

ON-DROP SEPARATION AND SENSING WITH COMPOUND DROPLET MICROFLUIDICS

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ABSTRACT

We present a new platform for analytical applications of droplet-based microfluidics in which flowing droplets function not only as isolated reaction flasks, but are also capable of *on drop* separation and sensing. To demonstrate this, ionic liquids with tunable chemical and physical properties have been selected as designer fluids. We create aqueous-ionic liquid compound droplets with various structures and present two analytical applications- separation of a binary aqueous mixture and dynamic pH sensing- to highlight the salient features of this scheme. By combining designer fluids with designer microfluidic emulsions, the present work opens a rich space of exploration for analytical microfluidics.

KEYWORDS: Compound Droplet, On-drop, Microfluidics, Ionic Liquid, Sensing, Separation

INTRODUCTION

Rapid compartmentalization and automated analysis of chemical and biological transformations on individual picoliter drops promises to revolutionize laboratory-based experimentation, enabling both time-resolved kinetic measurements and rapid exploration of large experimental parameter spaces. Droplet-based microfluidic systems are a technological platform that realizes this goal and have received tremendous attention in recent years [1]. We focus our attention on droplet-based microfluidics where the flowing droplets are composed of two (or more) immiscible fluid phases. More recently, such compound droplets have been of significant interest in the formation of tailored multiple emulsions and also in the fabrication of highly structured, spatially anisotropic polymeric beads. In this paper, we present a new and general droplet-based scheme where we demonstrate biphasic compound droplets capable of *on-drop* chemical separations and sensing. We choose ionic liquids as functional fluids whose chemical and physical properties can be tailored to be task-specific [2], and outline how aqueous-ionic liquid compound droplets can be generated with tunable structures through appropriate fluids selection and device operation. We further demonstrate and discuss two analytical applications - separation of a binary aqueous mixture of organic dyes and dynamic pH sensing. Our work paves the way for applications where a myriad of reactive and analytical processes occur concurrently within flowing microscale droplets, thus greatly expanding the realm of possibilities for droplet-based chemical, biochemical and materials analysis and screening.

EXPERIMENTAL

Microfluidic device patterns were fabricated onto silicon wafers by standard photolithography. Individual syringe pumps were used to deliver carrier fluid, IL and aqueous solutions to the microfluidic device. A 10:1 (v/v) mixture of perfluorodecalin (PFD) and perfluorooctanol (PFO) was used as the carrier fluid which will be referred to as fluorinated oil (FO) hereafter. *Liquid-liquid extraction:* An aqueous solution containing a binary mixture of Orange II (OrII) and Methyl Blue (MeB) was used. The individual flow rates of each stream, Q_{FO} , Q_{IL} and Q_{Aq} were $3 \mu\text{Lmin}^{-1}$, $1 \mu\text{Lmin}^{-1}$ and $3 \mu\text{Lmin}^{-1}$, respectively. *pH detection:* Aqueous p-toluenesulfonic acid (p-TSA monohydrate) solutions of varying concentration (5 mM, 10mM, 100 mM and 1 M) were used while the pH-detector was 1.6mM Thymol Blue in [EMIm][NTf₂]. The individual flow rates of each stream, Q_{FO} , Q_{IL} and Q_{Aq} were $3 \mu\text{Lmin}^{-1}$, $1 \mu\text{Lmin}^{-1}$ and $3 \mu\text{Lmin}^{-1}$, respectively. Quantification of the 'on drop' separation and pH sensing applications demonstrated in this work involves tracking color changes in the ionic liquid compartment. Once steady state operation was achieved the images of the flow were recorded at 23.6 fps by a CCD camera mounted on a stereo microscope.

THEORY

The formation and dynamics of droplets in microchannels are typically dominated by wettability and fluid-fluid interfacial considerations. When two immiscible fluids are continuously dispensed into a third immiscible fluid in a microchannel at low capillary numbers, as illustrated in the schematic of Fig. 1(A), the dispensed droplets can assemble into biphasic 'compound droplets' whose interfacial morphologies closely resemble the corresponding static cases [3, 4]. Three possible equilibrium interfacial morphologies are predicted by the theory developed by Torza and Mason: (1) completely engulfed drop-in-drop structures, (2) partially engulfed structures, where a three-fluid contact line is formed, and (3) non-engulfed droplet pairs where the two dispersed liquids remain unattached and isolated from each other by the continuous liquid phase. In this work, we particularly focus on partially engulfed compound droplets. Aqueous-ionic liquid compound droplet structures flowing in fluorinated or silicone-based oils are shown in Fig. 1(B).

RESULTS AND DISCUSSION

Liquid-liquid extraction is one of the most popular methods for isolation and purification of organic compounds, and involves the selective partitioning of molecules between two immiscible fluid phases brought in contact with each other [5]. As a first application example of aqueous-IL compound droplets, we demonstrate separation of a binary aqueous mixture of organic dyes. An aqueous mixture of two organic dyes (Orange II and Methyl Blue) that is initially brown is

dispensed into a microfluidic channel as compound droplets with IL. The orange dye is highly soluble in the IL-phase ([EMIm][NTf₂]) and rapidly extracted into the IL compartment, while methyl blue remains in the aqueous phase (Fig. 1(C)). We track color changes in flowing compound droplets and find that the extraction is completed in ~ 8 s. This extraction time is much smaller than the characteristic diffusion time $t_D \sim w^2/D = 1500$ s, where $D = 6.5 \times 10^{-12} \text{ m}^2\text{s}^{-1}$ is a Stokes-Einstein estimate of OrII diffusivity in [EMIm][NTf₂], and w is the microchannel width. This dramatically lowered extraction time can be attributed to convection-enhanced diffusive transport, where the characteristic extraction time (t_C) is decreased compared to diffusion time (t_D) by a flow-dependent factor $Pe^{-2/3}$ at short contact times ($t \ll t_D$) (where Peclet number (Pe) $\sim Uw/D$ and U is a flow speed). Taking this convection enhancement into account gives us an estimated convection-enhanced extraction time $t_C \sim 3$ s for a flow speed of $5 \times 10^{-3} \text{ m s}^{-1}$, which is in acceptable agreement with our measurements.

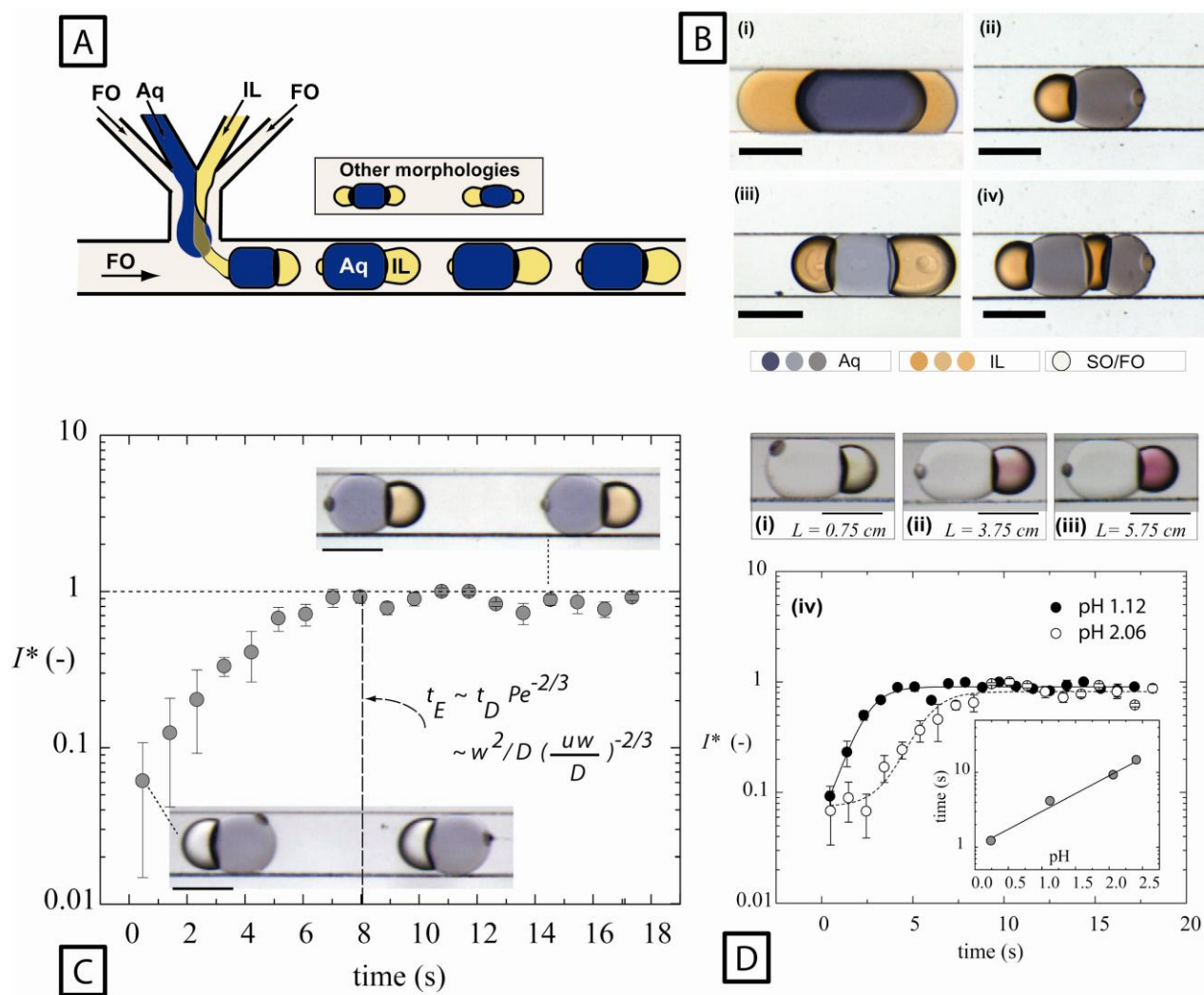


Figure 1: (A) A schematic illustrating our method (B) Stereomicroscope images of compound droplet structures generated in this work: (i) fully engulfed aqueous-in-ionic liquid (Aq-IL) compound droplets, formed in a continuous phase of silicone oil (SO), and (ii-iv) partially engulfed aqueous-ionic liquid droplets formed in a fluorinated oil (FO) continuous phase. (C) A plot of the average color intensity (normalized) in the ionic liquid compartment versus time. t_E and t_D are characteristic time of extraction and diffusion, respectively. (D) (i-iii) Stereomicroscopic images illustrating on-drop pH-sensing showing the ionic liquid compartment gradually changing color (from yellow to deep pink) as it translates along the length of the microchannel (iv) A plot of average color intensity (normalized) of the ionic liquid droplet versus time for two different pH values. The inset shows end-point measurements, i.e. the measured time for the saturation of color in the ionic liquid compartment at four different pH values. (L/v , where L is the distance along the microchannel and v is the velocity of the compound drops; $v = 0.005 \text{ ms}^{-1}$ obtained using image analysis.) All scale bars represent $300 \mu\text{m}$.

Measurements of pH in microfluidic devices are typically carried out either by electrochemical means with electrodes whose fabrication involves complex lithographic steps or by optical means using dissolved pH-sensitive dyes. We here, demonstrate *on-drop* pH sensing where the ionic liquid compartment serves as a non-invasive chemical sensor directly attached onto an aqueous droplet (Fig. 1(D)). An indicator-doped ionic liquid to measure the pH of an aqueous acidic phase has been used. In our case, the doped ionic liquid compartment simply changes color from yellow to pink as it becomes progressively acidic by mass transfer of the acid from the aqueous phase. Furthermore, steady-state operation enables us to calibrate pH of the aqueous phase versus dynamic color change of the ionic liquid as the compound droplets translate along the microchannel. We plot an average color intensity within the ionic liquid compartment as a function of aqueous-ionic liquid contact time in the microchannel, for two different pH values. The color change and saturation are clearly seen to occur more rapidly for the higher acid concentration. Therefore, this is not merely a qualitative endpoint measurement where a color change indicates a ‘yes’ or ‘no’ answer, but a quantitative measurement where the color change *dynamics* can be calibrated against pH (Fig. 1(D), inset). We envision this technique to eventually enable dynamic sensing of multiple chemical events in the aqueous phase.

CONCLUSION

In summary, we have introduced a compound droplet-based analytical method that makes *on-drop* reaction, separation and dynamic reporting possible, thus greatly broadening the spectrum of analytical droplet microfluidics applications [6].

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