Super-Resolution Fluorescence Assisted Diffraction Computational Tomography Reveals the Three-Dimensional Landscape of Cellular Organelle Interactome

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The emergence of super-resolution (SR) fluorescence microscopy has rejuvenated the search for new cellular sub-structures. However, SR fluorescence microscopy achieves high contrast at the cost of the lack of a holistic view of their interacting partners and surrounding environment. Thus we develop SR fluorescence-assisted diffraction computational tomography (SR-FACT) [1], which combines label-free three-dimensional optical diffraction tomography (ODT) with two-dimensional fluorescence Hessian structured illumination microscopy [2]. The ODT module is capable of resolving mitochondria, lipid droplets, the nuclear membrane, chromosomes, the tubular endoplasmic reticulum and lysosomes. Using dual-mode correlated live cell imaging for prolonged period of time, we observe a novel subcellular structure named dark-vacuole bodies, the majority of which originates from densely populated perinuclear regions and intensively interacts with organelles including mitochondria and the nuclear membrane, before ultimately collapsing into the plasma membrane. These works demonstrate the unique capabilities of SR-FACT, which suggest its wide applicability in cell biology in general.

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