

BROADER CAREER CHOICES ON THE HORIZON?

Understanding the brain is considered one of the grand quests of science, partly due to the conviction that the brain holds the key to what makes us human. The other reason is the intricacy of the organ itself, which James Watson has called “the most complex thing we have yet discovered in our universe.” That three-or-so-pound lump of soft tissue, housed within the cranium, has about 100 billion nerve cells or neurons (roughly equal to the number of stars in our galaxy), which form trillions of connections with each other, giving rise to millions of operations going on simultaneously. **By Steve Nadis**

Neuroscience encompasses a broad range of attempts to determine how the brain, its many components, and the nervous system as a whole function and, in some cases, malfunction, with one hope being to find remedies for when things go wrong. The good news for anyone contemplating a career in this field is that there is plenty of work ahead, and no shortage of problems to grapple with. The Nobel Prizing–winning neuroscientist **Eric Kandel** of Columbia University thinks it will take at least a century to understand normal brain processes, as well as major disorders like schizophrenia and depression.

For people operating on a shorter time frame, there is good news as well, for in the past decade or so, there has been substantial progress in this field. Partisans like **Robert Desimone**, director of the McGovern Institute for Brain Research at MIT, believe “there hasn’t been a better time to go into neuroscience,” owing to the powerful new tools at a researcher’s disposal. The field, according to Desimone, is benefiting from scientific revolutions in genetics and genomics, molecular biology, brain imaging, computer modeling, and so-called “systems neuroscience,” which focuses on how entire brain systems operate rather than looking at individual neurons, genes, and proteins. One area that has just come to the fore involves optogenetic techniques, which allow neuroscientists to selectively manipulate the activity of specific neurons using light.

Although jobs may be tight amidst the current economic slowdown, Desimone is optimistic about the field’s long-term prospects. “Universities will start hiring again, and private companies will start expanding again,” he says. “New opportunities are opening up due to the breathtaking pace of technological development.”

To those still seeking employment, he counsels patience as well as flexibility regarding the types of positions one might consider. Rather than getting fixated on one approach, it’s better for scientists to get broader training that puts them in a position to show competence in any number of new techniques. As for those in senior postdoctoral positions ready for the next step, he says, “Just hang on. Things will turn around.”

Academia is an appealing choice to many in the present economic climate. “There has been a massive [50 percent] increase in the number of Ph.D. applicants this year—270 applicants for six places,” says **David Attwell**, the University College London (UCL) neuroscientist who oversees the four-year Ph.D. fellowship program funded by the Wellcome Trust charity. And at the postdoctoral level, Attwell says, “As long as the grants keep coming, people will stay in academia longer than they have in the past until outside jobs start picking up again.”

UCL—already a major center of neuroscience with 450 principal investigators on its faculty—is set to expand further, assuming plans of the Wellcome Trust and Gatsby Charitable Foundation are realized to build a \$260-million neuroscience institute there. The proposed institute would engage a dozen or more research groups in the task of figuring out how human or animal behavior springs from information processing at the level of neural circuits. [continued »](#)



Robert Desimone



Claudia Kawas

“There hasn’t been a better time to go into neuroscience.”

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NEUROSCIENCE

“Our philosophy is that only through basic research can you undertake novel approaches to disease.”
—Morgan Sheng



Meanwhile, new neuroscience complexes are sprouting up elsewhere, including the Ernst Strüngmann Institute in Frankfurt, Germany, named after the founder of the drug company Hexal. Andreas and Thomas Strüngmann, his successors, donated more than \$300 million for this facility. This marks the first time Germany’s Max Planck Society has used private money to establish a research institute, says **Wolf Singer**, director of the Max Planck Institute for Brain Research and interim head of the new institute. “We hope it will set a precedent for other public-private research ventures in Germany.”

The center will create jobs for about 80 to 100 scientists, according to Singer, plus another 40 people for infrastructure. Though the focus will remain flexible, a priority will be placed on primate research, he says. “Given how rare this has become in Europe because of animal research restrictions, my feeling is that once we lose that, it’ll be gone forever.”

Much of what is known about nerve cell processing comes from single-cell recordings, Singer says. “But that’s clearly not the end of the story. The brain is a highly distributed system that uses distributed codes that can only be understood if you look at many cells at the same time.” The coordination of these distributed functions in the brain leads to specific behaviors, he adds. “That’s where animal models are essential. We can look at many nerve cells at the same time while simultaneously charting behavior.”

As the Strüngmann Institute is located on the university’s medical campus, it will take advantage of the availability of patients to probe what Singer calls “the highest integrated functions” and their pathologies. Arguably the most convenient and least invasive way of doing that is through functional magnetic resonance imaging, or fMRI—a technique that measures changes in blood flow and blood oxygen levels in the brain, thereby showing which parts of the brain are activated when people perform various tasks. By virtue of this tool, researchers have gained insights on how healthy brains work, while also identifying signs of brain abnormality.

Consequently, the use of fMRI has exploded worldwide since its invention in the early 1990s. “The last time I checked, 12,000 papers had been published on fMRI-related research since 1992,” says Washington University in St. Louis neuroscientist **Marcus Raichle**. The number of papers reflects both the excitement at having an unprecedented window into the brain at work and the increased availability of machines themselves. Devices that were once found only in elite radiology centers are now scattered throughout university departments. “The majority of research today is done on machines dedicated to researchers,” Raichle notes.

At first, fMRI was used primarily to explore classical questions in-

volving attention, memory, language, and perception. Its use was later extended to the study of diseases like Alzheimer’s, schizophrenia, autism, and stroke. A relatively new area is to look at the developing nervous system by scanning infants, children, and adults at rest, to chart changes in activity patterns as the brain matures. fMRI scanners also allow Raichle and other researchers to study the brain’s “dark energy”—baseline activities that are unrelated to external stimuli or the performance of overtly visible tasks, yet consume the vast majority of the brain’s energy. “It’s fair to say that a large fraction of the brain’s functional activity is unaccounted for,” notes Raichle, who’s hoping fMRI can help unlock this mystery.

As with functional brain imaging, the emerging technology of neuroprosthesis is opening up many new doors in the field. A team led by Brown University neuroscientist John Donoghue has implanted sensors in the brains of four quadriplegic patients that connect signals from the motor cortex to output devices, thereby enabling paralyzed patients to move computer cursors, control robotic limbs, and operate wheelchairs. Parallel efforts are under way at many other universities—all sharing the common goal of restoring functions to people with disabilities. The endeavor is bringing new people into neuroscience, including those accomplished in electronics, signal processing, sensor design, and other aspects of engineering.

“The diverse activities now under way illustrate that there are many different ways of being a neuroscientist,” says **Claudia Kawas**, a neurologist at the University of California, Irvine. “I work on a population study with more than one thousand 90-year-olds. Others in my department are studying learning and memory in sea slugs (*aplysia*) and songbirds. There are people who rarely see anything other than a cell culture, and those who spend all day looking at computer screens. There are also those who put mice in mazes and genes in mice. There is, in other words, something for everybody.”

Kawas focuses on the aging brain, which is a growth area, partly owing to demographics: In much of the world today, she says, people over 90 comprise the fastest-growing segment [continued »](#)

Featured Participants

Brown University
www.brown.edu

Columbia University
www.columbia.edu

Eli Lilly and Company
www.lilly.com

Gatsby Charitable Foundation
www.gatsby.org.uk

Genentech
www.genetec.com

Massachusetts Institute of Technology
www.mit.edu

Max Planck Institute
www.mpg.de/english

National Institute of Neurological Disorders and Stroke
www.ninds.nih.gov

Society for Neuroscience
www.sfn.org

The Wellcome Trust
www.wellcome.ac.uk

University College London
www.ucl.ac.uk

University of California, Irvine
www.uci.edu

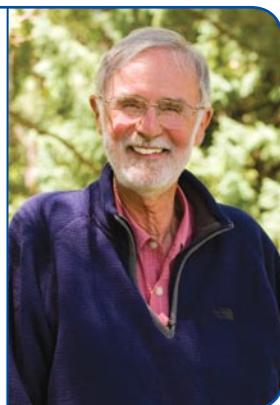
Washington University in Saint Louis
www.wustl.edu

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NEUROSCIENCE

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— Marcus Raichle



of the population. Though there are fewer than 2 million people in that category in the United States today, forecasts suggest there will be 10–12 million a few decades from now. Perhaps the biggest concerns for this portion of the population is dementia—including Alzheimer’s, the most common form—and other kinds of cognitive impairment. While getting to the root of Alzheimer’s has proved immensely challenging, there’s the further mystery of “Disease X.” Half the people over 90 who suffer from dementia have no obvious brain pathology, Kawas says. “It’s hard to know how to treat these people because we still don’t know what’s wrong with them.”

“When I started in this field 25 years ago,” she adds, “someone said they’ll cure Alzheimer’s and then there will be nothing to do. I now know that will never happen. We won’t run out of questions to explore. Alzheimer’s, like cancer, is not a single disease, and no single cure will take care of it all.”

Nevertheless, with tens of millions of people suffering from Alzheimer’s worldwide, there is keen interest in finding medical treatments for this disease. And the same holds for Parkinson’s, amyotrophic lateral sclerosis, and other neurodegenerative ailments.

Like much of the pharmaceutical industry, Eli Lilly and Company had focused its central nervous system drug development efforts on psychiatric illnesses, but is now making major forays into neurodegenerative diseases as well. “The need in this area is enormous and growing,” says **David Bredt**, who oversees the company’s neuroscience research. Lilly currently has two Alzheimer’s drugs in Phase 3 clinical testing (the final phase before seeking FDA approval). One drug blocks an enzyme essential to the formation of amyloid plaques that are thought to cause the disease. The second drug is intended to clear away the peptides that constitute the principal components of the plaque. “We’re getting a clearer understanding of the pathologies—amyloid plaques and their analog in Parkinson’s, Lewy bodies—and how we can thwart their formation,” says Bredt. Psychiatric illnesses like schizophrenia and depression are more mysterious, he adds, because there are no known brain lesions scientists can ascribe to those conditions.

“Neuroscience remains an area of tremendous unmet medical need,” Bredt notes. “With the burden of disease dramatically increasing along with an aging population, it constitutes among the largest therapeutic markets for drugs.”

Genentech, one of the world’s biggest biotech companies (recently purchased by Roche), seems to agree with that assessment. The company put its neuroscience program on hold a decade ago but is now making a renewed push in this area. The time is right owing

to recent advances in understanding how the brain works, claims the company’s neuroscience head **Morgan Sheng**, “coupled with the fact that most diseases of the nervous system are very inadequately treated.”

Genentech is focusing on neurodegenerative conditions, with additional efforts in pain and psychiatric illness. The company, which employs more than 100 postdocs, places a premium on basic (as well as translational) research, encouraging its scientists to publish in top journals. “Our philosophy is that only through basic research can you undertake novel approaches to disease,” Sheng says. “If you leave the basic research to academia, all you can do is react.”

Sheng left a tenured position at MIT as a professor and Howard Hughes investigator, moving to Genentech last year in order to have “a more direct impact on human well-being. My decision relates to the prospect that in the next 10 years we can come up with treatments for brain disease that really help people,” he says. “Obviously, you cannot fully do that in academia; you have to work with a drug company.”

Nevertheless, Sheng believes the wall between academia and industry is not nearly so pronounced as it once was. “There’s a lot of exchange between the two, with the flow going both ways,” he says. “Moreover, the kind of people we’re looking for—good scientists with solid training in multiple aspects of neuroscience—aren’t really different from what academic institutions are looking for.”

It is certainly the case that more career paths are open today, says **Thomas Carew**, president of the Society for Neuroscience (SfN) and chair of the University of California, Irvine’s Department of Neurobiology and Behavior. “When I started out 30 years ago, there was typically just a single path, which led to university professor. While that’s still the primary goal for many, there are other choices today.” In addition to jobs in industry and journalism, exciting new subfields are opening up for example in law, where neuroethics is playing an important role, and neuroeducation, which involves educational strategies that attempt to capitalize on neuroscience insights.

“Students shouldn’t try to figure out where the field is going,” Carew says. “They should make decisions based on what excites them and where their passion lies.” For those who are unclear as to what the possibilities may be, SfN—which has 38,000 members, a third of whom are graduate students and postdocs—offers an array of professional development programs that highlight various career choices.

One way of easing the transition from research fellow to working professional is through a National Institutes of Health grant. Pathway to Independence Awards, for instance, are specifically designed to smooth the transition from postdoc to independent research. Investigators with novel ideas, especially those who are in the early stages of their careers, might consider applying for New Innovator Awards. A variety of other funding sources can, of course, be pursued. “It’s a spectacular time to be a neuroscientist,” says **Story Landis**, a neuroscientist who heads the National Institute of Neurological Disorders and Stroke. “There are fantastic opportunities to do great science and really make a difference.”

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