

# Indirect NMR Detection in Solids with Multiple Cross-Polarization Periods

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**The use of indirect detection for signal enhancement in solids is much less common than in liquids, but has attracted renewed interest recently. In this work we describe an indirect detection scheme that offers a large signal enhancement for rare spins in solids. The method uses multiple periods of cross polarization, each followed by an evolution period. The latter is increased stepwise in a pseudo 2D experiment, in which the signal of the rare spin is detected as modulation of the abundant spin. As an illustration of this method, the natural abundance deuterium NMR spectrum of a static powder sample of 1,2,4,5-tetramethylbenzene is presented.** © 2001 Academic Press

**Key Words:** indirect detection in solid; natural abundance deuterium NMR.

## INTRODUCTION

For rare nuclei with low magnetogyric ratios or broad signals, insufficient sensitivity is often the major obstacle for successful application of NMR methods. Since the early days of NMR, various double-resonance techniques have been developed to improve the sensitivity in solids (1–5). Cross polarization (CP) (5) is one of the most efficient schemes. It is commonly used now in conjunction with magic angle spinning (MAS) for  $^{13}\text{C}$  and  $^{15}\text{N}$  experiments. For single contact, the theoretical maximum of the increase in signal-to-noise ( $S/N$ ) ratio of CP is  $\gamma_I/\gamma_S$ , the ratio between the magnetogyric ratios of the abundant ( $I$ ) and rare ( $S$ ) nuclei. When the number of abundant spin  $N_I$  in the sample is much larger than the number of rare spin  $N_S$ , it is possible to perform multiple CP contacts and get  $n \sim N_I/N_S$  spectra of rare nuclei in one scan. Coaddition of these spectra gives an additional factor about  $n^{1/2}$  for the  $S/N$  improvement. For  $\gamma_I > \gamma_S$ , indirect detection, i.e., using the spectrum of spins  $I$  to detect the signal of spins  $S$ , can give another increase in sensitivity by  $\gamma_I/\gamma_S$ , because the signal is proportional to the Larmor frequency as well as the polarization.

A very sensitive scheme called triggered detection was proposed in the early work of Hartmann and Hahn (2). It consists of a long CP period with stepwise increments of the phase of the RF field for the rare nucleus. By comparing the decay rate of the locked magnetization of the abundant nucleus with and without irradiation at the frequency of the rare nucleus, it is possible to detect the presence of weak diluted spins. McArthur *et al.* (3) proposed to make use of the change in the dipolar

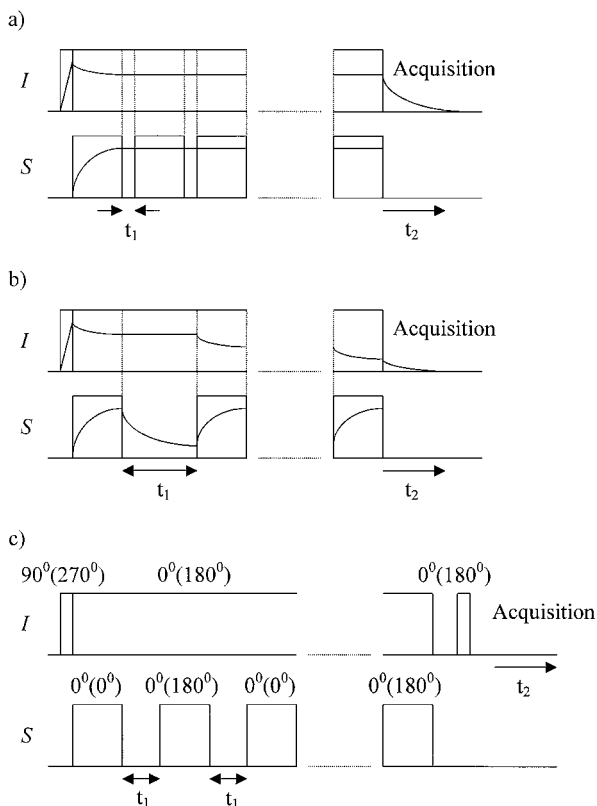
energy of abundant spins caused by contacts with rare spins. Later, Mansfield and Grannell (4) presented a scheme with multiple CP periods with fixed intervals between them. Using this technique, a single line of the rare nucleus was determined by observing oscillations of the abundant spins' signal as a function of the RF frequency of the rare spins. Bleich and Redfield (6) introduced another technique with multiple CP periods and saturation of the rare nucleus between them. It was also not a Fourier transform method and required a search of the resonance frequencies by sweeping the transmitter frequency for the rare nucleus. Pines *et al.* (5) suggested a Fourier transform scheme where variable intervals between the CP periods could be used in a 2D fashion as an additional dimension. This scheme takes advantage of the high sensitivity of the techniques mentioned above and produces the spectrum of the rare nucleus explicitly. It makes full use of the order stored in the polarization of the abundant nucleus. The scheme is especially efficient when the spectrum of the rare nucleus is broad, the case most difficult for conventional techniques.

In spite of these early investigations that promise tremendous  $S/N$  enhancement, reports on indirect detection for solids have been very rare. One of the successful implementations was the recording of  $^{14}\text{N}$  double-quantum spectra by observing a proton resonance with CP via the dipolar order (7). Recently, using very fast MAS to reduce the  $^1\text{H}$  linewidth, the indirect detection of  $^{15}\text{N}$  (8) and  $^{13}\text{C}$  (9) in solid samples has been described, and an improvement of  $S/N$  up to a factor of 3 has been achieved.

Here we present the results of using a modified version of the indirect detection method proposed by Pines *et al.* (5) to obtain the natural abundance  $^2\text{H}$  NMR spectrum of a static powder sample, and demonstrate that much higher  $S/N$  enhancement can be achieved.

## THE SCHEME OF THE EXPERIMENT

The idea of the experiment is illustrated in Fig. 1a. The preparation  $\pi/2$  pulse for spin  $I$  is followed by a long locking pulse. The RF field amplitudes for the two types of spins are matched to satisfy the Hartmann–Hahn (HH) condition, as in a standard CP experiment. The CP periods for spin  $S$  are alternated with the evolution periods, each of which has a duration  $t_1$ . The detection of the abundant spin is made by recording its FIDs in the



**FIG. 1.** (a, b) Schemes of experiments and magnetizations at different evolution times; (c) experimental pulse sequence showing the phase angles for odd and even (in brackets) transients, respectively.

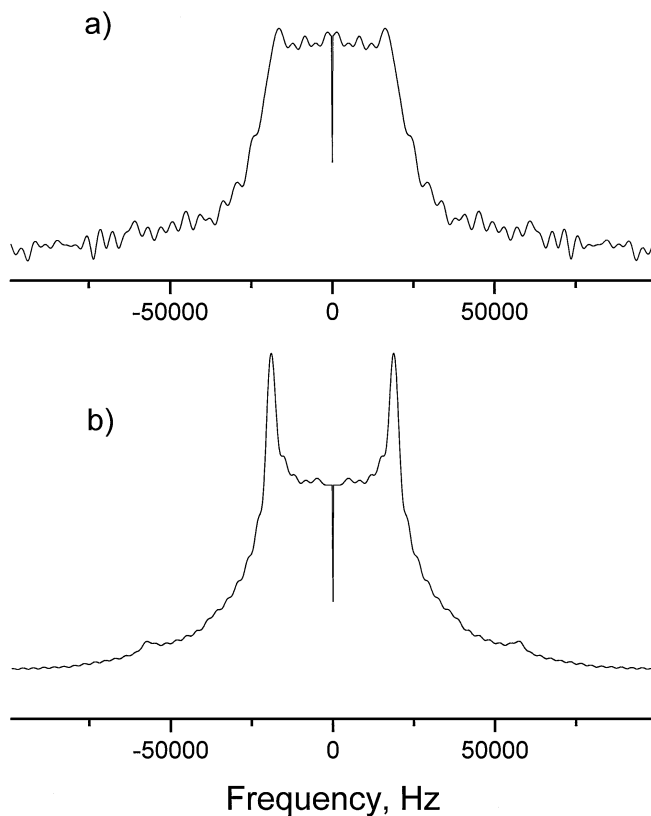
acquisition period  $t_2$ . When  $t_1$  is short compared to the decay time of the FID for spin  $S$ , the polarizations of the two types of spins reach their common value, which will result in only a small loss of polarization of the abundant spin (Fig. 1a). If the signal of the rare nucleus decays appreciably in the evolution time  $t_1$ , it would be restored during the next CP period. This causes an additional loss of polarization of the spin  $I$ , reducing the polarization of the abundant nuclei by a small amount during each of the CP periods (Fig. 1b). The reduction of the  $I$  polarization depends on the decay of the rare spin in time  $t_1$ . Even if the loss of the  $I$  spin magnetization may be quite small during a single contact, the total loss can be comparable to the initial magnetization of the spin  $I$  for a large number of CP periods. When the modulation of the spin  $I$  signal as a function of  $t_1$  is small compared to the total amplitude, this modulation is proportional to the FID of spin  $S$ . Therefore, the spectrum of the rare nuclei is obtained by Fourier transforming, with respect to  $t_1$ , the amplitude of the abundant nuclei signal (using the first point of the FID, the integrated intensity, or the height of the spectrum). For sufficiently long CP periods, the CP dynamics does not affect the signals, while  $T_{1\rho}$  relaxation of the spin  $I$  leads to corresponding broadening of the resulting spectra. On the other hand, if the relative modulation of the spin  $I$  signal is large, its dependence on

the spin  $S$  signal becomes nonlinear; then, a more complicated data processing procedure would be needed.

For the compensation of some of the experimental errors and more convenient data processing, the original indirect detection scheme was modified to eliminate all the  $I$  signal except for the part which is proportional to the FID of the  $S$  spin. The actual pulse sequence used in our experiments is shown in Fig. 1c. For both kinds of spins, the phases of the RF fields for odd and even transients are made different at fixed  $t_1$ , and the phases for odd and even transients are shown in brackets. The detected signal of spin  $I$  changes sign for every other transient. Simultaneously, the phase of the second, fourth . . . CP pulses for spin  $S$  is inverted, creating a contribution of different sign to the magnetization of spin  $I$ . Finally, a  $\pi/2$   $I$  pulse is added to create a solid echo before acquisition. It improves the lineshape for spin  $I$  and makes it less sensitive to instabilities of the spectrometer.

## RESULTS

As the demonstration of this indirect detection technique, a static sample of polycrystalline 1,2,4,5-tetramethylbenzene (durene) was studied, and its natural abundance (0.015%) deuterium NMR spectrum is shown in Fig. 2a. The spectrum was



**FIG. 2.** Indirectly detected  $^2\text{H}$  spectra for (a) a natural abundance sample of 1,2,4,5-tetramethylbenzene and (b) 4'-cyanobiphenyl 6-deuteriohexanoate with a monodeuterated methyl group.

obtained with the pulse sequence of Fig. 1c with only 64 transients for each of the 64 increments of  $t_1$ . It is the amplitude of the  $t_1$  Fourier transform of the height of the proton spectrum, which is the real part of a standard (phased) Fourier transform of its FID, starting from the maximum of the echo. The matched RF fields for both  $^1\text{H}$  and  $^2\text{H}$  were 33 kHz, the CP single contact time was 8 ms, the number of contacts was 17, and  $t_1$  was incremented in 5- $\mu\text{s}$  steps. The delay time between transients was set to 35 s. The experiment was performed with a Varian UNITY/INOVA NMR spectrometer operating at 9.39 T, with Larmor frequencies of 400.0 and 61.4 MHz for  $^1\text{H}$  and  $^2\text{H}$ , respectively. The mass of the durene sample was 0.19 g, which corresponded to a total number of about  $1.5 \times 10^{18}$  deuterons in the methyl groups.

For the  $^2\text{H}$  spectrum shown in Fig. 2a, we consider that the signal is due to the deuterons in the methyl group only because of two factors. First, the ratio between methyl deuterons and aromatic deuterons is 6:1. Second, the aromatic deuterons have a much larger quadrupole coupling constant ( $\sim 185$  kHz compared with  $\sim 56$  kHz for the methyl deuterons), so that their signal is very weak in the spectral range covered.

For comparison, the spectrum of 4'-cyanobiphenyl 6-deuteriohexanoate (10) with a monodeuterated methyl group is shown in Fig. 2b. It was obtained under exactly the same conditions, except that the number of transients for each of the  $t_1$  values was decreased to 4. The characteristic sharp "horns" in Fig. 2b indicate singularities in the powder pattern, and correspond to small-amplitude oscillation of the FID at long times. The shoulders in the high-frequency regions have decreased intensity compared with direct detection because of insufficiently high RF fields used for CP. The distortions of the spectrum in Fig. 2a are the result of limitations imposed by our hardware rather than intrinsic features of the method. The low power of the amplifiers (100 W) and safety limits of the probe did not allow us to use higher RF fields or longer irradiation times. This greatly decreased the efficiency of cross polarization. Instability of the spectrometer was another major problem, which did not allow the observation of small-amplitude oscillations. Consequently, "horns" are suppressed for the natural abundance sample. With more powerful amplifiers and a better probe, the CP can be carried out at higher RF fields with a larger number of contacts to obtain better spectra. At ambient temperature, the proton  $T_{1\rho}$  of durene is quite short, about 60 ms ( $T_1 = 8.1$  s). For measurements at a different temperature which corresponds to a longer  $T_{1\rho}$ , the result can be further improved.

## DISCUSSION

There are only a few reports on the study of natural abundance deuterium NMR (11–14). All of them take advantage of sufficiently narrow lines (about 100 Hz) for cases in which quadruple couplings are partially averaged by molecular motions, as for solids with rapid internal rotation (11, 12), or in liquid crystals (13, 14). It was also shown that a polarization transfer from  $^1\text{H}$  to

$^2\text{H}$  may enhance the sensitivity of the  $^2\text{H}$  resonance (12, 15, 16). However, to our knowledge, all such investigations were carried out with direct  $^2\text{H}$  detection.

In the most favorable cases, such as hexamethylbenzene (11) with fast MAS, the spectrum can be obtained with only a few minutes of direct acquisition. In other cases, even for sharp peaks with a small number of spinning sidebands, it would take hours and days. By performing a CP experiment with direct detection for a deuterated sample and measuring the  $S/N$  of the spectra with a line-broadening factor of 1 kHz, we estimated that a direct detection experiment with CP would take many days for the natural abundance sample to reach the  $S/N$  of the spectrum in Fig. 2a. For sufficiently long CP periods, the theoretical signal enhancement compared with the standard CP scheme is

$$R = (\gamma_I/\gamma_S)n_{\text{cp}} \cdot \exp(-n_{\text{cp}}\tau_{\text{cp}}/T_{1\rho}), \quad [1]$$

where  $n_{\text{cp}}$  is the number of CP contacts,  $\tau_{\text{cp}}$  is the length of each contact, and  $T_{1\rho}$  is the spin–lattice relaxation time in the rotating frame for spin  $I$ . In our experiment, this theoretical enhancement factor was about 15. The natural abundance  $^2\text{H}$  spectrum shown in Fig. 2a was obtained in 40 h using the multiple contact–indirect detection technique with a delay time of 35 s. Although the singularities of the typical powder pattern are severely truncated and the shoulders are too weak to be observed, the deficiencies are due to problems in our instrumentation rather than inherent problems of the scheme. They can be overcome by using more powerful RF amplifiers and a more rugged probe.

The pulse sequence shown in Fig. 1c collects information on the real part of the FID of the rare nuclei, and is appropriate for symmetric peaks. If the spectrum is asymmetric, the peaks will be superimposed with their mirror images. This can be avoided by setting the frequency outside the whole spectrum, but it may not work well if the spectral range is wide. In this case, the imaginary part of the FID can be obtained by performing an additional experiment with the same pulse sequence, except that the phase of each CP pulse for spin  $S$  should be incremented by  $90^\circ$  with respect to the phase of the preceding pulse.

Several modifications of the proposed scheme are possible. It can be advantageous, especially for MAS experiments, to use ramped-amplitude CP pulses (17) for the  $S$  channel. This can improve the efficiency of crosspolarization and, therefore, the total sensitivity of the experiment. For systems with inhomogeneous broadening, if the  $t_1$  intervals between the  $S$  pulses are changed into  $(\Delta + t_1/2) - \pi - (\Delta - t_1/2)$ , where  $2\Delta$  is the maximum evolution time and  $\pi$  denotes a  $\pi$  pulse for spin  $S$ , the  $T_{1\rho}$  effect of the abundant spin on the FID of the rare spin can be eliminated. Use of multipulse spinlocking for the acquisition period may further improve sensitivity.

Finally, we must point out the limitations of the present method. First, the spectral resolution is limited by the length of the evolution period  $t_1$ . It implies that, for any relaxation time

$T_{1\rho}$ , a compromise should be found between the total number of CP contacts, i.e., sensitivity, and the length of the evolution periods, i.e., resolution. To decrease  $T_{1\rho}$  relaxation, one can use purer samples, reduce the concentration of paramagnetic impurities, or perform the measurements at a different temperature if molecular motions are the main source of relaxation. The problem of spectral resolution makes the application of this method to the study of  $^{13}\text{C}$  and  $^{15}\text{N}$  technically more demanding. Second, if the spectral range of the  $S$  spin is very wide, the CP efficiency may drop off at the spectral edges even when ramped pulses are used. This problem may be more challenging for MAS experiments. In spite of these limitations, the indirect detection scheme with multiple CP contacts provides tremendous enhancement of NMR sensitivity, and may be useful for some specific systems.

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*Note added in proof:* Two other papers on indirect detection in solids have been published recently (18, 19).

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