30563 - Neuroscience Report Group 3

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Research Question

The research question we decided to explore is:
"How does neuronal spike activity vary among different brain regions in response to specific stimuli in mice, and can these variations be accurately classified to map functional brain regions?"

Introduction

The neuronal encoding of visual information in the brain is a fundamental aspect of how organisms interact with their environment and understanding it is a central objective of neuroscience.
Numerous studies attempted to map brain activities to specific cognitive functions. However, the precise mechanisms by which the brain interprets this complex stimuli remains to be further explored.
This project leverages machine learning techniques to analyze the dynamic firing patterns of neurons across various regions in mice's brains.
After exploring the complexity of neural activity, we hope to classify these neuronal responses in order to gain a deeper understanding of brain functionality.

Methods

Data Acquisition

We employed electrophysiological data from the Allen Brain Observatory, initially focusing on a dataset from one session, containing approximately 900 neurons. Recognizing the potential for a more robust analysis, we expanded the dataset by merging it with data from two additional sessions, increasing significantly our total sample size (approximately 2000 neurons).
The criteria we used to choose the sessions were the following: male mice with approximately the same age, high number of neurons overall and uniform distribution of neurons across brain areas.
After choosing the sessions we wanted to use, we proceeded with some Exploratory Data Analyses.

Data Preprocessing

The dataset had already been already cleaned and normalized, therefore we didn't encounter many issues of data quality.
However, we faced some challenges such as class imbalance (unequal representation of brain regions) and training bias due to the heterogeneous nature of the data across sessions. To address these issues, we removed underrepresented classes and employed stratified sampling to our dataframes to ensure a balanced data distribution for training and testing the model.

Model Selection and Training

We first built a dataset to perform our regression, choosing a time frame of 10000 bins to include all the spikes of the neurons during the experiment. We then decided to filter our dataset to consider only the stimuli coming from *natural scenes*, since they were numerous and the ones that we though could be more interesting for our analyses. We also tried considering other kinds of stimuli, like *static gratings*, obtaining overall the same results.
We briefly tried some models (Linear Regression, SVM, Random Forest, etc.) to perform our classification and we chose Logistic Regression as it was the most effective on our data. This model was trained both on the one-session dataset and on the expanded one using Grid Search for optimization.
To assess the model's robustness to variations in data initialization or shuffling, we employed validation techniques such as cross-validation and bootstrapping.
Additionally, we compared the Logistic Regression model's performance against a dummy classifier as a baseline reference. This comparison helped assess if the model learned meaningful patterns beyond random chance and checks for robustness.
Moreover, we tried removing the time bins that had no firing activity both to decrease sparsity and to see if our model improved.
Finally, we did some variance analysis and, motivated by the results, we removed neurons in *CA1* brain area to see how this would affect the performance of the model.

Results

The Logistic Regression model, initially trained on data from a single session, achieved a balanced accuracy of 37.1% on the test set and a mean cross-validation score of 44.6%. However, an accuracy around 99.6% on the training set suggested that the model was prone to overfitting.
This led us to the choice of integrating more sessions in order to have a model with more neurons that could generalize better on unseen data. However, some brain areas were represented by a very small number of neurons, therefore, to avoid any negative effect on our classification and ensure equal representation of brain areas, we decided to consider only those represented by at least {number of sessions}$\times$10 neurons. The model fitted to this dataset achieved a test accuracy of 46.4%, training accuracy of 98.7% and cross validation score of 43.8%: better than the previous one, but still suggested potential overfitting.
Plotting the mean cross-validation score and standard error against the number of neurons used for the classification, confirmed the improvement of our model with more sessions. Specifically, greater accuracy and reduced standard error were observed with increased neuron count.
Then, comparing our model with a random classifier, which performed with a mean accuracy of approximately 7%, we confirmed the robustness

of our model (with higher accuracy). We also used bootstrap and obtained consistent results.
When we analysed the variance across different brain areas, no significant pattern emerged, suggesting that it primarily contributed to noise rather than giving meaningful information in the model.
Additionally, the classification report shows variations in precision, recall, and f1-scores across different classes, indicating that the model's ability to recognize and classify neuronal spikes is uneven among the brain regions.
To reduce overfitting and sparsity, we removed all the columns with no spike activity at all (all zeroes). Our accuracy didn't increase much, but now our model was less computationally expensive. For this reason, we decided to keep it moving forward. After building a confusion matrix to better visualize our results, we realized that most of the misclassified areas ended up being labeled as *CA1*. This is an area related to autobiographical memory and not directly to visualization tasks. Therefore, we thought it might be a source of noise and, by removing it, we actually got better results.
We achieved an accuracy on the test set of 52.3% and 99.2% on the training set. This is our best and final model.

Discussion and Conclusion

The final model we built demonstrated promise in classifying neuronal spikes based on brain regions, identifying some patterns and offering a substantial improvement over random models.

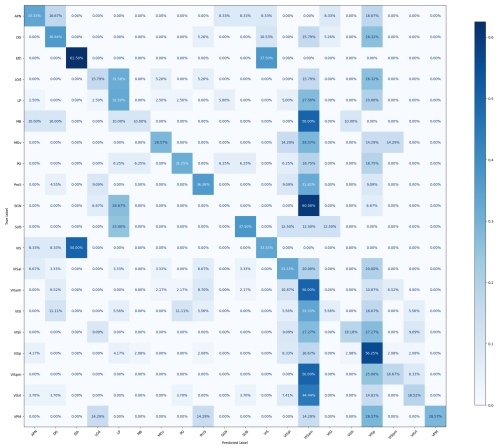


Figure 1: Confusion matrix of best classifier

We tried to understand why our classifier might be performing differently in different brain areas, and we noticed some relevant insights.
Firstly, we saw that our model performs better on areas primarily related to visualization tasks (such as VIS, VISal, VISam, VISp), or related to emotions and visual reflexes (Eth, ProS).
Then, we noticed that some areas related to memory are well classified, whereas others are not. For example, an area well classified is DG, which is crucial for memory encoding and retrieval and could be effectively activated by visual tasks involving new or remembered stimuli. On the other hand, MB is not classified well, and this might be because its role may not be directly engaged by simple visual tasks unless they specifically involve memory recall, leading to less distinct activity patterns. This shows that even if these brain areas have the same general function (memory in this case), they might react differently to a specific experiment or subject.
On the other hand, our classifier struggles with areas in general less directly related to visual or cognitive functions, such as those involved in integrating sensory and neural signaling beyond simple visual tasks (SUB, LP).
In conclusion, the final model demonstrated substantial improvement in classifying neuronal spikes across various brain regions with respect to random models, performing well in areas directly stimulated by the visual tasks and less effectively in regions involved in more complex cognitive functions.

Limitations and Developments

Despite the promising results achieved, our model remains prone to overfitting, as highlighted by its better performance on the training set compared to the test set.
While various strategies that we applied to overcome this problem have improved test accuracy, a discrepancy still persists. Future efforts should focus on identifying the underlying causes of this overfitting and trying to solve it with additional data and refined tuning techniques.
Later works could include developing more complex models to capture more effectively the characteristics of the data (such as XGBoost or Convolutional Neural Networks) or on considering other neuronal statistics for the classification task. In fact, the features used in the model may not effectively capture all the characteristics important for classifying activity in all regions. An example could be to classify brain functions by analyzing the presence of different neurotransmitters in different regions.
Finally, it might be also relevant to focus on other types of stimuli, considering the good results obtained in *static gratings*.

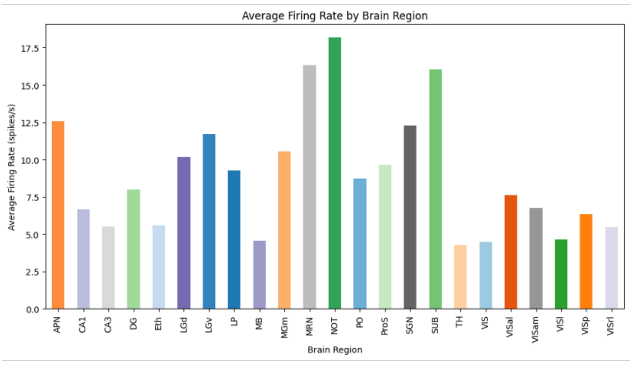
Applications

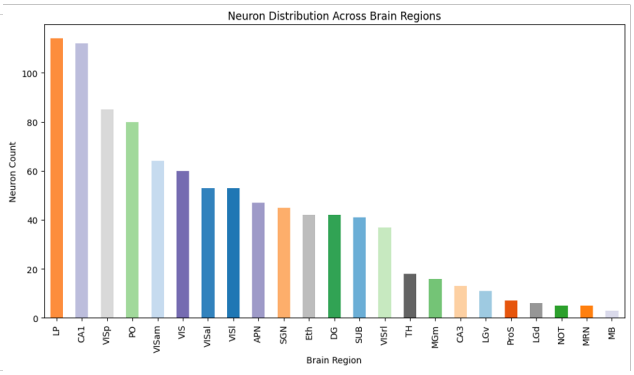
This research contributes to our understanding of brain functionality, offering valuable insights applicable to both neuroscience and clinical settings. The development and refinement of these models are crucial for deepening our understanding of how neural activity relates to brain functions and disorders.
Examining variations in spike activity contributes in generating more comprehensive and precise mappings of brain function.
Furthermore, investigating these variations in healthy brains could reveal distinctive features when compared with those affected by neurological disorders such as epilepsy, Parkinson's disease, or Alzheimer's disease.
Identifying specific activity patterns within particular brain regions may enable researchers to better comprehend the anomalies that lead to these conditions. This could pave the way for the development of new diagnostic tools and the formulation of targeted therapeutic strategies.

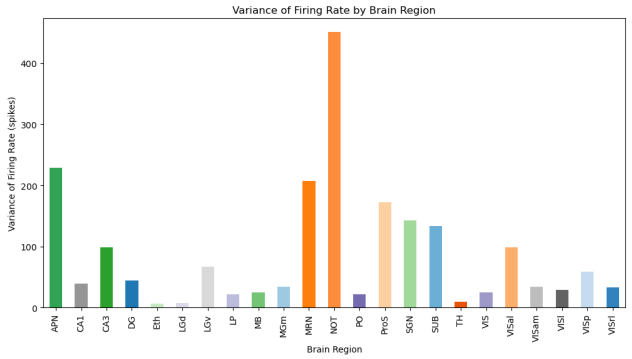
Appendix

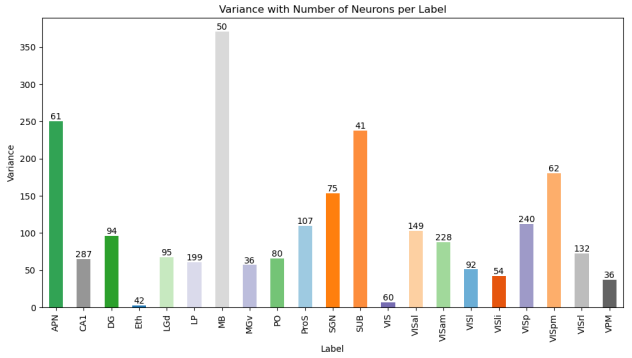
We add some images showing our results from the Exploratory Data Analyses and some confusion matrices from the classifications we performed.

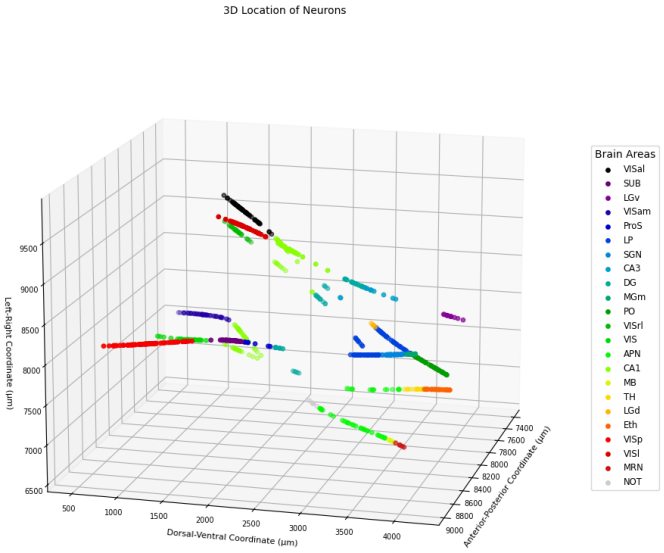
EDA

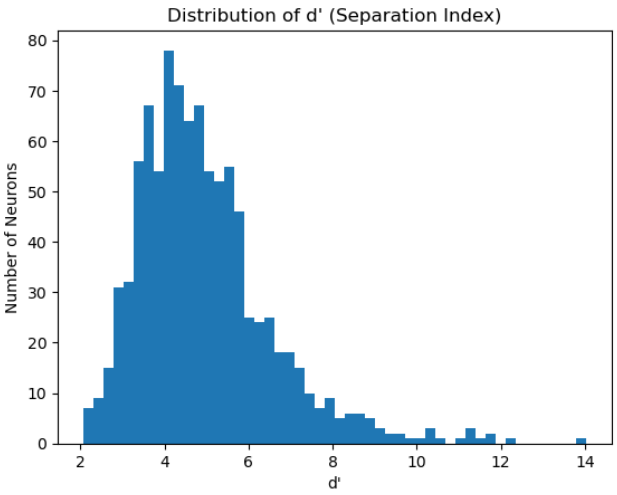


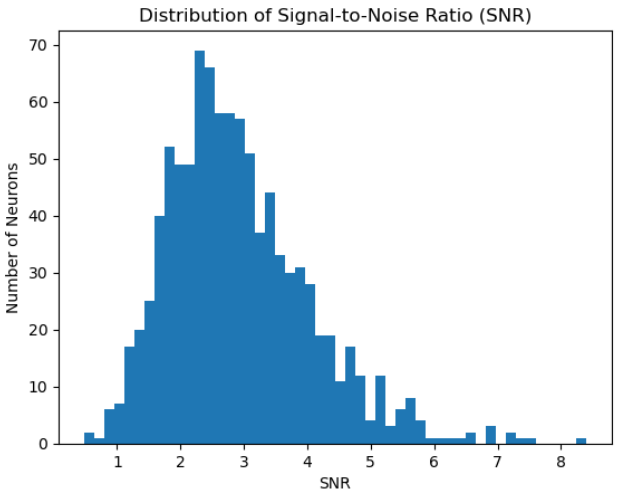


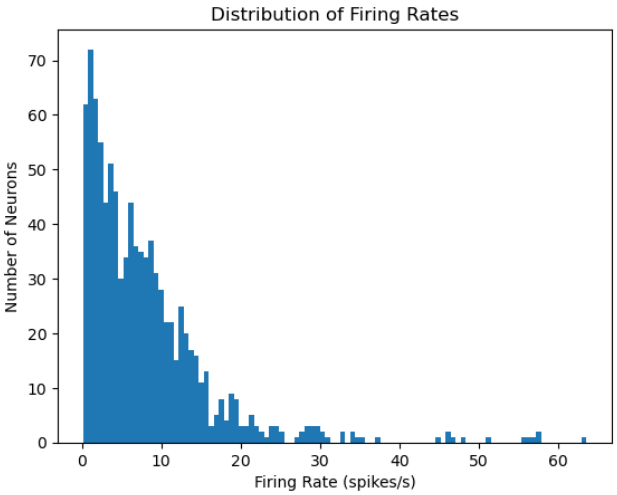


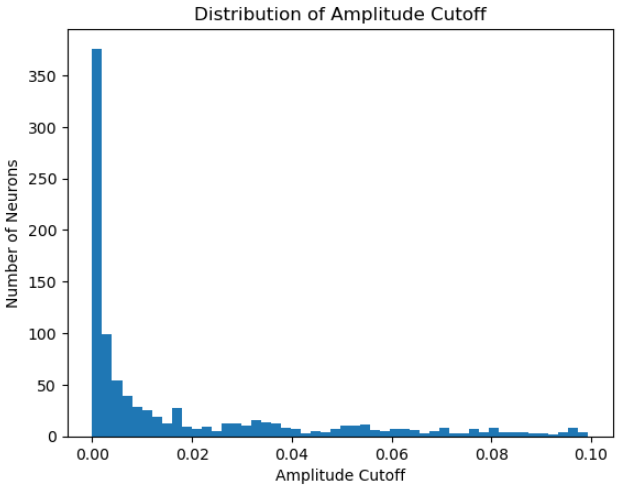




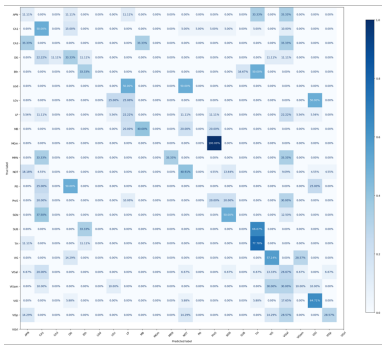

Distribution of d' (Separation Index)
Number of Neurons
d'


Distribution of Signal-to-Noise Ratio (SNR)
Number of Neurons
SNR

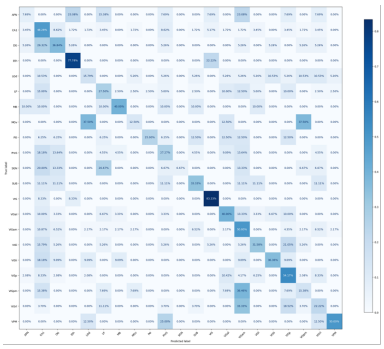

Distribution of Firing Rates
Number of Neurons
Firing Rate (spikes/s)


Distribution of Amplitude Cutoff
Number of Neurons
Amplitude Cutoff

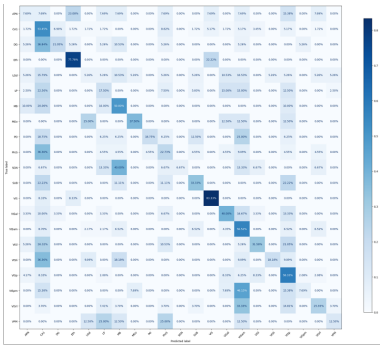
Classification results



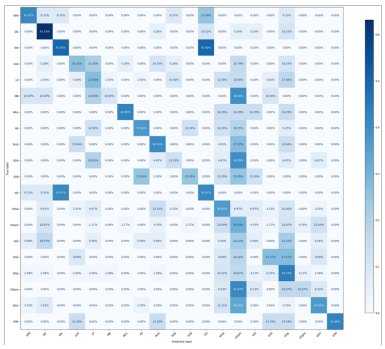
(a) Confusion Matrix of model on one session



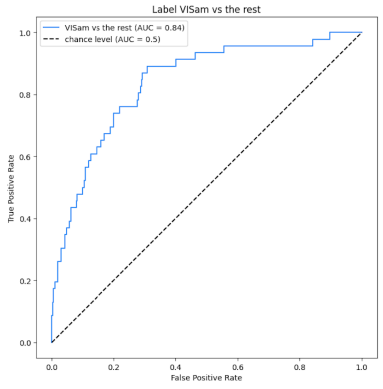
(b) CM of model on three sessions - unbiased



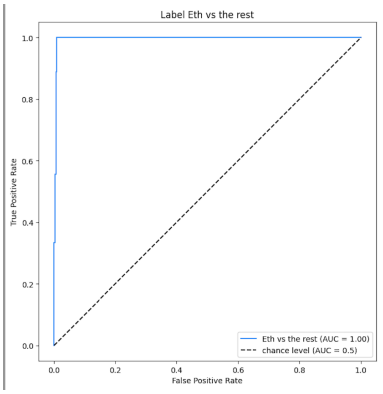
(c) CM of model on three sessions - no zeros



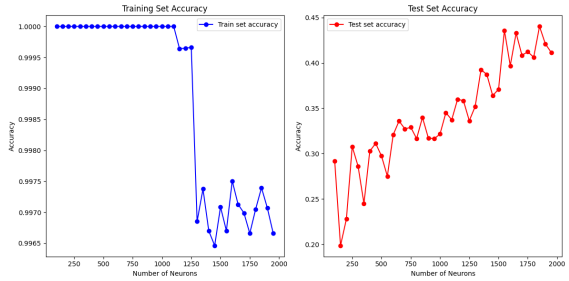
(d) CM of model on three sessions - no CA1



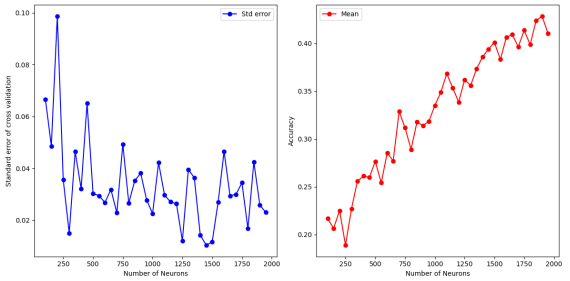
(e) ROC Curve for VISam



(f) ROC Curve for eth



(g) Accuracies vs. Number of Samples



(h) Cross Validation vs. Number of Samples