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Title: HYBRID MEG (MAGNETOENCEPHALOGRAPHY) SOURCE CHARACTERIZATION BY CORTICAL REMAPPING AND IMAGING OF PARAMATRIC SOURCE MODELS

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Hybrid MEG Source Characterization by Cortical Remapping and Imaging of Parametric Source Models

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1 Introduction

Reliable estimation of the local spatial extent of neural activity is a key to the quantitative analysis of MEG sources across subjects and conditions. In association with an understanding of the temporal dynamics among multiple areas, this would represent a major advance in electrophysiological source imaging.

Parametric current dipole approaches to MEG (and EEG) source localization can rapidly generate a physical model of neural current generators using a limited number of parameters. However, physiological interpretation of these models is often difficult, especially in terms of the spatial extent of the true cortical activity. In new approaches using multipolar source models [3, 5], similar problems remain in the analysis of the higher-order source moments as parameters of cortical extent. Image-based approaches to the inverse problem provide a direct estimate of cortical current generators, but computationally expensive nonlinear methods are required to produce focal sources [1,4]. Recent efforts describe how a cortical patch can be grown until a best fit to the data is reached in the least-squares sense [6], but computational considerations necessitate that the growth be seeded in predefined regions of interest.

In a previous study [2], a source obtained using a parametric model was remapped onto the cortex by growing a patch of cortical dipoles in the vicinity of the parametric source until the forward MEG or EEG fields of the parametric and cortical sources matched. The source models were dipoles and first-order multipoles.

We propose to combine the parametric and imaging methods for MEG source characterization to take advantage of (i) the parsimonious and computationally efficient nature of parametric source localization methods and (ii) the anatomical and physiological consistency of imaging techniques that use relevant *a priori* information. By performing the cortical remapping/imaging step by matching the multipole expansions of the original parametric source and the equivalent cortical patch, rather than their forward fields, we achieve significant reductions in computational complexity.

2 Methods

2.1 Parametric source imaging

Though the equivalent cortical patch may be seeded with the solutions from any parametric localization method, we routinely use Recursively Applied and Projected (RAP)-MUSIC which does not require that the number of sources be known *a priori*, as is the case for least squares fitting [7]. The version available in BrainStorm (http://neuroimage.usc.edu) estimates parameters for sources up to quadrupolar complexity.

2.2 Seeding the cortical growth

The first step consists of finding one or several best seeding locations from which to start growing a patch. We select the initial cortical locations for region growing using areas in which the local current density is larger than a predefined threshold in a Minimum-Norm (MN) image of the cortical currents.

Let $\mathbf{G}_o$ be the gain vector characterizing the estimated source $\mathbf{J}_o$ at location $\mathbf{r}_o$ for which an equivalent cortical patch is to be found. The cortical surface from a subject MRI is tesselated and an elemental current dipole allowed at each vertex on this surface. A gain vector $\mathbf{G}_i$ is assigned to the dipole at location $\mathbf{r}_i$ oriented normally to the cortical surface. Finding a cortical equivalent to $\mathbf{J}_o$ consists of finding the set of elemental cortical dipoles ζ and their amplitudes $\mathbf{y} = [y_i, i \in \zeta]$ so that $\mathbf{G}_o = \mathbf{G}_\zeta \mathbf{y} + \mathbf{b} = \sum_{i \in \zeta} \mathbf{G}_i y_i + \mathbf{b}$, where $\mathbf{b}$ is the error due to the discrepancy between the parametric source and its cortical counterpart. ζ is intialized by thresholding a regularized MN estimate of $\mathbf{y}$, $\hat{\mathbf{y}} = \underset{\mathbf{y}}{\operatorname{argmin}} \left\| \mathbf{G}_o - \mathbf{G}_\zeta \mathbf{y} \right\|^2 + \lambda \|\mathbf{y}\|^2$:

$$\zeta = \{ i \in C, |\hat{y}_i| \geq \tau \}. \quad (1)$$

where C denotes the entire set of N cortical vertices.

2.3 Iterative estimation of the source extension

The patch growth consists in a recursive estimation of the local current density on a growing number of source candidates in the vicinity of every seed in ζ until a functional U_k^i is minimized (for seed i at iteration k). The functional U_k^i is defined in the following section.

A. For every seed $i \in \zeta$,

1. Initialization: set k=1 and the patch around source i to $\vartheta_k^i = \{i\}$;
2. Estimate $\mathbf{y}_i$, then compute U_k^i;
3. If $U_{k-1}^i > U_k^i$,
   - (i) Grow the patch by including the vertices connected to the source(s) in ϑ_k^i,
   - (ii) Set k=k+1 and go back to A.2;

   else:
   - (i) Define $U^i = U_{k-1}^i$;
   - (ii) Define the best patch obtained from seed i, $\Pi^i = \vartheta_{k-1}^i$;
   - (iii) Proceed to the next seed.

B. Patch Merging:

Select a subset of patches $\{\Pi^i, i \in I\}$ with $I = \{ i, U^i < (\langle U^j \rangle - 3\sigma(U^j)) \}$, where $\langle U^j \rangle$ (res. $\sigma(U^j)$) is the mean (res. the standard deviation) of the set $\{U^j, j \in \zeta\}$. The final patch Π is then defined as: $\Pi = \bigcup_{i \in I} \Pi^i$.

For every seed i and at every iteration step k, the source amplitudes - which may be non-null only within ϑ_k^i - are estimated using a Bayesian estimator [1][4] as described in the following.

2.4 Bayesian imaging of the local current density

The local current density is modeled as a random field using extensions of models described in [4]. We characterized the current density at every vertex with a continuous random variable of dipole amplitude z_i and a binary indicator process x_i to model whether source i is on or off. The local equivalent source density can thus be written as $y_i = x_i * z_i$.

A MAP Bayesian estimator of $\mathbf{y}$ is given by:

$$\hat{\mathbf{y}} = \hat{\mathbf{X}} \cdot \hat{\mathbf{z}} = \arg\max_{\mathbf{x},\mathbf{z}} \frac{p(\mathbf{b}|\mathbf{x},\mathbf{z}) p(\mathbf{x}) p(\mathbf{z})}{p(\mathbf{b})}, \quad (2)$$

where $\hat{\mathbf{X}} = \operatorname{diag}(\hat{\mathbf{x}})$, and $\mathbf{x}$ and $\mathbf{z}$ are assumed to be independent. We assume that the source amplitudes $\mathbf{z}$ follow a zero-mean Gaussian process and that the indicator process $\mathbf{x}$ follows the assumption that cortical activity is focal and sparse. We hence define $p(\mathbf{x})$ to be a Gibbs distribution with the associated energy $V(\mathbf{x})$ function given by:

$$V(\mathbf{x}) = \sum_{j \in \vartheta_k^i} \left[\alpha_j x_j + \beta_j \sum_{u \in \upsilon_j} \frac{(x_j - x_u)^2}{\gamma_{ju}} \right], \quad (3)$$

where the parameters $\alpha_j > 0$ and $\beta_j > 0$ determine the relative weights of the sparseness and clustering terms; υ_j is the set of nearest neighbors of vertex j; and $\gamma_{ju} > 0$ is a coefficient translating the anatomic-functional priors between locations j and u. γ_{ju} is proportional to the distance between the 2 vertices and to the discrepancy between their orientations (see [8] for details).

The global functional to minimize for seed i at iteration k is thus:

$$U_k^i(\mathbf{x},\mathbf{z}) = \frac{1}{2} [\mathbf{G}_o - \mathbf{G}_\zeta \mathbf{X}\mathbf{z}]^T \mathbf{C}_n^{-1} [\mathbf{G}_o - \mathbf{G}_\zeta \mathbf{X}\mathbf{z}] + \frac{1}{2} \mathbf{z}^T \mathbf{C}_z^{-1} \mathbf{z} + V(\mathbf{x}), \quad (4)$$

where $\mathbf{C}_n$ (res. $\mathbf{C}_z$) is the covariance matrix for the perturbation process $\mathbf{b}$ (res. the amplitude process $\mathbf{z}$). The mixed-quadratic criterion is minimized using an approach based on the technique described in [4] with an ICM (iterated conditional mode) optimization of the binary indicator process.

2.5 Equivalent cortical patch estimation using scalar multipole expansions

A direct approach to remapping inspired by inverse problem techniques would be to define the gain vector $\mathbf{G}_i$ as the forward field of source i sampled at the sensor array. But there is no fundamental requirement that we directly match the sampled magnetic field $\mathbf{B}$ of the equivalent parametric and cortical sources. Indeed, as the current distribution is zero outside the head, $\mathbf{B}$ is the negative gradient of a scalar magnetic potential V_m obeying Laplace's equation. V_m can hence be expressed in terms of a spherical harmonic multipole expansion the moments of which are related to the current source density. Hence matching the magnetic fields everywhere outside the head reduces to matching the moments of the original source density. If the original source consists of dipoles for instance, it is straightforward to relate it to a multipole series about the origin [9]. Shift equations also exist to relate a multipolar expansion about a given point to one expanded also about the origin [10]. As potentials related to moments of order n fall off as $r^{-(n+1)}$, we may assume that most of brain sources may be reasonably described with moments of order up to 4 (i.e. octapoles). This means that the cortical remapping can be done with gain vectors describing only the first 15 moments of the scalar multipole expansion of the source about the origin (dipole: 3; quadrupole:5; octapole:7). Hence for every original and cortical source, we compute the following gain vector containing the 15 first moments of the multipole expansion of the source about the origin:

$$\mathbf{G}_i = \begin{bmatrix} \mathbf{I}_3 & & 0 \\ & \frac{1}{r}\mathbf{I}_5 & \\ 0 & & \frac{1}{r^2}\mathbf{I}_7 \end{bmatrix} \begin{bmatrix} \mathbf{m}_i \\ \mathbf{Q}_i^r + \mathbf{\Lambda}_1 \mathbf{m}_i \\ \mathbf{O}_i^r + [\mathbf{\Lambda}_{2,1}, \mathbf{\Lambda}_{2,2}] \begin{bmatrix} \mathbf{m}_i \\ \mathbf{Q}_i^r \end{bmatrix} \end{bmatrix} \quad (5)$$

where $\mathbf{m}_i = \frac{1}{2}\mathbf{r} \times \mathbf{J}(\mathbf{r})$ is the equivalent magnetic dipole of source $\mathbf{J}(\mathbf{r})$ located at $\mathbf{r}$; $\mathbf{Q}_i^r$ are the quadrupole moments of the source, and $\mathbf{O}_i^r$ its octapolar moments, both expanded about $\mathbf{r}$; $\mathbf{\Lambda}_j$ are matrix kernels derived for the shift equations (see [10] for details); and $\mathbf{I}_j$ stands for the identity matrix of size j. The matrix on the left in (5) - subsequently denoted by $\frac{1}{r^{\bullet}}\mathbf{I}_{\bullet}$ - allows a scaling of all the mutipole moments to the same unit and facilitates better conditioning of $\mathbf{G}_{\zeta}$. For dipoles, the multipole expansion is linear in terms of the equivalent magnetic moment and simplifies to:

$$\mathbf{G}_i = \frac{1}{r^{\bullet}}\mathbf{I}_{\bullet} \begin{bmatrix} \mathbf{I}_3 \\ \Lambda_1 \\ \Lambda_{2,1} \end{bmatrix} [\mathbf{r} \times \mathbf{o}_i], \quad (6)$$

$\mathbf{o}_i$ being the orientation of source i.

The advantages of this methodology include: (i) original and cortical sources are explicitly matched without reference to the source fields; (ii) there is no need to compute the forward fields on the entire set of several thousand cortical vertices, thus saving computation time, memory and storage; (iii) the remapping and imaging approaches also benefit from faster computational speed as the gain matrices to manipulate are 15 rows tall rather than having dimension equal to the number of sensors which could be several hundred for recent MEG systems (iv) patches need not have uniform activation fields. Our Matlab code for remapping on a 5,000-node cortex takes about 5secs on a PIII 650, 128MB.

3 Results

3.1 Simulations

A 5,000-node white/gray matter interface was extracted using the BrainSuite software (USC, http://neuroimage.usc.edu). Monte-Carlo (MC) simulations were performed by growing about 2300 cortical patches at randomly selected locations on the cortical surface with areas ranging from 0.3cm^2 to 15.3cm^2 (median 4.1cm^2). Uniform illumination was assigned to the cortical dipoles within a patch using a 100-time-sample waveform for active dipoles. MEG signals were simulated on 138 axial gradiometers (5cm baseline) uniformly distributed about the upper hemisphere of a spherical head. Gaussian white noise was added to the signals with a uniform level across all the channels of 10% of the peak of maximum amplitude.

At every MC trial, the parametric estimation with RAP-MUSIC consisted of finding the best dipole source that could account for the signal generated by the patch. Cortical remapping was then applied to the source found. $\mathbf{C}_n$ (res. $\mathbf{C}_z$) is chosen as $\sigma^2\mathbf{I}$ (res. $\sigma_z^2\mathbf{I}$) with $\sigma^2 = 10^{-2}$ (res. $\sigma_z^2 = 10\text{nA.m}$). α_j and β_j were set to 10^{-5} for every source, and no priors besides connectivity were taken into account when generating the original patches, hence $\gamma_{j,u} = 1$ for all pairs of neighbors.

3.2 Results

The patches generated in the MC simulations were gathered in 5 classes according to their area. Each class was labelled by the average value of the patch areas within that class. Following source remapping, the estimated area and the subspace correlation with the original cortical patch were computed. We designed an area-matching criterion from the original and the remapped patches: it consisted of a uniformly weighted sum of (i) the relative localization error of the patch centroid; (ii) the discrepancy with the original patch area; (iii) the overlap with the original patch and (iv) an affine transform of the resulting subspace correlation

$sc \in [0,1]$: $10\,sc-9$. This area-matching criterion takes its values between 0 (no match) and 100% (perfect match). Fig.1 shows there is no significant degradation of the remapping with increasing area of the original cortical patch (average matching criterion: 87%).

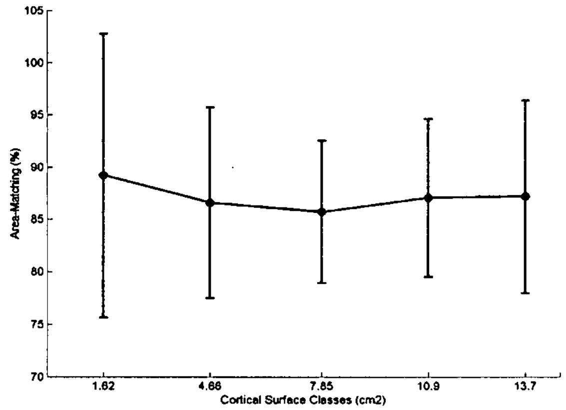

Figure 1: *Area-matching criterion for each of the 5 patch classes.*

More specifically, the subspace correlation with the original patch was excellent (average .993) even though the original parametric source tended not to fit the original forward field as well when the active cortical area increases (average .985) (see Fig.2).

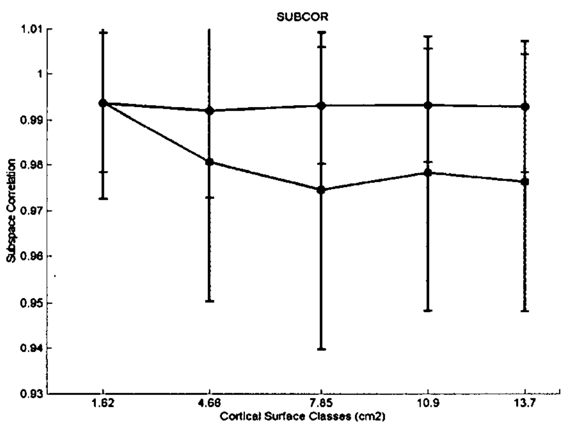

Figure 2: *Comparison of subspace correlation between the original patch and the parametric source (squares) or the remapped source (circles).*

A nice feature of the remapping method is that the original area is restored as shown Fig. 3 with surprising accuracy.

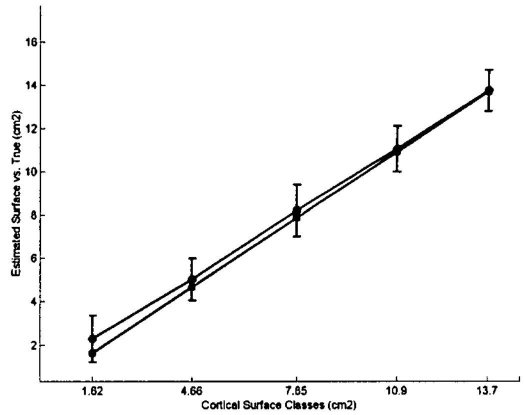

Figure 3: *Estimated (circles) vs. true (squares) value of the surface of the active cortical surface.*

The estimator succeeds in recovering quantitatively the area of the original surface with a correlation of .99.

4. Conclusion

We have presented a fast and promising method to localize and estimate the spatial extent of activated cortical regions in MEG. Further developments will consist of evaluating and correlating these new quantitative indices under various protocols and conditions.

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