

Written Statement of Carol Ann Mason, President, Society for Neuroscience
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Subcommittee on Commerce, Justice, Science, and Related Agencies
Appropriations Committee
In support of FY 2015 Appropriations for the NSF

Mr. Chairman and members of the Subcommittee, my name is Carol Ann Mason, PhD. I am a professor of pathology and cell biology, neuroscience, and ophthalmic science at Columbia University. I study the development of visual pathways in mammalian brains, with a focus on how neurons in the eye are encoded to project to the correct side of the brain, setting up the circuit for binocular vision. This statement is in support of increased funding for the NSF for fiscal year 2015. I am pleased to submit this testimony in my capacity as president of the Society for Neuroscience (SfN). On behalf of the nearly 40,000 members of SfN, thank you for your past support of neuroscience research at NSF.

The Society stands with others in the research community in requesting at least \$7.5 billion for NSF for FY 2015. Sequestration has taken an enormous toll on the research enterprise, coming on top of recent years when funding has failed to keep pace with the cost of research – let alone the scientific opportunities that are available. SfN urges Congress to reverse the current course and find ways to invest more in scientific discovery. Let's work to put research on a trajectory of sustained growth that recognizes its promise and opportunity as a tool for economic growth and for advancing the health and well-being of Americans.

Neuroscience: An Investment in Our Future

Even in the face of the difficult funding situation, the last several years have been a tremendously exciting and productive time for neuroscience discoveries. Major research advances in brain development, imaging, genomics, circuits, computational neuroscience, neural engineering, and many other disciplines are leading to new tools, new knowledge, and greater understanding that were unimaginable even a few years ago.

All told, there are more than 1,000 debilitating neurological and psychiatric diseases that strike over 100 million Americans each year, costing an estimated \$760 billion a year. Advances made possible by publicly-funded research will help us maintain and restore healthy brain function. Now more than ever, it is time to fan the flames of research in order to ensure life-changing breakthroughs continue.

Resources provided to NSF will support the nation's best and brightest researchers at the forefront of promising discoveries, graduate students at the start of their careers, and the development of advanced scientific tools and infrastructure that will be broadly available to the research community. These researchers are the ones who will be answering some of the vexing questions facing the field of neuroscience: how do the genetic, molecular, and cellular elements of the brain interact to allow for brain function and behavior? How will new tools such as brain-machine interfaces, computational models, and advanced imaging techniques deepen scientific capacity for inquiry, and contribute to better health and quality of life in the years ahead? NSF is uniquely positioned to address questions of this kind because of its emphasis on integrative and

interdisciplinary research and its long history of funding research that leads to the development of life-changing neurotechnologies.

NSF funding is an investment in America. Funding for research supports quality jobs and increases economic activity. In FY 2012 alone, NSF supported 39,862 senior personnel, 4,596 postdoctoral fellows, and 25,550 graduate students through 11,524 awards. Ninety percent of the NSF budget goes right back to fund extramural research in every state. Many of my colleagues can point to their first NSF grant as the launching pad for a career in science.

Finally, without robust, sustained investment, America's status as the preeminent leader in biomedical research is at risk. Other countries are investing heavily in biomedical research to take advantage of new possibilities. Even with the growing philanthropic support, private sector cannot be expected to close the gap. The lag time between discovery and profitability means that the pharmaceutical, biotechnology, and medical device industries need federally-funded basic (also known as fundamental) research to develop products and treatments. The foundation that basic research provides is at risk if federally-funded research declines.

The BRAIN Initiative

The Brain Research through Application of Innovative Neurotechnologies (BRAIN) Initiative – announced by the President last April – will enable NSF and other federal agencies to develop tools and plans that will help accelerate fundamental discoveries in neuroscience. The scientific community is providing direction through diverse workshops being held throughout the country.

The overarching goal of the BRAIN Initiative is to integrate across scales (e.g., genes to behavior) and disciplines (e.g., engineering and life sciences) to establish predictive theories of brain structure and function, and to use these theories to maintain and restore the healthy brain. The Initiative has a strong focus on technology and cyber tool development and the training of new generations of scientists to use the resources that emerge from the BRAIN Initiative, both of which have the potential to benefit all of neuroscience and even non-neuroscience research.

BRAIN – as with all the neuroscience research that takes place with federal support – can only be successful if it is part of a broad effort by Congress and the Administration to prioritize biomedical research so that it can reach its full potential. Such an investment will also help ensure the U.S. remains a global leader, even as other nations ramp up their investments in neuroscience research.

Cross-Disciplinary Neuroscience

NSF-funded basic research continues to be essential for discoveries that will inspire scientific and medical progress for generations. The work supported by NSF has led to the development of new technologies that have revolutionized neuroscience research. The following examples are just a few of the many basic research success stories in the science of the brain emerging now thanks to interdisciplinary research funded by a strong historic investment in NSF and other research agencies.

Green Florescent Protein

Basic research funded by NSF creates revolutionary advances in science, such as green fluorescent protein (GFP) — a transformative tool in cellular biology which allows scientists to look at the brain in unprecedented detail. The work that led to its discovery and development for use in research received the Nobel Prize in Chemistry in 2008.

The discovery of GFP revolutionized scientists' view of the nervous system by allowing them to add an incredible range and depth to images of the brain. With this protein and others like it, researchers are applying colors to brain cells to look at under the microscope. This enables them to map intricate details of brain cells, such as how they connect to each other. Understanding these connections and their susceptibility to change helps researchers better understand the healthy brain and how they might be damaged in a variety of disorders.

More than 100 years ago, scientists got their first glimpse at brain cells under a microscope after successfully staining cells with dark pigment. This and similar techniques are limited because they can't be used in living cells and they can only stain in a single color. GFP is a molecule that glows green under blue or ultraviolet light. Since its discovery, scientists have developed similar molecules that glow many different colors. Moreover, GFP can be used to visualize activity of a *living* cell. These light-emitting proteins have been used to illuminate the inner workings of brain cells by letting scientists track the movement of molecules inside the cells or watch how neurons react to environmental stimulation in living brains. Scientists have also used GFP to help answer questions about brain structure by using it to identify specific cells in specific areas and trace connections between two brain areas.

Recently, GFP has been adapted to help trace many brain regions at a time. In 2007, researchers found a way to make brain cells emit one of nearly 100 colors. They genetically engineered mice to carry multiple copies of a chain of three or four genes for different colored fluorescent proteins. In each cell, the combination of the colors emitted from each chain led to unique color blends. Just as a television produces a wide spectrum of colors by mixing red, green, and blue pixels, this so-called "rainbow" technique cast neighboring cells in colors from aquamarine to magenta. This technique allows scientists to map many pathways in the brain to a much larger extent than before and has allowed for a deeper understanding of brain circuits. GFP is now widely used to track everything from how nerve cells develop to how cancer spreads through the body to how HIV travels from infected to non-infected cells. In the field of neuroscience specifically, this technology will continue to evolve and will be instrumental in our efforts to understand brain structure and function.

Brain-Machine Interface

The brain is in constant communication with the body in order to perform every minute motion from scratching an itch to walking. Paralysis occurs when the link between the brain and a part of the body is severed, and eliminates the control of movement and the perception of feeling in that area. Almost two percent of the US population is affected by some sort of paralysis resulting from stroke, spinal cord or brain injury, or other cause. Basic research funded by the NSF has provided fundamental understanding of how the brain controls movement, which in turn has led to advances in next-generation prosthetics.

In the 1990s, scientists developed an array of electrodes that allowed them to study an unprecedented number of nerve cells at once—almost 50 at a time. This research demonstrated that brain cells communicate in clusters, not in isolation. In other words, cells work together to direct complex behaviors. Since then, scientists have found ways to translate messages from clusters of neurons into a language that an artificial device can understand and convert into movement. Fundamental research in humans and animals led to the discovery that thinking of a motion activates neurons in the same way that actually making the movement would—opening the possibility to control robotic devices using a person’s thoughts.

Thanks to successes in animal research, brain-controlled prosthetics are now being piloted in humans. Paralyzed humans implanted with electrodes can learn to guide a machine to perform various motor tasks such as picking up a glass of water. These advances, while small, enable substantial improvements in the quality of life for people suffering from paralysis. As deeper understanding of the language of the brain occurs in concert with advances in biomaterials, neurotechnologies, and computational power, scientists hope to eventually broaden the abilities of such devices to include thought-controlled speech and more.

Understanding the Development of Vision

My own area of research is the development of the circuits underlying vision. For binocular vision to function, the brain must receive information from both eyes. Nerve fibers from each retina grow to the ‘optic chiasm’ at the midline of the bottom of the brain. Here, nerve fibers from each eye cross to the other side of the brain. Other axons, however, are repelled at the midline and project to the same side of the brain. These connections underlie binocular vision which enables animals, including humans, to calculate how far objects lie in the distance.

One area of my research focuses on how this circuit develops, particularly the molecular mechanisms that prompt some growing retinal nerve fibers to “stop in their tracks” and reroute to the same side. These two groups of cells in the eye, each taking different routes, are endowed with distinct genes that direct their time of birth and their growth to the brain regions where they make their connections with other cells. Understanding their genetic “signatures” and growth helps us to learn how to encourage stem cells to become specific types of retinal cells and integrate into the diseased eye, and stimulate injured nerve fibers to regrow in the correct circuits. Moreover, understanding how tracts are laid down is essential for unraveling the basis of defects in fiber pathways and connections between neurons in neurodevelopmental disorders such as autism.

The development of my career has been made possible through NSF support starting with my NSF Summer Undergraduate fellowship. Next year I will apply for a NSF/NIH Collaborative Research in Computational Neuroscience with a colleague in Australia to model how nerve fibers grow based on live imaging data of developing fiber paths. This research is made possible by a foundation of NSF-funded advances in microscopy that revealed the dynamism of developing and mature neurons. My work further builds upon this foundation for future discoveries on brain circuits and new understanding about diseases of the eye and other neurodevelopmental conditions.

The Future of American Science

As the subcommittee considers this year's funding levels, please consider that significant advancements in the biomedical sciences often come from young investigators. The current funding environment is taking a toll on the energy and resilience of these young people. America's scientific enterprise — and its global leadership — has been built over generations. NSF alone has awarded over 46,500 Graduate Research Fellowships since 1952. Many young scientists receive their first grants from NSF on their way to having careers as independently-funded investigators. Without sustained investment, we will quickly lose that leadership. The culture of entrepreneurship and curiosity-driven research could be hindered for decades.

We live at a time of extraordinary opportunity in neuroscience. A myriad of questions once impossible to consider are now within reach because of new technologies, an ever-expanding knowledge base, and a willingness to embrace many disciplines. To take advantage of the opportunities in neuroscience we need an NSF appropriation that allows for sustained, reliable growth. That, in turn, will lead to improved health for the American public and will help maintain American leadership in science worldwide. Thank you for this opportunity to testify.