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Hole-Shell Microparticles from Controllably Evolved Double Emulsions

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ABSTRACT

In this work, we report a versatile strategy for fabrication of highly controlled hole-shell microparticles with a hollow core and a single, precisely-determined hole in the shell, and with simultaneous, independent control of the properties of the core interface. W/O/W double emulsions from capillary microfluidics are used as initial templates for the microparticles. By controlling the composition of organic middle phase, we vary the adhesion energy between the inner drop and outer phase to control the evolution of the emulsions from initial core-shell to desired acorn-shaped configuration; this produces versatile emulsion templates for controllable fabrication of monodisperse hole-shell microparticles with advanced shapes. Further adjustment of the hole-shell structures can be achieved by changing the size and number of the inner drop via tuning flow rates. Independent control of the interfacial property of the core is achieved by incorporating functional nanoparticles such as thermo-responsive nanogels and gold nanoparticles in the inner drop to coat only the core surface for modification. The hole-shell microparticles enable capture of living cells, size-match capture and size-classification of microspheres, and confined synthesis of functional materials. These microparticles create new opportunities as microcontainers for controlled capture/release, and as microreactors for catalysis and confined reaction. This approach based on controllably evolved double emulsions provides full versatility a versatile for preparation of hole-shell microparticles with advanced shapes and specific functions.

1. INTRODUCTION

Polymeric core-shell microparticles with hollow interiors have great potential for use as microencapsulation systems for controlled load/release (Im 2005, Zhu 2005, Amstad 2012), active protection (De Rose 2008), and confined microreaction (Ota 2009). Core-

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shell structures with solid shells provide effective encapsulation performance; however, transport of the encapsulants through the shell is more difficult to achieve. Addition of holes in the shell can provide more versatility for the microparticles by facilitating the mass transport through the shell based on size or functional selectivity of the holes; this produces microparticles with porous shells for myriad uses including controlled capture of particles (Im 2005, Ma 2012), controlled release of active molecules and very small particles (Chu 2002, Dinsmore 2002), and removal of pollutants (Guan 2007). Additional utility of these microparticles can be achieved through finer control of the holes in the shell: For example, a single, defined hole can provide a very versatile structure for selectively capturing particles for classification and separation, or capturing cells for confined culture. Even more versatility can be obtained through control of the shape of the hollow core: For example, microparticles with a dimple-shaped core is useful for size-selective capture of colloidal particles, whereas microparticles with a fishbowl-shaped core is more useful for loading objects such as cells and confining microreaction. Finally to make these structures fully functional, it is also desirable to control the interfacial properties of the core to enable precise interactions between encapsulants and the solid shell.

Colloidal-scale core-shell microparticles with a single hole in the shell are typically made with particle or emulsion-template methods: Polymerization-induced buckling of silicon drops (Sacanna 2010), freeze-drying solvent-swollen polymeric particles (Im 2005, Yin 2008), self-assembly of phase-separated polymers (Minami 2005), diffusion-induced escape of monomers (Han 2006) or solvents (Yow 2008, Lim 2009, Li 2011) from the microparticles during fabrication, selective polymerization of phase-separated drops (Ma 2003), and other means to control the phase behavior of the templates (Guan 2007, Chang 2010, Zhu 2011). These microparticles provide excellent performance when sizes less than a few microns are required. By contrast, larger microparticles provide additional versatility when the size requirements are not constrained to very small particles. These microparticles are typically formed using emulsion drops as templates and have sizes of tens of microns or larger. Even finer control over the monodispersity of the microparticles is achieved using microfluidic techniques to produce the emulsion templates (Utada 2005, Chu 2007, Wang 2011). The microparticle structure strongly depends on the configuration between the core-drop and shell-drop in the emulsion templates. With shell-drop partially wetted on the core-drop, organic-biphasic Janus drops produce truncated-sphere-shaped microparticles (Nie 2005, Nisisako 2007, Kim 2011, Lan 2012). With completely wetted core-shell configurations, aqueous-biphasic drops and water-in-oil-in-water (W/O/W) double emulsions respectively produce bowl-shaped (Ma 2012) and fishbowl-shaped (Wang 2012) microparticles. Surface modification of these microparticles has been recently achieved by introducing functional nanoparticles such as SiO_2 nanoparticles in the organic phase of emulsion templates (Kim 2011, Lan 2012, Wang 2012). Full versatility of the microparticles demands accurate and independent control of the shape and size of both the single-hole and the hollow-core, as well as the functionality of the core surface; this requires precise control of the configurations and interfacial properties of the emulsion templates. However, techniques to achieve this sort of fine control do not exist.

In this paper, we report a versatile strategy for fabrication of highly controlled hole-shell microparticles with a hollow core and a single, precisely-determined hole, and with simultaneous, independent control of the properties of the core interface. W/O/W double emulsions from capillary microfluidics are used as initial templates for the microparticles. By controlling the composition of organic middle phase, we vary the adhesion energy ΔF (Aronson 1980, Poulin 1998) between the inner drop and outer phase to control the evolution of the emulsions from initial core-shell to desired acorn-shaped configuration; this produces versatile emulsion templates for controllable fabrication of monodisperse hole-shell microparticles with advanced shapes. Further adjustment of the hole-shell structures can be achieved by changing the size and number of the inner drop via tuning flow rates. By incorporating nanoparticles in the inner drop, we controllably coat only the interface of the hollow core, thereby simultaneously, but independently controlling the interfacial properties. This method provides full versatility for preparation of hole-shell microparticles with single-hole in the shell.

2. HOLE-SHELL MICROPARTICLES WITH PRECISELY CONTROLLED STRUCTURES AND FLEXIBLY MODIFIED CORE SURFACE

We demonstrate the excellent controllability of our technique by starting with preparation of hole-shell microparticles from ordinary core-shell W/O/W emulsions. Capillary microfluidic device is used to generate monodisperse emulsion templates (Fig. 1a). Aqueous solution with 1 % (w/v) Pluronic F127 and 5 % (w/v) glycerol is used as the outer fluid (O.F.). Photocurable ethoxylated trimethylolpropane triacrylate (ETPTA) monomer with 1 % (v/v) 2-hydroxy-2-methyl-1-phenyl-1-propanone is used as the middle fluid (M.F.). Aqueous solution containing 0.01 g/mL fluorescein-isothiocyanate-labelled poly(*N*-isopropylacrylamide-*co*-methyl methacrylate-*co*-allylamine) (FITC-PNIPAM) nanogels is used as the inner fluid (I.F.). Drops of I.F. are first generated in the transition tube (Fig. 1b), with nanogels absorbed at the drop surface for stabilization. Then these water drops are encapsulated in the oil shell of M.F., resulting in monodisperse core-shell W/O/W emulsions (Fig. 1c,d). After collected in vessels, the inner drop is drawn to top of the oil shell due to density mismatch between I.F. and M.F. (Figs. 1e1 and 2b1). Polymerization of the eccentric core-shell emulsions by UV-irradiation for 5 min produces fishbowl-shaped microparticles with large hollow-core and small single-hole in the shell (Figs. 1e4 and 2e). The single-hole formation is due to the volume contraction and fast polymerization (within ~1 s) (Kim 2008) of the oil shell under UV light. The volume of oil shell decreases to ~59.1 vol.% after polymerization; this squeezes the inner drop out of the oil shell, while the fast *in situ* polymerization fixes this morphology and produces hollow microparticles with single-hole.

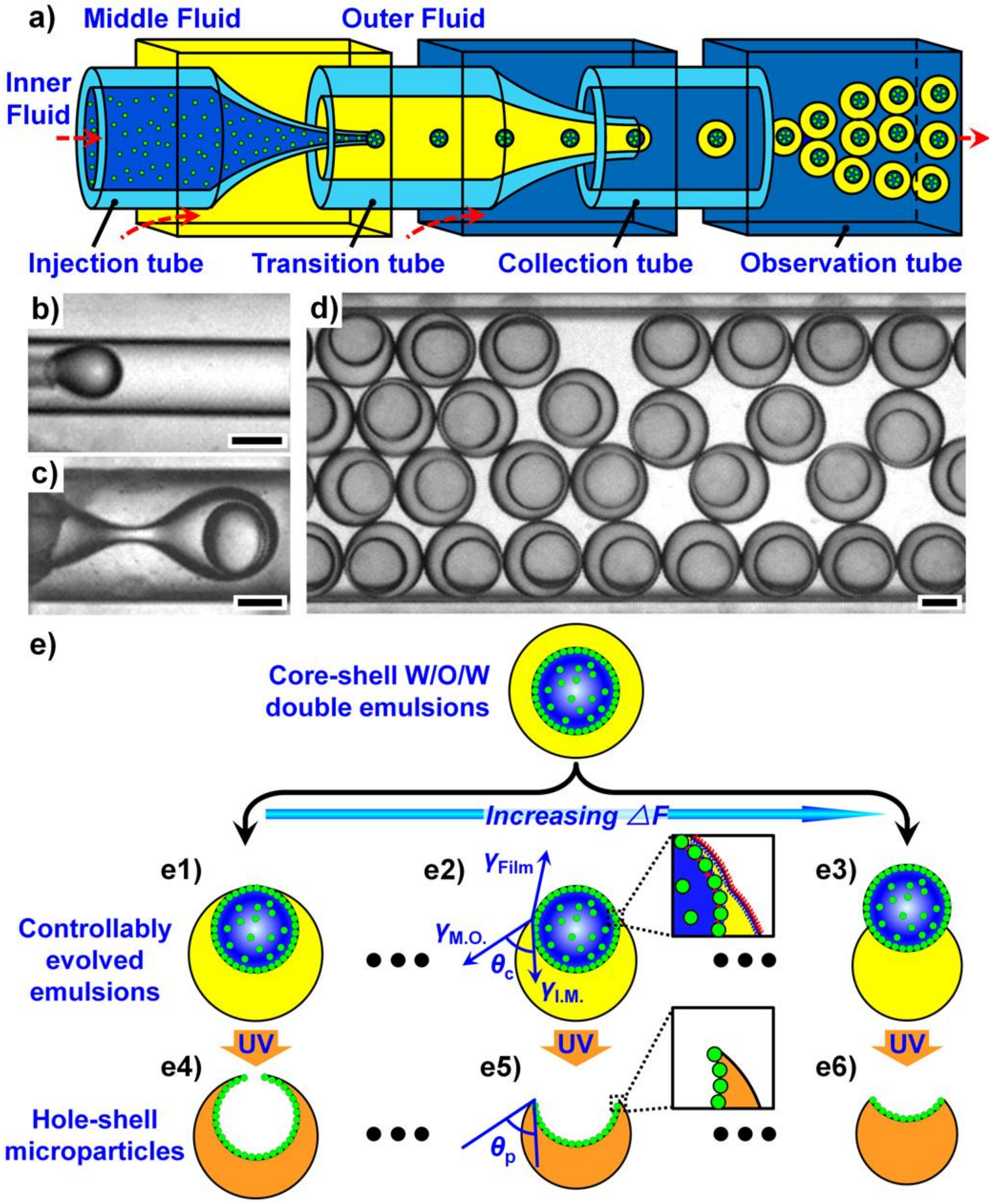

Fig. 1 Strategy for fabricating desired hole-shell microparticles from controllably evolved W/O/W emulsions. (a) Microfluidic device for generating monodisperse W/O/W emulsions with nanoparticle-containing inner drop. (b-d) Optical micrographs showing the generation of inner drops (b) and core-shell W/O/W emulsions (c,d). (e) Schematic illustration showing the template synthesis of hole-shell microparticles from controllably evolved W/O/W emulsions, with functional nanoparticles dispersed in the inner drop for modifying the core surface. Scale bars are 100 μm.

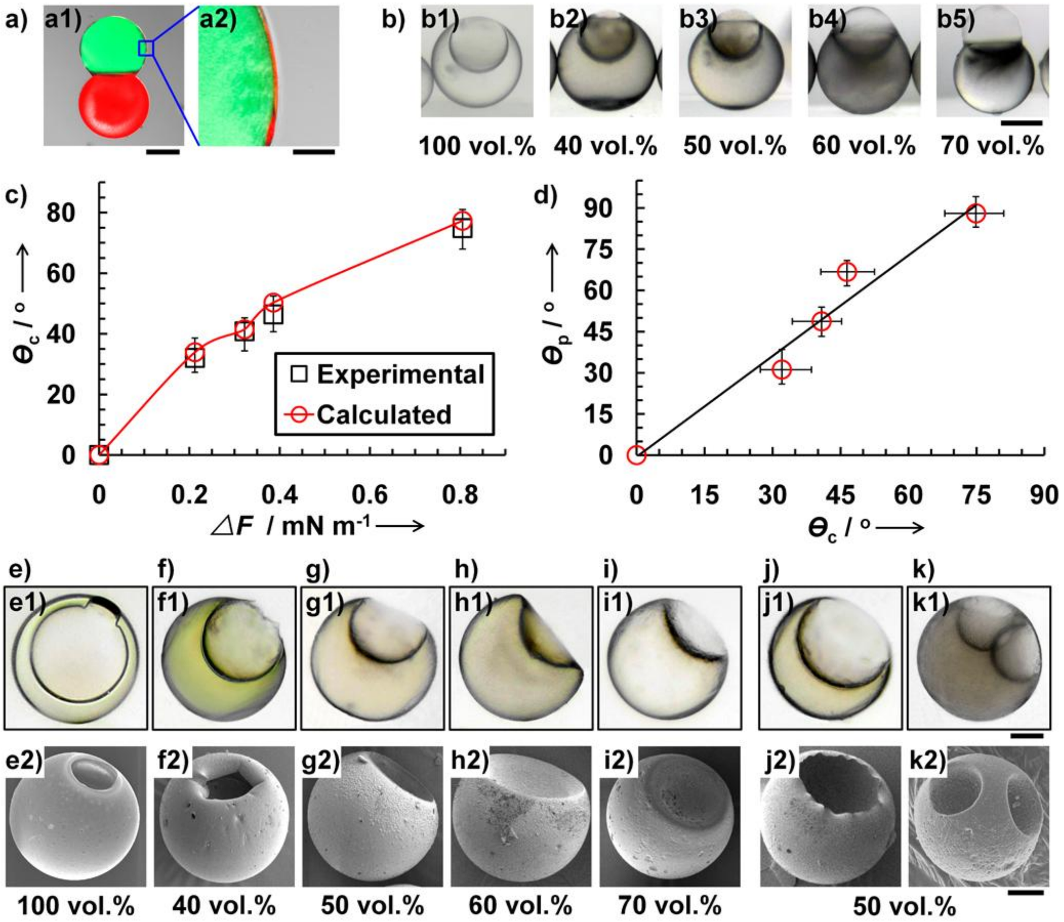

Fig. 2 Template synthesis of hole-shell microparticles from controllably evolved W/O/W emulsions. (a) CLSM images of evolved W/O/W emulsions with inner drop containing FITC-PNIPAM nanogels and oil shell containing fluorescent dye. Scale bar is 100 µm in a1, and 20 µm in a2. (b) Optical micrographs of side views of evolved W/O/W emulsions with oil phase containing different ETPTA fractions. Scale bar is 100 µm. (c) Effect of adhesion energy ΔF on the θ_c of W/O/W emulsions; the calculated θ_c values are obtained from the force balance of $\gamma_{I.M.}$, $\gamma_{M.O.}$ and γ_{Film} with an equation of $\theta_c = \arccos[(\gamma_{Film}^2 - \gamma_{I.M.}^2 - \gamma_{M.O.}^2)/2\gamma_{I.M.}\gamma_{M.O.}]$. (d) Relationship between the measured θ_p of microparticles and the measured θ_c of the emulsion templates. (e-i) Optical (e1-i1) and SEM (e2-i2) images of microparticles with fishbowl shape (e), bowl shape (f,g) and truncated-sphere shape (h,i). (j) Hole-shell microparticles with large core and large hole that fabricated by increasing the inner drop volume of emulsions. (k) Microparticles with dual hole-shell structures that fabricated by increasing the inner drop number of emulsions. Scale bars are 50 µm in e-k.

Controllable evolution of the W/O/W emulsions from core-shell to acorn-shaped configuration is achieved by inducing adhesion of the aqueous inner drop with outer phase. Organic solvent benzyl benzoate with ETPTA-poorly-dissolved surfactant polyglycerol polyricinoleate (PGPR) is added into the ETPTA as the M.F.. The poorly solubility of ETPTA for PGPR reduces the solvent quality and leads to adhesion of the inner drop with outer phase (Fig. 2a). The thin oil film that separates the inner drop and outer phase (Fig. 2a2) is associated with an adhesion energy (Aronson 1980, Poulin 1998):

$$\Delta F = \gamma_{\mathrm{I.M.}} + \gamma_{\mathrm{M.O.}} - \gamma_{\mathrm{Film}} \qquad (1)$$

where $\gamma_{\mathrm{I.M.}}$ and $\gamma_{\mathrm{M.O.}}$ are respectively the interfacial tensions between inner-middle and middle-outer phases, and γ_{Film} is the tension of the thin film. This ΔF is directly reflected by the contact angle θ_c between the adhesive inner drop and outer phase (Fig. 1e2) (Bremond 2012), which also defines the shape angle θ_p of the resultant hole-shell microparticles (Fig. 1e5). Thus, precise control of ΔF allows controllable evolution of the W/O/W emulsions for synthesis of hole-shell microparticles with advanced shapes (Fig. 1e). Moreover, the core surface of the microparticles can be independently modified by introducing nanoparticles into the inner drop and fixing them at the W/O interface by polymerization.

Precise control of the evolved emulsion morphologies is studied by investigating θ_c as a function of ΔF (Fig. 2b,c). For ΔF calculation, $\gamma_{\mathrm{I.M.}}$ and $\gamma_{\mathrm{M.O.}}$ are measured by pendent drop method; γ_{Film} is obtained from adhesion experiments of I.F. and O.F. drops in M.F. phase according to force balance (Aronson 1980, Poulin 1998). Precise manipulation of θ_c is achieved by tuning ΔF through adjustment of ETPTA fraction. For core/shell emulsions with 100 vol.% ETPTA as shell (Fig. 2b1), $\theta_c=0^o$ is observed (theoretically $\Delta F=0$). For acorn-shaped emulsions with mixed oil shell, the θ_c value increases with increasing the ΔF simply (Fig. 2b2-b5). The experimental θ_c results show good agreement with their calculated values (Fig. 2c). With precisely manipulated θ_c, these evolved emulsions enables synthesis of hole-shell microparticles with controlled θ_p for structure control (Fig. 2d). This produces controllable hole-shell microparticles, ranging from bowl shape (Fig. 2f,g), to truncated-sphere shape (Fig. 2h,I). The slight buckling at the hole mouth observed in Fig. 2f is due to the low mechanical strength caused by low ETPTA fraction. The microparticles and their holes show good monodispersity; for example, the coefficient of variation (*CV*) values of the sizes of microparticles and their holes shown in Fig. 2g are as low as 1.35 % and 2.26 % respectively. Moreover, besides fishbowl-shaped microparticles with large core and small hole, change of the inner drop volume by tuning flow rates allows creating large core and large hole within microparticles (Fig. 2j). Meanwhile, change of the inner drop number allows producing microparticles with dual hole-shell structures (Fig. 2k).

Flexibility of our strategy for independently modifying the core surface of hole-shell microparticles is first demonstrated by coating the core surface with FITC-PNIPAM nanogels. As confirmed by SEM, microparticles are featured with smooth outer surface (Fig. 3a) and rough core surface with densely-packed nanogels (Fig. 3b). The locations of FITC-PNIPAM nanogels in CLSM images (Fig. 3c,d) also prove their presence on the core surface. With thermo-responsive hydrophilic/hydrophobic transitions, these anchored nanogels would allow wettability control of the modified core surface by changing temperature. Since cell behaviours can be influenced by surface wettability (Sun 2011), the microparticles with such a controllable wettability would be potential for cell capture and confined culture. The cell capture is demonstrated by capturing algae cells (Fig. 3e) inside the microparticles. Versatility of our modification strategy is demonstrated by using gold nanoparticles with excellent catalytic property (Daniel 2004) for modifying the core surface (Fig. 3f).

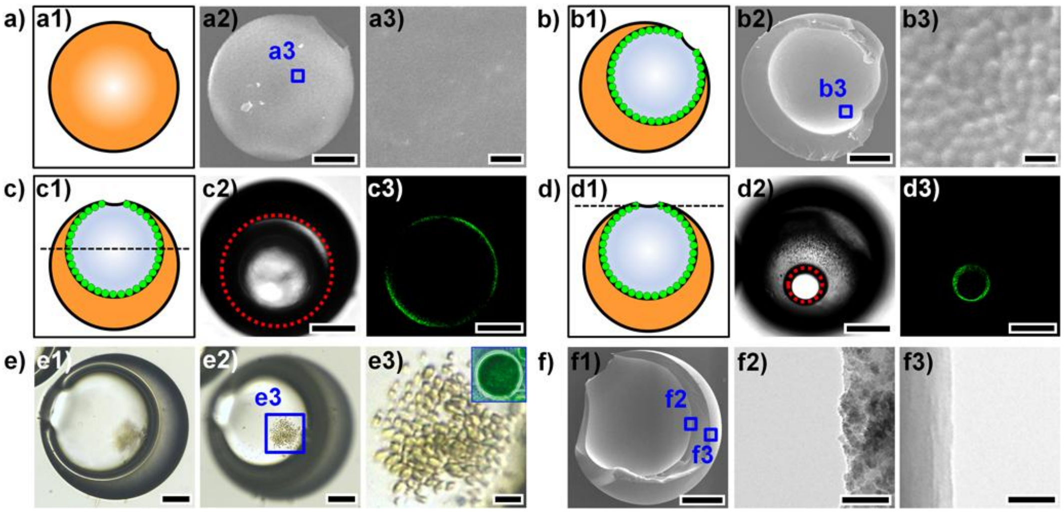

Fig. 3 Hole-shell microparticles with core surface independently modified with tunable functionalities. (a,b) Schematics (a1,b1) and SEM images of smooth outer surface (a2,a3) and core surface modified with FITC-PNIPAM nanogels (b2,b3). (c,d) Schematics and CLSM images that focus on the equator cross-section of hollow-core (c) and the hole mouth (d). The red circles in c2 and d2 mark the location of FITC-PNIPAM nanogels shown in the CLSM fluorescent images (c3,d3). (e) Optical micrographs of hole-shell microparticles loaded with algae cells. (f) SEM (f1) and TEM (f2, f3) images of hole-shell microparticle (f1) with gold-nanoparticle-modified core surface (f2) and unmodified outer surface (f3). Scale bars are 500 nm in a3 and b3, 10 μm in e3, 50 nm in f2 and f3, and 50 μm for the rest.

To further illustrate the diverse uses of hole-shell microparticles, demonstrations are performed on selective capture of microspheres, and confined synthesis of functional materials. Under ultrasonic-treatment, microspheres with size fitting the hole and core can be trapped into hole-shell microparticles based on “lock-key” size-match for 1:1 capture (Fig. 4a). Driven by ultrasonic vibration, the size-screening effect of the hole allows selective loading of microspheres smaller than the hole size (red colour) from larger ones in water for size-classification (Fig. 4b). Furthermore, we employ the hole-shell microparticles as microreactors for confined synthesis of thermo-responsive microgels inside the core as smart gate for “open-close” control of the hole (Fig. 4c), which provides a simple way to control the mass transfer into and out of the core.

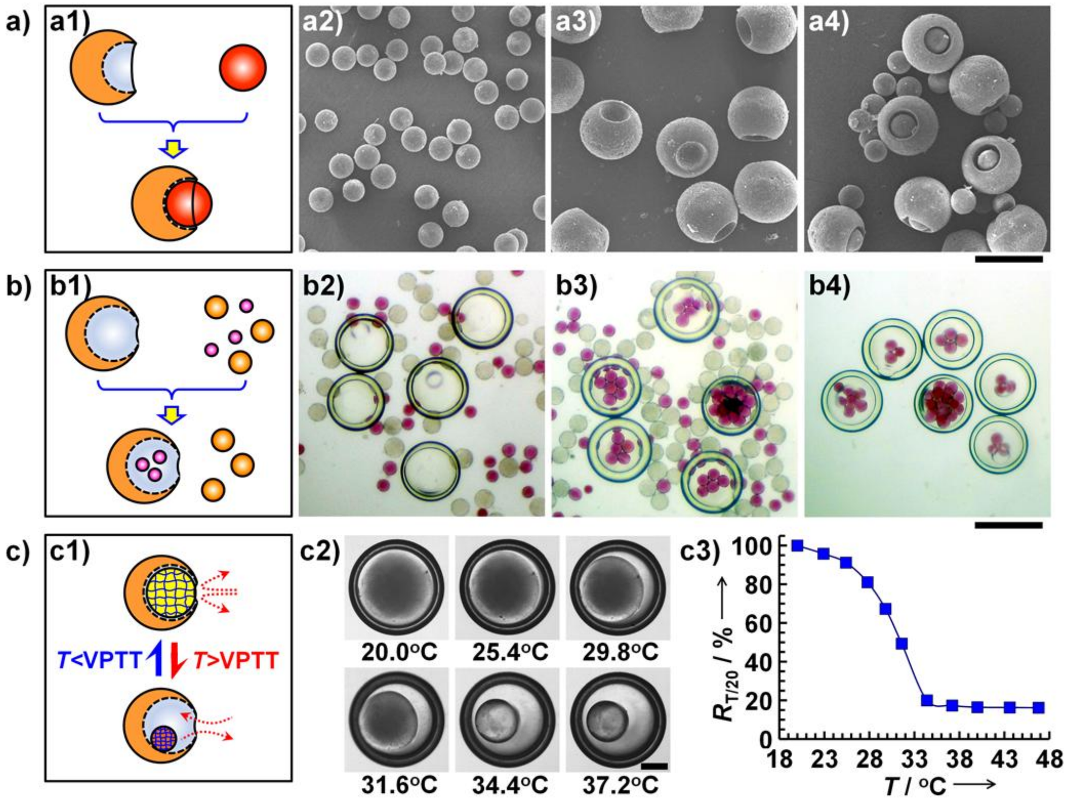

Fig. 4 Hole-shell microparticles for controlled capture (a), size-classification (b) and confined microreaction (c). (a) SEM images showing bowl-shaped microparticles capture microspheres based on “lock-key” size-match. (b) Optical micrographs showing fishbowl-shaped microparticles selectively capture smaller microspheres from larger microspheres for size-classification. (c) Confined synthesis of PNIPAM microgel in fishbowl-shaped microparticle for achieving thermo-responsive “open-close” control of the hole. Optical micrographs (c2) and temperature-dependent volume change curve (c3, $R_{T/20}$ is the ratio of microgel volume at T ^{o}C to that at 20 ^{o}C) showing excellent thermo-responsive property of the inside PNIPAM microgel. Scale bars are 200 μm in a and b, and 50 μm in c.

3. CONCLUSIONS

In summary, monodisperse hole-shell microparticles with precisely controlled structure and flexibly modified core surface have been fabricated by using controllably evolved W/O/W emulsions as templates. We achieve accurate control of the hole-shell structures by manipulating the adhesion-energy-dependent configuration of W/O/W emulsions with designer compositions. Further control of the hole-shell structure can be achieved by tuning the volume and number of the inner drop. Independent control of the interfacial property of the core is achieved by incorporating functional nanoparticles such as thermo-responsive nanogels and gold nanoparticles in the inner drop to coat only the core surface for modification. The hole-shell microparticles enable capture of living cells, size-match capture and size-classification of microspheres, and confined synthesis of functional materials. These microparticles create new opportunities as microcontainers for controlled capture/release, and as microreactors for catalysis and confined reaction. This approach based on controllably evolved double emulsions provides a versatile and promising way to fabricate hole-shell microparticles with advanced shapes and specific functions.

REFERENCES

Amstad, E., Kim, S.-H. and Weitz, D. A. (2012), "Photo- and Thermoresponsive Polymersomes for Triggered Release", Angewandte Chemie-International Edition, 51(50), 12499-12503.

Aronson, M. P. and Princen, H. M. (1980), "Contact angles associated with thin liquid films in emulsions", Nature, 286(5771), 370-2.

Bremond, N. and Bibette, J. (2012), "Exploring emulsion science with microfluidics", Soft Matter, 8(41), 10549-10559.

Chang, M.-W., Stride, E. and Edirisinghe, M. (2010), "A New Method for the Preparation of Monoporous Hollow Microspheres", Langmuir, 26(7), 5115-5121.

Chu, L.-Y., Utada, A. S., Shah, R. K., Kim, J.-W. and Weitz, D. A. (2007), "Controllable monodisperse multiple emulsions", Angewandte Chemie-International Edition, 46(47), 8970-8974.

Chu, L. Y., Yamaguchi, T. and Nakao, S. (2002), "A molecular-recognition microcapsule for environmental stimuli-responsive controlled release", Advanced Materials, 14(5), 386-389.

Daniel, M. C. and Astruc, D. (2004), "Gold nanoparticles: Assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology", Chemical Reviews, 104(1), 293-346.

De Rose, R., Zelikin, A. N., Johnston, A. P. R., Sexton, A., Chong, S.-F., Cortez, C., Mulholland, W., Caruso, F. and Kent, S. J. (2008), "Binding, Internalization, and Antigen Presentation of Vaccine-Loaded Nanoengineered Capsules in Blood", Advanced Materials, 20(24), 4698-4703.

Dinsmore, A. D., Hsu, M. F., Nikolaides, M. G., Marquez, M., Bausch, A. R. and Weitz, D. A. (2002), "Colloidosomes: Selectively permeable capsules composed of colloidal particles", Science, 298(5595), 1006-1009.

Guan, G., Zhang, Z., Wang, Z., Liu, B., Gao, D. and Xie, C. (2007), "Single-hole hollow polymer microspheres toward specific high-capacity uptake of target species", Advanced Materials, 19(17), 2370-2374.

Han, J., Song, G. and Guo, R. (2006), "A facile solution route for polymeric hollow spheres with controllable size", Advanced Materials, 18(23), 3140-3144.

Im, S. H., Jeong, U. Y. and Xia, Y. N. (2005), "Polymer hollow particles with controllable holes in their surfaces", Nature Materials, 4(9), 671-675.

Kim, S.-H., Jeon, S.-J. and Yang, S.-M. (2008), "Optofluidic encapsulation of crystalline colloidal arrays into spherical membrane", Journal of the American Chemical Society, 130(18), 6040-6046.

Kim, S.-H., Abbaspourrad, A. and Weitz, D. A. (2011), "Amphiphilic Crescent-Moon-Shaped Microparticles Formed by Selective Adsorption of Colloids", Journal of the American Chemical Society, 133(14), 5516-5524.

Lan, W., Li, S., Xu, J. and Luo, G. (2012), "A one-step microfluidic approach for controllable preparation of nanoparticle-coated patchy microparticles", Microfluidics and Nanofluidics, 13(3), 491-498.

Li, M. and Xue, J. (2011), "Facile Route to Synthesize Polyurethane Hollow Microspheres with Size-Tunable Single Holes", Langmuir, 27(7), 3229-3232.

Lim, Y. T., Kim, J. K., Noh, Y.-W., Cho, M. Y. and Chung, B. H. (2009), "Multifunctional Silica Nanocapsule with a Single Surface Hole", Small, 5(3), 324-328.

Ma, G. H., Su, Z. G., Omi, S., Sundberg, D. and Stubbs, J. (2003), "Microencapsulation of oil with poly(styrene-N,N-dimethylaminoethyl methacrylate) by SPG emulsification technique: Effects of conversion and composition of oil phase", Journal of Colloid and Interface Science, 266(2), 282-294.

Ma, S., Thiele, J., Liu, X., Bai, Y., Abell, C. and Huck, W. T. S. (2012), "Fabrication of Microgel Particles with Complex Shape via Selective Polymerization of Aqueous Two-Phase Systems", Small, 8(15), 2356-2360.

Minami, H., Kobayashi, H. and Okubo, M. (2005), "Preparation of hollow polymer particles with a single hole in the shell by SaPSeP", Langmuir, 21(13), 5655-5658.

Nie, Z. H., Xu, S. Q., Seo, M., Lewis, P. C. and Kumacheva, E. (2005), "Polymer particles with various shapes and morphologies produced in continuous microfluidic reactors", Journal of the American Chemical Society, 127(22), 8058-8063.

Nisisako, T. and Torii, T. (2007), "Formation of biphasic Janus droplets in a microfabricated channel for the synthesis of shape-controlled polymer microparticles", Advanced Materials, 19(11), 1489-1493.

Ota, S., Yoshizawa, S. and Takeuchi, S. (2009), "Microfluidic Formation of Monodisperse, Cell-Sized, and Unilamellar Vesicles", Angewandte Chemie-International Edition, 48(35), 6533-6537.

Poulin, P. and Bibette, J. (1998), "Adhesion of water droplets in organic solvent", Langmuir, 14(22), 6341-6343.

Sacanna, S., Irvine, W. T. M., Chaikin, P. M. and Pine, D. J. (2010), "Lock and key colloids", Nature, 464(7288), 575-578.

Sun, T. and Qing, G. (2011), "Biomimetic Smart Interface Materials for Biological Applications", Advanced Materials, 23(12), H57-H77.

Utada, A. S., Lorenceau, E., Link, D. R., Kaplan, P. D., Stone, H. A. and Weitz, D. A. (2005), "Monodisperse double emulsions generated from a microcapillary device", Science, 308(5721), 537-541.

Wang, J., Hu, Y., Deng, R., Xu, W., Liu, S., Liang, R., Nie, Z. and Zhu, J. (2012), "Construction of multifunctional photonic crystal microcapsules with tunable shell structures by combining microfluidic and controlled photopolymerization", Lab on a Chip, 12(16), 2795-2798.

Wang, W., Xie, R., Ju, X.-J., Luo, T., Liu, L., Weitz, D. A. and Chu, L.-Y. (2011), "Controllable microfluidic production of multicomponent multiple emulsions", Lab on a Chip, 11(9), 1587-1592.

Yin, W. and Yates, M. Z. (2008), "Effect of interfacial free energy on the formation of polymer microcapsules by emulsification/freeze-drying", Langmuir, 24(3), 701-708.

Yow, H. N. and Routh, A. F. (2008), "Colloidal buckets formed via internal phase separation", Soft Matter, 4(10), 2080-2085.

Zhu, M.-Q., Chen, G.-C., Li, Y.-M., Fan, J.-B., Zhu, M.-F. and Tang, Z. (2011), "One-step template-free synthesis of monoporous polymer microspheres with uniform sizes via microwave-mediated dispersion polymerization", Nanoscale, 3(11), 4608-4612.

Zhu, Y. F., Shi, J. L., Shen, W. H., Dong, X. P., Feng, J. W., Ruan, M. L. and Li, Y. S. (2005), "Stimuli-responsive controlled drug release from a hollow mesoporous silica sphere/polyelectrolyte multilayer core-shell structure", Angewandte Chemie-International Edition, 44(32), 5083-5087.