

Magn. Reson. Discuss., author comment AC1
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Reply on RC1

Francesca Camponeschi et al.

Author comment on "The long-standing relationship between paramagnetic NMR and iron-sulfur proteins: the mitoNEET example. An old method for new stories or the other way around?" by Francesca Camponeschi et al., Magn. Reson. Discuss., <https://doi.org/10.5194/mr-2021-2-AC1>, 2021

The manuscript describes the NMR characterization of the first coordination sphere of mitoNEET in its two oxidation states. Albeit a few NMR studies are available for the protein, the data reported here provide an advancement with respect to the current knowledge on the protein. Hence, to some extent, we agree with the reviewer that the manuscript, with very minor revisions, could be suitable also for other journals and for a more general audience.

However, we believe that the mitoNEET case is a very nice example of how a protocol based on the combination of various experimental approaches tailored to paramagnetic systems spanning from the more recent IR-HSQC-AP to the "ancient" 1D NOEs, could provide insights into the knowledge of a challenging system of high biological interest.

Tailored NMR approaches have recently contributed to advance the knowledge for many different cases in FeS proteins, see for example the cases of **Ciapin** (Proc Natl Acad Sci U S A. 2013 Apr 30;110(18):7136-41. doi: 10.1073/pnas.1302378110), **Glrx5** (Proc Natl Acad Sci U S A. 2014 Apr 29;111(17):6203-8. doi: 10.1073/pnas.1400102111), **ISCA2** (J Am Chem Soc. 2014 Nov 19;136(46):16240-50. doi: 10.1021/ja507822j, J Am Chem Soc. 2017 Jan 18;139(2):719-730. doi: 10.1021/jacs.6b09567), **NUBP1** (J Am Chem Soc. 2020 Jun 17;142(24):10794-10805. doi: 10.1021/jacs.0c02266), **IBA57** (J Am Chem Soc. 2018 Oct 31;140(43):14401-14412. doi: 10.1021/jacs.8b09061), **LIAS** (J Mol Biol. 2019 Nov 8;431(22):4514-4522. doi: 10.1016/j.jmb.2019.08.018) and also on **mitoNEET** (J Am Chem Soc. 2017 Jul 19;139(28):9479-9482. doi: 10.1021/jacs.7b05003). These studies were mainly performed in the frame of FeS proteins biogenesis and interactomics, and only sparsely discussed the NMR aspects from a methodological point of view. We thought that MR could be the suitable medium to emphasize how: - the combination of classical and tailored experiments circumvents the loss of information in the proximity of metal centers; - the continuous advancement in NMR methodology contributes to the understanding of FeS proteins, as overviewed in the first part of the article and outlined in the title.

We still believe this. We are, of course, ready to revise the manuscript according to reviewer suggestions but this might not affect the opinion of the reviewer on the appropriateness of the manuscript for MR.