Enhanced phase regression with Savitzky-Golay filtering for high-resolution BOLD fMRI

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Introduction

Functional magnetic resonance imaging (fMRI) based upon blood oxygenation level dependent (BOLD) contrast [1] remains the primary technique for non-invasive investigation of human brain function. The greater-than-linear increase in BOLD contrast with increasing magnetic field strength [2,3] has been a clear impetus for the steady increase in ultra-high-field (≥ 7T) sites worldwide. This increase in BOLD sensitivity can be readily exploited for functional imaging at higher spatial resolutions to reduce partial volume averaging effects and improve the specificity of activation and functional connectivity maps. However, gradient-echo acquisitions are also sensitive to large vessels and draining veins [4] that can be several millimeters away from the primary site of neural activation [5]. This degradation in spatial specificity is clearly undesirable. A post-acquisition method was previously proposed that uses the temporal evolution of phase in individual voxels to suppress BOLD fluctuations from larger vessels while preserving signal changes from microvascular effects [6]. This algorithm, known as *phase regression*, was originally applied to 4T data and works well when the phase time series exhibits high signal-to-noise ratio (SNR). However, our use of phase regression on 7T data acquired using both 2D echo-planar imaging (EPI) and 3D sequences such as PRESTO [7] has uncovered many instances in which the stability of the phase time series is insufficient to obtain adequate suppression of large vessels. An example of a noisy phase time series is the blue curve in Fig. 1D, and its use results in incomplete vessel suppression (blue curve in Fig. 1E). Therefore, the goal of this research is to investigate the use of Savitzky-Golay filters [8] to recover the underlying change in phase (e.g., red curve in Fig. 1D) and enhance the efficacy of phase regression (red curve in Fig. 1E). As temporal variance is dependent upon factors such as acquisition strategy and spatial resolution, we validate the robustness of these temporal smoothing filters using 7T data from 88 functional runs across 11 subjects acquired with four different pulse sequences at two in-plane resolutions.

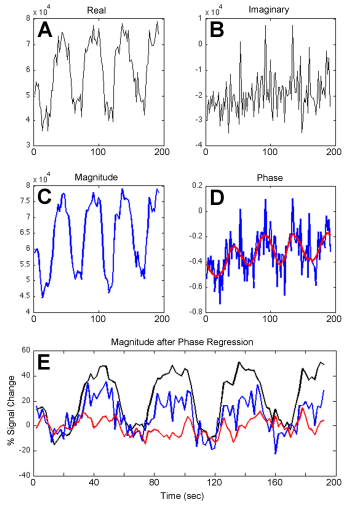

FIG. 1: Time series for a single voxel containing a vein. The (**A**) real and (**B**) imaginary time series add in quadrature to form the (**C**) magnitude. In (**D**) the blue curve is the noisy, unfiltered phase time series and the red curve is this phase time series after Savitzky-Golay filtering. In (**E**) the magnitude curve before phase regression exhibits a 38.8% signal change relative to baseline. The blue curve is the magnitude after phase regression using the unfiltered time series; the BOLD signal change is partially suppressed, but still exhibits a 16.8% signal change. Finally, the red curve is the magnitude after Savitzky-Golay filtered phase regression and exhibits complete suppression with a -0.55% BOLD signal change.

Methods

Experiments were performed on a Philips Achieva 7T scanner with a quadrature transmit coil and 16-channel receive-only head coil. A detailed description of data acquisition has been published [7]. In brief, data from eleven volunteers (eight females) were acquired under a protocol approved by the institutional review board. The visual paradigm was a block design with four segments of 24 sec baseline (central fixation) and 24 sec activation (stationary 8 Hz flashing checkerboard wedge). Slices (2 mm thick) were planned parallel to the calcarine sulcus. Eight functional runs were acquired using four sequences (2D EPI with 2.83 mm^3 voxels, 2D EPI with 9.59 mm^3 voxels, 3D fast field echo (FFE) [9,7] with 2.83 mm^3 voxels, and 3D PRESTO with 9.59 mm^3 voxels). Physiological noise correction via RETROICOR [10] (implemented using AFNI [11]) was applied to each run before the application of phase regression (PR). PR was applied either with or without Savitzky-Golay filtering (SGF). SGF (`sgolayfilt` in Matlab) requires two parameters to be specified (polynomial order and frame size) – the optimal values of which are unknown and can vary across voxels. Thus, the use of SGF considered many possible combinations of polynomial order and frame size (117 for EPI and FFE and 486 for PRESTO) for every voxel; the combination that produced the highest R^2 fit ($= 1 - \sigma_{PR}/\sigma_{orig}$) was selected as optimal. Resultant data were registered to the anatomical images (`3dAllineate` [11]) with a spatial weighting function to emphasize the anatomic features of each subject's occipital pole. For each subject, activation maps were computed using data acquired with each pulse sequence (`3dDeconvolve` [11]). Finally, to protect against analyses of false positive activations, only voxels with $t > 4$ (with or without either implementation of PR) in all four activation maps (for each sequence) were considered.

Results

Figure 2 displays *t*-score histograms of 19884 voxels from the four acquisition sequences for all subjects. These histograms are representative of the results for each of the single-shot or multi-shot acquisition sequences. Several authors have observed that the largest signal changes in BOLD fMRI can occur in larger vessels and draining veins (e.g., [3,12,13]); it thus follows that voxels containing larger vessels may also tend to have the highest *t*-scores. PR with SGF (Fig. 2B) suppresses signal changes in 62% of voxels with $t > 10$ and 89% of voxels with $t > 15$. In comparison, PR sans filtering (Fig. 2A) suppresses only 7.3% of voxels with $t > 10$ and 25% of voxels with $t > 15$. In both cases, PR preserves nearly all voxels with $4 < t < 8$, supporting the hypothesis that voxels with lower *t*-scores most likely reflect signal changes in gray matter.

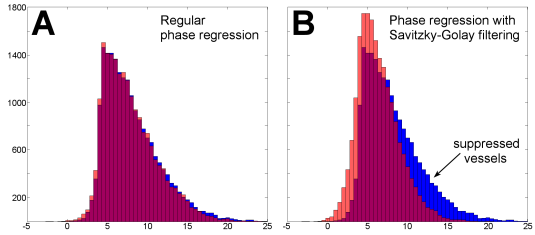

FIG. 2: Histograms of *t*-scores before (in blue) and after (in pink) phase regression (**A**) without filtering and (**B**) with Savitzky-Golay filtering. The overlapping region is represented in magenta. Although regular phase regression does suppress some high *t*-scores that are indicative of vessels, Savitzky-Golay filtering suppresses the majority of voxels with $t > 10$ while preserving nearly all voxels with $t < 8$.

Discussion

Phase regression can suppress BOLD signal changes from large vessels and draining veins in high-resolution gradient-echo data, thereby facilitating the construction of 'microvascular' activation maps that reflect signal changes from predominantly gray matter voxels [6]. However, our use of this algorithm at 7T has revealed that its efficacy is significantly hindered when the phase time series exhibits low SNR. We have demonstrated that the underlying modulation of phase can be recovered via Savitzky-Golay filtering, thus restoring the ability to suppress unwanted signal changes in large vessels and draining veins (Fig. 2B). We do not make *a priori* assumptions regarding the evolution of phase in any voxel (as it can be modulated by both ΔR_2^* and magnetic field inhomogeneities [14]) and therefore adopt an aggressive data-driven approach to identify the SGF parameters that minimize temporal variance in each voxel. This implementation preserves signal changes in nearly all voxels with lower *t*-scores, which is what we hypothesized to observe because gray matter tends to have smaller magnitude signal changes [3,12,13] and negligible BOLD-related phase changes [6]. Enhanced phase regression works on data acquired with single-shot and multi-shot pulse sequences, and should therefore be useful for human and animal gradient-echo fMRI at high spatial resolutions at high- and ultra-high fields.

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References – [**1**] Ogawa et al. PNAS USA 1990;87:9868. [**2**] Ogawa et al. Biophys J 1993;64:803. [**3**] Gati et al. MRM 1997;38:296. [**4**] Ogawa et al. MRM 1990;14:68. [**5**] Turner. Neuroimage 2002;16:1062. [**6**] Menon. MRM 2002;47:1. [**7**] Barry et al. Neuroimage 2011;55:1034. [**8**] Savitzky & Golay. Analytical Chem 1964;36:1627. [**9**] van der Meulen et al. MRI 1988;6:355. [**10**] Glover et al. MRM 2000;44:162. [**11**] Cox. Comput Biomed Res 1996;29:162. [**12**] Yacoub et al. Neuroimage 2005;24:738. [**13**] Harel et al. Neuroimage 2006;29:879. [**14**] Barry et al. MRI 2010;28:235.