PULSAR

Technical Note

Using **Pulsar** to measure spin-lattice relaxation data to determine the longevity of polarised spin-states produced by a parahydrogen based hyperpolarisation technique

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Introduction

The measurement of T_1 (spin-lattice) relaxation times is used to evaluate the longevity of a polarised state produced by hyperpolarisation techniques, which are applied to NMR and MRI. These measurements are typically performed at high magnetic field (typically around 9.4 T), but it is becoming increasingly more prudent to apply these techniques to obtaining images and spectra on low-field devices.

SABRE (Signal Amplification By Reversible Exchange), a *para*hydrogen based hyperpolarisation technique, is used for the production of molecules with non-Boltzmann distributions. An iridium centred complex is used to catalyse the spin-transfer. As the molecules that are typically polarised by this method are *N*-heterocycles, the aromatic region of the ^{1}H NMR spectrum can be crowded in that some chemical shifts are super-imposed on one another.

This application note describes the use of the **Pulsar** benchtop NMR instrument, in conjunction with the MNOVA software package for processing of acquired NMR data, to show that the T_1's of pyridine are readily ascertained under a range of physical constraints.

Experimental Set-Up

A Young's capped NMR tube (5 mm diameter) was charged with 5 μL of pyridine in 600 μL of d_4-methanol. This was then placed in the **Pulsar** benchtop NMR instrument, which was then tuned and matched. A standard ^{1}H NMR spectrum was acquired to give an indication of the sweep width required for the T_1 measurement. Following this the T_1 measurement was then completed.

The sample was subsequently used for other measurements, in which either the atmosphere above the sample, or the chemical composition of the solution were altered. Further measurements are made using the original sample, in the absence of air, and with the addition of 2 mg of [Ir(COD)(IMes)Cl] (spin-transfer catalyst, COD = cyclooctadiene, IMes = 1,3-Bis(2,4,6-trimethylphenyl)imidazole-2-ylidene) under an atmosphere of air or hydrogen.

Sample insertion point.

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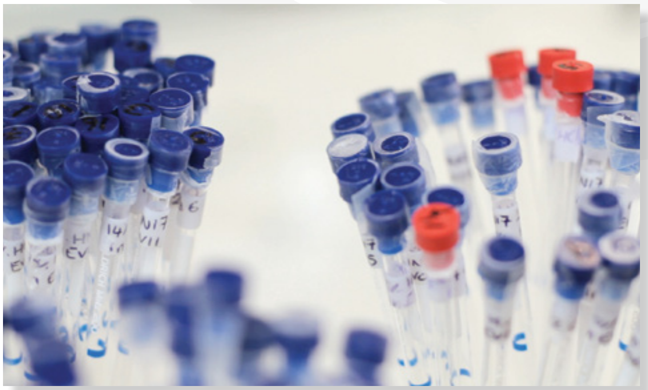
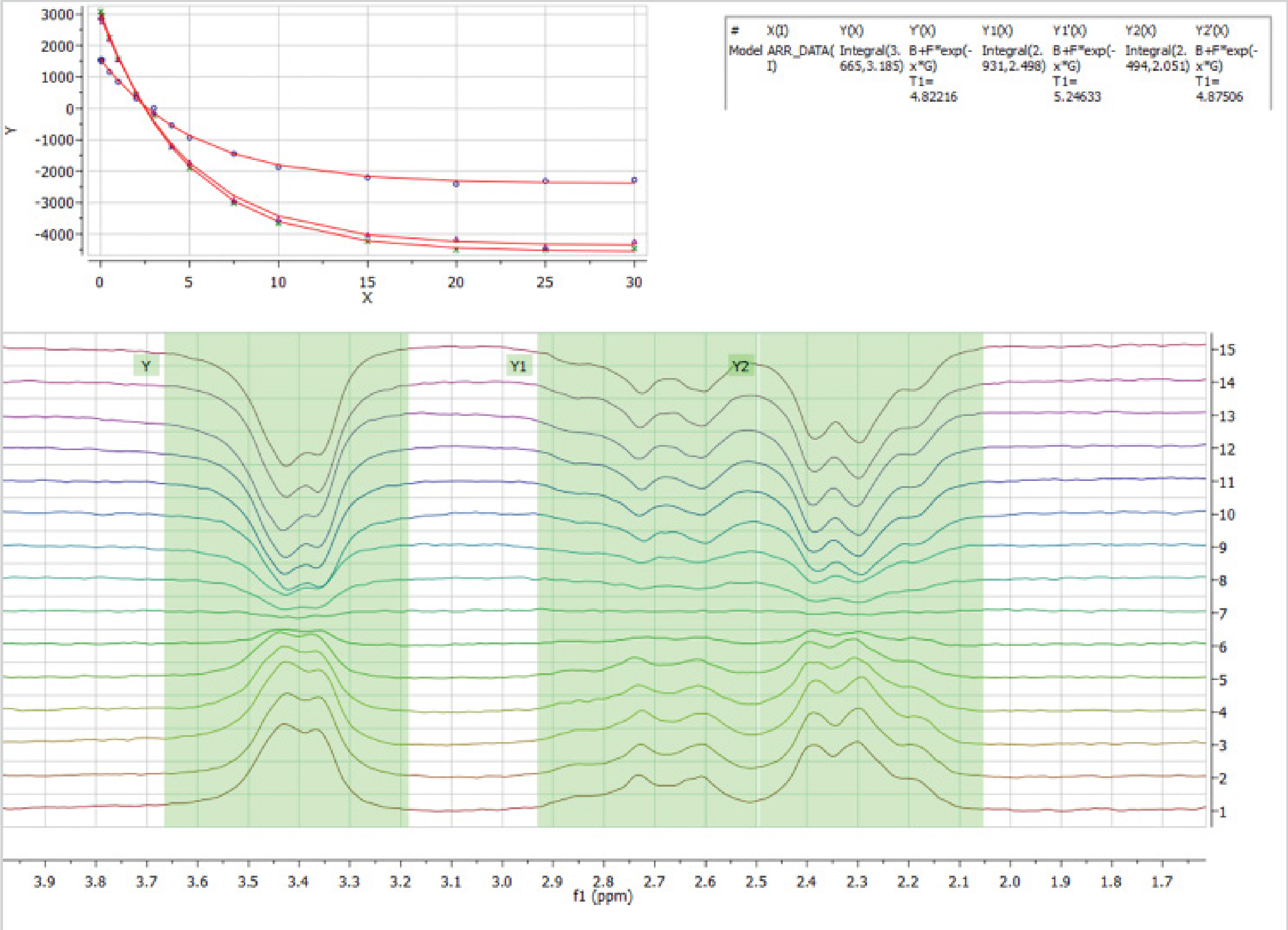
Results

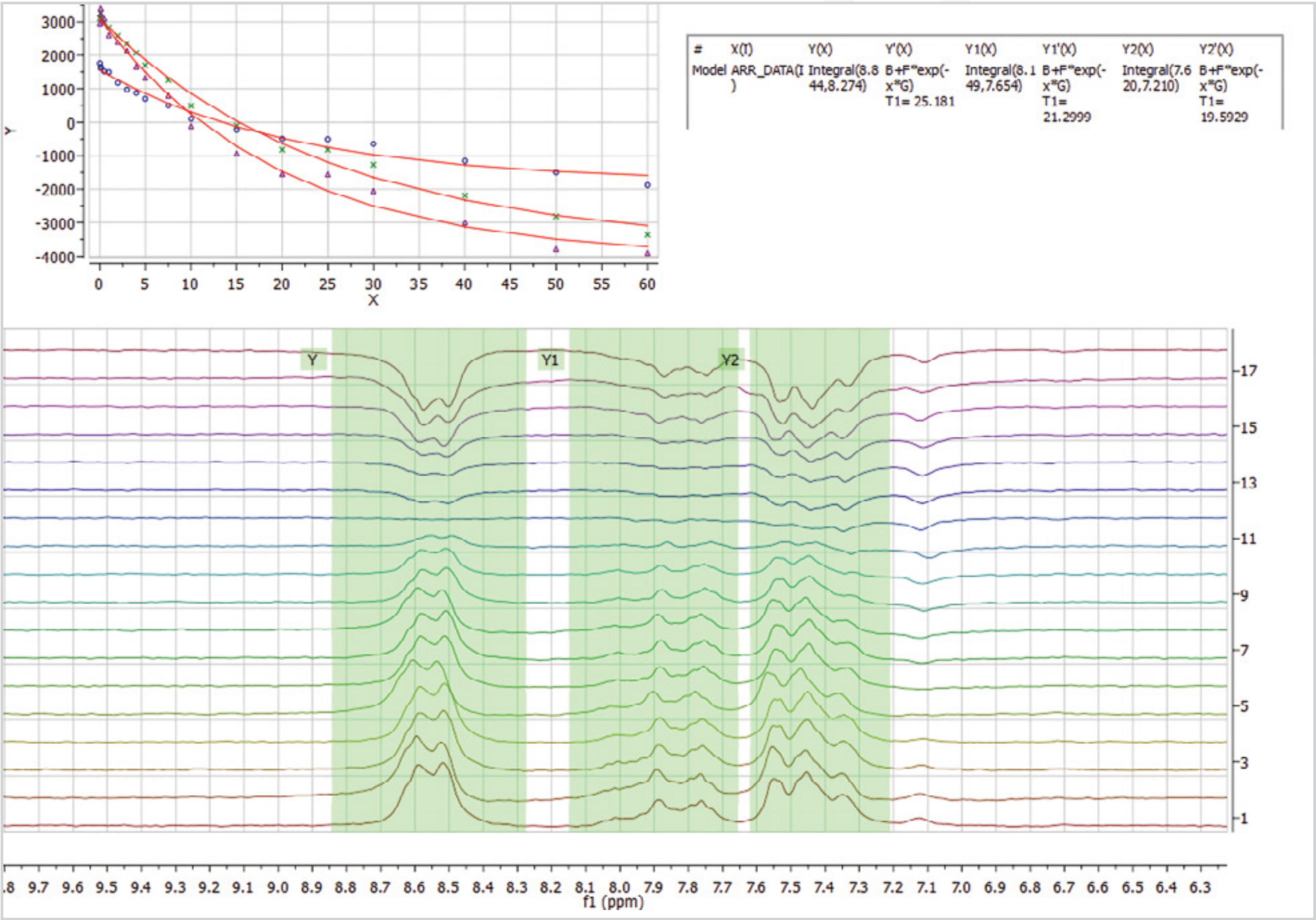
T_1 measurements of pyridine were successfully performed using the **Pulsar** benchtop NMR instrument. The data was then processed using MNOVA. The signals observed in the ^1H NMR spectrum are a lot wider at 60 MHz than they are at 400 MHz. This is because the *J*-coupling of the signals is ~7 times larger in units of chemical shift. Despite this, the three distinct regions for pyridine are readily identifiable, facilitating the calculation of T_1 values for the three different ^1H signals.





#	X(I)	Y(X)	Y'(X)	Y1(X)	Y1'(X)	Y2(X)	Y2'(X)
Model	ARR_DATA(I)	Integral(3.665,3.185)	B+F*exp(-x*G) T1= 4.82216	Integral(2.931,2.498)	B+F*exp(-x*G) T1= 5.24633	Integral(2.494,2.051)	B+F*exp(-x*G) T1= 4.87506

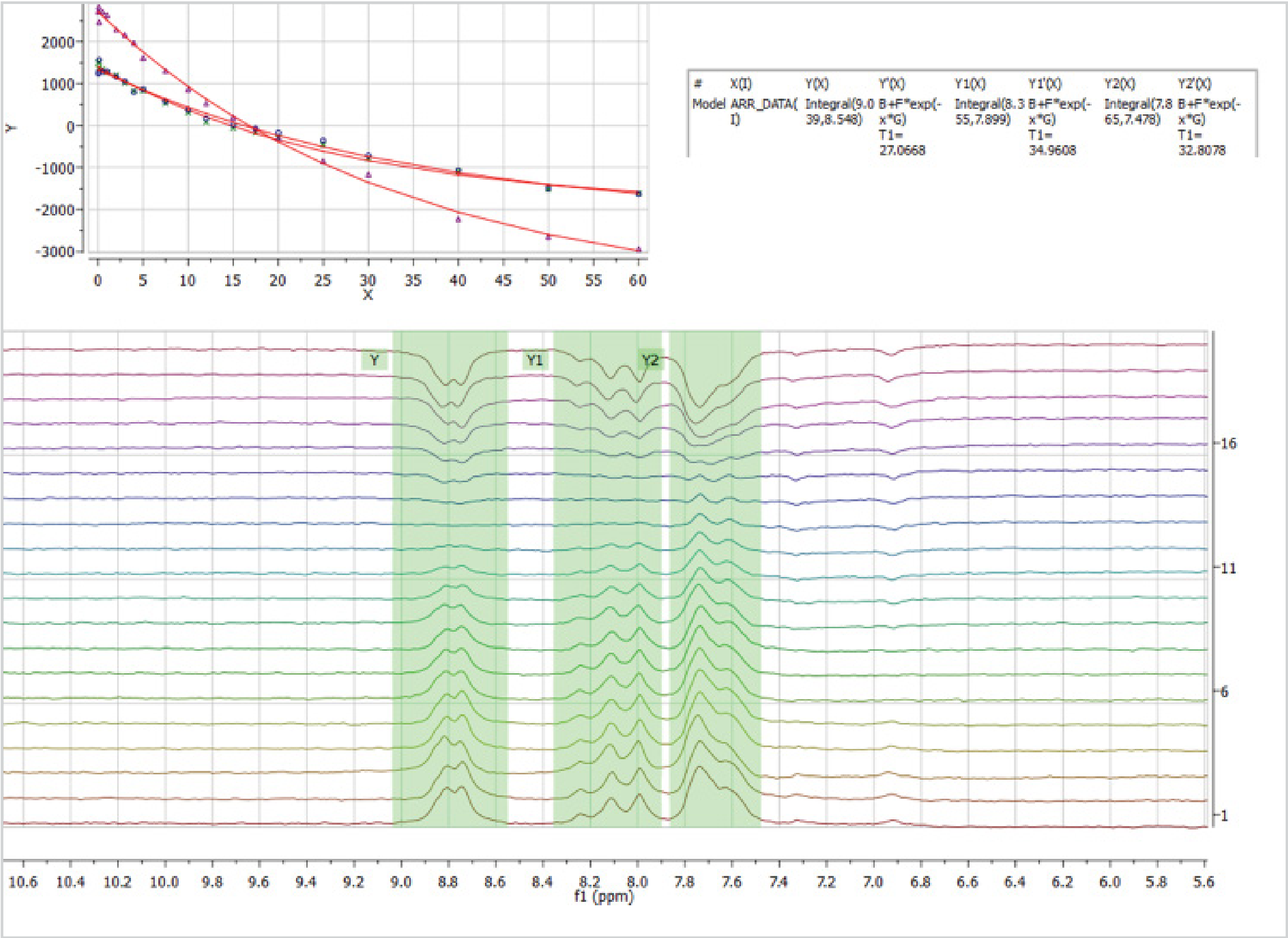
Figure 1: *^1H NMR T_1 data of a sample consisting of 5 µL of pyridine in 600 µL of d_4-methanol in the presence of air. The chemical shift scale has not been referenced to TMS. The variable delays used to collect the 15 different spectra were 0.01, 0.05, 0.1, 0.5, 1, 2, 3, 4, 5, 7.5, 10, 15, 20, 25 and 30 s. Using the data analysis function within MNOVA, the data integrals for the three ^1H signals of pyridine (ortho (Y), meta (Y2) and para (Y1)) were fitted to a T_1 decay. This gave the values of T_1 for the ortho-, meta- and para-protons of pyridine as 4.8, 4.9 and 5.3 s respectively.*



#	X(I)	Y(X)	Y'(X)	Y1(X)	Y1'(X)	Y2(X)	Y2'(X)
Model	ARR_DATA(I)	Integral(8.844,8.274)	B+F*exp(-x*G) T1= 25.181	Integral(8.149,7.654)	B+F*exp(-x*G) T1= 21.2999	Integral(7.620,7.210)	B+F*exp(-x*G) T1= 19.5929

Figure 2: *^{1}H NMR T_1 data of a sample consisting of 5 µL of pyridine and 2 mg [Ir(COD)(IMes)Cl] in 600 µL of d_4-methanol which has been degassed. The variable delays used to collect the 18 different spectra were 0.01, 0.05, 0.1, 0.5, 1, 2, 3, 4, 5, 7.5, 10, 15, 20, 25, 30, 40, 50 and 60 s. Using the data analysis function within MNOVA, the data integrals for the three ^{1}H signals of pyridine (ortho (Y), meta (Y2) and para (Y1)) were fitted to a T_1 decay. This gave the values of T1 for the ortho-, meta- and para-protons of pyridine as 25.4, 19.6 and 22.0 s respectively.*

The T_1 data collected in the absence of air, but in the presence of catalyst gave much longer T_1 times. This is due to the absence of oxygen, which increases spin-lattice relaxation because it is paramagnetic. Even with the added complexity of the spin-transfer catalyst in solution, the three proton environments of pyridine are readily observed and the T_1 values calculated. The measurement of T_1 can also be used to ascertain the effect of deuteration on a spin-system. Under a hydrogen atmosphere, the spin-transfer catalyst becomes active and promotes both spin-transfer and hydrogen-deuterium exchange. The latter is slow, but over long time periods, the ^{1}H signals of pyridine (in particular the ortho-peak) will decrease. Measurement of T_1 shows the effect of reducing the number of spins within a spin-system and thus its role in promoting longer lived polarised states when hyperpolarisation methods, such as SABRE, are employed.



#	X(I)	Y(X)	Y'(X)	Y1(X)	Y1'(X)	Y2(X)	Y2'(X)
Model	ARR_DATA(I)	Integral(9.039,8.548)	B+F*exp(-x*G) T1= 27.0668	Integral(8.355,7.899)	B+F*exp(-x*G) T1= 34.9608	Integral(7.865,7.478)	B+F*exp(-x*G) T1= 32.8078

Figure 3: *^{1}H NMR T_1 data of a sample consisting of 5 µL of pyridine and 2 mg [Ir(COD)(IMes)Cl] in 600 µL of d_4-methanol which has been under a hydrogen atmosphere for circa one week. The variable delays used to collect the 20 different spectra were 0.01, 0.05, 0.1, 0.5, 1, 2, 3, 4, 5, 7.5, 10, 12,15, 17.5, 20, 25, 30, 40, 50 and 60 s. Using the data analysis function within MNOVA, the data integrals for the three ^{1}H signals of pyridine (ortho (Y), meta (Y2) and para (Y1)) were fitted to a T_1 decay. This gave the values of T_1 for the ortho-, meta- and para-protons of pyridine as 27.1, 35.0 and 32.8 s respectively.*

Conclusion

The **Pulsar** system is fully capable of measuring T_1 data which is of interest in the employment of hyperpolarisation based techniques on low-field instrumentation. It also enables the deuteration of a molecule to be tracked and the subsequent change in the T_1 value to be monitored.

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