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SHORT COMMUNICATION

S. Horiguchi
K. Miyamoto
M. Tokita
T. Komai

Preparation of poly(*N*-normalpropylacrylamide) gel beads

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S. Horiguchi · K. Miyamoto
Prof. M. Tokita (✉) · Prof. T. Komai
Department of Chemistry for Materials
Faculty of Engineering
Mie University
Tsu 514
Japan

Abstract The gel beads of *N*-normalpropylacrylamide are prepared by the radical copolymerization of *N*-normalpropylacrylamide and *N*,*N'*-methylene-bis-acrylamide in water. The optimum reaction conditions to obtain the gel beads are revealed from the phase diagram of the reaction system together with the scanning electron microscopy of the reaction products. The scanning electron microscopy of the reaction products also indicates the formation of the spherical gel beads of sub-micron size ranging from 250 to 500 nm in diameter. The viscosity measurements of the suspension of the gel beads indicate that the concentration dependence of the viscosity of the suspension is well described by Einstein's theory of the viscosity of colloidal particles. The intrinsic viscosity of the suspension of gel beads is then determined. The density of the gel beads, which was obtained from the intrinsic viscosity of the suspension, indicates that the gel beads are in the swollen state at a temperature of 20 °C.

Key words Gel – volume phase transition – hydrophobic interaction – intrinsic viscosity

Introduction

Gel is a typical mesoscopic system that consists of a three dimensional polymer network and the solvent. It has been well established that the gel shows a volume phase transition under optimal conditions [1]. The aspects of the volume phase transition of the gel reflect the interactions between monomer units as well as the monomer unit and the solvent molecule. Many studies, thus, have been made to understand the details of the features of the volume phase transition of gels. Among others, to study the kinetics of the phase transition is of importance not only scientifically but also from the technological point of view. The kinetics of the phase transition is governed by the cooperative diffusion coefficient of the polymer network of the gel, which is the most important quantity that uniquely determines the viscoelastic properties of the gel. It has been shown that the characteristic time τ of the volume phase transition is given by the ratio of the square of the typical size of the gel R^2 and the cooperative diffusion coefficient of the gel D_{coop} [2]

$$\tau = \frac{R^2}{D_{\text{coop}}} , \tag{1}$$

where

$$D_{\text{coop}} = \frac{E}{f} . \tag{2}$$

Here, E and f represent the longitudinal modulus of the gel and the friction coefficient of the polymer network and the solvent [3]. The mechanical studies on the elasticity and the friction of the gels have been made so far [4, 5]. The results obtained in these studies confirm the equations given above. Recently, new phenomena of the gel systems, namely the multiple phases and the phase transition in heteropolymer gels, attract much attention of physicists and chemists [6, 7]. Studies are begun to clarify these new phenomena. The preliminary studies, however, suggest that the characteristic time of the swelling and the collapse of these gels are much longer than that of simple gels such as poly(acrylamide). It is clear from Eq. (1) that the characteristic time of the volume change of the gel is proportional to the square of the size of the gel. Smaller sample gels are, thus, useful to avoid the time consuming measurements of the swelling behaviors of the gels. It is, therefore, required to establish the method of synthesis to prepare small gel samples. It is already reported by Pelton that the gel beads of *N*-isopropylacrylamide (NIPA) can be prepared by radical copolymerization of NIPA and *N*, *N*′-methylene-bis-acrylamide in water [8]. Further studies are, however, clearly necessary for the establishment of the technology to prepare various kinds of gels.

Recently, we have reported that the phase transition of the poly(*N*-normalpropyl-acrylamide) gel (NNPA gel) is multiple under certain experimental conditions [9]. Although the size of the sample gel used in this study is 141 μm in diameter, it took more than three months to determine the multiple phases of the NNPA gel. It is, thus, required to prepare a smaller sample gel of NNPA for further studies on the volume phase transition of the NNPA gels. In this paper, therefore, we would like to report about the studies on the preparation of NNPA gel beads.

Experimental

The NNPA monomer was synthesized from *N*-normal-propylamines and acryloyl chlorides by a standard method. The monomer thus synthesized was distilled under vacuum. The cross-linker, *N*, *N*′-methylene-bis-acrylamide, and the initiator, ammoniumpersulfate, were purchased from BioRad (electrophoresis grade) and used without further purification. The solvent used in this study was water that was distilled, de-ionized, and finally purified by Milli-Q-system (Millipore Ltd.; specific resistance of purified water is $\sigma^{-1} = 18.3\ \mathrm{M}\Omega\,\mathrm{cm}$) immediately before the preparation of the pre-gel solution.

The pre-gel solution was prepared by dissolving monomer and cross-linker into water at desired concentrations. The tetramethylethylenediamine (accelerator) was also dissolved into the pre-gel solution at a concentration of 0.6 vol%. The pre-gel solutions were de-gassed for 20 min and sealed under nitrogen atmosphere. The pre-gel solution was kept at reaction temperatures for 10 min. The pre-determined amount of initiator solution was poured into the pre-gel solution and stirred for about 1 min. Then the solution was kept at the reaction temperature for 1 h without disturbance. The final concentration of the initiator in the reaction solution was fixed to be 0.1 wt%. The reaction solutions were inspected after the reaction to determine the phase diagram of the system. The reaction solution was dialyzed against water for two days to remove unreacted substances. Then the suspensions of the NNPA gel beads are centrifuged at 1.4×10^3 g for 30 min to remove larger aggregates of the NNPA gel beads and used for viscosity measurements.

The appropriate amount of the solutions, which were centrifuged and dialyzed, were freeze dried. The freeze dried material was further dried using the vacuum oven (Mini Oven, MO-10, Teraoka Co.) to ensure the complete evaporation of water. Then the concentration of the gel beads in the solutions were determined from the weight of the dried mass. The freeze dried material was also inspected by a scanning electron microscope to obtain information on the shape and size of the gel beads.

Results and discussion

Phase diagram of the reaction system

The reactions of the pre-gel solution are made under various experimental conditions of temperature, concentration of the NNPA, and concentration of the cross-linker. The reaction temperature is changed from 10 to 70 °C at an interval of 20 °. The monomer concentration and the cross-linker concentrations are changed independently as 100, 400, and 700 mM and 7, 21, and 42 mM at each reaction temperature.

The phase diagram of the system, which was determined by the naked eye observation of the solution after the reaction, is shown in Fig. 1. It is found from this figure that most of the reaction solutions are opaque at the reaction temperatures above 30 °C while all reaction solutions are transparent at a reaction temperature of 10 °C. The opaque nature of the reaction solution strongly suggests the formation of the colloidal particle of sub-micron size which is comparable to the wavelength of light. These results also indicate that the reaction solutions transform into bulk gels at higher concentrations of the monomer and the cross-linker. Such tendency becomes obvious when the reaction temperature is raised. In addition to this, the aggregation of reaction products also occurs at higher reaction temperatures. In such a system, we finally obtain the precipitates of the reaction products. It is worth noting that the pre-gel solution of the standard recipe (700 mM of NNPA and 7 mM of cross-linker reacted at 10 °C), by which we prepare the transparent bulk gel of NNPA for the swelling experiments, is in the solution state under the present experimental conditions. This may be due to the shorter reaction time of this experiment since

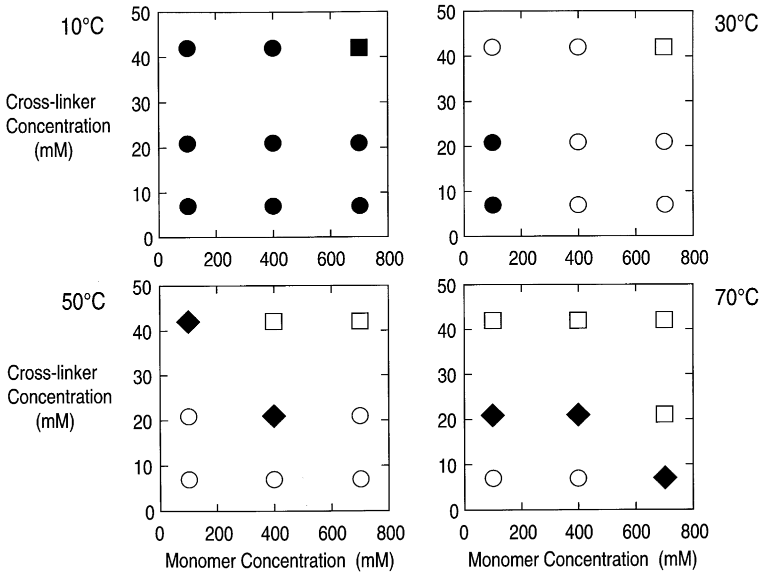

Fig. 1 The phase diagram of the reaction system. The reaction temperatures are, 10 °C; top left, 30 °C; top right, 50 °C; bottom left, and 70 °C; bottom right. The symbols indicate, ●; clear solution, ○; opaque solution, ■; clear bulk gel, □; opaque bulk gel, and ◆; precipitates

the reaction system is usually kept under the reaction conditions more than 12 h to obtain the bulk gel of NNPA. These results suggest that the reactivity of the NNPA monomer is lower than that of NIPA monomer in which we obtain the bulk gel within 1 h. These results are of interest because it may reflect the mechanism of the gelation reaction of the NNPA system but it is not the purpose of this paper. All the reaction solutions obtained here are first inspected by a scanning electron microscope. The results indicate that the gel beads are obtained at the reaction temperatures above 30 °C. The gel beads are obtained even in the transparent reaction solutions that reacted at 30 °C. These results suggest that the pre-gel solutions consisting of lower monomer concentrations which react at higher temperatures are preferable to obtain the NNPA gel beads. The optimum monomer concentration and reaction temperature range from about 50 to 200 mM and higher reaction temperatures than 30 °C, respectively.

Scanning electron microscopy

The NNPA gel beads are again synthesized at typical concentrations of the NNPA and the cross-linker at the temperatures of 30, 50 and 70 °C to study the reproducibility of the reaction. The concentrations of monomer and cross-linker are changed as follows: the ratios of the monomer and the cross-linker in the pre-gel solution, NNPA(mM)/cross-linker(mM), are 111/8 at 30 °C, 50/8, 111/8, 111/16, 111/24, and 200/8 at 50 °C, and 111/8 at 70 °C. The reaction solutions are dialyzed, centrifuged, and then freeze dried to obtain the samples for the scanning electron microscopy. The images of the scanning electron microscope of the dried gel beads are shown in Fig. 2. It is found from these images that spherical gel beads are obtained. The average diameter of the NNPA gel beads are determined from the images of the scanning electron microscope. The results are given in Table 1. The average diameters of these gel beads are found to be about 250–500 nm.

Intrinsic viscosity

The scanning electron microscopy of the reaction products is a direct experimental evidence for the formation of the NNPA gel beads of sub-micron size. These results should be, however, confirmed by combined experiments of the solution properties of the gel beads. One of the candidates of the experiments for such a purpose is the viscosity measurements of the gel beads solutions. The viscosity of the suspensions of the gel beads, prepared under various experimental conditions, is thus measured as a function of the concentration at a temperature of 20.0 °C. Then the intrinsic viscosity of the solution is determined. Typical experimental results are illustrated in Fig. 3. These results are obtained using the sample gel beads that were prepared under the conditions of the concentration ratio of monomer and cross-linker at NNPA/cross-linker = 111 mM/8 mM and the reaction temperature at 50 °C. It is clear from this figure that the specific viscosity of the

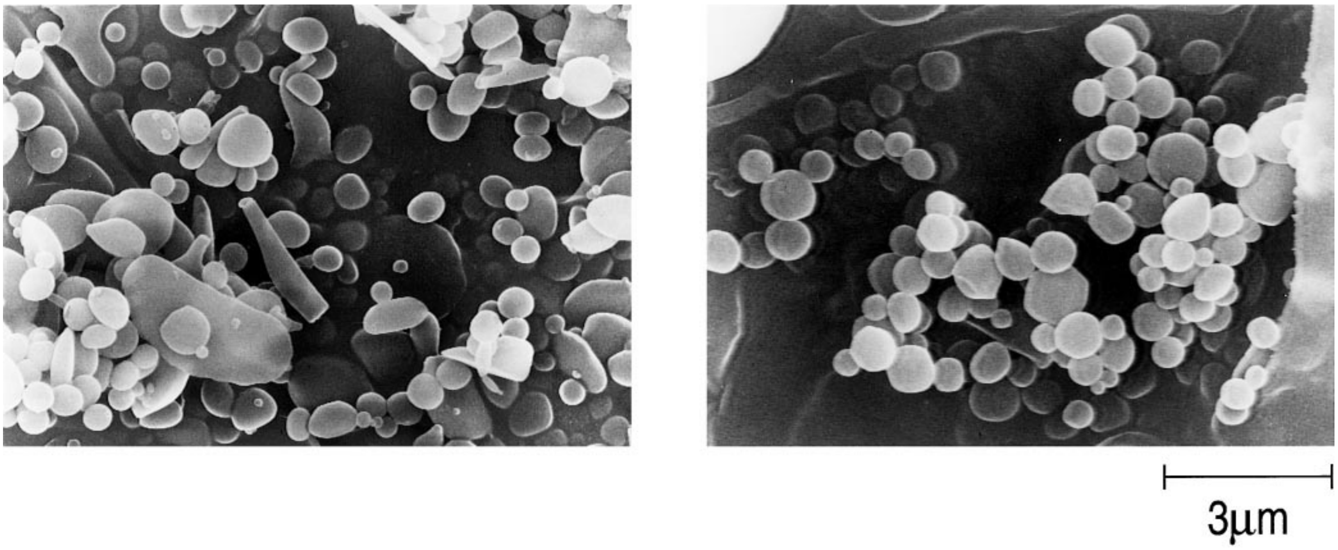

Fig. 2. The images of scanning electron microscope of the freeze dried gel beads. The composition of these sample gels are NNPA : cross-linker = 111 mM : 8 mM. The reaction temperatures are 70 (left) and 30 °C (right)

Table 1 Characteristic parameters of the NNPA gel beads

Reaction temperature [°C]	Composition (NNPA/Cross-linker) [mM/mM]	Diameter [nm]	Concentration of suspension [kg/dm^3]	Intrinsic viscosity (20 °C) [dm^3/kg]	Density (20 °C) [kg/m^3]
30	111/8	260	7.7×10^{-3}	38.3	65
50	50/8	274	2.4×10^{-3}	22.7	110
	111/8	333	7.6×10^{-3}	25.8	97
	111/16	302	7.9×10^{-3}	17.0	147
	111/24	435	5.5×10^{-3}	15.1	166
	200/8	406	11.9×10^{-3}	25.7	97
70	111/8	522	5.1×10^{-3}	21.4	117

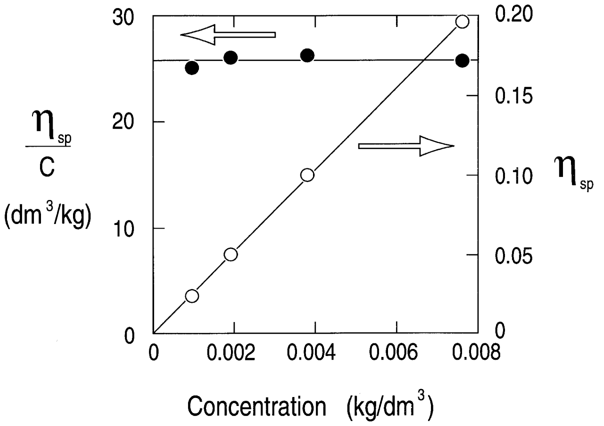

Fig. 3 The concentration dependence of the specific viscosity η_{sp} and the reduced viscosity η_{sp}/c. The measurements are made at a temperature of 20.0 °C using a Ubbelohde viscometer. The composition of the gel beads is NNPA : cross-linker = 111 mM : 8 mM. The reaction temperature is 50 °C

suspension is proportional to the concentration of the gel beads. The same concentration dependence of the specific viscosity is observed in the all gel bead systems prepared in this study.

It is well established that the specific viscosity of the suspension η_{sp} of the colloidal particle can be expressed by the following equation [10]:

$$\eta_{sp} = \frac{\eta - \eta_0}{\eta_0} = 2.5\phi \ , \tag{3}$$

where η_0, η, and ϕ denote the viscosity of the solvent, the viscosity of the suspension, and the volume fraction of the colloidal particle respectively. The volume fraction of the colloidal particle can be written as follows:

$$\phi = \frac{c}{\rho} = cv \ , \tag{4}$$

where, c, ρ, and υ are the concentration of the suspension (g/cm^3), the density of the particle (g/cm^3), and the specific volume of the particle (cm^3/g), respectively. The intrinsic viscosity of the suspension is, hence, expressed as follows:

$$[\eta] = \lim_{c \to 0} \frac{\eta_{sp}}{c} = 2.5\upsilon \ . \tag{5}$$

The specific volume, and hence the density, of the colloidal particle can be determined from the intrinsic viscosity of the suspension $[\eta]$. The results are analyzed according to the Eq. (5) and also plotted in Fig. 3 as a function of the concentration. It is clear from this figure that the reduced viscosity, which is given by the ratio of the specific viscosity and the concentration of the suspension, is independent of the concentration of the suspension. These results indicate that the viscosity of the suspension of NNPA gel beads is well explained by Einstein's theory of viscosity of colloidal particles. These viscometric behaviors of the gel bead solutions strongly suggest the formation of the NNPA gel beads of colloidal size in the solution. Furthermore, we can determine the density of NNPA gel beads ρ from the intrinsic viscosity of the suspension. The results of the viscosity measurements for various gel bead samples are analyzed in the same manner. The density of the gel beads thus obtained are given in the Table 1. It is found from these results that the values of the density of NNPA gel beads are rather low at a temperature of 20 °C; from about 70 to 170 kg/m^3.

It has been already reported that the NNPA gel (transparent bulk gel) shows a thermoreversible volume phase transition at about 24 °C as shown in Fig. 4. It is clear from this figure that the NNPA gel is in the swollen state below 24 °C. The swelling ratio of the gel gradually decreases upon increasing the temperature. Then the gel transforms into a compact state above 24 °C. The swelling ratio of the gel is independent of the temperature above 24 °C. These results indicate that the collapsed state of the gel is uniquely defined by a swelling ratio of the gel. In contrast, the swollen state of the gel involves many states that correspond to the various swelling ratios of the gel. Since the initial concentration of NNPA and the swelling ratio of the gel are known, the density of only the polymer network of NNPA bulk gel can be calculated from these values. The NNPA gel, which was used to determine the swelling behavior shown in Fig. 4, is prepared at a monomer concentration of 700 mM. Assuming that most of the NNPA monomers are incorporated into the polymer network, the density of the polymer network becomes about 80 kg/m^3 at a swelling ratio of unity. It is obvious from Fig. 4 that the swelling ratio of the NNPA gel is about 2 at 20 °C. On the other hand the swelling ratio of the collapsed state of the NNPA gel is about 0.1. Thus, the final density of the polymer network is calculated to be about 40 kg/m^3 at a temperature of 20 °C which increases up to about 800 kg/m^3 above the phase transition temperature in the case of the bulk gel of NNPA. The density of the polymer network of the NNPA gel bead is, however, much smaller than that of the bulk gel in the collapsed state. These results, therefore, indicate that the NNPA gel beads are in the swollen state at a temperature of 20 °C.

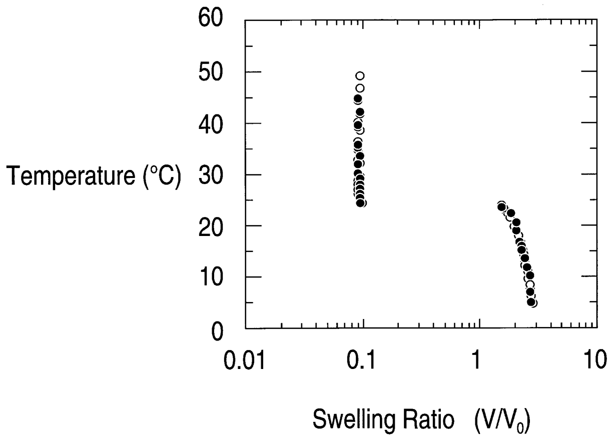

Fig. 4 The swelling curve of the bulk gel of NNPA (cited from Ref. [9]). The gel is prepared at a monomer concentration of 700 mM and at a reaction temperature of 5 °C. The open symbols represent the swelling ratio of the gel measured as a function of increasing temperature. The closed symbols are those measured upon lowering the temperature

Conclusions

We describe a convenient method to prepare the suspension of the *N*-normalpropylacrylamide gel beads of submicron size in this report. The density of the polymer network of the gel beads thus obtained can be determined from the intrinsic viscosity of the suspension. These results strongly suggest that the volume phase transition of the gel beads can be studied by the viscosity measurements of the suspension of the gel beads. The viscosity measurements of the suspension are, in some cases, much easier and efficient than the conventional method in which the bulk gels are used. It is, however, required to clarify the relationship between the physical properties of the gel beads and that of the bulk gels. For instance, the information on the temperature dependence of the radius of the gel beads is of importance to discuss the relationship between the phase transitions of the gel beads and that of the bulk gel. This information can be obtained by the dynamic light scattering study of the suspension of the gel beads. Therefore, the combined use of the viscosity and the light scattering data will promote a better understanding of the volume phase transition of the gel beads of the sub-micron sizes. Such studies are currently under way and will be reported in the near future.

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