A novel multi-echo fMRI weighting strategy using principal component analysis for BOLD contrast sensitivity enhancement

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Introduction: In functional magnetic resonance imaging (fMRI), acquisition parameters must balance the tradeoffs between spatial coverage and resolution, temporal resolution, and signal contrast. Blood oxygenation level dependent (BOLD) fMRI studies commonly employ a 2D multi-slice T2*-weighted echo-planar imaging (EPI) acquisition to capture changes in T2* decay due to BOLD signal fluctuation, with a single K-space traversal per slice, per radiofrequency excitation. Multi-echo imaging techniques extend this by acquiring images at various echo times (TEs) during the same excitation, sampling the T2* decay curve in more detail for each voxel and each repetition time (TR). Early functional spectroscopy experiments demonstrated contrast-to-noise ratio (CNR) benefits of multi-echo datasets [1]. Further investigation of multi-echo fMRI strategies has led to development of various weighting schemes to combine echoes for optimal BOLD contrast sensitivity [2,3]. More recently, a prototype multi-echo, coarse voxel (MECV) pulse sequence has been developed [4] and demonstrated in real-time neurofeedback experiments using existing weighting techniques [5]. Here, a novel method is presented for weighting multi-echo fMRI data using principal component analysis (PCA), validated by MECV-fMRI of a hand motor task.

Theory: An MECV data set from a single voxel consists of an n x m matrix $\boldsymbol{X}$ with n repetitions (TRs) and m echoes (TEs). Each row is a T2* decay curve at a given TR, whereas each column is a BOLD time-series at a given TE. To produce a single n x 1 time-series vector $\boldsymbol{v}$ per voxel, as in traditional fMRI datasets, requires a weighted sum of the multi-echo data along the echo dimension using a m x 1 weighting vector $\boldsymbol{w}$ [Equation 1]. The naive choice for $\boldsymbol{w}$ is the unity vector, which assigns equal weighting to all echoes (*Simple Weighting*). Posse et al. [2] chose $\boldsymbol{w}$ based on the expected BOLD contrast contribution from each echo [Equation 2], with T2* chosen from the literature (*T2* Weighting*). Poser et al. [3] chose $\boldsymbol{w}$ by estimating the contrast contribution of each echo from a separate resting state dataset (*CNR Weighting*). By determining the signal-to-noise ratio (SNR) of each echo, appropriate CNR weights were calculated [Equation 3].
Alternatively, $\boldsymbol{v}^T$ can be re-interpreted as a dimensionality reduction along the echo dimensions of $\boldsymbol{X}$, where the echoes are projected onto a single dimensional subspace defined by the basis vector $\boldsymbol{w}^T$. Principal component analysis (PCA) is a multivariate method of defining an orthogonal basis set based on directions of maximum variance, and has been used widely in neuroimaging analyses. Here, PCA is used to find the direction of maximum BOLD variance in the vector space defined by the echoes. The weighting vector $\boldsymbol{w}$ in this case can be defined as the PC that best corresponds to BOLD variance, giving most weight to those echoes that contribute most to BOLD fluctuation, as defined by the data itself. The *PCA Weighting* algorithm has 5 steps:

- **i.** Linearly detrend and mean centre the columns of $\boldsymbol{X}$ and find the covariance matrix, $\sum = \mathrm{Cov}(\boldsymbol{X})$;
- **ii.** Compute the eigen-decomposition of $\sum$, such that $\sum = \boldsymbol{PDP}^{-1}$, where the columns of $\boldsymbol{P}$ are the PCs;
- **iii.** Form a matrix $\boldsymbol{W}$ of all linear combinations of the 3 PCs with the largest eigenvalues [Equation 4] (typically > 95% of total signal variance is captured within PCs $\boldsymbol{p}_1$, $\boldsymbol{p}_2$, $\boldsymbol{p}_3$);
- **iv.** Calculate a model BOLD contrast vector based on a least-squares T2* estimate, and compute an r^2 correlation coefficient for each vector in $\boldsymbol{W}$;
- **v.** Let $\boldsymbol{w}$ be the vector in $\boldsymbol{W}$ that maximizes r^2, identifying the vector with maximal BOLD contrast.

$$\boldsymbol{v}=\boldsymbol{X}\boldsymbol{w} \qquad (1)$$

$$\boldsymbol{w}(TE) \propto TE \cdot e^{-TE/T2^*} \qquad (2)$$

$$\boldsymbol{w}(TE) \propto TE \cdot SNR(TE) \qquad (3)$$

$$\boldsymbol{W} = \begin{pmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ \vdots & \vdots & \vdots \end{pmatrix} \cdot \begin{pmatrix} 1 & 0 & 0 & 1 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 & 1 & 1 & 1 \\ 0 & 0 & 1 & 1 & 0 & 1 & 1 \end{pmatrix} \qquad (4)$$

Methods: Data were acquired with the MECV pulse sequence [4] at 1.5 T on a GE Signa MRI system (16 channel HDX, GE Healthcare, Milwaukee, USA) using a quadrature birdcage head coil, 256 echoes with 1ms echo spacing at a TR=1000ms and 32 coarse voxels (5x20x20 mm^3) along a linear column across both left and right primary sensorimotor cortices (SMC). 4 right handed participants (1 female) were scanned with a total of 20 datasets in a 200s, 20s off/20s on visually cued hand clenching experiment (8 right hand, 8 left hand). Four datasets were excluded from the analysis due to poor data quality (single echo equivalent CNR < 0.40). No additional resting state scans were performed, but resting state data were estimated through retrospective concatenation of rest block periods from the experimental data. Single voxel regions of interest were defined over the left or right SMC by inspection using a correlation analysis of simply weighted datasets with the boxcar task waveform to identify peak correlation coefficients. This analysis compares the resultant CNR of the *Simple*, *T2** and *CNR* weighted methods with the *PCA* method developed here, relative to the CNR obtained from a single echo acquired at TE=70ms. The CNR, $\Delta S/\sigma$, is defined as the ratio of task-related signal change ΔS with the standard deviation of the temporal noise fluctuations σ.

Discussion: Figure 1 compares the 4 methods for choosing $\boldsymbol{w}$ in a representative dataset. Aside from the uniform simple weighting vector, the $\boldsymbol{w}$ vectors obtained by the *T2**, *CNR* and *PCA* methods are very similar. The "noisy" appearance of the *CNR* and *PCA* weights and their deviation from the model curves indicate influences of non-monoexponential decay and spurious signal fluctuation. Noise suppression features are also evident from the reduced weighting of early echoes. Figure 2 shows mean CNR gains across the various weighting schemes. These results show that *PCA Weighting* and *CNR Weighting* methods perform equally well and achieve the highest relative CNR, *T2* Weighting* provides intermediate performance, and *Simple Weighting* provides the lowest CNR gain. The advantage of *PCA Weighting* is that it is data-driven and does not strongly rely on models or additional data (some model input is currently still required to guide the $\boldsymbol{w}$ selection process for identifying BOLD signal variance, and alternative approaches are being investigated). Also, the separate rest scan requirements for the *CNR Weighting* method can potentially suffer from cumulative effects of motion and scan-to-scan variability over an experimental session compared to *PCA* weights, which are derived from each dataset directly. The *PCA Weighting* algorithm is computationally inexpensive for multi-echo dataset sizes, and can potentially be used in the future for real-time data reconstruction. Additionally, more sophisticated multivariate classification methods, such as support vector machines can be investigated for further optimization of $\boldsymbol{w}$.

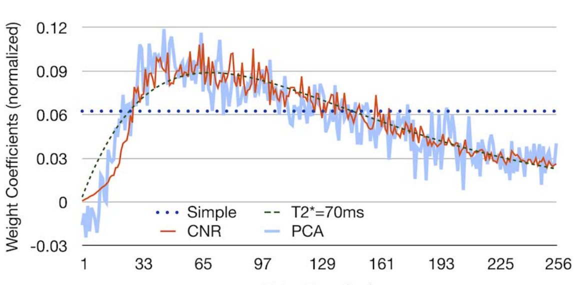

Figure 1 -Normalized $\boldsymbol{w}$ vectors calculated by each method for a representative dataset

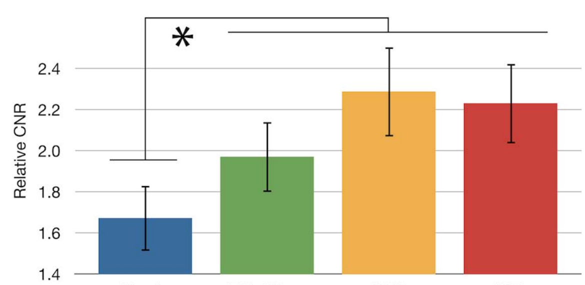

Figure 2 - Mean relative CNR gains over all (N=16) datasets. Error bars display standard error of the mean, * indicates significance (p<0.05, bonferroni corrected)

References

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