

Self-assembly of Hollow PNIPAM Microgels to Form Discontinuously Hollow Fibers*

Xiao-yun Liu^a, Jian-mao Yang^{a,b} and Liu-sheng Zha^{a,b**}

^a Research Center for Analysis and Measurement, Donghua University, Shanghai 201620, China

Zi-jun Jiang^b

^b State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, Donghua University, Shanghai 201620, China

Abstract A new kind of hollow hydrogel microfiber with discontinuous hollow structure was prepared by an ice-segregation-induced self-assembly process. Monodisperse thermo-responsive hollow poly(*N*-isopropylacrylamide) (PNIPAM) microgels were first synthesized by seed precipitation polymerization using colloidal SiO₂ nanoparticles as seeds, followed by removing the silica cores of the formed SiO₂/PNIPAM core/shell composite microgels with hydrofluoric acid. Then, the discontinuously hollow hydrogel microfibers were produced by unidirectional freezing of 1 wt% hollow PNIPAM microgel aqueous dispersion in liquid nitrogen bath, followed by freeze-drying to remove the formed ice crystals. Many orderly arrayed dents were observed on the surfaces of the hydrogel microfibers by field-emission scanning electron microscopy, indicating that they are constructed by closely packed monodisperse hollow PNIPAM microgels. The effect of freezing method and the hollow microgel concentration in the aqueous dispersion on the morphological structure of the hollow hydrogel microfibers was investigated.

Keywords: Discontinuously hollow microfiber; Ice-segregation-induced self-assembly; Thermo-responsiveness; *N*-isopropylacrylamide; Microgel.

INTRODUCTION

Hollow fibers are of great importance in material science due to their multiple applications in different fields, like environmental, electronic, biomedical technologies and gene therapy^[1–3]. The well-known hollow fibers are the fibers of continuously hollow structure, which have been widely used in hollow fiber membrane configuration for water purification and blood fractionation^[4, 5]. Hidalgo *et al.*^[6] synthesized polyacrylamide or poly(hydroxyethylmethacrylate) hydrogels confined to the macroporous structure of membranes by radiation-induced *in situ* polymerization, which was expected to be applied for the design of a bioartificial extra-corporeal liver.

Smart hydrogel microfibers possess not only the unique properties of the smart hydrogel, capable of swelling or deswelling in response to external stimuli^[7], but also the exceptionally large surface-to-volume ratio of the microfibers with the diameters down to submicrometer scale^[8]. Due to biocompatibility of hydrogels and faster response rate of a smart hydrogel microfiber than a conventional bulky hydrogel, smart hydrogel microfibers can enhance their biomedical applications as wound dressings, a scaffold for tissue engineering and

* This work was financially supported by the National Natural Science Foundation of China (Nos. 51073033 and 51373030) and the Fundamental Research Funds for the Central Universities (No. 2232014D3-43).

** Corresponding author: Liu-sheng Zha (查刘生), E-mail: lszha@dhu.edu.cn

Received January 24, 2014; Revised March 4, 2014; Accepted March 13, 2014

doi: 10.1007/s10118-014-1508-8

drug delivery carriers^[9, 10]. Smart hydrogels are crosslinked polymer networks, which are neither soluble nor meltable, thus it is impossible to produce smart hydrogel microfibers directly by electrospinning or conventional spinning process. Special treatment techniques, such as heat-induced crosslinking^[11], hydrolysis^[12], and an *in situ* photo-induced polymerization and crosslinking reaction^[13], have been used to prepare smart hydrogel microfibers. However, these techniques may inevitably destroy the activity of the component entrapped inside the microfibers.

Ice-segregation-induced self-assembly process (also referred to as “ice-templating method”) for preparing the materials used in biomedicine (*e.g.*, for tissue engineering and drug delivery purposes) attracts increasing attention most likely because of its biocompatible character^[14]. Furthermore, the process starts from an aqueous solution/suspension or from a hydrogel and proceeds in the absence of further chemical reaction or purification procedure, thus avoiding potential biomedical complications associated with residual byproducts or organic solvents. Over the past few decades, the technique has been applied for porous materials fabrication^[15], less for fiber preparation. In a pioneering study, Mahler *et al.*^[16] observed that unidirectional freezing of aqueous silicic acid can produce SiO₂ fibers with polygonal cross-sections. Organic fibers have also been prepared by this technique^[17]. In this case, the ice-segregation-induced self-assembly approach was applied to resorcinol-formaldehyde (RF) hydrogels obtained by sol-gel polycondensation of resorcinol with formaldehyde using sodium carbonate as a basic catalyst. It was found that polygonal fibers and a bundle of partly connected polygonal fibers can be formed by adjusting aging time before freezing RF hydrogels. Recently, Shi *et al.*^[18, 19] have used this strategy to produce fibers with alternating organic-inorganic arrangement and carbon/metal oxide microfibers with well-controlled pore structure and interface.

In this communication, we summarize our recent efforts for utilizing ice-segregation-induced self-assembly process to fabricate a new kind of hollow hydrogel microfiber with discontinuous hollow structure using thermo-responsive poly(*N*-isopropylacrylamide) (PNIPAM) hollow microgels as building blocks. Its discontinuous hollow structure was identified by field-emission scanning electron microscopy (FE-SEM) without any sample treatment under low accelerating voltage condition. The discontinuously hollow hydrogel microfibers are expected to have potential applications in some fields, such as controlled drug release system, bioreactor, bioprotective materials, *etc.*

EXPERIMENTAL

Preparation of Discontinuously Hollow PNIPAM Microfibers

Monodisperse SiO₂/PNIPAM core/shell composite microgels and the thereby produced hollow PNIPAM microgels were prepared according to the reference^[20]. The aqueous hollow PNIPAM microgel dispersion of 1 wt% concentration in a plastic tube was immersed into liquid nitrogen bath at a constant rate. Afterwards, the frozen aqueous microgel dispersion was placed quickly in the freeze dryer (EYELA, FDU-2200) for freeze-drying at -80 °C for 24 h to remove the ice by sublimation, such that a hollow microgel scaffold which consisted of interweaved microfiber bundles was produced.

Characterization

TEM micrographs of SiO₂/PNIPAM core/shell composite microgels and hollow PNIPAM microgels were obtained by a Hitachi H-800 TEM. The samples were stained by phosphate-tungstic acid of 1 wt% concentration. SEM images of SiO₂/PNIPAM core/shell composite microgels, hollow PNIPAM microgels and the microfiber bundle were observed by a JEOL JSM-5600LV microscope. The hydrodynamic diameter of hollow PNIPAM microgels at different temperatures were measured by a Brookhaven BI-200SM dynamic laser light scattering instrument with a 532 nm laser light source at the scattering angle of 90°. The fine topographical structure of discontinuously hollow fiber surface was analysed by a HITACHI S-4800 FE-SEM without any sample treatment under a low accelerating voltage (1–1.5 kV).

RESULTS AND DISCUSSION

Morphological Structure Characterization of Hollow PNIPAM Microgels and Their Thermo-responsiveness

The hollow PNIPAM microgels were prepared by removing the SiO₂ cores of SiO₂/PNIPAM core/shell composite microgels through chemical etching with hydrofluoric acid solution, which were synthesized by seed precipitation polymerization in the presence of 3-(trimethoxysilyl)propyl methacrylate modified colloidal SiO₂ nanoparticles as seeds, using *N*-isopropylacrylamide (NIPAM) as monomer and *N,N'*-methylene-bis-acrylamide (MBA) as crosslinker at 70 °C. The direct evidence of SiO₂ core elimination was the disappearance of its typical absorption band 1100 cm⁻¹ in the FTIR spectrum of the product. TEM and SEM observations provide additional evidences that the hollow PNIPAM microgels were produced after removal of the SiO₂ cores, as shown in Fig. 1. Comparing Fig. 1(a) and 1(b), it can be seen that the SiO₂ cores of SiO₂/PNIPAM core/shell composite microgels disappeared after HF acid treatment, resulting in hollow PNIPAM microgels. Compared with spherical SiO₂/PNIPAM composite microgels shown in Fig. 1(c), the hollow PNIPAM microgels exhibited in Fig. 1(d) have obvious dent depression on their surfaces due to capsule collapse at shell thin spots under the high vacuum required for SEM measurements. The cavity size and shape of the resulting hollow microgels are directly determined by the core particles with diameter ranging from tens to hundreds of nanometer.

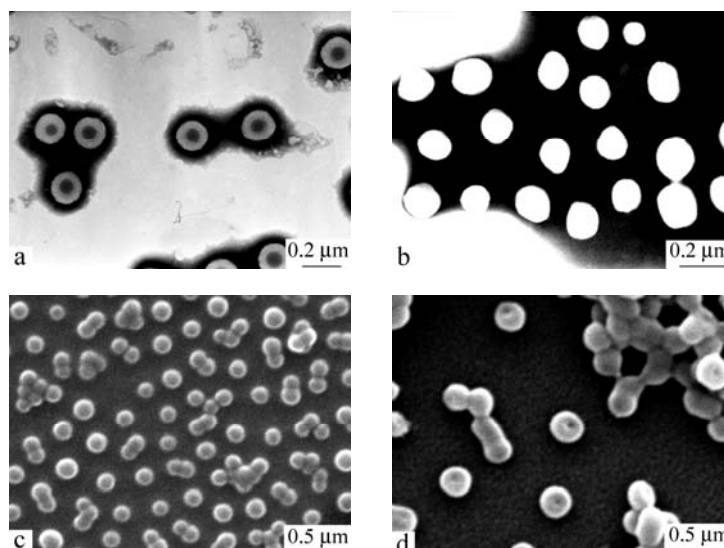


Fig. 1 TEM images of SiO₂/PNIPAM composite microgels (a) and hollow PNIPAM microgels (b); SEM images of SiO₂/PNIPAM composite microgels (c) and hollow PNIPAM microgels (d)

The temperature-induced diameter change of the hollow PNIPAM microgels with various crosslinking densities was investigated by dynamic light scattering, as shown in Fig. 2. When the temperature is elevated from 20 °C to 45 °C, their average hydrodynamic diameters decrease remarkably, indicating the hollow microgels deswells due to release of their entrapped water. Their volume phase transition take place at about 32 °C, which is consistent with the lower critical solution temperature of linear PNIPAM^[21]. It is also found from Fig. 2 that, with increasing their crosslinking density, their maximum deswelling extent lowers. The deswelling ratio of the hollow microgels defined as the cubic ratio of their diameters at 20 °C and 45 °C ($(D_{20\text{ °C}}/D_{45\text{ °C}})^3$) significantly decreases from 9.9, 6.1 to 4.5 upon increasing the molar percentage of the crosslinker MBA to the monomer NIPAM from 5%, 10% to 15% used in their synthesis recipes. Their deswelling and swelling cycles were repeatable and reproducible at least three times, even for the hollow microgels of low crosslinking density.

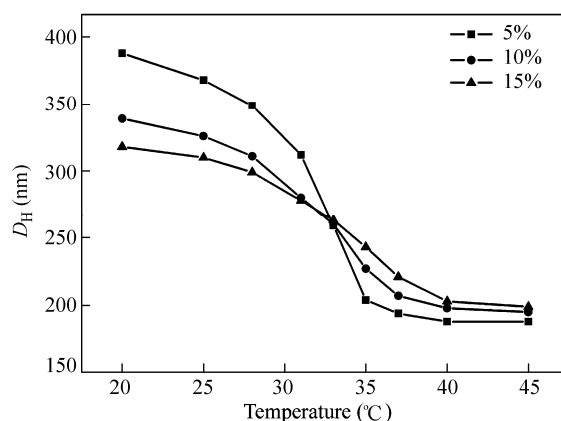


Fig. 2 Hydrodynamic diameters (D_H) of hollow PNIPAM microgels prepared by various molar percentage of MBA to NIPAM (5%, 10%, 15%) as a function of temperature

Fabrication of Discontinuously Hollow PNIPAM Fibers by Ice-segregation-induced Self-assembly Process

The discontinuously hollow fibers were fabricated by ice-segregation-induced self-assembly of the hollow PNIPAM microgels. The hollow PNIPAM microgels were dispersed in water and diluted to 1 wt% aqueous dispersion, followed by unidirectional freezing in liquid nitrogen bath. The ice was then sublimed by freeze drying at $-80\text{ }^{\circ}\text{C}$ and the discontinuously hollow fibers were produced. For comparison, the SiO_2 /PNIPAM composite fibers were also fabricated by ice-segregation-induced self-assembly of SiO_2 /PNIPAM core/shell composite microgels under the same conditions. The SEM images shown in Fig. 3 indicate that both the SiO_2 /PNIPAM composite fibers and the discontinuously hollow fibers are rounded, randomly orientated and interweaved, and their length varies from hundreds of micrometers to several millimeters. When the aqueous hollow PNIPAM microgel or SiO_2 /PNIPAM composite microgel dispersion was directionally frozen in the liquid nitrogen, the directional growth of ice crystals caused the microgels originally homogeneously dispersed in the aqueous medium to be expelled from the forming ice crystals and closely packed into fibrous structures by templating from the high-aspect-ratio ice crystals. In the freeze-drying process, the ice crystals were sublimed and the templated products of fibrous shape were formed. During the freezing process, the microgels were dehydrated and hydrogen bonds were formed between the amide groups of PNIPAM. Therefore, it is possible that the neighboring microgels can be “glued” together by the entanglement and the hydrogen bonding between the PNIPAM chains hanging on the surface of the adjacent microgels, leading to stable fibrous structures after freeze-drying. Such interactions integrated the microgels together and made the fibers mechanically strong enough for manipulation.

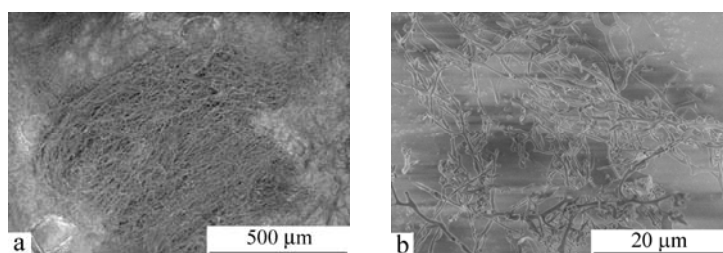


Fig. 3 SEM images of (a) the interweaved SiO_2 /PNIPAM composite fiber bundles and (b) the interweaved hollow PNIPAM fiber bundles

The Topographical Structure of Discontinuously Hollow PNIPAM Fiber Surfaces

In order to observe the fine structure of the fiber surface, the SiO_2 /PNIPAM composite fibers and the discontinuously hollow fibers were directly analysed by FE-SEM without any surface coating under very low accelerating voltage (1–1.5 kV). It can be found from Fig. 4(a) that the SiO_2 /PNIPAM composite fiber is

composed of hexagonally packed SiO₂/PNIPAM core/shell composite microgel particles. However, as shown in Fig. 4(b), no microgel particles but orderly arrayed dent depressions are observed on the surface of the discontinuously hollow fibers. During the freezing of the SiO₂/PNIPAM core/shell composite microgels, only PNIPAM shells were dehydrated and collapsed, so the microgels preserved their spherical shape in the formed fibers due to the support effect of SiO₂ cores. However, the hollow PNIPAM microgels were fully swollen and their interior cavities were full of water before freezing. Therefore, in the process of freezing, the hollow PNIPAM microgels were collapsed and dented due to the dehydration of PNIPAM wall and eduction of the water entrapped inside the hollow microgels, resulting in disappearance of the interface between the microgels and appearance of the orderly arrayed dent depressions.

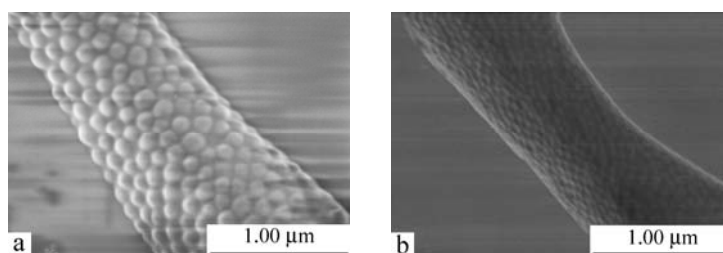


Fig. 4 SEM images of (a) the fiber formed from SiO₂/PNIPAM core/shell composite microgels and (b) the fiber formed from hollow PNIPAM microgels

The Main Factors Affecting the Fabrication of Discontinuously Hollow PNIPAM Fibers

Ice-segregation-induced self-assembly process consists of the freezing and freeze-drying of either a water solution or dispersion or a hydrogel, forming the materials with various morphological structure depending on the solute nature and size, the solute concentration and freezing conditions^[14]. In the fabrication of discontinuously hollow PNIPAM fibers, the unidirectional freezing of the microgel aqueous dispersion in liquid nitrogen bath at a constant rate is crucial for producing fibrous product. SEM images indicate that the assembly products showed obviously different morphological structure under different freezing condition. Under unidirectional freezing condition, the product was rounded, randomly orientated and interweaved fibers, as shown in Fig. 3(b). If the dispersion wasn't unidirectionally frozen, for example, the aqueous hollow microgel dispersion was frozen by refrigerator (−20 °C), the final product was the thin films with porous structure, as shown in Fig. 5. In addition, the microgel concentration in the aqueous dispersion was found to be another crucial factor for the morphology control of the product. For instance, unidirectional freezing a more concentrated microgel dispersion resulted in a mixture of fibers and flakes.

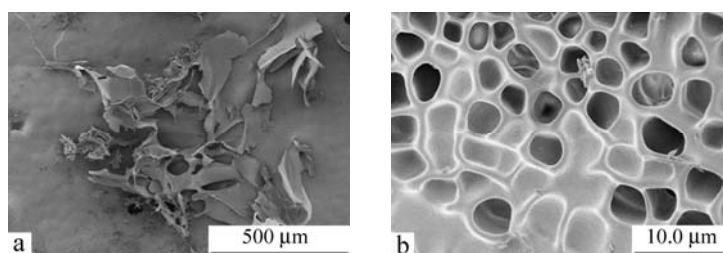


Fig. 5 SEM images of the thin films formed from hollow PNIPAM microgels under different magnifications

CONCLUSIONS

In summary, a new kind of hollow hydrogel microfiber with discontinuously hollow structure was prepared by ice-segregation-induced self-assembly of the thermo-responsive hollow PNIPAM microgels, which were produced by removing the SiO₂ cores of the SiO₂/PNIPAM core/shell composite microgels through chemical etching with hydrofluoric acid. Many orderly arrayed dents were observed on the surfaces of the microfibers by

FE-SEM, indicating that they are constructed by closely packed monodisperse hollow PNIPAM microgels. It was found that the unidirectional freezing approach of hollow PNIPAM microgels dispersion at a constant rate is crucial for producing the fibrous product, and the microgel particle concentration in the initial aqueous dispersion obviously affects the morphological structure of the hollow hydrogel microfibers.

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