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Beamformer-based spatiotemporal imaging of linearly-related source components using electromagnetic neural signals

Hui-Ling Chan [a,b], Li-Fen Chen [c,d], I-Tzu Chen [a], Yong-Sheng Chen [a,e,*]

[a] Department of Computer Science, National Chiao Tung University, Hsinchu, Taiwan
[b] Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Canada
[c] Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan
[d] Integrated Brain Research Unit, Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan
[e] Institute of Biomedical Engineering, National Chiao Tung University, Hsinchu, Taiwan

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ABSTRACT

Functional connectivity calculated using multiple channels of electromagnetic brain signals is often over- or underestimated due to volume conduction or field spread. Considering connectivity measures, coherence is suitable for the detection of rhythmic synchronization, whereas temporal correlation is appropriate for transient synchronization. This paper presents a beamformer-based imaging method, called spatiotemporal imaging of linearly-related source component (SILSC), which is capable of estimating connectivity at the cortical level by extracting the source component with the maximum temporal correlation between the activity of each targeted region and a reference signal. The spatiotemporal correlation dynamics can be obtained by applying SILSC at every brain region and with various time latencies. The results of six simulation studies demonstrated that SILSC is sensitive to detect the source activity correlated to the specified reference signal and is accurate and robust to noise in terms of source localization. In a facial expression imitation experiment, the correlation dynamics estimated by SILSC revealed the regions with mirror properties and the regions involved in motor control network when performing the imitation and execution tasks, respectively, with the left inferior frontal gyrus specified as the reference region.

Introduction

Elucidating the mechanisms and pathways involved in neural communication is increasingly important for understanding how information is processed within the brain (Averbeck and Lee, 2004) as well as for mapping a comprehensive functional connectome (Biswal et al., 2010; Smith, 2012). Previous findings have suggested that temporal correlation of neural activity may be an indication of communication and information flow between cortical neurons or neural assemblies (Salinas and Sejnowski, 2001; Singer and Gray, 1995; von der Malsburg, 1999). Neurons are capable of synchronizing their firings on a time scale of milliseconds to fulfill sensory-motor, perceptual, and cognitive functions (Azouz and Gray, 2000; Engel and Singer, 2001; Engel et al., 1999; König and Engel, 1995; Singer and Gray, 1995). The connectivity of neural networks presents rapid variations. Hence, it is beneficial to estimate connectivity by using magnetoencephalography (MEG) or electroencephalography (EEG) recordings with a high degree of temporal resolution (Schoffelen and Gross, 2009). This study proposes a temporal correlation-based source connectivity estimation method, which can be used to quantify the interdependency between a reference signal and source activity calculated from electromagnetic signals.

Numerous techniques have been developed to estimate connections among brain regions using MEG or EEG signals. Among them, correlation coefficient (Brazier and Casby, 1952) and coherence (Nunez et al., 1997) are the most commonly used measures to evaluate linear associations in the time and frequency domains, respectively. In measuring the degree of synchronization, phase synchronization methods can be used to estimate the relationship of oscillation phases between two signals (Hindriks et al., 2011; Lachaux et al., 1999; Mormann et al., 2000; Tass et al., 1998). Moreover, generalized synchronization methods measure the level of synchronization and provide the direction of information flow (Arnhold et al., 1999; Rulkov et al., 1995). In theory, these measures of functional connectivity are all related to correlation (Marrelec et al., 2005). Quiroga et al. (2002) showed similar results of connectivity estimation using the above-mentioned measures. In simulation experiments, Silfverhuth et al. (2012) demonstrated that the correlation coefficient technique is sensitive to direct causal connections. Ansari-Asl et al. (2006) and Wendling et al. (2009) further demonstrated that, with regard to coupling model parameters, both correlation coefficient and coherence techniques achieved sensitivity equal or

* Corresponding author at: Department of Computer Science, National Chiao Tung University, 1001 University Road, Hsinchu, Taiwan. Fax: +886 3 5721490.
E-mail addresses: hlchan@cs.nctu.edu.tw (H.-L. Chan), lfchen@ym.edu.tw (L.-F. Chen), quits.c@gmail.com (I.-T. Chen), yschen@cs.nctu.edu.tw (Y.-S. Chen).

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superior to other methods based on phase synchronization and general synchronization. Finally, in an EEG study by Guevara and Corsi-Cabrera (1996), the results obtained by coherence were highly similar to those obtained by correlation coefficient.

Coherence methods quantify the synchronization between two signals by comparing their spectral power dynamics, which makes these techniques suitable for detecting rhythmic synchronization (Nunez et al., 1997). Compared to coherence methods, correlation methods are better suited to detect the synchronization caused by time-locked responses (Kujala et al., 2007) or transient responses, such as P300 waves. Moreover, correlation methods achieve greater sensitivity than coherence methods when information related to time latency is provided beforehand (Ansari-Asl et al., 2005). To estimate latency, Gevins and Bressler (1988) introduced a measure called event-related covariance (ERC), which is the multi-lag cross-covariance between the time series of two channels. Latency is then determined according to the time lag with the maximum covariance. This measure has been applied to predict performance accuracy (Gevins et al., 1987), to study the function of gamma-band brain waves (Gevins et al., 1995; Menon et al., 1996), and to investigate propagation in both visuomotor tasks (Gevins et al., 1989a,b) and working memory (Gevins and Cutillo, 1993).

ERC was only applied to estimate connectivity or interdependency between a pair of electrodes. However, at the sensor level, connectivity may be over- or underestimated due to the effects of volume conduction on EEG or field spread on MEG (Hillebrand et al., 2012; Nunez and Srinivasan, 2006; Winter et al., 2007). These effects often result in artificial synchrony by a single cortical source contributing to multiple channels simultaneously (Palva and Palva, 2012). Schoffelen and Gross (2009) reported an example of overestimated connectivity using simulation data generated from uncorrelated sources. In a simulation study by Grasman et al. (2004), an estimated connectivity map displayed problematic distribution when two synchronized sources existed within the brain. In fact, data of a single MEG or EEG channel is a mixture of numerous sources with varying degrees of correlation among them. As a result, interpreting complex data related to MEG or EEG sensor-level connectivity poses significant challenges.

Connectivity estimation methods calculated at the cortical level could reduce the artificial synchrony at the sensor level caused by volume conduction and field spread (Palva and Palva, 2012). These methods first estimate cortical source activity and then calculate source connectivity by determining the level of interdependency among the estimated sources. For example, BESA source coherence can be used to calculate coherence between dipole sources estimated by using the dipole fitting method (Hoechstetter et al., 2004). Brookes et al. (2011a) estimated the functional connectivity by calculating the envelope correlation or coherence between two brain source signals obtained by beamfoming spatial filters. In the study conducted by Hipp et al. (2012), the artificial synchrony between two sources was reduced by orthogonalizing signals prior to the calculation of coherence.

Beamforming methods can estimate brain source activity with better spatial resolution than other source estimation methods (Dalal et al., 2008; Darvas et al., 2004; Sekihara et al., 2005). For beamforming methods, the neural activity is modeled by an equivalent current dipole and is estimated by a spatial filter for each position in the brain source space. Vector beamformer, such as linearly constrained minimum variance (LCMV) beamformer (Van Veen et al., 1997), calculates the components of dipole source activity in three orthogonal directions. For scalar beamformer, the dipole orientation has to be determined to obtain the beamforming spatial filter either by an exhaustive search, as in the synthetic aperture magnetometry (SAM) method (Robinson and Vrba, 1998), or by an analytical solution, as in the maximum contrast beamformer (MCB) method (Chen et al., 2006). In the experiments conducted by Vrba and Robinson (2000) and Chen et al. (2006), scalar beamforming methods can provide a better sensitivity and spatial resolution than LCMV beamformer.

Estimation of source activity for specific brain regions may include the contribution of multiple neural populations (Gross and Ioannides, 1999). In other words, each neural region contains multiple sources with various orientations and temporal profiles. Therefore, activity measured in individual brain regions may actually comprise multiple components and uncorrelated components may result in underestimated source connectivity. To decrease the influence of uncorrelated components in connectivity estimation, Gross et al. (2001) proposed a vector beamforming method, dynamic imaging of coherent sources (DICS), to calculate the source component with dominant coherence. DICS has been applied to investigate the functional network during reading (Kujala et al., 2007) and to estimate the connection density (Kujala et al., 2008).

This paper proposes a beamformer-based imaging method, called spatiotemporal imaging of linearly-related source component (SILSC), which is capable of estimating whole-brain functional connectivity with low artificial synchrony. For each targeted position, SILSC determines a spatial filter, which extracts the source component with the maximum temporal correlation to a given reference signal. The orientation of the dipole at the targeted position is accurately calculated in a closed-form manner. By calculating the correlation value between the reference signal and each cortical region within the brain, SILSC produces a correlation map for further identifying regions significantly correlated to the reference. Following the concept of ERC in determining time latency, SILSC uses a sliding time window to estimate the propagation latency between different regions of the brain. Experiments of simulation data and an MEG experiment involving the imitation of facial expressions demonstrated the feasibility of the proposed method.

Methods and materials

Beamformer-based correlation imaging

The correlation coefficient, R_θ, between the reference signal $a(t)$ and the source activity $s_\theta(t)$ is defined as follows:

$$R_\theta = \frac{E\{(s_\theta(t)-E\{s_\theta(t)\})(a(t)-E\{a(t)\})\}}{E\{(s_\theta(t)-E\{s_\theta(t)\})^2\}^{\frac{1}{2}}E\{(a(t)-E\{a(t)\})^2\}^{\frac{1}{2}}}, \tag{1}$$

where $E\{\cdot\}$ denotes the expectation value and the parameters $\theta = \{\mathbf{r}, \mathbf{q}\}$ represent the dipole located in position $\mathbf{r} \in \mathbb{R}^3$ with orientation $\mathbf{q} \in \mathbb{R}^3$. Source activity $s_\theta(t)$ can be estimated up to a scale factor λ_θ by applying a spatial filter $\mathbf{w}_\theta \in \mathbb{R}^N$ on the MEG measurements $\mathbf{m}(t) \in \mathbb{R}^N$:

$$s_\theta(t) = \lambda_\theta \mathbf{w}_\theta^{\mathrm{T}} \mathbf{m}(t). \tag{2}$$

In this paper, "T" indicates the transpose of a matrix or vector and N is the number of MEG channels. By substituting Eq. (2) into Eq. (1) and canceling the scale factor λ_θ, the correlation R_θ can be calculated as follows:

$$R_\theta = \frac{E\left\{\left(\mathbf{w}_\theta^{\mathrm{T}}\mathbf{m}(t)-E\left\{\mathbf{w}_\theta^{\mathrm{T}}\mathbf{m}(t)\right\}\right)(a(t)-E\{a(t)\})\right\}}{E\left\{\left(\mathbf{w}_\theta^{\mathrm{T}}\mathbf{m}(t)-E\{\mathbf{w}_\theta^{\mathrm{T}}\mathbf{m}(t)\}\right)^2\right\}^{\frac{1}{2}}E\{(a(t)-E\{a(t)\})^2\}^{\frac{1}{2}}}. \tag{3}$$

DICS

DICS is a vector beamforming method which can estimate the coherence or correlation between the reference signal and the source activity in each brain region (Gross et al., 2001, 2002). In vector beamforming, three spatial filters are computed for three