Controllable microfluidic fabrication of microstructured functional materials

Cite as: Biomicrofluidics 14, 061501 (2020); doi: 10.1063/5.0027907

Submitted: 1 September 2020 · Accepted: 21 October 2020 ·

Published Online: 4 November 2020

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ABSTRACT

Microstructured functional materials such as microfibers and microparticles are widely used for a myriad of applications. Precise manipulation of the functional components and structure is important for the microstructured functional materials to achieve desired functions for advanced application. This review highlights the recent progress on the controllable microfluidic fabrication of microstructured functional materials from liquid templates. First, microfluidic strategies for controllable generation of liquid templates including laminar jets and emulsion droplets are introduced. Then, strategies for fabricating microfibers and microparticles with diverse structures and advanced functions from the liquid templates are highlighted. These strategies mainly focus on precisely engineering the functional components and microstructures of the microfibers and microparticles by tailoring those of their liquid templates to achieve desired advanced functions. Finally, future development of microfluidic techniques for industrial-scale production of the microstructured functional materials is discussed.

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I. INTRODUCTION

Microstructured functional materials such as microfibers and microparticles are widely used for a myriad of applications including drug delivery, separation, detection, and tissue engineering.^{1–5} Precise engineering of the functional components and microstructure of the micro-scaled functional materials can achieve desired advanced functions for their applications. For example, creation of tubular structures in microfibers can provide channel-like microspace for the loading of drugs and enzymes and transportation of substances.^{6–8} Creation of more complex structures such as bamboo-like and spider-silk-like structures in microfibers allows for efficient encapsulation of cells for tissue engineering and biomimetic collection of water from air.^{9–11} In microparticles, engineering of functional porous structures can provide a large functional surface area for interaction with target molecules for adsorption.³ Alternatively, creation of compartmental structures in microparticles can provide confined internal microspaces for encapsulation of actives, while the functional shell around the compartments can protect the barrier for protection of the active and control of their release characteristics.^{1,2} Thus, for these microstructured materials to achieve desired functions, fabrication techniques with high controllability on their compositions and microstructures are required.

Microfluidic techniques allow flexible and precise manipulation of the flow and dispersion of multiple liquids in microchannels to produce microscale liquid systems.^{2,12} These liquid microsystems, including continuous liquid jets and discrete emulsion droplets, provide excellent templates for developing functional microfibers and microparticles.^{13–15} For example, one liquid phase with a controllable volume can be well dispersed in another immiscible continuous phase by using microfluidics to generate uniform droplets of single emulsions.¹⁶ These single emulsion droplets can provide confined microspaces to incorporate functional components for template synthesis of microparticles, with composition, shape, and size similar as those of the droplet templates to achieve advanced functions.¹⁷ With microfluidics, multiple liquid phases can also be engineered in a single droplet to create multiple emulsion droplets, such as double emulsions, triple emulsions, and even high-ordered multiple emulsions. These multiple emulsions can provide phase-separated structures to incorporate different functional components, such as inorganic nanomaterials and polymers, into each of the separated phases and onto the interface between the phases for the synthesis of microparticles with more complex structures and diverse functions.^{1,18} As compared to emulsion droplets, the use of continuous jets from microfluidics as templates allows the fabrication of

functional microfibers.¹⁹ For example, one liquid phase can be hydrodynamically shaped into a continuous laminar jet by the flow of another liquid phase with microfluidics. By the use of fast solidification processes such as fast interfacial cross-linking, UV-polymerization, and solvent extraction, the laminar jet can be continuously converted into functional microfibers, with their composition, shape, and size similar as those of the jet templates.^{12,19} Moreover, by incorporating the laminar jet with another jet and droplets, more diverse structures and functional components can be integrated into the microfibers to achieve advanced functions.^{9–11} Therefore, with excellent manipulation of the composition, structure, shape, and size of the liquid microsystems, microfluidic techniques provide vast opportunities for flexible design and controllable fabrication of diverse microparticles and microfibers with advanced functions.

In this review, we summarize recent progress on the controllable fabrication of microstructured functional materials from liquid templates produced by microfluidics. First, microfluidic approaches for controllably generating liquid templates including continuous jets and discrete emulsion droplets are introduced. Then, based on the liquid templates, fabrication of microstructure functional materials including microfibers and microparticles with diverse structures and functions are highlighted. For these microfibers and microparticles, we focus on the strategies based on precisely engineering their functional components and microstructures by adjusting those of the liquid templates to achieve desired advanced functions. Finally, perspectives on the further advancing microfluidic techniques for developing advanced functional microfibers and microparticles are provided.

II MICROFLUIDIC GENERATION OF CONTROLLABLE EMULSION DROPLETS AND LAMINAR JETS

A. Generation of simple jets and emulsion droplets

Microfluidic techniques enable flexible manipulation of the flow of multiple liquids in microchannels to controllably generate continuous jets and discrete emulsion droplets (Fig. 1).^{1,12,20} The generation of jets and emulsion droplets usually requires a separate injection of two liquid phases in different microchannels of a microfluidic device. When the two different liquid phases contact at the junction of the two microchannels, jets or emulsion droplets can be generated depending on the flow rates and physical/chemical properties of the liquid phases. Typically, microfluidic devices with cross-junction geometry and co-flow geometry are used for jet generation.²¹ The liquid phase that flows in the center can be hydrodynamically shaped into a cylindrical jet by the liquid phase that flows in the surrounding [Fig. 1(a)].²¹ The laminar flow behavior of liquids in microchannel benefits the formation of stable continuous jets in a microfluidic device. Moreover, based on the effect of liquid rope coiling, a coiled jet can be generated in the microchannel by matching the viscosities and flow rates of two liquid phases.^{22–24} By simply changing the microchannel dimensions and flow rates, the diameter of the laminar jet and the pitch of the coiled jet can be precisely controlled. These controllable jets can serve as templates for continuous synthesis of functional microfibers.

Emulsions are mixture systems with immiscible liquid phases, containing amphiphilic surfactants or nanoparticles for interfacial stabilization. Typically, by dispersing one liquid phase into another

immiscible one via shaking or stirring, simple single emulsions, such as water-in-oil (W/O) and oil-in-water (O/W) emulsions, can be produced. However, such preparation methods usually suffer from poor control over the shearing forces on the dispersed phase, leading to emulsion droplets with uncontrollable sizes and size distributions. With microfluidics to provide excellent control over the shearing process, the formation of each droplet can be precisely manipulated to produce monodisperse droplets with controllable sizes and size distributions. The microfluidic geometries used for droplet generation usually include the T-junction geometry, cross-junction geometry, co-flow geometry, and flow-focusing geometry.^{2,3} Typically, in a co-flow microfluidic device, the inner liquid phase that flowed in the injection capillary can be emulsified into uniform droplets by the outer liquid phase flowed in the collection capillary [Figs. 1(e) and 1(f)]. With proper wettability modification of the microchannel surfaces, each of these geometries can manipulate the flow of water and oil phases to controllably produce uniform W/O and O/W emulsion droplets. These controllable emulsion droplets are promising for template synthesis of functional microparticles.

B. Generation of complex jets and emulsion droplets

One of the great advantages of microfluidic techniques is their high scalability for controllable creation of complex liquid systems with diverse structures.^{25–27} The microfluidic geometries can be flexibly assembled to construct advanced microfluidic devices for generation of jets and emulsion droplets with desired complex structures. For generation of complex jets, a sequential arrangement of microfluidic geometries is usually required to manipulate multiple liquid phases. For example, a two-stage co-flow microfluidic device can be constructed by sequentially and coaxially assembling two co-flow geometries. The laminar jet formed in the first geometry can be encapsulated into another jet formed in the second geometry to produce a tubular jet [Fig. 1(b)].²⁸ Alternatively, the first co-flow geometry can be used to generate uniform droplets; these droplets can then be encapsulated into the jet created in the second co-flow geometry to produce a droplet-containing jet [Fig. 1(c)].¹⁰ Similarly, the droplet-containing jet can also be manipulated into a coiled jet based on the effect of liquid rope coiling [Fig. 1(d)].²⁹ With fine adjustment of the flow rate of each phase, the diameter of the jet and the inner droplets, the shell thickness, the distance between every two droplets, and the pitch of the coiled jet can be flexibly manipulated.

Scale-up of the microfluidic device by sequential and parallel arrangement of the microfluidic geometries enables the production of highly controllable multiple emulsion droplets. By combining two microfluidic geometries, uniform droplets generated in the first geometry can be encapsulated into the larger droplets from the second geometry. Such a sequential emulsification process can produce double emulsions with droplet-in-droplet structures [Fig. 1(g)].²⁶ With excellent control over each emulsification step, the double emulsions from microfluidic techniques show a highly controllable size and size distribution for their inner and outer droplets. Meanwhile, because the droplets are periodically generated in each geometry, by synchronizing the droplet-generating frequency in each geometry, the number of inner droplets in double emulsions can be accurately

FIG. 1. Controllable microfluidic generation of laminar jets and emulsion droplets. (a)–(c) Microfluidic generation of a laminar jet (a), a tubular jet (b), and a droplet-containing jet (c).^{28,33} Image (a) is reproduced with permission from Wu *et al.*, *J. Mater. Chem. B* **4**(16), 2455–2465 (2016). Copyright 2016 Royal Society of Chemistry. Images (b) and (c) are reproduced with permission from He *et al.*, *RSC Adv.* **5**(2), 928–936 (2015). Copyright 2015 Royal Society of Chemistry. (d) Microfluidic generation of a coiled jet containing deformed droplets.²⁹ Image (d) is reproduced with permission from Cai *et al.*, *ACS Appl. Mater. Interfaces* **11**(49), 46241–46250 (2019). Copyright 2019 American Chemical Society. Microfluidic generation of single [(e) and (f)], double [(g) and (h)], triple (i), and quadruple emulsion droplets (j).^{1,18,25,26,59} Images (e), (g), (i), and (j) are reproduced with permission from He *et al.*, *Adv. Mater. Technol.* **4**(6), 1800687 (2019). Copyright 2019 Wiley-VCH; Chu *et al.*, *Angew. Chem. Int. Ed.* **46**(47), 8970–8974 (2007). Copyright 2007 Wiley-VCH; and Mou *et al.*, *Adv. Sci.* **5**(6), 1700960 (2018). Copyright 2018 Wiley-VCH. Image (f) is reproduced with permission from Deng *et al.*, *Lab Chip* **11**, 3963–3969 (2011). Copyright 2011 Royal Society of Chemistry.⁶¹ Image (h) is reproduced with permission from Wang *et al.*, *Lab Chip* **11**(9), 1587–1592 (2011). Copyright 2011 Royal Society of Chemistry.

controlled. Moreover, by using a Y-junction geometry to connect two parallel co-flow geometries with a third one, double emulsions containing two types of inner droplets can be produced [Fig. 1(h)].²⁵ The two different types of droplets from the two parallel geometries can

be converged by the Y-junction and then encapsulated into the droplets formed in the third geometry to create double emulsions with distinct inner droplets. By matching the droplet-generating frequency of the three geometries, the number of each type of the droplets can

be precisely controlled. The double emulsions with two distinct droplets can also be created by using a capillary with θ -shaped dual-microchannels or two capillaries inserted in another capillary for generating the different inner droplets.^{30,31} The scale-up strategies for microfluidic devices can be further extended to controllably produce more complex high-order multiple emulsions such as triple emulsions [Fig. 1(i)],²⁶ quadruple emulsions [Fig. 1(j)],¹⁸ and quintuple emulsions,³² by increasing the number of microfluidic geometries for sequential and parallel arrangement. These highly controllable complex jets and multiple emulsion droplets from microfluidics provide diverse templates for fabrication of functional microfibers and microparticles.

III. CONTROLLABLE MICROFLUIDIC FABRICATION OF FUNCTIONAL MICROFIBERS FROM LAMINAR JETS

A. Functional microfibers with solid and tubular structures

Functional microfibers are widely used in myriad fields such as separation, energy storage, tissue engineering, and wound healing. Although traditional fabrication methods such as electrospinning and wet spinning can produce microfibers from a wide range of materials, the precise creation of microfibers with controllable internal microstructures still remains a challenge. The controllable jet templates from microfluidics enable continuous spinning of microfibers with diverse structures and functions.¹² Generally, by incorporating functional components into the laminar jets from microfluidics, functional microfibers can be fabricated via fast solidification processes. The laminar jets can usually achieve stable interfaces with the shearing of outer continuous flow in microchannels; thus, fast solidification of the jet templates is required for *in situ* synthesis of functional microfibers in the microfluidic device. Due to the tendency to achieve minimized interfacial energy, the cross section of the jet usually exhibits a circular shape. This allows production of microfibers with a cylindrical shape from these jet templates [Fig. 2(a)].³³ The diameter of the microfiber can be precisely and flexibly controlled by adjusting the flow rates of the liquid phases and microchannel dimensions of the injection and collection capillaries. Similarly, fast solidification of coiled jets in a microfluidic device can produce microfibers with a helical structure and circular cross section [Fig. 2(b)].^{22–24} Moreover, by manipulating the cross section of the microchannel for ejecting the jets, microfibers with non-circular cross sections, such as belt-like microfibers,³⁴ can also be produced by capturing the unstable jet interface via fast solidification immediately after the jet formation at the exit of the microchannel. The mild shearing conditions afforded by the laminar multiphase flows in microchannel provide a suitable microenvironment for efficient encapsulation of vulnerable cells and biomaterials in the resultant microfibers.

With tubular jets from microfluidics as templates, functional hollow microfibers can be fabricated by incorporating functional components into the outer sheath phase of the tubular jet. For example, tubular chitosan microfibers are fabricated by using a tubular jet with an outer sheath phase containing chitosan [Fig. 2(c)].²⁸ The chitosan in the outer sheath phase is quickly cross-linked by glutaraldehyde (GA) molecules that diffuse from the outer continuous water phase into the outer sheath phase for

shell construction. By using a tubular jet with an outer sheath phase containing *N,N*-dimethylacetamide and polyethersulfone (PES), tubular PES microfibers can be fabricated [Fig. 2(d)].³⁵ With *N,N*-dimethylacetamide in the outer sheath phase quickly extracted by the outer continuous water phase, the PES polymers can undergo a fast phase separation process to form the porous wall of the tubular microfiber. Furthermore, by adding K^+ -responsive microgels and poly(lactic-co-glycolic acid) (PLGA) in the outer sheath phase of a tubular jet, tubular PLGA microfibers with a K^+ -responsive microgel-embedded wall can be created via fast solvent extraction [Figs. 2(e) and 2(f)].²¹ The embedded smart microgels allow K^+ -responsive volume changes to regulate the permeability of the microfiber wall for controlled release of contents loaded in the hollow microfiber. Similarly, by simply adjusting the flow rates and microchannel dimensions, the diameters of the tubular microfibers and their hollow internals as well as the wall thickness can be precisely and independently manipulated. Moreover, although fast solidification of jet templates enables continuous *in situ* synthesis of microfibers in a microfluidic device, the fast solidification process based on interfacial cross-linking and solvent extraction can also lead to undesired microchannel blockage. By using a buffer phase to separate the continuous phase and sheath phase, the diffusion rate of cross-linkers and the extraction rate of solvents can be controlled to avoid microchannel blockage. For example, with a buffer layer to control the diffusion of Ca^{2+} from the continuous phase to the alginate-containing sheath phase, tubular Ca-alginate microfibers are stably and continuously fabricated [Figs. 2(g) and 2(h)].³⁶ Similar processes can be employed for the stable and continuous creation of tubular microfibers from different biocompatible materials such as chitosan and polyvinyl alcohol (PVA).³⁶ The functional microfibers with solid and tubular structures fabricated from microfluidics are promising for biomedical applications such as tissue engineering. For example, the belt-like solid microfibers with groove surfaces can provide unique topographical features to guide the migration, interaction, and organization of neuron cells.³⁴ On the grooved belt-like microfibers, the neuron cells migrate along the groove ridges, with neurites projected along the ridges to form oriented networks; while on smooth belt-like microfibers, they usually migrate toward the edges and form random networks of neurite connections. Thus, such grooved belt-like microfibers are promising as tissue engineering scaffolds for topographical control of the orientation of neuron cells for nerve regeneration. Moreover, tubular microfibers from microfluidics allow the manipulation of different types of cells for tissue engineering. For example, by encapsulating human umbilical vascular endothelial cells in the shell to imitate vascular vessel and human osteoblast-like cells in the tubular interior to imitate bone, tubular microfibers can serve as a biomimetic osteon-like structure, showing high potential for complex tissue regeneration.³⁷

B. Functional microfibers with complex biomimetic structures

The controllable droplet-containing jets from microfluidics provide more flexibility for template synthesis of complex functional microfibers that cannot be achieved by traditional fabrication methods. Generally, by separately adding functional materials into

FIG. 2. Controllable microfluidic fabrication of functional solid and tubular microfibers. Solid polyethylene glycol-based microfibers (a) and helical Ca-alginate microfibers (b).^{22,33} Image (a) is reproduced with permission from Wu *et al.*, *J. Mater. Chem. B* **4**(14), 2455–2465 (2016). Copyright 2016 Royal Society of Chemistry. Image (b) is reproduced with permission from Tang *et al.*, *Ind. Eng. Chem. Res.* **57**(29), 9430–9438 (2018). Copyright 2018 American Chemical Society. Tubular chitosan microfibers (c), tubular PES microfibers (d), and tubular PLGA microfibers with wall containing K⁺-responsive microgels [(e) and (f)].^{21,28,35} Image (c) is reproduced with permission from He *et al.*, *RSC Adv.* **5**(2), 928–936 (2015). Copyright 2015 Royal Society of Chemistry. Images (e) and (f) are reproduced with permission from Jiang *et al.*, *J. Mater. Chem. B* **4**(22), 3925–3935 (2016). Copyright 2016 Royal Society of Chemistry. Image (d) is reproduced with permission from Deng *et al.*, *J. Membr. Sci.* **526**, 9–17 (2017). Copyright 2017 Elsevier. (g) and (h) Microfluidic generation of tubular Ca-alginate microfibers from a tubular jet with a buffer layer.³⁶ Images (g) and (h) are reproduced with permission from Meng *et al.*, *Lab Chip* **16**(14), 2673–2681 (2016). Copyright 2016 Royal Society of Chemistry.

the sheath phase and core phase of the droplet-containing jets, microfibers with biomimetic structures such as peapod-like,^{28,38} bamboo-like,¹¹ and spider-silk-like structures^{9,10} can be developed. Typically, peapod-like chitosan microfibers containing oil droplets are developed from droplet-containing jets via fast interfacial cross-linking between chitosan and GA.²⁸ First, the core phase is emulsified into uniform oil droplets by the chitosan-containing sheath phase in the first co-flow geometry. Then, the sheath phase that carries the oil droplets is hydrodynamically shaped into a droplet-containing jet by the GA-containing continuous water phase in the second co-flow geometry. Meanwhile, the GA molecules diffuse from the continuous water phase into the sheath phase, and cross-link the chitosan to form microfibers with controllable peapod-like internals [Figs. 3(a) and 3(b)].²⁸ The peapod-like microfibers allow the synergistic encapsulation of multiple drugs with their hydrophilic chitosan network for loading water-soluble substances and the inner oil droplets for loading oil-soluble substances, showing potential for developing drug-loaded medical patches for wound healing. Similarly, bamboo-like Ca-alginate microfibers are developed from droplet-containing jets with the sheath phase containing alginate and the core phase containing volatile dimethyl carbonate and PLGA [Fig. 3(c)].¹¹ These bamboo-like microfibers show good performance for encapsulating living multicellular aggregates derived from mesenchymal stem cells (MSCs) for tissue engineering.¹¹ Moreover, with the droplet-containing jet as templates, spider-silk-like microfibers can be created by solidifying the sheath phase and the core phase [Figs. 3(d)–3(g)].¹⁰ The sheath phase contains alginate for constructing the hydrogel microfiber and the inner volatile oil droplets containing polystyrene and Fe₃O₄ nanoparticles for constructing the magnetic spindle-knots. Dehydration of the hydrogel matrix can create spider-silk-like microfibers with magnetic nodes for water collection. With an external magnetic field, the spider-silk-like microfibers can be flexibly assembled into different 2D and 3D structures. As shown in Figs. 3(h)–3(j), the spider-web-like structures assembled by these spider-silk-like microfibers on a circular magnet can collect water from the flow of water mist, exhibiting excellent water collection capacity.¹⁰ These complex biomimetic microfibers are promising as functional building blocks for engineering complex 3D scaffolds for water collection, cell culture, and tissue engineering. For example, the peapod-like microfibers allow efficient encapsulation of spheroids of mesenchymal stem cells (MSC) as peas for long-term cultivation.¹¹ These peapod-like microfibers can provide the encapsulated MSCs with higher cell densities than those in dish culture, protection against shear stress, and sufficient exchange of nutrients and oxygen. Thus, the MSC spheroids exhibit good viability and proliferation ability. Since the MSCs show enormous therapeutic potential for tissue repair, the MSC-encapsulated microfibers are promising for engineering biomimetic micro-sized tissues in regenerative medicine.

IV. CONTROLLABLE MICROFLUIDIC FABRICATION OF FUNCTIONAL MICROPARTICLES FROM EMULSION DROPLETS

A. Functional microparticles with controllable shapes

The highly controllable emulsion droplets from microfluidics provide excellent templates for controllable construction of diverse microparticles with advanced structures and functions.^{2,15} By

solidifying the emulsion droplets via chemical/physical processes such as free radical polymerization, cross-linking reaction, and physical deposition, solid microparticles can be created.^{2,3,15} Usually, the emulsion droplets are spherical shape due to their tendency to achieve a minimized interfacial energy. Thus, microparticles synthesized from these spherical emulsion droplets are usually spherical ones. With microfluidics to precisely control the flow behavior of emulsion droplets and the cross-sectional shape and size of microchannels, the shape of emulsion droplets can be flexibly manipulated for synthesizing nonspherical microparticles. Typically, by using a microchannel with inner dimensions smaller than the size of droplets, the droplets flowed in the microchannel can be deformed into nonspherical ones.¹⁷ The deformed shape of droplets is dependent on the cross-sectional shape of the microchannel. By *in situ* solidification of the deformed droplets in a microchannel, nonspherical microparticles, such as plug-shaped microparticles and disk-shaped microparticles,¹⁷ can be continuously synthesized. Due the uniform volume of the droplets, the nonspherical microparticles can also exhibit uniform shape and size. Alternatively, by tuning the microchannel dimensions and flow rates, generated droplets flowed in microchannel can also be hydrodynamically deformed into nonspherical ones. For example, by varying flow rates and inner dimension of collection capillary for droplet deformation [Fig. 4(a)], heart-shaped microparticles [Fig. 4(b)] and bullet-shaped microparticles [Fig. 4(c)] are prepared.³⁹ With the ratio of diameter of droplet to that of the collection capillary kept below 0.715, heart-shaped droplets can be obtained for microparticle fabrication, while bullet-shaped droplets can be obtained with the ratio higher than 0.715. The bullet-shaped microparticles can achieve improved embolization performances than spherical microparticles,³⁹ thus showing potential for uses in embolization therapy.

Besides the above-mentioned strategies for manipulation of droplet shapes, the shape of emulsion droplets can also be flexibly controlled via manual manipulation. For example, the precursor droplets can be encapsulated in stretchable PVA microfibers using droplet-containing jets as templates.⁴⁰ Manual stretching of the PVA microfiber deforms the encapsulated spherical droplets into different shapes. Meanwhile, twining the stretched PVA microfiber onto a steel wire can deform the inner droplets into a helical shape. With these deformed droplets as templates, microparticles with similar shapes, including rod-shaped [Fig. 4(d)] and helical microparticles [Fig. 4(e)], are obtained via UV-polymerization of the droplets followed with dissolution of the PVA networks.⁴⁰ Adjustment of the diameter and length of the rod-shaped microparticles and the pitch of the helical microparticles can be achieved by controlling the stretching ratio and the twining condition of the PVA microfibers. Moreover, by using droplet-contained jet to create a coiled jet, the inner droplets that encapsulated in the coiled jet can also be deformed into helical shapes. Typically, a coiled jet with alginate-containing sheath phase and photocurable oil cores can be generated in a microfluidic device by using a Ca²⁺-containing continuous phase.²⁹ The coiled structure can be stabilized based on the cross-linking between Ca²⁺ and alginate in the sheath phase. Thus, the droplets in the coiled jet can be stably deformed and then converted into helical microparticles via on-chip UV-polymerization [Fig. 4(f)].²⁹ In addition, by introducing

FIG. 3. Controllable microfluidic fabrication of functional microfibers with biomimetic structures. Peapod-like chitosan microfibers (a) with shell and core containing different substances (b).²⁸ Images (a) and (b) are reproduced with permission from He *et al.*, RSC Adv. 5(2), 928–936 (2015). Copyright 2015 Royal Society of Chemistry. (c) Bamboo-like Ca-alginate microfibers containing fluorescent PLGA microspheres.¹¹ Image (d) is reproduced with permission from Yu *et al.*, Adv. Mater. 26(16), 2494–2499 (2014). Copyright 2014 Wiley-VCH. Spider-silk-like Ca-alginate microfibers [(d)–(g)] and their assembly on a circular magnet [(h) and (i)] for water collection (j).¹⁰ Images (d)–(j) are reproduced with permission from He *et al.*, ACS Appl. Mater. Interfaces 7(31), 17471–17481 (2015). Copyright 2015 American Chemical Society.

FIG. 4. Controllable microfluidic fabrication of functional nonspherical microparticles. Adjustment of flow rate and capillary dimension (a) for creating heart-shaped (b) and bullet-shaped (c) microparticles.³⁹ Images (a)–(c) are reproduced with permission from Cai *et al.*, Chem. Eng. J. **370**, 925–937 (2019). Copyright 2019 Elsevier. Rod-shaped (d) and helical microparticles [(e) and (f)].^{29,40} Magnetic helical microparticles for transporting cargo (g) and removing clogging substance (h).²⁹ Images (d) and (e) are reproduced with permission from Wang *et al.*, Macromol. Rapid Commun. **38**(23), 1700429 (2017). Copyright 2017 Wiley-VCH. Images (f)–(h) are reproduced with permission from Cai *et al.*, ACS Appl. Mater. Interfaces **11**(47), 46241–46250 (2019). Copyright 2019 American Chemical Society.

magnetic nanoparticles into these droplets, magnetic helical microparticles can be fabricated for rotational and translational motion under a rotated magnetic field [Fig. 4(g)].^{29,40} With such a unique motion behavior, these helical microparticles can efficiently remove the clogging substance and transport micro-sized objects in a micro-channel [Fig. 4(h)].²⁹

B. Functional microparticles with controllable porous structures

Functional microparticles with porous structures have attracted great interest in a myriad of fields, such as adsorption, drug delivery, and tissue engineering.³ To create pores in microparticles, it usually

requires the addition of pore-templates such as sacrificed nanoparticles, microdroplets, and surfactant micelles in emulsion droplets for microparticle fabrication.³ For instance, SiO₂ microparticles with mesoporous structures are created from W/O emulsion droplets with assembled amphiphilic molecules as pore-templates [Fig. 5(a)].⁴¹ Their mesopores are used for efficient confined loading of phase change materials Na₂SO₄·10H₂O. With nucleating agents and crystal habit modifiers added in the mesopores, these microparticles can achieve reduced supercooling of Na₂SO₄·10H₂O with no phase separation for repeatable energy storage/release. By further incorporating with Fe₃O₄ nanoparticles for Fenton reaction and with Ag nanoparticles (AgNPs) for bubble-driven motion, mesoporous SiO₂ microparticles can achieve high performance for water remediation [Fig. 5(b)].⁴² Simply the addition of Fe₃O₄ nanoparticles in the W/O emulsion droplet templates can produce mesoporous SiO₂ microparticles embedded with Fe₃O₄ nanoparticles. These mesoporous SiO₂ microparticles containing Fe₃O₄ nanoparticles are further partially coated with polydopamine on their hemispherical surface for decorating AgNPs, based on the adhesion and reduction properties of polydopamine. The Fe₃O₄ nanoparticles can produce ·OH radicals from H₂O₂ at a low pH for a Fenton reaction; meanwhile, the AgNPs can decompose H₂O₂ into bubbles to power the movement of the microparticle. Thus, the Janus mesoporous SiO₂ microparticles show improved performance for degradation of organic dyes in water, as compared with mesoporous SiO₂ microparticles without AgNPs for bubble-driven motion. Porous microparticles that combine advantages of bubble-propelled motion and photocatalysis for water remediation can also be developed from single emulsion droplets [Fig. 5(c)].⁴³ O/W emulsion droplets containing surfactant micelles as pore-templates, photocatalytic metal organic frameworks (MOFs) as photocatalysts, and Fe₃O₄@Ag nanoparticles (Fe₃O₄@AgNPs) as nanoengines are used as templates. Driven by interfacial energy and magnetic field, the photocatalytic MOFs and Fe₃O₄@AgNPs can, respectively, transfer to the surface and the bottom of the emulsion droplets. UV-polymerization of such droplets can produce porous microparticles with MOFs-decorated surface and Fe₃O₄@AgNPs-decorated bottom. Based on the combination of bubble-propelled motion from Fe₃O₄@AgNPs/H₂O₂ and photocatalysis from MOFs and UV/H₂O₂ systems, the porous microparticles can achieve enhanced performance for degradation of organic dyes in water [Fig. 5(d)].⁴³

The incorporation of two different pore-templates in the droplets allows the fabrication of microparticles with hierarchical porous structures. Such microparticles can efficiently combine the advantages of pores with different pore sizes to achieve enhanced performance.^{44,45} By using homogenized oil droplets and assembled amphiphilic molecules as the dual pore-templates in water droplets, hierarchical porous SiO₂ microparticles with both mesopores and macropores are developed [Fig. 5(e)].⁴⁴ Because the macropores create easy paths in the mesoporous matrix of the microparticles, contaminant molecules can easily access the microparticle internals for efficient adsorption. Thus, the hierarchical porous SiO₂ microparticles exhibit a faster rate for removal of organic dyes in water than SiO₂ microparticles with only mesoporous structures. Furthermore, based on the flexible modification of silica-based materials, the hierarchical porous SiO₂ microparticles can be further functionalized with metal-chelators for efficient

removal of heavy metal ions. As compared to using homogenized droplets as pore-templates, employment of controllable microdroplets from microfluidics as pore-templates allow more flexible control over the pore structure and microparticle shape.^{45,46} For example, the controllable inner droplets in double emulsions from microfluidics can be used as pore-templates to create pores with micrometer-sizes in microparticles. Precise control of the size and number of the inner droplets allows accurate manipulation of the size and the number of the micrometer-sized pores in microparticles. Meanwhile, control of the number of the inner droplets also allows manipulation of the microparticle shape based on the packing structures of the inner droplets in double emulsions. Typically, hierarchical porous microparticles consisting of poly (methyl methacrylate-co-ethyleneglycol dimethacrylate) with precisely controlled pore size, porosity, functionality, and particle shape are developed from double emulsions, with assembled surfactants and inner droplets as dual pore-templates [Figs. 5(f) and 5(g)].⁴⁵ The microparticles possess nanometer-sized pores from the assembled surfactants and micrometer-sized pores from the inner droplets. By simply changing the number of inner droplets from two to four, the number of micrometer-sized pores and microparticle shape can be flexibly tailored [Figs. 5(f) and 5(g)]. Similarly, due to the features of hierarchical porous structures, the hierarchical porous microparticles can exhibit faster adsorption of oil pollutants and protein than microparticles with only nanometer-sized pores, showing good potential for use in water treatment and bio-separation. Moreover, further selective decoration of the hierarchical porous microparticles with Fe₃O₄@AgNPs [Fig. 5(h)] can integrate the intensified mass transfer of the bubble-driven motion and the advantages of hierarchical porous structures for enhanced adsorption of oil and heavy metal ions in water.⁴⁷

C. Functional microparticles with controllable compartmental structures

Functional microparticles with compartmental structures are promising for use in encapsulation, controlled release, and confined micro-reaction.^{1,2,15} Simple compartmental microparticles can be produced by employing interfacial reaction and assembly of copolymers or nanoparticles at the surface of single emulsion droplets.⁴⁸ The size and composition of the droplets determine the size of the microparticle and compartment and the content of the compartment, while the interfacial reaction and assembly processes determine the composition and thickness of the shell. Double emulsion droplets with separated phases provide more diversities for creating compartmental microparticles. The composition of inner and outer droplets can be flexibly manipulated to separately engineer the compartment and the shell. The outer droplets can be converted into a microparticle shell via processes such as interfacial cross-linking,^{49,50} UV-polymerization,^{51,52} and copolymer/nanoparticle assembly and polymer deposition based on solvent evaporation.¹⁶ Meanwhile, the size of the inner and outer droplets can be tailored to control the size of the compartment and the microparticle, as well as the shell thickness. Typically, by using UV-polymerization of the monomers in the middle aqueous phase of O/W/O double emulsions from microfluidics, compartmental microparticles with a stimuli-responsive shell, such as a glucose-responsive shell,⁵³ a

FIG. 5. Controllable microfluidic fabrication of functional porous microparticles. (a) and (b) Mesoporous SiO_2 microparticles loaded with $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ and selectively decorated with AgNPs.^{41,42} Image (a) is reproduced with permission from Li *et al.*, *Ind. Eng. Chem. Res.* **56**(12), 3297–3308 (2017). Copyright 2017 American Chemical Society. Image (b) is reproduced with permission from Li *et al.*, *Ind. Eng. Chem. Res.* **57**(13), 4562–4570 (2018). Copyright 2018 American Chemical Society. Porous microparticles with MOFs-decorated surface and Fe_3O_4 @AgNPs-decorated bottom for bubble-propelled motion (c) and photocatalytic water remediation (d).⁴³ Images (c) and (d) are reproduced with permission from Chen *et al.*, *ACS Appl. Mater. Interfaces* **12**(31), 35120–35131 (2020). Copyright 2020 American Chemical Society. (e) Hierarchical porous SiO_2 microparticles.⁴⁴ Image (e) is reproduced with permission from Zhang *et al.*, *Soft Matter* **16**(10), 2581–2593 (2020). Copyright 2020 Royal Society of Chemistry. Hierarchical porous microparticles with two (f) and four (g) micrometer-sized pores, and with two micrometer-sized pores and Fe_3O_4 @AgNPs-decorated bottom (h).^{45,47} Images (f)–(h) are reproduced with permission from Zhang *et al.*, *ACS Appl. Mater. Interfaces* **7**(25), 13758–13767 (2015). Copyright 2015 American Chemical Society; and Su *et al.*, *Ind. Eng. Chem. Res.* **58**(4), 1590–1600 (2019). Copyright 2019 American Chemical Society.

thermo-responsive shell,^{51,52} a pH-responsive shell,⁴⁹ and a K^+ -responsive shell,⁵⁴ are created. For example, double emulsions with outer droplets containing functional *N*-isopropylacrylamide (NIPAM) monomers can be converted into compartment microparticles with a thermo-responsive shell and an oil core compartment via UV-polymerization of the outer droplet [Fig. 6(a)].^{51,52} Their oil core can be used to load oil-soluble drug molecules and nanoparticles. Upon local heating, the poly(*N*-isopropylacrylamide) (PNIPAM) shell shrinks and generates pressure on the inner oil core. The PNIPAM shell finally ruptures due to the gradually increased pressure both on the shell and the oil core, and then the oil core is squeezed out with a high momentum for burst release [Fig. 6(a)].^{51,52} When nanoparticles with a diameter of 200 nm are loaded in the oil core as model drugs, the nanoparticles can achieve a travel distance of 359 μm within the first 1 s after the burst release.⁵¹ Such a distance is ~ 122 times longer than that in a diffusion-driven release process. The burst release rate for nanoparticles can be further manipulated by changing the cross-linking density and thickness of the shell, the viscosity of the oil core, and the rate of heating. Moreover, other triggers for the burst release such as pH and K^+ can be introduced into the microparticles by simply copolymerizing NIPAM with different functional comonomers.

By dissolving the oil cores, the compartmental microparticles with a hollow interior can be obtained to reload water-soluble drugs for stimuli-responsive controlled release. For instance, by removing the oil core of microparticles from double emulsions, glucose-responsive hollow microparticles with a hydrogel shell of poly(*N*-isopropylacrylamide-co-3-aminophenylboronic acid-co-acrylic acid) are prepared [Fig. 6(b)].⁵³ Their hydrogel shell allows reversible swelling/shrinking in response to variation of the glucose concentration. First, the microparticles are placed in a solution with 0.4 g L^{-1} glucose and a high concentration of insulin to ensure efficient loading of insulin molecules via their improved diffusion through the swollen shell. At low glucose concentrations, the hydrogel shell of microparticles remains shrunk and protects the loaded insulin in the hollow internal. With increased glucose concentration, the microparticle shell can reversibly swell at 37 °C to enhance the release rate of insulin due to the improved shell permeability. Thus, the microparticles allow self-regulated insulin release in response to glucose concentration changes within the physiological blood glucose concentration range at body temperature, showing high potential for treatment of diabetes. Further encapsulation of drug-loaded nanoparticles in the inner droplets of double emulsions can produce compartmental microparticles with the oil core containing the drug-loaded nanoparticles for sequential release. Typically, compartmental chitosan microparticles with an oil core containing drug-loaded PLGA nanoparticles are developed from W/O/W double emulsions via interfacial cross-linking [Fig. 6(c)].⁵⁰ The oil core and PLGA nanoparticles are used to load different drug molecules. The chitosan shell of these microparticles can remain intact in neutral pH conditions but decompose in acidic conditions to release their oil core and the drug-loaded PLGA nanoparticles within 60 s. Next, the drugs in the PLGA nanoparticles are slowly released for several days due to PLGA degradation [Fig. 6(c)].⁵⁰ For example, compartmental chitosan microparticles can be loaded with gastrointestinal anti-inflammatory drugs such as oleophilic curcumin and hydrophilic catechin for sequential release.⁵⁰ With curcumin

loaded in the oil core and in the PLGA nanoparticles, the compartmental chitosan microparticles can achieve first burst release of 56.2% curcumin within 60 s and then a sustained release of 19.3% curcumin for the next two days. When catechin is used instead of curcumin, the microparticles can achieve first burst release of 59.6% catechin within 60 s and then a sustained release of 32.3% catechin for the next two days. Since the hydrophilic catechin possesses a faster diffusion rate through the polymeric matrix of PLGA nanoparticles as compared to oleophilic curcumin, more catechin molecules are released within two days in the second sustained release stage. These compartmental chitosan microparticles are promising for the treatment of acute gastritis.

Multiple emulsions with more hierarchical structures are powerful for template synthesis of functional microparticles with more complex compartmental structures. These high-order multiple emulsions provide complex phase-separated structures to engineer the shell and compartments in the microparticles.^{18,55,56} Typically, with double emulsions containing two distinct inner droplets as templates, microparticles with one shell encapsulating dual compartments can be created for the co-delivery of two different contents. For example, microparticles with dual compartments loaded with different contents can be fabricated by polymerization of the outer droplets⁵⁵ or cooling-based solidification of the melted outer droplets into a thermo-responsive shell.⁵⁶ Control of the size and number of the distinct inner droplets enables independent and precise control over the size and number of each of the dual compartments as well as their loading levels of the distinct contents. The co-encapsulated contents can be released by destroying the shell via thermo-induced shell shrinking and shell melting.^{55,56} The use of quadruple emulsion droplets as templates allows the creation of two distinct shells into single dual-compartmental microparticles to separately control the release characteristics of contents from each compartment. With $O_1/W_2/O_3/W_4/O_5$ quadruple emulsion droplets from microfluidics as templates, Trojan-horse-like multicompartmental microparticles with capsule-in-capsule structures are developed for the programmed sequential release of their contents [Fig. 6(d)].¹⁸ By converting their inner (W_2) and outer (W_4) aqueous layers into two pH-responsive shells, the multicompartmental microparticles can achieve pH-triggered sequential release of contents separately loaded in their O_3 and O_1 cores. The O_3 core loaded with an inner chitosan capsule can be first released due to the decomposition of the outer chitosan shell in acid conditions. Then, the O_1 core can be released due to the shell decomposition of inner chitosan capsule. Alternatively, by converting the W_2 and W_4 aqueous layers into an inner chitosan shell and an outer PNIPAM shell, respectively, the multicompartmental microparticles can achieve a thermo-triggered burst release at the first stage and an acid-triggered burst release at the second stage. As shown in Fig. 6(d), with temperature increased from 25 °C to 50 °C, the outer PNIPAM shell of the multicompartmental microparticles shrinks for burst release of the O_3 core and inner chitosan capsule [Figs. 6(d1)–(d4)]. Next, by decreasing the pH to 2.5 and fixing the temperature at 25 °C, the inner chitosan shell disassembles to release the innermost O_1 core [Fig. 6(d5)–(d8)].¹⁸ The multicompartmental microparticles enable integration of multiple functions for advanced drug delivery.

FIG. 6. Controllable microfluidic fabrication of functional compartmental microparticles. (a) Thermo-responsive core-shell microparticles for burst release.⁵¹ Image (a) is reproduced with permission from Liu *et al.*, *Soft Matter* **6**(16), 3759–3763 (2010). Copyright 2010 Royal Society of Chemistry. (b) Glucose-responsive hollow microparticles.⁵³ Image (b) is reproduced with permission from Zhang *et al.*, *Soft Matter* **9**(16), 4150–4159 (2013). Copyright 2013 Royal Society of Chemistry. (c) PH-responsive core-shell chitosan microparticles loaded with drug-loaded PLGA nanoparticles for sequential release.⁵⁰ Image (c) is reproduced with permission from Yang *et al.*, *ACS Appl. Mater. Interfaces* **8**(16), 10524–10534 (2016). Copyright 2016 American Chemical Society. (d) Multicompartmental microparticles with an outer PNIPAM shell and an inner chitosan shell for programmable sequential release.¹⁶ Image (d) is reproduced with permission from Mou *et al.*, *Adv. Sci.* **5**(6), 1700960 (2018). Copyright 2018 Wiley-VCH.

V. CONCLUSION

This review provides a summary on the controllable fabrication of functional microfibers and microparticles, respectively, using continuous jets and emulsion droplets from microfluidics as templates. The microfluidic techniques allow controllable generation of continuous jets and emulsion droplets with highly controllable structures and compositions. With the diverse liquid jets as templates, functional microfibers with circular and non-circular cross sections and with solid, tubular, and complex biomimetic structures can be continuously created. From the controllable emulsion droplets, functional microparticles with spherical and nonspherical shapes and with solid, porous, and compartmental structures can be developed for many applications. Further improvement of the microfluidic techniques should focus on their use for industrial-scale production of the functional materials. Generally, robust materials and automatic processes are needed for large-scale production of microfluidic devices that can show good resistance to harsh preparation conditions such as harsh organic solvents and high temperature. Meanwhile, although the throughput of jets and droplets can be improved by using integrated microfluidic devices with an increased number of microchannels,^{57,58} robust and mass production of complex jets and multiple emulsion droplets still remains challenging. This restricts the mass production of microfibers and microparticles with complex structures from the liquid templates. Moreover, the use of the functional particles for biomedical application such as drug delivery usually requires the particle sizes in the nanometer range. Although particles with diameter down to several hundred nanometers can be fabricated by microfluidics,^{59,60} high-throughput generation of submicrometer emulsion droplets for mass production of nanometer-sized particles still remains difficult. This may require the development of integrated microchannels with new geometries and reduced dimensions and microfluidic dispersion techniques with powerful and controllable shearing processes. Thus, further innovations on the microchannel networks and emulsification process of microfluidic devices for robust and mass production of jets and droplets are required.

ACKNOWLEDGMENTS

The authors gratefully acknowledge support from the National Natural Science Foundation of China (NNSFC) (No. 21922809) and the Sichuan Science and Technology Program (No. 2019YJ0528).

DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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