NMR Investigations of Liquid State Zero Quantum Transitions in Homogeneous and Inhomogeneous Magnetic Fields

Dr. Aitor Moreno, Bruker Switzerland AG and
Dr. Prabhakar Anabathula, Bruker BioSpin, United Arab Emirates

For High-Resolution NMR, spatial homogeneity of the magnetic field exceeding 10-8 is often required to obtain chemical shift and scalar coupling information for a liquid sample [1]. Zero-Quantum Coherence (ZQC) has the remarkable property being independent of magnetic field inhomogeneities. This leads to a coresponding reduction of line width in a zero-quantum dimension compared to single-quantum dimension in inhomogeneous magnetic fields [2]. In this application note, we discuss a basic pulse sequence (shown in Figure 1, see Appendix) to acquire a ZQC spectrum and show how such data can be analysed.

Figure 1

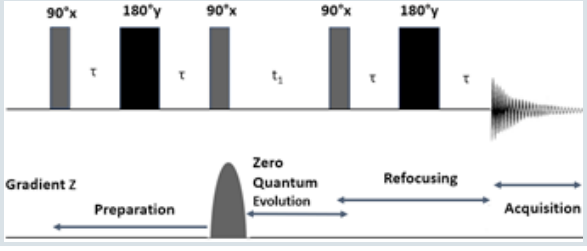
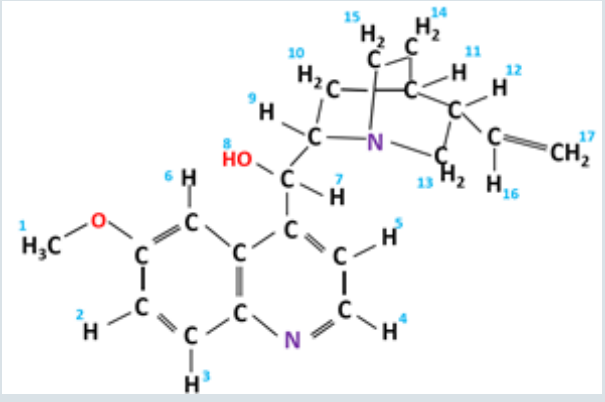


Figure 1: Pseudo-2D pulse sequence to excite and detect Zero-Quantum Coherence [3-4].

Antiphase magnetisation is prepared which is then transformed into multiple quantum coherence by the second 90°x pulse during the preparation period. Application of a pulsed field gradient ensures the destruction of all except ZQC which is unaffected by the field inhomogeneity during the evolution period t1. The third 90°x pulse then converts the ZQC into antiphase Single Quantum Coherence (SQC) which then evolves to inphase SQC during the refocusing period.

Scheme



Scheme : Quinine chemical structure and ^{1}H assignments.

Experiments were performed using a Bruker Avance NEO NanoBay 400 MHz spectrometer equipped with a cryogenically cooled 5 mm Prodigy broadband observe (BBO) probe with a pulsed field gradient of 5.3 G/cmA (see picture above). The used pulse sequence to acquire a 2D ZQC spectrum is shown in Figure 1. The spectral width's in indirect (F1) and direct (F2) dimensions were 1666.6 Hz and 4854.4 Hz, respectively. 512 increments were used to sample the indirect dimension and an evolution period of τ=60ms was used. The pulsed field gradient was applied for 60ms with a strength of 0.1 G/cm and data collected with a single scan per increment. Please note that only the F1 dimension is independent of magnetic field inhomogeneity. Magnetic inhomogeneity was introduced by misseting the Z shim by +1'000 units. Spectra were acquired on a 50mM quinine solution in d6-DMSO (Scheme).

Figure 2 shows SQC and ZQC ^{1}H NMR spectra acquired in homogeneous and inhomogeneous magnetic fields, respectively. Figure 2A shows an expansion of the conventional (SQC) ^{1}H NMR spectrum of quinine acquired in a properly shimmed, homogeneous magnetic field. After misseting the Z shim by +1'000units, the SQC ^{1}H NMR spectrum in Figure 2B is obtained. The observed SQC peak broadening is caused by the inhomogeneous magnetic field distribution. Figure 2C shows the F1 projection of the 2D ZQC spectrum in a homogeneous magnetic field. Different to the SQC spectrum in Figure 2A, the 1D ZQC spectrum only shows transitions from sets of protons with a mutual spin scalar coupling. The ZQC transition frequency between two chemically inequivalent protons hereby equals the chemical shift difference in the conventional SQC spectrum, see for example ZQC transition between protons H4 and H5 in Figure 2C. Please note that the intensive peak observed at 0 Hz results from longitudinal magnetisation restored during the ZQC evolut on period (Figure 1). Figure 2D shows the 1D F1 projection of 2D ZQC spectrum acquired in inhomogeneous magnetic field. Compared to the ZQC spectrum in 2C, similar linewidth's are obtained because ZQC's are independent of magnetic field inhomogeneities.

Figure 2

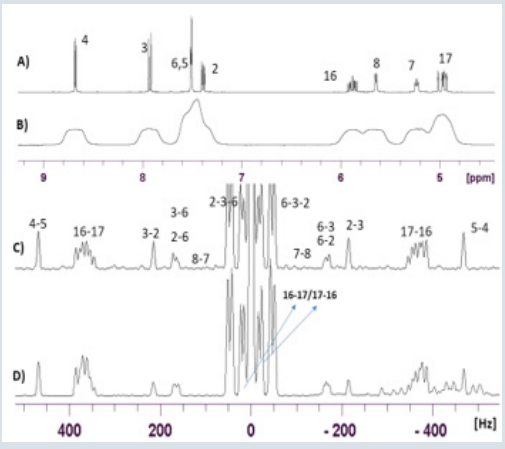


Figure 2: ^{1}H NMR spectra of quinine in d6-DMSO A) Conventional (SQC) spectrum in homogeneous magnetic field B) Conventional (SQC) spectrum in inhomogeneous magnetic field C) F1 projection of 2D ZQC spectrum in homogeneous magnetic field (plotted in Hz) with peak assignments D) F1 projection of 2D ZQC spectrum in inhomogeneous magnetic field illustrating the independence of ZQC lineshape on magnetic field inhomogeneity.

Figure 3

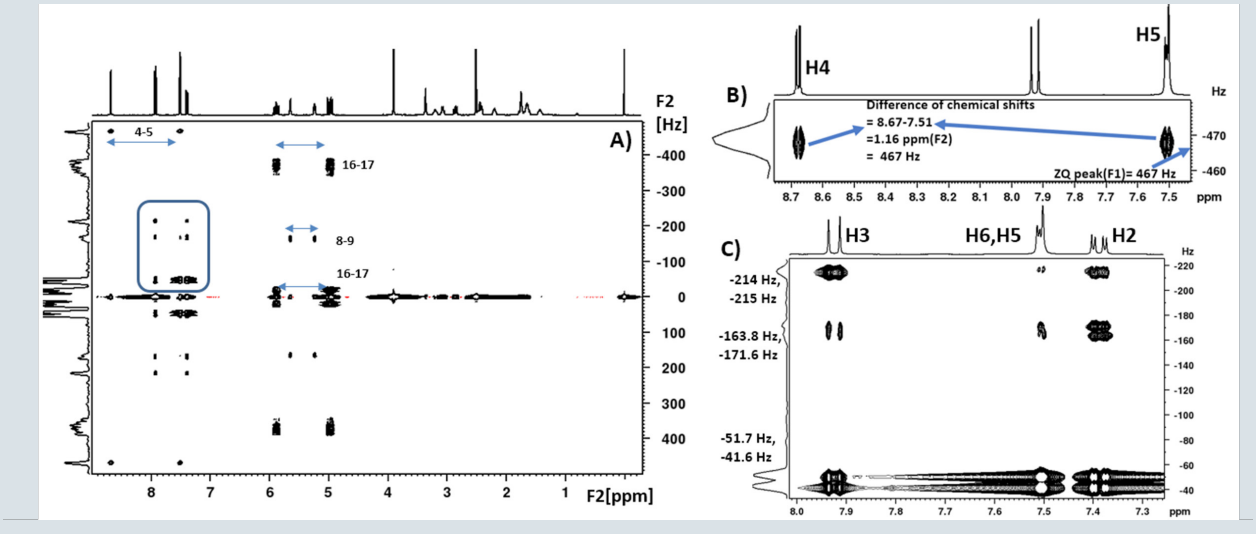


Figure 3: 2D ZQC spectrum in homogeneous magnetic field A) Full spectrum B) Expansion of H4-H5 transitions (AX spin system) C) Expansion of H2-H3-H6 transtions (AMX spin system).

The full 2D ZQC spectrum for quinine is shown in Figure 3A with conventional SQC proton spectrum plotted as F2 projection and internal ZQC projection in F1. As mentioned above, interpretation of ZQC spectra differs from conventional SQC spectra analysis, where chemical shift and J coupling information can readily be extracted. In contrast, as outlined in Table 1, ZQC peaks depend on differences in chemical shifts and J coupling constants between coupled spins [5]. We have applied these formulas for weakly coupled, homonuclear spins systems AX and AMX in the ZQC spectrum of quinine (Figure 3).

AX Spin System

An example of a two-spin AX spin system is the pair of aromatic protons H4-H5. Figure 3B shows the corresponding expansion of the ZQC spectrum. The difference in chemical shifts between these two protons is 1.16 ppm, or 467 Hz on a 400 MHz NMR spectrometer. This value of 467 Hz corresponds to the ZQC peak position in the F1 projection and can be calculated from the analytical expression in Table 1. Please note that for an AX spin system, the ZQC transitions are independent of the J coupling constant.

Spin System	Chemical shift (ppm) and J coupling constant (Hz)	Formula	Calculated ZQC transition from Formula (Hz)	Experimental ZQC transition from 2D (Hz)
AX	H4-H5			
	H4(A) = 8.67 H5(X) = 7.51 J(4-5) = 4.4	fA-fX	466.0	467.0
AMX	H2-H3-H6			
	H2(A) = 7.38 H6(M) = 7.51 H3(X)=7.92 J(2-3) = 9.2 J(2-6) = 2.8	(fM-fX)-(JAM-JAX)/2	-170.2	-171.6
		(fA-fX)-(JAM-JMX)/2	-220.6	-215.0
		(fA-fM)-(JAX-JMX)/2	-50.4	-51.7
		(fM-fX)+(JAM-JAX)/2	-47.6	-41.6
		(fA-fX)+(JAM-JMX)/2	-211.4	-214.0
		(fA-fM)+(JAX-JMX)/2	-163.8	-163.8

Table 1: Calculated and experimental ZQC frequencies for AX and AMX spin systems.

AMX Spin System

For a three-spin AMX spin system, the ZQC transitions depend on mutual chemical shift and J coupling constant differences, see Table 1. The ZQC transitions of an AMX spin system result in six individual peaks. For the AMX spin system of protons H2-H3-H6, transitions are observed at the six peak positions indicated in Figure 3C. The frequencies of these peaks match the values obtained using the corresponding formulas in Table 1.

In conclusion, we have applied a pseudo-2D pulse sequence to acquire the ZQC spectrum of quinine. Different to the regular SQC spectum, ZQC frequencies are only observed between sets of protons with mutual spin scalar couplings. A spin system dependent analysis of the ZQC spectrum then allows to extract chemical shift and J coupling constant information in an inhomogeneous magnetic field.

References

[1] Z. Chen, S. Cai, Y. Huang, Y. Lin, Prog. Nucl. Magn. Reason. Spectrosc., 2015, 90-91, 1–31

[2] A. Bax, T. Mehlkopf, J. Smidt, R. Freeman, J. Magn. Reason., 1980, 41, 3, 502-506

[3] L.D. Hall, T. J. Norwood, J. Chem, Soc., Chem. Commun., 1986, 44-46

[4] O.W. Sorensen, M.H. Levitt, R.R. Ernst, J. Magn. Reason., 1983, 55, 104

[5] G. Pouzard, S. Sukumar, L.D.Hall, J. Am. Chem. Soc., 1981, 103, 14, 4209-4215

© Bruker BioSpin 11/20 T182616

Appendix:

```
;ZQC2d
;avance-version (19/02/11)
;pseudo 2D sequence for measurement of Zero-Quantum Coherence (ZQC)
;
; L.D. Hall, T. J. Norwood,
;    J. Chem, Soc., Chem. Commun., 44-46 (1986)
; O.W. Sorensen, M.H. Levitt, R.R. Ernst,
;    J. Magn. Reason., 55, 104 (1983)
;
;$CLASS=HighRes
;$DIM=2D
;$TYPE=
;$SUBTYPE=
;$COMMENT=

#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>

"p2=p1*2"


"d11=30m"

"in0=inf1"

"d0=3u"

"acqt0=0"

1 ze
2 d11

  d1
  50u UNBLKGRAD
  p1 ph1
  d16
  p2 ph2
  d16
  p1 ph1
  p19:gp7
  d0
  p1 ph1
  d16
  p2 ph2
  d16
  4u BLKGRAD
  go=2 ph31
  d11 mc #0 to 2 F1QF(caldel(d0, +in0))

exit
ph1= 0
ph2= 1
ph31=0
;pl1 : f1 channel - power level for pulse (default)
;p1  : f1 channel -  90 degree high power pulse
;p2  : f1 channel - 180 degree high power pulse
;p19: gradient pulse
;d1  : relaxation delay; 1-5 * T1
;d16: delay for gradient recovery
;ns: 1 * n
;td1: number of experiments
;FnMODE: QF
;       use xfb and calculate F1 projection (f1sum) for ZQC spectrum

;for z-only gradients:

;gpz7: 0.2%

;use gradient files:

;gpnam7: SMSQ10.100
```