Towards automation of experiment-driven building and validation of a mesocircuit model

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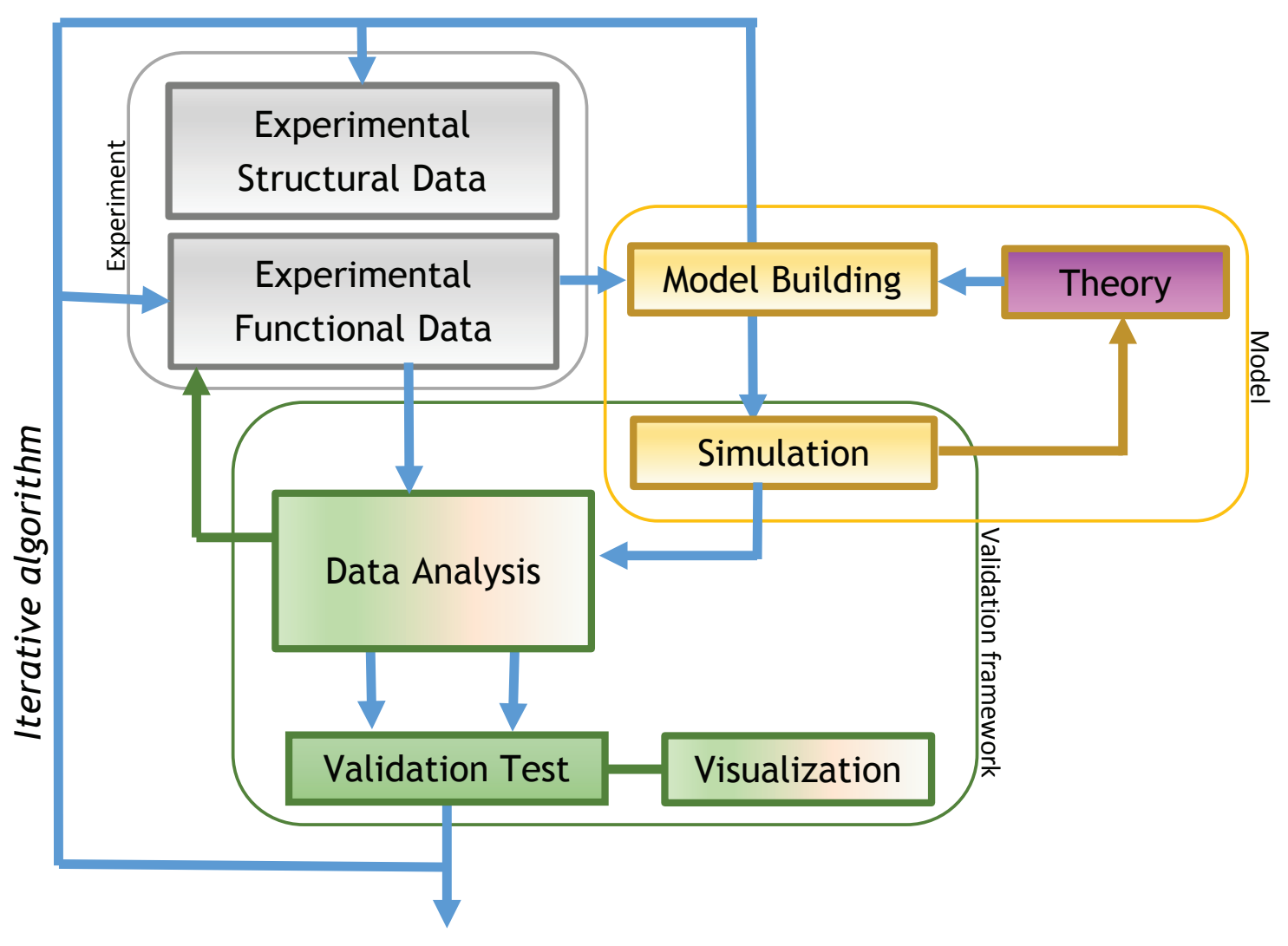
Integrative Loop Workflow



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 statistical neuronal activity as outlined in *Denker and Grün* (2016). The planned collaboratory based on this workflow 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 (*Potjans and Diesmann*, 2014), which is 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 (T6.4.4 [SGA1])**. Simulation runs will be realized with **UNICORE (T7.5.6 [SGA1])**.

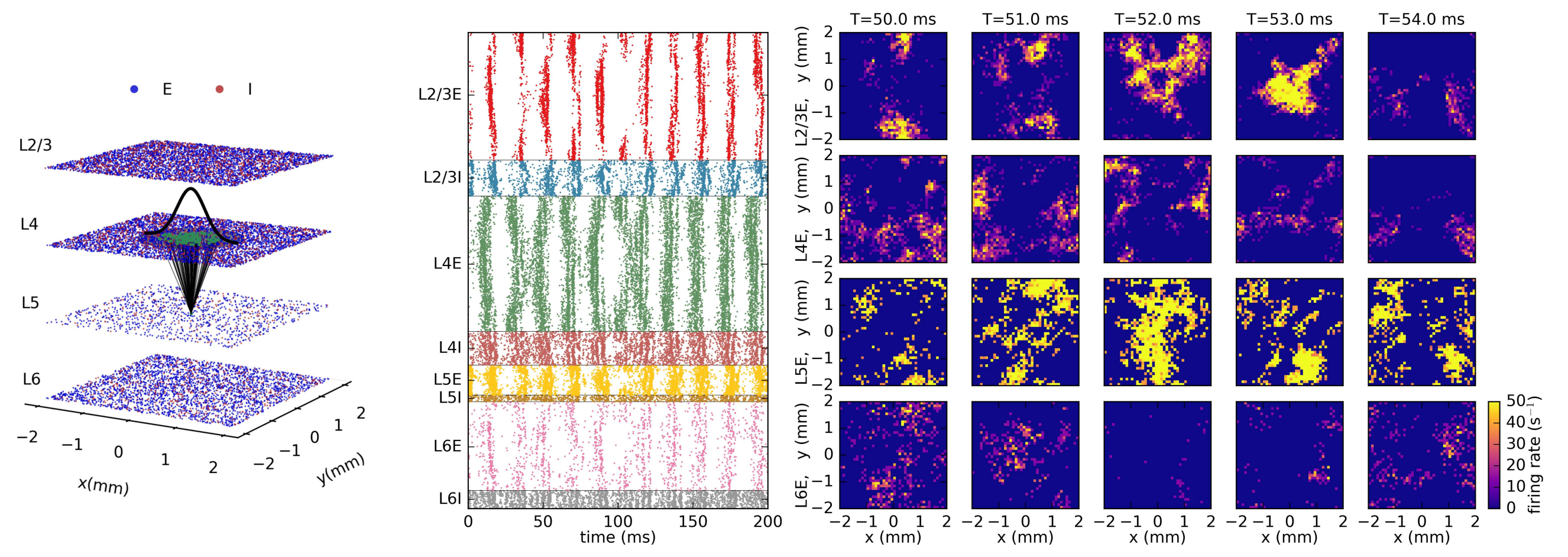
Within **T4.5.1 (SGA2) Comparing activity dynamics of models and living brains**, we outline here a workflow for electrophysiological research and show how existing tools are integrated, e.g. **T4.1.3 (SGA2) Mean-field and population models**, **T4.2.1 (SGA1) Simplified network models of different cortical areas**, **T5.7.1 (SGA2) Elephant**, and **T7.5.5 (SGA1) Simulator NEST as a Service**.

4×4 mm^2 Mesocircuit Model

The NEST spiking point-neuron model of cortical microcircuit by *Potjans & Diesmann* (2014) (1 mm^2 column, 8 populations, 4 layers) is extended to with distance-dependent connectivity and to be re-parameterized to (pre)motor cortex in order to reproduce experimental results.

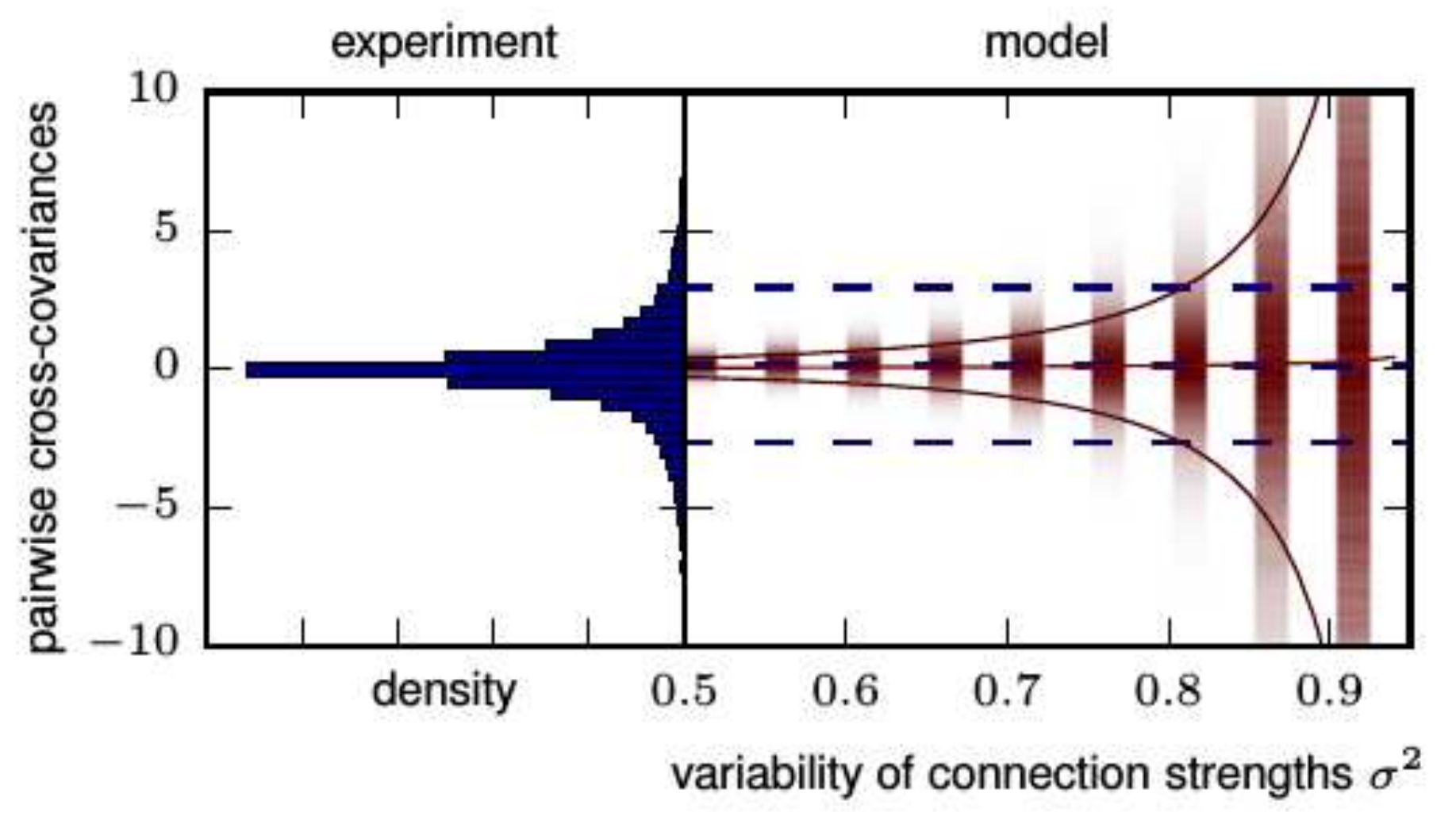
Network description

- ~1.2 million leaky integrate-and-fire (LIF) neurons in 4 layers with excitatory (E) and inhibitory (I) populations
- ~6 billion static current-based synapses
- External input with Poisson statistics
- Uniform neuron distribution with periodic boundary conditions (torus connectivity)
- Connection probabilities derived from experimental data [2]
- Distance-dependent connectivity with Gaussian profile (σ_E=0.5 mm, σ_I=0.2 mm) with maximum distance 2 mm
- Delay offset: 0.3 ms, axonal propagation speed 0.3 mm/ms



Mean-Field Theoretic Approach

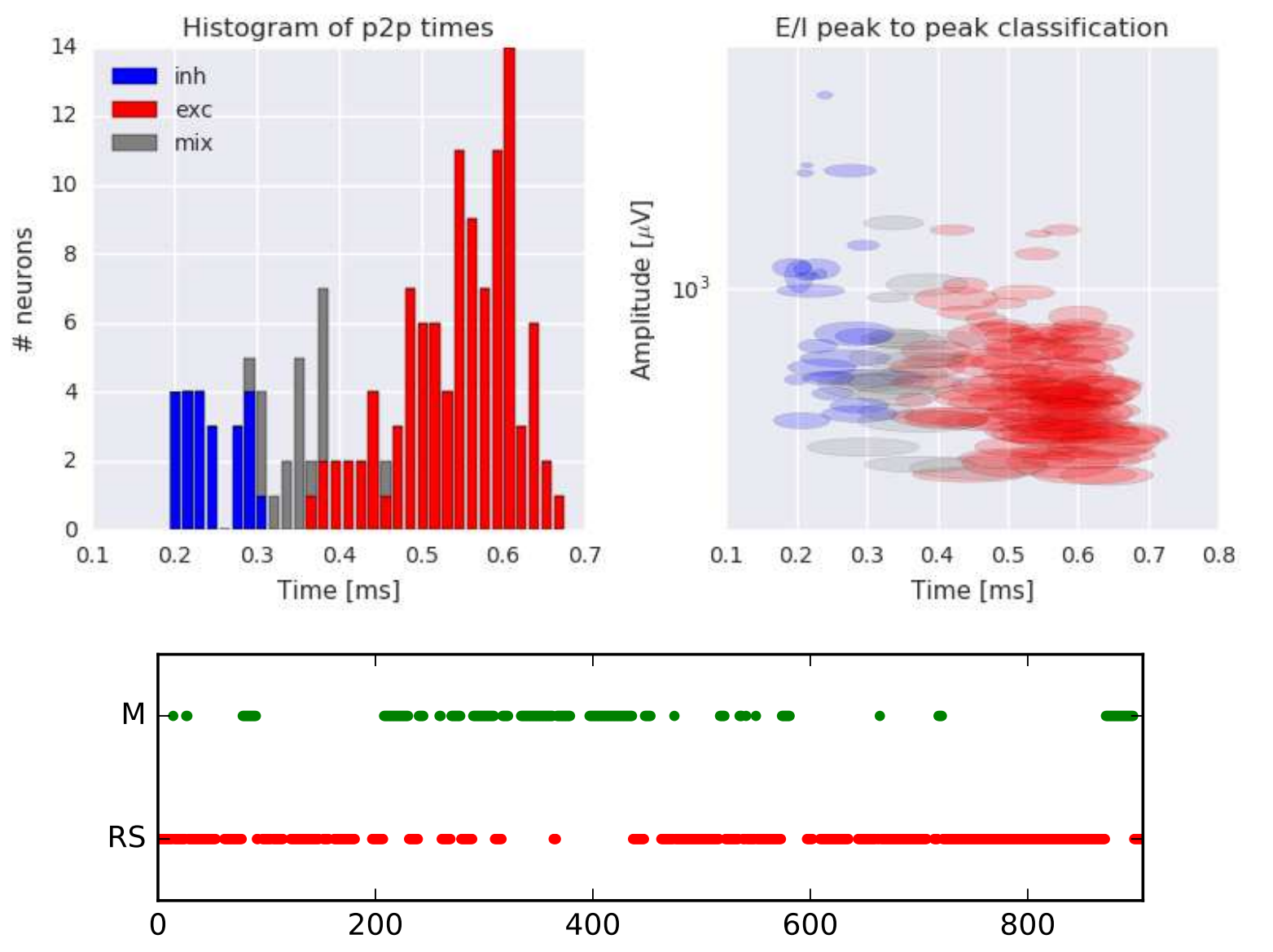
To **constrain the parameter space of the model**, we make use of a mean-field theory by *Dahmen et al.* (2016) that allows us to infer constraints on the statistics of effective connections from the experimentally observed first and second moment of the covariance distribution. Effective connections 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 spectral radius of the effective connectivity is predominantly determined by the width of the distribution of cross-covariances. The latter can thus be used to infer the operational regime of the network, i.e. the distance to criticality.



Analysis of Experimental Data

Data

Data are obtained from a **Utah array (100 electrodes)** in the (pre)motor cortex of macaque in **resting state**. **Spiking activity** and local field potentials were measured for 15 min and video recordings were used to **separate periods of rest and movement**. Spikes were sorted offline by our partner in Marseille [1] resulting in 147 single units.



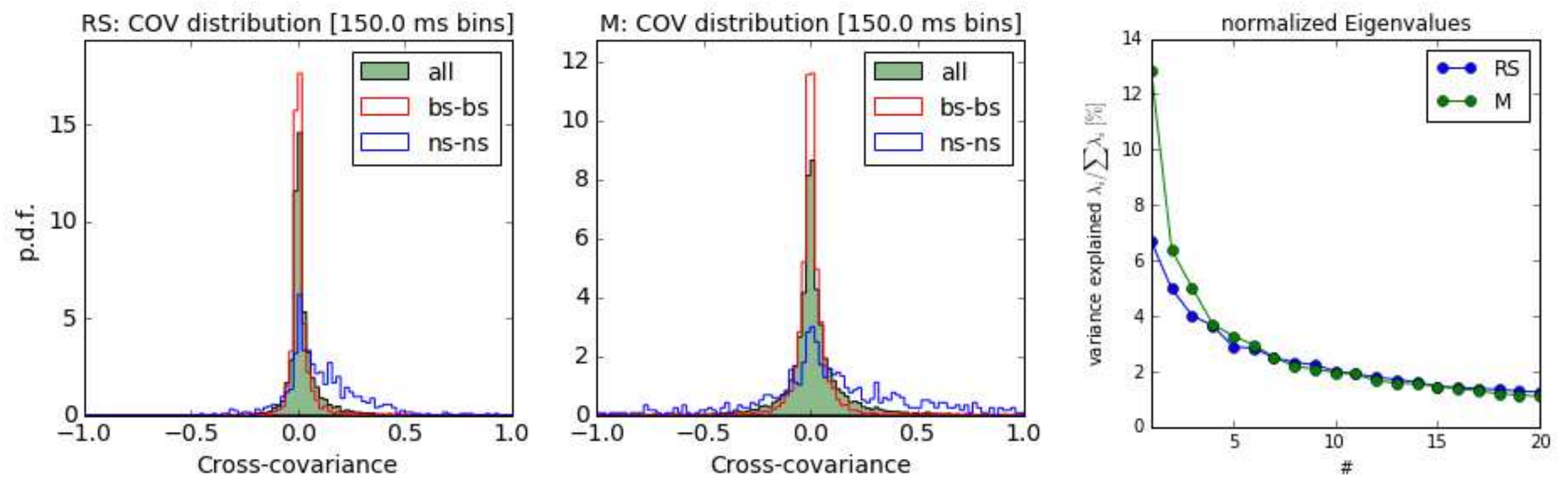
Analysis of experimental data from HBP collab #2493 [8].

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

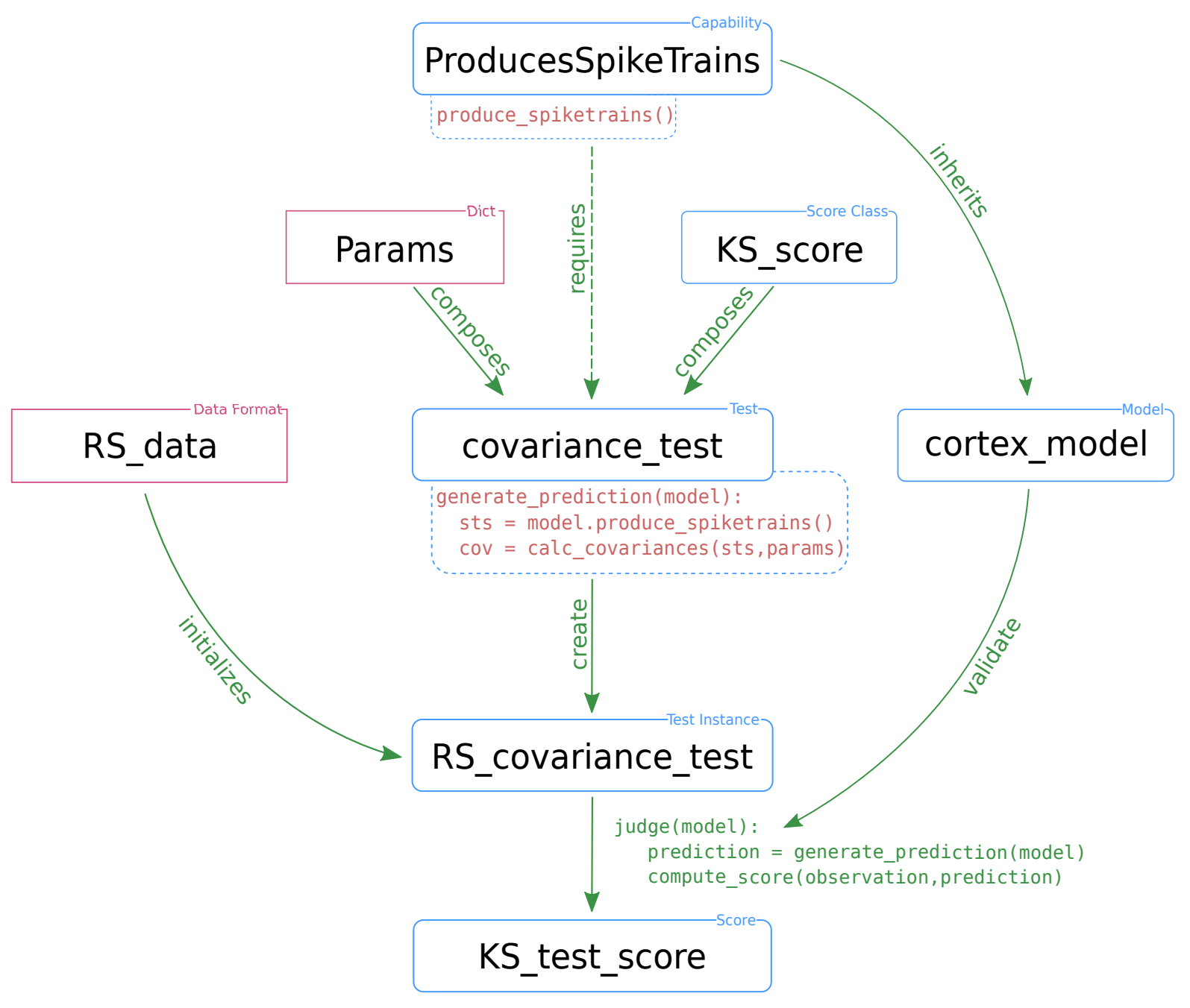
Cross-covariances are estimated from binned spike trains x and y with a binsize of 150 ms (after which the autocorrelation function has decayed to approximately zero) according to $c_{xy} = \langle xy \rangle - \langle x \rangle \langle y \rangle$. The p.d.f. of cross-covariances are computed for cell-type specific connections (bs-bs, ns-ns) as shown below. 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 indicates that the dimensionality is reduced during movement [5].



Validation

We validate the model with respect to experimental observation using the HBP validation framework (see other poster on this topic). Here validation means *to which degree a model accurately describes reality*. As the model is updated constantly, validation is an iterative process to increase confidence in the model. We make use of methods derived in **T9.1.5.** [6] for testing simulations on conventional computers against simulations on neuromorphic hardware (i.e. validation of the **SpiNNaker w.r.t. NEST** simulator). Among others, we test equality of distributions using the Kolmogorov-Smirnov distance (see below) and equality of variances using Levene score.

Validation Workflow

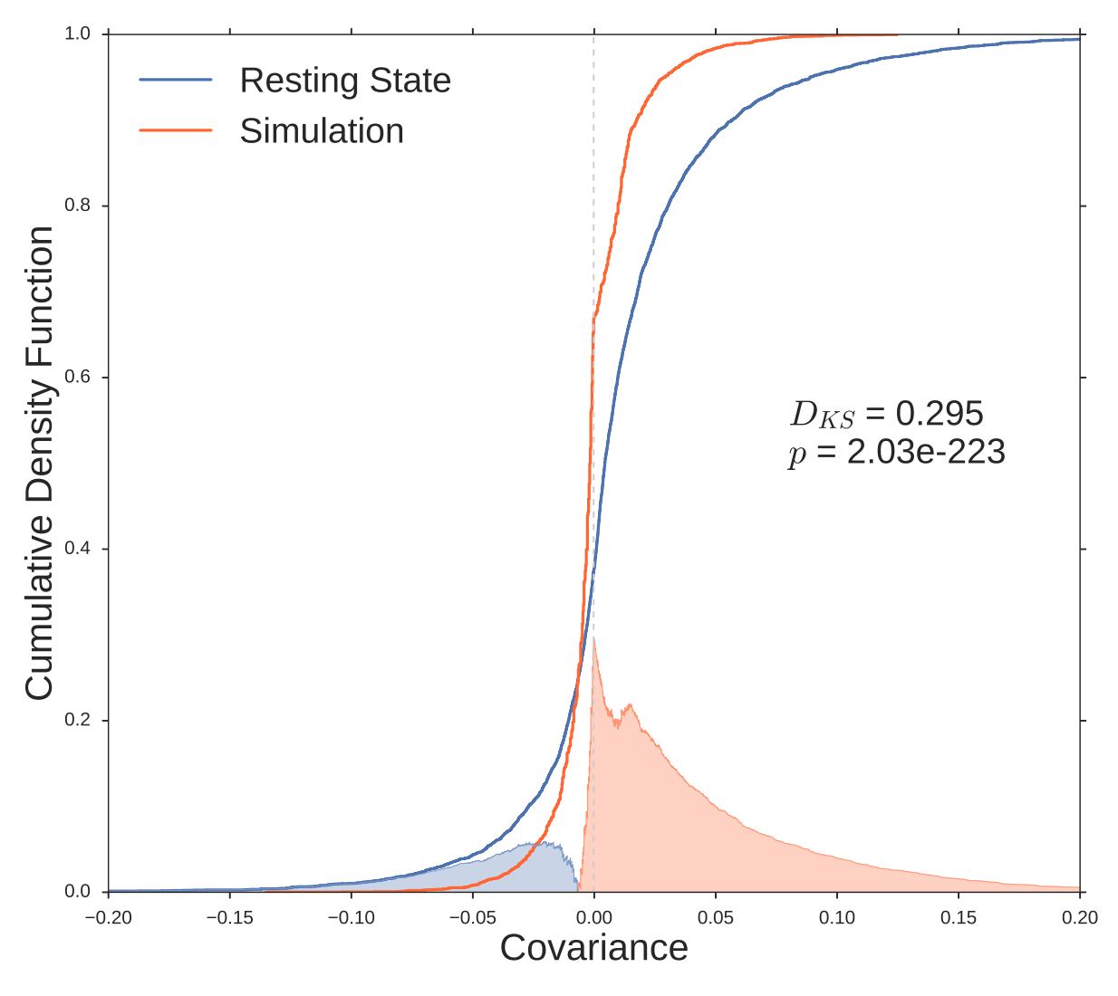


```
generate_prediction(model):
  sts = model.produce_spiketrains()
  cov = calc_covariances(sts,params)
```

```
judge(model):
   prediction = generate_prediction(model)
   compute_score(observation,prediction)
```

Structure of a typical test design in the validation framework. It shows the relation of the capability, test, score, and model classes in a validation test.

```
~$ RS_cov_test = covar_test_exc(RS_data)
~$ NEST_sim = cortex_model()
~$ RS_cov_test.judge(NEST_sim)
```



Comparison of covariance distributions of excitatory connections obtained from experimental (blue, at rest) and simulated (orange, layer 6 microcircuit) results. Small p-value indicates that there is still a significant difference (D_{KS} : maximal vertical distance between c.d.f.).

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] Riehle et al. (2013) Mapping the spatio-temporal structure of motor cortical LFP and spiking activities during reach-to-grasp movements. Front. Neural Circuits, 7(48).

[2] 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).

[3] Dahmen et al. (2016) Distributions of covariances as a window into the operational regime of neuronal networks. arXiv:1605.04153 [cond-mat.dis-nn]

[4] Denker and Grün (2016) Designing workflows for the reproducible analysis of electrophysiological data. In K. Amunts et al. (eds.), LNCS, 10087.

[5] Mazzucato et al. (2016) Stimuli reduce the dimensionality of cortical activity. Front. Syst. Neu., 10(11).

[6] Gutzen et al. (2017) NEST_SpiNNaker_Validation_Demo. in HBP Collaboratory: `https://collab.humanbrainproject.eu/#/collab/2366`.

[7] Senk et al. (2017) A collaborative simulation-analysis workflow for computational neuroscience using HPC. In E. Di Napoli et al. (eds.), LNCS, 10164.

[8] 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`.