# Improved High-Resolution MRS in Inhomogeneous Fields via Intermolecular Zero-Quantum Coherences

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## Introduction

High-resolution nuclear magnetic resonance (NMR) spectroscopy normally provides information of chemical shift, scalar couplings, and relative peak area for spectral assignment. However, variations in spatial and temporal homogeneity of the magnetic field may produce spurious field gradients that broaden resonance lines and hide fine spectral features. Intermolecular multiple-quantum coherences (iMQCs) provide a possible way for obtaining high-resolution spectra in inhomogeneous fields [1-4]. In this report, an improved iZQC pulse sequence with high acquisition efficiency was proposed.

## Methods

The designed pulse sequence is shown in Fig. 1. The second RF pulse is selective for solvent only. For a homogeneous liquid mixture consisting of an AX spin-1/2 system of $S$ component (solute, including $S_k$ and $S_l$ spins with scalar coupling constant $J_{kl}$) and a single spin-1/2 system of $I$ component (solvent), the iMQC treatment shows that the N-type intermolecular cross-peaks will center at $(\omega_I/2 - \pi J_{kl}, \omega_{S_k} + \pi J_{kl})$ and $(\omega_I/2 + \pi J_{kl}, \omega_{S_k} - \pi J_{kl})$, respectively and incline along a specific direction $\phi = \text{arctg}(2) = 63.4°$, where $\phi$ is the angle of spectral peaks with respect to the F1 axis, $\omega_m$ is the frequency offset of spin $m$ ($m = I, S_k, S_l$) in the rotating frame in the absence of magnetic field inhomogeneity. The $J$ coupling constants are scaled by a factor of $1 + \cot\phi = 3$.

Experiment was performed on a Varian Unity+ 500 MHz NMR spectrometer. The sample is a mixture of methyl ethyl ketone (solute) and cyclohexane (solvent). The gradient amplitude was $G \approx 0.08$ T/m and the duration $\delta = 2.0$ ms. The radiation damping effect was neglected by deliberately detuning the probe. The magnetic field was intentionally deshimmed to produce a line-width of 50 Hz. The spectral width of F1 dimension was 70 Hz and was 1200 Hz for F2 dimension.

Computer simulation [5] was also carried out to verify the theoretical prediction and experimental observation.



**Fig. 1.** iZQC pulse sequence

## Results and discussion

The 1D spectrum of the sample in a homogeneous magnetic field was first recorded (see Fig. 2a). The magnetic field was then intentionally degraded by deshimming the sample to produce a line-width of 50 Hz. The resulting 1D spectrum is shown in Fig. 2b, from which little useful spectral information can be deduced. The 2D iZQC spectrum obtained in such an inhomogeneous field from the pulse sequence shown in Fig. 1 is illustrated in Fig. 3b. The intermolecular cross-peaks align along the horizontal axis. Although the lengths of the streaks are susceptible to the inhomogeneity, the projection onto the F2 dimension of the 2D spectrum after a counterclockwise rotation of 63.4° is well resolved (Fig. 2c). The line-width is reduced from 50 to 3 Hz, remarkably similar to a conventional 1D high-resolution spectrum. The shearing projection spectrum maintains the spectral information of chemical shifts, relative peak areas, coupling constant, and multiplet patterns. The only difference of it from a conventional 1D spectrum is that the $J$ splitting distances are 3-fold magnified, i.e. the scale factor of the $J$ coupling constants is 3 (see Fig. 2a & 2c). This large scale factor makes it capable to reveal multiplet information of spin systems with small $J$ coupling constants. The above experimental measurement is supported by the result of computer simulation shown in Fig. 3a and in agreement with our theoretical prediction.

Compared to SEL-HOMOGENIZED sequences [3], all the streaks in the 2D spectra now align up along the center of the F1 dimension. This enables a substantial decrease of the F1 spectral width that needs to be sampled, thus reduces experimental time.

Theoretically, the time saving can be calculated to be $\propto \dfrac{\text{range of chemical shift}}{\text{range of field inhomogeneity}}$.

It opens a fast way to achieve 1D high-resolution NMR spectra in inhomogeneous fields. The method can conceivably be used in local spectroscopy and *in situ* analysis of chemical systems.



**Fig. 2.** 1D $^1$H NMR spectra of a mixture of methyl ethyl ketone and cyclohexane. (a) Conventional 1D high-resolution spectrum; (b) 1D spectrum acquiring in an inhomogeneous field; (c) projection of 2D iZQC spectrum.
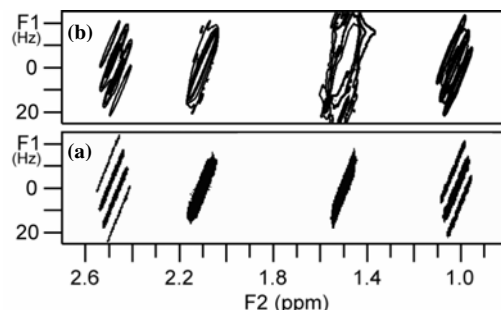


**Fig. 3.** 2D iZQC spectra of the mixture of methyl ethyl ketone and cyclohexane in an inhomogeneous field with 50 Hz line-width obtained from the pulse sequence shown in Fig. 1. (a) Simulation spectrum, (b) experimental spectrum.

## References

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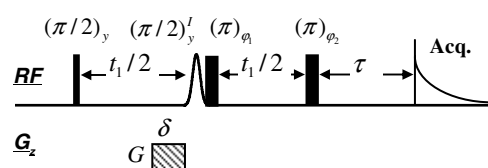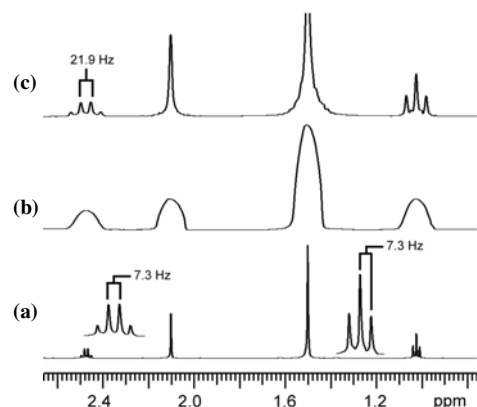[5] C.B. Cai, Z. Chen, S.H. Cai, J.H. Zhong. *J. Magn. Reson.* 172 (2005) 242.