BRAIN 2025: A scientific vision

Final report of the ACD BRAIN working group

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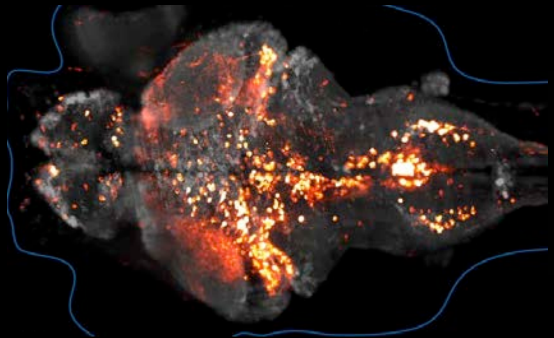
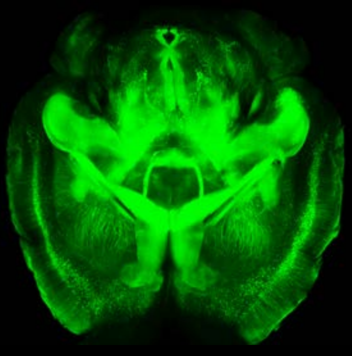
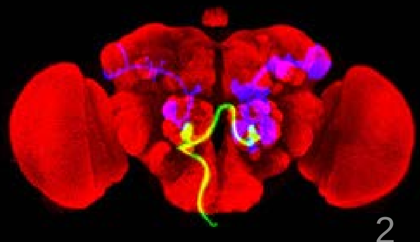
OUR CHARGE

Accelerate the development and application of ***innovative technologies*** to construct a ***dynamic picture*** of brain function that ***integrates neuronal and circuit activity over time and space.***

Build on neuroscience, genetics, physics, engineering, informatics, nanoscience, chemistry, mathematics, to catalyze an interdisciplinary effort of unprecedented scope.







BRAIN INITIATIVE WORKING GROUP

Cori Bargmann and Bill Newsome *(co-chairs)*

David Anderson, Caltech
Emery Brown, MIT & MGH
Karl Deisseroth, Stanford
John Donoghue, Brown
Peter MacLeish, Morehouse
Eve Marder, Brandeis
Richard Normann, Utah
Joshua Sanes, Harvard
Mark Schnitzer, Stanford
Terry Sejnowski, Salk
David Tank, Princeton
Roger Tsien, UCSD
Kamil Ugurbil, Minnesota

Ex Officio Members

Kathy Hudson, NIH
Geoffrey Ling, DARPA
John Wingfield, NSF
Carlos Peña, FDA

Executive Secretary

Lyric Jorgenson, NIH

OUR PROCESS

Spring/Summer 2013

- Reviewed neuroscience landscape
- 4 workshops, 48 expert participants, public commentary
- Presented interim report with FY2014 research priorities

Autumn/Winter 2013

Conversations, presentations, feedback:

- Society for Neuroscience leadership and general membership
- Presidents of major clinical neuroscience professional societies
- NAS neuroscience members, NAS general membership, AAAS
- Public and private partners (NSF, DARPA, HHMI, AIBS, Kavli)

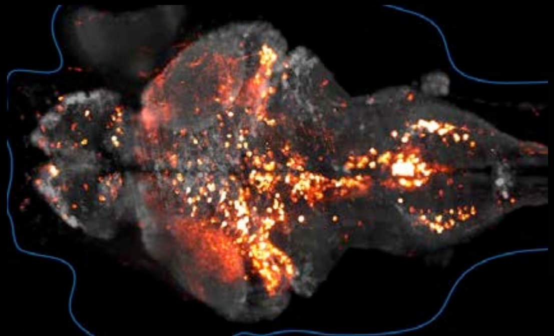
Spring 2014

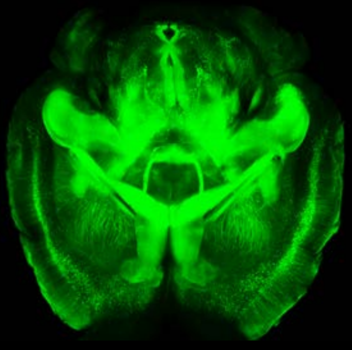
Deliverables, milestones, implementation, budgets

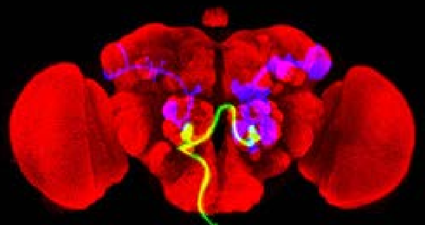
BRAIN 2025, A Scientific Vision

A FOCUS ON CIRCUITS AND NETWORKS

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.





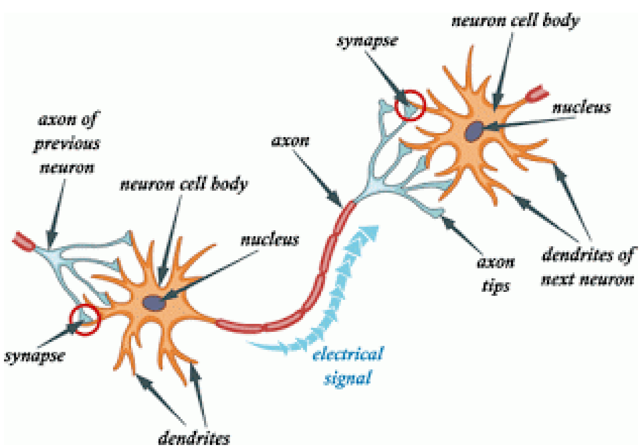


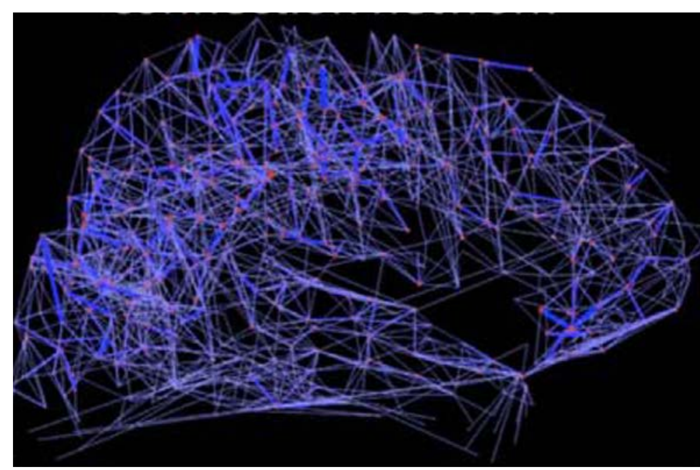
A FOCUS ON CIRCUITS AND NETWORKS

60 years	30 years	20 years
of single-neuron recordings	of molecular biology	of brain imaging (fMRI)

What is missing:

Cognition, emotion, memory, action are generated by circuits and networks of thousands to millions of interconnected neurons.
How do they work?





WHY NOW?

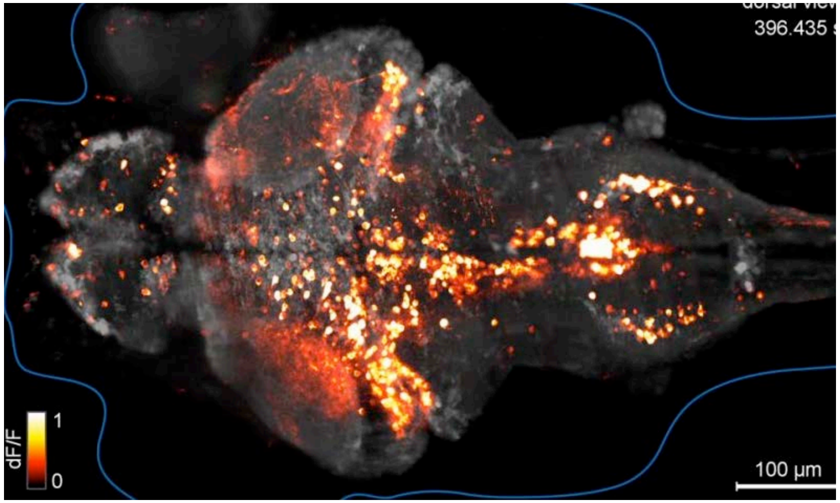
Technologies are expanding the range of the possible:

Recording technologies

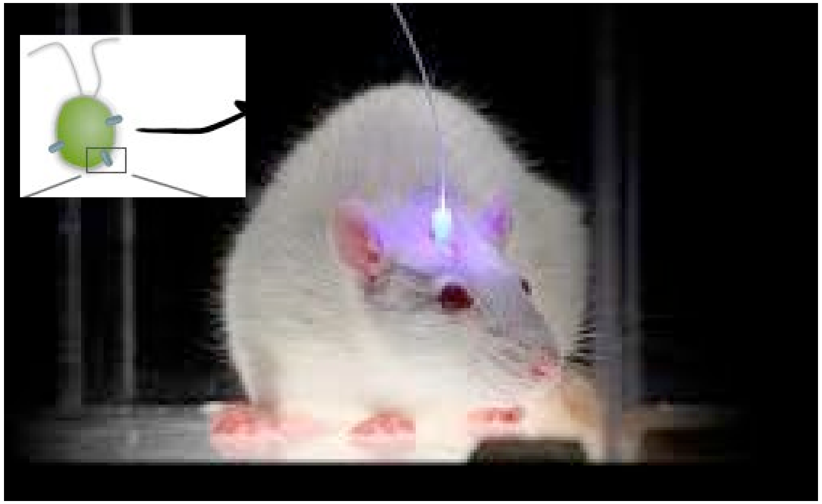
Microscopy and optics

Genetics

Computer science



Whole-brain optical recordings

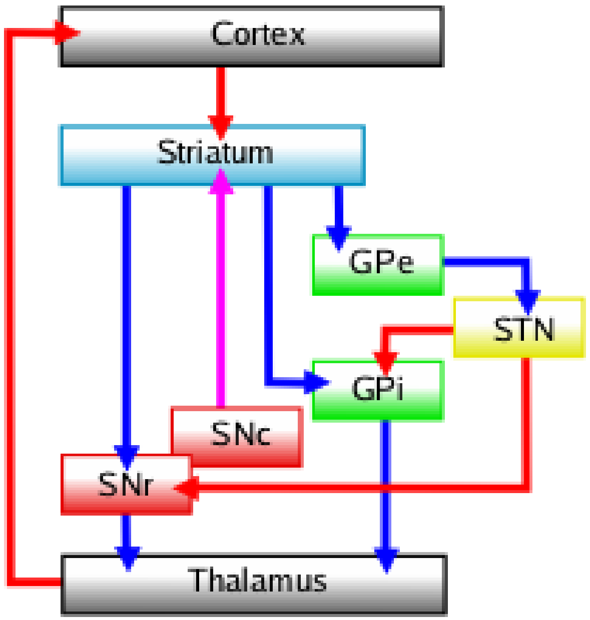


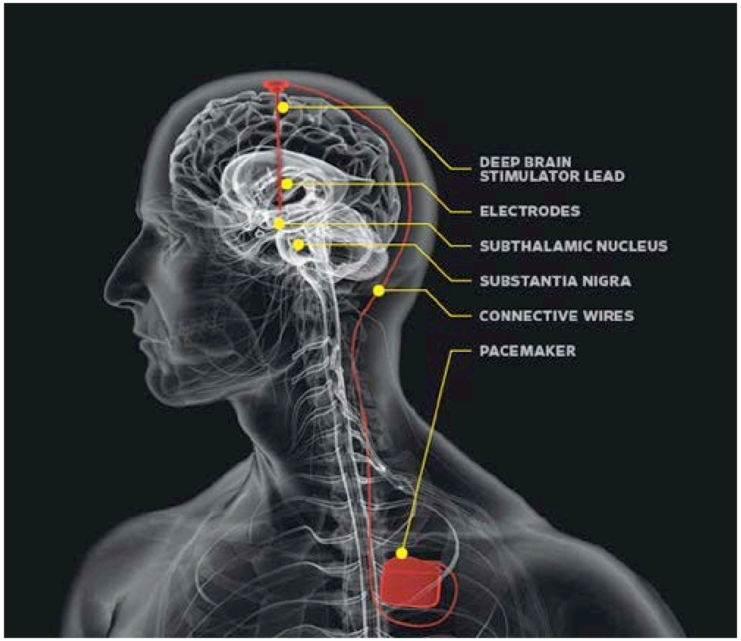
Optogenetics

THE PROMISE OF CIRCUIT-BASED INTERVENTIONS

Circuit-based interventions have great potential,
but first we must identify the circuits

Deep Brain Stimulation: A circuit-based treatment for Parkinson's Disease





THE SCIENTIFIC PLAN

FIRST FIVE YEARS	SECOND FIVE YEARS
Emphasize technology development	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.

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.

EXAMPLE DELIVERABLES, SHORT-TERM (5 years)

A census of neuronal and glial cell types in animal models (the “parts list”), and an intellectual framework for cell type classification.

Methods to map neural connections in human and animal brains with improved speed, cost, resolution and throughput.

New technologies for high density electrical and optical recording of neural activity in local and distributed neural circuits.

New technologies for perturbing electrical and biochemical activity in defined sets of neurons, at cellular resolution, in real time.

Integrated teams of clinicians, scientists, engineers, and ethical and regulatory specialists for advancing human subjects research.

EXAMPLE DELIVERABLES, LONG-TERM (10 yrs)

Extension of cell type census to humans. Tools to deliver genes, proteins, and drugs to defined neuronal and glial subpopulations.

Integrated systems for combining measurements of brain activity dynamics with perturbation, behavior, cell type information, connectivity maps, and theory.

New, 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.

OUTCOMES: VISION 2025 AND BEYOND

- Target specific human cell types to develop new therapies for neurological and psychiatric disorders.

- Discover circuit-level anatomical differences between healthy and disordered brains.

- Treat neurological and psychiatric disorders based on knowledge of each patient’s own circuitry and neural activity patterns.

- Discover general principles of neural coding, circuit dynamics and plasticity.

- Understand neural population dynamics associated with perception, learning, memory, emotion and action.

- Gain insight into the neural basis of human language, symbolic reasoning and consciousness.

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

NEEDED INFRASTRUCTURE

1. **Platforms for sharing data and data analysis tools**

   - Emphasis on accessibility, effective central maintenance
   - Partner with or learn from BD2K, AIBS, NIF, INCF, HCP

2. **Validate and disseminate new technology**

   - *Rigorous comparison of new technologies*
   - Iterative improvements to meet performance metrics

   - *Make new tools widely available*
   - *Pathway to production*
   - Practical training and courses
   - *Long-term: democratic access to complex technologies*

BUDGET DEVELOPMENT

Funding base of $40M in FY 2014 and $100M in FY 2015.

Project budgets FY 2016-2025.

FIRST FIVE YEARS

Emphasize technology development

SECOND FIVE YEARS

Emphasize discovery driven science

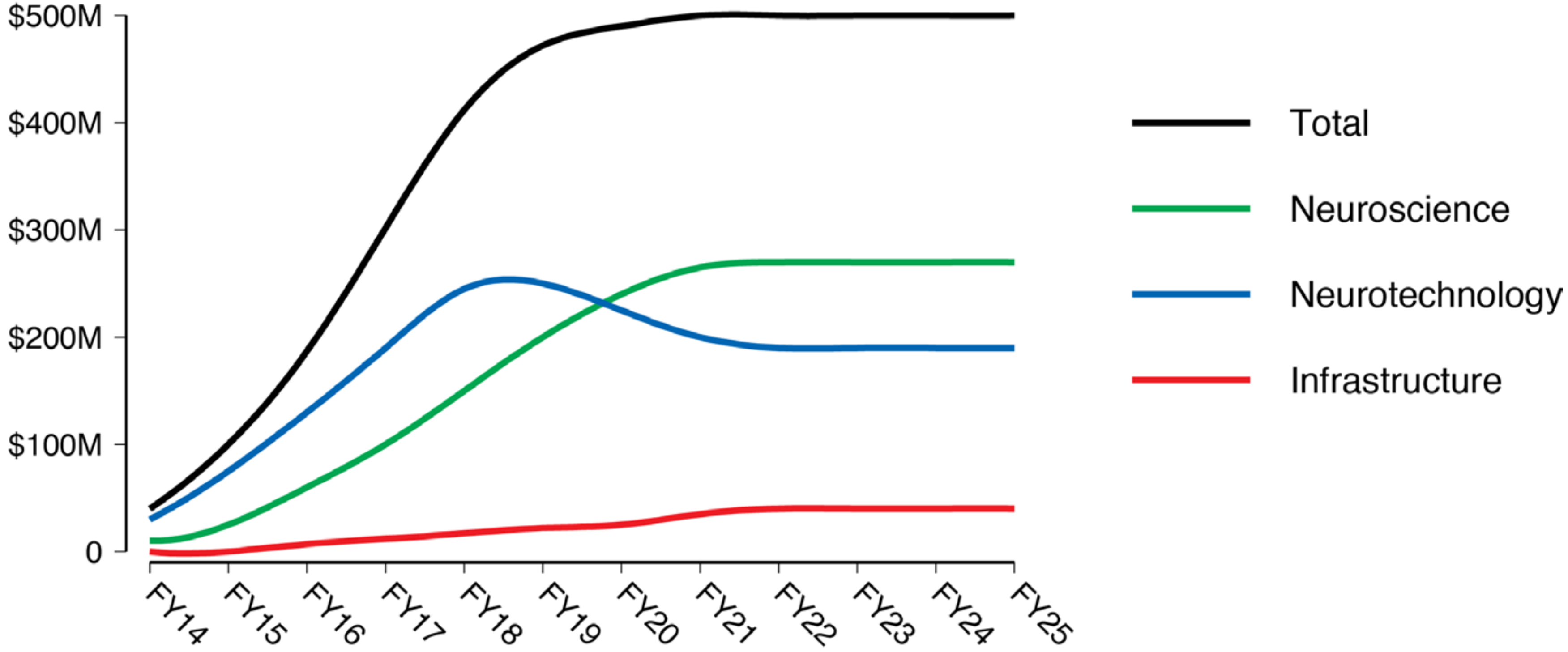
We considered:

What would it cost to implement individual goals?

What number and types of grants could be supported?

What do similar ongoing projects cost?

ESTIMATED BUDGET



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

Total investment of $4.5B by FY 2025

SOLVING FUNDAMENTAL PROBLEMS IN NEUROSCIENCE

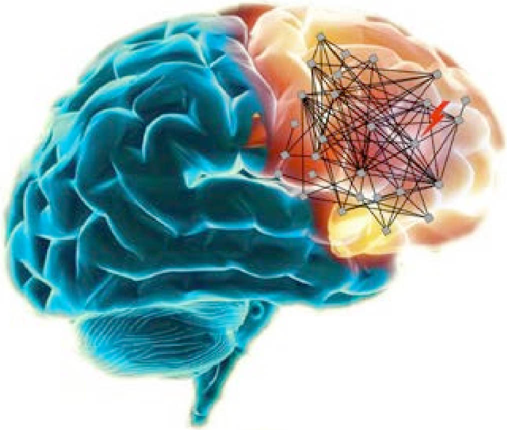
Perception

Emotion and Motivation

Cognition

Learning and Memory

Action



Discovering cellular diversity

Connectivity maps at multiple scales

Monitoring the brain in action

Demonstrating causality

Identifying fundamental principles

Advancing human neuroscience

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