Tuesday 11th August 2026
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Dear Editor of Magnetic Resonance,

Re: Manuscript No. mr-2026-9

Thank you for giving us the opportunity to revise our manuscript, "Line-Narrowing by Polychromatic Selective Spin-Locking in NMR", Manuscript No. mr-2026-9, for consideration in the journal Magnetic Resonance (Ampere). We appreciate the constructive feedback provided by the reviewers and have carefully addressed all their comments and suggestions in the revised version of our manuscript.

Below, we provide a point-by-point response to each of the reviewers' concerns, detailing the changes made to the manuscript. The reviewers' comments are in **boldface**, our replies are in lightface, and additions to the manuscript are in green. We hope that the revisions meet the expectations of the reviewers and the journal.

We have updated some figures in the manuscript and revised the description of the experiment, as we worked to improve it during the revision period.

Thank you for your time and consideration. We look forward to your decision.

Sincerely,

On behalf of the authors of the Manuscript No. mr-2026-9,
Hadi Loutfi

" Line-Narrowing by Polychromatic Selective Spin-Locking in NMR "

Reviewer Comments:

Reviewer #1 Pr. Dusan Uhrin:

The paper by Wiame et al presents a versatile approach to concurrently removing the fine structure of multiplets caused by homo- and/or heteronuclear coupling while achieving significant line-narrowing of NMR signals by eliminating the effects of inhomogeneous Bo. The paper is well-presented, with numerous examples, providing the NMR community with an excellent starting point for using this technique in a wide range of applications. As stated in the manuscript, "The data that support the findings of this study are available from the corresponding author upon request." I support the publication of this manuscript and like the authors to consider the points raised below.

Reviewer #1 (Remarks):

1. **The authors have provided typical parameters (pulse length, flip angle, power level, acquisition interval length, etc.), but they optimized these for different spectra (e.g., paragraphs 170 and 240). Could they provide some suggestions or rationale for choosing certain parameters? Additionally, what was the value of the after-pulse delay tau? The power deposition to the probe appears to be low; however, it would be desirable to put this into perspective using the technical specifications of current NMR probes.**

   The values of the parameters were written from lines 64 to 75 in the paragraph "2. Mono- or Polychromatic Selective Spin-Locking (SSL)". The parameters have to be optimized depending on the widths of the multiplets. To do this we started with a power for the decoupling pulses equivalent to 1.5 kHz. We optimized this value until we saw the best line-narrowing effect. After this, we optimized the

pulse duration to get the best narrowing effect. In addition, based on your observation concerning the value of the after-pulse delay tau, we have added in the manuscript on lines 66-67 the following: "The "soft" SSL pulses, separated by intervals τ = 1.1 µs, have a duration τ_p…".
To answer the last part of the comment, we added in the manuscript on lines 101 to 106: "The peak RF field amplitude of the short pulses is typically $\omega_1/(2\pi)$ = 2 kHz, so that the average RF field strength, is proportional to the duty cycle:

$$< \omega_1/(2\pi)> = \omega_1/(2\pi)\ \tau p/\Delta t \qquad (2)$$

In our work, the duty cycle is typically $\tau_p/\Delta t$=0.0125so that $< \omega_1/(2\pi)>$ = 25 Hz in our examples, corresponding to 2.05 mW for each of the M interleaved DANTE sequences, well below the maximum power that can safely be applied to commercial solution-state NMR probes."

2. **Some spectra contain low-intensity peaks on each side of the collapsed singlet. Some comments on their origin would be useful. For example, in Figures 3 and 4, are these peaks present due to signal density caused by Bo inhomogeneity, but in others, such as Figures 5 and 8, perhaps not? The acquisition times used are short, hence the chunking artifacts are positioned much further away. Is it possible to link the presence of these peaks to some parameter of the pulse sequence?**

   In the revised manuscript, where the concentrations of the samples were decreased by factors between 50 and 1000 compared to the original submitted manuscript, the low-intensity peaks are no longer visible in Figures 3, 4, 5, 6, and 8. There are some residual peaks for very large concentrations but we have not explored their origin any further because large concentrations are not often required. The intensity of the residual peaks is proportional to the intensity of the narrowed peak. We noticed that the position and intensity of the residual peaks are affected by the SSL pulse length τ_p: the longer τ_p, the smaller and farther apart the residual peaks become.

3. **The noise in the 31P SSL spectrum in Figure 11 is larger than in the reference spectrum. The stated peak height gains of approximately 3, 13, and 5 reflect the figure as presented, but perhaps not the SNR improvements, which should be considered when quantifying the signal enhancement.**

   Indeed, the SNR in Figure 11 decreased by about 50 % when using the SSL sequence, possibly because of electronic interference that we have not been able to suppress.
   Based on your insightful remark, we decided to substitute the peak heights comparison with SNR which we think is more interesting. We took out the sentence. All the peak heights comparison were changed to SNR comparison.

4. **Figure 9 demonstrates the use of polychromatic pulses, and it was interesting to see that the signals below 2.5 ppm preserved their multiplet structure, albeit with reduced intensities. The authors also demonstrated that applying SSL at frequencies 6.5 Hz apart is possible. It would be interesting to state how close 1H multiplets can be for one of them to be collapsed by SSL, yielding a quantitative response without interference from the signal next door. Would the off-resonance signal still be a multiplet, preserving its structure?**

   Indeed, the amplitude of the non-irradiated peaks is reduced by 29% due to as yet unknown interference effects. Furthermore, the HDO peak has been boosted by 29%, possibly because of cross-relaxation effects. We have not yet explored the efficiency of SSL as a function of the offset, but Fig . 9 shows and example where two multiplets near 3.8 ppm that are only 0.05 ppm (25 Hz) apart have been irradiated simultaneously, leading to satisfactory line-narrowing of the yellow and orange peaks. We have observed that off-resonance signals, if they are not directly coupled to signals hit with SSL, will preserve their multiplicity. However, if an off-resonance signal is directly coupled to the signal hit by SSL, we then observed a change in its multiplicity due to the decoupling effect of SSL.

5. **In the latest iteration of SHARPER pulse sequences, the authors have moved away from using selective pulses during acquisition. Although functional (Uhrin and co-authors, https://doi.org/10.1039/d2cc01325h open_in_new), they unnecessarily shortened T2eff, and a better outcome is achieved when the acquisition module consists of much shorter, hard pulses (Uhrin and co-authors, https://doi.org/10.1038/s41467-023-40130-2 open_in_new,**

https://doi.org/10.1021/jacs.5c11092 open_in_new). For the removal of J couplings only, typical chunk times (here AQ times) below 1 ms are used in combination with 90 or 180 deg pulses during the pulse/acquire period. It would be interesting to see how this approach compares to the SSL pulse in terms of the resulting signal linewidth, hence the signal hight and SNR.

We have not yet had the chance to compare SSL with SHARPER. In the introduction, we have said on line 31: "In its conventional form, however, SHARPER can refocus only one or two resonance frequencies, precluding simultaneous linewidth reduction across multiple chemically distinct spins."
We added the following reference in the introduction at line 31: "…and magnetic field inhomogeneities during acquisition (Jones et al., 2017; Davy et al., 2022; Dickson et al., 2022)."
Dickson, C. L., Peat, G., Rossetto, M., Halse, M. E., Uhrín, D. "SHARPER-enhanced benchtop NMR: improving SNR by removing couplings and approaching natural linewidths." Chemical communications, 58 (2022), 5534-5537.

6. **Reflecting on the previous two points, applying SSL to a single frequency (provided that nearby signals are not affected) would present an advantage over SHARPER (even if some intensity drop is registered) as it would avoid the need for selective excitation.**

   Our SSL technique starts with a preparation period that usually includes a "hard" "non-selective" π/2 pulse "hard" 90-degree pulse, followed by soft DANTE pulses which lead to selective spin-locking. We have not carried out a careful comparison between SSL and SHARPER for the reasons mentioned in the introduction.

7. **In paragraph 250, the authors stated as a reason for narrowing 31P signals: "Surprisingly, the experimental line-widths were even narrower, since Δ1/2 = 0.7 Hz at all three sites, which may be due to the cancellation of broadening due to chemical exchange with Mg2+ ions." What is the mechanism of this narrowing? Chemical exchange usually broadens the signal. Can SSL remove exchange broadening?**

   We have dropped this tentative explanation, since the multiplet of the alpha-31P site may result from scalar couplings to ribose protons.

   It is possible that SSL can remove some forms of exchange broadening, but this claim would require further experimental and theoretical investigations.

8. **In the concluding remarks, the authors list a number of areas with potential for the use of the SSL methodology, which is appreciated as it will accelerate the spread of this free-of-charge SNR enhancement methodology. As CPMG-type acquisition modules are widely used in applications where large Bo inhomogeneities need to be suppressed (e.g., the work of Prof Ville-Veikko Telkki and many others), it would be interesting to see if the SSL technique can also be applied in this field.**

   We have not yet compared our work with the ideas of Prof. Ville-Veikko Telkki and his team.

9. **With regard to referencing prior work, since one of the applications of SSL presented in this paper is to LLS, work achieving similar outcomes in the LLS space could be mentioned. See Bodenhausen and co-authors, DOI: 10.1103/PhysRevLett.109.04760, and Levitt and co-authors, https://doi.org/10.1039/c2cp42553j open_in_new.**

   We have inserted these two references in the manuscript.

10. **The approach taken by Andrew Simpson and co-workers (DREAMTIME, https://doi.org/10.1002/anie.202110044 open_in_new), a multi-focusing approach to increasing NMR sensitivity, should certainly be mentioned and discussed.**

    We added a reference to DREAMTIME in the manuscript, although this idea focusses on detecting resonances belonging to known compounds by doubly-selective double quantum excitation.

Reviewer #2:

This is an interesting ms with some nice results, well worth publishing, but it would benefit from some editing and from a more considered discussion and analysis.
Comments and corrections, trivial and otherwise, are listed below in order of page number.

Reviewer #2 (Remarks):

1. **Page 3: delete extra brackets following INFERNO**

   Correction was made.

2. **Page 4: The introduction to SSL lacks clarity and depth. It should be made clear in Fig. 1 that delta t is 1/sw, and that the period labelled "Acq" contributes just one complex point to the final FID; innocent readers will expect "Acq" to denote acquisition of an entire FID. Throughout the ms the description of experimental methods is missing small but critical pieces of information, e.g. the duration of the delay tau, whether "points" means complex points or real points, etc. I strongly encourage the authors to place their experimental data in a public repository so that interested readers can replicate their work, or at the least fill in some of the gaps left by the ms.**

   Based on your remark, we have reformulated the discreption of the experiment in paragraph "2. Mono- or Polychromatic Selective Spin-Locking (SSL)" from lines 64 to 75:

   "In SSL experiments, the preparation period usually includes a "hard" "non-selective" π/2 pulse, typically of 10 µs for a peak RF amplitude ω1/(2π) = 25 kHz, followed by the SSL sequence comprising M short equidistant pulses applied during the acquisition block. The "soft" SSL pulses, separated by intervals τ = 1.1 µs, have a duration τp, which ranges between 1.5 to 7 µs, with a peak RF amplitude on the order of 2 kHz. As a result, the individual pulses have small nutation angles in the range 1° < β < 10°. Each sequence of M short pulses $\tau_p^{m,n}$ with m = 1, 2 … M and n = 1, 2 … N constitutes a "comb" in the manner of DANTE (Carnevale et al., 2012; Bodenhausen et al., 1976; Morris et al., 1978). The phase of the π/2 pulse must be cycled from x to -x, to make up for artefacts arising from RF breakthrough. The phases of SSL pulses are applied along y, so that they are shifted by 90° with respect to the π/2 pulse but remain parallel between SSL pulses. The phase of the receiver must be perpendicular to the π/2 pulse, going from -y to y. These considerations entail that SSL experiments require a minimum of two scans."

   In addition, we added on lines 94 to 96: "The delay Δ*t* is equal to two times the dwell time, to ensure the receiver has enough time to acquire the sampling points. This implicates that two data points, one real and one imaginary, are acquired in each SSL loop.".

   We changed in Figure 1, its caption and the text the "Acq" to "t_{RX}". Some changes were done in the Figure 1 caption: "Figure 1: Schemes for (a) mono- or (b) polychromatic SSL, showing how a series of M short pulses separated by delays τ and associated with chemical shifts fm (where m = 1, 2, …, M), each having a duration τ_p, can be applied during each interval Δt (typically equal to 152 µs), to generate an FID. During the interval "t_{RX}" the receiver is activated to record sampling points, usually with oversampling. Each sequence of M short pulses is repeated N times, until the total number of points have been measured. Typically, N = 32k = 32768 in our experiments, so that the length of the FID is $N\Delta t$ = 4.98 s. The preparation period may consist of a simple π/2 excitation pulse, a T1 inversion recovery sequence, a T2 CPMG echo sequence, or indeed one of the very large number of two-dimensional (2D) experiments where the SSL sequence can be used in the detection interval. For in vivo or in vitro Magnetic Resonance Spectroscopy (MRS), the sequence must be preceded by a method to select a volume of interest."

   We shall deposit the pulse sequence and selected raw experimental data on Zenodo.

3. **Explanations are needed for the orders of magnitude chosen (e.g. pulse durations taup are limited by spectrometer RF bandwidths, flip angles need to be low enough to elicit linear responses, RF amplitudes are determined by beta and taup). It is unhelpful to describe the sequence of M short pulses as 'a "comb" in the manner of DANTE'; it is the M sets of N pulses that are such combs. It would be helpful to the reader to explain that sequence (a) is a DANTE selective irradiation on resonance; adding further phase-rolled pulses in (b) amounts to running a series of different DANTE sequences in parallel. It is not correct to describe the M pulses as "a superposition": that would place them one on top of another, they are a sequence or a succession not a superposition.**

   The soft pulse durations τ_p can be chosen freely regardless of probe bandwidth, the flip angles need not remain within the linear response regime. We have inserted a new Eq. (2) that defines the average RF amplitude:

   To answer the last part of the comment, we added in the manuscript on lines 101 to 106: "The peak RF field amplitude of the short pulses is typically $\omega_1/(2\pi)$ = 2 kHz, so that the average RF field strength, is proportional to the duty cycle:

   $$< \omega_1/(2\pi)>,= \omega_1/(2\pi)\ \tau p/\Delta t \qquad (2)$$

   In our work, the duty cycle is typically $\tau_p/\Delta t$=0.0125so that $< \omega_1/(2\pi)>$ = 25 Hz in our examples, corresponding to 2.05 mW for each of the M interleaved DANTE sequences, well below the maximum power that can safely be applied to commercial solution-state NMR probes."

4. **A significant problem with both the exposition and the analysis of polychromatic SSL is that the Bloch-Siegert effect appears to have been totally ignored. This is a major complication when RF irradiation is, as here, carried out at multiple frequencies simultaneously. The practical consequence here is that the effective DANTE irradiation frequencies produced will differ materially from those calculated using eq. (1). Packages such as Wavemaker routinely correct for such effects.**

   We are well aware of the consequences of Bloch-Siegert effects, inter alea in our early work: "Phase Shifts Induced by Transient Bloch-Siegert Effects in NMR. L. Emsley and G. Bodenhausen, Chem. Phys. Lett. 168, 297-303 (1990)". However, in the present work, the average RF amplitude are too weak to have any significant effects on neighboring resonances.

5. **A second significant complication that needs addressing is that modern NMR instruments do not acquire a single complex data point per dwell time; rather, digital signal processing is used to distil such single points from a much more rapid stream of data. Where that stream is, as here and in any "windowed" acquisition, interrupted, complications and distortions result that are an inevitable consequence of the loss of receiver data continuity while RF pulses are applied.**

   Indeed, complications may arise when the stream of digital processing is interrupted. This may be responsible for some of the interference effects and abnormal signal attenuations that are visible in Figure 9. Since the details of the "digital signal processing [that] is used to distil such single points from a much more rapid stream of data" are not accessible to the user of modern NMR instruments, we cannot compensate for the interference effects.

6. **Throughout the ms a range of different prescriptions are given for the choice of spin lock field amplitude. A clear explanation is needed of how to make rational decisions about this: too low an amplitude will degrade spin locking, too high will lead to spectra distorted by the B-S effect (v supra). Advice to use an RF amplitude comparable to J is unhelpful: many multiplets have widths much greater than any individual coupling, and using only a 10 Hz field with a 50 Hz wide multiplet will degrade the results obtainable.**

   Indeed, the average RF amplitude, as defined in the new Eq. (2) must be adapted to the width of the multiplet. As a rule of thumb, the average RF amplitude should be about equal to the full width of the multiplet or of the inhomogeneously broadened line. However, we have never encountered any problems that could be ascribed to Bloch-Siegert effects.

7. **Page 5: an N repetition -> N repetitions**

Correction was made.

8. **Page 5: It is a little misleading to say that "the novelty of SSL lies in the acquisition of data points in the intervals between the pulses". Windowed acquisition has been used for 60 years or so (e.g. in WAHUHA, and in multiple papers from the Freeman group), and is still available in some routine liquid state spectrometers for selective homonuclear decoupling.**

   We have removed this misleading claim. Indeed WAHUHA uses the same idea.
   We have also removed the (unnecessarily pretentious) expression "sustained" free induction decay.

9. **Page 6: 1 Hz FWHH is about twice the typical manufacturer's specification, so "careful shimming" is a bit of an exaggeration.**

   We have replaced "careful" by "rough".

10. **Page 6: If the natural abundance of 29Si is < 5% then the decoupling referred to cannot explain a 20% increase in peak integral.**

    Indeed. When calculating the signal-to-noise ratio, we found that the increase in SNR is by a factor of 5. We decided to substitute the peak heights comparison with SNR which we think is more interesting. We took out the sentence.
    We changed in the manuscript at line 135 the following: "The line-narrowing by a factor of ca. 5, leads to a gain in signal-to-noise (SNR) by a factor of ca. 5."

11. **Page 6: Here and throughout, the discussion of the linewidths achievable is a bit confused. Under the experimental conditions reported, the experimental linewidth contains a substantial contribution from the limited FID duration. The spins neither know nor care if a receiver is switched on during a DANTE sequence, so the T1rho measured during a windowed sequence should be exactly the same as that in the corresponding unwindowed sequence (see e.g. the comment at the foot of p. 9).**

    Correct. The length of the FID's should exceed by about 1.5 to 3 times T1rho so that the truncation effects can be safely neglected.

12. **Page 7: miss- -> mis-**

    Correction was made.

13. **Page 7: typically -> often [not all methylenes are in alkyl chains]**

    Correction was made.

14. **Page 8: both experiments -> experiments both**

    Correction was made.

15. **Page 9,11: Figs. 5 and 7 are missing basic information – "8 nonlinear steps" is not helpful!**

    Indeed. Short of inserting a boring list of steps, we have written in the captions of Figures 5 and 7 the following: "The interval between the SLIC-in and SLIC-out pulses was incremented in 8 steps of increasing size going from 0.1 to 30 s."

16. **Page 11: Applying Lorentzian broadening does not "improve the digital resolution" in the accepted sense of the term. Why were the data not zero-filled, rather than degraded in this way?**

To avoid any controversial terminology, we have written in the caption of Figure 7 and Figure 9 the following: "To increase the number of data point across the peaks, a Lorentzian line broadening of 0.3 Hz was applied so that each peak is represented by 5 points.".
Zero filling would also have been a good option.

17. **Page 12: The squiggly arrow in Fig. 8 and subsequent figures needs explanation (O1?)**

    We have explained in the text at lines 210 and 211, that the squiggly or wavy arrow correspond to the carrier frequency chosen: "The carrier frequency was set half-way between the two multiplets (wavy arrow in Fig. 8)". For the sake of clarity, we added the same sentence in the captions of Figs 8, 9 and 11: "The wavy arrow indicates the RF carrier frequency.".

18. **Page 12: The interesting observation that the proposed method can fail for the simplest possible coupled spin system, AX, needs both comment and explanation. Under what conditions does the breakdown occur? How can this be avoided?**

    We stated on line 216: "This effect is reminiscent of "recoupling" in solid-state experiments (Tošner et al., 2021). Furthermore, one may observe undesirable coherence transfer phenomena because of homonuclear cross-polarization if the Hartmann-Hahn condition is fulfilled (Sonnefeld et al., 2022b; Wiame et al., 2025). Such effects can be suppressed by using unequal average RF amplitudes of the selective fields applied to the chemical shifts A and X."

19. **Page 13: Lines narrowed -> Line-narrowed**

    We prefer the original text without hyphen.

20. **Page 13: The disappointingly messy results in Fig.9, where artefacts exceed some of the real signals in amplitude, need comment. Why are there so many spurious satellites (B-S effects? DSP artefacts?)? Why are they predominantly in negative absorption mode?**

    The artefacts may be attributed to electronic effects, in particular to the interruptions of the digital signal processing. As mentioned in our response to your fifth question: "Since the details of the digital signal processing method [that] is used to distil such single points from a much more rapid stream of data are not accessible to the user of modern NMR instruments, we cannot compensate for interference effects." We do not know why most artefacts appear in negative absorption mode.

21. **Page 15: The suggestion that SSL cancels broadening due to Mg2+ exchange is implausible: it would imply a shift change on binding that is small compared to the spin lock field amplitude.**

    Indeed. We have removed our comments on exchange broadening. This effect deserves further investigation.

22. **Page 17: The comparison with pure shift methods is more favorable than stated: in pure shift NMR the resolution limit is 1/(pi T2 star) not 1/(pi T2), and in the presence of a spin-lock field scalar contributions to T2 should be reduced, boosting the SSL signal still further.**

    We tend to agree, but short of an experimental comparison of SSL and pure shift methods, we prefer to refrain from any speculation.

23. **Page 17: Authors contributions -> Author contributions or Authors' contributions**

    Correction was made. We chose "Authors' contributions".

Community Comment by Gottfried Otting:

In response to Otting's legitimate request, we shall make the pulse sequence and selected raw figures available on Zenodo.