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A comprehensive study of sensitivity in measuring oscillatory magnetic fields using rotary saturation pulse sequences

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ABSTRACT

Detecting the oscillatory currents with a specific frequency distribution may have the potential to make neuronal current MRI (ncMRI) come true. The phase shift or dephasing induced by both positive and negative episodes of oscillatory neuronal currents is likely to be canceled out over the echo time in typical BOLD-contrast fMRI experiments. Based on the contrast of rotary saturation, both of the recently developed spin-locked oscillatory excitation (SLOE) and stimulus-induced rotary saturation (SIRS) pulse sequences have been demonstrated to be able to detect weak oscillatory magnetic fields in phantoms with 3 T MR scanners. In this report, through Bloch equation simulation as well as water phantom and anesthetic rats experiments, we comprehensively evaluate and compare the sensitivities of these two methods (SLOE and SIRS) in detecting the oscillatory magnetic fields for both high (100 Hz) and low (10 Hz) oscillation frequencies, while using their respective optimal imaging parameters. In agreement with the theoretical predications, both the simulated and experimental results showed that the SLOE method features a much higher detection sensitivity of weak magnetic fields than that of the SIRS method. SLOE was able to detect applied oscillatory magnetic fields as low as 0.1 nT in a water phantom and 0.5 nT in rat brains and the deteriorated noise levels in rat data may account for the reduced sensitivity *in vivo*. These promising results form the foundation for direct detection of *in vivo* neuronal currents using MRI.

1. Introduction

Neuronal current MRI (ncMRI) is a promising technique aiming at directly imaging neuronal currents with both high spatial and temporal resolutions. However, the feasibility of ncMRI is still in debate as previous studies showed controversial results [1–8].

Most previous ncMRI experiments were based on the measurements of phase shift and/or magnitude reduction resulting from evoked neuronal currents using a T_2^*-weighted gradient-echo EPI pulse sequence (see a review by Bandettini et al. [9]). From electrophysiological data, it is noted that the human brain neuronal currents are generally exhibited as oscillatory waveforms with a moderate frequency distribution rather than direct currents. Considering the measured ncMRI signals as the integral of the phase shift or dephasing over the echo time (TE) in EPI data acquisitions, the detection sensitivity will suffer from cancelation over time since the direction of phase change can be either positive or negative depending on the sign of neuronal currents. As a result, using the traditional magnetic field susceptibility (T_2^*) contrast-based pulse sequences may not be the optimal approach for measuring the oscillatory neuronal currents.

To improve the sensitivity in detecting weak oscillatory magnetic fields, a method named as stimulus-induced rotary saturation (SIRS) had been proposed and developed in the past a few years [10,11]. In the SIRS method, a spin-lock prepared pulse is first applied prior to the conventional imaging sequence. During the spin-lock time (TSL), the magnetization is locked in the rotating frame by a spin-lock RF field (B_{SL}). The magnitude of spin-lock field is carefully tuned so that its Larmor frequency ($\omega_{SL} = \gamma B_{SL}$) matches the frequency of the oscillatory neuronal field (ω_N). As a consequence, an oscillatory magnetic field generated by neuronal currents will act as an RF pulse in the doubly rotating frame, flipping **M** away from the spin-lock direction by a small angle. This effect was described as "rotary saturation" by Redfield [12]. At the end of the spin-lock pulse, **M** is flipped back to the longitudinal direction, and the change of the longitudinal magnetization acts as contrast whereas the transverse magnetization is crushed out. Based on the spin-locked rotary saturation contrast, the SIRS was reported to detect oscillatory

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magnetic fields of about 1 nanotesla (nT) at a 3 T MR scanner in a dipole model water phantom [10]. Considering the fact that *in vivo* neuronal magnetic field caused by evoked activities was estimated to be in the range of sub-nT [13], the sensitivity achieved by SIRS may still be insufficient in detecting *in vivo* neuronal activities.

To further push the boundary of detection sensitivity, a spin-locked oscillatory excitation (SLOE) method has been developed and its ability in detecting sub-nT oscillatory magnetic fields has been demonstrated in a preliminary phantom study [14]. Unlike the SIRS method that uses the reduction of M_z as image contrast, the SLOE method directly detects the magnetization excited in the transverse plane (M_{xy}). In this way, SLOE achieves a theoretical detection sensitivity that is much higher than that of SIRS. To fully exploit the capability and to achieve the best use of the SLOE technique, a comprehensive and quantitative analysis as well as parameter optimization of the imaging sequences is needed. In addition, lower frequency oscillatory fields that are within the range of neuronal activities should be considered. Furthermore, the comparison of these approaches should be extended to the experiments using a well-controlled living animal model.

In this report, a comprehensive evaluation and comparison of the sensitivities of these two methods (SLOE and SIRS) in detecting the oscillatory magnetic fields is presented. The timing diagrams for both SLOE and SIRS pulse sequences are shown in Fig. 1, and an optimized spin-lock preparation module that is insensitive to B_0 and B_1 field imperfections was applied [15]. The optimal imaging parameters for both SLOE and SIRS methods were obtained through numerical simulation on the time-dependent Bloch equation. Detection sensitivities and the contrast dependence on TSL in SLOE and SIRS methods were investigated. The simulation results were then verified in phantom experiments with a block-designed paradigm by applying oscillatory currents with high (100 Hz) and low (10 Hz) frequencies. Further, the feasibility of detecting applied sub-nT oscillatory fields in anesthetic rats' brains was explored, and the noise levels of both phantom and rat data were also analyzed and compared.

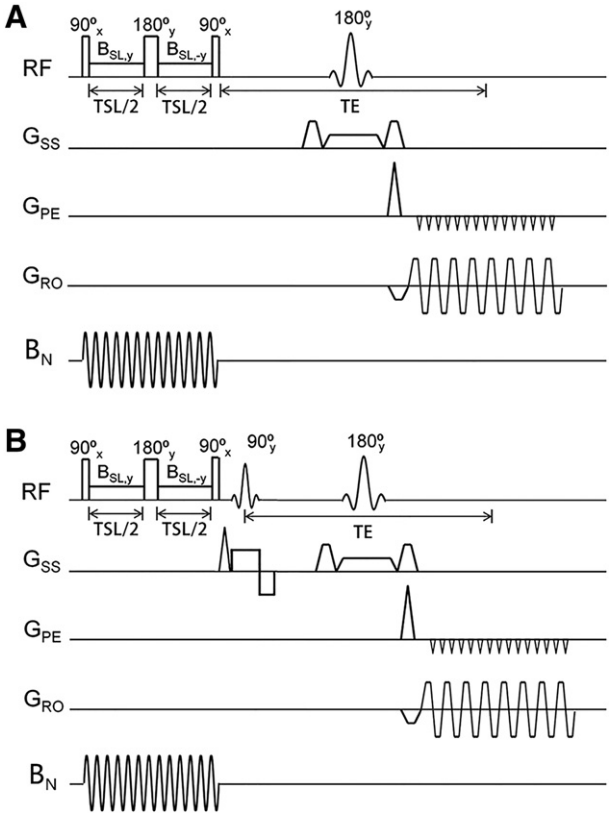

Fig. 1. Timing diagrams for SLOE (A) and SIRS (B) pulse sequences.

2. Material and methods

2.1. Bloch equation simulation

To quantitatively analyze the rotary saturation contrast, magnetization dynamics during spin-lock period was simulated without considering of 90 degree flipping pulses and 180 degree refocusing pulse. A doubly rotating frame (x″y″z″) was defined to preserve the analogy to the traditional rotating frame (x′y′z′). The z″ axis is defined by renaming the direction of B_{SL} (along y′ axis in our discussion), while the z′ and x′ axes in the singly rotating frame are renamed as x″ and y″ axes. The magnetic fields (B_N in amplitude) generated by oscillating currents can be separated into two counter-rotating components, each with an amplitude of $B_N/2$ and rotating at ω_N and $-\omega_N$ in the x″y″ plane, respectively. The magnetization will be flipped once the resonance condition is met, that is $\omega_N = \omega_{SL}$, and the effect of the component at $-\omega_N$ can be ignored because it rotates at $2\omega_N$ in the doubly rotating frame while the other component at ω_N will be stationary. Hence in the doubly rotating frame, B_{SL} is analogous to the static field, while the oscillatory field acts as the RF pulse. Thus, during the spin-lock period, the Bloch equations for the three components of magnetization are formulated in the doubly rotating frame as [16]:

$$\begin{aligned}\frac{dM_{x''}(t)}{dt} &= -\frac{M_{x''}}{T_{2\rho}} + \Delta\omega M_{y''}\\ \frac{dM_{y''}(t)}{dt} &= -\frac{M_{y''}}{T_{2\rho}} - \Delta\omega M_{y''} + \omega_m M_{z''}\\ \frac{dM_{z''}(t)}{dt} &= -\omega_m M_{y''} - \frac{M_{z''} - M_\rho}{T_{1\rho}}\end{aligned} \tag{1}$$

where $\omega_m = \gamma B_N/2$ is the spin frequency due to the oscillatory magnetic field and $\Delta\omega = \omega_{SL} - \omega_N$ is the off-resonant frequency. $T_{1\rho}$ and $T_{2\rho}$ represent the longitudinal and transverse relaxation times in the spin-locked doubly rotating frame, respectively. M_ρ denotes the equilibrium magnetization proportional to B_{SL} in the doubly rotating frame, and it can be safely ignored since B_{SL} is usually very small comparing to the static field (less than 10^{-5}). In this simplification, the motion of magnetization is supposed to be independent of B_{SL}, just as previous results indicated [10].

During the spin-lock period (immediately after the first 90 degree pulse), the initial magnetization vector of Eq. (1) could be written as $[M_{x'}(0)\ M_{y'}(0)\ M_{z'}(0)]\prime = [0\ 0\ M_0]\prime$, where M_0 represents the equilibrium magnetization at the main static magnetic field. By applying a matrix operation [17], the numerical solution of Eq. (1) can be obtained. It should be noted that the initial phase of the oscillatory field determines the direction of neuronal magnetic field in the doubly rotating frame as discussed previously [14]. In our simulation, the phase of oscillatory current was fixed at 0 so that the direction of oscillatory magnetic field will along the x″ axis. For SIRS, the contrast induced by currents is the decrease of magnetization along the direction of B_{SL}, and it could be represented by signal change defined as $|M_{z''}(\text{on}) - M_{z''}(\text{off})|/M_0$, where $M_{z''}(\text{on})$ and $M_{z''}(\text{off})$ represent the magnetization along z″ axis when the current is on and off, respectively. For SLOE, the component of magnetization along y″ axis flipped by the oscillatory field acts as the contrast, and its corresponding signal change can be written as $|M_{y''}(\text{on}) - M_{y''}(\text{off})|/M_0$ using similar definitions in SIRS.