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# NMR tools for studying large (>100 kDa) protonated proteins produced in human cells

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Our aim is to study proteins that are relevant for human diseases at atomic resolution. Many of the important drug target proteins –like G-protein coupled receptors –are difficult to study by NMR in solution, as they can often only be produced in eukaryotic expression hosts and are larger than 100160;kDa.
We have therefore developed protocols for isotope labeling in eukaryotic cell lines, including human HEK293 cells. However, to date we are not able to produce highly deuterated samples in these cell lines, that's why we developed an alternative approach to study large proteins based on <sup>13</sup>C-methyl group labeling and novel NMR experiments. Using a T<sub>1</sub>- and T<sub>2</sub>-relaxation optimized HMQC pulse sequence and introducing the concept of delayed decoupling, we are able to record spectra with more than 3-fold higher sensitivity. This enables studies of protonated membrane protein complexes of limited stability and characterizing clinically relevant antibodies (150 kDa) at natural <sup>13</sup>C abundance.

**Primary author:** Dr GOSSERT, Alvar (ETH Zürich)

**Co-authors:** Mr RÖSSLER, Philip (ETH Zürich); Dr RÜDISSER, Simon (ETH Zürich)

**Presenter:** Dr GOSSERT, Alvar (ETH Zürich)

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