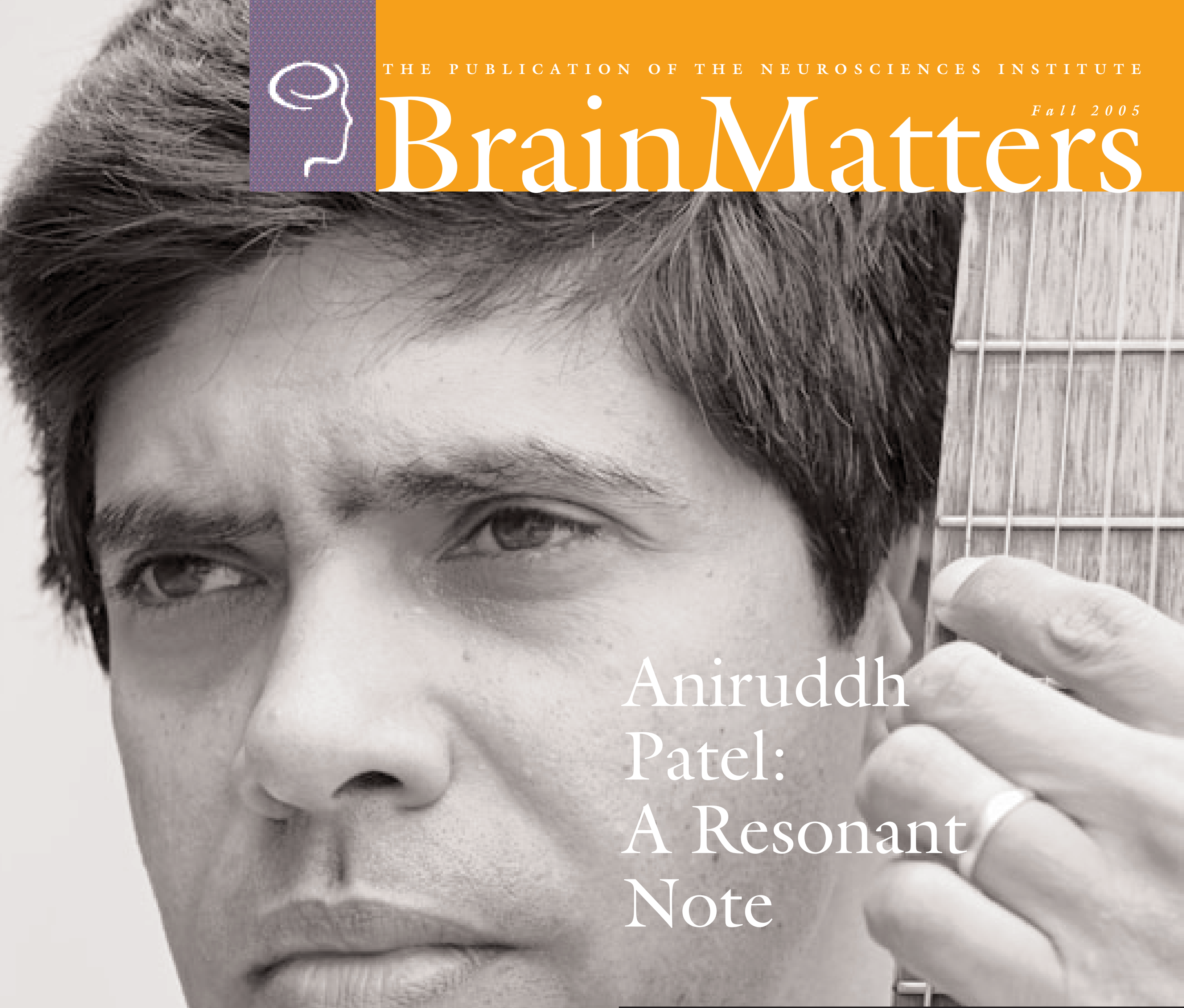
THE PUBLICATION OF THE NEUROSCIENCES INSTITUTE

BrainMatters

Fall 2005



Aniruddh Patel: A Resonant Note

It's something we've all experienced in our lives. You hear a melody, and you're suddenly overwhelmed by a complex cascade of memories and emotions.

Maybe it's a piece by Debussy, and you're back walking in the Left Bank on a serene summer evening. Or maybe it's a jumping swing tune by Count Basie, and now you're dancing in a sweltering ballroom in 1950s New York. Perhaps it's a powerful guitar solo by Eric Clapton, and you can feel the energy of

“As far as we know, humans are the only species that synchronize to a beat, that move or tap their feet to musical rhythms. What does that tell us about the human brain and its structure and function?”

the crowd in San Francisco’s Fillmore West.

Aniruddh Patel, the Esther J. Burnham Fellow at The Neurosciences Institute, is one of a relatively small group of scholars across the world who are determined to gain new insights about music and its powerful influence on the brain.

“A lot of people think that music is just a humanistic, cultural creation. Why would you choose to study music and the brain? How would that be any more related to brain function than painting and the brain?” says Patel.

“But that’s not really how studying music and the brain works. Music is a link to understanding fundamental aspects of brain function.”

An Outback Awakening

Patel’s path to his current studies has been circuitous. In the early 1990s, he was pursuing a doctorate at Harvard University and focusing on ecology and biology. In the third year of his studies, as he was doing fieldwork on the lives of ants in Northern Australia’s Outback, he had an epiphany.

“The research was going well, and I had an experiment lined up. But I realized that a Ph.D. is too much of an investment in one’s life to not do what you are really passionate about,” recalls Patel.

“So I wrote to my advisor, and I told him everything was fine. But I told him that what I really wanted to pursue was this issue of music and the brain. He wrote me back and said clearly you should pursue what you’re truly interested in. If that’s what you want to do, come back and we’ll start working on it.”

Since he was a child growing up in Delaware, Patel had been interested in music. He played clarinet as a youth, and he took up the study of classical guitar as an undergraduate at the University of Virginia. At Harvard, as he focused on biology and neuroscience, he began to see connections between his lifelong interest in music and its largely unknown effects on brain function.

“People have had theories about music and the brain for a long time. Plato talked about how music could reach the inner workings of the soul,” says Patel.

“Today, in terms of researchers who are really focusing on music and the brain, the community is still small. But over the last few years, we have really reached a critical mass, and we’re starting to meet regularly, interact with each other, and build on each other’s work.”

A Sense Of Place

Patel joined the Institute in 1997, following one of his advisors from Harvard to La Jolla.

He encountered a place where the interdisciplinary approach that is fundamental to his work was central. He was surrounded by scientists who were also musicians: Institute director Gerald Edelman is a classically trained violinist, and many of the research fellows were amateur musicians or music lovers.

And then there was the superb auditorium at the Institute where prestigious musicians from throughout the world converged to perform pieces ranging from those of Bach to those of Duke Ellington.

“I learned that Dr. Edelman was interested in the idea of studying music and brain function, and I saw this an ideal place where I could study fundamental neuroscience and also pursue questions related to music and the brain, which at the time was a very new field,” says Patel.

The Big Question

In this emerging field, researchers like Patel have an opportunity to pursue an array of issues and interests.

“The big questions are all there waiting to be tackled. There’s a chance of doing important things first,” he says.

As he sits in his office at the Institute, he quickly rattles off a series of questions that need to be answered.

“Some people can acquire astonishing motor skills. Playing the piano, in terms of the great pianists, can be comparable in skill to any professional sport. What changes in the brain accompany learning that ability? There’s formal evidence that musicians' brains differ from those of non-musicians," he says.

"There's a lot of discussion these days about how music can make you smarter. The latest evidence suggests that it's not just listening to music that has an impact, it's also studying a musical instrument. Learning that instrument over time that can have a positive effect on cognitive function."

"As far as we know, humans are the only species that synchronize to a beat, that move or tap their feet to musical rhythms. What does that tell us about the human brain and its structure and function?

"How can neuroscientists use music as a tool to explore how the brain deals with patterns in time, a question of fundamental importance to our understanding of how speech and language are processed by the brain?"

The Language Of Music

As he contemplates the myriad questions related to music and the brain, Patel has focused on an issue that is proving to be very fruitful: the relationship between music and language. While most of his work in this area has focused on brain function, he recently tackled a fascinating issue concerning the acoustic patterns of speech and music: How does language affect and define a culture's music?

He looked at two countries with powerful musical traditions and distinctive cultures—England and France. Patel wanted to know why, for example, the music of Sir Edward Elgar, who composed Pomp and Circumstance, sounded English. And what makes Debussy's music so distinctively French?

He says that musicologists and linguists had hinted that there were connections between the rhythms and cadence of spoken language and music, but the arguments were "largely anecdotal."

He and his team used new methods, focusing on measurements of the duration and pitch patterning of vowels in English and French speech that allowed them to directly compare rhythm and melody in music. Patel's team concluded "instrumental music in these two cultures does indeed reflect the prosody of the national language. Thus the language we speak may influence the music our culture produces."

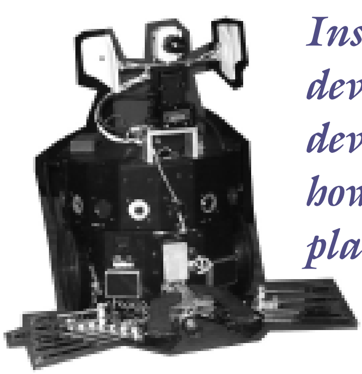
Patel moves seamlessly from one topic to another, from one discipline to another, and he believes that the Institute provides him with an ideal environment to pursue his varied interests.

"To do this kind of work, you need to be firmly rooted in neuroscience but have an open line of communication with people from linguistics, musicology, cognitive psychology—part of the fun of this is that I get to talk to people who are doing a wide variety of interesting things," he says.

"Right now, I'm dealing with the details of phonetic structure of language and how it's reflected in composers' work. And at the same time I'm also doing research on the neural relationship of music and language and working to tie these threads into a larger picture about the brain's processing of structured sound."

Make It Through the World

Institute researchers are developing brain-based devices that shed light on how we create a sense of place in a complex world



Jeff Krichmar came to The Neurosciences Institute in 1999 for a very specific reason—to enhance efforts to build highly complex and intelligent devices that model how the brain works. At the Institute, these brain-based devices were initially developed by Gerald Edelman and George Reeke, and from the beginning each was called “Darwin” after Charles Darwin.

The current version, Darwin X, stands about three feet tall and looks similar to a robot from Star Wars, but Krichmar is quick to tell you that Darwin is not a robot. It has a computer-simulated brain and nervous system that drives it. Neither is Darwin is an experiment in artificial intelligence. Rather, Darwin has become one of the most sophisticated models in the world, allowing Institute researchers to delve into how our brains learn from experience.

About three years ago, Krichmar and his colleagues Doug Nitz and Anil Seth accepted a challenge that, in the field of neuroscience, might be equivalent to scaling Mount Everest.

They were charged with creating an accurate model of the hippocampus, the part of the brain that drives the formation and recall of episodic memories, the autobiographical memories of one’s life. Among its many functions, the hippocampus is a key component in the system of interconnected brain regions that allows you to remember what you did a few moments ago and to play your next move—it provides context for the world around you. In Alzheimer’s disease, for example, hippocampal function is modified, resulting in a devastating loss of episodic memory and disorientation for those who suffer from the disease.

“Dr. Edelman had always wanted to incorporate a model of the hippocampus into a Darwin,” says Krichmar. “Inputs coming from many other areas of the brain converge on this small area, whose outputs are also widely distributed. The anatomy is distinct from that found anywhere else in the brain.”

The Challenge

To develop a functioning model of the hippocampus, the team needed to approach the problem from several different perspectives. Indeed, it was a classic Institute approach to science—bringing together people with divergent backgrounds to gain a new understanding of the brain.

“Doug knows more about the anatomy of the hippocampus than any of us,” says Seth. “And Jeff has this tremendous ability to create computer models. With my background in network theory and analysis, my task was to understand the causal interactions within the hippocampus

and between the hippocampus and the rest of Darwin's brain. I wanted to know how the neurons communicated."

The computer model of the hippocampus that the team created was complex—it included 90,000 neurons and about 1.4 million neural connections and reflected the principles of hippocampal anatomy and physiology.

To gauge how the model of the hippocampus functioned, Darwin had to go through a series of exercises in navigation. Darwin had to learn to locate where it was by assessing the pattern of colored objects on the walls of its 16 by 14 foot pen.

As Darwin roamed around its pen, a video camera allowed it "to see," to capture images sent through a wireless connection to its simulated brain running inside a computer. Krichmar says Darwin's brain tried to make sense of the image through the activity of its neurons and then it triggered motor commands, which were relayed to Darwin's body causing it to move in a particular direction within its pen.

Darwin's task was straightforward enough—it had to locate a particular place where it received an electronic reward, in essence a positive sensation.

But the beauty of this simple task, from the researchers' perspective, was gauging how the brain deals with previous and anticipated experiences, in terms of the neural activity within and between regions of the simulated brain.

"We really wanted to learn how the brain processes what is relevant, what is irrelevant, and what is marginally relevant," says Seth.

The Surprise

In a two-hour experiment, Darwin began the process of exploring its pen. Initially, it didn't know that there was a reward in the pen, but when it randomly came across the place leading to the positive electronic sensation, it began to learn and remember: Darwin used its simplified hippocampus to remember the recent episodes in its movements that led to its reward. The differently colored and shaped objects on the walls of the pen served as landmarks, or points of reference for its behavior. Thus, it navigated in much the same way mammals navigate to find food or a safe place.

The researchers anticipated this would happen—that Darwin would generally be successful in its task of navigating the pen and finding a positive reinforcement.

But then something interesting happened—instead of following the same path to the reward consistently, Darwin started taking shortcuts to the reward. As the team analyzed the cellular activity in Darwin's hippocampus, they made an important observation.

"It has long been known that the hippocampus has a distinct cellular architecture, incorporating multiple loops that allow it to process information," says Nitz. "Looping allows for a mixing of old information with new information."

As the team looked at Darwin's navigation behavior, they found that Darwin's brain was using different strategies for novel and for familiar environments. When the pen was new to Darwin, many of the loops in Darwin's hippocampus were involved in the processing. When the pen became familiar to Darwin, the device's simulated brain used fewer loops to make a good decision.

"That was a complete surprise," says Nitz, who has spent the majority of his research efforts looking at actual mammals rather than brain-based devices. "This was my first foray into modeling, and it opened my eyes to the fact that there is more promise there than I probably appreciated."

For Seth, who had the daunting task of analyzing the neural connections and what caused one neuron to prompt another neuron to fire, Darwin's navigation affirmed his belief in the possibilities of understanding causality in the tremendously intricate interactions of the brain.

"When I think about what I do on the most fundamental level, my task is pretty simple," says Seth. "I'm trying to take what looks like a mess and translate it into something understandable."

News & Events

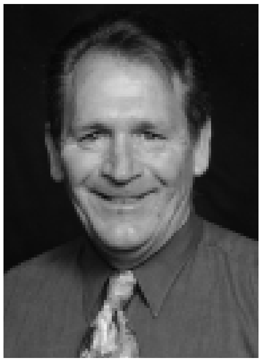
Institute Board Chairman Bill Walsh, Institute Director Gerald Edelman, and Vice Chairman Lewis Cullman (above, from left to right) view the new donor wall. At right, Institute researcher John Iversen talks with a group of volunteers and donors about his work related to music and its influence on brain function.

The Impact of Philanthropy

On May 14, more than 100 donors and trustees from around the country attended a morning of stimulating scientific presentations. Institute scientists described a range of examples of the theoretical and experimental research that they are pursuing. During the weekend, the Institute unveiled its new donor acknowledgment wall, which is located in the outdoor loggia of the auditorium. The wall recognizes individuals who have made cumulative gifts totalling $2,500 or more to the Institute.

IN MEMORIAM

Wayne E. Foster



All of us at The Neurosciences Institute are deeply saddened by the death of Wayne Foster, who lost his battle with cancer on August 28, 2005.

Wayne was a key contributor to life at the Institute for a decade. His careful attention to the big and small details of daily operations made it possible for us to be confident that lights would light, deliveries would be received, the grounds would be free of debris, and visitors would be properly escorted. Many were touched by his kindness and caring.

We shall miss his quiet humor, personal friendship, and deep commitment to the Institute.

Institute Team Wins RoboCup Soccer Tournament

In early May, researchers from The Neurosciences Institute competed at the 2005 RoboCup US Open in Atlanta, Georgia. The team consisted of a Brain-Based Device (BBD) using the Segway Robotic Mobility Platform and a human riding a Segway Human Transporter. The fully autonomous BBD is capable of all aspects of soccer play: passing, shooting, blocking, and planning routes up or down field.

Only two groups—The Neurosciences Institute and Carnegie Mellon University—have developed this type of technology, though the two organizations use very different approaches. The Institute's unique BBD model is based on a simulated brain that learns from its experiences, while Carnegie Mellon's robot is specifically programmed using an artificial intelligence aapproach. Both teams demonstrated Segway soccer with a series of games; this was the first time in RoboCup history that humans and robots interacted in complete games.

The Institute swept the competition with scores of 3-0, 4-0, 3-0, 3-0, and 2-1.

From the Director

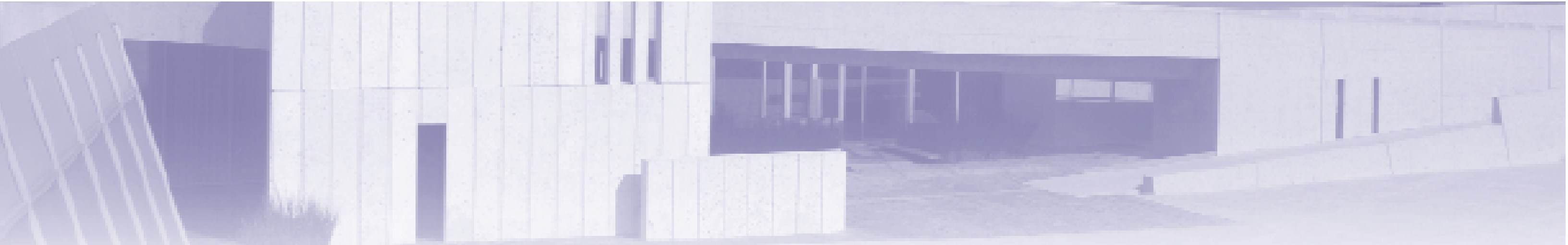
In considering the report in this issue of our work on music and the brain, I was prompted to recall two significant quotations. The first is by the great French physiologist, Claude Bernard, who said "Art is I, science is We." Suzanne Langer, a philosopher interested in the arts and the mind, said "Art is the objectification of feeling and the subjectification of nature." The two quotations are linked: Subjectification necessarily means "I", and objectification relates to the world that scientists explore—as "We."

The extraordinary progress of neuroscience has made it possible to explore characteristics of the human brain that lead to the production of artistic creations. While in the past, it was possible to study the psychological features of artistic creation, it is now possible to examine actual events in the living brain during the creation and response to graphic art and music.

We are now able to measure the most minute electrical currents in the brain as a person listens to and imitates rhythmic sequences. Drs. Ani Patel and John Iversen and their colleagues have used this methodology, called magnetoencephalography or MEG, to look at the patterns of brain responses. They have already found a great difference between rhythmic signals that are auditory and signals that are visual with the same timing. Untrained individuals can tap accurately to a metronomic beat, even after it has ceased. But if that beat is presented as rhythmic visual flashes in exactly the same pattern, it is very difficult to keep the precise rhythm. Thus, the two sensory modalities clearly differ in the way the brain treats their signals. Continued examination of brain responses by MEG or similar noninvasive techniques should greatly clarify the relationships between hearing and vision. They should also reveal interactions with the areas of the brain responsible for generating patterned movement.

One of the intriguing promises of current work on music at the Institute is the possibility of exploring the connection between rhythm, melody, and speech patterns. It may well be that the study of responses to music will provide a royal road to the understanding of key brain mechanisms involved in speech. What has already emerged from these studies relates to "subjectification." It has become clear that the brains of individuals are unique in their patterns. While, for example, we all respond similarly to certain patterned rhythmic inputs, the way in which we respond is often quite idiosyncratic. Understanding the basis of this individuality should shed a great deal of light on the range of our artistic responses, both as creators and as observers.

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



DONOR PROFILE

For the Love of Music and Science

Esther Burnham has long been passionate about opera. She is fascinated by this unique art form that brings so many disciplines together. She talks enthusiastically about how the singers, the instrumentalists, the costume and set designers, and the myriad other individuals work together to create an experience that is singular and powerful.

Ms. Burnham, a prominent San Diego volunteer and philanthropist who serves as a board member at The Neurosciences Institute, sees a clear link between the intricacies of opera and the multidisciplinary work of the Institute.

While she has had an opportunity to interact with many Institute scientists, she is particularly interested in the work of Associate Fellow Aniruddh Patel, who focuses on the connection between music and the brain. Ms. Burnham has established a Fellowship for Patel so he can pursue his important research.

Music has been a vital part of Ms. Burnham's life for almost all of her 90 years. She played the piano as a child in Brooklyn and developed a keen interest in classical music.

When she and her first husband, Stephen Newmark, moved to Los Angeles in the 1940s, she volunteered to enhance the visibility of classical music and opera. Newmark died in 1970, and Ms. Burnham met Donald Burnham, a prominent San Diegan, who shared Ms. Burnham's other passion—sailing. She and Burnham married and moved to San Diego in 1973, where she quickly became involved in the arts community. She has long served on the board of the San Diego Opera and continues to be involved in fundraising for the organization.

At the same time, she has become a strong advocate for The Neurosciences Institute, introducing friends and colleagues to the innovative work at the Institute.

"I am vitally interested in the work of the Institute, and I want others to support the Institute," says Ms. Burnham. "When I meet scientists or walk through the campus, I get a powerful sense of the fascinating research, and I am enthralled by what is happening there. It truly is a place where people work across disciplines to gain insights into issues that affect all of us."

"Music affects me a great deal," says Ms. Burnham. "It can bring tears to my eyes or it can elate me."

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