The Human Brain Project (HBP)

A proposal under the FET-Flagship program

October 20, 2010

Goal

The goal of the Human Brain Project (HBP) is to build the informatics, modeling and supercomputing technologies needed to simulate and understand the human brain. Major expected advances include new tools to fight the growing impact of brain disease on public health and well being, and a new class of technologies with brain-like intelligence, to empower people to make decisions in an increasingly complex information society.

More specifically, the HBP will:

1. Establish a global multidisciplinary program to organize and informatically analyze basic and clinical data about the brain and to model, simulate and understand animal and human brains at all levels of organization, from genes to cognition and behavior;
2. Design and implement an exascale supercomputer, with the power and functionality to make these goals feasible, including novel capabilities for real time model building, interactive simulation, visualization and data access; contribute to longer term prospects for brain-inspired supercomputing;
3. Derive novel technologies, beginning with enhancements to current telecommunications, multimedia, internet, ambient intelligence, data storage, real-time data analysis, virtual realty and gaming systems, but leading toward completely new kinds of information processing and genuine intelligence for robots;
4. Develop applications in medical and pharmacological research, including new diagnostic and disease monitoring tools, simulations of brain disease, and simulations of the effects and side effects of drugs.

Background

For at least two and half thousand years, humans have tried to understand what it means to perceive, to feel, to remember, to reason and to know. Today, this enquiry has turned into a quest to understand the brain. With the rise in brain disease as we adapt to an ever more complex society and as life spans increase, the quest has become urgent. And, as if this were not enough, we now have a new reason to study the brain: scientists have begun to see it as a source of *brain-derived* technologies.

The human brain has capabilities unmatched by any computer. It is energy-efficient and resilient to damage, it can effortlessly detect and categorize patterns in data, it can store and rapidly retrieve vast volumes of information, learn, adapt, make complex decisions, and pursue goalsm it can think abstractly and creatively and develop language. Information and Communiucation Technologies (ICT) with even some of these capabilities would hugely enhance our current computers and ICT devices, while opening the road to systems with completely new capabilities.

To derive such technologies, it will be necessary to delve deep into the workings of the brain and discover the key principles underlying its design and operation. Two key research developments make this possible. The first is the advent of *high throughput screening and neuroinformatics*, which allow scientists to collect and organize huge volumes of basic and clinical data on the brain. The Allen Brain Atlas has demonstrated that large-scale approaches can be very effective at exposing correlations and other patterns in data and in extracting general organizing principles. Other large-scale initiatives, such as the International Neuroinformatics Coordinating Facility (INCF), have begun federating worldwide data. The Human Connectome Project is working to obtain a deeper understanding of the brain's internal connections. However, this kind of informatics-based science, while incredibly valuable, is not enough, on its own, to show how the genome "unravels" to produce the brain and how the interactions between different elements in the brain support behavior and cognition. This requires new enabling technologies: modern *High Performance Computing* (HPC) and simulation-based science. Supercomputer-based simulations of the brain have the potential to model and simulate biological processes at every possible level of biological organization and thus to reveal the complex chains of causation leading from genes, molecules, cells and connections, to behavior and cognition. Brain simulations can organize and focus biological data and knowledge and allow us to address the ultimate questions concerning the roots of cognition and behavior. They are the key enabling technology for a new approach to brain disease. The knowledge they provide can lay the foundations for a completely new class of ICT.

The Project

The HBP is organized around a unified agenda to gather and informatically analyze data on the brain, derive organizing principles and build brain models with as much biological detail as technically possible. As brain science and medicine advance the models will evolve to further accelerate our understanding of the brain and its diseases. Building such models represents an extreme applications challenge that will shape the future of supercomputing, and provide the technologies we need to create realistic simulations of life processes. The new simulation technology will allow us to trace the causal chains of events leading from genes and molecules to cognition and behavior, and to design drugs targeting abnormalities leading to disease. Combined with high-level mathematical theories of brain function, it will be possible to build a new class of brain-like hardware devices and computer architectures. What follows is a brief description of the different facets of the project.

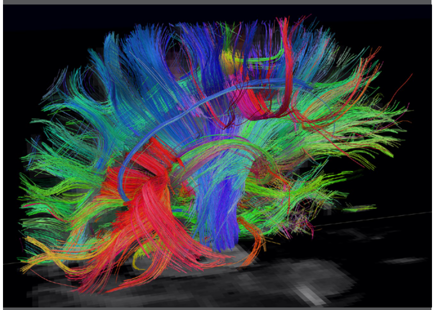
Modeling and simulating the brain

The HBP's main goal is to pave the way to simulating the complete human brain. The task is huge and enormously complex. The project aims to completely solve the technological challenges involved in simulating the human brain down to the molecular level, and accounting for its multiple levels of organization, development and plasticity. Meeting these challenges will drive rapid and radical innovations in HPC (see below). Neuroscientists, clinical researchers, and computational neuroscientists will use informatics and simulation technologies to facilitate collaboration, and to derive fundamental organizing principles for each level. These principles will allow us to understand how genes are differentially expressed in different types of neuron, how protein is produced, distributed and metabolized in cells, how subcellular organelles and different neuron morphologies are formed, how neurons are organized and connected in microcircuits, how microcircuits are arranged to form brain regions and how these regions are connected to form the brain. Understanding these principles will make it possible to model the human brain using data collected primarily with non-invasive techniques. The same principles will provide a solid foundation for new clinical diagnostic tools and new technologies.

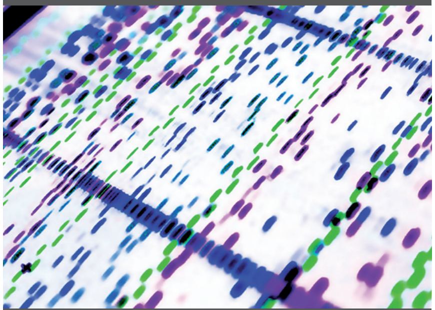
The project will build a sequence of biophysical, phenomenological and abstract models at various resolutions (molecular, subcellular, cellular) and scales (micro-, meso- and macrocircuits, whole brain), and in different species, including rat, mouse, cat, monkey and ultimately humans. This progression will make it possible to learn and transfer principles from one system to the next before reaching the human brain. The multi-scale approach also provides a natural way of optimizing the use of computational resources, in which highly active neurons are simulated at high resolution while simulation of less active neurons uses lower resolution models. The litmus test for success will be to compare the emergent properties of model neurons, circuits, systems and brains to the vast body of data from experimental neuroscience. As models are built scientists will refine them and use them to test their hypotheses. Ultimately, we will connect the models to robots in a closed loop system and to compare the memory, adaptability, behaviors and intelligence of brain-enabled robots to animal and human benchmarks established by the behavioral and cognitive neuroscience communities.

Facility for Brain Simulation

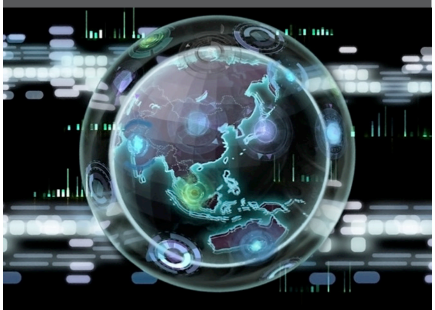
HBP brain modeling and simulation will be centered on a specially created *Facility for Simulation-Based Brain Research* that will integrate results from all the HBP's activities. The Facility's Internet portal will provide access to an integrated research environment that includes an HPC infrastructure and a wide variety of tools, data and services accessible remotely to scientists throughout the world. A *simulation cockpit* will integrate standardized data from neuroscience experiments and industrial-scale screening, clinical and experimental data on brain disease and models for all possible levels of brain organization. The Facility will collaborate with existing EU consortia to provide access to data on the brain in databases all over the globe,



Neuroscience: investigation of strategic aspects of brain function, critical for brain modeling.



Screening: large-scale production of data by high throughput facilities in industry and at selected universities.



Neuroinformatics: analysis, standardization and databasing of past and current knowledge; development of tools and techniques to extract fundamental organizing principles.

Brain Probes: development of new nano, micro, genetic, optical, and electrical technologies making it possible to study an ever broader range of brain structures and functions in greater depth, and more rapidly than is currently possible.

advanced informatics and data analysis tools, software to build, simulate, and analyze brain models and to visualize them interactively and tools to design customized simulation experiments, build virtual laboratories and set up teaching facilities.

Facility for High Performance Computing Research

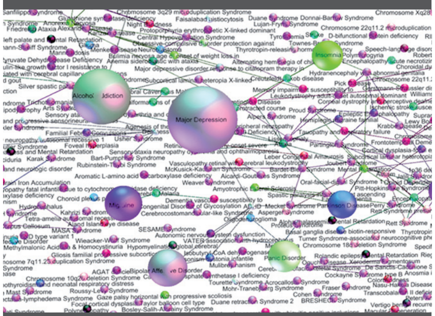
Building models of the complete human brain will require supercomputers at least a thousand times more powerful than today's largest machines. As the project's modeling effort comes closer to simulating the whole human brain, it will need dedicated access to progressively larger scale systems. Building such computers will demand new solutions for energy consumption, data transmission, resilience, programmability and interactivity, as well as completely new kinds of functionality. A particularly important requirement is interactivity, so that users can engage in real time with data, model building, simulations, visualization, and analysis. The HBP's strategy will be to find the best combination of existing and new hardware components from computer manufacturers and to drive the development of the middleware and other software needed to make the new systerms useful and usable for research communities. In line with this approach, the HBP will create a special *Facility for High Performance Computing Research*. The first task of the new Facility will be to work with manufacturers to explore possible hardware configurations. On this basis, the Facility will proceed to build a customized system that can scale to exascale levels of data storage and processing. In a longer-term perspective, the facility will investigate ways of exploiting the organizing principles of the brain in future supercomputers. This work will be based on the computing principles, hardware devices and systems developed by the *Facility for Brain-Derived ICT* (see below).

Facility for Brain-Derived ICT

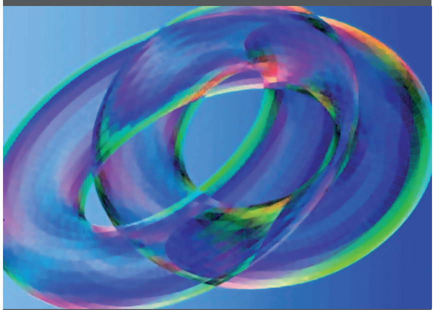
To turn knowledge of the brain into technology, it will be necessary to develop high-level mathematically-based theories of brain function, to segment and simplify models of neurons and brain circuitry, and to derive general principles of brain-like computing. This will be the mission of a new *Facility for Brain-Derived ICT*. As the HBP builds ever more sophisticated models of the brain, the facility will use simplified versions of these models as the basis for increasingly sophisticated hardware devices and systems. Key low level features are likely to include low energy consumption, resilience and robustness, new techniques of data storage and transmission, computing with noisy, error prone, and approximate information, adaptive problem solving, and self-repair. In parallel with this work, computational neuroscientists will develop and test cognitive architectures using top down approaches based on mathematical theories of brain function. At a relatively early stage of the project, the combination of the two approaches will enable the development of new sensors and measuring devices. It will also be possible to develop novel systems for pattern recognition, categorization, information retrieval and data analysis. As the HBP progresses, it will investigate more complex applications, in which brain-like architectures open the road to systems with genuine intelligence. This prospect promises to enormously enhance and ultimately to transform the computing and robotics we know today.

Facility for Neurorobotics

Despite numerous attempts that have yielded interesting results, no current robot can emulate the cognition and behavior of simple animals, let alone of humans. This would require a brain or brain-like system. To meet this challenge, the HBP will set up a *Facility for Neurorobotics*. The first task of the new facility will be to couple detailed brain models on supercomputers to virtual and physical robots in a closed loop. This will make it possible to study the emergence of cognition and behavior as brain-enabled robots adapt to their environment. The second task will be to simplify these models in ways that preserve desirable cognitive capabilities such as complex pattern recognition, decision-making, and goal-oriented behavior. This work will be informed by results from cognitive theory and modeling. The result will be reduced software and hardware architectures suitable for implementation in intelligent robots. Such robots will have many intelligent capabilities completely lacking in current machines. These will include the ability to create neural representations of the robot body, and its environment (including other animate systems) and their interactions. Such truly embodied intelligence would give the robot novel capabilities such as the ability to interpret the actions of human beings and human-made machines with which it interacts, goal-oriented navigation in novel environments and abstract action planning in real-world situations. Systems with this kind of capability would have an enormous range of applications for people on the move (as mobile personal assis-



Clinical Brain Research: exploitation of the power of ICT to study the 560 known human brain disorders as an interconnected complex system (the *diseasome*); derivation of constraints for modeling.



Modeling: capture of structural and functional properties and principles of the brain's operations in mathematical abstractions.

Simulation: creation of the software required for multi-scale modeling.

Supercomputing: design and optimization of an exascale computer optimized for brain simulation. Creation and management of an HPC facility for brain modeling and simulation.

tants) in the home (as domestic helpers, carers, and butlers), industry (in complex manufacturing, and security), health care (assistance for the sick and for elderly people, e-diagnosis, e-surgery), and education (as personal educators).

Facility for Informatics-Based Clinical Brain Research

The HBP will drive information-based approaches to brain disorders. To this end it will create a special *Facility for Informatics-Based Clinical Brain Research*. The Facility will network existing initiatives and consortia, hospitals and clinical research centers throughout the world to collect and standardize large volumes of data related to the diseases of the brain and to facilitate access to this data by relevant scientistic communities. It will then use statistics, advanced mathematics and informatics to study the differences and similarities among these diseases, identifying new diagnostic indicators and deriving novel principles of brain organization, that it will re-use in its modeling effort. The longer-term goal is to build biologically realistic models of Alzheimer's and Parkinson's Disease, schizophrenia, depression and other brain disorders, and to investigate their causes. Detailed computer models of disease will make it possible to simulate the action of drugs, potentially speeding the development of new treatments and reducing side effects.

Facility for Brain Screening

To build biologically accurate brain models, the HBP will need huge volumes of standardized data, including data on genes, proteins, cells, micro-, meso-, and macrocircuits, as well as images of the whole brain. Data on emergent properties of the brain will come from laboratories and will be federated by organizations such as the INCF, with whom the project will collaborate. Obtaining more basic data will require large-scale initiatives like the Allen Brain Atlas for all levels of biological organization. The *Facility for Brain Screening* will collaborate with industries and university with high throughput facilities to launch such initiatives wherever they are required and will drive the development of novel ICT approaches to screening in strategic areas (e.g. nano, micro-, and photonic technologies).

Ethical, legal and social issues

The HBP will raise important ethical, legal, social, political and philosophical issues both about the *research itself* and its *potential applications*. At the same time, its contributions to knowledge of the brain, cognition and behavior will have important philosophical and conceptual implications touching on basic concepts of what makes us human Against this background, the HBP will include a major program of activities dedicated to ethical, legal and social issues. The program will bring together scholars in the brain sciences, social sciences, and the humanities to study and discuss relevant issues and will use all available channels to encourage open, well-informed debate, to dissipate potential public concerns and to enhance appreciation of the potential benefits of the project's work.

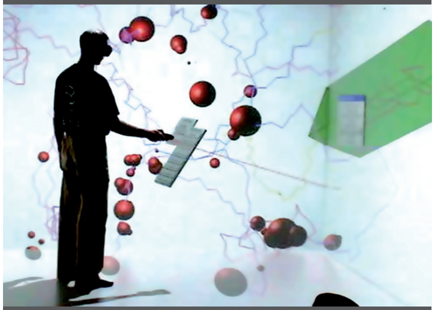
Education

The 21st century is witnessing a data deluge driven by the industrialization of many aspects of the scientific process, especially in the life science and medicine. The need to make sense of the growing volume of data is driving a rapid expansion in informatics-based and simulation-based science and medicine. The advent of supercomputers powerful enough to simulate life processes, the development of mathematical abstractions to describe them, and their application in simulations and models pose major challenges for the way we educate students and prepare the young researchers of the future. The HBP consititutes an extreme form of simulation-based research and is thus in an ideal position to teach this new science, and its applications in medicine and technology. The HBP will thus exploit the project's unique technology to build a novel educational platform where the science, medicine and brain-derived technologies can be demonstrated through internet-accessible hands-on interactions in virtual laboratories, lecture theaters, and realworld like enviornments (research labs, hospitals, factories). The project will use this platform as the basis for a unique program of transdisciplinary education for young scientists and technologists wishing to build a career in relevant disciplines. Additional educational activities will disseminate new knowledge generated by the project as it appears reaching out to the lay public, and to every level of the educational system.

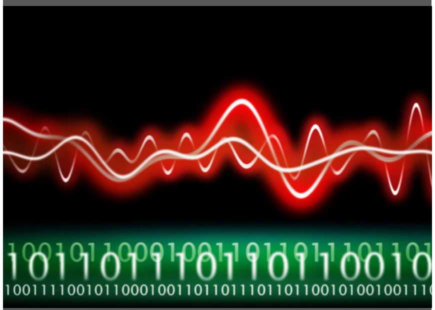
Impact

Neuroscience & Medicine

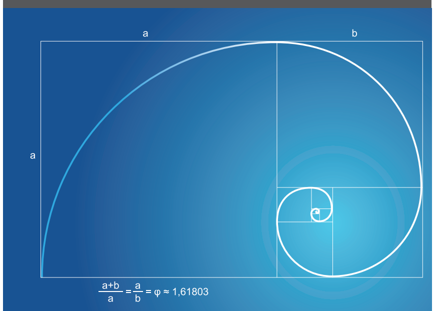
The first sign that biologically detailed brain models can support even the simplest form behavior - navigating through obstacles or remembering where a re-



Visualization: new techniques for interactive navigation and steering of supercomputing simulations.



Analytics: analysis of large volumes of data using a broad range of mathematical and statistical techniques.



Computation: understanding the fundamental mathematical principles of neural computation and the emergence of intelligence.

Neurorobotics: interfacing virtual and physical robots to brain models.

ward is located - would be a major breakthrough for the project and for brain science. Once such models are in place it will be become possible to trace the genes, molecules, cells, synapses, connections, pathways, and brain areas involved and identify vulnerabilities of the system that are implicated in disease. Models displaying more advanced functions, such as goal-oriented behavior, action-planning, reasoning more advanced intelligence and possibly language, will help unravel the elementary steps that lead to higher cognition and the multiple factors responsible for brain disease. Studies of clinical data and of the commonalities and dissimilarities among brain diseases will contribute rapidly to medical diagnostics. As the HBP expands its capabilities in molecular modeling, it will become possible to test specific hypotheses of disease causation and candidate treatments based on these hypotheses. Simulating drug effects will provide a firm foundation for rational drug design and for shortening the drug design cycle. The impact on medicine, industry and society will be far reaching. Disease and drug simulation will also lead to a drastic reduction in the use of animals in research, thus contributing to the EU's goal of *replacing, reducing and refining* animal testing.

High Performance, Low Energy Computing

Simulating the Human Brain will drive and guide the evolution of supercomputing and supercomputing-based simulation in the life sciences and elsewhere. Access to data in exascale data centers, interactive model building, molecular level brain simulation, and, visual steering of simulations, will create huge challenges for HPC technology. Meeting these challenges will make supercomputers far more capable, valuable and far more useful for specialists and non-specialists alike. The project will actively drive new concepts for cluster-based supercomputing and for interactive supercomputing. These solutions will allow users to visually explore vast volumes of data, build complex models, test hypotheses of brain function, simulate the brain, image simulations and analyse the brain's design and operations in real-time. The possibility of remote real-time visualization holds the potential to make supercomputing accessible to the general public, creating opportunities for mass-market applications including e-medicine, and virtual environments for schools, business and entertainment – even beyond current concepts of the 3D Internet. New insights into the way the brain computes, stores and transmits information will generate novel solutions for efficient energy management, memory, data movement, resilience and self-repair, addressing the growing challenges posed by the data deluge and laying the foundations for truly brain-inspired supercomputing.

Brain-derived ICT and Neurorobotics

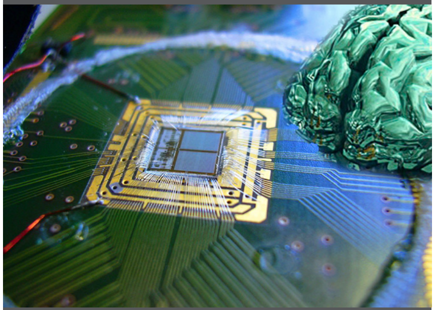
In the short-term, brain-derived technologies will add intelligence to a spectrum of devices by enhancing image and feature processing, data analysis, information retrieval, streaming and management of information, internet and mobile communications, and automated perception-action decisions. In the longer term, the HBP will lay the foundations for a paradigm shift in computing and robotics, offering valuable new capabilities such as, learning, adaptability, flexibility, goal-oriented behavior, and abstract action planning in novel real-world situations. These will allow the development of new types of personal computers and hand held devices, as well as genuinely intelligent robots with a huge range of potential applications in industry, health, education, research and the home.

Hightech and Biotechnology

The HBPs need for industrial scale, high quality data will drive high throughput screening technology, and will have a major impact on European hightech and biotech SMEs. New technologies from this effort (e.g. new techniques for genome analysis, single cell transcriptomics and proteomics, cellular resolution whole brain scanning, molecular level whole brain functional imaging) will have a major impact across the life sciences.

The Consortium

The project is proposed by a group of partners from Switzerland, Germany, Sweden, the UK, France, Spain, the Netherlands, Italy, Austria and other European and non-European countries, including representatives of existing large-scale initiatives in neuroscience, supercomputing, medicine, brain-inspired ICT and robotics and a broad range of computing, hightech, biotech and pharmaceutical industries, and many major hospitals, healthcare centers and clinics around the world.



Brain-derived ICT: construction of neuromorphic chips and larger systems derived from the circuitry of the brain.

Education: training students and educating the public about the brain, its diseases and the exploitation of knowledge about the brain in future ICT technologies.

Society: exploring the societal, ethical and philosophical implications of brain simulation and its application to brain disease and future ICT.

Coordination: management of the consortium, ensuring efficient integration and self-sustainability.

Contacts

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Leading scientists currently working in the HBP initiative include Jean-Piere Changeux, Collège de France, **France**, Ethics & Society; Javier DeFelipe, UPM, **Spain**, Neuroscience; Yadin Dudai, Weizmann Institute, **Israel**, Ethics & Society; Seth Grant, Sanger, **UK**, Large-scale Neuroscience; Andreas Herz, Bernstein Center, **Germany**, Modeling; Sean Hill, EPFL, Neuroinformatics, **Switzerland**; Alois Knoll, TUM, **Germany**, Neurorobotics; Jose Pena, UMP; **Spain**, Data Analysis; Danny Porath, Hebrew U, **Israel**, Brain Probes; Alois Saria, Innsbruck, **Austria**, Education; Thomas Schülthess, CSCS, **Switzerland**, HPC; Felix Schürmann, EPFL, **Switzerland**, Simulation; Idan Segev, Hebrew U, **Israel**, Modeling; Alex Thomson, U of London, **UK**, Neuroscience; Antoine Triller, CNRS, **France**, Neuroscience.

A large circle of scientists has expressed their interest in participation. They include: Jim Austin, Uni of York, **UK**, Integration; Wanda Andreoni, CECAM, **Switzerland**, Modeling; Alim-Louis Benabid, Grenoble, **France**, Diseasome; Driss Boussaoud, CNRS, **France**, Diseasome; Matthias Bethge, Bernstein Center, **Germany**, Retina Modeling; Raymond Campagnolo, Grenoble, **France**, Brain Probes; Angelo Egidio, U Pavia, **Italy**, Neuroscience; Sue Denham, U Plymouth, **UK**, Modeling; Peter Desain, Donders Institute, **Netherlands**, Cognition; Markus Diesmann, Riken, **Japan**, Modeling; Hans-Ulrich Dodt, TUW, **Austria**, Large-Scale Neuroscience; Gregor Eichele, Max-Plank, **Germany**, Large-Scale Neuroscience; Mark Ellisman, UCSD, **USA**, Neuroinformatics; Tamas Freund, HAS, **Hungary**, Neuroscience; Dario Floreano, EPFL, **Switzerland**, Neurorobotics; Fernando Ferri, Trier, **Germany**, Visualization; Steve Furber, U Manchester, **UK**, Neuromorphics; Oliver Faugeras, INRIA, **France**, Modeling; Lyle Graham, CNRS, **France**, Modeling; Christiane Gamrat, **France**, Neuromorphics; Michael Hausser, UCL, **UK**, Neuroscience; Allan Jones, Allen Brain Atlas, **USA**, Large-Scale Neuroscience; Viktor Jirsa, CNRS, **France**, Modeling; Mira Marcus-Kalissh, TAU, **Israel**, Brain Body; Marcus Kaiser, Newcastle U, **UK**, Data Analysis; Anders Lansner, KTH, **Sweden**, Modeling; Jeanette Hellgren Kotaleski, KTH, **Sweden**, Modeling; Edvard Moser, NUST, **Norway**, Neuroscience; David Lester, U Manchester, **UK**, HPC; Yusuf Leblebici, EPFL, **Switzerland**, Neuromorphics; Enrico Macil, Polito, **Italy**, Neuromorphics; Corinne Mestais, Grenoble, **France**; Brain Probes; Pierre Magistretti, EPFL, **Switzerland**, Neuroscience; Johnny Ottesen, RUC, **Denmark**, Modeling; Guy Orban, Leuven, **Belgium**, Neuroscience; Francesco Pavone, LENS, **Italy**, Large-scale Neuroscience; Alain Prochianz, CNRS, **France**, Neuroscience; Claire Prummel, Grenoble, **France**, Brain Probes; Ranolfo Romo, UNAM, **Mexico**, Neuroscience; Terry Sejnowski, Salk, **USA**, Modeling; Bernd Stahl, De Montfort University, **UK**, Ethics; Leslie Smith, U Sterling, **UK**, Neurorobotics; Paul Tiesinga, Donders Institute, **Netherlands**, Neuroscience; Yun Wang, Wenzhou Med Coll China, Large-scale Neuroscience; Paul Verschure, Pompeu Fabra U., **Spain**, Neurorobotics; Robert Williams, UT, **USA**, Neuroinformatics; Chris Zeeuw, NIN, **Netherlands**, ICT.

Many existing consortia and organizations (CECAM, PRACE, etc) and companies in HPC, ICT, Hightech, Biotech, Bioservices, and pharmaceuticals have also expressed their interest in contributing to the project as affiliate partners.