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LA-UR- 01-0643

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Title: ERROR BOUNDS IN MEG (MAGNETOENCEPHALOGRAPHY) MULTIPOLE LOCALIZATION

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Submitted to: 12th International Conference on Biomagnetism, Helsinki University of Technology, Espoo, Finland.

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Error Bounds in MEG Multipole Localization

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1 Introduction

Magnetoencephalography (MEG) is a non-invasive method that enables the measurement of the magnetic field produced by neural current sources within the human brain. Unfortunately, MEG source estimation is a severely ill-posed inverse problem. The two major approaches used to tackle this problem are "imaging" and "model-based" methods. The first class of methods relies on a tessellation of the cortex, assigning an elemental current source to each area element and solving the linear inverse problem. Accurate tessellations lead to a highly underdetermined problem, and regularized linear methods lead to very smooth current distributions. An alternative approach widely used is a parametric representation of the neural source. Such model-based methods include the classic equivalent current dipole (ECD) and its multiple current dipole extension [1]. The definition of such models has been based on the assumption that the underlying sources are focal and small in number.

An alternative approach reviewed in [4], [5] is to extend the parametric source representations within the model-based framework to allow for distributed sources. The multipolar expansion of the magnetic field about the centroid of a distributed source readily offers an elegant parametric model, which collapses to a dipole model in the limiting case and includes higher order terms in the case of a spatially extended source. While multipolar expansions have been applied to magnetocardiography (MCG) source modeling [2], their use in MEG has been restricted to simplified models [7]. The physiological interpretation of these higher-order components in non-intuitive, therefore limiting their application in this community (cf. [8]).

In this study we investigate both the applicability of dipolar and multipolar models to cortical patches, and the accuracy with which we can locate these sources. We use a combination of Monte Carlo analyses and Cramer-Rao lower bounds (CRLBs), paralleling the work in [3] for the ECD. Results are presented for both point sources and cortical patches.

This work was supported in part by the National Institute of Mental Health under Grant ROI-MH53213, and in part by Los Alamos National Laboratory, operated by the University of California for the United States Department of Energy under Contract W-7405-ENG-36.

2 Methods

2.1 MEG Multipolar Expansions

The external magnetic field is generated by the sum of the *primary neural activity*, designated by the current density vector $\boldsymbol{j}^P(\boldsymbol{r}')$, and the *volume* or *return currents* resulting from the electric field produced by the current source. It is the primary currents that are the sources of interest in MEG inverse problems [1]. In the special case treated here of radial measurements for sources confined to a spherical volume, the volume currents do not contribute to the measured field, and the radial component $b_r(\boldsymbol{r})$ of the magnetic field $\boldsymbol{b}(\boldsymbol{r})$ at location $\boldsymbol{r}$ is given by the well known equation:

$$b_r(\boldsymbol{r}) \equiv \frac{\boldsymbol{r}\cdot\boldsymbol{b}(\boldsymbol{r})}{r} = \frac{\boldsymbol{r}}{r}\cdot\frac{\mu_0}{4\pi}\int_V \boldsymbol{M}(\boldsymbol{r}')/d^3(\boldsymbol{r},\boldsymbol{r}')d\boldsymbol{r}' \qquad (1)$$

where $\boldsymbol{d}(\boldsymbol{r},\boldsymbol{r}') = \boldsymbol{r}-\boldsymbol{r}'$ is the distance vector between the sensor and source locations, $d(\boldsymbol{r},\boldsymbol{r}') = \|\boldsymbol{r}-\boldsymbol{r}'\|$ the corresponding scalar distance, $\boldsymbol{r}/r$ is a unit vector pointing in the radial direction, and V is any volume containing the primary source activity. We define the *magnetic moment density* or *magnetization* as $\boldsymbol{M}(\boldsymbol{r}') \equiv \boldsymbol{r}'\times\boldsymbol{j}^P(\boldsymbol{r}')$.

The first order multipolar representation is derived using a truncated Taylor series expansion of the distance $d(\boldsymbol{r},\boldsymbol{r}')$ about $\boldsymbol{r}_l$, the centroid of the region to which the primary source is confined:

$$d(\boldsymbol{r},\boldsymbol{r}_l+\boldsymbol{x})^{-3} \cong d(\boldsymbol{r},\boldsymbol{r}_l)^{-3} + 3d(\boldsymbol{r},\boldsymbol{r}_l)^{-5}(\boldsymbol{x}\cdot\boldsymbol{d}(\boldsymbol{r},\boldsymbol{r}_l)). \qquad (2)$$

We truncate the series after the 1st-order term, with the assumption that $x^2 \ll d(\boldsymbol{r},\boldsymbol{r}_l)^3$, which is to say that the source does not have a large radius relative to the distance to the observation point. Inserting *(2)* into *(1)* yields the magnetic multipolar expansion

$$b_r(\boldsymbol{r}) \cong \frac{\mu_0}{4\pi}\frac{\boldsymbol{r}}{r\|\boldsymbol{r}-\boldsymbol{r}_l\|^3}\cdot \left(\int \boldsymbol{M}(\boldsymbol{r}_l+\boldsymbol{x})d\boldsymbol{x} + \frac{3}{\|\boldsymbol{r}-\boldsymbol{r}_l\|^2}\left(\int \boldsymbol{M}(\boldsymbol{r}_l+\boldsymbol{x})\boldsymbol{x}d\boldsymbol{x}\cdot(\boldsymbol{r}-\boldsymbol{r}_l)\right)\right) \qquad (3)$$

where the integration is carried out over the volume of the primary source activity, centered on $\boldsymbol{r}_l$.

Equivalent Magnetic Moment (EMM):

Let the extent of the primary source activity V be sufficiently small that the second term in the multipolar expansion is negligible. As shown in [4], we can rewrite *(3)* as

$$b_r(r) = \frac{r}{r}\cdot\frac{\mu_0}{4\pi}\int\frac{M(r_l+x)}{\|r-r_l\|^3}dx = \frac{\mu_0}{4\pi}\frac{r\cdot m}{r\|r-r_l\|^3} \tag{4}$$

where we define m to be the *magnetic moment*

$$m(r_l) \equiv \int(r_l+x)\times f^P(r_l+x)dx\,. \tag{5}$$

Furthermore, if we define $q(r_l) \equiv \int f^P(r_l+x)dx$ to be the *equivalent current dipole*, we can express *(5)* as

$$m(r_l) = r_l\times q(r_l) + \tilde{m}(r_l) \tag{6}$$

where $\tilde{m}(r_l) \equiv \int x\times f^P(r_l+x)dx$ is the magnetic dipole moment centered at r_l due to the primary current density. Thus this model includes the equivalent current dipole as a limiting case where the source either has virtually no spatial extent or no net magnetic dipole moment.

First-Order Multipole:

If the spatial extent of the source is sufficiently large, then we retain the first two terms in the Taylor series and rewrite *(3)* as

$$b_r(r) \cong \frac{\mu_0}{4\pi}\cdot\frac{r}{rd^3(r,r_l)}\cdot\left(m(r_l)+\frac{3(Q(r_l)\cdot d(r,r_l))}{d^2(r,r_l)}\right) \tag{7}$$

where $Q(r_l)$ is the magnetic quadrupolar term defined as the 3×3 tensor product $Q(r_l) \equiv \int M(r_l+x)x dx$. We can rewrite this tensor using the Kronecker product $a\otimes b$, defined as the concatenation of the product of each element of a with the vector b, and the operator $\mathrm{vec}(A)$, defined as the concatenation of the columns of a matrix A into a vector:

$$b_r(r) \cong \frac{\mu_0}{4\pi}\left(\frac{r}{rd^3(r,r_l)}\cdot m+\frac{3(d(r,r_l)\otimes r)}{rd^5(r,r_l)}\cdot\mathrm{vec}(Q)\right) \tag{8}$$

where for notational convenience we drop the dependency of m and Q on r_l. We therefore characterize the first-order multipole using the combination of the three magnetic moment vector m, the nine magnetic quadrupolar terms in Q, and the location r_l.

2.2 Cramer-Rao Lower Error Bounds

The Cramer-Rao lower bound (CRLB) is an important result in estimation theory that establishes a lower bound on the variance of any unbiased estimator of a set of unknown parameters. We model the MEG data as

$$F = G(l)u + N \tag{9}$$

where $G(l)$ is the gain matrix at location l, and u is the magnitude and orientation of the source moments, i.e. $u = q$ or $u = m$ for the ECD and EMM models respectively. We restricted our theoretical error analysis in this paper to the dipolar models (see comments in Section 4. N is the additive noise assumed to be white and Gaussian. We denote the parameters to be estimated by $\theta = \{l, u\}$. The CRLB is given by the inverse of the Fisher Information Matrix (FIM):

$$J_{ij} = [CRLB(\theta)]_{ij}^{-1} = \frac{1}{\upsilon}\cdot\frac{\partial(Gu)^T}{\partial\theta_i}\cdot\frac{\partial(Gu)}{\partial\theta_j} \tag{10}$$

for $i,j=1, \ldots, P$, where P is the number of parameters and υ is the noise variance.

In this study, we are specifically interested in the additional localization error associated with using an equivalent magnetic multipole instead of the classical current dipole, even if the source is indeed only a current dipole. We are motivated by the simpler form of the magnetic moment model and the need to reduce the search complexity in inverse work. The equivalent CRLB expressions for the current dipole can be found in [3]. For the equivalent magnetic dipole, we rewrite *(8)* as

$$b_r(r) \cong \frac{\mu_0}{4\pi}\left[\frac{r}{rd^3}\right]\cdot m = G(l)\cdot m \tag{11}$$

The partial derivatives of G w.r.t. location l are given by

$$\frac{\partial G}{\partial l^T} \cong \frac{\mu_0}{4\pi}\cdot\frac{3}{rd^5}\cdot[rd]\,\cdot \tag{12}$$

where rd is a 3 x 3 tensor product.

3. Results

3.1 Performance of ECD vs. EMM for a dipolar field

We first evaluate the performance of the model in the simple case of a dipolar field produced by a point source. Fig. 1 and Fig. 2 show the CRLB in the positive x-z-quadrant for the ECD and EMM models

For both models we assumed a *y*-oriented dipolar source of 10 nA-m intensity, a 35 fT noise standard deviation and a 138 axial gradiometer sensor configuration located at 10.5 cm from the head origin and symmetrically covering the upper hemisphere. The contour lines are labeled with the standard deviation σ of the localization error bounds (in mm). Because the EMM has an extra degree of freedom that allows the addition of a magnetic dipole, we see a slight increase in error in the case of an EMM. The difference is negligible, however, for shallow regions, indicating that the EMM can safely be used as an adequate substitute for the ECD model.

To check the efficiency of our estimator, we performed Monte-Carlo simulations for both models based on a RAP-MUSIC estimator [6]. Several locations along the z-axis were tested with 100 random realizations of noise, and the root-mean-square (RMS) error was compared to the CRLB. The results in Fig. 3 and Fig. 4 confirm the formulas and demonstrate the closeness of the CRLBs to the actual RMS error results from the simulations.

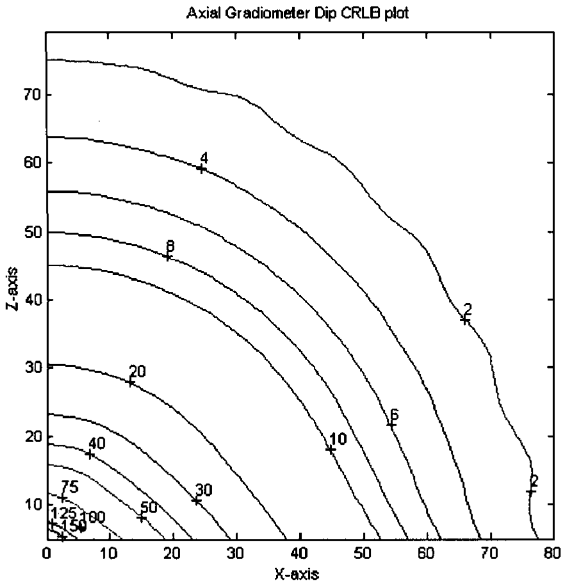

Figure 1: CRLBs for the localization error of an ECD in a spherical head model with radially oriented sensors.

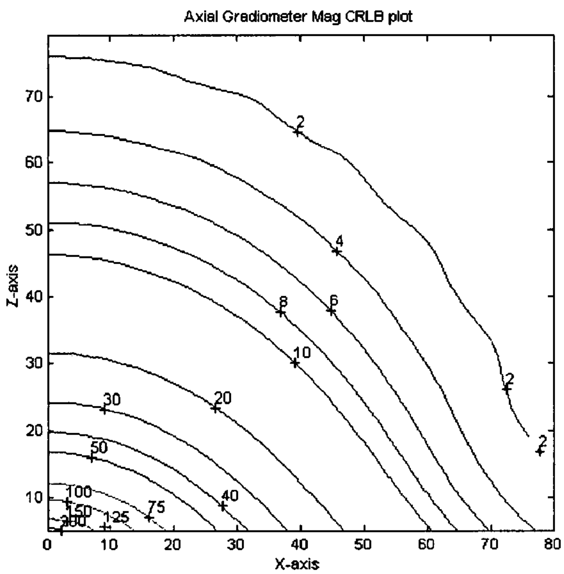

Figure 2: CRLBs for the localization error of an EMM in a spherical head model with radially oriented sensors.

3.2 Localization Error for Cortical Patch Activation

To evaluate the performance of the multipolar model for distributed sources, three activation patches were created on the cortical surface, as shown in Fig. 5. Patch #1 comprises 42 dipoles, each arranged normal to the local cortical surface, and each representing approximately 0.4 mm^2 area of cortex. We adjusted the current density in this patch to achieve three different source models, equivalent respectively to the current dipole, the magnetic

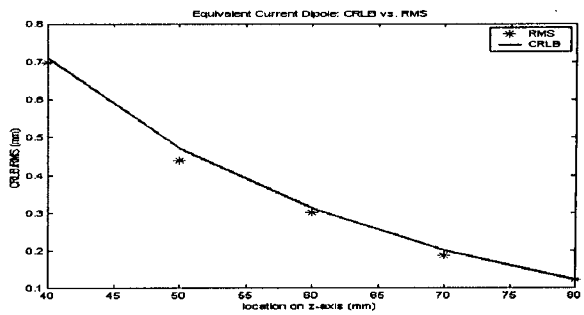

Figure 3: Monte Carlo RMS error and CRLB along the z-axis for the ECD model.

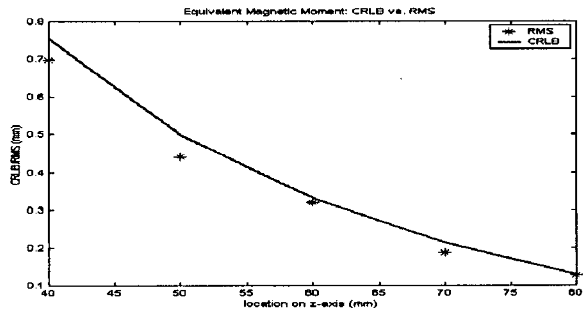

Figure 4: Monte Carlo RMS error and CRLB along the z-axis for the EMM model.

moment, and the multipole. The magnetic moment was formed by explicitly removing the current dipole model, then fitting the magnetic moment. Similarly, the multipole was formed by explicitly removing the magnetic moment, then fitting a multipole. In this manner we achieved a "pure" representations of each of our models for this patch. For each model, we adjusted the source intensity to achieve the same field peak of about 100 fT. We then ran 1,000 realizations of random noise added to this model, each time localizing using the appropriate model in "BrainStorm" (http://neuroimage.usc.edu). The RMS errors in localizing the true location are shown in Table 1. We then repeated this set of models for 100 realizations for Patches 2 and 3 in the figure, which comprised 134 and 137 cortical dipoles respectively, and their results are summarized in Table 2 and Table 3 respectively.

Table 1: Localization error in terms of CRLB and RMS for simulated cortical patch #1.

Patch #1	CRLB (mm)	RMS (mm)
ECD	3.85	3.90
EMM	5.24	5.29
1st-order Multipole	--	7.53

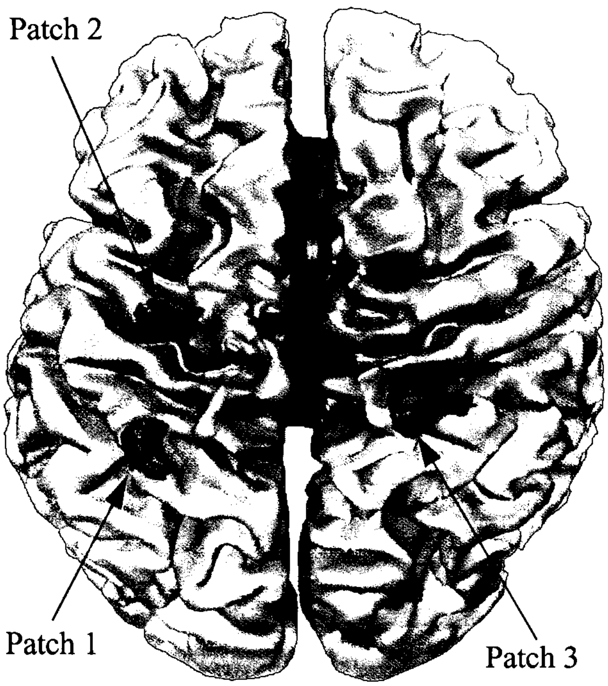

Figure 5: A tessellated human cortex showing mappings of three sources onto the cortical surface.

Table 2: Localization error in terms of CRLB and RMS for simulated cortical patch #2.

Patch #2	CRLB (mm)	RMS (mm)
ECD	2.56	2.53
EMM	6.63	6.67
1st-order Multipole	--	14.34

Table 3: Localization error in terms of CRLB and RMS for simulated cortical patch #3.

Patch #3	CRLB (mm)	RMS (mm)
ECD	2.73	2.67
EMM	7.40	7.07
1st-order Multipole	--	15.73

4. Discussion

Comparing the localization error for the *equivalent magnetic moment* to that of the *equivalent current dipole* model for a dipolar field, both theoretically and through Monte Carlo simulations, shows negligible deterioration in localization accuracy. It therefore appears safe within the proposed multipolar framework to use the EMM instead of the ECD to localize true current dipole sources.

The results for the simulated cortical patches show good agreement between the RMS errors and the CRLBs for the current dipole and the magnetic moment models, indicating the utility of the CRLBs in analyzing their performance, without the need for extensive Monte Carlos. We note, however, that the RMS errors for the multipolar model are in general substantially better than the CRLBs would indicate. Our multipolar model is unstable in some of its quadrupolar components, which we routinely regularize in BrainStorm. The regularization method chosen here was truncation of the smallest singular values, which introduces a transformation and bias of the variables. The CRLBs discussed here are for unbiased analyses only, and our future work will explore the more difficult analyses of regularized models. Moreover, we expect that further simulations as well as human data will reveal the flexibility and efficiency of the multipolar framework in localizing different neural source patterns thereby providing an important extension to the traditional ECD model for MEG source estimation.

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