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Multivariate Autoregressive Model Constrained by Anatomical Connectivity to Reconstruct Focal Sources

Brahim Belaoucha¹, Mouloud Kachouane¹,² and Théodore Papadopoulo³

Abstract—In this paper, we present a framework to reconstruct spatially localized sources from Magnetoencephalography (MEG)/Electroencephalography (EEG) using spatiotemporal constraint. The source dynamics are represented by a Multivariate Autoregressive (MAR) model whose matrix elements are constrained by the anatomical connectivity obtained from diffusion Magnetic Resonance Imaging (dMRI). The framework assumes that the whole brain dynamic follows a constant MAR model in a time window of interest. The source activations and the MAR model parameters are estimated iteratively. We could confirm the accuracy of the framework using simulation experiments in both high and low noise levels. The proposed framework outperforms the two-stage approach.

I. INTRODUCTION

EEG and MEG are two non-invasive modalities that allow us to measure brain activity with high temporal resolution. Obtaining the distributed sources activation from these measurements is an under-determined problem due to the small number of measurements with respect to the number of sources. To obtain a unique solution, different constraints can be added [1]. These can be divided into three different categories: spatial, temporal, and spatiotemporal constraints.

There are several studies that show that the reconstruction improves when including spatiotemporal constraints [2], [3]. In this work, we assume that the source signals follow a multivariate autoregressive (MAR) model. Fukushima et al. [3] proposed a MAR model in which matrix elements depend on the anatomical connectivity, but their method is time-consuming and hard to implement. Other studies, [4], [5], assume that sources increase or decrease by the same factor or interact with only their direct neighbors. These assumptions significantly reduce the degrees of freedom of the dynamics. We provide more degrees of freedom by allowing source interactions constrained by anatomical connectivity obtained from dMRI information. This allows us to generalize our work to the whole brain. Focal reconstructions are important because they are consistent with the notion of functional specialization of small cortical regions. Focal Underdetermined System Solver (FOCUSS) [6] is used to detect spatially localized sources. It is applied to each time sample and tends to set to zero sources with low activation at each time sample. This makes it unsuitable for MAR parameter estimation. Our framework estimates the source activation and the MAR parameters iteratively. This approach corrects the false activation and functional connections that can be obtained by two-stage approaches when working with low signal-to-noise ratio (SNR).

We have developed a framework constrained by a temporal dynamic over the whole brain to reconstruct sources. The source dynamics represented by the MAR model is based on the underlying anatomical connections obtained from dMRI information. Through simulations at different noise levels, we compare the accuracy of the proposed framework in the source reconstruction and MAR model parameters estimation with the ones obtained from a non-dynamical sparse solution based on mixed-norm estimates (MxNE) [7]. Our framework uses the MxNE estimates to initialize the source intensities then estimates the MAR entries iteratively.

II. DATA ACQUISITION AND PROCESSING

Structural and diffusion MRI data were taken from Wake-man et al. [8]. Cambridge University Psychological Ethics Committee approved all experimental procedures involving human subjects [8]. The T1 weighted images of size $256 \times 256 \times 192$ were acquired by a Siemens 3T Trio with GRAPPA 3D MPRAGE sequence (TR = 2250 ms; TE = 2.99 ms; flip-angle = 9°; acceleration factor = 2) at 1 mm isotropic resolution. The diffusion weighted images of size $96 \times 96 \times 68$ were collected by the same scanner at 2 mm isotropic resolution (64 gradient directions and $b$-value =1000 s/mm²), with one $b=0$ image. The cortical surface was extracted using Freesurfer [9] from T1 and remeshed to 2003 vertices (sources). The transformation between the anatomical and diffusion space was obtained by registering the brain in the two spaces using FSL [10]. The MEG/EEG forward problem, based on Boundary Element Method (BEM), is obtained using OpenMEEG [11], [12].

III. STRUCTURAL CONNECTIVITY

The structural connectivity of the sources (nodes on the mesh) is obtained from the dMRI information. Each node in the cortical mesh is considered as a seed. For each seed, we compute the connectivity profile, i.e. its connectivity with every voxel in the diffusion image space. Connectivity profiles are obtained by running probabilistic tractography for all seeds. We assume a model of multiple fiber orientations for each voxel developed in FSL [14] with $5 \times 10^3$ samples. The connectivity between node $i$ and $j$, $c_{ij}$, is the number of samples that were drawn from $i$ and arrived at $j$ divided by the total number of samples. $CM$ is the connectivity matrix with elements $CM(i,j) = \max(c_{ij}, c_{ji})$. The source $i$ and $j$ are considered to be structurally connected if $CM(i,j) \geq$...
We set \( c_{th} \) to 0.1 to remove weak connections. We obtained 3935 anatomical connections.

IV. ALGORITHM

The EEG/MEG measurements \((M \in \mathbb{R}^{n \times T})\) are related to the brain sources \((J \in \mathbb{R}^{m \times T})\) by the following linear relationship:

\[
M = GJ + \epsilon,
\]
where \( n \) and \( m \) are the number of sensors and sources respectively, \( T \) is the length of the time window, \( \epsilon \) is Gaussian observation noise and \( G \in \mathbb{R}^{n \times m} \) is the lead field matrix. We assume that the sources \((J_t)\) at time \( t \) are related to their past values by:

\[
J_t = AJ_{t-1} + \omega_t,
\]
where \( A \) is the MAR matrix and \( \omega_t \) is Gaussian generator noise. The elements of the MAR matrix are constrained by the structural connectivity obtained from dMRI information.

The only non-zero elements of \( A \) represent anatomically connected source pairs including self-connections. The dynamics of the model depend on the eigenvalues of \( A \). The sources can be obtained by minimizing the following functional:

\[
E(J) = \frac{1}{2T} \|M - GJ\|_2^2 + \lambda U(J), \tag{1}
\]
where \( U \) is some prior on sources and \( \lambda \) is a positive regularization parameter. In focial activation, most of the sources are inactive. This sparsity can be obtained by putting \( U(J) = \|J\|_1 \), where \( \|J\|_1 = \sum_i \sqrt{\sum_j|J_{ij}|^2} \). This norm, \( l_1 \), induces sparsity over the time window i.e. the sites of active sources will be the same over the entire time window of interest.

The solution of Eq. (1) is called the mixed-norm estimate (MxNE). More details about the MxNE can be found in [7]. To enhance the solution of the mixed-norm solution in low SNR values and to estimate the functional connectivity which is represented by the MAR model, we introduce an iterative framework. The MAR matrix, \( A \), is estimated over a time window of interest by minimizing \( D \):

\[
D(A) = \|J_{1,T} - AJ_{0,T-1}\|_2^2,
\]
where \( J_{1,T} \) and \( J_{0,T-1} \) are the values of the sources in a time window of \( T \) samples. This can be rewritten as:

\[
D(A) = \|J_{1,T} - J^*A\|_2^2, \tag{2}
\]
where \( A = \text{vec}(A) \) and \( J_{1,T} = \text{vec}(J_{1,T}) \)

\[
J^* = \begin{pmatrix}
J'_{0,T-1} & 0_{T \times m} & \cdots & 0_{T \times m} \\
0_{T \times m} & J'_{0,T-1} & \cdots & 0_{T \times m} \\
\vdots & \vdots & \ddots & \vdots \\
0_{T \times m} & 0_{T \times m} & \cdots & J'_{0,T-1}
\end{pmatrix},
\]
where \( 0_{T \times m} \) is a \( T \times m \) zero matrix and \((\cdot)'\) is the transpose operator. The solution of Eq. (2) is:

\[
A = (J^*J^*)^{-1}J^*J_{1,T}, \tag{3}
\]
Because of the block of zeros in \( J^* \), it is possible to estimate separately each row \( A_i \) of \( A \):

\[
A_i = (J_{0,T-1}J'_{0,T-1})^{-1}J_{0,T-1}J_{1,T}(i) \quad i \in \{1, \ldots, m\},
\]
where \( J_{1,T}(i) \) is the \( i^{th} \) row of \( J_{1,T} \). To estimate the source intensities and their interaction iteratively, we replace \( J_{1,T} \) by \( AJ_{0,T-1} \) in the data fit term of Eq. (1) and \( U(J) \) by \( U(J_{0,T-1}) \). Eq. (1) becomes:

\[
E(J_{0,T-1}) = \frac{1}{2T} \|[M_{1,T} - GA_{0,T-1}]\|_2^2 + \lambda \|J_{0,T-1}\|_{21} \tag{4}
\]

The framework, iterative Source and Dynamics Reconstruction (iSDR), is explained in Algorithm 1. We start by initializing the MAR matrix \( A \) with the identity \((I)\). \( J \) with the MxNE solution and the maximum number of iterations \( N \). In step 4, we estimate the sources by optimizing Eq. (1). Then \( A \) is updated by Eq. (3) in steps 6-8. The algorithm stops iterating if there is a small change in the data fit error, \( RSS = ||M_{1,T} - GA_{0,T-1}||_2 \), or after \( N \) iterations. The difference between Eq. (4) and Eq. (1) (MxNE) is that the lead field matrix, \( G \), is multiplied by the MAR matrix, \( A \). The columns and rows of \( A \) corresponding to inactive sources are set to zero in step 7. This allows the framework to reduce the effect of inactive sources on the measurements, i.e. reduce the number of unknowns resulting in better estimation of the source activation.

Algorithm 1 iterative Source and Dynamics Reconstruction (iSDR)

1: procedure iSDR(G, M, N)
2: Initialize:
3: \( A \leftarrow I, (n,m) \leftarrow \text{shape}(G), \varepsilon \)
4: for \( i=1:N \) do
5: \( \tilde{J}_{0,T-1} \leftarrow \text{arg min}_{J_{0,T-1}}(E) \quad \triangleright \text{Estimate } \tilde{J} \)
6: \( \tilde{J}_T \leftarrow \tilde{A}\tilde{J}_{T-1} \quad \triangleright \text{Update } \tilde{A} \)
7: for \( j=1:m \) do
8: \( \tilde{A}_j \leftarrow (J_{0,T-1}J'_{0,T-1})^{-1}J_{0,T-1}J_{1,T}(j) \quad \triangleright \text{Estimate } \tilde{A} \)
9: \( RSS' \leftarrow ||M_{1,T} - G\tilde{A}||_2 \)
10: if \( RSS' < RSS'^{-1} < \varepsilon \) then
11: break
12: end if
13: end for
14: return \( \tilde{J}, \tilde{A} \)
15: end procedure

V. RESULTS AND DISCUSSION

We used a realistic three layers head model. 70 EEG electrodes were considered. To test the framework, we first obtain the structural connectivity from the dMRI as explained in section III. Then, we investigate the parameter estimation accuracy of the proposed framework by using simulated data generated from a simple MAR model. Four sources \((S_1, S_2, S_3, S_4)\) are located in the Occipital lobe, see Fig. 1 (a) and connected anatomically, see Fig. 1 (b). We activated \( S_1 \) and \( S_2 \) while \( S_3 \) and \( S_4 \), and the other sources are inactive. We decided not to activate \( S_3 \) and \( S_4 \) to investigate the effect of the assumption that the sources functionally interact if they are anatomically connected. \( S_1 \) and \( S_3 \) are anatomically connected but functionally independent.
In this paper, we present an iterative framework for EEG and MEG source reconstruction constrained by a whole brain dynamics model based on dMRI information. In our simulation study, the proposed framework correctly reconstructed sources and estimated the MAR elements, while the non-dynamical two-stage approach based on MxNE solution detects false-positive sources resulting in false functional connections. The framework assumes that the source dynamics is constant over a time window of \( T \) samples. The optimal number of samples needed to estimate the MAR entries is proportional to the maximal number of anatomical connections per source. It is hard for the framework to detect sources that have small activation in time and duration. Like all initialization dependent approaches, the initialization has to be within some proximity to the true sources, in order to find the correct activation. This means that as long as the initial active set contains true active sources, we are able to recover correct activations and interactions.

Representing the source dynamics by linear autoregressive modeling would introduce errors to the estimated functional interactions for sources with non-linear relationships. In this work, we dealt with focal sources. Extended generators (constant activation per region) can be assumed on regions obtained from dMRI-based parcellation [3], [14] in the proposed framework. Higher-order MAR model can be assumed.

The two-stage approach found false-positive active sources in low SNR, Fig. 2 (b) and (c), which result in false functional connections. This is the limitation of two-stage approximation of the MAR model. The iterative framework could correct the false activation, see Fig. 2 (f) and (g). It could detect the correct connections between the sources for SNR \( \geq 5 \) dB (Fig. 2 (k)) and it underestimates the MAR coefficients for \( 5 \geq \text{SNR} \geq -5 \) dB (Fig. 2 (l)) because of the noise but they are still close to the ground truth.

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VI. CONCLUSION

We developed a source reconstruction framework constrained by a whole brain dynamical model based on dMRI information. The framework iteratively solves the source activation and MAR entries. In our study, the framework could correct the false activation in low SNR level generated by the two-stage approach and detect the correct functional interactions between sources. Application to real datasets and comparison of the solutions to the physiological literature is essential to validate this framework.

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