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## FAST DEPENDENT COMPONENTS FOR FMRI ANALYSIS

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### ABSTRACT

Canonical correlation analysis (CCA) can be used to find correlating projections of two datasets with co-occurring samples. Instead of correlation, we would typically want to find more general dependencies, measured by mutual information. Variants of CCA based on non-parametric estimation of mutual information have been proposed previously; they outperform traditional CCA for non-Gaussian data but require infeasible amounts of computation for already quite modest sample sizes. We introduce a novel variant that uses a semiparametric estimate leading to a considerably faster algorithm. We apply the method on searching for statistical dependencies between multi-sensory stimuli and functional magnetic resonance imaging (fMRI) of brain activity— in contrast to using regression on either of them.

**Index Terms**— Canonical correlation, component models, fMRI, mixture model, mutual information

### 1. INTRODUCTION

In fMRI analysis of brain signals related to natural stimulation, both the brain signals and the stimuli are very complex and difficult to analyze. Both contain variation that is not interesting to the analyst. The interesting aspects are the dependencies between the two datasets, and hence the analysis should be focused on those. The same setup of searching for statistical dependencies between datasets of co-occurring samples recurs in many applications.

A classical approach to searching for dependencies is to project the datasets onto lower-dimensional subspaces, in which it is easier to estimate dependencies than in the original high-dimensional spaces. When a projection is optimized to maximize dependency, it discards variation that is not present in the other dataset, while keeping the shared variation.

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The task of finding maximally correlating projections between two datasets can be solved by a classical method called canonical correlation analysis (CCA). The method is fast and robust, but for many applications correlation is too simple a measure; it only measures linear dependency.

Replacing correlation with mutual information makes discovery of more general types of dependency possible. However, mutual information cannot be computed as easily as correlation, and we need to resort to approximations. One option is to empirically estimate the probability density in the projection space, and estimate mutual information based on the density estimate. Earlier methods [1, 2] have used non-parametric Parzen-kernel estimates. We call these methods dependent component analysis (DeCA). An alternative solution would be to consider nonlinear projections while keeping correlation as the cost, e.g. by kernelizing CCA. Both approaches find non-linear dependencies, but DeCA has the advantage that linear projections can be interpreted in terms of the original features.

The Parzen estimates are consistent and accurate, but computationally demanding for large datasets. Replacing the non-parametric density estimates with semiparametric estimates should give comparable results while being scalable. We introduce a novel algorithm that uses a mixture of Gaussians to estimate the density in the projection space. An analogous method has been shown to improve efficiency in a related task of discriminant analysis [3].

We applied the novel DeCA-variant to the task of finding dependencies between measured brain activity and multi-sensory stimuli. Following an earlier application of CCA to the same task [4], we used a 2-step approach: First, spatially independent patterns of brain activity were extracted from fMRI data with independent component analysis (ICA) [5]. In the second step the new DeCA-variant was used to find dependencies between the brain patterns and the stimuli.

### 2. METHOD

The task in DeCA is to find linear projections of two datasets,  $\mathbf{X}$  and  $\mathbf{Y}$ , so that the mutual information between the projections  $\mathbf{s}_x = \mathbf{w}_x^T \mathbf{X}$  and  $\mathbf{s}_y = \mathbf{w}_y^T \mathbf{Y}$  is maximized. The

objective is thus to maximize

$$I(s_x, s_y) = \int \int p(s_x, s_y) \log \frac{p(s_x, s_y)}{p(s_x)p(s_y)} ds_x ds_y \quad (1)$$

with respect to linear transformations  $\mathbf{w}_x$  and  $\mathbf{w}_y$ . Here  $s_x$  and  $s_y$  are the random variables  $s_x = \mathbf{w}_x^T \mathbf{x}$  and  $s_y = \mathbf{w}_y^T \mathbf{y}$ , and  $\mathbf{x}$  and  $\mathbf{y}$  are random vectors corresponding to data sets  $\mathbf{X}$  and  $\mathbf{Y}$ . Mutual information has, however, two severe difficulties as a cost function: It requires knowledge of the joint probability density  $p(s_x, s_y)$ , and it involves an integral over the whole projection space. As a practical solution, we used a mixture of Gaussians-based density estimate  $\hat{p}(s_x, s_y)$ , and estimated the integral as an average over the observations. That is, we maximized the objective function

$$\hat{I}(s_x, s_y) = \frac{1}{N} \sum_{i=1}^N \frac{\hat{p}(s_x^i, s_y^i)}{\hat{p}(s_x^i) \hat{p}(s_y^i)}, \quad (2)$$

where  $N$  is the number of observations.

In earlier works,  $\hat{p}(s_x, s_y)$  has typically been a Parzen estimate, which is non-parametric. Hence, optimizing the cost of Eq. (2) has been straightforward; derive the gradient of the cost and use any standard optimization method to find a local optimum. Here, we consider parametric estimates of the form

$$\hat{p}(s_x, s_y) = \sum_{k=1}^K \pi_k \mathcal{N}([s_x; s_y] | \boldsymbol{\mu}_k, \boldsymbol{\Sigma}_k), \quad (3)$$

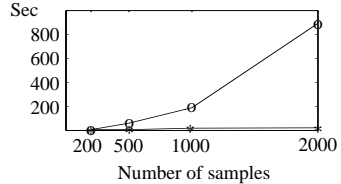
where  $\mathcal{N}(\mathbf{x} | \boldsymbol{\mu}, \boldsymbol{\Sigma})$  denotes the normal distribution with mean  $\boldsymbol{\mu}$  and covariance matrix  $\boldsymbol{\Sigma}$  evaluated at  $\mathbf{x}$ . The  $\pi_k$  represent the probabilities of the  $K$  mixture components. This estimate has a set of parameters  $\Theta$  that need to be learned,  $\Theta = \{\pi_k, \boldsymbol{\mu}_k, \boldsymbol{\Sigma}_k\}_{k=1}^K$ . Hence, straightforward optimization with respect to  $\mathbf{w}_x$  and  $\mathbf{w}_y$  is not possible.

We propose an alternating algorithm following the work in [3]. Starting with some initial projections, we learn a mixture of Gaussians in the projection space using the expectation maximization (EM) algorithm. After learning the density estimate, we optimize the projections  $\mathbf{w}_x$  and  $\mathbf{w}_y$ . The algorithm then proceeds by alternating these two steps.

The objective function Eq.(2) can be easily differentiated, so we can use gradient-based methods to learn the projections. We used a conjugate gradient method, with the number of iterations equal to the dimensionality of the parameter space. The density estimate was always optimized until convergence of the EM algorithm.

We optimized the components one at a time because density estimation in high-dimensional spaces is very difficult. By using 1-dimensional projections we can estimate the joint density  $p(s_x, s_y)$  in a 2-dimensional space, which can be done accurately enough already with a reasonably small datasets.

After finding the first component, we can proceed to search for the next maximally dependent component with the following constraint: The projections on the consecutive



**Fig. 1.** Running times of non-parametric DeCA (o) and mixture of 20 Gaussians DeCA (\*) in seconds as a function of the number of data samples.

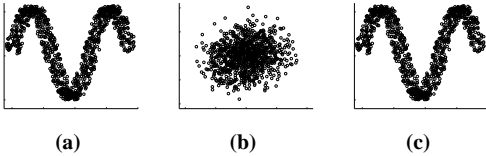
components should be independent of the projections on the previous components in both spaces. In practice, searching for a component that maximizes dependency with the other dataset while minimizing dependency with the earlier component(s) is difficult. We used an approximation, where instead of full independency, we required the components to be uncorrelated with the earlier projections, analogously to how successive CCA components are defined. This can be satisfied with a simple deflation procedure, as follows. After extracting a component  $\mathbf{w}_x$ , we transformed the data by

$$\bar{\mathbf{X}} = \mathbf{X} \left( \mathbf{I} - \frac{1}{\mathbf{w}_x^T \mathbf{X} \mathbf{X}^T \mathbf{w}_x} \mathbf{X}^T \mathbf{w}_x \mathbf{w}_x^T \mathbf{X} \right) \quad (4)$$

(and analogously for  $\mathbf{Y}$ ), and searched for the next component by applying the algorithm to  $\bar{\mathbf{X}}$  and  $\bar{\mathbf{Y}}$ . The procedure can be continued up to the minimum of the  $\mathbf{X}$ - and  $\mathbf{Y}$ -space dimensionalities, or until there are no significant dependencies left between  $\bar{\mathbf{X}}$  and  $\bar{\mathbf{Y}}$ .

### 3. TECHNICAL VALIDATION

The main advantage of the proposed method, compared to earlier DeCA methods, is in the computational speed. The Parzen estimate used in the earlier works has a computational complexity of  $\mathcal{O}(N^2)$ , and each iteration of a gradient-based optimization algorithm requires evaluating the densities again. A mixture model with  $K$  mixture densities has, however, only a complexity of  $\mathcal{O}(NK)$  for evaluating the density or the gradient with respect to the projections. We show in Fig. 1 the computation times as a function of data size,  $N$ . We also demonstrate the functionality of the DeCA variants compared to CCA on an artificial dataset. The data consisted of 10-dimensional data  $\mathbf{X}$  and 7-dimensional data  $\mathbf{Y}$  of 1000 samples, each dimension being uniform random noise except in one of the dimensions, where there was a clear dependency between  $\mathbf{X}$  and  $\mathbf{Y}$ , as shown in panel (a) of Fig. 2. CCA could not find such non-linear dependency, whereas both DeCA variants worked correctly.



**Fig. 2.** (a) Shows a dependent but uncorrelated subspace of the toy data. The CCA projection (b) completely missed the dependency, whereas DeCA found the true projections. (c) shows the result of the new mixture-based variant, but the non-parametric variant produced an indistinguishable solution. In both figures  $x$ -axis represents the projection of dataset  $\mathbf{X}$  and  $y$ -axis the projection of dataset  $\mathbf{Y}$ .

#### 4. APPLICATION TO FMRI ANALYSIS

Natural stimuli are increasingly used in fMRI studies to imitate real-life situations. Consequently, it is no longer feasible to assume single features of the experimental design alone to account for the measured brain activity. Instead, relevant combinations of stimulus features could explain the more complex brain activation patterns.

We have earlier proposed a 2-step approach [4, 6], where ICA was first used to identify spatially independent brain patterns. As the second step, temporal dependencies between stimuli and the brain patterns were detected using some CCA-variant, like DeCA. The idea is to look for dependencies between combinations of stimulus features and the corresponding combinations of brain patterns. The method differs from regression analysis, which is based on pre-selected regressors. In contrast to using regression on the ICA time-courses, we searched for dependencies between stimuli and brain signals without pre-specifying target classes, to automatically find the most relevant stimulus combinations.

This framework has been studied in two earlier papers, [4] and [6], one of which used non-parametric version of DeCA [1] and the other CCA for the dependency exploration step. We applied the new DeCA-variant to the data from study [4] where the fMRI measurements originally come from [7]. The preprocessed stimulus data and the result of ICA for the fMRI data (1932 data points) were taken from the earlier study without any modifications.

The original stimulation sequence consisted of 7 different stimuli: 1 tactile stimulus, 3 visual stimuli containing hands, faces or buildings, and 3 audio stimuli consisting of either tone pips, a voice reading about history, or a voice giving guitar fingering instructions. In [4], the original features of the stimuli were augmented with six features, extracted from the spectrogram of the actual auditory stimuli. The 13 stimulus time courses were quite far from being normally distributed, justifying the need for DeCA that does not make an implicit global normality assumption like CCA. Performing these ex-

periments using non-parametric DeCA, on the other hand, would have been computationally infeasible.

#### 5. EXPERIMENTS

We initialized the projection vectors  $\mathbf{w}_x$  and  $\mathbf{w}_y$  to the first PCA-components of the datasets  $\mathbf{X}$  and  $\mathbf{Y}$ , and initialized the mixture estimate in the projection space as follows. The initial values of means  $\mu_k$  and mixture probabilities  $\pi_k$  were determined by k-means separately in each projection space, by using the centroids as initial means of the mixture components and the proportions of cluster sizes as  $\pi_k$ . The initial covariance matrix  $\Sigma_k$  of each mixture component was set to a diagonal matrix  $\text{diag}(\sigma_x^2, \sigma_y^2)$  containing the variances of the initial projections  $s_x$  and  $s_y$ . Finally, the number of mixture components was initially set to 5, but if a mixture component was left empty during an EM-iteration, it was removed. The full algorithm was run for 10 iterations.

A critical issue in analyzing small datasets is to avoid overfitting. Already classical CCA suffers severely from overfitting with small enough data, which shows as spurious canonical correlations. Here we assessed the quality of the results by bootstrapping. DeCA (like CCA) identifies the components only up to a sign, and to average over a set of components obtained from the bootstrap replicates we matched their signs with an algorithm resembling a 1-component k-means (details omitted due to lack of space).

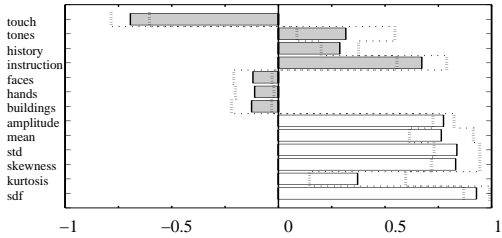
The statistical significance was tested with Wilcoxon signed rank test compared to zero factor loadings. We used the p-value threshold 0.01, corrected for multiple testing with Bonferroni correction.

#### 6. RESULTS

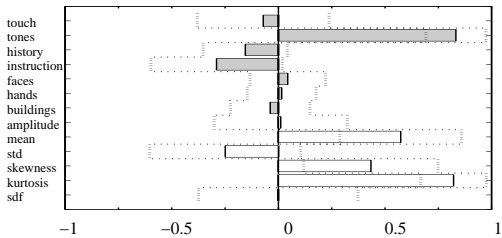
We were able to distinguish 8 individual significant DeCA components, which show clear discriminative patterns, and they can be roughly described as follows: Component 1 discriminates sound related features from other senses, especially from tactile stimulus. Component 2 discriminates tone pips and the related auditory features from speech. Component 3 discriminates between the two different speech features, *history* and *instruction*. Components 4–6 each represent one of the visual features *buildings*, *faces* and *hands*. Component 7 discriminates between two auditory features, *skewness* and *mean*. Component 8 represents the auditory feature *amplitude*. In Fig. 3, we show the factor loadings<sup>1</sup> of components 1–3, i.e., the correlations between the DeCA component and each of the original feature dimensions.

The main difference between results of DeCA and CCA was that DeCA was able to find more components. Some of the found DeCA components had counterparts in the CCA

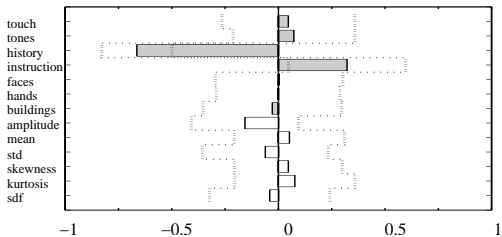
<sup>1</sup>An alternative would have been to study the projection vectors directly, but when there are within-dataset-correlations between the dimensions, the projection vectors might be misleading.



(a) DeCA component 1. All 13 features were significant.



(b) DeCA component 2. Significant features were tones, history, instruction, mean, std, skewness and kurtosis.



(c) DeCA component 3. Significant features were history, instruction and amplitude.

**Fig. 3.** Factor loadings of DeCA components 1–3 for the stimulus features. In each caption we list the features that both deviated from zero statistically significantly ( $P$ -value  $< 0.01$ ) and have factor loadings above 0.1. The gray bars illustrate the experimental stimulus features and the white bars the extracted stimulus features. The dotted lines indicate the level of one standard deviation between the bootstrap results.

results (DeCA components 1, 2 and 4). But there were also new ones; e.g. DeCA components 3, 7 and 8 discriminate fine differences between auditory signals, which could not be consistently distinguished with CCA.

## 7. DISCUSSION

We introduced an algorithm for finding linear projections of two datasets, so that the projections have high mutual infor-

mation. The proposed method improves earlier solutions by replacing non-parametric density estimators by mixtures of Gaussians, resulting in an optimization algorithm that is linear instead of quadratic in the number of data points.

We applied the method to a time-paired dataset from an earlier study. One of the datasets consisted of 13-dimensional time-series description of the stimuli presented to test subjects, and the other dataset of spatially independent brain patterns produced from fMRI measurements by so-called reliable ICA approach [8]. We found 8 different components that seem reasonable in terms of the stimulus features. Some of the found combinations of brain patterns were already familiar from the earlier study, and have there been interpreted to be meaningful [4]. In that study, CCA found only 5 components consistently from this data. DeCA was able to find more dependencies that were not shown in terms of the correlation, but still manifested themselves in mutual information.

We also showed with artificial dataset that the results of the novel semiparametric version and non-parametric version of DeCA are comparable and, indeed, can find dependency structures when correlation is zero and CCA fails. The novel variant was also verified to be considerably faster.

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