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Maximum Multiple-Correlation Beamformer for Estimating Source Connectivities in Electromagnetic Brain Activities

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***Abstract*— Synchrony is a phenomenon of local-scale and long-range integrations within a brain circuit. Synchronous activities manifest themselves in similar temporal structures that can be statistically quantified by temporal correlation. In previous studies, synchronous activities were estimated by calculating the correlation coefficient or coherence between a single reference signal and the activity in a brain region. However, a brain circuit may involve multiple brain regions and these regions may communicate to each other through different temporal patterns. Therefore, temporal correlation to multiple reference signals is effective in quantify the source connectivities in the brain. This paper proposes a novel algorithm to calculate the maximum multiple-correlation for each brain region which has an activity estimated by a beamformer. Furthermore, this algorithm can accommodate various latencies of activities in a circuit. Experimental results demonstrate that the proposed method can accurately detect source activities correlated to the given multiple reference signals, even when unknown latencies exist between the source and references.**

I. INTRODUCTION

Investigating temporal relationships between both neural activities and field potentials are crucial to understand how the brain works [1]. Temporally correlated neural activities may provide information for constructing the connectivities between brain areas. In [2], the temporal correlation in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) data was applied to study the functional connectivities. Compared to the slow hemodynamic changes in fMRI and PET data, magneto-/electroencephalography (MEG/EEG) measure the electromagnetic signals directly induced by the neural activities and have a high temporal resolution. Therefore, MEG and EEG are better suited for the investigation of the temporal dynamics of brain activities.

The electromagnetic signals detected by MEG/EEG sensors are a mixture of brain sources. There is no unique solution for unmixing the brain sources when no constraint or prior information is provided. The connectivity analysis at the source space is thus inherently affected by the accuracy of inverse solution [3]. It has been reported that the beamformer outperformed the minimum norm method in the source connectivity analysis [3]. Dynamic imaging of coherence sources (DICS) is a beamformer-based method which designs the spatial filter with maximum coherence between the filtered and reference signals at a specified frequency band [4]. However, DICS cannot tackle the latencies of coherent activities, resulting from propagation delays in either local-scale or long-range communication.

Compared to coherence, temporal correlation is a relatively more generalized measure for temporal relationship. It has been used to quantify connectivities at the sensor level [5], [6] and source space [7]. A beamformer-based method which optimizes spatial filter according to a maximum correlation criterion has been proposed to estimate source connectivities [7]. Compared to DICS, this method can provide closed-form solutions for dipole orientations. However, both methods can only estimate the coherence or temporal correlation according to one reference signal. The single reference signal can be obtained by averaging all the source signals in a reference region, at the expense of losing temporal information. Moreover, a brain circuit may involve multiple brain areas containing distinct brain activities. Therefore, estimating source connectivities with multiple reference signals is more appropriate than that with only one reference signal.

This paper presents a beamformer-based method for spatiotemporal imaging of temporally correlated brain activities with unknown latencies. For a targeted position, a spatial filter is designed to estimate the source activity which has maximum correlation to a linear combination of multiple reference signals. The dipole orientation is analytically determined with a closed-form solution. To accommodate the propagation delays in a neural circuit, we expand the reference signals by adding in their replicas with various latencies. The distribution of estimated multiple-correlation values reveals the source connectivities of the brain which are associated with the given reference signals. Moreover, our method can determine the major components and latencies for each source activity.

II. METHODS AND MATERIALS

A. Forward Model

A lead field vector $\mathbf{l}_\theta \in \mathbb{R}^C$ describes how a unit dipole source contributes to C MEG/EEG sensors as follows,

$$\mathbf{l}_\theta = \mathbf{G}_\mathbf{r}\mathbf{q} \ , \quad (1)$$

where $\theta = \{\mathbf{r}, \mathbf{q}\}$ is a set of parameters representing the dipole position $\mathbf{r} \in \mathbb{R}^3$ and orientation $\mathbf{q} \in \mathbb{R}^3$, $\mathbf{G}_\mathbf{r} \in \mathbb{R}^{C\times 3}$ is a C-channel gain matrix for the unit dipole located at $\mathbf{r}$.

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The ensemble of the brain activities can then be described by a forward model [8],

$$\mathbf{m}(t) = \mathbf{L}\mathbf{s}(t) + \mathbf{n}(t) \ , \tag{2}$$

where $\mathbf{m}(t) = [m_1(t)\, m_2(t) \dots m_C(t)]^{\mathrm{T}} \in \mathbb{R}^C$ represents the signals of all channels at time t, $\mathbf{L} = [\mathbf{l}_{\theta_1}\, \mathbf{l}_{\theta_2} \dots\ \mathbf{l}_{\theta_Z}] \in \mathbb{R}^{C\times Z}$ is the lead field matrix composed of Z lead field vectors, $\mathbf{s}(t) = [s_1(t)\, s_2(t) \dots s_Z(t)]^{\mathrm{T}} \in \mathbb{R}^Z$ represents the activities of all Z dipole sources at time t in a predefined source space composed of either the vertices constructing a cortical surface or the voxels in magnetic resonance (MR) images.

B. Spatial Filter Design

In the scalar-type beamforming method [9], the signal $y_\theta(t)$ for a dipole source with parameter θ is estimated by using a spatial filter $\mathbf{w}_\theta \in \mathbb{R}^C$ as follows:

$$y_\theta(t) = {\mathbf{w}_\theta}^{\mathrm{T}}\mathbf{m}(t) \ . \tag{3}$$

To minimize the contributions from other sources or noises while maintaining the amplitude of the targeted source, the minimum variance constraint and the unit-gain constraint, ${\mathbf{w}_\theta}^{\mathrm{T}}\mathbf{l}_\theta = 1$, are applied to calculate the optimal spatial filter $\hat{\mathbf{w}}_\theta$ as follows:

$$\hat{\mathbf{w}}_\theta = \arg\min_{\mathbf{w}_\theta} E\left\{|y(t) - E\left\{y(t)\right\}|^2\right\} + \alpha\|\mathbf{w}_\theta\|^2 \quad \text{s.t.}\ \ {\mathbf{w}_\theta}^{\mathrm{T}}\mathbf{l}_\theta = 1 \ , \tag{4}$$

where $E\{\cdot\}$ is denoted as expectation and α is a parameter of Tikhonov regularization. Eq. (4) can be solved by Lagrange multipliers and the optimal solution to the spatial filter is

$$\hat{\mathbf{w}}_\theta = \frac{(\mathbf{\Sigma} + \alpha\mathbf{I})^{-1}\mathbf{l}_\theta}{{\mathbf{l}_\theta}^{\mathrm{T}}(\mathbf{\Sigma} + \alpha\mathbf{I})^{-1}\mathbf{l}_\theta} \ , \tag{5}$$

where $\mathbf{\Sigma} \in \mathbb{R}^{C\times C}$ is the covariance matrix of the MEG/EEG measurements $\mathbf{m}(t)$ during a specified period of time.

C. Source Connectivity Estimation

In this study, the source connectivities are statistically quantified by means of the multiple correlation values between the filtered source signals, $a_\theta(t) = {\mathbf{w}_\theta}^{\mathrm{T}}\mathbf{m}_a(t)$, and a set of K reference signals, $\mathbf{b}(t) = [b_1(t), b_2(t), \dots, b_K(t)]^{\mathrm{T}}$. Notice that $\mathbf{m}(t)$ and $\mathbf{m}_a(t)$ are extracted from the same MEG/EEG recordings but probably with different time intervals. The time interval of $\mathbf{m}_a(t)$ is for calculating the multiple correlation value and should have the same length as each reference signal $b_k(t)$, $k = 1, \dots, K$. The multiple correlation is a measure of fitting in a linear regression model:

$$a_\theta(t) = \mathbf{f}^{\mathrm{T}}\mathbf{b}(t) + \epsilon(t) \ , \tag{6}$$

where $\mathbf{f} = [f_1, f_2, \dots, f_K]^T$ is a column vector composed of weights f_k for reference signals $b_k(t)$, $k = 1, \dots, K$, and $\epsilon(t)$ is the residual. The multiple correlation coefficient R_θ is generally defined as

$$R_\theta = \max_{\mathbf{f}} \mathrm{Corr}\left(a_\theta(t), \mathbf{f}^{\mathrm{T}}\mathbf{b}(t)\right) \ . \tag{7}$$

Under a minimum mean square error criterion, the optimal solution of the weighting vector is

$$\hat{\mathbf{f}} = \mathbf{\Sigma}_{\mathbf{bb}}^{-1}\sigma_{\mathbf{b}a_\theta} \ , \tag{8}$$

where $\mathbf{\Sigma}_{\mathbf{bb}} \in \mathbb{R}^K$ is the covariance matrix of reference signal $\mathbf{b}(t)$, and $\sigma_{\mathbf{b}a_\theta}$ is the vector of cross-covariance between $\mathbf{b}(t)$ and $a_\theta(t)$. Then the optimal approximation of $a_\theta(t)$ in terms of all K reference signals becomes

$$\hat{a}_\theta(t) = \hat{\mathbf{f}}^{\mathrm{T}}\mathbf{b}(t) = \sigma_{\mathbf{b}a_\theta}^{\mathrm{T}}\mathbf{\Sigma}_{\mathbf{bb}}^{-1}\mathbf{b}(t) \ . \tag{9}$$

Finally, the value of multiple correlation R_θ can be calculated by

$$R_\theta = \mathrm{Corr}\left(a_\theta(t), \hat{a}_\theta(t)\right) = \left(\frac{\sigma_{\mathbf{b}a_\theta}^{\mathrm{T}}\Sigma_{\mathbf{bb}}^{-1}\sigma_{\mathbf{b}a_\theta}}{\sigma_{a_\theta a_\theta}}\right)^{\frac{1}{2}} \ , \tag{10}$$

where $\sigma_{a_\theta a_\theta}$ is the variance of the filtered signal $a_\theta(t)$.

If the covariance matrix $\mathbf{\Sigma}_{\mathbf{bb}}$ is full-rank, $\mathbf{b}(t)$ can be linearly transformed to be a set of uncorrelated signals $\mathbf{p}(t) = [p_1(t), p_2(t), \dots, p_K(t)]^{\mathrm{T}}$ using the eigenvectors and eigenvalues decomposed from $\mathbf{\Sigma}_{\mathbf{bb}}$. The multiple correlation between $a_\theta(t)$ and $\mathbf{b}(t)$ equals to that between $a_\theta(t)$ and $\mathbf{p}(t)$, that is,

$$R_\theta = \left(\frac{\sigma_{\mathbf{p}a_\theta}^{\mathrm{T}}\Sigma_{\mathbf{pp}}^{-1}\sigma_{\mathbf{p}a_\theta}}{\sigma_{a_\theta a_\theta}}\right)^{\frac{1}{2}} = \left(\frac{\sum_{k=1}^{K}{\sigma_{p_k a_\theta}}^2}{\sigma_{a_\theta a_\theta}}\right)^{\frac{1}{2}} \ , \tag{11}$$

where $\mathbf{\Sigma}_{\mathbf{pp}}$ is the covariance matrix of $\mathbf{p}(t)$ and $\sigma_{\mathbf{p}a_\theta} = [\sigma_{p_1 a_\theta}, \dots, \sigma_{p_K a_\theta}]^{\mathrm{T}}$ is the vector of the cross covariance between the uncorrelated signals $\mathbf{p}(t)$ and the filtered signal $a_\theta(t)$. It can then be formulated in terms of the spatial filter and measurements as follows,

$$R_\theta = \left(\frac{{\mathbf{w}_\theta}^{\mathrm{T}}\left(\sum_{k=1}^{K}\sigma_{\mathbf{m}_a p_k}{\sigma_{\mathbf{m}_a p_k}}^{\mathrm{T}}\right)\mathbf{w}_\theta}{{\mathbf{w}_\theta}^{\mathrm{T}}\mathbf{\Sigma}_{\mathbf{m}_a\mathbf{m}_a}\mathbf{w}_\theta}\right)^{\frac{1}{2}} \ , \tag{12}$$

where $\mathbf{\Sigma}_{\mathbf{m}_a\mathbf{m}_a}$ is the covariance matrix of MEG/EEG recordings $\mathbf{m}_a(t)$ and $\sigma_{\mathbf{m}_a p_k}$ is the vector of cross covariance between $\mathbf{m}_a(t)$ and the k-th uncorrelated reference signal, $p_k(t)$, $k = 1, \dots, K$.

D. Maximum Multiple-Correlation Beamformer

The optimal spatial filter shown in (5) can be rewritten as

$$\hat{\mathbf{w}}_\theta = \frac{(\mathbf{\Sigma} + \alpha\mathbf{I})^{-1}\mathbf{G}_{\mathbf{r}}\mathbf{q}}{\mathbf{q}^{\mathrm{T}}\mathbf{G}_{\mathbf{r}}^{\mathrm{T}}(\mathbf{\Sigma} + \alpha\mathbf{I})^{-1}\mathbf{G}_{\mathbf{r}}\mathbf{q}} = \frac{\mathbf{C}_{\mathbf{r}}\mathbf{q}}{\mathbf{q}^{\mathrm{T}}\mathbf{D}_{\mathbf{r}}\mathbf{q}} \ , \tag{13}$$

where $\mathbf{C}_{\mathbf{r}} = (\mathbf{\Sigma} + \alpha\mathbf{I})^{-1}\mathbf{G}_{\mathbf{r}}$ and $\mathbf{D}_{\mathbf{r}} = \mathbf{G}_{\mathbf{r}}^{\mathrm{T}}\mathbf{C}_{\mathbf{r}}$. To extract the source component with maximum multiple correlation to the reference signals, we estimate the dipole orientation $\mathbf{q}$ by

$$\begin{aligned}\hat{\mathbf{q}} &= \arg\max_{\mathbf{q}} \frac{{\mathbf{w}_\theta}^{\mathrm{T}}\left(\sum_{k=1}^{K}\sigma_{\mathbf{m}_a p_k}{\sigma_{\mathbf{m}_a p_k}}^{\mathrm{T}}\right)\mathbf{w}_\theta}{{\mathbf{w}_\theta}^{\mathrm{T}}\mathbf{\Sigma}_{\mathbf{m}_a\mathbf{m}_a}\mathbf{w}_\theta} \\ &= \arg\max_{\mathbf{q}} \frac{\mathbf{q}^{\mathrm{T}}\mathbf{P}_{\mathbf{r}}\mathbf{q}}{\mathbf{q}^{\mathrm{T}}\mathbf{Q}_{\mathbf{r}}\mathbf{q}} \ ,\end{aligned} \tag{14}$$

where

$$\mathbf{P}_{\mathbf{r}} = \mathbf{C}_{\mathbf{r}}^{\mathrm{T}}\left(\sum_{k=1}^{K}\sigma_{\mathbf{m}_a p_k}{\sigma_{\mathbf{m}_a p_k}}^{\mathrm{T}}\right)\mathbf{C}_{\mathbf{r}} \ , \ \mathbf{Q}_{\mathbf{r}} = \mathbf{C}_{\mathbf{r}}^{\mathrm{T}}\mathbf{\Sigma}_{\mathbf{m}_a\mathbf{m}_a}\mathbf{C}_{\mathbf{r}} \ .$$

TABLE I

CONFIGURES OF TEMPORAL WAVEFORMS IN SIMULATIONS 1 AND 2

Simulation	Source	position	frequency (Hz)	amplitude (nAm)	peak time (ms)	reference design
1	1	$\mathbf{r}_1$	17 5	3 1	200 200	Ref 1.1
	2	$\mathbf{r}_2$	17 5	1 3	200 200	Ref 1.2
2	3	$\mathbf{r}_3$	17	3	200	Ref 2.2
	4	$\mathbf{r}_4$	5	3	200	Ref 2.7
	5	$\mathbf{r}_5$	17 5	2 1	500 500	

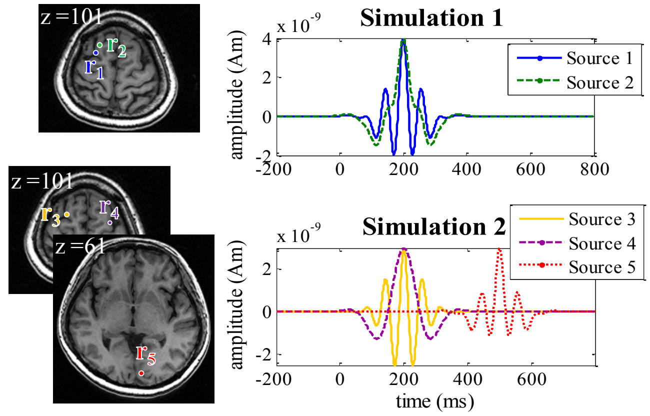

Fig. 1. Locations (left) and temporal waveforms (right) of dipole sources in Simulations 1 and 2

The optimal dipole orientation, $\hat{\mathbf{q}}$, is the eigenvector corresponding to the maximum eigenvalue of the matrix $\mathbf{Q}_\mathbf{r}^{-1}\mathbf{P}_\mathbf{r}$. Because $\mathbf{P}_\mathbf{r}$ and $\mathbf{Q}_\mathbf{r}$ are both 3×3 matrices, the optimal solution for (14) is a closed-form solution. With given reference signals together with the time period for extracting $\mathbf{m}_a$, we can calculate $\mathbf{P}_\mathbf{r}$ and $\mathbf{Q}_\mathbf{r}$ and then obtain $\hat{\mathbf{q}}$ according to (14). Finally, $\hat{\mathbf{w}}$ can be calculated by applying $\hat{\mathbf{q}}$ to (13) and the multiple correlation value for the dipole source at location $\mathbf{r}$ can be calculated by applying $\hat{\mathbf{w}}$ to (12).

E. Materials

The MEG data for Simulations 1 and 2 were both composed of 10 one-second trials contributed from two and three dipole sources, respectively. Each dipole source located at $\mathbf{r}_i$, $i = 1, \ldots, 5$, was associated with one or two amplitude-modulated cosine waveforms, as shown in Table I and Fig. 1. In Simulation 1, the locations of the two dipole sources were close and the associated temporal waveforms, Sources 1 and 2, were highly correlated (correlation value = 0.6110). In Simulation 2, Source 5 was the composite of Sources 3 and 4 with 300-ms time lags and the ratio of Sources 3 to 4 was $2:1$. Moreover, 3000 dipoles placed in random locations with strength 0.1 nAm were added to each of the MEG data for simulating background activities. The MEG data shown in Figs. 2(a) and 2(b) were generated by the forward model (2) according to the configure of a whole head 204-gradiometer system (Neuromag Vectorview).

For each simulation, as shown in Fig. 2, the time intervals for extracting $\mathbf{m}_a(t)$ and $\mathbf{m}(t)$ (the green dotted-boxes) are the same as the interval for extracting $\mathbf{b}(t)$ (the red dotted-boxes). In Simulation 1, two sets of 300-ms reference signals, as shown in Figs. 2(c) and 2(d), were applied to the source connectivity analysis. The first set composed of two signals (Refs 1.1 and 1.2) extracted from Sources 1 and 2 between 50 and 350 ms, whereas their average (Ref 1.3) was used as the reference signal in the second set.

In Simulation 2, two reference signals were extracted from Sources 3 and 4 between -25 and 625 ms. To accommodate the unknown latencies of activities, the set of reference signals was expanded by inserting replicas of the original two reference signals with peak times shifted to 100, 300, 400, and 500 ms, as shown in Fig. 2(e). Notice that the information of Source 5 was not used in the design of reference signals.

III. RESUTLS

In Simulation 1, the multiple-correlation map associated with the reference signals extracted from source signals is shown in Fig. 2(f). The two estimated peak positions are exactly at the ground-truth positions, $\mathbf{r}_1$ and $\mathbf{r}_2$, with high correlation values (0.9354 and 0.9424). However, as shown in Fig. 2(g), when a reference signal is the average of source signals, there is only one peak located between $\mathbf{r}_1$ and $\mathbf{r}_2$ in the multiple-correlation map with a low multiple-correlation value (0.1958).

In Simulation 2, the multiple-correlation map, as shown in Fig. 2(h), reveals three peaks exactly at the ground-truth positions, $\mathbf{r}_3$, $\mathbf{r}_4$, and $\mathbf{r}_5$. For the three peak positions, the associated optimal weights $\hat{\mathbf{f}}$ for linearly combining the reference signals are illustrated as the bar charts shown in Fig. 3. The bar charts demonstrate that the major components of the filtered signals at $\mathbf{r}_3$ and $\mathbf{r}_4$ are Refs 2.2 and 2.7, respectively. Moreover, Refs 2.5 and 2.10, which are Sources 3 and 4 with 300-ms latencies, respectively, constitute the major part of the filtered signal at $\mathbf{r}_5$ with around two-to-one ratio.

IV. DISCUSSION AND CONCLUSIONS

The two simulation studies have demonstrated that the proposed method can detect correlated activities with zero location errors when the reference signals provide adequate temporal information. On the other hand, incorrect design of reference signals may cause inaccurate estimation results of source connectivities. For example, the results of Simulation 1 demonstrate that using an averaged signal as a reference signal caused incorrect localizations of the correlated sources with low correlation values. Therefore, using temporal correlation to multiple reference signals stands a better chance of detecting source connectivities than that of using only one reference signal.

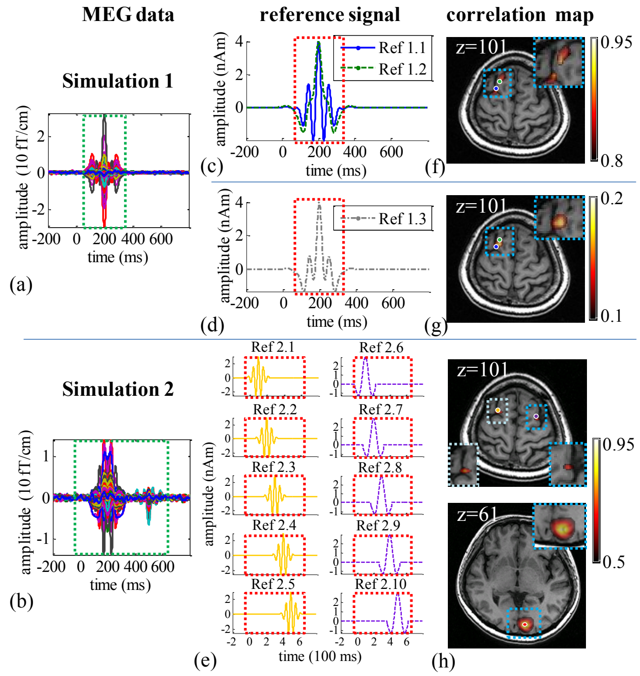

Fig. 2. MEG data generated in (a) Simulation 1 and (b) Simulation 2. Both MEG data are bandpass filtered with cutoff frequencies at 0.5 and 40 Hz. Three sets of reference signals are shown in (c)-(e) and the associated multiple-correlation maps calculated by the proposed method are shown in (f)-(h). The blue, green, yellow, purple, and red nodes overlaying these maps indicate the ground-truth positions, $\mathbf{r}_1$, $\mathbf{r}_2$, $\mathbf{r}_3$, $\mathbf{r}_4$, and $\mathbf{r}_5$, respectively. The time intervals of $\mathbf{m}_a(t)$ are the same as those of $\mathbf{m}(t)$, which are illustrated by the green dotted-boxes. The red dotted-boxes illustrate the time intervals of $\mathbf{b}(t)$.

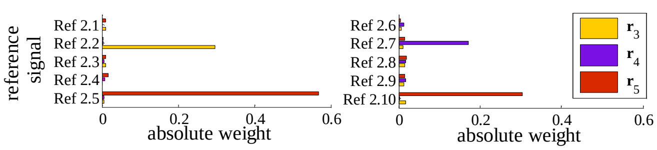

Fig. 3. Optimal weights $\hat{\mathbf{f}}$ for the linear combinations of the ten reference signals in Simulation 2.

In [7], the unknown latency problem of correlated activity estimation was tackled by sliding the reference signal within a time interval and repeating the whole correlation estimation procedure for each latency, at the expense of massively increased computational burden. On the contrary, as demonstrated by the results of Simulation 2, the proposed method efficiently estimate the latencies in a single step. This is because multiple reference signals including the replicas with various latencies can be simultaneously applied to estimate the correlated activities.

The results of Simulation 1 have demonstrated that the information from reference signals affects the results of source connectivity analysis. Moreover, the number of reference signals is limited by the duration of reference signals. To maintain a concise and informative set of reference signals, redundant ones should be detected and removed beforehand. If peripheral physiological signals are used as the reference signals, the estimated multiple-correlation maps will reveal the cortico-peripheral connectivities. If the reference signals are the source activities of the cortical regions of interest, the associated multiple-correlation map will reveal cortico-cortical connectivities. Independent components decomposed from MEG/EEG recordings can also be reference signals. The associated multiple-correlation map may represent the cortical distributions of components.

The latencies between correlated activities may be short and the period of correlated activities may be transient in real data. Therefore, the temporal resolution of the proposed method requires further investigation. Furthermore, for one reference signal, the latencies of its replicas can be different from other references. The latencies can be designed according to the spectral density of the reference signal or adaptively adjusted according to the estimation results. In this study, the orientations of correlated sources were assumed invariant during the time interval of $\mathbf{m}(t)$. If multiple dipole sources with different orientations are located at the same position, the source connectivity analysis may yield inaccurate results.

This paper presents a beamformer-based method which can estimate the spatiotemporal dynamics of correlated activities. For each targeted position, a spatial filter is designed to estimate its source activities with maximum multiple correlation to multiple reference signals. Distribution of the multiple correlation values can reveal source connectivities. Moreover, if the reference signals were expanded by adding their replicas with various latencies, the proposed method can also be applied to estimate the latencies of activities at interacting regions.

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