MULTIPLE TRIAL PROCESSING OF MULTIVARIATE PHASE SYNCHRONIZATION IN BRAIN SIGNALS

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ABSTRACT

The quantification of phase synchrony is important for the study of large-scale interactions in the brain. Current methods for computing phase synchrony are limited to the estimation of the stability of the phase difference between pairs of signals over a time window, within successive frequency bands. These approaches cannot quantify the synchrony across a group of electrodes and over time-varying frequency regions from multiple trials. In this paper, we address this issue by quantifying the frequency locking between groups of electrodes using a time-frequency based estimation of the instantaneous frequency. The instantaneous frequency maps of individual electrodes are combined to obtain the instantaneous frequency histogram as an estimate of the amount of frequency locking across electrodes. This analysis is then extended to the estimation of frequency locking across multiple electrodes and trials. Results are shown for both synthetic signal models and electroencephalogram (EEG) data collected from control and schizophrenic subjects.

Index Terms— Phase synchronization, Time-frequency analysis, Electroencephalography

1. INTRODUCTION

With the advance of neuroimaging technology, it is now possible to identify the oscillations of neuronal networks at high temporal and spatial resolutions, using multichannel recordings. Simultaneous recording of multiple oscillations between different cortical regions offers insight into how distributed neuronal oscillations interact with each other. These interactions, which can be used to study large-scale functional integration, are transient, time-varying, and frequency specific. Therefore, there is a need for time-frequency based methods for quantifying the time-varying nature of the phase synchrony.

Recently, new tools for detecting localized phase synchronizations, with respect to time and frequency, have been developed using the complex wavelet transform [1] and the complex bilinear time-frequency distributions [2]. These methods have the advantage of separating the amplitude component from the phase and quantifying phase synchrony over time and frequency. However, these measures are limited in the way that they can only quantify pairwise synchrony between neuronal oscillations, and cannot directly assess the large-scale interaction between groups of neuronal signals.

In this paper, we propose a new method for addressing this problem by quantifying multivariate phase synchrony across groups of neuronal oscillations. The proposed method is based on using the relationship between phase synchrony and frequency locking. Since phase and frequency are directly related to each other, two signals are synchronous whenever their instantaneous frequency is approximately the same. Using this relationship, we propose an instantaneous frequency estimation method in the time-frequency domain to quantify the amount of synchronization between groups of signals. The IF estimates for different signals are combined using an instantaneous frequency histogram (IFH) to indicate the amount of synchronization. The proposed method is then extended for multiple electrode and multiple trial EEG recordings. The K-means algorithm is used to extract the most significant IFH patterns across trials for a group of electrodes.

2. METHOD

Two monocomponent analytic signals, $x_1(t) = a_1(t)e^{\phi_1(t)}$ and $x_2(t) = a_2(t)e^{\phi_2(t)}$, are phase synchronous if the phase difference between the two signals is constant. To allow for a small amount of noise in the phase of synchronous signals, the phase difference can be approximately constant:

$$\Delta\phi_{1,2}(t) = m\phi_1(t) - n\phi_2(t) \approx \text{constant} \qquad (1)$$

where m and n are some integers, and $\Delta\phi_{1,2}$ is the phase difference between the two signals. The derivative of Equation (1) can be shown as:

$$\frac{\mathrm{d}\Delta\phi_{1,2}(t)}{\mathrm{d}t} = m\frac{\mathrm{d}\phi_1(t)}{\mathrm{d}t} - n\frac{\mathrm{d}\phi_2(t)}{\mathrm{d}t} = m\omega_1(t) - n\omega_2(t) \approx 0 \qquad (2)$$

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where $\omega_i(t) = \frac{\mathrm{d}\phi_i}{\mathrm{d}t}(t) > 0$ and $w_i(t)$ is the instantaneous frequency (IF) of $x_i(t)$ in radians/second. Therefore, when $n = m$, two monocomponent signals are phase synchronous if they have approximately the same IF. This relation can be extended to three or more monocomponent signals. If a set of signals all have approximately the same IF, then all the signals in the set are phase synchronous together [3].

The IF of a monocomponent signal can be computed by taking the time derivative of the phase of the analytic signal. Unfortunately, most real life signals, including brain signals, are not necessarily monocomponent. They tend to be multicomponent and are approximately equivalent to separable components in the following general form: $s(t) = \Sigma_k a_k(t) e^{\phi_k(t)}$. While the same concept of phase synchrony applies to multicomponent signals, computing their IFs requires the use of more sophisticated methods [3].

2.1. Estimating IF of Multicomponent Signals

Ideally, the IF of a multicomponent signal will be the union of the IFs of the separate components. Numerous techniques exist to estimate the IF of a multicomponent signal. Previous methods include time-frequency moments, adaptive recursive least squares, and adaptive least mean square [4, 5]. Since most biological signals are non-stationary it is not possible to estimate their IF from the signal in the time or frequency domain. For this reason, we propose a time frequency (TF) peak algorithm for estimating IFs for multicomponent non-stationary signals.

A bilinear TFD belonging to Cohen's class can be expressed as:

$$C(t,f) = \iiint \phi(\theta,\tau) s(u+\frac{\tau}{2}) s^*(u-\frac{\tau}{2}) e^{j(\theta u - \theta t - 2\pi\tau f)}\, du\, d\theta\, d\tau \tag{3}$$

where the function $\phi(\theta,\tau)$ is the kernel function and s is the signal. For the purposes of IF estimation it is important to choose $\phi(\theta,\tau)$ such that it corresponds to a reduced-interference distribution in order to remove the cross-terms. In this paper we use the Choi-Williams distribution to estimate the IF [6]. The proposed TF peak method can be summarized as follows:

1. Using the Choi-Williams kernel, compute the TFD of the signal, $s(t)$, to get $C(t,f)$.

2. Find the local peaks of $C(t,f)$ using the following:

$$B(t,f) = \begin{cases} 1 & \text{if } \{\frac{\partial C(t,f)}{\partial f} = 0\} \wedge \{\frac{\partial^2 C(t,f)}{\partial f^2} < 0\} \\ 0 & \text{otherwise} \end{cases} \tag{4}$$

   where $B(t,f)$ is a binary-valued image with ones at the local peaks of $C(t,f)$ and zeros everywhere else.

3. Assign all nonzero time-frequency points into connected components. A connected component D contains nonzero time-frequency points such that there is an 8-neighborhood path containing only points in D. Two time-frequency points are connected if $B(t_1,f_1) = 1$, $B(t_2,f_2) = 1$, $|t_2 - t_1| \leq 1$, and $|f_2 - f_1| \leq 1$.

4. Remove any connected component, D_i, from $B(t,f)$ if $|D_i| < \epsilon$ where $|D_i|$ is the support of D_i. The removal of connected components with a small support reduces the effect of noise in $s(t)$. The threshold, ϵ, is dependent on the application and the time support of the signal.

5. Compute the average energy of each component, D_j, as follows:

$$\xi_j = \frac{1}{|D_j|} \sum_{(t,f)\in D_j} C(t,f) \tag{5}$$

   Remove any connected component, D_i, from $B(t,f)$ if $\xi_i < \lambda$. The removal of low energy connected components reduces the effect of noise in $s(t)$. The threshold, λ, is application dependent and should depend on the maximum average energy component.

The remaining connected components of $B(t,f)$ form the IF estimate, $\hat{F}(t,f)$, of $s(t)$. The resulting $\hat{F}(t,f)$ is a binary image with ones indicating the time and frequency location of the IF.

2.2. Instantaneous Frequency Histograms

Given the fact that phase synchronous signals have similar IFs, the phase synchrony of multiple signals or multivariate phase synchrony can be represented using an instantaneous frequency histogram (IFH). If the collection of signals contains K signals, computing the IF for each signal results in K different IF estimates, $\hat{F}_i(t,f)$ for $i = 1, 2, \ldots, K$. Summing the IFs from the collection of signals results in the IFH, $\text{IFH}(t,f) = \sum_{i=1}^{K} \hat{F}_i(t,f)$. Since the IF estimate is a binary image, each value of the IFH is a discrete, finite value in the range from 0 to K. For a single trial EEG consisting of multiple electrodes, the IFH represents the multivariate phase synchrony of the trial.

2.3. Multiple Trial IFHs

Most EEG studies involve multiple trials of the same stimulus. Therefore, an EEG recording with N trials will result in N IFH surfaces across the electrodes. Each of the IFHs must be interpreted and analyzed to find general patterns of multivariate phase synchrony among the trials. We propose to use data reduction techniques on the IFHs to determine representative patterns of multivariate phase synchrony across trials.

Typically, principal component analysis (PCA) is the primary tool for the dimension reduction of data sets. However, because of the discrete, finite values of the IFH, PCA is not

the best option. For this reason, we propose to use the K-means clustering approach for reducing the N IFH surfaces across trials into a few, distinct IFH components. The centroids can be restricted to the finite values of the IFH. For K-means clustering, each time-frequency point of the IFHs is treated as a separate dimension in the clustering vector space, and each of the N IFHs is treated as a point in the clustering vector space. For indices $i = 1, 2, \ldots, N$ and $j = 1, 2, \ldots, K$, K-means clustering can be summarized as follows:

1. Choose the initial centroids, $M_j = \text{median}(\{\text{IFH}_i : \text{IFH}_i \in R_j\})$ where R_j is a set of randomly selected IFHs.

2. Assign each IFH to a cluster by finding its nearest centroid $C_i = \text{argmin}_j \|\text{IFH}_i - M_j\|_2$, where C_i is the cluster index that IFH_i is assigned to.

3. Calculate the new centroids based upon the new cluster assignments using $M_j = \text{median}(\{\text{IFH}_i : C_i = j\})$. The median is used rather than the mean to keep the centroids in the finite field.

4. If the centroids, M_j, have changed since the last iteration, go back to step 2. If the centroids, M_j, have not changed since the last iteration, stop. Once clustering is complete, the significance of each centroid is determined by the number of IFHs in that cluster.

2.4. Quantifying IFHs

In order to quantify the phase synchrony from IFHs we compute [3]:

$$p_{avg} = \frac{\sum_{(t,f)\in W} (\text{IFH}^2(t,f) - \text{IFH}(t,f))}{n_c(n_c-1)n_T n_F} \qquad (6)$$

where n_c is the number of signals, W is a time-frequency window of interest, n_T is the number of time samples in W, and n_F is the number of frequency samples in W. The p_{avg} is an indicator of phase synchrony per TF point. An IFH with a higher p_{avg} indicates more signals are phase synchronous.

3. RESULTS

In this section, we will first test the validity of the proposed method for determining the phase synchrony on a pair of synthesized signals and then apply it to EEG signals.

Example 1: IFH of Synthetic Signals: In this example, we consider two sinusoidal signals, $x_1(t) = \sin(2\pi f_1(t) + 2\pi/3)$ and $x_2(t) = \cos(2\pi f_2(t))$ where $f_1(t) = 3u(t) + 3u(t-2) - 6u(t-3)$ and $f_2(t) = 3u(t) - 3u(t-1) + 6u(t-2) - 6u(t-3)$ such that $u(t)$ is the unit step function. The sinusoids have the same IF of 3Hz from 0 to 1 seconds and 6Hz from 2 to 3 seconds. The resulting IFH in Figure 1 shows that the proposed method is effective at tracking the time-varying phase synchrony.

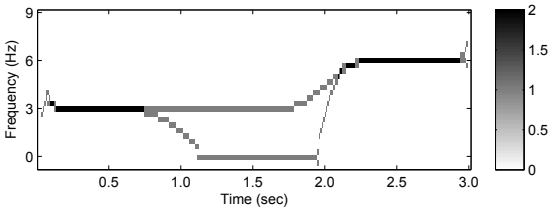

Fig. 1. The IFH of a pair of synthetic signals with common IF from 0 to 1 seconds and from 2 to 3 seconds.

Example 2: Gamma Band Synchrony in Schizophrenic Patients: In recent years, there has been evidence that large-scale functional integration of the brain is mediated by neuronal groups that oscillate in the gamma band range (30-60 Hz). It has been found that schizophrenic patients exhibit deficits in gamma band neural synchrony compared to normal subjects [7]. For the purpose of illustration, we examined the gamma band EEG activity in a schizophrenia patient and a non-psychiatric control subject who performed a continuous performance task (CPT). The IFH is computed over the P300 window (200-600 ms after the stimulus) and the γ band (30-55 Hz) for the frontal and parietal electrodes P3, P4, F3, and F4 for 80 trials. K-means clustering with $K = 10$, $\epsilon = 10$, and $\lambda = \xi_{max}/2$ is then performed on the 80 IFHs from each subject. Figures 2 and 3 show the four most significant cluster centroids for the control and schizophrenic subjects, respectively, over time and frequency. Overall, the four cluster centroids appear similar between the two subjects. However, the centroids with the most phase synchrony, Figure 2(b) for the control subject and Figure 3(a) for the schizophrenic subject, show more multivariate phase synchrony in the control subject in the higher frequencies. At 44 Hz and 48 Hz, three electrodes of the control subject are phase synchronous, while only two electrodes of the schizophrenic subject are phase synchronous. Tables 1 and 2 show the average correlations of the four most significant cluster centroids over two different frequency bands. The significance of the IFHs was tested using surrogate data, and the K-means cluster centroids were found to be significantly higher than the centroids obtained from trial-shifted data 90% of the time.

4. CONCLUSIONS

In this paper, we introduced a new method for quantifying the functional integration in the brain based on instantaneous frequency estimation in the time-frequency plane. The major contribution of the proposed method is that it can quantify synchronization across multiple trials and multiple electrodes as opposed to existing methods which focus on pairwise synchrony. The phase synchronization across multiple

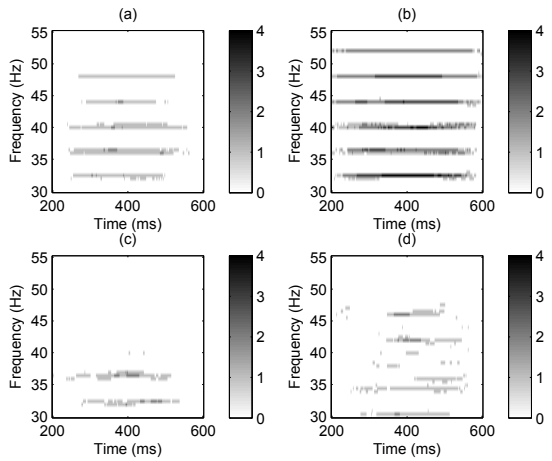

Fig. 2. The four most significant cluster centroids for the control subject. The number of IFHs belonging to each cluster: (a) 21, (b) 12, (c) 9, (d) 6.

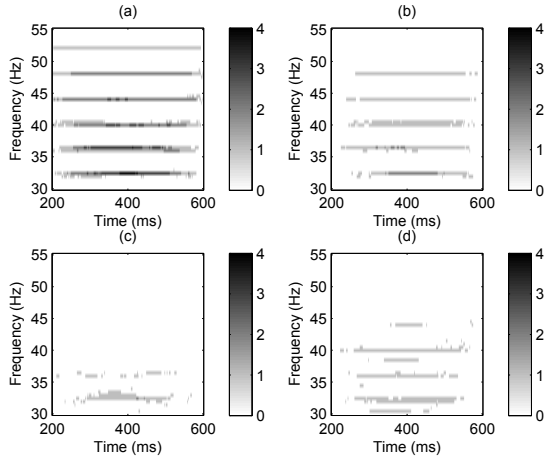

Fig. 3. The four most significant cluster centroids for the schizophrenia subject. The number of IFHs belonging to each cluster: (a) 20, (b) 13, (c) 8, (d) 8.

Comp #	Signif.	Freq. Band (Hz)	p_{avg}
1	21/80	30-40	0.001
		40-55	0.000
2	12/80	30-40	0.038
		40-55	0.037
3	9/80	30-40	0.002
		40-55	0.000
4	6/80	30-40	0.000
		40-55	0.001

Table 1. The correlation averages in two different frequency bands for the four most significant centroids of the control subject.

electrodes and trials is quantified using IFH and K-means algorithms. The proposed method has been applied to both synthetic and actual EEG signals, and was shown to be effective at determining phase synchronizations across time and frequency. The proposed measure can be extended to determine the functional network patterns in the brain across space, time and frequency.

Comp #	Signif.	Freq. Band (Hz)	p_{avg}
1	20/80	30-40	0.031
		40-55	0.016
2	13/80	30-40	0.004
		40-55	0.000
3	8/80	30-40	0.000
		40-55	0.000
4	8/80	30-40	0.000
		40-55	0.000

Table 2. The correlation averages in two different frequency bands for the four most significant centroids of the schizophrenic subject.

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