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Phase-coherence classification: A new wavelet-based method to separate local field potentials into local (in)coherent and volume-conducted components

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HIGHLIGHTS

- The novel wavelet-based phase-coherence classification (PCC) is introduced in detail.
- Local field potentials are split in time-frequency domain into three signal components.
- Spectra of incoherent, coherent and volume conducted components are analyzed separately.
- In Parkinson's disease components are differently modulated by medication and movement.
- The PCC components may represent activity of physiologically different networks.

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ABSTRACT

Background: Local field potentials (LFP) reflect the integrated electrophysiological activity of large neuron populations and may thus reflect the dynamics of spatially and functionally different networks.
New method: We introduce the wavelet-based phase-coherence classification (PCC), which separates LFP into volume-conducted, local incoherent and local coherent components. It allows to compute power spectral densities for each component associated with local or remote electrophysiological activity.
Results: We use synthetic time series to estimate optimal parameters for the application to LFP from within the subthalamic nucleus of eight Parkinson patients. With PCC we identify multiple local tremor clusters and quantify the relative power of local and volume-conducted components. We analyze the electrophysiological response to an apomorphine injection during rest and hold. Here we show medication-induced significant decrease of incoherent activity in the low beta band and increase of coherent activity in the high beta band. On medication significant movement-induced changes occur in the high beta band of the local coherent signal. It increases during isometric hold tasks and decreases during phasic wrist movement.
Comparison with existing methods: The power spectra of local PCC components is compared to bipolar recordings. In contrast to bipolar recordings PCC can distinguish local incoherent and coherent signals. We further compare our results with classification based on the imaginary part of coherency and the weighted phase lag index.
Conclusions: The low and high beta band are more susceptible to medication- and movement-related changes reflected by incoherent and local coherent activity, respectively. PCC components may thus reflect functionally different networks.

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1. Introduction

Data obtained from intracranial local field potentials (LFP) using macroelectrodes of ~1 mm diameter as well as EEG or MEG data generally reflect the integrated electrophysiological activity of pop-

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ulations of neurons at local and remote locations and mostly stem from post-synaptic potentials (Buzsáki et al., 2012). In order to concentrate on local electrophysiological activity one often uses first or second order derivatives of the measured signal, e.g. bipolar recordings or current source-density for LFP (Mitzdorf, 1985; Lempka and McIntyre, 2013) and average-reference or surface Laplacian for EEG (Hjorth, 1975; Nunez et al., 1997), which reduce the electrodes' spatial detection range as a large part of the remotely generated and volume-conducted signal is subtracted. However, there are some disadvantages associated to these techniques: (1) for first and especially for second order derivatives a large number of electrodes is needed; (2) not only activity generated at distant locations but also highly correlated and non-phase-shifted locally generated activity may be subtracted; and (3) incoherent local activity is spread out to neighboring electrodes and the volume-conducted signal is lost to further analyses.

The ability to distinguish between local incoherent and coherent signals may help to characterize activity of functionally specialized networks or neuronal populations (Schnitzler and Gross, 2005). Such spatial clusters of focal electrophysiological activity may be encountered in the target structures of clinical applications, e.g. deep brain stimulation of the subthalamic nucleus (STN) in case of Parkinson's disease (PD). Within the STN pathological activity with focal topography in the beta band (13–30 Hz) (Brown et al., 2001; Brown, 2003; Kühn et al., 2004; Kühn et al., 2005; Hammond et al., 2007) and different topographies of tremor clusters for postural and rest tremor (Reck et al., 2010) were observed indicating a functional and patho-anatomical segregation of subloops and symptoms. Further, activity within the beta band was reported to be subject to physiological modulations, e.g. induced by movement (Foffani et al., 2005; Engel and Fries, 2010), which need to be differentiated from pathophysiological signals in the same frequency band (Priori et al., 2004; López-Azcárate, et al., 2010).

In an attempt to allow for such a differential interpretation of LFP by identifying local (in)coherent and volume-conducted components we developed a novel method, namely the wavelet-based phase-coherence classification (PCC). As the oscillations in LFP are expected to be dynamic and localized in time-frequency space (Engel and Fries, 2010; Little et al., 2012; Zavala et al., 2015) the PCC separates the LFP in time-frequency space according to their pairwise statistical characteristics into three components associated with electrophysiological activity at local and remote locations. The local signal is further separated into coherent and incoherent activity. With this approach we can analyze the LFP in more detail and we hypothesize that the PCC components reflect functionally segregated networks of electrophysiological activity. Conceptually similar wavelet-based separation techniques have been shown to be of great value for the analysis and identification of coherent vortices in turbulent flows (Farge et al., 2001; Horbury et al., 2008).

The presented technique is not restricted to a certain type of electrode and is therefore of potential interest for several multi-electrode configurations. Although we focus here on intracranial LFP, the PCC can also be used to analyze MEG and EEG recordings. In M/EEG it can identify spurious coherencies caused by volume-conduction (Nunez et al., 1997) and thus help to determine functional connectivity of different cortical areas (Hipp et al., 2012). Furthermore, the PCC is in general also applicable to LFP obtained from microelectrode arrays such as tetrodes (O'Keefe and Recce, 1993) or Utah arrays (Maynard et al., 1997).

The basic assumption for the application of the PCC is the quasi-static approximation of the electromagnetic field (Plonsey and Heppner, 1967; Stinstra and Peters, 1998). Changes in the extracellular potential propagate across the tissue of the human brain by means of volume-conduction. Therefore, the phase lag of a volume-conducted signal measured at two different locations is negligible. As the sources of LFP and EEG can be approximated as dipoles (Buzsáki et al., 2012; Einevoll et al., 2013), volume-conducted signals generated at remote locations, i.e. postsynaptic terminals, can only generate phase differences of either 0° or 180° between different electrodes. The potential of a dipole source decreases quadratically with distance so that populations close to the electrode have considerably stronger effect on the measurement (Lindén et al., 2011). However, large populations with correlated synaptic input may generate a volume-conducted signal strong enough to be observed at several millimeters distance (Kajikawa and Schroeder, 2011; Lempka and McIntyre, 2013). Note that in our study the inter-electrode spacing is 2 mm and, therefore, it is unclear how much of the LFP stems from local activity that is only observed at a single electrode and how much from remote activity observed by several electrodes. For the derivation of our method we make use of the quasi-static approximation and assume that coherent signals with zero phase difference at two electrodes are volume-conducted and reflect activity at remote locations (i.e. distances larger than inter-electrode spacings). Signals observed at only one electrode and signals with a phase-shift between electrodes are considered to reflect local activity.

In this paper we introduce the PCC and show how to calculate power spectral densities for the separate components. We focus on the technical aspects of the method, namely its resolution properties and accuracy to determine the correct power spectral densities of the components. The resolution of the PCC is analyzed with synthetic time series and we test the accuracy of the PCC for non-stationary signals. We further derive reasonable parameters for its application to intracranial LFP and apply our method to a data set of LFP recordings from within the STN of patients with PD. First we present results obtained from standard analysis procedures (bipolar recordings) and then show that additional information can be obtained from the application of PCC. Particularly we indicate that PCC components differently reflect pathophysiological and motor-state related activity. Finally we show that the classification in time-frequency space prior to the separation of components can also be applied based on other coupling measures such as the imaginary part of coherency (IC) (Nolte et al., 2004) or the (weighted) phase lag index (wPLI) (Stam et al., 2007; Vinck et al., 2011).

2. Materials and methods

2.1. Wavelet transform

The wavelet transform (Farge, 1992; Torrence and Compo, 1998) of a discrete time series $x(t_n)$ with t_n being time is defined as

$$W_x(f_i, t_j) = \sum_{n=1}^{N} x(t_n)\Psi\left(\frac{t_n - t_j}{s_i}\right), \tag{1}$$

where N is the number of data points, Ψ the mother wavelet and s the temporal scale under consideration. Here, we use the Morlet wavelet with

$$\Psi(\eta) = \pi^{-1/4}\, e^{i\omega_0\eta}\, e^{-\eta^2/2}, \tag{2}$$

where the wavelet parameter ω_0 defines the number of oscillations in the wavelet and thus controls the frequency resolution $\Delta f/f$ (Meyers et al., 1993; Torrence and Compo, 1998). The scale s is related to the Fourier frequency f according to

$$f = \frac{\omega_0 + \sqrt{2+\omega_0^2}}{4\pi}\frac{1}{s}. \tag{3}$$

Using the wavelet cross-spectrum

$$W_{xy}(f, t) = W_x(f, t)\cdot W_y^*(f, t), \tag{4}$$

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