

## **Analysis of Nucleosome-protein interactions by NMR**

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The analysis and understanding of proteins, protein-protein interactions and their specificity are critical, both from a fundamental perspective and in structure-based drug discovery. Amongst structural biology techniques, NMR holds a special place as to its ability to capture dynamic events and observe low-affinity interactions. In this regard, the nucleosome constitutes a particularly interesting and challenging system. This large protein-DNA complex is central to multiple biological functions, including gene regulation, DNA damage repair response, and epigenetic mechanisms. In addition, defects and misregulations of such processes have been linked to diseases and particularly cancer, while healthy processes are used by viruses during their infectious cycle.

Here, we discuss the use of the novel sedimentation approach for studying nucleosomes by NMR. We demonstrate the successful use of sedimented nucleosomes for the acquisition of high quality  $^1\text{H}$ -detected spectra under very-fast MAS. We then use the approach to characterize the interaction between a viral peptide and the core of the nucleosome and from that modelled the structure of said complex. Through the combined use of NMR and SAXS we then demonstrate the general applicability of this method for the study of interactions with the nucleosome. Finally, we show a couple of examples of where NMR proved a powerful analytical tool for quality control of our experiments.