Droplet-Based Microfluidics for Emulsion and Solvent Evaporation Synthesis of Monodisperse Mesoporous Silica Microspheres

Nick J. Carroll,† Shailendra B. Rathod,† Erin Derbins,† Sergio Mendez,† David A. Weitz,‡ and Dimiter N. Petsev*,†

Department of Chemical and Nuclear Engineering and Center for Biomedical Engineering, University of New Mexico, Albuquerque, New Mexico 87131, and School of Engineering and Applied Sciences, Department of Physics, Harvard University, Cambridge, Massachusetts 02138

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A novel method for the fabrication of monodisperse mesoporous silica particles is suggested. It is based on the formation of well-defined equally sized emulsion droplets using a microfluidic approach. The droplets contain the silica precursor/surfactant solution and are suspended in hexadecane as the continuous oil phase. The solvent is then expelled from the droplets, leading to concentration and micellization of the surfactant. At the same time, the silica solidifies around the surfactant structures, forming equally sized mesoporous particles. The procedure can be tuned to produce well-separated particles or alternatively particles that are linked together. The latter allows us to create 2D or 3D structures with hierarchical porosity.

Introduction

The synthesis of mesoporous silicate solids using surfactant templating was discovered more than a decade ago.[1] A variation of the procedure, known as evaporation-induced self-assembly (EISA), involves confining all silica precursor and templating surfactant species within droplets. The solvent then progressively evaporates, and that leads to an increase in the concentration of templating surfactant which, upon surpassing the critical micelle concentration, assembles into spherical or cylindrical micellar structures.[2] When the solvent is fully evaporated, the silica solidifies around the surfactant structures. This is followed by surfactant removal via calcination, resulting in the formation of a well-ordered mesoporous silica material. EISA has been successfully utilized to fabricate well-ordered thin silica films[2] and particles[2,3] using a wide range of surfactants and block copolymers. However, the mesoporous silica particles obtained by EISA are usually characterized by substantial polydispersity.

Recently, Andersson et al.[4] demonstrated the synthesis of spherical mesoporous silica particles using an approach that combines previously established emulsion-based precipitation methods[5,6] with the EISA method. This synthesis route, referred to as the emulsion and solvent evaporation method (ESE), produced well-ordered 2D hexagonal mesoporous silica microspheres. The emulsions were prepared in the bulk using inhomogeneous vigorous stirring. As a result, the droplets, and therefore the particles, were produced with a relatively broad size distribution.

The fabrication of monodisperse silica microparticles containing highly ordered nanometer-scale pores (mesopores) of controllable size presents a fundamental challenge and is of practical interest.[7] They can be used for controlled drug delivery and molecular, biomolecular,[8] and cellular[9] encapsulation. Monodisperse particles can be ordered into 2D and 3D lattices,[10,11] which allow the fabrication of catalysts with well-defined pore hierarchy. Mesoporous particles also have significant potential for the design and implementation of chemical and biochemical sensors.[12]

Microfluidic flow-focusing devices (MFFDs) provide a straightforward and robust approach to the formation of highly monodisperse emulsion drops.[13] It has been demonstrated that microfluidic-generated drops can function as both morphological templates and chemical reactors for the synthesis of monodisperse polymer[13,15,16] and biopolymer[17] particles.

In this letter, we suggest a novel procedure for the fabrication of well-defined monodisperse mesoporous silica particles. It is based on MFFD emulsification of an aqueous-based sol[18] with subsequent EISA processing utilizing the ESE method.[4] The

* Corresponding author. E-mail: dimiter@unm.edu. Phone: (505) 277-3221.

† University of New Mexico.

‡ Harvard University.

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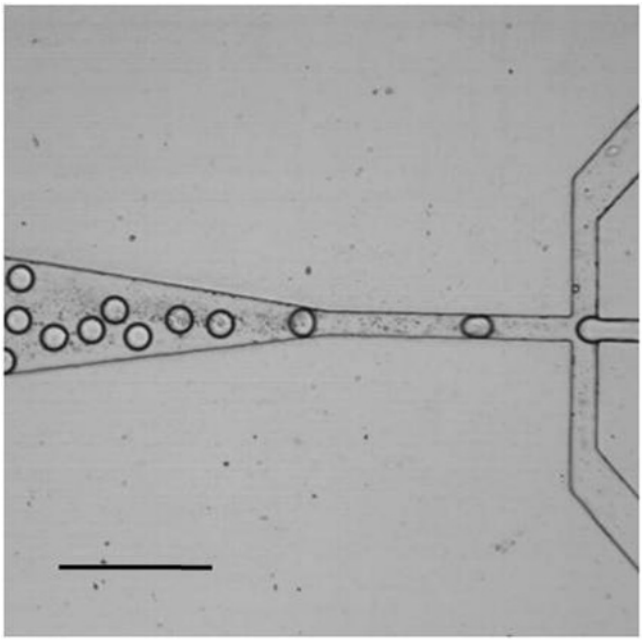

Figure 1. Optical microscopy image of droplets of silica precursor solution emulsified in a T-shaped microfluidic device in hexadecane. The channel dimensions of the orifice are 25 μm (width) by 30 μm (height). The scale bar is 100 μm. 72 × 71 mm^2 (150 × 150 DPI).

droplet-based microfluidic methodology can easily be developed further to allow for controlled loading and incorporation of cells, biomolecules, functionalized particles, and polymers within monodisperse, highly structured silica mesoporous microspheres.

Materials and Methods

The silica precursor solution was prepared by hydrolyzing 5.2 g of tetraethylorthosilicate (TEOS, Purum >98%) in 3 g of ethanol (99.7%) and 2.7 g of 0.01 N hydrochloric acid (pH 2) under vigorous stirring at room temperature for 30 min. Next, 1.4 g of the amphiphilic triblock copolymer templating molecule (Pluronic, BASF, P104) was dissolved in 5.43 g of DI water and subsequently mixed with the hydrolyzed TEOS solution to complete the preparation of the aqueous-based sol. We designed this particular recipe to allow the use of Pluronic surfactant as a templating reagent in the presence of a much lower concentration of ethanol than used by other authors.[4]

Emulsification of the aqueous siliceous precursor was achieved by supplying the sol-dispersed phase and organic oil continuous phase to the microfluidic device using two digitally controlled Harvard Pico Plus syringe pumps. The droplet (and therefore particle) production was approximately 100/s. The continuous phase was prepared by dissolving ABIL EM 90 (Degussa) surfactant in hexadecane (3 wt %), which served as an emulsion stabilizer. The volumetric flow rate for the dispersed sol was optimized to 0.5 μL/min, with a flow rate of 3.5 μL/min for the continuous oil phase. The SU-8 photoresist-templated poly(dimethylsiloxane) (PDMS) microfluidic device was fabricated using a well-established soft-lithography method.[19] The microfluidic device used in this study is shown in Figure 1.

The MFFD-produced droplets were transferred to a 50 mL round-bottomed flask and heated to 80 °C under a reduced pressure of 70 mTorr for 2 h. The flask was pretreated with RAIN-X solution to make it hydrophobic. This was necessary to prevent the droplets from sticking to the flask bottom. To prevent droplet flocculation and coalescence before the sol−gel transition was complete, the emulsion was subjected to constant stirring at 200 rpm. This stirring was sufficient to keep the droplets suspended and separated, and it did not lead to shear deformation. The particles were then collected and centrifuged, followed by calcination in air at 500 °C for 5 h to remove the templating surfactant.

Transmission electron microscopy (TEM) was conducted on JEOL 2010 and 2010F instruments, and scanning electron microscopy (SEM) was done on a Hitachi S-800 instrument.

Results and Discussion

Figure 2 shows silica particles obtained from TEOS precursor droplets formed in hexadecane oil. The hexadecane allows for the solvent (DI water and ethanol) to be expelled from the droplets, which leads to polymerization of the templated silica. Figure 2a shows particles that were obtained from a shaken bulk emulsion. The particles have a well-defined spherical shape but are very polydisperse. It is not possible to improve on this because a shaken emulsion produces polydisperse droplets, which later result in a wide particle size distribution. Increasing the energy input (stirring intensity) during emulsion formation narrows the size distribution but cannot produce monodisperse droplets. (See also ref 4.) Furthermore it will lead to the formation of smaller droplets on average. Therefore, varying the energy input does not allow us to decouple the size from the polydispersity.

Using the microfluidic device (Figure 1), we were able to form monodisperse droplets, which is the necessary condition for obtaining well-defined monodisperse particles. The size of the droplets depends on the dimensions of the microchannel, the flow rates in the central and side channels, the viscosity of the fluids (water/ethanol and oil), and the surfactant. Hence, a single device can produce monodisperse droplets of different sizes by varying the relative magnitude of the viscous and interfacial forces that are involved.[13] We were able to vary the droplet size by 1 to 3 times the channel width. Hence, to cover a wider range of sizes one may need more than one microfluidic device or may have several channels, each with different sizes, fabricated on the same device.

The evaporation of the solvent necessary to form the solid mesoporous silica spheres leads to an overall size reduction. Therefore, the final particles are approximately half the size of the original droplets. Figure 2a shows a histogram and an SEM image of particles obtained from a polydisperse bulk emulsion. The size distribution is broad and includes a wide range of particles, which is also evident from the image. Using microfluidics significantly reduces the polydispersity. The size distribution and the corresponding SEM image of the particles are shown in Figure 2b. These particles were obtained using the microfluidic device shown in Figure 1, which has 25 μm wide channels. This device can produce droplets between 25 and 75 μm and particles of about half that size. The particle size distribution in Figure 2b exhibits one well-defined peak centered at around 23 μm. Particles like these are obtained from droplets that were initially between 35 and 40 μm in diameter. After the solvent (water and ethanol) is expelled, the final size is the one shown in Figure 2b. There is a second peak at 30 μm that is most likely due to some coalescence that occurred before the droplets turned into silica particles.

The lower limit for the dimension for soft lithography is determined by the printing process that is used. Fabricating channels that are about 10 μm wide using soft lithography is quite plausible. Such channels will produce particles on the order of 5 μm in diameter. To produce smaller particles, one may need to fabricate smaller channels using different methods[20,21] or exploiting the extreme hydrodynamic regimes.[13]

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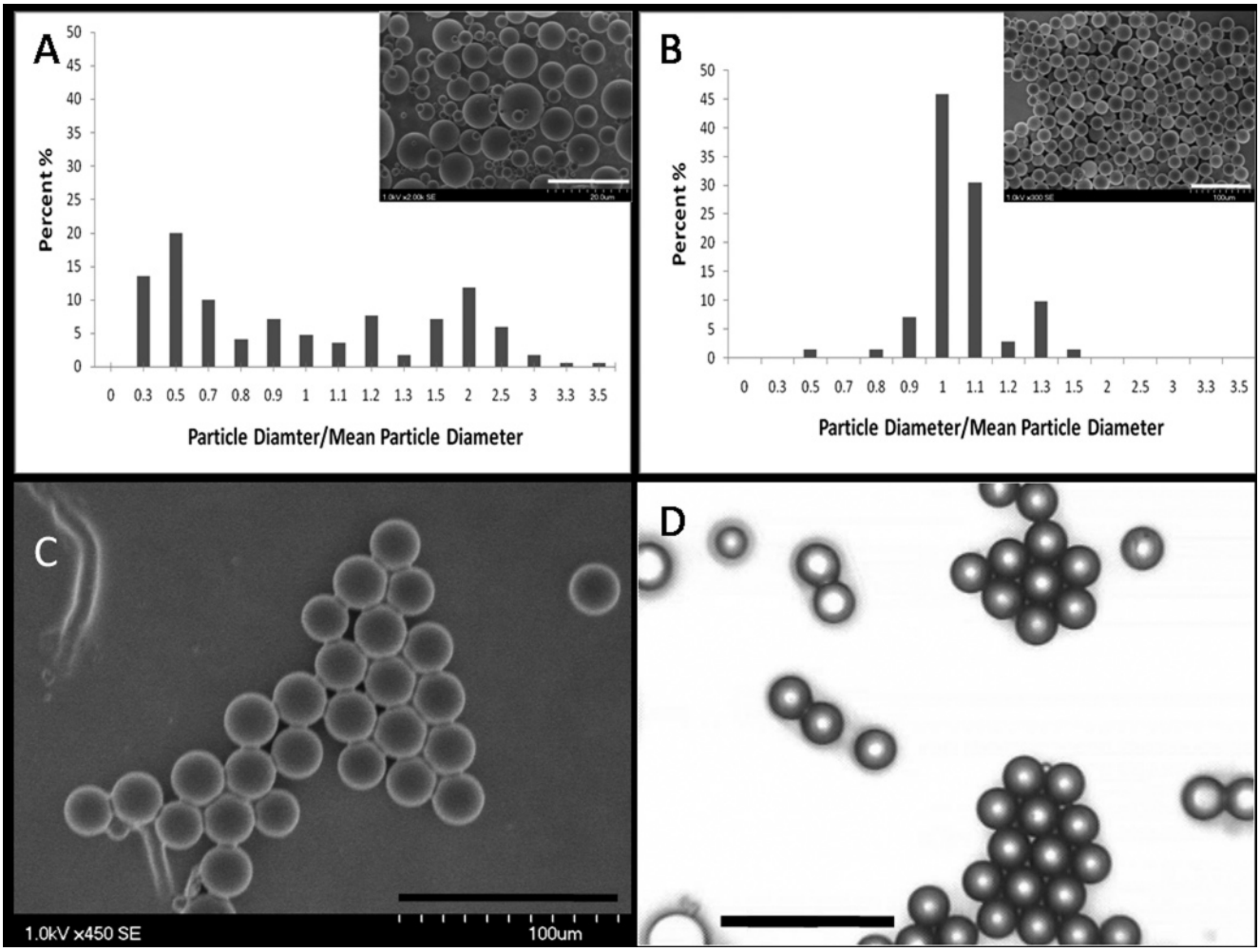

Figure 2. (A) Size distribution and SEM image of polydisperse silica microspheres templated from a shaken bulk emulsion. The scale bar is 20 μm. (B) Size distribution and SEM image of silica microspheres templated by monodisperse microfluidic device-generated droplets. The scale bar is 100 μm. (C) Scanning electron microscopy image and (D) optical photograph (scale bars for both images correspond to 100 μm) of particles that have fused together in a hexagonal array. The particles are connected by bridges that form when the particles come into contact before the completion of the gelation process. 174 $\times$ 131 mm^2 (150 $\times$ 150 DPI).

As we discussed above, the particles might stick together during the final stages of solvent evaporation unless some precautions are taken. However, this sticking could be exploited to obtain arrays of interconnected particles. Such interconnection adds to the structural integrity and allows robust 2D layers of well-defined monodisperse mesoporous particles to be fabricated. A layer of bound particles can be manipulated, transferred to different substrates, and incorporated into other applications in catalysis, sensing, and so forth. An example of such multiparticle 2D structure is depicted in parts c and d of Figure 2, which show a scanning electron microscopy image and an optical photograph of particles that have stuck together in a hexagonal array, respectively. The particles are connected by "bridges" that form when the particles come into contact before the completion of the gelation process.

Figure 3 shows a transmission electron microscope image of silica particles with internally ordered mesoporous structure. The particles were selected from the lower end of the distribution curve in Figure 2B. This allowed us to get a better image of the internal mesoporous structure. The pores have an approximately uniform size, which for the surfactant that we used is 6.4 nm, and a pore volume of 0.56 cm^3/g.[4] The pores seem to be closed at the surface, which is also the case reported by other authors.[4,18] Hence, microfluidics can be successfully used to fabricate silica spheres with well-defined size and internal porosity. Other types of water-soluble surfactants may be used for templating, which could extend the range of pore size and morphology.

Concluding Remarks

We have demonstrated that microfluidics can be successfully used to fabricate monodisperse mesoporous silica particles with well-defined size. A great advantage of monodisperse particles is that they can be ordered in 2D arrays on various substrates.[22,23] Controlled bridging and sticking of the particles allows the fabrication of arrays with sufficient structural integrity for subsequent manipulation and application. Monodisperse mesoporous particles can also be ordered in 3D structures, for example, by repeated deposition of layers following the technique in refs 22 and 23. This would allow structures with well-defined pore hierarchy to be obtained. Particles with surfactant-templated mesopores define two very different length scales: one in the

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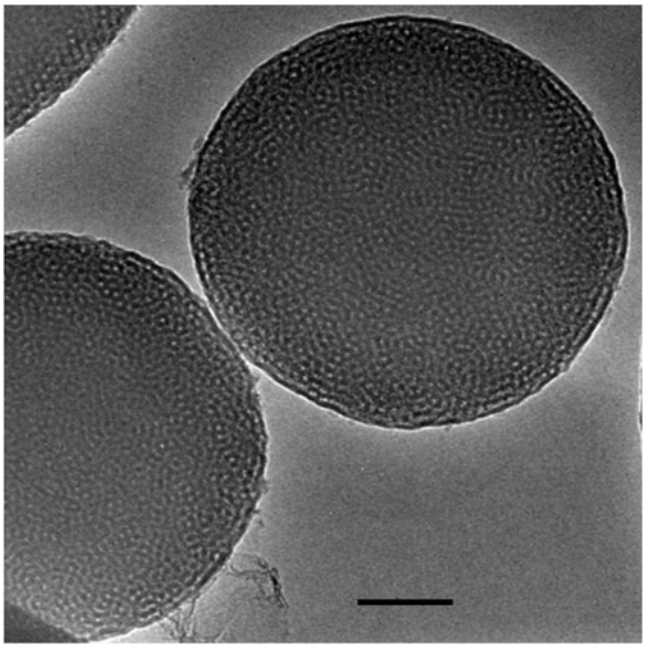

Figure 3. Transmission electron microscope image of silica microspheres containing mesostructured pores that are well ordered by the P104 surfactant. The scale bar is 100 nm. 126 × 126 mm^2 (150 × 150 DPI).

micrometer (particle size) range and the other in the nanometer (surfactant templates) range. The methodology developed here can be applied to derive mesoporous particles in a wide variety of sizes and can be modified to include other metal oxides.

The processing conditions for the surfactant templating described in this work are very different from those used in the alternative aerosol method.[7] The kinetics of solvent evaporation in our case is much slower because the solvents (water and alcohol) are transported across the continuous hexadecane phase. This means that the surfactant has a longer time to self-assemble into micellar structures that are closer to equilibrium. In the aerosol method, the solvent removal is very quickly, and some of the structures can be kinetically trapped. Thus, the slower kinetics will lead to better control of the pore structure and size. It also allows the study of the surfactant self-assembly process in silica, which is not tractable when solvent evaporation is too fast. Solvent evaporation and removal across the continuous organic (hexadecane) phase can also be used to obtain other mesoporous structures such as films and membranes. These structures do not require the use of microfluidics but may benefit from the slower kinetics.

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