

# Accurate Measurements of Small $J$ Coupling Constants in Inhomogeneous Fields

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## Introduction

Scalar coupling constant is an important parameter for structure analysis from nuclear magnetic resonance (NMR) spectra. However, for spin systems with small  $J$  coupling constants, it is difficult sometimes to obtain precise  $J$  coupling constants due to inconspicuous line splitting, especially when line-width is broadened in inhomogeneous fields. The line-widths of intermolecular multiple quantum coherence (iMQC) peaks in indirect dimension only depend on the relative homogeneity within the correlation distance in the sample [1]. Recently, we reported that high resolution spectra can be obtained in inhomogeneous field though iMQC detection [2-4]. In this report, a new pulse sequence which can scale  $J$  coupling constants arbitrarily was designed to acquire precise  $J$  coupling constants under inhomogeneous fields.

## Methods

The pulse sequence is shown in Fig. 1. The three selective pulses excite  $S$ ,  $I$ , and  $I$  spins respectively, where  $S$  represents solute and  $I$  represents solvent. The scaling factor (SF) of  $J$  coupling constant is  $1+1/m$ , where  $0 < m < 1/2$ . To test the proposed pulse sequence, <sup>1</sup>H NMR spectra of a sample of mixture of methyl ethyl ketone (solute) and cyclohexane (solvent) in an inhomogeneous field (~30Hz in line-width) were measured on a Varian Unity<sup>+</sup> 500 MHz NMR spectrometer. The gradient amplitude was  $G = 0.10$  T/m and the duration  $\delta = 1.2$  ms. We take  $m=1/4$  for example. Radiation damping effect was suppressed effectively by deliberately detuning the probe.

## Results and Discussion

The acquired 2D spectrum is shown in Figs. 3. The projection of Fig. 3a onto the F2 dimension after a counterclockwise rotation of 76° is shown in Fig. 2c. It can be seen that the projected spectrum maintains chemical shifts, relative peak areas, and multiplet patterns while inhomogeneous broadening is suppressed. Moreover, the  $J$  splitting distances are 5-fold magnified compared to Fig. 2a, in good agreement with the theoretical predictions. The magnification of  $J$  splits allows more accurate measurement of small  $J$  coupling constants. Furthermore, the solvent peak in Figs. 2c

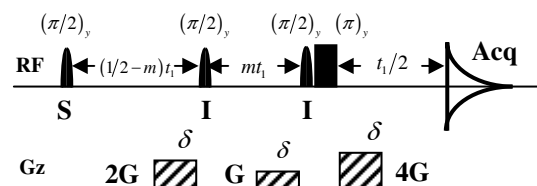
is much weaker than that in Fig. 2a. This suggests that solvent peak can be suppressed to some extent by the new pulse sequence. This is very useful for *in vivo* NMR spectroscopy. In view of the ability of scaling  $J$  coupling constants and extracting high-resolution spectra under inhomogeneous fields, the technique proposed herein can conceivably be used in local spectroscopy and *in situ* analysis of chemical systems.

## Acknowledgments

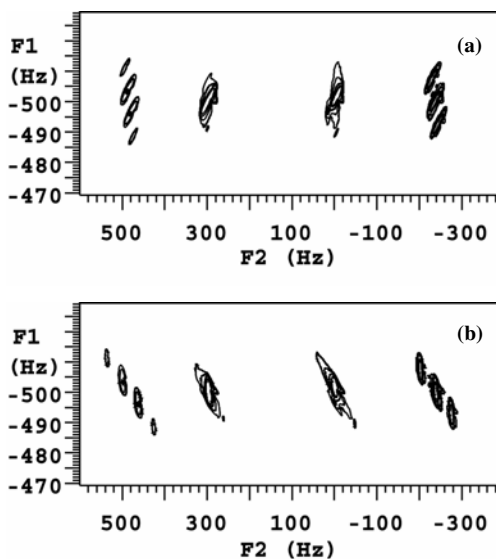
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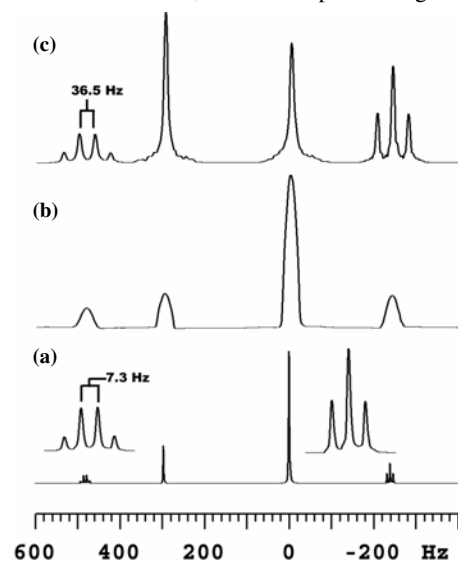
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**Fig. 1.** Pulse sequence for  $J$ -scaled high-resolution spectra in inhomogeneous fields via iMQCs.



**Fig. 3.** 2D <sup>1</sup>H NMR spectra of the mixture of methyl ethyl ketone and cyclohexane using the pulse sequence of Fig. 1 in the same inhomogeneous field as Fig. 2b. (a) Experimental spectrum with  $m = 1/4$ , (b) sheared spectrum of (a) after a counterclockwise rotation of 75.96°.



**Fig. 2.** 1D <sup>1</sup>H NMR spectra of the mixture of methyl ethyl ketone and cyclohexane. (a) Conventional 1D high-resolution spectrum in a well-shimmed field, (b) 1D spectrum acquired in an inhomogeneous field of about 30 Hz line-width, (c) accumulated projection of the sheared experimental spectrum shown in Fig. 3b.