Journal of Magnetic Resonance 213 (2011) 196–199

Contents lists available at SciVerse ScienceDirect

Journal of Magnetic Resonance

journal homepage: www.elsevier.com/locate/jmr

Communication

An efficient amplification pulse sequence for measuring chemical shift anisotropy under fast magic-angle spinning

Ivan Hung, Zhehong Gan *

Center of Interdisciplinary Magnetic Resonance, National High Magnetic Field Laboratory, 1800 East Paul Dirac Drive, Tallahassee, FL 32310, USA

ARTICLE INFO

Article history:
Received 11 July 2011
Revised 25 August 2011
Available online 10 September 2011

Keywords:
Chemical shift anisotropy
CSA
Magic-angle spinning
MAS
Spinning sidebands
Magic-angle turning
MAT
CSA amplification
Extended chemical shift modulation

ABSTRACT

A two-dimensional experiment for measuring chemical shift anisotropy (CSA) under fast magic-angle spinning (MAS) is presented. The chemical shift anisotropy evolution is amplified by a sequence of π-pulses that repetitively interrupt MAS averaging. The amplification generates spinning sideband manifolds in the indirect dimension separated by the isotropic shift along the direct dimension. The basic unit of the pulse sequence is designed based on the magic-angle turning experiment and can be concatenated for larger amplification factors.

1. Introduction

The chemical shift is one of the fundamental spin interactions of NMR spectroscopy. Measuring chemical shift anisotropy (CSA) parameters is of great interest because it can provide not only the magnitude of the spin interaction but also information on the electronic environment surrounding the nucleus [1–3]. For static solids, the orientation dependence of the NMR frequency due to CSA yields the so-called CSA powder pattern from which the three principal tensor components can be measured. For samples with multiple sites, overlap among powder patterns complicates CSA measurement and it is more desirable to perform the measurement under high-resolution magic-angle spinning (MAS) conditions. In the fast spinning regime, CSA powder patterns collapse completely to their isotropic chemical shifts and the anisotropic information is lost. At slow spinning, rotational modulation of the anisotropic chemical shift yields spinning sidebands. The relative intensity of these spinning sidebands can be used to extract CSA parameters, though the appearance of numerous sidebands can cause overlap among different sites, degrading spectral resolution. An ideal solution with the benefits of high spectral resolution and preservation of anisotropic chemical shift information is to separate the CSA and the isotropic shift into two dimensions. Various methods [4–31] have been developed to achieve this goal including recovering CSA using *rf* pulse sequences under fast MAS, rapidly switching the spinning rate or axis, discrete sample hopping, and the methods of phase-adjust sideband separation (PASS) and magic-angle turning (MAT). One class among the methods mentioned above involves applying a sequence of π-pulses that repeatedly interrupt the averaging of CSA by fast MAS. The timing of the pulses can be designed in such a way that the effective evolution results in spinning sidebands which are exactly the same as if the spinning rate is reduced or the CSA is magnified, such sequences have been dubbed extended chemical shift modulation (XCS) [12] or CSA enhancement/amplification in literature [9,32].

In this communication, an efficient CSA amplification sequence that overcomes some of the drawbacks of previous sequences is introduced. The original XCS sequence by Gullion [12] is efficient in terms of the number of pulses required for amplification, but the isotropic chemical shift is also amplified, which can cause problems for samples with multiple sites and/or inhomogeneous broadening. The CSA amplification sequences by Crockford/Shao et al. [33,34] and later by Orr et al. [35] overcame this problem by refocusing the isotropic chemical shift while amplifying the CSA. These sequences were designed following the development path of the PASS experiment, namely, by finding π-pulse timings that satisfy the PASS equations with an amplified CSA and zero isotropic shift evolution. Shao et al. [36] have also shown a modification to the original XCS sequence that compensates the

* Corresponding author. Fax: +1 850 644 1366.
E-mail address: gan@magnet.fsu.edu (Z. Gan).

1090-7807/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.jmr.2011.09.015

amplified isotropic chemical shift, though the compensation is possible only with a restriction of the t_1 evolution time. A recent review of this topic provides a thorough explanation and comparison of all CSA amplification sequences to date [32]. In this work, a different approach is taken, which does not require solution of any mathematical equations, to the design of CSA amplification sequences that refocus the isotropic chemical shift. The basic unit is based on the magic-angle turning condition, i.e., CSA frequencies at three rotor positions 120° apart average to zero.

For CSA amplification sequences, each π-pulse alternates the sign of time evolution for both the isotropic and anisotropic chemical shifts; this sign alternation interrupts the MAS averaging of CSA. The timing of the π-pulses is designed such that the effective evolution after the accumulated interruption is equivalent to an amplification of the CSA, i.e., the anisotropy $\delta = \delta_{zz} - \delta_{iso}$ ($\delta_{iso} = (\delta_{xx} + \delta_{yy} + \delta_{zz})/3$, $|\delta_{zz} - \delta_{iso}| \geqslant |\delta_{xx} - \delta_{iso}| \geqslant |\delta_{yy} - \delta_{iso}|$) is multiplied by a factor κ, while the asymmetry parameter $\eta = (\delta_{yy} - \delta_{xx})/\delta$ remains unchanged. Fig. 1a shows the basic unit of the original XCS experiment with two π-pulses per rotor period and an evolution time t_1. The π-pulses and corresponding sign alternation of the coherence order double the CSA evolution during t_1, since the CSA evolution would be zero at the end of the rotor period if no sign alternation takes place. Therefore, the unit amplifies the CSA by $\kappa = 2$ and repeating it n times multiplies the CSA evolution by $\kappa = 2n$, achieving efficient CSA amplification. The only drawback of XCS is that the isotropic shift is also amplified by the factor κ because the difference in total duration between the periods of $p = +1$ and -1 coherence order is $\kappa \cdot t_1$ as well. Amplification of the isotropic shift in addition to the CSA results in twisted-phase line shapes and baseline problems for samples with multiple sites and/or inhomogeneous broadening. The removal of isotropic shift evolution during CSA amplification has since been an important focus in the development of newer amplification sequences. This problem has been solved by following the approach used to develop the PASS experiment. By numerically solving the PASS equations for an amplified CSA without isotropic chemical shift evolution, pulse sequences have indeed been found with various numbers of π-pulses, rotor periods and amplification factors [33–36].

The approach taken here to the design of CSA amplification sequences employs the principle behind the magic-angle turning (MAT) experiment, namely, a sum at $N \geqslant 3$ rotor positions $2\pi/N$ apart averages the second-rank CSA. Fig. 1b illustrates the case with $N = 3$, which is the minimum required for second-rank tensors. The π-pulses are divided into two groups. The first group (black) is rotor-synchronous and used to encode CSA evolution. The three encoding pulses amplify CSA evolution by a factor of $\kappa = 6$. The encoding pulses are interspersed with a second group of π-pulses (blue), which satisfy the magic-angle turning condition; hence, these are called MAT pulses. There are several important aspects of the MAT pulses to consider. First, the MAT pulses are introduced to alternate the coherence order between $p = +1$ and -1, such that the CSA evolution from the encoding pulses is cumulative. Second, the MAT condition ensures that the MAT pulses do not themselves contribute to CSA evolution. Third, the MAT pulses can be shifted collectively relative to the rotor-synchronized encoding pulses. This type of shift changes the relative duration between the $p = +1$ and -1 periods and can thus be used to adjust isotropic chemical shift evolution. CSA evolution from the MAT pulses is kept null since the MAT condition remains satisfied. The MAT pulse timings in Fig. 1b are set so isotropic shift evolution is null. Fourth, changes in the order of the MAT pulses have no effect on either the CSA or the isotropic evolution. Fig. 1c shows a modification obtained by shifting the MAT pulses to the right by $\tau_r/6$, such that the first MAT pulse coincides with the first encoding pulse. The two coinciding π-pulses nullify each other, reducing the total number of π-pulses by two. The removal of two π-pulses leaves a blank period, such that a full rotor period can be omitted without affecting the CSA evolution. This modification reduces the basic amplification unit to four π-pulses that occupy two rotor periods, while keeping an amplification factor of $\kappa = 6$. Shifting of the MAT pulses changes the isotropic shift evolution. However, the removal of a complete rotor period makes the total $p = +1$ and -1 periods equal and therefore the isotropic shift is refocused. This is the basic building block employed here for CSA amplification, which can be repeated for larger amplification factors.

Fig. 2 shows the pulse sequence for the 2D CSA amplification experiment. The shortest version consists of two basic units, a stationary and an incrementing unit, separated by an evolution time t_1. The last π-pulse of the first basic unit (i.e., the stationary unit) is removed in order to have a CSA t_1 evolution. This leaves a long blank period such that the incrementing unit can be shifted to

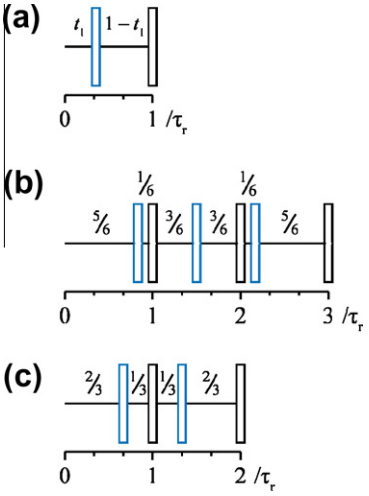

Fig. 1. The basic unit of (a) the original XCS, (b) a CSA amplification sequence with blue pulses satisfying the magic-angle turning condition, and (c) a modification of (b) by shifting the blue pulses to the right by $\tau_r/6$ and taking out the first full rotor period after the shift. The isotropic chemical shift evolution is amplified in (a) and is refocused in (b) and (c). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

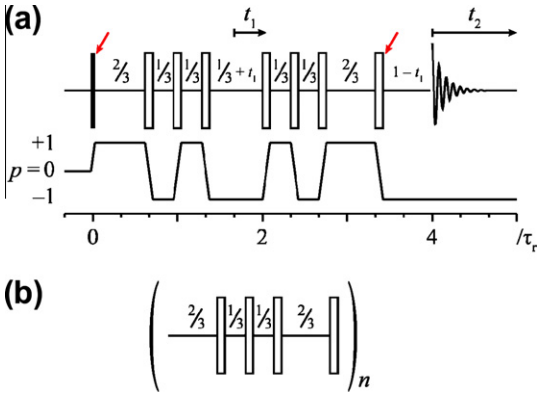

Fig. 2. (a) Pulse sequence and coherence transfer pathway for a $\kappa = 6$ CSA amplification experiment and (b) basic unit for insertion at the positions denoted by red arrows if additional CSA amplification is desired. In (a) a cogwheel phase cycle [37] is employed to select the desired coherence transfer pathway: 0 for all odd-numbered pulses starting from the excitation pulse, $\{0, 1, 2, \ldots 2a + 1\} \times \pi/(a + 1)$ for all even-numbered pulses, and $\{0, \pi\}$ for the receiver phase, where a is the total number of π-pulses. The t_1 increments span exactly one rotor period and a Fourier transformation of t_1 yields spinning sideband intensities corresponding to a spinning rate ν_r/κ. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)