Review "Optimized shaped pulses for 2D-SIFTER"

The paper by Paul Trenkler et al presents a great and comprehensive discussion of a number of different effects with respect to chirp SIFTER, in particular a comprehensive discussion of the different phase effects known to occur in chirp echo sequences. Further the authors provide an impressive, careful comparison of SIFTER and PELDOR data on the same RNA duplex, showing virtually quantitative agreement in a fraction of the data acquisition time by virtue of the broadband excitation, which is a great result. While many aspects, including chirp SIFTER, are known already as cited by the authors, the paper is definitely worth publishing in Magnetic Resonance as it goes beyond the current literature and enhances the applicability of chirp SIFTER, not least with the additional SIFTER pulse sequences. In particular, the different phase effects are comprehensively summarized, supported by simulations, and the importance for sequences like SIFTER is clearly explained, that this aspect could even be mentioned in abstract & conclusions.

To further improve clarity, I have the following comments prior to publication:

To show the complete SIFTER data, also the SIFTER raw data for the background-corrected traces in Fig. 10 a) need to be included somewhere as individual traces (ideally stacked like in Fig. 10a), particularly in the light of the uncertainties associated with the background correction (see below).

Discussion and simulations of optimal chirp pi-pulse amplitudes in Fig. 3 are great in their illustrative detail and show clearly why it was important to optimize chirp pulse amplitudes carefully as described in previous studies. Here, in the ideal simulations in the absence of B1-inhomogeneity, for a clear picture it would be important to state why the "Fidelity" already declines without the B1-inhomogeneity. Further, what is the direct consequence of the increasing B1-inhomogeneity, which causes the observed echo decline at high Qcrit? Is it a more severe phase roll delta_phi? This is assuming that the fixed echo phases phi_0 have been corrected for each Qcrit. Is that the case? In the text (p. 10) it should be "small sample", rather than "large sample" (the stated color is correct).

In relation to the nice simulations in Fig. 4, p. 10, the term "destructive interference pattern" is unclear. Also, please confirm/state in the text clearly that all sequences in Fig. 4 are set up in a way that complies with Eq. (8), as briefly indicated in the figure caption.

In line with the comment of Nino Wili, it should be correctly explained that working in the linear regime of the microwave amplifiers is not a requirement, contrarily to the authors' statement. It should be discussed that amplifier non-linearity or compression should be quantified and accounted for when calculating the microwave pulse shapes, or otherwise (when on purpose avoided for model studies) significant microwave power needs to be sacrificed to remain in the linear regime of a TWT amplifier. To avoid the caveat of sacrificing microwave power, software compensation with experimental amplitude compression appears preferable.

For the instrumentation, in the absence of high-speed clocks, it would be better to report a jitter time for single echoes (1 shot) for the standard and the high-speed detection variants because without high-speed clock synchronization there is also no fixed phase relation. I strongly suspect, that for down-conversion to 0 GHz before the ADC a small remaining jitter should have indeed only marginal influence (if any) – however, chirp echoes will include higher frequency components, hence jitter should be known before averaging shots to quantify echo amplitudes.

In agreement with the public comment of Maxim Yulikov, I share his opinion that the discussion of the SIFTER background and particularly of its correction here falls short of the potential offered by the presented data. It is a great first step that experimental SIDRE traces have been obtained, and surely also a 2-pulse Hahn echo decay should be known for these samples. Now that a strategy for background correction is published, as cited by Vanas et al 2023, it appears adequate to at least discuss why the presented approximation was chosen and explain how this could be justified over obtaining the SIFTER form factor F(t) with F(t) = [S_SIFTER(t) – S_unmodulated(t)] / [S_SIDRE(t) + S_2Hahn(t)], where S are the different time domain signals and S_2Hahn(t) is the decay of 2 Hahn echoes multiplied back-to-back as described by Vanas et al 2023. The approach taken here and the resulting quantitative agreement with the PELDOR data, suggests that the S_2Hahn(t) signals here may have a form very similar to the S_SIDRE signal for the length of the SIFTER traces shown here. These points appear important to test and clarify in order to provide solid grounds for the background correction employed here.

While indeed Chirp echoes are not the current experimental standard, the literature is somewhat less sparse than it sounds in the introduction. In addition to the works already cited, there are a number of notable applications optimizing and using chirp echoes, such as ESEEM (DOI 10.1063/1.4927088), chirp RIDME (doi:10.2533/chimia.2019.268), and CHEESY-detected EDNMR (DOI 10.1016/j.jmr.2018.02.001 & DOI: 10.1039/D0SC04436A). Also, experimental characterization of pulse excitation profiles has been shown and used as calibration (e.g. Fig. 6 b/e in DOI: 10.1039/c7cp01488k).

In the discussion of Fig. 2 it could be made clear that the sequence with pulse length ratios of 2-2-2 does not satisfy Eq.(8), while the ratio of 2-2-1 does. The expected result is the pronounced phase roll observed in panel (b) (for which the fig. captions is incomplete). The expectation based on Eq. (8) together with this result could be discussed more clearly.

p2 When discussing instrumental non-linearities, Ilya Kuprov's GRAPE paper (doi: 10.1063/5.0264092) could be cited as solution here to be aware of and discuss the approach to compensate for hardware imperfections in software.

p2 When other signals (here called unwanted) of SIFTER or DQC are discussed, it should be noted that most other coherence transfer pathways are not deleterious anymore, but instead can be explicitly taken into account during data analysis in DeerLab using multi-pathway fitting.

p3 As mentioned (and known, see e.g. Verstraete et al 2021) there is a difference between the nominal setting and the actual effective excitation bandwidth of chirp pulses. How much is that difference under the conditions used here? This is e.g. experimentally quantified in pulse excitation profiles.

p4 The finding that smaller Qcrit values (with large TBP values) for pi-pulses can lead to larger echo amplitudes is also discussed in the Verstraete 2021 paper. With the minimum value of TBP = 30 for pi-pulses, it would be helpful to also mention suitable values for the pi/2-pulses used here.

p6 While defining the different phases, please also define phi_p the parabolic phase shift, and for clarity please confirm that within your definitions that the Bloch Siegert shift and the term "dynamic phase shifts" are to be considered equal.

e.g. p9: Please don't omit "chirp" in 2-pulse chirp Hahn echo for clarity, as many might understand the conventional Hahn echo to have rectangular pulses.

p12 and appendix: What is an AWG input amplitude, considering that the AWG is a microwave source?

p16, Fig. 8a it would be nice to mark the 0 MHz offset point in the resonator profile for the other panels in Fig 8.

p17 In the brief introduction of orientation-selective PELDOR, particularly here with respect to X-band, also DOI: 10.1016/j.jmr.2011.12.024 would be adequate to cite.

p19 "SIFTER does not have these limitations and the frequency resolution is only limited by the homogeneous linewidth and the SNR…" Why homogeneous rather than inhomogeneous linewidth here? The EPR spectrum consists of a large number of inhomogeneously broadened EPR lines, some of which are excited at each frequency step during a chirp pulse.

p19 ".. dipolar frequencies from omega_dd to 2 omega_dd at the edges of the spectrum." Fig. 10 a looks like omega_dd is observed at the two edges, whereas 2 omega_dd is observed in the center (around 0 MHz offset in Fig. 10).

p26, Fig. 15 If a SIDRE trace is available as reference to the 6-pulse SIFTER, it would be nice to also show this in Fig. 15.