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Spurious cross-frequency amplitude–amplitude coupling in nonstationary, nonlinear signals

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HIGHLIGHTS

- Nonstationary oscillations can induce spurious amplitude–amplitude coupling (AAC).
- Nonlinear waveform can induce spurious AAC.
- The EMD-based AAC method performs better than the Fourier-based AAC method.

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ABSTRACT

Recent studies of brain activities show that cross-frequency coupling (CFC) plays an important role in memory and learning. Many measures have been proposed to investigate the CFC phenomenon, including the correlation between the amplitude envelopes of two brain waves at different frequencies — cross-frequency amplitude–amplitude coupling (AAC). In this short communication, we describe how nonstationary, nonlinear oscillatory signals may produce spurious cross-frequency AAC. Utilizing the empirical mode decomposition, we also propose a new method for assessment of AAC that can potentially reduce the effects of nonlinearity and nonstationarity and, thus, help to avoid the detection of artificial AACs. We compare the performances of this new method and the traditional Fourier-based AAC method. We also discuss the strategies to identify potential spurious AACs.

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1. Introduction

Various physical and physiological systems generate seemingly irregular outputs such as heart rate, motor activity, and brain activity that display complex oscillations/fluctuations over a range of frequencies [1,2]. These fluctuations are not simply caused by random external influences but possess intrinsic dynamic patterns that are of relevance to health [3–8].

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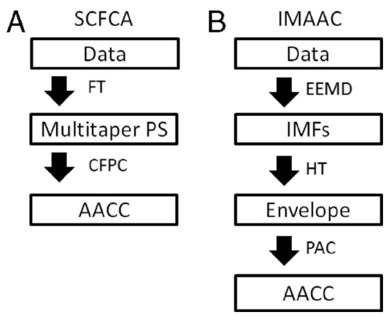

Diagram 1. The procedures of the two methods for the assessment of cross-frequency amplitude–amplitude coupling. (A) The spectral cross-frequency comodulation analysis (SCFCA). (B) The intrinsic mode amplitude–amplitude coupling (IMAAC). FT: Fourier transform; PS: power spectrum; CFPC: cross-frequency power correlation; AACC: amplitude–amplitude coupling comodulogram; EEMD: ensemble empirical mode decomposition method; IMF: intrinsic mode function; HT: Hilbert transform; PAC: phase–amplitude coupling.

Many recent studies have revealed cross-frequency coupling (CFC) in these complex fluctuations in which interactions occur between rhythms at different frequencies either within the same signals or in different signals [9]. CFC is of particular interest in the studies of brain activities because they are indicative of information propagation across different brain regions for specific neurophysiological functions [10–14]. There are three types of CFCs: phase synchronization (phase–phase CFC), phase–amplitude coupling (PAC), and amplitude–amplitude coupling (AAC). Most CFC studies have been mainly focused on the development and application of phase/frequency synchronization [15–18] and PAC [19–21]. However, few studies were conducted to validate/test the analytical tools for assessment of AAC despite the evidence for the physiological importance of AAC [22].

In this brief communication, we show that signals with nonstationary, nonlinear oscillations can lead to spurious AAC. The difficulties in identifying AAC while avoiding artifacts lie within the two required steps in assessing AAC: (1) extracting oscillatory components with varying amplitude, and (2) quantifying the coupling between the amplitudes of a pair of oscillatory components. To illustrate the difficulties, we test a previously used AAC method that is based on spectral analysis or Fourier transform [22]. In addition, we propose a new analytical tool for the assessment of AAC that is based on the empirical mode decomposition (EMD)—a decomposition that can better extract nonlinear and nonstationary oscillatory components from noisy signals [23–30]. We examine and compare the performances of the two methods using synthetic signals without AAC that are nonstationary and nonlinear as often observed in EEG recordings. The goal of this study is to illustrate certain pitfalls in AAC measures and to provide certain simulation results that can guild for appropriate result interpretation in AAC studies of real physiological data.

2. Methods

2.1. Assessment of AAC

2.1.1. Spectral cross-frequency comodulation analysis (SCFCA)

To assess AAC in local field potentials, the SCFCA was previously proposed and used to calculate the correlations [31] between the spectral power time series for all pairs of frequencies [22]. Briefly, for a signal, the method involves two steps (Diagram 1(A)): (1) multitaper spectral analysis is performed to obtain spectrum in sliding windows (window size $= 3$ s; step size $= 0.1$ s; taper number $= 9$) and to construct time $\times$ frequency spectrograms (frequency resolution $= 2$ Hz); and (2) cross-correlation is calculated for each pair of two power density time series at two frequencies to obtain an amplitude–amplitude power comodulogram. We note that the time and frequency resolutions of the SCFCA are determined by the selected parameters of the Fourier transform and filtering. For instance, with 3 s for the window size of each spectrum, it is not possible to identify the coupling between the amplitudes of two oscillatory components that only occurs at frequencies much greater than $>1/3$ Hz (Supplemental Figure 1, see Appendix A).

2.1.2. Intrinsic mode amplitude–amplitude coupling (IMAAC)

Strong evidence indicates that, as compared to the Fourier transform, the empirical mode decomposition (EMD) can better extract nonlinear and nonstationary oscillations [32]. Thus, we introduce a new EMD-based method for the assessment of AAC. This method, namely, intrinsic mode amplitude–amplitude coupling (IMAAC), involves the following steps (Diagram 1(B); Fig. 1). (1) The EMD is used to extract oscillatory components of a signal at different frequencies with each component (intrinsic mode function: IMF) representing true fluctuations in the raw data over a narrow band of frequencies. To avoid the mixed mode (i.e., specific signal may not be separated into the same IMFs every time) [33], we propose to use noised-enhance ensemble EMD (EEMD) with the noise level of 20% (where noise level 20% represents a standard deviation of 20%) and 400 realizations [34]. In addition, we use the updated version of the EMD algorithm that is proposed by Wang et al. and can be <1000 times less time consuming than the original EMD [35]. To avoid potential mode splitting (i.e., an oscillatory component is divided into different IMFs) [36], an orthogonal checking is performed and split