INVESTIGATING INTER-DROPLET MASS TRANSFER IN FLOW UTILIZING HIGH ACCURACY SYNCHRONIZATION

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ABSTRACT

We report a microfluidic system for the measurement of mass transfer between microfluidic droplets in flow. A high-accuracy droplet synchronization structure allows for the passive ordering of two droplet types which enabled quantification of both osmotic and diffusive transfer between droplets.

KEYWORDS: Microfluidic Droplet, Synchronization, Mass Transfer, Osmosis, Ordering

INTRODUCTION

Incubation and storage of microfluidic droplets is an essential step in many droplet-based biological and chemical assays[1]. To increase storage density and decrease back-pressure typically most of the continuous phase is removed resulting in tightly packed droplet streams[1]. It has previously been shown that cross-talk exists between stationary droplets in contact, leading to a homogenization of droplet contents over time[2]. Even though two immiscible phases are used for droplet formation, extensive interaction has been shown between the continuous and the dispersed phase[3]. Still, to our knowledge transfer between densely packed droplets in motion has not been quantified so far. In this work we utilize a novel passive droplet synchronization architecture, which allows us to create and investigate highly regular tightly packed droplet streams.

THEORY

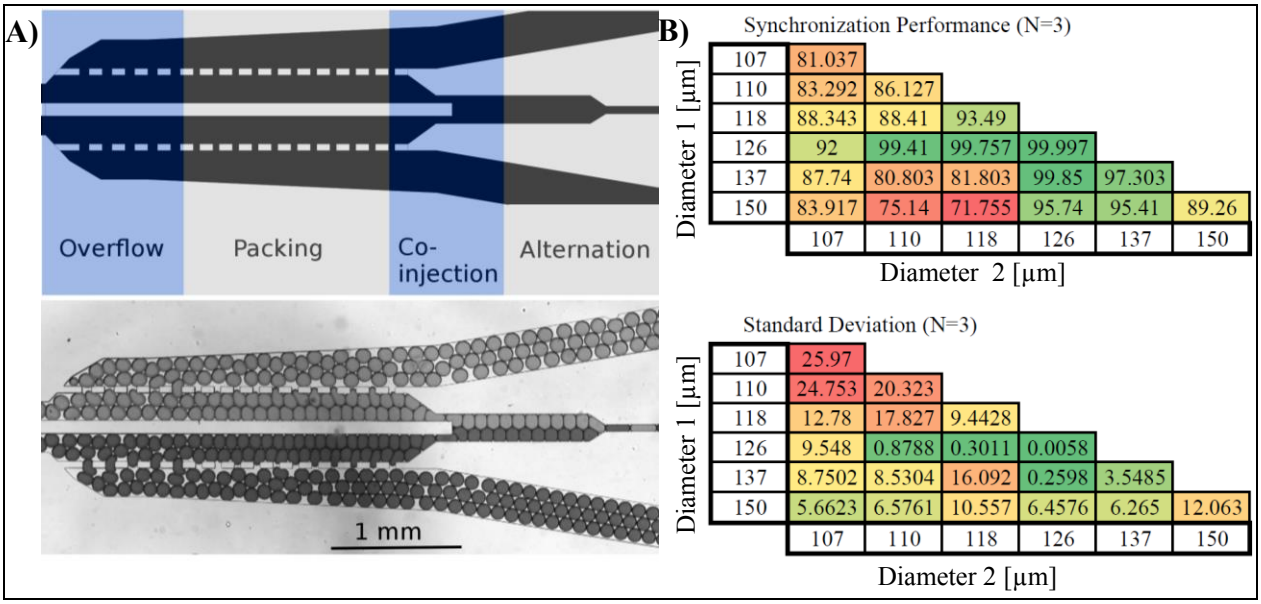
In recent years several studies have investigated the permeability of the interface between the continuous phase and the dispersed phase in microfluidic systems. It has been shown that water mass transfer due to osmosis between droplets is dependent on the concentration gradient, the contact area, contact time as well as the permeability of the interface between two droplets. Osmosis can effectively be used to alter droplet volume (concentration or shrinkage) without coalescence or injection, which was previously used to study crystallization in droplets[4], label-free detection of cell presence[2] and determination of droplet interface characteristics[5]. Further transfer of fluorescent dyes between static droplets has previously been investigated and a variety of molecules were shown to be able to permeate the droplet-droplet interface in static droplet systems.

Passive approaches to droplet synchronization provide the experimenter with additional control over droplet ordering whilst minimizing control architecture requirements. Ideal droplet synchronization architecture should process pre-formed droplets, such that droplet formation can occur independently from downstream operations. Previous studies have shown synchronization of preformed droplets can be achieved, albeit typically exhibiting unacceptably high error rates (approximately 15%)[6]. In the current study we used a structure for the continuous and passive synchronization of pre-formed droplets with very low error rates (Fig. 1). This is achieved by densely packing two (separate) component droplet populations (A and B) and co-injecting them into a single microchannel. This process results in an ordered ABAB droplet sequence. Such a sequence can then be rearranged into a single stream of alternating droplets. High error-tolerance is achieved due to a buffer structure which allows the removal of excess droplets during packing.

EXPERIMENTAL

All experiments were performed in microfluidic devices fabricated from Polydimethylsiloxane (PDMS), cast from wafers fabricated using photolithography. Stable droplets were formed using water as

the dispersed phase and fluorinated oil (FC-40) containing surfactant (4% *w/w*) as the continuous phase. Change of droplet volume and fluorescence of droplets in flow were monitored using high-speed microscopy.



Diameter 1 [µm] \ Diameter 2 [µm]	107	110	118	126	137	150
107	81.037					
110	83.292	86.127				
118	88.343	88.41	93.49			
126	92	99.41	99.757	99.997		
137	87.74	80.803	81.803	99.85	97.303	
150	83.917	75.14	71.755	95.74	95.41	89.26

Diameter 1 [µm] \ Diameter 2 [µm]	107	110	118	126	137	150
107	25.97					
110	24.753	20.323				
118	12.78	17.827	9.4428			
126	9.548	0.8788	0.3011	0.0058		
137	8.7502	8.5304	16.092	0.2598	3.5485	
150	5.6623	6.5761	10.557	6.4576	6.265	12.063

Figure 1: A) Passive droplet synchronization architecture. B) Dependence of droplet synchronization performance on the diameter of droplets used quantified by percentage of correctly synchronized droplets.

RESULTS AND DISCUSSION

Using the presented passive architecture we are able to synchronize thousands of droplets in three repeats with an error rate below 0.01% (Fig. 1B). Long-term stability was shown by synchronizing over 45,000 droplets in a continuous experiment (over 45 minutes) with an error rate below 0.02%. We have further evaluated the synchronization performance of the device with droplets of different sizes and have found that good synchronization (with an efficiency in excess of 90%) can be achieved in a broad size range (Fig. 1B). We note that droplet synchronization rates of up to 33 Hz are possible whilst maintaining a synchronization performance of over 99 %.

We have quantified concentration gradient dependence of osmotic transfer between water droplets in fluorinated oil stabilized by EA-surfactant. The microfluidic architecture allowed for the continuous monitoring of contacting droplets over a period of more than 180 seconds only limited by the available field of view. The presented setup was able to measure osmotic transfer between droplet pairs at 5 Hz which enabled us to deduce reliable variance data. Using this setup we were able to continuously increase the volume of osmotically active droplets by a factor of up to 1.9 within 130 seconds (Fig. 2A). We could not observe a decrease in the volume change rate which indicates the equilibration of the concentration gradient. Compared to previous measurements of osmotic transfer through static DIBS we could observe a decreased rate of volume change[4]. We have further used this system to determine the rate of H_3O^+ transfer between droplets through quantification of fluorescein quenching. Figure 2B) shows the decrease in fluorescence of a droplet containing fluorescein upon prolonged contact with an acidic droplet (pH 0.5).

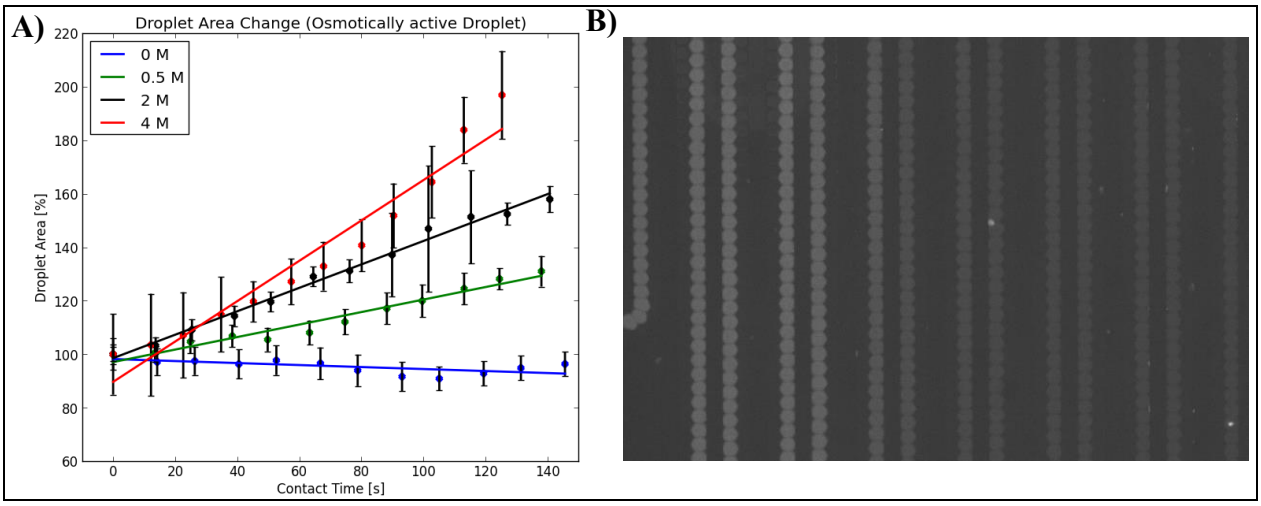


Figure 2: A) Droplet area change dependent on the $CaCl_2$ concentration. Saturation of osmosis could not be observed within the investigated time frame. B) Quenching of fluorescein in microfluidic droplets flowing beside acidic droplets (non-fluorescent) through a serpentine channel.

CONCLUSION

Passive synchronization of pre-formed microfluidic droplets was achieved showing error rates below 0.01%. The presented results highlight the permeability of the droplet barrier to both charged and neutral species. Results further suggest that the presented system could be used to alter the volume of aqueous droplets using osmosis, control the pH of a droplet population and quenching of a pH-sensitive reaction in droplets without the necessity of droplet coalescence.

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