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ScienceDirect

Journal of Magnetic Resonance 183 (2006) 142–144

JMR
Journal of Magnetic Resonance

www.elsevier.com/locate/jmr

Communication

IDEAL–A fast single scan method for X pulse width calibration

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Received 22 April 2006; revised 28 June 2006
Available online 4 August 2006

Abstract

In line with the recent development of the rapid single scan technique to calibrate proton flip angle, a new method that allows calibration of X-nucleus pulse width in a single scan is presented. The method involves observation of the anti-phase coherence of a proton coupled to a hetero-nuclear X-spin with nutation pulses applied at the X-spin resonance frequency in a gated decoupling experiment. The X-spin nutation causes the well-known illusions of decoupling, enabling estimation of rf amplitude level and the method is, thus, dubbed as IDEAL.

Keywords: Rapid single scan method; IDEAL method for pwx calibration

Sensitivity improvements in NMR due to modern probe designs and very high magnetic fields have opened up many avenues for fast data collection [1,2]. Multi-dimensional experiments have been developed that take only few seconds enabling real time monitoring of dynamic processes [3]. The ease of setup of such experiments heavily relies on the agile design of modern spectrometer hardware that is robust and which in turn allows use of only few calibrations to run experiments with many pulses of differing shapes and power levels. While many fast NMR methods have been developed in the past few years, only recently a fast pulse calibration method has been proposed [4]. The conventional method of calibrating pulse widths for a 90° excitation involves arraying the pulse width at a given power level and measurement of the excited signal intensity to obtain the maximum intensity that correspond to the desired pulse tip angle. This method often takes more time than the actual experiment and is not particularly suitable to be interleaved in an automated sample-changing environment. With the advent of ease of implementation of gated decoupling methods in the modern NMR spectrometers, the nutation spectroscopy has rendered itself as a fast method to determine the radio frequency pulse width in a single scan [4]. A strong isolated signal, such as a solvent proton magnetization is allowed to nutate by gated decoupling during observation and the nutation sidebands readily provides estimation of the decoupling field amplitude and hence a 90° pulse width in a single scan.

The extension of the rapid determination of pulse widths to low gamma nuclei (often referred as X-nucleus) by direct observation would be less efficient due to inherent low sensitivity and further by the low abundance of availability. It is needless to say that indirect observation of X-nucleus by transferring coherences from and to the attached protons is the common method to overcome such sensitivity issues. Recently published sequences such as CALIS-1 and CALIS-2 [5] are improvements over a HMQC based technique to yield accurate pulse-width calibration by indirect detection scheme. In this communication, a fast method that is based on indirect observation of X-nucleus for its pulse calibration in a single scan is presented. A proton anti-phase coherence that is generated due to the coupling to an X-nucleus is allowed to undergo nutation by the application of radio frequency pulses on the X-nucleus resonance position in a gated decoupling experiment. The anti-phase coherence is an ideal initial state to bring out the subtle effects of decoupling that is referred to as illusions of decoupling

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doi:10.1016/j.jmr.2006.07.010

[6]. Accordingly this method is dubbed as IDEAL for it uses illusions of decoupling to estimate rf amplitude level.

The IDEAL pulse sequence is given in Fig. 1. The experiment may be performed on an AX spins system, say, a proton (A) attached to a carbon-13 nucleus (X). The first 90°-pulse creates proton transverse magnetization that evolves under the *J* coupling to the carbon during the τ delay creating the desired anti-phase coherence $2A_xX_z$. The subsequent two 90° proton pulses sandwiching the gradient pulse act as ZZ/Z filter to clean up all the phase mixing components. Just before detection along with the desired anti-phase coherence, the in-phase *x*-coherence from uncoupled protons that have no information in the present context, are also retained. Application of rf pulses on the X-spin during observation in a gated decoupling mode nutate the anti-phase coherence and lead to a spectrum that is illustrated in Fig. 2.

A detailed description of the spin-dynamics leading to the observed spectrum in Fig. 2 involves the application of average Hamiltonian theory and is beyond the scope of this communication and will be attempted elsewhere. However, qualitatively, one could explain the features of the observed spectrum. The anti-phase coherence $2A_xX_z$ evolve under the X-spin nutation pulses applied on resonance as

$$\sigma(t) = 2A_xX_z\cos(\omega_{\mathrm{eff}}t) - 2A_xX_y\sin(\omega_{\mathrm{eff}}t), \tag{1}$$

where, $\omega_{\mathrm{eff}} = \delta\omega_{\mathrm{rf}}$ with the dutycycle δ given by the X-pulse rf on-time/dwell-time for the data sampling per point and ω_{rf} is the rf amplitude. Both terms on the right hand side of in Eq. (1) are unobservable. The hetero-nuclear *J* coupling also get affected by the application of nutation pulses on the X-spin and when the duty-cycle is small there is a residual *J* coupling (in Hz) given by J_{eff} as,

$$J_{\mathrm{eff}} = J\cos\theta \tag{2}$$

with $\theta = \tan^{-1}(\frac{\omega_{\mathrm{eff}}}{2\pi J})$.

The first term on the right hand side of Eq. (1) evolve under this residual *J* coupling and is converted into an observable signal with the anti-phase multiplet structure with splitting given by J_{eff} and appear as the center band of signal in the spectrum of Fig. 2. Indeed, a measurement of this splitting and knowledge of the unperturbed coupling value will enable the determination of rf amplitude.

The nutation side bands also appear on either side of the center band anti-phase signal and the phase of these side bands follow the phase of the center band signal. One could visualize two vectors, one corresponding to each of the anti-phase doublet, that are nutating about their respective effective field given by the effective rf amplitude (ω_{eff}) in the *x*-direction and the coupling constant m_aJ (m_a is $\pm 1/2$ for a spin 1/2 X-nucleus) along the *z*-axis when the pulses are applied on-resonance. The slow evolution of the anti-phase components under this modified effective field gives the anti-phase doublet in the middle and the sidebands with splittings $J_{\mathrm{eff}}/2$. As the duty-cycle increases the J_{eff} decreases leading to the collapse of the anti-phase components and cancellation of the central doublet and hence the side bands—a situation typical for the evolution of anti-phase coherence under decoupling field that becomes unobservable. In the above discussions it is assumed that X-spin pulses are applied on resonance and if the pulses are not on resonance then the effective nutation frequency will increase to $\sqrt{\omega_{\mathrm{eff}}^2 + \Delta\omega^2}$, where $\Delta\omega$ is the amount of shift from the resonance position.

The spectrum in Fig. 2 was recorded using a doped ($GdCl_2$ 0.3 mg/ml) sample that contained 1% H_2O, 0.1% ^{13}C-labeled methanol, and 0.1% ^{15}N-labeled acetonitrile in D_2O solvent on a 500 MHz Varian NMR system. A 5 μs pulse on the methanol carbon resonance was applied in a gated manner per sampling interval (200 μs) during data acquisition on the proton channel with a duty-cycle of 0.025. Only the methanol doublet region of the proton

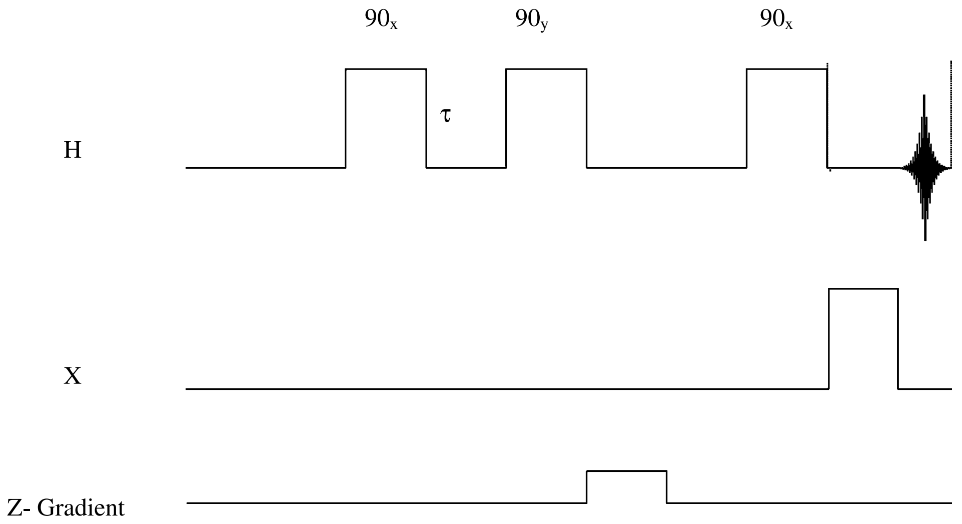

Fig. 1. The IDEAL pulse sequence used for calibration of X-nucleus 900 pulse width in a single scan. The rectangular pulses on the proton are 90° pulses with their phases shown as subscript. The pulse on the X-nucleus is of 5 μs duration applied along *x*-axis. See text for more details.

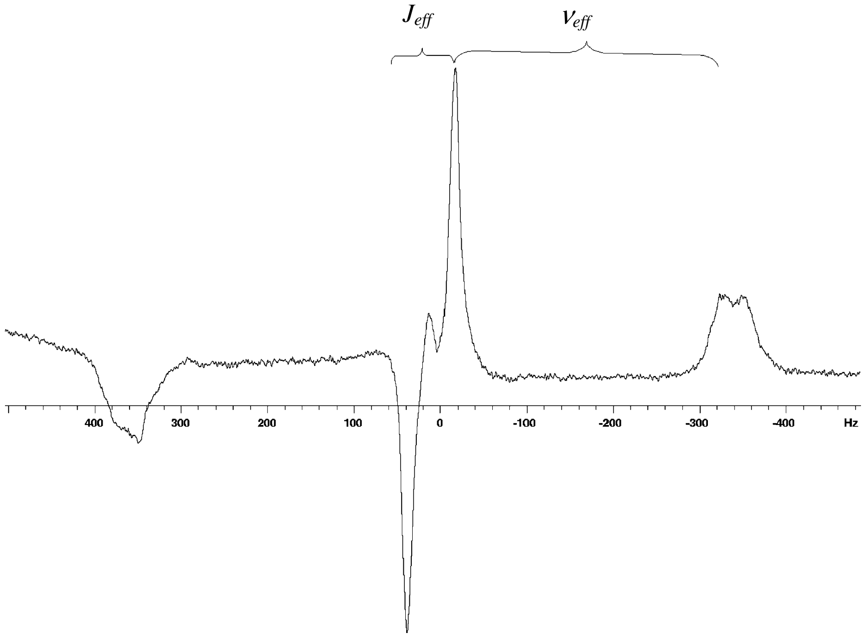

Fig. 2. ^{1}H-spectrum (500 MHz) recorded using the pulse sequence in Fig. 1. See the text for details.

spectrum is expanded for clarity. The central anti-phase doublet splitting corresponds to the residual J coupling and the separation between any one of the multiplet to the center of the sideband on the same side correspond to the nutation frequency $\upsilon_{\text{eff}} = \frac{\omega_{\text{eff}}}{2\pi}$. It is then straightforward to extract the X-nucleaus 90°-pulse width (pw90) using the relation $\tau_{90} = \frac{\delta}{4v_{\text{eff}}}$. The calculated pulse width of 20.1496 μs agreed very well (within 0.1 μs of a 20 μs pulse) with value obtained using the standard method of arraying the X-nucleus pulse width using a HMQC type pulse calibration sequence.

Usually in probes in which the X-nucleus is observed in indirect mode, such as in this experiment, pulse widths are not sensitive to sample conditions and do not vary from sample to sample. It is thus meaningful to use a standard sample that has an isolated AX spin pair that shows a coupling pattern without loss of generality. A typical duty-cycle of 0.025–0.05 is good enough to get an accurate calibration of pw90 value. As explained earlier, increasing the duty-cycle will attenuate the sideband intensity and would eventually become unobservable. The signals coming from uncoupled protons (not shown in Fig. 2) may be suppressed by a HMQC filter instead of the ZZ/Z filter which in turn requires pw90 value of the X-nucleus for maximum sensitivity of HMQC selection—a contradiction in a sequence that calibrates the very pulse width. However, any tip angle less than 90° on X-nucleus would do an effective filtering at the expense of signal to noise and may be used in case of a non-standard sample with spectral crowding. The IDEAL pulse sequence utilizes partial decoupling for X-nucleus pulse width calibration and is also a novel method that yields the result in just a single scan.

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