Hierarchical Latent Variable Models for Neural Data Analysis

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Abstract

Decision making is at the forefront of human minds, both in the concept of how people operate in their day-to-day lives, but also for neuroscience. In trying to understand the human brain better, this research investigates the neural mechanisms underlying decision-making by analyzing brain activity recorded from mice performing a visually guided choice task.

Code: https://github.com/vbommisetty/Hierarchical-Latent-Variable-Models-for-Neural-Data-Analysis

1 Objective

The objective of this project is to identify behaviorally sensitive neural clusters in the SCdg and SCiw brain regions and characterize their hidden dynamics using hierarchical latent variable models to uncover the underlying structure of neural activity during task-related events.

2 Introduction

Understanding how neural activity encodes behavior is a fundamental challenge in neuroscience. The brain's ability to process sensory information, make decisions, and execute actions relies on the coordinated activity of neurons across multiple regions. In this project, we focus on the **superior colliculus** (SC), a midbrain structure critical for sensorimotor integration, attention, and decision-making Jun et al. (2017). Specifically, we investigate two subregions of the SC—**SCdg** (dorsal gray) and **SCiw** (intermediate white)—which are implicated in integrating sensory inputs and generating motor outputs Krauzlis, Lovejoy and Zénon (2013).

Our study leverages large-scale neural recordings from 139 mice performing a decision-making task, collected as part of the International Brain Laboratory (IBL) initiative Jun et al. (2017). Using Neuropixels probes, we recorded activity from 621,733 neural units, of which 75,708 were classified as neurons, across 699 insertions. This rich dataset allows us to explore how neural activity in SCdg and SCiw encodes task-related events, such as stimulus presentation, movement initiation, and feedback.

The goal of this project is twofold:

- Identify sensitive neural clusters in SCdg and SCiw that respond to specific behavioral events.
- Analyze hidden dynamics in these clusters using hierarchical latent variable models, such as Probabilistic Canonical Correlation Analysis (PCCA), to uncover the underlying structure of neural activity during decision-making Gold and Shadlen (2007).

By combining advanced statistical methods with high-resolution neural recordings, we aim to shed light on how the brain transforms sensory information into action, providing insights into the neural basis of behavior. This work not only advances our understanding of the superior colliculus but also contributes to the broader effort of mapping brain-wide neural circuits underlying decision-making.

2.1 Literature and Prior Work

2.1.1 Superior Colliculus

The superior colliculus (SC) has long been recognized as a critical hub for sensorimotor integration, playing a key role in orienting behaviors, attention, and decision-making Jun et al. (2017). Previous studies have shown that the SC integrates multisensory inputs (e.g., visual, auditory) and generates motor outputs, such as eye and head movements Krauzlis, Lovejoy and Zénon (2013). The dorsal gray (SCdg) and intermediate white (SCiw) subregions, in particular, are involved in coordinating these processes, with SCdg implicated in sensory processing and SCiw in motor planning Krauzlis, Lovejoy and Zénon (2013).

Recent advances in large-scale neural recording technologies, such as Neuropixels probes, have enabled researchers to study neural activity at unprecedented resolution Jun et al. (2017). These tools have been instrumental in projects like the International Brain Laboratory (IBL), which aims to map brain-wide neural circuits underlying decision-making Jun et al. (2017). By combining high-density recordings with sophisticated analytical methods, such as Canonical Correlation Analysis (CCA) and Probabilistic Canonical Correlation Analysis (PCCA), researchers can uncover hidden dynamics in neural populations Gold and Shadlen (2007).

Building on this foundation, our project focuses on identifying sensitive neural clusters in SCdg and SCiw and analyzing their hidden dynamics during a decision-making task. By integrating large-scale neural recordings with hierarchical latent variable models, we aim to advance our understanding of how the SC encodes behavior and contributes to decision-making.

2.1.2 Real Data

The International Brain Laboratory (IBL) dataset represents one of the largest and most comprehensive collections of neural recordings in neuroscience Jun et al. (2017). It includes data from 139 mice performing a standardized decision-making task, with 699 Neuropixels probe insertions capturing activity from 621,733 neural units, of which 75,708 were classified as neurons. This dataset spans multiple brain regions, providing a unique opportunity to study brain-wide neural circuits underlying behavior.

The decision-making task involves visual stimuli, wheel-turning responses, and feedback, allowing researchers to investigate how neural activity encodes sensory inputs, motor outputs, and decision outcomes Jun et al. (2017). The use of Neuropixels probes ensures high spatial and temporal resolution, enabling the detection of single-neuron activity across multiple brain regions simultaneously Jun et al. (2017).

For our project, we focus on the superior colliculus (SC), specifically the SCdg and SCiw subregions, leveraging the IBL dataset to study how these areas contribute to sensorimotor integration and decision-making. The scale and quality of the IBL dataset make it an invaluable resource for identifying sensitive neural clusters and analyzing hidden dynamics

in neural activity.

Decision Making Task: The International Brain Laboratory (IBL) dataset was collected using a standardized decision-making task designed to study how neural activity encodes sensory, motor, and decision-related processes Jun et al. (2017). Mice were trained to perform a visual decision-making task where they had to make choices based on visual stimuli to receive rewards. The task involved presenting visual gratings (striped patterns) on either the left or right side of a screen, with the gratings varying in contrast and spatial frequency. Mice indicated their choice by turning a steering wheel—left turns for stimuli on the left and right turns for stimuli on the right. Correct choices were rewarded with a drop of a sucrose solution, while incorrect choices resulted in a timeout or a high-pitched sound (no reward). The reward size was kept constant to ensure consistent motivation across trials, and feedback (reward or timeout) was delivered immediately after the wheel-turning response. The task included both easy trials (high-contrast stimuli) and hard trials (low-contrast stimuli) to vary difficulty and study decision-making under different conditions. Each trial consisted of a stimulus presentation phase (1–2 seconds), a response period (wheel turn), a feedback phase (reward or timeout), and a short inter-trial interval (1–3 seconds) to allow the mouse to reset.

Neural activity was recorded using Neuropixels probes, high-density electrodes capable of capturing spikes from hundreds of neurons simultaneously Jun et al. (2017). Probes were inserted into the brain to record activity from multiple regions, including the superior colliculus (SC), visual cortex, and motor cortex. In addition to neural data, behavioral data such as wheel position, lick times (to measure reward receipt), and pupil diameter (to assess arousal and attention) were collected. The task was designed to be reproducible and scalable, with automated systems enabling high-throughput data collection across multiple labs and animals. This standardized approach ensures consistency and allows for the study of brain-wide neural circuits underlying decision-making Jun et al. (2017).

3 Methods

3.1 Preprocessing

Neural activity was recorded using Neuropixels probes, which captured spike times and waveforms from neurons Jun et al. (2017). These spikes were sorted into clusters, groups of spikes that appear to originate from the same neuron based on waveform similarity. Only high-quality clusters—those that passed three stringent quality control metrics—were retained for analysis. These metrics ensured that the clusters represented well-isolated, single-neuron activity with minimal noise or artifacts.

To focus on the superior colliculus (SC), we further sub-selected clusters from the SCiw (intermediate white) and SCdg (dorsal gray) subregions. This was achieved by identifying the boundaries between brain regions using additional electrophysiological signals, such as

the RMS of the high-frequency action potential (AP) signal and the power in the delta band of the local field potential (LFP). These signals helped localize the probe's position within the brain and ensured that only clusters from the SCiw and SCdg regions were included in the analysis.

3.2 Sensitive Cluster Identification

To identify sensitive clusters—neurons that significantly respond to specific behavioral events (e.g., stimulus onset, first movement, feedback)—we used permutation testing. This method compares the observed neural responses to a null distribution generated by randomly shuffling event labels. For each cluster, we calculated a test statistic (e.g., firing rate difference between conditions) and compared it to the null distribution to compute a p-value.

To account for **multiple comparisons** across clusters, we applied two correction methods:

Bonferroni Correction: This method adjusts the significance threshold (α) by dividing it by the number of tests (m): $\alpha_{\text{corrected}} = \frac{\alpha}{m}$. While stringent, it ensures control of the family-wise error rate (FWER), minimizing the chance of false positives Bonferroni (1936).

False Discovery Rate (FDR): This method controls the proportion of false positives among significant results. Using the Benjamini-Hochberg procedure, we sorted p-values and applied the threshold $p_i \leq \frac{i}{m}\alpha$, where i is the rank of the p-value and m is the total number of tests. FDR is less conservative than Bonferroni and is well-suited for high-dimensional neural data Benjamini and Hochberg (1995).

3.3 Latent Variable Modeling

3.3.1 Principal Component Analysis (PCA)

Principal Component Analysis (PCA) is a dimensionality reduction technique that identifies the principal components (directions of maximum variance) in a dataset. Given a dataset $X \in \mathbb{R}^{n \times p}$, PCA solves the following optimization problem:

$$\max_{w} \text{Var}(Xw),$$

where w is the weight vector for the principal component. The solution is obtained by performing eigenvalue decomposition on the covariance matrix $C = X^T X$:

$$C = W \Lambda W^T,$$

where W contains the eigenvectors (principal components) and Λ is a diagonal matrix of eigenvalues (explained variance) Gold and Shadlen (2007).

3.3.2 Canonical Correlation Analysis (CCA)

Canonical Correlation Analysis (CCA) identifies linear relationships between two datasets $X \in \mathbb{R}^{n \times p}$ and $Y \in \mathbb{R}^{n \times q}$ by finding weight vectors w_x and w_y that maximize the correlation

between their projections:

$$\max_{w_x, w_y} \text{corr}(Xw_x, Yw_y).$$

This is equivalent to solving the generalized eigenvalue problem:

$$C_{XX}^{-1} C_{XY} C_{YY}^{-1} C_{YX} w_x = \lambda w_x,$$

where C_{XX}, C_{YY}, and C_{XY} are the covariance matrices of X, Y, and their cross-covariance, respectively Gold and Shadlen (2007).

3.3.3 Probabilistic Canonical Correlation Analysis (PCCA)

Probabilistic Canonical Correlation Analysis (PCCA) extends CCA by modeling the shared latent structure between two datasets while accounting for noise and uncertainty. It assumes that X and Y are generated from a shared latent variable Z with added noise:

$$X = W_x Z + \epsilon_X, \quad Y = W_y Z + \epsilon_Y,$$

where W_x and W_y are factor loading matrices, and ϵ_X and ϵ_Y are noise terms. The goal is to maximize the likelihood of the observed data:

$$p(X, Y|Z) = p(X|Z)p(Y|Z).$$

The parameters W_x, W_y, and the noise covariance matrices Ψ_X and Ψ_Y are estimated using expectation-maximization (EM) Gold and Shadlen (2007).

Why Canonical Correlation Analysis? Canonical Correlation Analysis (CCA) and its probabilistic extension, PCCA, are powerful tools for studying relationships between neural activity and behavior. They allow us to identify shared variability and hidden dynamics in high-dimensional datasets, making them ideal for analyzing neural data Gold and Shadlen (2007).

Modifications to Gunderson's PCCA Implementation Our implementation of Probabilistic Canonical Correlation Analysis (PCCA) differs from Gunderson's original approach in several key aspects:

- **Factor Loading Matrix (W)**: Our implementation explicitly updates W using the formula:

  $$W = (XZ^T)(E[ZZ^T])^{-1},$$

  where Z is the posterior mean of the latent variables. This approach is done separately for different feature blocks, ensuring clarity but adding computational overhead. In contrast, Gunderson's method often uses a least-squares optimization approach, updating W in a single step by solving:

  $$W = XZ^T(ZZ^T)^{-1}.$$

- **Noise Covariance (Ψ)**: Our implementation explicitly computes the residual matrix and estimates Ψ_1 and Ψ_2 separately:

$$\Psi_1 = \frac{1}{n}\text{residual}_1\text{residual}_1^T + \lambda I,$$

$$\Psi_2 = \frac{1}{n}\text{residual}_2\text{residual}_2^T + \lambda I,$$

  where λI ensures numerical stability through regularization. Gunderson's approach typically uses a Bayesian prior-based method to estimate noise covariance, which provides a more probabilistically grounded way of handling variance Gold and Shadlen (2007).

These modifications make our implementation more explicit and modular but may introduce additional computational overhead compared to Gunderson's original method. However, they provide greater flexibility and control over the estimation process, particularly for the neural data that we use.

4 Results

4.1 Sensitive Cluster Analysis

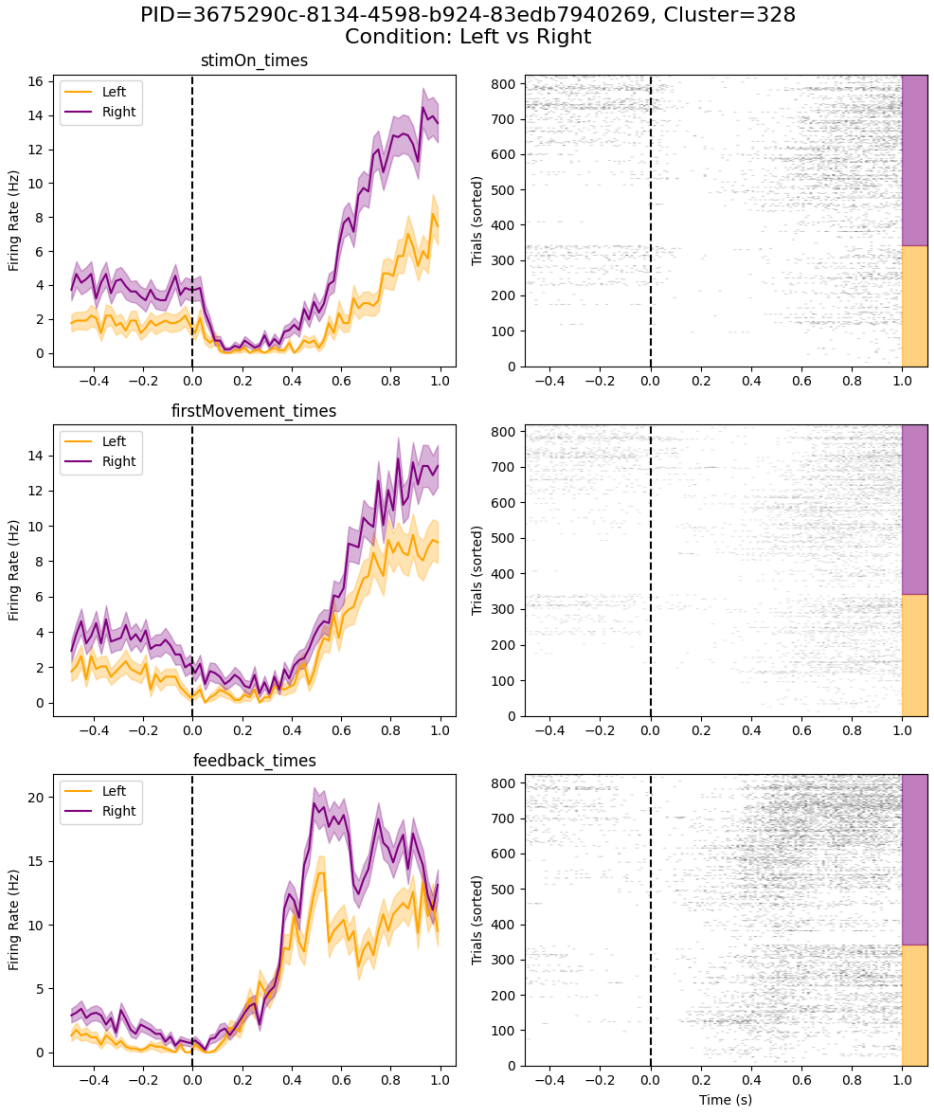

Figure 1: Cluster Analysis separated by Left and Right condition

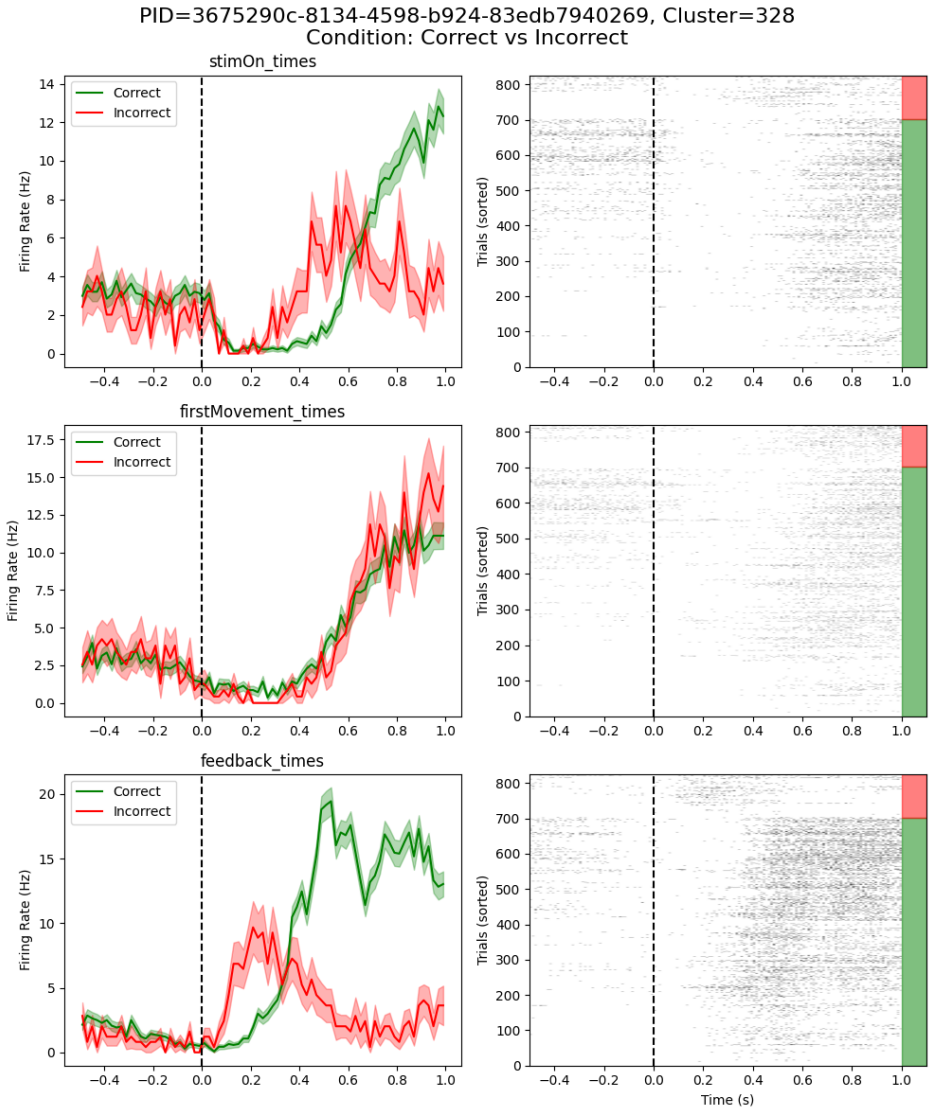

Figure 2: Cluster Analysis separated by Correct and Incorrect condition

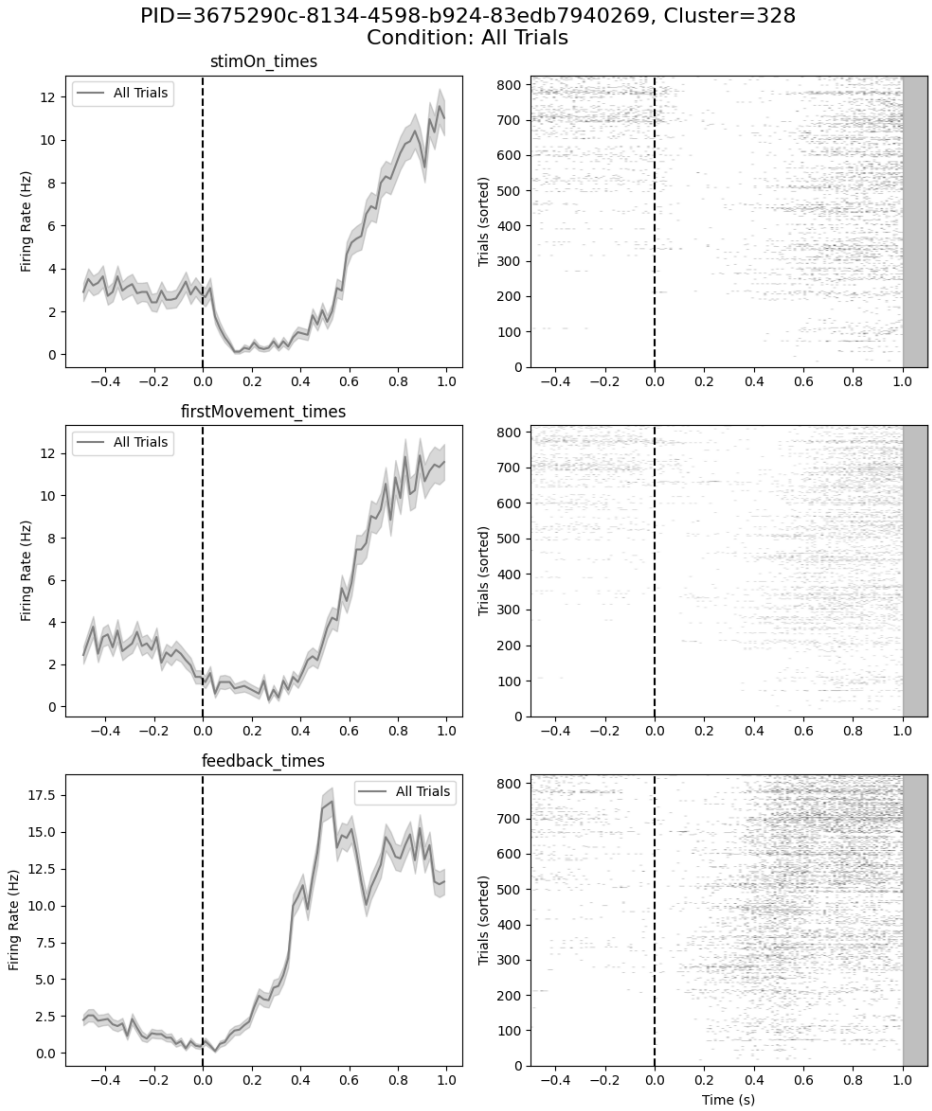

Figure 3: Cluster Analysis with no separation of trials

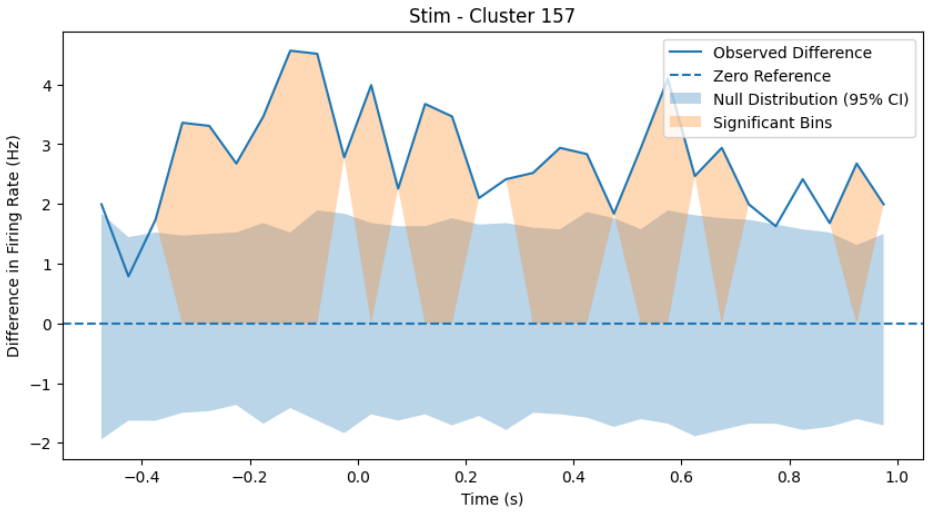

Figure 4: Sensitivity Cluster Analysis

4.2 Latent Variable Modeling Analysis

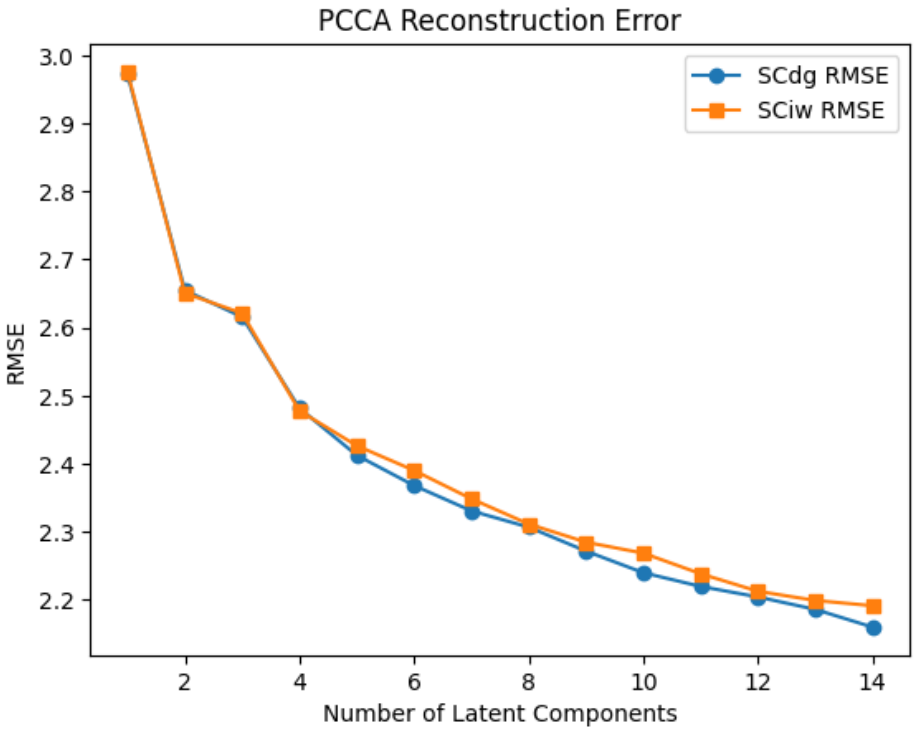

Figure 5: RMSE of PCCA Algorithm

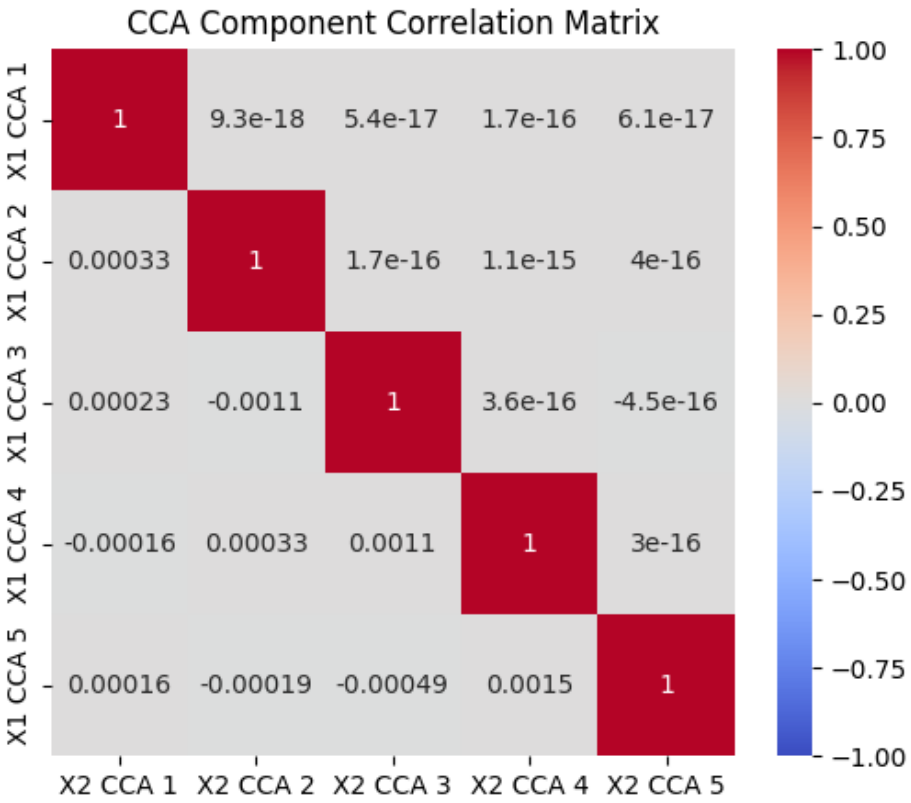

Figure 6: CCA Heatmap

5 Conclusion

This study explored the application of **Probabilistic Canonical Correlation Analysis (PCCA)** to analyze the shared neural dynamics between two distinct conditions: SCdg and SCiw. The results from our **sensitive cluster analysis** highlight clear differences in neural activity patterns across conditions, as observed in the **PSTH and raster plots**. These analyses suggest distinct neural representations of task-relevant variables, with firing rates varying systematically depending on task conditions (Left vs. Right, Correct vs. Incorrect).

The **latent variable modeling analysis** through **PCCA reconstruction errors** (RMSE plots) demonstrated that increasing the number of latent components reduces reconstruction error, indicating that a **higher-dimensional latent space better captures the shared variance** between the two conditions. However, the RMSE values remain relatively high compared to traditional PCA and CCA methods, suggesting that PCCA may not fully capture the structure of the data under the current assumptions **??**.

5.1 Limitations

Despite the insights gained, this work has several limitations:

- **Choice of Bin Size and Preprocessing:** The selection of bin size and preprocessing steps significantly impact the final results. Future work should explore different bin sizes and smoothing techniques to optimize model performance.
- **Limited Number of Clusters:** The analysis focused on a subset of clusters. While this allowed for computational efficiency, a broader analysis across more clusters may provide a more complete picture.
- **RMSE as the Primary Metric:** While RMSE is a useful reconstruction metric, it does not necessarily reflect biological interpretability. Exploring other measures such as **explained variance** or **predictive decoding accuracy** may be beneficial.
- **Correlation Matrix in CCA:** The low off-diagonal values in the **CCA component correlation matrix** suggest weak linear correlations between some canonical variables. This implies that alternative nonlinear methods might be needed to fully capture shared variance.
- **Potential Overfitting in PCCA:** The current PCCA model does not incorporate a **regularization or model selection framework**, which could lead to overfitting, particularly in high-dimensional latent spaces **?**.

5.2 Future Work

To address these limitations, several directions can be explored:

- **Time-Varying Latent Spaces:** Instead of static latent variables, **dynamic models** such as **Gaussian Process Factor Analysis (GPFA)** or **Hidden Markov Models (HMMs)** could better capture the temporal evolution of shared neural representations.
- **Cross-Validation on RMSE:** Instead of relying solely on training set RMSE, **cross-validated RMSE** should be computed to ensure the robustness of latent variable extraction.
- **Alternative Data Representations:** Future work could compare **wavelet-based features** or **convolutional neural network embeddings** for feature extraction before applying PCCA.
- **Higher-Dimensional PCCA Models:** Exploring **Bayesian hierarchical models** that explicitly model both **shared and condition-specific latent factors** could improve interpretability and generalizability.

This study provides a foundation for understanding shared neural representations between different conditions using **PCCA**. However, to fully uncover the underlying **task-relevant latent structures**, future studies should incorporate more flexible and dynamic latent variable models, particularly **GFPA and GPFA**, to better capture nonlinear and time-varying dependencies across neural populations.

References

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