An a contrario approach for the detection of activated brain areas in fMRI

Camille Maumet, Pierre Maurel, Jean-Christophe Ferré, Christian Barillot

An a contrario approach for the detection of activated brain areas in fMRI

Camille MAUMET[1], Pierre Maurel[1], Jean-Christophe Ferré[1,2], and Christian Barillot[1]

[1]Visages Project-team / U746, University of Rennes 1, INSERM, CNRS, Inria, RENNES, Brittany, France, [2]Department of Neuroradiology, CHU Rennes, Rennes, Brittany, France

Target audience: Medical doctors, computer scientists.

Purpose: BOLD functional MRI (fMRI) is now a widespread imaging technique to study task-related activity in the brain. However, getting the areas of activation at the individual subject level is still an open issue. The standard massively univariate statistical analysis is usually performed after smoothing the data and makes use of a single p-value for final thresholding of the results [1]. In group fMRI studies, the need for compensation of cross-subjects misregistrations clearly justifies the smoothing. However, at the individual level, where neat delineations of the activated areas are of interest, the use of gaussian smoothing as a pre-processing step is more questionable. In this paper, we propose to study the ability of an *a contrario* approach, recently adapted for basal perfusion abnormalities detection [2], to correctly detect areas of functional activity.

Methods: In the *a contrario* approach [2], pre-smoothing of the data is avoided by taking into account the spatial neighborhood into the statistical analysis. Starting from a voxel-wise probability map (obtained from a standard massively univariate general linear model (GLM)), a region-based probability map is built. To this aim, a grid of shapes is defined in the image of interest. In this study, we work with grids of spheres as we have no *a priori* shape for the detections. The initial voxel-wise probability map is thresholded using a set of pre-defined p-values $P=\{0.01, 0.005, 0.001\}$ and, then, the number of overthreshold voxels is counted for each pre-defined p-value in each region (sphere). In the general *a contrario* formulation, the region-based probability is then estimated, assuming spatial independence of the residuals, using a binomial distribution parametrized by the number of voxels in each sphere and the pre-defined p-values. To account for potential mismodeling, the null distribution used to define the voxel-wise probabilities was estimated with a non-parametric approach in the background of the image.

Results: 12 healthy subjects were involved in this study and underwent 3 BOLD fMRI sessions of a block motor paradigm [3]. In order to compare the performances of the standard massively univariate GLM with the proposed *a contrario* approach, we used Receiver-Operating-Characteristics (ROC) curves and estimated the area under the curve for false positive rates ranging from 0 to 0.1 (as only a small percentage of the voxels are expected to be active). Validation of fMRI analysis is still challenging due to the lack of ground truth. We focused on a well-studied right-hand motor paradigm in which the main activations are expected in the precentral and postcentral sulci (Left and Right) and in the Supplementary Motor Area (SMA) (Left and Right) [3]. We studied two different "ground truths". First, as suggested in [3], we targeted the activation of the grey matter in the right hand motor area as manually delineated by an expert neuro-radiologist, while the surrounding white matter was expected to be inactive. Second, we also tested a global criterion, in which activation in both the hand motor area and part of the SMA (as defined by the AAL atlas) were activation targets, while whole-brain white matter ($>70\%$) was expected to be inactive. We compared the standard massively univariate GLM (no smoothing and smoothing with a gaussian FWHM kernel of 6mm^3) with the *a contrario* approach.

Fig. 1 displays the expected active and inactive regions for a representative subject along with the associated ROC curves averaged over sessions and subjects. Overall the *a contrario* approach outperformed both the unsmoothed and smoothed massively univariate GLM in term of area under the curve. Two sample t-tests were performed in order to detect significant improvement at the group level (false discovery rate $q < 0.05$). The *a contrario* approach with local ground truth was significantly better than the smoothed GLM for all sessions ($p = 0.018$, $p = 0.038$, $p = 0.016$) and than the unsmoothed GLM for 2 sessions out of 3 ($p = 0.003$, $p = 0.005$). Moreover, using the global ground truth, the a contrario approach performed significantly better than the smoothed GLM for all sessions ($p = 0.003$, $p = 0.009$, $p = 0.006$) and than the unsmoothed GLM for 2 sessions out of 3 ($p = 0.002$, $p = 0.002$)
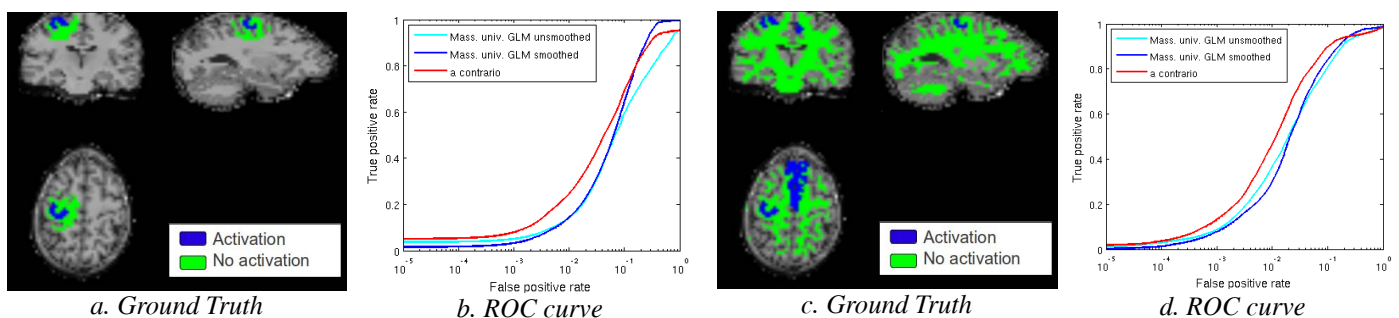

| *a. Ground Truth* | *b. ROC curve* | *c. Ground Truth* | *d. ROC curve* |

Figure 1 : Comparison of single-subject detections of activations between the massively univariate GLM and the a contrario approach. Local: a) Ground Truth for a representative subject, b) ROC curve; Global: c) Ground Truth, d) ROC curve.

Discussion: We proposed a new *a contrario* approach to detect fMRI activations. This method displayed better spatially defined activations with a more interesting trade-off between sensitivity and specificity by comparison to the standard massively univariate GLM.

References: [1] Gorgolewski et al. Front. Hum. Neurosci. 2012; [2] Maumet et al. Miccai, 2012; [3] Raoult et al. NeuroImage, 2011;