A Comparison of Surrogate Tests for Phase Synchronization Analysis of Neural Signals

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***Abstract*—Various studies show that advanced cognitive function is integrated by multiple interacted cortical regions. To investigate this mechanism, various measures, such as phase synchronization (PS) and partial directed coherence, has been applied to evaluate the pattern of neural connectivity among brain regions. However, some problems on quantifying neural connectivity are still open to be answered. For example, how to determine whether an estimated PS index (PSI) is significant big or not? Surrogate test is one main way to provide a threshold of significance for reference. Though many surrogate methods have been proposed, but which one is more suitable for PS analysis is not known yet. To deal with this question, this study performed a comparison of surrogate tests for the mean phase coherence based PSI with Electroencephalography (EEG) signals. Four different surrogate methods were compared, and results showed that among these methods, the rank-shuffled surrogate method is the most suitable one in providing significance test for PS analysis.**

I. INTRODUCTION

Functional neural connectivity plays an important role in human brain function [1], [2], and has been applied to not only reveal the mechanism of cognitive processing in human brain [2], [3], [4], but also gain new strategies for clinical treatments (e.g., Parkinson's disease) [5], [6]. Various methods, such as mutual information, phase synchronization (PS) analysis, and partial directed coherence, have been applied to quantify the connectivity among different brain units based on their functional neural signals, including electroencephalography (EEG), functional magnetic resonance imaging (fMRI) and etc. Some of these measures have been evaluated with both functional neural signals (EEG and fMRI) [7] and simulation data [8], and results show that these measures reveal similar global connectivity patterns but some differences between particular cortical regions [7]. Among these methods, PS analysis, which could effectively quantify the relationship between rhythms (i.e., instantaneous phase) extracted from the observed signals, but neglect the influence of instantaneous amplitude, is a suitable tool for analyzing neural signals, especially when the interaction between them is weak and may not be detected by other measures. Therefore, it has drawn increasing attention in recent years (for a review, cf. [3], [9], [10]).

To detect PS in observed signals, various definitions of instantaneous phase (IP) have been proposed [11], [12]. These IP definitions have been compared numerically with both simulation data and experimental signals [8], [13], and further unified into a framework which defines IP as the argument of the signal with a specific bandpass filter applied [14]. When the difference of the IPs of two coupled units (or extracted from a pair of signals) is bounded respect to time, the coupled units are said to be in PS. Various methods have been introduced to detect PS [13], [14]. However, to reliably detect PS is not so easy, especially with observed signals of a small number of samples and contaminated by noise as well [8], [13], [15]. Usually, the noisy data is pre-filtered with a bandpass filter.

The estimated PSI may falsely implicate that the corresponding signal pair is in a certain degree of PS if it is interpreted roughly with no significance level for reference. Surrogate test is one important way to offer a threshold of significance level for reference [10], [16]. Various surrogate methods have been applied to test the significance of estimated PSI. However, to the best of our knowledge, these surrogate methods have not been compared for PS analysis, and which surrogate is more suitable for PS analysis is not known yet. To answer this question, we perform a comparison of four surrogate methods for significance tests of PS with recorded EEG signals.

The organization of this paper is as follows. In Sec. II, the basic idea of PS and surrogate methods are introduced. In Sec. III, the EEG data used in this study are described. In Sec. IV, the results of comparison of surrogate tests are presented. Finally, conclusion is given in Sec. V.

II. METHODS

A. *Phase Synchronization Analysis*

For a real-value narrow-band signal $s(t)$, its analytic signal is defined as

$$z(t) = s(t) + j\mathcal{H}[s](t) = A(t)e^{j\phi(t)}, \tag{1}$$

where $A(t)$ and $\phi(t) = \arctan\frac{\mathcal{H}[s](t)}{s(t)}$ are the instantaneous amplitude and IP of signal $s(t)$, respectively, and $\mathcal{H}[s](t)$ is the Hilbert transform of $s(t)$, i.e.,

$$\mathcal{H}[s](t) = \frac{1}{\pi}\lim_{\delta\to 0}\left[\int_{-\infty}^{t-\delta}\frac{s(\tau)}{t-\tau}d\tau + \int_{t+\delta}^{+\infty}\frac{s(\tau)}{t-\tau}d\tau\right]. \tag{2}$$

In the frequency domain, $z(t)$ turns out to be

$$Z(w) = \begin{cases} 2S(w), & \text{if } w > 0 \\ S(w), & \text{if } w = 0 \\ 0, & \text{if } w < 0, \end{cases} \tag{3}$$

where $Z(w)$ and $S(w)$ are the Fourier transform of $z(t)$ and $s(t)$, respectively. Then, the analytic signal $z(t)$ can be easily obtained by performing inverse Fourier transform to $Z(w)$. In this study, the waves of EEG signals in particular frequency band are first extracted with bandpass filter, and then PS analysis is performed to the EEG waves.

Let $\phi_1(t)$ and $\phi_2(t)$ denote the cumulative IP of two coupled systems respectively. Then the coupled systems are said to be in PS when the inequality $|l\phi_1(t) - m\phi_2(t)| < \text{const.}$ holds, where l and m are positive integers. In this study, we focused on the case of 1:1 PS. More information on l:m PS can be found in [17], [18]. One popular index to quantify the level of PS is mean phase coherence (MPC) [19], which is defined as $\lambda = \|E[e^{j\varphi}]\|$, where $\varphi(t) = \phi_1(t) - \phi_2(t)$ is the IP difference. The value of λ is between [0 1], with $\lambda = 1$ implying perfect PS and $\lambda = 0$ indicating no PS at all.

B. Surrogate Test

Surrogate test is one important way to provide a reference of significance for an estimated PSI [10], [16], [19]. The surrogate methods usually produce artificial data by mimic only particular properties, such as the individual spectra, but randomizing the concerned property of the original signal [16], [20]. In this study, four different surrogate methods are compared in providing significance test for PSI estimated.

1) Rank-shuffled surrogate (RSS): This method generate surrogate data by randomly shuffling the rank of the original signals. Let $\{g(n)\}$ denote a random series of Gaussian distribution, and $R[g(k)]$ denote the rank order of $g(k)$ in time series $\{g(n)\}$, i.e., $R[g(k)] = 5$ if $g(k)$ is the 5th smallest sample in $\{g(n)\}$. Then $\{\tilde{s}(n)\}$ is a rank-shuffled surrogate of $\{s(n)\}$, where $\tilde{s}(n) = s[\kappa(n)]$, and $\kappa(n) = R[g(n)]$. By this way, the surrogate $\{\tilde{s}(n)\}$ has the same rank order with that of the Gaussian time series $\{g(n)\}$, but the samples of $\{\tilde{s}(n)\}$ all come from the original sequence $\{s(n)\}$, that is, the surrogate is a rank-shuffled version of the original signals [21].

2) Phase-shuffled surrogate (PSS): Let $\{S(k)\}$ denote the discrete Fourier transform of the original signal $\{s(n)\}_{n=0}^{N-1}$. Then a surrogate of $\{s(n)\}$ is generated by the inverse Fourier transform of $\tilde{S}(k)$, i.e.,

$$\tilde{s}(n) = \frac{1}{N}\sum_{k=0}^{N-1}\tilde{S}(k)e^{j2\pi kn/N}, n = 0, 1, \ldots, N-1, \quad (4)$$

where

$$\tilde{S}(k) = |S(k)|e^{j\nu(k)}, \quad (5)$$

and $\{\nu(k)\}_{k=0}^{N-1}$ is a uniform random sequence. This method shuffles the phase spectra of the original signal but keeping the amplitude spectra unchanged in the frequency domain.

3) RSS of instantaneous frequency (RSS-IF): RSS and PSS both generate surrogate data by shuffling particular features of the original signal, and surrogate test is further performed with IPs estimated from the so-obtained surrogate data. As PSI is calculated from the IP difference of a pair of signals, another strategy is to generate surrogate sequence of IP directly from the IP of the original signal. With this consideration, the third surrogate method is with the concept of instantaneous frequency (IF) [10]. The IF of $s(t)$ is defined as the derivative of the IP of $s(t)$, i.e.,

$$f(t) = \frac{1}{2\pi}\frac{d\phi(t)}{dt}. \quad (6)$$

For a discrete signal $\{s(n)\}$, its IF can be estimated by

$$f(n) = \frac{1}{2\pi}\frac{\hat{\phi}(n+1) - \hat{\phi}(n)}{\Delta t}, \quad (7)$$

where $\{\hat{\phi}(n)\}$ is the estimated IP sequence, and Δt is the sampling interval. With the IF sequence $\{\hat{f}(n)\}$ estimated, a surrogate sequence, $\{\tilde{f}(n)\}$, of $\{\hat{f}(n)\}$ can be generated with the RSS method introduced above. Then a surrogate sequence of $\{\hat{\phi}(n)\}$ can be obtained by

$$\tilde{\phi}(n+1) = \tilde{\phi}(n) + 2\pi\tilde{f}(n)\Delta t, \quad (8)$$

where $\tilde{\phi}(1) = \hat{\phi}(1)$.

4) PSS of instantaneous frequency (PSS-IF): This method generates surrogate sequence for $\{\hat{\phi}(t)\}$ in a similar way of RSS-IF [10]. The only difference lies in the step where the surrogate sequence, $\{\tilde{f}(n)\}$, of IF is produced from $\{\hat{f}(n)\}$ by the PSS method introduced in Sec. II-B2.

5) Statistical significance test: A (1-α)×100% level of significance corresponds to a probability α of a false rejection. To get a one-side test of 95% level of significance ($\alpha = 0.05$), $M = K/\alpha - 1$ surrogate realizations should be generated, where K is a positive integer. A larger value of K could offer a greater power in discrimination. In this study, we set $K = 5$, $\alpha = 0.05$, and $M = 99$, that is, 99 realizations of surrogate data are generated for each original signal set [20]. If a PSI of the original signal pair is larger then the 5th biggest value of all the 100 PSIs (the PSI of the original signal pair and the PSIs of its 99 surrogate pairs), the original signal pair is claimed to be in PS with a 95% level of significance ($\alpha = 0.05$).

III. EEG DATA RECODING AND PREPROCESSING

The EEG data used in this study were measured from ten right-handed healthy volunteers (21.3 ± 2.7 years) from Shanghai Jiao Tong University. All subjects reported normal hearing, normal or corrected-to-normal vision, and no history of neurological or psychiatric disorder. Each subject had given a written informed consent before the experiment, and the experiment protocols were complying with Helsinki declaration. In each trial, subjects were cued to switch attention to one sensory modality (auditory or visual) and maintain the intersensory selective preparatory state. As this study focused on methodology of EEG analysis, the protocol of this cognitive experiment is not introduced in detail here, but will be reported elsewhere [22]. EEG data was recorded with 32 scalp electrodes placed on an EasyCap$^{\text{TM}}$(BrainAmp amplifier, Brain Products GmbH, Germany) at 1000 Hz sampling rate. Horizontal and vertical electro-oculograms were recorded for rejecting eye movements and blinks off-line.

EEG preprocessing were conducted with Brain Vision Analyzer (Version 2.0). Raw EEG data were filtered with pass band [0.01 80] Hz and a notch filtering at 50 Hz off-line. Vertical and horizontal eye movements and blinks were corrected using independent component analysis. Then EEG data were referenced to the average, and other physical artifacts were rejected by Raw Data Inspection transform. After that, continuous EEG was segmented to trials of 2200 ms each, from 200 ms before the cue onset to 2000 ms post-cue. For each subject, one visual trial of EEG signals (30 channels) contained no significant artifacts were selected for subsequent surrogate tests.

IV. RESULTS

For the RSS and PSS methods, surrogate data of each channel of EEG signal are first generated. Then the theta waves ([4 8] Hz), alpha waves ([8 12] Hz), beta waves ([12 30] Hz), and gamma waves ([30 80] Hz) of the original signals and theirs surrogate data are extracted with FIR filters [23].

Let $\{s(n;i,p)\}$ denote the ith channel of EEG signals of the pth subject, and $\{\tilde{s}_k(n;i,p)\}$ denote the kth surrogate realization for $\{s(n;i,p)\}$. Let $\lambda(i,j)$ denote the MPC-based PSI of a pair of EEG channels, i.e., $\{s(n;i,p)\}$ and $\{s(n;j,p)\}$, in a particular frequency band, and $\tilde{\lambda}_k(i,j)$ denote the respective PSI of the pair of the kth surrogate realization (i.e., $\{\tilde{s}_k(n;i,p)\}$ and $\{\tilde{s}_k(n;j,p)\}$) in that frequency band. For each channel of EEG signals, 99 realizations of surrogate data are generated by each surrogate method. In this study, 30 channels of EEG signals of each subject are adopted, and thus there are 435 pairs of EEG channels and total 43 065 pairs of surrogate data for each subject. The histograms of MPC-based PSIs of the original signal pairs and their RSS surrogate pairs are presented in Fig. 1.

For each signal pair, the PSIs of 99 surrogate realizations and the original signal pair are sorted in ascending rank. Then the value of the PSI of the 5th largest one of these 100 PSIs is adopted as the threshold ($T_{.05}$) of 95% level of significance for the PSI of the original signal pair. Fig. 2 gives a scatter plot of PSIs of the original signal pairs with respect to the thresholds ($T_{.05}$) of 95% level of significance suggested by their RSS surrogate data. We can observe that the values of the thresholds $T_{.05}$ increase as the duration of the original EEG signals used for estimating PSI decreases. This is as expected, as the shorter length of the data used implies the higher probability to yield a nonuniform distribution of IP difference due to insufficient samples, and thus results in a larger PSI estimated. In addition, for the RSS method, the thresholds $T_{.05}$ show small correlation with respect to the PSIs of their original signal pairs in four frequency bands (i.e., the theta, alpha, beta, and gamma bands) and three different duration (i.e., 200 ms, 400 ms, and 800 ms). But as Fig. 3 demonstrates, the thresholds ($T_{.05}$) of 95% level of significance estimated by other three surrogate methods, especially RSS-IF and PSS-IF, show high correlation with respect to the PSIs of the original signal pairs. For a given segment of EEG signal pair, the significance level revealed by surrogate test is expected to be independent of the value of PSI of its original signal pair. Based on this point, RSS-IF and PSS-IF are not appropriate surrogate methods for PS analysis.

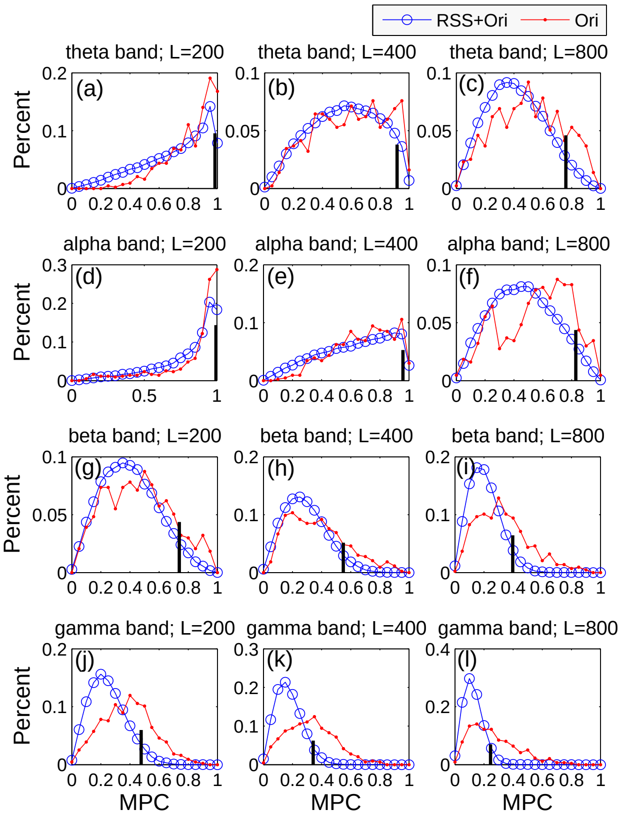

Fig. 1. Histograms of MPC-based PSIs for original EEG signals and their RSS surrogate data of one subject. The results for four frequency bands (i.e., the theta, alpha, beta, and gamma band) and three different duration (i.e., 200 ms, 400 ms, and 800 ms) of EEG signals are presented. The black bar indicate the value (x-axis) of the 5% largest PSIs of all the surrogate realizations (435 PSIs of the original signal pairs and the 435×99 PSIs of their surrogate pairs) and their original signal pairs (435 PSIs).

V. CONCLUSIONS

In this study, we perform a comparison of four surrogate methods, i.e., rank-shuffled surrogate (RSS), phase-shuffled surrogate (PSS), RSS of instantaneous frequency (RSS-IF), and PSS of instantaneous frequency (PSS-IF), in providing significance test for phase synchronization (PS) analysis. Results show that the RSS method can yield significant threshold which has rather small correlation to the PSI of the original signal pair, while the other three methods show big or relative big correlation to PSI of the original signal pair. From this point, we conclude that among the four surrogate methods, the RSS method is the most suitable one in providing significance test for PS analysis. Note that in this study, we only compared four surrogate methods from one aspect. Comparison of more other surrogate methods with criterions of various aspects are needed, and that is our next step work.

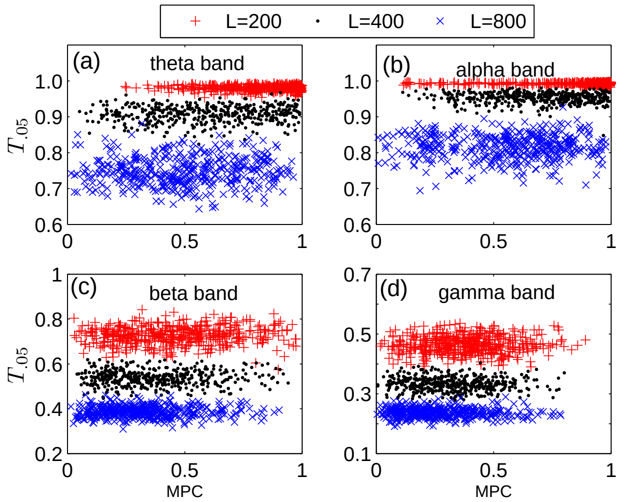

Fig. 2. Scatter plots of the thresholds ($T_{.05}$) of 95% level of significance suggested by RSS with respect to the MPC-based PSIs of their original signal pairs. The results for four frequency bands (i.e., the theta, alpha, beta, and gamma band) and three different duration (i.e., 200 ms, 400 ms, and 800 ms) are presented.

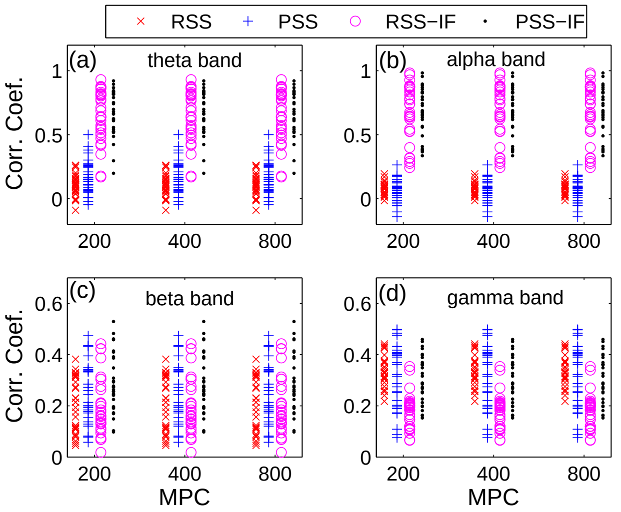

Fig. 3. Correlation coefficient between the PSIs of the original EEG pairs and their corresponding thresholds ($T_{.05}$) of 95% level of significance. The results for four frequency bands (i.e., theta, alpha, beta, and gamma band) and three different duration (i.e., 200 ms, 400 ms, and 800 ms) are presented. In each sub-figure, one symbol denotes the correlation coefficient for one subject at that case.

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