Sensing performance of a Mach-Zehnder interferometer with coherent phase readout in Al_2O_3

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Aluminium oxide (Al_2O_3) has emerged as a promising candidate material for sensing applications due to its low optical propagation loss over a broad wavelength range (UV-to-IR). These low propagation losses open up the possibility of using this material for different purposes, including integrated photonic sensors. One specific application for integrated photonic sensors is implantable sensors to, for example, continuously and non-invasively measure the physiological parameters of animals. For this purpose, an Al_2O_3 asymmetric Mach-Zehnder interferometer (aMZI) is developed. These developments include the surface functionalization of the Al_2O_3 waveguides.

To achieve higher sensitivity and a lower detection limit than conventional interferometric sensors, we implement a coherent phase readout detection scheme. In order to facilitate this, we adapt the aMZI design to incorporate a two-by-three 120° MMI downconverter, a crucial component for the readout scheme. The bulk refractive index limit of detection (LOD) of this device is measured to be 9×10^{-6} RIU by flowing solutions with different sodium chloride concentrations over the chip surface, and its sensitivity is 8.3×10^{4} rad RIU^{-1}. Furthermore, a functionalized sensor is used to measure concentrations of Interleukin-6 (IL-6). This work presents the experimental results and consequent data analysis that is required to fully utilize the coherent phase readout detection scheme.

Introduction

In this study, an asymmetric Mach-Zehnder interferometer (aMZI) with a 120º downconverter has been developed for sensing applications. An aMZI is chosen because it can operate at a single wavelength, eliminating the need for a tunable laser source which is required when working with resonator-based sensors. The ability to work with fixed wavelength sources simplifies future developments in integrating the photonic integrated circuit, source and detector into one module that could be used for *in vivo* sensing applications, i.e. monitoring physiological parameters in fish.

A traditional aMZI uses a single-output Y junction or 2-output couplers. The output intensities are a sinusoidal function of the phase change, resulting in zero sensitivity at the peaks and valleys. This study utilizes a 120º MMI downconverter with three outputs with a 120º phase difference. As a result, the need to tune the wavelength of the laser is eliminated and lower detection limits can be achieved [1].

The waveguides that constitute the photonic integrated circuits are designed in a way that ensures single mode propagation, while optimizing sensitivity of the sensor. The sensitivity is optimized by choosing waveguide dimensions that will ensure a large overlap of the optical mode with the region where the polymer brushes, onto which antibodies are immobilized to capture the antigen, will be located [1]. This approach resulted in a waveguide with a height of 450 nm and width of 800 nm in the case of an operating wavelength around 1040 nm.

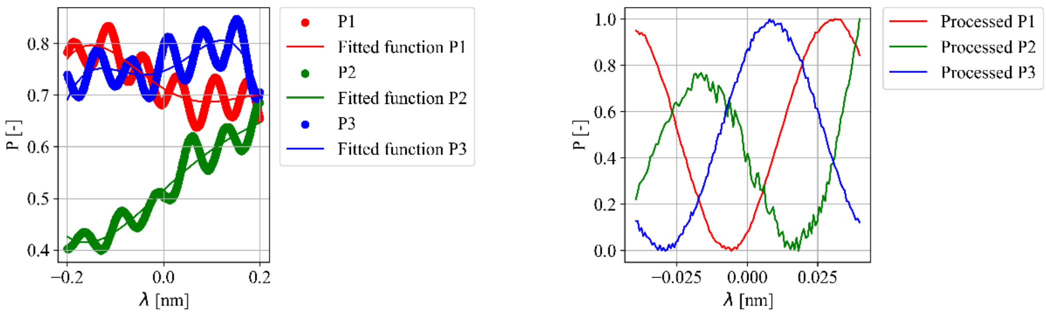
To evaluate the performance of the sensor, two sets of experiments were conducted. First, the sensitivity to bulk refractive index changes was assessed by flowing solutions of various sodium chloride (NaCl) concentrations over the surface of the chip. In the second experiment, the surface was functionalized with polymer brushes and IL-6 antibodies. The NaCl solutions were replaced with PBS in which varying concentrations of IL-6 antigens were dissolved. These tests aimed to demonstrate the sensitivity to bulk refractive index changes and specific biomolecular interactions.

Sodium chloride Concentration Experiment

Table 1) Concentrations of NaCl in DI water used during the experiment at different time intervals.

Time (min)	Reference flow	75	165	255	345	435	525	615	705	795
Concentration (g L^{-1})	0.3	0.5	0.7	1	1.5	2.3	3.5	5.2	7.8	12

To evaluate the aMZI, various concentrations of NaCl in demineralized (DI) water, as shown in Table 1, were introduced to the sensor. The refractive indices of these solutions were estimated from the observations reported by Xingcan Li et al. [2]. Initially, a reference solution was flowed for 75 minutes at a flow rate of 30 μL min^{-1}, followed by alternating 50-minute intervals with the NaCl solutions and 40-minute intervals with the reference solution. Spectral measurements were continuously obtained over a wavelength range of 1020 nm to 1070 nm using a TOPTICA CTL 1050 laser, operating at a scanning speed of 2 nm s^{-1}. Wavelength scanning was still required due to drift at the fiber alignment stages, which could not be monitored at a single wavelength.

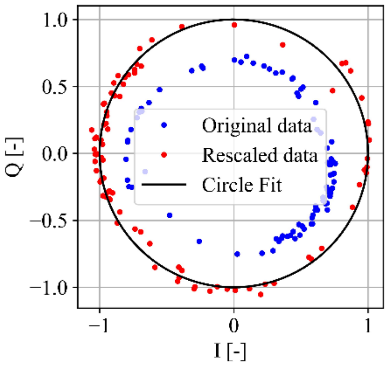


(a) *(b)*

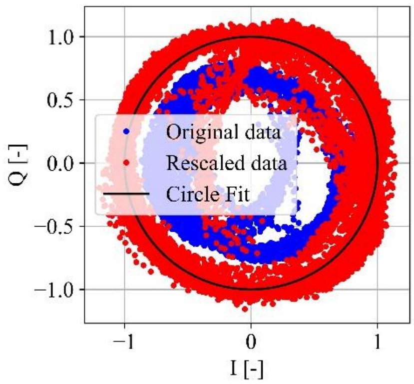
Figure 1) (a) Zoomed-in 0.4 nm window of the measured powers at the output of the 120-degree down converter, with a 4^{th}-order polynomial fit. (b) Normalized spectrum within an 80 pm window.

Figure 1a presents an example of the measured spectrum, zoomed into a 0.4 nm window. To correct for the Fabry-Pérot resonances, a 4^{th}-order polynomial fit was applied and subtracted from the measured data. Subsequently, the data were further refined by focusing on an 80 pm window around the wavelength of interest, after which normalization was performed again and the result is shown in Figure 1b. A clear 120° phase difference between the measured powers was observed. The normalized data were then transformed into in-phase (I) and quadrature (Q) components, as described by Equations 1 and 2, to extract the phase information from the signal [3]. The transformation, shown in Figure 2, was fitted to an ellipsoid and projected onto the unit circle, enabling the calculation of relative phase shifts. These shifts were referenced against the average phase shift calculated between minutes 10 and 70. This analysis was carried out over a wavelength range of 1025 nm to 1065 nm in steps of 1 pm.

$$I = P_2 - 0.5P_1 - 0.5P_3 \quad (1) \qquad Q = 0.5\sqrt{3}\,(P_1 - P_3) \quad (2)$$



(a)



(b)

Figure 2) Measured in-phase (I) and quadrature (Q) components, transformed and remapped to the unit circle with corrected data, for both (a) one single wavelength sweep and (b) a series of wavelength sweeps.

Due to the movement of the fiber alignment stages, the phase shift as a function of time revealed a linear drift in the measurements. This drift was corrected by applying a linear fit to the reference flow before and after the measurement and subtracting it from the results. Data within two minutes before and ten minutes after each flow transition were excluded to minimize transient effects. The remaining data from each flow were randomly divided into five subsets, and the average phase shift for each subset was calculated. A simple linear regression model was employed, the phase shifts were adjusted by multiples of 2π to enhance accuracy. The results are shown in Figure 3, from which the sensitivity of the system was determined to be 5.8×10^{5} rad RIU^{-1}. The corresponding detection limit (DL) was estimated to be 4×10^{-5} RIU [3].

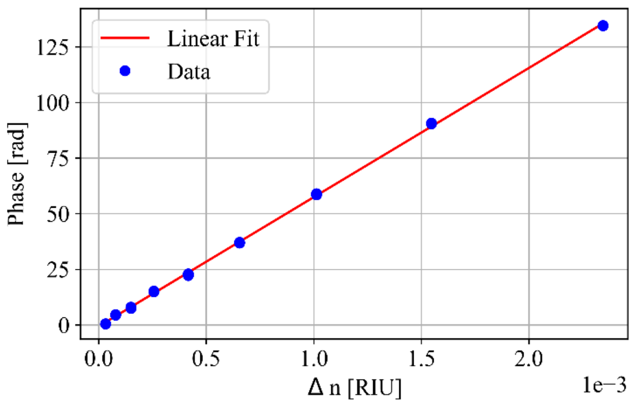


Figure 3) Measured phase shifts of the various NaCl solutions as a function of refractive index changes.

IL-6 Antigen Detection

To further test the MZI's capabilities, IL-6 antigen detection experiments were conducted. On the surface a functionalized antifouling coating was applied, utilizing a slightly modified version of the protocol from Kuzmyn et al. [4]. Instead of APTES, 12-aminododecylphosphonic acid was applied to the surface, following the protocol outlined by Roeven et al.[5]. For the polymer brushes, only CBMA monomers were used, which were subsequently functionalized with IL-6 antibodies (Biolegend 501101, 21 kDa). Additionally, the fiber alignment stages were replaced to reduce the power coupling drift from the system, thereby improving the sensor performance. Different concentrations of IL-6 antigen (Biolegend 570802) in PBS were flowed over the chip at 50 µL min^{-1} for 30-minute intervals, with PBS buffer washes between each flow.

Figure 3 shows the phase measurements over time. At several concentrations, a dip in the phase is observed after ~25 minutes. Shortly after the PBS flow is reinstated, the phase returned to previous measured values. Although some jumps and a small drift were present during the measurement, the new fiber alignment stages appear to have reduced these fluctuations. Despite the potentially short flow time and the remaining noise, these results suggest that IL-6 concentrations below 0.8 ng mL^{-1} can be detected.

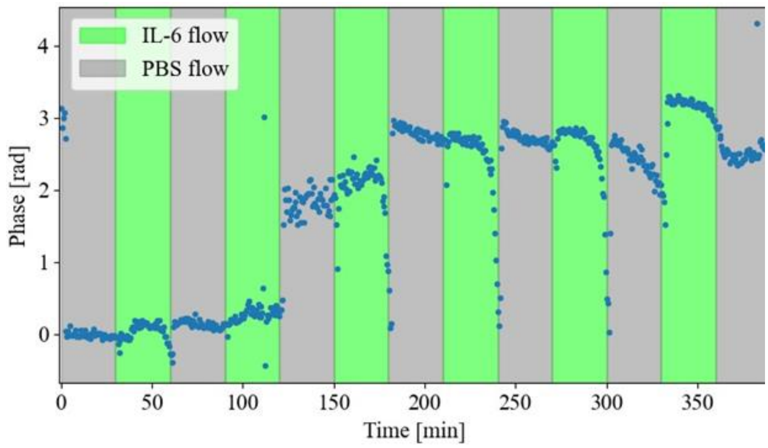


Figure 3) Phase shift over time during the IL-6 antigen experiments, showing the response to various concentrations of the IL-6 antigen.

Table 2 IL-6 concentrations used during the experiment.

Time (min)	**Concentration (ng mL^{-1})**
30	0.8
90	3.1
150	13
210	50
270	200
330	800

Conclusion

This study demonstrated the suitability of the Mach-Zehnder interferometer with coherent phase read out for precise sensing applications, including concentrations of NaCl and IL-6 antigen detection. The MZI provided excellent sensitivity and low detection limits. The system successfully detected phase shifts corresponding to different concentrations of NaCl, with a sensitivity of 5.8×10^5 rad RIU^{-1} and an estimated detection limit of be 4×10^{-5} RIU. Follow up experiments with IL-6 antigens suggested the ability to detect concentrations below 0.8 ng mL^{-1}, which is equal to 40 pM. However, additional experiments with extended flow durations are necessary to quantify the system’s capability for accurate IL-6 antigen detection.

References

[1] B. Kok *et al.*, “Numerical comparison of sensing performance of a microring resonator and Mach-Zehnder interferometer in Al2O3,” 2023.

[2] X. Li, L. Liu, J. Zhao, and J. Tan, “Optical properties of sodium chloride solution within the spectral range from 300 to 2500 nm at room temperature,” *Appl Spectrosc*, vol. 69, no. 5, pp. 635–640, May 2015, doi: 10.1366/14-07769R/ASSET/IMAGES/LARGE/10.1366_14-07769R-FIG11.JPEG.

[3] J. Leuermann *et al.*, “Optimizing the Limit of Detection of Waveguide-Based Interferometric Biosensor Devices,” *Sensors*, vol. 19, no. 17, 2019, doi: 10.3390/s19173671.

[4] A. R. Kuzmyn, L. W. Teunissen, P. Fritz, B. van Lagen, M. M. J. Smulders, and H. Zuilhof, “Diblock and Random Antifouling Bioactive Polymer Brushes on Gold Surfaces by Visible-Light-Induced Polymerization (SI-PET-RAFT) in Water,” *Adv Mater Interfaces*, vol. 9, no. 3, p. 2101784, 2022, doi: https://doi.org/10.1002/admi.202101784.

[5] E. Roeven, “Does it stick?: Macromolecular building blocks for antifouling coatings,” Wageningen University, Netherlands, 2021. doi: 10.18174/551763.