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Optimization of Residual Water Signal Removal by HLSVD on Simulated Short Echo Time Proton MR Spectra of the Human Brain

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Suppression of the residual water signal from proton magnetic resonance (MR) spectra recorded in human brain is a prerequisite to an accurate quantification of cerebral metabolites. Several postacquisition methods of residual water signal suppression have been reported but none of them provide a complete elimination of the residual water signal, thereby preventing reliable quantification of brain metabolites. In the present study, the elimination of the residual water signal by the Hankel Lanczos singular value decomposition method has been evaluated and optimized to provide fast automated processing of spectra. Model free induction decays, reproducing the proton signal acquired in human brain localized MR spectroscopy at short echo times (e.g., 20 ms), have been generated. The optimal parameters in terms of number of components and dimension of the Hankel data matrix allowing complete elimination of the residual water signal are reported. © 2001 Academic Press

Key Words: **STEAM localized proton spectroscopy; water signal removal; HLSVD method.**

INTRODUCTION

Accurate quantification of cerebral metabolites by *in vivo* proton magnetic resonance spectroscopy (MRS) is essential to the study of many brain disorders. In the spectra acquired at short echo times (e.g., 20 ms) with the stimulated echo acquisition mode (STEAM) localized MRS sequence, the residual water signal distorts the signals of several metabolites and prevents their accurate quantification. As a consequence, adequate water signal suppression remains a key and pending issue in the routine use of proton MRS to investigate human brain metabolism in a clinical context.

Several methods have been developed to suppress the water signal before acquisition (*1, 2*), but the results are not satisfactory. One of the problems inherent to these methods is to achieve complete elimination of the water resonance without altering the metabolite signals of interest. As a compromise, either the signals of metabolites close to the water signal are reduced or a significant residual water signal remains on the spectrum. In both cases, quantification of brain metabolites is inaccurate because of baseline distortion due to the residual water signal. Alternatively, numerical methods have been designed to remove the residual water signal after acquisition. However, due to magnetic field inhomogeneities and lineshape distortions caused by the water signal suppression sequence, the resulting water resonance proves very difficult to parameterize. Most of the postacquisition methods are based on bandpass filtering (*3–5*) or consist of subtracting the solvent signal calculated by either decomposition methods (*6–13*) or nonlinear least-squares methods (*14*). In addition, frequency domain filtering (*15*) or baseline correction (*16*) by fitting the water spectral region by a polynomial function has been proposed. All of these methods remove the residual water resonance but are limited by crude approximations regarding the fitting of the water resonance humps.

Pijnappel *et al*. (*9*) have developed the Hankel Lanczos singular value decomposition (HLSVD) method in the time domain. With this method, Van den Boogaart *et al*. (*11*) have reported a satisfactory elimination of the residual water resonance from a proton MR brain spectrum. The HLSVD water signal removal protocol is based on a choice of parameters such as the number of exponentially damped sinusoids and the size of data sets for fitting the entire signal. To our knowledge, no study has been devoted so far to the determination of the optimal values of all the parameters to be selected in the implementation of the HLSVD method, particularly with the goal of processing quickly and automatically short echo time human brain spectra. The objective of the present study was to determine the best values of the parameters, which afford an adequate removal of the residual water signal under the spectrum of brain metabolites. Under those optimized conditions, an accurate quantification of metabolites in the proton MR spectra of the human brain has become possible. Free induction decay (FID) models have been generated to best reproduce the proton MR signals acquired in human brain localized spectroscopy at short echo times and also the representative lineshape of the residual water signals obtained on clinical MRI/MRS systems. Large data sets representative of *in vivo* low-resolution brain spectra with limited signal-to-noise ratio were analyzed.

METHODS

Model signals in the time domain were generated on the basis of actual *in vivo* human brain proton MR spectra recorded

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at 1.5 T on a Siemens Magnetom SP63 using a STEAM (*17*) sequence (20-ms echo time, 30-ms mixing time, 1024-ms acquisition time, and 1.5-s repetition time) combined with a water suppression sequence using chemical shift selective excitation (CHESS) pulses.

Metabolite Signals

Based on actual *in vivo* human brain proton MR spectra recorded on N_{data} data points, signals of metabolites have been modeled using 19 exponentially damped sinusoids which correspond to the number of principal metabolite components in the spectra recorded on human brain as

$$\text{FID}_{\text{metabolite}}(n) = \sum_{k=1}^{19} A_k e^{i\varphi_k} e^{(-\alpha_k + 2\pi i \upsilon_k) n \Delta t}$$
$$n = 1, \ldots, N_{\text{data}}, \Delta t = 1 \text{ ms}. \quad [1]$$

The model function describes the sum of MR signals, A_k being the amplitude, υ_k the frequency, α_k the damping factors, and φ_k the phase of each signal. N_{data} is the number of data points on the FID. The parameters used to define the reference model signal of metabolites are listed in Table 1. The corresponding spectrum ($\text{SPE}_{\text{metabolite}}$) obtained by Fourier transform of $\text{FID}_{\text{metabolite}}$ is displayed in Fig. 1.

TABLE 1
$\text{FID}_{\text{metabolite}}$ Simulation Parameters Calculated from the Fit of *in Vivo* Human Brain Proton MR Spectra

Peak	υ_k (Hz)	A_k (au)	α_k (Hz)	ϕ_k (°)
1	−47	0.068	5.3	0
2	−56	0.086	8.0	0
3	−63	0.058	4.6	0
4	−70	0.071	4.6	0
5	−82	0.024	4.6	0
6	−92	0.118	6.4	0
7	−103	0.12	4.6	0
8	−113	0.005	2.3	0
9	−121	0.011	4.0	0
10	−128	0.099	8.0	0
11	−138	0.039	4.6	0
12	−145	0.068	8.0	0
13	−153	0.094	8.0	0
14	−160	0.128	6.4	0
15	−167	0.173	4.0	0
16	−191	0.033	15.0	0
17	−200	0.186	22.0	0
18	−228	0.219	33.0	0
19	−236	0.169	23.0	0

Note. Exponentially damped sinusoids are characterized by amplitudes A_k in arbitrary units (au). Frequencies υ_k and damping factors α_k are given in hertz and phases φ_k in degrees.

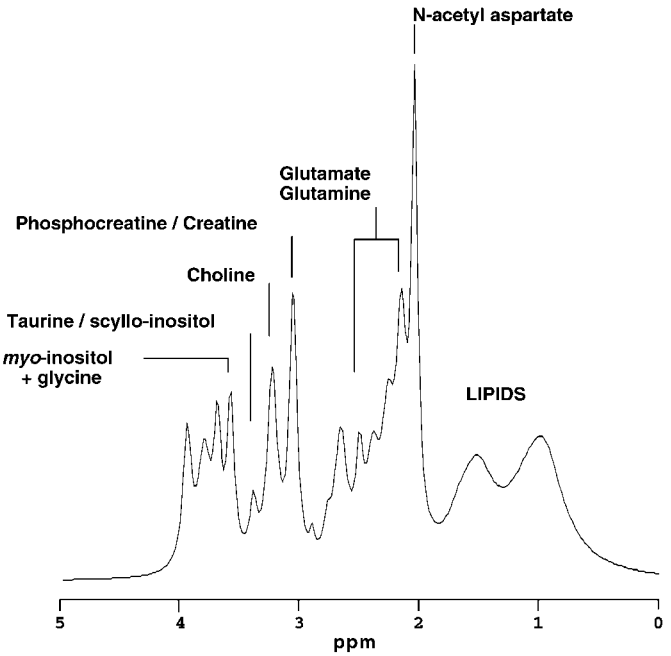

FIG. 1. Real part of a simulated human brain proton MR spectrum showing metabolite resonances between 0 and 4 ppm.

Residual Water Signals

The use of CHESS pulses, usually imposed on clinical MRI/MRS systems, largely distorts the residual water lineshape. Van den Boogaart *et al*. (*11*) proposed to describe the water resonance with 3 to 10 exponentials, but they reported that only 3 seem to be really significant. From a large set of different lineshapes acquired *in vivo*, we modeled the residual water signal with a linear combination of 4 to 6 exponentials in most cases. We constructed 15 different lineshapes of residual water signal ($\text{FID}_{\text{water},i}$, $i = 1$ to 15). The first group ($i = 1$ to 5) was constructed with the sum of 4 exponentials, the second group ($i = 6$ to 10) with 5 exponentials, and the third group ($i = 11$ to 15) with 6 exponentials. Figure 2 shows the five typical lineshapes of residual water spectrum within the second group.

Model Signals

Model FIDs have been obtained as a linear combination of signals of water, metabolites, and noise as

$$\text{FID}_{\text{model}} = \alpha \times \text{FID}_{\text{water},i} + \beta \times \text{FID}_{\text{metabolite}} + \Psi, \quad [2]$$

where α designates the amplitude factor of residual water contribution $\text{FID}_{\text{water},i}$ (i standing for the ith residual water model), β the amplitude factor of metabolite contribution, and Ψ the noise.

Values of parameters $\alpha = 45$ and β such that $0.5 \leq \beta \leq 2.5$ were selected to obtain spectra with metabolite signal to residual water signal ratios in the range of the ratios measured *in vivo*.

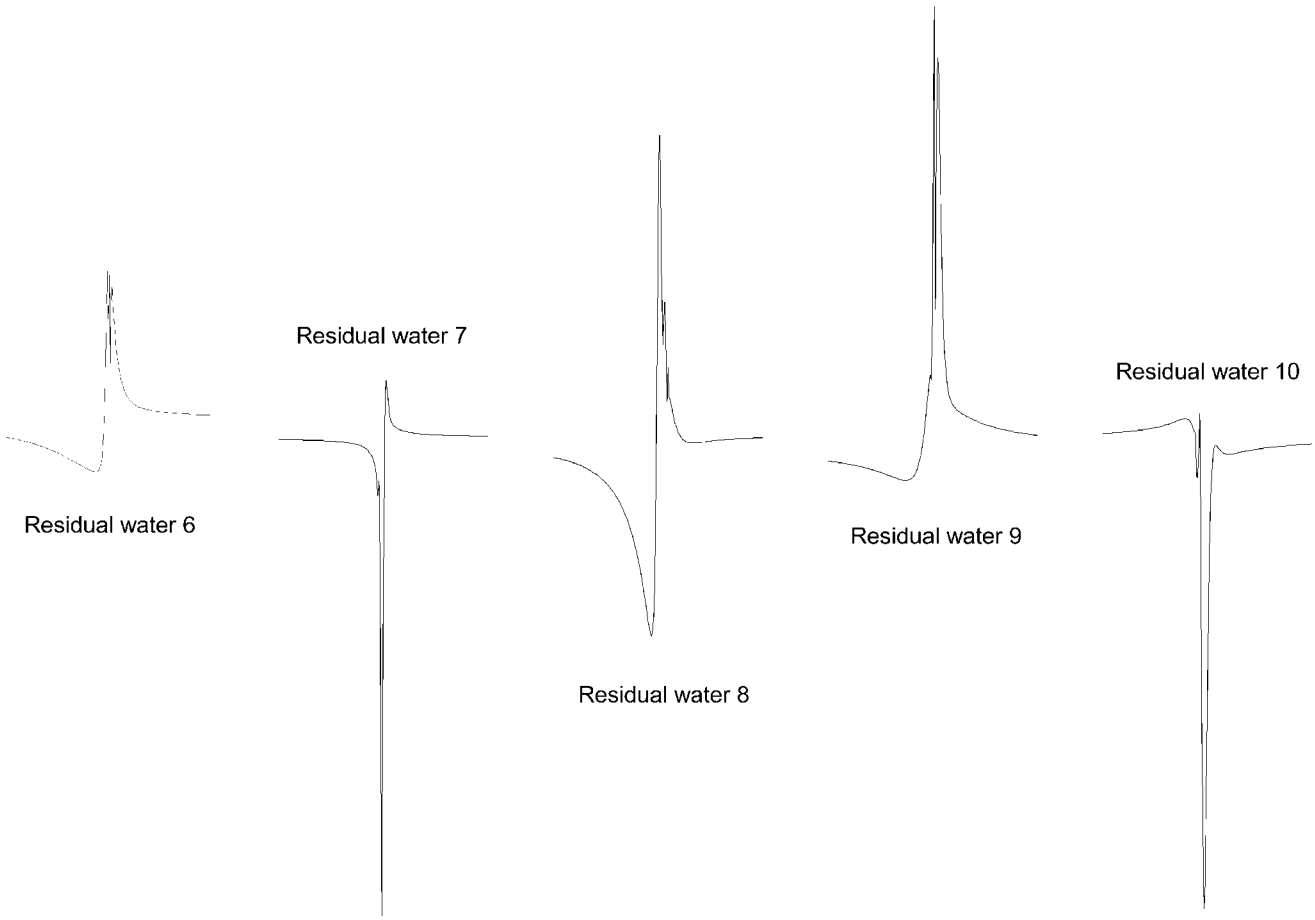

FIG. 2. Real part of the spectrum of five residual water model obtained with five exponentially damped sinusoids. Each residual water resonance is characterized by a typical lineshape.

The white gaussian noise Ψ, in the time domain, was chosen with a zero mean value and a standard deviation σ ranging between 0.005 (arbitrary unit) and 0.05 (arbitrary unit). The noise standard deviation was calculated on a spectrum region devoid of metabolite signals, measured on an actual brain spectrum. In the case of the inositol signal at -70 Hz, with $\alpha = 0$, $\beta = 1$, $\sigma = 0.025$, a signal-to-noise ratio equal to 4 (signal height/2 $\times$ SD of frequency noise) was obtained on the Fourier transform of the $\text{FID}_{\text{model}}$.

Residual Water Signal Removal by the HLSVD Method

The Hankel Lanczos singular value decomposition method is a so-called "black box" method which estimates the whole set of parameters of the model by making full use of the mathematical characteristics of the model function. This is done via an algorithm based on matrix algebra allowing singular value decomposition (*9*).

From N data points x_n of a signal and with $M \leq N$, a $(N - M + 1) \times M$ data matrix with a Hankel structure is constructed as follows:

$$X = \begin{bmatrix} x_0 & x_1 & \dots & x_{M-1} \\ x_1 & \dots & \dots & \dots \\ \dots & \dots & \dots & \dots \\ x_{N-M} & \dots & \dots & x_{N-1} \end{bmatrix}.$$

The HLSVD algorithm is applied to the X matrix, and a signal decomposition in K exponentially damped sinusoids is obtained (*9, 11, 18*).

Ideally, the FID signal is noiseless and results exactly from the addition of K exponentially damped sinusoids, which are characterized by amplitudes A_k, frequencies υ_k, damping factors α_k, and phases φ_k, as

$$X_n = \sum_{k=1}^{K} A_k e^{i\varphi_k} e^{(-\alpha_k + 2\pi i \upsilon_k) n \Delta t} \quad n = 1, \dots, N. \qquad [3]$$

In order to remove the residual water signal, the exponentially damped sinusoids whose frequencies are located in the water

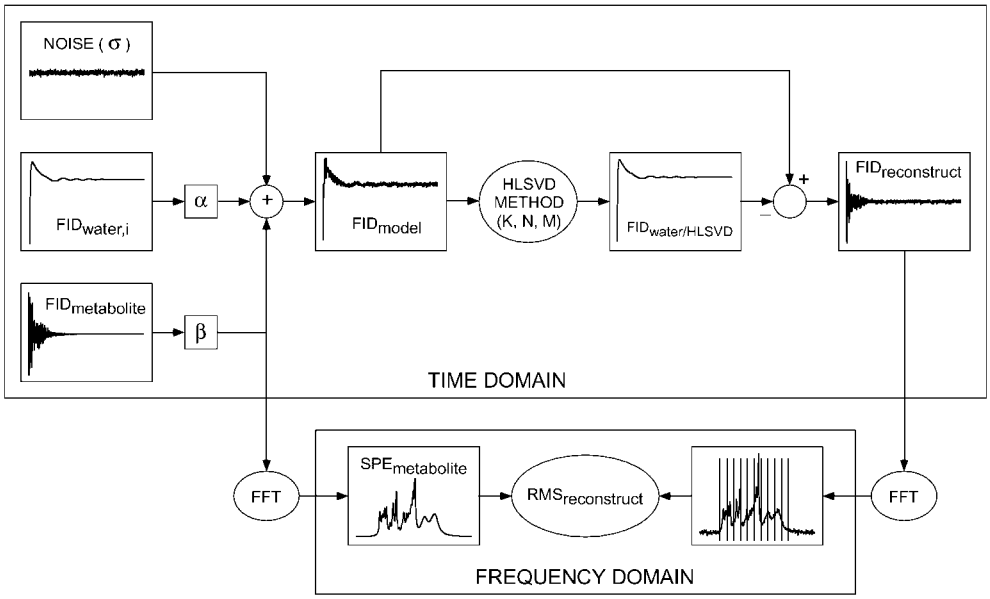

FIG. 3. Signal processing protocol. In the time domain, FID_{model} is obtained as a linear combination of $FID_{water,i}$, $FID_{metabolite}$, and noise. The HLSVD method is then applied to evaluate the residual water signal $FID_{water,i/HLSVD}$. Then the $FID_{reconstruct}$ is obtained. The accuracy of residual water signal removal by HLSVD method is finally evaluated in the frequency domain.

region are selected and subtracted from the original FID. Then, this new signal ($FID_{reconstruct}$) can be processed by fast Fourier transform or by any other appropriate methods for quantitative analysis.

With noisy FID signal, the crux of the method lies in the formation of the Hankel matrix X extracted from the acquired data points (N_{data}), i.e., in the choice of the values of N and M. In addition, the choice of total model order K is critical.

To our knowledge, no exact analytical theory exists currently that gives the optimal values of the N, M, and K parameters, for any kind of spectrum (with low- and/or high-resolution signals), any value of N_{data}, and any SNR level. There only exist approximated analytical theories (*19, 20*) based on high SNR level and applied only to one single exponential. These theoretical approximations have always been validated by numerical simulation and the authors (*19, 20*) had identified that requirement very early. In several studies (*9, 11, 21*), different empirical rules have been proposed to select the optimal values of the parameters. These rules are often inaccurate; they lack an exact analytical demonstration and are often associated with numerical simulations. It is in this unsatisfactory context that we have chosen to conduct numerical simulations to determine optimal practical values of the HLSVD parameters to be used for fast automated processing of human brain proton spectra.

Numerical Simulation with the HLSVD Method

Optimal values of K, N, and M have been determined by computer simulation. A tool for numerical simulation has been developed using IDL language (Interactive Data Language Research System, Inc., Boulder, CO) and HLSVD-MRUI FORTRAN code (www.mrui.uab.es/mrui) on a O2 Silicon Graphics workstation. Various HLSVD parameters have been applied to a large number of model data in order to analyze each decomposition and quantify the extent of residual water signal removal. A typical experiment involves a set of values of the HLSVD parameters (K, N, and M), a set of values of the FID_{model} parameters (α, i, β, and σ), and 100 different noise realizations ($IT_{model} = 100$). The water region was selected between $+40$ and -40 Hz. The metabolites of interest generated resonances range from -47 to -236 Hz (Table 1) in the spectrum. The protocol is summarized in Fig. 3.

Accuracy of Residual Water Removal by the HLSVD Method

In order to take numerical breakdown of the HLSVD method into account, routines have been inserted in the program to control some floating point exceptions errors (overflow, division by zero, invalid operation) and the infinite loop errors. In a given experiment, the total number of these errors is called ERR_{FPE}.

For one noise realization, when the HLSVD method does not numerically break down, two criteria were used to estimate its quality. The first one dealt with the accuracy of the decomposition. The HLSVD program calculates, in the time domain, the root mean square (RMS_{HLSVD}) between the model signal and the reconstructed signal. If the decomposition proposed by HLSVD method is absolutely exact, then the given RMS_{HLSVD} is equal to the standard deviation of the time noise. If this is not the case, there is a difference between the given model and the

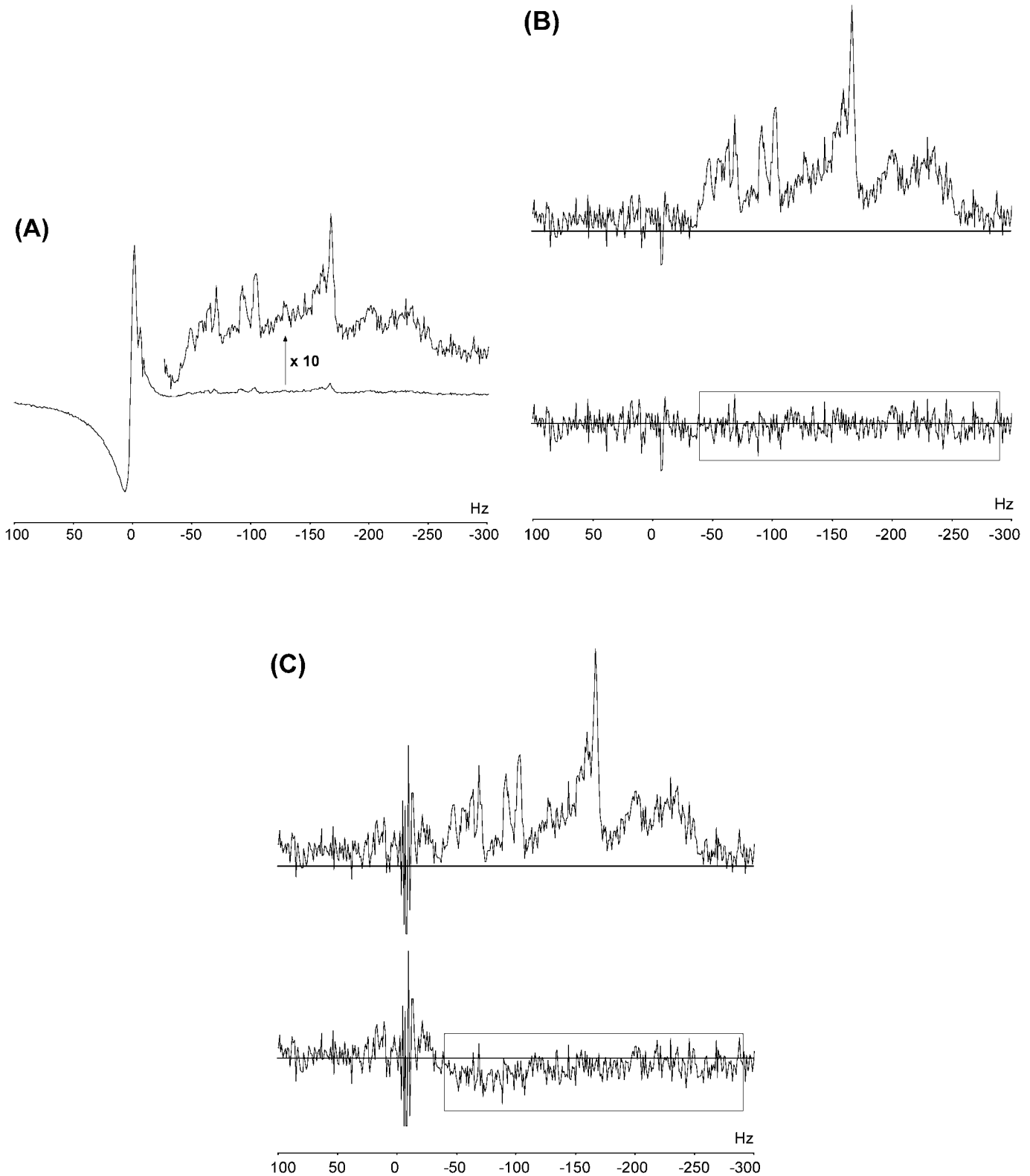

FIG. 4. Effects of two sets of HLSVD parameters on the extent of residual water signal removal. A shows the spectrum of a FID_{model} constructed with $FID_{water,8}$ ($\alpha = 45$), $FID_{metabolite}$ defined in Table 1 ($\beta = 1$), and one noise realization ($\sigma = 0.025$). B shows the spectrum of $FID_{reconstruct}$ and the spectrum of the residue $= FID_{metabolite} - FID_{reconstruct}$, obtained with $M = 320$, $N = 512$, and $K = 25$, conducting to $RMS_{reconstruct} = 8\%$. C shows the spectrum of $FID_{reconstruct}$ and the spectrum of the residue $= FID_{metabolite} - FID_{reconstruct}$, obtained with $M = 320$, $N = 512$, and $K = 10$, conducting to $RMS_{reconstruct} = 29\%$.

decomposition given by the HLSVD method. It is relevant (i) to assume that there is no correlation between this difference and the noise and (ii) to choose that the threshold of the RMS of this difference be inferior to the size of the standard deviation of the noise. Then, the threshold of RMS_{HLSVD} is equal to the square root of 2 multiplied by σ (the standard deviation of the time noise). Finally, if RMS_{HLSVD} exceeds $1.5 \times \sigma$ (where 1.5 is the approximate square root of 2), the global decomposition is rejected and the process is counted as an error of threshold ($ERR_{threshold}$).

Because our main interest was focused on the accurate measurement of metabolite concentrations, a second criterion was used in the frequency domain and refers to the accuracy of the residual water signal removal under the spectrum of metabolites. This criterion has been defined from the $RMS_{reconstruct}$ defined as

$$RMS_{reconstruct} = \sqrt{\frac{\sum_{j=1}^{Z}\left(1 - \frac{I_{reconstruct}(j)}{I(j)}\right)^2}{Z}}, \qquad [4]$$

where

- Z is the number of different regions selected on the metabolite spectrum ($SPE_{metabolite}$);
- $I_{reconstruct}(j)$ is the area of the jth region after Fourier transform of the signal $FID_{reconstruct} = FID_{model} - FID_{water/HLSVD}$, where $FID_{water/HLSVD}$ is the residual water signal reconstructed with the HLSVD method; and
- $I(j)$ is the area of the jth region after Fourier transform of the metabolite signal $\beta \times FID_{metabolite}$.

Areas are estimated using a numerical integration in the frequency domain.

For one noise realization, if the HLSVD method does not break down and if RMS_{HLSVD} does not exceed $1.5 \times \sigma$, then the $RMS_{reconstruct}$ is calculated. For one experiment ($IT_{model} = 100$), the number of calculated $RMS_{reconstruct}$ is given by

$$IT_{validate} = IT_{model} - (ERR_{FPE} + ERR_{threshold}). \qquad [5]$$

A typical result of one realization of residual water signal suppression is shown in Fig. 4 with different values of HLSVD parameters.

RESULTS AND DISCUSSION

In order to determine the optimal values of K, N, and M parameters providing the best conditions for residual water signal removal from human brain proton MR spectra, a four-step study was conducted using the FID_{model} signal (Eq. [2]) with the following conditions:

- $\alpha = 45$ and $i = 1$ to 15 for $FID_{water,i}$;
- $0.5 \leq \beta \leq 2.5$ and $FID_{metabolite}$ with 19 exponentially damped sinusoids (Table 1);
- $0.005 \leq \sigma \leq 0.05$ (arbitrary units), where σ is the standard deviation of the white gaussian noise.

The results are presented below as values of $IT_{validate}$ and of $RMS_{reconstruct}$.

Optimization of K

The first step consisted of evaluating the importance of prior knowledge of K. In an *in vivo* human brain proton FID signal, the number of components of the residual water is not exactly known because of the effects of the saturation pulses. Then, the number of total components of the FID signal (water + metabolites) is not perfectly determined. Values of K were varied from 10 to 45. Figure 5 presents the results obtained with $N = 512$, $M = 320$, $\alpha = 45$, $\beta = 1$, $\sigma = 0.025$. For each water signal ($i = 6$ to 10) the averaged value of the $RMS_{reconstruct}$ decreased and reached

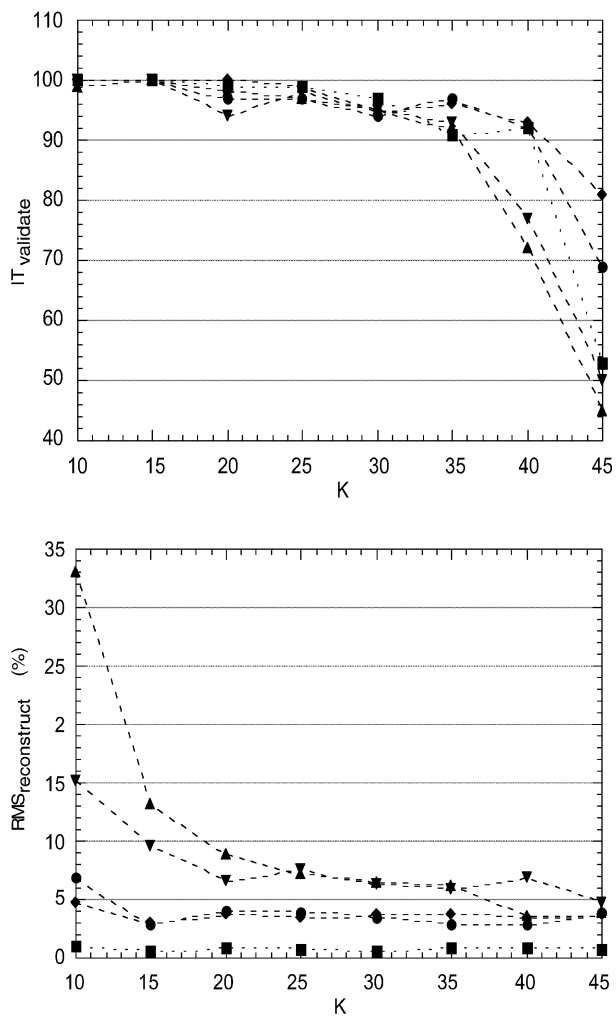

FIG. 5. $IT_{validate}$ and $RMS_{reconstruct}$ as a function of the number of exponentially damped sinusoids K. Results are displayed as a curve of averaged $RMS_{reconstruct}$ of water $FID_{water,i}$, ($i = 6$ to 10)), $\alpha = 45$, $\beta = 1$, and $\sigma = 0.025$, obtained with $N = 512$ and $M = 320$.

nearly steady state when K became greater than 30, but from $K = 35$, $IT_{validate}$ decreased dramatically.

Considering all results with the FID_{model} defined by $\alpha = 45$, ($i = 1$ to 15), $\beta = 1$, and $\sigma = 0.025$, obtained with $N = 512$ and $M = 320$, the value of K which maximizes $IT_{validate}$ and minimizes the $RMS_{reconstruct}$ was ca. 25. In the literature, the recommended value of K must be close to the model order value. This rule may be extended to simulated human brain proton MR spectra acquired at short echo time. Then, for *in vivo* human brain proton MR spectra, $K = 25$ constitutes a good choice for the use of the HLSVD method.

Optimization of the Hankel Matrix Size

Second, with the FID_{model} defined by $\alpha = 45$, $i = 1$ to 15, $\beta = 1$, $\sigma = 0.025$, and $K = 25$, the importance of the Hankel matrix size was evaluated. The results are presented as the distribution of $IT_{validate}$ and the distribution of averaged $RMS_{reconstruct}$ obtained for each residual water signal ($i = 1$ to 15). Figure 6A presents the results with $N = 512$ (the first half of the points of the FID_{model}) and with $64 \leq M \leq 448$. Figure 6B presents the results with $N = 1024$ (all the points of the FID_{model}) and $128 \leq M \leq 896$.

Figure 6 shows that the choice of the Hankel matrix size in the HLSVD method is then critical. Previous studies (*22, 23*) have advocated not to use all the data points, particularly the last points that bring in more noise. For acceptable $IT_{validate}$ values, the range of the choice of M was larger using $N = N_{data}$ than using $N = N_{data}/2$, but in contrast, the latter case gave always a better $RMS_{reconstruct}$. For example, if $IT_{validate}$ superior to 90% was selected, then for $N = 512$, the $RMS_{reconstruct}$ were inferior to 5% when $M = 192$ to 320 (Fig. 6A); for $N = 1024$, the $RMS_{reconstruct}$ were only inferior to 15% when $M = 256$ to 744 (Fig. 6B). Then, in our model signal, the HLSVD method does not break down on a larger range of M values, when all data points are included, but gives a worse removal of water signal under the metabolite signals.

Because our interest was to minimize $RMS_{reconstruct}$, the following optimal values of HLSVD parameters were selected for subsequent optimization: $N = 512$, $192 \leq M \leq 320$, and $K = 25$.

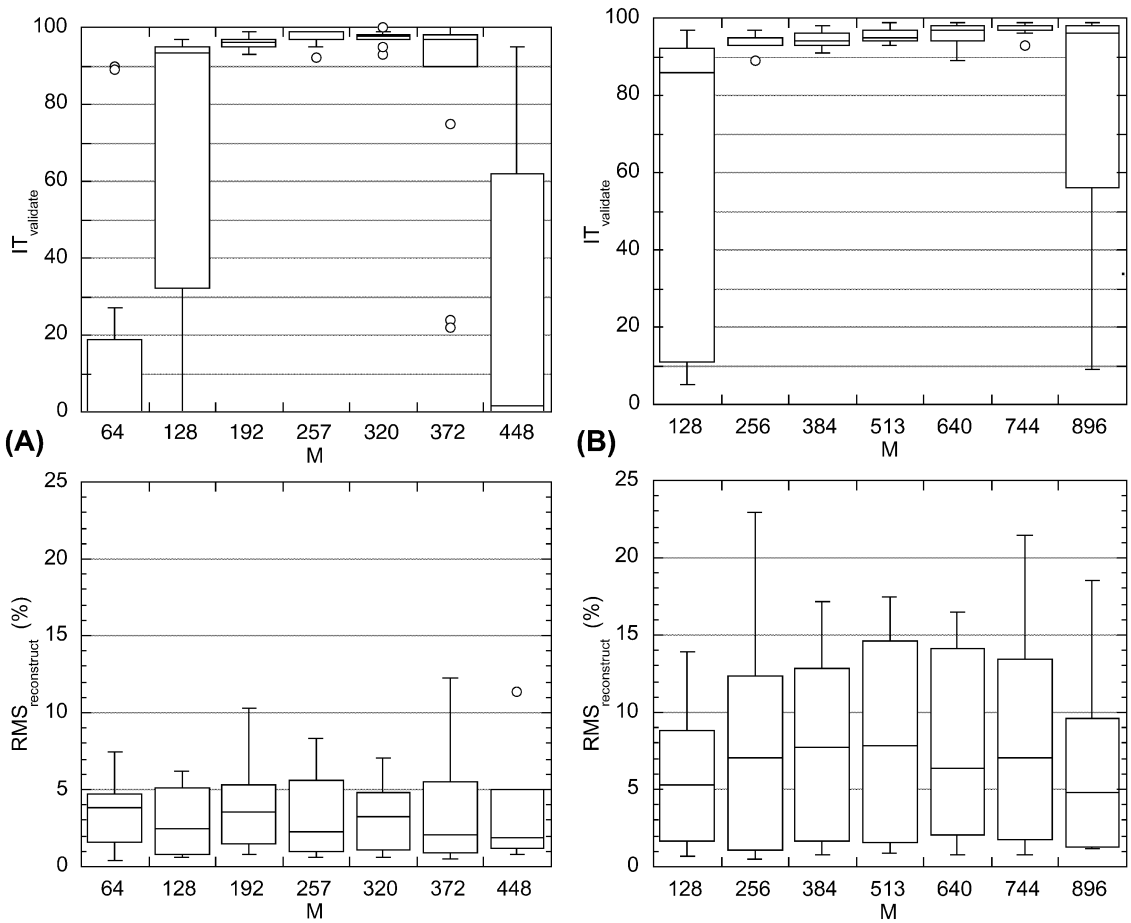

FIG. 6. $IT_{validate}$ and $RMS_{reconstruct}$ as a function of M. Results are displayed as a box plot distribution (5th, 25th, 50th (median), 75th, and 95th percentiles and outlier points) of $IT_{validate}$ and averaged $RMS_{reconstruct}$ for each $FID_{water,i}$, ($i = 1$ to 15), for $\alpha = 45$, $\beta = 1$, and $\sigma = 0.025$, obtained with $N = 512$ (A), $N = 1024$ (B), and $K = 25$.

Influence of Residual Water Signal to Metabolite Signal Ratio

Third, using the above parameters, the influence of the ratio between the amplitude factor ($\alpha = 45$) of the residual water signal and the amplitude factor ($0.5 \leq \beta \leq 2.5$) of the metabolite signal, for $i = 1$ to 15 and $\sigma = 0.025$, was evaluated. The range of the ratio (α/β) was in accordance with the variations observed *in vivo*.

The results are presented as the distribution of averaged $RMS_{reconstruct}$ obtained for each water signal ($i = 1$ to 15) versus β, the amplitude factor of metabolite. Figure 7 presents the results for $N = 512$ and $M = 192$ (Fig. 7A) or $M = 257$ (Fig. 7B) or $M = 320$ (Fig. 7C). In these three cases, $IT_{validate}$ was always superior to 90%. It can be observed that the $RMS_{reconstruct}$ decreased when the metabolite signals increased with respect to the water signal.

If a value of $RMS_{reconstruct}$ less than 5% was selected, the best results were obtained with β superior to 1 and $M = 320$. Then, for a standard noise ($\sigma = 0.025$), an acceptable performance ($IT_{validate} > 90\%$) of the HLSVD method was obtained for data with (α/β) ratio inferior to 45.

Influence of Signal-to-Noise Ratio

Fourth, with the FID_{model} defined by $\alpha = 45$, $i = 1$ to 15, $\beta = 1$, and with $N = 512$, $M = 320$, $K = 25$, the influence of the standard deviation σ of the noise in the range of 0.005 (arbitrary units) to 0.05 (arbitrary units) was evaluated. Figure 8 presents the distribution of the averaged $RMS_{reconstruct}$ obtained for each water signal ($i = 1$ to 15) versus σ values. $IT_{validate}$ was always superior to 90% for any noise level in the selected range (*in vivo* range). The good performance of the HLSVD method did not

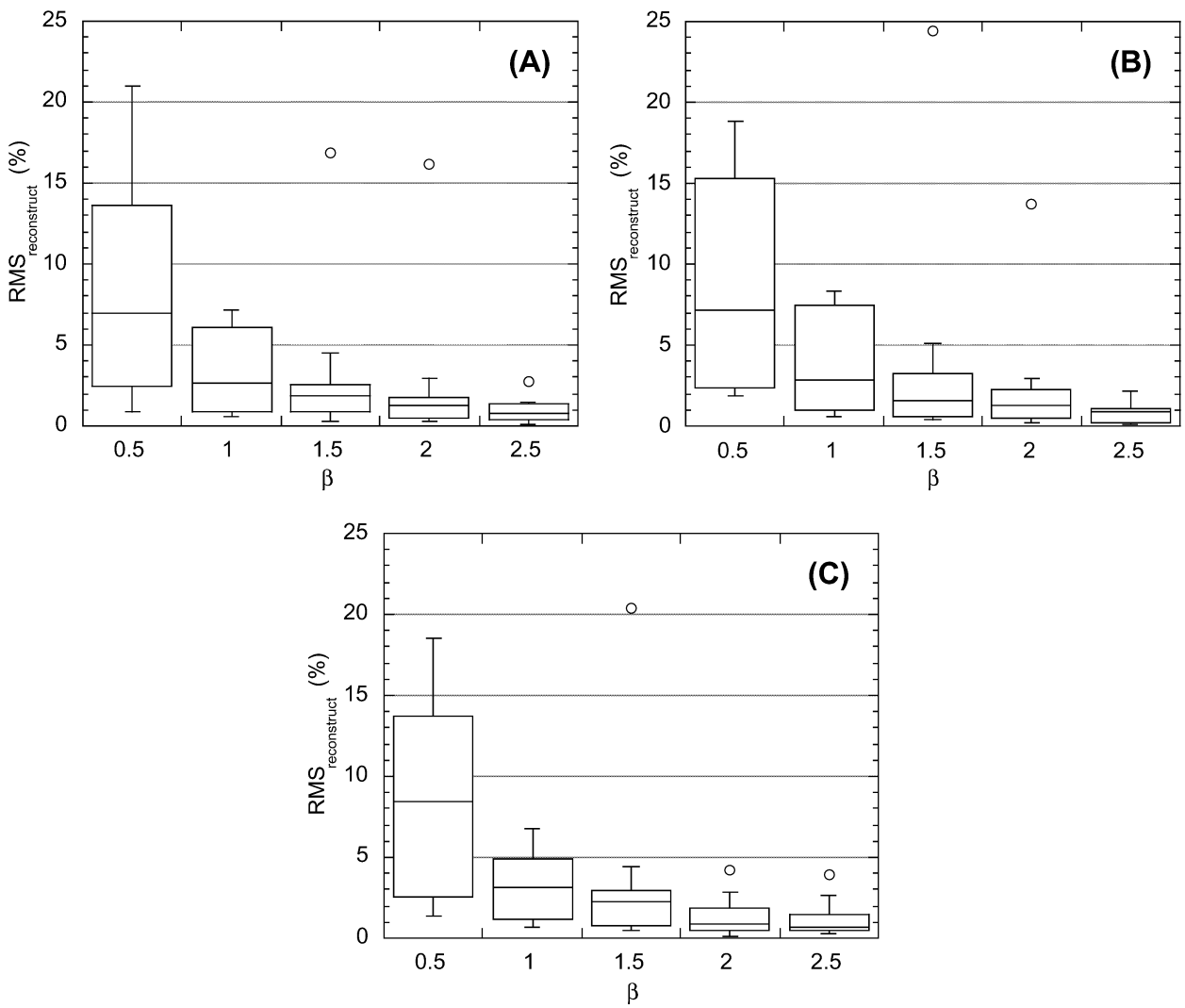

FIG. 7. $RMS_{reconstruct}$ as a function of amplitude factor β of the metabolite signal. Results are displayed as a box plot distribution (5th, 25th, 50th (median), 75th, and 95th percentiles and outlier points) of the averaged $RMS_{reconstruct}$ for each $FID_{water,i}$, ($i = 1$ to 15), for $\alpha = 45$, and $\sigma = 0.025$, obtained with $N = 512$, $M = 192$ (A), $M = 257$ (B), $M = 320$ (C), and $K = 25$.

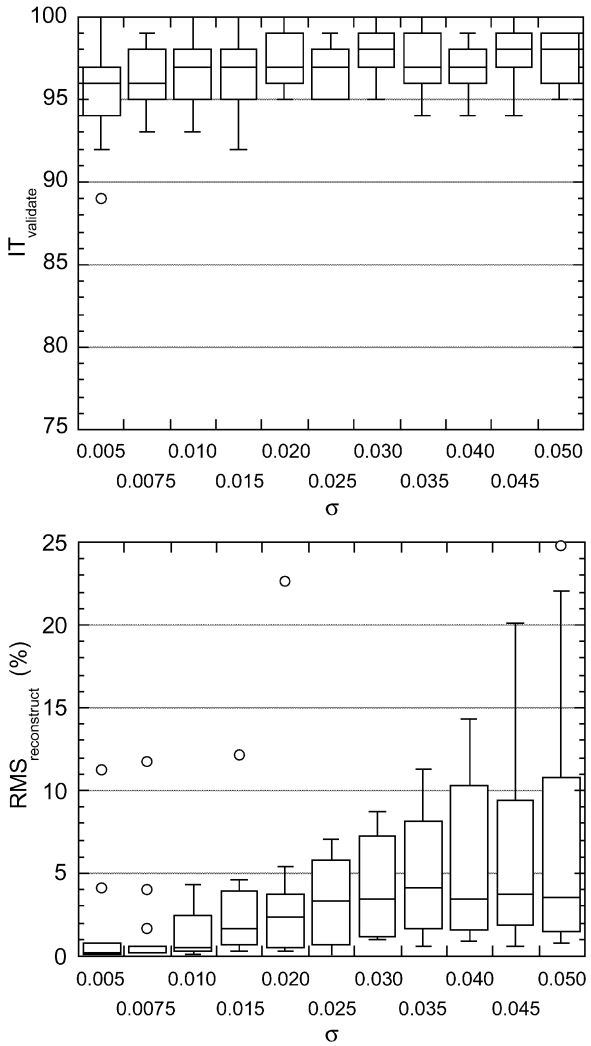

FIG. 8. $IT_{validate}$ and $RMS_{reconstruct}$ as a function of standard deviation σ of time noise. Results are displayed as a box plot distribution (5th, 25th, 50th (median), 75th, and 95th percentiles and outlier points) of the $IT_{validate}$ and the averaged $RMS_{reconstruct}$ for each $FID_{water,i}$, ($i = 1$ to 15), for $\alpha = 45$ and $\beta = 1$, obtained with $N = 512$, $M = 320$, and $K = 25$.

depend on the noise level when the previous optimal values were selected, but if we chose $RMS_{reconstruct}$ lower than 5%, a value of σ inferior to 0.025 gave better results.

CONCLUSION

Removal of the residual water signal from *in vivo* human brain proton MR spectra is required to quantify metabolites. With the objective of achieving fast automated processing of spectra, the optimal parameters for implementing the HLSVD method have been determined to obtain accurate removal of residual water signal without affecting the metabolite resonances of interest on simulated brain spectra corresponding to actual spectra recorded at short echo times. Different lineshapes of residual water signal, as well as a metabolite signal, have been modeled by appropriate decompositions in order to simulate actual *in vivo* spectra.

The HLSVD method is based on the choice of three parameters defining the order model K and the size $(N - M + 1) \times M$ of the Hankel matrix. The value $K = 25$ appears to be an optimal choice for *in vivo* human brain proton MR spectrum at short echo times. The optimal values of N and M parameters were $N = 512$ with M parameter chosen between 192 and 320 to obtain the best compromise between the minimum $RMS_{reconstruct}$ and maximum $IT_{validate}$.

On a large series of simulated MRS signals, optimal values of K, N, and M parameters have been determined. This set of values significantly improves the removal of residual water signal in brain proton spectra. Under these optimized conditions, the HLSVD method is robust ($IT_{validate} > 90\%$) and can be fully automated to obtain fast water removal on actual *in vivo* human brain spectra acquired at short echo times.

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REFERENCES

1. T. Ernst and J. Hennig, Improved water suppression for localized *in vivo* ^{1}H spectroscopy, *J. Magn. Reson. B* **106,** 181–186 (1995).
2. J. F. Shen and J. K. Saunders, Double inversion recovery improves water suppression *in vivo*, *Magn. Reson. Med.* **29,** 540–542 (1993).
3. Y. Kuroda, A. Wada, T. Yamazaki, and K. Nagayama, Postacquisition data processing method for suppression of the solvent signal, *J. Magn. Reson.* **84,** 604–610 (1989).
4. D. Marion, M. Ikura, and A. Bax, Improved solvent suppression in one- and two-dimensional NMR spectra by convolution of time-domain data, *J. Magn. Reson.* **84,** 425–430 (1989).
5. K. J. Cross, Improved digital filtering technique for solvent suppression, *J. Magn. Reson. A* **101,** 220–224 (1993).
6. N. Delprat, B. Escudié, P. Guillemain, R. Kronland-Martinet, P. Tchamitchian, and B. Torresani, Asymptotic wavelet and Gabor analysis: Extraction of instantaneous frequencies, *IEEE Trans. Inform. Theory* **38,** 644–664 (1992).
7. J. H. J. Leclerc, Distortion-free suppression of the residual water peak in proton spectra by postprocessing, *J. Magn. Reson. B* **103,** 64–67 (1994).
8. S. Van Huffel, H. Chen, C. Decanniere, and P. Van Hecke, Algorithm for time-domain NMR data fitting based on total least squares, *J. Magn. Reson. A* **110,** 228–237 (1994).
9. W. W. F. Pijnappel, A. Van den Boogaart, R. de Beer, and D. Van Ormondt, SVD-based quantification of magnetic resonance signals, *J. Magn. Reson.* **97,** 122–134 (1992).
10. L. Vanhamme, T. Sundin, P. Van Hecke, and S. Van Huffel, Frequency-selective quantification of biomedical magnetic resonance spectroscopy data, *J. Magn. Reson.* **140,** 1–16 (2000).
11. A. Van den Boogaart, D. Van Ormondt, W. W. F. Pijnappel, R. de Beer, and M. Ala-Korpela, in "Mathematics and Signal Processing III" (J. G. McWhirter, Ed.), pp. 175–195, Clarendon Press, Oxford, 1994.

12. T. Sundin, L. Vanhamme, P. Van Hecke, I. Dologlou, and S. Van Huffel, Accurate quantification of ^{1}H spectra: From finite impulse response filter design for solvent suppression to parameter estimation. *J. Magn. Reson.* **139,** 189–204 (1999).

13. J. P. Antoine, A. Coron, and J. M. Dereppe, Water peak suppression: Time-frequency vs time-scale approach, *J. Magn. Reson.* **144,** 189–194 (2000).

14. M. Derich and X. Hu, Elimination of water signal by postprocessing, *J. Magn. Reson. A* **101,** 229–232 (1993).

15. P. Tsang, Signal suppression in the frequency domain to remove undesirable resonances with dispersive lineshapes, *J. Magn. Reson.* **88,** 210–215 (1990).

16. N. Saeed, A knowledge-based approach to deconvolve the water component *in vivo* proton MR spectroscopy, *J. Comp. Ass. Tomogr.* **19,** 830–837 (1995).

17. J. Frahm, H. Bruhn, M. L. Gyngell, K. D. Merboldt, W. Hänicke, and R. Sauter, Localized high-resolution proton NMR spectroscopy using stimulated echoes: Initial applications to human brain *in vivo*, *Magn. Reson. Med.* **9,** 79–93 (1989).

18. A. Van. den. Boogaart, M. Ala-Korpela, J. Jokisaari, and J. R. Griffiths, Time and frequency domain analysis of NMR data compared: An application to 1D ^{1}H spectra of lipoproteins, *Magn. Reson. Med.* **31,** 347–357 (1994).

19. A. C. Kot, S. Parthasarathy, D. W. Tufts, and R. J. Vaccaro, The statistical performance of state-variable balancing and Prony's method in parameter estimation, in "Proceedings, ICASSP" (P. E. Papamichalis, Ed.), pp. 1549–1552, IEEE Press, 1987.

20. A. Okhovat and J. R. Cruz, in "Proceedings, Statistical Analysis of the Tufts-Kumaresan and Principal Hankel Components Methods for Estimating Damping Factors of Single Complex Exponentials, ICASSP" (T. Durrani, Ed.), pp. 2286–2289, IEEE Press, 1989.

21. R. de Beer and D. Van Ormondt, Analysis of NMR data using time domain fitting procedures, in "NMR Basic Principles and Progress," Vol. 26, pp. 201–248, Springer-Verlag, Berlin, 1992.

22. S. Van Huffel, H. Chen, C. Decanniere, and P. Van Hecke, Algorithm for time domain NMR data fitting based on total least squares, *J. Magn. Reson. A* **110,** 228–237 (1994).

23. A. Van den Boogart, F. A. Howe, L. M. Rodrigues, M. Stubbs, and J. R. Griffiths, In vivo ^{31}P MRS: Absolute concentrations, signal-to-noise and prior knowledge, *NMR Biomed*. **8,** 87–93 (1995).