Probing scalar coupling differences via long-lived singlet states

Stephen J. DeVience [a], Ronald L. Walsworth [b,c,d,*], Matthew S. Rosen [c,e,f]

[a] Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford St., Cambridge, MA 02138, USA
[b] Harvard-Smithsonian Center for Astrophysics, 60 Garden St., Cambridge, MA 02138, USA
[c] Department of Physics, Harvard University, 17 Oxford St., Cambridge, MA 02138, USA
[d] Center for Brain Science, Harvard University, 52 Oxford St., Cambridge, MA 02138, USA
[e] Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA
[f] A.A. Martinos Center for Biomedical Imaging, 149 Thirteenth St., Charlestown, MA 02129, USA

ABSTRACT

We probe small scalar coupling differences via the coherent interactions between two nuclear spin singlet states in organic molecules. We show that the spin-lock induced crossing (SLIC) technique enables the coherent transfer of singlet order between one spin pair and another. The transfer is mediated by the difference in *syn* and *anti* vicinal or long-range J couplings among the spins. By measuring the transfer rate, we calculate a J coupling difference of 8 ± 2 mHz in phenylalanine–glycine–glycine and 2.57 ± 0.04 Hz in glutamate. We also characterize a coherence between two singlet states in glutamate, which may enable the creation of a long-lived quantum memory.

Published by Elsevier Inc.

1. Introduction

Magnetic resonance experiments utilizing hyperpolarized media or exploring weak spin–spin interactions are often limited by the relatively short spin–lattice relaxation time, T_1, of the nuclear spins. Recently, the T_1 limit was greatly extended for a wide variety of molecules using nuclear spin singlet states, which can possess lifetimes $T_S > T_1$ [1–9]. The singlet state has subsequently been used to extend the lifetime of hyperpolarized spins for spectroscopy and imaging, to measure slow diffusion and transport, and to isolate targeted NMR spectra in heterogeneous samples via a quantum filter [10–18]. As a consequence of symmetry differences, the singlet state does not interact with its associated triplet states, and singlet state relaxation only occurs via weaker higher-order processes involving surrounding spins [8,19–22]. However, the same symmetry differences also make the singlet state inaccessible via conventional RF pulses. An early solution for creating singlet states was to start with pairs of inequivalent spins, such as those of citric acid or aspartate (Fig. 1a), and then create a singlet state using strong spin-locking. Subsequently, pulse sequences such as M2S and SLIC were developed to transfer polarization from the triplet states to the singlet state of two nearly equivalent spins by utilizing their small chemical shift difference,

thereby making spin-locking unnecessary [23–25]. Analogous techniques have been demonstrated for a particular 4-spin configuration of coupled spin pairs (Fig. 1b), which allows the singlet state of magnetically equivalent spins to be accessed, and for transferring polarization from parahydrogen to substrate molecules during signal amplification by reversible exchange (SABRE) polarization [9,26–30]. In all cases, the pulse sequences can be used not only to prepare singlet states, but also to determine spectroscopic parameters, such as J coupling and chemical shift differences, that would otherwise be hidden in a conventional spectrum due to spin state dressing.

In the symmetric 4-spin systems previously studied, the singlet state cannot be prepared selectively in one spin pair or the other. Instead, spin order is simultaneously transferred from two triplet states into two singlet states. Although that configuration creates ideal singlet populations for hyperpolarized work, in certain situations it would be useful to create a larger variety of spin states. For example, if one wishes to store quantum information in the form of arbitrary populations and coherences of long-lived singlet states, then each individual singlet state must be made accessible. To explore this possibility, we consider here a 4-spin configuration in which the two distinct singlet states in two nearly equivalent spin pairs of an organic molecule can be prepared and manipulated selectively (Fig. 1c). We show that coherent interactions occur between the two singlet states mediated by the difference in *syn* and *anti* vicinal or long-range J couplings. This interaction allows small J coupling differences to be measured, even when

* Corresponding author at: Harvard-Smithsonian Center for Astrophysics, MS 59, 60 Garden St., Cambridge, MA 02138, USA.
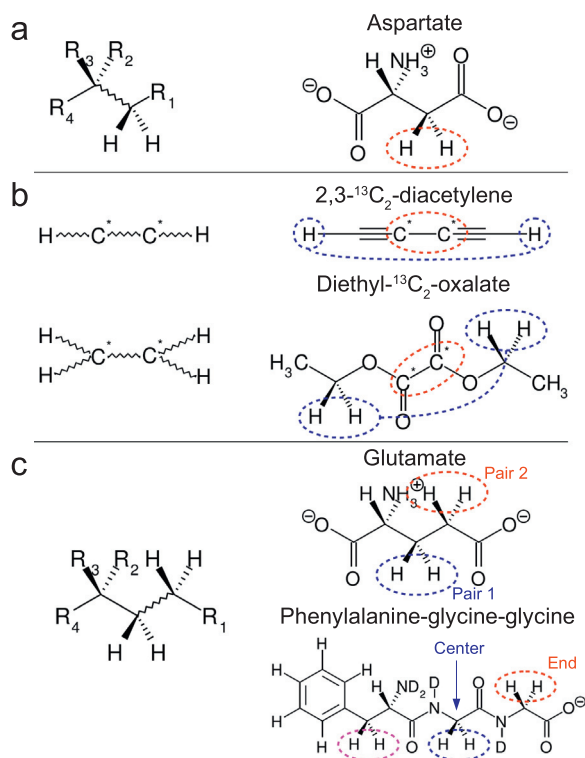 *E-mail address:* rwalsworth@cfa.harvard.edu (R.L. Walsworth).

Fig. 1. Example families of molecular structures used for singlet state experiments. Squiggly lines indicate that a variable number of intervening bonds is possible. (a) A pair of inequivalent or nearly equivalent geminal protons. Examples: aspartate, citric acid, glycerol formal. (b) One pair of identical spins sandwiched between one or more pairs of identical spins of a different nucleus (here * indicates locations enriched with ^{13}C). Examples: diacetylene, diethyloxalate. (c) Two or more pairs of nearly equivalent protons. Examples: glutamate, phenylalanine–glycine–glycine. Other geometries not shown include vicinal proton pairs, neighboring ^{15}N nuclei, and neighboring phosphate groups.

$\Delta J \ll 1/T_1$. Moreover, the singlet–singlet interaction can be controlled and used to create a coherent superposition between two singlet states.

We demonstrate the technique in proton pairs of the amino acid glutamate and the tripeptide phenylalanine–glycine–glycine (phe–gly–gly). These molecules are protein building blocks, and glutamate is an important neurotransmitter. In glutamate, we selectively prepare one singlet state and then perform both Rabi and Ramsey measurements in a subspace defined by the two singlet states. In the Rabi measurement, singlet state polarization is coherently transferred back and forth between the two spin pairs. The rate of transfer provides a measure of singlet–singlet interaction strength. In the Ramsey measurement, a coherent superposition of singlet states is created and allowed to evolve in the singlet–singlet subspace before being projected onto one spin pair or the other. The frequency of the associated oscillations provides a measurement of the energy difference between singlet states. We also implement a Rabi measurement in phe–gly–gly to demonstrate the technique's utility for measuring weak coupling differences. In phe–gly–gly, the scalar coupling between spin pairs is small compared with the spin–spin relaxation rate, i.e., $J \ll 1/T_2 \approx 1/T_1$, so that the coupling is difficult to measure from spectra or coherence transfer experiments. However, because the nuclear spin singlet state has a lifetime $T_S \gg T_1$, coherent interactions between singlet states are detectable, and we are able to measure a scalar coupling difference on the order of 10 mHz among the spins. We discuss possible applications of this technique in protein spectroscopy and biomedical imaging.

2. Theory

For a single spin in a static magnetic field B_0, the spin eigenstates can be described in the Zeeman basis as aligned or anti-aligned with B_0, i.e., $|\uparrow\rangle$ or $|\downarrow\rangle$. However, in a system with multiple spins, the wavefunctions can only be described exactly in the Zeeman basis in the case of non-interacting spins. Any spin–spin interactions cause the Zeeman states to mix, thereby creating dressed states that represent the true eigenstates of the system. In the case $|J| < |\Delta v|$, i.e., weak scalar coupling compared with any resonance frequency difference between spins, the dressed eigenstates can be calculated using perturbation theory, and they remain substantially similar to the Zeeman eigenstates. However, in the case $|J| \gg |\Delta v|$, perturbation theory fails and the dressed states must instead be calculated by diagonalizing the full Hamiltonian. The resulting eigenstates are very different from the Zeeman states and can possess unique properties, such as an extended lifetime in the case of the singlet state.

One of the simplest multiple spin systems consists of two spin-1/2 nuclei interacting via scalar coupling. If the coupling strength is zero, the spin states can be represented by the product states $|\uparrow\uparrow\rangle, |\uparrow\downarrow\rangle, |\downarrow\uparrow\rangle$, and $|\downarrow\downarrow\rangle$. When the scalar coupling between spins is strong compared with their resonance frequency difference ($|J| \gg |\Delta v|$), or if strong spin-locking is applied ($|v_n| > 5|\Delta v|$, where v_n is the spin-lock nutation frequency), then diagonalization reveals that the spin pair is instead described by singlet and triplet eigenstates. For the case of strong scalar coupling and magnetically equivalent spins, one finds a spin-0 singlet state $|S_0\rangle = (|\uparrow\downarrow\rangle - |\downarrow\uparrow\rangle)/\sqrt{2}$ and three spin-1 triplet states $|T_-\rangle = |\uparrow\uparrow\rangle, |T_0\rangle = (|\uparrow\downarrow\rangle + |\downarrow\uparrow\rangle)/\sqrt{2}$, and $|T_+\rangle = |\downarrow\downarrow\rangle$.

If the two spins are nearly but not exactly equivalent, then the small chemical shift difference, Δv, couples singlet and triplet states. As described elsewhere, this interaction can be used to prepare the singlet state by spin-locking at a nutation frequency such that triplet and singlet energy levels cross (spin-lock induced crossing or SLIC) [24,26,31,32]. The effect comes about because spin-locking rearranges the triplet states and perturbs their energy levels, leading to the spin-locked eigenstates:

$$|\phi_+\rangle = \frac{1}{2}(|\uparrow\downarrow\rangle + |\downarrow\uparrow\rangle + |\uparrow\uparrow\rangle + |\downarrow\downarrow\rangle) = \frac{1}{\sqrt{2}}|T_0\rangle + \frac{1}{2}(|T_-\rangle + |T_+\rangle)$$

$$|\phi_0\rangle = \frac{1}{\sqrt{2}}(|\uparrow\uparrow\rangle - |\downarrow\downarrow\rangle) = \frac{1}{\sqrt{2}}(|T_-\rangle - |T_+\rangle)$$

$$|\phi_S\rangle = \frac{1}{\sqrt{2}}(|\uparrow\downarrow\rangle - |\downarrow\uparrow\rangle) = |S_0\rangle$$

$$|\phi_-\rangle = \frac{1}{2}(|\uparrow\downarrow\rangle + |\downarrow\uparrow\rangle - |\uparrow\uparrow\rangle - |\downarrow\downarrow\rangle) = \frac{1}{\sqrt{2}}|T_0\rangle - \frac{1}{2}(|T_-\rangle + |T_+\rangle). \quad (1)$$

See Supplementary Materials for further details.

In a system composed of two pairs of spin-1/2 nuclei, the pairs can be labeled $i = 1$ and 2, with each pair's spins labeled $j = a$ and b. For the molecules studied, the interpair spin–spin coupling is weak compared with the intrapair coupling, so at first order the system can be approximated by 16 new product states formed from the singlet and triplet states of each spin pair. The relationships among these states form the basis for previous studies in which polarization was transferred from triplet product states $|TT\rangle$ to the singlet product state $|S_0S_0\rangle$ [26–28]. In the present study, we consider a different situation, in which we selectively transfer polarization to the singlet state of one spin pair while the other spin pair remains in the triplet state. We then only need to consider product states containing the triplet states of one spin pair and the singlet state of the other, represented by $|TS_0\rangle$ and $|S_0T\rangle$. Here, the overall triplet component is some combination of the individual triplet states and can be described by