Magnetic field dependence of singlet state lifetimes and implications for hyperpolarized magnetic resonance

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Purpose

Hyperpolarized magnetic resonance (HP-MR) faces a significant challenge - the fast decay of the hyperpolarization upon injection, which precludes the observation of biochemical processes that take longer than about one minute. Over the last decade, it has been shown that it is possible to restrict the fast decay by using *symmetry-protected singlet states*, enabling detection of low concentration molecules for tens of minutes to hours.[1] Here we examine the field dependence of singlet state relaxation rates and argue that the best magnetic field to conduct the HP-MR experiment may not be, as often believed, the highest accessible magnetic field, but rather the magnetic field at which the relaxation time is longest, which may very well be 1T or less.

Methods

We constructed a pneumatic shuttling setup that allows us to conduct field cycling experiments to measure the singlet state lifetime of many molecules at magnetic fields ranging from 0.01 T and the magnetic field strength of the magnet (8.5 T in the present case). The singlet state is prepared with specialized pulse sequences at 8.5T and then shuttled to the desired low field in less than 0.3 s. The sample is held at the low field for a variable delay and returned into the high field to probe the relaxation.

Results

We find very strong dependencies of the singlet state relaxation rates on the magnetic field as illustrated in Fig. 1 for a diazirine containing molecule. Diazirine moieties are particularly interesting because they can be added to metabolites such as amino acids without drastically altering metabolism. The diazirine moiety has a short singlet state lifetime of 6s at the high magnetic field of 8.5 T but at lower fields the lifetime approaches 8 minutes likely allowing for tracking of distribution and metabolism for half an hour or more. We will also be presenting corresponding field dependent relaxation times for the other molecules depicted in Fig.1 which already have much longer relaxation times at 8.5 T to begin with.[2,3]

Discussion

To appreciate the importance of the field dependent singlet relaxation lifetimes it is critical to understand that no signal-to-noise is sacrificed by going to lower magnetic fields: It is well known that in coil noise dominated NMR experiments the signal-to-noise ratio (SNR) scales with $B_0^{7/4}$. (signal ~B_0^2 , noise ~ $B_0^{1/4}$). For body noise dominated MRI, SNR scales with B_0 (signal ~B_0^2, noise ~B_0). For HP-MR the polarization source is independent of the main magnetic field of the scanner, thus SNR is roughly independent of the magnetic field (signal ~B_0 , noise ~B_0). SNR has even been shown to be better at mT-fields than at high fields of superconducting magnets.[4] Hence we believe that a detailed understanding of the relaxation properties at varying magnetic fields is critically important.

Conclusion

The relaxation mechanism with the strongest field dependence is Chemical Shift Anisotropy and scales with B_0^2. Given that the SNR is roughly independent of the main magnetic field it is very appealing to explore HP-MR experiments at low magnetic fields where signal lifetime can be extended significantly, possibly allowing for tracking of metabolites or perfusion agents for hours. The data suggests that chemical motifs exist that will make this promise a reality. The diphenyl-acetylene (DPA) derivatives depicted in Fig.1 represent a step in this direction: For example the butanoic acid functionalized DPA is reported as a diabetes drug. The forthcoming exploration of additional chemical motifs will likely yield biologically important molecules to be used HP-MR experiments probing metabolic diseases such as diabetes, cancer or cardiovascular disease.

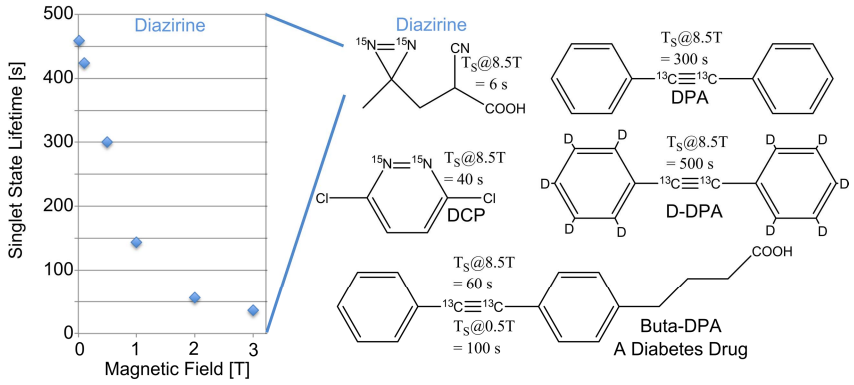

Fig. 1. The singlet state lifetime can exhibit very strong field dependence as exemplified by the diazirine compound. The singlet state lifetime for diazirine at 8.5 T is only 6s but at lower fields it approaches 8 minutes, likely enabling tracking of compounds with this moiety for half an hour in hyperpolarized experiments. In our presentation we will also detail the field dependence of all the other depicted molecules, where we already start from a much longer singlet state lifetime observed at the high magnetic field of 8.5 T.

References

1. Levitt (2012) *Ann. Rev. Phys. Chem.* 63, 89
2. Feng et al. (2013) *J. Am. Chem. Soc.* 135(26), 9632
3. Claytor et al. (2014) *J. Am. Chem. Soc.* 136 (43), 15118
4. Coffey et al. (2013) *J. Magn. Reson.* 237,169