Towards a quantitative theory for inhomogeneous magnetization transfer

Scott D. Swanson[1], Dariya I. Malyarenko[2], and Mario L. Fabiilli[2]

[1]*Department of Radiology, University of Michigan, Ann Arbor, Michigan, United States,* [2]*Department of Radiology, University of Michigan, Michigan, United States*

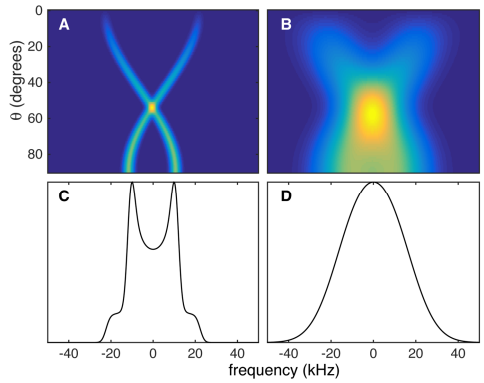

Figure 1. Pake pattern with line broadening of 100 μs (A,C) and 18 μs (B,D). A and B show the intensity of the two transitions as a function of $\boldsymbol{\theta_{ij}}$ and frequency. summing A and B over $\boldsymbol{\theta_{ij}}$ creates C and D. Other parameters are $\mathbf{S_{HH}}$ =0.7 and $\mathbf{b_{ij}}$ = 21.28 kHz.

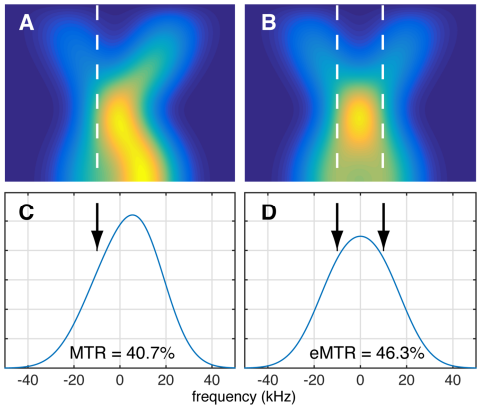

Figure 2. Simulation of RF saturation at 10 kHz (A,C) and at ±10 kHz (B,D) in a system with homogeneous and inhomogeneous broadening. Dashed lines and arrows show the frequency of RF saturation. Note the asymmetric line shape in A and C. The amount of ihMTR (= eMTR - MTR) in this example is about 6%.

Introduction: Recent work has shown that RF saturation applied at both positive and negative off-resonance frequencies creates enhanced MT (eMT) in CNS and PNS tissue and in certain lipid systems (1 - 3). This effect is termed Inhomogeneous MT (ihMT) and may prove useful for selective myelin imaging. The molecular origin of ihMT is thought to be a partially averaged dipole-dipole interaction between the CH_2 protons in myelin phospholipids (3). This work lays a theoretical foundation to derive quantitative ihMT parameters from experimental results.

Methods - Theory: The rigid lattice dipolar coupling, b_{ij}, for CH_2 protons separated by 1.78 Å is 21.28 kHz. As shown by extensive NMR, molecular dynamics, and EPR work, restricted lipid motion reduces the rigid lattice dipolar coupling to $d_{ij} = b_{ij}S_{HH}$, where S_{HH} is the order parameter, found to be between 0.2 and 0.8 for phospholipids (4). The Pake pattern of isochromatic frequencies (5) is calculated as $\nu(\theta_{ij}) = \nu_0 \pm 3/4\, d_{ij}(3\, cos^2\theta_{ij} - 1)$, where θ_{ij} is the angle between the H-H internuclear vector and the static magnetic field. The Pake pattern is shown with minimal broadening in Fig. 1A,C. Homogenous line broadening also occurs in lipids and convolving homogenous broadening with values appropriate for myelin is shown in Fig. 1B,D.

The Bloch equation for longitudinal magnetization of semisolid protons under RF saturation is given by $dM^b(t)/dt = R_1^b\left(M_0^b - M^b(t)\right) - R_{rf}^b M^b(t)$, where R_{rf}^b is the rate of saturation of the semisolid resonance given by $R_{rf}^b = \pi/2\ \omega_1^2 g^b(\delta\omega)$. At steady state, $M_{sat}^b = M_0^b R_1^b/(R_1^b + R_{rf}^b)$. The NMR spectrum of the semisolid component spectrum with RF saturation is generated by convolving the Pake pattern with RF saturation and line broadening; shown in Fig. 2 for RF saturation at 10 kHz (A,C) and at ±10kHz (B,D). MTR and eMTR are calculated as the percentage of saturation of the semisolid line. Saturation either -10 kHz (Fig. 2A,C) or +10 kHz (not shown) creates an asymmetric whereas saturation at ±10 kHz creates additional saturation of the semisolid line and additional or enhanced MT.

Methods - Experimental: Three samples, consisting of lamellar liquid crystals, Prolipid 161, and DPPC:Cholesterol phospholipids, were made in D_2O to reduce the water signal intensity and directly observe the semisolid protons. NMR spectra were obtained with RF offset, at +10kHz, -10 kHz and ±10kHz.

Results: ihMT effects in the semisolids are most evident as the difference between the spectra obtained with +10kHz and -10kHz RF saturation. When ihMT was not present (as in gelatin), the difference is zero (not shown). When ihMT is present, a dispersion-like shape is generated with amplitudes, peak frequencies, and broadening that can be compared with theory to derive corresponding quantitative metrics (M_0^b, S_{HH}, T_{2b}). Figs. 3 A-C show experimental results in a low molecular weight lamellar liquid crystal (A), a high molecular weight sample (Prolipid 161) (B), and in DPPC:Chosterol (C). Simulations with varying order parameter and line broadening are also shown (yellow lines).

Discussion: ihMTR creates images highly selective for the lamellar lipid bilayers found in myelin. Changes in myelin lipid structure and dynamics are known to occur in disease processes such as multiple sclerosis (MS) (6), yet no current imaging technologies can selectively measure these changes. Our results show that ihMT is very sensitive to lipid dynamics via order parameter estimation. Obtaining ihMTR images at different off-resonance frequencies will enable quantitative estimation of lipid content, order parameter and exchange rates to correlate with molecular measures of demyelinating disease progression.

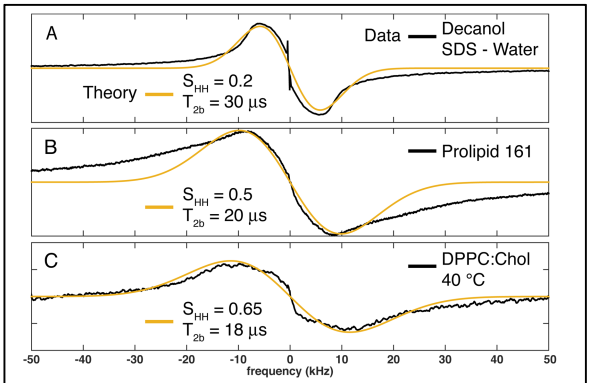

Figure 3. Difference between -10kHz and -10kHz RF saturation in lipid systems (black lines) and comparison to theory (yellow lines).

References: 1. Varma et. al. MRM, Online March 2014. 2. Girard et. al. MRM, June 2014. 3. Swanson et. al., Proc. ISMRM 2014; 309. 4. Marsh et. al. BBA, 1998, **1376** (267–96) 5. Pake, Phys Rev. 1948 **74** (1184-8); (6) Jana & Pahan, Neuromol. Med, 2010,**12**(351-361)