ADAPTIVE IDENTIFICATION OF OSCILLATORY BANDS FROM SUBCORTICAL NEURAL DATA

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ABSTRACT

Neural oscillations in various distinct frequency bands and their interrelations yield high temporal resolution signatures of the human brain activity. This study demonstrates solutions to some of the common challenges in the analysis of neurophysiological data by means of subthalamic local field potentials (LFP) acquired form patients with Parkinson's Disease (PD) undergoing deep brain stimulation therapy. Multivariate empirical mode decomposition (MEMD), being a data-driven method suitable for multichannel data, is employed. This method allows identification of oscillatory bands without the requirement of fixed *a priori* basis functions. Our study focuses on two issues: (i) Determination of data specific frequency bands and revealing the weak inconspicuous high frequency components in the data and (ii) validation of the biological meaningfulness of the MEMD oscillatory components via phase–amplitude coupling as previously shown to be inherent in subcortical PD LFP data.

Index Terms— local field potentials, oscillations, Parkinson's disease, coupling, multivariate empirical mode decomposition

1. INTRODUCTION

Identification of neural oscillatory activity in various distinct frequency bands and their cross interactions has been essential to characterize physiological and pathological mechanisms in the human brain [1]. Analysis of simultaneous multichannel brain signals, e.g., EEG and MEG data, is often handled under inexact assumptions of stationarity, linearity, predefined frequency bands and basis function models. This study concerns with local field potential (LFP) data acquired from the subthalamic nuclei (STN) of patients with Parkinson's disease (PD) undergoing deep brain stimulation (DBS) therapy. With such data at hand, we suggest solutions via the use of the recently introduced multivariate empirical mode decomposition (MEMD) method [2], which is suitable for multichannel and noisy data.

The first author is supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK # 112E562). In addition, the authors acknowledge support by the research commission of the medical faculty (# 9772562) and the strategic research fund of the Heinrich Heine University.

For many existing studies investigating neuronal oscillations, the determination of frequency bands is often not explicitly justified. It might be based on the specific dataset features such as spectral peak frequencies, however, lacking a clear and reproducible *modus operandi*. Importantly, the defined frequency band ranges affect analysis results when the spectral power change is assessed based on the power peak or even more in case of statistical comparison between different conditions.

Various EMD based algorithms has been suggested in neuroscientific and biomedical studies for purposes such as (i) sleep state classification from EEG data [3], (ii) estimation of the phase information for detecting the phase synchrony [4], (iii) estimation of the phase locking in time and frequency [5], and (iv) assessment of the directional coupling with the combination of partial directed coherence (PDC) [6].

Apart from the demonstration of an adaptive data-driven approach for the band limit determination of PD LFP data, this study aims to show that MEMD leads to "meaningful" oscillatory components and reveals power based "weak", but physiologically significant components at very high frequencies (>100 Hz), which may otherwise remain unnoticed.

2. MATERIALS AND METHODS

2.1. Data

Our study involved data from a 69-year-old male PD patient who underwent surgery for DBS. The data was part of a dataset used in a previous study [7]. The patient showed typical motor symptoms, such as rigidity and akinesia, while responding positively to pharmacological treatment with levodopa. He participated in the measurement with his written informed consent. The study was approved by the local ethics committee and was in accordance with the Declaration of Helsinki.

Electrodes were implanted bilaterally in the STN. There was no specific task, but the patient was instructed to rest on a comfortable chair with the least movement possible. Data were acquired simultaneously with an online bandpass filter of 0.1- 660 Hz and digitized at the sampling frequency of 2000 Hz. A notch filter was applied at 50 Hz (-/+ 2 Hz) to get rid of electrical power line noise.

Three bipolar LFP channels (1, 2, 3) were constructed by referencing the four adjacent contacts of the DBS electrode (Medtronic Inc, Minneapolis, MN USA, model

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3389). The labels 1 and 3 denote the most ventral and the most dorsal channels, respectively. Data were acquired both when the patient was not under dopamine medication (OFF) and after he was given dopaminergic medication (ON). Muscle activity was inspected to assure that the analyzed LFP data corresponds to "total rest", i.e., containing neither movement nor tremor. For this study, we used thirty seconds length LFP data collected from the left STN both for OFF and ON conditions.

2.2. MEMD

MEMD is a multivariate extension of empirical mode decomposition (EMD) [8], an adaptive, data-driven method that decomposes the signal into supposedly "meaningful" components called Intrinsic Mode Functions (IMF). Unlike the traditional decomposition methods such as Fourier and wavelet analysis, EMD extracts the oscillatory components without the requirement of fixed *a priori* basis functions, as they are characterized intrinsically by the input data dynamics. An IMF representing the different dynamic oscillatory modes in the signal is by definition required to have the following properties: (i) the number of extrema and zero-crossings should differ by one at most and (ii) the mean value of envelopes obtained from local minima and local maxima should be zero [8]. These properties for an IMF are practically satisfied by an iterative "sifting process".

MEMD aims to separate an N-dimensional (channel) data $\mathbf{x}$ into M oscillatory components $\mathbf{y}_i$, i.e., IMF's:

$$\mathbf{x}(n) = \sum_{i=1}^{M} \mathbf{y}_i(n) + \mathbf{r}(n)$$

where $\mathbf{r}$ stands for the residual. It operates the sifting process on the projections of the multichannel signal, which are called rotational modes. The projection on rotational modes enables the same number of uniform scales making MEMD suitable for multichannel data.

We used a noise-assisted version of MEMD, where we concatenate data with two additional random Gaussian white noise channels. Noise-assistance was reported to make MEMD more robust to noise and mode mixing [2]. The MEMD algorithm was executed via an open source Matlab function package provided in [9].

2.3. Determination of band limits

Oscillatory activity in the established frequency bands used in the clinics and research are known to be of limited validity due to the particular variability across individuals, tasks and medical conditions. One of the apparent discrepancies in the current PD LFP literature is the choice of frequency bands themselves and their ranges. For instance, beta band is regarded as low beta (13-20 Hz) and high beta (20-30 Hz) by [10], while in other studies high beta was taken as (20-35 Hz) [11] and low beta as (10-18 Hz) [12]. The upper limit of high beta could even be considered up to 40 Hz [13]. Many other studies consider the beta band without any further subdivision. However, they assumed different lower and upper limits such as 11-30 Hz [14], 15-30 Hz [15], and 14-35 Hz [16]. Similar discrepancies in the literature can also be observed for other frequency bands. Moreover, the diversity in the choice of frequency bands takes into account neither the variability between different medical conditions, nor the task at hand, e.g., resting vs. moving.

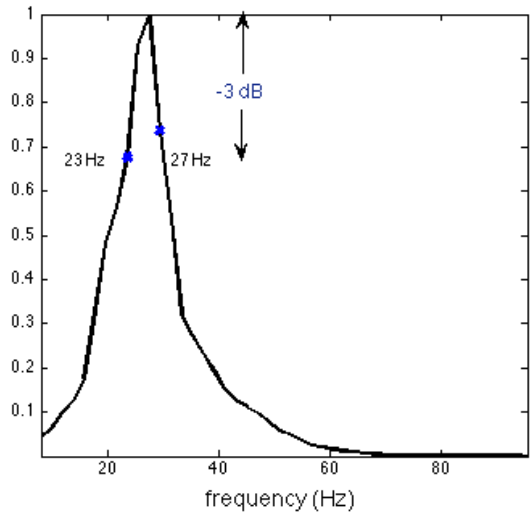

Fig. 1. An example showing a frequency band defined by the MEMD method.

We suggest the following simple algorithm for the determination of the limits (Fig. 1):

(i) Estimate the spectrum of the IMF corresponding to one oscillatory band.

(ii) Determine the minimum and maximum frequencies corresponding to power levels as 3 dB smaller than the spectral peak value.

For spectrum estimation, we used Welch's method with a Hanning window of 1024 samples length (corresponding to frequency resolution of ~0.5 Hz) with the overlapping length amounting to 512 samples. We also used the multitapering method with a frequency resolution of 20 Hz producing time-frequency portraits for frequencies > 100 Hz.

2.4. Marking cross-frequency relations

Recent studies [17,18] have shown a consistent coupling between the amplitude of high frequency oscillations (>100 Hz; HFO) and the phase of beta band activity in PD LFP data. The strength of this coupling changes both with respect to the location of the LFP contact within the STN and the medical condition. Here, we suggest a scheme investigating whether the IMF components corresponding to HFO and beta also show the previously described coupling behavior. This would give us clues about the biological plausibility of the obtained IMF's. Our scheme comprises the following steps:

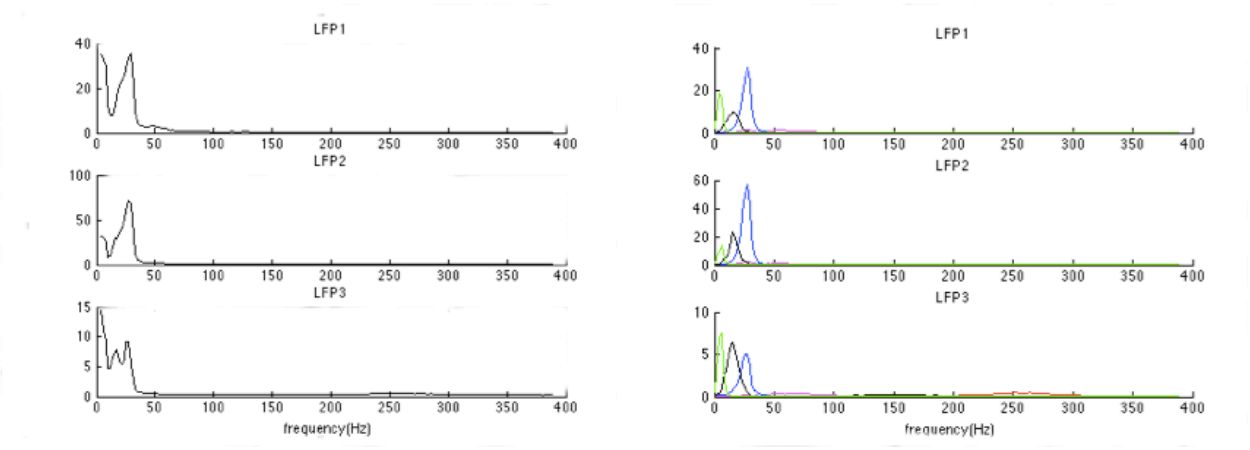

Fig. 2. Spectra of raw data (left) and IMF's (right) for all contacts

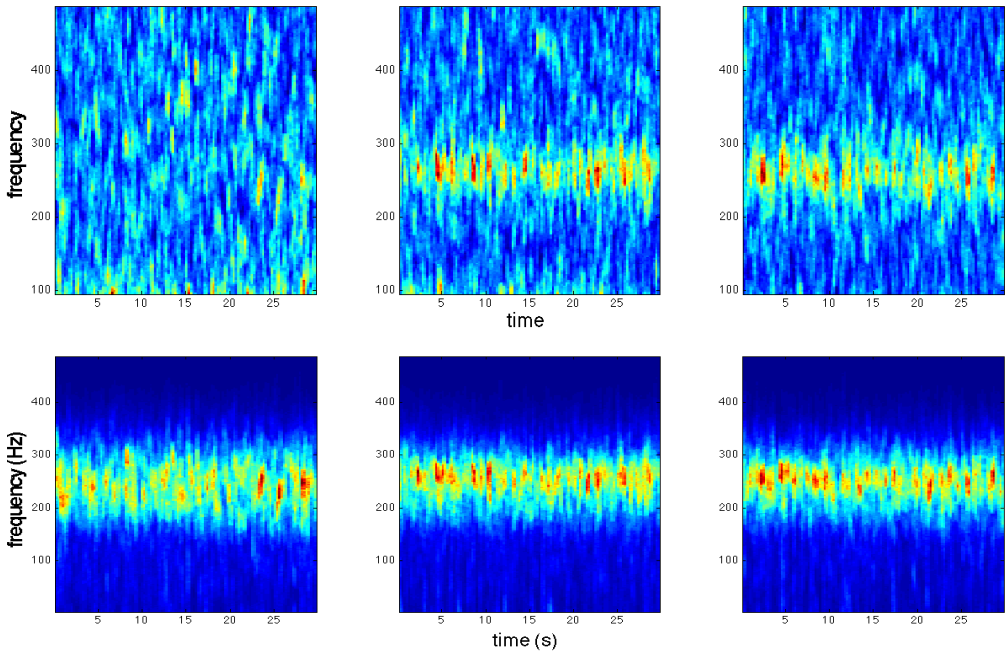

Fig. 3. Time-frequency portraits for high frequencies (top) and the IMF corresponsing to HFO (bottom). The range for the top figure was take above 100 Hz for the activity to be visible; this was not necessary for the IMF's.

(i) Determine the time points in the IMF corresponding to HFO where its amplitude is higher than a threshold and accept these points as "events". Threshold was chosen as one standard deviation further from the mean of the amplitudes.

(ii) Average the raw LFP data for segments centered on these events. The segment length was taken as 0.5 s.

(iii) Repeat the steps i) and ii) for surrogate data. The surrogate data are obtained by averaging the raw data around randomly chosen events.

(iv) Subtract the spectrum of the event-triggered average from that of the surrogate.

The resultant spectrum is expected to peak in the beta band because of the supposed coupling relation described above.

3. RESULTS

We determined the band limits from the obtained IMF's spectra for OFF and ON conditions (Table I). MEMD detects two different beta bands being low and high for the patient under study. Abnormally high beta power decreases with the dopamine for all three contacts. The computed band limits are not that different with respect to the medical conditions with the exception of HFO, whose range is drifted to higher frequencies with dopamine. This result tallies with earlier PD LFP studies [18]. Interestingly, gamma band activity is not observable in the medial contact LFP2 in either condition.

Please notice that it is hard to reach these inferences of oscillatory bands solely from observing the raw spectra of the contacts. For instance, although LFP3 shows two bands around the beta range (Fig. 2, left panel), this is not so obvious for the other channels. Even more

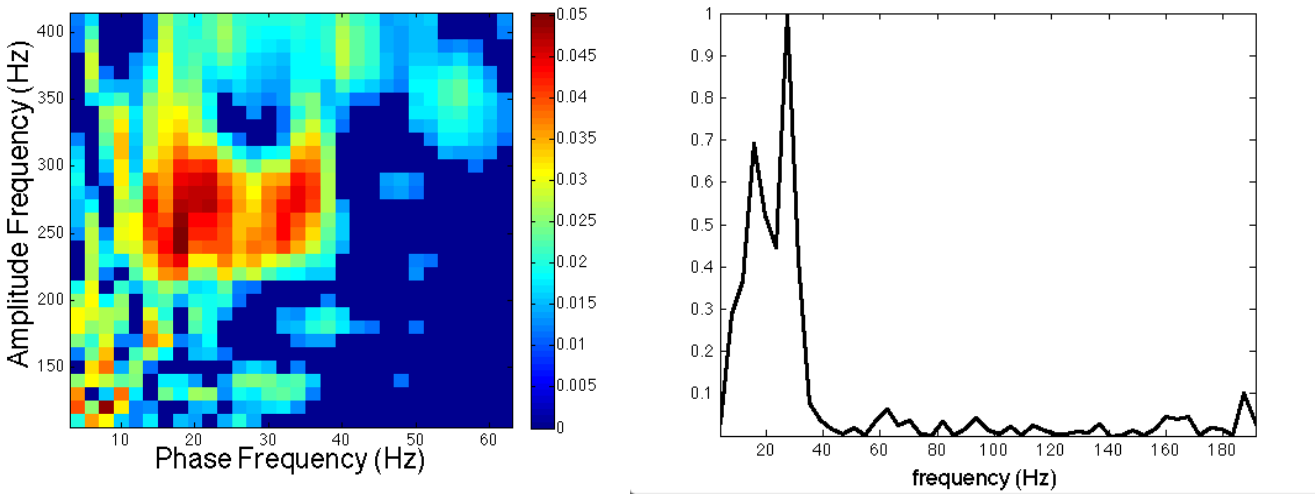

Fig. 4. Phase – amplitude coupling portrait using a classical method (left). The suggested algorithm showed that IMF corresponding to HFO band may also indicate this coupling as it led to averaged data with beta spectrum (right).

uncertain is the case of the weaker gamma band activity and HFO band, which can be captured by the use of MEMD (Fig. 2, right panel). Classical FFT based spectral estimation from raw data is not sufficient to discern HFO activity. This is primarily because of the much stronger activity occupying the low frequency bands of theta, alpha, and beta.

Even when one focuses on high frequencies and plots solely the power for over 100 Hz, HFO activity cannot really be discerned. Using multitapering spectrum estimation method on raw data could give some insight for HFO activity (Fig. 3, top panel). Nevertheless, HFO activity is still far from discernible, especially for the contact LFP1. In any case, one may reliably detect them through IMF's thanks to the separation capability of MEMD (Fig. 3, bottom panel).

We also wanted to explore whether the IMF's represent the oscillatory components properly. Do they conserve the phase and nonlinear features inherent in the neural signals? This is important as neural signals couple to each other through nonlinear interactions. Recent PD LFP studies have demonstrated consistently that beta phase is coupled to the HFO amplitude. Physiological meaning of this coupling is under fresh debate [19]. Fig. 4 (left panel) illustrates that our data also exhibit this coupling behavior. When the data were only locked for the points where HFO amplitude is above the threshold, a beta oscillation could be obtained (Fig. 4, right panel). Interestingly, the coupled spectrum has two peaks, which correspond to low and high beta bands. This result evidences that IMF's keep the inherent nonlinear nature of the oscillatory components reliably, even for very high frequencies.

4. CONCLUSION

MEMD has been applied on multichannel electrophysiological data for different purposes such as identification of steady-state visual evoked potentials, tracking alpha activity in BCI applications and denoising previously [2].

In this study, we pointed out applications specific to PD LFP studies. Accordingly, determination of data specific frequency band limits and disclosure of the weak inconspicuous oscillatory components were demonstrated. We also showed that the components obtained by MEMD conserve their coupling properties. Particularly, the phase–amplitude coupling between beta and HFO bands could be shown from the IMF corresponding to HFO. This was assessed in order to validate that IMF's obtained from the LFP data are biologically meaningful. Moreover, our algorithm implies that solely by using IMF's, one may detect phase-amplitude couplings by MEMD without having to filter data in the whole spectrum.

Employment of the suggested schemes may overcome aforementioned discrepancies in the choice of oscillatory bands in LFP's acquired from the subcortical regions of the brain. This is important for the consistency over studies. More importantly, there may be relevant oscillatory components hidden in the high end of the spectrum. We showed that HFO's in some channels might be unseen when the classical spectrum methods are applied. Instead, MEMD could reliably identify them for all channels. This allowed one to track the oscillatory power concentrated solely for HFO's in time. Future studies should be conducted to test the suggested schemes for larger datasets of different subjects and movement conditions.

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	OFF			**ON**		
	LFP 1	**LFP 2**	**LFP 3**	**LFP 1**	**LFP 2**	**LFP 3**
theta	4-8	4-8	2-8	2-6	2-6	2-8
low beta	14-20	14-20	12-20	12-20	12-18	12-18
high beta	23-31	23-31	23-29	23-31	21-31	23-31
gamma	47-63	-	78-102	47-61	-	76-92
HFO	248-258	264-270	254-270	305-322	264-287	254-285

Table 1. Band limits for OFF and ON conditions for the three contact pairs.