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A Beamforming Approach to Phase-Amplitude Modulation Analysis of Multi-Channel EEG

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Abstract

Phase-amplitude modulation is a form of cross frequency coupling where the phase of one frequency influences the amplitude of another higher frequency. It has been observed in neurophysiological recordings during sensory, motor, and cognitive tasks, as well as during general anesthesia. In this paper, we describe a novel beamforming procedure to improve estimation of phase-amplitude modulation. We apply this method to 64-channel EEG data recorded during propofol general anesthesia. The method improves the sensitivity of phase-amplitude analyses, and can be applied to a variety of multi-channel neuroscience data where phase-amplitude modulation is present.

I. INTRODUCTION

Oscillations are thought to underlie many aspects of brain function, but the mechanisms by which these oscillations organize neural activity across different temporal and spatial scales remains an area of active investigation. Recently, cross-frequency coupling has been observed where the phase of theta oscillations (4-8 Hz) modulates the amplitude of gamma oscillations (> 30 Hz) [1]. Similar phase amplitude relationships have been observed during different sensory, motor, and cognitive tasks [2]. These phase-amplitude relationships are usually estimated from single channel data, even when multi-channel data are acquired simultaneously, using non-parametric models of the relationship between phase and amplitude (e.g., constructing a histogram of amplitudes across discrete phase bins). The efficiency of these analyses could be improved substantially if data could be incorporated across multiple channels, and if parametric representations could be used to model the phase-amplitude relationship.

In recent work, we studied phase-amplitude modulation during general anesthesia. We examined how the phase of slow oscillations (< 1 Hz) influenced the amplitude of alpha-band oscillations (8-14 Hz), and found distinct patterns of modulation corresponding to different levels of consciousness under general anesthesia [3]. In this work, we describe a novel beamforming procedure to improve estimation of phase-amplitude modulation. In this

method, we model the phase-amplitude relationship parametrically using a low-order Fourier series. We then identify the optimal linear combination of channels to minimize the quadratic error for this phase-amplitude modulation curve. We apply this method to 64-channel EEG data acquired during induction of general anesthesia with the drug propofol. The method improves the sensitivity of phase-amplitude analyses, and can be applied to a broad range of multi-channel neuroscience data, such as EEG or local field potentials (LFP), where phase-amplitude modulation is present.

II. METHODS

A. EEG Recordings

We induced and maintained general anesthesia in healthy volunteers using the intravenous anesthetic propofol. The anesthetic induction was carried out by increasing the targeted effect-site propofol concentration to levels of 0, 1, 2, 3, 4, and 5 µg/ml every 14 minutes with a computer controlled infusion pump [4, 5]. We recorded 64-channel EEG continuously during this time (BrainAmp MRPlus, BrainProducts, GMBH). These studies were approved by the Massachusetts General Hospital Human Research Committee. In this paper, we analyze a subset of the data including n = 2 subjects to demonstrate our method for multi-channel estimation of phase-amplitude modulation between the slow (0.1-1 Hz) and alpha (8-14 Hz) bands.

B. Beamforming Formulation of Phase-Amplitude Coupling

Let $x(t) := [x_1(t), x_2(t), \cdots, x_N(t)]^T$ denote the EEG time-series corresponding to EEG channels for time $0 \le t \le T$. Let $a(t) := [a_1(t), a_2(t), \cdots, a_N(t)]^T$ and $s(t) := [s_1(t), s_2(t), \cdots, s_N(t)]^T$ denote the alpha rhythm and slow oscillation time-series which are obtained by band-pass filtering $x(t)$ in the frequency bands of 8-14 Hz and 0-1Hz, respectively [3]. Let $\alpha^H(t) := \alpha(t) + i\mathscr{H}(\alpha(t))$ and $s^H(t) := s(t) + i\mathscr{H}(s(t))$, where $\mathscr{H}(\cdot)$ is the discrete-time Hilbert transform. In [3] we showed that the amplitude of the alpha rhythm is modulated by the phase of the slow oscillation during general anesthesia, based on an analysis of single-channel Laplacian-derived EEG. Assuming that the phase-amplitude modulation arises from a unified and possibly spatially localized mechanism in the brain, the problem reduces to reconstructing a single phase-amplitude modulation relationship based on the observation through the multi-channel array of EEG sensors.

This problem is well-studied in array signal processing, and a viable solution is given by beamforming [6]. The idea of beamforming is to form a scalar signal based on the array observations in order to minimize an appropriate cost function representing the underlying system model. Let $w := [w_1, w_2, \cdots, w_N]^T$ denote a weight vector (beamforming vector) and consider the corresponding projection of the alpha rhythm and slow oscillation time-series given by $a_w(t) := w^T a^H(t)$, and $s_w(t) := w^T s^H(t)$, respectively. The amplitude of $a_w(t)$ and the phase (argument) of $s_w(t)$ are given by

$$A_w(t) := \sqrt{\left(\sum_{k=1}^{N} w_k \, \alpha_k(t)\right)^2 + \left(\sum_{k=1}^{N} w_k \, \mathscr{H}(\alpha_k(t))\right)^2} \quad (1)$$

and

$$\theta_w(t) := \arg\left(\sum_{k=1}^{N} w_k \, s_k(t) + i\sum_{k=1}^{N} w_k \, \mathscr{H}(s_k(t))\right), \quad (2)$$

respectively. Suppose that for a given value of the phase of $s_w(t)$, denoted by θ, the amplitude of the alpha rhythm $A_w(t)$ has a distribution given by the density $p_w(A; \theta)$. Then, the phase-amplitude modulation relation is defined as

$$A_w(\theta; t) := E_{p_w}\{A_w(t)|\theta\} \quad (3)$$

where the ensemble averaging E_{p_w} is with respect to the density $p_w(A; \theta)$. The function $A_w(\theta; t)$ is clearly periodic with the full period defined as $[-\pi, \pi]$. We further assume that $A_w(\theta; t)$ is stationary during the observation period $[0, T]$ and hence drop the dependence on t. Assuming that the function $A_w(\theta)$ has sufficient smoothness properties, it can be represented in the Fourier basis as follows:

$$A_w(\theta) = \mu + \sum_{k=1}^{\infty} a_k \sin(k\theta) + b_k \cos(k\theta) \quad (4)$$

where μ, a_k, and b_k denote the expansion coefficients. A suitable model for estimating $A_w(\theta)$ is given by its truncated Fourier expansion to the first L terms, with L 3. This reduced-order model enforces a smooth phase-amplitude modulation relation, which is consistent with empirical observations in [3]. A suitable cost function for estimating $A_w(\theta)$ is given by the following quadratic form:

$$R(\mu, \{a_k, b_k\}; w) := \int_{-\pi}^{\pi} \left\{ A_w(\theta) - \mu - \sum_{k=1}^{L} (a_k \sin(k\theta) + b_k \cos(k\theta)) \right\}^2 p(\theta) d\theta \quad (5)$$

Since the densities $p_w(A; \theta)$ are unknown, it is not possible to compute $A_w(\theta) = E_{p_w}\{A_w(t)|\theta\}$. Hence, we resort to an empirical quadratic cost function for estimating $A_w(\theta)$ by substituting the ensemble averaging operator E_{p_w} by the corresponding temporal averaging as follows:

$$R_T(\mu, \{a_k, b_k\}; w) := \int_{-\pi}^{\pi} \left\{ E_t\{A_w(t_w(\theta))\} - \mu - \sum_{k=1}^{L} (a_k \sin(k\theta) + b_k \cos(k\theta)) \right\}^2 p(\theta) d\theta \quad (6)$$

where $t_w(\theta)$ denotes the inverse function of $\theta_w(t)$, $p(\theta)$ is the prior distribution of the slow oscillation phase and E_t denotes temporal averaging. Note that we are implicitly assuming the ergodicity of the underlying processes during the observation period $[0, T]$ and hence are replacing ensemble averaging by temporal averaging. Since the prior $p(\theta)$ is unknown, the cost function can be further approximated by substituting the ensemble averaging over θ by the corresponding temporal averaging as follows:

$$\widehat{R}_T(\mu, \{a_k, b_k\}; w) := \frac{1}{T} \sum_{t=0}^{T} \left\{ A_w(t) - \mu - \sum_{k=1}^{L} (a_k \sin(k\theta_w(t)) + b_k \cos(k\theta_w(t))) \right\}^2 \quad (7)$$

For a given beamformer w, it is possible to minimize the cost function over the parameters μ, a_k, and b_k. Then, we can choose the best such beamformer by minimizing the resulting cost function over w. This, in fact, corresponds to a cost minimization formulation for estimating the reduced-order phase-amplitude modulation relation that is most consistent with the data (in the sense of the above quadratic cost function). Assuming that the beamformer elements are bounded as $\underline{w}$ w_k $\bar{w}$, for some constants $\underline{w}$ and $\bar{w}$, the overall optimization procedure can be expressed as:

$$\min_w \quad \min_{\mu, a_k, b_k} \widehat{R}_T \left(\mu, \{a_k, b_k\}; w \right) \quad s.t. \quad \underline{w} \le w_k \le \overline{w}, \forall k \quad (8)$$

The inner minimization can be easily carried out by linear regression and the resulting solution can be expressed explicitly in terms of $A_w(t)$ and $\theta_w(t)$. The outer minimization can be performed using standard optimization routines. In particular, since the constraints on w_k form a convex set, we have employed the interior point method for the outer minimization stage.

C. Data Analysis

For this analysis, the data from two subjects was used to compute optimal weight coefficients w. In our earlier studies, we showed that the phase-amplitude modulation of frontal EEG under GA [3] undergoes two different patterns of modulation, corresponding to depth of anesthesia. The first pattern, occurring before and after the point of loss of consciousness, consists of maximum alpha amplitude occurring at the trough (surface-negative) of the slow oscillation, which we refer to as the "trough-max" pattern. Under a deeper level of GA, the relationship reverses and maximum alpha amplitude occurs at the peak (surface-positive) of the slow oscillation, which we refer to as the "peak-max" pattern. In order to compute the electrode weights that would show both modes of the phase-amplitude modulation most clearly, equal-length segments of data from both modes were chosen and used to compute the optimal weights for each mode. These trough-max and peak-max data for the two subjects was were used to perform the averaging described in Equation (7). The data used in the optimization consisted of four-minute segments, chosen as periods during which the phase-amplitude modulation was relatively constant, based on phase-amplitude histograms computed using Laplacian-referenced data.

III. RESULTS

The alpha amplitude as a function of slow wave phase was fit for each of these data sets using the Fourier model in Equation (4), as well as a non-parametric model using 100 phase bins (Figure 1A). The Fourier model order was chosen using an F-test for inclusion of successive terms. Based on this test, a first order model was used everywhere except in the peak-max data segment from subject 2, where a second order model provided a better fit to the data.

The results of the optimization in all cases tended to give the greatest weight to one or two electrodes, and included smaller contributions from the other channels. The values of the weights for each electrode for subject 2 are shown in Figure 1, using the first Fourier harmonic for the trough-max period, and the first and second Fourier harmonics for the peak-max period.

To assess the efficacy of the beamformer weighting, we computed time-varying non-parametric phase-amplitude histograms using: 1) a single frontal channel with bipolar reference, 2) a single frontal channel with Laplacian reference (i.e., using the average of neighboring electrodes as the reference, as in [3]), and 3) the proposed method with optimal weights. These phase-amplitude histograms were computed using 100 phase bins, averaging over 1-minute windows with 30 seconds overlap, normalized by average alpha amplitude within each window. Figure 2 shows these time-varying phase-amplitude histograms for both subjects during periods of both trough-max and peak-max modulation. The modulation relationship appears clearest when the optimal weights w are used. To characterize this quantitatively, we computed the modulation depth for each of the methods by taking the average phase-amplitude histogram in each period (trough-max and peak-max), and taking the difference between the maximum and minimum points of the histogram. The

beamforming method produced the largest modulation depth, followed by the Laplacian method, with bipolar referencing showing the lowest modulation depth in both regimes.

IV. DISCUSSION AND CONCLUSIONS

Phase-amplitude modulation has been observed in a number of oscillatory neural systems sensory, motor, or cognitive tasks [2]. The modulation of alpha wave amplitude by slow wave phase is present in the EEG during general anesthesia, and could be an important variable for assessing brain activity and level of consciousness during general anesthesia. In EEG data, the ability to detect cross-frequency coupling is strongly influenced by the electrode reference scheme, and is often difficult to detect with a standard bipolar reference. The beamforming method presented here provides a means to obtain electrode weights that minimize the least-squares error in a parametric sinusoidal model of the phase-amplitude relationship. This optimal weighting of EEG electrodes allows for improved detection of phase-amplitude modulation across time and subjects. This method could be useful in studies of phase-amplitude modulation in the EEG under general anesthesia, as well as other conditions where this phenomenon might arise.

Acknowledgments

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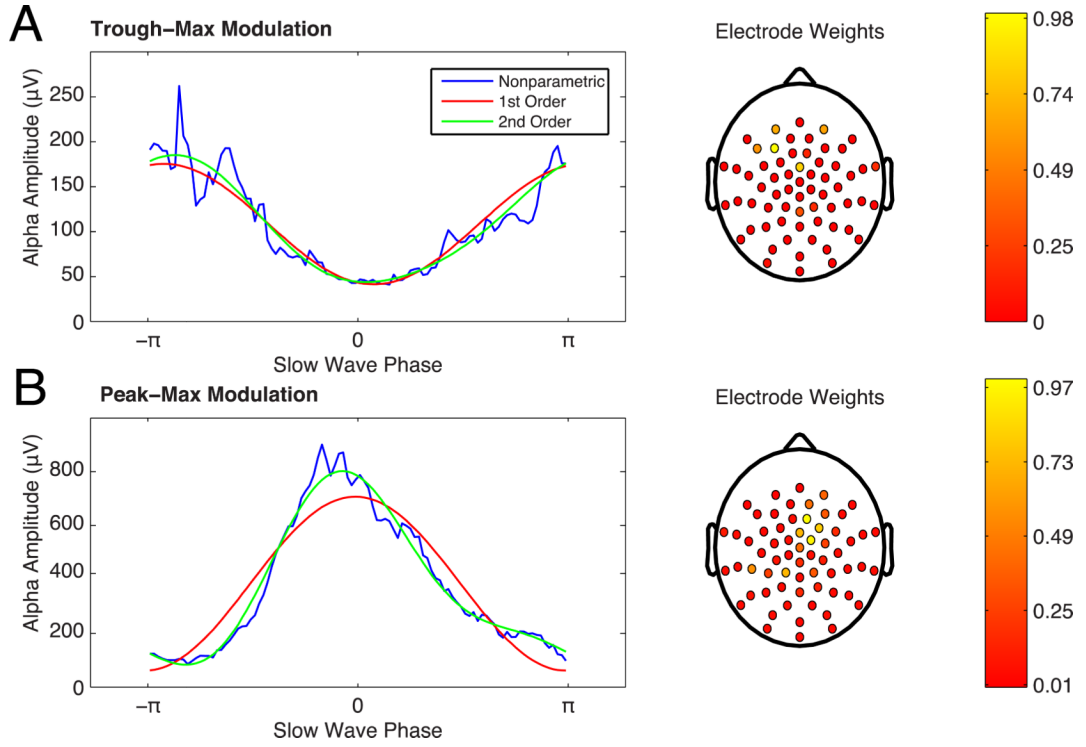
Fig. 1.
For trough-max modulation (A), and peak-max modulation (B), estimates of the empirical phase/amplitude relationship (blue) are shown along with first and second order model fits. The optimal weights for each electrode are shown to the right as estimated by the cost minimization procedure using the sinusoidal model of order 1 for trough-max and order 2 for peak max, chosen based on the corresponding F-statistics.
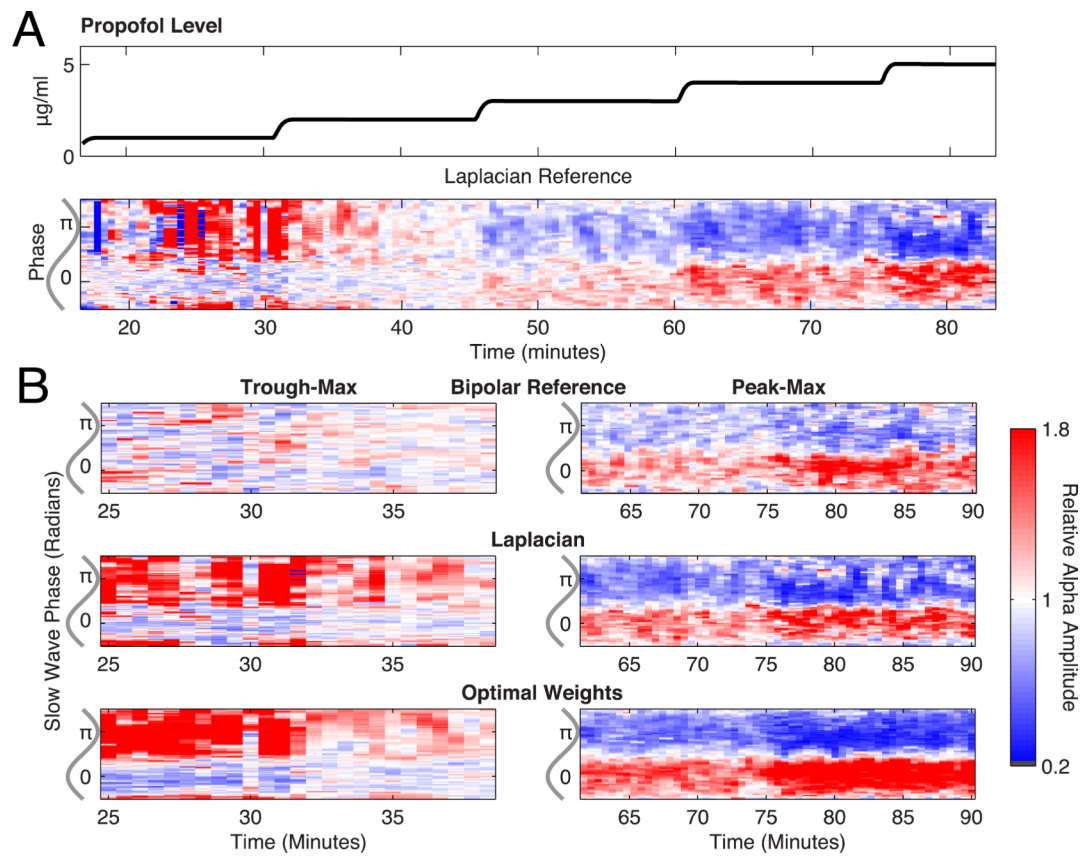
Fig. 2.
(A) The targeted effect-site propofol concentration is shown, along with the time-varying phase-amplitude histogram computed based on Laplacian-referenced data for a period spanning the trough-max and peak-max regimes of modulation. (B) Phase-amplitude histograms computed separately for a bipolar referencing, Laplacian referencing, and using the optimized combination of electrodes for both trough-max and peak-max data segments.

TABLE I

Modulation Depth For Different Methods

	Subject 1		Subject 2	
	Trough-Max	*Peak-Max*	*Trough-Max*	*Peak-Max*
Bipolar	0.26	0.39	0.22	0.76
Laplacian	1.08	0.73	0.98	1.00
Optimized	1.23	0.91	1.33	1.67