Efficient and Accurate Modeling of Pulsed Magnetization Transfer.

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Introduction. Detailed information about tissue composition including macromolecules could be most valuable for assessing pathology. Unfortunately, protons bound to immobile macromolecules can not be imaged directly on clinical MRI scanners, because of their extremely short T_2. However, information about macromolecules can be obtained indirectly from magnetization-transfer (MT) experiments using off-resonance saturation of the broad macromolecular resonance line and observation of the effect on the free water pool [3]. The preferred saturation technique would be continuous-wave (cw) irradiation, which is highly effective and can be analytically assessed by solving the Bloch equations. Unfortunately, cw-irradiation is not applicable on most clinical scanners, where the duration of radio frequency RF pulses is limited. As an alternative, pulsed saturation schemes have thus been proposed in studies involving human subjects [4,5,6]. A drawback of pulsed saturation is its substantially more complex mathematical description. We present a new approach of estimating MT parameters for arbitrary pulse sequences using a fast and accurate description of the pulse sequence by solving the McConnell equations numerically using matrix algebra.

Theory. Our approach for estimating MT parameters is based on the work of Helgstrand et al. [1] combining the differential equations for a two-state chemical exchange process with the Bloch equations. To simplify computation, the McConnell equations are rewritten in homogeneous form. Underlying first-order reactions are described according to d/dt $\mathbf{A} = \mathbf{K}\,\mathbf{A}$, where $\mathbf{A}$ is a vector of concentrations and $\mathbf{K}$ is the kinetic matrix. The formal solution is given by $\mathbf{A}(t) = \exp(\mathbf{K}t)\,\mathbf{A}(t_0)$. By defining pseudo first-order rate constants as proposed in [3], this model applies to the standard two-pool system for MT consisting of a liquid pool and a semisolid pool. By combining the Bloch equations with the kinetic matrix a 7×7 matrix is obtained. Transversal magnetization exchange between both pools was not considered, as it is generally assumed to be neglectible [8]. As a modification to [1], a Lorentzian lineshape was assumed for the liquid pool and a Gaussian (agarose) or a super-Lorentzian lineshape (human brain tissue) was assumed for the semi-solid pool by proper adaptation of the amplitude of the off-resonance irradiation in the fitting procedure. To obtain a closed-form solution, all elements of the matrix must be constants, which does not apply for a given pulse sequence with amplitude-modulated RF pulses. RF pulses were thus divided into N sections of constant amplitude and the matrix was successively solved for each time step.

Methods. Experiments were performed at 3T (MedSpec 30/100, Bruker) using a birdcage head coil. Sequences consisted of a saturation scheme followed by EPI. Two saturation schemes were compared: 1) 7s off-resonant cw irradiation; 2) 200 Gaussian off-resonant pulses (duration 14ms, separation 21 ms, bandwidth 300Hz). 13 logarithmically distributed off-resonant frequencies between 50Hz and 50kHz and 5 amplitudes were used. The mean amplitude in the pulsed scheme was chosen to match the power-equivalent of the cw irradiation [4]. Investigations were performed in a phantom (2% agarose in water) and a healthy human volunteer. In case of cw irradiation, MT parameters were extracted using the analytical steady-state solution from [3] and the modifications proposed in [4].

Results & Discussion. To verify the algorithm, synthetic MT based on the published results for agarose were computed with the analytic steady-state solution and the new approach yielding perfect agreement (Fig. 1). Results from fitting experimental data recorded from agarose by both cw and pulsed saturation are presented in Figs. 2a, b and Table 1. The parameters T_{1b} and RM_{0a} were fixed as proposed in [9]. Data points below 500 Hz were excluded from analysis, because increasing direct saturation caused artefacts in the EPI reconstruction. The obtained MT parameters for both experiments (f: ratio of the semi-solid pool to the overall pool size; T_{1a}: T_1 of the free pool; T_{2a}: T_2 of the free pool; T_{2b}: T_2 of the semi-solid pool) agree within the experimental accuracy. Similar results from fitting the in-vivo data recorded in normal human brain are given in Figs. 2c, d and Table 2. Again, the extracted parameters agreed within the experimental accuracy. By contrast, meaningful fits of the data recorded with pulsed saturation were not obtained when applying the simplified analysis scheme proposed by Ramani et al. [4] which is mainly due to an inappropriate estimation of the cw power equivalent [2,6].

The new fitting approach is promising for reliably estimating quantitative MT parameters from experiments with arbitrary saturation schemes and imaging sequences. While the current study was restricted to the standard two-pool MT model, expansion to more complex models is also possible.

	$f/R_a(1\text{-}f)$	T_{1a}/T_{2a}	T_{2b} in µsec
Cw	0.009 ± 0.003	67 ± 1	17.4 ± 5.0
Pulsed	0.012 ± 0.002	60 ± 1	19.9 ± 2.8

Table 1: Phantom results (2% agarose).

	$f/R_a(1\text{-}f)$	T_{1a}/T_{2a}	T_{2b} in µsec
Cw	0.10 ± 0.004	53 ± 3	12.6 ± 0.8
Pulsed	0.09 ± 0.005	42 ± 4	11.0 ± 0.9

Table 2: In vivo results (human brain).

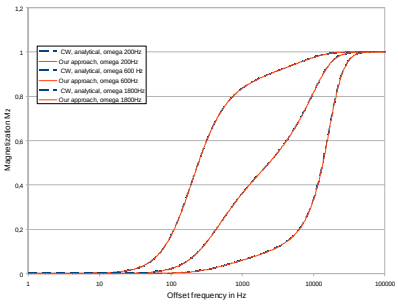

Fig 1: Simulation results.

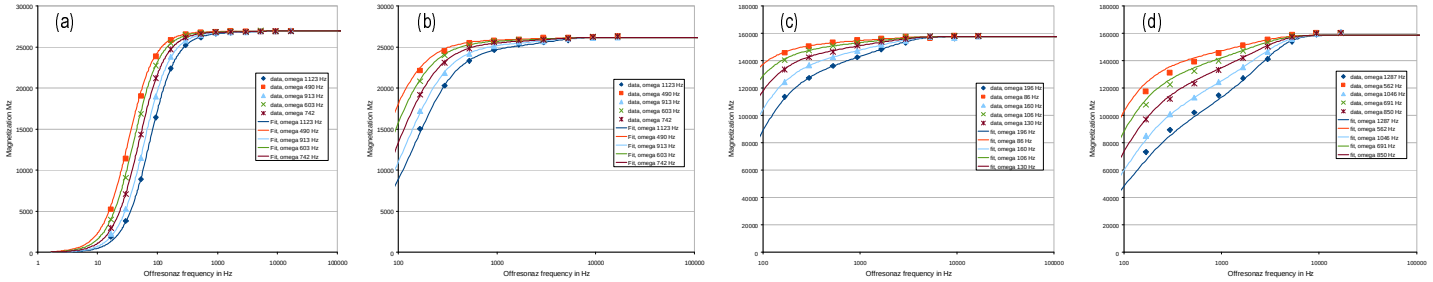

Fig. 2. Experimental data and fitting results for agarose and cw **(a)** and pulsed saturation **(b)** and for human brain with cw **(c)** and pulsed saturation **(d)**.

References. [1] Helgstrand M, JBNMR 2000;18:49. [2] Portnoy S, MRM 2007; 58: 144. [3] Henkelman RM, MRM 1993; 29: 759. [4] Ramani A, MRI 2002; 20: 721. [5] Sled JG, MRM 2001; 46: 923. [6] Cercignani M, MRM 2006; 56: 803. [7] Sharon P, MRM 2007; 58: 144. [8] Graham SJ, JMRI 1997;7:903. [9] Müller DK, ISMRM 2008;1416.