High-resolution heteronuclear NMR spectroscopy based on spatial encoding and coherence transfer

Kaiyu Wang[1], Zhiyong Zhang[1], Hao Chen[1], Shuhui Cai[1], and Zhong Chen[1]

[1]*Department of Electronic Science, Xiamen University, Xiamen, Fujian, China*

Target audience

The target audience is basic scientists and clinical scientists who are interested in high-resolution MRS.

Purpose

Two dimensional (2D) NMR fulfills a central role in the application of NMR on chemistry, biology and medicine. Heteronuclear single quantum correlation (HSQC) and heteronuclear multiple bond correlation (HMBC) are foremost two-dimensional (2D) NMR methods. Specially, in combination with spatially encoded technique, heteronuclear 2D NMR can be applied to monitor biochemical reaction.[1] However, high-resolution NMR spectra are difficult to be obtained in inhomogeneous fields caused by internal susceptibility heterogeneities of samples as well as the poor homogeneity of external magnetic fields. Inspired by the idea of tracing the difference of precession frequencies between two different spins to yield high-resolution spectra,[2,3] we propose a new method with two acquisition options to ultrafast obtain high-resolution HSQC spectra or heteronuclear *J*-resolved-like spectra in inhomogeneous fields.[4]

Methods

Figure1 shows the modified ultrafast HSQC sequence with correlation acquisition option and *J*-resolved-like acquisition option. When the two spatial encoding modules satisfy a certain request, the dephasing induced by field inhomogeneity in indirect dimension can be eliminated. A four-step phase cycling is used to select the desired coherence transfer path. EPI-detection-based acquisition scheme is the first acquisition option for correlation spectra. Assuming that the field inhomogeneity is linear along the orientation of encoding and decoding gradients, echoes will turn up at a time independent of the inhomogeneous field. A high-resolution heteronuclear correlation spectrum is obtained with peaks located at (Ω_S-1/4Ω_I, Ω_I), where Ω_S and Ω_I represent chemical shifts of carbon and proton. Data post-processing can easily move the peak to site (Ω_S, Ω_I), thus a high-resolution HSQC is achieved. *J*-detection-based scheme yields *J*-resolved-like spectra with carbon-proton *J* couplings at position of (Ω_S-1/4Ω_I, $\pm\pi J_{CH}$).

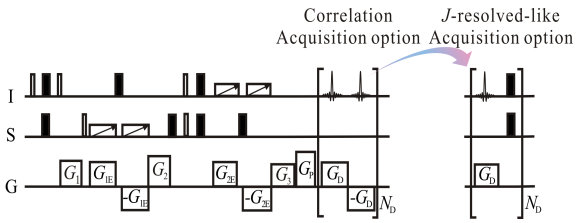

Fig. 1 Pulse sequence for ultrafast achieving high-resolution 2D HSQC spectra and heteronuclear *J*-resolved-like spectra in inhomogeneous fields.

Results and discussion

Experiments were performed on a Varian NMR System 500 MHz spectrometer. A sample of n-butyl bromide was used to test the sequence shown in Fig. 1 in an intentionally deshimmed inhomogeneous field with a line-width of 1400 Hz. Figure 2d shows the 2D reconstructed HSQC spectrum using the sequence with correlation acquisition option. The resolutions in both dimensions are greatly improved, and the line-widths are 101 Hz in F1 dimension and 38 Hz in F2 dimension. Compared to the ultrafast HSQC spectrum obtained in a homogeneous field (Fig. 2c), the reconstructed HSQC spectrum does circumvent the influence of field inhomogeneity.

The heteronuclear *J*-resolved-like spectroscopy experiment was implemented under the same circumstance. As shown in Fig. 3f, by projecting the peaks along the F2 dimension, ^{13}C-^{1}H *J* coupling constants can be measured. From up to down, the one-bond ^{13}C-^{1}H coupling constants are 122.6, 124.7, 148.2 and 123.9 Hz, respectively, the same as those measured in the homogeneous field (Fig. 2e) The center peaks in the F2 dimension are residual signals from the ^{1}H bonded with ^{12}C. Combining the *J*-resolved-like spectrum and the reconstructed HSQC spectrum, we can achieve J_{CH} coupling constants of each ^{13}C chemical sites without extra data post-processing. Both spectra (d) and (f) merely cost 40s by the present sequence.

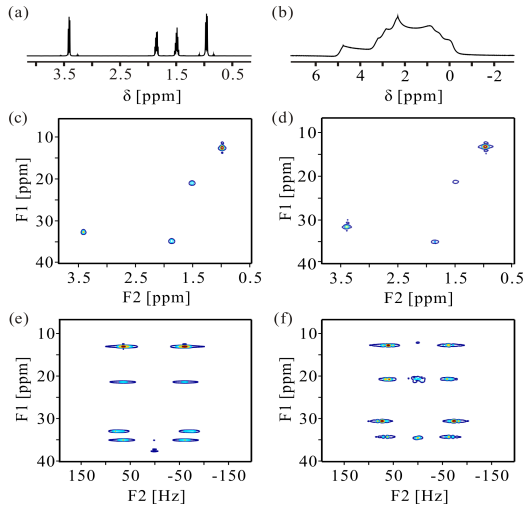

Fig. 2 NMR spectra of n-butyl bromide. (a, b) Conventional 1D ^{1}H spectrum in a well shimmed magnetic field (a) and in a deshimmed magnetic field with a line-width of 1400 Hz (b). (c, d)) Normal ultrafast HSQC spectrum (c) in the homogeneous field and reconstructed HSQC spectrum (d) acquired by the present sequence with correlation acquisition option in the inhomogeneous field. (e, f) Normal ultrafast hetero-nuclear 2D *J*-resolved spectrum[4] (e) in the homogeneous field and ultrafast *J*-resolved-like spectrum (f) acquired by the present sequence with *J*-detection acquisition option in the inhomogeneous field.

Conclusion

The combination of spatial encoding technique with coherence transfer is utilized to ultrafast achieve high-resolution HSQC spectra and *J*-resolved-like spectra in inhomogeneous fields. Though there is some sensitivity loss due to spatial encoding, the sensitivity can be improved by introducing new techniques such as the dynamic nuclear polarization. Moreover, the low signal to noise ratio of the resulting spectra in our experiments can be greatly improved by using ^{13}C enriched sample. This work may promote the application of NMR in structure analysis of complex organic compounds and bio-macromolecules and monitoring biochemical reactions.

Acknowledgement

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