Predictive Modeling of fMRI Brain States using Functional Canonical Correlation Analysis

S. Ghebreab[1,2], A.W.M. Smeulders[1], and P. Adriaans[2]

[1] ISLA lab, Informatics Institute, University of Amsterdam, The Netherlands
[2] HCS lab, Informatics Institute, University of Amsterdam, The Netherlands

Abstract. We present a novel method for predictive modeling of human brain states from functional neuroimaging (fMRI) data. Extending the traditional canonical correlation analysis of discrete data to the domain of stochastic functional measurements, the method explores the functional canonical correlation between stimuli and fMRI training data. Via an incrementally steered pattern searching technique, subspaces of voxel time courses are explored to arrive at (spatially distributed) voxel clusters that optimize the relationship between stimuli and fMRI in terms of redundancy. Application of the method for prediction of naturalistic stimuli from unknown fMRI data shows that the method finds highly predictive brain areas, i.e. brain areas relevant in processing the stimuli.

1 Introduction

Prediction of brain states directly from non-invasive measurements of brain activity has emerged as a powerful alternative to correlation of external stimuli with characteristic brain activity. The advantage of inverting the task from correlating external stimuli with brain activity to predicting stimuli from brain activity is that it facilitates evaluation of spatially distributed brain responses to complex uncontrolled stimuli [1]. Prediction of brain states from brain activity data, however, is a challenging task in its own right, requiring advanced data processing methods that go beyond conventional mass univariate data analysis of functional neuroimage data.

Various multivariate pattern classification approaches have recently been proposed for prediction of brain states directly from fMRI measurements. In these approaches, a classifier is trained on fMRI data to discriminate between different known brain states and then applied to predict brain states from unknown fMRI data. Several neuroimage studies (e.g., [2], [3]) successfully predicted complex stimuli from fMRI using multivariate pattern classification approaches, showing their ability to identify response patterns across the full spatial extent of the brain without attempting to localize function.

Here, we extend on the incremental functional multivariate regression method proposed in [4], which exploits the continuous nature of external stimuli and brain processes. Cast into an incremental pattern searching framework, this method performs functional principal component regression to find distributed voxel clusters that optimize a linear model in terms of F-statistic. In this work, we pursue canonical correlation analysis rather than principal component analysis in order to fully exploit correlated variation in stimuli and brain activity data. We show that in comparison to functional principal component analysis, functional canonical correlation analysis captures functional subspaces that are more appropriate for prediction of brain states.

2 Method

In the remainder, we consider stimuli and fMRI data as continuous functions of time, sampled at the scan interval and subject to observational noise. The functional form of the discrete data points is obtained by fitting a continuous curve through them.

2.1 Functional Data Representation

The four-dimensional fMRI data $I(\mathbf{x}, t)$, where $\mathbf{x} \in \Re^3$ denotes the spatial position of a voxel and t denotes its temporal position, defines the predictor set, i.e. the independent variable set. The image $I(\mathbf{x}, t)$ is preprocessed to arrive at a (spatially) normalized data set. We represent each voxel time course in functional form by $f(t)$, with t denoting the continuous path parameter. The vector $\mathbf{f} = [f_1, ..., f_S]^T$ of S functionalized voxel time courses contains the complete set of independent variables.

We represent the stimuli data by the functional $g(t)$, t being the continuous time parameter. We register $g(t)$ to each voxel time course $f_s(t)$ in order to be able to compare equivalent time points on stimulus and brain activity data, i.e. to capture subtle localized variations in Haemodynamic delays across brain regions and subjects. Curve registration here reduces to finding the small shift and nonlinear transformation that minimizes a global alignment criteria in least squares sense. Registration of $g(t)$ to all voxel time courses S results in the dependent variable set $\mathbf{g}(t) = [g_1(t), ..., g_S(t)]^T$.

2.2 Functional Canonical Correlation

We employ canonical correlation analysis to capture the relationships between the two sets of functions $\mathbf{f}(t)$ and $\mathbf{g}(t)$. Functional canonical correlation analysis [5] explores the dominant modes of correlation between each pair of functions $f_s(t)$and $g_s(t)$. Canonical weighting functions $\eta(t)$ and $\xi(t)$ are sought that maximize the sampled squared correlation of

$$\int \eta(t) f_s(t) dt \quad \text{and} \int \xi(t) g_s(t) dt \tag{1}$$

across all pair of functions. The correlation that results from the maximizing weight functions $\eta_1(t)$ and $\xi_1(t)$ is the first canonical correlation ρ_1. The corresponding first pair of canonical loadings are defined as

$$f_{s1} = \int \eta_1(t) f_s(t) dt \quad \text{and} \quad g_{s1} = \int \xi_1(t) g_s(t) dt. \tag{2}$$

The second pair of canonical weight functions $\eta_2(t)$ and $\xi_2(t)$ that maximize the correlation ρ_2 is found in the same manner. This second set is orthogonal to the first, i.e. satisfies the constraints

$$\int \eta_1(t) \eta_2(t) dt = 0 \quad \text{and} \int \xi_1(t) \xi_2(t) dt = 0. \tag{3}$$

This process in repeated until Q main modes of correlation have been found. In order to arrive a small number of meaningful modes of correlation, we regularize the weighting functions by penalizing their roughness (see [5] for more detail).

2.3 Overall Fit Function

To determine the amount of shared variance, we make use of the redundancy index [6], which is analogous to the R^2 statistic in multiple regression. This index provides a summary measure of the ability of the set of independent variables $\mathbf{f}(t)$ to explain variation in the dependent variables $\mathbf{g}(t)$. Here we compute

$$R = \frac{1}{Q}\sum_{q=1}^{Q}(\rho_q^2 \frac{1}{S}\sum_{s=1}^{S} g_{sq}^2) \tag{4}$$

where $\frac{1}{S}\sum_s g_{sq}^2$ is the amount of shared variance in $\mathbf{g}(t)$ explained by $\xi_q(t)$ and the squared canonical correlation ρ_q^2 is the amount of variance in $\xi_q(t)$ that can be explained by $\eta_q(t)$. We use this measure as the overall fit function that drives the search for voxel-time courses that are strongly related to the external stimuli.

2.4 Incremental Subspace Exploration

In order to efficiently find the subset of voxels that maximizes the overall fit R, we use the incremental search technique described in [7]. With help of this technique, at each increment a refined voxel subset is obtained and evaluated in terms of equation 4. At increment i, the subset of voxels time courses $S^i \subset S$ gives rise to canonical weight functions $\eta_q^i(t)$ and $\xi_q^i(t)$ and loadings

$$f_{sq}^i = \rho_q \int f_s(t)\eta_q^i(t) \quad \text{and} \quad g_q^i = \rho_q \int g(t)\xi_q^i(t). \tag{5}$$

Then, the set $\mathbf{F}^i = [\mathbf{f}_1^i, ..., \mathbf{f}_S^i]$ is explored using $\mathbf{g}^i = [g_1^i, ..., g_Q^i]$ as pilot. In short, elements are selected from $\mathbf{F}^i$ that have smallest Euclidean distance to $\mathbf{g}^i$ and form one or more spatially distributed clusters of a predefined size. These voxel elements are assumed to have some relationship with the stimulus and form the basis for computations at increment $i + 1$. This process is continued until convergence is reached with voxel subset $\mathcal{S} \subset S$, yielding scalar vector $\boldsymbol{\rho}_{\mathcal{S}}$ and vector of weight functions $\boldsymbol{\eta}_{\mathcal{S}}(t)$ and $\boldsymbol{\xi}_{\mathcal{S}}(t)$.

2.5 Brain State Prediction

We use $\boldsymbol{\rho}_{\mathcal{S}}$, $\boldsymbol{\eta}_{\mathcal{S}}(t)$ and $\boldsymbol{\xi}_{\mathcal{S}}(t)$ for prediction of brain states from new and spatially normalized fMRI data. The voxel time courses at spatial locations corresponding to those resulting from incremental exploration are extracted from this fMRI data and functionalized into $\tilde{\mathbf{f}}(t) = [\tilde{f}_1(t), ..., \tilde{f}_{\mathcal{S}}(t)]^T$. Then, following [8], prediction reduces to

$$\tilde{\mathbf{g}}(t) = \tilde{\mathbf{F}}\boldsymbol{\xi}_{\mathcal{S}}(t) \tag{6}$$

where the $\mathcal{S} \times Q$ canonical correlation loadings matrix $\tilde{\mathbf{F}}$ has elements

$$\tilde{f}_{sq} = \rho_q \int \tilde{f}_s(t)\eta_q(t) \tag{7}$$

and $\tilde{\mathbf{g}}(t)$ is the vector of predicted stimuli. We define the mean of $\tilde{\mathbf{g}}(t)$ as the stimulus that gave rise to the brain response represented by $\tilde{\mathbf{f}}(t) = [\tilde{f}_1(t), ..., \tilde{f}_S(t)]^T$. Hence, we have brain locations that are likely involved in processing the external stimulus as well as characterizations of the relationship between activity at these areas and the stimulus.

3 Experiments and Results

3.1 Experiment

Evaluation of our method is done on a data subset from the brain activity interpretation competition [9, 10], involving fMRI scans of three different subjects and two sessions. In each session, a subject viewed a new Home Improvement sitcom movie for approximately 20 minutes. All three subjects watched the same two movies. The scans produced volumes with approximately 35.000 brain voxels, each approximately 3.28mm by 3.28mm by 3.5mm, with one volume produced every 1.75 seconds. These scans were preprocessed (motion correction, slice time correction, linear trend removal) and spatially normalized to the Montreal Neurological Institute brain atlas.

After fMRI scanning, the three subjects watched the movie again to rate 30 movie features at time intervals corresponding to the fMRI scan rate. In our experiments, we focused on the 13 core movie features: Amusement, Attention, Arousal, Body Parts, Environmental Sounds, Faces, Food, Language, Laughter, Motion, Music, Sadness and Tools. The real-valued ratings were convolved with a standard hemodynamic response function, then subjected to voxel-wise non-linear registration as described in 2.1.

For training and testing our model, we divided each fMRI scan and each subject rating into 6 parts corresponding with movie on parts and functionalized these parts by fitting a 30 coefficient B-spline to their discrete data points. This resulted in 18 data sets for training (3 subjects $\times$ 6 movie parts) and another 18 for testing. We used movie 1 data for training and movie 2 data for prediction, and vice versa, with parameter values as in [4]. Functional cross correlation between manual feature rating functions and the automatically predicted feature functions was used as an evaluation measure.

3.2 Results

Average cross correlation results of 2×18 cross validations for all 13 movie features are shown in figure 1a. Also shown are previous results based on principal component regression. As can be seen, canonical correlation analysis produces higher cross correlation values for all features except for feature "Motion". Four features exceed the 0.5 threshold, indicating that there is a significant degree of match between the subject ratings and the predicted ratings. The average cross correlation across features for canonical correlation analysis is 3.7, against 3.2 for principal component regression. In almost all cross validation predictions, the number of voxels used were significantly smaller for canonical analysis than for principal component analysis.

The highest average cross correlation value of 6.9 is obtained for feature "Faces", with the best single result of 7.8 for prediction of subject 3 watching part 2 of movie 1. For this feature, first level analysis of each of the 18 training data sets associated with movie 2 produced a total number of 480 predictive voxels. In the second level analysis, these voxels were analyzed again to arrive at a reduced data set of 104 voxels for performing canonical correlation analysis and determining weight functions. Figure 2 shows gray level image with color overlay and surface rendering of a subset of the 104 voxels from second level analysis. The cross hair shows the voxel location in the occipital lobe that was found to be predictive across most subjects and movie parts.

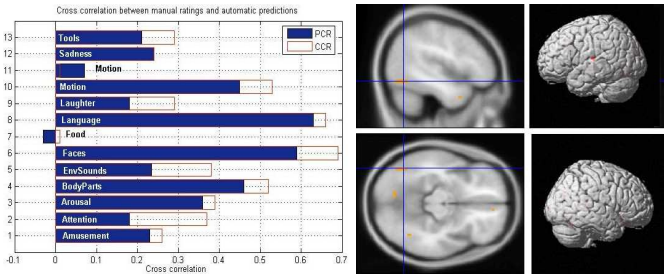

Fig. 1. Left: cross correlation values from cross-validation for 13 core movie features, using principal component analysis (PCR) and canonical corelation analysis (CCR) Right: gray level image with color overlay and surface rendering of a subset of predictive voxels from second level analysis. Color denotes predictive power and cross hair shows most predictive location.

4 Conclusion

We have proposed an incremental functional canonical correlation analysis method for prediction of brain states from fMRI. In comparison with the principal component regression method in [4], the proposed method produces better prediction results using a smaller amount of spatially distributed brain voxel clusters. We conclude that functional canonical correlation analysis captures important modes of correlation between fMRI and stimuli data that are very suited for prediction of stimuli based on new fMRI data. Given the high prediction results, we emphasize that our method is very promising for identifying and characterizing complex brain responses to intricate external stimuli.

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