Cell

Leading Edge
Commentary

Toward a Global BRAIN Initiative

Rafael Yuste[1,*] and Cori Bargmann[2,*]
[1]Neurotechnology Center, Kavli Institute of Brain Science, Department of Biological Sciences and Neuroscience, Columbia University, New York, NY 10027, USA
[2]Chan Zuckerberg Initiative, Palo Alto, CA 94301 and Lulu and Anthony Wang Laboratory of Neural Circuits and Behavior, The Rockefeller University, New York, NY 10065, USA
*Correspondence: rmy5@columbia.edu (R.Y.), cori@mail.rockefeller.edu (C.B.)
http://dx.doi.org/10.1016/j.cell.2017.02.023

Neuroscience is entering a collaborative era in which powerful new technologies, generated by large scientific projects in many countries, will have a dramatic impact on science, medicine, and society. Coordinating these international initiatives and ensuring broad distribution of novel technologies and open accessibility of the generated data will multiply their value, while tapping creativity and expertise from every source.

A New Era of Neuroscience

Neuroscience has undergone tremendous growth and development over the past decades. The field began more than a century ago with parallel attacks on nervous system structure and function, exemplified by the towering figures of Cajal and Sherrington. These approaches were symbolically united into one discipline in 1966 with the creation of the first neurobiology department at Harvard. In recent decades, the field has expanded to incorporate molecular genetics to explain the biophysical, cellular, and developmental properties of the nervous system. Today, we have an opportunity to link these approaches by understanding how circuits and systems—interconnected networks of neurons of various scales—work. The challenge in this field is to capture the rapidly changing functional states of the system that arise from neuronal interactions, which, by nature, are not revealed by examination of individual neurons.

One could define the central goal of neuroscience as breaking the neural code—deciphering the relationships between spatiotemporal patterns of activity across groups of neurons and the behavior of an animal or the mental state of a person. While much has been learned by studying the brain one neuron at a time, it is widely thought that emergent properties of ensembles of neurons determine functional states. Therefore, we must capture these states in our experiments by measuring the activity of many neurons and then manipulate the circuits in causal ways. Since many human disease states have a genetic component, we also need to incorporate genetic approaches into these studies. Finally, we need theoretical and computational power to understand the results that emerge. These needs are at the heart of the new global brain initiatives.

International BRAIN Projects

Partly as a reaction to the realization that neuroscience is poised to generate extraordinary insights, several large-scale neuroscience initiatives have been launched in the past five years in many different countries (Figure 1). A meeting in New York in September 2016, co-hosted by the Rockefeller University and Columbia University and sponsored by the NSF and the Kavli Foundation, brought together neuroscientists and neuroscience administrators from around the world, who reported about each of these initiatives (http://www.rockefeller.edu/research/intercenter/globalbrain; web links in Box 1, Figure 1).

The US BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies Initiative, or BRAINI) was launched by the White House in 2013. This initiative was seeded at a meeting supported by the Kavli and Gatsby Foundations, the Wellcome Trust, and the Allen Institute for Brain Science, where a group of scientists proposed the Brain Activity Map Project: systematic measurement and perturbation of neuronal activity in complete neural circuits, to be accomplished by importing methods and talent from the physical sciences into neuroscience (Alivisatos et al., 2012). After President Obama officially launched the BRAIN Initiative in 2013, a working group convened by the NIH elaborated and expanded these ideas in its BRAIN 2025 report, which provided a detailed plan for the systematic analysis of neural circuits and systems across spatial and temporal scales in animal models and in humans (Jorgenson et al., 2015). Since then, federal agencies such as NIH, NSF, DARPA, and IARPA have created BRAINI-funding programs that presently engage more than 300 laboratories in the US and abroad. With a current annual budget of over $300 million, the project is projected to be supported by several billion dollars of new research funds over its lifetime, of which $1.5 billion has been already committed to the NIH alone.

Near the same time, the European Union launched its Human Brain Project (HBP), a decade-long flagship project jointly funded by the European Commission's Future and Emerging Technologies Projects and the member countries and expected to have a total budget of one billion euros. The HBP's roots were in the Blue Brain Project, a large-scale brain data collection and simulation effort based in Switzerland. The HBP objectives are the development of a scientific infrastructure for brain research and cognitive neuroscience; gathering and disseminating data describing the brain and its diseases; simulating the brain; building theory and models of the brain; and developing brain-inspired computing, data analytics, and robots.

Japan, in turn, launched the Japan Brain/MINDS (Brain/Mapping by Innovative

 © 2017 Elsevier Inc.

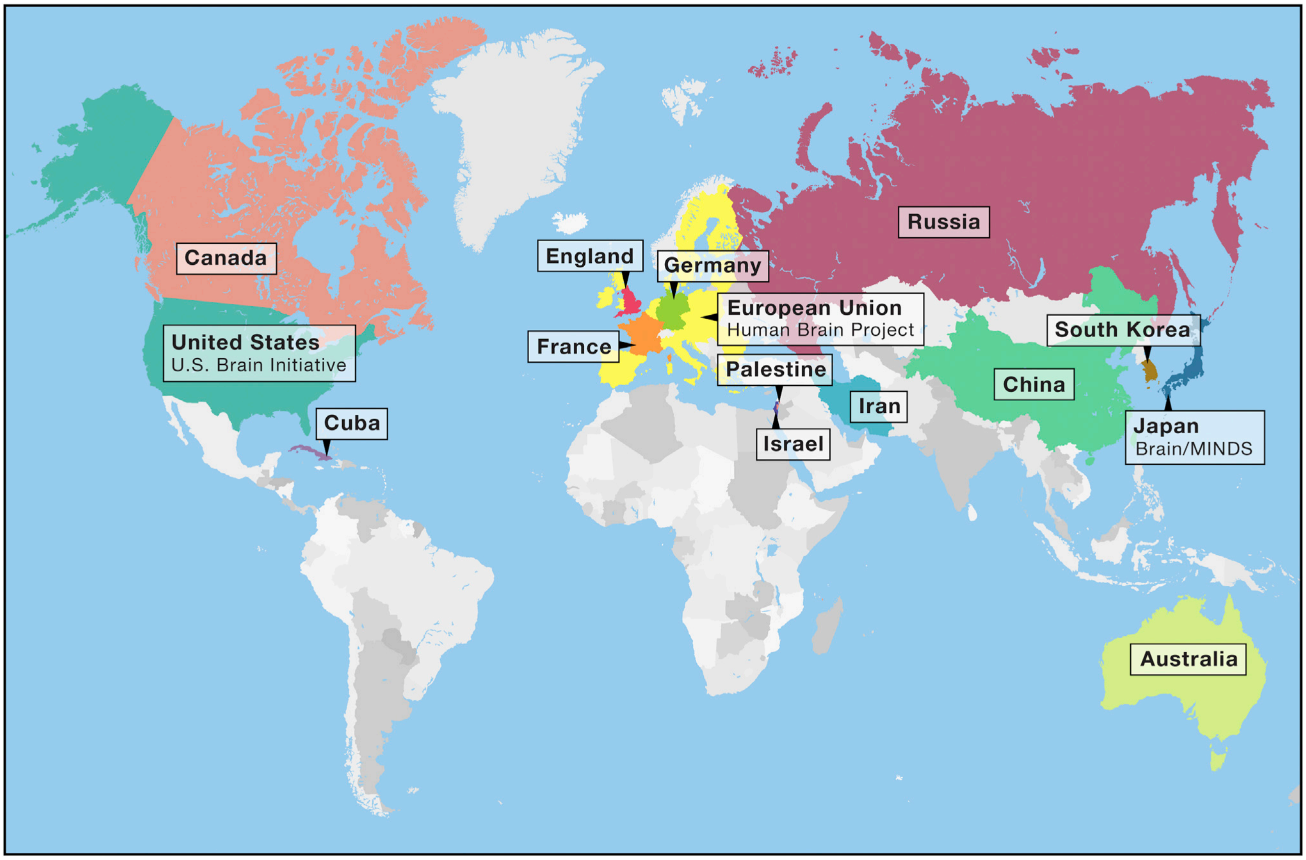

Figure 1. World Map Depicting Brain Initiatives and Related Programs around the World

Neurotechnologies for Disease Studies) project in 2014. Its three goals are to use the marmoset, a small primate with a short life cycle, for functional and structural brain mapping and genetic studies; to develop innovative tools to monitor and manipulate different aspects of neuronal activity; and to establish biomarkers for brain disorders.

South Korea announced a ten-year, $160 million brain-mapping project in 2016. Areas of interest are an atlas of the parietal lobe of the brain and a brain map addressing aging-associated brain diseases as part of a comprehensive plan to develop the country's brain science infrastructure.

Several countries are participating as partners in these existing international efforts, sometimes through private foundations, as well as national funding mechanisms. Scientists in Canada and Denmark whose research is judged as meritorious by the US BRAIN Initiative have their research funded by the host country or the Lundbeck Foundation; both countries also fund research through their own programs. Non-government groups such as the Kavli Foundation, the Simons Foundation, the Allen Institute for Brain Science, Brain Canada, the Brain and Behavior Research Foundation, and the Howard Hughes Medical Institute are each contributing to large-scale brain projects through their activities.

The September meeting also highlighted countries in the process of establishing their own large-scale brain projects. China is the furthest along, although its brain project is not formally launched. In China, studies of cognition will point toward human brain diseases along one axis and toward artificial intelligence along another axis. Neuroscientists in China are developing *Cygnomolgus* and *Rhesus* macaque primates as disease models; use of new CRISPR technologies is already yielding genetically modified macaques that model some human diseases. Areas in discussion on the medical axis include brain-machine interfaces and brain-training games.

Australia, Israel, Germany, France, and the UK were represented by delegates describing their current and planned brain research efforts. Within the audience of the meeting were scientists from Russia, Iran, Palestine, and Cuba, who spoke out about their own interest in brain science and potential projects in these countries. It is no exaggeration to say that brain projects are blooming all over the world.

Potential International Neuroscience Collaborative Projects

What models for international collaboration might neuroscientists emulate? An inspiring example is the success of the 1,000-plus-member LIGO Laboratory that was recently celebrated for detecting gravitational waves. One of LIGO's leaders, David Shoemaker, explained at the September meeting that the

Box 1. Web Resources Related to International Brain Initiatives

Belmont Report
https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report
Brain Initiative
https://www.braininitiative.nih.gov/
Brain 2025 report
https://www.braininitiative.nih.gov/2025/
BRAIN Canada
http://www.braincanada.ca/
BRAIN Foundation Australia
http://brainfoundation.org.au/
Coordinating Global Brain Projects Conference
http://www.rockefeller.edu/research/intercenter/globalbrain
Denmark Lundbeck Foundation-BRAINI
http://www.lundbeckfonden.com/nih-brain-initiative.516.aspx
Human Brain Project
https://www.humanbrainproject.eu/
Human Frontiers Science Program
http://www.hfsp.org/
Human Genome Organization
http://www.hugo-international.org
NeuroData Without Borders Initiative
http://www.nwb.org
Japan Brain/MINDS
http://brainminds.jp/en/
Simons Collaboration on the Global Brain Project
https://www.simonsfoundation.org/life-sciences/simons-collaboration-on-the-global-brain-2/
South Korean Brain Mapping Project
http://english.yonhapnews.co.kr/news/2016/05/30/0200000000AEN20160530008200320.html
State of the Brain Keystone Symposium
http://www.keystonesymposia.org/16R1

success of this large-scale project came in part because its scope—and funding agencies—demanded collaboration. The keys to LIGO's success included its coordination by scientific leaders, whose vision and determination were critical for the success of the project. They were supported by programmatic coordinators that provided coherent management and direction. Finally, the reward of membership accrued beyond the core project —access to data, expertise, and central infrastructure associated with LIGO provided leverage for each researcher's individual interests.

Neurotechnology Centers

Perhaps the strongest case for international collaboration for brain projects of different countries can be made from fields accustomed to sharing large-scale instrumentation, as has been the norm for astronomy (telescopes), physics (particle accelerators), electronics (foundries), computer science (supercomputers), space science (space stations), and structural biology (beam lines). This parallel has not gone unnoticed, as terms echoing these approaches, such as International Brain Stations or Brain Observatories, have been used to envision large-scale neuroscience facilities (Koch and Reid, 2012) (Alivisatos et al., 2015).

In several areas of neuroscience, there is already a case for pooling resources at a regional, national, or international scale for large-scale instrumentation. A special infrastructure is needed for connectomics, in the form of electron microscopy platforms to perform systematic ultrastructural reconstructions of brain tissue. Expense can be also minimized and expertise can be maximized by building shared facilities for cutting-edge magnetic or optical imaging. Nanofabrication of optical fibers and dense electrode arrays for neurophysiology, among other tools, can be conducted in specialized foundries. Some projects will benefit from joint data centers with advanced supercomputers. The US Department of Energy has examples of supercomputers, beam lines, foundries, and user facilities that might be deployed or imitated for this work, in addition to examples like the Cornell Nanofabrication Facility and the HHMI/Janelia Advanced Imaging Center.

Data Portals

In addition to physical neurotechnology centers, in the modern era, collaboration can be virtual, particularly for computational work. In an achievable ideal, a single web portal could serve as an entry point into data repositories, atlases, code collections, and an interactive ecosystem where researchers from around the world could work together and collaborate in the cloud (Neuro Cloud Consortium, 2016). Virtual data facilities could provide a major thrust to international collaborations and common data standards, as in the NeuroData Without Borders Initiative. Sharing neuroscience data and tools, and working together to store, analyze, integrate, and model neuroscience data, are particular interests of the NSF (US) and the HBP (Europe).

Virtual Centers

Virtual centers devoted to specific projects are also being considered and planned by many scientists. In these alliances, teams of laboratories working on the same focused question, the same part of the brain, or the same behavior are integrated to work together effectively (Mainen et al., 2016). Some of these alliances are grassroots efforts, and some have been initiated by funding agencies like the Simons Foundation in its Global Brain Project.

Funding Without Borders

The complementarity of the international brain projects has one potential problem, which is that expertise in a given project does not necessarily reside in a single country. We suggest that removing national barriers for funding opportunities is a desirable goal. Since it makes sense for scientists to move from one country to another in the pursuit and creation of knowledge, it is natural that funding should also follow suit. The HBP exemplifies this, but only within the European Union partner countries; the US Brain Initiative has gone a step further by making funding available to any researcher from any country in the world, as long at the proposed project is deemed worthy by the study sections that review it. A Global Brain Initiative could pioneer this style of funding for science in general as a model that could be copied by other fields.

Training Without Borders

Scientific talent exists everywhere, and scientific training should be open to anyone in the world, regardless of nationality. Many countries accept foreign students in PhD and postdoctoral programs, and the Human Frontiers Science Program has been a strong supporter of international training, but there are still significant barriers that could be reduced or removed. A first step would be thinking beyond formal degree-granting programs: summer schools or short courses have the potential to bring together teachers and students throughout the world, and investing in these courses will lead to connections that last for entire scientific careers.

Neuroethics and Societal Outreach

The ethical questions raised by the use, development, and application of neurotechnologies are international questions. Many are similar to questions in other areas of bioethics, but they can carry more ethical, legal, or social weight because the activity of our brains leads to our innermost selves. Monitoring or modifying human brain activity must be addressed with an international and humanistic mindset. In medicine, we have the Hippocratic Oath and the Patient's Bills of Rights, deontologically coded into the Belmont Report. In neuroscience, similar ethical standards should apply to neuroscientists and clinicians who create or use new neurotechnologies (Goering and Yuste, 2016).

Ethical and societal questions are not questions for experts alone, and the discoveries in brain science will affect the population as a whole. Outreach and communication must be aspects of the new brain projects. Engaging citizens of many countries will emphasize that global neuroscience is a truly international collaboration and will build public support for the importance of trans-national science efforts for the future of the world.

Moving Forward: An International BRAIN Consortium

The enthusiasm and energy of brain initiatives around the world calls for international collaboration, as did earlier projects in genomics, astronomy, and physics. How could this collaboration be achieved? By analogy with the international Human Genome Organization (HUGO), we suggest the formation of an International Brain Consortium (''iBrain'') assembled from all public and private groups. Regular meetings of an iBrain Committee with scientific and administrative leaders of these groups and public meetings would help build consensus and avoid duplicated effort. Based on the success of the September meeting and the enthusiasm at that meeting and an earlier ''State of the Brain'' Keystone meeting in Austria, we think that the time is ripe for such effort, and we call on the leaders of the international brain projects to act. The federation of different projects into a global brain initiative that aims to understand the scientific basis of our common humanity could play an inspirational role in this era of increased nationalism. It would be a befitting role for science, which has always operated as a network of researchers that stretches in space across national boundaries and in time across generations.

ACKNOWLEDGMENTS

We thank the National Science Foundation (Grant DBI 1644405) and the Kavli Foundation for support.

REFERENCES

Alivisatos, A.P., Chun, M., Church, G.M., Greenspan, R.J., Roukes, M.L., and Yuste, R. (2012). Neuron *74*, 970–974.

Alivisatos, A.P., Chun, M., Church, G.M., Greenspan, R.J., Roukes, M.L., and Yuste, R. (2015). Neuron *88*, 445–448.

Goering, S., and Yuste, R. (2016). Cell *167*, 882–885.

Jorgenson, L.A., Newsome, W.T., Anderson, D.J., Bargmann, C.I., Brown, E.N., Deisseroth, K., Donoghue, J.P., Hudson, K.L., Ling, G.S., MacLeish, P.R., et al. (2015). Philos. Trans. R. Soc. Lond. B Biol. Sci. *370*, 20140164.

Koch, C., and Reid, R.C. (2012). Nature *483*, 397–398.

Mainen, Z.F., Häusser, M., and Pouget, A. (2016). Nature *539*, 159–161.

Neuro Cloud Consortium (2016). Neuron *92*, 622–627.