A New Model for Canonical Correlation Analysis with Spatial Constraints

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Target Audience

This study provides important improvements in fMRI data analysis techniques for the detection of active brain areas.

Purpose

The purpose of this study is to improve techniques based on constrained canonical correlation analysis (cCCA), used to detect activation patterns in an episodic memory task. CCA has been used to determine active voxels in a group of neighboring voxels. Constraints are introduced in order to give more weight to the center voxel (the one which activation is being evaluated) in comparison to its 8 neighboring voxels. Two studied models[1] are given by the constraints $a_1 \geq \sum_{n=2}^{9} a_n$ and $a_1 \geq \max\{a_n : \geq 2\}$ respectively. We want to answer the following questions: is it possible to establish a family of constraints (indexed by real valued parameters) that naturally includes these two particular models? And if so, how good are these two particular models compared to optimal models from such family of models? To answer these questions we define a family of constraints that depends on a parameters $p \geq 1$ and $\psi \geq 1$. We obtain the two models when $(p, \psi) = (1,1)$ and $(p, \psi) = (\infty, 1)$ respectively. We show that excellent performance detecting activation is obtained for models such as $(p, \psi) = (2,10)$, among several others cases. We also study how changes in the two parameters p and ψ affect the optimal solution of the corresponding cCCA problem.

Methods

Imaging: Six normal subjects with previous fMRI experience were scanned. Subjects were instructed to perform an episodic memory task consisting of viewing faces and occupations with instruction, encoding, recognition and distraction (control) periods. FMRI was performed in a 3.0 T GE scanner (TE=30ms, FOV=22 cm×22 cm, 25 slices (coronal oblique), thickness/gap=4.0 mm/1.0 mm, resolution 96×96 interpolated to 128x128, 283 time frames, TR=2s.

Analysis: Each group of 9 voxels in a 3x3 neighborhood provides data $Y \in \mathbb{R}^{283\times 9}$ (the center voxel corresponds to the first column), while the 4 temporal reference functions that model *instruction*, *encoding*, *recognition* and *control* in the memory task provide data $X \in \mathbb{R}^{283\times 4}$. Given such a pair (Y, X) we solve the following optimization problem: find $\alpha \in \mathbb{R}^{9\times 1}$ and $\beta \in \mathbb{R}^{4\times 1}$, maximizing the correlation between $Y\alpha$ and $X\beta$, subject to $\alpha_1 \geq \psi \cdot \| (\alpha_2, \dots, \alpha_m) \|_p$, and $\alpha \geq 0$ (point wise). This formulation is equivalent to the multivariate regression problem of minimizing $\| Y\alpha - X\beta \|$ subject to $\alpha \geq 0$, $\alpha_1 \geq \psi \cdot \| (\alpha_2, \dots, \alpha_m) \|_p$ and $\alpha^T S_{YY} \alpha = \beta^T S_{XX} \beta$=1. Defining $B = X^+ Y$, $E = ((Y - XB)\alpha)^T ((Y - XB)\alpha)$ and $H = (CB\alpha)^T (C(X^T X)^{-1} C)^{-1} (CB\alpha)$, (where $C = [1,0,-1,0]$ is the contrast vector *encoding minus control*) we construct the Wilk's lambda statistic $\Lambda = \mathrm{E}/(\mathrm{E} + \mathrm{H})$. Then we define the statistic used to determine whether the center voxel is active or not as $\Pi = S \cdot sign(C \cdot B \cdot alpha)$, where S is the parametric p-value of the conversion of Λ to an F statistic. Given data Y corresponding to the local neighborhood we make the above computations, and declare the center voxel as active if the Π is no less than a certain threshold.

To measure the performance of this method (for fixed p, ψ), we use the area under the ROC curve in the interval [0,0.1]. We estimate each true positive rate throughout simulations, repeating 500 times the following experiment. We use wavelet-resampling in the temporal domain to obtain null data from resting state data of the whole brain. This gives us more than 90,000 time courses of *noise*. We then simulate data $Y \in \mathbb{R}^{t\times 9}$ for an *active* 3×3 neighborhood as follows. Initialize all the entries of Y as zero. Then redefine the first column of Y as the second column of X, i.e., the center voxel is now active by construction. Before adding noise, make other neighboring voxels active as well. For this select a number $l \in \{0, \dots, 8\}$ at random, and then select l different numbers from $\{2, \dots, 9\}$ at random. The corresponding l columns of Y are also redefined as equal to the 2nd column of X. Now select at random 9 time courses from the wavelet resampled data, forming an array $N \in \mathbb{R}^{283\times 9}$. Use $Y + N \cdot SNR$ as the data to input into the cCCA method (together with X). The false positive rate is estimated with the same procedure, except that we *do not* redefine the first column of Y as the second column of X.

Results We computed ROC curves for different values of p and ψ. Fig. 1 shows the ROC curve for the case $(p, \psi) = (2,10)$, which has an area under the curve that is almost 45% more than the area for $(p, \psi) = (1,1)$. We also include the case $(p, \psi) = (16,1)$, which is practically the same as the constraint $a_1 \geq \max\{a_n : \geq 2\}$ (see Discussion). Besides $(p, \psi) = (2,10)$, several other combinations give very good results as well. Fig. 2 shows an image corresponding to $(p, \psi) = (2,1)$ with p-value 10^{-4}. Note that no artifacts are introduced, and very distinct information of activation within the hippocampal areas are found, consistent with episodic memory activation.

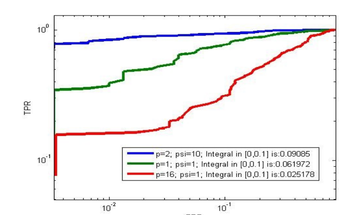

Fig.1

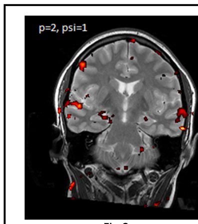

Fig.2

Discussion Due to the complexity of the constraints, the optimal solution α (on which the statistic to determine activation is constructed) can be described as the solution of a system of polynomial equations of degree p with coefficients dependent on the data (Y, X), hence practically impossible to be solved analytically. Instead, we find α numerically using a gradient descend approach with backtracking line search. The constraint $\alpha \geq 0$ requires to consider 512 different configurations for all the combinations of the last 8 coordinates being equal to 0. To speed up the computations the line search stops once the current point is outside the feasible region. These saves a substantial amount of time with a very low cost on the accuracy of the solution. Although for $p < 1$, $\|.\|_p$ is not a norm, all our computations and algorithm are still valid, and if fact we observe that as $p \to 0$, the more coordinates of the optimal α become equal to 0, until only 2 of them are non-zero ($\alpha_1$and some other one). Decreasing p even more does not change the optimal however (which can be verified analytically). On the other hand, as $\psi \to \infty$, the coordinates $\alpha_2 \dots \alpha_9$ are pushed to zero, and the optimal solution converges to that of single-voxel analysis. Note that the l_p norm converges to the l_∞ norm as $p \to \infty$, and in $\mathbb{R}^9$, l_{16} and l_∞ are practically the same.

Conclusion We propose and study a family of constraints for CCA, which naturally generalizes two interesting previously studied models. The solutions of these models can be found numerically and efficiently, and for several choices of these constraints, the performance of the method in determining active voxels is excellent as measured via ROC simulations.

References

1. Cordes, D., et al. Optimizing the performance of local canonical correlation analysis in fMRI (2012) Human Brain Mapping, 33(11), 2611-2626.