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EMD-Based, Mean-Phase Coherence Analysis to Assess Instantaneous Phase-Synchrony Dynamics in Epilepsy Patients

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Abstract

In this paper, an adaptive, non-linear, analytical methodology is proposed in order to quantitatively evaluate the instantaneous phase-synchrony dynamics in epilepsy patients. A group of finite neuronal oscillators is extracted from a multichannel electrocorticographic (ECoG) data, using the empirical mode decomposition (EMD). The instantaneous phases of the extracted oscillators are measured using the Hilbert transform in order to be utilized in the mean-phase coherence analysis. Finally, the dynamical evolution of phase-synchrony among the extracted neuronal oscillators within 1–600 Hz frequency range is assessed using eigenvalue decomposition. A different phase-synchrony dynamics was observed in two patients with frontal vs. temporal lobe epilepsy, as their seizures evolve. However, experimental results demonstrated a hypersynchrony level at seizure offset for both types of epilepsy during the ictal periods. This result suggests that hypersynchronization of the epileptic network may be a crucial, self-regulatory mechanism by which the brain terminate seizures.

I. Introduction

Dynamical evolution of synchrony level among neuronal networks is essential to decipher complicated brain functions during normal physiological conditions such as cognitive processing as well as pathological states such as epileptic seizures [1]. In a variety of neurological disorders such as epilepsy, the synchrony level can be altered relative to the normal brain functions. Epileptic seizure is conventionally considered as abnormal hypersynchronous states arising from an imbalance among inhibitory and excitatory inputs of large populations of neurons. Indeed, the high-amplitude, often-rhythmic activity corresponding to the ictal period of seizures mostly causes the aforementioned conclusion [2]. Therefore, assessing the evolution of synchrony dynamics may reveal essential

mechanisms crucial to clinical EEG analysis. It is also capable of providing a more in-depth understanding of the dynamics of epileptic seizures.

Identifying the synchronization level between non-linear, non-stationary, neuronal oscillators has been a challenging issue in neurological science. Recently, several mathematical methods have been proposed in order to detect the temporal synchrony changes among neuronal networks in the brain such as cross-correlation, Fourier, and wavelet analysis. These methods, while useful, suffer from several assumptions regarding linearity and/or stationarity of the underlying components of a time series and the frequency bandwidth of importance, which render them unsuitable for this purpose. Eigenvalue decomposition of a linear correlation matrix has been used to identify the synchrony level changes between a set of signals filtered below 70 Hz [3]. It has been shown that the synchrony between non-linear, non-stationary neuronal oscillators refers only to their relative phase dynamics rather than their amplitudes variations. Therefore, using the crosscorrelation matrix as a similarity matrix in the eigenvalue decomposition technique may result in spurious synchrony interpretation [4]. In addition, the phase synchronization can be detected between non-linear, coupled, oscillators even if their amplitudes are not synchronized [4]. Therefore, it is crucial to develop a non-linear method to accurately measure phase synchrony. Mean-phase coherence analysis has been used to evaluate the strength of phase connections between oscillators based on their pre-extracted instantaneous phase information [5]. However, the extracted instantaneous phases have no physical meaning in cases of multi-component time series signals. Therefore, some form of filtering of original data is necessary prior to the phase extraction stage. Most of the filtering methods, while useful, pose several assumptions about the underlying components of neurological signals, and fail to decompose them with respect to their intrinsic nonlinear, non-stationary properties.

Empirical mode decomposition (EMD) method introduced in [6], is capable of adaptively decomposing a signal into a set of finite, narrowband oscillatory components without posing any assumptions about its linearity and stationarity features. Therefore, it is capable of providing localized time-frequency analysis of electrophysiological signals.

This paper reports on assessing the instantaneous dynamics of phase-synchrony in epilepsy patients using a non-linear analytical methodology that merges the EMD, Hilbert transform, mean-phase coherence analysis, and eigenvalue decomposition technique. The rest of the paper is organized as follows. In section II, specifications of the adopted ECoG dataset along with the framework of the proposed phasesynchrony analysis are described. Section III presents the experimental results of the instantaneous phase-synchrony analysis among the extracted neuronal oscillators. Finally, Section IV provides conclusions to this research.

II. Dataset and Methods

A. Patients and ECoG Dataset

In this study, two sets of continuous, multi-channel ECoG dataset, recorded from two, de-identified epilepsy patients, are retrieved from the publicly available, online International Epilepsy Electrophysiology (IEEG) portal [7]. The first patient was diagnosed with frontal lobe epilepsy while the second one had temporal lobe epilepsy. seizure onset zones and its

timing have been clinically determined by the treating physicians at the Mayo Clinic, by the visual detection of clear ictal discharges. Data acquisition was carried out using a Neuralynx electrophysiology system with a 32 kHz sampling frequency, which was later downsampled to 5 kHz, and a 11500 Hz band-pass filtering. Moreover, in this study, bipolar derivations of the ECoG signals are measured through taking the voltage difference between the nearby electrodes, which represent their local neural activity. This is an essential step aims towards eliminating the confounding influences of both volume conduction and common reference signal [8].

B. Empirical Mode Decomposition (EMD) and Hilbert Transform

EMD is an adaptive, data-driven method of decomposing a signal into a set of finite intrinsic mode functions (IMFs), similar to basis functions in the Fourier transform, which together comprise the underlying oscillations within a time series signal. That is, IMFs are truly determined from the dynamics of the signal of interest. The EMD method does not pose any assumptions regarding underlying components of signals, which makes it ideal for the time-frequency analysis of non-linear, non-stationary neurological signals. The details about the EMD process has been described in [5]. It should be noted that the lower-index IMFs represent fast oscillation modes of a signal, while the higher-index IMFs capture the slower oscillation modes.

Hilbert analytic signal method is a well-established method of measuring instantaneous phase and frequency information from a narrowband signal. Multi-component or wideband signals yield a trajectory in the complex plane that contain several centers of rotation; however, in order to achieve an unambiguous phase reading, the complex trajectory of an analytic signal should have only a single center of rotation. The EMD method helps to provide a proper, instantaneous phase determination by separating the underlying oscillatory functions, IMFs, of a signal. This process results in several phase space traces, each with one center of rotation. In this study, the EMD of bipolar-derivate ECoG signals are carried out for each one-second window of data, prior to the use of the Hilbert transform, in order to measure the instantaneous phases unambiguously.

C. Mean-Phase Coherence Analysis

Once the instantaneous phases of the extracted IMFs from all channels within a one-second segment of the original data are obtained, it is desirable to determine the strength of their phase relationship. In order to do this, each IMF is treated as a row vector and stacked on each other to form an $m \times n$ matrix, in which m is the total number of IMFs extracted from all channels within a one-second segment of the bipolar-derivate data, and n denotes the length of the time series. In the next stage, the bivariate mean-phase coherence matrix is calculated using the following equation.

$$R_{nm} = \frac{1}{N} \sum_{n=1}^N \sum_{m=1}^N e^{[i(\phi_n(t) - \phi_m(t))]} \quad (1)$$

where i is equal to -1 , N is the total number of samples within the data segment, and $\phi(t)$ is the instantaneous phase of the analytic signal pair indicated by subscripts n and m . All the values in the bivariate mean-phase coherence matrix, $R_{N \times N}$, are normalized between zero to one.

D. Eigenvalue Decomposition and Synchrony Analysis

In order to achieve a multivariate measure that is capable of detecting phase-synchrony across all the extracted oscillators, eigenvalue decomposition of the square, mean-phase coherence matrix is performed. This decomposition compares all the values in the $R_{N \times N}$ and projects them into a set of principal directions with respect to the mean phase field. Besides, all the eigenvalues are sorted in ascending order to form an eigenvalue spectrum. Each one of the eigenvalues represents how strongly oscillators are phase-correlated in the direction of its corresponding eigenvector. This process is executed by solving $R_{N \times N} V_i = \lambda_i V_i$, in which λ_i and V_i are the resulted eigenvalues and their corresponding eigenvectors, respectively. It should be noted that sum of the eigenvalues is equal to the total number of the neuronal oscillators. Therefore, in order to keep the sum constant, any increase in one of the eigenvalues has to be compensated by a decrease in the other eigenvalues. This is the fundamental idea underlying assessing the phase-synchrony level among oscillators, which is clarified in detail in Fig. 1. The Fig. 1 demonstrates how changes in eigenvalue spectrum represent the phase-synchrony level in three different sets of IMFs.

Five extracted IMFs from a one-second, bipolar-derivate ECoG signal along with their corresponding mean-phase coherence matrix and eigenvalue spectrum is illustrated in Fig. 1. The IMFs decomposed from a same bipolar-derivate channel are nearly orthogonal, which means almost no phase-synchrony between them. Therefore, the resulted $R_{N \times N}$ values are very close to zero, color-coded as black, outside the diagonal and one, color-coded as white, on the diagonal. In this case, all the eigenvalues obtained from the eigenvalue decomposition of the $R_{N \times N}$ matrix are measured to be close to one. Fig. 1 (b) exhibits an IMF decomposed from a bipolar-derivate channel that are copied five times in order to create a fully phase-synchronized group of oscillators. As it is expected, the resulted $R_{N \times N}$ values are all equal to one. In this case, after performing the eigenvalue decomposition of the $R_{N \times N}$ matrix, the last eigenvalue is equal to the total number of the oscillators, $\lambda_N = N = 6$, while the rest of them are equal to zero, in order to maintain the sum of them constant. Fig. 1 (c) represents a phase-synchrony level between those in the case (a) and (b). The fifth IMFs that decomposed from five different, bipolar-derivate channels within a one-second ictal segment have been clustered to evaluate the phasesynchrony among them. The obtained eigenvalue spectrum indicates a decrease in the last eigenvalue compared to its counterpart in the case (b), which is compensated through an increase in its lower eigenvalues. Generally, considering the ascending order among eigenvalues, a small change in the values of a few higher-index eigenvalues causes a relatively large dynamic change in the large portion of the lower-index eigenvalues to compensate it. Therefore, in this paper, the average value of the large portion of the lower-index eigenvalues is measured, and reported in each second to assess the instantaneous phase-synchrony dynamics among the oscillators. In the Fig. 1, the mean value of the first 60% lower-index eigenvalues, $mean\lambda_{1:60\%}$, is reported for all the three cases in order to simplify the comparison between their synchrony levels. As the

phase-synchrony level increases between the oscillators from its minimum to maximum, the $mean\lambda_{1:60\%}$ value decreases correspondingly. That is, an increase/decrease in the value of the $mean\lambda_{1:60\%}$, reflects a decrease/increase in the phase-synchrony level, respectively.

III. Experimental Results

In order to magnify the very small, relative changes of the $mean\lambda_{1:60\%}$ variable over time, normalized $mean\lambda_{1:60\%}$ values are measured as follow. First, all of the $mean\lambda_{1:60\%}$ values are subtracted from their temporal average value, measured within a 2-minute pre-ictal period, and then divided by their standard deviation value, measured over the same reference time. The instantaneous phase-synchrony dynamics in the patient with frontal lobe epilepsy (FLE) is shown in Fig. 2. Fig. 2 (a) exhibits the anatomical position of the 36-channel ECoG electrode in the patient. Fig. 2 (b) illustrates a 5.5-minute, bipolar-derivate ECoG signal, comprising a seizure, which has been used for the instantaneous phase-synchrony analysis. The green dashed lines in the Fig. 2 denote the seizure onset and termination, which have been clinically determined by the treating physicians. The instantaneous, temporal changes of the normalized $mean\lambda_{1:60\%}$ variable resulted from the front-end, phase-synchrony analysis of the extracted IMFs, within 1 Hz to 600 Hz frequency range, is shown in Fig. 2 (c). The normalized $mean\lambda_{1:60\%}$ variable has a small increase around the seizure onset up to a few seconds after it, which reflects a short desynchronization around this period. Following this period, the normalized $mean\lambda_{1:60\%}$ starts to decrease gradually towards the seizure termination, which reflects a proportionally gradual increase in the phasesynchrony level during this period. It should be noted that the phase-synchrony level reaches to its maximum value at seizure termination, and then gradually decreases to reach to its pre-ictal level. Fig. 3 illustrates the dynamics of phasesynchrony in the patient with temporal lobe epilepsy (TLE). Fig 3 (c) demonstrates the instantaneous, changes of the normalized $mean\lambda_{1:60\%}$ variable, which are obtained from the front-end phase-synchrony analysis of the IMFs within 1 Hz to 600 Hz frequency range. The normalized $mean\lambda_{1:60\%}$ value starts to increase from 10 seconds preceding seizure onset, up to almost 20 seconds after this time, which reflects a desynchronization during this period. However, after this period, a gradual increase in the synchronization towards the seizure end, as indicated by a decrease in the normalized $mean\lambda_{1:60\%}$ value is noticeable. It should be noted that the desynchronization pattern observed in the patient with TLE is longer and more prominent than the one in the patient with FLE. Although the cause of this phenomenon is unknown to the authors, it may arise from the difference between the seizure onset zones in the patients, the difference in their seizure type, or perhaps due to a shorter ictal period in the patient with FLE.

IV. Conclusion

The aim of this study was to develop an adaptive, nonlinear, analytical methodology to assess the phase-synchrony among neuronal populations in epilepsy patients. A different evolution of phase-synchrony dynamics was observed in the two patients with FLE and TLE. However, synchronization achieved its maximum level at seizure termination for both types of epilepsy during ictal periods. However, the authors recognize that a higher number of epilepsy patients with different seizure onset zones and types will be required to draw a clinically robust conclusion to these phase-synchrony dynamics.

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Fig. 1.

Evaluating phase-synchrony levels among neuronal oscillators using eigenvalue decomposition of the mean-phase coherence matrix. All of the values in the mean-phase coherence matrix, $R_{N \times N}$ are normalized and color-coded between zero (black), to one (white). (a) Five decomposed IMFs from a one-second, bipolar-derivate ECoG signal using the EM D process, along with their corresponding mean-phase coherence matrix, eigenvalue spectrum, and the average value of the first 60% lower-index eigenvalues, $mean\lambda_{1:60\%}$, showing no phasesynchrony among the oscillators. (b) Five-time copied version of an IMF leads to a $R_{N \times N}$ matrix with all values equal to one, showing a full phase-synchrony among the oscillators. (c) A set of IMFs extracted from different channels within a one-second ictal period leads to a $R_{N \times N}$ matrix with values between cases (a) and (b), showing a partial phase-synchronization among the oscillators.

Fig. 2.

Evaluating the instantaneous phase-synchrony dynamics in the patient with frontal lobe epilepsy (FLE). (a) Anatomical position of the 36-channel ECoG electrode. (b) 5.5-minute, raw, bipolar-derivate ECoG signal containing a seizure, recorded from the patient with FLE. The green dashed lines denote the seizure onset and offset. (c) Relative, temporal changes of the normalized $mean\lambda_{1:60\%}$ value, after being smoothed with a 5-second moving average filter, for all the extracted IMFs within 1–600 Hz frequency range. An increase/decrease in the value of the $mean\lambda_{1:60\%}$, reflects a decrease/increase in the phase-synchrony level, respectively.

Fig. 3.

Evaluating the instantaneous phase-synchrony dynamics in the patient with Temporal lobe epilepsy (TLE). (a) Anatomical position of the 24-channel ECoG electrode. (b) 5.5-minute, raw, bipolar-derivate ECoG signal comprising a seizure, recorded from the patient with TLE. The green dashed lines denote the seizure onset and offset. (c) Relative, temporal changes of the normalized $mean\lambda_{1:60\%}$ value, after being smoothed with a 5-second moving average filter, for all the extracted IMFs within 1–600 Hz frequency range. An increase/decrease in the value of the $mean\lambda_{1:60\%}$, reflects a decrease/increase in the phase-synchrony level, respectively.