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Comment on mr-2021-11

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Referee comment on "Overhauser dynamic nuclear polarization (ODNP)-enhanced two-dimensional proton NMR spectroscopy at low magnetic fields" by Timothy J. Keller and Thorsten Maly, Magn. Reson. Discuss., https://doi.org/10.5194/mr-2021-11-RC2, 2021

This manuscript demonstrates two-dimensional NMR with quite decent resolution at a proton frequency of about 14 MHz, where Overhauser DNP is more easily applicable than at higher field. The authors also show that the "pure-shift" JRES experiment can be quite useful even in the strong-coupling regime, where pure-shift spectra cannot be obtained. Further, they present a simple - though not necessarily optimal - technique for dealing with magnetic field and phase drifts. Altogether, this manuscript demonstrates sufficient progress for a publication. However, I find several arguments lacking, as detailed below. This particularly regards the application potential of the technique. If sensitivity enhancement is the main argument, then the presented data is unconvincing. This technique will find a niche if and only if it can be applied to problems where the transfer of polarization from electron to nuclear spins provides information rather than "only" sensitivity gain. The authors should respond to the following comments before I can make a final recommendation on publication.

- (l. 49-50): It is not clear to me why the Dubroca method is limited to analytical chemistry. Do you mean that, while solutes in polar organic solvents can be polarized, this is not feasible in water? Please clarify.
- l. 56: dDNP experiments can be repeated, just not with the same sample. Please rephrase.
- l. 63: The wording "sample can be pumped" is unfortunate in a hyperpolarization context. It would help to specify "sample solution can be transferred from low to high magnetic field using a pump".
- Around l. 65: There is a Boltzmann factor penalty, but at the same time, enhancement is usually better at lower fields in Overhauser DNP. This should be mentioned earlier than in line 84. In general, the description of the state of the art is only loosely connected with the motivation of the present work. Please include one or two sentences that summarize the advantages and disadvantages of your approach with respect to measuring polarized samples at high field.
- Standard NMR spectrometers compensate for field drifts with a field lock ("deuterium lock"). Did you consider doing this and, if so, why did you decide against it? The interleaved referencing entails a loss in measurement time by a factor of two, giving up

square root of two in signal-to-noise ratio. Your effective enhancement for ethyl crotonate is only about 20 after that.

- l. 109: Just to be sure: "loaded resonator Q" commonly refers to the resonator being coupled to a 50-Ohm-line, not to it being "loaded" with a sample. Is it possible that 6900 is a loaded Q of the empty resonator and > 4000 is the loaded Q of the resonator with the sample inserted?
- l. 127: Please state explicitly that the linewidth of 0.16 ppm is not limited by shim quality but rather by the presence of the radical (you write so in l. 217). In fact, the statements in lines 216 and 217 are self-contradictory. If there is no significant line broadening due to the added paramagnetic polarizing agent, the linewidth cannot, at the same time, be "still limited by the polarizing agent". The caption of Figure S2 indicates that the polarization agent does determine linewidth.
- Related to 7, please specify the linewidth limit of the shims. It should be possible to measure water without polarizing agent.
- l. 154: "This makes processing 2D NMR spectrometer data possible without requiring transposing data." Why is this an advantage? Transposing a matrix is much faster than other processing steps and the processing time for 2D data is anyway insignificant with a modern computer.
- l. 157: Which window function was applied to 1D data? Line 214 states 1 Hz Lorentzian. What is the reason for this choice? Is this a matched filter? The numbers do not quite fit. You claim a linewidth of 2.3 Hz (l. 127, appears to be water) and a "native" linewidth of 7.3 Hz with a 1 Hz Lorentzian window (l. 214).
- l. 160: "a Gauss Lorentz transformation". Probably ä Lorentz Gauss transformation" is meant here, as correctly written in the caption of Figure 3.
- If the problem with the magnet is just a slow drift that can be addressed by interleaved reference measurements, wouldn't it also be possible to correct for it by analyzing 1D FT of the individual traces of the 2D spectrum?
- It is euphemistic to state that "some" resolution enhancement methods are known to decrease signal-to-noise ratio. Unless you know a method that doesn't entail such loss, please delete the "some".
- l. 227: A Lorentz-Gauss transformation with the same linewidth of 4 Hz for deconvolution and convolution should not change linewidth, but only lineshape. What measure of linewidth are you using here? Please also refer to Figure S3. How did you determine the improvement from 7.3 to 5.6 Hz? What happens if you do not use Lorentzian apodization, but a Hamming window (or even Chebyshev, this is no longer problematic with current computer power).
- l. 229 Instead of the Traficante et al. method, you could as well use a smaller convolution linewidth in the Lorentz-Gauss transformation. Did you try this?
- l. 270: "the possible applications are plentiful". Please list a few. What type of problem can be solved by high-resolution ODNP-enhanced NMR at low field (~14 MHz proton frequency) that cannot be solved by standard NMR? Your ethyl crotonate example would have better sensitivity with a 400 MHz spectrometer (your enhancement is 30). What can you potentially do that cannot be done better with standard NMR?
- l. 288-289: The argument about the Boltzmann penalty is wrong. You pay the same penalty when you measure at low field. The enhancement factor is higher, but sensitivity is not higher. In fact, detection at higher field does improve sensitivity at given polarization. The voltage induced in a coil is proportional to the rate of change of magnetic flux, which in turn is proportional to the resonance frequency.
- Section S3: What is the reason for the phase drift?
- Please refer to the ethanol data (Section S4) at some point in the main text rather than only stating that they exist.
- Supplement l. 54/55: What kind of peak integration would properly quantify the number of protons in the ethanol spectrum?

Typos:

- 10: “chemical cite” should read “chemical site”
- 31: “present large challenge” should read “present a large challenge”
- 140: “90-pulse length” should read “90°-pulse length”
- 165: “were reference” should read “were referenced”
- 176 : “which is on lower side” should read “which is on the lower side”
- 178: “lower viscosity as for example water” should read “lower viscosity than, for example, water”
- l. 254 “since the signal originate” should read “since the artifacts originate”