Optical Diffraction Tomography from Single-Molecule Localization Microscopy

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Single-molecule localization microscopy (SMLM) is an imaging modality that delivers nanoscale resolution. It does so by sequentially activating a subset of fluorescent tags and by extracting their super-resolved positions from the microscope images. The emission patterns of individual tags can be distorted by the refractive-index (RI) map of the sample, which reduces the accuracy of the molecule localization if not accounted for.

In this work, we show that one can exploit those sample-induced aberrations to reveal the structural information of the specimen. Our work is related to the optical diffraction tomography in that we aim to recover the RI map. To that end, we propose an optimization framework in which we reconstruct the RI map and optimize the positions of the molecules in a joint fashion. The benefits of our method are twofold. On one side, we effectively recover the RI map of the sample. On the other side, we further improve the molecule localization—the primary purpose of SMLM. We validate our joint-optimization framework on simulated data (Figure 1). Our results lay the foundation of an exciting and novel extension of SMLM.

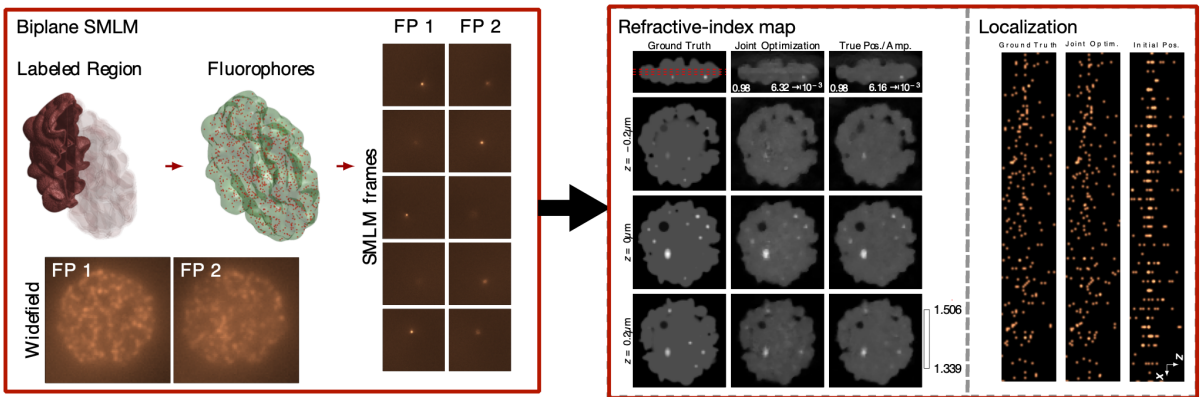

Figure 1. Left: Biplane SMLM. The simulated sample was populated with fluorophores. The spherical wave emitted by each fluorescent tag scattered through the sample and its intensity was recorded on two focal planes. Right: Joint-optimization framework. Based on biplane measurements and initial guesses of localization, our method reconstructs a refractive-index map and refines the positions of the fluorescent tags.