# Patrick David Roberts

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**University Address**
Department of Biomedical Engineering
Oregon Health & Science University, Mail code: CH13B
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**Education**

February 1993 Ph.D., Theoretical Particle Physics, University of Gothenburg, Sweden
Dissertation: "Modular invariance in string theory and conformal field theory"

May 1983 B.A., Physics, Reed College, Portland, OR, USA
Senior thesis: "The principle of exterior expressability"

**Experience**

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|---|---|
| Nov 2014 – present | Adjunct Faculty<br>Integrative Physiology & Neuroscience, Washington State Univ, Vacnouver, WA |
| Jul 2008 – present | Adjunct Associate Professor<br>Department of Biomedical Engineering, OHSU, Portland, OR |
| Jul 2008 – present | Adjunct Associate Professor<br>Systems Science Program, Portland State University, Portland, OR |
| Sep2007 – 2014 | Director of Computational Systems Pharmacology<br>In Silico Biosciences, Inc, Portland, OR (Lexington, MA) |
| May 2000 – 2008 | Assistant Scientist<br>Neurological Sciences Institute, OHSU, Portland, OR |
| Jul 2002 – 2008 | Assistant Professor (dual appointment)<br>Department of Biomedical Engineering, OHSU, Portland, OR |
| Jul 2005 – 2008 | Adjunct Assistant Professor<br>Systems Science Program, Portland State University, Portland, OR |
| March 1993 – 2000 | Research Associate, R.S. Dow Neurological Sciences Institute<br>Legacy Health Systems, Portland, OR |

**Research Interests**

To develop and apply quantitative methods, both analytical and numerical, for understanding the dynamics of activity patterns in the nervous system, and for understanding the relationship between levels of biological complexity.

**Honors, fellowships, and professional service**

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| 2011 - present | Section Editor, *Encyclopedia of Computational Neuroscience* , Springer-Verlag |
| July 2008 | Local host, Organization for Computational Neurosciences Annual Meeting, Portland OR |
| 2007 - 2011 | Board member, Organization for Computational Neurosciences |
| 2004 - present | Editor, *Biological Cybernetics*, Springer-Verlag |
| 2001 - 2007 | 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, 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**

"Mechanisms of selectivity to behaviorally relevant sounds in the auditory midbrain." Principal Investigator: Christine Portfors, Consultant: Patrick D. Roberts, Type: NSF (3 years) Period: July 1, 2013 to June 30, 2016. Total award amount: $660,158.

"Mechanisms underlying encoding of vocalizations in the auditory system." Principal Investigator: Christine Portfors, Consultant: Patrick D. Roberts, Type: NIDCD (R15, 3 years) Period: July 1, 2013 to June 30, 2016. Total award amount: $453,000.

"Learning and processing of electrosensory patterns in mormyrid electric fish," Principal Investigator: Patrick D. Roberts, Co-I: Todd K. Leen, Nathaniel B. Sawtell, Type: CRCNS (NSF, 3 years) Period: Sep 15, 2008 to Sep 14, 2012. Total award amount: $700,000

"Hippocampal synaptic dynamics during realistic patterns of afferent activity." Principal Investigator: Matthew E. Frerking, Co-I: Patrick D. Roberts, Type: R01 (NIMH, 5 years) Period: Dec 1, 2007 to Nov 30, 2012. Total award amount: $1,351,350

"Central control of electrosensory processing and learning in mormyrid electric fish." Principal Investigator: Patrick D. Roberts, 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, 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, Co-PI: Patrick D. Roberts, 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, Type: NSF (IBN-980887, 3 years) Period: September 1, 1998 to August 31, 2001.
Total award amount: $256,436.

**Grant reviewing**

NSF Integrative Strategies for Neural and Cognitive Systems, 2015
NSF Division of Mathematical Sciences, Mathematical Biology Panel, 2007
NSF Integrative Organismal Biology, Computational Neuroscience Panel, 2005
NIH CSR Special Emphasis Panel ZRG1 IFCN3-03 (ad hoc) CSR SEP,
Integrative, Functional & Cognitive Neuroscience 3, March 12, 2002
NIH CSR Special Emphasis Panel ZRG1 BDCN-6 03B December 2000
Various NSF proposal reviews, ad hoc, 1998-2007

**Teaching**

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

**Publications**


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

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

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

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

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 Fundamental Theories*, World Scientific.

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

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

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

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

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

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

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

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

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.

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

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

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

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

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

20. P. D. Roberts and C. C. Bell (2002) Spike timing dependent synaptic plasticity in biological systems. *Biol Cybern* **87**: 392-403.

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.

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

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

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

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.

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

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

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.

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

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.

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. *Neurocompu,* **69**:1191-1194.

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

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.

34. P.D. Roberts (2007) Stability of complex spike timing-dependent plasticity in cerebellar learning. *J Compu Neurosci* **22**: 283-296.

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.

36. P.D. Roberts, R. Santiago, C. Mello, T. Velho (2007) Storage of auditory temporal patterns in the songbird telencephalon. *Neurocomputing* **70**: 2030-2034.

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.

38. L. Holmstrom, P.D. Roberts, C.V. Portfors (2007) Responses to social vocalizations in the inferior colliculus of the mustached bat are influenced by secondary tuning curves. *J Neurophysiol* **98**: 3461-3472.

39. G. Lafferriere and P. Roberts (2007) Stable feedback models for electrosensory filtering in mormyrid fish. In *Decision and Control, 46th IEEE Conference:* pp609-614.

40. P.D. Roberts, R.A. Santiago, G. Lafferriere (2008) An implementation of reinforcement learning based on spike timing dependent plasticity. *Biol Cybern* **99**: 517-523.

41. P.D. Roberts, C.V. Portfors (2008) Design principles of sensory processing in cerebellum-like structures. Early stage processing of electrosensory and auditory objects. *Biol Cybern* **98**: 491-507.

42. V. Balakrishnan, S.P. Kuo, P.D. Roberts and L.O. Trussel (2009) Slow glycinergic transmission mediated by transmitter pooling. *Nature Neuroscience* **12**: 286-294.

43. C.V. Portfors, P.D. Roberts (2009) Over-representation of species-specific vocalizations in the awake mouse inferior colliculus. *Neuroscience* **162**: 486-500.

44. P.D. Roberts and T.K. Leen (2010) Anti-Hebbian spike-timing-dependent plasticity and adaptive sensory processing. *Front Comput Neurosci* **4**:156.

45. L. Holmstrom, L.B.M. Eeuwes, P.D. Roberts, C.V. Portfors (2010) Efficient encoding of vocalizations in the auditory midbrain. *J Neurosci* **30**: 802-819.

46. C.V. Portfors, Z.M. Mayko, K Jonson, G.F. Cha, P.D. Roberts (2011) Spatial organization of receptive fields in the auditory midbrain of awake mouse. *Neuroscience* **193**: 429-39.

47. A. Spiros, P. Roberts, H. Geerts (2012) A quantitative systems pharmacology computer model for schizophrenia efficacy and extrapyramidal side effects, *Drug Dev Res* **73**: 1098-1109

48. Z. Mayko, P. Roberts, and C. Portfors (2012) Inhibition shapes selectivity to vocalizations in the inferior colliculus of awake mice. *Frontiers in Neural Circuits*, **6**: 73.

49. H. Geerts, A. Spiros, P. D. Roberts, and R. Carr (2012) Has the time come for predictive computer modeling in CNS drug discovery and development? *CPT: Pharmacometrics & Systems Pharmacology*, **1**: e16.

50. P. D. Roberts, H. Geerts, and A. Spiros (2012) Simulations of symptomatic treatments for Alzheimers disease: Computational analysis of pathology and mechanisms of drug action. *Alzheimer's Research & Therapy*, **4**: 50.

51. H. Geerts, A. Spiros, P. Roberts, R. Twyman, L. Alphs, and A. A. Grace (2012) Blinded prospective evaluation of computer-based mechanistic schizophrenia disease model for predicting drug response. *PLOS One* **7**: e49732.

52. H. Geerts, P. Roberts, A. Spiros (2013) A quantitative system pharmacology computer model for cognitive deficits in schizophrenia. *CPT: Pharmacometrics & Sys Pharm* **2**: e36.

53. H. Geerts, A. Spiros, P. D. Roberts, and R. Carr (2013) Quantitative systems pharmacology as an extension of PK/PD modeling in CNS research and development. *J Pharmacokinet Pharmacodyn* **40**: 257-265.

54. H. Geerts, P. D. Roberts, A. Spiros, and R. Carr (2013) A strategy for developing new treatment paradigms for neuropsychiatric and neurocognitive symptoms in Alzheimers disease. *Frontiers in Pharmacology* **4**: 47.

55. T. Nicholas , S. Duvvuri, C. Leurent, D. Raunig, T. Rapp, P. Iredale, C. Rowinski , R. Carr , P. Roberts, A. Spiros and H. Geerts (2013) Systems pharmacology modeling in neuroscience: Prediction and outcome of PF-04995274, a 5-HT4 partial agonist, in a clinical scopolamine impairment trial. *Advances in Alzheimer's Disease* **2**: 83-98.

56. A. Spiros, P. Roberts, H. Geerts (2013) Phenotypic screening of the Prestwick library for treatment of Parkinson's tremor symptoms using a humanized quantitative systems pharmacology platform. *J Parkinsons Dis* **3**: 569-580.

57. C.V. Portfors and P.D. Roberts (2014) Mismatch of structural and functional tonotopy for natural sounds in the auditory midbrain. *Neuroscience* **258**: 192-203.

58. J. Liu, A. Ogden, T. A. Comery, A. Spiros and P. Roberts and H. Geerts (2014) Prediction of Efficacy of Vabicaserin, a 5-HT2C Agonist, for the Treatment of Schizophrenia Using a Quantitative Systems Pharmacology Model. *CPT Pharmacometrics Syst. Pharmacol.* **3:** e111

59. H. Geerts and A. Spiros and P. Roberts and S Potkin (2015) Understanding responder neurobiology in schizophrenia using a quantitative systems pharmacology model: Application to iloperidone. *J Psychopharmacol.* [Epub ahead of print]

**Invited Presentations**

P.D. Roberts, Simulations of symptomatic treatments for Alzheimer's disease, Fields Institute, Toronto, Canada, Jun 1, 2012

P.D. Roberts, Computational pharmacology: Simulating circuits of the brain for drug development, Engineering in Medicine and Biology Society, Portland, OR, Feb 24, 2010

P.D. Roberts, Over-representation of species-specific vocalizations in the midbrain of the awake mouse, Oregon Hearing Research Center, Portland, OR, Apr 17, 2008

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.

**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).

Roberto Santiago (Systems Science Ph.D. candidate, PSU, 2003-2007)

Dan Iancu (Biomedical Engineering Ph.D. candidate, OHSU, 2003-2008)

Lars Holmstrom (Systems Science Ph.D. candidate, PSU, 2005-2010)

Eran Agmon (Systems Science M.S. candidate, PSU, 20010-2011)

Zachery Mayko (Biological Sciences M.S. candidate, WSU, Vancouver, 20009-2012)

Andrew Tolman (Systems Science Ph.D. candidate, PSU, 2005-2012)

**Academic collaborations**

**Christine Portfors**, Washington State University, Vancouver. Auditory processing in the midbrain and brainstem of bats and mice (NFS and NIH funded).

**Laurence Trussell**, Oregon Hearing Research Center and Vollum Institute, OHSU. Auditory processing in the brainstem of mice.

**Gerardo Lafferriere**, Department of Mathematics, Portland State University. Dynamics of learning is biological neural networks and sensory processing pathways (previous NSF grant).

**Christof Teuscher**, Electrical Engineering Dept, Portland State University. Reservoir computing methods and applications.

**James McNames**, Electrical Engineering Dept, Portland State University. Co-advised (with Christine Portfors) PSU graduate students.

**Todd Leen**, Adaptive Systems Laboratory, OHSU. The effects of noise on sensory coding in weakly electric fish (previous NSF/CRCNS grants).

**Matthew Frerking**, Behavioral Neuroscience, OHSU. Synaptic plasticity of temporal patterns (current NINDS grant).

**Curtis C. Bell**, Neurological Sciences Institute, OHSU. Electrosensory processing.

### Industry collaborations

**Hugo Geerts, Athan Spiros, and Robert Carr**, *In Silico Biosciences, Inc.* Advise pharmaceutical companies on drug development and discovery projects for schizophrenia, Alzheimer's disease and Parkinson's disease from target validation to personalized medicine with the aim of improving the success rate of pharmaceutical research and development projects.

**In Silico Biosciences' contractual partners:** *Hoffmann-La Roche Ltd.*, *Pfizer Inc.*, *Johnson & Johnson*, *Abbvie*, *Bristol-Myers Squibb*, *Shire-Movetis NV.*

**Statement of Research**

The unifying aim of my research is to develop a dynamical understanding of complex biological systems. More specifically, my research program aims to develop and apply quantitative methods, both analytical and numerical, to extract *design principles of neurobiological function* in collaboration with neurobiologists. Theoretical studies of neurobiological systems can help bridge the gap between the fundamental level of biological processes and the systems level of biological function The following is a sketch my future research plans and a summary my past research activities with references to my publications in my curriculum vitae. *Future plans are shown in italics.*

***Principals of sub-cortical sensory processing****, Collaborators: Christine Portfors, Larry Trussell, Curtis C. Bell, Todd Leen, and Claudio Mello*

Considerable sensory processing takes place in the brainstem and midbrain to accelerate behavioral responses, and our study of neural representation in sub-cortical structures is revealing mechanisms of sensory processing. Studies focused on the cerebellum-like electrosensory lateral line lobe (ELL) in mormyrid electric fish, in collaboration with Curtis Bell, helped us to understand how the nervous system accurately stores the temporal flow of sensory information, and how past stimuli effect future sensory processing. We developed mathematical methods to estimate the average effects of STDP learning to correctly predict the system level adaptation [13, 14, 16, 17, 20]. In addition, progress 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]. finally, we developed mathematical methods adapted from statistical physics to quantify how noise affects learning and memory [24, 26, 27]. Our theoretical methods for understanding the circuit-level learning in the cerebellum-like ELL was extended to the cerebellum to explain how vestibular information is processed and stored to modulate balance and orientation. The results provided predictions of adaptive spike-responses of cerebellar neurons to natural vestibular stimuli [34].

An ongoing research project focuses on auditory processing in the mammalian and avian brain. In a current collaboration with Christine Portfors, we are investigating another cerebellum-like structure, the mammalian dorsal cochlear nucleus (DCN). 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], and found the first evidence of the predicted systems level sensory image cancelation in this mammalian structure [41]. We have applied dynamical models of neurons in the DCN to calculate the timing of synaptic inputs using extracellular recording data [37], investigated the circuit elements to better understand sensory processing [42]. *We are currently investigating the responses of neurons in DCN to natural mouse vocalizations, and extending our models to predict complex responses.*

We have found that many low-frequency tuned neurons of DCN and midbrain respond to ultra-high frequency natural vocalizations of mice [43]. We hypothesize that this is due to intermodulation distortions in the cochlea that are generating subharmonics. *Future work will pursue studies to formalize how this mechanism affects auditory processing from the cochlea through the brainstem to the midbrain.*

An important challenge of theoretical research in neural representations is to formalize and characterize the heterogeneity of neural response properties. We have demonstrated that many neurons in the inferior colliculus (IC) of awake mice and bats respond selectively and heterogeneously to vocalizations [43,45,46,48]. However, the known mechanisms do not explain the full diversity of responses to vocalizations observed in the mouse IC. *Our future plans will experimentally examine mechanisms for selectivity to vocalizations in the IC by testing changes with applications of drugs to IC and DCN, and to develop new theoretical methods for formalizing heterogeneous representations.*

***Quantitative systems pharmacology (QSP)***

New pharmaceutical treatments for mental illness have a failure rate greater than 90%, leading to high costs and inefficient development in the pharmaceutical industry. Although much is presently known about how psychoactive agents affect the nervous system, little effort has been expended within the industry to simulate drug effects at the functional level and predict the efficacy of drugs in clinic trials.

In recent years, I worked with In Silico Biosciences, Inc, a company that advises clients in the pharmaceutical industry and provides simulation support for schizophrenia [50,52], Alzheimer's disease [50,54] and Parkinson's disease [56] with the aim of improving the success rate of pharmaceutical development and discovery. The company's approach links neuropharmacology to simulations of neuronal activity using a simulation platform to predict the potential impact of drugs on the output of neuronal circuits by comparing their output to clinically measured effects [53,54]. The modeling platform has successfully preformed blind predictions of the clinical efficacy for several new compounds [51,55,58]. The In Silico Biosciences simulation platform currently includes a cortical model for working memory tasks [49], a striatal model for schizophrenia clinical symptoms scales [47,51,52], and a cortical-thalamic model for EEG predictions. *Future research will develop reduced neural models of psychiatric disease so that treatments can be optimized for individualize patients based on extensive data of patient history, co-medications and genotypes.*

***Learning dynamics of spike timing dependent plasticity***, *Collaborators: Curtis C. Bell, Todd Leen, Gerardo Lafferriere, and Christine Portfors*

An ongoing direction of my research has been to analyze the network-level neural dynamics that result from different spike timing dependent synaptic plasticity (STDP) learning rules. Since the timing relations of STDP learning rules result from molecular events at the synapse, this line of research helps to link the implications of processes at the molecular level, through dynamics at the network level, to the behavior of whole organisms. In collaboration with Curt Bell, we found that the precise timing relations of synapses in the brainstem of mormyrid electric fish was necessary to generate the systems level function of sensory image cancellation [14,15,17,18,21,25,32,39] and is stable in the presence of noise [27,44]. A secondary objective of the project was to classify the systems level learning that results from temporally correlated inputs for all possible STDP learning rules [13,16,20,44], and to identify the links from STDP learning rules to system level function such as reinforcement learning [40]. *Future research will investigate the system level effects of regulation of STDP through inhibition and modulators, particularly in relation to reinforcement learning in midbrain structures.*

***Development of neuromorphic hardware designs.***, *Collaborators: Gerardo Lafferriere, and Christof Teuscher*

Much of my research has focused on spike-timing dependent plasticity and processing of sensory information and motor control. The design principals of these neural systems could find broad application to many engineering systems. Recently, Hewlett-Packard developed an implementation of a memristor, a hypothesized circuit element that opens a new door on potential hardware design based on neurobiological principals. Such neuromorphic hardware could produce extremely high-speed, low-power computational algorithms that are presently cumbersome on highly parallel machines. *Two applications that I wish to pursue in the coming years are: (1) Develop hardware circuit designs using memristors for simulating biological neural circuitry and (2) Develop hardware circuit designs using memristors to implement action-selection algorithms for control systems based on the mammalian basal ganglia/cortical control loop with STDP learning.*

***Vestibular processing in the cerebellum***, *Collaborators: Neal Barmack and David Rossi*

Our long-term goal was to understand how the cerebellum processes information and stores a representation of that information that is be used to modulate balance and orientation. Our methodological approach combined formalized mathematical modeling with analyses of *in vivo* recorded data from Purkinje cells in the cerebellar uvula-nodulus during vestibular stimulation. The modeling consisted 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 predicted 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 vivo* recordings provided empirical data to test model predictions of spike-responses of cerebellar neurons to natural vestibular stimuli [16, 24, 26, 34].

***Neuroscience research early in my career***, *Postdoctoral advisor: Gin McCollum*

*Topological biomechanics*: In [6] we took advantage of global analysis used in the modern approach to nonlinear dynamics, and applied these techniques to the problem of body movement. We analyzed a set of coupled first order differential equations describing the possible movements constrained by muscles activity using Hamiltonian mechanics. This approach reduced the relevant phase space to a plane, in which theorems from topological dynamics elucidated the different strategies available to rise from sitting. The results united continuous physical properties of a multijointed system with discrete functional properties found in goal directed behavior.

*Conditional dynamics*: This mathematical formalism reveals the functional logic of the system and organizes experimental observations. Application of the formalism determines a mathematical structure that constrains observed behavior. In contrast to continuous modeling methods, the formalism does not depend on detailed assumptions of system parameters, but emphasizes functionally important aspects of the system and identifies gaps in experimental knowledge. Conditional dynamics was applied to the movements of the foregut of decapod crustaceans in [7] and provides predictions for possible behavioral modes.

*Rhythmic activity in small neural networks*: The study of rhythmic behavior of the gastric mill in crustaceans led to the development of methods to study the neural mechanisms underlying that behavior. In order to gain insight into the problem of predicting the activity modes of multiple pattern generators such as the stomatogastric ganglion, the rhythm space method was developed to classify the patterns of behavior to be expected given the synaptic connectivity and cellular properties of a biological network. This method was applied to the stomatogastric ganglion [9], the swim-reflex generator of Tritonia [11], cerebellar rhythmic activity [8], and vestibular rhythms of the oblique nystagmus in [12].

***String theory and conformal field theory***, *Advisors: Per Salomonson, Bengt Nilsson*

The majority of my graduate research work was the study of modular invariance in string and conformal field theories. My tools of investigation were self-dual lattices to insure modular invariance of conformal field theories, an important consistency condition of string theories. This technique proved to be quite powerful and was applied to the following areas of study:

*String phenomenology.* In [1] we made an orthodox application of the covariant lattice approach to four dimensional string model building. We constructed some three generation superstring models with a matter sector similar to the standard model. This study revealed an intimate relationship between the presence of three generations of leptons and quarks, the symmetries of the standard model, and supersymmetry in string theories.

*Modular invariance of conformal field theories.* In [2] and [4] we found that self-dual lattices can be used to the classification of modular invariant partition functions of conformal field theories. This has proven to be an efficient means of searching for new exceptional modular invariants of higher rank Kac-Moody algebras and classification of string theories.

*Strings on non-compact group manifolds.* In [3] we constructed characteristic functions for the SU(1,1) Kac-Moody algebra. We then used these characters to show that unitary, modular invariant string models could propagate on a non-compact group manifold. Interpretation of the SU(1,1) coset model as a string propagating on a black hole background, as well as applications to 2-D gravity [5].

**Teaching Interests in Interdisciplinary Topics**

It is my goal to bridge the disciplines of physics and biology in order to prepare students for the rapidly growing, multidisciplinary field of quantitative biology. This requires facilitating the interaction of students in both disciplines through common lab experiences and course offerings. In a previous position, I helped to developed a neuroengineering curriculum and research program that is able to accommodate students from diverse disciplines in collaboration with faculty during the formation of the Biomedical Engineering Department at OHSU. 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 is implemented in the development of four learning objectives in physics and interdisciplinary courses: (1) Learn how the mathematical problems are embedded in the context of scientific questions. (2) Learn how mathematical methods are *appropriately* 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 effectively communicate the results of mathematical analyses. 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 scientific questions. 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 into 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 have used the methods that were developed in my research in a graduate-level courses.

My recent experience in industry has convinced me that a new workforce will need to be trained for applying computational methods to the pharmaceutical industry and other industries that are presently dominated by biologists. These industries offer great opportunity, and will require a specialized type of employee who knows the possibilities and limits of mathematical analysis in a biological context.

I have a strong commitment to mentoring outside the classroom setting. Members of my research group have included graduate and undergraduate students from both the biological and mathematical departments. I have also developed an active partnership with Reed College and advised senior thesis students who were interested in my research. I find such educational activities highly rewarding, and I have continued mentoring students during my recent work in industry. 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 maintained joint lab meetings between several labs while at the Neurological Sciences Institute, OHSU, to provide opportunities for students to present and interpret recent work in the field, which fosters a collaborative, interdisciplinary atmosphere.

**Courses previously developed**

*Introduction to Computational Neurophysiology* (BME 565/BME 665 at OHSU)

In this course students explored 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 used a hands-on approach to develop and explain concepts from computational neurophysiology. The course had 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 included 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.

*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, and 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.

**Suggested courses for future development**
*Computational Neuropharmacology*
The purpose of this course is to introduce the mathematical methods necessary for evaluating the action of pharmaceutical agents on the nervous system. Concepts of neuromodulator receptor kinetics will be developed from principles of thermodynamics, but the emphasis will be on the cellular effects of receptor activation. The treatment of intracellular pathways will focus on the immediate and longterm effects on membrane and synaptic currents. Changes in network activity will be related to behavior, and pathology of human psychiatric and neurological disease will be linked to the underlying neurophysiology. Exercises will apply mathematical methods and physical understanding to simulated systems. Principles of drug design will be exercised in a final project that will demonstrate how mathematical reasoning can be used to answer specific medical questions.

*Mathematical Modeling of Biological Systems*
Biological applications for physics majors will be introduced in this course on mathematical biology. Some calculus will be required for background and the biological material will be self-contained. 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.

*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.