Research Article

Canonical Source Reconstruction for MEG

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We describe a simple and efficient solution to the problem of reconstructing electromagnetic sources into a canonical or standard anatomical space. Its simplicity rests upon incorporating subject-specific anatomy into the forward model in a way that eschews the need for cortical surface extraction. The forward model starts with a canonical cortical mesh, defined in a standard stereotactic space. The mesh is warped, in a nonlinear fashion, to match the subject's anatomy. This warping is the inverse of the transformation derived from spatial normalization of the subject's structural MRI image, using fully automated procedures that have been established for other imaging modalities. Electromagnetic lead fields are computed using the warped mesh, in conjunction with a spherical head model (which does not rely on individual anatomy). The ensuing forward model is inverted using an empirical Bayesian scheme that we have described previously in several publications. Critically, because anatomical information enters the forward model, there is no need to spatially normalize the reconstructed source activity. In other words, each source, comprising the mesh, has a predetermined and unique anatomical attribution within standard stereotactic space. This enables the pooling of data from multiple subjects and the reporting of results in stereotactic coordinates. Furthermore, it allows the graceful fusion of fMRI and MEG data within the same anatomical framework.

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1. INTRODUCTION

Source reconstruction in neuroimaging, particularly PET and fMRI, is usually into a standard anatomical space (e.g., that defined by the Atlas of [1]). Reconstruction into a canonical space facilitates the formal or informal meta-analysis of findings in imaging neuroscience and provides a useful framework within which to define structure-function relationships. In PET and fMRI the construction of spatially normalized images comprises two distinct steps. First, the raw data are reconstructed into images of source activity within the subject's own anatomical space. Second, these data are then spatially normalized into a standard space using a template matching approach (e.g., [2]). For EEG and MEG, however, source reconstruction and spatial or anatomical normalization cannot be separated because the reconstruction depends upon the spatial configuration of sources.

The central idea, upon which this work is based, is to include anatomical variability in a forward model that links MEG responses to canonical sources. Specifically, the

anatomical differences between a particular subject and a canonical subject (who conforms to the standard space) enter the forward model. Note that these differences are expressed in both cortical anatomy and in the geometrical and physical properties of other tissues (e.g., skull and scalp), through which electromagnetic fields propagate to the sensors. However, we restrict ourselves here to the effect of inter-subject variability in cortical anatomy, given that for MEG, spherical conductor models, which need not incorporate subject specific information about the head, generally provide a sufficiently good approximation compared with more realistic head models such as those using boundary element methods (BEM) see [3, 4]. In contradistinction, the inverse solution is highly sensitive to the source location and orientation, when defined by the cortical anatomy [5]. The nice thing about the approach used here is that spatial normalization becomes an implicit part of the inverse solution. In this paper, we describe how this can be implemented using fully automated procedures that are already in routine use and are freely available as academic software (see Software note).

The basic idea is to formulate a forward or generative model of how a specific subject's MEG data were caused and then invert this model using standard Bayesian techniques. We start with a canonical subject whose anatomy conforms to a predefined space; the MNI-space based upon the Talairach and Tournoux system [1]. This is the same space as used by the SPM software and, more generally, by the neuroimaging community when reporting fMRI and PET results. A canonical mesh is defined within this space, coding the position and orientation of dipolar sources. Warping the mesh to match the subject's anatomy creates a subject specific model. After warping, subject specific forward fields (i.e., a gain matrix) are computed using standard electromagnetic forward modelling procedures. In this paper, we use a single-sphere head model, fit to the template scalp surface. The resulting forward model has two components: an anatomical component that displaces and reorients the dipoles into subject specific anatomy and an electromagnetic component that projects the source activity to measurement space (i.e., channels). Reconstruction of the canonical sources corresponds to the inversion of this forward model, given some data. The conditional estimates of source activity can then be treated within a canonical space. In other words, the source activity is associated with the original mesh (before warping).

There are several advantages of the approach described in this paper. The primary advantage is that it allows for anatomically informed source reconstruction into a standard space that facilitates inter-subject pooling and standardized reporting of results. The second main advantage is that it does not entail the accurate extraction of a subject specific cortical surface. This means that the spatial constraints can be based upon any anatomical information, irrespective of whether its quality would support cortical surface extraction or not. Another advantage is that the estimation can proceed even in the absence of a subject's MRI. In this instance, the reconstruction assumes that the subject's anatomy was, in fact, canonical. A final advantage, which will be pursued in a subsequent paper, is that conditional uncertainty about the subject's anatomy can be handled gracefully during Bayesian inversion. It is worth noting that the two key methodologies, namely, estimating the mapping from canonical to subject specific anatomical space and Bayesian inversion of MEG forward models, are fully established and in routine use. Furthermore, because they are fully automated and deterministic, there is no need for human intervention, which renders the procedure totally reproducible.

The aim of this paper is first to motivate and to describe the operational details of a fully automated canonical source reconstruction. Second, we demonstrate, quantitatively, the performance of this inverse-normalized canonical mesh approach in comparison with (i) reconstructions based upon the subject's native mesh and (ii) the canonical mesh without any spatial transformation. In a later paper, we will use canonical reconstructions in a hierarchical model of multi-subject responses measured with EEG and MEG. This paper is restricted to the analysis of single subjects.

This paper is organized as follows. In Section 1 we review the theoretical aspects of the procedure. This entails a brief

review of our Bayesian approach to conventional forward models. We then consider spatial normalization. Finally, we see how these two components are integrated to enable canonical source reconstruction. The second section is an empirical demonstration of the utility of the approach. Because the estimation scheme is Bayesian, we can use Bayesian model comparison to evaluate different models. This comparison rests on the log evidence or likelihood of the data given a particular model (having integrated out any dependencies on the model's parameters or hyperparameters). Put simply, we can quantify the likelihood of any given data set given one model, relative to another. Here, we compare three sorts of models: first, a baseline model where the electromagnetic model was based upon a canonical mesh without spatial transformation. The second model, used to explain the same data, incorporated anatomically informed spatial transformations of the canonical mesh. We also evaluated a gold-standard model where the cortical mesh was obtained from a cortical surface extraction, using the subject's MRI data. We hoped to show that including the spatial transformation in the reconstructions would yield a greater log evidence than for the baseline model, and that this log evidence was not significantly less than for the gold-standard model based upon the subject's cortical surface.

2. THEORY

2.1. Bayesian source reconstruction

In a series of papers [6, 7] we have described a Bayesian approach to inverting forward models for EEG and MEG. These forward models start with a subject specific cortical dipole mesh or three-dimensional grid, referred to as the subject's source space. This, in conjunction with the position of the sensors, is used to compute a Gain matrix L in the usual way, under quasistatic Maxwellian assumptions. The inversion of the ensuing electromagnetic forward model uses a hierarchical linear observation model and conforms to parametric empirical Bayes (PEB) using restricted maximum likelihood (ReML). The Bayesian aspect accommodates the regularization required for ill-posed inverse problems. The empirical aspect allows us to identify the ReML estimators of hyperparameters λ controlling multiple noise and prior covariance components, $Q_i^{(1)}$ and $Q_i^{(2)}$, respectively. The key advantage of this approach is that it can accommodate multiple priors in a principled and efficient way. Its efficiency stems from the fact that the ReML scheme estimates covariance components in low-dimensional sensor space, as opposed to high-dimensional source space.

The objective function used by this scheme is equivalent to the ReML objective function, which, as shown in [8], is identical to the (negative) variational free energy

$$F = \langle \ln p(y | j, \lambda) + p(j | \lambda) - \ln q \rangle_q, \quad (1)$$

where y is the data, j are the source activities, and $q(j)$ is their conditional or posterior density. Under Gaussian assumptions, when F is maximized; $q(j) = p(j | y, \lambda)$, and the (negative) free energy becomes the log likelihood of the

FIGURE 1: Bayesian inversion scheme.

model or its log evidence $F \rightarrow \ln p(y | \lambda)$ [9]. We have shown how the log evidence can be used to compare and adjudicate among different models comprising different prior covariance components or different source configurations [7]. We use exactly the same approach below, to compare three different sorts of anatomical source models, each with slightly different configurations of a cortical mesh subtending the lead fields. Figure 1 provides a schematic that summarizes this Bayesian inversion scheme.

2.2. Spatial normalization

Spatial normalization is a term that refers to the warping or mapping of a subject specific image into a standard anatomical space. It is used routinely in fMRI and PET to enable inter-subject pooling. The parameters θ_i that define the transformation $x^{(0)} \rightarrow x^{(n)}$ are identified using

a Bayesian scheme that incorporates constraints on the smoothness of the transformation [2]. $x_i^{(n)}$ represents the position of the i th control point after n iterations. In brief, the warping is parameterized in terms of spatial basis functions (in SPM, we use a discrete cosine set). These encode the change in position effected by each transform parameter $\partial x / \partial \theta_i$. The coefficients of these basis functions maximize their conditional probability (i.e., maximize the likelihood and prior density). The likelihood is computed using a forward model, which mixes several canonical templates and then warps them to predict the observed image. The mismatch between the warped mixture of templates and the observed image constitutes a prediction error. Under Gaussian assumptions this error gives the likelihood of the observed image, given the mixing and warping parameters. Rough transformations are penalized by appropriate shrinkage priors on the coefficients, formulated

FIGURE 2: Spatial normalization scheme.

in terms of their covariance. The parameters are computed using a Newton method. The inverse of the template warping is applied to the image and the process iterated until convergence and the image is spatially normalized (see Figure 2 for a schematic).

Once the normalizing transformation has been identified, given some structural image it is usually applied to spatially normalize the subject's functional time series so that analysis can proceed in standard space. A full description of the assumptions and procedures entailed by spatial normalization can be found in a series of papers [10, 11]. Here, we do not use the spatial transformation to normalize reconstructed sources but to spatially *unnormalize* a canonical mesh to inform the forward model about how that subject's electromagnetic signals were generated. This simply involves applying the inverse spatial transformation $x^{(n)} \rightarrow x^{(0)}$ to the locations of the canonical mesh dipoles.

2.3. Canonical source reconstruction

Canonical source reconstruction is identical to our Bayesian source reconstruction (see Figure 1) with the addition of an

anatomical component to the forward model. This component is the spatial transformation of a canonical cortical mesh to match the subject's anatomy using the inverse of the spatially normalising transformation (see Figure 3). After transformation, the subject specific mesh is used in the usual way to create an electromagnetic forward model that is inverted as described above. The evidence for this model that comprises both the anatomical and electromagnetic components can then be used to compare different models.

In the next section, we apply the above theory to both synthetic and real MEG data. Our primary goal is to ascertain the relative likelihoods of the different models considered. However, we also take the opportunity to demonstrate the procedure and provide a worked example of its application.

3. MODEL COMPARISON

3.1. Anatomical models

In what follows, we use the following acronyms for the meshes used by the models, which differ only in their anatomical information.

FIGURE 3: Overview of canonical source reconstruction.

FIGURE 4: Surface rendering (upper row) and meshes (lower row) encoding the three cortical models: SCS (a), CCS (b), and TCS (c). CCS (red) and TCS (green) meshes are superimposed on the SCS mesh (blue).

FIGURE 5: (a) Sensor locations coregistered with the subject's MRI-derived meshes of the cortical, skull, and scalp surfaces; (b) sensor data for the difference between faces and scrambled event related fields.

TABLE 1: Log evidences obtained using the real MEG dataset for the three anatomical models.

	SCS	CCS	TCS
Log evidence	14084	14072	14058

It should be noted that our simple minimum-norm solution has favored superficial activity (a well-known property of minimum norm solutions); analyses of the same data using more realistic models (with multiple sensor and source covariance components) place the maximum response more ventrally in both the fusiform and orbitofrontal regions [17]. However, we used the simplest model because this is the most established and our focus here is on *differences* in the reconstructed activity.

The log evidences for the three models are relatively close. One can assess the differences (log ratios or Bayes factors) using the semantics proposed by Kaas and Raftery by analogy with classical inference [15, 18]. In this context, a Bayes factor of twenty means that the data are twenty times more likely to have been generated by one model relative to another (cf., of P -value of .05). A Bayes factor of twenty corresponds to a difference in log evidence of about three, which is the typical threshold one would use to declare that one model was

FIGURE 6: Caudal (upper row) and ventral (lower row) views of the cortical source energy estimated at the peak of the M170 for each of the three anatomical models: SCS (a), CCS (b), and TCS (c). Maps have been normalized to their maximum.

better than another. Given that the differences among the log evidences for our models were about twelve, there is strong evidence that SCS is better than CCS and that CCS is better than TCS. However, one cannot generalize from a single illustrative example. In Section 3.4, we present an extensive simulation study to assess quantitatively and statistically the difference between the three models.

3.4. Synthetic data

MEG data were simulated using the fine SCS mesh and the MEG setup described in Section 3.2 (see Figures 4(a) and 5, resp.). A hundred independent simulations were performed, each using a single-extended source. For each simulation, the active source comprised a cluster of dipoles. Each cluster was constructed by selecting a random dipole and its nearest mesh neighbors, up to second order (including the nearest neighbors of the nearest neighbors). The cluster size was 7 ± 3 dipoles. Since the dipoles are spread uniformly over the cortical surface, this random dipole selection ensures that all brain regions were represented equally, over simulations. The activity of each source was modelled (over 321 time bins) with two gamma functions, whose parameters were selected randomly, subject to the constraint that the simulated activity reached a peak within time window modelled. Finally, after projection to sensor space, white Gaussian noise was added ($\text{SNR} = 8 \text{ dB}$) (see Figure 7 for an example of simulated data).

The three models were inverted for each of the hundred simulated datasets. Since we know the true cortical activity,

FIGURE 7: Example of a synthetic MEG dataset and its associated inverse solutions. Each map has been normalized to its maximum.

we supplemented our model comparison using the log evidence with the localization error (LE). LE is the distance between the true source and the dipole exhibiting the maximum estimated energy. This comparative metric complements the log evidence and speaks to the performance of the inversion in terms of the deployment of reconstructed activity, which is an important consideration in multisubject studies. To calculate LE for the SCS-(resp., CCS and TCS) based solution, we used the dipole on the coarse SCS (resp., CCS and TCS) which was closest to the truly activated source on the fine SCS.

3.5. Simulation results

Figure 7 shows an example of synthetic data and the three solutions obtained for each mesh. Figure 8 shows the distributions (whisker plots) of the log evidence and LE over all simulations, for each of the three cortical models. The variance of the log evidences over source configurations is large. It is worth emphasizing here that a given log evidence has

FIGURE 8: Whisker plots of the log evidences and LE values obtained with synthetic MEG data (similar to the example shown in Figure 7) for each of the three anatomical models (SCS, CCS, and TCS).

no meaning in itself. It only becomes meaningful when compared to the log evidence of another model applied to the same data.

The means of the log evidences, over models, show the same tendency as in the real-data example. Furthermore, the one-way within-dataset ANOVA on the log evidences was significant ($F = 7.81$; $P < .0005^{***}$). Specifically, multiple comparisons with Bonferroni correction show that the only significant differences are between TCS and the two other models; suggesting that there is no demonstrable difference in the performance of the Bayesian inversion of the SCS and CCS models. Similarly, the one-way within-dataset ANOVA on the localization errors proved significant ($F = 15.25$; $P < .0005^{***}$). Again, multiple comparisons with Bonferroni correction show that the only significant pairwise differences are between TCS and the two other models.

To summarize, the localizations based on the reference mesh (SCS) are significantly better than the ones based on the anatomically uninformed template mesh (TCS). Critically, when we transform the template mesh into the subjects anatomical space (CCS) there is no significant difference in

4. CONCLUSION

The contribution of this work is twofold: first, conceptually we have formulated the problem of inter-subject anatomical variability as an explicit part of the forward model. This entails the notion of a canonical subject, whose cortical mesh is transformed anatomically to produce subject specific mesh. This places important constraints on individual meshes that enter the forward model; critically there must exist a diffeomorphic anatomical mapping between any subject and the canonical subject. We can exploit this constraint by always starting with the canonical mesh and warping it to match each subject. This has several fundamental advantages. First, it eschews the problems of cortical surface extraction from an individual’s MRI; second it uses all the anatomical information in the MRI to construct a subject specific forward model (this information is not just confined to the cortical surface but includes all the information used in spatial normalization). Third, it ensures the cortical mesh is topologically valid (because it is derived under the diffeomorphism constraint). Finally, it enforces a standard solution space that facilitates inter-subject averaging and reporting. These standard spaces have proved very useful in fMRI.

We used Bayesian model comparison and localization error to evaluate the advantage of anatomically informed mod-

To conclude, we have focussed on demonstrating the validity of the CCS model. This anatomically informed model has the twofold advantage of eschewing the need for cortical extraction and affording a one-to-one mapping with the canonical cortical surface. The latter is important for pooling results over subjects and reporting single subject or group localizations in the same stereotactic space. It also enables us to consider a full hierarchical model for multisubject analysis: namely, a unified inference scheme for group averages, instead of the conventional two-stage procedures (e.g., [17]). This includes, for example, incorporation of spatial priors on the MEG/EEG inverse solution based on normalized fMRI results from a group of subjects. This will be the focus of future work.

The algorithms described in this paper are available within SPM5 and can be downloaded from <http://www.fil.ion.ucl.ac.uk/spm>. It is worth emphasizing that the canonical cortical surface, given any subject's MRI, can be obtained automatically and robustly using the well-established spatial normalization schemes described in Section 2.2. SPM5 uses a unified forward model for anatomical deformations that includes tissue classification and inhomogeneity correction.

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REFERENCES

- [1] J. Talairach and P. Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*, Thieme, New York, NY, USA, 1988.
- [2] J. Ashburner and K. J. Friston, "Nonlinear spatial normalization using basis functions," *Human Brain Mapping*, vol. 7, no. 4, pp. 254–266, 1999.
- [3] M. Fuchs, R. Drenckhan, H. A. Wischmann, and M. Wagner, "An improved boundary element method for realistic volume-conductor modeling," *IEEE Transactions on Biomedical Engineering*, vol. 45, no. 8, pp. 980–997, 1998.
- [4] R. M. Leahy, J. C. Mosher, M. E. Spencer, M. X. Huang, and J. D. Lewine, "A study of dipole localization accuracy for MEG and EEG using a human skull phantom," *Electroencephalography and Clinical Neurophysiology*, vol. 107, no. 2, pp. 159–173, 1998.
- [5] J. C. Mosher, M. E. Spencer, R. M. Leahy, and P. S. Lewis, "Error bounds for EEG and MEG dipole source localization," *Electroencephalography and Clinical Neurophysiology*, vol. 86, no. 5, pp. 303–321, 1993.
- [6] C. Phillips, J. Mattout, M. D. Rugg, P. Maquet, and K. J. Friston, "An empirical Bayesian solution to the source reconstruction problem in EEG," *NeuroImage*, vol. 24, no. 4, pp. 997–1011, 2005.
- [7] J. Mattout, C. Phillips, W. D. Penny, M. D. Rugg, and K. J. Friston, "MEG source localization under multiple constraints: an extended Bayesian framework," *NeuroImage*, vol. 30, no. 3, pp. 753–767, 2006.
- [8] K. J. Friston, W. D. Penny, C. Phillips, S. Kiebel, G. Hinton, and J. Ashburner, "Classical and Bayesian inference in neuroimaging: theory," *NeuroImage*, vol. 16, no. 2, pp. 465–483, 2002.
- [9] K. J. Friston, J. Mattout, N. Trujillo-Barreto, J. Ashburner, and W. D. Penny, "Variational free energy and the Laplace approximation," *NeuroImage*, vol. 34, no. 1, pp. 220–234, 2007.
- [10] K. J. Friston, C. D. Frith, P. F. Liddle, and R. S. J. Frackowiak, "Plastic transformation of PET images," *Journal of Computer Assisted Tomography*, vol. 15, no. 4, pp. 634–639, 1991.
- [11] J. Ashburner and K. J. Friston, "Unified segmentation," *NeuroImage*, vol. 26, no. 3, pp. 839–851, 2005.
- [12] Y. Cointepas, J.-F. Mangin, L. Garnero, J.-P. Poline, and H. Benali, "BrainVISA: software platform for visualization and analysis of multi-modality brain data," in *Proceedings of the 7th Annual Meeting of the Organization for Human Brain Mapping (HBM '01)*, p. S98, Brighton, UK, June 2001.
- [13] J.-F. Mangin, "From 3D magnetic resonance images to structural representations of the cortex topography using topology preserving deformations," *Journal of Mathematical Imaging and Vision*, vol. 5, no. 4, pp. 297–318, 1995.
- [14] J. Sarvas, "Basic mathematical and electromagnetic concepts of the biomagnetic inverse problem," *Physics in Medicine and Biology*, vol. 32, no. 1, pp. 11–22, 1987.
- [15] W. D. Penny, K. E. Stephan, A. Mechelli, and K. J. Friston, "Comparing dynamic causal models," *NeuroImage*, vol. 22, no. 3, pp. 1157–1172, 2004.
- [16] R. N. Henson, Y. Goshen-Gottstein, T. Ganel, L. J. Otten, A. Quayle, and M. D. Rugg, "Electrophysiological and haemodynamic correlates of face perception, recognition and priming," *Cerebral Cortex*, vol. 13, no. 7, pp. 793–805, 2003.
- [17] R. N. Henson, J. Mattout, K. D. Singh, G. R. Barnes, A. Hillebrand, and K. J. Friston, "Population-level inferences for distributed MEG source localisation under multiple constraints: application to face-evoked fields," to appear in *Human Brain Mapping*.
- [18] R. E. Kass and A. E. Raftery, "Bayes factors," *Journal of the American Statistical Association*, vol. 90, no. 430, pp. 773–795, 1995.