Written Testimony of Dr. Narayanan (Bobby) Kasthuri
Neuroscientist, Argonne National Laboratory, and
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before the
Committee on Science, Space, and Technology, Subcommittee on Energy and Subcommittee on Research and Technology, of the U.S. House of Representatives
July 12th, 2018

SUMMARY

- We stand at a pivotal moment in our centuries-long quest to understand the brain—the moment when the worlds of computer science and neuroscience collide.
    - We can transform how we treat mental illness and brain diseases.
    - We can revolutionize how we think about and build future computers and algorithms.
    - We can bolster our artificial intelligence capabilities and national and economic security.
- Modern neuroscience is expensive and resource intensive.
    - Researchers encounter both financial and structural barriers to entry; needed investments in physics, engineering and computer science are typically beyond the scope of laboratories at single universities and institutes.
    - With the neuroscience community unable to efficiently utilize current capabilities, we are limiting the types of hypotheses we test to drive the next generation of innovation.
    - We must counteract the widening gap between the small fraction of laboratories utilizing the most recent technology and the remaining majority of neuroscientists.
- The DOE and the national lab system are perfectly suited to address this gap.
    - The national laboratories act as stewards of large-scale infrastructure supporting many of the nation's scientific programs; however, until recently there has been limited interaction between the labs and the neuroscience community.
    - A national clearinghouse will ensure that the necessary physics, engineering and computer science resources are vetted and freely accessible to measure brain structure and functions.
    - As stewards of the nation's advanced computing infrastructure, the labs can support efforts to understand the brain just as they supported mapping the human genome.
- With 100 billion brain-cells (neurons) making an average of 10,000 connections with each other, the human brain is the most complicated structure studied in the history of humanity.
    - Understanding how it functions will be the great intellectual achievement of the 21st century, revealing the physical bases of our most human abilities like reasoning and serving as the blueprint for reverse engineering those abilities into algorithms and robots.
    - Other countries like Japan, South Korea, and China, cognizant of the enormous economic and national security benefits of understanding the brain, have committed national efforts to both brain mapping and artificial intelligence; the United States has not.
- We went to the moon, we harnessed the power of nuclear energy, and we led the genomic revolution—now is the moment for the United States to lead again.
    - By mapping and reverse engineering the physical substrates of human thought, we will complete the most challenging quest of the 21st Century and cross what could be the last great scientific frontier.

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Chairman Weber, Chairwoman Comstock, Ranking Members Veasey and Lipinski, and members of the subcommittees, thank you for this opportunity to appear before you. My name is Bobby Kasthuri, and I am a neuroscience researcher at the U.S. Department of Energy's (DOE's) Argonne National Laboratory and an assistant professor of neurobiology at the University of Chicago.

I am here today because I believe that understanding the human brain is the most challenging quest of the 21st century—perhaps the last great scientific frontier—and that advanced capabilities and facilities of the DOE National Laboratories are critical to help usher in a new era of understanding. Scientists began and ended the great scientific challenge of the previous century—understanding the genetic basis of life—by creating two maps: one of the atomic structure of DNA in 1953, and another of every nucleotide in a human genome in 2003. The science enabled by Watson and Crick and the Human Genome Project is revolutionizing our understanding of the genetic bases of human health and disease.

A similar revolution awaits us when we understand how human brains acquire knowledge from experience—how we find patterns in our senses and use them to plan and act. When we know exactly how those processes work, we can connect prosthetic bodies to the paralyzed, design rational medical treatments for brain disease, and reverse-engineer human cognition into our computers, potentially at the energy cost of a fraction of a common lightbulb.

The medical ramifications alone are tremendous:

- The National Alliance on Mental Illness (NAMI) indicates that approximately 1 in 5 adults in the United States—43.8 million people—experiences mental illness in a given year, resulting in nearly $200 billion in lost earnings annually.

- The Alzheimer's Association reports that an estimated 5.7 million Americans of all ages are living with the disease; it is currently the sixth leading cause of death in the United States. In 2018, Alzheimer's and other dementias will cost the nation $277 billion, with costs rising as high as $1.1 trillion by 2050.

- The Centers for Disease Control and Prevention report that 1 in 59 children have autism-spectrum disorders that cause mild to severe social challenges and communication difficulties, as well as physical and medical issues.

Given the enormous benefits a better understanding of brains could provide, you could ask why we have not made more progress. Part of the problem is the sheer complexity of the human brain. The human brain contains around 100 billion cells, or neurons, which make thousands of connections called synapses with each other. The complexity of this intricate communication web cannot be overstated. Parts of our nervous system beyond our brain, some just mere atoms long, extend from foot to spine. The quest to understand how the brain works requires more cooperation across academic disciplines than any other human endeavor.

The good news is that we have defined the underlying hardware, so to speak. Every nervous system is based on the same principle—all representations, computations and actions mediated by the brain depend on neurons that are connected by synapses in highly complicated directional networks. Each neuron receives information from synapses that connect to its dendrites (branches) and sends information via its axon, which connects to dendrites of other neurons. One neuron might receive thousands of separate messages and convey the integrated information to thousands of other neurons.

You can picture each neuron as a hub that sends and receives signals to and from many thousands of other neurons. Neuroscientists propose that the map of how those 100 billion neurons make 1 quadrillion connections with each other, what we call the "connectome," is a map of who you are: your skills, your memories, your fears, and your personality. Disruptions or alterations in these maps—"mis-wirings" between neurons—are the basis of many neurological and psychiatric disorders.

The "Mind-Meld" Between Computer Science and Neuroscience

In our quest to understand the brain, one of the most important scientific collaborations is the "mind meld" between computer science and neuroscience. Given the complexity of the brain I just described, you can imagine that no matter how neuroscientists analyze the brain—whether we use laser beams, genetic engineering, fluorescent proteins, pharmaceuticals, virtual reality, metamaterials or robotics—tremendous computing power will always be a necessity.

Neuroscience, perhaps more than any other field of biology, operates at the cutting edge of big data. The raw data for the connectome, or map, I described will measure approximately 1 trillion gigabytes (an exabyte) and could not fit in the memory of any current computer. For comparison, the entire Human Genome Project measures only a few gigabytes. Indeed, if you could combine all the written material in the world into one dataset, it would be just a small fraction of the size of this brain map.

Scientists, including those at Argonne National Laboratory and the University of Chicago, and collaborators around the United States, are already working toward a human connectome by mapping smaller brains of other animals. To create even the smallest neural map teams of neuroscientists and computer scientists must work side by side to analyze the enormous brain datasets and use the latest artificial intelligence technology. Interestingly, we have discovered that although this collaboration clearly furthers neuroscience, this work is mutually beneficial to advancing computer science as well.

First, it turns out that problems to which computer scientists are eager to apply artificial intelligence—understanding pedestrian behavior to ensure the safe operation of a self-driving car or automatically interpreting changes in satellite images over time for strategic intelligence—involve the rapid analysis of large datasets at the same scales sought by neuroscientists. The only difference is that brain datasets are already orders of magnitude larger than any datasets humans have ever collected and are guaranteed to grow even larger. Deciphering the human brain by creating a new generation of artificial intelligence that is capable of analyzing the largest datasets ever created will inevitably aid every other field of human endeavor that struggles with big data.

Second, and perhaps even more importantly, understanding the brain more deeply could lead to a revolution in computing. Even as they herald recent gains in the computational abilities of artificial neural networks, computer scientists remain concerned that conventional approaches will soon plateau in performance. Almost every human brain possesses fundamental skills that even the most sophisticated algorithms do not: reasoning, humor, learning and creativity. If we can find the physical bases of these abilities in the brain, we can transform the landscape of computing.

The Future Is Here

Neuroscientists around the world—including a coalition comprised of both researchers from Argonne National Laboratory and collaborators from Princeton University (NJ), Baylor University (TX), Rice University (TX), the University of Notre Dame (IN), the Allen Brain Science Institute (WA), and other U.S. institutions—already have begun trying to reverse-engineer how brains work, to discover uniquely biological algorithms. For example, as part of the IARPA MICrONS program, a component of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, neuroscientists seek to reveal fundamental aspects of the brain's learning machinery from simpler animals. By observing the dynamics of the living mouse brain as it learns, and mapping the connections between neurons that mediate the learning, we hope to decipher how the brain uses its hardware in combination with programming language to recognize objects. Scientists will then be able to incorporate those principles into the next generation of computer programs. Artificial intelligence has progressed rapidly, but studying the best computer we know—the brain—has the potential to generate novel networks with leaps in performance that would otherwise take many years of chiseling and searching to achieve.

Indeed, computer scientists used the crudest visual maps of primate brains to develop what would become the ancestors of machine learning and other successful modern artificial intelligence. Given this past success, we expect that increasingly detailed maps of mouse brains will bear the next generation of computer algorithms. At only the halfway point of the 5-year MICrONS project, early results already suggest this historic data will yield countless insights for many years to come. Teams at Princeton, Baylor, Rice, and the Allen Brain Institute already have leveraged cutting-edge machine vision and artificial intelligence algorithms to produce exquisite maps of mouse brains with unprecedented detail, which already are changing the foundations of neuroscience and computer science. However, even the smallest part of the mouse brain, a small fraction in size and capability relative to the human brain, is the limit of most scientists, universities, and institutes. To map the human brain will require scholars with incredibly diverse expertise and skillsets, collaborating with federal scientific agencies like the National Institutes of Health, National Science Foundation, and the DOE and its National Laboratories. It is an interdisciplinary project of great scope and tremendous potential.

A National Resource for Neuroscience and Artificial Intelligence

Although neuroscientists and computer scientists are making remarkable progress, an unfortunate reality still prevents us from fully understanding the human brain and leveraging these discoveries for society—that is, most neuroscientists lack access to the tools and resources needed to test their ideas about the brain. Indeed, the enduring success of the BRAIN initiative will depend on widespread access to the technological advancements, computational tools and datasets the initiative creates.

Today the neuroscience community is underutilizing current technological capabilities, limiting the types of questions and hypotheses we can test to drive the next generation of innovation. We must counteract the widening gap between the small fraction of laboratories utilizing the most recent technology and the remaining majority of neuroscientists. A sophisticated national clearinghouse will ensure that the physics, engineering and computer science are vetted and freely accessible to measure brain structure and functions.

The DOE and the National Laboratory system are uniquely suited to convene leading researchers across the various scientific disciplines to overcome these barriers. At the forefront of discovery and innovation across fundamental sciences, the DOE National Laboratories are stewards of large-scale scientific user facilities, including light sources, accelerators, and supercomputing facilities that support advancements in a range of disciplines from astrophysics to chemistry to material science; however, until recently interaction between the neuroscience community and the National Laboratory system has been limited. Indeed, a Secretary of Energy Advisory Board (SEAB) reported to the DOE this exact sentiment (Secretary of Energy Advisory Board Report of the Task Force on Biomedical Sciences, September 22, 2016, p. 14)

"Brain research is supported across many institutes of the NIH, but the opportunities for DOE involvement are perhaps best appreciated in the context of the recent BRAIN Initiative. … BRAIN has begun a concerted effort to improve the methods available for brain research, both for experimental work and in the domain of theory and analysis. The ultimate goal is to understand large circuits of nerve cells: What are all the types of neurons involved? What is the structure and connectivity of the circuit? What are the signals flowing through the circuit? How do these circuit functions relate to behavior and cognition?" DOE laboratories clearly have expertise that relates to these goals ..."

As one of the first experimental neuroscientists at a DOE National Lab, I am amazed every day at the resources and tools that are at my disposal for brain science. The imaging technologies and advanced data-analysis techniques available through the Argonne Leadership Computing Facility (ALCF) and the Advanced Photon Source (APS) enable me to map the intricacies of brain function at the deepest levels and to describe these processes in greater detail than ever before. Those tools will be even more powerful in the future. The upgrade to the APS will create the ultimate 3-D microscope, producing the world's brightest hard x-rays and transforming our ability to understand and manipulate matter—including brains—at the nanoscale.

In 2021, Argonne will deploy the Aurora supercomputer at the ALCF. Aurora will be the first exascale-class system—at least 50 times faster than the nation's most powerful supercomputers in use today—in the United States. Aurora will enable us to explore new frontiers in artificial intelligence and machine learning; this will be the first time scientists have had a machine powerful enough to match the kind of computations the brain can do. It will be a breakthrough for neuroscience and for modeling biological processes. With the help of Aurora, I will be able to piece together millions of two-dimensional images, reconstructing the brain in three dimensions to create a map of the human brain.

These world-class user facilities—particularly when leveraged together—are and will continue to be critical to my efforts. For example, current recording and imaging methods can sample only a limited number of neurons or limited brain volumes, which constrains neuroscientific discovery. However, when data from imaging facilities like the APS is later modeled, simulated, and analyzed on a DOE supercomputer, neuroscientists can image and analyze every cell and blood vessel in a series of complete mammalian brains. Using one of the current fastest supercomputers on the planet at Argonne, called Mira, —I can quickly and efficiently analyze the millions of gigabytes of data this will produces. Imagine the game-changing possibilities of a resource where neuroscientists around the U.S., and ultimately around the world, utilize such technologies and infrastructure.

As members on the House Science, Space & Technology Committee, you understand that there are pivotal moments in science that we can harness to advance society in leaps, rather than small steps. Brain research is at that critical moment now. Neuroscientists are glimpsing a future where we can potentially understand the physical bases of mental illnesses that currently impose huge personal and financial burdens. Computer scientists see a future where the U.S. leads the world in computer science and artificial intelligence, which is critical for our national security and economic progress. The U.S. leads in both fields, for now, but we have not made brain mapping a national priority as Japan, South Korea, and China all have. The moment to cement our national leadership is now.

In 1962 at Rice University, President John F. Kennedy announced that the United States would put a man on the moon. Seven years later, Neil Armstrong walked on the face of the moon.

While some may say that the endeavor was a failure—where are moon bases now?—it is worth noting that when we landed on the moon in 1969, the average age of a NASA scientist was 29 years old. Seven years earlier, at the time of Kennedy's announcement, these scientists were college students seeking inspiration. The "moon shot" changed their lives and focused their passion so that they could change society in innumerable ways.

If we seize the opportunity now for a national moon shot for the brain, if we inspire the next generation of students to work at the intersection of brain science, computer science, and big data, we can make significant progress toward understanding the brain and curing brain diseases. We can create the next generation of computers and robots based on the brain, transforming our society and assuring U.S. leadership in these vital realms for the future. Thank you for your time and attention today. I welcome any questions you may have.

Dr. Kasthuri is the first Neuroscience Researcher at Argonne National Labs and an Assistant Professor in the Dept. of Neurobiology, University of Chicago. He has an MD from Washington University School of Medicine and a D.Phil. from Oxford University where he studied as a Rhodes scholar. As a post-doctoral fellow, Dr. Kasthuri developed an automated approach to large volume serial electron microscopy ('connectomics'). Currently, the Kasthuri lab continues to innovate new approaches to brain mapping including the use of high-energy x-rays from synchrotron sources for mapping brains in their entirety. The Kasthuri lab is applying these techniques to in service of answering the question: how do brains grow up, age, and degenerate?