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Supporting Information

Frequency-Selective Manipulations of Spins allow Effective and Robust Transfer of Spin Order from Parahydrogen to Heteronuclei in Weakly-Coupled Spin Systems

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1. **Total time of SP-SOT**

Total sequence time using SEPP-SPINEPT+ or SP-ESOTHERIC is $t_{tot} = \frac{1}{2J_{IS}} + \frac{1}{J_{SF}}$.

Total sequence time using phSPINEPT+ is $t_{tot} = 2\tau_1^0 + \frac{1}{2J_{SF}}$, where τ_1^0 is a result of $k = \sin(2\pi J_{IS}\tau_1)\sin(2\pi J_{SF}\tau_1) \rightarrow \max\limits_{conditional}$. Because of relaxation, k should not be maximized globally but with boundary conditions on τ_1^0. In the simulations below, τ_1^0 was minimized in the interval (0, 1 s) with a polarization threshold equal to 90%, 95% and 99% (**Fig. S1**) and 90% (**Fig. S2**).

In all three SP-SOTs it is reasonable to assign the spin S such that $|J_{SF}| \geq |J_{IF}|$. The performance of all sequences does not depend on the sign of J coupling constants and the third coupling J_{IF}.

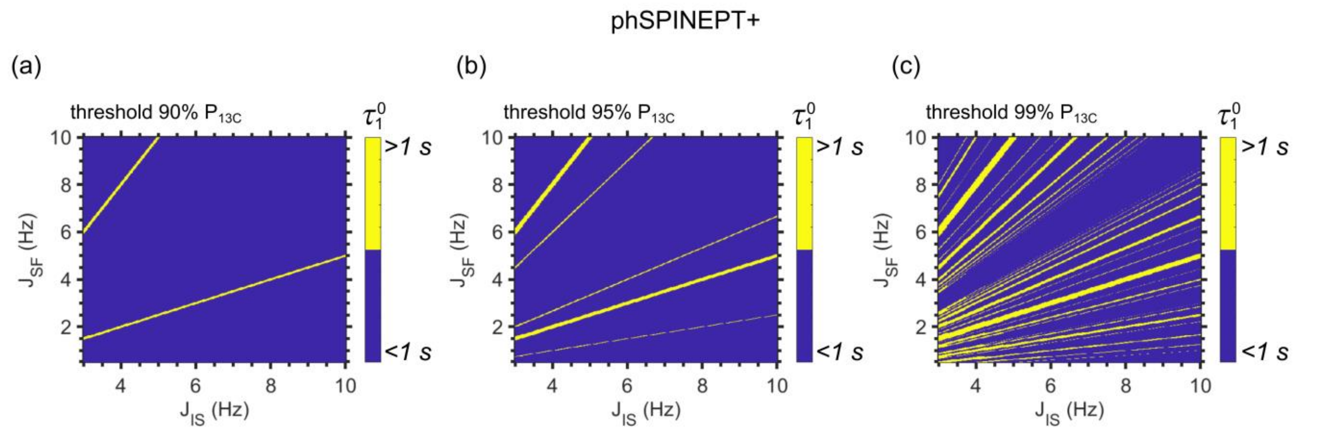

Figure S1. Effect of polarization threshold on phSPINEPT+ τ_1^0 parameter and total time t_{tot} of the sequence. Because phSPINEPT+ does not always provide 100% polarization, we considered three different thresholds of 90% (a), 95% (b), and 99% (c) of ^{13}C polarization. τ_1^0 was minimized in the interval (0, 1 s) with a given polarization threshold. If phSPINEPT+ can not reach the ^{13}C polarization threshold, then τ_1^0 is set to infinity: this situation is indicated as "$\tau_1^0 > 1\ s$" and appears as yellow color.

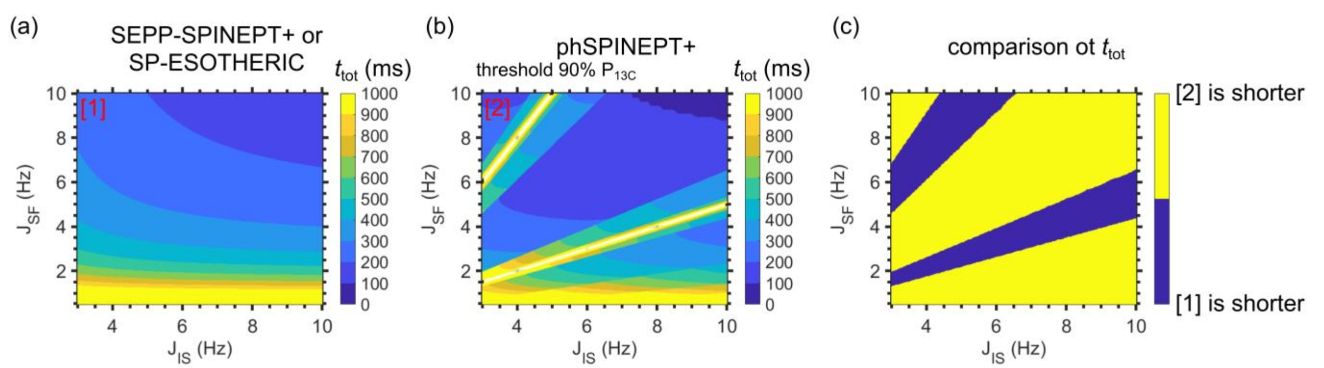

Figure S2. Comparison of the total time t_{tot} of SP-SOT sequences. SEPP-SPINEPT+ and SP-ESOTHERIC (a) and phSPINEPT+ (b). Total sequence time up to 1 s total length is plotted: $t_{tot} > 1$ s appears as 1 s in the plots (a) and (b). Because phSPINEPT+ does not always provide 100% polarization, we used a threshold of 90%. τ_1^0 was minimized in the interval (0, 1 s) with a polarization threshold equal to 90%. If phSPINEPT+ can not reach the threshold, then τ_1^0 is set to infinity (it will also appear as a white stripes in (b), see **fig. S1** for better visualization and examples of other threshold).

2. SP-SOTs applied to ethyl pyruvate and ethyl pyruvate-d8

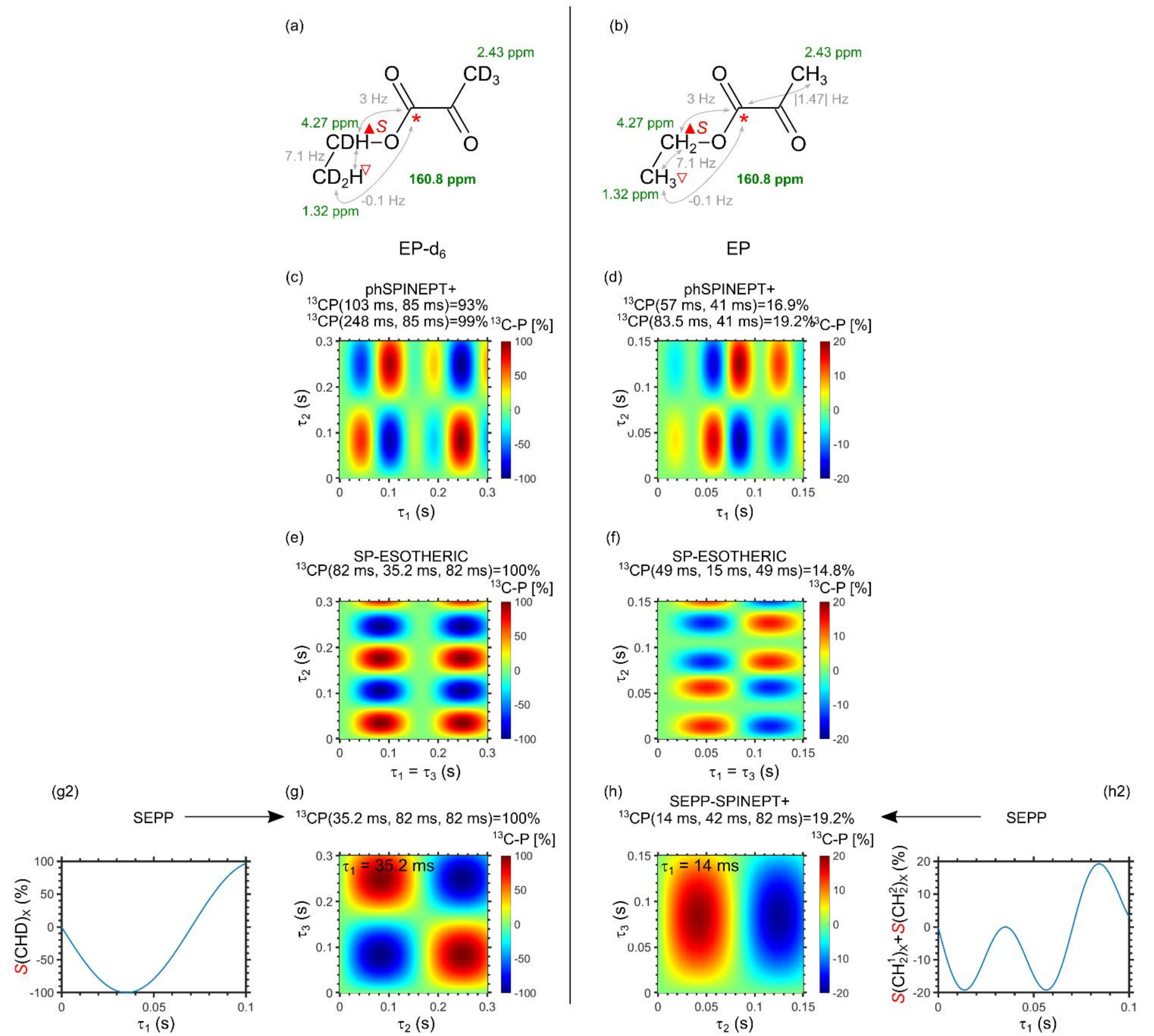

Figure S3. Structures of ethyl pyruvate-d6 (EP-d6) and fully protonated EP (a, b) and simulated ^{13}C polarization yield of three SP-SOT sequences: phSPINEPT+ (c, d), SP-ESOTHERIC (e, f), SEPP-SPINEPT+ (g, h). EP-d6 was modeled using three spins: two protons and one ^{13}C. EP was modeled using 9 spins: 8 protons and one ^{13}C. J-coupling constants and chemical shifts are given on (a, b). B_0 = 9.4 T was assumed. The total time and performance of SP-ESOTHERIC and SEPP-SPINEPT+ for EP-d6 is the same: $t_{tot} = 2(\tau_1 + \tau_2 + \tau_3) = 2(35.2 + 2 \cdot 82)$ms= 398.4 ms for 100% ^{13}C polarization. SP-SOT for fully protonated EP provide maximum 19.2 % polarization in phSPINEPT+ and SEPP-SPINEPT+. τ_1-intervals for SEPP-SPINEPT+ were adjusted additionally by maximizing net magnetization of CHD (g2) or CH_2 (h2) protons. In the case of SP-ESOTHERIC, τ_1=τ_3 was assumed that is not always optimal for EP. As a result, SP-ESOTHERIC provided lower P than the two other sequences. Total time for 19% ^{13}C polarization in phSPINEPT+ is $t_{tot} = 2(\tau_1 + \tau_2) = 2(45 + 83.5)$ms= 257 ms and in SEPP-SPINEPT+ is $t_{tot} = 2(\tau_1 + \tau_2 + \tau_3) = 2(14 + 42 + 82)$ms= 276 ms.

3. Effect of selective refocusing pulses on J- and Z-interactions

Table 1. Suppressing selected interactions and evolutions. Using a selective 180° refocusing pulse on any spin in a weakly coupled spin system allows suppressing certain interactions. For example, a 3-spin-½ system (I, S, F, e.g. $H_AH_B{}^{13}C_X$) can be manipulated such that the J_{IF} J-coupling appears to be the only one active (suppressing J_{IS}, J_{SF}, and Z_S or Z_I, Z_F, where Z is the Zeeman interaction). Of course, the other interactions take place during the □-180°-□ block, and relaxation of the intermittent spin states will occur. At the end of the block, however, these interactions are found to be "refocused," or, as we call it, suspended. The essential mechanism of this effect is that J-interactions between two nuclei will be "refocused" if the 180° pulse is applied to only one of them. If the pulse is applied to both (or none), the interaction will take place as usual.
This effect is beneficial, maximizing a specific term in the density matrix by choosing τ = 1/(4J) (because the system appears to be evolving under one J interaction only).

✔ - active

✗ - suspended

Refocusing 180° pulse on			Active spin-spin J-interactions			Active Zeeman Z-interactions		
I	S	F	J_{IS}	J_{IF}	J_{SF}	Z_I	Z_S	Z_F
✗	✗	✗	✔	✔	✔	✔	✔	✔
✗	✗	✔	✔	✗	✗	✔	✔	✗
✗	✔	✗	✗	✔	✗	✔	✗	✔
✗	✔	✔	✗	✗	✔	✔	✗	✗
✔	✗	✗	✗	✗	✔	✗	✔	✔
✔	✗	✔	✗	✔	✗	✗	✔	✗
✔	✔	✗	✔	✗	✗	✗	✗	✔
✔	✔	✔	✔	✔	✔	✗	✗	✗

The following section partially reproduces the more detailed derivation given in Ref. 1 (Appendix 10): Long-duration limit in spin-echo sandwiches (SES). SES is an RF block consisting of two equal time intervals and one π-pulse: $\tau - \pi - \tau$. Relaxation effects are not considered here.

The evolution of density matrix ρ is described using evolution propagators U:

$$\hat{\rho}(t) = \hat{U}(t)\hat{\rho}(0)/\hat{U}(t)$$

In the following, we will consider the propagator for the spin-echo-sandwich $\hat{U}_{SES}$(2□):

$$\hat{U}_{SES}(2\tau) = \hat{U}(\tau)\hat{R}_X(\pi)\hat{U}(\tau) =$$

$$= \hat{U}(\tau)\hat{R}_X(\pi)\hat{U}(\tau)\,\hat{R}_X(-\pi)\hat{R}_X(\pi) =$$

$$= \hat{U}(\tau)\hat{U}'(\tau)\hat{R}_X(\pi) =$$

$$= \exp\left(-\mathrm{i}\hat{\mathrm{H}}\tau\right)\exp\left(-\mathrm{i}\hat{\mathrm{H}}'\tau\right)\hat{R}_X(\pi)$$

If the spin system satisfies the weak coupling conditions $\left|\omega_k - \omega_j\right| \gg \pi|J|$, and the duration τ of the spin-echo sequence is sufficiently long $\left|\omega_k - \omega_j\right|\tau \gg 1$. Under the long-duration limit, secular approximations can be applied. Weakly coupled Hamiltonians commute and then the term simplifies to

$$\hat{U}_{SES}(2\tau) \cong \exp\left(-\mathrm{i}\hat{\mathrm{H}}^{weak}\tau\right)\exp\left(-\mathrm{i}\hat{\mathrm{H}}^{weak'}\tau\right)\hat{R}_X(\pi) =$$

$$\exp\left(-\mathrm{i}\left(\hat{\mathrm{H}}^{weak} + \hat{\mathrm{H}}^{weak'}\right)\tau\right)\hat{R}_X(\pi)$$

Here, the following operators were used:

$\hat{R}_X(\pi)$ –operators of rotation around X-axis on angle π,

Full liquid state Hamiltonians for nuclear spins in the magnetic field along Z-axis:

$$\hat{\mathrm{H}} = \sum_{k=1}^{N} \omega_k \hat{I}_{kZ} + 2\pi \sum_{k<m}^{N} J_{km} \hat{I}_k \cdot \hat{I}_m$$

The same Hamiltonian with secular approximations applied (“weak” coupling):

$$\hat{\mathrm{H}}^{weak} = \sum_{k=1}^{N} \omega_k \hat{I}_{kZ} + 2\pi \sum_{k<m}^{N} J_{km} \hat{I}_{kZ} \hat{I}_{mZ}$$

The spin-spin coupling part of the Hamiltonian (J, “weak”) under weak coupling regime:

$$\hat{\mathrm{H}}_J^{weak} = 2\pi \sum_{k<m}^{N} J_{km} \hat{I}_{kZ} \hat{I}_{mZ}$$

Hamiltonian after $\hat{R}_X(\pi)$ rotation:

$$\hat{\mathrm{H}}' = \hat{R}_X(\pi)\hat{\mathrm{H}}\hat{R}_X(-\pi)$$

Propagators:

$$\hat{U}(\tau) = \exp\left(-\mathrm{i}\hat{\mathrm{H}}\tau\right)$$

$$\hat{U}_J^{weak}(\tau) = \exp\left(-\mathrm{i}\hat{\mathrm{H}}_J^{weak}\tau\right)$$

$$\hat{U}'(\tau) = \hat{R}_X(\pi)\hat{U}(\tau)\hat{R}_X(-\pi) =$$

$$= \hat{R}_X(\pi)\exp\left(-\mathrm{i}\hat{\mathrm{H}}\tau\right)\hat{R}_X(-\pi) =$$

$$= \exp\left(-\mathrm{i}\hat{R}_X(\pi)\hat{\mathrm{H}}\hat{R}_X(-\pi)\tau\right) = \exp\left(-\mathrm{i}\hat{\mathrm{H}}'\tau\right)$$

In the following, we will consider three cases of SES application.

Case 1. No refocusing pulse is applied (no $\hat{R}_X(\pi)$).

When no refocusing pulse is applied during the SES block, then

$$\hat{\mathrm{H}}' = \hat{\mathrm{H}}$$

$$\hat{U}_{SES}^{case\ 1}(2\tau) = \exp\left(-\mathrm{i}\hat{\mathrm{H}}\tau\right)\exp\left(-\mathrm{i}\hat{\mathrm{H}}\tau\right) = \exp\left(-\mathrm{i}\hat{\mathrm{H}}2\tau\right)$$

So, the evolution of the system is going as expected under the action of the full Hamiltonian: the system evolves freely (without any RF pulses) during the time interval 2τ.

Case 2. Refocusing pulse is applied on all spins.

Here hard pulse refocuses all nuclear spins:

$$\hat{\mathrm{H}}^{weak\prime} = \hat{R}_X(\pi)\hat{\mathrm{H}}^{weak}\hat{R}_X(-\pi) =$$

$$= \sum_{k=1}^{N} \omega_k \hat{R}_X(\pi)\hat{I}_{kZ}\,\hat{R}_X(-\pi) + 2\pi \sum_{k<m}^{N} J_{km}\hat{R}_X(\pi)\hat{I}_{kZ}\cdot\hat{I}_{mZ}\,\hat{R}_X(-\pi) =$$

$$= -\sum_{k=1}^{N} \omega_k \hat{I}_{kZ} + 2\pi \sum_{k<m}^{N} J_{km}\hat{I}_{kZ}\cdot\hat{I}_{mZ}$$

$$\hat{\mathrm{H}}^{weak} + \hat{\mathrm{H}}^{weak\prime} = 2\hat{\mathrm{H}}_J^{weak}$$

hence

$$\hat{U}_{SES}^{case\ 2}(2\tau) \cong \exp\left(-\mathrm{i}2\hat{\mathrm{H}}_J^{weak}\tau\right)\hat{R}_X(\pi)$$

This propagator is equivalent to the sequence when all spins are first flipped with hard π-pulse and then evolve freely under the action of J-couplings only during 2τ.

Case 3. All but one spin L are refocused.

Now we apply such π-pulse which refocuses all spins $n = 1 \dots N$ and $n \neq L$. N – is a total number of spins.

$$\hat{\mathrm{H}}^{weak\prime} = \hat{R}_X^{not\ L}(\pi)\hat{\mathrm{H}}^{weak}\hat{R}_X^{not\ L}(-\pi) =$$

$$= -\sum_{k=1}^{N,not\ L} \omega_k \hat{I}_{kZ} + 2\pi \sum_{k<m}^{N,not\ L} J_{km}\hat{I}_{kZ}\cdot\hat{I}_{mZ} + \omega_L \hat{I}_{LZ} - 2\pi\hat{I}_{LZ}\sum_{k\neq L}^{N} J_{Lm}\cdot\hat{I}_{mZ} =$$

$$\hat{\mathrm{H}}^{weak} + \hat{\mathrm{H}}^{weak\prime} = 2\left(\omega_L \hat{I}_{LZ} + 2\pi \sum_{k<m}^{N,not\ L} J_{km}\hat{I}_{kZ}\cdot\hat{I}_{mZ}\right)$$

$$\hat{U}_{SES}^{case\ 3}(2\tau) \cong \exp\left(-\mathrm{i}\left(\hat{\mathrm{H}}^{weak} + \hat{\mathrm{H}}^{weak\prime}\right)\tau\right)\hat{R}_X^{not\ L}(\pi)$$

It means that the Zeeman interaction of this spin L is not refocused and that there is no effective J-coupling interaction with this spin over the evolution time interval 2τ.

This propagator reads as follows:

- All spins but L are flipped with π-pulse;
- Free evolution of the system under J-coupling Hamiltonian 2τ where all couplings with spin L are zero ($J_{Lk} = 0$ for k=1..N).
- Spin L evolves under Zeeman interaction for another 2τ interval.

Author Contributions

ANP, ABS: conceptualization, writing – original draft. All authors contributed to the investigation, funding acquisition discussions, and interpreting the results and have given approval to the final version of the manuscript.

REFERENCES

(1) Levitt, M. H. *Spin Dynamics. Basics of Nuclear Magnetic Resonance*, 2nd ed.; Wiley, 2008.