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Coherent transfer of nuclear spin polarization in field-cycling NMR experiments

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Coherent polarization transfer effects in a coupled spin network have been studied over a wide field range. The transfer mechanism is based on exciting zero-quantum coherences between the nuclear spin states by means of non-adiabatic field jump from high to low magnetic field. Subsequent evolution of these coherences enables conversion of spin order in the system, which is monitored after field jump back to high field. Such processes are most efficient when the spin system passes through an avoided level crossing during the field variation. The polarization transfer effects have been demonstrated for N-acetyl histidine, which has five scalar coupled protons; the initial spin order has been prepared by applying RF-pulses at high magnetic field. The observed oscillatory transfer kinetics is taken as a clear indication of a coherent mechanism; level crossing effects have also been demonstrated. The experimental data are in very good agreement with the theoretical model of coherent polarization transfer. The method suggested is also valid for other types of initial polarization in the spin system, most notably, for spin hyperpolarization. © 2013 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4848699>]

I. INTRODUCTION

Nuclear Magnetic Resonance (NMR) is a widely used method with numerous applications ranging from physics and chemistry to biology and medicine. Despite the power and popularity of NMR, all NMR methods suffer from their low inherent sensitivity. The reason for this is that the Zeeman interaction of nuclear spins with the external magnetic field, B , is very weak as compared to the thermal energy, kT , resulting in the poor Boltzmann polarization of spins at thermal equilibrium, $P_{eq} \approx \hbar\gamma_N B/kT$ (here, γ_N is the nuclear gyromagnetic ratio). Since the NMR signals are proportional to spin polarization, which is typically of the order of 10^{-5} – 10^{-4} , using thermally polarized spins results in reduction of the signal intensity by a few orders of magnitude. To tackle this problem and increase P_{eq} going to low temperatures is often not a choice; also, the technical realization of stable, homogeneous magnetic fields has reached its upper limits, in spite of enormous achievements during the last decades. An alternative way to overcome the sensitivity problem is using non-thermal spin polarization, also called hyperpolarization. Among the techniques based on this approach are Spin Exchange Optical Pumping (SEOP),¹ Dynamic Nuclear Polarization (DNP),^{2–4} Optical Nuclear Polarization (ONP),^{5,6} Chemically Induced Dynamic Nuclear Polarization (CIDNP),⁷ and Para-Hydrogen Induced Polarization (PHIP).^{8–11} All these methods employ strongly

non-thermally polarized spins, thus allowing one to boost the NMR signals by a few orders of magnitude.

Although the hyperpolarization techniques made numerous new NMR applications possible,^{4,12–28} there are still many problems to be solved in this field. In particular, it is of importance to further develop strategies of optimizing the efficiency of the hyperpolarization process; a second task is the transfer of spin order from the primarily polarized spins, e.g., in PHIP experiments^{8–11,28,29} the protons originating from para-dihydrogen, to the target nuclei of choice. It is common for all the techniques mentioned above that the spin polarization strongly depends on the strength of the external magnetic field; the same holds for the polarization transfer efficiency. In particular, it is often the case that hyperpolarization is maximal at low magnetic fields, whereas modern high-resolution NMR spectrometers are operating at high fields. For this reason, various field-cycling NMR methods^{30–35} have been developed to tackle this problem and also to study field-dependent relaxation phenomena^{36–38} in particular, because of their importance for the life-time of hyperpolarization. In this context, it is relevant for optimizing the performance of hyperpolarization techniques to understand on a quantitative level how the spin-spin interactions affect the evolution of multi-spin systems during the field variation.

In this work, we report a study of spin polarization transfer in field-cycling NMR experiments with a particular emphasis on coherent transfer phenomena. Coherent mechanisms of polarization transfer are advantageous, since (i) the transfer efficiency is usually much higher than in the case of incoherent processes such as cross-relaxation and (ii) in

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some cases coherent polarization transfer is highly selective and proceeds only between particular types of spin order thus allowing for efficient manipulation. A way^{39–44} to form spin coherences in field-cycling NMR experiments is polarizing the spin system at high field and subsequently transferring it to low field, at which the spins are coupled strongly. When the field switching is non-adiabatic the initial population difference is transferred into spin coherences.^{39–42} Their evolution results in a redistribution of polarization, which is particularly fast and efficient. Polarization transfer is most pronounced^{40,41,44–47} when the system is driven through an anti-crossing of the nuclear spin energy levels (also termed avoided level crossing). After the evolution of spin coherences has taken place, the system is brought to the high NMR detection field where polarized signals belonging to different nuclei are measured.

In the present contribution, we will demonstrate effects of coherent polarization transfer between homo-nuclei in field-cycling experiments taking systems of scalar coupled spins as an example. We will also elucidate the role of anti-crossings of the nuclear spin sublevels in the polarization transfer process. Experimental results will be accompanied by theoretical calculations to confirm the validity of our approach and to understand the results on a quantitative level. Non-equilibrium polarization will be created by applying RF-pulses to an initially thermally polarized spin system. Although such a method does not allow one to create hyperpolarization (because the starting polarization is the Boltzmann polarization), it is suitable for testing concepts of coherent polarization transfer. This is because one can start from a well-defined spin state of choice and thereby select specific coherent polarization transfer pathways. Experimental results will be presented for the amino acid N-acetyl-L-histidine (N-Ac-His), which has five scalar coupled protons. On the one hand, the protons of N-Ac-His represent a multi-spin system with a non-trivial coupling network; on the other hand, the evolution of polarization in this system can be rigorously analyzed theoretically and polarization transfer pathways can be precisely determined. The proposed strategy, however, is more general and is valid for any other polarization method and any kind of coupling as well. Thus, our study is of importance for all studies of spin systems off thermal equilibrium, in particular, for relaxation and hyperpolarization experiments which utilize fast field-cycling.

II. METHODS

A. Compounds and sample preparation

N-Ac-His was received from Bachem. The solvent D₂O, DCl, and NaOD were received from Sigma-Aldrich. DCl and NaOD were used to adjust pH. The NMR spectrum of N-Ac-His at pH 5.2 is shown in Figure 1 together with a simulation. The simulation parameters of N-Ac-His (proton chemical shifts, δ_i , in the delta-scale and their scalar spin-spin interactions, J_{ij}), which are also needed for modeling the polarization transfer effects, are given in Table I. The structure of N-Ac-His with assignment of protons is shown in Chart 1.

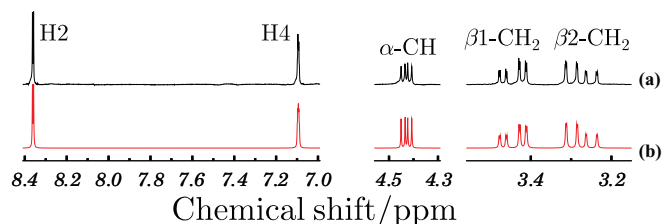


FIG. 1. NMR spectrum of N-Ac-His at pH 5.2 taken $B_0 = 7$ T (a); simulation (b) of the spectrum is also shown.

B. Field-cycling NMR

The field-cycling setup with mechanical shuttling of the NMR probe-head is described in detail in an earlier publication.³¹ This setup enables a unique combination of fast field-cycling (less than 0.3 s for shuttling the probe-head between the observation field, $B_0 = 7$ T, and the lowest magnetic field, ≈ 50 μ T, or vice versa) with high-resolution NMR detection (NMR line-width is about 0.3 Hz). The NMR spectra are recorded under permanent slow sample rotation (≈ 50 Hz). Evolution of the polarized spins can be studied at a variable B_{int} field in the range between 50 μ T and 7 T. The motion of the probe-head is digitally controlled and the field profile along the path is known; as a consequence, also the time profile, $B(t)$, of field variation is known precisely. The setup also allows one to hyperpolarize the spins at any magnetic field by means of photo-CIDNP by performing light irradiation³¹ or by PHIP by bubbling hydrogen gas enriched in its *para*-spin isomer through the sample.⁴⁰

C. Experimental protocol

To study the polarization transfer phenomena, we utilized the experimental protocol, which is depicted in Figure 2 and consists of 5 consecutive stages. During stage 1 (preparation), Boltzmann polarization is prepared at $B = B_0$ and converted into a non-thermal spin order by applying RF-pulses. Since preparation is done at the detection field the starting polarization pattern can be precisely determined. After preparation the field is rapidly switched to the value B_{int} (stage 2, reducing the field) during the time period τ_1 . Then after a variable period, τ , of free evolution (stage 3, free evolution) the field is switched back (stage 4, increasing the field) to the detection field B_0 during the time period τ_2 . Finally, the Free Induction Decay (FID) is measured, the Fourier-Transform NMR

TABLE I. J-couplings, chemical shifts, and high-field T_1 -relaxation times for N-Ac-His at pH 5.2.

J (Hz)	β_1	β_2	α	$H2$	$H4$
β_1		-14.8	4.9	...	-0.9
β_2	-14.8		8.2	...	-0.7
α	4.9	8.2	
$H2$		1.6
$H4$	-0.9	-0.7	...	1.6	
δ (ppm)	3.241	3.078	4.429	8.361	7.094
T_1 (s)	0.75	0.75	4.4	24.4	11.1

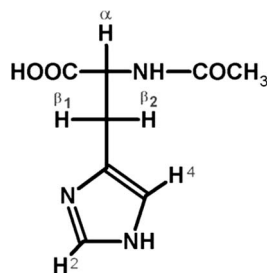


CHART 1. Structure of N-Acetyl-Histidine (N-Ac-His) with numbering and nomenclature of protons.

spectrum is obtained, and the NMR line intensities are determined (stage 5, detection).

The physical principles behind the experiments are described in Subsection II D.

D. Physical principles of coherent hyperpolarization transfer at low fields

In liquid systems where dipolar interaction is averaged out, the coupling strength of two spins is characterized by the angle

$$\theta = \frac{1}{2} \text{Arctan} \frac{J}{\Delta\nu}, \quad (1)$$

where J is their scalar coupling and $\Delta\nu = -\Delta\delta\gamma B_0/2\pi$ is the difference in their Zeeman interactions with the external field (both given in units of h); here, $\Delta\delta$ is the chemical shift difference for the two spins. The regime $|\theta| \ll \frac{\pi}{4}$ is that of weak, $|\theta| \simeq \frac{\pi}{4}$ is that of strong coupling.

An important property of strongly coupled spins is that their eigen-states can be mixed states (for instance, singlet and triplet T_0 states in the case of two spins $1/2$ at $B = 0$), i.e., cannot be presented as products of states of the individual spins. As a consequence, at low fields not individual spins but their collective states are polarized. Thus, apparently, polarization acquired at high field is efficiently transferred among strongly coupled spins.^{39,48–50} The transfer proceeds in a coherent way with a characteristic transfer time given by the inverse coupling, $\frac{1}{2J}$.^{39,50} Our recent field-cycling relaxometry experi-

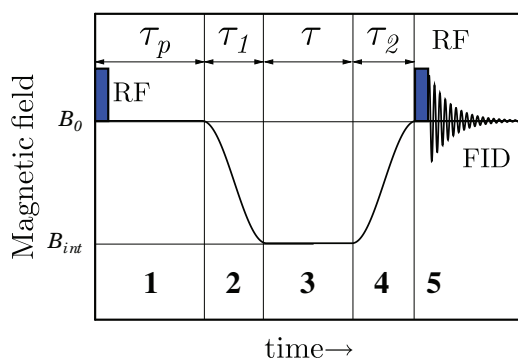


FIG. 2. Experimental protocol with 5 stages: preparation of polarization by RF-pulses at the NMR spectrometer field $B = B_0$ (stage 1, duration τ_p); going down to the intermediate field B_{int} (stage 2, duration τ_1); free evolution at the field B_{int} (stage 3, duration τ); going back to the NMR detection field B_0 (stage 4, duration τ_2); Fourier Transform NMR detection at $B = B_0$ (stage 5).

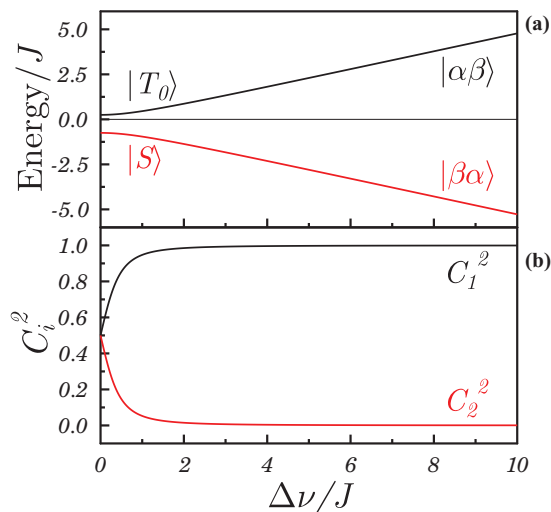


FIG. 3. Schematic dependence on $\Delta\nu$ for energy levels with $I_z = 0$ (a) and mixing coefficients (b) for a two-spin $1/2$ system. Here, the difference in frequencies, $\Delta\nu = |\Delta\delta|\gamma B/2\pi$, is given in units of the coupling strength, J . In (a) energy is also given in units of the coupling strength, J . Here, we have taken $J > 0$ (so that at zero-field the T_0 -state is higher in energy than the S -state) and $\delta_1 < \delta_2$ (so that at high field the $\alpha\beta$ -state is higher in energy as compared to the $\beta\alpha$ -state).

ments have also shown^{41,42} that strongly coupled spins tend to relax with a common longitudinal relaxation time even when their high-field T_1 -relaxation times are considerably different.

Now let us discuss how spin polarization can be transferred in experiments performed according to the protocol described above (Figure 2). Figure 3(a) shows the energies of the two states of a coupled two-spin $1/2$ system, which are characterized by zero projection, $I_z = 0$, of the total spin. At high fields (weak coupling of spins), these states are the Zeeman states, $|\alpha\beta\rangle$ and $|\beta\alpha\rangle$, with energies changing proportional to the field strength. As usual, the spin $1/2$ states are denoted as $|\alpha\rangle$ (spin-up state) and $|\beta\rangle$ (spin-down state). In the absence of coupling, they cross at zero field. However, in the presence of coupling the situation changes when the field is low: there is a “repulsion” of states, consequently, the crossing at zero field turns into an avoided crossing, or a Level Anti-Crossing (LAC).⁵¹ The minimal splitting between the anti-crossing levels is equal to the coupling strength $|J|$.

How the system goes from weak to strong coupling by changing the field can be visualized by showing the field dependence of the mixing coefficients of the Zeeman states (Figure 3(b)). The solution of the eigen-problem for an arbitrary scalar coupled two-spin system is simple and well-known; its eigen-states with $I_z = 0$ are as follows:

$$|1\rangle = C_1|\alpha\beta\rangle + C_2|\beta\alpha\rangle, |2\rangle = -C_2|\alpha\beta\rangle + C_1|\beta\alpha\rangle. \quad (2)$$

The coefficients C_1 and C_2 can be expressed via the mixing angle, θ , in the following way: $C_1 = \cos\theta$ and $C_2 = \sin\theta$. In the vicinity of the LAC (i.e., at $|\Delta\nu| \leq |J|$), there is an abrupt change in the coefficients (Figure 3(b)), which are equal to 1 and 0 at high field where the coupling is weak. The energies of the states are: $E_{1,2} = -\frac{J}{4} \pm \frac{1}{2}\sqrt{J^2 + (\Delta\nu)^2}$ and the splitting is $\Delta E = (E_1 - E_2) = \sqrt{J^2 + (\Delta\nu)^2}$ reaching its minimal value of $|J|$ at the LAC point at zero magnetic

field. In fact, for any coupled spin system of protons, there is a LAC at zero field. At the same time, at zero field the spin states are evenly mixed as $|\theta| = \frac{\pi}{4}$. Thus, the two concepts, i.e., strong coupling and LAC, are closely interrelated.

When low-field spin phenomena are discussed different definitions of “low magnetic field” are used depending on what interactions are compared. When the coupled spins are homonuclear, in our case protons, the difference of the Zeeman interactions, $\Delta\nu$, is only a few ppm of the Larmor frequency ν ; for nuclei with a larger span of chemical shifts (i.e., ^{13}C , ^{14}N , ^{19}F , or ^{31}P), it can reach a few hundred ppm still being a few orders of magnitude smaller than the Zeeman interactions of these nuclei. For this reason, it is relatively easy to achieve strong coupling in the homonuclear case without the necessity of going to really low fields. In particular, for nearly equivalent spins the condition for strong coupling can be fulfilled at high magnetic fields of a few Tesla. However, when hetero-nuclei are coupled, strong coupling is achieved only at very low fields, namely, considerably lower than the Earth field. The region of strong coupling is thus very narrow and the spins rapidly go to the weak coupling regime as the field increases. The case of zero-field, $J \gg \nu$, gives a very special situation. Modern developments make zero-field NMR feasible and useful as an analytical tool.^{15,16,52,53} This is because in contrast to the general low-field case (strong coupling) where the NMR spectrum of the spin system can be quite complicated at zero-field it becomes relatively simple again and also free from inhomogeneous broadening. A detailed classification of different coupling regimes depending on the field strength is given in Ref. 54 together with the corresponding NMR spectra of coupled spin systems. Finally, we emphasize that in this work we only go from weak to strong coupling for homonuclei (namely, for protons). Fulfilling the strong coupling condition for heteronuclei requires additional experimental efforts in shielding residual magnetic fields, static and fluctuating ones, including both their transversal and longitudinal components. In fact, when the z-component of the field is equal to zero this does not guarantee that very low fields are achieved.^{55,56} The presence of transverse field components gives additional effects, namely, LACs between the triplet states. Indeed, when $B_z = 0$ the triplet levels tend to cross but the transverse field splits them with the consequence that the crossing is avoided. The splitting can be rather large: for instance, for the transverse field being of the order of the Earth field it is about 2 kHz for protons. For this reason, the passage through the corresponding LAC is likely to be adiabatic, i.e., the spins tend to orient along the field direction during the passage through the point $B_z = 0$. Consequently, when the system is not shielded from even very small transverse fields reaching the zero magnetic field or even passing through the zero-field is not feasible. As a consequence, in our experiments the case of negative fields is not discussed; by “zero-field” we always imply that it relates to protons.

The strong mixing of states at LAC points makes efficient polarization transfer among spins possible. In experiments that include two field variations according to the protocol shown in Figure 2 polarization transfer can be performed in the following way: Let us assume that at the end of the preparation stage the spins have net polarizations, P_1

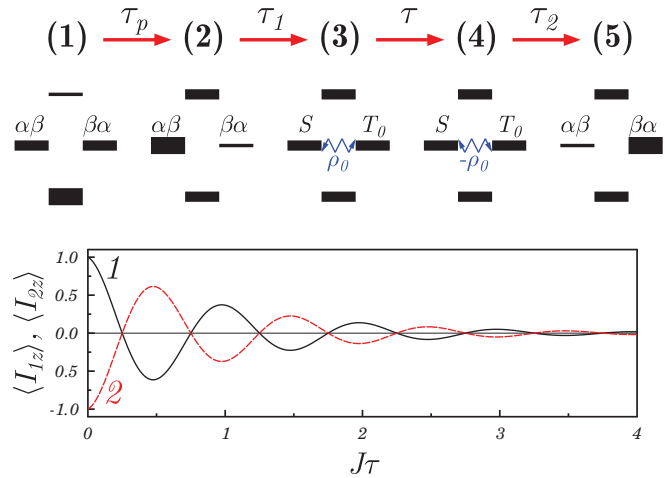


FIG. 4. Scheme of polarization transfer in field-cycling NMR experiments: spin evolution and state population patterns (PP) (top); transfer kinetics (bottom). First, spins have the same z-magnetization (PP 1); then a selective RF-pulse inverts magnetization of the second spin (PP 2). Fast jump to zero field converts the population difference between the $\alpha\beta$ - and $\beta\alpha$ -states into coherence, $\rho_{ST_0} = \rho_0$, between the low-field S- and T_0 -states (PP 3). Subsequent evolution during the time $\tau = 1/2J$ results in sign inversion of the coherence (PP 4); finally, after second switching to high field spin magnetizations are inverted (PP 5). Time evolution of magnetization as function of $J\tau$ contains quantum oscillations, which are damped due to relaxation.

and P_2 , of the same amplitude but of the opposite sign: $P_2 = -P_1$. Experimentally this can be done, for instance, by applying a selective π -pulse to one of the spins, which inverts its magnetization. In this situation, the populations of the high-field spin eigen-states (shown in Figure 4) are such that the two states characterized by $I_z = 0$ (namely, the $|\alpha\beta\rangle$ and $|\beta\alpha\rangle$ states) have different populations: $n_{\alpha\beta} \neq n_{\beta\alpha}$, while $n_{\alpha\alpha} = n_{\beta\beta}$. Let us also presume that after the preparation the field is instantaneously switched to a value of B_{int} (low field), which corresponds to strong coupling of the spins. Under such an assumption the initial (high-field) density matrix of the system, $\hat{\rho}_{hf}$, is projected onto a new eigen-basis at low fields, which is the singlet-triplet basis. As a consequence, the low-field density matrix, $\hat{\rho}_{lf}$, written in the eigen-basis of the system at low B_{int} has the following elements:

$$(\rho_{lf})_{T_+T_+} = (\rho_{lf})_{T_-T_-} = n_{\alpha\alpha} = n_{\beta\beta}, \quad (3a)$$

$$(\rho_{lf})_{T_0T_0} = n_{\alpha\beta} |\langle T_0|\alpha\beta\rangle|^2 + n_{\beta\alpha} |\langle T_0|\beta\alpha\rangle|^2 = \frac{n_{\alpha\beta} + n_{\beta\alpha}}{2}, \quad (3b)$$

$$(\rho_{lf})_{SS} = n_{\alpha\beta} |\langle S|\alpha\beta\rangle|^2 + n_{\beta\alpha} |\langle S|\beta\alpha\rangle|^2 = \frac{n_{\alpha\beta} + n_{\beta\alpha}}{2}, \quad (3c)$$

$$\begin{aligned} (\rho_{lf})_{T_0S} &= (\rho_{lf})_{ST_0} = n_{\alpha\beta} \langle T_0|\alpha\beta\rangle \langle \alpha\beta|S\rangle + n_{\beta\alpha} \langle T_0|\beta\alpha\rangle \langle \beta\alpha|S\rangle \\ &= \frac{n_{\alpha\beta} - n_{\beta\alpha}}{2}. \end{aligned} \quad (3d)$$

In our case, the S and T_0 states have the same population, while the initial population difference, $(n_{\alpha\beta} - n_{\beta\alpha})$, is converted into a coherence between the new eigen-states with $I_z = 0$ (zero-quantum coherence, or ZQC). Once created the ZQC starts oscillating at a frequency given by the splitting

between the S and T_0 states, which is equal to J :

$$(\rho_{lf})_{ST_0}(\tau) = (\rho_{lf})_{ST_0}(0)e^{2\pi i J \tau}. \quad (4)$$

When the second sudden field switching, $B_{\text{int}} \rightarrow B_0$, is applied the coherence is converted back into the population difference at high detection field. This quantity can be measured directly as the difference in NMR signal amplitude, $(\langle I_{1z} \rangle - \langle I_{2z} \rangle)$, of the individual spins. When the delay, τ , at $B = B_{\text{int}}$ is varied there are oscillations in the evolution of $\langle I_{1z} \rangle$ and $\langle I_{2z} \rangle$ (Figure 4): polarization is transferred back and forth between the spins with the frequency J . At $\tau = (2n + 1)/2J$ ($n = 0, 1, 2, \dots$), the spins have fully exchanged their polarizations. This process is coherent, therefore, fast and controllable. The experiments⁴¹ show that the oscillations are damped due to spin relaxation. When the field jump is performed from B_0 to $B_{\text{int}} \neq 0$, i.e., $|\theta| \neq \frac{\pi}{4}$, the amplitude of the quantum oscillations decreases, while their frequency increases. Indeed, the amplitude of the ZQC (the off-diagonal element of $\hat{\rho}_{lf}$) is equal to $|\sin 2\theta(n_{\alpha\beta} - n_{\beta\alpha})|/2$,⁵⁷ while the frequency (the energy difference for the corresponding eigenstates) is $\Delta E = \sqrt{J^2 + (\Delta\nu)^2} \geq |J|$. Thus, at the LAC point the mixing of states is maximal and the splitting is minimal.

Hence, coherent exchange of polarization among strongly coupled spins is possible, as has been demonstrated experimentally.^{40–42, 47, 50} The necessary conditions for the polarization transfer are as follows: (i) initial polarizations of spins, P_i , differ at high field; (ii) spins are strongly coupled at $B = B_{\text{int}}$; (iii) the two field switches are non-adiabatic. Condition (i) is provided by an appropriate preparation method. As far as (ii) is concerned, it is optimal that B_{int} coincides with the LAC position; at least during the “voyage” to the low field the system has to pass through a field region where the spins are coupled strongly. Condition (iii) is important first to create the ZQC and second to convert it back into the population difference, which is a NMR observable. In contrast, when the field is adiabatically varied the eigenstates from Eq. (2) keep their populations at all times. Thus, no coherences can be formed; moreover, the state populations are the same before and after the field-cycling (when relaxation effects are neglected). For this reason, methods based on adiabatic field-cycling are not suited for observing ZQCs and studying coherent phenomena; however, they can be used to investigate low-field relaxation phenomena, notably, for probing long-lived spin modes.⁵⁸ In general, the adiabaticity condition is described⁵⁹ by the set of parameters $\xi_{\mu\nu}(t)$, which describe mixing between states $|\mu\rangle$ and $|\nu\rangle$. In turn,

$$\xi_{\mu\nu}(t) = |\alpha_{\mu\nu}(t)/2\pi \Delta E_{\mu\nu}| \quad (5)$$

is expressed via two parameters, $\alpha_{\mu\nu}(t) = \langle \mu | (d|\nu\rangle)/dt$ (showing how the eigenstates change with time) and $\Delta E_{\mu\nu}(t)$ (which is the time-dependent splitting between the energy levels, here given in Hz). For example, for the states defined in Eq. (2), $\xi_{12}(t) = (2\pi \Delta E)^{-1} \left| \frac{d\theta}{dt} \right|$.

Importantly, in our experiments we can create and utilize only ZQCs, but no coherences of higher order: when the direction of the field does not change only states with the same I_z can be mixed by the Hamiltonian of the spin system. Evolution of a multi-spin system is generally quite complex as compared to the two-spin system described above; however,

there are situations where the simpler description valid for the two-spin system is also applicable to systems with more coupled spins. This is the case where there are pairs of levels that have isolated LACs, meaning that the anti-crossing levels do not have other LACs close by. In this situation by going through the specific LAC, it is possible to excite selectively the ZQC between the corresponding pair of levels. By adjusting the field variation speed and the residence time at low field, it is possible to exchange the populations of the anti-crossing levels in exactly the same way as for the two-spin system. We will thus exploit this strategy also for multi-spin systems. As will be shown below, the analysis of LACs is also helpful for elucidating the polarization transfer pathways because (i) typically ZQCs are excited only for pairs of levels having a LAC and (ii) each LAC corresponds to a particular pair of high-field states.

We want to note that the idealized situation of sudden field variation cannot be fulfilled experimentally. Accordingly, the theoretical method necessary for simulating the data is more complex. We will describe it below in more detail. The method is valid for an arbitrary number of scalar coupled spins and an arbitrary time profile of the field switching; it also takes into account spin relaxation, which is necessary to reproduce the damping of the oscillations in the transfer kinetics.

E. Calculation method

To simulate the experimental results, we used essentially the same method as described before.^{40–42, 44} We solved the Liouville-von Neumann equation for the spin density matrix, $\hat{\rho}(t)$, at times $\tau_p < t < \tau_p + \tau_1 + \tau + \tau_2$

$$\frac{\partial \hat{\rho}}{\partial t} = -i[\hat{H}(t), \hat{\rho}] + \hat{R}(\hat{\rho} - \hat{\rho}_{eq}). \quad (6)$$

Here, $\hat{H}(t)$ is the time-dependent Hamiltonian written in units of \hbar , which changes during stages 2 and 4 and is time-independent during stage 3 (see Figure 2). The Hamiltonian of K spin 1/2 nuclei represents contributions from the Zeeman interaction of the spins with the $B(t)$ field that varies with time and from their J -couplings, which are time-independent

$$\hat{H}(t) = 2\pi \left(-\sum_{i=1}^K v_i(t) \hat{I}_{iz} + \sum_{i<j}^K J_{ij} (\hat{\mathbf{I}}_i \cdot \hat{\mathbf{I}}_j) \right). \quad (7)$$

Here, $v_i(t) = \gamma B(t)(1 + \delta_i)/2\pi$ is the Zeeman interaction of the i th spin with the variable field, $B(t)$, determined by its chemical shift, δ_i ; γ is the proton gyromagnetic ratio; J_{ij} is the coupling constant between the i th and the j th spin. In the Hamiltonian, we consider only coupled protons and neglect all couplings to hetero-nuclei. This situation applies to N-Ac-His. In cases when it is necessary to consider spin 1/2 hetero-nuclei, this can be done with our formalism as well. In general, hetero-nuclei can have an effect on polarization transfer among protons even when the proton-hetero-nuclear coupling is weak.^{8, 40, 41, 60, 61} Particularly high effects are expected when the proton-hetero-nucleus coupling is strong;^{15, 16, 53, 62, 63} however, in this case the regime of

strong coupling is reached only at very low fields, which are much smaller than the Earth magnetic field.

The super-operator \hat{R} in Eq. (6) describes the relaxation of spins (both transverse and longitudinal), here in the model of fluctuating local fields.^{41,42} This model is rather simple⁶⁴ and requires as input parameters only the high-field T_1 -relaxation times of the individual spins, T_{1i} ; for small molecules in liquids, it is typical that $T_{2i} = T_{1i}$. These relaxation times can be easily measured at $B = B_0$. The form of the relaxation super-operator is given in the Appendix.

The matrix $\hat{\rho}_{eq}$ in Eq. (6) is the equilibrium density matrix at the corresponding magnetic field; its form is also given in the Appendix. In all cases under study, the initial condition for Eq. (6) corresponds to a spin system, which is characterized by different net polarizations, P_i , of the individual spins. Such states were created by applying RF-pulses. In our preparation method, other spin orders, for instance, multiplet polarization of the type $\hat{I}_{iz}\hat{I}_{jz}$, were negligible.

To solve Eq. (6), we considered relaxation effects only during stage 3 (evolution at low field) and neglected them during stages of the field variation because in our experiments the times τ_1 and τ_2 were always much shorter than the effective relaxation times. The algorithm of the calculation is described in more detail in the Appendix; a typical profile of field variation, $B(t)$, is also presented there.

III. RESULTS AND DISCUSSION

We ran experiments for N-Ac-His (molecular structure shown in Chart 1) containing 5 coupled protons (NMR parameters are given in Table I). Hereafter, the protons of N-Ac-His are always listed in the order [β 1-CH₂, β 2-CH₂, α -CH, H2, H4]; the same order applies to listing projections of spins for the high-field (Zeeman) states. Non-equilibrium polarization was prepared at B_0 field by applying a non-selective inverting π -pulse (to all five coupled protons) and introducing a suitable delay. Since all the spins have different relaxation times at high field (limit of weak coupling, see Table I), they acquire different polarizations at $t = \tau_p$. The delay $\tau_p = 5.2$ s was chosen so that the fast relaxing β -CH₂ protons almost completely restore the equilibrium polarization, $P_{eq}(B_0)$; the slowly relaxing aromatic protons, H2 and H4, have a considerable negative polarization being almost equal to $-P_{eq}(B_0)$, while the α -CH proton represents an intermediate situation having a small positive polarization. After the preparation, the field was rapidly switched to B_{int} . We systematically varied the magnetic field B_{int} and the delay τ . As will be shown below, our study revealed efficient coherent polarization transfer, predominantly among the aromatic protons.

Characteristic results of the study of polarization transfer are presented in Figure 5. It is clearly seen that polarization of the H2 and H4 protons changes with τ , exhibiting pronounced oscillations. The phase of the oscillations is opposite for the H2 and H4 protons, as a manifestation of the fact that these two protons exchange their polarizations. To understand the polarization transfer mechanism and the oscillation frequency, we performed theoretical modeling of the transfer in the way described above. The results of the theoret-

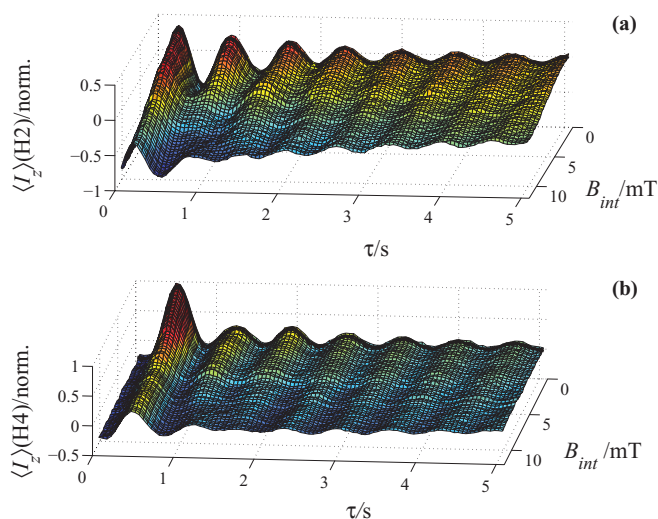


FIG. 5. Time evolution of polarization of the H2 proton (a) and H4 proton (b) measured at different external magnetic fields B_{int} in the field range from 0 up to 12 mT. In both subplots, the evolution at $B_{int} = 0.2$ mT is indicated by the bold contour.

ical simulation at low field $B_{int} = 0.2$ mT are presented in Figure 6(a): the calculated curves (solid lines) are in very good agreement with the experimental data. In the theoretical modeling, it was necessary to take into account all J -couplings in the entire five-spin system, the actual profile $B(t)$ of both field switchings, and relaxation effects during the free

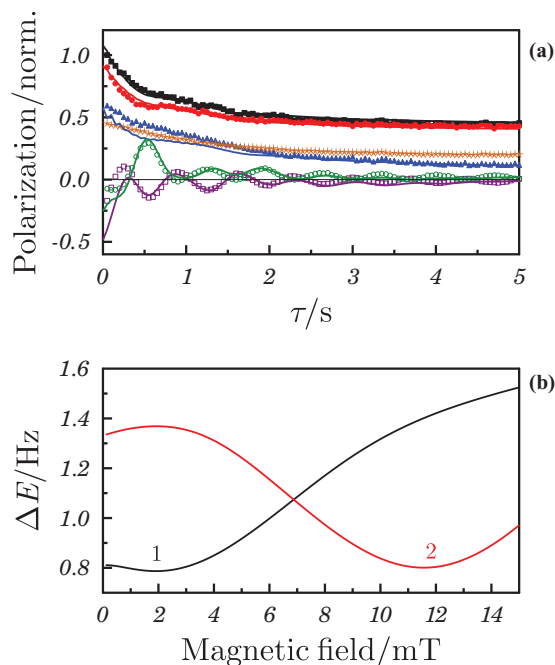


FIG. 6. Time evolution of polarization in N-Ac-His at $B_{int} = 0.2$ mT (a) and field dependence of the energy difference ΔE (in h units) between the levels, which are responsible for the transfer (b). Time traces are shown for β 1-CH₂ (filled squares), β 2-CH₂ (filled circles), α -CH (filled triangles), H2 (open squares), and H4 (open circles) protons and also for the average magnetization (stars, sum of all magnetizations divided by 5). Results of theoretical modeling are shown by solid lines in (a). Subplot (b) shows ΔE for the following pairs of states: $\alpha\beta\alpha\beta\alpha$ - $\beta\alpha\alpha\alpha\beta$ (curve 1) and $\beta\alpha\beta\alpha\beta$ - $\beta\beta\alpha\beta\alpha$ (curve 2). Here, spins are listed in the order: [β 1-CH₂, β 2-CH₂, α -CH, H2, H4].

evolution stage, which are responsible for damping the oscillations and for reduction of the overall polarization. The theoretical modeling reproduces the experimentally observed polarization transfer between the aromatic protons with the characteristic frequency of 1.35 Hz. Oscillations with this frequency also appear in the evolution of the β -CH₂ and α -CH protons; however, their amplitude is considerably weaker.

By calculating the energy levels of the Hamiltonian (7) as a function of field, we have managed to identify the coherences, which are responsible for the observed oscillations. As has been mentioned above, each pair of states having a LAC at low field behaves similar to the two-spin system. In this way, to analyze the polarization transfer pathway it is sufficient to determine, which levels cross at low fields so that ZQCs between them can be formed and to which high-field states they correspond. Then the consequence of mixing at low fields is population exchange in such pairs of states. Our treatment has shown that, first, the coherence between the states, which transform into the high-field states $|\beta\alpha\beta\alpha\rangle$ and $|\beta\beta\alpha\alpha\rangle$, has the experimentally observed frequency (see curve 1 in Figure 6(b)). Second, under our experimental conditions (i.e., the starting polarizations and field variation profile) this coherence is excited after the field variation $B_0 \rightarrow B_{\text{int}}$ as follows from our calculation. This is because for the given pair of levels there is an anti-crossing at the field of 11.5 mT: after going through this field the starting population difference is partly transformed into spin coherence, which is observed experimentally. The LAC can be readily seen from Figure 6(b): at the level crossing field, B_{lac} , the difference of the energies of the corresponding states is minimal. Since the states $|\beta\alpha\beta\alpha\rangle$ and $|\beta\beta\alpha\alpha\rangle$ (spins are always listed in the order described above) involve opposite projections of spins of the H2 and H4 protons, these two protons exchange polarization when the initial populations of these states differ at high field. For this pair of states, the spin projections of the α -CH and of one of the β -CH₂ protons (namely, of the β 2-CH₂ proton) are also exchanged. Indeed, the polarization of the α -CH and the β -CH₂ protons has an oscillatory component, which clearly shows that not only H2 and H4, but also other protons are involved in the transfer process: only the average polarization of all five protons (see Figure 6(a)) contains no oscillations and only exponentially decays with time. However, for the other protons the oscillations are much less pronounced, presumably, due to relaxation during field cycling and starting preparation. In principle, one can also expect polarization transfer between the H2 and H4 protons at lower frequency of ≈ 0.8 Hz, which is caused by the LAC of the states $|\alpha\beta\alpha\alpha\rangle$ and $|\beta\alpha\alpha\alpha\rangle$ (see Figure 6(b)). However, under our experimental conditions (namely, the initial spin state of the system and speed of field variation) this coherence has much lower amplitude. As revealed from our calculations this is because during the field variation $B_0 \rightarrow B_{\text{int}}$ the system does not go through the LAC but only to the LAC. From the discussion above, one expects maximal polarization transfer when $B_{\text{int}} = B_{\text{lac}}$ for the ideal case of sudden field variation. However, in practice the field variation speed is limited, in particular, at $B_{\text{int}} = B_{\text{lac}}$ the speed at the LAC point is zero. For this reason, coherences are excited more efficiently when $B_{\text{int}} < B_{\text{lac}}$: the LAC is then passed with non-zero speed so that ZQCs are

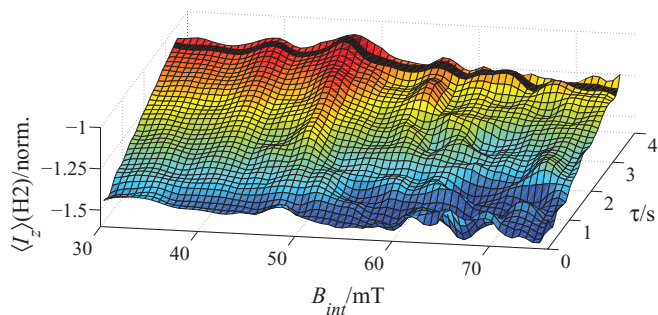


FIG. 7. Field dependence of the polarization of the H2 proton at various evolution times. Field dependence at $\tau = 3.4$ s is indicated.

formed with higher amplitude. As a consequence, the oscillations with the lower frequency are much less pronounced.

In addition to the low-field polarization transfer, we have studied in detail the polarization transfer effects in the intermediate field range, namely, from 30 to 100 mT. From our previous studies of spin relaxation of N-Ac-His, it is known that in this range there are multiple LACs in the five-proton system. It is of interest to also elucidate their role in the polarization transfer. The dependence of the polarization of the H2 proton on the field B_{int} and the delay τ is shown in Figure 7. In this presentation, it is seen that the field dependence of polarization at a given delay is not monotonous. At the same time, neither the features in the field dependence nor the quantum oscillations in the τ -dependence are well pronounced. This is because the number of LACs, which is a few dozens, in the corresponding field range is too large. As a consequence, there are numerous coherences excited; thus, there are many oscillatory contributions to the spin evolution with different frequencies. Because of destructive interference of the individual components the oscillations are efficiently suppressed. An additional problem in resolving the numerous LACs is the small splitting (about 0.1-0.2 Hz) between the crossing levels with the consequence that the resulting oscillations become slow and spin relaxation effects damp the coherent spin evolution already during the first period. Nevertheless, it is possible to visualize the LAC effects by taking a cut of the 3D-surface in Figure 7 at a fixed delay. Such a cut at $\tau = 3.4$ s is shown in Figure 8(a) together with the simulation. In this representation, several features are seen in the dependence of the polarization on B_{int} . These features are due to the LACs in the field range under study. The experimentally observed field dependence is in very good agreement with the theoretically predicted one (see Figure 8(a)). In previous relaxation measurements,⁴² we observed peaks and dips in the field dependence of the T_1 -relaxation times of the H2 and H4 protons (shown in Figure 8(b) for comparison), which were also explained as a level crossing effect. Although spin relaxation is not a coherent phenomenon, our treatment shows that it is related to the polarization transfer processes we are dealing with. This is because upon strong coupling of spins and, in particular, at the LAC points the eigen-states of the static Hamiltonian (7) change and there is no longer relaxation of individual spins but relaxation of coupled spin states. Thus, the LACs lead to maxima and minima in the field dependence of both relaxation and polarization transfer phenomena.

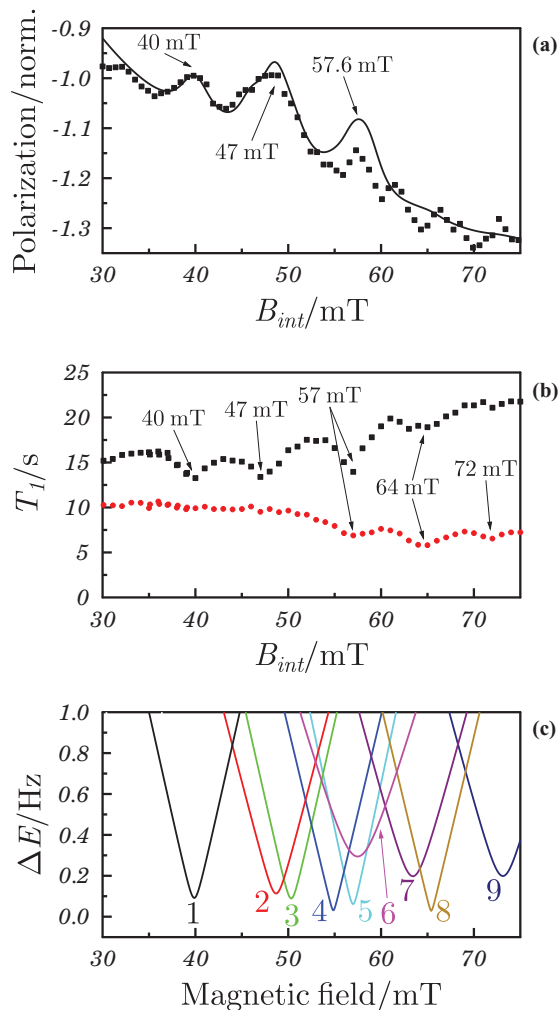


FIG. 8. Field dependence of polarization transfer efficiency to the H2 proton at $\tau = 3.4$ s (a); field dependence of T_1 -relaxation of the H2 (circles) and H4 (squares) protons (b); energy differences ΔE (in h units) between the levels experiencing LACs (c). Positions of features in (a) and (b) caused by LACs are indicated by arrows. Splitting is shown for the following pairs of states: $\beta\beta\alpha\beta\alpha-\beta\alpha\beta\alpha\beta$ (1); $\beta\beta\beta\alpha\beta-\beta\beta\beta\beta\alpha$ (2); $\beta\alpha\beta\alpha\alpha-\alpha\beta\alpha\alpha\beta$ (3); $\beta\alpha\beta\beta\alpha-\alpha\beta\alpha\beta\beta$ (4); $\alpha\alpha\alpha\beta\alpha-\alpha\alpha\alpha\beta\alpha$ (5); $\beta\alpha\beta\alpha\beta-\alpha\beta\beta\beta\alpha$ (6); $\alpha\alpha\beta\beta\alpha-\alpha\alpha\alpha\beta\beta$ (7); $\alpha\beta\alpha\beta\alpha-\alpha\alpha\beta\beta\alpha$ (8); $\alpha\alpha\beta\alpha\alpha-\alpha\alpha\alpha\beta\beta$ (9); the adiabatic levels are assigned at high fields where the spins are coupled weakly; spins are listed in the order: [β 1- CH_2 , β 2- CH_2 , α -CH, H2, H4].

Energy differences (frequencies) between the spin levels, which are responsible for features in polarization transfer and relaxation, are shown in Figure 8(c). Minima in the field dependences of the frequencies correspond to LACs, which give the features presented in Figures 8(a) and 8(b). Let us note, that sharp features in the same field range have also been observed³¹ in the field dependence of CIDNP of N-Ac-His. These features can also be accounted for by LAC effects; we will discuss this issue in a separate publication.

To demonstrate the LAC effects more clearly, it is desirable to study polarization transfer at an isolated LAC, so that there is no overlap of multiple coherences, which oscillate with different frequencies. It is expected^{39,40,42,47} that a system of three non-equivalent protons has only one isolated LAC at non-zero field. At fields larger than 80 mT, the coupling network in N-Ac-His can be described in good approximation by two separate sub-systems, consisting of

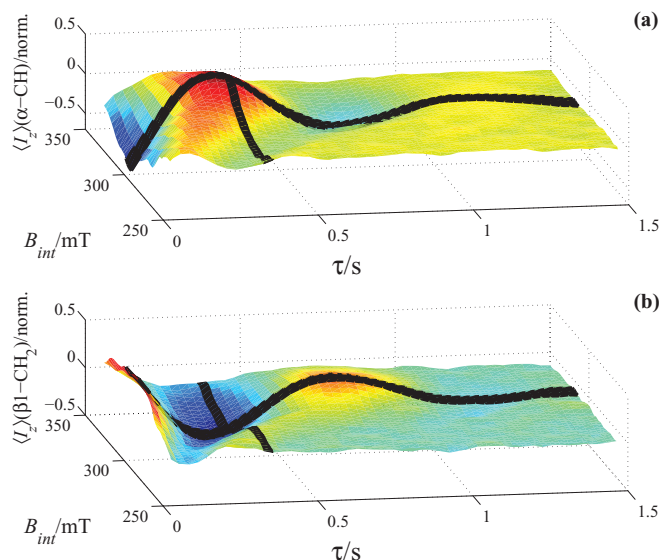


FIG. 9. Time evolution of polarization of the α -CH proton (a) and β 1- CH_2 proton (b) at different external magnetic fields B_{int} in the field range from 250 up to 340 mT. Time evolution at $B_{int} = 330$ mT and also field dependences at $\tau = 0.36$ s are indicated; to visualize coherent oscillations more clearly at all fields we subtracted from the time traces functions $f_i(\tau) = f_{i0} + f_i \exp(-\tau/\tau_i^*)$ (a decaying exponential and a constant) to reveal quantum beats, which are otherwise hidden on top of main curve. The values for τ_i^* were around 0.7 s for the β 1- CH_2 proton and around 1.5 s for the α -CH proton in this field range.

[β 1- CH_2 , β 2- CH_2 , α -CH] and the aromatic protons, respectively. Hence, the α -CH and β - CH_2 protons represent the desired three spin system. However, the situation is slightly more complex because this subsystem is slightly coupled to the H4 proton. Even though this coupling is weak, it can split the LAC as has been shown in our previous work.⁴¹ More specifically, it happens because the system [β 1- CH_2 , β 2- CH_2 , α -CH] is strongly coupled and the two β - CH_2 protons have slightly different couplings to the additional nucleus, the H4 proton. This situation results in a small splitting of ≈ 20 mT of the LAC, which is located at approximately 310 mT, into two LACs corresponding to the α - and β -states of the additional spin. However, since the splitting is relatively small, both LACs together work in almost the same way as a single LAC. In general, LACs are supposed to result in pronounced features in the field dependence of spin relaxation^{29,41,42,57} and polarization transfer.^{39-41,45-47} Here, we will study the polarization transfer at the LAC in the three-spin 1/2 system in detail and support the experimental results with theoretical calculations.

In our experiments, we prepared the following initial polarizations of spins: after establishing Boltzmann polarization at 7 T and applying a non-selective π -pulse together with an appropriately set delay $\tau_p = 1$ s the two β - CH_2 protons have positive polarizations of similar size, whereas the α -CH proton has negative polarization of the same magnitude because of the difference in the respective high-field T_1 -relaxation times. Our study shows (Figure 9) that one of the β - CH_2 protons, namely, the β 1- CH_2 proton, exchanges its positive polarization (Figure 9(b)) with the negative polarization of the α -CH proton (Figure 9(a)). The polarization exchange is most

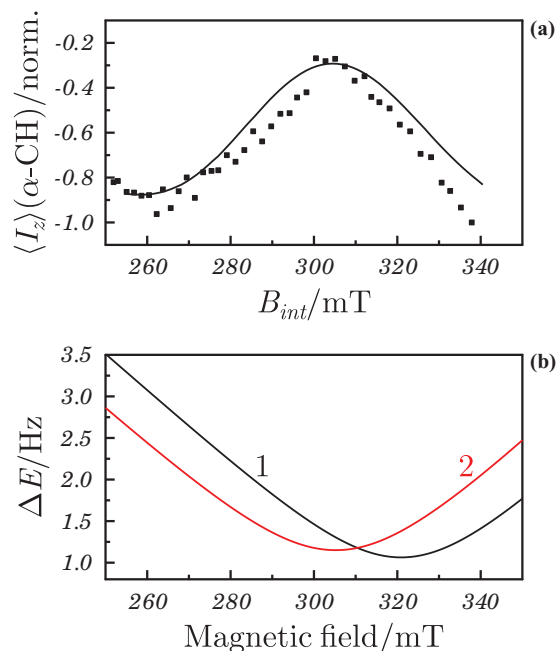


FIG. 10. Field dependence of polarization transfer efficiency to the α -CH proton from the β -CH₂ protons at $\tau = 0.36$ s (a) and energy differences ΔE (in h units) between the levels experiencing LACs (b). In subplot (a), theoretical simulation is shown by solid line; in subplot (b), splitting is shown for the following pairs of levels: $\beta\alpha\alpha$ - $\alpha\alpha\beta$ (curve 1) and $\beta\alpha\beta$ - $\alpha\alpha\beta$ (curve 2); the adiabatic levels are assigned at high fields where the spins are coupled weakly, spins are listed in the order: [β 1-CH₂, β 2-CH₂, α -CH, H4].

efficient at the LAC point as the amplitude of the spin coherence excited by the field variation is highest. That again the polarization transfer is coherent is readily concluded from the presence of an oscillatory component in the time evolution of the transfer. The oscillation frequency is smallest at the LAC, which clearly indicates that at this position the spacing between the corresponding spin energy levels is minimal. We also performed a theoretical simulation of the field dependence of the polarization transfer efficiency and the adiabatic spin energy levels of the system, which is shown in Figure 10. In each pair of the crossing levels, the protons in the α -CH and β 1-CH₂ positions have opposite z -projections at high field. After going to low field these two spins exchange their z -projections. Due to our preparation method the spin-up states of the β -CH₂ protons are overpopulated as compared to the states with the β -projections. For the α -CH protons, the situation is the opposite: spin-down states are overpopulated in comparison with the spin-up states. For this reason, after the preparation the $|\alpha\alpha\beta\rangle$ state (when the spins are numerated in the order [β 1-CH₂, β 2-CH₂, α -CH]) has a higher population than the $|\beta\alpha\alpha\rangle$ state. When the system is rapidly brought to the LAC the ZQC is formed. When at $B = B_{\text{int}}$ the delay τ is set properly so that the ZQC phase is inverted, then after two field switches the state $|\beta\alpha\alpha\rangle$ becomes overpopulated in comparison with the state $|\alpha\alpha\beta\rangle$. Accordingly, polarization is transferred selectively from the β 1-CH₂ proton to the α -CH proton. We have also checked by theoretical calculations that under our experimental conditions only coherences between the $|\alpha\alpha\beta\rangle$ and $|\beta\alpha\alpha\rangle$ states are excited, while all other coherences are negligibly small. As can also be seen from

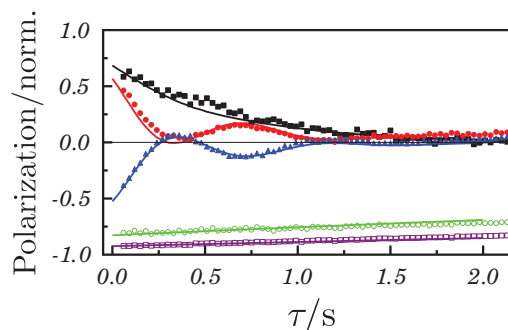


FIG. 11. Evolution of polarization in N-Ac-His at $B_{\text{int}} = 330$ mT. The kinetics is shown for β 1-CH₂ (filled circles), β 2-CH₂ (filled squares), α -CH (filled triangles), H2 (open squares), and H4 (open circles) protons. Results of theoretical modeling are shown by solid lines; frequency of the oscillatory component of the polarization transfer is ≈ 1.1 Hz.

Figure 10(a), the theoretical simulation is in excellent agreement with the experimental data: the calculated field dependence of polarization of the α -CH proton perfectly reproduces the experimental one. In this calculation, we did not use any fitting parameters: the field dependence was calculated with the known NMR parameters of the system and the known $B(t)$ profile. In particular, the polarization transfer frequencies observed for the three-spin system are in agreement with the calculated energy differences for the states, which are involved in LACs (Figure 10(b)).

The time profile of the coherent polarization transfer in the vicinity of LAC (namely, at $B_{\text{int}} = 330$ mT) is shown in Figure 11. In the curves for the β 1-CH₂ and α -CH protons oscillatory components are clearly seen, whereas polarization of the other protons relaxes exponentially. This is a clear indication of selectivity of the polarization transfer: by choosing a LAC it is possible to transfer polarization between a selected pair of spins. Again, the theoretical calculation is in very good agreement with the experimental results. Such a good agreement between theory and experiment is of particular importance because it indicates the precision of the theoretical approach, which can be used not only for modeling the experiments but also for predicting the polarization transfer behavior and determining the transfer rates. In addition, it allows us to find out, which particular spin coherences are excited in our experiments. This is very useful for understanding the polarization transfer pathway, its rate and efficiency.

IV. CONCLUSIONS

In this work, we demonstrated effects of polarization transfer among strongly coupled spins in NMR experiments with fast field-cycling. In particular, we have shown that such a transfer has a coherent nature, thus it is fast (as the transfer time is given by the inverse J -coupling), efficient (as it is possible to exactly exchange populations of the coupled levels), selective (as only particular spin orders are involved), and controllable (as the process can be manipulated by setting the experimental timing). We have shown that polarization transfer is occurring via ZQCs, which are excited by non-adiabatic changes of the spin Hamiltonian. Coherent effects clearly manifest themselves in the time evolution of the trans-

fer, which contains a pronounced oscillatory contribution. In our systems, polarization transfer between spins due to cross-relaxation is negligible. We have analyzed in detail coherent pathways of polarization transfer and elucidated the role of LACs in the observed phenomena. The good agreement of the experimental results with theoretical calculations allowed for identification and characterization of particular coherences responsible for the polarization transfer, for explanation of the transfer selectivity and for evaluation of the transfer frequencies. We have also demonstrated that the exploitation of LACs opens a way for selective population exchange between particular pairs of spin energy levels and thus for polarization transfer between well-defined spin orders. LACs result in pronounced features in the field dependence of the transfer efficiency; however, the positions of such features do not always coincide with those of the LACs. In general, correct interpretation of the observations inevitably requires support by numerical simulations. Then it becomes possible to correctly identify the transfer pathways and to map out particular LACs in the spin system.

It is worth noting that although we studied only scalar coupled $1/2$ spins our results are more general. In fact, other interactions (for instance, residual dipolar couplings in proteins^{65–67} or liquid crystalline samples^{68–70}) can lead to similar polarization transfer effects due to conversion of the state population differences into spin coherences. The mechanisms considered are always operative when (i) a polarized spin system goes to the strong coupling regime upon field variation and (ii) the field switch is non-adiabatic (preferably, sudden). Moreover, pronounced effects conditioned by LACs are expected for any kind of spin-spin interaction. An important example of a related phenomenon is given by the indirect detection of the quadrupolar ^{14}N nuclei:^{71,72} in a similar field-cycling protocol with two field jumps one can observe loss of polarization of protons due to their dipolar couplings to nitrogen in the molecule; such a loss of polarization becomes efficient at the LAC positions. Currently in these experiments, it is debated^{73,74} whether the mechanism for polarization exchange is based on cross-relaxation or on excitation of spin coherences. Our results show that coherent process should not be excluded.

In our experiments, non-thermal polarization has been prepared by applying RF-pulses to spin systems having different T_1 . Again, we anticipate that coherent polarization transfer effects in field-cycling NMR are inevitable and will be also manifest for other types of polarization, most notably, of hyperpolarization. In particular, Buljubasich *et al.*⁴⁵ have reported efficient transfer of PHIP in a four-spin system occurring due to LACs. Our own results⁴⁰ obtained for PHIP have shown that making use of LACs allows one to convert the initial multiplet polarization of a proton pair into net polarizations of selected protons. In a very recent work,⁷⁵ we have demonstrated that LACs are particularly important for understanding the field dependence⁷⁶ of the PHIP-based technique²⁸ termed Signal Amplification By Reversible Exchange (SABRE). Such a process is also based on excited ZQCs and population exchange between particular pairs of spin states. In fact, it is known that polarization transfer phenomena are common for low-field or

zero-field^{15,16,43,77–79} NMR experiments, which utilize spin hyperpolarization.

Our study opens additional opportunities for spectroscopic and dynamic studies of coupled spin systems. This is because the LAC positions and energy differences between the anti-crossing levels uniquely depend on the NMR parameters. For instance, they are sensitive not only to the absolute values of the couplings but also to their signs. In addition, at low fields the field inhomogeneity problem is minimized as compared to high-field NMR, where a B_0 inhomogeneity of the order of 10^{-9} is typically required for high spectral resolution. As a consequence, very small J -couplings can be determined by studying the polarization transfer kinetics at low fields. One can also measure the damping constants of ZQCs at low fields and thus obtain additional information on the relaxation properties of the spin system. Most notably, one can study so-called long-lived coherences (LLC),^{80–82} which are ZQCs of coupled spin systems in a situation where the difference in chemical shifts of spins is quenched. Our method gives an alternative way of observing ZQCs formed at low fields as compared to that proposed by Pileio *et al.*⁸⁰ who excited coherence between the singlet and T_0 states by pumping “forbidden” spin transitions with “extremely low-frequency” irradiation. Last but not least, the high precision of our theoretical approach, which can be straightforwardly extended²⁹ to consider dipolar relaxation, enables such studies on a quantitative level.

In summary, our study shows the importance of coherent phenomena in NMR experiments utilizing fast field-cycling techniques. The observed effects are of a general nature and, thus, are of importance for other experiments of non-thermally polarized spin systems as well. Moreover, the investigation of coherent polarization transfer effects can provide new spectroscopic and dynamic information on the system under study.

ACKNOWLEDGMENTS

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APPENDIX: DETAILS OF THE CALCULATION METHOD

1. Relaxation super-operator

To describe relaxation effects, we first introduced the Hamiltonian, $\hat{H}_{fl}(t)$, which describes interactions with the fluctuating local fields as follows:

$$\hat{H}_{fl}(t) = -\gamma \sum_{i=1}^N \{B_{ix}(t)\hat{I}_{ix} + B_{iy}(t)\hat{I}_{iy} + B_{iz}(t)\hat{I}_{iz}\}. \quad (\text{A1})$$

Here, B_{ix} , B_{iy} , and B_{iz} stand for the components of the local field for the i th spin. We will treat spin relaxation only

in the extreme narrowing limit, thus assuming that the motional correlation time, τ_c , is very short, i.e., $\gamma B \tau_c \ll 1$ in the whole field range. This is because N-Ac-His is a small molecule, which tumbles fast in room temperature aqueous solution. In this situation, the times T_{1i} and T_{2i} are field-independent and there is the following relation between the relaxation rates and the ensemble-averaged values of the auto-correlation functions:⁶⁴

$$\begin{aligned} \gamma^2 \int_{-\infty}^{\infty} \overline{B_{ix}(t)B_{ix}(t+\tau)} d\tau &= 2\gamma^2 \tau_c \langle B_{ix}^2 \rangle = 2\gamma^2 \tau_c \langle B_{iy}^2 \rangle \\ &= 2\gamma^2 \tau_c \langle B_{iz}^2 \rangle = \frac{1}{T_{1i}} = \frac{1}{T_{2i}}. \end{aligned} \quad (\text{A2})$$

Here, the over-bar stands for averaging over the ensemble; $\langle \dots \rangle$ denote the averaged quantities. In the averaging, we also assumed that fluctuations of B_{ix} , B_{iy} , and B_{iz} are independent of each other (i.e., for instance, $\langle B_{ix}B_{iy} \rangle = 0$); likewise, the local field components for the i th and j th spins fluctuate independently when $i \neq j$ (i.e., for instance, $\langle B_{ix}B_{jx} \rangle = 0$). The elements of the super-operator \hat{R} are as follows:⁸³

$$R_{\mu\nu, \mu'\nu'} = \frac{1}{2} \left(2J_{\mu\mu'\nu\nu'} - \delta_{\nu\nu'} \sum_{\kappa} J_{\kappa\mu', \kappa\mu} - \delta_{\mu\mu'} \sum_{\kappa} J_{\kappa\nu\kappa\nu'} \right), \quad (\text{A3})$$

where

$$J_{\mu\mu'\nu\nu'} = \int_{-\infty}^{\infty} \overline{\langle \mu | \hat{H}_{fi}(t) | \mu' \rangle \langle \nu' | \hat{H}_{fi}(t+\tau) | \nu \rangle} d\tau \quad (\text{A4})$$

and $\delta_{\mu\nu}$ is the Kronecker delta. For calculating the auto-correlation of $\hat{H}_{fi}(t)$ and performing the averaging, expressions (A2) should be used.

2. Initial condition and equilibrium density matrix

The matrix $\hat{\rho}_{eq}$ in Eq. (6) describes the multi-spin system being at thermal equilibrium at the corresponding magnetic field, B

$$\rho_{eq}(B) = \frac{1}{2^K} \left(\hat{E} + \frac{\hbar\gamma B}{kT} \hat{I}_z \right). \quad (\text{A5})$$

According to this expression, all spins have the same equilibrium magnetization, $P_{eq}(B)$, at the magnetic field equal to B . The initial condition for Eq. (6) at $t = \tau_p$ is as follows:

$$\hat{\rho}(\tau_p) = \frac{1}{2^K} \left(\hat{E} + \sum_{i=1}^K P_i \hat{I}_{iz} \right). \quad (\text{A6})$$

It describes the situation that the initial state is characterized by different net polarizations, P_i , of the individual spins. Such states were created by applying RF-pulses. In our experiments, all higher spin orders were negligible.

3. Calculation algorithm

First, we calculated changes in the density matrix, which is initially diagonal, see Eq. (A6), caused by dynamic spin

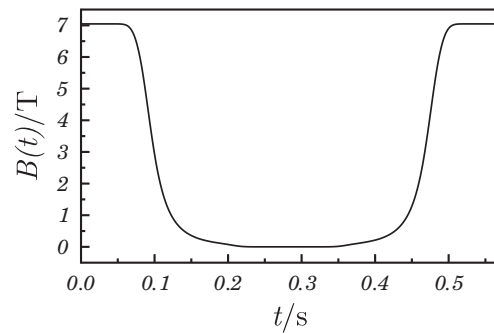


FIG. 12. Typical time profile, $B(t)$, of field variation used in our experiments. Here, $\tau_1 = \tau_2 = 0.283$ s, $\tau = 0$, $B_{int} = 0.45$ mT.

evolution while going to low field. The resulting density matrix is no longer diagonal in the basis of the Hamiltonian (7) at $B = B_{int}$, since there are ZQCs formed by non-adiabatic field variation. The density matrix at $t = \tau_p + \tau_1$ is the initial condition for the evolution at stage 3; to describe it we solved the Liouville-von Neumann equation for $\hat{\rho}$ also taking relaxation into account. The relaxation effects lead to both, a loss of non-thermal polarization in the system and a decay of all spin coherences. The density matrix at $t = \tau_p + \tau_1 + \tau$ is the initial condition for stage 4. Finally, we calculated changes caused by the second field variation during stage 4 neglecting spin relaxation effects. The main consequence of the second field variation is thus conversion of the ZQCs back to the state population differences at high field. Since the Hamiltonian is time-dependent during stages 2 and 4 (and, in addition, $\hat{H}(t_1)$ does not commute with $\hat{H}(t_2)$ when $t_1 \neq t_2$), we simulated the spin evolution splitting the time intervals τ_1 and τ_2 into small steps and calculating the evolution during subsequent steps. The number of steps was chosen such that the product of the duration of each step and the evolution frequencies given by energy differences between eigen-states of the Hamiltonian (7) were always very small; we also made sure that the calculation result did not depend on their duration. The field variation profile, $B(t)$, was rather complex and considerably different from linear, see Figure 12. To model the data precisely, it was thus necessary to take into consideration the actual $B(t)$ dependence, whereas modeling it with a simpler profile, such as a linear one, gives wrong results.

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