ABSTRACT – Ph.D. Thesis Contest

Contrast-enhanced CT imaging through hafnium oxide nanocrystals

Eline Goossens, Ghent University and University of Basel

In the PhD thesis, the potential of **hafnium oxide nanocrystals (HfO2 NCs) in computed tomography (CT) contrast-enhanced polymer nanocomposites** is explored. CT enables high-resolution imaging of the internal structure of materials by sending X-rays through the sample, unfortunately many materials suffer from poor contrast making (automatic) detection of components or defects impossible. Due to their high density and atomic number, HfO2 NCs are excellent CT contrast agents, yet practical applications were lacking. To overcome this problem, the PhD addressed the following key challenges:

- **Lack of proof-of-concept.** While HfO2 NCs showed promise as efficient CT contrast agents, no practical applications existed at the start of the thesis.
- **Surface chemistry optimization.** Nanocomposite stability was hindered by NC agglomeration, which made the NCs unsuitable as CT contrast agents until this issue was solved.
- **Synthesis scale-up.** Existing synthesis methods produced only milligram-scale batches, while a cost-efficient, gram-scale production was needed for applications.

To tackle these issues, we first unravelled the solvothermal synthesis **mechanism**, which challenged the current consensus that the nonaqueous synthesis is a slow, single-step synthesis. It was demonstrated that the existing theories of nucleation and growth do not apply to this synthesis, exposing their limitations. We discovered that an additional post-synthetic step reduced the reaction time from 4+ hours to 1 hour. Furthermore, the synthesis was **improved and upscaled** by introduction of (i) a new precursor with improved reproducibility and solubility in the solvent, (ii) a direct, more efficient post-synthetic ligand exchange protocol and (iii) a work-up procedure suited for gram-scale NC batches.

A first practical application was found the biomedical field, where the HfO2 NCs were added to a **vascular casting** resin by using careful surface chemistry design. Vascular casting visualizes the 3D vasculature *ex vivo* by injection of a polymer resin, but cannot be distinguished from the surrounding tissues due to a lack of contrast. After addition of the NCs, high-quality cardiovascular casts of both zebrafish and mice could be obtained with CT, revealing micrometer-scale details previously undetectable and without the need for corrosion.
In a second, engineering application, the HfO2 NCs were then integrated in **carbon fiber reinforced polymers (CFRPs)**, which are widely used in high-performance structural applications. Significant contrast enhancement was achieved by introducing the NCs either into the polymer resin or onto the fiber surface. We found that selecting and synthesizing the right surface chemistry was crucial, not only for ensuring stability before resin curing, but also to prevent stripping during the curing process. The strong control over our NCs and surface resulted in a homogeneous dispersion of the NCs without affecting the mechanical properties of the nanocomposite. Additionally, coating the fibers with NCs enabled their use as internal markers in digital volume correlation. The improved CT data enables the validation of damage initiation and propagation models, resulting in a better understanding of when these composites, used in cars, windmills and planes, will break.

In summary, this PhD thesis achieved, for the first time, homogeneous and stable dispersions of HfO2 NCs in several polymers. By demonstrating their feasibility as CT contrast agents, this work paves the way for further applications. Additionally, it emphasizes the critical role of **fundamental understanding**, not only in improving the NC synthesis, but also in ensuring stability in the polymer resin through surface chemistry optimization. Additionally, this research highlights the **importance of interdisciplinary collaboration** in tackling complex materials challenges, demonstrating how the combined expertise of nanochemistry, engineering and physics lead to practical, real-world advancements in each field.