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Volume-Selective Multipulse Spin-Echo Spectroscopy

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In the last few years a series of methods for spatially selective NMR spectroscopy has been suggested especially for in vivo investigations. We particularly refer to the work by Aue et al. (1), Ordidge et al. (2), and Doddrell et al. (3). The general aim of these techniques is to record a spectrum of a well-defined volume element preselected on the basis of a conventional slice image. In this communication we report on a new multipulse method for volume-selective spectroscopy (VOSY) which has the advantage of being simple, fast, and versatile. In contrast to the other techniques it selectively excites the desired volume element in the proper sense rather than to suppress signals from the undesired volume.

Three-pulse sequences have previously been used for pure imaging purposes (4, 5). As we will show in the following, special modifications of this sequence are also suitable for volume-selective spectroscopy. Despite the apparent similarity of the pulse programs to the imaging sequences suggested in Refs. (4, 5), the VOSY technique is based on a different philosophy which opens a new class of volume-selective NMR experiments and extensions to multipulse sequences.

Figures 1 and 2 show three-pulse VOSY RF- and field-gradient-pulse programs as examples and as demonstration of the principle (compare Hahn's paper (6)). Three slice-selective RF pulses with field-gradient pulses in the three spatial directions are applied. The pulse lengths are 90° but shorter pulses will serve also. Let us first describe how the different echo signals are formed in principle and then the methods for selective detection.

Each RF pulse is followed by a free-induction signal of the selected slice. Thus the signals \( A_i \) \( (i = 1, 2, 3) \) in Fig. 1 represent the corresponding three perpendicular slices. Each single excitation coherence is partially refocused by each of the following RF pulses so that the two-pulse echoes \( B_i \) \( (i = 1, 2, 3) \) are formed. Thus three line-selective signals \( B_i \) appear.

These line-selective coherences can again be partially refocused by one or more subsequent RF pulses. In the pulse scheme of Fig. 1 only one three-pulse echo of this type, namely the signal \( C_1 \), arises selectively for the volume element common to the three slices.

A further three-pulse signal appears as the stimulated echo \( C_2 \) which again is due to the volume element selected by the three slices. Its formation is based on the line-selective transfer of transverse magnetization in the \( z \) direction where the magnetization...
is stored for an interval $\tau_2$. The third pulse then selectively produces a spin coherence in the transverse plane leading to the stimulated echo $C_2$. This signal thus is influenced by a $T_1$ decay in the $\tau_2$ interval which interrupts the evolution of the initial spin coherence, and by $T_2$ decays in the other intervals ($T_1$ spin–lattice relaxation time; $T_2$ transverse relaxation time). The echoes $B_i$ and $C_i$, on the other hand, are formed without any $T_1$-sensitive interval.

The observation of the signals described above appears to be difficult because of two aggravating circumstances. First, the selection gradients simultaneously defocus the coherences if they are distributed asymmetrically over the echo formation intervals. Second, even with appropriate choice of the times $\tau_1$ and $\tau_2$, considerable signal overlap must be expected. These difficulties can however be safely overcome by special gradient-pulse programs.

In Fig. 2 we suggest a series of schemes for the selective detection of the signals $B_2$, $B_3$, $C_1$, and $C_3$. Two proposals are made for the selection of each of the different signals. One can either correct the dephasing tendency of the selection gradients by appropriate correction gradient pulses or use an appropriate combination of nonrefocusing and totally or partly self-refocusing selection gradients. In each case, the additional gradient pulses have to be optimized separately for maximum echo amplitude. As the schemes in Fig. 2 are self-explanatory, we do not go into further details.

Note, however, that unwanted coherences are, so to speak, automatically spoiled by the asymmetry of the slice-selection gradients in the course of the pulse sequence. If this homospoil effect should be insufficient, either additional gradient pulses can be applied or, preferably, the asymmetry can be increased by partial prolongation of the slice-selection gradients (Fig. 2). The latter method has been applied in the $C_2$-selective test experiment described in the following.

The $C_2$ selection in our test experiment has been performed with the gradient-pulse
sequence shown in Fig. 2 (version (a)). In order to ensure the perfect suppression especially of the $C_1$ echo, the $G_z$ gradient has been extended into the $\tau_2$ interval according to the dashed line in Fig. 2. We thus have taken advantage of the fact that the $C_2$ signal is insensitive to the length and strength of any gradient applied during the $\tau_2$ interval.

The experiments were carried out with a Bruker BMT 24/40 in vivo NMR spectrometer operating at 100 MHz proton resonance frequency. The magnet bore diameter was 40 cm. A phantom sample was used consisting of a cubic array of $3^3$ spherical plastic vessels with a diameter of 24 mm. The vessel in the center was filled with benzene; the surrounding spheres contained water (Fig. 3).
Figure 4 shows the 100 MHz one-scan $^1$H spectra selectively recorded in cubic volume elements (about (3 mm)$^3$) subsequently located at positions in the benzene, water, and interstitial space area, respectively, as indicated in Fig. 3. In this experiment the shape of the selective RF pulses was Gaussian for simplicity. The time intervals were $\tau_1 = 25$ ms and $\tau_2 = 67$ ms. The signal intensities correctly reflect the $^1$H densities in the three space areas. The $^1$H densities of water and benzene are related as 2.1:1.0. The suppression of signals originating from the space outside the selected volume elements was complete.

Note that, once the position of the sensitive volume element has been calibrated to the field gradients, any location can immediately be predetermined by calculating the corresponding frequencies of the RF pulses. Thus the spectra in Fig. 4 represent one-trial experiments.

The VOSY method has some remarkable advantages compared with other techniques: (a) The complete suppression of signals not originating from the selected volume element can be reached in a one-scan experiment. (b) There is only minor saturation of spins located outside of the observed volume element (namely those within the three perpendicular slices) so that a series of nonoverlapping volume elements can be investigated subsequently without any delay. If the reading pulse ($P_3$ in Fig. 1) is replaced by a sequence of reading pulses, a distribution of volume elements along a line defined by the first two slices in principle can be scanned with a rate equal to the reciprocal acquisition time. (c) The average RF power irradiated during one scan is intrinsically small and is expected to cause no complication under in vivo conditions.

A certain limitation for nuclei with short $T_2$ value is given by the signal reduction due to the $T_2$-sensitive intervals of the sequences, namely the $\tau_1$ periods. In the test experiments described above the typical $T_2$-sensitive time per scan was chosen to be $2\tau_1 = 50$ ms. This time can be reduced to the minimum needed for the gradient changes. At the present state of the art the $T_2$-sensitive time then would be about 30 ms for version (a) and somewhat less for version (b) of the C$_2$-selective gradient-pulse sequence (Fig. 2). Thus the technique will not be very advantageous for $^{31}$P spectroscopy. For proton resonance, on the other hand, the weakening of the water signal due to the short $T_2$ is quite desirable.

The minimum $\tau_2$ value is about 7.5 ms for the same reason as in the case of $\tau_1$. Practically it will not limit the applicability of the VOSY method particularly in the C$_2$ version where this interval is governed by spin–lattice relaxation.

![Diagram](image-url)  
**Fig. 3.** Mid-cross section of the phantom sample used in the test experiment. Central sphere: benzene; surrounding spheres: water. Diameter of the spheres: 24 mm; size of the selected volume elements: (3 mm)$^3$. 

[Image: Diagram of a mid-cross section of a phantom sample used in the test experiment. Central sphere is labeled as benzene, surrounding spheres as water. Diameter of spheres: 24 mm; size of selected volume elements: (3 mm)$^3$.]
FIG. 4. Application of the C₂ VOSY three-pulse sequence (Figs. 1 and 2) to volume-selective $^1$H spectroscopy of the volume elements indicated in Fig. 3 (I, water; II, benzene; III, interstitial space). The spectra are one-scan records with identical amplifier and vertical display settings. The zero position of the parts per million scale is arbitrary.

Because the pulse scheme in Fig. 1 is based on 90° refocusing pulses, the amplitude of the C₂ echo is reduced by a factor of 0.5, that of the C₁ echo even by a factor of 0.25 compared with a two-pulse echo refocused by a 180° pulse. On the other hand, in a given time more signals (of different volume elements) can be recorded than with the other volume-selective techniques which saturate all nuclei outside of the volume element under investigation. Thus, if one is interested in spectra of a series of volume elements all at once, as is likely the case in medical applications, the VOSY technique is expected to be effectively more sensitive.

The pulse scheme in Fig. 1 implies a series of special experiments promising the combination of spectroscopic and other information. We propose the following modifications based on the observation of the volume-selective echoes C₁ or C₂.
(a) Variation of \( \tau_1 \) or formation of additional echoes by adding further 180° pulses in order to permit records of stacked plots of \( T_2 \)-weighted \( C_1 \) or \( C_2 \) spectra.

(b) Variation of \( \tau_2 \) in order to permit records of stacked plots of \( T_1 \)-weighted \( C_2 \) spectra.

(c) Addition of equal gradient pulses with varying amplitudes in the intervals \( P_1 \ldots P_2 \) and \( P_3 \ldots C_2 \) in order to permit records of \( D \)-weighted stimulated echoes (7) (\( D \) self-diffusion is the coefficient). The data then can be represented as stacked plots of \( D \)-weighted \( C_2 \) spectra.

(d) Variation of one selective pulse in order to permit records of stacked plots of \( C_1 \) or \( C_2 \) spectra distributed along a line defined by the other two selective pulses.

(e) Adding the DEPT pulse sequence (8, 9) where the first heteronuclear 90° pulse is replaced by the \( C_1 \) or \( C_2 \) echo, in order to permit records of sensitivity-enhanced and volume-selective \( ^{13}C \) spectra (or of other proton-coupled nuclei).

(f) Choosing \( \tau_1 = (4J)^{-1} \) (\( J \) is a typical proton–proton coupling constant) in order to permit water and lipid signal suppression by multiple-quantum filtering (10).

(g) Suppression of signals from uncoupled spins (e.g., water protons) can also be achieved by choosing \( \tau_1 = (4J)^{-1} \) and applying selective heteronuclear pulses simultaneously with the second and third RF pulses (modified spin-echo double-resonance technique). The homonuclear version of the SEDOR technique can also be considered (11). Note that proposals (b) and (d) can also be carried out in a single scan by a sequence of reading pulses shorter than 90° (3).

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