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Mixed Selectivity Across Three Parietal Areas in Macaque During Eye-Hand Reaching

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1 INTRODUCTION

1.1 Overview of Neural Activity

Neurons communicate with each other and with their target cells via electrical and chemical signals. These signals, particularly electrical ones, are crucial for transmitting time-sensitive information quickly across long distances. Short-lived electrical changes, such as receptor potentials, synaptic potentials, and action potentials, are generated by fluctuations in ion currents across the cell membrane, altering the cell's resting potential. This ion flow, mediated by ion channels, underpins the transmission of neural signals within the nervous system (Kandel et al., 2021).

The intricate stimuli that we are constantly subject to are represented by the neuronal activity in the approximately 10^{11} neurons in our brains. Our internal thoughts, emotions and memories are also represented by these neurons and so are the commands sent to the muscles for motor output (Kreiman, 2004). Understand Neural coding involves understanding the way in which neurons represent and transmit information within the brain. Neurons employ various coding schemes, such as rate coding and temporal coding, to convey complex information. This understanding forms the basis for analyzing and modeling neural activity in order to define precise functional fingerprints. Neurons can also exhibit mixed selectivity, particularly within regions like the posterior parietal cortex (PPC). This characteristic enables them to respond to combinations of visuomotor and somatosensory stimuli, allowing for nuanced and coordinated responses crucial for motor control. Mixed selectivity represents an adaptive mechanism by which neurons can integrate multiple types of information, a feature that is especially relevant in tasks involving complex movements. Characterizing the relationship between stimulus and response is difficult because neuronal responses are complex and variable. Neurons typically respond by producing complex spike sequences that reflect both the intrinsic dynamics of the neuron and the temporal characteristics of the stimulus. Isolating features of the response that encode changes in the stimulus can be difficult, especially if the time scale for these changes is of the same order as the average interval between spikes. Neural responses can vary from trial to trial even when the same stimulus is presented repeatedly (Dayan and Abbott, 2001).

To interpret and comprehend the information that neurons encode, sophisticated statistical models must be used due to the intricacy and unpredictability of neural responses. The application of statistical models, such as Generalized Linear Models (GLMs), is one method that is frequently utilized in neuroscience. These models enable researchers to examine how many factors affect brain firing rates and to link neuronal activity to external variables, such as motor activities or sensory stimuli. In my thesis, brain activity captured during macaque eye-hand coordination tasks was analyzed using statistical modeling. This methodology facilitates an in-depth investigation of the ways neurons encode internal states, motor commands, or sensory input, helping to identify patterns of neuronal activity linked to certain functional role.

1.2 The Theory of Mixed Selectivity

Mixed selectivity is a fundamental concept in neuroscience, particularly in understanding the flexible and complex functions of cortical regions like the posterior parietal cortex (PPC), which includes areas V6A, PE, and PEc. Traditionally, selectivity in neurons was understood as a preference for specific sensory stimuli, motor commands, or cognitive states, with neurons responding predominantly to a single type of input (Burgess et al., 1997). However, mixed selectivity has expanded this understanding by demonstrating that many neurons exhibit a combinatorial response to multiple types of inputs. Neurons with mixed selectivity integrate visuomotor, somatosensory, and proprioceptive signals, enabling them to adapt their responses based on complex contextual cues, which is especially critical in sensorimotor tasks (Rigotti et al., 2013).

In the PPC, mixed selectivity is crucial for tasks that require coordinated movement, such as eye-hand coordination, as it allows neurons to encode information across spatial, temporal, and task-specific domains. For instance, neurons in the V6A area exhibit responses that are modulated by both gaze direction and arm movement, allowing for seamless integration of visual and motor information to guide reaching movements (Galletti et al., 1997). This ability to represent multiple dimensions of a task in a single neural response provides a versatile neural code that supports flexible behaviors (Raposo et al., 2014). Such mixed selectivity is essential for complex motor actions because it enables neurons to respond dynamically to multiple task-related parameters, reducing the need for distinct neural populations

dedicated to single, isolated functions.

The study of mixed selectivity also challenges conventional theories of neural coding, suggesting that neural responses are better described as high-dimensional representations rather than as responses to discrete variables (Fusi et al., 2016). In practical terms, this means that a single neuron in the PPC can contribute to multiple aspects of a task depending on the specific context, thus forming part of a high-dimensional network that underlies flexible cognitive and motor functions (Diomedi et al., 2020). By analyzing neurons with Generalized Linear Models (GLMs), researchers have demonstrated how different task epochs and parameters — such as eye position, movement direction, and arm posture — jointly contribute to shaping the firing rates of PPC neurons (Paninski, 2004; Diomedi et al., 2020). This approach reveals that mixed selectivity enables a more efficient and adaptable coding strategy for neurons involved in complex tasks, emphasizing the role of the PPC in coordinating spatial and motor information.

In summary, mixed selectivity represents a powerful mechanism that allows neurons in areas such as V6A, PE, and PEc to encode complex, multi-dimensional information. This integrative capacity is fundamental for sensorimotor coordination, supporting the hypothesis that the PPC operates as a highly flexible network capable of adapting to varied sensory and motor demands. The current study seeks to further investigate this phenomenon through the lens of eye-hand coordination, utilizing statistical models to quantify the extent and impact of mixed selectivity within PPC neurons.

1.3 Statistical Models for Studying Neuronal Activity

Statistical models and machine learning algorithms offer powerful tools for analyzing the complex dynamics of neuronal activity, particularly when studying high-dimensional data from brain recordings. Traditional statistical approaches, such as Generalized Linear Models (GLMs), allow researchers to examine how specific factors, such as task parameters or sensory inputs, influence firing rates in single neurons and across neural populations (Paninski, 2004). By using GLMs, it is possible to identify not only the primary drivers of neuronal response but also how different task phases contribute to modulating neural activity over time. In recent years, machine learning techniques, including dimensionality reduction and clustering, have enabled a shift from single-neuron analyses to population-based approaches. Techniques such as Principal Component Analysis (PCA) provide insights into the high-dimensional space in which neuronal populations operate, revealing underlying patterns and correlations that would be difficult to detect through traditional methods alone (Diomedi et al., 2020). These tools allow for the characterization of mixed selectivity, a phenomenon where neurons respond to combinations of variables, rather than isolated parameters, reflecting the neural system's adaptability in encoding complex sensorimotor tasks.

In my research, I apply these methodologies to analyze neuronal activity during a coordinated motor task, focusing on how different brain areas, such as the posterior parietal cortex, contribute to motor control and sensorimotor integration. This project aims to identify the contributions of different task-related variables within neuronal populations to explain the dynamic interactions within neural ensembles in the PPC . The use of these advanced analytical tools provides a comprehensive understanding of how distributed neuronal activity supports mixed selectivity and, ultimately, facilitates complex motor behaviors.

1.4 Posterior Parietal Cortex (PPC)

The posterior parietal cortex (PPC) has traditionally been studied as a key region for sensory processing. However, its role has since evolved to that of a critical hub for complex sensorimotor transformations, particularly in the context of visually guided actions. The PPC is part of the dorsal visual stream, which is heavily involved in the spatial localization of objects and the planning of goal-directed movements. This

stream processes "where" information, helping to guide actions such as reaching and grasping by integrating visual and somatosensory inputs. Research has established that the PPC is crucial for transforming sensory inputs into motor outputs, enabling complex behaviors such as spatial navigation, object manipulation, and coordinated limb movements. This integrative role is supported by the PPC's extensive connections with both cortical and subcortical regions. Specifically, the PPC interacts with visual areas to process spatial information and with motor regions to plan and execute goal-directed movements. The PPC can be broadly divided into several subregions (Figure 1), each contributing uniquely to different aspects of sensorimotor integration. These subregions (Figure 2) are interconnected and work in concert to support behaviors that require precise spatial awareness and motor coordination. Importantly, the PPC's role extends beyond simple sensory processing; it participates in higher-order cognitive functions such as attention, decision-making, and action planning. Studies have shown that PPC activity is modulated by task demands, indicating its dynamic involvement in context-dependent motor control (Gamberini et al., 2020).

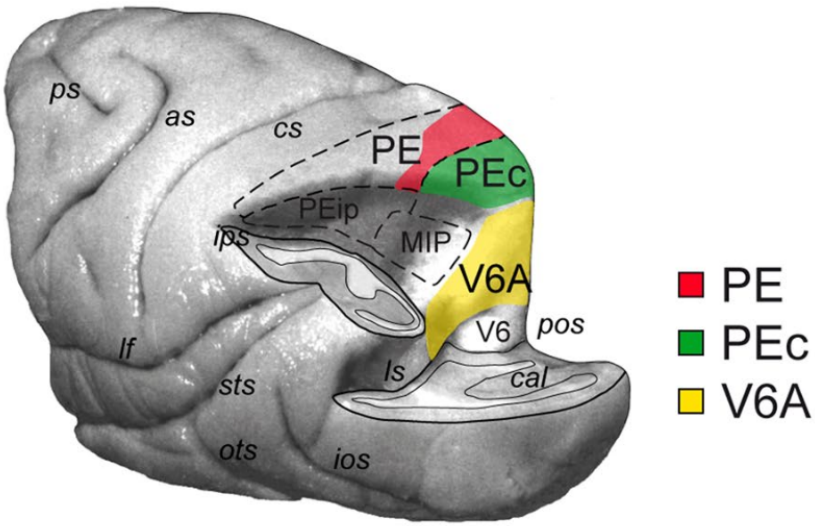

Figure 1: *Anatomical regions of the Posterior Parietal Cortex (PPC) highlighting areas V6A, PE, and PEc, involved in visuomotor integration and sensorimotor processing. Figure modified from* (Gamberini et al., 2020).

In addition to its integrative functions, the PPC plays a significant role in mixed selectivity, a phenomenon where neurons respond to combinations of sensory and motor signals. Mixed selectivity allows the PPC to encode information in a highly flexible manner, adapting to different task contexts and environmental changes. This

feature is thought to underlie the PPC's ability to support complex motor behaviors and precise visuomotor coordination (Vaccari et al., 2021). Given its central role in sensorimotor integration, the PPC has been extensively studied in tasks involving reaching, grasping, and spatial perception. In this study, we focus on three specific subregions within the PPC: V6A, PE, and PEc. By examining these subregions, our goal is to gain a deeper understanding of how the PPC contributes to sensorimotor transformations and adaptive behavior in complex tasks. Further details about each of these areas will be provided in the following sections.

1.4.1 Area V6A

Area V6A, located on the anterior wall of the parieto-occipital sulcus (POS), is distinguished by its strong visuomotor properties, with approximately 65% of its neurons responding to visual inputs essential for reach-to-grasp movements (Galletti et al., 1996). V6A neurons are finely tuned to parameters such as gaze direction, object orientation, and spatial position, making V6A crucial for coordinating upper limb movements during complex motor tasks (Fattori et al., 2017).

V6A is known to receive visual inputs from extrastriate areas such as V2 and V3, and it may also receive somatosensory inputs from PEc (Figure 3), which could contribute to its role in integrating sensory information during visually guided tasks (Gamberini et al., 2020). Additionally, 70% of its neurons modulate reaching actions based on direction and depth, while grip formation and wrist orientation influence around 60% of these neurons (Breveglieri et al., 2016; Hadjidimitrakis et al., 2014). In addition to its visual dominance, V6A exhibits mixed selectivity, responding to combinations of visuospatial, somatosensory, and motor parameters (Diomedi et al., 2020). This flexibility allows V6A to dynamically adjust motor outputs based on gaze, limb orientation, and object location, highlighting its role in visuomotor integration and its capacity to support precision and adaptability in reach-to-grasp tasks (Fattori et al., 2017; Gamberini et al., 2020).

1.4.2 Area PE

Area PE, located in the anterior part of the superior parietal lobule (SPL), is a somatosensory area that integrates sensory information from different parts of the body, particularly the upper limbs. It receives strong inputs from the primary somatosensory cortex (S1) and motor areas, forming a detailed proprioceptive map crucial for preparing and controlling limb movements during tasks requiring precision, such as grasping and reaching. PE also has direct connections to the spinal cord, which facilitate the transmission of somatomotor information for upper limb control (Murray and Coulter, 1981). Approximately 90% of PE neurons are activated by multi-joint somatosensory stimulation and limb posture, contributing to the creation of a detailed map of the body, with an over-representation of the upper limbs (De Vitis et al., 2019). However, these neurons are not exclusively selective for somatosensory inputs. Although mixed selectivity has not been demonstrated in PE, our work suggests its potential presence. This concept, well established in other PPC areas like V6A (Diomedi et al., 2020), leads us to hypothesize a contribution to complex processes such as voluntary movement and somatosensory integration.

Furthermore, somatosensory signals received from other parietal cortex areas (PEc, PEci, MIP, PEip, PGop, PFop, Ri) and from the supplementary motor area (SMA) allow PE to dynamically create an accurate proprioceptive information (Figure 3). This complex sensory and motor integration enables PE to play a crucial role in the control of upper limb movements, especially in actions that require precise coordination between visual and tactile information.

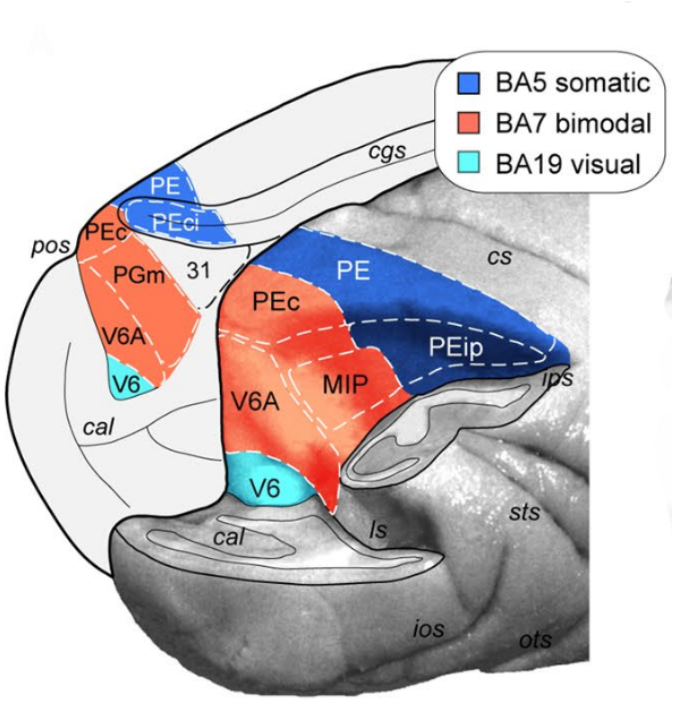

Figure 2: *Illustration of the posterior parietal cortex (PPC) areas in the macaque, highlighting their primary functional roles. According to (Gamberini et al., 2020), area V6 (BA19) is predominantly visual, area PE (blue, BA5) is mainly somatic, processing somatosensory information for limb positioning and movement guidance while area PEc (red, BA7) is bimodal, integrating visual and somatosensory inputs. Figure modified from* (Gamberini et al., 2020).

1.4.3 Area PEc

Area PEc, located caudally to PE in the superior parietal lobule (SPL), is characterized by its bimodal activity, responding to both visual and somatosensory inputs. It shares some cortical connections with PE, receiving inputs from various sensory areas. These connections suggest that, similar to PE, it integrates different sensory modalities. However, its functional role is more specifically focused on visuomotor integration, making it crucial for guiding movements through 3D space. PEc receives visual and somatosensory inputs and has strong connections with the medial parietal areas, particularly V6A and MIP (Figure 3) , which are involved in visually guided actions and somatosensory processing. In addition, PEc shares reciprocal connections with areas PG and PGop of the Lateral parietal lobule, as well as with mesial areas 23, 24, 31, and PEci, which are crucial for sensorimotor integration (Gamberini et al., 2021). These connections emphasize PEc's involvement in supporting upper and lower limb movements during complex motor tasks. Approximately 65% of PEc neurons are sensitive to somatosensory inputs, especially joint movements

(Gamberini et al., 2020). While PEc shares some similarities with PE in terms of cortical connections, it also exhibits notable differences, particularly in its inputs, showing stronger connections to visuomotor areas such as V6A and premotor areas involved in motor planning (Gamberini et al., 2020). PEc integrates informations in a flexible manner, supporting vision-guided motor behaviors such as hand-eye coordination and reach movements. Although mixed selectivity has not yet been demonstrated in PEc, our study aims to explore its potential presence, similar to what has been observed in other PPC areas, such as V6A (Diomedi et al., 2020).

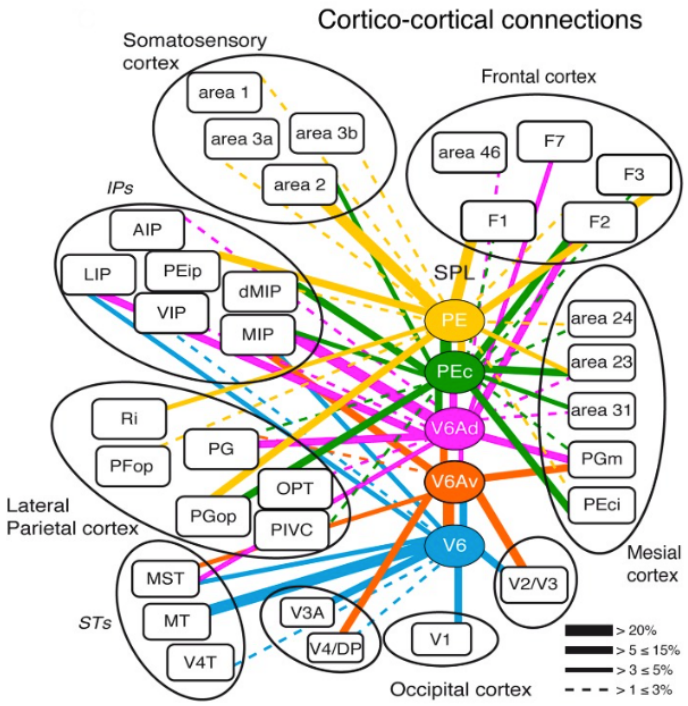

Figure 3: *Cortico-cortical connections of areas V6A, PE, and PEc. The image illustrates the main connections between the superior parietal lobule (SPL), occipital, somatosensory, and frontal regions. Areas V6A, PE, and PEc, highlighted in yellow, green, and orange, respectively, receive significant input from occipital regions (V1, V2/V3, V6) and lateral parietal regions (AIP, LIP, VIP, MIP). The connections are color-coded based on fiber density: black lines (> 20%), magenta (5–15%), yellow (3–5%), green (1–3%), and blue (< 1%). This network of connections underscores the critical role of areas V6A, PE, and PEc in visuomotor integration and multisensory processing required for motor control and movement planning. Figure modified from* (Bakola et al., 2010).

1.5 Homology Between Macaque and Human SPL in Visuomotor Integration

The comparison between macaque and human superior parietal lobule (SPL) highlights a striking homology in their structural and functional organization (Figure 4), with both featuring a somatosensory-dominated anterior region and a bimodal visual-somatosensory caudal sector (Gamberini et al., 2020). This similarity suggests that findings from macaque SPL, such as the roles of V6A, PE, and PEc in visuomotor transformations, can guide research into the human SPL's involvement in reaching and grasping tasks. Studies indicate that human SPL, akin to its macaque counterpart, is crucial for encoding visuospatial and proprioceptive information necessary for complex motor behaviors, such as arm-reaching and grasping movements (Astafiev et al., 2003; Filimon et al., 2009). This alignment supports leveraging the macaque model to deepen our understanding of human SPL functionality, including its potential applications in guiding prosthetic devices via neural signals, especially for individuals with motor impairments.

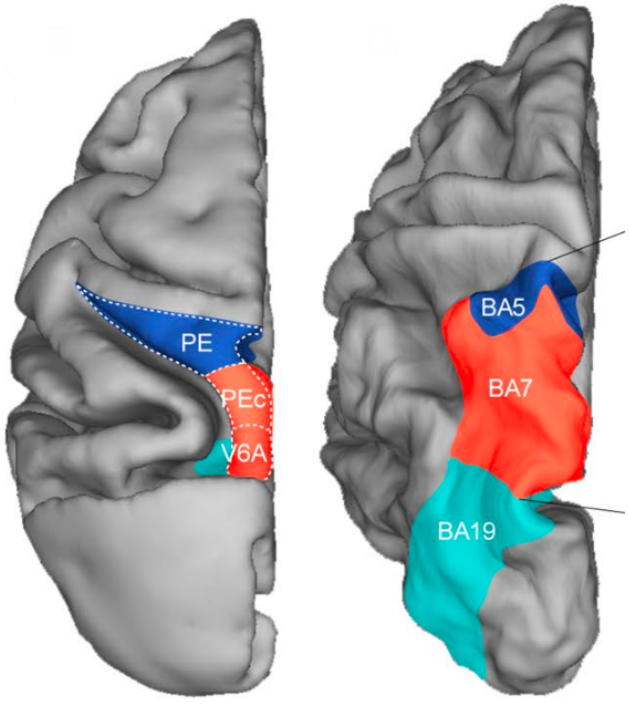

Figure 4: *Comparison of the superior parietal lobule (SPL) in humans (right) and macaques (left). The image highlights the structural organization of areas V6A, PE, and PEc, showing homologies in somatosensory (BA5), bimodal (BA7), and visual (BA19) regions. Figure modified from* (Gamberini et al., 2020).

The dynamic mixed selectivity observed in SPL neurons further underscores its role in seamlessly integrating sensory modalities to produce coordinated motor outputs. Future research could expand on this homology to investigate neural mechanisms underlying human motor control and their potential translational applications in neuroprosthetics.

1.6 Purpose and Significance of the Study

The purpose of this study is to investigate the neural mechanisms underlying visuomotor integration within specific areas of the posterior parietal cortex (PPC) — namely, areas V6A, PE, and PEc. These regions play essential roles in coordinating sensory and motor information, which is critical for complex tasks such as eye-hand coordination and reach-to-grasp movements. By examining the distribution of selectivity patterns across different task-related epochs, this research aims to elucidate how these cortical areas exhibit mixed selectivity, a phenomenon that enables neurons to respond to diverse sensory and motor cues in a flexible, context-dependent manner.

The study's significance lies in its contribution to understanding the nuanced functional roles of PPC subregions in dynamic sensorimotor integration. While previous research has established the involvement of V6A, PE, and PEc in visuomotor tasks, there is limited understanding of the specific response patterns and selectivity distributions that characterize each area. By providing insights into both shared and distinct features of neural selectivity in V6A, PE, and PEc, this research aims to expand current knowledge on how these cortical areas contribute to sensorimotor integration. The findings are expected to clarify the specific roles of these regions in enabling flexible and adaptive motor behavior, reinforcing the importance of mixed selectivity as a key organizational principle in the PPC (Vaccari et al., 2021; Diomedi et al., 2020).

1.7 Research Question

This study is guided by the following primary research question:

How do neuronal populations within areas V6A, PE, and PEc in the posterior parietal cortex exhibit mixed selectivity across task epochs, and how do the selectivity patterns differ across these areas in terms of multi-parametric coding during a reach task?

Sub-questions include:

- Is mixed selectivity, already established in V6A, also present in PE and PEc, and to what extent?
- Are there differences in how V6A, PE, and PEc encode multiple features during reach tasks, and how do these differences reflect the functional roles of these areas in visuomotor integration?

Addressing these questions will provide valuable insights into the cooperative roles of V6A, PE, and PEc in encoding multiple sensory and motor features. Through this investigation, the study aims to clarify whether the neural coding strategies of PEc and PE exhibit mixed selectivity, as already demonstrated for V6A, and to assess how these areas contribute to context-dependent visuomotor processing in complex tasks.

2 MATERIAL AND METHODS

2.1 Data Structure and Experimental Protocol

In this section, I will provide an overview of the datasets used in the study, including a detailed description of the data sources and their structure. The data analyzed in this investigation were recorded from neural activity in macaques during instructed delay reaching task. These data include marker events and spike timing captured from different regions of the Posterior Parietal Cortex (PPC), specifically V6A, PE, and PEc. The raw data, formatted in HDF5, is processed through MATLAB scripts to extract relevant spike and marker information. This section will also outline the preprocessing steps applied to the dataset, such as data filtering, and the methods used to prepare the data for further analysis, such as binning and the generation of functional fingerprints.

2.1.1 HDF5 Data Format

The HDF5 (Hierarchical Data Format version 5) is a versatile file format designed for efficient management of large scientific datasets. Its hierarchical structure enables the organization of complex datasets within a single file, making it ideal for neural recordings. HDF5 supports metadata, such as experimental conditions, recorded brain areas, and electrode configurations, providing essential context for the data. Key advantages include efficient data compression, fast input/output operations, and compatibility across platforms, as well as the ability to store multidimensional arrays, such as spike trains and behavioral event markers. The data was structured by neurons, trials, and conditions, facilitating processing and analysis in MATLAB. The format's scalability and metadata capabilities ensured well-documented, reproducible analyses, while its cross-platform compatibility made it suitable for long-term storage and collaborative research.

Each HDF5 file is organized into a hierarchy, similar to a file system with directories and subdirectories. The structure for neural data recordings can be represented as follows:

Level 0: `/DATA` – Contains all the data related to neural recordings.

-Level 1: `/DATA/unit` – Groups organized by each recorded neuron.

-Level 2: `/DATA/unit/condition` – Conditions (e.g., different tasks or trials)

-Level 3: `/DATA/unit/condition/trial` – Trials for each condition.

-Level 4: `/DATA/unit/condition/trial/spike_trains` – Contains the spike times of neural activity during each trial.

-Level 4: `/DATA/unit/condition/trial/event_markers` – Behavioral event markers (timing of key events in the task).

2.1.2 General Procedure

The neurophysiological recordings for this study were obtained from an adult male macaque monkey (Macaca fascicularis), referred as Monkey F. During the course of the experiments, Monkey F was aged between 5 and 8 years, weighing between 3.7 and 4.0 kg. The monkey underwent extensive training to perform a foveated reaching task, where he was required to direct his gaze and reach toward visual targets in a controlled environment. This training involved habituating the animal to sitting calmly in a primate chair and interacting with the experimental setup and experimenters. The training progressed until the monkey demonstrated consistent and accurate performance of the task. Following the completion of training, the animal underwent surgical procedure under general anesthesia (administered as sodium thiopental, 8 mg/kg/h, intravenously) to implant a head-restraint system and a recording chamber, which facilitated stable neural recordings. Post-surgical care included administering the analgesic ketorolac tromethamine (1 mg/kg immediately after surgery, followed by 1.6 mg/kg intramuscularly in the subsequent days) to alleviate discomfort. Antibiotic treatment (benzathine benzylpenicillin + dihydrostreptomycin + streptomycin, 1–1.4 ml/10 kg) was provided every 5–6 days to prevent infections.

All experimental and surgical protocols were approved by the Bioethical Committee of the University of Bologna and adhered to both Italian national regulations on the care and use of laboratory animals and the European Communities Council Directive on the protection of animals used for experimental purposes (2010/63/EU). Additionally, neural recordings and behavioral experiments were conducted only when the animal showed no signs of distress, ensuring the well-being of the monkey throughout the study.

2.1.3 Experimental Setup and Behavioural Task

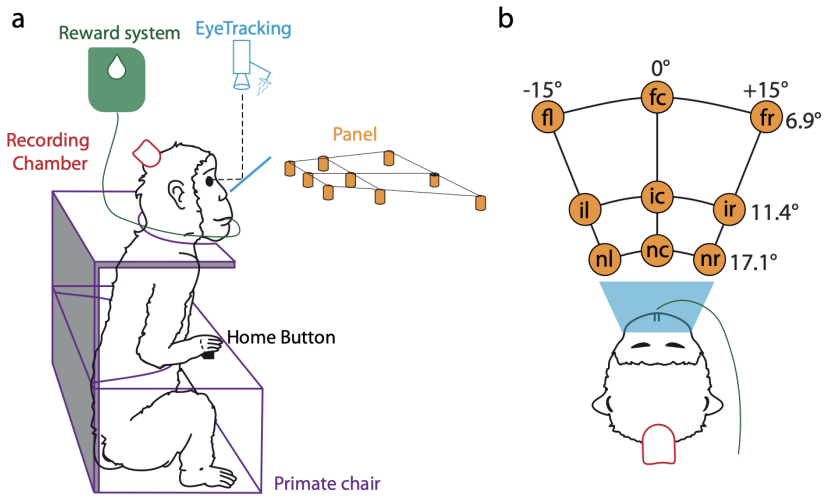

Figure 5: *(a) The monkey is seated in the primate chair, with its head fixed, facing a panel with 9 LED targets. Eye movements are tracked using an eye-tracking system, while neural activity is recorded via electrodes implanted in the Recording Chamber. The task begins when the monkey presses the Home Button (HB), and upon successful completion, a liquid reward is delivered. (b) Spatial layout of the 9 LED targets, with angular coordinates varying in version (horizontal direction) and depth. The targets are categorized as near, intermediate, and far, allowing the study of neural representations of reaching movements across different spatial conditions. Figure modified from* (Diomedi et al., 2024).

The setup consisted of several key components: a primate chair, an eye-tracking system, a panel equipped with multicolor LEDs, a reward delivery system, recording hardware, and custom software to control the experiment (Figure 5). In this task, monkeys were trained to use their contralateral hand relative to the hemisphere being recorded from to reach toward a series of visual targets. Reaching movements were directed toward nine visual targets (LEDs, 6 mm in diameter) distributed along three main directions—left, center, and right—at three distinct depths (Figure 5): near (10 cm), intermediate (15 cm), and far (25 cm) from the animal's eye. Eye position was continuously monitored using an ISCAN ETL200 eye-tracking system (sampling frequency: 100 Hz). The system utilized cameras positioned above the animal's head, recording pupil movements via a hot mirror placed at a 45° angle in front of the eyes. The reward system, designed to motivate the monkeys to perform the task correctly, consisted of a water delivery mechanism controlled by a solenoid valve. After each successful trial, a specific amount of water was dispensed to meet the daily hydration needs of the animal (Diomedi et al., 2024).

Neuronal activity was recorded extracellularly using a 5-channel multielectrode recording system (MiniMatrix; Thomas RECORDING GmbH, Giessen, Germany). The electrode signals were amplified (gain: 10,000) and filtered (bandpass: 0.5–5 kHz). Finally, histological reconstruction of electrode penetration sites was performed following established procedures described in previous studies conducted in the same laboratory (Gamberini et al., 2011). This step was crucial for confirming the precise recording locations within the PPC and ensuring data accuracy.

The task was performed in a dimly lit environment to reduce visual distractions, with brief background illumination between trials to prevent dark adaptation. Each experimental run consisted of 90 correct trials, corresponding to 10 successful trials per target, with the nine targets pseudo-randomly interleaved. Specifically, if an error occurred during a trial, the same target was immediately presented again, ensuring consistent exposure and allowing the monkey to attempt the movement once more. In contrast, after a successful trial, the target for the next trial was selected randomly from the remaining options. This design guaranteed that the animal performed a balanced number of reaching movements toward each target across multiple trials. A typical trial began when the monkey pressed the home button (HB). The task sequence was divided into distinct epochs, each representing a different phase of the trial (Figure 6):

- FREE epoch : During this initial phase, the monkey was free to look around without any constraints. After 1000 ms, one of the nine LEDs lit up in green, signaling the RT SACC epoch.
- RT SACC epoch: Upon the illumination of the LED, the monkey was required to perform a saccade and start fixating on the target. Once fixation was detected, the DELAY epoch commenced.
- DELAY epoch: During this interval, the monkey was required to maintain fixation on the target while continuing to press the HB. The duration of this epoch was randomly selected between two possible values (1850 ms or 2350 ms) to prevent the animal from predicting the timing of the next event. If the monkey released the button during this phase, the trial was aborted.

- RT MOVE OUT epoch: At the end of the DELAY epoch, the LED changed color from green to red, prompting the monkey to initiate the reaching movement. If the animal failed to start moving within 1 second, the trial was aborted.

- MOVE OUT epoch: Once the monkey began moving, it had 1 second to reach the target. If the reaching movement exceeded this time, the trial was aborted.

- HOLD epoch: Upon reaching the target, the monkey was required to hold its position at the target location for a randomly selected duration of 800 ms or 1200 ms. If the monkey released the target before the red LED was turned off, the trial was aborted.

- RT MOVE IN epoch: After the red LED turned off, the monkey was prompted to return its hand to the HB. A trial was aborted if the monkey took more than 500 ms to initiate this return movement.

- MOVE IN epoch: Once the hand movement back to the HB began, the monkey was required to complete the movement within 1 second. If the movement exceeded this time limit, the trial was aborted.

- WAIT END epoch: The animal maintained the fixation while the LED was turned on (from Green on to Red off events), during this period, if the animal broke the fixation, the trial was aborted.

Throughout the trial, it was critical for the monkey to maintain visual fixation on the target from the moment the LED turned green (during the RT SACC epoch) until the red LED turned off (end of the HOLD epoch). Any fixation break during this period resulted in the abortion of the trial. Notably, while most epochs had durations contingent on the animal's performance, specific epochs such as DELAY, HOLD, FREE, and WAIT END had fixed durations as described above (Diomedi et al., 2024). This experimental design ensured a precise evaluation of visuomotor coordination by imposing strict temporal and spatial constraints, while also allowing variability in trial timing to prevent anticipatory behaviors. Moreover, the use of pseudo-random interleaving of targets helped maintain consistent performance across all spatial directions.

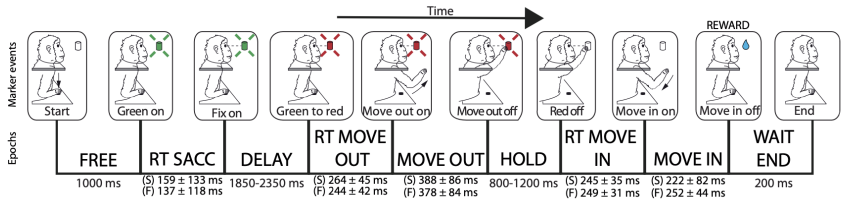

Figure 6: *Task sequence. The top row illustrates the sequence of task events: trial start (Start), target appearance (Green on), fixation onset (Fix on), go signal for the outward movement (Green to red), start of outward movement (Move out on), touch and beginning of target holding (Move out off), go signal for the inward movement (Red off), release of the target and start of inward movement (Move in on), end of inward movement (Move in off), and trial end (End). The bottom row shows the task epochs, each defined by the interval between adjacent event markers, with their corresponding duration. These epochs structure the behavioral task and are used to align neural recordings for subsequent analysis. Figure modified from* (Diomedi et al., 2024).

2.2 Statistical Model Used

2.2.1 GLM Models

Generalized Linear Models (GLMs) provide a versatile statistical framework to explore the complex relationships between neuronal activity and task-related variables. In this thesis, GLMs were employed to analyze the spike activity of neurons recorded from macaque brain regions V6A, PE, and PEc, which are crucial for visuomotor integration. By leveraging GLMs, we can assess how different task regressors affect neuronal firing rates. The choice of a Poisson distribution within the GLM framework is particularly appropriate for spike count data, as neuronal spikes are often modeled as a Poisson process. This approach is especially relevant in single-trial neural recordings where spike counts constitute discrete, non-negative data. Using Poisson GLMs allows us to model the neurons' firing rates based on task regressors, estimating the influence (or weights) of each task regressor on the neural response (Figure 7). This approach builds upon foundational work by (Paninski, 2004), who demonstrated the effectiveness of GLMs for modeling spike trains, emphasizing the practical and computational aspects of neural systems. This modeling framework proves particularly valuable in studying mixed selectivity, where neurons exhibit responses to combinations of task regressors rather than encoding just one isolated parameter. Neurons in regions like V6A are shown to integrate both sensory and motor signals, providing insights into how the brain flexibly encodes information during

complex behaviors. (Diomedi et al., 2020) highlighted this concept in their study of parietal areas, illustrating how neurons combine multiple sources of information during reaching movements.

In the context of this thesis, GLMs were employed to investigate mixed selectivity, where neurons respond to combinations of task regressors rather than isolated one. While our focus is on static covariates representing task conditions, previous work by (Truccolo et al., 2005) extended the GLM framework by incorporating dynamic covariates and spike history effects, enabling a more accurate modeling of temporal dynamics and network interactions. Although (Truccolo et al., 2005) approach primarily addresses dynamic neuronal interactions, their framework highlights the importance of incorporating multiple sources of information, which aligns with the concept of mixed selectivity, where neurons encode combinations of sensory and motor signals. By calculating several metrics (as we will discuss in Section 2.3.3), we can determine which task epochs contribute most to the neurons' firing patterns, furthering our understanding of the flexible encoding strategies in various brain areas.

GLM Structure and Technical Foundation:
The GLM framework in this context has three main components:

Random Component (Poisson Distribution)
In neural data, the number of spikes in a given time interval can be represented by a Poisson distribution, as this distribution models count data where the mean and variance are equal—an assumption commonly satisfied in neural recordings over short periods. The probability of observing a spike count is expressed by the following equation:

$$P(y \mid \mu, \Delta) = \frac{e^{-\mu\Delta}\mu\Delta^{y}}{y!} \tag{1}$$

where:

- y is the observed spike count,
- μ is the expected firing rate per unit time, and
- Δ is the time window or bin width used for analyzing the spike counts.

Systematic Component (Linear Predictor)

This component links task parameters (predictors) to a linear predictor η, representing a weighted sum of variables that influence the neural response:

$$\eta = \beta_0 + \sum_{i=1}^{p} \beta_i X_i \tag{2}$$

where:

- X_i are task-related regressors
- β_i represents the weight of each task variable on the firing rate.

This systematic component enables us to evaluate the relative influence of each task parameter on the neuronal activity, allowing for a nuanced understanding of the factors that modulate neuronal firing rates.

Link Function (Log Link)

Since spike counts are inherently non-negative, we apply a log link function to relate the linear predictor η to the expected firing rate μ. This ensures that the predicted firing rate remains positive, aligning with the biological reality of spike counts:

$$\log(\mu) = \eta$$

or equivalently,

$$\mu = e^{\eta}$$

where μ is the expected spike rate.

Parameter Estimation: Maximum Likelihood Estimation (MLE)

To determine the regression coefficients β, we apply Maximum Likelihood Estimation (MLE), which maximizes the likelihood of observing the given spike train given the model parameters. The log-likelihood function for a Poisson GLM is defined as:

$$l(y, \beta) = \log[L(y, \beta)] = \sum_{t=1}^{T} (y_t \log(\mu_t) - \mu_t) \tag{3}$$

where:

- y_t represents the observed spike count at time t,
- $\mu_t = e^{\eta_t}$ is the predicted rate from the model, and
- T is the number of time points.

By maximizing this log-likelihood function, we estimate the coefficients β that best fit the observed data, capturing how task variables modulate neuronal responses across time.

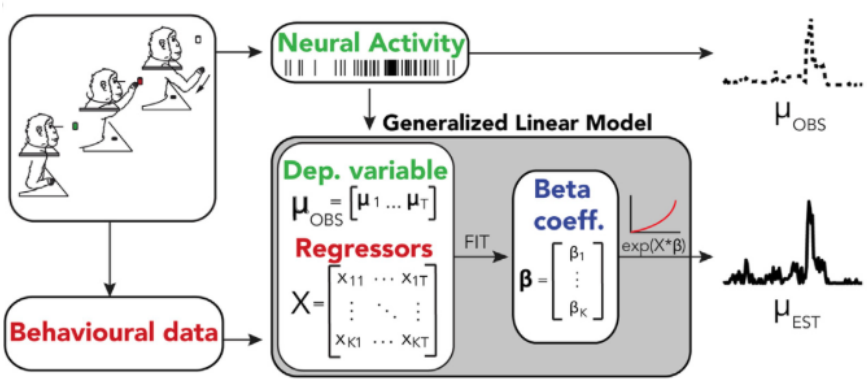

Figure 7: *Diagram illustrating the use of Generalized Linear Models (GLMs) to model neuronal activity in macaque brain regions during reaching tasks. Behavioral data and neuronal activity are used to construct regressors and estimate beta coefficients, allowing for the analysis of task-dependent firing rates and mixed selectivity in areas like V6A. Figure modified from* (Diomedi et al., 2020).

2.2.2 Regressors and Task Epochs: A Systematic Approach to Modeling Neural Activity

To investigate how task-related variables influence neuronal activity, we systematically constructed regressors reflecting the temporal and contextual structure of the behavioral task. This approach ensures that Generalized Linear Models (GLMs) accurately capture relationships between neural firing patterns and specific task phases. Building on established methodologies for neural data preprocessing (Diomedi et al., 2020), we adapted techniques to our experimental paradigm, focusing on two core components: a spike count vector Y (dependent variable) and a regressor matrix X (independent variables).

Raw neural recordings were preprocessed to segment spike trains into discrete 40 ms time bins per trial. This binning process balanced temporal resolution with

statistical robustness, adhering to Poisson distribution assumptions while preserving task-related dynamics. During the same time, behavioral markers that define task epochs were extracted. These markers enabled the definition of task epochs, rather than directly aligning spike times to each event. In our analysis, we considered the following task epochs: (1) FREE, (2) RT SACC, (3) DELAY, (4) RT MOVE OUT, (5) MOVE OUT, (6) HOLD, (7) RT MOVE IN, (8) MOVE IN, and (9) WAIT END. These epochs were chosen to capture the temporal evolution of neuronal activity across different phases of the reaching task. For each task epoch/regressor, we created 9 separate dummy variables, one for each of the nine spatial targets. Binary dummy variables (0/1) were constructed to represent task epochs and their association with target-specific conditions. For each neuron, condition, and trial, the custom MATLAB function generated epoch-specific binary vectors. A value of 1 indicated a bin's inclusion within an epoch (e.g., movement phase), with vectors pooled across trials to form the regressor matrix X. In trials involving reaches to nine spatial targets, this method isolated firing rate contributions from distinct phases, even with variable durations or overlapping events. Spike counts and regressors from individual trials were concatenated into unified matrices for modeling. The vector Y combined binned spike counts tip-to-tail across trials, while X integrated dummy variables with task-related predictors (e.g., target position). A critical challenge was maintaining temporal correspondence between Y and X: Each row of X corresponds to a single time bin in Y, ensuring that neuronal activity is mapped to the corresponding task epoch. For example, during a reach movement, the "movement" epoch regressor would be active in the same row of X, allowing the GLM to isolate its contribution to neural firing. This structure enables the model to assess how neuronal activity varies across different task phases, capturing the temporal dynamics of selectivity in areas V6A, PE, and PEc.

The construction of regressors is not merely a technical prerequisite for statistical modeling but a foundational step in interpreting how neurons encode task-related information. By anchoring dummy variables to behavioral epochs and pooling data across trials, we investigated mixed selectivity—the integration of multiple task variables into firing patterns (Figure 8). In visuomotor areas like V6A, PE, and PEc, this approach revealed shifts in single-neuron encoding strategies across task phases, advancing understanding of neural mechanisms underlying flexible behavior.

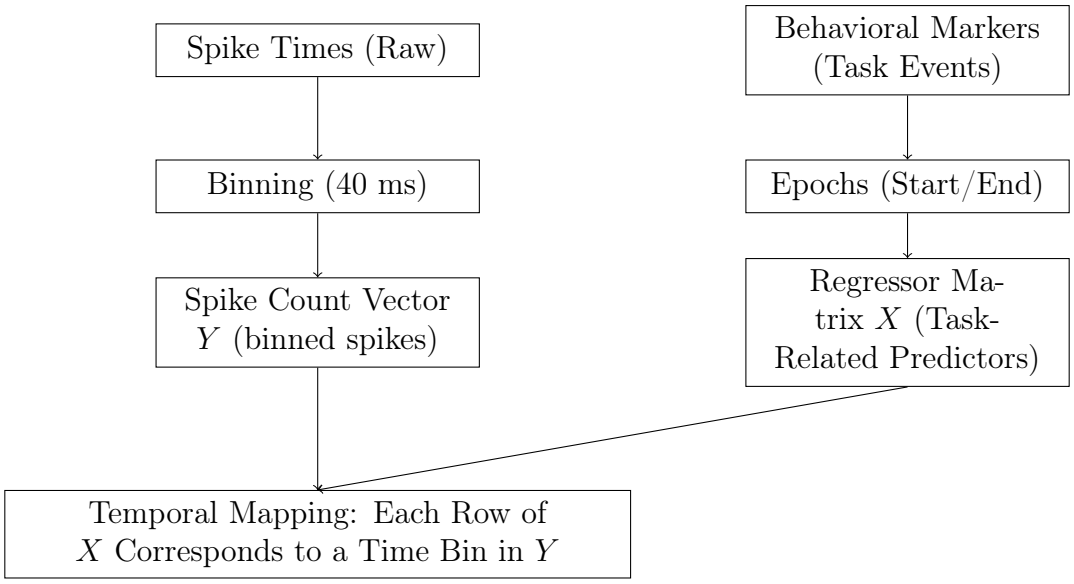

Figure 8: Neural and behavioral data preprocessing flow with temporal mapping.

2.2.3 Full and Nested Models

In this thesis, three key model types are used to analyze neuronal activity during task performance: the full model, nested models, and the null model (Figure 9). Each of these models serves a distinct purpose in understanding how different task variables contribute to neuronal firing rates and, ultimately, how mixed selectivity is expressed in regions such as V6A, PE, and PEc.

The full model includes all task-related regressors. This model is designed to capture the maximum amount of variance in the neuronal data by accounting for all the possible factors that could influence neuronal activity during the task. The full model provides the baseline for assessing how well neuronal activity can be explained when considering all relevant task phases together. In contrast, nested models are simplified versions of the full model, where one or more task variables or epochs are excluded. By systematically removing certain regressors, we can evaluate the relative contribution of each to the overall model. This process allows us to test specific hypotheses about which aspects of the task are most crucial in driving neuronal responses. For example, we can assess whether neuronal activity is more strongly influenced by movement initiation compared to fixation or holding phases. Nested models are particularly useful for identifying the key regressors that explain neural firing patterns, providing insights into the selectivity and responsiveness of neurons to specific task phases.

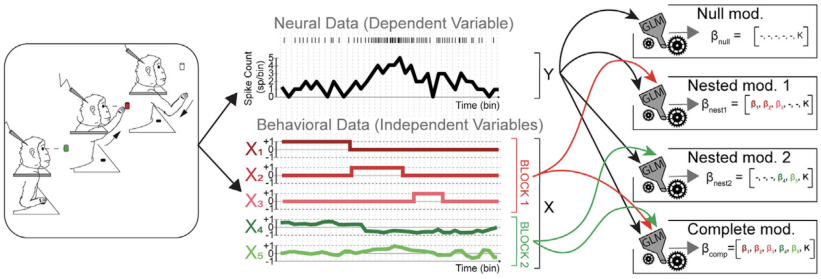

Figure 9: *Schematic representation of full, nested, and null models used to analyze neuronal activity during an eye-hand coordination task. The full model includes all task variables (X_1, X_2, ..., X_5) to explain neural firing rates, while nested models exclude specific variables to assess their contribution. The null model, serving as a baseline, excludes all task variables to measure task-related variance. Each model is fitted using a Generalized Linear Model (GLM), and the resulting beta coefficients (β) reflect the weight of each task variable in explaining the neural response. Figure modified from* (Vaccari et al., 2021).

Finally, the null model serves as a baseline comparison, where no task-related variables are included. This model assumes that neuronal activity is independent of the task and provides a measure of how well the model fits the data without considering any of the task epochs. The null model is essential for determining the overall explanatory power of the full and nested models. To quantitatively assess the significance of neural selectivity across task epochs, we leveraged the log-likelihood values obtained from the full and nested models to calculate the R^2_{pseudo}. This metric provides a relative measure of model fit, comparing the explanatory power of the full model (which includes all task epochs) to that of the nested models (which exclude one or more epochs).

Together, these three models offer a robust framework for dissecting the contributions of different task phases to neural responses. This approach, as applied in the work of Vaccari et al. (2021) and Diomedi et al. (2020), is central to understanding how neurons in parietal areas encode a combination of sensory and motor signals, and how these signals vary across different task conditions.

2.2.4 Generating Neural "Functional Fingerprints"

To explain the significance of neural selectivity across task epochs, we calculated two important metrics: w-values and R^2_{pseudo}. These metrics provide insights into how well the neuronal activity can be explained by different task-related variables.

R^2_{pseudo} is a relative measure of model fit, often used in generalized linear models (GLMs) to evaluate how well the model captures the variability in neuronal firing. In our implementation, we used a Poisson regression model to fit the spike counts, with predictors corresponding to the task epochs (e.g., fixation, movement). The formula for R^2_{pseudo} is:

$$R^2_{\text{pseudo}} = \frac{\mathcal{L}_{\text{nested}} - \mathcal{L}_{\text{null}}}{\mathcal{L}_{\text{full}} - \mathcal{L}_{\text{null}}} \tag{4}$$

Where:

- $\mathcal{L}_{\text{nested}}$: The log-likelihood of the nested model, which excludes one or more task epochs.
- $\mathcal{L}_{\text{null}}$: The log-likelihood of the null model, where no task regressors are included, representing the baseline fit.
- $\mathcal{L}_{\text{full}}$: The log-likelihood of the full model, which includes all task epochs and conditions.

This formula allows us to compare the full model, which includes all task epochs, with reduced models that exclude one epoch at a time. By calculating $\mathbf{R^2}$ pseudo for each epoch, we can determine the relative contribution of each task phase to the overall neural response (Diomedi et al., 2020; Vaccari et al., 2021). The calculation of w-values serves to quantify the relative importance of each task epoch in explaining the neural response. A higher w-value indicates that the corresponding epoch contributes significantly to the neuronal firing pattern. The formula for w-values is derived from the log-likelihood differences between nested models, each excluding one task epoch at a time, and the full model, which includes all epochs. The formula is:

$$\omega = 1 - R^2_{\text{pseudo}} \tag{5}$$

Where:

- ω: The omega value, which is a measure of the proportion of variance unexplained by the model (1 minus the R^2_{pseudo}).
- R^2_{pseudo}: The R^2_{pseudo} value , which measures the proportion of variance explained by the model relative to a null model.

These metrics were calculated for each neuron and task condition, providing a detailed profile of neural selectivity. This approach was heavily influenced by the methods proposed in (Vaccari et al., 2021) and (Diomedi et al., 2020), where Poisson GLMs were applied to model neuronal responses in similar tasks.In conclusion, the calculation of w-values R^2_{pseudo} allowed us to quantify the importance of different task epochs in driving neuronal activity. The w-values, in particular, quantified the contribution of each task epoch to neuronal activity and served as the foundation for constructing neural functional fingerprints (NFFs). By leveraging these metrics, it was possible to encapsulate how neurons selectively encode task-related information, creating a framework for exploring the mixed selectivity characteristic of areas V6A, PE, and PEc.

Neural functional fingerprints (NFFs) represent a comprehensive summary of the neural selectivity across different behavioral and cognitive conditions. These fingerprints are designed to capture how neurons respond to multiple stimuli and task parameters, providing a unique "signature" of neural functionality. By calculating NFFs, we can evaluate how different neurons contribute to sensory-motor integration and other cognitive processes, particularly in areas like V6A, PE, and PEc, which are involved in visuomotor coordination (Vaccari et al., 2021). In this thesis, I generated NFFs based on the neural activity recorded across several task conditions. The task conditions were defined by the combination of spatial targets and motor demands during the reaching task. For each neuron, we measured its response (in terms of spike counts) across different epochs of the task (e.g., fixation, movement, hold). These epochs were aligned with key behavioral events, allowing us to capture how each neuron responded to different phases of the task. The binned spike counts formed the basis of our functional fingerprint calculations, providing a detailed temporal profile of neural selectivity across conditions. By analyzing these spike counts within and across conditions, we aimed to uncover how neurons encode different aspects of the task. The generation of neural functional fingerprints was essential

for assessing the mixed selectivity of neurons, as discussed by (Diomedi et al., 2020) and (Vaccari et al., 2021). This mixed selectivity is particularly relevant in areas like V6A, where neurons exhibit complex responses that integrate both sensory and motor information (Vaccari et al., 2021).

2.2.5 Quantifying Task Epoch Contributions Using Omega Values

To determine the most influential task epochs in neuronal activity, we analyzed omega (ω) values, which quantify the contribution of each epoch to the overall firing rate modulation (Paninski, 2004). First, processes neuronal data, extracting spike counts and task event markers, and bins them according to pre-defined task epochs. This segmentation enables precise analysis of neural responses aligned with task phases and next the code calculates w-values by estimating the relative importance of each epoch in modulating neuronal activity. Finally, the script identifies key epochs by highlighting those that contribute at least 85% to the total omega value of each neuron, which are marked with asterisks in the figures. This threshold helps distinguish the most influential epochs in a neuron's functional fingerprint, indicating which task phases are most significant in driving neuronal modulation (Diomedi et al., 2020; Vaccari et al., 2021). This approach provides a rigorous statistical basis for capturing both selective and mixed-selective patterns across areas V6A, PE, and PEc, offering insights into how neurons integrate sensory and motor information essential for eye-hand coordination.

2.2.6 Principal Component Analysis (PCA)

Principal Component Analysis (PCA) is a powerful dimensionality reduction technique used to identify patterns in high-dimensional data. In the context of this thesis, PCA was applied to analyze the neuronal activity in areas V6A, PE, and PEc by reducing the dimensional complexity of w-values computed for task epochs. This approach highlights the principal directions (or components) that capture the most variance in the data, providing a concise representation of neuronal population behavior.

Mathematical Foundation

PCA operates by transforming the original data matrix $\mathbf{X}$ into a new coordinate system where the greatest variance by any projection lies on the first coordinate

(principal component), the second greatest variance on the second coordinate, and so on. This transformation is mathematically derived as follows:

Data Centering The data matrix $\mathbf{X}$ of size $n \times p$ (where n is the number of observations and p the number of variables) is centered by subtracting the mean of each variable:

$$\tilde{X}_{ij} = X_{ij} - \frac{1}{n}\sum_{i=1}^{n} X_{ij}. \tag{6}$$

Here, $\tilde{X}_{ij}$ represents the centered value of the data, X_{ij} is the original value, and the mean is subtracted across all observations for each variable.

Covariance Matrix The covariance matrix $\mathbf{C}$ of the centered data is calculated as:

$$\mathbf{C} = \frac{1}{n-1}\tilde{\mathbf{X}}^T\tilde{\mathbf{X}}. \tag{7}$$

The covariance matrix quantifies the relationships (covariance) between each pair of variables in the dataset, forming the basis for identifying the principal components.

Eigenvalue Decomposition The covariance matrix $\mathbf{C}$ is decomposed into eigenvalues (λ_k) and eigenvectors ($\mathbf{v}_k$) as:

$$\mathbf{C}\mathbf{v}_k = \lambda_k \mathbf{v}_k, \quad k = 1, \ldots, p. \tag{8}$$

The eigenvalues (λ_k) represent the amount of variance explained by each principal component, while the eigenvectors ($\mathbf{v}_k$) define the directions of these components in the original data space.

Projection Finally, the data is projected onto the principal components:

$$\mathbf{Z} = \tilde{\mathbf{X}}\mathbf{V}, \tag{9}$$

where $\mathbf{Z}$ is the transformed data, and $\mathbf{V}$ is the matrix of eigenvectors. This step transforms the original data into a new coordinate system defined by the principal components, simplifying its structure and highlighting the main sources of variance.

3 RESULTS

To investigate the neuronal mechanisms underlying visuomotor integration, we analyzed data from 30 sorted neurons recorded from each of the V6A, PE, and PEc areas in a non-human primate performing a reach-to-grasp task. Neuronal activity was examined across different task epochs to assess selective and mixed-selective responses. We applied Generalized Linear Models (GLMs) to fit neuronal firing rates using task regressors, quantifying the contribution of specific epochs through pseudo-R^2 and omega (ω) values. Functional fingerprints were then constructed to characterize how neurons encode sensory and motor information. The following sections present the results of this analysis, starting with single-cell activity patterns and progressing to population-level insights into mixed selectivity across cortical areas.

3.1 Analysis at the Single-Cell Level

3.1.1 Comparative Analysis of Observed and Estimated Firing Rates

The comparison between estimated and observed firing rates provides a crucial validation of the model's ability to predict neuronal activity (Figure 10). In this analysis, firing rates were modeled using a Poisson GLM, which estimated the neuronal responses based on task-related parameters. By calculating the estimated firing rates ($Y_{\text{estimated}}$) and comparing them with the observed rates (Y_{observed}), the model's accuracy in capturing the dynamic modulation of neurons during task epochs was evaluated. The moving average was implemented using a filter with a defined window size. Specifically, for each data point, the filter computed the average of a set number of surrounding points, creating a smoothed curve that retained essential fluctuations while minimizing high-frequency noise. In this case, a window size of 10 bins was chosen, meaning each data point in the smoothed series represents the average of 10 adjacent points. This window size strikes a balance: it is large enough to effectively reduce noise yet small enough to preserve meaningful variations related to task events.

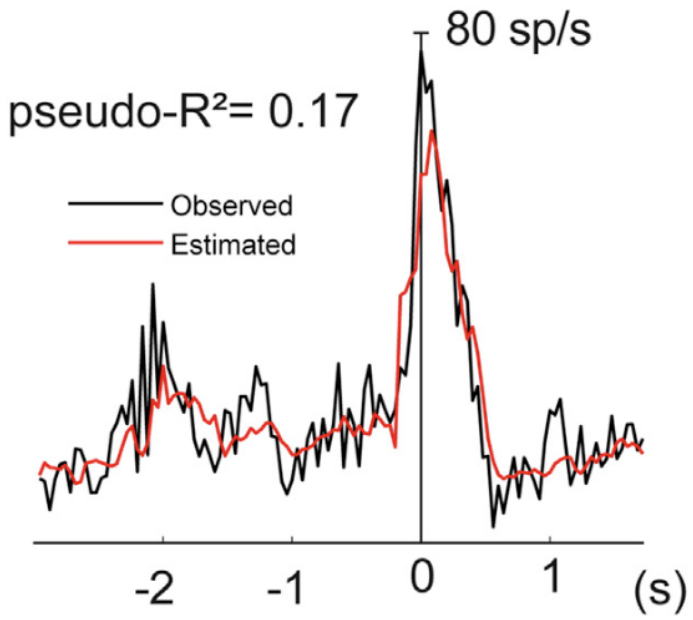

Figure 10: *Comparison of observed (black) and estimated (red) firing rates, smoothed with a moving average. The pseudo-R^2 value (0.17) indicates the model's accuracy in predicting neuronal responses during task-related events. Figure modified from* (Diomedi et al., 2020).

In this implementation, the filter moved across the data with a stride of one, meaning that it progressed by one data point at a time, without skipping any points. This choice of stride results in an overlapping window, where each new point in the smoothed series is influenced by the previous ones. The overlapping nature of the filter creates a continuous, gradual smoothing effect, enhancing the continuity of the firing rate data over time. Applying the moving average to both the observed and estimated firing rates helped reveal the general firing patterns of neurons during task conditions, filtering out random spikes that could obscure these patterns. By smoothing the data, it became easier to assess how well the model predictions aligned with actual neural responses, particularly across different task epochs. This approach, therefore, was crucial in accurately visualizing and interpreting neural firing rates, making the comparison between observed and estimated values more reliable. The chosen parameters — window size and stride — were selected to optimize the balance between reducing noise and retaining task-related trends, thus ensuring that the smoothed data retained its relevance to the underlying neural activity.

3.1.2 Neuronal Selectivity Patterns and Functional Fingerprints

Neurons in the posterior parietal cortex (PPC) exhibit diverse selectivity patterns, playing a crucial role in sensorimotor integration. The concept of mixed selectivity, extensively studied in electrophysiological recordings, captures the ability of neurons to respond to multiple task-related variables, rather than encoding a single feature in isolation. Understanding these selectivity patterns is fundamental for decoding neural representations of movement planning and execution. This chapter builds on the findings of (Diomedi et al., 2020; Vaccari et al., 2021) to explore how neurons in area V6A exhibit distinct functional fingerprints. The approach relies on the analysis of omega values (w-values), a metric that quantifies a neuron's selectivity across different task epochs. By examining the functional fingerprints of neurons, we aim to distinguish between those that exhibit broader integration across multiple epochs and those that show stronger modulation in specific task phases.

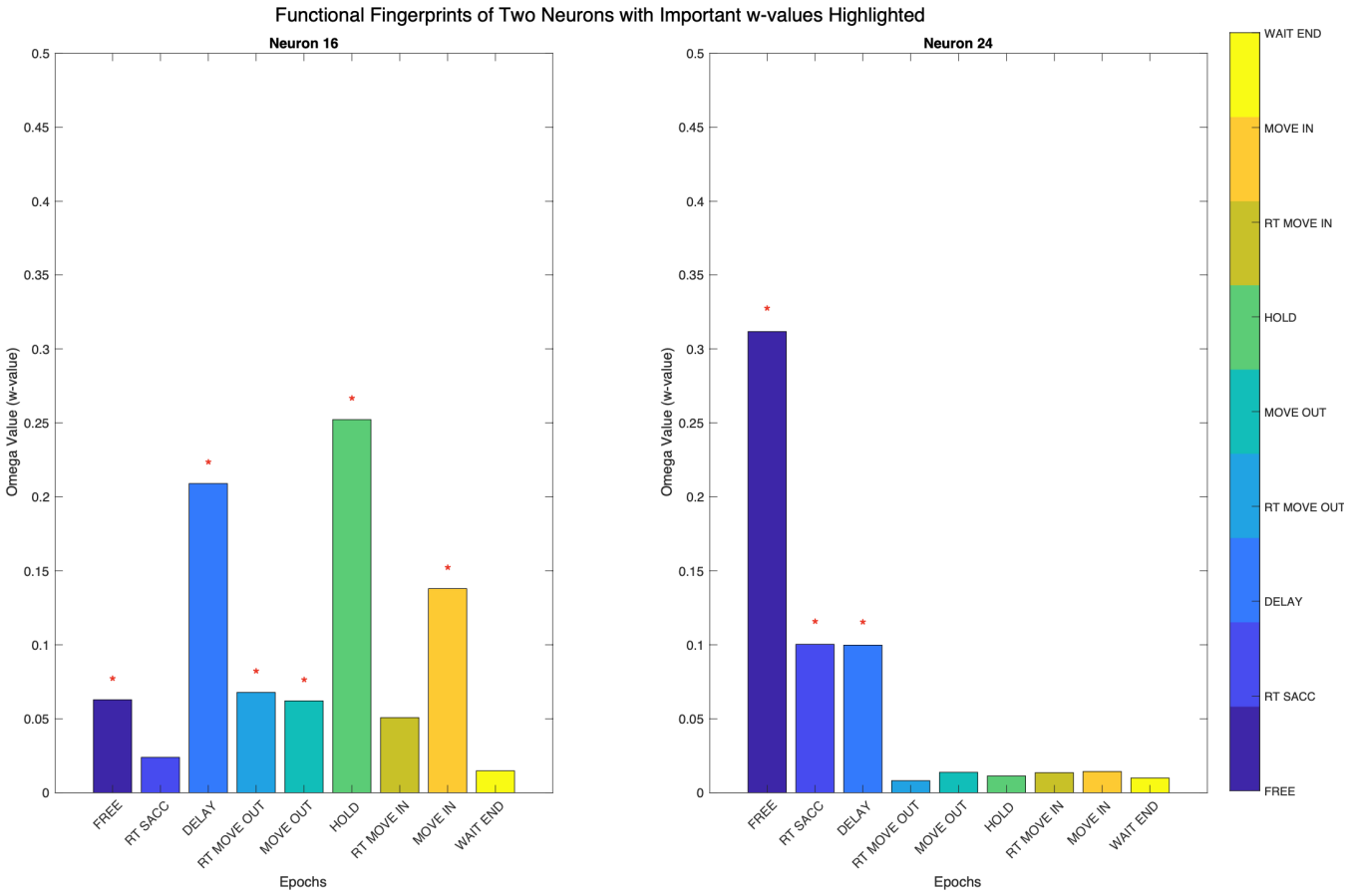

Figure 11: *Functional fingerprints of Neurons 16 and 24 in V6A highlight contrasting selectivity patterns.*

The functional fingerprint analysis of two representative neurons from area V6A is depicted in (Figure 11). The bar plots display the omega (ω) values associated with different task epochs, with higher values indicating stronger selectivity. The neuron on the left (Neuron 16) exhibits a mixed selectivity profile, responding to multiple epochs with comparable intensity. Notably, significant activity is observed during the DELAY (0.22), HOLD (0.27), and MOVE IN (0.15) epochs. The relatively uniform distribution of w-values suggests that this neuron integrates information from various task phases, reflecting its involvement in multiple aspects of visuomotor processing. In contrast, the neuron on the right (Neuron 24) demonstrates a strongly selective profile, with a predominant response during the FREE epoch (0.32), followed by lower activity in RT SACC (0.12) and DELAY (0.11). This indicates a preference for encoding information related to movement initiation or preparatory processes, with minimal contribution from later task stages. The stark difference in selectivity between these two neurons illustrates the heterogeneity in V6A. While Neuron 16 integrates signals across multiple epochs, Neuron 24 acts as a more specialized encoder for a specific task component. This contrast highlights the continuous spectrum of mixed selectivity observed in V6A neurons, reinforcing the idea that neuronal selectivity is not confined to distinct functional classes but instead varies along a gradient of task-related modulation. Such a spectrum may be crucial for optimizing sensorimotor transformations, allowing the PPC to flexibly contribute to different phases of action planning and execution.

(Figure 12) represents the functional fingerprints of two representative neurons from area PE, illustrating their task-related selectivity across different epochs. Neurons in PE are known to be involved in proprioceptive and motor-related processing, contributing to movement coordination somatosensory integration. By analyzing their activation patterns, we can observe differences in the way these neurons contribute to motor-related processing.

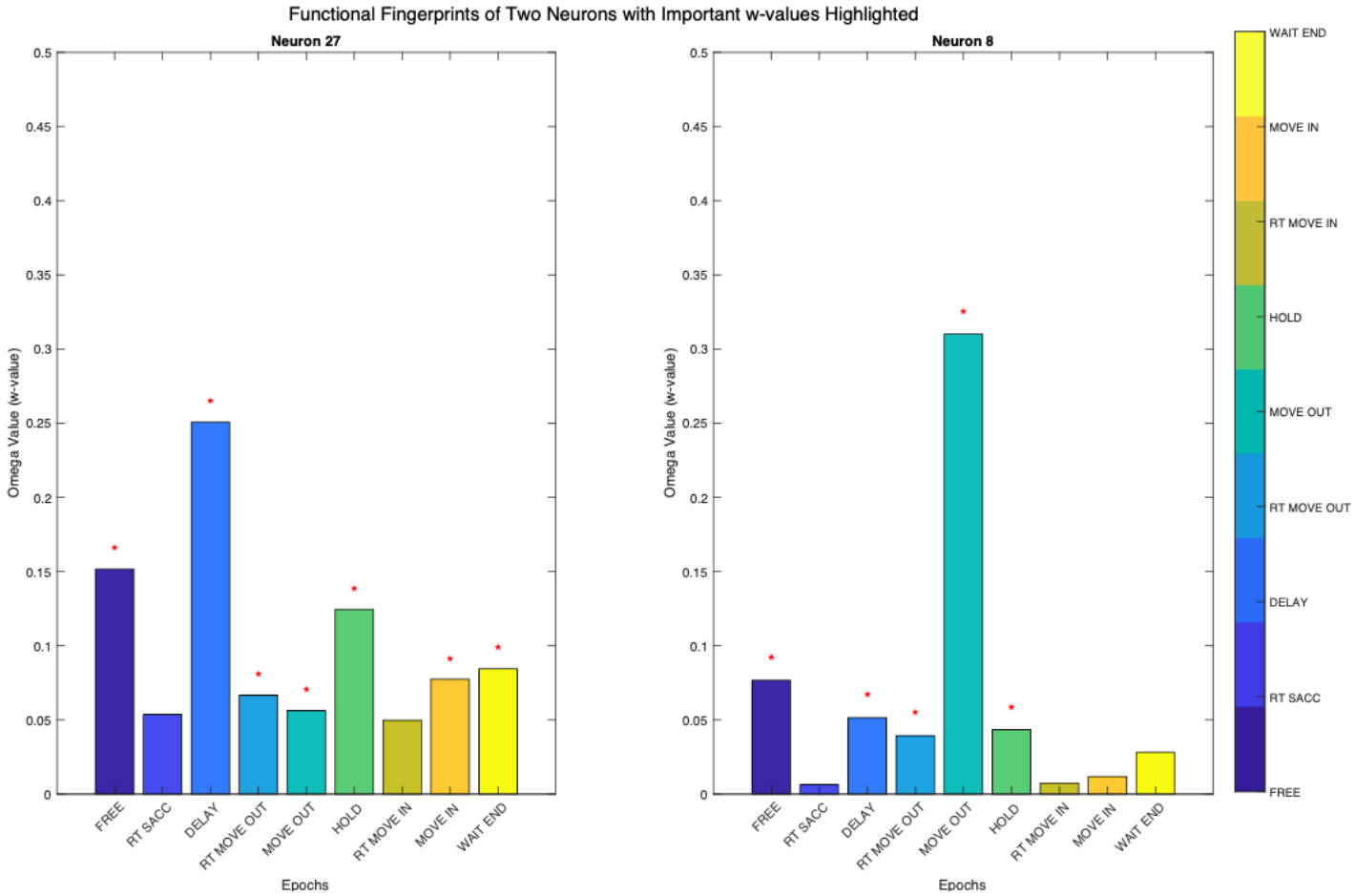

Figure 12: *Functional fingerprints of Neurons 27 and 8 in PE reveal distinct selectivity profiles.*

The neuron on the left (Neuron 27) exhibits a widespread selectivity, responding to multiple task epochs with varying degrees of modulation. The most prominent activity is observed during DELAY (0.26), followed by notable responses in FREE (0.16) and HOLD (0.12). Additionally, moderate activation is seen in MOVE IN (0.09) and WAIT END (0.10). This broad response pattern suggests that the neuron dynamically encodes task-relevant information across preparatory, execution, and post-movement phases. Conversely, the neuron on the right (Neuron 8) presents a more distinct tuning, with a pronounced peak in MOVE OUT (0.32), marking it as the dominant epoch of activation. Compared to this strong modulation, activity in other epochs, such as FREE (0.09), DELAY (0.07), and HOLD (0.08), remains relatively low. This distinct response profile suggests that Neuron 8 is primarily involved in motor execution, with a strong preference for the MOVE OUT phase, indicating a crucial role in movement initiation and limb displacement. Unlike Neuron 27, which integrates information across multiple task stages, Neuron 8 appears

to be more functionally specialized, predominantly encoding motor execution while showing minimal engagement in other task phases. The contrast between these two neurons highlights the variability in PE neuronal activity, where some neurons integrate information across multiple task stages, while others exhibit more constrained tuning to specific movement-related events.

(Figure 13) presents the functional fingerprints of two representative neurons from the PEc area, illustrating their selectivity related to the task in different epochs. Neurons in PEc are primarily involved in visuomotor coordination, integrating sensory and motor signals to support reach-related movements. By examining their activation across task epochs, we can observe differences in their response dynamics and the extent to which they contribute to action planning and execution.

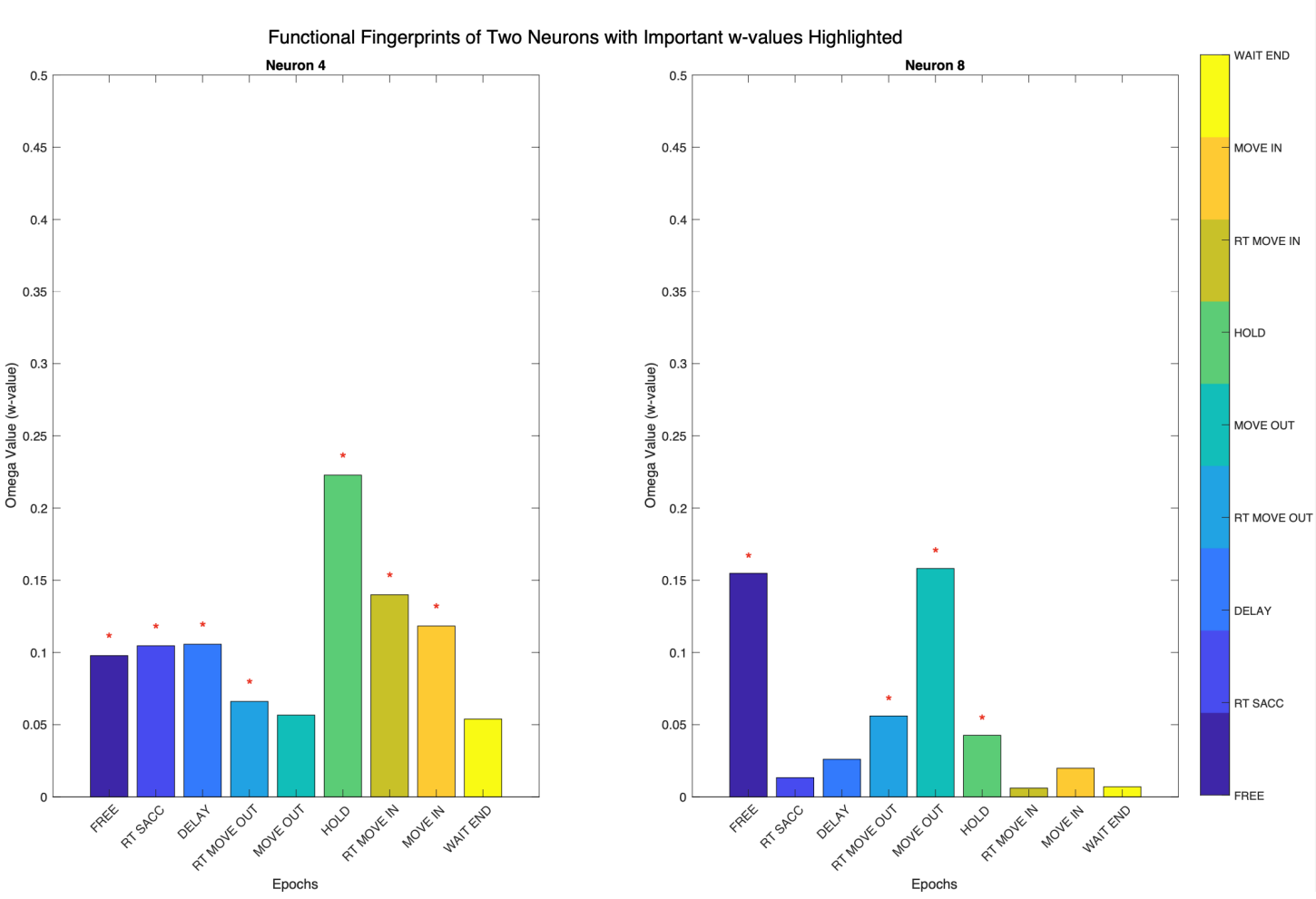

Figure 13: *Functional fingerprints of Neurons 4 and 8 in PEc reveal distinct selectivity patterns.*

The neuron on the left (Neuron 4) demonstrates a broad tuning, with moderate responses across multiple epochs and a notable peak in HOLD (0.27) and RT

MOVE IN (0.17). Smaller but significant contributions are observed in RT SACC (0.12), DELAY (0.11), and MOVE IN (0.13). This suggests that the neuron is engaged throughout different stages of movement preparation and execution, dynamically integrating information across task phases. In contrast, the neuron on the right (Neuron 8) exhibits a more focused response pattern, with pronounced activity in FREE (0.16) and HOLD (0.15) while showing weaker modulation in other epochs. Although some selectivity is maintained for MOVE OUT (0.08) and RT SACC (0.05), the overall distribution indicates a preference for encoding information primarily during early and intermediate movement phases, rather than across the entire task. The comparison between these two neurons highlights the variability in mixed selectivity within PEc. While Neuron 4 displays a distributed selectivity profile, integrating signals across both preparatory and movement-related epochs, Neuron 8 exhibits a more restricted modulation, preferentially encoding information at specific time points. This difference underscores the continuous nature of mixed selectivity, reinforcing the idea that PEc neurons do not belong to distinct functional subgroups but rather express a gradient of selectivity that varies depending on task demands.

3.2 Population-Level Analysis

3.2.1 Mixed Selectivity and Subpopulations

To further investigate the presence of mixed selectivity at the population level, we analyzed the distribution of w-values across task epochs using box plots for the three studied areas: V6A, PE, and PEc (Figure 14). These visualizations provide insights into the overall selectivity patterns across neurons, illustrating the variability and dispersion of w-values for each epoch. Each box plot represents the distribution of w-values across neurons, with the median (central line), interquartile range (IQR, box boundaries), and whiskers indicating the range of data distribution. Outliers, which represent neurons with particularly high selectivity for specific epochs, are denoted by red crosses. Despite minor differences, the overall structure of the box plots is remarkably consistent across V6A, PE, and PEc, reinforcing the idea that mixed selectivity is not confined to a specific subpopulation but is instead a widespread phenomenon throughout these parietal areas.

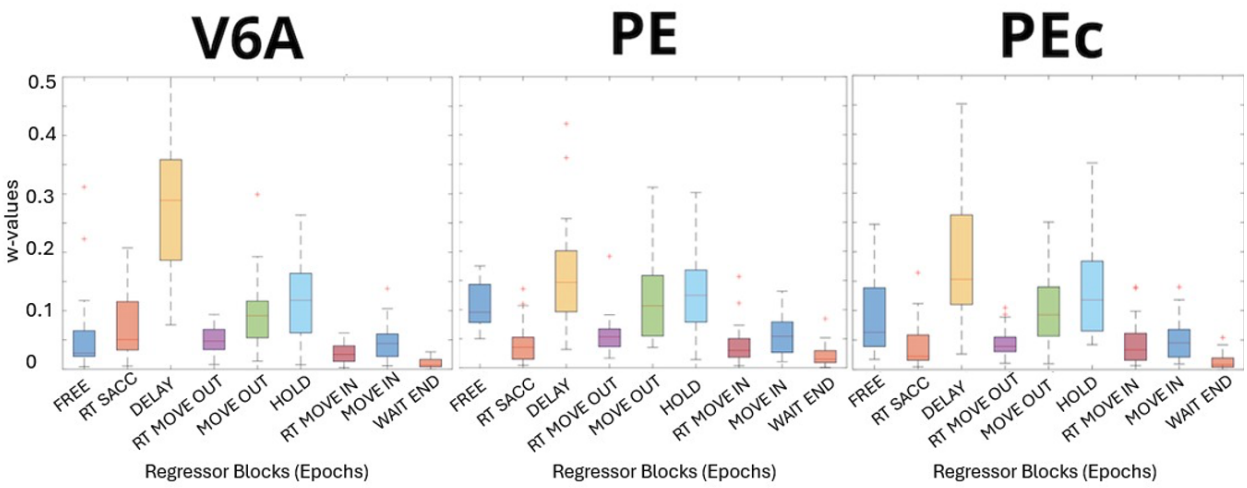

Figure 14: *Box plot of w-values across epochs for area V6A,PE,PEc*

In V6A, the highest median w-value is observed during the DELAY epoch, reaching approximately 0.25, with a broad interquartile range (IQR) spanning 0.15 to 0.35. This suggests that neurons in V6A exhibit strong selectivity for movement planning phases, with additional notable responses in RT SACC and HOLD, where upper whiskers extend beyond 0.2, indicating the presence of neurons that exhibit particularly strong modulation during these task phases. A similar trend emerges in PEc, where the DELAY epoch continues to show the highest median w-value (0.2), though with a slightly wider IQR compared to V6A, suggesting greater variability in neuronal responses. Notably, HOLD and MOVE OUT also exhibit high median values (0.15), reflecting significant neuronal engagement in both movement preparation and execution. This distribution hints at the role of PEc in integrating sensory and motor information across different stages of the task. The pattern observed in PE largely mirrors that of V6A and PEc, with the DELAY epoch again showing the highest w-values (0.2), followed by HOLD and MOVE OUT. However, PE exhibits a slightly wider IQR in the MOVE OUT and RT MOVE IN epochs, indicating a greater variability in neuronal selectivity during these task phases. This broader spread suggests that PE neurons may have a more heterogeneous role, with individual neurons displaying stronger selectivity for distinct movement-related components.

Although the FREE epoch exhibits relatively high w-values, we do not interpret it functionally, as it represents a baseline period rather than a specific task-related modulation. Its variability likely reflects general fluctuations in neuronal activity rather than selective encoding of task-relevant parameters. The presence of high w-values in multiple epochs, combined with the overlapping distribution patterns across V6A, PE, and PEc, highlights the continuous nature of mixed selectivity rather than the existence of discrete, functionally specialized neuronal subgroups. Importantly, no epoch appears to be exclusively dominant in any of the three areas, reinforcing the idea that these neurons do not encode a single feature in isolation but rather respond flexibly to multiple task conditions. Additionally, the spread of whiskers and the presence of outliers indicate that, while most neurons follow a general pattern of mixed selectivity, some show exceptionally strong selectivity for specific task phases. This could reflect task-dependent adaptation, where certain neurons become transiently more selective based on behavioral demands.

Implications for Sensorimotor Integration and Mixed Selectivity

To better define the presence of mixed selectivity across the three studied areas (V6A, PE, and PEc), we analyzed the distribution of w-values sorted in ascending order for each regression block (Figure 15). This approach provides insight into how neuronal populations in different cortical areas encode task-relevant information, highlighting both the proportion of neurons with low selectivity and those with strong modulation.

The overall structure of these distributions reveals a consistent pattern across the three areas, reinforcing the idea that mixed selectivity is a widespread characteristic of the posterior parietal cortex rather than being confined to specific neuronal subpopulations. The distribution curves show a progressive increase in w-values, indicating a gradual rise in neuronal selectivity across the population. Notably, in early epochs such as FREE and RT SACC, the curves suggest that neurons in V6A tend to reach higher w-values compared to PEc and PE, particularly in the upper percentiles. This could indicate that neurons in V6A contribute more prominently to motor preparatory processes. Similarly, the DELAY epoch, crucial for movement planning, exhibits a steep increase in selectivity values at higher percentiles in V6A, suggesting that a subset of neurons in this area may be more specialized for action planning. During movement-related epochs, including MOVE OUT, HOLD, RT MOVE IN, and MOVE IN, the distribution of selectivity remains largely comparable across all three areas, with no abrupt differences in the progression of w-values. This supports the notion that mixed selectivity is not functionally segregated but rather distributed along a continuous gradient, with neurons in all three areas encoding a mixture of task-related information.

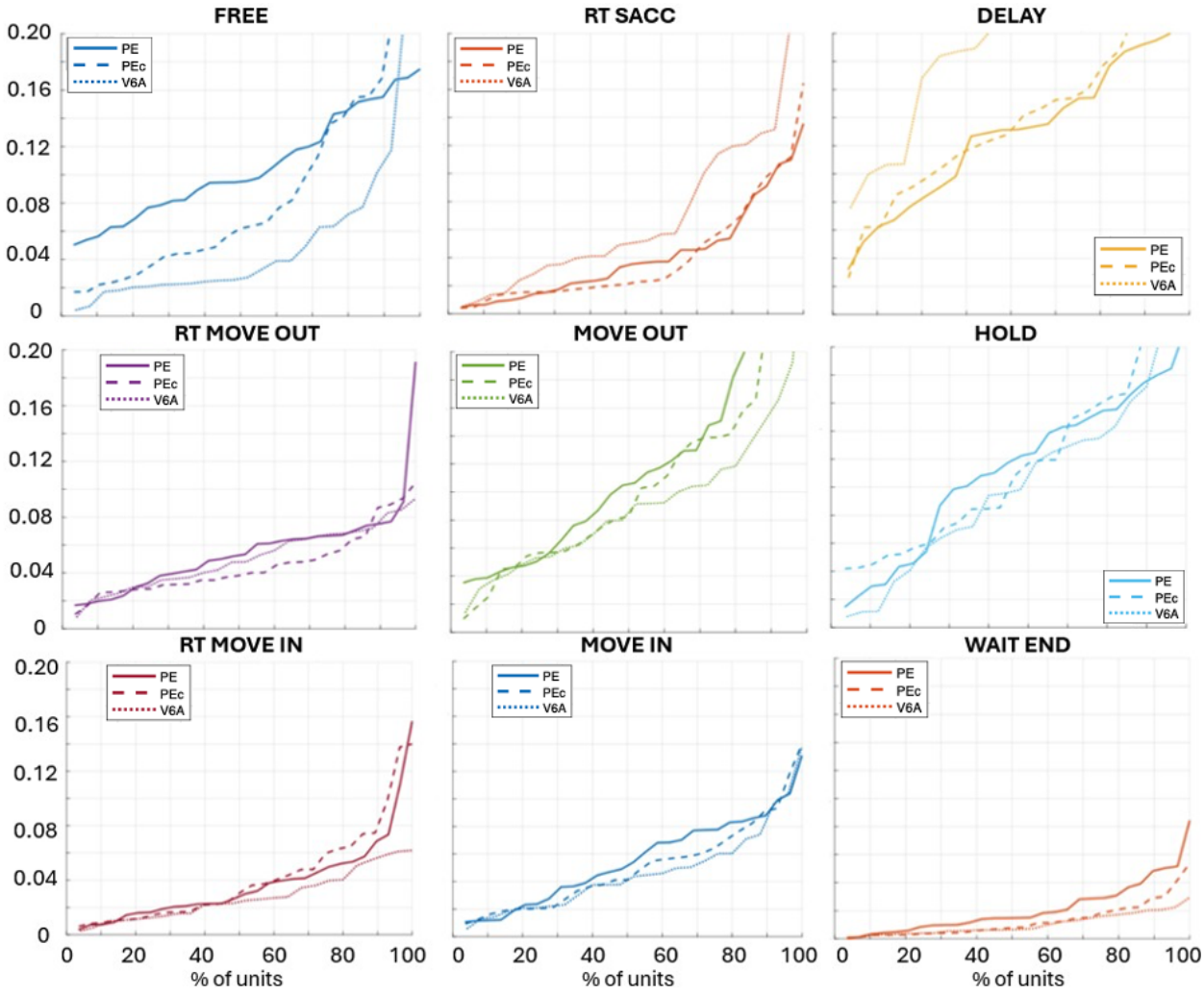

Figure 15: *Sorted w-values for different epochs in area V6A,PE,PEc*

To quantify these observations, we applied the Kolmogorov-Smirnov (KS) test to compare the distributions of w-values between cortical areas across epochs. For the FREE epoch, significant differences were found between PE and PEc ($p = 0.0070$), PEc and V6A ($p = 0.0256$), and PE and V6A ($p < 0.0001$), indicating that neuronal selectivity is not identically distributed across these areas during spontaneous activity. Similarly, in the DELAY epoch, differences were observed between PEc and V6A ($p = 0.0157$) and PE and V6A ($p = 0.0005$), further supporting the idea that V6A exhibits a slightly stronger selectivity for movement preparation compared to PE and PEc. The RT SACC epoch also displayed a significant difference between PEc and V6A ($p = 0.0157$), reinforcing the trend observed in preparatory activity. Conversely, no significant differences were found in HOLD, MOVE IN, and MOVE OUT, where the w-value distributions across the three areas remain statistically similar.

This finding aligns with the hypothesis that movement execution is encoded in a distributed manner across PPC neurons, rather than being confined to specific cortical regions.

3.2.2 Key Task Blocks Driving Neuronal Responses in Areas V6A, PEc, and PE

The histograms presented in (Figure 16) illustrate the distribution of the minimum number of important extrinsic regressor blocks required to explain 85% of the total w-values for each neuron across the three cortical areas: V6A, PE, and PEc. By examining these distributions, we can discern the extent of mixed selectivity and the degree of neuronal specialization in each area, shedding light on how different regions of the posterior parietal cortex (PPC) contribute to task-related processing. The x-axis in these histograms represents the number of significant regressor blocks, while the y-axis indicates the number of neurons that require this count of blocks to account for the majority of their activity. This analysis is crucial for understanding the variability in information encoding, as some neurons respond primarily to a few regressors (indicating higher specificity), while others exhibit distributed activity across multiple regressors (reflecting broader mixed selectivity).

In PE, the histogram displays a prominent peak around five to six regressor blocks, suggesting that a substantial portion of neurons in this area relies on multiple task parameters to reach the threshold of 85% explained variance. This distribution indicates a balanced representation of both specialized and broadly tuned neurons, supporting the concept that PE neurons integrate various sensory and motor signals in a flexible manner. The distribution for PEc shows a slightly different pattern, with the majority of neurons requiring around four to five regressor blocks. This narrower range suggests a more concentrated form of mixed selectivity, where neurons are predominantly driven by a default number of task-related variables. The narrower peak in PEc could indicate a more defined role in specific aspects of sensorimotor integration, focusing on fewer but highly influential parameters.

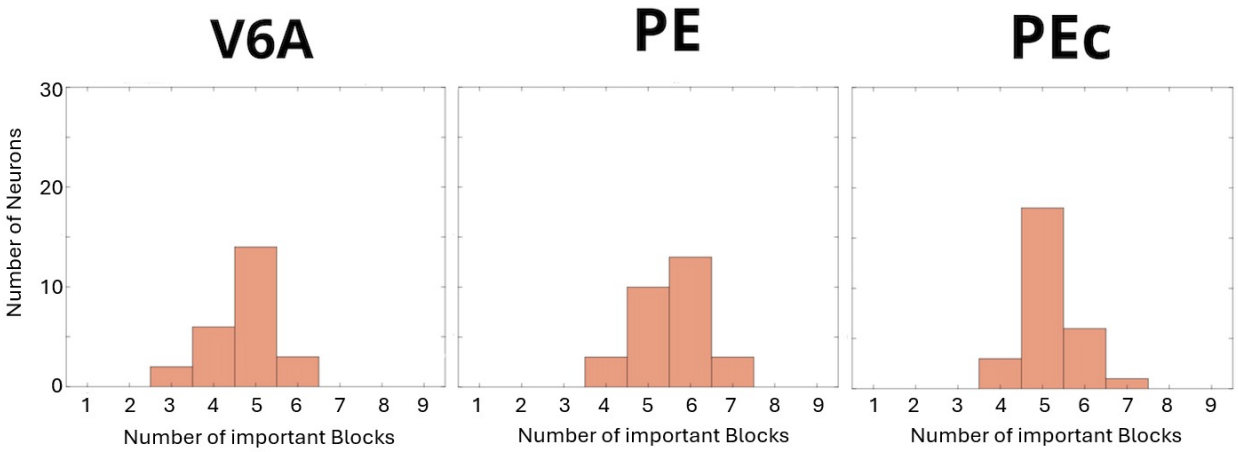

Figure 16: *Distribution of neurons in area V6A, PE, PEc based on the minimum number of regressor blocks driving their selectivity.*

In contrast, the histogram for V6A reveals a broader spread, with some neurons requiring as few as three regressor blocks, while others require up to six. While a slightly broader distribution is observed, the differences between V6A and the other areas are subtle, suggesting that all three regions exhibit a highly comparable structure of mixed selectivity. Rather than indicating distinct processing strategies, this slight variability in V6A may reflect the region's involvement in coordinating multiple visuomotor signals, leading to a minor increase in the number of regressors required to capture neuronal activity. This diversity in V6A aligns with its known role in the processing of complex visuomotor transformations, essential to guide coordinated eye and hand movements. These findings collectively underscore the continuum of mixed selectivity present in the PPC, where neuronal responses are not confined to distinct functional clusters but rather span a wide range of integrative capabilities. The ability of neurons to respond to multiple task parameters highlights the flexible and adaptive nature of cortical processing, enabling efficient sensorimotor transformations necessary for complex behaviors like reaching and grasping.

Overall, the histograms provide compelling evidence that mixed selectivity is a pervasive and intrinsic property of neurons in V6A, PE, and PEc. The variation in the number of regressor blocks required across these areas suggests that while all three regions engage in distributed processing, each area may exhibit unique specializations depending on the behavioral context and task demands. This nuanced understanding of neuronal encoding supports the broader concept that the PPC operates as a dynamic network, seamlessly integrating diverse sensory and motor inputs to facilitate goal-directed actions.

3.2.3 Exploring Neural Variability Through PCA

Understanding how neurons encode task-relevant information requires examining their selectivity patterns beyond individual epochs. Principal Component Analysis (PCA) provides a dimensionality-reduced visualization that captures the structure of neuronal modulation across the three cortical areas V6A, PE, and PEc.By projecting the w-values onto the first three principal components (PC1, PC2, PC3), we can assess whether neuronal responses follow distinct clustering patterns or instead form a continuum, supporting the hypothesis of mixed selectivity. In these three-dimensional representations, each dot corresponds to a single neuron, with its color reflecting the relative contribution of three key epochs: DELAY, MOVE OUT, and HOLD.

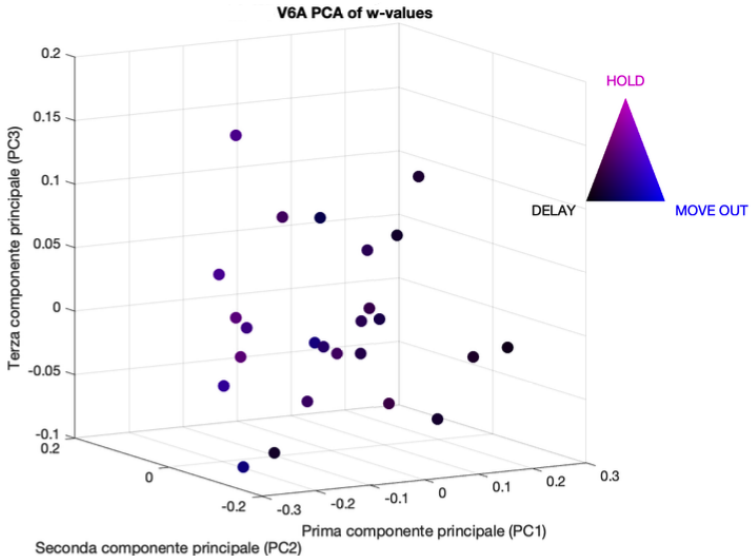

Figure 17: *Principal Component Analysis (PCA) of w-values for area V6A*

The triangular legend illustrates the color gradient, reinforcing that neurons encode information in a distributed fashion rather than being exclusively tuned to a single task phase. The overall distribution of neurons across PCA space reveals a continuous, overlapping pattern, with no indication of discrete functional subgroups, which aligns with the idea that neuronal activity in V6A, PE, and PEc operates along a gradient of task-related modulation. Across the three areas, the first three principal components account for a substantial portion of the total variance: 82.12% in V6A, 83.29% in PE and 81.53% in PEc. These high variance values indicate that the dimensionality reduction effectively captures the majority of task-related modulation in neuronal activity. Given that such a high proportion of the variance is explained by just the first three components, we can be confident that the main trends in neuronal selectivity have been preserved, and additional components would contribute only minimal new information. A comparison across the three regions highlights subtle differences in their respective distributions. In (Figure 18) the distribution of points remains relatively compact, indicating that neurons in PE share a more consistent selectivity profile, integrating task-related information in a more uniform manner. In contrast, PEc neurons exhibit a broader spread along PC1 and PC2 (Figure 19), reflecting greater variability in w-values across different task phases. The increased dispersion along these axes indicates that PEc neurons modulate their activity in a more heterogeneous manner, encoding multiple task-related features with varying weights.

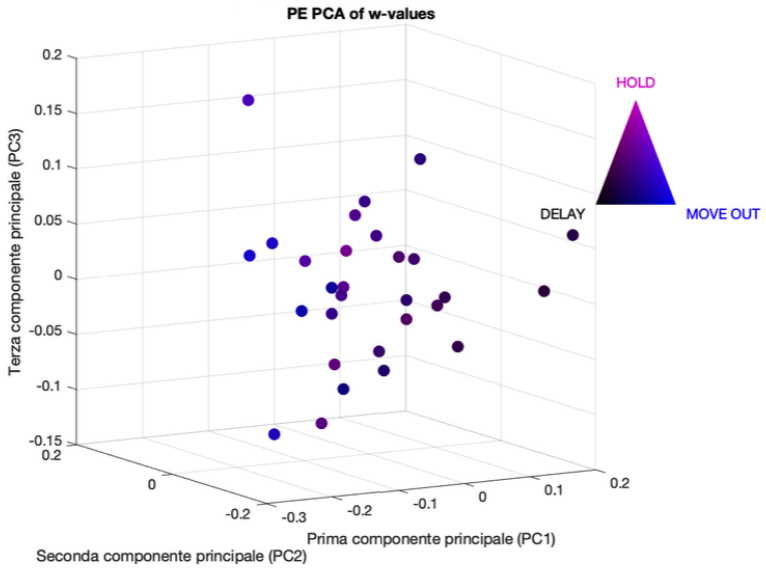

Figure 18: *Principal Component Analysis (PCA) of w-values for area PE*

In contrast, PEc neurons exhibit a broader spread along PC1 and PC2 (Figure 19), reflecting greater variability in w-values across different task phases. The increased dispersion along these axes indicates that PEc neurons modulate their activity in a more heterogeneous manner, encoding multiple task-related features with varying weights.

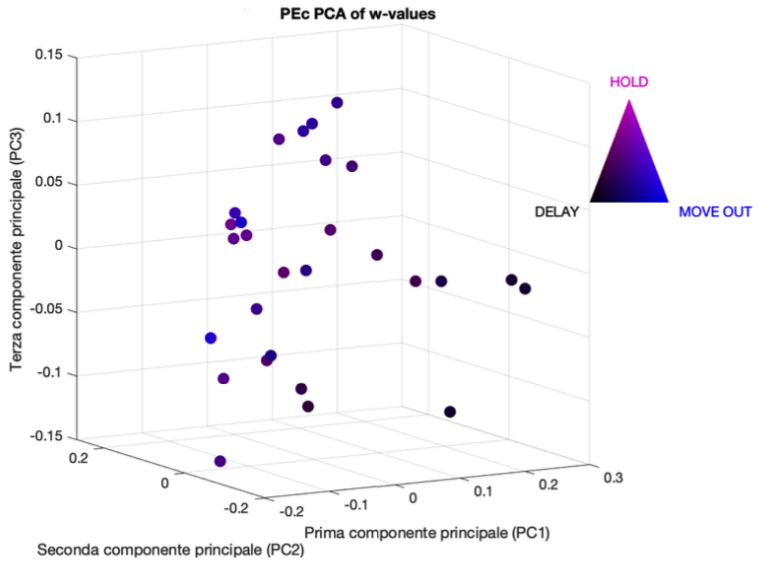

Figure 19: *Principal Component Analysis (PCA) of w-values for area PEc*

V6A neurons show a similarly dispersed distribution in PCA space compared to the other areas suggesting that neuronal encoding in V6A follows a similarly and overlapping complex pattern of mixed selectivity (Figure 17). Despite these nuances, the fundamental structure remains similar across all three regions, reinforcing the idea that selectivity is not confined to discrete neuronal subtypes but instead follows a continuous, integrative framework. This PCA-based visualization strengthens the conclusion that neuronal encoding in these areas is neither segregated nor specialized in distinct functional clusters. Instead, the findings further emphasize that PE, PEc, and V6A process reaching-related information through a flexible and distributed coding scheme, dynamically integrating sensory and motor signals without rigid functional boundaries.

4 DISCUSSION

In this study, we investigated how different regressors modulate neuronal activity in areas V6A, PE, and PEc, examining mixed selectivity through the application of Poisson GLMs. By analyzing neuronal firing patterns with this approach, we identified the functional fingerprint of each neuron, describing the ensemble of factors influencing its activity. Our results revealed that, in our sample of 30 neurons per area, we did not observe any neuron that was exclusively modulated by a single task variable. Instead, all analyzed neurons exhibited modulation by multiple factors, supporting the presence of a mixed selectivity encoding scheme. However, this does not exclude the existence of neurons with more selective tuning within these areas. This finding is consistent with the results of (Vaccari et al., 2024), where a decoding approach identified some neurons modulated by fewer parameters, although the majority still exhibited broad tuning across multiple task variables.

A fundamental question in sensorimotor processing is how different task-related inputs (e.g., visuospatial, motor, and somatic parameters) are integrated to drive coherent behavior. One possibility is that each area contains distinct neuronal subpopulations, each selectively encoding a specific feature (or fixed combinations of features). Alternatively, neurons could encode multiple parameters simultaneously, displaying full mixed selectivity. Our findings strongly support the latter hypothesis: across V6A, PE, and PEc, we observed that no neurons were highly tuned to a single variable, while most exhibited broad tuning across multiple task regressors. The distribution of w-values across neurons confirmed this pattern, resembling findings in other cortical areas, where only a small subset of cells show strong modulation by a single factor, while the majority display a continuum of mixed selectivity. The similarity in the distribution of w-values across V6A, PE, and PEc suggests that mixed selectivity is a fundamental and ubiquitous property of posterior parietal neurons, rather than being restricted to a particular cortical area. These findings support the idea that neuronal selectivity does not follow a strict categorical classification but instead varies along a continuous spectrum, allowing for flexible and adaptive sensorimotor transformations. The quantitative results, combined with the overall shape of the distribution curves, provide strong evidence that mixed selectivity is a pervasive and continuous property of PPC neurons, rather than being localized to discrete functional clusters. While V6A appears to exhibit a slightly stronger engagement during preparatory epochs, the general overlap of selectivity distributions

across V6A, PE, and PEc reinforces the idea that the parietal cortex does not rely on segregated functional modules but instead encodes task-related variables through a widely distributed and flexible neural representation.

From a computational perspective, mixed selectivity is advantageous because it allows for flexible sensorimotor integration and adaptive decision-making (Fusi et al., 2016). Previous studies suggest that neurons with mixed selectivity increase the computational capacity of a network, enabling efficient encoding of complex behaviors while maintaining robustness to noise and variability (Johnston et al., 2020). In associative cortical areas, such neurons may act as information hubs, integrating specialized inputs from different sources and distributing this information across the network with a increasing complexity moving away form the input. This idea is supported by theoretical models of parietal and associative cortices (Barak et al., 2013; Rigotti et al., 2010; Pouget and Snyder, 2000). Interestingly, other parietal areas, such as AIP (anterior intraparietal area), have been shown to exhibit partial mixed selectivity, where specific parameters (e.g., body parts involved in movement) are encoded in functionally segregated subpopulations (Zhang et al., 2017). However, in V6A, PE, and PEc, our analysis did not reveal such segregation: task-related parameters were randomly distributed across the neuronal population, reinforcing the idea of a fully mixed encoding strategy.

Overall, our findings indicate that mixed selectivity is a fundamental principle of neural processing in V6A, PE, and PEc, supporting their role in sensorimotor integration for eye-hand coordination and visuomotor transformations. Future studies should further explore whether specific subpopulations exist within these areas, or whether their encoding remains fully distributed, as suggested by our data.

4.1 The Importance of DELAY,HOLD and MOVE OUT in Mixed Selectivity

Our findings highlight the predominant role of the DELAY, MOVE, and HOLD blocks in shaping neuronal responses, emphasizing their fundamental contribution to the sensorimotor transformations occurring in these areas. This result aligns with prior literature on V6A, where it has been established that this area exhibits strong modulation during motor planning (Hadjidimitrakis et al., 2011), yet we extend this evidence to PE and PEc, suggesting a broader role for these regions in movement

preparation, execution, and postural maintenance. The strong involvement of these three task phases is consistent with recent studies applying decoding approaches, such as (Vaccari et al., 2024), who demonstrated that neural activity in V6A, PE, and PEc could effectively decode three distinct neural states corresponding precisely to DELAY, MOVE, and HOLD. This consistency between GLM-based modulation analysis and decoding approaches suggests a robust and reproducible neural representation of these task phases, reinforcing the notion that these areas do not merely encode discrete parameters but rather integrate multiple sources of information dynamically.

4.2 Study Limitations and Future Directions

While this study provides a detailed characterization of mixed selectivity in V6A, PE, and PEc, some limitations should be acknowledged. The fix-to-reach task used in our experiment allowed us to investigate neuronal modulation by various task-related factors (regressors).

A limitation of this study is the lack of recorded kinematic data during reaching movements. Our GLM models, while effective in capturing neuronal modulations, did not include regressors explicitly describing arm position and joint rotations. Given that somatosensory cells are present in V6A, PE, and PEc, future research should integrate detailed movement descriptors to explore how these areas contribute to the fine control of reaching movements. This could provide deeper insights into the sensorimotor transformations taking place in these regions. Furthermore, recent neuroimaging studies suggest the presence of a human homolog of area V6A in the superior parieto-occipital cortex. Applying similar GLM-based methods to human fMRI data could help distinguish the relative contributions of different task parameters in human PPC, bridging knowledge from non-human primate models to human sensorimotor processing. This would be particularly relevant for studying disorders affecting visuospatial and motor coordination.Beyond basic neuroscience, the functional fingerprints derived from this analysis could have practical applications in brain-machine interfaces (BMI). Specifically, our results could help identify the most informative neuronal populations for decoding movement intentions, optimizing BMI systems by selectively incorporating the most task-relevant neural units. This could enhance computational efficiency in neural decoding strategies. In summary, this study confirmed the presence of mixed selectivity across V6A, PE, and

PEc, with no clear evidence of functional segregation.

Future research should focus on refining spatial and temporal aspects of neuronal encoding, incorporating kinematic data, and extending these findings to human studies, ultimately contributing to a deeper understanding of parietal cortex function in action planning and execution.

5 CONCLUSION

This study highlights the pivotal role of the posterior parietal cortex (PPC) in facilitating visuomotor integration through mechanisms of mixed selectivity. By leveraging statistical modeling and advanced analytical approaches, this research revealed how areas V6A, PE, and PEc dynamically encode sensory and motor information across distinct task epochs. These findings provide valuable insights into the broader understanding of neural computations underlying adaptive behaviors, reinforcing the PPC's role as a central hub for sensorimotor transformations.

While certain methodological limitations and unanswered questions remain, this study establishes a solid foundation for future investigations into cortical dynamics. The integration of refined models and comparative analyses could further elucidate the complexities of neural processing, offering new perspectives on the interplay between sensory and motor signals in the brain. In addition to its theoretical contributions, this research has potential applications in areas such as neuroprosthetics and rehabilitation. Understanding the mechanisms of mixed selectivity could inform the development of more intuitive and effective interfaces for motor control, particularly for individuals with motor impairments. This thesis not only advances our knowledge of PPC functionality but also underscores the importance of interdisciplinary approaches in neuroscience research, paving the way for further exploration of the intricate relationship between neural systems and behavior.

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