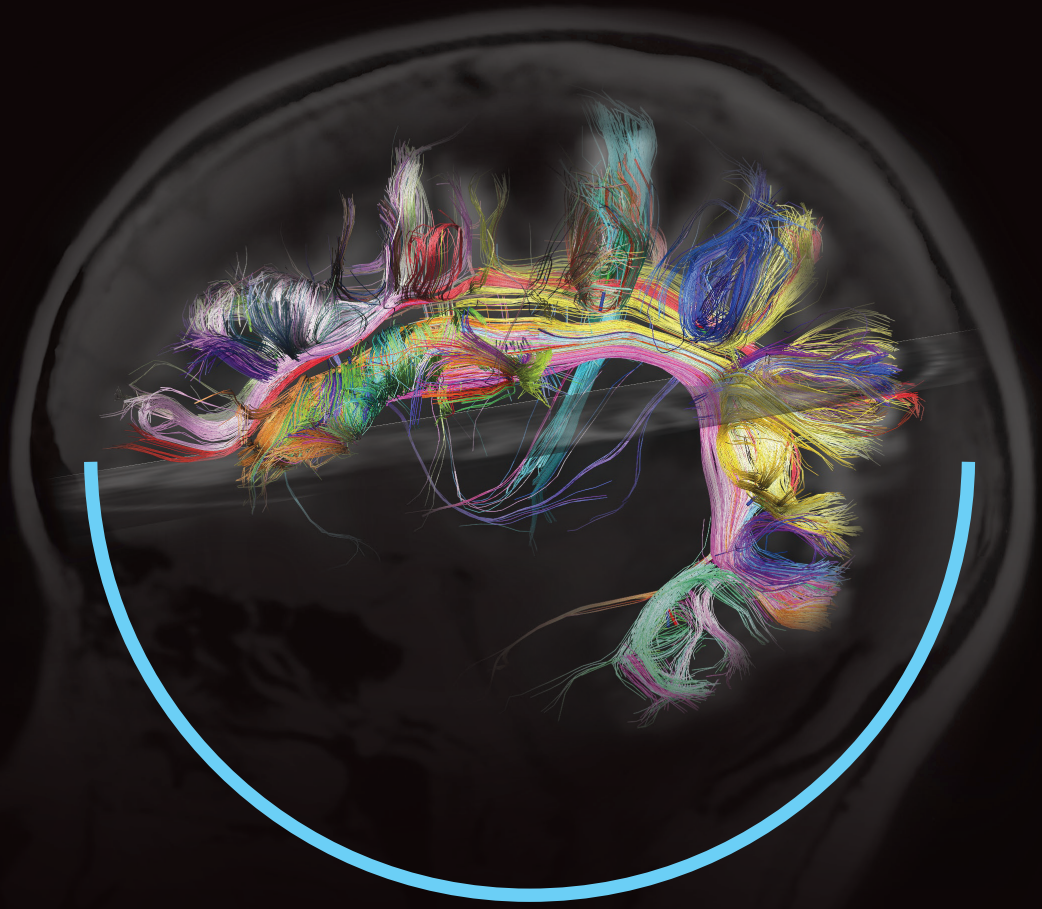


THE BRAIN INITIATIVE

NATIONAL INSTITUTES OF HEALTH

“THERE IS THIS ENORMOUS MYSTERY WAITING TO BE UNLOCKED, AND THE BRAIN INITIATIVE WILL CHANGE THAT BY GIVING SCIENTISTS THE TOOLS THEY NEED TO GET A DYNAMIC PICTURE OF THE BRAIN IN ACTION AND BETTER UNDERSTAND HOW WE THINK AND HOW WE LEARN AND HOW WE REMEMBER. AND THAT KNOWLEDGE COULD BE – WILL BE – TRANSFORMATIVE.”

PRESIDENT BARACK OBAMA, APRIL 2, 2013

WHAT IS THE BRAIN INITIATIVE?

Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative

The BRAIN Initiative will accelerate the development and application of new technologies to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought. These technologies will open new doors to explore how the brain encodes, stores, and retrieves vast quantities of information, and shed light on the complex links between brain function and behavior.

The National Institutes of Health (NIH), the Defense Advanced Research Projects Agency (DARPA), the National Science Foundation (NSF), and the Food and Drug Administration (FDA) are leading this national effort. Momentum is growing and additional partners are getting involved. President Obama has called for the BRAIN Initiative to be an “all hands on deck” effort and has encouraged participation from the private sector as well.

THE HUMAN BRAIN HAS 86 BILLION NEURONS ALONG WITH OTHER CELLS THAT MAKE MORE THAN 100 TRILLION CONNECTIONS.

WHY NOW?

100 million Americans suffer from devastating brain disorders at some point in their lives – neurodevelopmental disorders (such as autism), mood and anxiety disorders (such as depression and post-traumatic stress disorder), neurodegenerative diseases (such as Parkinson's and Alzheimer's diseases), among many others (such as epilepsy and stroke). Knowing more about the brain has the potential to improve so many areas of human health.

A recent revolution in modern neuroscience creates a unique opportunity to unlock mysteries of the brain with the promise of ultimately helping people with brain disorders. Recent progress has given us:

- Exciting insights into brain structure
- Advanced technologies for recording hundreds of neurons at once
- New methods for precisely manipulating activity within brain circuits
- Massive and complex data sets rich with valuable information

The time is right to inspire a new generation of researchers to undertake the most groundbreaking and integrated approach ever contemplated to understanding how the brain works in health and disease.

This is a moment in science when our knowledge base, our new technological capabilities, and our dedicated and coordinated efforts can generate great leaps forward. The answers to the mystery of how organized circuits of cells interact dynamically to produce behavior and cognition will not come easily, but the public health need and the scientific opportunity are so great that there has never been a better time to undertake this challenge.

NIH ROLE

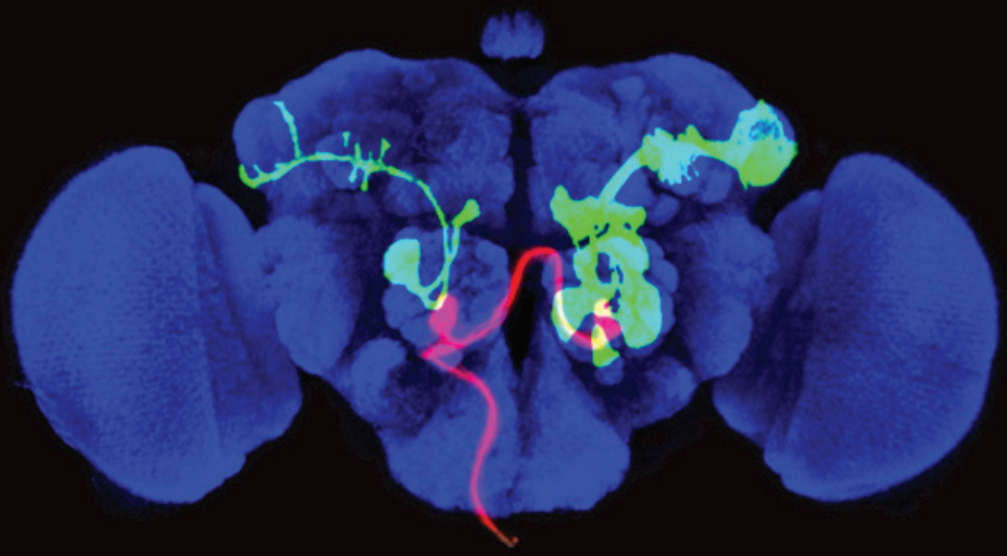
NIH Director Francis Collins convened an esteemed group of experts in neuroscience to develop a scientific plan for this bold endeavor. The group spent over a year and a half in extensive consultation, getting feedback from the basic, translational, and clinical research communities, in addition to patient advocates and the general public. The resulting June 2014 report, a 12-year scientific vision, spells out the NIH's role in the BRAIN Initiative (www.nih.gov/science/brain/2025).

12-YEAR SCIENTIFIC VISION

Overall Aim: To map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity, and understand how their interplay creates our unique cognitive and behavioral capabilities.

WHY FOCUS ON CIRCUITS?

60 years of studying one neuron at a time has taught us a lot about individual neurons. Imaging technologies have enabled us to observe the activity of thousands of neurons in the living brain. But there remains a gap in our knowledge of what happens in the middle of this spectrum – within the complex networks of neurons that form neural circuits. This is the level at which most of human cognition and behavior is generated. At any moment, thousands to millions of interconnected cells are rapidly transmitting information between themselves via chemical signals and electrical activity. We must understand how these circuits work to capture the full sense of what is happening in the healthy brain – and what goes awry in disease.



Advanced genetic techniques can label nerve cell circuits in real time at the level of single cells. This image depicts the circuitry a fly uses to smell. Credit: Liqun Luo, Stanford University, Palo Alto, CA

Brainbow is a technique that maps individual nerve cells with a wide array of colors in order to chart the circuitry of the nervous system. Credit: J. Livet and J.W. Lichtman, Harvard University

SCIENTIFIC GOALS

To achieve the long-term vision of the BRAIN Initiative, NIH is prioritizing seven scientific goals:

Parts list: Identify and provide experimental access to the different brain cell types to determine their roles in health and disease.

Maps: Generate circuit diagrams that vary in resolution from synapses to the whole brain.

The brain in action: Produce a dynamic picture of the functioning brain by developing and applying improved methods for large-scale monitoring of neural activity.

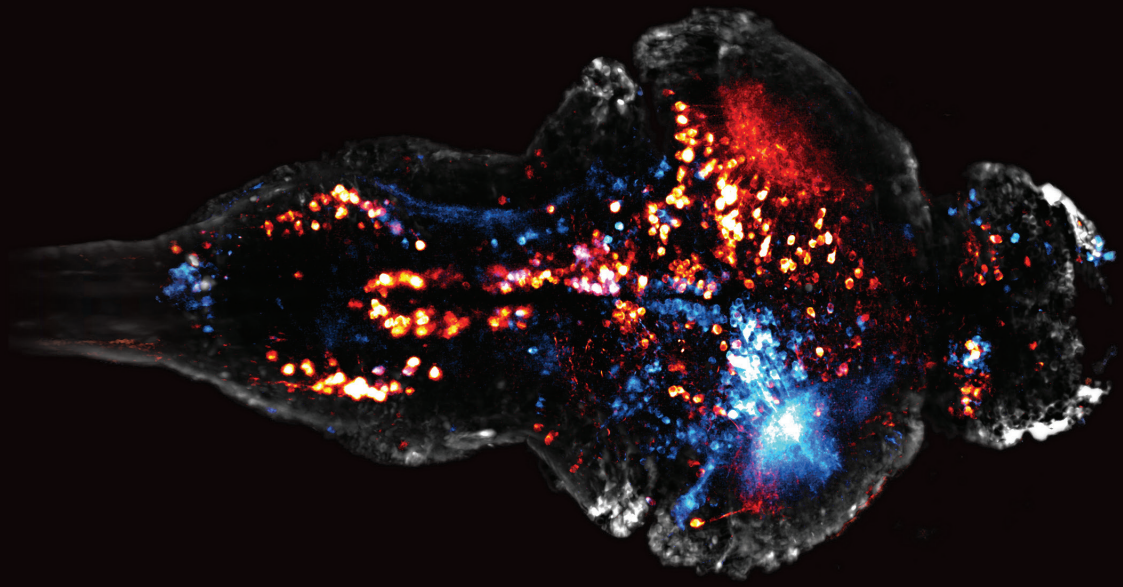
Causes: Link brain activity to behavior with precise interventional tools that change neural circuit dynamics.

Fundamental principles: Produce conceptual foundations for understanding the biological basis of mental processes through development of new theoretical and data analysis tools.

Human neuroscience: Develop innovative technologies to understand the human brain and treat its disorders; create and support integrated brain research networks.

From BRAIN Initiative to the brain: Integrate new technological and conceptual approaches produced in the other goals to discover how dynamic patterns of neural activity are transformed into cognition, emotion, perception, and action in health and disease.

THE BRAIN INITIATIVE HAS ENORMOUS POTENTIAL FOR SOLVING PERSISTENT MYSTERIES OF BRAIN FUNCTION, SPINNING OFF TECHNOLOGIES THAT SEED NEW INDUSTRIES, AND OPENING THE DOOR TO NEW TREATMENTS FOR DISEASES AND DISORDERS OF THE NERVOUS SYSTEM.



WHAT WILL IT TAKE TO ACCOMPLISH THIS GRAND CHALLENGE?

Collaborations

- Cross traditional neuroscience boundaries in interdisciplinary collaborations with geneticists, chemists, engineers, physicists, information scientists, and others
- Work with industry partners, who will bring experience developing products for use in patients

New technologies

- Integrate spatial and temporal scales, to go from cells to circuits as well as functions that can take milliseconds, minutes, or a lifetime
- Establish platforms to preserve and share data
- Validate and disseminate technologies

Rigorous standards and accountability

- Pursue human and non-human studies in parallel to reach scientific goals as expeditiously as possible
- Consider the ethical implications of research on the brain
- Ensure accountability to taxpayers and the community of basic, translational, and clinical neuroscientists

Substantial, sustained commitment

- More than a 10-year research effort
  - Years 1-5: technology development and validation
  - Years 6-10+: discovery-driven research to answer fundamental questions

Above: With lightsheet microscopy, activity in nearly every brain cell of the zebrafish can be monitored during behavior. Credit: Misha B. Ahrens & Phillip Keller, HHMI, Janelia Farm Research Campus

THE CHALLENGES

The brain is the most complex organ in the body; it may take decades for discoveries in basic neuroscience to lead to new treatments and cures for brain disorders. Researchers must first develop the tools for studying the brain to gain a fundamental understanding of how it works. This knowledge will provide much needed insights for solving the medical mysteries plaguing patients.

- In the 21st century, brain disorders – neurodevelopmental and neurodegenerative – will be the most disabling and most costly chronic diseases.
- 5 million+ Americans suffer from Alzheimer's disease. The cost of caring for these individuals is $200 billion+/year. Medicare and Medicaid spending on Alzheimer's disease alone dwarfs the NIH's total neuroscience research budget.
- 2.4 million+ Americans have schizophrenia. After 20 years of intense effort by the pharmaceutical industry, there are still no fundamentally new drugs.
- From 2000 through 2011, more than 235,000 service members were diagnosed with a traumatic brain injury.
- In 2009, an estimated 248,418 children (age 19 or younger) were treated in U.S. emergency departments for sports and recreation-related injuries that included a diagnosis of concussion or traumatic brain injury.

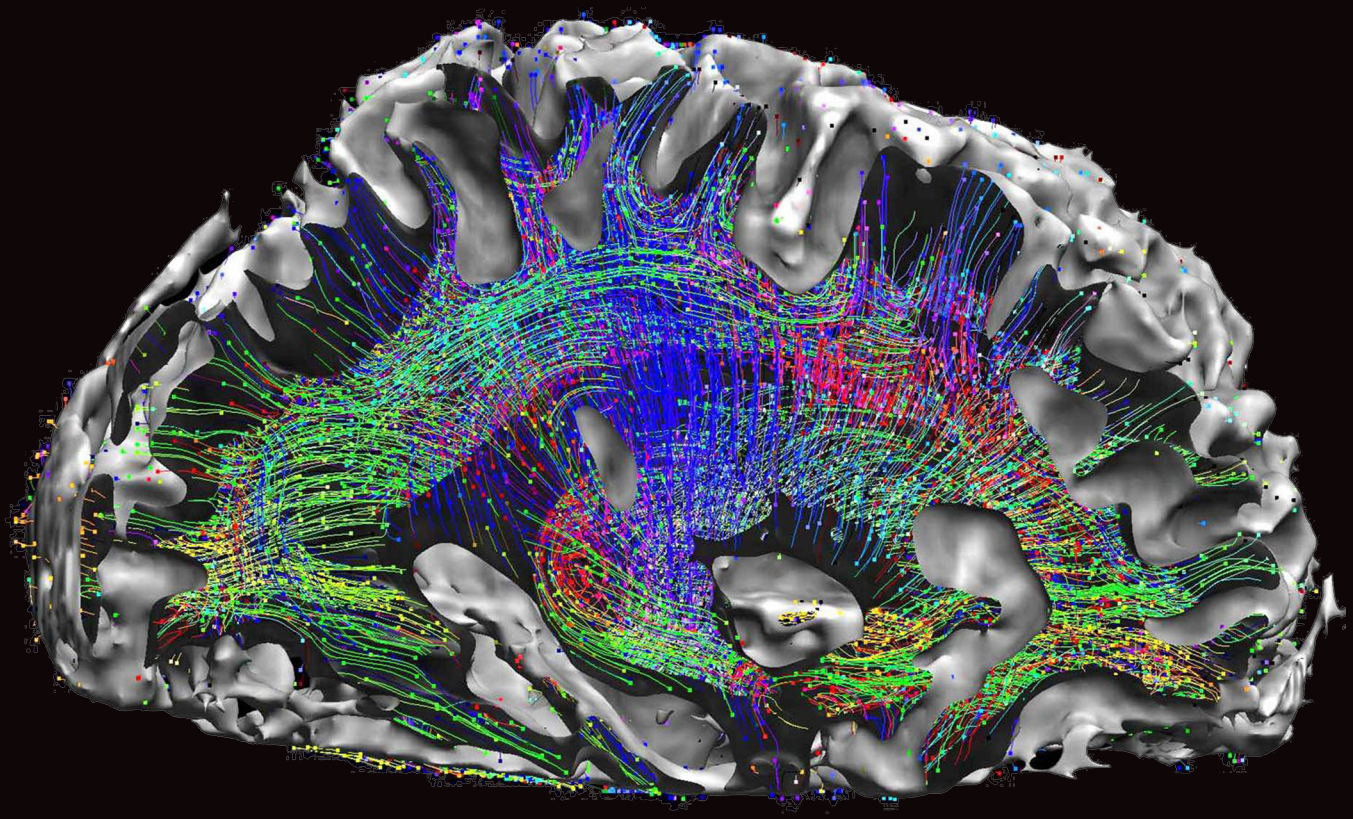
A FOCUSED, SUSTAINED INVESTMENT IN THE BRAIN INITIATIVE HAS THE POWER TO CHANGE THE FUTURE.

OPPORTUNITIES

Cochlear implants help more than 200,000 people overcome profound deafness. The same leap forward may be possible to restore vision for those with profound blindness. By understanding how the neurons in the retina and brain process streams of information from the visual world, it should be possible to devise intelligent retinal prostheses or other devices to restore sight.

Brain Computer Interfaces are being developed for patients paralyzed by injuries or stroke. But the technology needs better speed, reliability, and dexterity, which can come from better understanding of how the brain elicits targeted movements.

Deep brain stimulation has been used as a treatment for Parkinson's disease, chronic pain, and depression. The current technology could be improved through the development of electrodes capable of adapting stimulation parameters in real-time using feedback from neural activity, ultimately serving as sensors as well as stimulators.



New high-resolution, non-invasive imaging techniques produce detailed diagrams of neural tracts, enabling new analyses of how brain regions are connected. Credit: Washington University – University of Minnesota Human Connectome Project consortium

On the cover: Map of the wiring diagram of specific brain circuits, now called the "connectome" in the human brain. Credit: Harvard/MGH-UCLA Human Connectome Project consortium

“HOW THE BRAIN WORKS AND GIVES RISE TO OUR MENTAL AND INTELLECTUAL LIVES WILL BE THE MOST EXCITING AND CHALLENGING AREA OF SCIENCE IN THE 21ST CENTURY.”

NIH DIRECTOR FRANCIS COLLINS, JUNE 4, 2014

THE BRAIN INITIATIVE IS ONE PART OF THE NIH'S INVESTMENT IN BASIC, TRANSLATIONAL, AND CLINICAL NEUROSCIENCE. TO LEARN MORE ABOUT THE NIH BRAIN INITIATIVE, VISIT: www.nih.gov/science/brain

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