correlations among neurons for analyses both in the time domain and the frequency domain.
3. Assessment of between-trial/within-trial variability in peristimulus histogram analyses.
4. Characterizing synchronous firing activity in populations of neurons and how it relates to information encoding of specific stimuli.
5. Defining accurately stimulus response relations within a given neural system.
6. Measuring information encoding in neural ensembles.
7. Characterizing the differences in information representations between local field potentials and neural spike trains.
8. Conducting univariate and multivariate dynamic analyses of neural information encoding.
9. Making explicit the relationship between dynamical modeling of a neural system by means of differential equations, a statistically-based model, and analysis of the same system.
10. Devising accurate, real-time spiking sorting algorithms.

Workshop 4
***Olfaction System*: April 3-5, 2003**
Organizers:
Bard Ermentrout – Department of Mathematics, University of Pittsburgh; Alan Gelperin – Monell Chemical Senses Center

Summary of Speakers:

The first two talks were given by biologists, Brian Smith (OSU) and Mark Stopfer (NIH). Smith described a series of experiments on learning and plasticity in the honeybee olfactory system. He proposes that neural mechanisms that underlie this behavioral plasticity are those that are set up in early sensory processing. He made the important point that the understanding of behavioral and neural mechanisms of olfactory plasticity cannot be complete without knowledge of how natural odor objects vary from time to time and place to place. Stopfer also described experiments in an insect system: the locust antennal lobe (AL). He reported findings that showed that both the identity and concentration of odorants are represented as spatiotemporal patterns of activity across projection neurons (PNs) in the AL. By looking at principle components, he was able to show that the PN activity patterns could be represented as trajectories in a low-dimensional space.

The three afternoon talks were all theoretical. John Hopfield showed how synchronous activity and timing could be used to encode different sensory inputs. Maxim Bazhenov presented a detailed biophysical model of the system described by Stopfer, and his collaborators in the Laurent lab. He also explored a model of cells in the mushroom body and how they could use co-incidence detection to decode the output from the PNs in the AL. Mikhail Rabinovich presented a general theory called win-nerless competition, which is related to general Lotka-Volterra models. He showed that the near hetero-clinic cycles could account for many of the patterns seen in olfaction.

The morning sessions were a mix of experimental and modeling talks. Alan Gelperin and Bard Ermentrout spoke on the olfactory processing in the slug procerebral lobe (PC). Gelperin presented experiments showing that the slug was able to do all the classical behaviors associated with learning. He described the resting wave behavior and the synchronous odor-induced patterns recorded from the PC. Ermentrout presented several levels of modeling of the lobe. He described an abstract model of coupled oscillators with a frequency gradient and showed how this produced waves. Various experiments involving the cutting of the lobe were presented. He closed with a more detailed biophysical model in order to explain the role of NO and gap junctions.

Leslie Kay discussed behavioral-state dependent activity, and activity changes at the single cell and population level of mitral cells in the olfactory bulb of mice. She suggested that gamma oscillations (40-100 Hz) may actually be two behaviorally distinct bands, and preliminary studies from knockout mice show that the two types of oscillations, termed type 1 and type 2 gamma, may be dependent on different types of synaptic interactions and behavioral states.

Thom Cleland discussed some models of learning rules that allow one to overcome the difficulty of discriminating odors at different concentrations. He showed that a sparse representation of inputs can solve this conundrum, and presented a model to demonstrate that such a representation could be learned.

Kerry Delaney described circuitry in the frog olfactory bulb that could be used to enhance contrast between stimuli. He discussed a calcium activated non-specific current in granule cells that can be induced by action potential activity or large amplitude excitatory synaptic currents that are capable of elevating cytoplasm [Ca^{2+}]. This is the requisite "threshold" detector for discriminating large versus small signals.

Dan Lee and Eugene Balkovsky spoke in the last morning session. Lee described his efforts in controlling a robotic dog (the Sony Aibo) so that it could respond to sensory stimuli. He also discussed a recent example of fitting the robot with an electronic nose. Balkovsky described a model for how moths can find the source of a pheromone. He presents an effective algorithm for tracking the odor plume in a turbulent environment and shows that this is what the moth does as well.

Workshop 5
***Auditory System*: May 5-9, 2003**
Organizers:
Catherine Carr – Department of Biology, University of Maryland; John Rinzel – Center for Neural Science, New York University

Summary of Speakers:

At the biophysical and molecular level we heard reports of how low-threshold potassium channels contribute to the temporal precision of coincidence detection, that underlies sound localization at low frequencies. Evidence was presented for how the various subunits (Brew and Forsythe) in this family of potassium channels may be combined to give tunable channel characteristics that are specialized for enhancing one or another aspect of temporal precision and why/how these channels might be localized on particular cellular processes (e.g., at axonal initial segments or at synaptic terminals). Rinzel emphasized that some features of signal detection and discrimination (integration of subthreshold inputs prior to firing) may be well understood by using spike-triggered averaging, and that sodium current inactivation also contributes to this. Jonathan Simon used cable modeling to study the contribution of dendritic placement of synaptic inputs.

Benedikt Grothe presented recent experimental and modeling results that challenge a classical model (Jeffress, 1954) for sound localization, if considered for MSO computations, in two major ways: first, that ITD cues are "read off" by maximal slopes rather than the peaks in neurons' tuning curves and, second, that the tuning is strongly influenced by precisely-timed inhibition, not just excitation from bilateral inputs. Torsten Marquardt described how such inhibition-influenced tuning could be incorporated well into a neural code that is based on interaural phase differences (IPD) across frequencies.

The issue of how the coincidence detection circuitry could be established during development to give a slope code was addressed by Leo van Hemmen with models of spike-timing dependent synaptic plasticity. Anthony Burkitt, in a more general theoretical setting, also considered the importance of the timing window for synaptic input and cell firing. The dynamic nature of inhibitory synaptic gain as driven by background and environmental noise was emphasized by Dan Sanes who described in vitro results from gerbil superior olive, and by William Spain who presented similar studies from the chicken nucleus laminaris. Grothe had also discussed plasticity of inhibitory inputs during development (in MSO) with regard to the selective concentration onto proximal dendritic sites.

ITD Detection:

Philip Joris, Laurel Carney, and Ranjan Batra addressed the issues of what is needed for ITD detection, and whether ITD sensitive neurons act as cross correlators. Both Joris and Carney emphasized the importance of precise temporal information, and how it is enhanced in bushy cells relative to the auditory nerve. Joris reminded us that it is still possible that significant delays may be generated by frequency differences (sterausis). Simon used models of coincidence detection to refine present concepts of coincidence detection, while Peter Cariani used interspike interval statistics to support a theory of processing schemes for periodicity analysis in the nerve.

Auditory Computation and Physiology:

Several talks led the participants into issues about auditory computation and physiology at IC and AI levels. David Poeppel discussed how the human auditory cortex uses multiple timing-based mechanisms for complex sound analysis and representation, and that two temporal integration windows are significant (20-50 ms and 150-200 ms) and these are differentially weighted in left versus right non-primary auditory cortices. The transformation of representation in ascending levels was highlighted in talks by Monty Escabi and by Israel Nelken. Escabi used spectral-temporal response functions (STRFs) to suggest that modulation preferences and left/right ear disparities may enable auditory neurons to simultaneously and independently encode head related spatial cues and contextual information found in complex environmental stimuli. Heather Read discussed how changes in spectral encoding from ventral medial geniculate body to primary auditory cortex, using simultaneous recordings of MGBv and AI neurons. Mal Semple emphasized that in IC, and bird song system, the bird's midbrain and forebrain auditory regions show more heterogeneity and leseven more so in AI, many neurons show marked sensitivity to temporal modulation (time scale of 10s to 100s of ms) of auditory cues. In Nelken's talk we were told that while linear spectral-temporal filtering allows a reasonable

Local Scientific Advisory Committee

The Local Scientific Advisory Committee helps identify current topics workshops, future emphasis programs and organizers, and potential mentors for postdoctoral fellows.

- Jessie Au, College of Pharmacy
- Michael Beattie, Department of Neuroscience
- Albert de la Chapelle, Human Cancer Genetics
- Martin Feinburg, Department of Chemical Engineering
- Mauro Ferrari, Biomedical Engineering Center
- Paul Fuerst, Department of Evolution, Ecology, and Organismal Biology
- Erich Grotewold, Department of Plant Biology
- Fernand Hayot, Department of Physics
- Charles R. Hille, Department of Molecular and Cellular Biochemistry
- Lee Johnson, Department of Molecular Genetics
- Stanley Lemeshow, Center for Biostatistics
- Charles Orosz, Department of Surgery
- Dennis Pearl, Department of Statistics
- John Reeve, Department of Microbiology
- Andrej Rotter, Department of Pharmacology
- Wolfgang Sadee, Department of Pharmacology
- Joel Saltz, Department of Biomedical Informatics
- Brian Smith, Department of Entomology
- David Terman, Department of Mathematics
- Deliang Wang, Department of Computer and Information Science

representation in IC, in AI, nonlinear enhancement of rare and weak signals are found. Frederic Theunissen reported that while high selectivity is seen in neurons in the s selectivity. He found that the ensemble response properties of neurons are indeed tuned to modulations found in natural sounds, as he is finding with STRF analyses. While the phasic responsiveness of auditory neurons is widely studied, Xiaoqin Wang finds that in the awake primate auditory cortical neurons often show greater selectivity to particular stimulus parameters in their sustained discharges than in their onset discharges. At the same time, the neurons exhibit stronger context-dependent inhibition in the awake condition, likely contributing to increased selectivity to stimuli. Finally, a talk from Terry Takahashi combined neurophysiological and behavior studies to directly test localization performance with single neuron output in the inferior colliculus.

Workshop 6
***Sensory Motor Systems*:**
June 9-13, 2003
Organizers:
David Terman – Department of Mathematics, The Ohio State University; Charles Wilson – Dept. of Biology, University of Texas, San Antonio

Summary of Speakers:

The first speaker was Ann Graybiel. She discussed work in her laboratory to understand the role of the basal ganglia in learning and memory. She presented evidence for plasticity in the response properties of striatal units as animals undergo training in procedural learning tasks. This suggests that in order to develop a semi-automatic behavioral routine, it may be necessary to develop new neuronal firing patterns within the basal ganglia that represent action sequences. The next speaker was David Perkel, who described his work in the role of the basal ganglia in song birds for vocal learning. He presented the results of recent experiments that demonstrate that dopamine may have an important effect on cellular excitability, synaptic transmission, and on activity-dependent synaptic plasticity. These could play an important role in song learning.

There were three lectures during the first day's afternoon session. Mark Humphries and then David Hansel presented computational models for the basal ganglia's role in action selection. Hansel emphasized the role of multiple feedback loops connecting the basal ganglia with the thalamus and cortex. He hypothesized that for large dopamine depletion, synchronous oscillations driven by the hyperdirect loops emerge. The final speaker of this session was Hagai Bergmann who described experiments and theoretical results related to the role of the basal ganglia in motor learning. These results suggest that the normal basal ganglia activity represents an optimally compressed version of distinctive features of cortical activity. Changes in basal ganglia synchronization are caused by dopamine depletion and are correlated with clinical manifestations of Parkinsonian and its pharmacological treatment.

James Surmeier and Dieter Jaeger spoke during the second day's morning session. Jaeger presented anatomical evidence showing clusters of sodium channels at excitatory synapses on the dendrites of globus pallidus neurons. He then explored the consequences of this novel way of input coding in a modeling study. During the afternoon session, Charles Wilson described experiments to understand the ionic mechanism underlying rhythmic bursting patterns by cholinergic striatal interneurons. These neurons play an important but indirect role in synaptic integration in the neostriatum. Mark Bevan then discussed his experiments on the relationships between the intrinsic membrane properties of subthalamic nucleus neurons in vitro and their firing patterns in vivo. These membrane properties may underlie, in part, the normal operation of STN neurons in voluntary movement and their abnormal operation in Parkinson's disease. Jonathan Dostrovsky also spoke during the second day's afternoon session. He described the firing patterns and oscillatory activity of basal ganglia neurons in movement disorder patients.

There were three talks related to vocal learning in songbirds during the third day. Michael Brainard presented experimental evidence for a role of an avian basal ganglia circuit in the learning process. Allison Doupe then discussed studies showing that neural firing in this circuit is strongly modulated by social context. She further showed that variations in the degree of correlation in the network could alter information processing, as has been suggested in normal and diseased basal ganglia of mammals. Todd Troyer reviewed some basic models for how various representations of song might interact during the sensorimotor process of learning. There were several lectures during the third day's afternoon session that described mathematical and computational models for basal ganglia activity. Daniel Bullock described a model of how the basal ganglia might interact with a laminar model of frontal cortex to satisfy the staging and gating requirements of conditional voluntary behavior. David Willshaw and Andrew Gillies presented models for subthalamic pallidal interactions.

James Houk and James Tepper spoke during the fourth day's morning session. Houk presented a model of medium spiny neurons to explore the mechanism whereby reward likelihood modulates single unit responses. Tepper described experiments on the role of GABAergic inputs in controlling the firing patterns of dopamine neurons. The afternoon speakers during the fourth day were Patricio O'Donnell, Georgi Medvedev, Carmen Canavier, and Steve Lisberger. O'Donnell discussed how interactions between limbic and prefrontal cortical inputs depend on non-linear membrane properties. This may be important for the selction of behavioral responses appropriate to an animal's environment. Both Medvedev and Canavier showed how complex firing patterns can emerge in models for dopamine neurons.

During the final session, Erwin Montgomery, Cameron McIntyre, and Jonathan Rubin all discussed issues related to deep brain stimulation, a surgical procedure for Parkinson's disease. McIntyre described his model for the electric field generated by DBS electrodes and the coupling of the electric fields to 3D reconstructions of neurons surrounding the electrode. Rubin presented a computational model to test the hypothesis that DBS acts to replace pathological rhythmic basal ganglia output with tonic, high frequency firing. The final speaker was Leonid Rubchinsky who described a computational mode for the facilitation and inhibition of competing motor programs in basal ganglia circuits.

Conclusion:

This workshop was highly successful in nurturing cross-disciplinary interactions between theoreticians and experimentalists working on a variety of different animal models. The songbird experiments clearly demonstrate that the basal ganglia play a fundamental role in vocal learning. This may lead to new insights into the role of the basal ganglia of mammals in motor learning. Moreover, the experimental results clearly demonstrate that neurons within the basal ganglia display a variety of dynamic behaviors and patterns of neuronal activity differing between normal and pathological states. As these experiments continue to demonstrate the importance of temporal dynamics, the need for more realistic, biophysically based models, and the development of analytic tools to analyze these models, is becoming increasingly clear.

Current Topics Workshops

"Current topics" workshops are arranged on a short time notice, i.e., a few months. Their aim is to alert the mathematical sciences community to immediate opportunities that occur as a result of recent discoveries in the biosciences. Current Topics Workshops are also designed to articulate mathematical problems that arise during the annual program.

Current Topics Workshop
Non-local Integro-Differential Equations in Mathematics and Biology:
March 6-8, 2003
Organizers:
Bjorn Sandstede – Department of Mathematics, The Ohio State University; David Terman – Department of Mathematics, The Ohio State University

Summary of Speakers:
The first speaker was Shun-ichi Amari, a pioneer in this field. He revised the derivation of firing rate models for neuronal systems. In these models, the nonlocal interactions correspond to the excitatory and inhibitory coupling between neurons. He then discussed earlier work on the existence of so-called bump solutions in one-dimensional systems, and then more recent work on two-dimensional oscillatory and traveling wave patterns. He concluded by discussing how to incorporate generalized Hebbian learning rules into the models. The next speaker was Bard Ermentrout, who discussed several biological systems that give rise to integral equations. He considered the existence and stability of phase-locked solutions and traveling fronts in general neural networks. He presented a number of recently developed mathematical techniques for analyzing these patterns.

There were three lectures during the first day's afternoon session. These were by Amit Bose, Tim Lewis, and David Golomb. Bose discussed issues related to synchronization in a globally inhibitory network that is based on activity patterns in the hippocampal region. He demonstrated how geometric singular perturbation methods can be used to understand spatial synchronization in models that include short-term plasticity. Lewis considered wave propagation in networks of fast-spiking interneurons. A novel feature of these systems is that they include both direct electrical coupling and recurrent inhibitory synapses. He demonstrated how one could formulate an idealized model for this network that can be more easily analyzed. Golomb also considered issues related to synchronization and wave propagation in electrically coupled networks. He showed how the stability of asynchronous states can be reduced to an algebraic-integral eigenvalue problem.

The second day's 1-hour speakers were Carson Chow and Bjorn Sandstede. Chow considered localized pulse solutions in a one-dimensional equation similar to those discussed by Amari. He first demonstrated how these equations arise from a network of coupled spiking neurons. He then presented techniques to analyze how the existence and stability properties of the pulses depend on system parameters. Sandstede began his lecture with an overview of the so-called Evans function. This is a powerful technique to analyze the stability of solutions such as standing pulses and traveling waves. It has been used in a variety of biological and other systems. Sandstede concluded with recent extensions of the Evans function to equations that contain nonlocal terms, including those that arise frequently in nonlinear optics and in models of neuronal networks with nonlocal interactions.

There were four lectures in the second day's afternoon session. Steve Coombes discussed the analysis of traveling fronts on neural field theories which incorporate delays arising from the finite speed of action potential propagation. Bill Troy considered multi-bumps in partial integro-differential equations in two space dimensions. He showed how to derive a partial differential equation, which is equivalent to the integral equation. Using the PDE, he was able to predict the existence of a rich structure of patterns in systems with circular symmetry. Jon Rubin also considered bump-like solutions in integro-differential models. He demonstrated that these solutions can arise in models without recurrent excitation. Carl van Vreeswijk presented techniques to analyze large spatially extended networks of neurons. He showed how to derive a Fokker-Plank equation that can be used to determine the existence and stability of asynchronous states.

Peter Bates gave the 1-hour lecture during the third and final day. He considered a very general class of discrete and continuum bistable equations with indefinite interactions, and presented sophisticated analytic tools to characterize how both excitatory and inhibitory coupling can lead to both pattern formation and homogeneity. Wendy Hines considered an integral equation that models the dispersal of genes or organisms. She presented new analytic tools to determine the long-term dynamics of the system. Gabriel Lord considered traveling waves in a stochastically forced model of distributed dendritic spines along a diffusive cable. He derived a numerical scheme that can be used to examine the effect of changing smoothness of the stochastic forcing in space and the noise level in the system. The last speaker was Linghai Zheng. He showed how the Evans function method can be used to determine the stability properties of traveling waves arising in neuronal models with nonlocal interactions.

Conclusion:

This workshop clearly demonstrated that there are tremendous opportunities for interactions between both theoretical and experimental neurobiologists and mathematicians. Nonlocal integro-differential equations arise as models in many neuronal systems. These include models for working memory, sensory processing, and motor activity. The models have been extremely useful in testing hypotheses for the biological mechanisms underlying neuronal patterns, understanding how these activity patterns depend on parameters, and suggesting new experiments. This class of equations provides a rich source of spatial-temporal pattern formation that has attracted the attention of numerous mathematicians. This has motivated the development of sophisticated analytic tools to classify the types of patterns, along with their stability properties, that arise in a specific system.

Tutorials

***Tutorial on Neuronal Dynamics*:**
August 26-30, 2003
Organizers:
Brian Smith – Department of Entomology, The Ohio State University; David Terman – Department of Mathematics, The Ohio State University

***Tutorial on Neural Coding*:**
January 9-10, 2003
Organizers:
John Miller – Computational Biology Center, Montana State University; Alex Dimitrov - Computational Biology Center, Montana State University

Tutorial on Olfaction, Audition,
***and Sensory-Motor Systems*:**
March 31-April 2, 2003
Organizers:
David Terman – Department of Mathematics, The Ohio State University; Brian Smith – Department of Entomology, The Ohio State University; Catherine Carr – Department of Biology, University of Maryland; and Mike Reed – Department of Mathematics, Duke University

Period of Concentration

***Period of Concentration* - Functional Analysis of Nervous System - From Tasks to Implementation:**
February 17-28, 2003

Following Workshop 3, some participants stayed or came anew for 1 to 2 additional weeks. They gave 1 to 3 talks on the general topic: Functional analysis of the brain. Charles Anderson gave three talks about neural engineering, and Peter Foldiak gave two talks on stimulus selection for the experimental study of high-level cortex. John Hertz dealt with response variability in balanced cortical network models, and Barry Richmond discussed, in two talks, decoding spike trains. Mandyam Srinivasan described experimental results of flying insects with applications to autonomous robots.

Post-Workshop 5 Period of Study:
May 10 - 23, 2003

Following the workshops, some participants stayed on or came anew for 1 to 2 additional weeks of interactions. There were a few more talks, some lasting for 2 hours or more - allowing for much deeper questioning and exchanges. A few collaborations appeared to germinate during the 3-week span devoted to the auditory system (Marquardt and van Hemmen; Borisyuk and Borisyuk; Rinzel and Wenstrup).

Summer Program

July 14 – August 1:
Mathematical Neuroscience

Each summer the MBI hosts a 3-week education program. The first week is spent in a tutorial which combines morning lectures with active learning laboratories in the afternoon. The following two weeks are spent working on guided team projects and participating in a mini-conference to share project results. The participants include undergraduate students, graduate students, college teachers, and high school teachers. The topic of the program is related to the emphasis year program.

July 14-18 Tutorial:

Brian Smith: Biological introduction to neuroscience

David Terman: Mathematical introduction to Neuroscience

Afternoon visits to neuroscience labs.

July 21–30 Projects:

Title: Designing a neural control network for navigating a binary pheromone trail. Team leader - Daniel Dougherty.
Title: Propagation of signals along non-uniform axons. Team leader - Avner Friedman.
Title: How a neural network learns to smell. Team leader - Geraldine Wright.
Title: Image segmentation using neural oscillators. Team leader - Gheorghe Craciun.

July 31 – August 1
Mini-conference Reports

The project reports are available on the web: http://mbi.osu.edu.

Future Programs

September 2003 – August 2004
Mathematical Modeling of
Cell Processes

In the past few years, the importance of mathematical models in the study of cellular processes has become widely accepted. Mathematical models have played an important role, for example, in understanding how oscillations in cell cycles lead to regular cell division, and how intercellular calcium waves coordinate cellular response over large areas. During this year, we shall explore topics from cell growth and death, to intercellular communications, to the behaviors of large populations of cells such at those found in the immune system. Each quarter features tutorial sessions to provide important background information as well as in-depth workshops examining the issues described. Postdocs, graduate students, and faculty members interested in learning more about cell processes and the mathematical modeling of these processes are encouraged to attend.

Workshops

***Control of Cell Growth, Division, and Death*:**
September 29 – October 3, 2003
Organizers:
Jessie Au – College of Pharmacy, The Ohio State University; Baltazar Aguda – Department of Chemistry & Biochemistry, Boston University.

***Mathematical Models of Cell Proliferation and Cancer*:**
November 10-14, 2003
Organizers:
Jessie Au – College of Pharmacy, The Ohio State University; Marek Kimmel – Department of Statistics, Rice University

***Mathematical Challenges Arising in Cancer Models*:**
November 17-19, 2003
Organizers:
Avner Friedman - MBI, The Ohio State University; Marek Kimmel - Department of Statistics, Rice University

***Signal Transduction I: The Many Roles of Calcium*:**
January 26-30, 2004
Organizers:
James Sneyd – Department of Applied Mathematics, University of Auckland; Mike Anderson – Department of Mathematics, SUNY @ Stony Brook

***Signal Transduction II: Muscles and Motility*:**
March 8-12, 2004
Organizers:
James Sneyd – Department of Mathematics, University of Auckland; Ed Pate – Mathematics Department, Washington State University

Immunology Models: Cell Signaling and Immune Dynamics:
May 10-14, 2004
Organizers:
Denise Kirschner – Department of Microbiology & Immunology, University of Michigan Medical School; Jennifer Linderman – Department of Chemical Engineering, University of Michigan; Sergei Pilyugin – Department of Mathem-matics, University of Florida

***Disease Models: Host-pathogen Interactions*:**
June 21-25, 2004
Organizers:
Denise Kirschner - Department of Microbiology & Immunology, University of Michigan Medical School; Tom Kepler – Department of Biostatistics & Bioinformatics, Duke University

Tutorials

Tutorial on the Cell Cycle:
September 2-5, 2003
Organizers:
John Tyson - Department of Biology, Virginia Polytechnic Institute; Bela Novak, Technical University of Budapest; David Axelrod, Department of Genetics, Rutgers University

Tutorial on Cell Transduction:
January 5-9, 2004
Organizer:
James Sneyd – Department of Applied Mathematics, University of Auckland

Tutorial on Synapses and Muscles:
February 16-19, 2004
Organizer:
James Sneyd – Department of Applied Mathematics, University of Auckland

Tutorial on Immunology Models:
May 6-7, 2004
Organizers:
Denise Kirschner – Department of Microbiology & Immunology, University of Michigan Medical School; Tom Kepler - Bioinformatics and Computational Biology, Duke University

Tutorial on Host-Pathogen Interactions: June 17-18, 2004
Organizer:
Denise Kirschner – Department of Microbiology & Immunology, University of Michigan Medical School

Summer Program 2004

The theme for the summer program in 2004 (July 19 – August 6) will be mathematical modeling of cell processes. The tutorial will be given by James Sneyd (mathematical introduction to cell processes) and by Steve Osami, Andrea Doseff and Gustavo Leone (biological introduction to cell processes).

September 2004 – August 2005
Genomics, Proteomics, and Bioinformatics

GENOMICS was defined in the 1980s as the new discipline of mapping, sequencing and analyzing genomes, that is, the study of genes and their function in organisms on a global rather than a local scale. Proteomics, the study of the PROTEin complement to a genOME, emerged in the 1990s as the qualitative and quantitative comparison of proteomes under different conditions to further unravel biological processes. Both subject areas are at the forefront of the revolution taking place in biological and medical research, which is transforming them from data poor to data rich fields. While most biomedical research continues to be centered around single investigators or small groups of investigators, recording their experimental data in notebooks, increasing use is being made of novel technologies generating massive amounts of data, and requiring careful computational, mathematical, or statistical analyses. In this third year of the MBI, our focus is on these aspects of genomics and proteomics.

A major milestone in genomics was the completion of the mapping and sequencing of the human and mouse genomes in the period 2001-2003. This followed the sequencing of many bacterial genomes, as well as those of numerous other species of biological or medical importance, such as yeast, the roundworm, and the malaria parasite and its associated mosquito vector. This massive amount of DNA sequence data brings with it the ability to make progress on the molecular mechanisms of disease, including the complex interplay of genetic and environmental factors, and to generate thousands of new biological targets for the development of drugs, vaccines, diagnostics and therapies. Further, fundamental biological research is greatly aided by this wealth of data, permitting not only a genome-wide perspective in the study of particular organisms, but a greatly enhanced evolutionary perspective through the use of comparative genomics.

Analysis of Gene Expression Data:
Principles and Applications
Organizers:
Terry Speed – Department of Statistics,, The Ohio State University

Regulatory Networks
Organizer:
Jeff Hasty – Department of Bioengineering, Univ. of California, San Diego

Computational Proteomics and Mass Spectrometry
Organizers:
Vineet Bafna – The Center for the Advancement of Genomics; Tim Ting Chen – Departments of Biology, Computer Science, and Mathematics, University of Southern California

Emerging Genomic Technologies and Data Integration Problems
Organizers:
Terry Speed – Department of Statistics, University of California, Berkeley; Hongyu Zhao – Division of Biostatistics, Yale University

Biomarkers in HIV and Cancer Research
Organizers:
Victor De Grutolla – Department of Biostatistics, Harvard University; Mark Seigal - Department of Biostatistics, University of California, San Francisco; Alan Perelson - Los Alamos National Laboratory; Jeremy Taylor - Department of Biostatictics, University of Michigan; and Steve Skates - Department of Biostatistics, Massachusetts General Hospital

Evolutional Genomics
Organizers:
Rick Durrett – Department of Mathematics, Cornell University; Paul Fuerst – Department of Molecular Genetics, The Ohio State University

Tutorials

Tutorial on Microarrays:
September 13-17, 2004
Organizer:
Chandan Sen - Molecular and Cellular Biochemistry, The Ohio State University

Tutorial on Statistical Methods:
September 19-23, 2004
Organizers:
Nick Jewell - Department of Statistics, University of California, Berkeley; Sandrine Dudoit - Department of Statistics, University of California, Berkeley

Publications

The MBI began a series of technical reports; they are available on the web. An introductory volume on mathematical neurosciences will be prepared.

Technical Report No. 1
Authors: Avner Friedman and Gheorghe Craciun
Title: A model of intracellular transport of particles in an axon.
Date of Publication: March 2003

Technical Report No. 2
Authors: Jonathan E. Rubin and David Terman
Title: High frequency stimulation of the subthalamic nucleus eliminates pathological thalamic rhythmicity in a computational model.
Date of Publication: May 2003

Technical Report No. 3
Authors: Peter Szmolyan and Martin Wechselberger
Title: Relaxation Oscillations
Date of Publication: June 2003

Technical Report No. 4
Author: Roman Borisyuk
Title: Spatio-temporal activity of interactive neural oscillators
Date of Publication: August 2003

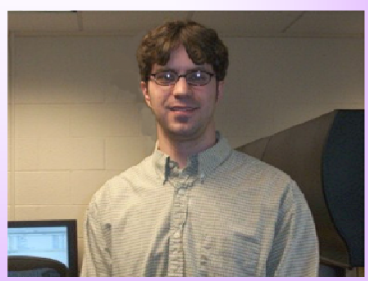
Staff

Kimberly Holle
Program Manager

Chris Conerby
Systems Manager

Stella Cornett
Program Assistant

Matt Thompson
Program Assistant



Rebecca Martin
Office Associate

Balance Sheet

INCOME

National Science Foundation		
Project 743058	$	1,323,030.00
Project 743168		676,970.00
TOTAL	**$**	**2,000,000.00**

EXPENSES

Project 743058

Salaries and wages	$	250,776.08
Postdoctoral stipends		201,723.12
Fringes		68,405.12
Computer services		125.00
Computer equipment		19,638,50
Materials and supplies		98,692.08
Travel – domestic (staff)		1,536.45
Other direct costs		18,795.55
F&A costs		304,025.37
Encumbered commitments		464,596.59
SUB-TOTAL	$	1,428,313.86

Project 743168

Salaries and wages	$	57,505.00
Fringes		9,488.37
Purchased services		500.00
Subcontracts		14,349.00
Other direct costs (participant hotels, etc.)		59,240.18
Travel – domestic (participants)		99,009.01
Travel – foreign (participants)		53,198.04
Encumbered commitments		207,501.06
SUB-TOTAL	$	500,790.66

TOTAL EXPENSES	**$**	**1,929,104.52**
BALANCE	**$**	**70,895.48**

OTHER FISCAL SUPPORT:

The Ohio State University		
Allocation	$	1,196,614.24
Expenditures		1,100,195.43
Encumbered commitments		13, 972.34
Balance	$	82, 446.47

MBI Institutional Partners		
Allocation	$	10, 500.00
Expenditures		2, 633.96
Encumbered commitments		0.00
Balance	$	7, 866.04

MBI Corporate Members: Pfizer		
Allocation	$	75,000.00
Expenditures		1, 079.00
Encumbered commitments		0.00
Balance	$	73, 921.00