Multi-Echo Simultaneous Multi-Slice fMRI: Reliable High-Dimensional Decomposition and Unbiased Component Classification

Prantik Kundu[1], Valur Olafsson[2], Souheil Inati[3], Peter Bandettini[1,3], and Thomas Liu[4]

[1]*Section on Functional Imaging Methods, NIMH, Bethesda, MD, United States,* [2]*UCSD, San Diego, CA, United States,* [3]*fMRI Core Facility, NIMH, Bethesda, MD, United States,* [4]*Center for Functional MRI, UCSD, San Diego, CA, United States*

Target Audience Researchers who are interested in acquiring simultaneous multi-slice (SMS) fMRI for fast imaging (TR<1s) of the resting state or task activation, especially for studies involving non-normative subjects, shorter scans, or individual subjects.

Purpose Here we demonstrate that a multi-echo (ME) SMS-fMRI approach can utilize TE-dependence analysis to provide automatic high dimensionality estimation, stable ICA, and empirical BOLD component classification (without the need for component templates). These capabilities utilize the existing ME-ICA framework originally developed for single-band ME-fMRI [3]. MESMS-fMRI extends blipped-controlled aliasing in parallel imaging (blipped-CAIPI), which has already received widespread interest for its application in the resting state fMRI studies of the Human Connectome Project (HCP) [1,2]. So far, SMS-fMRI has been used in conjunction with ICA-based artifact denoising based on fixed dimensionality estimates (e.g. 100 or 250) and group template-based component classification. While this pipeline may be optimized for the 1 hr resting state datasets acquired by the HCP, it may not represent a generalizable or unbiased approach for the analysis of SMS-fMRI from novel subjects or experiments.

Methods *Acquisition and Subjects* Data were acquired using a 3T GE MR750 system with a 32 channel receive coil (Nova Medical). MESMS-fMRI used 3-echo EPI (3.75x3.75x4mm, TR=0.87s, 690 volumes, TEs=13.9,33,52.1ms, FA=56°, blipped-CAIPI EPI with 3 sagittal slices per RF excitation, 36 slices (12 RF excitations) per volume, SENSE factor 1.33)[4,5]. Resting state fMRI data (10 minutes with fixation) were acquired from 11 subjects. An additional set of 10-minute resting state and video-watching scans was acquired for 3 subjects. *Preprocessing* used ME-ICA for: temporal and spatial alignment, T_2* weighted averaging for contrast optimization, and no additional smoothing or filtering. *Probabilistic Principal Components Analysis (P-PCA)* from FSL MELODIC [6] provided a conventional automatic dimensionality estimate based on comparing power of components in data versus components in a noise model. P-PCA was computed separately for high-pass filtered (f<0.01Hz) and unfiltered data. FastICA followed automatically. *ME-PCA Dimensionality Estimation* computed linear TE-dependence (κ) and TE-independence (ρ) model fits in PCA components to select those with BOLD (ΔR_2^*) and/or artifact (ΔS_0) loadings for FastICA unmixing, while excluding others as Gaussian/thermal noise. *ME-ICA Component Classification* involved separating BOLD from non-BOLD components by comparing TE-dependence and TE-independence model fits of spatial ICA components to classify each component as either ΔR_2^* or ΔS_0 weighted.

Results *P-PCA Dimensionality Estimation* of high-pass filtered data failed to produce convergent ICA for any dataset (Table 1; median 83% variance explained). P-PCA of unfiltered data yielded convergent ICA for 3 subjects, but with only 3-17 components total (due to a substantial drift component). *ME-PCA Dimensionality Estimation* yielded convergent FastICA for unfiltered resting state data from all subject datasets (Table 2; median 368 components and 93% dataset variance explained), based on automatic dimensionality estimates of 300-500. Video-watching scans (Table 3) had notably lower total dimensionality than respective rest scans (from the same session), indicating variability of data dimensionality with cognitive state. *ME-ICA BOLD Component Selection* The first group of 11 MESMS-fMRI resting state scans produced 42 to 110 BOLD components per subject (median 62) based on 10 minutes of acquisition (Table 3). ME-ICA rejected about 300 components per subject as non-BOLD. Video-watching data produced more BOLD components compared to rest, suggesting greater endogenous variability of BOLD signals from the video task. *ME-ICA Component Examples* include the default mode as well as an 'unconventional' caudate-medial thalamus component (Figure 1), with F-R_2* maps suggesting BOLD origins of both. In contrast, drift and multi-slice [physiologically related] artifacts do not show F-R_2* weighting despite explaining greater dataset variance, altogether justifying non-BOLD classification. Critically, the multi-slice artifact is shown to be clearly non-BOLD despite its physiological appearance, allowing unequivocal rejection.

Discussion FastICA non-convergence after P-PCA dimensionality reduction may be due to truncation producing Gaussian distributed signals, which FastICA cannot decompose. While shown for MESMS-fMRI, this limitation may affect single-echo SMS-fMRI as well. The stability of ME-ICA may lie in ME-PCA selecting low-variance but non-Gaussian signal components for FastICA. Possible dimensional variability related to cognitive state suggests that fixed dimensionality estimation would not have equal sensitivity across conditions. After decomposing data, ME-ICA removed SMS-fMRI artifacts on TE-dependence alone, suggesting that unforeseen SMS-fMRI artifacts may be handled likewise. This flexibility has already been demonstrated in removing complex motion and physiological artifacts from single-band ME-fMRI [3].

Conclusion ME-ICA enables robust analysis of MESMS-fMRI, likely with general applicability to data from various populations and experimental paradigms that can take advantage of high-speed fMRI.

Table 1 P-PCA Dimensionality Estimation (Gr oup 1)

Highpass	135	88	66	84	93	166	101	117	97	128	92
Unfiltered	N/A	127	126	3	9	17	125	153	125	122	88

Table 2 ME-PCA Dimensionality Estimation

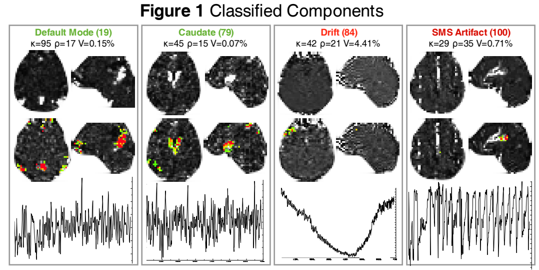
Group 1	503	359	378	323	385	379	368	289	376	366	302
Group 2	Rest	316	394	370		Video	313	246	265		

Table 3 Num. of Accepted BOLD Components

Group 1	110	42	57	64	100	81	58	62	53	51	71
Group 2	Rest	55	63	65		Video	75	63	82		

Table 1. Dimensionality estimation from P-PCA; **Table 2.** from ME-PCA. **Table 3.** Number of accepted ME-ICA BOLD components. Convergence: failed, error, pass. **Figure 1.** Component maps with κ, ρ, and component variance explained. Classification: BOLD, non-BOLD Intensity (above), overlaid with p<0.05 F-R_2* map (below), and time course.

Figure 1 Classified Components



References [1] Setsompop et al, MRM 2012. [2] Smith et al, Neuroimage, 2013. [3] Kundu et al, PNAS, 2013. [4] Wong, ISMRM 2012, 2209. [5] Olafsson et al, ISMRM 2013, 3318. [6] Beckmann, IEEE Trans. Med. 2004.