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Vector-based spatial–temporal minimum L1-norm solution for MEG

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Minimum L1-norm solutions have been used by many investigators to analyze MEG responses because they provide high spatial resolution images. However, conventional minimum L1-norm approaches suffer from instability in spatial construction, and poor smoothness of the reconstructed source time-courses. Activity commonly “jumps” from one grid point to (usually) the neighboring grid points. Equivalently, the time-course of one specific grid point can show substantial “spiky-looking” discontinuity. In the present study, we present a new vector-based spatial–temporal analysis using a L1-minimum-norm (VESTAL). This approach is based on a principle of MEG physics: the magnetic waveforms in sensor-space are linear functions of the source time-courses in the imaging-space. Our computer simulations showed that VESTAL provides good reconstruction of the source amplitude and orientation, with high stability and resolution in both the spatial and temporal domains. “Spiky-looking” discontinuity was not observed in the source time-courses. Importantly, the simulations also showed that VESTAL can resolve sources that are 100% correlated. We then examined the performance of VESTAL in the analysis of human median-nerve MEG responses. The results demonstrated that this method easily distinguishes sources very spatially close to each other, including individual primary somatosensory areas (BA 1, 2, 3b), primary motor area (BA 4), and other regions in the somatosensory system (e.g., BA 5, 7, SII, SMA, and temporal–parietal junction) with high temporal stability and resolution. VESTAL’s potential for obtaining information on source extent was also examined.

Keywords: Lead field; MEG; Minimum norm; Spatial–temporal; Median-nerve; L1-norm; Dipole

Introduction

MEG is a functional imaging technique that detects neuronal activity with millisecond temporal resolution. However, many different source configurations can generate identical magnetic field distribution at the MEG sensor array. In order to unambiguously localize the sources that generate the MEG signal, specific assumptions must be made about the nature of the neuronal sources. These are termed “source models.” A widely accepted source-modeling technique for MEG involves calculating a set of equivalent current dipoles (ECDs), assuming that the underlying neuronal sources are focal. This dipole fitting procedure is non-linear and over-determined since the number of unknown dipole parameters is much less than the number of MEG measurements. Automated multiple-dipole model algorithms such as multiple signal classification (MUSIC) (Mosher et al., 1992; Mosher and Leahy, 1998; Mosher et al., 1999a) and multistart spatial and temporal (MSST) multiple-dipole modeling (Huang et al., 1998; Aine et al., 2000; Huang et al., 2000; Shih et al., 2000; Stephen et al., 2002; Hanlon et al., 2003; Stephen et al., 2003; Huang et al., 2004a; Huang et al., 2004b) have been studied and applied to the analysis of human MEG responses. However, the ability of dipole models to adequately characterize neuronal responses is limited due to (1) difficulties in localizing extended sources with ECDs; (2) problems in accurately estimating the number of dipoles in advance; and (3) the sensitivity of dipole time-courses to errors in dipole location, particularly in depth.

Other methods of modeling MEG responses include lead-field-based imaging approaches. Unlike multiple-dipole modeling, lead-field approaches divide the source space into a grid containing a large number of dipoles, and the inverse problem is to obtain the dipole moments for the grid nodes (Hamalainen and Ilmoniemi, 1994). Here the inverse solution is a highly under-determined since the number of unknown dipole moments is much greater than the

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number of MEG sensors. Consequently, a large number of solutions can fit the data equally well. To handle this ambiguity, additional constraints are needed to reduce the non-uniqueness of the solution. The main advantage of lead-field approaches is that the number of sources to model does not need to be specified in advance. The minimum L2-norm inverse is a lead-field-based inverse solution that minimizes the total power (L2-norm) of the dipole moment (Hamalainen and Ilmoniemi, 1994). Such a solution can be easily obtained using a direct linear inverse operator (pseudo inverse calculation with regularization) of the lead fields. Dale et al. (2000) developed an anatomically constrained minimum L2-norm solution using noise covariance normalization to obtain statistical significance of MEG responses. Strengths of this solution included low computational cost and smooth source time-courses, making statistical comparison across different conditions quite simple. This anatomically constrained minimum L2-norm solution has been used in many MEG applications (Dale et al., 2000; Dale and Halgren, 2001; Marinkovic et al., 2003). However, the spatial resolution of the minimum L2-norm solution is relatively low and tends to provide distributed reconstructions even if the true generators are focal. Cross-talk between source time-courses of nearby grid points can also be relatively high.

Independent component analysis (ICA) is another signal processing tool that can separate different signals, which are statistically independent in time. ICA has been used to successfully identify and remove artifacts (e.g., eye blink, eye movement, muscle artifact, cardiac artifact, etc.) from contaminated EEG and MEG data (Vigario, 1997; Ikeda and Toyama, 2000; Jung et al., 2000a; Jung et al., 2000b). ICA has also been used to separate different brain sources (Makeig et al., 1997; Vigario and Oja, 2000; Vigario et al., 2000; Barros et al., 2000; Jung et al., 2001). However, it has been difficult to directly examine two major assumptions underlying ICA: that source time-courses of brain activation are (1) statistically independent, and (2) non-Gaussian. Statistical independence implies uncorrelated source time-courses; ICA has difficulties of resolving highly correlated brain sources.

To address these limitations, the present study examined the efficacy of a novel minimum L1-norm solution in analyzing MEG responses. The minimum L1-norm solution selects the source configuration that minimizes the absolute value of the source strength, and can handle highly correlated sources, since additional assumptions about their temporal dynamics are not needed. Like the minimum L2-norm, the minimum L1-norm method does not need information about the number of sources as a prerequisite. Unlike minimum L2-norm solutions, the minimum L1-norm solution can also provide focal high-resolution images for focal generators. The minimum L1-norm solution is a non-linear minimization approach that can be effectively implemented by linear programming (LP) (Matsuura and Okabe, 1995; Matsuura and Okabe, 1997; Uutela et al., 1999). Although LP is not as fast as the direct pseudo-inverse used by the minimum L2-norm solution, many LP algorithms can efficiently handle problems with thousands to millions of variables. Deviating from the LP implementation of minimum L1-norm approaches, Phillips et al. (1997) suggested a lead-field-based inverse method for MEG using a combination of L1-norm and neighborhood clustering function. However, their cost function needed to be minimized by a Markov random field (Geman and Geman, 1984), which results in a high computational cost, particularly when the number of dipoles on the grid is large.

Although minimum L1-norm methods, particularly the magnetic current estimation (MCE) L1-norm solution (Uutela et al., 1999), have been used in many MEG applications (Vanni and Uutela, 2000; Tesche, 2000; Stenbacka et al., 2002; Pulvermuller et al., 2003; Osipova et al., 2005; Auranen et al., 2005; Liljestrom et al., 2005), these conventional approaches have some limitations. The first is that the dipole orientation at each grid point must be known before applying L1-norm methods (Uutela et al., 1999); or the dipole orientation must be iteratively determined (Matsuura and Okabe, 1995, 1999). The latter approach can significantly slow down the computation, without appreciably improving the results (Uutela et al., 1999). In the former case, the dipole orientation on each grid point is chosen based on the orientation derived from the minimum L2-norm approach. However, when MEG data contain multiple generators, the L2-norm reconstructed dipole orientation may deviate from the true orientation (see Results for examples), which can then cause the minimum L1-norm analysis to misfit the data.

The most serious limitations of conventional minimum L1-norm approaches are their instability in spatial location and poor smoothness in reconstructed source time-courses. For instance, one often sees activity “jumping” from one grid point to (usually) neighboring grid points. Equivalently, the time-course of one specific grid point can show substantial “spiky-looking” discontinuities. This problem is also encountered in other focal localization methods using lead-field approaches (e.g., FOCUSS Gorodnitsky et al., 1995). Although averaging across many time points reduces the discontinuity in source time-courses, this results in a loss in temporal resolution (Uutela et al., 1999; Vanni and Uutela, 2000; Tesche, 2000; Stenbacka et al., 2002; Pulvermuller et al., 2003; Osipova et al., 2005; Auranen et al., 2005; Liljestrom et al., 2005).

In the present study, we introduce a novel vector-based *spatial–temporal* analysis using a L1-minimum-norm (VESTAL) solution. This approach is to ensure the linear relationship between MEG waveforms in sensors and the time-courses of the underlying neuronal sources. In the VESTAL approach, the temporal information in the data was used to enhance the stability of the reconstructed vector-based L1-minimum norm solution. Since this approach makes no additional assumptions about the temporal dynamics of the sources, it can also handle sources that are 100% correlated. VESTAL also effectively obtains source strength and dipole orientation without iteration or choosing a pre-fixed dipole orientation for each grid node. VESTAL was tested in computer simulations, and using data from human MEG responses. The results show that VESTAL provides high spatial stability and continuous temporal dynamics, without compromising spatial or temporal resolution.

Material and methods

Minimum L1-norm solution (general approach)

As in all lead-field-based MEG and EEG inverse approaches, we first divide the source space (the brain volume or just the cortex) into a grid of a large number of dipole locations. The $m \times s$ sensor waveform matrix $\mathbf{B} = [\boldsymbol{b}(t_1), \boldsymbol{b}(t_2), \ldots, \boldsymbol{b}(t_s)]$ contains MEG data where m is the number of MEG sensors and s is the number of time points, $\boldsymbol{b}(t_i)$ is an $m \times 1$ vector of the MEG measurements at given time point. For each column of $\mathbf{B}$, we have:

$$\boldsymbol{b} = \mathbf{G}\boldsymbol{q} + \text{noise} \tag{1}$$

where $\mathbf{G}$ is the $m \times n$ (lead-field) gain matrix, $\boldsymbol{q}$ is the $n \times 1$ dipole moment vector for given time point, and n is the number of