Preparation of photonic biosensors by inkjet printing technology

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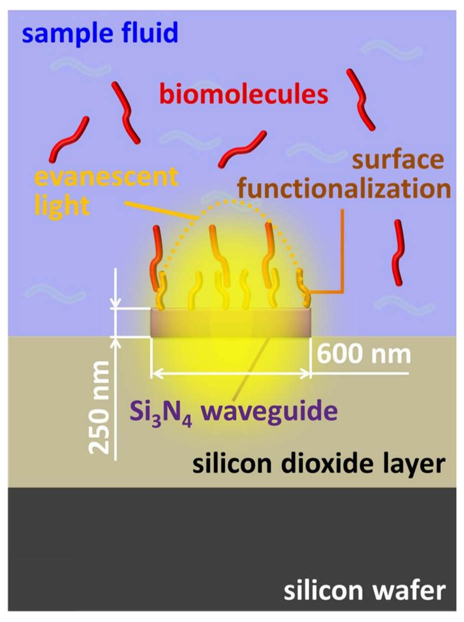
Abstract

In order to enable local functionalization of label-free optical waveguide biosensors in a cost effective mass-fabrication compatible manner, we investigate surface modification employing inkjet printing of a) functional polymers (biotin-modified polyethylenimine (PEI-B)) to implement high receptor densities at the surface and b) UV-curable benzophenone dextran (benzo-dextran) to form a voluminous porous hydrogel matrix. The combination of these approaches on a single chip is promising for the detection of biomolecules. We evaluate these functional polymers and hydrogels on an integrated four-channel silicon nitride (Si_3N_4) waveguide based Mach-Zehnder interferometric (MZI) sensor platform operating at a wavelength of 850nm (TM-mode).

Evanescent wave sensing

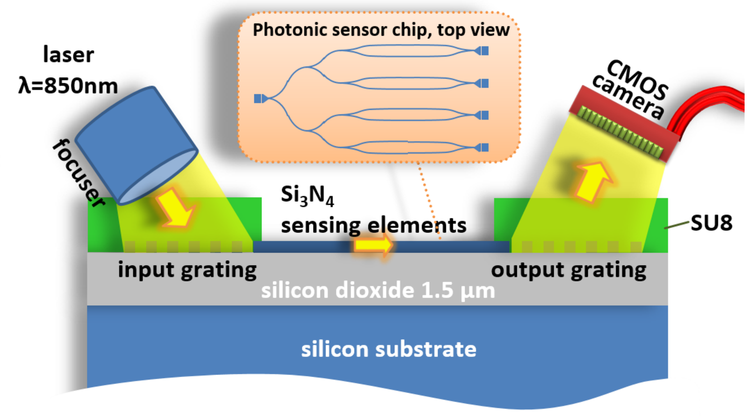
Detection principle

The binding of biomolecules to the functionalized sensor surface induces a local refractive index change that influences the light propagation in the waveguide. This leads to a phase shift between sensing and reference arm, which is translated into a sinusoidal modulation of the output power at the output of the MZI sensor [1].

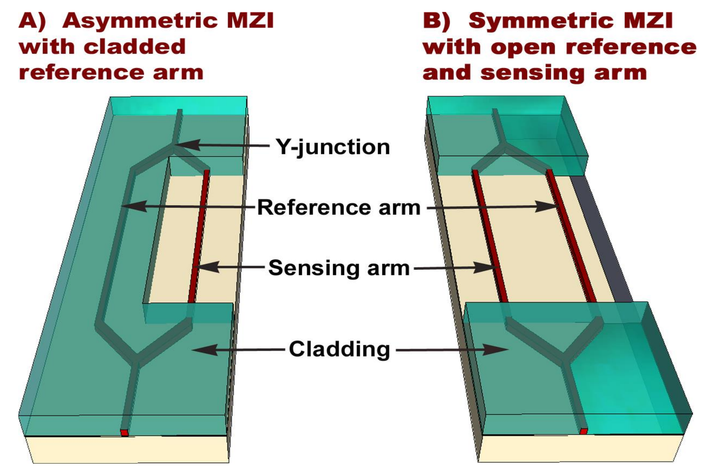


Measurement setup

We designed a four channel MZI-sensor array. The waveguides of the MZI have a cross-section of 600x250 nm². A fiber coupled focuser illuminated the input grating coupler. After passing the MZI sensor array ($L_{sensing\ arm}$=1 cm), the light deflected by the output grating couplers of the individual MZI sensors was detected by a commercial off-the-shelf CMOS camera.



MZI sensor configurations

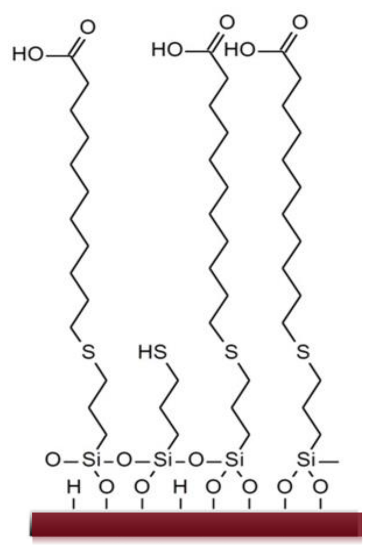


Inkjet printing allows modification of both configurations. Each of them possesses certain advantages – see result section.

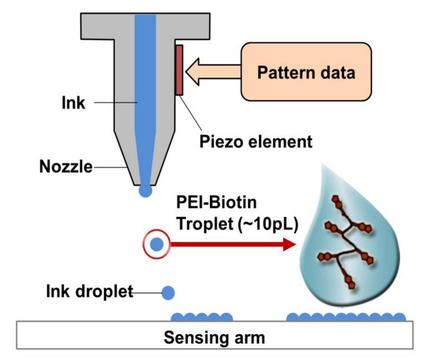
Surface modification

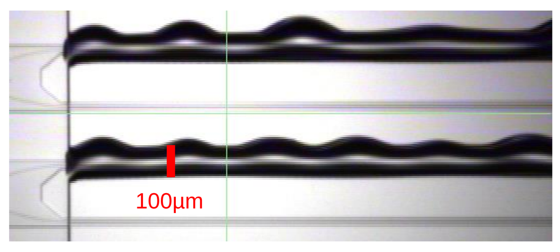
To enable biomolecular measurements, we developed inkjet printing procedures both for functional polymers (biotin-modified polyethyleneimine (PEI-B) macromolecules) and for hydrogel precursor solutions (benzophenone modified dextran (benzo-dextran) [3]). This allows the local functionalization of sensing waveguides in a cost effective and mass-fabrication compatible manner.

1. MPTS silanization
2. Thiol-ene reaction: 5mg/ml DMPA, 50%(v/v) 10-undecenoic acid in MeOH; UV-Light: 30min [2]
3. EDC/NHS Activation



I. Printing of functional polymer (PEI-Biotin)
+ TRIS block



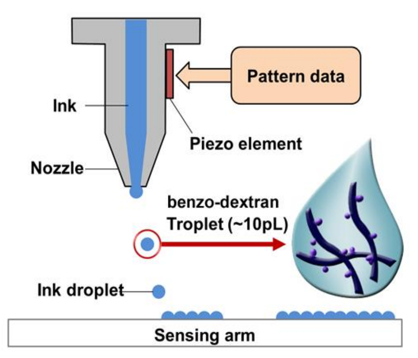


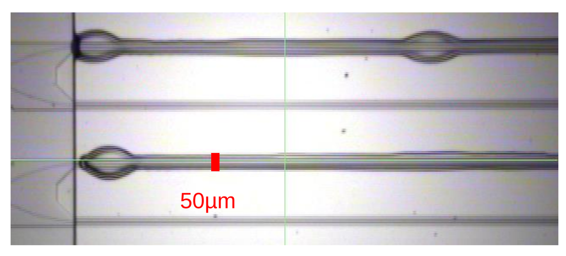
AND/OR

II. Printing of hydrogel *with/without* additional PEI-B
+ Irradiation with UV-light (1J/cm²)

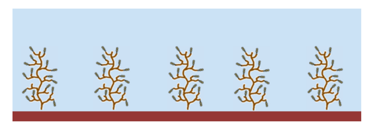
Combinations of both printing processes

Piezoelectric Dimatix material printer

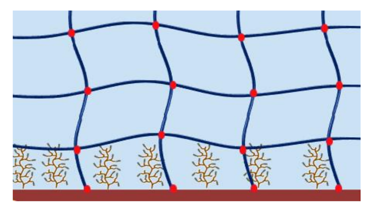




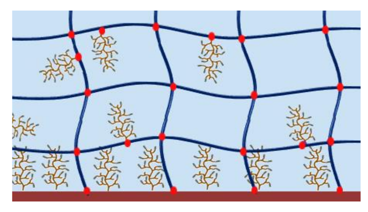
A: PEI-B surface



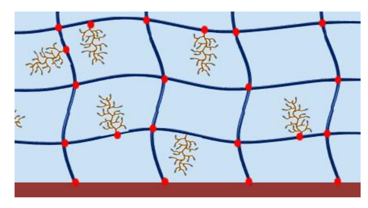
A1: Hydrogel on PEI-B surface



A2: PEI-B hydrogel on PEI-B surface



B2: Hydrogel on TRIS blocked surface

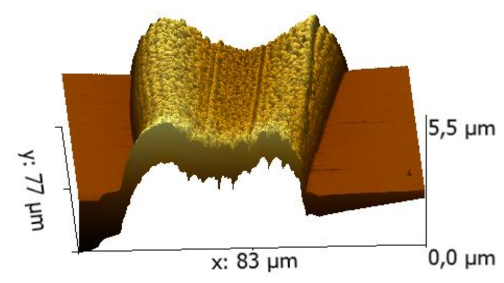


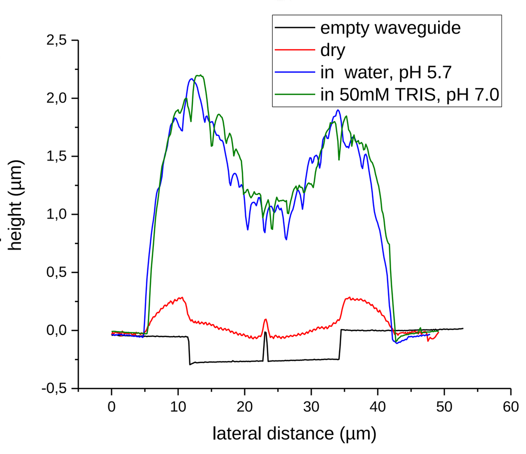
Results

Hydrogel modification

1) AFM-study towards swelling

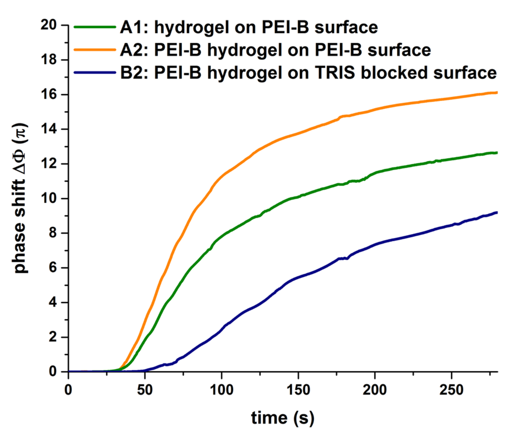
Hydrogels show a substantial uptake of water upon immersion in aqueous solutions, resulting in extensive swelling. The swelling behaviour of printed hydrogel films was investigated with AFM-measurements conducted in different buffers and air on two equally printed hydrogels layers. A swelling ratio of 7.5±1.5 and a thickness of 1000±300nm of the swollen film above the waveguide was determined.





2) Streptavidin binding on MZI

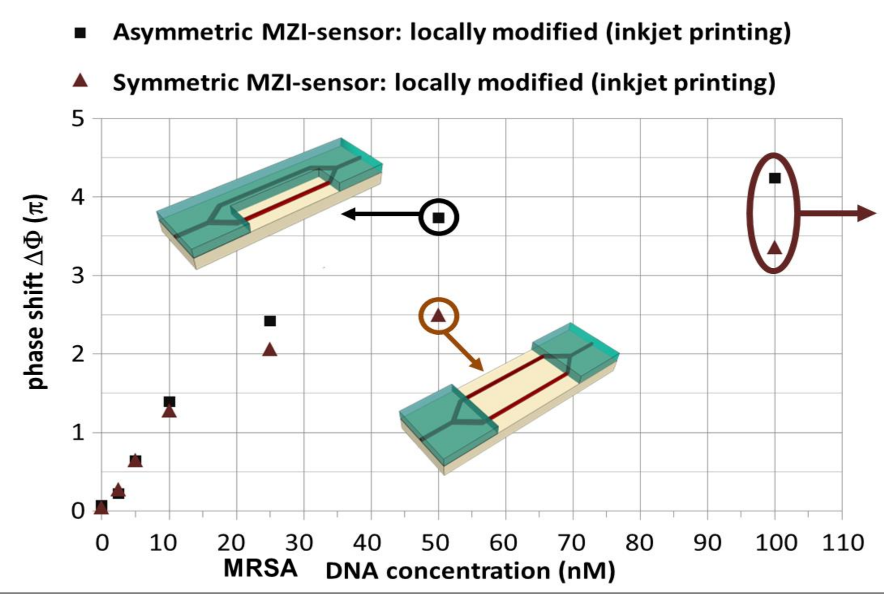
MZI-sensors were modified with the three different hydrogel-containing surfaces (A1, A2 and B2) and streptavidin binding measurements were performed. For the surface A1 and B2, signals of 14.5±1.2π (n=4) and 12.6±1.5π (n=4), respectively, were measured, proving the ability of streptavidin i) to diffuse through the hydrogel and ii) to bind to biotin within the hydrogel-matrix. Surface A2 - containing both surface bound and hydrogel bound PEI-B - lead to an increased response of 18.5±1.2π (n=4).

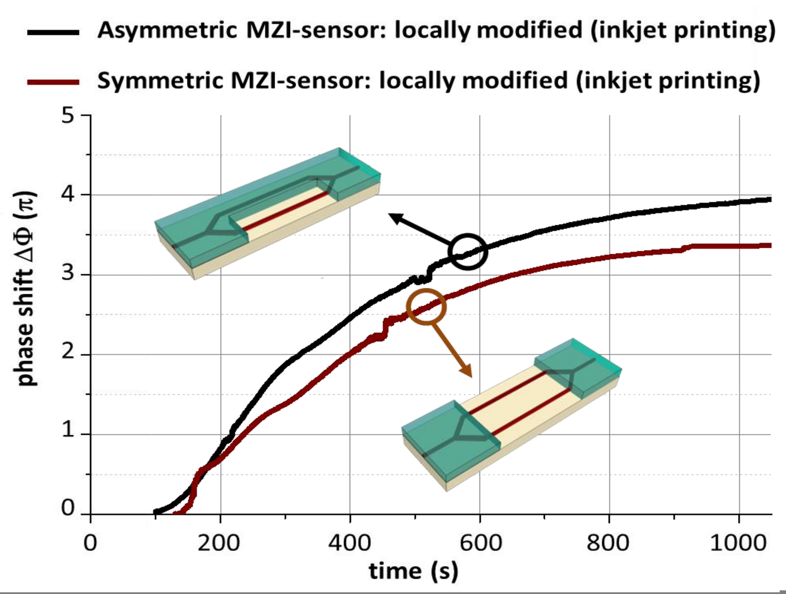


PEI-B surface: MRSA DNA measurements on MZI

Employing the strong biotin/streptavidin affinity, streptavidin was immobilized on the PEI-B modified sensor surface followed by attachment of biotinylated DNA single strands complementary to methicillin-resistant staphylococcus aureus (MSRA) specific DNA (150bp). A limit of detection (LOD**) of 1.60nM could be obtained for asymmetric sensors. Since inkjet printing allows to locally modify the sensing arm, the same measurement procedure was applied to symmetric sensors. A LOD of 0.44nM could be achieved for this MZI sensor-type. The improved LOD for the symmetric MZIs can be attributed to increased signal stability during the control measurement.

** LOD=$y_{\Delta\phi}$+3*σ; $y_{\Delta\phi}$ is the average value and σ the standard deviation of the control measurement - 0nM MRSA, 100nM non-complementary *vancomycin-resistant s. aureus* DNA sequence, 150bp.





References

[1] K. Tiefenthaler, W. Lukosz, J. Opt. Soc. Am. B 6:209–220 (1989).
[2] E. Melnik, P. Muellner, O. Bethge, E. Bertagnolli, R. Hainberger, M. Laemmerhofer, Chem. Commun. 50:2424 (2014).
[3] A. Brunsen, U. Ritz, A. Mateescu, I. Hoefer, P. Frank, B. Menges, A. Hofmann, P.M. Rommens, W. Knoll, U. Jonas, J. Mater. Chem. 22 (2012) 19590.

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