Electronic Supplementary Material (ESI) for Lab on a Chip.

Supplementary information to: Microfluidic Platform For Serial Mixing Experiments With *in operando* Nuclear Magnetic Resonance Spectroscopy

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Presented here is a microfluidic platform for serial mixing experiments with *in operando* detection by NMR spectroscopy. In the following, we discuss some additional details of the setup and its operation; in particular, the ancillary hardware and interfaces. The overall design is shown in Figure S1. This platform relies on the design versatility of the transmission-line probe (TLP), which accommodates planar microfluidic devices inside a standard NMR spectrometer. The probe and device are of corresponding geometry, such that the 2.5 μL detection chamber on the polymethyl methacrylate (PMMA) microfluidic chip coincides with the area of maximum sensitivity of the TLP. The key element of the PMMA chip is a set of pneumatic microvalves, positioned away from the detection area, and dictating the behaviour of sample liquid. The chip receives control input from external hardware: micro-syringe to inject the sample liquid, and pressurised air supply to actuate the microvalves. For functionality the PMMA chip is interfaced with 1/16 ” capillary tubing for liquids and 3 mm tubing for pneumatics via 3D printed chip holder and three elastomer membranes, covering the upper part of the chip (Fig. S2). Microvalve function relies on the deformation of the elastomer membranes, pushed by 5 bar pressurised air against the valve floor, as shown in Figure S3.

The experimental protocol for serial mixing is outlined in Figure S4. In preparation, two samples are consecutively loaded into the reservoir capillary extending from the micro-syringe to the microfluidic device, before connecting to the device inlet. The outgoing capillary is connected to 3 bar pressurised air to maintain the metering accuracy inside the microfluidic chip equal to the movement of the micro-syringe plunger. The micro-syringe push fills the device with the test solution, and the device is placed inside the spectrometer for calibration and to acquire initial spectra. A further push from the micro-syringe injects a fraction of the exchange solution into the chip, and the two solutions are mixed as result of a peristaltic motion induced by sequential actuation of the microvalves. Injection and mixing steps can be repeated many times, systematically changing the composition of the sample under investigation.

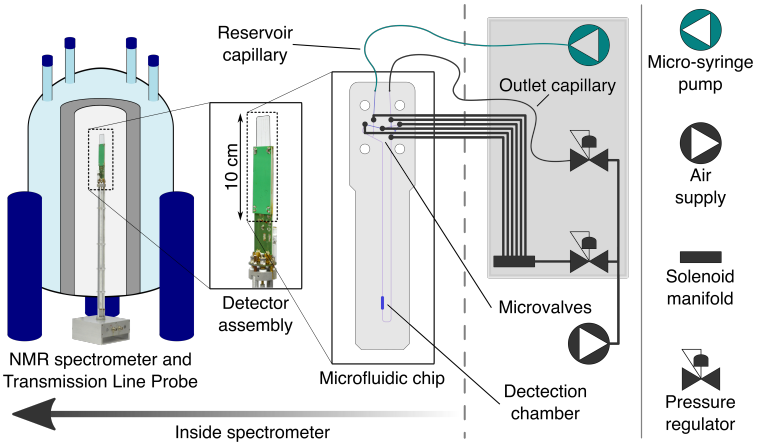

Figure S1: Macroscale to microscale (left to right) representation of the microfluidic device and its fit inside the NMR spectrometer. Remaining components, located away from the spectrometer, are represented in a schematic form.

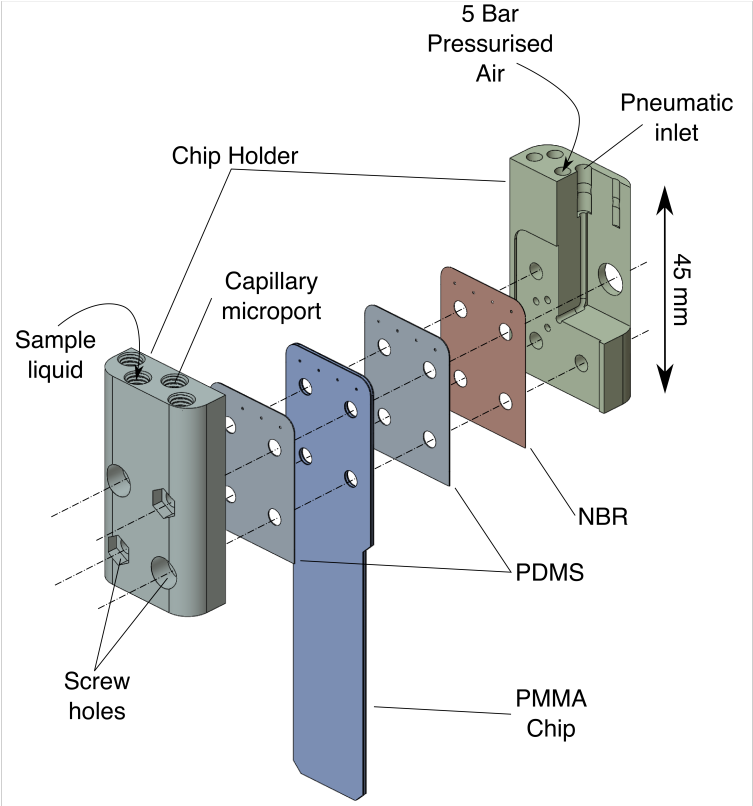

Figure S2: The microfluidic device is assembled from the central PMMA chip, where sample manipulation and detection takes place, three elastomer membranes acting as a gasket (PDMS) and gas barrier (NBR), and two holder blocks that connect to the external pressure and liquid supply systems. The assembly is held together by four M3 screws.

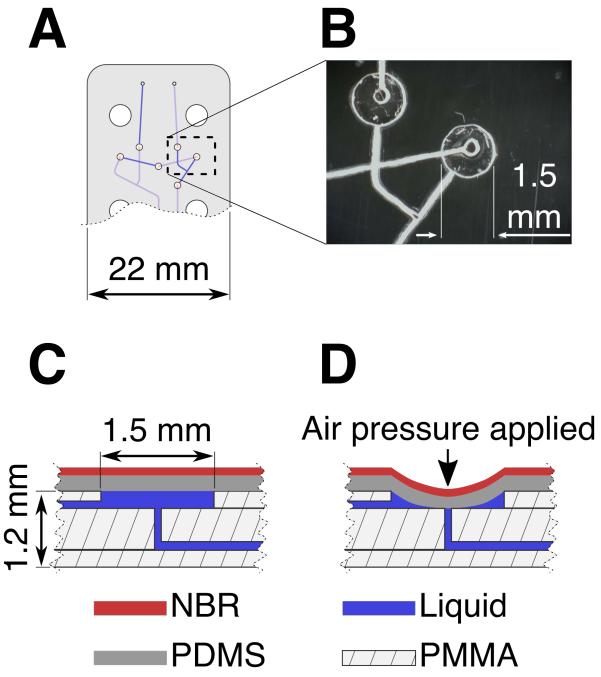

Figure S3: Detail view (A) and micrograph (B) of the chip microvalves. Cross section of a single microvalve (C) and its actuation principle (D).

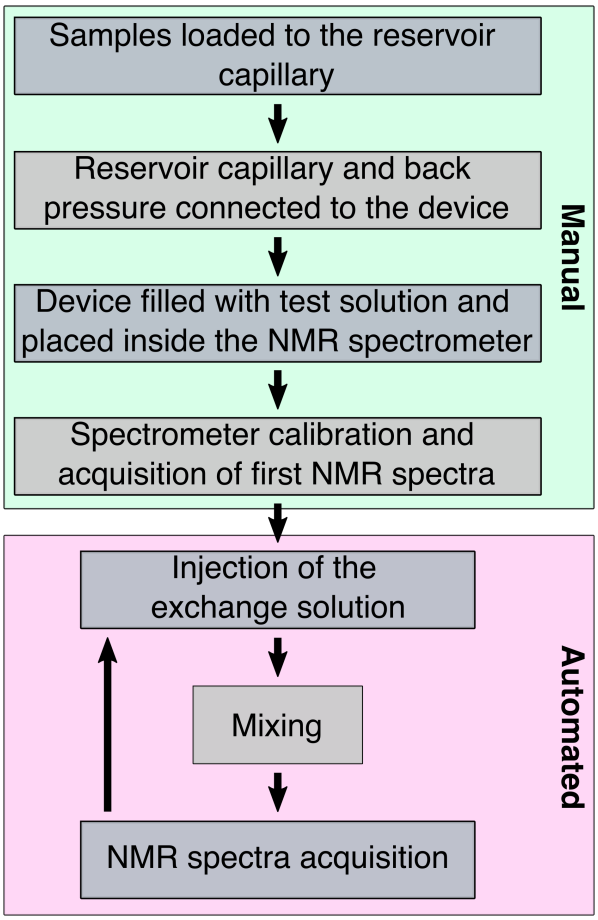

Figure S4: Flow chart of the operation algorithm for the successive two-solution serial mixing experiments.