Avalanching Amplification of MR Difference Imaging by Nonlinear Feedback Interactions at High Field

S. Y. Huang[1], J. D. Walls[1], M. Liong[1], Y-Y. Lin[1]

[1]Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, CA, United States

Introduction

With the advent of higher field strengths and increasing polarizations in magnetic resonance (MR), nonlinear feedback (reaction) fields emerge that depend on the spin state or magnetization itself. One such feedback field is radiation damping, which arises from the interaction between the magnetization and the RF coil [1, 2]. The transverse magnetization induces a current in the coil that is fed back to the spins, producing a radiation damping field that rotates the magnetization back to the +*z*-axis at a rate much faster than T_1 relaxation. The effect of radiation damping becomes more pronounced with higher fields (scaling as the 3/2 power of field strength) and more sensitive probes: for a typical high-*Q* probe at 600 MHz, the characteristic timescale for the radiation damping effect (τ_r) is 8 ms, and an even faster onset occurs in cryogenic probes with $\tau_r \approx 4$ ms. Moreover, radiation damping can be amplified in imaging applications by modifying the electronic circuit to provide positive feedback to the induced current [3].

This work demonstrates how sensitivity to the parameters governing the magnetization evolution can be amplified based on a positive feedback cycle mediated by radiation damping and RF pulses. This approach is applied in spectroscopy and imaging experiments to improve the sensitivity of the chemical exchange-dependent saturation transfer (CEST) effect [4]. By saturating the exchangeable protons on small metabolites and monitoring the associated decrease in the water proton signal, higher sensitivity can be achieved by CEST compared to direct detection. Still, the sensitivity enhancement provided by CEST is often limited for extremely dilute solutes with a small number of exchangeable protons or with slow exchange rates. Amplifying the CEST effect through radiation damping and external RF perturbations provides additional orders of magnitude of enhancement, which may prove useful in the design of more flexible molecular probes and contrast agents for CEST.

Methods & Results

Under radiation damping, inverted magnetization along the -*z* direction represents an unstable equilibrium and exhibits extreme sensitivity to small variations in the magnetization vector. As depicted in the pulse sequence in Fig. 1, following θ_1, which flips the magnetization vectors near the inverted state, the magnetization trajectories begin to diverge as the vectors nutate toward +*z* at rates dependent on their respective vector amplitudes. After τ, another pulse θ_2 flips the magnetization vectors near the inverted state again. Subsequent evolution under radiation damping further differentiates the magnetization vectors. This process is repeated *n* times until the trajectories reach maximal separation, which can be monitored by spectroscopy.

Figure 1 shows the results from a CEST experiment with radiation damping amplification for a sample of 10 mM ammonium chloride solution in a 5 mm sample tube on a Bruker Avance 600 MHz spectrometer with a triple resonance broadband inverse probe ($\tau_r \approx 8$ ms). In two successive experiments, saturation of the ammonium resonance produced a decrement of 2% in the water magnetization compared to irradiation applied at the same frequency on the opposite side of the water peak. While the CEST effect was limited in this sample, applying the pulse sequence in Fig. 1 with judiciously chosen θ_1, θ_2, *n*, and τ values optimized the positive feedback mechanism to differentiate the magnetization trajectories by radiation damping, leading to amplification of the initial magnetization difference due to CEST by up to 40 times.

Such avalanching amplification of small magnetization variations can be directly integrated into existing fast imaging sequences. This is demonstrated by microimaging experiments on the 600 MHz spectrometer conducted on the same sample of 10 mM ammonium chloride in a probe equipped with a Micro5 gradient system (1000 mT/m) and a 5 mm $^{13}C/^{1}H$ insert (saddle coil geometry) optimized for proton sensitivity ($\tau_r \approx 12$ ms). Figure 2 compares the one-dimensional projections of gradient echo difference images for CEST and radiation damping-enhanced CEST. The CEST effect in this case was enhanced by 12 times after applying the sequence shown in Fig. 1.

Discussion & Conclusions

As magnetic resonance progresses toward higher fields and more sensitive probes with active feedback circuits become available, amplification of small initial differences by radiation damping should be particularly advantageous in enhancing the images from such difference methods as CEST, flow alternating inversion recovery (FAIR), and magnetization transfer contrast (MTC). The work presented here offers a conceptual departure from conventional approaches to ascertaining the properties of the magnetization. By tailoring RF pulse manipulations to act in concert with nonlinear feedback fields in high-field MR, our approach provides a fundamentally new way to practice MR – allowing the spins themselves to play an active role in dictating their own evolution through positive feedback – which can lead to increased sensitivity to experimental parameters.

References

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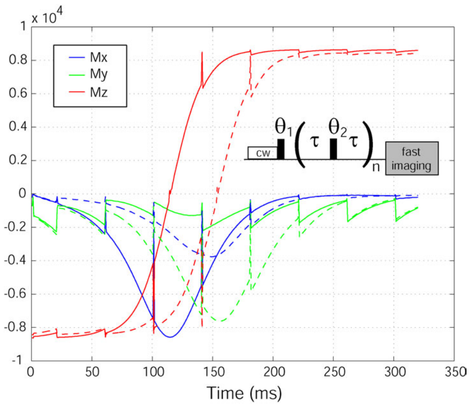

Fig. 1. Experimental trajectories showing the divergence of two magnetization vectors prepared by the sequence shown. The initial difference in magnetizations was prepared by CEST: continuous wave (cw) irradiation was applied at 60 mW for 150 ms at (dashed) and opposite (solid) the ammonium resonance. θ_1 = 175°, θ_2 = 10°, *n* = 3, and τ = 20 ms.

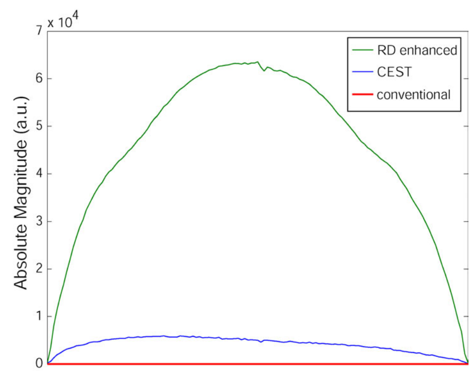

Fig. 2. One-dimensional projections of direct solute imaging (red), CEST difference imaging (blue), and radiation damping-enhanced CEST difference imaging (green; see sequence in Fig. 1). For CEST and radiation damping-enhanced CEST, cw irradiation was initially applied at 5mW for 1s at and opposite the ammonium resonance. θ_1 = 170°, θ_2 = 144°, *n* = 3, and τ = 30 ms. Imaging parameters included a matrix size of 128 × 128, an FOV of 5 × 5 mm^2, and an imaging slice thickness of 15 mm.