Investments Boost Neurotechnology Career Prospects

The past few years have seen some extraordinary activity in the neuroscience field. High-profile advances, from the Allen Brain Atlas to the Brainbow mouse, have injected an air of excitement into the study of the brain—an atmosphere that has been amplified by big funding initiatives in the United States and abroad. For budding neuroscientists, it's heady days—at least if you've got a knack for technology development, programming, and engineering. But it will take more than raw skill to land a job. **By Jeffrey M. Perkel**

Mark Cembrowski was a graduate student in applied mathematics with a taste for neurobiology at Northwestern University when he discovered a way to marry his two interests.

Two of his math professors were collaborating with physiologist Joshua Singer, also at Northwestern, who was keen to model the biology of a retinal cell called the AII amacrine interneuron. "Josh wanted someone to come in and build a model of single AII cells to try and understand how the AII works as an input/output device," Cembrowski explains. So, he joined Singer's team.

But models are only as good as their input data, and very quickly, Cembrowski says, he realized he needed more of it. Specifically patch-clamp electrophysiology data. And he was going to have to collect it himself.

Patch clamping isn't easy even for seasoned neuroscientists, let alone an applied mathematician who'd never set foot in a biology lab. "I was the worst of the worst," he concedes. "I broke a lot of things getting started."

Still, he persevered, and in 2012 published his first electrophysiology paper. "My whole perspective on this just flipped 180 degrees," he says. "When I found the confidence and the ability to do these experimental techniques, I felt like I was on top of the world."

As it turns out, researchers like Cembrowski are atop the neuroscience world, too, where research opportunities increasingly blend traditional neurobiology with technology development.

That marriage of disciplines underlies President Obama's recently announced Brain Research through Advanced Innovative Neurotechnologies (BRAIN) initiative. Seeded with $110 million from the U.S. National Institutes of Health (NIH), the National Science Foundation, and the Defense Advanced Research Projects Agency, the initiative has a heavy focus on technology development, says **Tom Insel**, director of the National Institute of Mental Health (NIMH), one of four NIH institutes that together contributed $40 million to the pot.

"This is a unique investment," Insel says. "It's not to expand all of neuroscience, but it's to invest in the area of tool development specifically, which is sometimes difficult to do with RO1grant funding."

In particular, he says, the initiative will support a new breed of neuroscientist, one trained not as a classical brain researcher but as a physicist or mathematician, computer scientist or engineer—researchers who may never have received NIH funding before. "One of the measures of success for me with the BRAIN Initiative is, when I see the pay plan of who's going to be funded, I'm hoping that I will not recognize most of the names," he says.

One name that won't be on the list is Cembrowski, who is still in training. Upon graduating with a Ph.D. in applied mathematics, he joined **Nelson Spruston**'s lab at the Howard Hughes Medical Institute's Janelia Farm Research Campus, a private research institute with a heavy focus on neurobiology. There, he pivoted again and again, from electrophysiology to RNA-sequencing data analysis, to anatomy and histology, and thence to behavioral analysis. "No technique is an island," he explains. "There's always other techniques that one can adopt as a way of validating and extending what you've done previously."

"This is a guy who just knows no boundaries," Spruston says. "He's going to go out and learn what he needs to learn to answer the questions that he wants to answer. And this is to me the phenotype of the successful neuroscientist these days."

Collecting techniques

So how can one develop that phenotype? Certainly, a solid technical background doesn't hurt. Popular flavors *du jour* include connectomics, functional magnetic resonance imaging (fMRI), and optogenetics.

But it's not the acquisition of techniques per se that matters, most say, so much as the willingness to try new things, coupled with sufficient neurobiology expertise to understand what questions to ask. continued>

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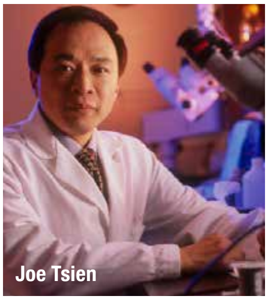
Joe Tsien

"We don't hire assistant professors because they know technique *x*, but because they are working on an interesting problem," says **Eve Marder**, a professor of neuroscience at Brandeis University. "We totally expect that in five or 10 years, they might be using a completely different technology."

Ed Boyden, a chemist and physicist turned electrical engineer who co-developed optogenetics, echoes that sentiment. "Skills are certainly good to have. But maybe even more important than having skills is having the ability to pick up new skills," he says. After all, today's hot technology is tomorrow's dinosaur.

In this era of "big data," strong computational skills and informatics expertise also are increasingly valuable for neuroscience success, says **David Van Essen**, alumni endowed professor of neurobiology at the Washington University School of Medicine and co-principal investigator (PI) of the Human Connectome Project (HCP). "That doesn't mean that they have to write new programs themselves," he says, "but they have to be comfortable with using computers in increasingly sophisticated ways."

Marder says her students inevitably become proficient in MATLAB. So, too, do researchers working with **Moritz Helmstaedter**, a connectomics expert and director of the Max Planck Institute for Brain Research in Frankfurt, Germany.

Helmstaedter says that in his experience, the best skillset for neuroscience in general, and connectomics in particular, is a background in physics. "That's almost always a convincing feature," he says, "because somebody who has that kind of background and is interested in neuroscience, very rarely fails on you." But barring that, he continues, interest in quantitative analysis is a must.

The brain, he notes, is a biological machine "of un-understood complexity," inevitably requiring sophisticated number crunching and quantitative approaches rarely found in pure biology. "Data is so massive that analysis has to be quantitative, of course, but also it has to involve high-dimensional pattern recognition. And these are topics that you have to have a very quantitative background for."

Such quantitative prowess can even help researchers leverage public datasets they didn't generate. **Van Wedeen**, another HCP PI at the Massachusetts General Hospital (MGH) Martinos Center for Biomedical Engineering, says the proliferation of neuroscience resources, such as those put out by the HCP and Allen Brain Atlas, can pay unexpected dividends for young researchers who lack the funds to collect such data themselves. In particular, they allow researchers to test-drive radical ideas and pivot to new areas of focus. "They enable everyone, young and old alike, to pursue hypotheses that are not heavily driven by preceding work," he says.

Spruston says that the postdocs he hires generally aren't afraid to take something apart and reassemble it, or write their own software rather than using off-the-shelf solutions. In part, he says, that's because he wants people who are "very quantitatively adept." But also it's because industry leaders tend to be people who understand a technology well enough to improve upon it. "If you just keep doing what you were doing five years ago or 10 years ago, it won't pay off in the same way as it will if you're on top of the technological advances as they happen."

Continuing education

One way neuroscientists can hone their technical edge is to take off-major courses in physics or engineering (if they are still in graduate school) or postdoc in a lab that can teach them new techniques.

But the burgeoning emphasis on technology development means that career development isn't just about teaching old neuroscientists new tricks; it's also about educating engineers, physicists, and computer scientists in the basics of neuroscience. **Joe Tsien**, co-director of the Brain and Behavior Discovery Institute at Georgia Regents University, has several computer scientists and physicists in his lab. "It's easier from my own experience to train these people to do the biology than to train the biologists [as] computer scientists," he says.

Some universities have begun offering graduate training specifically focused on neurotechnology, among them the Massachusetts Institute of Technology (MIT) Center for Neurobiological Engineering. Boyden, who codirects that center, says traditional neuroscience graduate programs typically focus on hypothesis-driven research—asking and answering "profound, deep mysteries of the brain." The MIT center, in contrast, "is about building tools."

"We really want to build technologies that enable us to answer questions that people might not even be able to ask right now," Boyden explains.

Martin Monti, assistant professor of psychology at the University of California, Los Angeles (UCLA), took a different path to boost his technological *bona fides*. In 2008, while a postdoc in the Medical Research Council Cognition and Brain Sciences Unit at the University of Cambridge, United Kingdom, Monti spent two weeks in sunny California at the UCLA Semel NeuroImaging Training Program (NITP).

NITP is a federally funded project whose agenda is "to take people with training that's nontraditional for neuroscience—engineers, mathematicians, statisticians, physicists, and so on—and to bring them up to speed on neuroimaging, a science that needs those sorts of technologies," says **Mark Cohen**, who directs the program. "It includes both a traditional one-year fellowship program open to UCLA graduate students, and a two-week immersive summer course continued>

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— Mark Cohen

PHOTOS: (FROM TOP) PHIL JONES; MARC ROSEBORO PHOTOGRAPHY (MROSEBOR@UCLA.EDU)

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— David Van Essen

Featured Participants

Brain and Behavior Discovery Institute, Georgia Regents University
www.gru.edu/mcg/discovery/bbdi

Brandeis University
www.brandeis.edu

Janelia Farm Research Campus
janelia.org

Max Planck Institute for Brain Research
www.brain.mpg.de/home.html

MGH Martinos Center for Biomedical Engineering
www.nmr.mgh.harvard.edu

MIT Center for Neurobiological Engineering
web.mit.edu/cnbe

National Institute of Mental Health
www.nimh.nih.gov

Northwestern University
www.northwestern.edu

UCLA Semel NeuroImaging Training Program
www.brainmapping.org/NITP

Washington University School of Medicine
medicine.wustl.edu

Additional Resources

BRAIN Initiative
www.nih.gov/science/brain

Human Brain Project
www.humanbrainproject.eu

Human Connectome Project
www.humanconnectome.org

in advanced magnetic resonance imaging methods and applications."

Limited to 35 or 36 attendees at all academic ranks, "the summer program combines classroom lectures, laboratory exercises, and a team-based research experience," says Cohen, "some of which result in publications and lasting collaborations."

The program also has a complementary agenda, he adds, which is to take people in more traditional neuroscience fields "and get them down and deep with the nitty-gritty of the technologies that we use in imaging, including math, physics, electrical engineering, and other things that are crucial to an understanding of the field."

According to Cohen, NITP—which is one of just three such programs around the country (the others are at MGH and the University of Pittsburgh)—offers its students a rare opportunity in interdisciplinary training. "Our students are expected to become sophisticates in digital signal processing, statistics, neurophysiology, electronics, measurement, and experimental design, simultaneously. Neuroimaging has become an unusually demanding high-technology field, and few places are equipped to offer these students the training that they need to become broad participants."

Monti already had substantial experience with fMRI when he signed up for NITP, he says, but was looking for a deeper understanding of the technology. The course, he says, "completely changed the way in which I understand experiments and analyze data," he says. He discovered he'd only scratched the surface of how fMRI works and what it can do—knowledge that he says helps him design better experiments, and may have boosted his career prospects.

Of course, a one- or two-week training course isn't going to make or break a resume, says **Robert Savoy**, an instructor in radiology at Mass General who runs several of the short-term training programs at the MGH Martinos Center. "This is not a degree-granting program," he says. "It isn't even CME [continuing medical education credit]-granting." But it is nevertheless valuable. Says Monti, "[NITP] certainly gave me a huge advantage in terms of talking about and conceiving experiments. Even just that made me a better candidate than many other people for any postdoc or faculty position."

A brain research brain drain?

There's no denying there's some big money in neuroscience these days. The BRAIN Initiative will dole out some $110 million in funding in its first year—about 2% of the $5.5 billion the NIH will spend this year on neuroscience overall, according to Insel—and President Obama has requested $200 million for 2015. A recent report by a working group of the Advisory Committee to the Director of the NIH, has recommended a subsequent investment of $4.5 billion over 10 years. The European Research Council spent some €250 million (~US$323 million) on neuroscience research in 2012. More recently, the European Union earmarked €1 billion (US$1.3 billion) toward the controversial Human Brain Project.

Such spending will undoubtedly produce new job opportunities at all levels of research, from technicians to postdocs to principal investigators. But the BRAIN Initiative, at least, says Insel, isn't a job program per se. "This is really about creating tools and resources for the broad community of people who want to study the brain."

China, too, is investing heavily in the brain, says Tsien, who in addition to his position in Georgia also is honorary chief scientist at the Brain Decoding Center at the BanNa Biomedical Research Institute in Yunnan Province, China. With comparatively fewer labs and scientists vying for research dollars, he estimates funding rates in China are "probably [around] 30%." In contrast, just 17.5% of RO1 applications were funded in 2013, according to the NIH. As a result, Tsien says, he is seeing a "fundamental shift," with many foreign postdocs who once would try to stay in the United States now heading home. "The vast majority go back to their country because there are more opportunities there."

Similarly, Helmstaedter says he has seen an increase in applicants from the United States for group leadership positions at the Max Planck Institute. "One hears about bad funding, but to [hear] that somebody would consider going to Europe from the United States, which for a long time was the place to do research, that's amazing," he says.

How that situation will evolve, of course, is anybody's guess. But neuroscience, at least, seems to be on the upswing. Says Spruston, "I think, if I were a student or a postdoc, I'd be encouraged about what's happening in the field now."

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