The Era of the Brain
U.S. Burden of Diseases: 291 Diseases and Injuries

**Leading Categories of DALYs 2010**

1. Neuropsychiatric Disorders
   - Mental and Behavioral Disorders: 13.6%
   - Neurological Disorders: 5.1%
   - Total: 18.7%

2. Cardiovascular and Circulatory Diseases
   - Total: 16.8%

3. Neoplasms
   - Total: 15.1%

4. Musculoskeletal Disorders
   - Total: 11.8%

5. Diabetes, Urogenital, Blood, and Endocrine Diseases
   - Total: 8.0%

6. Chronic Respiratory Diseases
   - Total: 6.5%

7. Other Non-communicable Diseases
   - Total: 5.1%

Percent of Total U.S. DALYs
The Challenge for the 21\textsuperscript{st} Century

• Chronic non-communicable diseases will be in the 21\textsuperscript{st} century what infectious diseases were in the 20\textsuperscript{th} century.

• Brain disorders – both \textit{neurodevelopmental} and neurodegenerative – will be the most disabling and most costly of these chronic diseases.

• We do NOT know enough about the brain to meet this challenge.
The BRAIN Initiative℠

- A focus on circuits and networks
- Measure the fluctuating electrical and chemical patterns within circuits
- Understand how all of this helps generate our unique thoughts and actions
The BRAIN Initiative

“a public and private effort”

Private Investments

NIH, DARPA, NSF, FDA, IARPA, HHMI, Kavli Foundation, Simons Foundation
The NIH BRAIN Scientific Plan

**FIRST FIVE YEARS**
Emphasize technology development

**SECOND FIVE YEARS**
Emphasize discovery driven science
Seven High Priority Research Areas

1. Discovering diversity: Identify and provide experimental access to the different brain cell types to determine their roles in health and disease. *also during development

2. Maps at multiple scales: Generate circuit diagrams that vary in resolution from synapses to the whole brain. *also during development

3. 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. *also during development

4. Demonstrating causality: Link brain activity to behavior with precise interventional tools that change neural circuit dynamics. *also during development
5. **Identifying fundamental principles:** Produce conceptual foundations for understanding the biological basis of mental processes through development of new theoretical and data analysis tools. *also during development*

6. **Advancing human neuroscience:** Develop innovative technologies to understand the human brain and treat its disorders; create and support integrated human brain research networks. *also during development*

7. **From BRAIN Initiative to the brain:** Integrate new technological and conceptual approaches produced in goals #1-6 to discover how dynamic patterns of neural activity are transformed into cognition, emotion, perception, and action in health and disease. *and lifespan effects of developmental brain states and disorders*
How to Accomplish These Goals: *Principles*

1. Pursue human and non-human animal studies in parallel
2. Cross boundaries in interdisciplinary collaborations
3. Integrate spatial and temporal scales
4. Establish platforms for sharing data and tools
5. Validate and disseminate technology
6. Consider ethical implications of neuroscience research
7. Accountability to NIH, taxpayers, and the scientific community
Estimated Budget

Ramp up to $400M/yr by FY 2018 ➔ Plateau at $500M/yr by FY2021
Total investment of $4.5B by FY 2025
Addressing **BRAIN 2025 Recommendations**

<table>
<thead>
<tr>
<th>Brain Cell Types</th>
<th>Tools for Circuit Diagrams</th>
<th>Tech. to Monitor Neural Activity</th>
<th>Precise Interventional Tools</th>
<th>Theory and Data Analysis Tools</th>
<th>Advance Human Neuroscience</th>
<th>Integrate Approaches</th>
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- **Cell-Type Classification**
- **Novel Tools - Cells and Circuits**
- **Next Generation Human Imaging**
- **Large scale Recording & Modulation Technologies**
- **Integrated Approaches to Understanding Circuit Function**
- **Early Stage Research for Recording & Modulation** *
- **Next-Gen Human Brain Recording & Modulation Devices** *
- **Short Courses** *
- **SBIR announcements** *

* New in FY 2015
Summary: BRAIN Initiatives by Fiscal Year

• 2014: **Six** BRAIN Funding Opportunities

• 2015: **Ten** BRAIN Funding Opportunities
  – Five reissues, Five new
  – Three SBIR/STTR initiatives

• 2016: Notice of Intent, Concepts for Clearance, Workshops
  – NOI: Research Opportunities Using Invasive Neural Recording and Stimulating Technologies in the Human Brain
  – Defining Cellular Phenotypes Workshop (4/21-4/22/15)
• **Brain development a key issue** in almost all of the RFA’s
  – Encourage neurodevelopmental research community to submit and engage

• **Age specific mechanisms of brain function**
  – Inform mental health, education, as well as pediatric and adolescent neuropsychiatric disorders

• **Lifespan approach**
  – Influence of environment and disease on developing pediatric and adolescent brain has impact on adult brain function
## Budget Summary: Will We Have Enough Gas in the Car?

Think big. Start small. Scale fast!

### Innovation

<table>
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<tr>
<th>Fiscal Year</th>
<th>Actual Budget</th>
<th>ACD WG Professional Judgment Budget</th>
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<tbody>
<tr>
<td>FY14</td>
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<td>$500M</td>
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BRAIN Initiative Investigators’ Meeting

First, Kick-off Meeting Nov. 20-21 2014

- Joint NIH-NSF meeting w/ DARPA and HHMI

“This can’t be business as usual ... This is a new culture bridging physicists, engineers, biologists, chemists ... with a big emphasis on showing new results and discoveries.” -- Cori Bargmann

Brainstormers: Obama’s big research push kicks off with a meeting of the minds
BRAIN Initiative: Exciting Advances Beginning to Emerge

High-speed label-free functional photoacoustic microscopy of mouse brain in action
Junjie Yao, Lidai Wang, Joon-Mo Yang, Konstantin I Maslov, Terence T W Wong, Lei Li, Chih-Hsien Huang, Jun Zou & Lihong V Wang

An acetylcholine-activated microcircuit drives temporal dynamics of cortical activity
Naiyan Chen, Hiroki Sugihara & Mriganka Sur

Highly Parallel Genome-wide Expression Profiling of Individual Cells Using Nanoliter Droplets

A New DREADD Facilitates the Multiplexed Chemogenetic Interrogation of Behavior
Eyal Vardy, J. Elliott Robinson, Chia Li, Reid H.J. Olsen, Jeffrey F. Diberto, Patrick M. Giguerre, Flori M. Sassano, Xi-Ping Huang, Hu Zhu, Daniel J. Urban, Kate L. White, Joseph E. Rittiner, Nicole A. Crowley, Kristen E. Pleil, Christopher M. Mazzone, Philip D. Mosier, Juan Song, Thomas L. Kash, C.J. Malanga, Michael J. Krashes and Bryan L. Roth
Multi-Council Working Group (MCWG)

MCWG:

- Respected experts looking at whole BRAIN initiative rather than at discrete parts
- Includes *ex officio* members from BRAIN agencies (IDARPA, FDA, IARPA, NSF)
- Connects to ICs and agencies with BRAIN-focused research
- Discuss funding plans and provide feedback for IC Councils
- Discuss concepts for potential FY 15 solicitations
NIH...

Turning Discovery Into Health