Fusion of Functional Brain Imaging Modalities via Linear Programming

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Table 1: *Notation*

Symbol	Meaning
N	Number of voxels, i.e. spatial resolution of high spatial resolution modality (FMRI)
M	Number of EEG sensors, i.e. spatial resolution of low spatial resolution modality
T	Number of time points of high temporal resolution modality (EEG)
U	Number of time points of low temporal resolution modality (FMRI)
$\otimes$	Kronecker product, $\mathbf{A} \otimes \mathbf{B} \equiv \begin{bmatrix} a_{00}B & \cdots \\ \vdots & \ddots \end{bmatrix}$
$\mathbf{I}_n$	$n \times n$ Identity matrix

Introduction

Fusion algorithms are employed in an attempt to construct a spatio-temporal estimate of neuronal activity using data gathered from multiple functional brain imaging modalities. Here, the estimate is built by placing a dipole in each voxel of the modality with highest spatial resolution, and estimating the time course of each dipole without constraining dipole orientations. The solution space thus consists of a matrix $\mathbf{S}$ of dimensionality $3N \times T$, which actually consists of 3 $N \times T$ matrices. Each such sub-matrix corresponds to the projection of the dipole to one axis [1]: $\mathbf{S} = \left[\; \mathbf{S}_x | \mathbf{S}_y | \mathbf{S}_z \; \right]^T$.

Table 2: *Forward EEG/FMRI equations.* $\tilde{\mathbf{S}}$ *is an* $N \times T$ *matrix holding the dipole strengths without orientation information, and* $\tilde{s}_{ij} = ||(s_{ij}^{(x)}, s_{ij}^{(y)}, s_{ij}^{(z)})||_2$

Modality	Matrix	Size	Estimate
EEG	$\mathbf{E}$	$M \times T$	$\hat{\mathbf{E}} = \mathbf{A}\mathbf{S}$
FMRI	$\mathbf{F}$	$N \times U$	$\hat{\mathbf{F}} = \tilde{\mathbf{S}}\mathbf{B}$

LP Approach

General LP Problem

Using abbreviations defined in Table 2 we formulate an initial LP problem as follows

$$\begin{aligned} \hat{\mathbf{E}} + \Delta_{\mathbf{E}} &= \mathbf{E} && \text{Constraints} && (1) \\ \hat{\mathbf{F}} + \Delta_{\mathbf{F}} &= \mathbf{F} && && (2) \\ \tilde{s}_{ij} &\geq 0 && \text{Region} && (3) \\ C &= \alpha \|\Delta_{\mathbf{E}}\|_1 + \beta \|\Delta_{\mathbf{F}}\|_1 && \text{Objective} && (4) \end{aligned}$$

where α and β control the relative influence of the two modalities.

Next we redefine each $|x|$, which are present in computation of C (4) and $\tilde{s}_{ij}$ (6), in a form suitable for LP as shown in Appendix A. This transformation leads to a side effect, namely minimization of the sum of absolute values $|s_{ij}|$, so we need to add another term $\gamma \|S\|_1$ to the objective function (4). This side effect could be considered a desired result - the minimization of L_1 norm of the solution results in its increased sparseness.

Transformation to LP

It is required to agree on the order of how we 'unfold' any 2D array into a 1D sequence. Each unfolded matrix $\mathbf{X}$ is presented as a vector $\bar{\mathbf{X}}$ and it is decomposed rowwise - rows compose unfolded matrix when taken sequentially. So for $\mathbf{S}$ $3N \times T$ matrix, which is the argument of optimization we want to obtain, we get vector $\bar{\mathbf{S}}$ $3NT \times 1$ where the order of dimensions growth within the vector is $t \rightarrow$ *sensor* $\rightarrow$ orientation(*axis*), so time is the fastest growing dimension.

EEG Equation in LP form

We can represent (1) in a form suitable for LP using the Kronecker product

$$(\mathbf{A} \otimes \mathbf{I}_T)\bar{\mathbf{S}} = \bar{\mathbf{E}} \qquad (5)$$

where $\mathbf{I}_Z$ is the identity matrix of size $Z \times Z$.

FMRI Equation in LP form

First we need to encode the definition of $\tilde{\mathbf{S}}$ into an LP constraint matrix using an approximation described in Appendix A,

$$\tilde{\mathbf{S}} = l(|\mathbf{S}_x|, |\mathbf{S}_y|, |\mathbf{S}_z|), \tag{6}$$

where $l(\cdot)$ is an LP approximation of the l_2 norm.

In a similar to (5) way we represent the product $\tilde{\mathbf{S}}\mathbf{B}$ in a form suitable for LP

$$\hat{\mathbf{F}} = (\mathbf{I}_N \otimes \mathbf{B}^T)\bar{\tilde{\mathbf{S}}} \tag{7}$$

Final LP form

Finally we group all the constraints and the objective function together into an extended LP canonical form,

$$(\mathbf{A} \otimes \mathbf{I}_T)\bar{\mathbf{S}} + \Delta_{\bar{\mathbf{E}}} = \bar{\mathbf{E}} \tag{8}$$
$$(\mathbf{I}_T \otimes \mathbf{B}^T)\bar{\tilde{\mathbf{S}}} + \Delta_{\bar{\mathbf{F}}} = \bar{\mathbf{F}} \tag{9}$$
$$\tilde{\mathbf{S}} - l(|\mathbf{S}_x|, |\mathbf{S}_y|, |\mathbf{S}_z|) = 0 \tag{10}$$
$$\bar{\tilde{\mathbf{S}}} \geq 0 \tag{11}$$
$$C = \alpha||\Delta_{\mathbf{E}}||_1 + \beta||\Delta_{\mathbf{F}}||_1 + \gamma||S||_1 \tag{12}$$

Simulations

Data

To check the method artificial data was created. Brain volume is simulated as a half-sphere 9 voxels in diameter, which gives us 132 voxels to be considered. A simple spherical model was used to generate a gain matrix for 11 EEG sensors distributed across the half-sphere surface. We generated a random activation map $\mathbf{S}$ consisting of 5 voxels firing within a 600ms interval after t_0=2 sec from the beginning of the timecourse (1 voxel at 0ms, 200ms, 400ms, and 2 voxels at 600ms after t_0) with the same amplitude but in different locations and random orientation. Using this map, clean EEG and FMRI were constructed through forward equations given in Table 2. EEG was sampled at 10Hz and FMRI at 1Hz.

Additive noise was used to corrupt EEG signal: Gaussian noise with SNR=-5dB[1] which equivalently constituted %RMS≈23%, where $\%RMS = (\sigma_{\text{noise}}/max(x)) \times 100\%$ for clean signal x. SNR for EEG was fixed across all experiments. An FMRI signal was also corrupted by additive Gaussian noise with variable SNR to do some noise sensitivity analysis (for FMRI SNR 2dB ≈ 35% %RMS).

[1]This value is so low due to the sparsity of the activation map - 5 activations within 16 seconds of simulation interval

Conditioning

Before analysis, both data sets (EEG E and FMRI F) and corresponding matrices (A and B) were normalized by the estimated noise standard deviation in order to properly scale the error terms. Then weights in error terms were used to remove dimensionality effect by assigning $\alpha = 1/(MT)$ and $\beta = 1/(NU)$.

As multiple tests with different SNR levels have shown, best estimates of activations were achieved when $\gamma = 1/(3NT\sigma_S)$, where σ_S is the standard deviation of the simulated activation map. Because this was possible only for synthetic data, a robust method to estimate γ is our next goal.

Results

Obtained solutions for FMRI, with a SNR of 3 dB returned all 5 original activations as the 5 highest obtained activations for duration of the experiment, with ≈ 50% of the energy spread through the rest of the volume. Lowering the SNR to 1dB lead to stable detection of 3/5 activations.

Future Work

Constrained Orientation

It is a common practice to use an anatomical MRI to constrain the inverse EEG solution to gray matter dipoles with orientation normal to the cortical surface [2]. With that assumption we do not need an l_2 approximation to represent $\tilde{\mathbf{S}}$ in a form suitable for LP, since the dipole magnitudes are linearly related to the potentials at the sensors.

Another issue to address here is that each voxel can cover area of more than one single dipole, when two or more triangulation elements from the cortical surface reconstruction has their area covered by the same voxel. Because these regions are separated in space, their impacts on changes in rCBF (regional cerebral blood flow) can be linearly added under reasonable assumptions.

Experiments

Real experiments require an efficient large-scale sparse LP solver with 'warm start'. After appropriate algorithms have been designed and implemented, experiments will be constructed in order to obtain good subject-specific estimates of HRF [3].

Discussion

Robust method for estimation of α, β and γ factors is required. There is a method suggested in [4] for weighting L_1 factor in estimating sparse convolution kernel, but it is ad-hoc and very computationally demanding when dealing with large arrays.

Conclusion

This method makes a number of simplifying assumptions which convert the EEG/FMRI integration problem into optimization of a convex function, of a form amenable to efficient solution as a very sparse linear programming problem. The assumptions made in doing this are, surprisingly, in general somewhat more robust than those generally used to cast EEG/FMRI integration as optimization of a non-convex function not amenable to efficient global optimization. This is because the L_1 norm used here corresponds to a more robust statistical estimator than the L_2 norm generally used. For this reason, even though this technique results in a tractable global optimization, it is more robust to non-Gaussian noise and outliers than approaches that make the Gaussian noise assumption [4].

References

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A Canonical Form for LP

Above we have freely used the minimum operator in formula like $a = \min(b, c)$, the absolute value function $y = |x|$, and other constructs not allowed in the canonical form of a linear program. In this section we describe a general technique for reducing a system of linear equalities and inequalities which include minimization of the L_1 norm, $|\cdot|$ and $\min(\cdot,\cdot)$ operators, along with a linear objective function, into a linear programming problem in standard canonical form.

Absolute Value

Commonly accepted way to deal with absolute value function $y = |x|$ in LP is to represent x as a difference of two non-negative numbers, with $|x|$ as their sum. Minimization of the sum would force one of them to become 0, with the other corresponding to $|x|$:

$$x = x^+ - x^- \tag{13}$$
$$|x| = x^+ + x^- \tag{14}$$
$$x^+ \geq 0 \tag{15}$$
$$x^- \geq 0 \tag{16}$$

while minimizing $|x|$

Minimal Value

To obtain $a = \min(b, c)$ we first relax it to

$$a \leq \min(b, c), \tag{17}$$

Inclusion of a $-a$ term in the objective function will lead to maximization of a thus achieving the necessary equality. Equality (17) can be easily represented in a form suitable for LP

$$a - b \leq 0$$
$$a - c \leq 0$$

Approximation of l_2 norm in LP

The magnitude of a dipole with moment vector $\mathbf{m} = (x, y, z)$ is $||\mathbf{m}|| = \sqrt{x^2 + y^2 + z^2}$. We assume that FMRI readings are related linearly to dipole magnitudes. In order to fit this into an LP framework, we need a way to approximate $e = ||\mathbf{m}||$ within an LP. Our solution is to note that the $\min(\cdot,\cdot)$ and modulus $|\cdot|$ functions can be used freely in a LP and then reduced to canonical form using the transformation described below. For our method, let $\{\mathbf{R}_i\}$ be a set of rotation matrices. To approximate $||\mathbf{m}||$ we let

$$e_i = ||\mathbf{R}_i \mathbf{m}||_1 \qquad e = \min_i e_i \tag{18}$$

where $||\cdot||_1$ denotes the l_1 norm. These can simply be added to the linear programming problem, enforcing the relation $e \approx ||\mathbf{m}||$. We can increase the number of matrices in the set to improve the accuracy of this approximation, at the expense of computational efficiency.