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Solvent Suppression Using Selective Echo Dephasing

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Many types of NMR experiments have benefited from the significant advances in B_0 gradient technology which have taken place over the past decade (*1–4*). In NMR spectroscopy, B_0 gradients can eliminate the need for phase cycling to select coherence pathways (*5–15*) and to achieve high-quality water suppression (*16–31*). Gradient-enhanced water suppression methods can generally be classified into two categories: (1) frequency-selective excitation followed by dephasing (spoiling) with gradient pulses (*16–23*), and (2) frequency-selective refocusing flanked by gradient pulses which dephase unwanted (nonrefocused) transverse magnetization (*24–31*). In the latter category, a technique known as excitation sculpting (*31*) offers the advantage that the transverse magnetization is returned to its original position, scaled by the square of the probability of spin inversion. This frequency-dependent inversion is determined by the choice of refocusing pulse S, which is applied an even number of times to eliminate phase distortions in the acquired even echo. S can be any sequence of RF pulses of any kind (*31*), although S is usually a composite sequence consisting of selective and nonselective 180° pulses (*32–36*). Excitation sculpting also has the advantage of being less sensitive to flip-angle errors than the related technique known as WATERGATE (*26, 27*).

As with any multiecho sequence, the minimum time (TE) required to execute excitation sculpting is limited by the time needed to apply at least two S sequences. In other words, the spins of interest (i.e., peaks outside the suppression band) must experience at least two refocusing pulses which may require a nonnegligible duration in certain applications. In practice, this situation arises in S sequences that employ composite, adiabatic, or spatially selective refocusing pulses which are longer than conventional (square) pulses. In this Communication, we describe a frequency-selective suppression method called MEGA (*37*) which offers many of the desirable features of excitation sculpting, with the additional advantage that the signals outside the suppression band are refocused with a single pulse (i.e., the signals of interest are refocused with a single echo).

Selective suppression can be achieved with MEGA in any sequence which forms a spin or stimulated echo. The subject of this Communication is limited to a simple spin-echo implementation of MEGA (Fig. 1a), which is compared with similar implementations of excitation sculpting (Fig. 1b) and WATERGATE (Fig. 1c).

MEGA can be understood using the same formalism that

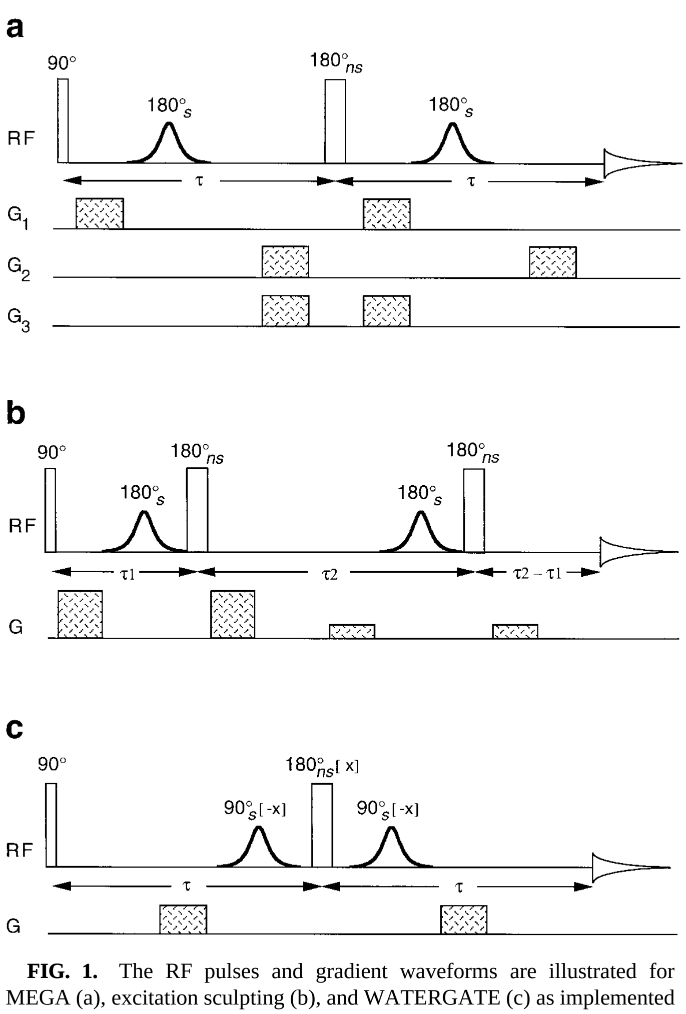

FIG. 1. The RF pulses and gradient waveforms are illustrated for MEGA (a), excitation sculpting (b), and WATERGATE (c) as implemented in a spin-echo sequence.

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was employed in the analysis of excitation sculpting (*31*). Accordingly, the unity transformation describing the effect of an arbitrary pulse is

$$S = \exp(-i\beta I_z)\exp(-i\theta I_y)\exp(-i\alpha I_x)\exp(i\theta I_y)\exp(i\beta I_z), \quad [1]$$

where α is the net flip angle about an effective rotation axis described by phase angle β and azimuthal angle θ. The spatially dependent phase shift induced by a gradient can be described by

$$G_j = \exp(-i\phi_j I_z), \quad [2]$$

where the index j (=1, 2, 3) denotes a unique (orthogonal) gradient axis. For optimal performance, MEGA requires triple-axis gradients. The complete propagator U describing the MEGA sequence that follows the initial 90° pulse (Fig. 1a) is then

$$U = G_2 S_s G_1 G_3 S_{ns} G_3 G_2 S_s G_1, \quad [3]$$

where S_s and S_{ns} represent selective and nonselective pulses, respectively. The final magnetization can be calculated from

$$M_\nu = \left(\frac{1}{2\pi}\right)^3 \int_0^{2\pi}\int_0^{2\pi}\int_0^{2\pi} \mathrm{Tr}\{I_\nu U \boldsymbol{\sigma}(0) U^\dagger\} d\phi_1 d\phi_2 d\phi_3, \quad [4]$$

where $\nu = x$, y, or z and the density matrix $\boldsymbol{\sigma}(0)$ (=$\mathbf{m}\cdot\mathbf{I}$) represents the magnetization at $t = 0$ (immediately after the initial 90° pulse). Integration of Eq. [4] yields the elements needed to construct the 3×3 rotation matrix

$$\mathbf{R} = \begin{bmatrix} ab\cos 2\beta_{ns} & ab\sin 2\beta_{ns} & 0 \\ ab\sin 2\beta_{ns} & -ab\cos 2\beta_{ns} & 0 \\ 0 & 0 & cd \end{bmatrix}, \quad [5]$$

where

$$a = \tfrac{1}{4}(1 + \cos\alpha_s\cos^2\theta_s + \sin^2\theta_s)^2$$
$$= [1 - \cos^2\theta_s\sin^2(\alpha_s/2)]^2, \quad [6]$$
$$b = \tfrac{1}{2}(1 - \cos\alpha_{ns}\cos^2\theta_{ns} - \sin^2\theta_{ns})$$
$$= \cos^2\theta_{ns}\sin^2(\alpha_{ns}/2), \quad [7]$$
$$c = (\cos\alpha_s\cos^2\theta_s + \sin^2\theta_s)^2, \quad [8]$$
$$d = \cos\alpha_{ns}\cos^2\theta_{ns} + \sin^2\theta_{ns}, \quad [9]$$

and the subscripts, s and ns, denote the angles associated with the selective and nonselective pulses, respectively.

R describes the transformation from the initial magnetization vector **m** to the final vector **M** according to **M** = **Rm**. When the phase of the nonselective pulse (β_{ns}) is constant, **R** is diagonalized by a final phase shift of $-2\beta_{ns}$, which can be achieved as part of the usual zero-order phase correction applied to the spectrum. Alternatively, when $\beta_{ns} = 0°$, **R** simplifies directly to

$$\mathbf{R} = \begin{bmatrix} ab & 0 & 0 \\ 0 & -ab & 0 \\ 0 & 0 & cd \end{bmatrix}. \quad [10]$$

Hence, MEGA avoids any interconversion of longitudinal and transverse magnetization and the phase of the transverse magnetization remains invariant, despite changes in the resonance offset and flip angles (α_s and α_{ns}). In these regards, MEGA is similar to excitation sculpting. However, these desirable properties can be realized with MEGA only when the rotation axis of the nonselective pulse (β_{ns}) is invariant with resonance offset and flip angle. Fortunately, the general utility of MEGA is not likely to be limited by this latter requirement, since a constant β_{ns} is afforded by many common refocusing pulses, including a simple square pulse, symmetric amplitude-modulated pulses (e.g., sinc- and Gaussian-shaped pulses), and certain composite pulses (*38*).

Like excitation sculpting, the suppression profile of MEGA is determined by the inversion profiles generated by the RF pulses in the sequence. When a RF pulse is flanked by gradient pulses, the inversion profile is given by the matrix element (*31*)

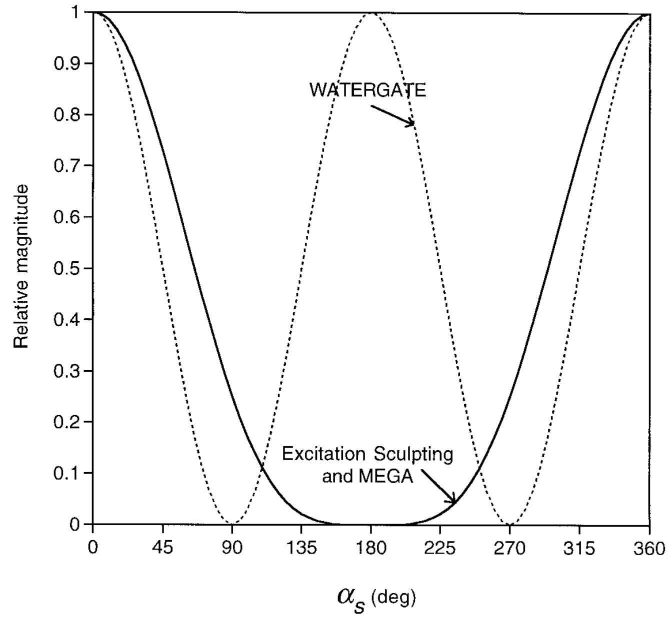

FIG. 2. Theoretical sensitivity of MEGA, excitation sculpting, and WATERGATE to errors in the flip angles of the selective pulses. The calculations assumed that the nonselective refocusing pulses were ideal (α_{ns} = 180° and θ_{ns} = 0°) and that the dephasing of the transverse magnetization was complete. These simulations indicate that WATERGATE is more sensitive to RF inhomogeneity and misset flip angles than either excitation sculpting or MEGA.

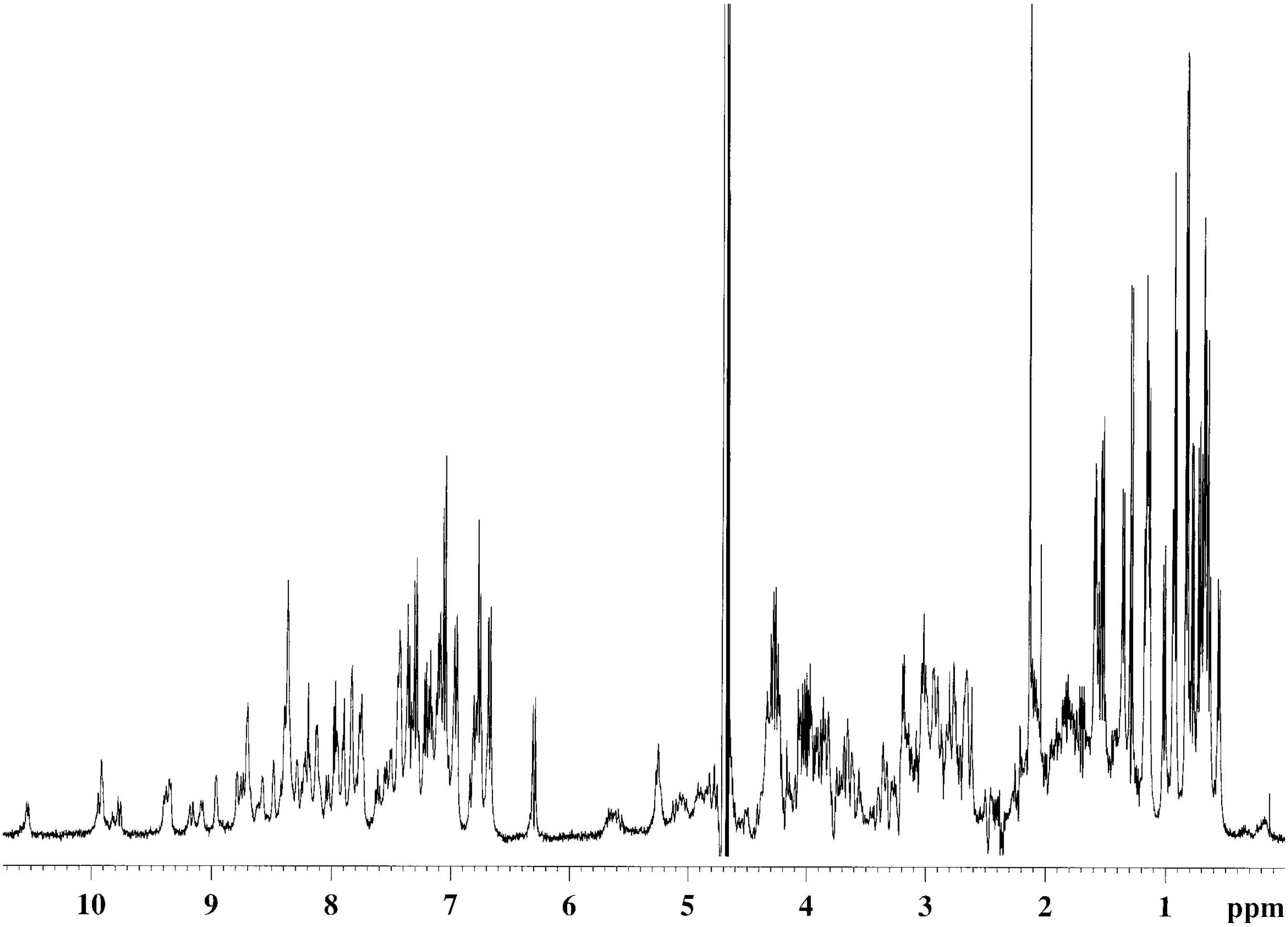

FIG. 3. ^{1}H spectrum of 1.5 m*M* BPTI in 90% H_2O using MEGA (TE = 19.56 ms). The phase relationship between the transmitter and receiver remained constant during signal averaging (NEX = 16). The spectrum was acquired with a Bruker DMX 500 spectrometer equipped with a triple-axis shielded gradient probe. Selective pulses were sinc-shaped (single-lobed, length = 5.77 ms). Sine-shaped gradient pulses (duration = 1 ms) had amplitudes of 27 G/cm along the *x* and *y* axes and 36 G/cm along the *z* axis.

$$\mathbf{T}(3,3) = \cos\alpha\,\cos^2\theta + \sin^2\theta. \qquad [11]$$

From Eq. [11], the probability of inversion is (*31, 39*)

$$P = \tfrac{1}{2}(1 - \cos\alpha\,\cos^2\theta - \sin^2\theta) = \cos^2\theta\,\sin^2(\alpha/2), \qquad [12]$$

or alternatively, the probability that the longitudinal magnetization is not affected by the pulse is

$$Q = \tfrac{1}{2}(1 + \cos\alpha\,\cos^2\theta + \sin^2\theta) = 1 - \cos^2\theta\,\sin^2(\alpha/2). \qquad [13]$$

Substituting Eqs. [6]–[9], [12], and [13] into Eq. [10] yields

$$\mathbf{R} = \begin{bmatrix} P_{ns}Q_s^2 & 0 & 0 \\ 0 & -P_{ns}Q_s^2 & 0 \\ 0 & 0 & (1 - 2P_{ns})(1 - 2Q_s)^2 \end{bmatrix} \qquad [14]$$

which shows that the suppression profile of MEGA is solely dependent on the inversion profiles of the selective and nonselective pulses.

The performance of the solvent suppression methods in Fig. 1 will degrade as the flip angles of the frequency-selective pulses deviate from the nominal values. In practice, flip-angle errors arise from RF inhomogeneity and inaccuracies in the calibration of pulse lengths (or power). With MEGA and excitation sculpting, the suppression diminishes equivalently as the flip angle of the selective pulses (α_s) deviates from 180°. Assuming that the nonselective pulse is ideal, Eq. [14] predicts residual (unsuppressed) signal proportional to $\cos^4(\alpha_s/2)$. In WATERGATE (*26*), the nominal value for α_s is 90°. From a theoretical analysis similar to that performed above, the predicted suppression with WATERGATE is proportional to $\cos^2(\alpha_s)$. Plots of these functions (Fig. 2) show WATERGATE to have the lowest tolerance to flip-angle errors.

The experimental performance of MEGA is demonstrated in Fig. 3, which shows a ^{1}H spectrum (500 MHz) of 1.5 m*M* BPTI in 90° H_2O. The spectrum exhibits excellent water suppression and is devoid of phase distortion outside the bandwidth of the frequency-selective pulses.

In summary, we have described a new solvent suppression method, MEGA, which is based on B_0 gradient dephasing of selective echoes. MEGA is closely related to two other gradient-enhanced solvent suppression methods, excitation sculpting and WATERGATE. Excitation sculpting has the advantage of generating constant magnetization phase for any choice of pulse S, whereas MEGA yields uniform magnetization phase only when a constant rotation axis is provided by the pulse used to refocus the spins of interest. Of the methods considered here, MEGA and excitation sculpting offer the highest tolerance to flip-angle errors of the selective pulses. MEGA and WATERGATE have the advantage of allowing short echo times, since the spins of interest are refocused in a single (primary) echo. In practice, the method of choice will depend on the particular requirements of each experimental application.

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