MEG-based Brain Functional Connectivity Analysis Using eConnectome

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***Abstract* — eConnectome (electrophysiological Connectome) is an open-source MATLAB software platform with graphical user interfaces for mapping and imaging brain functional connectivity from electrophysiological signals including EEG, ECoG and MEG. We introduce the software platform and report the newly included functionality of MEG connectivity analysis. Simulated and real MEG data were analyzed using the eConnectome. The results indicate the validity of the eConnectome for brain activity and connectivity mapping from MEG data.**

I. Introduction

The brain activity and neuronal network behavior provide important physiological and psychological information. It is significant to map brain activity and image brain functional connectivity to understand the brain functions and dysfunctions [1]. Electrophysiological signals including electroencephalogram (EEG), electrocorticogram (ECoG) and magnetoencephalogram (MEG) are widely used to reveal dynamic activity and functional connectivity of the brain due to their excellent temporal resolution on the order of milliseconds. Significant achievements have been made for mapping the brain activity [2], [3]. However, the brain activity mapping at every instant alone does not convey sufficient information regarding how brain regions communicate with each other. The brain functional connectivity thus plays an important role in understanding the organized behavior of brain regions beyond mapping and localization of their activities [4].

A number of methods can be used to assess the functional connectivity among different brain regions. The widely used directed transfer function (DTF) [5] is a method for extracting directional connectivity from multivariate time series data, and considers the multivariate time series as a stationary process. Previous studies have demonstrated its applications to study causal sources in normal brain functions [6], [7] or abnormal brain disorders [8], [9]. However, the process of real electrophysiological recordings may be dynamic, and the adaptive DTF (ADTF) [10] can then be used to extract time-varying directional connectivity. The ADTF has been demonstrated to hold the promise to reveal dynamic brain functional connectivity [10], [11]. Partial directed coherence (PDC) [12] and direct DTF (dDTF) [13] have also been proposed to estimate directional connectivity.

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eConnectome is a free and open-source MATLAB software developed by our lab for mapping and imaging brain functional connectivity [14]. The visualization module was jointly developed with Drs. Fabio Babiloni and Laura Astolfi at the University of Rome “La Sapienza”. The eConnectome provides graphical user interfaces for interactive analysis of electrophysiological signals, including preprocessing, spatial mapping, source imaging, connectivity estimation and visualization. There are many related software packages for analyzing brain activity from electrophysiological data, including EEGLAB [15], FieldTrip (http://fieldtrip.fcdonders.nl/), NUTMEG [16] and Brainstorm [17]. Compared to these software packages, a unique feature of the eConnectome toolbox is that it provides a flexible and easy-to-use platform to image brain functional connectivity and visualize functional connectivity patterns at both the sensor and source levels based on the standard Montreal Neurological Institute (MNI) brain [18] or a user-defined anatomy. The toolbox is aimed at addressing where, when and how neuronal assemblies are activated and coordinated, and allows users to obtain integrated connectivity visualization results. The first full version of the eConnectome supporting connectivity analysis from EEG and ECoG was released on August 19, 2010 [14]. The functionality of connectivity analysis from MEG was recently developed. In this paper, the functionality of EEG/ECoG connectivity analysis is introduced briefly, and the functionality of the MEG connectivity analysis and the methods implemented are described. Representative MEG analysis results from simulated and real data are presented.

II. Methods

A. EEG/ECoG Connectivity Analysis

The framework of the eConnectome is illustrated in Fig. 1. Major functions in EEG/ECoG connectivity analysis include EEG/ECoG preprocessing, scalp/cortex spatial mapping, cortical source estimation, connectivity estimation and visualization. Granger causality measures including DTF and ADTF were implemented to estimate the directional interactions of brain functional networks, over the scalp and cortical sensor spaces. Cortical current density inverse imaging was implemented using a generic realistic geometry brain-head model from scalp EEGs. Granger causality could be further estimated over the cortical source domain from the inversely reconstructed cortical source signals as derived from the scalp EEG. Estimated connectivity can be visualized over a realistic geometry scalp or cortex surface.

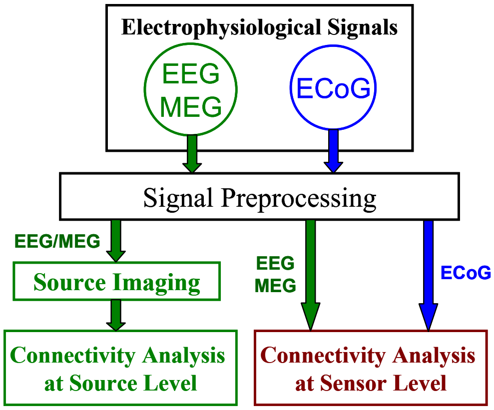

Fig. 1. The framework of the eConnectome. The electrophysiological signals including EEG, ECoG and MEG can be preprocessed before further analysis. Connectivity analysis of the preprocessed multi-channel EEG/ECoG/MEG data can then be performed at the sensor level. Cortical sources can be reconstructed from EEG/MEG data and then connectivity analysis can then be performed at the source level.

B. MEG connectivity Analysis

As illustrated in Fig. 1, preprocessing, source imaging and connectivity analysis can be integrated to analyze functional connectivity from MEG data at the sensor level, as well as the source level.

Multi-channel MEG data can be preprocessed in the time domain (e.g. artifact rejection, baseline correction, filtering). Time-frequency representation of each channel in a trial can be calculated using the Complex Morlet's wavelet [19] and visualized. Paradigm-related analysis and non-phase-locking type of analysis are available to obtain event-related fields (ERF) and event-related synchronization/desynchronization (ERD/ERS) [20], respectively.

MEG sensors are co-registered with the standard MNI brain. The cortical current density (CCD) source model is used to solve the inverse problem from the MEG sensors to cortical source distribution using minimum norm estimate (MNE) or lead field weighted minimum norm (WMN) algorithm. The lead field matrix is computed using the single sphere method [21] and the solution of MNE or WMN is derived using Tikhonov regularization in the regularization toolbox [22]. Cortical sources for a user-defined anatomy can also be reconstructed with the relative user-defined lead field matrix. Representative sources for the regions of interest (ROIs) can then be computed for cortical ROI connectivity analysis.

The DTF and ADTF [10] algorithms were implemented for the estimation of functional connectivity among MEG sensors or cortical ROIs. Statistic evaluation of the connectivity is conducted using the surrogate approaches [8]. Connectivity patterns among MEG sensors can be visualized over the MEG cap surface, while connectivity patterns among cortical ROIs can be visualized over a realistic geometry cortex surface.

C. Experiments and Results

1) Cortical Source Connectivity Analysis

Cortical source connectivity can be estimated from source imaging results. We simulated two fixed dipole sources at the MNI cortex with orientations perpendicular to the local cortical surface. The waveform of source 1 is a segment of real interictal ECoG spikes of 3 s sampled at 400 Hz, while the waveform of source 2 was generated based on a multivariate autoregressive model such that source 1 was the primary driver and source 2 was the sink. Locations and orientations of the MEG sensors and the MEG fiducial locations were from real MEG recordings. The MEG sensors were co-registered into the cortical space and continuous MEG (Fig. 2(a)) was generated by solving a MEG forward problem [21] with the addition of 10% Gaussian white noise.

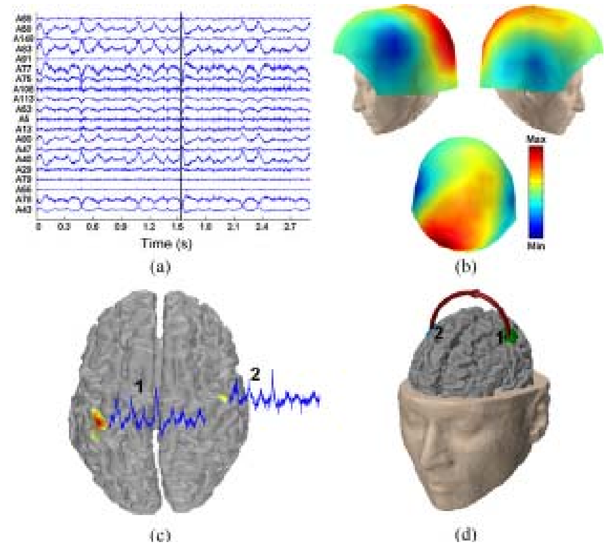

Fig. 2. (a) Waveforms of the simulated MEG. (b) Field map over the MEG sensors at a peak of the waveforms. (c) Cortical sources at the peak. (d) Directional information flow from source 1 to source 2 identified by DTF analysis.

The simulated MEG was processed in the eConnectome by forward modeling, followed by cortical source reconstruction using the MNE method. Field mapping over the MEG sensors and cortical source imaging at a peak of the waveforms are illustrated in Fig. 2(b) and Fig. 2(c), respectively. The visualization threshold for the source image was 50%. Two regions in agreement with the simulated dipole locations displayed significant source activity and thus were selected as source ROIs. Source waveforms at the two ROIs (Fig. 2(c)) were estimated, and the DTF analysis (Fig. 2(d)) showed directional information flow from source 1 to source 2 ($p < 0.05$), which is consistent with the simulation setting.

2) Analysis of Real MEG Data from Thumb Stimulation

Real MEG data from right thumb stimulation were analyzed. The somatosensory MEG recordings sampled by CTF machine (151 axial gradiometers) at 1250 Hz were made available by Dr. Sabine Meunier (Hopital de la Salpetriere, Paris) as part of the tutorial dataset distributed with Brainstorm [17]. The multi-channel waveforms and butterfly/GFP (global field power) of the average response for the right thumb stimulation are shown in Fig. 3(a) and Fig. 3(b), respectively. MEG field mapping and cortical source imaging at the GFP peak (44 ms) are shown in Fig. 3(c) and Fig. 3(d), respectively. The visualization threshold for the source image was 80%. The identified source was approximately in the middle of the left primary somatosensory cortex, which agrees with the right thumb stimulation pattern.

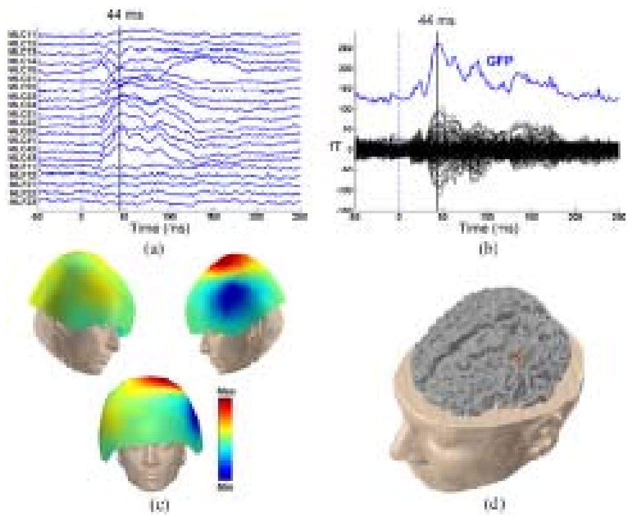

Fig. 3. (a) Multi-channel waveforms of the average response for the right thumb stimulation. (b) Butterfly and global field power of the average response. (c) Field map over the MEG sensors at the peak. (d) Cortical source at the peak.

III. Discussion

eConnectome is a useful software platform for analyzing activity and functional connectivity of the brain from electrophysiological signals including EEG, ECoG and MEG. It can be used to analyze directional connectivity among electrophysiological sensors, as well as cortical ROIs with the aid of cortical source imaging. Constant directional connectivity from stationary electrophysiological recordings can be estimated using the DTF method, while dynamic directional connectivity can be estimated using the ADTF method. Multi-style connectivity patterns including directional information flows, total outflows and total inflows can be visualized vividly at the sensor or source level. The functionality of the software platform will be enhanced gradually in the future to further facilitate brain functional connectivity analysis.

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