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Hydosomes: optically trappable femtoliter containers for studying single molecular complexes

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The success of single molecule (SM) techniques relies on methods to isolate and confine the biomolecule or molecular complex under study. Typical immobilization strategies currently include (1) binding or adsorbing molecules on a surface, (2) immobilization in porous materials, and more recently (3) encapsulation in a surface-tethered lipid vesicle. Here we demonstrate a new strategy for encapsulating and manipulating single molecules in optically-trappable aqueous nanocontainers that we call hydrosomes [1]. Hydrosomes have significant advantages over other immobilization or confinement strategies, in that they facilitate the study of transiently interacting molecular complexes on a single complex basis. Unlike liposomes, hydrosomes fuse on contact. The various components of a transiently interacting molecular complex can be isolated and confined in different hydrosomes, which can then be fused to form a single larger hydrosome. This larger hydrosome, which contains and confines all complex components and yet permits them to interact freely, can then be optically interrogated [2]. We present a comparison of FRET from single surface-attached RNA 16mers with FRET from single hydrosome-encapsulated RNA 16mers. Significant perturbation from the PEG tether used to immobilize the RNA on the surface is absent for the hydrosome encapsulated RNA. Our intent is to use hydrosome encapsulation and mixing to perform studies of transiently interacting RNA/protein complexes, and two examples will be discussed.

[1] Helmerson, K. et al. Optical manipulation of nanocontainers for biotechnology. Dholakia, K and Spalding, GC. Optical Trapping and Optical Micromanipulation(5514). 2004. Proc. SPIE.
[2] Reiner, J.E. et al. Optically trapped aqueous droplets for single molecule studies. Applied Physics Letters 89, (2006).