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Bayesian Tracking of Neural Activity in Biomagnetic Data

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Abstract

Magnetoencephalography (MEG) is a non-invasive brain imaging tecnique measuring the weak magnetic field due to neural activity. The analysis of the temporal evolution of the magnetic field, however, does not provide accurate spatial information about the neural activations in the cerebral cortex. Such information can be restored only by solving the inverse problem. We propose a probabilistic approach to solve this problem: a particle filter is implemented to realize a Bayesian tracking of the brain sources, modeled as pointwise currents.

Keywords: `inverse problem, Bayesian tracking, Magnetoencephalography.`

1. Introduction.

Magnetoencephalography (MEG) [1] is a brain imaging technique recording, in a completely non-invasive way, the magnetic field due to the neural currents lying in the cerebral cortex; from the temporal analysis of these measurements it is possible to infer information about the brain activity. The main advantage of MEG against other functional imaging modalities, such as Positron Emission Tomography (PET) or functional Magnetic Resonance Imaging (fMRI), is its temporal resolution of the order of the millisecond, that allows following the temporal evolution of the neural sources with great accuracy. The spatial resolution is not equally outstanding, being of the order of centimeter (but this is still a matter of debate, because several different factors affect the spatial accuracy of the

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inverse solution); other functional brain imaging procedures, such as PET and fMRI, reach the millimeter.

In the last years MEG has been employed for studying epilepsy, the re-organization of the somatosensory-cortex and more generally for neuroscientific investigations. The experimental paradigms concern the recording of both spontaneous cortical rhythms and evoked potentials after external stimulations.

The analysis of MEG data for obtaining information about the cerebral activity is a challenging task for a good number of reasons. First, the Signal-to-Noise Ratio (SNR) of the measurements is very low; this is due to several factors, including: (i) the brain magnetic field is very weak, only few hundreds of femtoTesla, so that only special sensors working thanks to superconductivity can in fact measure such low fields; (ii) while magnetic noise coming from external sources is generally strongly attenuated by the use of magnetically shielded rooms, the brain itself has to be considered as a source of noise, where noise is here all the magnetic field produced by cerebral currents not of interest in the present study. Second, the MEG problem is genuinely ill-posed: the solution is not unique, since many different configurations of neural sources may produce the same magnetic field; the inverse solution is characterized by a strong numerical instability.

Following [2,3,4], we use Bayesian tracking to solve this problem in a probabilistic framework. The computation of the forward problem, a necessary step in this approach, needs two models to be defined: a model for the geometry of the conductor, i.e the head, and one for the neural sources. In this work, the head is approximated by a homogeneous spherical conductor; this approximation is quite reliable for the posterior part of the brain. The neural currents can be modeled as a distributed source, in which the source locations are fixed and only their amplitudes are estimated from the measurements, or with a set of point-wise currents ("dipoles"), in which the activation is modeled by a small number of dipoles, defined by position, orientation and amplitude. In the dipole model the number of active dipoles cannot be fixed a priori, rather it can be considered as a time-varying variable varying with time. Here we employ the dipole model and show how the introduction of the Random Finite Sets theory [5,6] can be used to handle the varying number of sources. This work is organized in the following way: first we present the MEG problem and a Bayesian algorithm for its solution; then we show the results we obtain analyzing a real dataset and finally we propose our conclusion and discuss the problems still open.

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2. The MEG inverse problem.

The Biot-Savart law links the magnetic field to the currents and is therefore the key equation in the MEG problem:

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi} \int \mathbf{J}(\mathbf{r}') \times \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^3} dV \tag{1}$$

with $\mathbf{B}(\mathbf{r})$ representing the magnetic field in $\mathbf{r}$ due to the current distribution $\mathbf{J}(\mathbf{r}')$. The following theorems, proved respectively in [7] and in [8], demonstrate the ill posedness in the sense of Hadamard of the MEG problem:

Theorem 2.1. *The kernel of the Biot-Savart operator is not trivial.*

Theorem 2.2. *The Biot-Savart operator is compact.*

The dipole model for the neural sources

$$\mathbf{J}(\mathbf{r}) = \sum_i \mathbf{Q}_i \delta(\mathbf{r} - \mathbf{r}_{Q_i}) \tag{2}$$

where $\mathbf{r}_{Q_i}$ is the position of the i-th dipole and $\mathbf{Q}_i$ the dipole moment, induces a non-linear relationship between the position of the dipole and the magnetic field; in an unbounded, homogeneous conductor, the Biot-Savart equation directly reads:

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi} \sum_i \mathbf{Q}_i \times \frac{\mathbf{r} - \mathbf{r}_{Q_i}}{|\mathbf{r} - \mathbf{r}_{Q_i}|^3}; \tag{3}$$

the case of a bounded conductor is more complicated, as the neural current induces secondary (volume) currents in the conductor, whose contribution to the magnetic field is not null; the analytic solution is known in the case of a spherical conductor; for more realistic head geometries, Boundary or Finite Element Methods are needed to obtain approximate solutions; in all cases, the non-linearity holds.

In conclusion, solving the MEG inverse problem in the dipolar approximation involves solving a non-linear inverse problem, further complicated by the fact that the source parameters change in time (it's a dynamic problem) and the SNR of the data is rather low.

3. Bayesian tracking for the MEG problem.

For the reasons exposed in the previous section, the research of an exact solution may appear meaningless. So we decided to work in a Bayesian framework, in which all the data are modeled as random variables. The magnetic field $\mathbf{B} = \{\mathbf{B}_k\}_{k=1}^T$ and the unknown currents $\mathbf{J} = \{\mathbf{J}_k\}_{k=1}^T$ are considered as Markovian processes in which $\mathbf{B}_k$ and $\mathbf{J}_k$ are the random vectors representing, respectively, the measurement and the neural current at the time k. As we said before, the number of simultaneous sources, i.e. of dipoles, cannot be fixed a priori; moreover it can vary over the time. This implies that the random vector $\mathbf{J}_k$ could have different dimension at different time points. A more appropriate representation of such a problem can be given within the theory of Random Finite Sets (RFS) [6]. A RFS is a set with a variable number of elements, that are random vectors themselves. It can be viewed as a generalization of a random variable. We have to re-write the currents in terms of RFS: let $\mathcal{J}_k$ be the random finite set of currents and $J_k = (j_k^1, ...j_k^{m_k})$ its realization, with M_k the random variable representing the number of neural sources, and m_k its realization (in the implementation, this number is bounded for computational reasons). Using this theory, the number of neural currents at each time point is a random variable itself and needs not to be fixed a priori

The model equation can be written as:

$$\mathbf{B}_k = BS(J_k) + \mathbf{N}_k \tag{4}$$

where BS is the Biot-Savart operator and $\mathbf{N}_k$ represents the noise. The distribution of noise in the MEG problem is not known and we assume the general hypothesis it is zero-mean white Gaussian noise.

The choice of the probabilistic approach implies that all the information, and hence the solution, can be coded in probability density functions (pdf). In particular the posterior pdf $\pi_{post}(J_k|\mathbf{b}_{1:k})$ is the solution of the inverse problem in the Bayesian setting: it is the probability density for a dipoles set at time k, J_k, conditioned on the measurements up to time k, $\mathbf{b}_{1:k}$. The posterior pdf is computed at each time point from the prior density, with the Bayes theorem:

$$\pi_{post}(J_k|\mathbf{b}_{1:k}) = \frac{f(\mathbf{b}_k|J_k)\pi_{prior}(J_k|\mathbf{b}_{1:k-1})}{\pi(\mathbf{b}_k|\mathbf{b}_{1:k-1})} \tag{5}$$

and the prior pdf at the next time is given by the Kolmogorov-Chapman equation:

$$\pi_{prior}(J_{k+1}|\mathbf{b}_{1:k}) = \int p(J_{k+1}|J_k)\pi_{post}(J_k|\mathbf{b}_{1:k})\delta J_k \tag{6}$$

where the integral is the set integral [5], [6].

To apply the two previous equations, the following densities have to be defined:

- the prior pdf for $k = 1$, $\pi_{prior}(J_1)$ which is clearly needed for the initialization; we assume it is uniform in the position and Gaussian in the dipole moment with zero mean and standard deviation of the order of the expected sources magnitude;
- the likelihood function $f(\mathbf{b}_k|J_k)$ that is the probability to measure the magnetic field $\mathbf{b}_k$ when the current is J_k. Explicitly we choose $f(\mathbf{b}_k|J_k) = N(\mathbf{b}_k - BS(J_k), \sigma_{noise})$ where σ_{noise} is the standard deviation of the noise, computable from the data;
- the transition kernel $p(J_{k+1}|J_k)$ describing the dynamical evolution of our system. We have no knowledge of a model for the evolution and for sake of generality we assume it is a random walk. Moreover, with equal probabilities, a particle can preserve its dipoles number, or a dipole can die or born according to $\pi_{prior}(J_1)$.

The iterative application of the observation (5) and evolution (6) equations furnishes the solution of the MEG problem for each time k: in fact, using the prior at time $k = 1$ as an inizialization, we can compute the posterior pdf at time 1 and with the Kolmogorov-Chapman equation we can obtain the prior pdf at time 2 and so on.

The implementation of this procedure is perfomed by a particle filter [9]: the non linearity of the magnetic field with respect to the dipole position does not allow the use of a Kalman filter, generally and conveniently employed in presence of a linear model with Gaussian noise [10], [11]. In the particle filtering a set of N particles is considered as an approximation of the posterior pdf and it is recursively obtained by the discretization of Bayes theorem (5) and the evolution equation (6). At each time point, a weight, based on the likelihood function, is assigned to each particle, and then a resampling step is applied. The transit to the next time point is made be letting the particles evolve according to the transition kernel.

The algorithm can be summarized in the following steps:

- **initialization:** draw a sample $\{J_1^i\}_{i=1}^N$ distributed according to the density $\pi_{prior}(J_1)$;
- **observation:** compute the forward solution for each particle J_k^i and assign to it a weight based on the likelihood function $w_k^i = \frac{f(\mathbf{b}_k|J_k)}{\sum_{h=1}^N w_k^h}$;
- **resampling**: resample N particles from the set $\{J_k^i\}_{i=1}^N$ in order that the probability of extracting J_k^i is equal to its likelihood w_k^i; the set of uniformly weighted particles $\{\tilde{J}_k^i\}$ is a new approximation of

the posterior density at time k; this step is implemented for avoiding degeneracy of the algorithm;

- **evolution:** let each particle $\{\tilde{J}_k^i\}$ evolve according to the transition kernel, by drawing a new particle J_{k+1}^i from $p(J_{k+1}|\tilde{J}_k^i)$

. The particle filter gives, at each time point, an approximation of the posterior density function, that is the solution of our problem, but it is still necessary to extract from it the estimate of the solution. The estimation procedure involves two steps. First, the number of sources is dynamically estimated from the posterior density, by looking at the marginal distribution of M_k; in practice, this means that at each time point we assign to each source space (zero dipole, one dipole and so on) a weight computed by summing the weights of all the particles belonging to that space. The source space with the highest weight is considered as the space of the solution and its dimension determines the number of reconstructed dipoles. As for the source parameters, the weighted particles are used to compute a marginal quantity, named Probability Hypothesis Density (PHD) in the RFS theory, whose peaks represent the estimates of the source locations; the dipole moments are computed with linear least squares.

The algorithm is extremely time-consuming: at each time point we have to compute the forward solution for each particle. This operation is hence performed milions of time: in fact, we employ usually 100000 particles and the data last about 400 time point. A strong reduction of the computational cost can be obtained by constraining the dipoles to jump only between points of a pre-defined grid, enclosing the brain volume; the precomputation of the forward solution for the points of the grid reduces the computational cost of a factor about 1,000.

4. Results.

The particle filter has been previuosly applied in [2], [3], both to synthethic and to real MEG datasets. Here we present the results we obtained with a real dataset, recorded with a 306-channel whole-head neuromagnetometer (Elekta Neuromag Oy, Helsinki, Finland), which employs 102 sensor elements, each comprising one magnetometer and two planar gradiometers. The measurements were filtered in the range 0.1-170 Hz and sampled at 600 Hz.

An auditory stimulus, consisting in a perceptible but not annoying sound was presented to the subject for about 100 times. These repetitions are due to the necessity to have many recordings of the brain response to the stimulus: the data are averaged for obtaining a better SNR.

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The employed grid is a 3D cubic grid formed by about 40000 points with distance of 4 mm.

The typical brain response to this kind of simple auditory stimuli is well known and consists in a bilateral activation; the contralateral hemisphere (left hemisphere if the stimulus was presented to the right ear) is usually activated some milliseconds before the ipsilateral hemisphere

In figure 1 we show the model selection for the auditory experiment and in the figures 2 and 3 the reconstructions at different time points. The results are in agreement with the expected response and are obtained in an automatic and quite fast way. Moreover our results are comparable with the ones given by the dipole fitting modality [1], the technique most used in the MEG community.

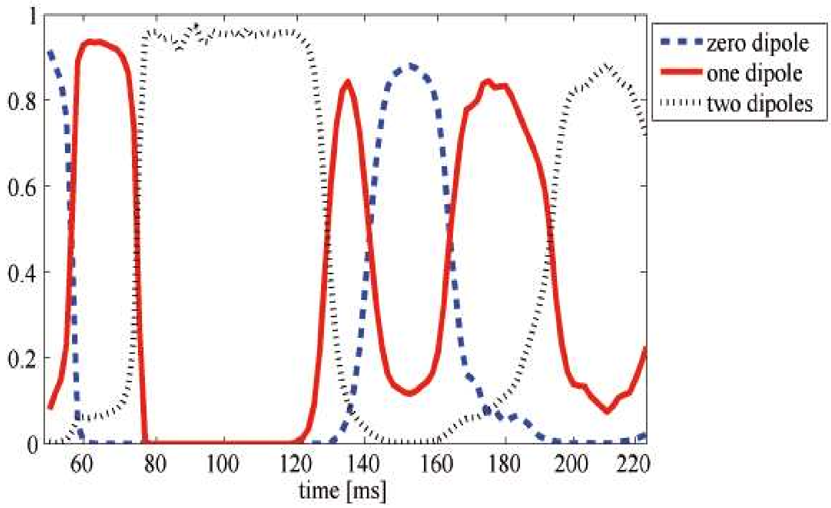

Fig. 1. Model selection: the probability to stay in the zero dipole space (blue dashed line), in the one dipole space (red line) and in the two dipole space (black dotted line)

5. Conclusions.

In this work we presented a Bayesian algorithm for the analysis of MEG data and suggested that the mathematical framework of Random Finite Sets is appropriate for dealing with the time-varying number of sources. For computational reasons we introduced a grid containing the brain volume. The grid used so far is a cubic grid, but it is possible to create a grid lying on the cortical surface for obtaining more accurate reconstructions: the neural currents are generated mainly on the brain cortex and not in the sub-cortical tissues.

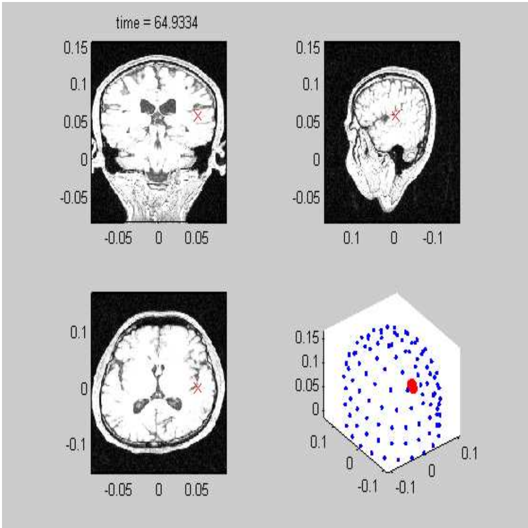

Fig. 2. Reconstructed dipole at the 64 ms: the panel shows in the first row the coronal and saggital views and in the second row the axial view and the sources inside the sensors' helmet. In according to the model selection at 64 ms, we have one reconstructed source

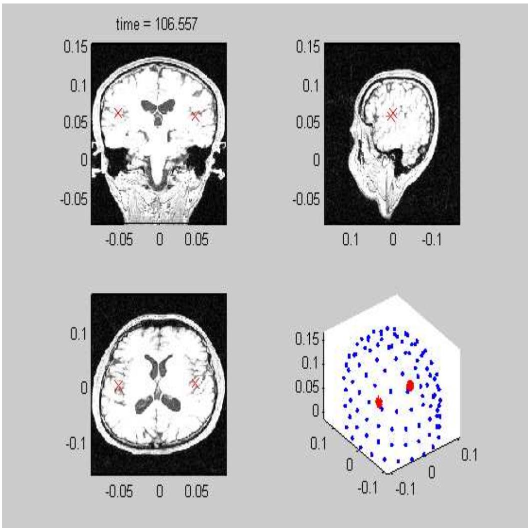

Fig. 3. Reconstructed dipole at the 106 ms: the panel shows in the first row the coronal and saggital views and in the second row the axial view and the sources inside the sensors' helmet. In according to the model selection at 106 ms, we show the two reconstructed sources

Future work will be concerned with applications both on data obtained during more complex stimulations and on the spontaneuos cortical activity,

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with the aim of investigating brain rhythms.

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