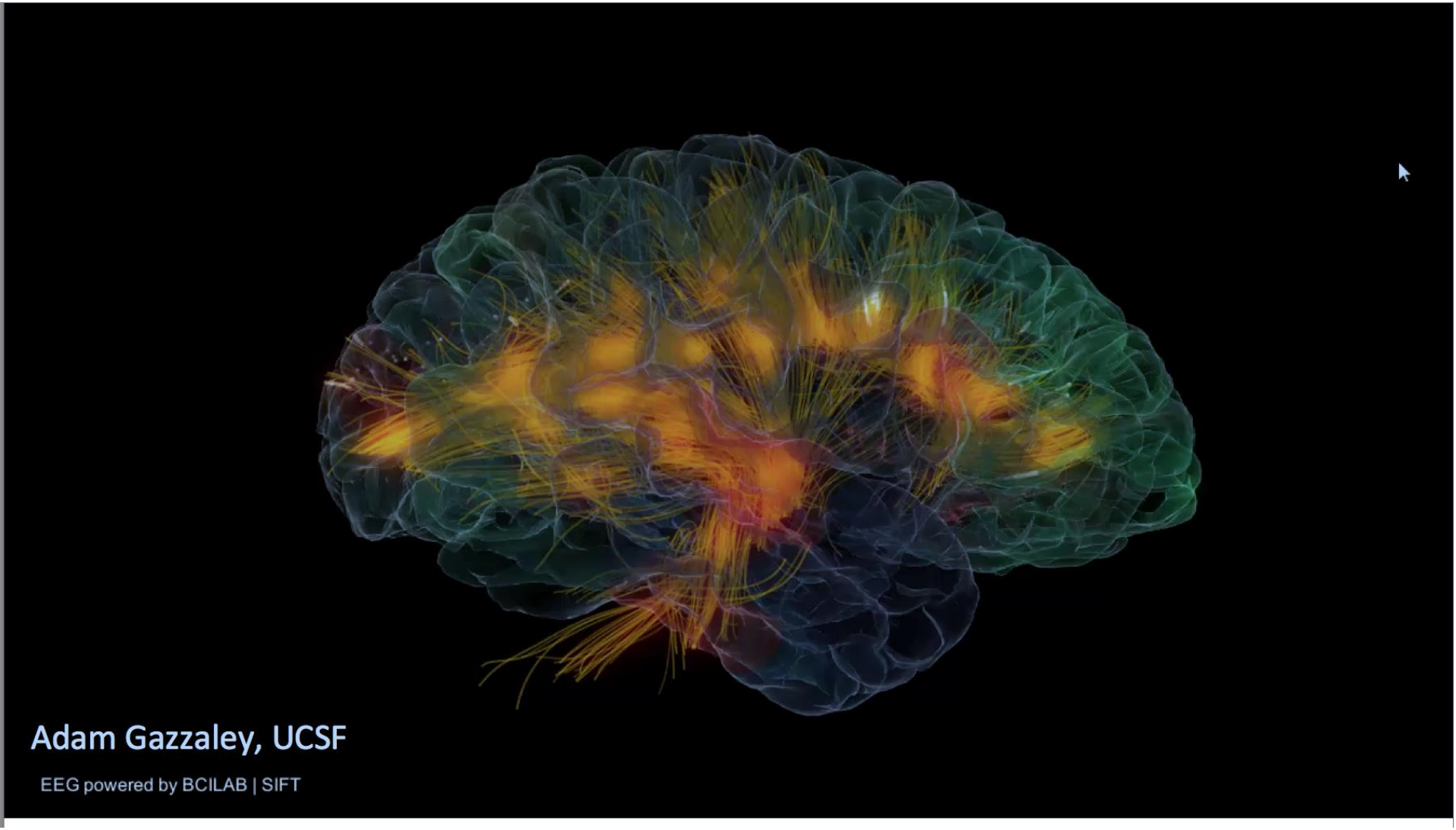
NIH and the BRAIN Initiative

Brain Research through Advancing Innovative Neurotechnologies

Walter Koroshetz, MD
Tom Insel, MD
December 17, 2014

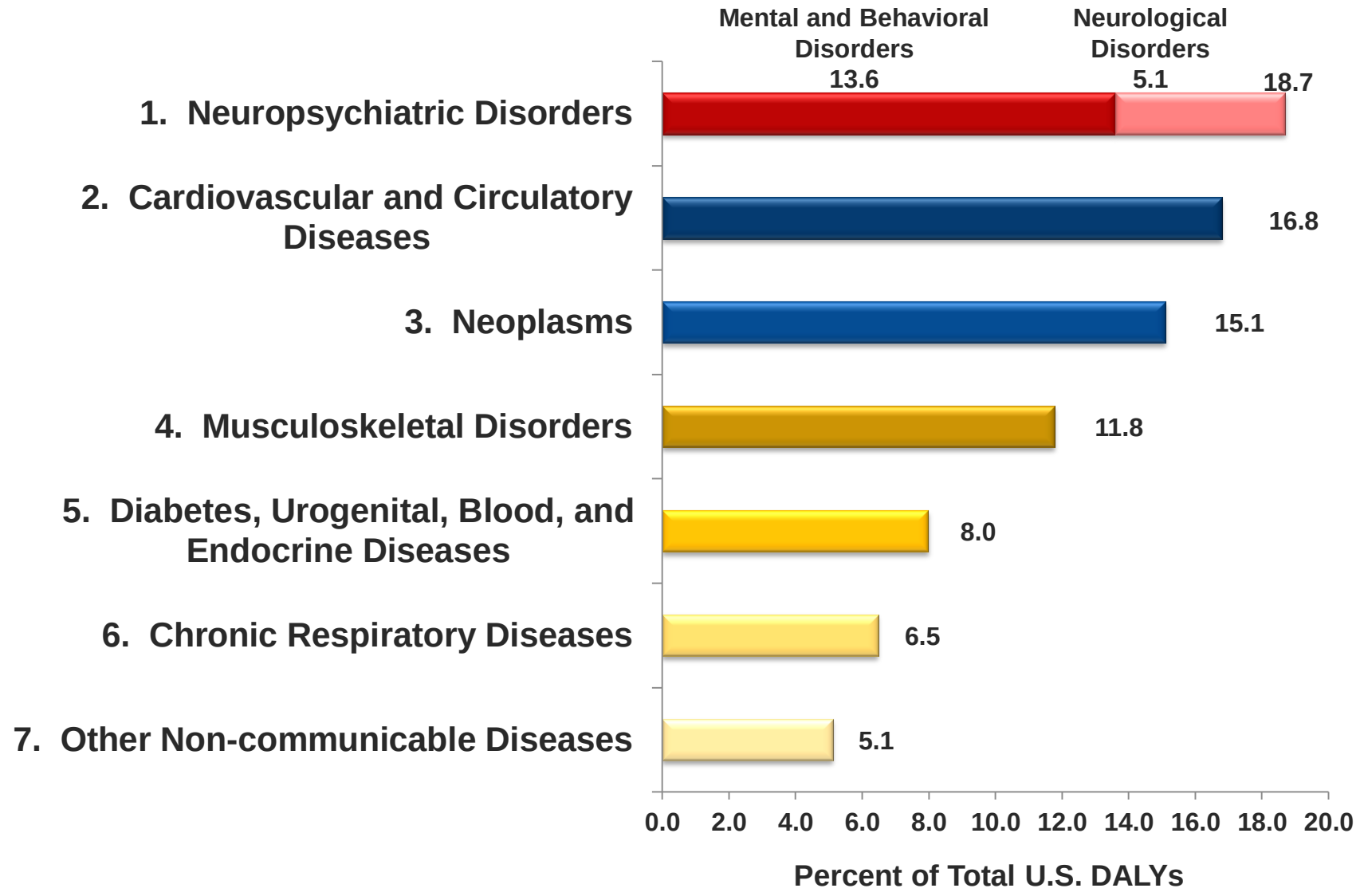
The Era of the Brain

The Problem: Mapping Activity at the Speed of Thought



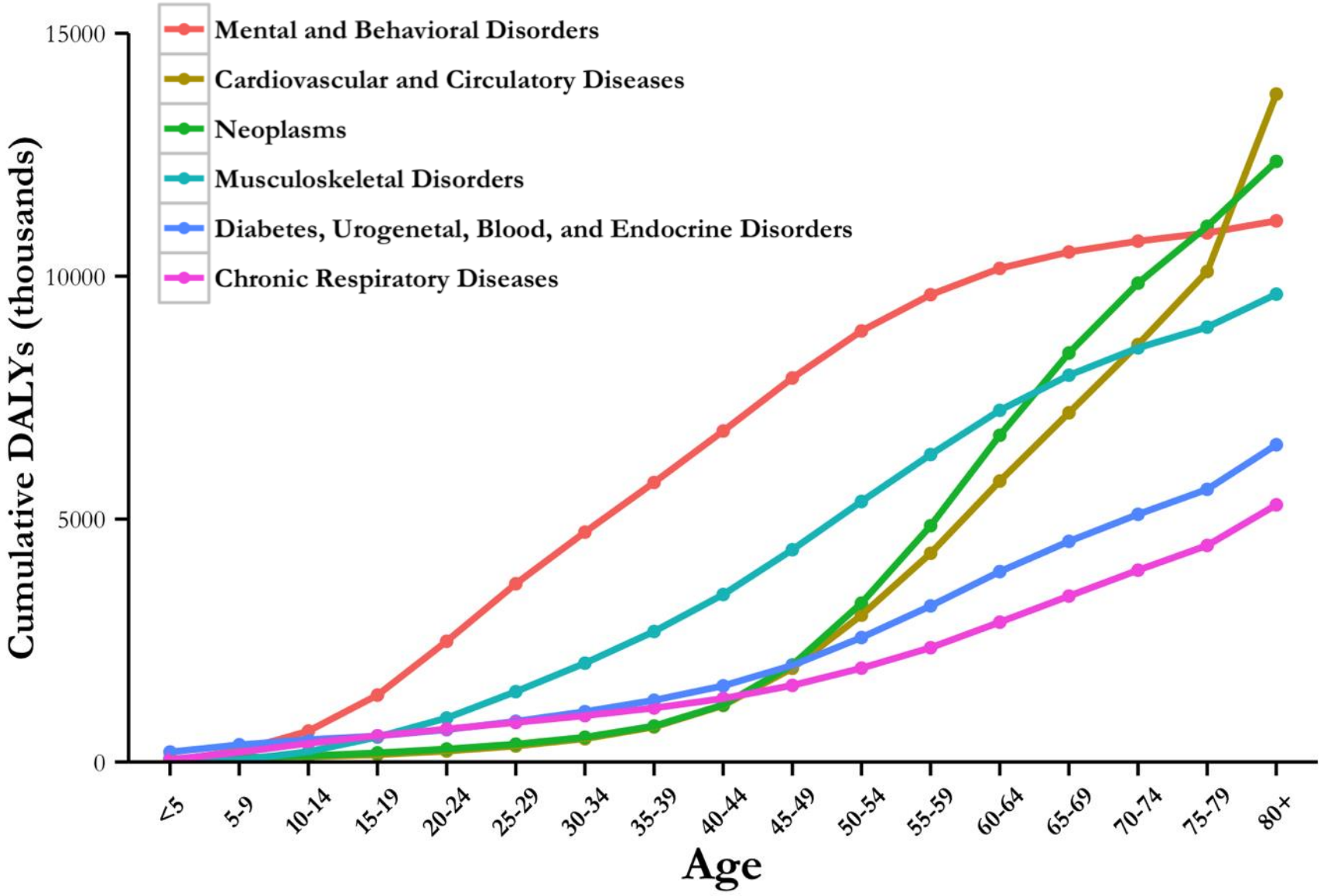
U.S. Burden of Diseases: 291 Diseases and Injuries

Leading Categories of DALYs 2010

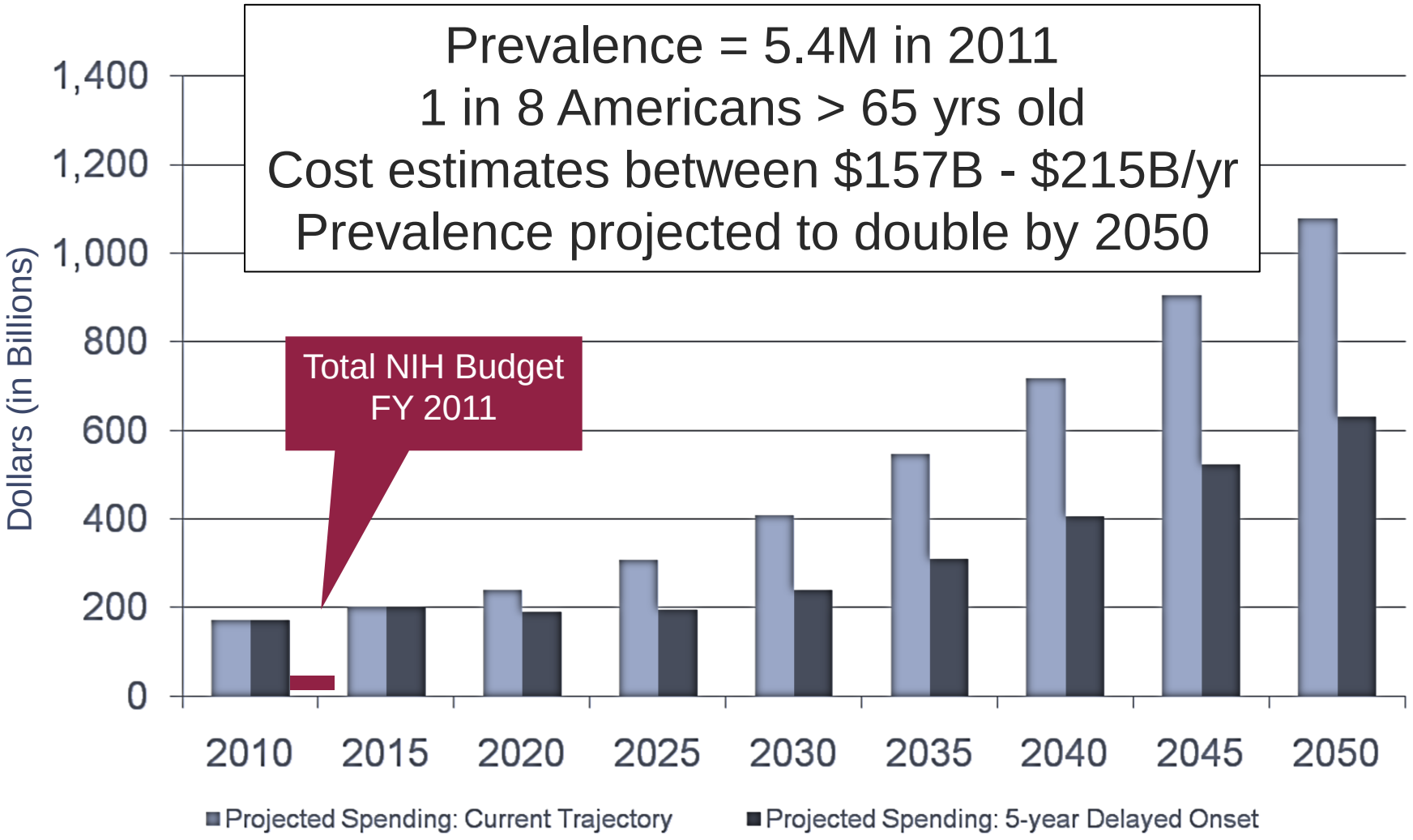


US Burden of Disease Collaborators, *JAMA*, 2013.

The Most Disabling Disorders Before Age 50

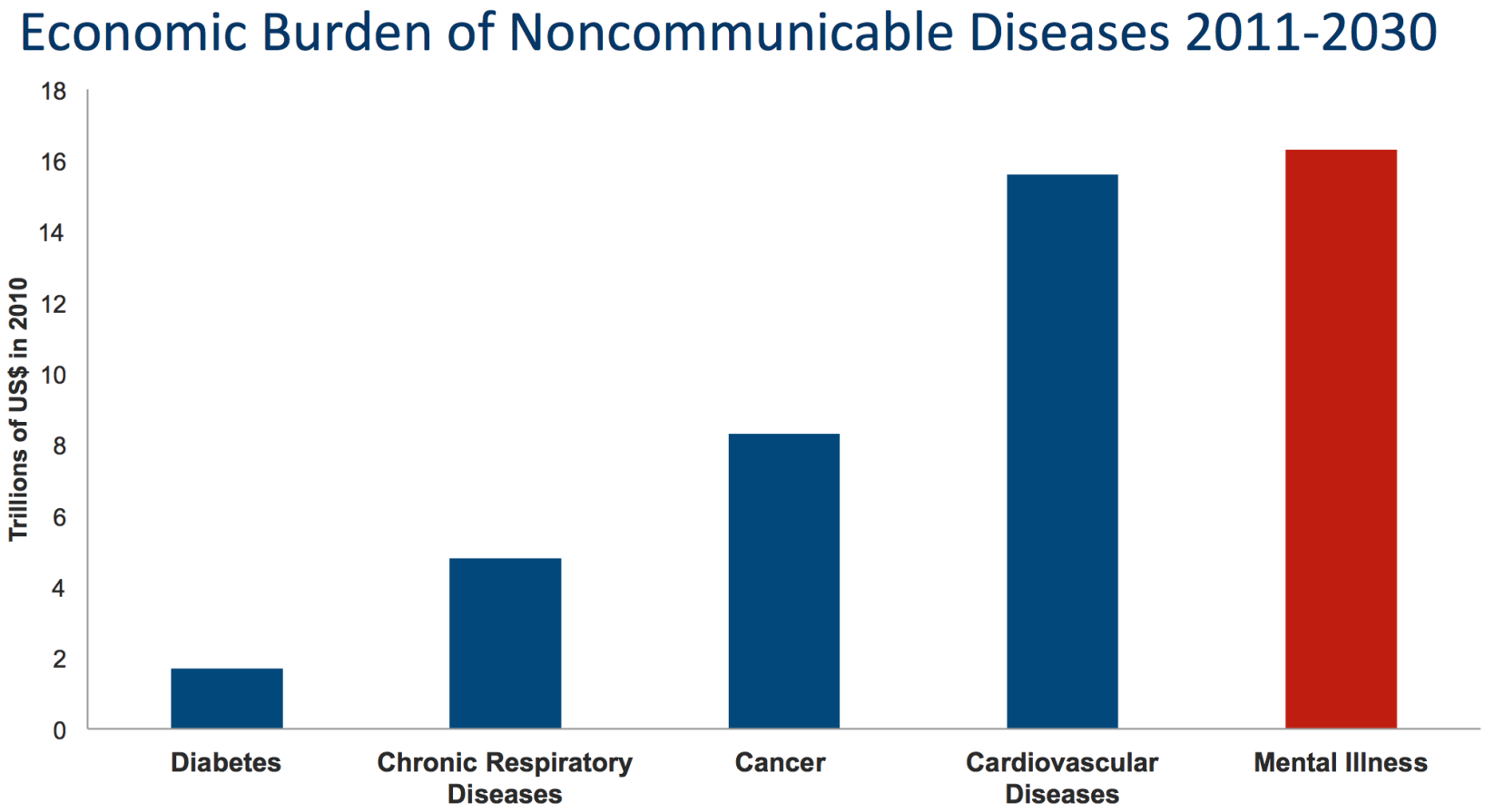


Burden of Alzheimer's Disease Over Time:
Projected Spending



Source: Alzheimer's Association, *Changing the Trajectory of Alzheimer's Disease: A National Imperative* (2010).

The Most Costly Conditions



US Annual Costs > $300B for SMI (Insel, AJP, 2008)

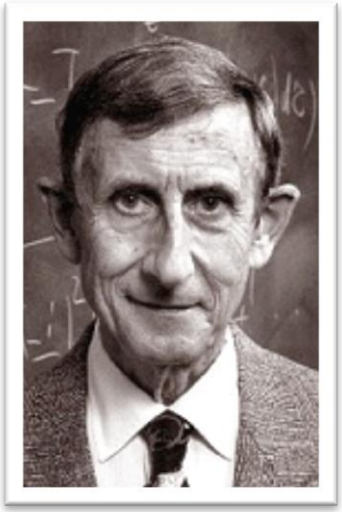
Source: The Global Economic Burden of Noncommunicable Diseases. WEF, 2011

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.**

Where Does Scientific Progress Come From?

"**New directions in science are launched by new tools much more often than by new concepts.** The effect of a concept-driven revolution is to explain old things in new ways. The effect of a tool-driven revolution is to discover new things that have to be explained."



Freeman Dyson (1997) *Imagined Worlds*
Harvard University Press, Cambridge, MA

“The Next Great American Project”

“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

“a public and private effort”

+

Private Investments

What is the Right Scale?

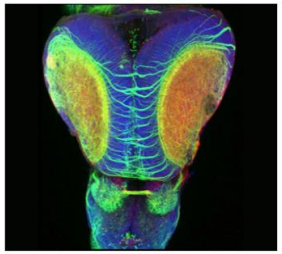
10^2

worm

10^5

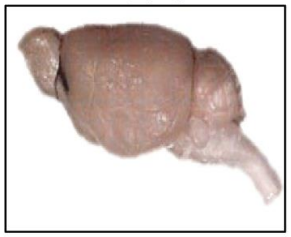
fly

10^6



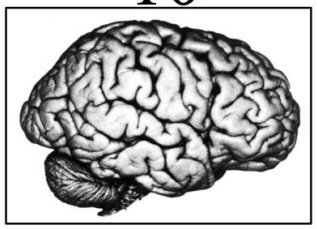
fish

10^7

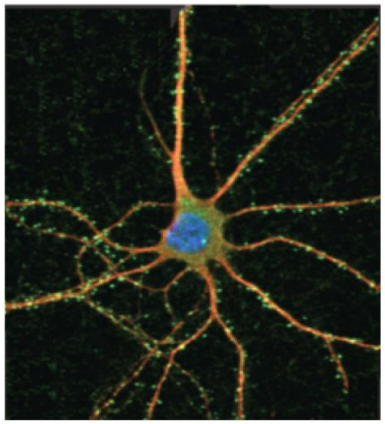


mouse

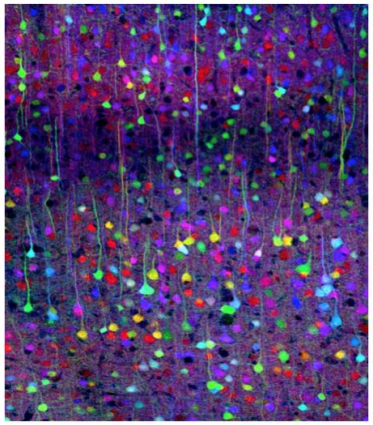
10^{11}



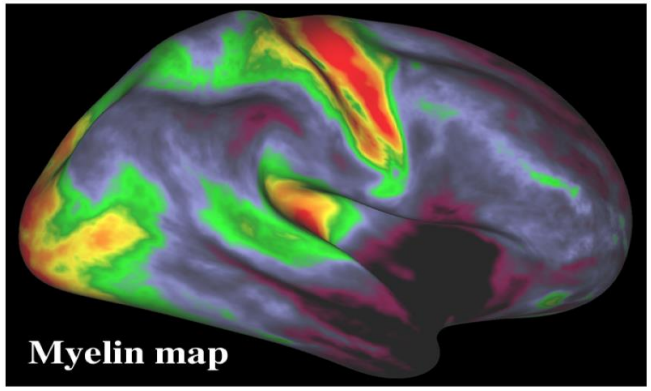
primate



Synapses
10^{14}



Neurons
10^{11}



Brain
1/person

Static → Dynamic

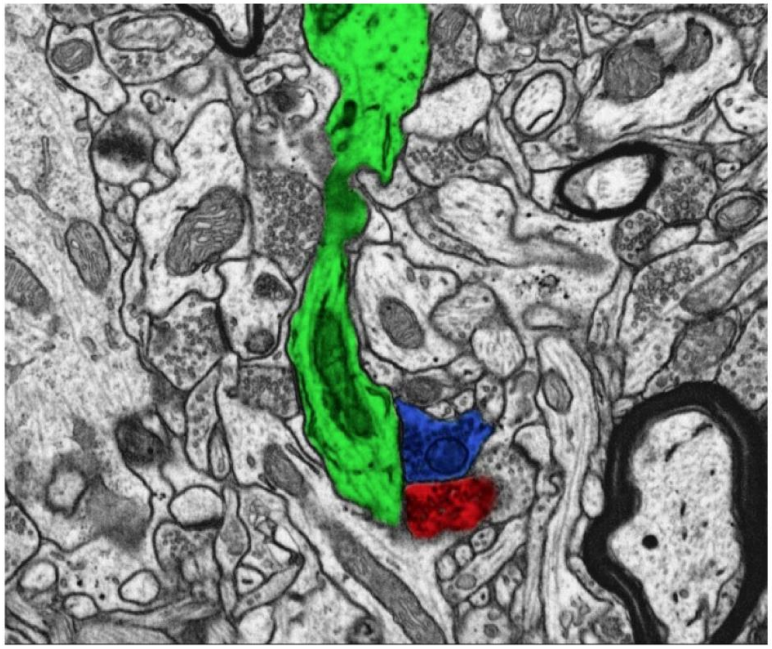
What Connectome Matters Most?

Macro-connectome
(whole-brain, long-distance)

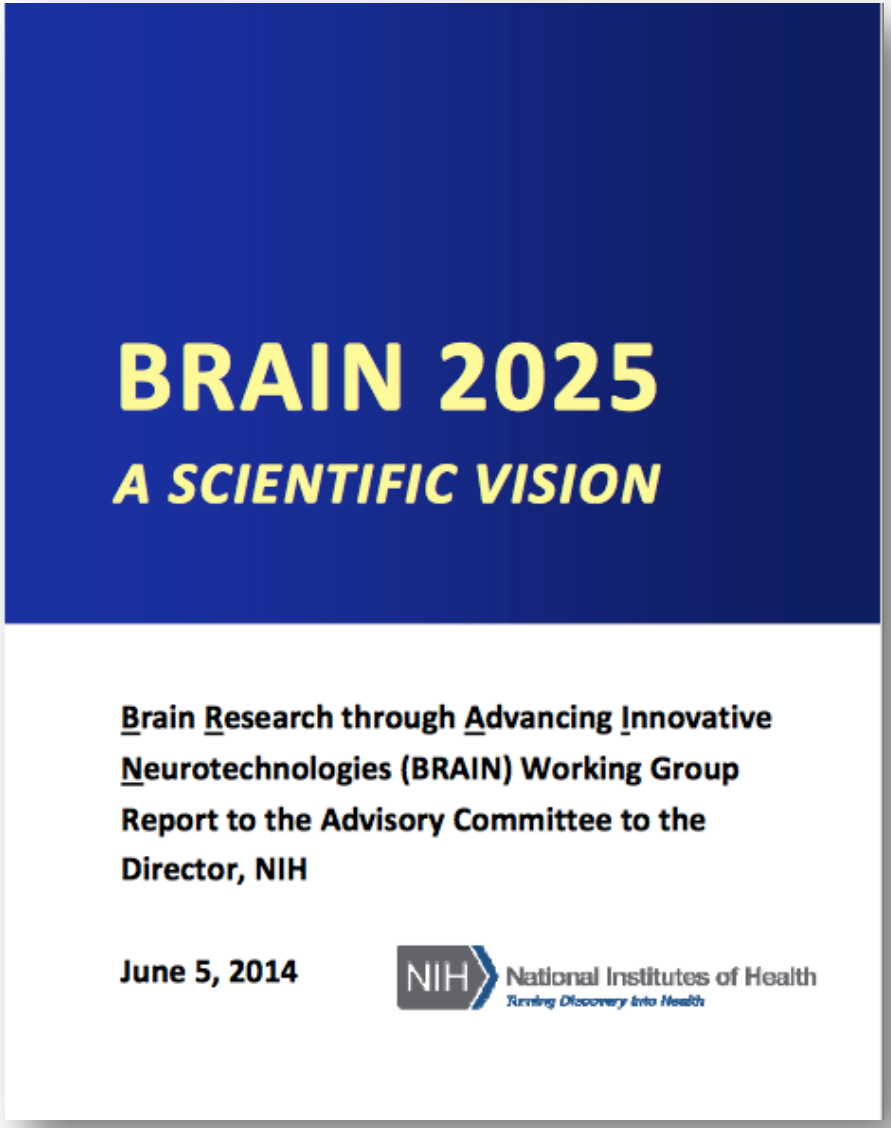
Resolution: 1 – 2 mm ‘voxels’

Micro-connectome
(every synapse, neuron, dendrite)

Volume reconstructed: <1 mm

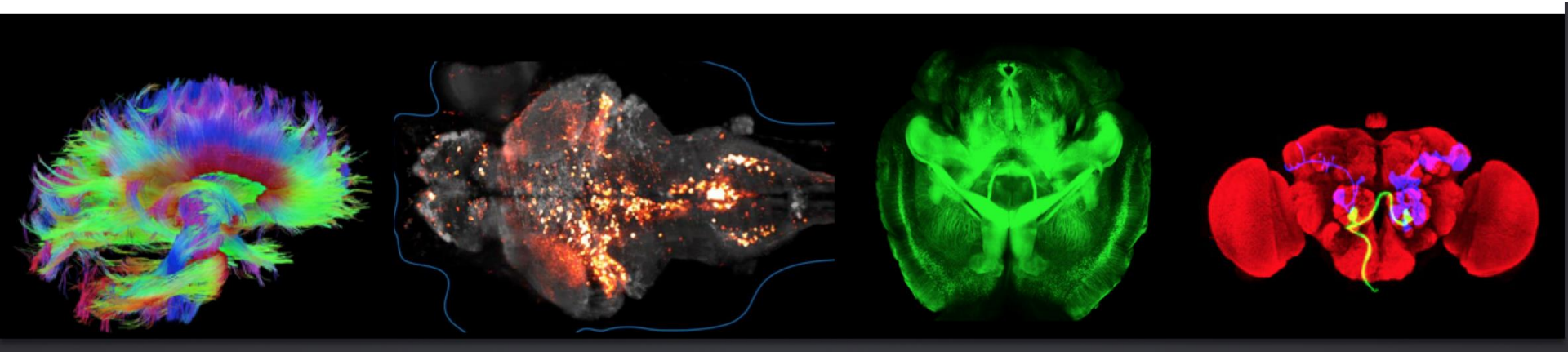


NIH BRAIN Workgroup Final Report



A Focus on Circuits and Networks

- Map the circuits
- Measure the fluctuating electrical and chemical patterns within circuits
- Understand how all of this helps generate our unique thoughts and actions



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.

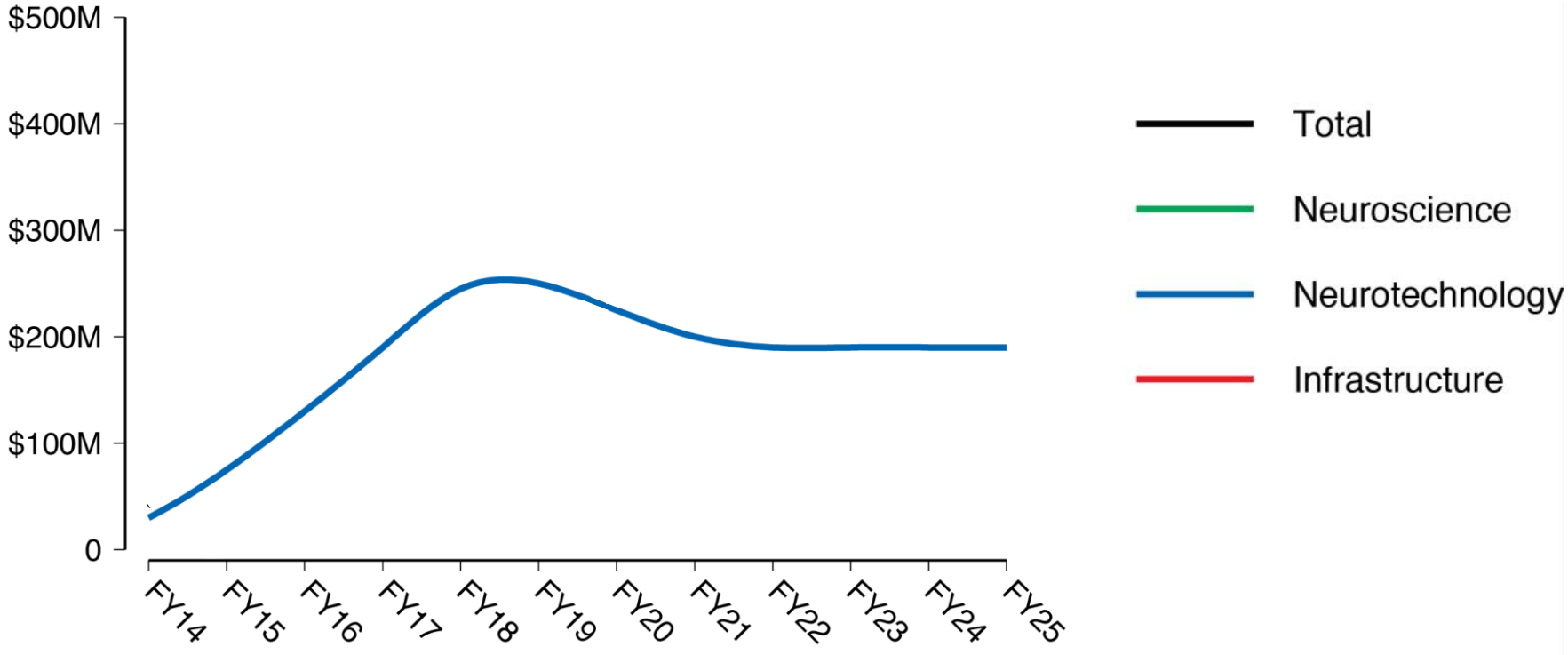
Seven High Priority Research Areas

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.

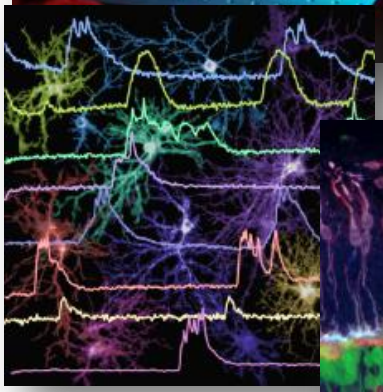
Estimated Budget

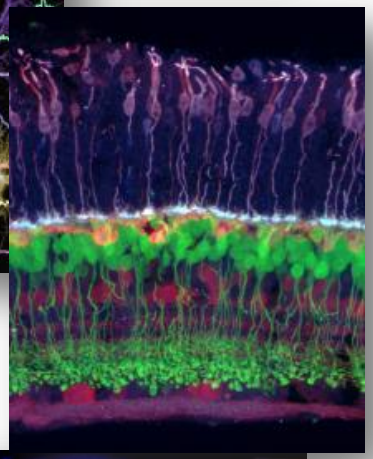


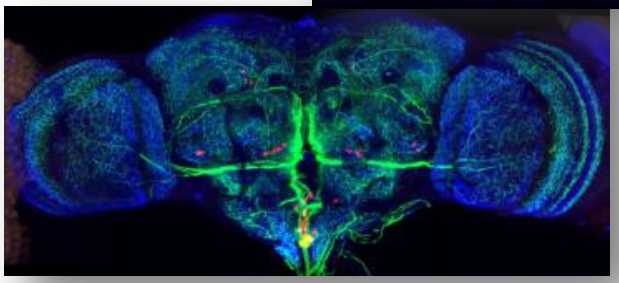
Ramp up to $400M/yr by FY 2018 ⟹ Plateau at $500M/yr by FY2021

Total investment of $4.5B by FY 2025

Funding in FY14



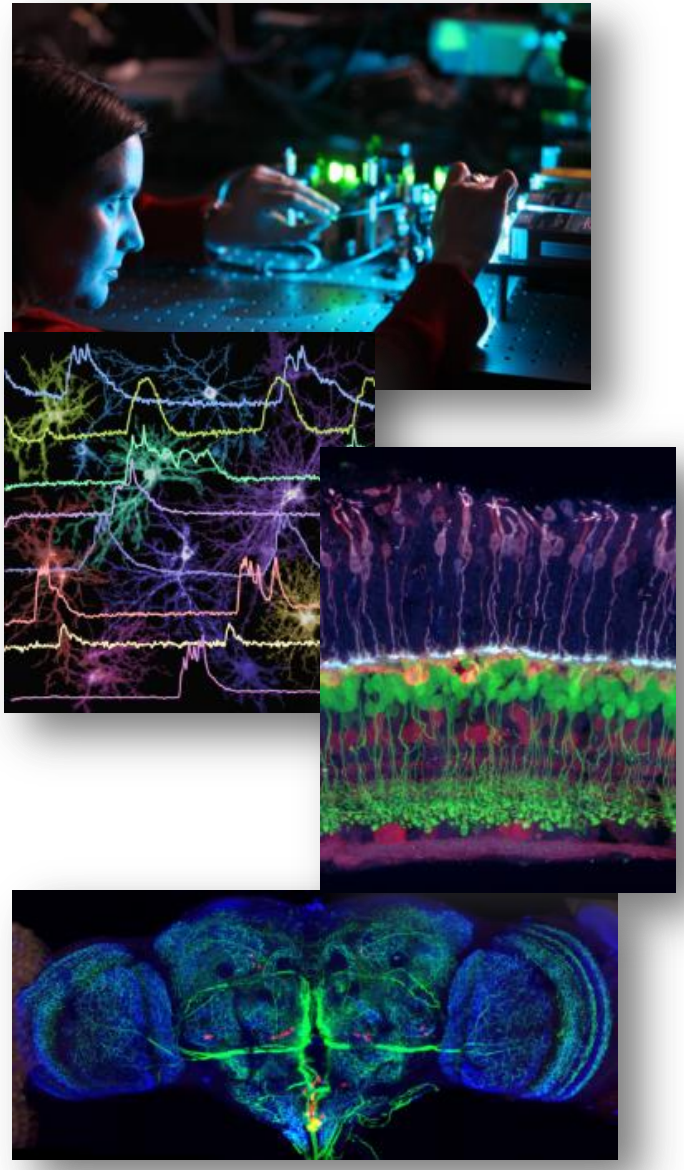




- $46M invested in 58 projects across 6 RFAs
- > 100 investigators in 15 states and 3 countries

RFA	Topic
MH-14-215	**Cell-Type Classification**
MH-14-216	**Novel Tools - Cells and Circuits**
MH-14-217	**Next Generation Human Imaging**
NS-14-007	**Large scale Recording & Modulation – New Technologies**
NS-14-008	**Large scale Recording & Modulation – Optimization**
NS-14-009	**Integrated Approaches to Understanding Circuit Function**

Funding in FY15

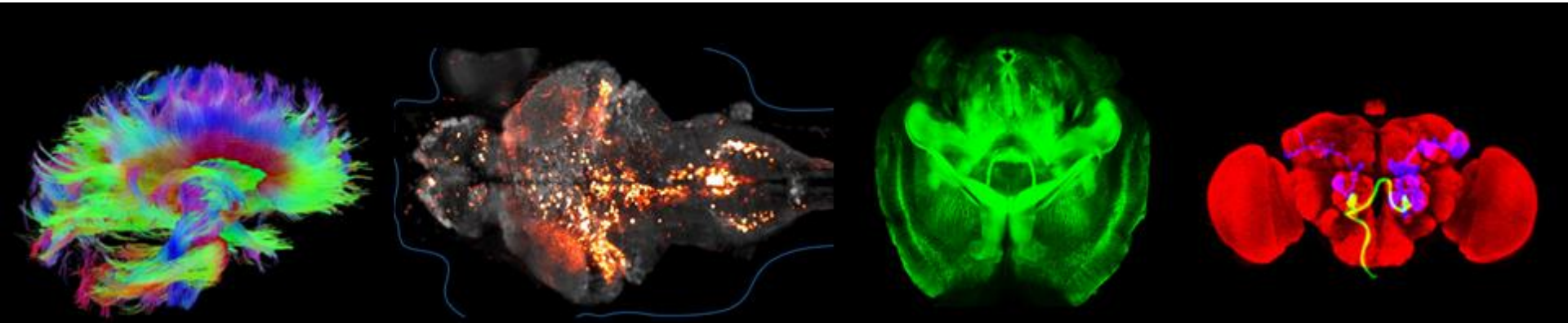


- $25M in new funds
- Plans for short courses and projects in human neuroscience
- Reissue:

RFA	Topic
MH-15-225	Novel Tools - Cells and Circuits
MH-15-200	Next Generation Human Imaging
NS-15-003	Large scale Recording & Modulation – New Technologies
NS-15-004	Large scale Recording & Modulation – Optimization
NS-15-005	Integrated Approaches to Understanding Circuit Function

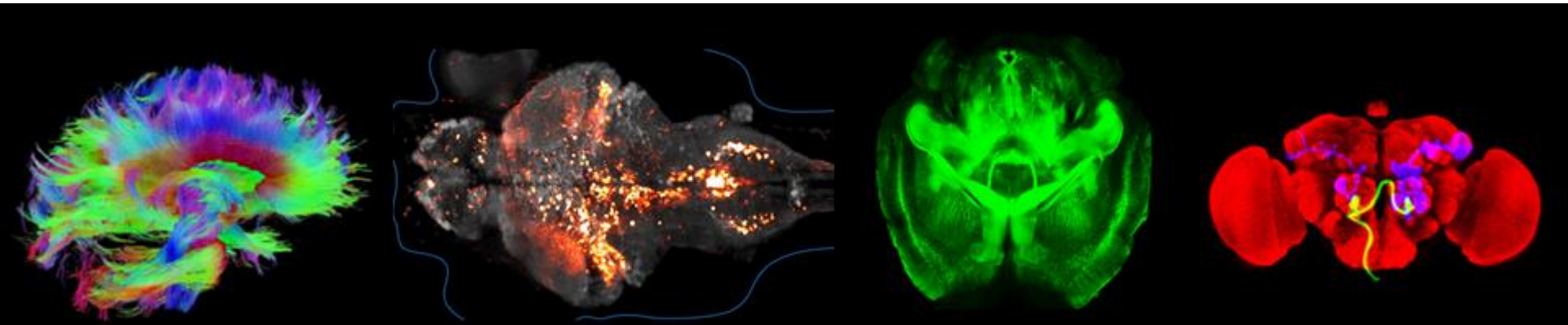
Example Deliverables: 5 Years

- **Census of neuronal and glial cell types** in animal models ("parts list") plus intellectual framework for cell classification
- Methods to **map neural connections** in human and animal brains with improved speed, cost, resolution, throughput
- Technologies for **high density electrical and optical recording** of neural activity in local and distributed circuits
- Technologies **for perturbing electrical and biochemical activity** in defined sets of neurons, at cellular resolution, **in real time**
- Integrated teams of clinicians, scientists, engineers, ethicists, regulatory specialists for **advancing human subjects research**



Example Deliverables: 10 Years

- **Extension of cell type census to humans;** tools to deliver genes, proteins, drugs to defined cell subpopulations
- **Integrated systems for combining measurements** of brain activity dynamics with perturbation, behavior, cell type information, connectivity maps, theory
- **Greatly improved, minimally invasive** technologies for monitoring and modulating human brain activity
- **Systematic theories** of how information is encoded in the chemical and electrical activity of the brain

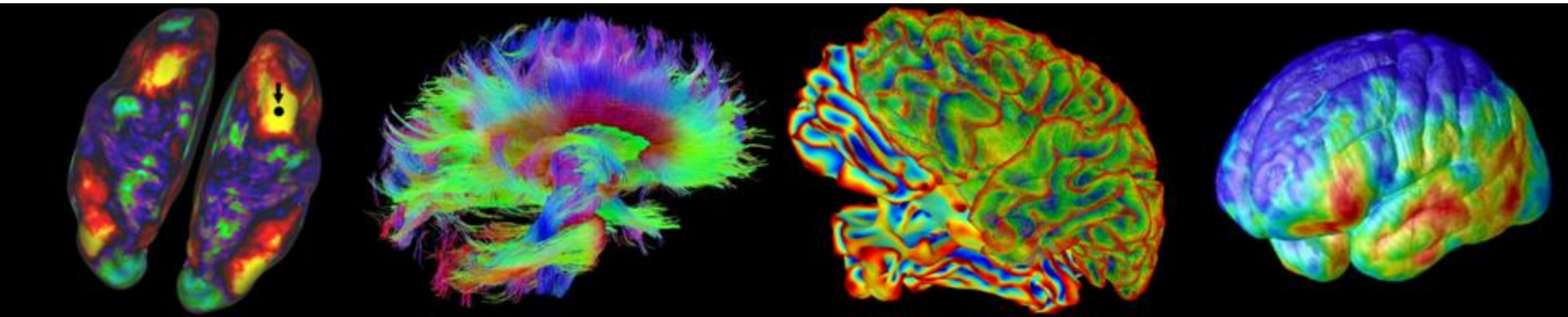


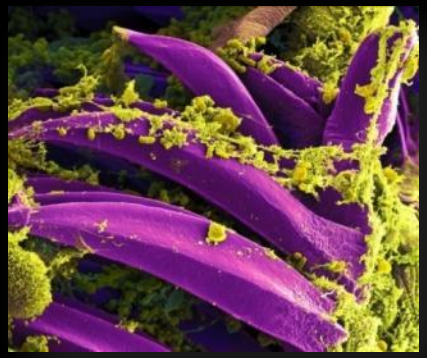
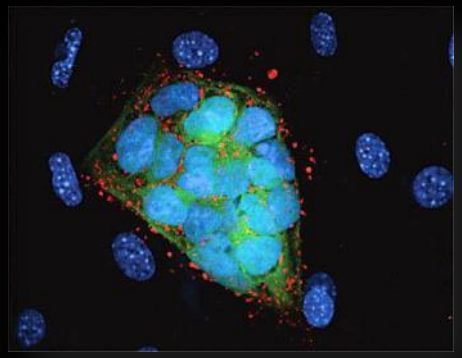
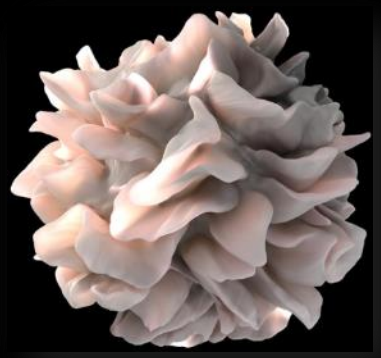
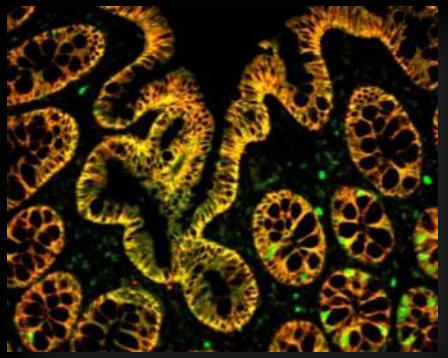
Summary

Brain disorders -- a leading source of disease burden and cost in the U.S.

Recent breakthroughs are transforming how we study brain structure and function.

The BRAIN initiative builds on this recent progress to create tools that will accelerate discovery and build the foundation we need to reduce the burden of brain disorders.



NIH…

Turning Discovery Into Health