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Short Communication

Faster droplet production by delayed surfactant-addition in two-phase microfluidics to form thermo-sensitive microgels

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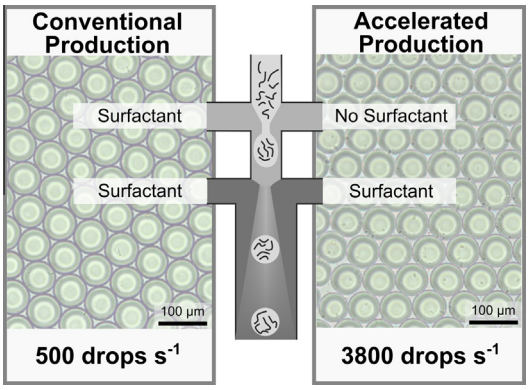
GRAPHICAL ABSTRACT



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ABSTRACT

Microfluidic droplet templating produces monodisperse particles of well controllable sizes, but this is limited by the necessity to operate microfluidic devices at low flow rates in the dripping regime. Here, the per-channel rate of droplet production could be substantially increased by delayed surfactant addition as applied and verified for microfluidic production of *N*-isopropylacrylamide based microgels.

1. Introduction

Microgels are micrometer-scale particles that consist of a cross-linked polymer network swollen by solvent, typically water [1,2]. Microgels can be designed to be sensitive to changes in their environment, for example, to changes in temperature, allowing them to be selectively swollen and deswollen in response to external stimulation [3,4]. Such responsivity relies on delicate hydrogen-bonding and hydrophobic interactions between the polymer and the solvent, which is achieved by the use of polymers that consist of amphiphilic monomer repeat units, the most prominent of which being poly(*N*-isopropylacrylamide) [4]. The original use of the term microgel referred to particles with sub-micrometer-scale colloidal dimensions, down to single, intramolecular crosslinked

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polymer coils [1], whereas recent contributions have extended its use to larger, above-micrometer-scale particles [5]. The prime utility of such above-colloidal microgels is their ability to encapsulate additives with above-molecular and above-colloidal sizes within a local environment similar to natural tissue [3,6]. As a result, these microgels are promising for applications in the biomedical field [7], especially when they exhibit environmental sensitivity to physiologically relevant changes of temperature or pH.

To optimize the utility of such above-colloidal-scale microgels, it is necessary to control their size and shape in addition to controlling their chemical function. This challenge can be addressed by droplet-based microfluidic templating [8,9]. In this approach, a stream of an aqueous pre-microgel solution (dispersed phase) is created in a microchannel and then periodically broken to form droplets by flow focusing with an immiscible oil (continuous phase). The size of the resulting pre-microgel droplets is controlled by the fluid flow rates, the dimension of the microchannel, and the fluid interfacial tension [10].

Despite its great promise, an intrinsic limitation in the use of droplet-based microfluidics for templating monodisperse microgels is the necessity to operate at low flow rates to avoid the transition from dripping to jetting regime [10]. When both the inner dispersed and the outer continuous phase are injected into a microfluidic device at low rates, individual monodisperse drops of the inner fluid within the outer fluid are formed periodically in a process termed dripping. By contrast, if the flow rate of either of these fluids is increased beyond a certain limit, this results in a jet of the inner fluid with drops forming far further downstream with, typically, a broader size distribution. The onset of the dripping-to-jetting transition is assessed by the capillary number $Ca = \eta \cdot \dot{V} \cdot \sigma^{-1}$ (Eq. (1)) of the outer fluid and the Weber number $We = \rho \cdot \dot{V}^2 \cdot d \cdot \sigma^{-1}$ (Eq. (2)) of the inner fluid.

In these equations, η is the viscosity, $\dot{V}$ the flow speed, and ρ the density of the respective fluid, along with d the channel diameter and σ the interfacial tension between the two immiscible phases. The Ca of the outer fluid reflects the balance between the drag of the outer fluid pulling on the inner fluid and interfacial tension that resists the flow in the jet as droplet pinch-off occurs. The We of the inner fluid reflects the balance between inertial forces of the inner liquid pushing the drop downstream and, again, interfacial tension resisting the flow. The boundary between dripping and jetting has previously been detected when either number, or their sum, is roughly in the range of unity, considering possible deviations up to one order of magnitude [10].

Thus, controlled microfluidic fabrication of particles must occur at low flow rates to keep both of the above numbers small. To overcome the resulting limitation of productivity that impairs the utility of microfluidic templates in industrial-scale processes, a parallelization of microfluidic channels being operated simultaneously or a droplet splitting has been suggested [11–13]. In addition to this approach, however, it would be desirable to increase the productivity of each individual microfluidic channel, too. This task must tackle the challenge of operating in the controlled dripping regime at higher flow rates. Here, we present a way to increase the per-channel rate in the production of water-based microgels in droplet-based microfluids by delayed surfactant addition.

2. Experimental

The used chemicals were fluorocarbon oil HFE-7500 (3 M), fluorinated surfactant Krytox 157 FSL (DuPont), *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED), *N*-isopropylacrylamide (NIPAAm), *N*,*N*′-methylene bisacrylamide (BIS) and ammonium persulfate (APS) (all latter by Sigma–Aldrich).

Microfluidic devices with a double cross-junction geometry (see Figs. 1 and 2) were fabricated through soft lithography in PDMS by bonding a PDMS replica of a pre-designed array of channels onto a glass slide using oxygen plasma treatment [14]. After the plasma treatment, the channels were coated by injecting a water repellent mixture of fluorinated compounds (Aquapel; PPG Industries, Pittsburgh, PA, USA) into the channels to render them hydrophobic and optimize their wettability for the formation of water-in-oil emulsions [15]. To operate the devices, three fluids were supplied by three syringe pumps (AL 1010, WPI, Sarasota, FL, USA) at given equal volume flow rates (q, see Fig. 2A–D) through polyethylene tubing (ID = 0.38 mm, OD = 1.09 mm, Becton Dickinson, Sparks, MD, USA).

Droplet formation was monitored by a digital high-speed microscope (VW 6000E with VH-Z100R lens and VW 100C camera, Keyence Deutschland GmbH, Neu-Isenburg, Germany). Images of the finally collected droplets were obtained on an optical microscope (DMI6000B, Leica, Wetzlar, Germany) and sizes were analyzed (more than 300 drops, each) after contrast adjustment and applying a watershed filter using ImageJ software (National Institutes of Health, USA). The droplet-number formation frequencies, $f = q \cdot V_{\mathrm{drop}}^{-1}$, were calculated from the volumetric throughput of the dispersed phase in the microfluidic experiments, q, and the droplet volumes (V_{drop}), which were calculated from the droplet average diameters. A tensiometer (K 100, Kruess GmbH, Hamburg, Germany) was operated at 25 °C with a density measurement setup (DE0701, silicon standard probe with 2.33 g cm^{-3}, Kruess GmbH, Germany) to determine the densities (ρ) of the different fluids used in this work; it was also operated with a Wilhelmy-plate (PL01, platinum, $19.9 \times 0.2 \times 10.0$ mm^3, Kruess GmbH, Germany) to estimate the interfacial tensions (σ) of the different pairs of fluids, respectively. Kinematic viscosities (ν) were determined at 25 °C using an Ubbelohde viscometer with Hagenbach correction (PVS1, S5 test stand, E200 thermostat, Koenigshofen, Germany). Dynamic viscosities (η) were calculated by $\eta = \nu \cdot \rho$.

3. Results and discussion

The conventional approach for microfluidic droplet formation in two-phase systems involves controlled dispersion of an inner fluid in a stabilizer-doped continuous phase with a microfluidic device operating in the controlled dripping regime, as shown in Fig. 1A. This may potentially be followed by addition of a further fraction of continuous phase that contains additives such as accelerators to induce downstream droplet-gelation [15], as shown in Fig. 1B. The limitation of this method is that increased Capillary (Ca) and Weber (We) numbers by increased volumetric flows will result in uncontrolled jetting, as shown in the inset of Fig. 1B. The approach presented in this paper aims to overcome this limitation and to increase the rate of droplet formation by decreasing Ca and We of the outer and inner fluids, which is achieved by increasing their interfacial tension (σ). With this strategy, microfluidic devices with a given channel size (d) can be operated at higher flow rates (q) before the undesired dripping-to-jetting transition occurs. To achieve this, an external phase without any surfactant is used, as illustrated in Fig. 1C. This mode of operation assures maximally possible interfacial tension with the inner pre-microgel phase. To prevent the pre-microgel droplets from coalescing, surfactant is added directly after their formation in the microfluidic channel, as also illustrated in Fig. 1C. With this approach, the droplet formation can be separated from the droplet stabilization, allowing the first to occur at maximal rate while still ensuring the second.

As a model material, poly(*N*-isopropylacrylamide) (pNIPAAm) is chosen because of its relevance for producing gels and microgels