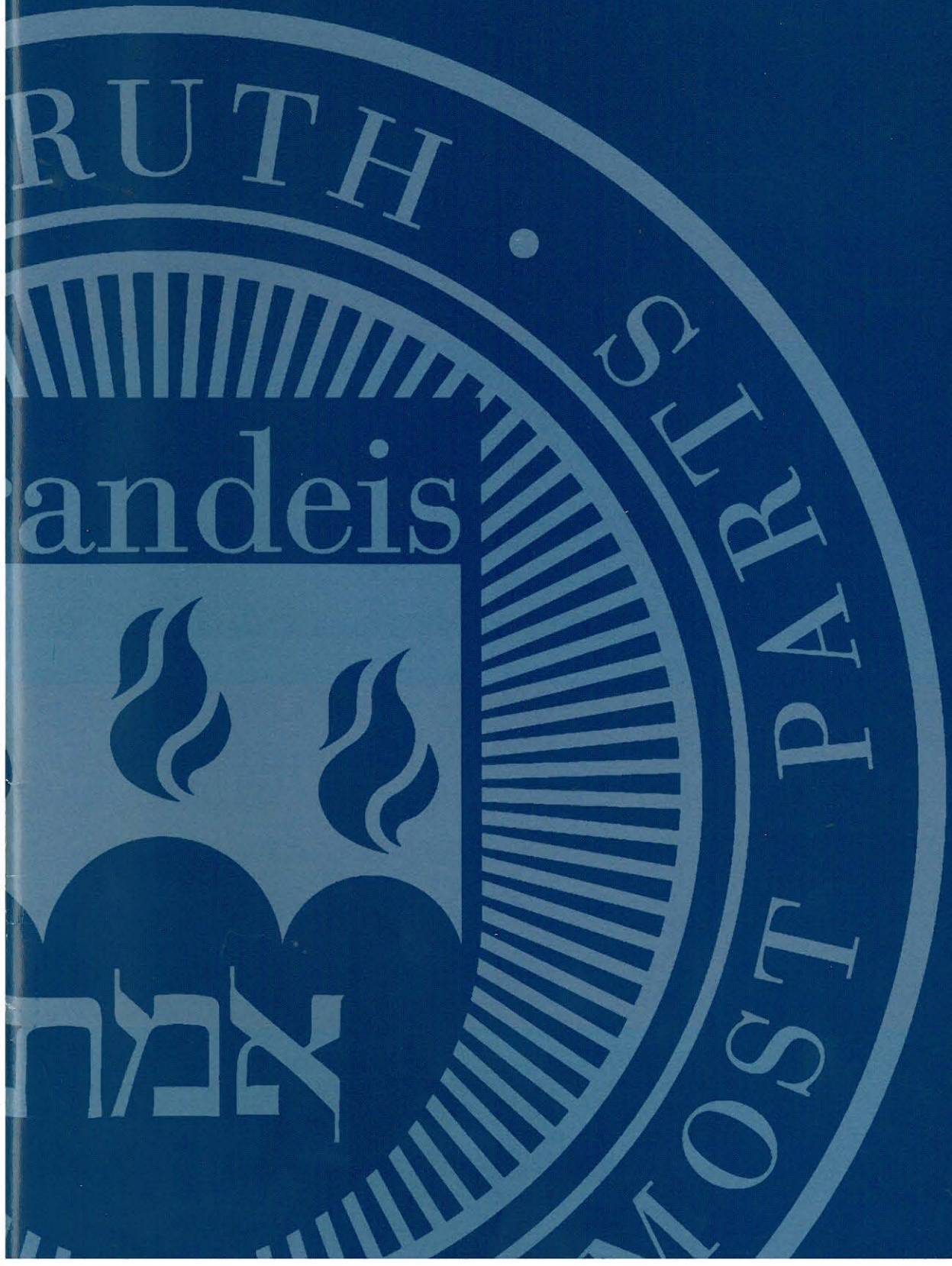
Brandeis University

Benjamin and Mae Volen National Center for Complex Systems

The M. R. Bauer Foundation Colloquium Series, Distinguished Lecturer Series, and Scientific Retreat

August 2008



The M. R. Bauer Foundation Colloquium Series, Distinguished Lecturer Series, and Scientific Retreat 2007–2008 Summary

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The 2008 M. R. Bauer Foundation Colloquium Series, Annual Scientific Retreat, and Distinguished Guest Lecturer Series

Introduction

As in previous years, I am very pleased to offer this introduction to the proceedings of the M. R. Bauer Foundation Colloquium Series, Scientific Retreat, and Distinguished Guest Lecturer Series at Brandeis University's Volen National Center for Complex Systems. For fourteen years, the generosity of the M. R. Bauer Foundation has underwritten these lectures, presentations, and discussions, all aimed at increasing the scientific community's knowledge and understanding of neuroscience. As these proceedings indicate, the foundation-sponsored activities have enriched the scientific dialogue within this field and will continue to do so in the coming years. I extend my own and the university's gratitude for the continuing support that makes these exchanges of information possible.

The 2007–2008 M. R. Bauer Colloquium Series featured six presentations by leaders within the field of neuroscience. These distinguished scientists represent prestigious universities from across the country. Four of the six speakers addressed the question of how the nervous system detects and encodes sensory information from the environment. **Peter Schiller**, PhD, professor in the Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, presented a topic titled, "How the Brain Moves Your Eyes About." The complex process of moving the eyes accurately from one location to another with rapid, saccadic eye movements is accomplished with the aid of numerous brain areas. His research focuses on the role of cortical brain areas V1 and V2 in generating eye movements. **Pamela Reinagel**, PhD, assistant professor of biology, University of California, San Diego, spoke on "Thalamic Coding." Dr. Reinagel discussed the possibility that thalamic bursts in the mammalian brain contain visual information. She reviewed evidence from animal models suggesting that visual information is encoded by such bursts, citing recent work that charts the different levels of such visually driven bursts. **Leslie B. Vosshall**, PhD, associate professor in the Laboratory of Neurogenetics and Behavior at the Rockefeller University and a Howard Hughes Medical Institute Investigator, moved from visual sensation to encoding of smell, with a talk titled, "A Glimpse into the Olfactory Universe of Insects and Humans." The lecture was divided into two parts. The first part discussed recent work deciphering the mechanism of insect olfactory signal transduction, and the second part presented a large-scale human olfactory psychophysical study in which interindividual differences in smell perception are linked to genetic polymorphisms in a human odorant receptor gene. **Kenneth Lohmann**, PhD, professor in the Department of Biology and Curriculum in Neurobiology, University of North Carolina, Chapel Hill, discussed his work in a lecture titled, "Beyond the Five Senses: The Maps, Compasses, and Sensory Biology of Sea Turtle Navigation." He described the extraordinary feats of orientation and navigation required for long-distance travel and the unique sensory, behavioral, and neural mechanisms that enable turtles to guide themselves across vast expanses of seemingly featureless ocean. The remaining two speakers addressed two fundamental issues in neuroscience. **Gene Robinson**, PhD, professor at the Institute for Genomic Biology at the University of Illinois, Urbana-Champaign, delivered a talk on "Feeding-Related Molecular Pathways and Division of Labor in Honey Bees." Dr. Robinson's laboratory studies how genes influence social behavior, and how social behavior in turn influences genome functioning. His group also researches other molecular mechanisms and related gene expression. The sixth speaker, **Don Cleveland**, PhD, professor at the Ludwig Institute for Cancer Research, Departments of Neurosciences and Cellular and Molecular Medicine, University of California, San Diego, and the Howard Hughes Medical Institute, delivered a lecture called, "From Charcot to Lou Gehrig: mechanism and treatment of ALS." His team's research implicates a central role of mutant SOD1 damage within non-motor neurons in initiating motor neuron degeneration. His group also has worked to develop gene therapies for targeting genes with certain critical features throughout the central nervous system (CNS).

Now in its tenth year, the M. R. Bauer Distinguished Guest Lecturer Series featured two visitors to the Volen Center—Daniel Choquet and Ralph Greenspan. During their lectures and the additional time they were able to spend with Brandeis faculty, postdocs, and students, these dynamic scientists offered their perspectives on intriguing subjects in neuroscience. **Daniel Choquet**, professor, Physiologie Cellulaire de la Synapse, CNRS-Université de Bourdeaux, France, conducts research on the fundamental question of how

brain cells communicate with one another. In his formal presentation to the Brandeis neuroscience community he spoke on the topic, "New Functions for AMPAR Mobility in Fast Synaptic Transmissions." Choquet described how his lab has established that ionotropic AMPA-type glutamate receptors (AMPARs) enter and leave synapses through lateral diffusion in the plane of the membrane. Choquet also has shown that receptor mobility is highly regulated by a set of protein-protein interactions. Recently, the Choquet lab investigated the function of the mobile AMPAR population in fast synaptic transmission. They found that the mobility of surface AMPARs participates in the recovery of synaptic depression. **Ralph Greenspan**, senior fellow in experimental neurobiology, The Neurosciences Institute, San Diego, California, gave as his formal presentation a talk titled, "From Sleep to Consciousness in *Drosophila*: the Sublime to the Ridiculous." His team's research explores the "cognitive potential" of the fruit fly *Drosophila melanogaster*. The Greenspan lab uses genetic, physiological, and behavioral approaches to investigate this potential and to study this fly's brain at various states, from deep sleep to completely alert status. At various levels, the fruit fly's brain shares some features of the mammalian brain when in a similar state.

One of the most important features of the M. R. Bauer Distinguished Guest Lecturer Series is the time that the guest lecturers spend on campus. They are able to immerse themselves in the Brandeis community for several days, exchanging ideas and building scientific relationships between their home institution and Brandeis.

The 2008 Volen Center Scientific Retreat, "A Neurogenetics Celebration to Honor Drs. Kalpana White and Jeffrey Hall," featured intriguing presentations from fourteen scientists from other universities. This two-day event honored the careers of Drs. Jeffrey Hall and Kalpana White, both recently retired Brandeis faculty, and the groundbreaking contributions they made to the beginnings of two fields: neurogenetics and behavioral genetics. It was held on the Brandeis campus and welcomed more than one hundred members of the Brandeis scientific community, as well as many guests. The speakers in this very special event all began their careers in the Brandeis laboratories of Jeffrey Hall, Kalpana White, or with Michael Rosbash, a close colleague and friend. Topics ranged from emerging directions in the study of the body's internal clock and how mosquitoes sense smells, to humorous recollections of time spent in the Hall and White laboratories. The keynote speaker was **Liqun Luo**, PhD, Stanford University and Howard Hughes Medical Institute, whose address was titled, "Probing Neural Circuits with Genetic Mosaics." Other presenters and titles included: **Paul Hardin**, PhD, Texas A&M University, "A Brief History of Clocks outside the Brain"; **Joel Levine**, PhD, University of Toronto at Mississauga, "Homage à un Clochard ('P. P. Dickey' Redux)"; **Jae H. Park**, PhD, University of Tennessee at Knoxville, "Neuropeptides in *Drosophila*"; **Kathleen Siwicki**, PhD, Swarthmore College, "Pheromones and Memory of Unsuccessful Courtship"; **Ralph Greenspan**, PhD, The Neurosciences Institute, "This Is Your Life, Jeffrey Hall: The Early Years"; **Vivian Budnik**, PhD, University of Massachusetts Medical School, "Wnts of change"; **Larry Zwiebel**, PhD, Vanderbilt University, "Exploring Mosquito Olfaction to Examine and (Perhaps) Modulate Critical Behaviors of Disease Vector Insects"; **Tony James**, PhD, University of California, Irvine, "Engineering Pathogen Resistance in Vector Mosquitoes"; **Ana Regina Campos**, PhD, McMaster University, "Chicken Soup for the Fly Pusher's Soul"; **Bentley Fane**, PhD, University of Arizona, "Structure, Function, and Evolution of Viral Scaffolding Proteins in a Two-Scaffolding Protein System"; **Josh Huang**, PhD, Cold Spring Harbor Laboratories, "Genetic Dissection of GABA Inhibitory Circuitry in Mice"; **Sandhya P. Koushika**, PhD, National Centre for Biological Sciences, "Regulation of Mitochondrial Transport in *C. elegans* Neurons"; and **Bambos Kyriacou**, PhD, University of Leicester, "From Brandeis to Infinity and Beyond."

The M. R. Bauer Foundation Colloquium Series, Scientific Retreat, and Distinguished Guest Lecturer Series at Brandeis University engage, challenge, and enrich our faculty, researchers, and students. Also, these forums help to build connections between visiting scientists and their counterparts on this campus and between Brandeis and other institutions. The scientific community is certainly global, and the M. R. Bauer Foundation–sponsored activities contribute to a worldwide dialogue in meaningful ways. So many synergies take place when researchers have the opportunity to step out of the laboratory and to speak with their colleagues who may be approaching

the same topic from a different perspective. It is my pleasure to thank the M. R. Bauer Foundation for its longstanding commitment to learning and discovery at Brandeis.

Arthur Wingfield, D.Phil.
Nancy Lurie Marks Professor of Neuroscience and
Director, Volen National Center for Complex Systems

The M. R. Bauer Distinguished Lecturer Series Summaries 2007–2008

Introduction

Diane Ackerman, a twentieth-century American poet and naturalist, once wrote, "We live on the leash of our senses." Although many of us only think of our senses as adding color, shape, or sound to our lives, this quote rightfully points out that our senses act as the sole connection between our minds and the outside world. Ackerman's words capture the essence of several of this year's M. R. Bauer Colloquium Series speakers, whose talks explored the biological underpinnings of this "leash."

Peter Schiller, PhD
Professor
Department of Brain and Cognitive Sciences
Massachusetts Institute of Technology
Cambridge, Massachusetts
December 3, 2007

How the brain moves your eyes about

In presenting these summaries we have departed from our usual practice of following the order of the speakers' visits, but instead have organized them to "tell a story" about human and animal senses and ending with the role of genes in behavior and disease. We begin with Dr. Peter Schiller who described his intriguing research dedicated to understanding eye movements in human vision.

Eye movements play a central role in the analysis of the visual scene. These movements are known as saccades, and are involved in refocusing the eyes to different stimuli. Humans make about three visually guided saccadic eye movements per second and more than 170,000 saccades a day. People perform this task with the greatest of ease and for the most part are not even aware of doing so. The retinae of primate eyes are highly specialized. Each eye has a small central area, known as the fovea, which is capable of high-acuity vision. Thus, shifting gaze from one location to another is essential for detailed, fine-grain analysis of the visual scene. With each shift in gaze, a new set of images to be analyzed appears on the retinae. Concurrently, a decision has to be made about where to shift the eyes next. This complex process of moving the eyes accurately from one location to another with rapid, saccadic eye movements is accomplished with the aid of numerous brain areas. These areas include the brainstem oculomotor centers, the superior colliculus, cortical areas V1, V2, the lateral intraparietal area, and the frontal and medial eye fields. The role of these areas in generating eye movements has been studied extensively using a variety of methods that include behavioral measures, anatomical studies, neural recordings, electrical microstimulation, and pharmacological manipulation. Using these methods, the research established that the cortical brain areas involved in saccade generation form two major systems: the *anterior* and the *posterior.* The *anterior system* from the frontal and medial eye fields has direct access to the brainstem oculomotor centers, whereas the *posterior system* gains access to the brainstem through the superior colliculus. Disruption of the *posterior system* eliminates a special class of saccadic eye movements, which have been called express saccades. Express saccades are generated with significantly shorter latencies than are regular saccades. Disruption of the *anterior system* produces deficits in target selection with saccadic eye movements. When both systems are inactivated, visually guided saccadic eye movements are eliminated. This suggests that these two systems are essential parts of saccadic eye-movement generation in primates. By manipulating GABAergic inhibitory circuits with local infusions of GABA agonists and antagonists, the Schiller lab has established that these inhibitory circuits play a central role in area V1 for visual analysis and in saccade generation in the frontal eye fields and the superior colliculus.

Pamela Reinagel, PhD

Assistant Professor
Department of Biology
University of California, San Diego
October 22, 2007

Thalamic Coding: How the Brain Gets News to the World

Like Dr. Schiller, Dr. Reinagel's laboratory also contributes to the field of vertebrate vision. Using the rat as a model organism, the electrophysiologists in the Reinagel lab have produced exciting new data in the field of neural coding in the visual system.

Dr. Reinagel's talk highlighted a current controversy in this field: whether or not thalamic bursts in the mammalian brain contain visual information. Bursts in the lateral geniculate nucleus (LGN) are due to specific types of calcium channels (T-type). Dr. Reinagel's lecture reviewed evidence that visual information is encoded by bursts. Each burst elicits distinct neural responses when an organism encounters a different scenario. Dr. Reinagel interpreted this as a mechanism for tagging visual signals according to how surprising the animal finds them to be. New data revealed that different burst lengths serve to represent different information. Thus, bursts act as a multisymbol code for transmitting information to downstream cells. This code relays information about the subthreshold voltage of presynaptic cells. Interestingly, anesthesia is known to dramatically affect bursting frequency in the mammalian brain. Because of this, recent work has incorporated the use of alert rats (that is, without anesthesia), and this preliminary data shows significant numbers of visually driven bursts in the LGN.

Leslie B. Vosshall, PhD

Associate Professor
Laboratory of Neurogenetics and Behavior
The Rockefeller University
Howard Hughes Medical Institute
New York, New York
April 7, 2008

A Glimpse into the Olfactory Universe of Insects and Humans

Like vision, the sense of smell (olfaction) is invaluable to an organism's ability to sense environmental cues and respond appropriately. The Vosshall laboratory is interested in the link between genes, environment, and olfactory-dependent behavior.

Dr. Vosshall's lecture was divided into two parts. The first part discussed recent work deciphering the mechanism of insect olfactory signal transduction, an investigation into the molecular targets of the DEET insect repellent, and the lab's efforts to improve upon DEET by high-throughput small molecule screening. The second part presented a large-scale human olfactory psychophysical study in which interindividual differences in smell perception are linked to genetic polymorphisms in a human odorant receptor gene.

Insects rely primarily on the sense of smell to find humans and are potently attracted to the characteristic scent of human sweat and the carbon dioxide present in breath, a behavior that is key to infectious disease transmission through blood-feeding. In collaboration with Kazushige Touhara from the University of Tokyo, the Vosshall Lab provided evidence that the insect olfactory receptors are a novel family of odor-gated ion channels. This is a surprising result because chemosensory receptors in nematodes and vertebrates use seven transmembrane domain G protein-coupled receptors that signal through heterotrimeric- G-proteins. This suggests that insects have evolved a completely novel strategy to couple odor binding to neuronal activation.

DEET (N,N-diethyl-meta-toluamide) is the most widely used active ingredient in topical insect repellents in the world. Discovered in 1946 by U.S. government entomologists and in civilian use since 1957, it has broad effectiveness against most classes of insects, but its mechanism of action remains unknown. It is thought to "confuse" or neutralize the sense of smell of mosquitoes when they approach a potential host, but no molecular targets have been identified. Work from the Vosshall lab has demonstrated that the repellent effects of DEET act in the volatile phase by blocking attraction to food odors, confirming previous efforts of other investigators. DEET inhibits both fruit fly and mosquito (*Anopheles gambiae*) olfactory sensory neurons normally responsive to attractive compounds. The repellent effect of DEET requires the *Or83b* gene in *Drosophila*, confirming that this compound acts on the olfactory system. Through expression in heterologous cells, the lab was able to show that DEET inhibits odor-evoked currents mediated by insect odorant receptors. This led to the conclusion that DEET exerts its repellent effects by masking the odors of insect hosts through direct inhibitory action on the insect odorant receptor complex. Using high-throughput small molecule screening, the lab was able to leverage the identification of a molecular target for DEET into the design of a new generation of safer and more effective insect repellents.

In the second portion of the lecture Dr. Vosshall presented a large-scale human olfactory study performed by her lab. Humans differ enormously in their response to odors. An odor that one person finds highly pleasant will be perceived as unpleasant by another person or odorless by yet a third person. The Vosshall lab has been asking whether this enormous perceptual variation between humans has a genetic basis, much like variation in color perception or color-blindness has been linked to mutations in visual photoreceptor genes. In collaboration with Hiroaki Matsunami at Duke University, the Vosshall Lab has shown that genetic variation in a single odorant receptor, OR7D4, explained up to one-third of the phenotypic variation in how human subjects sense the sex steroid-derived odors androstenone and androstadienone. This work provides a foundation for studying the general properties of odor coding in humans, and also for studying the link between the ability to smell these sex-steroid derived odors and human social and sexual behaviors.

Kenneth Lohmann, PhD
Professor
Department of Biology and Curriculum in Neurobiology
University of North Carolina
Chapel Hill, North Carolina
February 18, 2008

Beyond the Five Senses: the Maps, Compasses, and Sensory Biology of Sea Turtle Navigation

One usually thinks of humans and animals as having five senses: vision, hearing, smell, taste, and touch. As our next speaker pointed out, some might think of an innate navigational ability as a "sixth sense," combining aspects of all five traditional senses in order to find one's way in the world. For this study Dr. Lohmann looked to a well-known wayfinder—the sea turtle.

The long-distance migrations of sea turtles involve some of the most extraordinary feats of orientation and navigation in the animal kingdom. As hatchlings, turtles that have never before been in the ocean establish unerring courses toward the open sea and then maintain them after swimming beyond sight of land. Young juvenile turtles follow complex migratory pathways that often extend across entire ocean basins, and adults migrate between feeding grounds and distant areas used for reproduction. The itinerant lifestyle of sea turtles is thus inextricably linked to a suite of sensory, behavioral, and neural mechanisms that enable turtles to guide themselves across vast expanses of seemingly featureless ocean.

The navigational skills of sea turtles are based at least partly on several unusual sensory abilities. Hatchling turtles entering the sea for the first time establish offshore headings using ocean waves, which the turtles detect by monitoring acceleration sequences and orbital movements under water. In the open ocean, young turtles exploit the Earth's magnetic field both as a compass and also as a source of positional or geographic information. Turtles can detect the intensity of the field as well as the inclination of the field lines, abilities that permit them to distinguish among the magnetic signatures of different oceanic regions and exploit regional fields as open-sea navigational markers. These abilities are refined by older turtles, which settle into coastal feeding grounds and learn the surrounding magnetic topography, thus acquiring "magnetic maps" that can be used to navigate to specific areas. These remarkable abilities, perhaps supplemented by others yet to be discovered, endow turtles with a sophisticated navigational system well adapted to an open-sea environment with few visual references.

The principles that underlie navigation in sea turtles may be relevant to other ocean migrants. For example, spiny lobsters have been found to navigate using magnetic maps conceptually similar to those of turtles; the possibility exists that salmon might also use magnetic cues to guide themselves through the open ocean and into the vicinity of their home rivers, where chemical cues guide them to their final targets. An additional benefit of research on sea turtle navigation is that it may inspire new methods of position-finding that can be adapted for human use.

Gene Robinson, PhD

Professor
Institute for Genomic Biology
University of Illinois
Urbana-Champaign, Illinois
October 10, 2007

Eat, Drink, and Be(e) Merry: Feeding-Related Molecular Pathways and Division of Labor in Honey Bees

Behaviors seen among honey bees, such as feeding rituals and the division of labor, combine all six senses (including navigation). Dr. Robinson discussed advances in how genes influence social behavior, and how social behavior in turn impacts genome functioning.

Using the honey bee as a model organism, Dr. Robinson focused on the division of labor among workers and the dance language. Topics included a wide spectrum of molecular mechanisms, from insulin/IGF, reward, and endocrine pathways to pheromone regulation of brain gene expression.

Don Cleveland, PhD

Professor
Ludwig Institute for Cancer Research
Departments of Neurosciences and
Cellular and Molecular Medicine
University of California, San Diego
Howard Hughes Medical Institute
San Diego, California
May 12, 2008

From Charcot to Lou Gehrig: Mechanism and Treatment of ALS

Dr. Cleveland's lab, like many labs studying degenerative disease, focuses not on sensory loss, but instead on motor deficits. Just as sensory loss can isolate an organism from understanding its environment, motor dysfunction can cause a similar disconnect by limiting an organism's ability to respond to its surrounding environment.

Since its description by Charcot in 1869, the mechanism of selective death of motor neurons in Amyotrophic Lateral Sclerosis (ALS) has remained elusive. An inherited form is caused by mutation in superoxide dismutase (SOD1) that causes disease from an acquired toxicity unrelated to dismutase activity. Using mice carrying a deletable mutant gene or viral encoded siRNA to diminish mutant expression within motor neurons, disease onset is slowed, while progression is not. Conversely, reducing mutant SOD1 synthesis in a class of glial cells called microglia has little effect on disease onset, but strikingly slows disease progression.

Diminished mutant expression in another class of glial cells, astrocytes, also does not affect onset, but delays microglial activation and sharply slows later disease progression. Mutational damage within muscle does not play a significant role in the disease, and sustained increases in muscle mass and myofiber number (by AAV-encoded expression of follistatin to chronically inhibit myostatin) do not affect disease course. Damage within cells other than motor neurons does drive disease onset. The presence of wild type non-motor neurons delays motor neuron disease in chimeric mice that have high-level mutant

expression within 100 percent of motor neurons. This implicates a central role of mutant SOD1 damage within non-motor neurons in initiating motor neuron degeneration. Damaged non-neuronal cells implicated in disease onset include endothelial cells of the vasculature. Mutant-dependent microhemorrhages, accompanied by loss of capillary length and reduced blood flow within the spinal cord, initiate well before motor neuron degeneration. Thus, toxicity is non-cell autonomous, requiring mutant SOD1 acting within motor neurons, neighboring astrocytes, microglia, and the vasculature.

These findings validate therapies, including microglial or astrocytic stem cell replacement approaches, to slow disease progression in ALS by supplementing healthy astrocytes or modulating the toxicity within astrocytes to control an inflammatory response of microglia. Exploiting this insight, a gene therapy has been developed for targeting almost any gene using continuous infusion to deliver antisense oligonucleotides widely throughout the central nervous system. Such oligonucleotides catalytically target the mRNAs to which they hybridize for destruction by an endogenous, nuclear enzyme RNase H. Oligonucledotide infusion to reduce mutant SOD1 slows progression of ALS-like disease caused by mutant SOD1. Antisense oligonucleotide therapy can thus be an effective means of treating neurodegenerative diseases, including ALS, Alzheimer's, Parkinson's, and Huntington's, for which target genes have been identified.

The M. R. Bauer Distinguished Lecturer Series Summaries 2007–2008

Introduction

Once again, this year's M. R. Bauer Distinguished Guest Lecturer series was outstanding. The program, now completing its ninth year, brought two well-known and respected neuroscientists to campus: Daniel Choquet and Ralph Greenspan. During their weeklong visit, each of our distinguished visitors gave both formal and informal presentations to the Volen Center and visited individual laboratories for valuable one-on-one discussions with students and postdoctoral fellows. This mutual exchange of ideas and data remained a high point of the visits.

Daniel Choquet
Professor
Physiologie Cellulaire de la Synapse
CNRS–Université de Bourdeaux
Bourdeaux, France
February 2, 2008

New Functions for AMPAR Mobility in Fast Synaptic Transmissions

Throughout development and adulthood, the brain is constantly undergoing a variety of neuronal changes, often referred to as synaptic plasticity. These synaptic changes occur in response to everyday experiences and help the brain to better interact with the surrounding environment. The Choquet lab has identified a number of protein interactions that play a role in the dynamic regulation of such synaptic plasticity.

Ionotropic AMPA-type glutamate receptors (AMPAR) mediate most fast excitatory transmission in the central nervous system. Work from the last decade has shown that there is a dynamic component of glutamatergic synapses within the mammalian brain. The addition or removal of AMPAR to the postsynaptic density is known to directly influence the amplitude of the transmitter-evoked postsynaptic potential, which contributes to synaptic plasticity.

Using single molecule tracking techniques, the Choquet lab has established that AMPARs enter and leave synapses through lateral diffusion in the plane of the membrane. Surprisingly, more than half of AMPARs are mobile in synapses, dwelling for a few seconds in a given synapse. Thus, the number of AMPARs present at a synapse results from a dynamic equilibrium between the pools of intracellular, extra-synaptic, and synaptic receptors.

Dr. Choquet also has shown that receptor mobility is highly regulated by a set of protein-protein interactions, particularly by the interaction of the AMPAR-associated protein Stargazin with the major intracellular scaffold protein of excitatory synapses, PSD95. The lab also has shown that neuronal activity extensively controls AMPAR movements.

Recently, the Choquet lab investigated the function of the mobile AMPAR population in fast synaptic transmission. They found that the mobility of surface AMPARs participates in the recovery of synaptic depression, and does so in the tens of milliseconds time frame. Altogether, single molecule imaging techniques coupled with electrophysiological measurements have helped to elucidate unexpected roles for receptor trafficking in the hour to millisecond time range.

Ralph Greenspan
Senior Fellow in Experimental Neurobiology
The Neurosciences Institute
San Diego, California
June 16, 2008

From Sleep to Consciousness in *Drosophila*: The Sublime to the Ridiculous

The Greenspan lab studies the role of particular genes in producing complex behavior in the fruit fly. For years it has been known that flies share many behavioral traits and qualities with more complex organisms such as mammals. In this talk, Dr. Greenspan explored these characteristics to make a case for "consciousness" in the fruit fly. Although this is a highly controversial topic, Dr. Greenspan drew on a number of examples from his own work to make an interesting case for this both philosophical and scientific hypothesis.

Dr. Greenspan began his presentation by noting that the cognitive potential of the fruit fly *Drosophila melanogaster* has been extensively probed in recent years and, as a result, our estimation of its sophistication has grown considerably. How do they do it? Do these invertebrates accomplish such feats by an altogether different mechanism than we do? Dr. Greenspan's research addresses these questions from the standpoint of probing brain states in the fruit fly from the deepest sleep to the highest state of alertness, using a combination of genetic, physiological, and behavioral approaches.

At the molecular level, the fruit fly shares many features of sleep regulation with mammals, of which the dopaminergic and EGFR signal transduction systems are prominent. In the realm of higher arousal, the fruit fly displays many of the key elements of attention: orientation, expectancy, stimulus discrimination and suppression, and sustainability. Finally, they share a critical physiological feature with attention and consciousness states in humans: an increased degree of coherence (phase-locking) among multiple brain regions during the attention-related task. Dr. Greenspan suggested that while it is not productive to spend too much time worrying about whether fruit flies are conscious, they may possess some of the same requisite, underlying mechanisms, and thus are worthy of further study in this direction.

Brandeis University
The M. R Bauer Foundation
Scientific Retreat 2008

Introduction

The 2008 Volen National Center for Complex Systems Scientific Retreat was held on campus at the Shapiro Auditorium, the Volen Center Building, and the Kugler Lounge. This two-day event celebrated the careers of two recently retired distinguished faculty members, Drs. Jeffrey Hall and Kalpana White, and the groundbreaking contributions they made to the fields of neurogenetics and behavioral genetics. This retreat featured fourteen distinct talks given by former trainees of the Hall, White, and Rosbash laboratories at Brandeis. The event was a total success with excellent speakers, informative posters by postdocs and graduate students after the first day of talks, and a lunch and social hour capping the second day of talks.

Volen National Center for Complex Systems Annual Retreat, 2008

"A Neurogenetics Celebration to Honor Drs. Kalpana White and Jeffrey Hall"

Thursday, June 19, 2008

1:00 p.m.
Michael Rosbash, PhD
Brandeis University/HHMI
Opening Remarks

1:30 p.m.
Paul Hardin, PhD
Texas A&M University
"A brief history of clocks outside the brain"

2:00 p.m.
Joel Levine, PhD
University of Toronto at Mississauga
"Homage à un Clochard; (P. P. Dickey' Redux)"

3:00
Jae H. Park, PhD
University of Tennessee at Knoxville
"Neuropeptides in Drosophila"

3:30 p.m.
Kathleen Siwicki, PhD
Swarthmore College
"Pheromones and Memory of Unsuccessful Courtship"

4:00 p.m., Keynote Speaker
Liqun Luo, PhD
Stanford University/HHMI
"Probing Neural Circuits with Genetic Mosaics"

5:30 p.m.
Poster Session, Volen Center

Friday, June 20, 2008

9:30 a.m.
Ralph Greenspan, PhD
The Neurosciences Institute
"This Is Your Life, Jeffrey Hall: The Early Years"

10:00 a.m.
Vivian Budnik, PhD
University of Massachusetts Medical School
"Wnts of change"

11:00 a.m.
Larry Zwiebel, PhD
Vanderbilt University
"Exploring Mosquito Olfaction to Examine and (Perhaps) Modulate Critical Behaviors of Disease Vector Insects"

11:30 a.m.
Tony James, PhD
University of California, Irvine
"Engineering Pathogen Resistance in Vector Mosquitoes"

1:30 p.m.
Ana Regina Campos, PhD
McMaster University
"Chicken Soup for the Fly Pusher's Soul"

2:00 p.m.
Bentley Fane, PhD
University of Arizona
"Structure, Function, and Evolution of Viral Scaffolding Proteins in a Two-Scaffolding Protein System"

3:00 p.m.
Josh Huang, PhD
Cold Spring Harbor Laboratories
"Genetic Dissection of GABA Inhibitory Circuitry in Mice"

3:30 p.m.
Sandhya P. Koushika, PhD
National Centre for Biological Sciences
"Regulation of Mitochondrial Transport in *C. elegans* Neurons"

4:00 p.m.
Bambos Kyriacou, PhD
University of Leicester
"From Brandeis to Infinity and Beyond"

Paul Hardin, PhD
Chair and Professor
Department of Biology
Director, Center for Research on
Biological Clocks
Texas A&M University
College Station, Texas

"A Brief History of Clocks Outside the Brain"

Dr. Hardin was a postdoctoral fellow at Brandeis University from 1987–1991. He worked closely with Michael Rosbash and Jeff Hall on the topic of circadian rhythms (day/night sleep cycle) in the fruit fly.

Understanding how genes control behavior is a daunting challenge that attracted Dr. Hardin to Michael Rosbash's lab within the Brandeis Neurogenetics group in 1987. At this time the period (PER) gene had been cloned, and intriguing information showing that PER protein immunoreactivity cycled in a circadian manner prompted Dr. Hardin to explore whether this cycling was due to an underlying cycle of PER mRNA. His resulting work showed that not only did *per* mRNA cycle, but also that PER protein feeds back to control cycling of its own mRNA.

Subsequent analysis from many labs not only support the circadian feedback loop model but add to its mechanistic detail and demonstrate that conserved feedback loops also control circadian timing in mammals. Widespread expression of PER in flies suggests that feedback loops operate in many tissues. Dr. Hardin's lab went on to show that circadian feedback loops do indeed operate in the body tissues, and further analysis in the Hall and Kay labs using PER-driven luciferase reporter genes established that individual peripheral tissues contain autonomous light entrainable oscillators. However, the function of peripheral oscillators remained a mystery. Together with Stuart Dryer, the Hardin lab has shown that circadian oscillators in olfactory sensory neurons (OSNs) in the antenna were necessary and sufficient to control rhythms in the amplitude of physiological responses to odors. Recent work demonstrates that *G-protein coupled receptor kinase 2* (*Gprk2*) is rhythmically expressed, and that levels of GPRK2 protein determine the amplitude of odor-dependent responses by regulating the dendritic localization of heteromeric odorant receptor complexes within OSNs. The circadian clock in OSNs also controls the amplitude of spontaneous activity spikes, which implies that the clock controls basic aspects of OSN membrane physiology. By identifying the targets of GPRK2 and characterizing the mechanism underlying OR dendritic localization rhythms they hope to define the clock output pathway that controls rhythms in olfactory physiology.

Joel Levine, PhD
Assistant Professor
Department of Biology
University of Toronto
Mississauga, Ontario

"Homage à un Clochard ('P. P. Dickey') Redux"

Dr. Levine was a postdoctoral fellow in Jeff Hall's lab beginning in fall 1999 through 2004. A seasoned veteran of both circadian rhythms and courtship behavior, he reminisced over the good times and late nights spent during his time at Brandeis.

Dr. Levine's talk recounted a number of experiences in and out of biology that attracted him to the Hall lab at Brandeis. In addition, Dr. Levine emphasized the unique approach to neurogenetics that has developed at Brandeis and continues to shape current research activities in his own laboratory. Dr. Levine went on to describe in words and pictures the important people and themes that have affected him as a consequence of his association with Dr. Hall. In addition to others present at the meeting, such as Michael Rosbash, Paul Hardin, Ralph Greenspan, Bambos Kyriacou, Jae Park, Don Gailey and Adriana Villella among others, Dr. Levine fondly discussed his interactions with other influential Hall lab members such as John Ewer, Stephen Goodwin, Ralf Stanewsky, and Jeff Hall himself. Ultimately, it was Dr. Hall's powerful qualities as a researcher, a teacher, and a person that remain with Dr. Levine as links to the possibilities inherent in *Drosophila* genetics and a life in science.

Jae H. Park, PhD
Associate Professor
University of Tennessee at Knoxville
Knoxville, Tennessee

"Neuropeptides in *Drosophila*"

Dr. Park was a graduate student in the Hall lab from 1996 to 2000, working alongside Jeff Hall and Michael Rosbash on the topic of biological rhythms in the fruit fly.

Adipokinetic hormones (AKHs) are metabolic neuropeptides, mediating mobilization of energy substrates from the fat body in many insects. The *Drosophila* AKH (dAkh) gene is expressed exclusively in the neuroendocrine cells in the corpora cardiaca from late embryos to adult stages. Projection patterns emanating from the AKH neurons indicated that AKH has multiple target tissues, including the larval aorta and the adult crop and brain. Studies using transgenic manipulations of the *dAkh* gene demonstrated that AKH induced both hypertrehalosemia and hyperlipemia. Starved wild-type flies displayed prolonged hyperactivity prior to death. This novel behavioral pattern could be associated with foraging activities in response to starvation. In contrast, flies devoid of AKH neurons not only lacked this type of hyperactivity, but also displayed strong resistance to starvation-induced death, implying a role for AKH in the regulation of starvation-induced foraging behavior.

Kathleen Siwicki, PhD
Professor
Biology Department
Swarthmore College

"Pheromones and Memory of Unsuccessful Courtship"

Dr. Siwicki launched her career as a Drosophila neurobiologist studying rhythmic expression of the period gene as a postdoctoral fellow in Jeff Hall's lab. She studied with Dr. Hall from 1985 to 1989.

Dr. Siwicki's research focus shifted to courtship behavior shortly after reading Dr. Hall's influential 1994 review, *The Mating of a Fly*. While courtship is largely an innate behavior in male fruit flies, their sexual behavior can be influenced by unsuccessful attempts to court unreceptive females. When a male is paired with an unreceptive, mated female, he learns to suppress his courtship behavior toward this female, and it remains suppressed in subsequent pairings with virgins (Siegel and Hall, 1979). This experience-dependent modification of male courtship behavior is known as conditioned courtship suppression. Recent experiments in the Siwicki lab have addressed the role of female aphrodisiac pheromones in this learning and memory paradigm. Using genetic variants that produce flies with distinctive pheromonal blends, the researchers in the Siwicki lab have tested the requirement for specific compounds in both the acquisition and expression of males' memory of unsuccessful courtship. On the one hand, the results suggest that some components of the female pheromonal profile are required to elicit the males' memory of the aversive experience with mated females. On the other hand, work from the Siwicki lab has found that males can be trained to suppress their courtship by pheromonally depleted mated females. This suggests that they can acquire the memory even while courting females that lack the aphrodisiac pheromones in question. Additional behavioral studies with males carrying mutations or deletions of genes expressed selectively in chemosensory appendages further suggest a requirement for chemosensory signaling in both acquisition and expression of conditioned courtship suppression. The work discussed was completed by teams of talented Swarthmore undergraduates who have worked in her lab, in conjunction with the continuing influence of many colleagues who have shared the formative experiences of Brandeis neurogenetics.

Liqun Luo, PhD
Professor
Department of Biology
Stanford University
Investigator
Howard Hughes Medical Institute

"Probing Neural Circuits with Genetic Mosaics"

From 1987 to 1992 Dr. Luo was a graduate student at Brandeis University under the direction of Kalpana White, where his research focused on behavioral deficits in the fruit fly.

The Luo lab uses molecular genetics to study the logic of neural circuit organization and assembly. Much of the current knowledge of neuronal structure, connectivity, and development derives from Ramon y Cajal's classic studies a century ago. He used the Golgi staining method, which randomly labels a small number of individual neurons in their entirety, unobscured by the mass of other brain connections. The Luo lab has developed a modern genetic analog of Golgi staining: mosaic analysis with a repressible cell marker (MARCM), which labels small groups or isolated single neurons in the *Drosophila* brain. With MARCM, researchers also can genetically manipulate only these labeled neurons, such as deleting a gene of interest, to assess its function in the assembly of neural circuits. The Luo lab has used MARCM to study the morphological development of individual neurons and the formation of specific connections between neurons. Recently they have also developed an analogous method called MADM (mosaic analysis with double markers) in mice to study similar questions in the mammalian brain.

Ralph Greenspan, PhD
Senior Fellow in Experimental Neurobiology
The Neurosciences Institute
San Diego, California

"This Is Your Life, Jeffrey Hall: The Early Years"

Dr. Greenspan was the first graduate student in Jeff Hall's lab, working from 1974 through 1979. His talk recounted a number of the lesser-known events in Dr. Hall's life.

Born in Brooklyn, Jeff Hall grew up in Bethesda, Maryland, where his father worked as the Capitol Hill reporter for the Associated Press. This is where the family tradition of speaking truth to power was established—when his father was one of the only journalists willing to testify against Joe McCarthy. One of their neighbors was the distinguished biochemist Sid Udenfriend, whom Jeff met years later when Udenfriend's Institute at Hoffmann-LaRoche tried to recruit him. In high school, Jeff became an accomplished trumpet player, performing virtuoso concertos, such as the Bach Brandenberg No. 2 and the Haydn Trumpet Concerto, with local orchestras. For college, Jeff attended Amherst, where he became acquainted with fruit fly research, with Dr. Greenspan's brother, Peter, and with Dusty Dowse, his current collaborator. His undergraduate project resulted in his first publication, a study of aging in *Drosophila* that started off with a quote from the Rolling Stones, "What a drag it is getting old." He went west for graduate school to what was the only genetics department in the country at the time, Herschel Roman's department at the University of Washington, Seattle. Jeff always spoke of Roman in reverential terms, and of his experience in that department as formative. Its faculty included the pioneer phage geneticist Gus Doermann and the young Lee Hartwell, but the main attraction and influence was his adviser, the

virtuoso fly geneticist Larry Sandler. After graduate school, Jeff went south to Caltech where he introduced the first hard-core fly genetics into Seymour Benzer's lab and worked closely with Doug Kankel to develop internal markers for mosaics and identified the acetylcholinesterase gene in the fly. In 1973, he started at Brandeis as then almost the lone fly lab. And with constant oldies rock'n'roll in the background, he began the series of pioneering studies in neurogenetics that are his legacy.

Vivian Budnik, PhD
Professor of Neurobiology
University of Massachusetts
Medical School
Worcester, Massachusetts

"Wnts of Change"

Dr. Budnik was a graduate student in Kalpana White's lab from 1984 to 1988. Here she studied various modes of neurotransmission in the fruit fly brain.

Activity-dependent modifications in synaptic structure play a key role in synaptic plasticity and the development of neuronal circuits. However, the signaling mechanisms underlying this process are still poorly understood. Budnik demonstrated that glutamatergic *Drosophila* larval neuromuscular junctions (NMJs) undergo rapid and dynamic changes in synaptic structure and function in response to patterned stimulation. These changes, which depend on transcription and translation, include the formation of highly motile presynaptic filopodia-like structures, the elaboration of undifferentiated presynaptic varicosities, and potentiation of spontaneous release frequency. Experiments indicate that a bidirectional Wnt/Wg (Wingless) transduction pathway underlies these changes. Evoked activity induces Wnt1/Wg release from synaptic boutons, which stimulates both a postsynaptic DFz2 nuclear import pathway, as well as a presynaptic pathway involving GSK-3ß/Shaggy. The findings suggest that bidirectional Wg signaling operates downstream of synaptic activity to induce modifications in synaptic structure and function. Budnik proposes that activation of the postsynaptic Wg pathway is required for the assembly of the postsynaptic apparatus, while activation of the presynaptic Wg pathway regulates cytoskeletal dynamics. This mechanism might operate directly or through the activation of known plasticity pathways such as PKA and CREB.

Larry Zwiebel, PhD
Professor of Biological Sciences
Vanderbilt University
Nashville, Tennessee

"The Search for a New Generation of Insect Repellents"

Dr. Zwiebel was a postdoctoral fellow at Brandeis from 1985 to 1991. Much of his work was a collaboration between the Hall and Rosbash labs, the bulk of which focused on circadian rhythms (day/night sleep cycles). After leaving Brandeis, Dr. Zwiebel went on to study disease transmission in the mosquito.

The ability to sense and discriminate a large collection of chemical and visual cues is critical for several insect behaviors—insects, such as the *Anopheles gambiae* mosquito, which act as vectors for pathogens responsible for many important human diseases. In particular, olfaction plays a major role in host seeking and selection behaviors of blood-feeding female *Anopheles gambiae* mosquitoes, the species that acts as a vector for malaria. A long-term research objective in the Zwiebel lab is centered on an examination of the molecular genetics of the chemosensory system in *Anopheles gambiae* and other mosquitoes. Along with this, the lab is also interested in the chemosensory system's role in determining anthropophilic host preference in malaria vector mosquitoes. The Zweibel lab has identified, and continues to characterize, the complete repertoire of 79 odorant receptor (OR) genes from *Anopheles gambiae*, as well the complete set of 117 functional OR genes from the dengue and yellow fever virus vector mosquito *Aedes aegypti.* Through collaboration with other labs, the Zwiebel lab has completed a detailed analysis of the olfactory physiology, molecular neurobiology and odorant-binding characteristics of ORs on the adult maxillary palp and proboscis. They have also utilized behavioral and molecular elements of the larval stage olfactory system of *Anopheles gambiae* and *Aedes aegypti* to begin to define the functional "odor space" for these vector mosquitoes.

The Zwiebel lab leads a broad international network of five laboratories (also encompassing Yale University; Wageningen University, The Netherlands; Ifakara Health Research and Development Institute, Tanzania; The MRC Laboratories, The Gambia) that has been selected for a Grand Challenge In Global Health grant for the specific purpose of using these state-of-the-art molecular approaches to target odorant receptors in order to design a new generation of mosquito repellents and attractants.

Tony James, PhD

Professor
Microbiology & Molecular Genetics
(School of Medicine) and Molecular
Biology & Biochemistry (School of
Biological Sciences)
University of California, Irvine
Irvine, California

"Engineering Pathogen Resistance in Vector Mosquitoes"

Dr. James was a postdoctoral fellow from 1980 to 1985 who worked closely with Michael Rosbash and Jeff Hall on the topic of circadian rhythms (day/night sleep cycles) in the fruit fly. During this time Dr. James was adopted by, and happily integrated with, the members of the White lab, making him a true tri-lab citizen. Like Dr. Zwiebel, Dr. James also began to study the mosquito following his time at Brandeis.

Dr. James and his lab focus on vector-parasite interactions, mosquito molecular biology, and other questions of insect developmental biology. Dr. James described the efforts of his laboratory to use molecular biology and genetic tools to develop synthetic approaches for interrupting malaria parasite and dengue virus transmission by mosquitoes. His research group is the first to develop transgenesis procedures for mosquitoes, and they have been able to engineer single-chain antibodies that interfere with malaria parasite development in the mosquito. Dr. James is collaborating with other researchers to develop RNAi-mediated approaches to prevent dengue virus transmission.

Ana Regina Campos, PhD

Associate Professor of Biology
McMaster University
Hamilton, Ontario

"Chicken Soup for the Fly Pusher's Soul"

Dr. Campos was a graduate student in Kalpana White's lab from 1982 through 1988 during which she studied nervous-system development in the fruit fly.

Dr. Campos began her presentation by paying tribute to Kalpana White and Jeff Hall's early guidance in forging her academic identity and for the nuggets of wisdom that came her way as a graduate student with Kalpana and having Jeff as a member of her thesis committee. In her talk, Dr. Campos discussed two projects currently ongoing in her lab. One project, in collaboration with Andre Bedard, is aimed at dissecting the function of a human tumor suppressor gene called Menin. Using *Drosophila* as the model organism, this collaboration has led to the discovery that the Menin gene is required for the fly's response to environmental stress, and in this context it functions to maintain the integrity of the fly genome.

The second project is a classical screen for mutations that disrupt the *Drosophila* larval response to light. In this part of the talk, Dr. Campos described the behavior and the assay used, the phenotype of the mutant strain identified, and some aspects of the expression and possible function of this gene. Dr. Campos mentioned these experiments because they nicely illustrate many of the fundamental principles of behavioral and developmental genetics that were passed on to all of those who spent time in Kalpana's and Jeff's labs.

Dr. Campos also conveyed the long-lasting impact of being around Kalpana and Jeff (and Michael Rosbash, too) from a personal point of view. Her time at Brandeis has provided her with a lifelong treasure of wonderful memories that she reaches for often. Dr. Campos spoke of having left Kalpana's lab with a handful of brilliant friends, which she counts on for comfort and advice, scientific or otherwise. This group of people, in which Kalpana occupies a central position, has traveled far, both with Dr. Campos, and to see Dr. Campos in Canada and Brazil. She considers herself very lucky, and for this she wants to "thank Michael for opening this door, Kalpana for giving me shelter and overlooking many of my shortcomings, and Jeff for providing the soundtrack (rants and good music)."

Bentley Fane, PhD
Professor
University of Arizona
Tucson, Arizona

"Structure, Function, and Evolution of Viral Scaffolding Proteins in a Two-Scaffolding Protein System"

Dr. Fane was a former undergraduate student at Brandeis who spent much of his college career working under the direction of Kalpana White. During his introduction he spoke of the formative changes that Kalpana had on him both scientifically and personally. Memorably he spoke of her being the "jackhammer" that hewed chunks off the as-yet-unsculpted granite block he was as an undergraduate, thanking Kalpana for playing that role as he became a better scientist and person from his time with her.

Unlike most viral assembly systems, two scaffolding proteins, B and D, mediate bacteriophage phiX174 morphogenesis. The external scaffolding protein D is highly ordered in the atomic structure, and proper function is very sensitive to mutation. In contrast, the internal scaffolding protein B is relatively unordered, and extensive alterations do not eliminate function. Despite this genetic laxity, protein B is absolutely required for virus assembly. To address the biochemical functions of a dual scaffolding protein system and the evolution of complexity, progressive and targeted genetic selections were employed to lessen and finally eliminate B protein-dependence. The biochemical and genetic bases of adaptation were characterized throughout the analysis that led to the sextuple mutant with a B-independent phenotype, as evaluated by plaque formation in wild-type cells. The primary adaptation appears to be the over-expression of a mutant external scaffolding protein. Progeny production was followed in lysis-resistant cells. The ability to produce infectious virions does not require all six mutations. However, the lag

phase before progeny production is shortened as mutations accumulate. The results suggest that the primary function of the internal scaffolding protein may be to lower the critical concentration of the external scaffolding protein needed to nucleate procapsid formation. Moreover, they demonstrate a novel mechanism by which a stringently required gene product can be bypassed, even in a system encoding only eight strictly essential proteins.

Josh Huang, PhD
Professor
Cold Spring Harbor Laboratories
Cold Spring Harbor, New York

"Toward a Genetic Dissection of the GABA Inhibitory System in the Mouse Brain"

Dr. Huang got to know Jeff Hall and Kalpana White while working in the Rosbash lab. During his tenure at Brandeis from 1989 to 1994, his work focused on the contribution of a variety of genes involved in circadian rhythms (day/night sleep cycles).

A major challenge in modern neuroscience is to understand how behaviors emerge from the underlying neural networks and their cellular constituents. To take on this challenge, a productive approach aims to establish causal links between patterns of activity in specific groups of neurons (for example, cell types) and the computation of neural circuits that guides behavior. At the core of this approach is the identification and precise and flexible manipulation of distinct cell types, the functional units of neural circuits. However, the diversity and heterogeneity of neuron types in mammalian brains have been major road blocks. For example, GABAergic interneurons are crucial in establishing the functional balance, complexity, and computational architecture of neural circuits, but the heterogeneity of GABAergic cell types has been exceedingly difficult to penetrate by conventional anatomical and physiological techniques. Genetic strategies hold the promise to "de-convolute" this complexity because they tap into the intrinsic gene regulatory mechanism and logic that generate and maintain the heterogeneity of the GABAergic system.

The Huang lab uses cell type specific promoters and Cre/LoxP recombination-regulated gene expression to establish "genetic access" to all major classes GABAergic neurons. Using bacterial artificial chromosome (BAC) engineering technology, the Huang lab is generating more than twenty knockin "driver lines" expressing Cre or the inducible CreER in specific GABAergic cell types. In addition, they are constructing a new generation of Cre-activated "reporter" mice and, in particular, Cre-activated viruses to achieve high-level expression of fluorescent proteins (FPs) and "molecular switches"(MSs, such as ligand- or light-induced ion channels) *in vivo*. These genetic strategies will allow researchers to: 1) visualize the morphology and connectivity of GABA interneurons with synapse resolution (genetic neuroanatomy); 2) visualize the activity and activity-history of interneurons (genetic neurophysiology); 3) manipulate the firing and synaptic transmission of defined classes of cells at physiological time scales (genetic manipulation). Using this approach, the Huang lab has imaged the structural dynamics of a major class of GABA interneurons *in vivo* and manipulated their firing activity.

The genome-wide mapping of the transcriptome onto the mouse brain (that is, the Allen Brain Atlas) provides unprecedented opportunity to discover and define cell types by gene expression. The genetic access to specific cell types through Cre driver mice combined with efficient and flexible delivery of an array of conditional viruses to visualize and manipulate these cell types will herald a new era for studying the organization and function of complex neural circuits.

Sandhya P. Koushika, PhD

Principal Investigator
National Centre for Biological Sciences
Bangalore, India

"Regulation of Mitochondrial Transport in C. elegans Neurons"

Dr. Koushika was Kalpana White's very last graduate student. She spent her time with Dr. White from 1993 to 1998. Her thesis focused on the role of alternative splicing in neural development in the fruit fly. She spoke warmly during her introduction of the mornings that she sat next to Kalpana, both working at a microscope sorting their fruit flies, talking about science and life. Like Ana Marie Campos, Dr. Koushika remembered, with great gratitude, the wisdom that Dr. White imparted.

Kinesin-I is a heterotetrameric motor that consists of Kinesin heavy chain and light chain. This motor protein transports several cargoes such as mitochondria, vesicles, and mRNPs. Proteins such as UNC-16/SYD, UNC-76/FEZ1, UNC-14, UNC-51 and UNC-69 have all been implicated for their role in the Kinesin-I-dependent vesicular transport pathway. The Koushika lab has investigated the role of this complex in transporting mitochondria. While mitochondrial numbers in axons are reduced in the Kinesin-I, UNC-14, UNC-16, UNC-76 and UNC-51 mutants, the Koushika lab observes an increase in mitochondrial numbers in *unc-16* mutants. This increase in mitochondrial numbers is independent of Kinesin-I suggesting the recruitment of an alternate motor. Dynamic imaging also supports this hypothesis and reveals effects of UNC-16 in both the anterograde and retrograde pathway.

Charalambos Kyriacou, PhD

Professor of Behavioral Genetics
University of Leicester
Leicester, England

"From Brandeis to Infinity and Beyond"

Dr. Kyriacou was one of the first postdoctoral fellows in the Hall lab. Along with Michael Rosbash, Dr. Kyriacou and Jeff Hall together studied biological rhythms in the fruit fly.

Dr. Kyriacou joined the Hall lab during the great blizzard of '78 and was among Jeff Hall's first cohort of students/postdocs at Brandeis. Dr. Kyriacou's main colleagues were Laurie Tompkins, Ralph Greenspan, and Kristen White, all of whom remain firm friends to this day. During his first year, Dr. Kyriacou studied fly love songs and discovered the male song rhythm, which moved Jeff's laboratory into the field of biorhythm research. He left in 1981, now having "become bosom buddies (with Jeff) when he was no longer 'the boss.'" They consolidated their work over the next few years. Together with Michael Rosbash, they also initiated the molecular analysis of circadian and song rhythms.

In the past fifteen years or so, the work in Dr. Kyriacou's lab has moved into working on the functional implications of natural clock gene variation and has adopted a more evolutionary and ecological approach. They also have begun working on "omic" studies of mouse clocks. Dr. Kyriacou concluded by noting that his experience at Brandeis and with Jeff defined his subsequent scientific career in genetics and molecular biology.

Acknowledgements

We thank all the speakers who came to Brandeis over the past year for their time, lectures, and scientific discussions. The sharing of ideas is necessary for science to progress. We are grateful to each of our visitors for the lecture summaries they forwarded to us; these summaries served as the basis for this publication.

Additionally, we thank Sara Wasserman and Justin Slawson, two graduate students in the Life Science program at Brandeis for their editing of this publication and the humor and grace they brought to the process.