Communication

Life-times of long-lived coherences under different motional regimes

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ABSTRACT

The transverse relaxation rate R_2 of single quantum coherences, the relaxation rate R_{LLC} of long-lived coherences (LLC), and the ratio R_2/R_{LLC} have been studied by experiment, simulation and theory in the two-spin system formed by the Glycine aliphatic protons of the dipeptide Alanine–Glycine as a function of the correlation time of rotational diffusion.

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1. Introduction

Singlet and triplet states [1–3] associated with a pair of magnetically equivalent spins ½ belong to different irreducible representations of the permutation group. Transitions between singlet and triplet states are therefore symmetry-forbidden and have vanishing transition probabilities. However, in certain cases, it is possible to excite coherences that span such forbidden transitions. The evolution of such coherences can be monitored indirectly as a function of time by two-dimensional (2D) spectroscopy [4]. It has been shown recently [5] that a coherent superposition of a singlet state |S_0> and a central triplet state |T_0>, known as a *long-lived coherence* (LLC), can have a very long life-time. Its decay rate R_{LLC} can be significantly slower than the transverse relaxation rate R_2 of single quantum coherences (SQC) in the same system. This opens new perspectives for homogeneous line narrowing in NMR spectroscopy.

A pair of equivalent spins ½ is best described in the singlet–triplet basis (STB) $\Phi_{STB} = \{|T_{+1}\rangle, |T_0\rangle, |S_0\rangle, |T_{-1}\rangle\}$, where $T_{+1} = |\alpha\alpha\rangle$; $T_0 = N(|\alpha\beta\rangle + |\beta\alpha\rangle)$; $S_0 = N(|\alpha\beta\rangle - |\beta\alpha\rangle)$; and $T_{-1} = |\beta\beta\rangle$ with $N = 2^{-½}$. A long-lived coherence Q_{LLC} can be defined as a coherent superposition of the singlet state |S_0> and the central triplet state |T_0>:

$$Q_{LLC} = |S_0\rangle\langle T_0| + |T_0\rangle\langle S_0| \tag{1}$$

In terms of Cartesian angular momentum operators, Q_{LLC} can be written as:

$$Q_{LLC} = (I_x - S_x) \tag{2}$$

In order to observe a Q_{LLC} in a two-spin system with two magnetically *in*equivalent nuclei I and S, one must first excite a difference ($I_x - S_x$) and then render I and S magnetically equivalent by applying a strong radio-frequency field, in the simplest case a continuous-wave (CW) radio-frequency (*rf*) field with a carrier positioned half-way between the two chemical shifts. Starting from Boltzmann equilibrium ($I_z + S_z$), a semi-selective $(\pi)_x$ inversion pulse is first applied to the doublet of spin S to generate ($I_z - S_z$). A non-selective pulse $(\pi/2)_y$ converts this state into ($I_x - S_x$). When a CW field is applied along the x-axis of the rotating frame, the chemical shifts of the two spins are in effect suppressed. At this point, the system is best described in Φ_{STB} rather than in the product basis. The long-lived coherence Q_{LLC} oscillates with a frequency that corresponds to the separation between the singlet state |S_0> and the central triplet state |T_0> [5]. If the *rf* field is sufficiently strong, this splitting is equal to the scalar coupling constant J_{IS}. The transverse relaxation occurs with a rate constant R_{LLC}, so that the evolution of the long-lived coherence is described by:

$$\frac{d}{dt}Q_{LLC} = -(R_{LLC} + i\pi J_{IS})Q_{LLC} \tag{3}$$

In a two-spin system, the SQC relaxation rate is given by the usual expression:

$$R_2 = \left(\frac{b_{IS}^2}{20}\right)[9J(0) + 15J(\omega) + 6J(2\omega)] + R_2^{ext} \tag{4}$$

where $b_{IS} = -\frac{\mu_0}{4\pi}\frac{\gamma^2\hbar}{r_{IS}^3}$ is the strength of the homonuclear dipolar coupling, r_{IS} the inter-nuclear distance, $J(\omega) = \frac{\tau_c}{1+\omega^2\tau_c^2}$ the spectral density function, and τ_c the rotational correlation time. The term R_2^{ext} comprises contributions from external random fluctuating fields

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(including those arising from dissolved oxygen and other paramagnetic species), the modulations of the chemical shift anisotropies (CSA's), and dipolar interactions with further nuclei R, R', etc.

The relaxation rates R_{LLC} of LLC's can be significantly smaller than the transverse relaxation rates R_2 in the same system. If there are only two spins, the main mechanism that drives relaxation of R_{LLC} arises from dipolar interactions between the two 'active' spins I and S. (Note that this stands in contrast to the relaxation rate R_{LLS} of the population of the long-lived state $|S_0\rangle$, for which the dipolar interaction between I and S is completely ineffective.) The relaxation rate constant R_{LLC} can be calculated by Redfield theory [6]. If the rf field is sufficiently strong, it need not be taken into account explicitly and it is sufficient to retain the truncated Hamiltonian where the two spins I and S have the same Larmor frequency. The transverse relaxation rates R_{LLC} of long-lived coherences under strong rf irradiation can be evaluated in analogy to the longitudinal relaxation rates R_{LLS} of long-lived states [7–9]:

$$R_{LLC} = \left(\frac{b_{IS}^2}{20}\right)[J(0) + 3J(\omega) + 6J(2\omega)] + R_{LLC}^{ext} \quad (5)$$

Eqs. (4) and (5) were derived assuming isotropic reorientation, and are limited to rigid symmetric molecules, which may not be entirely satisfactory for the applications discussed below. The term R_{LLC}^{ext} again comprises contributions from external random fluctuating fields arising from dissolved oxygen and other paramagnetic species, the modulations of the chemical shift anisotropies (CSA's) of the two active spins (except if they are completely correlated), and dipolar interactions with further nuclei R, R'. If the external contributions R_{LLC}^{ext} are small, the long-lived coherence Q_{LLC} has a longer life-time than single quantum coherences. Eqs. (4) and (5) predict that the ratio R_2/R_{LLC} varies in the range $3 < R_2/R_{LLC} < 9$ depending on the rotational correlation time (Fig. 1). In the fast tumbling regime ($\tau_c \ll 1/\omega_0$), the spectral density functions are equal at all frequencies, i.e., $J(0) = J(\omega) = J(2\omega)$, hence $R_2/R_{LLC} = 3$. When molecular tumbling slows down, i.e., when $\tau_c \gg 1/\omega_0$, the ratio can approach the limit $R_2/R_{LLC} = 9$.

In this communication, we have sought to verify these predictions by experiments and simulations for the dipeptide Ala–Gly, which is admittedly neither a rigid nor an isotropic rotor. In this system, the two H^α protons of Glycine are diastereotopic with a difference in chemical shifts of 0.1 ppm (42.7 Hz at 9.4 T or 400 MHz for protons) and a scalar coupling $J(H^\alpha, H^\alpha) = -17.2$ Hz [10]. The experimental decay rates R_2 and R_{LLC} and the ratio R_2/R_{LLC} were compared with numerical simulations as a function of τ_c. In the simulations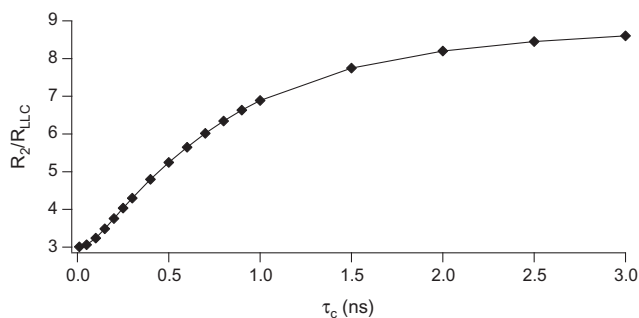 of Fig. 1, the correlation time of rotational diffusion was varied in the range $0.01 < \tau_c < 3$ ns. As described by Eqs. (4) and (5), the ratio R_2/R_{LLC} is close to 3 for fast motion and approaches 9 asymptotically in the slow motion limit.

Experiments were carried out to measure the ratio R_2/R_{LLC} in a sample of 1 M Ala–Gly dissolved in a 3:1 (v/v) D_2O/DMSO-d_6 mixture, where the viscosity strongly depends on temperature [11]. The relationship between the (microscopic) rotational correlation time τ_c and the (macroscopic) viscosity η is given by the Stokes–Einstein equation [12]. In the numerical simulations, we varied τ_c empirically to match the simulated and experimental R_2 rates at each temperature. The slow motion regime could not be fully explored because one cannot lower the temperature enough without causing excessive line-broadening, which makes LLC experiments difficult.

The rates R_2 were measured by on-resonance $R_{1\rho}$ experiments [5] and fitted with $I(t) = I_0 \exp(-R_2 t_1)$, assuming that $R_2 = R_{1\rho}$. The rates R_{LLC} were measured with the pulse sequence described by Sarkar et al. [5] and by fitting the intensities of the signals $(I_x - S_x)$ that oscillate as a function of t_1 with the function $I(t_1) = I_0 \cos(2\pi J_{IS} t_1) \exp(-R_{LLC} t_1)$. The role of the external contributions R_{LLC}^{ext} and R_2^{ext} has been evaluated as follows: The contributions of the chemical shift anisotropies (CSA's) of the two active spins can be neglected for aliphatic H^α protons in Glycine at 400 MHz. In the dipeptide Ala–Gly, dipolar interactions to further nuclei R, R' may arise from the lone H^α and three H^β protons of the neighbouring Alanine residue, the amide proton being replaced by a deuteron in this solvent. It turns out that, because of their distance, these four Alanine protons do not have a significant effect on the rate R_2 of the two Glycine protons, as evidenced by numerical calculations carried out with and without considering the four Alanine protons. Since the calculation of R_{LLC} rates in a 6-spin system is quite demanding, we have considered a reduced 3-spin system by dropping the three H^β protons of the Alanine residue, and found that the ratio R_2/R_{LLC} in Glycine is not affected by the remaining Alanine H^α proton, regardless of τ_c. We may therefore assume that the ratio R_2/R_{LLC} is not affected by the four remote protons in Ala–Gly.

On the other hand, paramagnetic oxygen was found to yield a significant contribution to R_{LLC}^{ext}. If one does not remove oxygen, the observed experimental ratio was in the range $2.2 < R_2/R_{LLC} < 2.5$ for $0.04 < \tau_c < 0.06$ ns (Fig. 2). After three freeze–pump–thaw cycles under Argon atmosphere, the ratio R_2/R_{LLC} increases, particularly in the fast tumbling regime, in comparison to the non-degassed sample (Fig. 2). As the correlation time τ_c increases with
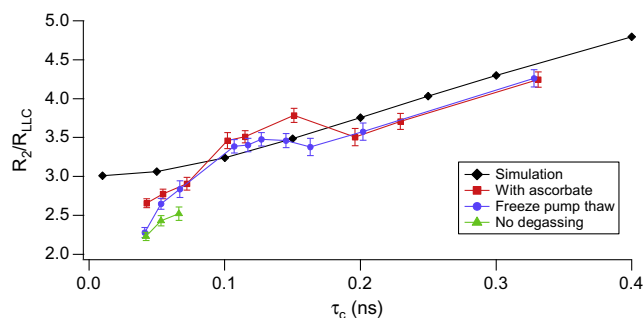

Fig. 1. Numerical simulations of the ratio R_2/R_{LLC} calculated by GAMMA [14] as a function of the rotational correlation time τ_c. The two H^α protons of Glycine in the dipeptide Ala–Gly were treated as an isolated two-spin system in a static field $B_0 = 9.4$ T (400 MHz for protons), $\Delta\nu_{IS} = 42.7$ Hz, $J_{IS} = 17.2$ Hz, $r_{IS} = 1.77$ Å, rf amplitude $\nu_1 = 1500$ Hz, with the rf carrier half-way between the two chemical shifts. Only the dipolar interaction between the two active nuclei I and S was taken into account.

Fig. 2. Simulations of the ratio R_2/R_{LLC} calculated by GAMMA [14] as a function of τ_c (black line with diamonds). The same parameters as in Fig. 1 were used. Experimental ratios R_2/R_{LLC} in 1 M Ala–Gly dissolved in a D_2O/DMSO 3:1 mixture without degassing (green triangles), after degassing with three freeze–pump–thaw cycles under Argon (blue circles), and after addition of 20 mM sodium ascorbate as a reducing agent to quench dissolved paramagnetic oxygen (red squares). The experimental points correspond to temperatures between 300 and 248 K. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

decreasing temperature, the trend of the ratio R_2/R_{LLC} agrees qualitatively with the simulations. Paramagnetic oxygen can be quenched by the addition of 20 mM sodium ascorbate (vitamin C) as a reducing agent [13]. Like in the degassed sample, the ratio R_2/R_{LLC} follows the simulated curve as τ_c decreases. In the range $0.04 < \tau_c < 0.06$ ns, the ratio R_2/R_{LLC} is even higher after degassing by freeze–pump–thaw cycles (Fig. 2). Nevertheless, the experimental ratio R_2/R_{LLC} remains lower than 9. This could be due to various contributions to R_2^{ext} and R_{LLC}^{ext}, such as residual paramagnetic oxygen in the sample and other sources of fluctuating fields.

2. Conclusions

We have compared the transverse relaxation rates R_{LLC} of long-lived coherences with the decay rates R_2 of single-quantum coherences. It was shown by theory and simulations that the ratio R_2/R_{LLC} varies from 3 to 9 as a function of the rotational correlation time τ_c. In the extreme narrowing regime, the experimental ratio was found to be about $R_2/R_{LLC} = 2.6$, somewhat lower than expected, even when paramagnetic oxygen was removed from the sample by freeze–pump–thaw cycles or scavenged by the addition of ascorbate. The slow motion regime could not be fully explored because one cannot lower the temperature below 248 K without causing excessive line-broadening, but the highest ratio was found to be $R_2/R_{LLC} = 4.6$. The experiments provide evidence of the efficiency of ascorbate as scavenger of paramagnetic oxygen.

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