THESIS DEFENSE: Optical Holographic Microscopy for Bio- and Nanoparticle Characterization

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April 21, 2023

15:00

ICFO Homage Room

Nowadays, being able to precisely characterize nanoparticles is of key relevance in a wide range of scenarios. For instance, chemical and pharmaceutical industries often rely in particle-sizing for quality control. In a clinical context, in contrast, sensitive bioparticle characterization platforms can lead to the diagnosis of early-stage illnesses. However, the needs between each scenario vary, due to the differences in samples' composition and the particle-property of interest. Hence, several nanoparticle characterization techniques have emerged, each one based on a different physical principle and best suited for particular usage scopes.

In this thesis, I improve the optical nanoparticle sizing techniques by using holography. I present different optical systems that image nanoparticles and record their scattering signal

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into holograms. I show how to reconstruct the scattered light's wavefront using holographic processing tools and how to extract the particle size information from it. I prove the capabilities of the holographic imaging systems that I introduce by providing their technical characterization and by measuring relevant samples.

First, I introduce an imaging system with an extended the dynamic range compared to conventional darkfield microscopes. I demonstrate the nanoparticle sizing capabilities of such holographic platform using calibration samples. Moreover, I provide a proof-of-concept in the form of the characterization of a clinical sample, composed by extracellular vesicles, to demonstrate the feasibility of the platform for the development of point-of-care systems.

Afterwards, I show how nanoparticle tracking analysis (NTA), that is to size particles from their diffusion, can be improved by using holography. The use of holography not only increases the NTA's precision, thanks to its ability to capture better the particles' diffusion, but also provides the refractive index information of the sample. The latter is of especial interest when measuring samples of unknown compositions, such as clinical extractions. I present experimental evidence of the improvements in the NTA's sizing precision and the simultaneous retrieval of the refractive index. Additionally, I measure the radial shift of the nanoparticles induced by the formation of protein-coronas, which I believe that proves the platform's relevance for studying the particles' behaviour in biological fluids.

Finally, I present a system that confines particles in the volume-of-view of a holographic imaging system for further improving the NTA's sizing precision. Such platform's design was motivated by the promising results obtained using holographic NTA and its potential usage on fundamental research of protein-corona formation. The idea behind the system is to obtain longer particle-diffusion trajectories for pushing the holographic NTA sensitivity down to what is necessary to detect the absorption of a single protein onto a nanoparticle. I demonstrate the capabilities of such platform by showing a thorough technical evaluation based on experimental evidence.

I foresee that the presented holographic platforms will find many applications of both fundamental and applied nature. In particular, considering the ability of such platforms to analyse polydisperse samples, I expect to contribute to advances in the fundamental research of extracellular vesicles.

Friday April 21, 15:00 h. ICFO Homage Room

Thesis Director: Prof Dr. Niek van Hulst

Hosted by: Prof Dr. Niek van Hulst