SUBSPACE APPROACHES FOR FMRI TIME SERIES ESTIMATION

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Abstract *We present a subspace approach for functional magnetic resonance imaging (fMRI) time series analysis. The signal subspace is formed of the eigenvectors of data correlation matrix. The approach is utilized both for single-trial estimation of blood oxygenation level dependent (BOLD) responses in fMRI time series and for studying the functional connectivity of BOLD responses from different spatial areas.*

Introduction

- fMRI is a noninvasive method for studying human brain function and constructing whole brain activation maps for sensory and mental functions with relatively high spatial resolution.
- The most common purpose on fMRI studies is to locate the cortical areas involved in processing the given stimulus.
- The relationship between stimulus, neural activation, and BOLD response has been studied since fMRI was introduced in 1992.
- The shape of BOLD response varies between subjects and also within subject depending on the type of the stimulus and active cortical area [1, 2, 3].
- The term functional connectivity is defined as the temporal correlations in neurophysiological events appearing between spatially remote cortical areas.

Methods

fMRI measurements and simulations

- The simulated BOLD responses were generated by using the Balloon model [4].
- In addition, two real fMRI measurements were acquired.
  1. A null data set for obtaining realistic noise. 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 x 64 matrix, 16 slices, slice thickness=5 mm, 1 mm gap, in-plane resolution 4 mm).
  2. A motor Go/NoGo task, i.e. button press for green squares and ignorance of red squares. 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 x 64 matrix, 16 slices, 3 mm isotropic voxels).
- Both data sets were preprocessed using SPM2 developed by the Wellcome institute in London, UK.

Subspace methodology

- Let us denote a single N-point BOLD response measurement with a column vector

$$z(t) = [z(1), \ldots, z(N)]^T$$

and an ensemble of M measurements with a matrix

$$Z = \begin{bmatrix} z_1(1) & \cdots & z_M(1) \\ \vdots & \vdots & \vdots \\ z_1(N) & \cdots & z_M(N) \end{bmatrix}$$

where $z_m(t)$ is the m'th BOLD measurement.

- The subspace for the estimation is constructed from the eigenvectors of data correlation matrix.
- The correlation matrix of the BOLD measurements can be estimated as

$$R_Z = \frac{1}{M} Z Z^T$$

and the eigenvectors u and the corresponding eigenvalues λ can be solved from the eigendecomposition $R_Z u = \lambda u$.

Single-trial BOLD response estimation

- Let us assume a nonlinear observation model

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

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

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

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

- The subspace regularized modification of the LS functional can be written in the form [5]

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

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

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

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

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

Functional connectivity estimation

- Let us consider two different cortical areas and denote the m'th response from area 1 with $z_m^1(t) = [z_m^1(1), \ldots, z_m^1(N)]^T$ and that from area 2 with $z_m^2(t)$ correspondingly. An augmented $2N \times M$ data matrix is then formed as

$$Z = \begin{bmatrix} z_1^1(t) & \cdots & z_M^1(t) \\ z_1^2(t) & \cdots & z_M^2(t) \end{bmatrix}.$$

- The subspace for the augmented data matrix is then constructed from the eigenvectors of the data correlation matrix.
- The first eigenvector u_1 (corresponding to the largest eigenvalue) is the best mean square fit of a single waveform to the set of augmented BOLD measurements, and thus, u_1 is similar to the mean of the augmented measurements.
- The next few eigenvectors are expected to cover the latency variations of the BOLD measurements as follows:
  1. If the latency variations of the BOLD responses in areas 1 and 2 are independent, at least two separate eigenvectors are needed to cover these latency variations.
  2. If there is strong functional connectivity between the two areas, the latency variations are expected to be mainly covered by a single eigenvector.

Results

- For the single-trial estimation a model of Cohen *et al.* [6] with four unknown parameters was used

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

- Single-trial BOLD estimates were calculated by using the ordinary LS and subspace regularized LS formulation.
- Typical single-trial estimates for simulated and real data are shown in Fig. 1.

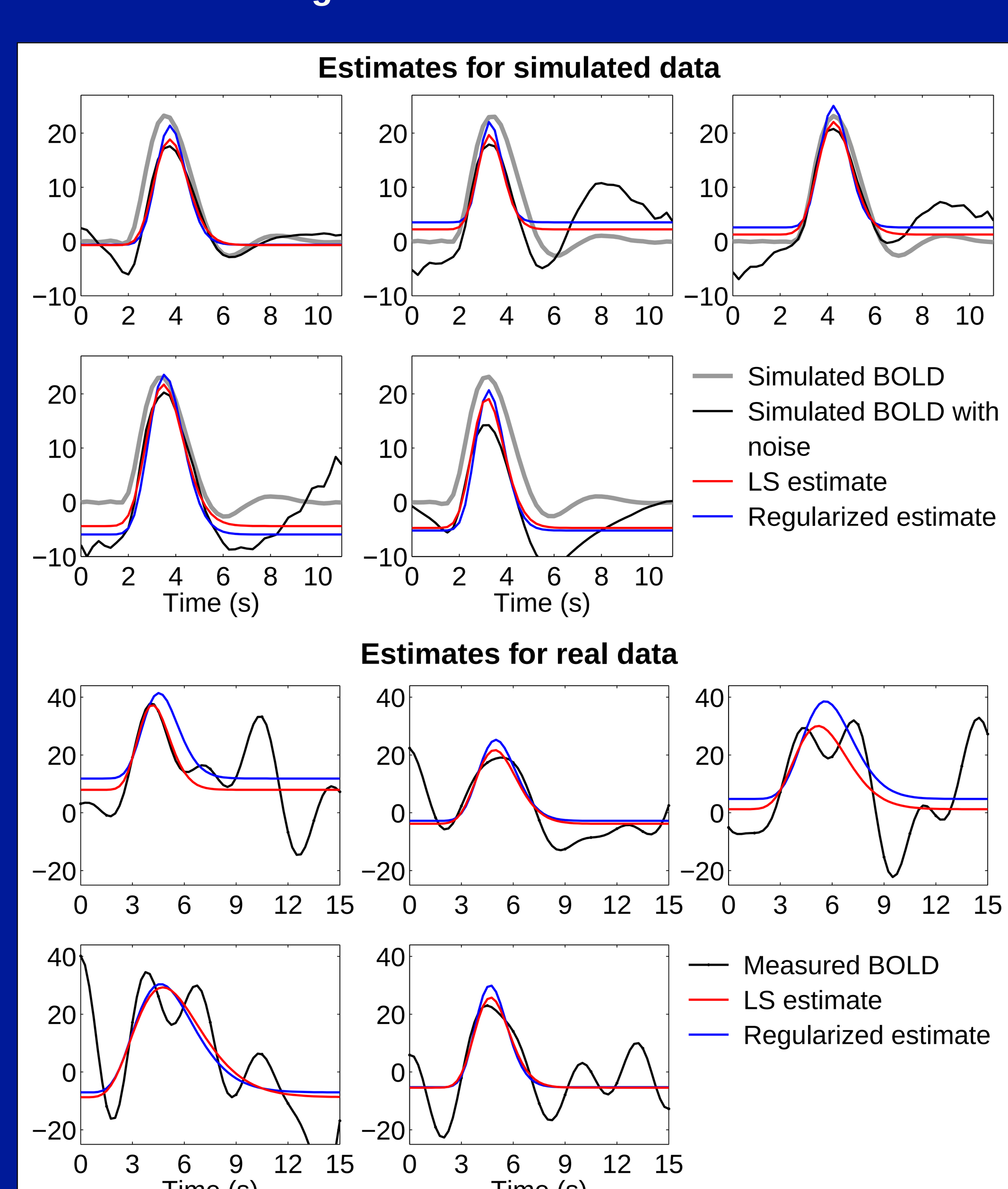

Fig. 1. Typical single-trial BOLD estimates for simulated and real data.

- Functional connectivity estimation was evaluated by simulating two data sets: 1) 70 BOLD responses from two cortical areas without temporal correlations (independent responses) and 2) with temporal correlations (dependent responses).
- The simulated BOLD responses were added into the real fMRI noise measurement.
- The augmented data matrices were then formed for both data sets by concatenating the simulated BOLD measurements from areas 1 and 2.
- The eigenvectors and corresponding eigenvalues were finally calculated for both data sets and the first three of them are shown in Fig. 2.

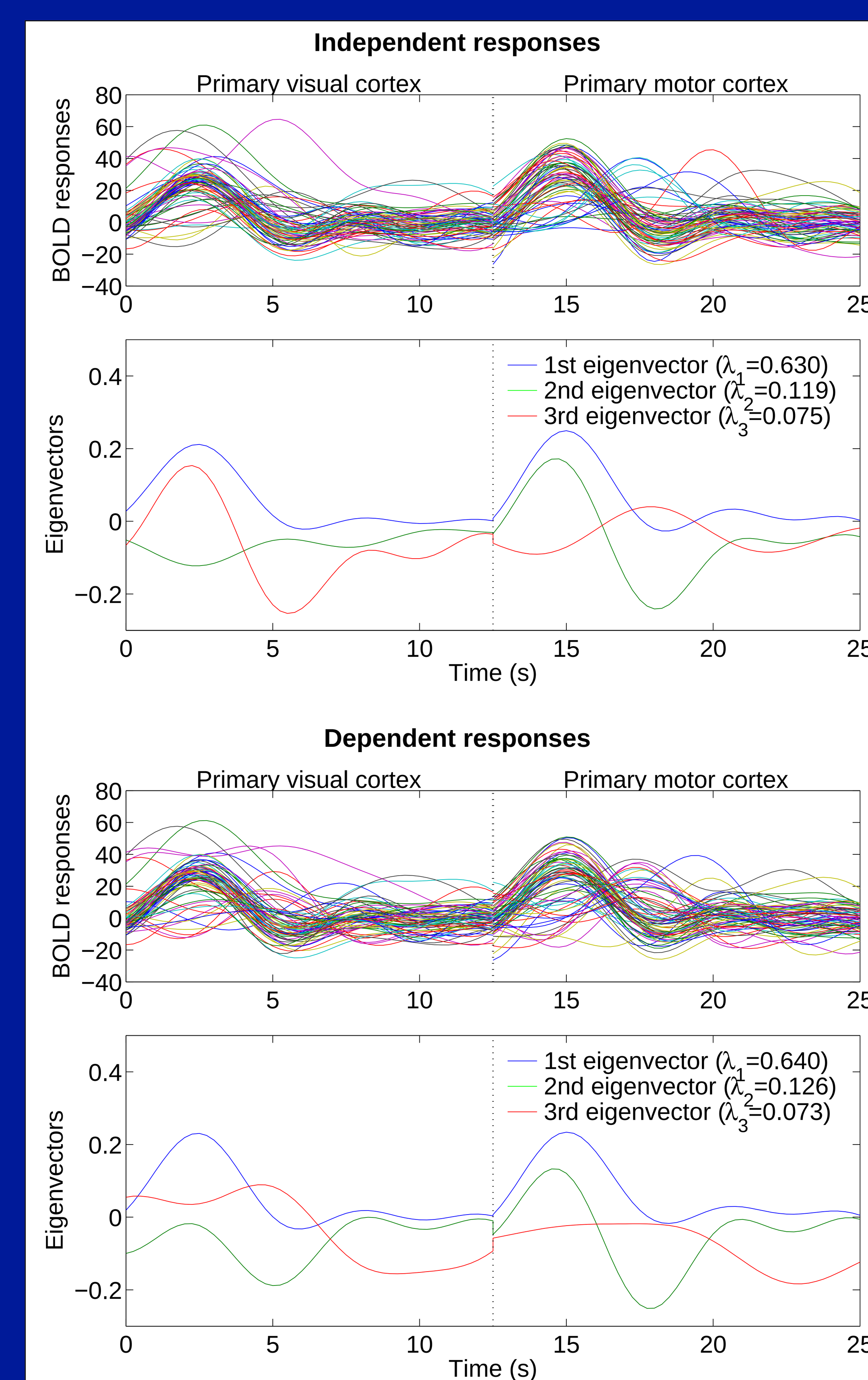

Fig. 2. Simulated BOLD responses and the corresponding eigenvectors for the independent and dependent case.

Discussion

- It has been shown how the subspace methodology can be used in the single-trial estimation of BOLD responses and in the estimation of functional connectivity.
- The subspace regularization seems to improve slightly the single-trial BOLD response estimates when compared to ordinary LS solution.
- In the future, more complex observation models for the BOLD response will be tested.
- The interesting difference in the functional connectivity estimation between the two cases was found from the second and third eigenvectors. That is, in the dependent case a single eigenvector seems to cover most of the latency variations of BOLD responses in both areas.

References

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