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Template Synthesis of Poly(*N*-isopropylacrylamide) Minigels Using Interconnecting Macroporous Polystyrene

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Thermosensitive uniform-sized poly(*N*-isopropylacrylamide) minigels with diameters of several micrometers were synthesized by a double template method using silica particles as original molds. The first template composed of the silica particles produced a macroporous polystyrene as the second template to decide the shape and the size of the minigels. The resultant minigels in the second template covalently interconnect with each other. After the minigels were collapsed in each compartment of the macroporous polystyrene, the separated minigel particles were obtained.

Introduction

Stimuli sensitive polymer gels that undergo reversible volume changes are of scientific and technological interest.¹ Most of the studies have, so far, been focused on a bulk gel whose size is bigger than submillimeter. However, the bulk gel needs a long time to reach swelling equilibrium because the time it takes for the swelling or shrinking of a gel is proportional to the square of the characteristic length of a gel such as the radius for a spherical or cylindrical gel and the thickness for a slab gel:²

$$\text{time} = (\text{characteristic length})^2/D_c \quad (1)$$

The diffusion coefficient, D_c , of a gel is usually considered to be constant and of the order of 10^{-7} cm²/s if the initial and final states of the swelling change are fixed.³ Therefore, the time needed for the volume change reduces as the size of the gel becomes smaller. For the determination of the physical properties and the technological applications of a gel, it is naturally desirable that its response time be as short as possible. Furthermore, as the size becomes small, the problem of the mechanical strength in the usage is also mitigated. Thus, minispherical gels have been the focus of constant attention over the past 20 years.^{1e–g,3,4}

Several studies have been reported on stimuli sensitive minigel particles, which can change their volumes in response to external change.^{1e–g} If there is one compound that has started to dominate the development of stimuli

sensitive polymer gels these days, it must be poly(*N*-isopropylacrylamide) (poly(NIPA)).⁵ The spread of usage of this polymer into many branches of scientific and technological fields is mainly due to the reversible thermosensitivity in a remarkable shrinking and swelling with changing temperature in aqueous solutions. Poly(NIPA) minigels and their derivatives have been studied in applications including the absorbents of proteins,^{1e} the removal of heavy metal ions,^{1f} and the controlled release of drugs.^{1g} To extend the possibility to various applications of the minigel particles composed of poly(NIPA), gel particles of all sizes with narrow particle size distributions need to be obtained. With the old technology, however, methods to control all of the sizes and compositions have not been established yet: minigels of 1–10 μm and <50 nm have not been prepared. On the other hand, the production technique of highly monodisperse silica gel particles has been established in various sizes.⁶ Silica gel is one of the very few materials that allows the facile synthesis of collections of uniform spheres with variable diameter. The aim of this work was to establish the method for making various sizes of the poly(NIPA) minigel particles by the double template method using the silica particles.⁷ This method was first developed by V. L. Colvin's group to make inorganic nanoparticles. We employed this method in order to make minigel particles with uniform size.

A few types of silica colloids with size distributions of less than 5% were able to form three-dimensional periodic colloidal crystals by a gravity sedimentation method,⁸ a hydrodynamic method,⁹ and a solvent evaporation method¹⁰ from dispersions in flat Petri dishes. It is known that the silica colloids are organized into a close-packed arrangement with a long-range order (Figure 1a). The stable dried crystals were obtained by the solvent evaporation method and then completely dried in vacuo at 60 °C. These silica–air crystals can serve as first minitemplates for the formation of macroporous polymers as second minitemplates to obtain minigels. The styrene monomer containing benzoylperoxide (BPO) as an initiator was

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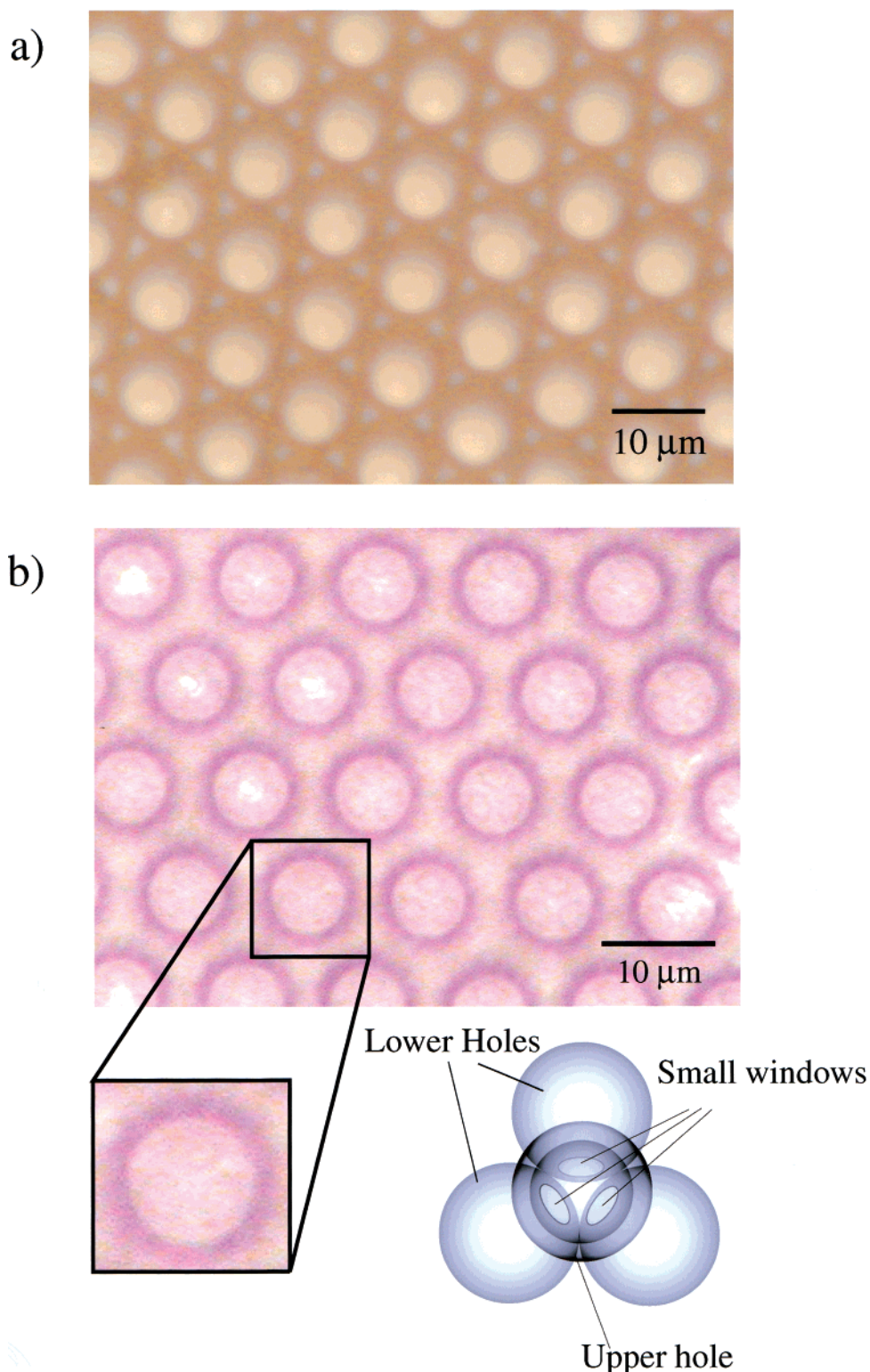


Figure 1. (a) Photograph of silica colloidal crystals. The diameter of a silica particle is $10\ \mu\text{m}$. (b) Photograph of templated macroporous polystyrene by silica colloidal crystals. Each void is connected to other neighboring voids through smaller windows (schematic representation).

infiltrated into the crystals and was polymerized at $60\ ^\circ\text{C}$ so as to trap their crystalline order. The obtained polymer membranes were soaked in 5% hydrofluoric acid solution for a few days to remove the silica colloids completely. Figure 1b shows a digital microscope photograph of the macroporous polystyrene membrane made by using the $10\ \mu\text{m}$ silica particles. The smaller inner pores that connect the macropores to each other appear in each macropore.

These pores allow the permeation of solutions into each compartment where silica particles are present.

NIPA and *N,N*-methylene-bis-acrylamide (BIS) were used as the main monomer and cross-linker, respectively, to obtain minigels. First, 5.933 g of NIPA, 0.531 g of BIS, and 0.135 g of BPO (1 mol %) were dissolved in a certain amount of ethanol (the final volume was 50 mL). The solution was degassed by bubbling nitrogen gas for 20

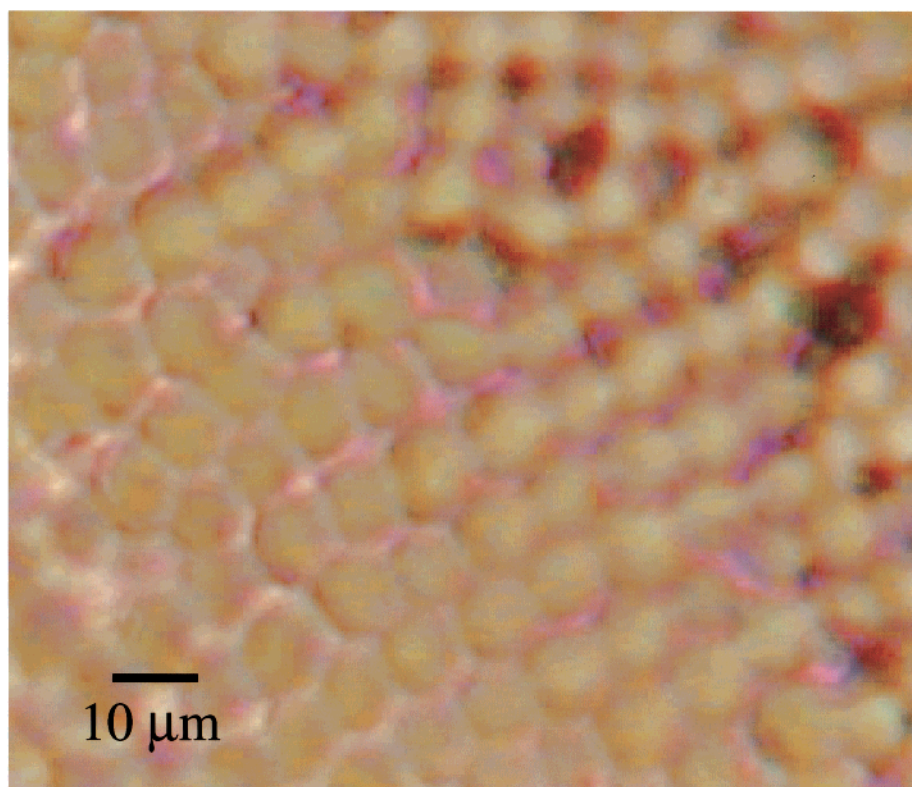


Figure 2. Photograph of a minigel particle assembly that is prepared by macroporous polystyrene.

min before the gelation. The macroporous polystyrene membranes were immersed into the pre-gel NIPA solution. Subsequently, polymerization was conducted by adding 0.102 g of dimethylaniline (1.5 mol %) to initiate a redox polymerization for 12 h at 4 °C. The membranes were taken out from the bulk gel and washed by toluene. The host macroporous polymer film can be easily removed, leaving behind an array of poly(NIPA) minigel particles that retain the structure of the initial silica crystals (Figure 2). The resultant gels are covalently interconnecting minigel particles.

Poly(NIPA) is known to undergo a reentrant coil-to-globule transition of individual polymer chains in water as well as many mixtures of water and water-mixable solvents, such as methanol, ethanol, and dimethylformamide.¹¹ For example, both water and ethanol are good solvents for poly(NIPA) at room temperature, but strangely, a mixture of them is not. This phenomenon has been called cononsolvency, and ternary phase diagrams have been observed. Therefore, poly(NIPA) gel also undergoes two transitions: a discontinuous collapsing followed by a continuous swelling when the solvent composition is varied systematically.¹² Figure 3 shows the degree of swelling of cylindrical poly(NIPA) gels in the aqueous solution of ethanol as a function of ethanol concentration.¹³ At room temperature (27 °C), poly(NIPA) gel is swollen in pure water. However, at an ethanol concentration of 20%, the gel undergoes a discontinuous volume collapse. The gel remains in the collapsed state under a further increase of ethanol concentration up to

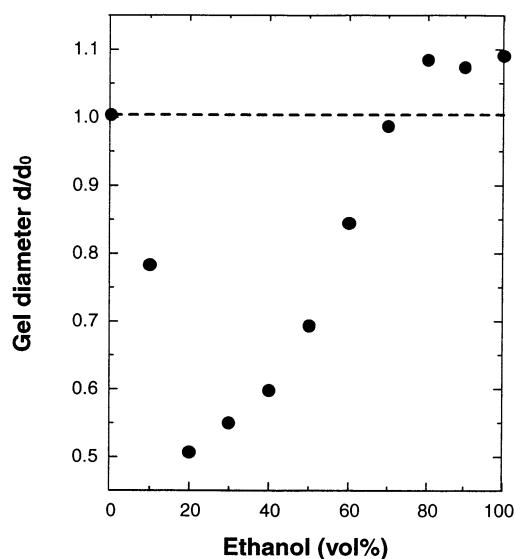


Figure 3. Swelling ratio of *N*-isopropylacrylamide gel in a mixture of EtOH and water at 27 °C. A ratio d/d_0 of unity denotes that the gel is the original size.

40%, and then the gel reswells continuously. This reentrant phase transition is reversible for a gradual change in the solvent compositions. However, when a swollen gel in a good solvent was suddenly immersed in a poor solution, it became opaque and wrinkled. In this case, the gel eventually became hollow, forming a tube.¹⁴ This means that polymer chains composing the gel were cut mechanically by suddenly changing the quality of the solvent.

This paper tried to isolate each minigel from the covalently interconnecting minigel particles to employ this phenomenon. The mechanism that was expected is as follows. The resulting gels in the macroporous polystyrene

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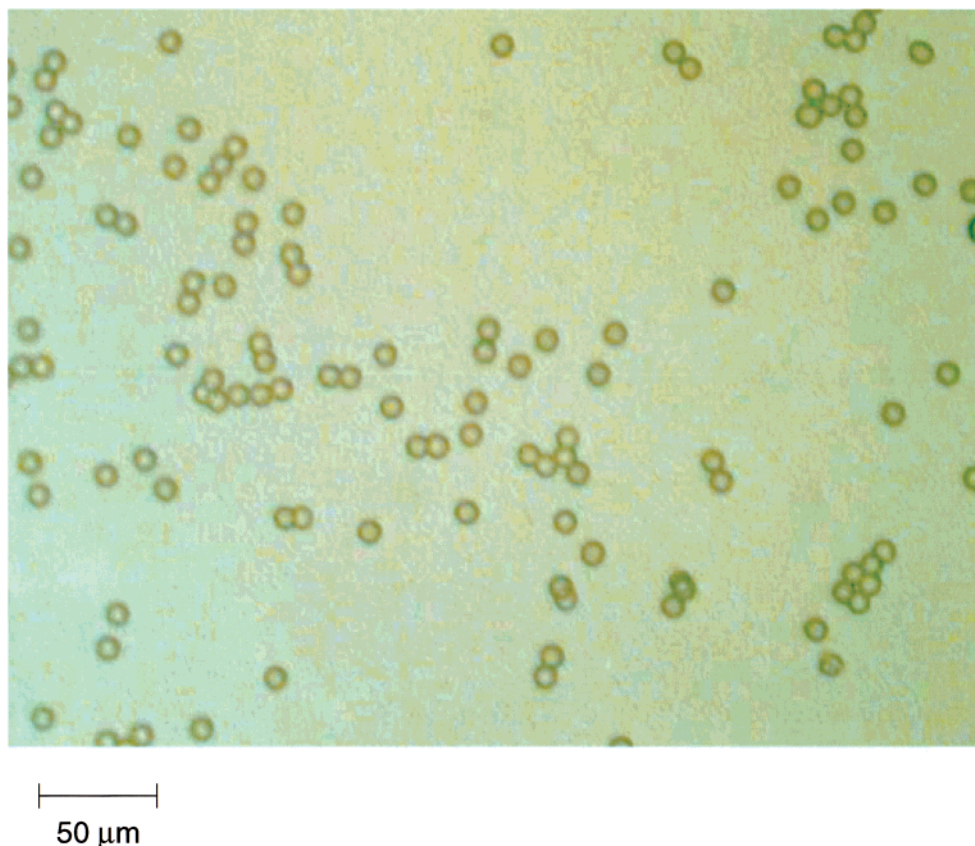


Figure 4. Photograph of separated minigel particles in water. The particles undergo a volume change in water with changing temperature, revealing that these are *N*-isopropylacrylamide gel particles.

were immersed in 30 wt % ethanol aqueous solution to reach a fully collapsed state at 25 °C. Each minigel undergoes a collapse transition in each compartment, thereby allowing separation of the minigels. Since there is a frame of polystyrene when mechanical stress starts by changing the solvent composition, each gel particle is cut from the weakest place: the portion with which the gel particles were connected. After such an operation was performed, the separated gel particles were obtained when the membrane was immersed in toluene to dissolve polystyrene, as was expected (Figure 4).¹⁵

In conclusion, poly(NIPA) minigels with diameters from 1 to 10 μm were synthesized by the use of macroporous

polystyrene films as minitemplates. If this method is used, it will become possible technically to prepare gel particles that have the desired particle diameter from nanometer to micrometer sizes. In this method, each compartment can be used as a small vessel to make gels. Therefore, the initial concentrations of monomer and cross-linker and the composition of monomers for making gels can be easily changed to obtain the desired properties of gels that are similar to those of bulk gels.¹⁶ Studies to confirm these hypotheses are under way.

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(15) In general, nonionic particle becomes so sticky that it becomes small. Micron-sized NIPA minigel particles composed of nonionic polymer are also sticky and form aggregates in water. Even micron-order silica particles aggregate with each other in water. However, these aggregates of minigel particles or silica particles can be separated when the solutions are stirred. We can observe that these aggregates are broken up to isolated particles in a stirred solution by an optical microscope. Therefore, we concluded that the separated minigel particles were obtained by our separation method.

(16) The same swelling behaviors can be observed in both the cylindrical gel and the 10 micron sized minigel in water.