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Quantifying the performance of MEG source reconstruction using resting state data

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ABSTRACT

In magnetoencephalography (MEG) research there are a variety of inversion methods to transform sensor data into estimates of brain activity. Each new inversion scheme is generally justified against a specific simulated or task scenario. The choice of this scenario will however have a large impact on how well the scheme performs. We describe a method with minimal selection bias to quantify algorithm performance using human resting state data. These recordings provide a generic, heterogeneous, and plentiful functional substrate against which to test different MEG recording and reconstruction approaches. We used a Hidden Markov model to spatio-temporally partition data into self-similar dynamic states. To test the anatomical precision that could be achieved, we then inverted these data onto libraries of systematically distorted subject-specific cortical meshes and compared the quality of the fit using cross validation and a Free energy metric. This revealed which inversion scheme was able to identify the least distorted (most accurate) anatomical models, and allowed us to quantify an upper bound on the mean anatomical distortion accordingly. We used two resting state datasets, one recorded with head-casts and one without. In the head-cast data, the Empirical Bayesian Beamformer (EBB) algorithm showed the best mean anatomical discrimination (3.7 mm) compared with Minimum Norm/LORETA (6.0 mm) and Multiple Sparse Priors (9.4 mm). This pattern was replicated in the second (conventional dataset) although with a marginally poorer (non-significant) prediction of the missing (cross-validated) data. Our findings suggest that the abundant resting state data now commonly available could be used to refine and validate MEG source reconstruction methods and/or recording paradigms.

1. Introduction

Magnetoencephalography (MEG) detects electromagnetic fields at sensors outside the head. The challenge for the researcher is to infer the neuronal current distribution responsible for the observed data, despite a much higher number of possible sources than sensors. The general approach is to restrict the number of potential solutions through a priori assumptions, including the temporal relationship between sources (i.e. source co-variance) and/or the anatomical manifold that gives rise to this function (e.g. the cortical mesh). These assumptions are continually being refined and debated (Baillet, 2015; Baillet et al., 2001; Lin et al., 2006; Wipf and Nagarajan, 2009). Two recurring issues make it difficult for the community to come to a consensus on optimal source reconstruction methods - the first is the choice of test scenario, the second is the lack of ground truth.

Firstly, the choice of task, or simulation set-up used to compare source localisations will introduce a selection bias towards a specific temporal pattern predominant in certain cortical areas, which will suit some inversion assumptions but not others. Here we set out a framework which utilises diverse spatio-temporal patterns and minimizes selection bias by using a Hidden Markov model (Baker et al., 2014) to parcel endogenous resting-state data into collections of self-similar and quasi-stationary time

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segments. Resting state data have been shown to arise from dynamic spatio-temporal network state fluctuations occurring on the scale of 100–200 ms (Baker et al., 2014; Koenig et al., 2002; Wackermann et al., 1993; Woolrich et al., 2013) that include the rehearsal of the transient dynamic patterns observed during task performance (O'Neill et al., 2017). These networks predominate in all M/EEG recordings (even those which are task based) and are key to healthy brain function (Barttfeld et al., 2015; Kaiser et al., 2015; Lewis et al., 2009; Li et al., 2012; Peterson et al., 2014; Philippi et al., 2015; Reineberg et al., 2015; Sheline and Raichle, 2013; Tessitore et al., 2012; Venkataraman et al., 2012; Wu et al., 2014; Wurina et al., 2012). We rely on these iterant dynamics, rehearsing multiple task scenarios, to provide a varied and unbiased spatio-temporal repertoire of the source reconstruction problems one might expect from any dataset on which to then test our inversion schemes.

The second problem then, having identified an appropriate and representative real dataset (as opposed to simulated data), is the lack of access to the ground truth with which to compare recording/inversion techniques. Here we leverage new analytic techniques to quantify the sensitivity of MEG source inversion schemes by progressively deforming the anatomical models (Lopez et al., 2013; López et al., 2017; Stevenson et al., 2014). Specifically, we quantify how distortions in the MRI-extracted cortical manifold (mesh) affect our ability to predict or model the underlying current distribution (using cross validation error and Free energy). The technique assumes that the MEG sensor level data are due to current flow normal to the cortical surface but makes no assumptions about how this current should be distributed. The rationale is that the best MEG inversion scheme will be the most sensitive to subtle distortions of the cortical anatomy (as we know that MEG data derives from grey matter structure). This spatial distortion metric then provides a principled basis for comparing different a priori inversion assumptions (i.e. different algorithms) and recording techniques. We are aiming for a generic method to provide a benchmark to refine inversion (or recording) methods based on human electrophysiological data from multiple labs.

The paper proceeds as follows: we first parcel resting state datasets into brief epochs using a hidden Markov model (Baker et al., 2014). The epochs for the four dominant networks were then amalgamated into four network-specific datasets for each subject and taken forwards for inversion. These datasets were then inverted onto a library of subject-specific distorted meshes, for which we had control over the spatial detail available in the forward model. For each of these meshes, and for each inversion scheme, we quantified the model fit using cross validation and Free energy metrics. As expected, we found that the greater the distortion from the true cortical mesh, the poorer the model fit. We then used this spatial quantification to compare different inversion schemes (implemented as different co-variance prior assumptions). For these data, we found that the beamformer-based priors (EBB) were the most sensitive to small deviations from the true anatomy. In addition to distinguishing between algorithms, here we also tested whether we could use the same methods to distinguish between datasets collected with and without a head-cast (Meyer et al., 2017a; Troebinger et al., 2014a; 2014b), where the accuracy of forward model is more precisely known, and those collected without and found marginal (but not significant) differences.

2. Methods

2.1. MRI

Subjects underwent two MRI scans using a Siemens Tim Trio 3 T system (Erlangen, Germany). For the head-cast scan, the acquisition time was 3 min 42 s, in addition to 45 s for the localizer sequence. The sequence implemented was a radiofrequency (RF) and gradient spoiled T1 weighted 3D fast low angle shot (FLASH) sequence with image resolution 1 mm^3 (1 mm slice thickness), field-of view set to 256, 256, and 192 mm along the phase (A–P), read (H–F), and partition (R–L; second 3D phase encoding direction) directions respectively. A single shot, high readout bandwidth (425 Hz/pixel) and minimum echo time (2.25 ms) was used. This sequence was optimized to preserve head and scalp structure (as opposed to brain structure). Repetition time was set to 7.96 ms and excitation flip angle set to 12° to ensure sufficient SNR. A partial Fourier (factor 6/8) acquisition was used in each phase-encoded direction to accelerate acquisition. For the anatomical scan later used to construct the cortical model, multiple parameter maps (MPM) were acquired to optimise spatial resolution of the brain image (to 0.8 mm). The sequence comprised three multi-echo 3D FLASH (fast low angle shot) scans, one RF transmit field map and one static magnetic (B0) field map scan (Weiskopf et al., 2013).

2.2. Head-cast construction

Scalp surfaces from the head-cast MRI data were extracted using SPM12 (http://www.fil.ion.ucl.ac.uk/spm/) by registering MRI images to a tissue probability map which classified voxels according to tissue makeup (e.g. skull, skin, grey matter etc.). The skin tissue probability map was transformed into a surface using the 'isosurface' function in MATLAB® and then into standard template library format with the outlines of three fiducial coils digitally placed at conventional sites (left/right pre-auricular and nasion). Next, a positive head model was printed using a Zcorp 3D printer (600 × 540 dots per inch resolution) and this model placed inside a replica dewar-helmet with liquid resin poured between the two, resulting in a flexible, subject specific, foam head-cast with fiducial indentations in MRI-defined locations (Meyer et al., 2017a).

2.3. MEG recording

Resting state data was acquired from 12 healthy subjects using head-casts (age: 26.6 ± 3.5 yrs (mean + sd)) and 12 other healthy subjects without head-casts (age: 25.2 ± 6.6 yrs). All subjects were right handed, had normal or corrected-to-normal vision, and had no history of neurological or psychiatric disease. Informed written consent was given by all subjects and recordings were carried out after obtaining ethical approval from the University College London ethics committee (ref. number 3090/001).

All subjects underwent a 10 min resting state scan with eyes kept open and instructed to fixate on a central cross on a screen, using a CTF 275 Omega MEG system. The head was localised using the three head-cast-embedded fiducials (head-cast subjects) or fiducials placed on the nasion and left and right pre-auricular points (non-head-cast subjects). Average range of absolute head movement within the 10 min resting state recording was 0.26 ± 0.06, 0.24 ± 0.05, 1.1 ± 0.54 mm (X,Y,Z directions; ± SEM) for head-cast and 3.2 ± 0.5, 3.0 ± 0.5, 3.3 ± 0.2 (X,Y,Z directions; ± SEM) for non-head-cast data. The data were sampled at a rate of 1200 Hz, imported into SPM12 and filtered (4th order butterworth bandpass filter: 1–90 Hz, 4th order butterworth bandstop filter 48–52 Hz) and downsampled to 250 Hz.

Traditional inverse problem solutions are based on the assumption that the data are stationary during the period of inversion. However, resting state data contains rapid dynamics that do not accord well with this assumption (Woolrich et al., 2013). Therefore, in order to improve stationarity within a given epoch, we parcellated the data into self-similar periods that capture the resting state network transitions (100–200 ms) using a Hidden Markov Model (HMM) that could identify the rapid formation and dissolution of recurring resting state networks (Baker et al., 2014). With this, a 'statepath' was estimated for each 10 min resting state block, which tracks the fine spatiotemporal dynamics and allocates each point in time to one of eight dominant network states (Baker et al., 2014). For this statepath determination, a copy of each subject's sensor level data was dimensionally reduced using principle component analysis (PCA) to derive 40 components of unit variance and mean (Woolrich et al., 2013). With these data, an 8 state Hidden Markov model (HMM; www.fmrib.ox.ac.uk/~woolrich/HMMtoolbox)