Fuzzy General Linear Model for functional Magnetic Resonance Imaging

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Introduction. Since the introduction of functional Magnetic Resonance Imaging (fMRI), the accurate delineation of brain activity is a relevant research topic. This is a difficult task, among other reasons, due to the fact that the Haemodynamic Response Function (HRF) varies over time, and across individuals or brain regions[1,2]. Hypothesis-free fMRI analysis methods (ICA, etc.) can alleviate the variability of the HRF, but these methods do not take advantage on existing knowledge regarding the shape of brain responses and the timing of the stimulation paradigm. A wrong assumption about the shape of the HRF can cause an increase in the false negative error rate[3].This work focuses on developing a computational fMRI processing tool more adequate to represent a broader range of possible shapes of the HRF, based on the framework of fuzzy variables.

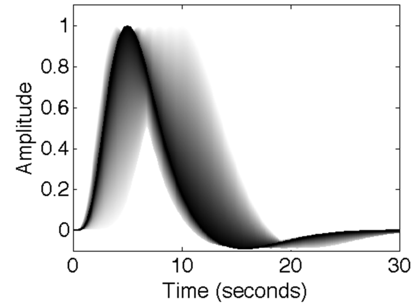


***Figure 1:** Fuzzy HRF.*

Methods. The fuzzy General Linear Model GLM for fMRI analysis is proposed. This technique is built by extending fuzzy linear regression models, developed within the soft-computing community.
The fuzzy HRF is generated as follows: given an analytical model of the HRF[4], we generated several suitable and possible shapes of such response by varying the parameters of that function. Each one of these shapes is weighted according to an estimation of its degree of possibility. Degrees of possibility are estimated for each time point by fitting triangular fuzzy sets. The highest degree of possibility at this time point is set to the value of the canonical HRF[4]. The obtained fuzzy HRF is presented in Fig. 1, where the degree of darkness corresponds to the degree of possibility of a value of the fuzzy HRF. To build the fuzzy design matrix $\tilde{\mathbf{X}}$, the convolution of the fuzzy HRF with the experimental paradigm is obtained by extending the convolution operator to deal with functions of fuzzy variables[5]. The fuzzy GLM method has the form $\tilde{\mathbf{Y}} = \tilde{\mathbf{X}} \diamond \boldsymbol{\beta} + \boldsymbol{\varepsilon}$, where $\tilde{\mathbf{Y}}$ is the BOLD signal observed at one voxel, interpreted as fuzzy singletons; $\boldsymbol{\beta}$ and $\boldsymbol{\varepsilon}$ are vectors of real numbers that represent the model parameters and the error term, respectively. The symbol "$\diamond$" represents matrix product operation defined for fuzzy matrices[5,6]. In order to obtain the Maximum Likelihood (ML) estimate of $\boldsymbol{\beta}$, fuzzy operations must be used. In this work we used those described by Yoon et al.[6]. Using the ML estimate of the fuzzy GLM and its asymptotic properties, the standard t-statistic can be derived to assess statistical activation maps. In order to validate the proposed fuzzy GLM, we first evaluated its performance simulating different HRF, whose definition in time varies. Two simulations were built, with the following ON/OFF stimuli: 5/40 s, 10/27 s, respectively. For each one of the periods when the stimulus is applied, a specific shape for the HRF is selected in a random manner. White noise was then added to the simulated signal. This simulation was repeated 10.000 times. At the same time, in order to simulate voxels with no brain activation present, another 10.000 signals made only with the same white noise were generated, obtaining at the end a contrast between active and non-active time courses.
ROC curves from t-scores of active/non-active time courses were created. We applied three strategies to detect activation: i) the proposed fuzzy GLM; ii) the standard GLM that uses the fixed canonical HRF; iii) the same standard GLM but whose design matrix was built on the precise HRF used to generate the specific simulated signals (GLM2).

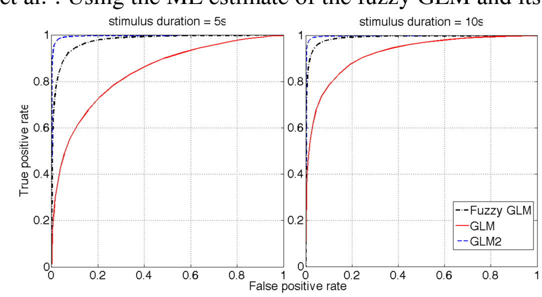


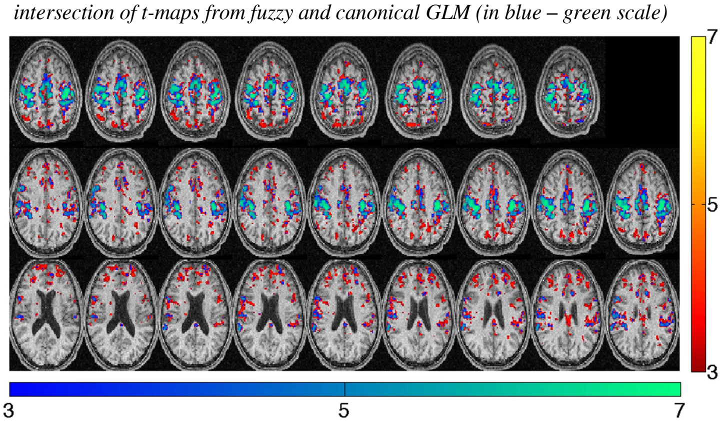
***Figure 2:** ROC curves obtained from simulated data experiments.*

A second step of validation was made on *in vivo* fMRI data. Data were acquired on a 1.5T Signa GE on a healthy volunteer (m., 25 y.o.). Task used was finger grasping between thumb and index in both hands simultaneously. Block design was used, beginning in OFF, with 30 s of no motion and 30 s of motion. Images were obtained with EPI with: TE/TR 60/3000 ms. Standard data preprocessing were done using SPM8[7].

Results. As expected, the best method to detect activation corresponds to GLM2, that is to say to the method based on the same precise HRF used to stimulate data: the corresponding ROC curves in Fig. 2 are almost perfect. Almost as good as GLM2, fuzzy GLM ROC curves show that fuzzy GLM performance is greatly improved with respect to canonical GLM, as fuzzy GLM permits to decrease the false negative rate in detection of activated pixels compared to canonical GLM. Fig. 3 presents activation maps obtained of a primary motor task on one healthy volunteer. All activated regions detected by the canonical GLM are also detected by the fuzzy GLM, but not all activated regions detected by the fuzzy GLM are detected by the canonical GLM: activated regions from fuzzy detection are broader and present in different brain areas.

Discussion and Conclusion. Promising results are obtained with fuzzy GLM in both simulation and data of healthy volunteer. In simulation, less false negative error are committed with a fuzzy GLM scheme, in agreement with the more extended activated regions obtained in volunteer data. To use a fuzzy definition of the HRF should allow a more robust adaptation of the GLM method to the uniqueness of brain response of each individual at one time point, but these are preliminary results that still need to be interpreted and validated thoroughly.

***Figure 3:** t-map obtained with fuzzy GLM (in red - yellow scale), and intersection of t-maps from fuzzy and canonical GLM (in blue – green scale)*



References. 1. Handwerker et al. (2004) *NeuroImage,* 21, 1639-1651. **2.** Proulx et al. (2014) *NeuroImage*, 93, 59-73. **3.** Lindquist et al. (2009) *NeuroImage*, 45, S187-S198. **4.** Glover (1999) *NeuroImage*, 9, 416-429. **5.** Hanss (2005), Fuzzy Arithmetic, Springer. **6.** Yoon et al. (2013), Soft Computing for Int Data Analysis, 190, 193-202. **7.** SPM8: http://www.fil.ion.ucl.ac.uk/spm/