Optofluidics characterization of individual virions and extracellular vesicles with deterministic sorting capacity

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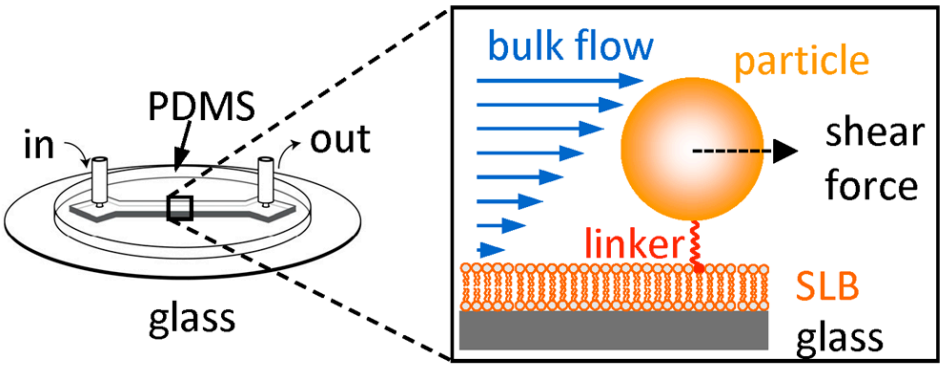
Abstract

Biological nanoparticles such as extracellular vesicles and exosomes are generating a rapidly growing interest due to the key roles they play in various biological processes and because of their potential use as biomarkers in clinical diagnostics and as efficient carriers in drug-delivery and gene-therapy applications. Their full exploitation, however, depends critically on the possibility to detect and classify them into different sub-populations, tasks that in turn relies on efficient means to identify their unique biomolecular and physical signatures. Due to their huge diversity, such information remains rather elusive and there is accordingly a need for new and complementary characterization schemes that can help expanding the library of distinct features of biological nanoparticles.

A diverse set of tools with single-nanoparticle sensitivity is now available, to which we recently contributed a concept that enables simultaneous fluorescent and scattering-based label-free imaging of thousands of surface-bound nanoscale entities.[1] With this setup, the fluorescence and scattering intensity of the nanoparticles can be very precisely determined, but their individual size remains unknown. The size of individual biological nanoparticles can instead be determined by simply tracking their 3D motion in a bulk solution, using e.g. nanoparticle tracking analysis (NTA).

However, due to the random motion of nanoparticles through the illumination volume, NTA does not offer reliable information about their individual scattering and fluorescence intensity. Hence, either the size or emission intensity can be determined, not both: Since the combination of size and content is decisive for the function of biological nanoparticles, this is has remained a severe analytical limitation. By replacing water as the mobile phase, as used in NTA, for a two dimensional fluid supported lipid bilayer, to which biological nanoparticles are directly anchored and imaged,[2] we have developed a new means to simultaneously determine both nanoparticle size and fluorescence / scattering intensity, including flow-cytometry-like sorting based on distinct features of individual nanoparticles. [3] This two dimensional flow nanometry concept, illustrated belwo, will be discussed in the context of improved characterization of individual nanoparticles of diagnostic and therapeutic significance.



[1] Agnarsson, B. et al. "Evanescent Light-Scattering Microscopy for Label-Free Interfacial Imaging: From Single Sub-100 nm Vesicles to Live Cells." (2015) **ACS Nano** 9:11849-11862.
[2] Block, S. et al. "Quantification of Multivalent Interactions by Tracking Single Biological Nanoparticle Mobility on a Lipid Membrane." (2016) **Nano Letters** DOI: 10.1021/acs.nanolett.6b01511.
[3] Stephan Block et al. "Two-Dimensional Flow Nanometry of Biological Nanoparticles for Accurate Determination of Their Size and Emission Intensity" (2016) **Nature Communications**; DOI: NCOMMS12956