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Undergraduate

BRAIN INITIATIVE: POWER IN NETWORKS

BY NINI LIU

EXPLORING THE BRAIN INITIATIVE'S TRAJECTORY AND DOMESTIC EFFECTS

Though the brain has been deeply analyzed and dissected in the past century, much of it remains a vast, unexplored terrain. In April 2, 2013, the White House launched the BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies) with the goal of creating innovative technologies to address, treat, and prevent brain disorders, such as Alzheimer's, epilepsy, and Parkinson's disease.⁶ Within the last decade, the BRAIN Initiative has launched an explosion of neurotechnology in the United States, driving brain research and opening windows for innovative treatments. The key to this golden age in neuroscience lies in new private-public partnerships and domestic collaboration across scientific fields.

The BRAIN Initiative's goal of modeling the active brain may seem trivial to everyday citizens; however, not understanding how our brain is wired imposes massive costs on the US economy.⁴ In a

2016 report by Information Technology and Innovation Foundation (ITIF), the price of mental-health related conditions cost the U.S. economy \$1.34 trillion dollars.¹⁸ This is enough to buy approximately 1.3 trillion giant Hershey's Milk Chocolate Bars or 30% of cars in the U.S. within a \$22,000 price range. This amount only accounts for financial costs related to direct treatments, care for related physical illnesses, increased crime rates, and lost productivity in the workforce.¹⁸ It does not factor in the indirect economic costs inflicted on caregivers or adults with

mental illness that can result from lower education, wages, productivity, and homelessness. As such, it is important to note that the initiative is not just focused on elevating neuroscience research or treating

brain-related disorders, but also on alleviating far-reaching economic and social burdens that directly or indirectly affect everyday U.S. citizens.

The crucial nature of the BRAIN Initiative has promoted public-private partnerships, which lie at the core of revolutionizing basic research and technology in neuroscience. Essentially, the BRAIN

Initiative exists only due to continued investments from federal research agencies and private research institutes, companies, and foundations (Figure 1).¹ Thus,

"...the price of mental-health related conditions costs the U.S. economy \$1.34 trillion dollars."

on legal and administrative technicalities.

A key challenge that the BRAIN Initiative recognizes and faces is data sharing. One of the problems in the neuroscience field is that there is no unified format to report findings and data, making replication and comparison of experiments difficult.¹⁸ And now with the BRAIN Initiative's nationwide projects, a standardized data system is more necessary than ever to ensure progress through collaboration between laboratories. Moreover, the 21st Century Cures Act also requires federal agency-supported research to be shared publicly, to pool data and advance rapid biomedical research.⁵

Therefore, in 2014 foundations and research institutes like the Howard Hughes Medical Institute, UC Berkeley, and Allen Institute for Brain Science collaborated and launched "Neurodata Without Borders: Neurophysiology" (NWB). This project aims to create a uniform data format for cellular-based neurophysiology data and optical physiology data (Figure 2).²¹ The challenge with this is individual laboratories



Federal agencies:
 National Institutes of Health
 National Science Foundation
 Intelligence Advanced Research Projects Activity
 Defense Advanced Research Projects Agency
 Food and Drug Administration

Foundations and private research efforts:
 Howard Hughes Medical Institute
 Allen Institute for Brain Science
 The Kavli Foundation
 The Simons Foundation
 University of Pittsburgh
 University of California, Berkeley
 Carl Zeiss Microscopy
 The Carnegie Mellon University

Private companies:
 General Electric
 GlaxoSmithKline
 Inscofix
 US Photonics Industry

Figure 1. Public-private partnerships involving key federal agencies, foundations, and private companies.

the importance of continuing brain research was highlighted in the 21st Century Cure Act, a bill passed by both Republicans and Democrats in the House of Representative and the Senate on July 10, 2015. Essentially, this bill gave the National Institute of Health (NIH), a key player in the BRAIN Initiative, authority over initiating private-public collaborations. Consequently, this allowed the Obama administration to propose \$300 million to be allocated to the BRAIN Initiative in the fiscal year 2016 budget with greater ease to Congress.¹ What this means is if NIH cannot meet the \$300 million budget, it can recruit private investors to meet this target. In summary, public-private partnerships helps sustain the BRAIN Initiative over a longer period of time by pooling financial resources from the federal to the private level.

Another way public-private partnerships accelerate progress with the BRAIN Initiative is to facilitate partnerships between researchers and manufacturers. One of the biggest problems recognized by the initiative was that researchers lacked powerful tools and technologies to understand the active neural circuitry. As part of NIH's Public-Private Partnership Program, NIH helps create partner-

ships between clinical researchers and manufacturers by acting as the middleman. According to NIH, basic research can progress and accelerate

"The importance of ... brain research was highlighted in the 21st Century Cure Act, a bill passed by both Republicans and Democrats in the House of Representative and the Senate..."

because clinical investigators have "early access to neuromodulation and recording devices for human clinical studies."¹⁷ Some examples of NIH's partnerships include NeuroNexus, Blackrock Device, and Second Sight, who provide researchers tools like multi-array electrodes to record large brain regions, spinal cord stimulators, and a bionic eye that uses electrical stimulation in the retina to "induce visual perception in blind individuals."^{12,13} With technologies and facilitated partnerships like these, researchers and manufacturers in the BRAIN Initiative can focus on progressing brain research with novel technologies rather than



Figure 2: Through Neurodata Without Borders, laboratories must overcome technological and cultural hurdles.

have different standards and conditions of obtaining recordings. Software developers and vendors have to translate multiple neurophysiology datasets and unify it into a new common language. Then, they have to make sure that its data software can be easily understood and used by researchers.¹⁸ Finally, as a key developer of the BRAIN Initiative Terrence Sejnowski states, “Investigators will have to be willing to part with their data,” which “will require a culture change because it’s not how most labs work today.”¹⁹

Essentially, creating a standardized data set like NWB plays only a smaller picture in ensuring continued federal funding and large scale collaborations for the BRAIN Initiative. For the BRAIN Initiative to be successful, laboratories across the U.S. must overcome cultural barriers.

Challenges aside, since the start of the BRAIN Initiative and new partnerships, there have been momentous breakthroughs. In 2015, Jeff Lichtman and his team at Harvard University finished a comprehensive 3-D reconstruction of 1,500 cubic microns of a mouse neocortex (Figure 3). While this is only about the width of a human hair, it is the “largest portion of the mammalian brain rendered in full detail,” containing 1,600 neurons and 1,700 synapses.¹⁴ Fundamentally, Lichtman cracked not only how synapses are formed, but also the beginning of the brain’s wiring diagram to provide insights on what happens in Alzheimer’s or Parkinson’s when brain circuits malfunction.

NIH funding to the Roth Lab in the University of North Carolina also yielded a unique tool: DREADD, or Designer Receptor Exclusively Activated by Designer Drugs. Basically, with DREADD researchers can turn neurons on and off in vivo by injecting DREADD non-invasively via a virus into specific neurons and activating it only by using a designer drug-- Clozapine-N-oxide.¹³ This tool al-

lows many labs around the world to control neuronal activity in living mammals. In the Susan M. Ferguson and John F. Neumair lab in the University of Washington, DREADD technology has been used to discover how the disruption of the striatonigral circuit in the brain can cause uncommon reward and learning behavior, which manifests in neuropsychiatric disorders.⁷

Another NIH breakthrough includes the blueprint for AMPET, a mobile brain scanning helmet developed by Dr.

the BRAIN Initiative under the proposed fiscal year 2017 budget? In March 2017, the Trump administration proposed an 18% cut to NIH’s \$31.7 billion budget. The key reason is to eliminate overhead payments and indirect expenses to universities and research institutes. This is mainly money that is not going directly towards research, but towards costs like running facilities, or even paying for staff needed to ensure experiments comply with ethical standards.⁹ Here is where the public-private partnerships act as a double-edged sword. If the budget proposal is approved in May, the BRAIN Initiative will face major setbacks due to its large dependence on the NIH. However, if it can garner greater financial support from private sectors, the initiative has a chance of weathering the budget cuts, but would be greatly delayed in expected scientific breakthroughs. To at least maintain the BRAIN Initiative’s current trajectory, research institutes, universities, private foundations, and everyday citizens need to unite and challenge the budget cuts.

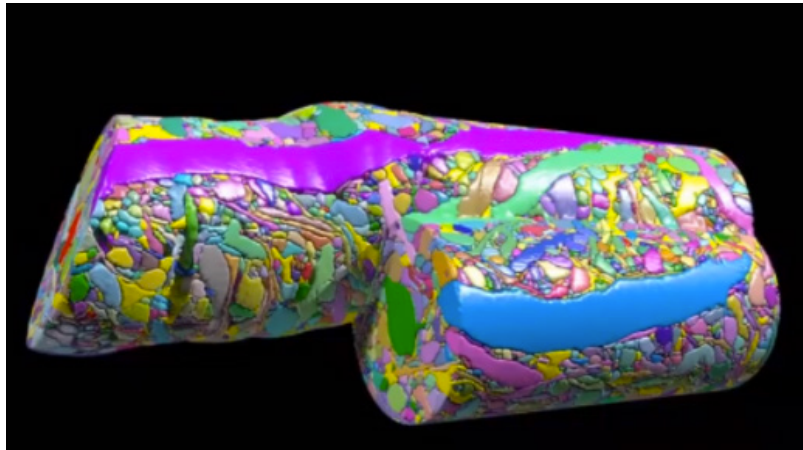


Figure 3: A 3-D rendering of a mouse neocortex by the Lichtman Lab.

Julie Brefczynski-Lewis and Dr. Kuang Gong at the West Virginia University (Figure 4).⁸ As opposed to previous immobile, low-resolution positron emission tomography (PET) scanners, AMPET images a moving person in their natural environment, allowing physicians to study biochemical changes as a diagnostic tool for diseases like Alzheimer’s, depression, as well as for seizure activity.² Overall, major developments like Dr. Lichtman’s reconstruction, DREADD, and AMPET were made possible through collaborations between researchers and manufacturers via public-private partnerships.

But are these collaborations and partnerships strong enough to sustain

Over the past few years, the BRAIN Initiative has yielded revolutionary discoveries in neuroscience, generating greater understanding towards curing neuropsychiatric and neurological disorders. It has also shown the benefits of cross-cultural collaborations between the scientific community and public-private partnerships. Most importantly, it has revealed the necessity and the power of creating unified networks to support biomedical and scientific progress. While networks do afford risks and challenges in shifting political environments, efforts to bolster these connections can overcome obstacles and continue the BRAIN Initiative’s trajectory.



Figure 4: Three AMPET models with varying mobilities and usages.

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