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# Broadband analytical decoupling in high-resolution NMR spectra

**L. Mahi, J. C. Duplan and A. Briguet***

Laboratoire de Résonance Magnétique Nucléaire, CNRS UPRESA 5012, Université Claude Bernard Lyon I–ESCPE, 43 Bd du 11 Novembre 1918, 69622 Villeurbanne Cedex, France

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ABSTRACT: A data processing method, based on double integral calculations, to obtain decoupled high-resolution NMR spectra in the weak scalar coupling approximation is described. Data are recorded from conventional spin echo experiments using different values of the delay of the echo. The collected echoes are processed in the time domain in such a way that resonances appear as single lines at their chemical shift frequencies in the resulting spectrum. The method described is a two-step post-acquisition treatment. In the first step, broadband decoupling of the spectrum is achieved. The second processing step suppresses the modulation of the amplitude by the scalar coupling *J*. Finally the spectrum obtained may be presented in the pure absorption mode without *J*-modulation. This technique, designed by analytical decoupling, improves the signal-to-noise ratio and facilitates the interpretation of complicated spectra. Intensities are not modulated by scalar coupling and they can be employed for quantitative analysis. The method was applied to proton NMR spectra of diethyl ether and 6-vinyl-1, 3-dioxane 1,3. It may be also applied to heteronuclear spin systems and an example of a broadband decoupled carbon-13 NMR spectrum of a mixture of diethyl ether and ethanol is given. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: broadband decoupled NMR spectra; spin echo experiment; *J*-modulation; scalar coupling

## INTRODUCTION

Complete homonuclear decoupling simplifies NMR analysis since spectral patterns due to scalar coupling may be reduced to single lines. The resonance intensity is no longer distributed over several lines and can be measured at the chemical shift frequency. This approach improves the signal-to-noise ratio, it makes easy studies such as spin–spin and spin–lattice relaxation measurements and it is a great asset when analyzing complicated spectra. Techniques to achieve broadband decoupling of heteronuclear systems[1–8] have been widely described. In the homonuclear case, and considering the offset effects due to the proximity of spectral lines, double resonance experiments must be carefully performed. The first method proposed for complete proton decoupling was described by Aue *et al.*[9] on the basis of a two-dimensional *J*-spectroscopy experiment. When the absolute-value mode is used with this technique, the 45° projection is just as good as a homonuclear broadband decoupling, but the spectral resolution is lowered. The 'constant-time' experiment[10] is based on a sequence similar to the method described by Aue *et al.*: the absorption decoupled spectrum is obtained by measuring the magnetization at a fixed time $\tau$ after the initial 90° pulse of a spin echo sequence, but the resonances amplitude are modulated by the scalar coupling constant. The two-dimensional version of the constant-time experiment[11] and time-reversal NOESY[12] are other possible techniques for observing decoupling via diagonal projection of the two-dimensional spectrum onto the $F_1$ axis.

A method for data processing was also proposed by Shaka *et al.*[13] in order to eliminate dispersion-mode components from two-dimensional NMR *J*-spectra. In this case, the 45° projection generates a proton spectrum from which all proton–proton splittings may be removed. Unfortunately, this technique fails in the presence of severe overlap and when signals have amplitudes comparable to noise. Ping *et al.*[14] proposed an interesting method for obtaining absorption-mode spectra without spin–spin splittings. The idea was to suppress dispersion components by using a so-called 'purging pulse'[15–17] applied during a conventional *J*-spectroscopy experiment. The projection of this form of *J*-spectrum on to the $F_2$ axis gives the decoupled spectrum. Woodley and Freeman[18] reported a considerable simplification of this method and achieved broadband decoupling without using any purging pulse. Another way to obtain homonuclear broadband decoupled spectra consists in taking the $F_2$ projection of phase-sensitive *J*-resolved spectra, obtained by extrapolating a 2D signal towards negative $t_1$ values by linear prediction.[19] Recently, a novel idea based on the use of selective pulses and weak gradients to achieve homonuclear broadband decoupling was described.[20]

Here we propose a new alternative to obtain decoupled spectra in the weak scalar coupling approximation,

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* *Correspondence to*: A. Briguet, Laboratoire de Résonance Magnétique Nucléaire, CNRS UPRESA 5012, Université Claude Bernard Lyon I–ESCPE, 43 Bd du 11 Novembre 1918, 69622 Villeurbanne Cedex, France.
E-mail: briguet@muzelle.univ-lyon1.fr

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termed analytical decoupling. Using a data processing method similar to that proposed for measuring long-range scalar coupling constants,[21] the method requires conventional spin echo experiments: a set of echoes is recorded for different values of the echo time, $T_E$, and a treatment is performed employing a two-stage procedure, giving a new signal in the time domain. Decoupled spectra with different amplitude modulations are obtained first. From this novel series of signals, the second processing step permits one to suppress the scalar modulation and a broadband decoupled spectrum is presented in the pure absorption mode. It is shown here how broadband decoupling can be performed with different $T_E$ values. A technique for suppression of the $J$-modulation in the resulting decoupled spectrum is then proposed. Examples of entirely decoupled proton spectra at 300 MHz for diethyl ether and 6-vinyl-1,3-dionaxane are presented. An application to heteronuclear systems is illustrated on $^{13}$C resonances in a mixture of diethyl ether and ethanol.

## ANALYSIS

### Decoupling

In the case of a weakly coupled system of two spin-$\frac{1}{2}$ nuclei subjected to a $(\pi/2)_x$–$T_E/2$–$(\pi)_y$–$T_E/2$–Acq$(t)$[22] sequence, the observed magnetization at the frequency $\nu_0 + J/2$, where $J$ is the scalar coupling of the nuclei, may be described by[1]

$$M(t, T_E) = M^0 \exp(-T_E/T_2) \times \exp(-t/T_2^*) \exp[i\pi J(t + T_E)] \exp(2i\pi\nu_0 t) \quad (1)$$

where the time $t$ is measured from the time of the echo formation, $T_2$ and $T_2^*$ are the spin–spin relaxation time and the transverse relaxation time in the presence of static field inhomogeneity, respectively, and $M^0$ represents the amplitude of the signal, $\nu_0$ is the chemical shift frequency of the considered nuclei. $T$ is the maximum value of $T_E$ obtained experimentally, hence a set of spin-$\frac{1}{2}$ echoes is recorded using different values of $T_E$. Letting $T_E = T - \tau$, $M(t, T_E)$ may be replaced by

$$M(t, \tau) = g(t) \exp(\tau/T_2) \exp[i\pi J(t - \tau)] \quad (2a)$$

where

$$g(t) = M^0 \exp(-T/T_2) \exp(i\pi J T) \exp(-t/T_2^*) \exp(2i\pi\nu_0 t) \quad (2b)$$

Starting from these signals, one may study formally the effect of the following transformation:

$$S(t, k) = \int_{\infty}^{\infty} \mathrm{d}\upsilon \int_0^T M(t, \tau) \exp[2i\pi\upsilon(t - \tau + kT)]\, \mathrm{d}\tau \quad (3)$$

where $\upsilon$ is a variable measured in Hz and $k$ is a positive dimensionless real number taken between 0 and unity.

The principle of the method suggested above is very similar to the pioneering homonuclear decoupling method[9] which uses the projection of a tilted conventional $J$-spectrum on to the $F_2$ axis. Summation over $\tau$ is the Fourier transform in the $F_1$ dimension, summation over $\upsilon$ is the projection on to the $F_2$ axis and the factor $\exp[i\pi\upsilon(t - \tau + kT)]$ represents the usual tilt. The modulated decoupled spectra obtained by calculating $S(t, k)$ for various values of $k$ are then used in a similar procedure for eliminating the $J$-modulation. The resulting spectrum is a pure absorption one and projecting a $J$-spectrum results in lineshape distortions since the peaks in the $J$-spectra have a phase twist lineshape.[23,24] Changing the order of integration with respect to the independent variables $\tau$ and $\upsilon$, one obtains

$$S(t, k) = g(t) \exp(-i\pi JkT) \int \exp(\tau/T_2)\, \mathrm{d}\tau \times \int_0 \exp[2i\pi(\upsilon + J/2)(t - \tau + kT)]\, \mathrm{d}\upsilon \quad (4)$$

Since $J$ is constant, the second integral is a Dirac distribution $\delta[\tau - (t + kT)]$ for $t \leqslant (1 - k)T$. In this case, with $\tau$ varying from zero to $T$, $S(t, k)$ is different from zero and one may write formally

$$S(t, k) = g(t) \exp(-i\pi JkT) \exp[(t + kT)/T_2] \quad (5)$$

and by inserting the expression for $g(t)$:

$$S(t, k) = M^0 \exp[-(1 - k)T/T_2] \exp[i\pi J(1 - k)T] \times \exp[t(T_2^{-1} - T_2^{*-1})] \exp(2i\pi\nu_0 t) \quad (6)$$

Notice that, for $t > (1 - k)T$, $\tau$ must be negative and $S(t, k)$ does not exist.

After Fourier transformation with respect to $t$, $S(t, k)$ shows pure absorption lines at the chemical shift frequency without splitting due to the scalar coupling. Note that each line which does not result from such coupling remains at its spectral position. However, $S(t, k)$ is still modulated by the scalar coupling. The line intensities will depend on the $J$ values, and the broadband decoupled spectrum cannot be used for quantitative NMR analysis. Varying $k$ allows one to obtain the decoupled spectrum with different amplitude modulations and this property will be turned into profit in the next section. Note also that for $k = 0$ one finds again the result of the 'constant-time' experiment.

### Suppression of intensity modulation

Scalar coupling modulation suppression requires a similar treatment to that described in the previous section. $S(t, k)$ given by Eqn (6) is calculated for a set of values of the parameter $k$, chosen such that $t \leqslant (1 - k)T$. Series of $S(t, k)$ are obtained and then employed to calculate the following sum:

$$S(t) = \int_{-\infty}^{\infty} \mathrm{d}\upsilon' \int_0^{k\max} \mathrm{d}k S(t, k) \exp[2i\pi\upsilon' T(1 - k)] \times \{1 + [\alpha(k_{\max}/2 - k)]^2\}^{-1} \exp(-akT) \quad (7)$$

where $\upsilon'$ is a variable measured in Hz, $k_{\max}$ is the maximum value of $k$ and $\alpha$ is a positive real value which must fulfil the condition $\alpha \gg (k_{\max}/2 - k)^{-1}$. The parameter $a$ may be considered as the mean value of the inverse of the spin–spin relaxation times observed along the spectrum and in further calculations it will be assumed that $\exp(kT/T_2)$ may be approximately the inverse of $\exp(-akT)$. This assumption is not necessary but it offers the possibility of making transverse relaxation time measurements in the broadband decoupled spectrum. Starting from Eqn (6), exchanging the order of integration in Eqn (7), using the hypothesis concerning $a$ and the properties of the Dirac function we obtain,

$$S(t) = M^0T^{-1}\{1 + [\alpha(1 - k_{\max}/2)]^2\}^{-1}\exp(-T/T_2) \times \exp[t(T_2^{-1} - T_2^{*-1})]\exp(2i\pi\nu_0 t) \qquad (8)$$

The Fourier transform of $S(t)$ with respect to time is a broadband decoupled spectrum and its line intensities are independent of the scalar coupling constants.

In practice, the collected echoes are numerically transformed to obtain the broadband decoupled spectrum. A good approximation of the infinite sum of Eqn (3) can be performed in the frequency domain from $-F$ to $F$, provided $F$ is taken as larger than the absolute value of the strongest coupling constant $J_{\max}$ in the spectrum considered. Integration over the variable $\tau$ must be limited to $T$ and taking $F \geqslant 4|J_{\max}|$, one may write

$$S(t, k) = \int_0^T 2FM(t, \tau)\operatorname{sinc}[2F(t - \tau + kT)]\,\mathrm{d}\tau \qquad (9)$$

where $\operatorname{sinc}(x) = \sin(\pi x)/\pi x$.

The last correlation product may be evaluated for each sampled value of $t$ using Romberg's integration method.[25] The second stage of the treatment is performed in the same way, in order to eliminate $J$-modulation effects. The frequency domain in Eqn (7) is limited to the range from $-F'$ to $F'$, leading to the convolution product which is also evaluated numerically:

$$S(t) = \int_0^{k\max} S(t, k)\{2F' \operatorname{sinc}[2F'(1 - k)T]\} \times \{1 + [\alpha(k_{\max}/2 - k)]^2\}^{-1}\exp(-akT)\,\mathrm{d}k \qquad (10)$$

where $F'$ is large compared with the value of the coupling constant.

## PRACTICAL EXAMPLES OF ANALYTICAL DECOUPLING

For homonuclear application to the proton spectrum of diethyl ether [Fig. 1(A)] taken at 300 MHz, 200 spin-$\frac{1}{2}$ echoes were recorded using an acquisition time of 1.4 s; $T$ was 1.44 s and was decreased in steps of 7.2 ms. Echoes were processsed as indicated above, using $k = 0$ and $F = 40$ Hz. The decoupled spectrum is shown in Fig. 1(B). It must be pointed out that the intensities of the lines are not in the expected 3:2 ratio since $J$-modulation occurs. A set of $S(t, k)$ was established for 200 values of $k$ incremented by $2.5 \times 10^{-3}$. These signals were treated using the following parameters: $k_{\max} = 0.5$, $F' = 150$ Hz, $\alpha = 44$ and $a = 0.4$ s$^{-1}$, and the spectrum obtained is shown in Fig. 1(C). Intensities in the 3:2 ratio demonstrate that $J$-modulation is fully suppressed. Figure 2(A) shows a decoupled spectrum of diethyl ether obtained by the 'constant-time' experiment with an acquisition time of 1.2 s and four scans. The sampling points were taken at a fixed time of 0.32 s after the 90° pulse of the conventional spin echo experiment. The peak intensities in the decoupled spectrum are clearly affected here by the scalar coupling modulation.

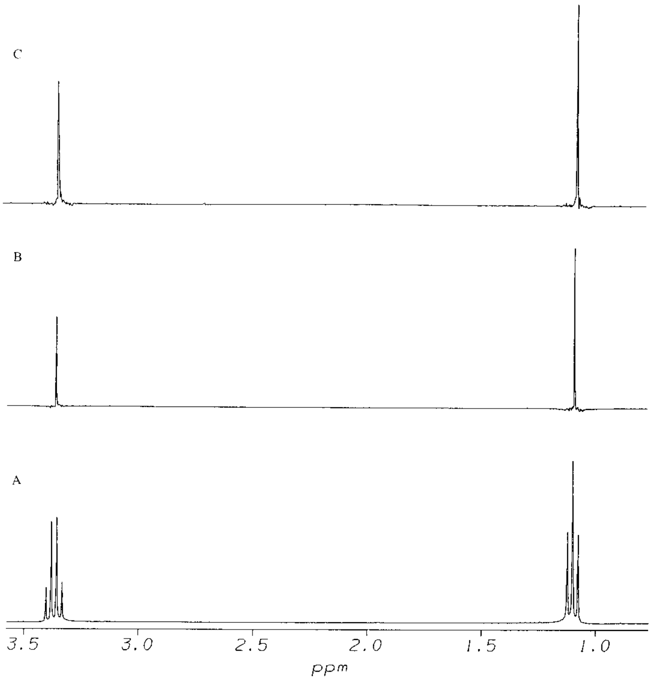

**Figure 1.** 300 MHz $^1$H NMR spectra of diethyl ether dissolved in chloroform-*d* (16% $Et_2O$–84% $CDCl_3$, at room temperature). The acquisition time was 1.4 s. (A) Normal spectrum. (B) Pure absorption decoupled spectrum: 200 recorded spin echoes treated in the time domain as explained in the text. $\tau$ and F were set to 7.2 ms and 40 Hz, respectively. The intensities of the lines depend on the coupling constant $J$ and are not in a 3:2 ratio. (C) Decoupled spectrum obtained by processing the series of echoes used in (B) for suppressing the modulation of intensities: 200 values of $k$ were used with a constant step of $2.5 \times 10^{-3}$; $k_{\max}$ was 0.5. In the spectrum obtained the intensities are no longer modulated by the scalar coupling $J$ and are in the theoretical ratio.

The method was also applied to the spectrum of 6-vinyl-1,3-dioxane [Fig. 3(A)]: 120 echoes were recorded using an acquisition time of 0.44 s and a step of 7.5 ms for $\tau$, with $T = 0.9$ s. Parameters used were $F = 35$ Hz, $k_{\max} = 0.5$, $F' = 200$ Hz, $\alpha = 45$ and $a = 0.5$ s$^{-1}$, and the decoupled spectrum is shown in Fig. 3(B).

For the AX heteronuclear spin system, a full spin echo sequence can be employed with the A resonance, and an inversion pulse is applied simultaneously to the X and A nuclei. The observed magnetization of spins A

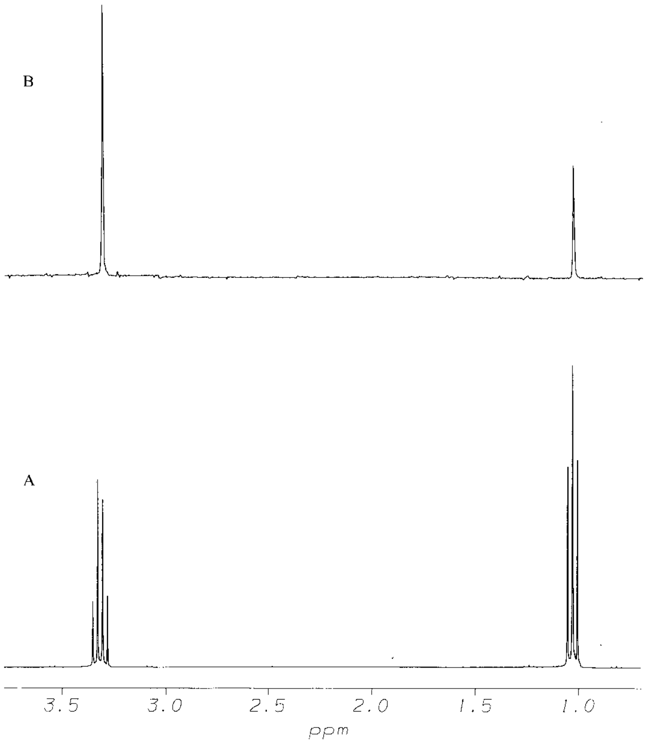

**Figure 2.** 300 MHz $^1$H NMR spectra of diethyl ether in chloroform-*d* (16% $Et_2O$–84% $CDCl_3$, at room temperature). (A) Simple spectrum obtained with an acquisition time of 1.2 s and four scans. (B) Broadband decoupled spectrum obtained by the 'constant-time' experiment. The magnetization was measured 0.32 s after the 90° pulse of the spin echo experiment for 2048 values of the echo delay.

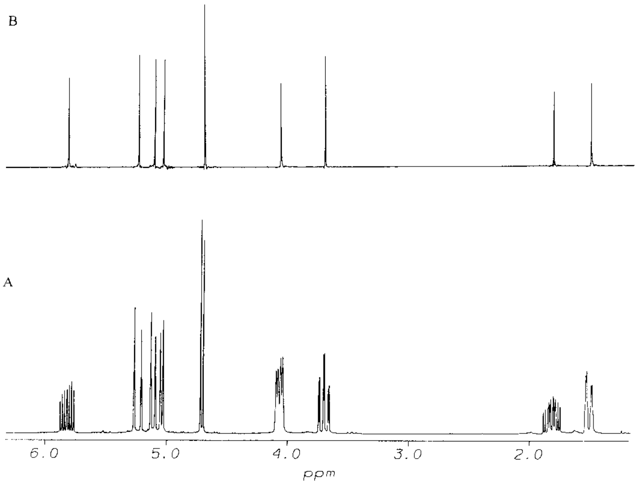

**Figure 3.** 300 MHz $^1$H NMR spectra of 6-vinyl-1,3-dioxane (20%) in chloroform-*d* (80%) at 298 K. (A) Simple spectrum recorded with an acquisition time of 0.44 s and eight scans. (B) Broadband decoupled spectrum obtained when treating 120 spin echoes recorded under the same conditions as in (A). The step of the echo delay was 7.5 ms.

may be described according to Eqn (1). The treatment is similar to the homonuclear case and the expression of the signal $S_A(t)$ is given by Eqn (8), where the spectral parameters have to be related to the A nuclei. A $^{13}$C–{$^1$H} analytical decoupling experiment was performed and the spectrum of a mixture of ethanol and diethyl ether [Fig. 4(A)] was observed using the carbon-13

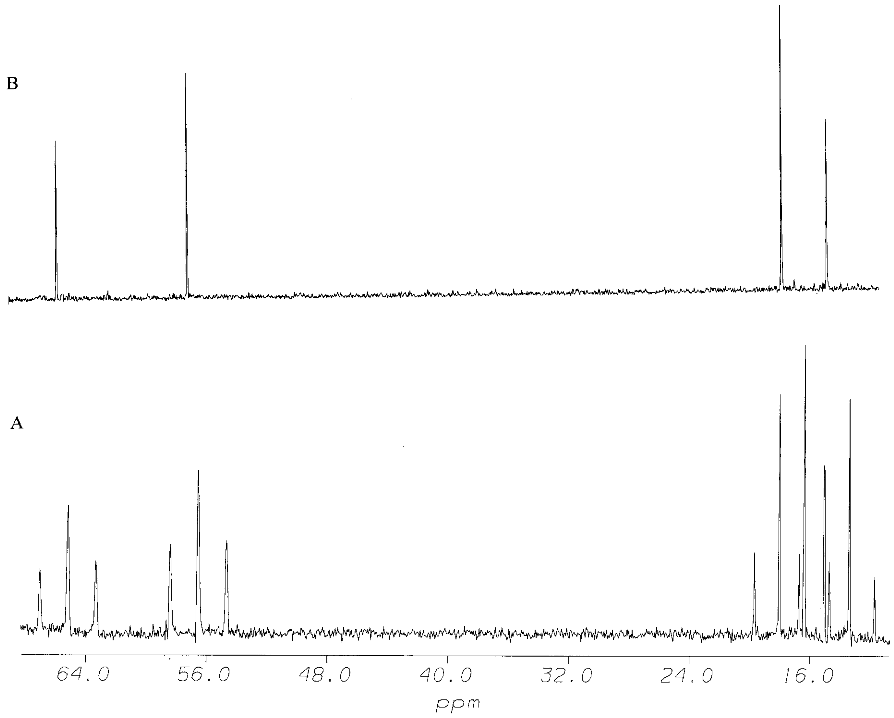

**Figure 4.** 75 MHz $^{13}$C NMR spectra of a mixture of diethyl ether and ethanol, dissolved in chloroform-*d* (45% $Et_2O$–40% EtOH–15% $CDCl_3$). (A) Simple spectrum recorded with an acquisition time of 0.4 s and 48 scans. The proton resonance was saturated for 1 s prior to the experiment. Proton decoupling was turned off during the acquisition. (B) Broadband decoupled spectrum obtained by treating 200 spin echoes recorded under the same conditions as in (A).

resonance: 200 spin echoes were recorded with an acquisition time of 0.4 s and a step of 4.25 ms for $\tau$, with $T = 0.85$ s; 48 scans were made for each echo. The proton resonance was previously saturated for 1 s in order to induce a $^{13}C$–$\{^1H\}$ NOE effect.[26,27] The following parameters were employed: $T = 0.85$ s, $F = 400$ Hz, $k_{max} = 0.5$, $F' = 800$ Hz, $\alpha = 45$ and $a = 0.6$ s$^{-1}$. The variable $k$ was then incremented by $2.5 \times 10^{-3}$ and 200 values of $k$ were used for each echo. The decoupled spectrum obtained is shown in Fig. 4(B).

## DISCUSSION

For scalar coupling outside the first-order approximation, let us consider the four resonances of an AB system denoted $A_1$, $A_2$, $B_1$ and $B_2$. Before the application of the inversion pulse of the spin echo experiment, the component $B_1$ rotates at an angular frequency $\omega_{12}$. After this pulse, the $B_1$ magnetization splits into two transverse components rotating with angular frequencies $\omega_{24}$ and $\omega_{34}$. The $\omega_{34}$ component is considered as the 'normal' component, whereas those rotating with $\omega_{24}$ is an additional one, generally called 'extra line.'[28] The corresponding expressions for the signals are then[28]

$$\begin{aligned} M_N(t, \tau) = {} & M^0 \exp[-(T - \tau)/T_2]\exp(-t/T_2^*) \\ & \times \exp[-i\pi J_{AB}(t + T - \tau)] \\ & \times \exp[i(2\pi\nu_{0AB} - D)t/2] \qquad (13) \end{aligned}$$

$$\begin{aligned} M_E(t, \tau) = {} & M^0 \exp[-(T - \tau)/T_2]\exp(-t/T_2\,^*) \\ & \times \exp[i\pi(D - J_{AB})(t + T - \tau)] \\ & \times \exp(2i\pi\nu_{0AB}\,t/2) \qquad (14) \end{aligned}$$

where $D = (\nu_{0AB}^2 - J_{AB}^2)^{1/2}$ and $\nu_{0AB} = \nu_{0A} - \nu_{0B}$; subscript N represents 'normal line' and E 'extra line.'

After decoupling and using the proposed method, the $B_1$ component gives rise to a 'normal line' at the chemical shift $(\nu_{0AB} - D)/2$ and an 'extra line' at $\nu_{0AB}/2$. Similar splitting occurs for the other components $A_1$, $A_2$, and $B_2$. Consequently, the application of analytical decoupling to a strongly coupled AB system creates two 'normal' lines of intensity $2\cos^2(2\theta)$ at $(\nu_{0AB} - D)/2$ and $(\nu_{0AB} + D)/2$ and an 'extra line' of intensity $4\sin^2(2\theta)$ at $\nu_{0AB}/2$, where $\theta$ is defined as $\theta = 0.5 \arctan(J_{AB}/\nu_{0AB})$.[24] Then for the AB system, the treatment has to be updated in such a way that it erases the 'extra lines' and that it delivers the decoupled spectrum with two 'normal lines' at their chemical shifts $\nu_{0A}$ and $\nu_{0B}$ only. Nevertheless, no practical and fast technique is available at present.

In conclusion, the method proposed to simplify analytically spectral features due to scalar coupling is very simple to carry out with weakly coupled systems. It is based on pure numerical analysis in the time domain. First the processing generates a set of decoupled spectra with different modulations according to the value of the introduced parameter $k$. These spectra are then used in a similar procedure to give broadband decoupled spectra, where the amplitudes are independent of scalar coupling. The method permits one to remove all spin–spin splittings, giving a single resonance at the chemical shift of each nucleus resonance. Such a simplification of NMR response renders the analysis of complicated spectra very easy. Since intensities are independent of the scalar coupling, the method appears suitable for quantitative studies. Generalization from homonuclear to heteronuclear spin systems has also been demonstrated. Using the example of diethyl ether, we have shown that the approach was able to provide broadband decoupled spectra with intensities in the expected theoretical ratio. With similar conditions, the examples of 6-vinyl-1,3-dioxane and a mixture of diethyl ether and ethanol show that analytical decoupling can be applied to spectra with a large number of resonance lines and to heteronuclear spin systems. The different examples of decoupled spectra obtained by this method show that the number of spin echo signals required can be restricted to less than 60.

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