The European Future Technologies Conference and Exhibition 2011

Introducing the Human Brain Project

Henry Markram [a], Karlheinz Meier [b], Thomas Lippert [c], Sten Grillner [d], Richard Frackowiak [e], Stanislas Dehaene [f], Alois Knoll [g], Haim Sompolinsky [h], Kris Verstreken [i], Javier DeFelipe [j], Seth Grant [k], Jean-Pierre Changeux [l], Alois Saria [m]

[a] *École Polytechnique Fédérale de Lausanne, Route Cantonale, Lausanne 1015, Switzerland*[v]
[b] *Kirchhoff Institute for Physics, Im Neuenheimer Feld 227, Heidelberg 69120, Germany*
[c] *Forschungszentrum Jülich, Stetternicher Straße, Jülich 52428, Germany*
[d] *Nobel institute of Neurophysiology, Karolinska Institute, Retzius väg 8, SE-171 77 Stockholm, Sweden*
[e] *Centre Hospitalier Universitaire Vaudois, Rue de Bugnon 21, Lausanne 1011, Switzerland*
[f] *Cognitive Neuroimaging Unit, CEA-Saclay Centre NeuroSpin, Gif-sur-Yvette 91191, France*
[g] *Technical University of Munich, Arcisstraße 21, Munich 80333, Germany*
[h] *Hebrew University of Jerusalem, Mount Scopus 91905, Jerusalem, Israel*
[i] *IMEC, Kapeldreef 57, Heverlee 3001, Belgium*
[j] *Universidad Politécnica de Madrid, Ramiro De Maeztu, 7, 28040 Madrid, Spain*
[k] *Wellcome Trust Sanger Institute, A1301, Hinxton, Cambridgeshire CB10 1, United Kingdom*
[l] *Institut Pasteur, 28 Rue Doct Roux, 75015 Paris, France*
[m] *Medical University of Innsbruck, Innrain 52, Christoph-Probst-Platz, 6020 Innsbruck, Austria*

Abstract

The Human Brain Project (HBP) is a candidate project in the European Union's FET Flagship Program, funded by the ICT Program in the Seventh Framework Program. The project will develop a new integrated strategy for understanding the human brain and a novel research platform that will integrate all the data and knowledge we can acquire about the structure and function of the brain and use it to build unifying models that can be validated by simulations running on supercomputers. The project will drive the development of supercomputing for the life sciences, generate new neuroscientific data as a benchmark for modeling, develop radically new tools for informatics, modeling and simulation, and build virtual laboratories for collaborative basic and clinical studies, drug simulation and virtual prototyping of neuroprosthetic, neuromorphic, and robotic devices.
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Selection and peer review under responsibility of FET11
Keywords: Human brain; neuroscience; neuroinformatics; modeling; simulation; supercomputing; HPC; medicine; neuromorphics; neuroprosthetics; neurorobotics

1. Rationale

Psychiatric and neurological disease is estimated to affect 135 million Europeans (calculated from [1,2]). A 2005 study estimated the total cost to the European economy at between 390 and 700 billion euros per year [3]. Today the correct figure is almost certainly higher. However, the pharmaceutical companies that traditionally fund a large proportion of European brain research are pulling out [4] and academic neuroscience is fragmented. A hundred years of research has studied the brain at different levels of organization, in different species, at different stages of development. New technologies are providing a flood of data about genes and gene expression, the production and distribution of proteins, protein interactions, cells, the connections between cells, and the fiber tracts that connect different regions of

the brain. To exploit this knowledge, we need a strategy to put it all together. The HBP proposes a new approach that uses supercomputer technology to integrate everything we know in multilevel brain models.

2. Brain Simulation as the Integration Strategy

The brain has many different levels of organization, each with its own characteristic elements, interactions, emergent properties, and time scales. Integrating the data from these different levels poses a massive challenge. The strategy proposed by the Human Brain Project is grounded in two major trends.

1. Modern supercomputers will soon be powerful enough to support multilevel computer models of the human brain. Terascale computers have already allowed EPFL's Blue Brain Project [5] to make the leap from simulations of single neurons to cellular level simulations of neuronal microcircuits. Petascale computers, now available, are potentially powerful enough for cellular-level simulations of the whole rodent brain, or for molecular level simulations of single neurons. Exascale computers, predicted for the end of the decade, could allow cellular level simulations of the complete human brain with dynamic switching to molecular-level simulation of parts of the brain when required.
2. New informatics and modeling approaches are making it possible to reverse engineer the detailed structure of the human brain without resort to invasive methods of data collection. By analyzing very large volumes of data, from different –omics levels, we can identify principles of design that cannot emerge from smaller studies and that make it possible to extrapolate data collected in one species to others, including humans. This *Predictive Reverse Engineering* will allow us to predict how different patterns of gene expression produce neurons with different morphologies expressing different molecules, and different synaptic connections. Other generalizing rules will predict the way neurons migrate into position and grow their arbors and the way they connect with each other to form micro- meso- and macro-level circuits. Models of non-neuronal cells and blood vessels, integrated in the overall model, will allow simulation of metabolism and nutrition. Data collected with non-invasive methods will further constrain the model. This kind of *Multiomic Model Integration* will enable ever more accurate models of the human brain, providing a focus for the project's integration strategy.

3. Scope of the Simulations

Simulating the brain is a major challenge that calls for industrial capabilities and organization. The project will develop these capabilities and make them available to relevant scientific communities through a remotely accessible Brain Simulation Facility, whose capabilities will be continually upgraded over the duration of the project. The Facility will implement well-defined workflows and tool chains, many of which have already been tested in preliminary work. The project will support the work of the INCF to federate data from multiple sources (literature, laboratory experiments, screening, clinical testing, etc.) and to reconstruct missing data. Rules extracted from the data will be transformed into mathematical models of specific brain structures and functionality (e.g. electrical behavior of neurons, protein interactions, synaptic transmission and plasticity, neuro-glial-vascular coupling, etc.). Software tools ("builders") will allow researchers to instantiate these models with their own hypotheses and to collaboratively define *in silico* experiments. The project's HPC capabilities (see below) will make it possible to simulate the models' emergent properties and behavior. In this way, researchers will be able to interact with simulations using tools ("virtual instruments") equivalent to those they use in *in vivo* and *in vitro* experiments. Discrepancies between *in silico* and laboratory experiments will help to refine models and to identify areas where more data is needed or rules need to be revised.

Like other large-scale science projects, the HBP will scale up gradually. In the first years, the focus will be on modeling the neurons, synapses, microcircuits, brain areas and brain systems of the rodent brain. As our software and computing capabilities expand, we will simulate larger brains (cat, macaque) with more and more biological detail, moving steadily towards the complete human brain. A special "pillar of activity" will be dedicated to the emergence of human cognition and behavior. Today, it is not known what level of biological detail we will need to explain behavior, cognition and intelligence. The HBP research platform will help to answer such questions. As part of this work, we will connect brain models to robots functioning in real or virtual environments, test their capabilities on "benchmark problems", and trace the causal chain of events leading to these capabilities.

4. The HBP and High Performance Computing

The Human Brain Project would not be possible without modern High Performance Computing (HPC). HPC capabilities are required to store, analyze and visualize basic and clinical data, and will play an essential role in Predictive Reverse Engineering, multiomic model building, simulation, and *in silico* experiments. Exascale supercomputers, planned to be available before the end of the decade, will be sufficient for cellular level models of the complete human brain and for simulations that dynamically switch to the molecular level in selected areas. The project will develop digital acceleration techniques (based on FPGAs or ASICs) and neuromorphic accelerators that further enhance its HPC capabilities. The design and configuration of the necessary hardware and software will be performed in close collaboration with manufacturers. The project's work in this area will place a special emphasis on visual steering and interactivity for supercomputing applications – critical not just for brain simulation but for simulation-based research throughout the life sciences. To achieve these goals, we will build a HPC Design Cockpit to facilitate the customization and optimization of HPC systems and a Simulation Cockpit, allowing interactive global collaboration on model building and *in silico* experiments.

5. The HBP and Medicine

Today, there are only very few brain disorders whose causes are fully understood, and very few drugs whose mechanism of action is known or that offer more than symptomatic relief. The HBP will offer new opportunities for clinicians and for researchers. Groups working in the project have already collected and analyzed very large volumes of imaging data from hospitals, and have used informatics-based analysis to achieve highly effective early diagnosis of brain disease [6]. The HBP will develop this work, which we expect to yield clinically useful results in the relatively short term. In a medium-term perspective, the HBP simulation platform will make it possible to explore hypotheses of causation for brain diseases, and begin simulating the effects of drug candidates. Simulation-based prototypes will enormously facilitate the development of neuroprosthetic devices. These new possibilities will shorten design cycles, lower costs and improve prospects for the development of effective treatments. To allow effective drug simulation, the project will make an important effort to explore and simulate molecular level mechanisms.

6. The HBP and Information Technology

Although modern computing technology outperforms the human brain on many tasks, it cannot match its cognitive capabilities, flexibility, robustness, and energy-efficiency. The HBP will provide the technology and knowledge to replicate some of these capabilities in novel computing devices and systems. The project will build on the work of European projects such as SenseMaker [7], FACETS [8], BrainScales [9] and SpiNNaker [10] that have already built "neuromorphic chips". Meanwhile, HBP theoretical neuroscientists will analyze brain models and simulations to reveal fundamental principles of neural computation. An important goal will be to identify the simplest neuronal circuit capable of providing specific functionality and to "export" the circuit for theoretical analysis and implementation in neuromorphic technology. We anticipate that the first devices, based on small scale, low granularity models, will be released at an early stage of the project. As the project progresses towards the human brain, they will become ever more powerful, robust, and energy efficient. A key application will be as controllers for truly intelligent robots with broad applications in industry, services and the home.

7. Summary

The HBP sets academia and industry on a new road to understanding the human brain. On the way, it will unify existing biological knowledge, generate new approaches and methods, for the brain sciences, and develop new intelligent technologies. Finally, the HBP will provide a new tool for investigations of the brain's diseases and for easier, faster, and cheaper development of new treatments. The potential social and economic impact is enormous. Necessarily, the project will dedicate a significant effort to educating young scientists in its new integrated approach to science, medicine and technology, and to dialog with the public on critical ethical, legal and social issues.

Supplementary material related to this article found, in the online version, at doi:10.1016/j.procs.2011.12.015.

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