



Signals and Systems Project

PHASE 1

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

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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.

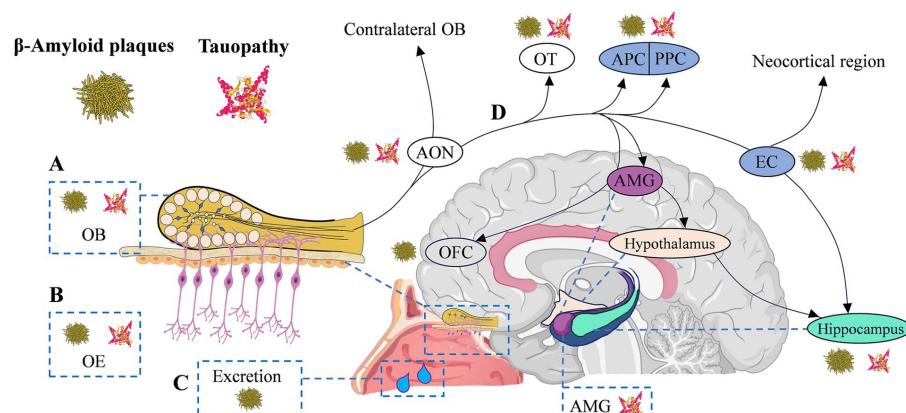


Figure 1: Early invasion of β -amyloid and tau pathology via the olfactory system: A potential route for Alzheimer's disease progression into the brain.

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).

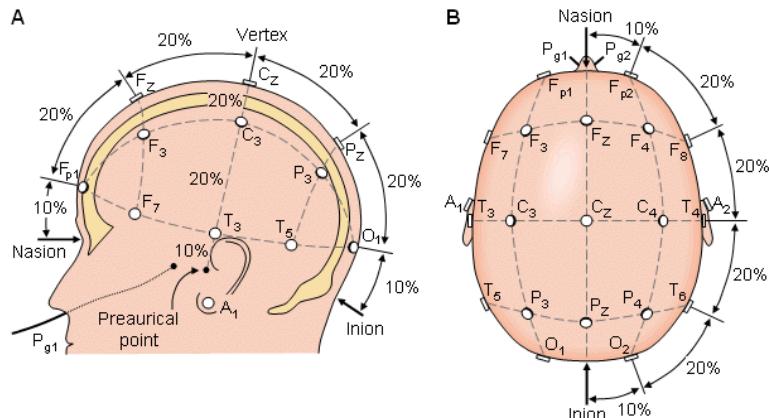


Figure 2: EEG 10-20 system Placements

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

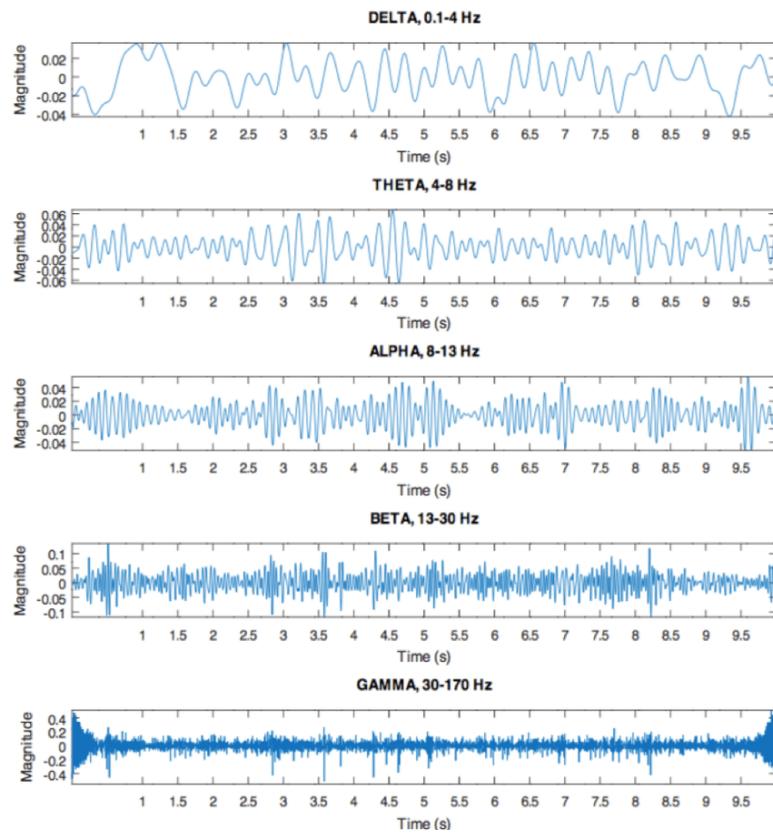


Figure 3: EEG frequency bands

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

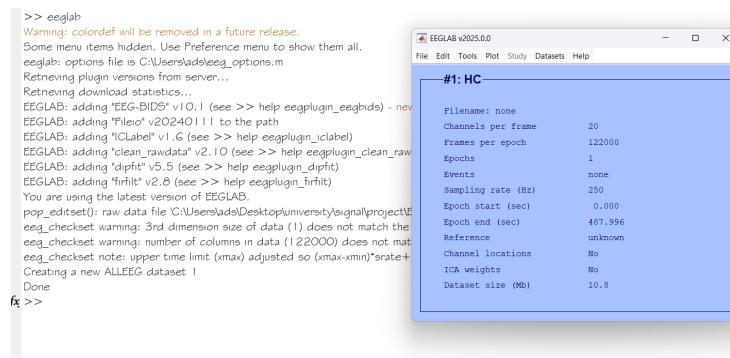
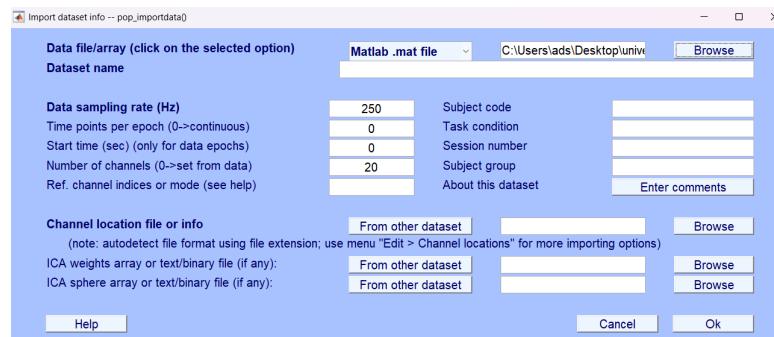
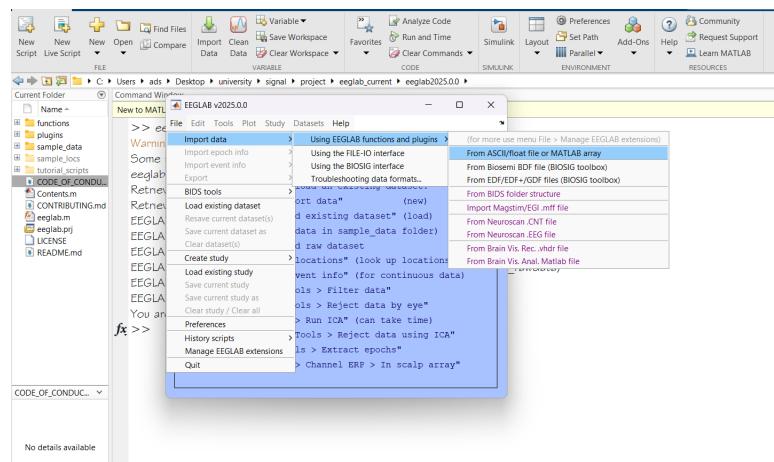
Each subject's EEG was recorded during the odor trials, and the onset times were logged using the tagging channel to facilitate event-related analysis.

3.2 Preprocessing Pipeline (EEGLAB)

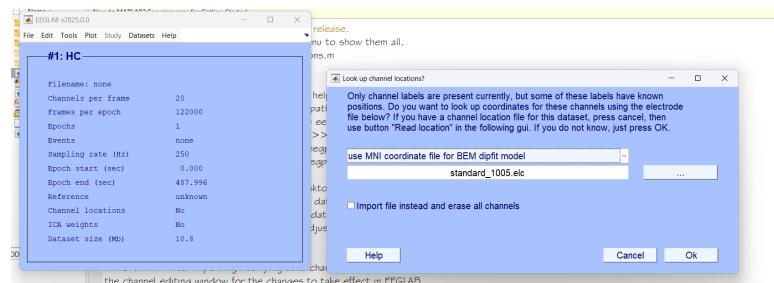
Preprocessing was conducted using EEGLAB, a MATLAB toolbox for EEG analysis. Below is the pipeline in detailed steps:

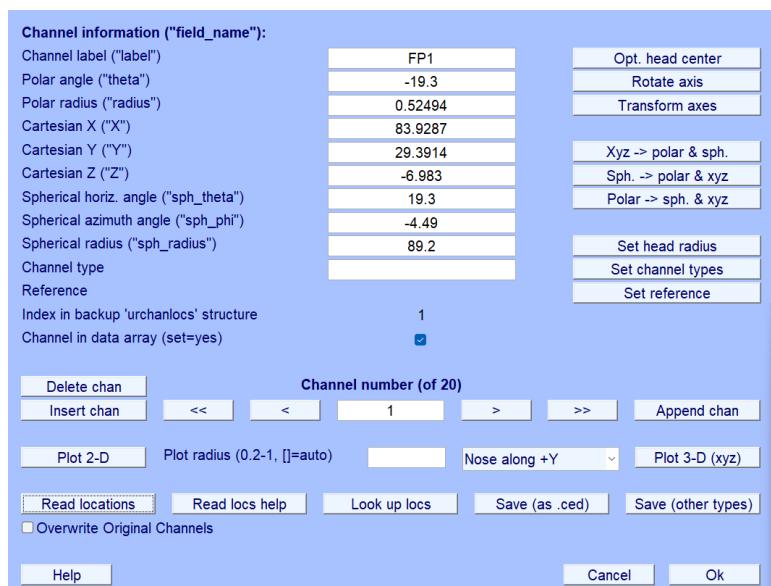
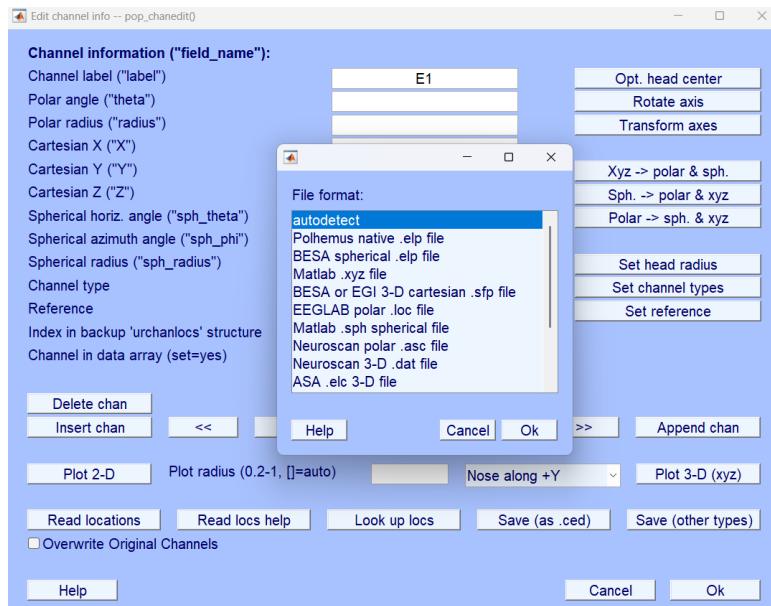
1. Load EEG Data and Set Channel Locations

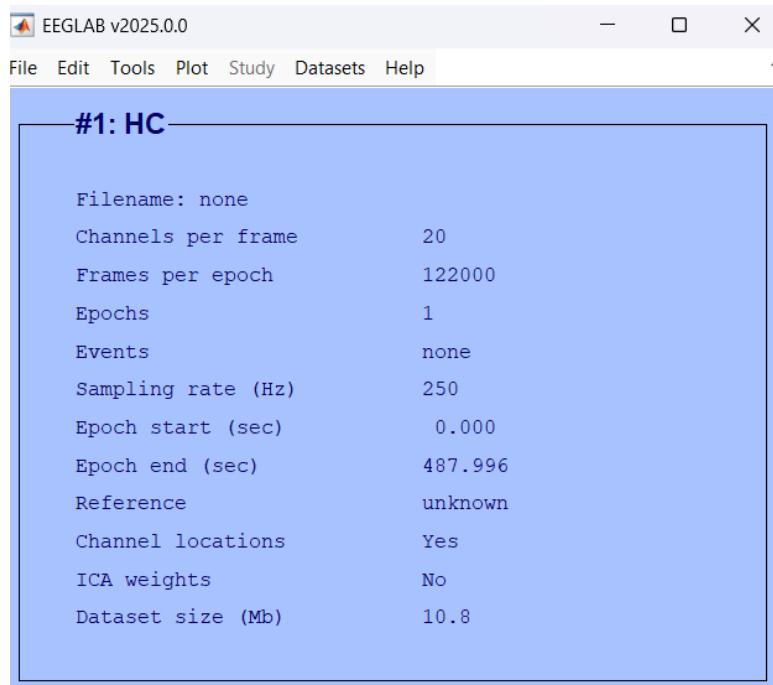
- Load .mat files containing raw EEG data.



- Assign standard electrode positions using a predefined montage (Electrodes_loc_19chan_plusTAG)

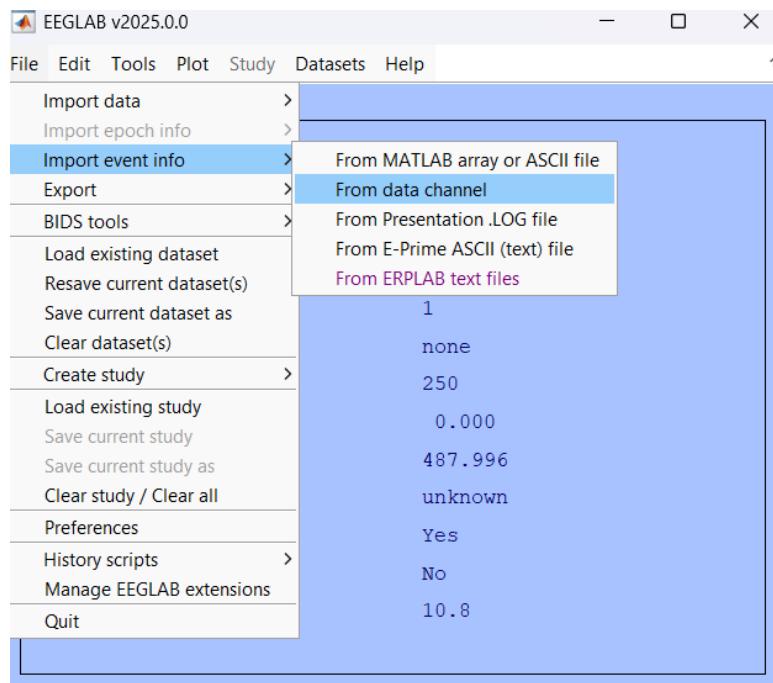


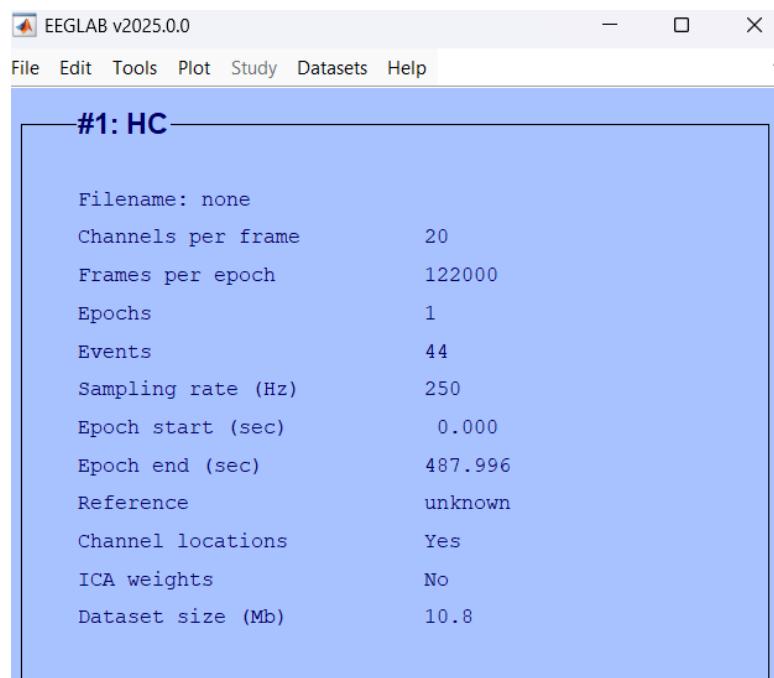
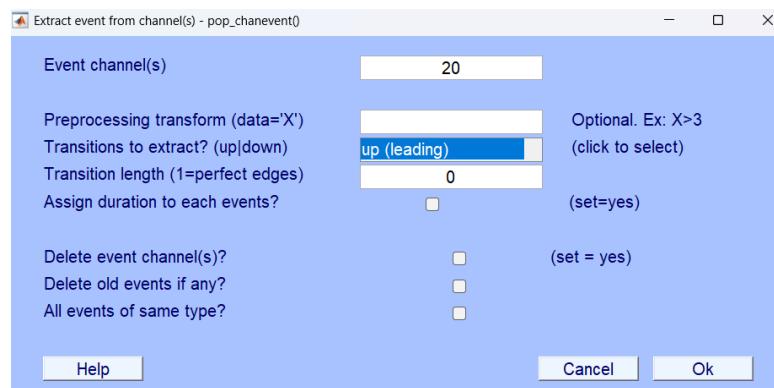




2. Import Event Information

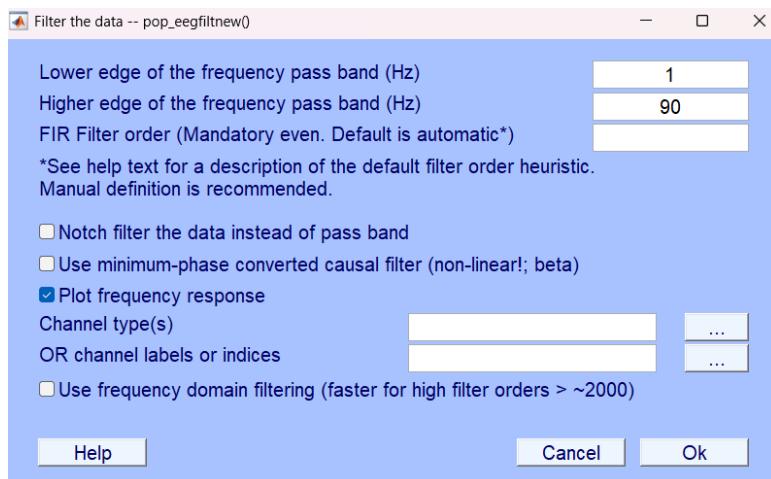
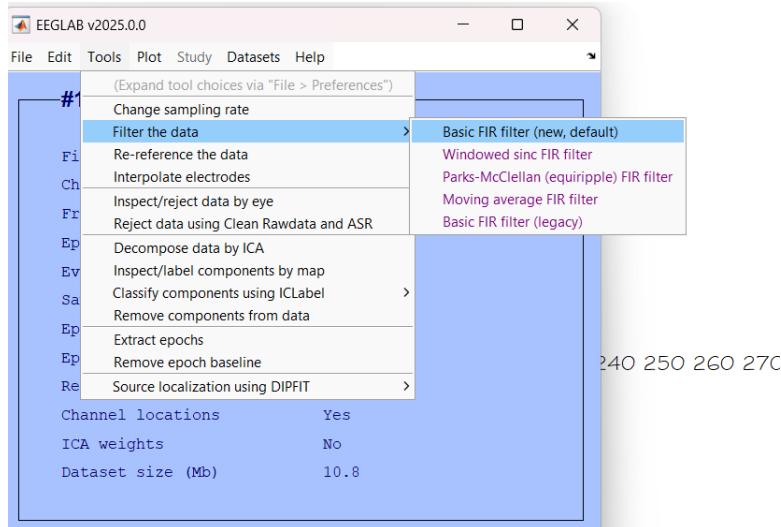
- Extract event markers (odor triggers) from channel 20 using EEGLAB's "Import Event Info from Data Channel" feature.

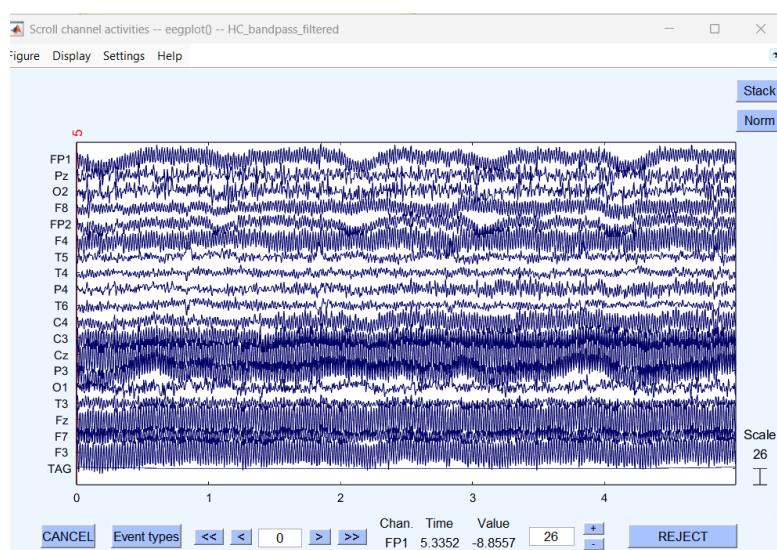
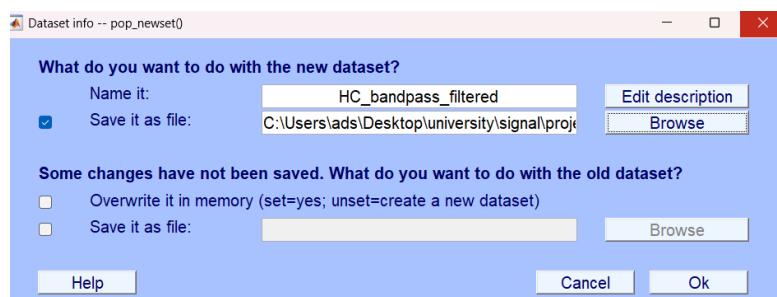
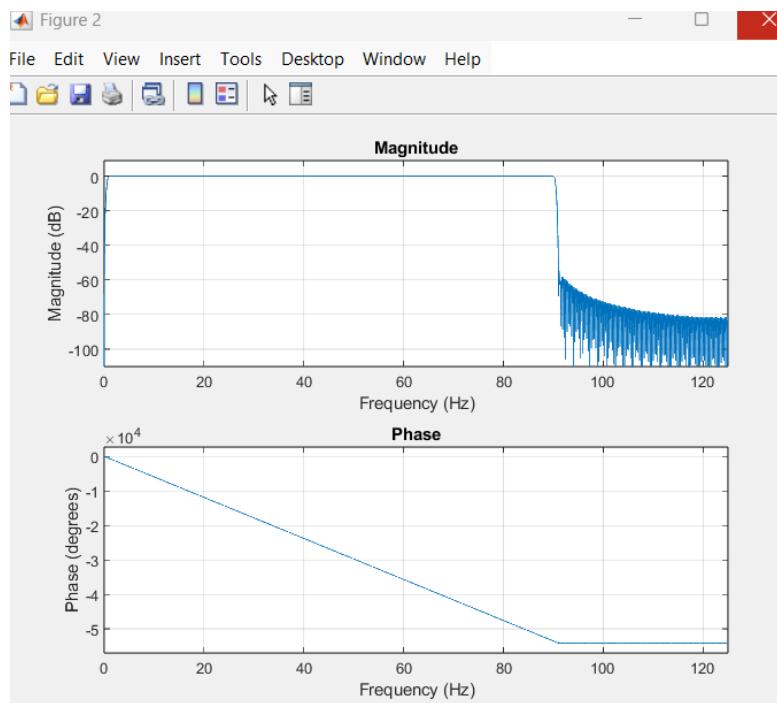


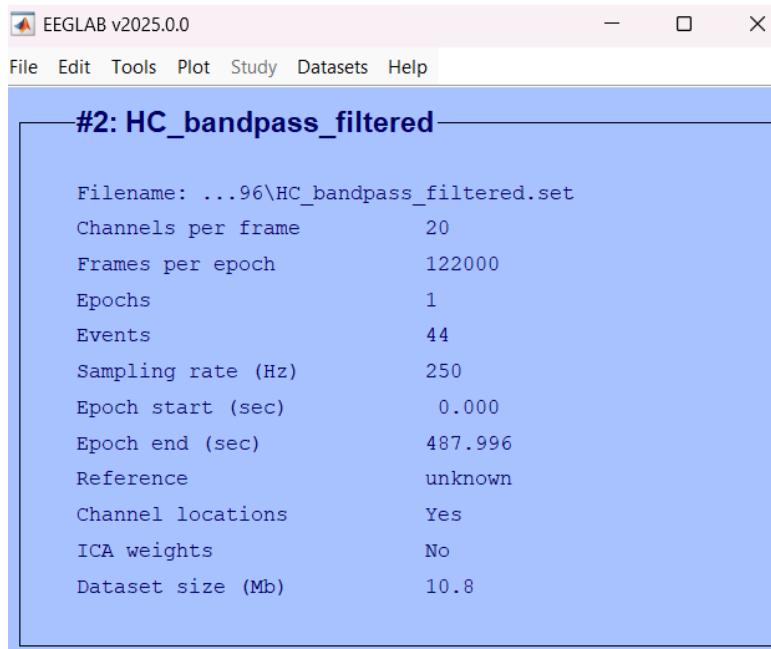


3. Filtering

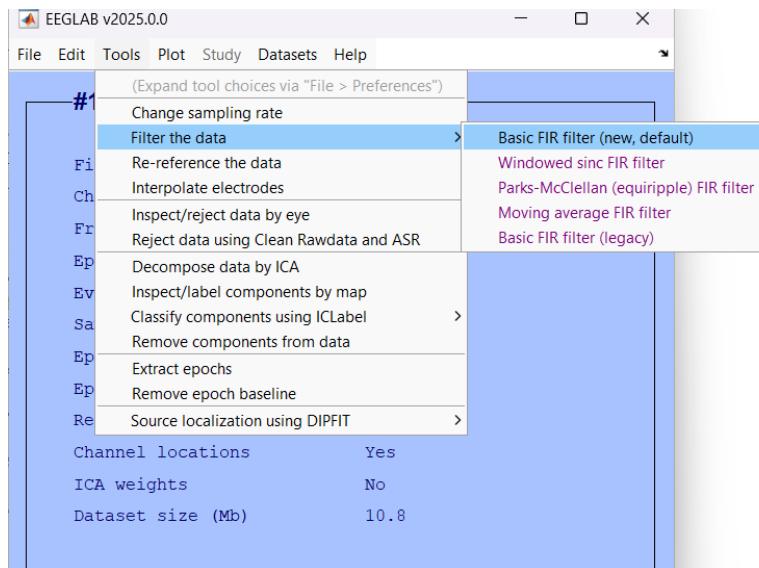
- Apply a bandpass filter (1-90 Hz) to remove slow drifts and high-frequency noise.

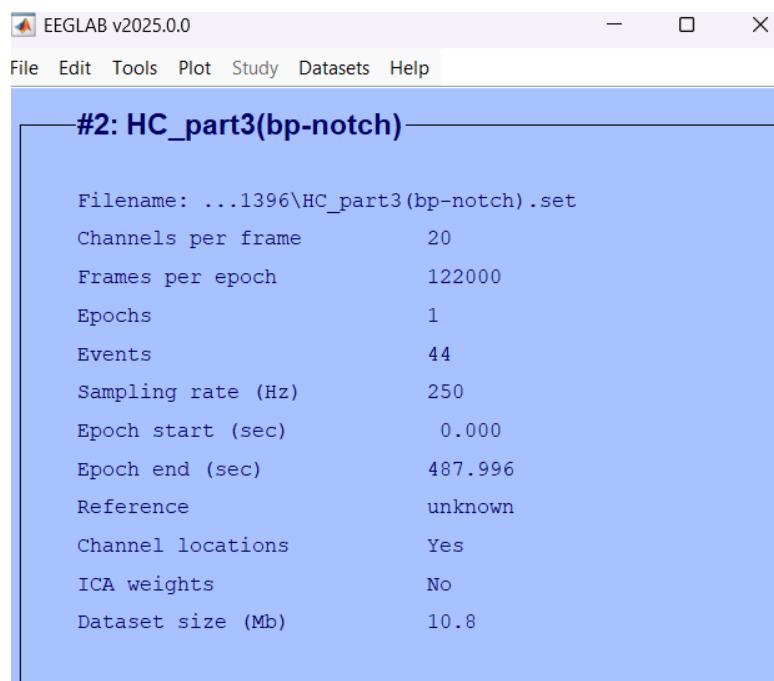
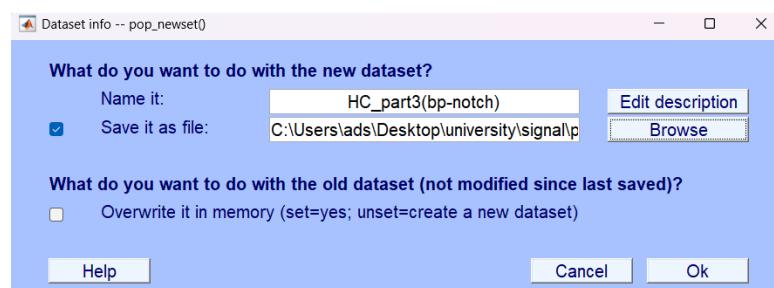
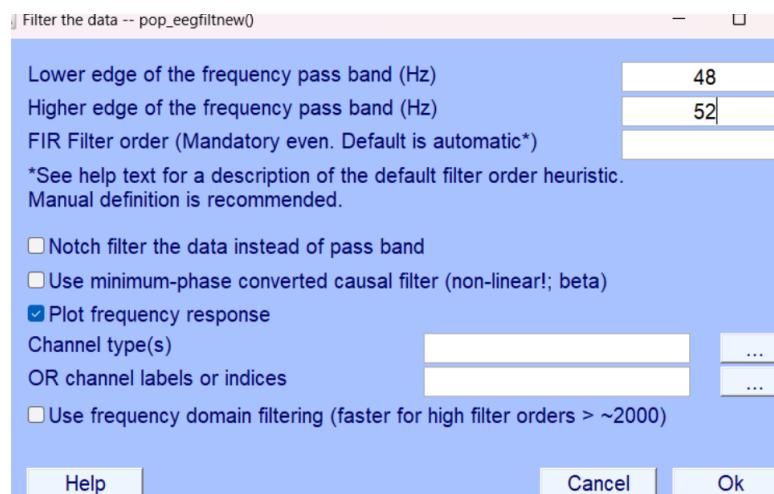


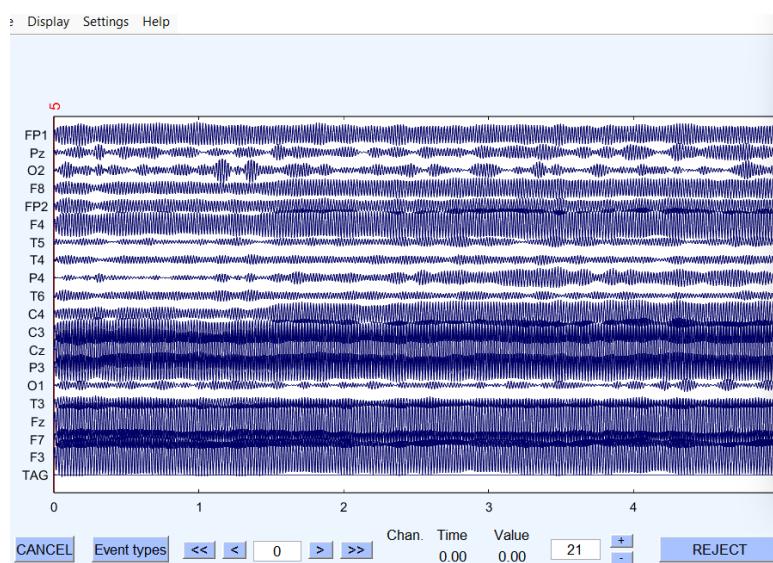
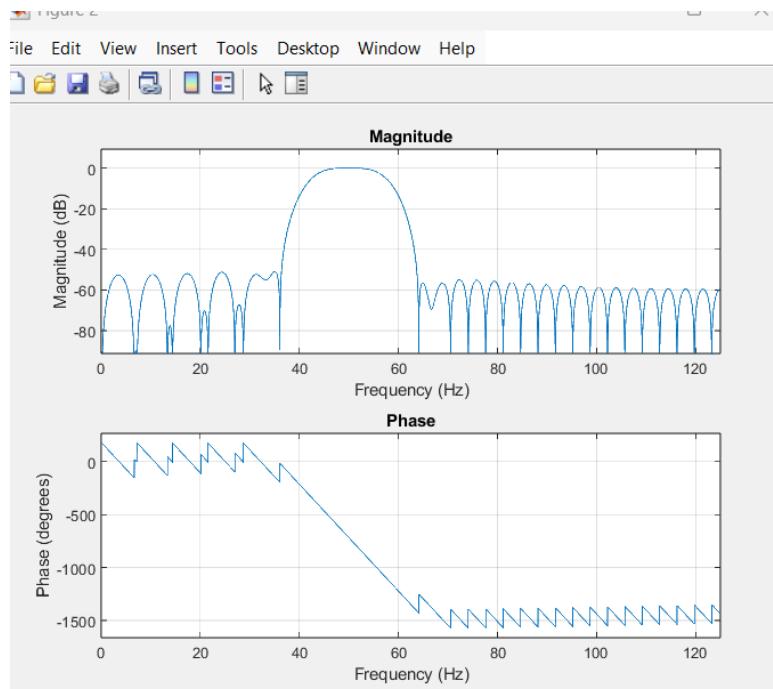




- Apply a notch filter (48-52 Hz) to eliminate line noise.

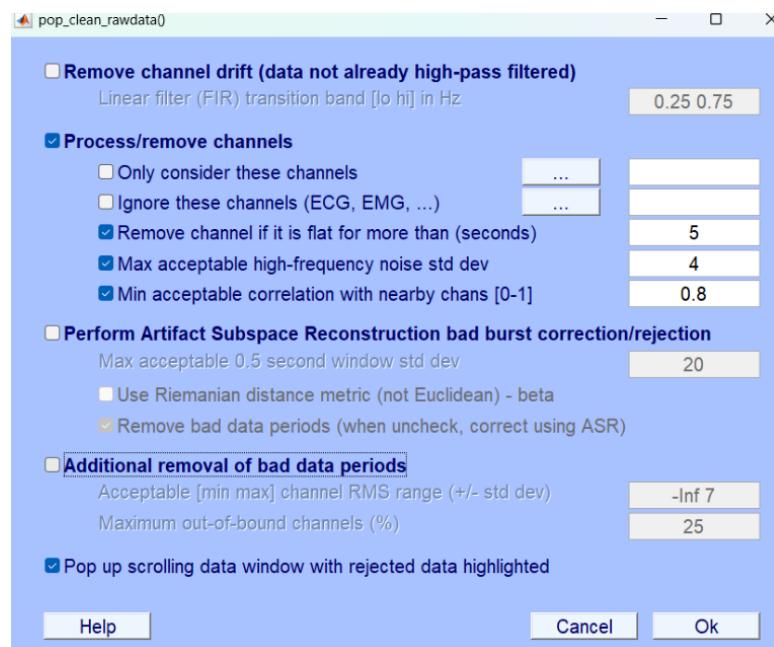
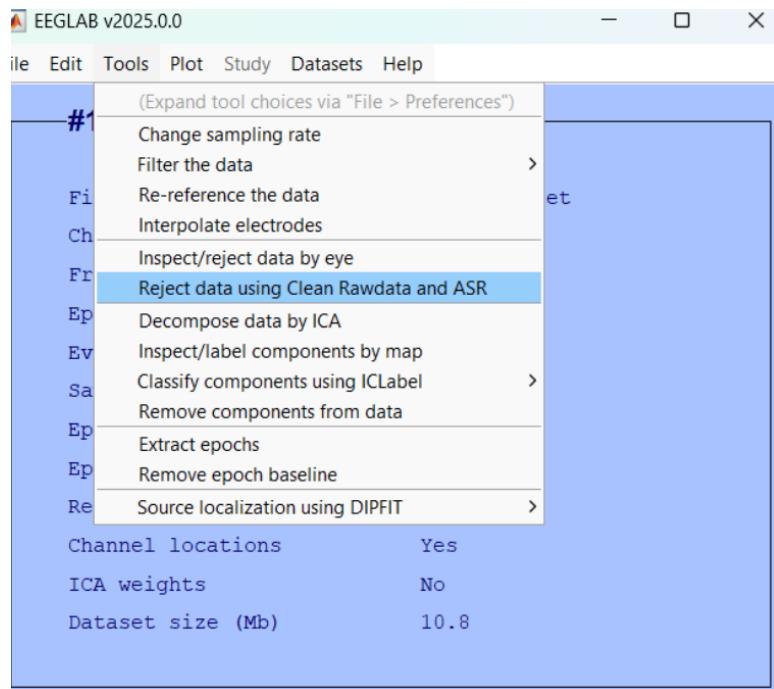


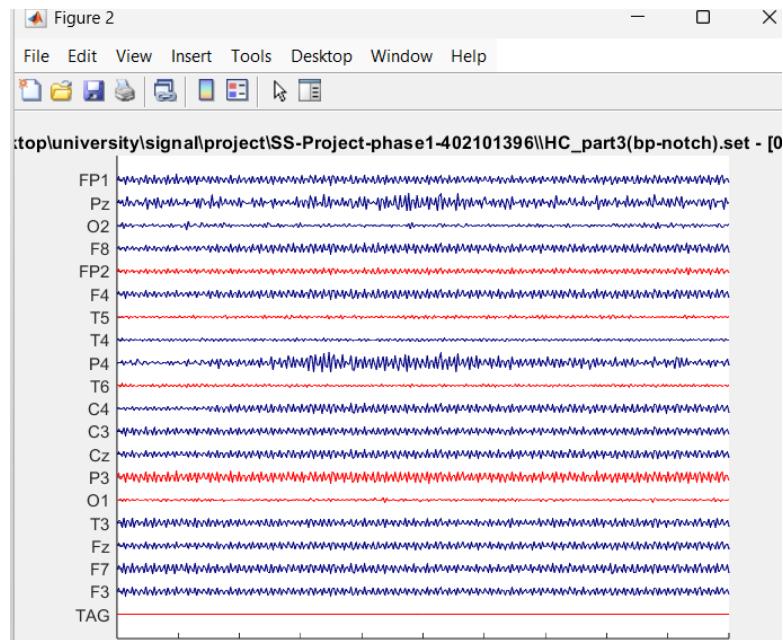




4. Identify and Remove Noisy Channels

- Use `clean_rawdata()` to detect and exclude noisy or flatline channels.

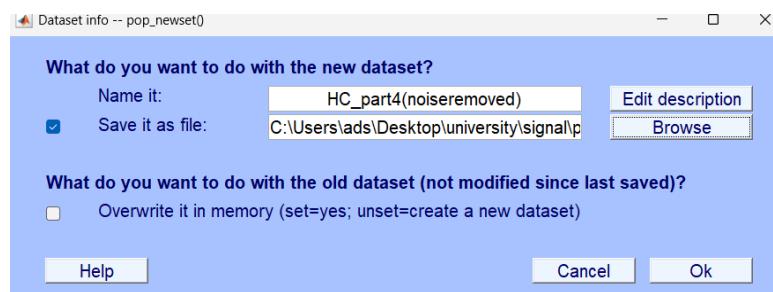




```

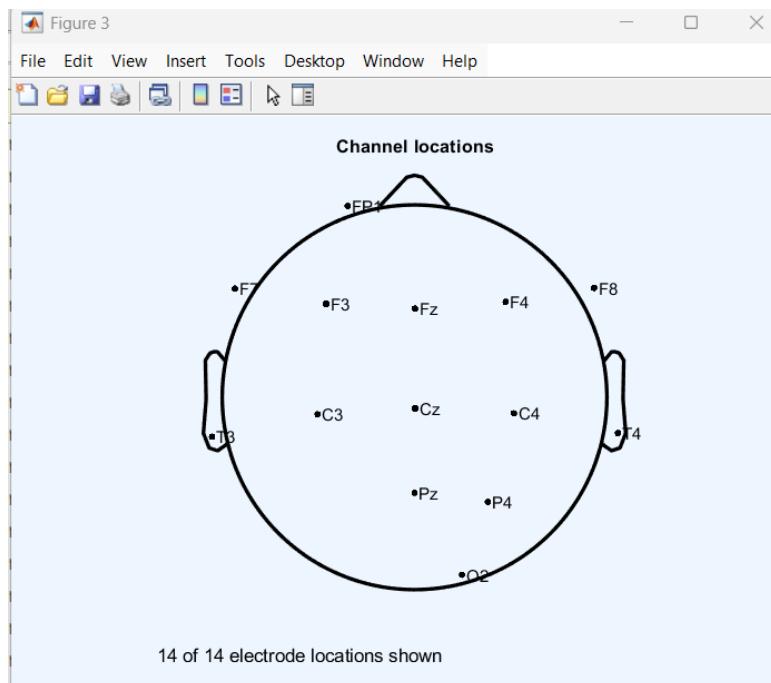
clean_channel: 79/97 blocks, 0.0 minutes remaining.
clean_channel: 80/97 blocks, 0.0 minutes remaining.
clean_channel: 81/97 blocks, 0.0 minutes remaining.
clean_channel: 82/97 blocks, 0.0 minutes remaining.
clean_channel: 83/97 blocks, 0.0 minutes remaining.
clean_channel: 84/97 blocks, 0.0 minutes remaining.
clean_channel: 85/97 blocks, 0.0 minutes remaining.
clean_channel: 86/97 blocks, 0.0 minutes remaining.
clean_channel: 87/97 blocks, 0.0 minutes remaining.
clean_channel: 88/97 blocks, 0.0 minutes remaining.
clean_channel: 89/97 blocks, 0.0 minutes remaining.
clean_channel: 90/97 blocks, 0.0 minutes remaining.
clean_channel: 91/97 blocks, 0.0 minutes remaining.
clean_channel: 92/97 blocks, 0.0 minutes remaining.
clean_channel: 93/97 blocks, 0.0 minutes remaining.
clean_channel: 94/97 blocks, 0.0 minutes remaining.
clean_channel: 95/97 blocks, 0.0 minutes remaining.
clean_channel: 96/97 blocks, 0.0 minutes remaining.
clean_channel: 97/97 blocks, 0.0 minutes remaining.
Removing 5 channel(s)...
Use vis_artifacts to compare the cleaned data to the original.
Current plot held
Done.

```



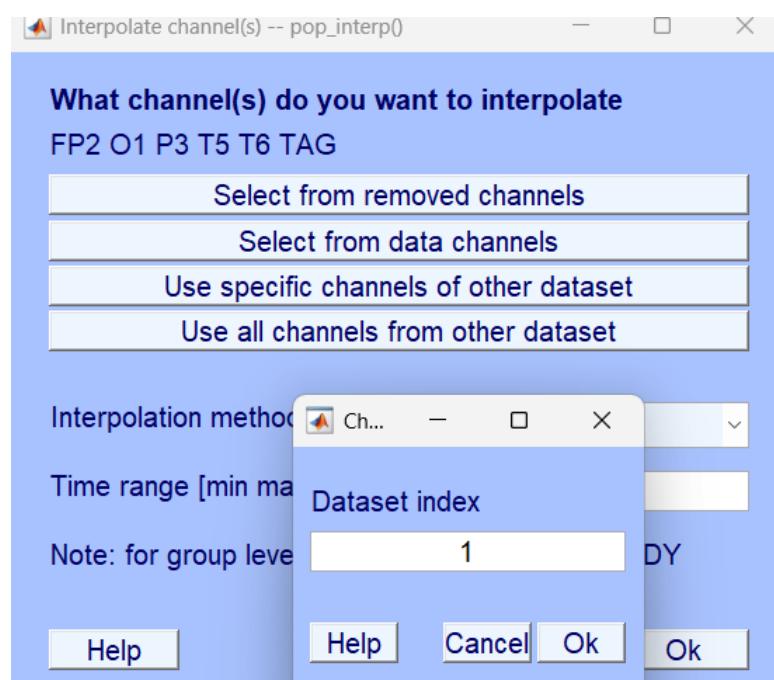
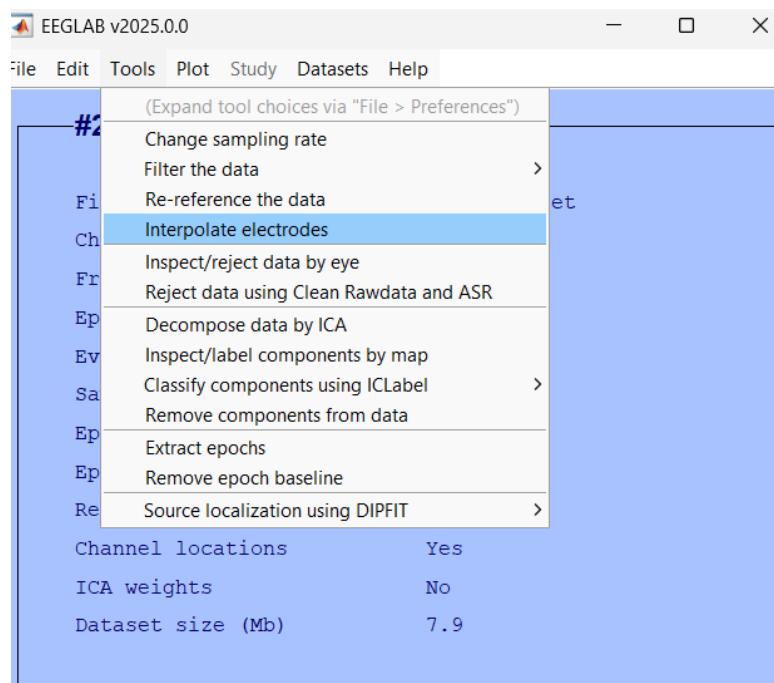
#2: HC_part4(noiseremoved)

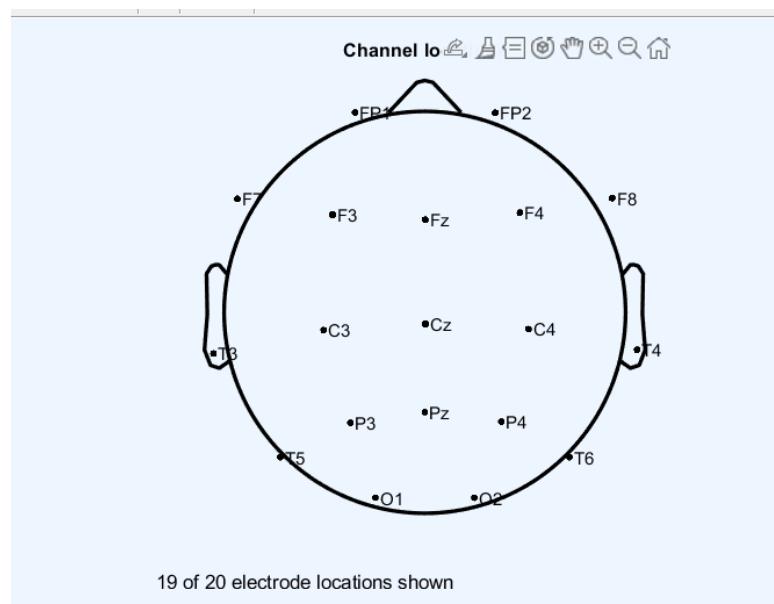
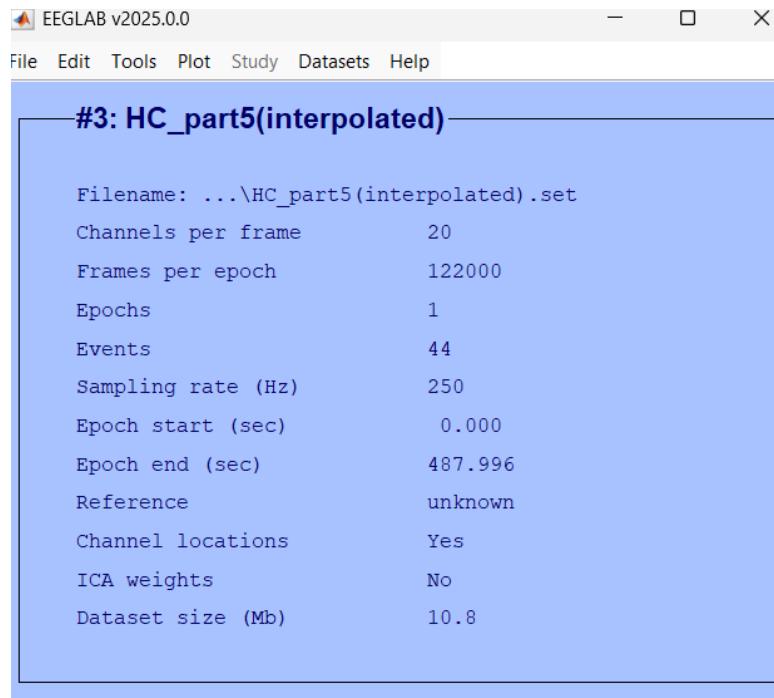
```
Filename: ...\\HC_part4 (noiseremoved).set
Channels per frame      14
Frames per epoch        122000
Epochs                  1
Events                  44
Sampling rate (Hz)      250
Epoch start (sec)       0.000
Epoch end (sec)         487.996
Reference                unknown
Channel locations        Yes
ICA weights              No
Dataset size (Mb)       7.9
```

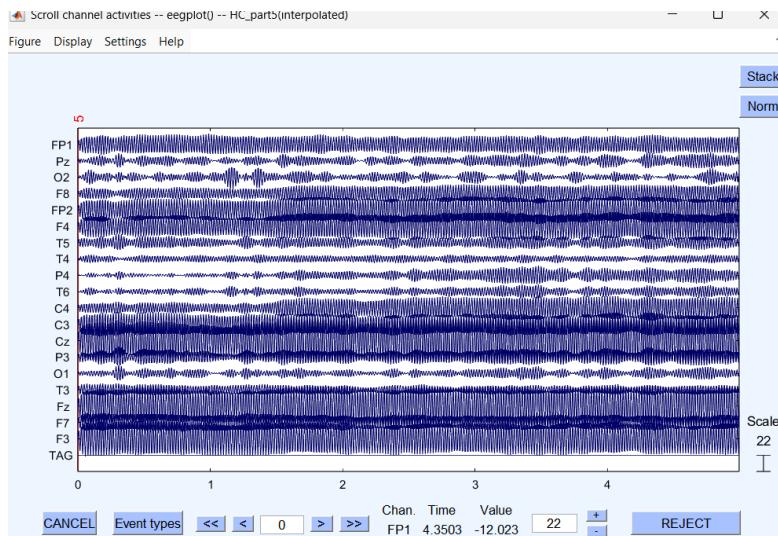


5. Interpolate Removed Channels

- Use spatial interpolation to restore missing channels and preserve the full montage.

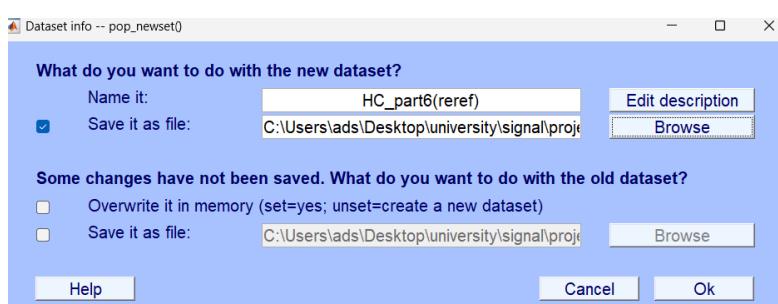
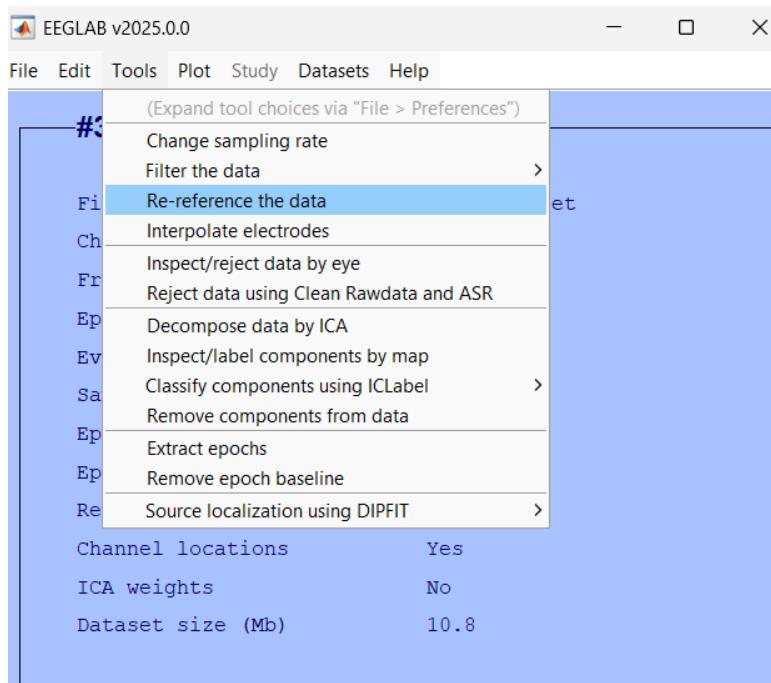


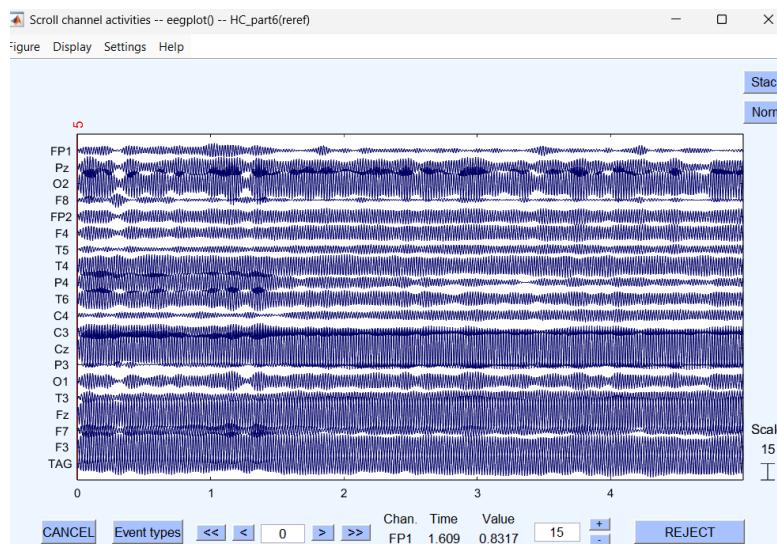
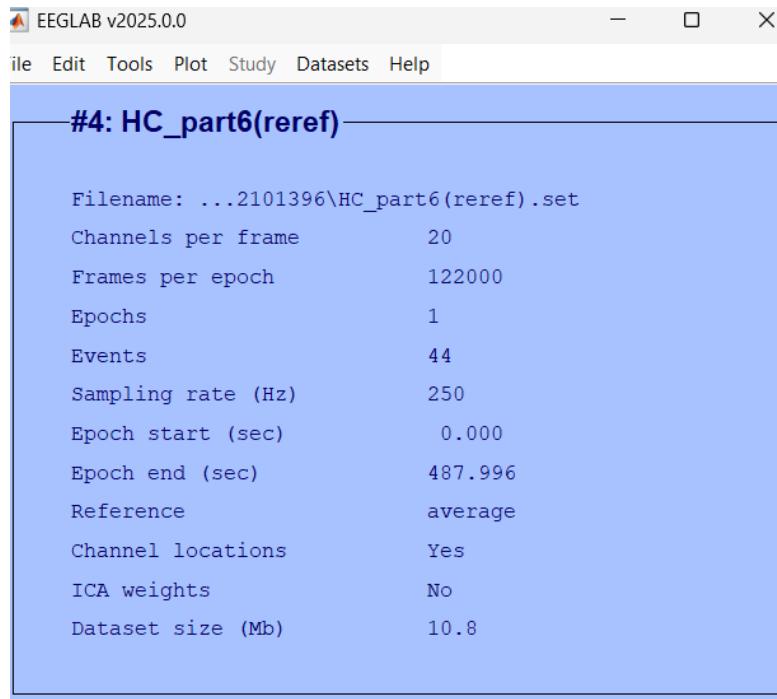




6. Re-reference EEG (First Pass)

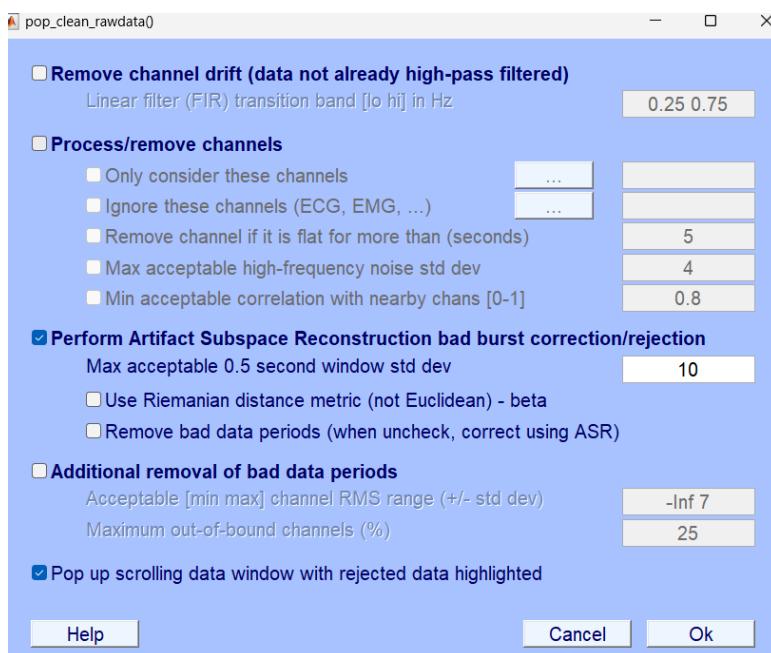
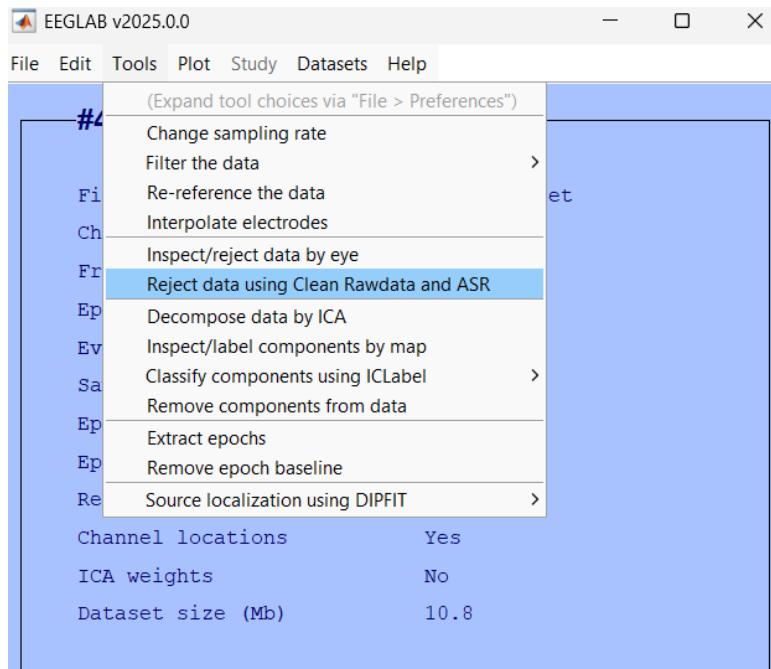
- Re-reference signals to the average of all EEG channels to remove common-mode noise.

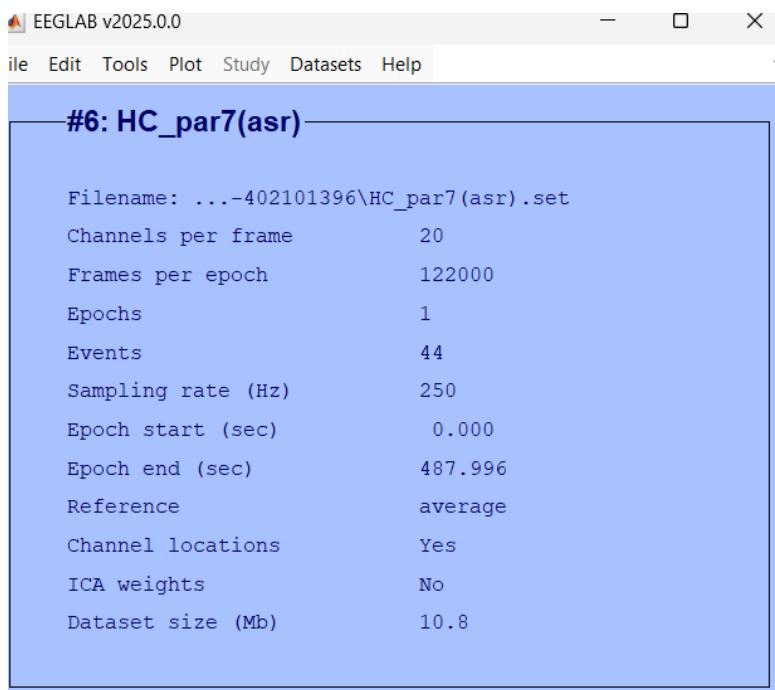
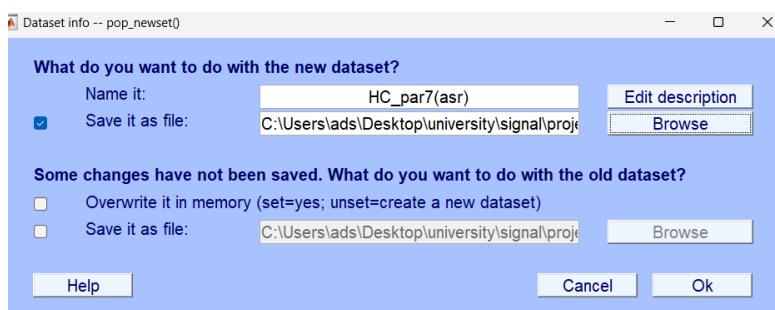
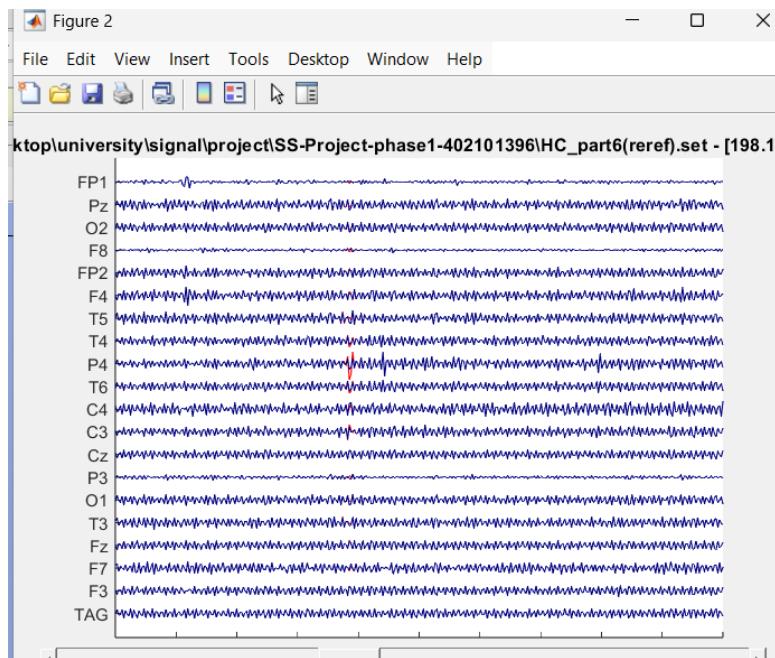




7. Artifact Subspace Reconstruction (ASR)

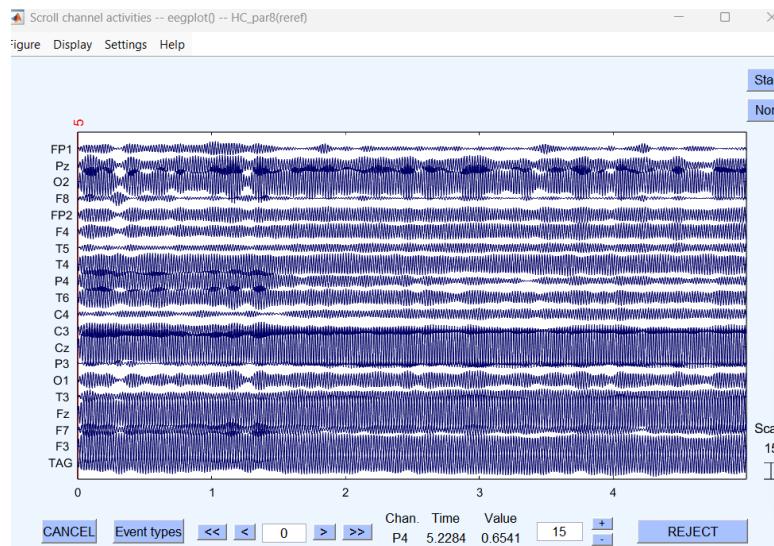
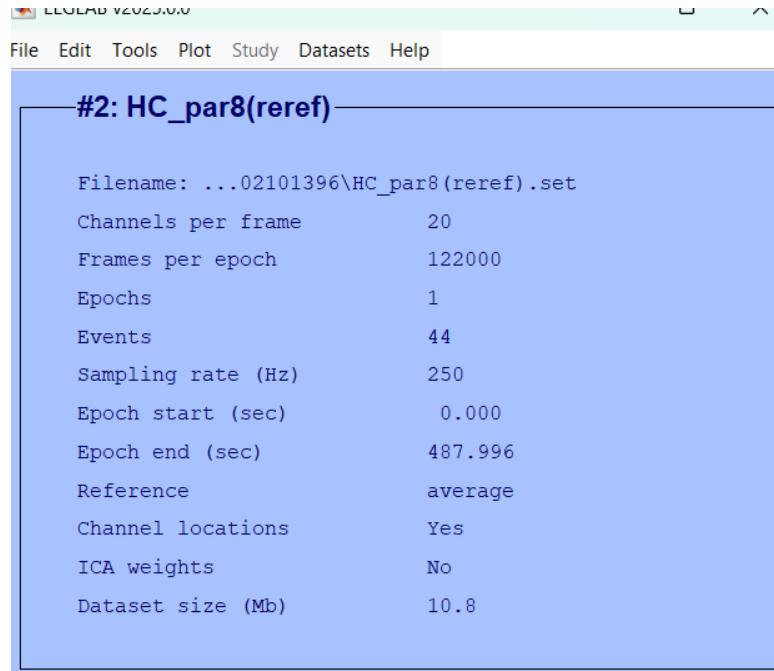
- Apply ASR with default settings via `clean_rawdata()` to eliminate transient artifacts such as muscle bursts.





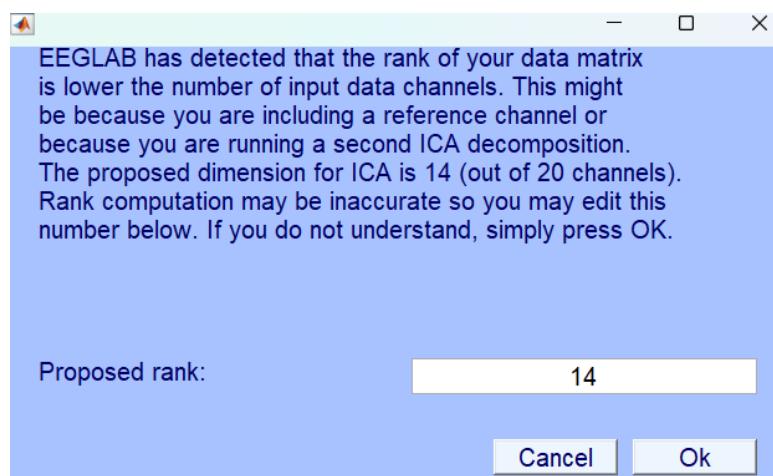
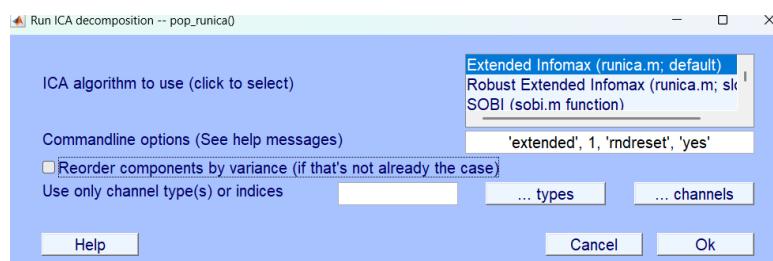
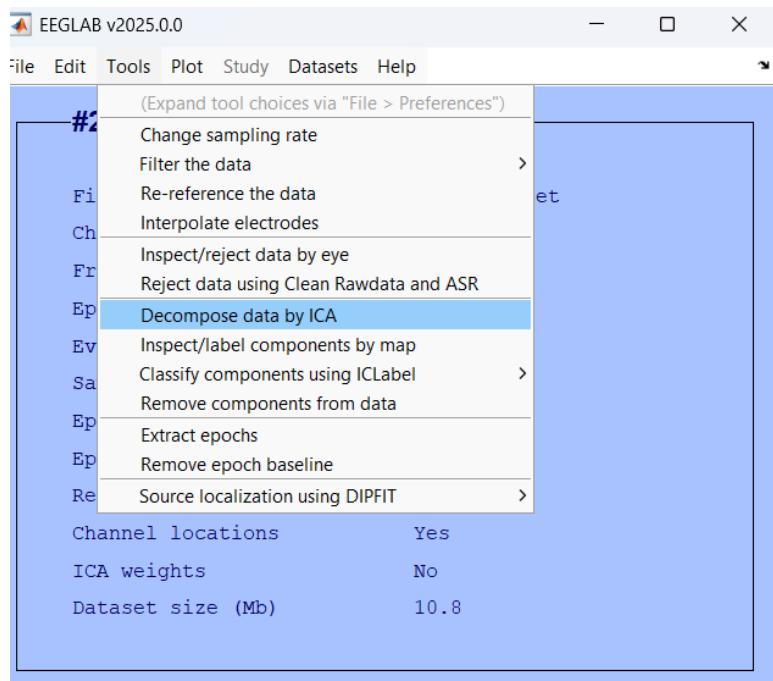
8. Re-reference EEG (Second Pass)

- 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).



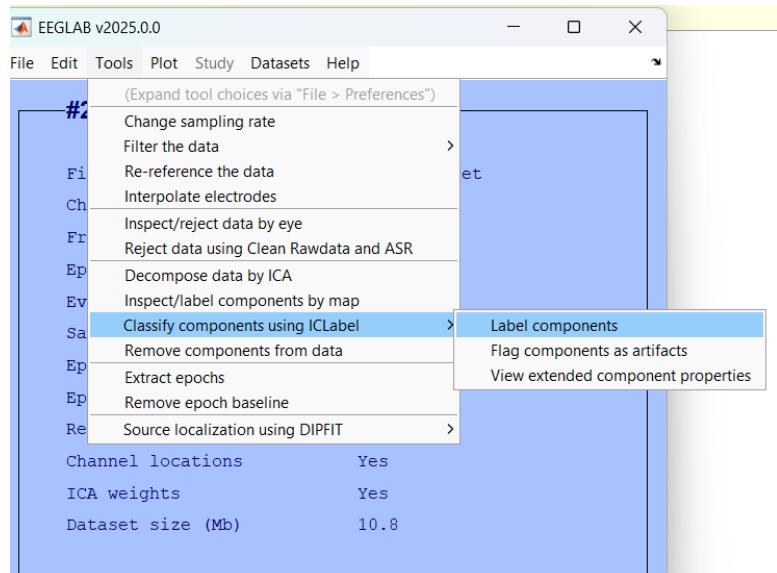
```

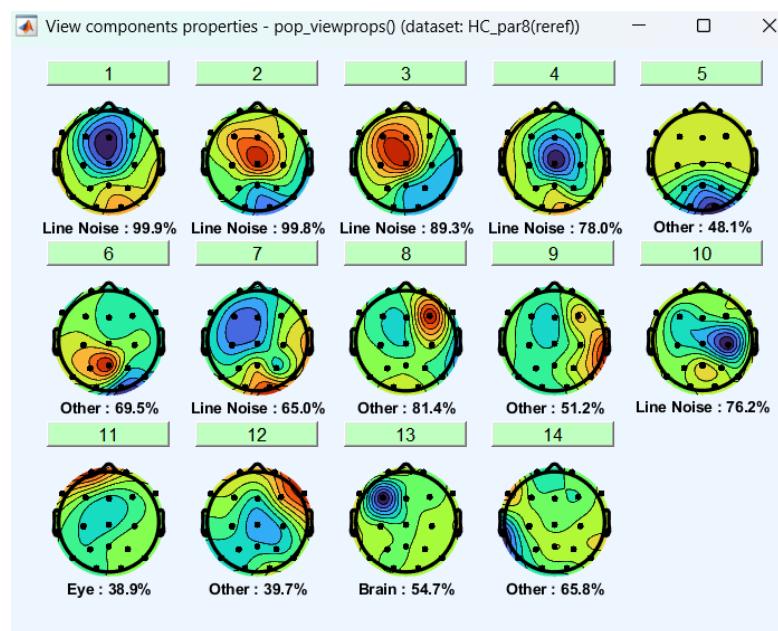
Attempting to convert data matrix to double precision for more accurate ICA results.
Attempting to convert data matrix to double precision for more accurate ICA results.
Data rank (14) is smaller than the number of channels (20).

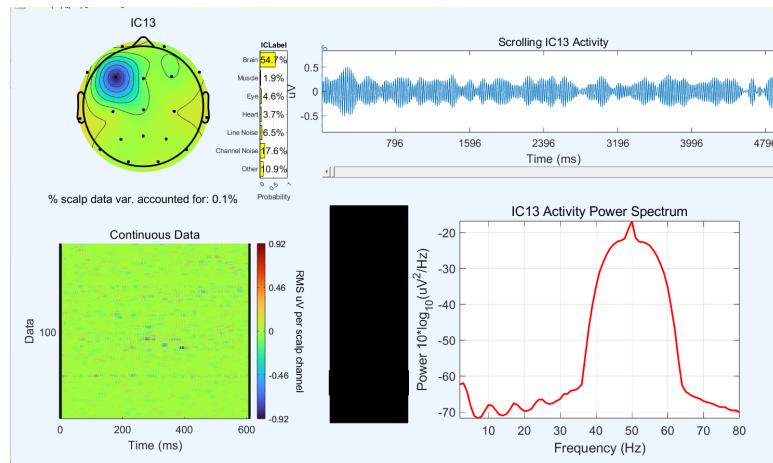
Input data size [14,122000] = 14 channels, 122000 frames/After PCA dimension reduction,
    finding 14 ICA components using extended ICA.
Kurtosis will be calculated initially every 1 blocks using 6000 data points.
Decomposing G22 frames per ICA weight ((19G)^2 = 122000 weights, Initial learning rate will be 0.001, block size 59.
Learning rate will be multiplied by 0.98 whenever angledelta >= 60 deg.
More than 32 channels: default stopping weight change 1E-7
Training will end when wchange < 1e-06 or after 512 steps.
Online bias adjustment will be used.
Removing mean of each channel ...
Final training data range -29.1169 to 29.0843
Reducing the data to 14 principal dimensions...
Computing the sphering matrix...
Starting weights are the identity matrix ...
Sphering the data ...
Beginning ICA training ... first training step may be slow ...
step 1 - lrate 0.001000, wchange 6.68366677, angledelta 0.0 deg
step 2 - lrate 0.001000, wchange 0.23201972, angledelta 0.0 deg
step 3 - lrate 0.001000, wchange 0.11228789, angledelta 80.4 deg
step 4 - lrate 0.000980, wchange 0.06368429, angledelta 77.8 deg
step 5 - lrate 0.000960, wchange 0.03503818, angledelta 100.8 deg

step 290 - lrate 0.000005, wchange 0.00000446, angledelta 110.5 deg
step 294 - lrate 0.000003, wchange 0.00000626, angledelta 92.9 deg
step 295 - lrate 0.000003, wchange 0.00000367, angledelta 123.9 deg
step 296 - lrate 0.000003, wchange 0.00000370, angledelta 99.9 deg
step 297 - lrate 0.000003, wchange 0.00000295, angledelta 110.8 deg
step 298 - lrate 0.000003, wchange 0.00000365, angledelta 89.9 deg
step 299 - lrate 0.000003, wchange 0.00000260, angledelta 116.8 deg
step 300 - lrate 0.000002, wchange 0.00000232, angledelta 104.0 deg
step 301 - lrate 0.000002, wchange 0.00000222, angledelta 101.2 deg
step 302 - lrate 0.000002, wchange 0.00000384, angledelta 129.9 deg
step 303 - lrate 0.000002, wchange 0.00000237, angledelta 94.8 deg
step 304 - lrate 0.000002, wchange 0.00000226, angledelta 122.7 deg
step 305 - lrate 0.000002, wchange 0.00000235, angledelta 120.7 deg
step 306 - lrate 0.000002, wchange 0.00000145, angledelta 107.4 deg
step 307 - lrate 0.000002, wchange 0.00000170, angledelta 120.2 deg
step 308 - lrate 0.000002, wchange 0.00000160, angledelta 109.3 deg
step 309 - lrate 0.000002, wchange 0.00000099, angledelta 102.8 deg
Composing the eigenvector, weights, and sphere matrices
    into a single rectangular weights matrix; sphere=eye(14)
Sorting components in descending order of mean projected variance ...
Using pseudo-inverse of weight matrix to rank order component projections.
Scaling components to RMS microvolt
Scaling components to RMS microvolt
Scaling components to RMS microvolt

```

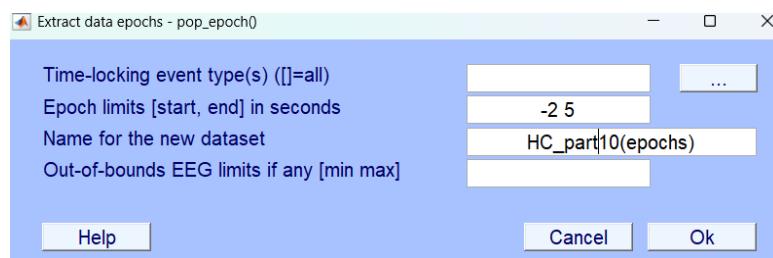
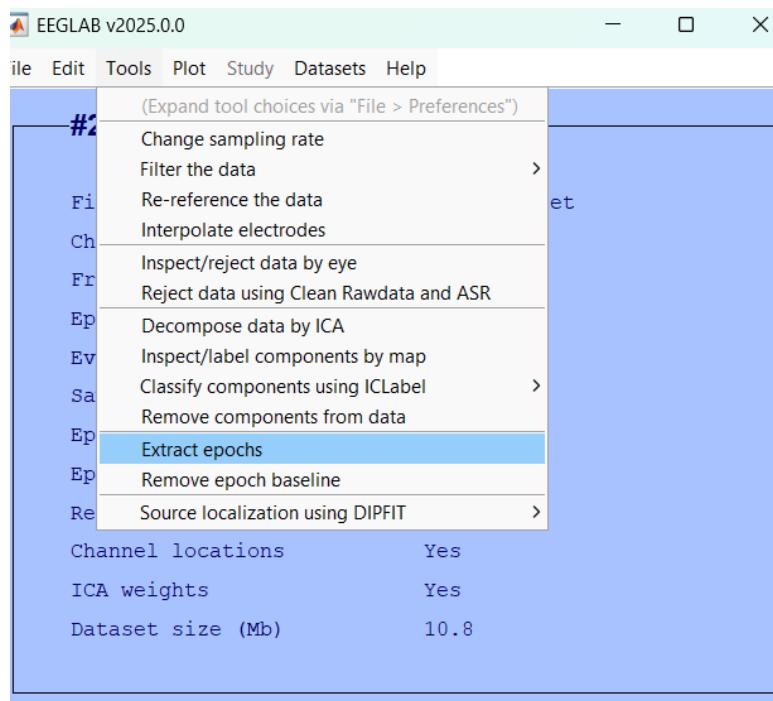


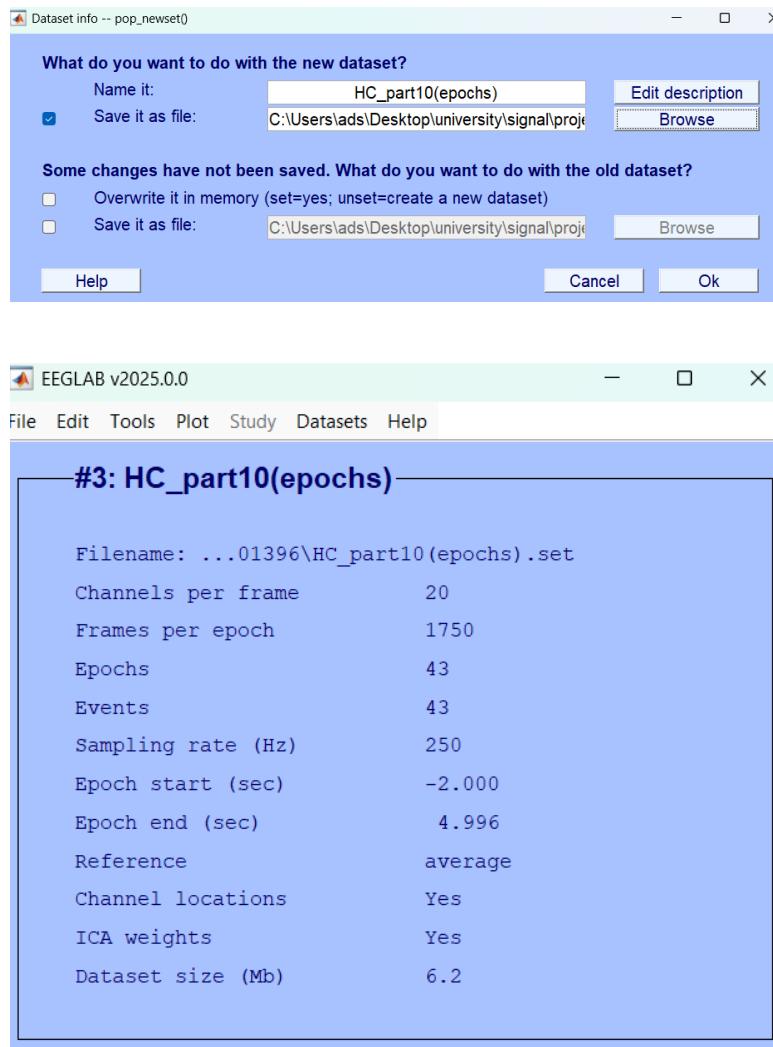




10. Epoching

- 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., $z > 3.5$).

```
% load the depoched dataset
EEG = pop_loadset('filename', 'HC_part10(epochs).set', ...
    'filepath', 'C:\Users\ads\Desktop\university\signal\project\SS-Project-phaseI-402\01396\');
EEG = eeg_checkset(EEG);

% Compute mean absolute signal per epoch and z-score it
epoch_amplitude = squeeze(mean(abs(EEG.data), 2)); % [channels x trials]
mean_amplitude = mean(epoch_amplitude, 1); % average over channels
z_scores = zscore(mean_amplitude); % z-score over trials

% Find bad epochs and reject
threshold = 3.5;
bad_epochs = find(z_scores > threshold);

fprintf('Rejecting %d epochs (z > %.1f)\n', length(bad_epochs), threshold);

EEG = pop_rejepoch(EEG, bad_epochs, 0); % 0 = do not use GUI
EEG = eeg_checkset(EEG);

% Save the cleaned dataset
pop_saveset(EEG, 'filename', 'HC_part10(trialrejection).set', ...
    'filepath', 'C:\Users\ads\Desktop\university\signal\project\SS-Project-phaseI-402\01396\');

disp('Done! Cleaned dataset saved as HC_part10(trialrejection).set');
```

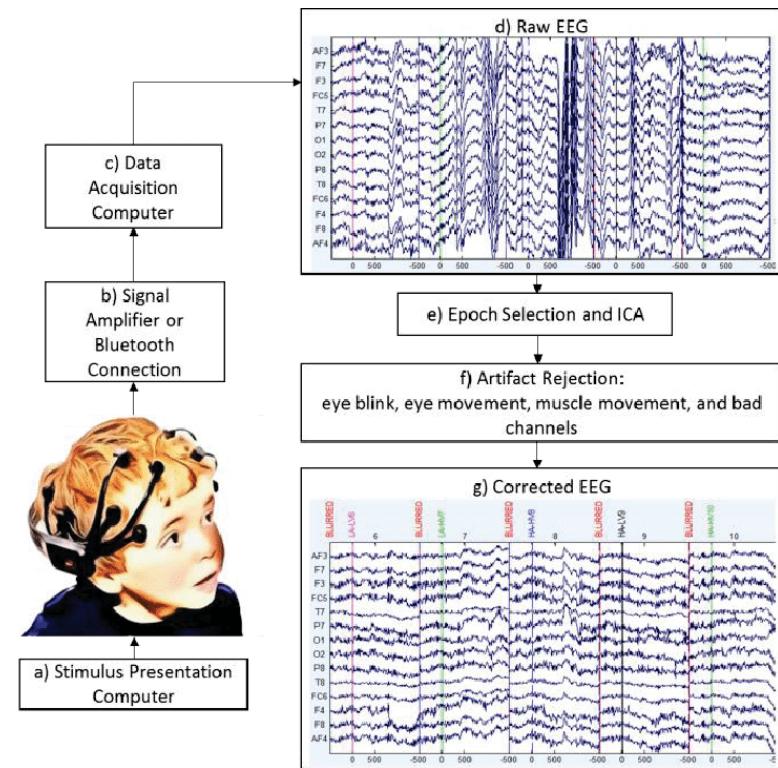
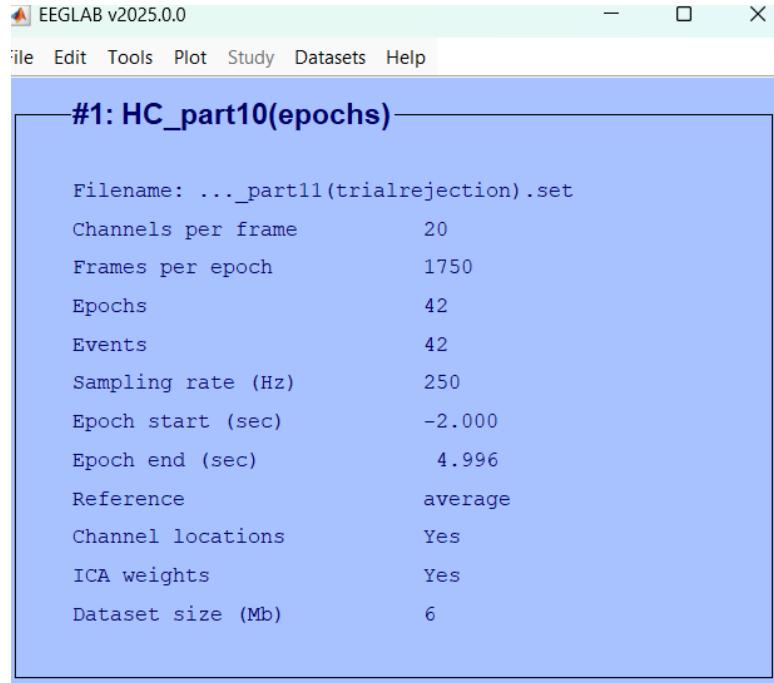


Figure 4: Data aquistion to Clean data

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:

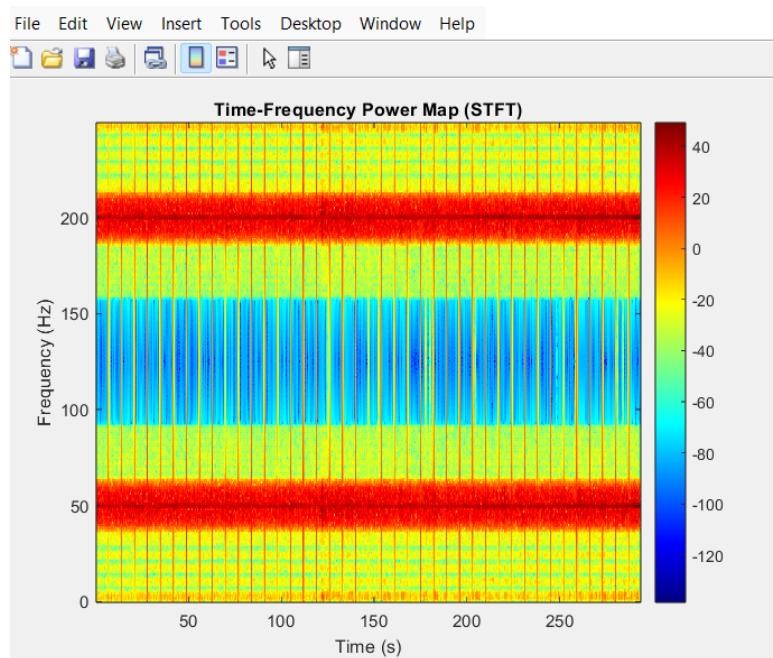
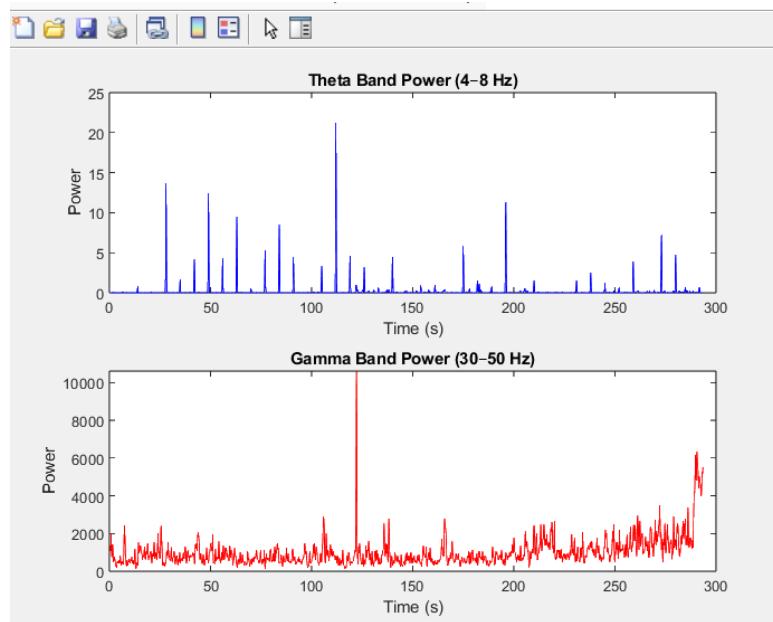
$$\text{Power}(t, f) = |\text{STFT}(t, f)|^2 \quad (1)$$

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.

```

1 % Load cleaned dataset
2 EEG = pop_loadset('filename', 'HC_part1 | (trialrejection).set', ...
3   'filepath', 'C:\Users\adel\Desktop\university\signal\project\SS-Project-phase1-402101396\');
4 %Select channel and prepare data
5 chan = 1; % e.g., Cz or any relevant channel
6 fs = EEG.srate;
7 signal = EEG.data(chan,:,:);
8 signal = reshape(signal, 1, []); % Concatenate all epochs
9 % STFT Parameters
10 win_duration = 1.0; % 1 second window for better frequency resolution
11 overlap_ratio = 0.90; % 90% overlap for smooth transitions
12 win_samples = round(win_duration * fs);
13 overlap_samples = round(overlap_ratio * win_samples);
14 %Compute STFT
15 [S, F, T] = stft(signal, fs, ...
16   'Window', hann(win_samples), ...
17   'OverlapLength', overlap_samples, ...
18   'Centered', false);
19 % Power Spectrogram
20 power = abs(S).^ 2;
21 % Extract theta and gamma power
22 theta_idx = find(F >= 4 & F <= 8);
23 gamma_idx = find(F >= 30 & F <= 50);
24 theta_power = mean(power(theta_idx, :), 1);
25 gamma_power = mean(power(gamma_idx, :), 1);
26 % Plot power over time
27 figure;
28 subplot(2,1,1);
29 plot(T, theta_power, 'r');
30 xlabel('Time (s)');
31 ylabel('Power');
32 title('Theta Band Power (4-8 Hz)');
33 subplot(2,1,2);
34 plot(T, gamma_power, 'r');
35 xlabel('Time (s)');
36 ylabel('Power');
37 title('Gamma Band Power (30-50 Hz)');
38 % Plot full power spectrogram
39 figure;
40 imagesc(T, F, 10*log10(power)); % Convert to dB scale
41 axis xy;
42 xlabel('Time (s)');
43 ylabel('Frequency (Hz)');
44 title('Time-Frequency Power Map (STFT)');
45 colorbar;
46 colormap jet;
47

```



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.

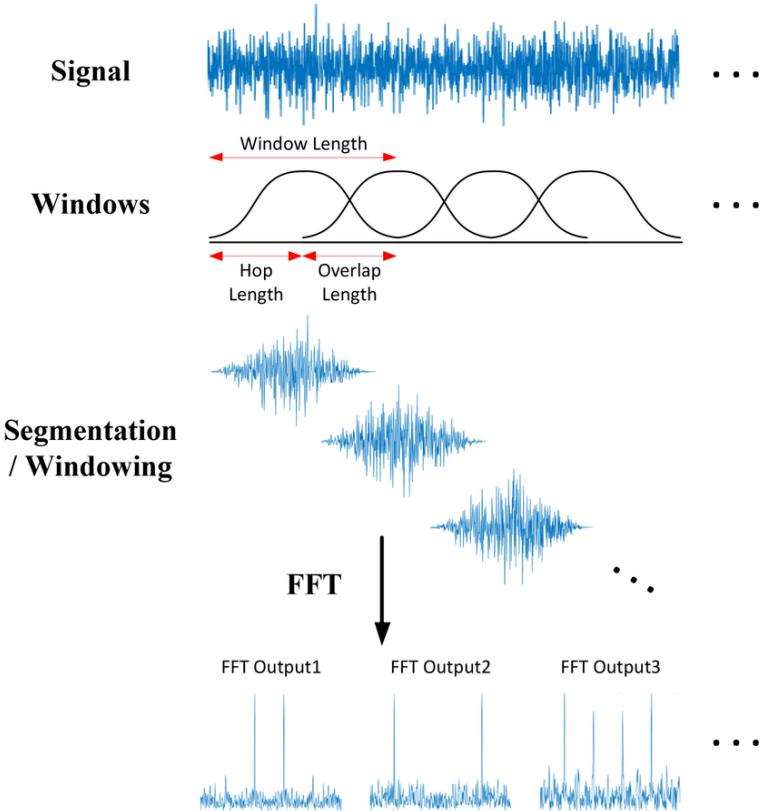


Figure 5: Short-time Fourier transform (STFT) overview

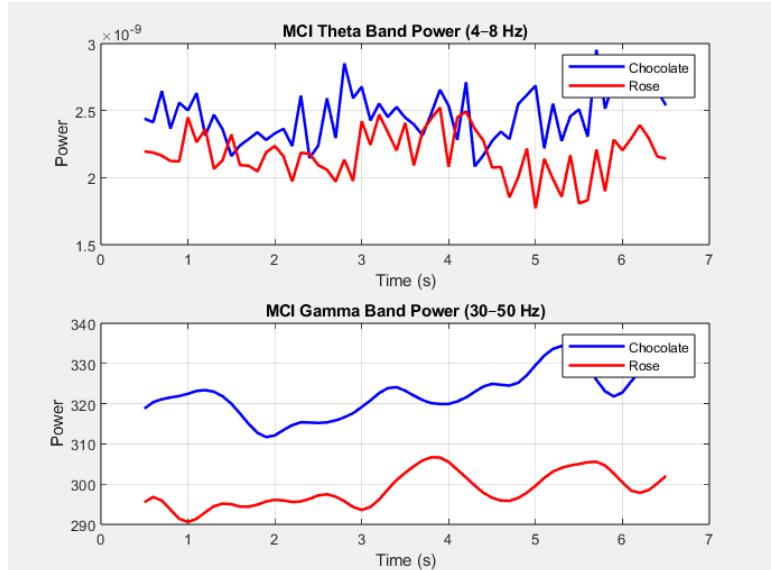
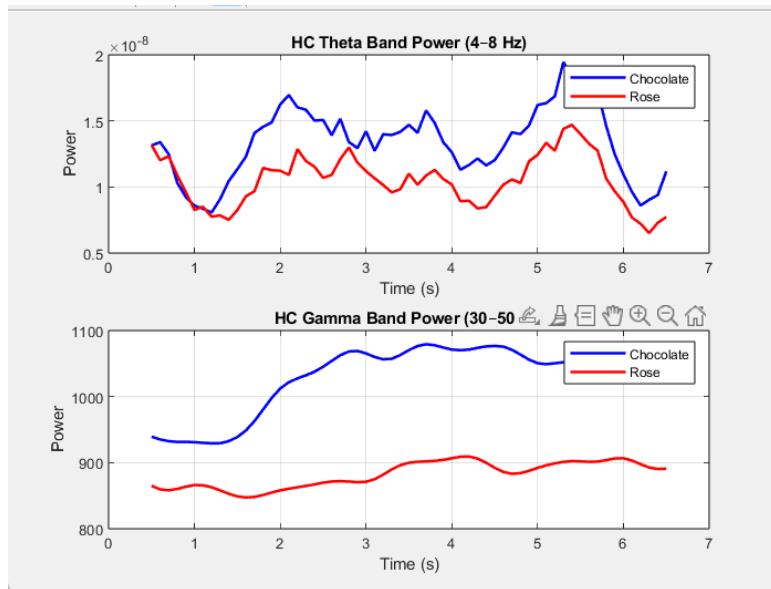
4.4 Building Power-Time Matrices and Comparison

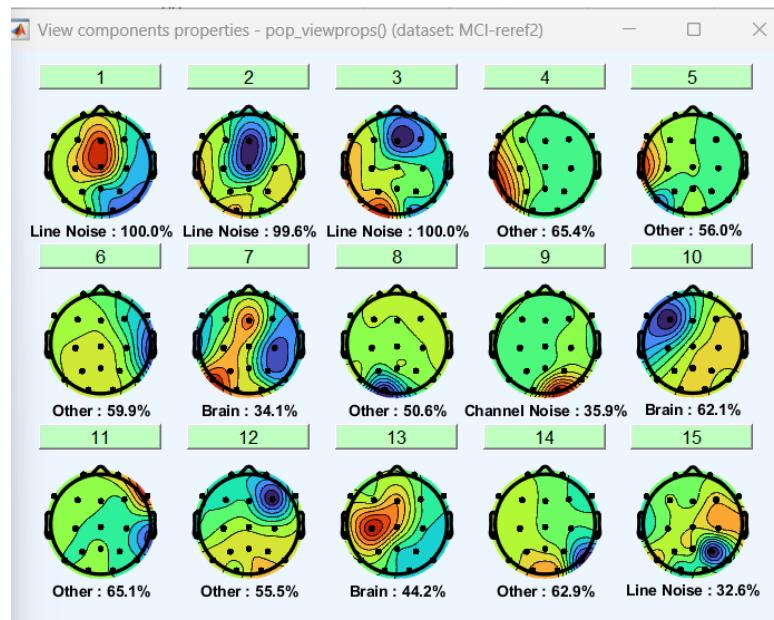
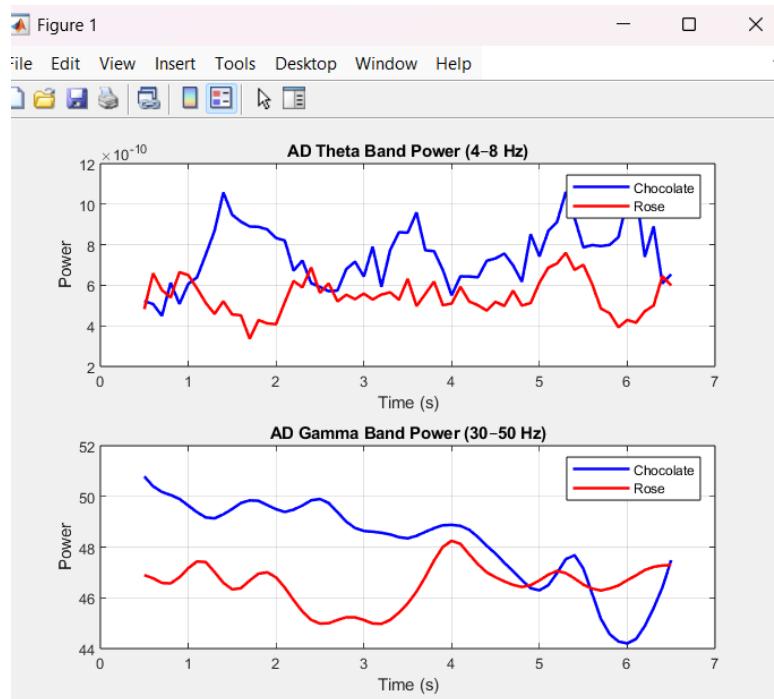
Once the power has been calculated for all trials, organize the data into a 2D matrix for each condition:

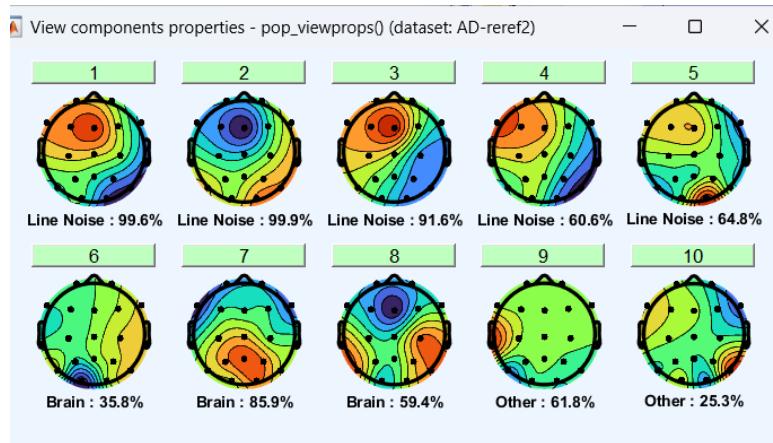
- One axis is time, and the other is trials.
- Average across trials to create a single power vs. time curve for each subject, odor, and frequency band.
- Create plots for each odor condition (chocolate and rose), and include one line per subject on each plot-comparing Healthy Control, MCI, and Alzheimer's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

i did all the last parts for MCI and AD subjects and the results are put in my delivered file. the average power of all the subjects and odors: the code is also attached in a text file.







4.5 What to Look For

When interpreting your plots, consider:

- Do any subjects show stronger or earlier peaks in power?

Peaks in HC are stronger and earlier.

- Are power patterns different for chocolate vs. rose?

In all groups, chocolate consistently elicits higher power than rose — especially in the theta and gamma bands. This is expected, as chocolate is more arousing, engaging both emotional and cognitive networks more strongly than rose.

- Is there a consistent delay or drop in response in the MCI or Alzheimer's subjects?

our results indicate that both MCI and AD subjects exhibit flatter or delayed power curves compared to HC, mostly in the theta band. Notably, the AD subject demonstrates the most significant drop.

- Does theta or gamma seem more affected in impaired states?

Both are affected, but gamma appears more dramatically suppressed in AD.

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?

we used short-time Fourier transform (STFT) to extract time-resolved power in theta (4–8 Hz) and gamma (30–50 Hz) bands. This method allowed us to visualize the temporal dynamics of power in response to odors, clearly distinguishing between conditions and subjects. The method was particularly effective in revealing temporal patterns and latency differences, which static power measures or full-spectrum plots wouldn't show as clearly.

- How did your choice of window length and overlap affect the resolution or interpretability of the signal?

Our STFT setup appeared to strike a reasonable balance. We captured smoothed temporal power curves without too much noise, but with enough temporal detail to distinguish peaks. However, gamma band results were more susceptible to noise due to their higher frequency and faster dynamics, suggesting that a shorter window or more overlap might help resolve rapid changes better in future analyses.

- Did you observe consistent differences in power between subjects or odors?

Yes. Consistent patterns were evident:

HC subjects showed stronger and clearer peaks in both theta and gamma bands, especially for chocolate.

MCI and AD subjects had weaker or delayed peaks, with less pronounced power especially in the gamma band.

Across groups, chocolate odor consistently evoked higher power than rose, particularly in gamma, suggesting a potentially stronger neural engagement or sensory association.

- What preprocessing choices might have influenced your results, and what would you try differently next time?

Preprocessing steps like filtering, epoching, and trial rejection could influence power calculations.

Next time, consider independent component analysis (ICA) to remove artifacts more precisely, and possibly baseline normalization to better compare across subjects.

Using a log-transform of power or normalization to baseline might also improve interpretability

- How do these power dynamics set the stage for phase-amplitude coupling in the next phase?

The distinct theta and gamma patterns across subjects suggest that phase-amplitude coupling (PAC) could differ significantly across conditions:

In HC, strong and temporally aligned theta/gamma power may reflect robust PAC.

In AD or MCI, disrupted or weaker theta/gamma dynamics may lead to weaker or misaligned coupling. These findings form a solid hypothesis: PAC might be impaired in Alzheimer's or cognitive decline, particularly during odor processing, and chocolate might enhance or restore PAC more than rose.

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.

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