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3D Super-Resolution Optical Fluctuation Imaging for Molecular Parameter Estimation

The LBEN at EPFL is offering a master project related to super-resolution imaging. Several techniques have been developed in order to overcome the diffraction limit in fluorescence microscopy. They rely on exploiting a priori knowledge about the quantum mechanical properties of fluorophores. For super-resolution optical fluctuation imaging (SOFI), higher order statistics (cumulants) of a time series of blinking fluorescence emitters are computed. SOFI analysis yields essentially background free images and is ideally suited for fast, 3D imaging using a multi-plane microscope. Balanced (b)SOFI deals with the nonlinear image contrast and enables up to fivefold improved spatial resolution in 2D. It allows extraction of molecular parameter maps such as the density and state lifetime of molecules. Molecular counting (or density estimation) based on SOFI is robust against imaging artifacts, which makes SOFI a unique tool in the super-resolution microscopy research field . We recently used bSOFI to investigate clustering of membrane proteins in T cells with an aim to understand their response In this project, you will explore the extension of bSOFI parameter estimation to 3D imaging. Based on an existing 2D simulation framework, different multi-plane configurations and fluorophore properties can be simulated (brightness/ signal-to-noise, blinking parameters, photo-bleaching) and evaluated using SOFI processing. You will perform super-resolution imaging of cells and/or DNA origami/protein calibration standards on our custom multi-plane microscopes. We aim to demonstrate multi-plane bSOFI parameter estimation for the first time. Depending on your skills and interests, the in silico or experimental aspects of the project can be emphasized.

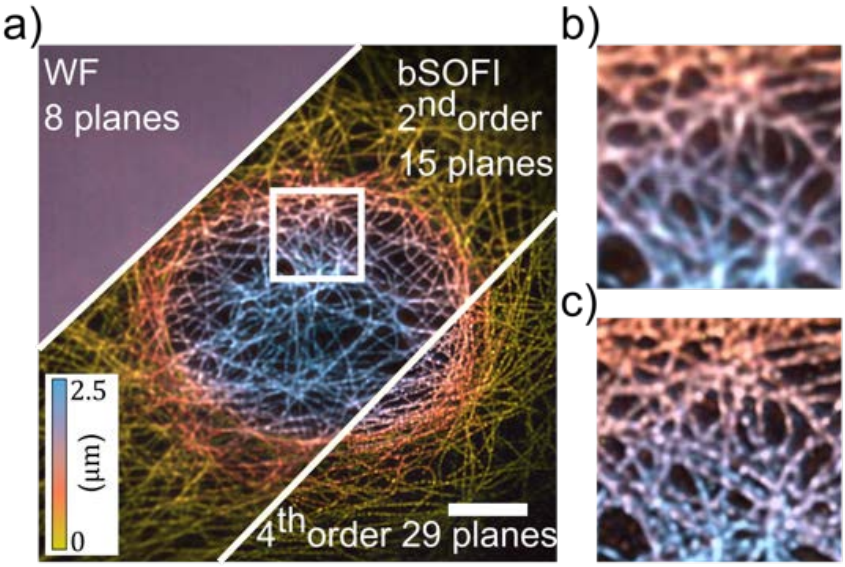

Figure 1. Multi-plane high-order SOFI with a self-blinking dye : COS-7 cells immunostained microtubules with AbberiorFlip565. a) Pseudo widefield image, 2nd & 4th order SOFI; b) and c) close-up. <2kWcm-2 532nm. Scale bar 5µm.

Skills: Optics, microscopy, data analysis (Matlab), signal processing, cell culture, labelling of cells and preparation for super-resolution microscopy.

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References:

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2. Geissbuehler, S. et al. Live-cell multiplane three-dimensional super-resolution optical fluctuation imaging. Nature Communications 5, 1–7 2014
3. Jungmann, R. et al. Multiplexed 3D cellular super-resolution imaging with DNA-PAINT and Exchange-PAINT. Nat Methods 11, 313–318 (2014).