UNDERSTANDING THE BRAIN (UtB)

Overview

Understanding the brain (UtB) is one of the grand scientific challenges at the intersection of the physical, life, behavioral, and engineering sciences. The National Research Council report, "*Research at the Intersection of the Physical and Life Sciences*" (2010),¹ identified "Understanding the Brain" as one of the top five grand challenges for research that will significantly benefit society. The National Academy of Engineering has also recognized "*Reverse-Engineer the Brain*" as a Grand Challenge for Engineering (2008).²

Many incremental advances in research and technology in recent decades are elucidating individual elements of the nervous system and brain and their relationships to individual cognitive processes and behaviors. However, there remains much to discover to attain a comprehensive understanding of 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.

The critical challenge to this comprehensive understanding is to integrate research and innovation across multiple scales of space and time, from molecular, physical (e.g., biophysical and biochemical), physiological, and genetic to cognitive and behavioral, with the ultimate goals of establishing integrative, quantitative, and predictive theories of brain structure and function.

To address this challenge, NSF is making major investments in collaborative fundamental science, in innovative enabling technologies, and in workforce development to accelerate discovery and revolutionize our understanding of the brain. NSF is leveraging and substantially expanding 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 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.

(Dollars in Millions)				
	FY 2015	FY 2016	FY 2017	
	Actual	Estimate	Request	
UtB	\$109.39	\$146.93	\$141.62	
BRAIN	\$50.12	\$73.46	\$74.16	

Total Funding for Understanding the Brain (UtB)

NSF is uniquely positioned to advance research on understanding the brain by bringing together a wide range of scientific and engineering disciplines to reveal the fundamental principles underlying brain structure and function. The co-mingling of these disciplinary and interdisciplinary fields is expected to

¹ www.nap.edu/openbook.php?record_id=12809

² www.engineeringchallenges.org/File.aspx?id=11574&v=ba24e2ed

yield enhanced understanding of the brain, cognition, and behavior, through the development of new technologies and theories. 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 optogenetics, 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 exemplified by NSF's long-term supporting role in the International Neuroinformatics Coordinating Facility (INCF).

In 2012, Congress encouraged NSF to create a cross-foundation activity in cognitive science and neuroscience, and also encouraged the White House to form the Interagency Working Group on Neuroscience (IWGN) under the National Science and Technology Council, which is co-chaired by NSF. In FY 2013, the President announced the multi-agency Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, with NSF as one of the lead participating agencies. The Understanding the Brain activity draws together and consolidates NSF's ongoing activities in cognitive science and neuroscience and the BRAIN Initiative.

Since its inception, this cross-foundation activity has brought the relevant but disparate scientific communities together, and that has resulted in the funding of novel collaborative efforts and innovative research and technology awards. In FY 2013, NSF released a cross-foundation Dear Colleague Letter (DCL) "Accelerating Integrative Research in Neuroscience and Cognitive Science (AIR-NCS)" and funded nine new Integrated NSF Support Promoting Interdisciplinary Research and Education (INSPIRE) awards and one new Research Coordination Network (RCN) as a result. In FY 2013 and FY 2014, NSF sponsored a series of workshops across the participating science and engineering directorates to provide input on research priorities and engage in preparatory collaborative activities. NSF used the resulting reports, white papers, and research articles to develop this multi-year roadmap of investment priorities and to devise targeted calls for research proposals. For example, in FY 2014 the Directorate for Biological Sciences (BIO) published a DCL for Early-concept Grant for Exploratory Research (EAGER) proposals for "catching circuits in action" projects to apply innovative neurotechnologies to study neural circuits responsible for cognition and behavior. This resulted in 36 highly interdisciplinary awards focused on elucidating the functional roles of neural circuits, funded by multiple NSF directorates. These awardees were invited to a joint meeting with the first cohort of NIH BRAIN Initiative awardees following the annual meeting of the Society for Neuroscience in Washington, D.C. as part of the President's BRAIN Initiative.

Goal

The overall goal of UtB is to enable scientific understanding of the full complexity of the brain in action and in context. This multi-year goal is being pursued across the four ongoing priority areas:

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

This priority area is aligned with the objectives of the Administration's BRAIN Initiative. These objectives are focused on development of innovative technologies, tools and instrumentation, computational infrastructure, theory, and models that will accelerate the integration of knowledge across experimental scales from molecular to behavioral; across multiple science, engineering, and computational disciplines; and across species and lifespans. Expected outcomes include the development of new neurotechnologies, predictive models, and theories of brain and nervous system function that can guide follow-on experimental research and foster further technical and theoretical achievements.

2. Identify the fundamental relationships among neural activity, cognition, and behavior.

This priority area aims to foster increased understanding of the causal relationships between neuronal activity in the brain, cognitive processes, and behavior. Advancements in this area require increased collaboration among the neuroscience, neuroengineering, cognitive science, science, technology, engineering, and mathematics (STEM) education, and behavioral and social science disciplines; adoption of innovative technologies and methods to monitor and manipulate brain activity, such as the recent development of optogenetics; and the utilization of cyberinfrastructure platforms and computational tools for performing multi-scale analysis of neuroscientific and behavioral data. NSF-planned investments are designed to provide an agile means for research teams to form around specific behavioral paradigms and adapt and/or develop technologies and models. Expected outcomes include an increase in the number of such teams working together on specific neural-behavioral paradigms utilizing advanced methods and models.

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

This priority area aims to expand support for exploring the links among the environment, behavior, and brain function, as well as the enhancing and restorative neurotechnologies that can be brought to bear in these areas. NSF research investments will catalyze the formation of new teams to elucidate basic brain mechanisms and their relationships to complex environments (including educational environments), cognition and behavior, and related neuroengineering. The expected outcome is measurable progress in developing specific mappings between brain functional/structural changes, changes in behavior and cognition, and changes in psychosocial, external physical, and technological environments; and acceptance of those mappings more widely in the community via citation and use/re-use.

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

This priority area focuses on development of a scientific workforce for understanding the brain that is better prepared for interdisciplinary and global collaboration, data analysis and sharing, and adoption of new and innovative technologies, tools, and models. In order to transform the workforce, the activities funded under priority areas one to three will require special training and professional development for multi-disciplinary research and international collaboration. The expected outcome will be a future workforce fully engaged in and facile with technologies and data science to understand the brain in action and in context.

Approach

Using existing mechanisms including workshops, DCLs, RCNs, targeted solicitations, and special mechanisms such as EAGERs and Ideas Labs, NSF will bring together the diverse relevant scientific communities in biology, chemistry, behavior, cognition, computational and information science, education, engineering, physics, psychology, mathematics, and statistics to identify scientific priorities and needed research infrastructure, establish cross-disciplinary standards, integrate data and methods, and catalyze the development of conceptual and theoretical frameworks. This will be accomplished through:

Specific Investment 1: Integrative and transdisciplinary team-based brain research.

NSF will seek proposals from interdisciplinary teams of researchers poised to promptly address targeted issues, such as innovative experimentation in realistic and complex environments; neurotechnology development; computational modeling and simulation; educational applications of neuroscience and neuroengineering research; and quantitative theory development. Such teams will also contribute to

defining requirements for cyberinfrastructure and analytic tools required to address the expected data surge from these experimental, modeling, and theoretical efforts. One major objective of these investments is to establish truly transdisciplinary team-based brain research – integrated collaborative research environments that rise above existing disciplines. Examples of expected outcomes include noninvasive or minimally invasive imaging technologies for brain mapping, and advanced neuroprosethetics for neuron repair or regeneration based on neuron decoding including deciphering neural coding and circuits and mechanisms underlying dynamic decisions and communication within and across scales in the brain.

Specific Investment 2: Data science, infrastructure, and tool development for understanding the brain.

NSF will provide new opportunities for building infrastructure, cyberinfrastructure, and analytic capabilities for data integration and interpretation across scales and disciplines, with the objectives of transforming data to knowledge for advances in cognitive science, neuroscience, neuroengineering research and education. Proposals will also be sought to address outcome goals of establishing policies and community practices for data management, open access, data sharing, and methods for exploiting large-scale neuroscience and behavioral data. This will be coordinated within the context of further developing the concept of a National Brain Observatory. A major NSF objective will be to encourage stronger connections with other NSF-funded communities that are dealing with similar Big Data issues and multi-modal data integration, such as those focused on earth, ocean, and climate observing, high energy physics, astronomy, and related large-scale computing. NSF will fund planning workshops and other community engagement activities to identify and clarify specific needs for infrastructure and analytic tools.

<u>Specific Investment 3:</u> <u>Specialized training and professional development in multidisciplinary and international research and large-scale data management and analysis.</u>

To develop a scientific workforce that is better prepared for interdisciplinary and global collaboration in understanding the brain, NSF will provide opportunities for training and professional development of supported personnel (students, postdoctoral scholars, and principal investigators) in areas of multidisciplinary research and international collaboration. Opportunities for multidisciplinary training will require mentoring and professional activity in collaboration and co-located collaborations with experts from intellectually distinct disciplines. Supporting this effort, the NSF Research Traineeship (NRT) program will feature Understanding the Brain as one of its emphasis areas. For international training, opportunities must be provided for students and professionals to train and/or collaborate abroad for a defined period of time. Award supplements will be tracked separately for evaluation purposes.

Investment Framework

(Dollars in Millions)				
	FY 2015	FY 2016	FY 2017	
Dir/Office	Actual	Estimate	Request	
BIO	\$38.48	\$44.38	\$46.00	
CISE	16.50	29.72	23.58	
EHR	5.00	11.00	11.00	
ENG	11.00	16.75	16.75	
MPS	15.44	19.49	18.70	
SBE	22.97	25.00	25.00	
OISE	-	0.59	0.59	
Total, UtB	\$109.39	\$146.93	\$141.62	
BRAIN	\$50.12	\$73.46	\$74.16	

LItP Euroding by Directorate

Totals may not add due to rounding.

<u>FY 2015 – FY 2016</u>

In FY 2015, NSF invested \$50.12 million in the BRAIN Initiative to catalyze fundamental research and new collaborations across neuroscience, neuroengineering, and cognitive science. An additional \$59.27 million, through core research activities, focused on accelerating fundamental research and associated development of new technologies for neuroscience and neuroengineering, bringing the total for UtB to \$109.39 million. FY 2015 included a new solicitation sponsored by the Directorates for Social, Behavioral, and Economic Sciences (SBE); Computer and Information Science and Engineering (CISE); Engineering (ENG); and Education and Human Resources (EHR) on Integrative Strategies for Understanding Neural and Cognitive Systems (NSF-NCS), and an Ideas Lab, "Cracking the Olfactory Code," sponsored by BIO and the Directorate for Mathematical and Physical Sciences (MPS) in partnership with the Janelia Farm research campus of the Howard Hughes Medical Institute. The NSF-NCS solicitation resulted in an investment of approximately \$13 million for 16 new awards as part of NSF's support for integrative, fundamental brain research and the BRAIN Initiative. Also in FY 2015, EHR and SBE funded a crossagency White House workshop on neuroscience and learning, and SBE, ENG and CISE released a DCL through the Industry/University Cooperative Research Centers (I/UCRC) program to foster collaborations between industry and academia in the field of brain imaging and in identifying structure-behavior relationships. An interagency working group was formed to initiate conceptual planning for a National Brain Observatory. A report was submitted to Congress on their current planning efforts.

In FY 2016, NSF increases its investment to \$146.93 million for the UtB activity, with \$73.46 million of these funds devoted to projects related to the BRAIN Initiative, \$3.0 million of which will be directed to furthering the development of the concept of a National Brain Observatory. These investments will drive integration of research at multiple scales of analysis and accelerate the development of new theoretical, experimental, and analytical approaches, including cyberinfrastructure platforms, computational and data-enabled modeling and tools, 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 complex neural systems, and their interactions with changing physical, technological, and social environments throughout the lifespan.

To understand the full complexity of the brain, it will be crucial to increase collaborations among relevant scientific communities, which have traditionally focused on discipline-specific experimental questions. Consequently, FY 2016 investments will also fund new interdisciplinary and transdisciplinary team

formation and workforce development through the development of up to two solicitations sponsored by unique combinations of our disciplinary directorates. In FY 2016, SBE, CISE, ENG, and EHR reissued the solicitation Integrative Strategies for Understanding Neural and Cognitive Systems. Funding will also support increases in interagency collaboration, coordination, and communication through the BRAIN Initiative and the efforts of the IWGN. In FY 2016, NSF takes a leadership role in international coordination through its support for a conference entitled, "Coordinating Brain Projects Across the Globe," that will be co-sponsored by the Kavli Foundation and organized to coincide with the United Nations Meeting of the General Assembly in September of 2016. The purpose of this conference is to bring together government representatives and leading scientists from countries already collaborating with the U.S. and/or making major investments in neuroscience research to exchange ideas about activities and identify opportunities to coordinate efforts where possible.

FY 2017 Request

In FY 2017, NSF total investment in the UtB activity is \$141.62 million, a 3.6 percent reduction. Within this amount, \$74.16 million will support activities related to the BRAIN Initiative. NSF will maintain the UtB focus initiated in FY 2015 and FY 2016 by continuing to employ investment strategies designed to enable the transformational research, engineering, infrastructure development, and training required to accomplish the overall multi-year goal across the priority areas identified earlier. These activities will include continuing efforts to further the development of the concept of a National Brain Observatory.

FY 2018 and Beyond

The NSF-wide UtB Coordinating Group will assess NSF's UtB investment using the assessment metrics discussed below to determine which priority areas had the highest impact on the field and how best to build upon them. The results of this assessment will guide NSF's UtB investment in FY 2018 and beyond.

Evaluation Framework

The NSF-wide UtB Coordinating Group will oversee evaluation of the progress on scientific and programmatic activities. Assays of success for each priority area below will be compared against the expected outcomes described above, using measures including:

- Priority Area 1: level of deployment and adoption of innovative technologies by the scientific community via reuse and citations;
- Priority Area 2: increases in the number of transdisciplinary teams funded to work and publish in this area;
- Priority Area 3: acceptance by the research community of new mappings between brain functional/ structural changes and identified changes in psychosocial, external physical, technological, and educational environments; and
- Priority Area 4: number of participants, and demographics of collaborations in publications before and after the investment period.

The progress of the implementation of this investment will be monitored and reviewed quarterly to ensure that it is on track as part of the FY 2016 Performance Goal 1: Ensure that Key Program Investments are on Track. This aligns with all objectives of Strategic Goal 1: Transform the Frontiers of Science and Engineering and Strategic Goal 2: Stimulate Innovation and Address Societal Needs through Research and Education. For more information about monitoring key program investments, see the FY 2016 Annual Performance Plan in the Performance chapter of NSF's FY 2016 Budget Request to Congress³ and the FY 2017 Annual Performance Plan in the Performance chapter of this Budget Request.

³ www.nsf.gov/about/budget/fy2016/pdf/57_fy2016.pdf