The members of the HBP are saddened by the open letter posted on neurofuture.eu on 7 July 2014, as we feel that it divides rather than unifies our efforts to understand the brain. However, we recognize that the signatories have important concerns about the project. Here we try to clarify some of the main issues they touch on. We also invite the signatories to discuss their concerns in a direct scientific exchange with scientists leading the HBP and its subprojects.

**What is the nature of the HBP?** The HBP is a multi-disciplinary research project, funded by the European Commission’s (EC) Future and Emerging Technologies (FET) programme, which aims to develop an information and communication technology (ICT) platform that will be made available to the scientific community worldwide as a collaborative research tool. The project aims to exploit the creativity generated by the interaction between disciplines, with a view to developing new technologies for neuroscience, medicine, and computing. In this respect, the HBP is a project of unprecedented cross-disciplinary scope, bringing together mathematicians, physicists, engineers, computer scientists, experimental and theoretical neuroscientists, clinical neuroscientists, neurologists, philosophers, and ethicists. The level of collaboration required for such a team to succeed will challenge us all. With the burden of brain diseases in Europe costing more than 800 billion EUR per year, we strongly believe that such collaboration is a prerequisite for achieving new frontiers in brain research and that they cannot be reached with a multitude of individual research projects.

**HBP’s impact and scope.** The technologies we are developing are expected to provide a new methodology for studying the brain as a multi-level integrated system from genes all the way to cognition and behaviour. This will also allow for the classification of brain diseases based on biological data, and for the configuration of neuromorphic computing systems based on the design principles of the brain. To bring all these new capabilities together, the HBP aims to build a unified ICT platform that will enable all researchers to share information resources and work together collaboratively or in complementary ways, across disciplinary boundaries and regardless of where they are in the world. The HBP was not conceived as a data generation project, but recognizes that some data, critical to the development of the platforms and unlikely to be generated by others, will be essential. The unified platform is being designed to support large-scale collaborative projects, and will include modules for neuroinformatics, medical informatics, brain simulation, high performance computing, neuromorphic computing and neurorobotics. It is already on track to be opened to the neuroscience, medical, and computing communities in 2016. Neuroscientists, clinicians and computer scientists are key to specifying and shaping the development of the platforms, and will forge the paths for their respective communities to adopt the platforms. Creating and supporting an open user community for the platforms is among the most important goals of HBP and an essential part of the current work programme.
What is the HBP’s unique contribution to neuroscience? Each year, neuroscience research receives an estimated 1 billion EUR in Europe, and at least 7 billion USD globally. While this work generates a vast amount of valuable data, there is currently no technology for sharing, organising, analysing or integrating this information, beyond papers and even databases. The HBP will provide the critical missing layer to move towards a multi-level reconstruction and simulation of the brain. This will require the development of novel supercomputing software and hardware, analysis software, algorithms, search technology and much more. The target is the mouse brain, and ultimately the human brain.

How is HBP contributing to medicine? The HBP also aims to provide the medical community with the missing technological layer to access unused patient data while respecting privacy. New technologies are needed to search multi-level clinical data for unique biological patterns across vast numbers of patients with all kinds of disorders. These patterns could help to achieve better classifications of brain diseases and to develop a draft map of brain diseases; point to possible causes of disease, help drug companies understand why drugs succeeded or failed, and allow the modelling of brain disease. As neuroscientists we must ensure that our work is benefitting society. While the HBP does not guarantee cures, its technologies will at least provide better chances for diagnosing brain-related diseases and for finding new therapeutic targets.

How is HBP harnessing and developing computing? The HBP will use neuroscience data to configure neuromorphic computing systems. This is a truly exciting and unique opportunity for Europe that will allow us to apply and test our knowledge of brain circuits and computational principles. For the first time, it will be possible to construct large-scale neuromorphic computing systems that fully exploit the capability of modern electronics technologies, including brain-inspired features like energy efficiency and the ability to self-organize and adapt. This could open up a whole new paradigm for computing. To succeed, we will build a strong cross-disciplinary link between the neuroinformatics and simulation modules to derive circuits from the biological data as a foundation for neuromorphic systems.

What are the concerns of the open letter? The open letter expresses the concern that these goals are so unrealistic that they will damage all of neuroscience, and states that not enough is known to take on such a challenge. We share this uncertainty. However we contend that no one really knows how much neuroscience data is currently available because it has never been organized, and that no-one even knows how much data is needed to begin such an endeavour. Reconstructing and simulating the human brain is a vision, a target; the benefits will come from the technology needed to get there. That technology, developed by the HBP, will benefit all of neuroscience as well as related fields. Many other areas of science have demonstrated that simulation can be a tool to create new knowledge, not just to confirm existing results.

What is the HBP Approach? The HBP wants to galvanize the scientific community to take on the challenge of finding out what we know, what we can predict, and what we still need to measure. This is a proposal for a methodological paradigm shift, to combine our data to get more value out of what we already generate. It also comes with a cultural paradigm: be it to reconstruct and simulate a single synapse, neuron, brain region, whole brain or a disease, large teams of scientists, clinicians, and engineers need to work side-by-side on a single problem. It pushes all of us beyond what we are used to and are comfortable with. This is an essential state change that is needed to leverage everyone’s data and synthesize all our knowledge. If we do not begin such an effort, neuroscience will not be in a position to shape and exploit emerging supercomputing and big data technologies. The European Commission was forward-thinking to accept our proposal, and the spirit of the Flagship initiatives is to go far beyond what we would normally do.
**What is the global perspective?** Some media comments related to the open letter suggest that the US BRAIN Initiative is a better plan for neuroscience research because it distributes funding broadly to many areas of independent investigation. There is no question that such an initiative is of enormous value. The HBP, however, is a data integration project, not a data generation project, and has an annual budget that is a small fraction of the BRAIN Initiative’s targeted USD 500 million per year. Europe has a chance to do something unique for the brain, medicine, and computing that is synergistic with and complementary to other ongoing brain initiatives. The common platform for data integration, a central goal of the HBP, is a key missing ingredient in the arsenal of approaches available in neuroscience.

**How will HBP be reviewed?** The Flagship proposal was rigorously evaluated during nearly four years of pre-proposal discussions, with a final evaluation by a panel of 25 world experts across the relevant disciplines. The project is described in detail with milestones and deliverables, which are carefully monitored by the EC. After 12 months of operation the project will undergo its first formal review in which every milestone and deliverable will be verified and judged by an independent panel of experts. The EC has all the mechanisms in place to monitor and course correct the project should that become necessary.

**Is cognitive neuroscience part of HBP?** The open letter claims that cognitive neuroscience has been removed from the project. There is no question that cognition and behaviour are vital for the HBP. A group of cognitive neuroscientists was recently repositioned to what are called HBP Partnering Projects, where they can continue their independent investigations. The core HBP project will focus on building the ICT platforms. As they become established and evolve with detailed biological and theoretically inspired models, cognitive neuroscientists will be essential to experiment with the models and to perform biological experiments. Cognitive and behavioural neuroscience will therefore become an increasingly important component in the Core Project to shape the technologies as they are developed and to prepare the way for the whole cognitive and behavioural neuroscience community to engage with the platforms. In fact, cognitive and behavioural neuroscience will become the most significant component of neuroscience in HBP over the course of the project. However, for this to happen the platforms have to be in place first.

**How and why is the HBP structure changing?** With the completion of the Ramp-Up Phase and the beginning of the Operational Phase in 2016, the structure of the HBP will be modified. As agreed by the EC and EU Member States earlier this year, the project will be divided into a Core Project (CP) and Partnering Projects (PPs), each with an annual budget of EUR 50 million. The HBP Board of Directors agreed that the CP would focus on operation and improvement of the ICT platform while the PPs would conduct independent, investigator-driven research, exploiting the services offered by the ICT platform. The Board also decided that, in the Operational Phase, some cognitive neuroscience activities would fit better in the Partnering Projects, where they could focus on the investigator-driven research advocated by the signatories of the open letter. The need to synchronize the subprojects and meet the EC’s criteria for the Core and Partnering Projects did give rise to debate and tough decisions had to be made. The estimated 10,000 independent neuroscience investigators in Europe now all have a fair opportunity to participate in the HBP through the Partnering Projects and a fair opportunity to become involved in the Core Project. Some could enter the CP at different stages of the roadmap.
How are the Core Project and Partnering Projects funded? CP funding does not take away from existing neuroscience budgets, since it comes from the ICT arm of the EC. Funds for Partnering Projects come from individual member states. Partnering Projects are a label that any existing or future project can obtain if it is synergistic with the CP. Aside from a small amount of transnational funding, there is currently, no dedicated funding involved. However, projects that do become Partnering Projects are considered part of the matching funds for each member state. The experimental neuroscience component is planned to be around 20% of the project’s budget for both the core and partnering projects. Members of the core HBP consortium will themselves have the possibility to develop Partnering Projects, and will not have privileged access to funding for their own research. Partnering Projects also provide a mechanism for industry to become involved in the HBP.

How is HBP run? The project recognizes that governance must evolve as it moves into the next phase and the Executive Committee has already met with the project’s advisors to begin this evolution. Additional changes are expected following the EC’s evaluation of the Framework Partnership Agreement proposal, and further changes are expected during the lifetime of the HBP, as the project becomes a global resource for neuroscience, medicine and computing. The structural changes are intended to safeguard the project’s objectives and ensure that the neuroscience, medical and computing communities are fairly represented.

HBP is a united effort. We would like to end by stating that the fundamental objective of the HBP is to serve the neuroscience, medical and computing communities worldwide. Our hope is that this project will unite these communities and that, together with the Partnering Projects, we will be able to make significant broad advances. The HBP is not a funding mechanism and unfortunately it cannot include all relevant and worthy work at all stages. The HBP aims to unify by building technologies that everyone, including the signatories of the open letter, finds useful. Our strongest hope is that we can work together, and make the HBP a model Flagship for Europe.

The HBP Board of Directors
The HBP Executive Committee