

Estimation of microscale connectivity from spiking activity of macaque visuomotor cortices

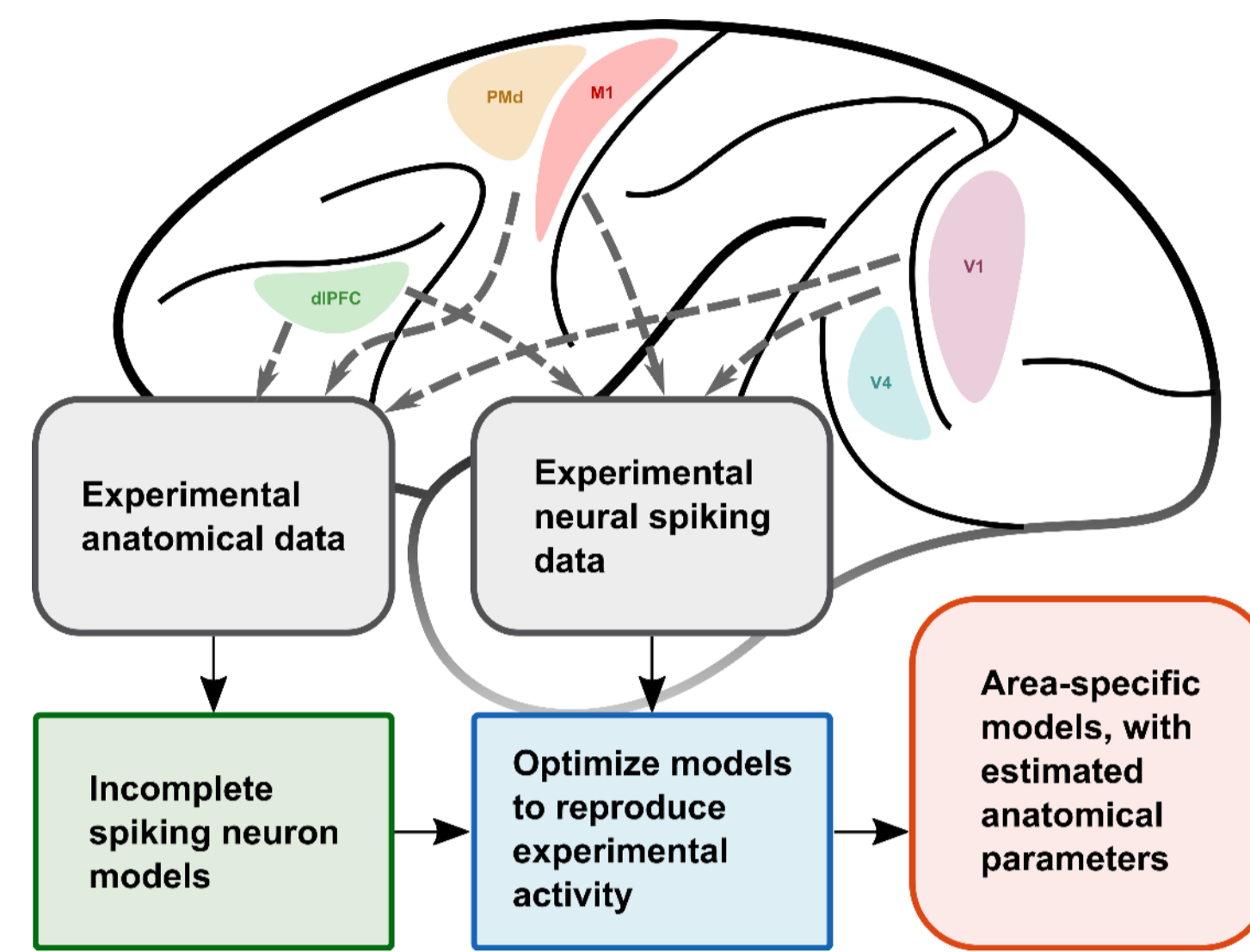
Aitor Morales-Gregorio^{1,2*}, Robin Gutzen^{1,3}, Paulina A. Dąbrowska^{1,3}, Alper Yegenoglu^{4,5}, Sandra Diaz-Pier⁴, Sarah Palmis⁶, Sofia Paneri^{7,8}, Alexandre René^{1,9}, Panagiotis Sapountzis⁷, Markus Diesmann^{1,10,11}, Sonja Grün^{1,3}, Johanna Senk¹, Georgia G. Gregoriou^{7,8}, Bjørge E. Kilavik⁶, Sacha J. van Albada^{1,2}

¹ Institute of Neuroscience and Medicine (INM-6) and Institute for Advanced Simulation (IAS-6) and JARA-Institut Brain Structure-Function Relationships (INM-10), Jülich Research Centre, Jülich, Germany. ² Institute of Zoology, University of Cologne, Cologne, Germany. ³ Theoretical Systems Neurobiology, RWTH Aachen University, Aachen, Germany. ⁴ SDL Neuroscience, Jülich Supercomputing Centre (JSC), Institute for Advanced Simulation, JARA, Jülich Research Centre, Jülich, Germany. ⁵ Institute of Geometry and Applied Mathematics, Department of Mathematics, RWTH Aachen University, Aachen, Germany. ⁶ Institut de Neurosciences de la Timone (INT), CNRS Aix-Marseille Université, Marseille, France. ⁷ Institute of Applied and Computational Mathematics, Foundation for Research and Technology Hellas, Heraklion, Greece. ⁸ Department of Basic Sciences, Medical School, University of Crete, Heraklion, Greece. ⁹ Department of Physics, University of Ottawa, Ottawa, Canada. ¹⁰ Department of Psychiatry, Psychotherapy and Psychosomatics, School of Medicine, RWTH Aachen University, Aachen, Germany. ¹¹ Department of Physics, Faculty 1, RWTH Aachen University, Aachen, Germany.

Contact: a.morales-gregorio@fz-juelich.de Twitter: @AitorMoraGre

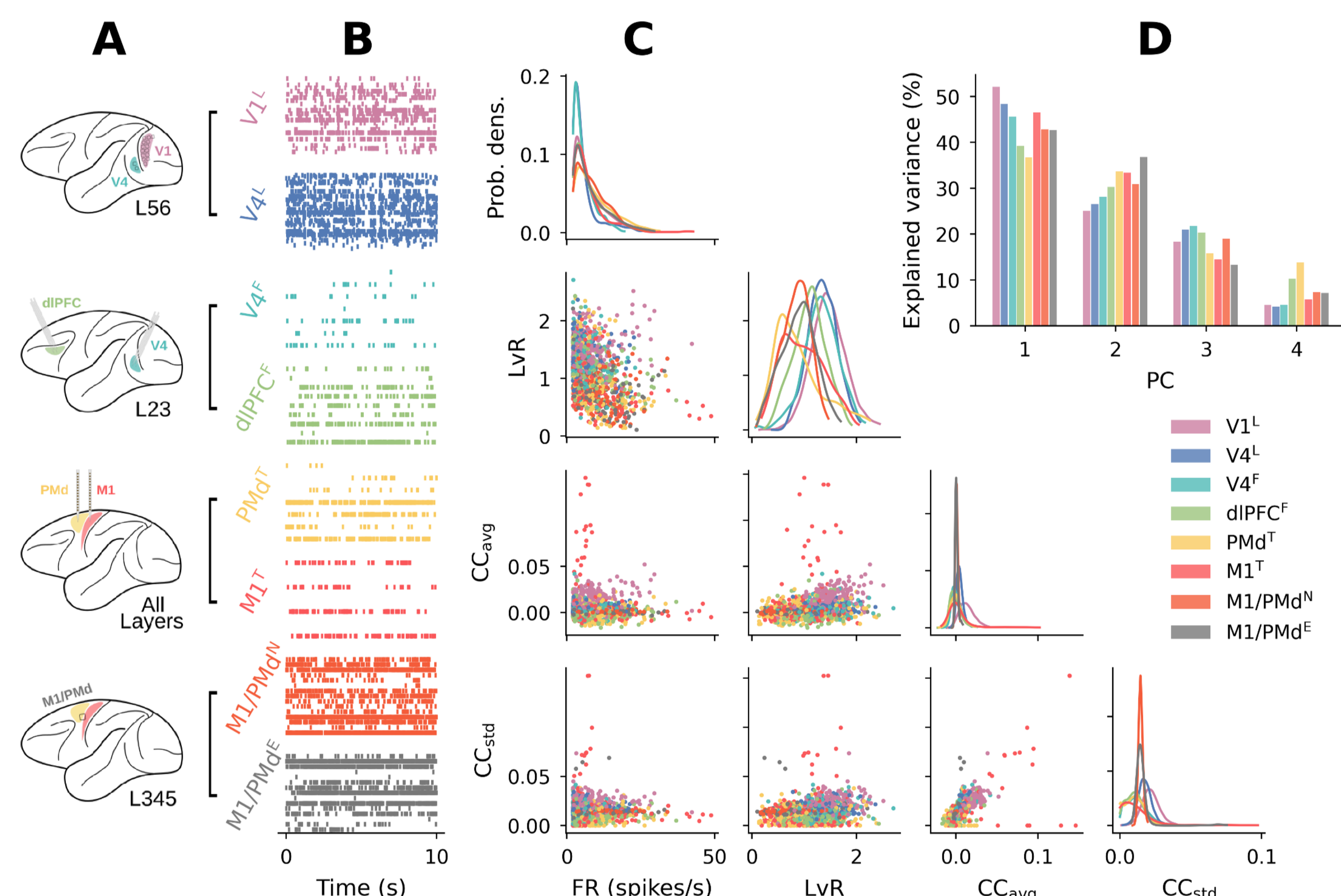
Introduction

Connectivity structure is essential to understanding the activity and function of neuronal networks in the central nervous system. While the long-range connectivity in the macaque cortex has been thoroughly studied [1, 2], relatively little is known about the microscale connectivity within cortical areas and across cortical layers—the microconnectome—outside of the early sensory and primary motor areas. It has been hypothesized that the microconnectome follows a canonical motif across the cortex, but quantitative measurements to date are still insufficient to fully verify this claim. Here, we present a novel method to estimate the microconnectome from neuronal spiking activity across the visuo-parieto-frontal gradient.



Summary statistics of spiking data

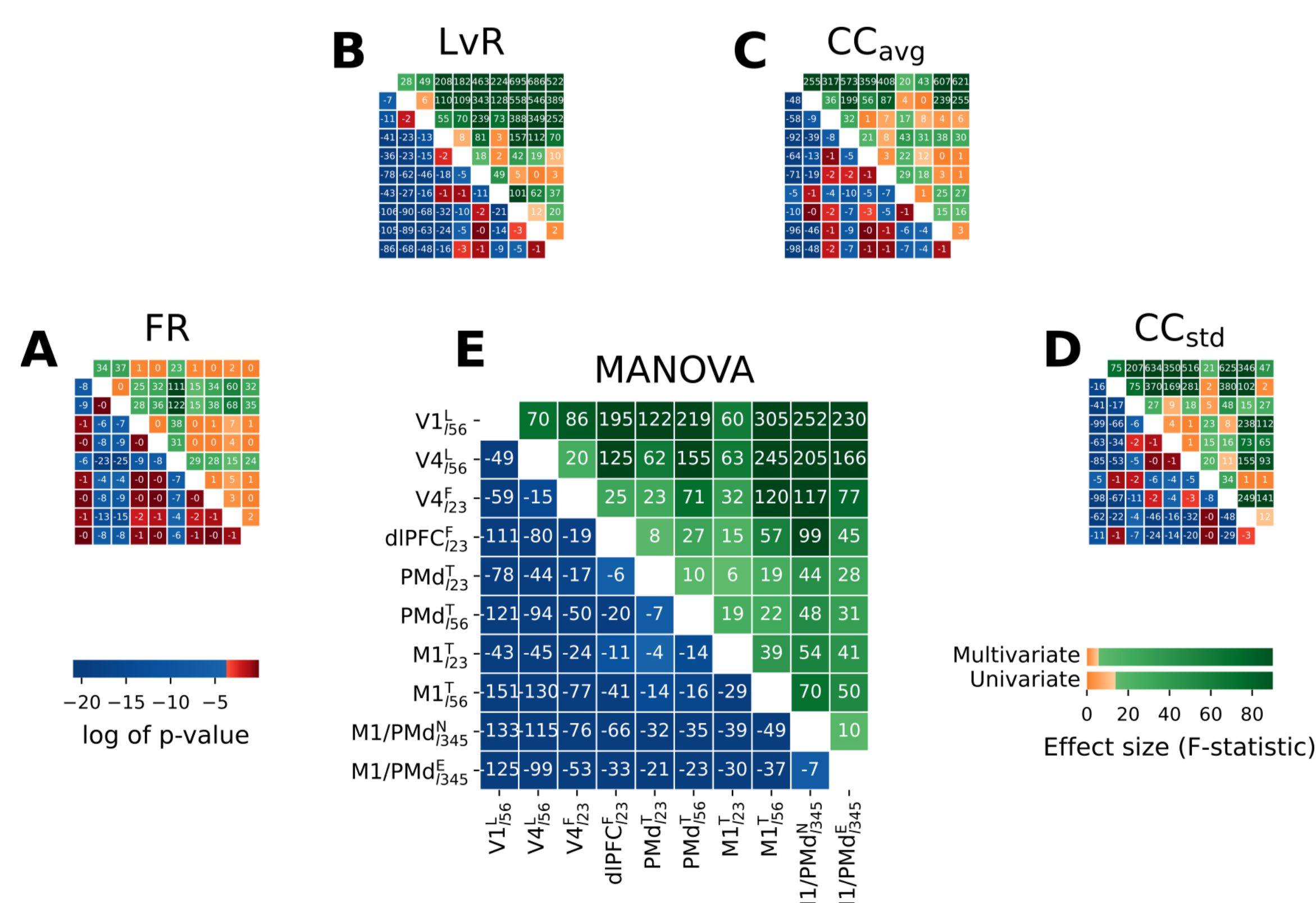
We measured the resting-state activity from several cortical areas (V1, V4, M1, PMd, dIPFC) in macaque monkeys (Macaca mulatta) [3-6]. From the spike-sorted activity, we calculated several single-neuron summary statistics for 10 s data slices, quantifying the firing rates, irregularity, and correlations. The analysis was implemented using the NetworkUnit framework to ensure reproducibility and interoperability [7].



Overview of experimental data and summary statistics. **A)** Schematic representation of the data recording location [3-6]. **B)** Sample recordings of simultaneous spike trains. **C)** Summary statistics of the single-unit spike trains. Each point in the scatter plot corresponds to a 10 s spike train of a single neuron. CC refers to the cross-correlations of the neuron with all other neurons in the recording. **D)** Variance explained by the first four principal components (PC) of the multi-dimensional summary statistics.

Distinct summary statistics in each area

To elucidate whether the resting-state activity is a unique signature of each cortical area, we test the differences of the multi-dimensional summary statistics across areas and layers. Indeed, a multivariate analysis of variance (MANOVA) reveals significant differences between cortical areas within and across experiments.



Pairwise statistical testing. **A-D)** Univariate (ANOVA) and **E)** multivariate (MANOVA) pairwise test results over the summary statistics. We test the null hypothesis that two or more groups have the same population mean. In all panels, lower triangular entries show the logarithm of the p-values and the upper triangular part shows the F-statistic. Significance level ($\alpha = 0.05$) corrected for multiple testing (Bonferroni).

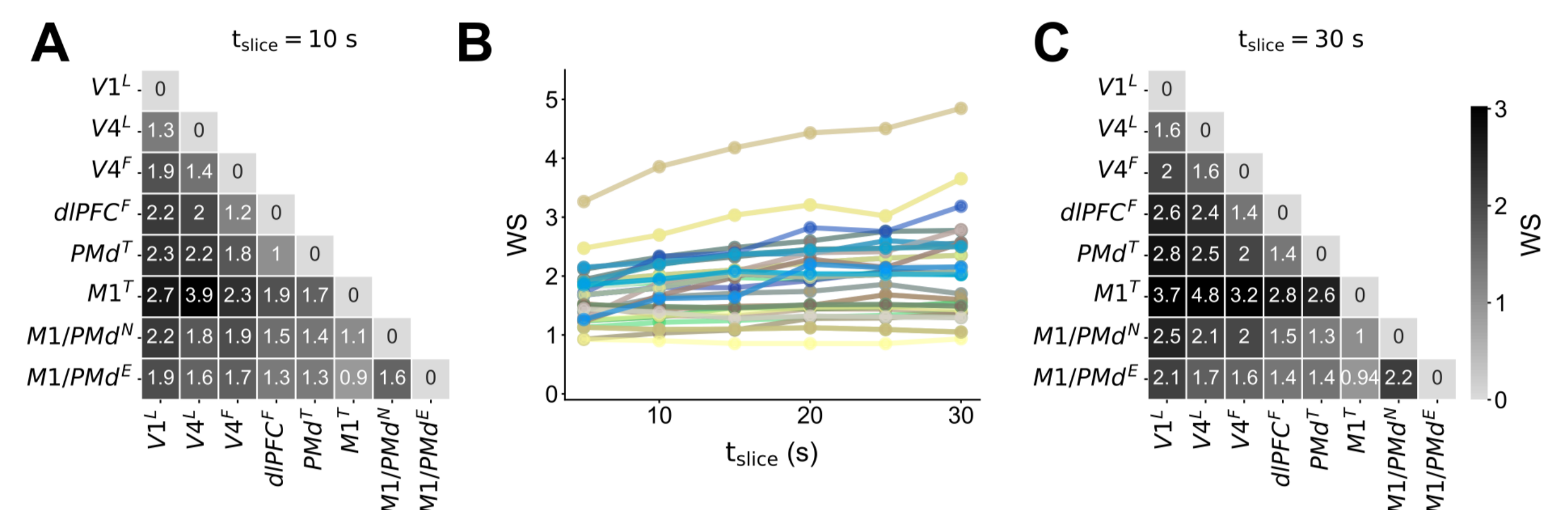
References

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Wasserstein distance: robust similarity metric

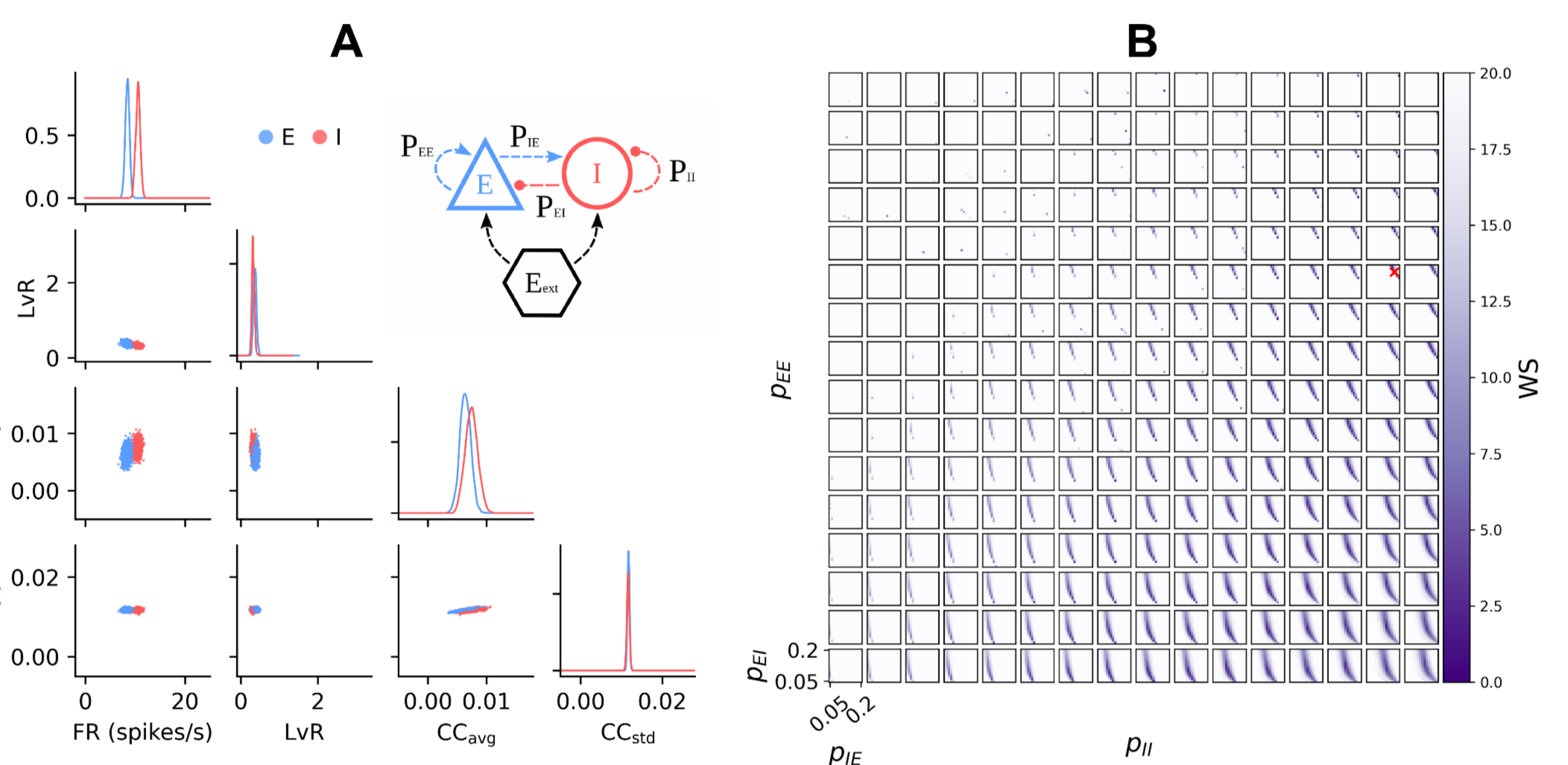
The Wasserstein distance (WS) is ideal for our use case because it can be applied to data sets with different sample sizes, is symmetric and does not require any assumptions of a certain distribution.



A, C) Wasserstein distance (WS) between all experimental data summary statistics for $t_{\text{slice}} = 10$ s and $t_{\text{slice}} = 30$ s, using the same color scale for both panels. **B)** WS as a function of t_{slice} . Each line represents one pair of recordings, colors are arbitrary.

Synthetic data and parameter scan

We generated synthetic data by simulating spike trains with a random balanced spiking neuron network [10]. We calculated the summary statistics of the synthetic data and performed a parameter scan. We calculated the WS distance with respect to our target parameter set and show that our cost function is smooth in parameter space.

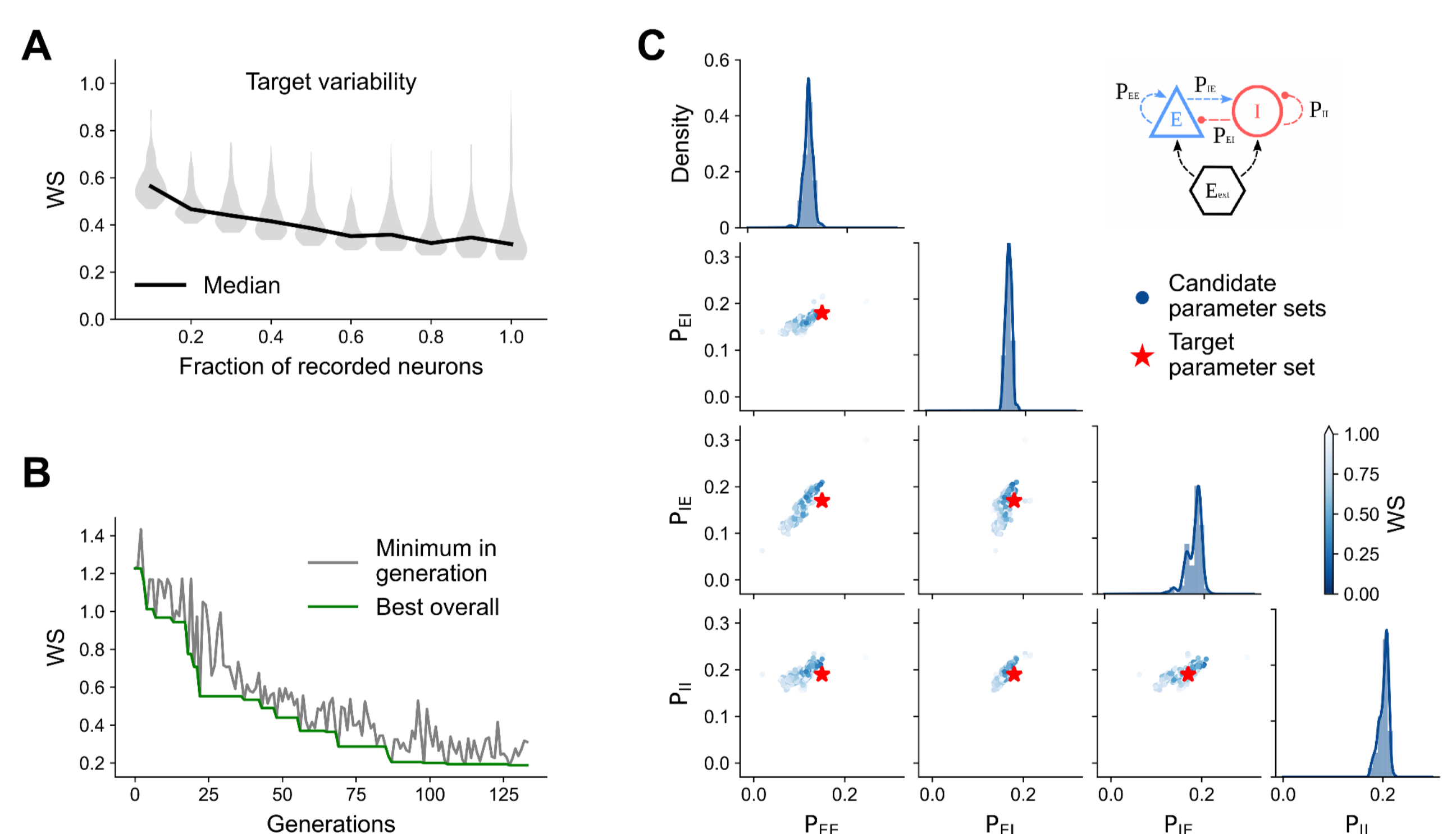


A) Summary statistics of spiking neuron model. **B)** Parameter scan. WS distance with respect to the target simulation.

Estimating connectivity from synthetic data

We used the summary statistics from the synthetic data as a target for our proof of concept. We could recover the connectivity parameters used to generate the synthetic data from the summary statistics alone (quantified via the Wasserstein distance) using the following heuristic:

1. population ← generate random individuals
2. for generation ≤ N do
3. population_fitness ← evaluate(population)
4. survivors ← select(all individuals)
5. mutants ← mutate(survivors)
6. newcomers ← generate random individuals
7. population ← newcomers and mutants
8. end for



Proof of concept of the optimization algorithm using synthetic data from a random balanced spiking neuron network. **A)** Variability of the Wasserstein distance (WS) in the target simulation when recording only a certain fraction of the neurons in the model. **B)** Progress of the optimization algorithm, showing lowest WS overall and within each generation. **C)** Pairplot of estimated parameter sets.

Discussion

The aim of this study was to estimate connectivity parameters of the cortical microcircuit from activity data alone. We presented a novel method for model-to-data comparison, using a multi-dimensional single-neuron statistic cloud. We showed that the multi-dimensional summary statistics vary across the cortex, and are robust to data duration lengths. Additionally, we presented a novel optimization approach that minimizes the distance between some specific target spiking activity and some spiking neural network model. Finally, we provided a proof of concept of our optimization method using synthetic data. Future work will see this approach extended to larger more biologically realistic models, which we will use to estimate local cortical connectivity parameters.