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Fully complex magnetoencephalography

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Abstract

Complex numbers appear naturally in biology whenever a system can be analyzed in the frequency domain, such as physiological data from magnetoencephalography (MEG). For example, the MEG steady state response to a modulated auditory stimulus generates a complex magnetic field for each MEG channel, equal to the Fourier transform at the stimulus modulation frequency. The complex nature of these data sets, often not taken advantage of, is fully exploited here with new methods. Whole-head, complex magnetic data can be used to estimate complex neural current sources, and standard methods of source estimation naturally generalize for complex sources. We show that a general complex neural vector source is described by its location, magnitude, and direction, but also by a phase and by an additional perpendicular component. We give natural interpretations of all the parameters for the complex equivalent-current dipole by linking them to the underlying neurophysiology. We demonstrate complex magnetic fields, and their equivalent fully complex current sources, with both simulations and experimental data.

Keywords: MEG; Steady state response; SSR; Equivalent-current dipole; Auditory

1. Introduction

Physiological questions of the human brain that demand temporal resolution commensurate with neuronal activity require electromagnetic techniques, particularly electroencephalography (EEG) (see, e.g. Gevins et al., 1995) or magnetoencephalography (MEG) (see, e.g. Hari and Lounasmaa, 1989; Lounasmaa et al., 1996). A compelling advantage of MEG is that it allows simultaneous spatial localization ("imaging") and high temporal resolution physiology of the neural sources (Roberts et al., 2000; Krumbholz et al., 2003). Neural sources' ionic currents generate measurable magnetic fields according to the classical physical equations of electrodynamics. The small magnetic signals (hundreds of femtoteslas) propagate outward transparently and can be measured with superconducting quantum interference devices (SQUIDs) (Hamalainen et al., 1993). The types of MEG responses whose source location and stimulus-related properties are commonly interpreted include evoked fields at specific latencies, e.g. the auditory N100 response (Hari et al., 2000) or evoked high frequency responses (Hashimoto et al., 1996); evoked or induced oscillatory responses (Hari and Salmelin, 1997; Lin et al., 2004); and steady state responses (SSR) to ongoing stimuli (Ross et al., 2000). SSR responses are a rich source of neurophysiological data but have received comparatively less attention.

Complex numbers arise naturally whenever any data, such as that from MEG, are analyzed with the Fourier transform. 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 a 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. The magnitude is a non-negative number, and the phase is an abstract angle that varies from 0 to 360° (equivalently, 2π radians, or 1 cycle). 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

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to complex valued vector fields. In the case of MEG signals, the Fourier transform of the time-varying magnetic field generates a complex valued magnetic field, for every spatial point (channel) the field is measured. Related transforms, such as wavelet and other short time Fourier transforms, also result in complex valued magnetic fields.

The utility of these complex valued responses can especially be seen in experiments and analysis that use SSR paradigms. In such paradigms, a stationary stimulus with periodic structure generates a neural response with the same periodic structure. Example auditory stimuli include: narrow- or broad-band carriers with periodically modulated amplitude, and periodic trains of clicks or tone-pips. In each case, there is a corresponding neural response with the same periodicity. The MEG SSR for sinusoidally amplitude-modulated tones has been well documented (Ross et al., 2000; Ross et al., 2002; Schoonhoven et al., 2003) and the SSR in EEG has a long and rich history (Galambos et al., 1981). The strongest frequency response is at the stimulus modulation frequency (harmonic responses are substantially weaker and so are not treated here directly, though their generalizations are straightforward). The response at the modulation frequency gives a complex magnetic field: a magnetic field with amplitude as well as phase as information.

The amplitude simply gives the strength of the response at the modulation frequency. The phase corresponds to the time-delay of the response in units of the modulation frequency, when the phase is measured in cycles. Thus, a 0.010 s delay for a 10 Hz modulation frequency gives a phase of 0.1 cycles (36°, or 0.2π radians). The periodicity property of phase arises from the inability to distinguish time shifts longer than one cycle from the equivalent time shifts shorter than one cycle.

Beyond this simple interpretation, however, the complex nature of these data is not often exploited (some statistical techniques used in EEG do embrace the complex nature of the response, e.g. Picton et al., 2001, 2003). A simple example is the spatial distribution of phase over the whole-head. Multi-channel MEG and EEG data is known for difficulty in its visualizability due to high dimensionality: many channels, many experimental conditions, and many repetitions, each a function of time. A greatly simplified picture results from replacing, for each channel, the entire dimension of time with the single value of the phase (of the frequency of interest). This representation has been used for EEG data analysis (Herdman et al., 2002). Examples of MEG whole-head complex fields in response to auditory stimuli are shown in Fig. 1. In each case, the complex whole-head SSR can be analyzed visually at once, whereas the comparable whole-head response in the time domain (a time waveform displayed over every sensor) is difficult to absorb visually.

The utility of the complex nature of the data goes beyond the field distribution. A complex magnetic field is generated by its complex neural current source, a concept that has only been partially exploited in analysis of data from MEG (Lutkenhoner, 1992) and EEG (Lehmann and Michel, 1989, 1990; Michel et al., 1992).

Several approaches are typically used in MEG analysis to determine the neural current sources of a measured magnetic field (Baillet et al., 2001). One of the simplest is the equivalent-current dipole approximation, which uses a least-squares minimization algorithm, plus simplifications of the physics due to Sarvas (1987). The result of this method is a set of equivalent-current source dipoles. When applied to real magnetic field configurations, the resulting equivalent-current dipoles are real. A real equivalent-current dipole is defined by its location and a real dipole vector **q**. Three real numbers are needed to fully describe a real vector: the three Cartesian components (q_x, q_y, q_z), or equivalently, a two-dimensional orientation (θ, ϕ) and an intensity (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. These can be seen as three complex components, or equivalently the six numbers given by the real and imaginary parts of the three Cartesian components $(\mathrm{Re}\{q_x\}, \mathrm{Re}\{q_y\}, \mathrm{Re}\{q_z\}, \mathrm{Im}\{q_x\}, \mathrm{Im}\{q_y\}, \mathrm{Im}\{q_z\})$. One may attempt to describe a complex dipole vector solely by its orientation (two real numbers) and a complex generalization of the intensity (two real numbers, e.g. a magnitude and phase), but this does not cover all six degrees of freedom. Nevertheless, a generic, complex, equivalent-current dipole can be described naturally and physiologically, in such a way that four of the six degrees of freedom do correspond to orientation and a complex intensity, and the two others are described below.

We discuss the roles and properties of the complex magnetic fields measured by MEG and SSR, which naturally lead to a visualization tool, the "whole-head complex SSR". The inverse problem is solved for a complex magnetic field distribution by determining the complex equivalent-current dipoles. The properties of complex dipoles are described, including all six degrees of freedom. Simulations are shown, and the method's utility is demonstrated with an example of a transfer function computation and an analysis of the variability of neural sources as a function of stimulus parameters.

The general methods outlined here are not special to MEG. Only small modifications are necessary to apply several of these methods to EEG and related techniques.

2. Methods

2.1. Complex magnetic fields from MEG and SSR analysis

A whole-head map of complex SSR responses is obtained by Fourier transforming each channel's response and focusing on the stimulus modulation frequency. For a stimulus with modulation frequency f_{mod} and response measurement duration T, and an integer multiple of the cycle period