Biomaterials are natural or artificial substances in contact with biological systems. CENIDE is involved in the investigation of this interaction between materials, surfaces, particles, and macromolecules. The research area benefits from expertise in material science and bioscience and the chemically or physically orientated sciences – for example, in the exciting field of nanobio photonics.

First of all, we welcome our new colleagues, Lawrence Livermore engineer Brian Giera and our new collaboration partner Stephan Link (Rice University/USA), both of whom have been awarded with Mercator Fellowships by the DFG. Brian Giera has recently begun a three-year visiting professorship at the University of Duisburg-Essen. In collaboration with Barcikowski he will be developing a method for uniformly coating neural implants with biocompatible metallic nanoparticles, adding his computational expertise, in particular, to nanoparticle-based simulation of electrophoretic deposition (EPD) for the coating of objects with materials using electrical fields. Stephan Link, internationally recognized for his work on single-particle spectroscopy in plasmonics, will support Stephan Barcikowski’s work in destroying multi-resistant pathogens (MRE) with so-called guided nanorockets, equipped with drugs which have the great advantage of releasing nanosilver in place and thus destroying the bacteria. MRE has led to thousands of complications, sometimes life-threatening, in German hospitals every year. No one who becomes infected after implantation is susceptible to antibiotics. The challenge is to create nanoparticles which dissolve at the right time and place, i.e., only where the anti-microbial silver meets the pathogens, thus preventing the destruction of cell tissue. In addition, with its expertise in the preparation of biocompatible nanoparticles, Stephan Barcikowski’s research group is a project partner of the new Research Training Group within the University Alliance Ruhr (UA Ruhr) “Precision Particle Therapy – Applied Physics and Chemistry at the Interface with Medicine”, which will be funded by the Mercator Research Center Ruhr for four years.

New nanomaterials such as fluorescing calcium phosphate nanoparticles were developed in a joint project of Matthias Epple and Jens Voskuhl. The surface of silica-coated calcium phosphate nanoparticles was covalently functionalized by azide groups. Alkynylated molecules can be covalently attached by copper-catalyzed azide-alkyne cycloaddition (CuAAC) and by strain-promoted azide-alkyne cycloaddition (SPAAC) via click chemistry, leading to a high packing density at the particle surface compared to the previous biotin-avidin binding concept. This was demonstrated for a number of dyes, e.g., FAM, TAMRA, Cy5, Alexa FluorTM 488. These nanoparticles (200 nm) are suitable for cellular uptake, as demonstrated by fluorescence imaging microscopy, confocal laser scanning microscopy, and structured illuminated microscopy. Correspondingly, other molecules can be bound by clicking, e. g., for targeting or as therapeutic agent. Overall, this paves the way for multimodal theranostic nanoparticles.\(^1\)
Nanohybrids in theranostics

Michael Farle, Ulf Wiedwald, and co-workers, in collaboration with Russian colleagues, have developed magnetite-gold nanohybrids as an ideal all-in-one platform for theranostics. The octahedral 25 nm Fe$_3$O$_4$-Au hybrid nanoparticles exhibit bulk-like magnetic properties. Due to their high magnetization and octahedral shape, the hybrids show superior in vitro and in vivo T$_2$ contrast for magnetic resonance imaging (MRI) as compared to other hybrids and commercial contrast agents. The nanohybrids provide two functional surfaces for loading with fluorescent dyes and drugs which allow the simultaneous tracking of the nanoparticle vehicle and the drug cargo in vitro and in vivo. The delivery to tumors and payload release is demonstrated in real time by intravital microscopy.

Additionally, investigations on size-selected Fe$_3$O$_4$–Au hybrid nanoparticles of 6–44 nm (Fe$_3$O$_4$) and 3–11 nm (Au) size for improved magnetism-based theranostics were carried out. The 25 nm Fe$_3$O$_4$–Au nanohybrid exhibited the best characteristics for application as a contrast agent in MRI and for local heating using magnetic particle hyperthermia in aqueous and agarose systems. These nanohybrids used in vitro hyperthermia test for the 4T1 mouse breast cancer cell line demonstrated efficient cell death and nanoparticle visualization.

Daniel Erni and his work group studied the effect of hepatic vein on gold nanoparticle-mediated hyperthermia in liver cancer. The gold nanoparticle-mediated hyperthermia is a non-invasive, target-based cancer treatment with significantly reduced side effects compared to conventional treatments. A multiphysics simulation model was performed to investigate the case of a liver tumor located in the vicinity of a hepatic vein. Then, size-optimized gold nanorods are embedded in the liver, and the temperature raise under CW laser illumination is calculated, while taking into account the convective heat transfer through blood perfusion. The results show that an effective temperature raise is barely achievable when the tumor is located in the vicinity of the hepatic vein due to the heat drain into the blood stream. Moreover, it has been proven that for up to 90% of vein occlusions the temperature raise is not effective for tumor ablation.

In a collaborative effort of Daniel Erni and Sebastian Schlücker’s groups, computational studies and optical single-particle experiments were performed in order to evaluate the signal brightness of molecularly functionalized plasmonic nanoparticles for diagnostic purposes. Specifically, different classes of plasmonic nanoparticles such as gold nanoparticles,
hollow gold/silver nanoshells, gold nanostars, and gold core/gold satellite particles were tested for their signal brightness in surface-enhanced Raman spectroscopy (SERS) as an ultra-sensitive detection technique in nanodiagnostics. Correlative SERS/SEM experiments have enabled the identification of single particles by electron microscopy as well as the characterization of both their elastic (LSPR) and inelastic (SERS) scattering spectra. Experimental observations were compared with predictions from FEM computer simulations. For single nanostars and core/satellite particles detectable SERS signals are shown. The very bright core/satellite particles were then integrated in lateral flow assays (LFA) with clinical serum samples. A 15-fold improved sensitivity in comparison to commonly used assays and a fast readout (5 sec) via an in-house developed portable SERS reader with line illumination for point-of-care testing (POCT) could be achieved.

**Model for the formation of self-evolving structures**

Based on a new model of the possible origin of life, Christian Mayer and co-workers proposed an efficient and stable system undergoing structural reproduction, self-optimization, and molecular evolution. The proposed system could also become a model for the formation of self-evolving structures, leading up to the creation of the first living cell. The system is formed by the interaction of two cyclic processes: one offers vesicles as the structural environment, the other supplies peptides from a variety of amino acids as versatile building blocks. Structures growing in a combination of these two cycles can support their own existence, to undergo chemical and structural evolution, and to develop as yet unpredicted functional properties. The key mechanism is the mutual stabilization of the peptides by the vesicles and of the vesicles by the peptides together with a constant production and selection of both. Clear evidence for a vesicle-induced accumulation of membrane-interacting peptide could be identified by LC-MS. The studied peptide has an effect on the vesicles, leading to (i) reduced vesicle size; (ii) increased vesicle membrane permeability; and (iii) improved thermal vesicle stability.
Mayer and Eppe, along with co-workers, coated ultra-small gold nanoparticles (1.8 nm) with L-cysteine. By employing isotope-labeled cysteine, the surface structure and the coordination environment of the cysteine ligands on the nanoparticle were studied using $^{13}$C- and $^{15}$N-NMR spectroscopy. This was necessary for the interpretation of the complex 1H-NMR spectra, which could otherwise not be unambiguously assigned. By using the DOSY technique it was shown that the organic ligand is only present at the gold nanoparticle surface, with no residual cysteine molecules in the solution. The particle size data and the NMR-spectroscopic analysis showed three different binding sites for cysteine in the gold nanoparticle surface and a particle composition of about Au174(cysteine). This can be used to identify possible binding sites for cysteine with a different crystallographic environment.9

Serious respiratory tract diseases can be caused by airborne fungal pathogens (e.g., aspergillus fumigatus). Shirley Knauer and associates have demonstrated, that by using controlled nanoparticle models, those nanoparticles without specific functionalization rapidly and stably assemble on fungal spores. The complex formation of nanoparticle spores was enhanced by small nanoparticle size and was reduced in a concentration dependent manner by the formation of environmental or physiological biomolecule coronas. The assembly of nanoparticle spores affected their pathobiology and reduced the sensitivity against defensins, uptake into phagocytes, lung cell toxicity, and TLR/cytokine-mediated inflammatory responses. Nanoparticle-spore complexes were detectable in the lung tissue of mice after infection and were less efficiently eliminated by the pulmonary immune defense. This has resulted in enhanced A. fumigatus infections among immunocompromised animals. Collectively, the assembly of nanoparticle-fungal complexes affects their (patho)biological identity and may cause impacts on both environmental and human health.9

Nanoantibiotics
Furthermore, Shirley Knauer’s group identified the first resistance mechanism specific for nanoantibiotics and provided a novel explanation as to why nanoantibiotics show reduced activity in clinically relevant environments. Nanoparticles are being investigated as novel antibiotics but are often inefficient in practical applications. It has furthermore been demonstrated that the resistance to antibiotics, mediated by biomolecule coronas acquired in pathophysiological environments, especially the antibiotic activity of metal nanoparticles against multidrug-resistant clinical isolates (MDR) strongly depends on a physical binding to pathogens. The nanoparticle-bacteria complex formation was enhanced due to the smallness of the particle. However, complex formation and MDR killing effects could be restored by low-pH nanoparticle formulations, thereby breaking bacterial resistance. Two independent in vivo models, Galleria mellonella and mice, show that low pH-induced complex formation was essential in order to significantly inhibit MDR Staphylococcus aureus skin wound infections with silver nanoparticles. The Knauer group recommends their model for studying the therapeutic and/or toxicological impact of nanoformulations in vivo prior to performing extensive studies in mammals.10

In the group of our new CENIDE member Katja Ferenz from the University Hospital Essen (UKE), an investigation on albumin-derived perfluorocarbon-based capsules (A-AOCs) as artificial oxygen carriers by means of holographic optical trapping was performed in cooperation with Cemal Esen’s group (Applied Laser Technologies, Ruhr-University Bochum). The aim of this study is the characterization and provision of the holographic optical tweezer (HOT) to investigate individual A-AOCs for future use as artificial blood in a physiological environment. Furthermore, the motion behavior of capsules in a ring-shaped or vortex beam is being analyzed. HOT was successfully applied for initial examinations of surface interactions between A-AOCs in an experimental in vitro setting, and was highly effective in mimicking the (in vivo) physiological conditions of blood plasma.11

In addition to the selected highlights from our CENIDE research activities, it is worth mentioning that NanoBio materials benefits from the full spectrum of advanced instrumental analytics (AUX, DLS, NTA, ADC, AFFF) combined with scalable colloid synthesis from liter scale-batch.

Artificial blood in a physiological environment

CENIDE Scientific highlights:
Nanomaterials for health

Artificial blood in a physiological environment

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Gas-phase synthesis of nanomaterials


Nanomaterials for health


Magnetic materials


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Nanotechnology in energy applications


