

Method for Measuring Spin Relaxation During Production of Hyperpolarized ^{13}C

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INTRODUCTION: The use of hyperpolarized tracers for MR imaging and spectroscopy has become an interesting topic in recent years. Hyperpolarized ^{13}C can be produced by transferring the spin order from parahydrogen by the method of parahydrogen-induced polarization (PHIP). The spin order is transferred by means of a series of RF pulses mixed with free precessions in an external magnetic field. A variety of pulse sequences have been proposed [1,2], and in ideal cases they result in a completely polarized heteronucleus. To our knowledge the effect of relaxation has not been considered in this context. We have therefore investigated conditions under which relaxation could lead to a significant reduction in the polarization of the ^{13}C nucleus; the ultimate goal is to determine how to maximize this polarization in spite of relaxation effects.

METHODS: We have performed a numerical integration of the Liouville-von Neumann equation using a fourth-order Runge-Kutta algorithm with an adaptive step size. The software was written in C++ by the authors based on an existing algorithm [3]. The computer was an Intel-based PC running the Linux OS. As an example, we studied deuterated hydroxyethyl propionate ($\text{CD}_2\text{HCDH}^{13}\text{COOCD}_2\text{CD}_2\text{OD}$). Because coupling to the deuterons is assumed to be negligible, we consider only the spins of the two protons (denoted \mathbf{I}_1 and \mathbf{I}_2) and the ^{13}C (\mathbf{S}). The Hamiltonian and initial density matrix are:

$$H = \omega_I(I_{1z} + I_{2z}) + \omega_S S_z + 2\pi(J_{12}\mathbf{I}_1 \cdot \mathbf{I}_2 + J_{1C}I_{1z}S_z + J_{2C}I_{2z}S_z), \quad \rho_0 = (1 - 4\mathbf{I}_1 \cdot \mathbf{I}_2)/8.$$

In this approximation the terms of the form $\mathbf{I}_1^+ \mathbf{S}^+$ are also ignored. The parameter $J_{12}=7.50$ Hz represents the coupling between the two protons, and $J_{1C}=8.22$ Hz and $J_{2C}=-5.02$ Hz represent the couplings between the ^{13}C and each proton. The spins evolve in an external magnetic field of 17.52 G. The pulse sequence which was studied is illustrated in Figure 1. In this initial study, T_1 relaxation was assumed to be negligible (although this should be revisited in a more detailed study). Coherences were assumed to decay exponentially with a time constant T_2 . The same relaxation time was assumed to apply to the density matrix components $\mathbf{I}_1^+ \mathbf{I}_2^-$ and $\mathbf{I}_1^+ \mathbf{I}_2^- S_z$, but a different time constant might apply to the components \mathbf{S}^+ , $\mathbf{S}^+ \mathbf{I}_{1z}$, $\mathbf{S}^+ \mathbf{I}_{2z}$, and $\mathbf{S}^+ \mathbf{I}_{1z} \mathbf{I}_{2z}$. We allowed for four independent time constants which we associate with $\mathbf{I}_1^+ \mathbf{I}_2^-$, \mathbf{S}^+ , $\mathbf{S}^+ \mathbf{I}_1^+ \mathbf{I}_2^-$, and $\mathbf{S}^+ \mathbf{I}_1^- \mathbf{I}_2^+$. Complex conjugate elements were assumed to have identical decay time constants. In the ideal execution of the pulse sequence shown in Figure 1, no other off-diagonal components of the density matrix will become populated.

Relaxation was modeled by adding a relaxation term to the Liouville-von Neumann equation:

$$d\rho/dt = i[\rho, H] - R(\rho)$$

The matrix R was computed by dividing each element of ρ by the appropriate decay constant for that element. A more accurate treatment of relaxation was beyond the scope of the present study.

Some flexibility is allowed in choosing the delays in the pulse sequence of Figure 1. The constraints will be explained elsewhere; here we merely state that the two examples indicated in Table I will both result in 100% polarization of the ^{13}C nucleus, assuming ideal RF pulses and the absence of relaxation effects. Both of these patterns were studied. For simplicity we considered the decay time $T_2=100$ ms, and in general only one of the four decay times was set to a small value while the others were set to 100 s, which for this problem is essentially infinite.

RESULTS: It was verified that when all of the decay constants explicitly described here were set to 100 s and the other off-diagonal coherence terms in the density matrix decayed with a time constant of 1 ms, the effect was negligible and the polarization transfer was essentially 100% efficient.

Table II compares calculations of the two different sequences of delays. Note that in the case where all four decay constants were set to 100 ms (shown in the far right column), the result is roughly equal to the product of the results from the four calculations in which only one constant was set to 100 ms.

DISCUSSION: When the delays are changed, the contribution of each relaxation constant to the ultimate polarization also changes. Because these effects are multiplicative, it may be possible to determine the relaxation time constants by "inverting" the results of an experiment in which the ^{13}C polarization is measured for a number of combinations of delay times. In addition, each of the delays can be extended by a multiple of the precession period (in this case, 99.963 ms) without changing the results in the ideal case. When either of the first two delays are so extended, only the relaxation of the $\mathbf{I}_1^+ \mathbf{I}_2^-$ coherence decreases the polarization; conversely, relaxation of this coherence causes no additional polarization loss when the last two delays are extended (results not shown).

CONCLUSION: A relatively straightforward series of experiments can be used to determine relaxation parameters in a PHIP system, permitting pulse sequence optimization. A more detailed model of relaxation should be considered.

REFERENCES: [1] H Sengstschmid *et al.*, *J Magn Reson* **A120**:249-257 (1996). [2] M Goldman & H Jóhannesson, *CR Physique* **6**:575-581 (2005). [3] WH Press *et al.*, *Numerical Recipes in C*, 2nd ed., Cambridge University Press (1992).

	t_1	t_2	t_3	t_4
Case A	41.288	21.114	21.114	41.288
Case B	27.254	36.354	57.254	8.330

Table I: Example delay times (in milliseconds) which may be used in the sequence in Figure 1.

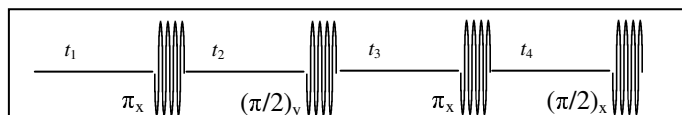


Figure 1: Schematic representation of the polarization transfer pulse sequence. The indicated pulses are applied to ^{13}C . Refocusing pulses during each delay are omitted for brevity.

	$\mathbf{I}_1^+ \mathbf{I}_2^-$	\mathbf{S}^+	$\mathbf{S}^+ \mathbf{I}_1^+ \mathbf{I}_2^-$	$\mathbf{S}^+ \mathbf{I}_1^- \mathbf{I}_2^+$	all
Case A	0.714	0.710	0.873	0.873	0.383
Case B	0.621	0.622	0.924	0.923	0.324

Table II: For the two sequences of delays in Table I, the computed polarizations are shown for the case where the indicated coherence has a decay constant of 100 ms and the other three have a decay constant of 100 s. All decay constants were set to 100 ms for the calculation in the right column.