

Magn. Reson. Discuss., referee comment RC2
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Comment on mr-2022-19

Anonymous Referee #2

Referee comment on "Time-domain R-PDLF NMR for molecular structure determination in complex lipid membranes" by Anika Wurl et al., Magn. Reson. Discuss.,
<https://doi.org/10.5194/mr-2022-19-RC2>, 2022

Wurl et al. report fitting of recoupled dipolar oscillations in the time domain and take into consideration the RF inhomogeneity of the probe. Measurement of the RF field inhomogeneity using a gradient, though not new, may be useful. I see several major issues with the manuscript. 1st, time domain fitting of dipolar recoupled spectra is not new. See for example the extensive work with DIPSHIFT, REDOR, including fitting of multiple distances (see for example *J. Phys. Chem. B* 2007, 111, 27, 7802–7811). 2nd, from a theoretical standpoint, the authors do not explain why time domain analysis is better than frequency domain analysis; since the FT is a linear operation, it should not result in any loss of information. Each point from the time domain produces a 'basis function' of multiple points in the frequency domain, such that it seems fitting either should be possible. The authors did not make a direct comparison between time domain and frequency domain fitting, but showed only comparisons of the freq. domain data without fitting and sometimes without even considering RF inhomogeneity, though that part is not always clear. 3rd, consideration of RF inhomogeneity in time domain fitting of similar recoupled dipolar interactions has been reported before (e.g. in *J. Phys. Chem. Lett.* 2022, 13, 18–24). I think that if the authors take the above into consideration, that the article could still be helpful for those working in the more dynamic application areas, such as lipid properties.

More minor things:

In the abstract, R-type is rather colloquial. 'R symmetry sequence' or similar would be more precise.

Perhaps there is a review article that could be helpful in the introduction (first paragraph)?

Duplicate citation line 34

Line 49: a strategy to develop a strategy ...

Line 52: more recent work in this area is: J. Chem. Phys. **150**, 134201 (2019);
<https://doi.org/10.1063/1.5088100>

And

J Magn Reson 2020 Oct;319:106827. doi: 10.1016/j.jmr.2020.106827

Line 59, the authors probably mean rather a reduction in the maximum time in the indirect dimension.

Line 69. Considering comments above, mention of the exceptions to this statement are relevant here.

Line 101. kHz would seem to be the more natural unit (at what magnetic field(s) is this statement relevant).

Fig. 2. values in ppm are probably not meaningful without knowing the magnetic field. values in Hz/kHz would be more important. Indication of units for the offset missing. Which

R sequence was used? Ok, it is mentioned in Fig. 1, but the choice of R sequence could be discussed somewhere.

Line 106. more details would be helpful in main text. this is critical to the story since application of this Gradient method seems to be the main innovation. In SI, is the sample static? is Z-gradient better than X or XZ?

Fig. 3. what were the fit parameters? Amplitude (fraction of each species) or only couplings? Why are the FTs of the red and blue curves of panel D not shown?

Fig 4. did both the time domain as well as freq. domain fits include the same treatment of RF inhomogeneity? How does the fit differ if done in the freq. domain (with all other parameters the same)?

Line 171. How were assignments done unambiguously?

Line 193. 'considerably higher' what is considerable? Quantification here would be good.

Line 194. Label of gamma missing in fig 1A.

Line 218. 'higher accuracy' compared to what ? 2H accuracy is not compared (just references to literature values which may have been acquired somewhat differently, and error bars which represent precision).

Fig S7 bottom left. two axes labeled the same. they should be Indexed. panel C explain the labels u and i (maybe that is an L?). also applies to other supplement figures.

Gaussian: capitalize