Exploring Neuronal Synchronization Dynamics in Epilepsy Using the Kuramoto Model: Insights from iEEG Data Analysis

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Abstract

This project investigates the synchronization dynamics within complex networks of neuronal activity during epileptic seizures, utilizing the Kuramoto Model adapted for phase-coupled oscillators with varying natural frequencies. Intracranial electroencephalogram (iEEG) data from epilepsy patients were processed and analyzed to explore how synchronization patterns manifest across different brain regions during seizure events. The methodology involved converting iEEG data corresponding to left mesial temporal from HDF5 to CSV format for analysis, filtering the data to focus on the Delta frequency band (1-4 Hz), and reconstructing the time series to capture the dynamics around seizure events. A network of interactions was constructed using a phase correlation matrix, which was then binarized to define the connectivity in the Kuramoto Model. The model parameters, including coupling strength and natural frequencies, were systematically varied to study their impact on network synchronization, assessed through the phase coherence metrics.

Key findings reveal distinct synchronization patterns across epileptogenic zones, with the order parameter fluctuating in response to changes in coupling strength. These fluctuations highlight the critical thresholds needed for the network to achieve synchronization, offering insights into the mechanisms of seizure propagation and the potential onset of seizures. The study underscores the importance of coupling strength and network structure in the synchronization dynamics of epileptic seizures.

Note: This research not only enhances our understanding of epilepsy through network synchronization but also suggests new avenues for developing predictive tools and targeted interventions based on the synchronization dynamics observed in neuronal networks. The application of the Kuramoto Model in this context demonstrates its potential as a powerful tool for elucidating complex biological phenomena and improving the management and treatment of epilepsy.

Introduction

Overview of Synchronization in Complex Networks

Synchronization phenomena are ubiquitous in nature, observed in systems ranging from celestial mechanics to biological networks. In complex networks, synchronization refers to the process where system components, though operating on individual rules, achieve a collective behavior due to interactions. This concept is particularly intriguing in neuroscience, where neuronal synchronization affects both normal and pathological brain functions.

Importance of Studying Synchronization in Epilepsy

Epilepsy is characterized by the occurrence of spontaneous seizures, resulting from the abnormal, excessive synchronization of neuronal activity. Understanding these synchronization patterns can provide crucial insights into the mechanisms of seizure generation and propagation, which is essential for developing better diagnostic and therapeutic strategies.

Introduction to the Kuramoto Model

The Kuramoto Model is a mathematical model used to describe synchronization in a system of coupled oscillators with differing natural frequencies. It has been widely applied in various fields, including physics, chemistry, and biology, to study emergent collective behavior from simple rules of local interactions. In the context of epilepsy, applying the Kuramoto Model allows for the analysis of how local interactions between neurons can lead to the global synchronization observed during seizures.

Relevance of the Kuramoto Model to the Study

The Kuramoto Model is particularly suited for epilepsy studies as it provides a framework to model the complex interactions within neuronal networks. By adapting the Kuramoto Model to include the specific connectivity and coupling strengths derived from iEEG data, this project aims to capture the dynamics of neuronal synchronization in relation to epileptic seizures. This approach not only aids in the understanding of the underlying network dynamics but also in identifying potential targets for disrupting pathological synchronization.

Objectives of the Project

The main objectives of this project are:

1. To preprocess and analyze iEEG data from an epilepsy patient, focusing on seizure onset zones.
2. To construct a phase correlation network based on the preprocessed data.
3. To apply and modify the Kuramoto Model to study synchronization dynamics within this network.
4. To interpret the synchronization patterns in the context of epilepsy and assess the model's effectiveness in providing insights into seizure dynamics.

This introduction sets the stage for a detailed exploration of synchronization in neuronal networks through the lens of the Kuramoto Model, emphasizing its application to understanding and potentially mitigating epileptic seizures.

Methodology

Data Preparation

The initial step involves converting the iEEG data from HDF5 format to CSV for easier manipulation and analysis in Python. The h5py library is used to read HDF5 files, which are commonly used for storing large datasets due to their efficient storage capabilities. The conversion process extracts EEG data and channel names, converting them into a pandas DataFrame, which is then saved as a CSV file. This step is crucial for making the data accessible for subsequent preprocessing and analysis stages.

Data Filtration

The raw iEEG data is filtered to focus on specific frequency bands relevant to epileptic activity. For this project, the Delta band (1-4 Hz) is chosen, which is significant in sleep and pathological conditions such as epilepsy. A Butterworth bandpass filter is applied using the scipy.signal library. This type of filter is preferred for its flat response in the passband and effective suppression of unwanted frequencies, making it ideal for EEG data analysis where retaining the shape of the waveform within the frequency band of interest is crucial.

Sampling Rate and Filter Order: The sampling rate is set at 200 Hz based on the data acquisition parameters. An order of 5 for the Butterworth filter provides a balance between effectively filtering out frequencies outside the desired range and maintaining the integrity of the waveform within the band.

Data Reconstruction and Fragmentation

To analyze the synchronization around seizure events:

- **Data Truncation**: The data is truncated to include 5000 time points before and after each seizure, providing a comprehensive view of the pre-seizure, seizure, and post-seizure stages.
- **Channel Cleaning**: Channels that are references or start with 'G', 'F', 'I' are removed to avoid artifacts and focus on relevant EEG channels.
- **Fragmentation**: The truncated data is divided into 14 equal parts to analyze changes over time, with a specific focus on the seizure event. This scheme allows for detailed analysis of the dynamics before, during, and after the seizure.

Network Construction

- **Phase Correlation Matrix**: A correlation matrix is constructed using phase correlation, a method that is robust against noise and amplitude variations, making it suitable for EEG data where non-stationarity and amplitude differences can pose challenges.

- **Binarization**: The correlation matrix is binarized by setting a threshold that ensures all channels are included in the network, facilitating the study of complete network dynamics. ***The thresholding approach involves gradually lowering the threshold until all nodes (channels) are part of a single connected component, ensuring the network's integrity.***

Kuramoto Model

The implementation of the Kuramoto Model in this project is specifically tailored to understand how synchronization dynamics manifest in complex networks, such as the neuronal networks observed in epilepsy. Here is an expanded explanation of the key components and considerations in applying the Kuramoto Model to iEEG data from epilepsy patients:

Model Basics

The Kuramoto Model describes the dynamics of a system of coupled oscillators where each oscillator has a phase (θ_i) and a natural frequency (ω_i). The evolution of each oscillator's phase is influenced by its natural frequency and the coupling with other oscillators. The generalized equation for the (i)-th oscillator in a network of (N) oscillators is given by:

$$\dot{\theta}_i = \omega_i + \sum_{j=1}^{N} K_{ij} \sin(\theta_j - \theta_i)$$

where (K_{ij}) represents the coupling strength between oscillators (i) and (j), and ($\sin(\theta_j - \theta_i)$) is the sinusoidal coupling function that models the tendency of oscillators to synchronize.

Natural Frequencies

The natural frequencies (ω_i) of the oscillators are assumed to be normally distributed, which is a common assumption that allows for the modeling of variability in intrinsic frequencies of different brain regions. This variability is crucial for modeling real-world systems where components (such as neurons) do not behave identically. In this project, the mean and standard deviation of the natural frequencies can be adjusted to explore different scenarios of frequency distributions, reflecting the heterogeneity of neuronal firing rates.

Coupling Matrix and Network Structure

The coupling matrix (K) is derived from the adjacency matrix of the network, which is constructed based on the phase correlations between different EEG channels. Each element (K_{ij}) of the matrix is set based on the binarized correlation matrix, which reflects whether there is a significant interaction between pairs of channels. This approach allows the model to incorporate the actual connectivity pattern observed in the EEG data, making the simulations more realistic and relevant.

Integration and Time Parameters

The differential equations of the Kuramoto Model are integrated using the odeint function. The choice of the time step (dt) and total simulation time (T) is crucial:

Time Step (dt): A smaller (dt) provides a finer resolution, capturing more detailed dynamics of phase changes. This is important for EEG data where rapid changes in phase relationships can occur.
Total Time (T): The total time determines how long the simulation runs and should be sufficient to allow the system to exhibit its long-term behavior, including reaching a steady state or showing persistent dynamic patterns

For each coupling value, we create a new Kuramoto model with that coupling value, a time step dt = 0.1, a total time T = 1000, and a number of nodes n. We then set the natural frequencies of the model to be normally distributed with a given mean and standard deviation. The model is then run with an adjacency matrix/binary matrix, which describes the connections between the nodes in the model. The result of the simulation is then processed in the next part.
The next part corresponds to calculating the mean and standard deviation of the phase coherence for each simulation. Phase coherence is a measure of how synchronized the nodes in the model are. For each coupling value, it calculates the phase coherence for the last 8000 time steps of the simulation. It then calculates the mean and standard deviation of these phase coherence values that we build the plots upon.

Analysis Metrics

Two primary metrics are used to analyze the output of the Kuramoto Model:

- Phase Coherence: This metric measures the overall synchronization of the system. It is calculated as the magnitude of the average of unit vectors pointing in the direction of each oscillator's phase. A higher coherence indicates stronger synchronization.
- Order Parameter (R): Similar to phase coherence, the order parameter quantifies the degree of synchronization among oscillators. It is particularly useful for examining how synchronization varies across different network regions or under different coupling strengths.

Visualization and Interpretation

The results from the Kuramoto Model are visualized to show how synchronization (measured by phase coherence and the order parameter) varies with changes in coupling strength and across different network configurations. These visualizations help in understanding the conditions under which synchronization is enhanced or suppressed, which is directly relevant to understanding the dynamics of epileptic seizures.

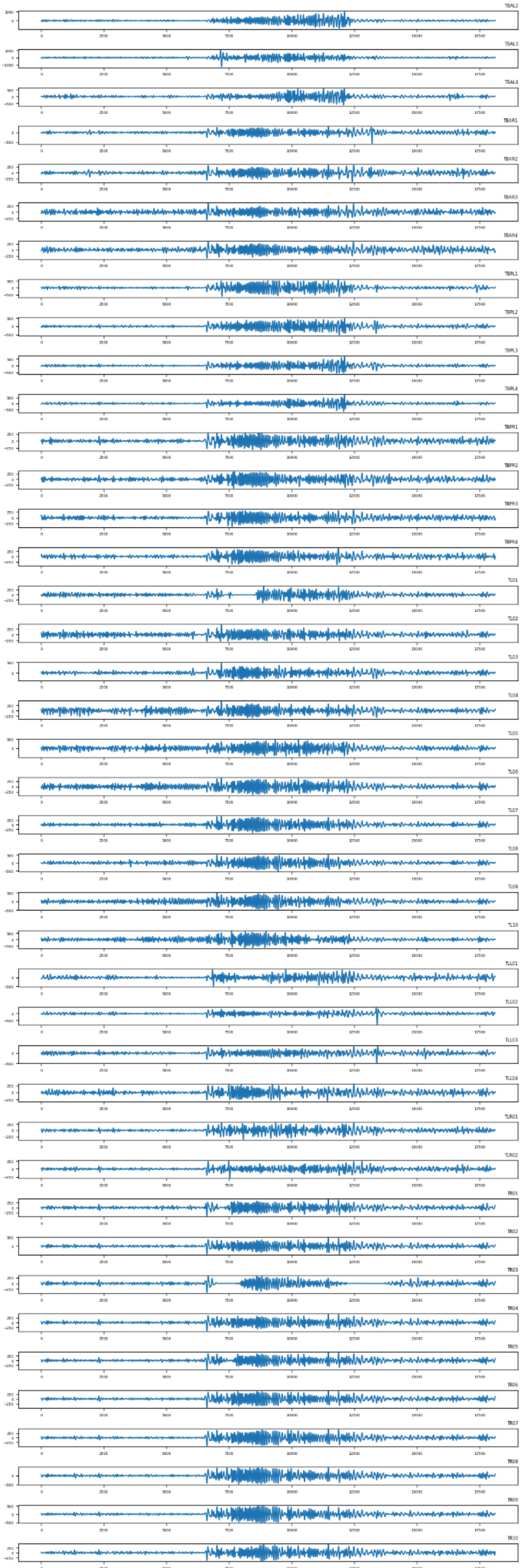
By applying the Kuramoto Model in this manner, the project aims to bridge the gap between mathematical models of synchronization and practical, clinical insights into epilepsy, potentially leading to improved strategies for intervention and management of this complex neurological condition.

Results

Visualization of Data

The initial visualization involves plotting the time series data extracted from the iEEG recordings. These plots serve as a fundamental tool to observe how epilepsy influences different brain regions (represented by different channels). Although these time series plots provide a basic visualization of the data, they offer limited information regarding the dynamic interactions between channels during seizure episodes. Graphs depicting the time series for each channel illustrate these patterns, helping to set the stage for more complex analyses.

Below figures visualize the data 111g0L (L) and 112g0L (R) after reconstructing the timeseries to focus on the part corresponding to the occurrence of epilepsy.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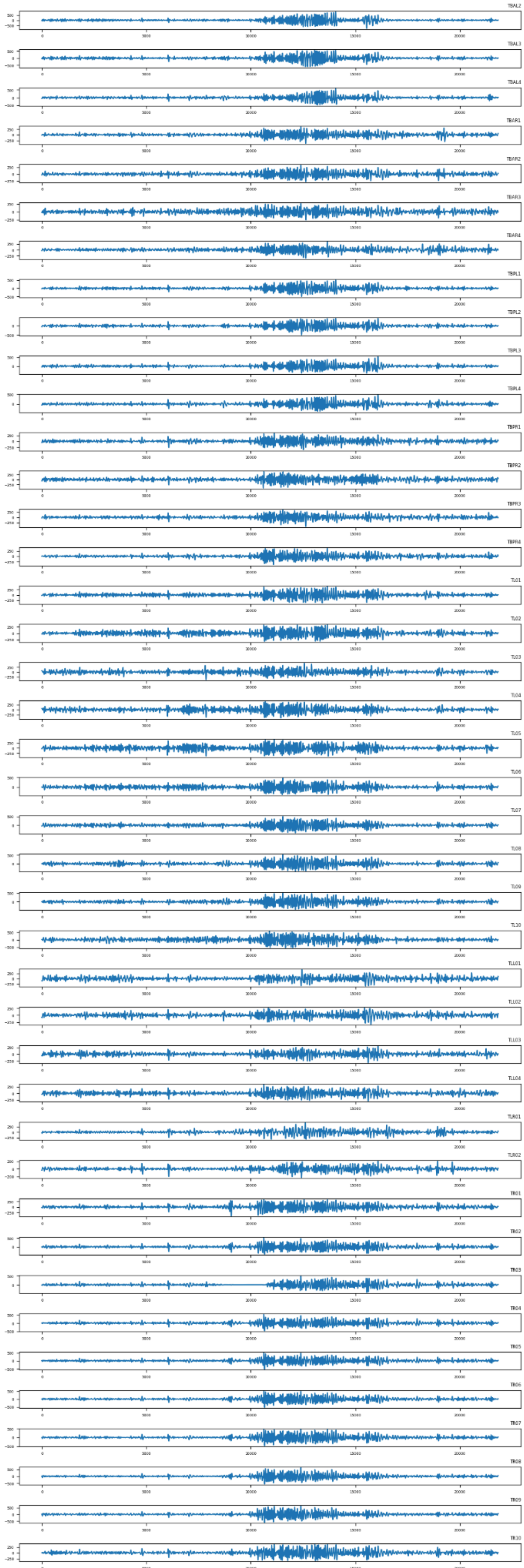
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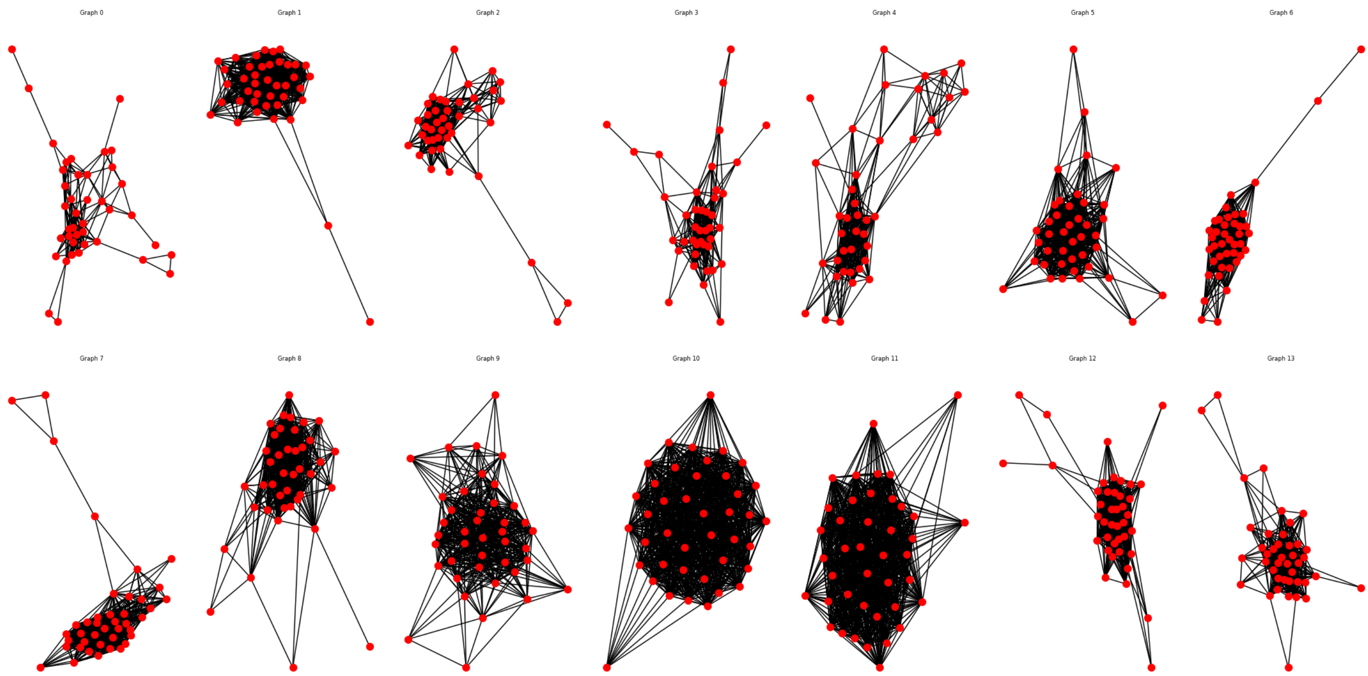
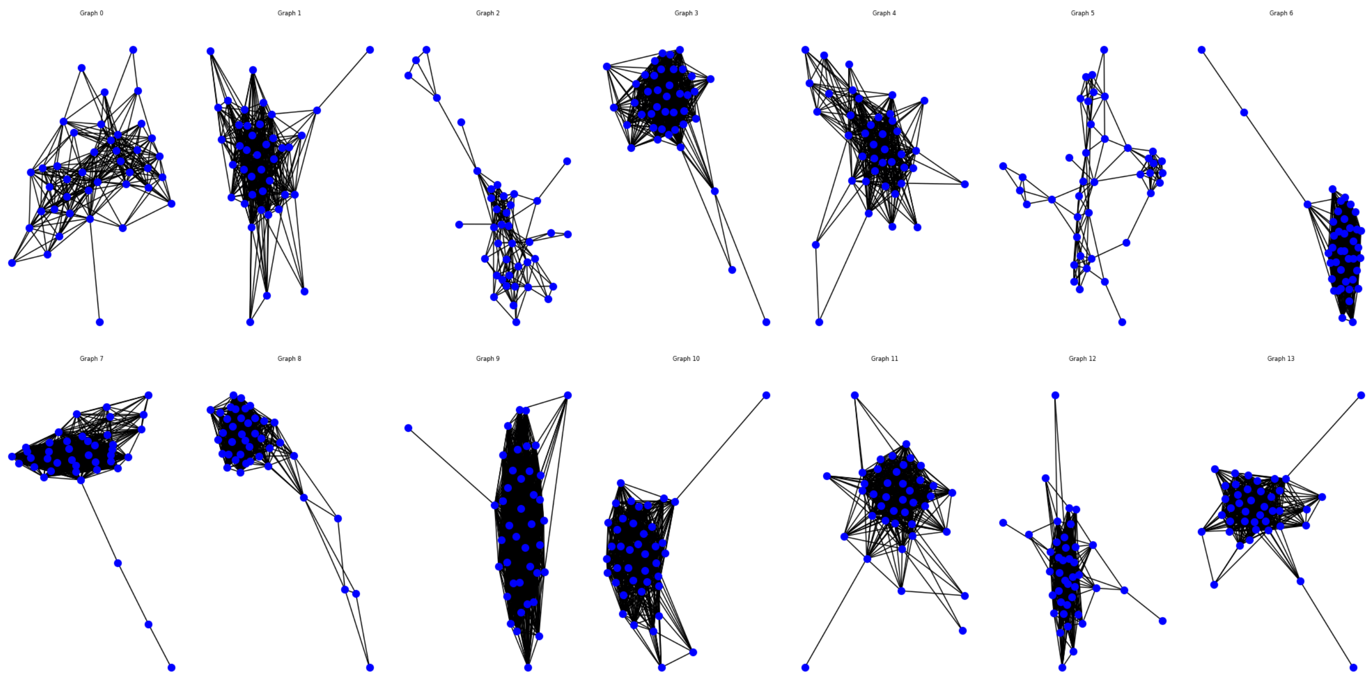
TR10

Network Analysis

To delve deeper into the interactions between different brain regions during seizures, a correlation matrix is computed. This matrix measures the strength of the relationship between the relative movements (phase changes) of pairs of channels. By converting the original data, which consists of 41 channels over numerous timesteps, into a 41 x 41 correlation matrix, we effectively capture the pairwise correlations across all channels. This transformation is crucial for understanding the network structure and is visualized through heatmaps of the correlation matrix, highlighting the strength of connectivity between different channels.



111g0L



112g0L

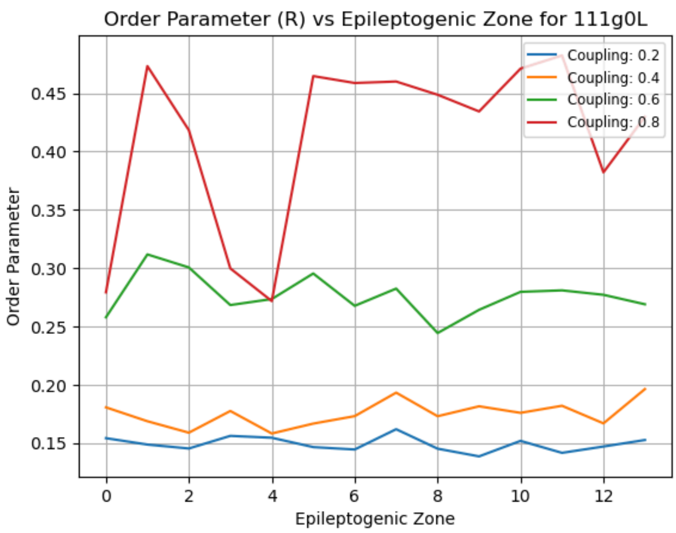
Kuramoto Order Analysis

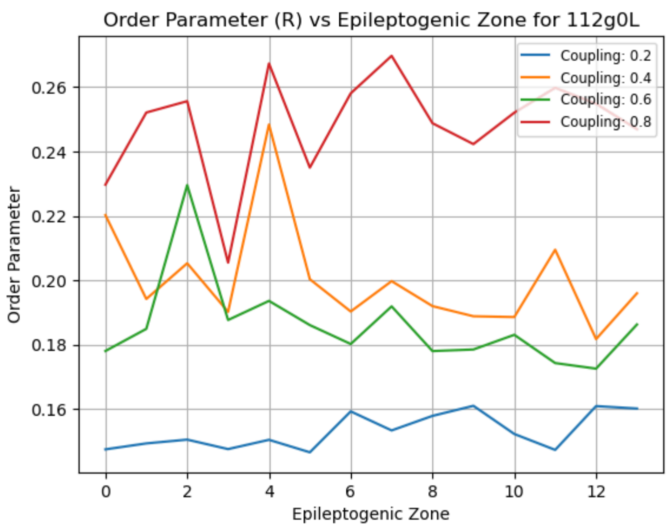
The synchronization across different epileptogenic zones is analyzed by varying the coupling strengths (0.2, 0.4, 0.6, 0.8) and observing the resultant order parameter, (R). The order parameter, a crucial metric derived from the Kuramoto model, quantifies the overall synchronization of the system. The formula used to compute the order parameter is:

$$R = |\frac{1}{N}\sum_{j=1}^{N} e^{i\theta_j}|$$

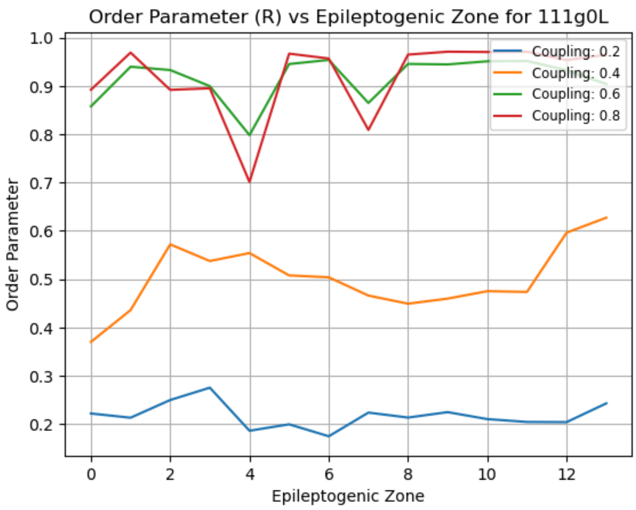
where (θ_j) is the phase of the (j)-th oscillator and (N) is the total number of oscillators. Plots of (R) versus different epileptogenic zones for various standard deviations (SD) of the natural frequencies (Mean = 0, SD = 0.8, 0.2, 1) are provided, showing how synchronization varies across the brain during seizures.

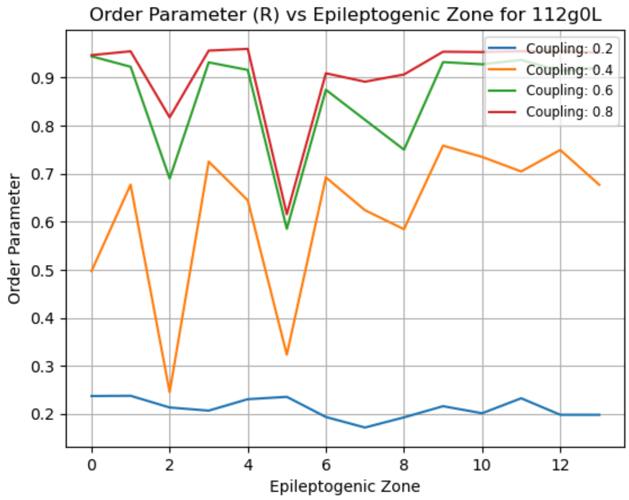
1. Mean = 0, SD = 0.8



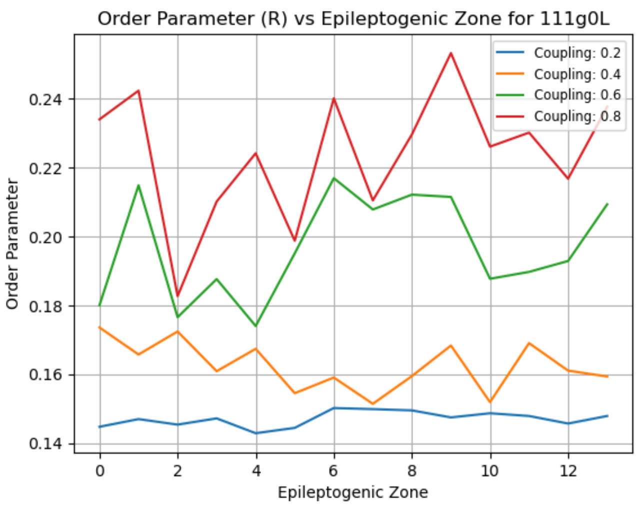


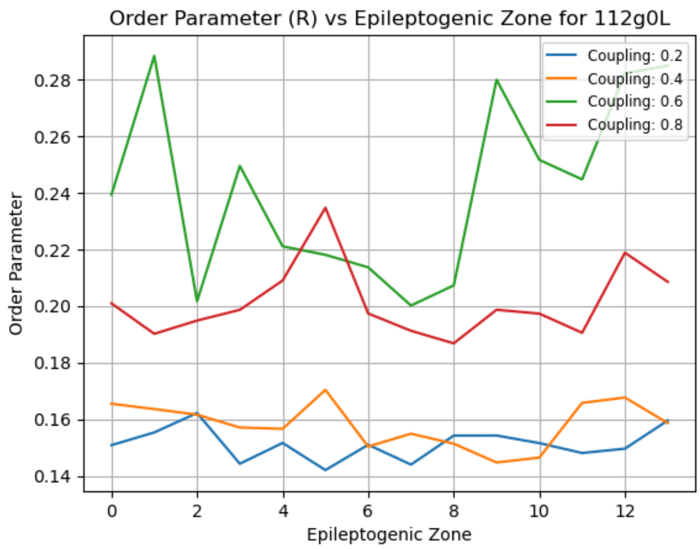
2. Mean = 0, SD = 0.2





3. Mean = 0, SD = 1

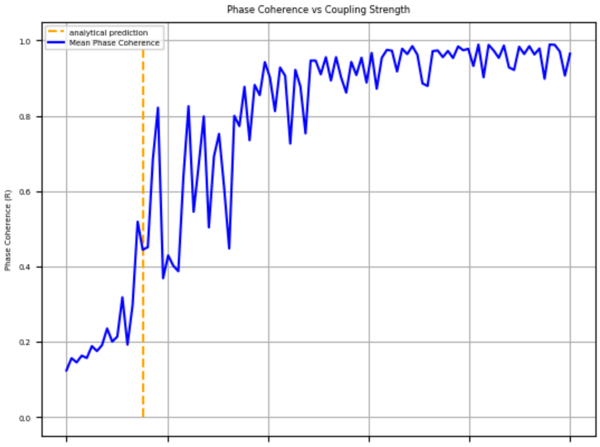




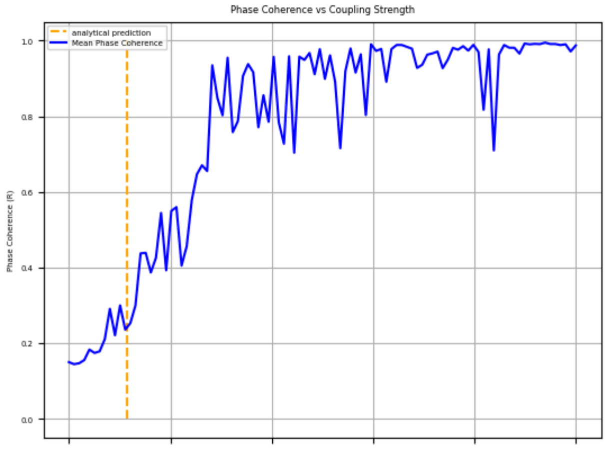
This analysis helps identify the critical coupling strength at which the system transitions to a synchronized state ((R) approaches 1). By gradually increasing the coupling strength and plotting the corresponding values of (R), we can pinpoint the threshold beyond which the oscillators in the network start to synchronize significantly. This is critical for understanding the conditions under which epileptic seizures enhance neuronal synchronization, potentially leading to the onset of a seizure.

Graphs for datasets 111g0L and 112g0L, representing different segments (0, 4, 9, 13), illustrate these dynamics, showing how synchronization varies not only with coupling strength but also across different segments of the data.

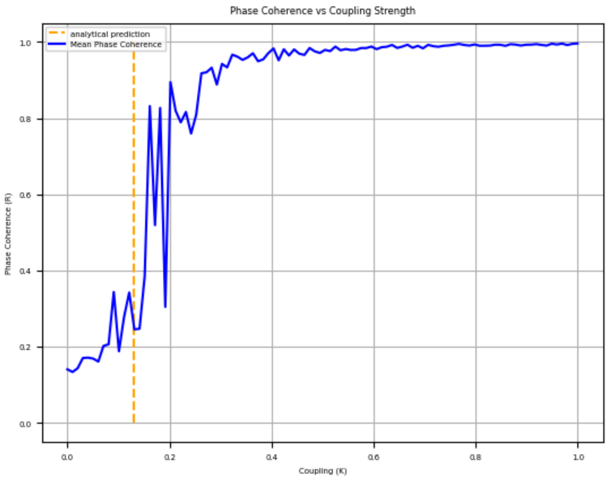
111g0L



0



4



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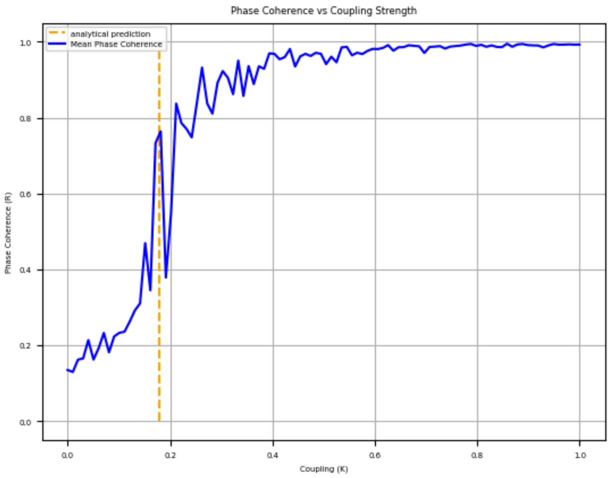
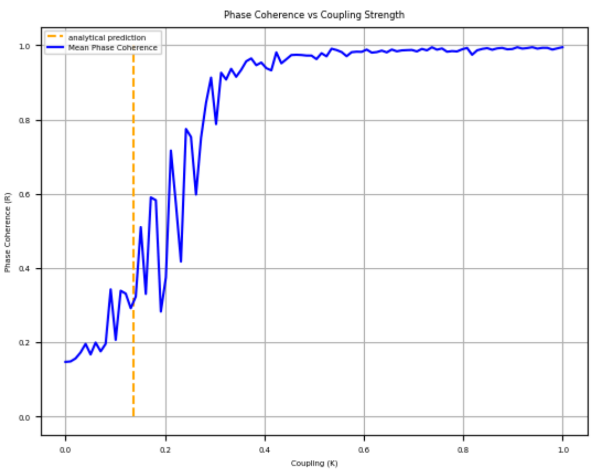
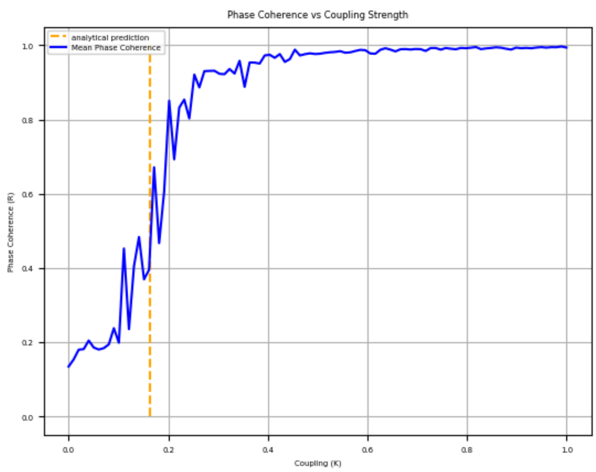


13

112g0L



0



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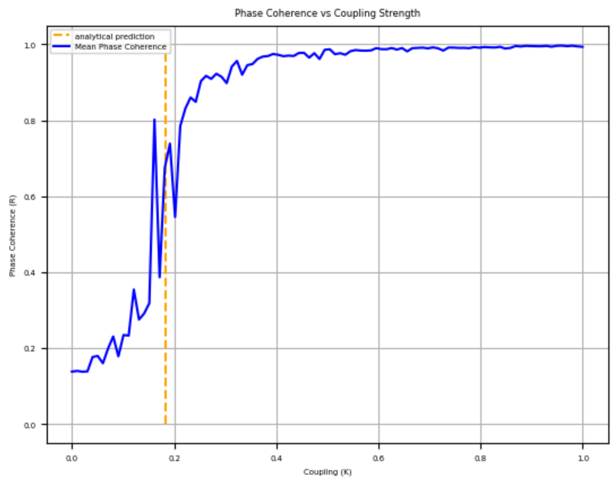

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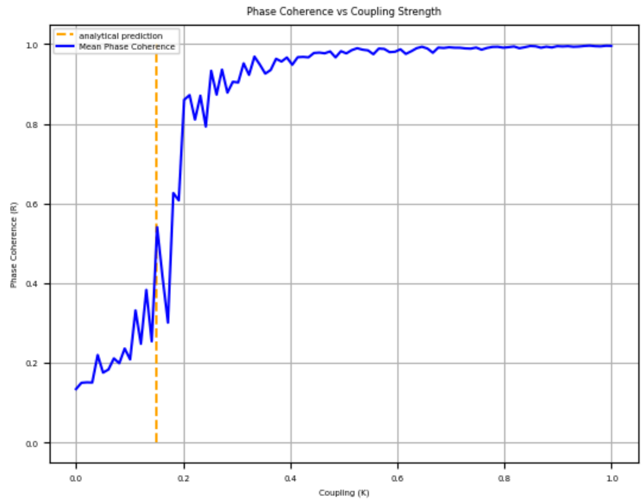
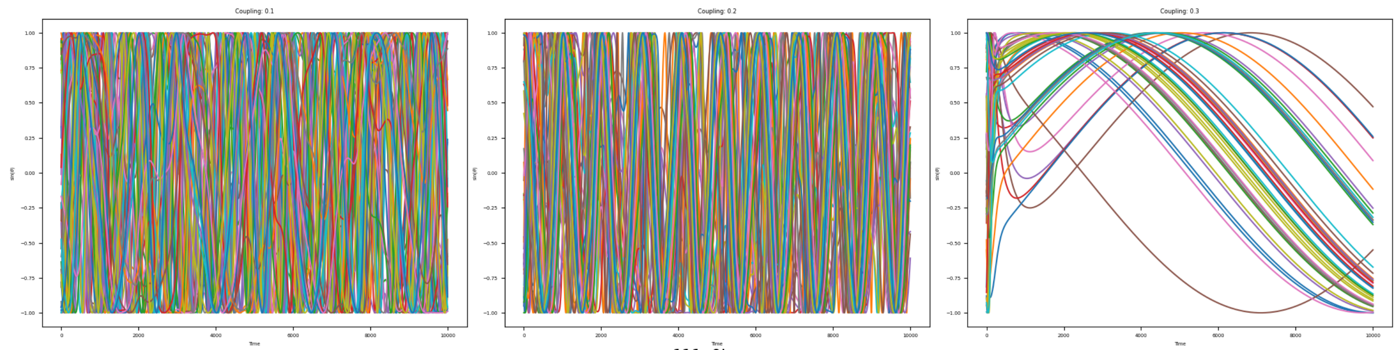


13

We also plotted the phases (sinΘ) against the timesteps for the same fragments to visualize the coherence attained by the oscillators as time progresses. The graphs have 3 subplots each corresponding to 3 coupling values situated around critical K, 0.1, 0.2 and 0.3.

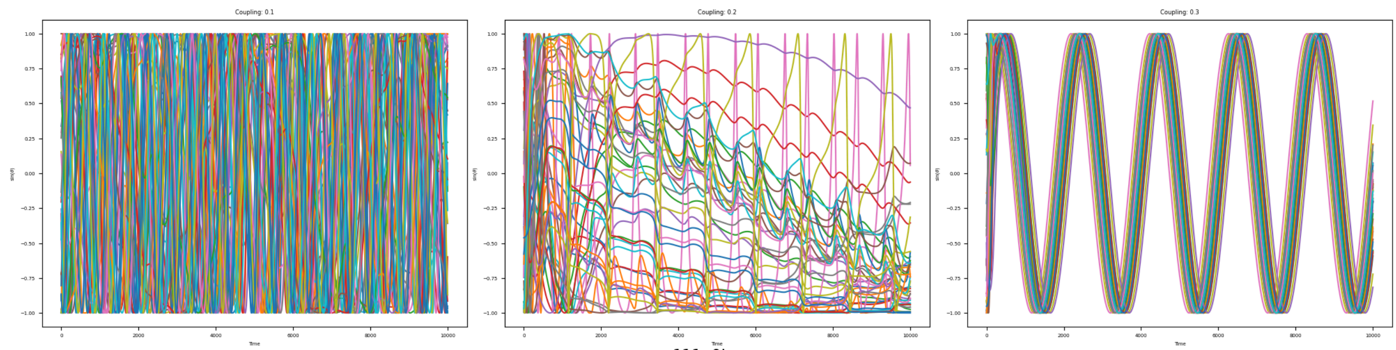
111g0L

0



111g0L

4



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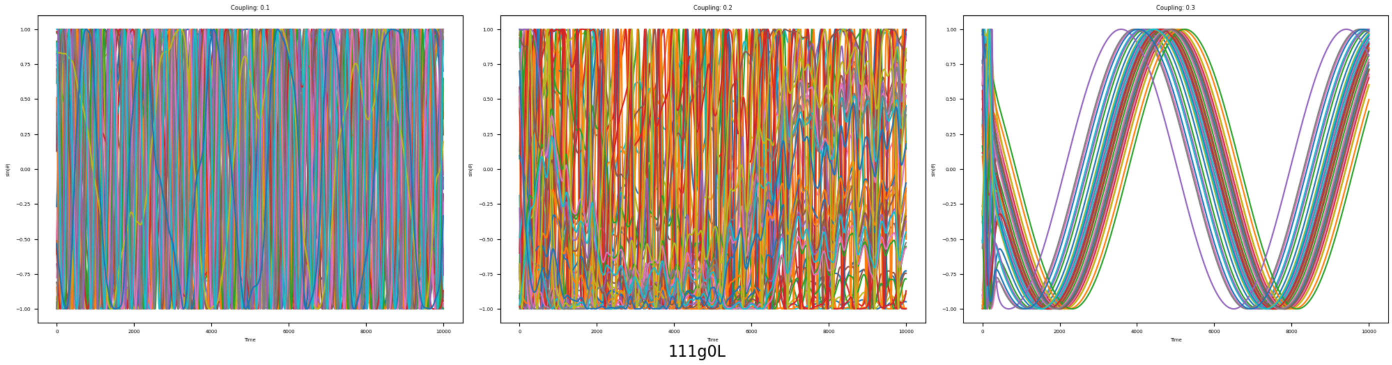

111g0L

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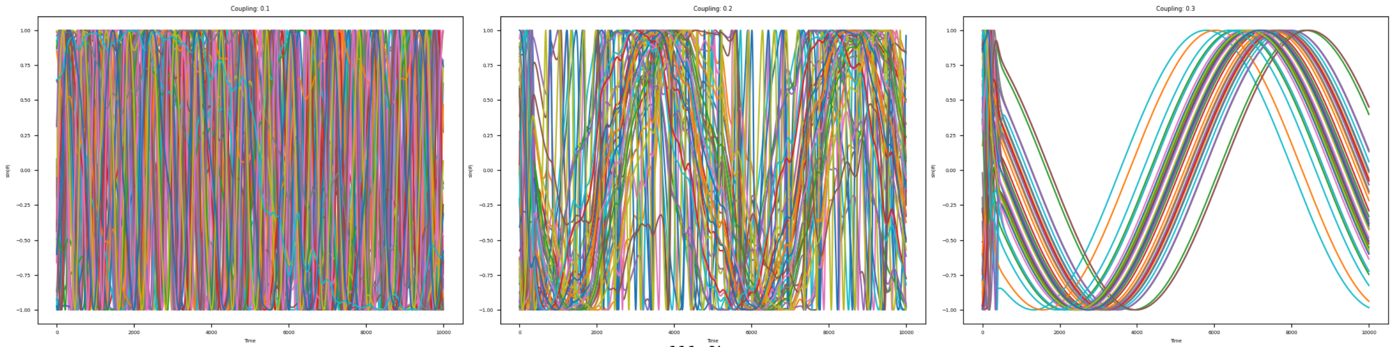
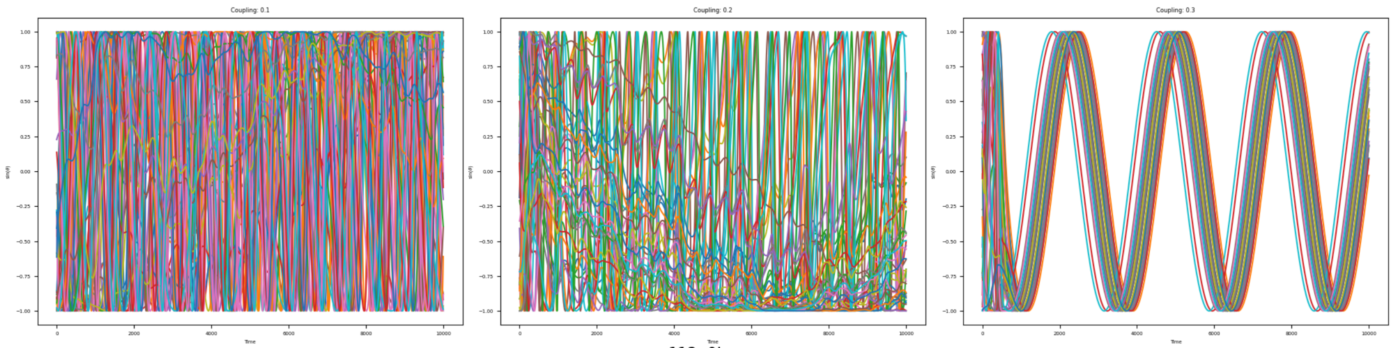


111g0L

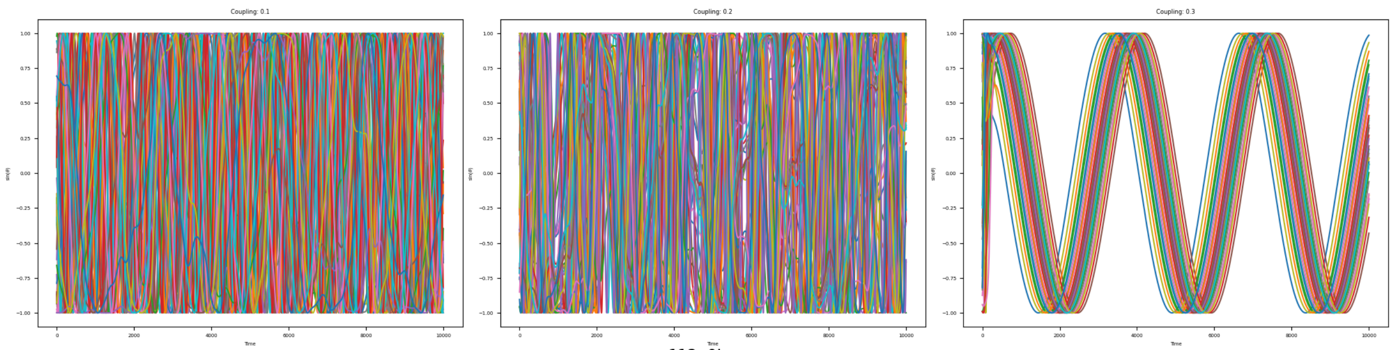
112g0L

0



112g0L

4



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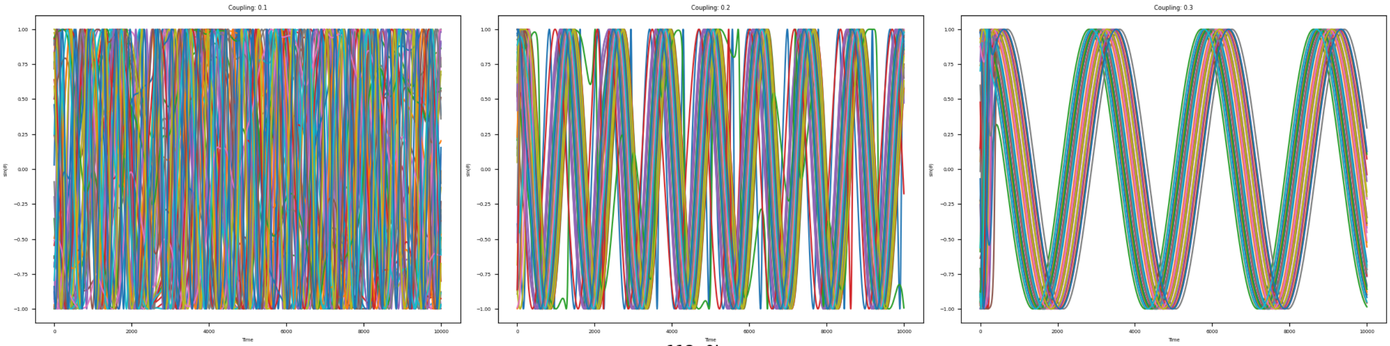

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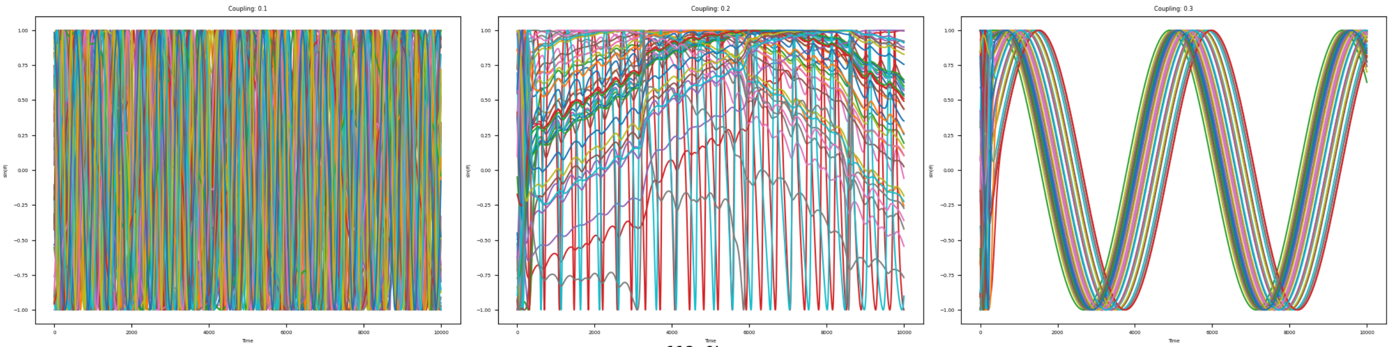
13



112g0L

Conclusion

The application of the Kuramoto Model to iEEG data from epilepsy patients provided significant insights into the synchronization dynamics during epileptic seizures. Key findings from this study include:

Distinct Synchronization Patterns: The analysis revealed distinct patterns of synchronization in the epileptogenic zones, particularly around the seizure onset. The phase coherence and order parameter metrics demonstrated clear fluctuations corresponding to different stages of the seizure cycle (pre-seizure, seizure, and post-seizure).

Influence of Coupling Strength: The study highlighted the critical role of coupling strength in the synchronization behavior of the network. ***A decrease in coupling strength led to a decrease in the order parameter, indicating reduced synchronization among the oscillators.*** This suggests that the degree of connectivity and interaction strength among neurons critically influences seizure dynamics.

Network Connectivity and Seizure Propagation: The construction and analysis of the network based on phase correlations provided a deeper understanding of how different brain regions interact during seizures. The binarized correlation matrix used to define the coupling matrix in the Kuramoto Model helped in identifying potential pathways of seizure propagation.

Coherence across Coupling Values: One can observe that ***the value of critical coupling value sees a slight increase during the 4th and 9th fragment in the case of 112g0L and a slight decrease in the same fragments for 111g0L.*** We can possibly infer that, during the fragments concerning the onset of epilepsy, a higher coupling value is required to get the system to a coherent state. ***We also see a more synchronized graph (for 111g0L) at the coupling value of 0.3 for fragments 4 and 9 as compared to the other pre and post-seizure fragments.***

Fluctuation in Order Parameter with Coupling Strength: The observed fluctuation in the order parameter with decreasing coupling strength can be attributed to the reduced effectiveness of the network's ability to achieve a coherent state. ***As the coupling strength decreases, the influence that each oscillator exerts on its neighbors diminishes, leading to a less synchronized state.*** This is particularly critical in understanding epileptic seizures, where excessive synchronization needs to be controlled or modulated to prevent or mitigate seizure activity.

Our analysis revealed distinct synchronization patterns between two groups (labeled 111g0L and 112g0L) when the inherent variability (standard deviation, SD) of the oscillators was relatively low (less than or equal to 0.8).

- In 111g0L, under these conditions, we observed a **decrease** in synchronization around the **fourth fragment**.
- Conversely, 1112g0L exhibited an **increase** in synchronization at the same fragment.

In conclusion, this project has not only advanced the understanding of synchronization in epileptic seizures using the Kuramoto Model but also opened new avenues for improving epilepsy treatment and monitoring through network-based approaches.

References

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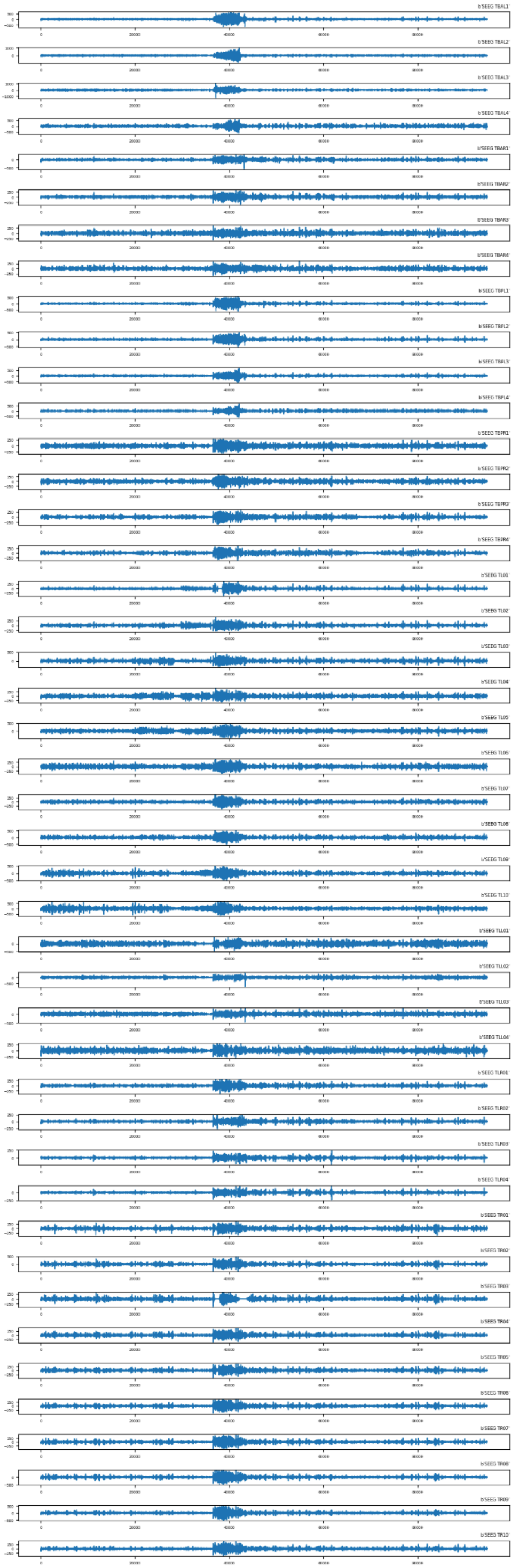
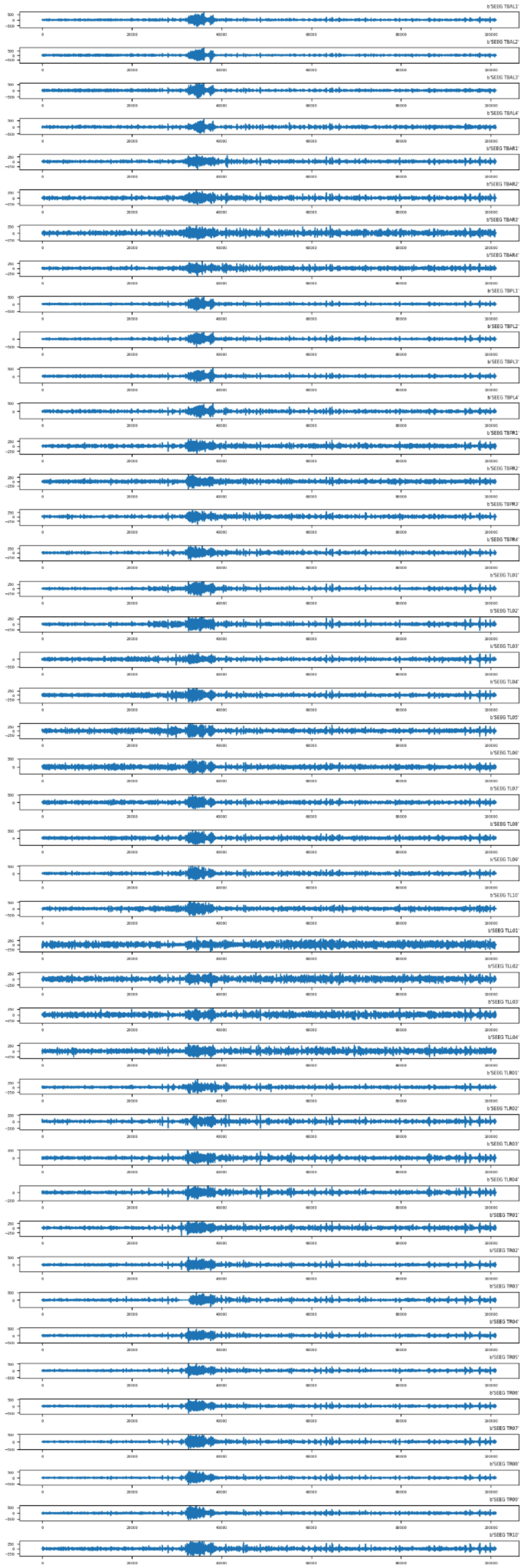
Appendix

Filtered Data





Custom Thresholding

ID	111g0L	112g0L
0	0.5	0.4
1	0.3	0.4
2	0.4	0.5
3	0.4	0.5
4	0.4	0.5
5	0.5	0.4
6	0.4	0.4
7	0.5	0.5
8	0.4	0.4
9	0.5	0.4
10	0.2	0.5
11	0.6	0.4
12	0.6	0.6
13	0.6	0.5