

GRAND CHALLENGES FOR THE GLOBAL BRAIN SCIENCES

PARTICIPANTS OF THE GLOBAL BRAIN WORKSHOP¹

Understanding the brain and curing it are among the most exciting challenges of our time. Consequently, national, transnational, and private parties are investing billions of dollars (USD). To efficiently join forces, Global Brain Workshop 2016 was hosted at Johns Hopkins University’s Kavli Neuroscience Discovery Institute on April 7–8. A second workshop, Open Data Ecosystem in Neuroscience will happen July 25–26 in DC to continue the discussion specifically about computational challenges and opportunities. A third conference, Coordinating Global Brain Projects, will take place in New York City on September 19th in association with the United Nations General Assembly. So vast are both the challenges and the opportunities that global coordination is crucial.

To find ways of synergistically studying the brain, the kickoff workshop welcomed over 60 scientists, representing 12 different countries and a wide range of subdisciplines. They were joined by 15 observers from various national and international funding organizations. Participants were engaged weeks before the conference and charged with coming up with ambitious projects that are both feasible and internationally inclusive, on par with the International Space Station (i.e., worthy of a global, decade-long effort). Over the course of 36 hours, scientists discussed, debated, and gathered feedback, ultimately proposing several “grand challenges for global brain sciences.” The workshop was covered in [media piece](#) in Science April 15, 2016. The newly established working groups have continued refining ideas, incorporating feedback from other participants and interested scientists who were unable to participate to compile a list of meaningful challenges.

The group began with 60+ ideas, each forged independently by one of the scientific participants. Each participant proposed a unique challenge that was designed to meet the following desiderata:

1. *Significant*: it will yield tangible societal, economic, and medical benefits to the world.
2. *Feasible*: it can achieve major milestones within 10 years given existing funding opportunities.
3. *Inclusive*: nations throughout the world can meaningfully contribute to and benefit from each challenge, and the collection of challenges are collectively scientifically diverse.

Interestingly, a lot of the proposed ideas were similar to one another and others were complementary. This allowed the group to converge on three grand challenges

¹See <http://brainx.io> for a complete list

for global brain sciences, each depending on a common universal resource.

Challenge 1: What makes our brains unique?

Both within and across species, brain structure is known to exhibit significant variability across many orders of magnitude in scale — *including anatomy, biochemistry, connectivity, development, and gene expression* (ABCDE). It remains mysterious how and why the nervous system tightly regulates certain properties, while allowing others to vary. Understanding the design principles governing variability may hold the key to understanding intelligence and subjective experience, as well as the influence of variability on health and function.

The grand challenge — **Anatomical Neurocartography** — **a global project to coordinate obtaining comprehensive multiscale maps of the ABCDEs of multiple brains from multiple species using multiple cognitive and mental health disease models.** Within a decade, we expect to have addressed this challenge in brains including but not limited to *Drosophila*, Zebrafish, Mouse, and Marmoset, and to have developed tools to conduct massive neurocartographic analyses. The result will be a state-of-the-art “Virtual NeuroZoo” with fully annotated data and analytic tools for analysis and discovery. This virtual NeuroZoo can be utilized by neuroscientists and citizens alike, both as a reference and for educational materials. By incorporating disease models, we explicitly link this challenge with the third challenge.

Challenge 2: How does the brain solve the complex computational problems of intelligence?

Brains remain the most computationally advanced machines for a large array of cognitive tasks — whether navigating hazardous terrain, translating languages, conducting surgery, or recognizing emotional states — despite the fact that modern computers can utilize millions of training samples, megawatts of power, and tons of hardware. While the ABCDEs establish the “wetware” upon which our brains can solve such computations, to understand the mechanisms we need to measure, manipulate, and model neural activity simultaneously across many spatiotemporal resolutions and scales — including wearables, embedded sensors, and actuators — while animals are exhibiting complex ecological behaviors in naturalistic environments.

The grand challenge — **Functional Neurocartography** — **is a global project to coordinate identifying how the multiscale distributed components of neural architecture orchestrate complex behavior in naturalistic environments.** The challenge differs from previous efforts in three key ways. First, it requires studying animals in complex environments and behaviors, ideally resembles zoos or even more natural habitats. Second, it requires coordinated attacks at many different scales by many different investigators while the animals are performing the same complex behaviors. We foresee groups of 20–30 investigators all

operating together on shared data and experimental design. Third, the richness of the mental repertoire of cognition suggests that deciphering its codes will require *many parallel investigations* to uncover different facets of brain function. These experiments in turn will produce multiscale models of neural systems with the potential to accomplish computational tasks that no current computer system can perform. Mechanistic studies will help to ask how perturbations of those systems lead to aberrant function, thereby linking this challenge with the next one.

Challenge 3: How can we augment clinical decisionmaking to prevent disease and restore brain function?

Psychiatric and neurological illnesses levy enormous burdens upon humanity: impairment, suffering, financial costs, and loss of productivity. Despite a growing awareness of the challenges, clinicians consistently battle the lack of objective tests to guide clinical decisionmaking (e.g., diagnosis, selection of treatments, prognosis). Compounding these limitations are societal stigmas regarding mental illness that increase the suffering of patients and their families. The ABCDEs of neurobiological variability, coupled with multiscale mechanistic models of cognition will provide new approaches to neurobiologically informed clinical decision making.

The grand challenge — **Medical Neurocartography — a global project to coordinate, acquire, and model both brain and behavioral data for brainbased disorders with the goal of augmenting clinical decisionmaking with neural mechanisms of dysfunction.** These datasets, and the tools developed to explore and discover novel treatment therapies will be the foundation upon which the next decades of experiments and clinical decisions will be based. The distributed and multimodal nature of these datasets further motivate the need for an allpurpose computational platform, upon which models of disease can be developed, deployed, tested, and refined.

A Universal Resource: The International Brain Station

All three of the above grand challenges for global brain sciences contain within them severe methodological challenges, including both technological and computational. The technological developments required for each of the challenges are essentially nonoverlapping. By contrast, regardless of the nature of the scientific questions or data modalities involved, each project will require computational capabilities including collecting, storing, exploring, analyzing, modeling, and discovering data. Although neuroscience has developed a large number of computational tools to deal with existing datasets, the datasets proposed here bring with them a whole suite of new challenges. The International Brain Station (TIBS) is a comprehensive computational platform, deployed in the cloud, that will provide Webservices for all the current “pain points” in daily neuroscience practice associated with big data. TIBS will realize a new era of brain sciences, one in which the bottlenecks of discovery transition away from data collection and processing to data enriching

exploring, and modeling. While science has always benefited from standing on the shoulders of giants, TIBS *will enable science to stand on the shoulders of everyone*. Today, essentially every practicing neuroscientists productivity is limited due to computational resources, access to data or algorithms, or struggling with determining which data and algorithms are best suited to answer the most pressing questions of our generation. TIBS will create a future where those limitations will feel as archaic as fitting the data with paper and pencil feels today.

We have identified six stages of science that utilize computational resources. For each, we have identified the pain points for typical practicing neuroscientists and have designed a system to minimize those painpoints as effectively (i.e., easily and inexpensively) as possible.

1. **Collection** The first necessary step for any brain investigation, can be tedious and tiresome, requiring manually and locally running the measurement devices. *Data Collection Dashboards* will directly interface with the machines, to provide live status summaries, and enable remote control as appropriate.
2. **Storage** The data must be deposited somewhere, and as it gets larger and more complicated, neuroscientists are developing custom data management solutions. *Multimodal Data Store* will interface with the data store to organize data in a fashion readily amenable for access and exploration with version control.
3. **Analysis** The raw data is often noisy, fragmented, and otherwise messy. *Data Analysis Pipelines* will convert raw messy data to clean data, automatically and on demand, by pooling the best algorithms and implementations from around the world to make them readily available for everyone to better explore and model, including exhausting quality control on both data and algorithms.
4. **Exploration** Whether your own data or shared reference datasets, we want access to the data from anywhere at anytime. *Interactive Data Explorers and Notebooks* will dynamically pull both raw and processed data to enable navigating and exploring the data in augmented reality environments, mobile devices, and other devices.
5. **Modeling** The final step, prior to suggesting a new experiment, is modeling and synthesizing the data. Establishing efficient integration of data and models comes with a dual challenge. Both datasets and models will be contributed according to a set of community driven specifications, such that *Data Modeling Bots* will automatically fit existing models to new data, and fit new models to existing data, significantly tightening links between models and data, to accelerate neuroscientific discovery.
6. **Discovery** To be useful, neuroscientists of all types must be able to quickly and easily find data appropriately matched to their scientific goals. To that end, a *Metadata Query Service* will link to a community established set of metadata fields, to enable both searching and juxtaposing similar and disparate datasets.

7. **Education** the above steps represent a transformation in the practice of brain sciences, and therefore, its success will depend on extensive training and educational material, designed from the ground up to be culturally sensitive and universally accessible.

Crucial to the success of TIBS will be tight integration with each of the three above motivating grand challenges, and the neuroscientists engaged in pursuing them. Moreover, community involvement and feedback at each stage will be key. TIBS will be entirely open source and community driven: both data and tools will be voted on and reviewed, forming the meritocracy the science deserves. In this sense, TIBS will be the most inclusive aspect of all of the proposed grand challenges, because the barrier to enter will be as low as possible.

Common Threads

In addition to TIBS linking all three grand challenges of global brain sciences, there are two key threads to this proposal that differentiate it from previous efforts. First, the data collection efforts will be multimodal and multiscale. Historically most neuroscientists focus on a small number experimental modalities and scales (e.g., extracellular electrophysiology), answering the above challenges satisfactorily will require **many groups jointly investigating** both across modalities and scales. Because designing and completing these experiments for even a single modality and scale will be a monumental task, coordinating across brain scientists will be essential. Second, the data and tools will be designed and developed at the outset to be **reference, rather than personal**. Collecting reference datasets, and writing reference implementations is different than standard academic practice. In particular, it requires considerable investment in training and support to facilitate other people effectively using the provided resources. Thus, to be effective, investigators will have to commit a sizable fraction of effort to supporting those activities.

Societal Considerations

Each nation affords different societal opportunities and restrictions, due to ethical, policy, and cultural considerations. Because these grand challenges are inherently inclusive, manifesting them will require understanding and mitigating issues that will arise in any crosscultural endeavor. Indeed, addressing the vast diversity of partnerships in such an endeavor is a challenge in itself. We therefore recommend the following. First, form a **cultural sensitivity committee** to consider and investigate potentially sensitive issues. Second, bolstered by their research, establish **crosscultural collaboration education materials**, including written guidelines and videos, which will be recommended to all participating scientists. Third, to deepen the understanding of transnational collaborations, develop **trainee exchange programs**, where participating trainees will spend six months to a year working and training in a foreign country. This will also facilitate crosscultural knowledge dissemination and fertilization. Fourth, require **frequent assessments**

to ensure maintenance of cultural sensitivities. These assessments will feedback into the educational materials, and be used to modify the exchange programs, thereby facilitating consistent considerations even as the goals and individuals change over the timecourse of these grand challenges.

Next Steps

Crucial to the success of this endeavor is a sequence of actionable steps that the community can follow. Because we are not actually proposing any additional funding, realizing the eventual goals of these grand challenges will rely on marshalling existing funds. Due to the incoming leadership changes, both on national and transnational levels, time for acting is of the essence. Therefore, we have taken the following steps:

- We have created a webpage, <http://brainx.io>, containing the following:
 - the current working version of this document, and
 - a list of all scientific participants and observers who attended the original brainstorming meeting leading to this document.
- We will provide (possibly via <https://neurostars.org/>):
 - a platform for discussion and improving the ideas presented herein,
 - a forum for “teaming,” that is, openly discussing these ideas to develop more specific and concrete plans for individual teams to pursue, and
 - a list of potential funding mechanisms that might support these endeavors, such as NSF’s **NeuroNex** and their **NSF 16076**.
- The following conferences will continue to refine the ideas discussed herein:
 - Open Data Ecosystem for the Neurosciences on July 25/26, 2016
 - Coordinating Global Brain Projects at Rockefeller on September 19, 2016, which will be publicly broadcast
 - A planned United Nations General Assembly Side Event, also in September.

We encourage anybody who feels inspired by this document to join the discussion, begin teaming activities, and get in touch with program officers with your ideas.