

## Nanoliter NMR Spectroscopy in a Microfluidic Chip

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The miniaturization of the transceiver coil has become an interesting approach to overcome one of the major limitations of NMR, i.e. its low sensitivity compared to other analytical techniques. Reducing the diameter of the RF coil, increases the signal-to-noise ratio (S/N) [1]. A reduction in coil diameter results in a decrease in the sample volume. Therefore, mass and volume-limited samples are highly suitable for these microcoils, as an optimum filling factor (ratio between the sample volume and the coil volume) is obtained which enables a highly sensitive detection in the NMR experiment.

A microfluidic chip (1 x 1.5 cm) with an integrated planar microcoil has been designed and fabricated [2] as an alternative approach to hold such as small sample volume ( $V_{\text{detection}} = 50$  nl).

The planar transceiver RF microcoil can be used for the detection of both high-resolution <sup>1</sup>H and <sup>19</sup>F NMR spectroscopy in nanoliters volumes and absolute quantities at the picomol level.

Focused on the optimization of the NMR-chip at the proton resonance frequency (<sup>1</sup>H NMR) [3], the self-assembly of calixarene dimelamine with dimethyl barbiturate (the so-called rosette) has been investigated inside the NMR chip. The high resolution reachable enables the monitoring of the encapsulation of a guest (alizarine) between the two rosette floors forming a self-assembled trimer structure with molecular weight of ~10kda.

As a proof of concept for the <sup>19</sup>F detection, supramolecular interaction of hexafluorophosphate anion and cyclodextrin at picomol level has been investigated inside the NMR chip. We monitored the shift of the fluorine peaks upon change of the host-guest ratio to determine the host-guest stoichiometry (1:1 PF<sub>6</sub><sup>-</sup>: cyclodextrin), and upon change of the concentration of cyclodextrin to obtain the association constant ( $K_{\text{ass}} = (0.4 \pm 0.15) 10^5 \text{ M}^{-1}$ ). The minimum concentration of NaPF<sub>6</sub> detected was 1mM which, corresponding to 50 picomol (8 nanograms) of NaPF<sub>6</sub> [4].

The combination of small volumes with the possibility of detecting both nuclei (<sup>19</sup>F and <sup>1</sup>H) opens the window for applications from microfluidic lab-on-a-chip devices to screening of biologically relevant molecules.

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