

Nonspherical Colloidosomes with Multiple Compartments from Double Emulsions**

Daeyeon Lee* and David A. Weitz*

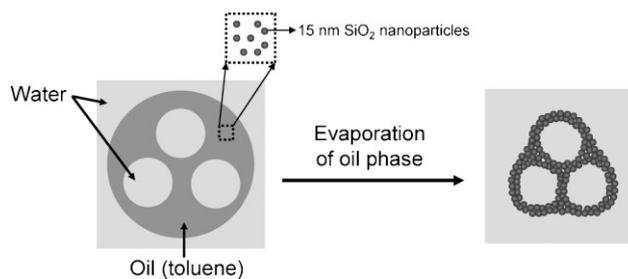
Colloidosomes are hollow capsules whose walls are composed of densely packed colloidal particles.^[1–4] Colloidosomes are typically prepared by creating particle-covered water-in-oil (W/O) emulsion droplets. These particle shells in the oil phase are subsequently transferred into an aqueous phase to generate the colloidosomes. We recently reported a new approach to fabricate monodisperse colloidosomes by using double emulsions as templates.^[5] Water-in-oil-in-water (W/O/W) double emulsions with a core-shell structure are created using a glass capillary microfluidic device.^[6] Hydrophobic SiO₂ nanoparticles, suspended in the oil phase, become the wall of colloidosomes upon removal of the oil. The functionality and physical properties of colloidosomes such as permeability, selectivity, and biocompatibility can be precisely controlled by suitable choice of colloidal particles and processing conditions.^[1,2,4,7,8] Such versatility makes these colloidosomes attractive candidates for applications in encapsulation and delivery of foodstuffs, fragrances, and active ingredients.

Further advantages could be obtained from colloidosomes and capsules with a non-spherical geometry, or with multiple-compartments. Nonspherical particles can pack more densely than spherical ones.^[9,10] Nonspherical capsules, therefore, can be used to store a larger amount of encapsulated materials compared to spherical capsules. Nonspherical capsules could also facilitate the delivery of encapsulated materials through constrictions; red blood cells (RBC) are one of many examples in nature where a nonspherical compartment is utilized.^[11,12] In addition to the nonspherical nature, multiple-compartment colloidosomes would enable encapsulation and storage of multiple types of cells and materials in a single capsule without

risk of cross contamination.^[13] Colloidosomes that have been reported to date, however, are spherical in shape, and have only one compartment. Interfacial tension between the two immiscible phases favors minimizing the surface area and thus leads to the formation of spherical droplets.^[14] This tendency naturally limits the fabrication process to the generation of spherical colloidosomes. Moreover, the traditional method of using simple W/O emulsions to template colloidosomes leads to generation of spherical colloidosomes with only one compartment.^[1–4]

In this report, we demonstrate the generation of nonspherical colloidosomes with multiple compartments. We use glass capillary microfluidics to prepare W/O/W double emulsions with different morphologies.^[6,15] These double emulsions have a different number of internal aqueous drops in the oil drop. Hydrophobic SiO₂ nanoparticles, suspended in the oil phase, and poly(vinyl alcohol) (PVA), dissolved in the continuous aqueous phase, stabilize the double emulsions. The nanoparticles in the oil phase eventually become the shell of colloidosomes upon the removal of the oil.^[5] During the oil removal, the internal W/O interface retains their spherical shapes whereas the outer O/W interface deforms; this process leads to the generation of nonspherical colloidosomes with multiple compartments (Scheme 1).

A glass capillary microfluidic device that combines a co-flow and a flow-focusing geometry is used to generate double emulsions with controlled morphology (see Supporting Information, Scheme S1).^[6] W/O/W double emulsions with a different number of internal aqueous drops per oil drop (n) were generated by controlling the flow rates of three phases independently as shown in Figure 1.^[15] The outer O/W interface was stabilized by a partially hydrolyzed PVA in the continuous phase and the inner W/O interface was stabilized by 15-nm hydrophobic SiO₂ nanoparticles; the nanoparticles dispersed in the oil phase adsorbed to the two W/O interfaces as evidenced by



Scheme 1. Generation of nonspherical colloidosome from W/O/W double emulsions with multiple internal aqueous drops. Oil phase comprises toluene and 15-nm hydrophobic silica nanoparticles.

[*] Prof. D. Lee
Department of Chemical and Biomolecular Engineering
University of Pennsylvania
Philadelphia, PA 19104 (USA)
E-mail: daeyeon@seas.upenn.edu

Prof. D. A. Weitz
School of Engineering and Applied Sciences/Department of Physics
Cambridge, MA 02138 (USA)
E-mail: weitz@seas.harvard.edu

[**] This work was supported by the NSF (No. DMR-0602684) and the Harvard MRSEC (No. DMR-0213805). Hydrophobic silica nanoparticles were generously provided by Nissan Chemicals Inc (Japan). We also thank Ho Cheung Shum and Prof. Vinodhan N. Manoharan of Harvard University for insightful discussions.

Supporting Information is available on the WWW under <http://www.small-journal.com> or from the author.

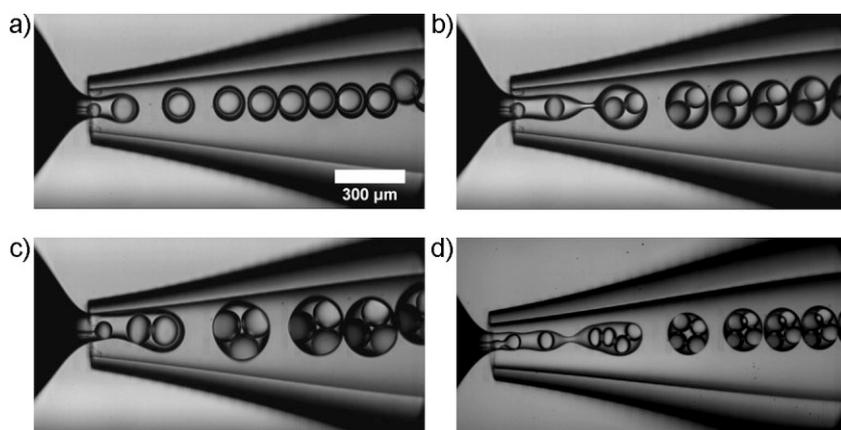


Figure 1. Generation of double emulsions with varying number of internal drops.

a) $Q_o = 20\,000\ \mu\text{L h}^{-1}$, $Q_m = 3\,000\ \mu\text{L h}^{-1}$, and $Q_i = 1\,500\ \mu\text{L h}^{-1}$. b) $Q_o = 20\,000\ \mu\text{L h}^{-1}$, $Q_m = 7\,000\ \mu\text{L h}^{-1}$, and $Q_i = 1\,500\ \mu\text{L h}^{-1}$. c) $Q_o = 10\,000\ \mu\text{L h}^{-1}$, $Q_m = 3\,000\ \mu\text{L h}^{-1}$, and $Q_i = 1\,700\ \mu\text{L h}^{-1}$. d) $Q_o = 35\,000\ \mu\text{L h}^{-1}$, $Q_m = 6\,000\ \mu\text{L h}^{-1}$, and $Q_i = 2\,000\ \mu\text{L h}^{-1}$.

the formation of wrinkles in the O/W interface during evaporation of the solvent due to the buckling of the adsorbed nanoparticle layers.^[5,16] Double emulsions with multiple compartments could be generated in the so-called dripping-to-jetting transition regime. In the typical dripping regime, the interfacial tension between the middle and outer phases dominates the droplet breakup process^[17]; the double emulsions generated tend to have one internal aqueous drop ($n=1$) (Figure 1a). As the inertial force of the middle and inner phases becomes comparable to the interfacial tension, the droplet breakup occurs in the dripping-to-jetting transition regime and n increases above one.^[17] For example, by increasing the flow rate of the middle phase (Q_m), n increases gradually as shown in Figure 2. In general, n increases with increasing Q_i and Q_m and with decreasing Q_o (see Supporting Information, Figure S1). Eventually, the middle and inner phases form a jet as the inertial force of these phases overcomes the interfacial tension.^[17] The double emulsions formed in this jetting regime have a wide distribution in size and n .

The morphology of double emulsions with the same n can also be controlled by varying the ratio of Q_i and Q_m . For example, double emulsions with $n=2$ with spherical structure can be created by adjusting Q_m to be greater than Q_i by three-

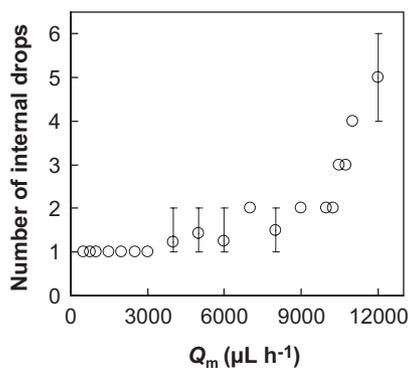


Figure 2. Effect of Q_m on the number of internal drops (n) in double emulsions. Q_o and Q_i are kept constant at $20\,000$ and $1\,250\ \mu\text{L h}^{-1}$.

fold as shown in Figure 3a (see Supporting Information, Figure S2). When the ratio of Q_m to Q_i is smaller than 3, ellipsoidal double emulsions are formed as seen in Figure 3b. The outer W/O interface rather than the inner one is deformed. This behavior can be easily explained by the fact that smaller droplets have a higher Laplace pressure acting across the interface given that the interfacial tension is the same.^[18] Thus the internal aqueous drops are less deformable than the encapsulating oil drop. This approach provides a new way to generate nonspherical emulsion droplets without relying on the jamming of the particles in solid-stabilized emulsion drops.^[19,20]

Evaporation of solvent from double emulsions in Figure 3 results in generation of colloidosomes with two internal compartments. Depending on the morphology of the double emulsions with $n=2$, the colloidosomes have different morphology. In the case of the spherical double emulsions with $n=2$, the resultant colloidosomes are ellipsoids as shown in the scanning electron microscopy (SEM) image in Figure 3c. In case of the ellipsoidal double emulsions, the resultant colloidosomes resemble peanuts (Figure 3d). Interestingly, these peanut-shaped colloidosomes have a saddle structure (black arrow in Figure 3d), which would be unstable due to the negative curvature.^[19] However, the structure is maintained because of the solid structure formed by the SiO_2 nanoparticles that become jammed during the evaporation of the oil phase.

Evaporation of the oil (toluene) from double emulsions with $n > 2$ leads to nonspherical colloidosomes with interesting geometry as shown in Figure 4. By increasing n , colloidosomes with 3D structures can be prepared as illustrated in Figure 4b–d. In addition to the nonspherical geometry of these colloidosomes with $n \geq 2$, each colloidosome has more than one compartment as the thin walls between internal aqueous droplets are maintained. Drying of the samples for SEM often leads to the rupturing of the thin walls of the colloidosomes, exposing the hollow interiors of colloidosomes. Similar damage has been observed where evaporation of water leads to rupturing of the capsule walls in spherical capsules.^[5,21] Optical microscopy and SEM images of intact colloidosomes are shown in the Supporting Information (Figure S3).

Colloidal particle clusters generated by evaporating solvent from particle-containing droplets leads to generation of polygons whose second moment of mass distribution is minimized.^[22] In the case of double emulsions with multiple n , however, such structures are not always observed. While double emulsions with $n \leq 3$ lead to colloidosomes with a unique geometry for each n , those with $n \geq 4$ can lead to structures that were not observed in the particle polygon study. The colloidosome with $n=5$ in Figure 4c, for example, is a square pyramid. Sometimes planar colloidosomes with $n \geq 4$ are observed as well (see Supporting Information, Figure S4); in case of the particle polygon with $n=5$, however, only triangular bipyramids were observed.^[22]

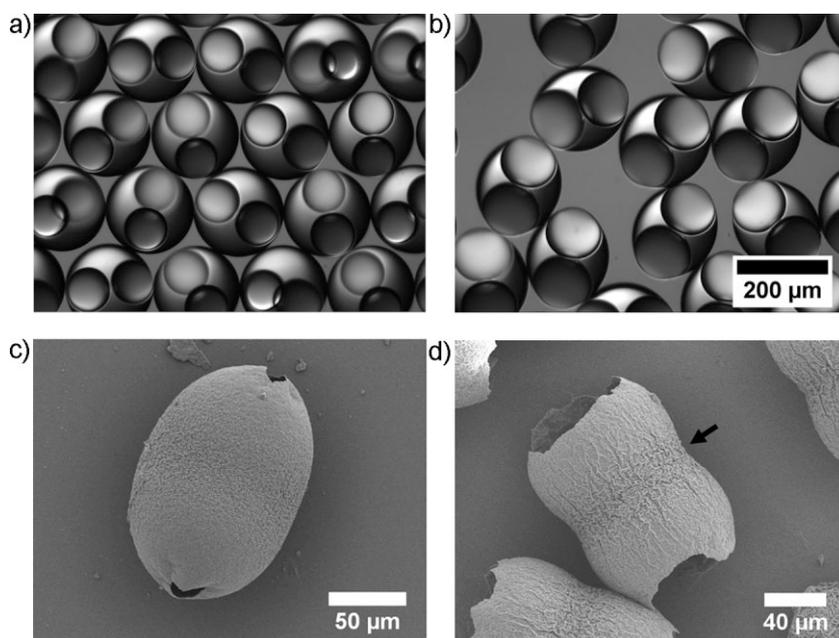


Figure 3. Optical microscopy images of W/O/W double emulsions with different volume ratios of V_m/V_i . a) $Q_o = 15\,000\ \mu\text{L h}^{-1}$, $Q_m = 7\,000\ \mu\text{L h}^{-1}$, and $Q_i = 1\,500\ \mu\text{L h}^{-1}$, and b) $Q_o = 20\,000\ \mu\text{L h}^{-1}$, $Q_m = 2\,000\ \mu\text{L h}^{-1}$, and $Q_i = 1\,500\ \mu\text{L h}^{-1}$. SEM images of dimer colloidosomes with varying shapes. The volume ratios of internal drops to middle phase (V_m/V_i) are 3.64 (c) and 1.94 (d). Colloidosomes shown in (c) and (d) are formed with middle phase containing hydrophobic nanoparticles.

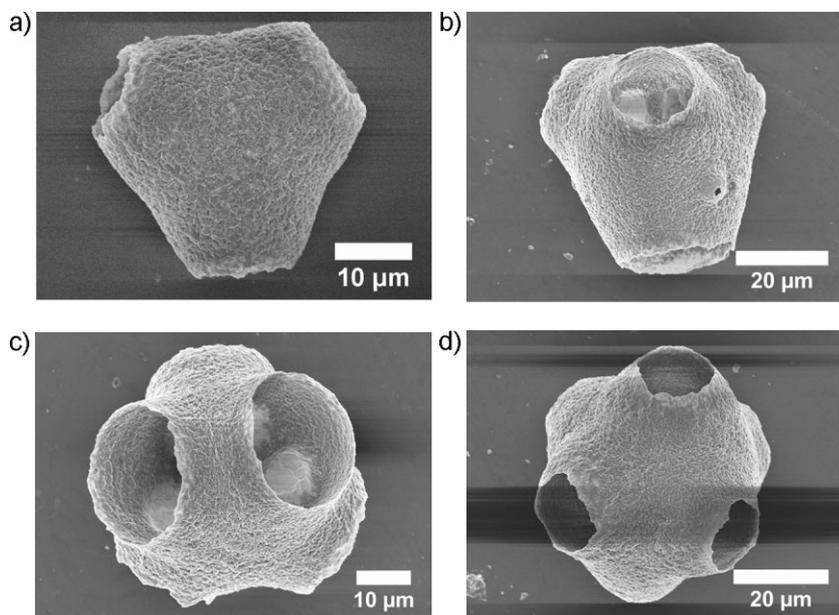


Figure 4. SEM images of nonspherical colloidosomes with $n = 3$ (a), 4 (b), 5 (c), and 6 (d) internal voids.

Some major differences exist between the colloidal particle polygons and the nonspherical colloidosomes obtained in this study. In the case of particle polygons, the particles adsorb to the interface between the two immiscible fluids during the solvent evaporation process.^[22] This process is critical in determining the final geometry of polygons.^[23] In the case of

colloidosomes, however, the internal droplets do not attach to the interface but rather stay completely encapsulated. There are also hydrophobic SiO_2 nanoparticles that fill the interstices between the internal drops. These nanoparticles may stabilize colloidosome structures that have not evolved into the “equilibrium structures” whose second moment of mass is minimized. In addition, nanoparticle layers coating the internal drops could generate friction between the internal drops and restrict the structures formed. These differences may have contributed to the different structures we have observed with colloidosomes.

In summary, we have shown that nonspherical colloidosomes with multiple compartments can be created by using double emulsions with different morphology as templates. The morphology of double emulsions is precisely controlled by using glass capillary microfluidic devices. We believe our approach provides a unique opportunity in generating multi-compartmentalized nonspherical structures that could be utilized in the encapsulation of several components in a single capsule.^[24] It should also be possible to generate more complex structures, such as asymmetric colloidosomes, where the inner and outer surfaces of the shell are composed of different nanoparticles. This could be achieved by using two nanoparticles with different wettabilities, one in the oil and the other in the continuous phases.^[25]

Experimental Section

Materials: Glass microcapillaries were purchased from World Precision Instruments, Inc. and Atlantic International Technologies, Inc. Hydrophobic silica nanoparticles suspended in toluene (average size is 15 nm as determined by transmission electron microscopy (TEM)) were generously provided by Nissan Chemical Inc. Toluene and PVA (89%–92% hydrolyzed, Mw 13 000–23 000) were purchased from Sigma Aldrich. Chemicals were used as received without further purification.

Microcapillary device fabrication and generation of double emulsions: The detailed preparation of glass microcapillary devices was described previously [6]. Briefly, cylindrical glass capillary tubes with an outer diameter of 1 mm and inner diameter of 580 μm were pulled using a Sutter Flaming/Brown micropipette puller (P-97). The dimension of tapered orifices was adjusted using a microforge (Narishige MF-830, Japan). Typical dimensions of orifice for inner

fluid and collection were 10–50 μm and 30–500 μm , respectively. The glass microcapillary tubes for inner fluid and collection were fitted into square capillaries that had an inner dimension of 1 mm. By using the cylindrical capillaries whose outer diameter match the inner dimension of the square capillaries, an axisymmetric alignment could be easily achieved to form a coaxial geometry. The distance between the tubes for inner fluid and collection was adjusted to be 5–30 μm . A transparent epoxy resin was used to seal the tubes where required. Solutions were introduced to the microfluidic device through polyethylene tubing (Scientific Commodities) attached to syringes (Hamilton Gastight or SGE) that were driven by positive displacement syringe pumps (Harvard Apparatus, PHD 2000 series). The drop formation was monitored with a high-speed camera (Vision Research) attached to a Leica inverted microscope.

For the generation of W/O/W double emulsions, three fluid phases are delivered to the glass microcapillary devices. The outer aqueous phase comprises 0.2–2 wt% PVA solution and the inner aqueous phase comprises 0–2 wt% PVA solution. The middle phase typically consists of 7.5 wt% hydrophobic silica nanoparticles suspended in toluene.

Double emulsion droplets were converted to nanoparticle colloidosomes by either exposing them to vacuum or to atmosphere overnight. The nanoparticle colloidosomes were then washed with a copious amount of deionized water to remove the remaining oil phase. The colloidosomes did not show any signs of aggregation, likely due to the PVA that adsorbed to the surface of colloidosomes. SEM was performed on a Zeiss Ultra55 field emission SEM at an acceleration voltage of 5 kV. Samples were coated with approximately 5–10 nm of gold.

Keywords:

capsules · colloids · emulsions · microfluidics · nanoparticles

- [1] A. D. Dinsmore, M. F. Hsu, M. G. Nikolaidis, M. Marquez, A. R. Bausch, D. A. Weitz, *Science* **2002**, *298*, 1006.
[2] A. Boker, J. He, T. Emrick, T. P. Russell, *Soft Matter* **2007**, *3*, 1231.

- [3] Y. Lin, H. Skaff, A. Boker, A. D. Dinsmore, T. Emrick, T. P. Russell, *J. Am. Chem. Soc.* **2003**, *125*, 12690.
[4] D. Y. Wang, H. W. Duan, H. Mohwald, *Soft Matter* **2005**, *1*, 412.
[5] D. Lee, D. A. Weitz, *Adv. Mater.* **2008**, *20*, 3498.
[6] A. S. Utada, E. Lorenceau, D. R. Link, P. D. Kaplan, H. A. Stone, D. A. Weitz, *Science* **2005**, *308*, 537.
[7] H. Skaff, Y. Lin, R. Tangirala, K. Breitenkamp, A. Boker, T. P. Russell, T. Emrick, *Adv. Mater.* **2005**, *17*, 2082.
[8] B. P. Binks, *Adv. Mater.* **2002**, *14*, 1824.
[9] A. Donev, I. Cisse, D. Sachs, E. Variano, F. H. Stillinger, R. Connelly, S. Torquato, P. M. Chaikin, *Science* **2004**, *303*, 990.
[10] J. W. Kim, R. J. Larsen, D. A. Weitz, *Adv. Mater.* **2007**, *19*, 2005.
[11] T. W. Secomb, *Cell Biophys.* **1991**, *18*, 231.
[12] D. Halpern, T. W. Secomb, *J. Fluid Mech.* **1991**, *231*, 545.
[13] Z. H. Nie, S. Q. Xu, M. Seo, P. C. Lewis, E. Kumacheva, *J. Am. Chem. Soc.* **2005**, *127*, 8058.
[14] P.-G. de Gennes, F. Brochart-Wyart, D. Quere, *Capillarity and Wetting Phenomena: Drops, Bubbles, Pearls, Waves*, Springer, New York **2003**.
[15] L. Y. Chu, A. S. Utada, R. K. Shah, J. W. Kim, D. A. Weitz, *Angew. Chem. Int. Ed.* **2007**, *46*, 8970.
[16] Z. H. Nie, J. Il Park, W. Li, S. A. F. Bon, E. Kumacheva, *J. Am. Chem. Soc.* **2008**, *130*, 16508.
[17] A. S. Utada, A. Fernandez-Nieves, H. A. Stone, D. A. Weitz, *Phys. Rev. Lett.* **2007**, *99*, 4.
[18] A. W. Adamson, *Physical Chemistry of Surfaces*, 3rd ed, Wiley, New York **1976**.
[19] A. B. Subramaniam, M. Abkarian, L. Mahadevan, H. A. Stone, *Nature* **2005**, *438*, 930.
[20] J.-W. Kim, D. Lee, H. C. Shum, D. A. Weitz, *Adv. Mater.* **2008**, *20*, 3239.
[21] N. Tsapis, D. Bennett, B. Jackson, D. A. Weitz, D. A. Edwards, *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 12001.
[22] V. N. Manoharan, M. T. Elsesser, D. J. Pine, *Science* **2003**, *301*, 483.
[23] E. Lauga, M. P. Brenner, *Phys. Rev. Lett.* **2004**, *93*, 4.
[24] S. Okushima, T. Nisisako, T. Torii, T. Higuchi, *Langmuir* **2004**, *20*, 9905.
[25] B. P. Binks, A. K. F. Dyab, P. D. I. Fletcher, in *Third World Congress of Emulsions*, CME, Lyon, France **2002**.

Received: February 28, 2009
Published online: April 16, 2009