Pattern recognition of deep and superficial layers of the macaque brain using large-scale local field potentials

Omar Costilla-Reyes (costilla@mit.edu)

André M Bastos (abastos@mit.edu)

Earl K Miller (ekmiller@mit.edu)

Picower Institute for Learning and Memory and Department for Brain and Cognitive Sciences
Massachusetts Institute of Technology
46 Vassar St
Cambridge, MA 02139

Abstract

Robust identification of cortical deep (layers 5 and 6) and superficial (layer 2 and 3) layers of the brain based on neurophysiological recordings is a challenging and unsolved problem in neuroscience. We still lack a complete understanding of the fine-grained neural computations in these layers. In this paper, we introduce a machine learning approach to identify deep and superficial layers patterns. We use multilaminar probes to capture local field potentials (LFP) data in cortical layers of the macaque brain. Here we present experimental modeling results of deep and superficial layers in the prefrontal cortex (PFC) and visual area four (V4) during a delayed match to sample task. Recordings spanned all six cortical layers simultaneously over 10 experimental sessions in these 2 areas. Our experimental results demonstrate that an ensemble machine learning approach applied to the LFP data is able to provide robust levels of identification of the layers with an optimal f-score of 0.8 and 0.84 for areas V4 and PFC respectively in combined data of 10 experimental sessions and across two monkeys.

Keywords: machine learning, cognitive neuroscience, deep and superficial layers, local field potentials

Introduction

The local field potential (LFP), originating largely from neural synaptic activity, has long been known as a summation signal of excitation and inhibitory dendritic potential around a single recording point in the brain (Quiroga & Panzeri, 2009). The LFP is a complex signal that depends on the electrodeposition, the dendritic morphologies of synaptic neurons, and on the spatial distribution and temporal correlations of synaptic inputs. The temporal structure of the LFP can provide sensory and motor-related signals that can be modulated by a cognitive process, providing additional information to single unit activity recording in the brain (Fries et al., 2001). Traditionally, time series analysis methodologies such as spectral analysis are used to characterize and study field potentials recordings (Halliday et al., 1995). Nowadays with the explosion of innovative machine learning inference techniques, the analysis is now shifting to an efficient way to extract meaning from larger sets of neural recordings. Modern tools for inference, are increasingly able to extract meaningful patterns in large volumes of neural data (Pesaran et al., 2018). However, efficient computational methodologies are still needed to properly identify patterns within the LFP neural signal to fully explain its underlying functionality.

Recently, neuroscience has started paying attention to the contribution of deep and superficial layers of the brain. These layers have distinct functional roles (Bastos et al., 2018) and have different anatomical structure and connectivity.

It has been well known for over 100 years that deep and superficial layers differ anatomically. However, a robust method to identify deep and superficial layers from neurophysiological recordings alone in an unbiased and automatic way is currently lacking.

Established methods for laminar classification such as current source density analysis (Schroeder et al., 1998) are based on assumptions which are mostly violated outside sensory cortex and are prone to human error and bias. Thus, a method that can robustly identify layers throughout cortex in-vivo would greatly aid the neuroscientific goal of understanding fine-grained computations that take place in specific layers of the brain.

In this paper, we introduce a machine learning methodology to identify deep and superficial patterns of activities in the brain. Figure 1 shows the areas of the brain studied and the methods for electrophysiology recording.

Methods

Delayed match to sample task

During the task, the monkeys fixated at a point on the screen, then they were cued with a sample stimulus, held the cue over a delay period, and finally reported the identity of the sample with a saccade. Experiments were performed in two rhesus monkeys, one male, and one female.

All procedures followed the guidelines of the Massachusetts Institute of Technology Committee on Animal Care and the National Institutes of Health. Further information on the task design and methodology can be found in (Bastos et al., 2018).

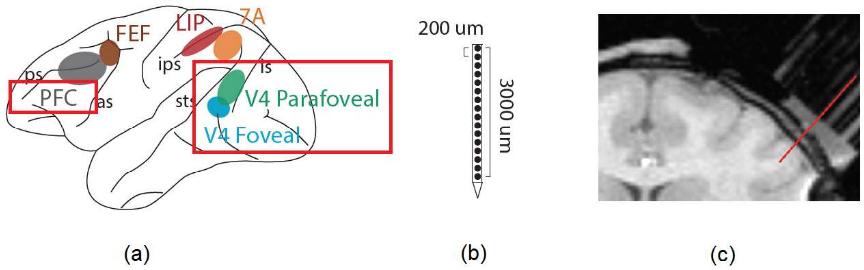

Figure 1: Areas of the macaque brain studied and neurophysiological data recording methodology. a) Areas of the brain (highlighted in red) b) Multi-contact laminar probe used to obtain the neuronal recordings c) Example of the trajectory recordings

Preprocessing of cortical layers

The six-layer LFP recordings were categorized either as deep or superficial for machine learning modeling. The neuronal layers were labeled based on the current source density analysis technique, the most established method for this task (Schroeder et al., 1998).

Dataset

Ten separate session recordings were used for modeling the two areas (V4 and PFC). In area V4 there were 58,099 trials for deep layers and 57,672 for superficial layers yielding a total of 115,771 trials in that area. For area PFC there were 55,146 trials for deep layers while 56,780 were obtained for superficial layers yielding a total of 111,926 trials.

Samples, features and experimental time window

For the analysis, the trials from the electrodes were the samples for the machine learning modeling, while the LFP temporal signals were the features in all the analysis of this paper. The experimental time was divided into non-overlapping 200 ms time windows that encompass the duration of the experiment, a unique machine learning model (with tuned hyperparameters) was trained for each of the windows. The windows allowed to analyze the task as a function of experimental progression. The modeling was conducted in the scikit-learn library (python) and its computing libraries such as Scipy, Numpy, and Pandas (Pedregosa et al., 2011).

Electrode group

The electrodes trials were separated in groups to accommodate them in a cross-validation strategy, this allows trials of a specific electrode to go only to one of the folds. This approach was used for a robust generalization strategy to prevent trials a single electrode to leak in both the training and testing set.

Cross-validation and evaluation

We performed model validation with a 3-fold cross-validation (Hastie et al., 2009) technique for robust model generalization. The cross-validation strategy was adopted for all the experiments presented in this paper. The F-score, a harmonic average of the precision and recall score was used to report classification performance score estimates of all the experimental time windows. The standard deviation of the folds was calculated to obtain performance confidence intervals, indicated as error bars.

Results

Model search and selection

In a model search procedure, several machine learning algorithms were tested in their ability to classify deep or superficial layers of the brain. One monkey and the initial 200 ms window was used for both the model search and hyperparameter search procedures, this in order to do the model and hyperparameter search in a small subset of the dataset and then aim to generalize the model and parameter search to several sessions and 2 monkeys with the obtained parameters, which was successfully in the case presented here.

The following algorithms were tested in the model search procedure: nearest neighbors, linear support vector machine (SVM), SVM with an RBF kernel, Gaussian process classifier, decision tree, random forest, neural network, AdaBoost, naive Bayes, quadratic classifier, Xgboost, extremely randomized trees (extra-trees) classifier and Logistic Regression (Hastie et al., 2009; Pedregosa et al., 2011). The performance results are shown in Figure 2.

The highest performance was delivered by the nearest neighbor algorithm (0.68 f-score) followed by a neural network and an extra-tree (0.67 f-score). The lowest ranking algorithm was obtained with an SVM model with RBF kernel (0.38 f-score).

Extremely randomized trees

The extra-trees model delivered a very close performance with the nearest neighbor algorithm to classify deep and superficial layers in the brain as shown in Figure 2. The main advantage of the extra-trees approach was that it offered the fastest times for training and testing compared to the other algorithms, therefore the extra-trees algorithm was selected as the main algorithm. The extra-tree algorithm is an ensemble method (Hastie et al., 2009) able to combine the predictions of several base estimators in order to improve generalization and robustness. On average, the combined estimator is usually better than any of the single base estimator because its variance is reduced. The extra-trees is also a computational

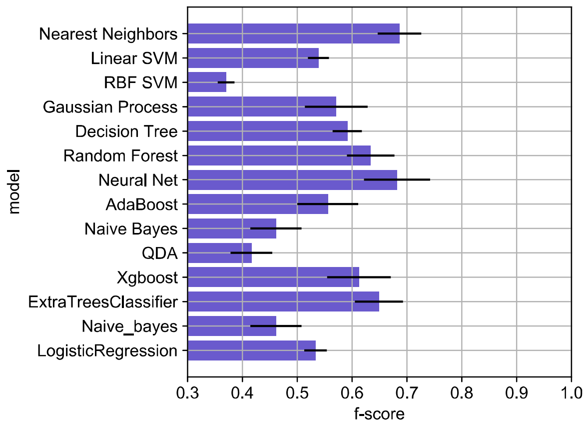

Figure 2: Machine learning model performance comparison

Features	R1	R2	R3	R4	R5
Number of trees	606	686	287	269	58
Min. samples split node	11	15	11	6	18
Min. samples leaf node	3	3	5	6	2
maximum features	0.3	1	0.2	1	0.35
mean val. f-score	.681	.681	.677	.676	.676
STD (%)	.072	.074	.076	.071	.071

Table 1: Top-5 Hyper-parameter optimization models

efficient ensemble algorithm: it splits a decision tree node during feature learning (Geurts et al., 2006), this allows decreasing variance at the expense of slightly increasing the bias.

Hyper-parameter optimization

A randomized search of hyper-parameters with a 3-fold cross-validation strategy was implemented to fine-tune the extra-tree model (Pedregosa et al., 2011). Hyper-parameters were sampled from the following feature distributions: number of trees (1-700), minimum samples to split a node (2-30), minimum samples to leaf a node (1-30) maximum-features (0-1, with a 0.05 step). We randomly sampled hyper-parameters in 100 runs for the randomized search. The top 5 hyper-parameters set for the extra-tree simulation area shown in Table 1.

From the top 5 results, the rank #5 result was selected since it offered the least number of trees that maximizes the f-score performance. The approach is advantageous since the smallest number of trees to train is equal to the least computational time spent in training the models.

Unique session deep and superficial layers identification of PFC and V4

Once the model and the hyper-parameters were defined, then unique sessions were modeled in both monkeys and both areas PFC and V4. Figure 3 shows the average performance of unique sessions (f-score and STD of the fold) in both monkeys.

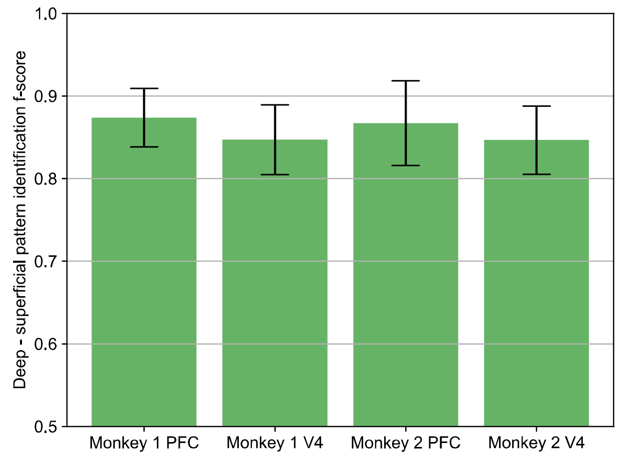

Figure 3: Unique session performance

Multisession deep and superficial layers identification of PFC and V4

To improve generalization, all the sessions from both monkeys were combined in models for V4 and PFC areas. The modeling results of areas PFC and V4 are shown in Figure 4. For both areas, the models delivered a steady f-score in the deep-superficial layers of 0.8 and 0.84 (approximately) respectively throughout the execution of the task.

The results demonstrate that there is a steady f-score level identification of the deep and superficial layers across the tasks. F-scores below the horizontal grey dotted line were the same as random chance. In this case, due to generalization error, the f-score dropped by approximately 5% compared to unique session experiments.

Laminar Similarity Maximization algorithm

This method seeks to identify deep and superficial layers of the brain by obtaining the best possible match between laminar probes with an alignment algorithm. The reader should be referred to (Bastos et al., 2019) for further explanation of the methodology.

Conclusions and future directions

We have presented for the first time in the literature a methodology to classify deep and superficial layers of the brain from a data-driven approach with a machine learning methodology. We have presented experimental results in both unique session and multi-session modeling from LFP data in the prefrontal cortex and visual area 4. Our results delivered a robust f-score above 0.8 throughout the execution of the delayed match to sample task in a challenging multisession scenario in two monkeys to identify the deep and superficial layers of the brain.

As a future direction, we aim to test whether a unique model can generalize to PFC and other higher-order and sensory areas. Ideally, this generalization would be robust that given

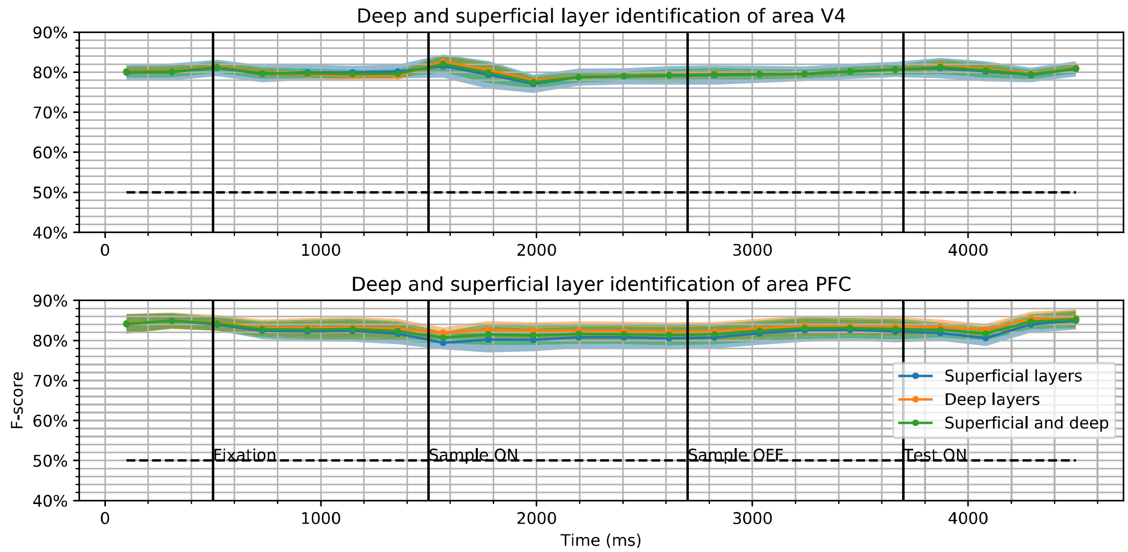

Figure 4: Multisession deep and superficial layers identification of PFC and V4

LFP data recorded in any brain area, the model would be able to accurately resolve the layer of origin of that electrode. This would enable laminar identification for areas in which perpendicular electrode recordings are not possible such as in cortical sulci.

We also intend to include in the modeling specific features from the LFP data such as frequency or power to be able to relate frequency (alpha, beta, and gamma) to cortical layers of the brain.

If these spectral features are indeed different among different layers it would suggest that unique computations take place in deep and superficial layers, and perhaps in the separation of time scales of processing. To summarize, the methodology presented here for laminar identification is the first step in discovering the functional properties of the different cortical layers, a long-standing and unresolved mystery in neuroscience.

Acknowledgments

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