Improving M/EEG source localization with an inter-condition sparse prior

Alexandre Gramfort, Matthieu Kowalski

IMPROVING M/EEG SOURCE LOCALIZATION WITH AN INTER-CONDITION SPARSE PRIOR

Alexandre Gramfort

Odyssée Laboratory,
ENS Paris - INRIA, France

Matthieu Kowalski

LATP, CMI, Université de Provence

ABSTRACT

The inverse problem with distributed dipoles models in M/EEG is strongly ill-posed requiring to set priors on the solution. Most common priors are based on a convenient ℓ_2 norm. However such methods are known to smear the estimated distribution of cortical currents. In order to provide sparser solutions, other norms than ℓ_2 have been proposed in the literature, but they often do not pass the test of real data. Here we propose to perform the inverse problem on multiple experimental conditions simultaneously and to constrain the corresponding active regions to be different, while preserving the robust ℓ_2 prior over space and time. This approach is based on a mixed norm that sets a ℓ_1 prior between conditions. The optimization is performed with an efficient iterative algorithm able to handle highly sampled distributed models. The method is evaluated on two synthetic datasets reproducing the organization of the primary somatosensory cortex (S1) and the primary visual cortex (V1), and validated with MEG somatosensory data.

Index Terms— Magnetoencephalography, Electroencephalography, Inverse problem, Elitist-Lasso, Proximal iterations

1. INTRODUCTION

Distributed source models in Magnetoencephalography and Electroencephalography (collectively M/EEG) use the individual anatomy derived from high resolution anatomical Magnetic Resonance Images (MRI) [1]. They consist in sampling the automatically segmented cortical ribbon with a high number of equivalent current dipoles (ECD). Each dipole adds linearly its contribution to the measured signal leading to a linear solution to the forward problem. The measurements $M \in \mathbb{R}^{N \times T}$ (N number of sensors and T number of time instants) are obtained by multiplying the current sources $X \in \mathbb{R}^{I \times T}$ (I number of dipoles) by a forward operator $G \in \mathbb{R}^{N \times I}$, called the lead field matrix, i.e., $M = GX$.

While solving the forward problem consists in computing G taking into account the electromagnetic properties of the head, solving the inverse problem consists in estimating the neural currents X^* that can explain the observed measurements. However, this latter problem is strongly ill-posed. It implies that X^* can only be computed if priors are set on the solution. Standard priors assume that a weighted ℓ_2 norm of X^*, denoted $\|X^*\|_{\mathbf{w};F}$ (Frobenius norm), is small. The estimated distribution of cortical currents X^* is obtained by solving :

$$X^* = \arg\min_X \|M - GX\|_F^2 + \lambda \|X\|_{\mathbf{w};F}^2 \ , \lambda \in \mathbb{R}_+ \quad (1)$$

with $\|X\|_{\mathbf{w};F}^2 = \sum_{t=1}^T \sum_{i=1}^I w_i x_{it}^2$, $\mathbf{w} = (w_i)_i \in \mathbb{R}_{+,*}^I$. Such priors are fast to compute and provide relatively accurate localizations, although they tend to smear the activations and therefore to over estimate the extent of the active regions.

During an experiment, a subject is generally asked to perform different cognitive tasks or to respond to various external stimulations. They are referred as different experimental conditions. With a standard ℓ_2 prior, it may occur, that the estimated active cortical region in condition 1 overlap the active region of condition 2, which may in practice be unrealistic considering what is known about neuroanatomy. In order to take into account this anatomical knowledge, and estimate more accurate mappings of some brain functional organizations, this contribution proposes to use a prior on the solution that integrates this dependency between multiple experimental conditions.

With ℓ_p norms, a value of p close to 1 induces *"sparsity"*, i.e., a small number of non zero coefficients, while a value of p close to 2 induces *"diversity"*, i.e., no non zero coefficients. Therefore, reducing the overlap of active regions, i.e., imposing each source to explain a small number of conditions, can be achieved by setting a ℓ_1 prior between conditions.

The rest of this contribution consists of three parts. Section 2, introduces the mixed norm with a ℓ_1 norm between conditions and a ℓ_2 norm over space and time. The iterative optimization procedure is also detailed. Section 3, presents some simulation results on two synthetic datasets reproducing the organization of the primary somatosensory cortex and the primary visual cortex. Finally the method is validated on MEG somatosensory data in Sect. 4.

2. METHOD

In order to introduce inter-condition sparsity constraints, currents corresponding to all conditions have to be estimated simultaneously. Let K denote the number of conditions. It is achieved by concatenating all measurements, $M \in \mathbb{R}^{N \times KT}$. Let $X \in \mathbb{R}^{I \times KT}$ have its elements now indexed by (i,k,t), i indexes space, k the condition and t the time.

Definition (Mixed norm). *Let $\mathbf{x} \in \mathbb{R}^{IKT}$ be indexed by a triple index (i,k,t) such that $\mathbf{x} = (x_{i,k,t})$. Let $p,q,r \geq 1$ and $\mathbf{w} \in \mathbb{R}^{IKT}_{+,*}$ be a sequence of strictly positive weights labelled by a triple index (i,k,t). We call mixed norm of $\mathbf{x}$ the norm $\ell_{\mathbf{w};p,q,r}$ defined by*

$$\|\mathbf{x}\|_{\mathbf{w};pqr} = \left(\sum_{i=1}^{I} \left(\sum_{k=1}^{K} \left(\sum_{t=1}^{T} w_{i,k,t} |x_{i,k,t}|^p \right)^{q/p} \right)^{r/q} \right)^{1/r} .$$

The problem that is addressed here is :

$$X^* = \arg\min_X \|M - GX\|_F^2 + \lambda \|X\|^2_{\mathbf{w};212} \ , \lambda \in \mathbb{R}_+ \quad (2)$$

A ℓ_1 prior is set over the index k corresponding to the condition, while an ℓ_2 prior is used over space and time. Each dipole has an incentive to explain a small number of conditions. The conditions are not supposed to change during the time window. Note that $\|X\|_{\mathbf{w};222} = \|X\|_{\mathbf{w};F}$ and that if $K = 1$, i.e., only one condition, $\|X\|_{\mathbf{w};212} = \|X\|_{\mathbf{w};F}$. Solving (2) is based on the notion of proximity operator, intensively used in convex analysis.

Definition (Proximity operator). *Let $\phi : \mathbb{R}^P \to \mathbb{R}$ be a lower semi-continuous, convex function. The proximity operator associated with ϕ and $\lambda \in \mathbb{R}_+$ denoted by $\text{prox}_{\lambda\phi} : \mathbb{R}^P \to \mathbb{R}^P$ is given by*[1]

$$\text{prox}_{\lambda\phi}(\mathbf{y}) = \arg\min_{\mathbf{x}\in\mathbb{R}^P} \|\mathbf{y} - \mathbf{x}\|_2^2 + \lambda\phi(\mathbf{x}) \ .$$

The proximity operator associated with the mixed norm $\|.\|^2_{\mathbf{w};212}$ is analytically given by the following proposition. We denote $\mathbf{y}_{i,k,\bullet} = (y_{i,k,1}, y_{i,k,2}, \ldots, y_{i,k,T})$.

Proposition. *Let $\mathbf{y} \in \mathbb{R}^{IKT}$ be indexed by a triple index (i,k,t). Let $\mathbf{w}$ a sequence of strictly positive weights such that $\forall t,\ w_{i,k,t} = w_{i,k}$. For each i, let w_{i,k'_i}, $[y_{i,k'_i}] = \sqrt{w_{i,k'_i} \sum_t |y_{i,k'_i,t}|^2}$ and $r_{i,k'_i} = [y_{i,k'_i}]/w_{i,k'_i}$ be ordered such that, for a fixed i, $\forall k'_i, r_{i,k'_i+1} \leq r_{i,k'_i}$. $\mathbf{z} = \text{prox}_{\lambda\|\cdot\|^2_{\mathbf{w};212}}(\mathbf{y})$ is given for each coordinate (i,k,t) by*

$$z_{i,k,t} = y_{i,k,t} \left(1 - \frac{\lambda\sqrt{w_{i,k}}}{1 + K_{\mathbf{w}_i}\lambda} \frac{\sum_{k'_i=1}^{K_i} [y_{i,k'_i}]}{\|\mathbf{y}_{i,k,\bullet}\|_2} \right)^+ .$$

with $K_{\mathbf{w}_i} = \sum_{k_i=1}^{K_i} w_{i,k_i}$, and the index K_i is the number such that

$$\lambda \sum_{k'_i=1}^{K_i} w_{i,k'_i} \left(r_{i,k'_i} - r_{i,K_i} \right) < r_{i,K_i} \leq \lambda \sum_{k'_i=1}^{K_i+1} w_{i,k'_i} \left(r_{i,k'_i} - r_{i,K_i} \right)$$

Sketch of the proof: Done using [2, Theorem 3] which gives $\text{prox}_{\lambda\|\cdot\|_{\mathbf{w};21}}(\mathbf{y})$ and $\text{prox}_{\lambda\|\cdot\|^2_{\mathbf{w};12}}(\mathbf{y})$ ♢

Remark.

1. *If $T = 1$, then $\text{prox}_{\lambda\|\cdot\|^2_{\mathbf{w};212}}(\mathbf{y}) = \text{prox}_{\lambda\|\cdot\|^2_{\sqrt{\mathbf{w}};12}}(\mathbf{y})$ which corresponds to the Elitist-Lasso problem [3].*
2. *The proximity operator is known analytically. It is simply a shrinkage operator. It implies that the solution is exact and relatively fast to compute.*

The steps of the iterative algorithm are :

Algorithm.

- Initialize *: Choose $X^{(0)} \in \mathbb{R}^{I\times KT}$ (for example* $\mathbf{0}$*).*
- Iterate *:*

  $$X^{(t+1)} = \text{prox}_{\mu\lambda\|\cdot\|^2_{212}} \left(X^{(t)} + \mu G^T (M - GX^{(t)}) \right)$$

  where $0 < \mu < \|G^T G\|^{-1}$.
- Stop *if $\left\|X^{(t+1)} - X^{(t)}\right\| / \left\|X^{(t)}\right\|$ is smaller than a fixed tolerance criterion.*

Theorem. *Algorithm 2 converges to a minimizer of Eq. 2, for any choice of $\mu \in [\epsilon, \|G^T G\|^{-1} - \epsilon]$, $\epsilon \in \mathbb{R}_{+,*}$.*

Sketch of the proof: The convergence of this algorithm is given by applying results of forward-backward proximal algorithm studied by Combettes et al. in [4] or by a Landweber iterative thresholding algorithm originally introduced by Daubechies et al. in [5] and used for mixed norms in [2]. ♢

Columns $(G_{\cdot i})_i$ of M/EEG forward operators are not normalized. The closer the dipole i from the head surface, the bigger $\|G_{\cdot i}\|_2$. This implies that a naive inverse procedure would favor dipoles close to the head surface. Using a weighted norm is an alternative to cope with this problem. With the mixed norm $\|.\|_{\mathbf{w},212}$, it is done by setting $w_{i,k} = w_i = \|G_{\cdot i}\|_2$.

3. SIMULATION STUDY

By setting a ℓ_1 prior between conditions, the mixed norm proposed penalizes overlap between active cortical regions. In order to illustrate it, two synthetic datasets have been generated. The first reproduces part of the organization of the primary somatosensory cortex (S1) [6]. Three, non overlapping, cortical regions with a similar area (cf. Fig. 2a), that

[1] Original Def. is $\arg\min \frac{1}{2}\|\mathbf{y} - \mathbf{x}\|_2^2 + \lambda\phi(\mathbf{x})$, but in *our* case the paper becomes more readable without the $\frac{1}{2}$.

could correspond to the localization of 3 right hand fingers, have been computed and used to generate synthetic measurements corrupted with an additive gaussian random noise. The amplitude of activation for the most temporal region (colored in red in Fig. 2), that could correspond to the thumb, was set twice bigger than the amplitudes of the two other regions. In practice the source amplitudes differ between conditions. The inverse problem was then computed with a standard $\|.\|_{\mathbf{w};F}$ norm and the $\|.\|_{\mathbf{w};212}$ mixed norm. Within the 3 neighboring active regions, a label corresponding to the maximum of amplitude in each of the three conditions was assigned to each dipole. Quantification of performance was done for multiple values of signal-to-noise ratio (SNR) by counting the percentage of dipoles that have been wrongly labeled. The SNR is defined here as 20 times the log of the ratio between the norm of the signal and the norm of the added noise. Results are also presented in Fig. 1. Results with an ℓ_1 prior, referred as *Lasso*, has also been added (corresponds to $\|.\|_{\mathbf{w};111}$, and the associated proximity operator is the well-known soft-thresholding operator). It can be observed that the $\|.\|_{\mathbf{w};212}$ produces systematically the best result. The ℓ_1 is very rapidly affected by the decrease of SNR, which is known in the M/EEG community. In order to have a fair comparison between all methods, the λ was set in each case to have $\|M - GX^*\|_F$ equal to the norm of the added noise, known in the simulations.

Results are illustrated in Fig. 2b and 2c on a region of interest (ROI) around the left primary somatosensory cortex. It can be observed that the extend of the most temporal region, obtained with $\|.\|_{\mathbf{w};F}$, is overestimated while the result obtained with the $\|.\|_{\mathbf{w};212}$ mixed norm is relatively accurate. Similar simulations have been performed in the primary visual cortex (V1), reproducing the well known retinotopic organization of V1. Results are presented in Fig. 3. Simulations lead to the same conclusion about the superiority of the $\|.\|_{\mathbf{w};212}$ mixed norm for the mapping of such brain functional organizations.

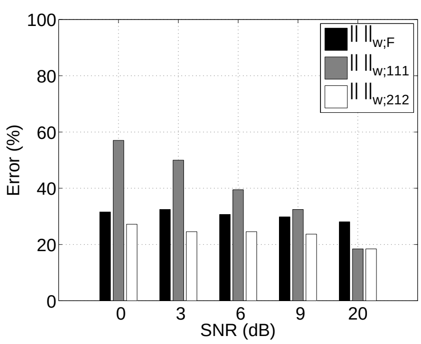
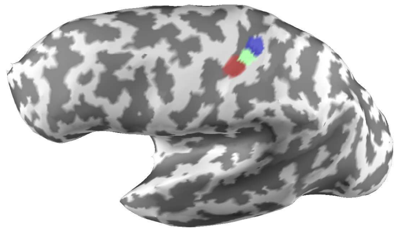
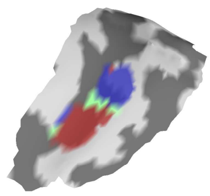


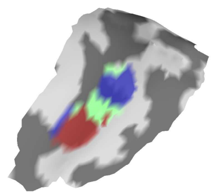
Fig. 1. Evaluation of $\|.\|_{\mathbf{w};F}$ vs. $\|.\|_{\mathbf{w};212}$ vs. $\|.\|_{\mathbf{w};111}$ estimates on synthetic somatosensory data. The error represents the percentage of wrongly labeled dipoles.



(a) Simulation data



(b) $\|.\|_{\mathbf{w};F}$ result (ROI)



(c) $\|.\|_{\mathbf{w};212}$ result (ROI)

Fig. 2. Illustration of result on the primary somatosensory cortex (S1) (SNR = 20dB). Neighboring active regions reproduce the organization of S1.

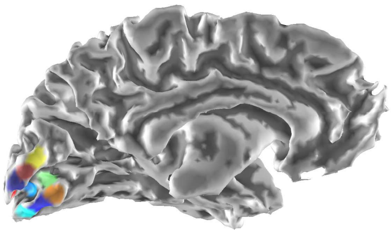
4. MEG STUDY

Results of the proposed algorithm using MEG data from a somatosensory experiment are now presented. The data acquisition was done using a CTF Systems Inc. Omega 151 system with a 1250 Hz sampling rate. The somatosensory stimulation was an electrical square-wave pulse delivered randomly to the thumb, index, middle and little finger of each hand of a healthy right-handed subject. Evoked data were computed by averaging 400 recordings of the same finger stimulation. To produce precise localization results, the triangulation over which cortical activations have been estimated was sampled with a very high number of vertices (about 55 000). The forward modeling was performed with a spherical head model[2] using dipoles with fixed orientations given by the normals to the cortex [1].

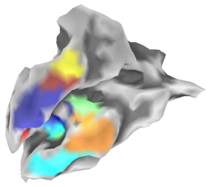
Prior to the current estimation, data were whitened using the noise covariance matrix Σ, estimated on the period before stimulation. Let $\Sigma = L^T L$ the Cholesky factorization of Σ. Whitening consists in replacing G by $L^{-1}G$ and M by $L^{-1}M$. With an additive gaussian noise model this implies that the noise, given by $M - GX \in \mathbb{R}^{N \times TK}$, is assumed to have a standard normal distribution. This provides a good estimate of $||M - GX^*||_F$ equal to $\sqrt{NTK}$. Therefore, the regularization parameter λ was set in order for X^* to be also the solution of the constrained problem : $X^* = \arg\min_X ||X||$ subject to $||M - GX||_F \leq \sqrt{NTK}$.

Results obtained with the right hand fingers during the period between 42 and 46 ms are presented in Fig. 4. Knowing

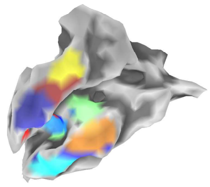
[2] http://neuroimage.usc.edu/brainstorm/



(a) Simulation data



(b) $\|.\|_{\mathbf{w};F}$ result (ROI)



(c) $\|.\|_{\mathbf{w};212}$ result (ROI)

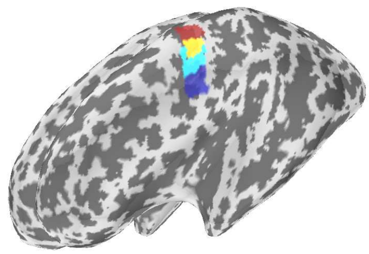
Fig. 3. Illustration of result on the primary visual cortex (V1) with $\mathrm{SNR} = 20\mathrm{dB}$. Neighboring active regions reproduce the retinotopic organization of V1.

that for this somatosensory dataset active parcels should have negative activations around 45 ms, regions with positive activations were first removed. Within the remaining regions, a label was assigned to each dipole based on its maximum amplitude across conditions. For each condition, equivalently each label, the biggest connected component was kept. Each of the 4 estimated components, corresponding to the 4 right hand fingers are presented in Fig. 4. Solutions using both norms $\|.\|_{\mathbf{w};F}$ and $\|.\|_{\mathbf{w};212}$ are detailed. With $\|.\|_{\mathbf{w};212}$ the well known organization of the primary somatosensory cortex [6] is successfully recovered, while with $\|.\|_{\mathbf{w};F}$, the component corresponding to the index finger is overestimated leading to an incorrect localization of the area corresponding to the thumb.

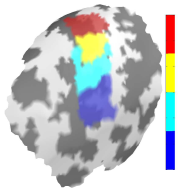
5. DISCUSSION

This contribution presents an alternative to the standard ℓ_2 priors, widely used in the M/EEG community, that improves the localization of cortical activations by offering the possibility to use a prior between different conditions. By proposing to perform the inverse problem on multiple conditions simultaneously and to use a mixed norm that sets an ℓ_1 prior between each condition, the method penalizes current estimates with an overlap between the corresponding active regions. When such an hypothesis holds anatomically, the more conditions are recorded and used in the inverse problem, the better is the localization of neuronal activity. By keeping an ℓ_2 prior over space and time, the proposed method guarantees a good robustness to noise like standard ℓ_2 based methods. This is confirmed by the simulations and the MEG somatosensory data, with which the method is successfully illustrated.

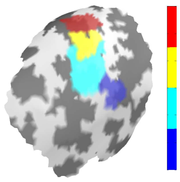
(a) Fingers color coded



(a) $\|.\|_{\mathbf{w},212}$ result



(b) $\|.\|_{\mathbf{w},212}$ result (ROI)



(c) $\|.\|_{\mathbf{w},F}$ result (ROI)

Fig. 4. Labeling results of the left primary somatosensory cortex in MEG

Acknowledgments : The authors are grateful to Dr Sabine Meunier from La Salpêtrire Hospital, INSERM, Paris, for permission to use parts of her somatosensory MEG data.

This work was supported by the EADS Foundation grant no. 2118 and the ANR ViMAGINE.

6. REFERENCES

[1] A. Dale and M. Sereno, "Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach," *J. Cogn. Neurosci.*, vol. 5, no. 2, pp. 162–176, 1993.

[2] Matthieu Kowalski, "Sparse regression using mixed norms," Tech. Rep., LATP, Marseille, France, 2008, http://hal.archives-ouvertes.fr/hal-00202904/.

[3] M Kowalski and B Torrésani, "Sparsity and persistence: mixed norms provide simple signals models with dependent coefficients," *Signal, Image and Video Processing*, 2008.

[4] P. L. Combettes and V. R. Wajs, "Signal recovery by proximal forward-backward splitting," *Multiscale Modeling and Simulation*, vol. 4, no. 4, pp. 1168–1200, Nov. 2005.

[5] I. Daubechies, M. Defrise, and C. De Mol, "An iterative thresholding algorithm for linear inverse problems with a sparsity constraint," *Commun. Pure Appl. Math.*, vol. 57, no. 11, pp. 1413 – 1457, Aug 2004.

[6] W. Penfield and T. Rasmussen, *The Cerebral Cortex of Man: A Clinical Study of Localization of Function*, Macmillan, 1950.