BRAIN Initiative (and Imaging)

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The Challenge for the 21st Century

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

• Brain disorders – both 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.
“So 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 Obama, April 2, 2013
# BRAIN Initiative: Partners

## FY2014 Investments

<table>
<thead>
<tr>
<th>Government Agencies</th>
<th>$ in Millions</th>
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<tbody>
<tr>
<td>National Institutes of Health</td>
<td>$40</td>
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<tr>
<td>Defense Advanced Research Projects Agency</td>
<td>$50</td>
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<tr>
<td>National Science Foundation</td>
<td>$20</td>
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<tr>
<th>Private Organizations</th>
<th>$ in Millions</th>
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<tbody>
<tr>
<td>Allen Institute for Brain Science</td>
<td>$60</td>
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<tr>
<td>Howard Hughes Medical Institute</td>
<td>$30</td>
</tr>
<tr>
<td>Salk Institute for Biological Studies</td>
<td>$28</td>
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<tr>
<td>The Kavli Foundation</td>
<td>$4</td>
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FIRST FIVE YEARS
Emphasize technology development

SECOND FIVE YEARS
Emphasize discovery driven science
To map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity flowing within those circuits, and understand how their interplay creates our unique cognitive and behavioral capabilities.
The BRAIN Initiative

- Provides the roadmap for the NIH initiative
- "imaging" appears 103 times in the document and "quantitative" appears 41 times
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.

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

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.

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

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

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.
Funding in FY14

- $46M invested in 58 projects across 6 RFAs
- > 100 investigators in 15 states and 3 countries

<table>
<thead>
<tr>
<th>RFA</th>
<th>Topic</th>
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<tbody>
<tr>
<td>MH-14-215</td>
<td>Cell-Type Classification</td>
</tr>
<tr>
<td>MH-14-216</td>
<td>Novel Tools - Cells and Circuits</td>
</tr>
<tr>
<td>MH-14-217</td>
<td>Next Generation Human Imaging</td>
</tr>
<tr>
<td>NS-14-007</td>
<td>Large scale Recording &amp; Modulation – New Technologies</td>
</tr>
<tr>
<td>NS-14-008</td>
<td>Large scale Recording &amp; Modulation – Optimization</td>
</tr>
<tr>
<td>NS-14-009</td>
<td>Integrated Approaches to Understanding Circuit Function</td>
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**BRAIN Funding Opportunities in FY2014**

- **Brain Cell Types**
- **Tools for Circuit Diagrams**
- **Tech. to Monitor Neural Activity**
- **Precise Interventional Tools**
- **Theory and Data Analysis Tools**
- **Advance Human Neuroscience**
- **Integrate Approaches**

**Cell-Type Classification:** 10 awards in FY14

**Novel Tools – Cells and Circuits:** 10 awards in FY14

**Next Generation Human Imaging:** 9 awards in FY14

**Large-scale Recording & Modulation (2 RFAs):** 19 awards in FY14

**Integrating Approaches to Understand Circuit Function:** 10 awards in FY14
Funding Opportunities in FY15

- Reissued FOAs include:

<table>
<thead>
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<tr>
<td>MH-15-200</td>
<td><strong>Next Generation Human Imaging</strong></td>
</tr>
<tr>
<td>NS-15-003</td>
<td>Large scale Recording &amp; Modulation – New Technologies</td>
</tr>
<tr>
<td>NS-15-004</td>
<td>Large scale Recording &amp; Modulation – Optimization</td>
</tr>
<tr>
<td>NS-15-005</td>
<td>Integrated Approaches to Understanding Circuit Function</td>
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- The cell census FOA was not reissued
Funding Opportunities in FY15

- $38M in new funds
- New FOAs included:

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<tr>
<td>MH-15-215</td>
<td>Short Courses in Computational Neuroscience (R25)</td>
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<tr>
<td>MH-15-220</td>
<td>Short Courses in Research Tools and Methods (R25)</td>
</tr>
<tr>
<td>PAR-15-090</td>
<td>Development, Optimization, and Validation of Novel Tools and Technologies for Neuroscience Research (STTR)</td>
</tr>
<tr>
<td>PAR-15-091</td>
<td>Development, Optimization, and Validation of Novel Tools and Technologies for Neuroscience Research (SBIR)</td>
</tr>
<tr>
<td>RFA-EY-15-001</td>
<td>New Concepts and Early-Stage Research for Large Scale Recording (R21)</td>
</tr>
<tr>
<td>RFA-NS-15-008</td>
<td>Next Generation Invasive Devices for Recording and Modulation in the Human CNS (UH3)</td>
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• In FY16, we expect to spend at least $150M on new and existing BRAIN awards.
• A total of 14 new program announcements were released.
• 7 of the 14 announcements were new, and 2 of those announcements will be of special interest to quantitative imagers.
Funding Opportunities in FY16

- **RFA-EB-15-006**: Theories, Models and Methods for Analysis of Complex Data from the BRAIN (R01)

- **RFA-MH-16-750**: Foundations of Non-Invasive Functional Human Brain Imaging and Recording – Bridging Scales and Modalities (R01)
BRAIN Imaging Awards – Next Gen Devices – FY14

- Julie Brefczynski-Lewis (West Virginia) – Wearable PET Brain Imager
- Wei Chen (Minnesota) – Ultra-high Dielectric Constant Materials
- Bob Desimone (MIT) – Vascular Interfaces for Brain Imaging and Stimulation
- David Feinberg (Berkeley) – Microscale Cortical Imaging
- Michael Garwood (Berkeley) – Portable MRI
- Allen Song (Duke) – Neuro-Electro-Magnetic Oscillations
- Doris Tsao (Cal Tech) – Ultrasonic Neuromodulation
BRAIN Imaging Awards – Next Gen Devices – FY15

• Peter Basser (NIH) – In vivo Brain Network Latency Mapping

• Jeff Bulte (Kennedy Krieger) – Nanoparticles to localize the source of EEG signals

• Charles Caskey (Vanderbilt) – Ultrasound neuromodulation

• Alan Jasanoff (MIT) – Functional Molecular Neuroimaging using Vasoactive Probes

• Yoshio Okada (Children’s Hospital) – sonoelectric tomography (SET), to tag specific locations in the brain using ultrasound

• Russell Witte (Arizona) - 4D Acoustoelectric Brain Imaging
Next Generation Devices – FY17

• Each of the FY 14 and FY15 awards were for three years to build teams and to do preliminary work toward building next generation imaging devices.

• We have received concept clearance for a second phase of the program to allow teams (not only the funded awardees) to actually build next generation imaging devices.
New and Ongoing International Partnerships

Goals:

• Strengthen and develop health research cooperation

• Develop a coordinated program to foster collaborative research in areas of mutual interest
  • Jointly support research projects involving Danish and U.S. scientists; exchange of scientific information

• Similar MOU signed as with ongoing partnerships between NIH and research organizations like Brain Canada and Australia’s National Health & Medical Research Council
BRAIN Neuroethics

November 2014 NIH workshop: *Ethical Issues in Neuroscience Research*

- Recommended priority empirical neuroethics research areas for NIH to consider funding

**BRAIN Neuroethics Workgroup**

- A consultative ethics group to work with BRAIN leadership and BRAIN investigators
- Services:
  - Recommend overall approaches for how the BRAIN Initiative should handle issues and problems involving ethics
  - Provide ethics consultations
  - Advise NIH on neuroethics questions important for BRAIN that could be answered through focused empirical research
• The first few years of the BRAIN Initiative were focused on tools and techniques.
• It is now clear that in one or two areas (cell census and likely invasive technologies) the new tools are ready to be applied to generating significant data.
• The awards in some of the FY16 imaging FOAs may also fall into this category in a few years.
• We are talking about setting up centers with the following structure
• One major purpose of the center would be to work with a defined research community to define standards. Those standards would then serve as the basis for data aggregated by the centers.
• The areas where we are considering informatics centers seem ready to do this.
• The second major purpose of the center would be to work with other BRAIN Initiative Informatics Centers and other parties to find ways to enhance searches across multiple databases and to work on data discoverability in the funded centers.

• An aspirational goal for the centers would be to work on ways to integrate data across scales and modalities.
BRAIN Initiative Data

• Landscape of Data Repositories

Data repository with a specific focus (PDB, Human Connectome, ADNI)

“Long tail” archive. Heterogeneous data, but data have some quality (DRYAD, CRCNS, NDA). There may be no easy way to search across datasets, but it is possible to attempt to integrate multiple data types.

(buckets of data)

BRAIN Initiative – set up specific data archives in a particular research area (cell census, invasive data). Allow each repository to aggregate data in their area (and hopefully to define standards). Require that each repository work to integrate their data sets with each other, as appropriate.
NIH...
Turning Discovery Into Health