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Label-free biosensing using cascaded double-microring resonators integrated with microfluidic channels

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ABSTRACT

Fast and accurate quantitative measurement of biologically relevant molecules has been demonstrated for medical diagnostics and drug applications in photonic integrated circuits. Herein, we reported a highly-sensitive optical biosensor based on cascaded double-microring resonators. The sensor was integrated with microfluidic channels and investigated with its label-free detection capability. With a wavelength resolution of 0.47 nm, the measured binding capacity of the antibody on the surface exhibits reliable detection limit down to 7.10 μg/mL using human immunoglobulin G (hIgG).

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1. Introduction

Integrated optical waveguide biosensors offer the promise of fast and accurate solutions for detection and analysis in biomedical diagnostics, environment monitoring and food safety applications. Great attention has been attracted owing to their superior advantages such as immune to electromagnetic interference, label free detection and integration of multifunctional devices on one chip [1,2]. Recently, special interest was focused on silicon-on-insulator (SOI) sensor based on evanescent field. With its natural benefit of high sensitivity, ultra-compactness and manufacture compatibility with the standard complementary metal–oxide–semiconductor (CMOS) process [3,4], advanced SOI sensors were able to be fabricated with low cost and mature industrial infrastructure [5]. Under this category, many relevant results have been reported, including surface plasmon resonance(SPR) [6], photonic crystals [7], Mach–Zehnder interferometer [8], micro-disk [9] and microring resonator [10].

Among various types of optical sensors, microring resonators have been regarded as a promising solution for biomolecular recognition and chemical analysis [11,12]. The sensing light is coupled into the resonators under resonant condition and confined near the waveguide surface of the resonators with an evanescent field exponentially decaying into the surrounding medium. The propagation of light in the resonator is thus influenced by the refractive index (RI) of the reagent contact to the waveguide surface. Compared with Mach–Zehnder interferometer, the degree of interaction of light in microring resonators is determined by the amount of rotations of light, and not restricted by the physical length [13]. The high-Q microring resonator can thus provide a higher sensitivity due to the sharper resonance peak. However, the interrogation of high-Q optical microring resonator requires a narrow line width tunable laser or a high-resolution optical spectrum analyzer. These equipments are very expensive and cannot be integrated into one chip. To address these problems, our group has previously proposed and demonstrated a highly sensitive optical sensor based on cascaded double-microring resonators with Vernier effect [14–17]. The method was then adopted by several other research groups and respectable results have been achieved [18–20]. We have previously reported a double-microring resonator based sensor exhibiting sensitivity up to 24,300 nm per refractive index unit (RIU) using different concentration solutions of NaCl [17], far surpassing the sensitivity of 135 nm/RIU for a SOI single ring resonator [21] and 12.7 nm/RIU for the polymer dual ring resonators [22]. To detect streptavidin, the cascaded double-microring resonators were further made biotin film immobilized on the surface [23]. However, this type of sensor cannot be applied for kinetic measurement of molecular interaction as it is not integrated with microfluidic channels.

In this paper, we further demonstrate the label-free detection of cascaded double-ring sensor in biosensing by measuring the refraction index change induced by the biorecognition molecular interaction. The sensor was fabricated by conventional photolithography and integrated with microfluidic channels to detect the concentration of human immunoglobulin G (IgG). By using the standard silicon surface functionalization procedure, the anti-human IgG is immobilized on the surface of the sensing area in the

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optical waveguide sensor. The measuring results demonstrate this cascaded double-microring resonator to be a promising real time sensor of measuring the molecules binding kinetics for biomedical and chemical applications.

2. Device fabrication

The sensor includes two layers: the integrated optical waveguide structure layer and the microfluidic system layer. The optical waveguide structure based on SOI substrate with a 220 nm-thick top silicon layer and 2 μm-thick buried oxide layer is composed of an input waveguide, a reference ring and a sensing ring cascaded by a common bus waveguide, and an output waveguide, as shown in Fig. 1(a). The optical waveguide wafer is covered by SU-8 upper cladding layer, while the sensing ring is exposed to the analyzed sample in the sensing window. The diameters of the reference and sensing ring of the sensor are 230 μm and 252.2 μm, respectively and directional couplers of 50 μm length with a gap of 1 μm are employed in all the ring resonators. All the ridge waveguides are designed with 30 nm shallow etched depth and 1 μm width enabling traditional contact photolithography patterning with single mode operation.

The fabrication started by spin-coating a thin film of photoresist on the SOI wafer. After conventional photolithography, the pattern of the photoresist was transferred to the SOI wafer by inductively coupled plasma reactive ion etching. The wafer was then spin coated with SU-8 as the upper cladding of the optical waveguide, and sensing window was opened by photolithography. Improved performance could be further realized with smaller patterns by employing a stepper or electronic beam lithography. More details of the operational principle and fabrication process of cascaded double-rings sensor were described in the reference [24].

The microfluidic channels are fabricated with polydimethylsiloxane (PDMS) [13]. The PDMS (Sylgard 184, Dow-Corning, USA) is degassed to remove air bubbles using vacuum pump. Then the PDMS is casted on the master to a thickness of 2 mm, and cured at 85 °C for 30 min in an oven. The fluidic structure is then peeled off from the master and cut out, and holes are punched for liquid input and output ports. The optical sensor is integrated into a chip by bonding with the microfluidic channels using epoxy glue, as shown in Fig. 1(b). The microfluidic system can control and manipulate small volumes of liquid samples or reagents required for testing and analysis quickly and reliably.

3. Measurement setup

The sensor was tested under the end-fire system. As shown in Fig. 2, the measurement setup mainly includes two parts: the controllers of liquids and the controllers of optics. Liquid flow is

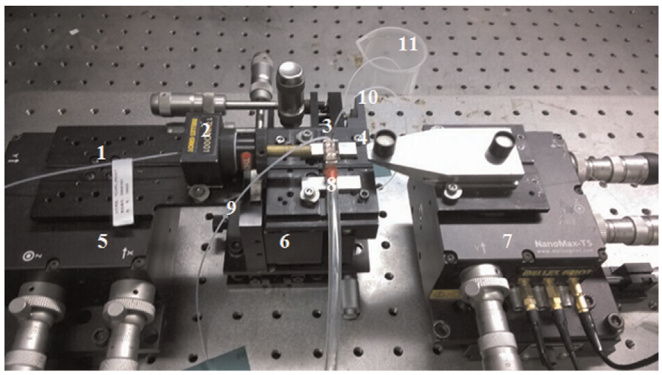

Fig. 2. The end-fire system. Liquid flow is maintained by syringe pumps. Laser wavelength tuning and signal read out are automated by computer control. (1) Input fiber; (2) fiber polarization controller; (3) sensor; (4) output fiber; (5, 6, 7) three-dimensional nanopositioning stages; (8) pipe for vacuum pump; (9) pipe for sample input; (10) pipe for sample output; and (11) waste reservoir.

controlled by syringe pumps (MICROINFUSION PUMP WZS-50F6), which supply a continuous flow of buffer or samples through the microfluidic channels passing by the sensing window and then to the waste solution bottle. The transverse electric (TE) mode light from the tunable light source (Agilent 81600B) is coupled into input waveguide of the sensor by the polarization maintaining lensed fibers. The output light is collected by the power meter (Agilent 81635A). For the optical measurement system, three three-dimensional nanopositioning stages (Thorlabs MAX312) are employed to accurately place the optical input fiber, output fiber and the chip. In addition, an infrared camera is used to assist the fiber alignment with the input waveguide. A fiber polarization controller is applied to adjust the TE polarization with a polarization filter. The whole measurement setup is automated by the computer.

4. Experimental results and discussions

4.1. Volume sensing

Volume sensing experiment is performed to prove the cascaded double-microring resonators sensing ability and eliminate the influence of background refractive index, where non-functionalized sensor was used. The optical sensitivity of the sensor was calibrated by using aqueous solutions of NaCl with different concentrations (0%, 2%, 4%, 6%, 8%). As shown in Fig. 3, the measured refractive index sensitivity is 1804 nm/RIU. Different solutions of proteins were prepared by serial dilutions in 10 mM PBS and injected to the microfluidic channel. The transmission spectrum and real time resonance wavelength of the cascaded double-microring resonators are shown in Fig. 4(a) and (b), respectively. From Fig. 4

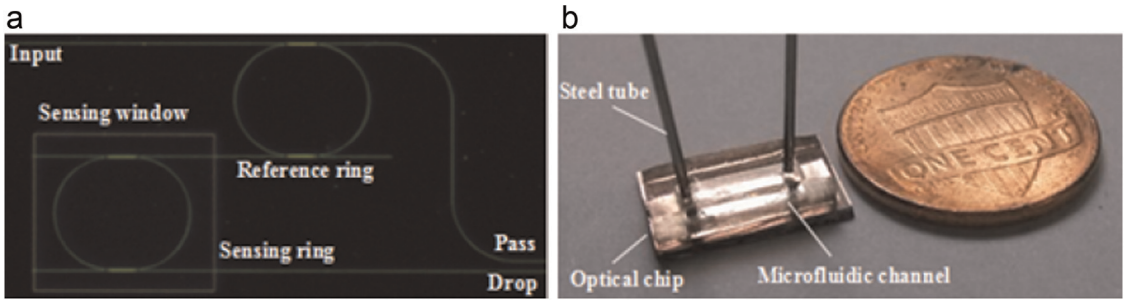

Fig. 1. (a) Optical microscope image of the cascaded double-microring. The reference ring and the waveguide are covered with an upper cladding layer SU-8 while the sensing ring is exposed to the air. (b) Photograph of one of the fabricated sensor. The steel tubes make fluidic flow to the microfluidic network below.

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