Quantitative comparison of a mesocircuit model with resting state activity in the macaque motor cortex

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Abstract

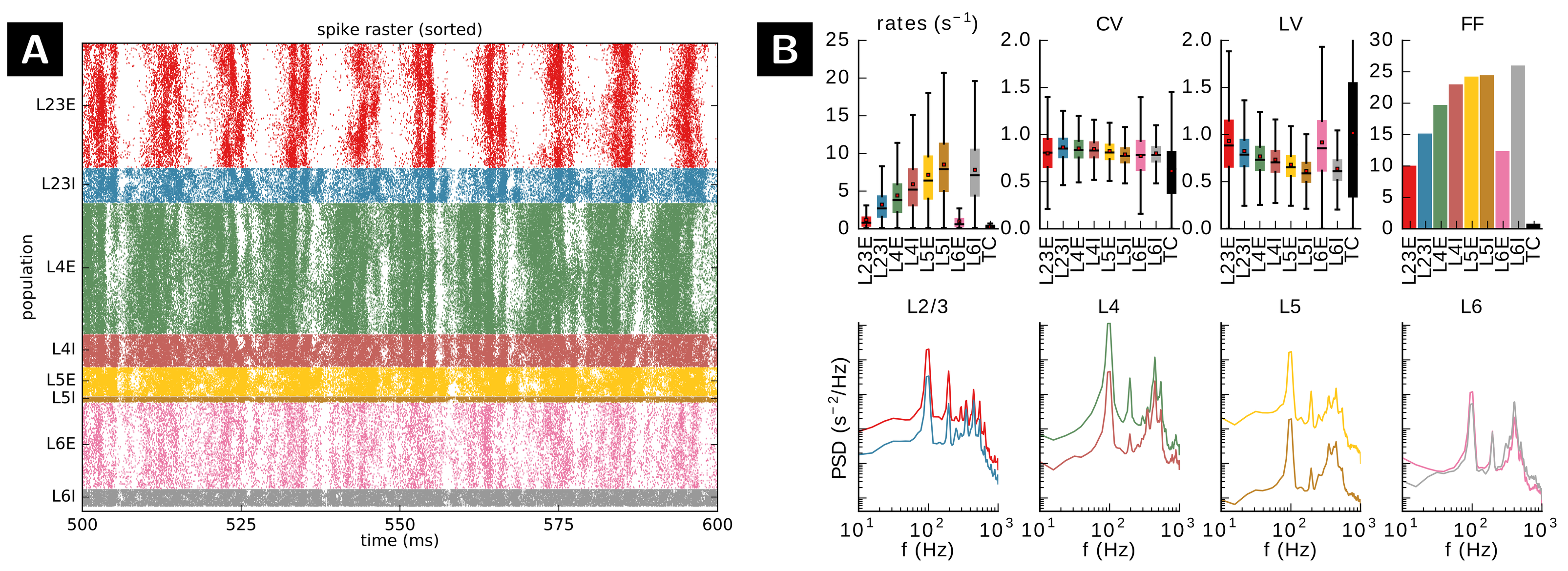
In this study, **we aim to derive a full-scale spiking network model** [7, 5] of part of the macaque motor cortex **that statistically reproduces experimental observations**. For that matter we designed a **validation workflow using the Python module NetworkUnit** [4]. The validated model will reveal possible underlying structural architectures and enable in-silico experiments, e.g. modification of structural connectivity to probe its influence on neural activity. At the current stage average spiking statistics are qualitatively similar for simulated and experimental data. Discrepancies might be caused by non-stationarities in experimental data. Further parameter adaptation of the model is to be guided by mean-field theoretic approaches [3].

4×4 mm^2 mesocircuit model

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

A spiking point-neuron model of the cortical microcircuit by Potjans & Diesmann (2014), proposed for the cat visual cortex, is extended to 4×4 mm^2 with distance-dependent connectivity. We aim to re-parameterize the model to macaque motor cortex in order to reproduce experimental data.

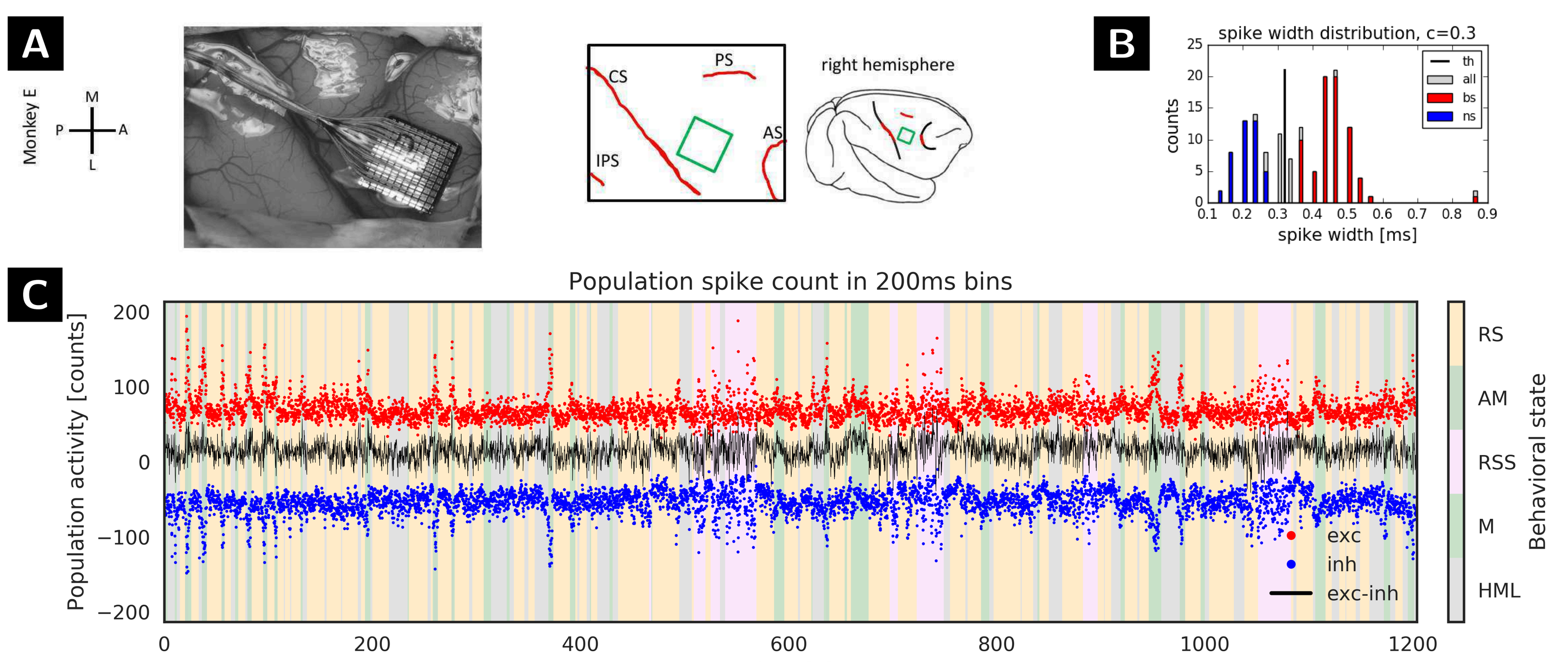
- $\sim$1.2 million leaky integrate-and-fire (LIF) neurons in 4 layers with excitatory (E) and inhibitory (I) populations
- ~ 5.5 billion static current-based synapses
- External input with Poisson statistics (8 sp/s)
- Uniform neuron distribution with periodic boundary conditions (torus connectivity)
- Connection probabilities derived from experimental data [7]
- Distance-dependent connectivity with Gaussian profile (σ=0.3 mm) with maximum distance of 2 mm
- Transmission delay at least 0.3 ms, axonal propagation speed 0.4/1.1 (E/I) mm/ms



A: raster plot of simulated data in a temporal window of 100 ms. **B, top row**: population resolved firing rate (FR), coefficient of variation (CV), local coefficient of variation (LV) of inter-spike intervals, and Fano factor (FF) of per-neuron firing rates. **B, bottom row**: Power spectral densities of population spike rates reveal a prominent 100 Hz fluctuation in all layers (colors according to raster plot).

Spiking activity in macaque motor cortex

Data are obtained from (pre)motor cortex (see Figure A) of two macaque monkeys (E and N) during a **resting state** experiment in which the monkeys are sitting in a chair without task. **Spiking activity** was recorded in one session 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 140/147 single units for monkeys E/N, respectively [2]. Putative excitatory and inhibitory neurons were classified according to waveforms into broad (bs) and narrow spiking (ns), respectively (Figure B). For monkey E and N we find 82/33 and 95/36 putative excitatory/inhibitory units. **Population activity** is significantly correlated ($\rho > 0.43$, $p \ll 10^{-9}$) between putative excitatory and inhibitory populations and activity increases during movement and sleepiness.



Example results for monkey E: **A**: Utah array location in (pre)motor cortex; **B**: separation into putative excitatory and inhibitory units with consistency of 70%. **C**: population activity of putative excitatory (red) and inhibitory (blue) units. Black line denotes difference of population activity. Colored areas indicate rest (RS), arm movement (AM), sleepiness (RSS), head movement (HML), and body movement (M).

Conclusions and discussion

- **NetworkUnit** (*https://github.com/INM-6/networkunit*) [4] sets a reproducible and modular framework for the quantitative comparison of network activity.
- **Balanced population activity** is observed between inhibitory and excitatory populations with increased activity during movement and sleepiness compared to rest.
- Average quantities of firing rate, inter spike interval and local coefficient of variation are **qualitatively comparable** (effect sizes < 1) in experimental and simulated data. However, **statistical hypothesis tests fail** and a layer localization of the experimental recording is so far not possible.
- **Neuron-type dependent cross-covariance distributions** are only observed in experimental data. First and second order of distributions can be related to effective connectivity.

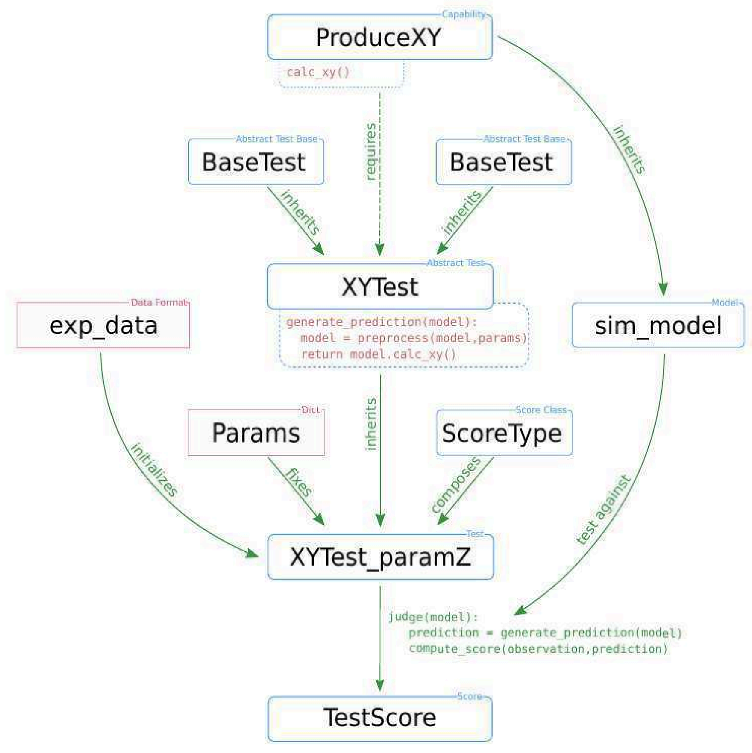
Non-stationary alternation of **connectivity patterns** during rest might explain discrepancy with simulated results. This is revealed by k-means clustering of 1st eigenvector of covariance matrix in sliding window (3 s) analysis [1] used to estimate recurring connectivity patterns of correlated structures.

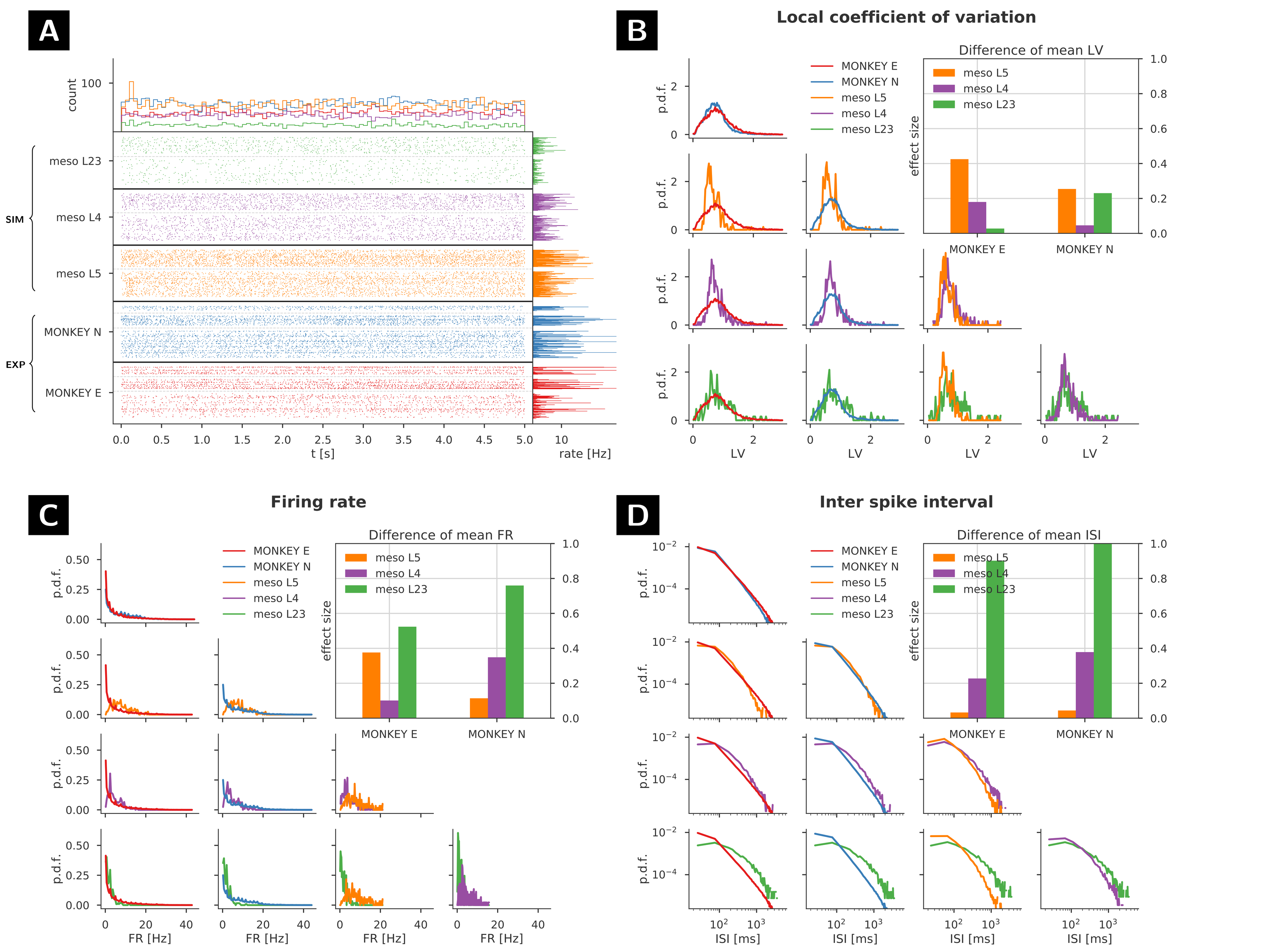
Comparison of spiking statistics

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

The model is to be validated using **NetworkUnit** (*github.com/INM-6/networkunit*) [4], a Python module for the quantitative comparison of neural network activity. It is based on SciUnit [6] and places the data, models and tests within the workflow in a reproducible framework.

Mono- and bivariate spiking statistics such as B) local coefficient of variation (LV), C) firing rate (FR), D) inter-spike intervals (ISI), and cross-covariances (see box below) are extracted in the form of probability density functions (p.d.f.). The difference between simulated and experimental data is quantified by the effect size $d = (\mu_1 - \mu_2)/\sigma_{12}$ and from statistical hypothesis tests. While **effect sizes** are generally below one **indicating at least qualitative similarity**, statistical tests for equality of mean (e.g. Welch's t-test) still show a **significant difference between simulated and experimental distributions** requiring further model calibration.

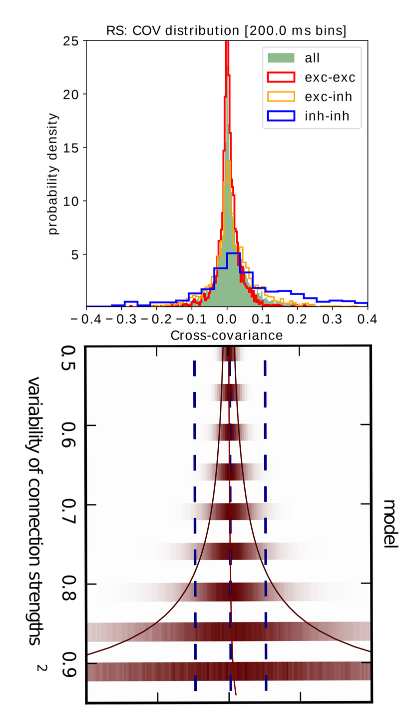




A: raster plots of simulated and experimental data showing 140 single units each Dots are separated for excitatory (below gray lines) and inhibitory units (above gray lines). Experimental data has an additional third group of unclassified units (uppermost group). Comparison of local coefficients of variation (B), mean firing rates (C), and inter spike intervals (D) between monkeys E and N and different layers within the mesocircuit model. Effect sizes of experimental results with respect to simulated data are shown in top right corner.

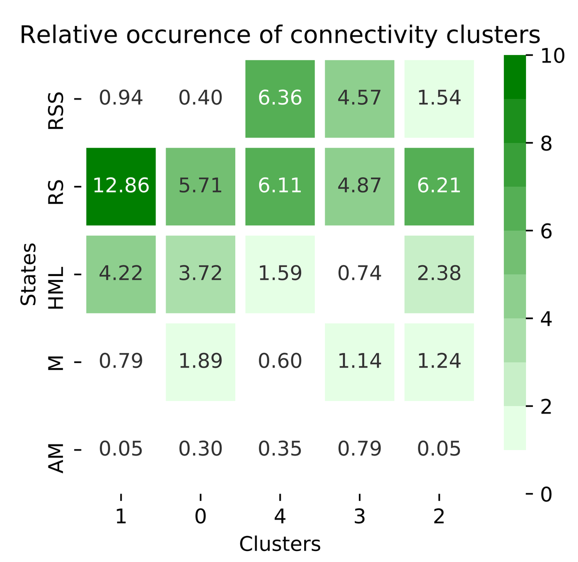
Mean-field theoretic approach

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



To constrain the parameter space of the model, we will make use of mean-field theoretic approaches [3]. This allows to **infer constraints on the statistics of effective connections** from the experimentally observed first and second moment of the covariance distributions. Effective connections measure the sensitivity of the postsynaptic firing to a spike of the presynaptic neuron and can be derived from the model parameters. 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 (**see also Poster #82**).

The figure shows schematically how experimentally observed cross-covariances (top, using 200 ms binsize) can be related to the modeled variability of connections (bottom). Cross-covariance distributions are wider for inhibitory than for excitatory pairs, which is consistent with mean-field theoretical estimations. The simulated data, however, do not display a neuron-type specific cross-covariance distribution (not shown).



Relative occurrence in percent of clusters (recurring connectivity patterns) and behavioral states (RSS: sleepiness, RS: rest, HML: head movement, M: body movement, AM: arm movement).

References

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