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# Core-Shell-Nanoparticles with Superparamagnetic Properties for Novel Applications as Biomaterials

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**Abstract:** Due to the increasing average age of the population, the number of implants is also increasing and with it the number of explantations. Therefore, facilitated implant removal is of great interest. A nanocomposite consisting of superparamagnetic core-shell nanoparticles (CSNPs) and a synthetic polymer is supposed to be used as implant coating, aiming for a stimulus-inducible modification of the composite's rheological properties by hyperthermia. Here, the first steps following this concept, the synthesis and modification of the CSNP are reported. In this work magnetite nanoparticles build the core and are surrounded by a periodic mesoporous organosilica (PMO) shell. For this reason, the CSNP are referred to as magnetic PMO (mPMO) particles in the following.

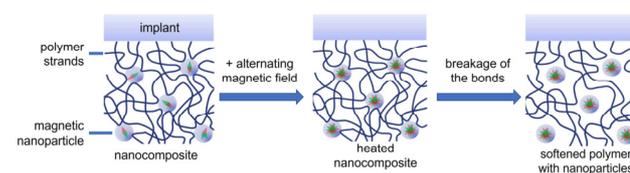
**Keywords:** hybrid materials, superparamagnetic, periodic mesoporous organosilica, magnetite, core-shell nanoparticles, biomaterial, nanocomposite

## 1 Introduction

More than 700 000 cochlea implants (CIs) are registered in 2019 all over the world [1]. By the transmission of sound waves into electrical signals, the CI is able to directly stimulate the remaining spiral ganglion neurons and replace the function of the inner hair cells in the human cochlea. As a result, people who are suffering from sensory hearing loss will regain a hearing impression. Despite these successes, an explantation

may still become necessary. Possible reasons for this can be infections that cannot be treated, a defective device, or a more advanced technology. However, since the implant is supposed to integrate well inside the body and because connective tissue may form on the implant surface, removal of the implant is often associated with tissue damage, which can even lead to trauma [2-3]. To prevent this, different CSNPs are developed and combined with a synthetic polymer to serve as a system for intentional implant removal. Superparamagnetic magnetite nanoparticles in the size range of 10-20 nm build the core. A biostable shell around them makes them accessible for modifications and increases their stability in body fluids. Suitable materials include organosilicas, zeosiles, or titanium dioxide, while this work focuses on an organosilica shell [4-5].

The developed CSNPs with superparamagnetic properties can further serve as crosslinking points inside synthetic polymers (e.g. hydrogels), forming a nanocomposite. By introducing functional groups to the polymer and the nanoparticle surface, a covalent and thermoreversible bond between nanoparticles and polymer chains can be formed (e.g. by Diels-Alder reaction). Through subsequent modification reactions with silanes, the interactions between polymer and nanoparticle can be adjusted. Superparamagnetic CSNPs, brought into an alternating magnetic field, can develop thermal energy to induce thermoreversible reactions (e.g. Retro-Diels-Alder reactions).



**Figure 1:** Schematic illustration of the concept for facilitated implant removal. By local heating, the crosslinks between the CSNPs and the polymer can be broken when the bonds are thermo-labile, as a consequence the nanocomposite softens.

Due to the thermally induced bond cleavage, the nanocomposite, becomes softer. As a result, implant removal is facilitated. This concept is illustrated in Figure 1.

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## 2 Materials and methods

All chemicals were used without further purification. Iron(II) chloride tetrahydrate ( $\geq 99\%$ ), iron(III) chloride hexahydrate (99%), sodium citrate tribasic dihydrate ( $\geq 99\%$ ), cetyltrimethylammonium bromide (CTAB,  $\geq 98\%$ ), ammonium hydroxide solution ( $\geq 25\%$   $\text{NH}_3$  in water), 1,4-bis-(triethoxysilyl)-benzole (BTEB, 96%), toluene (anhydrous, 99.8%), absolute ethanol ( $\geq 99.5\%$ ) and ammonium nitrate ( $\geq 99\%$ ) were purchased from Sigma-Aldrich Corporation (München, Germany). 1-[3-(triethoxysilyl)propyl]-1H-pyrrole-2,5-dione (maleimide silane, 95%) was purchased from Astatech (Bristol, USA).

Transmission electron microscopy (TEM) was measured on a Tecani G2 F20 TMP instrument ( $C_s = 2 \text{ mm}$ ,  $C_c = 2 \text{ mm}$ ) from FEI Company (Hillsboro, USA). Measurements were performed with a 200 kV field emission gun in bright-field mode. For preparation, 400-mesh carbon-coated copper grids from Plano GmbH (Wetzlar, Germany) were used. The samples were dispersed in ethanol, dropped onto the grid, and dried. The particle size was determined using NIH ImageJ, therefore 100 particles were measured.

Fourier-transform infrared spectroscopy (FTIR) was measured on a Tensor 27 type spectrometer in transmission from Bruker (Billerica, USA). The obtained measured values were normalised to the silica band at  $1070 \text{ cm}^{-1}$ .

Dynamic light scattering (DLS) and zeta potential measurements were performed on a Zetasizer type Nano ZS from Malvern Instruments (Malvern, UK), wherefore the sample was dispersed in water.

### Synthesis of magnetic periodic mesoporous organosilica (mPMO)

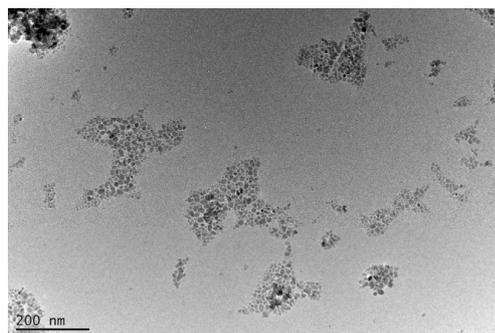
In the first step, the citrate stabilised magnetite nanoparticles (MNPs) were synthesised according to literature [6]. The MNPs (40 mg) were dispersed for 15 minutes in  $90 \mu\text{L}$  water and  $7.2 \text{ mL}$  ethanol, using an ultrasonic bath. Then  $28 \text{ mL}$  water,  $1.4 \text{ mL}$  ammonium hydroxide solution, and  $4.2 \text{ mL}$  of  $0.11 \text{ M}$  CTAB solution in water/ethanol (2:1) were added. The reaction mixture was shaken vigorously for 24 h at room temperature and afterwards placed in the convection oven at  $80 \text{ }^\circ\text{C}$  for another 24 h. The mPMOs were collected by centrifugation, washed three times with ethanol and dried under vacuum. The surfactant CTAB was removed by extraction in ethanol and ammonium nitrate for 2 h at  $80 \text{ }^\circ\text{C}$ . Again, the extracted particles were collected by centrifugation, washed three times with ethanol and dried in vacuum.

Afterwards, the particles were modified with the maleimide silane by post-grafting method. To do so, the mPMOs were dispersed in  $30 \text{ mL}$  anhydrous toluene and stirred under

nitrogen. Then,  $40 \text{ mg}$  of the maleimide silane was added and the reaction mixture heated up to reflux and stirred overnight. The particles were collected by centrifugation, washed three times with ethanol and dried under vacuum.

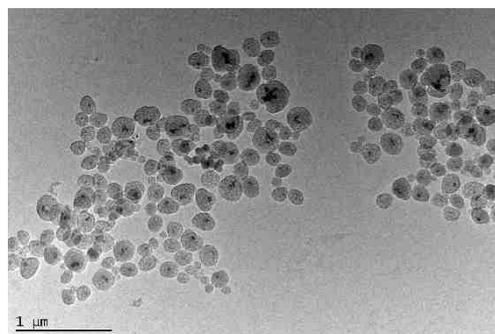
## 3 Results and discussion

In Figure 2 the obtained MNP, which later build the core of the MNP, are shown. They are of spherical shape and show a size distribution of  $10 \text{ nm}$  (SD  $2 \text{ nm}$ ).



**Figure 2:** TEM image of MNPs with a size range of  $10 \text{ nm}$  (SD  $2 \text{ nm}$ .)

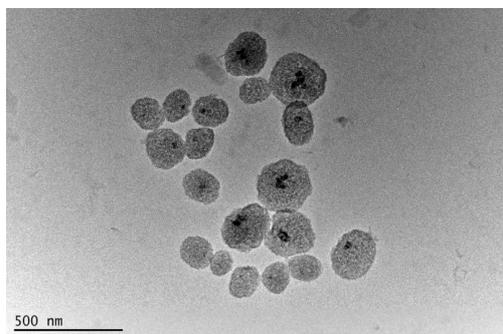
The synthesised mPMO particles are of spherical shape and show a size distribution of  $168 \text{ nm}$  ( $42 \text{ nm}$  SD), as determined by TEM, shown in Figure 3. As clearly visible in the TEM image, the dark spots are the citrate-capped magnetite nanoparticles, which are surrounded by the organosilica shell. This proves a successful formation of core-shell nanoparticles and it can be stated that almost every PMO particle has magnetic cores inside. The few particles without a magnetic core are smaller and were not taken into account for the size determination.



**Figure 3:** TEM image of mPMO. The dark spots (magnetite core) are surrounded by an organosilica shell.

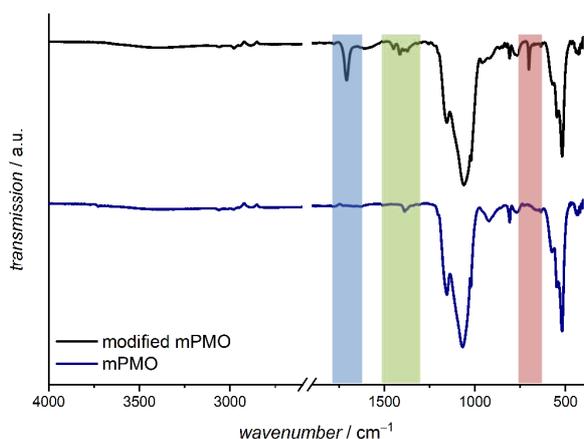
By comparing the TEM images before and after the modification reaction, shown in Figure 4, it can be noticed that the mor-

phology and size of the particles does not change after the maleimide modification, neither the surrounding shell, nor the core.



**Figure 4:** TEM image of mPMO after the maleimide modification. The dark spots (magnetite core) and organosilica shell do not change after the modification.

In order to confirm the successful attachment of maleimide groups, Fourier transform infrared spectroscopy (FTIR) and zeta potential measurements of the particles, before and after the modification reaction, were performed. Figure 5 shows the related FTIR spectra. After the modification additional bands at  $1704\text{ cm}^{-1}$ , which is related to the carbonyl stretching vibrations and highlighted in blue, at  $1446\text{ cm}^{-1}$ , which is related to the methyl bending vibrations and highlighted in green and at  $694\text{ cm}^{-1}$ , which is related to the maleimide ring deformation vibration and highlighted in red, occur.



**Figure 5:** FTIR spectra of mPMO before and after modification with the maleimide silane. Additional bands are visible after the modification at  $1704\text{ cm}^{-1}$  (blue),  $1446\text{ cm}^{-1}$  (green) and  $694\text{ cm}^{-1}$  (red), indicating a successful modification.

After the modification, the zeta potential of the mPMOs surface raises from  $-29\text{ mV} \pm 0.4\text{ mV}$  to  $-17\text{ mV} \pm 0.6\text{ mV}$ . The typically negatively charged silanol groups of the PMO shell are partially replaced after the surface functionalisation by the uncharged organic maleimide groups. This explains on the one hand the change of the zeta potential and also indicates, together with the appearance of new vibration bands in FTIR

spectra which can be assigned to the maleimide group, a successful modification of the particles with maleimide groups [7].

In the next steps, the material's capability of magnetic heating should be tested. In literature, Retro-Diels-Alder reactions with cleavage temperatures at  $90\text{ }^{\circ}\text{C}$  can be found [8]. By using a subnanometer local temperature probe, a temperature increase of  $70\text{ K}$  can be reached. This effect is strongly localised to the surface of the superparamagnetic nanoparticle and decreases within the first nanometers of surface and therefore should not damage the surrounding tissue by heating [9]. Also, inductive heating of the non-magnetic conductive platinum contacts has to be considered. Due to the higher heating efficiency of ferromagnetic and superparamagnetic materials, the heating of platinum contacts and wires was neglected in a study [10].

## 4 Conclusion

In summary, superparamagnetic core-shell nanoparticles were successfully synthesized. Citrate-capped magnetite nanoparticles build the core and are surrounded by a periodic mesoporous organosilica shell. Additionally, the CSNPs were successfully modified with a maleimide silane for further application as crosslinking points between polymer strands using the Diels-Alder reaction. With these newly designed materials, we are now able to proceed in realizing our materials concept of a stimulus-inducible modification of rheological properties of a polymer-nanoparticle composite by hyperthermia.

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### Author Statement

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