

Trapping, characterization and reactions of biocolloids in a salinity gradient

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Abstract. The properties of soft matter nanoparticles like exosomes are interesting for drug delivery and diagnostics applications. However, the simultaneous characterization of multiple properties, e.g., size and zeta potential, can only be done serially and is highly sensitive to the purification prior to characterization. Here we show how a salt gradient established in a nanofluidic channel induces opposing transport of particles and liquid that trap the particles. Particles are thus accumulated in the trap. We show how optical microscopy images of the particle positions in the salinity gradient provide a measurement of the size and surface charge. We demonstrate the method on a sample of exosomes and on individual particles. Finally, we show how biomolecular reactions at the surface of the nanoparticle can be detected from the optical microscopy analysis of the particles' trapping position.

Nanometer-sized biocolloids play an important role in many research fields, e.g., in drug delivery and diagnostics, and their size and surface charge are important parameters for their performance. The zeta potential, which depends on the surface charge, is an indicator of the biocolloids' stability in dispersions and is crucial for their initial adsorption on the cell membrane. Hence the zeta potential is both a key parameter when designing liposomes for drug delivery and for understanding the body's cell-to-cell communication with exosomes [1]. The particle size influences the endocytotic uptake rate after adsorption on the cell membrane, so the size is also important for their efficiency as drug delivery vehicles [2]. Current nanoparticle characterization techniques all have challenges. Measurements of size and zeta potential are routinely performed by dynamic light scattering (DLS) and laser Doppler electrophoresis (LDE), but they require multiple experiments and are challenged by polydisperse samples [3]. Alternatively, the size of individual particles can be measured by nano tracking analysis (NTA). Combined with refractive index measurements by interferometric imaging, this provides the two parameters simultaneously [4].

Here we present a nanofluidic-based method for determining the size and zeta potential from a single measurement with data acquisition times less than a minute [5]. In our method, we establish a salinity gradient across a funnel-shaped nanochannel. The nanochannel has a height of 240 nm, and the widths at the ends are 5 μm and 20 μm , see Figure 1a. The salinity gradient induces both a diffusio-phoretic particle migration towards higher salt concentration and an oppositely directed diffusio-osmotic fluid flow in the nanochannel [5]. Particles in the nanochannel are trapped where the diffusio-phoretic velocity $v_{dp}(x)$ and the diffusio-osmotic

fluid velocity $v_{do}(x)$ balance each other. The trapping position depends on the particles' diameter and zeta potential.

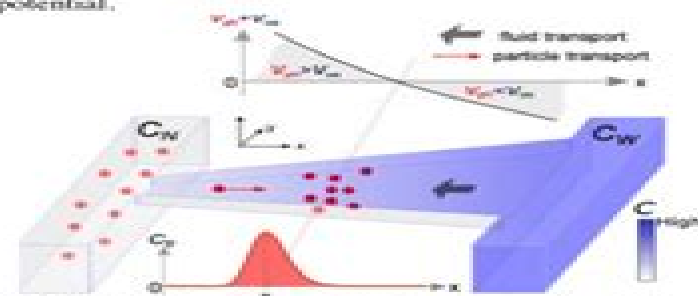


Fig. 1. Schematic of nanoparticle trapping in a funnel-shaped nanochannel by diffusio-osmosis and diffusio-phoresis. The salinity gradient is maintained by a continuous flow of solutions with PBS concentrations C_L and C_R ($C_L < C_R$) in the microchannels.

Figure 2a,b shows fluorescence microscopy images of trapped exosomes extracted from human blood serum and from a sample with two subpopulations of liposomes, respectively. The liposome subpopulations have different lipid compositions, and hence different zeta potentials, which causes a separation into two bands (Fig. 2b,c). The sizes and zeta potentials of both exosomes and liposomes are obtained from a fit of the fluorescence intensity along the nanochannel to a model that includes both the diffusion and the diffusio-phoretic and -osmotic velocities (Fig. 2c). The fitted values for the particle sizes and zeta

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