COVARIANCE NMR WITH MINIMAL DATASETS
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Introduction

Covariance NMR spectroscopy [1] is an alternative method to 2D Fourier transform (2D FT) NMR to establish spin correlations in molecules. The covariance spectrum $C$ is determined using the mixed time-frequency domain data $S$, $C = (S^T S)^{1/2}$, where $S$ is the $N_1 \times N_2$ mixed time-frequency domain matrix after Fourier transform along the detection dimension $t_2$. The matrix square-root can be efficiently determined by singular value decomposition [2].

Results and Discuss

An advantage of covariance spectra over traditional 2D FT is that the indirect dimension is not required to be sampled with a time increment that fulfills the Nyquist theorem, $1/(\text{spectral width})$. Importantly, if $N_1$ is to be minimized to achieve maximal speed up, undersampling in $t_1$ can be advantageous by probing a wider range of $t_1$ evolution times. The conventional FT spectrum obtained from the time-domain of the same size ($N_1=48$) shows severe line broadening along the indirect dimension $\omega_1$, and thus is unsuitable for simple analysis. The covariance spectrum has the same high resolution along both dimensions by definition. Comparison with the 2D FT spectrum with 2048 increments reveals, however, the presence of extra peaks reflecting the onset of poor sampling effects due to the small size of the dataset. These effects can be removed by a masking scheme that uses predicted spurious correlations caused by finite sampling. Application of the resulting mask to the covariance spectrum leads to the spectrum (upper right) that is essentially void of false peaks while most of the true peaks are present [3].

Conclusions

The enhanced covariance method presented here provides high-resolution 2D spectra from minimal $t_1$ datasets. The undersampling and cross-validation schemes represent powerful means to suppress spurious correlations. The scheme, which offers substantial savings of measurement time for TOCSY- and COSY-type spectra, is readily applicable to high-throughput screening such as in metabolomics.

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References