CLUSTERED COMPONENT ANALYSIS FOR FMRI SIGNAL ESTIMATION AND CLASSIFICATION *†

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ABSTRACT

In this paper, we introduce a method for estimating the statistically distinct neural responses in an sequence of functional magnetic resonance images (fMRI). The crux of our method is a technique which we call clustered component analysis (CCA). Clustered component analysis is a method for identifying the distinct component vectors in a multivariate data set. CCA is distinct from principal components analysis (PCA), and independent components analysis (ICA), because it is not constrained to produce orthogonal component vectors and it does not assume that components are indepedent. CCA employs Bayesian estimation methods such as expectation-maximization (EM) and Rissanen order identification to determine the best set of component vectors.

1 INTRODUCTION

Functional magnetic resonance imaging (fMRI) attempts to analyze the neural response to a stimulus by measuring small temporal changes in a sequence of MRI images. Typically, the subject stimulus is assumed to be periodic in time. For example, two alternating visual stimuli might be presented to a subject using a regular on/off pattern. In this case, the input is effectively a squarewave, so any steady state neural response must also be a periodic signal with the same period. Importantly, the output signal will be periodic even if the neural response is a nonlinear function of the input stimulus.

Generally, signal detection methodology in fMRI assumes that the fMRI response to neuronal stimulation is the same in all regions of the brain and for all stimuli. Very little data exists on the validity of this assumption.

Recently, there has been considerable interest in not only detecting activated neural regions, but also quantifying the so-called hemodynamic response function for each stimulus and region of the brain. This is a particularly difficult task when one considers that the blood oxygen level detection (BOLD) signal-to-noise ratio for a typical 1.5T MRI scanner is quite low.

In order to increase signal-to-noise ratio, we use a method similar to that used by Bullmore, *et al* [1]. This method decomposes the temporal response at each pixel into harmonic components corresponding to a sine and cosine series expansion at the appropriate period. We have found that it is possible to further increase the signal-to-noise ratio by estimating an M dimensional signal subspace [2]. This is done by estimating the signal covariance as the positive definite part of the difference between the total signal covariance and the noise covariance. Each pixel's response is then represented by an M dimensional feature vector.

Our objective is to determine which statistically distinct responses exist in particular regions of interest. Two waveforms that differ only in amplitude, but not shape, are not considered distinct. Therefore, each distinct response corresponds to a unique *direction*, independent of amplitude, in the M dimensional feature space. Researchers have used principal components analysis (PCA) [1], and independent components analysis (ICA) [3] to extract these distinct directions. However, both these methods have potential disadvantages. PCA results in principal components (eigenvectors) that are orthogonal. In practice, it is unlikely that the distinct behaviors in the data correspond to orthogonal signals. Alternatively, ICA attempts to determine the transformation that results in independent rather than simply uncorrelated components. However, it is not necessary that statistically distinct components be independent. Finally, both methods are constrained to produce exactly M components.

In this paper, we present a new methods for analyzing the multivariate fMRI feature vectors which we call clustered component analysis (CCA). This method depends on a explicit model of the feature vectors and is implemented through Bayesian parameter estimation. The estimation procedure is similar in in many respects to traditional clustering algorithms; however, it differs from existing methods because it produces component *directions* rather than traditional cluster means. The CCA method incorporates the expectation-maximization (EM) algorithm [4] together with a cluster merging technique which is used to estimate the true number of clusters [5].

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2 CLUSTERED COMPONENT ANALYSIS

Let Y_n be an M dimensional feature vector for pixel n. Furthermore, let $E = [e_1, \cdots, e_K]$ be K component directions in the feature space, each with unit norm. The basic assumption of our method is that

$$Y_n = \alpha_n e_{X_n} + W_n$$

where α_n is the unknown amplitude for pixel n, $1 \leq X_n \leq K$ is the class of the pixel, and W_n is Gaussian noise. The parameters α_n are critical because they model the unknown amplitude variations across pixels in the BOLD response. Without loss of generality, we assume that $E[W_n W_n^t] = I$. We also assume that class labels are independent and identically distributed with $P\{X_n = k\} = \pi_k$.

Our objective is then to estimate the model order K, the component vectors E, and the prior probabilities π from observations of $\{Y_n\}_{n=1}^N$. We do this by maximizing the minimum description length (MDL) criterion.

$$MDL = \log p(y|E, \pi) - KM \log(NM)$$

Here the log likelihood of Y may be computed by

$$\begin{aligned} MDL &= \sum_{n=1}^{N} \log \left(\sum_{k=1}^{K} p_{y_n|x_n}(y_n|k, E)\pi_k \right) \\ &\quad -KM \log(NM) \ . \end{aligned}$$

If we define the projection operator $P_k = I - e_k e_k^t$, then the log likelihood of the data given the class is

$$\log p_{y_n|x_n}(y_n|k, E) = -\frac{1}{2}\left(||P_k y_n||^2\right) - \frac{M-1}{2}\log(2\pi) + \text{const} \ .$$

This expression results from the fact that the signal orthogonal to e_k is Gaussian and white. In addition, any observation along the direction e_k is equally likely, and therefore may be considered to have constant likelihood. Without loss of generality, we will assume this constant to be 0.

The optimization of the MDL criterion may be performed using the EM algorithm where X_n is the incomplete data. To do this, we iteratively optimize the Q function.

$$Q(E, \pi; E^{(i)}, \pi^{(i)}) = E\left[\log p_{y,x}(y, X|E, \pi)|y, E^{(i)}, \pi^{(i)}\right] - KM \log(NM)$$

For our problem, $Q(E, \pi; E^{(i)}, \pi^{(i)}) =$[1]

$$\sum_{k=1}^{K} \left\{ -\frac{1}{2} tr(P_k \bar{R}_k) - \frac{(M-1)\bar{N}_k}{2}\log(2\pi) + \bar{N}_k \log \pi_k \right\} - KM \log(NM)$$

where

$$\begin{aligned} \bar{N}_k &= \sum_{n=1}^{N} p_{x_n|y_n}(k|y_n, E^{(i)}, \pi^{(i)}) \\ \bar{R}_k &= \sum_{n=1}^{N} y_n y_n^t \, p_{x_n|y_n}(k|y_n, E^{(i)}, \pi^{(i)}) \end{aligned}$$

[1]This equation differs from its original form in the ICIP proceedings due to the correction of a typographical error.

The EM update equations are then

$$(E^{(i+1)}, \pi^{(i+1)}) = \arg\min_{E,\pi} Q(E, \pi; E^{(i)}, \pi^{(i)}) \ , \quad (1)$$

and the solution is given by

$$\begin{aligned} e_k^{(i+1)} &= \text{principal eigenvector}\{\bar{R}_k\} \\ \pi_k^{(i+1)} &= \bar{N}_k / N \ . \end{aligned}$$

The question remains of how to maximize the MDL criterion with respect to K. Our approach will be to start with K large, and then sequentially decrement it. For each value of K, we will apply the EM algorithm updates until they converge to a local maximum of the MDL functional. After we have done this for each value of K, we may simply select the value of K and corresponding parameters that resulted in the largest value of the MDL criterion.

One method to effectively reduce K is to constrain the parameters of two classes to be equal. Let classes l and m be constrained so that $e_l = e_m$. Furthermore, let E^* and $E^*_{l,m}$ be the unconstrained and constrained solutions to (1). Then we may define a distance function

$$\begin{aligned} & d(l, m) \\ = \ & Q(E^*, \pi^*; E^{(i)}, \pi^{(i)}) - Q(E^*_{l,m}, \pi^*; E^{(i)}, \pi^{(i)}) \\ = \ & \sigma_{max}(R_l) + \sigma_{max}(R_m) - \sigma_{max}(R_l + R_m) \geq 0 \end{aligned}$$

where $\sigma_{max}(R)$ denotes the principal eigenvalue of R.

At each step, we compute the two components

$$(l^*, m^*) = \arg\min_{(l,m)} d(l, m)$$

that minimized the class distance. We then merge these two classes to decrement the value of K.

3 EXPERIMENTAL RESULTS

3.1 Synthetic Data

To test the validity of the method, synthetic fMRI images were generated using the averaged functional images gathered from the real data set used below as baseline images. The BOLD response signals were modeled using the methods given in [6], and were injected into 3 locations of 8x8 pixels. The mixture weights, as well as time constant and time delay parameters, were varied between the 3 locations in order to simulate responses from different functional cortices. The amplitudes of these signals were modulated by the baseline pixel intensities and then multiplied by a normalized Gaussian window to simulate the variation in amplitudes across the functional regions. Additive white Gaussian noise was then added to all the pixels at a standard deviation of 2% of the baseline pixel intensity.

PCA, CCA, and the fuzzy c-means clustering (FCM) package in Matlab were then applied to the synthetic data. All data were first preprocessed using PCA, and signal subspace estimation [2] resulted in 14 dimensions. Then, PCA, CCA, and FCM were each applied and constrained to yield 3 components. The mean squared error between the resulting components and their best matching true components was then computed. The results of this analysis methods are shown in Table 1 and Fig. 2. The CCA methods had 1/4 the MSE of the FCM method, and $1/20^{th}$ the MSE of the PCA method.

3.2 Real Data

Whole-brain images of healthy subjects were obtained using a 1.5 T GE Echospeed MRI Scanner (GE Medical Systems, Waukeshau, WI). T1-weighted anatomic images were acquired for reference with the following parameters: axial spin echo 2D, TE/TR = minimum full/500 ms, matrix = 256x128, 15 locations with thickness of 7.0 mm and gap of 2.0 mm covering the whole brain, field-of-view = 24×24 cm. The paradigm was designed to activate the auditory, visual, and motor cortex. The visual cortex was activated using a flashing 8Hz checkerboard pattern (6×8 squares) viewed through fiber-optic goggles (Avotec, Jensen Beach, FL). The auditory cortex was activated using backwards speech through pneumatic headphones (Avotec). The motor cortex was activated through finger tapping. The paradigm was arranged so all activation occurred in sync at a cycle length of 64 seconds: 32 seconds on, 32 seconds off. The paradigm contained 4 cycles. BOLD-weighted functional images were acquired with the following parameters: gradient echo EPI, TE/TR = 50ms/2000ms, flip angle = 90^o, matrix = 64x64, 160 repetitions, the same locations and field-of-view as the anatomic images.

The functional image data were analyzed pixel-by-pixel for evidence of activation using a least squares analysis [7]. ROI's were drawn on the resulting statistical maps in the cortical regions corresponding to primary activated regions for each of the three stimuli (i.e. precentral gyrus for the motor stimuli, superior temporal gyrus for the auditory stimuli, and the calcarine fissure for the visual stimuli).

The functional data in the ROI's were then analyzed using the harmonic component decomposition with 31 components [2]. The signal subspace was found to have $M = 7$ dimensions. The resulting 7-dimensional feature vectors were then analyzed using the CCA method described above.

The analysis returned $K = 5$ classes and the components E from the feature space. The timesequence realization of components of E are given in Fig. 1. Each pixel was then assigned to the class with the highest a posteriori probability. The ROI's are shown in Fig. 3 the accompanying anatomic data, using red for the first class, green for the second, blue for the third, yellow for the fourth, and magenta for the fifth.

It can be seen from the experimental results that a distinct functional behavior does not correlate directly with each of the functional ROIs, at least for the motor and auditory cortices. Rather, the classes are distributed along patterns of vascularization and sulcal-gyral boundaries. This can be seen in the motor and auditory cortices. However, the visual cortex does display a behavior distinct from the other two cortices.

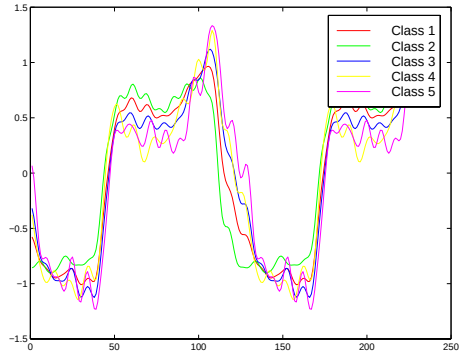


Figure 1: Timesequence realizations of the feature space for the real data set

Component	CCA	PCA	FCM
1	$2.5X10^{-4}$	$2.2X10^{-3}$	$1.8X10^{-3}$
2	$1.1X10^{-4}$	$4.7X10^{-4}$	$1.2X10^{-4}$
3	$1.0X10^{-4}$	$7.7X10^{-3}$	$1.2X10^{-4}$
Total	$1.6X10^{-4}$	$3.5X10^{-3}$	$6.7X10^{-4}$

Table 1: Mean squared error for each method of analysis

4 REFERENCES

[1] E. T. Bullmore, S. Rabe-Hesketh, R. G. Morris, L. G. S. C. R. Williams, J. A. Gray, and M. J. Brammer, "Function magnetic resonance image analysis of a large-scale neurocognitive network," *Neuroimage*, vol. 4, no. 1, pp. 16–33, August 1996.

[2] S. Chen, C. A. Bouman, and M. J. Lowe, "Harmonic decomposition and eigenanalysis of BOLD fMRI time-series data in different functional cortices," *Proc. of the ISMRM Eighth Scientific Meeting*, April 3-7 2000, Berkeley CA, p. 817.

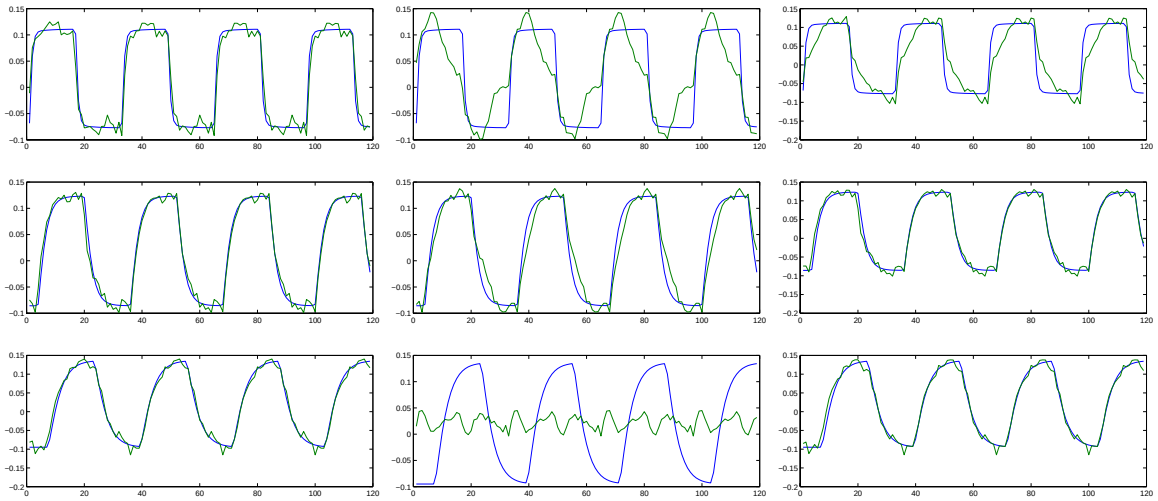
[3] M. J. McKeown and T. J. Sejnowski, "Independent component analysis of fMRI data: Examining the assumptions," *Human Brain Mapping*, vol. 6, pp. 368–372, 1998.

[4] E. Redner and H. Walker, "Mixture densities, maximum likelihood and the EM algorithm," *SIAM Review*, vol. 26, no. 2, April 1984.

[5] C. A. Bouman, "Cluster: an unsupervised algorithm for modeling Gaussian mixtures." Available from http://www.ece.purdue.edu/~bouman, April 1997.

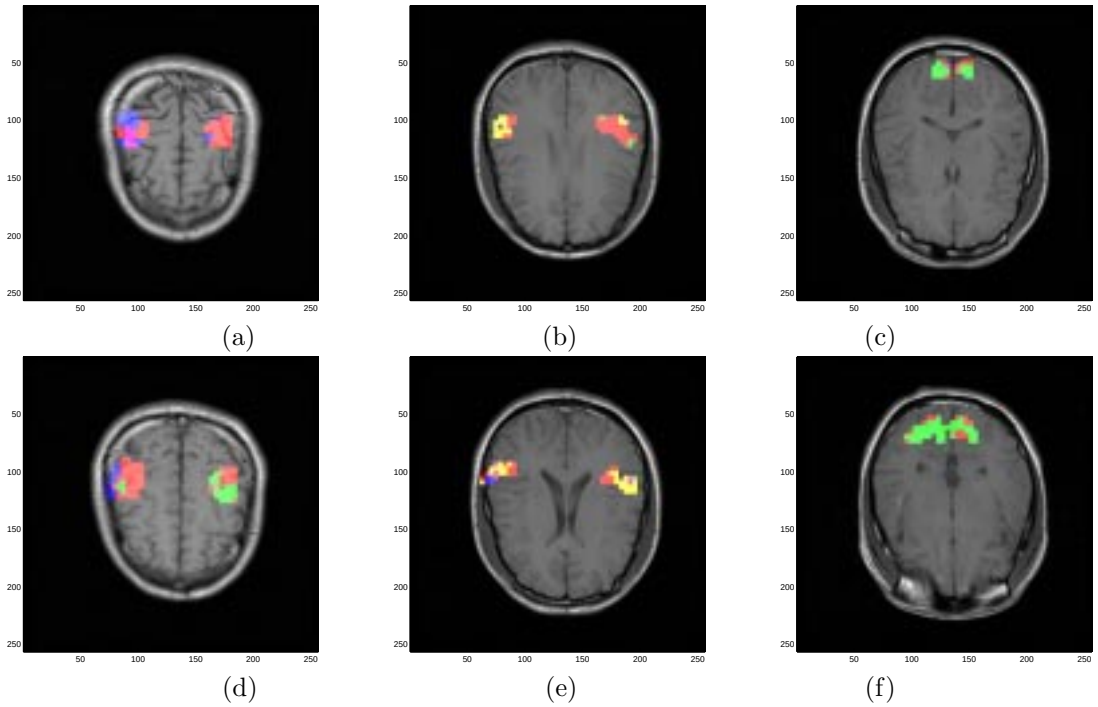
[6] P. Purdon, V. Solo, E. M. Brown, and R. Weisskoff, "Functional MRI signal modeling with spatial and temporal correlations," *submitted to Neuroimage*, May 1999.

[7] M. J. Lowe and D. P. Russell, "Treatment of baseline drifts in fMRI time series analysis," *Journal of Computer Assisted Tomography*, vol. 23, no. 3, pp. 463–473, 99.



(a) (b) (c)

Figure 2: Estimation methods plotted against injected synthetic signal: (a) CCA, (b) PCA, (C) FCM



(a) (b) (c)

(d) (e) (f)

Figure 3: CCA applied to the real data set: (a), (b), and (c) - upper motor, auditory and visual cortex slices; (d), (e), and (f) - lower motor, auditory and visual cortex slices;