Collaborative Research in Computation Neuroscience

CRCNS

Annual PI Meeting

June 9 – 11, 2013

Hosted by McGovern Institute for Brain Research at MIT
CRCNS Annual PI Meeting 2013

SCHEDULE

ALL CONFERENCE EVENTS WILL BE HELD IN MIT NEUROSCIENCE BUILDING 46
McGOVERN INSTITUTE ENTRANCE - 300 BLOCK OF MAIN STREET, CAMBRIDGE MA
(across from Citibank and Catalyst Restaurant)

SUNDAY, June 9, 2013 - Atrium

3:30 – 5:30  Registration
5:30 – 730  Dinner
Welcoming Remarks:  Emilio Bizzi, Robert Ajemian
Opening Remarks:  Kenneth Whang, Dennis Glanzman
8:00 – 10:00  Poster Session A

MONDAY, June 10, 2013 – Morning Session

8:00 – 8:30  Continental Breakfast – Atrium
Talks held in Singleton Auditorium (46-3002)
8:30 – 8:50  Adaption to inclined surfaces in locomotor trained spinal cats: Michel Lemay
8:50 – 9:20  Dynamical Architecture for Responding to Unpredictable Mechanical Loads During Rhythmic Behavior: Hillel Chiel, Peter Thomas
9:20 – 9:35  Discussants: Emilio Bizzi, Dagmar Sternad
9:35 – 9:55  Extreme functional generality in multiple-demand regions of frontal and parietal cortex: Nancy Kanwisher
9:55 – 10:05  Discussants: Bin He, Charles Jennings
10:05 – 10:20  BREAK
10:20 – 10:40  Hierarchical reinforcement learning: Mathew Botvinick
10:40 – 11:10  Investigation of distributed plasticity in olfactory memory by integrating behavior, neural activity and neuroanatomy through computational modeling: Brian Smith, Maxim Bazhenov, Ramon Huerta
11:10 – 11:25  Discussant: Nathaniel Daw, Rob Haslinger
11:55 – 12:10  Discussant: Mayank Mehta
12:10 – 1:10  LUNCH - Atrium
MONDAY, June 10, 2013 – Afternoon Session

1:10 – 1:30  Spontaneous and Evoked Release Are Independently Regulated at Individual Active Zones: Troy Littleton.
Discussant: Andreas Neef.

Discussant: Todd Sacktor

2:55 – 3:10  Discussant: TBA

3:10 – 3:25  BREAK - Atrium

3:25 – 3:55  Statistical models of natural scenes in the visual cortex: Tai Sing Lee, Alan Yuille

3:55 – 4:25  Neural Population Coding of Dynamic Natural Scenes: Chris Rozell, Bruno Olshausen
4:25 – 4:40  Discussants: Gabriel Kreiman

4:40 – 5:10  Making the case for natural stimulation: examples for inter-subject alignment and dynamics of visual attention: Michael Hanke, Peter Ramadge.
5:10 – 5:25  Discussant: Reza Rajimehr

5:30 – 7:30  DINNER - Atrium

8:00 – 10:00  Poster Session B - Atrium
TUESDAY, June 11, 2013

8:00 – 8:30  Continental Breakfast - Atrium

8:30 – 9:00  A framework to unify and control seizures and spreading depression: Steven Schiff, Markus. Dahlem

9:00 – 9:15  Discussant: Stephanie Jones

9:15 – 9:45  Memory consolidation, slow wave sleep and weak (electric) stimulation: Lisa Marshall, Thomas Martinetz, Lucas Parra, David Reato

9:45 – 10:00  Discussant Eric Halgren

10:00 – 10:20  BREAK

10:20 – 10:50  Cerebellar nuclear integration of behavior related Purkinje cell activity: theory, experiments and modeling: Dieter Jaeger, Detlef Heck

10:50 – 11:05  Discussant: Paul Katz

11:05 – 12:05  Panel Presentation: Why does the Brain still outperform Computers/Robots in so many sensory/motor modalities given the underlying inferiority of neurons as “hardware”

11:05 – 11:25  Jim DiCarlo – Does the brain still outperform computers in visual object recognition?

11:25 – 11:45  Neville Hogan – Controlling physical interaction

11:45 – 12:05  Robert Ajemian – The eternal dynamism of biological memory and how it differs profoundly from computer bytes

12:05 – 12:20  Discussants: Wasim Malik, Kurt Thoroughman

12:20 – 1:30  LUNCH

1:30 – 2:00  Evidence and a computational role for discrete state jumps in neural processing: Donald Katz, Paul Miller

2:00 – 2:15  Discussant: Bijan Pesaran

2:15 – 2:35  Limb coordination in crayfish swimming: the neural mechanisms and mechanical implications: Tim Lewis

2:35 – 3:05  Neuronal activity in the isolated mouse spinal cord during spontaneous deletions in fictive locomotion: Ilya Rybak, Ronald Harris-Warrick

3:05 – 3:20  Discussant: Joe Ayers

3:20 – 3:35  BREAK - Atrium

3:35 – 3:55  Optogenetics, Scalable Electrophysiology, and Other Neural Circuit Tools In order to help discover how neural circuits implement brain functions: Ed Boyden

3:55 – 4:05  Discussant: Bob Desimone

4:05 – 4:25  A theory of invariant object recognition by visual cortex: Tomaso Poggio

4:25 – 4:35  Discussant TBA

4:35 – 5:30  Panel and Discussion. Future Directions in Computational Neuroscience: Big Science or Little Science? Eve Marder, Sebastian Seung, Fritz Sommer, Yuan Liu, Kenneth Whang

CONFERENCE END
CRCNS Poster Session I – Sunday June 9, 2013

1. Tiffany Glenn-Hall, Pavel Sanda, Nitin Gupta, Mark Stopfer, Maxim Bazhenov
   Title: Feedforward vs. feedback inhibition to regulate the sparse firing of olfactory neurons

2. J. Lee, R. Estrada, S. T. Tokdar, J. M. Groh
   Title: Monkeys can localize more than one simultaneous sound, but how they do it is mysterious: behavior and neural activity in the inferior colliculus

3. Konstantin Mergenthaler, Dipanjan Roy, Jeremy Petravicz, Mriganka Sur, & Klaus Obermayer
   Title: A computational study on changes in orientation tuning in V1 by astrocyte glutamate uptake

   Title: Poster is requested. Explicit belief-state space strategies for latent inference with and without reversals

5. Jeremy Petravicz, Nikolaos Mellios, Sam- El-Boustani, Chuong Le, Mriganka Sur
   Title: Role of Astrocyte Glutamate Transporters in Ocular Dominance Plasticity and Response Properties of Visual Cortex

6. Melanie Lee, Mark Goldman, Emre Aksay
   Title: 'The role of dendritic processing in persistent neural activity

7. Patrick Sadtler, Kristin Quick, Matt Golub, Stephen Ryu, Byron Yu, Aaron Batista
   Title: Neural Constraints on Motor Learning

8. Brian J Fischer, José L Peña
   Title: Role of nonlinearity in optimal cue combination

9. Robert Morton, Alexander Grabenhofer, and Venkatesh Gopal
   Title: A Fast Centroid-Finding Algorithm for Particle Tracking

10. Grigori Enikolopov and Alex Koukakov
    Title: Disposable stem cell hypothesis: A model for neurogenesis in adult hippocampus

11. Camille Gomez-Laberge, Alexandra Smolyanskaya, Gabriel Kreiman, Rick Born
    Title: Silencing V2/V3 reduces spiking variability in MT: implications for excitatory/inhibitory balance

    Title: View-invariance and mirror-symmetric tuning in a model of the macaque face-processing system

13. Alan M. Litke and John M. Beggs
    Title: Large-Scale Electrical Recording, Imaging and Stimulation of Neural System Activity In Vitro
14. Wei Ji Ma, James Cotton, Edgar Walker, and Andreas Tolias
   Title: Visual categorization under variable uncertainty

15. Michelle M. McCarthy, Xue Han, Nancy Kopell, Allison Quach, Tyler X. Gu
   Title: Propagation and suppression of striatally-generated beta oscillations

   Title: Spike sorting for spatially dense, high channel count extracellular recordings

17. Catherine E. MyersAhmed A. MoustafaMark W. GilbertsonScott P. Orr & Richard J. Servatius
   Title: Computational Model of Hippocampal-Amygdala Interactions: Implications for PTSD

   Title: A probabilistic temporal context model for tracking mental context using neural and behavioral data

19. J. Sheynin, R.J. Servatius, M.W. Gilbertson, S.P. Orr, C.E. Myers
   Title: Computer-based approach for studying avoidance behavior: Behavioral findings, computational modeling and implications for PTSD

   Title: Awake Autopatching: Automatic whole cell patch clamp of hippocampal neurons in awake behaving animals

21. Fritz Sommer
   Title: Data sharing on CRCNS.org The poster will present the current status of the CRCNS.org repository for sharing of electrophysiology data and discuss the current developments of unified schemes for storing electrophysiology data in HDF5.

   Title: Contextual effects on perceptual and neuronal sensitivity to kinematic tactile features in the vibrissa pathway

   Title: High-affinity novel-scaffold monoamine transporter ligands revealed via in silico chemical library screening with the S1 substrate pocket of the serotonin transporter

   Title: Awake Autopatching: Automatic whole cell patch clamp of hippocampal neurons in awake behaving animals
Title: Spatiotemporal dynamics underlying recognition of occluded objects

26  Gregory J. Gerling, Isabelle I. Rivest, Daine R. Lesniak, Jacob R. Scanlong & Lingtian Wan
Title: Validating a Population Model of Tactile Mechanotransduction of Slowly Adapting Type I Afferents at Levels of Skin Mechanics, Single-unit Response, and Psychophysics

27  Daine R. Lesniak, Kara L. Marshall, Yuxiang Wang, Yoshichika Baba, Ellen A. Lumpkin, & Gregory J. Gerling
Title: Computational modeling predicts that tactile end-organ remodeling offsets changes in skin thickness during hair growth

28  Russell A Poldrack, Deanna M Barch, Jason Mitchell, Tor Wager, Anthony D Wagner, Joseph T Devlin, Chad Cumba, Oluwasanmi Koyejo, Michael Milham
Title: Towards open sharing of task-based fMRI data: The OpenfMRI project

29  Ranjan P. Khan and Kurt A. Thoroughman
Title: Human reward expectations during a novel motor task: experimental and theoretical foundations

30  Gabriela Costello, Dantong Zhu, Terrence R. Stanford, and Emilio Salinas
Title: Saccadic choices without attentional selection during an urgent-decision task
1. Jean-Marc Fellous, Amy Truong, Yimin Nie and Masami Tatsuno  
   Title: Long Term Reactivation in Hippocampus: Experimental evidence and Information Geometric Approach

   Title: Unraveling CNS Regeneration - From Data/Text Mining to Experimental Design

3. Pascal Ravassard, Ashley Kees, Bernard Willers, David Ho, Daniel A. Aharoni, Jesse Cushman, Zahra M. Aghajan, Mayank R. Mehta  
   Title: Multisensory control of hippocampal spatio-temporal selectivity

4. Yan Wong, Margaret Fabiszak, Nathaniel Daw and Bijan Pesaran  
   Title: Coherent neural activity coordinates movement decisions across the posterior parietal cortex

5. Evan Kirsch, Mohsen Mollazadeh, Vikram Aggarwal, Nitish V. Thakor, and Marc H. Schieber  
   Title: Primary motor cortex neurons correlate better with finger joint kinematics than with their principle components

   Title: Spike correlations and direction encoding in the retina

7. Roland Fleming and Steven W. Zucker  
   Title: US-German Collaboration: Color in Cortex: Orientations, flows, and surface inferences

8. Mengchen Zhu, Allison Del Giorno, Christopher J. Rozell  
   Title: Biophysically accurate non-classical responses and inhibitory interneuron properties in a sparse coding network

9. Mengchen Zhu, Ian Stevenson, Urs Köster, Charles M. Gray, Bruno A. Olshausen, Christopher J. Rozell  
   Title: Sparse coding model and population response statistics to natural movies in V1

10. Urs Köster, Charles M Gray  
    Title: Laminar Structure of Gamma Activity in Cat Visual Cortex

11. Urs Köster, Bruno A Olshausen  
    Title: Characterizing Nonlinear V1 Responses to Natural Movies with Kernel Methods

12. Fanny Cazettes, Brian J Fischer, José L Peña  
    Title: Likelihood representation in the owl's sound localization system

    Title: Open web atlas for high-resolution 3D mouse brain data
14. Uri Eden, Ming Cheng, Sridevi Sarma,  
   Title: Identifying and tracking transitions in neural spiking dynamics in the subthalamic nucleus of Parkinson’s patients

15. Eric Halgren, Rachel MakMcCully, Maxim Bazhenov, Syd Cash, Terry Sejnowski  
   Title: How does the human cortex produce isolated downstates (K-Complexes)? Combined modeling and empirical studies

16. Timothy Horiuchi and Cynthia Moss  
   Title: Functional organization of the midbrain superior colliculus for spatially-guided behaviors

17. Alex Huk & Jonathan Pillow  
   Title: Encoding and decoding of decisions in the parietal cortex

   Title: The dynamics of invariant object recognition in the human visual system

19. Stephanie Jones, Shane Lee, Maxwell Sherman and Christopher Moore  
   Title: Computational Investigation of A Novel Neocortical Beta Origin Hypothesis: From Mechanism to Meaning Beta frequency (15–29 Hz)

20. Akira Sakurai, Charuni A. Gunaratne, Paul S. Katz  
   Title: A comparative and computational analysis of central pattern generators reveals multiple solutions to the same problem

21. Adam Kohn, Ruben Coen-Cagli, Odelia Schwartz  
   Title: Flexible gating of contextual influences in natural vision

22. J.Kostek, R.J. Servatius, M.W. Gilbertson, S.P. Orr, C.E. Myers  
   Title: Acquired equivalence in veterans with symptoms of post-traumatic stress disorder (PTSD): More severe symptoms, particularly re-experiencing symptoms, are associated with better generalization

23. Ethan Meyers  
   Title: The advantages of using population decoding - and a Matlab decoding toolbox

24. Andreas Neef  
   Title: Neuronal encoding properties of individual neurons studied with continuous dynamic photostimulation

25. KaWai (George) Leung, Aylia Mohammadi, Ilya Nemenman, William Ryu  
   Title: Quantification of Nociceptive Escape Response in C. elegans

26. Boris I. Prilutsky, Alexander N. Klishko, Michel A. Lemay, David Cofer, Gennady Cymbalyuk  
   Title: Neuromechanical modeling of spinal control of rhythmic behaviors
   Title: Sensory Processing and Intrinsic Dynamics in the Rod Pathway of the Retina

   Title: Multiscale Dynamics of Thermal Memory in C. elegans

29. Panayiotis Tsokas, Changchi Hsieh, André Antonio Fenton, Harel Shouval, Todd Charlton Sacktor
   Title: Memory Storage at the Synaptic Level: Imaging and Modeling

30. Songqing Lu, Emmanuel A Michaelides, Namrata Mohapatra, Thomas Kuner Peter Jedlicka and Fidel Santamaria
   Title: Using Clomeleon to measure chloride dynamics in Purkinje cells

31. Frederic Theunissen, Wendy deHeer, Alex Huth, Jack Gallant, Tom Griffiths
   Title: Cortical representation of spectral, articulatory, syntactic and semantic information in natural speech revealed by BOLD responses

32. Davide Reato, Marom Bikson, Lucas C. Parr
   Title: Long-term effects of low amplitude electrical stimulation on pharmacologically-induced gamma oscillations in-vitro

33. Park A., Havekes R., Nie T., Huang T., and Abel T.
   Title: Subregion-specific PKA anchoring in the hippocampus is critical for synaptic tagging and contextual memory formation
Adaption to inclined surfaces in locomotor trained spinal cats: Michel Lemay

Rehabilitation strategies for the recovery of locomotor function after spinal cord injury (SCI) involve enhancing the neuronal networks controlling locomotion. Body-weight supported treadmill training is a rehabilitation strategy that through repetitive stepping on a treadmill leads to autonomous weight-bearing stepping in trained complete spinal animals. Patterned afferent inputs promote functional recovery of treadmill locomotion in complete spinal cats by shaping the spinal locomotor network organization through repetitive training. Afferent inputs are also important in modifying the motor output to accommodate walking on graded surfaces, i.e. incline or decline, although questions remains as whether the adaptation is at the spinal or supraspinal level. The performance of locomotor trained spinal cats on graded surfaces has not been reported, although this information could provide important clues about the contribution of spinal reorganization in the lumbar circuitry to locomotion on graded surfaces. We report on the effects of level treadmill training on the recovery of graded locomotion in two complete spinal cats. Each animal was implanted with chronic EMG electrodes in 11 hindlimb muscles pre-transection. Following spinal cord transection at the T11/T12 level, the animals received approximately 4 â?? 6 weeks of body-weight supported training on a level treadmill until the kinematics of stepping on the level surface plateaued. The animals were then recorded on a 10 degree incline and 10 degree decline treadmill surface. Kinematics of the forelimb and hindlimb, as well as hindlimb muscle EMGS, were recorded. Locomotor recovery was measured by the ability for an animal to make 10 consecutive weight bearing plantar steps at the speeds tested. Both animals were able to step on the 2 graded surfaces (incline and decline). However, toe height was significantly greater during inclined locomotion (compared to flat and decline) as a result of greater flexion in the hip, knee and ankle joints during swing (as observed for locomotion on incline in intact cats). Statistical analysis of step length and swing length post-transection showed no significant differences in these measures between grades (flat, incline, decline). However, to height was significantly greater during inclined locomotion (compared to flat and decline) as a result of greater flexion in the hip, knee and ankle joints during swing (as observed for locomotion on incline in intact cats). Statistical analysis of soleus activation showed no significant difference in the pre-stance onset activation time between all grades post-transection, however soleus burst duration increased significantly on the incline after transection. These results indicate that modifications in afferent feedback at the spinal level sufficiently modify the spinal motor output to adapt to changes in grades, particularly for the incline condition. Overall, we demonstrate that level treadmill training modifies sensory feedback such that walking on 10Â° grades is possible in the spinal cat. We are currently evaluating if removal of major ankle extensor afferents prevents recovery of graded stepping in the complete spinal cat. Supported by NIH grants: EB01285.
Dynamical Architecture for Responding to Unpredictable Mechanical Loads During Rhythmic Behavior: Hillel Chiel, Peter Thomas

Although many animals generate rhythmic motor behaviors when the environment is not changing (e.g., breathing, heartbeat, walking, swimming or flying), animals can respond rapidly and appropriately to unpredictable changes: increasing breathing and heart rate if oxygen demands increase during exercise, walking through muddy or swampy terrain where each step may vary, swimming through unexpected changes in current flow, and continuing to fly during an unexpected down draft. A typical simplifying assumption is that the operating conditions are stationary, and this allows effective approximations of the system as a limit cycle, affording reduction to a much simpler phase oscillator description. Incorporating nonstationarity arising from environmental variability enriches the problem mathematically and experimentally. Decomposition of rhythmic behaviors into functional components, often by using fast/slow analysis, has served as an effective way to begin to explore differential sensitivity of a cycle to perturbations that may act differently depending on the phase. We have explored a dynamical architecture based on stable heteroclinic channels (SHCs), i.e., a cycle composed of saddle points whose unstable manifolds lead to the stable manifold of a successor saddle point, but whose final connection is made to the original saddle point, forming a closed cycle. In previous work, we showed that it was possible to create a piecewise-linear version of such a system that allowed us to find an analytical solution for the instantaneous phase response curve (Shaw et al., SIADS 2012). We are currently using a nominal neuromechanical model to explore the effect of varying mechanical perturbations. The simple neural model that we are using can vary from smooth limit cycle (LC) dynamics to a stable heteroclinic channel, based on the value of a single parameter. Using this model, we have found that mechanical perturbations at a particular phase of the cycle are better accommodated by the SHC than the LC. However, because the SHC depends on sensory input to drive it from one saddle point to the next, complete removal of sensory input leads to much greater slowing of overall cycle times for the SHC than the LC. We compare these predictions to data obtained from the biological system upon which the nominal neuromechanical model is based, the feeding apparatus of the marine mollusk Aplysia californica, and show that (a) the response to increased mechanical loading is a slowing of a single phase of the pattern generator (the retraction phase), and (b) removal of most or all of the sensory input (by looking at patterns in reduced preparations or the isolated ganglia controlling feeding) lead to overall slowing of all phases of the motor pattern. These results may be of general interest for understanding many other pattern generators that must be sensitive to unpredictable loads at different points in their cycles.
Extreme functional generality in multiple-demand regions of frontal and parietal cortex: Nancy Kanwisher

In contrast to brain regions that respond selectively to specific kinds of information content (e.g., Kanwisher, 2010), a number of frontal and parietal regions are thought to be domain- and process-general, i.e., active during a wide variety of demanding cognitive tasks (e.g., Cabeza & Nyberg, 2000; Duncan, 2010). However, most previous evidence for this functional generality comes from methods that are known to overestimate activation overlap across tasks (Nieto-Castañon & Fedorenko, 2012). Here we present fMRI evidence from single-subject analyses in humans for extreme functional generality of a specific set of brain regions in frontal and parietal cortices: the same sets of voxels are engaged across tasks ranging from arithmetic to storing information in working memory, to inhibiting irrelevant information when selecting task-relevant responses. These brain regions – which can be identified at the individual-subject level using widely different “localizer” tasks – have a specific topography within frontal and parietal cortex, often lying directly adjacent to domain-specific regions. Thus, in addition to domain-specific regions tailored to solve particular problems of longstanding importance to our species, the human brain also contains a set of extremely functionally general brain regions that endow us with the cognitive flexibility necessary to solve novel problems. These findings suggest that intersubject averaging in the common anatomical coordinate system precludes detailed analysis of multiple demand areas and call for a different strategy for establishing functional correspondences across subjects. Our recent work aims to explicitly model intersubject functional variability when building a population template of the functional organization of the brain.
Hierarchical reinforcement learning: Mathew Botvinick

Research on human and animal behavior has long emphasized its hierarchical structure, according to which tasks are comprised of subtask sequences, which are themselves built of simple actions. The hierarchical structure of behavior has also been of enduring interest within neuroscience, where it has been widely considered to reflect prefrontal cortical functions. In recent work, we have been reexamining behavioral hierarchy and its neural substrates from the point of view of recent developments in computational reinforcement learning. Specifically, we've been considering at a set of approaches known collectively as hierarchical reinforcement learning, which extend the reinforcement learning paradigm by allowing the learning agent to aggregate actions into reusable subroutines or skills. A close look at the components of hierarchical reinforcement learning suggests how they might map onto neural structures, in particular regions within the dorsolateral and orbital prefrontal cortex. It also suggests specific ways in which hierarchical reinforcement learning might provide a complement to existing psychological models of hierarchically structured behavior. A particularly important question that hierarchical reinforcement learning brings to the fore is that of how learning identifies new action routines that are likely to provide useful building blocks in solving a wide range of future problems. Here and at many other points, hierarchical reinforcement learning offers an appealing framework for investigating the computational and neural underpinnings of hierarchically structured behavior. In addition to introducing the theoretical framework, I'll describe a first set of neuroimaging and behavioral studies, in which we have begun to test specific predictions.
Investigation of distributed plasticity in olfactory memory by integrating behavior, neural activity and neuroanatomy through computational modeling: Brian Smith, Maxim Bazhenov, Ramon Huerta

Biogenic amines released into the neural networks of the vertebrate Olfactory Bulb and the insect Antennal Lobe are fundamentally important for generating both non–associative and associative plasticity in response to odors. We use the AL of the honey bee as a model for investigating how biogenic amines target specific cell types to give rise to known plasticity. Our recent studies show that the response dynamics of uniglomerular projection neurons (uPNs) to an odor change after association of that odor with sucrose reinforcement. Octopamine (OA), released by the ventral unpaired median neuron (VUM), is necessary for this plasticity. Using anti-OA staining, we found that the varicosity-like distributions of VUM branch mostly in the cortex of the glomerulus, where it potentially modulates olfactory receptor neurons (ORNs), local interneurons (LNs) and uPNs. Importantly, the key receptor of octopamine, AmOA1, is expressed on GABAergic inhibitory neurons in the AL and, therefore, can affect the strength of LN-mediated inhibition to other LNs and to uPNs. We have developed a biophysical model of the AL circuit to investigate modulatory mechanisms that can explain existing data on the dynamical changes of uPNs during associative learning, and lead to insights for new experiments. Using principle component analysis (PCA) and correlation coefficient analysis, we described quantitatively the degree of similarity of the spatiotemporal patterns of odor responses across model PN activities in the AL. We progressively varied the concentration of each odor in a binary mixture and showed that spatiotemporal responses of projection neurons in the AL also varied smoothly from one pure component to the other. However, following reinforcement learning mixture responses moved towards the pure odor component that was learned. Enhancement of LN‐PN strength based on presynaptic activities causes neurodynamic change corresponding to associative learning as observed in experiments. In contrast, enhancement of synaptic strength based on postsynaptic activities was found to cause neurodynamic change similar to effects of nonassociative learning reported before. These results suggest that reinforcement mechanisms including synaptic facilitation of GABAergic synapses can explain supervised learning in the honeybee AL. To further investigate how nonassociative and associative learning rules modify olfactory circuits of honeybee, we proposed a set of generic learning rules that together account for a variety of experimental data on reinforced and unreinforced odor learning. These rules have been implemented in an existing model of the honey bee olfactory system. Associative conditioning combined with the mutual inhibition between the output neurons produced an abrupt increase in performance in spite of smooth changes of the synaptic weights, as observed experimentally. The results show that an integrated set of learning rules implemented using fan-out connectivities together with neural inhibition can explain the broad range of experimental data on learning behaviors.
Collaboration on High-Resolution Maps of Synapses on Hippocampal Neurons William Kath and Steve Smith

Mechanistic understanding demands knowledge of both structure and function. In the case of the brain, both structure and function are complex beyond any present capacity of science to fathom, but new experimental and computational tools are rapidly advancing capacities to map brains through both functional and structural imaging.

We are collecting functional data from hippocampal CA1 pyramidal neurons using patch-clamp recording in brain slices combined with two-photon glutamate uncaging and calcium imaging. We are also collecting structural and molecular data from the same dendritic branches using array tomography, which provides the highest possible resolution using light microscopy. These methods allow determination of the distribution of excitatory dendritic spines and synaptic weights, as well as the distribution of inhibitory synapses from different interneuron subtypes. Compartmental models of CA1 pyramidal neurons are being used to combine this data into a functionally consistent picture, and the experimental data is informing improvements on our current models of these neurons. In turn, computational simulations with the models generate experimentally testable predictions concerning the integration of synaptic inputs, informing future work on these neurons and the circuits in which they reside.

These investigations are providing critical data concerning the structure and function of pyramidal neurons in the hippocampus, and advancing our understanding of synaptic integration in dendrites and the contribution of excitable dendrites to synaptic plasticity. They provide a unique case study showing how proceeding from maps to mechanisms benefits from closely conjoint mapping of activity and structure and a back-and-forth between experiments and computational modeling.
Spontaneous and Evoked Release Are Independently Regulated at Individual Active Zones. Troy Littleton

Neurotransmitter release following synaptic vesicle fusion is the fundamental mechanism for neuronal communication at synapses. Most studies of neurotransmitter release have focused on electrophysiological responses of released neurotransmitters on postsynaptic cells that occur over a large population of individual release sites (active zones). We have generated transgenic tools that allow imaging of single synaptic vesicle fusion events at individual active zones at Drosophila neuromuscular junctions. This toolkit allows characterization of the spatial and temporal dynamics of single exocytotic events that occur spontaneously or in response to an action potential, as well as the relationship between these two modes of fusion across a population of individual active zones. We find that a majority of active zones participate in both modes of fusion, although release probability is not correlated between the two modes of fusion and is highly variable across the population. We also observe a population of active zones that are specifically dedicated to either spontaneous release or nerve-evoked release, suggesting that some postsynaptic receptors are uniquely activated by spontaneous fusion (minis). These findings indicate synapses contain two channels of information transfer that can occur at mode-specific active zones and that can be independently regulated.
A quantitative account of the first biochemical steps in LTP induction: Sridhar Raghavachari John Lisman

CaMKII is a major synaptic protein required for LTP induction and memory. Work using traditional biochemical methods revealed that CaMKII was activated during LTP induction, but provided no information about the kinetics. Recently it is has become possible to optically measure the activation in living dendritic spines. This method provides quantitative data about both CaMKII activation during LTP induction and the subsequent deactivation of the enzyme. It is furthermore possible to measure the Ca2+ elevation during LTP induction that results from Ca2+ entry through the NMDAR (in zero Mg). Thus both stimulus (Ca2+) and response (CaMKII activation) are known, providing a unique test-bed for understanding intermediate biochemical reactions involving calmodulin (CaM). We first developed a microscopically accurate, mean-field model of the holoenzyme that accounts for the recently discovered structural processes by which CaM binding enhances the further binding of CaM. We validated this model against a fully stochastic, particle-level reaction diffusion model, which uses rule-based kinetics to account for the multi-subunit, multi-state nature of CaMKII and CaM. Then, using known properties of calmodulin (and its buffering by neurogranin), we asked whether the Ca2+ influx through the NMDAR (modeled as stochastic channel openings) could predict the measured magnitude (nearly 100%) and kinetics of CaMKII activation and deactivation. Our results, which did not depend on adjustable parameters, show an excellent fit. With this verified model, we analyzed underlying principles and came to the following conclusions: 1) The recently discovered ultra-fast binding of Ca2+ to the CaM N-lobe is crucial for successful CaMKII activation; 2) The majority of CaM activation (either lobe) is driven by the binding of Ca2+ to CaM anywhere in the spine head and not primarily in the nanodomain of the NMDAR. 3) This diffuse activation of CaM results from the fact that free Ca2+ throughout the spine head is strongly elevated during each opening of the NMDAR. 4) CaMKII activation (autophosphorylation) is a steep function of Ca2+ (Hill Coeff=6), creating a virtual Ca2+ threshold. 5) This property depends crucially on the recently discovered structural cooperativity; 6) Within the spine, the kinase is an integrator of Ca2+ pulses, having a time-constant of roughly 10 sec. 7) The time-constant of CaMKII deactivation is determined primarily by the time-constant of T286 dephosphorylation by phosphatase 8) The measured deactivation time constants are complex, indicating that phosphatase activity can be rapidly altered even by single pulses. Taken together, these results provide the first biophysically and biochemically explicit explanation of the measured activation of CaMKII during LTP induction.
Dynamic Modeling of Synaptic Vesicle Fusion Machinery: Anand Jagota Maria Bykhovskaia

Neurotransmitters are packaged into synaptic vesicles that fuse with the synaptic membrane. Although molecular components of fusion have been identified, it is not yet understood how they interact dynamically. Vesicles dock tightly at the plasma membrane via a specialized protein complex (SNARE), which is thought to provide the necessary force to overcome inter-membrane repulsion. SNARE complexes form between the synaptic vesicle protein synaptobrevin (Syb) and the plasma membrane proteins syntaxin (Syx) and SNAP25 to drive membrane fusion. A cytosolic protein, complexin (Cpx), binds to the SNARE bundle, and functions to “clamp” synaptic vesicle fusion. To understand the fusion clamping mechanism, we performed molecular dynamics simulations of the SNARE/Cpx. To simulate the effect of electrostatic repulsion between vesicle and membrane on the SNARE complex, we calculated the electrostatic force and performed simulations under external forces. We found that electrostatic forces are likely to produce a subtle separation of the C-terminus of the SNARE complex, which may represent a “clamped” pre-fusion state. Importantly, we found that the partially unzipped state of the SNARE bundle can be stabilized by interactions with Cpx, suggesting a simple mechanistic explanation for the role of Cpx in fusion clamping. More specifically, our simulations support a model whereby the Cpx clamps fusion by binding to the Syb C-terminus, thus preventing full SNARE zippering. To test this model, we performed experimental and computational characterization of the Drosophila mutant, which has a point mutation in Syx that causes increased spontaneous fusion. We found that this mutation disrupts the interaction of the Cpx with Syb, partially imitating the cpx null phenotype. To test the predictive power of our model more directly, we generated Drosophila lines with single point mutations in Syb or Cpx, which were predicted to disrupt interactions between these proteins and thus alter the clamping function. In agreement with this prediction, we found that both mutations produced a “superclamping” phenotype, manifested as a decrease in spontaneous activity. Thus, we demonstrate that our model can provide the theoretical basis for directed mutagenesis.
One of the fundamental problems of vision is how the brain can recognize objects and scenes within 150 msec. The difficulty of this problem can be appreciated by realizing that the set of input images is practically infinite and there are an estimated number of 30,000 objects and 1,000 classes of scenes. Our project is based on the conjecture that the neural system adapts to the statistical structures of the environment. We will first give experimental evidence on how neurons in the visual cortex encode statistical models of 3D surface in natural scenes through their tuning properties and connectivity, as a proof of concept that visual cortex does exploit statistical models. Then we will describe two new and richer models of statistics of natural scenes: a model of the appearance of image patches with a generic dictionary of mini-epitomes, and a hierarchical compositional model that can rapidly perform inference over an exponentially large class of objects by bottom-up and top-down processing. We will discuss our on-going research to evaluate these models in V2 and V4 of the primate visual cortex.
Neural Population Coding of Dynamic Natural Scenes: Chris Rozell, Bruno Olshausen

The goal of this project is to determine how local populations of neurons in visual cortex process dynamic natural scenes. Our approach is to combine large-scale neural recordings (silicon polytrodes) with computational models to provide a functional account of cortical network dynamics. Our findings thus far reveal that the responses of most V1 neurons can not be well described purely as a function of the stimulus when using natural movies. Fitting a model to account for the joint activity of the entire recorded population, including the LFP, yields dramatic improvement in predicting the responses of individual neurons. These findings suggest that network effects, as opposed to stimulus properties per se, predominate the responses of neurons in visual cortex. On the theoretical side, we have been developing biophysically realistic models of sparse coding that are more closely tied to specific neural constraints and mechanisms, such as obeying Dale's law and using spiking rather than real-valued activities. We show that nCRF effects, as well as the observed decorrelation between neurons with overlapping receptive fields, can be accounted for in terms of sparse coding principles.
Making the case for natural stimulation: examples for inter-subject alignment and dynamics of visual attention: Michael Hanke, Peter Ramadge

We will discuss research that aims to discover a coding scheme that is common across brains. The methods being investigated align brain activity across subjects by projecting individual brain data into a common, high-dimensional space. This will allow one to build common models of brain representational spaces for different cortical areas that are valid both across brains and across a wide range of stimuli and cognitive states. We are developing two algorithms – hyperalignment and functional connectivity. Hyperalignment rotates the voxel spaces of individual brains into a single high-dimensional space in which each dimension is a profile of differential responses to stimuli that is common across brains. Functional connectivity hyperalignment aligns voxel spaces based on the functional connectivity profile for each cortical location rather than the functional response profile. Functional connectivity profiles afford models of areas that do not respond to external stimuli in a consistent manner, e.g. those areas in the default-intrinsic system that play a central role in social cognition.
A framework to unify and control seizures and spreading depression: Steven Schiff, Markus. Dahlem

Epileptic seizures and spreading depression (SD) are two pathological conditions in the brain characterized by distinct neuronal patterns of activities, characteristic ionic concentration changes, and a known dependency on oxygen supply. These phenomena have always been considered as separate physiological events. The classic Hodgkin-Huxley model of neuronal dynamics assumed that the ionic concentrations inside and outside of the neuron were fixed, that cellular and extracellular volume were constant, and that the neuron had an infinite supply of energy to pump and restore ionic gradients dissipated during activity. By extending the Hodgkin-Huxley formalism to include the ion flux dynamics of potassium, sodium, and chloride, permit the extracellular space to dynamically adjust as the cell swells during activity, and critically to include the energy requirements of ion pumps and oxygen supply as part of neuronal dynamics, we discover a unique fusion of the dynamics of seizures and spreading depression. By now adjusting the dual parameters of potassium and oxygen, we realize a wide range of neuronal dynamics, from tonic spiking, to seizures, to spreading depression (whether potassium or hypoxia induced), to mixed seizure and spreading states, and the terminal wave of death at very limited oxygen supplies. Because the transitions between these states are the boundaries we seek for control, we are examining them in detail to better understand their bifurcation structure. We have discovered that the tonic spiking transition to the onset of spreading depression is a subcritical torus bifurcation, while the transition from tonic spiking to seizures are observed as long transients, indicating a critical slowing down. We therefore offer a unified framework that places the fundamental membrane dynamics of spiking, seizures and spreading depression as realizable states within a single dynamical membrane system. In addition to substantially extending the predictions from the Hodgkin-Huxley formalism, these findings offer novel strategies to understand and control these pathological states.
Memory consolidation, slow wave sleep and weak (electric) stimulation: Lisa Marshall, Thomas Martinetz, Lucas Parra, David Reato

In general our studies support the idea that weak oscillatory electric stimulation given at the frequency characteristic for the behavioral state facilitates the ongoing behavior. In contrast to auditory stimulation, the electric stimulation is subthreshold. Thus, although also clinically relevant, subthreshold stimulation is more relevant for its primary potential to explain self-regulatory mechanisms of the brain. We will show Long term effects of repetitive stimulation.

The mechanisms underlying acute effects of weak electric stimulation on nervous tissue have been extensively explored in vivo and in vitro. How these acute effects translate into long lasting behavioral effects that are routinely observed in human clinical studies has remained fundamentally addressed. We explored the effects of constant current stimulation on hippocampal gamma activity. In this dynamical system we find that the acute effects of stimulation on the strength of gamma oscillation are no-uniform even within nearby recording locations (within CA3) and in fact suppress spatial coherence of network oscillations -- a disruptions that lasts long after the electric stimulation.

Finally, memory consolidation is closely associated with sleep slow oscillations which hallmark slow wave sleep. Here we present recent results which show that auditory stimulation in sleeping humans in-phase with the ongoing rhythmic occurrence of slow oscillation up-states enhances the slow oscillation rhythm, phase-coupled spindle activity, and alongside profoundly enhances the consolidation of declarative memories. We present preliminary results of a cortico-thalamic neural-mass model for simulating the influence of phase-coupled acoustic stimulation on the slow oscillation rhythm and spindle activity. Acoustic stimulation appears to provide a simple means to enhance sleep rhythms and their functional efficacy.
Cerebellar nuclear integration of behavior related Purkinje cell activity: theory, experiments and modeling: Dieter Jaeger, Detlef Heck

In this joint project between the Jaeger lab at Emory University and the Heck lab at the University of Tennessee Health Science Center. The main goal combined experimental and modeling study is to determine the mechanisms of neuronal interaction between the cerebellar cortex and the cerebellar nuclei, from where cerebellar output originates. Neuronal activity from single unit cerebellar Purkinje cells, mossy fibers and CN neurons is recorded in awake behaving mice. Purkinje cells and CN neurons have characteristically high baseline firing rates. We analyze the correlation of spike firing in these units with behavior at different times scales ranging from spike duration (~1 ms) to slow (~1 sec) fluctuations of spike rates. These data are then incorporated into our published biophysically realistic CN neuron model (Steuber V, Schultheiss NW, Silver RA, De Schutter E, Jaeger D (2011). The objective of this work is to determine which structure the synaptic input needs have in order to generate physiologically realistic output firing as measured in awake behaving mice. Our inputs to the model are derived from Purkinje cell (PC) and mossy fiber (MF) recordings obtained under the same conditions in awake mice as the CN neuron recordings. The spike trains of all 3 structures are characterized by their mean rate, regularity (CV and local variability (LV)), interspike-interval distribution, power spectrum, and behavioral modulation, which in this study is related to the control of respiration. Purkinje cell inputs to the model are constructed as rate modulated gamma – distributed spike trains with a refractory period. We show that these artificial spike trains can match all the properties of recorded spike trains listed above when carefully constructed. Because we have seen temporal correlations in the rate fluctuations of paired PC recordings but not any fast single spike cross-correlations, we incorporate only a rate correlation structure into our artificial PC spike trains by using a common rate template in constructing gamma distributed time series. 50 such spike trains converge onto the model neuron. Similarly, we allow for a behavioral co-modulation of PC inputs to the model via a common behavioral modulation of the rate template at the time of measured expiration. We find that using published parameters for the synaptic conductances of PC and MF inputs to our CN model that our rate modulated gamma – distributed spike trains with a refractory period can control model output to match CN spike train properties on all measures. Important signals can be carried both by MF and by PC input, and only a fraction of the inputs need to show behavioral modulation in order to drive realistic behaviorally modulated CN output. These findings support the notion that a spike rate code is sufficient to account for all observed firing patterns.
Why does the Brain still outperform Computers/Robots in so many sensory/motor modalities given the underlying inferiority of neurons as hardware: Jim DiCarlo, Neville Hogan, Robert Ajemian

Jim DiCarlo -- Does the brain still outperform computers in visual object recognition?

Neville Hogan -- Controlling Physical Interaction
Contact and physical interaction are essential for that quintessentially human ability, object manipulation and the use of tools. Despite slow muscles and long neural delays, humans achieve astonishing dexterity, far superior to anything yet achieved in robotic systems. I will review how the unique properties of muscle may contribute to this remarkable fact.

Controlling physical interaction presents unique challenges; for example, individually stable systems may be de-stabilized on contact. Physical interactions are bi-lateral; composite behavior is not a simple composition of operators. As a result, signal processing theory does not work well. Instead, concepts grounded in physical system theory have proven effective. Computers and brains essentially process information; physical systems process energy. The main constraints on computation and signal processing are temporal causality and boundedness. Physical systems are additionally constrained by mechanical physics. For example, connections between physical systems must be linear even if the systems are highly nonlinear.

Muscles are at the interface between information processing and energy processing and are well-modeled by a generalization of classical equivalent networks. One of their key properties is modifiable mechanical impedance which can dramatically simplify control of physical interaction. Examples include: multi-joint motions while interacting with a challenging kinematic constraint; operation at and through singularities in the map between end-point and joint motions; compensation for dynamic destabilization due to contact; compensation for static destabilization due to force production. In fact, the limits of human force exertion appear to be determined by the limits of muscular impedance production.

Robert Ajemian -- The eternal dynamism of biological memory and how it differs profoundly from computer bytes
Evidence and a computational role for discrete state jumps in neural processing: Donald Katz, Paul Miller

Neural activity related to behavioral choice has been described to build up slowly, in a ramp-like manner; in cortical responses to tastes, for instance, information related to consumption decisions (i.e., firing related to the tastes’ palatability) appears to build across a 500-msec period—a period that precedes the emission of palatability-related behavior (the decision to either swallow or expel). Here we show, however, that this apparent ramp of palatability-related activity is an artifact of across-trial averaging: while activity correlated with the palatability of different taste compounds does appear to build up slowly according to single-neuron analyses aligned on stimulus onset, neural ensemble activity within individual trials actually forms sequences of discrete states with sudden, coherent transitions between states. Furthermore, when trials are “re-aligned” to the onset of the state dominant at the peak of the apparent “ramp”, the rise of correlation with palatability is significantly steepled, and in fact becomes nearly as steep as that observed in “ideal” simulations in which palatability appears instantaneously. These results suggest that, at least in this naturalistic context, cortical ensemble responses predicting consumption decisions do not accumulate slowly, but rather appear suddenly, in an “a-ha” moment. We demonstrate how such neural dynamics can arise in circuits of “noisy” spiking neurons via stochastic transitions between attractor states. Finally, we show that by enforcing certain biological constraints—such as limited ranges of firing rates and presence of internal circuit noise—a system producing decisions via state-transitions can outperform a perfect integrator. Thus such computations by state transitions can be optimal and an aspect of natural behavior.
Limb coordination in crayfish swimming: the neural mechanisms and mechanical implications: Tim Lewis

A fundamental challenge in neuroscience is to connect behavior to the underlying neural mechanisms. Networks that produce rhythmic motor behaviors, such as locomotion, provide important model systems to address this problem. A particularly good model for this purpose is the neural circuit that coordinates limb movements in the crayfish swimmeret system. During forward swimming, rhythmic movements of limbs on different segments of the crayfish abdomen progress from back to front with the same period but neighboring limbs are phase-lagged by 25% of the period. This coordination of limb movements is maintained over a wide range of frequency. We examine different biologically plausible network topologies of the underlying neural circuit and show that phase constant rhythms of 0%, 25%, 50% or 75% phase-lags can be robustly produced. In doing so, we obtain necessary conditions on the network connectivity for the crayfish’s natural stroke pattern with 25% phase-lags. We then construct a computational fluid dynamics model and show that the natural 25% back-to-front phase constant rhythm is the most efficient stroke pattern for swimming. Our results suggest that the particular network topology in the neural circuit of the crayfish swimmeret system is likely the result of natural selection in favor of more effective and efficient swimming.
Neuronal activity in the isolated mouse spinal cord during spontaneous deletions in fictive locomotion: insights into the locomotor central pattern generator organization. Ilya Rybak, Ronald Harris-Warrick.

One method to study the structure of neural networks for behavior is to study changes in neuronal activity during spontaneous errors in network output. We explored the organization of the spinal central pattern generator (CPG) for locomotion in the isolated neonatal mouse spinal cord, by analyzing the activity of identified spinal neurons during spontaneous deletions of motor activity during fictive locomotion. Most spontaneous deletions were non-resetting, with rhythmic activity resuming after an integer number of cycles; this indicates the existence of an autonomous rhythm generator that can continue to cycle during loss of motoneuron rhythmic output. Flexor and extensor deletions showed marked asymmetry: flexor deletions were accompanied by sustained ipsilateral extensor activity, while rhythmic flexor bursting was not perturbed during extensor deletions. Rhythmic activity on one side of the cord was not perturbed during non-resetting deletions on the other side, and non-resetting deletions could occur with no input from the other side of the cord. These results were confirmed by intracellular recordings from motoneurons, commissural interneurons and the V2a class of excitatory interneurons. Different neuron classes clearly showed either deletion or maintenance of rhythmic synaptic drive during motor deletions, suggesting their location in the locomotor network. These experimental results could be successfully reproduced by a computational model of the locomotor CPG. This model has an asymmetrical two-level organization with rhythm-generating (RG) networks that drive pattern-forming (PF) networks; only the flexor RG network is intrinsically rhythmic, while the extensor RG network provides only tonic drive to the PF networks. The model makes explicit predictions about the pattern of synaptic drive neurons at different levels in the network should receive during deletions, which are currently being tested.

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Optogenetics, Scalable Electrophysiology, and Other Neural Circuit Tools In order to help discover how neural circuits implement brain functions: Ed Boyden

In order to help discover how neural circuits implement brain functions, and how these computations go awry in brain disorders, my group invents technologies to enable the scalable, systematic observation and control of biological structures and processes in the living brain. We have developed genetically-encoded reagents that, when expressed in specific neuron types in the nervous system, enable their electrical activities to be precisely driven or silenced in response to millisecond timescale pulses of light. I will give an overview of these “optogenetic” tools, adapted from natural photosensory and photosynthetic proteins, and discuss new tools we are developing, including molecules with novel color sensitivities (e.g., the multicolor channelrhodopsin pair Chronos and Chrimson) and other unique capabilities (e.g., the noninvasive red-light sensitive halorhodopsin Jaws). Often working in interdisciplinary collaborations, we have developed microfabricated lightguide-bearing and electrode recording hardware to enable complex and distributed neural circuits to be controlled and observed in a fully 3-D fashion, as well as robots that can automatically record neurons intracellularly and integratively in live brain (see companion presentations). These tools are in widespread use to enable systematic analysis of neural circuit functions, are also opening up new frontiers on the understanding and treatment of brain disorders, and may serve as components of new platforms for diagnosing and treating brain disease.
A theory of invariant object recognition by visual cortex: Tomaso Poggio

The talk explores the theoretical consequences of a simple assumption: the computational goal of the feedforward path in the ventral stream of visual cortex -- from V1, V2, V4 and to IT -- is to discount image transformations, after learning them during development.

The initial assumption is that a basic neural operation consists of dot products between input vectors and synaptic weights which can be modified by learning. It proves that a multi-layer hierarchical architecture of dot-product modules can learn in an unsupervised way geometric transformations of images and then achieve the dual goals of invariance to global affine transformations and of robustness to deformations. These architectures learn in an unsupervised way to be automatically invariant to transformations of a new object, achieving the goal of recognition with one or very few labeled examples. The theory should apply to a varying degree to a range of hierarchical architectures such as HMAX, convolutional networks and related feedforward models of the visual system and formally characterize some of their properties.