

Dear Professor Perunthiruthy Madhu,

Thank you for efficiently organizing the review of our paper: Analytical treatment of proton double-quantum NMR intensity build-up: multi-spin couplings and the flip-flop term. We also thank both reviewers for their kind attitude to our work and helpful comments, which we have tried to take into account in the present version. You can see the niche answers below:

“Response to anonymous Referee #1

The manuscript focuses on the application the Anderson-Weiss approximation for an interpretation of double-quantum (DQ) NMR experiments in many-spin systems ( $s = \frac{1}{2}$ ). The authors proposed new theoretical methods for the analysis of inter-chain flip-flop processes in such experiments. I believe that the manuscript will be interesting and useful for both experimentalists and theoreticians.

I suppose that the manuscript should be completed with materials showing connection of the developed approach with the theory of average Hamiltonian and the Floquet theory. From my point of view the manuscript deserves to be published in Magnetic Resonance.

*We thank Reviewer 1 for supporting our work.*

*If a mathematical equation is solved exactly, without approximations, then the final answer does not depend on the method of solution. If we are talking about approximations, of course such universality is lost, generally speaking. Average Hamiltonian theory and the Floquet formalism are to best of our knowledge the most popular approaches to problems in solid state NMR. In our case, the Floquet formalism is not really suitable as it is almost exclusively applied to solve problems in MAS NMR, i.e. cases with periodic modulations. Average Hamiltonian theory is in turn in fact used by us to derive eq. (3). In revised manuscript we will add some relevant references:*

*(Haeberlen, U., High Resolution NMR in Solids- Selective Averaging, Supplement 1, Adv. Magn. Reson., Academic Press, New York, 1976 and Ivanov K.L., Mote K.R., Ernst M., Egbal A., K. Madhu P.K.: Floquet theory in magnetic resonance: Formalism and applications, Prog. NM Spectr. 126–127, 17-58, <https://doi.org/10.1016/j.pnmrs.2021.05.002>, 2021).*

*We are trying to develop the variant of DQ theory for cases when one cannot neglect spatial displacements of the investigated spins during the experiment motion, with lattice variables being considered classically. In contrast to the usual theoretical approaches, we make the transition to the interaction (Dirac) representation in two steps:*

*In the first step, the lattice Hamiltonian is included along with the Zeeman interaction in the zeroth-order Hamiltonian of the interaction, which asymptotically leads to the DQ - Hamiltonian (15). In the Hamiltonian (15) we extract the part, see relation (16), responsible for the flip-flop transitions commuting with the z-projection of the total spin of the system, which is essentially an observable quantity in experiment, see relation (19). Then, which to the best of our knowledge is done for the first time, we make another transition to the interaction representation by taking the previously extracted flip-flop part as the new zero-*

*point Hamiltonian. On this basis we obtain the exact relations (23) and (24), with respect to which further approximations can be made in the future. In this paper the simplest approximations are investigated. A nontrivial result is obtained already in the zero approximation with respect to the Hamiltonian of flip-flop transitions for the spin 1/2 system: an exactly solvable multispin system (eq. (27-29)). Next, we study the first non-zero corrections associated with flip-flop transitions and their Anderson-Weiss generalizations.*

*We will make this clearer in the revised manuscript.*

Response to anonymous Referee #2

*We are grateful to the second reviewer for his careful review of the manuscript and comments, which will incorporate in the new version of our paper.*

The manuscript describes an analytical treatment of DQ excitation in solids in large spin systems where dynamics and spin flip-flop processes lead to time modulations of the dipolar couplings. In an iterative process of interaction-frame transformations, it is shown that the DQ build up can be calculated analytically while taking the action of the dynamics and spin flip-flop transitions into account. For this an additional interaction-frame transformation with the part of the DQ Hamiltonian that commutes with  $I^z$  (flip-flop part) is performed. This leaves just a  $yy$  part of the Hamiltonian that commutes with itself at all times and allows the calculation of an analytical phase factor that describes the DQ intensity. Results are compared to numerical simulations in relatively small spin systems (6 spins) which shows reasonable agreement with the analytical calculations. Can the authors at least comment whether they expect better agreement if state of the art spin system sizes of 10-12 spins (doable without sparse matrix implementations) would give better agreement?

*To discuss possible improvements in the agreement between simulations and predictions, one should consider that our (still limited) approximation is for now limited to times  $\tau_{DQ} \leq T_2^{eff}$  (see lines 470-480); for longer times, additional work (e.g. evaluating higher-order corrections) is required. Generally, of course, we expect better agreement between simulations and either better predictions or experimental results for more spins. Our (outdated) code is unfortunately limited to 9 spins at present. But the main limitation is in fact the consideration of a realistic spin system, where our alkyl cut-outs are already a bit of a stretch. With nowadays' improved simulation codes such as SPINACH, handling tens of spins, we shall in the future focus on trajectories from MD simulations for the most realistic modelling of fast local conformational dynamics and in particular inter-molecular couplings. We will add corresponding remarks in the paper.*

The manuscript is clearly inside the scope of MR and presents interesting new results that are of interest to the MR readership. However, I believe that the presentation could be improved and that there are a larger number of typos and very colloquial expressions that make it difficult to follow the text.

The authors start from a secular high-field truncated dipolar Hamiltonian (Eq (1)) which has the usual form. But then the authors say: "The Hamiltonian (1) in this paper plays the role of the original spin-lattice interaction Hamiltonian. In the lowest order of perturbation theory, it induces in a spin system 0-quantum transitions (dephasing processes or 0-quantum coherence) by terms proportional to .... 1-quantum transitions (transitions with a flip of one of a pair of interacting spins or 1-quantum coherence) and 2-quantum transitions (coordinated transitions of two spins or 2-quantum coherence) by terms proportional ...." (equation cut out of text). Why would this (static) ZQ Hamiltonian induce DQ or SQ transitions. This would be true for the untruncated dipolar Hamiltonian but not for the high-field truncated one used here, or am I missing something?

*The reviewer is right: the properties of the full Hamiltonian of magnetic dipole-dipole interactions, which was written in this part of the paper in the very first version, are attributed to its secular part. Corresponding changes will be made in the revised version of the paper: “ The Hamiltonian (1) in this paper plays the role of the original spin-lattice interaction Hamiltonian. In the lowest order of perturbation theory, it induces in a spin system only 0-quantum transitions (dephasing processes or 0-quantum coherence) through terms proportional to  $\hat{I}_i^z \hat{I}_j^z$  and flip-flop processes proportional to  $\hat{I}_i^+ \hat{I}_j^- + \hat{I}_i^- \hat{I}_j^+$ . We also note that the non-secular part of the Hamiltonian of magnetic dipole-dipole interactions inducing the processes of spin-lattice relaxation describes the processes of 1-quantum and 2-quantum coherence. However, at the times of interest  $t \ll T_1$  they can be neglected.”*

There are a lot of very colloquial and not very clear and precise statements that could be improved. Examples are:

Line 74: "In solids, the joint effect of mentioned factors, in the limit  $\Delta \rightarrow 0$ , where  $\Delta$  is time interval between the nearest RF pulses" which joint effects are meant here?

*This will be improved in the following way:*

*“ In solids, the joint effect of the BP sequence and the Hamiltonian (1), in the limit  $\Delta \rightarrow 0$ , where  $\Delta$  is time interval between the nearest RF pulses, the spin system’s time evolution can be described in terms of an effective DQ Hamiltonian having the following structure:*

$$\hat{H}_{DQ}^n = (-1)^{n\theta(t-\tau_{DQ})} \sum_{i < j} \hbar \omega_{ij} (\hat{I}_i^y \hat{I}_j^y - \hat{I}_i^x \hat{I}_j^x) = (-1)^{n\theta(t-\tau_{DQ})} \sum_{i < j} \frac{\hbar \omega_{ij}}{2} (\hat{I}_i^+ \hat{I}_j^- + \hat{I}_i^- \hat{I}_j^+), \quad (3)$$

*where  $\theta(x)$  is the Heaviside step function,  $n = 0, 1$ . The case  $n = 0$  corresponds to the first mentioned version of DQ experiment without phase change, i.e. to the signal  $A_0(2\tau_{DQ})$ , and  $n = 1$  to the second version with  $90^\circ$  phase shift, i.e. to the signal  $A_1(2\tau_{DQ})$ . ”*

Line 78: "Note, that  $n = 0$  corresponds to the first mentioned version of DQ experiment no phase change and  $n = 1$  to the second version  $90^\circ$  phase shift." The English is wrong (replace "no" with "without") and it could be stated clearly that you refer to A-0 and A\_1 signals here.

*This will be improved.*

Line 84: "At time moment DQ  $t = t$  the operator (3) changes time for the case, when  $n = 1$ ." A Hamiltonian cannot change time. I can change the sign.

*This is considered in the above passage referring to eq. (3).*

Line 95: "where the role of the zero Hamiltonian is sum of the lattice Hamiltonian and the Hamiltonian of Zeeman interaction of investigated spins with an external magnetic field." What is a zero Hamiltonian? It is defined later but I find this a very colloquial expression. Maybe the "dominant part of the Hamiltonian" would be a better term.

*To be improved:*

*“...zeroth-order Hamiltonian, i.e. the zero-point Hamiltonian or the dominant part of the Hamiltonian (see also expr. (8)), is sum of the lattice Hamiltonian and the Zeeman Hamiltonian of the investigated spins with an external magnetic field...”*

There are more such unclear statements and the manuscript would profit from a careful reading and checking for consistency of notation (see also minor points) as well as the English language.

*The revised version will be carefully edited.*

I think the manuscript would benefit from making section 3 really a discussion without pages and pages of equations that could be moved to an appendix. At the moment section 3.1-3.3 is more a theory section that is very hard to follow and gives little insight for the non-specialist.

*We will move these sections of the paper to the theoretical part (as we believe that moving it into an Appendix would disrupt the flow of arguments unnecessarily)*

Minor points - many typos (?) or unclear expressions in equations:

line 39: two full stops

line 58: quantum instead of quntum

Eq. (4): This should probably be a  $\omega_{ij}(t)$  and not  $\omega_{ij}^{(n)}(t)$  which is only defined in (5)

*All the above corrections will be implemented*

Line 102: Give a reference for AW approximation.

*We will add references to:*

*Anderson P.W., P.R. Weiss P.R.: Exchange narrowing in paramagnetic resonance, Rev. Mod. Phys., 25, 1, pp. 269-276, 1953.*

*Kimmich R.: NMR Tomography Diffusometry Relaxometry, Springer-Verlag Berlin Hedelberg (1997)*

line 164: Are  $I_z$  and  $I^z$  the same or different quantities?

*They are the same, to be improved.*

line 164: What is  $H_0$  here? the Zeeman Hamiltonian or the flip-flop part of the DQ Hamiltonian?

*Here, the zeroth-order average Hamiltonian is still given by expression (12): Zeeman + lattice. This will be clarified.*

Eq. 14 and 15: Is  $U_0(t)$  on the first line of Eq. 14 the same as  $U_0^{(DQ,n)}$  on the first line of Eq. 15?

*This misprint will be fixed.*

Eq. 15: Is  $H^{(0)}_{DQ}$  the same as  $H^{(n)}_{DQ}$  in Eq. 16

*Yes, to be stated clearly.*

Line 205: There is no section 2b

*To be fixed.*

Eq. 32: Is  $\{\tilde{l}_i^y \tilde{l}_j^y\}^{\text{fl}}_t$  the same as the  $(l_i^y l_j^y)^{\text{fl}}_t$  on line 205 and Eq. 31? If not then please define.

*Yes, to be improved.*

There are probably many more that I did not see.

*We will do our best to carefully check the manuscript again.”*

On behalf of all contributors, with respect,  
Nail Fatkullin