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Fix-Wavelength Multi-Analyte Detection with Serial SOI Ring Resonators †

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Abstract: We present a method for the read-out of five serially arranged SOI ring resonator-based biosensors at a speed of 3 Hz/sensor and a fixed wavelength of 1550 nm. The system uses the high thermo-optical coefficient of silicon by applying AC voltages to periodically heat up electrodes adjacent to each sensor. A time-division multiplex scheme allows the allocation of the measured optical output from the mutual spectrum to each specific resonator. We demonstrate our system by immobilizing two different antibodies (biotin and a hexa-His-peptide) at the surface of selected resonators and successfully showing the selective binding characteristics of analyte probing in a microfluidics supported experiments.

Keywords: biosensors; ring resonators; silicon-on-insulator; thermo-optical tuning; sensor multiplexing; microfluidics

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1. Introduction

When it comes to biosensing, optical microcavities such as rings, disks and spheres are a popular solution for the detection of antibody–antigen binding events [1]. Particularly, silicon-on-insulator (SOI) sensor platforms are highly promising due to their strong light confinement, which enables small sensor footprints, and their large sensitivity to refractive index changes [2,3]. Usually, the sensor read-out is performed by optical coupling to a tunable laser source that performs wavelength sweeps and a photodiode. Unfortunately, the speed of these measurements is highly restricted by the lasers sweep repetition rate, which usually lies in the range of seconds. Many different applications for massive parallel detection were demonstrated within the last years [4,5], but they still require expensive components such as lock-in amplifiers or tunable laser sources. The method presented here demonstrates the read-out of serially arranged SOI ring resonators at a speed of 3 Hz/sensor and a fixed wavelength of 1550 nm by exploiting the high thermo-optical coefficient of silicon and at low cost. AC voltages are applied to electrodes adjacent to each sensor in a time-division multiplex scheme which enables quasi-simultaneous read-out of the sensor-array while allowing the attribution of the measured optical output from the mutual spectrum to each specific resonator. The system is capable of a modulation frequency of 100 Hz/sensor and a variety of signal shapes. We demonstrate our system by immobilizing one of two different antibodies (biotin and a hexa-His-peptide complex) at the surface of selected resonators and successfully showing the selective binding characteristics of analyte probing in microfluidic experiments. The fast sampling of each resonator can be realized with cost-effective equipment and allows deeper insights into antibody–antigen binding kinetics.

2. Materials and Methods

2.1. SOI Sensor Platform

The sensor test platform consisted of an array of five racetrack resonators, all coupled to one common bus waveguide (add-drop-configuration) and equipped with a buried heating electrode. The structure was cladded by a top layer of SiO_2, which was partly opened on four resonators to enable evanescent field sensing on the resonators waveguide surfaces, while one ring was completely covered and acted as a reference ring tracking the temperature change. The resonators were formed by rib waveguides with a 220 nm × 450 nm cross section and a 70 nm slab. The circumference was 641 µm, resulting in a Free Spectral Range (FSR) of 1 nm at the operating wavelength. Optical in- and outcoupling was enabled by grating couplers supporting the fundamental TE mode. The sensitivity was ascertained to be 10 nm/RIU.

2.2. Sensor Surface Functionalization

All sensor chips were cleaned in isopropanol, acetone and DI water. Silanization was performed with 3-Aminopropyltriethoxysilane (APTES) in toluene for 1 h (2% v/v), followed by intense toluene rinsing, 10 min ultrasonic bath in toluene and thermal curing at 100 °C on a heating plate for 1 h.

Surface functionalization was realized following the scheme depicted in Figure 1; the first ring resonator R1 is the reference ring mentioned above. Ring resonators R2 and R3 were used for NHS-biotin immobilization (3 mg/mL DI-water for 1h), while R4 and R5 were dedicated for ac-hexa-His immobilization (ac-HHHHH-H with (3-dimethylaminopropyl) carbodiimid (EDC) and O-succinimide (OSu), for 3 × 15 min). The chips were intensely rinsed with DI water and dried under nitrogen flow. Figure 1 illustrates the selective surface functionalization of the sensor array.

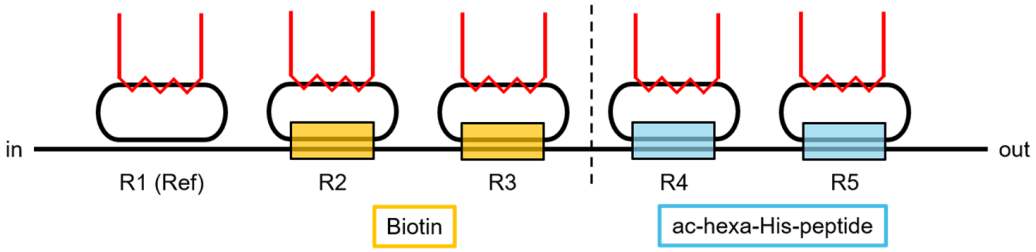

Figure 1. Functionalization scheme of the ring resonator arrays in use.

2.3. Measurement Setup

In our measurements, we used AC voltages applied to heating electrodes buried in the oxide on top of the ring resonators waveguide. The resulting temperature causes the effective refractive index n_{eff} of the sensor to change. Therefore, the wavelength coupled into the sensor structure could be kept fixed, and the resonance wavelength λ_{res} could be changed by thermo-optical modulation only, considering a resonance refractive index regime, n_{res}. This connection is described in Equation (1):

$$\lambda_{res} = \frac{n_{eff} \cdot L}{m} \leftrightarrow n_{res} = \frac{\breve{}_0 \cdot m}{L}, m \in N \quad (1)$$

where L is the ring resonator circumference and λ_0 is the fixed wavelength of operation. Modulation signals were generated by an Arduino Duo microcontroller board, which was controlled via PC. Its periodic output voltage was chosen to have a square root time dependence to induce a linear power increase at the heating electrodes. The frequency of the signal was divided into five channels by a demultiplexer and amplified, providing a modulation speed of 3 Hz/sensor. The amplitude was chosen to be 4 V, which enables good sensor modulation. The signal of channel 1 was tracked along with the allover

output power, thus the fix switching scheme of the sensor modulation by the time-division-multiplex (TDM) allowed an assignment of the responses of the individual sensors within the common output spectrum. More information can be found in [6]. The laser used for this experiment is an Agilent 81960A and was operated at 1500 nm. The optical power meter measuring the optical output power was an Agilent 81636B. A Zurich Instruments MFLI was used for data acquisition at 107 kSa/s. The setup is depicted in Figure 2.

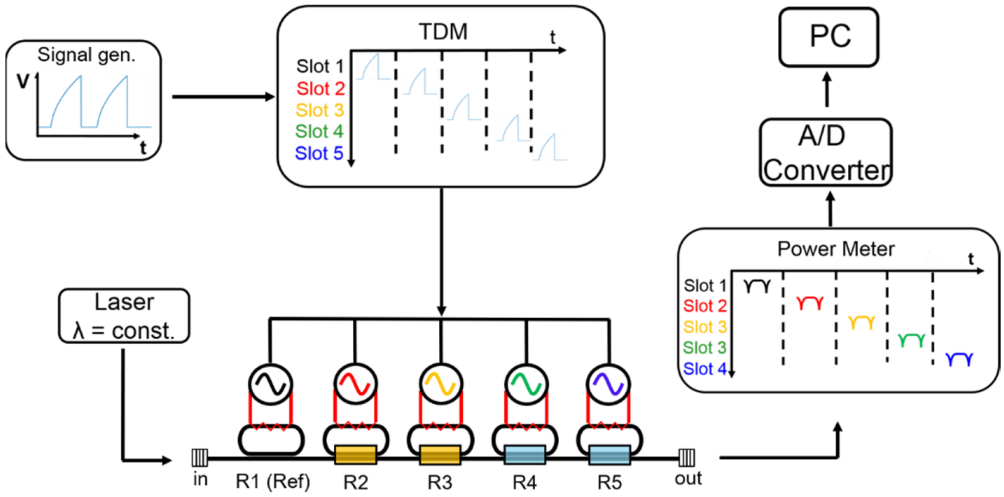

Figure 2. Electro-optical setup used for sensor modulation and read-out.

2.4. Experimental Procedure

For the experiments, the antigens streptavidin (0.1 mg/mL phosphate-buffered saline (PBS)) was prepared and brought into contact with the chip assisted by a LabSmith microfluidic system operated at a flow rate of 100 µL/min and a 3D-printed flow cell made of polylactic acid (PLA) mounted on top of the chip. The experiment was initiated by a PBS step, flushing the chip for 2 min before it was replaced by streptavidin for 2 min. During the experiment, the chip was mounted on top of a temperature-controlled stage. All experiments were conducted at 25 °C room temperature.

3. Results

Two ring resonators (R2 and R3) were functionalized with biotin in order to accept streptavidin binding, and two ring resonators (R4 and R5) with ac-hexa-His functionalization. Within the experiment, the sensor array was brought into contact with the antigen and the sensor response was tracked via thermo-optical modulation in a demultiplex scheme over time. The results were smoothed with a 10-point moving average filter and are shown in Figure 3.

Both ring resonators (R2 and R3) with immobilized biotin responded to their antagonist antigen streptavidin, while the hexa-His-functionalized resonators (R4 and R5) stayed, aside from smaller fluctuations, mostly unaffected. A slight temperature drift during the experiment was visible from R1.

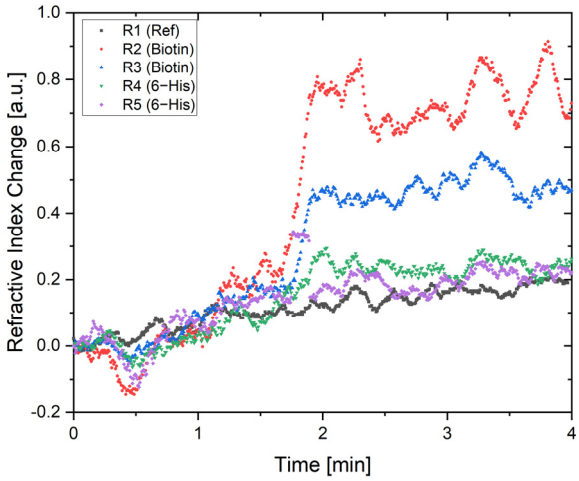

Figure 3. Resonance positions for all five ring resonators are displayed over time for the experimental condition of streptavidin detection.

4. Discussion

The fixed-wavelength sensor using five ring resonators as sensing elements was successfully applied to multiparameter experiments without labeling. Several parameters can lead to deviations within the actual experiment. Due to pressure fluctuations within the µ-fluidic system, a relatively high noise level, as visible in Figure 3, limits the analysis of the binding kinetics. The antibody cross reactivity is low, offering the potential to analyze a diverse array of biomolecules in a single assay. Sensitivity differences in sensor responses might be caused by variations in concentration of immobilized antibodies, or they may be due to flow velocity variations over the array surface. Furthermore, the thermal flux on the chip surface due to thermo-optical modulation must be considered, especially when organic material is tested. Modulation amplitudes are therefore to be kept low to avoid unintended kinetic influences or protein degeneration.

5. Conclusions

In this paper we present an effective way of fixed-wavelength low-cost analyte detection with multiple serial SOI ring resonators for biosensor applications. Using an Arduino Due for function generation and a time-division multiplex for thermo-optical modulation enables an easy and effective way for reducing experimental setups in size and complexity.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/I3S2021Dresden-10108/s1.

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Conflicts of Interest: The authors declare no conflict of interest.

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