Identifying Subpopulations of Neurons in Six Visual Areas in the Mouse

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Introduction

- This work is part of an ongoing effort to develop methods for analyzing spike train data across multiple brain areas of interest.
- Here we analyze 6 different visual areas in a mouse recorded at the Allen Institute using Neuropixels multielectrode probes.
- We aim to describe population patterns of activity subsequent to display of oriented drifting gratings, as well as sub-populations that show differing response patterns.

Data and Experiment

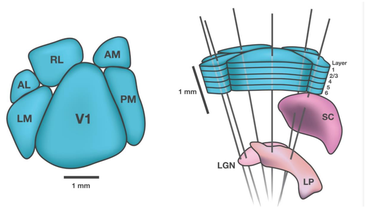

Figure 1: Placement of NeuroPixel Probes in six brain regions associated with visual processing. Source: allentinstitute.org

- The six visual areas recorded were the Primary Visual Cortex (V1), the Lateromedial Area (LM), the Anterolateral Area (AL), the Rostrolateral Area (RL), the Posteromedial Area (PM), and the Anteromedial Area (AM). The six probes were placed as shown in Fig. 1.
- The mouse observed was shown drifting gratings with varying configurations. This included eight orientations [0°, 45°, 90°, 135°, 180°, 225°, 270°, 315°] and five frequencies [1 Hz, 2 Hz, 4 Hz, 8 Hz, 15 Hz]. Each configuration was presented for 2 seconds and repeated over 15 trials. We chose to concentrate our analysis on 300 ms post stimulus.

Curve-Fitting Methods

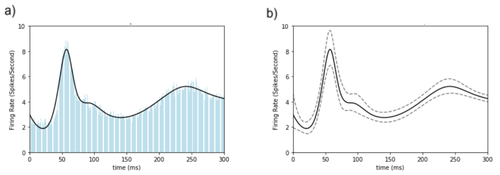

Figure 2: Panel A shows a fitted firing-rate function as it evolved over time. Panel B shows the 95% confidence pointwise bootstrap bands (dotted lines) calculated using statsmodels. The dotted lines represent the pointwise bootstrap bands on the GLM fit.

- For each brain area studied, we normalized the pooled the spike counts over all configurations using 1 ms time bins to create a PSTH.
- The averaged firing rates were smoothed using natural cubic splines. We fit a Generalized Linear Model with Poisson regression from the statsmodels module in Python. The Poisson regression formula for times i=1, …, τ is

$$Y_i \sim P(\lambda_i)$$
$$\log \lambda_i = x_i\beta.$$

where τ is the maximal time point. We visually chose knots that produced a nice-looking fit to our PSTH.

Comparison Across Visual Areas

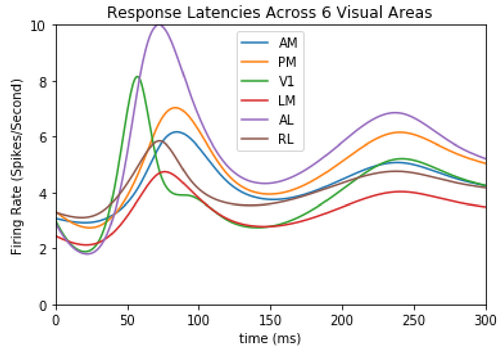

Figure 3: A comparison of the GLM fits to all 6 visual areas. The knots that were visually fit based on data from area V1 are [30, 58, 73, 93, 120, 240, 275, 300].

- Initial response latency relationships conform to qualitative expectations, with the first peak in activity in V1 leading LM and AL.
- Latencies across areas at the second peak in activity, if they exist, appear more subtle.
- Observed a large contrast in overall activity level, with the Anterolateral Area (AM) exhibiting the highest firing rate, on average.

Comparison Across Configurations

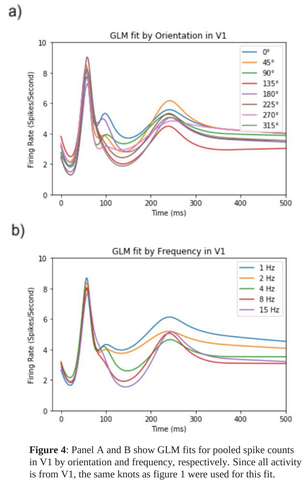

Figure 4: Panel A and B show GLM fits for pooled spike counts in V1 by orientation and frequency, respectively. Since all activity is from V1, the same knots as figure 1 were used for this fit.

- There were no obvious differences in firing rate latencies with differing orientations in drifting gratings.
- Due to the effects of orientation tuning, there are no apparent differences in response patterns between orientations that are separated by 180°.
- We observe a sequential increase in frequency as we decrease the predicted firing rate around 150 ms.
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- At around 150 ms, we observe, for all areas, a decrease in firing rate with increasing frequency.

Identifying Subpopulations of Neurons

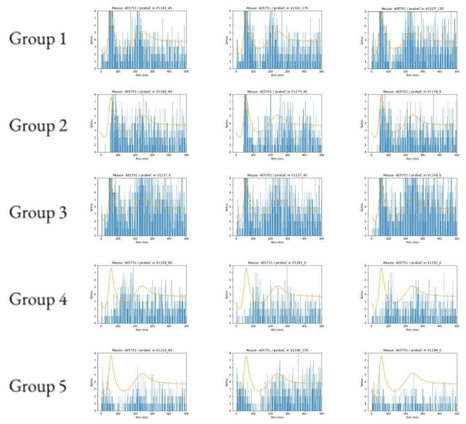

Figure 5: Three sample neuron recordings are shown for the five identified subgroups.

- Five subpopulations of neurons, shown if Fig. 5, were identified in area V1. The defining characterisitics of these subpopulations were used to categorize the remaining five visual areas. Key features forr each group over all areas are summarized in the table below.
- Activity from drifitng gratings with orientations separated by 180° and all frequencies were pooled to reduce noise.
- The time stamps for the first and second peak in area V1 were used as a reference for the remaining five visual areas.
- Neurons that did not meet a threshold firing rate of 3 spikes / ms were filtered out for sparse activity.

	Characteristics	Group Average Firing Rate (+/- SE, spikes per second)	1st peak time (ms)	2nd peak time (ms)
Group 1	Strong, short first and second peak	2.50 (+/- .70)	61	229
Group 2	Delayed initial activity	1.51 (+/- .35)	85	248
Group 3	Strong first peak and high activity	4.32 (+/- .69)	59	246
Group 4	Temporal shift in first peak	1.33 (+/- .30)	95	261
Group 5	Initial burst preceding first peak	1.62 (+/- .18)	20	255

Automation of Categorization

- PhD student Motolani Olarinre has successfully created an algorithm to determine if a single neuron is contributing to a subpopulation's initial change point.
- Comparison of the algorithm results to prior visual coding found that all of the neurons labeled as contributing by the algorithm were accurate. However, we found that it misses some neurons that were visually identified.
- This method can be expanded to other features to automate and improve the categorization of neurons.

Discussion

- The order first peaks across the six visual areas is consistent with the expected order of events suggested by Glickfeld et al. (2017).

$$V1 < \begin{pmatrix} AL \\ LM \end{pmatrix} < PM$$

- The subpopulations identified in area V1 were found in the remaining five areas. Categories such as these could be used to identify key features of neural firing rates to develop a general firing-rate function.

Future Plans

- Analyze data using the updated dataset containing the responses of 58 mice provided by the Allen Institute.
- Apply the methods of Behsta et al. (2007) in order to test the null hypothesis that the firing-rate curves that were fit to neurons under different configurations are equal.
- Create a general firing-rate function for mouse visual neurons, with drifting gratings as stimuli. We aim to be able to identify a set of factors that can be applied to most neurons.

References

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3. Kass, R., Brown, E., & Eden, U. (2014). *Analysis of neural data* . New York, NY ;: Springer.
4. Kass, R. E., Amari, S.-I., Arai, K., Brown, E. N., Diekman, C. O., Diesmann, M., … Kramer, M. A. (2018, March). Computational Neuroscience: Mathematical and Statistical Perspectives. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/30976604