Investigation of Efficient Implementation of Local Constrained Canonical Correlation Analysis for fMRI

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Introduction In previous work [1], following the early development of canonical correlation analysis (CCA) methods [2-4], local constrained CCA (cCCA) methods were proposed to utilize the spatial dependence of fMRI data and to avoid model overfitting and loss of specificity. A region-growing based cCCA (cCCA-RG) method was demonstrated to be more computational efficient and to have similar detection performance, if not better, compared with the branch-and-bound method (cCCA-BB) originally proposed in [3,5]. However, only first order canonical correlation (CC) was considered in [1]. In this work, we investigate the efficient implementation of local cCCA**.** Both simulated and real fMRI data are used to compare different cCCA-RG methods, an exhaustive search cCCA method, and conventional univariate methods with and without Gaussian smoothing.

Methods Spatially adaptive filtering can be performed using CCA on fMRI data. Unlike fixed Gaussian smoothing in fMRI data analysis, the filter weights (i.e. the spatial coefficients) in CCA are determined from data to yield the maximum canonical correlation with temporal regressors. To mitigate the effect of false positives, the first constraint is to require all components of the spatial coefficients $\boldsymbol{\alpha}_c$ of cCCA to be positive. This constraint enforces lowpass filtering (smoothing). We also propose a second constraint for the spatial weight α_1 of the center voxel using an empirically-determined parameter δ in [0,1] according to: $\alpha_1 \geq \delta \max(\boldsymbol{\alpha}_c)$. This additional constraint can further decrease the false positives, especially at boundary regions of activations. The local adaptiveness of the cCCA method allows versatile filtering kernels with flexible shape and size within a pre-specified region.

As proved in [5], the solution of cCCA with the first positive constraint (if it exists,) can be found through searching all subsets of spatial vectors and is the one that gives the maximum correlation satisfying this constraint. For the second constraint, the nonlinearity of maximum function prevents a tractable analytic solution. Nevertheless, the search method can still be applied to achieve an optimal solution if proper changes are made. In [1], it was already showed that cCCA-RG is computationally more efficient than cCCA-BB, both with first order CC. In this work, we further investigate cCCA-RG with including higher order CCs. The new cCCA-RG method can be implemented in the same way as [1] except that all orders of CCs will be examined in the step (2) (refer to [1]).

Results and discussions Functional MRI (fMRI) was performed in a 3.0T GE HDx MRI scanner equipped with an 8-channel head coil using the following parameters: ASSET=2, ramp sampling, TR/TE=2sec/30ms, FA= 70deg, FOV=22cmx22cm, thickness/gap=4mm/1mm, 25 oblique-coronal slices perpendicular to the long axis of the hippocampus, in-plane resolution 96x96 interpolated to 128x128. For each subject of eight we acquired two fMRI data sets. The first data set was collected during resting-state where the subject stayed calm and refrained from executing any particular task with eyes closed. The second data set was collected while the subject was performing a memory paradigm. Briefly, this paradigm consisted of memorization of novel outdoor scenes containing 6 periods of instruction, encoding, distraction, and recall tasks.

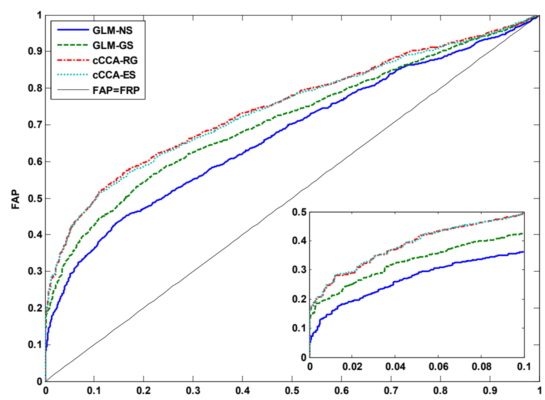

Fig. 1. Modified ROC Curves

First, we generated one million randomly shaped and sized activations within a 3x3 grid of pixels. The time courses of the activated pixles were simulated to be linear combinations of the 4 formerly-mentioned memory regressors with random amplitudes uniformly distributed in [0 1]. Different levels of noise were added randomly. We tested five methods: (1) univariate general linear model (GLM) without smoothing ("GLM-NS"); (2) GLM with Gaussian smoothing (FWHM=2.24 pixels, "GLM-GS"); (3) old cCCA-RG (cCCA-RG1); (4) new cCCA-RG (cCCA-RG2); and (5) cCCA exhaustive search (cCCA-ES). The mean square errors (MSE) of estimated first temporal coefficient (while other temporal coefficients lead to similar results and are omitted here due to the space limitation.) for different methods are: (1) GLM-NS: 0.0844; (2) GLM-GS: 0.1172; (3) cCCA-RG1: 0.0279 for δ=0 and 0.0948 for δ=1; (4) cCCA-RG2: 0.0279 for δ=0 and 0.0948 for δ=1; and (5) cCCA-ES: 0.0274 for δ=0 and 0.0949 for δ=1. From these results, we can see that the cCCA methods can dramatically increase the estimation accuracy by as much as 3 folds of GLM-NS for δ=0. GLM-GS did the worst because of the small and irregularly defined activations. When δ increases to 1, the benefit of cCCA methods on parameter estimation diminishes, both cCCA-RG1 and cCCA-RG2 converge to the same solution and their performance has negligible difference from cCCA-ES. Actually, we found that the solution for both cCCA-RG1 and cCCA-RG2 only contains first order CC for different δ's and there are 99.91% for the first order CC, 0.09% for the second, and zero for higher orders for δ=0 in cCCA-ES (for δ=1, up to forth order CC solution exists but the majority (>96%) is the first order). We also tested on the purely random time courses and found that only the first order CC solution exists in cCCA-RG methods. Since both RG methods converge to the same solution, we will not distinguish them in the following experiments.

Second, we use the novel CCA test statistic [6] and modified receiver operating characteristic (ROC) technique [7] to assess the detection power of different methods. As an example, the results for the contrast "Encoding minus Distraction" were plotted as Fraction of Active Positives (FAP) vs Fraction of Rest Positives (FRP) in Fig. 1 for δ=0 (where the insertion shows the portion of FRP<0.1). The cCCA methods perform notably better than the GLM methods, while the difference between cCCA-RG and cCCA-ES is marginal. We also tested on other values of δ and found that better results can be achieved when δ is close to zero.

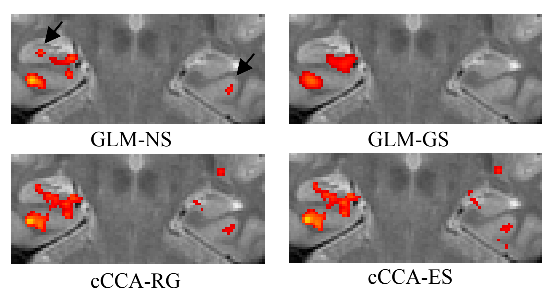

Fig. 2. Activation maps (corrected p<0.05)

Finally, shown in Fig. 2 are typical activation maps of the contrast "Encoding minus Distraction" with nonparametrically corrected p<0.05 [8]. It appears that GLM-GS yields bulgy activations and fails to detect activations in dentate gyrus and parahippocampal gyrus that were detected by GLM-NS (black arrows). Note that cCCA-RG leads to similar symmetric activation patterns as cCCA-ES and both cCCA methods reveal more activations than GLM-NS.

From these results, we conclude that only the first order CC is necessary for cCCA-RG. In terms of the estimation and detection power, it seems that small values of δ work better. The current implantation of cCCA-RG using MATLAB on a computer equipped with Intel Core 2 2.4GHz CPU and 4GB memory takes about 10 minutes (δ=0) for a brain-masked 128X128X25 volume and is about 10 times faster than cCCA-ES, a reasonable amount of time for fMRI data analysis.

References [1] Jin, M. et al., 2009 ISMRM 1708. [2] Friman, O. et al., 2001. Magn. Reson. Med., 323-30. [3] Friman, O. et al., 2003. NeuroImage, 837-45. [4] Nandy, R. et al., 2004. Magn. Reson. Med. , 947-52. [5] Das, S. et al., 1994. Lin. Algebra Appl, 29-47. [6] Jin, M. et al., 2009 ISMRM 1713. [7] Nandy, R. et al., 2003. Magn. Reson. Med., 1152-62. [8] Nandy, R. et al., 2007. NeuroImage, 1562-76. *This work is partially supported by the NIH (1R21AG026635).*