Unsymmetrical Covariance Processing of COSY or TOCSY and HSQC NMR Data to Obtain the Equivalent of HSQC-COSY and HSQC-TOCSY Spectra

INTRODUCTION

Brüschweiler and co-workers have recently described various aspects of covariance NMR spectroscopy in a series of reports. In their report that specifically dealt with indirect covariance NMR, Zhang and Brüschweiler noted that artifacts can arise in the indirect covariance spectrum due to the overlap of proton resonances. In subsequent work, we reported the analysis of two different types of artifact responses. Unsymmetrical covariance processing was initially developed based on the separation of the positively and negatively phased responses in an IDR (Inverted Direct Response)-HSQC-TOCSY experiment.

RESULTS & DISCUSSION

The indirect covariance processed IDR-HSQC-TOCSY spectrum of a complex polyacridane hetero-aromatic model compound, naptho[2’-1;& 5;& 6]&naptho[2’-1;& 4;& 5]thieno[2;& 3;& 4]-quinoline, is shown in Figure 1. Type II artifact responses are inverted (red contours and solid red lines). Type II artifact responses have a phase identical to legitimate carbon-carbon vicinal correlation responses, and are denoted by dashed black lines.

For a vicinally coupled pair of resonances in the IDR-HSQC-TOCSY spectrum, a diagonally symmetric pair of responses is generated in the usual fashion during unsymmetrical indirect covariance processing, as shown in Figure 3. In the case of artifact responses (see Figure 1), unsymmetrical covariance processing gives rise to a diagonally asymmetric Type II response as shown in Figure 4, which can subsequently be removed by the use of the symmetrization routine familiar to anyone who has ever processed COSY data.

Using unsymmetrical covariance processing as a point of departure, it is possible to explore co-processing data from disassociated experiments with identical proton (F2) spectral widths. Our first exploration of this area of research involved the co-processing of HSQC and HMBC data to afford a presentation containing long-range carbon-carbon connectivity information that would normally require a substantial sample and the acquisition of one of the variants of the ADEQUATE experiment. Most recently we have communicated the application of this technique to the co-processing of HSQC and either COSY or TOCSY data to yield the equivalent of HSQC-COSY or HSQC-TOCSY spectra with considerable time savings and substantially improved s/n ratios.

CONCLUSIONS

The ability to use unsymmetrical covariance processing to generate data presentations that have equivalent information content to much lower sensitivity 2D NMR experiments such as HSQC-TOCSY may help to facilitate the more widespread application of these methods in structure elucidation studies. Further studies will be necessary to determine the utility of unsymmetrical covariance processing when dealing with molecules whose proton spectra are congested, such as steroids, terpenes, etc. The co-processing of other pairs of 2D NMR experiments should also be investigated.

REFERENCES