Preserving nuclear polarization for longer than T1 time scale

Eric Han Literature Seminar November 13 2019

One major advantage of nuclear magnetic resonance (NMR) is the relatively long lifetime of excited nuclear spin states, which allows studies of slow molecular motion, diffusion, flow, etc by NMR as well as utilizing NMR in quantum computation. However, any manipulation of the nuclear spin interactions by radio-frequency (rf) pulses in such studies is limited by the time scale of the nuclear spin order relaxing to thermal equilibrium of the system, characterized by T_1, also known as spin-lattice, or longitudinal, relaxation time constant. Being able to preserve the magnetization for a longer period would greatly enhance the performance of NMR in the studies described above as well as aid technology advancement in the field of NMR.

In 2004, Carravetta et al reported a method of generating and storing nuclear magnetic spin order for significantly longer than T_1 time scale[1]. This method involves manipulating magnetization of a spin system consists of two identical nuclei at different chemical to generate a non-equilibrium nuclear spin singlet state which is immune to intramolecular dipole-dipole relaxation. The pulse sequence for generating the long-lived spin order and a schematic depiction of the process are shown in FIG 1.

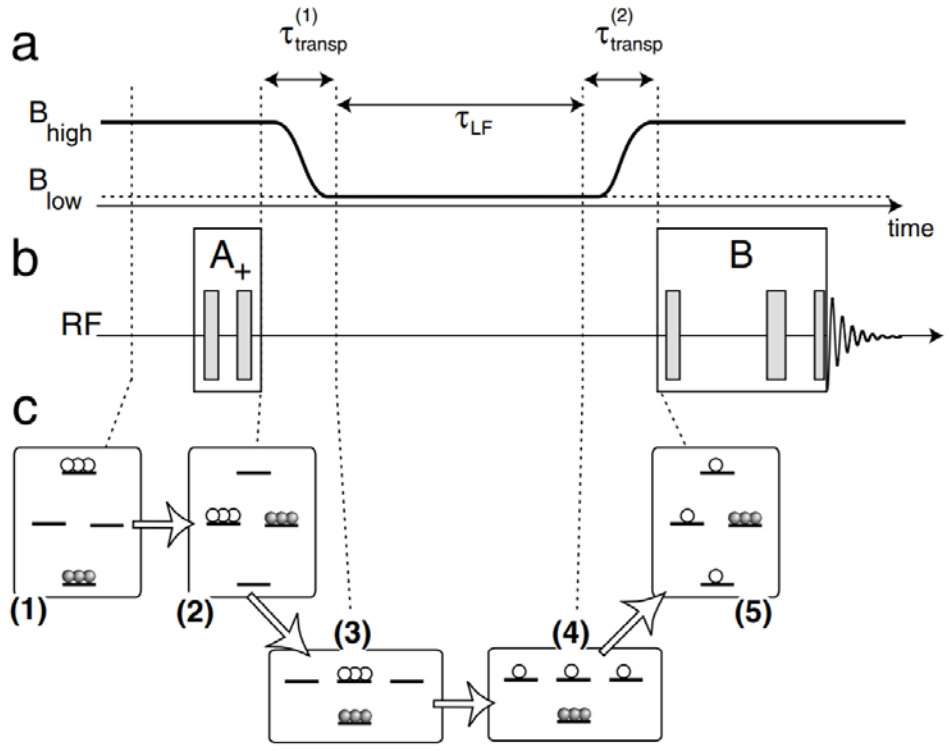

FIG 1. (a) Magnetic field scheme used in generating long-lived singlet state; (b) pulse sequence used to generate long-lived singlet state; (c) a schematic depiction of the two-spin system during the period of experiment.

The sample is transported physically between a high magnetic field and a low magnetic field, in the range of 0-20 mT [1,10], over a short τ_{transp}. The pulse sequence described in FIG 1 was performed at Larmor frequencies in high field.

Before any pulsing is performed on the system in high magnetic field, shown in time point (1) in FIG 1(c), the $|\alpha\alpha\rangle$ and $|\beta\beta\rangle$ states are occupied, with slightly more population in $|\alpha\alpha\rangle$ state which is demonstrated by the filled balls in the scheme. It is assumed that chemical shift $\delta_2>\delta_1$ so that energy $E_{\alpha\alpha}<E_{\alpha\beta}<E_{\beta\alpha}<E_{\beta\beta}$. The pulse sequence segment A+ and its alternative form A- is designed to only affect spin state of one of the two spins. As a result of pulse sequence, A+, the population of $|\alpha\alpha\rangle$ is exchanged with that of $|\alpha\beta\rangle$ and the population of $|\beta\beta\rangle$ is exchanged with that of $|\beta\alpha\rangle$. The system is then adiabatically transferred to low magnetic field in which J-coupling, described by Hamiltonian $\hat{H}=2\pi J I_1 \cdot I_2$, is much more dominant than Zeeman effect. The J-coupling Hamiltonian has four eigenstates: three components of a triplet state denoted by $|T_1\rangle=|\alpha\alpha\rangle$, $|T_0\rangle=(1/\sqrt{2})(|\alpha\beta\rangle+|\beta\alpha\rangle)$, and $|T_{-1}\rangle=|\beta\beta\rangle$ with the same eigenvalue $+1/2\pi J$ and a singlet state $|S_0\rangle= (1/\sqrt{2})(|\alpha\beta\rangle-|\beta\alpha\rangle)$ at lower energy $-3/2\pi J$. The populations originally on $|\alpha\beta\rangle$ and $|\beta\alpha\rangle$ transfer to the $|T_0\rangle$ and $|S_0\rangle$ states due to mixing of the two states, with slightly more population on $|S_0\rangle$. The population on $|T_0\rangle$ distributes evenly over the three degenerate triplet states over the period that the system is in low magnetic field, τLF. Then the system is adiabatically transferred back to high magnetic field in which states $|\alpha\alpha\rangle$, $|\alpha\beta\rangle$, $|\beta\alpha\rangle$ and $|\beta\beta\rangle$ are established again. The population on low field singlet state $|S_0\rangle$ is transferred to $|\alpha\beta\rangle$ under high magnetic field.

The population distribution shown in time point (4) of FIG. 1(c) can maintain indefinitely if dipolar coupling is the only relaxing mechanism and if the low field is exactly 0 because dipole-dipole coupling is symmetric with respect to exchange thus cannot interconvert singlet and triplet states [2]. The only way of detecting the singlet state is to transfer the system to a high magnetic field and pulse sequence segment B has been shown to be able to convert population on state $|\alpha\beta\rangle$ to observable NMR signal which is very distinguishable from T1 relaxation signal. Decay time constants of such singlet spin orders in 2,3-dibromothiphene and 2-chloroacrylonitrile have been measured to be 104 ± 5 s and 141 ± 7 s, respectively, while their T_1 relaxation time are about 17 s and 7.8 s. The storage effect is also relatively independent from field strength of the low magnetic field for fields under 20 mT [1,10].

Application of this effect had been demonstrated in various types of study involving nuclear spins. Shen et al showed that hyperpolarized $^{15}N_2$-diazirine sustains both singlet and magnetization states and leads to great signal enhancement as well as long-lasting polarization in nuclear magnetic resonance imaging [4]. Imaging studies utilizing singlet states tagging had also been demonstrated in monitoring macroscopic diffusion in real space and slow flow by Pileio et al [5] and Ahuja et al [6]. This could also potentially be implemented in in vivo MRI if biocompatible agents can be found [5]. Buratto et al had demonstrated that long-lived state of a ^{19}F-^{19}F system can be used to accurately measure dissociation rate of weak ligand-protein complexes [7]. Long-lived singlet state had also been shown to aid hyperpolarization experiments and result in better polarization [8,9].

Reference

1. Carravetta, M.; Johannessen O. G.; Levitt, M. H. Beyond the T1 Limit: Singlet Nuclear Spin States in Low magnetic Fields. Phys. Rev. Lett. 2004, 92 (15).
2. Carravetta, M.; Levitt, M. H. Long-Lived Nuclear Spin States in High-Field Solution NMR. J. Am. Chem. Soc. 2004, 126, 6228-6229.
3. Levitt, M. H. Long live the singlet state! J. Magn. Res. 2019, 306, 69-74.
4. Shen, K.; Logan, A. W. J.; Colell, J. F. P.; Bae, J.; Ortiz, G. X., Jr.; Theis, T.; Warren, W. S.; Malcomson, S. J.; Wang, Q. Diazirine as Potential Molecular Imaging Tags: Probing the Requirements for Efficient and Long-Lived SABRE-induced Hyperpolarization. Angew. Chem. Int. Ed. 2017, 56, 12112-12116.
5. Pilieo, G.; Dumez, J.; Pop, I.; Hill-Cousins, J. T.; Brown. R. C. D. Real-space imaging of macroscopic diffusion and slow flow by singlet tagging MRI. J. Magn. Res. 2015, 252, 130-134.
6. Ahuja, P.; Sarkar, R.; Vasos, P. R.; Bodenhausen, G. Diffusion Coefficients of Biomolecules Using Long-Lived Spin States. J. Am. Chem. Soc. 200, 131, 7498-7499.
7. Buratto, R.; Mammoli, D.; Canet, E.; Bodenhausen, G. Ligand-Protein Affinity Studies Using Long-Lived States of Fluorine-19 Nuclei. J. Med. Chem. 2016, 59, 1960-1966.
8. Elliot, S. J.; Meier, B.; Vuichoid, B.; Stevanato, G.; Brown, L. J.; Alonso-Valdesueiro, J.; Emsley, L.; Jannin, S.; Levitt, M. H. Hyperpolarized long-lived nuclear spin states in monodeuterated methyl groups. Phys. Chem. Chem. Phys. 2018, 20, 9755-9759.
9. Roy, S. S.; Rayner, P. J.; Norcot, P.; Green, G. G. R.; Duckett, S. B. Long-lived states to sustain SABRE hyperpolarized magnetization.
10. Carravetta, M.; Levitt, M. H. Theory of long-lived nuclear spin states in solution nuclear magnetic resonance. I. Singlet states in low magnetic field. J. Chem. Phys. 2005, 122, 214505.