Indirectly-Detected Heteronuclear MR Spectroscopy & Imaging by Amplified Solvent Proton Signals

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Target audience Physicians and physicists interested in the research of heteronuclear MR spectroscopy and imaging, indirect detection, nonlinear spin dynamics, and sensitivity enhancement.

Purpose Low sensitivity is particularly problematic in heteronuclear MRI, where insensitive and/or dilute heteronuclear spins are detected. A general spin amplification scheme was developed to enhance the sensitivity of heteronuclear spins based on dynamic instability of the solvent magnetization under collective feedback fields. The heteronuclear solute spins are first detected by the solvent proton spins through various magnetization transfer mechanisms and serve as small "input" signals to perturb the solvent proton magnetization, which is prepared in an unstable state. The weakly detected signal is then amplified through subsequent nonlinear evolution of the solvent proton magnetization. By manipulating bulk solvent proton spins near the threshold of instability to detect dilute heteronuclear solute spins, sensitivity and signal-to-noise ratios (SNR) of the heteronuclear MR spectroscopy and imaging can be markedly improved.

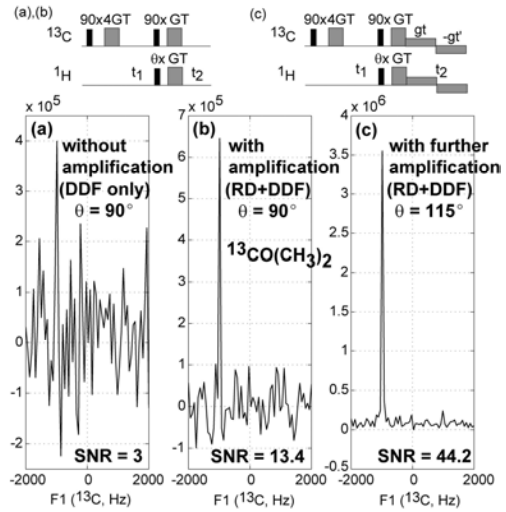

Fig. 1: Indirectly detected spectra of 10% 2-^{13}C acetone at 600 MHz (a) without amplification, (b) with amplification, and (c) with further amplification, using the pulse sequences at top.

Methods & Results This general spin amplification scheme is shown here to amplify indirectly detected heteronuclear solute signals. Low-gyromagnetic ratio nuclei can be detected through the large solvent ^{1}H magnetization by the distant dipolar field (DDF) [1,2]. As shown in Fig. 1 (pulse sequence at top, a+b), the modulated ^{1}H transverse magnetization precesses under the DDF created by the spatially modulated ^{13}C longitudinal magnetization, generating an echo in the ^{1}H solvent magnetization that carries information about the ^{13}C spins. Recently discovered self-refocusing of dephased solvent magnetization due to the joint action of radiation damping and the DDF [2] is exploited to enhance the indirectly detected echo signal. The extreme sensitivity of the first and largest self-refocused echo's phase and amplitude to the phase and amplitude of the initial triggering magnetization (here, the indirectly detected signal) suggests that the nonlinear spin dynamics can serve as a high-gain spin amplifier to enhance the small initial magnetization transferred to the solvent from the dilute ^{13}C solute spins. The resulting SNR of the amplified indirectly detected echo signal, *e.g.*, 10% 2-^{13}C acetone solution, is improved by ~3-4x (Fig. 1b) compared to without amplification (Fig. 1a, DDF only). The amplification factor can be further improved by controlling the nonlinear spin evolution under the feedback fields. For example, if the ^{1}H pulse flip angle $\theta>90°$, the instability of the inverted net ^{1}H longitudinal magnetization under radiation damping aids in refocusing more ^{1}H transverse magnetization. Moreover, field inhomogeneity or weak continuous gradients may also be exploited to accelerate the self-refocusing process [3] and increase SNR by more than 10x overall (Fig. 1c). Application of this approach to ^{13}C MRI is shown in Fig. 2 and Fig. 3 for a phantom sample and carrot stem, respectively.

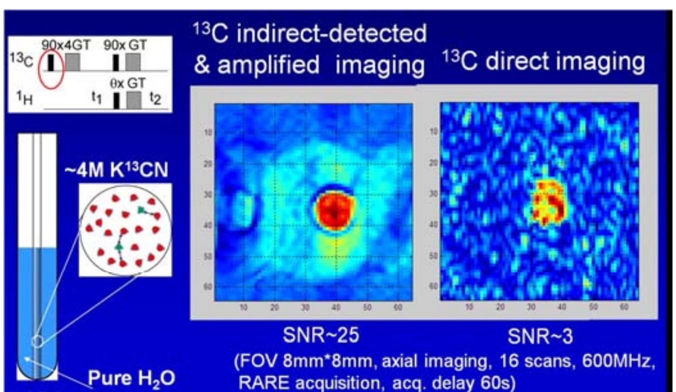

Fig. 2: ^{1}H axial indirect-detected spin-amplified images at 600 MHz of a capillary containing 4M K^{13}CN. Compared with direct detection of ^{13}C images (right), an enhancement of ~8 times in SNR is achieved for the difference image (left), where the 1st ^{13}C excitation pulse is on or off, respectively.

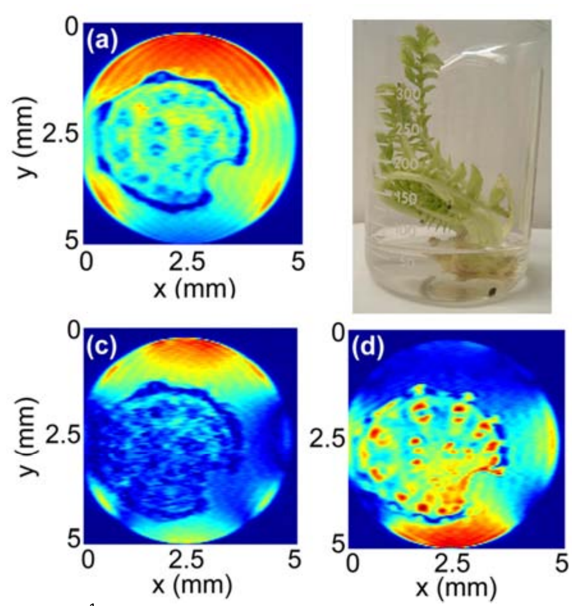

Fig. 3. ^{1}H axial images at 600 MHz of carrot stems, acquired after being immersed in 1 M U-^{13}C glucose for 48 hours: (a) T_2-weighted, (b) the carrot, (c) T_1-weighted, and (d) the difference image acquired when the 1st ^{13}C excitation pulse is on or off, superimposed on the ^{1}H density image.

Discussion & Conclusion Sensitivity enhancement by the dynamic instability of solvent proton magnetization represents a new direction for surmounting a long-standing weakness of poor sensitivity in heteronuclear MR spectroscopy and imaging.

Reference [1] R. Bowtell, *J. Magn. Reson.* **100**, 1 (1992) [2] Warren et al. *J. Chem. Phys.* **108,** 1313 (1998) [3] Y.-Y. Lin et al. *Science* **290**, 118 (2000).