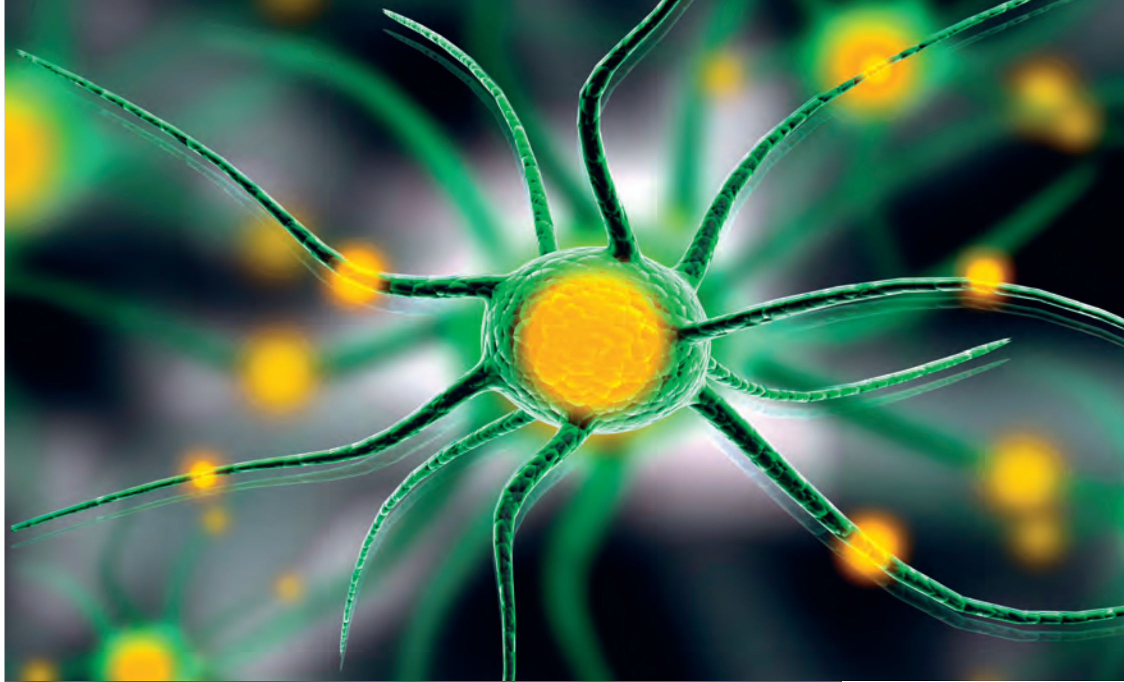

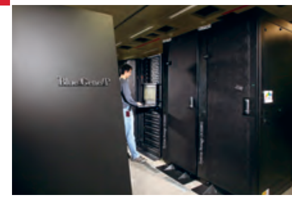

Conference series "The Big Six –
Spotlight on the EU-Flagship-Initiative"

Summary of the Conference "Perspectives of High Power Computing in Neurosciences"

by Denis Monard, past president SCNAT

Organisation: SCNAT and SAMS
Location: UniS, Schanzeneckstrasse 1, Bern
Date: 20 January 2012

sc | nat

Swiss Academy of Sciences
Akademie der Naturwissenschaften
Accademia di scienze naturali
Académie des sciences naturelles

SAMS Swiss Academy of Medical Sciences

General Summary

The conference was organised to meet a need expressed by the scientific community, which considered that solid scientifically-based information and discussion should be provided in the fields covered by each of the EU-Flagship Initiative projects. This conference provided discussion related to the “Human Brain Project” initiative. It must be emphasissed, though, that its purpose was not to evaluate this project.

Except for the first speaker, who gave the introductory talk, all invited speakers were computer-modeling specialists, and it was therefore not unexpected that certain issues and arguments related to aspects of the flagship enterprise regarding modeling the human brain were raised. The contributions and following debate were lively. The majority of the speakers expressed critical arguments claiming that today’s available data was insufficient to support and justify a fully integrated computer modeling of the human brain. The content and the controversy of the conference resulted in several media reports. The vast majority of the 170 participants appreciated this opportunity to get more detailed scientific information on a field of research, which will undoubtedly develop further in the future.

Summaries of the Presentations

Speakers (following the sequence of the presentations):

Andreas Papassotiropoulos, University of Basel
Introduction
The psychologist Andreas Papassotiropoulos, basing his research on molecular genetics and epigenetics, provided the perspective of a neuroscientist not specialised in modeling. Using citations of highly reputable neuroscientists, he illustrated the multiplicity of approaches and the diversity of opinions concerning the present and future progresses in neurosciences. Despite the impressive knowledge gained during the last decades, he estimateds that there are still many gaps in solid data, which render an obvious evaluation of the future successful approaches in brain research difficult. His presentation is best summarised by two of his statements: “It’s all about claims (and the justification for these claims)” and “The only intellectually honest answer is that there is no way to know. One can prefer to be an optimist or a pessimist, but the best approach is to be an empiricist.”

Rainer Friedrich, Friedrich Miescher Institute for Biomedical Research, Basel
Inter-Disciplinary Approaches to Understand Neuronal Circuits
Rainer Friedrich emphasised that one of the outstanding challenges in science and health care is to understand how interactions between large numbers of neurons give rise to higher brain functions and dysfunctions. According to Friedrich, emergent properties of circuits and hypercircuits cannot be extrapolated from the biophysical principles governing the function of individual neurons because of brains’ enormous potential complexity, and because they were created by serendipity (evolution and experience). Understanding brain function is not a well-defined, singular problem, but presents a diverse array of technical and scientific challenges. Brain research therefore combines an exceptionally broad spectrum of approaches to measure, analyse and conceptualise neuronal circuit function.

Taking the perspective of a basic researcher, Friedrich argued that a set of very solid data, obtained by different molecular, electrophysiological, optical imaging, optogenetics, and novel 3-D electron microscopy techniques is an absolute requirement to initiate the modeling of the patterns of activity across large numbers of individual neurons. The presented results illustrated nicely that computational modeling and related mathematics merely provide an important step to verify the relevance of the data and to design new types of experiments, whose results should lead to a refinement of the model or to a new model. The solid set of data presented illustrated very well the need for a continuous crosstalk between modeling and multiple interdisciplinary experimental approaches. The need to rely on appropriate animal models and to reach or redefine milestones was also considered as a priority.

For Rainer Friedrich, the primary role of high power computing is not to integrate the highest amount of data, but to simplify it on the basis of clearly defined questions. Key problems in basic neuroscience include, but are by no means limited to, the measurement of activity patterns across large numbers of individual neurons, the exhaustive reconstruction of connectivity between individual neurons, the precise manipulation of neuronal activity in the intact brain as well as a rigorous analysis of structure-function relationships. Finally, the main role of computing is to generate new ideas, new concepts how to design creative and innovative experimental approaches.

Rodney Douglas, ETH Zurich

Reality and Illusion in Computational Modeling in Neuroscience

Rodney Douglas first insisted that neuronal networks cannot only be considered as made of "point neurons", but that up to 15,000 connections (synapses) can trigger or modulate the activity of each of these neurons. Because the size of complex neuronal circuits in the human brain is not even adequately defined, he therefore estimated that a petabyte range of computer capacity would be needed to register all these parameters, corresponding to the registration of the amount of all the sentences spoken since the existence of mankind. According to Douglas, a huge database including all the information accumulated by research in the neurosciences cannot lead to the understanding of the functional integration of neuronal circuits as long some basic principles have not been discovered. An agnostic simulation of high range neuronal circuits just defined by the accumulation of an incredible amount of data will not automatically lead to more detailed knowledge. For Rodney Douglas, brain activities cannot simply be assimilated to conventional computing. As a consequence, multiple approaches and the creativity and the innovative power of young generation neuroscientists are still needed to lead to the definition of such new principles required to approach an integration of different human brain functions.

Henry Markram, EPF Lausanne

Simulation Based Brain Research

At the outset, Henry Markram insisted on the need to involve high power computing to integrate the incredible amount of information, which is accumulating week after week in neuroscience research. The increasing complexity in the electrophysiological properties of each neuronal cell, types and number of neurotransmitter receptors characterising each neuron, enzymatic equipment specific to each neuron, multiple synaptical connections affecting the activity of each individual neuron involved in a circuit, interactions between different neuronal circuits, is described by the generation of about 60,000 new publications per year. High-power

computing is required to register such an amount of data and to make its comprehensive unifying integration possible. On that basis, high-power computer modeling of neuronal circuits, and eventually the entire human brain, should become possible. At a later stage, simulation should mimic higher brain functions.

Henry Markram described the first steps of such an approach by the on-going Blue Brain Project, which aims at the complete description and understanding of a cortical column in slices of the cortex of the rat brain.

Many of his statements related to the Human Brain Project were challenged by questions from other specialists in the field. Furthermore, Henry Markram stepped down from statements he had made in the press, claiming that high-power computing human brain modeling would make animal experimentation superfluous, and that it would lead to an understanding of consciousness as well as complex neurodegenerative diseases such as Alzheimer.

David Willshaw, University of Edinburgh, Scotland

Principles of Computational Modeling in Neuroscience

Using the vertebrate visual system, David Willshaw underlined some of the principles that should drive computational modeling. Theories of the natural world should lead to predictions. Modeling should be an aid to but cannot replace reasoning. Modeling should remove ambiguity from theories and bring consistency. Wrong models can still be useful. Computational modeling can help to perform the right experiment. David Willshaw stressed the following issues associated with modeling in the nervous system: 1) Need to clearly formulate the question; 2) Verification of the quality of the experimental data used; 3) Decision of the level that needs to be modelled; 4) Matching the model to the computing infrastructure (computer power is, in fact, not the bottleneck in neuroscience; in many institutions, such as in Edinburgh, today's infrastructure is not fully used); 5) Computer modeling, not massive modeling, is essential for neuroscience. David Willshaw considered that the small number of publications generated by the Blue Brain Project until now (18 papers, only one in a high impact journal, 1 million Euro/paper) raises questions about the expectations of massive modeling. He also mentioned that two of the software products developed by Markram and colleagues, the BBP BrainBuilder and BrainSimulator, are not generally used or available. According to Willshaw, the larger the project, the more likely it is to fail, especially if the goals are ill defined.

Finally, David Willshaw argued that the development of new experimental technologies, such as optogenetics, is actually the driving force in neuroscience.

Alexandre Pouget, University of Geneva

Where is the Bottleneck in Linking Neural Activity and Behaviour?

For Alexandre Pouget, the main goal in neuroscience is to understand how neurons control behaviour. He first addressed the level of computer investment required in relation to the desired goal as well as the feasibility to trigger realistic brain simulations. He insisted on the lack of a general theory that would offer explanations for tasks such as perceptual learning, decision making, multisensory integration, arithmetic, which precisely link neuronal code with behavioural performance. Alexandre Pouget expressed doubts about a brute force approach consisting of random simulation of extremely complex networks of firing neurons when considering the enormous diversity of their characteristics (number and types of synapses, number and types of neurotransmitters, number and types of receptors, number and types of ion channels, etc.). In this regard he cited Rainer Friedrich's "The goal of modeling effort is to simplify". Alexandre Pouget proposed different levels of simplification (which would nevertheless leave a nonlinear network with 27 free parameters), which would then allow studying the impact of more precise simulations. According to him, performance has to be mathematically predicted and then estimated. In summary, too many neuronal parameters have to be integrated at this stage and too little behavioural data is available. Alexandre Pouget concluded with a set of questions: "1) How is it possible to avoid over-fitting in "zero tweaks models"?; 2) What do we learn from a simulation?; 3) How do we develop theory in such large networks?; 4) What types of learning rules can we use?"

Larry Abbott, Columbia University, USA

How does a Spike Mean?

For Larry Abbott as well, the aim of modeling is to understand how behaviour is generated by the activity of neural circuits. His presentation impressively illustrated the type of modeling that can be performed upon analysis of multiple multicellular recordings. Using data obtained by his group and others in the visual cortex and in the olfactory system, he showed that, merely on the basis of experimentally recording simplified firing spikes and rates, modeling can "reproduce aspects of behaviour and neuronal activity in a framework respecting the essential features of the neural circuit". In other words, Larry Abbott showed that the dynamics of neuronal circuitry can be faithfully reproduced in much simpler models, in which the neuronal activity can be reproduced, such a task not being possible in the complexity of the human brain. For Larry Abbott "bigger is not better" but rather "smaller is better".

Conclusions

The round-table discussion with the speakers, joined by Thomas Schulthess, CSSS, Lugano, and Klaus Hepp, ETH Zurich, led to a lively and even passionate debate, as previously experienced throughout the day. The audience asked sharp questions as well. Here are some of the issues that were debated:

- Support of multidisciplinary approaches by young generation neuroscientists providing better chances to discover new principles in brain function than uniquely focusing on modeling
- Computer modeling not being able to reduce animal experimentation, but rather suggesting new types of experiments and animal models
- Illusory vision that modeling will solve psychiatric diseases or complex neurodegenerative conditions such as Alzheimer's disease
- Lack of solid and clearly defined background justifying a modeling of the human brain at the present moment
- Problem of sharing the presently available computer facilities
- Lack of interest by neuroscientists to use the computer facilities presently available at the Centre in Lugano
- Agreement on the importance of computer modeling, but disagreement on the capacity required and on the priority of the types of approaches
- Problem of the type of simulation that would be relevant to the physiological in vivo conditions

The conference resulted in a radio report and a series of articles in the press.
In this regard, it is worth to conclude by citing two sentences from Mitchel Waldrop's conference report in Nature (482, 456-458, 23 February 2012):

"Officially, the Swiss Academy of Sciences meeting in Bern on 20 January was an overview of large-scale computer modeling in neuroscience. Unofficially, it was neuroscientists' first real chance to get answers about Markram's controversial proposal for the Human Brain Project (HBP)."

"The description of the HBP as an open user facility sparked interest and enthusiasm at the Bern meeting. But much more vocal were Markram's critics, many of whom focused on the perceived inadequacies of the Blue Brain model — and of Markram's approach to data integration."

The Big Six – Spotlight on the EU-Flagship-Initiative

The Swiss Academies of Arts and Sciences organized the conference series "The Big Six – Spotlight on the EU-Flagship-Initiative", aiming to inform the Swiss scientific community about the planned EU projects. The meetings provided a platform to discuss both general and specific questions concerning the potential, ambitions and trends and helped to form an opinion on the priority of a Swiss participation in such programs:

- **Perspectives of High Power Computing in Neurosciences,** 20 January 2012, Bern
- **Exploring the Potential of Graphene**, 8 March 2012, Bern
- **Medicine in the 21st century: IT as a magic bullet**, 16 March 2012, Bern
- **Participatory Computing for our Complex World,** 21 March 2012, Zurich
- **Guardian Angels for a Smarter Life – innovations enabled by Zero-Power technologies**, 17 April 2012, Zurich
- **Rise of Sentient Machines? Robot Companions for Citizens,** 22 May 2012, Bern

Further information: www.akademien-schweiz.ch/flagshipseries