A new method for quantifying chemical exchange rates from CEST MRI using the solutions to the time-dependent Bloch equations with and without spin locking

Kenya Murase[1], Junpei Ueda[1], Koji Itagaki[1], Shigeyoshi Saito[1], and Atsuomi Kimura[1]
[1]*Medical Physics and Engineering, Osaka University, Suita, Osaka, Japan*

INTRODUCTION

Recently, there have been an increasing number of studies that have used the chemical exchange effect to probe the tissue microenvironment and provide novel imaging contrasts that are not available from conventional magnetic resonance imaging (MRI) techniques. Most of these studies adopted either a chemical exchange saturation transfer (CEST) or a spin-locking (SL) approach. Jin et al. [1] performed CEST and SL experiments to compare the characteristics of the CEST and SL approaches in the study of chemical exchange effects, and pointed out that the SL approach has a higher signal-to-noise ratio (SNR) than the CEST approach. On the other hand, the numerical solutions to the time-dependent Bloch equations including the chemical exchange effect are useful not only for investigating the contrast mechanism and optimal conditions of CEST MRI but also for quantifying chemical exchange rates. The purpose of this study was to present a simple and fast method for solving the time-dependent Bloch equations with SL and to propose a new method for quantifying chemical exchange rates from CEST MRI using this method.

MATERIALS AND METHODS

The Bloch equations in the 2-pool CEST model consisting of pools of bulk water protons (w) and water-exchangeable solute protons (s) are given by $d\mathbf{M}(t)/dt=\mathbf{A}(\omega,\omega_1,\phi)\cdot\mathbf{M}(t)$...(1) [2], where $\mathbf{M}(t)=[M_x^w(t)\ M_x^s(t)\ M_y^w(t)\ M_y^s(t)\ M_z^w(t)\ M_z^s(t)\ 1]^T$ and superscripts *w* and *s* show the parameters in pool w and pool s, respectively. For example, $M_x^w(t)$ denotes the x component of the magnetization in pool w at time *t*. $\mathbf{A}(\omega,\omega_1,\phi)$ in Eq. (1) is given by Eq. (2), where R_1^w ($=1/T_1^w$) and R_2^w ($=1/T_2^w$) denote the longitudinal and transverse relaxation rates in pool w, respectively, R_1^s ($=1/T_1^s$) and R_2^s ($=1/T_2^s$) those in pool s, k_{ws} the exchange rate from pool w to pool s, k_{sw} the exchange rate from pool s to pool w, and M_0^w and M_0^s the thermal equilibrium z magnetizations in pool w and pool s, respectively. $\Delta\omega_w$ and $\Delta\omega_s$ are given by $\omega_w-\omega$ and $\omega_s-\omega$, respectively, where ω_w and ω_s are the Larmor frequencies in pool w and pool s, respectively, ω and ω_1 are the frequency and nutation rate of RF-pulse irradiation, and ϕ is the angle of RF-pulse irradiation with respect to the x-axis. The solution of Eq. (1) can be given by $\mathbf{M}(t)=e^{\mathbf{A}(\omega,\omega_1,\phi)t}\cdot\mathbf{M}(0)$...(3) [2], where $\mathbf{M}(0)=[0\ 0\ 0\ 0\ M_0^w\ M_0^s\ 1]^T$ and $e^{\mathbf{A}(\omega,\omega_1,\phi)t}$ is the matrix exponential that can be computed using diagonalization [2].

$$\mathbf{A}(\omega,\omega_1,\phi)=\begin{pmatrix} -(R_2^w+k_{ws}) & k_{sw} & \Delta\omega_w & 0 & -\omega_1\sin\phi & 0 & 0 \\ k_{ws} & -(R_2^s+k_{sw}) & 0 & \Delta\omega_s & 0 & -\omega_1\sin\phi & 0 \\ -\Delta\omega_w & 0 & -(R_2^w+k_{ws}) & k_{sw} & \omega_1\cos\phi & 0 & 0 \\ 0 & -\Delta\omega_s & k_w & -(R_2^s+k_{sw}) & 0 & \omega_1\cos\phi & 0 \\ \omega_1\sin\phi & 0 & -\omega_1\cos\phi & 0 & -(R_1^w+k_{ws}) & k_{sw} & R_1^w M_0^w \\ 0 & \omega_1\sin\phi & 0 & -\omega_1\cos\phi & k_{ws} & -(R_1^s+k_{sw}) & R_1^s M_0^s \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}\cdots(2)$$

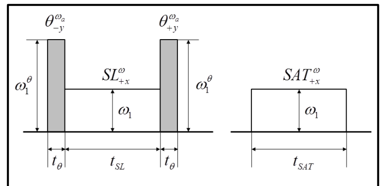

Fig. 1 (a) (b)

Figure 1 illustrates the diagram of the pulse sequence with (a) and without SL (b). When spins are locked by an SL pulse that is applied on the x-axis at an offset frequency Ω [Fig. 1(a)], the effective SL magnetic field (B_1^{eff}) is given by $B_1^{eff}=(\omega_1^2+\Omega^2)^{1/2}/\gamma$, where γ is the gyromagnetic ratio. To achieve SL, the magnetization is first flipped by the θ-degree pulse to the x-z plane, then locked by B_1^{eff} for a duration of SL (t_{SL}), and then flipped back to the z-axis for imaging. On the analogy of Eq. (3), the θ-degree rotation matrices [$\mathbf{R}$(θ)] and [$\mathbf{R}$(-θ)] are given by $e^{\mathbf{A}(\omega,\omega_1\theta,-\pi/2)t\theta}$ and $e^{\mathbf{A}(\omega,\omega_1\theta,\pi/2)t\theta}$, respectively, where $\theta=\tan^{-1}(\omega_1/\Omega)$ and t_θ is a duration of the θ-degree pulse irradiation given by $t_\theta=\theta/\omega_1^\theta$ [Fig. 1(a)]. Thus, we obtain the magnetization after SL as $\mathbf{M}(t_{SL})=\mathbf{R}(-\theta)e^{AtSL}\mathbf{R}(\theta)\mathbf{M}(0)$...(4). When the SL pulse is not applied [Fig. 1(b)], the magnetization is simply given by $\mathbf{M}(t_{SAT})=e^{\mathbf{A}(\omega,\omega_1,0)tSAT}\mathbf{M}(0)$...(5), where t_{SAT} denotes a duration of saturation [Fig. 1(b)].

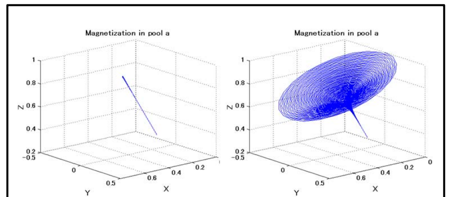

Fig. 2 With SL Without SL

If we assume that the T_1 and T_2 values in the two pools are known, the parameters to be estimated (**x**) are reduced to k_{ex} ($=k_{ws}+k_{sw}$) and M_0^s/M_0^w, i.e., $\mathbf{x}=[k_{ex}\ M_0^s/M_0^w]^T$. These parameters can be estimated from the z component of magnetization in pool w [$M_z^w(\mathbf{x}, t)$] by use of the nonlinear lease-squares (NLSQ) method, i.e., $\mathbf{x}'=\arg\min \Sigma_t\|M_z^w(\mathbf{x}, t)\|^2$...(6), where *t* corresponds to t_{SL} and t_{SAT} for cases with and without SL, respectively. It should be noted that k_{ws} and k_{sw} can be calculated from k_{ex} as $k_{ws}=k_{ex}/(1+M_0^w/M_0^s)$ and $k_{sw}=k_{ex}/(1+M_0^s/M_0^w)$, respectively, because it holds true that $k_{ws}M_0^w=k_{sw}M_0^s$ at equilibrium.

As illustrative examples, we assumed that t_θ=200 μs, Ω=2000 Hz, $\omega_w-\omega_s$=2400 Hz, ω_1=1000 Hz, T_1^w=1.5 s, T_2^w=60 ms, T_1^s=0.77 s, and T_2^s=33 ms in this study. Rician noise was added to $M_z^w(\mathbf{x}, t)$ in order to investigate the effect of statistical noise on the accuracy of parameter estimation. Furthermore, to quantitatively evaluate the accuracy of parameter estimates, the root-mean-square error (RMSE) and bias against the true values were calculated for k_{ex} and M_0^s/M_0^w across 100 simulations. The RMSE and bias were calculated from sqrt{mean[$(\mathbf{x}'/\mathbf{x}-1)^2$]} and mean[$|\mathbf{x}'-\mathbf{x}|/\mathbf{x}$], respectively, where **x** and **x'** denote the true and estimated parameter values, respectively.

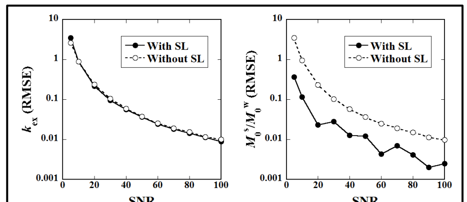

Fig. 3 (a) (b)

RESULTS AND DISCUSSION

Figure 2 shows the 3-dimensional plots of the magnetization in pool w with (left) and without SL (right), which were calculated from Eqs. (4) and (5), respectively. As shown in Fig. 2, the effect of SL is clearly visualized. Figures 3(a) and 3(b) show the RMSE values for k_{ex} and M_0^s/M_0^w as functions of SNR, respectively, while Figs. 4(a) and 4(b) show the bias values for k_{ex} and M_0^s/M_0^w, respectively. In these figures, closed and open circles represent cases with and without SL, respectively. As shown in Fig. 3, the RMSE value for M_0^s/M_0^w in the case with SL was smaller than that without SL, while the RMSE value for k_{ex} was almost the same. The bias in the case with SL was slightly smaller than that in the case without SL for both k_{ex} and M_0^s/M_0^w (Fig. 4).

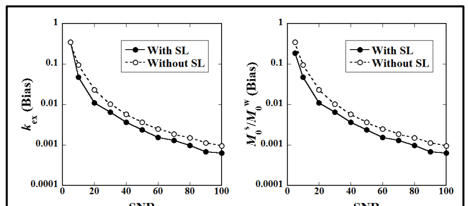

Fig. 4 (a) (b)

In our method, matrix operation was used not only for solving the time-dependent Bloch equations but also for taking into account the relaxation and chemical exchange effects during RF-pulse irradiation. Although an ordinary differential equation (ODE) solver can also be used, the computation time was considerably reduced when using our method (by a factor of approximately 5000 compared to the ODE solver), indicating that our method is preferable to estimating parameters such as chemical exchange rates using the NLSQ method. In this study, we treated the 2-pool CEST model as an illustrative example. However, CEST agents often have more than one type of exchangeable proton. For such cases, it is necessary to expand the Bloch equations to multi-pool exchange models. Our method can easily be extended to multi-pool models by modifying the matrix **A** given by Eq. (2).

CONCLUSION

We presented a simple and fast method for solving the time-dependent Bloch equations in CEST MRI with SL, and proposed a new method for quantifying chemical exchange rates from CEST MRI with and without SL using this method. Our results suggest that the CEST MRI with SL is more reliable than that without SL for quantifying parameters such as chemical exchange rates, and that our method will be useful and effective for this purpose.

REFERENCES

[1] Jin T, et al. Magn Reson Med 2011; 65:1448-1460. [2] Murase K, et. al. Magn Reson Imaging 2011; 29:126-131.