JOURNAL OF MAGNETIC RESONANCE **124,** 286–289 (1997)
ARTICLE NO. MN961060

# Post-Acquisition Solvent Suppression by Singular-Value Decomposition

GUANG ZHU,*,† DAVID SMITH,* AND YINGBO HUA‡

*Department of Biochemistry, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong; and
‡Department of Electrical and Electronic Engineering, University of Melbourne, Parkville, Victoria 3052, Australia

Received November 14, 1996

Solvent resonance suppression is critical in many nuclear magnetic resonance spectroscopy applications. For a protein dissolved in 90% $H_2O$/10% $D_2O$, the concentration of solvent protons ($\approx$100 *M*) is about five orders of magnitude greater than the concentration of the protons of interest in the solute (typically $\approx$ 1 m*M*). Consequently, the strong solvent resonance that dominates the NMR spectrum of the solute can hide signals of interest. A great number of experimental and numerical methods have been designed to suppress solvent signals. These have been reviewed in detail (*1, 2*). The experimental methods can be divided into two classes: solvent irradiation methods and solvent nonexcitation methods (*3*). While these methods are suitable for many situations, they have a variety of disadvantages such as incomplete solvent suppression leading to dispersive signals in the spectrum, the generation of artifacts, and the saturation of signals close to the solvent resonance (*3*). Another class of techniques, known as post-acquisition methods, has been developed to attempt to correct some of these difficulties (*4*). Most of the post-acquisition solvent-suppression methods are based on bandpass filtering (*5–7*) or subtracting the synthetic solvent peak which is calculated by either LPSVD (linear-prediction method based on singular-value decomposition) type of methods (*8*) or nonlinear least-squares methods (*9*).

In this Communication, we present an alternative approach in which a Toeplitz matrix is formed from a 1D FID, and the corresponding solvent suppressed 1D FID is then constructed by removing the largest singular value of the Toeplitz matrix. This method has proved to be effective in removing a strong solvent peak even when it is $10^{14}$ times larger than the other resonances in a simulated spectrum. This indicates that, theoretically, little or no solvent suppression is needed in an experiment if this post-acquisition solvent-suppression method is applied. We show the effectiveness of this method in removing the residual water signal from a 2D NOESY spectrum of the protein lysozyme in 90% $H_2O$/10% $D_2O$, in which presaturation of the water resonance by selective low-power irradiation during the relaxation delay was applied.

A 1D FID is composed of the summation of *K* exponentially damped sinusoids which are characterized by amplitudes $a_k$, frequencies $f_k$, damping factors $d_k$, and phases $\phi_k$. The 1D FID is defined by

$$x_n = \sum_{k=1}^{K} a_k \exp(i\phi_k)\exp[(-d_k + 2i\pi f_k)n\Delta t] \quad [1]$$

with $x_n$ and $\Delta t$ being the *n*th data point and the sampling interval, respectively. A forward Toeplitz matrix $\mathbf{T}$ can be formed as

$$\mathbf{T} = \begin{bmatrix} x_1 & x_2 & \cdots & x_M \\ x_2 & x_3 & \cdots & x_{M+1} \\ \cdot & \cdot & \cdots & \cdot \\ x_{N-M+1} & x_{N-M+2} & \cdots & x_N \end{bmatrix}, \quad [2]$$

where *N* is the number of data points in the 1D FID, and *M* is the window size of the Toeplitz matrix. This matrix is exactly the same as that used in the forward linear-prediction method (*10*).

It is well known (*11*) that for *M* vectors in an $(N - M)$-dimensional vector space with $M \leqslant (N - M)$, an orthonormal basis which spans the same subspace can be calculated by SVD (singular-value decomposition). That is, an $(N - M) \times M$ matrix $\mathbf{T}$ can be expressed as the product of an $(N - M) \times (N - M)$ unitary matrix $\mathbf{U}$, an $(N - M) \times M$ diagonal matrix $\mathbf{\Sigma}$, and an $M \times M$ unitary matrix $\mathbf{V}$ according to

$$\mathbf{T} = \mathbf{U\Sigma V}^{+}, \quad [3]$$

where $^{+}$ denotes conjugate transpose. The diagonal elements, $\sigma_i$, of the matrix $\mathbf{\Sigma}$ are positive and its off-diagonal elements are zero. Furthermore, the largest component, $\sigma_1$, corre-

† To whom the correspondent should be addressed.

1090-7807/97 $25.00



Copyright © 1997 by Academic Press
All rights of reproduction in any form reserved.

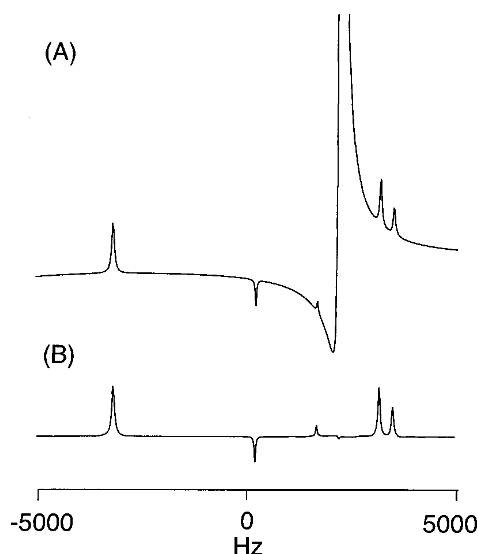



**FIG. 1.** (A) The 1D spectrum obtained by Fourier transformation of a simulated 1D FID consisting of 512 complex data points. (B) The corresponding 1D solvent-suppressed spectrum obtained by Fourier transformation of the 1D FID after it was processed by the proposed post-acquisition solvent-suppression method with a window size of 40.

sponds to the largest sinusoid component in the 1D FID, and the noise will have the smallest singular values, $\sigma_{M+1}$, . . . , $\sigma_{N-M}$. By zeroing the largest singular value and constructing a new Toeplitz matrix $\mathbf{T}'$ in the following manner

$$\mathbf{T}' = \mathbf{U}\Sigma'\mathbf{V}^{+}, \qquad [4]$$

where $\Sigma'$ is the matrix $\Sigma$ with $\sigma_1 = 0$ and the rest of the elements are unchanged, a new 1D FID can be constructed from the Toeplitz matrix $\mathbf{T}'$ according to Eq. [2]. The spectrum obtained from Fourier transformation of the reconstructed FID will have the solvent resonance removed from it if the solvent peak is much stronger than the other resonances, which is normally the case in the NMR applications. By zeroing the smallest singular values, the noise can be removed from the corresponding spectrum provided there is a clear division in the singular-value distribution between the noise and the signals (*12*). Similarly, solvent suppression can also be achieved by the same procedure on the backward Toeplitz matrix.

The SVD solvent-suppression method was demonstrated on a synthetic 1D FID and experimental 1D and 2D FIDs. First, we composed a synthetic noise-free, 1D FID with 512 complex data points which was processed with the proposed method. The window size, $M$, for this test was chosen to be 40. As shown in Fig. 1, the largest solvent peak was effectively removed with this method. Our simulations also showed that the method was successful even when the strong solvent peak was $10^{14}$ times larger than the rest of the resonance peaks. When the peak ratio exceeded $10^{14}$, the round-off errors of the computational method became a dominating factor.

It should be noted that when other resonances are close to the solvent peak there is a residual solvent peak left after applying the proposed SVD solvent-suppression method. The amplitude of this residual solvent peak depends on how close other resonances are to the solvent resonance. In general, it is much smaller than the amplitudes of the peaks close to the solvent resonance. Despite this residual peak, the large tail of the solvent peak is removed and the baseline is much flatter. Another point to note is that if the solvent peak is much larger than the other resonance peaks, a smaller window size, $M$, can be used; otherwise, a larger window size should be employed. The computation needed for SVD with large $M$ will be much more demanding than with smaller $M$ since the computational complexity is proportional to $M^2(N - M)$ (*11*). Solvent suppression with smaller $M$ may leave a small solvent residue partly due to insufficient degrees of freedom to categorize the signal components of the FID according to their amplitudes. Therefore, a compromise between computational speed and the quality of solvent suppression may be required. This technique, though, works well if the solvent signal is much larger than the rest of signals, and the method is independent of the experimental setup as shown in Fig. 1.

We also applied the SVD solvent-suppression method to

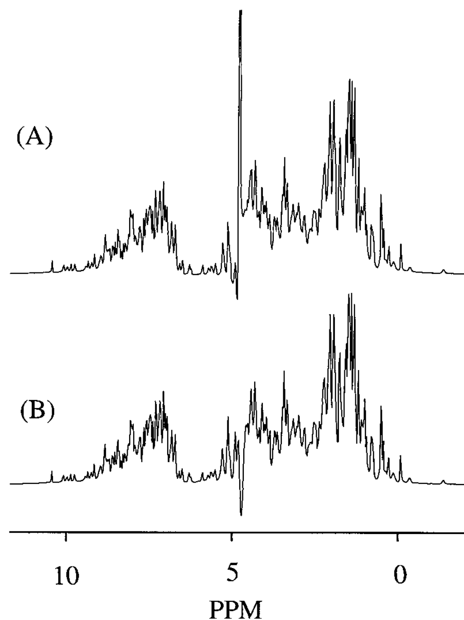
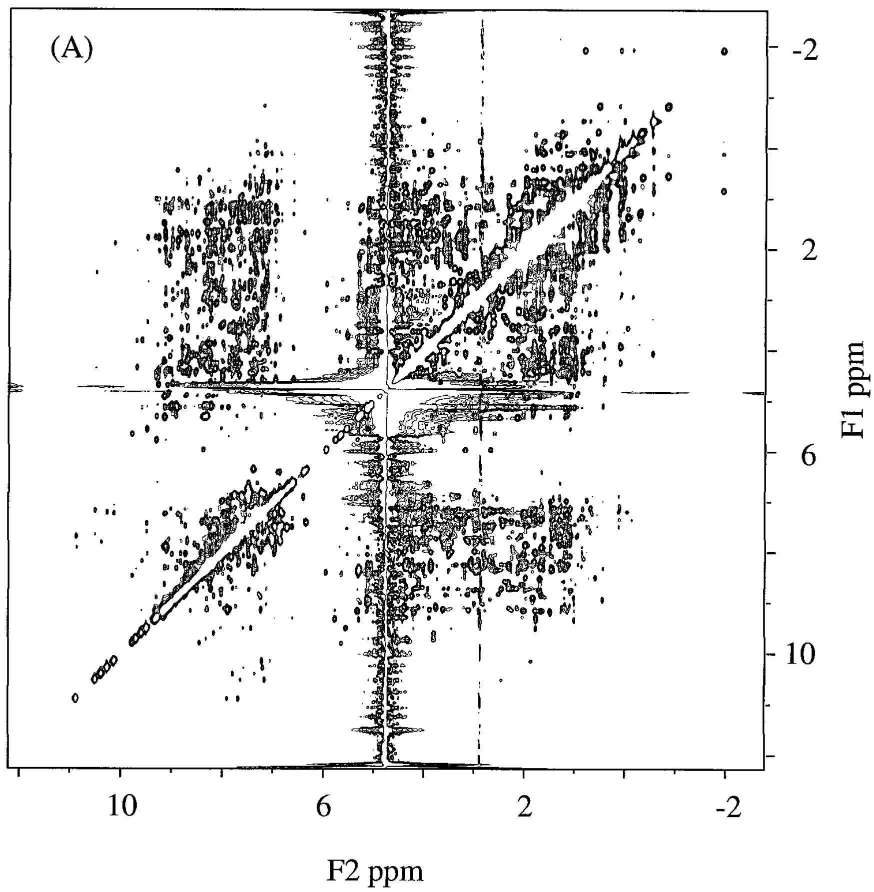
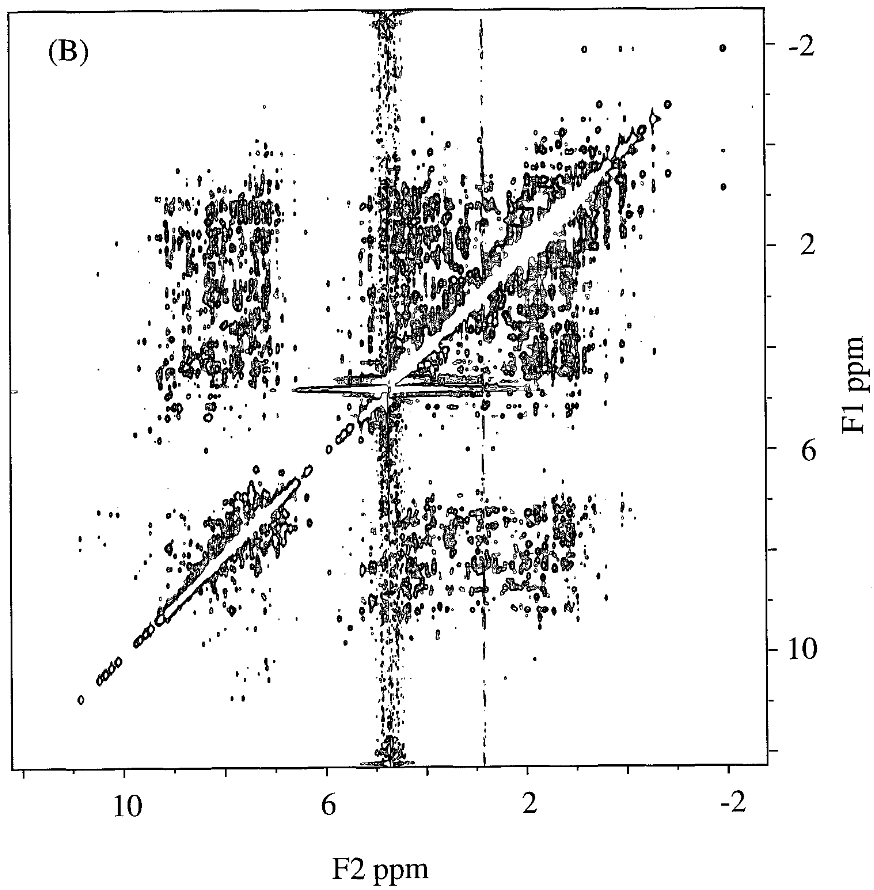



**FIG. 2.** (A) The 1D spectrum obtained by Fourier transformation of the first FID of a 2D NOESY experiment on the protein lysozyme recorded with water presaturation. (B) The corresponding water-suppressed 1D spectrum processed in the same manner as in (A) after applying the solvent-suppression method with a window size of 60 to the FID.


(A)
-2
2
6
10
F1 ppm
10
6
2
-2
F2 ppm


(B)
-2
2
6
10
F1 ppm
10
6
2
-2
F2 ppm

a 1D FID which is the first FID of a 2D NOESY spectrum of the protein lysozyme recorded on a Varian Inova-400 spectrometer with the 2D FID matrix being 512* × 200* in States format. Water presaturation was used in the experiment, giving the spectrum in Fig. 2A. The SVD-solvent-suppressed 1D spectrum (Fig. 2B) was obtained with the window size, *M*, equal to 60. The residual water signal in the processed spectrum as shown in Fig. 2B may come from the presaturation or imperfect shimming which could split the water peak into many resonances and the algorithm described has only removed the largest component of these resonances.

Finally, we applied this solvent-suppression method to the complete 2D NOESY spectrum. A Fourier-transformed 2D NOESY spectrum with matrix size of 1024 × 512 was obtained by applying sine-bell and sine-squared bell window functions to the $t_1$ and $t_2$ domains, respectively, and zero filling and is shown in Fig. 3A. Constant baseline correction was also used in the $t_2$ domain to remove $t_2$ ridges from the spectrum. The $t_1$ ridges were removed by multiplying the first data point of each FID in the $t_1$ domain by 0.5 (*13*).

In Fig. 3B, the water-suppressed 2D NOESY spectrum which was obtained by applying the proposed solvent-suppression technique to the $t_2$ domain with a window size *M* of 30 is shown. The figure clearly demonstrates that the water peaks in the $t_2$ domain have been effectively removed with only very small residual peaks remaining for the reason mentioned above. Small residual water peaks in the $t_1$ domain can also be seen. This is characteristic of this solvent-suppression method when it is applied to 2D homonuclear NMR spectra. The computational time required by SVD for this example was 2 h on a Sun SPARC 20 computer. We are currently in the process of designing faster and more efficient SVD methods by exploiting the matrix structure described in Eq. [2].

In conclusion, this method utilizes the fundamental characteristics of a Toeplitz matrix constructed from the sampled data points of the sinusoidal signals. This method is much less complicated than the previously proposed method (*8*) which needs to go several steps further before the solvent peak can be simulated and subtracted. It is also different from the approach proposed by Mitschang *et al.* (*4*) where an autocorrelation matrix was formed and a Karhunen–Loeve (KL) transformation was applied. As indicated in the paper by Brown and Campbell (*14*), SVD, KL, and PCA are different and they may not yield the same results in 2D image processing. The computer program used to implement the solvent-suppression algorithm was written in C and is available from the author. The SVD subroutine was modified such that it could be used for processing a complex data set. After applying the SVD solvent-suppression method to the 2D NOESY spectrum, the nmrPipe (*15*) package was used to carry out the remaining spectral processing.

## ACKNOWLEDGMENTS

We thank Dr. David Live for providing the 2D NOESY spectrum of the protein lysozyme. The work is supported by the Hong Kong Research Grants Council (HKUST563/95M) and the young Asian scholars program of the University of Melbourne, Australia.

## REFERENCES


1. P. J. Hore, *in* "Methods in Enzymology" (N. J. Oppenheimer and T. L. James, Eds.), Vol. 176, p. 64, Academic Press, San Diego, 1989.
2. M. Gueron, P. Plateau, and M. Decorps, *Prog. NMR Spectrosc.* **23,** 135 (1991).
3. T. A. Frenkiel, "NMR of Macromolecules. A Practical Approach" (G. C. K. Roberts, Ed.), p. 35, IRL Press, Oxford, 1993.
4. L. Mistchang, C. Cieslar, T. A. Holak, and H. Oschkinat, *J. Magn. Reson.* **92,** 208 (1991).
5. Y. Kuroda, A. Wada, T. Yamazaki, and K. Nagayama, *J. Magn. Reson.* **84,** 604 (1989).
6. D. Marion, M. Ikura, and A. Bax, *J. Magn. Reson.* **84,** 425 (1989).
7. K. J. Cross, *J. Magn. Reson. A* **101,** 220 (1993).
8. J. H. J. Leclerc, *J. Magn. Reson. B* **103,** 64 (1994).
9. M. Deriche and X. Hu, *J. Magn. Reson. A* **101,** 229 (1993).
10. H. Barkhuijsen, R. De Beer, W. M. M. J. Bovee, and D. Van Ormondt, *J. Magn. Reson.* **62,** 465 (1985).
11. G. H. Golub and C. F. Van Loan, "Matrix Computations," Johns Hopkins Univ. Press, Baltimore, 1983.
12. Y. Y. Lin and L. P. Hwang, *J. Magn. Reson. A* **103,** 109 (1993).
13. G. Zhu, D. Torchia, and A. Bax, *J. Magn. Reson. A* **105,** 219 (1993).
14. D. E. Brown and T. W. Campbell, *J. Magn. Reson.* **89,** 225 (1990).
15. F. Delaglio, S. Grzesiek, G. Vuister, G. Zhu, J. Pfeiffer, and A. Bax, *J. Biomol. NMR* **6,** 277 (1995).


**FIG. 3.** (A) The 2D NOESY spectrum of the protein lysozyme recorded with water presaturation and processed with sine-bell and sine-squared-bell window functions applied to the $t_2$ and $t_1$ domains respectively, constant baseline correction in the $t_2$ domain, and with zero filling. (B) The water-suppressed 2D NOESY spectrum obtained by applying the SVD-based solvent-suppression technique in the $t_2$ domain to the same NOESY data which was then processed as described for (A).