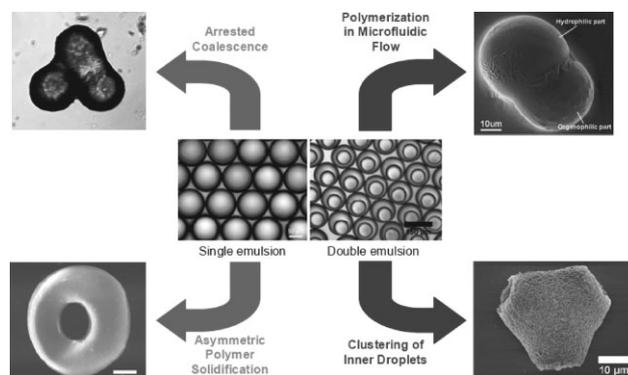


# Droplet Microfluidics for Fabrication of Non-Spherical Particles

Ho Cheung Shum, Adam R. Abate, Daeyeon Lee, André R. Studart, Baoguo Wang, Chia-Hung Chen, Julian Thiele, Rhutesh K. Shah, Amber Krummel, David A. Weitz\*

We describe new developments for controlled fabrication of monodisperse non-spherical particles using droplet microfluidics. The high degree of control afforded by microfluidic technologies enables generation of single and multiple emulsion droplets. We show that these droplets can be transformed to non-spherical particles through further simple, spontaneous processing steps, including arrested coalescence, asymmetric polymer solidification, polymerization in microfluidic flow, and evaporation-driven clustering. These versatile and scalable microfluidic approaches can be used for producing large quantities of non-spherical particles that are monodisperse in both size and shape; these have great potential for commercial applications.



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## Introduction

Virtually all colloidal-scale particles are naturally spherical, as the forces of surface tension typically dominate all others during synthesis, resulting in spherical particles. However, non-spherical particles can also be of great potential for a broad range of applications including cosmetics,<sup>[1]</sup> biotechnology,<sup>[2]</sup> structural materials,<sup>[3]</sup> and pharmaceuticals,<sup>[4]</sup> as the non-spherical shape can offer unique properties by comparison to spherical particles. For example, non-spherical particles can pack more densely than spherical ones.<sup>[5]</sup> Anisotropically shaped particles can also behave differently from spherical ones under the same hydrodynamic,<sup>[6]</sup> electric,<sup>[7]</sup> and magnetic conditions.<sup>[8]</sup> Lightweight composite materials with unique mechanical properties have been produced by taking advantage of the reinforcing ability of non-spherical particles such as fibers and platelets.<sup>[3,9]</sup> Moreover, non-spherical particles of custom-engineered geometry can also simulate the shape of molecules for the studies of self-assembly, as most



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molecules are non-spherical.<sup>[10]</sup> These exciting properties can lead to new applications and create new opportunities for areas that have traditionally used spherical particles.

Most current uses of colloidal particles focus on spherical ones because of the relative ease and robustness of the steps involved in their synthesis. Interfacial tension between two immiscible phases naturally favors minimization of surface area, which facilitates production of spherical shapes. Since the properties of non-spherical particles are strongly dependent on their shape, methods to control not only size, but also shape, are crucial to create particles with reproducible and uniform behavior. Strategies to fabricate such particles include template molding,<sup>[11,12]</sup> seeded emulsion polymerization,<sup>[13]</sup> self-assembly of spherical particles through liquid protrusions,<sup>[14]</sup> and “stretching” of spherical particles.<sup>[15]</sup> However, it remains difficult to produce large quantities of monodisperse non-spherical particles of tunable geometry and adjustable properties.

Recent advances in microfluidic technologies for manipulating fluids in controlled environments have led to new approaches for the fabrication of non-spherical particles. One approach to fabricate particles in a microfluidic device is by forming droplets which are used as precursors for the final particles. By confining the droplets in microfluidic channels of different sizes and shapes<sup>[16,17]</sup> or by manipulating the droplets by electric fields,<sup>[18]</sup> non-spherical particles can be generated. Another approach to form non-spherical particles using microfluidics is through the combination of lithography and photo-chemistry. Typically, a photo-mask with patterns of the desired particle shape is used as a template for the final polymer particles, which are formed by UV-initiated photopolymerization of the monomer that flows periodically<sup>[19]</sup> or continuously<sup>[20]</sup> in the microfluidic devices. Using this approach, 2D<sup>[19,20]</sup> and 3D<sup>[21]</sup> polymer particles of desired shapes can be fabricated. For particles to be generated continuously at a high production rate, the photopolymerization reaction has to be fast, restricting the use of the approach to a limited choice of materials.

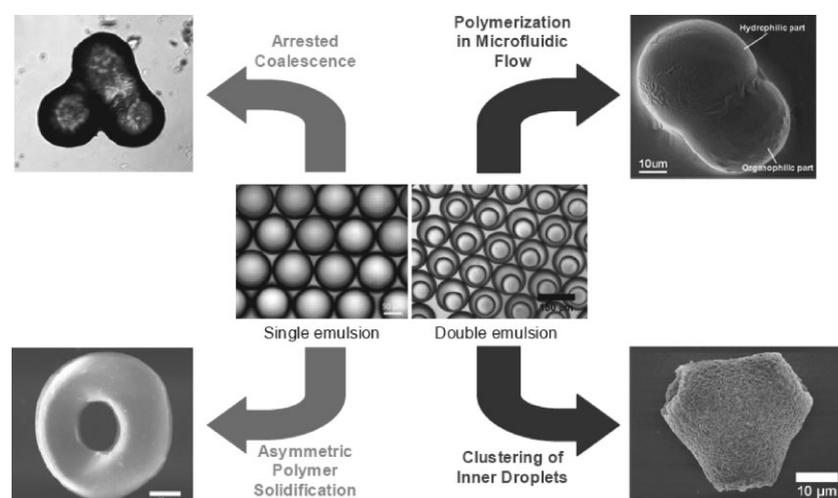
In this paper, we discuss various efforts to utilize droplet-based microfluidic technologies to fabricate non-spherical particles. We take advantage of the high degree of control afforded by microfluidics to form single and multiple emulsion droplets that are afterwards transformed to non-spherical particles through further simple, spontaneous processing steps.

Single emulsions are droplets of one fluid, the dispersed phase, suspended in

an immiscible fluid, the continuous phase. Double emulsions consist of drops of one phase inside a larger drop of another phase and the drops-in-drops are dispersed in an outer continuous phase;<sup>[22]</sup> these are an example of a more general class of multiple emulsions. In this paper, we discuss how single and double emulsions can be used as templates for forming non-spherical particles using strategies that are summarized schematically in Figure 1. The spherical single emulsion precursors are converted into non-spherical particles through arrested coalescence of particle-stabilized droplets and asymmetric solidification of droplets of polymer solutions. Double emulsion precursors are transformed into non-spherical particles following polymerization in microfluidic flow and evaporation-driven clustering. The details of these different approaches are discussed below. Examples using both stamped lithography-based poly(dimethyl siloxane) (PDMS) microfluidic devices and 3D glass-capillary microfluidic devices are shown. While lithography-based PDMS devices are chosen for the simplicity of the manipulation of device geometry, 3D glass devices are used when aggressive chemicals are used in the fabrication procedures.<sup>[22]</sup>

## Arrested Coalescence

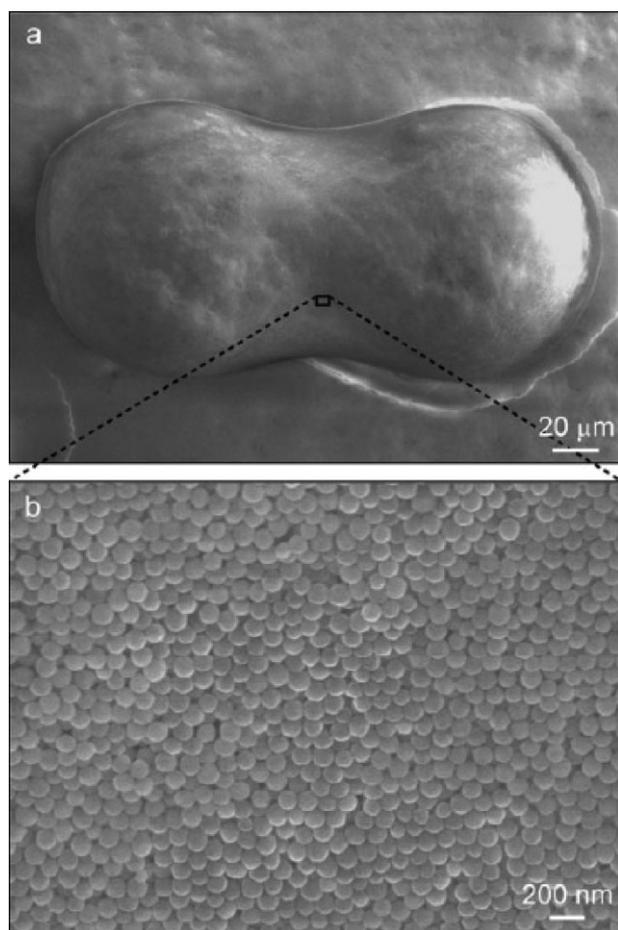
One way to use single emulsion droplets as precursors to form non-spherical particles is by initiating the coalescence of droplets and freezing their shapes before they relax into spheres. We have demonstrated this approach using single emulsions containing droplets stabilized through interfacially adsorbed particles, also known as Pickering



**Figure 1.** Schematic of the different strategies for converting emulsion precursors prepared with microfluidic devices into non-spherical particles. (Arrested coalescence: reproduced with permission from ref.,<sup>[23]</sup> © 2009 American Chemical Society; Asymmetric polymer solidification: reproduced with permission from ref.,<sup>[29]</sup> © 2009 Wiley-VCH; Polymerization in microfluidic flow: reproduced with permission from ref.,<sup>[32]</sup> © 2009 American Chemical Society; Clustering of inner droplets: reproduced with permission from ref.,<sup>[43]</sup> © 2009 Wiley-VCH).

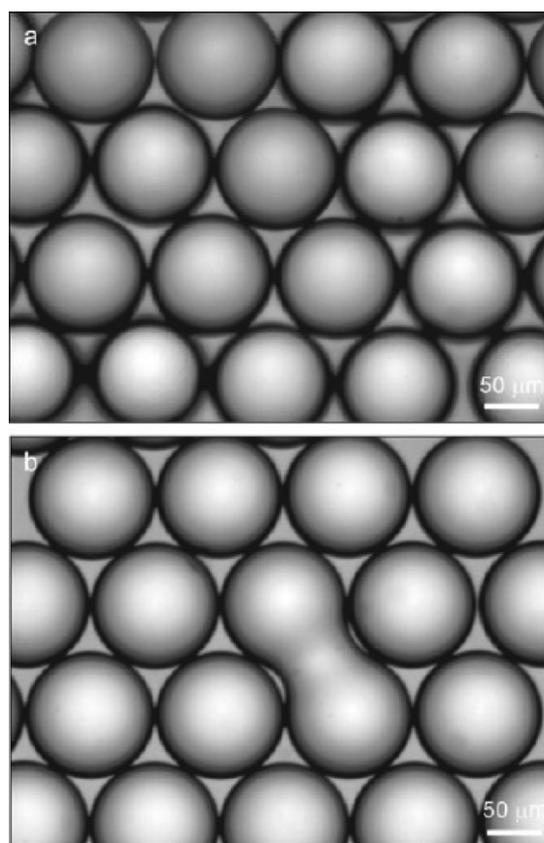
emulsions. Non-spherical supracolloidal structures are created from the partial coalescence of such particle-coated droplets.<sup>[23]</sup> While Pickering emulsions can be kinetically stable for long periods of time,<sup>[24–26]</sup> incomplete coverage of the droplet surface by particles results in the formation of unprotected surface patches that can initiate droplet coalescence. For particles irreversibly adsorbed at the oil–water interface, the reduction in droplet surface-to-volume ratio accompanying the coalescence process leads to an increase of up to 26% in the droplet surface coverage by the particles.<sup>[23]</sup> We have shown that such increase in surface coverage can arrest the coalescence process by irreversibly jamming the particles adsorbed at the oil–water interface (Figure 2). Assuming that two-dimensional jamming occurs when the interfacial coverage of particles approaches 0.90, arrested coalescence between two identical droplets is expected to occur with the initial surface coverages ranging from 0.71 to 0.90.

The phenomenon of arrested coalescence can be exploited to produce supracolloidal structures with



**Figure 2.** (a) Non-spherical structure highlighting (in b) the colloidal particles jammed in the neck region between droplets. (Reproduced with permission from ref.<sup>[23]</sup> © 2009 American Chemical Society).

intricate, non-spherical geometries.<sup>[23]</sup> To achieve structures with well-defined shape, monodisperse droplets produced in a glass microfluidic device can be used as building blocks. Arrested coalescence of such droplets is induced by partially coating the droplets with colloidal particles. The flow rates of the inner and outer fluids used for droplet formation in the microfluidic device are tuned to obtain droplet surface coverages within the range required to achieve arrested coalescence. Although the coalescence process itself takes place within tenths of microseconds, coalescence only occurs when the unprotected surfaces of two adjacent droplets are exposed to each other.<sup>[23]</sup> This implies that droplet rotation or particle rearrangement at the interface are required to initiate coalescence. We observe that these rearrangements occur within a few seconds after contact between droplets. One can take advantage of this delayed process to arbitrarily position single droplets into target geometries before the onset of coalescence. Using toluene as inner phase, e.g., we produced oil droplets that cream to the top of the emulsion and self-assemble into compact ordered arrays at the air–water interface prior to coalescence [Figure 3(a)]. Arrested



**Figure 3.** (a) Top view of an array of toluene droplets partially coated with 100 nm colloidal particles and (b) non-spherical structure formed through the arrested coalescence of adjacent droplets. (reproduced with permission from ref.<sup>[23]</sup> © 2009 American Chemical Society).

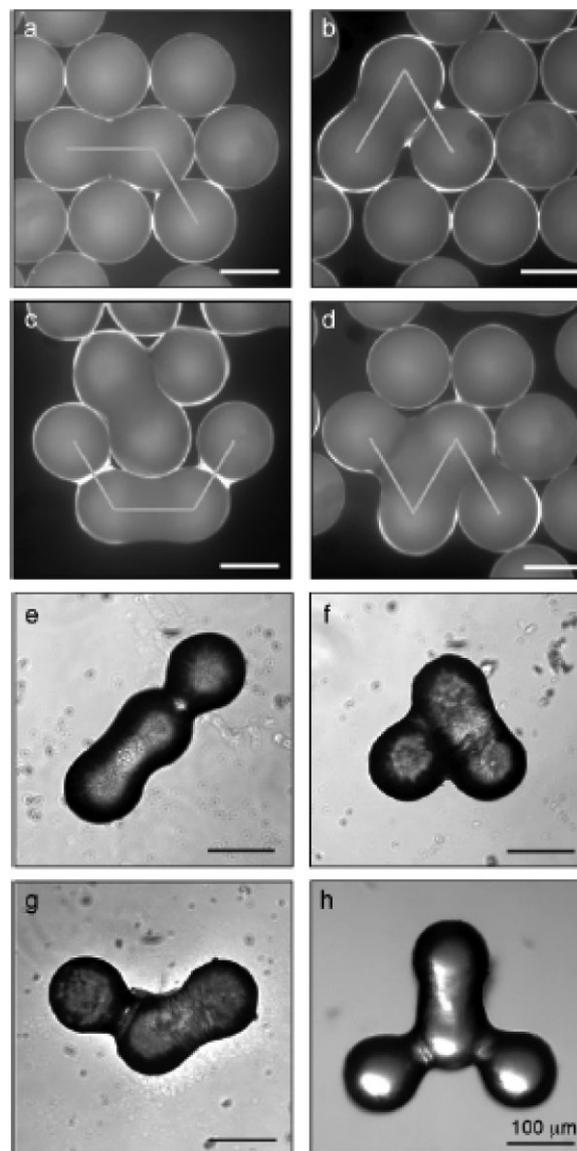
coalescence of adjacent single droplets then lead to supracolloidal structures with non-spherical shape [Figure 3(b)]. Interestingly, coalescence at one site of the droplet surface does not lead to particle jamming throughout the entire oil–water interface. As a result, particle-free patches are still present on other sites of the droplet surface, allowing each single droplet to undergo arrested coalescence with more than one adjacent droplet.

The possibility of fixing the position of droplets into specific arrays before coalescence and the ability to induce multiple fusion events enables the production of multi-unit structures with tailored bonding angles between the merging droplets. Structures formed from droplets previously assembled in a hexagonal array, e.g., must exhibit bonding angles that are integral multiples of  $60^\circ$ . Examples of multi-unit supracolloidal structures displaying bonding angles of  $60$  and  $120^\circ$  are shown in Figure 4(a)–(d). Anisotropic shapes with intricate geometries can also be achieved, as exemplified by the structures with zig-zag [Figure 4(d)] and boat-like [Figure 4(c)] conformations.

These multi-unit structures can be dried and harvested without impairing their well-defined structure by polymerizing the inner dispersed phase; typical results are shown in Figure 4(e)–(h). While anisotropic shapes have, so far, been obtained only by the random coalescence of neighboring droplets, positioning droplets into templates with arbitrary configurations would enable precise control over the size and shape of the final structures. Moreover, this method is not limited to the type of particles used; other particles can be used so long as their surface chemistry is properly controlled to induce particle adsorption at the liquid interface.<sup>[27]</sup> Supracolloidal structures with tailored surface chemistry can potentially be created by adsorbing different types of colloidal particles onto the outer shell.<sup>[28]</sup> These concepts can possibly also be extended to bulk emulsification techniques for the preparation of non-spherical structures in larger quantities, albeit with a poorer control over the droplet size and monodispersity. This approach is thus a promising route toward the controlled fabrication of anisotropic supracolloidal structures with deliberately designed shapes and surface chemistry.

### Asymmetric Polymer Solidification

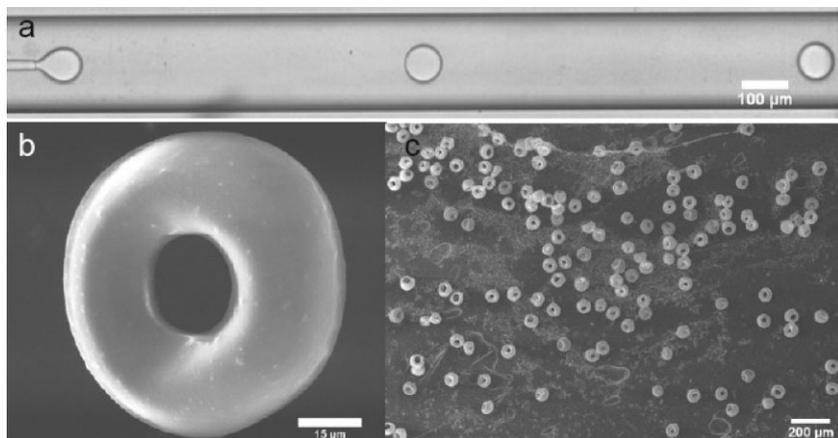
Another way to make particles from single emulsion precursors is by polymer solidification. Polymer is first dissolved in a volatile good solvent. The resulting polymer solution is used as the dispersed phase of the emulsion. Polymer particles can be obtained after evaporation of all the solvent. Typically, solvent is evaporated isotropically through the surrounding continuous phase into air, resulting in spherical particles. However, if solvent diffu-



**Figure 4.** Non-spherical oil droplets with well-defined geometries obtained by positioning the droplets in regular arrays shortly before coalescence (a–d) and the resulting non-spherical structures after polymerization of the oil phase and harvesting (e–h). (Reproduced with permission from ref.,<sup>[23]</sup> © 2009 American Chemical Society).

sion can be manipulated such that it takes place non-isotropically, non-spherical polymer particles can also be formed. We have demonstrated such approach to form toroidal particles in microfluidic devices.<sup>[29]</sup>

Droplets of polymer solution are prepared by coflowing the polymer solution in the continuous phase inside a glass capillary microfluidic device,<sup>[30]</sup> as shown in Figure 5(a). Solvent removal from the droplets takes place in the cylindrical microchannel. Even though the continuous phase is immiscible with the solvent of the dispersed phase, a finite amount of solvent can nevertheless still be dissolved

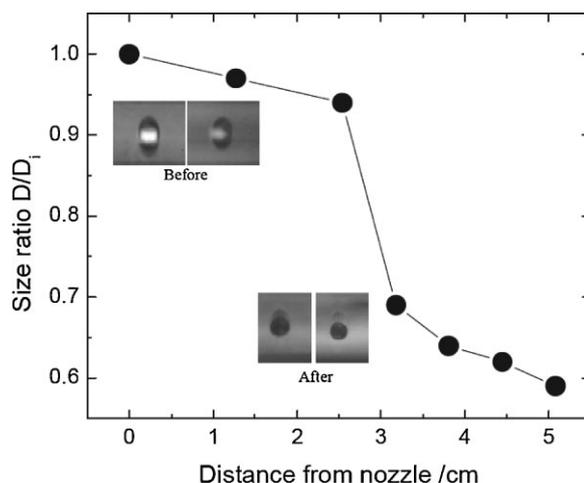


**Figure 5.** Fabrication of torroidal polymer particles using phase separation in an axisymmetric laminar flow field provided by a microcapillary device. (a) Droplets of polymer solution being generated inside a capillary microcapillary device. (b) Scanning electron microscopy (SEM) image of a typical torroidal polymer particle. The particle was prepared by solidifying a droplet of 10 wt.-% PSF dissolved in DMF, generated with a dispersed phase flow rate,  $Q_{\text{inner}}$ , of  $20 \mu\text{l} \cdot \text{h}^{-1}$  and a continuous phase flow rate,  $Q_{\text{out}}$ , of  $2500 \mu\text{l} \cdot \text{h}^{-1}$ . (c) SEM image of torroidal PSF particles prepared under the same conditions in (b). The particles have an average diameter of  $52.9 \mu\text{m}$  with a standard deviation of  $1.5 \mu\text{m}$ . (Reproduced with permission from ref.,<sup>[29]</sup> © 2009 Wiley-VCH).

tion. If the asymmetric polymer solidification is completed within the microchannel, a doughnut-shaped torroidal structure can be formed, as shown in Figure 5(b),(c). We plot the variation in polymer droplet size as a function of the distance from the exit of the injection nozzle, where the droplets are generated, in Figure 6. The droplets initially decrease in size, due to diffusion of solvent from the droplet into the continuous phase. Then, the size of the polymer droplet drops dramatically, as the droplets begin to solidify. The droplets become smaller in size and turn opaque following solidification, as shown in the insets of Figure 6.

This strategy is completely general and applicable to a range of polymers, including poly(ether sulfone) (PES), polysulfone (PSF), poly(methyl methacrylate) (PMMA), and poly(vinylidene fluoride) (PVDF), when an appropriate solvent,

in the continuous phase. Therefore, as the droplets translate inside the microchannel, solvent diffuses into the surrounding continuous phase until it becomes saturated with the solvent. Since the flow is laminar and no turbulent mixing takes place inside the microchannel, the velocity of the continuous phase differs across streamlines in different radial positions. Along the axial direction, the continuous phase directly in front of and behind the droplet moves at the same velocity as the droplet. As a result, local stagnation zones are formed at the front and the back of the droplet and in these regions the continuous phase remains saturated with the solvent. By contrast, the streamlines of the continuous phase farthest from the center of the droplet moves at a different speed and flow around the droplet, thereby carrying away solvent dissolved in the continuous phase. Therefore, in this circumferential region around the droplet, solvent does not become saturated and continues to diffuse into the continuous phase. Solidification of the droplet takes place in regions where the local concentration of polymer exceeds a critical concentration. Thus, in the microchannel, solidification of the polymer solution droplet begins at the circumferential surface. As the solvent continues to diffuse into the continuous phase in the circumferential region, the remaining polymer in the droplet continues to solidify and deposit on the solidified surface.<sup>[31]</sup> This leads to a decrease in the polymer concentration in the center of the droplet. Eventually, the originally spherical droplet becomes stretched and pinched, and almost all the polymer is solidified around the circumferential region. We refer to such solidification within the microchannel as asymmetric polymer solidifica-



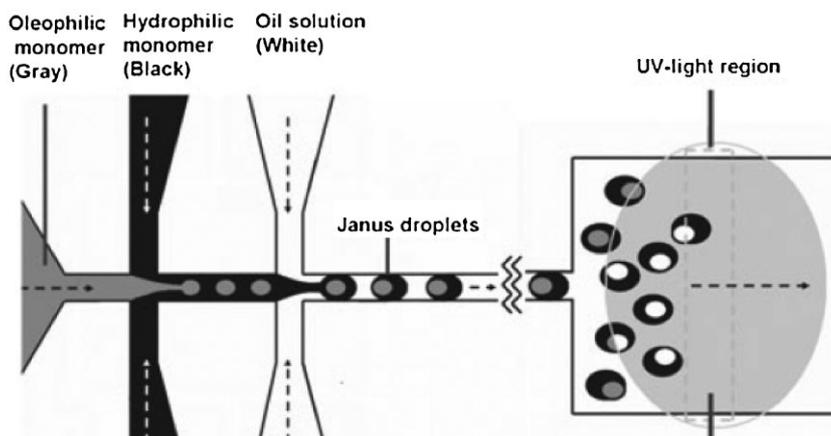
**Figure 6.** Variation of polymer droplet size with the distance from injection tube exit. Droplet size,  $D$ , is expressed as a size ratio relative to the initial droplet size,  $D_i$ , at the exit of capillary tube. Droplets of polymer solution first decrease slowly in size and then experience a sudden drop at about 2.6 cm from the exit of the capillary tube. The sudden decrease in droplet size reflects solidification of the droplet. The transparent liquid drops, as shown in the inset images labeled “Before,” become opaque solid particles following the sudden reduction in size. While the droplets in the inset images labeled “Before” appear non-spherical, they are indeed spherical due to interfacial tension effects. The apparent elongation in the vertical direction is due to the lensing effect associated with imaging through the cylindrical capillary with a wall thickness of  $400 \mu\text{m}$ . The droplets are generated with a dispersed phase flow rate,  $Q_{\text{inner}} = 50 \mu\text{l} \cdot \text{h}^{-1}$  and a continuous phase flow rate,  $Q_{\text{out}} = 5000 \mu\text{l} \cdot \text{h}^{-1}$ . The polymer solution consists of 10 wt.-% PSF in DMF. (Replotted and reproduced with permission from ref.,<sup>[29]</sup> © 2009 Wiley-VCH).

such as *N,N*-dimethylformamide (DMF) is used. To stabilize the emulsion precursor over the course of the droplet solidification, a surfactant is added to the continuous phase, which should be immiscible with the solvent while still allowing solvent to diffuse into it. The size of the torroidal particles generated depends on the size of the emulsion precursors, which in turn depends on the size of the nozzle of the microfluidic device and the flow rates used. Typical sizes of the particles generated range from 6 to 120  $\mu\text{m}$ . By incorporating additional functional components, such as fluorescent dyes and magnetic nanoparticles, into the solvent mixture, composite torroidal particles with specific functionalities can be fabricated, as shown in Figure 7. Such functional torroidal particles have many potential uses; examples include anisotropic imaging probes for biomedical applications and agents for magnetic actuation.<sup>[29]</sup>

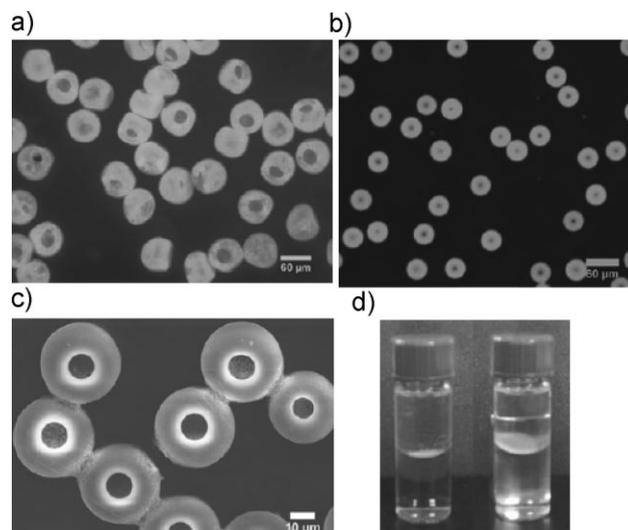
Our results show that even though droplets prepared microfluidically tend to be spherical due to interfacial tension effects, the spherical droplets formed can be manipulated and transformed into non-spherical particles inside controlled environments. With carefully designed environments for solvent removal, achieved, for instance, by tuning the fluid flow, it is possible to fabricate even more complex geometries.

### Polymerization in Microfluidic Flow

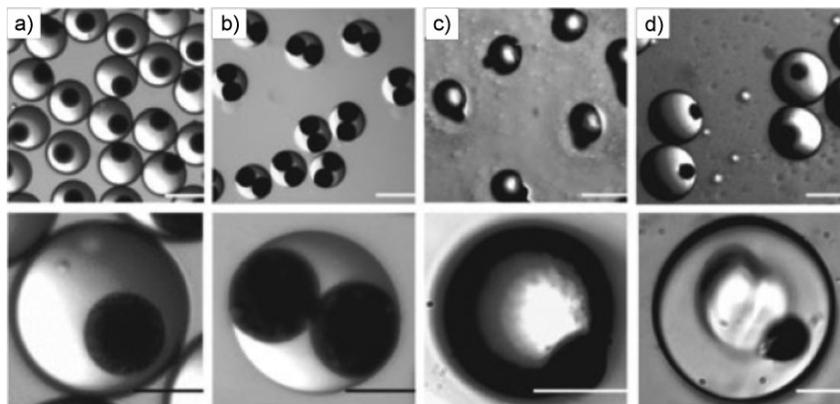
While single emulsion drops are simpler to generate, the more complex structure of double emulsion drops enables even more sophisticated engineering of the shape and functionality of the resulting non-spherical particles. When double emulsion drops are generated inside a microfluidic device, the inner droplets usually do not sit at the center of the drops due to fluid flow induced by viscous forces within the double emulsion drops and the difference between the densities of the two fluids.<sup>[32]</sup> If the diameter of the double emulsion drops is larger than the height of the channel, the drops will be deformed into non-spherical shapes as they flow through the channels. Non-spherical particles can be formed by locking in the structure of the double emulsion drops. This can be achieved easily with solidification of the drops through polymerization. Since it is simpler to control the dimensions of the channels in a PDMS lithographic device,<sup>[33,34]</sup> we conduct this work in a PDMS double emulsion device shown in Figure 8.



**Figure 8.** Schematic of PDMS double emulsion maker. In order to form double emulsions in a PDMS device, spatial control of channel wettability is critical. Using a photoreactive sol-gel coating we make the first drop maker hydrophilic and the second hydrophobic. The first thus produces oil drops dispersed in water, which flow into the second drop maker where water drops containing an inner oil drop are formed and dispersed in oil, forming an O/W/O double emulsions. To force the drops to adopt a non-spherical shape, we flow them down a long, narrow channel. Hydrodynamic forces cause the inner drops to move toward the back of the double emulsion, forming a Janus drop. To lock in the Janus structure, we use UV illumination of the drops in the channel to polymerize, and thereby solidify them. (Reproduced with permission from ref.,<sup>[32]</sup> © 2009 American Chemical Society).



**Figure 7.** Composite particles with a torroidal structure. (a) An optical microscope image of PSF torroidal particles containing fluorescein sodium salt at less than 0.1 wt.-%. The PSF particles were prepared from a solution of 10 wt.-% PSF dissolved in DMF. (b) An optical microscope image of PMMA torroidal particles containing rhodamine B of less than 0.1 wt.-%. (c) An electron microscope image of PMMA torroidal particles containing 10 nm magnetic particles at  $\approx 0.5$  wt.-%. The PMMA particles were prepared from a solution of 10 wt.-% PMMA dissolved in DMF. (d) Magnetic torroidal particles are attracted toward a magnet placed behind the glass vial (right), and stay at the interface of the PDMS oil and water in the absence of a magnetic field (left). (Reproduced with permission from ref.,<sup>[29]</sup> © 2009 Wiley-VCH).



**Figure 9.** Optical microscope images of uniformly anisotropic magnetic double emulsions containing (a) one core and (b) two cores synthesized using PDMS microfluidic devices. After polymerization, the double emulsions are solidified, (c) dried, and (d) re-dispersed in water where they re-hydrate and swell. The scale bars in the top row are 50  $\mu\text{m}$  and in the bottom row are 20  $\mu\text{m}$ . (Reproduced with permission from ref.,<sup>[43]</sup> © 2009 Wiley-VCH).

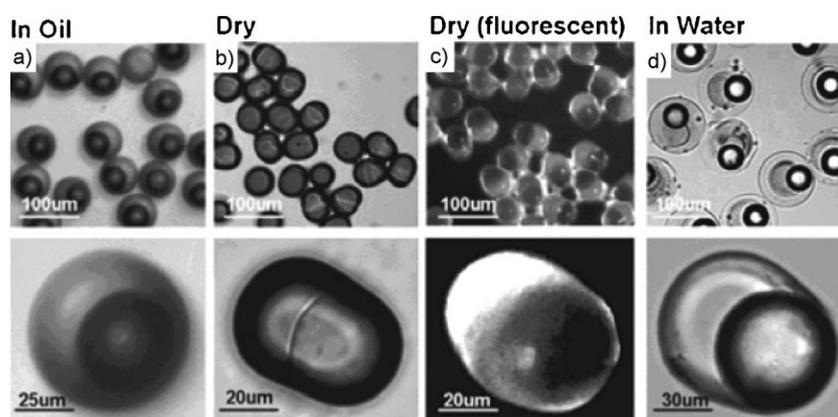
As a demonstration of the utility of this approach for the synthesis of non-spherical particles, we form magnetically responsive microparticles with uniformly anisotropic internal structure.<sup>[32]</sup> The particles consist of a hydrogel shell within which is encapsulated a magnetic core. They are formed by first producing an oil-in-water-in-oil (O/W/O) double emulsion<sup>[35]</sup> and then locking-in the anisotropic structure using photo-polymerization. The shell of the double emulsion drop is composed of acrylamide monomer solution and the core is composed of a styrene/ferro-fluid mixture; the ferro-fluid makes the drops magnetically responsive while the styrene and acrylamide monomers make them photo-polymerizable. By adjusting flow rates during formation, we control the size and internal structure of the particles, encapsulating one, two, or several magnetic cores in each particle, as illustrated in Figure 9(a),(b). The solidified particles are then dried and re-dispersed in water, as shown in Figure 9(c),(d). In water, the particles re-hydrate, swelling in size but maintaining their anisotropic structure, as shown in Figure 9d. These particles can be used as microstir bars to mix fluids at small scales by spinning them using a rotating magnetic field, as in a stirring hotplate.

As a second demonstration, we synthesize size biphasic Janus particles.<sup>[32]</sup> These particles are composed of two halves: an oleophilic half composed of an oil-based polymer and a hydrophilic half composed of a hydrogel polymer. Such particles are useful for a myriad of applications

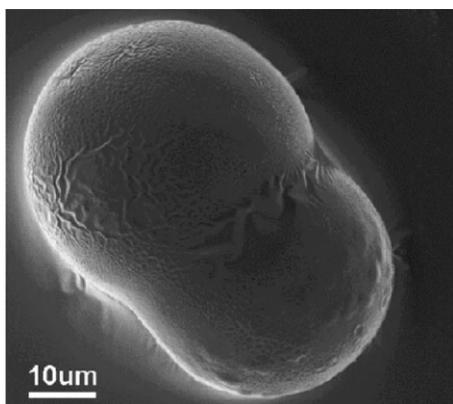
including emulsion stabilization and optical probing of chemical, biological, and rheological phenomena. We form them employing our double emulsification/solidification strategy: we flow the double emulsions down a small micro-channel forcing them to adopt a non-spherical shape. Using photo-polymerization, we then lock-in the structure by solidifying the drops. The resulting particles have a biphasic Janus shape, as shown in Figure 10(a),(b). To visualize the internal structure of the particles, we dye the hydrophilic halves with fluorescein. When viewed in a fluorescent microscope the hydrophilic halves are bright while the un-dyed oleophilic halves remain dark, confirming the Janus structure, as shown in Figure 10(c). As with the magnetic particles, the solidified Janus

particles can be re-dispersed into other solvents, such as water, and maintain their non-spherical shape, as shown in Figure 10(d) and Figure 11. To control the size of the particles and the relative proportions of the oleophilic and hydrophilic portions, we control the dimensions of the PDMS drop maker and flow rates used to form the drops; this allows synthesis of Janus particles with a range of tailored sizes and structure.

This approach combines the high degree of control offered by droplet microfluidics with the ability to tune the particle chemistry to fabricate non-spherical particles. It is also very general and is independent of the choice of



**Figure 10.** Hydrophilic/oleophilic double emulsions synthesized using PDMS microfluidic devices. Optical microscopic images of solidified Janus particles (a) suspended in oil and (b) dried in air. Fluorescent microscopic images of (c) dried Janus particles and solidified Janus particles in water. The hydrophilic half of the particles dyed with fluorescein appears bright in (c), while the un-dyed oleophilic half appears dark. The Janus structures are locked in by photo-polymerizing Janus-shaped double emulsions flowing through a long, thin PDMS channel. (Reproduced with permission from ref.,<sup>[32]</sup> © 2009 American Chemical Society).



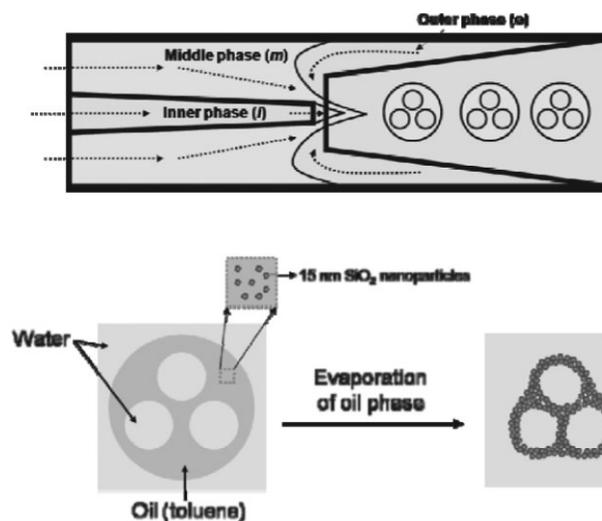
**Figure 11.** Scanning electron microscopy (SEM) image of Janus particle synthesized using a PDMS double emulsion device. The sizes of the two sides of the Janus particle can be controlled by controlling flow rates during formation in microfluidic devices. (reproduced with permission from ref.,<sup>[32]</sup> © 2009 American Chemical Society).

monomer, as long as an appropriate polymerization strategy is available. Therefore, this approach offers the possibility to choose the materials of the non-spherical particles according to the requirements of the specific application.

### Clustering of Inner Droplets

Another means of using double emulsion droplets as precursors for forming non-spherical particles is by packing multiple inner droplets inside a small volume of the middle shell phase. If the interface between the inner and the middle phases is less deformable than that between the middle and the outer phases, non-spherical double emulsion droplets will form. We illustrate this approach by using double emulsions with multiple inner droplets to form non-spherical colloidosomes with multiple compartments.

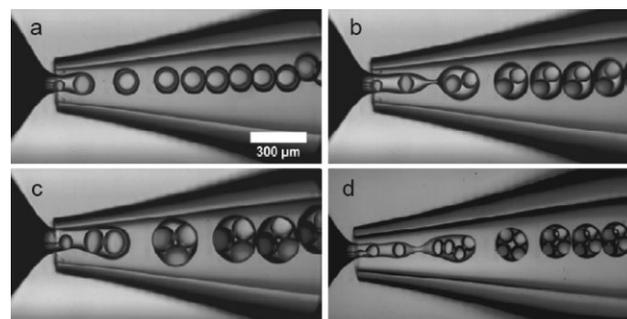
Colloidosomes are capsules whose shell consists of densely packed colloidal particles.<sup>[36]</sup> These colloidosomes are typically prepared by creating particle-covered water-in-oil (W/O) emulsion droplets, which are subsequently transferred into an aqueous phase.<sup>[36–39]</sup> Properties such as permeability, biocompatibility, and functionality of these colloidosomes can be tuned by using different particles to form the shells; such features make these structures ideal for applications in drug delivery, encapsulation, and controlled release. While a number of colloidosome preparation methods have been suggested, it is difficult to control the colloidosome shape using these conventional techniques. Interfacial tension between the immiscible liquids leads to spherical droplets and thus spherical colloidosomes. Non-spherical colloidosomes could potentially be used to improve the flow properties of these



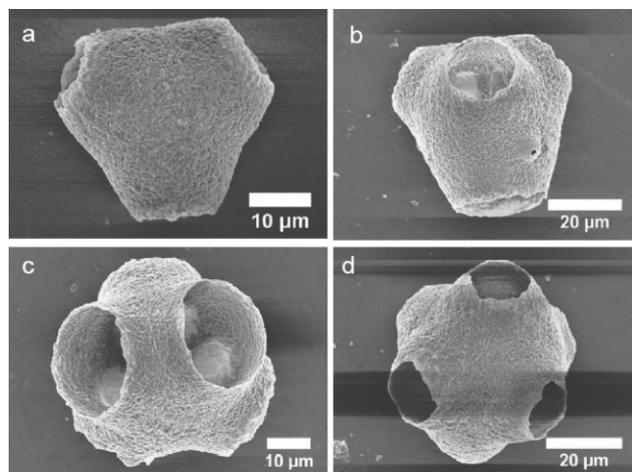
**Figure 12.** Schematic representation of generation of double emulsions with multiple aqueous cores (top) and generation of non-spherical colloidosome (bottom). (Reproduced with permission from ref.,<sup>[40]</sup> © 2009 Wiley-VCH).

capsules through constrictions mimicking the non-spherical structure of red blood cells.<sup>[40]</sup> They can also be used to increase storage efficiency due to higher packing density of non-spherical objects.<sup>[5]</sup>

We generate non-spherical colloidosomes using double emulsion drops as templates. Double emulsions with different number of inner aqueous drops are generated by tuning the flow rates of three fluid phases as shown in Figure 12. Non-spherical multi-compartment colloidosomes are subsequently generated by removing the oil phase from double emulsions with multiple inner drops, as shown in Figure 13. Since the Laplace pressure across W/O and O/W interfaces depends on the curvature of the interface, the inner drops are able to retain their spherical shapes while the outer interface deforms during solvent removal. This process leads to the generation of non-spherical colloidosomes with multiple compartments as shown in Figure 14. Multi-compartmental non-spherical



**Figure 13.** Generation of double emulsions with multiple inner droplets using a glass capillary microfluidic channel. (Reproduced with permission from ref.,<sup>[40]</sup> © 2009 Wiley-VCH).

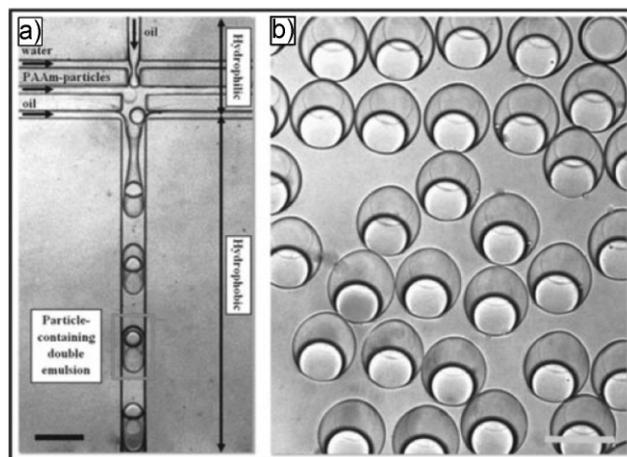


**Figure 14.** Scanning electron microscopy (SEM) images of non-spherical colloidosomes templated with double emulsions containing (a) three, (b) four, (c) five, and (d) six inner drops. (Reproduced with permission from ref.<sup>[40]</sup> © 2009 Wiley-VCH).

capsules could potentially be used to encapsulate several components in a single capsule without the risk of contamination. In addition, non-spherical geometry could afford advantages in achieving favorable flow properties through constrictions as exemplified by non-spherical red blood cells in nature.

The use of this approach for forming non-spherical particles is not limited to the fabrication of colloidosomes, which rely on the jamming of the particles for the solidification of the precursor emulsion drops. The only requirements for this approach to work are that the inner droplets are less deformable than the encapsulating middle drops, and that the double emulsion droplets are stable enough to maintain the non-spherical interface between the middle and the outer continuous phases. As long as these requirements are satisfied, non-spherical particles can be formed when this approach is used together with an appropriate strategy for solidifying the emulsion drops.

In fact, the inner, less deformable entities do not have to be fluidic. They can be solid particles too. As an example, we form non-spherical particles by using a mixture of fluid drops and solid particles, which we call internal particle scaffolds, as the inner entities. Instead of having inner fluid drops only, we encapsulate small particles as well as fluid drops into the shells of double emulsions, causing them to adopt a unique, non-spherical equilibrium shape. To insert the particles, a double emulsion device is outfitted with particle injection channels,<sup>[41]</sup> shown in Figure 15(a). The inner fluid drops are formed in the first droplet generator, while particles are injected into the middle shell phase through the particle injection channels. By close-packing the small particles in the particle injection channels, a controlled number of particles can be inserted evenly into the drop when the particle injection rate is set to an integer



**Figure 15.** Particle-scaffolded non-spherical double emulsions. (a) Optical microscope image of PDMS double emulsion device outfitted with particle injection channels. The injection channels insert a single particle into the shell of each double emulsion; additional particles are inserted by adjusting injection rate to an integer multiple of the drop formation rate. (b) Optical microscope image of a monodisperse population of particle-scaffolded non-spherical double emulsions. The scale bars are 100  $\mu\text{m}$  for the left image and 50  $\mu\text{m}$  for the right image.

multiple of the double emulsion formation rate. This allows formation of non-spherical double emulsions that are perfectly monodisperse, as shown in Figure 15(b). By controlling the size and packing arrangements of the particle scaffold, we can precisely position the inner drops.

The main advantage of the clustering approach for forming non-spherical particles is that the double emulsion precursors maintain their non-spherical shape even in the absence of flow or confining walls, because it is the equilibrium state of the system. It is therefore possible to form the double emulsion templates in one step and solidify them in a separate step. Unlike the previous approach locking in the structure with polymerization, formation of non-spherical particles therefore does not require ultra-fast polymerization techniques for solidifying the droplets in microfluidic devices; these techniques can be difficult to implement and are not always feasible.

## Conclusion and Outlook

Microfluidics offers new approaches for fabricating non-spherical particles. Single and multiple emulsion drops prepared in microfluidic devices can be converted into non-spherical particles with complex geometries using subsequent processing steps including arrested coalescence, asymmetric polymer solidification, polymerization in microfluidic flow, and evaporation-driven clustering. With traditional synthesis techniques, it is challenging to prepare micron-sized non-spherical particles that are

monodisperse in both size and shape. As more microfluidic-based fabrication techniques emerge, more novel applications will also be discovered. For these applications to be commercially feasible, it is important to have technologies for producing non-spherical particles in large quantities. One way to meet this challenge is to scale-up the production of droplets by parallelization.<sup>[35,42]</sup> Efforts on such parallelization suggest that production rates on the order of  $1 \text{ ton} \cdot \text{d}^{-1}$  might ultimately be attainable. Advances in the scale-up of microfluidic devices will also make it possible for non-spherical particles to be used in commercial applications.

Another challenge for the fabrication of non-spherical particles using microfluidics is to achieve non-spherical particles that are in the sub-micron size range. While the microfluidic approaches that have been demonstrated for fabricating micron-sized particles should be applicable for fabricating nanometer-sized particles, practical aspects of microfluidic devices, such as the pressure required for pumping fluids and the choice of materials, have prevented simple and cost-effective operation of these devices for production of sub-micron sized droplets in large quantities. These challenges must be addressed to extend the same level of size and shape control achieved for micron-sized particles to nanometer-sized particles.

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