SUPER-RESOLUTION OF LARGE BIOLOGICAL SAMPLES BY MEANS OF SELECTIVE PLANE ILLUMINATION MICROSCOPY

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The recent development of super-resolution techniques, based on localization of single molecules (such as PALM, STORM and GSDIM), allowed to push below the diffraction limit the reachable spatial resolution of fluorescence microscopy. Even if these techniques have been established to investigate structures at the molecular scale in thin samples (<15 μm), a growing of interest is still addressed to the widening of super-resolution application to thick samples (>50 μm).

Within this scenario, light sheet based fluorescence microscopy techniques provide optical sectioning and imaging depth capability allowing imaging of thick living samples [1]. Here we demonstrate 3D super-resolution imaging through thick biological specimens, by coupling far-field individual molecule localization (IML) and selective plane illumination microscopy (SPIM). A PALM approach [2], implemented into a selective plane illumination architecture, allowed to image cellular spheroids with < 35 nm lateral precision and sub-diffraction axial resolution [3]. Furthermore, two photon excitation microscopy implemented into a light sheet based configuration can be exploited for reduction of the scattering effects thus improving the signal to noise ratio and imaging capabilities of thick samples [4]. 3D imaging of mammary cell spheroids in depth has been also performed using 2PE-SPIM [5].