Proceedings of the 2nd International IEEE EMBS
Conference on Neural Engineering
Arlington, Virginia · March 16 - 19, 2005

Complex Valued Equivalent-Current Dipole Fits for MEG Responses

Yadong Wang[1], Nayef E. Ahmar[2], Juanjuan Xiang[2], Ling Ma[3], David Poeppel[1,4], Jonathan Z. Simon[2,3,4]
[1]Cognitive Neuroscience of Language Laboratory
[2]Department of Electrical and Computer Engineering
[3]Bioengineering Program
[4]Department of Biology
University of Maryland, College Park
jzsimon@eng.umd.edu

Abstract - Complex numbers appear naturally in biological systems in the context of the Fourier transform. In particular, physiological magnetic field data from whole head magneto-encephalography (MEG) is complex after a Fourier transform. The whole-head MEG Steady State Response (SSR) to a stationary modulated stimulus results in a complex magnetic field for each MEG channel, from the frequency corresponding to that of the stimulus modulation. This complex data set is used to estimate the neural current sources generating the magnetic field, naturally leading to complex current sources. We show that standard inverse methods of estimating the current sources, such as the single equivalent-current dipole, generalize to complex sources in a useful and straightforward manner. The usage and utility of the complex magnetic field and the complex neural current source are demonstrated using examples from auditory SSR experiments.

I. Introduction

The Fourier transform takes a real valued time-varying signal and represents the same signal by a complex valued function of frequency. The original signal, at one time instant, is represented by a single real number, but the Fourier transform, for a particular frequency, is represented by two real numbers, e.g. a magnitude and a phase.

Magnetoencephalography (MEG) measures the magnetic fields generated by neural currents. These electrical currents generate measurable magnetic fields according to the classical physical equations of electrodynamics. The small (hundreds of femtoteslas) signals can be measured with superconducting quantum interference devices (SQUIDs) [1]. Just as real numbers can be usefully generalized to complex numbers, real valued fields can be generalized to complex valued fields, and, in particular, real valued vector fields can be generalized to complex valued vector fields. In the case of MEG signals, the Fourier transform of the time varying magnetic field generates a complex magnetic field, for every spatial point (channel) the field is measured, at each frequency. Related transforms, such as the wavelet transforms, also give complex valued fields.

The utility of these complex valued responses can be seen in experiments that use the Steady State Response (SSR) paradigm. In this paradigm, a time-stationary stimulus with periodic structure generates a neural response with the same periodic structure. Example stimuli from auditory studies include pure tones with periodically modulated amplitude and periodic trains of short-duration clicks (or tone-pips), and others. In each case, there is a corresponding neural response with the same periodicity. The MEG SSR for sinusoidally amplitude modulated (SAM) tones has been well documented [2-4] and the sister phenomenon in electroencephalography (EEG) has a long and rich history [5]. For SAM tones, the frequency at which the response is strongest is the stimulus modulation frequency. The magnetic field response at the stimulus modulation frequency gives a complex magnetic field: both phase and amplitude information.

The interpretation of the amplitude is standard: it is the strength of the response at the stimulus modulation frequency. The interpretation of phase is also straightforward: it corresponds to the time-delay of the response in units of the stimulus modulation frequency (for phase measured in cycles).

The measured magnetic fields are typically not the final result; rather, the neural currents generating them. There are several approaches used to tackle this "inverse" problem [6]. One of the simplest is the equivalent-current dipole approximation, which uses a classic least-squares minimization algorithm, along with physical simplifications due to Sarvas [7]. The result is one or more equivalent-current source dipoles, which generate a magnetic field configuration approximating the observed magnetic field configuration.

Applying this procedure to a real magnetic field leads to real equivalent-current dipoles, each of which, in addition to its location, is described by the three real numbers needed to fully describe a real vector: the three components (q_x, q_y, q_z), or equivalently, a two-dimensional orientation (θ, φ) and a magnitude (q). A complex magnetic field configuration leads to complex equivalent-current dipoles, each of which, in addition to its location, is described by three *complex* numbers, or equivalently *six real* numbers. It is tempting to describe a complex dipole vector solely by its orientation (two real numbers) and a complex magnitude (two real numbers, e.g. magnitude and phase), but this does not cover all six of the necessary degrees of freedom.

II. Methods

A. Complex Magnetic Fields from MEG and SSR Analysis

For specificity, we present the case of a stimulus with a single modulation frequency (f_{mod}), and a response

0-7803-8709-0/05/$20.00©2005 IEEE

measurement window of duration (T) which is much longer than a single cycle period ($T_{mod} = 1/f_{mod}$) and is an integer multiple of it ($T = NT_{mod}, N >> 1$). In this case, the SSR complex response is given by the Nth component of the discrete Fourier transform of the time waveform of the response (where the DC response is the zeroth component). We make the further simplifying assumption that the MEG sensors are simple magnetometers or gradiometers (e.g. not vector magnetometers), giving a scalar (single real number) valued waveform. This gives a time-waveform at each MEG channel, derived from the time-varying real magnetic field, spatially discretized and spatially projected into each sensor. Each channel's time-waveform is discrete Fourier transformed and only the component corresponding to the stimulus frequency is examined. The result is a map of complex SSR responses, i.e. a map of (spatially discretized) complex magnetic field projections. A typical response pattern is shown in Fig. 1, for $f_{mod} = 32$ Hz and $T = 100$ s, for a single subject. Each sensor's complex response is depicted by a phasor, i.e. a vector arrow whose magnitude is proportional to the response magnitude and whose direction corresponds to the phase.

The whole head complex SSR can connect visually with commonly used magnetic field contour maps by projecting the complex values onto a complex line of constant phase. That is the complex numbers are turned into real (positive and negative) numbers by rotating them by the phase of this complex line and then taking the real part. This visual aid can greatly increase a viewer's ability to see natural structures in the array of complex responses. One straightforward method is to use the phase of the peak of the spatial variance as measured over half the modulation cycle.

B. Complex Single Equivalent-Current Dipole

1) Forward Problem

The whole-head magnetic field is calculated using the complex version of the Sarvas spherical head model [7]. Outside the spherical conductor (head), the *complex* magnetic field $\mathbf{b}$ at a sensor with location $\mathbf{r}$ is given by [8]:

$$\mathbf{b}(\mathbf{r}) = \frac{\mu_0}{4\pi F^2(\mathbf{r},\mathbf{r_q})}(F(\mathbf{r},\mathbf{r_q})\mathbf{q}\times\mathbf{r_q} - (\mathbf{q}\times\mathbf{r_q}\cdot\mathbf{r}\ \nabla F(\mathbf{r},\mathbf{r_q})) \quad (1)$$

where $\mathbf{r}_q$ is location of the *complex* current dipole $\mathbf{q}$, $F(\mathbf{r},\mathbf{r_q}) = d(rd + r^2 - (\mathbf{r_q}\cdot\mathbf{r}))$, $\mathbf{d} = \mathbf{r} - \mathbf{r_q}$ and $d = |\mathbf{d}|$ .The complex magnetic field at a sensor due to multiple current dipoles is the simple sum of the contributions from each individual dipole.

For an axial gradiometer system a measurement is given by

$$m(r_i) = \mu(b(r_{upper}) - b(r_{lower})), \quad (2)$$

where r_{upper} and r_{lower} are locations of two adjacent coils, μ is a constant, and i ranges over the channels.

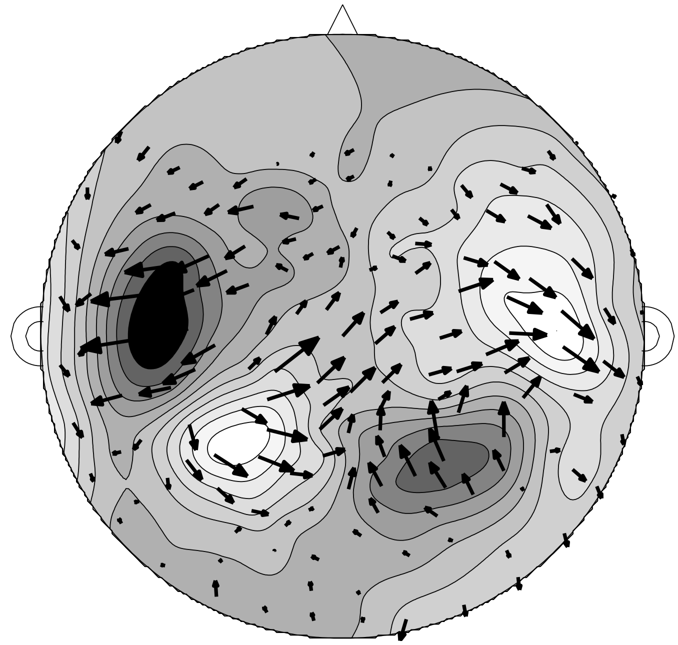

Fig. 1. Whole-head SSR from one subject in an auditory MEG experiment. The 157 channels are shown on the surface of a flattened head. Each arrow represents the complex field value at a sensor.

2) MRI-MEG Matching and Realistic Head Models

Accurate solutions to forward problem require anatomical information obtained from high-resolution volumetric brain images obtained with MRI. If this is not available, a virtual MRI file may be generated from Polhemus data, consisting of head shape file and marker coil file. The measurement given by our system is based on MEG machine coordinates. The virtual MRI coordinates must be aligned with the coordinate system in MEG machine before analysis can begin. This process is done with help of 5 markers in our system. The transform matrix between MEG machine coordinates and MRI coordinates is given as

$$\begin{bmatrix} x_{mri} \\ y_{mri} \\ z_{mri} \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix} \begin{bmatrix} x_{meg} \\ y_{meg} \\ z_{meg} \end{bmatrix} + \begin{bmatrix} x_d \\ y_d \\ z_d \end{bmatrix} \quad (3)$$

where $\begin{bmatrix} x_d & y_d & z_d \end{bmatrix}^T$ are displacements. This matrix enables us to transform between the coordinate systems.

The closed-form solution for the forward problem has been discussed in previous section for heads with conductivity profiles that can be modeled as a set of nested concentric homogeneous and isotropic sphere. In real experiments, however, heads usually are inhomogeneous, anisotropic and not spheres. Nevertheless a spherical head may approximate the real head. The sphere should be the best fit possible (in the sense of least mean square error) with the head shape. The spherical models approximation work reasonably well as reported by Baillet et al. [6].

3) Calculate Lead Field for Spherical Heads

If the primary sources were specified in both locations and moments, then calculation of (1) could proceed directly, given the sensors location. The inverse problem, however, involves finding both a suitable set of sources and their corresponding location, which best approximate the data given. This can be implemented in a two-step approach, where the location is found before the source moments are calculated. It is applicable because the complex magnetic field is linear with respect to the dipole moment and nonlinear with respect to the location, as seen in (1).

Since the complex magnetic field is linear with respect to the complex dipole moment $\mathbf{q}$, we may decompose moment $\mathbf{q}$ into three orthogonal complex dipole components and calculate the magnetic field for each of them. Denote the dipole location as $\mathbf{r}_q = [r_x \quad r_y \quad r_z]^T$, or in polar format as $\mathbf{r}_q = (|\mathbf{r}_q|, \theta, \phi)$. We may treat the direction of $\mathbf{r_q}$ as a new x-axis and define a new 3 dimensional coordinate system. Then the projection of $\mathbf{q}$ into this new three dimension coordinate system can be represented by

$$\begin{bmatrix} q'_x \\ q'_y \\ q'_z \end{bmatrix} = \begin{bmatrix} \sin(\theta)\cos(\phi) & \sin(\theta)\sin(\phi) & \cos(\theta) \\ \cos(\theta)\cos(\phi) & \cos(\theta)\sin(\phi) & -\sin(\theta) \\ -\sin(\phi) & \cos(\phi) & 0 \end{bmatrix} \mathbf{q} \quad (4)$$

Sarvas [7] shows that radically oriented dipoles do not produce any external magnetic field outside a spherically symmetric volume conductor, regardless of the sensor orientation. Since q'_x is always radically oriented, we may ignore its effect on the magnetic field. Instead having three free components of $\mathbf{q}$, we need calculate only two. We may project $\mathbf{q}$ into q'_y and q'_z, and the lead field $\mathbf{A}$ can be easily computed.

4) *Inverse Problem*

Using the above spherical head model for the forward problem, we follow a linear model to solve the inverse problem [6]. As above, the complex magnetic field is linear with respect to the complex dipole moment $\mathbf{q}$ and nonlinear with respect to the location $\mathbf{r_q}$. For simultaneous MEG measurements made at N sensors by p dipoles, $\mathbf{M} = \mathbf{A}\mathbf{S}^T$, where $\mathbf{M}$ is an array of the complex MEG measurements at the N sensors, $\mathbf{S}^T$ is an array of $2p$ complex dipole magnitudes (a pair for each dipole, corresponding to the spatial projections of the two independent orientations, q'_y and q'_z, perpendicular to the radial direction), and $\mathbf{A}$, the *lead field matrix* is defined by the linear relationship between $\mathbf{M}$ and $\mathbf{S}^T$ in (1).

In the presence of measurement errors, the forward model may be represented as $\mathbf{M} = \mathbf{A}\mathbf{S}^T + \varepsilon$, where ε is a complex spatio-temporal noise (error) matrix. By defining the cost function as the measure of fitness, the least-squares estimation minimizes the cost function

$$J_{LS} = \left\| \mathbf{M} - \mathbf{A}\mathbf{S}^{\mathbf{T}} \right\|_F^2, \quad (5)$$

where the cost function is calculated by the Frobenius norm of the complex error matrix.

For any selection of sensor locations and complex dipole locations, the matrix $\mathbf{S}$ that will minimize J_{LS} is $\mathbf{S}^T = \mathbf{A}^+\mathbf{M}$, where $\mathbf{A}^+$ is the pseudoinverse of $\mathbf{A}$. We then solve for J_{LS} by minimizing the adjusted cost function:

$$J_{LS} = \left\| \mathbf{M} - \mathbf{A}(\mathbf{A}^+\mathbf{M}) \right\|_F^2 = \left\| (\mathbf{I} - \mathbf{A}\mathbf{A}^+)\mathbf{M} \right\|_F^2 \quad (6)$$

Minimization methods range from grid search and downhill simplex searches to global optimization schemes [9].

It should be emphasized that the key feature of this method is the generalization of the magnetic field and the source vectors to complex quantities. Aside from this essential difference, the algorithm is unchanged from the real version [6].

C. *Complex Multi-Equivalent-Current Dipole Fitting*

MEG is especially sensitive to neuronal activity in auditory cortical areas. MEG auditory responses lateralize strongly (in contrast to EEG responses which mix across cortical hemispheres and are strongest medially), making multi-equivalent-current dipoles fitting necessary.

III. Example from Auditory SSR

As an example of the utility of the complex equivalent-current dipole analysis method, we calculate a transfer function: the response (strength and phase), at the stimulus frequency, as a function of stimulus frequency. The auditory whole-head SSR is measured for several frequencies.

Sinusoidally amplitude-modulated sounds of 1 s duration were presented to each subject. The 4 stimuli were made with a carrier of 400 Hz and modulation frequencies 16 Hz, 32 Hz, 48 Hz and 64 Hz. All 4 stimuli were presented 100 times in a random order with interstimulus intervals from 400 to 550 ms, interspersed with other modulated stimuli. The loudness was approximately 70 dB SPL.

Recordings were performed in a magnetically shielded room. The magnetic signals were recorded using a 160-channel, whole-head axial gradiometer system (KIT, Kanazawa, Japan).

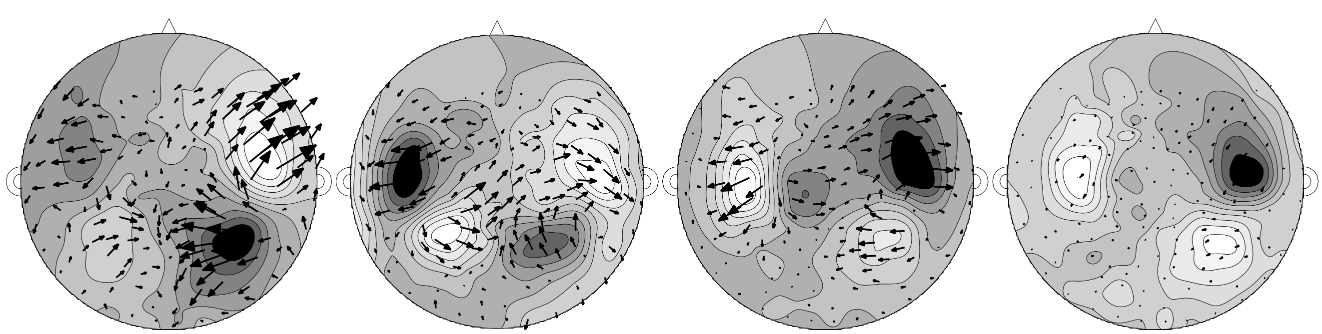

Fig. 2 Responses from the same subject for four different modulation frequencies: 16 Hz, 32 Hz, 48 Hz, 64 Hz. In every case, each hemisphere is dominated by a classic pattern of dipole-like generated activity, with variation in location, size, and strength across stimuli.

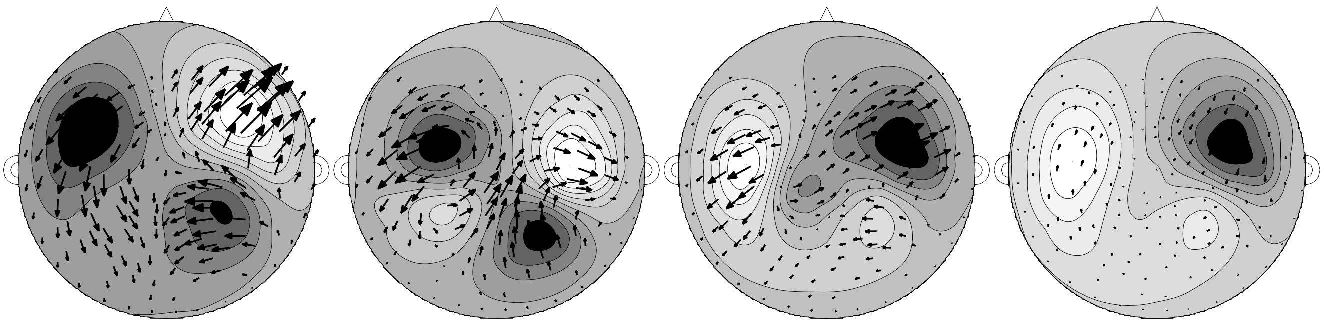

Fig. 3. Results of two-equivalent-current dipoles fitting for the whole head configurations in Fig. 2.

The magnetic signals were bandpassed between 1 Hz and 200 Hz, notch filtered at 60 Hz, and sampled at the rate of 1000 Hz.

The measured responses from 50 to 1050 ms post-stimulus were concatenated, giving 4 total responses (100 s duration) for each channel. The discrete Fourier transform was applied to the concatenated data, giving 4 frequency responses (0.01 Hz resolution) for each channel. The whole-head SSR is the magnitude and phase at the modulation frequency for each channel. The response is characterized by two complex, equivalent-current dipoles responsible for both the right and left-hemispheric portions of the response. The response strength is measured by the two complex dipoles' semimajor axis (of the ellipse swept out by the complex vector), and its phase by the semimajor axis' phase (subtracting the component due the 50 ms delay).

In Figure 2, the whole-head SSR, as a function of stimulus modulation frequency, dramatically shows the MEG response as a function of modulation frequency. Figure 3 shows the results of two equivalent-current dipoles for the same responses. The two hemisphere transfer functions for this subject, as measured by the two complex equivalent-current dipoles, are illustrated in Figure 4, with separate plots for amplitude and phase. This summarizes concisely the data seen in both hemisphere responses in Figure 2: the amplitude graph captures faithfully the visible strength in each hemisphere, and the phase graph captures faithfully the corresponding changes of phase in the same plots.

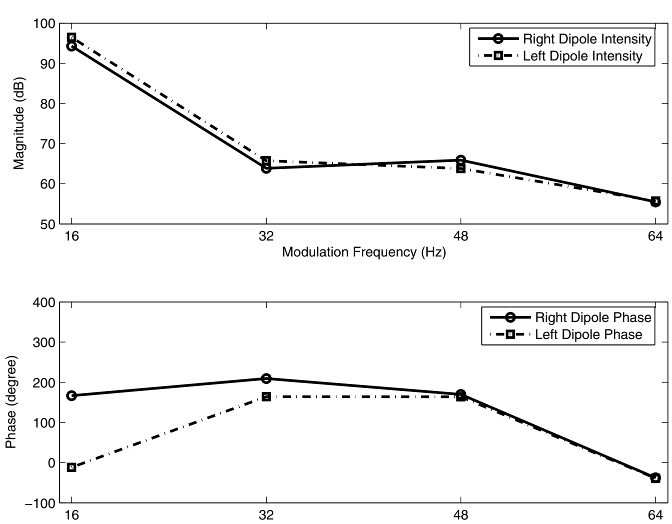

Fig. 4. The transfer function derived from two equivalent dipoles fitting of the whole head aSSRs shown in Fig. 2. Upper graph: Amplitude in dB. Lower graph: Phase in degrees.

IV. Discussion

The complex magnetic field distributions arising in Fourier analyzed MEG studies have a natural interpretation as oscillations with the specified amplitude and phase. Visual representations of the complex responses over the whole head are invaluable in identifying structure and patterns in the whole head response. Additionally, complex magnetic field distributions arise from presumed neural sources with similarly complex properties. None of the methods outlined here are particular to MEG. Only small modifications are necessary to apply the methods to EEG, or related techniques.

References

[1] Hamalainen, M., Hari, R., Ilmoniemi, R. J., Knuutila, J. & Lounasmaa, O. V. Magnetoencephalography - Theory, Instrumentation, and Applications to Noninvasive Studies of the Working Human Brain. *Reviews of Modern Physics* **65**, 413-497 (1993).

[2] Ross, B., Borgmann, C., Draganova, R., Roberts, L. E. &. Pantev, C. A high-precision magnetoencephalographic study of human auditory steady-state responses to amplitude-modulated tones. *J Acoust Soc Am* **108**, 679-91 (2000).

[3] Ross, B., Picton, T. W. & Pantev, C. Temporal integration in the human auditory cortex as represented by the development of the steady-state magnetic field. *Hear Res* **165**, 68-84 (2002).

[4] Schoonhoven, R., Boden, C. J., Verbunt, J. P. & de Munck, J. C. A whole head MEG study of the amplitude-modulation-following response: phase coherence, group delay and dipole source analysis. *Clin Neurophysiol* **114**, 2096-106 (2003).

[5] Galambos, R., Makeig, S. & Talmachoff, P. J. A 40-Hz auditory potential recorded from the human scalp. *Proc Natl Acad Sci U S A* **78**, 2643-7 (1981).

[6] Baillet, S., Mosher, J. C. & Leahy, R. M. Electromagnetic brain mapping. *Ieee Signal Processing Magazine* **18**, 14-30 (2001).

[7] Sarvas, J. Basic mathematical and electromagnetic concepts of the biomagnetic inverse problem. *Phys Med Biol* **32**, 11-22 (1987).

[8] Mosher, J. C., Leahy, R. M. & Lewis, P. S. EEG and MEG: forward solutions for inverse methods. *IEEE Trans Biomed Eng* **46**, 245-59 (1999).

[9] Uutela, K., Hamalainen, M. & Salmelin, R. Global optimization in the localization of neuromagnetic sources. *IEEE Trans Biomed Eng* **45**, 716-23 (1998).