Signals and Systems Project

Phase 1

Instructor: Prof. Hamid Aghajan

Sharif University of Technology

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

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Authors:

Kimia Fakheri — kimia.fakheri@gmail.com
Matin M.babaei — babaeimatin22@gmail.com

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Preface

Notes on the project:

- Phase 1 Due date: May 18^{th} 2025 (1404/02/28)

- The project must be done individually. Each individual will present his results in an online session. The date of the online session will be announced later and will take place after the submission of Phase 2.

- Please submit your project report as a `.pdf` file. Include all outputs and final results in the report. Make sure to list the practice text questions and provide a concise explanation of your problem-solving approach in each section.

- Ensure that all codes are provided in a separate `.m/.py/.ipynb` file. If a code cannot be tested accurately upon submission, the reported results will be considered invalid, and no points will be awarded in such cases.

- You have the flexibility to utilize either `MATLAB` or `Python` for your project. However, please be aware that `MATLAB` is recommended since certain aspects of the project rely on `MATLAB` toolboxes.

- Ensure that you save all files, including your report, codes, helper functions, and any additional outputs, if required, in a compressed file format such as `.zip` or `.rar`. This compressed file should then be uploaded to the Course-Ware (CW) submission platform.

- Your file names must be in the following format:

  `SS-Project-Phase[1/2]-[#StudentID].[zip/rar/pdf/m/py/ipynb]`

- In this project, it is essential to uphold the principles of academic integrity and refrain from any form of cheating or copying. Cheating undermines the learning process, diminishes personal growth, and compromises the trust placed in us as students/researchers/professionals. It is crucial to recognize that engaging in dishonest practices not only tarnishes our own reputation but also has serious consequences, both ethically and academically. We want to emphasize that if anyone is found to have cheated, their results will not be accepted in this project, and they will receive a zero mark.

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Grading

The grading will be based on the following criteria, with a total of 0.6 points for Phase 1 and 1.4 points **(0.4 mandatory + 1.0 bonus)** for Phase 2. Note that Phase 1 of the project is **mandatory** and must be completed by all students. The total grade for Phase 1 is 0.6 points, contributing to the final project evaluation.

Task	**Points**
Phase 1:	0.6 points
Data and Preprocessing	50%
Power Analysis of EEG Signals	25%
Online Q&A Session (Evaluation)	20%
Clarity and Quality of Report	2.5%
Clarity and Quality of Code	2.5%
Bonus: Writing your report in Latex	5%

1 Introduction

1.1 Alzheimer's Disease and Olfactory Function

Alzheimer's disease begins its silent progression years before memory symptoms emerge, with two pathological hallmarks - amyloid-beta plaques accumulating between neurons and tau protein tangles forming inside them. These destructive processes first target key brain regions that serve dual roles in both smell processing and memory formation. The olfactory bulb, which acts as our brain's smell detector, along with the memory-critical entorhinal cortex and hippocampus, show some of the earliest signs of this damage.

This overlap between smell and memory systems explains why olfactory dysfunction frequently appears as one of the first noticeable symptoms, often preceding obvious memory problems by several years. During the transitional stage of Mild Cognitive Impairment (MCI), when subtle cognitive changes begin to exceed normal aging but haven't yet progressed to full dementia, these smell-related changes may offer particularly valuable early warning signs. About 10-15% of MCI cases progress to Alzheimer's each year, making this an important window for early detection.

What makes this connection especially promising for research is that the same vulnerability linking smell and memory systems also makes them ideal for non-invasive monitoring through EEG. When we smell something, it activates a coordinated dance of electrical activity across these interconnected brain regions. By examining how different frequency bands of brain waves interact during this process - particularly through phase-amplitude coupling between slower theta rhythms and faster gamma waves - we can gain insights into the functional integrity of these neural networks.

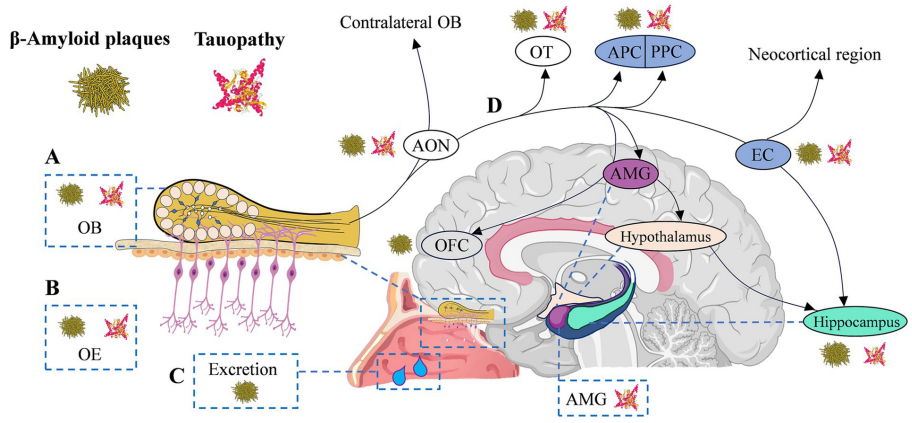

Figure 1: Early invasion of $\beta-amyloid$ and tau pathology via the olfactory system: A potential route for Alzheimer's disease progression into the brain.

1.2 Project Motivation and Goal

This project is driven by the search for early, reliable biomarkers of cognitive decline, specifically Alzheimer's Disease, using non-invasive EEG recordings collected during olfactory tasks. While our long-term focus is on Phase-Amplitude Coupling (PAC) as a key mechanism underlying sensory-memory integration and its deterioration in disease, we will explore that in Phase 2 of the project.

In this initial phase, our primary objective is to analyze how the power of the EEG signal evolves over time in response to olfactory stimuli. By doing so, we aim to:

- Develop an intuitive understanding of the signal characteristics for each subject and odor.
- Observe dynamic changes in neural activity across brain regions.
- Lay the groundwork for more advanced coupling analyses later.

To achieve this, we'll use Short-Time Fourier Transform (STFT) to visualize time-varying power across trials and subjects. This will help us detect event-related neural responses and understand the energetic landscape of the brain during sensory stimulation.

2 EEG and Brain Oscillations

EEG captures electrical signals from the scalp via electrodes positioned using the international 10-20 system, ensuring consistent spatial representation of brain regions (frontal, parietal, temporal, and occipital).

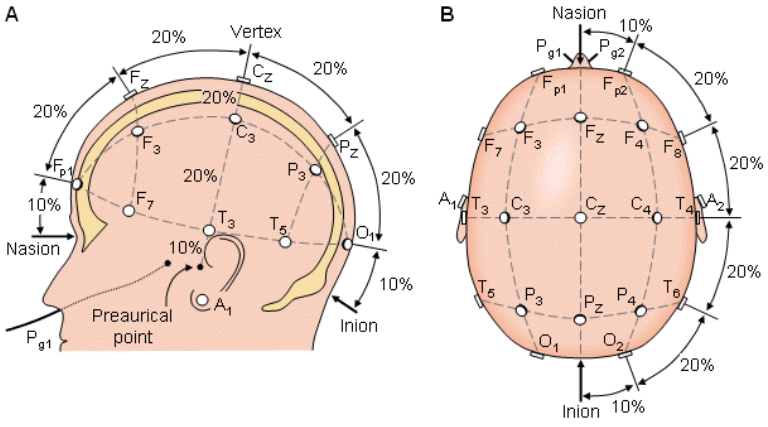

Figure 2: EEG 10-20 system Placements

2.1 EEG Frequency Bands

EEG signals are divided into standard frequency bands, each linked to distinct neural processes:

- Delta (0.5-4 Hz): Deep sleep and unconscious states
- Theta (4-8 Hz): Working memory and attention
- Alpha (8-13 Hz): Relaxation and passive processing
- Beta (13-30 Hz): Active thinking and motor control
- Gamma (30-90 Hz): Sensory processing, cognitive binding, memory

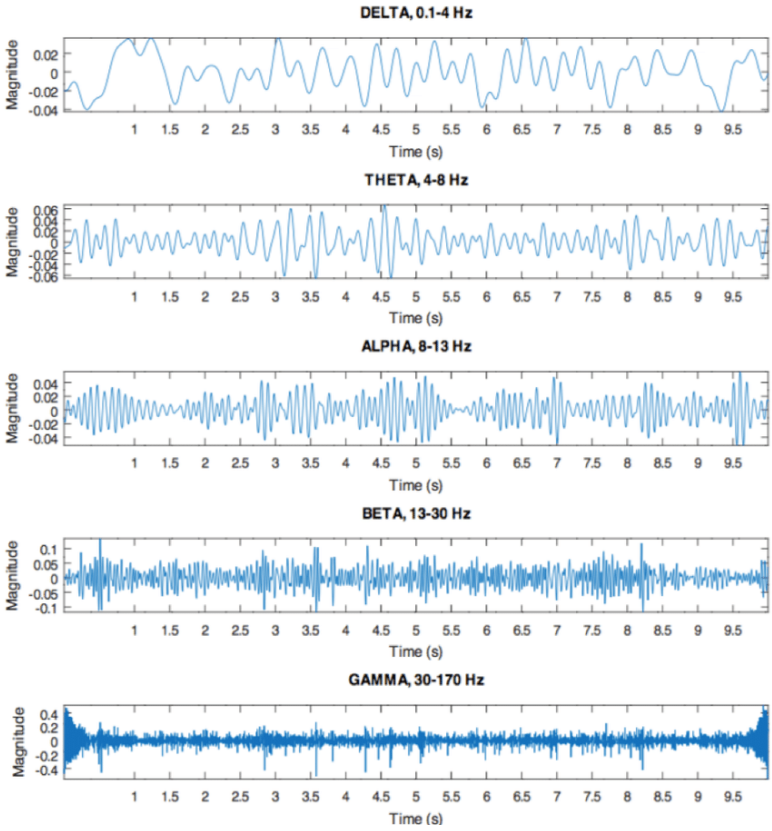

Figure 3: EEG frequency bands

Power in theta and gamma is of particular interest due to its involvement in memory and perception tasks.

3 Data and Preprocessing

3.1 Experimental Design

Subjects participated in an olfactory stimulation task where they were exposed to two distinct odors: chocolate and rose.

- Odor Presentation Time: 5 seconds
- Rest Period: 6 seconds of odorless airflow between trials (baseline period)
- Trial Count: 22 trials per odor per subject
- Event Tagging:
  - Tag 5: Chocolate
  - Tag 6: Rose
- Subjects:
  - One Healthy Control (HC)
  - One Mild Cognitive Impairment (MCI) subject
  - One Mild Alzheimer's Disease (AD) subject
- EEG Configuration:
  - 19 scalp channels + 1 tagging channel (Channel 20)
  - Sampling frequency: 250 Hz

Each subject's EEG was recorded during the odor trials, and the onset times were logged using the tagging channel to facilitate event-related analysis.

3.2 Preprocessing Pipeline (EEGLAB)

Preprocessing was conducted using EEGLAB, a MATLAB toolbox for EEG analysis. Below is the pipeline in detailed steps:

1. **Load EEG Data and Set Channel Locations**
   - Load .mat files containing raw EEG data.
   - Assign standard electrode positions using a predefined montage (Electrodes_loc_19chan_plusTAG
2. **Import Event Information**
   - Extract event markers (odor triggers) from channel 20 using EEGLAB's "Import Event Info from Data Channel" feature.
3. **Filtering**

- Apply a bandpass filter (1-90 Hz) to remove slow drifts and high-frequency noise.
- Apply a notch filter (48-52 Hz) to eliminate line noise.

4. **Identify and Remove Noisy Channels**
   - Use clean_rawdata() to detect and exclude noisy or flatline channels.
5. **Interpolate Removed Channels**
   - Use spatial interpolation to restore missing channels and preserve the full montage.
6. **Re-reference EEG (First Pass)**
   - Re-reference signals to the average of all EEG channels to remove common-mode noise.
7. **Artifact Subspace Reconstruction (ASR)**
   - Apply ASR with default settings via clean_rawdata() to eliminate transient artifacts such as muscle bursts.
8. **Re-reference EEG (Second Pass)**
   - Perform a second average re-reference post-ASR for normalization.
9. **Independent Component Analysis (ICA)**
   - Run ICA and use ICLabel to classify components.
   - Remove components identified as artifacts (e.g., eye blinks, muscle noise).

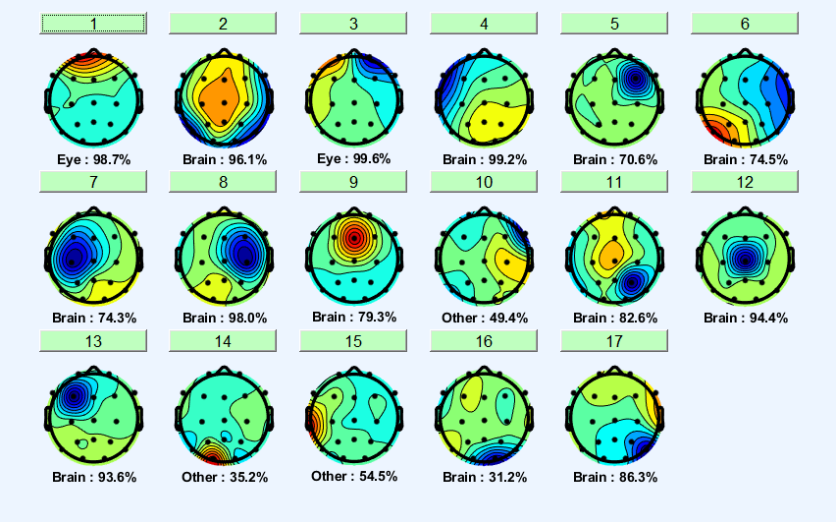

Figure 4: An example of ICA components

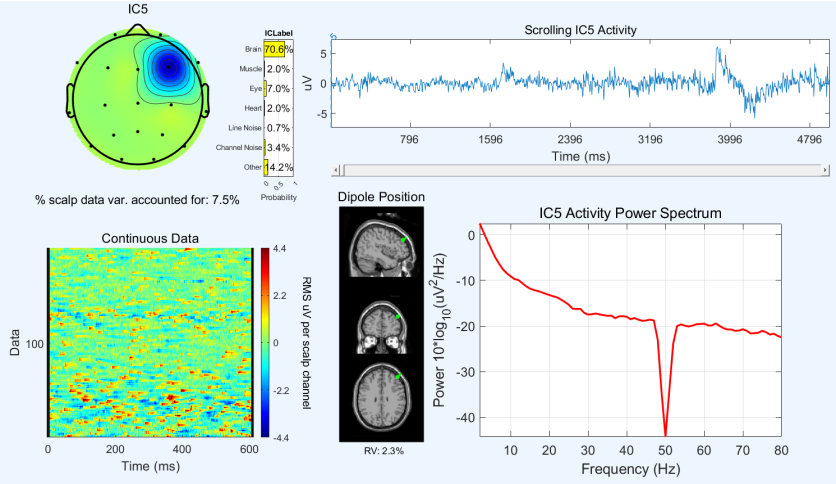

Figure 5: One component's all detailed activity

10. **Epoching**

- Segment trials from -2 to +5 seconds around odor onset to capture pre-stimulus, stimulus, and post-stimulus dynamics.
- (Note: These time ranges are suggestions; slight adjustments can be made.)

11. **Trial Rejection**

- Reject noisy trials manually or using z-score thresholding (e.g., $z > 3.5$).

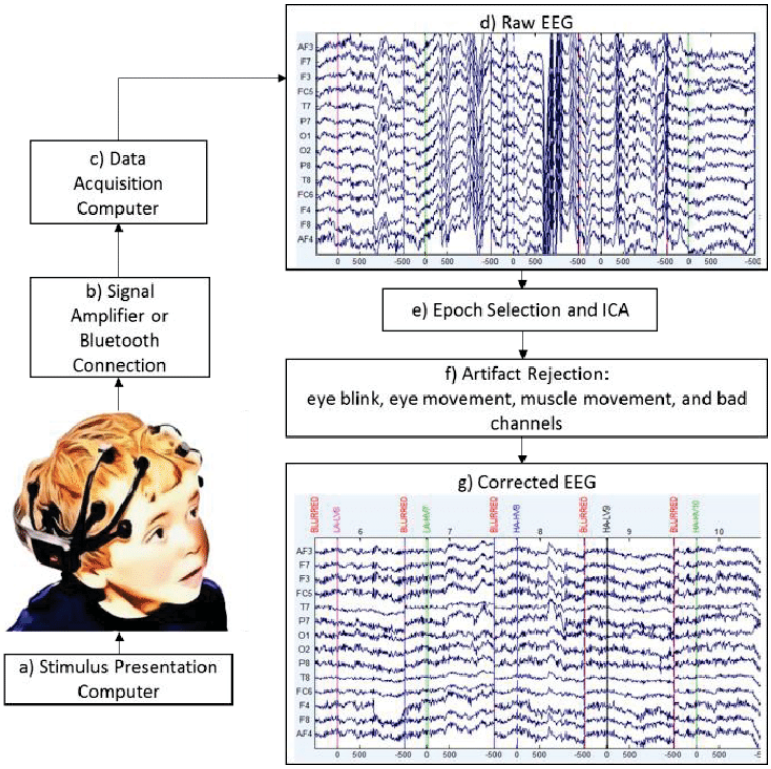

Figure 6: Data aqusition to Clean data

4 Power Analysis of EEG Signals

Before diving into cross-frequency interactions, it's important to first understand the core characteristics of the EEG signal. Power analysis offers a direct and insightful view into brain activity, allowing you to observe how energy in specific frequency bands changes over time in response to external stimuli.

This part of the project focuses on quantifying and visualizing power dynamics across time, with special attention to different subject states and odor conditions.

4.1 Why Power Analysis?

Think of EEG signals like a set of radio stations. Before investigating how they interact (as in PAC), it's crucial to know which ones are broadcasting and how strong their signals are. Power analysis reveals:

- When the brain responds most strongly to stimuli.
- Which frequency bands are most active.
- How responses differ across subject groups (Healthy Control, MCI, Alzheimer's).

By tracking power over time, it becomes possible to recognize the neural signature of responses to odors like chocolate and rose, and to begin differentiating between healthy and impaired cognitive processing.

4.2 Power Calculation Using STFT

The time-varying power is calculated using the Short-Time Fourier Transform (STFT). This method breaks the signal into overlapping time windows, then computes how frequency content changes over time.

Once the STFT is computed, the power at each point is calculated by taking the squared magnitude of the complex coefficients:

$$\text{Power}(t, f) = |\text{STFT}(t, f)|^2 \tag{1}$$

This gives a two-dimensional map of how much energy is present in each frequency band at each moment in time. From here, focus on extracting power in the theta (4-8 Hz) and gamma (30-50 Hz) bands, which are most relevant to the next phase of this project.

4.3 Choosing Window Length and Overlap

To analyze how power evolves over time, use time windows of 0.5 to 1 second, with 85-95% overlap between consecutive windows. The specific parameters can be adjusted based on the signal quality and the level of detail you want to observe.

Smaller windows give better timing resolution; larger ones provide clearer frequency resolution. The overlap helps capture smooth transitions in activity and avoids missing brief but meaningful changes around the stimulus.

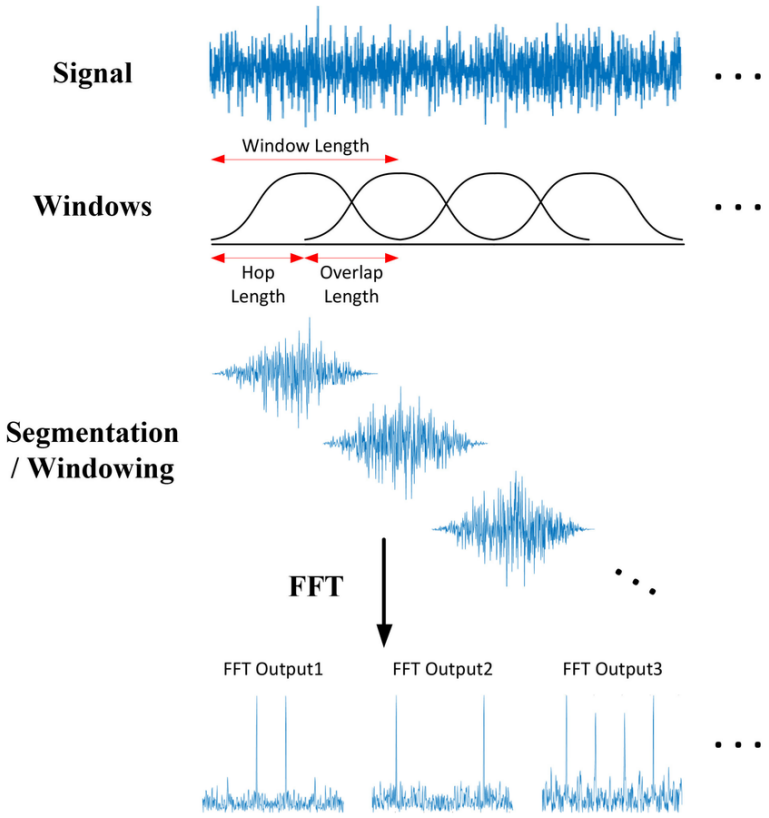

Figure 7: Short-time Fourier transform (STFT) overview

4.4 Building Power-Time Matrices and Comparison

Once the power has been calculated for all trials, organize the data into a 2D matrix for each condition:

- One axis is time, and the other is trials.
- Average across trials to create a single power vs. time curve for each subject, odor, and frequency band.
- Create plots for each odor condition (chocolate and rose), and include one line per subject on each plot-comparing Healthy Control, MCI, and Alzheimer's responses side by side.

This visualization highlights differences in neural activity between groups and provides early insight into how odor processing may change with cognitive decline.

4.5 What to Look For

When interpreting your plots, consider:

- Do any subjects show stronger or earlier peaks in power?
- Are power patterns different for chocolate vs. rose?
- Is there a consistent delay or drop in response in the MCI or Alzheimer's subjects?
- Does theta or gamma seem more affected in impaired states?

These patterns can help form early hypotheses for what may later be observed in PAC analyses.

4.6 Reflective Questions

To deepen your analysis and guide your thinking:

- Which method of power extraction gave you clearer or more informative results?
- How did your choice of window length and overlap affect the resolution or interpretability of the signal?
- Did you observe consistent differences in power between subjects or odors?
- What preprocessing choices might have influenced your results, and what would you try differently next time?
- How do these power dynamics set the stage for phase-amplitude coupling in the next phase?

5 Conclusion

This study demonstrates the potential of EEG signal analysis, particularly through power dynamics and phase-amplitude coupling measures, to reveal distinctive neural patterns during olfactory processing across different cognitive states. The findings suggest that both time-frequency power analysis and cross-frequency coupling provide valuable, complementary insights into brain function that may serve as sensitive markers for early cognitive decline. While further validation with larger cohorts is needed, this work establishes a foundation for developing non-invasive electrophysiological biomarkers that could aid in early detection and monitoring of Alzheimer's disease progression.

References

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