Computational connectomics

The brain is a complex network of billions of nerve cells giving rise to our sensory, motor and cognitive abilities. Understanding the structure of this network is an important step towards understanding how it functions. Today the field of neuroscience has entered the age of *connectomics*, with the ultimate goal of providing a comprehensive description of the physical and functional coupling among all neural elements of the brain. Great international efforts are currently devoted to studying brain network organization at multiple scales, from the detailed connectivity of cellular neural circuits to the large-scale connection patterns among entire brain areas. The multiscale network structure is studied both at the anatomical or structural level and at the functional level defined by the activity patterns of neural elements. As both anatomical and functional connectivity patterns change across several time scales, the dynamics of brain connectivity and its relation to development, learning, aging and disease are also of great importance.

Recent progress in experimental techniques as well as continuing advances in information technology have led to improved reconstruction of local circuits at a scale of millimetres as well as the macroscopic wiring patterns among brain areas in different species. High-throughput approaches promise to produce data sets of unprecedented size at unprecedented speed but just as deciphering the genome has not meant that we now completely understand genetic networks, charting the brain's wiring diagram does not directly imply that we will understand its function. To fully capitalize on the new technological developments in obtaining wiring diagrams of the brain, the refinement of experimental techniques

must be accompanied by corresponding computational and theoretical advances. Specifically, as experimental techniques are maturing there is a growing need to develop new computational approaches to facilitate the automated reconstruction of connectivity from various kinds of imaging data sets, to support the curation and open access distribution of large-scale data sets, to undertake systematic analyses of complex connectivity networks and to build computational models and develop theories to ultimately truly understand the brain's wiring. The German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) has recently established a new priority program “*Computational connectomics*” (SPP 2041) to address this rapidly growing need. In this special issue, experts in connectomics review the state of the art of the field and highlight future challenges and opportunities. The articles cover a broad range of approaches from the micro-connectomics based on electron microscopy to macroscopic connectomics of the human brain. Together they provide an up to date view of this emerging new field within the neurosciences.

In “Connectomics with cellular precision,” Helmstaedter gives an update on recent progress regarding electron microscopy-based techniques for obtaining wiring diagrams of local brain circuits. He reviews the insights about network function that have been obtained so far through such efforts and discusses future promises and challenges. Whether the wiring of cortical circuits in mammals is predominantly random or whether it utilizes precisely targeted connectivity, is identified as a major open question for this field.

Rumpel and Triesch, in their contribution “The dynamic connectome,” highlight the very dynamic nature of the connectome even in the adult brain. The surprisingly high rates of creation and deletion of synaptic connections raise fundamental questions about the mechanisms of learning and the stability of neural representation and long-term memory. The authors argue how the dynamic nature of the connectome can be reconciled with stable function and long-term storage of memory and emphasize the benefits of a close integration of experimental and theoretical research.

While substantial effort in the field of connectomics is devoted to investigating the brains of mammals, much is to be gained by studying brain structures across other phyla. Laurent, in his contribution “Connectomics: a need for comparative studies,” highlights the benefits of comparative work. He encourages us to exploit the diversity of circuit mechanisms generated by evolution as we are trying to establish the fundamental computational principles of circuit function.

Hilgetag and Amunts, in “Connectivity and cortical architecture,” review the relationship of macroscopic brain connectivity to other aspects of brain architecture, particularly the cytoarchitectonic differentiation of the mammalian cerebral cortex. Architectonic criteria, such as the density of neural populations in the different cortical layers, have a long history in neuroanatomy but only the recent introduction of big data approaches has allowed the systematic quantitative characterization and analysis of brain architecture. The multivariate analysis of extensive architecture and connectivity data has revealed a close relationship between the architectonic similarity of cor-

tical areas and the features of their interconnections. These findings suggest general wiring principles relating intrinsic cortical circuits to extrinsic cortico-cortical connections, as a generic basis for computational models of cortical connectivity.

Finally, Stefanovski et al. in “Linking connectomics and dynamics in the human brain,” highlight the promise of whole brain network modelling and simulation. They present an open source platform for this approach, the virtual brain. The virtual brain combines microscopic circuit models and macroscopic connectivity measurements based on diffusion tensor imaging. The authors emphasize the potential of this approach for supporting individualized diagnostics, prognostics and treatment of neurologic disorders and discuss the challenges lying ahead.

inspired vision systems. Together with Claus Hilgetag he has initiated the newly established German Research Foundation (DFG) priority program “Computational connectomics.”

Claus C. Hilgetag studied Biophysics at Humboldt University Berlin and Neuroscience at the universities of Edinburgh, Oxford and Newcastle. He completed his PhD on the organization of mammalian brain connectivity in 1999. Subsequently, he was a postdoctoral fellow at Boston University, where he still holds a faculty appointment in the Department of Health Sciences. In 2001, Hilgetag became part of the founding faculty of the new International University Bremen (later Jacobs University). In 2011 he became the Director of the Institute of Computational Neuroscience at University Medical Center Eppendorf, Hamburg University. His research is focused on understanding general principles of brain connectivity, particularly the structural connectivity of the mammalian cerebral cortex. He also uses computational modelling to study neural activity patterns arising from the characteristic topology of brain networks, and studies lesions of brain networks by multivariate analysis approaches. Hilgetag is a member of the DFG research centers SFB 936 “Multi-site communication in the brain” and TRR 169 “Cross-modal learning: adaptivity, prediction and interaction” as well as the Academy of Sciences in Hamburg.

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Jochen Triesch received his diploma and PhD degree in physics from the Ruhr University Bochum, Germany, in 1994 and 1999, respectively. After 2 years as a postdoctoral fellow at the Computer Science Department of the University of Rochester, NY, USA, he joined the faculty of cognitive science at UC San Diego, USA as an assistant professor in 2001. In 2005 he became a fellow of the Frankfurt Institute for Advanced Studies (FIAS), in Frankfurt am Main, Germany. Since 2007 he is the Johanna Quandt Research Professor for Theoretical Life Sciences at FIAS, where he currently serves as the vice chairman of the board of directors. He also holds professorships at the Department of Physics and the Department of Computer Science and Mathematics at the Goethe University in Frankfurt am Main, Germany. In 2006 he received a Marie Curie Excellence Center Award of the European Union. From 2009–2011 he co-coordinated the Bernstein Focus Neurotechnology Frankfurt, a large center grant focusing on biologically