NONLINEAR SUBSPACE REGULARIZATION METHOD FOR THE SINGLE-TRIAL ESTIMATION OF BOLD RESPONSES IN EVENT-RELATED fMRI

UNIVERSITY OF KUOPIO

Eini Niskanen*,[1], Mika Tarvainen[1], Mervi Könönen[2], Hilkka Soininen[3,4], Pasi Karjalainen[1]

[1]Department of Physics, University of Kuopio, Kuopio, FINLAND

[2]Department of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, FINLAND

[3]Department of Neuroscience and Neurology, University of Kuopio, Kuopio, FINLAND

[4]Department of Neurology, Kuopio University Hospital, Kuopio, FINLAND

*Email: *Eini.Niskanen@uku.fi*

URL: *http://bsamig.uku.fi/*

Abstract

In this work, a method for single-trial estimation of BOLD responses in fMRI time-series is presented. The method is based on subspace regularization approach in which eigenvectors of data correlation matrix are used prior information in modelling the BOLD responses. The performance of the proposed method is evaluated using both simulated and real event-related fMRI-data and the results are compared to those obtained without subspace regularization.

Introduction

- The shape and size of BOLD responses vary between and within subjects across stimuli, active cortical area, and trial [1, 2, 3].
- By using a fixed model in BOLD response estimation, the sensitivity of activation detection is diminished and the study of the variability of the BOLD responses is biased toward the selected model.
- We propose a method based on the subspace regularization method [4] for the single-trial estimation of BOLD responses.
- From a set of measured BOLD responses second order statistical information is extracted using eigenvalue decomposition. This information creates a signal subspace that is used as prior information in the regularization method.

Materials and methods

The subspace regularization method was evaluated using both simulated and real fMRI data.

Simulated data

- The simulated BOLD responses with varying delay were created using the Balloon model [5].
- For obtaining realistic noise a null dataset was obtained. A young healthy volunteer was scanned in a 1.5 T Siemens Vision scanner with a gradient echo EPI sequence (TR = 2.5 s, TE = 70 ms, FOV = 256 mm, 64 $\times$ 64 matrix, 16 slices, slice thickness = 5 mm, 1 mm gap, in-plane resolution = 4 mm). The null data was spline-interpolated to 2 Hz sampling rate.

Real data

- A young healthy volunteer was scanned in a 1.5 T Siemens Magnetom Avanto scanner with a gradient echo EPI sequence (TR = 1.5 s, TE = 50 ms, FOV = 192 mm, 64 $\times$ 64 matrix, 16 slices, 3 mm isotropic voxels).
- The paradigm was a simple motor Go/NoGo task (button press for green squares and ignorance of red squares). The squares were presented in a random order (62 green squares and 62 red squares). The interstimulus interval was randomized to be between 15 and 20 seconds.
- The data was preprocessed (motion and slice timing difference correction, coregistration with a high-res. T_1-image, smoothing) and analyzed using SPM5 (the Wellcome Department of Cognitive Neurology, London).
- The time series of the voxel with strongest activation in SPM5-analysis in primary motor cortex (see Fig. 1) was extracted from the unsmoothed SPM5-preprocessed images and used in subspace regularization analysis.

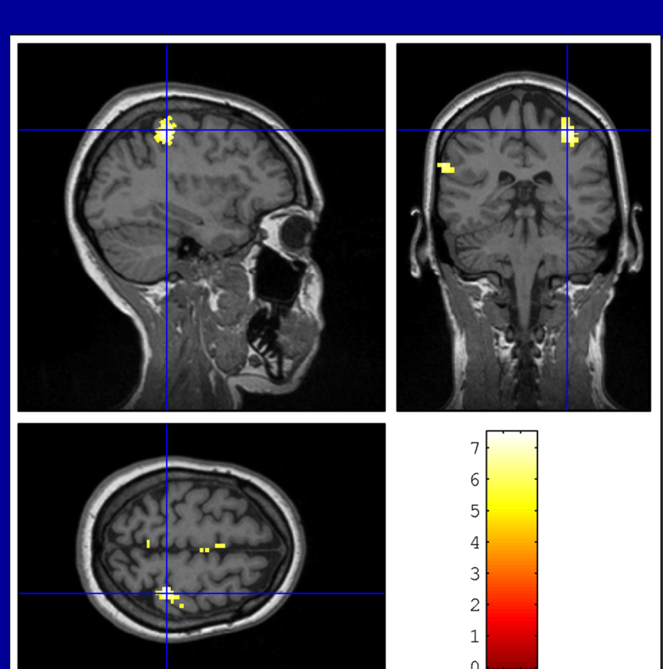

Fig. 1. The results from SPM5-analysis (button pressing, $p < 0.001$ FWE-corrected). The crosshair is located on the voxel with strongest activation.

Subspace regularization

- Let us assume a nonlinear observation model

$$z = s + v = h(\theta; t) + v,$$

where z is the sampled measurement, s is the BOLD response, $h(\theta; t)$ is some nonlinear model for the BOLD response, and v is the measurement noise.

- The ordinary least squares (LS) solution for parameters θ is obtained by minimizing the functional

$$l(\theta) = \|z - h(\theta; t)\|^2.$$

- Parameters θ can be solved e.g. by using the iterative Levenberg-Marquad algorithm

$$\hat{\theta}_{i+1} = \hat{\theta}_i + \kappa \left(J_h^T J_h + \lambda I\right)^{-1} \left[J_h^T \left(z - h(\hat{\theta}_i)\right)\right],$$

where κ defines the length of the iteration step, J_h is the Jacobian determinant of the nonlinear model $h(\theta)$, and λ is a positive constant.

- The subspace regularized modification of the LS functional can be written in the form

$$l = \|z - h(\theta)\|^2 + \alpha^2 \|(I - H_S H_S^T) h(\theta)\|^2,$$

where α is the regularization parameter. H_S is consisted of the eigenvectors of data correlation matrix and forms an orthonormal basis for a signal subspace. The distance of $h(\theta)$ from this subspce is $\left(I - H_S H_S^T\right) h(\theta)$.

- The Levenberg-Marquad algorithm for the subspace regularized solution becomes

$$\hat{\theta}_{i+1} = \hat{\theta}_i + \kappa \left(J_h^T J_h + \alpha^2 J_h^T (I - H_S H_S^T) J_h + \lambda I\right)^{-1} \cdot \left[J_h^T \left(z - h(\hat{\theta}_i)\right) + \alpha^2 J_h^T \left(I - H_S H_S^T\right) h(\hat{\theta}_i)\right].$$

Results

Next steps were performed both for the simulated and real data.

- The trend in the fMRI time series was removed and the time series was divided into adequate BOLD responses (Fig. 2).

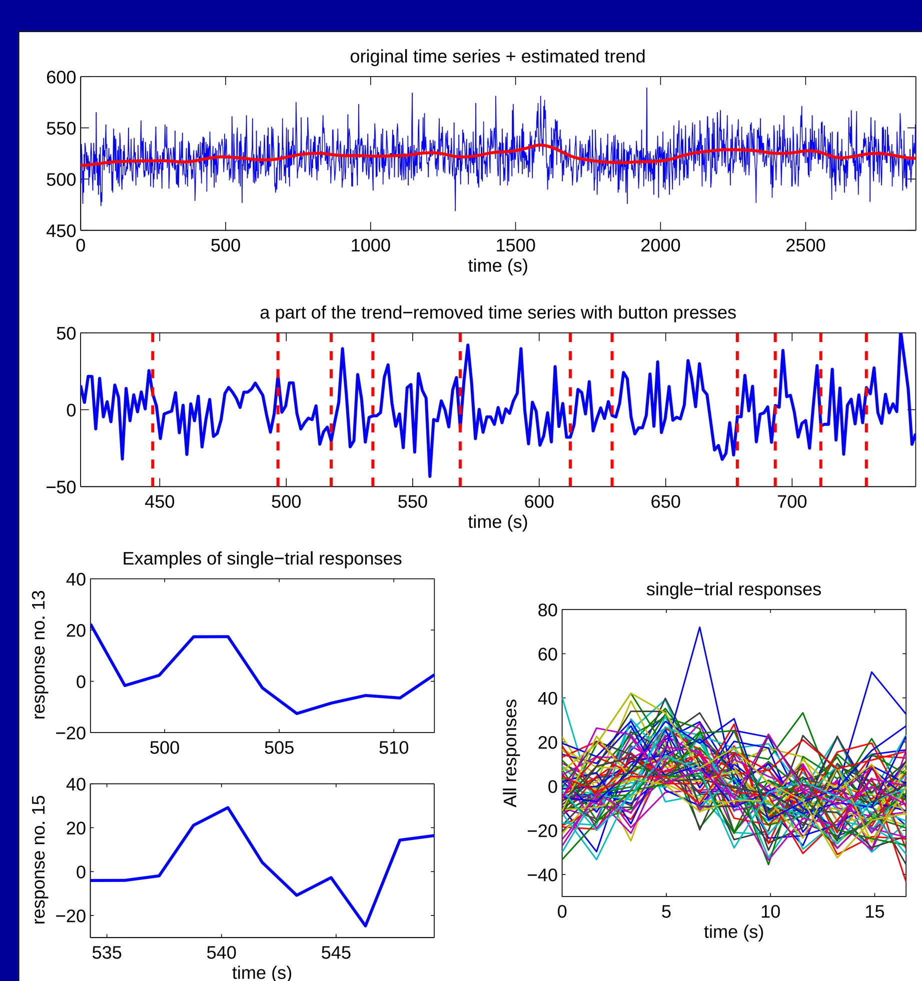

Fig. 2. The original real data time series with an estimated trend (up). A part of the trend-removed time series with red markers of button pressing (middle). Examples of single-trial responses (bottom left). All single-trial responses plotted as they occur in the data matrix z (bottom right).

- The first four eigenvectors of the data correlation matrix were used as the orthonormal basis H_S of the signal subspace.
- The model of Cohen *et. al* [6] was used as the nonlinear model for the BOLD responses $h(\theta; t)$

$$h(\theta; t) = A t^{\delta} e^{-t/\tau}$$

with A, δ and τ as the unknown parameters θ.

- The value of the regularization parameter was selected experimentally and the estimates for the BOLD responses were calculated using the parameters solved with regularization.
- Nonregularized estimates for the BOLD responses were calculated also for comparison.
- The estimates for some typical responses are illustrated in figures 3 and 4.

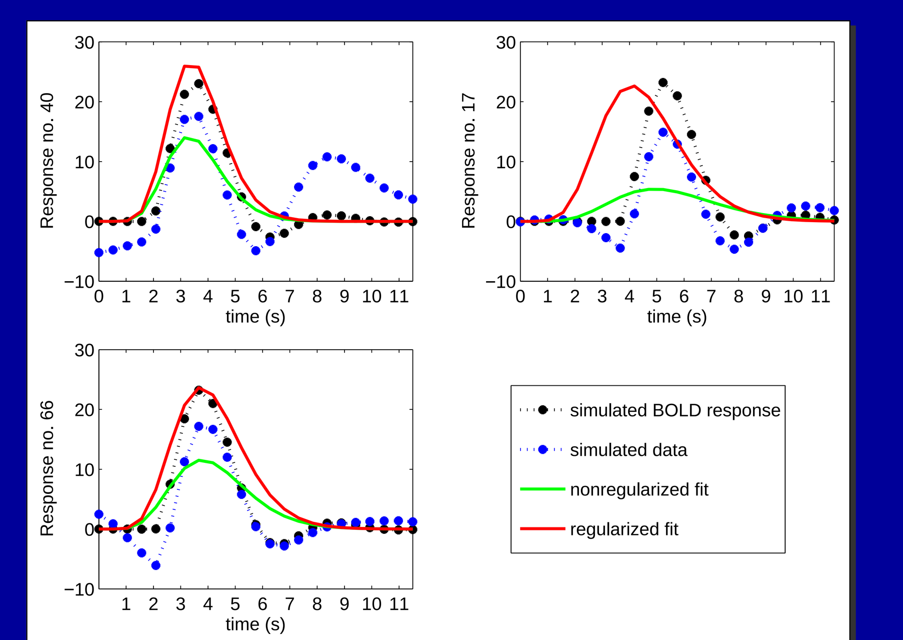

Fig. 3. Typical BOLD response estimates for the simulated data.

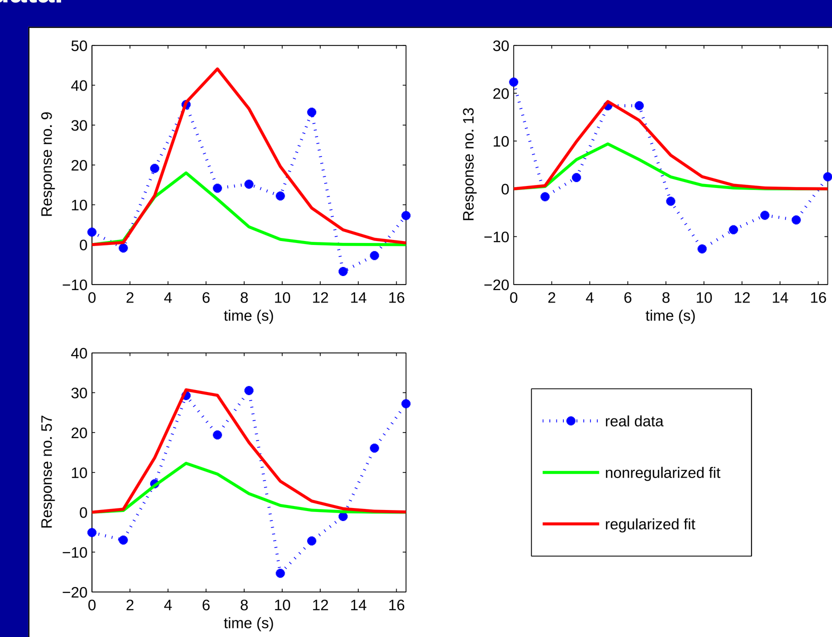

Fig. 4. Typical BOLD response estimates for the real data.

Discussion

- The proposed subspace regularization method enhances the estimates of the BOLD responses in cases with a lot of noise. Especially the estimate of the BOLD response amplitude is significantly enhanced.
- The low number of data points in a BOLD response constricts the number of estimated parameters in the BOLD model. Too complex model with many parameters cannot be estimated in single-trial manner. Therefore a compromise between the number of the parameters and the goodness of the fit must be made.
- The model used in this work is unfortunately not capable of modelling the poststimulus undershoot or the initial dip. It also fails in modelling the response with large delay after the stimulus.
- An optimal regularization parameter α could be found using some model evaluation method e.g. the cross-validation approach.

References

[1] A. L. Vazquez and D. C. Noll, "Nonlinear aspects of the BOLD response in functional MRI," *NeuroImage*, vol. 7, no. 2, pp. 108–118, 1998.

[2] J.-R. Duann, T.-P. Jung, W.-H. Kuo, T.-C. Yeh, S. Makeig, J.-C. Hsieh, and T. J. Sejnowski, "Single-Trial Variability in Event-Related BOLD Signals," *NeuroImage*, vol. 15, pp. 823–835, 2002.

[3] V. D. Calhoun, T. Adali, G. D. Pearlson, and J. J. Pekar, "Spatial and Temporal Independent Component Analysis of fMRI Data Containing a Pair of Task-Related Waveforms," *Human Brain Mapping*, vol. 13, no. 1, pp. 43–53, 2001.

[4] P. A. Karjalainen, J. P. Kaipio, A. S. Koistinen, and M. Vauhkonen, "Subspace Regularization Method for the Single-Trial Estimation of Evoked Potentials," *IEEE Transactions on Biomedial Engineering*, vol. 46, pp. 849–860, July 1999.

[5] T. Obata, T. T. Liu, K. L. Miller, W.-M. Luh, E. C. Wong, L. R. Frank, and R. B. Buxton, "Discrepancies between BOLD and flow dynamics in primary and sipplementary motor areas: application of the balloon model to the interpretation of BOLD transients," *NeuroImage*, vol. 21, pp. 144–153, 2004.

[6] M. S. Cohen, "Parametric Analysis of fMRI Data Using Linear Systems Methods," *NeuroImage*, vol. 6, no. 2, pp. 93–103, 1997.