Steady-state Functional MRI Using Spoiled Small-tip Fast Recovery (STFR) Imaging

Hao Sun[1], Jeffrey A. Fessler[1], Douglas C. Noll[2], and Jon-Fredrik Nielsen[2]

[1]*Electrical Engineering and Computer Science, the University of Michigan, Ann Arbor, MI, United States,* [2]*Biomedical Engineering, the University of Michigan, Ann Arbor, MI, United States*

Introduction: Most functional brain MR imaging uses T2*-weighted gradient-echo sequences with single-shot readout (BOLD fMRI), providing high activation contrast but suffering from off-resonance-induced image artifacts (signal drop, distortions or blurring). Steady-state fMRI based on balanced steady-state free precession (bSSFP) uses segmented readouts and can produce excellent image quality, but is susceptible to dark "banding" artifacts, and generally has lower functional contrast than BOLD [1]. Small-tip fast recovery (STFR) imaging is a recently proposed steady-state imaging sequence that has similar signal level to bSSFP, but with reduced signal variations (banding) due to resonance offsets [2,3]. STFR relies on a tailored "tip-up," or "fast recovery," RF pulse to align the spins with the longitudinal axis after each data readout segment (Fig. 1(a)). The design of the tip-up pulse uses a separate off-resonance (B0) map. Using Monte Carlo Bloch simulation and preliminary *in vivo* experiments, it has been demonstrated that STFR can produce detectable fMRI signal [4]. Here we investigate the spoiled STFR fMRI sequence in more detail by: (1) performing a quantitative comparison between simulation and *in vivo* experiments, and (2) estimating test–retest reliability of STFR (and BOLD) functional maps following [5, 6].

Theory: The transverse magnetization for an isochromat of STFR is [1]:

$$M_T = M_0 \sin\alpha \frac{e^{-T_g/T_1}\left(1-e^{-T_f/T_1}\right)\cos\beta + \left(1-e^{-T_g/T_1}\right)}{1-e^{-T_g/T_1}\ e^{-T_f/T_2}\ \sin\alpha\sin\beta\cos\left(\theta_f-\phi\right) - e^{-T_g/T_1}\ e^{-T_f/T_1}\ \cos\alpha\cos\beta} \qquad (1)$$

Where T_f is the free procession time, T_g is the duration of the gradient crusher, θ_f is the accumulated phase during the free procession, ϕ is the phase of the tip-up pulse, and α, β are the flip angle of tip-down and tip-up pulse, respectively. Figure 1 (b) shows Eq. (1) as a function of the phase mismatch between the phase of tip-up pulse and free procession accumulated phase ($\theta_f - \phi$). The total signal from a voxel is the weighted integral of the isochromat profile over $\theta_f - \phi$, within a voxel (illustrated in Fig. 1(b)). Note that the tip-up pulse phase ϕ is the same during both active and rest states, but the distribution of intra-voxel off-resonance introduced phase θ_f depends on the BOLD effect; therefore, this dependence can be used to detect the BOLD functional signal.

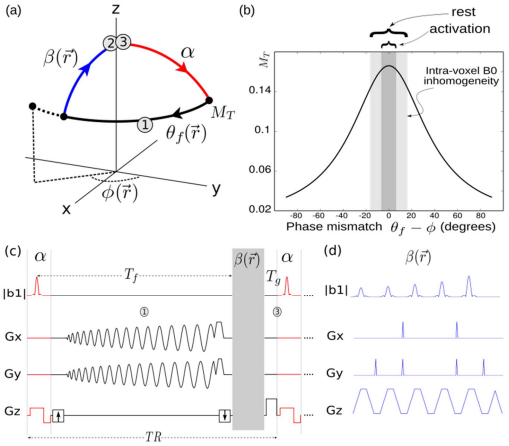

Figure 1: Small-tip fast recovery (STFR) imaging. (a) Steady-state spin path. The tip-up pulse (blue) is tailored to the mean free precession angle ($\theta_f(r) = \omega(r)T_f$) within each voxel, and there is in general a mismatch between the isochromat spin phase in that voxel and the tip-up phase. (b) Transverse magnetization profile vs. phase mismatch. The observed voxel signal is obtained by integrating the profile over the intra-voxel B0 distribution, which depends on the BOLD effect. (c) STFR pulse sequence diagram. (d) fast-kz (spoke) tailored pulse for the tip-up block.

Method: We performed Monte Carlo Bloch simulation as in [3], but with parameters matched to our *in vivo* experiments. We performed high-resolution fMRI experiments with bilateral finger-tapping on 5 healthy volunteers, using segmented stack-of-spirals imaging as shown in Fig. 1(c) (3 cm axial slab; 10 z partitions; 8 spiral kx-ky segments supporting 128x128 matrix size; FOV 24 cm; T_f 10 msec; flip angle for STFR/bSSFP/BOLD = 16°/32°/16°). We repeated the fMRI run 3-5 times for each subject, to quantitatively compare STFR and BOLD in terms of test-retest reliability [5, 6]. This analysis is based on calculating activation maps using multiple activation thresholds, and obtaining a maximum likelihood estimate (MLE) of sensitivity and false positive rate at each threshold. These rates are then plotted to form a receiver operating characteristic (ROC) curve for each subject.

Results: Figure 2 (a) shows the thresholded correlation map obtained with STFR, BOLD, and bSSFP in subject "A". Both STFR and BOLD show high correlation in the motor cortex areas. bSSFP imaging shows some activation in the motor cortex area, but also displays correlations in other regions. The time course (Fig. 2 (c)) shows that STFR has slightly smaller percent signal change than BOLD, but higher than bSSFP, which agrees well with simulation (Table 1). Figure 3 shows ROC curves for STFR and BOLD in 5 subjects, STFR shows good reliability in general, but slightly lower than conventional BOLD. In addition, our simulation results indicate that spin diffusion does not impact the functional contrast in STFR significantly (not shown).

Discussion and Conclusions: Monte Carlo Bloch simulations and *in vivo* experiments indicate that STFR is a sensitive and reasonably robust technique for detecting BOLD functional signal, and has the potential to become a high resolution 3D functional imaging modality that does not suffer from signal loss near air cavities. In the future, we plan to evaluate the feasibility of whole-brain STFR fMRI, which requires 3D tailored tip-up pulses. We expect the design of such 3D pulses to benefit greatly from parallel transmission systems.

[1] Zhong et al, MRM 2007; [2] Nielsen et al, MRM 2012; [3] Sun et al, MRM 2013; [4] Nielsen et al, ISMRM 2013; [5] Genovese et al, MRM 1997; [6] Noll et al, MRM 1997; [7] Forman et al, MRM 1995. *This work was supported by NIH Grants R21EB012674 and R01NS058576.*

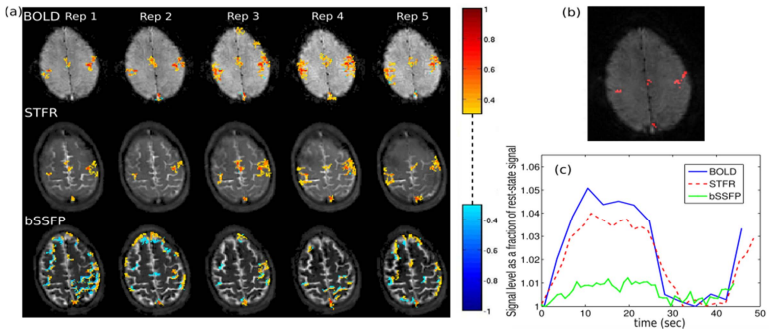

Figure 2: Repeated motor cortex imaging using STFR, BOLD and bSSFP in subject "A". (a) Activation maps with correlation threshold 0.3 and cluster size 10 [7]. All five scans demonstrate that STFR can produce similar activation maps as BOLD, which are well localized to the motor cortex area. (b) ROI used to calculate the mean time course for each sequence, obtained by selecting the pixels showing activations in at least 4 scans in both BOLD and STFR. (c) One cycle of the mean time course over the ROI (the rest state signal is normalized to be 1). STFR has slightly lower functional contrast than BOLD, but higher than bSSFP. Table 1 reports the calculated percent functional signal changes.

Table 1: Percent functional signal change

	BOLD	STFR	bSSFP
Simulation	5.2 %	3.6 %	0.8 %
Measurement	4.1 %	3.1 %	0.7 %

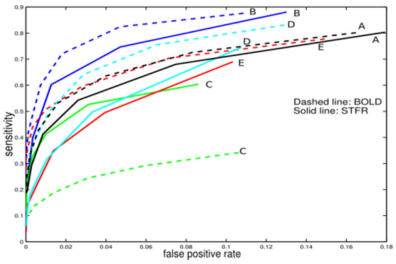

Figure 3: Test-retest reliability results for 5 different subjects, calculated using the method in [5, 6]. The ROC curves for STFR are generally slightly lower than BOLD, but still demonstrate that it is a reliable sequence for detecting functional activity. One BOLD curve is much lower than other curves, which is probably due to motion artifact observed in that data set.