Matrix-Algebra-Based Modeling Approach to MT, NOE and CEST for an Arbitrary Number of Interacting Spin Pools

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Target Audience: Researchers interested in modeling MR experiments, magnetization transfer, and CEST.

Purpose. An introduction into numerical simulations of MR sequences is given that uses the Bloch-McConnell equations to consider any type of magnetization transfer. To account for cases with more than two spin pools involved in processes exchanging magnetization, an extension of previously published technique [1] for matrix-algebra-based simulation of the binary spin bath model is implemented. By describing a method for dynamically extending the underlying matrices for a system of n spin pools, the resulting model allows straightforward simulation of any MR experiments with combined effects from chemical exchange saturation transfer (CEST) [2] and cross-relaxation via the nuclear Overhauser effect (NOE) between water and small molecules [3] as well as magnetization transfer (MT) involving a macromolecular pool [4]. A fast implementation of the method in MatLab is presented. Solutions for time-efficient simulations, in particular dealing with shaped RF pulses, are discussed.

Outline of the Method

Matrix-Algebra-Based Model: We start from the homogeneous matrix form of the Bloch equations, Eqs. (1) & (2) in the rotating frame with appended constant (1/2) to include equilibrium magnetization [5], where $\omega_{1,x} = -\gamma_p B_1 \cos(\phi)$, $\omega_{1,y} = -\gamma_p B_1 \sin(\phi)$, $\Theta \overset{\text{def}}{=} R_1 M_z^0$, ϕ is the RF phase, and $\Omega = \omega_0 - \omega_{RF}$ with ω_{RF} the irradiation pulse frequency. R_1 was omitted in the definition of $\boldsymbol{L}_{in}$. The above system of equations can be dynamically extended for n spin pools by evaluating [5] $\boldsymbol{L}_{in,n} = \mathbf{1}_n \otimes \boldsymbol{L}_{in}$ where $\mathbf{1}_n$ denotes the n-dimensional unity matrix and $'\otimes'$ is the Kronecker vector product. $\boldsymbol{L}_n$ then corresponds to $\boldsymbol{L}_{in,n}$ with the appended row and column of zeros and $L_{n,j1} = -2\Theta^i$ for $j = 4i$.

$$\frac{d}{dt}\begin{pmatrix}1/2\\ M_x\\ M_y\\ M_z\end{pmatrix} = -\underbrace{\begin{pmatrix}0 & 0 & 0 & 0\\ 0 & R_2 & \Omega & -\omega_{1,y}\\ 0 & \Omega & R_2 & \omega_{1,x}\\ -2\Theta & \omega_{1,y} & -\omega_{1,x} & R_1\end{pmatrix}}_{\overset{\text{def}}{=} \boldsymbol{L}_1}\begin{pmatrix}1/2\\ M_x\\ M_y\\ M_z\end{pmatrix} \quad (1)$$

$$\boldsymbol{L}_{in} \overset{\text{def}}{=} \begin{pmatrix}R_2 & \Omega & -\omega_{1,y}\\ \Omega & R_2 & \omega_{1,x}\\ \omega_{1,y} & -\omega_{1,x} & 0\end{pmatrix} \quad (2)$$

Inclusion of CEST and NOE Effects: Firstly, effects from chemical exchange are included using the Bloch-McConnell equations [6]. Considering all $\binom{n}{2}$ possible chemical exchange interactions k_{ij} among the spin pools (exchange from spin pool j to i), we obtain the preliminary kinetics matrix $\widetilde{\boldsymbol{K}}_n$ with $\widetilde{K}_{ij} = c_i k_{ji}, \widetilde{K}_{ji} = c_j k_{ji}$ for $i \neq j$ and $\widetilde{K}_{ii} = -\sum_{l=1,l\neq i}^{n} c_l k_{il}$.

Similarly, cross-relaxation effects are included based on the Solomon equations [7] by considering the cross-relaxation rates σ_{ij} for a system of n spins (corresponding to magnetization transfer from spin j to spin i). The relaxation matrix is defined as $\widetilde{\boldsymbol{R}}_n$ with $\tilde{R}_{ij} = \sigma_{ij}$, $\tilde{R}_{ii} = R_1^i - \sum_{l=1,l\neq i}^{n} \sigma_{li}$, where R_1^i denotes the longitudinal relaxation rate for spin i, and the condition $c_i\sigma_{ji} = c_j\sigma_{ij}$ is fulfilled. Both matrices $\widetilde{\boldsymbol{K}}_n$ and $\widetilde{\boldsymbol{R}}_n$ must be transformed to meet the $(3n+1)\times(3n+1)$ dimensions of the Bloch-coefficient matrix, $\boldsymbol{L}_n$ (as defined in Eq. (1) for the specific case of n=1). This is accomplished as shown below in Eqs. (3)–(6):

$$\boldsymbol{K}_n = \widetilde{\boldsymbol{K}}_n \otimes \begin{pmatrix}1 & 0 & 0\\ 0 & 1 & 0\\ 0 & 0 & 1\end{pmatrix} \quad (3) \qquad \widehat{\boldsymbol{K}}_n = \begin{pmatrix}0 & \cdots & 0\\ \vdots & & \\ 0 & & \boldsymbol{K}_n\end{pmatrix} \quad (4)$$

$$\boldsymbol{R}_n = \widetilde{\boldsymbol{R}}_n \otimes \begin{pmatrix}0 & 0 & 0\\ 0 & 0 & 0\\ 0 & 0 & 1\end{pmatrix} \quad (5) \qquad \widehat{\boldsymbol{R}}_n = \begin{pmatrix}0 & \cdots & 0\\ \vdots & & \\ 0 & & \boldsymbol{R}_n\end{pmatrix} \quad (6)$$

The Bloch-coefficient matrix is changed accordingly: $\boldsymbol{L}_n^{K,R} = \boldsymbol{L}_n - \widehat{\boldsymbol{K}}_n + \widehat{\boldsymbol{R}}_n$, and the above definition of Θ is rewritten as $\boldsymbol{\Theta} \overset{\text{def}}{=} \widetilde{\boldsymbol{R}}_n \cdot \boldsymbol{M}_n^0$, with $\boldsymbol{M}_n^0$ now denoting the vector of initial longitudinal magnetizations for n spin pools. Finally, the behavior of the spin system is obtained from Eq. (7), where $\boldsymbol{M}_{n,hom}$ denotes the magnetization vector for n spin pools with the appended constant (1/2) for the homogeneous form of equations, as mentioned above.

$$\frac{d}{dt}\boldsymbol{M}_{n,hom} = -\boldsymbol{L}_n^{K,R}\boldsymbol{M}_{n,hom} \quad (7)$$

Summary. The above model can be used for simulating any number of spin pools (with different relative spin concentrations) with consideration of potential MT-, NOE- and CEST-related interactions individually and without unwarranted simplifications. Combined with a previously published technique for efficient calculation of the matrix exponentials [1], it is possible to simulate MR pulse sequences by multiplying the matrix exponentials for each time step, containing the coefficient matrices that are constructed as above. An example for a simulated experiment considering 3 spin pools with NOE and CEST interactions is shown in Fig. 1. As the complexity of the spin system increases with the number of considered pools, so does the number of free parameters.

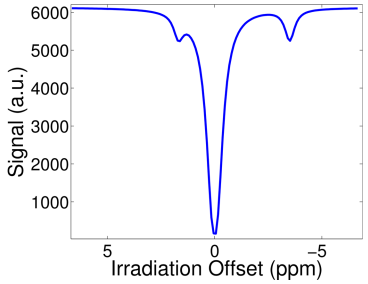

Figure 1: Simulation results showing the application of matrix-algebra-based model using a 3 spin-pool approach (with NOE between water and spin pool at -3.5ppm, and CEST between water and spin pool at 1.7ppm).

Conclusion. With the extension of the matrix-algebra-based pulse sequence simulation it is possible to consider an arbitrary number of coupled spin pools.

References. [1] Müller et al., JMR 230, 88 (2013). [2] Ward et al., JMR 143, 79 (2000). [3] Overhauser, Phys. Rev. 92, 411 (1953). [4] Henkelman et al., MRM 29, 759 (1993). [5] Helgstrand et al., J. Biomol. NMR 18, 49 (2000). [6] McConnell, J. Chem. Phys. 28, 430, (1958). [7] Solomon, Phys. Rev. 99, 559 (1955).