Optical Nanoscopy and Raman Spectroscopy Using an Integrated Photonic Chip Platform

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Integrated photonics is a rapidly emerging field, with great potential in e.g. microelectronics. There are, however, a plethora of other possible applications where photonics circuits can have a big impact in the years to come. Here, we present two on-chip applications: super-resolution imaging and spectroscopy. The photonic circuits reduces costs vastly, increases simplicity and can even outperform traditional set-ups[1,2].

Single molecule localization based microscopy techniques, such as direct stochastical reconstruction optical microscopy (*d*STORM), often use total internal reflection excitation to avoid out-of-focus light. The evanescent field excitation is typically generated by using special total internal reflection fluorescence (TIRF) objective lenses with high magnification and numerical aperture. Since both excitation and collection are done through the TIRF lens, the field of view is restricted. Here, we show that planar optical waveguides can be used to hold the sample and the evanescent field inherently present at the interface to the stained sample. As the evanescent field is restricted to around 100 nm from the surface, it gives excellent optical sectioning. The intensity of the evanescent field can be made sufficiently high for fluorophore blinking as required in *d*STORM imaging (1-10KW/cm^2) by using thin waveguides of high refractive index material such as Si_3N_4 or Ta_2O_5. The TIRF illuminated area can be made almost arbitrarily large by using wide and long waveguides. Separation of excitation and collection light pathways allows us to acquire *d*STORM over large areas using low magnification objectives. We demonstrate sub-100 nm optical resolution over 500x500 µm^2 area, imaging more than 50 liver sinusoidal endothelial cells simultaneously. The same set-up can also give higher resolution over smaller regions simply by switching the objective lens. Photonic chip-based nanoscopy therefore enables high-throughput nanoscopy.

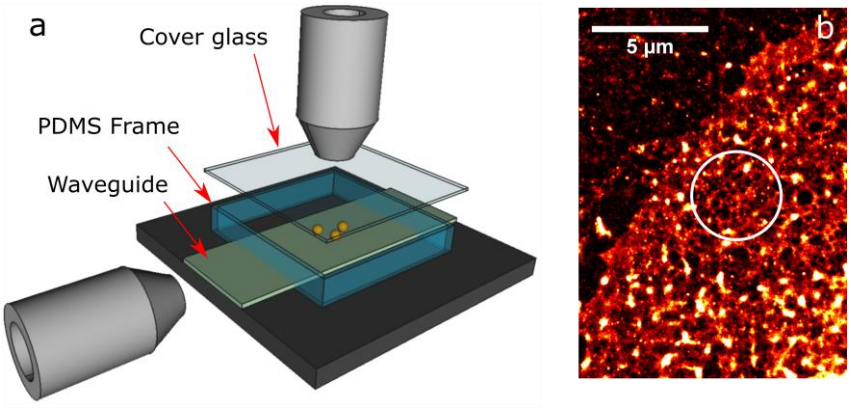

Figure 1: (a) Schematic overview of the chip-based nanoscope. A coupling lens (far left) couples light into the waveguide. The light is guided along the waveguide and excites samples in contact with the surface (yellow spheres) through the evanescent field. A hollow PDMS frame is used to contain the sample and blinking buffer. The area is sealed off with a cover slip and the sample is imaged from the top using a

conventional optical microscope. (b) dSTORM image of a small section of the plasma membrane stained liver sinusoidal endothelial cells. Nanoscopic fenestrations (diameter between 50 and 200 nm) in the plasma membrane are highlighted with the white circle. The image is captured with a 60x/1.2 NA objective lens.

The planar waveguide platform used for *d*STORM imaging can also be used for other, label-free applications. The high intensity evanescent field gives rise to Raman scattering in the sample. Waveguide based Raman spectroscopy is an emerging field, and can offer intrinsic enhancement, miniaturization and high reproducibility (compared to e.g. SERS)[1]. Here, we present some recent development towards resonant Raman measurements of hemoglobin using the waveguide platform.

1. Dhakal, A. *et al.* Nanophotonic Waveguide Enhanced Raman Spectroscopy of Biological Submonolayers. *Acs Photonics* **3,** 2141 - 2149 (2016).

2. Diekmann, R. *et al.* Chip-based wide field-of-view nanoscopy. *Nat. Photonics* **11,** 322 - 328 (2017).