TECHNICAL NOTE

Double emulsions with controlled morphology by microgel scaffolding

Julian Thiele*[a] and Sebastian Seiffert[bc]

Double emulsions are valuable structures that consist of drops nested inside bigger drops; they can be formed with exquisite control through the use of droplet-based microfluidics, allowing their size, composition, and monodispersity to be tailored. However, only little control can be exerted on the morphology of double emulsions in their equilibrium state, because they are deformable and subject to thermal fluctuations. To introduce such control, we use droplet-based microfluidics to form oil-in-water-in-oil double emulsion drops and arrest their shape by loading them with monodisperse microgel particles. These particles push the inner oil drop to the edge of the aqueous shell drop such that the double emulsions adopt a uniform arrested, anisotropic shape. This approach circumvents the need for ultrafast polymerization or geometric confinement to lock such non-spherical and anisotropic droplet morphologies. To demonstrate the utility of this technique, we apply it to synthesize anisotropic and non-spherical polyacrylate–polyacrylamide microparticles with controlled size and shape.

Double emulsions are drops of one fluid nested inside drops of another fluid;[1] they are useful to compartmentalize active ingredients such as nutrients, cosmetics, and drugs[2–4] or to template complex microparticles with structured interiors.[5] To produce these valuable emulsions, bulk methods such as membrane emulsifiers or shear cells are typically used.[6] These methods form a large number of double emulsion drops, albeit with poor control over the individual drop formation.[7] This limitation is overcome through the use of droplet-based microfluidics: with this technique, double emulsions are produced in a drop-by-drop fashion with a high degree of control.[1]

Microfluidic devices can be fabricated from materials such as polydimethylsiloxane (PDMS) with micron-scale precision using the methods of soft lithography.[8] This allows the drop formation to be optimized and double emulsions with tailored size, composition, and monodispersity to be created.[9,10] However, droplet-based microfluidics offers only limited control over the morphology of double emulsion droplets. Since these droplets consist of liquid phases, their shape is deformable, and a uniform, arrested morphology cannot be achieved as long as this deformability persists. This circumstance is detrimental if double emulsion droplets shall be used as templates for the synthesis of microparticles with anisotropic[11] or core–shell-type

structure,[12] as it limits controlling the morphology of these particles.

Many previous attempts to template anisotropic microparticles from emulsion droplets, both single and double emulsions, are based on rapidly locking a distorted, non-equilibrium droplet morphology rather than altering the equilibrium shape of the droplets. For example, polymer particles with Janus-type structure[13] have been formed from single emulsion and higher-order emulsion droplets by the groups around Doyle,[14] Weitz,[11,15,16] Nisisako,[17] and Kumacheva.[18] Yet, all these approaches require rapidly locking an anisotropic, non-equilibrium shape of the Janus-type precursor droplets before they randomize their morphology after exiting the microfluidic device. In another approach, Kumacheva and colleagues employed geometric confinement of single emulsion droplets in microchannels to force their shape into a non-spherical form, which then serves to template non-spherical particles.[19] This concept can basically be extended to double emulsions, but again, it requires ultrafast polymerization to lock the geometrically confined structure of the droplets to intercept a non-equilibrium structure before the droplets can relax into their equilibrium shape outside the controlled environment of the microfluidic device. This drawback greatly limits the versatility of all these approaches. A superior method would be one where morphology control is exerted on an equilibrium droplet structure, allowing slow and gentle or even stepwise polymerization to be applied to form solid microparticles from the droplets.

In this note, we present the formation of double emulsions with controlled equilibrium morphology. We use PDMS-based microchannels to form oil-in-water-in-oil (O/W/O) double emulsion drops. To arrest their shape, we load them with monodisperse polyacrylamide (pAAm) microgel particles. These

[a]*Physical Chemistry I, Bayreuth University, Universitätsstraße 30, D-95447 Bayreuth, Germany. E-mail: julian.thiele@uni-bayreuth.de; Fax: +49 921552780; Tel: +49 921554376*
[b]*F-I2 Soft Matter and Functional Materials, Helmholtz Zentrum Berlin, Hahn-Meitner-Platz 1, D-14109 Berlin, Germany. E-mail: sebastian. seiffert@helmholtz-berlin.de; Tel: +49 30806242294*
[c]*Institute of Chemistry and Biochemistry, FU Berlin, Takustr. 3, D-14195 Berlin, Germany. E-mail: seiffert@chemie.fu-berlin.de; Tel: +49 3083856082*

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microgel particles push the inner oil drop to the edge of the aqueous shell drop such that the double emulsions adopt an arrested, anisotropic shape. The position of the inner drop is controlled by the size and packing of the microgel particles. To demonstrate the utility of this approach, we use it to synthesize anisotropic and non-spherical polyacrylate–polyacrylamide microparticles with controlled size and shape.

Methods and experiments

PAAm microgel preparation

Monodisperse polyacrylamide particles are prepared from a water-in-oil emulsion made in a PDMS-based microfluidic device with rectangular 25 × 25 μm channels. The dispersed aqueous phase is a solution of 60 g L^{-1} acrylamide (Aldrich) and 1.8 g L^{-1} N,N-methylenebisacrylamide (Fluka) along with 8.8 mmol L^{-1} ammonium persulfate (Sigma). This monomer solution is dispersed to form monodisperse droplets by flow-focusing with fluorocarbon oil (HFE 7500, 3M) which contains N,N,N′,N′-tetramethylethylenediamine (Sigma) (0.4% v/v) and surfactant (Krytox® 157 FSL, ammonium salt, DuPont) (1.8% w/w). The volume flow rates are 700 μL h^{-1} for the aqueous and 1200 μL h^{-1} for the oil phase. Thermal gelation of the aqueous droplets is achieved by storing the emulsion at 65 °C for 1 h. The resultant pAAm particles are consecutively washed with fluoro-carbon oil containing perfluorooctanol (Aldrich) (20% v/v), hexane that contains Span 80 (Aldrich) (0.5% w/w), plain hexane, water that contains Triton X (Aldrich) (0.1% w/w), and plain water. The particles are then densified in a centrifuge (Eppendorf MiniSpin Plus, 3000 rpm, 30 s) and supernatant water is removed.

Microfluidic device fabrication

Microfluidic devices with geometries as shown in Fig. 1 are fabricated by soft lithography in PDMS.[8] The channel width at the first, the second, and the third cross-junction is 50 μm, 100 μm, and 100 μm. All channels have a fixed height of 50 μm. A PDMS replica of this array of channels is bonded to a glass slide using oxygen plasma treatment. Within 5 minutes after plasma treatment, the device is coated with a fluorinated sol–gel layer that contains a methacrylate silane, providing a durable hydrophobic surface while allowing the microchannel wettability to be modified in defined regions of the device by grafting patches of hydrophilic poly(acrylic acid).[20] To form O/W/O double emulsions, the first and the second cross-junction are patterned to be hydrophilic, whereas the third cross-junction is left hydrophobic.

Formation of microgel-scaffolded double emulsions

We form oil-in-water single emulsions at the first drop-forming cross-junction by injecting fluorocarbon oil at 200–250 μL h^{-1} and water with sodium dodecyl sulfate (SDS) (0.5% w/w) at 400 μL h^{-1}. Dense-packed, monodisperse pAAm particles with diameters of 40 μm are added to the aqueous phase at the second cross-junction at 120 μL h^{-1}. At this flow rate, exactly one particle is encapsulated into each double emulsion droplet. As the particles are deformable, and as the microfluidic device exhibits no constriction that is significantly smaller than the particles, the microgels do not clog the channels. At the third cross-junction, fluorocarbon oil with the ammonium salt of Krytox® 157 FSL (1.8% w/w) is added at 2000 μL h^{-1} to produce microgel-scaffolded O/W/O double emulsions.

Polyacrylate–polyacrylamide microparticle fabrication

To produce polyacrylate–polyacrylamide microparticles, an inner phase that consists of toluene (75% w/w), 1,6-hexanediol-diacrylate (15% w/w) (Sigma-Aldrich), and trimethylolpropane ethoxylate (14/3 EO/OH) triacrylate (7.5% w/w) (Sigma-Aldrich), along with photoinitiator Darocur 1173 (2.5% w/w) (CIBA) is injected into the microfluidic device shown in Fig. 1 at a volume flow rate of 300 μL h^{-1}. This phase is then emulsified by a middle phase that is an aqueous solution of 60 g L^{-1} acrylamide (Aldrich) and 1.8 g L^{-1} N,N-methylenebisacrylamide (Fluka) as well as 8.8 mmol L^{-1} ammonium persulfate (Sigma), injected at 800 μL h^{-1}. Scaffolding of the inner toluene-based monomer droplet is achieved through the injection of 40 μm pAAm microgel particles at the second cross-junction of the microfluidic device, and double emulsion droplets are formed in the third cross-junction by flow focusing with an outer phase of
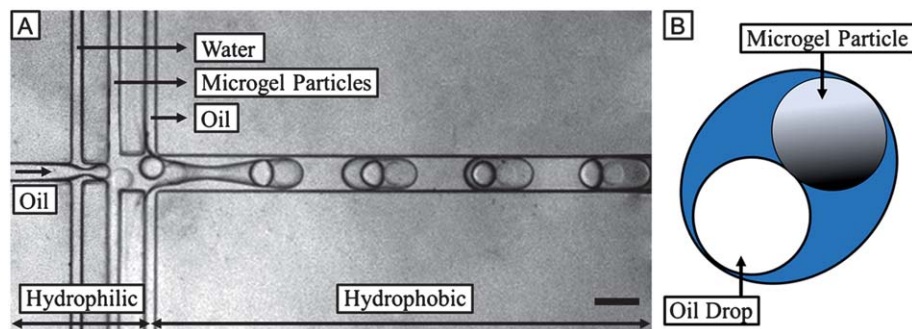

Fig. 1 Microfluidic fabrication of microgel-scaffolded double emulsions. (A) Photomicrograph of a polydimethylsiloxane (PDMS) microfluidic device forming oil-in-water-in-oil (O/W/O) double emulsions with controlled morphology. The device is equipped with an additional set of inlet channels to inject 40 μm polyacrylamide (pAAm) microgel particles. A single particle is injected into the shell of each double emulsion droplet. The left part of the device is hydrophilic to form oil-in-water single emulsions. By contrast, the right part of the device is hydrophobic to encapsulate these single emulsions in an outer oil phase. This yields the desired microgel-scaffolded oil-in-water-in-oil double emulsions. (B) Schematic of an O/W/O double emulsion droplet containing a single pAAm particle. The scale bar denotes 100 μm.
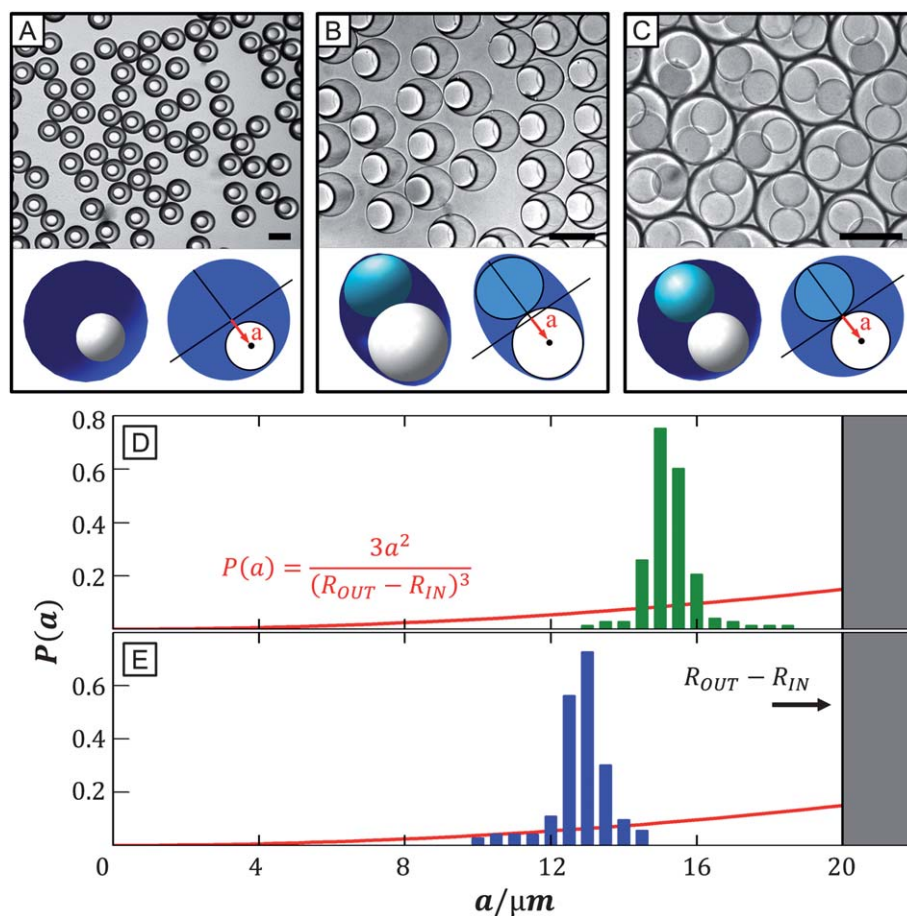
Fig. 2 Conventional and particle-loaded double emulsions. (A) Optical micrograph of a conventional O/W/O double emulsion with random inner drop position. (B and C) Monodisperse populations of O/W/O double emulsions with controlled morphology through particle encapsulation: (B) non-spherical and (C) spherical. We define a as the distance between the center of a double emulsion droplet and the center of its innermost drop to determine the control over this morphology. (D and E) Probability distributions for the position of the inner drop of the particle-scaffolded double emulsions shown in panel B (D) and panel C (E). For comparison, the random probability distribution for a spherical drop with radius R_{IN} sitting in a spherical double emulsion shell with radius R_{OUT} is plotted as red curve. For $a = 0$, the inner drop is centered, for $a = 20$ μm $= a_{MAX}$, the inner drop is at the periphery of the double emulsion shell. Scale bars are 50 μm.

fluorocarbon oil (HFE 7500, 3M) loaded with the ammonium salt of Krytox® 157 FSL (1.8% w/w), injected at a volume flow rate of 1800 μL h⁻¹. Droplet solidification is achieved in two subsequent, separate steps by exposing the collected double emulsion to UV light to polymerize the acrylate monomers in the inner oil phase, followed by heat-induced polymerization of the acrylamide monomers in the aqueous shell phase. Post-processing of the product particles is performed by the same procedure used to post-process the scaffolding pAAm microgels. To image the product particles, scanning electron micrographs are recorded on a LEO 1550 Ultra Field Emission SEM (Zeiss SMT AG).

Results and discussion

We conduct our experiments in microfluidic devices equipped with an array of three cross-junctions. We control the wettability of the channel walls to render the first and second junctions hydrophilic and the third junction hydrophobic.[20] This pattern allows O/W/O double emulsions to be formed,[21,22] while the device geometry is engineered such that micrometre-sized

hydrogel particles can be encapsulated into the aqueous middle phase of the double emulsion droplets. In detail, oil drops are dispersed in water at the first junction and then enter the second junction, where monodisperse, micrometre-sized pAAm particles are added. At the third junction, additional oil is injected to encapsulate the oil-in-water drops and the pAAm particles. This yields the desired particle-scaffolded O/W/O double emulsions, as shown in Fig. 1A and B.

If the microgel particles are perfectly monodisperse and close-packed with a volume fraction close to 74%, they enter the microfluidic device with high periodicity. This allows us to synchronize their injection with the double emulsion formation; the number of encapsulated particles is therefore controlled by adjusting the particle flow rate to an integer multiple of the drop formation rate. Thus, exactly one, two, three, or more particles can be encapsulated into each double emulsion droplet, with an efficiency that exceeds that obtained by Poisson-type encapsulation statistics.[23] Encapsulation of more than three particles has only limited control on the position of the inner oil drop since it gives too much freedom for particle and droplet arrangement.

Hence, we focus on the encapsulation of one, and only one, pAAm particle per double emulsion droplet and compare the position of the innermost oil droplet in these particle-loaded double emulsions with that in conventional double emulsions, as illustrated in Fig. 2.

The conventional O/W/O double emulsion drops shown in Fig. 2A are deformable, and hence, subject to thermal fluctuations. This leads to a non-uniform distribution of the inner drop in each double emulsion shell: while the inner drop is centered in some shells (Fig. 2A, left), others are off-centered (Fig. 2A, right) at the moment of observation. By contrast, the particle-loaded double emulsions shown in Fig. 2B exhibit a uniform and arrested morphology which is maintained even if the double emulsion is subjected to external stress. Due to the encapsulation of a microgel particle into these double emulsion shells, the position of their inner drop is determined relative to the center. If the volume of the aqueous shell droplet is insufficient to host both the microgel particle and the inner oil droplet in a spherical shell with a diameter $d_{shell} = d_{inner\ drop} + d_{microgel\ particle}$, the double emulsion droplets are distorted and adopt a non-spherical shape, as seen in Fig. 2B. This is because the liquid shell droplet can be deformed more easily than the encapsulated microgel particle, which exhibits an elastic modulus in the kilopascal range. To form particle-loaded double emulsions with a spherical shape, we account for this circumstance and match the volumes of the outer drop, the inner drop, and the microgel particle by adjusting the respective flow rates, as shown in Fig. 2C.

To quantify the degree of control over the morphology of the particle-loaded double emulsions, we define a as the distance between the center of a double emulsion droplet and the center of its inner drop, as sketched in Fig. 2A–C. The normalized probability distributions, $P(a)$, of non-spherical and spherical particle-loaded double emulsions are plotted in Fig. 2D and E. Both distributions are narrow, substantiating the confinement of the inner drop by the encapsulated pAAm particle in the shell. To describe the morphology of a conventional, density-matched O/W/O double emulsion, we assume a random distribution of a spherical oil drop with radius R_{IN} inside a spherical aqueous drop with radius R_{OUT}, plotted as red curves in Fig. 2D and E. As opposed to the distributions of particle-loaded double emulsions, the distribution of the inner drop position in these conventional double emulsions is broad. The maximum of $P(a)$ of these random distributions is located at the cut-off a_{MAX}; this corresponds to double emulsion droplets with completely off-centered inner droplets, which are similar to that obtained by the particle scaffolding. However, these random distributions have significant values of $P(a)$ at any other a too, reflecting the poor control of the droplet morphology in the absence of particle scaffolding.

To demonstrate the utility of the shape-arrested double emulsions, we apply them to template anisotropic and non-spherical microparticles. Such particles are useful for applications as optical crystals or emulsion stabilizers, requiring them to be monodisperse in both their size and shape. We adopt our technique to form distorted double emulsion droplets such as those shown in Fig. 2B by encapsulating micrometre-sized pAAm microgel particles as well as fluid drops into the shells of double emulsions, causing them to adopt a unique, non-
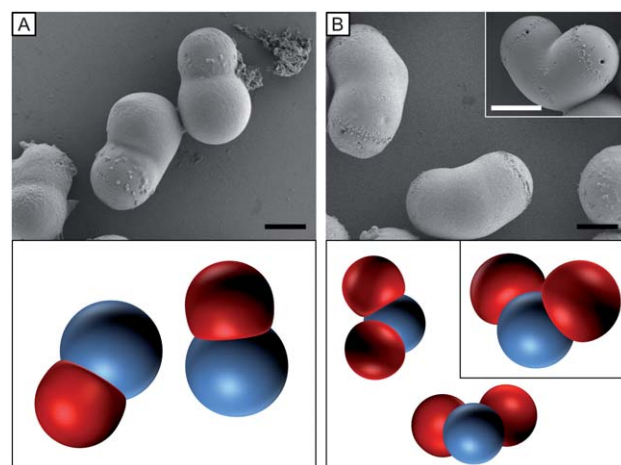

Fig. 3 Scanning electron micrographs and schematics of anisotropic, non-spherical polyacrylate–polyacrylamide microparticles with one internally hydrophilic (blue) and (A) one or (B) two internally hydrophobic (red) lobes, covered by a purely hydrophilic shell (not indicated in the schematics). The shape of these particles differs from that of the double emulsion templates shown in Fig. 2B, because the SEM micrographs of the particles are recorded in a dry state, whereas the double emulsion templates shown in Fig. 2B contain solvent; since the solvent content of the polyacrylamide phase is 94% (w/w) compared to only 75% (w/w) for the polyacrylate phase, we observe non-affine deswelling of the two polymerized species that causes a significant deformation of the particles during the drying process. The scale bars denote 10 μm.

spherical equilibrium shape. The fluids used are two polymerizable monomer solutions: we use an aqueous solution of acrylamide and bisacrylamide along with a thermal initiator, ammonium persulfate, as aqueous shell phase along with a solution of two hydrophobic acrylates and photoinitiator Darocur 1173 in toluene as inner oil phase. Emulsifying these compounds in a microfluidic device yields double emulsion precursors that maintain their non-spherical shape if pAAm microgel scaffolding is applied. It is then possible to solidify these shape-arrested droplets in two subsequent, separate steps; we achieve this by exposing the collected double emulsion to UV light, triggering a free-radical polymerization of the acrylate monomers in the inner oil phase, followed by heat-induced polymerization of the acrylamide monomers in the aqueous shell phase. With this stepwise procedure, we decouple the solidification of the two lobes of the particles and circumvent the need for harsh, ultrafast polymerization. As a result, we obtain anisotropic and non-spherical polyacrylate–polyacrylamide particles, as shown in Fig. 3. These particles consist of two lobes, one hydrophilic and the other hydrophobic in its bulk, whereas the exterior of the particles is fully hydrophilic. As a result, solvents with different polarities are absorbed differently by the lobes of these particles, causing them to alter their shape depending on the solvent composition;[11] this behavior renders these particles interesting for applications as particulate surfactants, self-assembling at a solvent–solvent interface depending on the polarity difference.[24–26] By varying the number of oil droplets in the double emulsion precursors, we are able to template particles with one (Fig. 3A) or two (Fig. 3B) lobes of inner hydrophobicity.

Conclusions

The encapsulation of elastic polymer particles is an excellent tool to form double emulsions with controlled anisotropic morphology. This method extends the performance of droplet microfluidics by adding the ability to control the droplet morphology, particle chemistry, and scaffolding structure in a single step. Particle-loaded double emulsions are useful for the encapsulation and delivery of multi-component systems as well as for synthesizing particles with anisotropic properties, greatly extending the utility of these fascinating structures.

Acknowledgements

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