Opening up the Human Brain Project (HBP) to the neuroscience community

The Human Brain Project is an ambitious research and technology development project. In the course of 2014 the project experienced protest from the neuroscience community. As a result, a mediation process was initiated. The present newsletter reports on the outcome of an open forum seminar where HBP researchers discussed collaboration in a seminar titled "Theory and data for advancing future neuroscience and the Human Brain Project (HBP)"

In May 2015, researchers from the Human Brain Project (HBP) meet with scientists from the neuroscience community. The purpose of the meeting was to begin a conversation on the contribution of the HBP to neuroscience, and explore possibilities for future collaborations. Before the meeting, a 'mediation report' had been published on the HBP. The mediation report had its background in a protest letter published over the summer of 2014. Among other suggestions, the mediation report recommended that the HBP begin efforts of 1) the building of a user community for use and co-design of the ICT platforms, and 2) The development of an on-going dialogue with the international neuroscientific community on the data and theory required for developing the platforms. The seminar was designed to address these two points.

What passed were two days spent in intense and constructive discussions on the goals and approaches of the HBP. In this newsletter, we report on the key discussion points that emerged during these discussions. You will also find the points summarised as recommendations in the box to the right.

Recommendations from the seminar:

- Communicate more about the research being done in the subprojects
- The project should still have several objectives, e.g.:
  - assist in understanding how brains fail
  - take a particular disease or drug design as a starting point
  - network building between internal and external researchers could be a success in itself
- Develop plans for how the horizontal integration should take place. It will not 'just happen'.
- Find a point of connection between bottom-up and top-down approaches and create a bridge between the molecular and the cognitive level (multi-level integration)
- Prioritise building in plasticity and neuromodulation in the ICT brain models
- Set up a 'brainstorming structure mechanism' where crazy ideas can develop and be tested

Brain models and simulations in HBP

The HBP takes a specific approach to simulation. As Richard Walker of the

HBPs sub-project 6 (SP6) explained, the simulation tools are developed to be 'multi-scale and multi-level'. As he explained, the simulation tools are

developed on the basis three principles: There will be no custom built models designed for specific problems; builders do not draw on any high-level hypothesis; and the models developed will be statistical models of the brain with data input coming from many animals.

Richard Walker' comments were well received, but also prompted questions from the audience. Albert Gjedde pointed out that the use of the rat/mice as a model organism seems a bit strange. To this question Richard Walker explained that the choice of model organism has to do with the projects origin. Henry Markram' aim was to understand human brains, and rightly or wrongly, the project team had been convinced that it would learn more from studying rat/mice models.

Richard Morris raised the point of the apparent failure of the models to take into account plasticity and neuro-modulation. This point was recognised as a critical issue for the simulation models of SP6. As Richard Walker explained, the plan is to incorporate neuromodulation into the model at some stage. The ambition is also to build plasticity into the models. In the current stage of the HBP SP6 refers to its models as 'skeleton' models. The limitations mentioned are serious ones, and how long it will take to modify them is unknown.

Richard Walker also clarified that the simulation models are not completely hypothesis free. They include theory on e.g. electrophysiology, but they do not include high-level hypothesis e.g. on how the brain performs cognitive functions.

The insistence on excluding high-level hypothesis thrust the participants into a discussion on the balance between bottom-up and top-down approaches. Several of the partici-pants spoke favourable about a combination of top-down with bottom-up approaches. One reason for support-ing such an idea, was as Jean-Pierre Changeux explained, the HBP' need to perform research on data from different levels. According to him, the project needs to incorporate di-verse data, and to bridge the levels between molecular and cognitive levels. Richard Morris gave one of his favourite examples of a success-ful combination between top-down and bottom-up: the work on the barn owl by Eric Knudsen at the Califor-nia Institute of Technology. Others, like Marcel van Gerven, pointed to the opportunity to work with scien-tists outside the HBP who have expe-rience integrating behavioural and top-down constraints. The essential question is then how collaboration could be facilitated.

Multidisciplinary collaboration
The external participants raised the issue of representation of the HBP. From their perspective, the HBP has taking on an 'imperial' position with regards to its contribution to neuro-science, and science generally. They explained that to them, representing a project, its approach and models, as *the approach* is highly counterpro-ductive to the mission and reception of the project.

At the seminar, several HBP re-searchers gave presentations of their work in the HBP. This peek into the diversity of the work that is ongoing was highly appreciated. As Albert Gjedde pointed out, the SP presenta-tions at the seminar gave an interest-ing view to the research taking place, and confirmed that the individual projects are well set up and worth-while. Similar sentiments were ex-pressed by several of the participants.

The challenge might now lay in the horizontal integration within the HBP, and the integration and collabo-

ration with the neuroscience community outside the HBP.

Horizontal integration within the HBP

Several of the HBP researchers explained that the original idea with the HBP was that the SPs should be strong in their own right, but that over time a unified picture would emerge. As Richard Walker explained, the unified picture is the high-level ambition, and the project is trying to steer towards that. However, one should be realistic as well as to what is possible. It should not be so integrated that everyone should necessarily talk to each other all the time. Instead collaboration will happen in pairs.

The lack of a common set of problems is part of the difficulty with horizontal integration in the project. As Nikolas Rose explained, you will have many disciplinary groups with different ways of understanding and approaching human and animal neurobiology, and each with their own set of problems. The challenge is then not only about integrating different ways of working, but also different philosophies. One could take one of three stances when faced with this problem: 1) that it is possible to integrate, and that it should be done; 2) that integration is possible but that it is too early; 3) that integration is not what the HBP should aim for because it is not how science works.

Jean-Pierre Changeux argued for 1), drawing on the creation of the concept 'neuroscience' to show how integration among disciplines often lead to innovation and progress.

Andreas Roepstorff, saw the aim for horizontal integration as perhaps the greatest ambition of the project. As he explained, however, it would be a mistake to think that integration would happen by itself. The project would very soon need to have an explicit strategy for how to do integration. Having a few cross-cutting projects was, according to Andreas Roepstorff, not ambitious enough and not a guarantee for horizontal integration. If the HBP has the ambition to transcend the different disciplines, then it should be matched with specific ideas as how to do it. If there is no aggressive experimentation from the very beginning, chances are that the HBP will end up doing disciplinary work and not much more.

Jean-Pierre Changeux pointed to concepts such as 'memory' and 'consciousness' as possible drivers an integration process. Naturally, there is an important empirical element to research, but conceptual development is what leads research to new ground. Therefore there should be a balance between experiments and theory. The European Institute for Theoretical Neuroscience (EITN) is unique for providing a place for the HBP to have a debate on ideas to drive the project instead of hanging on to one concept or idea of the brain.

Closing the gap between HBP and future users

A first step in closing the gap between the HBP and future users would be to identify the (end) users, and then connect with them. As Marcel van Gerven expressed it, at the moment it is very unclear how one could get involved with the HBP project or what could be interesting tools coming out of the project for others.

Several participants mentioned the Open Worm project as an example for the HBP to connect and collaborate with (please see the note at the end of this newsletter on another SP12 initiative to facilitate this type of collaboration). Not only is the Open Worm project interesting in itself, but it is also an example of a

transparent approach to science, where users and others are invited to participate from the beginning. The participants also urged the project to connect with the other big research initiatives on the brain that are on-going in e.g. the U.S. and China.

The critical importance of the involvement of users is well recognised by the HBP. As Richard Walker explained, several initiatives are underway in the HBP to connect with (end) users and to create collaborations with them. Florian Röhrbein explained SP10, who are developing the neurorobotics platform are very eager to interact with neuroscientists. Richard Walker also explained how the idea is to open up all the six ICT platforms to the public before the end of the first ramp-up phase of the HBP.

It was clear from the reactions of the participants in the seminar that they would welcome and recommend a community-driven approach to model-building and validation in HBP platforms. However, critical to the success of network building effort would also be the way the project represents itself to potential partners.

A brainstorming structure

The discussion on horizontal integration in the HBP and the creation of connections with users led to a discussion on the role of human actors to facilitate and take part in the integration process. Danilo Bzdok wanted to know what the role and importance of people with a foot in more than one project in the HBP could be. Albert Gjedde answered that young people have a very important role to play in generating the 'sparks of imagination' necessary for multidisciplinary work and successful integration across different disciplines in the HBP. However, such work needs to be seen as rewarding, and necessary, and there perhaps

could lay a real challenge in the incentive structures of science.

Drawing on the example of Francis O. Schmitt and the introduction of the Neuroscience Research Program at the Massachusetts Institute of Technology, the participants came up with the idea of human agents acting as 'cross-worlds' influences (concept courtesy of Christine Aicardi, the HBP Foresight Lab). Persons, who can bridge disciplinary boundaries, would be important for the integration efforts in the HBP. However, not only people, but also the structure for being creative is important. The HBP could set up a 'lab' or a brainstorming structure where people could be allowed to work on 'crazy', 'stupid' or 'mad' ideas.

Many of the participants were enthusiastic about this idea. Albert Gjedde referred to the group assembled as already a being an experiment a 'lab' for 'leaps of imagination' to occur. As Richard Walker and Nikolas Rose explained, the HBP is set up in a way that is effective from a management point of view, but a stifling to creativity. One could imagine a free space for experimentation for up to 3-6 months. It should be possible, at which Alain Destexhe reiterated the point of the EITN as an open space for experimentation.

The contribution of the HBP

At present the participants saw the HBP as having one very high-level goal: to contribute to a unified understanding of how the brain works. However, many argued that the HBP should have several objectives.

Jean-Pierre Changeux argued for the importance of orienting at least part of the efforts of the HBP at understanding mental disease and at the development of new drugs. There is already a part of the work devoted to research on mental disease and dis-

covery of new opportunities for drugs. The suggestion was that such effort should be more visible and even strengthened.

To this Omar Gutierrez-Arenas added that the development of models and research on drug development is already intertwined. The question might be more of realising the interconnections and explicitly taking advantage of them in the project.

Albert Gjedde added that perhaps a goal is not even drug design per se, but more the development of an understanding of the extent to which it is possible to predict how brains fail.

Finally, as Nikolas Rose pointed out, the question is not to have the one or the other objective as most important, but to collect and implement all the objectives, so to have efforts directed at: mental diseases, drug design, brain failure and as Andreas Roepstorff added the creation of an immense network of skilled people, which is a feat in and of itself.

The value of open forums for discussion

Perhaps it was due to the hospitality and excellent service at the EITN institute, perhaps it was the food, but many of the participants at the seminar expressed their appreciation of the opportunity to meet and discuss honestly in a small setting.

A few comments from the evaluation of the event were:

"I feel the workshop was very useful, and an essential point is that we have to set up mechanisms to facilitate the collaboration between HBP partners, as well as collaborations with partners outside of HBP."

"As a non-HBP partner it was very informative to view the projects from the inside and to be able to interact with HBP partners. This also resulted

in some new ideas for collaboration and an incentive to submit a proposal for the new call."

So, to answer the question that Albert Gjedde asked the seminar participants "Should we have more of this?" - Yes we should.