

Magn. Reson. Discuss., referee comment RC3
<https://doi.org/10.5194/mr-2021-48-RC3>, 2021
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Comment on mr-2021-48

Anonymous Referee #3

Referee comment on "Virtual decoupling to break the simplification versus resolution trade-off in nuclear magnetic resonance of complex metabolic mixtures" by Cyril Charlier et al., Magn. Reson. Discuss., <https://doi.org/10.5194/mr-2021-48-RC3>, 2021

This is an interesting manuscript with an important approach for metabolomics. It describes a high resolution HSQC approach without decoupling. For this it uses two HSQCs that are combined by software to obtain a quasi-decoupled spectrum.

Unfortunately the approach is not obvious from the description in the manuscript - a software is mentioned where spectra are first processed at low resolution for peak picking, followed by some undescribed approach for the high resolution spectrum.

I assume that both spectra are shifted and the size of the shift is determined by initial peak picking. As couplings in metabolites vary massively there is no common shift that works for all.

The paper would be better if this process was clearly described. What are the limitations? Does this work for overlapping peaks (of species with different or similar coupling constants)? Can this also be used for ^{13}C -labelled metabolites where adjacent ^{13}C -atoms can lead to long range ^2JCH couplings? What is the sensitivity of the experiment - this is crucial for often dilute metabolomics samples.

Overall this manuscript will be excellent with some minor revisions and is meaningful for a growing community of scientists looking at complex small molecule mixtures.

