B12(N)

Bioinspired Nanocomposites for Early Detection of Complications in Gastrointestinal Surgery

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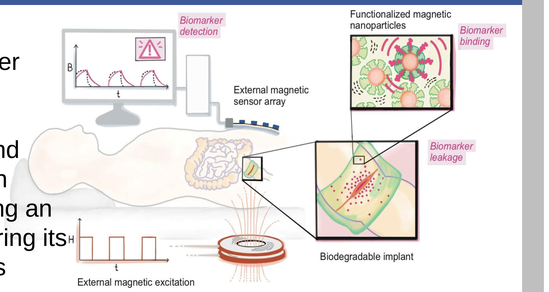
biomagnetic sensing SFB 1261

Motivation and Objectives

Problem:

- Anastomotic leakage after intestinal surgery
- Risk of sepsis with subsequent operation and prolonged hospitalization
- No direct way of detecting an anastomotic leakage during its formation or early stages



Proposed approach:

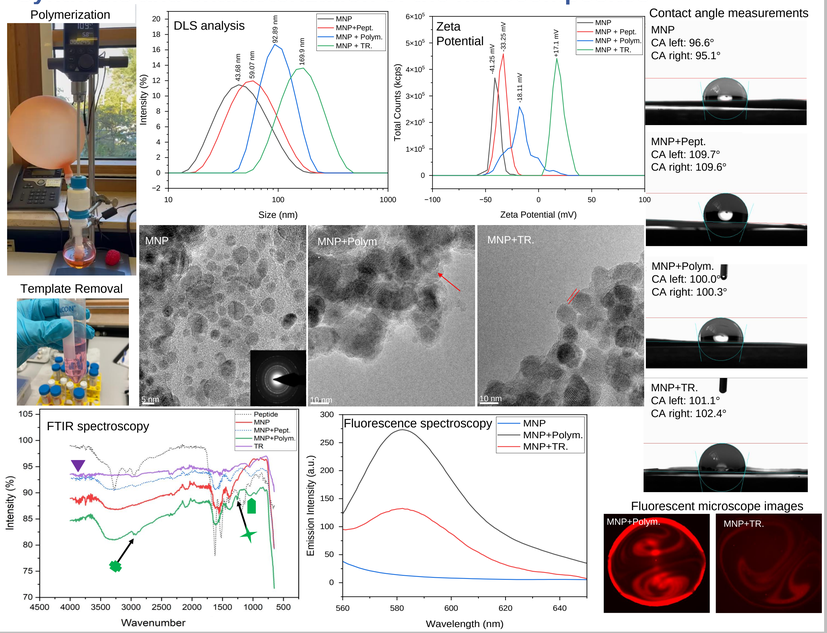
Development of an ***in vivo*** **diagnostic implant** to **detect the biomarkers** overexpressed in the leak relying on **magnetically labeled synthetic receptors** combined with **a wireless magnetic-field readout system** based on **magnetoelectric sensors**

Main objectives:

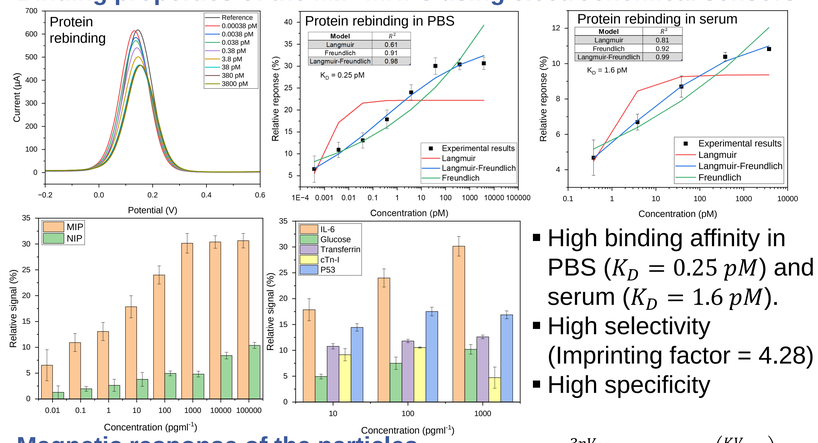
- Identification of suitable biomarkers
- Development of a bio-implant based on magnetic nanoparticles functionalized with molecularly imprinted polymers (MIP-MNP)
- Realization of a readout system based on magnetic field detection
- Validation of the approach on a cell assay, *in vitro* and *in vivo*

Preliminary Work

Synthesis and characterization of the nanocomposites

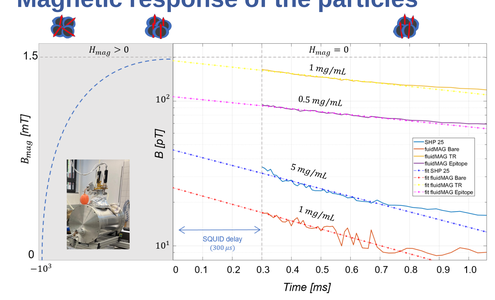


Binding properties of the MIP-MNPs using electrochemical sensors



- High binding affinity in PBS ($K_D = 0.25\ pM$) and serum ($K_D = 1.6\ pM$).
- High selectivity (Imprinting factor = 4.28)
- High specificity

Magnetic response of the particles



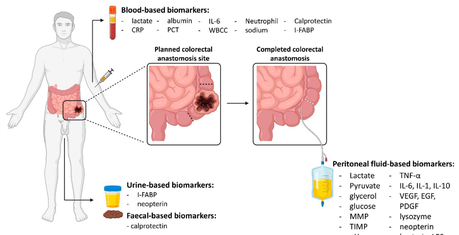
$$\tau_B \sim \frac{3\eta V_{HD}}{k_B T} \qquad \tau_N \sim \tau_0 \exp\left(\frac{KV_{MNP}}{k_B T}\right)$$

	d_{hd}	τ_{exp}	τ_B	B_{est}
SHP-25	44 nm	1.87 ms ± 0.02 ms	0.03 ms	46 pT
fluidMAG - Bare	44 nm	1.76 ms ± 0.01 ms	0.03 ms	25 pT
fluidMAG + TR	170 nm	4.50 ms ± 0.11 ms	1.87 ms	189 pT
fluidMAG + Epitope	–	4.80 ms ± 0.09 ms	–	107 pT
fluidMAG + Protein*	196 nm	–	2.90 ms	–

d_{hd}: *hydrodynamic diameter*, τ_{exp}: *experimental time constant* $1/e$, τ_B: *theoretical Brownian relaxation time*, B_{est}: *estimated magnetic field at* $t = 0$
*: *estimated value*

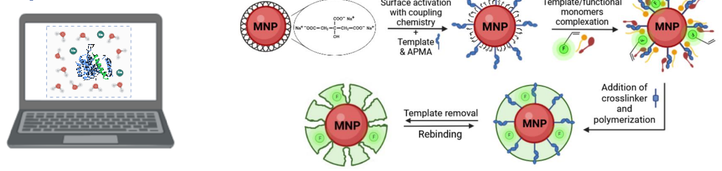
Preliminary work with SQUID system for magnetorelaxometry. Example curve of magnetization of disordered MNPs by 1.5 mT field and magnetization relaxation signal in the pT-range after turning off the excitation field. The relaxation time constant τ_{exp} is slower than the expected values from theoretical Brownian relaxation times.

Work Plan for Third Funding Period



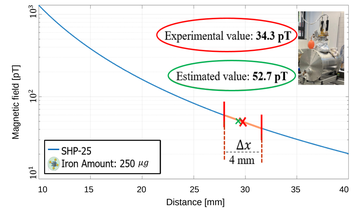
WP1: Detection of suitable biomarkers by the analysis of drainage fluid of patients

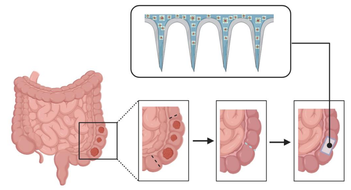
WP2: Development of optimum production recipes for MIP-MNP using computation methods



WP3: Hydrogel-forming implantable smart dressing

WP4: ME sensors for MNP detection

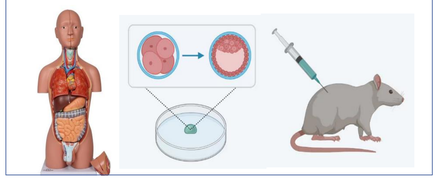




WP5: Torso phantom experiments:

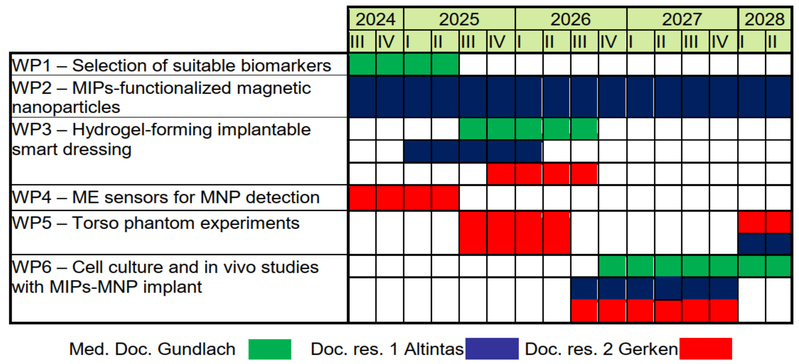
Large coil placed outside the body and the sensor system attached to it. The MIP-MNP implant is at a distance of up to 15 cm away on the inside of the body.

Torso phantom, *in vitro* & *in vivo*



WP6: *In vitro* and *in vivo* studies

Investigation of cytotoxicity of the MIPs-MNP implants on cells and rodents.



Med. Doc. Gundlach Doc. res. 1 Altintas Doc. res. 2 Gerken

Collaborations

A4: ΔE–Effect sensors obtained from A4. Experimental results to A4.
A6: MIPs-functionalized MNPs provided to A6 for TEM analysis.
A7: Converse ME sensors obtained from A7. Experimental results to A7.
A8: Simulations on MNP ensemble behavior during biomolecular binding. Experimental results given by A8 modelling group.
A9: SAW sensors obtained from A9. Experimental results provided to A9.
B1: Readout electronics developed in close interaction with B1.
B2: Digital signal processing developed in close interaction with B2.

Funds Requested

2 Doctoral researchers + Consumables (100%)
1 Medical doctor + Consumables (50%)

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