Estimation of the cortical microconnectome from *in vivo* spiking activity in the macaque monkey

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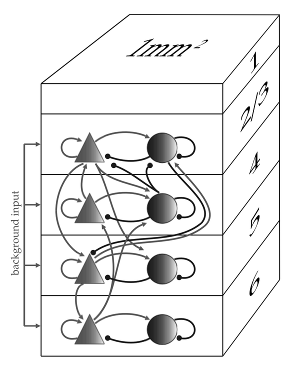
Introduction

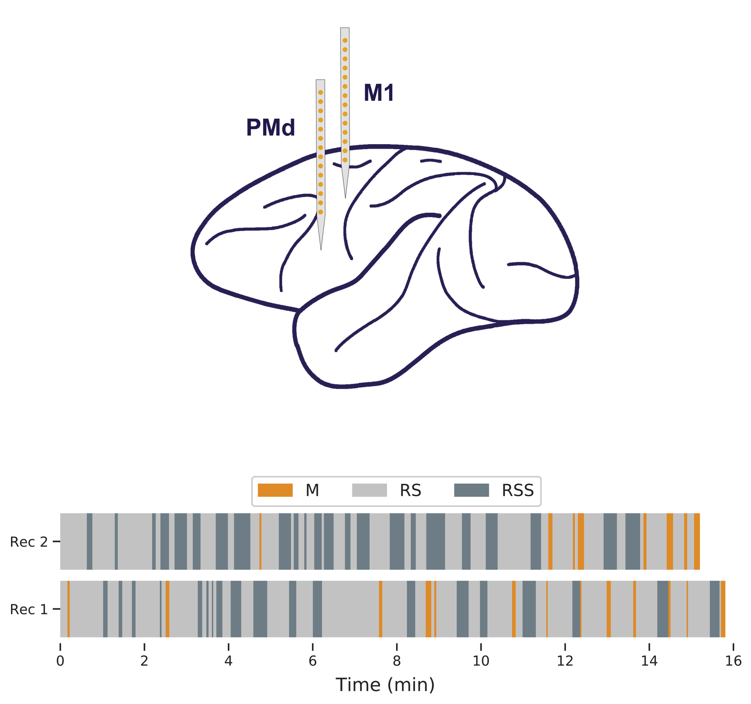
The primate brain is a complex system and many aspects of the relation between its cortical structure and network activity remain to be understood. Bottom-up simulation approaches have been able to partially describe the dynamics of the visual cortex, relying on anatomical parameters [1]. Despite extensive knowledge of cortical architecture, quantitative studies have focused on few areas of interest and the properties of large portions of cortex remain unknown. We aim to overcome the limitations of available structural parameters by constraining a cortical microcircuit model [2] with experimental electrophysiological data.



Microcircuit model [2]

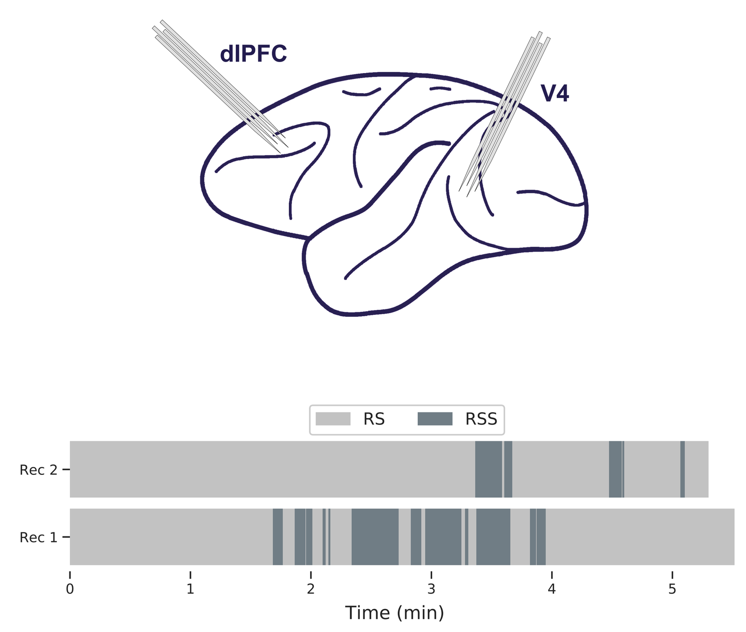
Electrophysiological recordings

M1/PMd recordings



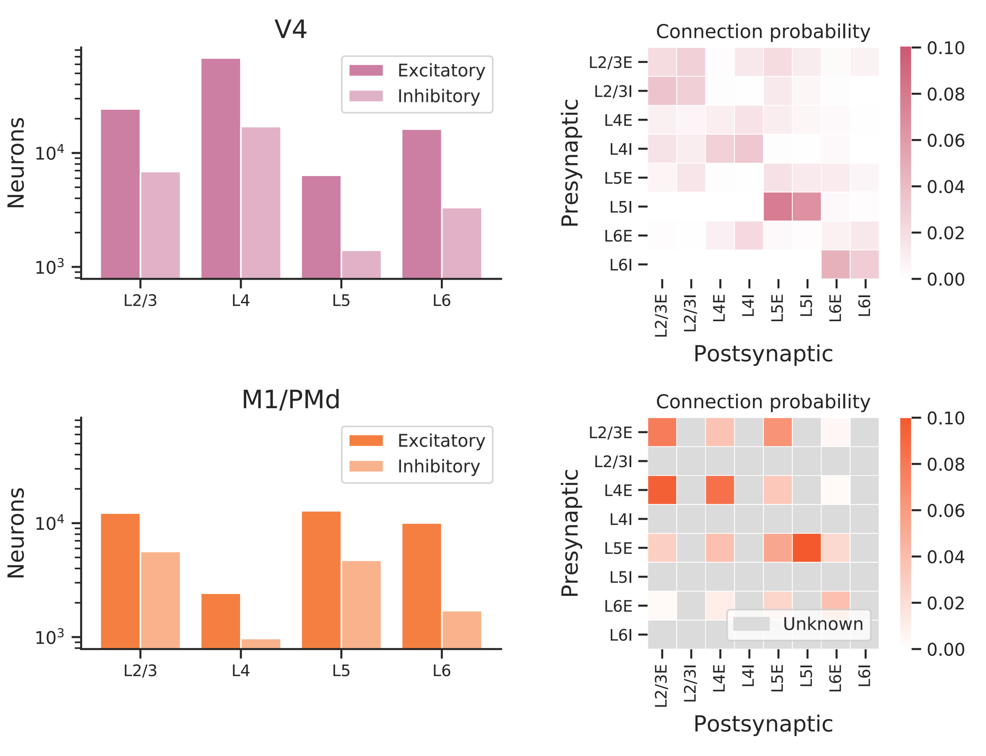
Acute simultaneous recordings of macaque primary motor (M1) and premotor (PMd) cortices (n=1 subject, n=18 sessions) with laminar probes (Plexon and Alpha Omega, 24 contacts, 100 and 200 μm pitch) during dedicated resting state sessions [3]. Video-based behavioral segmentation: RS (eyes open, no movement), RSS (eyes closed), M (movement). Spike sorting identified 5-13 clean single units per probe and session. Two sample behavioral segmentations shown.

V4/dlPFC recordings



Acute simultaneous recordings of macaque visual area V4 and dorsolateral prefrontal (dlPFC) cortices (n=1 subject, n=58 sessions) from superficial layers (L2/3) during resting state with up to 4 Plexon electrodes. Eye pupil size signal based segmentation: RS (eyes open), RSS (eyes closed). Spike sorting identified 4-10 clean single units per area and session. Two sample behavioral segmentations shown.

Anatomical parameters



Number of neurons under $1\ \mathrm{mm}^2$ of cortical surface and connection probability between any two neurons in each layer.

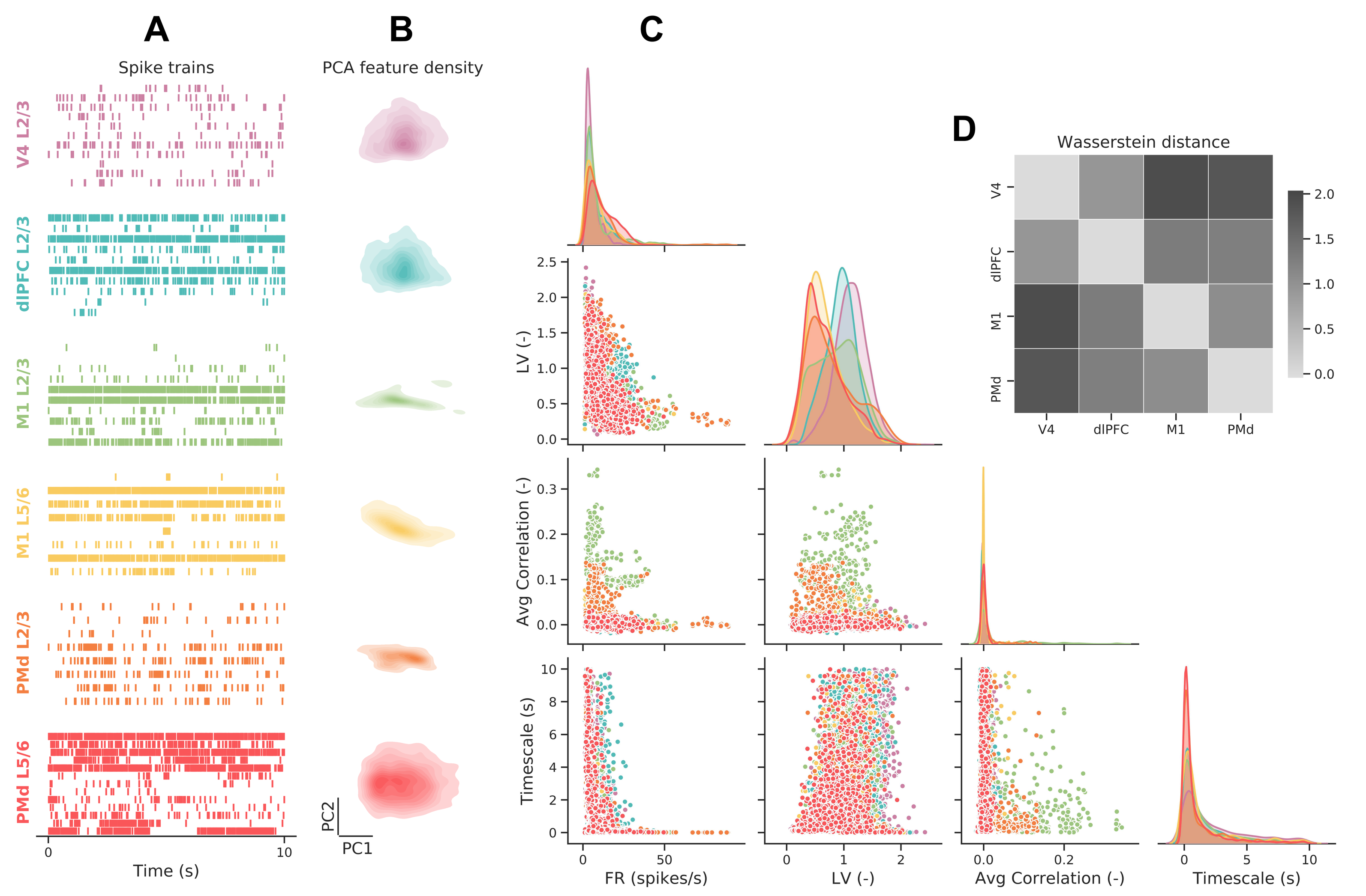
Prior knowledge of the anatomical structure of the cortical areas is incorporated at the initialization of the model for each area. We rely on previously calculated estimates of the V4 parameters [4]. Motor cortex (M1, PMd) neuron counts [5, 6] and connectivities [7] were obtained from the available literature. These anatomical estimates rely on data from mice, rats, cats and macaques; measured in different settings.

Spiking data features

Spike trains were sliced into 10 second long slices and several statistics were calculated for each unit. We use a multi-dimensional cloud of these metrics to represent the activity in one area. The metrics are:

- Average firing rate (FR)
- Local variability of the inter-spike intervals (LV)
- Average cross-correlation with units in the same layer
- Decay constant of the autocorrelation function (Timescale)

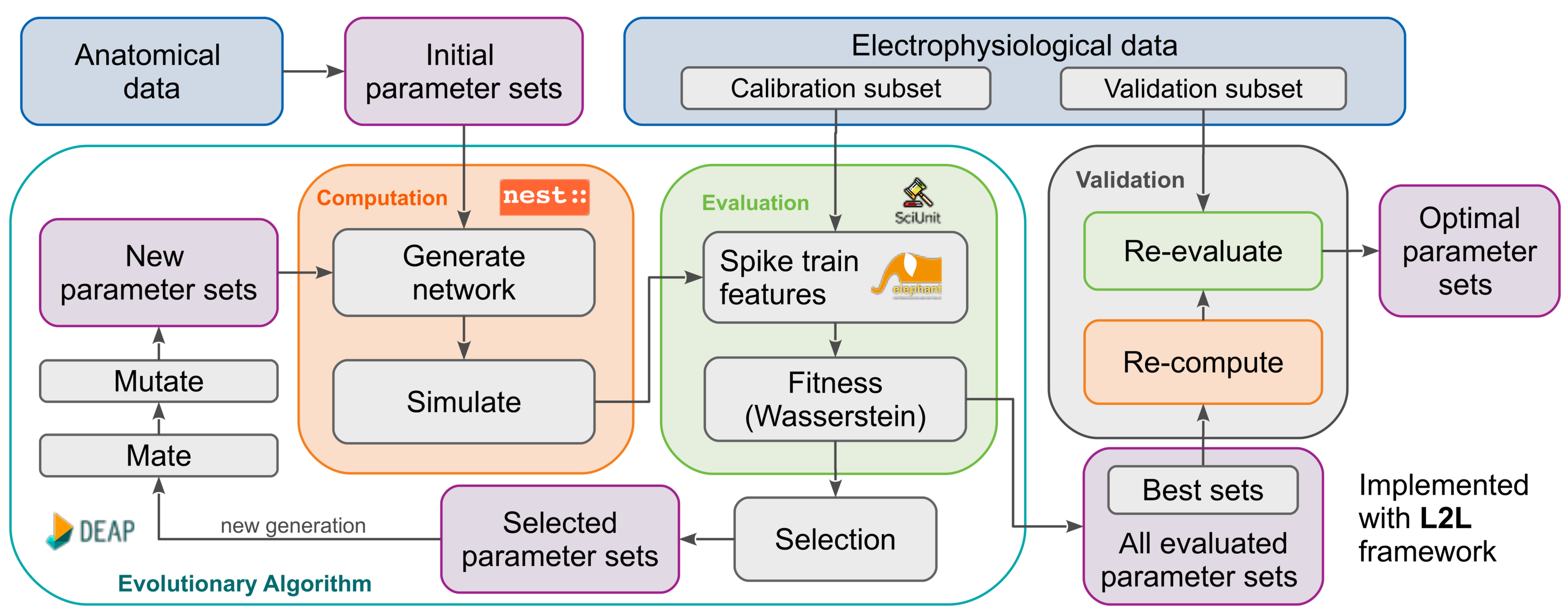
We quantify the differences between these feature clouds with the Wasserstein distance (i.e. Earth mover's distance). All statistical tests are implemented in the NetworkUnit [8] validation library, allowing to flexibly construct a reproducible calibration workflow.



Overview of spiking data features. **A** Spike trains simultaneously recorded in each layer. **B** Distribution of the first two principal components of the features for each area and layer. **C** Pair plot of all features from experimental data and density distribution of each feature. **D** Layer-wise Wasserstein distance between feature clouds of the different cortical areas.

Evolutionary optimization

We have chosen to estimate the connectivity parameters of the cortical microcircuits using a gradient-free Evolutionary Algorithm (EA). We search for a variety of optimal parameter settings, based on findings that disparate parameters can lead to similar dynamics [9]. The cost function (i.e. fitness) is given by the Wasserstein distance between the simulated and experimental data features. We use the learning to learn (L2L) optimization framework [10] on high-performance computers [11] to compute the cortical parameter estimates.



Conceptualization of the optimization algorithm used for the estimation of anatomical parameter sets from electrophysiological recordings.

Outlook

This is an ongoing project. Future work will include: Exploration of further data features (e.g. spectral power); extensive optimization runs to estimate parameter sets; comparison of models with white or colored noise input; assessment of obtained parameters, similarities and differences within and across areas. The area-specific microcircuit models developed in the present project will be incorporated into a multi-area model of all vision- and motor-related areas of macaque cortex [1, 4] to enable studying visuomotor interactions.

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