HYPERSPHERICAL PHASE SYNCHRONY MEASURE FOR QUANTIFYING GLOBAL SYNCHRONIZATION IN THE BRAIN

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ABSTRACT

Phase synchronization has been proposed as a plausible mechanism to quantify both linear and nonlinear relationships between neuronal populations and to assess functional brain connectivity. However, bivariate phase synchrony is not sufficient for complex system analysis such as the brain where the bivariate relationships do not always reflect the underlying network structure. Recently, multivariate extensions of bivariate phase synchrony has been of interest in investigating the interactions within a group of oscillators. Current extensions are based on either averaging all possible pairwise synchrony values or eigen decomposition of a matrix of bivariate synchronization indices to estimate multivariate synchrony using the entropy of the normalized eigenvalues. All of these approaches are sensitive to the accuracy of the bivariate synchrony indices, cause loss of information, computationally complex and are indirect ways to quantify the multivariate synchrony. In this paper, we propose a novel and direct measure to estimate the multivariate phase synchrony by forming direction vectors in a multidimensional hyperspherical coordinate system. The proposed method is evaluated through application to electroencephalogram (EEG) data containing error-related negativity (ERN) related to cognitive control. We compare the new measure with existing methods and show its effectiveness in quantifying multivariate synchronization of different brain regions.

***Index Terms*—** Multivariate phase synchrony, Global phase synchronization, Functional brain connectivity

1. INTRODUCTION

Cooperative behavior of chaotic dynamics of complex systems is relevant in many fields of research, from climactic processes and electric circuits to human cardio-respiratory system and neuroscience. Usually, this complex dynamics is analyzed through bivariate measures of signal interdependence such as traditional cross-correlation and spectral coherence techniques or nonlinear measures such as mutual information. More recently, tools from nonlinear dynamics, in particular, phase synchronization have received much attention since they offer a way of extracting information on the interdependence of weakly interacting systems that cannot be obtained by traditional methods [1, 2, 3]. Phase synchronization of chaotic oscillators occurs in many complex systems including the human brain, where both linear and nonlinear dependencies are quantified though bivariate phase synchrony using noninvasive measurements such as electroencephalogram (EEG) data [4].

Classically, synchronization of two signals is understood as adjustment of their rhythms due to interaction, referred to as phase locking, which occurs when $\Phi_{i,j}(t,\omega) = |\Phi_i(t,\omega) - \Phi_j(t,\omega)| mod 2\pi <$ constant, and $\Phi_{i,j}(t,\omega)$ is the generalized phase difference between signals i and j at time t and frequency ω. Two steps are needed for quantifying phase synchrony. First, instantaneous phase of each signal is estimated at a particular frequency of interest and second, a statistical criterion is used to quantify the degree of phase locking. The first step has been addressed using the analytic signal concept through the Hilbert transform, convolution with a complex wavelet function, commonly the Morlet wavelet [5], or the recently proposed RID-Rihaczek complex time-frequency distribution [3]. For the second step, the deviation of the empirical distribution of the relative phase difference from a uniform distribution is usually quantified using indices based on either Shannon entropy or circular variance of phases [6].

Recently, phase synchronization of a group of oscillators, which is referred to as global or multivariate phase synchronization, has been of interest for understanding the group dynamics and characteristic behavior of complex networks [7]. Contrary to the bivariate phase synchrony, which is limited to pairwise relationships, multivariate synchrony captures the global synchronization patterns quantifying the degree of interactions within a group of oscillators. Existing approaches to multivariate phase synchronization rely on the computation of the whole set of pairwise synchrony values. A preliminary approach is the partial synchrony adapted from partial coherence to reveal the indirect interactions among the oscillators within a network [8]. However, this method still infers bivariate relationships and cannot quantify group dynamics. Recently, cluster analysis has been proposed to maximize group connectivity within each cluster while minimizing the connectivity between clusters [9, 10]. Allefeld et al. have proposed a mean-field approach to analyze EEG data, where each signal is contributing to a single cluster to a different extent [11]. The existence of a single synchronization cluster is not a reasonable assumption since the underlying clustering structure of brain networks, which usually consist of multiple clusters, cannot be inferred. In order to address this limitation, an approach based on the eigenvalue decomposition of the pairwise bivariate synchronization matrix has been proposed [12]. Multiple synchronization clusters are detected based on the number of eigenvalues greater than 1. The strength of each cluster depends on the magnitude of its associated eigenvalue and the corresponding eigenvectors account for the internal structure. However, it has recently been shown in cases where there are clusters of similar strength that are slightly synchronized with each other, the assumed one-to-one correspondence between eigenvectors and clusters is not realistic [13]. One of most prominent and commonly used measures for quantifying multivariate synchrony is based on the spectral decomposition of the bivariate synchronization matrix and is known as the S-estimator [7, 14]. However, the accuracy of this measure is affected by the accuracy of the bivariate synchrony estimates.

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All of these prior approaches depend on the estimation of bivariate phase synchrony values and offer an indirect and a limited way to estimate the multivariate synchrony within a network. With respect to prior work, in [15], we proposed a novel and direct method, which is referred to as 'Hyperspherical Phase Synchrony' (HPS), to compute the multivariate phase synchronization within a group of oscillators. HPS is a direct extension of 'Phase Locking Value', which is the most prominent index of bivariate phase synchrony [3] and offers a novel way to exploit the circular variance of phase differences among multiple oscillators to compute global synchronization. We applied HPS to simulated signal models using Hilbert transform for phase estimation. Simulation results showed improved results in terms of robustness to noise and lower computational complexity of the proposed method compared to the existing methods. The contributions of this paper is two fold. First, we use the RID-Rihaczek distribution [3] to allow definition of a time and frequency dependent multivariate phase synchrony measure. Second, we apply the proposed HPS measure to a set of EEG data containing event related potentials and compare its performance with the S-estimator in determining functional connectivity networks of the human brain.

2. BACKGROUND

2.1. Phase Estimation

In order to quantify bivariate or multivariate phase synchrony among multiple time-series, one needs to extract the time and frequency dependent phase of each signal. For this purpose, we propose to use a new time-varying phase estimation method based on the Reduced Interference Rihaczek (RID-Rihaczek) distribution belonging to Cohen's class [3]. Compared to the existing measures, such as the Hilbert transform or the continuous wavelet transform using Morlet wavelet, RID-Rihaczek based phase estimator is robust to noise and offers phase estimates having uniformly high time-frequency resolution with less bias. Therefore, it performs superior at detecting actual synchrony within a group of oscillators [3]. In this paper, time and frequency dependent phase, $\Phi_i(t,\omega)$, of a signal, $x_i(t)$, is estimated as: $\Phi_i(t,\omega) = \arg\left[\frac{C_i(t,\omega)}{|C_i(t,\omega)|}\right]$ where $C_i(t,\omega)$ is the complex RID-Rihaczek distribution of $x_i(t)$:

$$C_i(t,\omega) = \int\int \underbrace{\exp\left(-\frac{(\theta\tau)^2}{\sigma}\right)}_{\text{Choi-Williams kernel}} \underbrace{\exp(j\frac{\theta\tau}{2})}_{\text{Rihaczek kernel}} A_i(\theta,\tau)e^{-j(\theta t+\tau\omega)}d\tau d\theta \tag{1}$$

and $A_i(\theta,\tau) = \int x_i(u+\frac{\tau}{2})x_i^*(u-\frac{\tau}{2})e^{j\theta u}du$ is the ambiguity function of $x_i(t)$.

2.2. Bivariate Phase Synchrony

Once the instantaneous phases of signals, $x_1(t)$ and $x_2(t)$, and the corresponding phase difference, $\Phi_{1,2}(t,\omega) = |\Phi_1(t,\omega) - \Phi_2(t,\omega)|$, are estimated, one needs to employ a statistical criterion to quantify the degree of phase locking [3]. The most prominent index of bivariate phase synchronization is the 'Phase Locking Value' (PLV), based on circular variance of the distribution of the phase differences:

$$PLV_{1,2}(t,\omega) = \frac{1}{L}\left|\sum_{k=1}^{L}\exp\left(j\Phi_{1,2}^k(t,\omega)\right)\right| \tag{2}$$

where L is the number of trials and $\Phi_{1,2}^k(t,\omega)$ is the time and frequency dependent phase difference estimate for the k^{th} trial. The phase difference between the signals, $\Phi_{1,2}^k(t,\omega) \in [0,2\pi)$, is mapped onto the unit circle by forming a direction vector and this index is a measure of how the relative phase is distributed over the unit circle. The relative phase will occupy a small portion of the circle if the two signals are synchronized, which results in a larger PLV value. PLV is equal to 1 for perfect synchronization and approaches to zero for independent oscillators.

2.3. Multivariate Phase Synchrony

For a network consisting of N nodes, bivariate synchrony has been extended to multivariate synchronization using S-estimator [7, 14], which exploits the eigenvalue spectrum of the $N \times N$ bivariate synchronization matrix, $\{PLV_{i,j}(t,\omega)\}_{i,j=1,\ldots,N}$, as follows:

$$S(t,\omega) = 1 + \frac{\sum_{m=1}^{N}\lambda_m \log(\lambda_m)}{\log(N)} \tag{3}$$

where $S(t,\omega)$ quantifies the group synchrony at time t and frequency ω, $PLV_{i,j}(t,\omega)$ is the bivariate synchrony between the i^{th} and j^{th} nodes and λ_ms are the N normalized eigenvalues.

This index is a complement to the entropy of the normalized eigenvalues of $\{PLV_{i,j}(t,\omega)\}_{i,j=1,\ldots,N}$ and the more disperse the distribution of the eigenvalues, the higher the entropy would be. If the network is completely synchronized, i.e., $PLV_{i,j}(t,\omega) = 1\ \forall\ i,j$, then the maximum eigenvalue will be equal to N whereas the remaining eigenvalues will be equal to zero which results in $S(t,\omega) = 1$, indicating perfect multivariate synchrony.

However, this measure is an indirect way of estimating the multivariate phase synchrony since it needs the computation of $\binom{N}{2}$ bivariate synchrony values to compute the global synchrony within the group. Furthermore, computational complexity is also an inherent drawback of the S-estimator since it requires the eigenvalue decomposition of the bivariate synchrony matrix at each time and frequency point.

3. HYPERSPHERICAL PHASE SYNCHRONY

Bivariate phase synchrony is based on the circular variance of the two-dimensional direction vectors on a unit circle (1-sphere), obtained by mapping the phase differences, $\{\Phi_{1,2}^k(t,\omega)\}_{k=1,\ldots,L}$, between the two time-series onto a Cartesian coordinate system. If the circular variance of these direction vectors is low, the time-series are said to be locked to each other. In this paper, we propose an extension of this idea to the multivariate case and define $\{\theta_1^k(t,\omega), \theta_2^k(t,\omega), \ldots, \theta_{N-1}^k(t,\omega)\}$ as the $(N-1)$ angular coordinates at time t and frequency ω for the k^{th} trial, where $\theta_i^k(t,\omega) = \Phi_i^k(t,\omega) - \Phi_{i+1}^k(t,\omega)$ is the phase difference between the i^{th} and $(i+1)^{th}$ time series within a group of N oscillators[1]. We map these $(N-1)$ angular coordinates onto an N-dimensional space by forming direction vectors in an N-dimensional hyperspherical coordinate system. For any natural number N, an $N-1$-sphere of radius r is defined as the set of points in (N)-dimensional Euclidean space which are at distance r from a central point, where the radius r may be any positive real number. The set of coordinates in N-dimensional space, $\gamma_1, \gamma_2, \ldots, \gamma_N$, that define an $(N-1)$-sphere is represented by:

$$r^2 = \sum_{i=1}^{N}(\gamma_i - c_i)^2 \tag{4}$$

[1]Note that the sequence of the phases when computing the angular coordinates does not have any effect on the circular variance of the resulting direction vectors.

where $\boldsymbol{c} = [c_1, \ldots, c_N]$ is the center point and r is the radius. In this paper, $r = 1$ and the center point is the origin. Fig. 1 shows an example of a 2-sphere where the 3-dimensional direction vectors are shown by the line crossings.

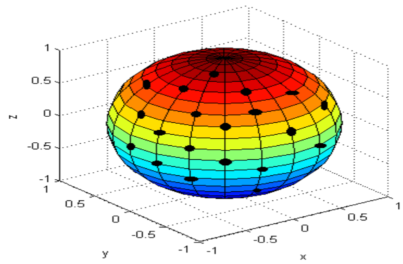


Fig. 1. Line crossings, such as the black dots, indicate the sampled 3-dimensional direction vectors based on uniform angular sampling of a 2-sphere.

Using the $N-1$ angular coordinates, $\{\theta_1^k(t,\omega), \ldots, \theta_{N-1}^k(t,\omega)\}$, we define the set of N Cartesian coordinates on a unit $N-1$ sphere which forms a direction vector, $\mathbf{\Gamma}^k(t,\omega) = [\gamma_1^k(t,\omega), \ldots, \gamma_N^k(t,\omega)]$, as[2]:

$$\begin{aligned}
\gamma_1^k(t,\omega) &= \cos(\theta_1^k(t,\omega)),\\
\gamma_2^k(t,\omega) &= \sin(\theta_1^k(t,\omega)) \times \cos(\theta_2^k(t,\omega)),\\
\gamma_3^k(t,\omega) &= \sin(\theta_1^k(t,\omega)) \times \sin(\theta_2^k(t,\omega)) \times \cos(\theta_3^k(t,\omega)),\\
&\vdots\\
\gamma_{N-1}^k(t,\omega) &= \sin(\theta_1^k(t,\omega)) \times \cdots \times \sin(\theta_{N-2}^k(t,\omega)) \times \cos(\theta_{N-1}^k(t,\omega)),\\
\gamma_N^k(t,\omega) &= \sin(\theta_1^k(t,\omega)) \times \cdots \times \sin(\theta_{N-2}^k(t,\omega)) \times \sin(\theta_{N-1}^k(t,\omega)),
\end{aligned} \tag{5}$$

Therefore, for N signals, we define the hyperspherical phase synchrony (HPS) as:

$$HPS(t,\omega) = \frac{1}{L}\left\|\sum_{k=1}^{L}\mathbf{\Gamma}^k(t,\omega)\right\|_2 \tag{6}$$

where $HPS(t,\omega)$ is the multivariate synchronization value at time t and frequency ω, $\|.\|_2$ is the Euclidean norm and L is the number of trials. Note that HPS is equivalent to PLV for a network consisting of two signals. In the case of perfect multivariate phase synchronization of the network, HPS is equal to 1 and equals to zero when the oscillators are independent.

4. APPLICATION TO EEG DATA

4.1. EEG Data

In order to evaluate the performance of the proposed measure in quantifying the multivariate synchronization across different brain regions, we use a set of EEG data containing the error-related negativity (ERN). The ERN is an event-related brain potential that occurs following performance errors in a speeded reaction time task [16] and is observed as a sharp negative trend in EEG recordings which typically peaks around 75-80 ms after the error response. Previous work indicates that there is increased phase synchrony associated with ERN for the theta frequency band (4-8 Hz) and ERN time window (25- 75 ms) between frontal and central electrodes versus central and parietal [17]. Cavanagh *et al.* have shown that lateral prefrontal cortex (lPFC) activity is phase-synchronous with medial-frontal theta, supporting the idea that medial prefrontal (mPFC) and lPFC regions are functionally integrated during error processing [18]. Therefore, in this paper, application of the proposed measure to EEG data is based on the hypothesis that the medial-frontal region will play a central functional role during the ERN, and will have significant integration with frontal areas within the theta frequency band. Therefore, multivariate phase synchronization is expected to be higher for frontal and central electrode group compared to parietal and central one.

EEG data from 62-channels was collected in accordance with the 10/20 system on a Neuroscan Synamps2 system (Neuroscan, Inc.)[3]. A speeded-response flanker task was employed, and response-locked averages were computed for each subject. Before applying the proposed measure, all EEG epochs were transformed to current source density (CSD) to accentuate local activity and distal activity (e.g. volume conduction), using published methods [19, 20]. In this paper, we analyzed data from 32 subjects corresponding to the error responses.

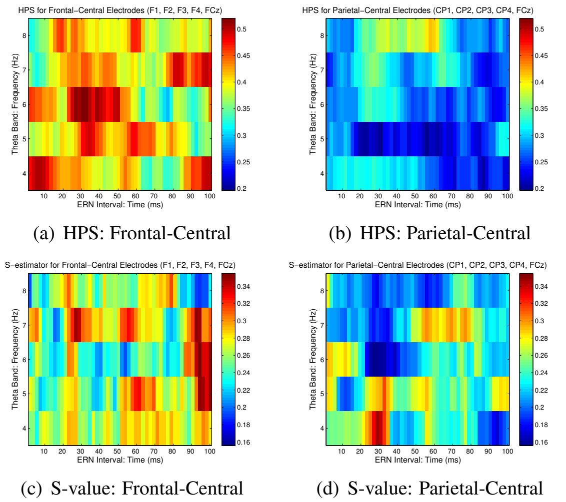
4.2. Results

The proposed hyperspherical multivariate synchrony measure is applied to both the frontal (F1, F2, F3, F4)-central (FCz) electrode group and the central parietal (CP1, CP2, CP3, CP4)-central (FCz) group. For each subject, we focused on the ERN interval, $[t_a, t_b]$, and theta frequency band, $[\omega_a, \omega_b]$, and compared the mean HPS value, $\overline{\text{HPS}} = \frac{1}{T\times\Omega}\sum_{t=t_a}^{t_b}\sum_{\omega=\omega_a}^{\omega_b}\text{HPS}(t,\omega)$, where T and Ω are the total number of time and frequency bins, respectively, to identify if the frontal-central group has stronger multivariate synchronization compared to the parietal-central group. For all subjects, frontal-central electrode group resulted in significantly larger HPS values compared to the parietal-central group using a Welch's t-test at 1% significance level. This result is consistent with previously observed interactions in the theta band between medial prefrontal cortex (mPFC) and lateral prefrontal cortex (lPFC) during error-related negativity [18]. Figs. 2(a) and 2(b) show the mean HPS values computed over all subjects at each time and frequency point within the ERN interval and theta band for the two electrode groups. Moreover, we compared the performance of HPS with the S-estimator in discriminating between the multivariate synchronization of the two groups. Figs. 2(c) and 2(d) show the mean S-values computed over all subjects. We found that the HPS values for frontal-central group in Fig. 2(a) are significantly larger compared to parietal-central group in Fig. 2(b) with $p < 0.01$. On the other hand, the S-values in Fig. 2(c) are significantly larger compared to parietal-central group with $p < 0.05$. Therefore, the proposed measure yields more significant differences and outperforms S-estimator in discriminating between the multivariate synchronization of the two groups.

We also compare our proposed measure with S-estimator for detecting significant multivariate synchronization for the frontal-central electrodes using an ROC curve. In this paper, for each subject, a true positive (detection) is determined when the mean

[2] In this paper, to generate a suitable set of direction vectors, unit hyperspheres are sampled based on uniform angular sampling methods.

[3] The authors would like to acknowledge Dr. Jason Moser from Michigan State University for sharing his EEG data with us.



(a) HPS: Frontal-Central

(b) HPS: Parietal-Central

(c) S-value: Frontal-Central

(d) S-value: Parietal-Central

Fig. 2. The mean HPS ((a) and (b)) and S-values ((c) and (d)) computed over all subjects at each time and frequency point within the ERN interval and theta band for the two electrode groups.

multivariate synchrony value within the ERN interval and theta band for the frontal-central electrodes is larger than the threshold, whereas a false alarm is defined when the mean multivariate synchronization for the parietal-central group is larger than the threshold. Fig. 3 shows the ROC curves for HPS and S-estimator. One can clearly see that HPS performs better than the S-estimator in detecting frontal-central multivariate synchronization.

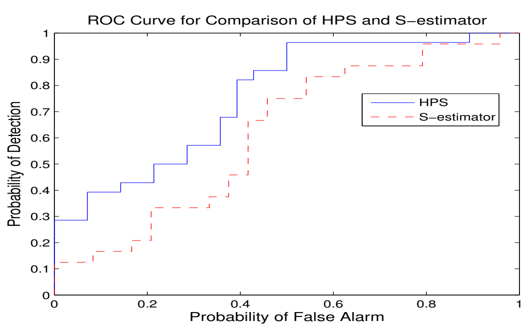


Fig. 3. ROC curves for HPS and S-estimator

5. CONCLUSIONS AND FUTURE WORK

In this paper, a novel and direct method is proposed to compute the multivariate phase synchrony for quantifying global coupling across different brain sites. Application to real EEG data containing the ERN supports the effectiveness of the proposed measure in revealing the increased phase synchrony associated with ERN between frontal and central electrodes versus central and parietal.

Future work will concentrate on exploring different sampling point-sets such that the resulting direction vectors are distributed uniformly on the N-sphere since the set of direction vectors based on uniform sampling in the angular coordinate system results in nonuniformly distributed direction vectors as shown in Fig. 1. The proposed measure will also be applied to EEG data containing event related potential due to both error and correct responses to get a more complete understanding of cognitive control. In the current application to EEG data, one limitation of the proposed measure is that the groups of oscillators to be analyzed have to be identified a priori and an exhaustive search to find synchronization clusters would be computationally complex. Therefore, it would be valuable to first use preprocessing methods, such as eigenvalue decomposition or measures of association and complexity, which can help us to discover the underlying networks.

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