Processing of Monolithic Magnetic Gels for Magnetophoresis

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Received May 26, 1994

Magnetite particles and monosized polystyrene beads were trapped in a silica sol–gel, which was then dried by using supercritical fluid extraction. When the monolithic dried gel is sintered, the polystyrene beads are pyrolyzed, leaving a porous magnetized piece of ceramic with controlled pore sizes. These "magnetic gel" ceramics provide a novel class of materials for use in gel magnetophoresis and other biophysical applications.

We report the synthesis of a "magnetic gel" oxide glass with controlled pore sizes intended for magnetophoresis applications in biology. Magnetophoresis, where magnetically labeled cells or DNA are trapped by high magnetic field gradients, is a rapidly evolving technique that is complementary to the more widely used electrophoresis method. Existing implementations of high magnetic field gradients use either steel wool[1] or metal spheres.[2] However, there exists a need for finer control of the pore sizes and a way to tailor the magnetic and structural properties of the filter material for specific applications, while at the same time ensuring that metal filters do not react with salt solutions that comprise most biological samples.

The goal of the present research is to separate magnetically labeled biological particles, which are either targeted cells or DNA molecules bound to magnetic beads. This application immediately specifies the engineering properties that must be displayed by the processed materials: (i) The magnetic "gel" has to generate large field gradients ($\sim 10^4$–10^5 T/m) in order to generate sufficient forces to effectively trap small magnetic particles. (ii) The material must have a low remnant magnetization in order to allow trapped particles to be eluted after switching off an external magnetic field. (iii) The pore sizes should be controllable, to suit the specific application—whether it is to filter magnetically labeled nucleic acids or target biological cells. This report describes a procedure for the rational synthesis of materials that satisfy these criteria.

There has been considerable interest in adapting sol–gel processing to the rational synthesis of composite materials engineered for specific applications by including inorganic and organic molecules into the sol–gel.[3] The chief advantage of this approach is that is allows for processing at much lower temperatures than direct fusion of mixed solids, thus making it possible to introduce guest molecules into the glass without destroying them during the high temperature treatment. By use of this approach, oxide glasses have been engineered with specific optical properties with applications in nonlinear optics and optical information storage.[4–5] Recently, Chaput et al.[6] have reported synthesizing a novel magneto-optic oxide gel with permanent optical birefringence. The possibility of incorporating composite nanoparticles with desired optical, electrical, or magnetic properties (see, for example, Lukehart et al.[7]) makes sol–gel processing ideal for applications in biotechnology, where control of materials properties often have to be tailored for specific applications.

I. Materials and Methods

A sol was made from tetraethoxysilane (TEOS), ethanol, and water with the volume ratio 1.5:1:1 and was left stirring for 24 h. Aliquots of this solution were placed in Pyrex tubes (~2 mL each) and then mixed with 1 mL of ferrofluid (EMG 705 from Ferrofluidics), which is an aqueous suspension of highly monodisperse colloidal particles of magnetite (Fe_3O_4) of ~100 Å diameter, stabilized by a surfactant.[8] Commercial polystyrene bead suspensions of varied amounts (Duke Scientific) were added to these mixtures to obtain a final material with controlled porosity, according to the method originally developed by Sonuparlak and Aksay.[9] A gel formed within a few minutes of the addition of the ferrofluid, suggesting that constituents of the ferrofluid enhance the gelation of the TEOS. In order to retain uniformity, the samples were shaken during gelation. Larger fractions of ethanol resulted in flocculation of the ferrofluid particles, whereas too little ethanol prevented complete hydrolysis of TEOS. Solvent extraction was performed above the critical point of the ethanol–water solution using a supercritical fluid extraction method.[10] The supercritical fluid extraction method has been described extensively in the literature and provides the most reliable and convenient method for drying gels while retaining monolithicity without cracking.[11,12]

To determine an appropriate temperature profile for the sintering, a piece of the aerogel was placed in a thermogravimetric analyzer (TGA, Perkin-Elmer). A steep drop in the mass of the sample was observed at around 300 °C, indicating the pyrolysis

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⊗ Abstract published in *Advance ACS Abstracts,* September 1, 1994.

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(12) Because the solvent has been removed from these materials, they might be more appropriately called "magnetic xerogels". We prefer to use the short form "magnetic gels".

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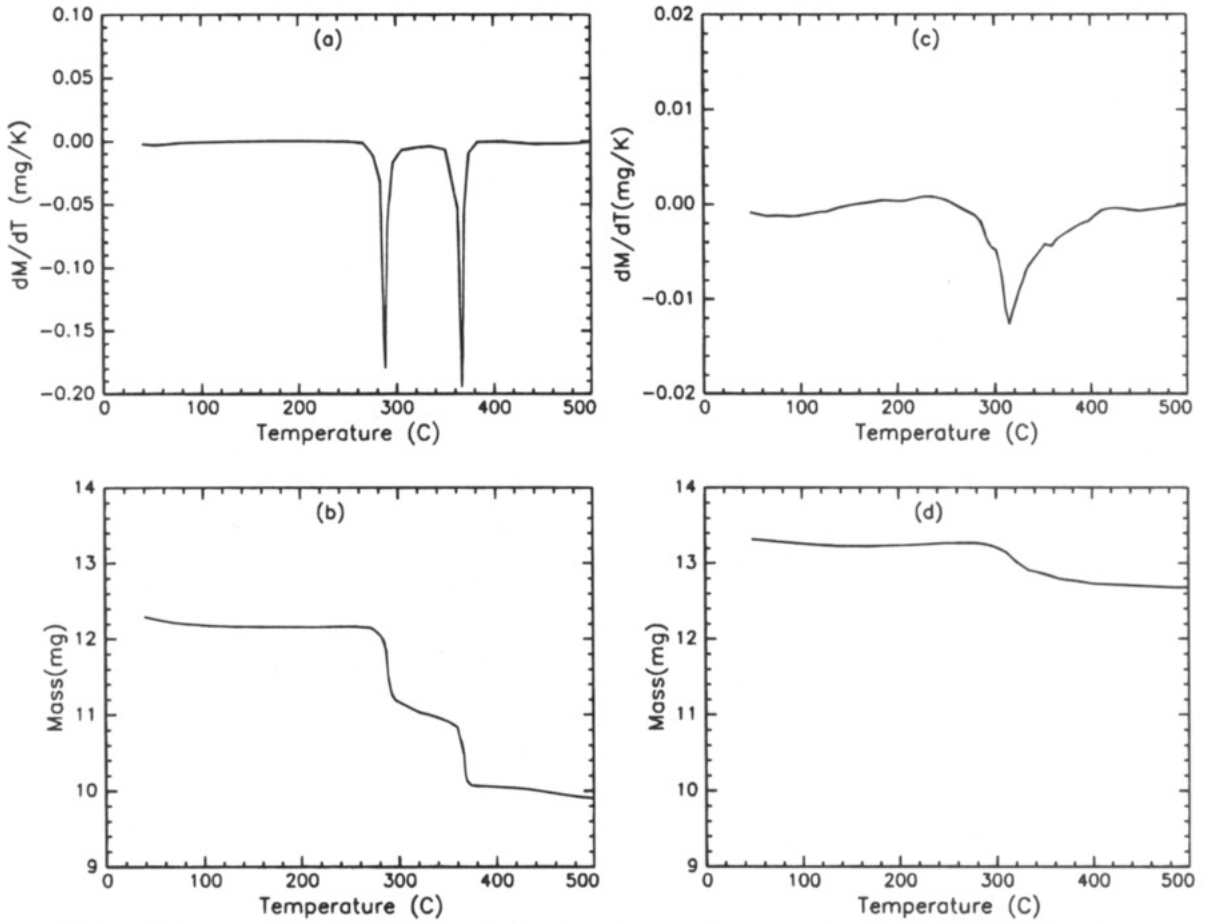

Figure 1. TGA profile for porous magnetic gels. (a) Derivative of the multistep mass loss profile shown in (b) is for a sample with a polystyrene beads with 3.4 μm diameter beads at a starting concentration of 0.02 (v/v). (c) Derivative of the mass loss profile shown in (d), for a sample with 10.2 μm diameter polystyrene beads also at 0.02 (v/v).

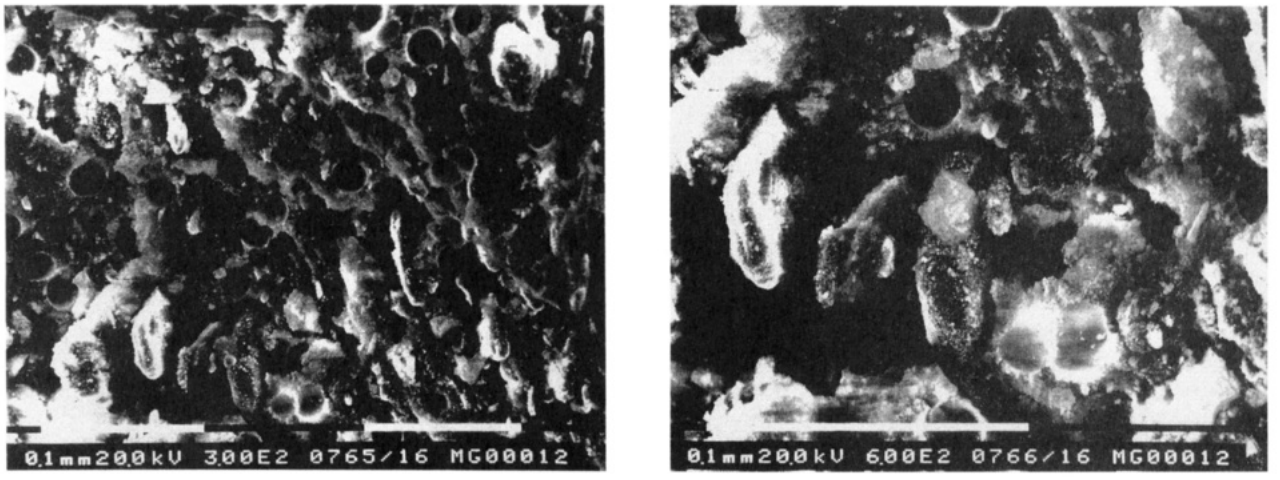

Figure 2. SEM of sintered porous magnetic gel. The circular holes are the locations of the polystyrene beads (21.7 $\pm$ 3.2 μm diameter), at a starting volume fraction of 0.015. The voids are the remnants of the polystyrene beads that were thermally removed, while the structure of the gel is maintained.

of polystyrene beads (Figure 1). Samples with large polystyrene beads (~10 μm diameter) showed only one step in the TGA loss-of-mass profile, similar to the in vacuo decomposition of polystyrene. Samples with smaller beads (~3 μm) showed a more complex multistep profile. Differently sized polystyrene beads may have different decomposition profiles, even in open air.

Sintering was done as follows. The sample was initially placed in an open air oven at 300 °C for a period of 45 min to ensure full oxidation of the polymer. The sample was then slowly heated in a nitrogen atmosphere to 700 °C and soaked for 3 h to give it greater structural integrity. The slightly reducing atmosphere had the advantage of reversing the partial oxidation of magnetite, which is inevitable during polymer oxidation at 300 °C. The sample was then allowed to cool to room temperature. The result of this processing was a black porous ceramic. In samples that were sintered in ambient air at 700 °C, the magnetite in the ceramic appeared to oxidize and formed an extremely friable reddish brown ceramic resembling hematite with poor magnetic properties.

II. Analysis

Since the morphology of the gel is one of the most interesting parameters, the microscopic structure was characterized by scanning electron microscopy (SEM, Phillips 515). An SEM image of a gel with controlled

porosity is shown in Figure 2. The porosity was further characterized by measuring the BET isotherm, using helium gas as the adsorbate (Micromeritics). The surface area per gram was measured to be 22.76 ± 0.46 cm^2 g^{-1}. A careful study of a number of such SEM micrographs suggests that the voids left by the polystyrene spheres may not be randomly distributed; some clustering, perhaps as a result of van der Waals attraction between the spheres, is observed. While the microscopic origin of this phenomenon is not understood, clustering lowers the percolation threshold required to form a continuous channel across the sample. Nonrandom clustering may also be enhanced by preparing the gel in the presence of an external magnetic field, which can orient the magnetic particles to form field induced structures.[13,14]

Magnetic susceptibility measurements were performed using a SQUID magnetometer (Quantum Design) (see Figure 3). The magnetic property of particular interest is the saturation magnetization M_s and the remnant magnetization. The measured value of M_s is 39.8 ± 0.1 erg/(G g) and the remnant magnetization is 0.9 ± 0.02 erg/(G g) with saturation setting in at an applied field strength of ~2000 G. The large M_s is needed to obtain large field gradients to trap magnetically labeled particles, and the small remnant magnetization, which results from the small size of the superparamagnetic particles, ensures that particles can be eluted after switching off an externally imposed magnetic field.

The pore size and shape can be tailored for the specific filtration application by simply changing the diameter, shape, and volume fraction of the included polystyrene beads. A systematic investigation of the filtration characteristics of these new materials has begun. We believe that sol–gel technology can be used to synthesize new classes of materials that can be designed specifically to satisfy needs in biotechnology.

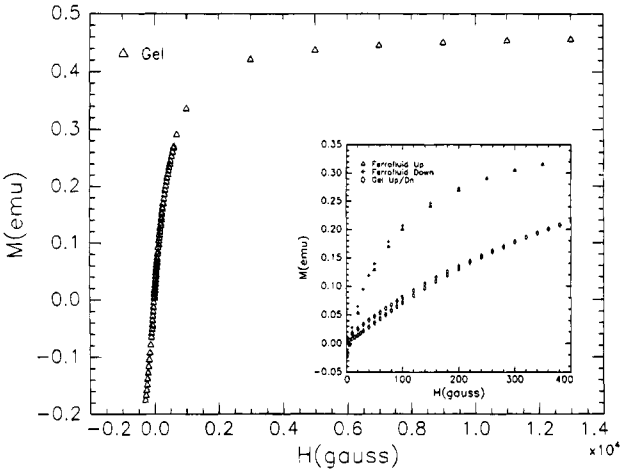

Figure 3. Magnetization of the porous magnetic gel. Inset shows the same data showing the extent of the hysteresis at lower values of the magnetic field. Also shown for comparison is the magnetization profile of the ferrofluid used.

Acknowledgment. We thank Ray Goldstein, Mi Hong, Pablo Debenedetti, Stanislas Leibler, Jay Benziger, and Nai Phuan Ong for advice. Also, assistance from Yasutomo Uemura, Graeme Luke and Weidong Wu of the condensed matter physics group at Columbia University in making magnetization measurements is gratefully noted. This work was supported in part by grants from the NSF (DMR), the Office of Naval Research, and the AFOSR (F49620-93-0259).

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