3D Single-Particle Tracking in the Short-Wave Infrared to study diffusion in Complex Soft Matter Systems as Models for (neuro)biological tissues

Exploration of the brain extracellular space (ECS) using diffusing nanoparticles has gained interest in recent years, as these regions are microenvironments for signaling molecules, neurotransmitters and toxic metabolites, and exhibit heterogeneities and spatial variations with changes in health, and development. This exploration is primarily achieved with the use of single particle tracking (SPT) strategies in the shortwave infrared (SWIR) range (950-1300 nm), particularly using single-walled carbon nanotubes (SWCNT) whose emission lies in the transparency window of biological tissues, enabling SPT at depths of hundreds of µm.

Similarly, the SWIR nanoparticles exploring interstitial spaces in highly autofluorescent mouse liver tissues show significant variations in diffusion from healthy to fibrosed tissues. Thus, understanding the physical aspects of diffusion in complex biological tissues is crucial to explain the nanoscale topology and local molecular mobility in the context of health and disease.

Here we present a soft matter system composed of packed emulsion droplets as a biophysical model to mimic ECS in tissues that can be studied with SWIR SPT. These bio-inspired emulsions used to study macroscopic tissue responses to mechanical forces and cell adhesion form a network of interstitial voids that provides a model system for various tissues, including brain ECS.

Using widefield optical sectioning, and a double helix point spread function (DHPSF) phase mask for 3D SPT, we obtain correlative images of the droplet system with individual diffusing nanoparticles with a localization accuracy of less than 20 nm at SWIR wavelengths. Using ultra-short SWCNTs of ~50 nm length, fluorescing at ~1100 nm as nanoprobes, we obtain 3D SPT at depths greater than 100 µm. The choice of SWCNT surfactant allows us to tune their diffusion at the droplet surface or in interstitial volumes. Furthermore, we show the variation in exploration and diffusion of nanotubes of different sizes. Finally, we also propose an opal model to study diffusion in rigid structures relative to droplets.

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