NEUROMAGNETIC SOURCE RECONSTRUCTION

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ABSTRACT

In neuromagnetic source reconstruction, a functional map of neural activity is constructed from noninvasive magnetoencephalographic (MEG) measurements. The overall reconstruction problem is under-determined, so some form of source modeling must be applied. We review the two main classes of reconstruction techniques—parametric current dipole models and nonparametric distributed source reconstructions. Current dipole reconstructions use a physically plausible source model, but are limited to cases in which the neural currents are expected to be highly sparse and localized. Distributed source reconstructions can be applied to a wider variety of cases, but must incorporate an implicit source model in order to arrive at a single reconstruction. We examine distributed source reconstruction in a Bayesian framework to highlight the implicit nonphysical Gaussian assumptions of minimum norm based reconstruction algorithms. We conclude with a brief discussion of alternative non-Gaussian approachs.

1. INTRODUCTION

In magnetoencephalography (MEG), the minute magnetic fields generated by neural activity are measured at the surface of the head by superconducting quantum interference device (SQUID)-based gradiometers [1]. Neuromagnetic source reconstruction is the process of deducing the sources of these fields in order to produce a functional mapping of the brain. MEG is attractive because the millisecond temporal resolution of the measurements. This high resolution enables the analysis of dynamic brain processes such as evoked responses. Alternate functional imaging modalities such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) cannot provide comparable temporal resolution.

The difficulty in using MEG for functional mapping lies in its inverse problem. The general neuromagnetic source reconstruction problem—determining the three dimensional neural current distribution from the head surface magnetic field—is under-determined [2]. To address this problem, prior assumptions must be made about the neural source configuration.

Two distinct approaches have been used in dealing with the basic indeterminacy of the inverse problem. The first, and most wide spread, is a parametric, model-based approach in which the neural currents are assumed to be sparse and localized. The currents in each active region of the brain are modeled by a current dipole or low order multipole. Locations of the brain's active regions are found via a least squares fit of the nonlinear source model to the measurements. These techniques can provide accurate source mappings with resolutions in the millimeter range when the modeling assumptions are met. Model-based approaches are also amenable to array processing algorithms such as MUSIC [3] and statistical performance analyses such as Cramer-Rao error bounds [4].

A second, nonparametric approach to MEG source reconstruction has arisen in an attempt to handle cases with more distributed source currents—source configurations that may not be sparse and localized. By applying sampling theory, the overall reconstruction problem can be discretized and reduced to computing currents in a set of fixed volume elements (voxels) in the brain. This approach is much less restrictive than dipole source modeling. And the resulting linear form permits straightforward incorporation of anatomical constraints and an easy comparison to PET and fMRI results.

Although the formulation is linear, it is highly under-determined. The challenge in this approach is to pick a single reconstruction out of an infinite set of possibilities. Distributed source reconstruction methods make this decision by applying a quality metric to the solution. The metric represents an implicit model of the source configuration. Metrics have included solution norms (e.g. minimum norm solutions) [5,6] and sparseness measures (e.g. minimum source solutions) [7,8].

In this paper, we review both approaches to MEG source reconstruction. We examine distributed source reconstruction in a Bayesian framework to highlight the implicit nonphysical Gaussian assumptions of minimum norm based reconstruction algorithms. We conclude with a brief discus-

This work was supported by the Los Alamos National Laboratory, operated by the University of California for the United States Department of Energy under contract W-7405-ENG-36, and by NIMH Grant R01-MH53213.

0-7803-2431-5/95 $4.00 © 1995 IEEE

sion of non-Gaussian models which can potentially capture the advantages of both approaches.

2. BASICS

The relation between the primary neural source currents inside the head and the resultant magnetic field strength outside of the head can be expressed as [2,9,10]

$$b(\hat{s}, \boldsymbol{r}, t) = \int_{V'} \boldsymbol{g}(\hat{s}, \boldsymbol{r}, \boldsymbol{r}') \cdot \boldsymbol{j}(\boldsymbol{r}', t) dV' , \qquad (1)$$

where $b(\hat{s}, \boldsymbol{r}, t)$ is the magnetic field component in the $\hat{s}$ direction at location $\boldsymbol{r}$ outside the head, $\boldsymbol{j}(\boldsymbol{r}', t)$ is the primary current density at $\boldsymbol{r}'$ inside the head, $\boldsymbol{g}(\hat{s}, \boldsymbol{r}, \boldsymbol{r}')$ is the magnetic lead field, V' is the volume inside the head, and t is the time index. The magnetic lead field $\boldsymbol{g}$ relates the primary current density (the current directly resulting from neural activity) to the resulting external field and includes the effect of the ohmic "return currents" [9]. The form of $\boldsymbol{g}$ depends on the head geometry and conductivities. For the radial component of the magnetic field outside of a head modeled as a sphere with spherically symmetric conductivity [2], the lead field is

$$\boldsymbol{g}(\hat{s}, \boldsymbol{r}, \boldsymbol{r}') = \boldsymbol{g}(\frac{\boldsymbol{r}}{|\boldsymbol{r}|}, \boldsymbol{r}, \boldsymbol{r}') = \frac{\mu_o}{4\pi} \frac{\boldsymbol{r} \times \boldsymbol{r}'}{|\boldsymbol{r} - \boldsymbol{r}'|^3 |\boldsymbol{r}|}, \qquad (2)$$

where μ_o is the permeability of free space. For realistic head models, $\boldsymbol{g}$ must be computed numerically [1].

Using (1), an MEG measurement i can be expressed in the basic form

$$b_i(t) = \int_{V'} \boldsymbol{g}_i(\boldsymbol{r}') \cdot \boldsymbol{j}(\boldsymbol{r}', t) dV' + n_i(t) , \qquad (3)$$

where $n_i(t)$ represents measurement error or noise. And $\boldsymbol{g}_i(\boldsymbol{r}')$ is derived from a linear combination of lead fields that accounts for both multiple gradiometer coils and finite coil area [10].

In the general case, knowledge of the external magnetic field is insufficient to reconstruct the primary current density. This is because there exist "silent," nonzero distributions that produce no external magnetic field, i.e. $\int_{V'} \boldsymbol{g}(\hat{s}, \boldsymbol{r}, \boldsymbol{r}') \cdot \boldsymbol{j}(\boldsymbol{r}') dV' = 0$ for all $\hat{s}$ and $\boldsymbol{r}$. Of course any two current distributions that differ by a silent distribution will produce exactly the same external magnetic field. The ambiguity can be further compounded by the finite number of measurements available.

3. DIPOLE SOURCE MODELS

One approach to resolving the ambiguity in neuromagnetic source reconstruction is to represent the primary current density by a physiologically plausible parametric model. In cases where the neural activity is expected to be localized—restricted to a small number of regions of the brain—point source current dipole models are widely employed. In this approach, the neurally-driven primary current density $\boldsymbol{j}$ is modeled as a small set of l current dipoles

$$\boldsymbol{j}(\boldsymbol{r}', t) = \sum_{k=1}^{l} \boldsymbol{j}_k(t) \delta(\boldsymbol{r}' - \boldsymbol{r}_k) , \qquad (4)$$

where $\boldsymbol{j}_k$ is the dipole moment and δ is a Dirac impulse. From (3), the measurements can be expressed as

$$b_i(t) = \sum_{k=1}^{l} \boldsymbol{g}_i(\boldsymbol{r}_k) \cdot \boldsymbol{j}_k(t) + n(t) . \qquad (5)$$

For m measurements, the problem formulation is

$$\begin{bmatrix} b_1(t) \\ \dots \\ b_m(t) \end{bmatrix} = \begin{bmatrix} \boldsymbol{g}_1(\boldsymbol{r}_1) & \dots & \boldsymbol{g}_1(\boldsymbol{r}_l) \\ \dots & & \dots \\ \boldsymbol{g}_m(\boldsymbol{r}_1) & \dots & \boldsymbol{g}_m(\boldsymbol{r}_l) \end{bmatrix} \begin{bmatrix} \boldsymbol{j}_1(t) \\ \dots \\ \boldsymbol{j}_l(t) \end{bmatrix} + \begin{bmatrix} n_1(t) \\ \dots \\ n_m(t) \end{bmatrix}, \ or$$

$$B(t) = G(R)J(t) + N . \qquad (6)$$

Using (5) or (6), neuromagnetic source reconstruction reduces to finding the unknown parameters l—number of dipoles, $\boldsymbol{r}_k$—dipole locations, and $\boldsymbol{j}_k$—dipole moments. Typically l is small enough so that the number of parameters is far less than the number of measurements. As a result, the parameters can be estimated using nonlinear least squares and/or subspace projection techniques [1,3].

Dipole models also have a mathematical interpretation as the leading term in a multipole expansion (vector Taylor series). If the measurements are made at a distance that is much greater than the spatial extent of the source, then the dipole term will dominate. Judicious use of low order multipole terms in addition to the dipole can allow parametric models to handle less sharply localized neural sources [11].

4. DISTRIBUTED SOURCE MODELS

If the primary current density $\boldsymbol{j}$ is sampled spatially with adequate resolution, then it can be expressed in terms of its l voxel samples $\boldsymbol{j}_k$ as

$$\boldsymbol{j}(\boldsymbol{r}', t) = \sum_{k=1}^{l} \boldsymbol{j}_k(t) \Phi_k(\boldsymbol{r}') , \qquad (7)$$

where Φ_k are the set of basis or interpolation functions associated with the sampling. Substituting into (3) and interchanging the order of the summation and integration yields

$$b_i(t) = \sum_{k=1}^{l}\left(\int_V g_i(r')\Phi_k(r')dV'\right)\cdot j_k(t) + n_i(t). \quad (8)$$

Defining g_{ik} to be the integral inside the parentheses, (8) can be expressed as

$$b_i(t) = \sum_{k=1}^{l} g_{ik}\cdot j_k(t) + n_i(t). \quad (9)$$

For m measurements, the problem formulation is

$$\begin{bmatrix} b_1(t) \\ \dots \\ b_m(t) \end{bmatrix} = \begin{bmatrix} g_{11} & \cdots & g_{1l} \\ \dots & & \dots \\ g_{m1} & \cdots & g_{ml} \end{bmatrix}\begin{bmatrix} j_1(t) \\ \dots \\ j_l(t) \end{bmatrix} + \begin{bmatrix} n_1(t) \\ \dots \\ n_m(t) \end{bmatrix}, \textit{ or}$$

$$B(t) = GJ(t) + N. \quad (10)$$

Note that the dipole model (5) is a special case of (9) where the basis functions are Dirac impulses. A critical difference however, is that in the dipole model the number of "samples" (l) is small and both the number of samples and their locations are unknown parameters. In (9) the number of samples and their locations are known *a priori*. As a result, neuromagnetic source reconstruction reduces to finding the voxel values j_k which are linearly related to the measurements.

Although the problem has been cast in a linear form, the underlying ambiguity still remains since the number of voxels is generally much larger than the number of measurements. A number of ad hoc techniques have been proposed to deal with this. Each of these approaches has in some way replaced the explicit assumptions of the dipole model with implicit assumptions that are often buried within the reconstruction algorithms. In the next section we cast distributed source reconstruction in a Bayesian framework and use this interpretation to examine the underlying assumptions of different approaches.

5. BAYESIAN FRAMEWORK

To overcome the structural ambiguity of (10), prior information must be incorporated in order to pick a single reconstruction from the infinite set of primary current distributions consistent with the measurements. A Bayesian framework provides a formal way in which to incorporate nonparametric prior information. From (10), dropping the time index, the measurement model is $B = GJ + N$. Both J and N are treated as random vectors and prior information about them is represented as the probability density functions (pdf) $p(J)$ and $p(N)$.

The additional knowledge of J provided by the measurements B is then represented by the posterior conditional pdf $p(J|B)$. By Bayes rule

$$p(J|B) = \frac{p(B|J)p(J)}{p(B)}. \quad (11)$$

The neuromagnetic source reconstruction is then derived as an estimate of J based on $p(J|B)$. The maximum a posteriori (MAP) estimate is the most probable current distribution.

$$\hat{J} = \underset{J}{\operatorname{argmax}}\,[p(J|B)]. \quad (12)$$

The MAP estimate can be derived from the log of the posterior pdf [12].

$$\hat{J} = \underset{J}{\operatorname{argmax}}\,[\ln p(B|J) + \ln p(J)] \quad (13)$$

From (13) it is clear that the MAP estimate strikes a balance between consistency with the measurements (first term) and consistency with prior knowledge of the neural current distribution (second term).

If both J and N are independent and normally distributed, then the MAP estimate is

$$\hat{J} = \underset{J}{\operatorname{argmax}}\Big[-(B-GJ)^T C_N^{-1}(B-GJ) - (J-M_J)^T C_J^{-1}(J-M_J)\Big] \quad (14)$$

where M_J and C_J are the mean and covariance of J, and C_N is the covariance of the zero mean noise N. In this case, the first term is chi-square, which measures compatibility of the solution with the measurements, and the second term is a norm on J. The closed form solution of the MAP estimate in (14) is [12]

$$\hat{J} = C_J G^T\left[GC_J G^T - C_N\right]^{-1}(B - GM_J) + M_J. \quad (15)$$

(Due to the symmetry of $p(J|B)$, this is also the minimum mean square estimate of J.)

If J is zero mean ($M_J = 0$) and the noise is negligible ($C_N = 0$), then the MAP estimate reduces to a weighted minimum norm solution to (10).

$$\hat{J} = C_J G^T\left[GC_J G^T\right]^{-1}B. \quad (16)$$

The elegance and simplicity of minimum norm solutions have attracted many MEG researchers [5,6,13–17]. However, the underlying implicit model of a zero mean Gaussian distributed current density has little physiological basis. Indeed, minimum norm current reconstructions are invariably smooth and suffer systematic geometric bias.

6. NON-GAUSSIAN PRIORS

Although easy to generate, the smooth, diffuse current reconstructions produced by minimum norm techniques do not provide a good match to our understanding of neural functioning. In many dynamic brain functions, the neural responses are known to be sparse and localized. The current dipole represents an extreme of this model. Indeed, in the Bayesian framework, dipole models correspond to priors in which only small sets of Dirac impulses are allowable for $\boldsymbol{j}$.

Ideally, one would like to maintain the generality provided by the distributed source model, while at the same time favoring solutions that are sparse and localized. Jeffs [17] minimizes a p-norm where $p < 1$ instead of the traditional 2-norm. The implicit prior of this approach, $p(J) \propto \exp\{\|J\|_p\}$, clumps the probability density along the axes of the vector space. An alternative is to directly minimize the number of nonzero sources [5,8]. A third approach has been to implicitly derive focal solutions by iterative minimum norm weightings [6,7].

A particularly interesting class of image models are Markov random field (MRF) priors which have been used to great effect in many other branches of image processing [18]. These models have densities in the form of Gibbs distributions, $p(J) = (1/z)\exp\{-U(J)\}$, where z is a constant and $U(J)$ is a Gibbs energy function which consists of a sum of potential functions, each of which is defined on a set of voxels which are mutual neighbors of each other. By carefully choosing the neighborhood system and the potential function, it is possible to construct a prior which reflects prior physiological information. For example, functional localization in the cerebral cortex can be reflected in a prior for which images consisting of a relatively small number of clusters of active pixels occur with high probability. Such a model can be developed within a MRF framework. Furthermore, MRF models provide a natural framework for incorporating additional functional information extracted from PET or fMRI by providing increased probability of current sources in regions showing activation in these other functional modalities.

Non-Gaussian priors pose a challenging computational problem, since they typically result in non-concave posterior densities and hence are subject to trapping of gradient based searches in local optima. Methods to circumvent this problem include the use of genetic algorithms [8] and deterministic and stochastic annealing methods [18].

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