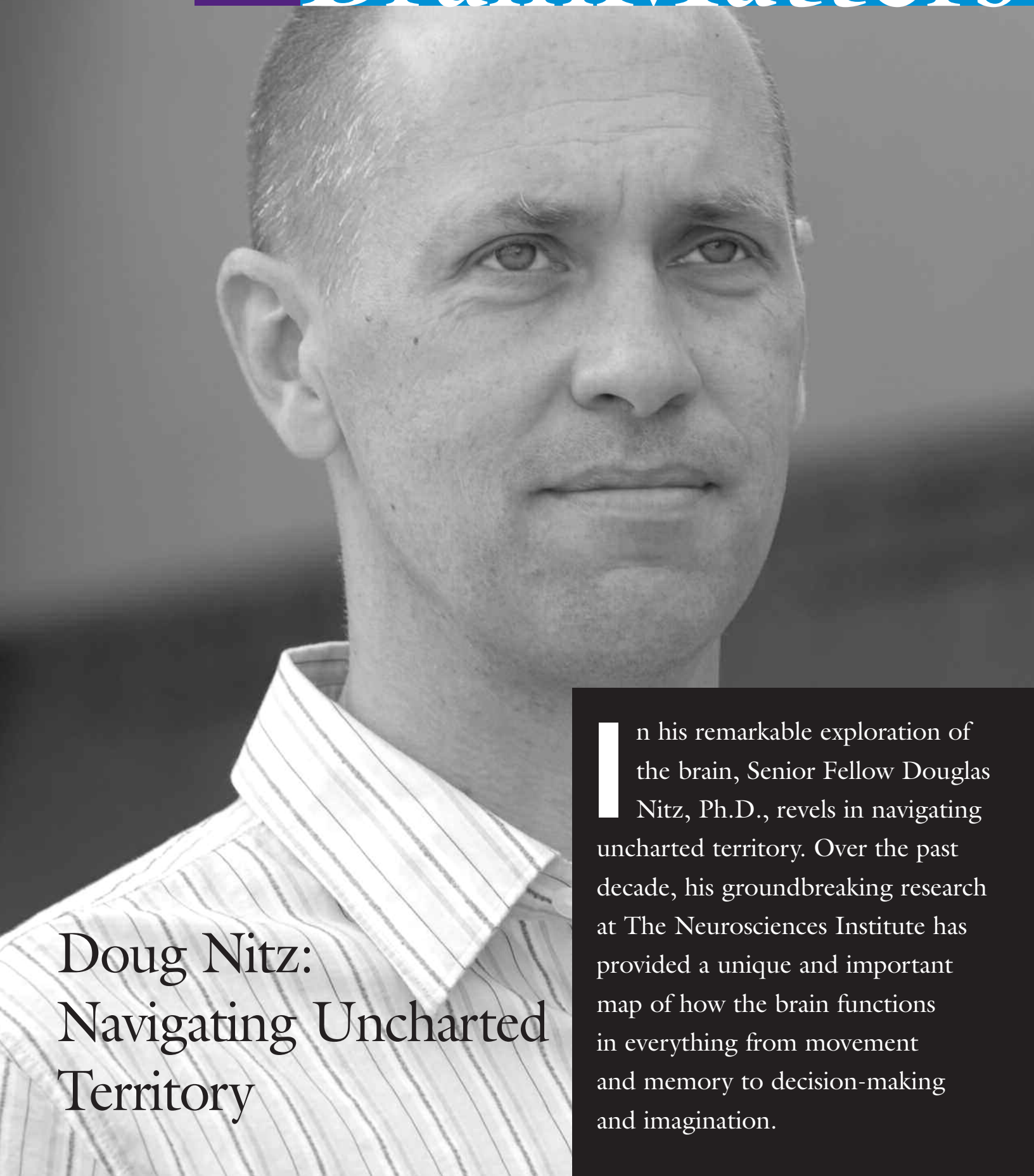
THE PUBLICATION OF THE NEUROSCIENCES INSTITUTE

Fall/Winter 2008

BrainMatters



Doug Nitz: Navigating Uncharted Territory

In his remarkable exploration of the brain, Senior Fellow Douglas Nitz, Ph.D., revels in navigating uncharted territory. Over the past decade, his groundbreaking research at The Neurosciences Institute has provided a unique and important map of how the brain functions in everything from movement and memory to decision-making and imagination.

A significant chapter in Nitz' career—and for the Institute as well—came to a close in September when he joined the faculty of UCSD as an Assistant Professor in the Cognitive Science Department. However, as a sign of the deep esteem that the neuroscientist and the Institute have for each other, Nitz will continue his association part-time with the Institute as Affiliated Fellow in Experimental Neurobiology.

"I'm eager to tackle a new set of challenges at UCSD," Nitz says, "but I'm also really pleased to continue working with an institute that has played such a crucial role in my development as a scientist. My 10 years at The Neurosciences Institute have contributed much of what I know and think about the brain, and the incredible environment here has enabled me to delve into the brain in ways that would not have been possible anywhere else."

Nitz' achievements are some of the most wide-ranging at the Institute, in part because he measures widespread neuronal activity—including that of single neurons—not just in one brain region but in several, including the hippocampus, subiculum, parietal cortex, basal ganglia, and prefrontal cortex.

It is precisely this ability to measure activity in more than one brain region at the same time that is the key to his research success. He is one of the foremost experts in the nation in a technique that allows him to make real-time and simultaneous recordings of multiple brain regions in freely behaving rodents as they perform various navigational tasks, an approach that has revealed much about how these regions interact across time.

These skills have enabled Nitz and his team to make significant strides in three different areas. His investigation into activity patterns in the premotor cortex and prefrontal cortex is showing the role of uncertainty or confidence in an animal's ability to make a decision. More specifically, Nitz has been able to shed light on the mechanisms involved when a decision with a cost-benefit outcome must be faced, when decisions among possible behaviors with different costs and benefits are made, and the implications for behavior when that function is impaired or disrupted. Nitz believes this work eventually could help explain and possibly treat obsessive compulsive disorder, substance abuse, and other types of self-destructive behavior.

Nitz' study of the hippocampus has revealed that while that brain region is critical to memory, and episodic memory in particular, it appears that the hippocampus doesn't create memories for every specific episode. Instead it creates a set of rules or templates that enable the brain to recognize, organize, and store the various similarities it perceives in the outside world.

A vigorous surfer, Nitz uses an example to illustrate this point. Imagine, for example, the first lifeguard to derive the rule "always swim parallel to shore to escape a riptide." One learns that the reliability of such rules is based not on one, but on multiple experiences. However, these experiences may be very different in content--different people, different settings, etc. In the brain, different content of episodic memories usually means that different neuronal groups are active. The hippocampus appears to be capable of producing neuronal groups that are activated by subtle, but meaningful similarities between situations. Their activation makes for a common neural bond between different memories; that neural bond is, literally, the rule itself. Knowledge of this relationship has potential uses in education, for example, where a teaching environment could be structured to enable a child's brain to utilize this connection to increase his or her learning comprehension and efficiency.

Some of Nitz' most exciting research involves the parietal cortex, showing that its capabilities go well beyond helping mammals to navigate in space. His study of rats moving through a complicated spiral-shaped track revealed that the animal's brain—thanks to the contribution of its parietal cortex—has the ability not only to keep track of three different spatial relationships simultaneously but also track a temporal relationship so that the rat knows where it is at any given time or space.

A second key aspect of parietal activity is that the mappings of multiple spatial relationships may be based on the space defined by any arbitrary set of items in the environment. For example, if a noise wakes you up in the middle of the night and out of curiosity or concern you proceed down the stairs to investigate. You can imagine where the stair steps are and the space between the furniture in the dark while moving toward the perceived location of the noise without falling and stumbling. "We think we can show that this higher brain function may be one of the underpinnings of human imagination, and we're the first to do that," Nitz says. "I don't think it was a coincidence that the analysis of Einstein's brain showed that the one region that was thicker than any other was his parietal cortex. He was extremely good at imagining novel ways of looking at spatial relationships."

Although he says that applying this research is years in the future, Nitz does believe that teaching geometry and other spatially related subjects may someday be accomplished in a much more visual manner by taking full advantage of the parietal cortex's unique function.

Education and improving learning techniques are important to Nitz. It's appropriate that he's moving to a university setting where he will have teaching duties in addition to his research responsibilities. "In most of my research, discovering new and better ways to help kids learn is always in the back of my mind. I really hope to make some contributions through what we're finding about the how the brain organizes and learns to use information."

Outside of his professional work, Nitz is already making a contribution to education by volunteering to help create the Inaugural San Diego Brain Bee. This question-and-answer competition

which tests the neuroscience knowledge of high school students will be held January 31st at the Institute and is being sponsored by the San Diego Chapter of the Society for Neuroscience, Invitrogen, and Jean and Mike Collins.

"For me, it's a fun way to give back to the community and my field, but the contest is really important for motivating kids to learn about the brain," Nitz says. "They're at the perfect age where by capturing their imagination, we have a good chance of inspiring some of them to consider a career in neuroscience."

As Nitz looks back on his own career at this time of transition, he marvels at what he and the entire Institute have been able to accomplish over the past decade. He credits the unique scientific environment created by Gerald Edelman, M.D., Ph.D., Institute Founder and Director.

"Neuroscience is still a relatively young field and we still know far less about the brain than we would like, but I'm always amazed when I stop to think about what my colleagues and I have achieved across such a wide spectrum of brain inquiry," Nitz says. "In part it's because of the flow of ideas that comes from the constant interaction we have with each other, as well as from the great scientists who visit the Institute, that has been so inspiring.

"But above all, the flexibility and freedom Dr. Edelman has given us to pursue great science wherever we find it is the reason we've been able to generate a host of important discoveries no one could have ever predicted. For this, as well as the great friendships I've made here, I consider myself truly fortunate to have worked at The Neurosciences Institute."

"EXTREME ENGINEERING"

When it comes to innovative ideas and experiments, the scientists at The Neurosciences Institute are leaders in their field. But sometimes finding the best method or the right equipment to conduct their experiment can stump even the best of them. That's when they call on the team of James Snook and Donald Hutson, the Institute's resident engineers. What they can create from an idea, a microprocessor, some hardware, metal, and occasionally a piece of discarded equipment is no less than a remarkable art that is engineered to support the science at the Institute.

Jim Snook came to the Institute with a degree in the multidisciplinary study of Cognitive Science from UCSD. He had worked at several commercial electrical engineering enterprises before landing what he calls "a dream job" that combines his interests, education, and obvious talent. Jim can take an idea from design to completed part, often in just one day. He is proud to have worked on a series of ever-evolving robotic platforms that are key elements of the Institute's research using Brain-Based Devices. These devices can sense and act on their environment under the control of a neural simulation, and they learn from their 'experience.' In addition to this more traditional engineering work, he has built devices for other projects ranging from equipment that supported sleep deprivation studies in fruit flies to specialized treadmills for behavioral studies in rodents and just about everything in between.

"Jim was one of the first people I got to know when I started at the Institute", says Associate Fellow David Edelman. "In the years since we met, he has demonstrated a keen engineering expertise that spans a wide range of applications. The breadth of Jim's knowledge was made crystal clear to me when I came to him a couple of years ago seeking help with an old neurophysiology rig that I had to adapt to a new computer I intended to use for sleep studies of rats. The rig hadn't been used in years, so it didn't have a compatible interface for modern PCs. Upon quick inspection, Jim knew exactly what was needed and, in short order, built a working interface and a software module to control everything". The Institute's ability to attract creative and talented individuals to its small campus is

testimony to its unique style and approach to scientific research and engineering applications.

Jim first met Donald Hutson in 1999 at a competitive robotic program called BattleBots; Donald remains as one of the heavyweight division's world champions. He was persuaded to join the Institute to work on Brain-Based Devices in 2001. From an early age, Donald enjoyed working with his hands and tinkering with parts. But now he uses sophisticated computer-aided design software and oftentimes expensive, complex mechanical components to engineer his colleague's ideas into reality. He's the "go-to-guy" when any of the scientists need help with the physical design and construction of their experimental equipment, such as the automatic feeding devices in a rat maze or an infrared-beam reward system.

Weimin Zheng, Associate Fellow in Experimental Neurobiology studying auditory neurophysiology, sums it up succinctly when he describes several devices Donald designed and built for his rat stereotaxic systems. "These devices are critical for our experiments, fully customized to our needs, and commercially unavailable."

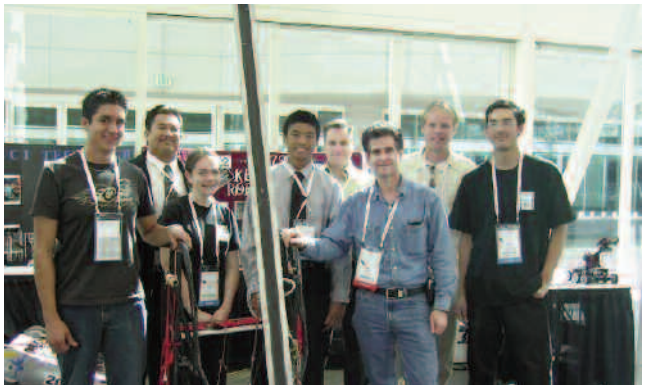
Several of the Institute's scientists study individual nerve cells by maintaining them in tissue culture in chambers suitable for observation of the cells under a microscope. Neurons can be extremely sensitive to drastic changes in the temperature and acidity of the culture medium, making them quite difficult to keep alive. Finding an 'off-the-shelf' solution to this life support problem, and particularly one that would fit under a microscope, could have been quite costly. But as David Edelman says, "in our lab we're acutely aware of the cost of instrumentation and reagents, and we try to get the biggest bang for our buck, choosing often to build equipment rather than ordering pricey—and often overly specialized—devices from commercial vendors. When I explained our cellular life support problem to Donald, he intuitively grasped the core issues and immediately went to work on a practical solution."

After some heavy-duty troubleshooting, Donald had fabricated a working microscope stage-top incubator that is capable of keeping the cultured neurons alive indefinitely and is significantly more flexible and adaptable than any commercially available.

Jim and Donald both have similar interests outside of The Institute. In addition to BattleBots, Jim and Donald also mentor local students as part of the For Inspiration and Recognition of Science and Technology ("FIRST") robotics curriculum. Their FIRST team at Kearny High School reached 3rd place at the San Diego regional competition this year. Jim also started FIRST robotic programs at both Muirlands Middle School and La Jolla High School last year. "I have a profound appreciation for what teachers go through every day," he says.

A fun-loving fellow, Donald gets very serious when he talks about his role in supporting brain science. "Providing the best tools available," he says, "to the best minds in neuroscience—that's my job." And he clearly enjoys doing it. With the new FIRST season coming up in early 2009, he plans to mentor again, too.

During the week you'll find both Jim and Donald surrounded by the tools of their trade, meeting with the scientists on staff, immersed in figuring out the next engineering step in the puzzling and complex brain science we do. Outside of the Institute walls you'll more than likely find them surrounded by those same kinds of tools and among the young scientists of the future.



Fresh Faces

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STEPHEN COWEN
Birthplace: Fredonia, Wisconsin
Education: B.S. in Marketing and Management, The University of Wisconsin, Madison, Peace Corps Volunteer, Honduras, Ph.D. in Psychology, The University of Arizona, Tucson
Hobbies: Capoeira (Brazilian style of martial art, acrobatics and dance), Surfing, Exploring California beaches, snorkeling

"Why you are interested in studying the brain?"

I have always been fascinated by how thoughts emerge, how they give us a sense of identity, and how we learn. My curiosity led me to brief adventures in linguistics, artificial intelligence, and philosophy, but my first course in neuroscience changed everything. I found researchers asking specific questions about the neural basis of thought and from that point on I was hooked.

"What are you researching at The Institute?"

My research is concerned with understanding how the brain helps to estimate the costs and the benefits of an action in order to produce a decision. The ultimate goal of this research is to uncover the patterns of neural activity that underlie the various stages of decision making.

"What do you hope to achieve at The Institute?"

The question that originally drew me to neuroscience was to understand how brains produce thought. I am realizing how unbalanced this question may have been after becoming aware of some of the subtle ways that we use our bodies and the environment to shape our thinking. One of my long-term goals is to integrate embodied theories of the mind with insights developed from observing neural activity in order to produce theories of the mind that combine the body, environment, and neural activity.

JARY DELGADO
Birthplace: Caguas, Puerto Rico
Education: Ph.D., University of California, Los Angeles
Hobbies: Woodcraft, bread making, cooking, hiking, swimming with my daughter

"Why you are interested in studying the brain?"

My passion for neuroscience arose with my brother's struggle with severe generalized anxiety disorder. His attacks were sometimes elicited with just a simple intrusive thought. This experience motivated me to learn more about the processes involved during memory formation in hope that one day I could help him and others.

"What are you researching at The Institute?"

My research spans various levels. At the molecular level, I am studying the role of a protein involved in changing the number of receptors between nerve cells. At the cellular level, I am testing how different levels of neuronal activity limit the ability to form memories.

"What do you hope to achieve at The Institute?"

I hope to gain a better understanding of the cellular and molecular mechanisms responsible for the recycling and delivery of neurotransmitter receptors to the synapse. In particular, I want to see how the protein phosphorylation regulates the movement of intracellular vesicles containing neurotransmitter receptors, vesicle distribution, and fusion with the cell membrane.

CYNTHIA L. HUGHES
Birthplace: Wyandotte, Michigan
Education: B.A. University of California, Berkeley
Ph.D., Indiana University
Hobbies: Hiking, spending time with her new son, Malcolm

"Why you are interested in studying the brain?"
Human behavior is endlessly fascinating and frustrating, and it's natural to want to understand what makes us tick, which makes neuroscience really fun.

With my background in genetics, I also wonder how changes in genes create new behavioral circuits and how specific genes are able to code the development and differentiation of the neurons for a behavioral circuit. For example, how does the spider genome grow a brain that knows how to spin a web?

"What are you researching at The Institute?"
I am using fruit flies to study the neural circuits that control two important behaviors -- appetite and sleep. Once we learn about the basic circuit in flies, we can design better experiments to see what's going on in mammals.

"What do you hope to achieve at The Institute?"
My goal is to establish the fundamental organization of these behavioral circuits at the genetic level, laying the groundwork for more detailed studies into how individual neurons are genetically programmed to carry out specific functions in a circuit.

RUGGERO SCORCIONI
Birthplace: Pavullo (Modena), Italy
Education: Ph.D., George Mason University
Masters in Software Engineering, University of Modena
Hobbies: Salsa dancing, hiking, canoeing

"Why you are interested in studying the brain?"
The brain is one of the most complex structures known to man with the amazing ability to interpret the world, make decisions, take actions and experience the full range of human emotions.

"What are you researching at The Institute?"
The brain is a highly parallel system, composed of a multitude of different subregions that are interconnected with precise anatomical patterns. These patterns depend not only on the specific subregion, but also on the peculiar neuronal classes that are being connected. My research focuses on understanding how these anatomically accurate connections affect the activity of the brain.

"What do you hope to achieve at The Institute?"
My hope is to elucidate the relationship between connectivity, activity and, hopefully, function in the brain.

A Familiar Face: *Tom Coldiron*

If you've ever attended an event at The Neurosciences Institute then you've probably seen Tom Coldiron, the Institute's chief security guard. Tom, born in Long Beach, entered the U.S. Navy in 1972 where he served as an Aviation Ordinance Technician on land and at sea, including in the USS Constellation. Retiring after 21 years in the Navy, he joined the team at the Institute in 1996, where he continues to provide security for our campus and at 100 concerts a year in the Auditorium. He has two passions in his life–sports and his family, including wife Elisa, 3 stepchildren and 5 granddaughters. He is a supporter of the Disabled American Veterans and never misses a Dodgers or a Lakers game!

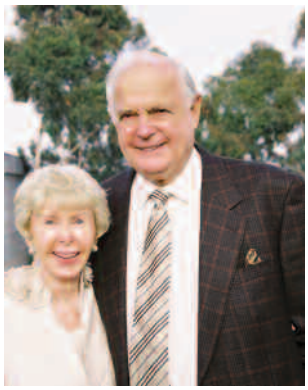
News & Events

Sixth Annual Fundraising Gala
Minding the Arts

On Sunday, September 14, 2008, The Neurosciences Institute hosted its sixth annual Minding the Arts benefit to raise critical funds for the Performing Arts Program. Since the inception of the program in 1996, the Institute has donated the use of its acclaimed auditorium to many non-profit arts and educational organizations for events ranging from classical piano to jazz quartets, poetry readings to sitar concerts.

Nuvi Mehta, the Director of Special Projects at the San Diego Symphony was the Master of Ceremonies for the event, which included an outdoor cocktail reception with delicious food and beverages donated by San Diego's best culinary venues followed by a concert in the auditorium. The concert featured the incredibly talented young Bunnell Strings ensemble, presented by the San Diego Youth Symphony, the heavenly voices of the Pacific Coast Harmony ensemble, and the remarkable pianist Gustavo Romero.

As the program has grown in popularity, the burden to the Institute's budget has also grown, and it now costs the Institute more than $300,000 a year! We are deeply grateful to the sponsors, in-kind donors, caterers, entertainment, planning committee, and volunteers who made this event possible. Their support, as well as the support of all who attended the event, will help keep the Performing Arts Program running for the benefit of the San Diego community.



Minding the Art

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Sammy's Woodfired Pizza
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Get INVOLVED!

"We were absolutely stunned by the kind of advanced experiments and neurobiological studies that are taking place [at the Institute]…It was a great pleasure to "Meet the Fellows" and enjoy a lunch with them." - Brenda and Lou Alpinieri, Members

The basis of The Neurosciences Institute's ability to conduct ground-breaking and innovative research is our reliance on funding from foundations and individuals rather than restrictive government grants. Members of the Institute, through their annual contributions, help to ensure that our brand of forward-thinking research continues in an uninhibited environment. Membership opportunities begin at the Friends level with an annual gift of $250 or more.

FRIENDS: $250 - $999
- Invitations to special community lectures
- Invitation to Minding the Brain scientific presentations
- Subscription to BrainMatters, the Institute's newsletter
- Advance invitations to our Library Roundtable lecture series
- Quarterly "Members Only" email newsletter

PATRONS: $1,000 – 4,999
- Invitation to a Fellows Symposium luncheon and private tour of the Institute
- Invitation to "Meet the Fellows" monthly events
- Plus "Friends" level benefits

FOUNDERS CIRCLE: $5,000 AND MORE
- Signed book by Dr. Gerald Edelman
- Annual Founders Circle luncheon with Dr. Gerald Edelman
- Plus "Patrons" level benefits

In addition to advance invitations to Library Roundtable lectures by Dr. Ranulfo Romo and Dr. John Searle in 2008, The Neurosciences Institute was pleased to extend invitations to our members to attend several members-only events:

- The Magic of Science & The Science of Magic – A magic show by the world-class magician Mark Mitton and discussion by Dr. Gerald Edelman about the mysteries of perception and illusion.
- Presentations by our scientists in the intimate setting of Casa de Mañana in La Jolla:
  - Dr. Aniruddh Patel: "Music and The Brain: Three Links to Language"
  - Dr. Ralph Greenspan: "Understanding Human Health & Disease: The Fruit Fly's Role in Medical Discovery"
  - Dr. Geoffrey Owens: "CSI Mitochondria: Investigating the Brain's Power Source to Shed Light on Aging and Disease"

Legacy Council

The Legacy Council recognizes those visionary benefactors who have made gifts to The Neurosciences Institute in their estate plans. Their gifts build an endowment, an investment fund whose interest is used to support our work in perpetuity. This permanent source of income provides essential funding for the ongoing research being conducted at the Institute. A special panel on our donor recognition wall in the loggia of the auditorium is reserved for individuals on the Legacy Council. For more information on the benefits of membership in the Legacy Council or to discuss estate planning options, please contact Rachel Jonte at (858) 626-2018 or jonte@nsi.edu.

Current list:
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Nancy L. Vaughn
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From the Director

Consciousness and the Ultimate Aim of Neuroscience

Neuroscience is increasingly mentioned in the media these days. The prefix "neuro" is applied more and more to subjects of general interest: "Neuroeconomics," "neuroethics," and even "neurohistory." This prompts the question: How far can our knowledge of the workings of the brain go? The answer to this question cannot be given before the fact. But the biological basis of consciousness is one key area of human concern that may fairly be considered as an ultimate goal of neuroscience. Once the exclusive precinct of philosophers, the study of consciousness has attracted the attention of neuroscientists all over the world. Scientists at The Neurosciences Institute have been concerned with the neural basis of consciousness for the last three decades, and a brief review of the shift from philosophy may be of interest.

In 1637 and 1641, the French philosopher René Descartes proposed the notion of dualism. According to this view, the world is divided into two kinds of areas: res extensa (extended things subject to scientific study) and res cogitans (thinking things which cannot be so studied). In one sense, this philosophy removed the mind from nature. Although subsequently the subject was vigorously debated by philosophers, the possibility that science could study the issue awaited the analysis by the great American psychologist and philosopher William James at the beginning of the 20th century. He recognized that consciousness was a process, not a thing, and gave an account of its properties chief among which was the seminal idea of the stream of consciousness.

The field went into scientific darkness with the advent of behaviorism, a doctrine that deliberately removed the subject from experimental consideration. With the resurgence of interest in cognitive psychology and the appearance of new methods of studying brain activity from the 1950's on, the mind was put back into nature. Indeed, beginning in the mid 1980's, a veritable explosion of scientific attention and study is taking place. In scientific circles, Descartes' dualism has been rejected and the search for explanations of consciousness as a result of brain activity has intensified. What do we know so far?

Using humans as models and with non-invasive brain imaging and clinical methods of study, the evidence accumulated so far suggests that the key brain element in producing consciousness is the so-called thalamocortical system. This consists of a walnut sized brain area, the thalamus, and its two-way connection with the wrinkled structure enveloping our brains, the cerebral cortex. Strokes damaging the thalamic relay system can lead to permanent loss of consciousness. Those involving the cortex can lead to losses of conscious contents, eg. sight, hearing, speech, etc. Human speech and language lend us the remarkable ability to be conscious of being conscious. While certain animals show signs of consciousness, they lack this ability, which like language itself, distinguishes our species as unique.

Arguably, one may claim that understanding the brain and bodily bases of consciousness is the ultimate goal of neuroscience. The complexity of the subject, while daunting, is actually beginning to yield to scientific analysis. One of the most exciting prospects would be the design and construction of a conscious artifact. This prospect was once the domain of science fiction but it now appears as a distinct possibility, provided that one aims only to produce so-called primary consciousness, not the language-based higher order consciousness of humans. Successes at The Neurosciences Institute in constructing brain-based devices capable of perception and learning provide a very early basis for considering this endeavor.

This enterprise is challenging, but, if achieved, it would allow us to study this most marvelous of processes in scientific detail. Next to analyzing messages received from outer space, a more exciting and revealing enterprise is hard to imagine. Scientists at The Neurosciences Institute are gearing up to lay the groundwork, or shall we say, the "thoughtwork" necessary for success.

Gerald M. Edelman, M.D., Ph.D.
Director

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