Validation of Simulated on Experimental Spiking Activity: The Human Brain Project Perspective

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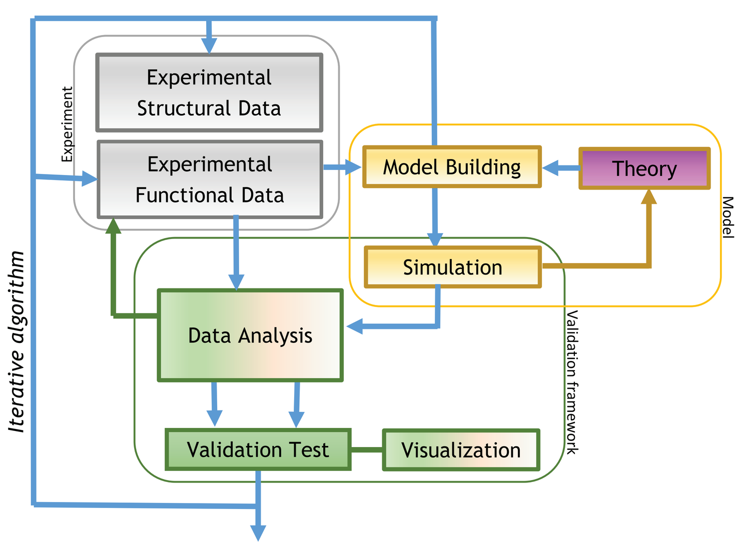
Integrative Loop Workflow



The integrative loop describes an iterative process of comparison and validation of experimental and simulated data. Here we use it to derive a mesocircuit model of the macaque (pre)motor cortex validated in terms of the statistics of neuronal activity as outlined in *Gutzen et al.* (2018). The workflow will be implemented into the HBP Collaboratory [4] and will have the role of providing an integrated solution for reproducibility.
Senk et al. (2017) have implemented a similar workflow (see **collab #507**) to compare simulation results of NEST and SpiNNaker for the same cortical model [5, 8], which was continued in **T9.1.5 (SGA1) Model simplification and validation**. The comparison of experimental and modeled data is currently developed within the Collaboratory using the **validation framework (T6.4.5, SGA2)**. Simulation runs will be realized with **UNICORE (T7.5.6, SGA1)**.
Within **T4.5.1 (SGA2) Comparing activity dynamics of models and living brains**, we outline here a workflow for electrophysiological research and show how existing tools are integrated, e.g. **T4.1.3 (SGA2) Mean-field and population models**, **T4.2.1 (SGA1) Simplified network models of different cortical areas**, **T5.7.1 (SGA2) Elephant**, and **T7.5.5 (SGA1) Simulator NEST as a Service**.

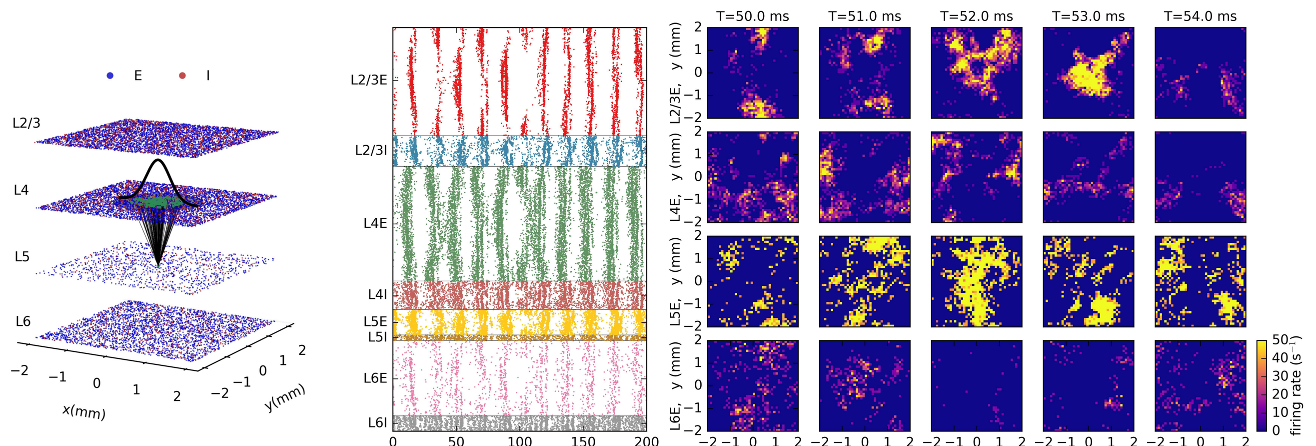
4×4 mm^2 Mesocircuit Model

Senk et al., 2018, arXiv:1805.10235 [q-bio.NC]

The NEST [5] spiking point-neuron model of the cortical microcircuit by *Potjans & Diesmann* (2014) (1 mm^2) is extended to 4×4 mm^2 with distance-dependent connectivity and is to be reparameterized to the macaque (pre)motor cortex in order to reproduce experimental results. Here we show an example parameter combination that is within biologically plausible bounds.

Network description

- ~1.2 million leaky integrate-and-fire neurons in 4 layers with excitatory (E) and inhibitory (I) populations
- ~ 5.5 billion static current-based synapses
- External input with Poisson statistics
- Uniform neuron distribution with periodic boundary conditions
- Connection probabilities derived from experimental data [8]
- Distance-dependent connectivity with Gaussian profile (σ_E=0.5 mm, σ_I=0.2 mm) with maximum distance of 2 mm
- Transmission delay: 0.3 ms, axonal propagation speed 0.3 mm/ms

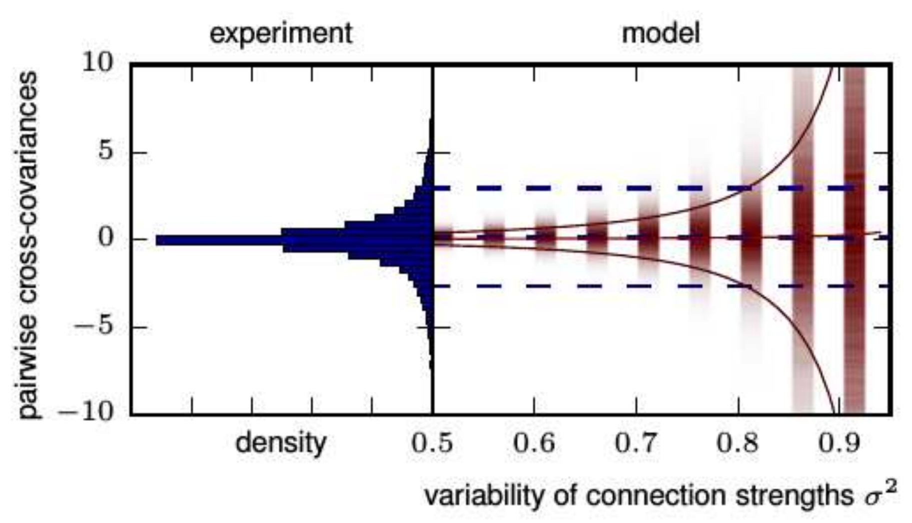


Left: Distance-dependent connectivity profile and neuron density; middle: raster plots of spiking activity in a small time window of 200 ms; right: neural activity (firing rates) projected on cortical area.

Mean-Field Theoretic Approach

Dahmen et al. (2017), arXiv:1711.10930 [cond-mat.dis-nn]

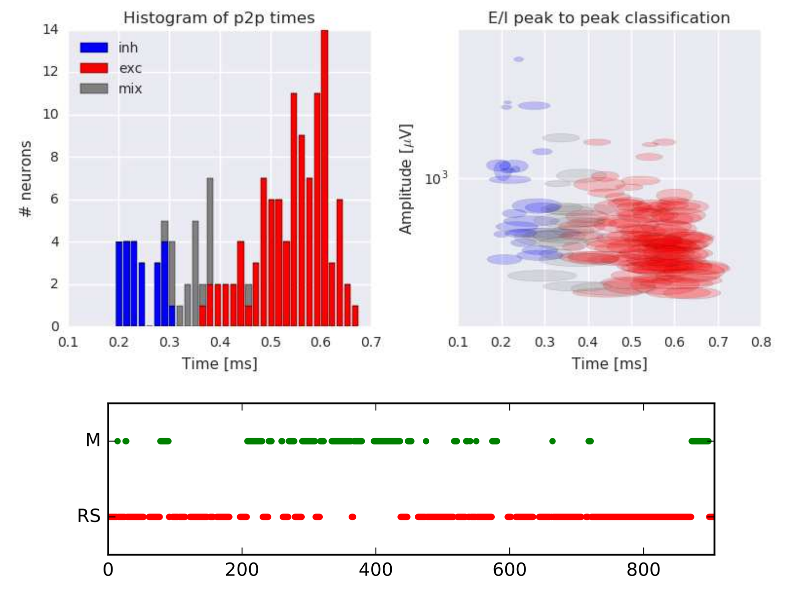
To **constrain the parameter space of the model**, we make use of a mean-field theory [2] that allows us to infer constraints on the statistics of effective connections from the experimentally observed first and second moment of the covariance distribution. Effective connections hereby measure the sensitivity of the postsynaptic firing to a spike of the presynaptic neuron. The figure shows how low mean and large standard deviation (blue dashed horizontal lines) of experimentally observed cross-covariances (blue) are explained by a model network (red) with high variability of connections ($\sigma^2 = 0.8$). The experimental data can thus be used to infer information on the statistical distribution of the underlying structural connectivity and to gain insight into the operational regime of the network.



Analysis of Experimental Data

Data

Data are obtained from (pre)motor cortex of macaque during a **resting state** experiment in which the monkey is sitting in a chair without task. **Spiking activity** were measured for 15 min using a Utah array (100 electrodes) and **behavior** (rest, movement, sleepiness) was identified from video recordings. Spikes were sorted offline resulting in 147 single units [1].



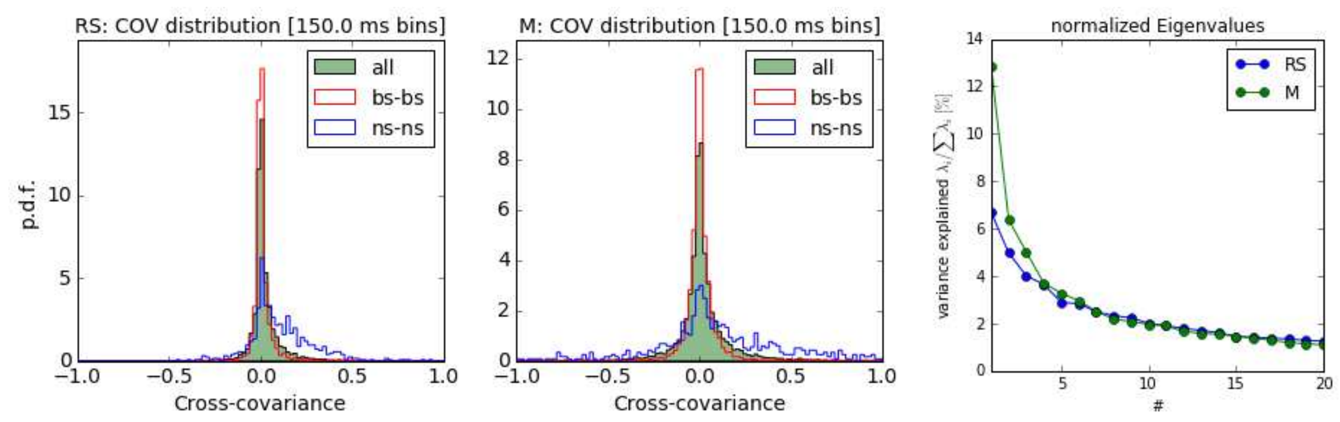
Analysis of experimental data on HBP collab #2493 [7]. Top: separation of putative excitatory and inhibitory units according to peak to peak (p2p) amplitude (left) and peak to peak time (right). Bottom: Behavioral segmentation into rest and movement.

Preprocessing

To identify putative excitatory and inhibitory neurons, we classify waveforms into broad (bs) and narrow spiking (ns). For a given threshold (350 ms) the percentage consistency of each unit is calculated. Forcing at least 60% consistency we find 95 putative excitatory (bs) and 37 putative inhibitory (ns) units.

Estimation of Covariances and Eigenvalues

Cross-covariances are estimated from binned spike trains x and y with a binsize of 150 ms according to $c_{xy} = \langle xy \rangle - \langle x \rangle \langle y \rangle$. The p.d.f. of cross-covariances are computed for cell-type specific connections (bs-bs, ns-ns) during rest (left panel) and movement (middle panel). As expected from mean-field theory [*Deutz et al.*, in prep.], inhibitory neurons lead to broader distributions. A singular value decomposition of the covariance matrix (right panel) indicates that the dimensionality is reduced during movement [6] as eigenvalues are larger during movement (green line) than during rest (blue line).



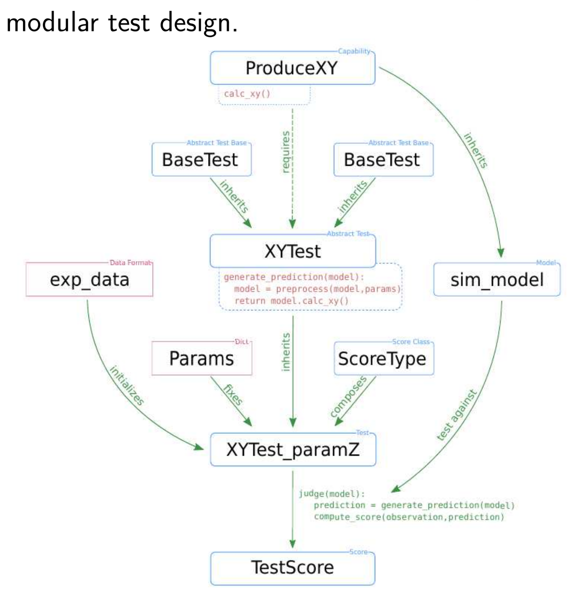
Validation

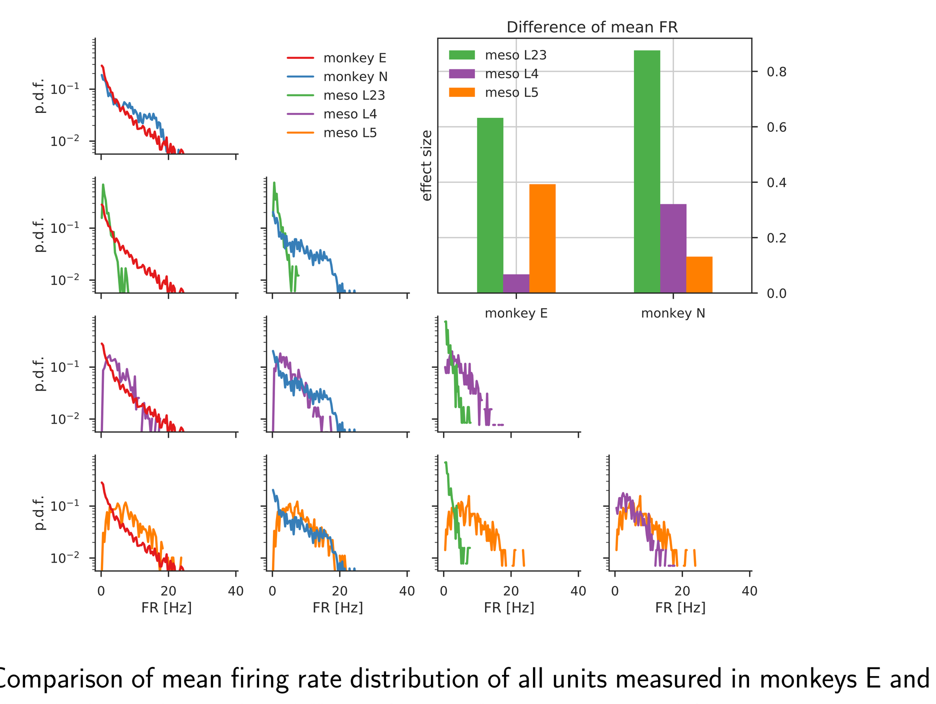
Gutzen et al. (2018), Front. Neuroinf., submitted

The model is to be cross-validated with respect to the observed network activity within several monkeys using the Python module NetworkUnit (`github.com/INM-6/networkunit`). We make use of methods derived in **T9.1.5.** [3, collab #2366] for testing simulations on conventional computers against simulations on neuromorphic hardware (i.e. validation of the **SpiNNaker w.r.t. NEST** simulator). For the mesocircuit model the effect sizes of the firing rate distributions (bottom right) show a qualitative fit (effect size < 1) but statistical hypothesis tests for equality of the mean (e.g. Welch's t-test) still fail, thus demanding a further parameter adaptation of the model.

Validation Workflow

Schematic structure of the validation framework using NetworkUnit. Capabilities, tests, scores and models are defined as classes and allow for a respective flexible and modular test design.





Comparison of mean firing rate distribution of all units measured in monkeys E and N with those observed in different layers of mesocircuit model.

Outlook

- Additionally constrain parameter space based on firing rates and coefficient of variation
- Incorporate UNICORE-based computation of mesocircuit on JUELICH clusters
- Add experimental data in Neural Activity Resource NAR (T5.7.2 [SGA2])
- Generate algorithm to automatically update model parameters based on the quantitative results obtained from statistical comparisons

[1] Brochier et al. (2018) Data Descriptor: Massively parallel recordings in macaque motor cortex during an instructed delayed reach-to-grasp task. Sci. Data, 5.
[2] Dahmen et al. (2017) Two types of criticality in the brain. arXiv:1711.10930 [cond-mat.dis-nn]
[3] Gutzen et al. (2018) Reproducible neural network simulations: model validation on the level of network activity data. Front. Neuroinf., submitted
[4] `https://collab.humanbrainproject.eu`
[5] `http://www.nest-simulator.org`
[6] Mazzucato et al. (2016) Stimuli reduce the dimensionality of cortical activity. Front. Syst. Neu., 10(11).
[7] von Papen et al. (2017) Analysis of single unit activity during rest and movement in the macaque (pre)motor cortex. in HBP Collaboratory: `https://collab.humanbrainproject.eu/#/collab/2493`.
[8] Potjans and Diesmann (2014) The cell-type specific cortical microcircuit: Relating structure and activity in a full-scale spiking network model. Cereb. Cort., 24(3).
[9] Senk et al. (2017) A collaborative simulation-analysis workflow for computational neuroscience using HPC. In E. Di Napoli et al. (eds.), LNCS, 10164.
[10] Senk et al. (2018), Reconciliation of weak pairwise spike-train correlations and highly coherent local field potentials across space. arXiv:1805.10235 [q-bio.NC].