Séminaire de l'axe Formulation et analyse du médicament

Deconstructing molecular and nanoparticle interactions with simple single-molecule imaging

Radin Tahvildari, Ph.D.
Associé de recherche
Dép. de physique, The Leslie Lab
Université McGill

à l'invitation du professeur Davide Brambilla

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Key challenges in the development of functional nanoparticles include the characterization of their size distributions and aggregation tendencies, as well interaction rates and affinities with other molecules. While standard characterization tools like Dynamic Light Scattering (DLS) are limited to bulk measurements, averaging over millions of NPs and obscuring important details about sample variations, high-throughput Convex Lens-induced Confinement (CLiC) imaging can resolve the properties of each nanoparticle and construct a distribution of properties. More broadly, CLiC enables direct visualization of nanoparticle interactions and dynamics, such as binding and unbinding without tethers and away from surfaces, encapsulation and release, fusion and self-assembly, with real-time control over the solution environment. This helps elucidate the impact of particle variations, such as aggregation, on functional properties of interest, such as the capacity to carry and deliver drug cargo. Beyond discussing new sights from CLiC into the nanoparticle dynamics, I will also discuss key applications of our research and development.

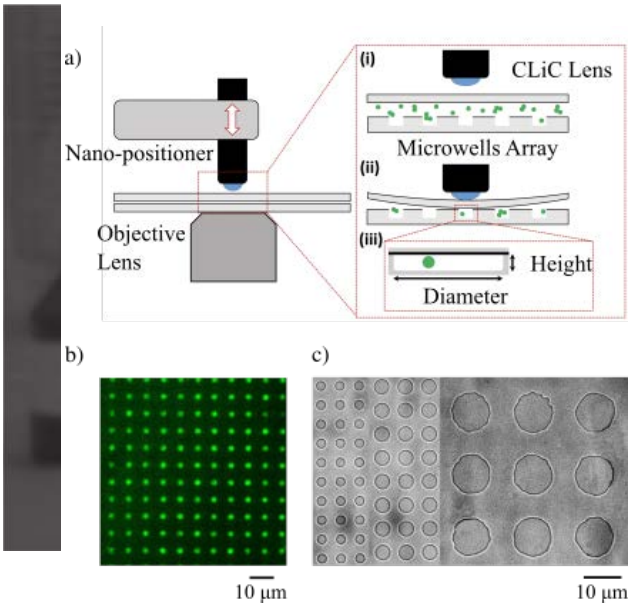

Figure 1. (a) CLiC instrument and schematic cross section of a typical flow cell placed between the objective lens and CLiC lens. The CLiC lens *(i)* deflects the top surface downward and traps sample in the *(ii)* microwells embedded in the bottom surface. *(iii)* Typical microwell diameter is 1-10 μm and depth is 350 nm, less than the focal depth. **(b)** Fluorescent image of nanoparticles in 3 μm wells. **(c)** Images of 3, 5 and 10 μm arrays.

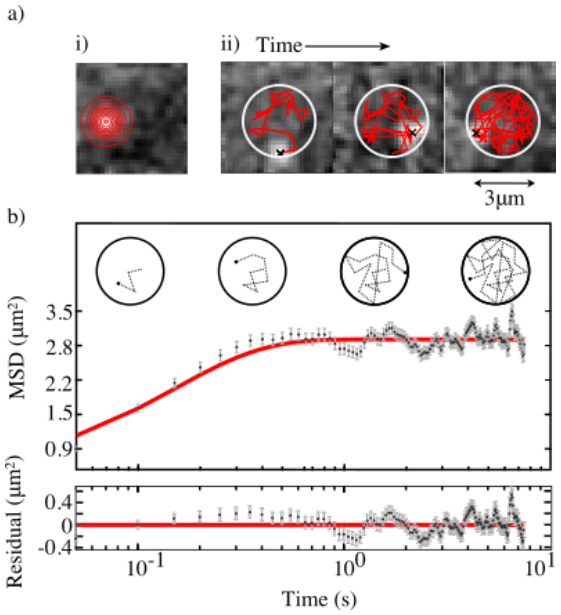

Figure 2. Imaging and tracking a single nanoparticle in a 3 μm well. **(a)** *(i)* Identifying a particle; *(ii)* Consecutive 50 ms exposure frames with the particle's Brownian motion trajectory represented by a growing red line. The circle shows the microwell boundary. **(b)** Typical mean squared displacement (MSD) curve of a diffusing nanoparticle. The plateau at longer times is due to confinement of the particle in the microwell. **(c)** Residual plot of the MSD fit.

Figures from: Tahvildari *et al*, *in preparation* (2019).