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Estimation of nonlinear neural source interactions via sliced bicoherence

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ABSTRACT

Neural oscillations and their spatiotemporal interactions are of interest for the description of brain mechanisms. This study offers a novel third order spectral coupling measure named "sliced bicoherence". It is the diagonal slice of cross-bicoherence allowing an efficient quantification of the nonlinear interactions between neural sources. Our methodology comprises an indirect estimation method, a parametric confidence level formula and a subtracted version for robustness to volume conduction. The methodology provides an efficient estimation of third-order nonlinear cross relations reducing the complexity to the same order of second-order coherence computation. Unlike other bispectral measures, the suggested measure solely holds terms related to cross relations between channel sources and omits the possible strong autobispectral relations. Feasibility and robustness of the methodology are demonstrated both on simulated and publicly available MEG data. The latter were collected for a motor task and an eyes-open resting state. Analytical confidence level marked the non-significant couplings. Simulations confirmed that the subtracted bicoherence enabled robustness to volume conduction by avoiding the spurious nearby channel couplings. Central regions were shown to be coupled with muscular activity by sliced bicoherence. Couplings for spontaneous data occurred particularly at theta and alpha bands. Volume-conduction related bicoherence values originated especially from the low frequencies below 5 Hz. The suggested nonlinear measure is promising to be a part of the rich collection of the multichannel electrophysiological brain connectivity metrics.

1. Introduction

Neural oscillations have been assumed to play a fundamental role during the functioning of normal and pathological brain. Specifically, neural synchronization is known to be an essential means for the communication of spatially distant oscillatory networks in the brain [1,2]. Synchronization is achieved through interaction of massive neural populations either at one frequency or multiple frequencies. Coherence is a well-known measure to obtain linear phase and/or amplitude relations between two sites at one specific frequency. Recent years have also witnessed the ubiquitous use of cross-frequency measures [3] such as phase-amplitude coupling which quantifies low frequency phase and high frequency amplitude synchronization [4] and amplitude-amplitude correlation [5,6]. Various studies have shown that synchronization measures may signify genuine neural interactions characterizing the fundamental mechanisms of the brain for medical [7], task-related [8] and resting states [9].

Rapid estimation of neural synchronization measures is of utmost importance while revealing the brain networks from macro scale electrophysiological multichannel data. Thus, employed methods need not only yield computationally affordable estimations of synchronization measures but should also allow efficient determination of statistical significance. Examples for the latter utilize the simple parametric formulae assuming standard distributions (Gaussian, uniform etc.) for the assessment of coherence [10] and phase-amplitude coupling [11] confidence limits.

There have been various studies using bispectrum and its normalized version named as bicoherence on EEG and MEG data [12–16]. We would like to emphasize the expensive computational cost as one of the main obstacles over the bispectral measures. A pairwise bispectral analysis of multichannel data requires estimates in the order of $\sim N^2 \times M^2$, where N and M denote the number of channels and the number of sampled frequencies, respectively. In order to alleviate the huge computational cost of bispectral analysis, Chella et al. [16] applied principal component analysis to reduce

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the data dimension prior to the parameter estimation. However, this operation alone still cannot decrease the degree of the complexity but rather reduces the number of channels to the number of principal components.

Current study presents an efficient indirect estimation of diagonal slice of cross-bicoherence (normalized cross-bispectrum), hence reducing the complexity to the same order of coherence computation. We also present simple formulae to obtain the confidence limits of the estimate. The suggested procedure allows feasible extractions of higher-order spectra related brain connectivity from data with high number of channels and low computational cost, making it computationally comparable to that of the classical coherence and the power spectrum.

2. Methods

The 1,1,2 cross-bicoherence for two signals $x_1(n)$ and $x_2(n)$ is given by

$$b_{12}(f_1, f_2) = \frac{|E\{X_1(f_1)X_1(f_2)X_2*(f_1+f_2)\}|^2}{S_1(f_1)S_1(f_2)S_2(f_1+f_2)} \quad (1)$$

where superscript * stands for the complex conjugate and $E\{\}$ is the statistical expectation operator [17]. Here X and S denote Fourier coefficients and spectra respectively. Please note that the rest of the text shall consider a particular slice of bispectrum, i.e., the diagonal slice where $f_1 = f_2$. Despite not being explicitly stated, higher-order couplings in this slice were commonly observed in empirical neuroelectrophysiological studies (see Section 4, for some examples). Nevertheless, in principle, it is straightforward to select any other slice of the cross-bispectrum to proceed with the suggested methodological approach.

2.1. Diagonally sliced 1,1,2 cross-bicoherence: definition and relation to coherence

For the sake of brevity, the measure in the subtitle shall be called "sliced bicoherence" throughout this paper. We would like to consider sliced bicoherence in analogy with the well-known coupling measure of coherence, which is defined for two signals $x_1(n)$ and $x_2(n)$ as [18,19]:

$$c_{12}(f) = \frac{|S_{12}(f)|^2}{S_1(f)S_2(f)} = \frac{|E\{X_1(f)X_2*(f)\}|^2}{S_1(f)S_2(f)}. \quad (2)$$

Similar to the coherence, sliced bicoherence for the signals $x_1(n)$ and $x_2(n)$ can be formulated as:

$$b_{12}(f) = \frac{|B_{112}(f,f)|^2}{{S_1}^2(f)S_2(2f)} = \frac{|E\{{X_1}^2(f)X_2*(2f)\}|^2}{{S_1}^2(f)S_2(2f)} \quad (3)$$

where B denotes (cross) bispectrum.

Please notice the structural similarity of coherence (Eq. (2)) and sliced bicoherence (Eq. (3)) formulations. Some essential distinctive properties may be listed as follows:

1. Coherence is a 2nd order cross-spectral measure. While sliced bicoherence is a 3rd order one.
2. Coherence is a linear measure. Input and output signals of a linear filter are also perfectly coherent. While sliced bicoherence is a nonlinear measure.
3. Unlike coherence, sliced bicoherence is not symmetric, i.e., $b_{12}(f) \neq b_{21}(f)$. As it is clear from Eq. (3) that $b_{12}(f)$ implies the relation of the frequency component at f in the first signal to the component at $2f$ in the second one, while the other way around is the case for $b_{21}(f)$.
4. Two signals are perfectly coherent if they are 1:1 linear phase locked at the same frequency f. While two signals are perfectly sliced bicoherent if they are 1:2 quadratic phase locked at a frequency f for one signal and its double $2f$ for the other signal.
5. A signal is perfectly coherent with itself, i.e., $c_{11}(f) = c_{22}(f) = 1$ for $\forall f$. This is not the case for sliced bicoherence.

2.2. Estimation

The IDFT of the numerator of Eq. (3) for "autobispectrum", i.e., $B_{111}(f,f)$ was called as "sum-of-cumulants" (SOC) in signal processing [20]. It has been used for various purposes such as system identification [21], signal reconstruction [22], detection of nonlinearity [23] and robust speaker recognition [24]. It should be noted that these studies utilized SOC to capture only "auto" bispectral features in the aforementioned literature. The current study instead aims at seeking cross-frequency couplings via the cross-bispectrum related measures.

In order to estimate b_{12}, one may compute the average over a number of segments, just like in coherence. Computing the whole total bispectrum to obtain the numerator of Eq. (3) would take considerable time, as its dimension is higher than the spectrum. Instead, we suggest using an indirect formula computing the cross-bispectral slice:

$$\hat{B}_{112}(f,f) = \mathcal{F}\{x_1(n)*x_1(n)*y_2(n)\} \quad (4)$$

where $\mathcal{F}$ stands for Discrete Fourier Transform, * is the convolution operator and

$$y_2(n) = \begin{cases} x_2(N-1-n/2), & n \text{ is even} \\ 0, & n \text{ is odd} \end{cases}. \quad (5)$$

A similar formula to Eq. (4) has been used for the computation of "auto" bispectrum in some studies [22,24]. The validity of Eq. (4) can be shown using the convolution theorem (see Appendix A).

2.3. Confidence limit

Halliday et al. [10] suggested a plain parametric formula depending on the number of segments in order to compute a statistical limit for coherence. Analogously, Özkurt [11] derived a formula that gives a statistical limit for direct phase-amplitude coupling measure. The latter formula solely depends on data length. Both studies assumed standard and reasonable probability distributions (such as Gaussian and uniform) that are fairly easy to manipulate and hence obtain simple confidence limits. They enable efficient statistical thresholds for the coupling estimates.

In a similar fashion, Haubrich [25] showed that the 0.95 confidence level for bicoherence is $3/N$ for signals with Gaussian probability distributions, where N denotes the number of segments. One should note that Gaussian signals ideally would have zero bicoherence. Hence the derived formula provides a lowest limit while deciding the reliability of the resultant bicoherence value. Elgar and Guza [26] compared this formula to the results of numerical simulations.

We here show that Haubrich's formula is only valid for the bicoherence $b_{12}(f_1, f_2)$ of different frequencies, that is for $f_1 \neq f_2$. Our numerical derivation indicated that specifically for the diagonal sliced bicoherence $b_{12}(f)$, the confidence limit becomes $6/(N+1)$ instead, that is for $f_1 = f_2$. Please see Appendix B for the derivation and note that we additionally validated the confidence level derivation with a Monte Carlo simulation.

2.4. Use in electrophysiology

One can reliably estimate the oscillatory coupling between a frequency of a signal in a channel and the double frequency in another