Testimony of

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Overview

The human brain is arguably the most complicated biological entity we are aware of in the universe. With roughly 100 billion neurons and 100 trillion synaptic connections linking them together, the brain is responsible not only for controlling basic physiology, such as breathing, but also for higher-level functions such as learning, memory, emotions and cognition.

NSF's goal is to enable scientific understanding of the full complexity of the brain in action and in context. In order to meet this goal, fundamental research is needed to explore and discover the general principles underlying how cognition and behavior relate to the brain's structural organization and dynamic activities, how the brain interacts with its environment, and how the brain can recover from lost functionality.

To address these issues, NSF is supporting interdisciplinary teams to develop the needed tools and to integrate their respective scientific disciplines at a rate they have not done in the past. NSF is strategically targeting its resource investments to advance the basic research needed to understand how healthy brains work and how they achieve cognition. An improved understanding of the healthy human brain is essential for dealing with the increasing frequency of neurological disorders that affect the human population.

Why NSF?

Throughout its history, NSF has been a catalyst for transformative breakthroughs in brain research and related technologies. For example, the fundamental research that led to the development of functional magnetic resonance imaging (fMRI), of the optogenetics technology for manipulating specific neurons in living brains, the CLARITY transparent brain preservation technique, brain-machine interface systems, and the first FDA-approved artificial retina began with NSF support. In addition, NSF's capacity for enabling integrative activities in neuroscience at a global scale is demonstrated by NSF's long-term supporting role in the International Neuroinformatics Coordinating Facility (INCF) as well as partnerships with the German Federal Ministry of Education and Research (BMBF), the French Agence Nationale de la Recherche (ANR) and the US-Israeli Binational Science Foundation (BSF) for the Collaborative Research in Computational Neuroscience program. The latter is the flagship Federal program that supports research in mathematical and computational aspects of neuroscience, which is pivotal for interpreting neural data and formulating conceptual models of brain function. NSF's cross-foundation activity has brought the relevant, but disparate, scientific communities together, and has resulted in the funding of novel collaborative efforts and innovative research and technology awards.

Many of the current innovations in medical technology that provide relief from debilitating human conditions are made possible by advances in basic research. For example, NSF has played a key role in supporting the development of Brain-Computer Interfaces, which has the potential to restore function such as voluntary motor control to paralyzed patients. An award from the Biological Sciences Directorate in the mid-80s to Dr. Apostolos Georgopoulos at the University of Minnesota supported the development of a mathematical framework for interpreting the relationship between neural signals in the brain and the direction of limb movement. Building on Dr. Georgopoulos' discoveries and other technical advances, in part supported by NSF, Dr. Miguel Nicolelis of Duke University developed techniques to decode brain signals from primates to physically move robotic arms in remote locations. This work was supported by an award from the multidisciplinary Knowledge and Distributed Intelligence Initiative that ultimately paved the way for subsequent developments of Brain Computer Interfaces, so stunningly demonstrated at the recent FIFA Soccer World Cup. NSF continues to fund research today that may help us understand the brain many years from now, but that is not currently classified as "brain-related." Thousands of researchers around the world are currently investigating brain mechanisms in both normal and disease states, such as post-traumatic stress syndrome, Parkinson's and schizophrenia, with a powerful new tool called optogenetics. Optogenetics, which was developed with partial funding from NSF, enables researchers to selectively turn on and off individual neurons in living animals by exposing them to light. The development of optogenetics was made possible by earlier NSF-funded research on light sensitivity in algae that was conducted purely out of curiosity about the survival strategies of algae and without any knowledge that it would eventually be pivotal to the seemingly far-flung field of brain research. Building on this achievement, a recent award from NSF's Engineering Directorate to Ute Hochgeschwender at Central Michigan University describes an integrated research, education, and outreach program which focuses on developing a new generation of genetically encoded light sources for non-invasive manipulation of optogenetic sensors. If successful, this will be a key threshold advance that will provide the foundation for new technologies enabling minimally invasive and highly efficient diagnostics and therapies.

Optogenetics is just one example of how significant advances in brain research have resulted from broad areas of research in neuroscience and other fields. Both the principles of electrical activity in the brain and the molecular basis of memory formation were discovered in simple animal systems (squid and sea slug). Decades of research have demonstrated that these mechanisms are similar across the animal kingdom, including humans, and that knowledge derived from a variety of animal systems provides a strategic advantage in understanding how the healthy human brain works.

By funding research in all disciplines of science and engineering, NSF is uniquely positioned to advance research on understanding the brain by bringing together a wide range of scientific and engineering disciplines, each of which brings its own unique perspective to the challenge.

History of NSF Support for Neuroscience Research

Neuroscience is a relatively young field and NSF began funding brain research in 1951 with awards to study nervous system function and neurological responses. In 1976, a Division of Behavioral and Neural Science was established, which subsequently expanded to eight programs from 1982 to 1989. These programs resided in different Directorates and many have changed names over the years. NSF's current programs that focus exclusively on neuroscience or cognitive science include:

- Organization; Activation; and Modulation Programs in the Neural Systems Cluster in the Biological Sciences (BIO) Directorate;
- Collaborative Research in Computational Neuroscience Program in the Computer and Information Science and Engineering (CISE) Directorate;
- Perception, Action and Cognition; Cognitive Neuroscience; and Science of Learning Programs in the Social, Behavioral and Economic Sciences (SBE) Directorate.

Many other programs across the Foundation also support research on neuroscience and cognitive science, but their broader scope also includes other types of research. Examples include:

- Physics of Living Systems and Mathematical Biology programs in the Mathematical and Physical Sciences (MPS) Directorate;
- Information and Intelligent Systems program in CISE;
- Biomedical Engineering, Biophotonics, Nano-biosensing, Fluid Dynamics, Communications, Circuits, and Sensing-Systems (CCSS), Electronics, Photonics, and Magnetic Devices (EPMD), as well as Engineering Research Center (ERC) programs in the Engineering (ENG) Directorate;
- Advances in Biological Informatics program in BIO;
- Graduate Research-Fellowships (GRF) and Improving Undergraduate STEM Education (IUSE) programs in the Education and Human Resources (EHR) Directorate.

Between 2009 and 2013, this combination of NSF core programs invested approximately $70 million per year in neuroscience and cognitive science research. Moreover, a new level of excitement for the possibilities of neuroscience research has emerged from the recent and rapid development of powerful new experimental methods and technologies, some of which were described above.

Summary of Recent Investments and Activities

Based on its long support for neuroscience, in FY 2013 the Congress encouraged NSF, "…to establish a cognitive sciences and neurosciences crosscutting theme." In response, NSF articulated a cross-cutting theme in a Dear Colleague Letter (DCL) to the community entitled: "Accelerating Integrative Research in Neuroscience and Cognitive Science (AIR-NCS)." This DCL resulted in nine new interdisciplinary awards under the Integrated NSF Support Promoting Interdisciplinary Research and Education (INSPIRE) program and one new Research Coordination Network (RCN) award.

On April 2, 2013 President Obama announced The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. As described on the White House webpage, "The initiative will accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought." In response, NSF created a publicly accessible website to provide information about the related "Cognitive Science and Neuroscience" and "The BRAIN Initiative" activities as well as NSF-wide funding opportunities.

NSF now refers to this joint effort as "Understanding the Brain" (UtB). The UtB website (http://www.nsf.gov/news/special_reports/brain/) describes an overarching framework for all NSF activities associated with The BRAIN Initiative and the "Cognitive Science and Neuroscience" cross-cutting theme, and identifies five thematic areas for NSF research

- **Multi-scale Integration of the Dynamic Activity and Structure of the Brain**
  To elucidate and link dynamics of the brain and neural circuits with brain function, including its real-time physiological, behavioral and cognitive outputs.
- **Neurotechnology and Research Infrastructure**
  To create tools to image, sense, record and affect real-time brain function and complex behavior, and develop theories and systems to collect, visualize, analyze, model , store, and distribute BRAIN data.
- **Quantitative Theory and Modeling of Brain Function**
  To reveal emergent properties of the brain and provide predictive theoretical frameworks to guide future research.
- **Brain-Inspired Concepts and Designs**
  To strategically capitalize on insights gained from BRAIN to inspire novel conceptual paradigms and innovative technologies and designs that will benefit society.
- **BRAIN Workforce Development**
  To educate a BRAIN workforce and create new career opportunities for BRAIN discovery and innovation.

In FY 2014, BIO released another DCL expressing interest in Early-concept Grant for Exploratory Research (EAGER) proposals that would apply innovative neurotechnologies to the study of the neural circuits responsible for cognition and behavior. The result was 36 highly interdisciplinary awards focused on elucidating the functional roles of neural circuits, and funded by five NSF directorates for a total of approximately $10 million. Subsequently, these NSF BRAIN EAGER awardees participated in a joint meeting with the first cohort of NIH BRAIN Initiative awardees that was held following the 2014 annual meeting of the Society for Neuroscience in Washington D.C. This initial joint meeting was extremely successful in developing new research collaborations and in sharing new and innovative ideas.

An example of the integrative nature of these BRAIN EAGER awards is illustrated by Dr. Andrea Chiba, who, in collaboration with researchers at the University of California-San Diego, is working to better understand how the human brain functions during social interactions and decisions. Currently, our knowledge regarding the function of neurons in the brain is based on recordings from animals or humans isolated from their social counterparts – essentially quarantined from other humans. Chiba and her colleagues are using funding from NSF's Directorate for Social, Behavioral & Economic Sciences to develop sensors and robotics to study how our interaction with other humans in our environment may influence our behavior and related brain function. Her work synthesizes and builds on research produced from fields of not only social and behavioral science, but also engineering, materials science, intelligent systems and biology.

NSF has also continued to engage leaders across all scientific and engineering disciplines through a series of cross-disciplinary workshops sponsored by multiple NSF directorates. These workshops have identified a number of key gaps in scientific understanding of the brain and needed technologies which will help guide NSF's investment strategies for FY 2015 and FY 2016. These investments will drive integration of research at multiple scales of analysis and accelerate the development of new theoretical, experimental, and analytical approaches, including computational and data-enabled modeling and new neural engineering and technology research and development. Funding will also enable transformative scientific progress toward understanding of the functional dynamics of the brain, and how those interactions evolve over time with changing physical, technological, and social environments.

To understand the full complexity of the brain, it will be crucial to further increase collaborations among relevant scientific communities that have traditionally focused on discipline-specific experimental questions. FY 2015 investments will fund new interdisciplinary and transdisciplinary teams and workforce development. A recently released solicitation entitled, "Integrative Strategies for Understanding Neural and Cognitive Systems (NSF-NCS)," issued by SBE, CISE, ENG, and EHR, invites bold, potentially transformative, interdisciplinary proposals around two research themes: Neuroengineering and Brain-Inspired Concepts and Designs; and Individuality and Variation. This solicitation has received approximately 160 proposals that are currently undergoing peer review.

Another solicitation just released by the BIO and MPS directorates is entitled, "Cracking the Olfactory Code: An Ideas Lab Activity." Olfaction is an evolutionarily primitive sense critical for survival across the animal kingdom – finding food, searching for mates, or avoiding predation all depend on detecting, identifying and discriminating odors. Although early steps in olfactory processing are relatively well understood, significant gaps remain in our understanding of higher-order odor representations and processing during on-going behavior. The goal of this solicitation is to facilitate the generation and execution of innovative research projects aimed at understanding the nature of olfactory processing and sensory representations in the brain. The aspiration is that mixing researchers from diverse scientific backgrounds will engender fresh thinking and innovative approaches that lead to research projects that will transform our understanding of olfactory processing and create new opportunities to elucidate the general nature of sensory representations in the brain. The Howard Hughes Medical Institute (HHMI) will partner with NSF in this Ideas Lab and is providing a workshop venue at its Janelia Farm research campus.

Congress recently encouraged NSF to organize an International Conference on BRAIN research as well as begin conversations with the Department of Energy and others to consider the creation of a National Brain Observatory. NSF is in the process of planning both of these activities and has reached out to its respective potential partners.

NSF's perspective of its specific role in The BRAIN Initiative centers on the development of physical tools and conceptual theories to understand better how a normal healthy brain functions and how cognition arises from normal brain function. In order to accomplish this goal, NSF is working with its partner agencies and institutions (NIH, DARPA, and more recently FDA and IARPA as well as the academic and private partners). Each agency has its own primary mission and set of mechanisms to support science. Because of this, each agency and institution brings its own unique perspective to the BRAIN challenge. NSF believes that the concurrent integration of these diverse perspectives is essential for moving forward quickly to understand the brain.

Understanding the Brain in FY16

In NSF's FY 2016 budget request, the Understanding the Brain (UtB) framework was initiated as a multi-year effort that continues the previously titled "Cognitive Science and Neuroscience" activity and includes NSF's participation in The BRAIN Initiative. The UtB activity draws together and consolidates NSF's ongoing activities in Cognitive Science and Neuroscience and the BRAIN Initiative.

With UtB, NSF aims to leverage its existing investments and foster greater collaboration among research and technology disciplines to accelerate fundamental discoveries in neuroscience, cognitive science, and neuroengineering.

NSF will build off its FY 2014 and FY 2015 investments and continue to leverage and substantially expand its investments in high-risk/high-reward exploratory and transformational scientific and engineering research with emphasis on integration across scales and disciplines. Novel experimentation, multimodal data integration, and theoretical developments that span the molecular, biophysical, biochemical, systems, genetic, organismal, and social scales will elucidate the mechanisms linking dynamic brain activity to behavior and physiology of the whole organism in its environmental context. New conceptual and physical tools with the associated technologies will expand the limits of detection, refine the level of experimental manipulation, and improve computational capability, allowing a fuller characterization and analysis of temporal and spatial patterns of the activity of networks of neurons that drive behavior. Other UtB investments will aim to improve education through discoveries in the neural bases of learning, and enhance our understanding of how the brain adapts to changing environments.

NSF increased investments in UtB related activities by $22.6 million in FY 2014, raising it from about $70 million annually in previous years to $92.6 million. In FY 2015, NSF anticipates $106.4 million with $48.5 million being targeted for The BRAIN Initiative, and for FY 2016 NSF is requesting $143.9 million for UtB with $71.6 million being dedicated for The BRAIN

Initiative. This multi-year effort, which includes The BRAIN Initiative but encompasses broader NSF work, is being pursued across the four ongoing priority areas that will build and extend upon FY 2014 and FY 2015 investments:

1. Develop innovative neurotechnologies to monitor and analyze brain activity, as well as new tools, experimental approaches, theories, and models to integrate neuroscience information across scales and scientific disciplines.

2. Identify the fundamental relationships among neural activity, cognition, and behavior. This priority area, aligned with the Neuroscience and Cognitive Science activity, aims to foster increased understanding of the causal relationships between neuronal activity in the brain, cognitive processes, and behavior.

3. Transform our understanding of how the brain responds and adapts to changing environments and recovers from lost functionality.

4. Train a new generation of scientists, engineers, and educators for a transdisciplinary, globally competitive workforce in neuroscience and neuroengineering.

Internal Management and Coordination

Multiple divisions of nearly all NSF science and engineering directorates will participate in the proposed activities. During the last two years, a high-level Steering Committee for Understanding the Brain and two programmatic-level working groups were established by NSF senior management under formal charge to ensure cross-directorate coordination of all ongoing and proposed activities, including those related to NSF's participation in The BRAIN Initiative.

In FY 2015, NSF has streamlined these three groups into a single Understanding the Brain Coordinating Group (UtBCG) to improve communication and efficiency related to support for The BRAIN Initiative, neuroscience, and cognitive science research across the Foundation. The UtBCG is charged with ensuring implementation of the programmatic roadmap as well as interfacing with other federal entities and coordinating the formation of an interagency working group to discuss the creation of a National Brain Observatory (NBO) as specified in the explanatory statement that accompanied the Consolidated and Further Continuing Appropriations Act of 2015 (P.L. 113-235). NSF has formally contacted the DOE, and the UtBCG is in the process of finalizing the membership of the NBO working group. The NBO working group will coordinate with member agencies of the Interagency Working Group on Neuroscience (IWGN) in making recommendations.

Summary and Future Directions

NSF supports the most innovative neuroscience possible by strategically investing in new technologies, seeking input from the scientific community and often funding research in a variety of different organisms to provide unique opportunities for deep scientific and technical advances.

The Understanding the Brain framework promises innovative and integrated solutions to challenges in our ability to predict how collective interactions between brain function and our physical and social environment enable complex behavior. NSF's strategic investments will support research and infrastructure designed to transform our view of who we are and how we relate to and interact with each other and our ever-changing environment[1].

NSF will continue to work with scientific communities, international partners and other stakeholders as we coordinate with federal and private partners to identify important gaps in our current knowledge, and to enable scientists working across species, disciplines, technologies, institutions and nations to efficiently collect, integrate, share, and analyze new data that will reveal the biological principles that produce the functioning human brain.

Our goal, as always, is to ensure the best possible science for the country.

[1] http://www.nsf.gov/news/special_reports/brain/initiative/

Jim Olds is currently Assistant Director for Biological Sciences at the National Science Foundation. He is on leave from George Mason University where he is a Professor of Neuroscience. The Biological Sciences Directorate funds the majority of non-biomedical research at U.S. colleges and universities. He is also editor-in-chief of *The Biological Bulletin* published by the Marine Biological Laboratory in Woods Hole.

Prior to his appointment at NSF, Olds spent 16 years as Chief Academic Unit Officer and Director of George Mason's Krasnow Institute for Advanced Study. Olds has served on numerous private and public boards and has played a central role in scientific public policy development at all levels, ranging from the White House to advising heads of ministries internationally. He spent eight years as chair of Sandia National Laboratory's External Cognitive Science Board. In the non-profit world, Olds was treasurer of American's for Medical Progress. Olds has also served as a Virginia State Commissioner, appointed by Virginia Governors of both political parties.

Prior to taking the leadership role at Krasnow, Olds led one of the oldest and most prestigious scientific societies, The American Association of Anatomists as CEO. Olds received his undergraduate degree from Amherst College in chemistry and his doctorate from the University of Michigan in Ann Arbor in the field of neuroscience. His postdoctoral research at the National Institutes of Health led to fundamental advances in understanding the molecular basis of learning and memory, for which he was awarded the NIH Merit Award in 1993.