The Effect of Strong Homonuclear Proton Coupling on a PRESS-Localized ge-HMQC Sequence

A. Yahya[1], P. S. Allen[1]

[1]University of Alberta, Edmonton, Alberta, Canada

Introduction: It is well known that ^{13}C coherences can be detected indirectly from the protons coupled to ^{13}C. It has also been demonstrated that by combining the standard PRESS localization sequence with the ge-HMQC (gradient enhanced heteronuclear multiple quantum coherence) technique [1] such coherences can be detected from 3D volumes in a single scan at the same time as suppressing any resonances from protons not coupled to ^{13}C nuclei. However, the effects of strong homonuclear proton coupling on the outcome of this sequence have not previously been investigated. The issue is relevant because at clinical field strengths (e.g. 3.0 T), metabolites often detected by ^{13}C MRS such as glutamate (Glu) and glutamine (Gln) exhibit strong homonuclear proton coupling in addition to the heteronuclear $^{13}C/^{1}H$ coupling. Neglecting the proton homonuclear coupling suggests an outcome of a ge-HMQC sequence that is 50% signal from ^{13}C-coupled protons, and zero signal from ^{12}C-bonded protons. In this report we illustrate, using Glu at 3.0 T, that the strong proton coupling indirectly links the ^{13}C spin to protons not bonded to it, thereby preventing complete elimination of signal from ^{12}C-bonded protons and giving rise to a reduced signal yield for ^{13}C-coupled protons. Lack of anticipation of this can result in quantification errors in ^{13}C labelling measures. These same effects have been previously observed with the Proton Observe Carbon Edited (POCE) sequence [2,3].

Methods: *Numerical method:* Numerical solutions of the equation of motion of the density matrix of each spin system in response to the pulse sequence were carried out in MATLAB. Both strong homonuclear proton coupling and weak heteronuclear coupling interactions were included in the Hamiltonian. Numerical models for the selective pulses were also incorporated. The responses of C_3- and C_4-labelled Glu to the sequence shown in figure 1 were calculated. A ratio of G_1:G_2 of 3:5 [4] was used for coherence selection and the gradients were 2 ms in length. To simulate ^{13}C decoupling, all heteronuclear scalar coupling constants were set to zero in the Hamiltonian used during the acquisition period (otherwise J_{CH} = 135 Hz).

Experimental methods: All experiments were carried out using an 80 cm bore, 3 T magnet (Magnex Scientific PLC, Abingdon, UK) in conjunction with a SMIS console, a home-built 7 cm diameter ^{1}H birdcage RF coil, and a 3 cm diameter ^{13}C surface coil. A 2 cm diameter sphere containing 35 mM labelled Glu with the C_3 carbon enriched 99% in ^{13}C was used to verify experimental calculations. To improve suppression of unwanted resonances the phase of the first 90° ^{13}C pulse as well as that of the receiver was alternated between ±x. The experiments employed the following parameters: a voxel size of 1.0×1.0×1.0 cm^3, $1/2J_{CH}$ = 3.7 ms, and a repetition time of 3 s. The coherence selection gradients were applied in all three directions with a duration of 2 ms each. The ^{1}H nuclei were ^{13}C decoupled during acquisition using the WALTZ-16 sequence.

Results: Figure 2 shows a contour diagram of the numerically calculated intensity of the protons bonded to the C_3 carbon of Glu (MN protons of the AMNPQ spin system) in response to the sequence of figure 1, and as a function of the two PRESS echo times (TE_1 and TE_2). The rapid drop in signal intensity with increasing echo times was similarly observed with $^{13}C_4$-Glu. For optimal proton signal reflecting either $^{13}C_3$-Glu or $^{13}C_4$-Glu, it is therefore important to minimize the PRESS echo times. To illustrate the response shown in figure 2(a) of a $^{13}C_3$-Glu molecule first, to the PRESS sequence, and secondly, to the PRESS-ge-HMQC combined sequence a choice of {TE_1, TE_2} = {10 ms, 10 ms} was made. The spectra were experimentally confirmed and are displayed in figure 2(b). The area of the MN multiplet (1.8–2.25 ppm) calculated from the ^{13}C edited spectrum of figure 2(a) is only about 30% that of the MN multiplet of the PRESS spectrum (instead of 50%), while about 8.5% of the PQ peak (2.25-2.55 ppm) remains unsuppressed. Very similar ^{13}C bonded proton signal loss accompanied by unbonded proton residual signal were observed from $^{13}C_4$-Glu. It was determined that these effects are not only due to the spin evolution that occurs during PRESS but also due to the evolution which takes place during the ge-HMQC sequence itself. It was calculated that in response to the basic ge-HMQC sequence without any localization that the MN peak of a $^{13}C_3$-labelled Glu molecule was about 38% of that of the corresponding peak obtained with a single excitation pulse, while a residual 11% PQ signal remained instead of zero.

Discussion and Conclusion: It has been demonstrated in this work, using Glu at 3.0 T, that when ^{13}C-coupled protons are also involved in strong homonuclear proton coupling, the signal yield of ^{13}C-coupled protons in response to a PRESS-localized ge-HMQC sequence is less than the expected 50%. Moreover, because of the polarization transfer mediated by that homonuclear coupling the ^{12}C-bonded protons become indirectly linked to the ^{13}C spin. This results in the incomplete elimination of signal from ^{12}C-bonded protons. If integration between fixed frequency limits is being employed to quantify the ^{13}C fractional enrichments then it is likely that overestimations will take place because of the unexpected residual signal from ^{12}C-bonded protons. A more accurate method of quantification would be to exploit a spectral fitting routine, e.g. LC model [5] with the correct basis lineshapes. Although the effects observed are in part due to the strong proton scalar coupling evolution that takes place during the ge-HMQC itself, the effects are exacerbated by PRESS localization and the response to the sequence is highly echo-time dependent.

Figures:

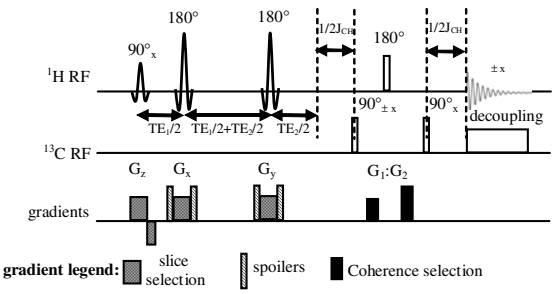

Figure 1: The combined pulse sequence

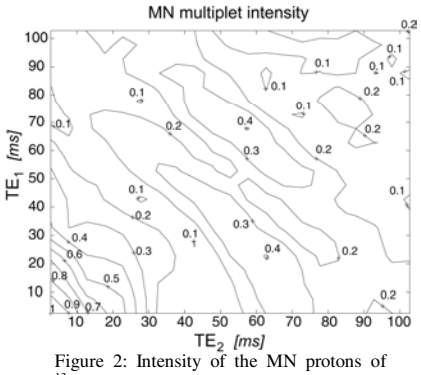

Figure 2: Intensity of the MN protons of $^{13}C_3$-labelled Glu to the PRESS-localized ge-HMQC sequence as a function of the two PRESS echo times.

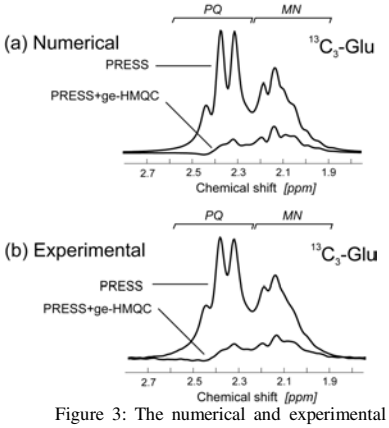

Figure 3: The numerical and experimental response of C_3-labelled Glu to the PRESS sequence (TE_1 = TE_2 = 10 ms) and to the PRESS-localized ge-HMQC sequence.

References

1. A. Yahya, P.S. Allen, *Proceedings of the 12th annual meeting of ISMRM,* Kyoto, 2004: 680.
2. P-G Henry, M. Marjanska, R. Gruetter, K. Ugurbil, *Proceedings of the 13th annual meeting of ISMRM,* Miami, 2005: 57.
3. A. Yahya, P.S. Allen, *Magnetic Resonance in Medicine*, in press.
4. J. Ruiz-Cabello, G.W. Vuister, C.T.W. Moonen, P. van Gelderen, J.S. Cohen, P.C.M. van Zijl, *Journal of Magnetic Resonance* **100**, 282 (1992).
5. S.W. Provencher, *Magnetic Resonance in Medicine* **30**, 672 (1993).

Acknowledgements: The authors would like to thank the Canadian Institutes of Health Research, the Alberta Heritage Foundation for Medical Research, the Natural Sciences and Engineering Research Council of Canada and the Alberta Informatics Circle of Research Excellence.