ON-CHIP GENERATION AND EXTRACTION OF HYDROGEL MICROPARTICLES USING RAILING MICROPOSTS

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ABSTRACT

We present a microfluidic system for continuous on-chip generation, extraction, and washing of alginate microparticles (AMPs). Internal gelation, a technique whereby calcium carbonate nanoparticles are dissociated by acetic acid to trigger the release of calcium ions, was used to gelate the AMPs. To perform on-chip extraction, railing microposts spanning across a laminar oil-water (O/W) interface continuously guides and gently transfers the AMPs from the oil phase into the collecting water phase.

KEYWORDS: Droplet microfluidics, hydrogel microparticles, on-chip collection.

INTRODUCTION

Microfluidic generation of hydrogel microparticles by water-in-oil inverse emulsion is gaining popularity owing to the ease of generating large numbers of homogeneous particles for applications such as drug delivery, tissue engineering, and biosensors. However, the extraction of the microparticles from the oil into water needs to be done off-chip using filtration and/or multiple cycles of centrifugation, which is cumbersome and often leads to loss of particles. Whereas on-chip extraction methods have been proposed, they necessitate >13 fluidic connections to accommodate the high W/O flow ratio, making them impractical [1,2]. Recently, microfluidic rails were proposed to direct particles across interfaces [3], and, using multiple laminar streams of oils and aqueous solutions, the extraction of rigid nanoparticles from water-in-oil (W/O) droplets was shown [4]. **Here, we introduce a microfluidic system for the streamlined production, extraction, and washing of soft alginate hydrogel microparticles.**
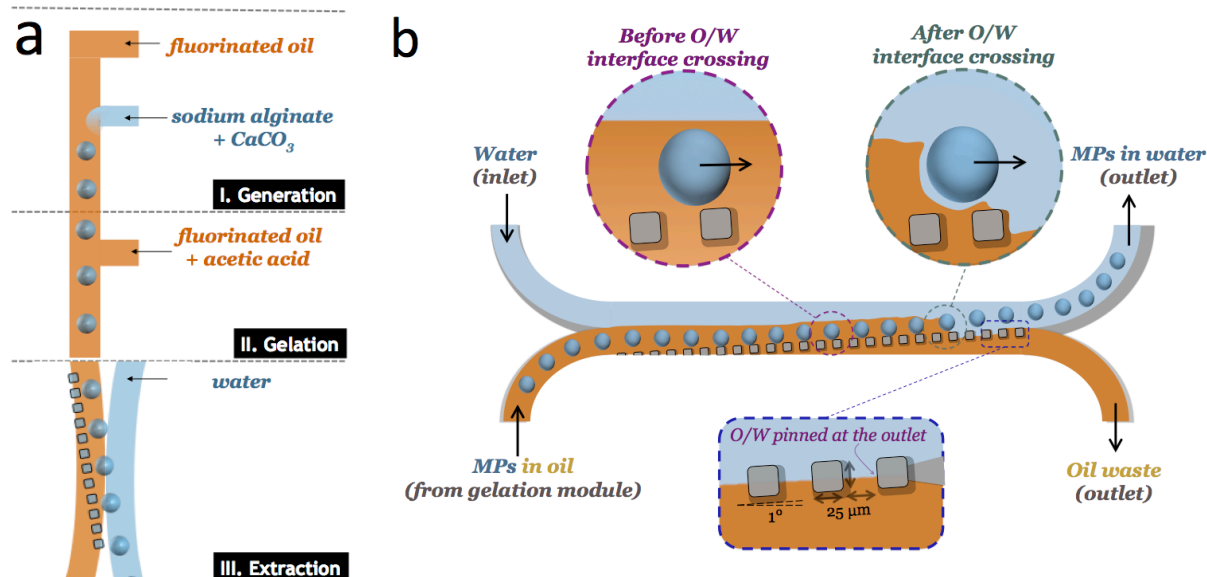

Figure 1: Conceptual illustration of the microfluidic device. *(a) In the generation phase, droplets of alginate in oil containing CaCO₃ nanoparticles were formed using a T-junction. Downstream, alginate gelation is kickstarted after the addition of acetic acid in oil. In the third module, the microparticles are extracted from oil to water. (b) Detailed schematic of the extraction module (III): the microparticles are gently guided by microposts towards the oil-water interface which they eventually cross. Oil is fully removed from the waste outlet.*

METHODS

A microfluidic chip with 100 μm deep channels was fabricated in polydimethylsiloxane (PDMS) through replica molding of SU-8 molds. The chip consisted of three modules: generation, gelation, and extraction (Fig. 1a). A T-junction with oil and water inlet widths of 150 μm was used for W/O droplet generation (Fig. 2a). In the extraction module, the continuous oil phase is merged with an aqueous phase, forming a 2-phase laminar flow. The guiding rail, crossing the O/W interface at a 1° angle, is made of 25 μm square microposts with 100 μm height separated by 25 μm gaps (Fig. 1b & Fig. 2c).

RESULTS AND DISCUSSION

The microfluidic device, shown in fig. 2, was tested by generating, gelating, and extracting alginate microparticles (AMPs). Gelation of the AMPs was performed using internal gelation, whereby calcium is released from $CaCO_3$ nanoparticles through the addition of acetic acid to the continuous phase. W/O droplets were generated using a T-junction junction consisiting of 1% sodium alginate with 50mM $CaCO_3$ nanoparticles as the dispersed phase dispensed at 0.02 μL/s. The continuous oil phase (Q_{O1}=0.2 μL/s) consisted of a fluorinated oil (Novec 7500 EF) with 1% w/v Krytox 157 FSH as surfacant. Gelation of the alginate emulsions was triggered by the downstream addition of 0.1% v/v acetic acid in the same oil (Q_{O2}=0.2 μL/s). Gelation proceeded in the incubation line for 30 s to allow for protons to diffuse from the oil phase into the microparticles and dissolve the $CaCO_3$ nanoparticles. In the extraction module, an aqueous solution was injected at Q_W=0.4 μL/s flowing parallel to the oil. To pin the water-oil interface to the outlet fork, a water-to-oil flow ratio of $Q_W/Q_O = 1$ was found to be sufficient (Fig. 3A). This is attributed to the low viscosity of
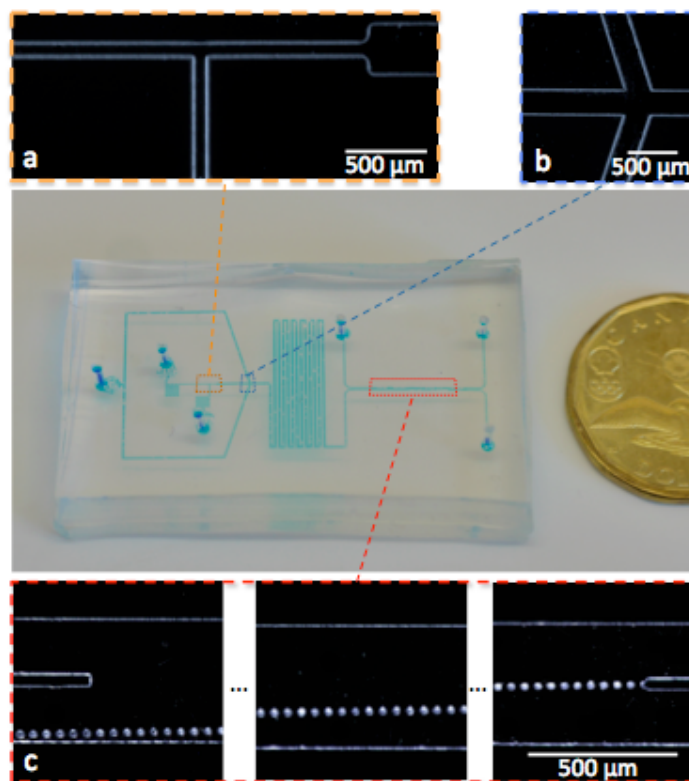

Figure 2: Images of the fabricated SU-8 mold and PDMS device . (a) Dark-field image of the T-junction for droplet generation, (b) gelation junction where 1% acetic acid in fluorinated oil is added, and (c) three images along the length of the extraction module (total length=1.3 cm) showing the 20μm microposts arrayed at 1°. the microposts end at the outlet fork separating the collection channel (top) from the oil waste (bottom).

Novec 7500 (~0.44 cst). By comparison, the use of more viscous hydrocarbon oils such as mineral oil (~15 cst) required a flow ratio of Q_W/Q_O =15 at least. As such, the AMPs were gently guided by the rail, without getting trapped between the posts. The addition of a surfactant (0.1% Triton-X100) to the aqueous phase facilitated the wetting of the aqueous solution and transfer of the AMPs out of the oil. Using this setup and aforementioned flow rates, AMPs were extracted at an average rate of ~12 Hz into the water phase (Fig. 3C). The average diameter of collected microparticles was 180 μm (Fig. 3B), indicating that the extraction did not compromise their integrity.

A

Δt=0 ms

Δt=25 ms
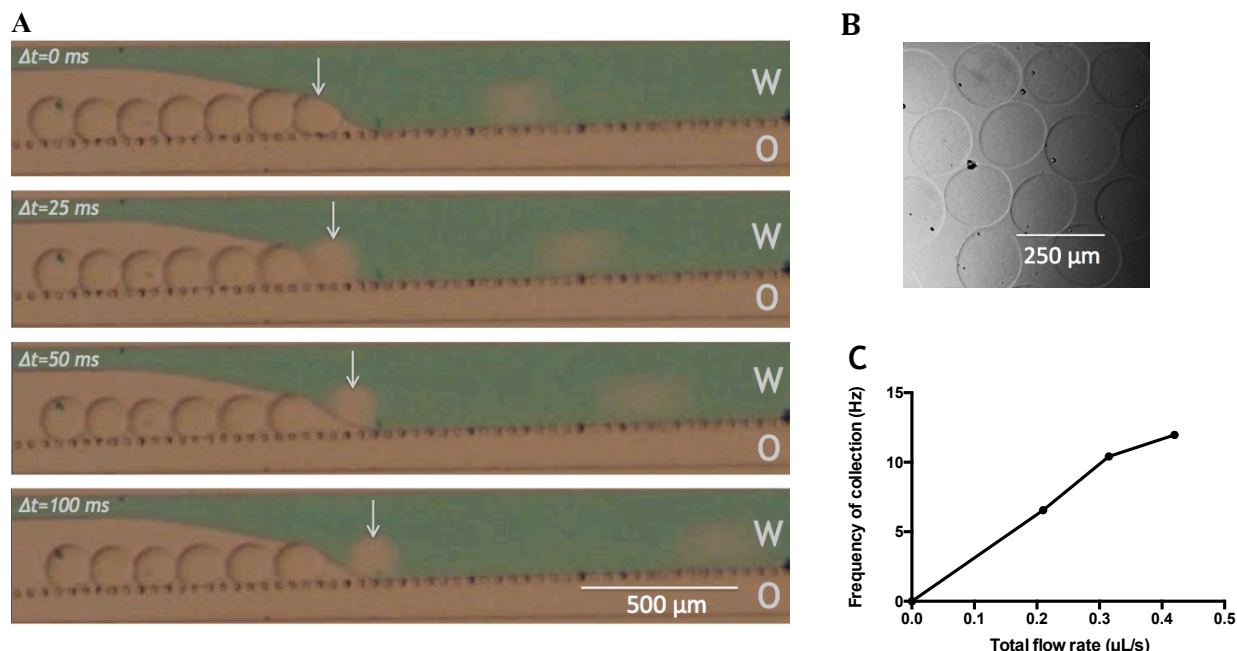
Δt=50 ms

Δt=100 ms

B

250 μm

C

500 μm

Figure 3A: Time-series image demonstrating AMPs crossing the oil/water interface. Stills from a video taken of the collection zone (module III shown in fig.1 inset). The AMPs are arriving from left in oil (bottom fluid), guided by the microposts. The arrows point to the microparticles which is crossing the interface. Figure 3B: Representative image of microparticles viewed directly after extraction without further manipulation. Figure 3C: Extraction frequency of AMPs with respect to total flow rate of combined fluids (oil and alginate).

CONCLUSION

We demonstrated a practical design to generate and extract AMPs using minimal fluidic connections at a rate of 12 Hz**.** Further, the flow rate ratio of W/O in the extraction outlet was decreased 15-folds from previous designs [1,2] through the use of a fluorinated oil with lower viscosity. This system may be further optimized to produce AMPs of different sizes and to increase the throughput, either by increasing the flow rates, or by multiplexing, or a combination of both.

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