## Large-scale model development from the NEST perspective

## Sacha van Albada

Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulation (IAS-6) and JARA Institute Brain Structure-Function Relationships (INM-10), Jülich Research Centre

We view models of cortical networks at the resolution of neurons and synapses as formal frameworks for the integration of experimental data from different sources and scales. On the structural level these models assess the consistency of experimental data and expose gaps in our knowledge. Furthermore, only mathematical models bring anatomical data into contact with data on the neuronal activity emerging in cortical networks. The vision is that such models serve as building blocks for ever more complete models of brain function and testbeds for theoretical investigations.

A recent full-density model of a 1 mm² microcircuit of early sensory cortex [1] illustrates this role of physiology-based models as integrators and platforms by bringing together knowledge from over 50 papers, being used in at least 17 peer-reviewed studies, and cited in at least 61. The reasons for the wide and rapid uptake have not been formally investigated. However, the availability of an executable model description in the metasimulation language PyNN [2], inclusion as an example in current releases of the NEST simulation code, as well as publication via Open Source Brain [3] likely contribute. Shimoura et al. [4] achieved a reproduction of the work using the Brian simulator [5].

The problem of reproducibility of results in computational neuroscience [6] became apparent a decade ago when the first large-scale projects formed in Europe [7], and the field is still striving for suitable terminology and technology, as demonstrated by the recent special issue "Reproducibility and Rigour in Computational Neuroscience" of Frontiers in Neuroinformatics. The NEST Inititative is working with the community and in international projects like the European Human Brain Project (HBP) to foster collaboration and advance methodology that promotes reproducibility.

Despite its success, the microcircuit model can be criticized as underconstrained, as each neuron receives half of the synapses from distant sources. In addition, the model does not exhibit prominent characteristics of cortical activity like substantial power at low frequencies. Cortical architecture, i.e. the area-specific cellular and laminar composition of the cortical network, is related to the connectivity between areas, which forms a hierarchical and recurrent network at the brain scale. Based on the aforementioned work on the cortical microcircuit, our recent study [8] integrates data on cortical architecture and axonal tracing data into a multi-scale framework describing one hemisphere of macaque vision-related cortex. We represent each area by the network below 1 mm<sup>2</sup> of cortical surface. These circuits are modeled with their natural number of neurons and synapses. Simulations confirm a realistic activity regime after adjustments of the connectivity within the margins of error [9] with the help of mean-field theory. At a sufficiently large coupling between the areas, spike patterns, the distribution of spike rates, and the power spectrum of the activity are compatible with in-vivo resting-state data. Furthermore, the matrix of correlations between the activities of areas is as similar to the experimentally measured functional connectivity of resting-state fMRI as can be expected based on inter-individual differences. This correspondence on multiple spatial scales is achieved in a metastable state exhibiting time scales much larger than any time constant of the system.

The increased complexity of brain-scale models poses new challenges for the reproducibility and reusability of results by the computational neuroscience community.

First, only executable model descriptions enable the effective communication between scientists and the reproducibility of results. Furthermore, the information required to instantiate a model in the memory of a computer is only one aspect of the modeling process. The experimental data entering the model span multiple scales and come from different sources. Algorithms are required to collate the data and derive the final model parameters. Often, data are only partially available such that quantitative hypotheses need to be formulated to bridge the gaps. As a consequence researchers can only add new data to the model or modify assumptions if they have access to the construction process. Hence, the workflow of data integration also needs to be documented in an executable format. The complete model description comprises a substantial amount of source code. Therefore, we explore the transfer of our experience from software development to model construction using a code review platform. On the example of our multi-area model, we trace the development of a publishable executable workflow of model construction and discuss the difficulties we encountered in the process.

Second, simulating multi-area models at the level of resolution of neurons and synapses taxes the largest supercomputers available. Thus, models are only reproducible in practice if the community has access to corresponding computer resources. Alongside the hardware, a simulation code is needed which reduces the required resources in terms of memory and time to a minimum while providing the neuroscientist with a homogeneous environment from laptops to supercomputers. The talk presents our recent progress [10] and points out that the phase of network instantiation as opposed to the propagation of the dynamics can become the bottleneck of a simulation [11]. High-level model descriptions need to be designed such that simulation engines can efficiently parallelize the instantiation.

Still, solving the equations for microscopically parallel system on conventional computers with their rather coarse-grained parallelism consumes considerable energy, and reaching real-time or accelerated speeds is difficult. Therefore, we also explore neuromorphic computing as an alternative computing platform. The talk presents recent progress in this area [12], in which we ported the full-density microcircuit model to the SpiNNaker hardware system. The finding is relevant because it lays the foundation for simulating even larger cortical networks by already approximating the full number of synapses per neuron.

The open development of NEST is guided by the NEST Initiative. Partial funding comes from the Human Brain Project through EU grants 604102, 720270, and 78590; and from the German Research Council (DFG grant SPP 2041). Use of the JUQUEEN supercomputer in Jülich was made possible by the JARA-HPC Vergabegremium and provided on the JARA-HPC Partition (VSR computation time grant JINB33).

- [1] Potjans T, Diesmann M (2014) The cell-type specific cortical microcircuit: relating structure and activity in a full-scale spiking network model. Cereb Cortex 24:785-806 [2] Davison AP, Brüderle D, Eppler J, Kremkow J, Muller E, Pecevski D, Perrinet L, Yger P (2009). PyNN: a common interface for neuronal network simulators. Front Neuroinform 2:11 [3] Gleeson P, Cantarelli M, Marin B, ... van Albada SJ, van Geit W, R Silver RA (2018) Open Source Brain: a collaborative resource for visualizing, analyzing, simulating and developing standardized models of neurons and circuits, bioRxiv:29484.
- [4] Shimoura RO, Kamiji NL, Pena RFO, Cordeiro VL, Ceballos CC, Romaro C, Roque AC (2018) [Re] The cell-type specific cortical microcircuit: relating structure and activity in a full-scale spiking network model. ReScience 4:1
- [5] Goodman DF, Brette R (2009) The Brian simulator. Front Neurosci 3:192-197[6] Brette R, Rudolph M, Carnevale T, ... Davison AP, El Boustani S, Destexhe A (2007).Simulation of networks of spiking neurons: a review of tools and strategies. J Comp Neurosci

23:349-398.

- [7] Plesser HE (2018) Reproducibility vs. replicability: a brief history of a confused terminology. Front Neuroinform 11:76.
- [8] Schmidt M, Bakker R, Hilgetag CC, Diesmann M, van Albada SJ (2018) Multi-scale account of the network structure of macaque visual cortex. Brain Struct Func 223:1409-1435 [9] Schuecker J, Schmidt M, van Albada SJ, Diesmann M, Helias M (2017) Fundamental activity constraints lead to specific interpretations of the connectome. PLOS Comput Biol 13:e1005179
- [10] Jordan J, Ippen T, Helias M, Kitayama I, Mitsuhisa S, Igarashi J, Diesmann M, Kunkel S (2018) Front Neuroinform 12:2
- [11] Ippen T, Eppler JM, Plesser HE, Diesmann M (2017). Constructing neuronal network models in massively parallel environments. Front Neuroinform 11:30
- [12] van Albada SJ, Rowley AG, Senk J, Hopkins M, Schmidt M, Stokes AB, Lester DR, Diesmann M, Furber SB (2018) Performance comparison of the digital neuromorphic hardware SpiNNaker and the neural network simulation software NEST for a full-scale cortical microcircuit model. Front Neurosci 12:291