

Dynamic nuclear polarisation enhanced solid-state NMR spectroscopy and magnetic resonance force microscopy for structural biology

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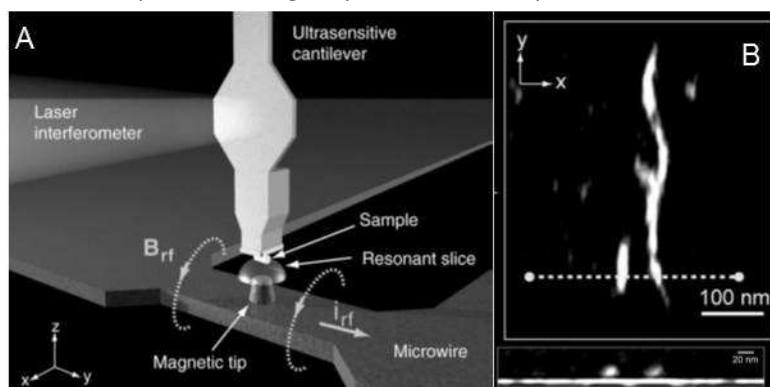
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Low sensitivity is always a central concern in the NMR community and a number of techniques have been developed to improve the sensitivity. In particular, high-field magic-angle-spinning dynamic nuclear polarisation (MAS-DNP) has been proven to be a powerful technique to enhance the sensitivity of solid-state NMR in many different types of systems. We have recently developed a new technique to selectively enhance surface signals using MAS-DNP and demonstrated “on-cell” NMR on bacterial cells, which will be a great investigation tool for “on-cell” studies [1].

However, application of MAS-DNP is not always straightforward mainly due to the use of frozen DNP-matrices which uniformly distribute polarising agents around the sample of interest at low temperature. In order to successfully perform MAS-DNP experiments, we have recently demonstrated matrix-free DNP [2, 3]. This utilises a binding affinity of polarising agents, clearly evidenced during the on-cell MAS-DNP studies above. We have obtained very encouraging results where only 20 minutes were sufficient to record natural-abundance 2D ^{13}C - ^{13}C correlation experiments on cellulose [2]. Furthermore, intermolecular constraints were obtained on self-assembled peptide nanotubes at natural ^{13}C abundance, which demonstrates the feasibility of supramolecular structure determination of such nano-assemblies without isotopic labelling [4].

Though above technique will allow one to reduce the sample amount dramatically, conventional NMR still requires $> 10^{10}$ molecules. Magnetic resonance force microscopy (MRFM) which utilises force detection instead of traditional inductive detection has been emerging as a promising technique to study structures of single nano-objects (see Figure) [5]. We will present our approach towards structural biology using MRFM, including the use of isotopic labelling for regional image contrast. We will also discuss potential target systems, such as proteins embedded in membranes.



A: Basic principle of MRFM. B: 3D images of virus particles at a spatial resolution of about 5 nm.

[1] H. Takahashi, et al. *J. Am. Chem. Soc.* 2013, 135, 5105. [2] H. Takahashi, et al. *Angew. Chem. Int. Ed.* 2012, 51, 11766. [3] H. Takahashi, et al. *Chem. Commun.* 2013, 49, 9479. [4] H. Takahashi, et al. *Angew. Chem. Int. Ed.* 2013, 52, 6979. [5] C. L. Degen, et al. *PNAS*, 2009, 106, 1313.