GUIDING OF LIQUIDS VIA PATTERNED SURFACE COATINGS TO FACILITATE SOLID-PHASE EXTRACTION IN TWO-PHASE FLOW

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ABSTRACT

We present a concept for solid phase extraction of compounds from reactions contained in the dispersed phase of two-phase flow based on the manipulation of liquids via patterned surface chemistry. Approaches to guiding of liquids via patterned surface coatings have been proposed by several groups [1-3]. However, few practical applications of such approaches have been reported to date. We demonstrate a simple and efficient method for extraction of compounds from nanoliter-sized liquid plugs using magnetic beads as carrier.

KEYWORDS: solid-phase extraction, plugs, two-phase flow, patterned surface chemistry, magnetic beads

INTRODUCTION

Two-phase systems such as droplet-based systems are increasingly popular for miniaturized, high-throughput performance of analytical (e.g. digital PCR) or chemical reactions [4]. The majority of reactions which are carried in two-phase flow are homogeneous reactions. Here, all reactants remain in the liquid phase and analysis of the reaction product can be performed in-situ (e.g. through a color change). However, many reactions require purification of the analyte for downstream analysis (e.g. the purification of DNA prior to PCR). But at the micro scale the interface between the two phases aggravates conventional means of solid-phase extraction (e.g. via magnetophoresis)[5]. In our concept we perform extraction by defined breakage of the micro emulsion via manipulation of the solid/liquid interface.

CONCEPT

We selectively alter the wettability of surfaces of microfluidic structures to manipulate the flow of immiscible liquids. This allows to access species which are contained in the dispersed phase of segmented flow. For this purpose magnetic beads are added to the aqueous plugs for specific binding of the target compound. To facilitate extraction of the bead-bead compounds from the plugs the micro-emulsion is broken. This is achieved by flowing the train of plugs through a channel section with a patterned surface coating (Figure 1). One side of the channel is coated with a hydrophobic fluoropolymer. It is wetted preferably by the continuous phase. The other side is coated with a surface-attached hydrogel (i.e. a hydrophilic area) which is wetted by the aqueous phase (Figure 2). Thus, when plugs are flown in this channel section, they spontaneously orientate towards the hydrophilic side of the channel. There they add to a co-flowing aqueous stream, which is applied for purification of the bead-bound species. The underlying mechanism for this surface-induced breakage of the plugs is the reduction of the free surface energy of the plug. Accordingly, in areas of the channel that are homogeneously coated with the fluoropolymer, the surface is wetted preferably by the fluorocarbon solution. Thus, the fluorocarbon solution encloses the aqueous plug (Figure 1A). However, if the plug flows in a channel section that is partly rendered hydrophilic, it can lower its interfacial energy by wetting the hydrophilic solid surface (Figure 1B).

Figure 1: schematic illustration of the mechanism guiding of liquids via different surface chemistries. Above: microfluidic chip with hydrophilic and hydrophobic areas. Below: cross-sectional views at locations (A & B) along the channel.

Figure 2: water drops on planar substrate coated with hydrophobic fluoropolymer (top) and with hydrophilic hydrogel (bottom). Surrounding medium is fluorocarbon solution. The liquid-liquid interfacial tension was 30 mN/m.
EXPERIMENTAL

The fabrication process of the fluidic devices is illustrated schematically in Figure 3. The channel structures were micro-milled into PMMA. The width of the channel was 500 µm in the narrower (Figure 1A) and 750 µm in the wider section (Figure 1B), the depth was 300 µm. Different polymer layers were applied via dip-coating. The fluoropolymer was poly-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-heptadecafluorodecyl acrylate co 1% methacryloyloxybenzophenone) [6]. The hydrogel was formed from poly-(N,N-dimethylacrylamide co 5% methacryloyloxybenzophenone co 2.5% Na-4-styrenesulfonate [7]. Patterning of the coatings was achieved by incorporation of photo reactive cross-linker moieties in the polymer chains. This allows for simple structuring of polymer coatings via photolithography analogously to photoresists. Upon short UV-exposure the polymers crosslink in the irradiated areas while simultaneously covalent attachment of the forming network to the microfluidic structure and optionally functionalization (e.g. with biomolecules) is achieved [7].

Figure 3: schematic illustration of the fabrication process of the microfluidic structures with patterned surface coatings

The two immiscible phases which were employed comprise of FC-43 (3M, Germany) which was used as continuous phase and aqueous solution containing red dye or superparamagnetic beads (1 µm, Chemicell, Germany), respectively. The interfacial tension between the two liquids was lowered by addition of a fluorosurfactant (25% (V/V) to the continuous phase. The fluorosurfactant solution was prepared from Zonyl FSO-100 (Sigma Aldrich) following a protocol from Roach et al. [8]. Plugs were generated at a flow ratio \( r \) of continuous phase and dispersed phase of \( r = 5 \). The volume per plug was about 120 nL.

RESULTS AND DISCUSSION

First, continuous streams of both immiscible liquids were flown through a channel section with differently patterned surface chemistry. As shown in Figure 4 the aqueous solution stays on the “hydrophilic” tracks. Thereby even an overcrossing of the two phases could be achieved.

Figure 4: A) schematic illustration of a microfluidic structure that was selectively coated with two different polymers. Hydrophobic areas were achieved by coating with a fluoropolymer, hydrophilic area with a surface-attached hydrogel. B) Image of the microfluidic chip. Two immiscible phases were flown in from two inlets. The aqueous phase preferably stays on the hydrophilic areas of the channel. Overcrossing of both phases can be observed.

A similar device was used to manipulate a segmented flow of plugs. As shown in Figure 5 the plugs show the expected behavior: segmented flow in areas that were homogeneously coated with hydrogel and a transition to a side-by-side flow in the channel section with both hydrophilic and hydrophobic surface properties. In this channel section the plugs orientated instantaneously towards the hydrophilic channel area and added to the co-flowing aqueous stream (compare Figure 5).
The surface-induced breakage of the plugs allows to extract particles which are contained in the plugs for specific binding of target compounds. This is shown in Figure 6 where particles were continuously extracted from aqueous plugs. Thereby, the magnetic beads with bound species are hold stationary by the magnetic field. Simultaneously, purification of the bead-bound compound is achieved. Free compounds are washed away by the continuous flow of aqueous washing solution.

CONCLUSION

We demonstrated a simple method that allows to extract and isolate specific compounds from liquid plugs. This process can be performed successively for a train of plugs at a rate of > 5 Hz. Thereby, the sequence of the plugs is preserved which is important if individual plugs have different contents and their identity is encoded in the order of the plugs. We assume that this concept can simplify the performance of heterogeneous reactions in two-phase flow.

REFERENCES