Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative

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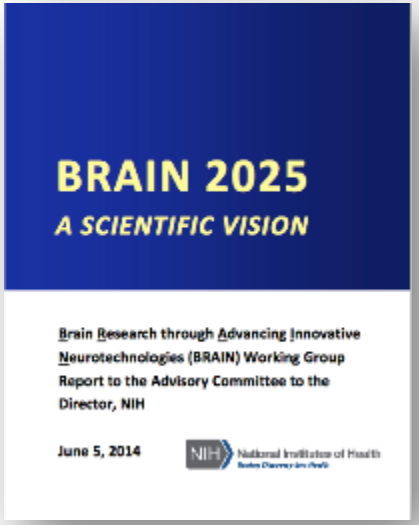
BRAIN Multi-Council Working Group
Co-Chairs

Foster Innovation: *Focus on Brain Circuits*



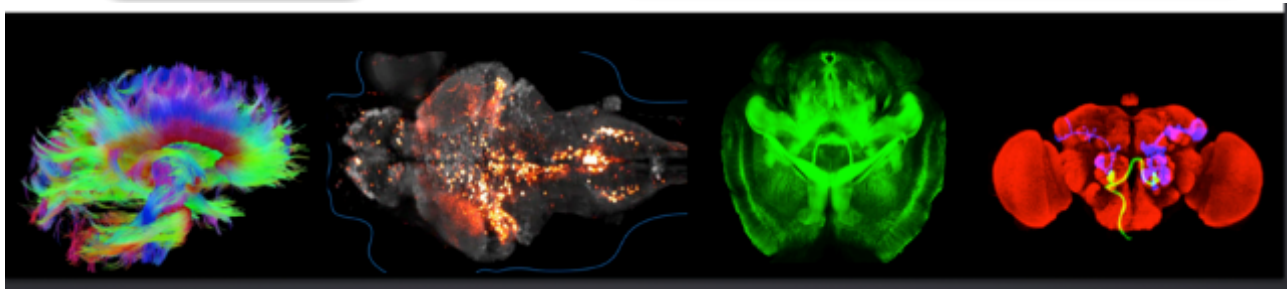
Goal: Elucidate circuit structure and function to understand:

- How the brain moves, plans, executes
- How to monitor/manipulate circuits for improved function
- That disordered brain circuits cause neuro/mental/substance abuse disorders

Long-term goal: Make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention

FIRST FIVE YEARS	SECOND FIVE YEARS
Emphasize technology development	Emphasize discovery driven science

Molecular/Structural Pathology → **Circuit Dysfunction** → **Neuro/Mental/Substance Abuse Functional Disability**



National Institutes of Health
Turning Discovery Into Health

Seven High Priority Research Areas

Brain Cell Types

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

Tools for Circuit Diagrams

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

Tech. to Monitor Neural Activity

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.

Precise Inter-ventional Tools

4. **Demonstrating causality:** Link brain activity to behavior with precise interventional tools that change neural circuit dynamics.

Seven High Priority Research Areas

Theory and Data Analysis Tools

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

Advance Human Neuro-science

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

Integrate Approaches

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.

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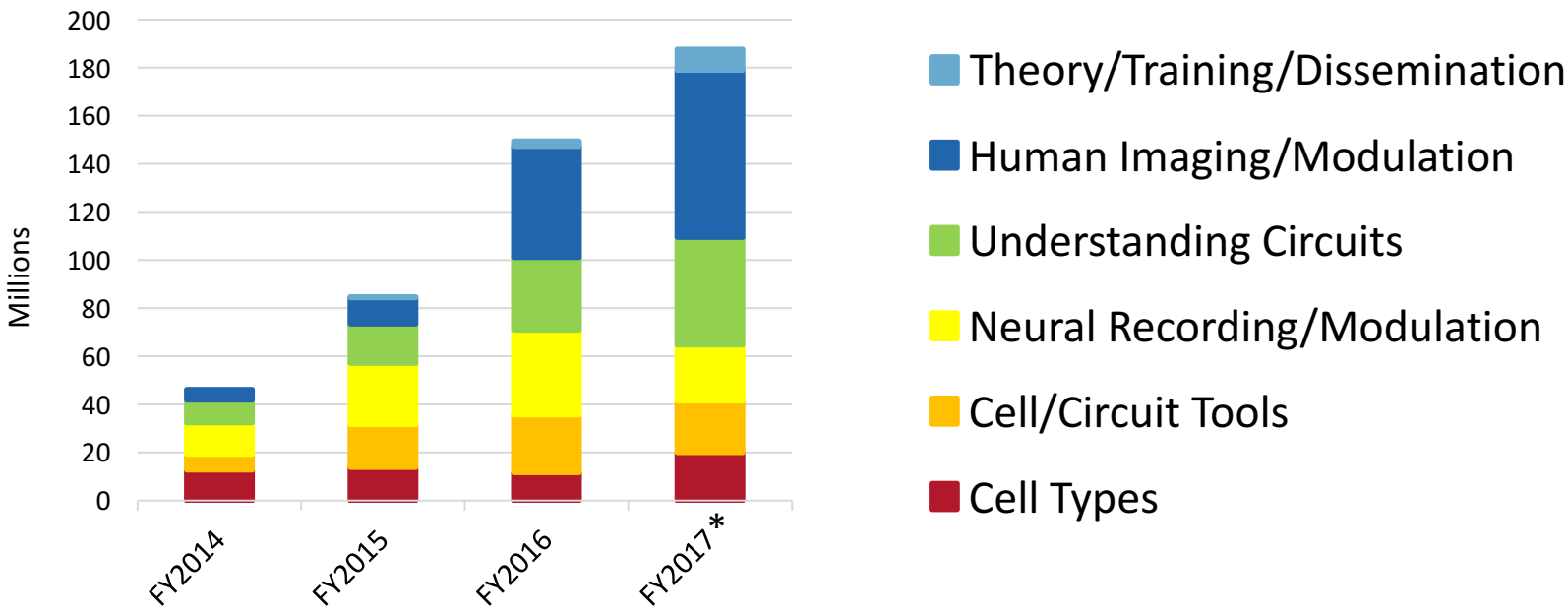
Scientific Stewardship: *NIH BRAIN Investment*



Scientific goals and overarching principles of the *BRAIN 2025* report and the BRAIN Multi-Council Working Group (MCWG) continue to guide NIH funding decisions

BRAIN MCWG assessed progress in Feb. 2017, recognized investments towards 65/74 short-term goals

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**All FY17 information is an estimate, as we do not know the FY17 budget. President's budget ~$195M*

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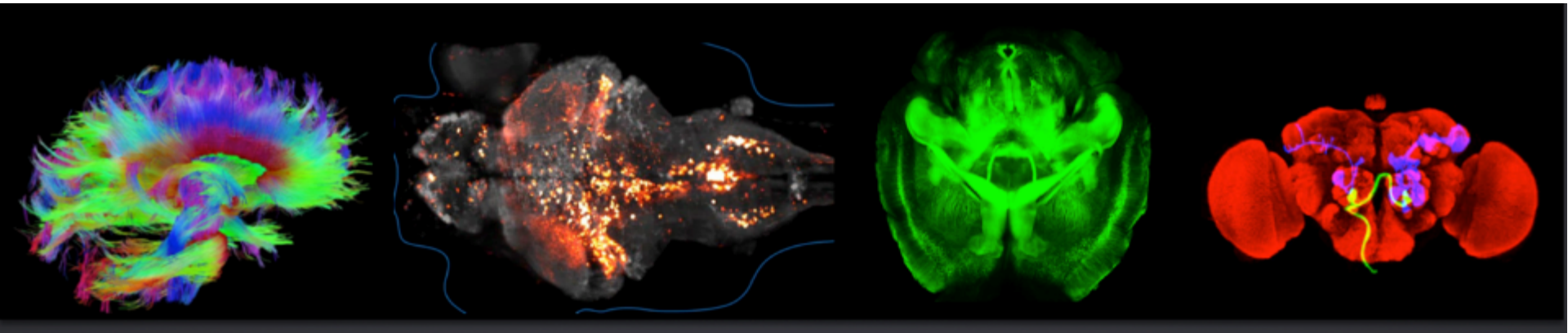
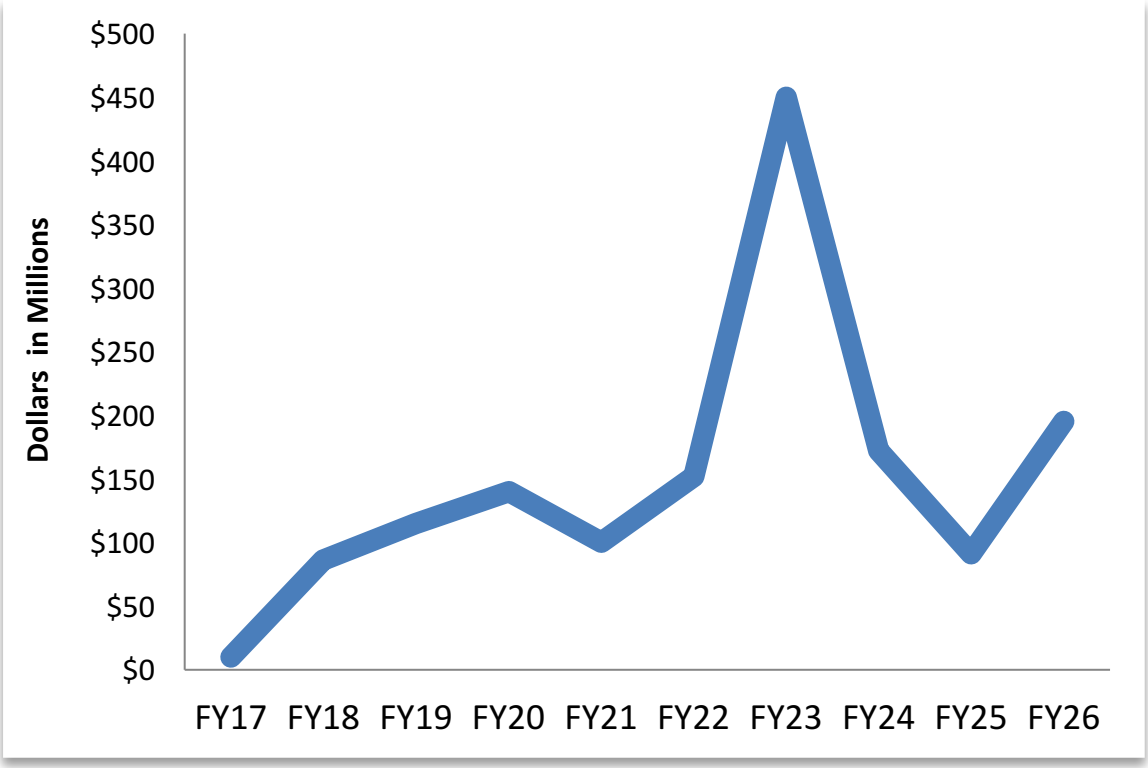
NIH BRAIN Investment

Fiscal Year	Actual Budget	# New BRAIN Awards	21st Century Cures	ACD WG Recommendation
FY14	$46.1M	58		
FY15	$85M	67		$100M
FY16	$154M	108		$190M
FY17	TBD		$10M	$300M
FY18	TBD		$86M	$400M
FY19	TBD		$115M	$500M

- Blueprint
- NCCIH
- NEI
- NIA
- NIAAA
- NIBIB
- NICHD
- NIDA
- NIDCD
- NIMH
- NINDS
- OBSSR
- OD
- ORWH



BRAIN 21st Century Cures Innovation Funds



21st Century Cures Act authorizes $1.511 billion to be transferred from the ***Beau Biden Cancer Moonshot & NIH Innovation Account*** for BRAIN research through 2026

Funds need to be appropriated each year, not to exceed these amounts:

- FY 17: $10,000,000
- FY 18: $86,000,000
- FY 19: $115,000,000
- FY 20: $140,000,000
- FY 21: $100,000,000
- FY 22: $152,000,000
- FY 23: $450,000,000
- FY 24: $172,000,000
- FY 25: $91,000,000
- FY 26: $195,000,000

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Innovation Fund Budget Scenario

FY Year	Original Cures Fund	Competing	Noncompeting	Multi Year Funded	Total
2017	10,000,000	10,000,000	-		10,000,000
2018	86,000,000	38,000,000	10,000,000	38,000,000	86,000,000
2019	115,000,000	33,500,000	48,000,000	33,500,000	115,000,000
2020	140,000,000	_____	81,500,000	58,500,000	140,000,000
2021	100,000,000	28,500,000	71,500,000		100,000,000
2022	152,000,000**	45,000,000	62,000,000	45,000,000	152,000,000
2023	450,000,000**	45,000,000	73,500,000	331,500,000	450,000,000
2024	172,000,000**		118,000,000	54,000,000	172,000,000
2025	91,000,000		89,500,000	1,500,000	91,000,000
2026	195,000,000		89,500,000	105,500,000	195,000,000
Total	1,511,000,000	200,000,000	598,500,000	712,500,000	1,511,000,000

** Potential time frame to take advantage of emerging scientific opportunities and/or to use funds to advance dissemination of new tools/technologies or develop new data sharing platforms.

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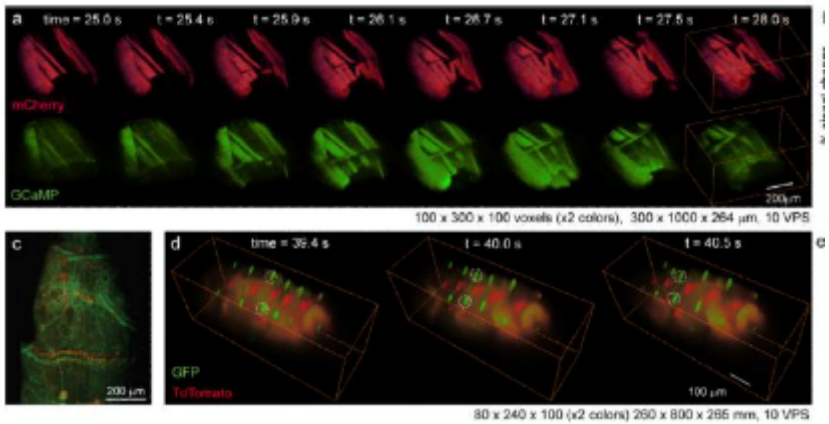
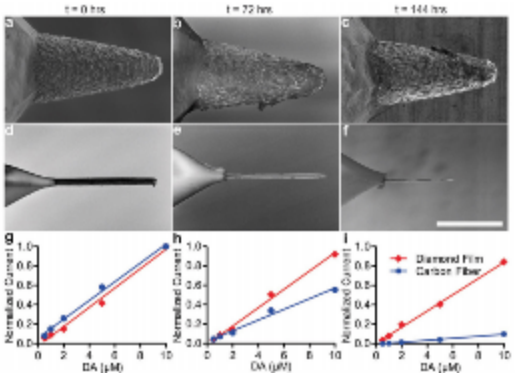
BRAIN-supported Technology Leaps to Catalyze Neuroscience



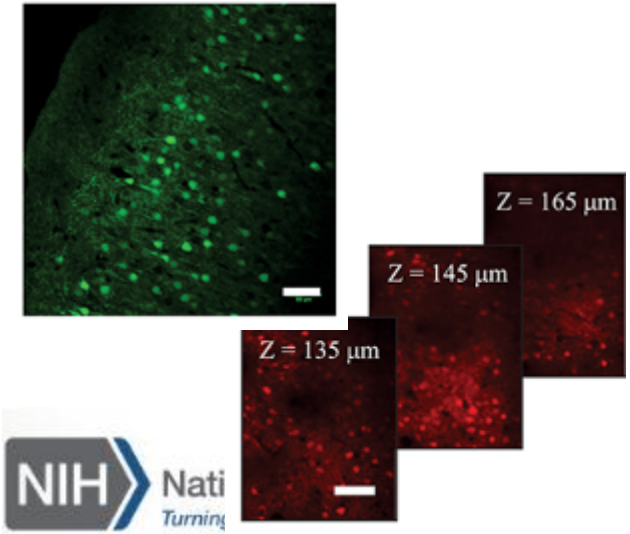
SCAPE: Novel 3D microscopy method for high-speed, volumetric imaging of living tissue visualizes spontaneous neuronal firing in whole-brain of awake, behaving mice and *Drosophila* larvae

Bouchard et al., *Nature Photonics,* 2015



Diamond electrodes can measure stimulation-driven monoamine transmitter release in basal ganglia of humans with greater longevity and strength

Bennet et al., *Frontiers in Human Neuroscience,* 2016



Two-Photon Holographic Stimulation of red-shifted opsin, ReaChR: Red-shifted opsins react to longer wavelengths of light, may reach deep brain structures

Chaigneau et al., *Frontiers in Cellular Neuroscience,* 2016

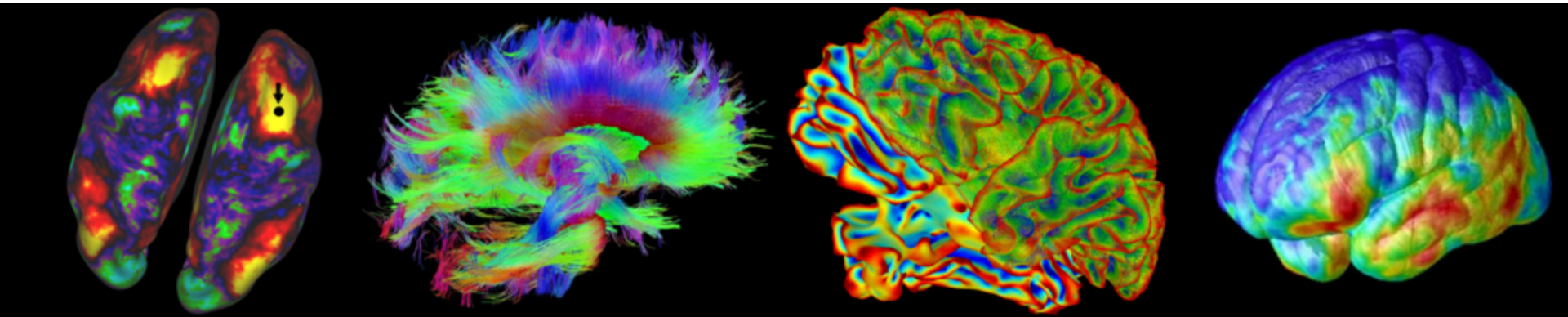
21st Century Cures Innovation Funds: *Strategies for BRAIN*

Maintain flexibility to allow us to take advantage of emerging scientific opportunities

Utilize a variety of funding approaches to ensure sustained funding

Balance regular and multi-year funding of grants

- Ability to spread funds over more than one year to provide a more steady stream of resources
- Leverage administrative and competitive supplements
- Ensure full funding of all grants by 2026



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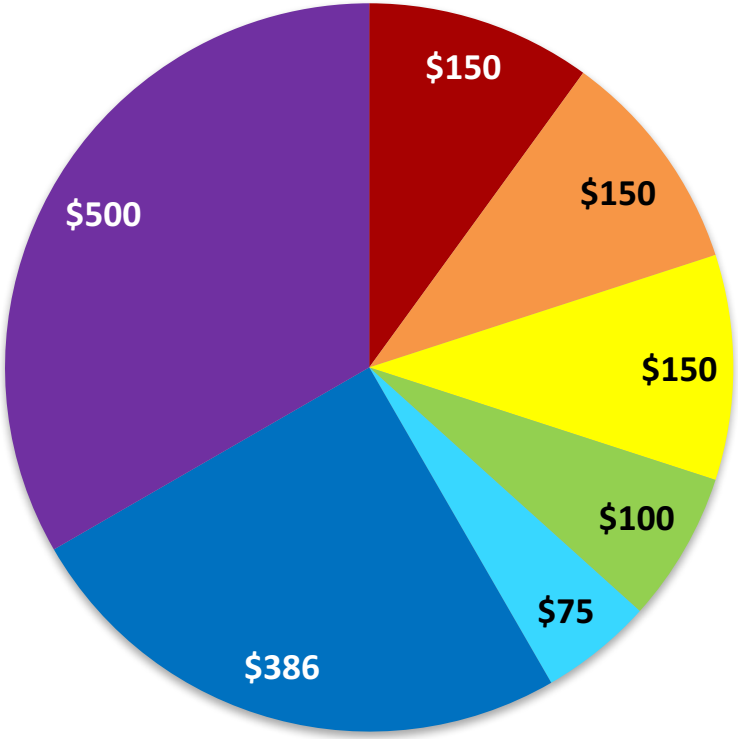
21st Century Cures Innovation Funds: *Potential Distribution*

Brain Cell Types	Tools for Circuit Diagrams	Tech. to Monitor Neural Activity	Precise Inter-ventional Tools	Theory and Data Analysis Tools	Advance Human Neuro-science	Integrate Approaches & Principles



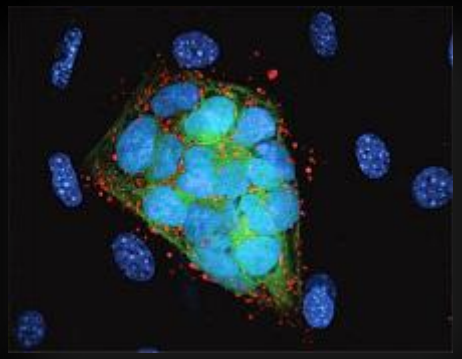
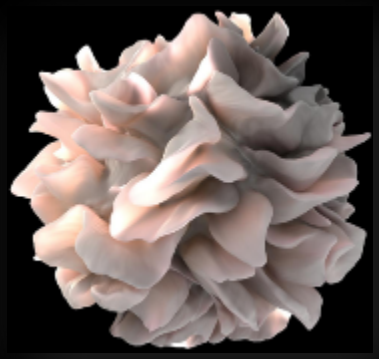
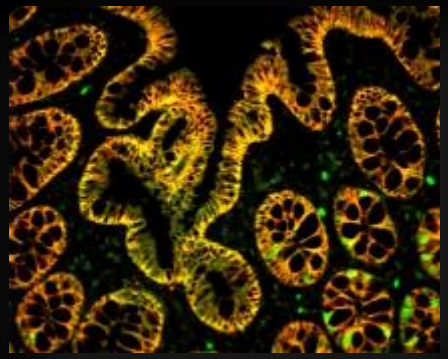
Dollars in millions

High level estimate of potential distribution of Innovation Funds over the next 9 years

FY 2022, 2023, 2024 large funding increases may be opportunity to take advantage of scientific opportunity to rapidly advance an area and/or devote additional funds to one of the BRAIN initiative priorities, particularly costly goals e.g.:

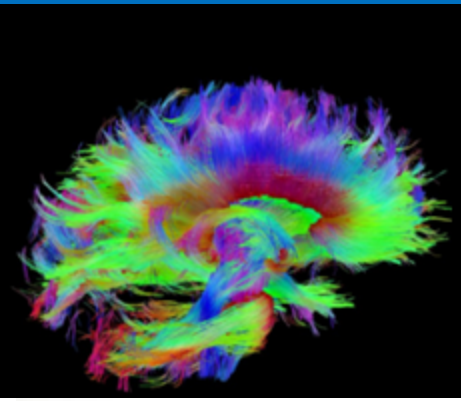
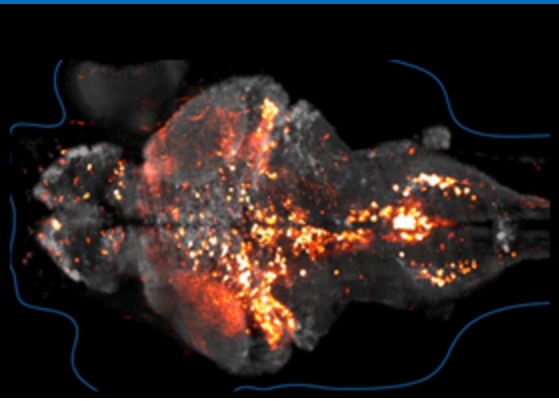
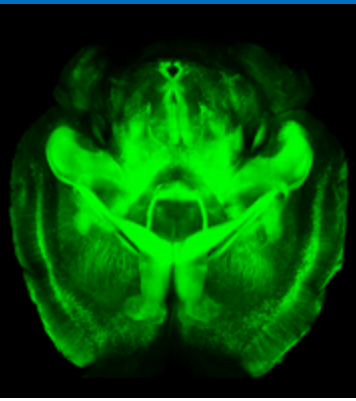
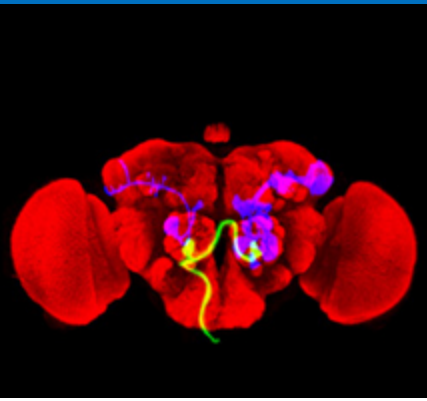
- Human studies
- Dissemination of new technologies/training
- Infrastructure for data science and new data sharing platforms

NIH National Institutes of Health
Turning Discovery Into Health

BRAIN…

mapping brain activity at the speed of thought

Advancing Research through Partnerships:

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BRAIN Initiative Alliance

Mission : *To coordinate and facilitate communications from its members related to the BRAIN Initiative*

Website provides platform for funding opportunities, news, achievements, resources, and more gathered from across the federal and non-federal participants of the BRAIN Initiative

www.braininitative.org

Allen Institute for Brain Science | Food and Drug Administration | Intelligence Advanced Research Projects Activity | The Kavli Foundation | National Institutes of Health | National Science Foundation | Simons Foundation

Recruiting Outstanding Workforce: *Engaging Many Disciplines*

Department Category (for Contact and Multi PIs)	FY15	~FY16
Biochemistry	11	12
Biology/cell biology/Microbiology/Pathology/Immunology	43	36
Chemistry	17	11
Genetics	4	3
Biostatistics/math/computer science	12	33
Physics	16	14
Engineering (all categories)	119	141
Neuroscience/ Neurology	146	141
Neurosurgery	14	47
Psychiatry/Psychology	17	69
Radiology/ Radiation-Diagnostic	31	61
Bioimaging/ Imaging	15	8

Recruiting Outstanding Workforce: *New, Early Stage Investigators*

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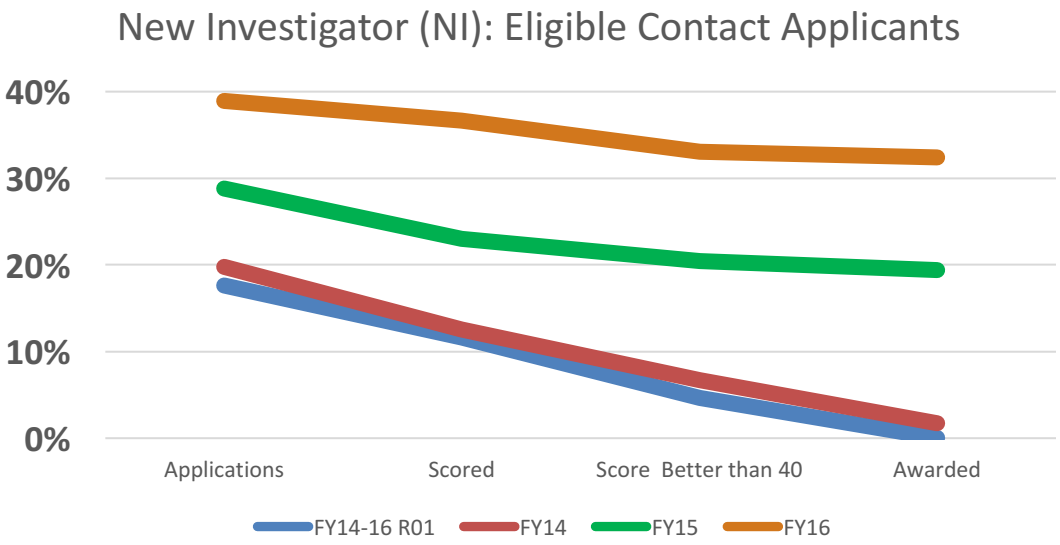
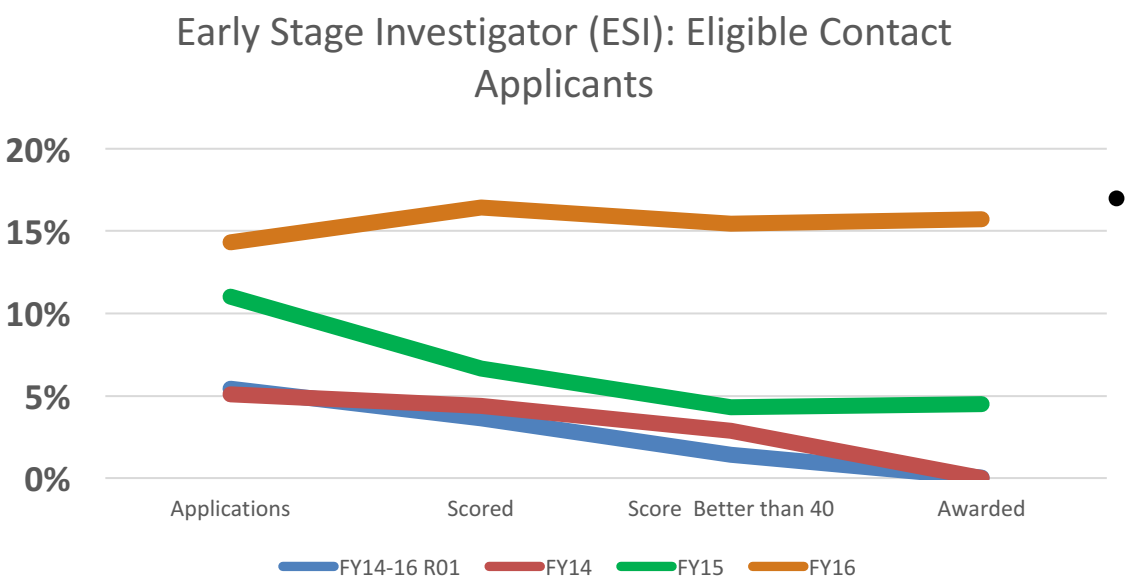
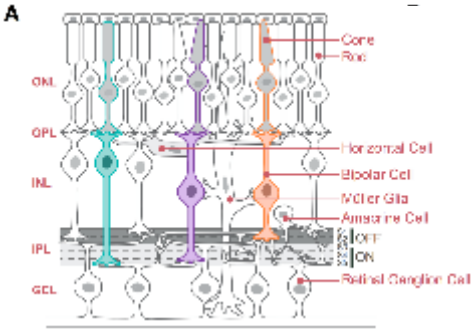




- The BRAIN Initiative is reaching early stage investigators and their applications are doing spectacularly well
- New BRAIN FOAs attract both NI and ESI applicants. Source of the increase in FY 15 and FY16
- The R21 Funding opportunity for large scale recording continues to attract NI and ESI applicants

Control is neuroscience across all ICs.

BRAIN-supported Technology Leaps to Catalyze Neuroscience

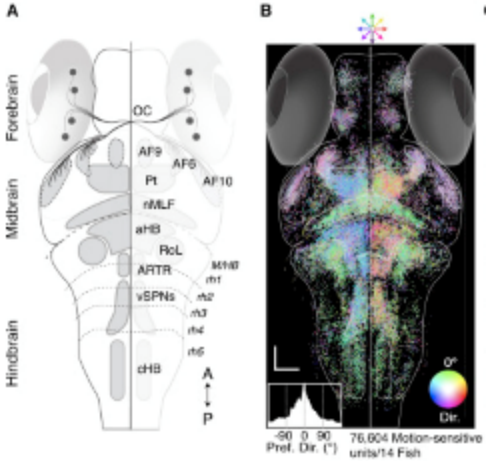


Novel method for classifying cell types using high throughput genetic sequencing allowed comprehensive classification of retinal bipolar neurons

Shekhar et al., *Cell,* 2016

Genome editing of synthetic target arrays for lineage tracing **(GESTALT) tracks cell fate in whole complex, multicellular organisms**

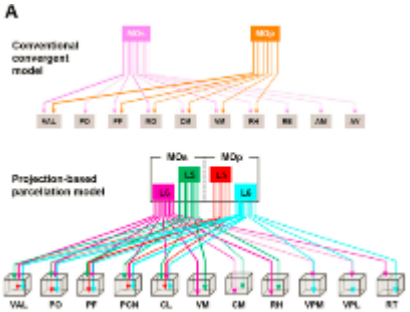
McKenna et al., *Science,* 2016



The zebrafish optomotor response: Integration of whole-brain imaging, behavioral analysis, functional perturbations, and network modeling to build a brain-scale circuit model of an orienting behavior

Naumann et al., *Cell* 2016

3D map of motor cortex tract pathways in mice **reveal a systematically organized connectome of motor output projections**



Jeong et al., *Scientific Reports* 2016

Scientific Advancements: Cell Types

Dr. Arnold Kriegstein and colleagues identify candidate entry receptor for Zika virus in neural stem cells

Single cell RNA-seq analysis of different cell types during early development (*Cell Stem Cell*)

- Examined expression of several candidate entry receptors for Zika virus
- Candidate AXL is highly expressed in several cell types, including human radial glial cells
  - Loss of radial glia founder populations leads to microcephaly
  - AXL expression pattern is conserved in mice, ferrets, and human iPSCs – models for infectivity and developmental effects of Zika virus