

Division of Neurobiology and Behavior

John Koester, PhD, Division Chief

Department of Psychiatry, Columbia University College of Physicians and Surgeons
New York State Psychiatric Institute

Annual Report for July 1, 2007 – June 30, 2008

Overview

The Division of Neurobiology and Behavior consists of seventeen independent basic research laboratories in the Kolb Research Annex. The research philosophy shared by the division's faculty holds that an integrated approach, ranging from cellular and molecular biology to neural systems and behavioral analysis, is required to understand the basis of normal and abnormal human behavior. As part of this endeavor, experimental approaches are complemented by a broad range of theoretical and computational techniques. The main foci of research in the division are on basic science aspects of neural development and on the functions of the nervous system that underlie normal and abnormal behavior. The subjects investigated in these studies range from simple invertebrates to humans. Many of the studies carried out in the division focus on processes such as learning and memory, attention, perception, and affective behavioral traits that may be involved in mental illness. Several ongoing projects may someday contribute to the field's understanding of the etiology of, and new therapeutic approaches to, anxiety disorders, benign-age-related memory loss, cerebral palsy, fragile-X syndrome, Rubinstein-Taybi Syndrome, schizophrenia, and spinal cord trauma.

The Division of Neurobiology and Behavior is also home to four specialized research entities:

- Drs. Kandel and Siegelbaum are members of the Howard Hughes Medical Institute.
- The David Mahoney Center for Mind and Brain Research, which is headed by Dr. Michael Goldberg, includes Drs. Abbott, Das, Ferrera, Gottlieb, Miller, Qian, and Salzman. The members in the Mahoney Center work in the area of cognitive and systems neuroscience.
- The Kavli Institute for Brain Science, headed by Dr. Eric Kandel, includes Drs. Bailey, Siegelbaum, Goldberg, Salzman, Abbott, and Miller. This group focuses on the development of novel experimental and computational strategies for analyzing and deciphering how signaling in neural circuits controls behavior. The goal is to develop more powerful tools to enable one to move from the study of individual nerve cells to that of complex neural systems that underlie higher mental function.

- The Center for Theoretical Neuroscience, directed by Drs. Abbott and Miller, includes Dr. Qian and Fusi. The goals of this center are to determine how neurons encode and process information and to help extend the understanding from single-neuron to network-level analyses of neural systems.

Staff

Laurence Abbott, PhD, Professor of Neuroscience and Physiology & Cellular Biophysics
Craig Bailey, PhD, Research Scientist V
Aniruddha Das, PhD, Assistant Professor of Neuroscience
Vincent Ferrera, PhD, Research Scientist VI
Stefano Fusi, PhD, Assistant Professor of Neuroscience
Claude Ghez, MD, Research Scientist VI
Michael E. Goldberg, MD, Research Scientist VII
Jacqueline Gottlieb, PhD, Assistant Professor of Neuroscience (in Psychiatry)
Robert Hawkins, PhD, Research Scientist VI
Eric R. Kandel, MD, Director; Research Scientist VIII
John Koester, PhD, Research Scientist VII
John Martin, PhD, Research Scientist IV
Kenneth Miller, PhD, Professor of Neuroscience and Physiology & Cellular Biophysics
Ning Qian, PhD, Research Scientist V
Daniel Salzman, MD PhD, Research Scientist VII
Samuel Schacher, PhD, Research Scientist V
Steven Siegelbaum, PhD, Professor of Neuroscience and Pharmacology

Current Research

Systems and Cognitive Neuroscience

Three laboratories study visual cortex with the goal of gaining insights into general principles of cortical function:

- Drs. Aniruddha Das and Gene Sirotin have discovered a novel expectation-related signal in the visual cortex that prepares the brain for any predicted visual task by increasing the flow of arterial blood shortly preceding the task-onset. This finding likely describes a hitherto unknown mechanism of attentional preparation in the brain. Further, this attentional signal has a very different relation to local neuronal activity as compared with stimulus-evoked signals. Simultaneous electrode recordings demonstrated that the novel attentional signal is not predicted by local neuronal spiking or 'gamma band' local field potentials, even though these same measures of local neuronal activity reliably predict visually-evoked signals. This finding may require a major shift in the interpretation of functional brain imaging results obtained with fMRI.

- Dr. Ning Qian's lab has been conducting computational studies on the mechanisms of orientation plasticity and the Pulfrich effect, wherein the lateral movement of an object is perceived as having a depth component. For the orientation project, they have compared systematically the plastic properties of feed-forward and recurrent models of cortical circuitry, and found that only recurrent models can explain the extant experimental data. They have further demonstrated that two key features of the recurrent models, the broadly tuned feed-forward inputs and subsequent sharpening of the inputs by intracortical interactions, are essential for replicating the experimental data. For the Pulfrich project, they have compared models that code motion and binocular disparity either jointly or separately, and found that under physiologically plausible assumptions, only joint coding models can explain the Pulfrich effects. These studies have important implications for the origin of orientation tuning and the nature of motion-depth integration processes in the brain.
- Dr. Ken Miller's research focuses on understanding cerebral cortical circuitry, with a particular emphasis on primary visual cortex as a model system. One main line of work is aimed at understanding the structure of the mature circuitry underlying functional responses. Dr. Miller's research has previously shown how response selectivity can be understood from the structure of feed-forward input to cortex. In current studies of the role of the recurrent intracortical circuitry, he has found that the combination of strong recurrent excitation and strong feedback inhibition is required to explain the modulation of response gain by stimulus context, and that this recurrence yields interesting and novel dynamical properties that both explain previous data and make novel predictions. His other main line of work focuses on understanding the neuronal plasticity that underlies the development of mature cortical circuitry. He has developed a model for the onset of the critical period for visual plasticity in young animals and developed a unified model of three separable components of plasticity that have been separated pharmacologically. The model provides a unified account of a wide variety of data on critical period plasticity and its dynamics.

Dr. Laurence Abbott and colleagues use both mathematical analysis and computer simulation of network models in two projects focused on the flow and integration of information within the brain:

- Neuronal activity recorded in vivo arises from an interaction between ongoing activity generated spontaneously by neural circuits and responses driven by external stimuli. They have determined how a neural network that intrinsically generates complex patterns of activity can remain sensitive to external input. They have found that input not only drives network responses, it also actively suppresses ongoing activity, ultimately leading to a transition in which intrinsic activity is completely eliminated. As a result, internally generated "noise" accompanying a sensory response can, in some cases, be more sensitive to parameters characterizing a stimulus than the response itself. Experimental tests of these ideas are currently underway.

- Cognitive processing requires precise control over signal transmission within and between brain regions. Abbott and colleagues introduced an idea for signal gating called “detailed balance,” in which incoming excitatory signals are normally cancelled by locally evoked inhibition, leaving the targeted layer unresponsive. Transmission is gated on by modulating excitatory and inhibitory gains to upset this balance. The failure modes of these network models exhibit effects reminiscent of clinically observed pathologies, such as the gating deficits and hallucinatory symptoms of schizophrenia, when the balance between excitation and inhibition is not properly maintained.

Three labs are engaged in studies examining the mechanisms that underlie higher cognitive functions such as selective attention and decision-making:

- Dr. Michael Goldberg studies the physiological mechanisms underlying visual attention and spatial perception. He uses the techniques of multiple single unit recording, psychophysics, and computational modeling to understand how the brain chooses attended objects in space and makes eye movements to look at them. In particular he is interested in the contribution of the parietal and frontal lobes to these problems. Projects currently underway in the lab include examining the role of surround inhibition in the decision to move the eyes to one of two competing objects; using the technique of saccadic adaptation to understand the coordinate system of the cortical oculomotor and attentional systems; examining the role of oculomotor proprioception in spatial perception; studying how the brain remembers spatial locations between trials; studying the role of GABA in attentional decisions; and studying mutual inhibition between proprioception and vision.
- Dr. Jacqueline Gottlieb’s lab studies the neural mechanisms of selective attention in the parietal cortex. Results from her laboratory suggest that the parietal lobe participates in the higher-level decisions as to which of many sources of information is most attention-worthy at a particular moment. It also implies that attentional decisions are task-specific and can be trained or optimized for specific behaviors. Current experiments aim to understand the mechanisms of learning and plasticity in the parietal cortex and their relation to flexible decision-making and learning of sensorimotor tasks.
- Dr. Vincent Ferrera’s lab studies the neural basis of decision-making in sensory-motor behavior, with an emphasis on visual perception and visual-motor behavior. They use classical neurophysiological approaches in awake, behaving monkeys. Monkeys are trained to perform visual discrimination tasks while they record the activity of individual neurons in prefrontal cortex and basal ganglia. They complement the lab’s neurophysiological studies with functional imaging (fMRI). They perform fMRI studies in humans and monkeys under identical conditions to make direct cross-species comparisons of activity in brain circuits that underlie higher cognitive function.

Dr. Claude Ghez's research is directed at identifying and distinguishing between the different neural processes responsible for planning and performance of reaching movements in humans. Earlier studies in his laboratory revealed that the mechanisms responsible for learning and generating straight hand trajectories are distinct from those producing the torques that rotate the joints. In the past two years he and his colleagues have discovered that the postural control mechanisms that assure hand stability at the desired endpoint are themselves superimposed on trajectory commands. Recent experiments have shown that the former depend importantly on proprioceptive feedback to assure positional control while the latter are more closely regulated by errors estimated from visuospatial information arising during the course of the movement. These findings imply that different brain regions and networks are used for each mode of control and are recruited in parallel. Current work is aimed at developing valid and effective methods for using sensory substitution to enhance performance in normal subjects and in patients with sensory and motor deficits.

Organisms decide to initiate a behavior in the context of continuously changing and often ambiguous stimuli. The nervous system must evaluate such stimuli and make discrete decisions. John Koester and colleagues have used the neural circuit that controls *Aplysia* consummatory feeding behaviors as a model system for exploring cellular and circuit processes that underlie choice and decision-making and their modulation. Most recently they have described the neural correlates of the delay period that precedes each consummatory act, in terms of the voltage-gated and synaptically gated ion channels that control the firing activities of individual identified circuit elements.

Learning and Memory

Five labs use the giant neurons of the sea slug *Aplysia californica* and/or the mammalian hippocampus as model systems to study the cellular and molecular mechanisms of learning and memory:

- Dr. Craig Bailey, in collaboration with Dr. Kandel, has continued to examine the molecular events that underlie both the initiation and maintenance of learning-related synaptic growth in *Aplysia*. Recently, they have identified a temporal memory window wherein local protein synthesis is engaged in synapse stabilization. This late phase of local protein synthesis lasts for approximately two days and is importantly regulated by the *Aplysia* homolog of cytoplasmic polyadenylation element binding protein (CPEB), which promotes translational activation. These results define a specific stabilization phase for long-term synaptic plasticity and demonstrate that synapses formed after a memory-inducing stimulus are initially labile and require subsequent events involving sustained CPEB-dependent local protein synthesis to acquire the more stable properties of mature synapses necessary for the persistence of memory storage.

- Dr. Sam Schacher's lab has found that in *Aplysia*, formation and maturation of specific synapses during development share common cellular and molecular mechanisms with long-term synaptic plasticity at those very same synapses that are cellular analogs of learning and memory in the adult. They have found that stimulus- or target-dependent increases in the activation of protein kinase C is required for the synthesis and release of a neurotrophin-like peptide from sensory neurons, and that the peptide plays a crucial role in the formation and maturation of specific synapses and long-term facilitation of the synapses. Local translation of the mRNA encoding that neuropeptide, after being transported to the synapses, is critical for both the synapse formation and the synaptic plasticity underlying learning. The secretion of the neurotrophin-like peptide near synaptic terminals contributes to synapse maturation and long-term plasticity. These studies suggest that a common response to external stimuli – secretion of a neuropeptide – regulates synapse formation both during development and when stimuli are sufficient to produce long-term memories in the adult.
- Dr. Robert Hawkins' lab has continued their studies of neuronal mechanisms underlying long-term learning in *Aplysia* and in mammalian hippocampus. In *Aplysia* they have continued to study mechanisms for short-, intermediate, and long-term facilitation at sensory-motor neuron synapses in isolated cell culture and for behavioral dishabituation and sensitization of siphon withdrawal in a semi-intact preparation. They have found in both systems that presynaptic mechanisms play important roles in the early stages of facilitation, and that postsynaptic mechanisms become important later on. Moreover, spontaneous transmitter release from the presynaptic neurons recruits the postsynaptic mechanisms of facilitation. In parallel studies of the mammalian hippocampus they have found that long-term synaptic potentiation is accompanied by rapid (10 min) and more gradual growth of synaptic structures and aggregation of both pre- and postsynaptic proteins, which require protein synthesis for their long-term maintenance.
- Dr. Steven Siegelbaum's laboratory examines the cellular and molecular mechanisms that underlie the regulation of long-term synaptic plasticity that is important for learning and memory. Their focus is on the hippocampus, a region of the brain important for spatial memory, where they examine how the HCN1 (hyperpolarization-activated cation-permeant) ion channels regulate the integration of synaptic information and synaptic plasticity in CA1 pyramidal neurons, which is a key step in memory-storage. Studies from other labs demonstrated that HCN1 levels can be up-regulated by patterns of neural activity important for memory storage and down-regulated by pathological activity associated with seizures. However, the mechanism for this regulation is not known. In the past year the Siegelbaum lab has found that HCN1 channels are regulated by a brain-specific cytoplasmic protein TRIP8b. Different isoforms of TRIP8b have opposing effects to either up- or down-regulate the trafficking of HCN1 to CA1 dendrites. In addition, all TRIP8b isoforms modulate the voltage-gating of these channels. Thus, TRIP8b functions as an auxiliary subunit of

HCN1 channels that may provide a mechanism for the activity-dependent regulation of HCN1 expression and neural activity.

- The Kandel lab has explored bi-directional communication between the synapse and the nucleus during learning and memory storage. Using *Aplysia* sensory-motor neuron co-culture as a model neural circuitry for this research they have asked: 1) whether the nucleus to synapse communication by axonal transport is affected by learning induced signals? 2) what molecules are transported in response to stimulation, and 3) whether the transport could be specific to stimulated synapses? Their approach to isolate and characterize kinesin transport complexes in this circuitry has yielded valuable insights into the molecular mechanisms underlying memory storage. They have found that molecular motor kinesin, involved in fast axonal transport, is transcriptionally upregulated by serotonin, a physiological signal produced in the intact animal. This upregulation is critical for the induction of long-term memory storage, but necessary for the short-term memory or for the maintenance of long-term memory. They have further shown that by simply enhancing fast axonal transport, they could facilitate induction of long-term memory storage. Thus, this up-regulation of kinesin is a rate-limiting step in the storage of long-term memory. Additionally, they have identified proteins involved in the active zone formation such as piccolo and bassoon, and shown that proteins involved in synapse formation such as neuroligin and neuroligin, are protein cargos transported by kinesin.

The neurotrophin family of secreted growth factors and their cognate Trk tyrosine kinase receptors play central roles in mammalian brain development and function but have not been found in invertebrates. In a major advance a postdoctoral fellow in the Kandel lab, Stefan Kassabov, recently cloned the first invertebrate neurotrophin Trk receptor in *Aplysia californica* and showed that it is conserved both structurally and functionally with its mammalian counterparts. He then went on to identify and clone the even more elusive cognate neurotrophin ligand for this receptor – ApNT1, and showed that this is a single ancestral neurotrophin gene which has a novel multi-exon gene structure. After proving that this is a functional receptor-ligand couple Stefan demonstrated that this signaling system controls various growth processes in *Aplysia* neurons like neurite outgrowth and branching and synaptogenesis. It also regulates both the induction and maintenance of serotonin dependent long-term facilitation (LTF) in sensory-motor neuron co-cultures. In addition to clarifying a longstanding conundrum in evolutionary biology, this finding enables analysis of the role of this key signaling system in learning-related growth in the *Aplysia* sensory-motor co-culture system at a level of detail previously unattainable in mammalian model systems.

In collaboration with Dr. Joy Hirsch's neuroimaging facility within the Program for Imaging and Cognitive Sciences, Kandel and colleagues are currently evaluating the results of a study investigating the neural circuitry

underlying learned safety in people using a paradigm paralleling the recently published mouse study. They have found that the presentation of the safety signal leads to a pattern of brain activity supporting the proposed antidepressant role of learned safety in humans.

Dr. Stefano Fusi applies theoretical analyses in combination with empirical approaches to study the role of synaptic complexity in learning and memory. Memories are continuously overwritten by ongoing plasticity and they are forgotten rapidly when the synapses are restricted to vary in a limited range, as it is reasonable to assume for any realistic synapse. In 2005 he introduced with Dr. Abbott and P.J. Drew a model of a synapse that has a cascade of states, each characterized by a different degree of plasticity. Memories are stored by modifying both the synaptic efficacy and the degree of plasticity (metaplastic modifications). The cascade model is meant to capture the aspects of the biological complexity of the synapse that are important for memory preservation. In fact, the cascade model outperformed synaptic models that did not have metaplastic states, indicating that biological complexity plays an important role. In recent years he continued to study the memory problem along three lines of research:

- Theoretical: can memory performance be improved without resorting to synaptic complexity? The lab has preliminary evidence that biological complexity is actually necessary, and that both sparseness and different ways of imposing synaptic boundaries cannot solve the problem of catastrophic forgetting.
- Experimental: he started a joint project with John Krakauer (neurology) to model how human subjects adapt to a cursor rotation. Interestingly, adaptation is more rapid upon relearning. They can explain the data with a simple model based on the cascade synapses, in which adaptation to cursor rotation restores the plasticity of the synapses.
- Applied: metaplasticity can greatly extend the memory lifetime of biological systems. The same principles could be used to build an efficient electronic memory device. As the microelectronics technology is reaching its physical limits, there is an urgent need to develop new approaches that are robust to noise and heterogeneities. As part of collaborative project with IBM and K. Boahen at Stanford, Fusi is involved in developing a neuromorphic device that imitates basic brain functions including simple forms of learning and memory.

Dr. Daniel Salzman's lab studies the neuronal basis of reinforcement learning and emotion in non-human primates. Using single neuron recordings from awake behaving monkeys they showed that the amygdala has neurons that assign positive or negative values to conditioned stimuli, and that amygdala activity correlates with the subject's learning those associations. They have also discovered that activity in the amygdala encodes unexpected rewards and punishments. Such activity may underlie the role of

the amygdala in both valence-specific emotional processes, like fear-learning, as well as in valence non-specific processes, such as arousal and enhanced attention.

Translational Research

John Martin's laboratory works in two areas of relevance to clinical problems. In the first set of experiments they study a process that is defective in cerebral palsy patients – the postnatal development of the corticospinal tract, the principal motor pathway for controlling voluntary movements. When neural activity of the corticospinal tract is limited in developing animals, aberrant connections form with spinal motor circuits and movements become impaired. Rebalancing activity later in development can restore normalcy to connections and motor function. In the second set of experiments they are exploring novel approaches for promoting motor function after brain or spinal cord injury. They found that electrical stimulation of corticospinal tract axons that survive after injury promotes reactive sprouting and strengthens their connections. In addition, they have developed an approach to bridging the gap across a spinal cord injury, using a novel nerve bypass. These findings show that activity-dependent processes and constructing novel spinal circuitry can be implemented to repair the damaged motor systems.

Education

The faculty of the Division of Neurobiology and Behavior is actively involved in training medical, dental and pre-doctoral students and post-doctoral fellows and post-graduate clinical trainees. Together with their colleagues from throughout the university's neuroscience community, they organize and teach the course in basic neural science for first year medical and dental students, several graduate courses in neuroscience for pre-doctoral students, and a CME review course in basic and translational neuroscience. The pre-doctoral and postdoctoral trainees in the division are supported by three training grants from NIH.

New Grant Awards

- Gatsby Initiative in Brain Circuitry Neural Correlates of Context-Dependent Actions in Prefrontal and Parietal Cortex. (Gottlieb)
- Gatsby Initiative in Brain Circuitry: Brain Circuitry for Simple Contextual Modulation and Perceptual Learning in the Human Visual System (Das)
- Mathers Charitable Foundation: Genomic Approaches to Neuronal Diversity and Plasticity (Kandel)
- NARSAD: From Thought to Action: Interactions between Prefrontal and Parietal Cortex for Context-Dependent Actions (Gottlieb)
- NEI R01: A Study of the Neurophysiology of Visual Search (Goldberg)
- NIDA R01: Neural Mechanisms Underlying Reinforcement Learning (Salzman)
- NIDA R01: A Molecular Analysis of the Gateway Hypothesis in Mice (Kandel)

- NIMH R01: HCN1 Channels in Hippocampal Function and Spatial Memory (Siegelbaum, Kandel)
- NIMH R01: Neurophysiology Underlying Neural Representations of Value (Salzman)
- Professional Schools Diversity Fellowship, Columbia University, Neural Mechanisms of Attention, Reward and Plasticity (Gottlieb)
- The Dana Foundation Program in Brain and Immuno Imaging: Relating fMRI Signals to Neuronal Activity using a Novel Optical Imaging Technique in Alert Monkey (Das)

Honors

Dr. Michael Goldberg:

- President-Elect, Society for Neuroscience

Dr. Eric Kandel:

- Doctor of Philosophy, Honoris Causa, the Weizmann Institute of Science, Israel
- Doctor of Science, Honoris Causa, Watson School of Biological Sciences
- Doctor of Science, Honoris Causa, Harvard University
- Keynote Lecturer, Karolinska Institute Symposium, Stockholm, Sweden
- Royal Society Public Lecture, London, UK
- Nobel Symposium: Genes, Brain and Behavior, Stockholm, Sweden
- Kavli Prize Public Lecture, Trondheim, Norway

Dr. Daniel Salzman:

- Harold and Golden Lampert Award for Excellence in Clinical Science Research, Columbia University

Highlights

- Dr. Vincent Ferrera and colleagues have shown that categorical decision-making in humans involves a fronto-striatal cortical network different from the network involved in signal detection decisions. In ongoing research using fMRI in awake monkeys, they have found that monkeys have a categorical decision-making network similar to that in humans. This finding validates the hypothesis that the monkey can be used as a model system to understand the physiology of decision-making in humans.
- Drs. Eric Kandel and Daniela Pollak have found that learned safety acts as a behavioral antidepressant in mice. It induces cell-biological and molecular changes characteristic of pharmacological antidepressants (i.e. effect on survival of newly generated hippocampal neurons and increased expression of BDNF in the dentate gyrus of the hippocampus) while acting through serotonin-independent signaling pathways.
- Memory storage is thought to depend on activity of neurons in the hippocampus. Abnormal patterns of activity can however lead to seizures. Dr. Siegelbaum and

colleagues have recently described a new mechanism that regulates hippocampal electrical activity through the actions of a protein that controls the trafficking of an ion channel within hippocampal neuron dendrites, the site of synaptic input.

- Ken Miller and colleagues have found that cat primary visual cortex, which is a model system for cerebral cortical processing more generally, operates in a regime in which recurrent excitation is strong enough to drive cortical activity to instability, and that this instability is controlled by feedback inhibition.

Publications:

Abbott LF, Luo SX: A step toward optimal coding in olfaction. *Nature Neurosci* 2007; 10:1342-1343.

Abbott LF, Rohrkemper R: A simple growth model constructs critical avalanche networks. *Prog Brain Res* 2007; 165:13-19.

Antonov I, Ha T, Antonova I, Moroz LL, and Hawkins RD: Role of nitric oxide in classical conditioning of siphon withdrawal in *Aplysia*. *J Neurosci* 2007 27:10993-11002.

Bailey C, Kandel ER: Synaptic remodeling, synaptic growth and the storage of long-term memory in *Aplysia*. *Prog Brain Res* 2008; 169:179-198

Bailey CH, Kandel ER: Activity-dependent remodeling of presynaptic boutons In: L Squire (ed), *New Encyclopedia of Neuroscience*, Elsevier Press, 2008

Beg AA, Sommer JE, Martin JH, Scheiffele P Alpha2-chimaerin is an essential EphA4 adapter in the assembly of neuronal locomotor circuits *Neuron* 2007; 55:768-778.

Belova MA, Paton JJ and Salzman CD Moment to moment tracking of state value in the amygdala. *J Neurosci* 2008; 28:10023-30.

Ben Dayan Rubin DD, Fusi S: Long memory lifetimes require complex synapses and limited sparseness, *Frontiers in Comput Neurosci* 2007; 1:7.

Brader JM, Senn W and Fusi S: Learning real world stimuli in a neural network with spike driven synaptic dynamics. *Neural Comput* 2007; 19:2881-2912.

Brozovic M, Abbott LF, Andersen RA: Mechanisms of gain modulation at single neuron and network levels *J Comput Neurosci* 2008; 25:158-168

Brus M, Carmel JB, Chakrabarty S, Martin JH: Electrical stimulation of spared corticospinal axons augments connections with ipsilateral spinal motor circuits after injury. *J Neurosci* 2007; 27:13793-13801

Campos L, Chakrabarty S, Haque R, Martin JH: Regenerating motor bridge axons refine connections and synapse on lumbar motoneurons to bypass chronic spinal cord injury: *J Comp Neurol* 2008; 506:838-850

Cassanello C, Ferrera VP: Neuronal responses to moving targets in monkey frontal eye field. *J Neurophysiol* 2008; 100:1544-56

Dudman JT, Tsay D, Siegelbaum SA: A role for synaptic inputs at distal dendrites: instructive signals for hippocampal long-term plasticity. *Neuron* 2007; 56:866-879

Friel K, Martin JH: Rebalancing corticospinal activity promotes recovery of motor skill and anatomical integrity after inactivation during a critical period. *J Neurosci* 2007; 27:11083-11090

Fusi S: A quiescent working memory *Science* 2008; 319:1495-1496.

Ganguli S, Bisley JW, Roitman JD, Shadlen MN, Goldberg ME, Miller KD: One-dimensional dynamics of attention and decision making in LIP. *Neuron* 2008; 58: 15-25

Gee AL, Ipata AE, Bisley JW, Gottlieb J, Goldberg ME: On the agnosticism of spikes: salience, saccades, and attention in the lateral intraparietal area of the monkey *Attention and Performance* 2007; ed. P Haggard, Y Rosetti and M Kawato, Oxford University Press XXII: 1-26

Gee AL, Ipata AE, Gottlieb J, Bisley JW, Goldberg ME: Neural enhancement and pre-emptive perception: the genesis of attention and the attentional maintenance of the cortical salience map. *Perception* 2008; 37: 389-400

Ghez C, Scheidt R, Heijink H: Different learned coordinate frames for planning trajectories and final positions in reaching. *J Neurophysiol* 2007; 98:3614-3626.

Gottlieb, J, Balan P F, Oristaglio, J and Schneider D: Task specific computations in attentional maps. *Vision Research* 2008; epub ahead of print

Grinband J, Wager T, Lindquist M, Ferrera VP, Hirsch J: Detection of time-varying signals in event-related fMRI designs. *NeuroImage* 2008; Published Online

Hawkins RD: Trans-synaptic signaling by NO during learning-related synaptic plasticity. In Byrne, J (Ed) *Learning and Memory: A Comprehensive Reference* 2008; Elsevier, Oxford, UK

Hawkins, RD, Kandel, ER, and Bailey, CH: Presynaptic facilitation. In Squire, L R (Ed.) *Encyclopedia of Neuroscience* 2008, Academic Press, Oxford, UK

Hu JY, Chen Y, Schacher S: Multi-functional role of protein kinase C in regulating the formation and maturation of specific synapses. *J Neurosci* 2007; 27:11712-11724

Hu JY, Chen Y, Schacher S: Protein kinase C regulates synthesis and secretion of a neuropeptide required for activity-dependent long-term synaptic facilitation. *J Neurosci* 2007; 27:8927-8939

Huang Y-Y, Kandel ER, and Levine, A Chronic nicotine exposure induces a long-lasting and pathway-specific facilitation of LTP in the amygdala *Learning & Memory*; 2008; 15:603-610

Hurwitz I, Ophir A, Korngreen A, Koester J, Susswein AJ Currents contributing to decision making in neurons B31/B32 of *Aplysia*. *J Neurophysiol* 2008; 99:814-30

Ipata AE, Gee AL, Bisley JW, Goldberg ME: Neurons in the lateral intraparietal area create a priority map by the combination of disparate signals. *Exp Brain Res* 2008

Itskov V, Abbott LF: Pattern capacity of a perceptron for sparse discrimination *Phys Rev Lett* 2008; 101:018101

Jeffries SM, Bisley JW, Kusunoki M, Goldberg ME: Rhesus monkeys mislocalize saccade targets flashed for 100 ms around the time of a saccade. *Vision Res* 2007; 47: 1924-34

Kim J, Jung S-Y, Lee KY, Park S, Choi, J-S, Lee C-J, Kim H-S, Choi Y-B, Scheiffel P, Bailey CH, Kandel ER, Kim, J-H: Neuroligin-1 is required for normal expression of LTP and associative fear memory in the amygdala of adult animals. *Proc Nat Acad Sci, USA* 2008; 105:9087-9092

Koendgen H, Geisler C, Fusi S, Wang X-J, Luscher H-R and Giugliano M The dynamical response properties of neocortical neurons to temporally modulated noisy inputs in vitro. *Cerebral Cortex* 2008; 18:2086-2097.

Lee, Y-S, Bailey, C H, Kandel, E R, and Kaang B-K Transcriptional regulation of long-term memory in the marine snail *Aplysia*. *Molecular Brain* 2008; 1:3-40

Miniaci MC, Kim J -H, Puthenveetil S, Si K, Zhu H, Kandel ER, Bailey CH: Sustained CPEB-dependent local protein synthesis is required to stabilize synaptic growth for persistence of long-term facilitation in *Aplysia*. *Neuron* 2008; 59:1024-1036

Mitra S, Indiveri G, Fusi S: Learning to classify complex patterns using a VLSI network of spiking neurons, *NIPS Proceedings* 2008;.

Mitra S, Indiveri G, Fusi S: Robust classification of correlated patterns with a neuromorphic VLSI network of spiking neurons. *BioCAS Proceedings* 2007; online

Nicholls RE, Alarcon JM, Malleret G, Carroll RC, Grody M, Vronskaya S, Kandel ER: Transgenic mice lacking NMDAR-dependent LTD exhibit deficits in behavioral flexibility. *Neuron* 2008; 58:104-117.

Palmer SE, Miller KD: Effects of inhibitory gain and conductance fluctuations in a simple model for contrast-invariant orientation tuning in cat V1. *J Neurophysiol* 2007; 98:63-78

Parga N, Abbott LF: Network model of spontaneous activity exhibiting synchronous transitions between up and down states. *Frontiers in Neurosci* 2007; 1:57-66.

Pian P, Bucci A, DeCostanzo A, Robinson RB, Siegelbaum SA: Modulation of cyclic nucleotide-regulated HCN channels by PIP2 and its role in signaling through receptors coupled to phospholipase C. *European J Physiol*; 2007; 455:125-145.

Pollak DD, Monje FJ, Zuckerman L, Denny CA, Drew MR, Kandel ER: An animal model of a behavioral intervention for depression. *Neuron* 2008; 60: 149-161.

Salimi I, Friel K, Martin JH: Pyramidal tract stimulation restores normal corticospinal tract connections and visuomotor skill after early postnatal motor cortex activity blockade. *J Neurosci* 2008; 28:7426-7434.

Scheidt RA, Ghez C: Separate adaptive mechanisms for controlling trajectory and final position in reaching. *J Neurophysiol* 2007; 98:3600-3613

Sharpee TO, Miller KD, Stryker MP: On the importance of static nonlinearity in estimating spatiotemporal neural filters with natural stimuli. *J Neurophysiol* 2008; 99:2496-509

Squire L, Kandel, ER: *Memory: From Mind to Molecules*, 2nd Ed. 2008; Roberts and Company, Colorado

Tsay D, Dudman JT, Siegelbaum SA: HCN1 channels constrain synaptically evoked Ca²⁺ spikes in distal dendrites of CA1 pyramidal neurons. *Neuron* 2007; 56:1076-1089

Vogels TP, Abbott LF: Gating deficits in model networks: a path to schizophrenia? *Pharmacopsychiatry* 2007; 40:S73-S77

Xu H, Dayan P, Lipkin RM, Qian N: Adaptation across the cortical hierarchy: Low level curve adaptation affects high level facial expression judgments. *J Neurosci* 2008, 28:3374-3383

Zhang M, Wang X, Goldberg ME: Monkey primary somatosensory cortex has a proprioceptive representation of eye position. *Prog Brain Res* 2008; 171:37-45

Zhou L, Siegelbaum SA: Effects of surface water on protein dynamics studied by a novel coarse-grained normal mode approach. *Biophys J* 2008; 94:3461-3474