

# High Resolution NMR Spectra in Inhomogeneous Fields via Intermolecular Double Quantum Coherences

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## SYNOPSIS

Intermolecular double quantum coherence (iDQC) technique is used to yield high-resolution NMR spectra in inhomogeneous magnetic fields. The method is based on the long-range dipolar interactions between solvent and solute spins. The technique was applied to a mixture of isopropanol and dimethyl sulfoxide, a mixture of major brain metabolites, and a sample of homogenized brain tissue from a rat. Experimental results showed that the chemical shifts, coupling constants, and relative intensities obtained in an inhomogeneous field are in agreement with those in a homogeneous field. This technique may find potential applications in *in-vivo* MR spectroscopy.

## INTRODUCTION

The pursuit for higher resolution in NMR spectroscopy never stops. A variety of techniques have been designed to extract spectral information from inhomogeneously broadened spectra.<sup>[1,2]</sup> Recently, intermolecular zero-quantum coherences (iZQCs) from long-range dipolar interactions were shown to result in high-resolution spectra with substantial and predictable intensities at high fields.<sup>[2]</sup> The main challenge in the method is to isolate the iZQC signals from the much stronger conventional single-quantum signals. In this abstract a new approach is presented in an attempt to remedy the shortcomings of current techniques.

## THEORIES AND EXPERIMENTS

iDQCs have similar characteristics as iZQCs. Our previous works suggested that there is no need to use additional phase cycling to obtain "pure" iDQC signals and their intensities are higher than those from iZQCs.<sup>[3]</sup> Since the spins on solute and solvent molecules coupled by long-range dipolar interactions are physically close to each other and experience similar magnetic field over the distance between the two spins, the DQ spectrum mimics the conventional single-quantum spectrum of the solute, but is shifted by the chemical-shift of the solvent. Thus, chemical shift difference and coupling information for the solute could be retained, and inhomogeneous broadening and field drift would be almost completely canceled. The pulse sequence (Fig. 1) was designed to obtain high-resolution spectra in extremely inhomogeneous magnetic field without removing chemical shifts and *J* couplings. We call this detection scheme IDEAL (Intermolecular Dipolar-interaction Enhanced All Lines) method. A sample of a mixture of isopropanol and dimethyl sulfoxide (DMSO) was tested at Varian INOVA 600. The conventional <sup>1</sup>H spectrum of this sample in well-shimmed field is shown in Fig. 2c. The sample was then deshimmied to produce a linewidth of ~105Hz (Fig.2a). IDEAL sequence was then applied to the deshimmied sample, resulting in the DQ spectrum (Fig. 3). The same technique was also applied to a mixture of major brain metabolites and a sample of homogenized brain tissue from a rat. Similar results were obtained.

To understand the essence of the sequence, we consider an *I* (solvent) and *S* (solute) spin systems of different resonance frequencies, with the second RF pulse selective for the *I* spin only. If  $\Delta B(x,y,z)$  is the width of the spatially dependent field inhomogeneity, the resonance frequency for the *S* spins in the F2 dimension ranges between  $\omega_{SQ}(x,y,z) = \omega_s \pm 0.5\gamma \Delta B(x,y,z)$ , the frequency in the F1 dimension ranges between  $\omega_{DQC}(x,y,z) = (\omega_I + \omega_S) \pm \gamma \Delta B(x,y,z)$ . If the spectrometer reference frequency coincides with the resonant frequency of the *I* spin, i.e.  $\omega_I = 0$ , the intermolecular cross peaks between *I* and *S* spins will be centered at  $(\omega_s, \omega_s)$  with separate streaks along the specific direction  $\phi = \arctan 2$  (Fig. 3). A projection of the cross peaks along the special axis perpendicular to  $\phi$  gives a 1D high-resolution spectrum without inhomogeneous broadening. Since the spatial correlation via dipolar field of the solvent affects all the spins of the solute equally, the relative signal intensities and chemical shifts from iDQCs are the same for all resonances as those in routine 1D NMR spectrum. On the other hand, the correlation of spatial distribution of field inhomogeneity is independently of *J* couplings, so the spins of the solute evolve under *J* coupling in both F1 and F2 dimensions. Therefore, the trace in the F2 dimension has the same multiplicity patterns with the scale factor  $1 + \cot \phi = 1.5$  of the *J* coupling. To obtain a projection spectrum which is similar to a conventional 1D one, a rotation of  $\phi$  around the centers of individual *J*-multiplets was performed. After this shearing procedure, a horizontal summing projection maintains the frequency separation between the cross peaks while the inhomogeneous broadening is suppressed (Fig. 2b). In addition, the projection of the 2D spectra (inset in Fig. 2b) has much higher resolution than the original 1D spectrum shown in Fig. 2a. The linewidth is reduced from 105 to 2 Hz, remarkably similar to the conventional high-resolution <sup>1</sup>H spectrum (Fig. 2c).

## CONCLUSION

A novel method to obtain 1D high-resolution NMR spectra in inhomogeneous fields is developed. Chemical shifts, coupling constants, multiplicity patterns, and relative signal intensities can all be retained. It has significant advantages over their iZQC counterpart. This technique may find potential application in *in-vivo* localized homo- and hetero-nuclear MR spectroscopy, and work in these directions is currently under way.

## ACKNOWLEDGMENT

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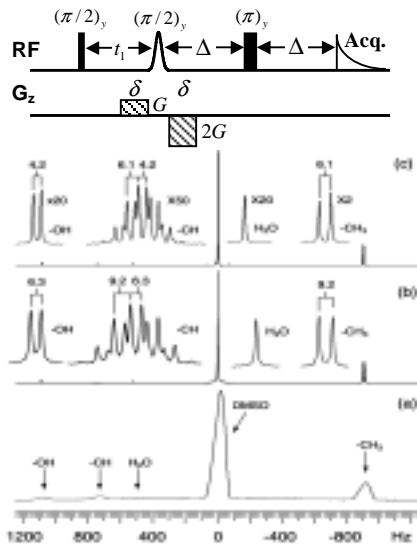


Fig 1. The IDEAL sequence, which produces high-resolution spectra in inhomogeneous fields. (see left)

Fig 2 (LEFT). (a) Conventional 1D <sup>1</sup>H spectrum in the inhomogeneous field; (b) accumulated projection of the sheared spectrum shown in Fig. 3, and (c) single-pulse spectrum in a well shimmed field. Insets are magnified in both vertical and horizontal directions.

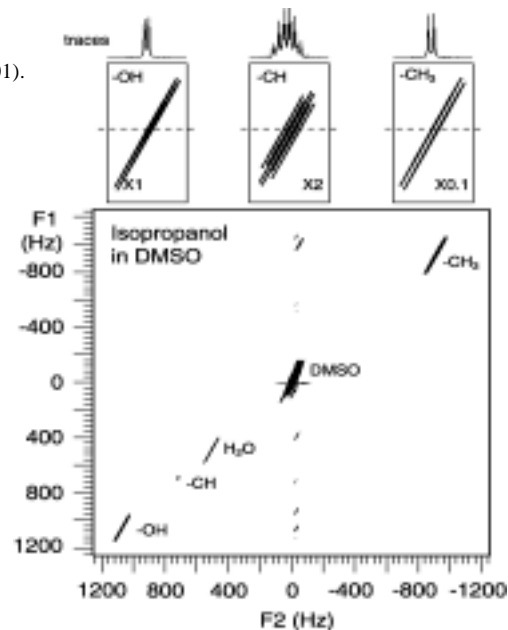


Fig 3 (RIGHT). 2D iDQC spectrum in an inhomogeneous field. The -OH, -CH, and -CH<sub>3</sub> regions are expanded in both vertical and horizontal directions. The 1D spectra are the traces along the dashed line.