Quantitative Analysis of *In Vivo* 2D ^{1}H-^{13}C HSQC Spectra Using a Complex Nonlinear Least-Squares Curve-Fitting

H. Watanabe [1], M. Umeda [1], Y. Ishihara [1], K. Okamoto [1], M. Oda [2], T. Kanamatsu [2], Y. Tsukada [2]
[1] Toshiba Medical Systems R&D center, Otawara, Japan, [2] Institute of Life Science, Soka University, Hachioji, Japan

Introduction

Two dimensional (2D) correlation ^{1}H-^{13}C spectroscopy, which can resolve glutamate and glutamine *in vivo* via ^{13}C chemical shifts (δ_C) with ^{1}H sensitivity, is one of the best ^{13}C MRS methods. We have proposed a multislice ^{1}H-^{13}C heteronuclear single quantum coherence (HSQC) method (1, 2) and demonstrated that it enabled the detection of several amino acids from a human brain after the oral administration of glucose C1 (Fig. 1). In this sequence, a simple reverse polarization transfer using 90°(^{13}C) and 90°(^{1}H) is utilized after t_1 to minimize a number of RF pulses, so that ^{1}H chemical shifts (δ_H) are not refocused and a magnitude-mode display is needed. In this paper, we present a quantitative analysis method for 2D spectra, in which phasing is difficult because of heavy baseline distortions, by using a complex nonlinear least-squares (NLLS) curve-fitting and demonstrate *in vivo* application. This method is also useful for 2D spectra acquired without ^{13}C decoupling to be free of heating problems and decoupling noise by using a model which includes the J_{CH} splitting.

Methods

In the 2D HSQC spectra, these following parameters are detectable: δ_H, J_{HH} and J_{CH} in F_2; δ_C and J_{CC} in F_1. Since each peak is well resolved, each J_{CH} doublet can be curve-fitted respectively. One doublet can be written as 2D Lorentzian model with 7 parameters, neglecting J_{CC} splitting, because J_{HH} cannot be resolved under *in vivo* conditions:

$$F(\omega_1, \omega_2; V, \omega_{01}, \omega_{02}, \alpha_1, \alpha_2, \phi_0, \phi_1)$$
$$= \exp(i\phi_0)V[A_1 + iD_1][(A_{21} + iD_{21}) + \exp(i\phi_1)(A_{22} + iD_{22})]$$

with

$$A_1 = \alpha_1 / [\alpha_1^2 + (\omega_1 - \omega_{01})^2]$$
$$D_1 = -(\omega_1 - \omega_{01}) / [\alpha_1^2 + (\omega_1 - \omega_{01})^2]$$
$$A_{21} = 0.5\alpha_2 / [\alpha_2^2 + (\omega_2 - (\omega_{02} - 2\pi J_{CH}/2))^2]$$
$$D_{21} = -0.5\alpha_2 / [\alpha_2^2 + (\omega_2 - (\omega_{02} - 2\pi J_{CH}/2))^2]$$
$$A_{22} = 0.5\alpha_2 / [\alpha_2^2 + (\omega_2 - (\omega_{02} + 2\pi J_{CH}/2))^2]$$
$$D_{22} = -0.5\alpha_2 / [\alpha_2^2 + (\omega_2 - (\omega_{02} + 2\pi J_{CH}/2))^2]$$

Thus,

$$F_{real} = V[R\cos(\phi_0) - I\sin(\phi_0)]$$
$$F_{imag} = V[R\sin(\phi_0) + I\cos(\phi_0)]$$

with

$$R = A_1[A_{21} + (A_{22}\cos\phi_1 - D_{22}\sin\phi_1)] - D_1[D_{21} + (A_{22}\sin\phi_1 + D_{22}\cos\phi_1)]$$
$$I = A_1[D_{21} + (A_{22}\sin\phi_1 + D_{22}\cos\phi_1)] + A_2[A_{21} + (A_{22}\cos\phi_1 - D_{22}\sin\phi_1)]$$

Using this model, a 2D frequency domain data is approximated as follows:

$$\begin{bmatrix} R \\ I \end{bmatrix} \cong \begin{bmatrix} F_{real}(\mathbf{x}_0) \\ F_{imag}(\mathbf{x}_0) \end{bmatrix} + \begin{bmatrix} A_{real}(\mathbf{x}_0) \\ A_{imag}(\mathbf{x}_0) \end{bmatrix} \Delta\mathbf{x}$$

$$\mathbf{x} = \mathbf{x}_0 + \Delta\mathbf{x}$$

where $\mathbf{x}$ is a parameter vector, R and I are real and imaginary parts of 2D spectra, and A_{real} and A_{imag} are those of Yacobians of F_{real} and F_{imag}.

Complex spectra are curve-fitted to this model using a modified Marquardt algorithm. In this NLLS method, good initial parameter estimates are importance for convergence. For this estimation, first, 5 sets of parameters (V, ω_{01}, ω_{02}, α_1 and α_2) are calculated from a magnitude-mode spectrum and ϕ_1 is obtained from a dead time in the sequence. Developed curve-fitting procedure is as follows:

(1) estimation of ϕ_0 using a LS fitting
(2) estimation of V, α_1, α_2, and ϕ_0 using a NLLS
(3) estimation of all parameters using a NLLS

It is possible to avoid convergence to local minimum using above procedure.

Results & Discussion

Using the developed complex NNLS method, the *in vivo* 2D HSQC spectrum of a human brain (Fig. 1) was curve-fitted. Figure 2 shows the F_2 cross sections at δ_C for a glutamate C4 resonance of the 2D spectrum shown in Fig. 1, the best fit and the residual F_2 sections.

Conclusions

A presented complex NLLS curve-fitting method is a useful tool for *in vivo* 2D HSQC spectra. It also enables quantitation of 2D HSQC spectra without ^{13}C decoupling. Moreover, this method can be applied to *in vivo* 2D spectra for which phasing is difficult.

Acknowledgments

This work was performed as part of the National Research & Development Programs for Medical and Welfare Apparatus under entrustment by the New Energy and Industrial Technology Development Organization (NEDO).

References

1. Watanabe, H. et. al., 5th Annual Meeting, ISMRM, 1436, 1997.
2. Watanabe, H. et. al., 6th Annual Meeting, ISMRM, 360, 1998.

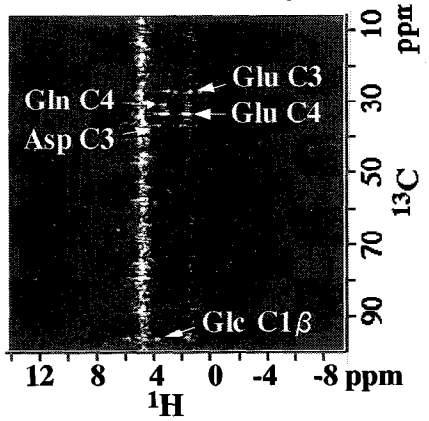

Fig. 1. A 2D ^{1}H-^{13}C HSQC spectrum obtained from a human brain (volume size = 36 ml, total acquisition time = 100min) after an oral administration of glucose C1.

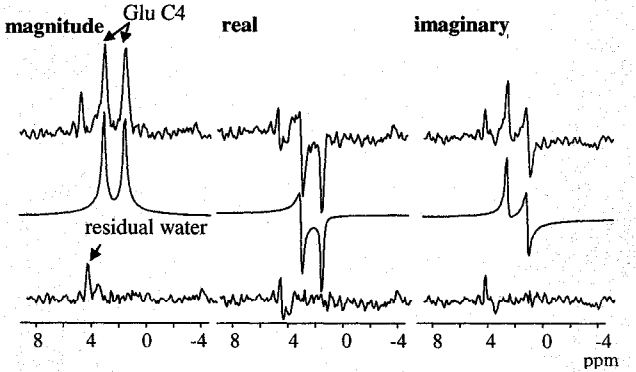

Fig. 2. The F_2 cross sections through glutamate C4 (top) of the 2D spectrum shown in Fig. 1, the best fits (middle), and the residuals (bottom).