

Multiplexed 3D super-resolution imaging of whole cells using spinning disk confocal microscopy and DNA-PAINT

Single-molecule localization microscopy (SMLM) can visualize biological targets on the nanoscale, but complex hardware is required to perform SMLM in thick samples. Here, we combine 3D DNA Points Accumulation for Imaging in Nanoscale Topography (DNA-PAINT) with spinning disk confocal (SDC) hardware to overcome this limitation. We assay our achievable resolution with two- and three-dimensional DNA origami structures and demonstrate the general applicability by imaging a large variety of cellular targets including proteins, DNA, and RNA deep in cells. We achieve multiplexed 3D super-resolution imaging at sample depths up to $\sim 10\ \mu\text{m}$ with up to 20 nm planar and 80 nm axial resolution, now enabling DNA-based super-resolution microscopy in whole cells using standard instrumentation.