Continuous Flow Hyperpolarisation in a Microfluidic Chip

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NMR is an ideal tool to follow chemical and biochemical processes in microfluidic lab-on-a-chip (LoC) devices due to its non-invasive properties and its generality and specificity. In spite of this, NMR is rarely used in the context of LoC systems due to limited sensitivity. Hyperpolarisation techniques such as parahydrogen-induced polarisation (PHIP) may overcome this limitation. However, hyperpolarised spin states are susceptible to spin-lattice relaxation. It is reasonable to bring the production of hyperpolarised species as close as possible to the point of use. In this work, we demonstrate the integration of PHIP on a flexible microfluidic platform. The combination of hyperpolarisation with a highly optimised transmission line NMR probe leads to exceptionally good sensitivity. Moreover, the integrated system allows operation under continuous flow. This enables detailed kinetic studies of the hydrogenation, polarisation transfer, and relaxation processes.

In our recent work we demonstrate that PHIP on a chip improves the mass limit of detection by nearly three orders of magnitude from what was previously reported [1]. Our setup comprises a microfluidic chip made from three PMMA layers with laser-cut channels and a semi-permeable PDMS membrane, all held together by 3D printed holders with nano-channels that enable delivery of substrates (fig. 1a). The precursor solution, which contains propargyl acetate and a rhodium catalyst, are delivered to the chip via a syringe pump. Para-hydrogen is delivered through a separate channel and penetrates the PDM membrane to dissolve into the precursor solution; hence the hydrogenation reaction takes place on the chip (fig 1b). The resulting PASADENA signals are detected in the 2.5 μL sample chamber using a home-build probe.

Once a dynamic equilibrium state between the reactants was established, a stable signal enhancement of 1800 was observed (fig 1c). Constant supply of fresh hyperpolarised products together with excellent stability of the signal enabled us to acquire hyperpolarised 2D NMR spectra (fig 1d black) which is otherwise impossible due to the limited lifetime of hyperpolarised species [2]. Figure (fig 1 d blue) shows simulated spectra.

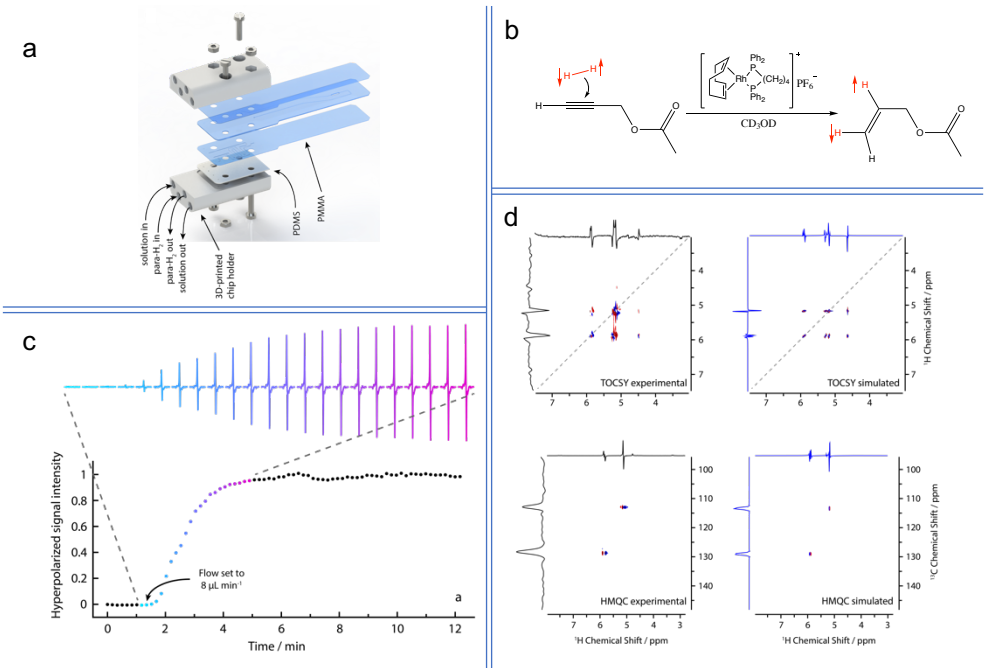

Fig 1 a) chip assembly b) scheme of the hydrogenation reaction c) build-up of the hyperpolarised signal d) experimental (black) and simulation (blue) 2D NMR spectra of the hyperpolarised reaction mixture.

References:
[1] G. Finch, A. Yilmaz, M. Utz, Journal of Magnetic Resonance **262**, 73 - 80 (2016).
[2] C.L. Swisher et. al., Journal of Magnetic Resonance **257**, 102 - 109 (2015)