Single-particle imaging of biological nanoparticles for therapeutic 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 insights into microscopic properties which can be inherently heterogeneous.

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 drug-loading 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 insights into the distribution of size and loading properties relevant to therapeutic use.

Further, we investigate the pH-dependent size and dynamic properties of lipid nanoparticles designed for drug delivery, including real-time measurements of pH-induced dynamics such as fusion or drug-release. More broadly, CLiC imaging of nanoparticles opens the door to visualizing a range of nanoparticle interactions and dynamics, such as binding and unbinding, encapsulation and release of drugs, with single-particle resolution and real-time control over the solution environment.