Magnetic Functionalization of Poly(N-isopropylacrylamide) Hydrogels for Sensor Applications

Christian Keßler* and Gerald Gerlach

To develop a hydrogel sensor system using the Hall effect to detect the degree of swelling, gels containing high concentrations of magnetic particles are necessary to induce a strong magnetic field. For this purpose, hydrogels based on poly(N-isopropylacrylamide) cross-linked with Laponite XLS are modified with various magnetic nanoparticles. The focus of this work is to introduce high particle densities with a homogeneous distribution into the gel. Particles are coated with 3-[trimethoxysilyl]propyl methacrylate to bind them into the network structure. The swelling behavior and temperature response of gels containing pure and modified particles are compared to the unmodified clay gel. Ferrogels are further synthesized in a magnetic field to permanently align magnetic nanoparticles in the network. This results in permanently embedded rod-like structures spanning the entire length of the gel. The influence of this anisotropic distribution on the mechanical properties of the hydrogel is investigated through compression measurements.

1. Introduction

Hydrogel-based microsystems are currently a highly investigated field both as sensors and actuators.\[1,2\] The usage of piezoresistive bending plates has become an established method of detecting the degree of swelling due to the simple yet precise measuring principle.\[3-6\] This, however, imposes certain limitations on the gel. Since it has to exert force on the bending plate, it is not possible to measure the free swelling of the gel. Furthermore, nanocomposite hydrogels with high degrees of swelling can potentially damage the plate, requiring advanced flexible materials.\[7\]

A currently highly investigated alternative detection method is based on the detection of stray magnetic fields from magnetic nanoparticles (MNPs) and microbeads. Potential biomedical applications have been demonstrated by detecting biomolecules labeled with MNPs using giant magnetoresistive spin valves.\[8-10\] Similar applications have been reported using Hall crosses to detect magnetic microbeads.\[11,12\] The implementation of MNPs into hydrogel networks to form ferrogels provides further potential applications for drug delivery and cancer therapy.\[13,14\] The detection of such ferrogels has also been demonstrated using the giant magnetoresistance.\[15-17\]

Based on these works, a novel method to detect the degree of swelling of ferrogels was proposed by Koseva et al. using a newly developed bismuth Hall sensor.\[18\] The potential of this approach was demonstrated by adding NdFeB particles on the surface of a hydrogel and placing it on top of the Hall sensor. The drying of the gel led to an increasing Hall voltage. Using this method, the free swelling process of a gel can be observed in real time ranging from the deswollen to the equilibrium swelling state.

The previously mentioned works mainly focus on the implementation of biocompatible maghemite with particles concentrations below 10%. Since the induced Hall voltage is directly linked to the stray field of the MNPs, this investigation focuses on the synthesis of ferrogels containing high amounts of different MNPs to maximize the potential sensor signal of a stimuli-responsive ferrogel. The usage of large particle concentrations inevitably leads to agglomeration and sedimentation, especially when using pure magnetic particles.\[19\] This effect can be countered by coatings that reduce interaction between particles and enable solubility.\[20,21\] Commercially available coated particles though are kept stable in solution only at low concentrations reducing the possible output signal.\[22\] Methods to introduce large quantities of MNPs into a hydrogel network while ensuring a homogeneous distribution were therefore investigated in this work.

Temperature-responsive Laponite-based poly(N-isopropylacrylamide) (PNIPAM) hydrogels were chosen due to their enhanced mechanical properties and high degree of swelling and loaded with up to 50 wt% magnetic particles.\[23,24\] The focus was on CrO₂ particles due to their unique accicular shape.\[25\] These were further coated with 3-[trimethoxysilyl]propyl methacrylate to ensure permanent fixture into the network structure. Lastly, the ferrogels were magnetized during synthesis with magnetic flux densities of up to 200 mT to achieve a permanent alignment of the particles in the network. The effects on the swelling behavior and mechanical properties for the different implementations were investigated.
2. Results and Discussion

2.1. Ferrogel Synthesis

The ferrogels were synthesized using Laponite XLS as multifunctional cross-linkers. Keeping the concentration at 10 mol L\(^{-1}\) prevents interactions between the individual clay particles and the subsequent change of the gel properties after applying mechanical stress.\(^{[24]}\) PNIPAM serves as the temperature sensitive component. The further discussion will focus on CrO\(_2\) with Fe\(_3\)O\(_4\) and SrFe\(_{12}\)O\(_{19}\) showing similar results.

Using high amounts of magnetic particles, it is first necessary to prevent sedimentation and ensure a homogeneous particle distribution throughout the gel. Due to the magnetic nature of the added particles, standard mixing equipment cannot be used. Constant flushing of the dispersion with argon was performed as a replacement for stirring. Contrary to stirring or shaking, the gas flow accelerates the gelation process when kept up after initializing the polymerization. By keeping the flow up for 45 s after the initialization, the viscosity is still low enough for further processing. The rapid increase of the viscosity afterward traps the nanoparticles in the network and prevents sedimentation.

To validate this method, the magnetization of the top and bottom parts of a 10 cm long cylindrical sample loaded with 20 wt% CrO\(_2\) were investigated using a vibrating sample magnetometer (VSM). VSM measurements were performed on dry samples and should therefore only be used to compare individual samples; as they do not reflect the magnetic properties, a swollen gel would exert. The comparison in Figure 1a shows a remanence of 0.06 emu for both the top and bottom sections. Based on this, samples containing 10 to 50 wt% CrO\(_2\) were prepared using the same method. The linear increase ranging from 0.03 to 0.15 emu in Figure 1b indicates that the particles remain in the network even at high concentrations.

The thermogravimetric analysis (TGA) in Figure 2a shows an increasing amount of CrO\(_2\) in the unreacted components of the sol content ranging from 0.16 to 3.18 wt%. The visible lack of particles in the outer region of the gel seen in the microscopic image in Figure 2b indicates that the particles get washed out during the initial swelling process as a result of the expansion.
of the network. Due to the comparatively small surface area, this amount was not significant at the current scale but would pose problems when working in the micrometer range. An integration of the particles into the network structure was therefore necessary.

### 2.2. Coating of MNPs

Silanes were chosen to connect the magnetic particles with the polymer network, due to their ability to attach to hydrated surfaces, allowing for flexibility in both particle type and hydrogel material. 3-(trimethoxysilyl)propyl methacrylate (TMSPMA) was used for the PNIPAM-based gel to add double bonds to the particle surface enabling them to participate in the propagation reaction. Infrared (IR) measurements in Figure 3a show the stretch vibrations of C=O at 1701 cm⁻¹ and C=C at 1629 cm⁻¹. TGA measurements (Figure 3b) also show an additional decomposition process starting at 320 °C. Both measurements indicate the presence of a TMSPMA layer with double bonds on the CrO₂ surface. The coated particles were therefore used for further studies. Microscopic examination of the resulting gels shows that the swelling process does not lead to a loss of particles in the surface region.

### 2.3. Ferrogel Synthesis in a Magnetic Field

Applying a magnetic field after the formation of the hydrogel can result in relaxation and rotation of MNPs after the removal of the field. This would reduce the magnetic field exerted by the ferrogel over time. A magnetic flux density of 200 mT was therefore applied during the synthesis, resulting in a permanent alignment of the particles in the network structure. Figure 4 shows a visible change from the uniform particle distribution to rod-like structures, which run along the magnetic field lines. These consist of large agglomerations of magnetic particles varying significantly in size and diameter, spanning throughout the entire gel with lengths of up to 7 cm. The structures remain stable within the network even after multiple swelling and deswelling cycles.

While ferrogels containing only magnetic particles as cross-linkers have been shown before, this concept cannot be applied here due to anisotropic distribution of the particles. The surrounding matrix contains almost no magnetic particles meaning that cross-linking via the TMSPMA coating mainly occurs between the magnetic particles and adjacent polymer chains. Lowering the magnetic flux density to 100 mT still gave similar results while further decreasing to 50 mT does not result in a visible change of the particle distribution.
2.4. Temperature Response

Increasing the amount of MNPs in the gel shows little impact on the relative degree of deswelling of the gel samples increasing by 10% when going from 0 to 50 wt% (Figure 5). An increase in the sample variance can also be observed due to the higher absolute degree of swelling. TMSPMA-coated particles cause a reduced temperature response due to the increased cross-linking density, which is in agreement with previous reports. The magnetized samples show similar deswelling behavior to the unmodified clay gels. The sample variance for both the coated and magnetized samples are improved when compared the sample containing 20 wt% uncoated MNPs. Since the measured deswelling process occurs parallel to the inflexible rods and the surrounding matrix is mostly free of magnetic particles, this results in the rods barely influencing the swelling behavior in that direction. While there were no observable differences in the swelling behavior perpendicular to the rods, potential deformation effects due to the inhomogeneous cross-linking density have to be investigated for thin layers.

Repeated heating and cooling cycles in Figure 6a show reproducible results after the first cycle. The swelling experiments had to be performed over a period of 24 h due to the swelling taking significantly longer than the deswelling process, taking multiple hours as opposed to about 8 min (Figure 6b). This can be attributed to the skin effect generally observed with stimuli-responsive gels.

2.5. Average Chain Length

Compression measurements were performed to calculate the average chain length $M_C$ of PNIPAM. These also show the minimal effect of the magnetic particles on the polymer chains at low concentrations (Figure 7). The influence of uncoated nanoparticles on the mechanical stability of the ferrogel becomes apparent when going to 50 wt% particle loads and beyond. At 60 wt%,
gels break easily once swollen, and at 70 wt%, no stable gels are formed. The TMSMPA-coating leads to a reduced average chain length of about one third of the pure Laponite clay gel. This is in agreement with the nanoparticles functioning as additional cross-linkers and thus increasing the overall cross-linking density of the network. The coating can therefore be used to increase the amount of embedded particles.

Magnetization of the samples shows a noticeable decrease in the calculated chain length. This is however due to the force being applied perpendicular to the rods, which are stabilizing the gel in one direction. \( M_c \) can therefore not be accurately calculated for samples with such an anisotropic composition. The measurement still shows the improved mechanical properties resulting from the magnetization and deliberate agglomeration. It was also observed that the large variance in thickness and length of the rods has almost no influence on the average chain length across the total length of the gel.

The magnetization of the MNPs during the ferrogel synthesis can therefore be used to tune the mechanical properties of the gel depending on the direction of the field. Such gels offer the potential for improved stability in the flow direction in microfluidic systems while still maintaining high degrees of swelling. This method can be also applied to other hydrogel systems and MNPs due to its universal approach.

3. Conclusions

Different methods of integrating large amounts of MNPs into nanocomposite PNIPAM hydrogels were investigated. Sedimentation effects could be minimized for pure particles using an argon flow during the initiation reaction. The particles were further successfully coated with TMSMPA and integrated into the polymer network leading to enhanced mechanical stability resulting from the increased cross-linking density.

It was shown that the application of a magnetic field during the ferrogel synthesis can be used to induce a deliberate inhomogeneous distribution of the MNPs by forming rod-like structures along the magnetic field lines. This provides a stable integration of the MNPs into the network structure as well as improved mechanical stability perpendicular to the rods. Furthermore, there is little effect on the swelling properties parallel to the rods compared to pure Laponite hydrogels and low variation between multiple samples. This allows the tuning of the gel properties depending on the direction of the magnetic field and makes this a promising method for the future use in a Hall sensor system.

4. Experimental Section

**Materials:** Laponite XLS was provided by Rockwood Additives Ltd. NIPAM (Acros Co.) was recrystallized from n-hexane before use. N,N,N',N'-tetramethyl ethylenediamine (TEMED, ≥99.0%), Magnetsieve (CrO₃, 300 nm by 50 nm), magnetite (Fe₃O₄, 50–100 nm), strontium ferrite (SrFe₁₂O₁₉, <100 nm), and 3-(trimethoxysilyl)propyl methacrylate (TMSMPA, 98%) were purchased from Sigma-Aldrich.

**Ferrogel Synthesis:** Laponite XLS (0.33 g) was dissolved in water (4 mL) and stirred for 12 h until a clear solution was obtained. After adding NIPAM (0.5 g), the solution was flushed with argon for 15 min. Magnetic particles were added relative to the amount of NIPAM and the suspension placed in an ultrasonic bath for 10 min. After adding potassium peroxodisulfate (10 mg in 0.5 mL water) and TEMED (20 μL in 0.5 mL water), the solution was flushed with argon for 45 s and then injected into the sample containers and cooled overnight. For the magnetized samples, the reaction was performed in a magnetic field using a Bruker B-E25 electromagnet with magnetic field strengths of 50–200 mT. The samples were prepared as described and placed in the magnetic field for 15 min after filling them in the desired container. All samples were conditioned in water for 1 week with the water changed daily.

**Coating of Magnetic Particles:** Magnetic particles (0.3 g) were suspended in 20 mL dry acetone under argon atmosphere. After adding TMSMPA (0.2 mL), the suspension was placed in an ultrasonic bath for 30 min. The particles were washed three times with acetone and water, respectively, and vacuum-dried at room temperature overnight.

**Characterization:** The remanence of dried cylindrical gel samples were measured with a VSM (VSM Modell 7307. Lake Shore Cryotronics). The swelling properties were observed with a stereo microscope (Zeiss Stemi 2000-C with Axiocam ICc 1) using cylindrical samples. Lower critical solution temperature behavior was induced by switching between 22 and 40 °C. Compression measurements were performed on cylindrical samples (height =6 mm, diameter =8 mm) in water by measuring the indentation of the gel after applying force and in the relaxed state. The average chain length \( M_c \) was derived from the rubber elasticity theory using

\[
M_C = \frac{\Delta C}{C_0} = \frac{\Delta \lambda}{\lambda} = \frac{P}{K} \text{RT} \text{Q}(\lambda - 1)^{-2}
\]

where the front factor is 1 for the affine network, \( \rho_i \) is the polymer density (1 g cm⁻³), \( Q \) is the degree of swelling, and \( \lambda \) is the deformation ratio compared to the initial height of the gel.

Fourier-transform infrared spectroscopy (FT-IR) was performed with a Nicolet 5700 IR-spectrometer (Thermo Elektron, Dreieich) with MCT detector using the KBr method. Thermogravimetric analysis was done using a TGA 50 by Mettler. Dried powder samples were used.

**Acknowledgements**

We thank Johannes Henrich for the VSM measurements and his support during the hydrogel synthesis in magnetic fields. This work was performed as part of the GRK 1865: Hydrogel-based microsystems. Funding was provided by the DFG.

Open Access funding enabled and organized by Projekt DEAL.

**Conflict of Interest**

The authors declare no conflict of interest.

**Data Availability Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Keywords**

ferrogels, hydrogels, nanocomposite material, surface coating

Received: January 14, 2022
Revised: April 7, 2022
Published online: May 20, 2022

[1] A. Richter, G. Paschew, S. Klatt, J. Lienig, K. F. Arndt, H. J. P. Adler, Sensors 2008, 8, 561.
