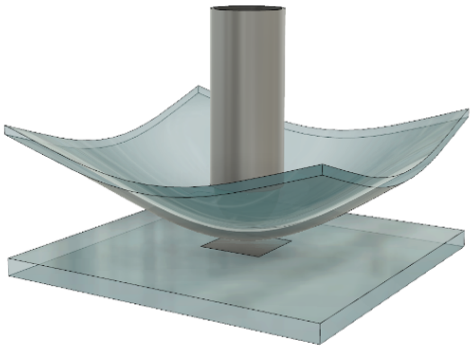
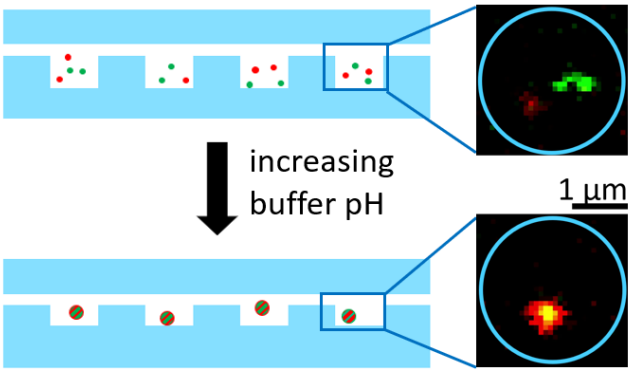


A deflectable flow-cell of the CLiC device



Watching Lipid nanoparticle dynamics – in real-time – as a function of pH

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Single-particle imaging of lipid nanoparticles for drug delivery applications

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A wide range of biological nanoparticles are being developed for diverse applications including therapeutics, cosmetics, and textiles. Key challenges in nanoparticle engineering involve resolving, understanding, and predicting important functional properties, such as size and loading, as well as aggregation and interaction properties. Typical characterization tools average over thousands of particles or more to obtain a bulk result, obscuring detailed understanding.

In this work, we introduce a general imaging and analysis method to isolate and track many copies of single diffusing nanoparticles at once. We confine the particles in an array of circular microwells using the CLiC (Convex Lens-induced Confinement) imaging technique. This enables simultaneous measurements of the size and intensity of each particle, without using tethers. We establish agreement between our measurements and the mean particle size reported using other methods such as Dynamic Light Scattering; and provide detailed size and loading distributions.

Further, we investigate the pH-dependent size and dynamic properties of lipid nanoparticles designed for drug delivery, such as real-time measurements of particle fusion. The CLiC platform enables direct investigation of nanoparticle interactions and dynamics under cell-like conditions - such as binding and unbinding, encapsulation and release, and fusion of nanoparticles - and in contexts extending from "glass cells", to model endosomes, living cells, using the same device.