The Virtual Brain

P. Ritter

published in

NIC Symposium 2018
K. Binder, M. Müller, A. Trautmann (Editors)

Forschungszentrum Jülich GmbH,
John von Neumann Institute for Computing (NIC),
Schriften des Forschungszentrums Jülich, NIC Series, Vol. 49,
ISBN 978-3-95806-285-6, pp. 145.
http://hdl.handle.net/2128/17544

© 2018 by Forschungszentrum Jülich
Permission to make digital or hard copies of portions of this work for personal or classroom use is granted provided that the copies are not made or distributed for profit or commercial advantage and that copies bear this notice and the full citation on the first page. To copy otherwise requires prior specific permission by the publisher mentioned above.

The Virtual Brain

Petra Ritter

Dept. Neurology, Charité Universitätsmedizin Berlin & Berlin Institute of Health,
Charitéplatz 1, 10117 Berlin, Germany
E-mail: petra.ritter@charite.de

The study of the brain often involves experiments on individual elements of function and structure. It is difficult, however, to appreciate how these elements come together in support of healthy brain function and when they change in clinical conditions. We have built an open-access brain modelling platform "The Virtual Brain" that links directly to experimental data and combines the elements to simulate a brain and facilitate new discoveries about brain function and dysfunction.

1 Introduction

Brain research generates a plethora of unique data on nervous system function across multiple scales and species. New technologies reveal aspects of brain dynamics that heretofore were unimaginable. A challenge with these activities is the difficulty in integrating disparate data sources to appreciate their complex interdependencies in brain function. Computational modelling and simulation provide a principled means to merge such data and begin to understand such relations. We have developed The Virtual Brain (TVB, `http://thevirtualbrain.org`), as an open-source platform to model large-scale brain networks by merging different data sources in a dynamical systems framework. We are currently expanding the platform to make it more accessible to other projects creating better links between data, analysis and modelling. We have recently enhanced the usability of TVB through the systematic reduction of key barriers to adoption including improvement of simulation speed, development of methods for parameter choices and model comparison. In future, this will be further supported by a model registry where users can access published models for replication and extension. New models will be added to the registry as the user-base grows. The proposed developments will provide an innovative and scalable whole brain modelling platform that is designed to facilitate data-sharing and open-science.

Brain functions emerge from interactions at multiple spatial (from synapses to areas) and temporal (milliseconds to days) scales. Dynamical interactions in the healthy brain and their alterations in neurological disorders can be identified experimentally using different modalities (e.g. EEG: electroencephalography, fMRI: functional magnetic resonance imaging), but extracting general rules that apply across scales and support whole brain dynamics is difficult due to the size and complexity of empirical data sets. Tackling questions about brain network dynamics in healthy and clinical populations requires a great deal of data, but simply gathering more data is not an answer in and of itself. The neuroscience community is immersed in the collection of large datasets to provide greater sensitivity for understanding brain function and dysfunction. Such initiatives span normal function (Human Connectome Project), development (NIH Pediatric Database), brain disorders such as Alzheimer's disease (ADNI) and psychiatry (RDoC: Research Domain Criteria Project).

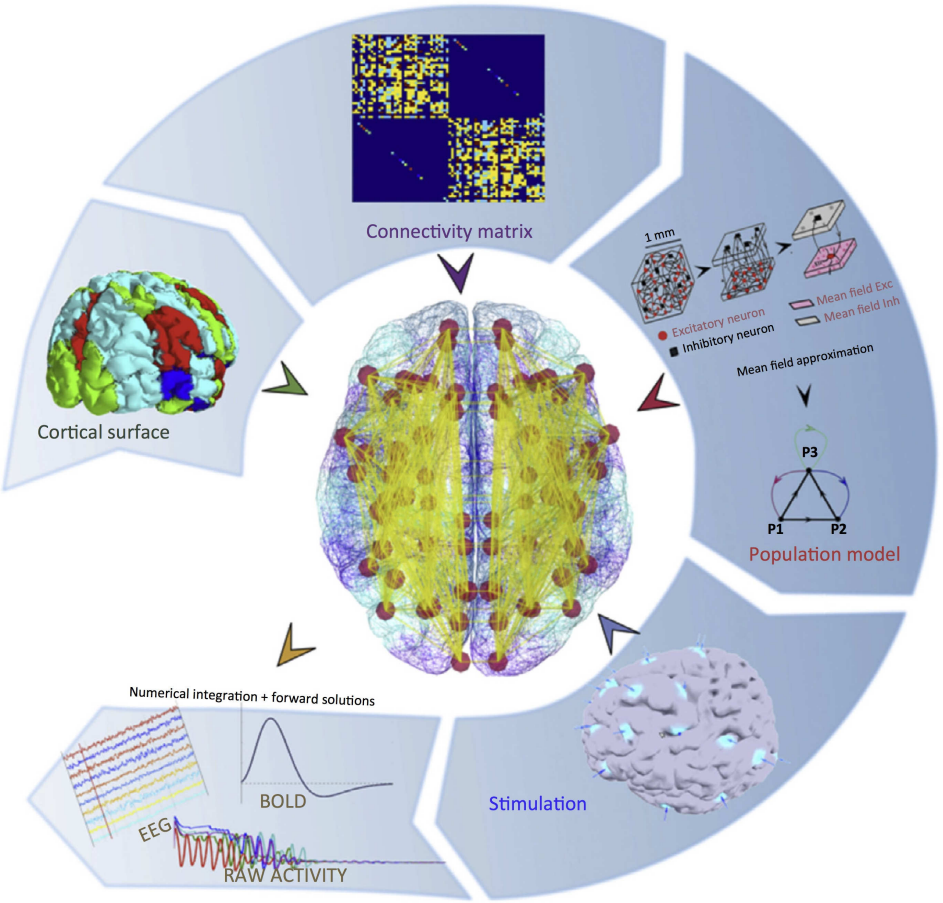

Figure 1. **The Virtual Brain Workflow.** A large scale model (centre), is built from the geometry of the cortical (and subcortical) surface, the anatomical connectivity, and cell population models for the local dynamics. Dynamics can arise from intrinsic activity alone and through direct stimulation of one or more cell populations. Simulations generate raw activity, which are essential local field potentials (LFP). Through forward models, the LFPs can be converted to EEG, MEG or fMRI BOLD data to map to empirical data to assess the model fit. Figure is taken from Ref. 20.

The Virtual Brain (TVB) is an open-source software platform designed to build computational models of whole-brain network dynamics, where the network's connectivity is based either on published anatomical connectivity matrices[1,2], or empirical estimations using diffusion MRI-based connectoms[3] (Fig. 1). The connectivity matrix acts as a starting point for dynamical systems modelling, where the nodes are then imparted with dynamics derived from one of several neural mean field equations. These can range from simple oscillators (2D oscillator, Kuramoto), to multicomponent population firing rate models (Wilson-Cowan, Stefanescu-Jirs 3D[4]), to phenomenological models such as the Epileptor[5]. The local parameters and effect of other nodes via the long-range connection, constrain the node dynamics generating simulated data, which are effectively local field potentials that

come from each node. Through forward models, EEG, MEG, fMRI can also be created. Stereotaxic EEG data can also be modelled based on user-specified electrode locations or to deliver focal stimulation. These data are generated in standard formats to enable the user to analyse them as if they were empirical data, including the comparison with empirical data for the purposes of model fitting and validation.

TVB was first released as an open-source software platform in 2012. It is written in Python and can be downloaded directly from the TVB website (`http://thevirtualbrain.org`) or through GitHub. Since its release, there have been over 4000 downloads with an active user community of about 160 who interact via Google groups. There has also been a steady stream of papers using TVB, including primary descriptions of the platform[3,6] and applications[7–12]. These applications serve as proof-of-principle of the value of TVB across many research programs currently supported under the BRAIN Initiative, as elaborated below.

2 Network Dynamics

TVB was specifically designed to simulate network dynamics, particularly at the whole brain level. Some of the first applications were simulations of Resting-State, or intrinsic, networks that had been measured in many fMRI studies. The work from TVB indicated that the intrinsic dynamics could be best explained by biophysical noise that drives the reconfiguration on network interactions atop a relatively deterministic anatomical skeleton[13,14]. The subsequent work has refined this observation to link with concepts of criticality, indicating that the intrinsic dynamics help the brain establish an optimal working point to facilitate information processing and response to external perturbation[15]. The ability of TVB to link to empirical data enables tighter integration of the model to the data.

3 Multiscale Dependencies and Mechanisms

By construction, TVB integrates local and global aspects of brain dynamics. Some neural mass models approximate the interactions between local cell populations, where parameters can be related to excitatory and inhibitory influences[16,17]. The forward models (monitors) in TVB then project the outcome of the local dynamics and the ensuing cascades across the network into EEG or fMRI data. TVB simulates local field potentials that reflect both the local dynamics and the larger network context, and how these translate to other scales of measure (EEG and fMRI). TVB can thus provide additional evidence to explain links between scales (microcircuit within a node, network, and neuroimaging signals) and by modifying model parameters (e.g., global coupling). The capacity to bridge scales is a decided advantage of TVB over simple data analysis and enables a test bed to ascertain how multiscale organisation is realised.

4 Network Perturbation

While much of the published work with TVB has focused on intrinsic dynamics, some recent studies have examined perturbations of nodes and the impact on network dynamics. For example, Spiegler *et al.*[18] stimulated more than 16,000 sites in a TVB model

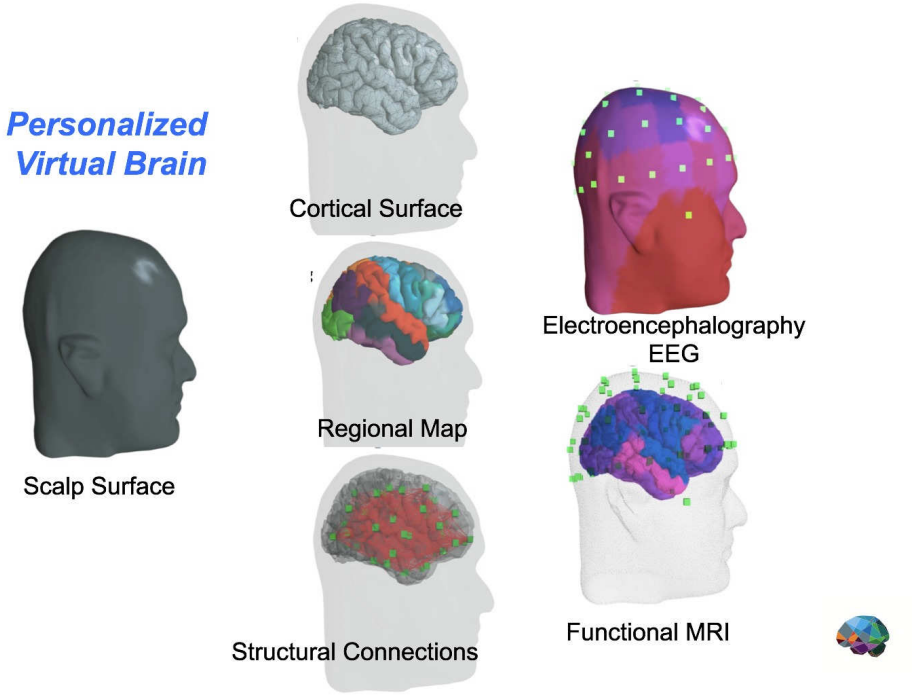

Figure 2. Minimum self-consistent dataset needed for TVB with potential functional output. The foundation for the model comes from structural MRI data giving scalp and cortical surface, and with diffusion tensor MRI, structural connectivity estimations. Parcellation schemes are used to derive regional maps. The dynamics for each region are imparted by a selected mean field model, generating local (field potential) dynamics, which cascade across the network through the structural connections. Using forward models, the network dynamics are converted to other data types, such as fMRI and EEG. Figure is taken from Ref. 21.

to compare the stimulation efficacy in terms of broad network engagement. Subsequent work simulated tDCS effects[19], finding new dynamic states emerge from interactions in the connectome that were not observable in an isolated brain area, and not necessarily be predicted from the structural connectivity. Stimulation-induced synchronisation is a key mechanism underlying changes in the spatiotemporal pattern formation. The stimulation module in TVB provides a complementary bioengineering design platform for work on brain stimulation.

References

1. R. Kotter, *Online retrieval, processing, and visualization of primate connectivity data from the CoCoMac database*, Neuroinform **2**, 127–144, 2004.
2. N. T. Markov *et al.*, *Weight consistency specifies regularities of macaque cortical networks*, Cerebral Cortex **21(6)**, 1254–72, 2011.
3. P. Sanz Leon *et al.*, *The Virtual Brain: a simulator of primate brain network dynamics*, Front Neuroinform **7**, 10, 2013.

4. R. A. Stefanescu and V. K. Jirsa, *A low dimensional description of globally coupled heterogeneous neural networks of excitatory and inhibitory neurons*, PLoS Comput Biol **4(11)**, e1000219, 2008.
5. V. K. Jirsa *et al.*, *On the nature of seizure dynamics*, Brain **137(Pt 8)**, 2210-30, 2014.
6. M. M. Woodman *et al.*, *Integrating neuroinformatics tools in TheVirtualBrain*, Front Neuroinform **8**, 36, 2014.
7. A. Gosh *et al.*, *Noise during Rest Enables the Exploration of the Brain's Dynamic Repertoire*, PLoS Comput Biol **4(10)**, e1000196, 2008.
8. P. Ritter *et al.*, *The virtual brain integrates computational modeling and multimodal neuroimaging*, Brain Connect **3(2)**, 121–45, 2013.
9. G. Deco *et al.*, *Key role of coupling, delay, and noise in resting brain fluctuations*, Proc Natl Acad Sci USA **106(25)**, 10302–7, 2009.
10. E. C. Hansen *et al.*, *Functional connectivity dynamics: modeling the switching behavior of the resting state*, Neuroimage **105**, 525–35, 2015.
11. M. I. Falcon, V. Jirsa, and A. Solodkin, *A new neuroinformatics approach to personalized medicine in neurology: The Virtual Brain*, Curr Opin Neurol **29(4)**, 429–36, 2016.
12. V. K. Jirsa *et al.*, *The Virtual Epileptic Patient: Individualized whole-brain models of epilepsy spread*, Neuroimage **145(Pt B)**, 377–388, 2017.
13. G. Deco, V. K. Jirsa, A. R. McIntosh, *Emerging concepts for the dynamical organization of resting-state activity in the brain*, Nature Rev. Neurosci **12(1)**, 43–56, 2011.
14. G. Deco, V. K. Jirsa, A. R. McIntosh, *Resting brains never rest: computational insights into potential cognitive architectures*, Trends Neurosci **36(5)**, 268–74, 2013.
15. G. Deco, V. K. Jirsa, *Ongoing cortical activity at rest: criticality, multistability, and ghost attractors*, J Neurosci **32(10)**, 3366–75, 2012.
16. G. Deco *et al.*, *How local excitation-inhibition ratio impacts the whole brain dynamics*, J Neurosci **34(23)**, 7886–98, 2014.
17. M. Schirner *et al.*, *Bridging multiple scales in the human brain using computational modeling*, BioRxiv, 2017.
18. A. Spiegler *et al.*, *Selective Activation of Resting-State Networks following Focal Stimulation in a Connectome-Based Network Model of the Human Brain*, eNeuro **3(5)**, 2016.
19. T. Kunze *et al.*, *Transcranial direct current stimulation changes resting state functional connectivity: A large-scale brain network modeling study*, Neuroimage **140**, 174–87, 2016.
20. M. L. Kringelbach *et al.*, *The Rediscovery of Slowness: Exploring the Timing of Cognition*, Trends in Cognitive Sciences **19(10)**, 616–628, 2015.
21. L. Stefanovski *et al.*, *Linking connectomics and dynamics in the human brain*, Neuroforum **22(3)**, 64–70, 2016.