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Magn. Reson. Discuss., referee comment RC1
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Comment on mr-2022-19

Anonymous Referee #1

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-RC1, 2022

General comments:

The manuscript by Wurl et al. describes a maximum likelihood approach to fitting data from R-type 1H-detected local field experiments in which simulated data computed by forward-modeling, including empirically-determined field inhomogeneity. While this is a promising approach in principle, the method described lacks an effort at error analysis or propagation other than cross-validation against results from 2H experiments. There is also no discussion of model order selection. These deficits undermine the support fot the claims that the method yields better accuracy. **In addition to performing error analysis, the authors should attend to poor English usage in the manuscript**.

Specific comments:

The comment that time-domain fitting avoids the problems of short data records is incorrect, as error analysis would demonstrate (the errors will increase as the data records become shorter). The discrete Fourier transform is, after all, also a maximum likelihood method in which the model is a Fourier series. The time domain fitting approach here works better because it has fewer degrees of freedom (so long as the assumptions are valid, e.g. the field inhomogeneity). Apropos degrees of freedom, the authors do not consider the problem of model order selection – e.g. one vs. two components. A two component model will always fit the empirical data better. The question is whether the better fit is statistically significant in light of the increase of degrees of freedom. This can be approached using the minimum description length or other measures of information content.

While various methods for error analysis could be applied to the maximum likelihood approach described by the authors (e.g. Cramer-Rao), a more rigorous approach would be to use Bayesian analysis, in which the field inhomogeneity is treated as a prior probability. This would allow the impact of the uncertainty in the determination of the inhomogeneity to be propagated to the posterior probability distribution. It would be a natural extension of the maximum likelihood approach described here.