HHS Public Access

Author manuscript

Proc IEEE Int Symp Biomed Imaging. Author manuscript; available in PMC 2017 September 27.

Published in final edited form as:

Proc IEEE Int Symp Biomed Imaging. 2015 April ; 2015: 1372–1375. doi:10.1109/ISBI.2015.7164131.

OPTIMAL SIGNAL RECOVERY FROM INTERLEAVED FMRI DATA

David Parker[1] **[Member, IEEE]**, **Raphael T. Gerraty**[2], and **Qolamreza R. Razlighi**[1,3] **[Senior Member, IEEE]**

[1]Biomedical Engineering Department, Columbia University, NYC

[2]Psychology Department, Columbia University, NYC

[3]Neurology Department, Columbia University, NYC

Abstract

Due to the nature of fMRI acquisition protocols, slices in the plane of acquisition are not acquired simultaneously or sequentially, and therefore are temporally misaligned with each other. Slice timing correction (STC) is a critical preprocessing step that corrects for this misalignment. STC is applied in all major software packages. To date, little effort has gone towards assessing the optimal method of STC. In this study, we examine the most popular methods of STC, and propose a new optimal method based on the fundamental properties of sampling theory. We evaluate this method using 20 simulated fMRI data and demonstrate the utility of STC in general as well as the superiority of the proposed method in comparison to existing ones.

Index Terms

Slice timing correction; Interleaved acquisition; Interpolation; fMRI; EPI

1. INTRODUCTION

Typically, fMRI data are acquired slice by slice through a fast acquisition technique called echo planar imaging (EPI) in which each slice's acquisition takes about 30–100 ms and follows a single RF pulse excitation [1]. By rapidly acquiring and stacking 2D slice images; a 3D brain volume image can be constructed anywhere between fractions of a second or several seconds, depending on the number of slices and the slice thickness. Such sequential acquisition results in an accumulating offset delay between the first slice and the remaining ones. Furthermore, to eliminate or attenuate leakages of a single slice RF pulse excitation to adjacent slices, interleaved slice acquisition techniques are performed regularly in fMRI scanners. In interleave slice acquisition adjacent slices are not acquired sequentially, a process which imposes irregular offset delay to the sequential slices.

Ideally, we would like the entire brain volume to be captured at one instance. While sequential acquisition of slices is tolerable for many aspects of fMRI analysis, non-contiguous temporal sampling of spatially adjacent voxels in interleaved acquisition becomes problematic for any process that requires voxels expanding over more than one slice. Spatial smoothing with 3D kernel is one such process that becomes problematic with interleaved acquisition of the data. Involuntary head motion during the scan is also

challenging to model and correct with interleaved data. To resolve this problem, slice timing correction (STC) is proposed and widely used in the field. STC corrects a given slice's temporal offset by shifting and interpolating the signal in the reverse direction of the imposed offset delay. The benefits of STC have been shown in numerous studies[2] [4]. However, all the existing methods are interpolation based meaning that they estimate the signal values between two sampling points. Therefore they are all considered to be essentially sub-optimal methods.

In this study, we aim to completely reconstruct the signal from its sampled version with no Interpolation. According to Shannon-Nyquist sampling theorem such reconstructed signal will be independent from the offsets of sampling and thus eventually eliminates the need for STC altogether. Section II describes the existing methods from signal processing point of view, and section III describes in detail the proposed method. Section IV examines results comparing statistics from our STC method to those present in popular software packages, and section V offers our concluding observations and remarks.

2. EXISTING METHODS OF STC

Almost all the existing slice timing correction methods are based on interpolation techniques that estimate the signal value between sample points. If $f(s,t)$ is the underlying true fMRI signal at location $s(s=(x,y,z)$ in Cartesian coordinate system) and time instance t, then sampled version of the true signal will be

$$F[s,n]=f(s,nT_s+\varphi(z)) \quad \varphi(z)=mod_\gamma[\delta z] \tag{1}$$

where T_s is the sampling period (TR), z is the slice number, γ is the total number of slices, δ is the interleaved parameters, and $\varphi(z)$ is the offset delay imposed for each slice by interleaved acquisition. The slice-timing problem arises since the offset $\varphi(z)$ changes as a function of z. Fig. 1 shows the effect of such dependency in the sample's offset delay for five adjacent voxels with different z coordinate. The goal of STC is to make these five sampled signals as close as possible to each other. conventional interpolation-based techniques attempt to operate on the discrete signals (Fig. 1b) and estimate the signal value between the sample points. Mathematically this can be represented by the convolution of the sampled signal, $F[s,k]$ with an interpolation kernel h:

$$\hat{f}[s,n]=\sum_{k=0}^{N-1} F[s,k]*h(nT_s-k+\varphi(z)) \tag{2}$$

where $\hat{f}$ is the shifted/interpolated signal. Linear, cubic *spline*, *sinc*, or a windowed *sinc* functions are commonly used in the literature for the purpose of STC. Fig. 2 shows the time and frequency domain of these interpolation kernels. It is clear from the frequency response that linear and cubic spline interpolation kernels are suboptimal for fMRI data, since the

BOLD signal is generally believed to contain information in the frequency range [0.01 0.2] Hz. Furthermore, two of the dominant fMRI data analysis software packages use different version of Sinc interpolation (SPM: Sinc, FSL: Hanning Window Sinc) for their implemented STC module. Because of this, we will focus on Sinc interpolation. Sinc interpolation can be described as convolution with the following kernel,

$$h_s(t)=\frac{\sin(\pi t/T_s)}{\pi t/T_s} \quad (3)$$

Fig. 2 shows the time and frequency domain of this kernel. It should be emphasized that ripples in the pass band of the Sinc kernel are due to truncation of the signal in the time domain. To attenuate the rippling artifact, a smooth window function such as Hanning has been proposed by FSL to be applied to the Sinc kernel.

$$w_{hann}(n)=0.5\left(1-\cos\left(\frac{2\pi nT_s}{T_sN-1}\right)\right) \quad (4)$$

where N is the length of the sequence, By examining the frequency domain of this kernel we can see that ripples are removed at the expense of BOLD signal cut-off. It is clear that the accuracy of the final result depends highly on the shape of $H(\omega)$. The more $H(\omega)$ preserves the original shape of true fMRI signal, the more accurate the result will be after interpolation.

3. OPTIMAL SIGNAL RECOVERY

In the previous section we have formulated the existing interpolation-based STC techniques as filtering of the sampled fMRI signal with different kernels with irregular and slice dependent offset delay $\varphi(z)$. As can be seen in Fig. 2b, such irregular offset delay has no effect on the magnitude of the frequency domain. In other words, no matter what $\varphi(z)$ is, the frequency domain of the interpolation's kernel will be the same. In fact, from the signal theory standpoint, since all slices will be acquired with the same sampling rate, as long as the sampling rate is twice the maximum bandwidth of the underlying BOLD signal of interest, it can be optimally recovered (Shannon-Nyquist sampling theory). This means all sampled signals in Fig. 1b for all the slices can be reconstructed to give the signals in Fig. 1a, no matter what is the offset of the sampling.

If we assume that the canonical double gamma HRF curve, commonly used in linear modeling of hemodynamic response, is realistically close to the shape of the real HRF, then spectral analysis of this curve reveals that the hemodynamic response function has 99.9% of its energy in the frequency range of [0, 0.21] Hz. For a typical fMRI sampled at 0.5 Hz (TR = 2), this is sufficient to reconstruct the signal completely according to the sampling theorem. By up-sampling/zero-padding the data to 20Hz and then low pass filtering with cut

off frequency of 0.21 Hz we aim to reconstruct the true signal which will no longer require STC.

One issue we encounter is that the limited length of the fMRI data prevents us from using an optimal or near optimal filter due to the lengthy initialization period. This resembles the problem discussed earlier for interpolation based techniques. In this study we addressed this issue with two different tactics. First, we used the non-causal structure of the fMRI time series to properly apply mirror padding to both ends of the time series to generate a contiguous circular time series to reduce the initialization period significantly. Furthermore, we used a Kaiser multiplicative windowing function to further attenuate the rippling of the impulse response function tails of the filter.

$$w_{kaiser}(n) = \begin{cases} \dfrac{I_0\left(\pi\alpha\sqrt{1-\left(\frac{2nT_s}{T_sN-1}-1\right)^2}\right)}{I_0(\pi\alpha)} & 0 \le n \le N-1 \\ 0 & otherwise \end{cases} \quad (5)$$

where I_0 is the zero order modified *Bessel* function of the first kind, and α is an arbitrary shaping coefficient. This kernel in plotted in Fig. 2 for the comparison purpose. It is clear from Fig. 2b that Kaiser window preserve the BOLD signal and remove the uninteresting signal variability more effectively than the Hanning window. It should be emphasized that we also reduced the low-pass cut-off frequency to 0.21 Hz. Mathematically, the method we propose is a tradeoff between the two existing methods associated with Sinc interpolation. To achieve a smoother, steeper cutoff band, and there for a cleaner signal, the order of the filter can be increased. This is achieved by using an interpolation kernel that samples the continuous Sinc function over a larger time period. However, higher order filters have a longer initialization period. Because of this, increasing the filter order arbitrarily would require excessive padding to remove any initialization artifacts, which can greatly increase computation time. Therefor, it is desirable to truncate the Sinc signal so it contains a low number of time points. This truncation results in discontinuities at the end of the Sinc function that would add rippling to the signal if not corrected for. In our method, the filter order is raised modestly, by sampling more of the continuous Sinc function, while a Kaiser window is added to help smooth the ends of the signal and remove any discontinuities. This can be seen in the inset of Fig. 2, where our Kaiser windowed Sinc function tapers off gently, while the non-windowed Sinc ends abruptly. From the new upsampled function, the signal can be resampled at the appropriate offset with no need for interpolation.

3. EXPERIMENTAL EVALUATION

In this study we have synthesized 20 fMRI scans to evaluate the effectiveness of the proposed method. We generated 10 minutes of scanning, with an in-plane acquisition matrix of 112×112, and 37 slices. The voxel size was set to 2×2×3 mm^3 and the TR equal to 2 seconds. In total, neuronal stimuli consisting of sequences of 20 pulses with jittered onsets (at least 10 sec apart) and randomly-generated durations (5 to 30 sec) were created for each ROI. Then the neuronal stimulus for each voxel was convolved with the canonical HRF

included in SPM to generate the hemodynamic response. Both HRF and neuronal stimuli were sampled at high frequency, f_s=20 Hz. The 20 Hz sampling rate was chosen to be able to simulate the interleaved slice-timing acquisition. Null data (random noise) were assigned to regions outside the ROIs. To simulate cardiac and respiratory variations in the fMRI signal, a simplified approach was taken, using a single sinusoid at f_c=1.005 Hz for cardiac and another sinusoid at f_r=0.25 Hz for respiratory noise. These sources of variability were added to the signal. The magnitude of the cardiac signal is modulated with the inverse of the distance of the voxel from the nearest artery. Three different levels (0, 20, 40 percent) of white noise were also added to the signal to simulate thermal noise. Then a real subject's fMRI scan was temporally averaged to obtain the mean value at each voxel, which was used to shift the mean of the hemodynamic signal and to scale the standard deviation of the signal to 1% of the mean value comparable to a robust signal in the visual cortex. We used the same mean image to control the significant difference in the morphology of the brain which eliminates the need for second level analysis to compare the results.

To have the most realistic simulation of motion, interleaved slice acquisition, and their interaction, we have simultaneously simulated the motion and slice acquisition. We have up-sampled three real subjects' motion parameters to 20 Hz using spline interpolation. By applying the up-sampled parameters to the volume at the initial point we can specify the exact position of the volume relative to the two sampling points (TR). Slices are then sampled from the appropriate 20 Hz volume, corresponding to the offset of any given slice.

Our STC method was executed in the following steps. First, the fMRI signal was upsampled from 0.5 Hz to 20Hz by zero padding between each data point. Then, a 908 order Kaiser windowed Sinc FIR filter was created with a cutoff frequency of 0.21Hz, transition width 0.08Hz, and stop gain of −60dB. To help accommodate the large order of the filter and eliminate edge effects and ringing, half of the upsampled signal was mirrored on both ends to double the total length of the signal.

Filtering was then preformed on the mirrored, upsampled data. The output of this process is a 20Hz reconstruction of the original BOLD signal. The signal was then trimmed to its original duration, and resampled to 0.5Hz at any desired time shift. Because each slice has the same offset over all x and y, this process can be parallelized so that each slice is operated on independently, and reincorporated into the final image. All computations were carried out using python.

In addition to our pipeline, we also ran the standard SPM and FSL slice timing correction methods for comparison. To quantify the quality of each pipeline, we ran a standard first level GLM on the processed data using a default FSL statistical analysis with no additional slice timing, image filtering, or prewhitening. This analysis was also run on the original uncorrected images for comparison purposes. 12 regressors corresponding to the known, noiseless, underlying BOLD signal in 6 pairs of left/right brain regions (Superior Frontal, Supramarginal, Insula, Middle Temporal, Lateral Occipital, and Post Central) of varying size and geometry were examined. Resulting z scores were compared within the given ROI. Higher z scores indicate that the signal more closely resembles the true underlying bold.

4. RESULTS AND DISCUSSIONS

Using standard preprocessing and GLM analysis of FSL we analyzed the 20 simulated data. We examined each of the brain regions listed above. The z value of the voxel wise z-test in the group level analysis of these 20 simulated data is used as the measure of effectiveness of the STC methods in this study. Fig. 3 summarizes the results using violin plots. For each level of motion and noise we compare the proposed optimal recovery of the signal with STC methods used in FSL and SPM. As predicted, optimal recovery outperforms FSL and SPM STC techniques for when there is no motion or noise. All STC methods had significantly higher z statistics than the uncorrected data. In the no noise condition, our method proved significantly higher than both SPM and FSL. Adding noise to the simulation reduced the magnitude of the z statistic for all methods, however even in the lowest SNR condition, where 60% of the signal's energy is from noise, all methods still scored significantly better than uncorrected data, and our method maintained significantly higher z scores than both SPM and FSL. A typical distribution of z scores for a medium noise subject can be seen in Fig. 3.

Motion proved to be the most harmful source of signal contamination in our simulations. At low motion, all methods still preformed significantly better than uncorrected data, while our method remained significantly higher than SPM and FSL. At medium motion, our method no longer preformed significantly better than the others. The overall benefits of slice timing correction are greatly diminished, but z scores in STC images still remained significantly higher than in uncorrected images. In high motion, there was no significant difference between z scores in STC and uncorrected images. This is likely due to the complex and nonlinear interaction between motion and slice acquisition.

These results are interesting in that when there is significant motion artifact, it is challenging to assess the effectiveness of the STC methods. It should be emphasized that these results were obtained while controlling for differences in baseline fMRI activity and brain morphology, both of which have stronger a deteriorating effect on the results than the interleaved slice timing itself. Taken together, these might explain why evaluating STC methods under real data is extremely difficult if not impossible.

6. CONCLUSION

Based on a signal theory concept of sampling and reconstruction we have proposed and developed an optimal signal recovery technique that eliminates the need for slice timing correction. This optimal method has the disadvantage of requiring long initialization which we addressed by mirror padding and thus introducing contiguous circularity to the signals. We have generated a set of 20 simulated data with different level of noise and motion and shown that our method resulted in significantly higher z scores over all noise conditions, as well as low motion conditions. For medium and high motion conditions, our method generated z scores equivalent to those generated by other traditional STC techniques. In the future, we hope to show similar results on real data sets, though comparing methods aimed at signal recovery is becomes difficult without knowledge of the true and uncontaminated underlying BOLD signal.

Acknowledgments

This work was supported in part by NIA K01 AG044467 and R01 AG026158 grants.

References

1. Stehling MK, Turner R, Mansfield P. Echo-planar imaging: magnetic resonance imaging in a fraction of a second. Science. Oct; 1991 254(5028):43–50. [PubMed: 1925560]
2. Henson R, Buechel C, Josephs O, Friston K. The slice-timing problem in event-related fMRI. NeuroImage. 1999; 9:125.
3. Sladky R, Friston KJ, Tröstl J, Cunnington R, Moser E, Windischberger C. Slice-timing effects and their correction in functional MRI. NeuroImage. Sep; 2011 58(2):588–594. [PubMed: 21757015]
4. Vogt, K., Ibinson, J., Small, R., Schmalbrock, P. Slice-timing correction affects functional MRI noise, model fit, activation maps, and physiologic noise correction. Int Soc Magn Reson Med; Proceedings 17th Scientific Meeting; 2009. p. 3679

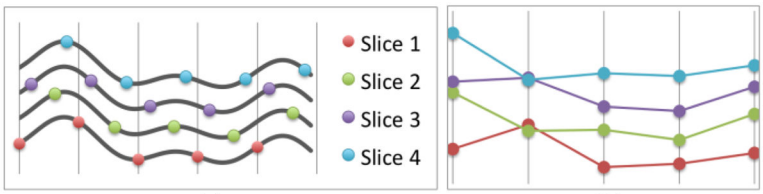

Fig. 1.

(a) Five adjacent slices acquired with interleaved acquisition all sample the same underlying bold signal. (b) Without correction, reconstruction yields five different signals, despite being having the same underlying shape.

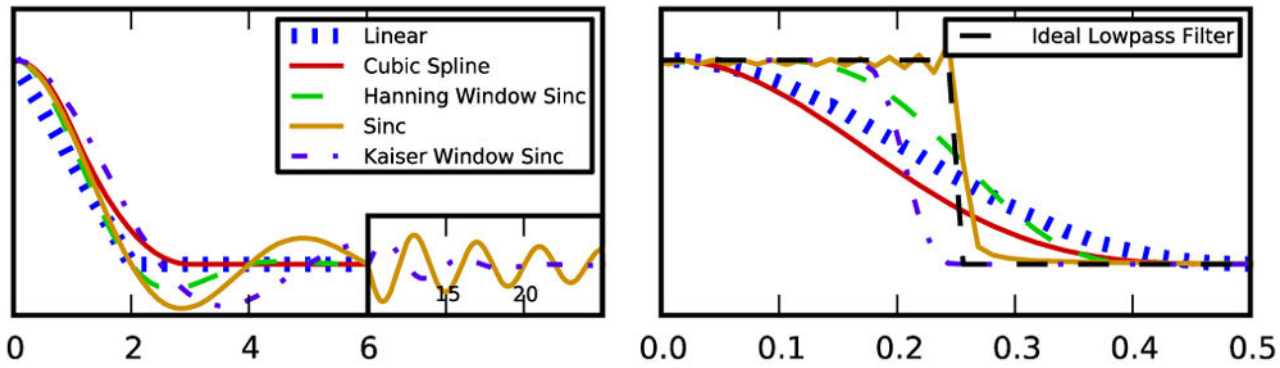

Fig. 2.

Examples of time domain interpolants (convolution kernels) for linear, cubic, sinc, hanning sinc, and kaiser sinc interpolation (left), and their respective frequency domains (right). It is easy to see from this the impact various interpolants will have on a signals frequency spectrum.

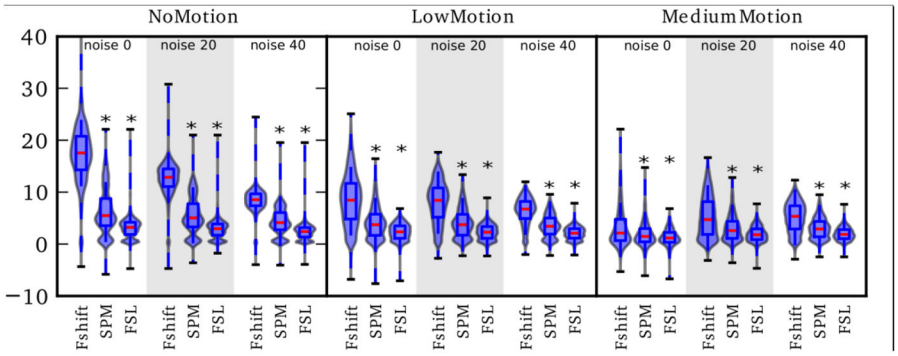

Fig. 3.

Voxel-wise Z statistic difference between STC data and uncorrected data. Higher values indicate that a STC method had higher z scores than data that was analyzed with no STC. Violin plots include all voxels from all six ROI's. Stars indicate that these z differences are also significantly different from our method (Fshift) after Bonferroni correction.