Patrick David Roberts

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Research Interests: To develop mathematical methods, both analytical and numerical, for applications in understanding the dynamics of biological systems, and for advancing our understanding of the relationship between levels of biological complexity.

Degrees

February 1993 Ph.D., Theoretical Particle Physics, University of Gothenburg, Sweden

May 1983 B.A., Physics, Reed College, Portland, OR, USA

Experience

May 2000 – present	Assistant Scientist (primary appointment) Neurological Sciences Institute, OHSU, Portland, OR
July 2002 – present	Assistant Professor (dual appointment) Biomedical Engineering Department, OHSU, Portland, OR
July 2005 – present	Adjunct Assistant Professor Systems Science Program, Portland State University, Portland, OR
March 1993 – May 2000	Research Associate, R.S. Dow Neurological Sciences Institute Legacy Health Systems, Portland, OR

Honors, fellowships, and professional service

2004 - present	Editor, *Biological Cybernetics*, Springer-Verlag
2001 - present	Web Manager, Neurological Sciences Institute, OHSU
1993 - 2001	Review Author, Mathematical Reviews, American Mathematical Society
1994	Complex Systems Summer Fellowship at the Santa Fe Institute
1990 - 1992	The American-Scandinavian Foundation Fellowship, Thorn-Gray Memorial Fund
1982 - 1983	Commendation for Excellence, Div. of Math and Natural Science, Reed College

Professional societies

Organization for Computational Neurosciences (board member)
American Physical Society
American Physiological Society
American Association for the Advancement of Science
Society for Mathematical Biology
International Society for Neuroethology
Society for Neuroscience

Grant support

"Central control of electrosensory processing and learning in mormyrid electric fish." (Current) Principal Investigator: Patrick D. Roberts, Ph.D. Type: NSF (IOB-0445648, 3 years) Period: March 1, 2005 to February 28, 2008. Total award amount: $312,112

"Dynamics of neural activity in the cerebellum." Principal Investigator: Patrick D. Roberts, Ph.D. Type: R01 (MH60364, 5 years) Period: April 15, 2000 to March 31, 2005.
Total award amount: $566,250.

"The effects of noise on the electrosensory system of mormyrid electric fish." Principal Investigator: Todd Lean, Ph.D., Co-PI: Patrick D. Roberts, Ph.D. Type: NSF (IBN-0114558, 3 years) Period: September 1, 2001 to August 31, 2004. Total award amount: $390,000.

"The Storage of Temporal Patterns in Cerebellum-like Structures." Principal Investigator: Patrick D. Roberts, Ph.D. Type: NSF (IBN-980887, 3 years) Period: September 1, 1998 to August 31, 2001. Total award amount: $256,436.

Grant reviewing

NSF review panel, Division of Mathematical Sciences, 2007
NSF review panel, Integrative Organismal Biology, 2005
NIH CSR Special Emphasis Panel ZRG1 BDCN-6 03B March 2002
NIH CSR Special Emphasis Panel ZRG1 BDCN-6 03B December 2000
Various NSF proposal reviews, ad hoc, 1998-2007

Teaching

Spring 2007	Quantitative Methods in Systems Science Systems Science Program, PSU
Winter 2007	Introduction to Computational Neurophysiology Biomedical Engineering Department, OHSU
Winter 2006	Quantitative Methods in Systems Science Systems Science Program, PSU
Spring 2004	Introduction to Computational Neurophysiology Biomedical Engineering Department, OHSU
September 1981 – June 1983	Physics lab instructor, Physics Department Reed College, Portland, OR
September 1980 – June 1981	Physics tutor and Math Lab instructor The Evergreen State College, Olympia, WA

Publications

37. C.V Portfors, P.D. Roberts (2007) Temporal and Frequency Characteristics of Cartwheel Cells in the Dorsal Cochlear Nucleus of the Awake Mouse. *J Neurophysiol* **98**: 744-756.

36. P.D. Roberts, R. Santiago, C. Mello, T. Velho (2007) Storage of Auditory Temporal Patterns in the Songbird Telencephalon. *Neurocomputing* **70**: 2030-2034.

35. O. Iancu, P.D. Roberts, J. Zhang, C.C. Bell (2007) Postsynaptic modulation of electrical EPSP size investigated using a compartmental model. *Neurocomputing* **70**: 1685-1688.

34. P.D. Roberts (2007) Stability of Complex Spike Timing-Dependent Plasticity in Cerebellar Learning. *J Compu Neurosci* **22**: 283-296.

33. N.B. Sawtell, A. Williams, P.D. Roberts, G. von der Emde, C.C. Bell (2006) Effects of sensing behavior on a latency code. *J Neurosci.* **26**: 8221-8234.

32. P.D. Roberts, G. Lafferriere, N. Sawtell, A. Williams, C.C. Bell (2006) Dynamic regulation of spike-timing dependent plasticity in electrosensory processing. *Neurocomputing,* **69**: 1195-1198.

31. P.D. Roberts, C.V. Portfors, N. Sawtell, and R. Felix (2006) Model of auditory prediction in the dorsal cochlear nucleus via spike-timing dependent plasticity. *Neurocomputing,* **69**: 1191-1194.

30. C.V. Mello and P. D. Roberts (2005) Neuronal substrates of sensory processing for song perception and learning in songbirds: Lessons from the mormyrid electric fish. In J. S. Kanwal and G. Ehret, editors, Behavior and Neurodynamics for Auditory Communication, pp 265-293, Cambridge England, Cambridge University.

29. P.D. Roberts (2005) Recurrent neural network generates a basis for sensory image cancellation. *Neurocomputing,* **65-66**: 237-242.

28. G. McCollum and P. D. Roberts (2004) Dynamics of everyday life: Rigorous modular modelling based on blochs dynamical theorem. *J. Integ. Neurosci.,* **3**: 397-413.

27. A. Williams, T. K. Leen, and P. D. Roberts. (2004) Random walks for spike-timing dependent plasticity. *Phys. Rev. E.* **70**: 021916.

26. P.D. Roberts (2004) Recurrent biological neural networks: The weak and noisy limit. *Phys. Rev. E* **69**: 031910.

25. P. D. Roberts and C. C. Bell (2003) Active control of spike-dependent synaptic plasticity in an electrosensory system. *J.Physiol. (Paris)* **96**: 445-449.

24. P. D. Roberts (2003) Effects of noise on recurrence in networks of spiking neurons. *Neurocomputing* **52-54**: 893-899.

23. C. Mohr, P. D. Roberts, and C. C. Bell (2003) Cells of the mormyrid electrosensory lobe: II. Responses to input from central sources. *J. Neurophysiology* **90**: 1211-1223.

22. C. Mohr, P. D. Roberts, and C. C. Bell (2003) Cells of the mormyrid electrosensory lobe: I. Responses to the electric organ corollary discharge and to electrosensory stimuli. *J. Neurophysiology* **90**: 1193-1210.

21. A. Williams, P. D. Roberts, T. K. Leen, (2003) Stability of negative image equilibria in spike-timing dependent plasticity. *Phys. Rev. E.* **68**: 021923.

20. P. D. Roberts and C. C. Bell (2002) Spike-timing dependant synaptic plasticity: mechanisms and implications. *Biol. Cybern.* **87**: 392-403.

19. P. D. Roberts (2001) Cooperative field theory is critical for embodiment. *Beh. Brain Sci.* **24**:59-60

18. P. D. Roberts and C. C. Bell (2001) Mutual inhibition increases adaptation rate in an electrosensory system. *Neurocomputing* **38-40**: 845-850.

17. P. D. Roberts (2000) Modeling inhibitory plasticity in the electrosensory system of mormyrid electric fish. *J. Neurophys.* **84**: 2035-2047

16. P. D. Roberts (2000) Dynamics of temporal learning rules. *Phys. Rev. E* **62**: 4077-4082

15. P. D. Roberts (2000) Electrosensory response mechanisms in mormyrid electric fish. *Neurocomputing* **32-33**: 243-248.

14 . P. D. Roberts and C. C. Bell (2000) Computational consequences of temporally asymmetric learning rules: II. Sensory image cancellation. *J. Compu. Neurosci.* **7**: 67-83.

13. P. D. Roberts (1999) Computational consequences of temporally asymmetric learning rules: I. Differential Hebbian learning. *J. Compu. Neurosci.* **7**: 235-246.

12. P. D. Roberts (1998) Rhythmic behavior generated by neural ensembles. *Int. J. Theor Phys.* **37**: 3051-3068.

11. P. D. Roberts (1998) Classification of temporal patterns in dynamic biological networks. *Neural Comp.* **10**: 1831-1846.

10. P. D. Roberts (1997) Stochastic recruitment in parallel fiber activity patterns. *Beh. Brain Sci.* **20**: 263-264.

9. P. D. Roberts (1997) Classification of temporal patterns in the stomatogastric ganglion. *Neuroscience* **81**: 281-296.

8. P. D. Roberts, G. McCollum, and J. E. Holly (1996) Cerebellar rhythms: Exploring another metaphor. *Beh. Brain Sci.* **19**: 146-147.

7. P. D. Roberts and G. McCollum (1996) The stomatogastric nervous system: A formal approach. *Neuroscience* **72**: 1089-1105.

6. P. D. Roberts and G. McCollum (1996) Dynamics of the sit-to-stand movement. *Biol. Cybern.* **74**: 147-157.

5. S. Hwang and P. Roberts (1993) Interaction and modular invariance of strings on curved manifolds, in L. Brink and R. Marnelius (eds.), *Pathways to Fundemental Theories*, World Scientific.

4. P. Roberts and H. Terao (1992) Modular invariants of Kac-Moody algebras from covariant lattices. *Int. Jour. of Mod. Phys.* **A7**: 2207-2218.

3. M. Henningson, S. Hwang, P. Roberts and B. Sundborg (1991) Modular invariance of SU(1,1) strings. *Phys. Lett.* **B267**: 350-355.

2. P. Roberts (1990) Modular invariant partition functions of minimal models from self-dual lattices. *Phys. Lett.* **B244**: 429-434.

1. B.E.W. Nilsson, P. Roberts and P. Salomonson (1989) Standard model-like string theories from covariant lattices. *Phys. Lett.* **B222**: 35-42.

Presentations

Invited presentations

P.D. Roberts, Design principles of biological sensory processing, Bernstein Symposium on Object Localization, Herrsching am Ammersee, Germany, Sep 29, 2007

P.D. Roberts, Design principles of biological sensory processing, Office of Naval Research NeuroSilicon Workshop, Portland, OR, Aug 2, 2006

P.D. Roberts, Stochastic Approaches to Biological Physics: Electrosensory adaptation, Systems Science Seminar, Portland, OR, February 18, 2005

P.D. Roberts, Spike-timing dependent plasticity in adaptive sensory processing, International Congress of Neuroethology, Nyborg, Denmark, Aug 13, 2004

P.D. Roberts, Stochastic approaches to spike-timing dependent plasticity: Electrosensory adaptation, Monte Verita Workshop on Spike-Timing Dependent Plasticity, Ascona, Switzerland, Mar 5, 2004.

P.D. Roberts, Stochastic approaches to biological physics: Electrosensory adaptation.
Mathematics Department, Portland State University, Portland, OR; Nov. 4, 2003.
Physics Department, Reed College, Portland, OR; Dec. 10, 2003.
Department of Computer Science and Engineering, OHSU, Portland, OR; October 15, 2004.

P.D. Roberts, Effects of recurrent connections on spike-timing dependent plasticity, Activity-dependent Synaptic Plasticity Workshop, Fifteenth Annual Conference on Neural Information Processing Systems, Whistler, British Columbia, Canada; Dec 7, 2001.

P.D. Roberts, Spike-time dependent synaptic plasticity in an electrosensory system, Dynamics of Neural Networks: From Biophysics to Behavior, Kavli Institute for Theoretical Physics, University of Santa Barbara, CA; Nov 01, 2001.

P.D. Roberts and C.C. Bell, Modeling electrosensory processing in mormyrid electric fish, Neurobiology of Electrosensory Organisms, Poppelsdorfer Schloss, Bonn, Germany; July 29, 2001.

P.D. Roberts and C.C. Bell, Mutual inhibition increases adaptation rate in an electrosensory system, Featured presentation at Ninth Annual Computational Neuroscience Meeting, Brugge, Belgium; July 21, 2000.

Selected conference presentations

P.D. Roberts, Effects of recurrent inhibition on sensory processing in the cerebellar granule cell layer, Dynamical Neuroscience X, Orlando, FL, Nov. 1, 2002.

P.D. Roberts, Analysis of learning dynamics in neural networks with recurrent connectivity, The American Physical Society March Meeting, Seattle WA; Mar 22, 2001.

P.D. Roberts, Analysis of learning dynamics in neural networks with recurrent connectivity, The American Physical Society Centennial Meeting, Atlanta, GA; Mar 12, 1999.

P.D. Roberts and G. McCollum, Temporal pattern generation in dynamic biological networks, *Soc. Neurosci. Abstr.*, Vol. 21, Part 1, p. 225, 1995.

P.D. Roberts and G. McCollum, A formal approach to the function and behavior of the stomatogastric nervous system, *Soc. Neurosci. Abstr.*, Vol. 20, Part 1, p. 324, 1994.

P.D. Roberts and G. McCollum, The dynamics of rising from a seated position, *Soc. Neurosci. Abstr.*, Vol. 19, Part 2, p. 1687, 1993.

Physics presentations

P.D. Roberts, Modular invariance of strings on curved manifolds.
Physics Department, McGill Univ., Montreal, Canada; Dec. 4, 1992.
Physics Department, The Johns Hopkins Univ., Baltimore, MD; Dec. 6, 1992.
Physics Department, Brown Univ., RI; Dec. 12, 1992.
Newman Laboratory Of Nuclear Studies, Cornell Univ, Ithaca, NY; Dec. 13, 1992.

Department of Physics, Cal. Inst. Tech., Pasadena, CA; Jan 7, 1993.
Physics Department, Univ. So. Cal., LA, CA; Jan 16, 1993.
Lyman Laboratory of Physics, Harvard Univ., Cambridge, MA; Jan 23, 1993.

Students advised

Kunal Dalal (Yale undergraduate summer student, 2001) Presentation: How does internal calcium concentration relate to spike-timing dependent synaptic plasticity?

Evan Vickers (Reed College thesis student and summer student, 2001-2002) Thesis: Computational modeling of the active electrosensory system in a weakly electric fish, *Gnathonemus petersii* (Reed psychology advisor, Dr. Stephan St. John).

Owen Gross (Reed College thesis student and summer student, 2003-2004) Thesis: Biophysical Mechanisms of Spike Generation in Direction Selective Ganglion Cells (Reed physics advisor, Dr. John Powel).

Matthew Davidson (Reed College thesis student and summer student, 2005-2006) Thesis: Spatial Frequencies of Natural Scene Stimuli Determine the Response Functions in LIF Model Neurons (Reed physics advisor, Dr. John Powel).

Dan Iancu (Biomedical Engineering Ph.D. candidate, OHSU, 2003-present)

Roberto Santiago (Systems Science Ph.D. candidate, PSU, 2003-present)

Andrew Tolman (Systems Science Ph.D. candidate, PSU, 2005-present)

Lars Holmstrom (Systems Science Ph.D. candidate, PSU, 2005-present)

Active collaborations

Curtis C. Bell, NSI, OHSU. Electrosensory processing (active NSF grant).

Christine Portfors, Washington State University, Vancouver. Primary auditory processing in the dorsal cochlear nucleus (NIH grant proposal, submitted 7/2007).

Todd Leen, Dept. of Computer Science and Engineering, OGI. The effects of noise on sensory coding (previous NSF grant and planned submition of joint NSF-NIH grant proposal, 10/2007).

Neal Barmack, NSI, OHSU. Dynamics of neural activity in the cerebellum (previous NIH grant).

David Rossi, NSI, OHSU. Dynamics of granule cell activity in the cerebellum (submitted NIH grant proposal, 10/2006).

Matthew Frerking, NSI, OHSU. Synaptic plasticity of temporal patterns (submitted NIH grant proposal, 3/2007).

Claudio Mello, NSI, OHSU. Auditory learning in songbirds (planned submition of NSF grant proposal, 10/2007).

Gerardo Lafferriere, Department of Mathematics, Portland State University. Dynamics of biological neural networks and biochemical signalling pathways (previous NSF grant).

James McNames, Electrical Engineering Dept, Portland State University. Co-advise (with Christine Portfors) a PSU graduate student (Lars Holmstrom) on modeling neural responses in the auditory system.

Statement of Research

The major theme of my research is to understand dynamics of complex biological systems. To achieve this goal, my research approach applies mathematical analysis and computer simulation techniques to elucidate underlying mechanisms of biological systems, and to extract principles of biological function. Although my focus has been on the processing of sensory information in the nervous system, the mathematical methodologies that I use for neural systems could find broad application to many biological systems.

Modeling studies, such as those developed by my lab at the Neurological Sciences Institute (NSI), OHSU, can help bridge the gap between the level of fundamental biological processes and the systems level. In addition, by developing new models of complex biological processes, we are forced to develop new mathematical methods and expand the domain of application for present methods. My background in theoretical physics has provided me with excellent training to develop new mathematical techniques in pursuit of answers to fundamental scientific questions.

I presently collaborate with biologists at OHSU and Washington State University, Vancouver who have expertise in exploring primary sensory processing. These scientists are presently involved in research programs in a variety of sensory modalities, such as auditory, vestibular, electrosensory, and visual. Our lab is involved in an expanding program of collaborations with other scientists in the Portland area to develop mathematical methods and introduce student with a quantitative background to biological research. These collaborations extend to the Systems Science Program at Portland State University, as well as the Nonlinear System Group and the Biological Signal Processing Lab, bringing expertise in artificial learning systems, hybrid and hierarchical systems, and observability issues in control.

Electrosensory Processing, (Collaborators: Curtis C. Bell, Todd Leen, and Gerardo Lafferriere)

Primary sensory information is processed at the earliest stages by complex neural circuitry. Understanding how the central nervous system stores information about sensory signals is a prominent challenge facing neuroscience today. At present, little is known about what features are extracted, or how sensory processing is modulated by adaptation and recurrence from higher stages. Our understanding is particularly poor concerning the connection between synaptic plasticity at the cellular level and the storage of actual sensory patterns as examined in systems-level studies. New theoretical methods are needed to help in the design of experimental protocols and the analysis of data.

The first goal of this project has been to understand how the nervous system accurately stores the temporal flow of sensory information, and how past stimuli effect future sensory processing. Our studies focused on the cerebellum-like electrosensory lateral line lobe (ELL) in mormyrid electric fish in collaboration with NSI scientist Dr. C. Bell. *In vitro* experiments on these structures have revealed precise learning rules of spike-timing dependent synaptic plasticity. However, due to the complexity of cerebellum-like structures, it was unclear how the rules of adaptive learning measured *in vitro* explain the collective neural activity observed *in vivo*. The difficulty of experimentally exploring the roles of various learning rules, sites of adaptive change, and intracellular connections make theoretical and modeling work a necessary adjunct to experimental study. We developed mathematical methods to estimate the average effects of precise synaptic learning rules to correctly predict the system level adaptation [13, 14, 16, 17, 20].

The second goal of this project has been to identify the mechanisms of central control that are used in sensory processing and adaptation. Recent studies of primary sensory processing structures are revealing that they are far more than simple relays that transfer sensory information from the receptors to "higher centers." Not only does some significant sensory processing take place at these primary structures, but feedback from targets of these structures also influences the processing that takes place. However, it is presently unknown what "higher-level" processing takes place in these primary structures, or how that processing is influenced by experienced. We have studied mechanisms of recurrent control by constructing detailed mathematical, conductance-based models of neurons involved in the initial processing of sensory information and by determining how the interactions between peripheral and central inputs to cerebellum-like structures affect information transfer and adaptation. In addition, progress towards our goals necessitated the development of analytical methods to determine the stability of recurrent control, and to analyze the biological evidence for the presence of control mechanisms [15, 18, 22, 23, 25, 32].

The third goal of this project has been to understand how the nervous system accurately stores the temporal flow of sensory information in the presence of noise. This research investigates how noise effects the storage and retrieval of temporally ordered responses to sensory stimuli in the electrosensory system of mormyrid electric fish. The long-term objective is to understand how noise affects multimodal sensory processing. The types of noise that we investigate arise from the sensory receptors and the variability of synaptic contacts within the sensory processing circuit. We developed mathematical methods adapted from statistical physics to quantify how noise affects learning and memory [24, 26, 27].

Auditory Processing, (Collaborators: Christine Portfors, Claudio Mello, and James McNames)

A key challenge for the central auditory system is to filter predictable sounds so that novel sounds can be better processed and perceived. Auditory neurons achieve this filtering by altering their responses based on recent experience. This type of adaptive mechanism, or plasticity, has been observed in the mammalian dorsal cochlear nucleus (DCN); the first site in the central nervous system where acoustic cues are processed. Our long term goal is to understand the mechanisms of auditory processing in the DCN and determine how auditory processing is affected by adaptive mechanisms. We have adapted our models from the electrosensory system to predict the adaptive properties of processing in the DCN of the mammalian auditory system [31].

A fundamental function of the auditory system in humans is to process speech. When individuals suffer from age-related hearing loss, they have difficulty understanding basic speech sounds important in everyday life. The long term goal of this second research project on auditory processing is to understand how speech processing mechanisms are affected by age-related hearing loss. The objective of the current research is to understand how age-related hearing loss alters encoding of vocalizations in the inferior colliculus (IC). To achieve this objective, empirical studies of single neuron responses in the mouse IC will be combined with mathematical modeling to test our central hypothesis: age-related hearing loss disrupts the selectivity of neurons in IC to frequency combinations that are important for encoding vocalizations.

The long-term goal of a third project is to understand higher-order auditory processing in biological systems. Our research focuses on the auditory forebrain of songbirds, a system well-suited for the study of adaptive auditory processing. We use mathematical modeling and novel experimental paradigms to advance towards a better understanding of auditory processing and adaptation. One specific goal is to develop quantitative models of the auditory forebrain and simulate the adaptive responses of neurons to conspecific songs. The model predicts the adaptive responses of neurons in caudomedial nidopallium (NCM), and quantifies how properties of neural response properties change in response to selective changes of conspecific songs. The objective of this research is to develop and test a model of habituation to auditory patterns, a model that predicts the neural activity of auditory neurons to any spectral-temporal pattern [36].

Vestibular Processing in the Cerebellum, (Collaborators: Neal Barmack and David Rossi)

Our long-term goal is to understand how the cerebellum processes information and stores a representation of that information that is be used to modulate balance and orientation. Our immediate objective is to formalize the spike activity of parallel fibers in the cerebellum as dynamical equations in order to understand the spike responses of Purkinje cells to time-dependent input stimuli. Our research is expected to contribute to our knowledge of how the spike activity of Purkinje cells is dependent on circuitry, adaptive mechanisms, and properties of other neurons in the circuitry. By developing accurate mathematical predictions of how changes in spike activity of specific neurons affect the collective spike activity of the neural population, we will learn more about how brain circuitry works. Such predictions will ultimately provide a means to forecast how particular pharmaceutical interventions will affect the function of the brain.

Our methodological approach combines (1) formalized mathematical modeling with (2) empirical experimentation using *in vitro* patch clamp recordings in mammalian cerebellar slices and (3) analyses of *in vivo* recorded data from Purkinje cells in the cerebellar uvula-nodulus during vestibular stimulation. The modeling consists of: 1) numerical modeling of cerebellar granule cells and unipolar brush cells, and 2) analytical network modeling of cerebellar circuitry based on spiking neuron models of cerebellar neurons. Our analytic network models predict the spatial-temporal spike probability patterns of cerebellar neurons, and these results are be compared with numerical computer simulations of neural spike-activity. The *in vitro* recordings provide empirical data to test our predictions of synaptic plasticity in granule cells and characterize cellular dynamics of granule cells and UBCs. The *in vivo* recordings provide empirical data to test model predictions of spike-responses of cerebellular neurons to natural vestibular stimuli [16, 24, 26, 34].

Dynamics of Neural Circuitry, (Collaborators: M. Frerking, S. Prasad, and G. Lendaris)

Synaptic transmission is a major mechanism underlying the intercellular transfer and processing of signals in the nervous system. The output of synapses is highly dynamic, owing to the existence of several forms of activity-dependent synaptic plasticity that range in duration from milliseconds to hours. Although individual forms of synaptic plasticity have been well described, the simple stimulus patterns used to define each form of plasticity bear little resemblance to the activity seen *in vivo*, where most synapses are activated by temporally complex patterns of afferent firing. These complex patterns of activity are expected to engage several forms of synaptic plasticity simultaneously in a complex combination, which we will refer to as synaptic dynamics. Synaptic dynamics define how the synaptic output produced by each spike is influenced by the pattern of the preceding spike train. These dynamics are widely presumed to be an important component of signal processing during synaptic transmission, and may be affected by drugs or neurological diseases; however, synaptic dynamics during realistic patterns of afferent activity are poorly understood. We are actively developing mathematical methods to predict the changes in synaptic response to complex spike trains, and to predict how those responses change following activity dependent plasticity.

Activity dependent changes at individual synapses combine to generate neuronal algorithms of learning that can be mathematically predicted from synaptic learning rules. However, the verification of neuronal learning algorithms is limited by our inability to develop highly controlled neural networks for experiments *in vitro*. Microelectrode arrays (MEA) coupled with electric field based manipulation (EFM) offers the capability of developing experiments *in vitro* that precisely control neural connectivity and electrical activity. Hence, MEAs coupled with EFM will provide a means to verify the validity of the neuronal learning algorithms as predicted by theoretical studies, and significantly progress our understanding of how the nervous system learns. We will develop a specific neural network design to verify the neural learning algorithms that emerge from the known spike-timing dependent learning rules of hippocampal neurons [13].

Our objective is to establish the validity of the temporal-difference learning algorithm that arises from spike-timing dependent synaptic plasticity by utilizing the MEA experimental platform. The central hypothesis for the proposed research is that the antisymmetric spike-timing learning rule at synapses between cultured hippocampal neurons leads to differential Hebbian plasticity when the input neurons spike in a series of delays. We will test this hypothesis by electric field based manipulation of neural cultures on planar micro electrode platforms, leading to the development of an experimental model with immense control over individual cell electrical behavior essential for verifying neural algorithms of learning.

Statement of Teaching

It is my goal to bridge the disciplines of mathematics and biology in order to prepare students for the rapidly growing, multidisciplinary field of mathematical biology. This requires facilitating the interaction of students in both disciplines through common lab experiences and course offerings. To this end, in collaboration with faculty at the Biomedical Engineering Department at OHSU, I helped to developed a neuroengineering curriculum and research program that is able to accommodate students from these diverse disciplines. My teaching philosophy focuses on structuring the curriculum so that students develop the quantitative and communication skills that will prepare them for the challenges beyond their graduation.

This philosophy has been implemented in the development of four learning objectives in applied mathematics courses: (1) Learn how the mathematical problems are embedded in the context scientific questions. (2) Learn how mathematical methods are appropriate applied to the specific problem, emphasizing the comparative advantages of some methods over others. (3) Develop proficiency in calculation techniques, both analytical (formal) and numerical (computational) methods, through exercises. (4) Learn how to communicate the results of mathematical analyses effectively. To attain these objectives I have developed an approach that combines lectures with exercises, projects, and presentations (both written and oral). Homework exercises are intended to induce the student to practice the calculation techniques. Projects are intended to apply those techniques in the context of a scientific question. Presentations are structured so that the student must justify the reasons for application of the methods, and motivate the results in a cogent manner.

I have found it enriching to incorporate my research activities in education because mathematical models have proven to be an excellent explanatory tool for understanding how biological systems work. For example, I use detailed numerical models of neurons to introduce and to explain concepts of neural dynamics and synaptic plasticity to students, colleagues, and the general public. I also use graphics generated by computer simulations of mathematical models in outreach activities and in educational modules posted on my web site. I also use the methods that are developed in my research in a graduate-level course on systems science.

I have a strong commitment to mentoring outside the classroom setting. The members of my lab have included graduate and undergraduate students from both the biological and mathematical departments. I have also developed an active partnership with a Reed College and advised senior thesis students with interest in my active research projects. I find such educational activities highly rewarding. As part of this process I try to ensure that students participate in various activities that further their abilities and career goals, including attending international conferences, presenting seminars and publishing in peer-reviewed journals. I also maintain joint lab meetings between several labs in the Neurological Sciences Institute to provide opportunities for students to present and interpret recent work in the field, which fosters a collaborative, interdisciplinary atmosphere.

Courses previously developed

Quantitative Methods of Systems Science (SySc 512 at PSU)

An introduction to the quantitative representation and investigation of systems for early graduate level or advanced undergraduates. Lectures focus on the appropriate application of mathematical methods to example systems, while exercises emphasize tools more than applications. Topics include nonlinear dynamics, optimization, and probability. The level of presentation assumes familiarity and proficiency with calculus. The course is intended as part refresher mathematics course, part survey course, in quantitative methods applied to complex systems analysis. Methods from linear algebra unify the topics, and those methods will be practiced with calculations. Required course work includes both calculations to be done on a computer and formal analysis.

Introduction to Computational Neurophysiology (BME 565/BME 665 at OHSU)
In this course students will explore how neurons communicate through electrical signals, how information transmission between neurons occurs, and how connectivity between neurons determines activity patterns and results in specialized behavior. This course uses a hands-on approach to develop and explain concepts from computational neurophysiology. The course has two goals: to help students understand how computational models can be used to analyze, explain and predict the physiological behavior of neurons and assemblies of neurons; and to provide students with an opportunity to use current research tools to investigate the concepts underlying these computational models. The course will include a very brief review of relevant concepts from cellular neurophysiology (action and membrane potentials, channels, etc.) and of mathematical concepts needed to understand the material.

Suggested courses for future development
Statistics and Experimental Design
The purpose of this course is to understand statistical reasoning in the context of experimental design. Concepts of statistics will be developed from principles of probability theory, but the distinction will be drawn between the estimation of a likelihood and the underlying probability distribution. Course material will include common distributions and their uses, the central limit theorem, tests of significance, and analysis of variance. Historical and philosophical development of statistical methods will be discussed, and exercises will apply statistical methods to simulated data. Principles of experimental design will be exercised in a final project that will demonstrate how statistical reasoning can be used to answer specific scientific questions.

Mathematical Modeling of Biological Systems
Mathematics for life science majors will be introduced in this course on mathematical biology. Some calculus and high-school algebra will be required for background. Spatial and temporal models will be applied to population biology, behavior, and development (pattern formation). Techniques to be presented will include difference equations, continuous processes and ordinary differential equations, spatially distributed systems and partial differential equations. Concepts from linear algebra will be introduced as needed. Lectures will demonstrate how and why the mathematical methods are appropriate for particular applications, and homework exercises will provide practice in the techniques, mostly through numerical calculations. Group projects will elaborate the course material for a specific application.

Brain, Behavior and System Adaptation
This course explores the neural basis of animal behavior. The emphasis is on the information processing problems that animals face in complex natural environments and how nervous systems have evolved to solve these problems. The course introduces students to the use of computer modeling and simulation techniques for exploring principles of nervous system design and function. Ecological models of interacting species, and the adaptive effects of interactions on behavior, will be studied through simulations. Current literature in computational neurobiology and neuroethology will be incorporated in readings and class discussion.

Scientific Communication
Effective communication skills are essential for collaborative research and for progress in an interdisciplinary research environment. This course will explore how to develop a scientific "narrative" out of a collection of fact such as numerical data. Formats for scientific articles will be discussed, and exercises and editing will be examined. In addition, graphical presentation of scientific data and ideas will be explored, and students will learn effective use of graphics and animation in oral presentations. The final project will be a 15 page written proposal and 20 minute oral presentation.

References

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