Modelling and correcting the impact of RF pulses for continuous monitoring of hyperpolarized NMR

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The manuscript summarizes work carried out to analyse the effect of radio frequency (rf) pulses on the polarization dynamics of samples in low temperature dynamics nuclear polarization experiments. The authors use a simple three parameter model to simulate a set of data assuming equally spaced rf pulses applied to monitoring the nuclear spin polarization buildup during microwave irradiation. Alternatively, they consider the decay of nuclear spin polarization after a non-thermal state was generated and the microwave irradiation was switch off. In their model they considered an electronic polarization reservoir, a rate by which electron spin polarization is converted into nuclear spin polarization and a rate by which nuclear spin polarization is lost by longitudinal relaxation processes. Furthermore, they added noise to the simulated data to generate data with a particular signal-to-noise ratio (SNR).

The simulated data were used to test three different correction scheme to correct for the polarization loss due to the application of the train rf pulses. The objective was to find differences in how well these correction schemes can recover the actual polarization buildup and decay rates, and the signal enhancement that are given by the choice of the simulation input parameters. The correction schemes used were i) a computational iterative scheme proposed by the authors (and based on their simple model) that provides corrected buildup time constant, longitudinal relaxation time constant and enhancement, an analytical correction formula published by Capozzi et al (2017) for the buildup time constant (in the manuscript called the CC method) and a correction based on the simple $\cos^n \theta$ formula, that corrects for the loss of nuclear spin polarization due to the application of rf-pulses with a pulse angle θ.

Furthermore to these simulations, the three correction methods were applied to experimental data acquired with samples of 50mM 4-oxo-TEMPO in fully protonated water/glycerol or partly deuterated DNP juice.

Such an analysis is useful and should be interesting to a wider readership that uses samples with non-thermal polarization in their own research.

Assuming that I have correctly understood the data presented in tables 2 and 3 and Figs. 4 and 5, the key findings of the authors can be summarized by

(i) All three correction schemes seem to work work well and give similar results for the longitudinal relaxation time constant provided that the pulse angle θ of the pulse train is kept reasonably small (e.g. 5 degree). For bigger excitation pulse angles, the simple $\cos^n \theta$ formula seem to fail when applied to experimental data for the DNP juice sample.

(ii) The analytical formula of the CC method and the computational more demanding iterative scheme seem to give very similar results for the buildup time constants with, as claimed by the authors, the iterative scheme offering the additional advantage to also providing the corrected enhancement factor.

A number of questions arise mainly caused by the less-than-ideal presentation of the data in this manuscript:

i) Fig. 2: It is not clear how much noise was added (see green dots) in these simulations (later in the discussion a SNR of 40 is quoted). The level of noise used should be added in the captions. Are all six subplots really necessary or is it not possible to provide the same information by just using 4 plots? The key information (apart from the obvious fact that data must be corrected to recover the true polarization dynamics) seems to be here that the iterative correction scheme tends to fails if noise is added to the model data and big rf pulse angles are used for the excitation. Therefore, it would be interesting to see how the quality of the iterative correction scheme depends on different added levels of noise and how this relates to the expected SNR in real experimental data. In the discussion, the authors conceded that they have assumed a much lower SNR (40) in their simulations in comparison to the SNR of 1000 obtained by a 2.4 degree excitation rf pulse for the fully protonated sample. Does this mean that the robustness of their iterative correction method against low SNR is actually not really required since for experimental data the SNR is much higher than the assumed low value in the simulations?

ii) Presentation of data in Fig. 3 should be improved: The captions do not explain the black curve in (a). Furthermore, in (b) it is very difficult to distinguish between the open diamond and open square box symbols. Why not using different colours instead ?

iii) I suggest to move the lengthy tables 2 and 3 into an appendix or into the SI, since all the key information of these tables is already summarised in Fig. 4 and 5. In Fig. 5 (c) there seems to be excellent agreement for the relaxation time constant for all three correction methods when applied to the experimental data of the fully protonated sample (the existence of the green dots for the $\cos^n \theta$ correction scheme can only be inferred from the few green error bars in this subplot).

However, the $\cos^n \theta$ correction scheme seems to fail for smaller pulse angles when applied to the DNP juice sample (see Fig 4 c). In the discussion the authors imply that the SNR of the fully protonated sample is smaller than the SNR of the DNP juice sample due to the shorter FID caused by stronger dipolar broadening in the solid state sample. What is then the possible explanation that apparently the $\cos^n \theta$ correction scheme seems to fail when applied to correct for smaller pulse angles with a sample with higher SNR (i.e. the DNP juice sample) ?

It would be useful to include (e.g. in Tables 2 and 3) also the SNR (e.g. measured under steady state polarization conditions) of the two different sample depending on the pulse angles used.

Why is the symbol ϕ used for the pulse angle in the axes titles for Fig 4 and 5 instead of θ ?

Provided that the CC method gives a reliable correction for the buildup time constant, should it not be possible then to also obtain a reliable estimate of the enhancement value if the thermal polarization can be measured ?

iv) The authors should consider using a more consistent terminology and rephrase some of their sentences. Instead of polarization ‘injection’, I suggest to use ‘polarization transfer’ and I would definitely avoid the use of ‘RF relaxation-rate’ and ‘RF relaxation’ (e.g. see page 10) since in NMR terminology relaxation is used to describe incoherent processes while the depletion or loss of nuclear spin polarization caused by application of rf pulses is usually an entirely coherent process.

v) The information included in the SI document is very badly explained and is very difficult to understand by the interested reader without the addition of further details either in the captions of the supplementary figures or additional text in the SI document.

vi) A more cosmetical detail: Please check the use of the multiplication symbol in your formulas. You have not consistently used it in all terms of your formulas (e.g. see eqn 7 and 8). Its use is rather unconventional and I would delete it in all formulas.

In summary, while this manuscript covers some interesting aspects that need to be considered when analysing experimental data of non-thermal spin polarization dynamics, the current version requires significant improvements in both data presentation and careful analysis and discussion. In particular, a thorough analysis of how the various correction scheme depend on the SNR of the data would provide useful insight which scheme should be applied in which experimental scenario. In the current version no convincing arguments are made that the proposed iterative correction scheme for the buildup time constant would be superior to the already published CC method or that it would be superior to the $\cos^n \theta$ scheme for obtaining a properly corrected relaxation time constant.

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