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Detecting phase-amplitude coupling with high frequency resolution using adaptive decompositions

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HIGHLIGHTS

- Narrowband filtering can lead to poor frequency resolution, incorrect frequency assignment, and false negatives in PAC assessment.
- Accurate PAC assessment can be obtained with adaptive and broadband decompositions, but these decompositions give little frequency information.
- Coupling adaptive, broadband decompositions with time-local frequency assessment allows for PAC assessment that is both accurate and highly frequency resolved.

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ABSTRACT

Background: Phase-amplitude coupling (PAC) – the dependence of the amplitude of one rhythm on the phase of another, lower-frequency rhythm – has recently been used to illuminate cross-frequency coordination in neurophysiological activity. An essential step in measuring PAC is decomposing data to obtain rhythmic components of interest. Current methods of PAC assessment employ narrowband Fourier-based filters, which assume that biological rhythms are stationary, harmonic oscillations. However, biological signals frequently contain irregular and nonstationary features, which may contaminate rhythms of interest and complicate comodulogram interpretation, especially when frequency resolution is limited by short data segments.

New method: To better account for nonstationarities while maintaining sharp frequency resolution in PAC measurement, even for short data segments, we introduce a new method of PAC assessment which utilizes adaptive and more generally broadband decomposition techniques – such as the empirical mode decomposition (EMD). To obtain high frequency resolution PAC measurements, our method distributes the PAC associated with pairs of broadband oscillations over frequency space according to the time-local frequencies of these oscillations.

Comparison with existing methods: We compare our novel adaptive approach to a narrowband comodulogram approach on a variety of simulated signals of short duration, studying systematically how different types of nonstationarities affect these methods, as well as on EEG data.

Conclusions: Our results show: (1) narrowband filtering can lead to poor PAC frequency resolution, and inaccuracy and false negatives in PAC assessment; (2) our adaptive approach attains better PAC frequency resolution and is more resistant to nonstationarities and artifacts than traditional comodulograms.

Abbreviations: PAC, phase-amplitude coupling; EEG, electroencephalogram; LFP, local field potential; EMD, empirical mode decomposition; IMPAC, intrinsic mode phase-amplitude coupling method; BPAC1, Butterworth filter phase-amplitude coupling method 1; BPAC2, Butterworth filter phase-amplitude coupling method 2; EEMD, ensemble empirical mode decomposition; DFPAC, dyadic filter bank phase-amplitude coupling method.

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1. Introduction

Complex biological systems contain rhythmic components at multiple frequencies, and these rhythms are rarely independent, exhibiting many forms of coupling including phase synchronization and amplitude comodulation (Rosenblum et al., 1997; Tass et al., 1998; Fries, 2005; Womelsdorf et al., 2007; Lo et al., 2008; Sauseng et al., 2008; Darvas et al., 2009; Fell and Axmacher, 2011; Bartsch et al., 2012; Hu et al., 2012; Schutter and Knyazev, 2012). Recently, a great deal of attention has been paid to phase-amplitude coupling (PAC) in neuronal signals, in which two rhythms co-exist and the amplitude of the higher frequency rhythm itself oscillates in phase with the lower frequency rhythm (Lakatos et al., 2005; Buszaki, 2006; Jensen and Colgin, 2007; Cohen et al., 2009; Canolty and Knight, 2010; Axmacher et al., 2010). For instance, there is extensive evidence of phase-amplitude coupling between theta (∼4–10 Hz) and gamma (∼40–100 Hz) rhythms in electroencephalogram (EEG) and local field potential (LFP) recordings (Bragin et al., 1995; Canolty et al., 2006; Montgomery et al., 2008; Sirota et al., 2008; Tort et al., 2009; Scheffzuk et al., 2011). This PAC is empirically linked both to neuronal circuit dynamics and to cognitive processes, and is believed to reflect neural coding and information transfer within the complex neural network of the brain (Jensen and Lisman, 1996; von Stein and Sarnthein, 2000; Lakatos et al., 2005; Jensen and Colgin, 2007; Cohen et al., 2009; Canolty and Knight, 2010; Axmacher et al., 2010). In addition, PAC phenomena have been observed in other complex systems in geology and finance (Rennert and Wallace, 2009; He et al., 2010). Thus, PAC and other types of cross-frequency coupling may serve as generic, promising tools for investigating the multiscale interactions underlying complex systems (He et al., 2010).

Reliable estimation of PAC requires not only identifying the existence of certain rhythms by their average spectral power, but also determining the precise profiles of individual cycles of these rhythms. Thus, neurophysiological time series present a number of challenges for PAC assessment: their multiple component oscillations may be buried under complex and nonstationary noise, may be present only intermittently, and may exhibit seemingly unstable waveforms varying in amplitude and frequency. Thus, the frequency domain representations of neural signals – like the underlying neural activity they measure – are broadband, even when rhythms of interest are not, and decomposing data to extract these rhythms is far from trivial. The Fourier transform can introduce non-physiological oscillations to account for nonsinusoidal and nonstationary properties of these signals (Kramer et al., 2008; Lo et al., 2009a), a difficulty that may be aggravated in short time series, for which frequency resolution (as measured by the Rayleigh resolution – the difference between consecutive frequencies represented in the Fourier transform) is severely limited.

To address some of these issues, we introduce a novel PAC measurement method which couples a broadband, adaptive decomposition method – the empirical mode decomposition (EMD) (Huang et al., 1998) – with time-local frequency assessment. The EMD iteratively applies a procedure called “sifting” to extract the fastest timescale fluctuations from a signal, resulting in a series of successively lower-frequency oscillatory components called intrinsic mode functions (IMFs). The original signal can be represented as the sum of these IMFs, each of which is unique to the data. As the IMFs are derived in the time domain without the assumption of constant frequency, amplitude, and functional form, each IMF may be frequency- and/or amplitude-modulated.

Due to the broadband and data-derived nature of these IMFs, combining current methods with the EMD or another adaptive decomposition would yield, at best, PAC measurements with very broad frequency resolution (i.e., PAC measurements computed between oscillations with energy over a wide range of frequencies), and at worst, PAC measurements incomparable between data segments (i.e., PAC measurements computed between oscillations with frequency content that is highly variable between data segments). Our method, called Intrinsic Mode Phase-Amplitude Coupling (IMPAC), resolves this issue. It calculates a measure of phase-amplitude coupling between each IMF and its higher-frequency IMFs. Rather than assigning this measure to a single frequency pair, determined by, for instance, the average frequency content of the phase-giving and amplitude-giving IMFs, IMPAC redistributes the calculated coupling across the phase frequency-amplitude frequency plane. This redistribution is done according to the proportion of time the two IMFs spend at each phase frequency-amplitude frequency coordinate, as determined by the cycle-by-cycle frequencies of the two IMFs.

While IMPAC is built around the EMD, similar approaches may be implemented on the output of any adaptive or otherwise broadband decomposition method, such as wavelet decomposition. As an illustration, we have applied the IMPAC approach to the output of a serial, dyadic filter bank with an average frequency response similar to the EMD (Flandrin et al., 2003, 2005; Wu and Huang, 2004) and many similarities to the wavelet transform, a method we call the Dyadic Filter bank PAC method (DFPAC).

We compared the performance of IMPAC and DFPAC to two standard Fourier-based PAC methods on both simulated signals and real EEG data. Our simulated signals contained PAC at frequencies chosen to mimic theta and gamma rhythms in brain activity – the phase of a 6 Hz rhythm modulates the amplitude of a 65 Hz rhythm – as well as a number of data processing challenges that are often present in neurophysiological data: measurement noise; missing data; random trends or measurement drift; the presence of uncoupled, frequency- and amplitude-modulated oscillations; and coupled oscillations with amplitude proportional to frequency. The coupled rhythms were for the most part stationary and sinusoidal, but we also examined frequency-modulated and asymmetric coupled oscillations. We simulated a total of 150 s of signal for each challenge, divided into 3 s epochs. Each epoch was designed to capture the same system – i.e., there is some stationarity across epochs – and we measured the average performance of each measure on the 50 epochs. We also tested all PAC measurement methods on mouse intracranial EEG recorded during REM sleep, a state in which brain signals have been shown to exhibit robust theta-gamma PAC (Scheffzuk et al., 2011), as well as multiple nonstationarities and artifacts in combination.

Our results show that, perhaps counter intuitively, standard comodulograms can yield poor frequency resolution of PAC, inaccurate PAC frequency assignment, and false negatives in PAC assessment. The novel strategy of recovering PAC from broadband oscillations and determining its frequency characteristics time-locally and post-decomposition attains better PAC frequency resolution and is more resistant to the effects of nonstationarities than standard comodulograms. We also obtain novel results regarding the effects of uncoupled oscillations. While these uncoupled rhythms a priori should not affect PAC measurement, we show that they distort both narrow- and broadband PAC measurements in characteristic ways, suggesting differential use of these approaches to minimize the effects of constant-frequency vs. frequency-modulated uncoupled oscillations.

2. Methods

2.1. PAC quantification

Several methods of exploring PAC have been employed in the literature. One popular analysis is the comodulogram, in which a “coupling palette” is computed and used to indicate, for wide