Photonic chip-based linear SIM with 2.4x resolution enhancement

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Structured illumination microscopy (SIM)[1] has proven to be one of the most popular super-resolution methods for live-cell imaging due to its fast temporal resolution, compatibility with most fluorescent dyes and ease of use. However, the resolution of conventional linear SIM is hindered by the optics and does not exceed 2x over the diffraction limit. In conventional SIM microscopes, the structured illumination is generated via the microscope objective lens, which acts as a low-pass filter stopping fringe formation with smaller fringe spacing than what can be supported by the NA of the objective lens.

Recently, we have shown that photonic-chip based TIRF nanoscopy based on the principles of single-molecule localization can support super-resolution imaging over extra-ordinary large areas (0.5 x 0.5 mm^2 with a resolution of 75 nm)[2, 3] In this work, we have expanded the usefulness of photonic circuit chips towards TIRF-SIM[4]. We generate the structured illumination using a photonic integrated circuit chip (PIC) allowing fringe formation which is independent of the microscope objective lens. A photonic chip acts as the sample substrate, where at the top surface of the chip, integrated optical waveguides are shaping the excitation light forming a standing wave interference pattern. The standing wave excites fluorescence in the specimen via evanescent fields, exponentially decaying away from the waveguide surface up to around 100 nm. The fringe spacing determines the resolution enhancement of SIM, and by using waveguide materials with a high refractive index (e.g. silicon nitride or tantalum pentoxide), and using counterpropagating light the resolution enhancement is shown up to 2.4x, exceeding the 2x resolution enhancement possible in conventional SIM. We further demonstrate different phase-shifting methods, and finally, showcase the method by imaging both biological and artificial samples.

In this work, we will present SIM-on-chip and will also discuss the multi-modality aspect of photonic-chips which can enable different nanoscopy methods (SIM, *d*STORM, ESI, SOFI, etc) using a standard optical microscope, which could pave the road for an affordable and wide-spread TIRF-nanoscopy solution.

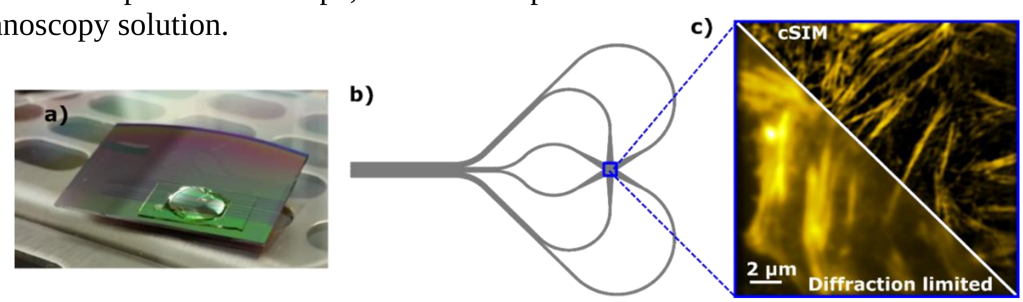

Figure 1: a) A silicon chip is used as the sample substrate and excite fluorescence via evanescent fields. b) By shaping the waveguides in the chip surface, standing wave interference patterns are formed which can be used as the excitation light in SIM. c) Biological specimen is imaged using cSIM showing a clear resolution enhancement

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