TESTIMONY
of
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Good morning, Chairman Bucshon, Ranking Member Lipinski, and members of the Subcommittee. Thank you for the opportunity to provide testimony today on the frontiers in human brain research and the importance of an interdisciplinary and interagency approach to neuroscience. My name is Gene E. Robinson and I am the Swanlund Chair of Entomology and Neuroscience and the Director of the Institute for Genomic Biology at the University of Illinois at Urbana-Champaign. I am a member of the US National Academy of Sciences and currently serve on the Advisory Council of the National Institute of Mental Health.

Today I will address three topics: first, the importance of basic research on brain and behavior; second, the wisdom of studying a diverse set of animal models; and third, the power of interdisciplinary research, which is essential for building new tools to study the human brain.

A few years ago, the National Science Foundation (NSF) sponsored a workshop that I chaired to address the challenges of 21st century biology. Our report, published in 2010 in *BioScience*, concluded that, "Addressing the challenges of 21st century biology requires integrating approaches and results across different subdisciplines of biology…as well as technologies, information, and approaches from other disciplines…" This applies to many areas of biology, including neuroscience, and in particular, the recently announced Brain Initiative, that is, the Brain Research through Advancing Innovative Neurotechnologies Initiative. The BRAIN Initiative needs to develop a broad and inclusive agenda that funds basic research on brain and behavior, both in humans and in a variety of animal species.

Why is a broad approach necessary? What are the benefits of studying a wide array of species in our efforts to understand the human brain? One of the goals of the BRAIN Initiative is to understand how the brain produces human behavior, with all of its complexity and potential for disorder. We are fortunate that the diversity of animal life on the planet provides us with many potential models for aspects of human behavior, so long as we have the knowledge to recognize and take advantage of them. This approach of exploring and capitalizing on the resources provided by nature falls perfectly within the mission of NSF. NSF supports a wide scope of basic science on brain and behavior that provides the breadth of knowledge necessary for continued advancement of the field of neuroscience.

It is necessary to understand how healthy brains work in order to cure the many devastating brain disorders that afflict our society. This involves basic research on animal models—the type of science championed by the NSF. The role of NSF in meeting societal challenges is to support basic research—research that examines how a healthy system functions and adds to our knowledge of how living things work. This knowledge makes it possible to generate hypotheses that describe what changes occur in a dysfunctional system, and to propose and test possible interventions for those disorders. The process is interconnected, interdisciplinary, and progressive. Let me give you one example from my own research to illustrate the benefits of integrating research on the brain with research on behavior in an interdisciplinary manner, as well as the synergy between basic science and its sometimes unexpected applications.

I study social behavior, specifically how it arises in nature and what mechanisms govern it. I use honey bees to address these questions. The reason I use honey bees is that they live in one of the most complex societies on the planet, with tens of thousands of individuals involved in intricate forms of communication and division of labor. Intriguingly, they produce all this complex social behavior with a brain the size of a grass seed! How can such a tiny brain produce such complex behavior and what does this say about our own brains?

One question my laboratory has addressed is how do bees know what job to perform in their hive. There are about a dozen different jobs that bees perform, including feeding the baby bees, foraging for nectar and pollen from flowers, and turning nectar into honey. Bees divide labor in a very organized fashion, with different groups specializing in the different jobs. But bees don't do these jobs like little robots; rather they adjust their behavior to the needs of the whole group. When a hive of bees loses some of its foragers, others will drop what they're doing and start to forage. Thanks to a new system of tracking bees with Radio Frequency ID tags developed in my laboratory by retired computer entrepreneur and current citizen scientist Paul Tenczar, we can now automatically detect these adaptive behavioral shifts, enabling us to more easily explore the underlying neurobiological questions.

One intriguing aspect of job-switching in bees is that they do it without receiving commands from centralized control. Neither the queen nor any other individual directs the actions of the rank and file worker bees, but everyone in the beehive does what needs to be done. Each bee is able to synthesize information about the environment inside and outside the hive, along with internal cues about its physiological state, to appropriately direct its own behavior. We suspected that this might involve reprogramming the bee's brain to perform the different job, but we needed new tools to monitor brain activity.

In the early 2000s, with the advent of more advanced genome sequencing technology, we pushed to sequence the honey bee genome, the assemblage of all the genes, in order to develop powerful new tools for brain analysis. Fortunately the NIH's National Human Genome Research Institute at the time was considering additional species for sequencing in order to better understand the human genome and the honey bee was selected because of its compelling social behavior. The United States Department of Agriculture also contributed to this effort because of the vital role bees play in pollinating our nation's food and fiber crops, contributing approximately $20B per year to our economy.

With new tools in hand we obtained a grant from the NSF Frontiers of Science program, which was designed to promote interdisciplinary research. My laboratory performed a series of experiments that explored the relationship between job shifts in the beehive and changes in brain gene activity, which leads to changes in how much of the brain's proteins are produced.

We found that the brain of the bee is indeed reprogrammed to perform a different job, but the way this reprogramming occurs was a big surprise. Not only does the genome provide a script for building and operating the brain; when it comes to behavior, the genome also improvises—it is sensitive to the environment and alters the activity of genes in a dynamic way. When a bee detects a decrease in the number of foragers in its hive, thousands of genes in its brain change their activity, and this causes the bee to start to forage. The bee's experience is embedded in its genome in the brain so that it can change its behavior appropriately.

It turns out that bees are not the only ones with dynamic genomes in their brains. Birds, fish, mice, and other animals also have been found to exhibit dynamic brain genomes. In addition, as expected when a feature of biology is similar in many different organisms, humans also appear to exhibit the same dynamic brain genome. It is much more difficult to study this phenomenon in humans than in animals, and it likely never would have been done without animal discoveries paving the way.

Last year I co-chaired a special meeting of the National Academy of Sciences and the Canadian Institute for Advanced Research to explore the human health implications of this discovery. Social scientists have carefully documented the developmental and health consequences of early exposures to adversity, and now they badly want to know how the experiences of childhood adversity get "under the skin," into the body's systems that influence vulnerability and resilience. The conference imagined a new "science of adversity," with a new partnership among psychologists, sociologists, political scientists, neuroscientists and geneticists.

The question of biological embedding—how social influences are perceived, processed, and ultimately transformed into signals inside brain cells--is one of the most important questions in neuroscience, with profound health and public policy implications. It is clear that early adversity changes behavior, learning capacities, and social functioning, but how this happens –how the brain develops differently under adversity—can only be studied in animals in a basic research framework. Our research on honey bees helped initiate this line of research, but it will take the integration of this and many other research efforts to reach a complete answer, including research on animals funded by the NSF Directorate for Biological Sciences and research on humans funded by the NSF Directorate for Social, Behavioral and Economic Sciences.

My laboratory's research on honey bees shows the value of combining the power of new technology with knowledge derived from basic research on both brain and behavior. The BRAIN Initiative similarly needs to commit to an effective blend of basic and applied research, to increase the opportunity for transformative discoveries. The initiative will likewise benefit from the selection of experimental models and behaviors that provide illuminating contexts in which to apply them. However, neuroscientists are increasingly relying on the study of just a few species to understand behavior and brain function. These classic model organisms, including the fruit fly and mouse, do offer experimental advantages. They are easy to breed in the laboratory and they are easy to use for many types of genetic experiments to learn the functions of different genes. As attractive as these advantages are, the use of only a few model organisms is unnecessarily limiting. Many aspects of biology are the same across species, but each species has unique characteristics as well; to distinguish between these two possibilities, multiple species must be studied and compared. The unique features of some organisms offer research opportunities that more traditional study organisms do not, often because they represent an extreme of a biological property of interest. Studies that make strategic use of well-chosen, and diverse, animals models can have tremendous impact on a field. Neuroscientists have long known this—the lowly squid essentially launched the modern era of neuroscience because its nerve cells are so big that their activity could be studied even with the primitive techniques of the late 1940s. Because an increasing number of species have had their genomes sequenced over the past few years, there are more choices than ever before for high-powered molecular analyses of the brain.

Our 21st century biology report also concluded that, “biologists need devices to continuously record the activity of cellular components as they interact naturally in living cells.” This recommendation has been embraced by the BRAIN Initiative, and future technological innovation will be central to uncovering the workings of the human brain. Here, again, NSF’s contributions will be vital because of its tradition of encouraging and facilitating interdisciplinary approaches to integrate engineering, computer science, physics and chemistry. The new tools to record brain activity are most easily developed by individuals who combine knowledge of physics or math, or expertise in the applied skills of computer science or engineering, with understanding and appreciation of the challenges and technological needs of biology. The University of Illinois at Urbana-Champaign provides an excellent example of an environment that fosters this type of interdisciplinary work. Modern research institutes such as the Institute for Genomic Biology and the Beckman Institute for Advanced Science and Technology bring together top engineers and biologists in a spirit of open communication and collaboration. This atmosphere has led to remarkable innovations. For example, an NSF-sponsored partnership between the University of Illinois and the Cray Corporation built Blue Waters, one of the world’s most powerful supercomputers, the computational capacity of which will vastly improve our ability to model the most complex biological systems, including the human brain.

Understanding how the brain works represents a formidable challenge to our collective ingenuity and dedication. It is important that we consider carefully how to best direct our efforts and resources to meet this challenge, united by our common interest in improving the health and structure of our society. I appreciate the opportunity to be here today with you and the committee to discuss this important topic. We must remember that basic science research is called “basic” not because it is simple, but because it provides the foundation for innovation. I am confident that this initiative will bring great improvements to our understanding of the human body, the brain, and our health by promoting the continuation of impressive work in our university research centers and government laboratories, in partnerships with private organizations, and enabled by funding from government agencies. Through the united effort of biologists and mathematicians, engineers, physicians, and other explorers of the brain, both big brains and little brains, we must –and we will-- find the answers we need.