Waveguide chip-based super-resolution microscopy enables multi-modal imaging over large fields-of-view

Robin Diekmann[1#], Øystein I. Helle[2], Cristina I. Øie[2], Peter McCourt[3], Thomas R. Huser[1], Balpreet S. Ahluwalia[2], Mark Schüttpelz[1]

[1] Department of Physics, Bielefeld University, Bielefeld, Germany.
[2] Department of Physics & Technology, The Arctic University of Norway, Tromsø, Norway.
[3] Department of Medical Biology, The Arctic University of Norway, Tromsø, Norway.
[#] E-mail: rdiekmann@physik.uni-bielefeld.de

The advent of large area, highly sensitive (primarily sCMOS) cameras facilitates high throughput super-resolution imaging due to the extensive fields-of-view (FOV) enabled by these detectors. Consequently, researchers are aiming for plain sample illuminations over unprecedented large regions [1],[2]. Pursuing this trend, we demonstrate an integrated imaging platform based on waveguide chips that provides TIRF excitation over an almost arbitrarily wide FOV, limited in its dimensions only by the waveguide layout. Our approach completely decouples the excitation and illumination light paths (Fig. 1a) and allows for multi-modal, scalable nanoscopy where the choice of the detection objective lens in terms of magnification and numerical aperture (NA) can be tailored to the particular application.

Using a 20×/NA0.45 objective lens, we demonstrate *d*STORM imaging over a FOV of 0.5 mm width (Fig. 1b) at resolutions down to 140 nm. Swapping to a 60×/NA1.2 objective lens results in sub-50 nm resolution and is used to visualize the interplay of the cytoskeleton and plasma membrane sieves in liver sinusoidal endothelial cells.

Planar multi-mode waveguides provide dynamic near-field fluorescence excitation patterns with high spatial and temporal frequencies. Explicitly exploiting this fluctuating sample illumination allows for fluctuation-based super-resolution imaging, whereas averaging over multiple frames yields uniform fluorescence excitation that enables diffraction limited as well as *d*STORM imaging. As standard low cost setups can easily be retrofitted with this approach and biological sample preparation is possible following standard protocols, the chip-based implementation has the potential to contribute to the dissemination of nanoscopy for a wide range of users.

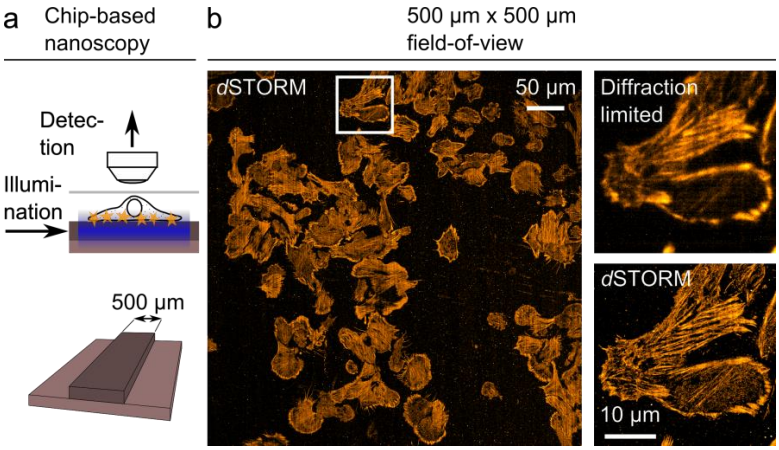

Figure 1:
(a) Waveguide chips provide TIRF excitation over almost arbitrarily large regions. Illumination and detection are completely decoupled, so a simple upright microscope can be used to capture the fluorescence emission. (b) Choosing a 20×/NA0.45 objective lens enables *d*STORM imaging over a 500×500 µm² large FOV.

[1] K.M. Douglass, Ch. Sieben, A. Archetti, A. Lambert, S. Manley, "Super-resolution imaging of multiple cells by optimized flat-field epi-illumination," *Nat Photonics* **10**, 705–708 (2016)
[2] J. Deschamps, A. Rowald, J. Ries, "Efficient homogeneous illumination and optical sectioning for quantitative single-molecule localization microscopy," *Opt Express* **24**, 28080-28090 (2016)