High-resolution NMR Spectra of Heterogeneous Biological Tissues via Intermolecular Single-quantum Coherences

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Introduction

High-resolution NMR spectroscopy offers a powerful tool to analyze molecular structures and compositions through the measurement of chemical shifts, scalar coupling constants, multiplet patterns, and peak areas. However, it is difficult to obtain high-resolution information under the circumstances where the spatial homogeneity of the magnetic field is degraded due to intrinsic variations in magnetic susceptibility. Intermolecular multiple-quantum coherences (iMQCs) provide a feasible way to obtain high-resolution spectra [1]. Recently, we proposed several pulse sequences based on intermolecular zero- or double-quantum coherences [2-4]. In this abstract, intermolecular single-quantum coherences (iSQCs) were employed to obtain high-resolution spectra for heterogeneous biological tissues with high acquisition efficiency and water suppression while retaining the same information as conventional single-quantum coherence (SQC) spectra.

Methods

The pulse sequence is shown in Fig. 1. The first and the third RF pulses are selective for solvent while the second RF pulse is selective for solute. Three linear coherence selection gradients with an area ratio of 1:0.7:-2.4 are applied along *z* direction to select the coherence transfer pathway $0 \rightarrow +1 \rightarrow +2 \rightarrow +1$. In such a way, only the interesting solute-solvent iSQCs are chosen while both conventional SQCs and iMQCs from solvent are filtered out. Furthermore, the excitation sculpture before acquisition and a specially designed phase cycling improve solvent suppression efficiency. The observable signal at the detection period can be written as

$$M^{+}_{iSQC}(t_1+t_2) = \frac{i\pi\Delta_s t_2}{6\tau_d^I}\left(\frac{kT}{\hbar\omega_I}\right)^2 M_0^S e^{-i\omega_1 t_1}[e^{i(\omega_{Sk}+\pi J_{kl})t_2} + e^{i(\omega_{Sk}-\pi J_{kl})t_2}],$$

where $\tau_d^I = 1/\mu_0\gamma M_0^I$ is the dipolar field time constant and γ is the gyromagnetic ratio.

Experiments were performed at 298 K using a Varian NMR System 500 MHz spectrometer, equipped with a 5 mm indirect detection probe with three-dimensional gradient coils. An 8-step phase cycling was applied: the phases for the first RF pulse, the third RF pulse and receiver were (*x*, -*x*, *x*, -*x*, *x*, -*x*, *x*, -*x*), (*x*, *x*, -*x*, -*x*, *x*, *x*, -*x*, -*x*), and (*x*, -*x*, -*x*, *x*, *x*, -*x*, -*x*, *x*), respectively. A sample of intact pig brain tissue was used to test the feasibility of this sequence for biologic samples with intrinsic macroscopic susceptibility gradients and intense water signal. Moreover, a PRESS-like module [5] was implemented to this sequence to obtain the spatially localized iSQC spectra on a sample in a test tube with pig brain tissue closely packed against a piece of cucumber.

Results and Discussion

The 1D spectra of the intact pig brain tissue are presented in Fig. 2. It is noticed that hardly any spectral information can be obtained from the conventional SQC spectrum. In the 1D accumulated projection of the 2D iSQC spectrum after a counterclockwise rotation of 45°, the line-widths are greatly reduced and several multiplet patterns of metabolites such as lactate (Lac, 1.31 ppm) and alanine (Ala, 1.47 ppm) can be resolved.

The localized iSQC spectra of the sample packed with pig brain tissue and cucumber are shown in Fig. 3. No information can be obtained from the 1D SQC spectrum with a line-width of 100 Hz and intensive water signal (Fig. 3a). When different regions of the sample are selected, the corresponding iSQC signals can be obtained, as shown in Fig. 3b-d. The results suggest that the method provides a feasible way for *in vivo* magnetic resonance spectroscopy.

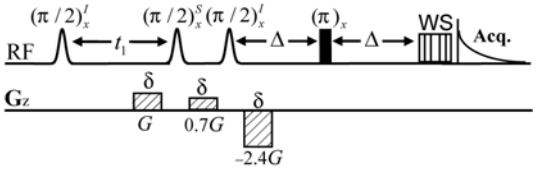

Fig.1 Pulse sequence for high-resolution spectra of heterogeneous biological tissues via iSQC acquisition.

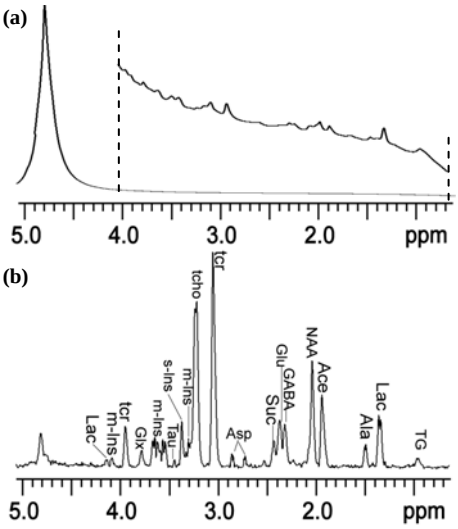

Fig.2 Spectra of pig brain tissue. (a) Conventional 1D SQC spectrum; (b) 1D accumulated projection of 2D iSQC spectrum using the pulse sequence in Fig. 1.

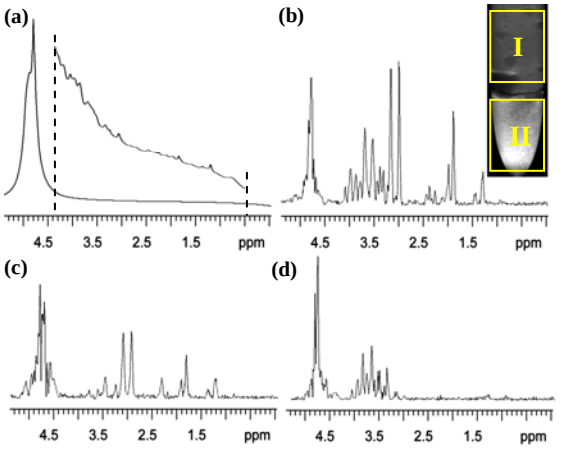

Fig.3 Spectra of a sample packed with pig brain tissue and cucumber. (a) Conventional SQC spectrum with 100 Hz line-width; (b) ~ (d) localized iSQC spectra of the whole sample, the pig brain tissue, and the cucumber, respectively. The spin echo image of the sample is shown on the top right and the localized region of the pig brain tissue and cucumber are marked by I and II respectively.

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