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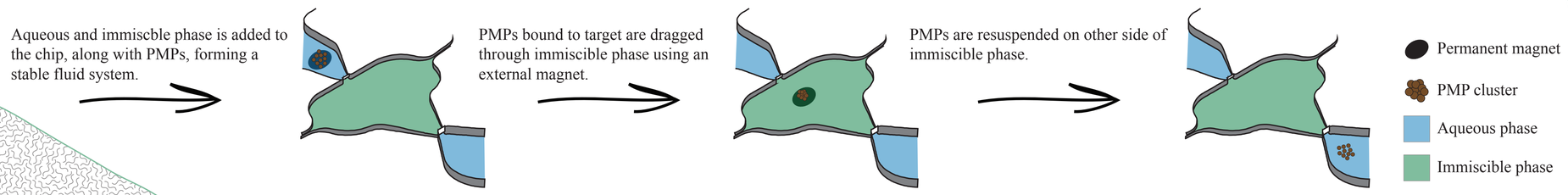
LIQUID CARRY-OVER IN AN ALL-POLYMER CHIP SYSTEM FOR MAGNETIC BEAD-BASED MOBILE SOLID PHASE EXTRACTION

MOTIVATION

Paramagnetic particles (PMPs) are commonly used as the solid phase matrix for mobile solid phase extraction (MSPE). A variant of PMP-based MSPE exists, where an immiscible phase is used as a filtering step in order to circumvent the washing steps otherwise needed to perform a successful extraction [1-3].
It works the following way:



In this study we characterise an injection moulded COC polymer planar chip system that has been bonded together using ultrasonic welding – both techniques that can be readily applied in mass production and it is what sets this system apart from ones previous published. The chip is fitted with geometric capillary micro valves for PMP-based mobile solid phase extraction (MSPE) using the immiscible phase filtration approach, see figure 1 for a photograph of the chip.

We quantify the carry-over volume of the system and further investigate the influence of surfactants on the efficacy of the system. The carry-over volume directly contaminates down stream analyses and it is therefore important to know its size.

[1] K. Sur, S.M. McFall, E.T. Yeh, S.R. Jangam, M. a Hayden, S.D. Stroupe, et al., Immiscible phase nucleic acid purification eliminates PCR inhibitors with a single pass of paramagnetic particles through a hydrophobic liquid., J. Mol. Diagn. 12 (2010) 620–8. doi:10.2353/-jmoldx.2010.090190.

[2] S.M. Berry, E.T. Alarid, D.J. Beebe, One-step purification of nucleic acid for gene expression analysis via Immiscible Filtration Assisted by Surface Tension (IFAST)., Lab Chip. 11 (2011) 1747–53. doi:10.1039/c1lc00004g.

[3] R.C. den Dulk, K. a Schmidt, G. Sabatté, S. Liébana, M.W.J. Prins, Magneto-capillary valve for integrated purification and enrichment of nucleic acids and proteins., Lab Chip. (2012) 106–118. doi:10.1039/c2lc40929a.

RESULTS

The chip was performance tested by first ensuring that a stable fluid system could be achieved using Milli-Q water and FC40 “teflon” oil. The chip was then tested with various surfactants and the carry-over volume was quantified. We used MyOne SILANE magnetic beads (Ø = 1 µm) for all the experiments.

Characterization was performed for solutions with different types and amounts of surfactant. Table 1 shows the compatibility of the system with different solutions.
In general, the solutions were compatible if;

- the solution-oil interfacial energy was above 7 mN/m.
- the solution-air contact angle was above 25°.

Figure 2 shows the determination of volume carry-over vs. amount of MyOne SILANE magnetic beads for pure water and a typical DNA binding buffer.
We find that the volume carry-over;

- is proportional to the amount of beads through a linear correlation.
- is the same for the two investigated solutions.

We have estimated that the PMPs constitute 13.6% of the total solution-PMP aggregate.

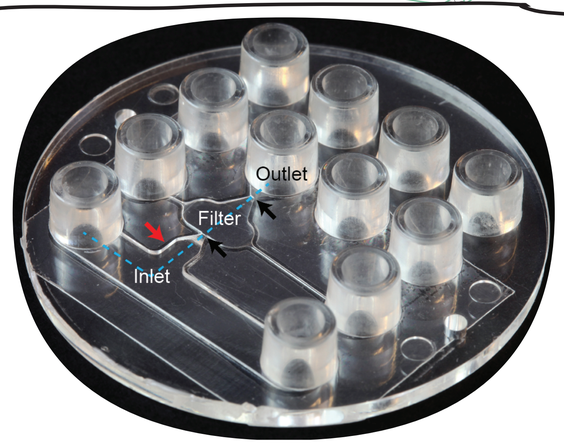


FIGURE 1 **Photograph of a welded chip** with the different compartments highlighted. The red arrow indicates the welding seam following the channel circumference. The black arrows indicate the positions of the geometric capillary micro valves. The blue dotted line shows the pathway of the PMP bead cluster. Ø = 50 mm.

CHIP DESIGN AND VOLUME CARRY-OVER DETERMINATION

The assembled chip is disc shaped and features a Luer-Slip layout with an inlet channel, oil-containing “filtration” channel and an outlet chamber, all interconnected by geometric capillary micro valves, see Figure 1.
The chip was mounted in a setup with a movable magnet situated under the inlet Luer fitting. A fluorophore containing solution was added to the inlet channel and a blank solution to the outlet chamber. FC40 oil was then added to the middle channel to complete the loading. Various volumes of PMPs was then added to the inlet and transferred from inlet to outlet by moving the magnet. The PMPs were resuspended, removed and the outlet volume was transferred to a microtiter plate. The carry-over volume was estimated by analysing the dye content of the wells. This concentration could then be calculated into a volume by correlating with the dye concentration of the inlet and the respective volumes of the inlet and outlet.

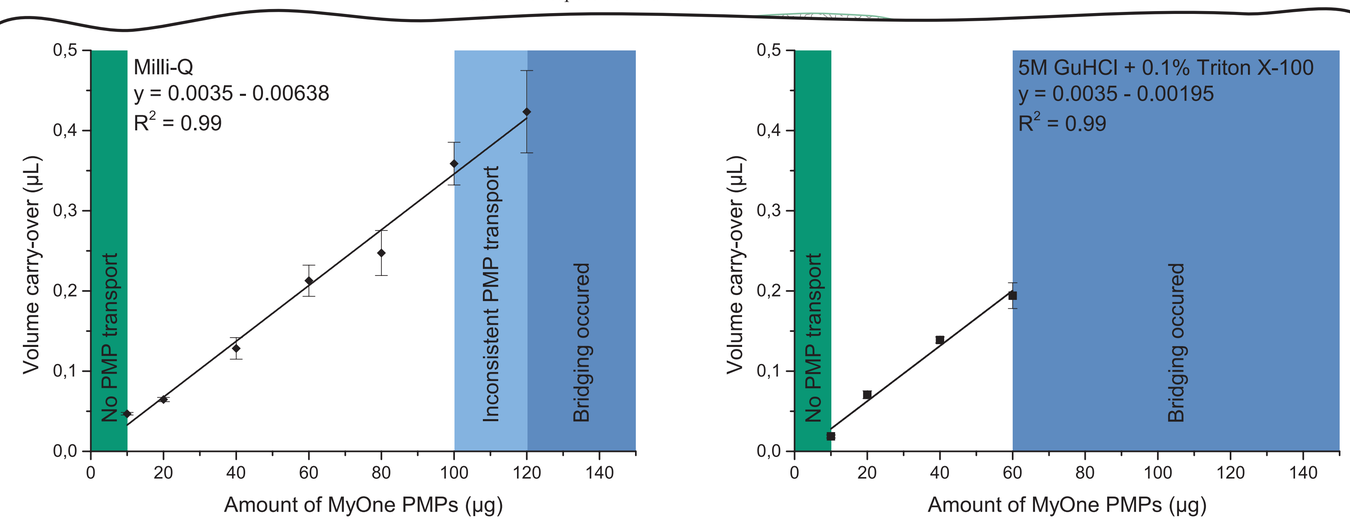


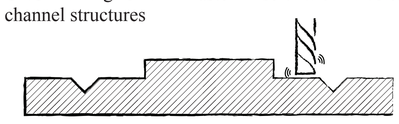
FIGURE 2 **Volume carry-over for various amounts of MyOne SILANE PMPs**. The left part shows the carry-over of Milli-Q water whilst the right part shows the carry-over of a 5M guanidine hydrochloride solution with 0.1% Triton x-100. A good correlation was found in both cases with an average carry-over of 0.0035 µl/µg. It was not possible to transfer less than 10 µg of PMPs. For Milli-Q water, PMP transfer became problematic above 100 µg and bridging occured above 120 µg. For the surfactant containing solution bridging occured already at loads of 60 µg PMPs.

CHIP FABRICATION

The chip consists of two Cyclic Olefin-Copolymer (COC) parts of the grade TOPAS 5013; An injection moulded main part and a 0.152 mm extruded film.
The fabrication process is as follows:

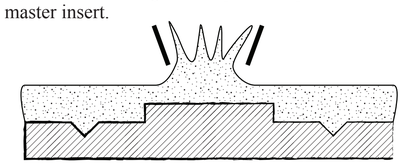
(A) MILLING OF MOULD INSERT

CNC milling of Al master insert with inverted channel structures



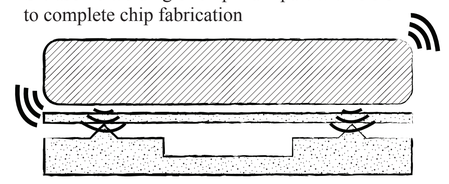
(B) INJECTION MOULDING

Injection moulding of chip main part based on master insert.

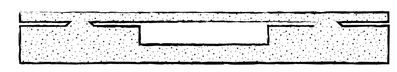


(C) ULTRASONIC WELDING

Ultrasonic welding of chip main part with COC film to complete chip fabrication



(D) FINISHED CHIP



HAVE A LOOK AT THE CHIP

CONCLUSION

The results showed that

- One can expect a linear correlation between the amount of volume of carry-over and the mass of PMPs for a polymer system with a water-air contact angle of around 90°.
- A dilution factor of atleast 250 can be expected when using 100 µg of PMPs.
- The system is compatible with various surfactants in low concentration.
- Adding surfactants does not affect the carry-over volume.

Surfactants decrease the interfacial energy and potentially allow for more carry-over. One explanation for the observed normalisation could be the geometrical capillary micro valves. This forces the PMP cluster to be tightly packed at the interface, affecting the forces governing the cross-interface transport. If this is the case, one can effectively normalise the amount of carry-over by using a geometrical capillary micro valve instead of one based on chemical modifications.

The COC used here is not optimal for a system where you wish to employ surfactants. A polymer with a higher surface energy, such as polypropylene or a chemical surface coating would increase the surfactant compatibility of the chip.

TABLE 1 **Compatibility of surfactants with the chip**. A chip was deemed compatible if the fluids could be pippetted onto the chip and form a stable fluid system after which 40 µg of PMPs could be successfully transported through the oil phase. The interface tension of FC40 oil in the noted solution (γ) and the contact angle (θ) of the noted solution with air was recorded using a goniometer.

Solution ((v/v)%)	γ (mN/m)	°θ (°)	Compatibility
Milli-Q water	44.0 ± 1.6	87.8 ± 0.5	YES
0.1% Triton X-100	9.5 ± 0.1	46.0 ± 0.7	YES
0.25% Triton X-100	6.2 ± 0.1	19.7 ± 0.7	NO
0.0625% Sarkosyl	7.8 ± 0.2	35.6 ± 2.0	YES
0.125% Sarkosyl	5.4 ± 0.4	12.8 ± 3.1	NO
1% Span 80	25.1 ± 0.4	78.0 ± 1.2	YES
1% Tween-20	8.3 ± 0.1	29.8 ± 0.3	YES

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