

## In Situ Preparation of Nanocrystalline $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> in Iron(II) Cross-Linked Alginate Gels

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Alginic acid is a naturally occurring polysaccharide that forms rigid cross-linked gels in the presence of di- and trivalent cations.<sup>1</sup> Recently, magnetic forms of alginate have been made by incorporation of micrometer-scale iron oxides into the calcium cross-linked gels.<sup>2,3</sup> In addition, alginic acid, together with other polysaccharides, have served as templates for the preparation of various magnetic substrates.<sup>4</sup> Magnetic gels are the subject of intense current research for potential applications in medical diagnostic technologies, such as magnetic drug delivery<sup>5</sup> and cell-sorting systems,<sup>2</sup> and in sensors and actuator systems.<sup>6</sup> Here we report a new approach to the preparation of magnetic alginate that utilizes the cross-linking ion as the reaction center for the in situ formation of nanocrystalline iron oxides. The resulting gel was isolated in the form of spherical beads that are superparamagnetic and stable indefinitely at room temperature.

Typically, the iron oxide–alginate nanocomposites were prepared as follows. An aqueous solution of sodium alginate (25 mL, 3 wt %, alginic acid, sodium salt, Aldrich Chemicals) was added dropwise at room temperature and using a syringe fitted with a 17 gauge stainless steel needle to a degassed solution of FeCl<sub>2</sub> (0.1 mol L<sup>-1</sup>, 250 mL, 1:1 v/v methanol/deionized water). The pale-yellow Fe(II)-cross-linked beads, ca. 2 mm in diameter, formed instantaneously. At the end of the addition, the beads were kept in the reaction solvent, for several hours under N<sub>2</sub>. They were washed with copious amounts of methanol (MeOH)/water (1/1 v/v) to remove excess ferrous ions. Methanol served to inhibit the alginate depolymerization. Next, an aqueous solution of sodium hydroxide (0.5 mol L<sup>-1</sup>, 200 mL, pH 13) was added at once to the Fe<sup>2+</sup>-cross-linked beads kept under nitrogen in a MeOH/water solution, resulting in a change in the color of the beads from light orange to

dark green. After 2 h oxygen was bubbled through the mixture for 2 h. The resulting orange beads were washed with MeOH/water to neutral pH. To increase the amount of iron oxide in the gel beads, the two steps were repeated up to four times with the same batch, in the manner reported by Ziolo et al.<sup>7</sup> for the preparation of high loadings of iron oxides in cross-linked sulfonated polystyrene ion exchange resins. This technique allowed us to prepare gels containing 0.5–5.5 wt % of Fe in the wet beads or 10–50 wt % of Fe in the dehydrated form. The iron content was determined spectrophotometrically on acid-treated freeze-dried beads using *o*-phenanthroline.<sup>8</sup> We note that related systems, such as swollen ionic alginate fibers,<sup>9</sup> were resistant to multiple loadings.

The ability to perform multiple loadings on the same batch of beads suggests a regeneration of the reactive oxygen-bearing ionic sites in the polysaccharide following oxide formation. The ionic nature of the iron oxide containing gels is evidenced further by volume changes in the beads when exposed to solutions of varying pH. In an acidic environment (0.1 M HCl) where the carboxylate groups are expected to exist in their protonated form, the gels shrink to approximately one-half the volume they occupy in neutral conditions. Alternatively, swelling occurs in aqueous base (0.1 mol L<sup>-1</sup> NaOH).<sup>10</sup> Methanol was used as a cosolvent throughout the preparation to prevent depolymerization of the alginate, which is promoted by oxygen and ferrous ions.<sup>11</sup> Accordingly, the beads can be stored indefinitely in a MeOH/water solution and can be subjected to at least six reaction cycles.

A transmission electron micrograph (TEM) of iron oxide alginate beads is shown in Figure 1. Here, the beads were subjected to two reaction cycles, embedded in a Spurr resin, and sectioned prior to analysis with a JEOL JEM 1200 EXII TEMSCAN microscope. The observed *d*-spacing values (Table 1) from both the electron diffraction pattern (inset, Figure 1) and the powder X-ray diffraction pattern of the magnetic nanocomposite were consistent with those for either  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> or Fe<sub>3</sub>O<sub>4</sub> (Table 1). The iron oxide particles are approximately isometric in shape and range in diameter from 4 to 15 nm.<sup>12</sup> The beads are light-brown and optically similar to the  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> nanocomposites reported in ref 6. This color suggests that Fe<sub>3</sub>O<sub>4</sub>, usually dark-brown to black, is not present in the beads. Further analysis of the materials, in particular Mössbauer spectroscopy, is in progress in order to confirm this point.

The broad size range of the oxide nanocrystals presumably results from the inhomogeneity in the composi-

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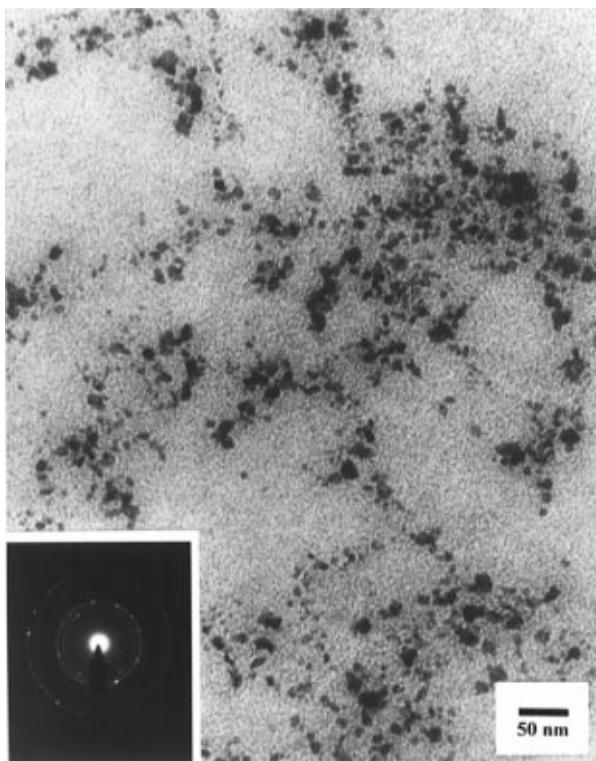
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(10) As suggested by a referee, the pH-induced changes in volume need not indicate cross-linking of the oxide to the alginate. Even if the iron oxide is only embedded in the gel, pH changes will induce changes in the charge of both the gel and the hydroxylated surface of the oxide, which will affect the volume of the beads.

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(12) Iron analysis in combination with magnetic data suggest that about 10% of the iron exists in a nonmagnetic form of iron oxide, such as  $\alpha$ -FeOOH.

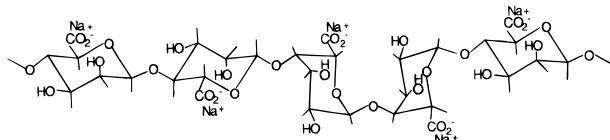


**Figure 1.** TEM micrographs of a section of an alginate/iron oxide composite bead; magnification 20 000; 50 kV. Inset: electron diffraction pattern from an oxide crystal.

**Table 1. Electron Diffraction Data for the Iron Oxides in Magnetic Alginate Beads**

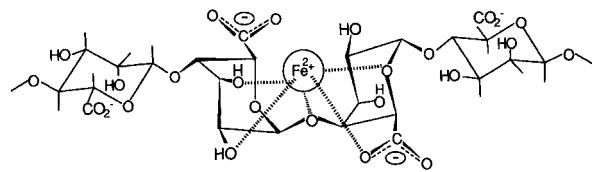
<i>d</i> spacings (Å) <sup>a</sup>	$\gamma$ -Fe <sub>2</sub> O <sub>3</sub> <sup>c</sup>	$\gamma$ -Fe <sub>2</sub> O <sub>3</sub> <sup>d</sup> (Miller indices)
2.93	2.97	2.95 (220)
<b>2.50</b>	<b>2.52</b>	<b>2.52 (311)</b>
2.07	2.10	2.08 (400)
1.60	1.61	1.61 (511, 333)
<b>1.45</b>	<b>1.47</b>	<b>1.48 (440)</b>

<sup>a</sup> Bold values indicate the most intense reflections. <sup>b</sup> Measured values averaged over five selected-area diffraction patterns. <sup>c</sup> Cu K $\alpha_1$  data acquisition 40 min. <sup>d</sup> X-Ray Data-Joint Committee on Powder Diffraction Standards, Selected Powder Diffraction Data for Minerals, 1st ed., 1974.

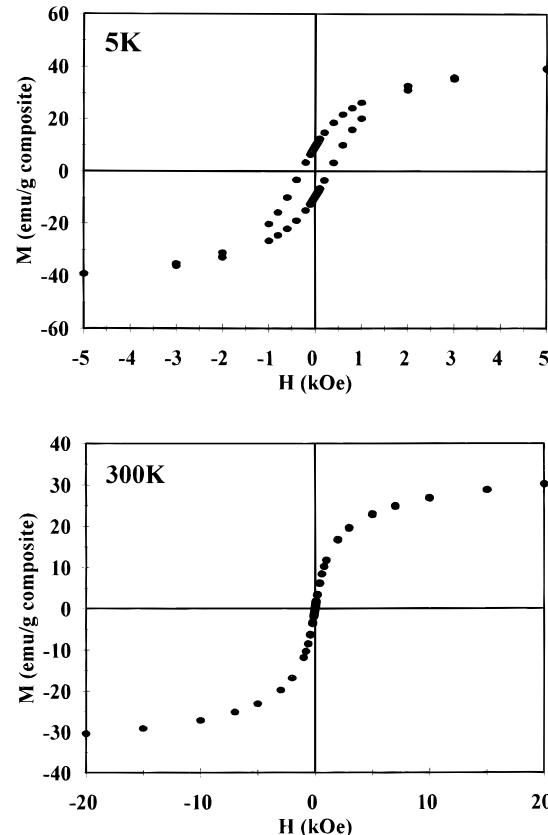


**Figure 2.** Chemical structure of alginic acid.

tion of alginic acid. This polysaccharide is composed of two pyranosides,  $\beta$ -D-mannuronic (M) and  $\alpha$ -L-guluronic (G) acids, linked by 1  $\rightarrow$  4 glycosidic bonds (Figure 2). The distribution of the mannuronic and guluronic units along the polysaccharide chain is random. The polysaccharide presents extensive homopolymeric blocks (MMM, GGG) and regions of alternating sequences (MGMG) of the monomeric constituents.<sup>13</sup> Since the intra- and interchain cooperative complexation of cations occurs primarily between regions of diaxially linked G blocks<sup>10</sup> (Figure 3) the degree of cross-linking is dependent on the population of homopolymeric G blocks in the polymer sample.



**Figure 3.** Schematic representation of the Fe(II) cross-linking shown to occur between two diaxially linked guluronic acid (G) units.



**Figure 4.** Magnetization curves of alginate/iron oxide composite beads (dry sample, five reaction cycles). Top: zero-field-cooled magnetic hysteresis loop at 5 K. Bottom: room-temperature curve.

Beads subjected to several reaction cycles are strongly magnetic. Gels obtained after five consecutive loading cycles and dehydrated have a room temperature saturation magnetization of 30 emu/g of composite at 20 kOe, as determined with a Quantum Design SQUID MPMS magnetometer. At room temperature, no hysteresis is observed (Figure 4, bottom), suggesting superparamagnetism, consistent with the small size of the iron oxide. At low temperature, the magnetization curves of the gels exhibit hysteresis. At 5 K, for example, the coercivity is 0.30 kOe and the isothermal remanent magnetization is 10 emu/g (Figure 4, top). The blocking temperature is estimated to occur below 50 K. Zero-field cooled and field-cooled magnetization data also suggest superparamagnetic behavior. The value of the zero-field cooled maximum shifted from 50 to 20 K when the applied field was increased 10-fold, indicative of the behavior expected for superparamagnetic and spin-glass materials.<sup>14</sup>

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This investigation has demonstrated the feasibility of preparing highly magnetic alginate in the form of a stable nanocomposite by a direct route involving the cross-linking points of the network as reaction centers for the synthesis of the iron oxide. Future studies will explore the possibility of obtaining hydrogels responsive not only to a magnetic field but also to a change in pH and in temperature, thus leading the way to pluriresponsive materials.

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