

Improved Multi-Echo BOLD fMRI Visual Activation Detection by Applying Spatiotemporal Maps Reconstruction

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Impact

Applying spatiotemporal map model to the multi-echo fMRI dynamic reconstruction provides increased tSNR and functional contrast while preserving spatial resolution, offering potential for high-resolution (e.g., layer-) fMRI.

Synopsis

Motivation: Multi-echo fMRI (ME-fMRI) could disentangle TE-dependent signal from artifactual constituents related to spin density fluctuations, but requires more aggressive under-sampling, which may result in increased image artifacts and SNR loss.

Goals: Explore using a spatiotemporal reconstruction framework and evaluate its impact on the estimated T_2^* and S_0 dynamic changes in fMRI visual task.

Approach: Apply a new dynamic reconstruction framework, namely spatiotemporal maps (STM), to reconstruct the ME-fMRI time-series.

Results: STM shows comparable tSNR and functional contrast to spatially-smoothed CG-SENSE reconstruction, but preserves spatial resolution. We also observed spurious activations that may be due to the limited representation capability of our STM implementation.

Introduction

Multi-echo (ME)-fMRI enables T_2^* decay to be modeled on a voxel scale at each time point. Compared to the standard single-echo approach, ME-fMRI can differentiate BOLD-related signal from artifactual constituents that are caused by S_0 changes [1], such as head motion, cardiac effects, and hardware instability (e.g., B0 drift). However, estimating dynamic changes in T_2^* and S_0 parameters by fitting the multi-echo time series to an exponential model is very sensitive to noise [1].

Recently, a subspace-based [2,3] dynamic reconstruction framework called spatiotemporal maps (STM) was proposed [4]. The STM model decomposes the dynamic image series into voxel-level temporal bases and static coefficient maps. It has been shown in fMRI data that STM has denoising and/or de-aliasing characteristics. Here we apply the STM model to reconstruct the entire ME-fMRI time series (including individual echos), and evaluate its impact on the estimated T_2^* dynamic changes in response to a visual stimulation task, in comparison with conventional framewise CG-SENSE least-squares (FW-LS) reconstruction.

Methods

STM Model

The STM model decomposes the image series $\rho(\vec{x}, t)$ into the form:

$$\rho(\vec{x}, t) \approx \sum_{l=1}^{L(\vec{x})} s_l(\vec{x}, t) \rho_l(\vec{x}), \quad (1)$$

where the temporal bases $s_l(\vec{x}, t), l = 1, \dots, L(\vec{x})$ are called the spatiotemporal maps, and $\rho_l(\vec{x})$ are called the coefficient maps. Here we chose $L(\vec{x}) = 5$ for all locations. The temporal bases $s_l(\vec{x}, t)$ are efficiently computed from the auto-calibration signal (ACS) region acquired at each time point (cf., Figure 1) by leveraging the autoregressive properties of the $(\vec{k}, t)$ -space [4].

Once we have the STMs $s_l(\vec{x}, t)$, we estimate the coefficient maps $\rho_l(\vec{x})$ by solving:

$$\{\hat{\rho}_1, \dots, \hat{\rho}_L\} = \arg \min_{\{\rho_l\}_{l=1}^L} \frac{1}{2} \|\mathbf{A}(\sum_{l=1}^L \mathbf{S}_l \rho_l) - \mathbf{d}\|_2^2 + \beta \mathcal{R}(\rho_1, \dots, \rho_L), \quad (2)$$

where $\mathbf{A}$ is the measurement matrix, $\mathbf{d}$ is the multi-channel k-data, ρ_l is the vectorized coefficient map, and $\mathcal{R}$ is the regularization term. We compare the STM reconstruction with a framewise CG-SENSE reconstruction where each echo image is reconstructed independently.

Weighted Exponential Fit

After obtaining the multi-echo image series, R_2^* ($1/T_2^*$) at each "slow-time" point was estimated by fitting a mono-exponential model:

$$S(TE_n) = S_0 e^{-R_2^* TE_n}, \quad (3).$$

We used a weighted least squares log-linear fit to account for the lower SNR of later TEs. The weighting for the n th echo is $|S(TE_n)|$ as this is an approximation of the inverse log-signal variance.

fMRI Experiment

A 4-echo 2D-EPI sequence with $TE = [12, 33, 54, 75]$ ms, $TR = 0.8$ s and $3\times$ acceleration (*cf.*, [Figure 1](#)) was used in a 5-cycle 20s-on 20s-off flashing-checkerboard visual task fMRI experiment. The activation was analyzed based on t-statistic of estimated R_2^* dynamic changes, and the 2nd-echo signals ($TE = 33$ ms). We compared 1) the R_2^* -based activation with the single-echo activation; and 2) the activations of three different reconstructions: framewise (FW-LS) without and with spatial smoothing, and STM model. The spatial smoothing is done by low-pass filtering the FW-LS image k-space anisotropically to match the spatial frequency of the STM ACS region. The fMRI experiment was repeated 4 times to evaluate the test-retest reliability of each method by using a mixed-binomial model [5,6].

Results

[Figure 1](#) shows the flowchart of the STM framework. [Figure 2](#) shows the percent change of 2nd-echo signals, of R_2^* and S_0 "slow-time" dynamics for an activated voxel. [Figure 3](#) shows the activation maps based on 2nd-echo signals and R_2^* "slow-time" dynamics, as well as tSNR maps. Both the spatially-smoothed FW-LS and STM percent change curves ([Figure 2](#)) have less temporal noise compared to FW-LS. This is also evident in the tSNR maps, in which both methods have a $2.5\times$ higher average tSNR than FW-LS. This denoising feature leads to a stronger visual activation. Note that the STM model shows comparable tSNR and activation intensity to spatially-smoothed FW-LS but preserves high spatial resolution. [Figure 4](#) shows the TE-dependency of R_2^* - and S_0 -related activations. FW-LS shows a cleaner separation of TE-dependent and TE-independent activations compared to STM. [Figure 5](#) shows the ROC curves for single-echo and R_2^* -based activation maps with different reconstructions. ROC analysis shows that the R_2^* activation maps have similar test-retest reliability for both FW-LS and STM reconstructions.

Discussion/Conclusion

It should be noted that there seems to be spurious activations outside the brain in the STM activation maps. This artifact could be from the locally-low-rank feature of the STM model. We hypothesize that this issue may be alleviated by choosing a larger (or spatially-dependent) $L(\vec{x})$. Increasing $L(\vec{x})$ may also result in better separation of TE-dependent and TE-independent signals.

In conclusion, we demonstrated that STM produces comparable tSNR and functional contrast to spatially-smoothed FW-LS reconstruction but preserves high spatial resolution. These results point to the potential of STM to improve high-resolution (e.g., cortical-column-specific and layer-specific) fMRI.

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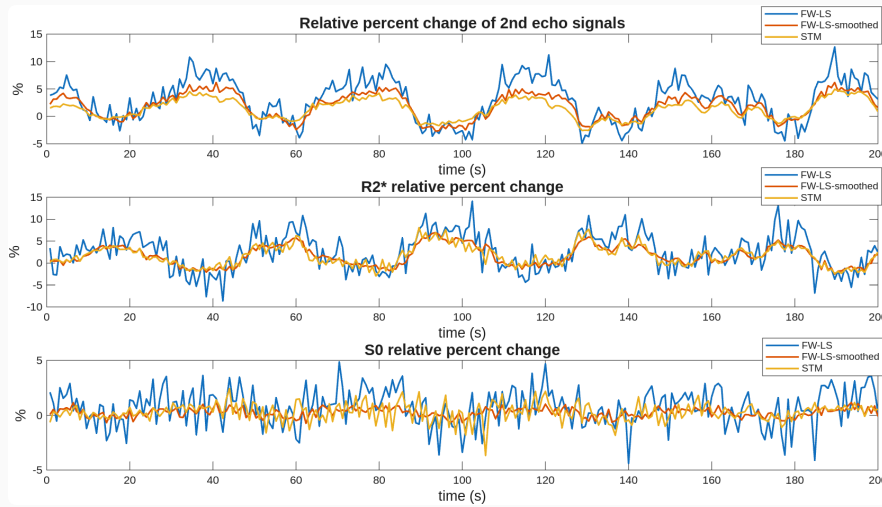
▶ **Animated Figure 1**

This figure contains animation/video content. To view the animation, scan the QR code with your mobile device or visit the online version of this abstract.



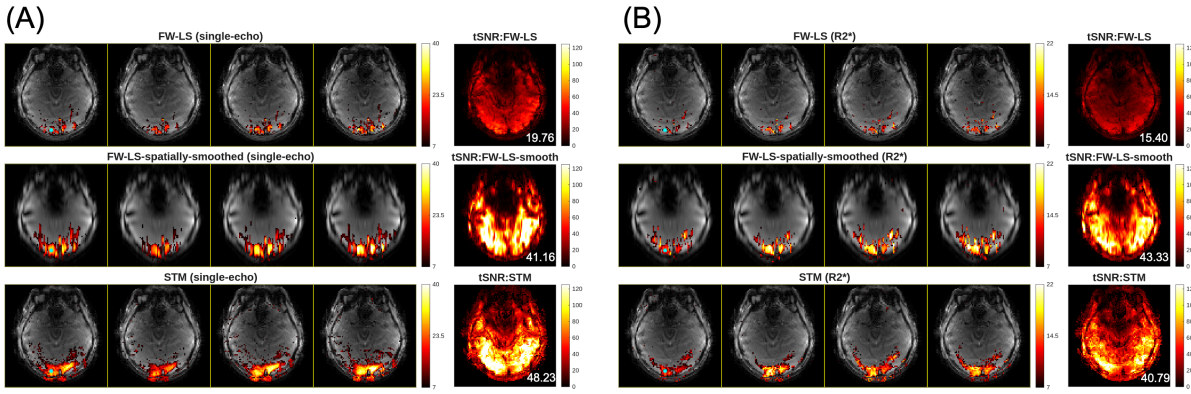
Figure 1: Flowchart of STM framework.

The ACS data at each acquisition is zero-padded and then used to generate the STMs. The coefficient maps are computed by solving Eq. (2). STMs are then multiplied by the coefficient maps to obtain the multi-echo image series. Alternatively, the image series can be obtained by using CG-SENSE at each acquisition independently (called FW-LS). Matrix size = 90×90 , resolution = 2.4mm iso., acceleration $R_y=3$, ACS width $N_{ACS}=18$.



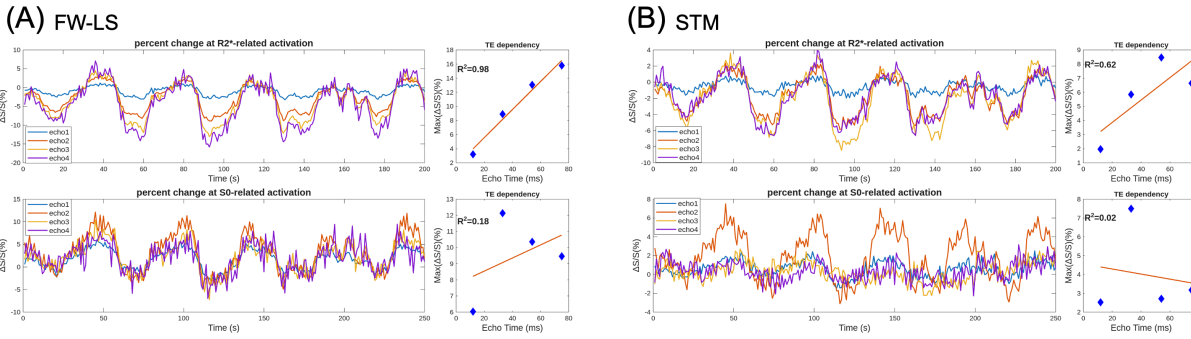
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Figure 2: Relative percent change of 2nd-echo signal, and R_2^* and S_0 ("slow-time") dynamics, in the voxel marked as cyan asterisk in Figure 3. Both spatially-smoothed FW-LS and STM "slow-time" series show less temporal noise compared to FW-LS.



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Figure 3: T-statistic maps of four runs based on (A) 2nd-echo signal and (B) R_2^* "slow-time" dynamics overlaid on structural images for a visual task. The task regressors for 2nd-echo signal and R_2^* dynamics are half-a-cycle out of phase. tSNR for each method is shown on the right. From top to bottom, the multi-echo image series are reconstructed using FW-LS, FW-LS with spatial smoothing, and STM. Average tSNR within the brain is marked in the bottom-right corner of each tSNR map.



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Figure 4: Spatially-averaged percent changes of R_2^* - and S_0 -related activations for (A) FW-LS and (B) STM reconstructed time series. The activated voxels in Fig.3(A) are categorized into R_2^* - and S_0 -related activations by comparing the t-statistic of R_2^* and S_0 dynamics. TE-dependency is quantified by a linear regression of the maximal percent changes against TEs. FW-LS shows a cleaner separation of TE-dependent and TE-independent activations than STM.



Figure 5: ROC curves for different activation analysis methods estimated from the mixed-binomial model [5,6]. Area-under-curve (AUC) up to false-positive-rate = 0.02 for each method is indicated in legend. The numbers next to the markers indicate the threshold levels used for t-statistic. "Single-echo" refers to 2nd-echo signal.