PO171 SABRE-enhanced real-time pure shift NMR spectroscopy

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NMR Methodology Group

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1. Introduction

Analysis of ^{1}H NMR spectra is often impeded by signal overlap (Figure 1, top), caused by the ubiquity of homonuclear scalar (J) coupling. Suppression of J-coupling effects to produce spectra containing a singlet at the chemical shift (δ) of each chemical environment, using pure shift NMR methods[1], significantly improves spectral resolution (Figure 1, bottom). However, broadband pure shift methods suffer from reduced sensitivity, and require extensive signal averaging to obtain useful spectra at thermal equilibrium. Here, we employ SABRE (Signal Amplification By Reversible Exchange)[2] hyperpolarization to circumvent low sensitivity in single-transient real-time Zangger-Sterk pure shift ^{1}H NMR experiments.

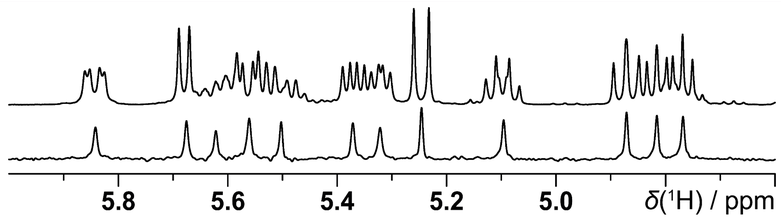

Figure 1: Excerpts from the (top) conventional ^{1}H, and (bottom) pure shift ^{1}H NMR spectrum of cyclosporin.

2. Pure shift ^{1}H NMR concepts

Most pure shift ^{1}H NMR methods combine:

- A J-refocusing element, which refocuses the effects of J-coupling for active spins (those observed) using a hard 180° pulse and an active spin refocusing (ASR) element
- Chunked data acquisition, which exploits the slow rate of J-evolution to acquire sections of FID with minimal J-modulation

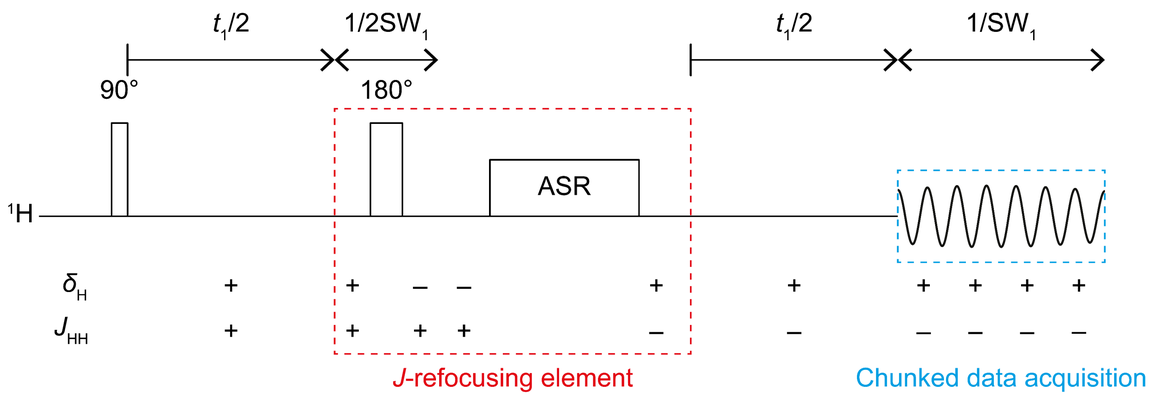

Figure 2: General scheme of a pure shift ^{1}H NMR pulse sequence, using a J-refocusing element (red) and chunked data acquisition (blue) to suppress the effects of J-evolution.

3. Pure shift ^{1}H NMR sensitivity: active spin refocusing element

ASR elements (Figure 3) divide the spins in the sample into active spins (observed), and passive spins (manipulated to suppress effects of J-coupling to active spins).

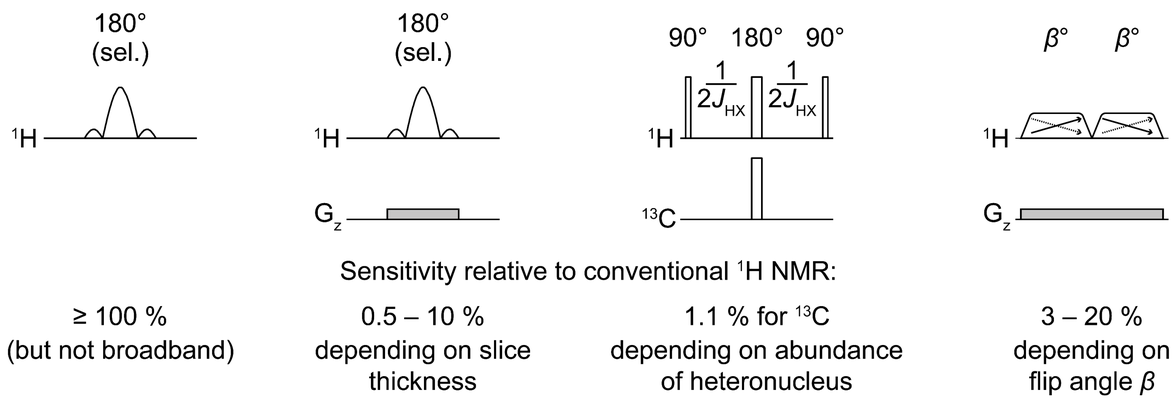

Figure 3: Common active spin refocusing elements used in pure shift ^{1}H NMR, and their corresponding sensitivities.

The approach of Zangger and Sterk[3] uses shift and slice selection to invert the magnetization for each chemical shift in a different slice of the sample. Sensitivity depends on the slice thickness, determined by the required selectivity of the soft 180° pulse and the spectral width to be decoupled.

4. Pure shift ^{1}H NMR sensitivity: chunked data acquisition

Chunked data acquisition reduces experiment time compared with point-by-point data acquisition. J-evolution is refocused at the centre of each chunk; J-modulation is negligible in a chunk of duration $1/SW_1 \ll 1/J$.

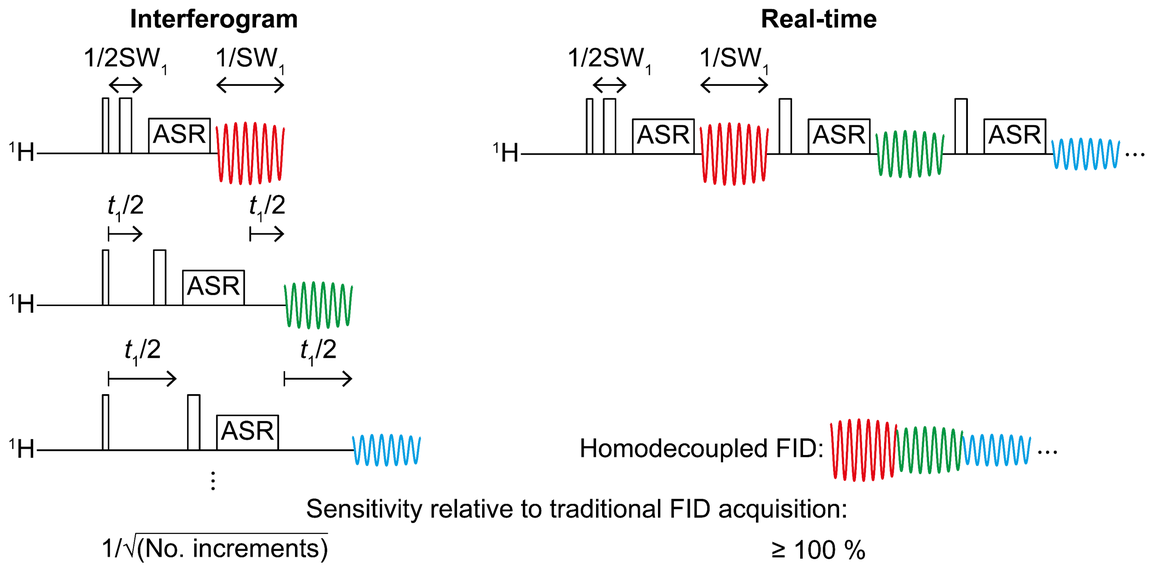

Figure 4: Chunked data acquisition approaches used in pure shift ^{1}H NMR, and their corresponding sensitivities.

Single-shot real-time[4] (as opposed to pseudo-2D interferogram[3]) acquisition, periodically interrupts data measurement to refocus J. Relaxation during the active spin refocusing element reduces practical resolution.

5. Increasing pure shift ^{1}H NMR sensitivity

Hyperpolarization circumvents low NMR sensitivity: bulk nuclear spin polarization is increased, a greater proportion of spins contribute to the detected NMR signal. SABRE[2], which transfers spin order to a substrate from singlet state parahydrogen (pH$_2$) upon transient binding at an iridium centre, is quick and requires only simple equipment. Figure 5 demonstrates compatibility of SABRE with the real-time Zangger-Sterk pure shift ^{1}H NMR experiment[5].

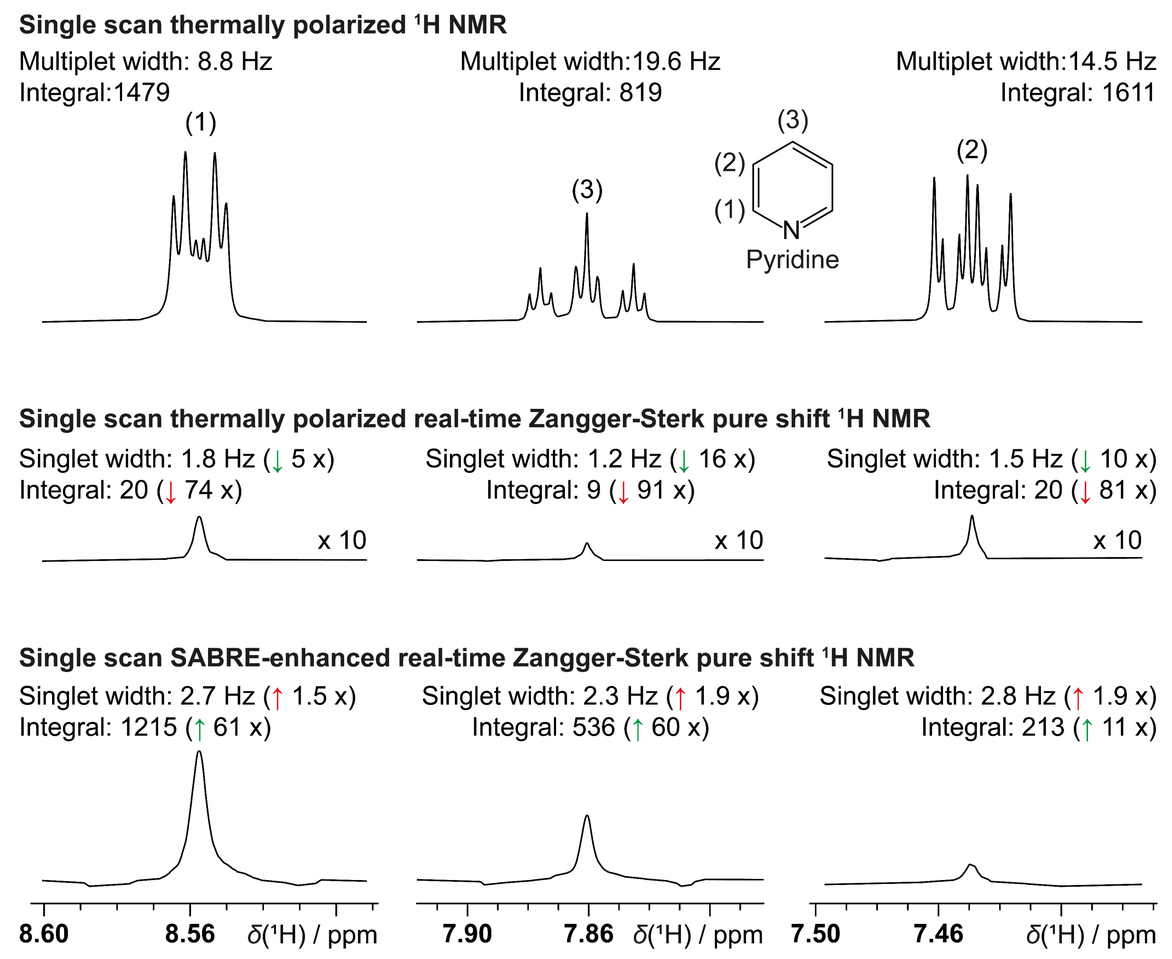

Figure 5: Expansions of the single-scan (top) thermally polarized conventional ^{1}H, (middle) thermally polarized real-time Zangger-Sterk, and (bottom) SABRE-enhanced real-time Zangger-Sterk NMR spectra of pyridine in methanol-d_4. In SABRE-enhanced experiments the sample was pressurized to 3 bar with 50 % pH$_2$, and polarization was transferred by shaking for 10 s in a 130 G field.

Combining SABRE with the real-time Zangger-Sterk pure shift ^{1}H NMR experiment provides:

- Reduced signal width (singlet linewidth over 9 times smaller than multiplet width in conventional spectrum, despite poorer field homogeneity)
- Enhanced signal integrals (up to 60-fold compared with integrals in thermally polarized real-time Zangger-Sterk spectrum)
- Useful pure shift ^{1}H NMR spectra in a single transient

6. Mixture application

Shake and drop polarization transfer discriminates in favour of molecules amenable to SABRE hyperpolarization. Signals from thermally polarized species are negligible in the pure shift ^{1}H NMR spectrum when the sample is hyperpolarized.

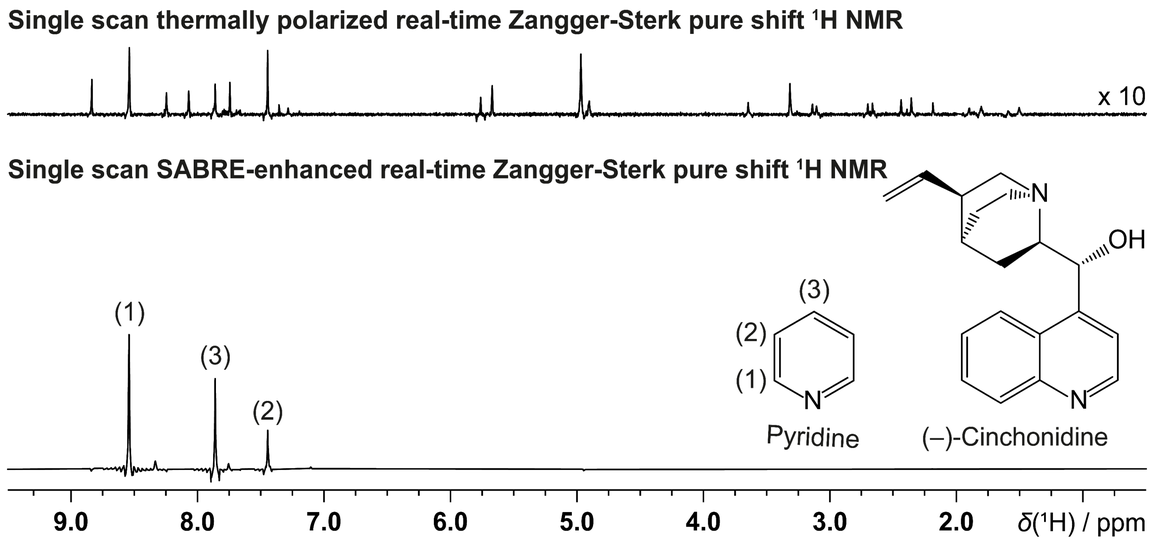

Figure 6: Single-scan (top) thermally polarized, and (bottom) SABRE-enhanced real-time Zangger-Sterk NMR spectra of a mixture of pyridine and (–)-cinchonidine in methanol-d_4.

References

1. *Prog. Nucl. Magn. Reson. Spectrosc.*, 2015, **86–87**, 1–20
2. *Science*, 2009, **323**, 1708–1711
3. *J. Magn. Reson.*, 1997, **124**, 486–489
4. *J. Magn. Reson.*, 2012, **218**, 141–146
5. *Magn. Reson. Chem.*, 2021, **59**, 1244–1252

Acknowledgments

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