High-resolution localized 2D J-resolved Spectroscopy for Biological Tissues

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Target audience

Magnetic resonance spectroscopy (MRS) provides useful metabolite information complementing the insight delivered by MRI for biological systems, and enables an impartial investigation of changes in metabolic status due to diseases, toxic insult, genetic manipulation, etc. [1,2] An effective MRS approach applied for high-resolution localized 2D *J*-resolved information in biological tissues is presented in this report, and people who perform metabolic study in biological systems may be interested.

Purpose

1D MRS approach is a common tool in metabolomics with the advantages of fast spectral acquisition. However, there are two main reasons limiting applications of 1D MRS in biological tissues. Firstly, 1D MRS measurement of biological samples with complex metabolites generally yields highly congested spectra with overlapping signals and severely hinders metabolite identification and quantification. Secondly, MRS study on biological tissues is generally impacted by the field inhomogeneity originated from variations of macroscopic magnetic susceptibility, resulting in spectral line broadening and loss of the desired information for metabolite identification. Although localized 2D *J*-resolved spectroscopy (*J*RES), *J*PRESS, can provide a feasible solution for the signal overlapping problem in 1D MRS of biological tissues by separating chemical shift and *J* coupling information along two different dimensions,[3] the *J*PRESS still suffers from inhomogeneous effects from macroscopic susceptibility variations in biological tissues. It is well known that intermolecular multiple-quantum coherences (iMQCs) provide a feasible way to obtain high-resolution spectra in inhomogeneous fields.[4] In this report, a new MRS sequence based on intermolecular double-quantum coherences (iDQCs) is introduced to eliminate inhomogeneous effects and recover high-resolution localized 2D *J*-resolved spectra from biological tissues.

Methods

The iDQC *J*RES sequence is schematically shown in Fig. 1. It can be understood intuitively using the raising and lowering operator formalism in the following:

$$I_zS_z \xrightarrow{(\pi/2)_x} \frac{1}{4}I^+S^+\left(t_1/2\right) \xrightarrow{(\pi/2)_x^I} \frac{1}{8}I_zS^+\left(t_2/2\right) \xrightarrow{(\pi)_x,\ D_{IS}I_zS_z} \frac{1}{8}S^-\left(t_1/2+t_2/2+t_3\right),$$

where I spin (corresponding to the solvent) and S spins (corresponding to solutes) are spin-1/2 systems and D_{IS} is distant dipolar interactions for iDQCs between solvent and solute spins. And a PRESS-like module is used for spatial localization. After the 3D acquisition and corresponding data processing, the location for the observable signal is ($\omega_I/2+\gamma\triangle B/2$, $\pm\pi J$, ω_S), high-resolution 2D *J*-resolved spectrum can be extracted by projecting the processed 3D data into F2-F3 plane. Although 3D acquisition is needed, two indirection dimensions only cover half of inhomogeneous broadening and *J* coupling respectively, thus acquisition efficiency is greatly improved.

A layered biological sample of pig brain tissue closely packed against a piece of cucumber in a 5 mm NMR tube was applied. The voxels were set to 4×4×16 mm^3, 4×4×7 mm^3, and 4×4×7 mm^3 for localizing the whole stratified sample, the pig brain tissue, and the cucumber tissue, respectively. The pulse repetition time was 1.0 s, a 4-step phase cycling was applied, and 12 × 40 × 150 points were acquired with spectral widths of 100 Hz × 100 Hz × 4000 Hz (F1×F2×F3) in 32 min. The data was processed using our custom-written program on MATLAB 7.8 (The MathWorks, Natick, MA). For comparisons, a traditional *J*PRESS experiment is also performed under the same condition. All experiments were performed at 298 K using a Varian NMR System 500 MHz spectrometer, equipped with a 5 mm indirect detection probe with 3D gradient coils.

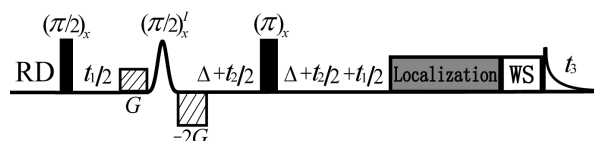

Fig.1 Pulse sequence for high-resolution localized 2D *J*-resolved spectroscopy from inhomogeneous fields.

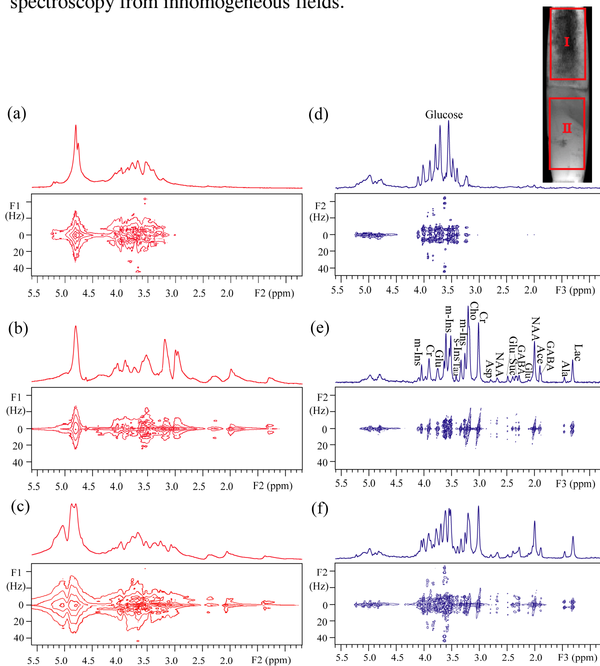

Fig.2 Localized 2D *J*-resolved spectra on a layered sample of pig brain tissue and cucumber tissues. Localized regions of the cucumber and pig brain tissues are marked by I and II respectively and sagittal GRE image of the sample is on upper right. (*a* ~ *c*) 2D *J*PRESS spectra localized on region I (*a*), region II (*b*), and the whole sample (*c*); (*d* ~ *f*) iDQC 2D *J*RES spectra localized on region I (*d*), region II (*e*), and the whole sample (*f*).

Results and discussion

The comparison results on the layer sample acquired from *J*PRESS and iDQC *J*RES methods are presented in Fig. 2. The *J*PRESS spectra for region I, region II, and the whole layered sample are shown in Fig. 2*a*, *b* and *c*, respectively. It can be noticed that these 2D *J*PRESS spectra are subject to inhomogeneous line broadening along the F2 dimension due to macroscopic susceptibility variations, which results in spectral peak overlap and loss of exact chemical shift and *J* coupling information. The iDQC localized 2D *J*-resolved spectra for the corresponding regions are given from Fig. 5*d*, *e*, and *f*, respectively. The spectral resolution is greatly enhanced and the linewidth is reduced from 90 Hz to 15 Hz along F3 dimension in Fig. 5*d*, *e*, and *f*, then the main metabolites for brain and cucumber tissues can be clearly assigned. The *J* coupling information for metabolites can be obtained along F2 dimension. It's clear that the iDQC *J*RES method still holds the ability of eliminating the field inhomogeneity from macroscopic magnetic susceptibility and provides a useful tool for studying metabolites in biological tissues.

Conclusion

Here, we present an iDQC *J*RES method for achievement of high-resolution localized 2D *J*RES spectra under inhomogeneous magnetic fields. With immunity to field inhomogeneity from macroscopic magnetic susceptibility and efficient water suppression, iDQC *J*RES method is well suitable for localized 2D *J*-resolved detection on biological tissues. Compared to the existing *J*PRESS technique, high-resolution *J*-resolved information can be obtained for the analysis of metabolites. The iDQC *J*RES method is merely based on pulse sequence design and can work on standard NMR spectrometers without any hardware requirement, providing a convenient and effective way for metabolic study of biological systems, even *in vivo* systems.

References

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