

A Fast Method for Obtaining 2D J -Resolved Absorption Spectra

Two-dimensional homonuclear J spectroscopy (1) is a useful method both for unraveling complicated spectra (2) and for the study of spin-spin coupling constants. The principle of the technique has been described by Aue *et al.* (1). By means of one or more 180° pulses a spin echo is created at a time t_1 after an initial 90° pulse. The second half of this echo is acquired for a series of t_1 values. Two-dimensional Fourier transformation then generates a 2D frequency spectrum.

This method needs a rather long measuring time and does not give the optimum sensitivity. Another disadvantage is that it is impossible to get 2D absorption spectra in an easy way (3, 4), and therefore one usually calculates an absolute-value spectrum, which introduces line broadening, and decreases the obtainable resolution. As has been shown earlier (5), processing of complete spin echoes can remove this disadvantage. Slightly different measuring techniques are described, which allow a shorter measuring time and can also produce 2D J -resolved absorption spectra.

The essence of J spectroscopy is that spin echoes are modulated by spin-spin coupling. The phase ϕ_{jk} of the frequency component k of a set of magnetically equivalent nuclei j at the center of a spin echo, t_1 seconds after an initial 90° pulse, is given by

$$\phi_{jk} = \left(\sum_l 2\pi J_{jl} m_{lk} \right) t_1 = \omega_{jk} t_1, \quad [1]$$

where J_{jl} are the coupling constants and m_{lk} the magnetic quantum numbers of nuclei l . As explained by Freeman and Hill (6), Eq. [1] holds independent of the numbers of 180° pulses between the initial 90° pulse and the middle of the echo considered, if the coupling is sufficiently weak and if the condition

$$1/2T \ll \sigma_{jl} \quad [2]$$

is satisfied (7), where $2T$ is the distance between two successive 180° pulses and σ_{jl} is the difference in chemical shift between the nuclei j and l . Because of the 180° pulses the amplitude of magnetization component jk at the center of an echo is in first order not influenced by magnetic field inhomogeneity and depends only on the transverse relaxation T_{2jk} . After the center of an echo the behavior of the magnetization is a free decay expressed by

$$M_{jk}(t_1, t_2) = M_{jk}(0, 0) \cos(\omega_{jk} t_1 + \Omega_{jk} t_2) \times \exp(-(t_1 + t_2)/T_{2jk} - t_2/T_2^*), \quad [3]$$

where Ω_{jk} is the resonance frequency of line jk and T_2^* denotes the influence of magnetic field inhomogeneity. Because $M_{jk}(t_1, t_2)$ is independent of the number of 180° pulses given during t_1 , we can acquire a whole set of echoes for different values of t_1 by sampling all the echoes of a CPMG pulse sequence (Fig. 1). If the distance between the 180° pulses is $2T$, the values of t_1 for which an echo signal is acquired are

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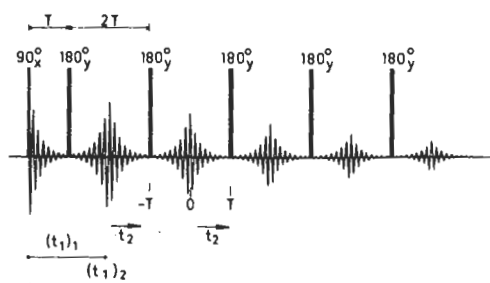


FIG. 1. A 2D time signal $M_y(t_1, t_2)$ from one CPMG sequence.

$t_1 = 2nT$, $n = 1, \dots, N$, where N is the total number of 180° pulses. An echo signal for $t_1 = 0$ is necessary to avoid frequency-dependent phase errors after Fourier transformation with respect to t_1 .

To obtain an echo-like signal for $t_1 = 0$, one can mirror the free-induction decay acquired after the first 90° pulse, because for $t_1 = 0$ Eq. [3] represents a pure decaying cosine for all magnetization components M_{jk} . So a complete set of data can be obtained for

$$t_1 = 2nT, \quad n = 0, 1, 2, \dots; \quad T < t_2 < T. \quad [4]$$

If one wants to obtain a 2D spectrum out of one single CPMG sequence, the Shannon conditions for the sampling frequency along the t_1 axis must be fulfilled. This sampling frequency, which equals $1/2T$, must be larger than the maximum multiplet width, which gives

$$1/2T > \sum_l J_{jl} I_l, \quad [5]$$

where I_l is the maximum value of the magnetic quantum number of nucleus l . An absolute-value-mode display of a 2D spectrum obtained from the second halves of the echoes of one CPMG sequence is given in Fig. 2a. The spectrum is computed from a 128×48 data matrix. The measuring time was about 7 sec. Because the Meiboom-Gill modification of the Carr-Purcell sequence does not correct the 180° pulse imperfections for magnetization components with ν_{jk} not equal to zero (8), both the lines of the doublet and the outer lines of the triplet are clearly broader in the ω_1 dimension than the center line of the triplet. Because of the short sampling time of the second halves of the echoes, which has a maximum value of T and is set by Eq. [5], resolution along the ω_2 axis is poor. Absorption spectra obtained by the processing of the complete echoes (5) are shown in Fig. 2b. The spectrum is obtained from the same measurement as the spectrum of Fig. 2a, only here a 128×96 data matrix is processed because the number of data in the t_2 dimension is doubled. The spectrum of Fig. 2b shows better resolution in both dimensions than the spectrum of Fig. 2a because of the two-dimensional absorption character.

The method described is restricted to cases where Eqs. [2] and [5], which can be contradictory, are both satisfied, and homonuclear coupling is sufficiently weak. Another disadvantage of the method is that imperfections of the 180° pulses give rise to severe signal loss because of the large number of successive 180° pulses.

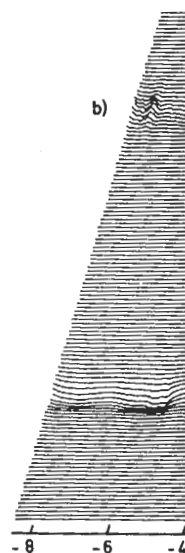
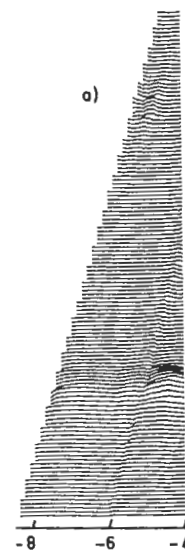


FIG. 2. 2D J spectra of 1, value-mode display. (b) Ab

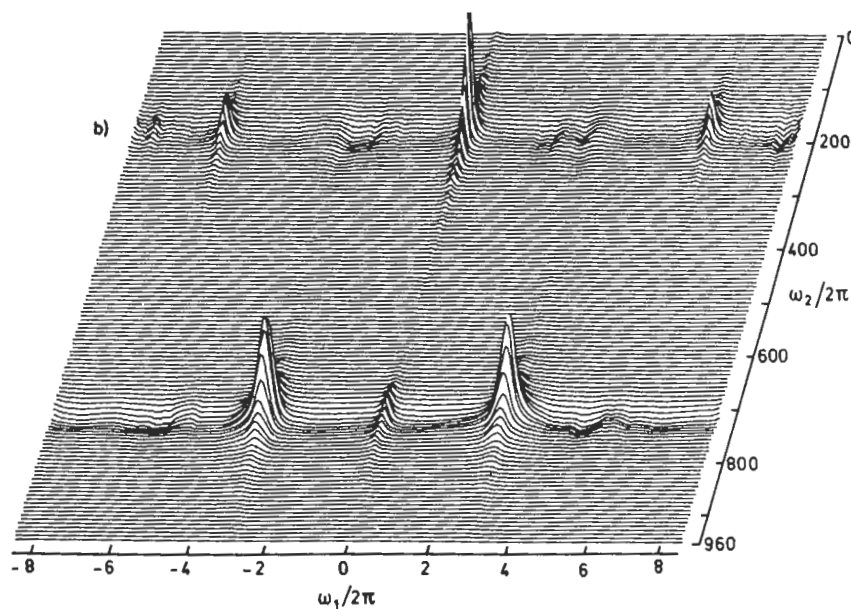
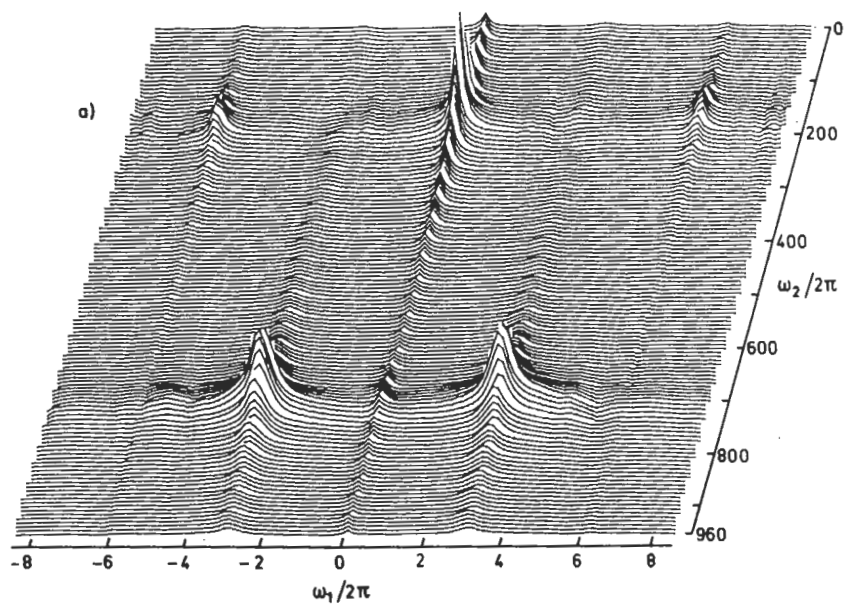


FIG. 2. 2D J spectra of 1,1,2-trichloroethane obtained from one single CPMG sequence. (a) Absolute-value-mode display. (b) Absorption display. The total measuring time was about 7 sec.

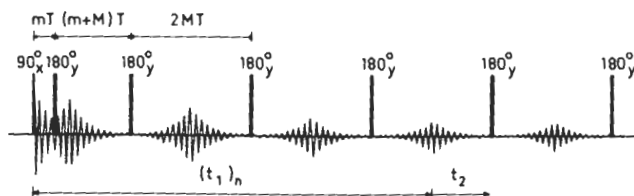


FIG. 3. Pulse scheme of the m th spin-echo sequence of a relatively shifted multiple-echo 2D experiment, used to obtain a J -modulated time signal $M_y(t_1, t_2)$. The complete experiment consists of M similar spin-echo sequences. During this sequence a set of second halves of echoes is acquired for $(t_1)_n = 2mT + (n-1) \times 2T$. Complete echoes can be acquired for $(t_1)_n = 2mT + 2nT$.

Resolution along the ω_2 axis is still determined by the maximum value of T , and thus by the maximum multiplet width, as is clear from Eq. [5].

All the problems mentioned above arise from the fact that the time between two successive 180° pulses cannot be larger than the maximum value, as given by Eq. [5]. However, we can make this time M times larger by applying a scheme which consists of M relatively shifted CPMG-like pulse sequences of the form $90^\circ_x - mT - 180^\circ_y - (m+M)T - 180^\circ_y - 2MT - 180^\circ_y - 2MT - 180^\circ_y \dots$, $m = 1, \dots, M$, as is shown in Fig. 3. During the m th pulse sequence spin echoes are generated for $t_1 = 2mT + (n-1) \times 2MT$, $n = 1, \dots, N$, where N is the number of 180° pulses per sequence. During all the M pulse sequences spin echoes will be generated for the values of t_1 given by Eq. [4]; thus a full set of echoes will be generated.

As is clear from Fig. 3, complete echoes will be generated only for $n \geq 2$, so for $t_1 < 2MT$ no complete echoes can be acquired. With this method the maximum value of T is set by Eq. [5] again, while Eq. [2] is transformed into $1/2MT \ll \sigma_H$ which can be satisfied more easily than Eq. [2]. A second advantage is that the resolution in the ω_2 dimension, because of limited acquisition time, is M times better than that in the case of one single CPMG sequence. Because the number of 180° pulses per echo train will be M times smaller, the effect of an imperfection in the 180° pulse will be less severe. Obtaining the absolute 2D spectrum again requires the acquisition of the second halves of all echoes in the M relatively shifted sequences. Processing these half echoes in the way described by Aue *et al.* (1) results in a 2D spectrum with absolute-value lineshapes.

If we want to obtain a 2D absorption spectrum, complete echoes must be acquired. As mentioned before, each first echo of a sequence is incomplete. The easiest way to circumvent this problem is simply given by not acquiring these incomplete echoes, and a data processing of only the complete echoes. The missing of the first M incomplete echoes means in the time domain that the first M sampling points along the t_1 axis are missing. This gives rise, after Fourier transformation, to a linear frequency-dependent phase shift ϕ_1 , which equals $\phi_1 = 2M\pi$ and can be corrected automatically. However, such a strong frequency-dependent phase correction changes the absorption character of the lines in the 2D spectrum slightly. A 2D absorption spectrum of 1,1,2-trichloroethane obtained with this method is shown in Fig. 4. The pulse scheme consisted of eight pulse sequences ($M = 8$) containing sixty-five 180° pulses each ($N = 65$), with a spacing $2MT$ of 416 msec. The spectrum was computed from a 512×768 data matrix. The total measuring time was about



FIG. 4. 2D absolute-value multiple-echo experiment. The total measuring time was

10 min. Resolution is better because the same direction is better as mentioned by conventional methods.

The comparison of new methods will be both experimentally and τ_2 , respectively. The total measuring time is a number of 90-180 pulses. The method introduced in this communication has a sampling frequency dictated by the maximum value of M'' equals 1 if all arguments of Au are $T_a' \approx \tau_1/2 + \tau_2 + 1$ calculation shows $T_a'' \approx \tau_1 + \tau_2 + 1.2$ thus

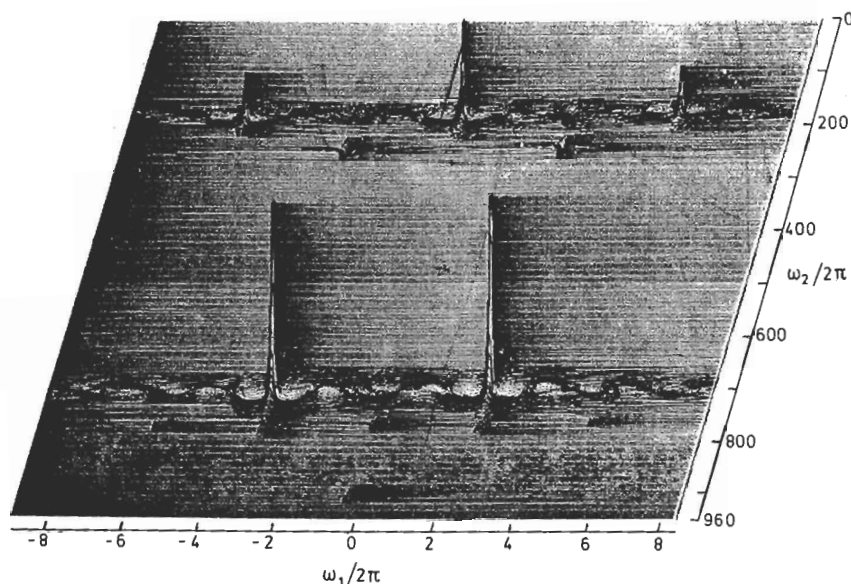


FIG. 4. 2D absorption J spectrum of 1,1,2-trichloroethane obtained with the relatively shifted multiple-echo experiment. The spectrum was computed from a 512×768 data matrix. The total measuring time was about 10 min.

10 min. Resolution in the ω_2 dimension was improved compared with Fig. 2b, because the sampling time in the t_2 dimension is 8 times longer. Resolution in the ω_1 direction is better because the effect of imperfections in the 180° pulses is less severe, as mentioned before. Measuring time is about 50 times shorter than with the conventional method of Aue *et al.* (1).

The comparison of the S/N ratios for the original method of Aue *et al.* (1) and our new methods will be done by calculating the measuring times of these methods. In both experiments the sampling times along the t_1 axis and the positive t_2 axis are τ_1 and τ_2 , respectively, so the resolution in the resulting spectra should be equal. The total measuring time for a complete 2D spectrum (T_t) is equal to MT_a , if M is the number of $90-180^\circ$ pulse sequences, and T_a is the average time of these sequences. In the method introduced by Aue *et al.* (1), M is given by $M' = 2\tau_1 \sum_i J_{ii} I_i$ if the sampling frequency along the t_1 axis is equal to the minimum allowed value, which is dictated by the maximum multiplet splitting, as in Eq. [5]. In the methods introduced in this communication M is given by $M'' = 4\tau_2 \sum_i J_{ii} I_i$ if τ_2 equals $M''T$. The quantity M'' equals 1 if all data are acquired in one single CPMG sequence. Following the arguments of Aue *et al.* (9) the optimum average time of a $90-180^\circ$ sequence is $T'_a \approx \tau_1/2 + \tau_2 + 1.27 T_1$, with T_1 the longitudinal relaxation time. An analogous calculation shows that the optimum average time per pulse train for our methods is $T''_a \approx \tau_1 + \tau_2 + 1.27 T_1$. The total measuring time of the method of Aue *et al.* (1) is thus

$$T'_t \approx 2\tau_1 \sum_i J_{ii} I_i \times (\tau_1/2 + \tau_2 + 1.27 T_1), \quad [6a]$$

while for new methods the time is given by

$$T_1'' \approx 4\tau_2 \sum_l J_{lI} I_l \times (\tau_1 + \tau_2 + 1.27 T_1). \quad [6b]$$

Taking only the second halves of the echoes the gain in S/N (G) is given by $(T_1'/T_1'')^{1/2}$. From Eq. [6], G is given by $(\tau_1/4\tau_2)^{1/2} \leq G \leq (\tau_1/2\tau_2)^{1/2}$. Processing of the complete echoes gives an extra gain of a factor $2^{1/2}$, if we neglect the signal loss of the first M'' noncomplete echoes.

The new measuring techniques can be used advantageously if $\tau_1 > 2\tau_2$, because of the shorter measuring time and the elimination of diffusion effects (1). Especially if $\tau_1 \gg \tau_2$, e.g., in the 2D studies of coupling constants or transverse relaxation times via linewidth determination, they can be used with much profit. The methods are applicable only in the case of weak scalar coupling. The derivations for line positions and intensities in the 2D spectra of strongly coupled spin systems (10, 11) do not hold for these multiple refocusing methods. The applicability of the new methods is shown only for homonuclear 2D J spectroscopy, but the principle of multiple refocusing can also be applied in the case of the heteronuclear "proton-flip" experiment (4), which can be used for the study of, for example, C-H coupling constants. Here the gain in signal-to-noise-ratio can be of even more practical importance. Because the large number of data in the multiple-echo sequences should be acquired continuously, the spectrometer must possess either a large main memory or a fast background storage.

The spectra shown were recorded on our home-built 7-T HR-NMR spectrometer (12), which does the time averaging in double precision on a HP 7905 disk. To minimize the imperfection in the 180° pulses due to the offset frequency, which has a rather severe effect in our new methods, quadrature detection should always be applied.

ACKNOWLEDGMENTS

One of the authors (A.B.) sincerely acknowledges stimulating discussions with Prof. Dr. R. R. Ernst and Dr. K. Nagayama, concerning subjects dealt with in this communication. This research was made possible by a stipend of the Delft University Fund (A.B.).

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Received November 22, 1979; revised February 22, 1980