Human Brain Project

Mediation Report

Editor:

Mediation of the Human Brain Project
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Executive Summary

Background: *The HBP is a large international collaboration funded by the EU as a FET-(Future and Emerging Technologies)-Flagship with a budget of about € 500 million for the Core Project over 10 years. Another € 500 million is expected to come from national research agencies via Partnering Projects or by member institutions through in-kind-contributions in the form of matching funds which are not yet secured. The coordinator of the project is the École Polytechnique Fédérale de Lausanne (EPFL). The HBP aims to build an IT-infrastructure to integrate research data from neuroscience and medicine in an effort to understand the human brain by simulation and ultimately to emulate its cognitive capabilities by computational technologies. In 2014 a debate emerged in the project in reaction to the repositioning of cognitive and systems neuroscience from the Core Project in the ramp-up phase to Partnering Projects in the following operational phases. The debate rapidly spread in the neuroscience community, escalated and then culminated in July 2014 in an Open Letter to the European Commission co-signed by several hundred scientists. The signatories requested an evaluation of the HBP's governance and scientific approach, and called for an independent external steering committee. If these objectives were not achieved, the signatories threatened to boycott the project.*

The Mediation Process: *In an attempt to deal with the growing controversy, a mediation process was solicited by several stakeholders related to the HBP and formally set in motion by the HBP's Board of Directors in September 2014. Wolfgang Marquardt, the Chairman of the Board of Forschungszentrum Jülich, agreed to act as a mediator. The objectives of the mediation were defined in the Terms of Reference; they include the development of a "proposal for a restructured concerted governance structure and a balanced scientific structure". The mediator invited 27 international experts from the EU and beyond to form a mediation committee. The committee members were selected such that they cover a broad range of expertise in the management of scientific institutions, large-scale research projects and infrastructures and in relevant scientific disciplines. They are involved with the HBP in various ways, ranging from being a Principal Investigator (PI) to being completely unrelated to either the HBP or its direct scientific communities. The mediation committee developed its recommendations to the HBP in a series of meetings including a hearing between the mediator and the HBP's Board of Directors. The report has been presented to the Board of Directors and made available to the public. According to the Terms of Reference, for the mediation process to be successful, HBP will have to agree and faithfully implement the recommendations of this report.*

Report of the mediation committee: *The report comprises 5 sections, i.e., i) background information on the HBP; ii) summary of the emerging critique of the HBP; iii) the mediation process; iv) the debate within the mediation committee and between the mediation committee and the HBP's Board of Directors; v) recommendations, and an appendix containing supplementary information. The mediation committee acknowledges that HBP has visionary and pioneering ambitions, but also emphasizes the substantial risk involved. In order to significantly increase the HBP's chances of success in delivering innovative and valuable research results and technology platforms substantial reforms are considered essential. The mediation report was endorsed by all but two members of the mediation committee. The remainder of this executive summary outlines the recommendations.*

Recommendations on science: *Five recommendations address the scientific program of the HBP.*

The HBP should define a unique set of concrete and achievable long-term objectives, which can be realized within the projected timeframe and with the financial resources available. To this end, it is recommended that the scientific program be carefully re-evaluated. Concentration on a smaller number of properly prioritized activities will be required. Research activities should focus on the development of a set of models that complement each other and integrate multiple scales and perspectives, together with the specification, design, implementation and testing of IT platforms enabling and exploiting these models. The HBP should provide access to existing experimental neuroscientific data. It should not attempt to fill all the gaps in structural and functional data, but should rather focus on dedicated and targeted experiments, which will be required for the development and provisioning of the IT platforms.

Cognitive and systems neurosciences should be (re-)integrated by means of a new subproject comprising at least 3-4 work packages. These should cut across, and thereby link, the existing subprojects, which are organized largely within traditional scientific disciplines. These crosscutting activities should demonstrate the value that the evolving IT platforms can add to the solutions of concrete and ambitious problems in cognitive and systems neuroscience in an interdisciplinary research approach. These crosscutting activities should be substantially funded by a reallocation of the budget based on an assessment of the scientific quality and programmatic fit of the work planned in the subprojects.

Scientific project management should be revised to facilitate the assignment of properly defined research tasks to research teams with excellent track records and, in particular, to allocate the budget in a transparent manner. To facilitate the delivery of mature IT platforms that can serve as computational research infrastructures for a broad base of users it will be crucial to establish a significant level of coordination within and across work packages. These research processes will thus need to include continual quality assurance.

The research objectives and program should be viable even if funding is only available for the core projects. Part of the core budget should be devoted to the integration of scientists outside the HBP by suitable means. Funding of partnering projects that contribute directly to the objectives of the HBP at a comparable level to core funding, should be sought with the highest priority. The scientists leading the partnering projects will have to be given a determining role in driving and shaping the overall scientific program of the HBP.

The HBP and the EC have a fundamental responsibility to clearly and faithfully communicate the HBP's sharpened mission and objectives. Furthermore, the HBP should systematically take and create opportunities for constructive scientific dialogues with scientists, with science policy makers and with the interested public. Furthermore, a strong reputation in the science community can only be built by publishing convincing scientific results and generating widely used IT platforms. Appropriate target setting, resource allocation, project coordination and communication will be essential for success.

Recommendations on governance: *Four recommendations are formulated regarding the revision of the HBP's governance.*

It is essential that the responsibility of the HBP and the role of the coordinator be transitioned from EPFL to a new legal entity jointly represented by those institutions that most strongly contribute to the project. Such a distribution of responsibilities will help the HBP grow into an international hub. As such, it will continue to further develop the HBP's platforms, ensure their maintenance, and sustainably provide them to the scientific community, to clinical medicine and to industry in the EU and beyond.

The revised governance of the HBP shall adhere to good governance practice. The separation of functions and responsibilities and a robust system of strong checks and balances will have to be implemented. In particular, scientific strategy development, executive and administrative management, as well as supervisory, auditing and advisory committees will have to be clearly distinguished. To ensure transparency of the process, decision-making and supervisory bodies will have to be entrusted to external experts who are not beneficiaries of their own decisions. A framework – detailing function, reporting lines, membership and leadership – is provided, in order to guide the implementation of the revised governance.

Finally, a migration process from the current to the new governance is suggested which ensures appropriate participation of the whole partnership of the HBP.

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1. Background

The Human Brain Project (HBP) has been set up as a FET (Future and Emerging Technologies) Flagship, which is a new funding instrument of the European Commission (EC). Flagships are intended to be "… ambitious large-scale, science-driven, research initiatives that aim to achieve a visionary goal. The scientific advance should provide a strong and broad basis for future technological innovation and economic exploitation in a variety of areas, as well as novel benefits for society." (http://cordis.europa.eu/fp7/ict/program/fet_en.html). They are long-term initiatives bringing together excellent research teams across various disciplines, sharing a unifying goal and an ambitious research roadmap on how to achieve it. Flagships are expected to run for about 10 years, with an annual budget of around € 100 million. About half of the budget is provided by the EC *via* Core Projects (CPs), while the other half has to be covered by other sources, including in-kind contributions by the partnering institutions, contributions by the private sector and, in particular, research grants provided by national funding agencies of the member states *via* Partnering Projects (PP). Instruments or budget corridors for PP funding have not yet been developed. This division into CPs and PP was introduced to accommodate the transition from the Seventh Framework Program (FP 7) to Horizon 2020, the current funding program of the EC. There was no distinction between CPs and PP under FP7; however, EC funding was also limited to about half of the total cost, while matching funds had to be provided by the partnering institutions.

The HBP builds on the European projects on brain simulation and neuromorphic computing FACETs (Fast Analog Computing with Emergent Transient States under the 6th Research Framework Program (FP) of the EU), Brain-i-Nets (Novel Brain-Inspired Learning Paradigms for Large-Scale Neuronal Networks under EU FP-7) and BrainScaleS (Brain-inspired multiscale computation in neuromorphic hybrid systems under EU FP-7) and on the Swiss Blue Brain project. The experience gathered in the Partnership for Advanced Computing in Europe Initiative (PRACE) will help to coordinate access and operation of supercomputing resources for the HBP. The Blue Brain Project, funded primarily by the Swiss government, has a special role as a precursor project, whose goal was to demonstrate the feasibility of large-scale, biologically realistic simulations of the brain using supercomputer technology. The Blue Brain project began in 2005 with an agreement between École Polytechnique Fédérale de Lausanne (EPFL) and IBM, the supplier of the BlueGene/L supercomputer. The project is headed by the coordinating scientist of the HBP, Henry Markram of EPFL.

The HBP FET Flagship proposal was submitted in 2012. The goal of the HBP is "to build a completely new ICT infrastructure for neuroscience, and for brain-related research in medicine and computing, catalysing a global collaborative effort to understand the human brain and its diseases and ultimately to emulate its computational capabilities" (http://ec.europa.eu/programs/horizon2020/en/news/human-brain-project-video-presenting-flagship-project). Hence, the HBP is primarily an IT project with the goals of generating new forms of IT platforms to empower brain research and clinical neurology and psychiatry and of contributing to new forms of brain-inspired computing. These tools include platforms for neuroinformatics, brain simulation, high performance computing, medical informatics, neuromorphic computing and neurorobotics. Accordingly, the HBP is financed by the ICT section of the EC. In communicating the project to the general public and also to the wider scientific community much emphasis has been placed on possible long-term societal benefits as a result of the

research in the HBP, such as improved understanding of brain function, novel diagnostic methods and therapies for brain diseases and development of novel brain-inspired information technologies. The proposal was accepted in January 2013 after multiple peer reviews. The reviewers' evaluation report (https://www.humanbrainproject.eu/documents/10180/538356/HBP_FPA_PRINT_29-07-14.pdf) recommended the "development of a clear strategy for access to clinical data and for an adequate representation of clinical data which comprises the successful development of the medical informatics platform and a better establishment of the links between the brain models and the clinical practices". The reviewers also stated that some of the projected claims are "overly ambitious in relation to the simulation of the whole human brain and in relation to potential health outcomes". Concerning the HBP governance the reviewers stated that the "overall governance structure is adequate, but [that] the proposal does not clarify in sufficient detail how the General Assembly will relate its decisions to, and interact with, the rest of the governance bodies. The administrative functions of the consortium are commendable. The roster of the Executive Committee is not identified." At the same time, the reviewers acknowledged in their report that the "proposal adheres well to the Flagship concept as specified in the work program. It is visionary, highly ambitious, science-driven, goal-oriented, large-scale, multi-disciplinary and builds on well-established research. The proposal is integrative, employing a large distribution of international laboratories, and takes advantage of current scientific and technological advances".

The HBP is organized in several phases, starting with the ramp-up phase, during which research collaborations are initiated and governance bodies and project management structures are established. The ramp-up phase is funded under FP7 starting 1 October, 2013, and will run until 30 September, 2016. The next (operational) phase will start (with 6 months overlap) in April 2016 and will last until September 2023, divided into three Specific Grant Agreement (SGA) periods.

The implementation of the operational phase of the HBP was outlined in a Framework Partnership Agreement (FPA), which is the legal basis for the execution of the project under Horizon 2020. The FPA proposal was submitted to the EC in June 2014 and refines the original proposal with an emphasis on the operational phases SGA-1 to SGA-3. The comments of the (anonymous) review panel and the recommendations of the EC on the FPA proposal were submitted to the Consortium in September 2014. The expert panel rated the HBP allocating 4.5/5 points for "Excellence", 4.5/5 for "Impact" and 3.5/5 for "Quality and efficiency of the implementation and the management". The experts made numerous suggestions, including a re-evaluation of the governance structures as well as the reintegration of systems and cognitive neuroscience into the project. The evaluation report (https://www.humanbrainproject.eu/documents/10180/538356/650003-HBP+FPA-ESR-Ares.pdf) and comments by the EC (https://twitter.com/ eurohumph/status/511836521604083712) are publicly available.

A first scientific review of the HBP covering the first year took place from 26-28 January, 2015. This review not only looked at the progress in science and technology, but also evaluated the governance and the overall management of the project and the mobilization and coordination of its resources. The (anonymous) expert panel compiled an evaluation report, which was submitted to the HBP in early March 2015. The summary of this report reads as follows (http://ec.europa.eu/information_society/newsroom/cf/dae/document.cfm?doc_id=8923): "The reviewers acknowledge the good

quality of the work that has been carried out by the consortium in the first year of the Human Brain Project (HBP) and recognize the huge task the creation of the HBP flagship represents but recommend also the implementation of important corrective actions. (…) The leaders of the project and of the subprojects have demonstrated that they maintain a clear vision for the HBP and that their firm ambition is to achieve the overall goal of HBP. However, whilst the participants were all excited by and fully engaged in their own subprojects, it is clear that very significant efforts remain to be made, in terms of coordination and integration, for the HBP to become a truly large unified project. There is a clear need for a tighter and more carefully managed integration and realignment of the work in the Data and Theory subprojects, both with the development of the ICT platforms, and within and between these subprojects themselves. A more rigorous methodology for infrastructure construction and operation is also required for ensuring success in translating the platforms into a solid ICT integrated infrastructure. Moreover, it is crucial that the consortium engages with the wide scientific community in the co-design and development of the ICT platforms. In the first year, the consortium has set up all the governance and management structures as proposed in the DoW. However, the reviewers recommend that changes are made to ensure that the decision making processes are simple, fair and transparent. (…) It is important for the HBP to better articulate its strategic goals and to communicate them in a clear and realistic way, within the HBP, to the wider scientific community and to the public, and to avoid at all costs creating unrealistic expectations. The goals must be communicated to the scientists outside HBP in a manner which allows an engagement in open debates that would help clarify the scientifically and technically achievable targets of the project."

Both the review of the FPA proposal and the scientific progress during the first year will require some significant modifications which have to be presented by the HBP Consortium in an amended version of the FPA to be re-submitted to the EC.

2. Emerging Criticism of the HBP

The governance and management of the HBP as well its scientific objectives and research approach became the target of increasing criticism. The concentration of functions and responsibilities among the small group of leading scientists forming the Executive Committee (ExCo) led to increasing dissatisfaction among a number of PIs in the HBP: ExCo members not only fill most of the instrumental positions in the governance bodies of the HBP, they are also able to control the Board of Directors (BoD), i.e., the major scientific decision making body of the HBP. In order to achieve the two-thirds majority needed for decisions, the BoD depends on the votes of the ExCo members. Further issues raised by some PIs of the HBP refer to the decision and management practices, the lack of transparency, and the (at least perceived) lack of pluralistic scientific discourse among the PIs.

The controversy escalated during the drafting of the FPA proposal in the second quarter of 2014, because of the envisioned repositioning of cognitive and systems neuroscience in the operational phase of the HBP (SGA-1 to SGA-3). Whereas cognitive neuroscience is one of 13 subprojects (SP) in the core during the ramp-up-phase, no consensus could be reached on a plan for continuing this work in the operational phase, and as a result the BoD of the HBP suggested transferring these activities from the core to PP in the operational phase. The significant uncertainty related to the PP, i.e.,

the time schedule, the available budget and the application procedures in the national funding systems, created significant irritation and strong opposition among neuroscientists, who had intended to contribute to the HBP. As a result, a dispute developed in the neuroscience community, within as well as outside of the HBP, which was no longer limited to management and decision-making structures, but also raised questions about the validity of the HBP's objectives and scientific approach.

The scientific objectives of the HBP as stated in the FET Flagship and the FPA proposals, and elaborated upon in a number of scientific contributions by leading HPB scientists and in the public announcements of the HBP public relations office and of the EC, were regarded as ambitious and disruptive by some neuroscientists and as overstated and unrealistic – to the point of seriously questioning the credibility of the whole project – by others (see, e.g., http://www.nature.com/news/computer-modelling-brain-in-a-box-1.10066). The latter position is also reflected in the recommendations of the EC on the HBP Flagship 2012 proposal as quoted above. The goal of reconstructing the mouse and human brain *in silico* and the associated comprehensive bottom-up approach is viewed by one part of the scientific community as being impossible in principle or at least infeasible within the next ten years, while another part sees value not only in making such simulation tools available but also in their development, in organizing data, tools and experts (see, e.g., http://www.bbc.com/future/story/ 20130207-will-we-ever-simulate-the-brain). A similar level of disagreement exists with respect to the assertion that simulating the brain will allow new cures to be found for brain diseases with much less effort than in experimental investigations alone. The public relations and communication strategy of the HBP and the continuing and intense public debate also led to the misperception by many neuroscientists that the HBP aims to cover the field of neuroscience comprehensively and that it constitutes the major neuroscience research effort in the European Research Area (ERA).

In an attempt to resolve the escalated conflict, the provost of EPFL and the Executive Committee met with the HBP Internal Advisory Board (IAB) and the chair of the External Advisory Board (EAB) in Paris in June 2014 to discuss the FPA proposal and governance issues. The results of this meeting, though never formally agreed by the BoD, were published in a press release and can be summarized as follows:

- The Research Board (the equivalent of the BoD after the ramp-up phase) will elect the chairperson of the board. This position should not be held by any of the HBP subproject leaders.
- The Research Board will elect its Executive Committee on a three-year term basis, with possibilities for renewal. The scientific coordinator of HBP is always part of the Executive Committee.
- The Research Board will elect a new Strategic Advisory Board, which will be comprised of the chairperson and eight members. The term will be three years.

However, the debate among the PIs in the HBP continued. Considerable differences of opinion emerged in the HBP as to whether the measures agreed upon should be implemented immediately or only with the beginning of the operational phase (SGA-1). The change in governance discussed in the Paris Meeting has not been implemented, since a mediation process was initiated before action was taken.

Notwithstanding the reforms announced after the Paris Meeting a group of neuroscientists published an open letter to the EC in July 2014, expressing strong concerns regarding the general structure of the HBP (http://www.neurofuture.eu/). This letter was signed by hundreds of neuroscientists from around the world within a few weeks. The criticism addressed the "narrowing of goals [in the Framework Partnership Agreement for the second round of funding] and funding allocation, including the removal of an entire neuroscience subproject and the consequent deletion of 18 additional laboratories". The signatories strongly questioned "whether the goals and implementation of the HBP are adequate to form the nucleus of the collaborative effort in Europe that will further our understanding of the brain." In addition they voiced concern about the "quality of the proposed governance and management structure" and called attention to the "sparse community support" of the HBP. They requested the establishment of an "external steering committee […] [whose] members would need to be fully independent of the project (i.e. receiving no funding)."

In the event that these objectives were not secured, the demands of the signatories were "to reallocate the funding currently allocated to the HBP core and partnering projects to broad neuroscience-directed funding to meet the original goals of the HBP – understanding brain function and its effect on society." The signatories "strongly support the mechanism of individual investigator-driven grants as a means to provide a much needed investment in European neuroscience research." They also threatened to boycott the PP and urged other scientists to join them.

The ExCo and the BoD of the HBP responded to the open letter in a public declaration (https://www.humanbrainproject.eu/documents/10180/17646/HBP-Statement.090614.pdf) explaining that its project funding comes from the "European Commission's (EC) Future and Emerging Technologies (FET) "program" thus making clear that it could not be reallocated to neuroscience funding as requested by the signatories. They then went on to elaborate on the objectives of the project stating that "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 behavior. 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."

The contribution of the FET Flagship to neuroscience was described by the HBP as follows: "Each year, neuroscience research receives an estimated 1 billion Euro 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, organizing, analyzing 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 hard-

ware, analysis software, algorithms, search technology and much more. The target is the mouse brain, and ultimately the human brain."

Following this public exchange of positions the dispute spread and was continued in a number of scientific journals as well as in daily newspapers. In some contributions, for example in a "Nature" article (http://www.nature.com/news/neuroscience-where-is-the-brain-in-the-human-brain-project-1.15803), the HBP was criticized as "decreasing the emphasis on experimental neuroscience" and hence advancing a "concept in which *in silico* experimentation becomes a 'foundational methodology for understanding the brain' thus "building a massive database to feed simulations without corrective loops between hypotheses and experimental tests". This was considered "at best, a waste of time and money".

Criticism ccontinued to be voiced that the simulation of the human brain, one of the major goals of the HBP, is unrealistic and its potential overstated (e.g., http://news.sciencemag.org/brain-behavior/2014/07/updated-european-neuroscientists-revolt-against-e-u-s-human-brain-project, http://www.nzz.ch/wissenschaft/biologie/flaggschiff-auf-schlingerkurs-1.18344079). This perspective is broadly shared by parts of the scientific community and had already been expressed in the evaluation report of the peer review of the original FET Flagship proposal as noted above.

However, the review panel also stated that the project "is visionary, highly ambitious, science-driven, goal-oriented" (see quotation above). This position matches the perspective of the HBP leadership who view the project as an endeavour that is disruptive and high risk – thus fulfilling the necessary requirements for EC-FET-Flagships. These were initiated precisely **"**to promote high-risk research" supporting projects "that aim to achieve a visionary goal" (http://cordis.europa.eu/fp7/ict/program/fet_en.html). The HBP leadership underlines its position with the need to establish such ambitious and high-risk projects, which, in contrast to the US, are still not well appreciated and realized in the European funding systems. The HBP project leadership's response to claims that the "goals are unrealistic […] and that not enough is known to take on such a challenge" reads as follows (https://www.humanbrainproject.eu/documents/10180/17646/HBP-Statement.090614.pdf): "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 endeavor. 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."

3. Mediation Process

A mediation process was sought independently by a number of stakeholders within and outside the HBP in July 2014 and formally set in motion by the scientific coordinator Henry Markram with in a letter to the members of the HBP consortium dated 10 September 2014 in order to react to and ad-

dress the continuing critical debate on the HBP within and outside the project. The mediation was supposed to reconcile the conflicting positions with the help of external advisors.

The BoD of the HBP invited Wolfgang Marquardt to act as a Mediator. Marquardt has been Chairman of the Board of Directors of Forschungszentrum Jülich since July 2014, and, prior to that, he served as Chairman of the German Council of Science and Humanities, an advisory body to the German federal and state governments, and as a professor for process systems engineering with a focus on computational engineering science at RWTH Aachen University, Germany. He is not a member of any governance organ or body of the HBP, neither is he scientifically involved with the HBP. However, scientists from the Forschungszentrum Jülich and their research groups are actively involved in the HBP. Two of them are members of the BoD. Marquardt agreed and accepted the role as Mediator of the HBP after agreeing with the BoD on a Terms of Reference (ToR) document, which was signed by all members of the BoD by 8 September, 2014.

The main objectives of the mediation according to the ToR are "the development of a proposal for a restructured Concerted Governance Structure (CGS) and a Balanced Scientific Structure (BSS) for the HBP by the Mediator and its implementation in HBP by the responsible bodies facilitated by the Mediator." The ToR also defined the major steps of the mediation process as well as the criteria for successful completion of the mediation.

3.1. Experts Supporting the Mediation Process

After his appointment, the mediator invited a number of internationally recognized experts to take part in the mediation process as advisors to the mediator. The experts were selected according to the following criteria to address the relevant management and scientific issues: (i) their expertise should cover a broad range of fields ranging from science management, management of large-scale research projects to the scientific disciplines and fields relevant for HBP; (ii) a varying degree of relationship with the HBP, ranging from being a PI in the HBP to being completely unrelated to the HBP and its scientific communities; (iii) a wide spread of nationalities in the EU and beyond.

A mediation committee (MC) was formed that consists of 27 members. Five of them are subproject (SP) leaders of the HBP, four are members of the HBP's Internal Advisory Board (IAB) and External Advisory Board (EAB), and one expert on the committee also acted as a reviewer in the panel evaluating the scientific progress of the HBP after the first year. The other members are not involved in the HBP. The range of expertise of the committee members complies with the criteria formulated above.

The committee is organized in two working groups (WG): one WG addressed suggestions for "readjusting the scientific balance" within the HBP, while the other group focused on recommendations for "restructuring the governance" of the HBP. However, there has been active communication and an intense exchange between the two WGs, as the two areas necessarily impact on each other. Some of the experts were members of both groups, facilitating close interaction between the two groups. This report has been finalized in a joint meeting of both WGs which ensured that governance and scientific issues were considered in an integrated manner and a consistent set of recommendations to the HBP were formulated.

The members of the working group "Science" are as follows:

Prof. Dr. Bjoern Bergh
Zentrum für Informations- und Medizintechnik, Universitätsklinikum Heidelberg, Germany

Prof. Dr. Barbara Chapman
Department of Computer Science, University of Houston, Texas, USA

Prof. Dr. Peter Dayan
Gatsby Computational Neuroscience Unit, University College London, United Kingdom

Prof. Dr. Kathinka Evers
Centre for Research Ethics & Bioethics (CRB), Uppsala University, Sweden
Subproject Leader "Ethics and Society"

Prof. Dr. Angela Friederici
Max-Planck-Institut für Kognitions- und Neurowissenschaften, Leipzig, Germany

Prof. Dr. Karl Friston
Welcome Principal Research Fellow and Scientific, Welcome Trust Centre for Neuroimaging, London´s Global University (UCL), London, United Kingdom

Prof. Dr. Steve Furber
School of Computer Science, University of Manchester, United Kingdom
Subproject Co-Leader "Neuromorphic Computing Platform"

Prof. Dr. Rainer Goebel
Cognitive Neuroscience, Maastricht University, Netherlands

Prof. Dr. Sten Grillner
Department of Neuroscience, The Nobel Institute for Neurophysiology, Karolinska Institute, Stockholm, Sweden
Subproject Leader "Neuroinformatics Platform "

Prof. Dr. Hans-Jochen Heinze
Universitaetsklinik fuer Neurologie, Otto-von-Guericke-Universitaet, Universitaetsklinikum Magdeburg, Germany

Prof. Dr. Andreas Herz
Computational Neuroscience, Department Biology II, Ludwig-Maximilians-Universitaet Muenchen, Germany

Prof. Dr. Henry Kennedy
Stem-Cell and Brain Research Institute, Lyon, France

Prof. Dr. Alois Knoll
Institut fuer Informatik VI, Technische Universitaet Muenchen, Germany
Subproject Leader "Neurorobotics Platform"

Prof. Dr. Gordon Pipa

Chair of Neuroinformatics, Institute of Cognitive Science, Universitaet Osnabrueck, Germany

Prof. Dr. Haim Sompolinsky
The Edmond and Lily Safra Center for Brain Sciences, Hebrew University of Jerusalem, Israel

Prof. Dr. Keiji Tanaka
Cognitive Brain Mapping, Riken Brain Science Institute, Saitama, Japan

Prof. Dr. Torsten Wiesel
President Emeritus of The Rockefeller University New York, USA
Member of Strategic Advisory Board

The members of the working group "Governance" are as follows:

Prof. Dr. Winfried Denk
Department of Biomedical Optics, Max Planck Institute for Medical Research, Heidelberg, Germany

Prof. Dr. Ray Dolan
Wellcome Trust Centre for Neuroimaging, London´s Global University (UCL), London, United Kingdom

Dr. Ulrich Drees
Boehringer Ingelheim GmbH, Ingelheim, Germany

Prof. Dr. Kathinka Evers
Centre for Research Ethics & Bioethics (CRB), Uppsala University, Sweden
Subproject Leader "Ethics and Society"

Prof. Dr. Sten Grillner
Department of Neuroscience, The Nobel Institute for Neurophysiology, Karolinska Institute, Stockholm, Sweden
Subproject Leader "Neuroinformatics Platform: user support and community building"

Prof. Dr. Paul Herrling
Vice President, Board of the Swiss Federal Institute of Technology (ETH-RAT)

Prof. Dr. Herbert Jaeckle
Max-Planck-Institut fuer biophysikalische Chemie, Abt. Molekulare Entwicklungsbiologie, Goettingen, former vice-president of Max-Planck-Gesellschaft, Germany

Dr. Matthias Kaiserswerth
Director IBM Research-Zurich, Switzerland

Prof. Dr. Walter Kroell
Former President of Helmholtz Association, Berlin, Germany

Prof. Dr. Francesco Pavone
University of Florence, Physics Department, European Laboratory for Non Linear Spectroscopy (LENS), Florence, Italy

Prof. Dr. Thomas Schulthess
Institut fuer Theoretische Physik, ETH Zurich, Switzerland

Subproject co-Leader "High Performance Computing Platform: integration and operations"
Member of the Internal Advisory Board

Prof. Dr. Torsten Wiesel
President Emeritus of the Rockefeller University, New York, USA
Member of the External Advisory Board

Prof. Dr. John Womersley
Chief Executive, Science and Technology Facilities Council, Swindon, UK
Chairman of the European Strategy Forum on Research Infrastructures, DG-RTD, European Commission

3.2. Course of the Debate

After the ToR document was signed on September 28, the mediator met with the BoD to get their perspective on the critical debate. Furthermore, the mediator collected the positions of many informed stakeholders. The information gathered was used to prepare for the meeting of the WGs of the MC. After the ToR document was signed, the mediator met with the BoD to get their perspective on the critical debate on September 28. Furthermore, the mediator collected positions of many informed stakeholders. The information gathered was used to prepare the meetings of the WGs of the MC. Both WGs met for two one-day meetings at Frankfurt Airport on 5 and 6 December, 2014, and on 22 and 23 December, 2014. Together they drafted a first set of recommendations ("Draft 13 January 2015 – Recommendations of the Mediation Committee for the HBP"). Then this draft was sent to all members of the BoD, including the ExCo, and the members of the EAB and the IAB of the HBP on 13 January 2015 and served as a basis for the discussion between the BoD, the EAB and IAB, and the mediator, which took place in a meeting on 16 and 17 January 2015, at Frankfurt Airport. The comments of the BoD, IAB and EAB members have been integrated into the second draft document, which was sent to the members of the MC on 3 February 2015. This document was discussed in the

final meeting of the MC on 10 February 2015. The comments of the members of the MC (including representatives of the BoD of the HBP) have been taken into account in preparing the final version of the recommendations. The final draft was sent again to the members of the MC for review.

A final version of the report, which represents the compromise reached regarding structure, content and wording of the document, was agreed on by the members of the MC by 9 March 2015. *Two members of the mediation committee, Prof. Steve Furber and Prof. Francesco Pavone, could however not agree and have therefore not endorsed the mediation report.* They feel that the report is overly negative about the current position of the HPB, the achievements of its participants and its leadership, and the ambitious vision which underpins the entire HBP mission. Furthermore, they claim that the report is giving too much weight to critical opinions about the HBP. They regard the recommendations as being overly prescriptive and that the report contains elements of a scientific review. Finally, they do not agree that the report should be published.The EC has not been directly involved in the mediation process. However, there was a close interaction between Thierry van der Pyl and Thomas Skordas, the responsible representatives of EC, and the mediator to exchange information

on the progress of the mediation and the scientific review, two processes which were running in parallel. The results of the review of the FPA proposal have been taken into consideration in the mediation process from the very beginning. The MC has taken note of the preliminary results and conclusions of the scientific review before finalizing its report. Likewise, the members of the review panel of the first year scientific review had access to the first draft of the mediation report and to a short written summary of the mid-January meeting between BoD, IAB, EAB and the mediator.

The mediator informed the provost of EPFL, Philippe Gillet, who is also the representing EPFL in the HBP leadership, on the progress of the mediation process.

3.3. Preparation of the Members of the MC

Since the members of the WG come from a variety of backgrounds and have different types of expertise and degrees of familiarity with the HBP, comprehensive documents were prepared by the mediator to summarize background information on the HBP and on the current controversy with references to key documents. These key documents included

- Description of Work (DoW) of the HBP,
- Results of the Review of the HBP Proposal,
- HBP Consortium Agreement,
- Paris Meeting Minutes; Paris Meeting Press Release,
- Open Letter to EC,
- Official HBP Response to the Open Letter,
- Official EC Response to the Open Letter,
- Framework Partnership Agreement Proposal,
- Results of the Review of the FPA Proposal,
- Blog of Robert Madelin, Director General at the EC for DG Connect,
- HBP Blue Book Edition 12,
- HBP Heidelberg Summit, BoD Minutes.

The preparatory documents summarized comments collected in numerous telephone conversations by the mediator with informed stakeholders regarding internal and external views on the HBP, the results from an anonymous online survey sent to all Principal Investigators (PIs) of the HBP as well as the input provided by the BoD to the mediator in their September meeting.

The objectives of the mediation according to the ToR were translated into the following guiding questions to be addressed by the WGs:

1) Should the research program and the research process of the HBP be readjusted?
2) How can the Partnering Projects (PPs) be adequately funded and integrated?
3) How can a constructive interaction between the HBP and the wider neuroscience community be achieved?
4) How can the field of “cognitive architecture” be appropriately (re-)integrated into the operational phase of the HBP (SGA-1 to SGA-3)?
5) How can funds and resources be made available for this purpose?
6) How can the transparency of project governance and operational management be ensured?

7) How can the roles and tasks of the organs, bodies and boards of the HBP – in particular, the division of responsibilities between the ExCo, the BoD and the General Assembly (GA) – be clarified and readjusted?
8) How can structure, processes, roles and responsibilities of central project management be improved?

4. Debate during the Mediation Process

This section summarizes the debate in the MC and refers to the discourse between the MC and the BoD of the HBP.

During its first meeting the MC reflected on how it saw its own role, how it viewed the HPB and how the HPB is perceived in the scientific community at the start of the mediation process.

The MC has been well aware that it had to try mediating between a well-defined group, the HBP leadership and a rather diffusely defined group, the part of the scientific community which is critical of the HBP. The MC was also aware of the fact that its task was not to provide yet another review of the project. The MC largely agrees, however, that the mediation process should assess whether the scientific focus of the project and its governance structures have evolved in the course of the project in such a way that the HBP can achieve its objectives successfully. Consequently, an analysis of the scientific program of the reviewed and accepted FPA proposal was considered to be necessary. It was, however, decided to distinguish between ***"recommendations"*** and ***"observations"***. While agreement on the recommendations by the BoD will decide on successful completion of the mediation process, the observations are intended to support the HBP in evolving its scientific program, governance and management.
Furthermore, the MC was determined from the very beginning to publish the results of the mediation process. In its final meeting, the MC agreed that the full mediation report should be published regardless whether or not the BoD decides to accept the recommendations.

In conclusion, the MC largely supports and emphasizes the critique voiced by parts of the scientific community regarding objectives, scientific approach, governance and management practices (see Section 2). Most of the members of the MC agree that the way the HBP was presented to the public and to the scientific community lacked self-reflection, and thus contributed to a loss of credibility of the HBP in the scientific community. They pointed out that the HBP's leadership neglected its responsibility to prevent this through adjustment of the HBP's public relations and to introduce sound expectations management. It was largely agreed that there is a need to communicate the goals of the HBP clearly, honestly and more modestly. Most of the members of the MC agreed that major changes are necessary to create value for the scientific community as well as for society. A perceived deficit in the governance of the project and a perceived lack of transparency regarding operational management, criticism of the scientific program and a lack of trust in the leadership of the project, not only among the HBP partners, but also between the HBP and part of the wider neuroscience community, have been identified as major reasons for the current crisis in the HBP. These issues could put the entire project at risk and pose a serious obstacle to the success of HBP.

The following Sections, 4.1 and 4.2, summarize the debate on science and governance along the lines of the questions listed in Section 3.3. The presentation reflects not only the debate in the MC but also includes the perspective of the BoD as expressed during the meeting with the mediator on 16 and 17 January 2015.

4.1. Science

In this section, the discussion related to the first five guiding questions concerning science as formulated in Section 3.3 is presented.

4.1.1. Research Program and the Research Process Coordination

The research program as presented in the proposal and in the communication of the HBP (cf. https://www.humanbrainproject.eu/de/discover/the-project/strategic-objectives) proposes three largely independent research tracks:

- *"Future Neuroscience:* Achieve a unified, multi-level understanding of the human brain that integrates data and knowledge about the healthy and diseased brain across all levels of biological organization, from genes to behaviour; establish *in silico* experimentation as a foundational methodology for understanding the brain.
- *Future Computing:* Develop novel neuromorphic and neurorobotic technologies based on the brain's circuitry and computing principles; develop supercomputing technologies for brain simulation, robot and autonomous systems control and other data intensive applications.
- *Future Medicine:* Develop an objective, biologically grounded map of neurological and psychiatric diseases based on multilevel clinical data; use the map to classify and diagnose brain diseases and to configure models of these diseases; use *in silico* experimentation to understand the causes of brain diseases and develop new drugs and other treatments; establish personalized medicine for neurology and psychiatry."

The MC agrees that the HBP's visionary and ambitious scientific long-term goals formulated in the research program should be re-evaluated and more sharply articulated. A reformulation of the scientific goals should be considered. This is not only due to but is reinforced by the fact that (i) the budget for the HBP's CP during the current negotiations with the EC has been reduced by about 15%, and that (ii) the newly introduced PP covering half of the initial budget are left without secured funding. In particular the scientific program should be contrasted with other large-scale brain-related efforts including Allen's Institute's MindScope, and the NIH BRAIN initiative, which, in addition to stating long-term visions, specify concrete, short and medium-term goals in the deliverables, which can be realistically achieved with the resources available.

Most members of the MC are of the opinion that the HBP should concentrate on enabling methods and technologies, in particular on developing, demonstrating and maintaining innovative IT software and hardware platforms for neuroinformatics, emphasizing multi-perspective/multi-scale modelling and brain simulation. These platforms should be co-designed in an interdisciplinary collaboration

between neuroscience and information technology to empower future neuroscience research and – in the longer run – related clinical medicine.

The majority of the members of the BoD claim that focusing the current, visionary and broad objectives as stated in the mission statement reproduced above would turn a visionary project into an average one. They consider the current goal as unique and consequently as inspiring and motivating. They are of the opinion that the HBP's mission may sound unrealistic but they claim that valuable research results will be achieved, even if the mission of simulating the whole brain could not be fulfilled. However, some members of the BoD agreed with the MC that the budget cut forces the HBP to rephrase its goals.

Questions about the balance and coherence of the HBP's scientific program revolved around the role of cognitive – and more generally – experimental neurosciences. There seems to be consensus that the contributions of systems and cognitive neuroscience are essential for the HBP. However, there are differing viewpoints on how to implement those tasks in the HBP, whether and what kind of dedicated experiments on cognitive neuroscience issues are necessary to accomplish the project goals with the funds available in the project. The MC emphasizes that the HBP should integrate and evaluate the potential of data already available or generated outside the HBP, before venturing into new experiments. While the BoD largely agrees with this assessment, suitable mechanisms – organizational and technical – to absorb relevant experimental data produced in the global neuroscience community by means of the neuroinformatics platforms under development in the HBP still need to be established. Hence, existing activities need to be strengthened to both satisfy the needs of the HBP itself and to provide an information hub for the neuroscience research community. Since existing data are estimated as being far from adequately satisfying the needs of the project, some stakeholders propose that the implementation of experimental neuroscience (including but not limited to cognitive neuroscience) be one of the main pillars in the HBP research program. This request has been extended to include experiments with non-human primates (NHP) in the HBP. Obviously, the generation of all the experimental data needed to build brain models is not possible within the HBP.

Most neuroscience experiments are not targeted to the needs of model and platform development. Therefore, a suitable number of well-chosen experiments have to be performed as part of the HBP to support platform development. In contrast to the position taken in the FPA, the MC believes that the active participation of systems and cognitive neuroscientists is essential during platform development in order to include their current and future requirements in the development process. If they were to merely utilize the platforms once they have been built without having had any substantial input during the development, the risk of a misalignment between platform functionalities and existing or emerging needs would increase tremendously. In addition, incentives for external experimental groups will have to be created, to ensure that they provide data that cannot be generated in the HBP because of resource limitations, in particular in the first period of the HBP.

The objectives regarding the long-term goal of the simulation was viewed as premature by some members of the MC also because of the lack of understanding and data for parameterizing microscopic models. The MC proposes to extend the objective beyond the simulation of the human brain using a largely mechanistic, bottom-up approach to provide a diverse set of methods and tools for

multi-perspective, multi-scale and multi-faceted modelling and simulation as well as for data mining for the correlation of existing data by data-driven models. These tools should be aimed at testing modelling hypotheses regarding brain function and cognitive behaviour in particular. The BoD, however, considers brain simulation as the unique selling point of the HBP and therefore insists on focusing on simulation models, which should be built bottom-up incorporating biological knowledge at every step.

According to most members of the MC, the HBP should avoid raising far-reaching expectations about how much the use of the IT platforms under development in the HBP will be able to rationalize diagnostic and therapeutic approaches. However, there is consensus that such platforms can be essential for making progress in systems and cognitive neurosciences and that HBP has a unique opportunity to provide such tools to the scientific community. Neuroinformatics platforms, software and hardware systems for brain simulations and data mining, and a simulation platform for neurorobotic systems development could eventually support the neuroscience community in its quest to understand cognition and the control of behaviour by the brain. It is important that these co-designed platforms evolve in a continuous specify/design/test/validate cycle and in in close cooperation with the end users. Specifications regarding current and future needs have to be drafted as a first step in developing these IT platforms. These tools will have to be continually validated in neuroscience and clinical research while they are evolving in the HBP to implement feedback of user experience and expectations into the platform construction process. Thus, a continuous improvement cycle can be established ensuring – by integrating technology push and application pull – that the methods and tools resulting from the HBP will facilitate neuroscience in an unprecedented way. The added value of the IT platforms used to support the research processes can be demonstrated during this improvement cycle, if suitable scientific cases are chosen. Regarding the value of this approach the BoD and the MC are in agreement. There is also consensus that metrics of success will not only include peer-reviewed publications but also the acceptance of the platform technologies by the neuroscience community. Suitable project management tools will have to be implemented.

The MC and the BoD agree that these objectives require a significant degree of coordination of the research activities within and across the subprojects to make sure that the IT platforms are delivered, demonstrated, validated and maintained at a level of maturity satisfying the needs and expectations of the users. This “big science” approach is unusual and has not been experienced by the neuroscience community at large. It is important that (i) all PIs and their groups are open-minded and accept the necessary degree of coordination and that (ii) professional project management is established that carefully balances the degree of coordination necessary for the development of mature IT platforms with the diversity and autonomy that successful research and creative technology development requires. Consequently, the participating neuroscientists should focus their contribution on supporting the development and demonstration of technology platforms. The operational project management must be set up in such a way as to enable coordination and alignment of research activities within and across subprojects.

4.1.2. Funding and Integration of Partnering Projects (PPs)

Neuroscientists outside the HBP can contribute to the project both by (i) creating a particular type of data that can be smoothly fed into the platforms and (ii) by giving feedback on the usability of the HBP platforms and offering suggestions on how to improve them. Both activities are indispensable for the development of enabling IT platforms and should be funded either via PPs or the core budget.

According to the EC, the budget for PPs, which is planned to be approximately half of the HBP's total budget, is expected to come from national funding sources of the Member and Associate States. However, such sources cannot be relied on, because there are yet not any high-level agreements in place. Furthermore, the recent Flag-ERA call for PP proposals does neither cover the specific needs of the HBP as outlined above nor is it sufficiently supported by those Member and Associated States strongly involved in the project. Serious and continuing efforts should be made by the HBP to engage with the neuroscience community to build trust in the HBP and thus increase the chances to obtain funding from national sources.

If, however, funding for PPs cannot be secured during the ramp-up phase either by the EC or the Member or Associated States, plans have to be made to achieve the HBP's goals with substantially reduced PP funding. Consequently, any incentives targeting the participation of the wider neuroscience community must come from the CP budget. At the beginning, a subcontractor model might be the best way to ensure a perfect fit of the research contribution to the needs of the HBP. Subsequently, after the IT platforms show a reasonable level of maturity, a "beamline model" similar to the one used to assess external contributions to collaborating research group (CRG) at the European Synchrotron Radiation Facility (ESRF), for example, could be applied. In particular, a transparent peer-review process has to be established to select those PPs that complement the CP and are designed to help the HBP to succeed. The selection process has to strictly follow scientific criteria assuring quality and proper alignment with the HBP's objectives.

This model will only work if the platforms suit the needs of the neuroscience community, such that the scientists will benefit from using the platforms. At this point, they should be willing to contribute their own money for access to the platforms.

4.1.3. Interaction between the HBP and the Neuroscience Community

The HBP needs to reach out to a large community, because the success of the HBP strongly depends on acceptance of the developed IT platforms by the scientific user community. While the BoD believes that there is already a strong involvement of neuroscientists in the development, demonstration and use of the evolving IT platform, the MC is convinced that additional incentives have to be established to make neuroscientists, who are not involved in the CP, participate in and benefit from the HBP.

While the resources needed to develop mature platforms have to come from the CPs of the HBP, other research activities (funded from whatever sources) have to be associated with the HBP in a

constructive way. The HBP can only be successful in the long run, if a substantial number of non-HBP scientists use the HBP-created IT platforms in their own work.

The lack of opportunities for researchers to propose PPs funded by the HBP or from matching funds specifically targeted towards such projects at the initially planned scale is interpreted as a sign of failure of the HBP by the neuroscience community, because they not only feel excluded but may also feel betrayed after having supported the HBP during the application phase. This is because many research groups interested in participating in the HBP but who have not been included in the FPA, have been referred to opportunities provided by PP funding. Hence, PP funding by national or EC funding instruments is an essential element not only for the scientific success of the HBP but also for reconciling the conflict between the HBP and the wider neuroscience community.

Communication within the HBP, between the HBP and the science community, as well as between the HBP and the public is regarded as a major weakness of the project. The MC considers the initiation of a transparent scientific discourse within the HBP and between the HBP and the science community as being a pre-requisite for the process of steering the HBP to a set of realistic objectives, which are accepted by the HBP Consortium and appreciated by the scientific community. Given the complexity of the project's research topics and the uncertainty that is inherent in any scientific endeavour aiming at ground-breaking results, a lively and dynamic continuing scientific discourse among all scientists involved in the project regarding the mission and objectives of the HBP should be routinely practiced. This discussion should particularly address issues related to the balance between research on neuroscience and IT platforms, structurally and functionally oriented neuroscience, between theoretical and empirical research and between top-down and bottom-up modelling towards

an understanding of the brain. This discourse also needs to cover research planning regarding the degree of coordination among and the scheduling of the various activities in the course of the project.

Some members of the BoD hold the view that a highly visionary project such as the HBP that is disruptive usually lacks support from its wider community, although they are confident that support will grow over time. However, deficits in communication were acknowledged by most of the BoD members. The mission statements on the HBP website were recognized as being oversimplified and thus giving a misleading impression. Members of the BoD also suggested starting a well-documented socratic dialogue in the public between scientists within and outside the HBP. It was also pointed out by a BoD member that part of the neuroscience community is not yet familiar with simulation approaches. Therefore, HBP has to emphasize activities aimed at promoting the potential of simulation in neuroscience.

4.1.4. Reintegration of Systems and Cognitive Neurosciences

An important issue, also brought up in the recommendations of the FPA review, is related to the (re-) integration of systems and cognitive neuroscience into the HBP during the operational phase (SGA-1 to SGA-3). The following positions compiled by the MC were favourably commented upon by the BoD.

The MC suggests that the current project structure should be expanded for this purpose. At present, the HBP is organized in vertical subprojects. These could be supplemented by cross-cutting activities organized in horizontal work packages possibly aggregated into a horizontal subproject, thus creating a matrix structure. In addition to existing implicit links the current subprojects would then also be explicitly linked by the cross-cutting work packages, which should address a few concrete challenging problems in systems and cognitive neuroscience, each focusing on a certain behavioural phenomena (see Appendix A.1). They should be structured in such a way that they can be successfully tackled by modelling, theory-building and simulation during the course of the HBP.

As many of the existing tasks (or even work packages) in the (vertical) SP as is reasonable with regard to the scientific alignment should be assigned to cross-cutting (horizontal) work packages emphasizing a concrete systems and/or cognitive neuroscience problem. In this way, method-oriented research approaches, largely covered by the SP, will be combined with problem-oriented research approaches in a productive manner. This will also help to overcome fragmentation. It would not only entail team building across disciplines and foster interaction between different fields, but would also provide an appropriate environment for the validation of the IT platforms in the sense outlined above. Systems and cognitive neuroscience would thus become part of all or at least the majority of the subprojects sending a strong message to the wider neuroscience community.

Currently, the HBP concentrates on the generation of experimental data for mice and humans in the CP. Some of the experts on the mediation committee strongly agree with those members of the neuroscience community within and outside the HBP that regard research on NHP as being essential for bridging the gap between the mouse and the human brain. Experiments with NHP should, therefore,

not be excluded on principle if relevant data are not available and if dedicated experiments are essential to fulfil the objectives of the HBP. It is emphasized that a successful integration between established neuroscience and evolving simulation-based neuroscience research also requires the design of new experiments that leverage the capability of the evolving IT platforms. Such research activities should also be part of the newly introduced cross-cutting work packages. Experiments either on mice, NHP or human brains that generate data but that do not help the development of IT platforms, should not be included in the CP.

4.1.5. Funding of Cross-Cutting Activities

Since the HBP has to be set up in a self-contained manner relying exclusively on secured CP funding, the budget for cross-cutting activities has to be either provided as additional core funding by the EC, or funding has to be reallocated from the CPs in the SPs to the cross-cutting activities. The MC analysed the scientific content of all SPs to make suggestions for such a reallocation, which is unavoidable if no extra core funding from the EC becomes available, using the criteria scientific quality and relevance to the mission and the objectives of the HBP. The results of this analysis are summarized in Appendix A.2.

Tasks and work packages that are not in alignment with the overarching goals of the HBP or lack scientific quality should be identified by the HBP using some kind of internal mechanism that relies on the scientific discourse between the members of the HBP and is modelled on established peer-review procedures. For example, work package funding could be competitively awarded on a formal ranking by the decision-making body in the HBP governance. This would encourage excellence and ensure coherence between subprojects. Another source for funding cross-cutting activities could be SP 11 (Management and Coordination).

While most members of the MC are in favour of bold cuts to focus the scientific program and further improve coherence and quality, the BoD prefers small cuts across all SPs. While the BoD suggests to realign research in a SP so that it contributes to a cross-cutting activity, but to keep the funding of the cross-cutting activities in the SPs, the MC is convinced that the work packages implementing cross-cutting activities should have their own funding.

4.2. Governance

Although the MC greatly appreciates the dedication, commitment and contributions of the coordinating institution and its representatives – in particular the coordinating scientist – in successfully applying for the FET Flagship project, they are convinced that the role of the coordinating institution and the leading scientists have to be re-defined to prepare for the challenges the HBP will face.

4.2.1. Transparency of Project Governance and Operational Management

A lack of transparent governance and project management structures provides an easy target for widespread criticism, but more importantly, increases the risk that the whole project will fail. Professional, independent and transparent management is indispensable to assure the scientific community and the public that the project is credible and that its goals are sensible. Appropriate governance structures and processes can only be established if clear rules and constraints are specified by the EC, in particular, with respect to funding mechanisms as well as governance and integration of PPs into Flagship projects.

The EPFL is the major recipient of HPB funding and also serves as the coordinating institution. While the EPFL has substantially co-funded parts of the HBP in the ramp-up phase *via* the Blue Brain Project, and thus expects appropriate representation in decision-making, the current governance is biased towards EPFL: the coordinating scientist, who has been representing EPFL, is not only a member of all decision-making, executive and management bodies within the HBP, but also chairs them and supervises the administrative processes supporting these bodies. Furthermore, he is a member of all the advisory boards and reports to them at the same time. In addition, he appoints the members of the management team and leads the operational project management.

The tension between the decision-making and executive bodies of the HBP, such as the ExCo, the General Assembly (GA), and the BoD largely results from tasks and responsibilities not being clearly assigned. Most at odds with good governance practice is the lack of separation between those who make decisions and those who benefit from them. While some overlap between those groups may be inevitable during the initial phase of a project, such overlap needs to be minimized for the operational phases.

There is a strong consensus among most members of the MC and the BoD that transparency of decision-making and professional management will be essential for the success of the project. Consequently, the concentration of too many tasks and responsibilities with the members of the ExCo and the lack of separation of duties and power has to be eliminated. The roles and responsibilities in the leadership of the HBP need to be disentangled and appropriate checks and balances must be established.

Finally, there must be mechanisms in place that ensure that the governance outlined in the Consortium Agreement is implemented and properly executed. Though this requirement seems to be obvious, it has not been always fulfilled in the HBP.

Separating responsibilities for science from those for management was appreciated by most members of the BoD though some regarded joint responsibility as advantageous. The BoD largely agreed on the need to mark the transition from the ramp-up to the operational phase by modifying the governance and further professionalizing project management.

4.2.2. Roles and Tasks of the Organs, Bodies and Boards of the HBP

The HBP is a large-scale scientific project composed of scientists coming from widely differing scientific backgrounds and cultures, which complicates the task of governing it tremendously. The HBP should therefore learn from other big science projects.

The concentration of scientific and leadership tasks, decision-making power and executive responsibilities among the ExCo members is seen as inherently problematic. It has to be overcome to avoid work overload of individuals but also to improve transparency. Furthermore, the decision-making power of the ExCo members needs to be put on a broader platform. They not only fill most of the instrumental positions in the governance bodies, but they are also able to control the BoD, i.e., the major scientific decision-making body of the HBP. In order to achieve the two-thirds quorum needed for decisions, the BoD depends on the votes of this particular group of people. While the MC appreciates that the members of the ExCo and selected SP leaders have been instrumental in successfully acquiring funding for the HBP, they are convinced that their involvement in the leadership of the HBP has to be revised. While it is imperative that tasks, functions, responsibilities and accountabilities are

disentangled and distributed to a larger group of people, the members of the current ExCo should continue taking responsibility in the HBP as PIs and as WP/SP leaders.

According to the FPA proposal, strategic decisions are to be taken by the BoD, executed by the ExCo, and approved by the GA. This, in theory, makes the BoD the main decision-making body of the HBP, while the ExCo's role is to execute those decisions and the role of the GA is to control them. This separation of tasks and responsibilities (decision-making, execution, supervision) does not only need to be implemented in day-to-day management practice, but also has to be refined. The task of allocating funds currently lies by the BoD and is approved by the GA. This is not without its dangers since many BoD members benefit directly from their own funding decisions, which cannot be effectively supervised by an organ such as the GA, composed of more than hundred members, mostly task and WP leaders or administrative staff, who do not see all implication of their decisions. To alleviate this problem, a truly independent body, such as a scientific advisory or a supervisory board, needs to be asked to review and approve funding decisions.

4.2.3. Structure, Processes, Roles and Responsibilities of Central Project Management

The central project management team has been and still is directed by representatives of EPFL. In the beginning this team was physically located in the premises of a lab at EPFL in Lausanne and was integrated with the administration of this lab. Recently, however, the team moved to Geneva together with the research team of the Blue Brain Project. The tasks of the HBP management team overlap with the administrative tasks of the Blue Brain Project and the management of SP 5 (Brain Simulation), the subproject led by the coordinating scientist. As a consequence of the discussions between EFPL, the EC and the mediator, the provost of EPFL took over responsibility for the central project management team, at least until completion of the mediation process. He appointed a Chief Operating Officer (COO), who is reporting to him and who is acting as the interim head of the central project management team. The COO was a member of one of the management subdivisions and is thus familiar with the HBP.

The MC recommends separating the project management of the HBP from any organizational unit of EPFL. This includes a separation of legal functions, possibly even a physical separation of the management office from EPFL premises, and a clear distinction between the tasks of the scientists in the ExCo in HBP central management, the tasks in the SP they lead and the tasks in the Blue Brain Project, headed by the coordinating scientist. In the operational phase, the HBP should rely on a governance structure that distributes responsibilities over a number of institutions. Executive management decisions should be taken by a directorate staffed by individuals, who are experienced in science management and policy and who have not been involved with the HBP yet.

Most of the members of the MC also concluded that the current central project management of the HBP is not optimally positioned regarding cost-benefit ratio. Despite the fact that SP 11 (Management and Coordination) also provides funds for IT support, outreach and education, a careful evaluation of the budget is necessary. The MC expects that substantial budget cuts are identified to be feasible.

5. Recommendations

Section 4 documents positions on the HBP governance and the scientific balance of the MC and the BoD. The MC has drawn up a number of concrete recommendations, which are presented in this section. The HBP will have to agree and faithfully implement all these recommendations for the mediation process to be successfully completed (cf. ToR of the mediation). Section 4 should be considered as additional advice to be taken into account during the implementation of the recommendations.

It is useful to distinguish the following four phases when formulating the recommendations:
Phase 1 extends until the completion of the negotiation of the FPA with the EC in May 2015 and is focussed on updating the FPA, thereby integrating the mediation committee's recommendations on governance and science. The Mediator will support the Consortium where necessary, e.g. to interpret the recommendations and put them into the context of the observations.
Phase 2 is an intermediate phase, which could last until the beginning of the operational phase in April 2016 or at most until September 2016. In Phase 2, the transition from the current to a new governance and project structure should be implemented gradually and should be completed by the start of SGA-1 in April 2016. While the EPFL will act as the coordinating institution during Phase 2, the implementation of a legal entity acting as an umbrella for the HBP (see Recommendations G2) will be prepared and established before the end of Phase 2.
Phase 3 covers the remainder of the time until the end of the HBP, which is planned for September 2023. The legal entity coordinating and managing the HBP must be fully operational at the beginning of this phase (see Section 4.2, for the specific recommendations for a revised governance of the HBP and the new legal entity replacing EFPL as the coordinating institution), and the recommendations regarding the scientific program and the project structure must be fully functional at the beginning of this phase.
Phase 4 covers the period after the HBP has come to an end, i.e., it will start after funding of the HBP has ended, in October 2023 according to the current plan. If the HBP succeeds in establishing an IT infrastructure accepted and used by the global neuroscience community and clinical practitioners, the legal entity, which has been operational in Phase 3, could be the vehicle to implement a transition from project funding to institutional funding, and would be responsible for ensuring that support for evolving and maturing the IT infrastructure continues. The "ownership" of the legal entity operational in Phase 3 should be transferred to a few Member or Associated States in Phase 4.

5.1. Recommendations on Science

The MC has identified several points that disturb the scientific balance of the HBP and has provided suggestions to solve those constraints by adjusting the scientific program and the project structure of the HBP. The recommendations on the science in the HBP are presented in this section. For a detailed exposition of the arguments as well as for additional important considerations and suggestions the reader is referred to Section 4.1. Further observations on the scientific program as described in the FPA are compiled in Appendix A.2. All the recommendations apply at least to Phases 1 to 3, as outlined in Section 5. Their implementation has to be prepared by introducing concrete measures in the revision of the FPA during Phase 1 (before its submission to the EC). Implementation should be started during Phase 2. Obviously, many of the recommendations require continuous effort not only during Phase 2 but also during Phase 3.

S1: Focus the Research Program on the HBP's Mission and Objectives

Issue: The HBP addresses very ambitious long-term objectives, which may not be achieved within the projected time-frame and with the financial resources available.

Recommendation: The HBP should re-evaluate and accordingly re-adjust its scientific program. The research program has to be designed to follow a unique mission and set of objectives, which can be successfully fulfilled with the budget available for CP. This will require focusing on properly prioritized activities contributing to the main goal of the HBP. In particular this requires directing any neuroscience research in the HBP towards the development of a set of complementing and integrating models and the specification, design, implementation and testing of IT platforms, built on those models. The HBP should not attempt to fill *all* the gaps in structural and functional data, as desirable as such data may be for the neuroscience community. It should emphasize the development of Data Hubs that could eventually provide access to experimental neuroscientific data that already exist or will emerge over the course of the project. The HBP is expected to take a leading role in establishing partnerships to support this endeavour. Dedicated and targeted experiments for different species, including NHP, carried out in the HBP should serve the mission and the objective of the HBP, i.e., the development and provision of IT tools to empower research in the neurosciences, and – in the longer run – in clinical neurology and psychiatry.

S2: (Re-)Integration of Systems and Cognitive Neuroscience

Issue: The absence of systems and cognitive neuroscience subverts the multi-scale and multi-perspective ambitions of the HBP to integrate and validate various approaches to a unifying modelling and simulation platform. It also impairs the validation of other IT platforms developed in the HBP regarding the value added to future neuroscience research and clinical practice.

Recommendation: The SPs (and the constituent WPs) suggested in the FPA should be consolidated and integrated with a set of new cross-cutting horizontal tasks to form a matrix-type project structure. These cross-cutting activities should be organized in at least 3 - 4 WPs to address challenging problems of systems and cognitive neuroscience which are led by PIs with a strong scientific background in the respective areas. These WPs should be aggregated to a new cross-cutting subproject "Cognitive and Systems Neuroscience: CSN". Both, the PI leading the cross-cutting (horizontal) WP and the PI leading the vertical WP in the SPs defined in the FPA, need to take joint responsibility for the research in the cross-cutting activity (see the schematic in Figure 2). The problems addressed by the cross-cutting activities should be chosen in order to demonstrate the added value of the IT platforms and, if successful, to facilitate new and unprecedented insight in brain function and cognitive behaviour. The selection of concrete problems is at the discretion of the HBP, but illustrative examples are given in Appendix A.1 for orientation. This may require dedicated experiments with different species. The solution of these problems will likely require specific data that presently neither exist nor are likely to be collected by other international initiatives in the next 5 years. The budget allocation has to properly account for such dedicated experiments. The funding for each WP implementing a cross-cutting activity should therefore be at least at a level of € 2-3 million p.a. in all the SGA phases. Based on this estimate at least € 45 million (about 10 % of the planned total budget) is required to properly fund the cross-cutting activities during the operational phases. The funding must come from core funding of the HBP. If the EC cannot make additional core funding available for this purpose, the necessary budget has to be generated by re-allocating funds from the SPs in the core, including SP 11 (Management and Coordination). The budget should be taken from those SPs that contribute the

least to the mission and scientific objectives of the HBP, or where there is doubt regarding the scientific excellence. This should be achieved in a peer reviewed and quality controlled process implemented by the HBP.

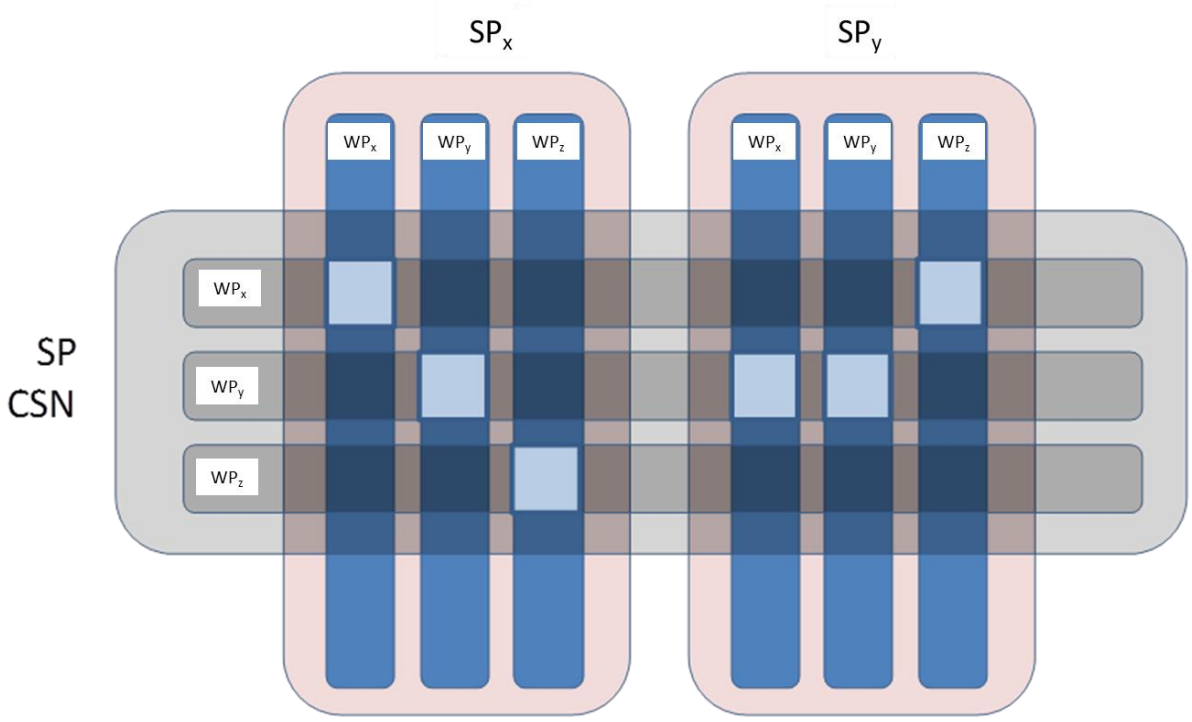

Figure 1: Schematic of crosscutting (cognitive in systems neuroscience) subproject – in which each (vertical) work package is assigned to a (horizontal) thematic work package (and named principal investigators). Light patches identify joint research between WPs and crosscutting activity.

S3: Scientific Project Management and Coordination

Issue: Scientific project management and coordination is not carried out with sufficient stringency in SPs and in particular across SPs. Especially problematic are (i) poor definitions of tasks, (ii) mismatch between research teams, often with excellent research track records, and tasks, and (iii) a lack of coherence and transparency during the allocation of a task budget.

Recommendation: SPs and constituent WPs should be consolidated and substantially streamlined to avoid resource dilution and underfunding of tasks. In particular, the number of PIs contributing to each WP should be reconsidered and ideally be reduced. In addition, the SP leadership should create incentives that promote the formation of groups of researchers (Postdoctoral Research Fellows and Ph.D. Students) from different laboratories. Those groups would be working closely together and its members would spend a significant amount of time at a common location, possibly rotating between the labs of the participating PIs. This would help to create an interdisciplinary research environment, a sense of shared intellectual ownership, and a training legacy. Even more important is the establishment of effective scientific project management on all levels of the HBP which aims at appropriate coordination towards the delivery of mature IT platforms. At the same time the project management should foster not only creative, methodologically as well as discovery-oriented research on theory and tool development, but also in the demonstration of the tools' capabilities by applying them to demanding problems in systems and cognitive neuroscience. Joint leadership of WPs by PIs with different scientific backgrounds should be considered where appropriate, but in particular for the cross-cutting WPs. Furthermore, continuing quality assurance should inherently be embedded in

the research processes and monitored by project management. The partnership in the SPs should develop mechanisms for an open scientific discourse that builds on established principles of peer review to assess the quality of the research. Budget allocation has to account for scientific quality and how well the research matches the objectives of the HBP. The PIs should make suggestions, but cannot decide on budget allocation.

S4: Partnering Projects

Issue: At present, no substantial additional funding for PPs has been secured and the future of these funds is uncertain. The project has to be successful, if – in the worst case – no substantial PP funding were available. Nevertheless a gate to the communities has to be opened somehow.

Recommendation: The research program should be designed such that core objectives of the HBP can be successfully fulfilled with the budget available for CPs. This level of funding will require both, substantial concentration on a smaller number of properly prioritized activities contributing to the main goal of the HBP, namely developing and demonstrating new IT tools for future neuroscience research, and the integration of scientists outside the HBP by suitable means. Despite this repositioning of the HBP, accommodating a possibly much lower budget than initially planned, the realization of PPs and their funding at about the same level as the CP funding has to be aimed at with the highest priority. This task is a joint responsibility of the HBP and the EC. Properly set-up PP programs and their targeted integration in the HBP core must be established as a mechanism to productively interact with relevant scientific communities. PPs have to be designed such that they contribute directly to the objectives of the HBP. HBP governance has to accommodate the PP leaders and give them an appropriate role in driving and shaping the overall scientific program of the HBP which should accept contributions from both CPs and PPs.

S5: Interaction between the HBP and the Science Community

Issue: Public announcements by the HBP leadership and by the EC overstated objectives and the possible achievements of the HBP. Unrealistic expectations were raised, such as tools for predictive simulation of the human brain to enable understanding of brain function or to support diagnosis and therapy of neurodegenerative diseases within the course of the project. This resulted in a loss of scientific credibility of the HBP.

Recommendation: The HBP and the EC should clearly and openly communicate the project's sharpened mission and objectives. Furthermore, the HBP should systematically create and use opportunities to enter a constructive scientific discourse with the science community, with science policy makers and with the interested public. Ultimately the reputation of the HBP in the science community will rest on the publication of convincing scientific results and the generation of widely used IT platforms. The leadership of the HBP should therefore aim both at publications of high impact and at mature IT platforms that will eventually be made available. This will require appropriate target setting, resource allocation and project coordination. The HBP should be assessed by a very specific metric of success, namely the acceptance and adoption of the HBP's IT platforms and the demonstration of added-value created by IT-empowered research processes. The HBP should establish appropriate processes for research process coordination and quality assurance to meet these expectations.

5.2. Recommendations on Governance

A revision of the governance structures is regarded as necessary as the project enters the operational phase. The governance structure must ensure that the leading scientists (PIs, WP and SP Leaders) are adequately involved in strategic decision making. However, the approval of decisions on the allocation of funds has to be the responsibility of an independent governance body. An individual not related to the HBP and experienced in science policy, science management and project execution should be appointed as the CEO.

The establishment of an independent legal entity is recommended before the end of Phase 2. Members of the MC and the BoD believe that the HBP could in the long run become a hub for simulation-based or even computational neurosciences in Europe. In this role, the project should aim at providing and maintaining IT platforms and services for the scientific community and clinical practice. For this purpose the consortium of the HBP will, in close cooperation with the end-users, carry out applied IT-related research to the degree necessary to support the community. Further it will act as an organisational centre to induce and support the implementation of collaborations between academia and industry.

G1: Guiding Principles for a Revision of the Governance Structure

Issue: While the current governance of the HBP might have been useful for the ramp-up phase, it does neither meet the requirements for the operational phase nor does it comply with established standards of good governance.

Recommendation: The project governance has to be developed further and implemented in a short timeframe. Such a thorough revision of the governance should adhere to the following principles:

- The governance structure should serve the scientific goals of the project and implement scientific leadership, while safeguarding a conscientious, transparent and appropriate use of resources. The scientific goals need to be identified in a transparent and open discourse. The governance should be designed to establish a fair and transparent process for reaching consensus on major strategic objectives. The set-up should be lean and avoid unwarranted complexity. The revised governance should be tailored to the implementation phase of the HBP (Phase 3), but should be adequate for Phases 2 and 4 as well. It should assure stability, but should also allow flexibility to react to changes in the scientific program, to unforeseen events, and to new project partners.
- The governance should combine effective scientific leadership with professional management in execution and administration of the project, its financing and implementation. Allocation of funding for the SPs and WPs should be decided by an independent board consisting of non-beneficiaries of the funding decisions. An appropriate system of checks and balances between the internal stakeholders and the external members of the governance bodies has to be established.

- The governance should distinguish and establish a functional separation between advising, decision-making (on project scope, content and governance), operating, supporting and controlling (or auditing) bodies. Separation between execution, strategic decision-making, and quality control must be strictly followed. Each governance body should have a clearly defined charter describing scope, roles and responsibilities, membership, meetings (agendas and minutes) and deliverables. Each governance body will be chaired by a different person.
- The HBP governance should be separated from the governance of other projects and scientific institutions. If there is an overlap in staff, the regulations for working and reporting into different projects need to be made transparent. Potential conflicts of interests need to be disclosed.
- Clear and transparent escalation and conflict resolution mechanisms must be put in place as part of the governance regulations.
- Each governance body will have a defined charter describing its scope, function, responsibilities, reporting lines, membership and leadership.

- Representatives of partnering projects should have to be involved in the decision-making progress regarding the scientific objectives and program of the HBP.

G2: Establishment of a Legal Entity

Issue: The current governance is centred at EPFL, the initiator and the coordinating institution of the HBP. While this model has been suitable during the competition for winning the Flagship project, the concentration of responsibility on a single institution restricts a future extension of its objectives – like an evolution of the HBP into a European hub for simulation-based or even computational neuroscience, which provides and maintains tools for the global science community, and, in the longer run, for clinical neurology and psychiatry as well as for commercial service providers.

Recommendation: The responsibility for the HBP has to be taken by more than a single institution. In particular, the "ownership" of the project should be associated with a new and neutral legal entity acting as an umbrella for the HBP. The envisaged entity shall act independently from the self-interests of the institutions participating in the HBP and thus requires legal independence from all organisations participating in the HBP. It should be incorporated and physically established in one of the states of the participating institutions. This new institution will take responsibility for properly executing the project, maintaining and eventually further developing the IT platforms, organizing user access based on peer review, or license the IT platforms to commercial service providers. It will oversee any IP generated by the HBP, which should be made widely available to the scientific communities. The legal entity should be fully operational by the end of Phase 2. During Phase 3, the proprietors of this legal entity should consist of the most relevant institutions (with the strongest commitment) that are willing to take (financial and legal) responsibility for the HBP. The HBP should decide on 3 to 7 participating institutions taking a major role in the HBP. One of them has to be EFPL to acknowledge its significant contribution to the HBP. Though not all institutions participating in the HBP can become "owners" of the legal entity, they will nonetheless participate in an appropriate role in the governance of the HBP.

If the HBP is successful, the project-based funding under Horizon 2020 should be transferred to an institutional funding in Phase 4. The legal structures and the governance have to be adjusted accordingly. The specific governance design needs to be re-evaluated based on the scientific progress made in Phase 3 and the objectives set for Phase 4.

There are various options to set up the legal entity in both Phases 3 and 4, either under European law or under national law of one of the member or associated states. The particular kind of legal entity cannot yet be decided, because the choice of the entity will require a thorough assessment, in particular of financial issues such as the liability of the owners and tax exemption. Several options for the legal entity have been identified and compiled in Appendix A.3. While the legal entity will be owned by public institutions in Phase 3, all those options in A.3, that require the Member or Associated States to act as "owners" of the legal entity are not eligible. The *European Economic Interest Grouping* is an interesting option under European law for Phase 3.

In Phase 4, the legal entity should be migrated to an international organisation that is governed by a few Members or Associated States. The European Molecular Biology Laboratory (EMBL) can act as a role model for an international entity hosting the HBP. Alternatively, the HBP could also become a division of EMBL such as the European Bioinformatics Institute (EMBL-EBI).

G3: Governance Structure

Issue: The governance structure outlined in the FPA needs revision to meet the rules of good governance practice, as outlined in G1 above, and the requirements that the HBP will face during the operational phases and beyond.
Recommendation: The HBP leadership should develop a revised governance structure following the guiding principles outlined in Recommendation G1. This governance should be implemented step by step during Phase 2 and be fully functional at the latest at the beginning of Phase 3. Its basic principles should be valid regardless of the type of legal entity recommended in G2 for Phases 3 and 4. The MC provides a revised governance structure, which presents a framework for the HBP presenting a more detailed governance structure in the revised FPA.

A sketch of the recommended architecture of the new HBP governance is given in Figure 1. It is the governance of the HBP legal entity after it has been established. The **Assembly of Contracting Partners** (ACP) constitutes the owners of the HBP legal entity, 3 to 7 research institutions from different countries participating in the HBP in Phase 3, a set of Member and Associated States in Phase 4. All the research institutions participate in the **Partners Assembly** (PA) which receives and approves the report of the HBP bodies during Phase 3. The PA may not be necessary anymore in Phase 4. The **Supervisory Board** (SB) has multiple functions: (i) it approves decisions of the **Directorate** (D) regarding the scientific strategy, (ii) selects and decides on the integration of PP*,* and (iii) monitors executive management of the D. The SB comprises the representatives of the ACP and the same number of external experts. The SB is chaired by an external member who has an additional vote in a tie. It establishes a **Partnering Project Subcommittee** (PPS) for the preparation of decisions on PP selection and integration. The SP leaders are *ex officio* members of the PPS; the same number of external members is appointed by the SB. The **Scientific Advisory Board** (Sc_AB) and the **Ethics Advisory Board** (Et_AB) provide advice on scientific and ethical issues, respectively, to the Supervisory Board and to the Directorate. While the Sc_AB will supersede the EAB and IAB, the Et_AB will be established by merging the current Research Ethics Committee (REC) and the current Ethical, Legal and Social Aspects Committee (ELSA). The **Directorate**, consisting at least of the Chief Executive Officer (CEO) and the Chief Administrative Officer (CAO) implements the executive and operational management with a split of responsibilities for scientific progress and technology platforms (CEO) and administration and finances (CAO). The CEO holds the overall responsibility. The **Scientific Board** (ScB) is the assembly of the SP leaders. It (i) develops a scientific strategy and proposes it to D, (ii) proposes budget allocation for all WPs to D, and (iii) is responsible for scientific coordination and management across the SPs. The Chairman of the ScB is elected by its members and represents the ScB in the D as well as in the SB as a non-voting guest. Each SP is led by a subproject leader who is coordinating the research process in the SP. The **Enabling Functions Committee** (EFC) is responsible for all administrative issues and enabling functions. It is chaired by the CAO. The **Audit Committees** (ACs) are regularly auditing the project emphasizing finances, scientific quality and good governance practice.

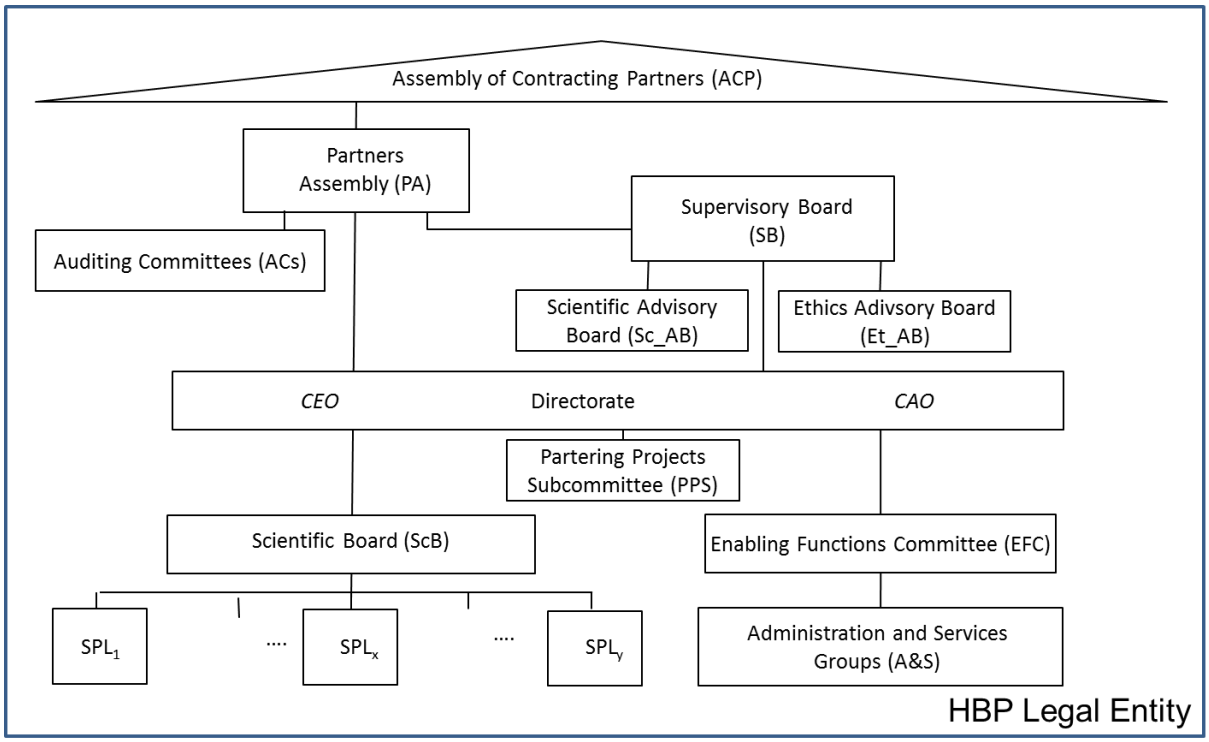

Figure 2: Draft of a revised HBP governance structure showing the bodies and their major interactions

The various bodies, their roles, functions and members are described by means of the following tables. These tables do not intend to provide a complete specification of all the technical details, but focus on the basic principles. Details may be added in the presentation of the new governance in the revised FPA. A complete specification (in the sense of a "constitutional document") with all relevant technical details will be compiled during the transition period (see G4: Transition phase).

Assembly of Contracting Partner (ACP)

Function	• Liaison between EC and HBP legal entity in Phase 3 • Liaison between state governments and HBP legal entity in Phase 4 • Sets policy for scientific targets and constraints of scientific program; also sets overall budget in Phase 4
Reporting line	• Reports to EC in Phase 3 • Reports to Member and/or Associated State governments in Phase 4
Members	• One representative of each of the owning institutions in Phase 3 (who is also member of PA) • One representative of each of the owning Member and/or Associated States in Phase 4 • Members are nominated by a nomination committee and appointed by PA (for details, see G4)
Leadership	• Chairperson elected by the members • One member – one vote

Partners Assembly (PA)

Function	• Receives and approves the regular reports of D • Decides on regular or premature termination of HBP • Decides on legal framework of HBP legal entity • Appoints the members of SB • Appoints members of Directorate nominated by SB
Reporting line	• Reports to ACP
Members	• One representative of each institution participating in CP (or a delegate) • One representative of each institution participating in PP (or a delegate)
Leadership	• Chairperson appointed by ACP based on nominations from PA in Phase 3 • Chairperson appointed by owning Member or Associated states based on nomination by PA in Phase 4 • One member – one vote

Supervisory Board (SB)

Function	• Approves scientific strategy • Approves overall budget allocation for all SPs • Monitors executive management by D • Approves decision from D regarding admission of PIs to CP • Approves adoption of PP, selected by D based on suggestions of PPS • Proposes all members of D to PA • Approves Chairperson of ScB, elected by its members • Approves decision on appointment of SP leaders • Escalation and final decision body in case of major disputes between SB, PPS, and D • Approves report of D on project progress to EC in Phase 3 and to ACP in Phase 4
Reporting line	• Reports to PA
Members	• All members of the ACP (one representative of each of the owning institutions in Phase 3, one representative of each of the owning states in Phase 4) • External scientists and science managers from academia or industry, equal in number to ACP members; nominated by nomination committee and appointed by PA (for details, see G4). • CEO (non-voting guest) • CAO (non-voting guest) • Chairperson of ScB (non-voting guest) • Representative of EC in Phase 3 (non-voting guest)
Leadership	• Chairperson: an external member of the SB, proposed by SB and appointed by PA • 50 % of the votes are with the members of the ACP, 50 % of the votes are with external members; Chairperson has an additional vote in case of a tie of votes • Four years per term in office with a maximum of two terms in office for each member

Directorate (D)

Function	• Represents the HBP • Executes internal and external communication • Executive management of the HBP according to approvals by SB • Decides on proposal for scientific strategy by ScB and forwards its own proposal for approval to SB • Executes scientific strategy approved by SB • Proposes budget allocation for each SP to SB • Decides on budget allocation for all WPs based on proposals from ScB • Decides on all administrative measures and enabling functions proposed by EFC • Decides on admission of PIs to CP suggested by SPL • Decides on SPL suggested by PIs of respective SP • Decides on selection of PP suggested by PPS
Reporting line	• Reports to SB and PA • Reports to the EC on project progress after approval of the report by SB in Phase 3 • Reports to ACP on project progress after approval of the report by SB in Phase 4
Members	• Chief Executive Officer: scientific & technological leadership, overall executive responsibility for the HBP • Chief Administrative Officer: administrative and financial leadership • In addition to CEO and CAO, further Directors can be appointed if necessary • Chairperson of ScB (non-voting guest)
Leadership	• Each Director has one vote; CEO has additional vote in case of a tie of votes

Scientific Advisory Board (Sc_AB)

Function	• Advises SB and D on scientific strategy and scientific issues
Reporting line	• Reports to SB and D
Members	• 7 – 10 external scientists nominated by the ScB and appointed by the SB
Leadership	• Chairperson to be elected by Sc_AB members

Ethics Advisory Board (Et_AB)

Function	• Advises SB and D on ethical issues
Reporting Line	• Reports to SB and D
Members	• All members of the present Research Ethics Committee on Human and Animal research • 5 members of the present Ethical, Legal and Social Aspects Committee
Leadership	• Chairperson to be elected by the Et_AB members

Partnering Project Subcommittee (PPS)

Function	• Preparation of decisions on PP selection and integration; suggests PP for integration to SB
Reporting line	• Reports to SB
Members	• SPL (born members) • External members equal in number to SPL, suggested by ScB, nominated by D and appointed by SB
Leadership	• Chairperson elected from group of external members by all members of PPS • One member – one vote; Chairperson has additional vote in case of a tie of votes

Scientific Board (ScB)

Function	• Develops scientific strategy and proposes it to D • Proposes budget allocation for all WPs to D • Enacts scientific project management and coordination across SPs
Reporting line	• Reports to D
Members	• All SPLs
Leadership	• One member – one vote • Chairperson nominated by ScB and approved by SB; term in office is defined by the length of one SGA, starting after one half of the SGA1 period; reappointment is possible

Subproject Leader (SPL)

Function	• Coordinates research activities of respective SP • Suggests assignment of tasks and budget allocation per WP in the respective SP to D • Suggests admission of PIs to respective SP to D
Reporting line	• Reports to ScB
Leadership	• Nominated by all PIs of all SPs (majority vote, one vote each), approved by D and appointed by SB • Term in office is defined by the length of one SGA, starting after one half of the SGA1 period; reappointment is possible

Enabling Functions Committee (EFC)

Functions	• Deals with all administrative measures and enabling functions and proposes to D • Manages IT platforms and other infrastructure necessary for administration • Manages IP rights (based on agreement for legal entity) • Provides legal support
Reporting line	• Reports to D
Members	• Chief Administrative Officer (CAO) • Head of each management and services group
Leadership	• Lead by CAO

Audit Committees (ACs)

	• Regular audits on financial issues, scientific work and good governance practice
Reporting line	• Reports to PA in Phase 3 • Reports to PA and ACP in Phase 4
Members	• 3 external expert teams, one per specific audit field, appointed by EC (financial audit and scientific review) and by ACP (governance practice) during Phase 3, appointed by ACP during Phase 4
Leadership	• Chairperson appointed as part of appointment of audit teams

G4: Transition Phase

Issue: The transition from the current to the new governance has to be properly managed. It should evolve according to the outline of Phases 1 to 4 at the beginning of Section 5. The transition has to be smooth to guarantee appropriate leadership and professional project management at any time.

Recommendation: The new governance should be implemented as quickly as possible in a step-by-step manner starting immediately after approval of the report of the MC by the BoD. The existing governance bodies are dissolved as soon as their counterparts are in place. The process should be carried out as outlined next.

i) The GA approves the report of the MC and agrees to Recommendations S1 to S5 and G1 to G4. It renames itself to PA.

ii) A nomination committee, comprising at least 9 presidents of the HBP's partnering institutions, is elected by the PA. Presidents may delegate their task to a representative of their choice.

iii) The nomination committee identifies and nominates all members of the ACP. The PA appoints the members of the ACP according to the standards established for the GA. Subsequently the ACP will be implemented.
In parallel, the nomination committee identifies and proposes the external members of the SB to the PA, which appoints the external SB members. Subsequently the SB will be implemented. The members of the SB propose a chairperson among its external members to the PA, which appoints the chairperson of the SB. The SB chairperson will act as the CEO until the D will have been formed.

iv) The PIs of all SPs nominate an SP leader and propose him/her to the SB. The SB approves the nomination and appoints the SP Leaders as members of the ScB. The ScB will be implemented; it elects a chairperson who will be approved by the SB. The ExCo is dissolved at the latest after the SB and the ScB are operational.

v) The members of the D are nominated by the SB and approved by the PA by the end of Phase 2 at the latest, starting with the CEO. The profile of eligible CEO candidates should adhere to the following key aspects: candidates must have no self-interests in HBP; candidates must have proven experience in the management of large-scale international and interdisciplinary projects and a strong expertise in change management. The identification of further members of the D is performed by the SB in reconcilement with the CEO.

vi) All other governance bodies will be established in due time according to the principles laid out in Recommendation G3.

Appendix A: Observations

This section compiles various observations resulting from an analysis of the scientific program of the HBP. These observations – in contrast to the recommendations compiled in Section 4 – are meant to advise the (current and, in particular, the new) HBP leadership in decision-making with respect to the readjustment of the scientific program in relation to the (re-)integration of systems and cognitive neuroscience as cross-cutting activities and the reallocation of funds from the SPs to these newly introduced activities as described in the FPA proposal.

A.1 Guidelines for Defining Newly Introduced Cross-Cutting Activities

As indicated in Recommendation S2, a list of examples is presented to guide the selection and definition of the problems implemented as cross-cutting activities. Each is intended to form a single WP. These WPs must integrate multidisciplinary expertise: in addition to systems and cognitive neuroscience groups, they must include computational neuroscientists and researchers who will interface these activities with the relevant neuroinformatics, imaging, brain simulation, high performance computing, neuromorphic and neurorobotics platforms. It is crucial that the cross-cutting activities should integrate the various brain modelling and simulation services most appropriate to their specific needs, and so will ensure that a broad range of scales and a diversity of data (including recordings, imaging, sensory and behavioural data) characterizing contemporary neuroscience research is covered. Experimental research on rodents, non-human primates and humans that generates new data may be covered if it supports the development and use of the IT platforms, especially modelling and brain simulation as outlined in Section 4. A few inspiring examples of such cross-cutting activities, which promise substantial advances and, most importantly, demonstrate the usefulness of the new IT platforms, are sketched below.

Spatial navigation and related episodic memory: Build models based on existing data and targeted experiments to characterize these functions in rodents and humans, and realize the results in robots. In rodents, detailed and more abstract simulations of hippocampal circuits and their inputs and outputs are possible. In humans - coarser, high-level simulations can be constructed based on general insight from rodents, imaging and behavioural data in humans, combined with high-level theoretical principles. All can be tested using robotic navigation in realistic environments.

Goal-directed Decision-making: There is a wealth of electrophysiological, pharmacological, neuroimaging and behavioural data on monkeys, rodents and humans, together with sophisticated theory to prefrontal cortices in place, address decision-making related to frontal lobe - basal ganglia - neuromodulatory circuits with a behavioural readout in terms of motor behaviour.

Visually guided behaviour: Model and simulate the sensory-motor loop in relatively simple visually guided motor tasks based on behavioural data in monkeys and humans and emerging data in rodents. These can be used to inform/test BMI tools and robotic systems, and will provide stringent tests of high-level theories of action perception loops.
Cortical local structure-function: Generate an experimentally constrained interpretation of the function of cortical micro-circuitry (detailed simulations with full morphologies, estimated/measured connections, and cell types, including inputs and output afferents in several cortical areas including simulations in rodents constrained by the relative abundance of data, and exploratory studies in humans, test under several states and sensory stimuli). Compare with established abstract models, test multi-scale methods, test statistical estimations of connectivity against actual data, test plasticity rules. Use to inform/test high-level theories about the generic function of cortical columns.

Large-scale cortical networks structure and function: Complex cognitive functions typically depend on networks involving more than one brain region. Each network consists of a number of well-defined brain regions that are structurally (white matter) and functionally connected. Deficiencies in the integrity of these white matter fibre tracts lead to behavioural deficits in humans and are, therefore, relevant for clinical neurology. Decomposing the cognitive functions into local and integrated components by analysing these deficits could provide substantial insight into different scales of neural information processing.

Parkinson's Disease: Use data from monkeys and rodents in the motor cortex and basal ganglia to understand the pathogenesis of the disease, its circuit level disruption and motor deficits (combination of phenomenological models and simulations of basal ganglia circuitry); also test normative theories of the effect of dopamine on motivation, planning, and decision making. This could potentially be a key tool for understanding circuit aspects of the disease and its therapies, including DBS.

Schizophrenia: Build on increasing, although still fragmented, data on various molecular pathways, and circuit dynamic dysfunction: excitation – inhibition imbalance, pathological neuronal oscillations, and disruption in large-scale brain functional and structural connectivity). Synthesizing fragmented data at multiple levels into a coherent simulation and computational model would constitute an important achievement for HBP tools.

Other suitable health-related topics include epilepsy, addiction, obsessive-compulsive disorder, Huntington's, ADHD, depression, and consciousness disorders. Each of these topics deals with a vastly complex set of phenomena, and comprehensive breakthroughs will almost certainly take longer, and require greater efforts, than accommodated by the HBP.

All the cross-cutting activities have to be tightly integrated with platform development and usage to demonstrate their capabilities and identify shortcomings.

The existing SPs should be screened for tasks or even work packages which could rather go into the cross-cutting activities. In particular, it could be checked whether SP 9 (Neurorobotics) and its WPs could qualify as a cross-cutting activity in its own, complementing the newly introduced ones.
Interim goals should be specified in the form of milestones for all the cross-cutting activities that need to be achieved jointly with the vertical SPs as a precondition for approving the following funding cycle.

A.2 Comments on Subprojects of the FPA Proposal

The material in this appendix was prepared by members of the MC during an analysis of the scientific program of the HBP as presented in the FPA proposal to ground the discussion on the balance of the scientific program, acknowledging that the mandate of the mediation panel was to mediate on scientific balance and not to critique the research program. Unfortunately, an imbalance in the assessment has been unavoidable because only a few scientific fields were represented in the MC both by experts inside and outside the HBP, whereas others were represented only either by insiders or outsiders. Full balance could therefore not be achieved in the following comments. Reconciliation of the often opposing views was not always possible, though this was pursued as far as possible.

The comments are not intended to be read as specific criticisms of SP leaders – the draft FPA, on which they are based, reflects various constraints. They are rather intended to help the leadership of

the HBP in making decisions as to how to evolve the SPs and how to reallocate the budget to fund mission-critical cross-cutting activities.

SP 1 and SP 2: Targeted Maps for the Mouse Brain and the Human Brain

The goals formulated for SP 1 and SP 2 are certainly very ambitious and are considered unrealistic by a number of members of the MC. The CPs of these two SPs are set up to generate new structural data for the mouse and the human brain. The generation of functional data has been shifted to the PP, the funding of which has, however, not been secured. Many of the data generation activities seem to be generic in the sense that their overall aim is to build various maps of the brain, rather than for specific tasks related to the development and validation of the IT platforms.

The difference in the approaches regarding mouse and human brain mapping are not sufficiently explicit. Adequate coverage of NHP research has not been included despite the consensus in some sections of the neuroscience community that an understanding of the human brain, which has been publicized in the media as a major long-term objective of the HBP, is impossible without research on NHP. Given the fact that experimental techniques applicable to the human brain are limited, and that the differences between the mouse and the human brain are much larger than between human and NHP brains, work on NHP should be considered in the HBP to meet the objectives of developing, demonstrating and validating IT platforms contributing to an understanding of the human brain. For example, according to one member of the committee, a need for an in-depth structural analysis of the mouse, marmoset and macaque brain, particularly given that the marmoset is an NHP model that will soon allow molecular approaches that are currently only available in mouse. It is considered particularly important that PIs participating in the HBP can use core funding to carry out such NHP research. Likewise, data on the human brain have to be acquired in the HBP to support the development of the IT platforms.

With respect to the collaboration between SP 1 and SP 2, it is crucial to identify similarities and differences between the different species in detail. This has direct implications for modelling and simulation (“constraints”), and has consequences for basic neuroscience. Finally, it is relevant because it determines the strategy for defining what has to be analysed in the mouse brain, what can be transferred to the human brain, and what can be done exclusively in the human brain. Obviously, such similarities and differences depend again on the spatial and temporal scale.

The over-arching problem, however, is that insufficient rationale has been provided as to what experimental data need to be generated within the HBP. Obviously, the resources of the HBP are not sufficient to produce comprehensive atlases for the mouse, some NHPs and the human brain. Dedicated experiments for the generation of knowledge and data covering only carefully selected issues from the variety described above should be included in HBP core projects, where they are targeting the development and validation of novel IT platforms, including brain simulation models, behavioural models or brain atlases. Such data generation should include functional data, such as recordings, functional imaging, as well as sensory and behavioural environments. Functional data are desirable from network through system to whole brain levels. Complementary data generation activities by other international initiatives, such as the Allen Brain Institute (e.g., with respect to gene expression data), Janelia or the US BRAIN Initiative (e.g., with respect to diffusion tensor imaging data of connectivity) need to be constantly monitored. The emerging interaction of the HBP with these and other initiatives is encouraged to develop and exploit complementary scientific expertise, with a focus on data acquisition and knowledge generation to leverage the work of the international community. This broad community of neuroscientists, working in both, SP 1 and SP 2, as well as their collaborative partners should be the early adopters of the platforms in order to achieve new scientific

knowledge, as well as making other groups familiar with this new kind of research. This dissemination activity is expected to have a big impact and to contribute to a better standing of the HBP in the scientific community.

Some members of the MC were in favour of restructuring SP 1 and SP 2 so that instead of being organized around mouse and human brains, respectively, that SP 1 would concentrate on structural data, and SP 2 on functional data in different species.

More specific individual comments for SP 1 and SP 2 are as follows.

SP 1: *Targeted Maps for the Mouse Brain.* While some details have been specified at the molecular/cellular levels, no mention has been made as to the strategy for assembling the necessary anatomical data (micro- and macro-connectomics). This would not only allow the tasks at the different spatial and temporal scales to be better integrated within the project, but also aid its interaction with SP 2. There is a need for a focus on functional *and* structural data. Functional data are required especially from network through system to whole brain levels, at which it is more difficult to make useful models purely via bottom-up, mechanistic, approaches. Support for molecular mappings, complementing structural and functional data, requiring gene-manipulated mice strains (note that SP 1 plans to spend € 18.5 million for "housing and care of mice") is particularly problematic, considering the existing facilities in Europe where such data could be generated in PP. SP 1 is very much focused on a few PIs, which cover almost all aspects of the SP and receive the major amount of the budget. This may lead to a very one-sided approach within the mouse brain project, and potentially neglect strong groups both inside and outside.
SP 2: *Targeted Maps for the Human Brain.* While an in-depth structural analysis of the human (and, to a lesser extent, marmoset and macaque) brain is lacking, significant effort is spent for the generation of experimental data on the mouse brain in SP 1. The lack of anatomical and physiological data about the human brain represents an outstanding problem which is tackled in SP 2. This demanding scientific problem is a truly "big science" problem which – in contrast to similar efforts on rodent and NHP brains – is currently not targeted by any other major international effort and is well-positioned in the HBP to provide the structural and functional data forming the basis for virtual human brain atlases.

SP 3: Theory

The overall objective of SP 3 is to provide solid theoretical and mathematical foundations for work performed in other SPs to enable computational advances. The CP has four goals: The first is to enable horizontal collaboration between researchers from different SPs – reflecting the recommendation for horizontal cross-cutting activities. The second goal is to develop theoretically grounded methods that reduce high-fidelity models to their simplest form, enabling comparisons between bottom-up and top-down models, a goal which is consistent with the recommendation for multi-level integration and the use of dimension-reduction theories. The third goal is to integrate top-down models with advanced learning algorithms that replicate the learning and cognitive behaviour observed in non-human species and ultimately in humans. This goal is consistent with our proposed emphasis on systems and cognitive neuroscience. The fourth goal is a readjustment of the program of SP 3 which should result in an adaptation of the WPs as outlined as follows. Obviously, the interlinking with the cross-cutting activities should be the guideline for the selection of particular topics investigated in the WP of SP 3.

WP 3.1 (Theory across SP boundaries) seems to be sensible regarding the prediction of function from structure and clinical implications. Since such issues have also been addressed by the Virtual Brain

Project (http://ins.univ-amu.fr/cross-cutting-research/the-virtual-brain-project/), complementary research activities and close collaboration are essential for making progress effectively on this massive undertaking. WP 3.2 (Bridging scales) focuses on biophysical models, as simulation engines to emulate neuronal function. It does not seem to acknowledge fully the pragmatic (and possibly more important) role of modelling in providing observation (e.g. neuronal state-space) models of empirical time-series. In addition to the tasks covered by WP 3.4 (Models of cognitive processes), the multi-scale aspect of theoretical constraints on neuronal dynamics may be exploited by mean field and neural mass models – both in simulations and as a metaphor for neuronal processing. Though the topics of WP 3.5 (Large-scale brain models) are potentially exciting and useful, any successful related research will require theoretical approaches beyond random networks that are informed by brain organisation.

Theoretical neuroscience and simulation technologies should play an even stronger role in the HBP than outlined in the FPA. However, given the numerous research activities and modelling paradigms the HBP has to make a choice that will endow it with a unique selling point regarding theory development. Ideally, a coherent modelling framework combining existing and emerging modelling paradigms should be formulated as the target of the research in SP 3. The success of the entire enterprise depends on the ability to connect multiple scales and levels of description. Thus, developing effective mathematical and numerical methods for multi-scale modelling is a primary challenge for the SP 3. SP 3 should, on the one hand, provide a tool-building infrastructure for mathematically formulated models that the simulations need to emulate, as well as the appropriate range of parameters, scales and tolerances. Likewise, SP 3 should develop methods for data analysis and interpretation, including clustering, feature extraction, and dimensionality reduction to be implemented in the neuroinformatics platform, on the other hand.

To ensure coherence and to reduce redundancy, the various WPs addressing theoretical foundations of simulation-based neuroscience currently present in many of the SPs should be consolidated under SP 3, whenever possible. Another major instrument to ensure the coherence of the neuroscience work within HBP, and to reduce redundancy and fragmentation, is provided by newly introduced WPs which implement cross-cutting activities and address concrete challenge problems in systems and cognitive neuroscience (see Recommendation S2). All these cross-cutting and problem-driven WPs have to be properly linked with the methods-driven activities forming the core of SP 3.

SP 4: Neuroinformatics

The amount and diversity of neuroscience is growing exponentially. Developing tools and formats for standardized data storage and sharing, overlaying data from different scales, allowing direct visualization and comparison of experimental and simulation data, etc., will all be of enormous value for neuroscience in the next decades. Thus, SP 4 is one of the most important activities of HBP. To fulfil its goals at an acceptable level of risk, SP 4 needs to be funded with adequate resources. On the other hand, SP 4 should complement rather than duplicate similar neuroinformatics programs elsewhere, such as at the Allen Institute or INCF. The relation and division of labor between SP 4 and INCF in particular must be clearly specified. Failing to resolve this complicated issue has the potential to hamper real progress in this SP.

The description of the neuroinformatics goals in the FPA emphasizes "predictive neuroinformatics" (e.g. in WP 4.4). This terminology creates the misleading impression that statistical analysis of sparse data can alleviate the need for further experimentation to collect new data. The goal of "predictive neuroinformatics" and the underlying idea of filling gaps in knowledge by predictions based on models which have not been (and in most cases cannot yet be) validated are ill-founded. The resulting

false impression is most dangerous, given the very critical discussion of animal experiments per se, and may make future tests of the data based on animal experiments more difficult or even impossible. The data collected in the neuroinformatics platform do provide some opportunity for model validation. However, model validation is lacking in the tasks and objectives of this and other SP and should be properly integrated. This may be supported by targeted experiments.

Part of the activities of SP 1 and SP 2 should support the establishment and maintenance of an HBP Data Hub in SP 4. This would be responsible for integrating existing structural and functional experimental data from rodents, non-human primates and humans, and from continuing experiments in research laboratories within and outside the HBP. The HBP Data Hub should also include data for stimuli and resulting behaviour. The data-related needs of neuroinformatics and neurorobotics should also be accounted for. Collaborative arrangements should be established for this purpose among the research groups participating in the HBP and, in particular, with other research groups and institutions. These arrangements should define standards and formats for the acquisition of data and identify specific datasets that need to be generated to support the development of IT platforms within the HBP that will (most likely) not be generated by other initiatives.

SP 4 should concentrate on the ideas formulated in the CP, and should not implement tasks defined for PP. If additional funds can be realized in the future, they should rather be used to support the ideas pursued in the CP and to provide services to the community.

SP 5: Brain Simulation

SP 5 contains a very important part of HBP, the development of a simulation platform that will allow the modelling neural processes at multiple levels - from the subcellular to synapses, glia and microcircuits, toward the systems level. This represents much of the core of the HBP and will most likely be of fundamental importance for developing an understanding of how the brain functions in a multiscale perspective extending from the subcellular level to microcircuits and beyond.

This SP, however, contains two work-packages (WPs 5.4 and 5.5) that have led a significant part of the neuroscience community to reject the HBP as being non-realistic. WPs 5.4 and 5.5, aim to model, respectively, the mouse and human brain in its entirety, from the subcellular to the whole brain level ("develop models of the mouse brain (WP 5.4) / the human brain (WP 5.5) at the subcellular, cellular, micro (column / module / nucleus), meso (region), and macro (whole brain) levels"). Members of the MC agree with many of the criticisms voiced by substantial parts of the neuroscience community and recommend that the research in this part should be redirected. With regard to many aspects of brain function, knowledge is still much too limited to permit a credible bottom-up simulation. For instance, an extensive simulation of cortical circuits will not in itself determine essential information about global brain function, though it might be an important first step. Cortex is entirely dependent on the vast input from thalamus, on the many modulatory systems and on a great number of subcortical circuits, including the basal ganglia, amygdala, hypothalamus, and the midbrain. It depends for execution on also the brainstem and spinal cord. The only credible way to proceed when addressing complex functions at the systems (cognitive) level, is to test specific functional hypotheses in behaviourally relevant subsystems, in which sufficient information is available to provide at least the backbone of the simulations, and to allow the bottom-up perspective to be combined with behavioural constraints and top-down considerations. SP 5 should be tightly linked with those theoretical foundations of simulation-based neuroscience which address multi-scale and multi-perspective modelling in SP 3. SP 3 and SP 5 should collaborate intensively with the newly introduced cross-cutting activities on challenging problems in systems and cognitive neuroscience (Recommendation S2). Examples of such systems problems in which this could be credibly attempted are provided in Appendix A.1.

SP 6: High Performance Computing

SP 6 involves designing and operating HBP's HPC platform, which consists of a central system and 3 satellite systems with specific functionality, connected *via* a high-speed network. Further, it supports the design, implementation and deployment of software capabilities and algorithms for brain simulation, and adapts existing software to the HBP hardware and to develop interactive visualization. The WP includes (i) the development of software tools (model libraries, DSLs etc.) to facilitate the creation of brain simulation software, (ii) programming models for data-intensive supercomputing paving the path to exascale computing, (iii) techniques for large-scale visual data analysis, and interactive, immersive visualization at scale, (iv) infrastructure for dynamic resource allocation including the co-scheduling of workflows (e.g., to perform in situ data analysis during a running computation), and (v) infrastructure for modelling the behaviour of software on different architectures to derive information on performance and possibly energy consumption to support decision-making on important hardware design choices.

There are significant in-kind contributions to the HBP project that substantially reduce the cost of providing exascale-level HPC infrastructure to the project and bring added value to HBP. However, given the competition of the various scientific disciplines to get access to the most powerful computing capabilities and the technology to fully exploit the computing power in challenging applications, the HBP should contribute a substantial investment to expand the capacity of existing HPC systems contributed in-kind by the participating HPC centres in order to secure the availability of compute cycles for emerging simulation-based neuroscience applications.

The main objective of SP 6 is to provide a fully functional exascale platform that meets the needs of HBP. The creation of a production-quality program development and execution environment is a mammoth undertaking that cannot be accomplished by the project alone, nor is the expertise in the HBP sufficient for all parts of this work. Some portions will most likely have to come from vendors. Fortunately, there are other exascale projects in the EU and elsewhere pursuing similar goals. For example many, but not all, of these efforts are also funded by the US DoE ramping up its exascale R&D, which also includes vendor development of new technologies to provide viable exascale platforms. Therefore, much will be accomplished by contributing to related global community efforts, adopting/adapting other results, and ensuring that the vendors of choice provide critical functionality. However, the emphasis on large memory distinguishes the efforts in SP 6 from other emerging exascale projects. If such a platform can be constructed at a reasonable cost, it will be of clear benefit not only to HBP, but also too many other projects, in particular in the Life Sciences, and indeed, would help many technical applications scale to this level. As a result, SP 6 contains an innovative component and specific challenges to address when adapting solutions from other exascale development efforts.

In order to develop HPC platforms, in particular, continuous interaction with the application subprojects and the user community is essential. It seems imperative that such interactions – not only to specify requirements, but also to ensure co-design and iterative improvement of all user-level software – are explicitly provided for. Only if close collaboration with the end users is established can the upgrading of computational capabilities *b*e of great value for the future study of the brain. So far, the HBP has neither fully exploited the collaboration between SP 6 and the simulation-based neuroscience activities in SP 3, SP 4 and SP 5, nor has it engaged with the wider neuroscience community in such a dialogue. The research therefore runs the risk of constructing expensive software tools that will have only a marginal impact on neuroscience. In addition to providing appropriate HCP platforms, the technology providers have to reach out and help interested neuroscientists who need to scale-up their computational problems and to exploit HPC technology. Access to HPC systems has to

be opened up to the neuroscience community, following a competitive process relying on peer review.

SP 7: Medical Informatics

The main objective of SP 7 is to re-use existing data from various sources (clinical, biomedical, genetic, etc.) for the purpose of further analysis. In order to achieve this, an IT-architecture is planned to be established in which a common portal will grant access to distributed data, which mainly reside in the systems at the source sites, and are only to a limited extent replicated in a central instance. The envisaged objectives are very broad but certainly valid. They constitute and circumscribe some of the most fundamental and unsolved research topics and problems in today's Medical Informatics (MI).

However, a possible solution would affect various domains of MI as well as Healthcare IT (HC-IT), in particular because operational systems have to be taken into consideration. The intended federated architecture requires a data collection from the partner's source systems. No Chief Information Officer (CIO) and hospital trust will allow direct queries to their operational and mission critical IT-systems. Hence a local node will have to be installed at all partners' sites. This node will have to collect data from the source systems and communicate with the central components (e.g. the portal). This local node can also be considered as a kind of Research Information System (REIS), which is usually designed around a Data Warehouse (DWH) architecture. Most frequently, off-the-shelf industrial warehouse components are deployed for this purpose and extended by additional mandatory components usually not delivered by the DWH vendors. Examples would be components for patient consent and identity management, in particular, a Master Patient Index (MPI).

Many university hospital and medical faculties are currently considering or even working on the implementation of a REIS. In order to avoid duplication of interfaces and work tasks, most approaches use one core-DWH, and integration work is only done once ideally with standardised protocols. To avoid interference with those activities, the HBP local node would have either to serve as the generic WH, or tightly and seamlessly integrate with the other local installations.

At present, the vast majority (ca. 90 %) of clinical documentation is in the form of free text, and is hence unstructured. The current scientific state-of-the-art does not allow free text to be de-identified. Re-use for scientific purposes would either require text mining and extracting structured concepts, or double documentation into a dedicated research documentation system (similar to electronic data capture systems in clinical trials). This step would have to be followed by a semantic annotation of the data to ensure semantic interoperability across borders, which must use internationally accepted standards. Finally an international, federated architecture like the intended one must deploy international communication and interoperability standards (such as IHE).

All these issues should be properly addressed by this SP. A project of this scope requires in depth knowledge and skills in various areas of MI, including profound competence in HC-IT systems architectures accounting for the necessary integration of local nodes and source systems. Proprietary architecture should be avoided.

The revision of the task description of this SP should be oriented at the following guidelines: The main objective has to be the design of an open and flexible IT architecture blueprint based on international standards at least for syntactic and sematic interoperability. The second step should be a solution outline followed by a detailed technical specification, all of which should be approved by an advisory board. The consortium should strive to extend its competence by including healthcare in-

formation systems architects and/or hospital CIOs. The surveillance of the implementation process should be addressed separately.

SP 8: Neuromorphic Computing

There are two development lines in SP 8 because these are the two European large‐scale neuromorphic developments that were ongoing before HBP and which are distinct and complementary: The Heidelberg system uses a physical model – the neural equations are mapped into analogue electronic circuits – and runs 10,000 times faster than biological real time. The Manchester system uses a massively-parallel many-core computing approach with a bespoke communications infrastructure to run in biological real time. The two systems represent different trade-offs between performances, flexibility, repeatability, energy-efficiency, and so on. There are also other groups around the world building various forms of neuromorphic hardware, including IBM, Qualcomm, Neurogrid at Stanford University, and others. The IBM TrueNorth chip is a very impressive piece of silicon, implementing a million neurons on a single (very large!) chip. The architecture is digital and runs at biological speeds. It is rather considered to be an application delivery platform and therefore is less flexible than the European designs, which are primarily research platforms and are generally viewed as being more advanced.

The WPs of SP 8 have been carefully designed and are required to fulfil their mission. Since the costs of building the initial machines have effectively been covered outside the HBP budget (NM-MC-1 (SpiNNaker) has been funded by the UK EPSRC, and NM-PM-1 has been funded within the EU FACETS and BrainScaleS projects), the HBP ramp-up phase has largely been funding the software development required to make these machines available as HBP platforms. Later phases of the project aim at the development of subsequent generations of the two platforms, guided by user experience gained on the current machines. Both platform development programs represent very substantial engineering enterprises. Given the substantial investment for further developing two neuromorphic computing platforms, the HBP leadership should reflect on and carefully evaluate the cost-benefit ratio for the HBP.

WP 8.4 is of a different nature from than the other WPs in SP 8. It is the one place in SP 8 where direct neuroscience input is offered to the neuromorphic platform teams. This WP would benefit from more theory, including cognitive neuroscience, provided neuroscientists were committed to implementing their models on the neuromorphic platforms as they emerge. It could be the driver for linking SP 8 *via* cross-cutting activities with SP 3.

SP 9: Neurorobotics

Neurorobotics can help to assess the scope and robustness of models of neural function, and to understand the sensory-motor milieu in which brains operate. Complementary virtual robotic implementations may significantly aid the development of high-level cognitive models, since virtual reality scenarios allow one to generate well-defined control conditions and quickly explore larger parameter ranges using closed-loop experiments. Since they do, however, lack a key feature of true (robotic) experiments in real worlds, namely the many unaccounted for but potentially crucial details of physical reality, real experiments are considered to be indispensible.

The current focus on virtual robots and virtual environments (WP 9.1, WP 9.2, WP 9.4, WP 9.7, WP 9.10) might thus be most valuable to speed up the development cycle of robotic hardware. However, it risks being irrelevant for the main goals of HBP, because it is based on the limitations of bottom-up

models (in particular in WP 9.2, WP 9.3, WP 9.5, WP 9.6, WP 9.11-WP 9.14). It is questionable whether sensation and actuation can be coupled to a detailed whole-brain model and achieve a worthwhile outcome (IMP 9.1, IMP 9.2), because such a model may not be deliverable over the course of the HBP.

The goals of SP 9 and its specific tasks should therefore be reformulated to include systems and cognitive neuroscientists in task specification and implementation. Instead of aiming at connecting bottom-up full-scale brain models with virtual robots or virtual animals populating virtual environments, SP 9 should rather focus on connecting high-level cognitive models and their simulations with robots. This would also provide a valuable direct link to systems and cognitive neuroscience and strengthen their integration into HBP.

If this reformulation is not accepted, individual WP within SP 9 should nevertheless be adjusted: Parts of WP 9.3, i.e., the development of value systems and motivation, as well as the entire WP 9.6 seem to be out of reach given the resource constraints of the HBP. In addition, WP 9.4 is important but seems to be misplaced as an individual WP and might better become an integral part of WP 9.1, WP 9.2, WP 9.3, and WP 9.5.

In addition, it remains an open question whether virtual neurorobotics could qualify as a horizontal cross-cutting activity. Proponents argued that SP 9 addressed many interesting cognitive neuroscience questions such as embedding existing models of cognitive architectures into the anatomical realities of the mouse nervous and muscular system. Initial research could focus on the shortest sensory-motor loops to untangle the division of labour between body, muscles, peripheral and central nervous systems. Later, larger sensory-motor loops could move into focus, including basic models of sensory motor control and low-level behaviour selection. Finally, higher-level cognitive tasks such as navigation in a maze, decision making and joint perception/action could be considered. Within this framework, SP 9 would benefit from a joint roadmap with SP 1 and SP 2 to provide the required data, with SP 3 to provide appropriate theoretical foundations for brain modelling and with SP 5 regarding simulation aspects. In short, SP 9 would refine WP 5.4 and 5.5 to include sensory-motor loops and the animal's environment. Based on the same bottom-up methodology and need for highly detailed data, SP 9 would, however, be subject to the same general critique as WP 5.4 and 5.5. Furthermore, it will suffer from the lack of experiments needed to generate the required detailed data about the mouse musculature and body.

SP 10: Ethics and Society

The overall goal of SP 10 is to explore HBP's social, ethical and philosophical implications, the benefits of research on the brain and its technological applications, and any potentially risky implications for early discussion. It also aims to inform and establish dialogue among the general public and decision-makers, and to ensure that the project complies with legal and ethical norms. SP 10 comprises 5 WP: A foresight lab aims to foresee the social implications in order to identify key ethical issues. The philosophical team analyses core concepts in HBP such as simulation, and consciousness. A dialogue with the public, decision-makers and stakeholders is being established. Ethical awareness among the HBP-researchers is to be developed and surveys have been done within HBP to identify attitudes and views in this regard. Ethical governance within HBP, directed from SP 10, includes an independent Ethical, Legal and Social Aspects Committee, and a Research Ethics Committee on Human and Animal research. The work of these committees could be rendered more clearly and more efficiently if they are merged into one. In that aim, a maximum of 5 names should be selected from the present ELSA committee for inclusion into the present REC that retains all its present members. The new, enlarged committee would retain all the tasks of the present REC, adding some broader social and legal aspects when relevant.

All the WP and tasks of SP 10 seem relevant to HBP, and necessary to achieve the overall aims. However, whilst SP 10 has from the beginning operated in a collaborative cross-SP manner, its cross-cutting activities must be further developed, in line with the Mediation's recommendations. The philosophical team, for example, (WP 10.2) should strengthen its collaboration with cognitive neuroscience. In some measure, it has already has done so, e.g. through publishing joint articles, and holding the first joint conference, but these collaborations must be further developed. Joint early stage researchers between SP 10 and other SPs could be highly beneficial on a mutual basis, for HBP and for SP 10. Developing strategies for RRI is a crucial task for HBP that also requires cross-SP collaboration. This is under development within several SP 10 WPs, notably those focusing on foresight, public dialogue, and ethical awareness, but further cross-cutting activities must be encouraged and developed.

A.3 Analysis of Legal Structures Available for HBP

This section provides a first, so far incomplete assessment of legal structures which could be adopted to implement a legal entity for the HBP.

Legal Framework Available under International Law

International organisations

International organisations are established through intergovernmental agreements and have a legal personality which is governed by international law. For example, the *European Organisation for Nuclear Research (CERN)* was founded in 1954 as the first European research organization based on an inter-governmental agreement and was a model for other scientific organizations such as the European Molecular Biology Laboratory (EMBL) and the European Organisation for Astronomical Research in the Southern Hemisphere (ESO). A more recent example is the *International Thermonuclear Energy Reactor* (ITER)[1].

These agreements are concluded by intergovernmental conventions between states and other international subjects. Usually they are made of a number of standard provisions, which encompass the legal personality, the establishment of the organisation and its purpose, the members and organs, privileges and immunities of the organisation, an accession clause and the settlement of disputes.

These organisations operate under their own rules and bylaws regulating a wide range of issues such as staff and financial rules, and procurement procedures. The financial contributions of the participating countries are either fixed by negotiations (*ITER*) or calculated according to the net national income of each country (*CERN*). Prior to the agreement, there are often long discussions between the countries (the partners) about the funding of resources, the site and all other necessary elements to commission and to operate the facility.

This legal form typically allows significant advantages such as tax exemptions (VAT and salary taxes)[2]. Regarding staff policy, the specific status of personnel (international civil servant or United Nation-like type), with privileges and immunities, makes it possible to attract very highly skilled collabora-

[1] The Joint Implementation Agreement was signed on 21st November 2006 (Annex to Council of the EU 212731/06 of 21.9.2006)

[2] "Very Large Scientific Facilities in Europe: Analysis of Institutional Co-operation", OCDE/GD(95)80.

tors. The more than 60 years' experience of *CERN*, and the more recent experience of *ITER*, make it feasible to emphasise the well-established long-term advantages, constraints and/or parameters, which can be drawn from an intergovernmental agreement or convention.

Legal Frameworks Available under EU Law

Joint Undertakings

Article 187 of the Treaty on the Functioning of the European Union (TFEU) allows the Union to set up joint undertakings or any other structure necessary for the efficient execution of the Union's research, technological development and demonstration programs. The decision to set up a joint undertaking is taken by the Council based on a proposal from the European Commission. This possibility has been used for setting up Joint Technology Initiatives under Horizon 2020[3].

This structure ensures the single effective management of a program combining various funding sources from the public and private sectors. However, since the EU is contributing to these initiatives, it is worth noticing that these Joint Undertakings have been considered by the Council as "EU Bodies" with the corresponding characteristics and constraints.

European Research Infrastructure Consortium (ERIC)

The legal framework for an ERIC[4] has been designed to facilitate the establishment and operation of research infrastructures of European interest with the involvement of several European countries. Complementing national and inter-governmental schemes, the ERIC Regulation provides a common legal framework based on Article 1872 of the TFEU.

An ERIC is a legal entity with legal personality and full legal capacity recognised in all the Union's Member States. Its basic internal structure is very flexible, leaving the members to define in the statutes, case by case, membership rights and obligations, the bodies of the ERIC and their competences. The liability of the ERIC's members will generally be limited to their respective contributions.

An ERIC is recognised by the country hosting its seat as an international body or organisation for the purposes of the directives on value added tax (VAT) and excise duties. It also qualifies as international organisation for the purpose of the directive on public procurement. An ERIC may therefore, under certain limits and conditions, benefit from exemptions from VAT and excise duties on its purchases in all EU Member States and it may adopt procurement procedures respecting the principles of transparency, non-discrimination and competition but not subject to the directive on public procurement as implemented in national law.

The following entities may become members of an ERIC: Member States, Associated Countries to Horizon 2020, third countries and intergovernmental organisations. An ERIC must include at least three Member States as members.

European Economic Interest Grouping (EEIG)

[3] Innovative Medicines 2 (IMI2); Fuel Cells and Hydrogen 2 (FCH2); Clean Sky 2 (CS2); Bio-based Industries (BBI); Electronic Components and Systems for European Leadership (ECSEL);Shift2Rail

[4] Council Regulation (EC) No 723/2009 of 25 June 2009 on the Community legal framework for a European Research Infrastructure Consortium (ERIC), OJ L 206, 8.8.2009, p. 1.

The EEIG is explicitly designated as a means to "cooperate effectively across frontiers"[5]. Its purpose is to facilitate or develop economic activities of its members. It can comprise companies or firms as well as other legal bodies governed by public or private law and natural persons. It was one of the first legal instruments to bring about the single European market. The members of the grouping have unlimited joint liability for its debts and other liabilities of whatever nature.

European grouping of territorial cooperation (EGTC)

This is a relatively new cooperation instrument at EU level, based on Article 159 of the Treaty, for the creation of cooperation groupings in the Community territory. The objective of an EGTC is to facilitate and promote cross-border, trans-national and/or inter-regional cooperation between its members, primarily regional and local or other public bodies, but covering national authorities as well, with the aim of strengthening economic and social cohesion[6]. This may include using it for research purposes, as research is recognised as a tool for fostering regional development. EGTCs can be set up by national research authorities only and may therefore, in some cases, be used for the purpose of European research infrastructures.

The European Cooperative Society (ECS)

Its purpose is to complete the EU internal market and to provide a legal framework for cooperatives on a community scale[7]. It is considered that the operating principles of cooperatives are "different from those of other economic agents" in the sense that they require a democratic structure and distribution of net profits on an equitable basis, with a very strong participation of employees. As with all cooperatives under domestic law, its main feature is the supply of goods and services. Consequently, its focus is the participation in economic activities, which rules out the suitability for scientific large-scale facilities.

European Company (also known as Societas Europaea SE)

This legal framework derives from Council Regulation (EC) No. 2157/2001 of 8 October 2001. Following a long discussion on how to enable public limited companies (i.e. plc) to carry on their business on a community scale, this regulation was meant to ensure that companies with a "European dimension" can be created and managed.

A European Company can only be created if existing companies in more than two Member States (MS) are concerned. It is exclusively foreseen in 4 cases: i) by the merger of two or more existing public limited companies from at least two different Member States; ii) by the formation of a holding company promoted by public or private limited companies from at least two different MS; iii) by the formation of a subsidiary of companies from at least two different MS and iv) by the transformation of a public limited company which has, for at least two years, had a subsidiary in another MS. The European Company addresses primarily the needs of large industrial firms, whose capital is divided into shares to operate under the legal framework of a European law.

[5] Council Regulation (EEC) No 2137/85 of 25 July 1985 on the European Economic Interest Grouping.

[6] The (Regulation (EC) No 1082/2006) is the first EU instrument offering a legal framework to set up a legal body under Community law for territorial cooperation.

[7] Council Regulation (EC) No. 1435/2003 of 22nd July 2003.

Legal Frameworks under National Law

Companies

Companies are often used to set up research infrastructures in Europe because they are well adapted to public-private needs and are better integrated into the legal framework of the country where the research infrastructures are located (e.g. French *Société civile*, UK *Limited liability Company* (Ltd), German *Gesellschaft mit beschraenkter Haftung* (GmbH)). There are many different legal types, most of which are limited liability companies. The shareholders have a limited liability in proportion to their contribution to the capital. One distinguishes non-profit making companies in which members wish to develop a specific activity from commercial and profit-making ventures in which the shareholders invest a capital essentially for their financial interest. Generally, companies can be set up with partners, public or private, coming from the host country and/or from any other state.

Foundations

This legal form is typical for non-profit organisations, governed by national law. In The Netherlands, this legal form is commonly used for research organisations. It emphasises the non-profit character of the research work and allows for a flexible governance structure with a board consisting of representatives from the stakeholders/financing parties and a management, reporting to the board, but having full authority for the daily management of the organisation.

AISBL (international non-profit organisation under the Belgian Law)

This legal form is typical for non-profit organisations, governed by the Belgian national law, but allowing international partners and activities. It allows for a flexible governance structure with a board consisting of representatives from the stakeholders/financing parties and a management, reporting to the board, but having full authority for the daily management of the organisation.

Appendix B: Abbreviations

AC	Audit Committee
ACP	Assembly of Contracting Partners
AISBL	International non-profit organisation under the Belgian Law
BoD	Board of Directors
CAO	Chief Administrative Officer
CEO	Chief Executive Officer
CIO	Chief Information Officer
COO	Chief Operating Officer
CP	Core Project
D	Directorate
DoW	Description of Work
DWH	Data Warehouse
EC	European Commission
ECS	European Cooperative Society
EAB	External Advisory Board
EPFL	École polytechnique fédérale de Lausanne
ERA	European research Area
Et_AB	Ethics Advisory Board
EU	European Union
ELSA	Ethics, Legal and Social Aspects Committee
EMBL	European Molecular Biology Laboratory (
EMBL-EBI	European Bioinformatics Institute
EFC	Enabling Functions Committee
FPA	Framework Partnership Agreement
GA	General Assembly
HC-IT	Healthcare-IT
HBP	Human Brain Project
IAB	Internal Advisory Board
iCEO	Interim CEO
ICT	Information and Communication technology
MC	Mediation Committee
MI	Medical Informatics
MPI	Master Patient Index
PA	Partner's Assembly
PI	Principal Investigator
PP	Partnering Projects
PPS	Partnering Projects Subcommittee
PRACE	Partnership for Advanced Computing in Europe Initiative (PRACE)
RB	Research Board
REIS	Research Information System
SAB	Strategic Advisory Board
SB	Supervisory Board
Sc_AB	Scientific Advisory Board
ScB	Scientific Board
SE	Societas Europaea
SGA	Specific Grant Agreement
SP	Sub Project
WP	Work Package