A NOVEL TEMPORAL FILTERING STRATEGY FOR FUNCTIONAL MRI USING UNFOLD

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Introduction

UNFOLD [1] is used to increase sampling rates in fMRI to detect transient BOLD signal modulations. Spatial aliasing artifacts due to interleaved k-space sampling are removed by temporal filtering before statistical mapping in the time domain is carried out. So far, low-pass filtering and zero-filling have been proposed. Particularly at high UNFOLD factors both methods are non-optimal since low-pass filtering degrades temporal resolution and zero-filling leads to serial correlations (non-white noise) known to bias linear modeling of fMRI data [2-8]. In this work, we propose a novel temporal filtering strategy intrinsically introducing less non-white noise compared to zero-filling. In this event-related finger-tapping experiment, we demonstrate that the number of significantly activated voxels is increased when the proposed filtering strategy is used.

Material and Methods

Four male healthy subjects (28±2 years) were measured twice on a 3.0 Tesla whole-body MR system (TimTrio, Siemens Healthcare, Erlangen, Germany) equipped with a 12 channel head coil. A 3D version of a Multi-Echo FLASH imaging sequence [9] was eightfold accelerated with UNFOLD using an acceleration factor of two and four in slice and phase encode direction, respectively (TE/TR=35ms/93.6ms, matrix size=256x256x16, FOV=190x190x48 mm^3, slice-thickness=3.0 mm, flip angle=22°, bw=520Hz/Px, 3D-encoding direction: head-foot (dk_z=2), phase-encoding direction: anterior-posterior (dk_y=4)). A fat-saturation pulse of 5 ms was applied before a 3D slab was acquired yielding an effective temporal resolution of 3.05 s per single time frame with UNFOLD. In the first run, the volunteers received a short auditory stimulus presented at a rate of 1/15 Hz. At each stimulus, bilateral finger tapping was performed for three seconds. In a total scan time of 13 minutes, 256 image volumes were acquired. In the second run, the imaging protocol was kept the same but no finger-tapping was performed (null-dataset). The power spectrum of a representative voxel exhibits equispaced aliasing peaks at the frequencies $\omega_{alias} = -\omega_{Nyq} + 2\cdot\omega_{Nyq}\cdot n/(dk_y\cdot dk_z)$ with $n \in \{0,1,2,.., dk_y\cdot dk_z\}$, and $\omega_{Nyq}=0.5\cdot TR^{-1}$ (Figure 1). After phase trend removal, as proposed by Yanle Hu [10], the width of each aliasing peaks was in average narrowed to approx. $4\cdot 10^{-3}$ Hz corresponding to three frequency components. Besides zero-filling a novel filtering strategy was tested replacing aliasing peaks by Gaussian noise with mean $\mu = \langle A^2(\omega)\rangle$ and standard deviation $\sigma = [\mathrm{var}(A^2(\omega))]^{1/2}$ estimated from the power spectrum $A^2(\omega)$ in each voxel. The frequency components $A^2(\omega_{alias})$, the fundamental stimulation frequency and higher harmonics were excluded from this estimation process. After temporal filtering, the fMRI datasets were post-processed and statistically analyzed with SPM5 (http://www.fil.ion.ucl.ac.uk/spm). For spatial smoothing a Gaussian kernel with a FWHM of 1.4x1.4x3.0 mm^3 was used. In order to compare both filtering strategies at an unbiased significance level, the t-value distribution in the null-datasets was used to calculate the cumulative distribution function for each subject. Adjacently, the number of significant voxels were counted for both filtering strategies at an actual significance level of α<2.5% and cluster size of 50 voxels

Results

The proposed filtering strategy increased the average number of activated voxels by a factor of 2.3 with a significant increase in three of four subjects and a slight decrease in the remaining subject compared to zero-filling (Table 1). Representative activation maps of subject 2 (Figure 2) show clearly more robust activation in the sensory and supplementary motor cortex when the proposed filtering strategy was used. A more complete picture of the filtering effects provides the modified receiver-operator-characteristics (ROC) for both temporal filtering strategies (Figure 3). The proposed strategy increased the number of positive responses at all thresholds nearly by a factor of two for a given level of false positives.

Discussion and Conclusion

The key objective of this work was to demonstrate that the proposed temporal filtering strategy improves statistical inference in fMRI when UNFOLD is applied. It has to be mentioned that the unbiased fMRI results shown may not be a ground truth since the t-distribution observed in the null-datasets considerably depended on the slice and the specific location within the slice. However, the unbiased statistical results and the modified ROC curves consistently showed a significantly increased BOLD sensitivity for the proposed filtering strategy. This is particularly important for fine scale fMRI measurements typically suffering from low temporal SNR impairing the detectability of neuronal activation. In conclusion, we have successfully demonstrated that statistical inference is increased in fMRI using UNFOLD using the proposed temporal filtering strategy.

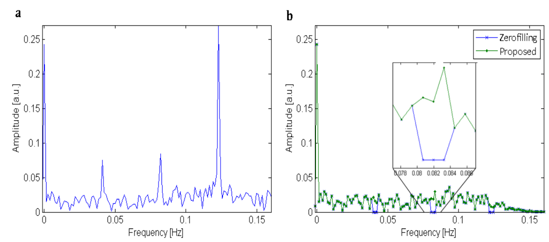

***Figure 1.** Typical power spectrum of a single voxel acquired with UNFOLD before **(a)** and after **(b)** temporal filtering using the zero-filling and the proposed filtering strategy. Panel **b** shows attenuated high frequencies due to low-pass filtering to improve temporal SNR.*

Subject	Zero-filling	Proposed
1	503	369
2	2100	7393
3	56	549
4	116	851
Average	**694**	**2291**

***Table 1.** Total number of activated voxels detected in the finger-tapping datasets for the zero-filling and the proposed filtering strategy.*

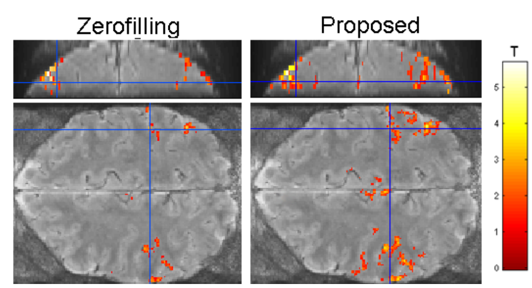

***Figure 2.** Activation maps acquired during bilateral finger-tapping using the zero-filling and the proposed filtering strategy.*

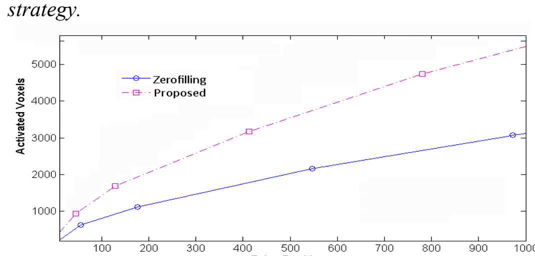

***Figure 3.** The modified receiver operator characteristics show the number of significant voxels detected during task activation versus the number of significant voxels (false positives) detected during the resting state. These are mean values of four subjects.*

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