Supporting Information: High-Resolution Nuclear Magnetic Resonance Spectroscopy With Picomole Sensitivity by Hyperpolarisation On A Chip

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PHIP@chip setup

Fig. S1 shows the solution (blue line) of propargyl acetate and catalyst in methanol being fed into the magnet via syringe pump. Simultaneously, para-H₂ is fed in (red line) at the desired



Figure S1: Drawing of PHIP@chip setup



Figure S2: ¹H spectrum obtained under continuous flow with thermal hydrogen.

pressure regulated to a flow rate of 20 mlmin^{-1} using a mass flow controller. Both these are fed into the microfluidic device, comprised of 3 layers of PMMA as well as a layer of PDMS and 2 3D printed holders as shown in Fig. 1 of the main article, that is inserted into the probe inside the 11.7 T magnet.

Thermal ¹H NMR spectrum

The thermal spectrum shown in Fig. S2 was collected using a flow rate of 2 μ lmin⁻¹ and a thermal H₂ pressure of 5 bar. The spectrum was processed using Mnova by Mestrelab and peaks of products assigned using values taken from literature.

Ortho-para conversion of H₂ dissolved in PDMS

The PHIP@chip experiment, as introduced here, requires diffusion of parahydrogen through a PDMS membrane. To determine the potential losses of polarisation due to hydrogen ortho-para conversion in PDMS, the ortho-para conversion time of H_2 dissolved in PDMS was measured. A high-pressure NMR tube of 5 mm outer diameter (Sigma-Aldrich) was filled with PDMS resin (Sylgard 84, 3M). A teflon capillary of 1/16 inch outer diameter was pushed into the NMR tube along the central axis, and the PDMS was allowed to cure. The capillary was then removed, leaving a cylindrical void in the centre of the NMR tube. The tube was then exposed to vacuum for varying amounts of time, in order to study the effect of residual oxygen



Figure S3: Ortho-para conversion of H₂ in PDMS.



Figure S4: Overview of finite element simulations. a: Overview of the finite element simulation domain, consisting of the PDMS membrane, gas channel, and fluid channel including sample chamber. b: Detail of the finite element mesh; c: flow velocity profile in the sample chamber at an overall flow rate $q = 1 \ \mu l \min^{-1}$.

on the ortho-para conversion time. The detectable thermal signal in the ortho-para conversion experiment is given by $1 - \frac{1}{3}(4f - 1)$, where *f* is the para-enrichment level of the H₂ gas. Therefore, the equilibrium ratio of f = 0.25 gives a signal of 1, and pure parahydrogen gas gives no signal. Hence, our signal starting at 50% enrichment should vary from 2/3 to 1. The data was fit to a function of the form $A - B e^{-\frac{t}{T_s}}$, with *A*, *B* and *T_s* as variables.

Simulated H₂ concentration in chip

Finite element simulations were carried out using COMSOL version 5.3a. The simulation domain was imported from a SolidWorks model, and consisted of the PDMS membrane, and the fluid channel with the sample chamber. The gas channel was not explicitly modelled, but a



Figure S5: Simulated partial pressure of H_2 in the PDMS membrane and the flow channel and sample chamber. At low flow rates, the hydrogen partial pressure is able to equilibrate between the hydrogen gas channel and the sample chamber (input hydrogen pressure: 5 bar). Higher flow rates lead to lower hydrogen partial pressures in the sample chamber.

constant hydrogen partial pressure condition was imposed on the boundary between the PDMS membrane and the gas channel (Fig. S4a). A tetrahedral mesh was used, with a maximum element size of 50 μ m in the fluid channel (Fig. S4b). Three separate finite element models were coupled: a laminar flow model, using nominal values for the viscosity and density of methanol, and an flow rate boundary condition at the liquid inlet; a dilute species diffusion model for H₂ in the PDMS membrane, and a diffusion/convection model for H₂ in the flowing liquid. Values for the Henry constants of molecular hydrogen in PDMS and in methanol, as well as the diffusion coefficient of hydrogen in PDMS, were obtained from the literature.^{1,2} The H₂ partial pressures at the boundary between the PDMS and the liquid were matched. Overall, the mesh consisted of 1.6 M elements, and the computation involved 1.5 M independent degrees of freedom. The flow profile in the sample chamber at a flow rate of $q = 1 \,\mu l \min^{-1}$ is shown in Fig. S4c. The H₂ partial pressure in the flowing liquid decreases with increasing flow rate, as shown in Fig. S5.



Figure S6: Saturation recovery of the hyperpolarised NMR signal as a function of flow rate (filled circles). The solid lines are guides to the eye only.

Saturation recovery data

The data and the fit obtained for each set are shown in Fig. S6. Here all signal intensities have been normalised to those obtained at the optimal flow rate of 8 μ l min⁻¹. The data shows the variation in maximum signal achieved at each flow rate consistent with the curve shown in the main article. It is also important to observe that the signal build up constant, that depends on T₁ and a, varies greatly at lower flow rates below optimum and seemingly remains constant afterwards at the time of writing this relationship is not understood fully.

2D Pulse Sequences

The pulse sequences used for the PH-TOCSY and the PH-HMQC spectra are shown in Fig. S7.

The peaks in the PH-TOCSY spectrum appear with dispersive phase components. This is not evident from the magnitude mode spectra shown in the main article. Fig. S8 shows



Figure S7: Pulse sequences used for the PH-TOCSY and the PH-HMQC experiments.

phased spectra. While the peak positions and intensities agree well between the simulated and experimental spectra, there are significant discrepancies in the phases. We attribute this to imperfections in the isotropic mixing pulse sequence which were not modelled; the simulations assumed a perfectly isotropic Hamiltonian during the mixing period. At this point, it is not clear whether a variant of the PH-TOCSY sequence can be derived that yields purely absorptive spectra.



Figure S8: Experimental (left) and simulated (right) TOCSY spectrum plotted in phased (real) mode.

References

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