The New York Academy of Sciences

ASPENBRAINFORUM

Present

Cracking the Neural Code: Third Annual Aspen Brain Forum

AUGUST 23 – 25, 2012

www.nyas.org/NeuralCode

Aspen Meadows Resort, Aspen, CO

KEYNOTE SPEAKERS

George Church, PhD
Harvard Medical School

Sean Hill, PhD
Ecole Polytechnique Federale de Lausanne

Allan Jones, PhD
Allen Institute for Brain Science

Christof Koch, PhD
Allen Institute for Brain Science

David Van Essen, PhD
Washington University in St. Louis

WELCOME

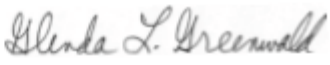
The Aspen Brain Forum Foundation and The New York Academy of Sciences are pleased to welcome you to the Third Annual Aspen Brain Forum, ***Cracking the Neural Code***. Our goal is to facilitate a lively and interactive discussion of cutting-edge developments in our quest to understand the neural code.

One of the greatest challenges in neuroscience today is deciphering how the activity of individual neurons and neuronal circuits gives rise to higher order cognition and behavior, including sensation, perception, memory, and attention. Speakers at this conference will present research from systems and computational neuroscience that is advancing our understanding of the complexities of translating neuronal activity, on the micro, meso, and macro scale, into behavior. Advances in tools, technology, imaging methods, informatics, and computational models will also be highlighted.

The Third Annual Aspen Brain Forum represents a partnership between The New York Academy of Sciences and The Aspen Brain Forum Foundation intended to build a live and virtual network of innovators that will ultimately lead to new collaborations and breakthroughs in research.

We hope that this conference will provide a unique forum for communication among researchers working to solve this crucial challenge and lead to foundational advances in our understanding of the human brain as well as improved diagnosis and treatment of brain disorders.

Ellis Rubinstein
President and CEO
The New York Academy of Sciences



Glenda L. Greenwald
President and Founder
Aspen Brain Forum Foundation

Joseph Dial
Chair, Scientific Advisory Board
Aspen Brain Forum Foundation

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All faculty participating in this activity are required to disclose to the audience any significant financial interest and/or other relationship with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in his/her presentation and/or the commercial contributor(s) of this activity.

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FACULTY DISCLOSURES

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Christof Koch, PhD
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Anthony Zador, MD, PhD
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AGENDA

Day 1: Thursday, August 23, 2012

The Doerr-Hosier Center: McNulty Room

5:00 PM **Registration**

5:30 PM **Welcome Remarks**

5:45 PM ***Consciousness: Confessions of a Romantic Reductionist***
Christof Koch, PhD, Allen Institute for Brain Science

6:30 PM **Networking Reception**

7:30 PM **Meeting Adjourns**

Day 2: Friday, August 24, 2012

The Doerr-Hosier Center: McNulty Room

8:00 AM Registration and Continental Breakfast

SESSION 1: KEYNOTE LECTURES

9:00 AM ***Neural Coding: Building Brain Observatories at the Allen Institute***
Christof Koch, PhD, Allen Institute for Brain Science

9:30 AM ***Mapping Gene Expression and Connections in the CNS: Tools and Data from the Allen Institute for Brain Science***
Allan Jones, PhD, Allen Institute for Brain Science

10:00 AM ***The Human Macro-connectome***
David Van Essen, PhD, Washington University in St. Louis

10:30 AM ***Blue Brain: Insights From the Synthesis of a Cortical Column***
Sean Hill, PhD, Ecole Polytechnique Federale de Lausanne

11:00 AM **Coffee Break**

11:30 AM ***Reading and Writing All Basepairs in a Genome and All Impulses in a Brain***
George Church, PhD, Harvard Medical School

AGENDA

12:00 PM **Panel Discussion**
Innovation and Collaboration: Successful Models for Multi-scale Neuroscience Research
Moderator: **Fred H. Gage**, PhD, The Salk Institute for Biological Studies

Panelists:

George Church, PhD, Harvard Medical School

Sean Hill, PhD, Ecole Polytechnique Federale de Lausanne

Allan Jones, PhD, Allen Institute for Brain Science

Christof Koch, PhD, Allen Institute for Brain Science

David Van Essen, PhD, Washington University in St. Louis

12:30 PM Lunch

SESSION 2: ADVANCES IN TOOLS, TECHNOLOGY, AND METHODOLOGY: INNOVATIVE TOOLBUILDING, NEUROIMAGING, AND NEUROINFORMATICS

1:30 PM ***New Tools for Analyzing and Engineering Brain Circuits***
Ed Boyden, PhD, Massachusetts Institute of Technology

1:50 PM ***Sequencing the Connectome***
Anthony Zador, MD, PhD, Cold Spring Harbor Laboratory

2:10 PM ***Imaging Neuronal Activity in the Freely Moving Animal: From the Eye to the Cortex***
Jason N.D. Kerr, PhD, Networking Imaging Group, Max Planck Institute for Biological Cybernetics, Germany

2:30 PM ***New Approaches for Correlated LM and 3D EM Applied to MULTISCALE CHALLENGES: Bridging Gaps in Knowledge and Understanding***
Mark H. Ellisman, PhD, The National Center for Microscopy and Imaging Research (NCMIR), University of California, San Diego

2:50 PM ***Developing an International Neuroinformatics Infrastructure***
Sean Hill, PhD, Karolinska Institute

AGENDA

SESSION 3: ADVANCES IN TOOLS, TECHNOLOGY, AND METHODOLOGY: COMPUTATIONAL MODELS

3:10 PM ***Prediction in the Retina***
Stephanie E. Palmer, PhD, University of Chicago

3:30 PM Coffee Break

4:00 PM ***Bayesian Inference with Efficient Neural Population Codes***
Alan A. Stocker, PhD, University of Pennsylvania

4:20 PM ***The Orchestral Brain: Coding with Correlated and Heterogeneous Neurons***
Rava Azeredo da Silveira, PhD, Ecole Normal Superieure, Paris

4:40 PM ***View from the Top: What Probabilistic Models of Perception Can Teach Us about Neural Computation***
Wei Ji Ma, PhD, Baylor College of Medicine

5:00 PM ***Computing Intelligence: Mind, Brain and Machine***
Tomaso Poggio, PhD, Massachusetts Institute of Technology

5:20 PM Meeting Adjourns

Day 3: Saturday, August 25, 2012

Paepcke Memorial Building: Paepcke Auditorium

8:30 AM Registration and Continental Breakfast

9:00 AM ***Neural Plasticity and Neuronal Diversity***
Fred H. Gage, PhD, The Salk Institute for Biological Studies

SESSION 4: MICRO-LEVEL CELLULAR BEHAVIOR

9:30 AM ***Model Building: From Coding of Fundamentals to Validation of a High-performance Neural Prosthetic***
Andrew Schwartz, PhD, University of Pittsburgh

9:50 AM ***Predicting Every Single Spike — Beyond Generalized Linear Modeling***
Matthias Bethge, PhD, Werner Reichardt Centre for Integrative Neuroscience, University of Tübingen

AGENDA

10:10 AM ***A New Class of Neural Population Codes***
Ila R. Fiete, PhD, University of Texas at Austin

SESSION 5: MESO-LEVEL CIRCUITS

10:30 AM ***Neural Circuits Controlling Innate Emotional Behaviors***
David J. Anderson, PhD, California Institute of Technology

10:50 AM Coffee Break

11:10 AM ***Sparse High-order Interaction Networks Underlie Learnable Neural Population Codes***
Elad Schneidman, PhD, Weizmann Institute of Science

11:30 AM ***A Statistical Approach to Understanding Decision-related Signals in Parietal Cortex***
Jonathan W. Pillow, PhD, University of Texas at Austin

11:50 AM Lunch

SESSION 6: MACRO-LEVEL SYSTEMS

1:10 PM ***Learning Volitional Control of Neural Activity: Natural Repertoire or Arbitrary Patterns?***
Richard A. Andersen, PhD, California Institute of Technology

1:30 PM ***Imaging Regional Connections in the Living Human Brain***
Tim Behrens, DPhil, Oxford University

1:50 PM ***Neural Syntax: Oscillations Promote Cell Assembly Sequences***
Gyorgy Buszaki, MD, PhD, The Neuroscience Institute, New York University Langone Medical Center

2:10 PM ***Representational Transformations in Memory Consolidation***
Yadin Dudai, PhD, Weizmann Institute of Science

2:30 PM ***Mapping the Retinal Connectome with EyeWire, an Online Community for "Citizen Neuroscience"***
Sebastian Seung, PhD, Massachusetts Institute of Technology

AGENDA

SESSION 7: APPLIED NEUROTECHNOLOGY

2:50 PM ***Decoding Vision: A Retinal Prosthetic Strategy with the Capacity to Restore Normal Vision***
Sheila Nirenberg, PhD, Weill Medical College of Cornell University

3:10 PM ***Neuronal Ensembles: Harnessing their Power in BrainGate and Epilepsy Research***
Leigh R. Hochberg, MD, PhD, Brown University

3:30 PM ***Glucose Powered Neural Prosthetics***
Rahul Sarpeshkar, PhD, Massachusetts Institute of Technology

3:50 PM **Panel Discussion**
The Future of Neural Coding and Brain Modeling

Q&A with Speakers:

Richard Andersen, PhD, California Institute of Technology

Andrew Schwartz, PhD, University of Pittsburgh

David Anderson, PhD, California Institute of Technology

Gyorgy Buszaki, MD, PhD, The Neuroscience Institute, New York University Langone Medical Center

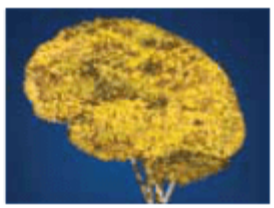
Mark Ellisman, PhD, The National Center for Microscopy and Imaging Research (NCMIR), University of California, San Diego

Yadin Dudai, PhD, Weizmann Institute of Science

Tomaso Poggio, PhD, Massachusetts Institute of Technology

4:20 PM **Closing Remarks**

4:30 PM **Aspen Brain Forum Concludes**



ABSTRACTS

Speaker abstracts are listed in order of presentation.

Day 1: Thursday, August 23, 2012

Consciousness: Confessions of a Romantic Reductionist

Christof Koch, PhD, Allen Institute for Brain Science, Seattle, WA

What links the conscious experience of joy, color, lust and smell to bioelectrical activity in the brain? How can anything physical give rise to nonphysical, subjective, conscious states? Neuroscientist Christof Koch has devoted much of his career to bridging the seemingly unbridgeable gap between the physics of the brain and phenomenal experience. Koch recounts not only the birth of the modern science of consciousness but also the subterranean motivation for his quest—his instinctual (if "romantic") belief that life is meaningful. Koch describes his own groundbreaking work with Francis Crick in the 1990s and 2000s and the gradual emergence of consciousness (once considered a "fringy" subject) as a legitimate topic for scientific investigation. Koch gives us stories from the front lines of modern research into the neurobiology of consciousness as well as his own reflections on a variety of topics, including the distinction between attention and awareness, the unconscious, how neurons respond to Homer Simpson, the physics and biology of free will, dogs, sentient machines, and *Der Ring des Nibelungen*.

Day 2: Friday, August 24, 2012

SESSION 1: KEYNOTE LECTURES

Neural Coding: Building Brain Observatories at the Allen Institute

Christof Koch, PhD, Allen Institute for Brain Science, Seattle, WA

The Allen Institute for Brain Science is initiating a ten-year project to study the principles by which information is encoded, transformed and represented in the mammalian cerebral cortex and related structures. The Institute will build a series of brain observatories to identify, record and intervene in the neuronal networks underlying visually guided behaviors in the mouse, including visual perception, decision making and consciousness. This is a large-scale, in-house team effort to synthesize anatomical, physiological and theoretical knowledge into a description of the wiring scheme of the cortex, at both the structural and the functional levels. The fruits of this cerebroscope will be freely available to the public.

ABSTRACTS

Mapping Gene Expression and Connections in the CNS: Tools and Data from the Allen Institute for Brain Science

Allan Jones, PhD, Allen Institute for Brain Science, Seattle, WA

The Allen Institute for Brain Science is a non-profit research organization dedicated to providing tools and data for the larger research community. Since 2003, the Allen Institute has created a suite of large-scale data efforts along with a web portal to view and analyze the data. These efforts include gene expression atlases of the developing and adult mouse brain and spinal cord, developing and adult human and non-human primate gene expression studies, and more recent efforts on connectivity atlases of the mouse brain. This presentation will cover an overview of the Allen Institute, its current projects and infrastructure, a few data highlights, and a look at future directions.

The Human Macro-connectome

David Van Essen, PhD, Washington University in St. Louis, St. Louis, MO

Recent advances in noninvasive neuroimaging have set the stage for the systematic exploration of human brain circuits in health and disease. One such effort is the Human Connectome Project (HCP), which will characterize brain circuitry and its variability in healthy adults. A consortium of investigators at Washington University, University of Minnesota, University of Oxford, and 7 other institutions is engaged in a 5-year project to characterize the human connectome in 1,200 individuals (twins and their non-twin siblings). Information about structural and functional connectivity will be acquired using diffusion MRI and resting-state fMRI, respectively. Additional modalities will include task-evoked fMRI and MEG/EEG, plus extensive behavioral testing and genotyping. Advanced visualization and analysis methods will enable characterization of brain circuits in individuals and group averages at high spatial resolution and at the level of functionally distinct brain parcels (cortical areas and subcortical nuclei). Comparisons across subjects will reveal aspects of brain circuitry which are related to particular behavioral capacities and which are heritable or related to specific genetic variants.

Data from the HCP will be made freely available to the neuroscience community. A user-friendly informatics platform will enable investigators around the world to carry out many types of data mining on these freely accessible, information-rich datasets. Altogether, the HCP will provide invaluable information about the healthy human brain and its variability.

ABSTRACTS

Blue Brain: Insights From the Synthesis of a Cortical Column

Sean Hill, PhD, Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland

The Blue Brain Project aims to provide a generic facility for large-scale neuroscience data integration, modeling and simulation. A prototype facility has been completed, which is capable today of building neural microcircuits or modules of the rat brain with cellular level resolution. This prototype was founded on a novel data-driven and data-constrained process for creating, validating and researching the neocortical column. Recent models recreate key experimental findings of structural and functional properties of neocortical circuitry *in vitro* — including connectivity, synaptic responses and network dynamics. We present insights gained from this process including principles underlying invariance and robustness in cortical microcircuitry.

Reading and Writing All Basepairs in a Genome and All Impulses in a Brain

George Church, PhD, Harvard Medical School, Boston, MA

We have brought down the cost of reading and writing DNA (in genomes and epigenomes) by about a million-fold in the past 8 years. Higher quality and comprehensiveness have greatly improved genomic models, software, and applications. Synthetic biology plus the decreasing size of components in wireless circuits will likely enable analogous exponential progress in brain-computer interfaces. The ability to inexpensively record, hyperpolarize, and depolarize precise combinations of neurons on demand is likely to be quite helpful for rapidly generating and testing models (see also PMID: 22726828).

ABSTRACTS

SESSION 2: ADVANCES IN TOOLS, TECHNOLOGY, AND METHODOLOGY: INNOVATIVE TOOLBUILDING, NEUROIMAGING, AND NEUROINFORMATICS

New Tools for Analyzing and Engineering Brain Circuits

Ed Boyden, PhD, Massachusetts Institute of Technology, Cambridge, MA

Understanding how neural circuits implement brain functions and how these computations go awry in brain disorders, is a top priority for neuroscience. Achieving this understanding will require new technologies. Over the last several years we have developed a rapidly-expanding suite of genetically-encoded reagents that, when expressed in specific neuron types in the nervous system, enable their electrical activities to be powerfully and precisely activated and silenced in response to pulses of light. First, I will briefly give an overview of the field and then I will discuss a number of new tools for neural activation and silencing that we are developing, including new molecules with augmented amplitudes, improved safety profiles, novel color and light-sensitivity capabilities, and unique new capabilities. Second, we have begun to develop microfabricated and robotic hardware to enable complex and distributed neural circuits to be precisely controlled and for the network-wide impact of a neural control event to be measured using distributed electrodes, fMRI, and automated intracellular neural recording. We explore how these tools can be used to enable systematic analysis of neural circuit functions in the fields of emotion, sensation, movement, and in neurological and psychiatric disorders.

Sequencing the Connectome

Anthony Zador, MD, PhD, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

The brain is an extremely complex network, consisting of billions of neurons connected by trillions of synapses. The details of these connections—which neurons form synaptic connections with which other neurons—are crucial in determining brain function. Malformation of these connections during prenatal and early postnatal development can lead to mental retardation, autism or schizophrenia; loss of specific connections later in life is associated with neurodegenerative diseases such as Alzheimer's. We are developing an entirely novel approach based on high-throughput DNA sequencing technology. Sequencing technology has not previously been applied in the context to neural connectivity. The appeal of using sequencing is that it is fast and cheap. Moreover, like microprocessor technology, sequencing technology is improving exponentially. An efficient method for determining the brain's wiring diagram would provide a foundation for understanding how neural circuits compute and could transform neuroscience research.

ABSTRACTS

Imaging Neuronal Activity in the Freely Moving Animal: From the Eye to the Cortex

Jason N. D. Kerr, PhD, Networking Imaging Group, Max Planck Institute for Biological Cybernetics, Tübingen, Germany

Motivation underlies the performance of self-determined behavior and is fundamental to decision making, especially with regard to seeking food, mates, and avoiding peril. As many decision making based behaviors in rodents involve a combination of head movements, eye movements, vestibular driven neuronal activity and multimodal active sensing of the environment to guide the behavior, studying the freely moving animal is paramount. To achieve this, what is also necessary is the precise tracking of the animal's movement and interaction with the environment. Here, I will outline work from our group that focuses on how freely moving rodents use their vision during decision making tasks and resulting cortical activity. I will introduce methods that allow accurate recording of neuronal activity from populations of cortical neurons, using multi-photon imaging techniques, while simultaneously tracking behavior, using eye and head tracking techniques, during decision making in the freely moving rodent. The second half of the presentation will focus on recent results from our lab showing how rodents have a distinct eye movement strategy that is of major evolutionary benefit.

New Approaches for Correlated LM and 3D EM Applied to MULTISCALE CHALLENGES: Bridging Gaps in Knowledge and Understanding

Mark H. Ellisman, PhD, The National Center for Microscopy and Imaging Research (NCMIR), University of California, San Diego, San Diego, CA

A grand goal in cell biology is to understand how the interplay of structural, chemical and electrical signals in and between cells gives rise to tissue properties, especially for complex tissues like nervous systems. New technologies are hastening progress as biologists make use of an increasingly powerful arsenal of tools and technologies for obtaining data, from the level of molecules to whole organs, and at the same time engage in the arduous and challenging process of adapting and assembling data at all scales of resolution and across disciplines into computerized databases. This talk will highlight projects in which development and application of new contrasting methods and imaging tools have allowed us to observe otherwise hidden relationships between cellular, subcellular and molecular constituents of cells, including those of nervous systems.

New chemistries for carrying out correlated light and electron microscopy will be described, as well as recent advances in large-scale high-resolution 3D reconstruction with LM, TEM and SEM based methods. Examples of next generation cell-centric image libraries and web-based multiscale information exploration environments for sharing and exploring these data will also be described.

ABSTRACTS

Developing an International Neuroinformatics Infrastructure

Sean Hill, PhD, Karolinska Institute, Stockholm, Sweden

The International Neuroinformatics Coordinating Facility (INCF) was launched in 2005, following the proposal by the Global Science Forum of the Organization for Economic Cooperation and Development (OECD) to create an organization to coordinate an open international infrastructure to integrate heterogeneous neuroscience data and knowledge bases and enable new insights from analysis, modeling and simulation. Here we present the INCF multi-phase strategy to deploy such an infrastructure with specific capabilities and milestones. The first phase is to establish a globally federated data space with searchable metadata. The second phase will deploy an object-based data integration layer employing web services to ensure the unique identification of all data through ontologies and spatial coordinates, while using data models to access diverse data formats through standard interfaces. The third phase would enable standard workflow management for analysis, visualization, modeling and simulation can then be built on top of the data integration layer. The development of portal interfaces will be critical to provide interactive user access to data, analyses and simulation results. The aim of this infrastructure is to facilitate international sharing, publication and integration of neuroscience data across multiple levels and scales from genes to behavior.

SESSION 3: ADVANCES IN TOOLS, TECHNOLOGY, AND METHODOLOGY: COMPUTATIONAL MODELS

Prediction in the Retina

Stephanie E. Palmer, PhD[1], Olivier Marre, PhD[2], Michael J. Berry, II, PhD[3], William Bialek, PhD[3]; [1]University of Chicago, Chicago, IL, [2]Paris VI University, Paris, France, [3]Princeton University, Princeton, NJ

In the natural world, temporal correlations between events exist on many timescales, allowing organisms to anticipate the future state of their environments. A neural system that uses predictions to guide behavior must encode the future values of sensory inputs. This suggests a new approach to neural encoding. While most studies have, historically, sought to characterize what stimuli in the past gave rise to a response (the classical receptive field picture of encoding), we ask instead what stimuli those responses predict. We have found such "predictive information" in the population responses of retinal ganglion cells (RGCs) in the larval salamander. To quantify predictive information, we ask how much RGCresponses at some time "now" *(Rp)* tell us about the future state of the stimulus (Sf). This information, *I(Rp;Sf)*, is bounded by correlations in the stimulus itself, *I(Sp;Sf)*. For particular classes of stimuli, this bound can be calculated analytically. We have shown that certain patterns of population firing in the retina approach this bound, suggesting that the retina may be optimized for prediction. Coding for prediction may be a useful strategy for neural systems to adopt, making transfer of sensory information more efficient by compressing signals along dimensions relevant for behavior.

ABSTRACTS

Bayesian Inference with Efficient Neural Population Codes

Alan A. Stocker, PhD, University of Pennsylvania, Philadelphia, PA

The accuracy with which the perceptual brain can infer the value of stimulus variables in the world depends on both the amount of stimulus information that is represented in a population of sensory neurons (encoding) and the mechanism by which this information is subsequently retrieved from the population's response pattern (decoding).

Previous studies have mainly focused either on the encoding or the decoding aspect of the problem, providing evidence for two general optimality principles: The efficient coding hypothesis (Barlow 1961) states that neural representations are optimally adapted to encode a given stimulus ensemble, while the Bayesian hypothesis proposes that the brain is able to optimally decode a stimulus variable by combining sensory evidence with prior information (e.g. Knill/Richards 1999).

Here, I present recent work of my laboratory in which we developed a new theoretical framework that functionally links optimal (efficient) encoding with optimal (Bayesian) decoding. More specifically, I demonstrate that efficient population codes allow the accurate emulation of Bayesian inference with a relative simple, neural decoding mechanism based on a generalized form of the population vector read-out. Stimulus priors (bottom-up) are intrinsically represented by the tuning curves distribution in the neural population, while top-down attentional priors can be incorporated by gain changes in neural firing. The framework makes specific predictions about perceptual behavior based on stimulus-specific parameters such as stimulus prior, strength- and time-constants, as well as physiological parameters such as spontaneous firing rates. The framework is a concrete example for the duality between neural representation and computation.

The Orchestral Brain: Coding with Correlated and Heterogeneous Neurons

Rava Azeredo da Silveira, PhD, Ecole Normal Superieure, Paris, France

While single-cell activity may be well correlated with simple aspects of sensory stumuli, rich stimuli or subtly differing stimuli require concomitant coding by several neurons in a population. It is then natural to ask whether the nature of the coding is "orchestral" in that it relies upon correlation and physiological diversity among cells. Positive correlations in the activity of neurons are widely observed in the brain and previous studies stipulate that these are at best marginally favorable, if not detrimental, to the fidelity of population codes, compared to independent codes. Here, we put forth a scenario in which positive correlations can enhance coding performance by astronomical factors. Specifically, the probability of discrimination error can be suppressed by many orders of magnitude. Likewise, the number of stimuli encoded—the capacity—can be enhanced by similarly large factors. These effects do not necessitate unrealistic correlation values and

can occur for populations with as little as a few tens of neurons. The scenario relies upon "lock-in" patterns of activity with which correlation relegates the noise in irrelevant modes. We further demonstrate that, quite generically, coding fidelity is enhanced by physiological heterogeneity. Finally, we formulate heuristic arguments as to the plausibility of "lock-in" patterns and possible experimental tests of the theoretical proposal.

View from the Top: What Probabilistic Models of Perception Can Teach Us about Neural Computation

Wei Ji Ma, PhD, Baylor College of Medicine, Houston, TX

Sensory information is often noisy and ambiguous and perception is uncertain as a result. Under such circumstances, organisms can maximize their performance by using a decision strategy known as probabilistic or Bayesian inference. In simple perceptual tasks such as cue combination, Bayesian models describe human behavior extremely well. Here, we show that the formalism extends to more cognitive tasks, where inference is typically categorical and hierarchical, and resource limitations might play a role. As examples, we will discuss visual search, change detection, and categorization under ambiguity. Probabilistic models of perceptual and cognitive behavior provide strong constraints on theories of the underlying neural computations and yield testable predictions for physiological experiments. We will illustrate this using cue combination, a realm in which these physiological predictions have partially been confirmed.

Computing Intelligence: Mind, Brain and Machine

Tomaso Poggio, PhD, Massachusetts Institute of Technology, Cambridge, MA

I conjecture that the sample complexity of object recognition is mostly due to geometric image transformations and that a main goal of the ventral stream is to learn and discount image transformations. The theory predicts that the size of the receptive fields determines which transformations are learned during development; that the transformation represented in each area determines the tuning of the neurons in the area; and that class specific transformations are learned and represented at the top of the ventral stream hierarchy. If the theory were true, the ventral system would be a mirror of the symmetry properties of motions in the physical world.

ABSTRACTS

Day 3: Saturday, August 25, 2012

Neural Plasticity and Neuronal Diversity

Fred H. Gage, PhD, The Salk Institute for Biological Studies, La Jolla, CA

The first part of the talk will focus on evidence supporting the birth and maturation of new neurons in the adult dentate gyrus of the hippocampus in the mammalian brain. The mechanism by which the cells integrate and become functional will be discussed. In addition, the potential functional significance for adult neurogenesis in the context of the normal function of the hippocampus will be discussed. The focus will be on how the mature brain cellular and molecular structure changes with experience, which results in a dynamic processing of information. In the second part of the talk, I will focus on the recent finding that LINE-1 (Long Interspersed Nucleotide Elements-1 or L1) retroelements are active in somatic neuronal progenitor cells providing an additional mechanism for neuronal diversification. Together with their mutated relatives, retroelement sequences constitute 45% of the mammalian genome with L1 elements alone representing 20%. The fact that L1 can retrotranspose in a defined window of neuronal differentiation, changing the genetic information in single neurons in an arbitrary fashion, allows the brain to develop in distinctly different ways. The characterization of somatic neuronal diversification will not only be relevant for the understanding of brain complexity and neuronal organization in mammals, but may also shed light on the differences in cognitive abilities.

SESSION 4: MICRO-LEVEL CELLULAR BEHAVIOR

Model Building: From Coding of Fundamentals to Validation of a High-performance Neural Prosthetic

Andrew Schwartz, PhD, University of Pittsburgh, Pittsburgh, PA

The fundamental feature of neural processing begins with neural integration of synaptic input to raise a neuron's membrane potential to fire an action potential. The combination of inputs that generate this non-linear event has a structure. In general, some combinations of events are more likely than others and this probability is captured by tuning functions which plot firing rate against measureable parameters. Accurate tuning functions allow predictions of the parameters from neural activity. This is the basis for neural prosthetics. I will review motor cortical tuning, its utility for motor prosthetics, and current progress in controlling advanced robotic arms and hands.

ABSTRACTS

Predicting Every Single Spike — Beyond Generalized Linear Modeling

Lucas Theis[1], Dan Arnstein[1], Andre Maia Chagas[1], Cornelius Schwarz, PhD[1,3] and **Matthias Bethge**, PhD[1,2,3]; [1]Werner Reichardt Centre for Integrative Neuroscience, University Tübingen, Tübingen, Germany, [2]Max Planck Institute for Biological Cybernetics, Tübingen, Germany, [3]Bernstein Center for Computational Neuroscience, Tübingen, Germany

A ubiquitous challenge in sensory systems neuroscience is to characterize the relationship between external stimuli and neuronal responses. Here, we describe a generative modeling approach towards a functional characterization of single-cell responses. A popular approach for modeling neuronal responses is to use a generalized linear model (GLM). However, for GLMs to work well, choosing an appropriate set of nonlinear stimulus features is often crucial but difficult. This problem can be elegantly tackled by taking a generative approach which not only tries to model the conditional distribution of observing a spike given the stimulus, but jointly models the full joint distribution of stimulus and response. We start by modeling important spike-dependent distributions such as the spike-triggered distribution and the interspike-interval distribution. Subsequently, Bayes' rule allows us turn these distributions into a model of the neuron's response conditioned on the stimulus and spike history, subject to certain assumptions. By using flexible distributions such as mixtures of Gaussians, we are able to extract complex dependencies between responses that cannot be captured by a generalized linear model. We apply our model to single-cell recordings of primary afferents of the rat's whisker system and how quantitatively that it significantly improves the prediction of neural spike generation. In particular, the model captures exceedingly high information rates between stimulus and neural response up to 529 bits/s.

A New Class of Neural Population Codes

Ila R. Fiete, PhD, University of Texas at Austin, Austin, TX

The brain represents and transforms external variables to accomplish goals. Representation and transformation are inherently noisy when performed by neurons. One way to extract a less noisy estimate of the encoded variable is by averaging over neural populations. Population coding is widely used by human observers to estimate the encoded variable, and has been interpreted as a model of how downstream brain areas may readout the variable. The population codes observed in the sensory and motor peripheries, however, lead only to modest – polynomial – improvements in estimation for the number of neurons involved.

Is there a better way? I will show that the entorhinal grid cell code for animal location is capable of exponentially strong removal of noise from noisy estimates of the animal's position, in contrast with common population codes. Noise control is enabled by the peculiar structure of the grid code, and does not rely on the existence of external cues. I will show how a simple neural network model of the entorhinal-hippocampal loop performs this noise removal for improvements in accuracy easily exceeding 10^4 compared to a place cell population code using the same number of neurons.

ABSTRACTS

SESSION 5: MESO-LEVEL CIRCUITS

Neural Circuits Controlling Innate Emotional Behaviors

David J. Anderson, PhD, California Institute of Technology, Pasadena, CA

Research interests in my laboratory focus on understanding how emotional behavior is encoded in the brain, at the level of specific neuronal circuits, and the specific neuronal subtypes that comprise them. We want to understand the structure and dynamic properties of these circuits and how they give rise to the outward behavioral expressions of emotions such as fear, anxiety, or anger. This information will provide a framework for understanding how and where in the brain emotions are influenced by genetic variation and environmental influence ("nature" and "nurture"), and the mechanism of action of drugs used to treat psychiatric disorders such as depression. We are using both mice and the vinegar fly *Drosophila melanogaster* as model systems. A central focus of the laboratory is on the neural circuits underlying aggression and fear. We are using molecular genetic tools, as well as functional imaging and electrophysiology, to establish cause-and-effect relationships between the activity of specific neuronal circuits and behavior. We hope that this research will lead to new insights into the organization of emotion circuits, and their dysregulation in psychiatric disorders.

Sparse High-order Interaction Networks Underlie Learnable Neural Population Codes

Elad Schneidman, PhD, Weizmann Institute of Science, Rehovot, Israel

Information is carried in the brain by the joint activity patterns of large groups of neurons. Understanding the structure and function of population neural codes is challenging due to the exponential number of possible activity patterns and dependencies between neurons. By studying groups of 100 retinal neurons responding to natural movies, we found that these neurons are strongly correlated and that pairwise maximum entropy models, which are highly accurate for small networks, are no longer sufficient. We show that because of the sparse nature of the neural code, the higher order interactions can be easily learned with surprisingly high accuracy using a novel pseudo-likelihod model and that a very sparse interaction network underlies the code of large populations of neurons. Additionally, we show that the interaction network is organized in a hierarchical and modular manner, suggesting scalability of the code. Our results suggest that learnability is a key feature of the neural code.

A Statistical Approach to Understanding Decision-related Signals in Parietal Cortex

Jonathan W. Pillow, PhD, University of Texas at Austin, Austin, TX

A central problem in systems neuroscience is to decipher the neural mechanisms underlying sensory-motor decision making. The lateral intraparietal area of parietal

cortex (LIP) forms a primary component of neural decision making circuitry in primates, but its exact role in choice behavior is hotly debated. In this talk, I will describe recent work aimed at developing a statistical model of the information carried by LIP neurons during a decision making task. This approach differs in taking a "data first" perspective, aiming to describe the rich statistical structur e of observed spike trains in LIP, rather than looking to validate for a particular "normative" theory of evidence accumulation, learning, or choice. First, we formulate an explicit encoding model of LIP responses, which allows us to distinguish the effects of various sensory, motor, and reward-related variables on spiking. These dependencies are highly variable across neurons, and depend on spike history in a manner inconsistent with a Poisson rate code. Secondly, we use the model to perform Bayesian decoding of decisions from LIP spike responses on single trials. I will discuss the implications for various hypothesized decoding schemes, and for understanding the decision-related computations performed in LIP.

SESSION 6: MACRO-LEVEL SYSTEMS

Learning Volitional Control of Neural Activity: Natural Repertoire or Arbitrary Patterns?

EunJung Hwang, PhD and **Richard A. Andersen**, PhD, California Institute of Technology, Pasadena, CA

Recent brain machine interface (BMI) studies have proposed that it may be more efficient to learn arbitrary relations between individual neuron activity and the control signals necessary for assistive devices than to utilize the complex relations observed between activity and natural movements. This idea is based on the assumption that neurons can be conditioned independently from one another regardless of how they respond together for natural behaviors. We tested this assumption in an important candidate area for BMIs, the parietal reach region (PRR) in which neurons encode goal locations for reaching movements. Monkeys could learn to elicit seemingly arbitrarily assigned activity patterns; However, on closer examination, it was found that the animals were producing these patterns by imagining particular movements, drawing on the natural repertoire of movement activity. Moreover, neurons free from conditioning showed correlated responses with the conditioned neurons as though they encoded common reach goals. Thus, the learning was accomplished by finding imagined goals for which the natural response could well approximate the arbitrary patterns. Our results suggest that animals learn to volitionally control single neuron activity, at least in PRR, by preferentially exploring and exploiting their natural movement repertoire. Thus, for optimal performance, BMIs utilizing neural signals in PRR should harness – not disregard – the activity patterns found in the natural repertoire. This rule may also apply to other brain areas that are candidates for controlling BMIs. The findings reinforce a strategy of choosing brain sites for recording whose natural repertoires are best suited for particular BMI applications.

ABSTRACTS

Imaging Regional Connections in the Living Human Brain

Tim Behrens, DPhil, Oxford University, Oxford, England, United Kingdom

Recent advances in non-invasive neuroimaging have enabled the measurement of connections between distant regions in the living human brain, thus opening up a new field of research: Human Connectomics. Different imaging modalities allow the mapping of structural connections (axonal fiber tracts), as well as functional connections (correlations in time series). Individual variations in these connections may be related to individual variations in behavior and cognition. Connectivity analysis has already led to several important advances. Segregated brain regions may be identified by their unique patterns of connectivity, structural and functional connectivity may be compared to elucidate how dynamic interactions arise from the anatomical substrate, and the architecture of large-scale networks connecting sets of brain regions may be analyzed in detail. Collectively, advances in human connectomics open up the possibility of studying how brain connections mediate regional brain function and thence behavior.

Neural Syntax: Oscillations Promote Cell Assembly Sequences

Gyorgy Buszaki, MD, PhD, The Neuroscience Institute, New York University Langone Medical Center, New York, NY

The dominant theoretical form of mental structure of the last century was implicitly a neuropsychological model. At the center of this model, necessary for episodic free recall, planning or logical reasoning, is Hebb's phase sequences of neuronal assemblies, i.e., hypothetical self-propagating loops of neuronal coalitions connected by modifiable synapses. These phase sequences can be activated by exogenous or endogenous (internal) sources of stimulation, independent from environmental determinants of behavior. The neurophysiological implication of this conjecture for episodic recall is that hippocampal networks are endowed by an internal mechanism that can generate a perpetually changing neuronal activity even in the absence of environmental inputs. Recall of similar episodes would generate similar cell assembly sequences and uniquely different sequence patterns would reflect different episodes. Using large-scale recording of neuronal ensembles in the behaving rat, I will show experimental support of self-perpetuating activity neuronal assemblies and demonstrate how oscillations support precise spike timing across neuronal populations. The physiological characteristics of these assemblies are virtually identical to features of hippocampal place cells controlled by environmental and/or idiothetic stimuli. I hypothesize that neuronal mechanisms introduced for navigation in the physical environment in "simpler" animals are identical to those needed for memory recall and/or planning in animals with larger brains. The different appearance of representations in the hippocampus of different species and different segments of the hippocampus in the same species may reflect its functional connectivity with the neocortex and other structures.

ABSTRACTS

Representational Transformations in Memory Consolidation

Yadin Dudai, PhD, Weizmann Institute of Science, Rehovot, Israel

Long-term memory of personal events reorganizes over time over distributed brain circuits in a process termed "systems consolidation". This process involves transformation of event information into variants that come to differ from each other in their contextual and factual details, cue-induced retrievability, the ability to reenact the original experience, and the dependency on the brain circuits that have encoded the information in the first place. I will discuss how the transformation of the cognitive representation relates to cellular and systems activity in identified brain circuits.

Mapping the Retinal Connectome with EyeWire, an Online Community for "Citizen Neuroscience"

Sebastian Seung, PhD, Massachusetts Institute of Technology, Cambridge, MA

According to a doctrine known as connectionism, brain function and dysfunction depend primarily on patterns of connectivity between neurons. Connectionism has been explored theoretically with mathematical models of neural networks since the 1940s. It has proved difficult to test these models through activity measurements alone. For conclusive empirical tests, information about neural connectivity is also necessary, and could be provided by new imaging methods based on serial electron microscopy. The bottleneck in using these new methods is now shifting to the data analysis problem of extracting neural connectivity from the images. Our capacity to acquire "big data" from the brain has far outpaced our ability to analyze it. My lab has been developing computational technologies to deal with this data deluge. Based on these innovations, we have launched EyeWire, an online community that mobilizes the public to map the retinal connectome by playing a coloring game. Players analyze nanoscale images by interacting with one another and with artificial intelligence based on machine learning. I will describe preliminary efforts to map the retinal circuits presynaptic to JAM-B and orientation-selective types of ganglion cells.

SESSION 7: APPLIED NEUROTECHNOLOGY

Decoding Vision: A Retinal Prosthetic Strategy with the Capacity to Restore Normal Vision

Sheila Nirenberg, PhD, Weill Medical College of Cornell University, New York, NY

A pressing problem in systems neuroscience is determining the neural code. We know that neurons send their signals in the form of trains of action potentials, but we don't know what the code is, that is, we don't know what the unit of information is. Is it the number of spikes per unit time? Is it the individual spike or some pattern of spikes? Getting a clear answer to this

affects a great deal of work in systems neuroscience, both basic and applied. For basic research, it tells us what quantity we need for building models of neural computations (i.e., what spike train features we need). For applied research, it tells us what quantity we need to effectively transmit information from one brain area to another via prosthetic devices. Here, we describe a strategy for finding neural codes and use it to develop a novel retinal prosthetic.

Neuronal Ensembles: Harnessing their Power in BrainGate and Epilepsy Research

Leigh R. Hochberg, MD, PhD, Brown University, Providence, RI

Decades of fundamental neuroscience research have begun to crack the neural code yielding an evolving understanding of how neural activities contribute to perception, cognition, behavior, decision making, and memory. Some of the earliest inspiration for computational neuroscience research has been its long anticipated translation to the creation of neural interface systems that might serve to restore the communication, mobility, and independence of people with paralysis or limb loss. With the use of investigational technologies that have permitted chronic intracortical recording (in one case, for more than five years), the ongoing BrainGate pilot clinical trials are evaluating the feasibility of persons with tetraplegia controlling a computer cursor or other devices simply by imagining movement of their own hand. Recently, two people with tetraplegia controlled a robotic arm to make multi-dimensional reach and grasp movements; one used a BrainGate-enabled robotic arm to pickup a thermos of coffee and to drink from it—the first time in nearly 15 years she had been able to pickup any drinking vessel and sip her morning coffee solely of her own volition. In related neuronal ensemble-based research, early glimpses into the activities of dozens of individual cortical neurons in humans are providing new insights into the understanding of neuronal activities before, during, and after seizures. Such research might provide new diagnostic and therapeutic modalities for people with epilepsy.

Glucose Powered Neural Prosthetics

Rahul Sarpeshkar, PhD, Massachusetts Institute of Technology, Cambridge, MA

Nature is a great analog and digital circuit designer. She has innovated circuits in the biochemical, biomechanical, and bioelectronic domains that operate very robustly with highly imprecise parts and with incredibly low levels of power. This talk will discuss how analog, RF, and bio-inspired circuits and architectures have led to and are leading to novel ultra-low power neural prosthetics for the deaf, blind, and paralyzed. It will conclude by discussing how, in the future, some of these highly energy efficient implantable prosthetics may be completely self-powered by harvesting their energy from the glucose in the body.

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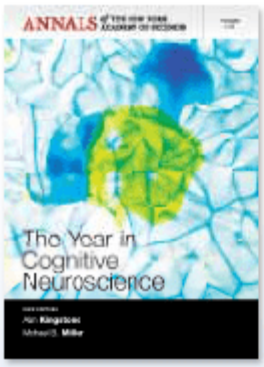
ADDITIONAL INFORMATION



THE YEAR IN COGNITIVE NEUROSCIENCE

Edited by Alan Kingstone (University of British Columbia, Vancouver, British Columbia) and Michael B. Miller (University of California, Santa Barbara, Santa Barbara, California)

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The latest installment of The Year in Cognitive Neuroscience series features in-depth reviews of the major issues and emerging topics in cognitive neuroscience, including the role of strategies in motor learning; efficient coding and the neural representation of value; the emotion paradox in the aging brain; perceptual foundations of bilingual acquisition in infancy; understanding disgust; color through the lens of art practice, history, philosophy and neuroscience; functional imaging studies of emotion regulation; and neuropeptides and social recognition.

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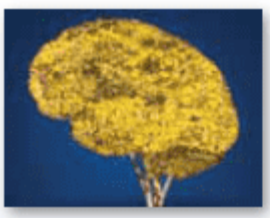

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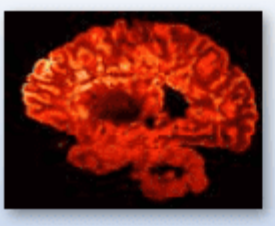
Neural prosthetic devices to replace motor, sensory, and cognitive function lost by disease or trauma hold great therapeutic promise but have not been widely used in people. This conference examined how to use neural prosthetics therapeutically.



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www.nyas.org/MSImaging-eB

This eBriefing provides an overview of the currently accepted and newly emerging imaging techniques for diagnosis and monitoring of multiple sclerosis.

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