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Promotionsverfahren von **Herrn M.Sc. Andreas Neusch**
**Auslage** der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

**Design and Optimisation of a Superparamagnetic Nanoparticle based on Ferritin - Towards Probing and Manipulating Cellular Functions**

von den Berichterstattenden Prof. Dr. C. Monzel und Prof. Dr. P. Kollmannsberger beantragt. Sie kann zusammen mit den Gutachten in der Zeit

**vom 19.12.2024 bis 13.01.2025**

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen (§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

**16.01.2025 um 13:30 Uhr**

im **Hörsaal 6B** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Prof. Dr. A. Kedrov, Priv.-Doz. Dr. G. Lehmann und Prof. Dr. M. Getzlaff.

Die Öffentlichkeit ist bei der Befragung zugelassen.

Mit freundlichen Grüßen
im Auftrag

Amina Diekmann

# Design and Optimisation of a Superparamagnetic Nanoparticle based on Ferritin

Towards Probing and Manipulating Cellular Functions


## Summary of Dissertation

Cellular signalling has been the source of a multitude of unanswered questions regarding its activation, underlying mechanisms, and role in disease outbreak and development. However, these questions can only be answered with reliable and precise methods to control the related signalling pathways. With this intention, various techniques have been developed during the past decades to manipulate and control selected pathways through external stimuli. One promising technique in this repertoire is magnetogenetics, which utilises magnetic nanoparticles (MNP) and external magnetic fields to remotely activate, redistribute, or heat selected components of signalling pathways.

This work used and developed a semisynthetic MNP platform based on the human iron storage protein ferritin, commonly referred to as Magnetoferritin (MFt). MFt consists of two distinct compartments: a protein nanocage and a synthetic, magnetic iron oxide core. It was shown in the past that the performance of the magnetic core during magnetogenetic actuation was unsatisfactory due to weak responses. Also, while being an effective shield against environmental conditions, the protein shell's functionality and targeting capabilities are limited. Thus, both of MFt's components were engineered in this work to maximise the overall effectiveness of the MNP.

On the one hand, the magnetic properties of the core were enhanced by introducing 7% of cobalt to the iron oxide core with the goal of increasing the magnetic anisotropy. Even at these comparatively low doping levels, the core's magnetic properties increased drastically – namely, its blocking temperature, coercivity, and, most notably, heat dissipation via magnetic hyperthermia in an alternating magnetic field. The adjustments of these properties led to a fivefold increase in effective heat dissipation compared to undoped MFt. While cobalt doping of MFt increased its heat dissipation significantly, similar MNPs with larger magnetic cores exhibited enhanced response and thermal effectiveness under identical conditions. Hence, doping of MFt's core qualifies the nanoagent as a mild heat mediator. However, its heating capabilities are limited.

On the other hand, the protein shell of MFt was genetically modified to be both fluorescent and specifically targetable to selected proteins. This selectivity was achieved by fusing a minimal binding domain of Protein A from Staphylococcus aureus to the surface of MFt. Protein A is capable of coupling to the constant part of antibodies. Hence, decorating MFt with an antibody of choice was achieved easily. Thus, the functionalised MFt could bind to the antibody's original target. With this approach, it was possible to bind the death receptor CD95, induce cluster formation, and subsequently apoptosis.

The modifications applied to the components of the nanoagent MFt in this work enhanced its performance and applicability in cellular contexts while maintaining high biocompatibility, owing to the passivating character of MFt's protein cage. Even in the presence of cobalt in MFt's core, biocompatibility was high, and usability in cell experiments was not impeded. Compared to synthetic iron oxide MNPs with a dextran shell, MFt was more readily taken up by cells. Also, the mobility of MFt in the cytosol was significantly higher during magnetic redistribution for up to 5 h after incubation.

Conclusively, MFt's increased heat dissipation, its biocompatibility, as well as the possibility to target any protein via antibody-mediated coupling make it a potent MNP for the investigation of signalling pathways in the context of magnetogenetics.