Balanced Steady State Free Precession (bSSFP) from an effective field perspective: application to the detection of exchange (bSSFPX)

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INTRODUCTION: CEST (and the closely related off-resonance $T_{1\rho}$) method is gaining popularity and many promising applications have been investigated[1]. Typically, the method utilizes the application of a long pulse followed by acquisition[1]. Often, CEST employs a series of off-resonance saturations, the so-called Z-spectrum, which is time consuming. Moreover, quantification methods that could lead to metabolite maps or pH measurements require repetition of the entire experiment with different saturation time or power[2]. Recently, steady-state methods were reported, where the long saturation is split into short parts with intermittent acquisition[3]. The extreme case of this approach would be a train of excitation pulses[9] with intervals for acquisition. We observe that this is, in essence, a balanced Steady-State Free Precession (bSSFP) sequence: a train of pulses intermittent with windows and balanced gradients for the image acquisition.

At the core of our work is the realization that the bSSFP experiment IN ITSELF is sensitive to the exchange processes. Thus, no additional saturation/preparation is needed. Instead, the bSSFP data is collected at multiple frequency offsets (or, alternatively, using continuous RF phase advance). The analysis of this bSSFP spectral profile (bSSFPX spectrum in the following) provides information about the exchanging moieties; similar to CEST or off-resonance $T_{1\rho}$ experiments. In essence, *the acquisition is performed during saturation*. It may speed up the acquisition. Also, it would allow acquisition while the system approaches the steady-state, thus providing the data for QUEST-like quantification in a "single-shot". In this method we are observing the XY component of magnetization and not Z, as is standard in Z-spectroscopy.

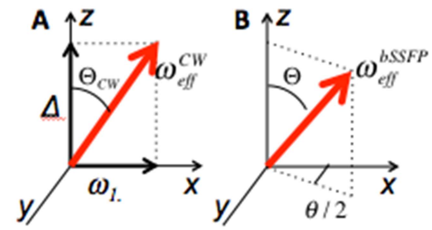

Figure 1.The effective RF fields generated during CEST/$T_{1\rho}$ experiment (A) and bSSFP (B).

bSSFP has been applied to the exchange before[4] and asymmetries, akin to the ones presented here were observed[5]. However, to the best of our knowledge this is the first time that the analogous nature of bSSFP and CEST/$T_{1\rho}$ experiments is realized and explored.

THEORY: The basic repetitive unit of the bSSFP is: $[(\alpha)_{\Delta\varphi}\text{-TR}]$, where α is the flip angle and Δφ is the phase advance between the two consecutive units. Typically, Δφ=π or Δφ=0. The gradients are balanced and can be ignored from the treatment[4,5]. Using Euler transformations we can show that the train of pulses generates an effective field:

$$\boldsymbol{H_{eff}}=\sin(\Theta)[\Phi/TR]\boldsymbol{I_{xy}}+\cos(\Theta)[\Phi/TR]\boldsymbol{I_z},$$

with $\cos(\Theta)=\cos(\alpha/2)\sin(\theta/2)/\text{sqrt}(1-\cos^2(\alpha/2)\cos^2(\theta/2))$, $\cos(\Phi/2)=\cos(\alpha/2)\cos(\theta/2)$, $\boldsymbol{I_{xy}}=\boldsymbol{I_x}\cos(\theta/2)+\boldsymbol{I_y}\sin(\theta/2)$, where θ is the effective rotation angle due to the RF off-resonance Δ: $\theta=2\pi\Delta TR+\Delta\varphi$[6]. Hence, the strength of the effective field generated in bSSFP is equal to $\omega_{eff}^{bSSFP}=\Phi/TR$. For comparison, in the CW spin-lock (or saturation) experiment using RF along **x**, the effective field is: $\boldsymbol{H_{eff}}^{CW}=\sin(\Theta_{CW})\,\omega_{eff}^{CW}\boldsymbol{I_x}+\cos(\Theta_{CW})\,\omega_{eff}^{CW}\boldsymbol{I_z}$ and $\Theta_{CW}=\text{atan}(\omega_1/2\pi\Delta)$ with ω_1 to be the RF intensity. The effective fields for bSSFP and CEST/$T_{1\rho}$ are shown schematically in Fig.1 and the analogous nature of the experiments is apparent.

In the steady state, the magnetization is locked along the effective field. Similar to the CEST/$T_{1\rho}$ experiments, it can be shown that in the presence of exchange, there is an additional contribution to the relaxation: $R_{ex}=p_Ap_B\Delta_{CS}k_{ex}/([\Phi_B/TR]^2+k_{ex}^2)$, where $p_{A/B}$ is a fractional population of pool A/B, Δ_{CS} is chemical shift difference between the two pools and k_{ex} is the exchange rate[7]. Maximum R_{ex} is achieved when the effective field on pool B is minimal, i.e. when $\Phi_B=0\pm2N\pi$ (N is an integer). For small α, this condition converts to $\Delta=\Delta_{CS}\pm2N/TR$: i.e. maximum R_{ex} is achieved when pool B is on-resonance with the center-band or the saturation sidebands of bSSFP. This is again in the complete analogy with the CEST/$T_{1\rho}$ experiment (e.g. see ZAPI[8])

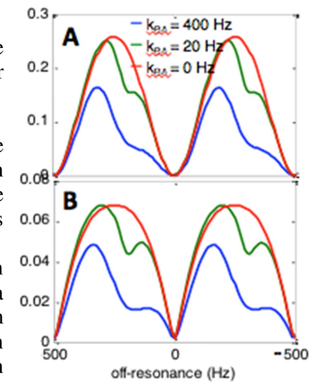

Figure 2. (A) Z-spectrum and (B) bSSFPX spectrum (XY component of the magnetization)

METHODS: Simulations were performed in Matlab 8.0 (The Mathworks, Natick, MA), different relaxation and exchange parameters were investigated. All experiments were performed at a 3T Philips Achieva scanner using a 32 channel head array coil. The phantom consisted of a bottle with 50mM Choline immersed in water. Choline possesses a hydroxyl group with exchanging protons resonating at ~1ppm from water. The bSSFP sequence with TR=2msec and Δφ=π was used. In the current implementation, dummy prep echoes were used to reach the steady-state, followed by a single image acquisition. In the future, we intend to collect images, instead of dummy prep echoes, and use this information for quantification. Due to the long T_1 of the samples, an 8 sec prep time was used to reach the steady state. Other imaging parameters were: FOV = 220×220 mm, matrix =112×112, slice thickness = 8 mm. The bSSFP analysis was performed on the pixel-by-pixel basis and followed the procedure analogous to common CEST analysis leading to Magnetization Transfer asymmetry (MTR_{asym}). Namely, the bSSFPX spectra were collected using offsets (Δ) in the range ±500Hz, with steps of 10Hz. The spectra were fitted to a single-pool bSSFP profile to determine the B_0 shift. The spectra were shifted according to the B_0 with the additional 1/2TR shift to account for Δφ=π Asymmetry was calculated and normalized by the values at negative frequencies ($bSSFPX_{asym}$). Standard CEST images were also acquired, using 5sec pulsed saturation, ±500Hz and 25Hz step, and processed using standard methods with WASSR correction for B_0 inhomogeneities.

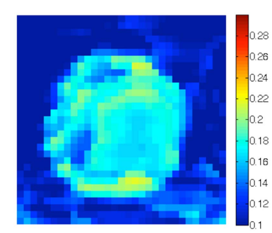

Figure 3. $bSSFPX_{asym}$ image of 50mM Cho solution

RESULTS AND DISCUSSION: Fig.2 shows typical simulation results using M_{0B}/M_{0A}=0.05 for concentration, T_{1A}=2 s, T_{2A}=0.05 s, T_{1B}=1 s, T_{2B}=1 s, Δ_{CS}=200 Hz and k_{BA}=0, 20 and 400 Hz. The asymmetries due to exchange are apparent. The whole spectrum repeats itself every 1/TR, in accordance with repetitive nature of the bSSFP profile. Again, in this approach we are measuring the XY component (Fig.2b) and not Z-component (Fig.2a) of the magnetization.

An image collected using bSSFPX is shown in Fig.3. The $bSSFPX_{asym}$ for Choline is 17±1% while MTR_{asym} is 14±1%. Thus, the quantitative measures are comparable between CEST and bSSFPX, At the same time, substantial $bSSFPX_{asym}$ was observed in water (~10%). This is probably an artifact of the current processing used for bSSFPX analysis. We are exploring other, more advanced methods (similar to what was gradually developed for CEST) that may lead to better quantification of the exchanging moieties without contamination of non-exchanging pools.

CONCLUSION: bSSFP can be viewed from the effective field perspective, which reveals its complete analogy with CEST/$T_{1\rho}$ experiments. The bSSFPX approach described here offers a novel way of collecting the data, essentially while the saturation/lock occurs. This may lead to fast acquisition and quantification approaches. We are focusing on the XY component of magnetization, previously ignored. The treatment presented here may also impact the application and understanding of bSSFP. Work is in progress to incorporate quantification and to apply the bSSFPX *in-vivo.*

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