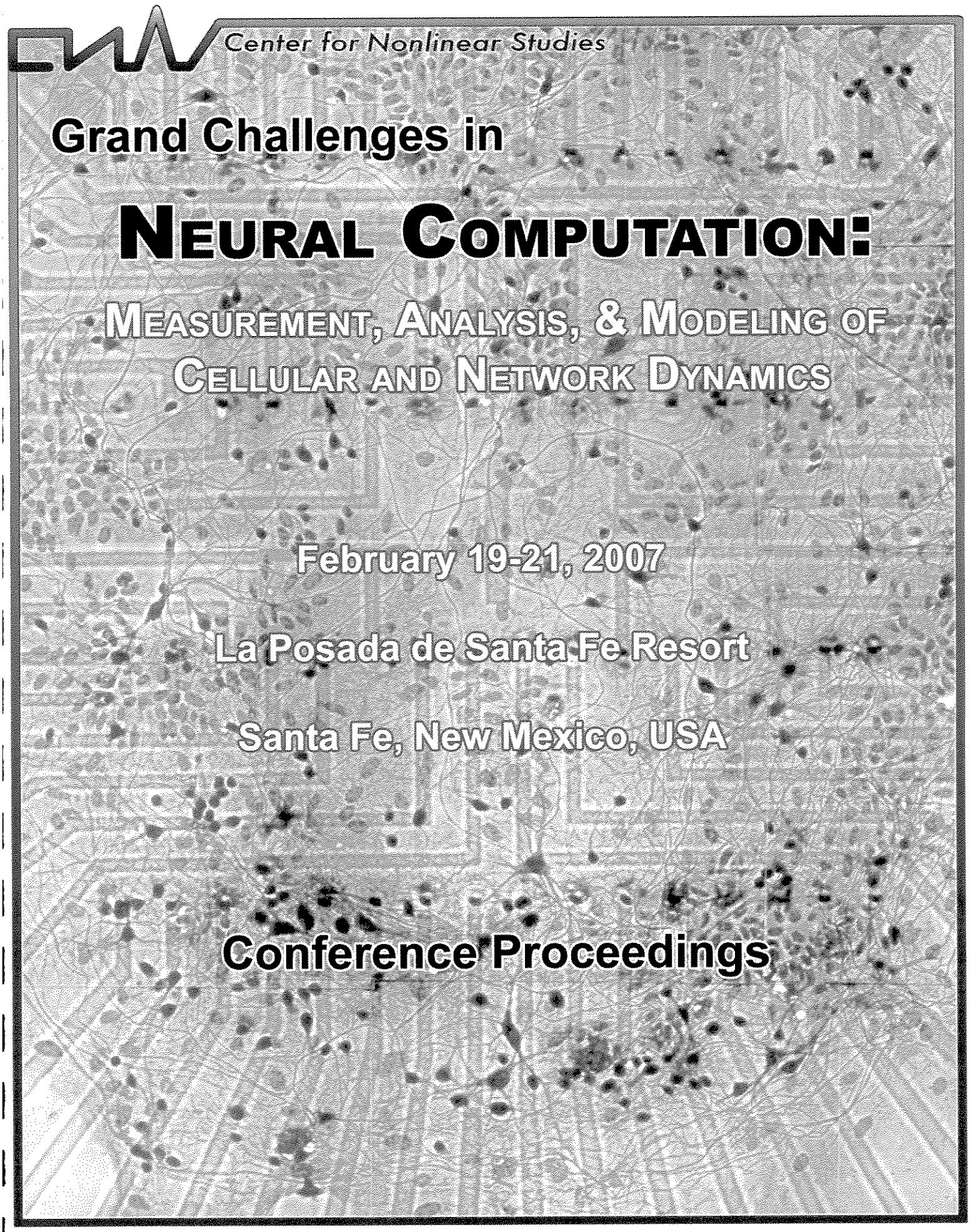
Center for Nonlinear Studies
Grand Challenges in
NEURAL COMPUTATION:
MEASUREMENT, ANALYSIS, & MODELING OF
CELLULAR AND NETWORK DYNAMICS
February 19-21, 2007
La Posada de Santa Fe Resort
Santa Fe, New Mexico, USA
Conference Proceedings

Monday, February 19, 2007

Measurement and Analysis I
8:05 AM – 12:00 PM

Theory, Modeling, and Applications I
1:30 PM – 5:30 PM

Banquet
7:30 PM

Tuesday, February 20, 2007

Theory, Modeling, and Applications II
8:15 AM – 12:00 PM

Measurement and Analysis II
1:30 PM – 5:30 PM

Poster Reception
7:00 PM

Wednesday, February 21, 2007

Theory, Modeling, and Applications III
8:00 AM – 12:05 PM

Neuroscience in New Mexico
1:30 PM – 5:20 PM

Organizers:
Luis Bettencourt, John George, Garrett Kenyon, & Ilya Nemenman (LANL)

Advisory Committee:
David Sharp (LANL), Bill Priedhorsky (LANL), Chris Wood (SFI), John Rasure (MIND), Tom Bowles (NM Science Advisor), Gerold Yonas (Sandia), Robert Duncan (IAS-NM), Yoshio Okada (BRAIN Inst), Joysree Aubrey (Advisory Committee Coordinator)

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Monday, February 19, 2007

Session 1: Measurement and Analysis I

Session Chairs: Garrett Kenyon & Ilya Nemenman

8:00-8:05	Welcome from Robert Ecke, CNLS Center Director
8:05-8:10	Welcome from Robert Duncan, Institute for Advanced Studies
8:10-8:25	Introduction by Tom Bowles, NM Science Advisor
8:25-8:30	Introduction of Keynote Speaker by Garrett Kenyon
8:30-9:10	**David Van Essen** (Washington University & Society for Neuroscience President) *Neural Circuits and Neural Computation: A Systems-level Perspective*
9:10-9:50	**Apostolos Georgopoulos** (University of Minnesota) *Encoding Information in Neurons, Encoding it from Neuronal Populations*
9:50-10:00	Poster Previews
10:00-10:15	Break
10:15-10:55	**Rob de Ruyter van Steveninck** (University of Indiana) *Insect Vision: Physical Constraints in Natural Information Processing*
10:55-11:35	**William Bialek** (Princeton University) *Searching for Principles, and Letting the Data Guide Us*
11:35-12:00	Grand Challenges Panel Discussion

Session 2: Theory, Modeling, and Applications I

Session Chair: Henry Abarbanel

1:30-2:10	**Henry Abarbanel** (University of California at San Diego) *The Threefold Way in Computational Neuroscience*
2:10-2:50	**Roger Traub** (SUNY Downstate Medical Center) *The Critical Role of Electrical Coupling in the Generation of Population Oscillations in Neocortex, at Frequencies from <1 Hz to >100 Hz*
2:50-3:30	**Reza Shadmehr** (Johns Hopkins University) *Internal Models, Adaptation, and the Timescales of Memory*
3:30-3:45	Break
3:45-4:25	**Sebastian Seung** (Massachusetts Institute of Technology) *Toward a New Science of Connectomics*
4:25-5:05	**Kenneth Miller** (Columbia University) *Understanding Cortical Circuits*
5:05-5:30	Grand Challenges Panel Discussion

Banquet

7:30-9:30	Banquet
8:30-9:10	**C. Randy Gallistel** (Rutgers University) *Memory and the Computational Brain*

Neural Circuits and Neural Computation: A Systems-level Perspective

David C. Van Essen
Washington University in St. Louis

The amazing computational capabilities of the human brain reflect the dynamic flow of information through its fabulously complex neural circuitry. Elucidating the wiring diagram of the primate brain in general and the human brain in particular represents one of the grand challenges of neural computation. As the dominant structure of the brain (and in humans the most variable structure), the cerebral cortex is especially intriguing but also especially challenging to decipher. This presentation will focus on new neuroimaging approaches that show much promise for revealing the circuitry and functional organization of cerebral cortex in humans and nonhuman primates. A quantitative understanding of neural connectivity patterns at both macroscopic and microscopic levels will allow fundamental advances in modeling biologically plausible neural circuits that emulate many functions of the human brain.

Insect vision: Physical constraints in natural information processing.

Rob de Ruyter van Steveninck
Department of Physics, Indiana University, Bloomington

Information processing by the brain is often understood to be constrained by the properties of the neural hardware that carries out the underlying computations. However, living systems cannot freely choose the quality of their sensory input. That is dictated by physical properties of the environment and by the necessity to respond to external stimuli in time. In other words, there are constraints on information processing, independent of the animal or its neural substrate, and these constraints are to some extent universal. Our knowledge of neural processing has mostly come from laboratory experiments, and so our understanding of those constraints, as they arise in real natural conditions, is still in its infancy. It will be interesting to quantify them, to see how they affect information processing strategies in real animals, and to assess whether the solutions that animals use are close to optimal in a way that we can understand.

The visual system is a good model for a study of these questions, because vision naturally operates over an enormous range of light intensities, that is, an enormous range of signal to noise ratios. Insect visual systems in particular are generally very amenable to quantitative analysis. I will introduce the subject with some historic examples that illuminate problems and solutions in insect vision, ranging from the optics of the insect eye, to motion vision, and behavior. Then I will discuss some of our early experiments and analyses on motion estimation in a natural context, illustrating the need for the system to adapt its computational strategies in order to cope with large variations in signal and noise. Work in this vein is still in its early stages. For the not too distant future, it is my hope that a combined effort in experiment and theory can achieve a deeper and more quantitative understanding of sensory information processing in the much richer context offered by the complexities and uncertainties of the natural world.

Searching for principles, and letting the data guide us

William Bialek
Princeton University

What would it mean to have a theory of the brain? I can imagine at least two very different answers to this challenge. In one version, we want to show how brain function emerges from the microscopic dynamics of molecules, cells, and synapses. Most of the things we find really mysterious about the brain involve the activity of many such elements, and so a theory in this spirit might look something like statistical mechanics. A second approach would focus on what we mean by "function;" since the brain is not a general purpose computer, some computations are done more efficiently than others, and some specific tasks seem to be performed as well as possible. A theory thus could start by taking these examples of near-optimal performance seriously, and articulating optimization principles from which essential aspects of neural circuitry could be derived. These two styles of theorizing are not completely separate, nor do they exhaust the possibilities, but they pose very different problems. In the shortest possible phrasing, the first approach responds directly to "how does the brain work?", while the second approach starts with "what does the brain do?". It surely is worth pausing to emphasize that we don't have a precise answer to the second question.

In this talk I hope to discuss two examples, one from each style of theorizing.

The Threefold Way in Computational Neuroscience

Henry Abarbanel
University of California, San Diego

There appear to be three (at least) identifiable approaches to Computational Neuroscience. After trying to identify these views, and comment on them with my own opinion, I will focus on the view I think will be most productive both for Neuroscience as a whole and for organizations such as the Los Alamos National Laboratory specifically.

This op-ed introduction will be followed by a discussion of a specific problem solved by neural systems in a variety of different ways: telling time. On scales from a few microseconds to many hours animals need to address the passage of time. I will review some of the known strategies for this and speculate on others.

Not to be too mysterious about the connections between this and the beginnings of the talk: I choose the second of the three fold approaches.

The critical role of electrical coupling in the generation of population oscillations in neocortex, at frequencies from <1 Hz to >100 Hz

Roger Traub
SUNY Downstate Medical Center

The neocortex generates oscillations at many different frequencies, the pattern of which correlates (in vivo) with the sleep/wake cycle and, in the waking state, with sensory stimulation and cognitive tasks. There are also correlations with the initiation and progression of epileptic seizures. Many of these oscillations can be replicated in brain slices, from both rodents and (more recently) humans, with a remarkable similarity, at the cellular level, to in vivo oscillations. In addition, detailed network simulations have advanced to the state where cellular oscillation patterns can be replicated and specific experimentally testable predictions offered - in some cases, already verified. Remarkably, most oscillation types in the neocortex, and hippocampus also, depend on electrical coupling between pyramidal neurons, and such coupling appears to exist at an unexpected site - between axons. I shall review the morphological data on this type of coupling, and also the phenomenology and mechanisms of gamma (30 - 80 Hz), beta2 (20 - 30 Hz) and very fast (>80 Hz) oscillations; and I shall outline how large-scale modeling of a thalamocortical column, using multi-compartment, multi-conductance neurons, has contributed to our understanding.

For the future, it is safe to say that models and theories of neocortical function will need to take account of electrical coupling between neurons, in addition to chemical synaptic interactions.

Internal models, adaptation, and the timescales of memory

Reza Shadmehr
Johns Hopkins University

When the brain generates a motor command, it also predicts the sensory consequences of that command via an "internal model". The reliance on predictions makes the brain able to sense the world better than is possible from the sensors alone. However, this happens only when the models are accurate. To keep the models accurate, the brain must constantly learn from prediction errors. Here I use examples from saccade and reach adaptation to demonstrate that learning is guided by multiple timescales: a fast system that strongly responds to error but rapidly forgets, and a slow system that weakly responds to error but has good retention. What are these systems learning? In principle, the brain could be learning to more accurately predict the sensory consequences of motor commands and correct movements as they occur (i.e., learn a forward model). Using the theoretical framework of stochastic optimal control, I show that such adaptation should leave its signature in saccade trajectories. Experiments on a novel form of saccade adaptation seems to bare out the predictions. Therefore, it appears that motor errors give rise to multiple timescales of adaptation, and the fastest timescales learn forward models.

Toward a new science of connectomics

Sebastian Seung
Howard Hughes Medical Institute and MIT

Judging from current progress in nanoscale imaging and cutting, histochemical and genetic methods for staining, and computational algorithms for image analysis, it should soon be possible to create automated systems that will take a sample of brain tissue as input and generate its "connectome," a list of all synaptic connections between the neurons inside. Such systems will give rise to a new field called "connectomics," defined by the high-throughput generation of data about neural connectivity, and the subsequent mining of that data for knowledge about the brain. I will discuss the possible impact that connectomics could have on our understanding of how the brain wires and rewires itself, the dynamics of activity in neural networks, and the neuropathological basis of mental disorders.

Memory and the Computational Brain

C. Randy Gallistel
Rutgers University

A read-write memory (Turing's tape) is implied by behavioral evidence for the kinds of computations performed by even insect brains (e.g., dead reckoning) together with what computer scientists understand about the limitations that a finite state architecture places on computational power. However, neuroscientists have not looked for and (therefore?) not found a read-write memory mechanism. The absence of such a mechanism is often taken as a virtue, despite its relegation of the nervous system to the computationally weaker class of finite state machines. Computational models in contemporary cognitive science routinely presuppose the much more powerful Turing architecture, which is why they are "neurobiologically implausible." I argue that this is a problem for neuroscience, not cognitive science. There must be a read-write memory mechanism. Its role in the causation of behavior is as central as the role of the read-only molecular genetic memory mechanism in the causation of biological structure. Its discovery will transform our understanding of neurobiology, just as the discovery of the structure of the gene transformed biochemistry.

Tuesday, February 20, 2007

Session 3: Theory, Modeling, and Applications II

Session Chair: John Hopfield

8:15-8:20 Introduction of Keynote Speaker
8:20-9:00 **John Hopfield** (Princeton University & American Physical Society President)
Assorted Problems
9:00-9:40 **Yann LeCun** (New York University)
Can a Single Learning Algorithm Build the Visual Cortex? The Challenges of Training an Artificial Vision System
9:40-10:20 **Steven W. Zucker** (Yale University)
Principles of Computational Abstraction for Visual Cortex
10:20-10:35 Break
10:35-10:55 Poster Previews
10:55-11:35 **David McCormick** (University of California at Berkeley)
Cortical Networks: From Subcellular Processes to Models
11:35-12:00 Grand Challenges Panel Discussion

Session 4: Measurement and Analysis II

Session Chair: Yoshio Okada

1:30-2:10 **Gilles Laurent** (California Institute of Technology)
Circuit Dynamics, Synaptic Learning Rules and Computation in an Olfactory System
2:10-2:50 **E.J. Chichilnisky** (Salk Institute)
Ensemble Coding of Visual Motion in the Primate Retina and Its Readout in the Brain
2:50-3:30 **Israel Nelken** (Hebrew University)
Grand Challenges in Auditory Research
3:30-3:45 Break
3:45-4:25 **Charles Gray** (University of Montana)
Distributed Processing in the Cerebral Cortex: How Can We Get the Data to Ask the Questions?
4:25-5:05 **Jack Gallant** (University of California at Berkeley)
Discovering the Neural Code for Vision
5:05-5:30 Grand Challenges Panel Discussion

Posters and Reception

7:00-8:30 Reception
7:30-10:30 Contributed Posters

Assorted problems

John Hopfield
Princeton University

How can we build useful, suitable models of brain function? Why/how is neurobiology so effective? How is analyze electophysiological data to be analyzed, cast in light of structure and cell biology, in such a way as to get at computational questions? What are appropriate collective coordinates? How do we bridge the gap from stimulus-response tasks to tasks that require planning, considering alternatives, or multiply reusing the same neural circuits? How is ongoing 'mental life' to be described and studied at the neuron level?

Can a Single Learning Algorithm Build the Visual Cortex? The Challenges of Training an Artificial Vision System.

Yann LeCun
The Courant Institute, New York University

It may come as a surprise to many neuroscientists that some of the best artificial vision systems for detecting human faces, recognizing everyday objects, or recognizing handwritten characters, are based on Hubel and Wiesel's old ideas. Feed-forward neural networks with multiple, alternated layers of simple cells (non-linear filters) and complex cells (which locally pool simple cell outputs) can perform those tasks with high accuracy, in real time, and with robustness to variations of pose, illumination and clutter.

Until recently, these networks had to be trained using biologically implausible supervised learning algorithms, which require a large number of training samples. Hinton recently showed how to train "deep" networks (with many layers) using unsupervised algorithms. Applying similar ideas to the multi-stage Hubel-Wiesel architecture leads to artifical vision systems that can learn invariant feature hierarchies in an unsupervised way, by simply being shown natural images.

One of the biggest challenges of learning research is to devise better learning procedures that can train such "deep" architectures, and that can be scaled up to produce full-fledged artificial perception systems.

Principles of Computational Abstraction for Visual Cortex

Steven W. Zucker
Yale University

The visual system is distributed across dozens of cortical areas, each of which exhibits detailed cytoarchitectonic and connection structures. At a cartoon level the functional architecture of many of these areas appears columnar, with rich long-range horizontal connections in some layers. The grand challenge is to determine the principles of neural computation that derive from these structural constraints for solving real vision problems. These principles would then support an abstract theory of vision which would specialize to neural implementations, was amenable to computational abstraction (not just simulation), and could transfer to engineering applications.

Cortical Networks: From Subcellular Processes to Models

David A. McCormick
Yale University School of Medicine

How does the cerebral cortex operate? A leading hypothesis that was proposed more than 50 years ago was that the cortex operates through dynamic functional connectivity through the temporary formation of neuronal assemblies. It has been tacitly assumed in these models that information transmission between elements in these assemblies occurred almost exclusively through the rate and timing of action potentials. Intracellular recordings in waking and sleeping animals demonstrate that cortical networks flip between preferred states of activity and that these states determine neuronal responsiveness (gain) – and therefore intracortical functional connectivity. In addition, detailed investigations of communication between cortical neurons reveal that synaptic transmission may be influenced by more than just the rate and timing of action potentials arriving from the presynaptic cell. It is also dependent upon the membrane potential of the communicating cell, indicating that information transfer within local networks in the cortex may operate in a mixed "analogue" and "digital" model. These investigations reveal that the cortex operates in a mode that is fluid, holistic, and dynamic, in which the real time interactions of subcellular, cellular, and network components precedes and determines the flow of information throughout the network as well as its response to outside information. A grand challenge in the study of cortical networks is to integrate information from the subcellular level all the way to large scale networks in order to understand how cortical activity flows and controls its own excitability.

Circuit dynamics, synaptic learning rules and computation in an olfactory system

Gilles Laurent
Caltech

Olfactory systems solve, with very reduced circuitry and thus, presumably, with high efficiency, the most basic and typical problems of pattern learning, classification and recognition. By studying small brains (insects, fish), we are attempting to describe and understand some of the basic building blocks of such circuits. I will describe some of our results, focusing especially on the relationships between circuit architecture, cell and synaptic function, dynamics, synaptic learning rules and computation. Finally, I will try and describe some of the most obvious remaining challenges.

Ensemble coding of the visual motion in the primate retina and its readout in the brain

E.J. Chichilnisky
The Salk Institute

One of the great challenges in neuroscience is to understand the function of population codes. This entails answering at least three major questions: (1) how do populations of neurons encode information in their collective activity? (2) how are population codes read out by downstream neurons? (3) how do population codes influence sensation and behavior? The primate visual system illustrates these problems in abundance. Specifically, as signals flow from the peripheral to the central visual system, receptive fields become increasingly large and complex, reflecting readout of population coded signals at successive stages of processing. A comprehensive investigation of these computations therefore requires that one be able to experimentally monitor the entire population code and its readout, a demand that until recently has been technically prohibitive. In this talk I will describe our studies of a behaviorally important population code and its readout in the primate visual system. Visual motion is represented in the retina by traveling waves of activity in many non-direction-selective neurons. The direction and speed of these waves are read out by downstream neurons to control perception and behavior. We exploited a newly developed large-scale electrophysiological recording system to measure a substantial fraction of the population code for visual motion over a significant region of primate retina. To test how effectively the population code is read out by central neurons, we compared speed estimates obtained from retinal activity to speed estimates performed by human observers in matched stimulus conditions. We find that for brief, small stimuli, behavioral motion sensing performance approaches the limits imposed by the retinal signal, suggesting that population code readout can be efficient and nearly noiseless. On the other hand, for extended stimuli, behavioral motion sensing performance falls far short of limits imposed by the retinal signal, indicating that central readout of the peripheral population code can place the ultimate limit on sensation and behavior. We discuss the implications of these findings for how motion is computed in the brain. We also discuss the factors that have made it possible to obtain a comprehensive view of the population code, and the parallels that might be expected in future investigations of neural population codes.

Grand challenges in auditory research

Israel Nelken
Hebrew University

The auditory system has highly developed subcortical structures which are among the best understood in the brain. Furthermore, a number of rather simple rules, with rough understanding of peripheral representations, are sufficient to account for a surprisingly large number of perceptual phenomena. Nevertheless, we understand very little about the way these lower representations are combined to solve the 'hard' problems of audition, such as pitch representation, spatial localization in realistic conditions, speech understanding, or even such seemingly simpler processes such as segregating the incoming sound into its component 'objects'. I will argue that the common feature of these hard problems is the need to integrate information across both frequency and time, neither of which occur at the lower representation levels. I will present a number of (not necessarily mutually-exclusive) views of how auditory cortex may participate in these tasks. In order to discriminate between these possibilities it will be necessary to combine behavioral studies, multi-single neuron recordings and active manipulation of neural activity at a single-neuron resolution.

Distributed Processing in the Cerebral Cortex: How Can We Get the Data to Ask the Questions?

Charles Gray
Center for Computational Biology, Montana State University

Anatomical, physiological and functional imaging studies have established that mammalian cognitive functions involve the concerted action of populations of interconnected neurons distributed throughout the brain. Although this perspective is widely accepted, we continue to know surprisingly little about the details of distributed neuronal processing, its underlying physiological mechanisms, and its relation to behavior. This lack of understanding stems largely from technical limitations in our ability to make appropriate electrophysiological measurements. To overcome this limitation, we have designed a new class of instrumentation that will enable investigators to simultaneously monitor neuronal activity from hundreds of independently movable microelectrodes that are semi-chronically implanted in widespread regions of the brains of awake, behaving monkeys. I will present this design and discuss its implications, as well as its limitations, for gaining a greater understanding of large scale brain dynamics.

Discovering the neural code for vision

Jack L. Gallant
University of California at Berkeley

Mental processes are mediated by a complex network consisting of hundreds of closely coupled computational modules. Understanding how these various modules encode and represent information is an important goal of computational neuroscience. Its solution will also simplify other problems in this area and facilitate applications (e.g., brain-machine interfaces). I will summarize some of the theoretical and practical constraints that limit our ability to investigate neural coding and representation, using the visual system as a model. These constraints include the inherent complexity of natural images, the fundamental nature of neural computation, and practical limits in data acquisition. I will also review modern approaches to solving this problem using various tools of nonlinear system identification, and offer some speculations about future directions in this area.

Wednesday, February 21, 2007

Session 5: Theory, Modeling, and Applications III

Session Chair: John George

8:00-8:40	**Yang Dan** (University of California at Berkeley) *Visual Cortical Coding of Natural Stimuli*
8:40-9:20	**Guenter W. Gross** (University of North Texas) *Nerve Cell Networks on Microelectrode Arrays: Platforms for Investigations of Neuronal Dynamics Underlying Information Processing*
9:20-10:00	**Kwabena Boahen** (Stanford University) *Neurogrid: Emulating a Million Neurons in the Cortex*
10:00-10:20	Break
10:20-11:00	**Sara Solla** (Northwestern University) *Decoding Neural Signals for the Control of Movement*
11:00-11:40	**Charles F. Stevens** (Salk Institute) *Design Principles that Endow the Brain with a Scalable Architecture*
11:40-12:05	Grand Challenges Panel Discussion
12:00-12:05	Main Workshop Adjourns

Session 6: Neuroscience in New Mexico

Session Chair: Chris Wood

1:30-1:40	**Rob Duncan** (Director of Institute for Advanced Studies)
1:40-1:50	**Dan Savage** (University of New Mexico)
1:50-2:00	**Claudia Tesche** (University of New Mexico) *Imaging Associative Neural Plasticity in Man*
2:00-2:10	**Elba Serrano** (New Mexico State University)
2:10-2:20	**Chaouki Abdallah** (University of New Mexico)
2:20-2:35	**Yoshio Okada** (BRAIN) *Neuroimaging Research at the BRAIN Imaging Center*
2:20-2:35	**Yoshio Okada** (BRAIN) *Origins of Macroscopic Electrical and Magnetic Signals from the Brain: Theoretical and Experimental Analyses*
2:35-2:45	**Wolfgang Mueller** (BRAIN) *Presynaptic Plasticity of Vesicle Turnover and Short-term Plasticity*
2:45-3:00	Break
3:00-3:10	**John Rasure** (MIND) *Overview of the MIND Research Network*
3:10-3:20	**Michael Weisend** (MIND) *The Challenge of Pooling Neuroimaging Data across Different Laboratories: A Pilot Investigation with MEG*
3:20-3:30	**Vince Clark** (MIND) *Brain Networks in Learning and Mental Illness*
3:30-3:40	**Rex Jung** (MIND/Sandia) *NS2: Neuroscience for National Security*
3:40-3:50	**Danny Rintoul** (Sandia) *Big Computing & Neuroscience: Where is the low-hanging fruit?*
3:50-4:00	**Ann Speed** (Sandia)
4:00-4:15	Break
4:15-4:25	**David Sharp** (LANL) *Neuroscience at Los Alamos*
4:25-4:35	**John George** (LANL) *Dynamic Mapping and Imaging of Neural Population Function*
4:35-4:45	**Garrett Kenyon** (LANL) *Analysis of multiunit data: Getting more from each spike*
4:45-5:00	**Chris Wood** (Santa Fe Institute)

Nerve cell networks on microelectrode arrays: platforms for investigations of neuronal dynamics underlying information processing

Guenter W. Gross
University of North Texas, Denton

It is unlikely that we will achieve a quantitative understanding of information processing in the vertebrate brain until we understand spatio-temporal action potential pattern processing in small neuronal ensembles or networks. All information enters in parallel, is processed in parallel, and shapes behavioral patterns in parallel. Computation seems to be performed primarily by colliding patterns with associated constructive and destructive interference. These phenomena are superimposed on spontaneous activity with complex effects on gating sensory information. In the extreme, spontaneous activity is either anticipatory, which facilitates rapid output pattern generation, or antagonistic, which can block incoming sensory information, as is seen in thalamo-cortical circuitry during sleep.

The requirement to quantify spatio-temporal patterns is unavoidable, and methods must be developed that capture the simultaneity of neuronal output patterns in neuronal circuits, networks, or ensembles. Although single neuron behaviour cannot be ignored, it is the cell group that provides reproducibility, fault tolerance, storage or experience-dependent responses, and (possibly) "decision states". Cell group dynamics must receive emphasis for a "bottom-up" construction of brain function, but is difficult to study in situ. Primary cultures on microelectrode arrays (MEAs) form stable, spontaneously active networks that provide superior, long-term readout from many discriminated units, and simultaneous optical information on network morphology. In the past decade they have received extensive pharmacological and toxicological attention and can be considered "histiotypic", as their responses are highly similar to those of the parent tissue in situ.

Given their thorough pharmacological characterization, it is now prudent to explore the more difficult domains of structure-function relationships and network dynamics with these platforms. Electrical stimulation is possible through the recording electrodes and responses to weak, pulsed magnetic fields have been demonstrated. Recently, it was shown that such networks in culture are weakly disassortative small world graphs, which differ significantly in their structure from randomized graphs with the same average connectivity (1). It is now possible to explore the internal dynamics of self-organized neuronal systems and ask key questions such as: (a) What is the origin and purpose of spontaneous activity? (b) What is the nature of biological fault tolerance? (c) How do networks select or develop specific spatio-temporal patterns? (d) What are the mechanisms and manifestations of pattern storage? (d) Can specific patterns be imposed on network via external stimulation? How do several networks interact if coupled electrically? Spontaneously active mammalian tissue on MEAs opens a window to the internal dynamics of networks with realistic applications to studies of pattern processing and to basic theoretical questions on the nature of information processing. They also find applications as tissue-based biosensors, and in areas such as toxicology and drug development. This presentation will summarize the progress made with these platforms, discuss the remaining problems, and outline realistic future research efforts.

(1) Bettencourt et al, 2007, Physical Review E. (in press).

Neurogrid: Emulating a million neurons in the cortex

Kwabena Boahen
Stanford University

I will present a proposal for Neurogrid, a specialized hardware platform that will perform cortex-scale emulations while offering software-like flexibility. Recent breakthroughs in brain mapping present an unprecedented opportunity to understand how the brain works, with profound implications for society. To interpret these richly grow-ing observations, we have to build models—the only way to test our understanding—since building a real brain out of biological parts is currently infeasible. Neurogrid will emulate (simulate in real-time) one million neurons connected by six billion synapses with Analog VLSI techniques, matching the performance of a one-megawatt, 500-teraflop supercomputer while consuming less than one watt. Neurogrid will provide the programmability required to implement various models, replicate experimental manipulations (and con-trols), and elucidate mechanisms by augmenting Analog VLSI with Digital VLSI, a mixed-mode approach that combines the best of both worlds. Realizing programmability without sacrificing scale or real-time op-eration will make it possible to replicate tasks laboratory animals perform in biologically realistic models for the first time, which my lab plans to pursue in close collaboration with neurophysiologists.

Decoding neural signals for the control of movement

Sara A. Solla
Northwestern University

The activity of neurons in primary motor cortex provides the signals that control our ability to execute movements. One of the crucial questions, still unresolved, is that of identifying the coordinate system used in the execution of movements: is it an euclidean representation of the external space, or an actuator representation of the state of the muscles? We address this question through the analysis of data obtained for an awake behaving monkey. The data includes both simultaneous recording of the activity of about one hundred neurons in motor cortex and of the activity of about ten muscles in the relevant limb. The analysis of this data involves a variety of techniques, from linear regression models to nonlinear methods for dimensionality reduction. I will review the current level of achievement in this active area of research and discuss its implications, both for understanding aspects of neural information processing that relate to natural behaviors and for extracting from these neural signals the information needed to guide prosthetic limbs and other types of external devices

Design Principles that Endow the Brain with a Scalable Architecture

Charles F. Stevens
Salk Institute

One of the Grand Challenges is to learn what mathematical operations are performed by neuronal circuits. The vertebrate brain has a scalable architecture – the computations become better in some way as the size of a circuit is increased – and understanding the scalability can place constraints on the types of computations done or offer clues about the nature of the computations. I will outline some methods for studying scalability rules in vertebrate brains, and illustrate these methods with a particular example of a universal scaling law and its underlying principle.

Imaging Associative Neural Plasticity in Man

Claudia D. Tesche
University of New Mexico

Magnetoencephalography (MEG) provides an opportunity to observe the dynamics of human brain function with exquisite temporal resolution. Aversive (fear) conditioning may result from the repeated pairing of a neutral â€œconditionedâ€ visual stimulus (CS) with an aversive â€œunconditionedâ€ auditory stimulus (US). This association leads to a learned response: presentation of the CS in isolation elicits behaviors associated with the US, even though no such stimulus is presented. Although aversive conditioning has been studied intensively in animal models, little is known about the dynamics of the conditioned response in the normal human brain. We utilized a MEG array to study associative neural plasticity in normal adults. CS presented in isolation following training elicited activation of auditory cortex and amygdala. In a subsequent study, the inter-stimulus interval between CS and US was shortened from 1500 ms to 418 ms. Visual CS predictive of aversive noise continued to elicit responses in auditory cortex, as well as frontal areas and cerebellum, although activation of amygdala was strongly suppressed.

Presynaptic plasticity of vesicle turnover and short term plasticity

Wolfgang Müller
BRAIN

Long term synaptic plasticity (LTP and LTD) is believed by many to be expressed postsynaptically by insertion or removal of receptors into the postsynaptic membrane. This would not directly affect short term dynamics associated with facilitation of presynaptic neurotransmitter release due to buildup of residual calcium and depression due to depletion of vesicles. Using direct two- photon imaging of vesicle turnover in mature presynaptic terminals in brain slice we demonstrate LTP and LTD of presynaptic vesicle release and relate these changes to changes in synaptic short term dynamics that may contribute to memory and coding of temporal relations.

MIND Research Network Overview

John Rasure
MIND

The MIND Institute performs pioneering research in technology development for better understanding of brain function and diagnosis of mental illness and neurological disorders. MIND executes its research through the National MIND Research Network, an established, cross-disciplinary, collaborative partnership with leading universities and national laboratories: Sandia National Laboratories, Los Alamos National Laboratory, the National Center for Genome Resources, the University of New Mexico, Massachusetts General Hospital (Harvard and MIT), and the University of Minnesota.

The National MIND Research Network has assembled a world-class, highly integrated neuroimaging and neuroinformatics capability. This shared infrastructure supports MIND's iterative research process: 1) diagnostic technology development; 2) neuroscience discovery; 3) translational application of research into clinical practice. The interplay of the three themes is critical to our success. New clinical hypotheses drive technology development while new diagnostic methods result in pursuing clinical questions that were previously inaccessible.

MIND is currently leading three National Programs. The FIRST (Functional Imaging for Research and Schizophrenia Treatment) Program, led by Dr. Charles Schulz, M.D., University of Minnesota, links multi-modal brain imaging, genetics and pattern recognition to develop a definitive diagnostic tool for mental illness. The Neurodevelopmental Program, led by Dr. Yoshio Okada, University of New Mexico, is a multi-site program to develop novel diagnostic techniques based on MRI, NIRS, MEG, and EEG for studying brain development and to apply these techniques to understanding the consequence of brain injury in babies and children with autism. The MEG Tech Program led by Dr. Mike Weisend, The MIND Institute, is focused on developing cross-platform (CTF, 4-D, Neuromag) openly distributed software that is fully characterized for sensitivity, accuracy and reliability.

NS2: Neuroscience for National Security

Dr. Rex E. Jung, PhD
Sandia National Laboratories

National security threats are inherently "wicked", involving non-linear processes, diverse stakeholders, shifting social/political/economic contexts, and poorly defined parameters. Our working hypothesis is that we can gain traction in addressing "wicked" problems through increased understanding, manipulation, and control of brain processes – an approach we call "neurosystems engineering." Particular applications of such an approach might include: training "resilient" soldiers; deception detection; rapid decision-making under stress; and accelerated learning. Computational neuroscience will accelerate our progress toward understanding and controlling brain processes by increasing our ability to analyze large data sets (106kb) across a large number of variables (1011neurons) with adequate resolution to discern latent relationships amid the noise. The National Laboratories are well situated to partner with the neuroscience community to meet the demands of an increasingly complex and interdependent (i.e., "wicked") world.

Big Computing & Neuroscience: Where is the low-hanging fruit?

Mark D. (Danny) Rintoul III, Ph.D.
Sandia National Laboratories

There is a computational revolution in biology right now related not to computational advances but to experimental ones. Our ability to generate large amounts of "messy" data is rapidly improving in many areas, and neuroscience is leading the way both in the massive amounts of data and the messiness associated with the data. I will give a brief introduction to the state-of-the-art in high-performance computing and how that applies to the problems of analyzing neuroscience data. I will then touch on how these data can be used to populate models. I will emphasize where high-performance computing can be used now to make a significant impact, and where I believe is will not play a significant role in the near future.

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Spike Timing Precision and the Influence of Cortical Dynamics

4 **Garrett Kenyon** (LANL, P21)
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Finding Correlations Using Frequent Patterns Analysis: Application to Neuroimaging Data

Andrea Benucci
Smith-Kettlewell Eye Research Institute

Persistent population activity in primary visual cortex

Andrea Benucci, Robert A. Frazor, Vincent Bonin, and Matteo Carandini Smith-Kettlewell Eye Research Inst, San Francisco, CA

The primary visual cortex is a layered network of neurons with a columnar organization of preferred orientation and topographic mapping of the visual space. During natural vision, this network is constantly driven by rapidly changing visual input. How does the network switch from one activity pattern to the other under these conditions? What are the rules governing the interactions between these patterns and how do they depend on the underlying cortical connectivity? To address these questions, we used a sequence of oriented stimuli. If the sequence is rapid, the responses in primary visual cortex (V1) to the individual orientations might interact with each other via summation, suppression, or other possible dynamics. We measured population responses by imaging voltage-sensitive dye (VSD) signals in area V1 of anesthetized, paralyzed cats (dye RH-1692, Grinvald & Hildesheim, 2004) with 5-10 ms resolution. Stimuli were 6 s sequences of 30-40 ms flashed gratings of random orientation (Ringach et al., 1997). We computed the preferred orientation for each pixel in the image to obtain population responses as a function of time and preferred orientation. The population responses to successive orientations exhibited apparently complex dynamics. If two orientations in a sequence were separated by less than 30-45 deg, the population response seemed to shift seamlessly from one orientation to the other. A larger step in orientation seemed to elicit a suppressive interaction between population responses. We asked whether these dynamics could be explained on the basis of the average response to a single orientation, i.e. a linear filter. We computed this filter through stimulus-triggered averaging; its amplitude had a center-surround organization in orientation, increased rapidly 40-70 ms after stimulus onset and decayed after 150-200 ms. We computed a linear prediction of the responses to the whole sequence of orientations by convolving the filter with the stimulus. This simple linear model provided a good description of the data (correlation $r = 0.997 \pm 0.002$). In particular, whenever a stimulus was followed by another stimulus, the dynamics of model responses closely resembled those seen in the measured responses. The structure of the linear filter thus explains the apparent interactions between orientations. However, we observed a consistent discrepancy between the predicted and measured responses when a stimulus was not followed by another stimulus (blank condition). The linear model predicts a rapid decay of the response to the background level. The actual response, however, persists for a few tens of ms after the disappearance of the last grating. We conclude that population responses to rapidly changing stimuli switch rapidly between stimulus-driven states, and are predicted by a simple linear model. This fast switching, however, is supplemented by persistent activity whenever the sensory drive is removed. This brief maintenance of cortical activity might be supported by intracortical recurrent connections, and may be associated with perceptual phenomena of visual persistence. Supported by the National Eye Institute and by the McKnight Endowment Fund for Neuroscience

Tim Blanche
UC Berkeley, Redwood Center for Theoretical Neuroscience

Spike timing precision and the influence of cortical dynamics

Timothy J Blanche, Kilian Koepsell Olshausen Lab, Redwood Center, University of California, Berkeley

The prevailing wisdom that visual cortex neurons are noisy and temporally imprecise is based largely on evidence from sequential single unit recordings in response to reduced visual stimuli such as drift gratings or spots of light. Moreover the benchmark for quantifying spike timing precision is the trial to trial variability in the post-stimulus time histogram (PSTH) of repeated presentations of the same stimulus, which explicitly ignores ongoing (or stimulus independent) cortical dynamics. We are exploring the limits of spike timing precision in local neuronal populations evoked by complex stimuli (natural scene movies), taking into account the ongoing activity as measured by the local field potential (LFP). High-density silicon electrode arrays (polytrodes) were used to make simultaneous recordings of 100+ neurons spanning all cortical layers in anesthetized cat primary visual cortex [1]. Brief 5s natural scene movie segments [2] were presented 25-75 times (50Hz frame rate, 200Hz refresh). The complex analytic signal was used to obtain an instantaneous measure of LFP phase from 1-150Hz. LFP modulation of spike timing was quantified by fitting a von Mises distribution (circular Gaussian) to the histograms of spike phases relative to the LFP oscillation. Evoked responses to natural scenes were characteristically sparse, punctuated with highly reliable events (Fano factors 0.1). Neurons showed varying degrees of phase locking to the LFP with predominant peaks in all the classically defined EEG bands. Individual neurons often had multiple peaks. The LFP itself also showed transient stimulus-dependent phase alignment across trials at several frequencies. Without considering the role of the LFP the full-width half-maximum of many spiking events was around 15ms. Dejittering the spike trains based on the phase of the LFP in the gamma band revealed ms-precise temporal patterns within the events. Taken together we suggest that neurons in the primary visual cortex are capable of high spike timing precision comparable to that reported in the lateral geniculate and retina, but ongoing cortical dynamics introduces temporal jitter that may obscure this precision. References [1] Polytrodes: high-density silicon electrode arrays for large-scale multiunit recording. Blanche TJ, Spacek MA, Hetke JF, Swindale NV. J Neurophysiology 93(5):2987-3000, 2006. [2] Responses to natural scenes in cat V1. Kayser C, Salazar RF, Konig P. J Neurophys 90(3):1910-20, 2003.

Garrett Kenyon
LANL, P21

Evidence for Extreme Synergy in a Retinal Code

Over the brief time intervals available for processing natural scenes, approximately 50 msec to 200 msec, the number of additional spikes generated by individual retinal ganglion cells, even when strongly stimulated, fluctuates randomly from 20% to 50%, a noise level seemingly incompatible with the acuity of visual perception. Here, computer-generated spike trains were used to demonstrate how substantial increases in signal-to-noise might be achieved by taking advantage of the spatiotemporal correlations among retinal neurons drawn from extended neighborhoods containing hundreds of cells. Realistic spatiotemporal correlations were produced by modulating the instantaneous firing rates of all stimulated neurons by a common oscillatory input whose temporal structure was consistent with measured local field potentials. Singular Value Decomposition (SVD) was then used to simultaneously analyze both pairwise and higher-order correlations across retinal patches containing up to 32x32 ganglion cells, corresponding to over one-million cell pairs, or across smaller patches containing up to seventeen-million cell triplets. Our results suggest that rather than operating independently, ganglion cells employ a highly synergistic code in which the value of each pixel can only be rapidly extracted by taking into account the concurrent firing activity across contiguously activated elements.

Sean Escola
Columbia University

HMMs applied toward the inference of neural states and the improved estimation of linear RFs

Sean Escola and Liam Paninski, Columbia University

Several recent experimental results suggest that neurons are associated with multiple firing regimes, or states (e.g. tonic and burst modes of LGN cells and up-and-down states in the cortex). We develop a general framework for estimating neural receptive fields (RFs) from paired spike-train and stimulus data assuming that neurons transition between several discrete hidden states. Previous approaches applied to RF estimation such as the spike-triggered average, the linear-nonlinear-Poisson (LNP) point-process model, and information theoretic techniques are predicated on the assumption that all spikes are equally informative about thestimulus. If, instead, some spikes occur while the neuron is in a stimulus-ignoring state, then including those spikes in the RF estimation will necessarily worsen the estimate. Furthermore, if the neuron moves between several states, each of which responds to different features of the stimulus, then these techniques will discover some composite RF that may differ significantly from all of the individual, state-specific RFs. By discovering the hidden state of the neuron at every point in time, each of the individual RFs can be estimated for each of the hidden states. We have modified the traditional hidden Markov model (HMM) theoretical framework (Rabiner, 1989) to allow for point-process observables (i.e. spike-trains) and to be parameterized by N^2 linear filters of the time-varying stimulus (where N is the number of states) rather than static, conditional probability tables. Specifically, each state is associated with its own N filters: N − 1 of these determine the transition rates from the current state to the other states, and the remaining filter determines the firing rate for the current state. This latter filter is the canonical RF (although now there are N of them, one for each state), while the former filters are "RFs" for the state dynamics, a new concept in sensory neurophysiology. The actual transition and firing rates are the result of nonlinear transformations of the dot-products of the filters and the stimulus (i.e. as in LNP models). Stimulus-dependent transition rates are required to ensure that the neuron can be prompted by the stimulus to enter a particular state needed to respond to a feature of the stimulus. The filters are learned using expectation-maximization (EM)—specifically the Baum-Welch algorithm—to maximize the log-likelihood as with traditional HMMs. Assuming the nonlinearities used in the model conform to a certain class of functions (Paninski, 2004), the M-step of EM is concave in the parameter space with a unique solution easily found via gradient ascent. We show the results of training from a number of simulated spike-train and stimulus pairs. The linear filters recovered by our algorithm nicely match the filters used to generate the data. **References: Paninski, L. (2004). Maximum likelihood estimation of cascade point-process neural encoding models. Network: Computation in Neural Systems, 15:243–262. Rabiner, L. (1989). A tutorial on hidden Markov models and selected applications in speech recognition. Proceedings of the IEEE, 77:257–286.

Kilian Koepsell
UC Berkeley

Retinal oscillations carry visual information to cortex

Neuroimaging with PET and MRI have shown that ongoing activity in the resting brain accounts for more than 90% of energy consumption in the brain. The function of ongoing activity, which is often oscillatory, is one of the big mysteries in Neuroscience. Here we report the discovery of an information channel that is mediated by ongoing oscillations and can be used to transmit information from the eye to the brain. Specifically, retinal oscillations provide a previously unknown independent second channel of information using a form of multiplexing similar to methods used in technical communication systems: The two different channels are assigned to separate frequency bands of the spike train of single relay cells in the thalamic lateral nucleus. We were able to unmask this novel channel by combing experiment, model and theory. First, we used whole cell recording in vivo to gain direct access to the precise timing of both retinal inputs (EPSPs) and thalamic spikes during the presentation of natural movies. Second, we developed new methods to detect intracellular events and to quantify the information carried in spike timings with respect to ongoing activity. Third, we devised a model of the thalamic relay cell that reproduced the experimental findings. Previously, we showed that much of the variance in responses of thalamic relay cells to repeated stimuli could be explained by intrinsic retinal oscillations that are not time-locked to the stimulus. Specifically, we found that spike latencies with respect to the stimulus were far more variable than spike timing with respect to retinal EPSPs, which showed millisecond fidelity. Here we explored how the stimulus and the intrinsic oscillations influence spike timing by building a multiplicative model of the relay cell. The model described spiking by a point process where the density is given by the product of two functions. One is the usual stimulus transfer function, i.e., the low-passed convolution between visual input and the receptive field. The second function represented the impact of intrinsic retinal oscillations; its periodicity and phase were determined from recent synaptic input. The degree to which thalamic activity phase-locked to the retinal oscillations was described by a von Mises distribution whose two parameters were tailored for each cell. The model was able to reproduce experimentally measured spiking statistics and information rates and thus revealed a multiplicative scheme for thalamic spike trains to generate dual channels for visual information to reach cortex. It is likely that the two channels transmit different types of information downstream. Stimulus-locked coding is suited to provide information about local patterns that fall on individual receptive fields. By contrast, oscillation-based coding, which is produced by spatially distributed retinal networks, could provide information about global context. Thus, beginning at the sensory periphery, the code formed by neural spike trains can be parsed into parallel streams that communicate complementary information about local detail and the big picture. Recent experiments in frog support the prediction that oscillations convey such contextual information.

Stephanie Palmer
Princeton University

Predictive information in simultaneously recorded retinal ganglion cells

SE Palmer, MJ Berry and W Bialek Princeton University

Making predictions is important, and difficult. To explore the problem of prediction in a tractable context, we consider the responses of multiple (simultaneously recored) retinal ganglion cells to a natural movie. We divide time into slices of duration dt such that each cell produces zero or one spike; the signal transmitted to the brain in each slice is, thus, a binary word; we consider the problem using one binary word at time t to predict the next word at time t + dt. For small groups of cells, we can estimate this predictive information accurately given reasonable data sets. We then imagine a "neuron" that receives these inputs, and gives as output a single bit (spike or no spike). Can this output capture the available predictive information? What is the structure of the algorithm that maps inputs to predictive outputs? For four cells, we can sample all possible deterministic input/output rules for converting input responses into a binary output. We find that the best rules can capture more than 95% of the predictive information in the input firing. Rules which capture such a large percentage of the predictive information also retain a large amount of stimulus information, so that solving the unsupervised problem of prediction would allow the brain to identify combinations of inputs which are especially informative about the visual world. These best rules can be reliably learned by a perceptron model, meaning that instantiating such a coding of predictive information in the brain might be biologically plausible.

Greg Schwartz
Princeton University

Synchronized Firing among Retinal Ganglion Cells Signals Motion Reversal

Greg Schwartz, SamTaylor, Clark Fisher, Rob Harris, and Michael J. Berry II

In order to make coordinated movements, the brain must compensate both for delays in the firing of neurons and for delays in the movement of limbs to their intended location. The only way to compensate for such delays is to use an object's past trajectory to predict its future location. Such prediction is likely to fail, however, when there is a motion discontinuity. Thus, it is important for the brain both to make predictions about the future location of a moving object as well as recognize when those predictions are wrong. Here, we show that these forms of processing begin in the retina. When an object moves at constant velocity, the retina anticipates its location, such that ganglion cells fire early and correct for their own latency. But when an object suddenly reverses its direction of motion, a large population of ganglion cells fire a synchronous burst of spikes. This synchrony labels the firing pattern as a distinct neural event and can be easily recognized by the brain. We present a decoding strategy for distinguishing this special 'reversal' response from other ganglion cell firing events.

Aonan Tang
Indiana University, Bloomington

A second-order maximum entropy model predicts correlated network states, but not their evolution over time

Aonan Tang1, David Jackson2, Jon Hobbs1, Wei Chen1, Jodi L. Smith3, Hema Patel3, John M. Beggs1 1Indiana University Department of Physics, 2Brown University, 3Indiana University Purdue University Medical School

Highly correlated network states are often seen in multielectrode data, yet are predicted to be rare by independent models. What can account for the abundance of these multi-neuron firing patterns? Recent work [1, 2] has shown that it is possible to predict over 90% of highly correlated network states, even when correlations between neuron pairs are weak. To make these predictions, both groups used a maximum entropy model that fit only the firing rates and the pairwise correlations (a second-order maximum entropy model), and which was maximally uncommitted about all other model features. This new work raises several questions. First, how general are these results? Both previous reports largely used retinal data. Could this maximum entropy approach also succeed when applied to cortical slices? Although the original model explained correlations among spikes, could it also be used to explain the abundance of correlated states of local field potentials (LFPs)? A second issue concerns the abundance of correlated states over time. Can a second-order maximum entropy model predict sequences of correlated states? To examine the generality of this approach, we applied a second-order maximum entropy model to a variety of in vitro cortical networks, including acute slices from rat (n = 3) and human epileptic tissue (n = 1), as well as organotypic (n = 3) and dissociated cultures (n = 3) from rat. We explored its effectiveness in predicting correlated states of both spikes and LFPs at one time point. On average, the model accounted for 90 ± 6% (mean ± s.d.) of the available multi-information, in good agreement with previous studies. In all cases, the maximum entropy model significantly outperformed an independent model, demonstrating its effectiveness in explaining correlated states in cortical spikes and LFPs at one time point. We also explored how well the maximum entropy model predicted sequences of correlated states over time. Here, the model often failed to account for the observed sequence lengths. In 8/10 preparations, the distribution of observed sequences was significantly longer (p ≤ 0.003). We conclude that a second-order maximum entropy model can predict correlated states, but not their evolution over time. This suggests that higher-order maximum entropy models incorporating temporal interactions will be needed to account for the sequences of correlated states that are often observed in the data. Acknowledgments This work was supported by NSF grant number 0343636 to JMB. References [1] Weak pairwise correlations imply strongly correlated network states in a neural population. E Schneidman, MJ Berry, R Segev and W Bialek, Nature 440(7087):1007-1012, April 9, 2006. [2] The structure of multi-neuron firing patterns in primate retina. J Shlens, GD Field, JL Gauthier, MI Grivich D Petrusca, A Sher, AM Litke and EJ Chichilnisky, J Neuroscience 26(32):8254-8266.

Ilya Nemenman
LANL

Neural coding of a natural stimulus ensemble: Uncovering information at sub–millisecond resolution

Ilya Nemenman, Geoffrey Lewen, William Bialek, Rob de Ruyter van Steveninck

Our knowledge of the sensory world is encoded by neurons in sequences of discrete, identical pulses termed action potentials or spikes. There is persistent controversy about the extent to which the precise timing of these spikes is relevant to the function of the brain. We revisit this issue, using the motion--sensitive neurons of the fly visual system as a test case. New experimental methods allow us to deliver more nearly natural visual stimuli, comparable to those which flies encounter in free, acrobatic flight, and new mathematical methods allow us to draw more reliable conclusions about the information content of neural responses even when the set of possible responses is very large. We find that significant amounts of visual information are represented by details of the spike train at millisecond and sub--millisecond precision, even though the sensory input has a correlation time of $\sim 60\,{\rm ms}$; different patterns of spike timing represent distinct motion trajectories, and the absolute timing of spikes points to particular features of these trajectories with high precision. Under these naturalistic conditions, the system continues to transmit more information at higher photon flux, even though individual photoreceptors are counting more than one million photons per second, and removes redundancy in the stimulus to generate a more efficient neural code.

Florin Chirila
University of West Virginia, School of Medicine

Development of Temporal Delayed Sensitivity In MSO Neurons

Florin V. Chirila1,2, Kevin C. Rowland1,3, Jesse M. Thompson1,3, and George A. Spirou1,2,3 Sensory Neuroscience Research Center1 Departments of Otolaryngology2, Physiology and Pharmacology3 PO Box 9303, West Virginia University School of Medicine Morgantown, WV 26506-9303

Interaural temporal delay (ITD) is an important cue for sound localization, first encoded in mammals by neurons of the medial superior olive (MSO). The sensitivity of MSO neurons to differences of tens of microseconds in ITD derives in part from the development of ionic conductances and timing of the excitatory and inhibitory inputs. The maturational sequence of physiological and anatomical characteristics that lead to adult-like ITD sensitivity are little studied, especially in relationship to the onset of auditory experience. Using brain slices maintained at physiological temperature, we reveal that MSO neurons are sensitive to small temporal delays, TD<1.5 ms, by the onset of hearing at P10 for excitatory stimuli of 6-10 ms. Development of membrane properties such as relative increase of input conductance, action potential amplitude, spike threshold, and max dV/dt is described by a Bernoulli (logistic) type dynamic dx/dt=bx(1-x). Anatomical and synaptic properties such as dendritic length, number of twigs per cell, fractal dimension, and duration of inhibitory postsynaptic potentials (IPSP's) follow the same logistic law. Three key developmental points, P10, P13, and P16 where observed in the transition to adult-like properties. Temporal delay sensitivity is quantified by the slope of TD curves (probability of spiking versus TD). TD sensitivity increases with age and with the decrease in duration of EPSC's. The discriminability of temporally delayed stimuli is measured by just noticeable difference (JND) and shows an improvement with age. The effect of evoked inhibition on TD sensitivity was also studied. A range of relative onset times less than 1 ms yielded responses showing sensitivity to temporal delay (JND<100 ms). We propose that shaping of excitatory circuitry to mediate TD can begin before many animals are able to detect airborne sound, and that inhibitory inputs having suboptimal neural delays can be pruned by cellular mechanisms activated by sensitivity to ITD.

Michael Ham
University of North Texas

Comparison of stimulation efficacy in vitro using naturally and artificially generated patterns

We investigate network-network interaction using spontaneously active neuronal ensembles derived from dissociated embryonic central nervous system tissue that self assembles in vitro on microelectrode arrays. Each network, which develops without external stimulation, displays unique patterns and levels of spontaneous electrophysiological activity. This study focuses on how such networks interact when electrically coupled to each other. As a first step in this direction, we tested whether electrically stimulated target networks are more responsive to naturally or artificially generated patterns. Natural stimulation patterns, from the output activity of a single representative neuron in a driver network, stimulated the target network via single or multiple inputs. Our findings show single and multi input artificial stimulation and single input natural stimulation cause momentary deviations in activity without major long-term changes. However, preliminary data on multi-site stimulation with duplicate natural input patterns suggests that target networks are greatly influenced during stimulation as evident by pattern synchronization. Removal of the input stimulus caused target network bursting and most spike activity to cease for several minutes before native patterns could resume. We hypothesize that networks in culture, which have no overt input and output structures, require multi -site stimulation to induce long term changes. We hope information obtained by this approach will be useful to designing favorable stimulation patterns. Further, we anticipate that basic strategies for optimal network-network interaction may emerge from such studies.

Joseph Jun
Princeton University

Development of neural circuitry for precise temporal sequences through spontaneous activity, axon remodeling, and synaptic plasticity

Precisely timed spike sequences are observed in many brain areas, including songbird premotor nucleus, cat visual cortex, and primate motor cortex. How neurons are wired into networks that produce such sequences is not understood. Here we propose a computational model of the development of neural circuitry for precise temporal sequences through spike-time dependent plasticity of synapses, and axon remodeling triggered by the formation of strong synapses. Driven by an external input that intermittently activates a subset of neurons and by the spontaneous activity, a feedforward chain network gradually emerges through a recruiting process, in which neurons connect to the tail of the chain started by the subset. The network topology is essentially that of a synfire chain, which can support stable propagation of a precisely timed spike sequence through the feedforward connections. The model is robust to varying parameters, as well as natural events like neuronal turnover and massive lesions.

Olaf H.-U. Schroeder
NeuroProof GmbH

Dynamics of Neuronal Microcircuits – Recent Empirical Observations

Olaf H.-U. Schröder1, Alexandra Gramowski1,2, Konstantin Jügelt1,2, Dieter G. Weiss2 1 NeuroProof GmbH, F. Barnewitz St. 4, 18119 Rostock, Germany 2 University of Rostock, Dept. of Biological Sciences, Cell Biology and Biosystems Technology, 18051 Rostock, Germany

During the last three decades neuronal networks from dissociated embryonic brain cells grown in culture on microelectrode arrays were studied extensively. These self organized networks reveal various interesting features such as spontaneous, and brain region-specific activity patterns as well as a wide range of specific distinguishable spike train responses following exposure to chemicals. Up to this day the different activity patterns cannot be modelled with sufficient accuracy. Here we discuss a variety of effects which are difficult to explain but are in our opinion crucial for the understanding of burst phenomena and dynamic states of neuronal networks. The activity patterns of neuronal networks recorded with microelectrode arrays show a rich burst structure which is significantly and reproducibly influenced by treatment with neuroactive drugs (Gramowski et al 2004, 2006). We studied the therapeutic drugs Diazepam and Clonazepam, two structurally very similar agonists acting as allosteric modulators at the benzodiazepine binding site of the GABA-A receptor. However, Diazepam is acting via two different binding sites on this receptor while Clonazepam does not show this behaviour. The two binding sites of Diazepam differ in a gamma-subunit conformation of the GABA-A receptor associated chloride channel. Diazepam and Clonazepam have a wide dynamic range over 6 orders of magnitudes from 10-10 to 10-4 M. A detailed description of the network activity states was performed by 200 parameters derived from the spike and burst patterns and their degrees of regularity and synchronicity. While the spike rate is decreasing with increasing concentrations for both compounds, we found some parameters describing the burst structure, the burst amplitude, the duration of the burst plateau and others which showed biphasic concentration-response-curves with turns in their course from decrease to increase for higher Diazepam but not for Clonazepam concentration range. New computational models have to reflect (2000), that Diazepam has a second binding site in the micromolar concentration range. New computational models have to reflect the complex variety of significant molecular mechanisms causing the activity changes of neuronal networks. Successful modelling of this behaviour would be helpful to understand such complex phenomena. Our future work will be aimed at two topics. • By hypothesis, mechanisms which control burst generation by different conformations of receptors should be modelled. More work should be done to uncover similar effects in the model system of microelectrode arrays with neuronal network cultures. • In contrast to invariant burst types different excitement states need to be described for the different burst structures by dynamic systems (Izhikevich 1999) in order to better explain the nature of burst generating. Gramowski, A., Jügelt, K., Weiss, D.G., Gross, G.W.: Substance identification by quantitative characterization of oscillatory activity in murine spinal cord networks on microelectrode arrays. Eur J Neurosci. 19: 2815-2825 (2004) Gramowski, A., Jügelt, K., Stüwe, S., Schulze, R., McGregor, G.P., Wartenberg-Demand, A., Loock., J., Schröder, O., Weiss, D.G.: Functional Screening of Traditional Antidepressants with Primary Cortical Networks grown on Multielectrode Neurochips. Eur J Neurosci. 24: 455-465 (2006) Izhikevich EM: Weakly pulse-coupled oscillators, FM interactions, synchronisation, and oscillatory associative Memory, IEEE Transactions on neural networks, 10: 508-526 (1999) Walters RJ, Hadley SH, Morris KD, Amin J: Benzodiazepines act on GABAA receptors via two distinct and separable mechanisms. Nature Neurosci 3: 1274-1281 (2000) Santa Fe 2007

Nachum Ulanovsky
University of Maryland

The comparative challenge to neural computation, and the need to find across-species invariants: a case study of hippocampal activity in freely-moving echolocating bats

Neural activity and functional brain organization may differ between species: prominent examples include the lack of orientation columns in the visual cortex of rodents versus the columnar structure in cats and primates, and the seemingly-different computations performed by birds and mammals for sound localization. A central challenge for neural computation is to find the underlying principles, or 'invariants' of neural coding, that could explain the function of a particular brain region across species – or at least across the mammalian species. Here I will attempt such an across-species explanation of neural activity in mammalian hippocampus, by presenting data on hippocampal activity in freely-moving echolocating bats, and comparing it to rodents and primates. The hippocampus is a brain region crucial for episodic and spatial memory. In freely-moving rodents, hippocampal pyramidal neurons exhibit spatially-selective firing when the animal passes through a neuron's 'place field', and theta oscillation is continuously present during locomotion. In primate hippocampus, some studies have found place cells, whereas others reported 'spatial-view cells' that are active when the animal is looking at a certain location in the room; theta oscillation in primates is weak and often intermittent. Here we addressed these reported differences between rodent and primate hippocampus by studying hippocampal activity in another mammalian species – the echolocating bat, Eptesicus fuscus. We found place cells in hippocampal area CA1 of the bat that were as common, as stable and as spatially-selective as the place-cells of rodents. We also found spatial-view cells, and are currently examining the relations between these two types of cells. However, unlike in rodents, theta oscillation occurred only when the bats explored the environment without locomoting, using distal sensing through echolocation. Furthermore, theta was not continuous but occurred in short bouts. The intermittent nature of theta suggests that in bats – and possibly in other mammals, such as primates – there may be need to reconsider models of hippocampal function that rely explicitly on continuous theta. Our data support the hypothesis that theta oscillation in mammalian hippocampus is involved in sequence learning and hence, theta power should increase with sensory-input rate – which explains why theta power correlates with running speed in rodents and with echolocation call rate in bats.

Rhonda Dzakpasu
University of Michigan

Causal Entropy as a Measure of Temporal Relationships and Direction of Information Transfer in Neural Systems

There are billions of neurons in the brain, each of which participates in the execution of various functions. How does the brain organize the operations of these fundamental units? What relationships exist, on a temporal scale, between neurons? Is there an ordering between the temporal patterns of neurons? In order to begin to address these questions, we have developed a novel analytical tool that measures temporal interdependencies between coupled neurons. The technique involves the real time monitoring of inter-event intervals between the coupled neurons. We demonstrate the feasibility of the measure on a mathematical model consisting of two, coupled non-identical Hindmarsh–Rose models of thalamo-cortical neurons. We show that the measure may be better than more conventional methods at detecting changes in asymmetrical temporal patterns. Finally, we demonstrate how the technique can be modified to study networks of coupled neurons and discuss the application of the measure in the analysis of experimental data.

Robert Haslinger
Harvard-Martinos Imaging Center

The Computational Structure of Spike Trains

Neurons are computational devices, but identifying the computations they carry out has proved difficult, not least because synaptic inputs are generally unknown. Here we present a practical, theoretically-grounded method for inferring the computational structure of a neuron from its output spiking activity, which is directly observable. We show that the expected algorithmic information content of a spike train can be split into three parts: (1) a minimal sufficient statistic describing the time-invariant structure of the spike generating process, (2) a minimal description of the part of the history of the spike train relevant to its future and (3) a residual pure noise term. Our minimal sufficent statistic takes the form of a Causal State Model (CSM), essentially an optimally-predictive hidden Markov model. These CSM's are automatically generated from the data, making only mild regularity assumptions, via the Causal State Splitting Reconstruction (CSSR) algorithm. From the CSM we can objectively quantify the number of bits needed to describe both the complexity (structure) and the randomness of the spiking process as a whole, as well as their variation over time. We demonstrate these methods using both simulated spike trains and experimental data recorded in rat barrel cortex during vibrissa stimulation. The method presented here complements more traditional spike train analyses by describing the computational structure of spike trains, information which has previously been unavailable.

Christopher Honey
Indiana University, Bloomington

The Network Structure of Cerebral Cortex Influences Functional Connectivity Patterns on Multiple Time Scales

In the cerebral cortex, complex patterns of neural activity are observed in the absence of any external input. These spontaneous fluctuations are organized into anticorrelated functional networks whose transient activation has been linked to attentional processes. Here we use a forward modeling approach in an attempt to relate the functional features of cortical dynamics to the structural features of the anatomical network on which they unfold. We simulate nonlinear neuronal dynamics on a network that captures the large-scale interregional connections of a large part of macaque neocortex, and apply information theoretic and wavelet analysis to construct corresponding functional networks. Functional networks recovered from long windows of neural activity (minutes) exhibit significant overlap with underlying structural networks. As a result, hubs in these "slow" functional networks largely correspond to hubs in structural networks. However, the sequence of functional networks recovered from consecutive shorter time windows (seconds) exhibits fluctuations in topology and the functional centrality of individual nodes thus varies across time. These fluctuation occur in a coordinated manner that reveals two anticorrelated functional clusters which are in turn linked by prefrontal and parietal regions that are known to be hubs in the underlying structural network. At an even finer time scale (hundred of milliseconds), we detect individual episodes of interregional synchronization, and we are able to relate the statistics of these brief synchronous episodes to the patterns of information flow observed on slower time scales.

James Rebesco
Northwestern University

Analysis of functional connectivity in large-scale network models

J.M. Rebesco 1, S.A. Solla 1,2, and L.E. Miller 1 1 Department of Physiology, Northwestern University, 2 Department of Physics and Astronomy, Northwestern University

Numerous methods exist in the literature for assessing the functional connectivity of small networks of neurons. Among existing principled methods, we focus on those based on Granger causality [1], maximum-likelihood estimates over stochastic spiking processes [2], and nonlinear optimization of deterministic spiking models [3]. Up to now, these methods have typically been validated in application to very small networks of the order of ten neurons, where the activity of all the neurons in the network is monitored. In this scenario, the activity at every node in the network, as either a continuos or a point process variable, provides input to the algorithm that determines functional connectivity. This scenario is drastically different from realistic cortical recordings, where the population of observed neurons, of O(100), is embedded in a much larger network of unobservable units, of O(10,000,000,000). In the case of such an extremely large number of missing variables, a useful algorithm for the determination of functional connectivity must account for the effects of the dynamical activity of the underlying network. To investigate the ability of various functional connectivity algorithms [1-3] to capture such effects, we have developed a model network of O(10,000) neurons. The parameters of the network reflect the physiological literature on cortical networks. In this simulation environment we treat a small number of neurons, O(10), as observable units; the remaining neurons are not observed, and they provide a background activity. This environment allows us to compare the effectiveness of the various functional connectivity algorithms. The dynamical equivalence of the "functional" and "real" networks is demonstrated through comparisons of the statistical properties of the spiking activity of the observed neurons, both at the single neuron level (interspike interval statistics) and at the level of pairs on neurons (pairwise correlations). This type of systematic numerical experiments allow us to refine the specification of effective connectivity in a situation that mimics the outcome of multielectrode cortical recordings in awake, behaving animals. An additional aspect of functional connectivity in cortical networks is their nonstationarity. One of our goals is to refine the existing algorithms so as to monitor changes in network configuration associated with switches among tasks as well as with learning. References [1] Using partial directed coherence to describe neuronal ensemble interactions. Sameshima, K. and L.A. Baccala, Journal of Neuroscience Methods 94:93-103, 1999. [2] Analyzing functional connectivity using a network likelihood model of ensemble neural spiking activity. M. Okatan, M.A. Wilson, and E.N. Brown, Neural Computation 17:1927-1961, 2005. [3] A method for determining neural connectivity and inferring the underlying network dynamics using extracellular spike recordings. V.A. Makarov, F. Panetsos, and O. de Feo, Journal of Neuroscience Methods 144:265-279, 2005.

Luis Bettencourt
LANT, T7

Identification and dynamics of functional cell modules in dissociated neural networks

Information processing and memory in neural systems are collective properties of networks of neurons involving groups of cells that together constitute functional modules. These modules may be organized as partially redundant circuits involved in short term memory, or may combine information from other cells to generate new functional output. We use concepts of information theory and time series analysis applied to spike trains from dissociated networks of neurons living in vitro, grown over microelectrode arrays, to identify groups of cells that together form such functional groups. Such ensembles are identified via the measurement of specific ranges of the difference between their cells' multi-information to the information of the their joint state conditional on the state of extra units. These differences can be used to explicitly distinguish cell groups associated with short time memory circuits or instead connected with (logical) information processing. Identified structures are further characterized in terms of specific functional relations among cells and the dynamics of these circuits is studied over time. This analysis showns that dissociated cortical networks exhibit large numbers of modules associated with information relay, which are stable over our recording times (many hours). We also show that modules associated with simple logical functions are present in living cultureds neural networks, although in fewer numbers.

Stephanie Jones
MGH Martinos Center For Biomedical Imaging

Neural Correlates of Tactile Detection: Combined MEGand Biophysically Based Computational Modeling Study

S. R. Jones1, D. L. Pritchett2, S. M. Stufflebeam1, M. Hämäläinen1, C. I. Moore1,2 1Athinoula A. Martinos Center for Biomedical Imaging, Mass. General Hospital, Charlestown, MA, 2McGovern Institute, MIT, Cambridge, MA.

Cortical correlates of sensory perception have typically been observed in higher order cortical areas, while there are conflicting reports as to their presence in primary sensory cortex. To investigate the cortical correlates of somatosensory perception in humans, we conducted studies of tactile detection using MEG. To this end, we developed an MEG compatible piezoelectric tactile stimulator with real time regulation of stimulus amplitude as a function of psychophysical response. We recorded 306-channel MEG signals (Elekta NeuroMag VectorView) and extracted somatosensory evoked dipoles by combining MEG with structural MR images. A stimulus-level dependent equivalent current dipole (ECD) in the hand area of SI was observed in all subjects. Perception of the threshold level stimuli was predicted from ongoing 'state' properties and from post-stimulus evoked responses in SI. Perceived trials at threshold showed lower power in alpha (7-12Hz) and/or beta frequency bands (15-35Hz) in the signal immediately prior to stimulus onset (-500ms to onset; N = 6/7 Ss). In the evoked response, the magnitude and timing of peaks in the early SI ECD waveform predicted perception as early as 70ms post-stimulus (N = 7/7). To make a direct and principled connection between the observed phenomena and the underlying neural dynamics, we developed a biophysically realistic computational neural model of a laminar SI cortex. The model incorporated the dendritic morphology and physiology of large pyramidal neurons known to be the primary generators of MEG ECDs. Results from the model led to the novel hypothesis that polarity and magnitude of peaks in the evoked SI ECD were induced by a sequence of feed-forward (from the periphery and thalamus) and feedback (from a "higher order" cortical area) input into the local SI network, characterized by the laminar location of their synaptic inputs. Further, specific manipulations of these inputs led to predictions on the neural dynamics underlying conscious perception. The observed signatures of perception in the SI ECD were reproduced in the model by simulating feedback and late thalamic inputs with earlier latencies and stronger magnitudes during perceived trials. An investigation with the model of ongoing state dynamics and their relation to evoked responses and perception is currently in progress. Taken together, our results suggest that evidence of conscious perception exist in SI both in the ongoing state dynamics and in the evoked response, and that these effects can be investigated using biophysically realistic computational cortical modeling. This work was supported by NIH: K25MH072941, 1RO1-NS045130-01, T32 GM007484. NSF: 0316933

Krastan Blagoev
LANL, T10

Stimulus induced changes in the intra-cortical magnetic field: theory and detection using MR spectroscopy

Krastan B. Blagoev, B. Mihaila, B.J. Travis, D. Ranken, A. Franco, C. Gasparovic, A. Mayer, P. Mullins, I. Ulbert, M. Morita, W. Müller, J. Connor, E. Halgren

An imaging modality with the tomographic precision of magnetic resonance imaging (MRI) and the high temporal resolution of electrophysiological techniques, such as electro-encephalography (EEG) and magneto-encephalography (MEG), would be of great utility to neuroscience and medicine, allowing researchers and clinicians to directly map the changes in the neuronal dynamics associated with a given stimulus. Currently, the predominant MRI technique to study brain function, functional MRI (fMRI), provides only an indirect measure of the neuronal (electrophysiological) response and is limited in temporal resolution to several seconds. While electrophysiological techniques such as electro- and magneto-encephalography (EEG/MEG) have superb temporal resolution, the spatial localization of these techniques suffer from an ill-posed inverse problem. In this poster, based on large-scale computer simulations, the stimulus induced magnetic field changes that occur in cortical tissue will be discussed. The expected contrast that can be detected using magnetic resonance techniques will also be presented. The models are based on detailed data from optical imaging. Recent single voxel MR spectroscopy (MRS) data at 4T suggesting that MR spectroscopy is a promising technique for direct detection of neuronal currents in cortical tissue will be shown. At the end a geometric analysis approach to whole brain imaging using MRS will be presented.

John George
LANL, P21

Lateral Interactions in Outer Retina Disclosed by High Resolution Dynamic Optical Imaging of Neural Activation

John S. George and Xin-cheng Yao

We have recently demonstrated the feasibility of dynamic near-infrared imaging of fast intrinsic optical changes directly associated with the electrophysiological response in isolated frog retina activated by visible light. High Resolution CCD image sequences acquired with transmitted light (bright field) illumination disclosed large fractional responses and showed evidence of multiple response components with both negative and positive-going signals with different timecourses. Dark field imaging further enhanced the contrast and sensitivity of optical measures of neural activation. High resolution imaging disclosed optical responses in single pixels often exceeding 5%, of background light, allowing dynamic imaging at the resolution of single cells, in single passes. Based on cell location and response dynamics (including correspondence with identified components of the ERG), we identified responses consistent with photoreceptors, horizontal and bipolar cells. Some cells were classified according to functional criteria, including ON, OFF and ON/OFF responses. Optical responses showed complex but consistent spatiotemporal dynamics from frame to frame and trial to trial. Following photoreceptor activation we observed a rapid diffuse response of opposite polarity in the surrounding retina, distant regions of punctate activity and development of an enhanced response associated with the perimeter of the stimulated region. Our experimental results and theoretical analysis suggest that the optical responses may result from dynamic volume changes corresponding to ion and water flow across the cell membrane. Transient intrinsic optical responses associated with neural activation offer an attractive strategy for studying the computation performed by extended neural networks such as the retina. Our studies and theoretical analysis of optical responses in other neural systems suggest that such fast light optical responses can be detected with high sensitivity in reflected light and therefore might enable non-invasive methodology for diagnostic imaging of retinal function.

H. Jeremy Bockholt
MIND

The MIND Clinical Imaging Consortium as a case study for novel neuroinformatics tools to support multi-institutional heterogeneous psychiatric research studies

H. Bockholt1, J. Ling1, M. Scully1, V. A. Magnotta3, R. L. Gollub2, T. White4, S. C. Schulz4, N. C. Andreasen3, INSTITUTIONS (ALL): 1. The MIND Institute, Albuquerque, NM, USA. 2. Massachusetts General Hospital, Boston, MA, USA. 3. The University of Iowa, Iowa City, IA, USA. 4. The University of Minnesota, Minneapolis, MN, USA.

The MIND Clinical Imaging Consortium (MCIC) was founded in 2003 as a collaboration among four university research groups engaged in multi-site psychiatric research: The University of Minnesota, The University of New Mexico, The University of Iowa, and Harvard University. The psychiatric research domains utilized in the MCIC research protocol include: socio-demographic assessments, comprehensive neurological and psychiatric assessments, a neuropsychological battery, genetic sample, an anatomical neuroimaging session that collects morphological and diffusion weighted sequences, and a functional neuroimaging session that collects calibration information and two cognitive tasks conditions. The design of the MCIC study includes two connected sub-studies: a cross-sectional component, and a longitudinal component. The cross-sectional component of the protocol evaluates chronically ill patients with schizophrenia and matched healthy normal volunteers (HNV)s. The longitudinal component of the MCIC evaluates first episode patients with schizophrenia compared to a matched group of HNVs. Neuroinformatics is a hybrid of neuroscience and computer science disciplines whose major goal is to efficiently manage, manipulate, and provide access to the vast amounts of data produced in neuroscience studies. A comprehensive set of requirements and neuroinformatics tools including a research database, web-based data-entry, tablet-pc application, and a collaboration portal have been developed and implemented to support the needs of the MCIC project. The solution to efficiently manage, manipulate, and provide access to vast amounts of data is to apply best practices learned from other disciplines that engage in multi-center projects, create a team of people representing all sites and facets of the research, understand and identify the requirements of tools needed, and collaborate with other members in the community that have similar problems. The neuroinformatics tools implemented and tested for conducting the MCIC project can serve as a generic solution of how to meet the demanding needs of large multi-center psychiatric research projects that integrate heterogeneous data sources.

Wolfgang Müller
University of New Mexico

Dynamics of vesicle turnover in mature presynaptic terminals in acute brain slice

Vesicular release and vesicle pool replenishment are basic mechanisms in the maintenance of synaptic transmission. In primary neuronal culture a readily releasable and rapidly recycling pool (RRP) rapidly exchanges with the reserve pool while we find very slow exchange in brain slice. This discrepancy suggests fundamental differences for synapses that have formed in culture and appear to be immature, in comparison to mature synapses in acute brain slices. Further, in dissociated cultures miniature postsynaptic potentials seem to result from spontaneous recycling of a separate pool of vesicles (SRP). Using two-photon laser-scan microscopy (TPLSM) in brain slice to image staining (vesicular uptake) and destaining (vesicular release) of the styryl dye FM 1-43 for action potential (AP)-independent spontaneous recycling, action potential-dependent recycling with electrical stimulation (1200 AP @ 10 Hz, 2 sec each 4 sec) and total pool recycling with 45 mM K+-ACSF we demonstrate separate pools of vesicles in hippocampal slice CA1 stratum radiatum: an RRP with about 18 %, an SRP of 51% and a reserve pool of 31% of total pool. Slow and fast AP-dependent destaining kinetics after loading the SRP or the RRP, respectively, suggest limited exchange between these two pools. In all experiments spontaneous activity was blocked by the AMPA glutamate receptor antagonist CNQX. Activity dependent synaptic plasticity is believed to underlie memory and learning. Previously we have shown presynaptic RRP changes after low-frequency stimulation-induced long-term depression (LTD) and high-frequency stimulation-induced potentiation (LTP) (Stanton et al. 2003, 2005). When using a spike-timing induction protocol, LTP and LTD induction enhanced or decreased, respectively, both, spontaneous and stimulated endocytosis by synaptic boutons in stratum radiatum of area CA1. For memory and learning cholinergic input from the basal forebrain/septum to the hippocampus is known to be critically involved. Blocking muscarinic receptors by atropine during spike-timing induction of LTD and LTP strongly inhibited LTD and LTP of field EPSPs, respectively. Interestingly, atropine blocked presynaptic changes in AP-dependent RRP recycling, but not in spontaneous SRP recycling. In conclusion, our results suggest novel roles of SRP and RRP recycling in synaptic information processing and storage.

Jeremy Lewi
Georgia Tech

An Efficient Algorithm for Sequential Optimal Design of Neurophysiology Experiments

We present an efficient algorithm for selecting optimal stimuli for estimating the conditional response function of a neuron. Stimuli are selected by optimizing an objective function which quantifies the expected reduction in uncertainty about the unknown response function. Our objective function is based on mutual information and leads to an optimality criterion known as D-optimality~\\cite{Fedorov72}. Our implementation overcomes the computational hurdles of sequential optimal experimental design in this setting. Simulations show that using optimally chosen stimuli can reduce the number of trials needed to estimate the conditional response function by more than an order of magnitude. Our algorithm has three main components. 1) We model the conditional response function by more than an order of magnitude. Our algorithm has three main components. 1) We model the conditional response parametrically using General Linear Models (GLMs). This a very flexible nonlinear model which can capture many firing rate statistics of a neuron. Furthermore, it is possible to incorporate effects such as adaptation, refractory periods, and burstiness. We consider a restricted class of nonlinearities for the GLM which ensures the log-likelihood is concave ~\\cite{Paninski04}. Concavity of the likelihood improves the tractability of many of the necessary computations. 2) We approximate the posterior distribution on the parameters of the conditional response function as a Gaussian distribution. Asymptotically this approximation is accurate~\\cite{Paninski05}. The normal approximation makes it easier to update the estimated parameters and to compute the mutual information. 3) We show that choosing the stimulus to maximize the mutual information requires at worst one 2-d optimization per trial. We present a number of simulations to demonstrate the potential utility and applicability of our algorithm to neurophysiology experiments. A theoretical and empirical analysis shows that the running time of our algorithm grows on average as the square of the dimensionality. We compared the estimated parameters using stimuli drawn according to our algorithm to the estimated parameters using I.I.D stimuli drawn from a uniform distribution. These simulations looked at the performance when: 1) the parameters are very high dimensional 2) spike history effects are included and 3) the parameters are non-stationary. The validity of our Gaussian approximation is tested using Monte-Carlo methods to measure the Kullback-Leibler distance to the true posterior. Finally we show that asymptotically our uncertainty about the unknown parameters decreases at a rate near that predicted by a theoretical analysis of the information maximizing approach.

John Pearson
LANL

The Principle of Corresponding States for Multimeric Ion Channels

Analogous to van der Waals\' principle of corresponding states we show that the mean open and closed times ($\\tau_O$ and $\\tau_C$) from IP3 receptors, Ryanodine receptors, and BK channels, when scaled by an estimate of the minimum mean open time, all fall near a universal $\\tau_C$ versus $\\tau_O$ curve with $\\tau_C$ being a monotone decreasing function of $\\tau_O$. The existence of such curves is theoretically unexpected since there is not usually a one to one relationship between $\\tau_C$ and $\\tau_O$ in the space of Markov models used to model ion channel gating. This similarity among diverse channels suggests that it is a consequence of the one feature they all have in common: tetrameric structure. We propose an explanation based on Markov models with identical independent subunits, deriving a universal $\\tau_C$ versus $\\tau_O$ curve that is largely independent of the details of the gating kinetics. The universal curve contains no free parameters, and {\\it predicts} a factor of two variation in $\\tau_O$ for the IP_3 receptor in good agreement with experiment.

Thimo Rohlf
Santa Fe Institute

Topological self-organization and critical dynamics of input-driven neural threshold networks

Based on a simple model of network self-organization by local rewiring rules, we study topological evolution of input-driven neural threshold networks. In addition to the original (completely autonomous) system, a subset of network nodes is driven by stochastic external signals with a spiking rate ρ_{in}, that serves as a convenient new control parameter. Depending on this spiking rate, we find a much faster convergence towards topological and dynamical criticality than in the original (undriven) model. In particular, our extensive numerical simulations indicate that, at a critical driving rate $\rho_{in}^c(N)$, networks become self-organized critical even for finite numbers N of nodes. Several dynamical order parameters exhibit pronounced power-law scaling, long-range correlations and 1/f noise (including, e.g., the average neural activity on the whole network). Finally, we discuss possible applications of this model to problems in two fields: control of neural activity in the brain, and the evolution of signal processing by gene regulatory networks in biological cells.

Per Danzl
University of California Santa Barbara

Partial Phase Synchronization of Uncoupled Populations: An Application of Phase Reduction Methods

This poster outlines a model reduction method used to derive the phase response curve for conductance-based neuron models. We compare results for population-level dynamics of large populations of phase-reduced neuron models to full-dimensional conductance-based models and show excellent correlation for biologically relevant stimulus magnitudes. We also present a novel computational technique to estimate the phase of a conductance-based neuron model with high accuracy. We use the phase-reduced models to enable the investigation of partial phase synchronization due noise across a large parameter space.

Marc'Aurelio Ranzato
Courant Institute - New York University

Learning Sparse and Invariant Features Hierarchies

Understanding how the visual cortex builds invariant representations is one of the most challenging problems in visual neuroscience. The feed-forward, multi-stage Hubel and Wiesel architecture [1,2,3,4,5] stacks multiple levels of alternating layers of simple cells that perform feature extraction, and complex cells that pool together features of a given type within a local receptive field. These computational models have been successfully applied to handwriting recognition [1,2], and generic object recognition [4,5]. Learning features in existing models consists in handcrafting the first layers and training the upper layers by recording templates from the training set, which leads to inefficient representations [4,5], or in training the entire architecture supervised, which requires large training sets [2,3]. We propose a fully unsupervised algorithm for learning sparse and locally invariant features at all levels. Each simple-cell layer is composed of multiple convolution filters followed by a winner-take-all competition within a local area, and a sigmoid non-linearity. For training, each simple-cell layer is coupled with a feed-back layer whose role is to reconstruct the input of the simple-cell layer from its output. These coupled layers are trained simultaneously to minimize the average reconstruction error. The output of a simple-cell layer can be seen as a sparse overcomplete representation of its input. The complex cells add the simple cell activities of one filter within the area over which the winner-take-all operation is performed, yielding representations that are invariant to small displacements of the input stimulus. The training procedure is similar to [6], but the local winner-take-all competition ensures that the representation is spatially sparse (and the complex-cell representation locally invariant). The next stage of simple-cell and complex-cell layers is trained in an identical fashion on the outputs of the first layer of complex cells [7], resulting in higher level, more invariant representations, that are then fed to a supervised classifier. Such a procedure yields 0.64% error on MNIST dataset (handwritten digits), and 54% average recognition rate on the Caltech-101 dataset (101 object categories, 30 training samples per category), demonstrating good performance even with few labeled training samples. References [1] Neocognitron: A new algorithm for pattern recognition tolerant of deformations and shifts in position. K. Fukushima, S. Miyake, Pattern Recognition 1982. [2] Gradient-Based Learning Applied to Document Recognition. Y. LeCun, L. Bottou, Y. Bengio, P. Haffner, IEEE 1998. [3] Learning Methods for Generic Object Recognition with Invariance to Pose and Lighting, Y. LeCun, F.-J. Huang, CVPR 04. [4] Object Recognition with Features Inspired by Visual Cortex. T. Serre, L. Wolf, T. Poggio, CVPR 05. [5] Multiclass Object Recognition with Sparse, Localized Features. J. Mutch, D. Lowe, CVPR 06. [6] Efficient Learning of Sparse Representations with an Energy-Based Model. M. Ranzato, C. Poultney, S. Chopra, Y. LeCun, NIPS 06. [7] Reducing the dimensionality of data with neural networks. G.E. Hinton and R.R. Salakhutdinov, Science 06.

Dirk B. Walther
Beckman Institute, University of Illinois at Urbana-Champaign
Modeling attention to proto-objects in natural scenes

Selective visual attention is believed to be responsible for serializing visual information for recognizing one object at a time in a complex scene. But how can we attend to objects before they are recognized? In coherence theory of visual cognition, so-called proto-objects form volatile units of visual information that can be accessed by selective attention and subsequently validated as actual objects. I propose a biologically plausible model of forming and attending to proto-objects in natural scenes. I demonstrate that the suggested model can enable a model of object recognition in cortex to expand from recognizing individual objects in isolation to sequentially recognizing all objects in a more complex scene. Furthermore, I will present neural network implementations of two key operations of the model. All code is available in a Matlab toolbox at: http://www.saliencytoolbox.net

Greg Stephens
Princeton University
Dimensionality and dynamics in the motor behavior of C. elegans

Neural computations function to produce desired behavior. Yet, while there has been substantial effort towards understanding the encoding of sensory information and the dynamics of neural response, investigations of motor output are comparatively underdeveloped, in part due to the complexity of natural behaviors and the lack of canonical descriptions of relevant behavioral states. Here we provide a quantitative and principled analysis of motor behavior in a domain which is both rich enough to be interesting yet simple enough so that movements can be explored exhaustively: the motions of C. elegans freely crawling on an agar plate. In this case, the worm movements are completely characterized by the dynamics of its two-dimensional shape. While {C. elegans possesses a modest nervous system consisting of about 300 neurons, worms perform a variety of complex behaviors from forward and backward crawling, to swimming, turning, chemotaxis and thermotaxis. Using high-resolution tracking video-microscopy we capture a worm's image and extract the skeleton of the shape as a head-to-tail ordered collection of tangent angles sampled along the curve. We use the tangent angle representation to directly explore the full space of shapes, making no a priori assumptions about what aspects of shape are important. Applying principal components analysis we show that the space of shapes is remarkably low dimensional, with four dimensions accounting for ~95% of the shape variance. We show that these dimensions are robust, applying across worms and environments, and informative, aligning naturally with behaviorally relevant states. Two dimensions, with weak excursions into a third, are naturally expressed as phase and amplitude and this corresponds to sinuous crawling movements and reversals. A fourth dimension, weakly dependent on the phase defined by the other two, captures both gentle turns and the Omega-like shapes associated with large changes in the worm's trajectory. We use our detailed representation to search for a vocabulary of behavioral states, primitive stereotyped patterns upon which more complex behavior is based. Focusing upon the evolution of the phase we show that forward crawling and reversals arise as attractors in a dynamical system built directly from the time series of the modes. This suggests identifying behaviors through the representative trajectories of a derived dynamical system. Such a notion is intrinsically appealing, avoiding the bias associated with an observer-defined state and is suggestive of further analysis such as nature of the transitions between the attractors of forward and backward motion. In summary, our full and quantitative description of C. elegans movement provides a powerful tool, useful in a wide variety of contexts, from the linking of motor output with neural circuitry and response to the genetic basis of adaptive behavior.

Bruce Wheeler
University of Illinois
Building a Brain on a Chip

We use lithography to control geometric position of neurons cultured on microelectrode arrays. We are building the technology to explore how geometric form influences computation within an in vitro neural network.

Gennady Berman
LANL, T13
Finding Correlations Using Frequent Patterns Analysis: Application to Neuroimaging Data
Gennady Berman (T-13), Krastan Blagoev (T-10), Vyacheslav Gorshkov (T-13)

Irreducible frequent patters (IFPs) are used to analyze patterns in transactional databases. Frequent pattern is a set of events in the database. • A frequent pattern is irreducible (IFP) if the joint probability p(x,y,z,...) of the frequent pattern xyz..., cannot be reduced to a product of the probabilities of two (or more) other FPs of smaller lengths, e.g. p(xyz...)≠ p(xy)p(z...). • Previously, we have developed an algorithm for searching IFPs in transactional databases. Here we show that the analysis of multidimensional data sets in terms of IFPs captures the multi-event correlations in the database and is a useful tool for characterizing the internal structure of data sets. We discuss the possible application of this data analysis tool in Neuroimaging data analysis. An important problem in event related as well as in resting state magneto- and electro-encephalography (MEG/EEG) data analysis is how to characterize the spatial-temporal correlations in the data, how to analyze the data to be able to find the sequence of information processing events, as well as how to discover the causal connections between different brain regions in a given task. Using IFPs we will be able to look at the correlations between 2,3, etc brain regions or sensors and discover the multi-region correlations in the data.