Photonic chip-based multi-modality TIRF nanoscopy platform

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We propose a multimodal optical nanoscopy platform based on photonic integrated chips. Optical waveguide generate an evanescent field all along their surface that can be exploited for multi-modality total internal reflection fluorescence (TIRF) nanoscopy. Here, we present the methodology and the results for photonic chip-based a) TIRF microscopy, b) single molecule localization microscopy (SMLM), c) TIRF structured illumination microscopy (SIM), and d) fluctuation based microscopy (Fig.1). The biological material (cells) are placed directly on top of the waveguide chip (Fig. 1) and illuminated by the evanescent field.

Conventional TIRF nanoscopy techniques typically use special high NA oil immersion objectives with high magnification, leading to a limited field of view (f-o-v). By generating light illumination patterns using waveguides [1], the chip-based nanoscopy platform decouples excitation and collection light paths. As the evanescent field is generated independent of the collection objective lens, a lower magnification objective lens can be used to extend the f-o-v for SMLM. This property is exploited in chip-based SMLM, where we report optical resolution of 80 nm over millimeter large f-o-v, (0.25 x 0.5 mm^2). Moreover, by making optical waveguides using high-refractive index material (n=2), the laser light is more tightly confined inside the waveguide than what can be achieved using an oil-immersion objective lens (typically the refractive index of oil is = 1.5). We harness this property to show chip-based SIM with a resolution enhancement of 2.3X, and fluctuation based methods [2,3] with highly extended resolution.

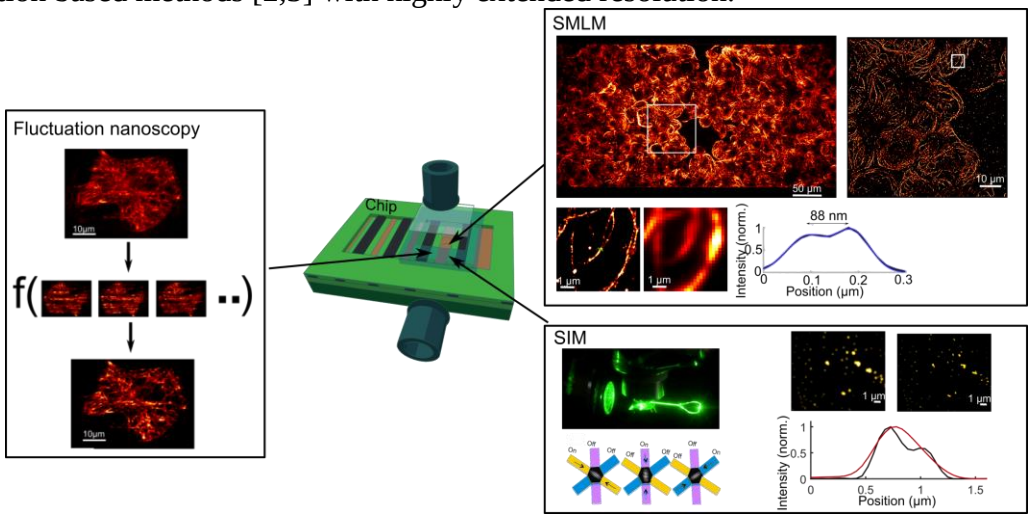

Fig.1: Chip-based multi-modality TIRF nanoscopy: Fluctuation nanoscopy utilize intrinsic intensity fluctuations to generate a stack of images and an algorithm to extract a super-resolved image. Chip based *d*STORM generate super-resolved images over large fields of view. The photonic chip also supports SIM that harness standing waves generated by interfering waveguide structures.

[1] R. Diekmann, Ø. I. Helle, C. I. Øie, P. McCourt, T. R. Huser, M. Schüttpelz, and B. S. Ahluwalia, "Chip-based wide field-of-view nanoscopy," Nat Photonics **11**, 322 (2017).
[2] K. Agarwal and R. Macháň, "Multiple signal classification algorithm for super-resolution fluorescence microscopy," Nature Communications **7**, 13752 (2016).
[3] I. Yahiatene, S. Hennig, M. Müller, and T. Huser, "Entropy-Based Super-Resolution Imaging (ESI): From Disorder to Fine Detail," ACS Photonics **2**, 1049-1056 (2015)