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# Multilayered Polymer Microspheres by Thermal Imprinting during Microsphere Growth

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***Abstract:*** Modulation of the polymerization temperature in precipitation polymerizations was used to form onion-type polymer microspheres consisting of multiple nested layers. Specifically, the copolymerization of chloromethylstyrene and divinylbenzene-55 in acetonitrile, at temperatures ramping between 65 and 75 °C, led to monodisperse, cross-linked microspheres of about 10 $\mu$m diameter that have radial density profiles closely reflecting the thermal profiles used. This thermal imprinting is attributed to the copolymer formed being close to its theta point during the polymerization. As the microspheres grow by continuously capturing oligomers from solution, the resulting transient surface gel layer expands and contracts with temperature, and thus records the reaction temperature profile in the form of a corresponding density profile, even as it cross-links.

## Introduction

Multishell microspheres are receiving significant attention, due to their interesting structures and their potential use in photonic band gap devices.[1,2] Several approaches to forming these fascinating materials have recently been described, including layer-by-layer deposition of polyelectrolytes onto colloidal cores[3] and multistep emulsion polymerization.[4] Okubo et al. demonstrated earlier that mixtures of graft copolymers and homo polymers trapped within spherical droplets can undergo phase separation into onion-type multilayer spheres.[5] Finally, Farrer et al. prepared large multilayer hydrogel beads by successive in-diffusion of protecting and deprotecting agents.[6] The present Article describes a different approach to multilayer, onion-type microspheres, based on thermally inscribing different cross-link densities into microspheres as they grow.

It was shown earlier that cross-linked monodisperse microspheres could be formed by polymerization of divinylbenzene-55 in near-theta solvents such as acetonitrile.[7] These microspheres self-seed and grow by capturing oligomers from the reaction medium. The resulting surface gel sterically stabilizes the microspheres, even as it is coated by more oligomers and cross-links to build up the body of the microsphere.[8] Chosing appropriate solvents allowed incorporation of alkyl methacrylates,[9] chloromethylstyrene,[10] maleic anhydride,[11] methacrylic acid, and poly(ethylene glycol) methacrylate,[12] with a wide range of porosities[13] and cross-link levels[10,11] and final particle diameters ranging from 0.5 to 8 $\mu$m.[8,11,13]

This present Article describes the thermal imprinting of radial density profiles into such microspheres during their formation. The particular system involves temperature oscillations between 65 and 75 °C during the copolymerization of chloromethylstyrene with divinylbenzene in acetonitrile, with a cross-linker content of close to 10 vol % of total monomers.

## Experimental Section

**Materials.** Divinylbenzene-55 (DVB-55, 55% divinylbenzene isomers, 45% ethylstyrene isomers, Aldrich), chloromethylstyrene (vinylbenzyl chloride, mixture of 3- and 4-isomers, Aldrich), acetonitrile, methanol, and tetrahydrofuran (HPLC grade, Caledon Labs) were used as received. 2,2′-Azo-bis-(2-methylpropionitrile) (AIBN, Eastman Kodak Co.) was recrystallized from methanol.

**Procedure.** The polymerizations were carried out in 30 mL HDPE or in 20 mL glass screw cap vials placed in an oven consisting of a silicone-encased flat sheet heating element, a set of steel rollers, a temperature controller, an internal air-circulating fan and a thermally insulating cover, as described previously.[8]

The polymerizations employed 2 vol % total monomer in acetonitrile and 2 wt % AIBN relative to monomer. The nomenclature E8, E9, E10, and E11 is used to describe the volume percent of effective cross-linker, i.e., meta and para DVB isomers, in the total monomer. Since commercial divinylbenzene-55 (DVB-55) contains 55% divinyl isomers,

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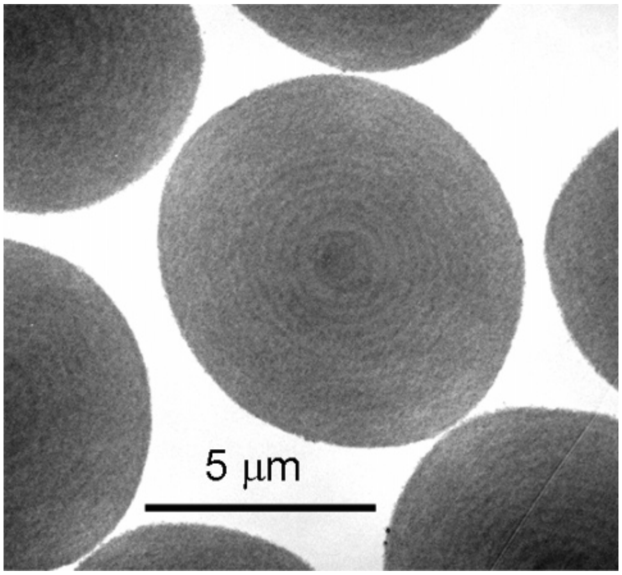
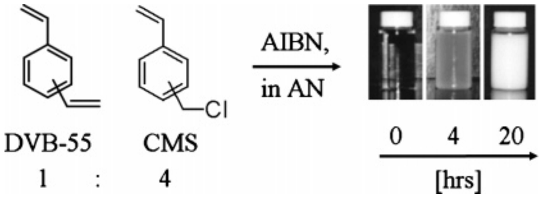


***Figure 1.*** TEM image of poly(chloromethylstyrene-*co*-divinylbenzene-55) microspheres containing 11% divinylbenzene (E11) formed by copolymerization in acetonitrile at 70 °C in the presence of an accidental thermal oscillation with 20 min period length.

***Scheme 1.*** Precipitation Copolymerization of DVB-55 and Chloromethylstyrene in the Presence of 2% AIBN at 65 °C



a typical E11 polymerization thus consists of dissolving 0.480 mL (0.520 g) of chloromethylstyrene (CMS), 0.120 mL (0.109 g) of DVB-55, and 0.0126 g of AIBN in 30 mL of acetonitrile in a 30 mL HDPE bottle.

Polymerizations were conducted in parallel by placing several bottles on the rollers in the oven, rotating at 4 rpm while the reaction temperature was ramped from room temperature to 65 °C over 1 h, followed immediately by a series of 65−75−65 °C triangular heating and cooling ramps as described in the figures and discussion. These temperature profiles are denoted by the time required to complete one heating−cooling cycle. For example, in the 2 h profile each cycle involves a linear 1 h ramp from 65 to 75 °C followed by a 1 h linear ramp from 75 to 65 °C. The control polymerizations involving flat profiles were ramped from room temperature to 70 °C during 1 h, and then kept at 70 °C for 22 h. The progressive thermal profile is as described in Figure 6. All thermal profiles were programmed using a thermal controller and reflect the actual temperature measured within the oven to within 0.5 °C. With the use of a small thermometer embedded in a 30 mL reaction vial, we confirmed that the temperature within the vial was never more than 1 °C from the oven temperature.

At the end of the reaction, the microspheres were separated from the reaction medium by centrifugation, successively washed three times each with tetrahydrofuran, and dried under vacuum at 50 °C overnight. Yields of microspheres were determined by gravimetry and consistently ranged from about 1−2% for E8 to 10% for E11. The final reaction mixtures also contain significant amounts of soluble, branched polymer.[13]

**Characterization.** Microsphere diameters were determined from images obtained with an Olympus optical microscope and by using Image Pro software to measure typically 100 microspheres. The surface morphology of the microspheres was studied with an ISI DC-130 scanning electron microscope. The internal texture of the microspheres was studied using a JEOL 1200EX transmission electron microscope (TEM). For TEM study, the microspheres were embedded in Spurr epoxy resin, ultramicrotomed to about 100 nm thickness, and the resulting sections deposited on 3 mm open TEM copper grids.

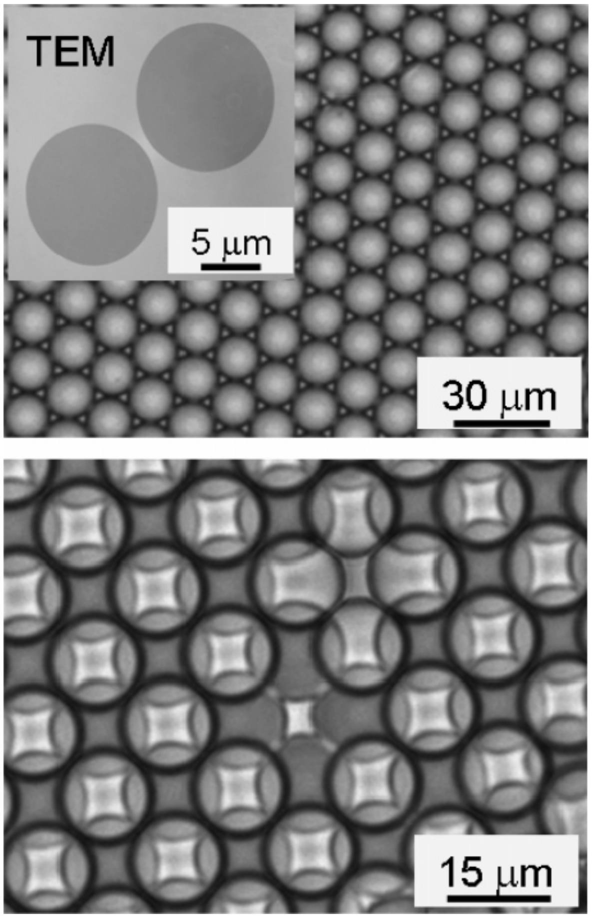


***Figure 2.*** E11$^{flat}$ microspheres formed at 70 °C without thermal oscillations: optical microscopy images of microspheres swollen in THF containing 5% polystyrene (ref 15) and assembled into single (top) and double layers (bottom) by capillary action. Note that the top image shows hexagonal close packing, while the bottom one shows a square-packed array with two void locations. Inset: TEM image of a thin cross section of microspheres embedded in Spurr resin.

## Results and Discussion

During an earlier copolymerization of DVB-55 with chloromethylstyrene in acetonitrile in a 1:4 volume ratio (11% effective cross-linker, or E11), we had obtained microspheres with multiple internal layers as seen in the TEM image in Figure 1.[14] This internal structure was subsequently attributed to an accidental thermal feedback loop in the temperature control system used at the time, with a periodicity of about 20 min. The nonspherical nature of the TEM image is attributed to inadvertent stretching of the microtomed film during sectioning.

The present Article reports for the first time the use of thermal oscillations to imprint radial structure into growing microspheres. Scheme 1 illustrates the general process of precipitation polymerization used in the present experiments. The reactions are carried out in HDPE or glass vials rotating horizontally on a set of steel rollers in a thermally controlled enclosure. The originally clear solutions turn turbid during particle nucleation,

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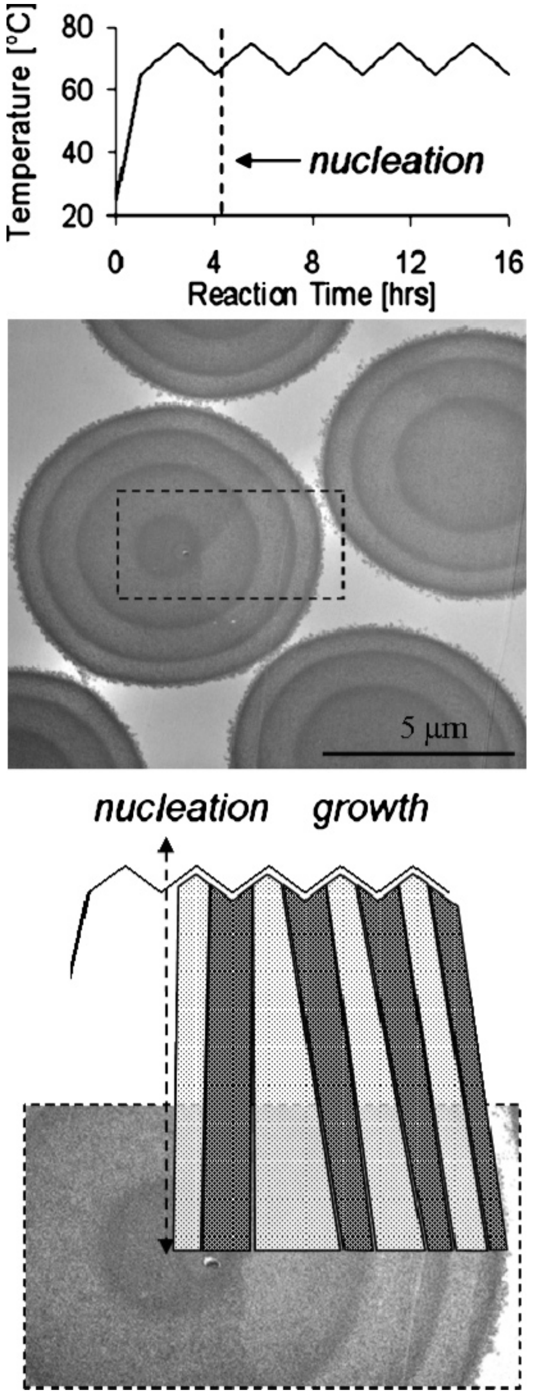

***Figure 3.*** TEM image of $E9^{3h}$ microspheres formed using a 5 × 3 h 65−75−65 °C thermal profile and embedded in Spurr resin. The enlarged section relates the postnucleation thermal profile to the polymer layers formed.

which occurs after about 1.5 h for DVB-55 and after about 3−4 h for E11. The final reaction mixtures are white due to the presence of dispersed microspheres.

Initial copolymerizations of DVB-55 and chloromethylstyrene were carried out using a flat thermal profile of 70 °C, following a 1 h ramp from room temperature to 70 °C. The resulting monodisperse microspheres have diameters of around 10 $\mu$m in the dry state and swell to about 15 $\mu$m in diameter in tetrahydrofuran. Both the optical microscopy images and the TEM image of $E11^{flat}$ microspheres embedded in Spurr epoxy (Figure 2) demonstrate the absence of internal structure in these microspheres formed without thermal oscillations.

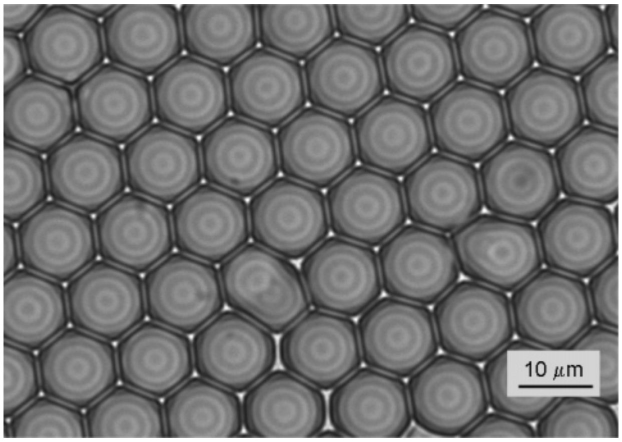

***Figure 4.*** Transmission optical microscope image of $E9^{3h}$ microspheres swollen in THF containing 5% polystyrene.

The particle yield obtained with this flat thermal profile increases from 1−2% for E8 to 10% for E11. This yield pattern as well as the significant degree of swelling reflect their low effective cross-link density. This in turn should make them responsive to thermal oscillation due to either changes in initiation rate or coil expansion. Periods of higher polymerization temperature would have higher rates of radical formation, shorter kinetic chain lengths, and lower effective cross-link density and should hence produce a polymer layer of higher swellability. As well, the proximity to the theta condition, indicated by the aggregation of these microspheres in acetonitrile upon cooling to room temperature, suggests that coil expansion during periods of higher polymerization temperature should also contribute to the deposition of a more swollen cross-linked polymer layer.

**Effect of Oscillations in the Polymerization Temperature.** Thermal oscillation experiments were mainly carried out at cross-linker contents between E8 and E11. No microspheres could be isolated at lower DVB content, and the internal structure faded at higher DVB content. Figure 3 shows the TEM image of $E9^{3h}$ microspheres formed using five 65−75−65 °C segments, each lasting 3 h, following an initial 1 h ramp from room temperature to 65 °C. The microspheres, embedded in Spurr epoxy resin prior to sectioning, show several alternating light and dark layers, corresponding to different degrees of swelling by the epoxy resin. The dark rings are attributed to more highly cross-linked regions of the particles, which contain relatively more CMS/DVB-55 polymer and less epoxy resin than the lighter regions. Layer thickness decreased from core to surface, in accord with decreasing monomer and initiator concentrations and with increasing shell volumes.

The enlarged section permits matching the thermal profile to the polymer layers. Following particle nucleation at approximately 4 h, the light, resin-swollen layers are attributed to high-temperature periods, while the darker layers are formed during lower temperature periods. This assignment is compatible with both larger coil expansion and lower cross-link efficiency during the higher temperature portion of the profile. The layers have an asymmetric appearance where for each dark layer, the density decreases more sharply toward the particle surface than it does toward the core. This likely reflects the temperature experienced just after deposition of the material on the particle surface. Polymer deposited during the temperature up-ramp experiences increasing temperature just after deposition and may

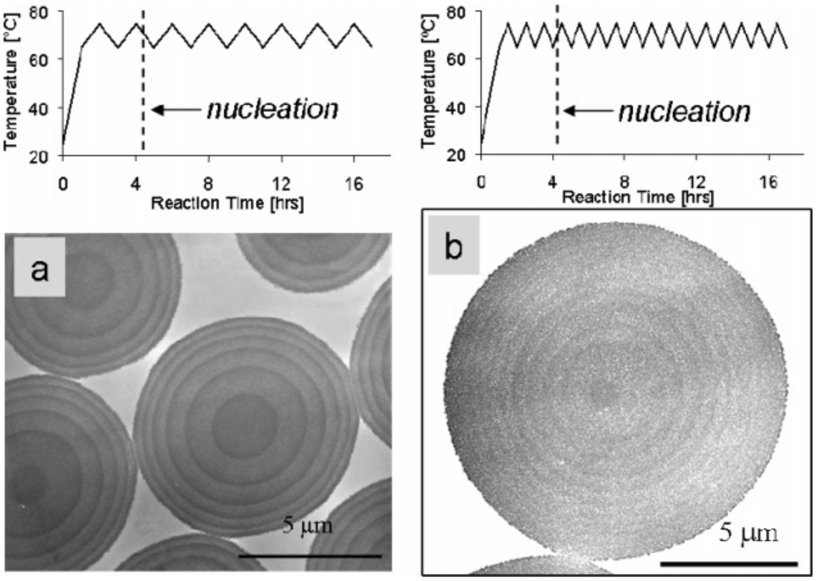

***Figure 5.*** TEM images of the internal structure of E9$^{2h}$ and E9$^{1h}$ microspheres formed using a series of 65−75−65 °C thermal segments with periodicities of (a) 2 h and (b) 1 h.

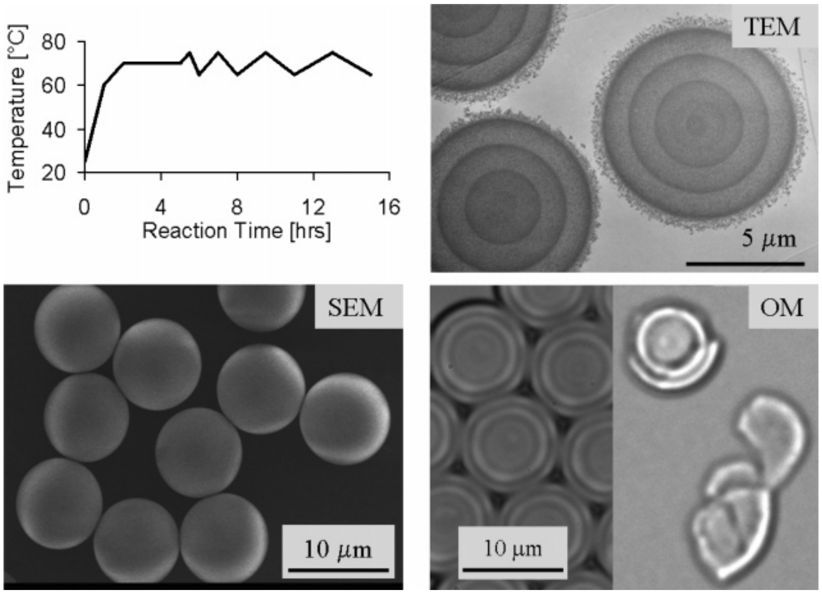

***Figure 6.*** TEM, SEM, and OM images of E9$^{prog}$ microspheres formed using a progressive thermal profile. The temperature is ramped to 60 °C and then to 70 °C in 1 h each, and then kept at 70 °C for 3 h, until after nucleation. The remainder of the profile consists of four oscillations with ramp rates corresponding to 0.5, 1, 1.5, and 2 h per 10 °C. The OM images (transmission mode) show THF-swollen microspheres before and after delamination by shearing between two glass slides.

remain swollen, or swell further, as cross-linking locks this morphology in place.

Layers formed at 75 °C retain their swellability even after exposure to several subsequent high/low temperature segments, demonstrating that it is the temperature regime at the time of polymer formation and deposition on the particle surface that determines the cross-link density. The fuzzy surface layer visible in Figure 3 and other images is attributed to lightly cross-linked surface layers formed late in the reaction.

Figure 4 shows a transmission optical microscope image of an array of E9$^{3h}$ microspheres swollen in THF containing 5% polystyrene, with the layer structure clearly visible. Closer inspection reveals two examples of nonspherical onions formed by coating of irregular core particles.

Parts a and b of Figure 5 show the internal structures of E9$^{2h}$ and E9$^{1h}$ microspheres, formed using analogous 65−75−65 °C thermal profiles of 2 and 1 h periodicity, respectively. These microspheres also permit a correlation between thermal profile and the number of dense and resin-swollen layers, analogous to that shown in Figure 3. These microspheres also start recording their thermal profiles following nucleation at about 4 h.

Microspheres with evenly spaced layers would be of particular interest for photonic applications. Figure 6 shows the internal structure of E9$^{prog}$ microspheres formed using a progressive thermal profile based on thermal excursions that increase in duration during the reaction. This progressive slowing of the temperature cycling roughly compensates for the decreasing monomer loading and changing layer volumes and leads to near-constant layer thickness.

Both SEM and optical microscopy images confirm the monodispersity of the E9$^{prog}$ microspheres. The optical microscopy image of the THF-swollen E9$^{prog}$ microspheres shows density patterns that closely match the internal structure revealed by the TEM above, though with reverse contrast. The optical microscopy image also shows one THF-swollen microsphere that had been purposely delaminated at a weakly cross-linked layer by manually shearing it between glass slides.

The internal layer structure of these microspheres proved most visible when they are swollen by THF or embedded in Spurr epoxy resin. Other embedding resins, based on higher molecular weight epoxy and amine components, did not swell the microspheres and accordingly did not bring out the internal contrast as well as Spurr resin. Similarly, allowing the polymerizations to continue past the end of the thermal profiles resulted in reduced layer contrast, presumably through post-curing of the more swollen layers.

Unlike the DVB-55/4-methylstyrene microspheres described earlier,[8] the present chloromethylstyrene-rich microspheres are colloidally stable in acetonitrile only at elevated temperature and reversibly aggregate upon cooling to room temperature. This suggests that the corresponding oligomers and hence surface gel layers are close to their theta condition at the polymerization temperature and, hence, may undergo significant thermal coil expansion upon heating from 65 to 75 °C, leading to more resin-swellable layers that appear lighter in the TEM images. Future work will involve studying the theta temperature of styrene−CMS and DVB−CMS copolymers as a function of composition.

Freeze-drying such microspheres swollen in benzene should give rise to high refractive index contrast, onion-type microspheres of interest for photonic band gap applications. In addition to their interesting onion-type structure, these particles also represent the largest monodisperse cross-linked microspheres reported for dispersion or precipitation polymerization.[16,17]

This concept of forming cross-linked microspheres with radial density profiles, using thermal oscillations during precipitation polymerization involving thermally responsive polymers, should be general. We will explore the use of other comonomer systems, including functional comonomers and water-soluble analogues.

## Conclusions

Thermal oscillations have been used to imprint corresponding density profiles into polymer microspheres prepared by precipitation polymerization under near-theta conditions. This is a novel concept for forming polymer microspheres with well-controlled radial structure. The resulting multilayer, onion-type microspheres are of fundamental interest due to the opportunity to control morphology through polymer−solvent interactions. They may also find uses in photonic band gap devices on the basis of their periodically varying refractive indices.

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(15) We added 5 wt % polystyrene (150 K) to this THF in order to slow the solvent and particle motion and reduce the rate of solvent evaporation. We verified that this added polystyrene does not significantly alter the swelling behavior of the microspheres, compared to that in neat THF.

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