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Stimuli-responsive hydrogel patches for resolving pH with magnetic particle spectrometry (MPS)

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Abstract

Magnetic particle spectrometry (MPS) enables the characterization of magnetic nanoparticles (MNPs) in terms of their nonlinear magnetic behavior, which also depends on the particles' hydrodynamic mobility and, consequently, on the local environment. Therefore, MPS can be used to examine particle-matrix interactions. In this work, the pH value of a solution is resolved using MPS. The underlying principle is based on a pH-responsive magnetic hydrogel patch, which exhibits reversible volume alteration in response to a change in the surrounding pH value. This swelling behavior affects the particle-matrix interactions of embedded MNPs, resulting in a modified magnetic signal. A correlation was observed in which the hydrogel swelling increases with rising pH. In MPS measurements, the amplitudes of the spectra were found to correlate with the extent of swelling and, consequently, with the pH value. As a consequence, the measured MPS spectra can be assigned a specific pH value.

I. Introduction

Magnetic particle spectrometry (MPS), developed as a related technique to magnetic particle imaging (MPI), is a zero-dimensional characterization method that relies on the non-linear properties of MNPs [1]. MPS is able to elucidate particle-matrix interactions in complex media, as prior research has demonstrated the dependence of MPS spectra on temperature and viscosity [2]. This work aims to resolve the pH value from a given MPS signal on the basis of the change in the local environment of MNPs through hydrogel swelling. A stimuli-responsive hydrogel patch induces a pH-dependent volume change, which results in a modification of the MPS amplitude spectrum of embedded MNPs. Consequently, it is possible to assign a specific MPS spectrum to a swelling ratio of a hydrogel, and thus to a corresponding pH value. A possible application includes the use of pH-responsive hydrogel patches for pH resolving in multicontrast MPI.

II. Methods and materials

The synthetic copolymer hydrogel 5-poly(2-hydroxyethyl methacrylate-co-acrylic acid) (PHEMA-AA) is used to fabricate patches with 2.5 mm diameter using photopolymerisation. First, 820 µl of monomer hydroxyethyl methacrylate with 30 mg of photoinitiator 2-dimethoxy-2-phenylacetophenone are briefly vortexed. Subsequently, 18 µl of crosslinker ethylene glycol dimethacrylate and 460 µl of monomer acrylic acid are added, and the solution is mixed using a vortex for 10 min and ultrasonic agitation for 20 min. The solution is pipetted into a silicone mold and irradiated with UV light. The integration of MNPs into the cured hydrogel patches is achieved through the immersion of the dry hydrogel patches in a solution of Synomag-D (50 nm, micromod Partikeltechnologie GmbH, Rostock, Germany) for min. 24 h. Solutions of sodium hydroxide and hydrochloric acid at pH levels 2, 4, 7 and 10 are prepared by diluting stock solutions. The hydrogel swelling ratio (percentage increase in weight) is calculated using the weight of the dry and swollen hydrogels. The MPS measurements are conducted with a magnetic field strength of 20 mT and an excitation frequency of 25 kHz. The MPS signal is measured for dry magnetic hydrogel patches and for patches immersed in solutions with different pH values after 24 h. Subsequently, the MPS spectra are correlated with the pH values of the solutions, and the mean MPS spectrum of 6 samples per pH value is calculated.

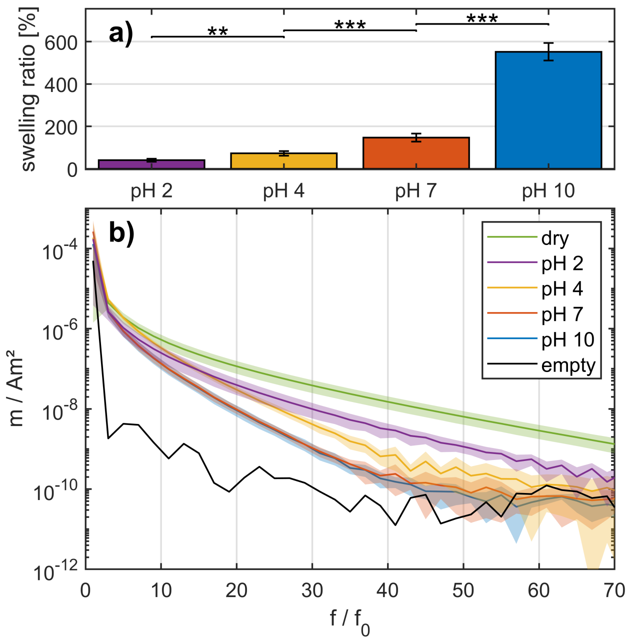

Figure 1: a) Mean swelling ratio (percentage increase in weight) for magnetic hydrogel patches in different pH solutions, stars indicating statistical significance, **b)** MPS spectra (odd harmonics) comparing patches in dry state before swelling and in swollen state for pH values 2, 4, 7, and 10, mean values of 6 samples per pH, colored corridors indicate standard deviation

III. Results and discussion

Figure 1a illustrates the mean swelling ratio for magnetic hydrogel patches measured in MPS. It was shown that there is a correlation in which the swelling ratio increases with increasing pH levels. Linear swelling behavior can be observed in the acidic pH range, while pH 10 shows considerably stronger swelling. All investigated pH values exhibited a statistically significant difference in hydrogel swelling. Figure 1b shows a decline in the MPS signal as the pH value increases. The highest signal is generated by hydrogels in the dry state, followed by samples in solution at pH 2 and pH 4. The values for pH 7 and pH 10 are almost identical in the spectrum, resulting in the lowest signal. It can thus be postulated that an elevated swelling ratio, indicative of a higher pH value, is associated with a reduction in the MPS signal, most likely caused by a change in particle interactions by increasing interparticle distance. This reduction in signal can be compared to a signal reduction as a result of a reduced particle concentration. The small difference in the spectrum signals from the samples at pH 7 and pH 10 is still under investigation and needs further research.

IV. Conclusion

The amplitudes in the MPS spectra are found to correlate with the pH-dependent swelling ratio of magnetic hydrogel patches. A linear relationship exists between the swelling ratio and the pH value in the acidic pH range, which allows a specific MPS spectrum to be assigned to a pH value. So far, statistically significant differentiation between MPS spectra has been observed in pH 2, 4, and 7. Further investigations should address signal generation, dynamic behavior, and a more narrower pH range.

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Author's statement

Conflict of interest: Authors state no conflict of interest.

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