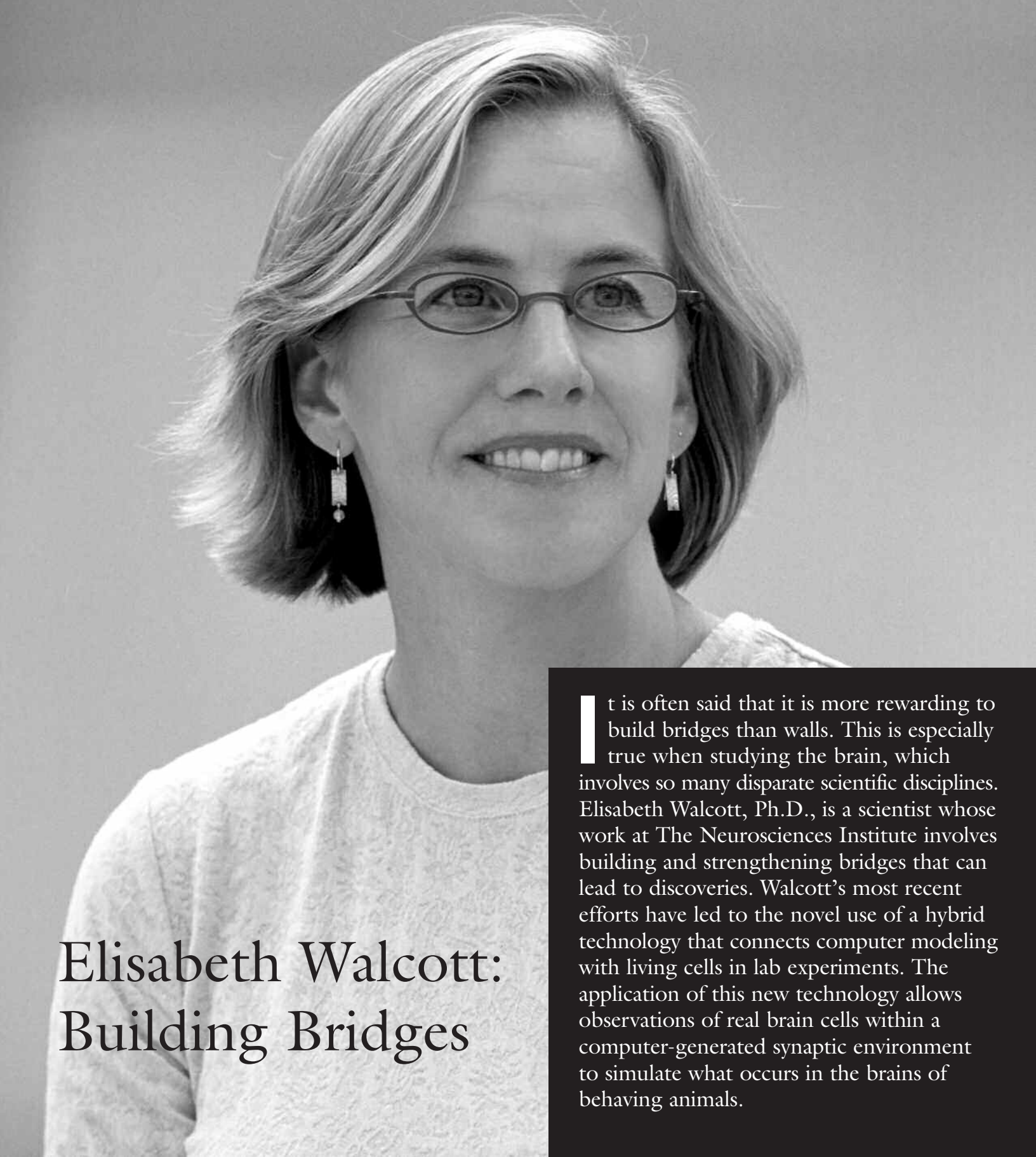
THE PUBLICATION OF THE NEUROSCIENCES INSTITUTE

BrainMatters

Fall/Winter 2006



Elisabeth Walcott: Building Bridges

It is often said that it is more rewarding to build bridges than walls. This is especially true when studying the brain, which involves so many disparate scientific disciplines. Elisabeth Walcott, Ph.D., is a scientist whose work at The Neurosciences Institute involves building and strengthening bridges that can lead to discoveries. Walcott's most recent efforts have led to the novel use of a hybrid technology that connects computer modeling with living cells in lab experiments. The application of this new technology allows observations of real brain cells within a computer-generated synaptic environment to simulate what occurs in the brains of behaving animals.

"My goal is to understand how the brain changes at the cellular level as a result of experience, and I hope to one day get a handle on the altered brain functions that lead to behavioral disorders."

— Elisabeth Walcott

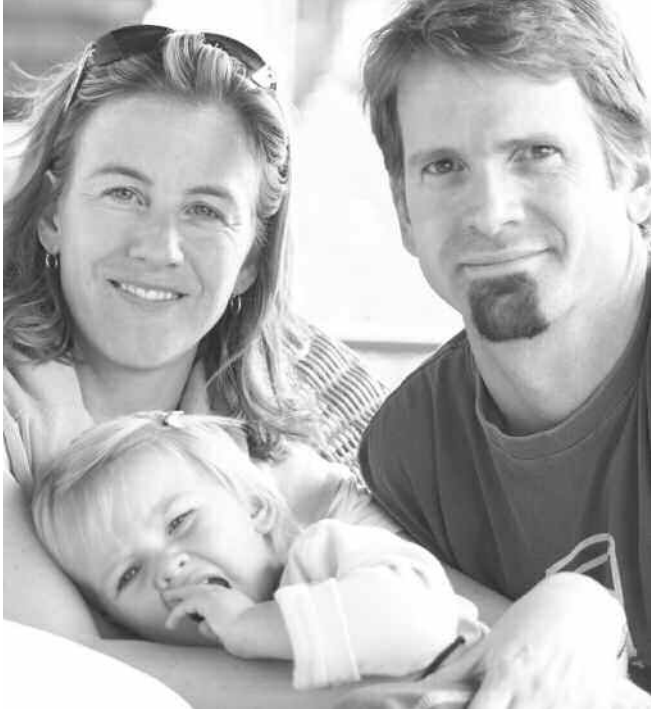


Photo: Greg O'Loughlin, www.GregO.com

As she pursues her groundbreaking investigation of brain function at the level of synapses and small groups of neurons, Elisabeth Walcott is simultaneously engaged in an equally fascinating and much more personal experiment: to balance the challenging dual roles of professional neuroscientist and dedicated mom. Her daughter Lila just turned two years old.

"The demands of science and motherhood are both so great that balancing the two requires planning and discipline, as well as being flexible and willing to modify my expectations," says Walcott. She is quick to give credit to her husband, Dr. Stephan Miller, and to the Institute for enabling her to attempt this juggling act. "I've been very fortunate," Walcott says. "My husband has a busy career as a medical writer, but he shares a lot of the childrearing and household duties, including serving as the family chef. His contribution has been crucial, especially during those frequent periods when I need to concentrate on my research. The Institute has also been tremendously understanding and supportive in every way possible. They've allowed me to work part-time, which amounts to a four-day week, to accommodate my family responsibilities," explains Walcott.

Walcott maximizes her productivity in those four days. As a Research Fellow in Experimental Neurobiology, she is an integral part of the Institute's cellular electrophysiology group. The primary focus of her work is to understand the physiology of the microcircuitry in the cerebral cortex by recording the electrical activity of brain cells in real time, under different physiological and pharmacological conditions. Walcott studies rodent brain slices which can stay alive for up to 12 hours outside the animal. Inserting them into an apparatus that combines electrical recording tools with various microscopy modes to visualize individual neurons, she can peer into the inner workings of complex cortical circuits.

Walcott's early interest in neuroscience, combined with her intense curiosity about the world, led her to major in psychobiology at Harvard. Later, as she developed an interest in neurobiology, she entered the doctoral program in biology at the University of California, Irvine. There she dove into molecular biochemistry, including assisting with a key study on the effects of nicotine at the cellular level. "At the end of graduate school I felt as though I had swung too far from my interests in the brain. I had shifted from behavioral psychology to studying neurotransmitter receptors in frog eggs, not even neurons," says Walcott.

The seeds of Walcott's future were planted a year before she got her Ph.D. when she visited The Neurosciences Institute. She was recruited by Ronald Langdon, a former Senior Fellow in Experimental Neurobiology, to help him study neuronal electrophysiology.

Her early contributions involved examining how synaptic plasticity—communication between neurons at the level of synaptic connections—occurs in the neocortex. The neocortex is involved

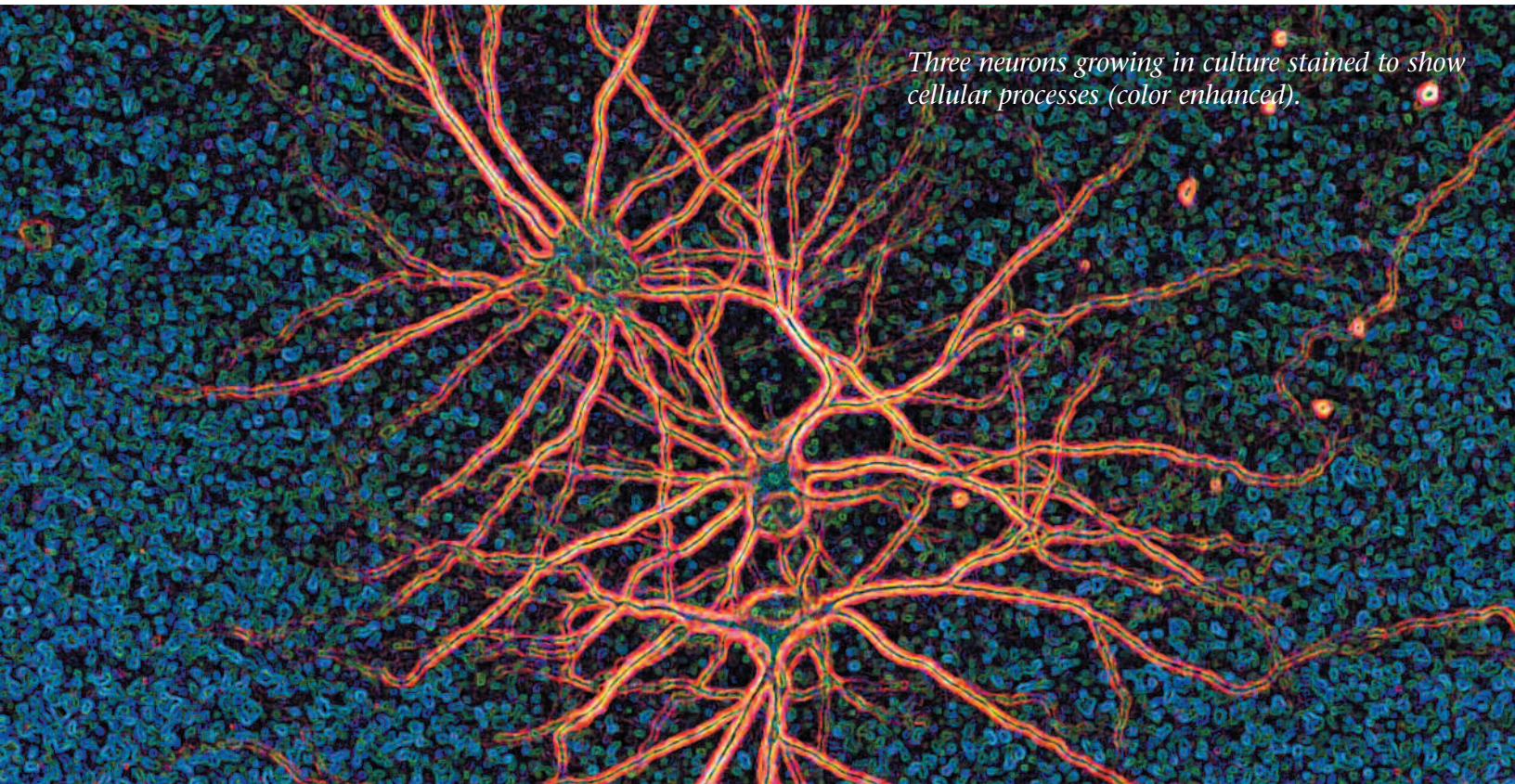
in higher functions such as sensory perception, conscious thought, generation of motor commands, and spatial reasoning. Synaptic plasticity is the ability of the connection, or synapse, between two neurons to change in strength. Memories are thought to be stored in synapses of the brain. Therefore, synaptic plasticity plays an important role in the process of learning and development of memory.

One important question was whether all brain synapses were the same in their capacity to become strengthened or weakened with use. Walcott demonstrated that unlike some other synapses, several types of neocortical synapses got weaker very quickly during a strong burst of stimulation. This type of short-term plasticity is temporary, but it is thought to be especially important in the neocortex for preventing runaway excitation, or epileptic-like activity, since the cortex is such a highly interconnected structure.

Like many post-docs, Walcott envisioned staying at the Institute for two or three years. However, she was encouraged to stay on. As she took on more responsibility and gained the respect and confidence of her fellow scientists, Walcott realized she had found a home.

Currently, Walcott has been working with Niraj Desai, an Associate Fellow in Experimental Neurobiology, to make measurements in single neurons that act like those found in the brain of awake, behaving animals. To do this they took advantage of a system that combines real neurons in a brain slice with computer-simulated events that modify the neurons' electrical and chemical environment. This is a big step forward, as many studies of synaptic communication have been conducted either in neuronal cultures that lack appropriate neuroanatomy or in "quiet" slices that do not have normal levels of neuronal activity. The ability to record from neurons in a more realistic environment will help provide detailed mechanisms for behavioral changes observed in live animals and could even be used to improve the types of testing available for potentially therapeutic drugs.

The two scientists used this hybrid method to study the effects of the potent brain chemical acetylcholine on excitability of neurons in the motor region of the neocortex. Acetylcholine is a chemical released into the neocortex during periods of wakefulness, and it has been shown to be required for certain types of learning. Notably, it is the acetylcholine-producing neurons that



Three neurons growing in culture stained to show cellular processes (color enhanced).

deteriorate in Alzheimer's disease, so understanding how they operate is of great interest. Walcott and Desai showed that acetylcholine increases the excitability of neurons in the motor cortex. This increased sensitivity might just be the thing that allows plasticity and learning to occur.

Walcott believes that the work she is doing serves as an important bridge for many group projects at the Institute. In addition to her own work in the neocortex, she is eager to get involved and learn about her colleagues' projects. She has recorded from brainstem neurons as part of a modeling project with Eugene Izhikevich, from large networks of neurons in cultures exposed to caffeine with Fred Jones, and from developing neural precursor cells with Kathryn Crossin, all Fellows at The Neurosciences Institute. However, she feels strongly that cellular neurophysiology is more than a bridge. "It is a field unto itself with vast potential for generating breakthroughs of its own," says Walcott. She explains that our ability to observe how chemicals affect single neurons in a simulated "live system" can lead to technology that will allow for better testing of the beneficial and harmful properties of new drugs.

The ultimate goal for Walcott, however, is one she acknowledges may take a few more years to track down. "Wouldn't it be amazing to see what an abnormal brain circuit looks like in real time, in a human? Right now, there's no way to do it. One thing that we can study is how synaptic activity levels influence and shape responses of neurons in different brain regions. My goal is to understand how the brain changes at the cellular level as a result of experience, and I hope to one day get a handle on the altered brain functions that lead to behavioral disorders," explains Walcott.

"The brain is vastly complicated and malleable, with circuitry that is puzzlingly adaptable. It's going to take a lot of hard work to uncover the brain's underlying processes. I'm definitely one who takes the long-range view of science. This field is so promising, and the technology is improving so rapidly, that I know we'll get there, even if it takes a decade or more. When we do, I think we'll see the development of some sophisticated diagnostic and surgical tools that will turn the tide against many diseases," says Walcott.

Despite the hectic schedule, Walcott actually seems to relish straddling her two worlds. "I love going to the lab and really miss it when I'm not there," she says. "The thought of discovering something that no one has ever seen and which might benefit mankind is incredibly exciting. I also love being a mom. I'm committed to our family and raising a healthy and happy child. Watching Lila develop and learn about the world at such an astonishing rate reminds me of how incredible the human body is, especially the brain. It makes me realize that my two lives aren't really that separate. Right now, I'm enjoying the challenges of doing both," says Walcott.

"I am constantly searching for female role models who have continued to work at the highest levels of science while raising a family," says Walcott. Ironically, while searching for the ideal role models, Walcott has become a strong role model herself, by building bridges both in her cooperative work and between motherhood and a professional career in science. Clearly, she has now joined the ranks of the many professionals who manage the challenges of raising their families while working towards important scientific goals.

Do You *Hear* What *I* Hear?

The rushing sound of the freeway traffic is a steady companion for the highway worker. The waitress knows her busy restaurant is noisy, but she hardly notices as she races around filling customer orders. Young people walk about with their iPods plugged into their ears and even make claims that they can study while listening to music. Our lives are well intertwined with many types of pleasurable and unpleasant sounds.

How is our brain changed, for better or worse, by sound? And when we listen, what factors influence what we actually hear? Different people listening to the same sounds might have completely different perceptions, because our brain is not like a tape recorder, but instead it is actively interpreting the world around us.

Two innovative scientists at The Neurosciences Institute, Drs. Weimin Zheng and John Iversen, focus on these fundamental questions about auditory perception. Using complementary levels of analysis, they both look at how the brain responds or changes based on our sound-related experiences. Zheng's research is at the cellular level and focuses on how the properties of individual neurons in the auditory processing centers of the brain can change under a variety of sound exposure conditions. Iversen uses non-invasive brain imaging to examine the activity of many thousands of neurons to understand the fundamental brain mechanisms that enable us to perceive rhythm, music, and language. The two may work on different projects, but they have a great deal to talk about during their lunch hours at the Institute's daily Fellows Symposium, where the Fellows gather to discuss their research and share insights and new ideas.

Zheng, who is an Associate Fellow in Experimental Neurobiology, has carried out groundbreaking research which shows that, in rats, continual exposure to seemingly harmless ambient noise can lead to a rewiring of the brain's auditory circuitry. Such a rewiring could impair our normal abilities to distinguish between sounds, to understand language, or to enjoy music. He was recently awarded $65,000 by The San Diego Foundation's Blasker-Rose-Miah Science & Technology Fund. This grant will allow him to continue and expand his studies of changes in the brain's hearing centers induced by long-term exposure to noise at intensity levels similar to those of human conversation, traffic noise, and many workplace environments.

Iversen, Karp Foundation Fellow in Theoretical Neurobiology, studies how our mind shapes our perception of the world. Perception is not simply the passive recording of events in the world—our minds are active participants in shaping what we

"Weimin Zheng thinks that hearing problems of millions of Americans may result not from ear damage caused solely by high sound levels or by aging, but from alterations in the brain's auditory circuitry resulting from its effort to adapt to ordinary sounds in our environment."

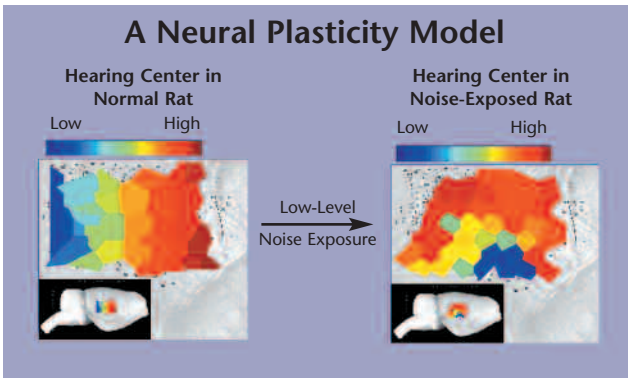
perceive. He focuses especially on how we experience complex patterns of sound as they unfold in time, a process that is the foundation of our capability to find meaning in speech, music, and other sounds that are central to our lives as humans.

In a recent study, he examined how we "hear the beat" of music. The beat—what we clap or tap our foot to when listening to music—is actually a product of our mind as it interprets and organizes the sonic rhythms. Using measurements of brain activity in human volunteers listening to rhythmic sounds, Iversen is seeking to understand just how the imagination influences perception in the brain.

Iversen and Zheng each bring their own special approaches to examine how the brain processes various types of sound.

"John is working in a higher, much more theoretical realm of auditory processing, whereas I'm working at a very basic level—looking at how the neurons in the auditory system of the brain identify and make sense of what the animal is hearing. But both of our investigations are showing that the brain is remarkably plastic in its ability to process and adapt to changes in response to all types of auditory stimuli," says Zheng.

"Normally, there is a well-organized map, called the tonotopic map, in the primary hearing center of our brains that represents the pitch of sounds in an orderly way. This map is crucial in our daily life for understanding the spoken word, enjoying music, and detecting and recognizing all sorts of sounds."



Zheng's findings showed that the regular map of the auditory cortex region (tonotopic map as shown above, left) of the rat gets rearranged as a result of exposure to noise (above, right). The different colors indicate the regions that respond to the lowest to highest frequencies of sound. The map in the noise-exposed rats showed a significantly disrupted pattern. The insets show the location of the auditory region on the surface of the rat brain.

Zheng's many years of research on experience-dependent neuroplasticity—the brain's ability to reorganize itself based on an individual's experience—has led him to theorize that the hearing problems of millions of Americans may result not from ear damage caused solely by high sound levels or by normal aging, but from alterations in the brain's auditory circuitry resulting from its ongoing efforts to adapt to sounds in our environment.

Zheng is particularly interested in the brain's response to "white" noise (sound containing a very

"John Iversen, who has had a lifelong interest in Japanese taiko drumming, is looking to achieve a deeper understanding of how the brain processes rhythmic sound."

broad spectrum of frequencies) that is a normal part of so many work environments. He exposed laboratory rats for a month to continuous, low-level "white" noise that was no louder than the level of normal conversation. Mapping of the animal's primary auditory cortex before and after the experiment showed that, even in that short period, a dramatic reorganization of the animal's tonotopic map had occurred. Zheng then showed, using behavioral tests, that the animals had lost their ability to discriminate small pitch differences, suggesting that the map shift actually had a detrimental effect on the animal's hearing.

"Discovering that the animals had lost some of their ability to distinguish between certain sounds was the critical finding, and it's the one that has me so concerned that people in all types of jobs with prevalent white noise may be suffering from these adaptive changes that may lead to significant brain alteration," says Zheng.

"Unlike the proven damaging effects of working around jet aircraft or playing in a rock band, the noise level I used in my experiment was well within the safe workplace decibel limits established by the federal Occupational Safety and Health Administration (OSHA)," Zheng adds. "This could mean that millions of workers are unknowingly at risk for potential sound-induced changes that could severely affect their hearing abilities."

Zheng hopes that publication of his research will spur government, consumer, and health groups to take a closer look at the effects of ambient noise. In the meantime, his own concern is so deep that he has already begun a series of new experiments.

"Now that I know that sound-induced reorganization in the brain is a reality, I'm testing whether the tonotopic map can be restored when the animal is returned to a normal sound environment," Zheng says. "If not, I'm going to test whether the brain might have the ability to develop a new and different map that would enable the animal to go back and forth between the two environments and process sound properly in both."

Zheng's long-term goal for his research is even more ambitious. "Ultimately, what I want to show is how experience-dependent brain plasticity works," he says. "It's this plasticity that forms the basis of learning and memory. If we can better understand the mechanisms, there's an excellent chance we'll be able to harness this plasticity to help people recover from brain damage or disease and perhaps to rejuvenate the brains of our aging population."

Iversen's goal is to achieve a basic understanding of how the brain processes sounds. In his research he has been able to combine a lifelong passion for drumming, which he learned to do before he ever walked, with a deep interest in how the brain functions.

"I'm fascinated with rhythm and how what we hear—or think we hear—influences brain activity," Iversen says. "In particular, I'm intrigued by the concept that our perceptions of the world are not just a passive recording of stimuli, but rather they

reflect constructive mental processes in which our interpretation shapes what we perceive.

"When we hear music, for example, the perceptual experience of a rhythm depends on how the listener interprets the meter—where in the sequence of notes they hear the downbeat. While the location of the beat is often implied and supported by the music, it is in fact subject to our control," says Iversen.

In his recent work on the mechanisms of rhythm perception, Iversen works with volunteers who sit in a magnetoencephalography (MEG) machine that measures, in real time, the minute magnetic fields produced by electrical activity in the brain. During the experiment, the volunteer first listens to repeated pairs of two identical tones that have no inherent beat. After brain responses are measured during that baseline session, the subject is then asked to imagine the beat on the first tone, and then, in a separate series, on the second tone. Where they imagine the beat to fall dramatically changes the perception of the rhythm.

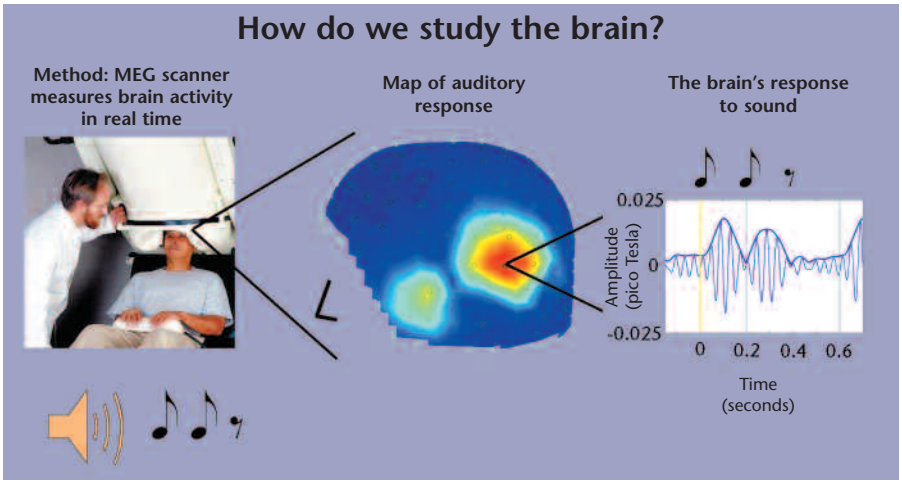
"Because the actual tone stimulus remained unchanged in this experiment, and the only thing that changed was the individual's own experience internally, the experiment really allowed us to examine how a listener's imagination—'marching to the beat of one's own drum'—can change what's happening in our brain," Iversen explains.

The fascinating result was that the brain responded more strongly to the tone with the imagined beat, although the tones were not different in loudness. Iversen has also shown that listening to a tone that is louder has just the same boosting effect.

"The brain responses appear to originate in the auditory cortex, suggesting that imagining the downbeat actually modifies brain responses to sound at an early stage, maybe even changing perception," Iversen says. "A second interpretation, based on the known role of these brain signals in motor processing and long-distance coupling in the brain, suggests that the motor system is an essential component of a purely perceptual act."

For Iversen, this opens up an entirely new world to research. "I'm excited about where this is going to lead. Discovering this connection between the brain's auditory and motor systems has truly wide-ranging implications for the integration of perception and action," he says. Finding a brain response that is sensitive to a listener's imagination opens up possibilities not only for understanding how we create our perceptions, but also it could lead to new kinds of brain-computer interfaces allowing people to control a computer by "just thinking." It also has implications for new therapies using rhythm to help people suffering from movement disorders, such as Parkinson's disease.

What will be next for the two? Iversen and Zheng will continue to pursue their questions in their immediate research areas. However, possibilities for their collaboration at the Institute, which encourages creativity and flexible interactions among researchers, are endless. By combining forces, they could begin to approach fundamental questions about the links between mind and brain. How does our rich perception of the world arise from the activity of neurons? Does noise exposure also affect the perception of the timing of sounds, as well as the frequency? Will rhythm and music therapy reorganize sensory maps in the brain, perhaps leading to the development of treatment methods for serious neurodegenerative disorders? These are just a few examples of the possibilities that these two colleagues might explore.



MEG Scanner Photo: 4-D Neuroimaging

News & Events

Minding the Brain – Celebrating 25 Years of Advances in Brain Research

The Neurosciences Institute celebrated 25 years of pioneering brain research on Saturday, September 30. Dr. Gerald Edelman, the Founder and Director of the Institute, described some of the Institute's major research discoveries and advances along with a historical review of activities from 1981-2006. Several of the Senior Fellows presented their recent research. Jeffrey Krichmar highlighted the latest on brain-based devices; Eugene Izhikevich showed how computers can be used to simulate the brain; Ralph Greenspan gave an account of how genes influence behavior in fruit flies; Fred Jones related how genes in nerve cells are affected by caffeine; and Ani Patel spoke about the advances in studies relating music, language, and the brain. The event brought together over 250 community members interested in learning about the Institute's research innovations and their potential for future applications. After the presentations, guests celebrated this landmark birthday at a reception in the Institute's plaza.

Minding the Brain Celebration from top down and left to right: Patti Cooprider and Lou Alpinieri, Lewis Cullman and Gerald Edelman, Lucy Killea, Reena Horowitz, Reception in the Plaza.

Minding the Arts

Gordon and Annika Kovtun, with Lael and Jay Kovtun, Honorary Chairs (left to right)

Event gathering with Theory Center in background

Fifth Annual Minding the Arts Gala

The Institute's fifth annual Minding the Arts benefit to support our performing arts program was held on Sunday, September 17. Chaired once again by Linda Satz, with Lael and Jay Kovtun as Honorary Chairs, the event raised funds so that the Institute can continue to make its acoustically superb auditorium available at no charge to local nonprofit arts and educational organizations. Dr. Nicolas Reveles, the Geisel Director of Education at the San Diego Opera, was the Master of Ceremonies.

The event included an outdoor cocktail reception amidst the stunning architecture of the Institute's campus, followed by a concert in the auditorium. The concert featured operatic vocal performances from Daniel Hendrick and Elliott Wulff of The Hendrick-Montaño Artist Foundation, classical Persian music of The Darvak Ensemble, presented by The Center for World Music and Persian Cultural Center, and a Haydn piano sonata by Anne-Marie McDermott, presented by Mainly Mozart. In addition to the artists, who donated their efforts, many local vendors generously donated food and beverage stations. Our thanks go to A.R. Valentien at The Lodge at Torrey Pines, Best Beverage Catering Company, Elegant Events Catering Company, the Fish Market, FRESH Seafood Restaurant and Bar, Girard Gourmet, Gourmet Group Catering, Orfila Vineyard & Winery, Sammy's Woodfired Pizza, St. Tropez Bakery & Bistro, Sydney Frank Importing – JC Cognac, TK&A Custom Catering, Top of the Cove, Greene Music, and Sharrie Woods Floral Design.

Jeff Enslin and Jennifer Satz, with Event Chair Linda Satz, and Joe Satz (left to right)

We are truly grateful to our Minding the Arts sponsors: Audrey Geisel/San Diego Foundation's Dr. Seuss Fund, San Diego Foundation's Isabella Fund, Sempra Energy, The Mandell Weiss Charitable Trust, The San Diego Foundation's Weingart-Price Fund, Pfizer, Inc., and Merck Research Laboratories.

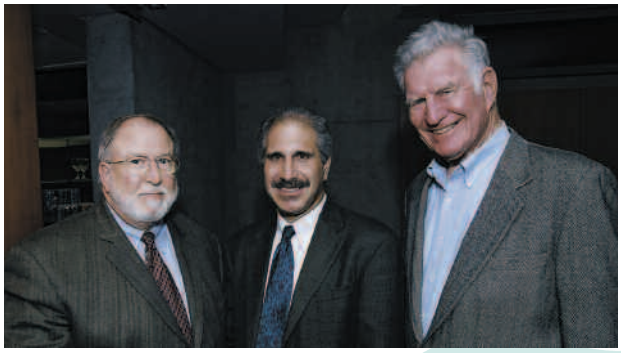
All the event proceeds will be used to defray the costs associated with lending the auditorium, including maintenance, security, energy, and staff support. Through the "Performing Arts at The Neurosciences Institute" program, the Institute effectively saves San Diego's arts community more than $300,000 per year, by lending our facility for nearly 100 concerts annually. Over twenty thousand people attended events in the auditorium last year.

Educating the Community through our Library Roundtable Presentations

The Neurosciences Institute presents its own community lecture series, the Library Roundtable program. It is offered several times each year at no charge to the public. These lectures, delivered by leading figures in science and technology as well as other fields that pertain to neuroscience, are followed by a discussion session.

On November 16, Robert Malenka, M.D., Ph.D., spoke about "Experience, Memory, and Addiction" at the latest presentation in the Library Roundtable series. Dr. Malenka received his professional degrees from Stanford University and then completed a residency in psychiatry at Stanford. He is a world leader in elucidating the mechanisms underlying the action of neurotransmitters in the mammalian brain and in revealing the molecular mechanisms by which neural circuits are reorganized by experience.

Dr. Malenka discussed the progress, to which he has been a key contributor, over the last 25 years in understanding the mechanisms of neuronal communication through synapses and of the adaptations in synaptic function that underlie all forms of normal and pathological behavior, such as addiction. Because of his training as both a cellular neurobiologist and a clinical psychiatrist, he has been at the forefront of helping to apply the knowledge gained from basic neuroscience research to the treatment and prevention of major psychiatric disorders. For information about our next Library Roundtable presentation, visit our website at www.nsi.edu.



Drs. Einar Gall, Robert Malenka, and Bill McColl

Miriam Goldberg and Jeanette Stevens

Daniel Hendrick at the piano, and the young and talented Elliott Wulff at the Minding the Arts Gala performance.

"Mainly Mozart is proud to have called the acoustically superb Auditorium at The Neurosciences Institute "home" since 1995. Dr. Gerald Edelman's remarkable vision and passion for the arts has turned this local treasure into one of the top concert halls in the region. The magnitude of The Neurosciences Institute's gift to arts organizations and patrons over the past eleven years is staggering. We at Mainly Mozart are profoundly and eternally grateful."

Nancy Laturno Bojanic
Executive Director, Mainly Mozart

Hot Off the Press!

Selected Recent Publications

The results of the Institute's research are made available to the world-wide scientific community by publication in various media. The following items are a sampling of recent work that may be of particular interest to the general public.

EDELMAN, G.M. (2006) *Second Nature: Brain Science and Human Knowledge,* Yale University Press.

This book offers a new theory of knowledge based on striking scientific findings about how the brain works. It also addresses the related question: Does the latest research imply that all knowledge can be reduced to scientific description? Edelman's brain-based approach to knowledge has implications for our understanding of the connections among the different ways we have of knowing, as well as for dissolving the differences between science and the humanities. He foresees a day when brain-based devices will be conscious and reflects on this and other fascinating ideas about how we come to know the world and ourselves.

DIERICK, H. AND R.J. GREENSPAN (2006) Molecular analysis of flies selected for aggressive behavior. *Nature Genetics* 38(9):1023-1031.

This study shows that flies can be made more aggressive by selective breeding, and it identifies a gene likely to be involved in fighting behavior. It represents an important step in learning more about the gene networks underlying a particular behavior.

IZHIKEVICH, E.M. (2006) *Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting,* MIT Press.

This book provides a comprehensive introduction to nonlinear dynamical systems theory and describes many novel applications of the theory to neuroscience. It is likely to become a key resource for advanced computational neuroscience courses in many universities worldwide.

McKINSTRY, J.L., G.M. EDELMAN, AND J.L. KRICHMAR (2006) A cerebellar model for predictive motor control tested in a brain-based device. *Proceedings of the National Academy of Sciences USA* 103(9):3387-3392.

This paper investigates the proposal that the cerebellum is a general purpose controller for adaptive control and motor learning. A model of the cerebellum based on this principle was incorporated into a real-world brain-based device, which successfully learned to adapt its motor outputs to different circumstances. The system described may be useful for developing intelligent machines.

DESAI, N.J. AND E.C. WALCOTT (2006) Synaptic bombardment modulates muscarinic effects in forelimb motor cortex. *Journal of Neuroscience* 26(8):2215-2226.

This paper examines the effect of complex synaptic background activity on how neuronal response properties are altered by the neuromodulator acetylcholine. To do this, the authors made novel use of a hybrid methodology that combines biological recordings with computer simulations. The findings have important general implications for the study of other neuromodulators and drugs.

NITZ, D.A. (2006) Tracking route progression in the posterior parietal cortex. *Neuron* 49(5):747-756.

This work's importance lies in the identification of a novel way that spatial relationships in the world are registered by brain activity. It appears that the parietal cortex is capable of assembling activity patterns which register the spatial relationships between any arbitrary pair of objects or places.

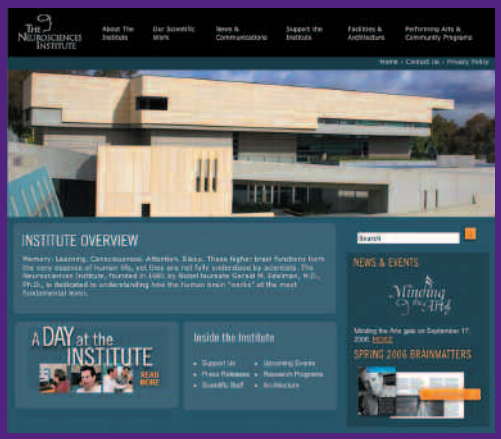
SETH, A.K., E.M. IZHIKEVICH, G.N. REEKE, AND G.M. EDELMAN (2006) Theories and measures of consciousness: An extended framework. *Proceedings of the National Academy of Sciences USA* 103(28):10799-10804.

This paper distinguishes key aspects of consciousness that can be measured. It then compares the strengths and weaknesses of three quantitative measures of dynamical complexity that have been applied to consciousness: neural complexity, information integration, and causal density.

The Neurosciences Institute Reaching Out to the Community

The Institute is committed to sharing the knowledge that we gain through our research with the community at large. Aside from publishing articles in scientific journals, we reach out to the public through our Library Roundtable lecture series and by various presentations to community groups. We hold monthly educational lectures at Casa de Mañana residence in La Jolla, and many of the Institute's Fellows frequently speak to various community groups about their latest research. Some of the recent presentations our fellows have made include:

- **Dr. Jeffrey Krichmar**, Senior Fellow in Theoretical Neurobiology, gave a lecture on the technology of brain-based devices at UCSD's California State Summer School for Mathematics & Science Program (COSMOS). This program provides residential academic experience for gifted high school students interested in careers in math and science.
- **Dr. Aniruddh Patel**, Esther J. Burnham Senior Fellow in Theoretical Neurobiology and an expert in studies of music and the brain, presented a lecture for UCSD's Grey Matters series, which has been broadcast by UCSD television. In addition, Patel has recently spoken about his research to the National Association of Teachers of Singing, the Wednesday Club of San Diego, and the Osher Lifelong Learning group.
- In the series "Discussing the Mind and Its Complexities" at Casa de Mañana, recent speakers were **Drs. Eugene Izhikevich, Elisabeth Walcott,** and **Fred Jones**. These short lectures have become very popular with the residents, and they have been followed by lively discussions about topics such as computational models of the brain, cellular mechanisms of communication, and the effects of drugs like caffeine on the brain.



The Institute's New Website

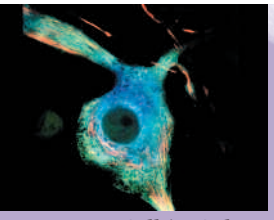
The new design of The Neurosciences Institute's website (www.nsi.edu) premiered on September 30 in celebration of our 25th anniversary. The new site offers a great deal of information about our scientific programs, campus architecture, and history. Our ongoing scientific research is presented in simplified summaries along with downloadable files of our technical scientific reports. In addition, look for electronic copies of our *BrainMatters* newsletters, press releases, a schedule of performing arts and other upcoming events at the Institute, and more. Please visit the website and find out about the many ways you can support the Institute's programs.

www.nsi.edu

Celebrating the Generosity of Lewis and Dorothy Cullman

On May 4, The Neurosciences Institute honored Lewis B. and Dorothy Cullman for their invaluable support and visionary generosity. Mr. Cullman is Vice Chairman of the Institute's Board of Trustees. Mr. and Mrs. Cullman have donated over $10 million to the Institute, largely through a challenge grant, that stimulated another $15 million in gifts from other donors. Their generosity has been recognized by naming Ralph Greenspan and Joseph Gally as the Lewis B. and Dorothy Cullman Senior Fellows.

The event honoring the Cullmans was held at the newly renovated Museum of Modern Art in New York City, where the Cullmans are also major benefactors. Many of the Institute's Trustees and a number of community leaders attended the dinner, joining together to thank Mr. and Mrs. Cullman for their combined imagination, foresight, generosity, and leadership. Dr. Edelman shared some of the Institute's main scientific accomplishments that were realized as a result of the Cullman's support. The dinner and festivities concluded with a song in tribute to Mr. and Mrs. Cullman.



Nerve Cell in Culture

Help Solve the Most Important Puzzle of Science: Become a Member of The Neurosciences Institute

"Without the brain you can not have sensation, perception, memory, consciousness, happiness, remorse, etc.,…and you wouldn't be able to read a novel." – Dr. Edelman

Deciphering how the brain works in the state of health is the key to understanding the processes that lead to diseases like Parkinson's and Alzheimer's and for the development of potential treatments for such diseases. The outstanding research programs of The Neurosciences Institute depend on the financial support of individuals and private foundations. The Institute has many opportunities for donors to get involved. For information about how to support the Institute and help advance brain research, visit our website at **www.nsi.edu**, or contact Rachel Jonte at jonte@nsi.edu, or 858-626-2018. All membership benefits are listed on the website. Contributions are tax-deductible to the extent allowed by law. The Neurosciences Institute is a nonprofit partner with the Endow San Diego program at The San Diego Foundation (see www.endowsandiego.org).

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THE NEUROSCIENCES INSTITUTE

From the Director

The celebration of the 25th anniversary of the Institute's founding prompted me to consider what has changed and what has remained constant over the years. What has remained unchanged includes our resolute commitment to understanding how the human brain works and our mode of organization as a scientific monastery. What has changed most significantly is the flowering of new discoveries and the flood of new talent which it has been our good fortune to attract.

We remain committed to supporting no more than forty remarkable young scientists in an atmosphere that encourages the sharpening of critical research questions and the choice of key problems in brain science. We continue to welcome Visiting Fellows from a wide range of fields to allow our young scientists to see across wider horizons. In this way, our interests remain diverse, but not too diverse.

What has been achieved in the last twenty-five years? First, we have trained and cultivated 52 former Fellows, who have gone on to distinguished, independent careers at research institutions here and abroad. Second, we have made a series of seminal discoveries ranging from innovation in embryonic brain transplants and the molecular biology of sleep to a number of theoretical achievements, culminating in the design for the first time of brain-based devices. These devices provide new ways of understanding brain action and promise to open up new applications in the design of intelligent machines.

One might ask how our organizational structure prompts such discoveries. In part, the answer rests in our style of funding research. Instead of judging a young person's work by how many grants he or she has obtained, we use a larger set of more flexible criteria—choice of problem, innovation, and, above all, imagination. Of course, we expect skill to dominate the design and execution of experiments, but beyond skill we judge the marks of taste in analyzing a problem and judgment in executing its solution.

Success in brain science (and in biology in general) rests in picking the right example of a target for research. The great variety and complexity of animal systems cannot be examined by any one institution or approach. Unlike physics, where a general problem can be expressed in mathematical form, the generalities of biology are best revealed by the inspired choice of animal species, tissues, and molecules to serve as exemplars of deep principles. Of course, as in physics, new methods and technologies play a major role. We strive to keep abreast of such advances from day to day.

While experimentation is our foundation, we realize that studying the brain, which is perhaps the most complicated object in the known universe, requires a global theoretical approach. We have steadfastly supported theory making and computer simulations of a variety of key brain systems, and our Fellows have made major contributions in this domain.

Clearly our efforts have grown and changed with the passage of time. Over the years, we have striven to make our work and facilities available to the community at large. We are particularly pleased by the response and support of the San Diego community upon hearing about our work. The philanthropic support of the community gives us a key impetus for our next period of accomplishment.

In sum, what has changed over the last two-and-a-half decades is the building of new concepts of understanding the brain as the center of human concern. What has remained constant is our mode of organization along with our steadfast dedication to understanding the human brain.

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

DONOR PROFILE

Einar Gall, Jinx Ecke, and Gerald Edelman

"Light tomorrow with today!"

— Elizabeth Barrett Browning

"Years ago when I was the leader of my daughter's Camp Fire group, I came across this line in the leaders' manual: 'Teach the girls to leave the campsite better than they found it.' I've always thought of that as pretty good advice, and my involvement with The Neurosciences Institute is my attempt to do just that."

The Neurosciences Institute salutes Elisabeth "Jinx" Kenney Ecke, our long-time benefactor and dedicated volunteer, for lighting the way to tomorrow through her involvement and investment in the Institute today. Jinx has been serving on the Board of Trustees of the Institute since 2002. She was instrumental in the planning and creation of our very first Minding the Arts gala event to raise funds for the Institute's Performing Arts program. Her efforts have increased community awareness for this important program, through which the Institute's Auditorium is made available to local nonprofit organizations at no charge for arts and culture events which enhance the community of San Diego. Minding the Arts was so successful that it has become an annual event for five years running, and Jinx remains actively involved on the Honorary Committee and as a sponsor.

A native of Bloomington, Indiana, and a graduate of San Diego State University, where she studied speech pathology, Jinx was married for 40 years to the late Paul Ecke, Jr. of Ecke Poinsettia Ranch in Encinitas. She has three children and seven grandchildren. Jinx has been very active along with her family in promoting and supporting the California 4-H Youth Development Program, which emphasizes citizenship, leadership, and life skills.

Jinx is an advocate of women's civil rights and has been a devoted supporter of Planned Parenthood, serving on their Board of Trustees for six years. She has been very active in helping to elect pro-choice candidates to public office, and she is a founding member of the San Diego Women's Foundation. Jinx cares deeply about children, arts, culture, and the environment, and she has funded many grants to local community organizations through her fund at The San Diego Foundation. She has also been actively supporting the San Diego Zoological Society. In 2005 she was honored as the distinguished alumna of the year by the San Diego State Alumni Association. Currently, she serves as Vice President of the Friends of the Library at San Diego State University.

Jinx became involved as an advocate for the Institute because she believes that its unique structure, leadership, capable scientists, and focus on fundamental brain research make it ideally positioned to make important headway in understanding the mysterious human brain. She is excited about where this new understanding may lead in treating illness and disease. The Institute is deeply grateful for her dedication, generosity, and wisdom.

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BrainMatters

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