Non-Parametric Statistical Thresholding for Spatial-Filter Source Reconstruction Images

Kensuke Sekihara[1], Maneesh Sahani[2], Srikantan S. Nagarajan[3]
Tokyo Metropolitan Institute of Technology, Tokyo, Japan, [2]Keck Center for Integrated Neuroscience, University of California, San Francisco, CA, USA, [3]Department of Radiology, University of California, San Francisco, CA, USA

ABSTRACT

This paper proposes a simple statistical method for extracting target source activities from spatio-temporal source activities reconstructed using MEG measurements. The method requires measurements in a control condition, which contains only non-target source activities. The method derives, at each pixel location, an empirical probability distribution of the non-target source activity using the time-course reconstruction obtained from the control period. The statistical threshold that can extract the target source activities is derived based on the empirical distributions obtained from all pixel locations. Here, the multiple comparison problem is taken into account by using two step procedure: standardizing these empirical distributions and deriving an empirical distribution of the maximum pseudo T value at each pixel location. The results of applying the proposed method to the auditory evoked measurements are presented to demonstrate the method's effectiveness.

KEY WORDS

Nonparametric statistics, MEG, Source reconstruction, Statistical significance test

INTRODUCTION

This paper proposes a simple method for this statistical subtraction between task and control measurements; the method is applicable to results of spatio-temporal source reconstruction from MEG/EEG measurements. This method assumes neural activities to be quasi stochastic, and it uses nonparametric statistics to derive an empirical probability distribution of these activities using the time course reconstruction in the control period. This empirical distribution is then used for deriving the statistical threshold; the thresholding can extract the target activities that exist only in the task measurements by eliminating other non-target activities that exist both in the task and control measurements. One method for implementing such statistical subtraction has been recently proposed[Pantazis,2003]. The method uses the permutation tests to assess the statistical significance of the source reconstruction results, and thus it is very computer intensive. On the contrary, the method proposed in this paper does not use such computer intensive re-sampling methods as the permutation tests or the bootstrap, and it can be implemented with much shorter computational time. In this paper, we explain the proposed statistical thresholding method with spatial filter source reconstruction[Sekihara,2004]. This is because the formulation of the spatial filter is relatively simple and the spatial filter techniques have been successfully applied to MEG source analysis[Robinson,1998][van Veen,1997]. However, the applicability of the proposed method is not limited to the spatial filter formulation and it can be used with any types of source estimation methods that can provide the spatio-temporal source reconstruction, i.e., that can reconstruct source time courses at all pixel locations.

PROPOSED NONPARAMETRIC STATISTICAL SIGNIFICANCE EVALUATION

We define the magnetic field measured by the mth detector coil at time t as $b_m(t)$, and a column vector $\boldsymbol{b}(t) = [b_1(t), b_2(t), \ldots, b_M(t)]^T$ as a set of measured data where M is the total number of sensor coils and superscript T indicates the matrix transpose. The spatial location is represented by a three-dimensional vector $\boldsymbol{r}$: $\boldsymbol{r} = (x, y, z)$. The magnitude of the source moment is denoted $s(\boldsymbol{r}, t)$. Spatial filter techniques estimate the source current density by applying a simple linear operation to the measured data, i.e.,

$$\widehat{s}(\boldsymbol{r}, t) = \boldsymbol{w}^T(\boldsymbol{r})\boldsymbol{b}(t) = \sum_{m=1}^{M} w_m(\boldsymbol{r}) b_m(t), \tag{1}$$

where $\widehat{s}(\boldsymbol{r}, t)$ is the estimated source magnitude. The column vector $\boldsymbol{w}(\boldsymbol{r})$ expresses a set of the filter weights, which characterizes the property of the spatial filter. Various types of spatial filter techniques have been proposed and applied to the MEG/EEG source reconstruction problems.

The measured data can be expressed as

$$\boldsymbol{b}(t) = \boldsymbol{b}_I(t) + \boldsymbol{b}_\xi(t) + \boldsymbol{n}(t), \tag{2}$$

where $\boldsymbol{b}_\xi(t)$ is the magnetic field generated from sources other than the signal sources, such as brain spontaneous activities or some evoked activities that are not the target of current investigation. This $\boldsymbol{b}_\xi(t)$ is often referred to as the brain noise. The problem with the parametric modeling described in the preceding section is that it cannot efficiently take the brain noise into account, because the Gaussianity assumption does not hold for $\boldsymbol{b}_\xi(t)$. Here, we propose a simple nonparametric method that can take such brain noise into consideration. The spatial filter outputs obtained from $\boldsymbol{b}(t)$ is expressed as

$$\widehat{s}(\boldsymbol{r}, t) = \boldsymbol{w}^T(\boldsymbol{r})\boldsymbol{b}_I(t) + \boldsymbol{w}^T(\boldsymbol{r})\boldsymbol{b}_\xi(t) + \boldsymbol{w}^T(\boldsymbol{r})\boldsymbol{n}(t) = \widehat{s}_I(\boldsymbol{r}, t) + \widehat{s}_c(\boldsymbol{r}, t), \tag{3}$$

where

$$\widehat{s}_I(\boldsymbol{r}, t) = \boldsymbol{w}^T(\boldsymbol{r})\boldsymbol{b}_I(t) \quad \text{and} \quad \widehat{s}_c(\boldsymbol{r}, t) = \boldsymbol{w}^T(\boldsymbol{r})(\boldsymbol{b}_\xi(t) + \boldsymbol{n}(t)) \tag{4}$$

The key assumption in the proposed method is that the control measurement that can provide $\boldsymbol{b}_c(t) = \boldsymbol{b}_\xi(t) + \boldsymbol{n}(t)$ is available. Using this control measurement, the proposed method first derive an empirical distribution of $\widehat{s}_c(\boldsymbol{r}, t)$, and with this empirical distribution, the method determines the statistical threshold. The proposed procedures are described as follows:

(i) Empirical distribution formation We calculate $\widehat{s}_c(\boldsymbol{r}, t_j)$, by applying the spatial filter to the control measurement $\boldsymbol{b}_c(t_j)$ where t_j is the discrete time point in the control measurement. We then calculate $\widehat{F}(x)$, which is the empirical distribution of the modulus of the time course $|\widehat{s}_c(\boldsymbol{r}, t_j)|$, such that $\widehat{F}(x) = \sharp\{|\widehat{s}_c(\boldsymbol{r}, t_j)| \leq x\}/K_c$ where $\sharp\{|\widehat{s}_c(\boldsymbol{r}, t_j)| \leq x\}$ indicates the number of $|\widehat{s}_c(\boldsymbol{r}, t_j)|$ which is less than or equal to x, and K_c is the number of time points in the control measurement. This procedure is repeated and the empirical distribution is calculated at all pixel locations. Since $\widehat{F}(x)$ is obtained at each pixel location $\boldsymbol{r}$, $\widehat{F}(x)$ is rewritten as $\widehat{F}(x|\boldsymbol{r})$ in the following explanation.

(ii) Statistical thresholding with multiple comparisons The proposed method uses the maximum statistics to incorporate the multiple comparison problems; the use of the maximum statistics has been studied in [Pantazis,2003][Nichols,2001]. To utilize the maximum statistics, we first studentize the empirical distribution of $|\widehat{s}_c(\boldsymbol{r},t_j)|$ by calculating $T(\boldsymbol{r},t_j)$ such that

$$T(\boldsymbol{r},t_j)=\frac{|\widehat{s}_c(\boldsymbol{r},t_j)|-\langle|\widehat{s}_c(\boldsymbol{r},t_j)|\rangle_c}{\widehat{\sigma}(\boldsymbol{r})},\quad \text{where}\quad \widehat{\sigma}^2(\boldsymbol{r})=\langle\widehat{s}_c(\boldsymbol{r},t_j)^2\rangle_c-\langle|\widehat{s}_c(\boldsymbol{r},t_j)|\rangle_c^2, \tag{5}$$

and $\langle\cdot\rangle_c$ indicates the time average over the control period, i.e.,

$$\langle\widehat{s}_c(\boldsymbol{r},t_j)^2\rangle_c=\frac{1}{K_c}\sum_{j=1}^{K_c}\widehat{s}_c(\boldsymbol{r},t_j)^2 \quad\text{and}\quad \langle|\widehat{s}_c(\boldsymbol{r},t_j)|\rangle_c=\frac{1}{K_c}\sum_{j=1}^{K_c}|\widehat{s}_c(\boldsymbol{r},t_j)|.$$

We then calculate the maximum T value $T_{max}(\boldsymbol{r})$ at each pixel location. The maximum T value at the ith pixel location is denoted T^i_{max} where $i=1,\ldots,K_N$ and K_N indicates the total number of pixels. We next obtain the empirical distribution of T^i_{max}, $\widehat{H}(x)$, such that $\widehat{H}(x)=\sharp\{T^i_{max}\le x\}/K_N$ where $\sharp\{T^i_{max}\le x\}$ is the number of T^i_{max} values which is greater than or equal to x. We can then obtain the threshold for the α-confidence level, T^{th}_{max}, such that $T^{th}_{max}=\widehat{H}^{-1}(1-\alpha)$. The inverse of this empirical distribution can be calculated by first sorting T^i_{max} in the increasing order

$$T^{(1)}_{max}\le T^{(2)}_{max}\le\cdots\le T^{(K_N)}_{max}, \tag{6}$$

and choose $T^{(p)}_{max}$ as T^{th}_{max} where $p=[(1-\alpha)K_N]$. We finally obtain the statistical threshold for the spatial-filter reconstruction, $\Sigma(\boldsymbol{r})$, by using

$$\Sigma(\boldsymbol{r})=T^{th}_{max}\widehat{\sigma}(\boldsymbol{r})+\langle|\widehat{s}_c(\boldsymbol{r},t_j)|\rangle_c. \tag{7}$$

We evaluate the statistical significance of the spatial filter outputs by comparing the outputs $|\widehat{s}(\boldsymbol{r},t)|$ with $\Sigma(\boldsymbol{r})$, and when $|\widehat{s}(\boldsymbol{r},t)|\ge\Sigma(\boldsymbol{r})$, the outputs $\widehat{s}(\boldsymbol{r},t)$ is considered to be statistically significant.

EXPERIMENTS

We applied the proposed method to auditory-evoked MEG data to test its effectiveness. The auditory-evoked fields were measured using the 275-channel Omega-275 ™ whole-cortex biomagnetometer. The auditory stimulus (1-kHz pure tone) was presented to the subject's right ear. A total of 400 epochs were measured for averaging. The eigenspace-projected adaptive spatial filter [Sekihara,2002] was applied to these averaged recordings. The snapshots of the source reconstruction results at 44 ms is shown in Fig. 1(a). The reconstructed results not only contain a clear localized source in the left temporal lobe probably near the primary auditory area but also contain another diffused activity. The time-averaged reconstruction obtained over the whole prestimulus period is shown in Fig. 1(b). These results contain a diffused source similar to that found in the snapshot at 44 ms, suggesting that these diffused sources were caused by the periodic background activities. The results of applying the proposed method are shown in Fig. 1(c). The diffused source activities contained in (a) have been removed in (c),demonstrating the effectiveness of the the proposed statistical thresholding for removing the influence of background source activities.

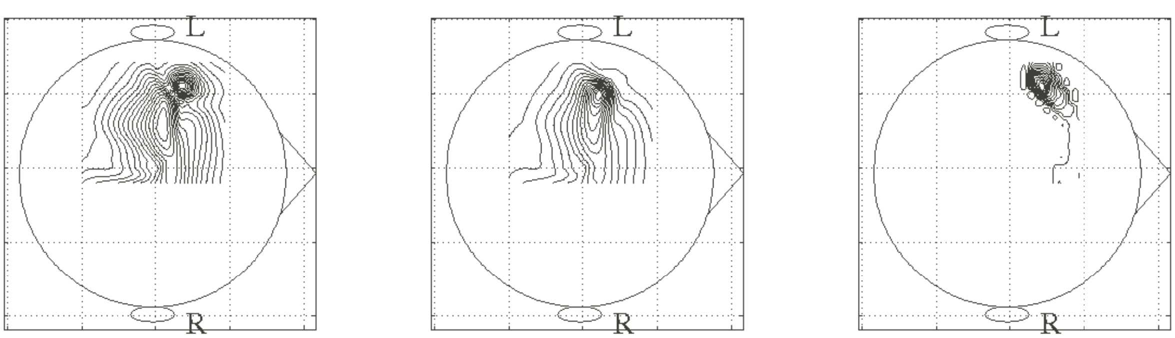

Figure 1: (a)Snapshot reconstruction at 44 ms. (b)Prestimulus-average reconstruction. (c)Results from proposed statistical thresholding.

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