Published in final edited form as:

Magn Reson Imaging. 2009 October ; 27(8): 1074–1087. doi:10.1016/j.mri.2009.05.023.

Rotating frame relaxation during adiabatic pulses versus conventional spin-lock: simulations and experimental results at 4T

Silvia Mangia^{*}, Timo Liimatainen, Michael Garwood, and Shalom Michaeli

Center for Magnetic Resonance Research, Department of Radiology, University of Minnesota, Minneapolis, Minnesota, USA

Abstract

Spin relaxation taking place during radiofrequency (RF) irradiation can be assessed by measuring the longitudinal and transverse rotating frame relaxation rate constants ($R_{1\rho}$ and $R_{2\rho}$). These relaxation parameters can be altered by utilizing different settings of the RF irradiation, thus providing a useful tool to generate contrast in MRI. In this work we investigate the dependencies of $R_{1\rho}$ and $R_{2\rho}$ due to dipolar interactions and anisochronous exchange (i.e., exchange between spins with different chemical shift $\delta\omega \neq 0$) on the properties of conventional spin-lock and adiabatic pulses, with particular emphasis on the latter ones which were not fully described previously. The results of simulations based on relaxation theory provide a foundation for formulating practical considerations for *in vivo* applications of rotating frame relaxation methods. Rotating frame relaxation measurements obtained from phantoms and from the human brain at 4T are presented to confirm the theoretical predictions.

Keywords

rotating frame relaxations; spin-lock; adiabatic pulses; dipolar interactions; anisochronous exchange; MR contrast

A. Introduction

Rotating frame relaxation rate constants, $R_{1\rho}$ and $R_{2\rho}$, characterize relaxation during radiofrequency (RF) irradiation when the magnetization vector $\vec{M}$ is aligned with or perpendicular to the direction of the effective magnetic field ($\vec{B}_{\text{eff}}$), respectively. $R_{1\rho}$ and $R_{2\rho}$ reflect the features of the spin dynamic processes, and depend on the properties of the RF irradiation [1-4]. The latter feature creates the possibility to “manipulate” the measured $R_{1\rho}$ and $R_{2\rho}$ by choosing different settings of the RF irradiation, thus leading to the generation of MR contrast [5,6]. Whereas the spin-lattice relaxation rate constant R_1 is sensitive to dynamic processes close to the Larmor frequency ($\omega_0/(2\pi)$), which is in the order of MHz for standard *in vivo* applications, in the majority of cases the rotating frame relaxations are additionally

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^{*}Corresponding author Silvia Mangia, Ph.D. Center for Magnetic Resonance Research University of Minnesota 2021 Sixth Street SE Minneapolis, MN 55455 USA Tel. 612-626-2001 FAX: 612-626-2004 Email: mangia@cmrr.umn.edu.

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sensitive to fluctuations close to the effective frequency ($\omega_{\text{eff}}/(2\pi)$, where $\omega_{\text{eff}} = \gamma B_{\text{eff}}$ and γ is the gyromagnetic ratio), which is in the order of kHz. The enhanced sensitivity of $R_{1\rho}$ and $R_{2\rho}$ to molecular dynamics in the kHz range makes rotating frame relaxations a practical tool for gaining information about water spin dynamics and interactions with endogenous macromolecules [7]. Application of these methods holds great potential for addressing several biological questions, especially at high magnetic fields.

A typical method to measure $R_{1\rho}$ and $R_{2\rho}$ is the conventional spin-lock (SL) experiment, where a continuous-wave (CW) pulse is applied on- or off-resonance (for review see [4]). In the presence of the CW pulse, relaxations due to different relaxation channels, such as dipolar interaction and exchange, are well investigated [3,8]. Advances in RF pulse design and experimental capabilities have led to the routine use of pulse sequences based on adiabatic RF pulses for *in vivo* applications [9]. Rotating frame relaxation experiments can also be performed with adiabatic pulses [10]. Although the theoretical investigation of rotating frame relaxations during adiabatic RF pulses has been recently extended [10,11], much work remains to be done to characterize the influence of the experimental parameters on the measured relaxations.

The aim of the present work is to describe the effects of different RF irradiation parameters on either CW (spin-lock) or adiabatic $R_{1\rho}$ and $R_{2\rho}$, due to dipolar interactions in the weak field limit (*i.e.*, fast motional regime) and in the presence of anisochronous exchange (*i.e.*, exchange between spins with different chemical shifts, $\delta\omega \neq 0$) in the fast exchange regime (FXR). Specifically, the simulations presented here exploit the dependencies of $R_{1\rho}$ and $R_{2\rho}$ on *i*) the amplitude and direction of the effective field during the CW SL pulse, and *ii*) the pulse length, bandwidth, and RF peak amplitude during adiabatic rotation. Finally the effect on relaxations introduced by different pulse modulation functions of adiabatic pulses is discussed, and a practical perspective of rotating frame relaxation methods for *in vivo* applications is provided. Experimental results obtained from phantoms and from the human brain at 4T are presented to confirm some relevant theoretical predictions.

B. Theoretical overview

B.1. Properties of the effective magnetic field during SL versus adiabatic rotation

During the CW SL pulse, $\vec{B}_{\text{eff}}$ is tilted from the quantization axis z' (*i.e.*, the longitudinal axis of the first rotating frame) by the angle α (Figure 1a), defined as:

$$\alpha = \tan^{-1} \left(\frac{\omega_1}{\Delta\omega} \right), \quad [1]$$

where ω_1 is the amplitude of the SL pulse in rad/s and $\Delta\omega = (\omega_0 - \omega_{\text{RF}})$ is the frequency offset in rad/s. The amplitude of the effective frequency $\omega_{\text{eff}} (= \gamma B_{\text{eff}})$, where γ is the gyromagnetic ratio) is given by:

$$\omega_{\text{eff}} = \sqrt{\omega_1^2 + \Delta\omega^2}. \quad [2]$$

During an adiabatic pulse, both amplitude and frequency are typically modulated (Figure 2a). In the present study, we use adiabatic pulses of the hyperbolic secant (HS_n) family [9,12,13]. The amplitude of HS_n pulses is given by:

$$\omega_1(t) = \omega_1^{\text{max}} \text{sech} \left(\beta \left(2t/T_p - 1 \right)^n \right), \quad [3]$$

where $\omega_1^{\max}$ is the maximum value of $\omega_1(t)$ in rad/s, β is a truncation factor ($\text{sech}(\beta) = 0.01$), T_p is the pulse duration, $t \in [0, T_p]$, and $n = 1$ and 4 for HS1 and HS4 pulses, respectively. With respect to the carrier frequency ω_c , i.e., the center frequency in the bandwidth (BW) of interest, the frequency modulation for HS1 pulse is given by:

$$\omega_{\text{RF}}(t) - \omega_c = A \tanh\left(\beta\left(2t/T_p - 1\right)\right), \quad [4]$$

and for the HS4 pulse is given by:

$$\omega_{\text{RF}}(t) - \omega_c = A \int_0^t \text{sech}^2\left(\beta\left(2t'/T_p - 1\right)\right) dt', \quad [5]$$

where A is the amplitude of the frequency sweep in rad/s, with the bandwidth of the pulse being $BW = 2A$. One fundamental property of the adiabatic pulse is the so time-bandwidth product given by:

$$R = (AT_p) / \pi. \quad [6]$$

From Eq. [6], it is evident that at a given T_p settings, the amplitude of the frequency sweep (A) is determined by the R -value. Note that if A is given in Hz, then $R = 2AT_p$, and consequently:

$$BW = R/T_p. \quad [7]$$

During the application of adiabatic pulses, both magnitude and orientation of the effective field vary continuously (Figure 2c,d); therefore, $\omega_{\text{eff}}(t)$ and $\alpha(t)$ are functions of time:

$$\omega_{\text{eff}}(t) = \sqrt{\omega_1^2(t) + \Delta\omega^2(t)}, \quad [8]$$

$$\alpha(t) = \tan^{-1}\left(\frac{\omega_1(t)}{\Delta\omega(t)}\right). \quad [9]$$

The time-dependent precession angle around the effective field direction is given by:

$$\psi(t) = \int_0^t \omega_{\text{eff}}(\zeta) d\zeta. \quad [10]$$

The adiabatic condition is well satisfied when the change in orientation of the effective field is significantly slower than the rotation of $\vec{M}$ around the effective field: $\omega_{\text{eff}} \gg |d\alpha/dt|$. An adiabatic pulse which performs a π rotation of $\vec{M}$ (Figure 2b) is called adiabatic full passage (AFP).

B.2. Relaxations during conventional spin-lock versus adiabatic rotation

The relaxation mechanisms occurring during the application of CW pulses depend on the initial orientation of $\vec{M}$ relative to $\vec{B}_{\text{eff}}$. Specifically, when $\vec{M}$ is collinear with $\vec{B}_{\text{eff}}$, the relaxation is

governed solely by $R_{1\rho}$ process; if the angle between $\vec{M}$ and $\vec{B}_{\text{eff}}$ is 90° , the relaxation is governed by $R_{2\rho}$. For any other orientation, the relaxation is governed by the combination of $R_{1\rho}$ and $R_{2\rho}$. Typically, the CW SL $R_{1\rho}$ experiment is performed by tilting $\vec{M}$ to the $x'y'$ plane, followed by application of the CW pulse with a 90° phase difference relative to the phase of the excitation pulse phase [14]; for the $R_{2\rho}$ measurements the phase difference needs to be 0° or 180° , as was originally proposed by Solomon [15].

When applying adiabatic pulses, the relaxation mechanisms occurring during the RF irradiation depend on the initial orientation of $\vec{M}$ [10]. In fact, when $\vec{M}$ is originally aligned along the z' axis and the adiabatic pulse is applied, $\vec{M}$ remains oriented along the time-dependent direction of the effective field. In this case the decay of $\vec{M}$ is characterized by the time-dependent rate contrast $R_{1\rho}(t)$. If $\vec{M}$ is instead initially in the $x'y'$ plane and the adiabatic pulse is applied, $\vec{M}$ precesses in the plane perpendicular to $\vec{B}_{\text{eff}}$, and the relaxation is characterized by $R_{2\rho}(t)$.

In the following, we will overview the formalism utilized to describe relaxation due to dipolar interactions in the case of two identical spins and anisochronous exchange. The formalism was initially formulated to describe relaxation during CW SL experiments, where ω_{eff} and α are constant during the RF irradiation [1,2,16,17]. Recently, the theoretical expressions of $R_{1\rho}(t)$ and $R_{2\rho}(t)$ have been generalized to the case of time-dependent $\omega_{\text{eff}}(t)$ and $\alpha(t)$ [6,18,19]. It has been shown that the relaxations during adiabatic rotation in the weak field approximation could be represented as an average of instantaneous time-dependent contributions due to the different relaxation channels:

$$\bar{R}_{1,2\rho} = \frac{1}{T_p} \int_0^{T_p} R_{1,2\rho,\text{ex}}(t) dt + \frac{1}{T_p} \int_0^{T_p} R_{1,2\rho,\text{dd}}(t) dt, \quad [11]$$

where $R_{1,2\rho,\text{dd}}$ and $R_{1,2\rho,\text{ex}}$ are the rotating frame relaxations due to dipolar interactions and anisochronous exchange, respectively.

B.2.a. Relaxations due to dipolar interactions: two identical (like) spins—For a system of two equivalent nuclei of spin $I = 1/2$ and gyromagnetic ratio $\gamma = 2\pi \cdot 42.576 \cdot 10^6 \text{ rad/(sT)}$ in a single site, $R_{1\rho,\text{dd}}(t)$ and $R_{2\rho,\text{dd}}(t)$ due to dipolar fluctuations can be given by a simple, isolated two-spin description [6,11,16,18]:

$$R_{1\rho,\text{dd}}(t) = \frac{3}{20} b^2 \left[\frac{3\sin^2\alpha(t) \cos^2\alpha(t)}{1+\omega_{\text{eff}}^2(t) \tau_c^2} + \frac{3\sin^4\alpha(t)}{1+4\omega_{\text{eff}}^2(t) \tau_c^2} + \frac{2+3\sin^2\alpha(t)}{1+\omega_0^2 \tau_c^2} + \frac{8-6\sin^2\alpha(t)}{1+4\omega_0^2 \tau_c^2} \right], \quad [12]$$

$$R_{2\rho,\text{dd}}(t) = \frac{3}{80} b^2 \left[3(3\cos^2\alpha(t) - 1)^2 + \frac{30\sin^2\alpha(t) \cos^2\alpha(t)}{1+\omega_{\text{eff}}^2(t) \tau_c^2} + \frac{3\sin^4\alpha(t)}{1+4\omega_{\text{eff}}^2(t) \tau_c^2} + \frac{(20-6\sin^2\alpha(t))}{1+\omega_0^2 \tau_c^2} + \frac{8+12\sin^2\alpha(t)}{1+4\omega_0^2 \tau_c^2} \right],$$

[13]

where $b = -\mu_0 \hbar \gamma^2 / (4\pi r^3)$, $\mu_0 = 4\pi \cdot 10^{-7} \text{ H/m}$ is the vacuum permeability, $\hbar = 1.055 \cdot 10^{-34} \text{ Js}$ is Planck's constant, r is the internuclear distance in m, τ_c is the rotational correlation time in s characterizing the tumbling of the magnetic dipole. Eqs. [12-13] are written in a general form where ω_{eff} and α are time-dependent, and they can be used to calculate the time-courses of

$R_{1\rho,dd}$ or $R_{2\rho,dd}$ values during the adiabatic pulse (Eq. [11]). Eqs. [12-13] apply also for a CW SL experiment, with the only difference being that ω_{eff} and α are time-invariant [16]. For comparison purposes, the equations for the free precession relaxation rate constants are provided [20]:

$$R_{1,dd} = \frac{3}{20} b^2 \left[\frac{1}{1 + \omega_0^2 \tau_c^2} + \frac{4}{1 + 4\omega_0^2 \tau_c^2} \right], \quad [14]$$

$$R_{2,dd} = \frac{3}{80} b^2 \left[3 + \frac{5}{1 + \omega_0^2 \tau_c^2} + \frac{2}{1 + 4\omega_0^2 \tau_c^2} \right]. \quad [15]$$

B.2.b. Relaxations due to anisochronous exchange—We consider a two-site

chemical exchange process between sites m and q : $m \xrightleftharpoons[k_{-1}]{k_1} q$. The difference in chemical shifts between sites m and q is defined by $\delta\omega$ in rad/s. Here k_1 and k_{-1} represent the forward and backward exchange rate constants obeying the McConnell relationship [21]:

$$\tau_{\text{ex}} = \frac{P_m}{k_{-1}} = \frac{P_q}{k_1}, \quad [16]$$

and for anisochronous exchange in the fast regime

$$\tau_{\text{ex}} = \frac{1}{k_{\text{ex}}} \ll \delta\omega^{-1}. \quad [17]$$

Exchange-induced $R_{1\rho,\text{ex}}$ and $R_{2\rho,\text{ex}}$ under CW SL irradiation were derived in [1,2]:

$$R_{1\rho,\text{ex}} = P_m P_q \delta\omega^2 \sin^2 \alpha \frac{\tau_{\text{ex}}}{1 + (\omega_{\text{eff}} \tau_{\text{ex}})^2}, \quad [18]$$

$$R_{2\rho,\text{ex}} = P_m P_q (\delta\omega)^2 \left[\cos^2 \alpha \tau_{\text{ex}} + \frac{1}{2} \sin^2 \alpha \frac{\tau_{\text{ex}}}{1 + (\omega_{\text{eff}} \tau_{\text{ex}})^2} \right]. \quad [19]$$

The corresponding time-dependent relaxation functions during adiabatic rotation were detailed in [19]. Theory shows $R_{1\rho,\text{ex}}$ and $R_{2\rho,\text{ex}}$ to be dependent on the choice of the amplitude- and frequency-modulation functions of adiabatic pulses *via* their $\alpha(t)$ and $\omega_{\text{eff}}(t)$ dependencies. The exchange-induced $R_{1\rho,\text{ex}}(t)$ during adiabatic rotation follows from the relaxation functions derived in [10]:

$$R_{1\rho,\text{ex}}(t) = P_m P_q (\delta\omega)^2 \left[\sin \alpha(t) \cos \alpha(t) \int_{-\infty}^{\infty} \cos [\psi(t - \tau) - \psi(t)] e^{-\tau/\tau_{\text{ex}}} d\tau \right]. \quad [20]$$

In the FXR, Eq. [20] simplifies to

$$R_{1\rho,\text{ex}}(t) = P_m P_q \delta \omega^2 \sin^2 \alpha(t) \frac{\tau_{\text{ex}}}{1 + (\omega_{\text{eff}}(t) \tau_{\text{ex}})^2}. \quad [21]$$

The exchange-induced $R_{2\rho,\text{ex}}$ in the FXR during the adiabatic pulses is given by [18]:

$$R_{2\rho,\text{ex}}(t) = P_m P_q \delta \omega^2 \cos^2 \alpha(t) \tau_{\text{ex}}. \quad [22]$$

Note that the time-dependence of $R_{2\rho,\text{ex}}(t)$ originates from the time-dependence of $\alpha(t)$ and not from $\omega_{\text{eff}}(t)$. As in the presence of dipolar interactions, Eqs. [21-22] can be used to calculate the time-courses of the instantaneous contributions to be used in Eq. [11] to calculate the average relaxation rates during adiabatic pulses.

Finally, it is well known that anisochronous exchange does not contribute to the free precession longitudinal relaxation R_1 , but it generates a free precession transverse relaxation rate which is given by [3]

$$R_{2,\text{ex}} = P_m P_q \delta \omega^2 \tau_{\text{ex}}. \quad [23]$$

C. Material and methods

Simulations

The RF pulses with different amplitude and frequency modulation functions were generated using an even time scale with 500 points per millisecond according to Eqs. [3-5]. Then, $\omega_{\text{eff}}(t)$ and $\alpha(t)$ were computed according to Eqs. [8] and [9], respectively. Relaxation rates in the presence of dipolar interactions and anisochronous exchange were calculated separately for each time point, *i.e.* for certain $\alpha(t)$ and $\omega_{\text{eff}}(t)$, according to Eqs. [12,13], and [18,19,21,22] respectively. The time average over the pulse time duration was then estimated by numerical integration, according to Eq. [11]. All simulations were carried out using Matlab 7.3 platform (Mathworks Inc., Natick, CA).

Phantom experiments

Phantom experiments were performed on 4-T/90-cm Oxford magnet interfaced to Varian INOVA console. A linear coil consisting of a single loop with a 2-cm diameter was used. A water/ethanol sample was prepared at the molar ratio ~1.1:0.9 to investigate the dependencies of adiabatic $R_{1\rho}$ and $R_{2\rho}$ on RF parameters in the case of anisochronous exchange. Relaxation measurements were performed on the single line resulting from the fast exchange between protons from water and the hydroxyl group of ethanol. Adiabatic $R_{1\rho}$ and $R_{2\rho}$ measurements were performed by placing a train of HS_n pulses prior to or after the coherent excitation by adiabatic half passage (AHP) pulse, respectively. Localization was achieved by adiabatic selective refocusing (LASER) [9] for $5 \times 5 \times 5 \text{ mm}^3$ voxel selection. The pulse trains consisted of a variable number of HS1 or HS4 pulses (4, 8, 16, 32 and 64 pulses), with phases prescribed according to MLEV-4,-8,-12,-16,-32 [22] and $T_p = 6 \text{ ms}$. For exploiting the ω_1^{max} dependence, $\omega_1^{\text{max}}/(2\pi)$ values from 1.75 kHz to 4.4 kHz were used. For exploiting the BW dependency, R -values of 15, 20, 30 and 40 were used, corresponding to $BW = 2.5, 3.3, 5.0$ and 6.6 kHz for $T_p = 6 \text{ ms}$, respectively. The relaxation rate constants were calculated from the signal intensities using a linear regression algorithm with a mono-exponential decay function.

In vivo experiments

Two healthy subjects were investigated on the same 4-T/90-cm magnet used for phantoms experiments. A shielded quadrature transmit/receive half-volume RF coil consisting of two geometrically decoupled single-turn coils with diameter of 12 cm was used for spectroscopic measurements similar to the ones performed on phantoms, while a TEM volume coil [23] was used for imaging experiments. For the MRS experiments, the localization ($VOI = 20 \times 20 \times 20 \text{ mm}^3$) was performed as described for phantom experiments, with $TE = 39 \text{ ms}$, $TR = \text{variable}$ from 4.5 to 13 s (to comply with the FDA limits on the specific absorption rate, SAR). Other parameters were: number of pulses in the AFP pulse train was 4, 8, 16 and 32; $T_p = 6 \text{ ms}$. To investigate the BW dependency, we used R -values of 10 and 20 which correspond to $BW = \sim 1.6$ and 3.3 kHz , respectively, with $\omega_1^{\max}/(2\pi) = 1.25 \text{ kHz}$; to investigate the $\omega_1^{\max}$ dependency, we used $\omega_1^{\max}/(2\pi)$ values of 0.9 and 1.7 kHz , with R -value = 10; finally, to investigate the dependency on the modulation functions, we used HS1 or HS4 pulses with R -value = 20 and $\omega_1^{\max}/(2\pi) = 1.25 \text{ kHz}$.

The purpose of the imaging experiments was to compare the contrast (defined as the relative change in measured relaxation rate constants) generated by varying RF parameters of CW SL and adiabatic irradiation in the $R_{1\rho}$ configuration. Images were acquired by fast spin echo readout, $TR = 5 \text{ s}$, $TE = 0.60 \text{ s}$, matrix 128×128 , $FOV = 20 \text{ cm} \times 20 \text{ cm}$, and slice-thickness = 3 mm . In the adiabatic $R_{1\rho}$ configuration, a train of 4, 8, 12, or 16 HS1 or HS4 pulses was placed prior to the spectroscopic or imaging readout. The RF parameters of the adiabatic pulses were: $T_p = 6 \text{ ms}$, HS1 modulation functions with R -value = 20 and $\omega_1^{\max}/(2\pi) = 1.25 \text{ kHz}$, or HS4 modulation function with R -value = 20, and $\omega_1^{\max}/(2\pi) = 0.885 \text{ kHz}$. RF parameters of the two adiabatic pulses were chosen to achieve comparable RF power depositions. For the CW SL experiment, composite pulses were generated by placing a CW pulse with varying T_p between two 8-ms adiabatic half passage (AHP) pulses as described in [24]. The duration of the spin-locking time was the same as that used for the adiabatic $R_{1\rho}$ measurements (namely 24, 48, 72 and 96 ms), while $\omega_1^{\max}/(2\pi) = 0.625 \text{ kHz}$, which resulted in RF power deposition similar to the adiabatic $R_{1\rho}$ experiment. The carrier frequency of these composite pulses was chosen on resonance, or 0.625 kHz off-resonance from the water resonance, thus locking $\vec{M}$ at $\alpha = 0^\circ$ or 45° , respectively. The acquisition time of each relaxation map was $\sim 5 \text{ min}$.

SAR monitoring for human studies

The RF power delivered to the coil was limited to a safe operating range using the hardware monitoring module of the Varian console. In addition, the RF power output over the full range of settings used in these experiments was measured with an oscilloscope connected to the coil port. From these measured values, the average RF power delivered to the coil was computed by integration of all RF pulses in the sequence, and SAR was estimated assuming a tissue load of 3 kg in the coil. When using the longest pulse train, the estimated SAR was always below the FDA limit of 3 W/kg averaged over the head for 10 min (<http://www.fda.gov/cdrh/ode/mri340.pdf>).

D. Simulation Results

D. 1 $R_{1\rho}$ and $R_{2\rho}$ during continuous-wave spin-lock

Dependency of rotating frame relaxation rate constants on angle α —The dependencies of $R_{1\rho,dd}$ and $R_{2\rho,dd}$ during CW SL pulse on the rotational correlation time (τ_c) and a in the presence of dipolar interactions are shown in Figure 3a,b. It can be seen that, for dipolar interactions in the extreme narrowing case ($\omega_0\tau_c \ll 1$, $\omega_1 \ll \omega_0$), the $R_{1\rho}$ reaches its maximum value for $\alpha = 90^\circ$. In this condition ($\alpha = 90^\circ$), for dipolar interaction between identical spins, $R_{1\rho,dd} \equiv R_{2\rho,dd}$ (Eqs. [12,15]) [16]. On the other hand, the transverse relaxation $R_{2\rho,dd}$ reaches its minimal value at $\alpha = 90^\circ$, and at this angle $R_{2\rho,dd} < R_{1\rho,dd}$. This feature is inherently

different from the relationship between free precession relaxation rate constants R_1 and R_2 , since $R_2 \geq R_1$. It can be seen also from Figure 3a,b that the dependence of the rate constants on α is pronounced for $\tau_c > \sim 5 \cdot 10^{-9}$ s, and becomes negligible for shorter correlation times (fast tumbling).

In Figure 3c,d the dependency of $R_{1p,ex}$ and $R_{2p,ex}$ on the exchange correlation time (τ_{ex}) and the angle α are shown. The calculations were performed using Eqs. [21-22]. In the FXR, $R_{1p,ex}$ increases from zero to its maximum value and then decreases, reaching its maximum around $\tau_{ex} = 2\pi/\omega_{eff}$. In this region the greatest change of $R_{1p,ex}$ is observed. For $R_{2p,ex}$ a significant dependence of the rate constant on τ_{ex} is apparent as the system moves toward the slower correlation times and approaches (still in the FXR) the intermediate exchange regime. On the other hand, in the fast exchange limit, $R_{2p,ex} \rightarrow 0$.

Dependency of rotating frame relaxation rate constants on ω_{eff} —The dependencies of $R_{1p,dd}$ and $R_{2p,dd}$ during CW SL pulse on τ_c and ω_{eff} are shown in Figure 4a,b for $\alpha = 45^\circ$. It can be seen that over a wide range of τ_c values in the fast tumbling regime [10^{-11} - 10^{-9}] the dependence of the rate constants on ω_{eff} (in the range of $0 < \omega_{eff}/(2\pi) < 10$ kHz) is negligibly small at $\omega_0/(2\pi) = 169$ MHz. On the other hand, the dependence of the relaxation rates on τ_c is pronounced. The exchange-induced relaxation rate constants, $R_{1p,ex}$ and $R_{2p,ex}$, exhibit greatest change near $\tau_{ex} = 2\pi/\omega_{eff}$. Figure 4 c,d show a smaller change of $R_{2p,ex}$ as a function of ω_{eff} as compared to the $R_{1p,ex}$, as predicted by Eqs. [21-22]. Indeed, the dependence of $R_{2p,ex}$ on ω_{eff} (the second term in Eq. [21]) is a factor of $1/2$ smaller than the $R_{1p,ex}$ dependence on ω_{eff} . As in the case for the dipolar interactions, the dependence of $R_{1p,ex}$ and $R_{2p,ex}$ on τ_{ex} is pronounced.

The generation of contrast with continuous-wave spin-lock—The dependency of rotating frame relaxations using CW SL pulses on α and ω_{eff} provides the possibility to generate contrast *in vivo*. We have shown that the dependence of R_{1p} and R_{2p} on α is more significant as compared to ω_{eff} in the fast motional regime. From a practical perspective, α can be changed by changing either ω_1^{max} or the frequency offset (Eq. [1]). In fact, it is common to apply the CW SL pulse both on- or off-resonance and with different power settings in order to obtain independent relaxation measurements, thus generating contrast in MRI [25,26]

D. 2 R_{1p} and R_{2p} during adiabatic rotation

In the following section, we describe relaxations during AFP pulses, when the adiabatic condition is well satisfied.

Dependency of rotating frame relaxation rate constants on pulse duration and bandwidth—In Figure 5 the dependencies of $R_{1p,dd}$ and $R_{2p,dd}$ on the time duration (T_p) and bandwidth (BW) of the AFP pulse are shown. The calculations demonstrate an important property of the frequency swept pulses: the relaxation rates are affected by how the frequency sweep is achieved during the pulse rather than for how long the AFP pulse is applied. Indeed, when T_p increases, but the time-bandwidth product (R -value) of the pulse is constant (Figure 5a,b), $R_{1p,dd}$ and $R_{2p,dd}$ change with T_p . In this case, when increasing T_p , the BW of the pulse decreases according to R/T_p (Eq. [7]). The maximum variation observed in the range of the correlation times investigated corresponds to $\sim 25\%$ increase for $R_{1p,dd}$ and $\sim 10\%$ decrease for $R_{2p,dd}$, when T_p increases from 2 to 16 ms, in the case of R -value = 80 and $\omega_1^{max}/(2\pi) = 10$ kHz. As shown in Figure 5c,d, such variations are not observed increasing T_p for fixed BW , which is achieved by matching accordingly the R -value of the pulse (Eq. [7]). Similarly to $R_{1,2p,dd}$, the exchange-induced relaxation rate constants ($R_{1,2p,ex}$) depend on T_p when BW varies (Fig 6a,b), but remain constant when the R -value of the pulse scaled with

T_p , keeping the BW constant (Figure 6c,d). Note that when both BW and $\omega_1^{\max}/(2\pi)$ are kept constant (Figure 6c), the maximum of $R_{1p,ex}$ occurs at the same τ_{ex} for different T_p values.

Dependency of rotating frame relaxation rate constants on $\omega_1^{\max}/(2\pi)$ and pulse modulation functions—The dependencies of $R_{1p,dd}$ and $R_{2p,dd}$ on $\omega_1^{\max}/(2\pi)$ are shown in Figure 7 a,b for the HS1 pulse and in Figure 7 c,d for the HS4 pulse. It can be seen that, in the range of $\omega_1^{\max}/(2\pi)$ between 2 - 10 kHz, $R_{1p,dd}$ increases by 20% for HS1 and by 44% for HS4, whereas $R_{2p,dd}$ decreases by 6% for HS1 and by 10% for HS4. The range of the $\omega_1^{\max}/(2\pi)$ chosen here ensures the adiabatic condition to be satisfied. The reason why relative changes are larger for HS1 compared to HS4 pulse originates from the different amplitude modulation functions of the pulses. The modulation functions of HS4 are in fact stretched versions of those used in HS1 (Figure 2a), and resemble more closely the case of a CW pulse, for which the dependency of rates on $\omega_1^{\max}/(2\pi)$ is maximum (Figure 4).

As predicted by Eqs. [21-22], $R_{1p,ex}$ but not $R_{2p,ex}$ exhibits a Lorentzian - like dependency both on τ_{ex} and on $\omega_1^{\max}/(2\pi)$ via its ω_{eff} dependence (Figure 7). Similarly to the previous case of dipolar interactions, $R_{2p,ex}$ decreases with $\omega_1^{\max}/(2\pi)$, and relative changes of $R_{1p,ex}$ and $R_{2p,ex}$ are larger for HS4 as compared to HS1 pulses.

Generating contrast by altering the modulation functions of adiabatic pulses—Figures 9 and 10 show the contrast generated by HS1 and HS4 pulses in the case of dipolar interactions and anisochronous exchange, defined as $(R_{1,2p,dd,ex}(HS4) - R_{1,2p,dd,ex}(HS1))/R_{1,2p,dd,ex}(HS1) \cdot 100$, as a function of $\omega_1^{\max}/(2\pi)$ at a fixed BW , and as a function of BW at a fixed $\omega_1^{\max}/(2\pi)$, respectively. The plots demonstrate how the choice of BW and $\omega_1^{\max}/(2\pi)$ of HS1 and HS4 pulses can result in different contrasts. The contrast generated by different pulse modulation functions can be drastically different between anisochronous exchange and dipolar interaction at similar $\omega_1^{\max}/(2\pi)$ and BW , to the point that the contribution of one relaxation pathway can be eventually neglected from the contrast generated by alternating HS1 vs HS4 pulses. For instance, for the choice of intrinsic parameters shown in Figures 9 and 10, the $R_{1p,ex}$ contrast is zero when $\omega_1^{\max}/(2\pi) \sim 8$ kHz (Figure 9c) and when $BW \sim 3$ kHz (Figure 10c).

To summarize, results from simulations show that MR contrast can be generated with adiabatic pulses by using different pulse modulation functions, different $\omega_1^{\max}$, and different amplitudes of the frequency sweep (A) of the AFP pulses, whereas the pulse length of the AFP pulse in itself does not affect the relaxations. The influence of these parameters on the rotating relaxation rate constants strongly depends on the relaxation channel. For example, whereas the dependency of $R_{1,2p,dd}$ on $\omega_1^{\max}/(2\pi)$ is relatively small (Figure 7), it becomes significant in the case of the anisochronous exchange (Figure 8). This may provide a possibility to separate relaxation mechanisms *in vivo*.

E. Experimental Results

Results from the ethanol phantom (Figure 11) confirmed the theoretical predictions of the dependencies of adiabatic $RR_{1p,ex}$ and $R_{2p,ex}$ on $\omega_1^{\max}/(2\pi)$ (Figure 9c,d) and BW (Figure 10 c,d). In fact, $R_{1p,ex}$ values decreased with both $\omega_1^{\max}/(2\pi)$ and BW , while R_{2p} values decreased with $\omega_1^{\max}/(2\pi)$ but increased with BW . In addition, $R_{1p,ex}$ (HS4) was found to be greater than $R_{1p,ex}$ (HS1), while $R_{2p,ex}$ (HS4) was found to be smaller than $R_{2p,ex}$ (HS1).

Results from the human MRS experiments demonstrate that altering the modulation functions of the adiabatic pulses is the most effective way to generate contrast *in vivo* when changing the RF parameters of adiabatic pulses. Indeed, $R_{1\rho}$ and $R_{2\rho}$ values measured from the voxel localized in the visual cortex changed by 4% and -9% when increasing $\omega_1^{\max} / (2\pi)$ from 0.9 to 1.7 kHz at R -value = 10, respectively, and changed by 20% and 4% when increasing BW from 1.7 to 3.3 kHz at $\omega_1^{\max} / (2\pi) = 1.25$ kHz, respectively. However, differences in $R_{1\rho}$ and $R_{2\rho}$ values were considerably bigger, 63% and -13%, respectively, when alternating between the modulation functions of HS1 vs HS4 pulses at similar BW and $\omega_1^{\max} / (2\pi)$.

Results from the human MRI experiments were in agreement with theoretical predictions and with results obtained by MRS. In CW SL $R_{1\rho}$ experiments, varying the angle of the spin-lock α relatively to z' axis resulted in different $R_{1\rho}$ values (Figure 12a,b). Likewise, relaxation rates changed in adiabatic $R_{1\rho}$ experiments when varying the pulse modulation functions at constant BW and $\omega_1^{\max} / (2\pi)$ (Figure 12c,d). Specifically, the average CW SL $T_{1\rho}$ ($= 1/R_{1\rho}$) values measured from an ROI localized in the visual cortex were (84 ± 9) ms and (163 ± 20) ms for $\alpha = 0^\circ$ and 45° , respectively; the average adiabatic $T_{1\rho}$ values from the same ROI were (231 ± 30) ms and (160 ± 14) ms for HS1 and HS4 pulses, respectively.

F. Contrast generated by spin-lock and adiabatic pulses: a practical perspective

Rotating frame relaxation methods offer a powerful tool to generate MR contrast *in vivo* which can assess motional regimes relevant for biological applications. Notably, by proper modeling of the relaxation processes (see section B), the simultaneous analysis of several independent measurements of $R_{1,2\rho}$ obtained with different experimental settings of the RF irradiation potentially allows the extraction of fundamental relaxation parameters, as for instance rotational, translational or exchange correlation times. The estimation of these fundamental parameters holds great potential to quantitatively characterize the functionality of the tissue *in vivo*, since the intrinsic relaxation parameters might provide sensitive markers to differentiate healthy from diseased state [25]. Due to enhanced sensitivity to slow molecular motion as compared to the free precession relaxation rates, $R_{1\rho}$ MRI has proven to be sensitive to different factors related to cell death in several experimental disease models [27,28]. For example, in rat models of cerebral ischemia, the change in $R_{1\rho}$ relaxation measurements were associated with the tissue changes resulting from cessation of blood flow [29]. Importantly, the acute changes in $R_{1\rho}$ correlated with the outcome of the tissue even in those cases where initial changes in water diffusion transiently recovered upon reperfusion [27,30]. $R_{1\rho}$ MRI has been shown to be useful in detecting cartilage degeneration [31], in revealing tissue damage occurring in the amygdala stimulation model of epilepsy [28], in characterizing neoplastic tissue [32] and in providing an early surrogate marker for treatment response in tumors receiving chemotherapy [32] or gene therapy [33]. However, clinical exploitation of $R_{1\rho}$ contrast using clinical scanners has been delayed because of several technical obstacles, such as high RF energy deposition into the tissue. In addition, the paucity of $R_{2\rho}$ relaxation studies *in vivo* is a consequence of experimental challenges affecting accurate measurements obtained with CW SL methods.

Whereas the CW SL method is particularly flexible due to its great sensitivity to experimental settings (RF amplitude and frequency offset), the *in vivo* implementation of CW SL sequences has been shown to be problematic due to a variety of experimental problems, such as uncertainty of tilt angles due to variations of B_0 and B_1 [34,35]. These artifacts could be partially removed by proper pulse sequence design, although often such techniques are not easily implementable on clinical scanners. In addition, even if in principle CW SL can utilize low locking power, at high magnetic field this choice might be insufficient to lock spins, thus

leading to severe image artifacts. On the other hand, the utilization of high $\omega_1^{\max}$ is limited by SAR. With respect to adiabatic pulses, contrast can be generated by using different pulse modulation functions (for example HS1 and HS4), $\omega_1^{\max}$, and BW . However, for *in vivo* applications in humans, the generation of the contrast based on increasing $\omega_1^{\max}$ is not usually feasible. Indeed, for short pulse lengths (e.g., $T_p = 2$ ms) just the minimum $\omega_1^{\max}$ that achieves adiabaticity can be beyond the achievable range of $\omega_1^{\max}$ for human studies. Overall, the preferable choice to generate contrast *in vivo* by adiabatic pulses is by using different pulse modulation functions. Additionally, the insensitivity of the adiabatic pulses to B_1 inhomogeneities makes the utilization of these methods advantageous as compared to CW SL. These properties of adiabatic pulses have been already used to generate tissue contrast in the human brain [5,6] and applied for treatment monitoring in rat glioma [26]. Some studies have shown that adiabatic rotating frame relaxation measurements can be more informative than T_1 and T_2 in detecting certain pathologic changes occurring in neurodegenerative diseases. For example, in a recent pilot study of patients with Parkinson's disease, adiabatic R_{2p} was more sensitive than T_2 to pathological changes occurring in the brain, which is likely due to iron accumulation in substantia nigra. In addition, adiabatic R_{1p} reflected likely nigral neural degeneration [36], as confirmed by experiments performed on animal models of loss of dopaminergic neurons [37].

We conclude that changing the parameters of RF irradiation is a powerful and flexible tool to generate NMR contrast in the context of rotating frame relaxation measurements, which rely both on conventional spin lock methods and on adiabatic pulses. These methodologies offer potential to access water spin dynamics for addressing critical biological questions. However, several experimental limitations, ultimately related to SAR issues, need to be taken into account when applying both adiabatic and CW SL methodologies for human applications.

ACKNOWLEDGEMENTS

The authors thank the following agencies for financial support: Instrumentarium Science Foundation (TL), Orion Corporation Research Foundation (TL), Finnish Cultural Foundation Northern Savo (TL), NIH grants P30 NS057091, P41 RR008079, R01NS061866 and R21NS059813.

References

1. Abergel D, AG Palmer I. On the use of the stochastic Liouville equation in nuclear magnetic resonance: application to R_{1p} relaxation in the presence of exchange. *Concepts in Magnetic Resonance Part A* 2003;19A(2):134–48.
2. Davis D, Perlman M, London R. Direct measurements of the dissociation-rate constant for inhibitor-enzyme complexes via the T_{1p} and T_2 (CPMG) methods. *J Magn Reson B* 1994;104:266–75. [PubMed: 8069484]
3. Fischer M, Majumdar A, Zuiderweg E. Protein NMR relaxation: theory, applications and outlook. *Progr NMR Spectr* 1998;33:207–72.
4. Desvaux H, Berthault P. Study of dynamic processes in liquids using off-resonance RF irradiation. *Progr NMR Spectr* 1999;35:295–340.
5. Michaeli S, Grohn H, Grohn O, Sorce D, Kauppinen R, Springer C, Ugurbil K, Garwood M. Exchange-Influenced T_{2p} contrast in human brain images measured with adiabatic radio frequency pulses. *Magn Reson Med* 2005;53:823–9. [PubMed: 15799068]
6. Michaeli S, Sorce D, Springer C, Ugurbil K, Garwood M. T_{1p} MRI contrast in the human brain: modulation of the longitudinal rotating frame relaxation shutter-speed during an adiabatic RF pulse. *J Magn Reson* 2006;181:138–50.
7. Liepinsh E, Otting G. Proton exchange rates from amino acid side chains--implications for image contrast. *Magn Reson Med* 1996;35:30–42. [PubMed: 8771020]

8. Korzhnev D, Billeter M, Arseniev A, Orekhov V. NMR studies of Brownian tumbling and internal motions in proteins. *Prog NMR Spectrosc* 2001;38:197–266.
9. Garwood M, DelaBarre L. The return of the frequency sweep: designing adiabatic pulses for contemporary NMR. *J Magn Reson* 2001;153:155–77. [PubMed: 11740891]
10. Michaeli S, Sorce D, Garwood M. $T_{1\rho}$ and $T_{2\rho}$ adiabatic relaxations and contrasts. *Current Analytical Chemistry* 2008;4:8–25.
11. Sorce D, Michaeli S, Garwood M. Relaxation During Adiabatic Radiofrequency Pulses. *Current Analytical Chemistry* 2007;3:239–51.
12. Silver M, Joseph R, Hoult D. Highly selective $\pi/2$ and π pulse generation. *J Magn Reson* 1984;59:347–51.
13. Tannus A, Garwood M. Improved performance of frequency-swept pulses using offset-independent adiabaticity. *J Magn Reson A* 1996;120:133–7.
14. Ostroff E, Waugh J. Multiple spin echo and spin locking in solids. *Phys Rev Lett* 1966;16:1097–8.
15. Solomon I. Rotary spin echoes. *Phys Rev Lett* 1959;2:301–5.
16. Blicharski J. Nuclear magnetic relaxation in rotating frame. *Acta Physica Polonica* 1972;A41:223–36.
17. Jones G. Spin-Lattice Relaxation in the Rotating Frame: Weak Collision Case. *Physical Review* 1966;148:332–5.
18. Michaeli S, Sorce D, Idiyatullin D, Ugurbil K, Garwood M. Transverse relaxation in the rotating frame induced by chemical exchange. *J Magn Reson* 2004;169:293–9. [PubMed: 15261625]
19. Sorce D, Michaeli S, Garwood M. The time-dependence of exchange-induced relaxation during modulated radio-frequency pulses. *J Magn Reson* 2006;179(1):136–9. [PubMed: 16298149]
20. Abragam, A. Principles of nuclear magnetism. Clarendon Press; Oxford: 1986.
21. McConnell H. Reaction rates by nuclear magnetic resonance. *J Chem Phys* 1958;28:430–1.
22. Levitt M, Freeman R, Frenkel T. Broadband heteronuclear decoupling. *J Magn Reson* 1982;47:328–30.
23. Vaughan JT, Hetherington HP, Otu JO, Pan JW, Pohost GM. High frequency volume coils for clinical NMR imaging and spectroscopy. *Magn Reson Med* 1994;32:206–18. [PubMed: 7968443]
24. Grohn OH, Makela HI, Lukkarinen JA, DelaBarre L, Lin J, Garwood M, Kauppinen RA. Onand off-resonance $T_{1\rho}$ MRI in acute cerebral ischemia of the rat. *Magn Reson Med* 2003;49:172–6. [PubMed: 12509834]
25. Jokivarsi KT, Niskanen JP, Michaeli S, Grohn HI, Garwood M, Kauppinen RA, Grohn OH. Quantitative assessment of water pools by $T_{1\rho}$ and T_{2r} MRI in acute cerebral ischemia of the rat. *J Cereb Blood Flow Metab* 2009;29:206–16. [PubMed: 18827834]
26. Sierra A, Michaeli S, Niskanen JP, Valonen PK, Grohn HI, Yla-Herttuala S, Garwood M, Grohn OH. Water spin dynamics during apoptotic cell death in glioma gene therapy probed by T_{1r} and T_{2r} . *Magn Reson Med* 2008;59:1311–9. [PubMed: 18506797]
27. Grohn O, Lukkarinen J, Silvennoinen M, Pitkanen A, Zijl Pv, Kauppinen R. Quantitative magnetic resonance imaging assessment of cerebral ischemia in rat using on-resonance T_1 in rotating frame. *Magn Reson Med* 1999;42:268–76. [PubMed: 10440951]
28. Pitkanen A, Nissinen J, Nairismagi J, Lukasiuk K, Grohn O, Miettinen R, Kauppinen R. Progression of neuronal damage after status epilepticus and during spontaneous seizures in a rat model of temporal lobe epilepsy. *Prog Brain Res* 2002;135:67–83. [PubMed: 12143371]
29. Kettunen M, Grohn O, Penttonen M, Kauppinen R. Cerebral $T_{1\rho}$ relaxation time increases immediately upon global ischemia in the rat independently of blood glucose and anoxic depolarization. *Magn Reson Med* 2001;46:565–72. [PubMed: 11550250]
30. Grohn O, Kettunen M, Makela H, Penttonen M, Pitkanen A, Lukkarinen J, Kauppinen R. Early detection of irreversible cerebral ischemia in the rat using dispersion of the MRI relaxation time, $T_{1\rho}$. *J Cereb Blood Flow Metab* 2000;20:1457–66. [PubMed: 11043908]
31. Duvvuri U, Goldberg A, Kranz J, Hoang L, Reddy R, Wehrli F, Wang A, Englander S, Leigh J. Water magnetic relaxation dispersion in biological systems: the contribution of proton exchange and implications for the noninvasive detection of cartilage degradation. *Proc Natl Acad Sci USA* 2001;98:12479–84. [PubMed: 11606754]

32. Duvvuri U, Poptani H, Feldman M, Nadal-Desbarats L, Gee M, Lee W, Reddy R, Leigh J, Glickson J. Quantitative $T_{1\rho}$ magnetic resonance image of RIF-1 tumor in-vivo: detection of early response to cyclophosphamid therapy. *Cancer Research* 2001;61:7747–53. [PubMed: 11691788]
33. Hakumaki J, Grohn O, Tyynala K, Valonen P, Yla-Hertuala S, Kauppinen R. Early gene therapy-induced apoptotic response in BT4C gliomas by magnetic resonance relaxation T_1 in the rotating frame. *Cancer Gene Ther* 2002;9:338–45. [PubMed: 11960284]
34. Witschey WR 2nd, Borthakur A, Elliott MA, Mellon E, Niyogi S, Wallman DJ, Wang C, Reddy R. Artifacts in $T_{1\rho}$ -weighted imaging: compensation for B_1 and B^0 field imperfections. *J Magn Reson* 2007;186:75–85. [PubMed: 17291799]
35. Witschey WR, Borthakur A, Elliott MA, Mellon E, Niyogi S, Wang C, Reddy R. Compensation for spin-lock artifacts using an off-resonance rotary echo in $T_{1\rho}$ -weighted imaging. *Magn Reson Med* 2007;57:2–7. [PubMed: 17191245]
36. Michaeli S, Oz G, Sorce D, Garwood M, Ugurbil K, Majestic S, Tuite P. Assessment of brain iron and neuronal integrity in patients with Parkinson's disease using novel MRI contrasts. *Movement Disorders* 2007;22:334–40. [PubMed: 17149719]
37. Michaeli S, Burns TC, Kudishevich E, Harel N, Hanson T, Sorce DJ, Garwood M, Low WC. Detection of neuronal loss using $T_{1\rho}$ MRI assessment of $^1\text{H}_2\text{O}$ spin dynamics in the aphakia mouse. *Journal of neuroscience methods* 2009;177:160–7. [PubMed: 19027791]

Figure 1.

Effective magnetic field during conventional spin-lock pulse (a) and during adiabatic rotation (b). The effective magnetic field ($\vec{B}_{\text{eff}}$) is the vector sum of the RF generated magnetic field $B_1 \hat{x}'$ and a longitudinal field component $[B_0 - \omega_{\text{RF}}/\gamma] \hat{z}'$. In the first rotating frame $\vec{B}_{\text{eff}}$ is kept in the $x'z'$ plane, since the frame rotates around $z' (\equiv z)$ with frequency ω_{RF} . In the second rotating frame, z'' is aligned with the direction of $\vec{B}_{\text{eff}}$, and therefore this frame is tilted compared to z' by the angle α . The magnitude and the direction of $\vec{B}_{\text{eff}}$ are kept stationary in the first rotating frame during the conventional spin-lock pulse, whereas they are time-dependent during the adiabatic rotation, since $\vec{B}_{\text{eff}}$ is a function of the amplitude and frequency modulation functions.

Figure 2.

Properties of adiabatic full passage (AFP) pulses, namely the hyperbolic secant HS1 (solid lines) and HS4 (dotted lines) pulses. a) amplitude and frequency modulation functions., with $T_p = 4$ ms, R -value = 40, corresponding to $B = 10$ kHz, $\omega_1^{\max}/(2\pi) = 2.5$ kHz; b) trajectories showing the inversion of the magnetization for the isochromat centered at the carrier frequency of the pulse. Note that during the AFP, the magnetization of each isochromat within the BW becomes inverted by the end of the pulse; c-d) evolution of $\alpha(t)$ and $(\omega_{eff}/(2\pi))^2$ during the pulses. Since $\alpha(t)$ and $(\omega_{eff}/(2\pi))^2$ depend not only on the modulation functions but also on the pulse parameters, the cases corresponding to $\omega_1^{\max}/(2\pi) = 2.5$ kHz and 5 kHz are presented. Note that when $\omega_1^{\max}/(2\pi) = A$ ($\equiv BW/2$), i.e. when $\omega_1^{\max}/(2\pi) = 5$ kHz, then $(\omega_{eff}/(2\pi))^2$ during the HS1 pulse becomes time-independent. This is because the known trigonometric identity $\omega_{eff}^2 = A \cdot [\text{sech}^2(\beta(2t/T_p - 1)) + \tan^2(\beta(2t/T_p - 1))] = A$.

Figure 3.

Dependency of rotating frame relaxation rate constants on tilt angle α during CW SL pulse, for dipolar interactions (a,b) and for anisochronous exchange (c,d). The range of rotational correlation times (τ_c) and exchange correlation times (τ_{ex}) were chosen in order to satisfy the weak field approximation and the fast exchange limit, respectively. The $R_{1,2p,dd}$ and $R_{1,2p,ex}$ values were obtained using Eqs. [12-13] and [21-22], respectively. The effective frequency was chosen as $\omega_{eff}/(2\pi) = 2$ KHZ. Other parameters: $\omega_0/(2\pi) = 169$ MHz, which corresponds to proton frequency at 4 T; $\delta\omega = 0.85$ ppm (= 170 Hz at 4 T), $P_m = P_q = 0.5$; $r = 0.158$ nm.

Figure 4.

Dependency of rotating frame relaxation rate constants on $\omega_{\text{eff}}/(2\pi)$ during CW SL pulse, for dipolar interactions (a,b) and for anisochronous exchange (c,d). The range of rotational correlation times (τ_c) and exchange correlation times (τ_{ex}) were chosen in order to satisfy the weak field approximation and the fast exchange limit, respectively. The pulse frequency was placed off-resonance to satisfy the condition $\alpha = 45^\circ$. Other parameters: $\omega_0/(2\pi) = 169$ MHz, which corresponds to proton frequency at 4 T; $\delta\omega = 0.85$ ppm (= 170 Hz at 4 T), $P_m = P_q = 0.5$; $r = 0.158$ nm.

Figure 5.

Dependency of rotating frame relaxation rate constants on the adiabatic pulse duration (T_p), in the presence of dipolar interactions. The adiabatic pulse was HS1. a,b) R -value = 80, thus resulting in $BW = 40, 20, 10$ and 5 kHz for $T_p = 2, 4, 8$ and 16 ms, respectively, according to the relationship $BW = R/T_p$; c,d) the R -values were adjusted to keep $BW = 10$ kHz, namely R -value = 20, 40, 80 and 160 for $T_p = 2, 4, 8$ and 16 ms, respectively. The peak RF amplitude was chosen to satisfy the adiabatic condition for all pulses investigated ($\omega_1^{\max}/(2\pi) = 10$ kHz). The $R_{1p,dd}$ and $R_{2p,dd}$ values were calculated using Eqs. [12-13], with parameters: $\omega_0/(2\pi) = 169$ MHz and $r = 0.158$ nm. The range of rotational correlation times (τ_c) was chosen in order to satisfy the weak field approximation.

Figure 6. Dependency of rotating frame relaxation rates on adiabatic pulse duration (T_p), in the presence of anisochronous exchange. The adiabatic pulse was HS1. a-d) as in Figure 5. The $R_{1p,ex}$ and $R_{2p,ex}$ were calculated according to Eqs. [11-13], respectively, with parameters: $\omega_0/(2\pi) = 169$ MHz, $\delta\omega = 0.85$ ppm (= 170 Hz at 4 T) and $P_m = P_q = 0.5$. The range of exchange correlation times (τ_{ex}) was chosen in order to satisfy the fast exchange limit.

Figure 7.

Dependency of rotating frame relaxation rates on $\omega_1^{\max} / (2\pi)$ during the HS1 pulses (a,b) and the HS4 pulses (c,d), in the presence of dipolar interactions. For both pulses, $R = 80$ and $T_p = 8$ ms, corresponding to $BW = 10$ kHz. The $R_{1p,dd}$ and $R_{2p,dd}$ values were calculated using Eqs. [12-13], with parameters: $\omega_0 / (2\pi) = 169$ MHz and $r = 0.158$ nm. The range of rotational correlation times (τ_c) was chosen in order to satisfy the weak field approximation.

Figure 8.

Dependency of rotating frame relaxation rates on $\omega_1^{\max}/(2\pi)$ during HS1 pulse (a,b) and HS4 pulse (c,d), in the presence of an anisochronous exchange. For both pulses, $R = 80$ and $T_p = 8$ ms, corresponding to $BW = 10$ kHz. The $R_{1p,ex}$ and $R_{2p,ex}$ were calculated according to Eqs. [11-13], respectively, with parameters: $\omega_0/(2\pi) = 169$ MHz, $\delta w = 0.85$ ppm ($= 170$ Hz at 4 T) and $P_m = P_q = 0.5$. The range of exchange correlation times (τ_{ex}) was chosen in order to satisfy the fast exchange limit.

Figure 9.

Comparison of rotating frame relaxation rate constants in the presence of dipolar interactions (a,b) and anisochronous exchange (c,d) as a function of $\omega_1^{\max}/(2\pi)$ during HS1 (solid lines) and HS4 (dashed lines) pulses, with $BW = 10$ kHz. The relaxation rate calculations were obtained, respectively, according to Eqs. [12-13] with parameters: $\omega_0/(2\pi) = 169$ MHz, $r = 0.158$ nm and $\tau_c = 10^{-9}$ s, and according to Eqs. [21,22] with parameters: $\omega_0/(2\pi) = 169$ MHz, $\delta\omega = 0.85$ ppm ($= 170$ Hz at 4 T) and $P_m = P_q = 0.5$ and $\tau_{ex} = 2 \cdot 10^{-4}$ s. The range of $\omega_1^{\max}/(2\pi)$ was chosen to satisfy the adiabatic condition. The insets depicts the % contrast defined as $(R_{1,2p}(\text{HS4}) - R_{1,2p}(\text{HS1}))/R_{1,2p}(\text{HS1}) \cdot 100$.

Figure 10.

Comparison of rotating frame relaxation rate constants in the presence of dipolar interactions (a,b) and anisochronous exchange (c,d) as a function of BW during HS1 (solid lines) and HS4 (dashed lines) pulses, with $\omega_1^{\max}/(2\pi) = 10$ kHz. The relaxation rate calculations were obtained, respectively, according to Eqs. [12-13] with parameters: $\omega_0/(2\pi) = 169$ MHz, $r = 0.158$ nm and $\tau_c = 10^{-9}$ s, and according to Eqs. [21,22] with parameters: $\omega_0/(2\pi) = 169$ MHz, $\delta\omega = 0.85$ ppm (= 170 Hz at 4 T) and $P_m = P_q = 0.5$ and $\tau_{ex} = 2 \cdot 10^{-4}$ s. $\omega_1^{\max}/(2\pi)$ was chosen to satisfy the adiabatic condition. The insets depicts the % contrast defined as $(R_{1,2r}(\text{HS4}) - R_{1,2r}(\text{HS1}))/R_{1,2r}(\text{HS1}) \cdot 100$.

Figure 11.

Adiabatic R_{1p} and R_{2p} as a function of $\omega_1^{\max}/(2\pi)$ (a, b) and BW (c, d) measured from a phantom containing a mixture of water and ethanol at 4T during HS1 (bold symbols, solid lines) and HS4 (empty lines, dashed lines) pulses. The BW was varied by changing the amplitude of the frequency sweep, while remained constant (*i.e.* the pulse patterns were created using $R = 15, 20, 30$ and 40)

Figure 12.

$T_{1\rho}$ ($= 1/R_{1\rho}$) relaxation maps from the human brain at 4T. a) SL $T_{1\rho}$ map obtained with on resonance CW irradiation and $\omega_1^{\max} / (2\pi) = 0.625$ kHz; b) SL $T_{1\rho}$ map obtained with CW irradiation off resonance by 0.625 kHz and $\omega_1^{\max} / (2\pi) = 0.625$ kHz, which corresponds to $\alpha = 45^\circ$; c) adiabatic $T_{1\rho}$ map obtained with HS1 pulse, R -value = 20, $\omega_1^{\max} / (2\pi) = 1.13$ kHz; d) adiabatic $T_{1\rho}$ map obtained with HS4 pulse, R -value = 20, $\omega_1^{\max} / (2\pi) = 0.88$ kHz, $T_p = 6$ ms.