Journal of Materials Chemistry B

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/materialsB

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Multicompartment microfibers: fabrication and selective dissolution of composite droplet-in-fiber structures

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

We present a microfluidic method to continuously produce multicompartment microfibers, where embedded single or double emulsion droplets are regularly spaced along the length of the fiber. Both hydrophobic and hydrophilic compounds can be encapsulated in different microcompartments of the fiber for storage, selective dissolution, and delivery applications, as well as to provide multifunctionality.

One-dimensional, high aspect ratio flexible structures, such as micro and nanofibers, are useful materials because even though their properties, geometry and composition are controlled at the micron and sub-micron length scales,[1] they facilitate at larger length scales the creation of more complex assemblies and three-dimensional architectures, such as meshes and textiles.[2-3] As with any materials system, strategies that add versatility and functionality are advantageous as the demands for 'smart' materials increase for many life science and materials science applications. The utilization of composite structures is a common approach to add such multifunctionality, and composite fiber structures with tailored volume fractions of components, precise spatial control, and controlled chemistry and loading of cargo are appealing for many applications. Examples include scaffolds for the spatial control of cellular microenvironments in tissue engineering,[4] the local delivery of therapeutics for wound healing applications,[5] the immobilization and protection of bacteria in bioreactors,[6] as self-healing composite materials for load bearing applications,[7] and in food science.[8-9]

For the generation of composite fibers, a common approach is to use an emulsion as the pre-fiber solution.[8, 10, 11] With this process, cargos such as proteins,[10] antimicrobial compounds,[11] and self-healing compounds[7] have been incorporated into electrospun nanofibers. To avoid the mechanical stresses associated with bulk emulsification techniques on fragile cargo, such as using homogenizers and ultra sonication, other techniques have been developed, such as compound-jet electrospinning, coaxial electrospinning,[12-15] thermally induced in-fiber emulsification of an extruded core-shell fiber,[16] coaxial microfluidics,[3] microfluidics incorporating stratified flows for mosaicked fibers,[17] and valve-based microfluidics for coded fibers.[18] These techniques have been shown to generate micro/nanofibers containing various cargos, including cells,[14] drugs,[15] and proteins.[13]

Some methods for producing composite fibers, such as using bulk emulsification, are relatively simple to execute, but lack the spatial control desired for advanced applications. Others, while efficient at fabricating fibers with complex morphologies and a high level of spatial control, rely on complex device designs and externally controlled actuation.[18] We are interested in developing methods for the fabrication of a composite fiber structure that can exhibit a high level of spatial control within the fiber structure, where the fibers can be used for the efficient storage and release of multiple cargos; the fabrication process also allows for making the fibers magnetic to allow for external actuation. To achieve this goal, we developed a passive microfluidic process to combine droplet generation and fiber formation steps. To the best of our knowledge, Oh et al.[19] first showed that microfluidics can be used to capture droplets within a solid fiber, while investigating the formation of core-shell particles in a microfluidic device. More recently, Yu et al.[20] combined droplet microfluidics and off-chip wet spinning to generate uniform fibers containing oil droplets along the length of the fiber. While the authors showed that they can solidify the oil droplets and incorporate pre-formed cell spheroids in their fibers, they only hinted at the potential usefulness of their composite fiber structure for encapsulation.

In this work, we describe our microfluidic method for the *in situ* fabrication of novel composite fibers based on the droplet-in-fiber structure. We demonstrate that double emulsion droplets can be embedded in the microfiber, which provides a greater level of hierarchical structuring in the microfiber when compared to embedding single droplets in fibers. Unlike the method of solvent evaporation of the oil droplets to incorporate polymer spheres in a fiber,[20] our methods can make double emulsions inside the fiber, and use calcium alginate for the aqueous phase in the oil droplets to create hydrogel particles inside the fiber. These embedded double emulsion droplets arranged along the length of the fiber provide a heterogeneous microenvironment where the different microcompartments have alternating hydrophilic or hydrophobic characteristics, as well as contrasting physical states: solid versus liquid.

Encapsulation of various materials within the fiber is possible by dissolving or dispersing them in each of the phases, including the outer fiber body and each of the droplet compartments. We explore the encapsulation capabilities of our fiber structures by testing the ease of loading various cargos within each type of microcompartment in the fiber, where the cargo can be a model drug or a component that adds functionality to the fiber, such as

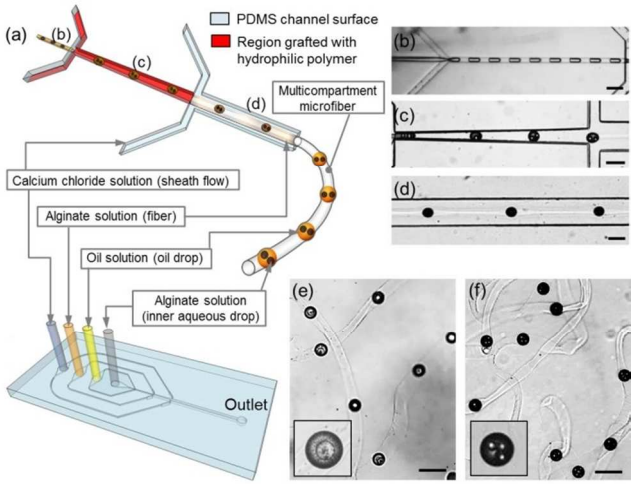

Fig.1 (a) The microfluidic device geometry designed for generating alginate particle-in-oil compartments encapsulated in an alginate fiber. The enlarged part of the channel shows each step of the *in situ* fabrication of the multicompartment fibers, with the hydrophilic region of the channel indicated in red. All the inlets for each solution to constitute the multicompartment fibers are indicated in the schematic device below. (b-d) Microscope images showing each step of the multicompartment fiber fabrication including (b) inner alginate particle generation in an oil phase, (c) alginate-in-oil double emulsion formation in the region grafted with hydrophilic polymer, and (d) the formation of the complete composite alginate fiber containing double emulsion droplets and sheathed by an aqueous solution of calcium chloride in the main channel. (e-f) The resulting fibers collected from the outlet containing double emulsions that consist of (e) a single alginate particle per oil compartment, and (f) multiple alginate particles per oil compartment. Scale bars = 200 μm.

magnetic properties. One example we present to illustrate the potential usefulness of fiber encapsulated cargos is to use the fiber as a cell scaffold, where we study the effect of loading chemicals in the droplet compartments on the spatial growth of cells within the fiber. We can easily encapsulate the cells in the fiber through the microchannel along with the double emulsion droplets, and the cells dispersed in the fiber can eventually grow for several days, into densely packed aggregates. In addition, we investigate the ability to selectively dissolve or remove the different microcompartments by adding suitable solvents.

For the work presented in this paper, we chose to use calcium alginate as the base composition of the fiber, although our microfluidic method can be adapted to other solidification methods such as photochemistry and solvent extraction.[21] Alginate is a biopolymer that can undergo a mild but rapid gelation in the presence of divalent cations to form a hydrogel.[22] Thus, the fundamental structure of the fiber consists of an alginate-in-oil-in-alginate configuration.

A schematic of the channel configuration and the multicompartment fiber is shown in Fig. 1a. We can encapsulate oil droplets in the fiber (Fig. S1) or water-in-oil double emulsion droplets in the fiber as in Fig. 1. The hydrophobic walls of the polydimethylsiloxane (PDMS) microchannel are necessary for making aqueous droplets in the oil continuous phase and to prevent adhesion during the production of the hydrogel fibers. In order to make oil droplets in an aqueous stream, the PDMS walls were chemically modified to become hydrophilic in that region of the microchannel. To achieve the hierarchical structuring, the microfluidic device is composed of a sequence of flow-focusing junctions. At the first junction, droplets of alginate solution are generated in the oil phase and the alginate droplets are gelled by the calcium ions in the oil phase (Fig. 1b). We chose to gel the inner aqueous phase because the alginate particles are more stable than aqueous droplets in the final fiber structure. At the second junction, oil droplets containing alginate particles are formed in alginate solution (Fig. 1c). At the third junction, the alginate fiber with embedded alginate particle-in-oil droplets is formed as the alginate stream is focused by an outermost aqueous sheath solution containing calcium ions, which triggers solidification of the alginate stream (Fig. 1d).

One advantage of using microfluidics for droplet generation is the ease of customization of the size and density of the droplet and particle microcompartments within the fiber structure. All of the details on the dimension and the stability of droplets in the fibers are in supplementary information (Table S1 and Figure S2). We can make fibers with one alginate particle per oil droplet (Fig. 1e) or multiple alginate particles per oil droplet (Fig. 1f) according to the flow rates described in Table S1. The flow rate of the oil phase contributes to the stability of the fiber because, at high flow rates, the oil solution may start wetting the channel wall. We kept the ratio of the flow rates of the inner alginate phase to the oil phase less than 0.4 so that the inner alginate phase formed stable droplets inside the oil phase. Also, the distance between the oil droplet compartments in the fiber can be

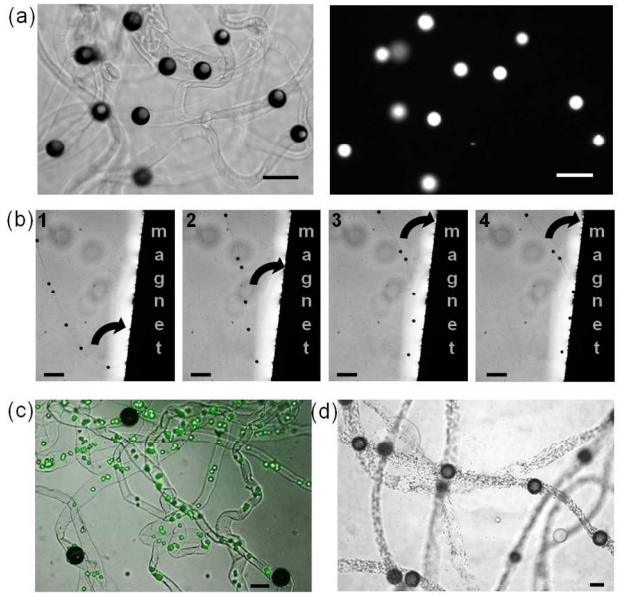

Fig. 2 Examples of encapsulation in the multicompartment fibers. (a) Bright-field and fluorescence images of alginate-in-oil-in-alginate fibers where fluorescent nanoparticles are encapsulated in the inner alginate particles of the fibers. The fibers are freely suspended in calcium chloride solution. Scale bars = 200 μm. (b) Bright-field images of an alginate-in-oil-in-alginate fiber where the alginate core particles contain magnetic microparticles that allow the fiber to be attracted to a magnet (at right), as indicated by the arrow. Scale bars = 500 μm. (c-d) Encapsulation of live cells in alginate-in-oil-in-alginate fibers. (c) Fibroblast cells growing in the alginate fiber compartment with ferrofluid inside the oil-droplet compartment, 3 days after the initial encapsulation. Live/dead assay is performed using calcein-AM (green fluorescence) and ethidium homodimer-1 (red fluorescence). (d) *E. coli* cells encapsulated in the oil-in-alginate fibers suspended in Luria–Bertani (LB) growth medium after 3 hours.

Table 1 Summary of multicompartment fiber encapsulation

Fiber compartment	Cargo	Fig.
inner alginate particle	fluorescent nanoparticles	2a, S3a, 4c
	FITC-conjugated BSA	S3b
	magnetic microparticles	2b
middle oil droplet	fluorescent dye (Nile Red)	4c, S5a,c
	ferrofluid	2c, S3c-f
	eugenol (antimicrobial)	3, S3c-f
alginate fiber	NIH/3T3 fibroblast cells	2c, S3e,f
	Escherichia coli	2d-e, 3, S4

controlled by the dimension of the channel and the flow rates (Fig. S2). Overall, the distance between the droplets is inversely proportional to the droplet generation frequency, which can increase with the flow rate of the oil phase and decrease with an increase in channel dimension (by producing larger volumes of the droplets). In this work, the distance between the droplet compartments ranged from 750 μm to 16 mm, while the diameters of the droplet compartments ranged from 113 μm to 187 μm. The width of the alginate stream ranged from 80 μm to 128 μm, where there are no droplets, and the region surrounding the droplets were 10-20 μm thicker. The uniformity of the fiber width can be improved by incorporating oil droplets with smaller diameters compared to the width of the fiber, and also by increasing the strength of the fiber using a higher concentration of alginate in the solution.

A wide variety of cargos can be added to the different compartments of the microfiber. Table 1, Fig. 2 and Fig. S3 summarize our efforts to encapsulate various materials in the three different microcompartments of the composite fiber. As calcium-crosslinked alginate is hydrophilic and has pore sizes on the order of 10 nm, the heterogeneous composite structure of the fiber is more suitable for storing materials with different sizes and chemistries, and so we have investigated small molecule, macromolecule, and micro- and nano-particulate cargo, some of which are hydrophobic and others hydrophilic.

As a model particle cargo, 200 nm fluorescent nanoparticles were added to the inner alginate particle to produce fluorescent core microfibers (Fig. 2a and Fig. S3a). The nanoparticles were clearly encapsulated in the inner particles of the fiber, and were not found anywhere else in the fiber structure. We also demonstrated encapsulation of protein by adding fluorescein isothiocyanate (FITC) conjugated bovine serum albumin (BSA; molecular weight: 66 kDa) to the alginate particles. FITC-conjugated BSA encapsulated in the inner alginate particle was also protected by the oil layer of the outer droplet compartment, and we observed the fluorescence for 20 hours (Fig. S3b).

Similarly, magnetic microparticles of 1 μm diameter were added to the inner alginate particle. The magnetic alginate particles allowed the fiber to respond to an external magnetic field, as shown in Fig. 2b, where the multicompartment fiber, suspended in calcium chloride solution, was drawn towards a magnet. The fibers can also exhibit magnetic properties by adding magnetic material to the oil phase. To illustrate this feature, we incorporated an oil-based ferrofluid, containing 10 nm diameter iron oxide nanoparticles, in the oil droplets of the fiber to produce magnetically responsive fibers (Fig. S3c-d).

A hydrogel fiber is a good material for studying three-dimensional cell growth and as a scaffold for tissue engineering.

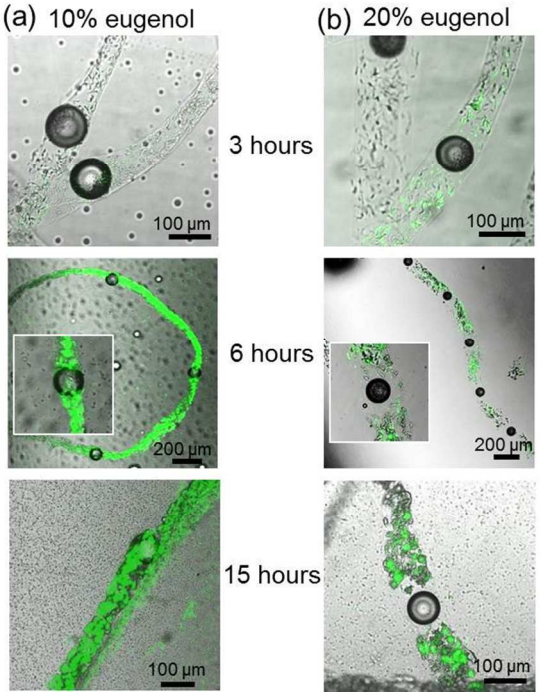

Fig. 3 Study of the antibacterial effect of eugenol oil on *E. coli* cells within the multicompartment fibers. (a) For the alginate fibers containing up to 10% (v/v) eugenol droplets inside, the GFP-expressing *E. coli* cells grew around the oil droplets and covered most of the fibers completely after 15 hours. (b) In 20% (v/v) eugenol droplets-in-alginate fibers, we observed the growth of *E. coli* already slowing down around the oil droplets after 3 hours, and showing no growth around the rim of the droplets even after 15 hours.

As researchers try to incorporate more functionality in the hydrogel used for cell encapsulation, such as magnetic property,[24] we can fabricate our multicompartment fibers with that function without having to disperse the magnetic particles in the hydrogel precursors. We added oil-based ferrofluid in the oil compartment of the fibers and grew mammalian cells inside the alginate fiber (Fig. 2c, Fig. S3e-f). The cells, which were randomly dispersed throughout the outer alginate regions of the fiber initially, grew and formed aggregates that continued to increase in size to form large spherical aggregates over the incubation period (Fig. S3e). A Live/Dead assay shows high viability (94% viability) of the cells after growing for 6 days inside fibers that are freely suspended in cell medium. Since the oil-based ferrofluid is localized only in the oil compartment, we can encapsulate very high concentrations of ferrofluid for strong magnetic attraction without affecting the cells in the fiber. Fibers spun with a motor formed a sheet of cells embedded with ferrofluid droplets (Fig. S3f). After 6 days, 84% of the cells grown in the sheet were viable, showing more death of the cells in the middle of the sheet possibly due to a deficiency of oxygen and nutrient transport.

With respect to the use of magnetic particles in the different compartments, we note that the fibers can be retrieved and separated from solution using a magnet, which subjects the fibers to less mechanical stress than many other separation methods. So for multistep procedures where the fibers need to be moved to different solutions, such as multiple washing steps, magnetic separation is convenient. Furthermore, the added magnetic

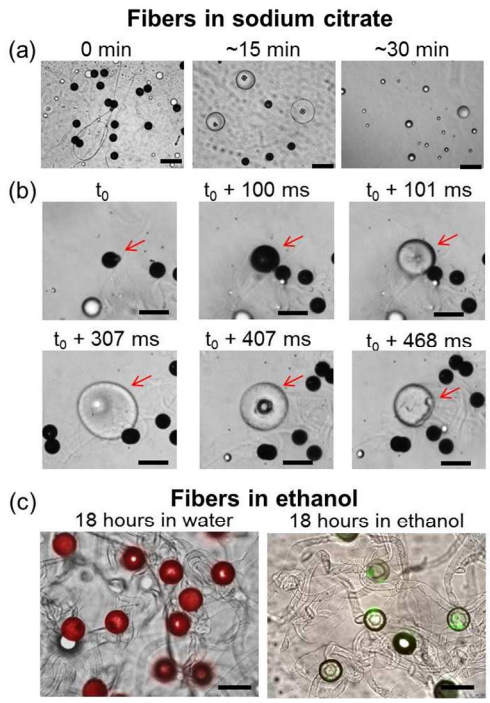

Fig. 4 Stability and dissolution studies of multicompartment fibers in (a-b) a solution of sodium citrate and (c) a solution of ethanol in water. (a) Bright-field images of alginate-in-oil-in-alginate fibers suspended in a solution of sodium citrate showing the dissolution of the alginate hydrogel, which leaves behind the oil droplets. (b) Bright-field images of alginate-in-ferrofluid oil-in-alginate fibers suspended in a solution of sodium citrate showing the partial dissolution of an inner alginate particle in an oil droplet (indicated by the red arrow), where the oil droplet is released from the dissolving alginate fiber, and then the inner alginate particle breaks open. After relatively long times, the broken inner alginate particle dissolves completely leaving only oil droplets. (c) Comparison of green NP alginate-in-Nile Red oil-in-alginate fibers left for 18 hours in DI water (left) and water/ethanol solution (right), showing the loss of the oil solution, containing Nile Red dye, in the case of the ethanol but not in the case of pure water. The fluorescent nanoparticles in the inner alginate particles remain intact in the presence of ethanol. Scale bars = 200 μm.

functionality suggests that the multicompartment fibers can be utilized in bioseparations[23] and assembly.[24]

We also tested the growth of bacterial cells, *Escherichia coli* (*E. coli)*, in the oil droplet-in-alginate fibers (Fig. 2d). The *E. coli* cells encapsulated in the fibers were suspended in the LB medium for 21 hours, and grew very well inside the fibers where they completely surrounded the oil droplets (Fig. S4). The oil microcompartments of the fiber potentially can be used to encapsulate hydrophobic drugs or antibacterial chemicals to test their effects on the cells. For example, eugenol is a known antibacterial compound found in clove oil.[25] We dissolved eugenol in the oil compartment composed of mineral oil with 5% (v/v) undecanol and 2 wt% Span 80. The undecanol was used to aid the mixing of eugenol oil with the mineral oil. Although we observed, qualitatively, a reduction in the overall growth rate of *E. coli* in the presence of the eugenol-oil droplets inside the fiber, at eugenol concentrations up to 10% (v/v), we did not observe any significant difference in the cell growth around the eugenol droplets (Fig. 3a), compared with the cells around oil droplets with no eugenol (Fig. S4). At 20% (v/v) eugenol-oil droplets, we started to observe a significant decrease in the cell population around the oil droplets (Fig. 3b). Thus, multicompartment fibers carrying either oil or water-based droplets can be used to study the effect of drugs on cells, even with chemicals of low solubility in water. Also, the encapsulated droplets provide another method to localize and pattern multiple cell types inside the fiber according to the attractive or repulsive characteristics of the cells towards the contents of the droplets.

The multicompartment fibers exhibited long-term stability when stored in water. We prepared alginate-in-oil-in-alginate fibers, and stored the fibers in deionized (DI) water. We observed the fibers periodically over a 30-day period and did not observe any significant changes in the fiber structure during this time (Fig. S5a). The fiber compartments – inner alginate particles, oil droplets, and the alginate fiber itself – remained intact during a month of storage in DI water, showing no evidence of droplet coalescence. Thus, our multicompartment fibers can be used as a stable storage system of the alginate particles or oil droplets. These experiments were conducted with mineral oil as the oil phase; however, if oil with higher miscibility in water, such as eugenol, is used (solubility in water, 2.46 mg mL^{-1}),[26] the fiber structure does change over time. We observed that the eugenol droplets (100% eugenol) embedded in the fiber dissolve in water, shrinking from 120 μm to 50 μm in diameter over a period of 2 hours (Fig. S5b). Depending on properties such as size and hydrophilic/hydrophobic affinity, the materials to be encapsulated in the droplet compartment can be stably stored or released over time from the fiber.

Upon demand, we can also release and recover the droplet compartment stored inside the fiber. Calcium alginate gels can be dissolved using chelating agents, such as sodium citrate, where the citrate anions remove the calcium cations from the alginate gel, thereby uncrosslinking the gel. In order to demonstrate the release of the oil compartments, an aqueous solution of sodium citrate was added to a suspension of our multicompartment fibers in DI water. The alginate gel that composes the main body of the fibers began to dissolve, releasing the oil droplets, which then floated to the surface of the solution (Fig. 4a). In the early stages of dissolution, the inner alginate particles in the oil droplets remained intact and were visible in the released oil droplets. The inner alginate particles did eventually dissolve leaving only oil droplets in solution. We noted that there was an intermediate step in the dissolution of some of the inner alginate particles as shown in Fig. 4b; upon release of the oil droplets from the fiber, the intact inner alginate particles, which we observed had shell structures, first ruptured and broke into pieces, and then eventually dissolved completely.

To study the effect of the hydrophobic chemical on the cells, we have used a lipophilic compound such as eugenol, which has slight solubility in water. If the miscibility of the compounds in the oil droplets is too low to cause passive release in pure water, we can add a suitable solvent, such as dimethylsulfoxide (DMSO), at low concentrations to aid in the removal of the contents of the oil microcompartments of the fibers. For non-biological applications, we can use stronger organic solvents. In this example, we used ethanol for a simple demonstration of the oil phase removal. The oil phase, which is a solution of mineral oil, 5% (v/v) undecanol, and 2 wt% Span 80 surfactant, is slightly miscible with ethanol, and thus is able to slowly escape the oil

microcompartments in the fiber in the presence of ethanol. To illustrate this idea, we prepared alginate-in-oil-in-alginate fibers with 0.3 mg mL^{-1} of a lipophilic fluorescent dye, Nile Red, in the oil droplets, and green fluorescent nanoparticles of 190 nm diameter in the inner alginate particles; one fiber sample was left in water, and the second fiber sample was left in an ethanol/water solution. The red fluorescence of the Nile Red dye in the oil microcompartments was observed in the fiber left over 18 hours in water (Fig. 4c; left). However, upon addition of ethanol, the red fluorescence in the oil droplets of the fibers became less intense and appeared more diffuse over time (Fig. S5c). After a longer time, we were not able to observe any red fluorescence in the fibers, which indicates that the lipophilic dye partitioned from the oil microcompartments into the suspending solution because of the presence of ethanol. In addition, the oil microcompartments lost their spherical shape as their contents were removed, as shown in Fig. 4c (right). We were still able to observe the green fluorescence from the nanoparticles encapsulated in the inner alginate particles of the fibers, indicating that the core structures were unaffected by the presence of ethanol. Materials that are already encapsulated inside the inner alginate particles will remain inside as long as the material has lower affinity towards the solvents. Depending on the solvents suitable for the specific application, we can choose to encapsulate materials either in the aqueous phase or the oil phase; as there is a broad range available for material selection, the multicompartment fibers can potentially be applied towards many applications.

Conclusions

We have demonstrated a passive microfluidic approach to the fabrication of multicompartment fibers that exhibit a droplet-in-fiber structure. Our work is the first to show embedding of double emulsion droplets in alginate fibers and to investigate the versatility of the fiber structure for encapsulating a wide range of materials, both hydrophilic/hydrophobic, solid/liquid, and biological/inorganic. We also provided more functionality to the fiber such that it can not only be used as an encapsulating material but it possesses magnetic property, or can be used to create a cell scaffold that can study the behaviors of the cells in response to certain chemicals compartmentalized within the fiber. The hierarchical structure allows us to have more choices on the materials to be encapsulated in the fiber itself, and also on the solvents used to release the material. We use the alternating properties of the microcompartments, where there are repeating regions with alternating hydrogel/oil/hydrogel environments for the co-encapsulation of both lipophilic and hydrophilic compounds, and propose this fiber structure as being potentially useful for the co-encapsulation and co-delivery of compounds with incompatible solubilities, selective dissolution, and multifunctionality. Our future work includes the systematic design of multicompartment fibers for the controlled release of compounds from each compartment. We are also investigating various materials to be used in our microfluidic system including UV-polymerizable poly(ethylene glycol) diacrylate for the multicompartment fiber material, where droplets and the sheath flow are in the oil phases.

The most immediate usage of the multicompartment fiber is as a droplet storage system in a one-dimensional array, where the temporal order of droplet production is preserved within the fiber structure. The ability to store the spatiotemporal information of products eliminates the need to index each droplet or particle as they are produced and collected. Our microfluidic method is modular and the device consists of different regions for the sequential generation of each of the components that makes up the final fiber structure. This modular approach makes it possible to add different droplet operations, such as alternating droplet flow for introducing different chemistries,[27] or modules to control the length and shape of the fibers,[28] which can be used to generate more advanced fiber structures with greater composition and geometry control for diverse applications. We expect that our multicompartment fibers can provide more architectural variety to the 1-D structure of conventional microfibers. They can facilitate studies of the effects of microenvironmental variations on the cell behaviours, and further be used as functional scaffold units to be assembled into 2-D and 3-D structural bases for tissue engineering.

Acknowledgements

We acknowledge Prof. B. L. Bassler, Dr. K. Drescher and M.-Y. Kim for providing bacteria strains and IPTG, as well as assistance with bacteria protocols. We thank Kyungeun Lee for assistance with figure graphics. The microfabrication work was performed at the Princeton Microfluidics Core Facility and we thank the director, Dr. S. Vyawahare. EU and HAS thank AFOSR (grant # FA9550-12-1-0368) for partial support of this research. EU was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (2013R1A6A3A03065994). JKN and HAS thank the Princeton MRSEC (DMR 0819860) for partial support of this research.

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† Electronic Supplementary Information (ESI) available: Experimental details, additional figures and video. See DOI: 10.1039/b000000x/

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1 Y. Jun, E. Kang, S. Chae and S.-H. Lee, *Lab Chip* 2014, **14**, 2145; D. Li and Y. Xia, *Adv. Mater.* 2004, **16**, 1151.

2 C. Burger, B. S. Hsiao and B. Chu, *Annu. Rev. Mater. Res.* 2006, **36**, 333.

3 H. Onoe, T. Okitsu, A. Itou, M. Kato-Negishi, R. Gojo, D. Kiriya, K. Sato, S. Miura, S. Iwanaga, K. Kuribayashi-Shigetomi, Y. T. Matsunaga, Y. Shimoyama and S. Takeuchi, *Nat. Mater.* 2013, **12**, 584.

4 M. Yamada, S. Sugaya, Y. Naganuma and M. Seki, *Soft Matter* 2012, **8**, 3122; M. Yamada, R. Utoh, K. Ohashi, K. Tatsumi, M. Yamato, T. Okano and M. Seki, *Biomaterials* 2012, **33**, 8304.

5 P. Zahedi, I. Rezaeian, S.-O. Ranaei-Siadat, S.-H. Jafari and P. Supaphol, *Polymer. Adv. Tech.* 2010, **21**, 77; M. Zilberman, E.

Golerkansky, J. J. Elsner and I. Berdicevsky, *J. Biomed. Mater. Res. A* 2009, **89A**, 654.
6 A. Nardi, R. Avrahami, E. Zussman, J. Rokem and C. Greenblatt, *J. Environ. Prot.* 2012, **3**, 164.
7 S. Sinha-Ray, D. D. Pelot, Z. P. Zhou, A. Rahman, X. F. Wu and A. L. Yarin, *J. Mater. Chem.* 2012, **22**, 9138.
8 A. Arecchi, S. Mannino and J. Weiss, *J. Food Sci.* 2010, **75**, N80.
9 K. Sultana, G. Godward, N. Reynolds, R. Arumugaswamy, P. Peiris and K. Kailasapathy, *Int. J. Food Microbiol.* 2000, **62**, 47.
10 B. Dong, M. E. Smith and G. E. Wnek, *Small* 2009, **5**, 1508; E. H. Sanders, R. Kloefkorn, G. L. Bowlin, D. G. Simpson and G. E. Wnek, *Macromolecules* 2003, **36**, 3803; J. C. Sy, A. S. Klemm and V. P. Shastri, *Adv. Mater.* 2009, **21**, 1814.
11 R. Korehei and J. Kadla, *J. Appl. Microbiol.* 2013, **114**, 1425; C. Kriegel, K. M. Kit, D. J. McClements and J. Weiss, *Langmuir* 2009, **25**, 1154.
12 A. Mickova, M. Buzgo, O. Benada, M. Rampichova, Z. Fisar, E. Filova, M. Tesarova, D. Lukas and E. Amler, *Biomacromolecules* 2012, **13**, 952.
13 C. H. Park and J. Lee, *Macromol. Mater. Eng.* 2010, **295**, 22.
14 A. Townsend-Nicholson and S. N. Jayasinghe, *Biomacromolecules* 2006, **7**, 3364.
15 L. Viry, S. E. Moulton, T. Romeo, C. Suhr, D. Mawad, M. Cook and G. G. Wallace, *J. Mater. Chem.* 2012, **22**, 11347.
16 J. J. Kaufman, R. Ottman, G. Tao, S. Shabahang, E.-H. Banaei, X. Liang, S. G. Johnson, Y. Fink, R. Chakrabarti and A. F. Abouraddy, *Proc. Natl. Acad. Sci. U.S.A.* 2013, **110**, 15549.
17 S. Cho, T. S. Shim and S.-M. Yang, *Lab Chip* 2012, **12**, 3676.
18 E. Kang, G. S. Jeong, Y. Y. Choi, K. H. Lee, A. Khademhosseini and S.-H. Lee, *Nat. Mater.* 2011, **10**, 877.
19 H.-J. Oh, S.-H. Kim, J.-Y. Baek, G.-H. Seong and S.-H. Lee, *J. Micromech. Microeng.* 2006, **16**, 285.
20 Y. Yu, H. Wen, J. Ma, S. Lykkemark, H. Xu and J. Qin, *Adv. Mater.* 2014, **26**, 2494.
21 J. K. Nunes, S. S. H. Tsai, J. Wan and H. A. Stone, *J. Phys. D: Appl. Phys.* 2013, **46**, 114002.
22 K. Y. Lee and D. J. Mooney, *Prog. Polym. Sci.* 2012, **37**, 106.
23 I. Munaweera, A.Aliev and K. J. Balkus, Jr., *ACS Appl. Mater. Interfaces*, 2014, **6**, 244.
24 F. Xu, C.-a. M. Wu, V. Rengarajan, T. D. Finley, H. O. Keles, Y. Sung, B. Li, U. A. Gurkan and U. Demirci, *Adv. Mater.* 2011, **23**, 4254.
25 R.-S. Pei, F. Zhou, B.-P. Ji and J. Xu, *J. Food Sci.* 2009, **74**, M379.
26 S. H. Yalkowsky, Y. He and P. Jain, *Handbook of Aqueous Solubility Data*, CRC Press, Boca Raton, FL, USA 2010.
27 E. Um, M. E. Rogers and H. A. Stone, *Lab Chip* 2013, **13**, 4674.
28 J. K. Nunes, H. Constantin and H. A. Stone, *Soft Matter* 2013, **9**, 4227; J. K. Nunes, K. Sadlej, J. I. Tam and H. A. Stone, *Lab Chip* 2012, **12**, 2301.

Multicompartment microfibers: fabrication and selective dissolution of composite droplet-in-fiber structures

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Table of contents

We present multicompartment microfibers embedded with double-emulsion droplets, which have great potential for encapsulating various functional cargos.