Preparation and Responsive Properties of Magnetically Soft Poly(*N*-isopropylacrylamide) Gels

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ABSTRACT: A novel polymer gel characterized by temperature and magnetic field sensitivity has been prepared. By incorporation of magnetite nanoparticles into poly(*N*-isopropylacrylamide) hydrogels, we are able to target and separate the gel beads by a magnetic field. It was established that the presence of magnetic material does not modify the temperature sensitivity of these gels.

Introduction

Novel polymer gels that are responsive to external stimuli have been developed in the past decade.[1−3] The stimuli that have been investigated to induce change in polymer gels are diverse, and they include temperature, pH, solvent and ionic composition, electric field, light intensity, and an introduction to specific molecules. The discovery of a discontinuous volume phase transition in gels, which is often called collapse transition, has rendered such soft materials technologically useful.[4,5] The applications of these gels can be utilized in mechanical devices or controlled release delivery and separation systems.

Poly(*N*-isopropylacrylamide) hydrogel, abbreviated as NIPA gel, is one of the most frequently studied temperature responsive gels. It exhibits a remarkable volume change in response to temperature changes. The transition temperature above which the network chains are in the collapsed state is called the lower critical solution temperature, LCST. For NIPA gels swollen in water LCST has been found to be 34 °C. There are several other gels showing reversible swelling and shrinking transition with different LCST or UCST. These gels are often used to immobilize enzymes and as carriers of certain functional groups important for biochemical or biomedical applications.[5] Usually small gel beads in the size range from approximately 0.1 μm to several millimeters are used. These gels are heated by a surrounding heat source to control the swelling degree. A more efficient heating was proposed recently by application of magnetic heating. Takahashi and coworkers immobilized needlelike γ-Fe_2O_3 powders with 0.5−0.8 μm length into polymer gels.[6,7] Due to the hysteresis loss of the hard magnetic material in the presence of an alternating magnetic field, the magnetic energy is converted into heat inside the gel, which increases the temperature. Thus, warming the gel beads only is an energetically more efficient method than heating the whole environment.

Magnetic field sensitive gels were also developed to increase the rate of shape change.[8−13] Magnetic nanoparticles of Fe_2O_3, called magnetite, were incorporated into chemically cross-linked poly(vinyl alcohol) hydrogels. It was established that the peculiar magnetic and magnetoelastic properties of these gels might be used to target magnetic gel beads to a certain place or to create a wide range of motions to control the shape of the gels.

The magnetic properties of γ-Fe_2O_3 powder and Fe_3O_4 nanoparticles are quite different. γ-Fe_2O_3 is a magnetically hard material showing a hysteresis loop on the magnetization curve. The shape of the hysteresis curve is dependent upon the hardness of the material as well as the magnitude and rate of the change of applied field. Hysteresis makes possible permanent magnetism, but it also represents an energy loss mechanism producing heat. Fe_2O_3 nanoparticles with a typical size of 10 nm are magnetically soft materials. They exhibit superparamagnetic behavior.[14] The monodomain ferromagnetic particles of colloidal size are the elementary carriers of a magnetic moment in the ferrogel. In the absence of an applied field they are randomly oriented due to thermal agitation, and thus the ferrogel has no net magnetization. As soon as an external field is applied, the magnetic moments tend to align with the field to produce a bulk magnetic moment, *M*. With ordinary field strengths the tendency of the dipole moments to align with the applied field is partially overcome by thermal agitation. As the strength of field increases, all particles eventually align their moments along the direction of field, and as a result, the magnetization saturates. If the applied field is turned off, the particles quickly randomize, and *M* is again reduced to zero. This means that the magnetization curve shows no hysteresis at all and can be fitted by a Langevin function corrected with the distribution of magnetic dipole moments.

Because of the significant difference between soft and hard magnetic particles incorporated into a gel matrix, the properties of magnetic gel beads are also different. If the gel is loaded with a magnetically hard filler material, it behaves like a permanent magnet. As a consequence—due to the magnetic interactions—the gel beads form aggregates, even in the lack of external magnetic field. To counterbalance the magnetic interactions, an intensive stirring is required to maintain individual gel beads.

If magnetically soft particles are introduced into the gel, then the beads have no permanent magnetization,

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and as a result, they form aggregates only in the presence of an external magnetic field.

The main purpose of the present work is to prepare magnetically soft NIPA gel, abbreviated as MNIPA gel. For the preparation we have to incorporate individual magnetic nanoparticles into the NIPA gel matrix. It was also an important task to study how strong the influence of the magnetic filler particles is on the swelling–shrinking behavior of these gels.

Experimental Part

A magnetic field sensitive gel is a special type of filler-loaded gel, where the finely divided filler particles have strong magnetic properties. Preparation of such a gel does not require a special polymer or a special type of magnetic particle. As a polymer network one may use every flexible chain molecule that can be cross-linked. The filler particles can be obtained from ferro- as well as ferrimagnetic materials.

Preparation of a MNIPA gel is similar to that of other filler-loaded elastomeric networks. One can precipitate well-dispersed particles in the polymeric material. The "in situ" precipitation can be made before, during, and after the cross-linking reaction.[15,16] At first, a ferrofluid, which contains magnetite sol particles, was prepared from $FeCl_2$ and $FeCl_3$ in aqueous solution. To counterbalance the van der Waals attraction and the attractive part of magnetic dipole interactions, colloidal stability has been maintained by a small amount of $HClO_4$, which induced peptization. The purified and stabilized magnetite sol having a concentration of 17.2 wt % was used for further preparative work.

Chemically cross-linked temperature-sensitive poly(*N*-isopropylacrylamide) gels were prepared from *N*-isopropylacrylamide, *N*,*N*-methylenebis(acrylamide) (BA), ammonium persulfate (APS), and *N*,*N*,*N*′,*N*′-tetramethylenediamine (TEMED) from Aldrich Chemicals. These chemicals were used without further purification. We have prepared both monolith gels and gel beads.

Preparation of Monolith MNIPA Gels. Poly(*N*-isopropylacrylamide) gels were prepared by free radical polymerization. 0.8475 g of *N*-isopropylacrylamide (monomer), 0.0075 g of BA (cross-linker), and 10 μL of TEMED (accelerator) were dissolved in 8 mL of distillate water. Then this mixture was placed under the nitrogen atmosphere to remove the residual oxygen. A 1.96 mL aliquot of ferrofluid (17.2 wt %) was added to the solution. Finally, 50 μL of APS (10 wt %) was added to the mixture as the initiator. The gelation took 2 h. The gels were then washed several times in pure water in order to remove remnants of chemical reaction. After the purification the gels were cut into small pieces which were used for magnetic and swelling experiments.

Preparation of MNIPA Gel Beads. We have prepared gel beads according to the method developed by Park and Choi.[17] An interpenetrated network (IPN) was prepared by simultaneous gelation of Ca alginate in spherical bead shape, with a concomitant free radical polymerization of MNIPA and cross-linker within the beads. Alginate dissolved in 25 mL of 0.01 M Tris buffer (1.75 w/v %) was degassed and then mixed with 1.92 g of NIPA monomer, 0.09 g of BA (4% to NIPA (w/v)), 0.125 mL of TEMED, and 0.89 mL of ferrofluid. The above solution was injected in a dropwise manner, by using a syringe needle, into 300 mL of 0.01 M Tris buffer solution, containing 3% $CaCl_2$ and 0.1% (w/v) APS. Gel beads were kept for about 30 min under nitrogen atmosphere. At the end of the polymerization (24 h) they were washed three times with distillate water to remove unreacted monomer, cross-linker, and initiators. Afterward the beads were incubated with 0.1 M EDTA solution (pH $\sim$ 7) for 2 or 3 h to chelate calcium ions and extract the alginate from the IPN beads. It is worth mentioning that bead size can, to some extent, be controlled by using different sized needles on the string. In this manner beads ranging from 0.5 to 4 mm may be conveniently prepared. Since our main intention was to study both temperature and magnetic field sensitivity, we have prepared gel beads with an average diameter of $d = 2.0$ mm and narrow size distribution for accurate measurements. It must be mentioned that none of these properties are size-dependent. It is worth mentioning that preparation of smaller beads requires another technique.

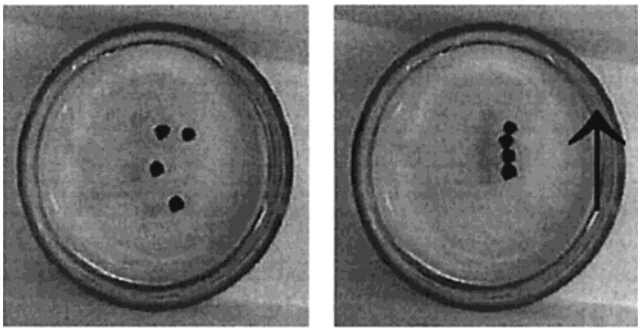

Figure 1. Needlelike aggregation of MNIPA gel beads in a uniform magnetic field: (a) no external field; (b) homogeneous magnetic field. The arrow indicates the direction of the field which has an intensity of 300 mT.

Magnetic Measurements. The static magnetization curves of different MNIPA gels have been determined at room temperature. The magnetic measurements were carried out in a homemade vibrating sample magnetometer. A small piece of monolith MNIPA gel, put into a copper sample holder, was made to vibrate uniformly in the air hole of a sensitive measure coil (1 cm long, 8000 turns of fine wires). This whole equipment was placed into a superconducting electromagnet (Oxford Instruments) being able to induce a well-controllable, homogeneous magnetizing field up to 14 T with a high homogeneity of the order of 0.1 mT/cm. We measured the voltage induced in the measure coil in cases of different magnetizing field strengths employing a lock-in amplifier (Stanford Research Systems, SR830 DSP, USA), which received the reference signal from the vibrating apparatus. This voltage was directly proportional to the magnetization of the sample.

Image Analyses. To determine the temperature dependence of swelling degree, experiments were monitored by a digital video system. A CCD camera with a $^1/_3$ in. video chip has been connected to a PC through a real-time video digitalizer card. The diameter, *d*, of MNIPA gel beads was followed on the magnified picture by a homemade program, which has properly mixed the digitalized picture coming from the video source with the computer screen image. By this method very small change in the diameter (1 pixel on the screen) can be monitored and measured on the real time video image. The error of the measurement depends on the magnification; however, in our cases it was within 0.01 mm. The reduced swelling degree defined below was used to characterize the degree of swelling and shrinking:

$$q_r = V/V_0 = (d/d_0)^3 \qquad (1)$$

where V and d represent the volume and diameter of the gel bead, respectively. The subscript refers to the reference state at temperature $T = 25$ °C.

Results and Discussion

Visual Observations and Magnetic Measurements. Several MNIPA gel beads were distributed randomly in a Petri dish (see Figure 1). Without an external magnetic field, the beads do not attract each other, and as a result, they do not form aggregates. This visual observation tells us that the gel beads have no significant remanent magnetization.

The situation is somewhat different if we put the magnetic gel beads into a homogeneous magnetic field.

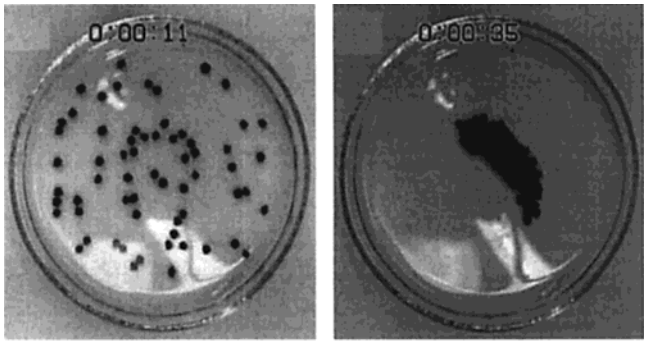

Figure 2. Magnetophoresis of MNIPA gel beads: (a) no magnetic field is applied; (b) nonuniform magnetic field is created by a permanent magnet.

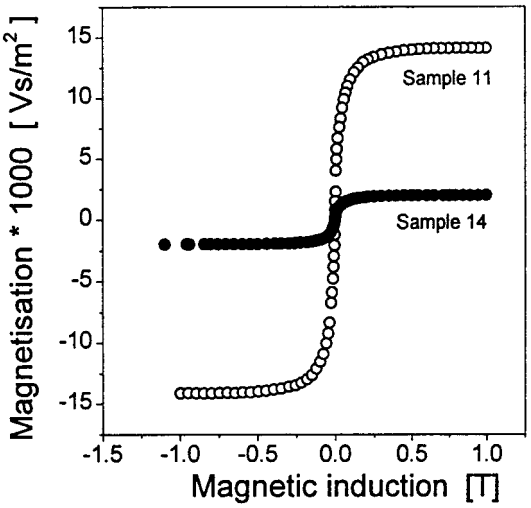

Figure 3. Magnetization curve of two monolith MNIPA gels.

In this case no force is exerted on gel beads, but the magnetic field polarizes the beads inducing a moment in them. The induced magnetic moment aligned parallel to the imposed field. The attractive interactions between induced magnetic dipoles lead to chain formation (see Figure 1b). When the field is turned off, the induced magnetic moment of the beads vanishes, and chaining can be destroyed by slight mechanical agitation.

Magnetizable particles, like MNIPA gel beads, experience a force only in a nonuniform magnetic field. This phenomenon, called magnetophoresis, is the result of a magnetoforetic force directed along the gradient of the magnetic field intensity (see Figure 2). The nonuniform magnetic field is induced by a permanent magnet (not seen in the figure) placed under the Petri dish. The beads are attracted to the magnetic field intensity maxima and repelled from minima. As a consequence, all the beads gather where the field intensity has the highest value. This position corresponds to the surface of the permanent magnet, which cannot be seen in the figure. It is also shown in the Figure 2 that the time required for collecting all the beads is rather short. This process took place within 24 s.

Although the visual observations support the expected superparamagnetic behavior, they cannot be considered as a rigorous experimental proof. Therefore, we have measured the magnetization curves. In Figure 3, as a demonstrative example, the magnetization curves for two significantly different samples are shown. The gel samples have a different amount of magnetite and cross-

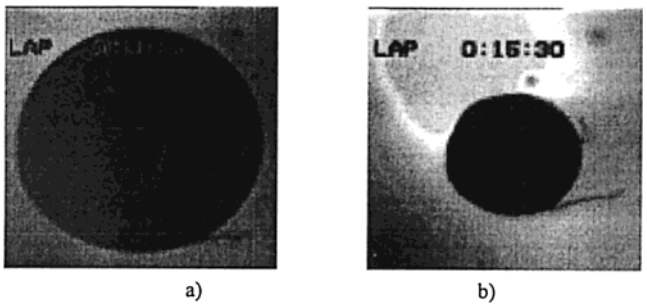

Figure 4. Collapse transition of a MNIPA gel bead: (a) temperature below the LCST, $T = 25$ °C and $d = 1.87$ mm; (b) temperature above the LCST, $T = 40$ °C and $d = 1.00$ mm.

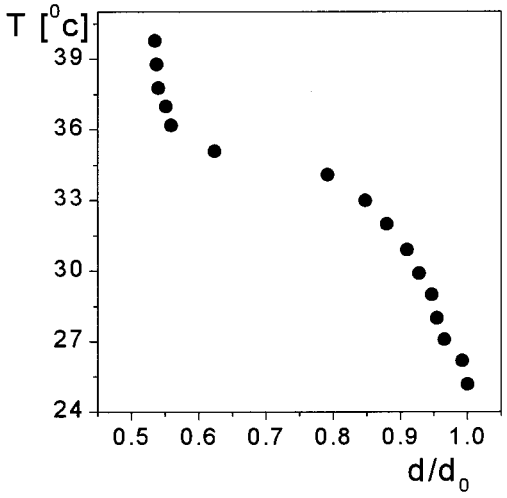

Figure 5. Dependence of the gel size on the temperature.

linking agent. As a result, the swelling degree of the gels are different. For sample 11, the concentration of magnetite is 23.1 mass %, whereas the sample 14 contains 3.3 mass %. The measured magnetization of these MNIPA gels is plotted against the magnetic induction. Two cycles have been measured and plotted. On the basis of the figure, we can conclude that, within the experimental accuracy, no hysteresis loop has been observed. This finding says that no remanent magnetization takes place in MNIPA gels at room temperature. This is an important result, which means that in alternating magnetic field the transformation of magnetic into thermal energy is rather small. For this reason, devices made of MNIPA gels and subjected to alternating magnetic field are characterized by small energy loss per cycle.

It is also seen that both the slope of the magnetization curves (at weak fields) and the value of saturation magnetization (at high field strengths) are different. The slope of the magnetization curve is identified as the initial magnetic susceptibility. Since both the saturation magnetization and initial susceptibility are proportional to the concentration of magnetic particles in the gel, therefore the ratio of the initial susceptibilities and the ratio saturation values should be equal to the ratio of magnetite concentration in the gel.

Careful analyses of the experimental data have shown that this ratio is 7.2, which—within the experimental accuracy—is in accordance with the ratio of magnetite concentrations, 7.0.

Collapse Transition of MNIPA Gel Beads. We have studied the temperature dependence of the magnetic gel beads. It was found that, similar to the

nonmagnetic NIPA gels, an abrupt volume change in response to temperature change has been observed (see Figures 4 and 5).

Because of an increase of the temperature, the volume of the gel bead is significantly decreased (see Figure 4). The reduced swelling degree has changed form 1 to 0.15. To study the effect of incorporated magnetite nanoparticles on the temperature sensitivity of the gels, we have determined the temperature dependence of the bead size (see Figure 5).

It is seen that the volume (or size) of MNIPA gels has a very similar temperature dependence to unloaded NIPA gels. This finding means that incorporation of magnetite nanoparticles into NIPA gels does not affect the temperature sensitivity significantly.

Summary

We have prepared magnetically soft temperature responsive poly(*N*-isopropylacrylamide) hydrogels. The temperature sensitivity of magnetic poly(*N*-isopropylacrylamide) gels is quite similar to that of the same gel containing no magnetic nanoparticles. Consequently, the collapse transition is not affected by the presence of magnetite nanoparticles. In a uniform magnetic field the gel beads form a straight chainlike structure, whereas in a nonhomogeneous field the beads aggregate due to the magnetophoretic force directed to the highest field intensity. The peculiar magnetic properties of these gels may be used to target and orient the temperature responsive gel beads, and it is easy to separate them from the environment by using a nonuniform magnetic field.

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References and Notes

(1) Peppas, N. A., Korsmeyer, R. W., Eds. *Hydrogels in Medicine and Pharmacology*; CRC Press: Boca Raton, FL, 1987.
(2) De Rossi, Kawana, K.; Osada, Y.; Yamauchi, A. *Polymer Gels*; *Fundamentals and Biomedical Applications*; Plenum Press: New York, 1991.
(3) Harland, R. S., Prud'homme, R. K. Eds. *Polyelectrolyte Gels*; ACS Symposium Series 480; American Chemical Society: Washington, DC, 1992.
(4) Tanaka, T. *Phys. Rev. Lett.* **1978**, *40*, 820.
(5) Okano, T., Ed. *Biorelated Polymers and Gels*; Academic Press: Boston, 1998.
(6) Takahashi, F.; Sakai, Y.; Mizutani, Y. *J. Ferment. Bioeng.* **1997**, *83* (2), 152.
(7) Kato, N.; Takizawa, Y.; Takahashi, F. *J. Intell. Mater. Syst. Struct.* **1997**, *8*, 588.
(8) Barsi, L.; Büki, A.; Szabó, D.; Zrínyi, M. *Prog. Colloid Polym. Sci.* **1996**, *102*, 57.
(9) Zrínyi, M.; Barsi, L.; Büki, A. *J. Chem. Phys.* **1996**, *104*, 20.
(10) Zrínyi, M.; Barsi, L.; Szabó, D.; Kilian, H.-G. *J. Chem. Phys.* **1997**, *106*, 5685.
(11) Zrínyi, M. *Trends Polym. Sci.* **1997**, *5* (9), 277.
(12) Zrínyi, M.; Barsi, L.; Büki, A. *Polym. Gels Networks* **1997**, *5*, 415.
(13) Szabó, D.; Szeghy, G.; Zrínyi, M. *Macromolecules* **1998**, *31*, 6541.
(14) Rosenweig, R. E. *Ferrohydrodynamics*; Cambridge University Press: New York, 1985.
(15) Mark J. E. *Br. Polym. J.* **1985**, *17*, 144.
(16) Haas, W.; Zrínyi, M.; Kilian, H.-G.; Heise, B. *Colloid Polym. Sci.* **1993**, *271*, 1024.
(17) Park, T. G.; Choi, H. K. *Macromol. Rapid Commun.* **1998**, *19*, 167.

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