Metabolic Mixture Analysis by Heteronuclear NMR

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Introduction

Identification of individual chemical components of biological systems and monitoring of their changes in response to a multitude of factors such as genetics, age, pathology, development, environment, stress, and treatment are key aspects of metabolomics and metabonomics. The comprehensive systems biological approach to the study of metabolic mixtures thereby promises a better understanding of complex biochemical processes in living systems.

Here we present a generalization of the recently introduced homonuclear TOCSY-based DemixC method to heteronuclear 2D HSQC-TOCSY NMR spectroscopy. The approach takes advantage of the high resolution afforded along the $^{13}$C dimension due to the narrow $^{13}$C line widths for the identification of spin systems and compounds. The method combines information from both 1D $^{13}$C and $^1$H traces by querying them against an NMR spectral database using our COLMAR query web server. The complementarity of $^{13}$C and $^1$H spectral information improves the robustness of compound identification.

Results and Discussion

Figure 1 shows importance index profile calculated from HSQC-TOCSY spectrum of model mixture (A) along $^1$H dimension and (B) along $^{13}$C dimension. At the peak positions picked in panels A and B (indicated by “x” symbols) a subset of traces is extracted in the HSQC-TOCSY spectrum, such as the lysine carbon trace obtained from the $^1$H importance index (panel C) and the lysine proton trace obtained from $^{13}$C importance index (panel D). The vertical arrows indicate the importance index peak positions where the traces were extracted in the HSQC-TOCSY. The diagonal arrows indicate the connections between the importance index and the traces picked linking the $^{13}$C (C) and $^1$H (D) traces to the same compound (lysine).

Conclusions

This metabolic mixture analysis by heteronuclear NMR is included in our COLMAR suite of Metabolomics Web Portals (http://spinportal.magnet.fsu.edu). This and the other COLMAR servers aid the identification and quantification of chemical components of metabolomics mixtures without requiring physical separation of individual components. This web portal, which allows users easy uploading and downloading of NMR data, significantly facilitates the analysis of a wide range of complex biological mixtures.

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References