Journal of Magnetic Resonance 230 (2013) 88–97

Contents lists available at SciVerse ScienceDirect

Journal of Magnetic Resonance

journal homepage: www.elsevier.com/locate/jmr

Matrix-algebra-based calculations of the time evolution of the binary spin-bath model for magnetization transfer

Dirk K. Müller, André Pampel, Harald E. Möller *

Max Planck Institute for Human Cognitive and Brain Sciences, Stephanstr. 1a, 04103 Leipzig, Germany

ARTICLE INFO

Article history:
Received 23 May 2012
Revised 21 January 2013
Available online 9 February 2013

Keywords:
Bloch–McConnell equations
Continuous-wave saturation
Matrix algebra
Polynomial interpolation
Pulsed saturation
Quantitative magnetization-transfer imaging

ABSTRACT

Quantification of magnetization-transfer (MT) experiments are typically based on the assumption of the binary spin-bath model. This model allows for the extraction of up to six parameters (relative pool sizes, relaxation times, and exchange rate constants) for the characterization of macromolecules, which are coupled via exchange processes to the water in tissues. Here, an approach is presented for estimating MT parameters acquired with arbitrary saturation schemes and imaging pulse sequences. It uses matrix algebra to solve the Bloch–McConnell equations without unwarranted simplifications, such as assuming steady-state conditions for pulsed saturation schemes or neglecting imaging pulses. The algorithm achieves sufficient efficiency for voxel-by-voxel MT parameter estimations by using a polynomial interpolation technique. Simulations, as well as experiments in agar gels with continuous-wave and pulsed MT preparation, were performed for validation and for assessing approximations in previous modeling approaches. *In vivo* experiments in the normal human brain yielded results that were consistent with published data.

1. Introduction

The proton signals from macromolecules or membranes (subsequently summarized under the single term 'macromolecules') are not directly visible to magnetic resonance imaging (MRI) because their associated transverse relaxation times are in the order of 10 μs. It is, however, possible to generate image contrast based on cross-relaxation and/or chemical exchange between macromolecules and highly mobile tissue water [1–3]. A common strategy is to saturate the macromolecular magnetization by off-resonance radiofrequency (RF) irradiation and to compare the image to one obtained without saturation. A simplifying, yet often sufficient approach to quantitative magnetization transfer imaging (qMTI), is the binary spin-bath (BSB) model [4,5], which consists of two proton pools: a pool "*a*" of "free" liquid water and a pool "*b*" of semisolid macromolecules with restricted motion [6,7].

Generally, off-resonance irradiation can be implemented in a continuous-wave (CW) or in a pulsed mode. The CW experiment achieves the best separation of the effects of RF irradiation on the two pools [8] and leads to a closed-form analytical solution for the BSB model [7]. For human MRI, however, repetitive pulsed off-resonance irradiation is typically necessary because only few scanners support CW operation. In most *in vivo* experiments, modified gradient-recalled echo (GRE) sequences have been employed to investigate the spin system at a periodic steady state. They consist of shaped off-resonance saturation pulses ("MT pulses") for generating magnetization-transfer (MT) contrast, which are interleaved with small-angle on-resonance excitation pulses ("imaging pulses") for image acquisition (e.g., [9–11]). Alternatively, transient techniques have been suggested, which investigate the approach to steady state after a train of equidistant MT pulses (e.g., [12,13]). A drawback of pulsed saturation is that it results in a mathematically more complex description, which may lead to computationally inefficient data analysis when MT parameters have to be determined voxel-by-voxel [14].

To simplify data analysis and overcome computational limitations, several approaches have been proposed. A relatively comprehensive one based on the Redfield-Provotorov theory was suggested by Sled and Pike [9]. For the liquid pool, the combined effects from MT and imaging pulses are approximated as an instantaneous fractional saturation in the absence of relaxation and exchange. For the semisolid pool, on-resonance irradiation is ignored, and each MT pulse is approximated by a period of constant–amplitude irradiation with equivalent frequency offset and power. Yarnykh [10] derived an expression by also employing a constant–amplitude approximation for the MT pulses and ignoring direct saturation of the liquid pool. Ramani et al. [11] modified the analytical CW solution by approximating pulsed off-resonance irradiation as having the same effect as CW irradiation of equivalent average power, which is calculated over the duty cycle

* Corresponding author.
E-mail addresses: dirk.mueller@cbs.mpg.de (D.K. Müller), anpa@cbs.mpg.de (A. Pampel), moeller@cbs.mpg.de (H.E. Möller).

1090-7807/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jmr.2013.01.013

of the MT pulse. This approach essentially ignores the pulsed fashion of the saturation.

In this paper, we present an approach for estimating MT parameters acquired with arbitrary pulse sequences. It uses matrix algebra [15], as previously employed for simulating nuclear magnetic resonance (NMR) experiments with chemical exchange [16–18]. The algorithm achieves high accuracy by a concatenation of analytical matrix solutions to the underlying Bloch–McConnell equations for piecewise constant RF irradiation, which allows for an exact sampling of digitized RF pulse shapes generated on an MRI scanner. A key feature of the implementation is a polynomial interpolation technique to achieve sufficient efficiency for voxel-by-voxel MT parameter estimations. Simulations and phantom measurements comparing CW and pulsed saturation schemes were performed for validation and to assess approximations used in previous modeling approaches. Application to human-brain qMTI was used to evaluate the performance under *in vivo* conditions.

2. Theory

2.1. Simplified BSB model

The Bloch equations in the rotating frame can be written in matrix form as

$$\frac{d}{dt}\begin{pmatrix} M_x \\ M_y \\ M_z \end{pmatrix} = -\begin{pmatrix} R_2 & \Omega & -\omega_{1y} \\ -\Omega & R_2 & \omega_{1x} \\ \omega_{1y} & -\omega_{1x} & R_1 \end{pmatrix}\begin{pmatrix} M_x \\ M_y \\ M_z \end{pmatrix} + \begin{pmatrix} 0 \\ 0 \\ R_1 M_0 \end{pmatrix}, \qquad (1)$$

$\mathbf{M} = (M_x\ M_y\ M_z)^T$ is the magnetization vector, M_0 is the equilibrium z-magnetization, t is time, and $R_1 = 1/T_1$, $R_2 = 1/T_2$, T_1, and T_2 are the longitudinal and transverse relaxation rate constants and times, respectively. The offset frequency is given by $\Omega = \omega_0 - \omega_{RF}$, and the x and y components (in rad/s) of the applied RF field with amplitude B_1 and phase ϕ are $\omega_{1x} = \omega_1 \cos\phi$ and $\omega_{1y} = \omega_1 \sin\phi$ with $\omega_1 = -\gamma B_1$. ω_0 is the Larmor frequency, ω_{RF} is the frequency of the RF field, and γ is the magnetogyric ratio.

For the further analysis, it is beneficial to append a constant to the magnetization vector to obtain a homogeneous form of the Bloch equations. Following previous suggestions [16,17], we choose a constant 1/2 because it leads to the same normalization as used in the product operator formalism [19]. To account for MT processes, the Bloch equations are then expanded by differential equations for first-order exchange to obtain the Bloch–McConnell equations [4]. We restrict our analysis to the BSB model with the two proton pools defined above. For biological tissues, with $T_2^b \approx 10\ \mu s$ [20], net exchange of transverse magnetization is commonly neglected [1,7,21] because the efficient relaxation of the semisolid pool rapidly destroys transverse magnetization. Transverse magnetization in the semisolid pool produced by the RF pulses is also negligible as long as $\omega_1 \ll R_2^b$ [21]. Under these conditions, simplified Bloch–McConnell equations are conveniently written in matrix form according to

$$\frac{d\mathbf{M}}{dt} = -\mathbf{L}\cdot\mathbf{M}, \qquad (2)$$

with $\mathbf{M} = \left(1/2\ M_x^a\ M_y^a\ M_z^a\ M_z^b\right)^T$ and the dynamic matrix [22]

$$\mathbf{L} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & R_2^a & \Omega & -\omega_{1y} & 0 \\ 0 & -\Omega & R_2^a & \omega_{1x} & 0 \\ -2R_1^a M_0^a & \omega_{1y} & -\omega_{1x} & R_1^a + RM_0^b & -RM_0^a \\ -2R_1^b M_0^b & 0 & 0 & -RM_0^b & R_1^b + RM_0^a \end{pmatrix}. \qquad (3)$$

R is the MT rate constant, which is defined through the pseudo-first-order rate constants $k_{ab} = RM_0^b$ and $k_{ba} = RM_0^a$ describing the transfers $M_z^a \to M_z^b$ and $M_z^b \to M_z^a$, respectively [7]. The factor 2 that is multiplied with $R_1^a M_0^a$ and $R_1^b M_0^b$ in the first column of $\mathbf{L}$ is required to account for using 1/2 as the constant term in the magnetization vector. We note that transfer of longitudinal magnetization can occur via direct chemical exchange [5] or via dipolar relaxation caused by the nuclear Overhauser effect (NOE) [23]. Because both processes lead to equivalent algebraic expressions [24], the MT experiment cannot distinguish between them.

2.2. Lineshape for the semisolid pool

The simplified dynamic matrix, Eq. (3), does not consider RF absorption by the semisolid pool b (due to ignoring M_{xy}^b and setting matrix elements $L_{5,2}$ and $L_{5,3}$ to zero). As a correction, an absorption lineshape is arbitrarily introduced by modifying the lower-right element ($L_{5,5}$) according to

$$\mathbf{L} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & R_2^a & \Omega & -\omega_{1y} & 0 \\ 0 & -\Omega & R_2^a & \omega_{1x} & 0 \\ -2R_1^a M_0^a & \omega_{1y} & -\omega_{1x} & R_1^a + RM_0^b & -RM_0^a \\ -2R_1^b M_0^b & 0 & 0 & -RM_0^b & R_1^b + RM_0^a + R_{RF}^b \end{pmatrix}. \qquad (4)$$

R_{RF}^b is the saturation rate constant defined through [7]:

$$R_{RF}^b = \pi\omega_1^2 g_b\left(\Omega, T_2^b\right), \qquad (5)$$

where g_b is the absorption lineshape function. It depends on the associated transverse relaxation time of the semisold pool, which is determined by the local microstructure [20]. A Gaussian lineshape was found to fit experimental data well for agar gels [7], whereas a super-Lorentzian lineshape [25] was successfully employed for modeling MT in tissues [20]. For more efficient computation, it is convenient to write these lineshape functions according to

$$g_b'(\zeta) = \frac{1}{\sqrt{2\pi}}\exp\left(-\frac{\zeta^2}{2}\right), \qquad (6)$$

and

$$g_b'(\zeta) = \int_0^{\pi/2} \sqrt{\frac{2}{\pi}}\frac{1}{|3\cos^2\theta - 1|} \times \exp\left[-2\left(\frac{\zeta}{3\cos^2\theta - 1}\right)^2\right]\sin\theta d\theta, \qquad (7)$$

respectively, with only one independent variable $\zeta \equiv \Omega T_2^b$. The omitted factor T_2^b in Eqs. (6) and (7) is then considered as a scaling parameter in Eq. (5), which is rewritten as

$$R_{RF}^b = \pi\omega_1^2 T_2^b g_b'(\zeta). \qquad (8)$$

2.3. Steady-state conditions under CW irradiation

Under conditions of CW irradiation for a sufficiently long time $\tau_{CW} \gg T_1^a, T_1^b$, a steady state establishes, and Eq. (2) reduces to a system of linear equations. After introducing a scaling factor σ, the signal from the liquid pool is [7,11]:

$$S^a = \sigma M_0^a \frac{R_1^b \frac{RM_0^b}{R_1^a} + R_{RF}^b + R_1^b + RM_0^a}{\frac{RM_0^b}{R_1^a}\left(R_1^b + R_{RF}^b\right) + \left[1 + \frac{\omega_1^2 T_2^a}{R_1^a\left(1+\Omega^2 T_2^{a2}\right)}\right]\left(R_1^b + R_{RF}^b + RM_0^a\right)}. \qquad (9)$$

In general, Eq. (9) permits the unique determination of six model parameters: $\sigma M_0^a, M_0^b/(R_1^a M_0^a), RM_0^a, R_1^b, 1/(R_1^a T_2^a)$, and T_2^b (from R_{RF}^b).