¹H DOUBLE QUANTUM NMR AT ULTRA FAST MAS: ANALYTICAL AND NUMERICAL INVESTIGATIONS[*]

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Abstract. Analytical and numerical investigations of ¹H Double Quantum (DQ) excitation efficiency under ultra fast magic angle spinning (MAS) conditions are performed. Specific features and excitation mechanisms have been found for two distinct pulse sequences, of which advantages for structural investigations by solid state NMR spectroscopy is discussed.

Key words: Solid State-NMR, ¹H DQ-NMR, ultra fast MAS, numerical simulations.

1. INTRODUCTION

The most important feature of dipole-dipole couplings is that they encode structural information through the $1/r^3$ dependence with respect to the corresponding spin-spin distance. Due to its high sensitivity and high natural abundance, ¹H is an attractive nucleus for NMR study of molecular structure hence, ¹H DQ-MAS experiments are commonly employed to determine proton-proton proximities in solid organic compounds. This technique implies the design of homonuclear recoupling pulse sequences capable to efficiently generate the so-called DQ correlations between spins of the same nuclear species. Among the large variety of recoupling methods (*e.g.* HORROR, CMR7, SPIP, RN_n^υ, POST-C7, BABA) [1-7] the later two are most frequently used in ¹H DQ-MAS experiments. Whereas POST-C7 implies a continuous irradiation of the sample with a radio-frequency (*rf*) field, and can be used only at moderate MAS rates ($\upsilon_R = 10$–15 kHz), BABA-2 is a pulsed recoupling sequence which is applicable also at larger spinning frequencies. The main drawback of using slow or moderate MAS frequencies comes from the magnitude of the recoupled ¹H-¹H dipolar interaction,

which is often too large compared to the cycling time of both, POST-C7 or BABA-2 sequences ($2\tau_R$), thus leading to a rapid DQ build-up compared to the minimal sampling period of the recoupling intervals. To overcome this, in a previous work it was shown that using submultiples of POST-C7 cycling time (*i.e.*, $2\tau_R/7$) the sampling period can be decreased, and smooth ^{1}H DQ build-up curves are obtained for β-AspAla dipeptide, at moderate sample rotation (12.5 kHz) [8]. An attractive alternative to this approach is the use of ultra fast MAS, which has became feasible since the development of equipment that allows spinning frequencies of up to 70 kHz.

In the present paper, a detailed theoretical investigation (both, analytical and numerical) of the efficiency in generating double quantum correlations by BABA and a conventional two-pulse (TP) sequence in ultra-fast MAS regime ($\upsilon_R = 30$–70 kHz) is performed. It was found in the both cases that smoother DQ build-up curves can be obtained by shortening the sampling period, whereas for the latter also an additional mechanism was identified which is related with the $1/\upsilon_R$ scaling of the recoupled effective dipolar interaction. It is also shown by numerical simulations that the proposed schemes fulfil most of the general requirements of an ideal DQ recoupling sequence described in [9].

2. ANALYTICAL INVESTIGATION

DQ excitation is an incremental process obtained by concatenating n basic BABA sequences, $\left[\left(P_x - \tau_R/2 - P_{\bar{x}}\right)\left(P_y - \tau_R/2 - P_{\bar{y}}\right)\right]_n$, or by increasing the free evolution period $n\tau_R$ in the TP sequence, $\left[\left(P_x - n\tau_R - P_{\bar{x}}\right)\right]$, where n is an integer, P stands for ideal 90^0 *rf* pulses around the specified direction, whereas $-t-$ designates free evolution during the time t under the rotor modulated dipolar Hamiltonian

$$H(t) = \sum_{m=-2}^{2} H_m \, \mathrm{e}^{im\omega_R t} = \sum_{m=-2}^{2}\sum_{j<k}^{N} \omega_D(j,k) b_m(j,k) \left[2I_{jz}I_{kz} - \frac{1}{2}\left(I_{j+}I_{k-} + I_{j-}I_{k+}\right) \right] \mathrm{e}^{im\omega_R t}, \quad (1)$$

with ω_R, the angular rotation frecuency $\omega_R = 2\pi\upsilon_R$, $\omega_D(j,k)$, the dipolar coupling constant between the j and k ^{1}H spins, and $b_m(j,k)$, characteristic functions of angular variables. Their explicit expressions can be found for instance in [10]. The effect of chemical shielding is disregarded in this analysis (thus $H_0 = 0$ in eq. (1) and below), which enables one to consider only simplified versions of the pulse sequences illustrated in Fig. 1.

Incrementing n in a DQ experiment gives rise to the so-called build-up curves, which are sampled in time-steps equal with the cycle time, τ_R. Obviously, smoother curves can be obtained for both sequences by reducing the sampling period, *i.e.*, by increasing the spinning frequency, $\upsilon_R \sim 1/\tau_R$. Differences between

them might however occur with respect to the characteristic DQ excitation mechanism, primarily due to the different values of the incorporated free evolution periods, $\tau_R/2$ in the case of BABA, and $n\tau_R$ for the TP sequence. Qualitatively, this can be analyzed by evaluating the density operator at the end of the excitation time, $\tau_{ex} = n\tau_R$, that is $\rho(\tau_{ex}) = \hat{U}(\tau_{ex},0)\,\rho(0)$, where $\rho(0) = I_z$, and

$$\hat{U}(t_2,t_1) = \sum_{p,q} \hat{C}_p^\dagger \mathrm{e}^{\,\mathrm{i}\,p\,\omega_R\,t_2}\,\mathrm{e}^{-\mathrm{i}\hat{H}_{e\!f\!f}\,(t_2-t_1)}\,\hat{C}_q\mathrm{e}^{\,\mathrm{i}\,q\,\omega_R\,t_1}\;, \tag{2}$$

Both, the ω_R-modulated operators, C, and the effective Hamiltonian, $H_{e\!f\!f}$, in eq. (2) are expressed as power series of which n-order terms are scaled with the nth power of the spinning frequency, $1/\omega_R^n$ [10]. For instance, the lowest order terms read

$$\hat{C}_m^{(0)} = \delta_{m0};\qquad \hat{C}_m^{(1)} = \sum_{m=-2}^{2}\frac{\hat{H}_m}{m\omega_R},$$

$$H_{e\!f\!f}^{(0)} = H_0;\qquad H_{e\!f\!f}^{(1)} = \sum_{m=-2}^{2}\frac{\left[H_m,H_{-m}\right]}{m\omega_R}. \tag{3}$$

The calculations of $\rho(\tau_{ex})$ closely follow the formalism developed in [10], so that only their final expressions obtained in first order of approximation will be explicitly given here. Specifically,

$$\rho_{BABA}^{(1)}(\tau_{ex}) = \sum_{j<k}^{N}\left\{\omega_D(j,k)\left[b_1(j,k)-b_{-1}(j,k)\right]DQ(j,k)\right\}\tau_{ex} \tag{4}$$

$$\rho_{TP}^{(1)}(\tau_{ex}) = \sum_{j<k<l}^{N}\left\{\frac{\omega_D(j,k)\omega_D(j,l)}{\omega_R}A(j,k,l)\left[DQ(j,k)I_{lz}+DQ(j,l)I_{kz}\right]\right\}\tau_{ex} +$$

$$+ \sum_{j<k<l}^{N}\left\{\frac{\omega_D(j,k)\omega_D(j,l)}{\omega_R}B(j,k,l)\left[ZQ(j,k)I_{lz}+ZQ(j,l)I_{kz}\right]\right\}\tau_{ex}, \tag{5}$$

where $ZQ(j,k) = \left(I_{j+}I_{k-}+I_{j-}I_{k+}\right)$ and $DQ(j,k) = \left(I_{j+}I_{k+}+I_{j-}I_{k-}\right)$ represent zero-quantum (ZQ) and DQ correlations, while $A(j,k,l)$ and $B(j,k,l)$ are functions of the angular parameters b_m within the specified (j,k,l) three-spin subsystem.

The truncation of the density operator to lowest order terms is well justified in the ultra fast MAS regime. Therefore, the above relationships are ideally suited to identify distinctive features of the DQ-excitation process in its early stage, $0 < \tau_{ex} < 1/\omega_D^{average}$. Here, $\omega_D^{average}$ defines a sequence specific average dipolar coupling of which order of magnitude can be estimated in principle from the corresponding eqs. (4)–(5). The major conclusions from such a comparative analysis are briefly summarized below:

(i) The DQ excitation mechanism is different under the two pulse sequences. This can be simply explained based on the fact that the DQ correlations in the two cases are generated by distinct components of the time-propagator (2), namely, the rotor-modulated factor, $\hat{C}_p^\dagger \, \hat{C}_q \, e^{i(p-q)\omega_R(t_2-t_1)}$, and the dephasing part, $e^{-i\hat{H}_{eff}(t_2-t_1)}$, in the case of BABA, and the TP sequence, respectively. There is no interference between them in the approximation described by eqs. (4)-(5): however, as shown in ref. [10], mixing is possible in higher orders, *i.e.*, at longer excitation times, but this perturbing effect can be reduced if the spinning frequency is further increased.

(ii) DQ excitation efficiency is expected to be larger under BABA, because in the lowest order it generates only DQ correlations, whereas the TP sequence gives rise also to ZQ terms in the expression (5) of the corresponding density operator.

(iii) While spin-pair interactions *(j,k)* are sufficient for exciting DQ correlations under BABA, this process requires mutual couplings among at least three spins *(j,k,l)* if the TP sequence is employed: in practice, this means that DQ experiments based on the two distinct sequences will provide complementary structural information.

(iv) Theoretically, the excitation efficiency can be directly related with the weighting coefficients of the DQ spin-correlation terms in the expression of the density operator, whereas experimentally it is estimated from the so-called DQ build-up rate (the slope of the corresponding build-up curve). Thus, according to eqs. (4–5), the build-up rates are expected to be independent on the spinning frequency in the case of BABA, and to decrease with increasing ν_R under the TP sequence. This makes the TP sequence quite attractive for practical applications, because of its flexibility in adjusting the measured build-up rates as function of the employed spinning frequency.

3. NUMERICAL SIMULATIONS

Numerical simulations of the DQ build-up curves under BABA and the TP sequences are performed using the SPINEVOLUTION program [11], considering a spin system composed of eight ^{1}H nuclei in the L-Tyrosine amino acid. These protons belong to the aliphatic, aromatic, and carboxylic region respectively. The spin system size is chosen large enough such as to capture the general behaviour of a compound in an experimental case, but also sufficiently small to avoid a very long computing time. The simulations were performed at $\nu_R = 30$, 50, and 70 kHz spinning frequencies, by averaging 100 crystallites orientations.

To better approach a real experimental situation, the simplified sequences discussed previously are replaced in practice with the improved versions shown in Fig. 1 (BABA-2, and the incorporation of rotor synchronized π pulses in the TP sequence), with the purpose of minimizing the disturbing effect of the ^{1}H chemical shift (CS) interactions. Consequently, typical isotropic chemical shift values for each ^{1}H nucleus in the spin system, that is, in the range 2-5 ppm for the aliphatic groups, 6-8 ppm for the aromatic CH, and 12 ppm for the OH proton, are explicitly considered into the simulations.
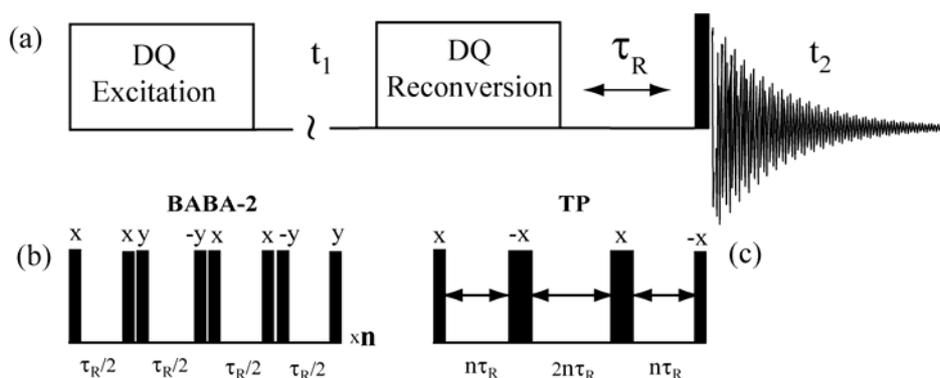

Fig.1 – a) General scheme for ^{1}H DQ NMR correlation experiments, where the recoupling sequences used in the excitation and reconversion periods are b) BABA-2, or (c) TP.

BABA-2 and TP recoupling sequences are applied during the excitation period τ_{ex} in order to transform the longitudinal magnetization into DQ correlations. During the recoupling period followed by a $\pi/2$ pulse, the DQ correlations are transformed to directly observable transverse magnetization. The numerical simulation of ^{1}H DQ build-up curves has been done by simultaneously incrementing n in the pulse sequences applied during the excitation and reconversion periods. Considering the indirect evolution time t_1=0 in Fig. 1a (a set-up called 1D DQ-filtered experiment), the first point in the NMR signal is recorded separately for each individual ^{1}H nucleus, thus giving rise to eight DQ build-up curves of the corresponding protons into the system. Each of these build-up curves includes contributions from all DQ correlations that are generated by an individual proton: in practice, they can be further separated by acquiring a set of 2D DQ spectra for different values of n, but this case will not be discussed in this work.

Fig. 2 compares two representative DQ build-up curves as a function of the excitation time τ_{ex} for the TP (a-c), and BABA-2 sequence (d-f), included in a DQ-filtered experiment for υ_R=30 (a,d), 50 (b,e), and 70 kHz (c,f). Specifically, the analyzed curves correspond to the fourth (H4 – open circles) and sixth (H6 – filled circles) ^{1}H nuclei in the L-Tyrosine molecule, of which structure is also drawn in Fig. 2. H6 is illustrative for a proton involved in a strong pair dipolar coupling (H6-H7), and two medium couplings (H6-H8 and H6-H4), that are associated with a

short, ~ 1.7 Å, and two medium, ~ 2.5 Å, internuclear distances. The other site, H4, is typical for protons that are subjected only to medium-sized pair dipolar couplings, corresponding to the H4-H3 and H4-H6 distances of about 2.5 Å.
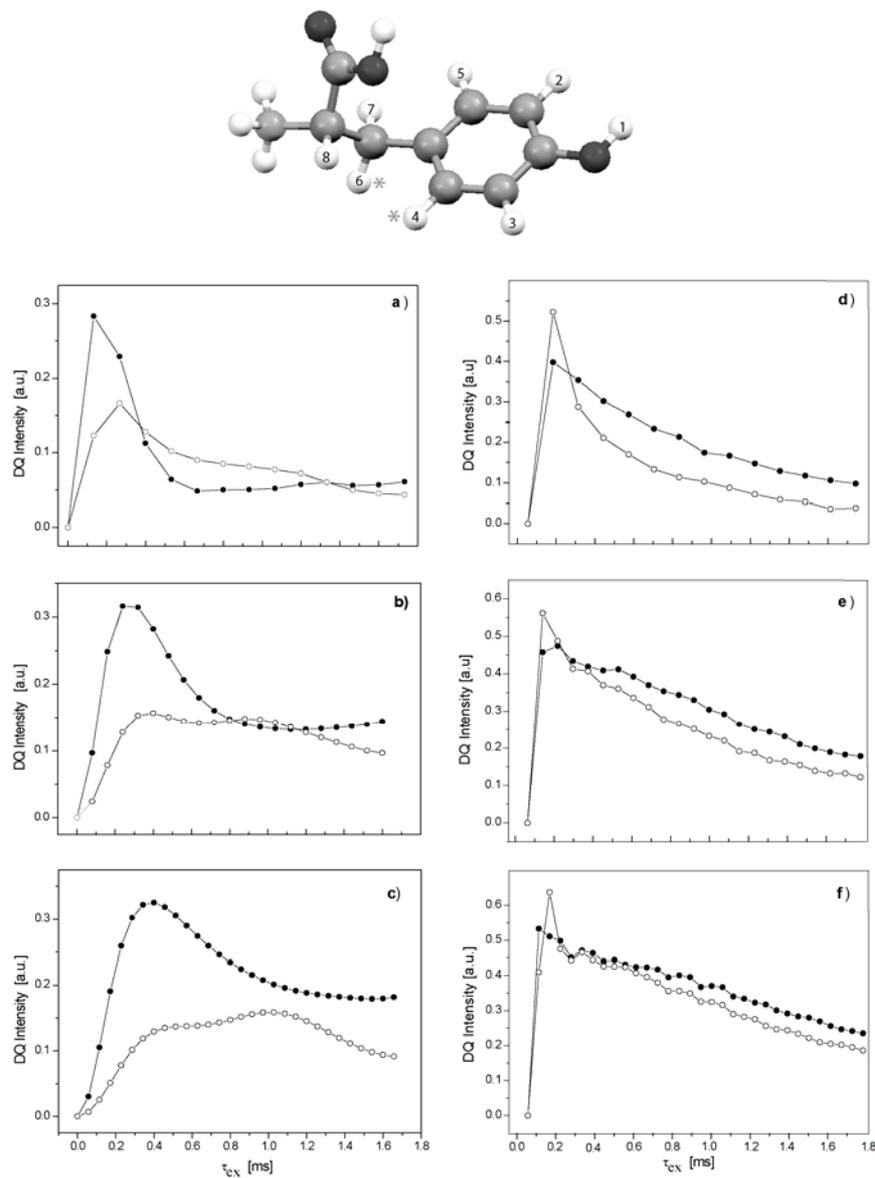

Fig. 2 – Comparison between simulated DQ build-up curves in L-Tyrosine recorded for two ^{1}H spin sites (H4 with open circles, and H6 with filled circles), using three different spinning frequencies υ_R= 30 (a–d), 50 (b–e), and 70 kHz (c–f).

A comparative analysis of the DQ excitation process under these two pulse sequences can be performed in a similar way as above, by relating the distinct features of the simulated DQ build-up curves with the conclusions (i) – (iv) derived from the analytical expressions (4–5). The major differences are observed with respect to the behaviour at short excitation times, and the overall DQ intensity obtained in the two distinct cases. In particular, the short τ_{ex} evolution corresponds to the raising part of the DQ build-up curve: as clearly seen from Fig. 2, their slopes, *i.e.* build-up rates, are independent of the spinning frequency in the case of BABA, whereas they are progressively reduced with increasing υ_R under the TP sequence. This is in perfect agreement with the conclusion depicted in (iv), and clearly demonstrates the practical importance of the DQ build-up curves obtained under the TP sequence, because their build-up rates can be easily manipulated by choosing different values of the spinning frequency. The result can be also discussed in connection with the statement (iii): H6 is subjected as mentioned above to a strong dipolar coupling with H7, but also to two medium couplings with H8 and H4 respectively. At the same time, the internuclear distance between H7 and H8 protons is situated in the same medium-range interval, so that H6-H7-H8 protons form a tightly packed spin-network. In contrast, the H4 proton belongs to a weaker spin couplings network, H4-H6-H3, than in the previous case, since the H3-H6 internuclear distance is a large one (~4.8 Å). The "compactness" of the spin-network is a measure of the DQ build-up rates in the TP case, so that the slope of the H4 build-up curves is more abrupt than that for H6 site, which emphasizes the increased selectivity of the TP sequence in distinguishing large and medium sized ¹H-¹H dipolar couplings.

This advantage of TP sequence is obtained at the expense of a lower sensitivity compared with BABA, where the intensities of build-up curves are almost twice higher due to the increased efficiency of BABA in generating only DQ correlation in the short excitation time approximation, as described in (ii). Finally, the long τ_{ex} behaviour in (i) is well described by the simulated build-up curves illustrated in Fig. 2, the main conclusion which can be drawn is that the loss in the DQ excitation efficiency reduces with increasing the spinning frequency for both recoupling sequences.

4. CONCLUSIONS

In the present paper, a comparative study on the efficiency of two recoupling sequences, TP and BABA in generating double-quantum correlations has been performed. As concluding remarks, the behaviour of the simulated DQ build-up curves, which correspond to the TP case in the short excitation-time approximation can be manipulated by increasing the spinning frequency. At ultra fast MAS, the build-up rates which correspond to the TP sequence vary from each other

depending on the proton site which is observed, while in BABA case the build-up rates are independent of the investigated proton sites, and the spinning frequency. This important advantage which results from the analytical investigation presented here makes the TP sequence a promising option for NMR molecular structure investigations at the currently available ultra-fast MAS frequencies.

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