Communication

# $^1$H–$^1$H double-quantum CRAMPS NMR at very-fast MAS ($\nu_R$ = 35 kHz): A resolution enhancement method to probe $^1$H–$^1$H proximities in solids

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ABSTRACT

A High-resolution two-dimensional (2D) $^1$H double-quantum (DQ) homonuclear recoupling experiments, combined with smooth amplitude-modulation (SAM) homonuclear decoupling is presented. The experiment affords highly resolved and clean $^1$H DQ–SQ 2D spectra at very-fast MAS rates ($\nu_R$ = 35 kHz). The method is well suited to probe $^1$H–$^1$H distances in powdered solids and demonstrations are applied on a NaH$_2$PO$_4$ powdered sample, an inorganic compound having hydrogen bonding networks.

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The potential of multiple-quantum MAS NMR spectroscopy, particularly DQ MAS, for the characterisation of solids is well-known. The use of solid-state NMR techniques that exploit the dipolar couplings to measure nuclear distances between heteronuclear spin-pairs is well established and many applications are available. The ability to probe proximities between hetero and homo nuclear spin-pairs, e.g., $^{13}$C–$^{15}$N [1], $^{13}$C–$^{13}$C [2] and $^{15}$N–$^{15}$N [3], is very important to study biological solids. However, such experiments are mostly dedicated to enriched samples owing to the low natural abundance of such nuclei. Because of its high sensitivity and high isotopical abundance, $^1$H is an attractive nucleus to probe molecular structure and dynamics. However, assessing $^1$H–$^1$H distances in rigid solids through dipolar couplings poses several well-known difficulties and some pioneering work toward this direction have been reported by Brown and Spiess [4]. The strong $^1$H homonuclear dipolar couplings typically result in broad and featureless lineshapes and poorly-resolved $^1$H spectra. The use of 1D $^1$H MAS and 2D $^1$H–$^1$H DQ recoupling experiments, employing fast sample spinning alone (∼30 kHz), has been shown to afford enough resolution to study hydrogen bondings and π–π stacking effects in crystalline systems [5].

$^1$H homonuclear recoupling NMR pulse sequences are among the most powerful techniques to obtain $^1$H chemical information in solids. A variety of methods are available to recouple homonuclear dipolar couplings (e.g., HORROR, R$^2$, RFDR, RIL, DREAM, CMR7, SPC5, POST-C7, BABA) [2,6], mainly employed on spins different from $^1$H. Among these, the later two are widely used as DQ recoupling schemes. Concerning applications under fast MAS conditions, these different pulse sequences have diverse efficiencies and are not equally well adapted for dipolar recoupling purposes, because they differ in the *rf* pulse requirements, excitation bandwidths, compensation for *rf* imperfections and perturbing interactions. To overcome this problem, alternative symmetry-based ($CN_n^\nu, RN_n^\nu$) pulse schemes, such as, SC14$_4^5$ [7] and R6$_6^2$ [8] have been proposed to allow recording spectra at higher spinning rates (up to 20 kHz). Alternative $^1$H line-narrowing methods (other than fast MAS alone), based on $^1$H CRAMPS decoupling schemes, such as DUMBO and PMLG sequences, have been successfully combined with the POST-C7 and the C9 DQ recoupling schemes, respectively, considerably improving the $^1$H spectral resolution in the single-quantum (SQ) and DQ dimensions and providing a better insight to probe $^1$H–$^1$H proximities [9,10]. However, such schemes may present certain difficulties on their optimisation, depending on the actual spectrometer console. Such $^1$H CRAMPS decoupling techniques contain multiple pulses (including tilted pulses [9]) with several discrete phase changes, which may introduce additional *rf* imperfections, i.e., phase transients, phase propagation delays and other artefacts. Up to now, the performance of these DQ excitation/reconversion and CRAMPS methods has been restricted to moderate MAS rates (up to *ca.* 25 kHz), because the available $^1$H decoupling methods did not perform well at higher spinning

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speeds, at least using moderate *rf* field strengths, due to interference between the spin- and real space-modulations of the homonuclear interaction. In most cases, the ^{1}H decoupling cycle times must be shorter than the rotor periods ($\tau_C < \tau_R$) to obtain efficient dipolar decoupling. Adapting CRAMPS decoupling to ultra-fast MAS probes now commercially available ($\nu_R$ up to *ca.* 70 kHz) is a very important issue in modern solid-state NMR. Here, we wish to show how to design a high-resolution 2D ^{1}H DQ–SQ correlation experiment employing ^{1}H homonuclear decoupling in both dimensions, that performs well at ultra-fast MAS rates, being easy to optimise, and offering considerable resolution improvement and clean 2D ^{1}H NMR spectra. The effectiveness of this pulse sequence (Fig. 1) is demonstrated on $NaH_2PO_4$, a model inorganic material, aiming to discriminate and assign all the ^{1}H resonances involved in a network formed by multiple O–H · · · O hydrogen bonding (Fig. 2).

The very recently reported SAM sequences, were employed for ^{1}H homonuclear decoupling, consisting of a Smooth Amplitude-Modulated decoupling strategy able to eliminate rotor-*rf* lines, zero-frequency peak, quadrature images and additional artefacts. SAM is a smooth version of $CN_n^{N/2}$ rotor-synchronized pulse sequence, which uses a Zero (instead of 360°) rotation basic element that corresponds to a z-rotation for chemical shift and does not cancel it. In our case, we have employed the $SAM_3$ [11] and $wSAM_3$ [12] decoupling versions during $t_1$ and $t_2$ evolutions, respectively. $SAM_3$ corresponds to a continuous version of the $C6_1^3$ symmetry sequence using three *rf* cosine modulation periods every rotor period $\tau_R$. This rotor-synchronization helps to avoid interferences during $t_1$ between MAS and *rf* decoupling. The $wSAM_3$ decoupling sequence consists in applying the $SAM_3$ blocks during $\tau_R$, followed by observation windows. The BABA sequence [13] was chosen for the excitation/ reconversion of the DQ coherences, since it is well adapted to fast ^{1}H MAS NMR experiments and is one of the most simple and robust recoupling methods.

Fig. 3 shows 2D DQ–SQ ^{1}H spectra recorded at 9.4 T (Bruker Avance-II spectrometer), with a spinning rate of 35 kHz, on a 2.5 mm double-resonance probe. Additional experimental details are provided in the figure caption. Fig. 3a shows the 2D DQ–SQ ^{1}H CRAMPS spectrum recorded using the pulse sequence in Fig. 1. For comparison, the 2D ^{1}H BABA spectrum ^{1}H decoupled in $t_1$ only (Fig. 3b) and the conventional BABA spectrum (Fig. 3c) are also depicted. The spectrum in Fig. 3a exhibits highly resolved lines in both the $t_1$ and $t_2$ dimensions, and all ^{1}H resonances are observed. The considerable improvement in ^{1}H resolution obtained using our method is better ascertained by comparing the $F_1$ projections (DQ dimension). Clearly, along this dimension, the conventional BABA experiment does not reveal all ^{1}H DQ resonances.

$NaH_2PO_4$ is monoclinic and, in addition to presenting two crystallographically non-equivalent phosphorous (P1 and P2) and so-
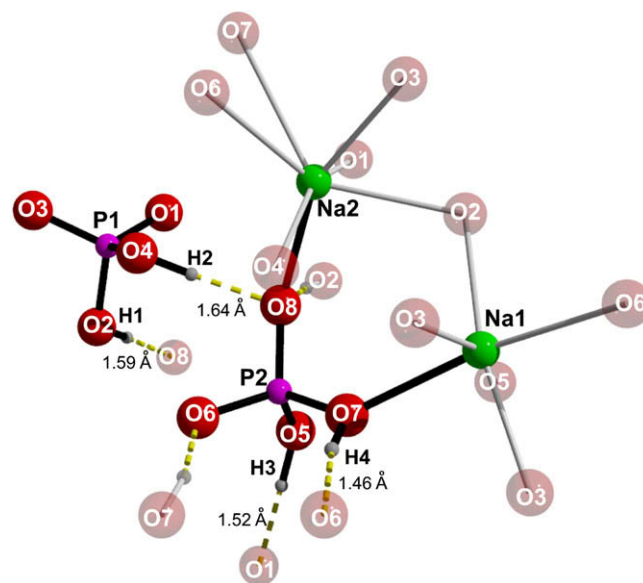


**Fig. 2.** Ball-and-stick representation of asymmetric unit and coordination environment of $NaH_2PO_4$, emphasising the O–H ···O hydrogen bonding (dashed lines) network involving the phosphate groups [14].

dium (Na1 and Na2) nuclei, the room-temperature neutron-diffraction study revealed four distinct proton environments (H1-4) involved in strong O–H · · · O hydrogen bonds (length 1.46–1.64 Å, Fig. 2). More details on the crystal structure may be found elsewhere [14].

Through observation of the $F_2$ projection relative to the classic (Fig. 3c) and $t_1$ [1]H decoupled (Fig. 3b) DQ spectra, it is possible to identify three resolved ^{1}H resonances at ca. 9.5 (H2), 11.5 (H1) and 13 (H3+H4) ppm (Fig. 2). However, the $t_1$ and $t_2$ [1]H decoupled DQ spectrum (Fig. 3a) resolves one additional ^{1}H peak at high frequency giving rise to two distinct peaks at *ca.* 12.9 and 13.3 ppm. Assignment of these four peaks can be made qualitatively, based on the well-known correlation between the low-field shift of ^{1}H resonances and the strength of hydrogen bonds, which may be estimated through hydrogen bond lengths (Fig. 2). The ^{1}H chemical shifts were calculated with two different exchange-correlation functionals and cluster or periodic models of $NaH_2PO_4$ in order to overcome the difficulties in the correct resonance assignment. The theoretical calculations corroborate the ^{1}H assignment made above with full details given as Supplementary Data.

The neutron-diffraction data [14] revealed that all the four proton sites are close to each other (<5 Å), enabling the observation of all the expected ^{1}H DQ–SQ contacts in 2D spectra. For example the proxim-
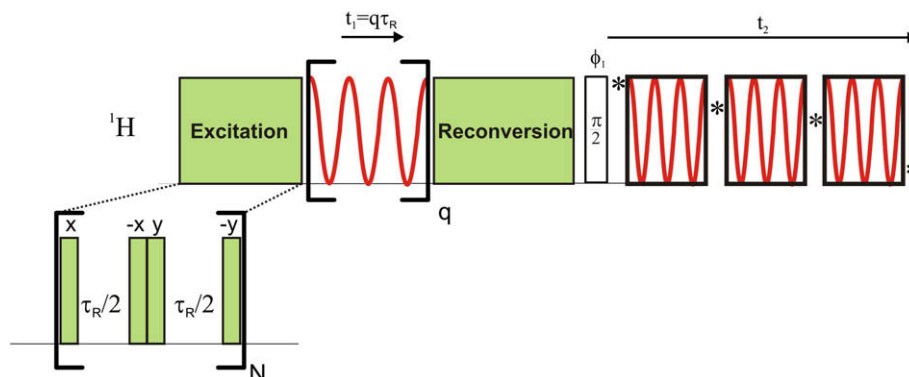


**Fig. 1.** Pulse sequence used to record the 2D [1]H–[1]H DQ–SQ correlation spectra of Fig. 3a. Asterisks depict a sampled complex data point.
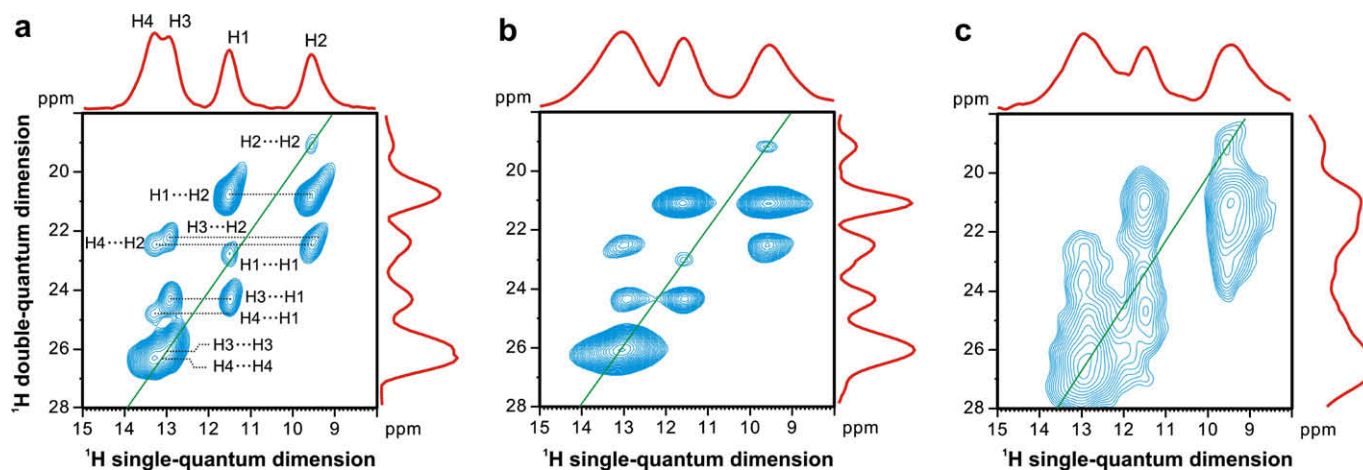
**Fig. 3.** 2D $^1$H–$^1$H DQ–SQ correlation spectra of $NaH_2PO_4$, recorded in 2 h, employing the ((a and b) BABA sequence using homonuclear decoupling during a) both indirect ($t_1$) and direct ($t_2$) dimensions using SAM3 and wSAM3, respectively (Fig. 1), (b) the indirect ($t_1$) dimension using SAM3 and employing the (c) classic BABA only. 224 $t_1$ points with 16 scans each were recorded using a recycle delay of 2s. A one rotor period version of BABA ($N$ = 1, Fig. 1) was used for excitation and reconversion ($\tau_{rcpl}$ = 28.6 μs) of DQ coherences employing 90° pulse lengths of 2.1 μs; $v_R$ = 35 kHz; (w)SAM3 decoupling conditions: the same *rf*-power decoupling was used in both SAM3 and wSAM3; $v_{mod}$ = 115 kHz; the cosine amplitude-modulated shapes were defined with 350 ns steps; the wSAM3 sampling window ($t_w$) was set to 7.1 μs. The carrier frequency was set to 17 ppm in both dimensions. The experimental scaling factor was $\kappa$ = 0.7–0.72 for both dimensions. $^1$H–$^1$H DQ spin-pairs are depicted in (a).

ities between equivalent proton environments may be seen along the diagonal. They correspond to inter-nuclear distances of 3.69, 3.12, 3.72 and 2.40 Å, for H1–H1 with SQ and DQ shifts of 11.5 ppm and 23 ppm, respectively; H2–H2 (SQ = 9.5 ppm; DQ = 19 ppm); H3–H3 (SQ = 12.9 ppm; DQ = 25.8 ppm) and H4–H4 (SQ = 13.3 ppm; DQ = 26.6 ppm). The off-diagonal contacts refer to proximities between protons from distinct environments and are also easily resolved in the high-resolution 2D DQ spectrum. It is worth noting that the off-diagonal contacts such as H3–H1/H4–H1 and H3–H2/H4–H2 may only be found by applying simultaneous $^1$H decoupling in the $t_1$ and $t_2$ dimensions. For example, these DQ–SQ contacts could not be separated from the spectra in Fig. 3b, which supports the importance of decoupling the $^1$H spins during the direct NMR signal observation. The $^1$H MAS spectrum, which is similar to the $F_2$ projections of the spectra in Fig. 3b and c is relatively narrow having a FWMH of *ca.* 1 and 0.8 ppm for H2 and H1 protons, respectively. In the fully highly resolved DQ spectra, a factor of 2–2.5 in resolution is obtained, comparing the $F_2$ projections of Fig. 3a–c.

As concluding remarks, we have shown the homonuclear decoupling performance of (w)SAM$_3$ adapted to high-resolution 2D $^1$H–$^1$H DQ–SQ correlation experiments recorded at very-fast MAS rates ($v_R$ = 35 kHz) where other previous CRAMPS methods failed up to now to deliver high-quality $^1$H spectra. This method allows separating all the DQ–SQ contacts involving the four $^1$H resonances of PO-H hydrogen bonded groups present in $NaH_2PO_4$. The method may be easily implemented on any spectrometer. Its calibration is very straightforward and the method does not suffer from *rf* pulse imperfections, thus, delivering a clean $^1$H spectrum. It is important to stress that the quest for higher MAS rates is not only required to further decouple dipolar coupled proton spins to enhance $^1$H resolution, but also to deliver a number of advantages such as: (i) reduced transverse losses, which is particularly interesting for all multi-dimentional experiments, (ii) reduced CSA effects at high static magnetic fields, (iii) hetero nuclear decoupling that can be performed with low *rf*-power, (iv) increased spectral-width in all rotor-synchronized experiments. In face of such advantages, related to very-fast MAS, we expect that cosine amplitude modulation $^1$H decoupling schemes may be easily adapted to other NMR sequences to facilitate the application of $^1$H CRAMPS methods at much higher spinning rates than the actual ones. Applications of such combination, on heteronuclear experiments, are underway and will be published elsewhere.

## Acknowledgments

## Appendix A. Supplementary data

DFT calculations, to determine the theoretical $^1$H chemical shifts of $NaH_2PO_4$. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jmr.2008.10.009.

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