National Institutes of Health
Advisory Committee to the Director (ACD) Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative Working Group 2.0
Workshop #3: From Experiments to Theory and Back | October 4, 2018 | Houston, TX

## EXECUTIVE SUMMARY

The Advisory Committee of the NIH Director (ACD) enthusiastically endorsed *BRAIN 2025: A Scientific Vision* as the strategic plan for the NIH BRAIN Initiative. Consistent with the *BRAIN 2025* report, in the second 5 years of the BRAIN Initiative, NIH plans to build upon its current emphasis on technology development and has convened a new working group (WG 2.0) to revisit the *2025* report's priorities through the lens of progress to date, rising scientific opportunities, and the new set of tools and technologies emerging from BRAIN. As with WG 1.0, WG 2.0 reports to the full ACD, which provides recommendations to the NIH Director. A companion WG, the NIH ACD BRAIN Initiative Neuroethics Subgroup (BNS), has been charged with developing a neuroethics roadmap for BRAIN 2025, taking into consideration any proposed updates to BRAIN 2025. Overlapping members of WG 2.0 participate in the BNS.

Beginning in April 2018, and led by co-chairs Catherine Dulac, Ph.D., and John Maunsell, Ph.D., WG 2.0 members have reviewed the existing BRAIN investment and progress and have considered potential areas for growth and expansion. In so doing, WG 2.0 is soliciting input from the broader neuroscience community and other BRAIN stakeholders through two principal means: i) a series of public workshops held between August 2018 and November 2018 ii) an RFI seeking input (comments are due by November 15, 2018). In addition to this October 4, 2018 workshop "From Experiments to Theory and Back," past workshops include a September 21, 2018 workshop "Looking Ahead: Emerging Opportunities" held in Chicago, Illinois and an August 24, 2018 workshop "Human Neuroscience" was held in Cambridge, Massachusetts. Other upcoming events include:

- Society for Neuroscience Town Hall and Networking Session (Sunday, November 4, 2018 6:30 PM-9:00 PM Pacific Time)

### Workshop #3: Invited Presentations – From Experiments to Theory and Back

Scientific collaboration/integration and data science/data sharing were two broad areas of discussion in presentations and surrounding discussion during and after Workshop #3's three speaker sessions (**Theory - Building Understanding of Brain Function**, **Data Tools and Management**, and **Team Science versus Individual Labs**). A brief description appears below, followed by session summaries.

*Scientific Collaboration/Integration*
The inherent complexity of the human brain necessitates various modes of investigation, many of which call for enhanced interdisciplinary collaboration and consequent integration of information and methods. This may take the form of team science, but it also requires migration of new expertise into the neuroscience landscape. Especially needed for both team approaches and individual discovery are theoreticians/computational neuroscientists and data scientists of various types including software developers and data-management specialists. Many of the latter work in the private sector, and thus creative strategies are needed to recruit them into academia/government. Sociological and cultural issues continue to impede progress in interdisciplinary teamwork. Enhanced integration of theory and experiment will likely lead to new approaches that can collect a range of data concurrently (anatomical data, recording, and other); integrating it will help to reconstruct circuits. There is a need to build links

and theories to explain how collective pictures emerge from interactions of diverse cell types and populations.

*Data Science/Data Sharing*
A key question facing the BRAIN Initiative and the broader biomedical research community is "How aggressive should we be about data sharing, task standardization, and data aggregation?" These activities can be difficult in practice; yet, they underlie research quality, reproducibility in particular. Re-use of data magnifies the research investment considerably; without proper standards, protocols – and a culture to support both – the BRAIN investment is limited: "If data is worth collecting, it is worth sharing." NIH/BRAIN 2.0 could advance data sharing and standardization through various actions, ideally in a cloud environment, by bringing compute to the data, enabling scalable computing, providing useful tools and interfaces, and facilitating interoperability.

**Session I: Theory - Building Understanding of Brain Function** featured presentations on the current theoretical landscape in neuroscience, in particular computational neuroscience. Our current theory of brain is grounded in single-unit recordings, yet brain activity is in reality very heterogenous and comprised of millions of interconnected events. Moreover, multiscale neural activity is itself extremely variable. One area of recent growth is understanding of neural population dynamics, and continued progress is expected in this arena. Creating a vibrant alliance between neuroscience and machine learning will provide a rich opportunity for advances. Opportunities for large-scale in silico experiments exist using deep-learning approaches that employ neural networks. These can be trained and optimized and thus used as a new type of model organism for human-brain investigations that are concrete and detailed and that enable iterative, unsupervised hypothesis-generation. Theory may also guide experiments to define or refute the etiology and function of cell types and brain regions that have been heretofore described anatomically. Despite these opportunities, and echoing previous workshops and other discussions, neuroscientific discovery is hampered by the lack of robust collaboration between theorists and experimentalists. Contributing to the divide are culture, resources, size of teams, and different incentives. BRAIN 2.0 could help resolve this gap by recruiting and retaining mathematicians, physicists, and engineers to work alongside neuroscientists. A particularly difficult challenge is how to conduct multiscale, multistructure experiments – theory input may help constrain complexity of experimental conditions to avoid assumptions (e.g. linearity) that may obscure the full range of conclusions. Neural theories can thus enable "targeted reductionism." A united approach that bridges theory and experiment can be grounded in behavior – the necessary common denominator.

**Session I** speakers included **Tatiana Engel, Ph.D.** (Cold Spring Harbor Laboratory); **Stephanie Jones, Ph.D.** (Brown University); **David Sussillo, Ph.D.** (Google Brain Group and Stanford University); **Surya Ganguli, Ph.D.** (Stanford University); and **Brent Doiron, Ph.D.** (University of Pittsburgh).

**Session II: Data Tools and Management** featured presentations on data-science and data-management strategies that are critical for investigation and focused in particular on the necessity of sharing/re-use for both theorists and experimentalists. One example is DataJoint, a free, open-source framework for building and operating shared data pipelines, which provide tools, interfaces, services, and applications to help craft a given project's data science plan that encompasses experimental design, data collection, data processing and analysis, and publication/sharing. In addition, several sets of neuroscience data standards exist but are not used/followed consistently. Many realities frustrate current progress in this arena. These include the vast size of datasets, data in many different formats, and an uneven level of corresponding metadata. Although required by many funders including NIH, data sharing may appear to be an unfunded mandate and is very expensive. Common arguments against wide availability/sharing of data and code include irrelevant focus of time, effort, and resources; no apparent immediate utility; and a disincentive to conducting hard/risky experiments. There are many ways to mitigate these objections, including creating reasonable data embargos, providing incentives for publication of valuable data and analysis, making data and code publication easier, and enabling publication of useful data extractions. There is widespread consensus that training in data use/analysis/data mining is insufficient on a national scale, despite scattered courses, funding supplements, a limited number of training grants, and other resources. NIH/BRAIN 2.0 is supporting these efforts, but much more can be done. In addition to addressing/incentivizing cultural change toward an open-science environment, other strategies include supporting cloud co-location of storage and compute platforms, recruiting data-science expertise, and developing broad, hands-on training opportunities (across the career trajectory) on how to make data Findable, Accessible, Interoperable, and Reusable (FAIR). NIH/BRAIN 2.0 must also address specific data issues tied to neuroethics, to ensure best practices are required by institutional review boards (IRBs) and followed by investigators.

**Session II** speakers included **Dimitri Yatsenko, Ph.D.** (Baylor College of Medicine, Vathes LLC); **Lydia Ng, Ph.D.** (Allen Institute for Brain Science); **Ariel Rokem, Ph.D.** (University of Washington); and **Daniel Marcus, Ph.D.** (Washington University School of Medicine in St. Louis).

**Session III. Team Science versus Individual Labs** featured presentations on how to support collaborative investigation in neuroscience. Various models exist for team science and due to the extraordinary complexity of the human brain, large-scale collaborative approaches are necessary. It is a myth that innovation and exploration are dissonant from collaborative science, yet careful planning and flexibility are needed to support and maintain an environment that supports each. Attention must be paid to incentives and rewards for individuals to participate in a larger, shared effort than is different from that which has been customary for most of the history of biomedical research. The International Brain Laboratory is an interesting model, with 21 labs working together around a common set of principles and involving both experimentalists and theorists. Several key components enable healthy team science and also support research discovery. These include select appropriate projects amenable to team science; managing operational challenges so as to not obscure scientific goals; developing effective project-management systems (with both people and tools); and allowing timely adjustment through frequent data analysis and feedback cycles. Team culture is vital and must support core values and leadership principles; clearly assign roles and responsibilities; fairly assign and distribute credit and contribution; and finally – enable opportunities for exploration and innovation. There are likely to be some areas of neuroscience riper for team science, but overall, there is a need to be flexible and dynamic – as technology and knowledge emerge and questions shift. BRAIN 2.0 can play a formative role in enabling various models of team science that have the flexibility to change according to progress – and that are not excessively top-down managed.

**Session III** speakers included **Alexandre Pouget, Ph.D.** (University of Geneva); **Andreas Tolias, Ph.D.** (Baylor College of Medicine); and **Hongkui Zeng, Ph.D.** (Allen Institute for Brain Science).