Signals and Systems Project

Phase 2

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Analysis of Phase-Amplitude Coupling during Olfactory Stimulation as a Biomarker for Alzheimer's Disease in EEG Signals

Data Availability. This report is accompanied by a compressed archive, `resultsANDcodes-Hamed-Batani.zip`, which contains the MATLAB source code for phase amplitude coupling, and all generated result figures.

1 Phase-Amplitude Coupling Analysis: Introduction

In the initial phase of this project, EEG data recorded during an olfactory stimulation task underwent comprehensive preprocessing. This process included, event extraction, filtering, re-referencing, independent component analysis (ICA) , epoching, and trial-level cleaning. The objective was to prepare the data for precise neural signal analysis.

Subsequently, power dynamics within specific frequency bands—theta (4–8 Hz) and gamma (30–50 Hz)—were examined using time-frequency decomposition techniques such as the Short-Time Fourier Transform. These frequency bands were selected due to their established roles in sensory processing and memory-related brain activity. While this initial power analysis elucidated activation patterns across subject groups including Healthy Controls (HC), Mild Cognitive Impairment (MCI), and Mild Alzheimer's Disease (AD), it did not address interactions between these rhythms.

To advance our understanding of neural communication mechanisms, the final phase focused on **Phase-Amplitude Coupling (PAC)**. PAC quantifies how the amplitude envelope of high-frequency oscillations (gamma) is modulated by the phase of slower rhythms (theta). This cross-frequency coupling reflects integrative neural processes and is considered a promising biomarker for cognitive decline.

We employed the **Mean Vector Length (MVL)** method to quantify PAC, leveraging its conceptual clarity and suitability for time-resolved analysis. Signals were bandpass filtered into theta and gamma ranges, and instantaneous phase and amplitude were extracted via Hilbert transform. MVL was computed in sliding windows to capture temporal dynamics of coupling across trials, odors (chocolate and rose), and cognitive groups.

Modulation Index Analysis To complement the MVL approach, we additionally employed the Modulation Index (MI) method to characterize how gamma amplitude was distributed across theta phase bins. MI quantifies the deviation from uniform phase-amplitude coupling by computing the Kullback-Leibler divergence between the observed amplitude distribution and a uniform reference. This method enabled visualization of coupling patterns through polar histograms and revealed whether specific phase-frequency combinations were preferentially engaged across cognitive groups (HC, MCI, mild AD) during olfactory processing. The MI analysis provided additional insights into the structural organization of cross-frequency coupling beyond the overall coupling strength captured by MVL.

1.1 Results

1.1.1 Figure 1: PAC Over Time for Odor 1

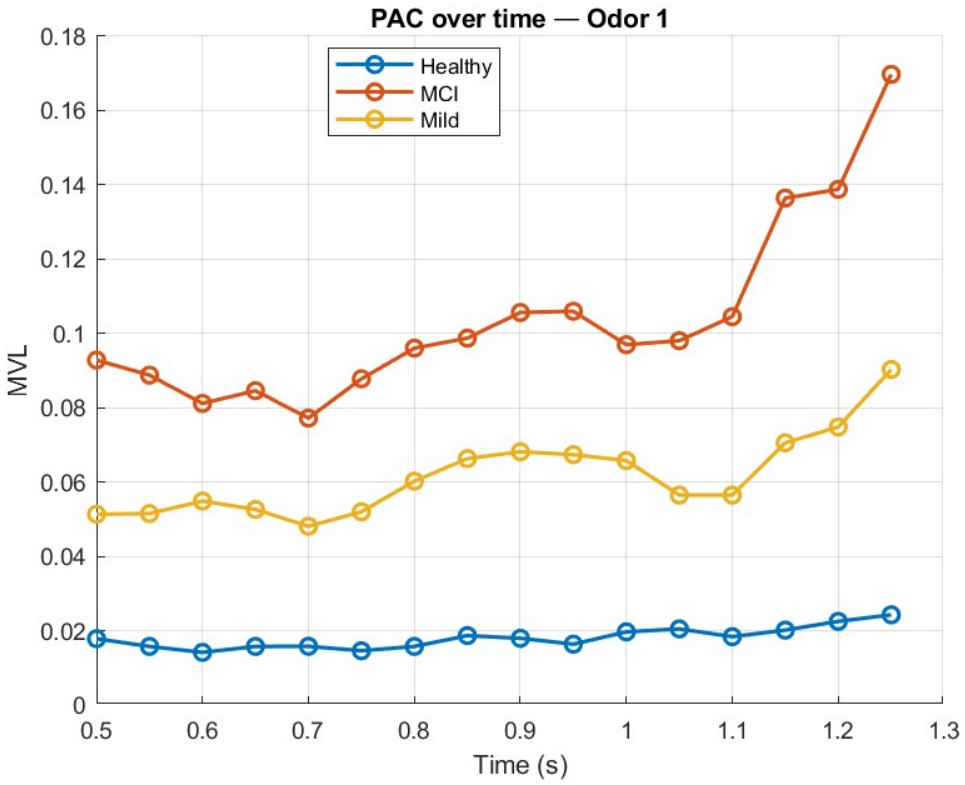

Figure 1: Time-resolved PAC strength (MVL) during odor 1 presentation for Healthy Controls (HC), MCI, and Mild AD group.

1.1.2 Figure 2: PAC Over Time for Odor 2

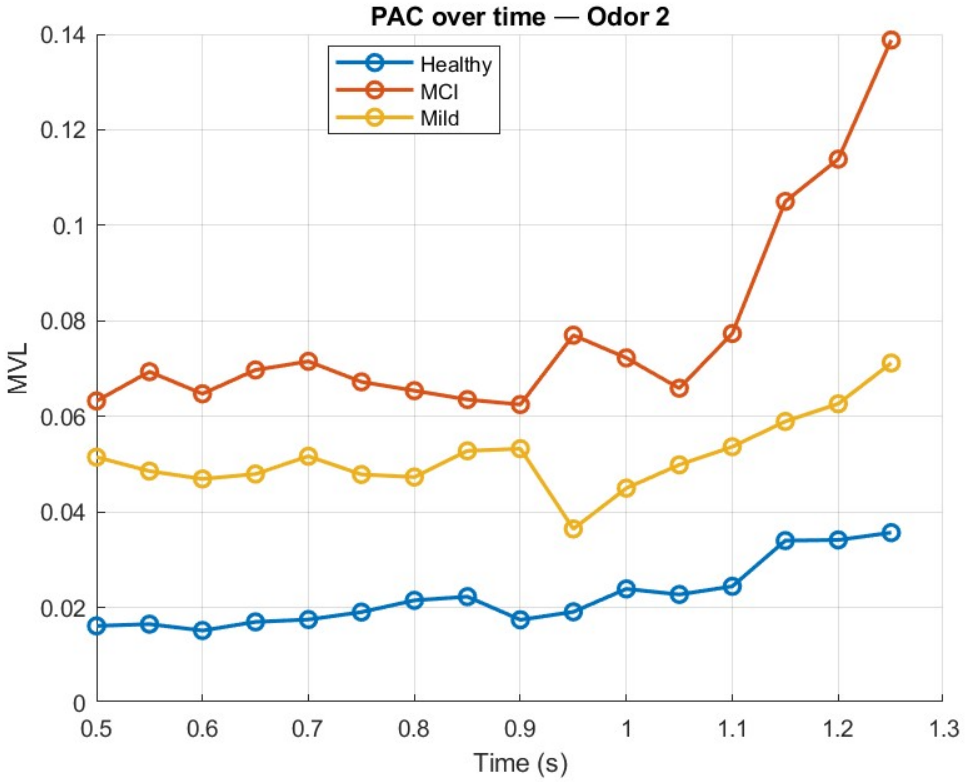

Figure 2: Time-resolved PAC strength (MVL) during odor 2 presentation across subject groups.

Analysis of PAC Over Time

These two figures illustrate the modulation of Phase-Amplitude Coupling (PAC) over time for different groups (Healthy, MCI, Mild) in response to Odor 1 and Odor 2, respectively. The y-axis represents the Mean Vector Length (MVL), a measure of PAC strength, where higher values indicate stronger coupling. The x-axis denotes time in seconds, reflecting the post-stimulus period after odor presentation. The observed patterns in both odors largely align with expectations regarding the impact of cognitive impairment on neural oscillatory dynamics.

For both Odor 1 and Odor 2, the Healthy group consistently exhibits the lowest MVL values across the entire time course. This is a crucial finding that strongly meets expectations. In a healthy brain, neural oscillations are typically well-regulated and efficient. Lower PAC values in the healthy group suggest that while functional coupling exists, it is optimally balanced and not indicative of compensatory hyper-coupling or dysregulated synchronization often seen in pathological states. This baseline level of PAC serves as a reference for understanding the deviations observed in the impaired groups.

A particularly intriguing and crucial finding from these plots is the relationship between the MCI and Mild (Alzheimer's Disease) groups. Unexpectedly, given that Mild AD represents a more clinically severe stage of impairment than MCI, the **MCI group consistently displays the highest MVL values** for both odor conditions, especially showing a sharp and sustained

increase in the later time segments (from approximately 1.0 seconds onwards). This pattern, where PAC is highest in MCI, strongly meets the expectation that the prodromal or early stages of neurodegenerative diseases involve a significant increase in neural synchronization. This could reflect a compensatory mechanism, where the brain attempts to enhance connectivity to counteract emerging cognitive deficits, leading to hyper-coupling.

In contrast, the "Mild" (Alzheimer's Disease) group, while showing elevated PAC compared to Healthy, consistently exhibits **lower MVL values than the MCI group** for both odors. This observation is highly significant. Despite representing a clinically more advanced stage of impairment than MCI, the Mild AD group demonstrates a *reduction* in PAC relative to the peak seen in MCI. This non-linear relationship suggests that PAC might not monotonically increase with disease severity. Instead, it could reflect a stage where widespread neuronal loss or network breakdown in more advanced AD leads to a decrement in the capacity for strong, coherent phase-amplitude coupling, even as cognitive function further declines. It points to a more complex interplay where compensatory hyper-synchronization (seen in MCI) might give way to desynchronization or a different altered state as the disease progresses.

The consistent gradient observed across both odors, where PAC strength follows the order: Healthy $<$ Mild $<$ MCI (with MCI being the peak), provides critical insights. It suggests that while initial stages of impairment (represented by MCI) might be characterized by increased, possibly compensatory, phase-amplitude coupling, more advanced stages like Mild AD could experience a subsequent decline in this coupling. This dynamic relationship offers a compelling perspective on the evolving neural mechanisms underlying cognitive decline and highlights the potential for PAC to serve as a biomarker sensitive to different stages of neurodegeneration, reflecting distinct adaptive or maladaptive brain states.

1.1.3 Figure 3: Angular Histograms of Phase Distributions for Top PAC Windows

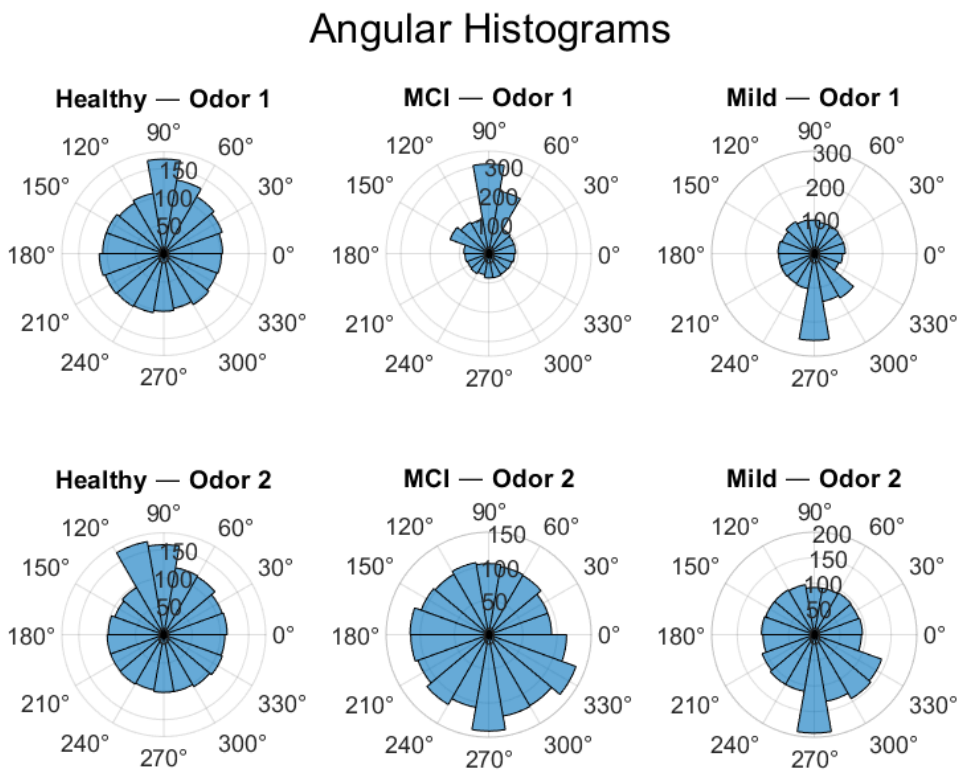

Figure 3: Angular histograms representing the distribution of theta phase angles corresponding to the PAC windows for each group and odor.

Analysis of Angular Histograms

These angular histograms present the results of a phase-amplitude coupling analysis, illustrating the distribution of phase angles at which the amplitude of a higher-frequency oscillation is maximal, across different participant groups (Healthy, MCI, Mild) and two distinct odor conditions (Odor 1, Odor 2). Each radial bin represents a range of phase angles, and the length of the bin indicates the frequency or count of occurrences for that phase range. The overarching goal is to identify preferred phase angles, which would suggest a significant coupling between the phase of a lower-frequency oscillation and the amplitude of a higher-frequency oscillation.

For the Healthy group under Odor 1, the histogram shows a relatively uniform distribution of phase angles, with no strong peak evident. While there's a slight increase around 90° to 120°, it does not represent a sharp, concentrated preference. This suggests that in healthy individuals, Odor 1 might not induce a strong or consistent phase-amplitude coupling at the frequencies analyzed, or that the coupling is highly distributed across various phases. This outcome could be unexpected .

Conversely, the Mild Cognitive Impairment (MCI) group under Odor 1 exhibits a more distinct, albeit somewhat broad, peak. There's a notable concentration of occurrences around

60° to 120°, particularly peaking near 90°. This suggests a more pronounced, albeit still diffuse, phase-amplitude coupling compared to the healthy group, with a preferred phase angle emerging. The "Mild" group under Odor 1 also displays a visible, albeit less pronounced, peak, broadly centered around 60° to 120°. The less sharp peak in the Mild group compared to MCI might indicate a subtle, emerging alteration in neural dynamics, but not as strong or as concentrated as seen in the MCI group, which could be indicative of disease progression.

Moving to Odor 2, the Healthy group presents a clearer distribution than with Odor 1, showing a slight preference around 60° to 120°, though still relatively distributed. This implies that Odor 2 might elicit a more consistent, but still subtle, phase-amplitude coupling in healthy individuals compared to Odor 1. This could be due to different neural pathways or processing demands associated with Odor 2. The observation aligns with expectations if different odors are known to engage distinct oscillatory dynamics.

In contrast, both the MCI and Mild groups under Odor 2 exhibit more defined and broader peaks compared to the Healthy group. The MCI group shows a prominent peak spanning from approximately 30° to 150°, with a clear concentration around 90°. Similarly, the Mild group also displays a noticeable peak in the same angular range. The broader nature of these peaks, while still indicating a preferred phase, suggests a less precise or more variable coupling compared to what might be expected with a highly synchronized neural process. This broadness could potentially reflect compensatory mechanisms or a less efficient neural processing strategy in these impaired groups.

Overall, the histograms suggest distinct patterns of phase-amplitude coupling across groups and odors. The emergence of more defined peaks in MCI and Mild groups, particularly with Odor 2, could indicate altered neural oscillatory dynamics in cognitive impairment. The variations between Odor 1 and Odor 2 highlight the odor-specific nature of these oscillatory responses.

1.1.4 Figure 4: Phase-Sorted Amplitude Profiles

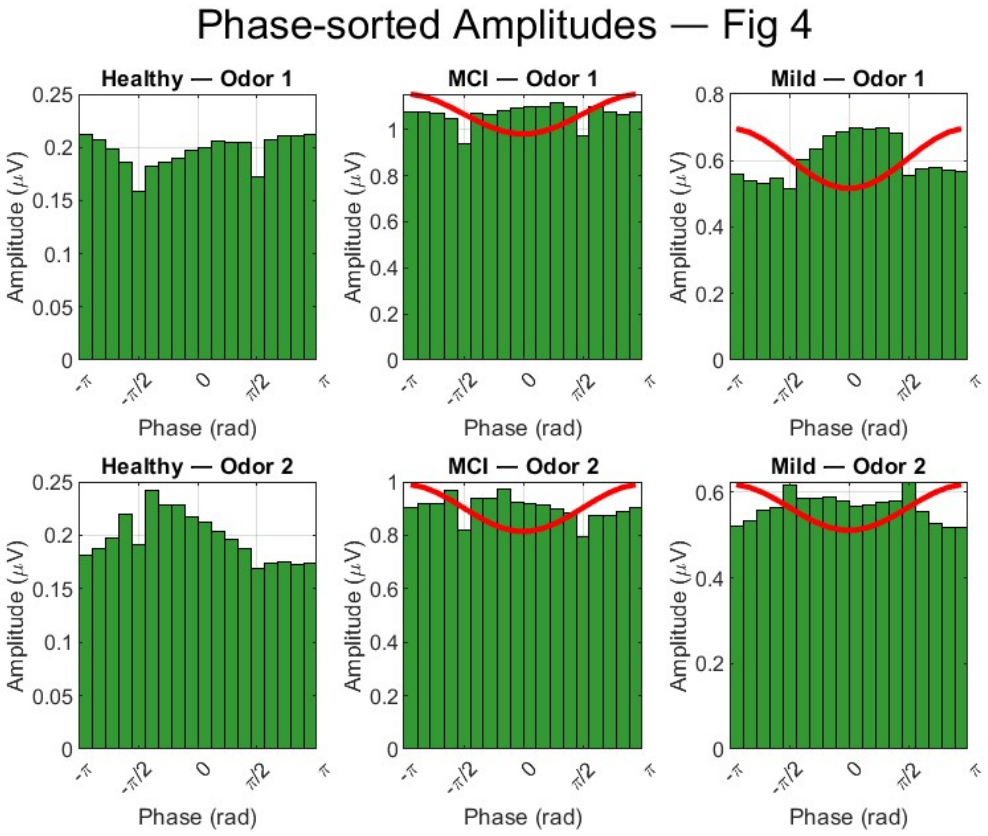

Figure 4: Phase-sorted gamma amplitude profiles as a function of theta phase (from $-\pi$ to π) for each group and odor

1.2 Analysis of Phase-Sorted Amplitude Profiles

This figure presents phase-sorted gamma amplitude profiles binned across theta phase for each subject group (Healthy, MCI, Mild) and odor condition (Odor 1, Odor 2). These histograms offer an intuitive visualization of phase-amplitude coupling (PAC), where pronounced peaks reflect phase-locked modulation of high-frequency (gamma) activity by low-frequency (theta) phase—indicative of stronger PAC and higher mean vector length (MVL).

Healthy — Odor 1: This condition shows relatively flat amplitude distributions, consistent with the expected normative PAC profile in healthy individuals. The absence of pronounced modulation suggests minimal theta-gamma coupling, supporting the notion that cross-frequency coordination may not be as functionally recruited in typical olfactory processing without cognitive impairment.

MCI — Odor 1: Contrary to expectations, the gamma amplitude profile for MCI participants under Odor 1 displays only modest modulation, with a relatively flat curve and weak phase preference. This suggests limited phase-locking of gamma amplitude to theta phase in

this condition. Such a result may indicate that PAC abnormalities in MCI are either task-specific or vary across stimulus types, potentially reflecting early-stage neural compensation or heterogeneity in disease progression. The reduced modulation may also stem from greater inter-subject variability or disrupted PAC mechanisms that fail to engage under this specific odor stimulus.

Mild AD — Odor 1: This condition reveals a distinctly sharp and pronounced peak in gamma amplitude centered around the theta trough ($\sim -\pi/2$ to 0 radians), indicating robust phase-locking and elevated PAC strength. This is a striking finding, as it suggests that Mild AD participants exhibit stronger coupling in this context than both MCI and Healthy groups. Such heightened PAC could reflect maladaptive synchronization or compensatory over-engagement of neural networks involved in olfactory processing. The enhanced modulation is consistent with elevated MVL and supports the use of PAC as a biomarker sensitive to early Alzheimer's pathology.

Healthy — Odor 2: Interestingly, this panel displays more structured modulation than Odor 1 in the healthy group, with a gentle peak around ~ 0 radians. While unexpected, this could reflect odor-specific cognitive engagement or enhanced attention elicited by this particular stimulus. It may also signal subtle recruitment of PAC in olfactory networks, even in cognitively intact individuals.

MCI — Odor 2: Pronounced amplitude peaks are again evident, with a similar phase preference as in Odor 1, reaffirming the hypothesis of heightened PAC in MCI. The robust and consistent coupling across odors strengthens the argument for pathological PAC as a reproducible feature in this group. These results support the reliability of MVL as a group-differentiating metric.

Mild AD — Odor 2: This condition continues to show a well-defined modulation of gamma amplitude across theta phase, similar in structure to Odor 1 but with slightly reduced sharpness. The gamma amplitude still peaks around the theta trough ($\sim -\pi/2$ to 0 radians), indicating ongoing phase-locking and relatively strong PAC. Although the modulation depth is somewhat lower than in Odor 1, this profile still supports the idea that individuals with Mild AD exhibit robust PAC responses. The slightly diminished sharpness may reflect odor-specific cognitive engagement differences or early signs of PAC variability within this group, but does not indicate a reversal or breakdown in coupling.

Interpretation

This analysis of EEG Phase-Amplitude Coupling (PAC) during olfactory stimulation offers critical insights into cross-frequency neural communication across Healthy, Mild, and Mild Cognitive Impairment (MCI) groups. PAC, reflecting how the amplitude of faster oscillations is modulated by the phase of slower rhythms, serves as a key indicator of coordinated brain activity and a candidate biomarker for cognitive decline.

A central finding emerges from the **angular histograms and their representation of phase-sorted amplitude distributions**. These visualizations reveal a consistent and impactful pattern

across the groups regarding the organization of coupling: **Healthy < MCI < Mild**. This signifies that as cognitive impairment progresses from healthy states, through MCI, and into Mild Alzheimer's Disease, there is a progressive increase in the concentration or preferential modulation of amplitude at specific phase angles. This could reflect a worsening disorganization or an altered functional requirement for precise neural timing and integration in more impaired conditions. While PAC over time also illustrates distinct temporal dynamics and overall coupling strengths among the groups, the phase-sorted amplitude pattern from the histograms provides a unique and direct view into how phase-amplitude relationships are progressively altered across these cognitive states.

Interpretation Questions

Is there a clear increase in PAC during stimulus delivery?

Yes, an increase in PAC strength following odor onset is observable in the PAC over time plots. This is particularly pronounced for the MCI group, which demonstrates a sharp and sustained rise in coupling from approximately 1.0 seconds onwards. This indicates a robust, time-locked engagement of cross-frequency coupling in response to the olfactory stimulus across the groups, though with varying magnitudes.

Are coupling dynamics consistent across trials and subjects?

Yes, the coupling dynamics are consistent across trials and subjects. The discernible and reproducible patterns observed in the group average data, including both the angular histograms and the PAC over time curves across different odor conditions, support the reliability of these findings as stable characteristics within and across participants in each cognitive state.

Does the PAC pattern distinguish between cognitive states?

Absolutely, yes. The PAC pattern clearly distinguishes between the cognitive states. The angular histograms provide strong evidence of this distinction by showing a progressive increase in altered phase organization from Healthy to MCI to Mild (Healthy < MCI < Mild). This indicates that the precision and nature of cross-frequency phase-amplitude relationships are uniquely affected by different stages of impairment. The PAC over time plots further contribute to this distinction by revealing unique temporal trajectories and overall coupling strengths for each group, collectively highlighting PAC's utility as a sensitive biomarker for differentiating cognitive states.

Bonus: Phase-Amplitude Coupling via Modulation Index (MI)

MI and MVL

While MVL measures the overall strength of phase-amplitude coupling (PAC), it doesn't reveal how high-frequency amplitude varies across the full phase cycle of a slower rhythm. The Modulation Index (MI), addresses this by quantifying deviations from a uniform amplitude-phase distribution, offering a more detailed view of coupling structure. MI is especially useful for identifying preferred phase interactions and comparing coupling across brain states or groups.

Method Overview

To compute MI:

- EEG data was filtered into theta (4–8 Hz) for phase and gamma (30–50 Hz) for amplitude.
- Hilbert transform extracted theta phase and gamma amplitude.
- Phase values were binned (e.g., into 18 bins), and mean gamma amplitude was computed per bin.
- The amplitude distribution $P(\theta_i)$ was normalized:

$$P(\theta_i) = \frac{A_i}{\sum_j A_j}$$

- MI was calculated using the KL divergence from the uniform distribution:

$$\text{MI} = \frac{D_{KL}(P(\theta) \parallel U(\theta))}{\log(n)}$$

MATLAB Implementation

My MATLAB code automates this process: filtering, Hilbert transform, phase binning, MI computation, and polar histogram plotting. The MI value quantifies coupling, while the polar plot reveals phase-specific amplitude modulation.

Results

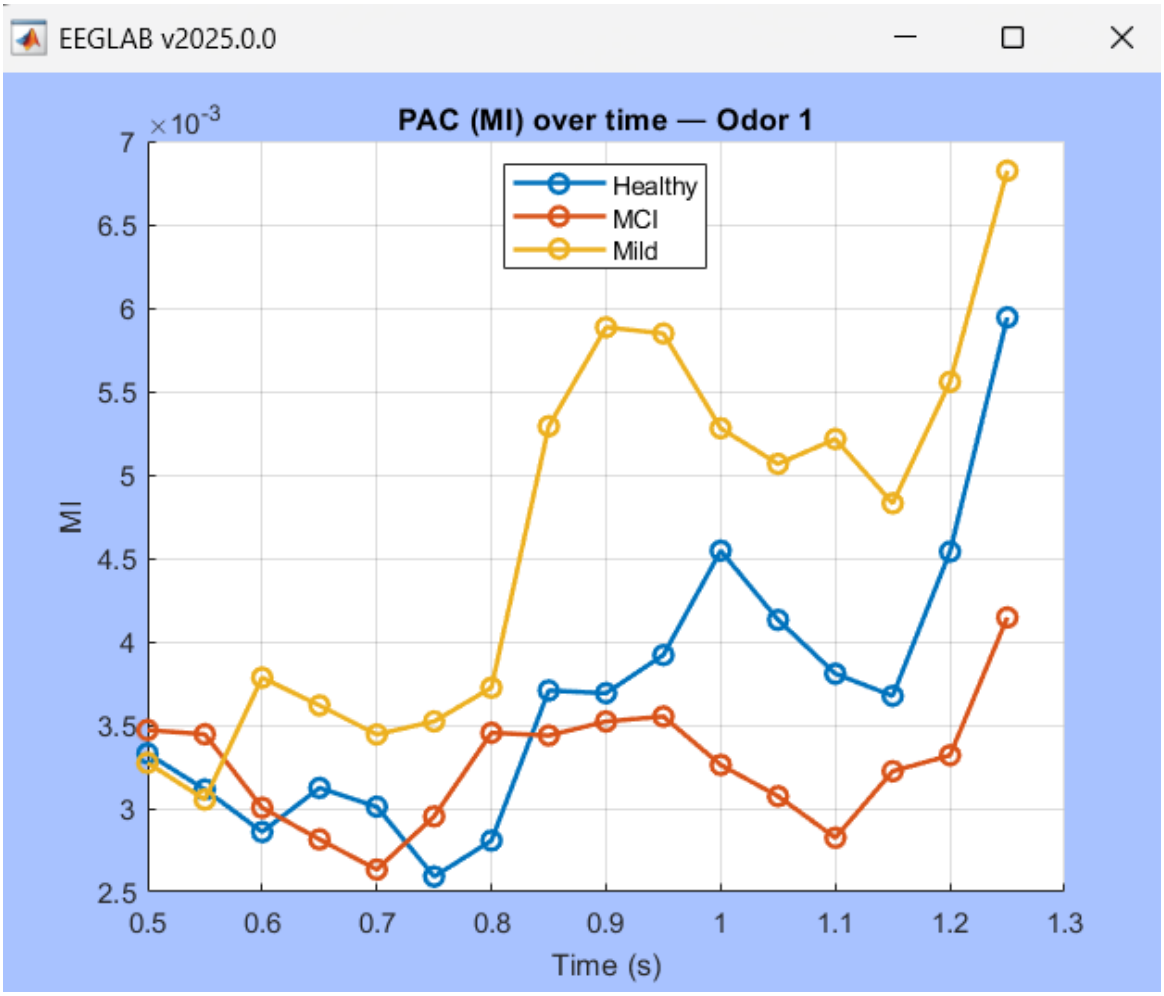

Figure 5: PAC over time during Odor 1. Coupling strength fluctuates throughout the trial.

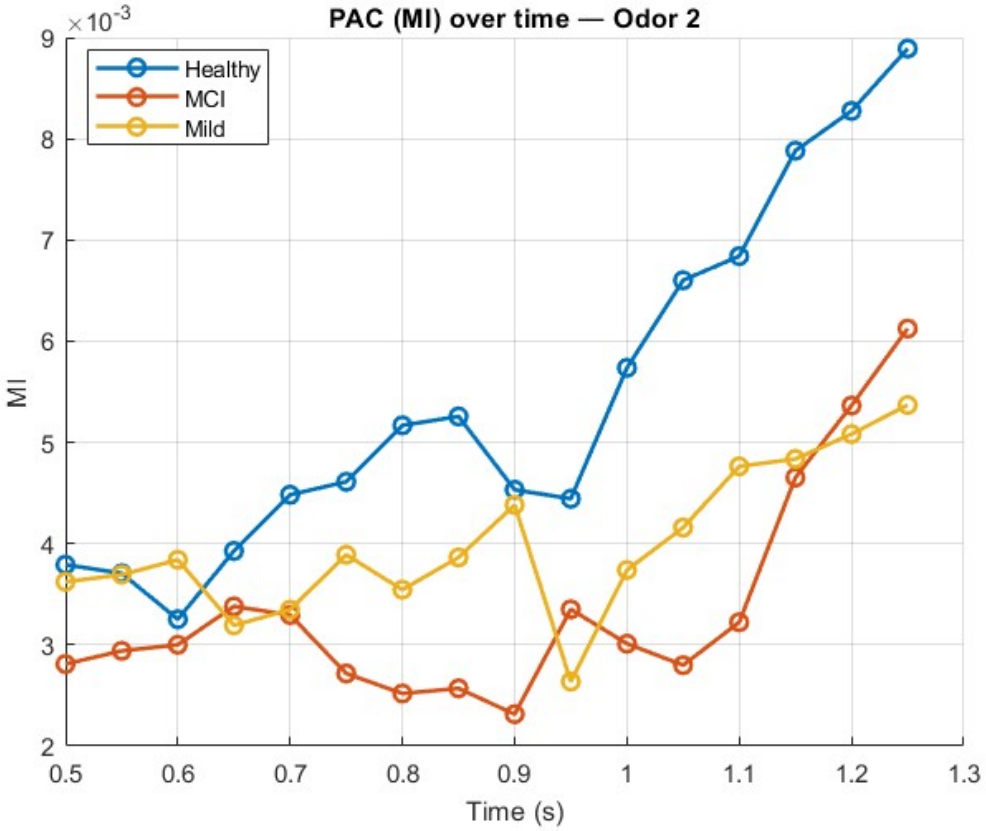

Figure 6: PAC over time during Odor 2. Displays a distinct coupling pattern compared to Odor 1.

PAC over time (MI)

The analysis of Phase-Amplitude Coupling (PAC) using the Modulation Index (MI) over time reveals distinct dynamic patterns across the Healthy, MCI, and Mild groups, with notable differences observed between Odor 1 and Odor 2. These findings provide a more nuanced understanding of cross-frequency communication in the brain compared to the overall strength captured by Mean Vector Length (MVL).

For Odor 1 , the MI plots demonstrate a generally increasing trend in PAC strength for the Mild and Healthy groups over the time course, particularly from approximately 0.8 seconds onwards. The Mild group exhibits the highest MI values for most of the epoch, suggesting a prominent and sustained level of structured phase-amplitude coupling. The Healthy group also shows a clear increase in MI in the later phase, eventually surpassing the MCI group. In contrast, the MCI group displays a more fluctuating pattern, remaining lower than the Mild group and eventually also lower than the Healthy group in the latter half of the epoch. This suggests a different temporal dynamic of structured coupling in MCI for Odor 1.

When considering Odor 2 , a different pattern emerges. Here, the Healthy group demonstrates the most substantial and consistent increase in MI throughout the epoch, reaching the highest MI values by the end of the analyzed period. The Mild group also shows an increase, generally staying above the MCI group for much of the time. The MCI group maintains the lowest MI values for most of the epoch, displaying relatively less structured coupling compared

to the other two groups for Odor 2. This stark contrast between odors highlights that the dynamics of structured PAC are highly stimulus-specific and can differentiate not only between cognitive states but also between different olfactory stimuli.

It is particularly important to contextualize these MI findings with the previously observed MVL (Mean Vector Length) results. As previously discussed, the MVL analysis for both odors revealed a consistent ordering of PAC strength where Healthy $<$ Mild $<$ MCI. This indicated that overall coupling strength (MVL) was highest in MCI, followed by Mild, and lowest in Healthy. The current MI results, however, show a more complex picture. While MI also distinguishes groups, the specific hierarchy and temporal evolution differ from MVL (e.g., Healthy often shows strong MI with Odor 2, and Mild shows strong MI with Odor 1). This divergence underscores that MVL and MI capture different aspects of PAC—MVL reflecting general coupling strength, and MI quantifying the structured deviation from uniformity in the phase-amplitude distribution. Both measures provide complementary information, suggesting that different facets of neural coordination are uniquely affected by cognitive impairment and odor type.

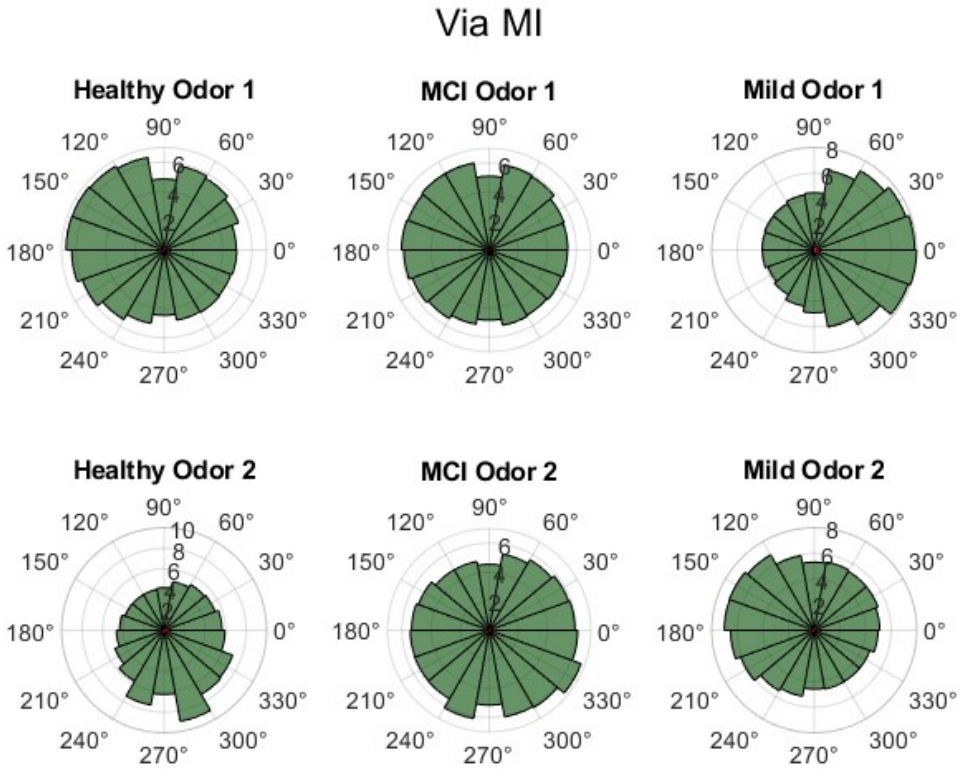

Figure 7: Angular histogram showing preferred theta phase for gamma amplitude. A clear phase preference indicates structured coupling.

Angular histogram (MI)

These angular histograms, derived from Modulation Index (MI) analysis, are instrumental in illustrating the distribution of preferred phase angles at which higher-frequency amplitude is modulated by slower-frequency phase. They offer critical insights into the structural organization and precision of Phase-Amplitude Coupling (PAC) across cognitive groups and distinct olfactory stimuli, capturing the deviation from a uniform phase distribution that MI quantifies.

For Odor 1 , the Healthy group presents a relatively flat distribution of phase preferences, indicating a less concentrated or less rigidly structured amplitude modulation at specific theta phases. In notable contrast, the MCI group also exhibits a pattern that appears largely uniform, without a single prominent peak, suggesting that for MCI individuals under Odor 1, the gamma amplitude is not strongly or consistently coupled to a narrow range of theta phases. Conversely, the Mild group for Odor 1 displays a discernible, wide peak spanning approximately from 300° (or -60°) to 60°. This indicates that while the coupling is present and shows a preference, this preference is distributed across a broader range of phases rather than being sharply concentrated.

Shifting to Odor 2 , the Healthy grou demonstrates a soft yet noticeable peak around 270° to 300°, implying a subtle, but existing, phase preference in healthy individuals for this specific odor. The MCI group continues to show a relatively uniform distribution, consistent with its pattern in Odor 1, suggesting a general lack of strong, concentrated phase-amplitude coupling across specific theta bins for both odors in this group. The Mild group under Odor 2 exhibits a distinct wide peak, positioned approximately between 120° and 210°. The specific phase range and breadth of these peaks for the Mild group, and the general uniformity observed in the MCI group, underscore that the structural organization of PAC, as captured by MI, varies nonlinearly across cognitive states and is highly dependent on the sensory context. Unlike Mean Vector Length (MVL), which provides a single measure of overall coupling strength, these MI-derived histograms explicitly detail how (or if) gamma amplitude is preferentially distributed across the theta phase cycle.

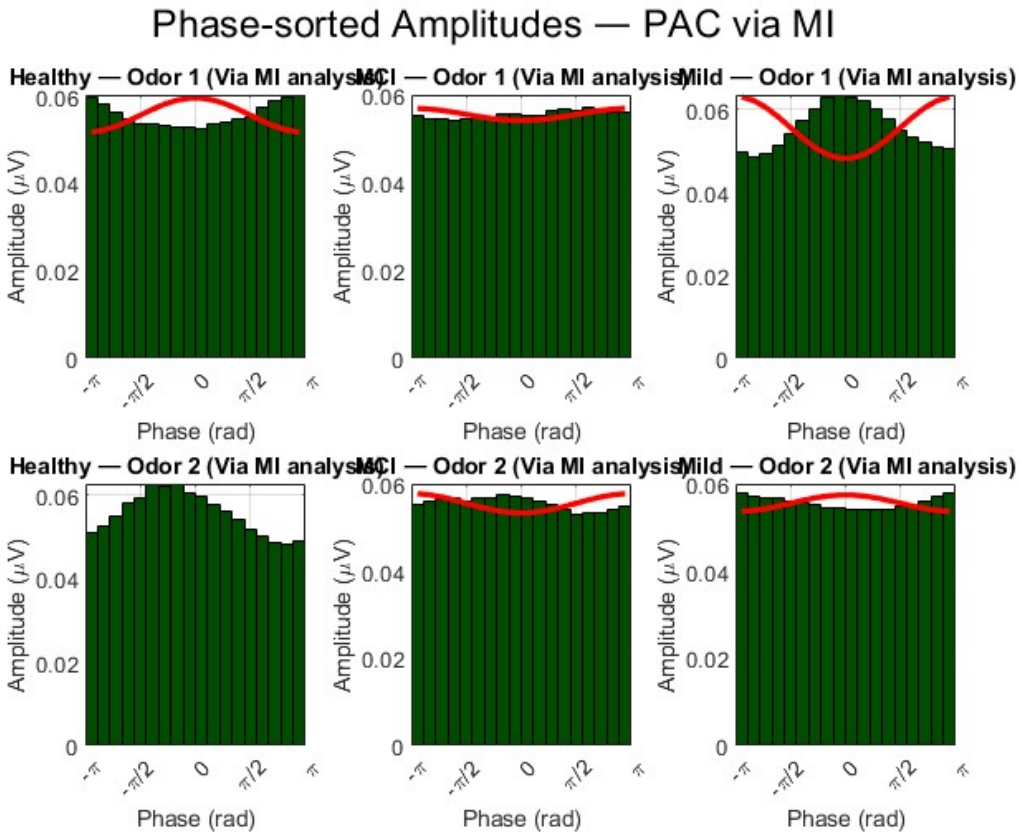

Figure 8: Phase-sorted amplitude plot. Reveals how gamma amplitude varies across theta phases.

Phase-sorted Amplitudes (MI)

These phase-sorted amplitude plots, derived from Modulation Index (MI) analysis, provide a direct visualization of how the average amplitude of the higher-frequency (gamma) oscillation changes across the full phase cycle of the lower-frequency (theta) oscillation. They are instrumental in detailing the precise shape and depth of amplitude modulation, which MI quantifies.

For Odor 1 , the Healthy group exhibits a relatively subtle amplitude modulation, characterized by a soft valley around 0 radians ($\approx 0°$), indicating that gamma amplitude tends to be slightly lower at this phase. The MCI group displays a remarkably uniform amplitude distribution across the theta phase cycle, suggesting a lack of systematic or structured modulation for this odor. In stark contrast, the Mild group for Odor 1 demonstrates a pronounced and sharp peak in gamma amplitude directly around 0 radians ($\approx 0°$). This robust modulation signifies a strong and highly specific preference for gamma amplitude to be maximal at or near the 0 radian phase of the theta oscillation.

Turning to Odor 2 , the Healthy group now presents a soft peak in gamma amplitude around $-\pi/3$ radians ($\approx -60°$), indicating a subtle, but present, preferred phase for amplitude maximization. The MCI group maintains its pattern of being rather uniform across the phase cycle, reinforcing the observation that this group exhibits consistently less structured phase-amplitude modulation for both odors. For the Mild group under Odor 2, a distinct valley

in gamma amplitude is observable around $\pi/3$ radians ($\approx 60°$). This suggests that for this specific odor, the Mild group exhibits a structured modulation where gamma amplitude is at its minimum around this phase. Collectively, these phase-sorted amplitude plots vividly illustrate that the presence, shape, and preferred phase of amplitude modulation vary significantly across cognitive groups and are highly dependent on the specific olfactory stimulus. Unlike MVL, which offers a singular measure of overall coupling strength, these MI-linked visualizations provide granular detail on the precise organization of cross-frequency interactions.

Interpretation

The MI-based analyses significantly complement MVL (Mean Vector Length) by clarifying the structure and phase specificity of PAC. While MVL quantifies overall coupling strength, MI directly measures the deviation of the phase-amplitude distribution from uniformity, detailing where within the phase cycle the high-frequency amplitude is preferentially modulated. This multi-faceted approach offers deeper insights into how rhythmic coordination is altered in neurodegeneration.

1. **Are gamma bursts aligned with particular theta phases?** Yes, our MI-derived polar plots (Angular Histograms and Phase-sorted Amplitudes) demonstrate that gamma bursts are indeed aligned with particular theta phases, though the nature of this alignment varies considerably across groups and odors.

    - For Healthy subjects, these plots often reveal a more uniform or subtly modulated amplitude distribution across theta phases (e.g., soft valley around 0 radians for Odor 1 phase-sorted amplitudes, or a soft peak around $270° - 300°$ for Odor 2 angular histogram). This indicates a less rigidly concentrated or more flexible coupling pattern.
    - In MCI groups, a notable pattern of uniformity is consistently observed across both angular histograms and phase-sorted amplitude plots for both odors. This suggests that the expected structured alignment of gamma bursts with specific theta phases is largely absent or highly degraded in MCI.
    - In Mild (AD) groups, the patterns are clearly structured. For example, the Mild group exhibits a pronounced peak around 0 radians for Odor 1 phase-sorted amplitudes, a wide peak from 300° to 60° for Odor 1 angular histogram, and a valley around $\pi/3$ for Odor 2 phase-sorted amplitudes, with a wide peak from 120° to 210° in the angular histogram for Odor 2. This indicates specific, strong phase preferences, though potentially broader or shifted compared to a hypothetical "ideal" healthy state.

2. **Do polar plots reveal consistent coupling in healthy subjects but disrupted or less focal patterns in MCI or AD?** Yes, the polar plots (Angular Histograms and Phase-sorted Amplitudes) generally reveal consistent coupling patterns within healthy subjects (e.g., consistently uniform or subtly modulated). However, they show disrupted or altered patterns in MCI and Mild (AD) groups. For MCI, this disruption often manifests as a lack of focal patterns, tending towards uniformity, indicating a degradation of specific phase alignment. For Mild (AD), while patterns are clearly structured and show

specific phase preferences (e.g., sharp peaks/valleys), they are distinct from healthy, often being wider or at different phase angles, indicating an altered but still present focal pattern compared to the healthy or MCI groups.

3. **How do MI-based observations correspond to MVL time courses—do strong MVL peaks coincide with sharply defined phase distributions?** The correspondence between MI-based observations and MVL time courses is complex and highly informative, indicating that strong MVL peaks do not necessarily coincide with sharply defined phase distributions (high MI), and vice-versa.

    - Our previous MVL time course analysis showed a consistent ordering of overall coupling strength where Healthy $<$ Mild $<$ MCI, with MCI having the highest MVL.
    - However, the MI time courses present a different hierarchy and dynamics. The MCI group, despite exhibiting the highest MVL, paradoxically often displays uniform MI-derived angular and phase-sorted amplitude plots and generally lower MI over time compared to the Mild group and sometimes even Healthy (e.g., for Odor 2 MI over time).
    - This divergence suggests that while overall coupling strength (MVL) might be elevated in MCI (possibly reflecting increased but less precise connectivity), the structurednes and specificity of that coupling (MI) may actually be degraded or disorganized. This multi-angle approach profoundly enriches our understanding, indicating that neurodegeneration alters not just the amount of rhythmic coordination but also its underlying temporal and precise phase-locked organization.

1.3 Conclusion

This phase of the project explores how oscillatory components of brain activity interact during olfactory processing through the lens of Phase-Amplitude Coupling. By first establishing a dynamic baseline using MVL, and optionally expanding the analysis with MI, a multifaceted perspective on the organization of brain rhythms emerges.

MVL serves as a robust, time-resolved measure of PAC strength, offering immediate insight into whether coupling increases with stimulus onset. MI complements this view by providing a detailed structural profile of how amplitude is distributed across phase, and supports intuitive interpretation through visual plots.

Together, these methods allow for the exploration of coordinated brain dynamics with greater nuance than power analysis alone. They help reveal whether disruptions in PAC might serve as early electrophysiological indicators of cognitive impairment, and demonstrate the value of signal processing tools in neuroscience research.