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BRAIN Initiative to Transform Human Imaging

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IN HER KEYNOTE ADDRESS AT THE NATIONAL INSTITUTES OF HEALTH'S (NIH'S) 50TH anniversary celebration of the discovery of the double helix structure of DNA, molecular biologist and Princeton President Shirley Tilghman observed that ideas are fundamental to advancing science, yet technological innovation is the engine of scientific progress (1). Indeed, there are many historical lessons to illustrate this truth.

During the dawn of the scientific revolution, the Milky Way was believed to be merely a nebulous cloud of light-reflecting dust. It was not until Galileo used the newly invented telescope in the early 1600s that this bright celestial cloud was discovered to actually be a constellation of individual stars. This was a tremendous revelation, not only advancing astronomy but also demonstrating the value of precise measurement and objective observation in revealing the laws of nature. It illustrated how precision tools are critical to new insights and new knowledge.

Today, we are encouraged to think beyond ourselves again and invent that which we do not currently have to help meet the bold new goals set by President Obama's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative. Unveiled in April 2013 and supported by the NIH (2), National Science Foundation (NSF), and Defense Advanced Research Projects Agency (DARPA), as well as private participants, the BRAIN initiative has been on a fast track to develop a complete picture of brain function through a four dimensional (4D) (space and time) mapping of the extensive network of neural circuits. With this goal in mind, the NIH Director's Advisory Committee BRAIN Working Group presented an interim report in September 2013, followed by the final report in June 2014 (3).

In the interim report, now underscored by the final report, the BRAIN Working Group made initial high-priority recommendations, which led to six NIH funding opportunities that were announced in December 2013 with funding planned by September 2014 (4). These initiatives will lead to new fundamental observations and knowledge about the brain by stimulating the development of various neurotechnologies. These technologies will be designed to explore and catalog neurons and neural system function across the full range of biophysical and physiological scales. One of these six high-priority initiatives, Planning for Next Generation Human Brain Imaging, is the only one focused on human imaging (5).

This particular high-priority initiative is the first from the NIH to challenge the research community to form new teams to innovate and invent a new generation of truly transformative human imaging methodologies. What are explicitly sought are systems that

will provide investigative capabilities far beyond those of even the most advanced and cutting-edge current systems. The goal is to exceed the spatiotemporal resolution limits of current imaging methods to observe human physiology at the cellular networks level. We at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the NIH foresee this specific BRAIN initiative as having a dual impact: It will help to solve some of the great neuroscience mysteries, while also spurring a transformation in imaging of all human organ systems. In elucidating the mysteries of the brain and human pathophysiology in general, the impact may well be comparable with that which Galileo had through his clarification of the Milky Way.

This vision is not an unjustified dream. Again, we have but to turn to recent history for a lesson in what innovation can bring in medical science. Just 40 years ago, the best noninvasive medical imaging system produced “planar” or 2D shadow-grams of internal organs. It completely lacked the 3D pinpoint accuracy that has become a central mainstay of modern health care. The development of computer-assisted tomography (CAT) in the early to mid-1970s was realized through the evolution of sophisticated image reconstruction mathematics, advances in electronics, and the creation of high-performance computers. Since its introduction, CAT (or CT) has had an impact on the delivery of effective health care and medical discovery that would be hard to overstate. Exploratory surgery has long been a procedure of the past, and gone is the guesswork about exactly where, how big, and how responsive to treatment an internal lesion is.

Indeed, this innovation resulted from interdisciplinary research that merited the 1979 Nobel Prize in Physiology or Medicine for two of its inventors, engineer and radar scientist Godfrey N. Hounsfield and medical physicist and radio astronomer Allan M. Cormack. Before their independent translational work, inspired in both by the clinical need for 3D human imaging, came the brilliant insights of mathematician Johann Radon. He defined the relationship between certain measurements that can be made from outside of an object to the object’s internal structure. Over the ensuing decades, the mathematics he pioneered was developed further in astronomy, for which scientists devised rigorous approaches to reconstructing the source of detected radio signals from the heavens. These mathematical advances, however, needed to be coupled with advances in x-ray technology, electronics, and computer science in order to realize a CAT scan prototype circa 1971.

A similar dramatic advance in human neuroscience is envisioned as a result of the innovation the BRAIN initiative intends to stimulate. The aspirations are tremendous: a dynamic picture of the brain showing the complex 4D interplay of cells and neural circuits. Since biologic systems from molecules to cells are continuously dynamic, investigative methods must provide information that is highly resolved in space and time. What are required are technologies that can observe human neuroprocesses not seen with current state-of-the-art human imaging systems. Achieving this does not necessarily require the discovery of a new physical phenomenon. It may well mean extracting more of the fundamental information contained within signals from current probes. Indeed, Hounsfield himself remarked in his Nobel lecture that in investigating the previous use of x-rays, “it became apparent that the conventional methods were not making full use of all the information the x-rays could give.”

This high-priority BRAIN initiative on next-generation human imaging technologies is a striking call for teams of our best and brightest minds from multiple disciplines to think big, aim high, and reach far beyond previous boundaries in human imaging science. Many basic and practical payoffs await us. These include assessing microcircuits and their interplay with hemodynamics, deciphering the blood-brain barrier construct and function, observing person-specific neurotransmitter dynamics, defining cellular metabolism and gene expression, investigating non-neuronal (glial) structure and function, measuring real-time drug distribution, and discovering ion channel dynamics (5). Like the examples from history, progress of this magnitude is born from a convergence of disciplines and backgrounds. It will require transdisciplinary science and engineering. With this level of technological innovation, the ultimate impact may extend well beyond the brain to other organ systems, helping to unravel the mysteries of human health and disease, and with this, how to heal, cure, and prevent some of our most challenging illnesses.

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Biography

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