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Line-Narrowing by Polychromatic Selective Spin-Locking in NMR

Coline Wiame [1], Hadi Loutfi [*,1], Kirill Sheberstov [1], Geoffrey Bodenhausen [1]

[1] Chimie Physique et Chimie du Vivant (CPCV, UMR 8228), Department of Chemistry, Ecole Normale Supérieure, PSL University, Sorbonne University, CNRS, Paris, 75005, France

**Corresponding author*: hadi.loutfi@ens.psl.eu

CW's ORCID: 0009-0008-3517-3354
HL's ORCID: 0009-0004-8617-6599
KS's ORCID: 0000-0002-3520-6258
GB's ORCID: 0000-0001-8633-6098

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Abstract: Selective Spin-Locking (SSL) of the magnetisation vectors of selected singlets or multiplets in high-resolution Nuclear Magnetic Resonance (NMR) spectra by mono- or polychromatic selective radio-frequency (RF) irradiation can reduce the line-widths to the limit given by homogeneous $T_{1\rho}$ relaxation. The resulting line-narrowing leads to an increase in signal height of spectra of ^{1}H, ^{19}F, ^{31}P or other nuclei that is in principle only limited by the ratio $T_{1\rho}/T_2{}^*$. At the same time, the scalar interactions that give rise to multiplets are decoupled, thus leading to an additional gain in signal height. Common one-dimensional (1D) experiments such as inversion recovery (IR) as well as the excitation and reconversion of Long-Lived States (LLS) by Spin-Lock Induced Crossing (SLIC) can significantly benefit from SSL.

1. Introduction

Line-widths in NMR spectra are often broad due to inhomogeneous broadening arising from susceptibility effects, sample heterogeneity, or imperfect static field inhomogeneity. The SHARPER (Sensitive, Homogeneous, And Resolved PEaks in Real time) method enables exceptionally narrow NMR resonances by suppressing dephasing arising from chemical shift evolution and magnetic field inhomogeneities during acquisition (Jones et al., 2017; Davy et al., 2022). In its conventional form, however, SHARPER can refocus only a single resonance frequency, precluding simultaneous linewidth reduction across multiple chemically distinct spins. To achieve line-narrowing on multiple peaks, we have developed a method that we shall refer to as Selective Spin-Locking (SSL), which is based on our earlier work on 'polychromatic decoupling' (Carnevale et al., 2012), where a number of short pulses with small flip angles are inserted in the intervals between the sampling points of the free induction decay (FID). Such short pulses are reminiscent of selective irradiation by Delays Alternating with Nutations for Tailored Excitation (DANTE) (Bodenhausen et al., 1976; Morris et al., 1978), and INFERNO ((Irradiation of Narrow Frequency Envelopes by Repeated Nutation and Orbiting)) (Morris et al., 1978), which are selective excitation methods that are widely used in NMR spectroscopy that use a comb of equidistant low-power RF pulses to achieve selective excitation of specific nuclear resonances. A suitable choice of the phases of these short pulses allows one to generate an irradiation spectrum where multiple peaks of interest are hit simultaneously. The combs of short pulses have the effect of *spin-locking* the magnetisation vectors belonging to the irradiated singlets or multiplets in their *local rotating frames*, thus preventing the phase dispersion due to the static field inhomogeneity and to *J-couplings*. In this case, the decay of the spin-locked transverse magnetisation will be determined by $\exp\{-t/T_{1\rho}\}$ rather than by $\exp\{-t/T_2^*\}$ so that the narrowest possible line-width, $\Delta\nu_{\min}^{SSL}$, is determined by the dissipation of the selectively spin-locked magnetisation in the rotating frame (Redfield, 1955), i.e., $\Delta\nu_{\min}^{SSL} = 1/\pi T_{1\rho}$.

Many common one-dimensional (1D) experiments designed to probe molecular motions can benefit from Selective Spin-Locking (SSL). Inversion Recovery (IR) experiments provide longitudinal relaxation times (T_1), enabling one to estimate rotational correlation times (τ_c), among other parameters. Carr-Purcell-Meiboom-Gill (CPMG) spin-echo experiments yield transverse relaxation times (T_2), allowing for the assessment of chemical exchange effects and other line-broadening mechanisms, such as scalar relaxation of the second kind. Other measurements that use pulsed field gradients (PFG) in order to determine diffusion coefficients can also benefit from SSL. Beyond 1D experiments, SSL can be combined with the many two-dimensional (2D) experiments used in NMR. For many studies, multiplet structures are essentially a nuisance, making the use of SSL valuable.

2. Mono- or Polychromatic Selective Spin-Locking (SSL)

The pulse sequence in Fig. 1 shows how mono- or polychromatic SSL during the acquisition of a Free Induction Decay (FID) is applied after a preparation period that can represent any arbitrary NMR experiment.

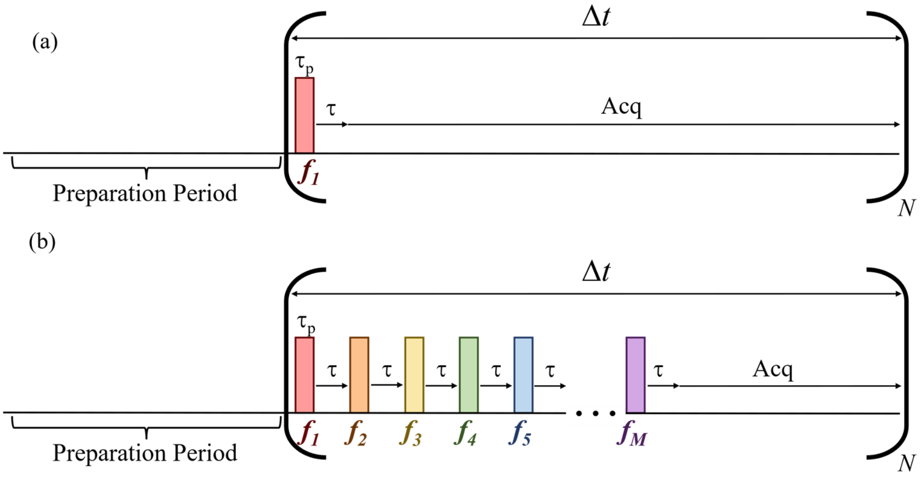

Figure 1: Schemes for (a) mono- or (b) polychromatic SSL, showing how a series of M short pulses separated by delays τ and associated with chemical shifts f_m (where $m = 1, 2, \ldots, M$), each having a duration τ_p, can be applied during each interval Δt between sampling points, to generate a "sustained" FID. Each sequence of M short pulses is repeated N times, until the total number of points have been measured. The preparation period may consist of a simple $\pi/2$ excitation pulse, a T_1 inversion recovery sequence, a T_2 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.

In SSL experiments, an initial non-selective $\pi/2$ pulse, typically of 10 μs for a peak RF amplitude $\omega_1/(2\pi) = 25$ kHz is applied and followed by a 90° phase shift of all M short equidistant pulses applied during the acquisition block. The SSL pulses have a duration τ_p, which ranges between 2 to 7 μs, and an attenuated peak RF amplitude on the order of 2 kHz. Typically, the individual pulses have small nutation angles in the range $1° < \beta < 10°$. Each sequence of M short pulses $\tau_p^{m,n}$ with $m = 1, 2 \ldots M$ and $n = 1, 2 \ldots N$ constitutes a "comb" in the manner of DANTE (Carnevale et al., 2012; Bodenhausen et al., 1976; Morris et al., 1978).

To irradiate M chemical shifts f_m simultaneously, one must apply a superposition of pulses $m = 1, 2, \ldots, M$, incrementing their phases from one interval Δt to the next ($n = 1, 2, \ldots N$) by phase-shifts $\Delta\Phi_{m,n} = n\Delta\varphi_m$, where the "phase roll" $\Delta\varphi_m$ can be calculated by the following equation:

$$\Delta\varphi_m = 2\pi\Delta t\Delta f_m \quad (1)$$

where, as shown in Fig. 2, Δf_m corresponds to the difference in frequency (in Hz) between the RF carrier frequency and the m^{th} peak of interest. Using Δf_m, the phase shift required to apply the m^{th} short pulse, $\Delta\varphi_m$, to the m^{th} peak of interest can be calculated using equation (1). For monochromatic SSL (Figure 1a), the carrier frequency can be set to be on-resonance with the peak of interest so that $\Delta\varphi_m = 0°$.

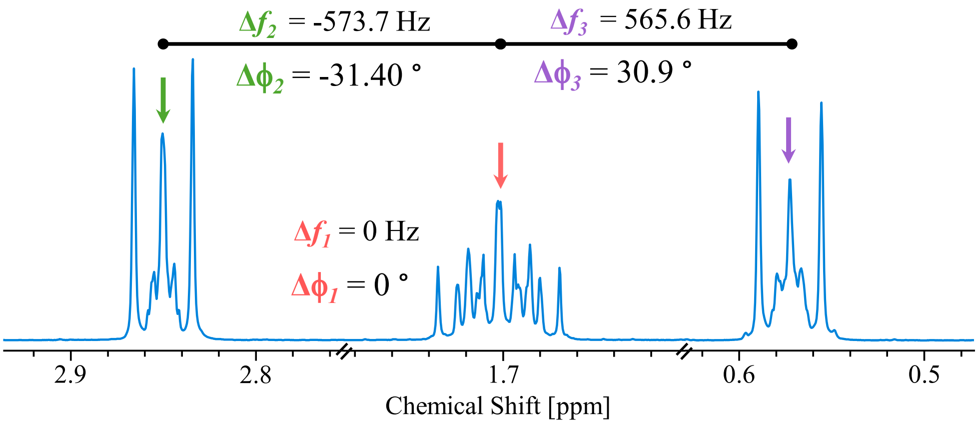

Figure 2: One-dimensional (1D) ^{1}H spectrum showing peaks corresponding to the three CH_2 groups of 200 mM sodium trimethylsilylpropanesulfonate (DSS) in 100 mM phosphate buffer solution (PBS, pH 7.2) in D_2O at 11.7 T (500 MHz for ^{1}H) showing the phase incrementation required for trichromatic SSL ($M = 3$) with $\Delta t = 152$ μs, the carrier frequency being set on the central peak (red arrow). The green and purple arrows designate the positions irradiated using phase incrementation which are calculated with Eq (1) to coincide with the central lines of the high- and low-frequency multiplets.

Signal acquisition occurs during a short time interval, designated by the delay "Acq" in the sequences above, during which the receiver is activated in so-called oversampling mode. As illustrated in Fig. 1, the delay Δt remains the same for mono- or polychromatic sequences; the variable delay is "Acq" which becomes shorter for experiments with large number of SSL pulses, M. The total number of points is observed through an N repetition of the SSL sequence (Fig. 1, bracketed section) to generate a "sustained" free induction decay. Since the precession is no longer "free", we may speak of a "sustained induction decay". Typically, N can be as large as 64 k or more. Although the novelty of SSL lies in the acquisition of data points in the intervals between the pulses, one can also replace the intervals marked "Acq" in Fig. 1 by empty delays, in which case the line-narrowing method can be inserted in one of several evolution intervals of n-dimensional experiments.

The peak RF field amplitude of the short pulses is typically $\omega_1/(2\pi) = 2$ kHz, so that the average RF field strength, $\langle\omega_1/(2\pi)\rangle$, proportional to the duty cycle $\tau_p/\Delta t$ (typically equal to 0.0125 in our work), is $\langle\omega_1/(2\pi)\rangle = 25$ Hz in our examples. The average RF field amplitude should be comparable to $1/(\pi T_2^*)$

if one wishes to narrow a single inhomogeneously broadened line, and comparable to *J* if one wishes to collapse a multiplet at the same time.

3. Monochromatic SSL for Line-Narrowing in the Absence of Couplings

The long-range *J*-couplings of the nine magnetically equivalent methyl protons in sodium trimethylsilylpropanesulfonate (DSS), to neighbouring protons are negligible, so that one can focus on the ability of SSL to overcome the effects of B_0 inhomogeneity. A conventional proton spectrum was measured after a $\pi/2$ pulse, using a 5 mm Bruker NEO iProbe at 11.7 T (500 MHz for ^{1}H), where a full width at half-height (FWHH) of approximately 1 Hz was achieved by careful shimming (Fig. 3, blue line). By deliberately miss-setting the z_1-gradient of Bruker's room temperature shim system, the line was broadened to ca. 40 Hz (Figure 3, light blue line).

As mentioned before, the smallest line-width that can be achieved is determined by the transverse relaxation time in the rotating frame, $T_{1\rho}$ (Redfield, 1955). For the methyl protons of DSS, $T_{1\rho} = 3.08$ s at 298 K and 11.7 T, as measured by applying selective monochromatic DANTE sequences (Morris et al., 1978) with increasing durations $0.1 < \tau < 15$ s after an initial $\pi/2$ excitation pulse. Therefore, the theoretical minimum line-width that can be achieved in the case of these methyl protons is $\Delta\nu_{\min} = 1/\pi T_{1\rho} = 0.103$ Hz. The T_1 of these protons is equal to 3.13 s; the fact that $T_{1\rho}$ and T_1 are nearly equal shows that the extreme narrowing regime ($\omega_0\tau_c < 1$) is fulfilled to a good approximation.

The monochromatic SSL sequence (Figure 1a), was applied to the middle of the inhomogeneously broadened resonance of the methyl groups of DSS, setting the duration of the short pulses $\tau_p = 1.9$ µs (nutation frequency = 1.9 kHz for ^{1}H), applied within $\Delta t = 152$ µs (spectral width 6579 Hz), to achieve an average RF amplitude $<\omega_1/(2\pi)> = 17$ Hz. The monochromatic SSL leads to a narrow peak (dark blue line in Fig. 3) with a FWHH of 0.28 Hz, about 2.7 times broader than the theoretical limit $\Delta\nu_{\min} = 0.103$ Hz. This demonstrates that SSL with very weak RF fields can overcome severe inhomogeneous broadening. Monochromatic SSL was also applied to the well-shimmed proton signal (Figure 3, blue line) with $\Delta\nu = 1.0$ Hz. The resulting line-narrowed spectrum, not shown in Fig. 3, has a FWHH of 0.2 Hz, only about 1.4 times broader than the theoretical limit. The line-narrowed peaks resulting from both the inhomogeneously broadened peak and from the well-shimmed peak have comparable line-widths which shows the ability of SSL to surmount different degrees of broadening.

Surprisingly, the line-narrowing by a factor of ca. 5 leads to a gain in peak height by a factor of ca. 6, because the gain is boosted by (heteronuclear) decoupling of the satellites due to ^{29}Si (natural abundance 4.67 %) (Rosman et al., 1998) with ^2J (^{29}Si, ^{1}H) = 6.6 Hz (Delmulle et al., 1980). Note the slight displacement of the line-narrowed peak (Figure 3, dark blue line), with respect to the conventional 1D spectrum peak arises from problems in accurately determining the centre of gravity of the inhomogeneously broadened light blue line. To verify that the quantitative aspect of proton NMR is conserved when applying monochromatic SSL, we compared the integrals of the conventional 1D and line-narrowed spectra and found them to be equal.

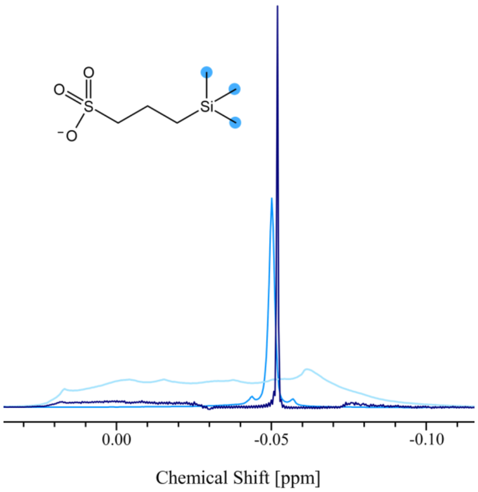

Figure 3: Line-narrowing by monochromatic SSL applied to the three equivalent CH_3 groups (blue circles) of 200 mM DSS in 100 mM PBS (pH 7.2) in D_2O. Blue line: Conventional 1D spectrum with a line-width $\Delta\nu = 1$ Hz. Note the satellites due to ^{29}Si with 5% natural abundance and $^2J(^1H,^{29}Si) = 6.6$ Hz. Light blue line (scaled x4): Broadened to a line-width of about 40 Hz by deliberately miss-setting a shim current. Dark blue line: Line narrowed to $\Delta\nu = 0.28$ Hz by monochromatic SSL applied to the broadened light blue resonance, as described in the text. All spectra were obtained with 32 k points and 1 scan.

135 4. Monochromatic SSL for Line-Narrowing and Decoupling of Multiplets

4.1 Applications to Proton NMR

4.1.1 Combination with one-dimensional spectroscopy

In ^1H NMR spectra, methylene protons (–CH_2–) typically appear as complex second-order multiplets due to couplings between magnetically inequivalent neighbouring CH_2 protons. Here, we 140 measured conventional spectra of a well-shimmed sample excited by a $\pi/2$ pulse (Figure 4, blue line), which features a complex multiplet structure covering about 40 Hz and a central line with a line-width $\Delta\nu = 2$ Hz. The inhomogeneously broadened peak (Figure 4, light blue line) spans an overall width of about 100 Hz. The same monochromatic SSL experiment applied to the methyl groups of DSS, described in the previous section, was applied to the central CH_2 inhomogeneously broadened multiplet 145 (Figure 4, light blue line) of DSS giving rise to a narrow singlet (Figure 4, dark blue line). We observed both a narrowing of the line-width, to $\Delta\nu = 0.38$ Hz, and a collapse of the multiplet, resulting in an approximately 8-fold increase in peak height.

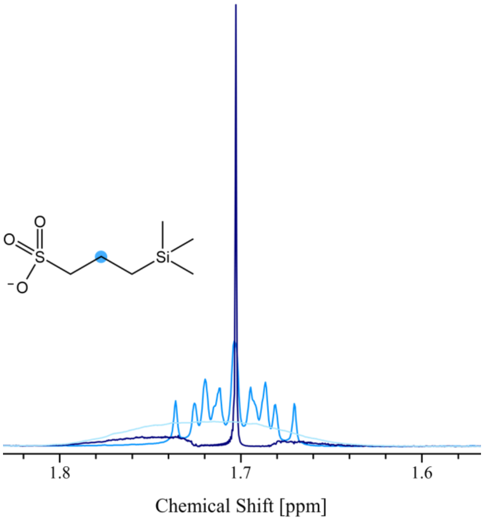

Figure 4: Line-narrowing and decoupling by monochromatic SSL applied to the central CH_2 multiplet (blue circle) of 200 mM DSS in 100 mM PBS (pH 7.2) in D_2O. Blue line (scaled x2): Conventional 1D multiplet with an overall width of ca. 40 Hz and a $\Delta\nu = 2$ Hz for the central line. Light blue (scaled x2): Broadened by deliberately miss-setting a shim current to an overall width of ca. 105 Hz. Dark blue line: The broadened spectrum was line narrowed and decoupled to a line-width $\Delta\nu = 0.38$ Hz by monochromatic SSL, resulting from the Fourier transformation of an FID obtained with short pulses of $\tau_p = 1.9$ µs, applied within delays of $\Delta t = 152$ µs, with an average RF amplitude of 17 Hz. All spectra were obtained with 32 k points and 1 scan.

4.1.2 Combination with Long-Lived States (LLS)

In recent years, we have developed methods to excite long-lived population imbalances and reconvert them into observable magnetisation in $(CH_2)_n$ chains by Spin-Lock Induced Crossing (SLIC) (Sonnefeld et al., 2022). The decays of the signals allow one to determine the lifetimes T_{LLS} of the superpositions of two-, four- or even six-spin order LLS terms. Applying monochromatic SSL (τ_p = 2.85 µs, applied within Δt = 152 µs, and 37 Hz average RF amplitude) to a multiplet that results from the reconversion of LLS in the low-frequency CH_2 group of β-alanine (Fig. 5b) collapses the multiplet of an overall width equal to 18 Hz and narrows the central line-width of 1 Hz to a sharp singlet of $\Delta\nu$ = 0.3 Hz. The gain in amplitude by a factor of ca. 7 (Figure 5) achieved by monochromatic SSL is particularly welcome for these types of experiments. Indeed, at least 90 % of the signal is lost during the creation and reconversion of LLS by SLIC experiments, so that boosting the peak height by SSL offers a significant advantage. The LLS lifetime was extracted by mono-exponential fitting and was found to be T_{LLS} = 18.9 s, for both experiments with and without SSL.

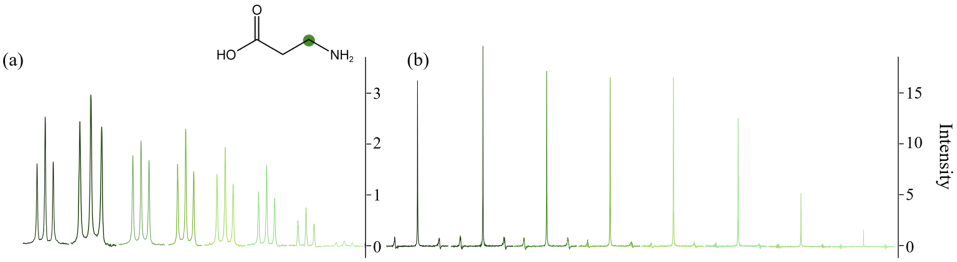

Figure 5: LLS signals of the low-frequency CH$_2$ group (green circle) of 100 mM β-alanine in 100 mM PBS (pH 7.2) in D$_2$O, obtained by the reconversion of LLS into magnetisation by SLIC. The LLS were created on both CH$_2$ groups by dichromatic SLIC-in and reconverted into magnetisation by dichromatic SLIC-out. (a) Without SSL one observes a $\Delta\nu = 1$ Hz. (b) With monochromatic SSL, as described in the text, applied to the low-frequency CH$_2$ group during acquisition, the line-width is narrowed to $\Delta\nu = 0.3$ Hz. The interval between the SLIC-in and SLIC-out pulses was incremented in 8 non-linear steps going from 0.1 to 30 s. The intensity of the signals was increased by a factor of ca. 7 when SSL is applied, as shown by the increased vertical scale in (b). Note that the signals increase initially before they decay, due to long-lived coherences (LLCs). Both experiments were obtained with 64 k points and 2 scans.

4.2 Applications to Fluorine-19 NMR

4.2.1 Combination with one-dimensional spectroscopy

Fluorine-19 spectra tend to show complicated multiplets because of the ubiquity of long-range couplings. Fig. 6 shows an application of a *monochromatic* SSL sequence (at 11.7 T or 470.53 MHz for ^{19}F and 298 K) to perfluorobutanesulfonic acid (PFBS), a typical example of per- and poly-fluoroalkyl substances (PFAS). The monochromatic SSL sequence was applied to the central CF$_2$ group of PFBS, with short pulses of $\tau_p = 3.8$ μs (nutation frequency = 2.1 kHz for ^{19}F) applied within delays $\Delta t = 21.2$ μs (spectral width 47.17 kHz) for an average RF amplitude of 120 Hz. These parameters were optimised to effectively collapse the entire multiplet which covers a region of ca. 76 Hz. This experiment resulted in a line-narrowing effect decreasing the FWHH from about 22 to 0.9 Hz, while the peak height of the signal is increased by a factor of ca. 23.

In molecules that are not perfluorinated but contain residual protons our method allows one to dispense with proton decoupling since both homo- and heteronuclear couplings are effectively supressed.

The transverse relaxation time in the rotating frame of these ^{19}F nuclei was measured to be $T_{1\rho} = 1.39$ s, so that the narrowest theoretically possible line-width achievable by SSL for these nuclei is $\Delta\nu_{\min} = 0.23$ Hz. The experimental value measured is therefore ca. 4 times larger than this limit.

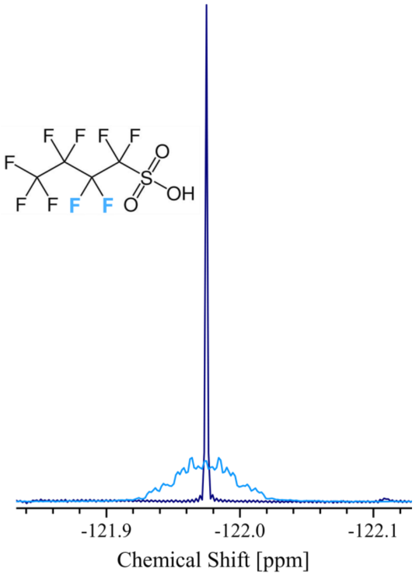

Figure 6: Fluorine-19 spectra of the central CF_2 multiplet (fluorine atoms highlighted in blue) of 100 mM PFBS in D_2O. Blue line (scaled x2): Conventional 1D spectrum with an overall width of about 75 Hz and a FWHH of 22 Hz. Dark blue line: Line narrowed and decoupled to a line-width $\Delta\nu$ = 0.9 Hz by monochromatic SSL as described in the text. Both spectra were obtained with 64 k points and 1 scan.

180 4.2.2 Combination with Long-Lived States (LLS)

In recent work, we investigated the creation and reconversion of LLS in $(CF_2)_n$ chains using SLIC (Wiame et al., 2025). The excitation yield of LLS in these fluorinated aliphatic chains by SLIC is only around 1 %, making SSL even more appealing than for applications to protons. In Fig. 7, we show the signal decay of LLS without and with monochromatic SSL (τ_p = 3.8 µs, applied in delays Δt = 42.0 µs for an average RF amplitude of 61 Hz) irradiating the central CF_2 peak of PFBS, resulting from the reconversion of LLS. Here, the LLS signal is line narrowed and decoupled, from a line-width of 21 Hz and an overall width of ca. 53 Hz to only $\Delta\nu$ = 1.3 Hz, while increasing the signal height by a factor ca. 12. In both experiments, it was found that T_{LLS} = 3.3 s.

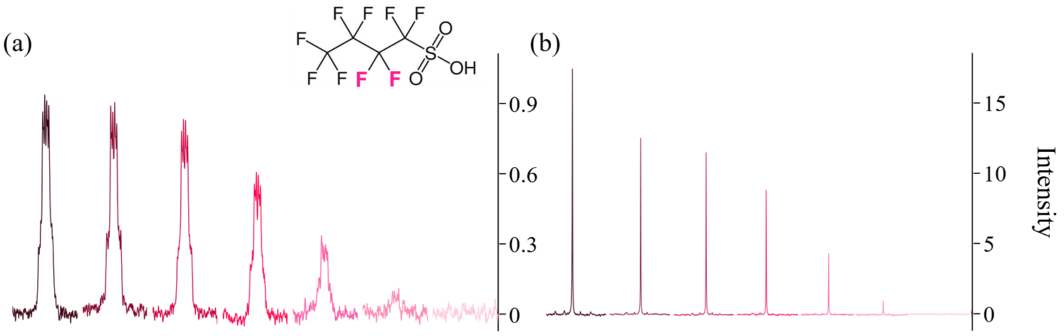

Figure 7: LLS signals of the central CF_2 group (highlighted in pink) of 100 mM PFBS in D_2O, obtained by the reconversion of LLS into magnetisation by SLIC. The LLS was created and reconverted by monochromatic SLIC-in and monochromatic SLIC-out. (a) Without SSL with overall span of about 53 Hz and a FWHH of 21 Hz. (b) With monochromatic SSL applied to the central CF_2 group during acquisition as described in the text, narrowing the line-width to $\Delta\nu$ = 1.3 Hz. The interval between the SLIC-in and SLIC-out pulses was incremented in 8 non-linear steps going from 0.1 to 60 s. The intensities of all signals were increased by a factor of ca. 12, as shown by the increased vertical scale in (b). Both experiments were obtained with 64 k points and 2 scans. To improve the digital resolution, a Lorentzian line broadening of 0.3 Hz was applied so that each peak is represented by 9 points.

5. Polychromatic SSL for Line-Narrowing and Decoupling

5.1 Applications to Proton NMR: Combination with one-dimensional spectroscopy

In addition, we applied a *dichromatic* SSL sequence (M = 2 in Fig. 1b) to both CH_2 groups in the antibiotic metronidazole (MDZ), achieving narrowing and decoupling of both multiplets from a line-width of $\Delta\nu$ = 1.7 Hz for the central line and an overall width of ca. 17 Hz of the multiplet to a singlet with a line-width of only 0.6 Hz (Fig. 8). The heights of both peaks were increased by factors close to 3. The parameters of dichromatic SSL were τ_p = 1.9 µs (nutation frequency = 1.9 kHz), applied within delays Δt = 152 µs, with an average RF amplitude of 25 Hz. The carrier frequency was set half-way between the two multiplets (wavy arrow in Fig. 8) so that the effective irradiation frequencies appear at Δf_1 = -148.3 Hz and Δf_2 = +148.3 Hz with respect to the carrier.

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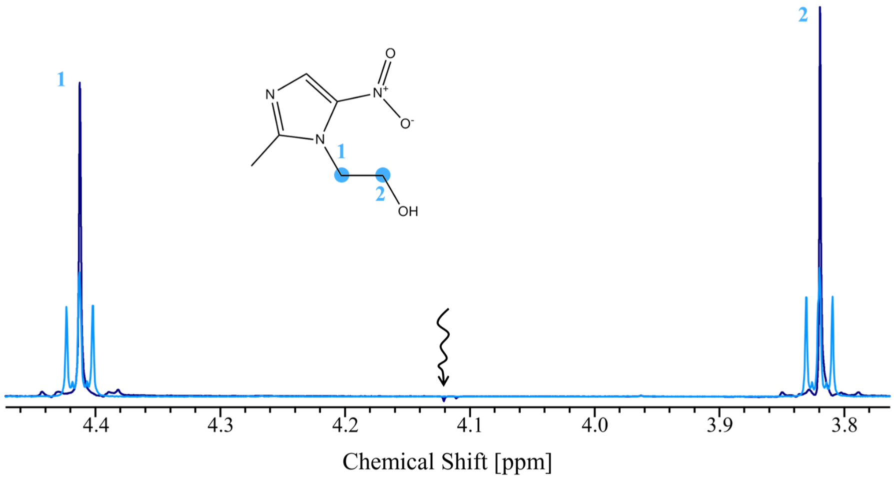

Figure 8: Line-narrowing and decoupling by dichromatic SSL applied simultaneously to the high- and low-frequency CH_2 peaks (highlighted by blue circles) of 40.3 mM MDZ in 100 mM PBS (pH 7.2) in D_2O at 11.7 T (500 MHz for ^1H) and 298 K. Blue line: Conventional 1D spectrum with a line-width $\Delta\nu$ = 1.7 Hz. Dark blue line: Lines narrowed and decoupled to a line-width $\Delta\nu$ = 0.6 Hz by dichromatic SSL as described in the text. The peak heights are increased by factors of ca 3. Both spectra were recorded with 64 k points and 1 scan.

When dichromatic spin locking is applied to the chemical shifts A and X of a coupled two-spin AX system, the effects of all couplings J_{AM}, J_{XM} to non-irradiated nuclei are suppressed, but the coupling J_{AX} between the two irradiated spins may not be perfectly cancelled. 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., 2021; 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.

We applied an *octa-chromatic* SSL ($M = 8$ in Fig. 1b) sequence to a mixture of various small molecules, i.e., metronidazole, vitamin B1, acetylcholine, β-alanine, taurine and γ-aminobutyric acid (GABA), as shown in Fig. 9. In this experiment, we could effectively narrow and decouple overlapping peaks, even if their central lines were only 6.5 Hz apart. The line-widths of all peaks irradiated by octa-chromatic SSL were decreased by a factor of ca. 2, while the peak heights were increased by factors ranging from 2 to 6. The same τ_p, average RF amplitude, and Δt used for the dichromatic SSL experiment described previously were used for octa-chromatic SSL. The carrier frequency was set to be on-resonance with the peak highlighted in light green, corresponding to a CH_2 group of acetylcholine (black wavy arrow in Fig. 9b) and the effective irradiation frequencies were $\Delta f_1 = 0$ Hz, $\Delta f_2 = +156.27$ Hz, $\Delta f_3 = +238.87$ Hz, $\Delta f_4 = +273.48$ Hz, $\Delta f_5 = +363.34$ Hz, $\Delta f_6 = -69.21$ Hz, $\Delta f_7 = -90.34$ Hz, $\Delta f_8 = -387.04$ Hz with respect to the carrier. The spectrum in Fig. 9b features a number of sharp spikes that do not arise from the nuclei but are due to intermodulation effects.

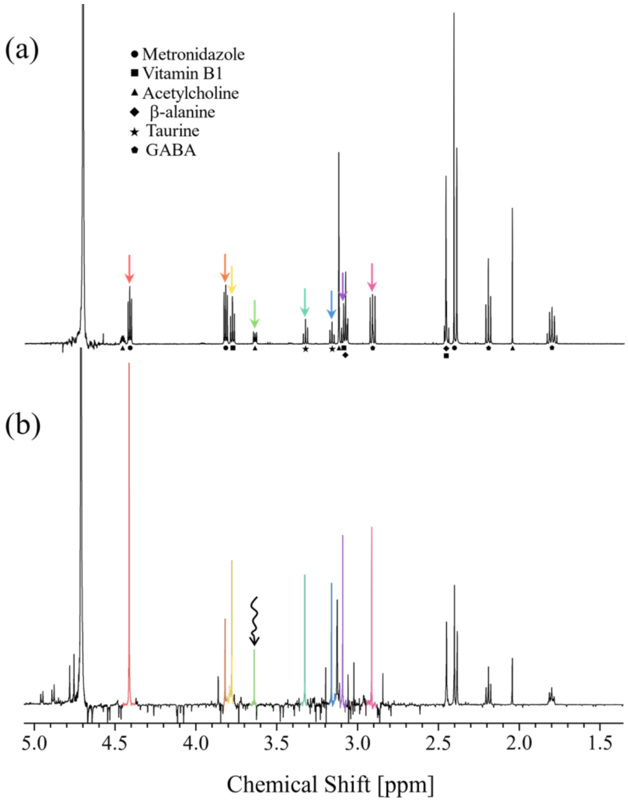

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Figure 9: Line-narrowing and decoupling by octa-chromatic SSL applied to a mixture of six small molecules: metronidazole, vitamin B1, acetylcholine, β-alanine, taurine and GABA, all at 10 mM concentrations in 100 mM PBS (pH 7.2) in D_2O. (a) Conventional 1D spectrum. (b) Lines narrowed and decoupled spectrum obtained by octa-chromatic SSL as described in the text. The 8 coloured arrows in (a) correspond to the irradiation frequencies of the pulses chosen to spin-lock 8 selected proton signals. The colour-coded peaks in (b) show the corresponding irradiated peaks after line-narrowing and decoupling by octa-chromatic SSL. To improve the digital resolution, a Lorentzian line broadening of 0.3 Hz was applied so that each peak is represented by 5 points. The peak heights are boosted by factor between 2 and 6. Both spectra were recorded with 16 k points and 1 scan.

5.2 Proton NMR: Combination with Inversion Recovery (IR)

We were also able to combine *dichromatic* SSL with the Inversion Recovery (T_1) experiment, as shown in Fig. 10b for the amino acid, β-alanine. The line-widths of the peaks equal to ca. 2 Hz and the overall width of the peaks equal to ca. 20 Hz were reduced to $\Delta\nu = 0.7$ Hz by dichromatic SSL and 225 the heights of the peaks, as shown by the vertical scale in Fig. 10b, showed a 5-fold increase. The T_1 was extracted by mono-exponential fitting and found to be ca. 2.6 s, both without and with SSL. Adding an SSL block after an IR sequence therefore provides a robust method for measuring T_1 values while boosting the peak heights by a sizable factor.

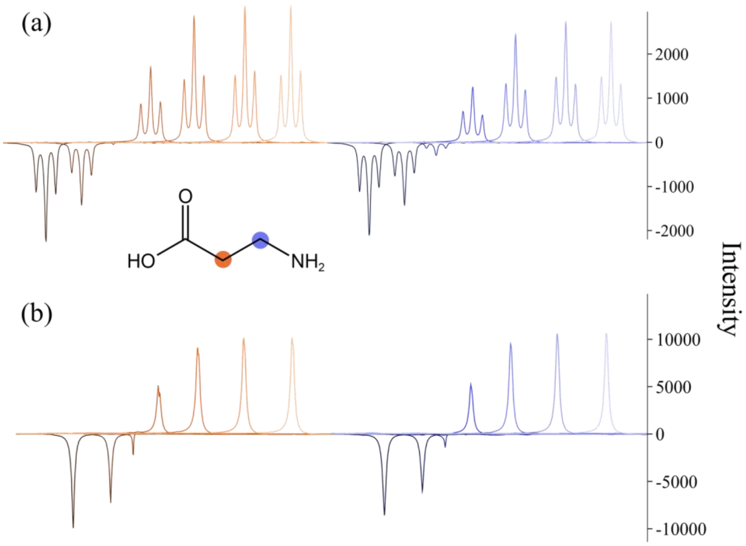

Figure 10: Inversion-Recovery (T_1) experiments showing the high-frequency CH_2 (orange) and low-frequency CH_2 (blue) groups of 100 mM β-alanine in 100 mM PBS (pH 7.2) in D_2O. (a) Without SSL with a line-width Δν = 2 Hz. (b) Lines narrowed and decoupled to line-widths close to Δν = 0.7 Hz by dichromatic SSL as described in the text. The interval between the inversion pulse and the excitation pulse was incremented in 8 non-linear steps going from 0.1 to 30 s. To improve the digital resolution, a Lorentzian line broadening of 0.3 Hz was applied so each peak is represented by 9 points. Both experiments were obtained with 64 k points and 1 scan.

Likewise, T_2 CPMG spin-echo experiments can benefit from SSL. Such experiments (not shown in this work) were run and yielded accurate relaxation times T_2.

6. Applications to Phosphorus-31 NMR

Although phosphorus-31 resonances at high fields are broadened due to rapid relaxation driven by the chemical shift anisotropy, which cannot be eliminated by SSL, various other line-broadening mechanisms are amenable to line-narrowing. To assess this, we looked at the three ^{31}P nuclei in Adenosine Triphosphate (ATP). In addition to the decoupling of homonuclear $J(^{31}P, ^{31}P)$ interactions, a significant line-narrowing effect was observed (Fig. 11). In the conventional spectrum, the individual lines of the left-hand doublet have widths of about Δν = 1.3 Hz, those of the central doublet have Δν = 13 Hz, and lines of the right-hand triplet have Δν = 2.3 Hz. The two doublets span widths of about 20 Hz while the triplet spans a width of ca. 40 Hz. By applying *trichromatic* SSL to the all three chemical shifts, the multiplets were decoupled and their lines were narrowed to line-widths of 0.7 Hz, boosting peak heights by factors of ca. 3, 13, and 5 for the signals from left to right. The optimised parameters for this experiment were $\tau_p = 3.8$ µs, applied within $\Delta t = 152$ µs and with an average RF amplitude of 35 Hz. The carrier frequency was set half-way between the outer multiplets at -16.9 ppm (black wavy arrow in Fig. 11). The irradiation frequencies were $\Delta f_1 = -1239.9$ Hz, $\Delta f_2 = -1132.3$ Hz and $\Delta f_3 = +1239.9$ Hz The fact that the three peaks have nearly the same heights suggests that SSL yields quantitative intensities, i.e., that the peak heights are proportional to the numbers of spins and hence to the concentrations.

The transverse relaxation time in the rotating frame of the central ^{31}P nucleus was measured to be $T_{1\rho} = 0.357$ s, so that the narrowest theoretically possible line-width achievable by SSL for these nuclei is $\Delta\nu_{\mathrm{min}} = 1/\pi T_{1\rho} = 0.89$ Hz. Surprisingly, the experimental line-widths were even narrower since $\Delta\nu = 0.7$ Hz at all three sites, which may be due to the cancellation of broadening due to chemical exchange with Mg^{2+} ions.

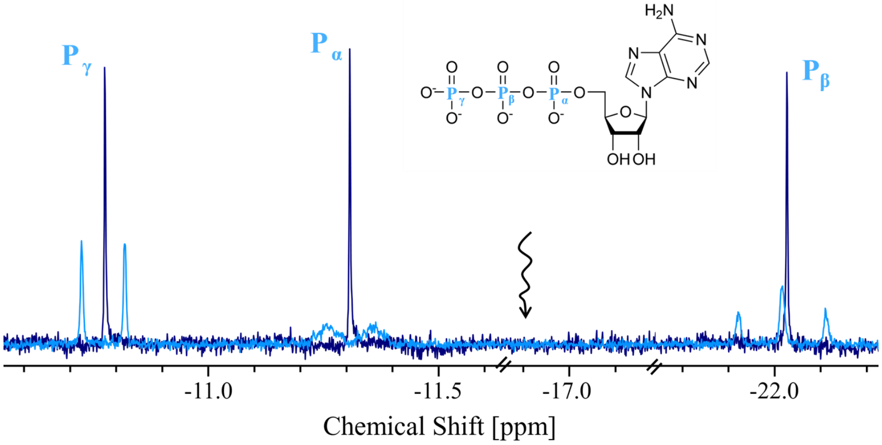

Figure 11: Phosphorus-31 spectra of 20 mM ATP (the three phosphorus atoms are highlighted in blue) in D_2O at 11.7 T (202.41 MHz for ^{31}P) and 298 K. Blue line: Conventional ^{31}P spectrum. Black line: Line-narrowed and decoupled spectrum obtained by trichromatic SSL, as described in the text, with line-widths $\Delta\nu = 0.7$ Hz at all three sites. Both spectra were obtained with 64 k points and 1 scan.

7. Conclusion

By applying mono- or polychromatic SSL to selected singlets or multiplets in high-resolution NMR spectra of ^{1}H, ^{19}F, ^{31}P and other nuclei, one can collapse both homo- and heteronuclear scalar couplings, eliminate inhomogeneous broadening, and thus obtain very narrow signals. The decay of the spin-locked transverse magnetisation is in principle limited by $\exp\{-t/T_{1\rho}\}$ rather than by $\exp\{-t/T_2^*\}$, so that the line-widths upon Fourier transformation can approach the theoretical limit $\Delta\nu_{\mathrm{min}} = 1/\pi T_{1\rho}$ rather than inhomogeneous width $1/\pi T_2^*$.

The reduction of line-widths and decoupling of multiplets leads to an increase in peak heights, ranging from factors 4 to 40 in the examples discussed in this work. This should make it possible to reduce the detection level, i.e., the minimum concentration of molecules that is required to detect their NMR signals, provided the identity of the molecules under investigation and their chemical shifts are known. This may be of interest for metabolomic studies.

The SSL method should also be useful for special probes where several samples can be studied in parallel, where the static homogeneity and hence the line-widths may suffer from imperfect shimming (Van Dyck et al., 2026).

Applications of SSL are not limited to small molecules. The line-widths in proton spectra of macromolecules at high fields are usually dominated by homogeneous T_2 relaxation, and $T_{1\rho}$ is usually close to T_2 rather than T_1 as in small molecules, so that line-narrowing by SSL is not likely to be very effective. However, although decoupling of homo- and heteronuclear scalar interactions (Cavanagh et al., 2007) such as $J(^1H, ^1H)$, $J(^{13}C, ^1H)$ and $J(^{15}N, ^1H)$ may be useful in macromolecules. Furthermore, the lines can be broadened by chemical exchange, in particular by exchange between major and minor conformers, and the effects of SSL should be investigated empirically.

All magnetic resonance imaging (MRI) methods achieve spatial resolution by using pulsed field gradients, including “frequency encoding” during signal observation. Spin-locking should obviously not be applied during signal observation (Mosher et al., 1990). However, in a sub-class of MRI experiments that have come to be known as magnetic resonance spectroscopy (MRS), where the signals are observed in the absence of gradients to determine the chemical shifts, spin-locking can be applied during signal observation. This can be used inter alia to determine the concentrations of various constituents or metabolites in the brains of rodents and humans, as well as phosphorylated molecules like ATP (Chung et al., 2024), phosphocreatine, etc., in various organs. At high fields, the line-widths in phosphorus-31 spectra are usually dominated by homogeneous T_2 relaxation, particularly if the chemical shift anisotropy (CSA) is the dominant line-broadening mechanism. A priori, such line-widths are not amenable to narrowing by SSL. However, we have shown that significant line-narrowing can be achieved in addition to decoupling of $J(^{31}P, ^{31}P)$ interactions. Furthermore, the line-widths of ^1H, ^{31}P or ^{13}C resonances in vivo are broadened by discontinuities in tissues, variations in susceptibility, and motions due to arterial or respiratory effects. Such static or dynamic line-broadening effects should be largely mitigated by mono- or polychromatic SSL during signal acquisition.

In Magic Angle Spinning (MAS) solid-state NMR, the line-widths in proton spectra are usually dominated by residual dipole-dipole interactions (Chávez et al.,2021) that cannot be supressed by SSL. However, the line-widths in MAS spectra of ^{13}C and other dilute nuclei are often broadened by disorder in amorphous or polycrystalline materials. Their line-widths could therefore be narrowed by SSL, in as far as the modulations due to sample spinning do not interfere with the short pulses used in SSL.

Synchronisation of these pulses with the rotor period can alleviate such problems (Caravatti et al., 1983).

In solids spinning at the magic angle, half-integer spins like ^{7}Li and ^{23}Na feature central transitions between the $m = \pm 1/2$ levels that are broadened by inhomogeneous second-order quadrupole interactions. Such line-shapes could be collapsed to their average positions by applying SSL near the frequency of their first moment. A superposition of *M* overlapping sites (as occurs in battery materials) could be separated by a two-dimensional method where *M*-chromatic SSL is applied in the detection period but not in the evolution interval.

The SSL method might be applicable to other two-level systems such as occur in optical spectroscopy, although broadening by Doppler effects might not be amenable to line-narrowing.

A wide range of methods collectively known as "pure shift spectroscopy" have been derived from two-dimensional J-spectroscopy (Aguilar et al., 2010; Castañar et al., 2015). These ingenious methods allow one to collapse multiplets due to scalar couplings. While the final result bears similarities to mono- or polychromatic SSL, in particular since decoupling is accompanied by line-narrowing (in principle limited only by the homogeneous relaxation rate $1/\pi T_2$ for pure shift spectroscopy), the mechanisms are quite distinct, and mono- or poly-chromatic spin-locking is more efficient in terms of signal-to-noise par unit time.

Data availability

The data that support the findings of this study are available from the corresponding author upon request.

Authors contributions

KS and GB designed the experiment. CW and HL carried them out. CW, HL, KS and GB prepared the manuscript.

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KeyWords: Spin-locking • Relaxation in the rotating frame • Polychromatic decoupling• Inhomogeneous line-broadening.

References

Aguilar, J.A., Faulkner, S., Nilsson, M., Morris G.A.. “Pure Shift 1H NMR: A Resolution of the Resolution Problem?” Angewandte Chemie International Edition. **49** (2010): 901-3903.

Bodenhausen, G., Freeman, R., and Morris, G. A., “A simple pulse sequence for selective excitation in Fourier transform NMR.” Journal of Magnetic Resonance **23**, (1976): 171-175.

Caravatti, P., Bodenhausen, G., and Ernst, R. R., Selective Pulse Experiments in High-Resolution Solid-State NMR.” Journal of Magnetic Resonance **55** (1983): 88-10.

Carnevale, D., Segawa, T. F., and Bodenhausen, G., “Polychromatic Decoupling of a Manifold of Homonuclear Scalar Interactions in Solution-State NMR.” Chemistry – A European Journal **18**, (2012): 11573-11576.

Castañar, L., and Parella, T., “Broadband 1H Homodecoupled NMR Experiments: Recent Developments, Methods and Applications.” Magnetic Resonance in Chemistry **53** (2015): 399– 426.

Cavanagh, J., Fairchild, W. J., Guiles, J. W., & Palmer, A. G. (2007). Protein NMR Spectroscopy: Principles and Practice (2nd ed.). Academic Press.

Chávez, M., Wiegand, T., Malär, A. A., Meier, B. H., & Ernst, M. “Residual dipolar line width in magic-angle spinning proton solid-state NMR.” Magnetic Resonance, **2(2)**, (2021): 499–509.

Chung, Y. J., Hoare, Z., Baark, F., Yu, C. S., Guo, J., Fuller, W., Southworth. R., Katschinski, D. M., Murphy. M. P., Eykyn, T. R., and Shattock, M. J. (2024). “Elevated Na is a dynamic and reversible modulator of mitochondrial metabolism in the heart.” Nature Communications, **15(1)**, (2024): 4277.

Davy, M., Dickson, C. L., Wei, R., Uhrín, D., & Butts, C. P. “Monitoring off-resonance signals with SHARPER NMR–the MR-SHARPER experiment.” Analyst, **147(8)**, (2022):1702-1708.

Delmulle, L., and Van Der Kelen, G. P., “NMR Study (^{1}H, ^{13}C and ^{29}Si) of $(CH_3)_{4-x}$ $Si(CHCH_2)_x$ Compounds where x = 0, 1, 2, 3, 4.” Journal of Molecular Structure **66** (1980): 309–14.

Jones, A. B., Lloyd-Jones, G. C., & Uhrín, D. “SHARPER reaction monitoring: generation of a narrow linewidth NMR singlet, without X-pulses, in an inhomogeneous magnetic field.” Analytical chemistry, **89(18)**, (2017): 10013-10021.

Morris, G. A., and Freeman, R., “Selective excitation in Fourier transform nuclear magnetic resonance.” Journal of Magnetic Resonance **29**, (1978): 433-462.

Mosher, T. J., & Smith, M. B. “A DANTE tagging sequence for the evaluation of translational sample motion.” Magnetic Resonance in Medicine, **15(2)**, (1990): 334–339.

Redfield, A. G.. “Nuclear magnetic resonance saturation and rotary saturation in solids.” Physical Review, **98(6)**, (1955): 1787.

Rosman, K. J. R., and P. D. P. Taylor. "Isotopic compositions of the elements 1997." Journal of Physical and Chemical Reference Data **27.6** (1998): 1275-1287.

Sonnefeld, A., Razanahoera, A., Pelupessy, P, Bodenhausen, G., and Sheberstov, K., “Long-Lived States of Methylene Protons in Achiral Molecules.” Science Advances **8**, (2022): 48.

Tošner, Z., Brandl, M. J., Blahut, J., Glaser, S.J., Reif, B. “Maximizing efficiency of dipolar recoupling in solid-state NMR using optimal control sequences.”, Sci. Adv. **7** eabj5913 (2021).

Van Dyck, S., Wiame, C., Loutfi, H., Sonnefeld, A., Pelupessy, P., Sheberstov, K., Wadhwa, S., Kampmann, R., and Bodenhausen, G., “Probe with Four Independent Samples for Parallel Detection in High-Resolution Solution-State NMR.” Review of Scientific Instruments, In press (2026).

Wiame, C., Van Dyck, S., Sheberstov, S., Razanahoera, A., and Bodenhausen, G., “Long-Lived States Involving a Manifold of Fluorine-19 Spins in Fluorinated Aliphatic Chains.” Magnetic Resonance (Ampere) **6** (2025): 273–7.