

ERIC T. SHEA-BROWN

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EDUCATION:

PRINCETON UNIVERSITY, Princeton, NJ, 1999 – 2004

Ph.D. (2004), M.S. (2001), Applied and Computational Mathematics

Advisor: Philip Holmes

Co-Advisor: Jonathan Cohen

Dissertation: *Neural oscillators and integrators in the dynamics of decision tasks*

UNIVERSITY OF CALIFORNIA AT BERKELEY, Berkeley, CA, 1994 – 1998

B.S. (1998), Engineering Physics (with High Honors)

OTHER RESEARCH EXPERIENCE:

Postdoctoral research fellow, Courant Institute for Mathematical Sciences and Center for Neural Science, New York University, New York, NY, Fall 2004-present

Mentor: John Rinzel.

Research in applied dynamics and mathematical neuroscience (neural mechanisms for the representation of time intervals, dynamics of structured oscillator networks, models of correlated spiking in neural populations).

Research associate, Program in Applied and Computational Mathematics, Princeton University, Princeton, NJ, Summer 2004

Research in applied dynamics and mathematical neuroscience (dynamics and neural mechanisms of optimal decision algorithms).

Research fellow, Lawrence Livermore National Laboratory (LLNL), Livermore, CA, 1996 – 1999

Associated Western Universities and U.S. Dept. of Energy (SERS) programs

Research in computational modeling of chemical transport through geologic domains.

AWARDS:

- **Recipient**, Burroughs Wellcome Career Award at the Scientific Interface (awarded Nov. 2005; term of support Jan. 2006 – Dec. 2010)
- **Recipient** of the 2004 Council of Graduate Schools / University Microfilms International Distinguished Dissertation Award in the field of Mathematics, Science, and Engineering (awarded Nov. 2004)
- **Mathematical Sciences Postdoctoral Fellow**, National Science Foundation (awarded Feb. 2004)
- **Porter Ogden Jacobus Fellow**, Princeton University (2003 – 2004)
- **Fellow**, Burroughs Wellcome Graduate Training Program in Biological Dynamics (2001 – 2004)
- **Fellow**, National Science Foundation Graduate Fellowship Program (1999 – 2002)
- **Fellowship Awardee**, National Defense Science and Engineering Graduate Fellowship (1999)
- **Recipient**, 1999 UC-Berkeley Departmental Citation in Engineering Science
- **Recipient**, U.S. DOE (SERS), Associated Western Universities Fellowships, LLNL (1996-1998)
- **Member**, Phi Beta Kappa, Tau Beta Pi Societies (1998 - present)

PUBLICATIONS:

- X. Feng, E. Shea-Brown, H. Rabitz, B. Greenwald, and R. Kosut. Optimal Deep Brain Stimulation of the subthalamic nucleus: a computational study. To appear, *Journal of Comp. Neuroscience.*, 2007.

- X. Feng, E. Shea-Brown, H. Rabitz, B. Greenwald, and R. Kosut. Toward Closed-Loop Optimization of Deep Brain Stimulation for Parkinson's Disease: Concepts and Lessons from a Computational Model. *Journal of Neuroengineering*, 4: L14-L21, 2007.
- S. Coombes, B. Doiron, K. Josic, and E. Shea-Brown. Toward blueprints for network architecture, biophysical dynamics, and signal transduction. *Phil. Trans. Royal Soc. A*, 364: 3301-3318, 2006.
- R. Bogacz, E. Brown, J. Moehlis, P. Hu, P. Holmes, and J. D. Cohen. The physics of optimal decision making: A formal analysis of models of performance in two-alternative forced choice tasks. *Psychological Review*, 113: 700-765, 2006.
- J. Moehlis, E. Shea-Brown, and H. Rabitz. Optimal inputs for phase models of spiking neurons. *ASME Journal of Computational and Nonlinear Dynamics*, 1(4): 358-367, 2006.
- M. Golubitsky, K. Josic, and E. Shea-Brown. Winding numbers and average frequencies in phase oscillator networks. *Journal of Nonlinear Science*, 16, 201-231, 2006.
- E. Shea-Brown, J. Rinzel, B. Rakitin, C. Malapani. A firing-rate model of Parkinsonian deficits in interval timing. *Brain Research*, 1070, 189-201, 2006.
- P. Holmes, E. Shea-Brown, J. Moehlis, R. Bogacz, J. Gao, G. Aston-Jones, E. Clayton, J. Rajkowski, and J.D. Cohen. Optimal decisions: From neural spikes, through stochastic differential equations, to behavior. *IEICE Transactions on Fundamentals of Electronics, Communications and Computer Science*, 88 (10), 2496-2503, 2005.
- E. Brown, J. Gao, P. Holmes, R. Bogacz, M. Gilzenrat and J.D. Cohen. Simple neural networks that optimize decisions. *Int. Journal of Bifurcation and Chaos*, Vol 15, No. 3, 2005. (Highlighted by P. Dayan in Journal Club section of *Nature* 435, p. 251 (2005).) Also appears in World Scientific Series on Nonlinear Science, Series B - Vol. 13, E. Doedel, G. Domokos, and I. Kevrekidis, eds.
- E. Brown, J. Moehlis, P. Holmes, E. Clayton, J. Rajkowski, and G. Aston-Jones. The influence of spike rate and stimulus duration on noradrenergic neurons. *Journal of Comp. Neuroscience* 17 (1), 5-21, 2004.
- E. Brown, J. Moehlis, and P. Holmes. On the phase reduction and response dynamics of neural oscillator populations. *Neural Computation*, 16: 673-715, 2004.
- E. Brown, P. Holmes, and J. Moehlis. Globally coupled oscillator networks. In: *Perspectives and Problems in Nonlinear Science: A Celebratory Volume in Honor of Larry Sirovich*, E. Kaplan, J. Marsden, K. Sreenivasan, Eds., pp. 183-215. Springer: New York, 2003.
- H. Rabitz, G. Turinici, and E. Brown. Control of Molecular Motion: Concepts, Procedures, and Future Prospects. In: *Handbook of Numerical Analysis, Volume X*, P. Ciarlet and J. Lions, Eds., pp. 833-887. Elsevier: Amsterdam, 2003. N.B. draws on E. Brown and H. Rabitz, 2002 (below).
- R. Cho, L. Nystrom, E. Brown, A. Jones, T. Braver, P. Holmes, and J. D. Cohen. Mechanisms underlying performance dependencies on stimulus history in a two-alternative forced choice task. *Cognitive, Affective, and Behavioral Neuroscience*, 2(4): 283-299, 2002.
- E. Brown and H. Rabitz. Some mathematical and algorithmic challenges in the control of quantum dynamics. *Journal of Mathematical Chemistry* 31(1):17-63, 2002. Also appears (in Russian) in *Control of molecular and quantum systems*, A.L.Fradkov, O.A.Yakubovskii, Eds., Moscow-Izhevsk, Institute for Computer Studies, 2003.
- E. Brown and P. Holmes. Modeling a simple choice task: stochastic dynamics of mutually inhibitory neural groups. *Stochastics and Dynamics* 1(2):159-191, 2001.

PREPRINTS:

- E. Shea-Brown, K. Josic, J. de la Rocha, and B. Doiron. A universal correlation transfer function for leaky integrate-and-fire neurons. *ArXiv* q-bio.NC/0703037, 2007.

- E. Shea-Brown, M. Gilzenrat, and J. D. Cohen. Optimization of decision making in multilayer networks: The role of Locus Coeruleus. Submitted to *Neural Computation*, 2007.
- J. de la Rocha, B. Doiron, E. Shea-Brown, K. Josic, and A. Reyes. Correlation between neural spike trains increases with firing rate. Submitted to *Nature*, 2006.
- C. Malapani, B. Deweer, E. Shea-Brown, J. Rinzel A. Benabid, Y. Agid. Effects of Subthalamic Deep Brain Stimulation on Encode and Decode Processes of Parkinsonian Timing. Submitted to *Movement Disorders*, 2006.
- K. Lin, E. Shea-Brown, and L-S. Young. Reliable and unreliable dynamics in driven coupled oscillators. *ArXiv* nlin.CD/0608021, 2006.

TECHNICAL REPORTS (ONLINE AT HOST INSTITUTIONS):

- E. Brown, M. Gilzenrat, and J. D. Cohen. The locus coeruleus, adaptive gain, and the optimization of simple decision tasks. *Technical Report #04-02*, Center for the Study of Mind, Brain, and Behavior, Princeton University (2004).
- J. Moehlis, E. Brown, R. Bogacz, P. Holmes, J. D. Cohen. Optimizing reward rate in two alternative forced choice tasks: mathematical formalism. *Technical Report #04-01*, Center for the Study of Mind, Brain, and Behavior, Princeton University (2004).
- E. Brown, S. Doss, F. Hoffman, R. Gelinias, K. Fox, and J. O'Boyle. Adaptive-grid computational model of VOC transport across fine-and coarse-grained sediment contacts. *LDRD Final Report, Lawrence Livermore National Laboratory* (UCRL-ID-129845), pp. 5.1-5.37, Livermore, CA, 1998.

OTHER ARTICLES:

- "Isochron," "Periodic Orbit," and "Stability" entries, co-authored with P. Holmes, J. Moehlis and K. Josic. In peer-reviewed *Scholarpedia, Dynamical Systems*, E. Izhikevich, Ed. (online). p.2509, p.2464, and p.4208 (respectively). 2006.

SELECTED SOCIETY FOR NEUROSCIENCE ABSTRACTS:

- C. Gooch, A. Wilson, E. Shea-Brown, J. Rinzel, and M. Matell. (abstract) Firing patterns of premotor cortex are correlated with temporal estimates in the rat. *Abstracts (online), Society for Neuroscience*, 15.5, 2006.
- E. Shea-Brown, X. Feng, H. Rabitz, B. Greenwald, and R. Kosut. (abstract) Optimal deep brain stimulation of the subthalamic nucleus -- a computational feasibility study. *Abstracts (online), Society for Neuroscience*, 174.9, 2006.
- E. Shea-Brown, J. Rinzel, B. Rakitin, C. Malapani. (abstract) A firing-rate model of Parkinsonian deficits in interval timing. *Abstracts (online), Society for Neuroscience*, 774.5, 2005.
- M. S. Gilzenrat, E. T. Brown, G. Aston-Jones, J. D. Cohen. (abstract) Locus coeruleus, adaptive gain, and the optimization of decision tasks. *Abstracts (online), Society for Neuroscience*, 899.6, 2004.
- R. Bogacz, J. Moehlis, E. Brown, P. Holmes, J. D. Cohen. (abstract) Neural mechanisms for decision optimization. *Abstracts (online), Society for Neuroscience*, 197.6, 2003.
- R. Cho, L. Nystrom, P. Holmes, E. Brown, B. Casey, and J. D. Cohen. (abstract) A connectionist model of conflict and control in a forced-choice task. *Abstracts, Society for Neuroscience*, v.26, 2000.

SELECTED TALKS:

- **Neuroscience Seminar, Princeton University**, Princeton, NJ. *Dynamics of correlation and coding in simple neural circuits*. (Feb. 2007)
- **Theoretical Biophysics Seminar, UC San Diego**, San Diego, CA. *Spike-to-spike correlation and neural coding: basic roles for membrane and circuit dynamics*. (Feb. 2007)

- **Biomedical Engineering Seminar, Duke University**, Durham, NC. *Dynamics of integration, correlation, and encoding in simple decision tasks.* (Feb. 2007)
- **Applied Mathematics Seminar, Northwestern University**, Evanston, IL. *Dynamics of correlation and coding in simple neural circuits.* (Feb. 2007)
- **Neural Engineering Seminar, Pennsylvania State University**, University Park, PA. *Spike-to-spike correlation and neural coding: basic roles for membrane and circuit dynamics.* (Jan. 2007)
- **Applied Mathematics Seminar, University of Washington**, Seattle, WA. *Spike-to-spike correlation and neural coding: basic roles for membrane and circuit dynamics.* (Jan. 2007)
- **Applied Mathematics Seminar, Columbia University**, New York, NY. *Dynamics of integration and correlation in neural encoding and decisions.* (Dec. 2006)
- **Neuroscience Seminar, Brandeis University**, Waltham, MA. *Dynamics of integration and correlation in encoding and simple decisions.* (Dec. 2006)
- **Courant Institute Applied Mathematics Seminar**, New York, NY. *A theory of correlations for spiking neurons.* (Oct. 2006)
- **Neuromath `06 Conference on Mathematical Neuroscience**, Andorra. *Reliability, recurrence, and rhythm in a pair of phase oscillators.* (Sept. 2006)
- **Sloan-Swartz Summer Meeting**, New York, NY. *Spike-to-spike correlations: modeling and mechanisms.* (July 2006)
- **Seminar, Center for Theoretical Neuroscience, Columbia University**, New York, NY. *Dynamics of integration and correlation in timing and decisions.* (June 2006)
- **Theoretical and Applied Mechanics Seminar**, Cornell University, Ithaca, NY. *Spiking Dynamics in Phase Oscillator Networks.* (April 2006)
- **Mathematical Biology Seminar**, New Jersey Institute of Technology, Newark, NJ. *How network architecture restricts spiking patterns in networks of phase oscillators.* (April 2006)
- **2006 Joint Mathematics Meetings**, San Antonio, TX. *How architecture restricts spiking patterns in networks of phase oscillators.* (Jan. 2006)
- **International Workshop on Applied Dynamical Systems**, Centre de recherches mathématiques, Montreal. *How architecture restricts spiking patterns in networks of phase oscillators.* (Oct. 2005)
- **Seminar, Applied Mathematics Laboratory**, Mount Sinai School of Medicine, New York, NY. *How network architecture and cell type restrict spiking patterns for phase oscillators.* (July 2005)
- **SIAM Conference on Applications of Dynamical Systems**, Snowbird, UT. *On the phase reduction and response dynamics of neural oscillator populations.* (May 2005)
- **Computational Neuroscience Seminar**, University College London, UK. *From spikes to speed-accuracy via the locus coeruleus.* (April 2005)
- **Interdisciplinary/Applied Mathematics Seminar**, University of Illinois at Urbana-Champaign, Champaign, IL. *Modeling optimal decisions with neural integrators and oscillators.* (March 2005)
- **Courant Institute Dynamical Systems Seminar**, New York, NY. *Spikes, Synchrony, and Decisions: A From-Scratch Tour of Some Dynamical Systems in Neuroscience.* (March 2005)
- **Courant Institute Mostly Biomathematics Seminar**, New York, NY. *On the phase reduction and response dynamics of neural oscillator populations.* (Dec. 2004)
- **Courant Institute Applied Mathematics Seminar**, New York, NY. *From spikes to speed-accuracy via the brainstem.* (Sept. 2004)
- **13th Annual Computational Neuroscience Meeting**, Baltimore, MD. *On the phase reduction and response dynamics of neural oscillator populations.* (July 2004)
- **SIAM Life Sciences Meeting**, Portland, OR. *A neural mechanism for optimizing task performance.* (July 2004)

2004)

- **AIMS 5th International Conference on Dynamical Systems and Differential Equations**, Pomona, CA. *On the phase reduction and response dynamics of neural oscillator populations*. (June 2004)
- **Seminar, Institute for Biophysical Dynamics and Center for Neural Computation and Engineering**, University of Chicago, Chicago, IL. *From spikes to speed-accuracy via the locus coeruleus*. (May 2004)
- **Mathematical Biology Seminar**, New Jersey Institute of Technology, Newark, NJ. *From spikes to speed-accuracy via the brainstem*. (March 2004)
- **SIAM Conference on Applications of Dynamical Systems**, Snowbird, UT. *Response dynamics and phase oscillators in the brainstem*. (May 2003)
- **Computational Neuroscience Forum**, New York University, New York, NY. *Response dynamics and phase oscillators in the brainstem*. (January 2003)
- **Seminar, Applied Mathematics Laboratory**, Mount Sinai School of Medicine, New York, NY. *The influence of spike rate and stimulus duration on response in locus coeruleus*. (December 2002)
- **Applied Mathematics Days**, Rensselaer, NY. *Modeling synchrony and spike probabilities in cognitive regulation*. (April 2002)
- **12th International Summer Symposium on Science and World Affairs**, Moscow, Russia. *The Accelerated Strategic Computing Initiative and the future of nuclear weapons simulations*. (August 2000)
- **Dynamical Systems and Nonlinear Science Seminar Series**, Princeton University, Princeton, NJ. *Stability, synchrony, and symmetry in coupled rotator oscillators* and *The Hodgkin-Huxley action potential: biophysical and experimental foundations*. (March 2001 / November 1999)

TEACHING EXPERIENCE:

Substitute / Guest Lecturer, New York University. Gave two 2-hour lectures in graduate courses on mathematical neuroscience. (2005)

Research Mentor, New York University. Supervised rotation by Center for Neural Science graduate student in Rinzel working group. Focussed on phase plane methods and applications to firing rate models for cognitive tasks. (2005)

Research Mentor, New York University, for Bronx Science High School student's project: "Biological Networks." (2005)

Research mentor, Princeton University. Graduate mentor for senior thesis on control theory and neuron dynamics. Helped undergraduate student to form research plan and advised on computational, mathematical, and biological aspects of work. (2003-2004)

Teaching Assistant / Unit Lecturer, Princeton University, APC/MOL/EEB 514 graduate course *Biological Dynamics* directed by David Tank. Taught weekly sessions for graduate students from a wide range of departments on subjects such as "random walks and stochastic differential equations" and "bifurcations and bursting neurons," many featuring interactive MATLAB-based tutorials. Delivered two 1.5 hr. course lectures on population models and synchrony in neuroscience. Developed some course materials and graded assignments. (half semester, Fall 2003)

Teaching Assistant, Princeton University, MOL437 senior-level course *Computing Networks and Computational Neurobiology* taught by John Hopfield. Led informal discussion sessions on course assignments and advised graduate and undergraduate students on course projects. Delivered course lectures, and developed assignment, on topic of Hidden Markov Models. Graded portions of exam, projects, and assignments. (Fall 2000)

Teaching Assistant, University of California at Berkeley, E24 freshman seminar *Exploring Curvature* (elementary ideas from geometry of surfaces). Some assistance with course planning, instruction, and evaluation. (Spring 1998)

INVITED WORKSHOPS AND OTHER ACADEMIC PROGRAMS:

Workshop on Symmetry and Bifurcation in Biology, Pacific Institute for the Mathematical Sciences, Banff International Research Station, Alberta, Canada. (1 week, June 2003)

Workshops on Neuronal Dynamics and Systems Neuroscience, Mathematical Biology Institute, Ohio State University, Columbus, OH. (~3 weeks, Fall 2002)

DIMACS Tutorial on Mathematical Epidemiology, Rutgers University, New Brunswick, NJ. (June 2002)

Complex Systems Summer School, Santa Fe Institute, Santa Fe, NM. (June 2000) Prepared summer school papers, “A neural model for chaotic dynamics in human decision tasks” with A. Kelley and “Modeling deforestation processes in the Amazon: Linking Empirical, Analytical, and Computational Methods” with L. Solorzano, A. Yuen, and M. Westphal.

PROFESSIONAL SERVICE AND AFFILIATIONS:

Member, Princeton University Graduate School Leadership Council (2006-present)

Referee for *Journal of Computational Neuroscience*, *Journal of Nonlinear Science*, *Cerebral Cortex*, *Physica D*, *Network: Computation in Neural Systems*, *Neural Computation*, *Communications in Math. Science*, *Science* (co-referee), and *SIAM J. Appl. Dynamical Systems*, (2003-present)

Co-organizer, Computational Neuroscience Forum, New York University (2004-2006)

Coordinated Burroughs Wellcome Fellows Seminars in Biological Dynamics, Princeton University (2001-2004)

Organized Applied Mathematics Graduate Student Seminars, Princeton University (2000-2002)

Member of Society for Industrial and Applied Mathematics (2000-present), Society for Neuroscience (2004-present), Union of Concerned Scientists (2002-present)

ADDITIONAL TEACHING AND LEADERSHIP EXPERIENCE:

Instructor, North Carolina Outward Bound School. Taught science, writing, and outdoor leadership for accredited high school Summer Scholars Program (Summer 1998) and outdoor leadership and rock climbing for general courses. (Summers 1996, 1997)

Expedition assistant and climber, Patagonian Bros. Expeditions, Argentinean Andes (Cerro Aconcagua, 22,800 ft.; Winter 1996)

RESEARCH SUMMARY, WITH REFERENCES TO PUBLICATIONS AND PREPRINTS:

The main body of my research is on the dynamics of structured networks of neurons and neural populations. The goal is to uncover mechanisms that enable these networks to encode, propagate, and make decisions about sensory inputs. This requires building collaborations with cognitive neuroscientists (as in my work on modeling decision tasks), with electrophysiologists (as in my studies of firing dynamics in the brainstem), and with psychiatrists and neurologists (as in my current work on models for the timing behavior of Parkinsonian patients).

Achieving this goal also requires generalizing mechanisms uncovered in these and other studies to develop the mathematical theory of spiking neural networks, a challenge which fascinates me and one on which I've worked with several different groups of applied mathematicians. The goal is a theoretical framework which describes and connects the neural dynamics occurring on different spatial and temporal scales, ranging from single neurons and small circuits to populations. At the finest scale, we describe how precise *patterns of spike times* emerge in structured networks. Examples are my work on spike ordering and network architecture, on optimal control of spike times, and on repeatable vs. chaotic dynamics in stochastically forced networks. At the gradually coarser scales, we study the *statistics of spike times* averaged over large groups of neurons. Examples here are my work on the response properties of neural oscillator populations, and studies of spike-to-spike correlations in neural populations.

1. Neural mechanisms for optimal decisions:

My work with Philip Holmes, Jonathan Cohen, Jeff Moehlis, Mark Gilzenrat, Rafal Bogacz, Gary Aston-Jones and collaborators (at Princeton and U. Penn) on the dynamics of simple decision tasks starts with models of neural "integrators." Each integrator represents, via a firing rate, the activity of a population of neurons that is selectively responsive to one of the possible stimuli in the decision task. We first develop a reduced model of the stochastic firing rate dynamics of neural integrators in a two-alternative decision task, via projecting solutions onto the slow manifolds along which they concentrate. This reduced description is useful in developing intuition and analytical estimates for the reaction times and error rates that the model predicts [*Stoch. Dyn.*, 2001]. These predictions compare favorably with behavioral data from human subjects (in one case elucidating complex dependencies of task speed and accuracy on stimulus histories [*Cog. Aff. Beh. Neurosci.*, 2002]), and make surprising predictions regarding effects of parameters (e.g., that reaction times, modeled as crossing times of firing rate thresholds, become longer but less variable as a "feedback" term changes). Moreover, the resulting models of drift-diffusion processes crossing thresholds can implement statistically optimal algorithms for decision making [*CSMBB Tech. Rpt. #04-01*, 2004; *Int. J. Bifn Chaos*, 2005; *Psych. Rev.*, 2006]. This connection between network dynamics and optimal signal processing provides a benchmark for parameterizing and interpreting neural models of decisions. Furthermore, the hypothesis that neural networks in the brain indeed implement these optimal algorithms makes strong predictions for both firing patterns of neural groups and statistical patterns of behavioral performance, some of which were later validated in psychophysics experiments conducted by Rafal Bogacz [*Trans. IEICE*, 2005; *Psych. Rev.*, 2006], in which participants are instructed to maximize their rates of decision-based reward.

Optimal decision algorithms require time dependent modulation of the sensitivity (gain) of neural integrators as task-relevant stimuli occur. An emerging hypothesis is that the brainstem area locus coeruleus (LC) is responsible for this modulation, via its release of the neurotransmitter norepinephrine to the cortex. Thus motivated, we analyze spiking models of LC neurons, exploring the role of baseline frequency and stimulus duration in shaping the firing dynamics of the LC population (and hence the dynamics of norepinephrine release). The results suggest a new mechanism which may contribute to the transition between LC firing patterns associated with different levels of cognitive performance, and also provide an explanation for differences in LC firing patterns observed across cognitive tasks [*J. Comp. Neurosci.*, 2004]. We then compare experimental LC firing patterns with the statistically optimal firing patterns that are predicted by reduced neural integrator models with optimized gain schedules. We use these optimized models to assess the benefits of LC-driven gain modulation via the behavioral metric of reward rate [*Int. J. Bifn. Chaos*, 2005, and *preprint*], and find that features of the optimal and experimentally observed LC dynamics do agree qualitatively, supporting a role for the LC in dynamically facilitating decisions -- for example, by implementing filters matched to the time course of incoming sensory information.

2. Neural mechanisms for the representation of elapsed time:

With John Rinzel at NYU as well as Chara Malapani and other members of the Temporal Cognition Laboratory at Columbia University, I am studying neural integrator models for the firing rates of neural populations involved in the estimation of seconds-scale time intervals. We apply these highly idealized models to behavioral data

from Parkinsonian subjects both on (control condition) and off L-dopa therapy, and find that modifying the feedback and net input parameters between on and off L-dopa states reproduces several non-intuitive features of Parkinsonian timing data [Brain Res., 2006]. In particular, we suggest that unbalanced feedback in the firing rate dynamics is a mechanism for the Parkinsonian timing deficits of “migration” (overestimation of short and underestimation of long time intervals) and the “violated scalar property” (anomalous scaling of errors in time estimates). Ongoing work extends this idealized modeling framework to describe timing behavior of patients on and off Deep Brain Stimulation [preprint]. Nevertheless, many unanswered questions remain, and Malapani and collaborators are conducting a series of experiments that will test several of the model’s predictions and will lead to its refinement. We are also collaborating with Matthew Matell and Cindy Gooch (Villanova) to analyze multiunit neuronal data from the cortices of rats performing timing tasks, using principle component and discriminant analyses to identify features in the spike trains that predict timed behavior. These analyses will also better constrain our models of the firing rate dynamics that underlie interval timing tasks.

3. Correlations in neural populations:

In developing models of neural populations, a primary challenge is to correctly include correlation among the firing times of the constituent cells. A mechanistic understanding is still lacking of how these correlations develop, and, critically, of how their strength depends both on the population’s operating range (that is, the rate and regularity of spiking) and on the membrane dynamics with which spikes are generated. With Jaime de la Rocha, Brent Doiron and Alex Reyes (NYU), and Kresimir Josic (U. Houston), we address these questions using linear response theory, numerical simulations, and *in vitro* experiments [preprints]. To our surprise, our theory predicts, and cortical slice experiments verify, that correlations increase dramatically with firing rate over ranges of up to approximately 20-30 Hz. This fundamental connection between rate and correlation holds regardless of the level of regularity in single-cell spiking, a counterintuitive result we establish using low-noise asymptotics for integrate-and-fire neuron models. Furthermore, the co-dependence of rate and correlation seems universal among many neuron models, a fact we explain using a simple statistical theory based on the thresholding process that underlies spike generation. Finally, we demonstrate that the relationship between rate and correlation enables enhanced information transfer across a feed-forward network of neurons, in particular increasing the accuracy with which similar signals can be discriminated. We quantify this accuracy by calculating Fisher information, and the resulting expressions isolate the contribution of rate-dependent correlations to neural encoding.

4. How network architecture determines spiking dynamics:

The simplest architecture with which cells can be connected, and the starting point for many theoretical studies of the synchronized and phase-locked behavior that results, is all-to-all or “global” coupling. Our work with globally coupled networks of phase oscillators (which serve as simplified models of some neurons) summarizes and adds to established results by describing how the form of their coupling determines the existence and stability of phase-locked states in which subgroups of oscillators are synchronized [in *Perspectives and Probs. in Nonlin. Sci.*, 2003]. Work with Josic and Marty Golubitsky (U. Houston) goes beyond the global coupling assumption, treating networks with more general coupling architectures and therefore building on the recent theory of coupled cell systems developed by Golubitsky, Ian Stewart, and colleagues. Our emphasis is on the new features of network dynamics that arise in this context from additionally assuming a phase or integrate-and-fire (i.e., one dimensional) description of the individual cells. Results to this point focus on the different classes of synchronized, partially synchronized, and spatio-temporally symmetric (i.e., phase-shifted) solutions that are forced to exist by the coupling architecture. We also investigate how the existence of some types of these solutions restricts the admissible winding numbers that subsets of cells can display over arbitrary intervals of time, thereby limiting the possible network spiking patterns (be they periodic or irregular). This has the interesting consequence that the order of certain temporal sequences of spikes must repeat, until an external input reorders the cells [J. Nonlinear Science, 2006].

With Lai-Sang Young and Kevin Lin at NYU, I investigate another general role of architecture: how the presence of feedback affects the *reliability* of spike trains in response to inputs. The reliability of an isolated neuron or neural model is a celebrated fact: if the same signal (an aperiodic current trace) is presented many times, after a short transient the neuron will typically display the same spiking response, regardless of its initial state. But what happens if this neuron is embedded in a network? The answer is not known but is fundamental for neural processing. We take a first step by adding a second cell “downstream” to that receiving the input, with either purely feedforward or both feedforward and feedback connections to the first. While the two-cell feedforward network still responds reliably (as the second neuron can be seen as an isolated cell receiving its inputs from the first), we find that the feedback network can be either robustly reliable or unreliable, each over broad parameter ranges. Based on

geometrical reasoning and computations of Lyapunov exponents, we identify an unexpected role for oscillations in driving the transition between reliable and unreliable responses [preprint].

5. Characterizing the response of neuron models to simple stimuli:

Different conductance-based models of individual neurons produce widely varying dynamics and involve a daunting number of parameters. One way to make progress in understanding these dynamics is to develop qualitative characteristics that describe the response of general categories of such models to stereotyped inputs. Work with Jeff Moehlis and Philip Holmes contributes by developing and extending phase reductions that show how both type of, and distance from, four typical transitions (bifurcations) to periodic firing determine a neuron's phase response curve, and hence the timing of its spikes in response to coupling currents and external inputs [*Neural Comp.*, 2004]. We then show how these phase reductions lead to general conclusions about the responses of neural populations to simple stepped stimuli. Our results include scaling relationships between the amplitude of a neuron's phase response curve and its baseline frequency, and an explanation of how this scaling is inherited in the amplitude of stimulus-evoked transients in population firing rates. We also find the counterintuitive effect that populations of neural oscillators with some classes of phase response curves (i.e. near certain bifurcations) respond more strongly to the offset of a stepped, positive stimulus than its onset.

In collaborative work with Herschel Rabitz, Xiao-Jiang Feng and colleagues (Princeton), we are pursuing a complementary, simulation-driven approach. Specifically, we are exploring how nonlinear, global parametric analysis, based on random sampling and Monte-Carlo integration, can determine both the sensitivity and cooperativity of parameters in conductance-based neuron models. Via tracking control, we also use these High Dimensional Model Representation [HDMR] methods to address the inverse question of how parameters determine the input currents required to produce a specified target "output" pattern of neuronal spikes.

6. Optimal control of spike patterns and timing:

With Rabitz and Feng, we take a computational approach to the novel question of whether optimal control methods will eventually identify distinct current waveforms that can serve as alternatives to the present high-frequency patterns used in Deep Brain Stimulation (DBS) therapies for Parkinson's disease. Specifically, we use global numerical optimization (running on a parallel cluster) to identify effective DBS inputs within a biophysically based model of subthalamopallidal neurons in the Parkinsonian state. Our algorithm seeks DBS waveforms that optimally alleviate the attendant pathological synchrony and rhythmic bursting in this model. Compared with simulations of the standard class of DBS inputs, the waveforms identified by our algorithm achieve comparable effects with a fraction of the current strength, and also operate by vastly different mechanisms (the standard inputs directly entrain cells while the optimal inputs more subtly perturb and desynchronize spike times) [*J. Neuroengineering*, 2007; *J. Comp. Neurosci.*, 2007].

A second collaborative project focuses on optimal control at the level of single cells. Here, we identify the minimum-strength current waveforms that perturb the time at which a single spike will occur. Interestingly, if the strength of an input current is measured by its square integral, these optimal currents have the same form and a related scaling to that of the neuron's phase response curve (cf. Sect. 5) [*J. Comp. Nonlin. Dyn.*, 2006]. These results connect the nonlinear dynamics of single neurons with a simple aspect of their signal processing.

7. Expository writing:

With Steve Coombes (at U. of Nottingham), Kresimir Josic, and Brent Doiron, we argue that mathematical neuroscience needs a new confluence of theoretical approaches to neural signal processing, single-cell dynamics, and networks of coupled dynamical systems [*Proc. Royal Soc.*, 2006]. As motivating examples, we review work showing how critical features of synaptic and spiking dynamics combine with network architecture to determine mechanistic "blueprints" for neural integrators and certain sensory networks. Doiron and I are also working with Marty Golubitsky to develop a website on 'Hodgkin and Huxley and the Mathematics of the Spike' as part of SIAM's online "WhyDoMath" initiative. The goal here is to show how mathematical thinking has played, and will continue to play, an integral role in neuroscience research. Finally, recently co-authored articles in the peer-reviewed *Scholarpedia* (online) provide accessible overviews of several underlying topics in dynamical systems.