Published in final edited form as:

J Magn Reson. 2018 August ; 293: 28–33. doi:10.1016/j.jmr.2018.05.006.

RAFFn Relaxation Rate Functions

Dennis J. Sorce¹ and Shalom Michaeli¹

¹Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, USA

Abstract

In the present study we derive expressions for relaxation rate functions due to dipolar interactions between identical spins in the rotating frames of rank greater than or equal to 3. The rotating frames are produced due to fictitious magnetic field as generated by amplitude and frequency modulated radiofrequency (RF) pulses operating in non-adiabatic regime. This solution provides a means for description of the relaxations during method entitled Relaxation Along a Fictitious Field (RAFF) in the rotating frame of rank n (RAFFn), in which a fictitious field is created in a coordinate frame undergoing multi-fold rotation about n axes (i.e., rank n). We validate the proposed model by comparison with the accepted trigonometric relations for relaxation rates between tilted frames. The agreement between the proposed model for RAFF3 and the trigonometric model is excellent.

Graphical Abstract

Introduction

As is documented by NMR researchers, transformations between rotating frames are at the heart of much of the formalism used to calculate relaxation rates and magnetization

*Address correspondence to: Dennis J. Sorce, Center of Magnetic Resonance Research, University of Minnesota 2021, 6th street SE, Minneapolis, MN, 55455, fax: (612)-626-2004, phone: (612)-626-2001, dennissorce1@comcast.net.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

trajectories in magnetic resonance, MR [1–3]. We use the transform from the Laboratory Frame (LF) to the First Rotating Frame (FRF) routinely for rotating frame MR imaging (MRI) and spectroscopy (MRS) to eliminate the rapid precession rotation around the B_0 field, and then the transformation from the FRF to the Tilted Doubly Rotating Frame (TDRF) to deal with cases where there is time-evolution during the radiofrequency (RF) irradiation [4–13]. Recently, we described transformation and evaluated relaxation and time-evolution in a third rotating frame, the so-called Tilted Triply Rotating Frame (TTRF). These transformations were necessary for describing relaxations in the high rotating frames of rank n during non-invasive MR contrast methods of RAFFn family (Relaxation Along a Fictitious Field in the rotating frame of rank n), and more colloquially the RAFF3 Frame with $n=3$. With this MRI contrast methods, the rotating frame relaxations in high rotating frames are generated during amplitude and frequency modulated radiofrequency (RF) pulses operating in non-adiabatic regime. We refer the reader to these detailed treatments for a careful consideration of the TTRF transform [14, 15]. Here we are content to outline the transform and then to detail the method for the calculation of relaxation rate constants in the higher RAFFn frames.

For the ease of the reader we state again the equation used in the TDRF transform and then the TTRF transform.

Recall we defined:

$$\omega_{eff}(t) = \sqrt{\omega_1(t)^2 + \Delta\omega(t)^2} \quad (1.0)$$

$$\alpha^{(1)}(t) = \text{ArcTan}\left(\frac{\omega_1(t)}{\Delta\omega(t)}\right) \quad (2.0)$$

Whereas previously defined $\omega_1(t)$ is the pulse amplitude and $\omega(t)$ is the time-dependent frequency offset. Here $\alpha(t)$ is the angle between quantization axis and the effective frequency $\omega_{eff}(t)$.

For the transform to the TTRF we must define another angular quantity and another vectorial contribution to the effective field in the TTRF [16].

To accomplish this, we write:

$$\omega_E(t) = \sqrt{\omega_{eff}(t)^2 + (\dot{\alpha}^{(1)}(t))^2} \quad (3.0a)$$

$$\text{where } \alpha^{(2)}(t) = \text{ArcTan}\left(\frac{\dot{\alpha}^{(1)}(t)}{\omega_{eff}(t)}\right) \quad (3.0b)$$

$$\phi_E(t) = \int_0^t \omega_E(t') dt' \quad (3.0c)$$

Here Eq[3.0c] gives the phase angle for rotation around the effective field $\omega_E(t)$. We also need to define specific forms for the RF modulation functions.

Some thought will lead the reader to conclude (see also [16] that the angle $\alpha^{(2)}(t)$ will be a constant in the TTRF with sine and cosine (SC) functions and that with SC functions the condition:

$$\omega_E = \sqrt{2}\omega_1^{\max} \quad (3.0d)$$

entails.

Also, we define explicitly:

$$\omega_1(t) = \frac{\omega_E}{\sqrt{2}} \left| \sin\left(\frac{\omega_E}{\sqrt{2}}t + \varphi_0\right) \right| \quad (4.0a)$$

$$\Delta\omega(t) = \frac{\omega_E}{\sqrt{2}} \cos\left(\frac{\omega_E}{\sqrt{2}}t + \varphi_0\right) \quad (4.0b)$$

We can now proceed to the derivation of the relaxation rates in the TTRF. For reference the reader is referred to the review by Hubbard [17]. We will define the complete transform from the LF to the TTRF.

$$U(t) = U_{x''}(t)U_{y'}(t)U_z(t) \quad (5.0)$$

With defining:

$$U_z(t) = \text{Exp}(i\omega_0 t I_z) \quad (6.0a)$$

$$U_{y'}(t) = \text{Exp}(i\alpha^{(1)}(t)I_{y'}) \quad (6.0b)$$

$$U_{x''}(t) = \text{Exp}(i\alpha^{(2)}(t)I_{x''}) \quad (6.0c)$$

We note that the subscript z corresponds to the LF, y' to the FRF and x'' to the TDRF. We next use the transform definitions as given for example in the review by Hubbard [17] as applied to an arbitrary irreducible tensor of rank 2:

$$U(t)T_{q_2}^2U(t)^{-1} = U_{x''}U_{y'}(t)U_z(t)T_{q_2}^2U_z(t)^{-1}U_{y'}(t)^{-1}U_{x''} \quad (7.0a)$$

We next write:

$$U_z(t)T_q^2U_z(t)^{-1} = T_q^2\text{Exp}(iq\omega_0t) \quad (7.0b)$$

Then:

$$U_{y'}(t)T_{q_1}^2U_{y'}(t)^{-1} = \sum_{q=-2}^2 T_q^2 d_{q_1,q}^{(2)}(\alpha^{(1)}(t)) \quad (7.0c)$$

$$U_{x''}T_{q_2}^2U_{x''}^{-1} = \sum_{q_1=-2}^2 T_{q_1}^2 \text{Exp}(iq_2\phi_E(t))d_{q_2,q_1}^{(2)}(\alpha^{(2)}(t)) \quad (7.0d)$$

We next give a demonstration how all these transforms together obtain rate functions. We start from using the Wigner rotation matrices acting on rank two Spherical Tensors to put into effect the transformation schematically shown above.

We first write:

$$\tilde{T}_{2q_1} = \sum_{q=-2}^{q=2} d_{q_1,q}^{(2)}(\alpha^{(1)}(t))\text{Exp}[iq\omega_0t]T_{2q} \quad (8.0a)$$

$$\tilde{T}_{2q_2} = \sum_{q_1=-2}^{q_1=2} d_{q_2,q_1}^{(2)}(\alpha^{(2)}(t))\text{Exp}[iq_2\phi_E(t)]\tilde{T}_{2q_1} \quad (8.0b)$$

Substituting Eq(8.0a) into Eq(8.0b), we obtain:

$$\tilde{T}_{2q_2} = \sum_{q_1=-2}^{q_1=2} d_{q_2, q_1}^{(2)}(\alpha^{(2)}(t)) \text{Exp}[iq_2\phi_E(t)] \sum_{q=-2}^{q=2} d_{q_1, q}^{(2)}(\alpha^{(1)}(t)) \text{Exp}[iq\omega_0 t] T_{2q} \quad (8.0c)$$

So this transform the Second Rank tensors from the so called Laboratory Frame to the so called Second Rotating Frame which is RAFF2 in the accepted nomenclature of the series of RAFFn [16].

Next, we follow Bloch-Redfield-Wangsness Theory [2, 18–20] by implementing Second Order Perturbation Theory on time-dependent Hamiltonians in the most widely used Semi Classical Approximation where the RF fields are treated Classically and the interaction with the Spin $\frac{1}{2}$ nucleus is treated quantum mechanically [21]. See especially the review article of M. Goldman for an introduction to this formalism [22]

First, we write the Liouville -von Neumann equation for the time dependence of the density matrix in the Second Rotating Frame [18–20].

$$\frac{d\tilde{\sigma}[t]}{dt} = -i[\tilde{H}_{DD}[t], \tilde{\sigma}[t]] \quad (9.0)$$

As is well documented the LvNeq can be solved exactly only for a few special cases. We seek in this treatment to use the Dipole-Dipole Interaction Hamiltonian for identical spin $\frac{1}{2}$ nuclei [18]. We next choose to define the Dipole Dipole Hamiltonian in the SRF using generic notation as (See for example Chapter 8 in [18]):

$$\tilde{H}[t] = \sum_{q_2=-2}^{q_2=2} F_{2q_2}[t] \tilde{T}_{2q_2} \quad (10.0.a)$$

Here the F functions provide the interaction of the spins system with the so-called lattice or bath and the Second Rank Spin Tensors take into account the behavior in the RF and DD field, of the spins.

$$\tilde{H}^\dagger[t] = \sum_{p_2=-2}^{p_2=2} F_{2p_2}^\dagger[t] \tilde{T}_{2p_2}^\dagger \quad (10.0b)$$

In Eq(10.0b) we take the adjoint which is the conjugate transpose of the Hermitian Dipolar Hamiltonian.

Now we finally get to the second order perturbation formalism. The idea is to first integrate Eq(13.0) first in time to obtain:

$$\tilde{\sigma}[t] = -i \int [\tilde{H}_{DD}[\tau], \tilde{\sigma}[\tau]] d\tau \quad (11.0)$$

And then to substitute back Eq(11.0) into Eq(9.0):

To obtain the following form of double commutators:

$$\frac{d\tilde{\sigma}[t]}{dt} = -i \int_0^t [\tilde{H}_{DD}[t], [\tilde{H}_{DD}^\dagger[t-\tau], \tilde{\sigma}[t]]] d\tau \quad (12.0)$$

The reasons for the chosen algebraic form will become clearer in the subsequent treatment. Next, we substitute Eqs(10 a,b) into Eq(12.0) to obtain:

$$\frac{d\tilde{\sigma}[t]}{dt} = \sum_{q_2=-2}^{q_2=2} \sum_{p_2=-2}^{p_2=2} \int_0^t \langle F_{2q_2}[t] F_{2p_2}^\dagger[t-\tau] \rangle [\tilde{T}_{2q_2}, [\tilde{T}_{2p_2}^\dagger, \tilde{\sigma}[t]]] d\tau \quad (13.0)$$

To be complete there are conditions on the various temporal variables for the validation of Wangsness Redfield Relaxation Treatments. The reader is referred to some of the vast literature [20, 22, 23].

We now substitute Eqs(10.0) into Eq(13.0) leaving the adjoint operation for now, also to obtain:

$$\begin{aligned} \frac{d\tilde{\sigma}[t]}{dt} = & \sum_{q_2=-2}^{q_2=2} \sum_{p_2=-2}^{p_2=2} \sum_{q_1=-2}^{q_1=2} \sum_{q=-2}^{q=2} \sum_{p_1=-2}^{p_1=2} \sum_{p=-2}^{p=2} \int_0^t F_{2q_2}[t] F_{2p_2}^\dagger[t-\tau] [d_{q_2, q_1}^{(2)}(\alpha^{(2)} \\ & [t]) d_{q_1, q}^{(2)}(\alpha^{(1)}[t]) \text{Exp}(iq_2\phi_E(t)) \text{Exp}(iq\omega_0 t) \tilde{T}_{2q_2}, \\ & [d_{p_2, p_1}^{(2)}(\alpha^{(2)}[t]) d_{p_1, p}^{(2)}(\alpha^{(1)}[t]) \text{Exp}(-ip_2\phi_E(t-\tau)) \text{Exp}(-ip\omega_0(t-\tau)) \tilde{T}_{2p_2}^\dagger, \tilde{\sigma}[t]] \\ & \quad (14.0) \end{aligned}$$

We next make an approximations based on the typical experimental conditions in liquid state NMR by assuming that $\tau \ll t$. So, we can write:

$$\phi_E(t-\tau) \simeq \phi_E(t) - \tau\omega_E(t) \quad (15.0)$$

Where $\omega_E(t)$ is defined in Eq(3.0a) and the tilt angles are defined in Eq(3.0b).

We next consider Eqs(14,15) and apply the Secular Approximation which basically says the large time dependent terms will cause rapid oscillation in the exponential terms which will tend to average to zero contribution upon integration in time when solving the system of equations. So, with this in mind we group the indices as:

$$\text{Exp}(i(q_2 - p_2)\phi_E(t)) \quad (16.0a)$$

$$\text{Exp}(i(q - p)\omega_0 t) \quad (16.0b)$$

So applying the Secular Approximation to Eqs(14.0a and 14.0b) we obtain:

$$q = p \quad (17.0a)$$

$$q_2 = p_2 \quad (17.0b)$$

$$\begin{aligned} \frac{d \langle \tilde{\sigma}[t] \rangle}{dt} = & \sum_{q_2=-2}^{q_2=2} \sum_{q_1=-2}^{q_1=2} \sum_{q=-2}^{q=2} \int_0^t \langle F_{2q_2}(t) F_{2q_2}^\dagger(t-\tau) d_{q_2, q_1}^{(2)}(\alpha^{(2)}[t]) d_{q_1, q}^{\dagger(2)}(\alpha^{(1)} \\ & [t]) \tilde{T}_{2q_2}, \\ & [d_{q_2, q_1}^{\dagger(2)}(\alpha^{(2)}[t]) d_{q_1, q}^{\dagger(2)}(\alpha^{(1)}[t]) \text{Exp}(iq_2 \omega_E(t)\tau) \text{Exp}(iq \omega_0 \tau) \tilde{T}_{2q_2}^\dagger, \tilde{\sigma}[t]] \end{aligned} \quad (18.0)$$

Next, we seek to take an ensemble average over the Bath Operators in Eq(16.0) which yield an assumed exponential correlation function. For simplicity and general applicability to liquid state data we assume the relaxation mechanism is intramolecular rotational isotropic diffusion. See for example [24]. Then we obtain for the correlation function:

$$KD = \frac{4}{5} \frac{\hbar^2 \nu^4}{r^6} \quad (19.0a)$$

$$C[\tau] = K \text{DExp}(-\tau/\tau_c) \quad (19.0b)$$

Where D is diffusion constant.

So now grouping integrand terms in τ and using the correlation function in Eqs (17.0a,b)

We obtain the following integral:

$$\int_0^t K \text{DExp}[-\tau/\tau_c + i(q\omega_0 + q_2\omega_E(t))\tau] d\tau \quad (20.0)$$

So we can perform this standard integral to obtain the Spectral Density as:

$$KDJ(q\omega_0 + q_2\omega_E(t)) \quad (21.0)$$

With the definition of the reduced Spectral Density function as:

$$J(\omega) = \frac{\tau_c}{1 + \omega^2 \tau_c^2} \quad (22.0)$$

We note that in obtaining the Spectral Density we assume that as previously stated the τ is on the order of the correlation time and the correlation time is much less than the magnitude of t. So as is common practice it is then legitimate to extend the upper limit of integration of the integral in τ to Infinity. Then Eq(20), ignoring the complex term, follows.

We next focus on the double commutators in the Tensors and the Density Matrix in the SRF for RAFF2. We note that to find the expectation value of an observable in the Schroedinger Picture of Quantum Mechanics one takes the Operator of Interest multiplied by the Density Matrix and takes the Trace Operation (See for example [22]). So one obtains the following form for the Trace of the double commutators with $\tilde{I}_\alpha$ defined as the spin angular momentum of the spin 1/2 nucleus:

$$\text{Tr}([T_{2q_2}, [T_{2q_2}^\dagger, I_\alpha]] \tilde{\sigma}(t)) \quad (23.0)$$

We note that in obtaining Eq(21.0) we used the cyclic property of the trace [17].

We also note that in Eq(23.0) we assume $\alpha = 0, -1, 1$. Also we can use results [24] for evaluating Eq(23.0) for the different α values.

It is given in, [24] that:

$$Tr([T_{2q_2}, [T_{2q_2}^\dagger, I_\pm]] \tilde{\sigma}(t)) = \frac{1}{8}(q_2 + 2)(3 - q_2)2I(I + 1) < \tilde{I}_\pm[t] > \quad (24.0a)$$

$$\text{And } Tr([T_{2q_2}, [T_{2q_2}^\dagger, I_0]] \tilde{\sigma}(t)) = \frac{1}{4}(q_2^2)I(I + 1) < \tilde{I}_0[t] > \quad (24.0b)$$

This leads to the following expressions in the SRF or RAFF2 frame:

$$R_{1\sigma, RAFF2}(t) = \frac{3}{20} \frac{\hbar^2 \nu^4}{r^6} \sum_{q=-2}^2 \sum_{q_1=-2}^2 \sum_{q_2=-2}^2 J(q\omega_0 + q_2\omega^{(2)}_E(t)) \quad (25.0a)$$

$$(d_{q, q_1}^{(2)}(\alpha^{(1)}(t)))^2 (d_{q_1, q_2}^{(2)}(\alpha^{(2)}))^2 (q_2)^2$$

$$R_{2\sigma, RAFF2}(t) = \frac{3}{40} \frac{\hbar^2 \nu^4}{r^6} \sum_{q=-2}^2 \sum_{q_1=-2}^2 \sum_{q_2=-2}^2 J(q\omega_0 + q_2\omega^{(2)}_E(t)) \quad (25.0b)$$

$$(d_{q, q_1}^{(2)}(\alpha^{(1)}(t)))^2 (d_{q_1, q_2}^{(2)}(\alpha^{(2)}))^2 (q_2 + 2)(3 - q_2)$$

We now seek to generalize this result for RAFF2 to the case for general RAFFn. We postulate the general expression and then validate it for RAFF3 against the Trigonometric Expression for RAFF3 [1–3, 18]. We use different indices to aid in see the generalization. Note these expressions for the Modulation Functions in the various frames are treated in detail in [25, 26] We give a brief definition of the Modulation Functions in Appendix I.

$$R_{1\sigma, RAFFn}(t) = \frac{3}{20} \frac{\hbar^2 \nu^4}{r^6} \sum_{m=-2}^2 \sum_{m'=-2}^2 \sum_{m''=-2}^2 \sum_{m'''=-2}^2 \sum_{m''''=-2}^2 \quad (26.0a)$$

$$\dots \sum_{m^{(N-1)}=-2}^2 \sum_{m^{(N)}=-2}^2 j(m\omega_0 + m''\omega^{(2)}_E(t) + \sum_{j=3}^N (m^j \omega^j_E(t)))$$

$$(d_{m,m'}^{(2)}(\alpha^{(1)}(t)))^2 (d_{m',m''}^{(2)}(\alpha^{(2)}(t)))^2 \prod_{j=3}^N ((d_{m^{(j-1)},m^{(j)}}^{(2)}(\alpha^{(j)}(t)))^2 (m^{(j)})^2$$

$$\omega^{(k)}_E(t) = \sqrt{\omega^{(k-1)}_E(t)^2 + \dot{\alpha}^{(k-1)}[t]^2}$$

$$\omega^{(4)}_E(t) = \sqrt{\omega^{(3)}_E(t)^2 + \dot{\alpha}^{(3)}[t]^2}$$

$$\omega^{(3)}_E(t) = \sqrt{\omega^{(2)}_E(t)^2 + \dot{\alpha}^{(2)}[t]^2}$$

$$\omega^{(2)}_E(t) = \sqrt{\omega^{(1)}_E(t)^2 + \dot{\alpha}^{(1)}[t]^2}$$

$$\omega^{(1)}(t) = \sqrt{\omega_1(t)^2 + \Delta\omega[t]^2}$$

$$\alpha^{(k)}[t] = \text{ArcTan}\left[\frac{\dot{\alpha}^{(k-1)}[t]}{\omega^{(k-1)}_E(t)}\right]$$

$$\alpha^{(4)}[t] = \text{ArcTan}\left[\frac{\dot{\alpha}^{(3)}[t]}{\omega^{(3)}_E(t)}\right]$$

$$\alpha^{(3)}[t] = \text{ArcTan}\left[\frac{\dot{\alpha}^{(2)}[t]}{\omega^{(2)}_E(t)}\right]$$

$$\alpha^{(2)}[t] = \text{ArcTan}\left[\frac{\dot{\alpha}^{(1)}[t]}{\omega^{(1)}_E(t)}\right]$$

$$\alpha^{(1)}[t] = \text{ArcTan}\left[\frac{\omega_1[t]}{\Delta\omega(t)}\right]$$

$$\begin{aligned}
R_{2\sigma, RAFFn}(t) &= \frac{3}{40} \frac{\hbar^2 \nu^4}{r^6} \sum_{m=-2}^2 \sum_{m'=-2}^2 \sum_{m''=-2}^2 \sum_{m'''=-2}^2 \sum_{m''''=-2}^2 \\
&\dots \sum_{m^{(N-1)}=-2}^2 \sum_{m^{(N)}=-2}^2 j(m\omega_0 + m''\omega^{(2)}_E(t) + \sum_{j=3}^N (m^j \omega^j_E(t))) \\
&(d_{m,m'}^{(2)}(\alpha^{(1)}(t)))^2 (d_{m',m''}^{(2)}(\alpha^{(2)}(t)))^2 \prod_{j=3}^N ((d_{m^{(j-1)},m^{(j)}}^{(2)}(\alpha^{(j)}(t)))^2 (m^{(j)} + 2)(3 - m^{(j)})) \\
\omega^{(k)}_E(t) &= \sqrt{\omega^{(k-1)}_E(t)^2 + \dot{\alpha}^{(k-1)}[t]^2} \\
\omega^{(4)}_E(t) &= \sqrt{\omega^{(3)}_E(t)^2 + \dot{\alpha}^{(3)}[t]^2} \\
\omega^{(3)}_E(t) &= \sqrt{\omega^{(2)}_E(t)^2 + \dot{\alpha}^{(2)}[t]^2} \\
\omega^{(2)}_E(t) &= \sqrt{\omega^{(1)}_E(t)^2 + \dot{\alpha}^{(1)}[t]^2} \\
\omega^{(1)}(t) &= \sqrt{\omega_1(t)^2 + \Delta\omega[t]^2} \\
\alpha^{(k)}[t] &= \text{ArcTan}\left[\frac{\dot{\alpha}^{(k-1)}[t]}{\omega^{(k-1)}_E(t)}\right] \\
\alpha^{(4)}[t] &= \text{ArcTan}\left[\frac{\dot{\alpha}^{(3)}[t]}{\omega^{(3)}_E(t)}\right] \\
\alpha^{(3)}[t] &= \text{ArcTan}\left[\frac{\dot{\alpha}^{(2)}[t]}{\omega^{(2)}_E(t)}\right] \\
\alpha^{(2)}[t] &= \text{ArcTan}\left[\frac{\dot{\alpha}^{(1)}[t]}{\omega^{(1)}_E(t)}\right] \\
\alpha^{(1)}[t] &= \text{ArcTan}\left[\frac{\omega_1[t]}{\Delta\omega(t)}\right]
\end{aligned} \tag{26.0b}$$

n is the number of RAFF higher order frames. This basically becomes equal to the number of distinct Wigner Rotation Element rotations used in the relaxation master equation. Here we list the Analytic Model Proposed for RAFF3 Relaxation for both longitudinal and transverse rates based on the general expressions shown in Eqs [26.0 a,b]

$$R_{1\sigma, RAFF3}(t) = \frac{3}{20} \frac{\hbar^2 \nu^4}{r^6} \sum_{q=-2}^2 \sum_{q_1=-2}^2 \sum_{q_2=-2}^2 \sum_{q_3=-2}^2 J(q\omega_0 + q_2\omega^{(2)}_E(t) + q_3\omega^{(3)}_E(t))$$

$$(d_{q,q_1}^{(2)}(\alpha^{(1)}(t)))^2 (d_{q_1,q_2}^{(2)}(\alpha^{(2)}))^2 (d_{q_2,q_3}^{(2)}(\alpha^{(3)}))^2 (q_3)^2$$

(27.0a)

$$R_{2\sigma, RAFF3}(t) = \frac{3}{40} \frac{\hbar^2 \nu^4}{r^6} \sum_{q=-2}^2 \sum_{q_1=-2}^2 \sum_{q_2=-2}^2 \sum_{q_3=-2}^2 J(q\omega_0 + q_2\omega^{(2)}_E(t) + q_3\omega^{(3)}_E(t))$$

$$(d_{q,q_1}^{(2)}(\alpha^{(1)}(t)))^2 (d_{q_1,q_2}^{(2)}(\alpha^{(2)}))^2 (d_{q_2,q_3}^{(2)}(\alpha^{(3)}))^2 (q_3 + 2)(3 - q_3)$$

(27.0b)

Here, we list the RAFF3 Relaxation Rates using the Trigonometric Relaxation as used in the literature [1–3, 18]:

$$R_{2\sigma, RAFF3}^{Trig}(t) = R_{2\sigma, RAFF2}(t) \cos(\alpha^{(2)}(t)) + R_{1\sigma, RAFF2}(t) \cos(\alpha^{(2)}(t)) \quad 28.0a$$

$$R_{1\sigma, RAFF3}^{Trig}(t) = R_{1\sigma, RAFF2}(t) \cos(\alpha^{(2)}(t)) + R_{2\sigma, RAFF2}(t) \cos(\alpha^{(2)}(t)) \quad 28.0b$$

The Trigonometric Relaxation Functions are found when one seeks to transform between rotating frames where the rotation is about a preferred axis with the angle of rotation α . We have found this relationship to be valid when transforming between the RAFF2 frame and the RAFF3 frame. Others also have found validity of these relations between the free precession laboratory frame and rotating frame R_{1p} and R_{2p} relaxation rate constants [1, 27, 28]. The physical meaning was illustrated clearly by expanding the density operator in an orthogonal set of basis operators [1]. Here, the motivation in using these relations is that the Wigner Rotation Operator based relations Eq [27.0a and 27.0b] are fairly involved and the Trigonometric relations fairly simple. For these expressions to produce such a perfect equality between the two we feel strongly indicates the correctness of the derived relations presented in the text.

As defined in [14, 25, 26], the relaxation rate constant during frequency modulated pulses of RAFF method is given as:

$$R_{RAFF3}^{Wig} = \frac{1}{2T_p} \int_0^{T_p} (R1\sigma_{RAFF3}(t) + R2\sigma_{RAFF3}(t))dt \quad (29.0a)$$

$$R_{RAFF3}^{Trig} = \frac{1}{2T_p} \int_0^{T_p} (R1\sigma_{RAFF3}^{Trig}(t) + R2\sigma_{RAFF3}^{Trig}(t))dt \quad (29.0b)$$

Here T_p is the duration of the RAFFn pulse. In Figure 1 the results of the calculations of the relaxation rate constants due to dipolar interactions between identical spins are shown using Eqs [27–29]. The comparison between two independent approaches indicate remarkable similarity between relaxation rate constants when the condition of the fast tumbling is well satisfied. To further demonstrate the remarkable similarity between the results provided by two approaches,

Wigner Transformations and Trigonometric Relationship, we calculated the normalized difference between rate constants as follows: $[R(RAFF3, Wig) - R(RAFF3, Trig)] / R(RAFF3, Wig)$ for both longitudinal and transverse relaxation rate constants. The results of this calculation are presented in Figure 2, and clearly indicate that the difference between two approaches is negligibly small.

Conclusion

We have provided a model for higher order RAFF relaxation functions. We have provided validation for the equivalence of the proposed model with the trigonometric relaxation expressions cited in the literature [1, 3]. The RAFFn pulse sequences have proved to be of interest in terms of detection of slow motion in MRI studies [14, 25, 26]. In fast tumbling regime the trigonometric identity could be used for the calculations of relaxation rates due to dipolar interactions in high rotating frames.

Acknowledgments

One of the authors (DJS) thanks Sanford Simon for discussion and support over the years. This work was supported by the NIH core grant P41-EB015894.

References

1. Abergel D, Palmer AG. On the use of the stochastic Liouville equation in nuclear magnetic resonance: Application to R-1 rho relaxation in the presence of exchange. *Concept Magn Reson A*. 2003; 19a(2):134–148.
2. Fischer M, Majumdar A, Zuiderweg E. Protein NMR relaxation: theory, applications and outlook. *Progr NMR Spectr*. 1998; 33:207–272.
3. Palmer AG 3rd, Kroenke CD, Loria JP. Nuclear magnetic resonance methods for quantifying microsecond-to-millisecond motions in biological macromolecules. *Methods Enzymol*. 2001; 339:204–38. [PubMed: 11462813]

4. Borthakur A, Mellon E, Niyogi S, Witschey W, Kneeland JB, Reddy R. Sodium and T1rho MRI for molecular and diagnostic imaging of articular cartilage. *NMR in biomedicine*. 2006; 19(7):781–821. [PubMed: 17075961]
5. Grohn OHJ, Kettunen MI, Makela HI, Penttonen M, Pitkanen A, Lukkarinen JA, Kauppinen RA. Early detection of irreversible cerebral ischemia in the rat using dispersion of the magnetic resonance imaging relaxation time, T1rho. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism*. 2000; 20(10):1457–66.
6. Hakumaki JM, Grohn OH, Tyynela K, Valonen P, Yla-Herttuala S, Kauppinen RA. Early gene therapy-induced apoptotic response in BT4C gliomas by magnetic resonance relaxation contrast T1 in the rotating frame. *Cancer Gene Ther*. 2002; 9(4):338–45. [PubMed: 11960284]
7. Kettunen MI, Sierra A, Narvainen MJ, Valonen PK, Yla-Herttuala S, Kauppinen RA, Grohn OH. Low spin-lock field T1 relaxation in the rotating frame as a sensitive MR imaging marker for gene therapy treatment response in rat glioma. *Radiology*. 2007; 243(3):796–803. [PubMed: 17517934]
8. Michaeli S, Grohn H, Grohn O, Sorce DJ, Kauppinen R, Springer CS Jr, Ugurbil K, Garwood M. Exchange-influenced T2rho contrast in human brain images measured with adiabatic radio frequency pulses. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2005; 53(4):823–9.
9. Michaeli S, Oz G, Sorce DJ, 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 : official journal of the Movement Disorder Society*. 2007; 22(3):334–40. [PubMed: 17149719]
10. Michaeli S, Sorce DJ, Idiyatullin D, Ugurbil K, Garwood M. Transverse relaxation in the rotating frame induced by chemical exchange. *Journal of magnetic resonance*. 2004; 169(2):293–9. [PubMed: 15261625]
11. Michaeli S, Sorce DJ, Springer CS Jr, Ugurbil K, Garwood M. T1rho MRI contrast in the human brain: modulation of the longitudinal rotating frame relaxation shutter-speed during an adiabatic RF pulse. *Journal of magnetic resonance*. 2006; 181(1):135–47. [PubMed: 16675277]
12. Solomon I. Rotary Spin Echoes. *Physical Review Letters*. 1959; 2(7):301–302.
13. Witschey WRT, Borthakur A, Elliott MA, Mellon E, Niyogi S, Wang CY, Reddy R. Compensation for spin-lock artifacts using an off-resonance rotary echo in T-1 rho(off)-weighted imaging. *Magnet Reson Med*. 2007; 57(1):2–7.
14. Liimatainen T, Hakkarainen H, Mangia S, Huttunen JM, Storino C, Idiyatullin D, Sorce D, Garwood M, Michaeli S. MRI contrasts in high rank rotating frames. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2015; 73(1):254–62.
15. Sorce DJ, Mangia S, Liimatainen T, Garwood M, Michaeli S. Exchange-induced relaxation in the presence of a fictitious field. *Journal of magnetic resonance*. 2014; 245:12–6. [PubMed: 24911888]
16. Liimatainen T, , Nissi MJ, , Nieminen MT, , Michaeli S, , Garwood M, , Grohn H. Relaxation Along Fictitious Field (RAFF) Contrast in Bovine Articular Cartilage. *Proceedings 18th Scientific Meeting and Exhibition of the International Society for Magnetic Resonance in Medicine (ISMRM); Stockholm, Sweden. 1 – 7 May 2010; 2010*
17. Hubbard PS. Quantum- Mechanical and Semi-Classical Forms of the density Operator Theory of Relaxation. *Rev Mod Phys*. 1961; 33:249–264.
18. Abragam A. *Principles of Nuclear Magnetism* Clarendon Press; Oxford: 1991
19. Redfield AC. *Adv Magn Reson*. 1965; 1(1)
20. Slichter C. *Principles of magnetic Resonance* Berlin, Heidelberg, New York: Springer-Verlag; 1996
21. Haase A. Snapshot Flash Mri - Applications to T1, T2, and Chemical-Shift Imaging. *Magnet Reson Med*. 1990; 13(1):77–89.
22. Goldman M. Formal theory of spin--lattice relaxation. *Journal of magnetic resonance*. 2001; 149(2):160–87. [PubMed: 11318616]
23. Bendall MR, Garwood M, Ugurbil K, Pegg DT. Adiabatic Refocusing Pulse Which Compensates for Variable Rf Power and Off-Resonance Effects. *Magnet Reson Med*. 1987; 4(5):493–499.

24. Blicharski J. Nuclear magnetic relaxation in rotating frame. *Acta Phys Pol A*. 1972; 41(2):223–236.
25. Liimatainen T, Mangia S, Ling W, Ellermann J, Sorce DJ, Garwood M, Michaeli S. Relaxation dispersion in MRI induced by fictitious magnetic fields. *Journal of magnetic resonance*. 2011; 209(2):269–76. [PubMed: 21334231]
26. Liimatainen T, Sorce DJ, O'Connell R, Garwood M, Michaeli S. MRI contrast from relaxation along a fictitious field (RAFF). *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2010; 64(4):983–94.
27. Davis DG, Perlman ME, London RE. Direct measurements of the dissociation-rate constant for inhibitor-enzyme complexes via the T1 rho and T2 (CPMG) methods. *J Magn Reson B*. 1994; 104(3):266–75. [PubMed: 8069484]
28. Zinn-Justin S, Berthault P, Guenneugues M, Desvaux H. Off-resonance rf fields in heteronuclear NMR: Application to the study of slow motions. *J Biomol NMR*. 1997; 10(4):363–72. [PubMed: 20859782]

Appendix I: Definition of RAFFn Modulation Functions

$$\omega_1^{(1)} = \omega_1^{\max} \quad (\text{I.1})$$

$$\Delta\omega^{(1)} = \omega_1^{\max} \quad (\text{I.2})$$

The following recursion relations are used to generate the RAFFn Modulation Functions for even and odd n as follows:

$$\omega_{1\text{even}(t)}^{(n)} = \Delta\omega_{\text{odd}}^{(n-1)}(t) \text{Sin}\left(\int_0^t \omega_{1\text{odd}}^{(n-1)}(t_n) dt_n\right) \quad (\text{I.3a})$$

$$\Delta\omega_{1\text{even}(t)}^{(n)} = \Delta\omega_{\text{odd}}^{(n-1)}(t) \text{Cos}\left(\int_0^t \omega_{1\text{odd}}^{(n-1)}(t_n) dt_n\right) \quad (\text{I.3b})$$

$$\omega_{1\text{odd}(t)}^{(n)} = \omega_{1\text{even}}^{(n-1)}(t) \text{Sin}\left(\int_0^t \Delta\omega_{\text{even}}^{(n-1)}(t_n) dt_n\right) \quad (\text{I.4a})$$

$$\Delta\omega_{odd(t)}^{(n)} = \Delta\omega_{even}^{(n-1)}(t) \cos\left(\int_0^t \Delta\omega_{even}^{(n-1)}(t_n) dt_n\right) \quad (\text{I.4b})$$

Appendix II: Definition of RAFFn Effective Fields and Tilt Angles

For the benefit of the reader we give the equations for the RAFFn Effective Fields

And Tilt Angles for $n=0,1,2,3$. For greater detail please see [14, 25, 26]

$$\omega_1(t) = \frac{\omega_E}{\sqrt{2}} \sin\left(\frac{\omega_E}{\sqrt{2}}t + \varphi_0\right)$$

$$\Delta\omega(t) = \frac{\omega_E}{\sqrt{2}} \cos\left(\frac{\omega_E}{\sqrt{2}}t + \varphi_0\right)$$

$$\omega_E[0, t] = \frac{\omega_1^{\max}}{\sqrt{2}} \quad (\text{II.1})$$

$$\omega_E[1, t] = \frac{\omega_1^{\max}}{\sqrt{2}} \quad (\text{II.2})$$

$$\omega_E[2, t] = \sqrt{\omega_E(1, t)^2 + \dot{\alpha}^{(1)}(t)} \quad (\text{II.3})$$

$$\omega_E[3, t] = \sqrt{\omega_E(2, t)^2 + \dot{\alpha}^{(2)}(t)} \quad (\text{II.4})$$

$$\alpha^{(n)}(t) = \text{ArcTan}\left(\frac{\omega_1(t)}{\Delta\omega(t)}\right) \text{ for } n = 1 \quad (\text{II.5})$$

$$\alpha^{(n)}(t) = \text{ArcTan}\left(\frac{\omega_1^{\max}}{\omega_1^{\max}}\right) \text{ for } n = 0 \quad (\text{II.6})$$

$$\alpha^{(n)}(t) = \text{ArcTan}\left(\frac{\dot{\alpha}^{(n-1)}(t)}{\omega_E^{(n-1)}(t)}\right) \text{ for } n = 2, 3 \quad (\text{II.6})$$

$$\alpha^{(0)}(t) = \frac{\pi}{4} \quad (\text{II.7})$$

$$\alpha^{(1)}(t) = \frac{\omega_1^{\max} t}{\sqrt{2}} \quad (\text{II.8})$$

$$\alpha^{(2)}(t) = \frac{\pi}{4} \quad (\text{II.9})$$

Figure 1.

Relaxation rate constants due to dipolar interactions between like spins are plotted during the duration of RAFF3 pulse.

Normalized difference between RAFF3 rates obtained with Wigner Transformstions and Trigonometric Identity

Figure 2. Relative differences between the Trigonometric Model for relaxation during RAFF3 pulse and proposed analytic model using Wigner Rotation Matrices.