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Reconstructing spatially extended brain sources via enforcing multiple transform sparseness

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ABSTRACT

Accurate estimation of location and extent of neuronal sources from EEG/MEG remain challenging. In the present study, a new source imaging method, i.e. variation and wavelet based sparse source imaging (VW-SSI), is proposed to better estimate cortical source locations and extents. VW-SSI utilizes the L1-norm regularization method with the enforcement of transform sparseness in both variation and wavelet domains. The performance of the proposed method is assessed by both simulated and experimental MEG data, obtained from a language task and a motor task. Compared to L2-norm regularizations, VW-SSI demonstrates significantly improved capability in reconstructing multiple extended cortical sources with less spatial blurredness and less localization error. With the use of transform sparseness, VW-SSI overcomes the over-focused problem in classic SSI methods. With the use of two transformations, VW-SSI further indicates significantly better performance in estimating MEG source locations and extents than other SSI methods with single transformations. The present experimental results indicate that VW-SSI can successfully estimate neural sources (and their spatial coverage) located in close areas while responsible for different functions, i.e. temporal cortical sources for auditory and language processing, and sources on the pre-bank and post-bank of the central sulcus. Meantime, all other methods investigated in the present study fail to recover these phenomena. Precise estimation of cortical source locations and extents from EEG/MEG is of significance for applications in neuroscience and neurology.

Introduction

Electroencephalography (EEG) and magnetoencephalography (MEG) are promising noninvasive neuroimaging technologies to probe human brain activities with excellent temporal resolutions (milliseconds), as compared with other neuroimaging technologies, e.g. functional magnetic resonance imaging (fMRI). Meantime, the precise reconstruction of brain sources behind EEG/MEG still remains challenging, which are usually obtained by solving so-called EEG/MEG inverse problems (Baillet et al., 2001). Accurate estimation of EEG/MEG source locations and extents, however, is of significance in understanding human brain functions (Dhond et al., 2001; Hillyard, 1993) and addressing clinical needs (Brodbeck et al., 2011). EEG/MEG inverse solutions based on equivalent current dipole (ECD) source models provide localizations for single or a few focal brain activations (Stefan et al., 2003; Wood, 1982), when the number of dipoles is known or can be estimated (Wood, 1982). However, ECD solutions provide no estimation of source extents since ECDs are only discrete source points, which can even potentially cause bias in locating spatially extended brain sources (Ou et al., 2009; Plummer et al., 2008).

Recognizing the limitation of ECD, distributed current density (DCD) models have been developed to model extended brain sources, in which the source space is defined as a set of distributed dipoles over a three dimensional (3D) brain volume (Ding and He, 2008; Pascual-Marqui et al., 1994) or a two dimensional (2D) cortical surface (cortical current density, i.e. CCD, models) (Dale and Sereno, 1993). It is thus theoretically possible to infer both source locations and extents in inverse solutions. Practically, the estimation accuracy still largely depends on how efficiently DCD-based inverse problems can be solved, which have infinite number of solutions to a given set of measurements (Baillet et al., 2001). Unique solutions are typically obtained by introducing anatomical and/or functional priors, via a procedure known as regularization (Vega-Hernández et al., 2008). The most common regularization approach is to have minimum overall energy (i.e. L2-norm) in inverse solutions, such as minimum norm estimate (MNE) (Hämäläinen and Ilmoniemi, 1994) and its variants, i.e. weighted MNE (wMNE) (Dale and Sereno, 1993) and low-resolution electromagnetic tomography (LORETA) (Pascual-Marqui et al., 1994). L2-norm regularizations

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belong to quadratic regression problems (Hoerl and Kennard, 1970), which assume Gaussian source fields (Uutela et al., 1999) and produce over-smooth estimations (Pascual-Marqui et al., 1994; Vega-Hernández et al., 2008). The nature of smoothness makes them not suitable for estimating source extents from early sensory brain responses and focal epilepsy, in which sources are proved to be compact (Allison et al., 1989; Oishi et al., 2002).

Other regularizations utilizing non-quadratic regression schemes, such as minimum current (i.e. L1-norm), have demonstrated sparse solutions to address the smoothness problem (Ding and He, 2008; Tibshirani, 1996; Uutela et al., 1999). However, most of them, including selective minimum-norm method (Matsuura and Okabe, 1995), minimum current estimate (MCE) (Uutela et al., 1999), least absolute shrinkage selection operator (LASSO) (Tibshirani, 1996), and sparse source imaging (SSI) (Ding and He, 2008), produce over-focused solutions, which do not reflect accurate source extents either (Chang et al., 2010; Ding et al., 2011). The over-focality is caused by insufficient consideration of source extents in models due to the enforcement of sparseness in the original source domain, which leads to the idea of enforcing sparseness in transform domains (Chang et al., 2010; Ding, 2009), where signals (i.e. current densities) can be sparser or more compressible (Candès and Romberg, 2007). Variation transform, which computes the difference between neighbored elements, has been first reported to use transform sparseness (Ding, 2009). Inverse solutions of variation based L1-norm regularizations allow the reconstruction of extended sources, in which source extents can be inferred. Laplace transform has also been proposed to compress current densities using the second-order spatial derivative (Chang et al., 2010), which promotes smoothness in neighborhoods. However, since the minimization of both variation and second-order derivative does not limit the global energy of inverse solutions, L1-norm regularizations with these transforms must incorporate additional priors to constrain global energies. Wavelet transforms, efficient methods in compressing signals and/or images, have been developed for complex 2D surfaces with either regular subdivisions, e.g. spherical wavelets (Schröder and Sweldens, 1995), or irregular subdivisions, e.g. face-based wavelets (Liao et al., 2012; Valette and Prost, 2004), which can be applied to compress current densities on highly convoluted cortical surfaces, i.e. CCD models. The L1-norm regularizations based on wavelet transforms have thus been pursued (Chang et al., 2010; Liao et al., 2012). Liao et al. (2012) further indicates that the L1-norm regularizations using face-based wavelets have better accuracy in recovering sources than spherical wavelets (Chang et al., 2010). Furthermore, adaptive estimation of source extents of both focal and extended sources has been suggested possible by controlling the level of wavelet compression (Chang et al., 2010), which is, however, challenging without a priori knowledge about the size of sources.

In the present study, a new sparse source imaging method, i.e. variation and wavelet based SSI (VW-SSI), is proposed using multiple penalties in L1-norm regularization, i.e. enforcing sparseness in both variation and wavelet domains (with the face-based wavelet). It aims to address the limitation in the variation-based method since the wavelet penalty term constrains the global energy, and to stabilize the issue of selecting the wavelet compression level with the variation penalty term. With the hybrid sparseness constraints integrated, it is expected that SSI techniques can achieve better accuracy in estimating source locations and extents even in data with low signal-to-noise ratio (SNR). The performance of the proposed method was evaluated in simulated and experimental MEG data. In simulations, neural activations of various extents were randomly located. The VW-SSI inverse solutions were assessed using multiple metrics on the accuracy of both locations and extents, as compared with other SSIs and L2-norm methods. The sensitivities of VW-SSI to SNR, wavelet compression level, and hyper-parameter for multiple penalty terms were studied. Experimental MEG data collected from both language and motor tasks in an epilepsy patient were analyzed to evaluate and compare all methods in reconstructing distributed neural activations.

Material and methods

Sparse source imaging using L1-norm regularization

Giving the CCD source model and the conductive profile of the head, the relationship between MEG measurements $\vec{\phi}$ and source $\vec{s}$ can be expressed as (Nunez, 1981):

$$\vec{\phi} = \mathbf{A}\,\vec{s} + \vec{n} \tag{1}$$

where $\vec{n}$ denotes the noise and $\mathbf{A}$ is the lead field. Since the number of measurements M is much smaller than the number of dipoles N, its inverse problem has no unique solution. L1-norm regularizations have been proposed to search for a unique solution by enforcing sparseness in either original source domain or transform domains (Chang et al., 2010; Ding, 2009; Ding and He, 2008; Liao et al., 2012; Tibshirani, 1996; Uutela et al., 1999), which can be universally expressed as a constrained optimization problem:

$$\min \left\| \mathbf{H}\,\vec{s} \right\|_1 \quad \text{subject to} \quad \left\| \vec{\phi} - \mathbf{A}\,\vec{s} \right\|_2 < \varepsilon \tag{2}$$

where the matrix $\mathbf{H}$ is either an identity matrix or any matrix for a transform. The regularization parameter ε is estimated by the discrepancy principle (Morozov, 1966). Assuming Gaussian white noise with variance σ^2, $\left(1/\sigma^2\right)\left\|\vec{n}\right\|_2^2$, where $\vec{n} = \vec{\phi} - \mathbf{A}\,\vec{s}$, can be treated as a χ^2-distribution with degree of freedom as the number of sensors. To make the probability of $\left\|\vec{\phi} - \mathbf{A}\,\vec{s}\right\|_2 \geq \varepsilon$ small enough, ε is selected as the upper bound of the confidence interval [0, ε] that integrates to 0.99 probabilities.

Using different transform matrix $\mathbf{H}$, various L1-norm regularizations can be formed: (1) SSI (Ding and He, 2008) where $\mathbf{H}$ is the identity matrix; (2) variation based SSI (V-SSI) (Ding, 2009) using the variation operator $\mathbf{V}$ as $\mathbf{H}$ (Variation transform section); (3) wavelet based SSI (W-SSI) (Liao et al., 2012) using the wavelet transform matrix $\mathbf{W}_m$ as $\mathbf{H}$ (Face-based wavelet transform section), where the index m stands for the level of wavelet compression ($m = 1,2,3,4$).

Variation transform

In the CCD model meshed with triangles (see Simulation protocol section for details), the variation transform is defined as (Ding, 2009):

$$\mathbf{V} = \begin{bmatrix} v_{11} & v_{12} & \cdots & v_{1N} \\ v_{21} & v_{22} & \cdots & v_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ v_{P1} & v_{P2} & \cdots & v_{PN} \end{bmatrix} \qquad \begin{cases} v_{ij} = 1; v_{ik} = -1; & \text{if elements } j,k \text{ share the same edge } i \\ v_{ij} = 0; & \text{otherwise} \end{cases} \tag{3}$$

where P is the number of triangular edges. Each element in the variation vector, $\mathbf{V}\,\vec{s}$, is defined on each triangular edge indicating the change of values over neighbored triangles.

Face-based wavelet transform

To define wavelet transform on the cortical surface, a multi-resolution cortical model (Fig. 1) is firstly constructed by iteratively compressing the highly convoluted cortical structure to create a series of spaces for multi-resolution wavelet analysis (Valette and Prost, 2004). The compression procedure is accomplished by hierarchically merging multiple triangles on a finer level into one triangle on a coarser level. With the multi-resolution cortical model, the scaling function supported on a triangle at level m is designed as one on the triangle and zeros otherwise. Then, its decompositions to approximations (scaling coefficients) and details (wavelet coefficients) at the next coarse level $m + 1$ can be obtained by directly applying analysis matrices $\mathbf{A}^m$ and $\mathbf{B}^m$ (Liao et al., 2012). See details on how to construct $\mathbf{A}^m$ and $\mathbf{B}^m$ in