Bayesian shrinkage as an alternative to spatial smoothing for multi-echo BOLD fMRI

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Target Audience: Investigators using (or considering using) multi-echo acquisitions for functional MRI or other applications.

Purpose: Spatial smoothing is the most popular way to enhance sensitivity in fMRI analysis. However, this improvement is achieved at a cost of coarsened spatial resolution and reduced specificity, which may be unwanted in fine resolution studies or single patient studies [1,2]. Multi-echo acquisitions can improve specificity in fMRI by allowing analysis of effective transverse relaxation rate via least-squares (LS) fitting to each voxel's echo decay [3]. Bayesian shrinkage is an approach in which the parallel simultaneous estimation of many similar parameters is improved by "borrowing strength" from parallel measurements [4,5]. Here, we "shrink over grey matter" by applying Bayesian shrinkage to estimation of the effective transverse relaxation rate from echo decays in grey matter voxels. A previous study demonstrated that shrinkage improved sensitivity of *resting-state* multi-echo BOLD fMRI [6]. The purpose of this study was to assess application of shrinkage to *task based* multi-echo BOLD fMRI. Results show that shrinkage increases fMRI sensitivity (with respect to LS fitting) without the "blurring" caused by spatial smoothing.

Methods: Acquisition: Six healthy adults gave informed consent to participate in IRB-approved research. Data were acquired at 3 T using multi-echo BOLD fMRI. Acquisitions used echo times of 10, 30, 50, and 70 ms, a SENSE acceleration factor of 3.0, TR of 2.5 s; 88 volumes were acquired in each of two runs. The acquired/reconstructed voxel size was 3.0x3.0 mm^2 / 2.5x2.5 mm^2 with a slice thickness of 4 mm plus a 0.5 mm gap using 31 slices. An MP-RAGE image was acquired at isotropic 1 mm resolution. Stimulus: Visual stimulus used 7.5 Hz flashing checkerboard, with five cycles of 10 s on and 10 s off. Initial analysis: Standard preprocessing, including slice-timing correction, motion correction and normalization to MNI template, was performed using SPM8 [7]. The effective transverse relaxation rate, R_2^*, was computed for each voxel of each volume using least squares (LS) fitting to the echo-time decay. Shrinkage: The Bayesian shrinkage estimator was applied over all voxels of each tissue type at each time point. For each voxel, the adjusted R_2^* was $R_2^{*shrink} = \overline{R_2^*} + (1-\lambda)\times(R_2^* - \overline{R_2^*})$. The shrinkage factor λ is given by $\lambda = (n-3)\sigma^2 / \mathrm{sum}(R_2^* - \overline{R_2^*})^2$, where σ^2 is the temporal variance in R_2^* during baseline, and $\overline{R_2^*}$ denotes the spatial mean within the tissue type. Statistics: Visual activation was estimated at the single-subject level using a general linear model. The P value was threshold using family wise error correction. For each subject, the spatial extent of activation determined from the "LS" fitted R_2^* values was compared with that obtained using R_2^* values following empirical Bayes ("EB") shrinkage, and also with that obtained following modest spatial smoothing ("SM") using a Gaussian kernel with full width at half max (FWHM) 5mm. Reproducibility was assessed by eta-squared (η^2) score; contrast to noise ratio (CNR) was quantified by percentage BOLD signal change (β_1/β_0, where β_1, β_0 are coefficients of general linear model) divided by percentage BOLD fluctuation (temporal STD / temporal mean) during baseline.

Results and Discussion: Table 1 shows that shrinkage increased the spatial extent (number of significant voxels) of activation for each subject and each run (p<0.05 paired t-test). Shrinkage also improved reproducibility (p=0.04). The shrinkage factor λ was on the order of of 10^{-3} for every dynamic R_2^* voxel, suggesting that changes in R_2^* due to shrinkage were modest, and that spatial resolution was preserved (Figure 1, left & middle). Shrinkage did not significantly increase CNR, but the majority of subjects showed moderate improvement (Table 1). Table 2 shows that modest spatial smoothing outperformed shrinkage. However, spatial smoothing reduced effective spatial resolution as shown by the "blurring" evident in Figure 1 (right).

Sub. ID	Number of voxels of activation (FWE p=0.05)				Reproducibility score (η^2)		CNR			
	Run1		Run2		Run1 VS Run2		Run1		Run2	
	LS	EB	LS	EB	LS	EB	LS	EB	LS	EB
1	1375	3391	1307	3592	0.846	0.887	1.581	1.636	1.568	1.642
2	2009	2362	3214	4031	0.772	0.782	1.512	1.524	1.994	1.998
3	2534	3971	3689	5617	0.763	0.804	1.763	1.769	1.895	1.921
4	1224	1288	1404	1474	0.763	0.767	1.857	1.858	1.499	1.506
5	1882	1954	1488	1532	0.801	0.803	1.486	1.484	1.480	1.478
6	3096	4423	3538	5309	0.831	0.854	1.828	1.842	1.822	1.780
Mean	2020	2898	2440	3593	0.796	0.816	1.671	1.686	1.710	1.721
Std	706	1224	1151	1787	0.0361	0.0455	0.165	0.161	0.221	0.215
P	0.048		0.034		0.039		0.15		0.50	

Table 2. Group-level visual activation determined using R_2^* values from: **EB**: Empirical Bayesian shrinkage; **SM**: Spatial smoothing with 5 mm FWHM.

	Number of voxels of activation (FWE p=0.05)		Eta score (η^2)	CNR	
	Run1	Run2	Run1 VS Run2	Run1	Run2
EB	2898±1224	3593±1787	0.816±0.0455	1.686±0.161	1.721±0.215
SM	5277±1702	5785±1917	0.873±0.0344	1.721±0.207	1.769±0.238
P value	0.024	0.011	0.001	0.221	0.025

Table 1. Subject-level visual activation determined using R_2^* values from: **LS**: Least square (conventional) fitting; **EB**: Empirical Bayesian shrinkage.

Conclusion: Bayesian shrinkage may serve as an alternative to spatial smoothing for multi-echo BOLD fMRI, improving subject-level sensitivity at no cost to spatial resolution and specificity.

References: **1.** Speck O and Turner R. Der Radiologe 53(5):415, 2013. **2.** Chen L. et al., Neuroimage 29(10):1330 2011. **3.** Kundu P et al., Proc. Natl. Acad. Sci. 40:16187, 2013. **4.** Stein, Proc. 3rd Berkeley Symp. Math. Statist. Prob. 1:197, 1956. **5.** James & Stein, Proc. 4th Berkeley Symp. Math. Statist. Prob. 1:361, 1961. **6.** Xu F Proc. ISMRM 2013. **7.** The Wellcome Trust Centre for Neuroimaging UCL, London, UK.

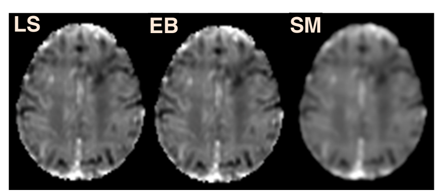

Figure 1. Example maps of R_2^* from: **LS:** Least squares (conventional fitting to echo decay); **EB:** Empirical Bayesian shrinkage; **SM:** Spatial smoothing.