Optofluidic chip with directly printed polymer optical waveguide Mach-Zehnder interferometer sensors for label-free biodetection

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Abstract: Optofluidic devices hold great promise in biomedical diagnostics and testing because of their advantages of miniaturization, high sensitivity, high throughput, and high scalability. However, conventional silicon-based photonic chips suffer from complicated fabrication processes and less flexibility in functionalization, thus hindering their development of cost-effective biomedical diagnostic devices for daily tests and massive applications in responding to public health crises. In this paper, we present an optofluidic chip based on directly printed polymer optical waveguide Mach-Zehnder interferometer (MZI) sensors for label-free biomarker detection. With digital ultraviolet lithography technology, high-sensitivity asymmetric MZI microsensors based on a width-tailored optical waveguide are directly printed and vertically integrated with a microfluidic layer to make an optofluidic chip. Experimental results show that the sensitivity of the directly printed polymer optical waveguide MZI sensor is about 1695.95 nm/RIU. After being modified with capture molecules, i.e., goat anti-human immunoglobulin G (IgG), the polymer optical waveguide MZI sensors can on-chip detect human IgG at the concentration level of 1.78 pM. Such a polymer optical waveguide-based optofluidic chip has the advantages of miniaturization, cost-effectiveness, high sensitivity, and ease in functionalization and thus has great potential in the development of daily available point-of-care diagnostic and testing devices.

1. Introduction

Rapid and accurate detection of disease biomarkers at the point of care (POC) has become increasingly important for enhancing health care services and improving patient-centered outcomes [1–4]. It is particularly demanded to develop cost-effective biomedical diagnostic devices for daily testing and widespread applications in responding to public health crises. Currently the most common POC method is lateral flow immunoassay (LFIA) techniques because of their ease of use and short analysis time [5–8]. However, they can provide a qualitative result with limited sensitivity and specificity, compared to laboratory-based immunochemical methods. One of promising solutions to overcome these limitations is lab-on-a-chip (LoC) devices that integrate many kinds of microscale components to complete various processes on a chip scale. Particularly, integrated optofluidic chips that combines photonic microsensors with microfluidic components have been widely considered as the most promising solution for high-sensitivity biodetection because of the abundance of light-matter interactions as well as the high sensitivity and high signal-to-noise ratio of lightwave technology [9–12]. For instance,

Q. Liu *et al.* demonstrated a two-step sample-to-answer device with silicon Mach-Zehnder interferometer (MZI) sensors and a sample pretreatment module to detect malaria parasites [13]. X. Ouyang *et al.* developed an optofluidic chip with polymer whispering gallery mode (WGM) microlaser sensors for enzyme-linked immunosorbent assay (ELISA), which can detect vascular endothelial growth factor (VEGF) at the femtogram level [14].

Especially, optical waveguide-based photonic sensors hold great promises in the development of integrated optofluidic devices due to their well-known flexibility in on-chip integration [9,15]. They can guide light wave within a strip or rib with a very low propagation loss, and thus enable the creation of many kinds of micro-interferometers or micro-resonators to harness lightwave technology for high-sensitivity biosensing. Light wave is well confined within the guiding layer to make up interference or resonance with well-defined structures, meanwhile it may interact target molecules within surrounding medium via its evanescent field [16–18]. One of most widely used waveguide structures for bio-detection is MZI micro-sensors. Patricia. *et al.* proposed a MZI sensor based POC device for tuberculosis detection [19]. A photonic chip with six silicon nitride MZI sensors was fabricated and integrated with a disposable microfluidic cartridge for simultaneous detection of multiple disease biomarkers. It was demonstrated to detect tuberculosis in un-diluted urine at the concentration level of 475 pg/mL and its detection time is less than 15 mins. Densmore *et al.* demonstrated a silicon photonic MZI biosensor array for detection of two biomarkers at the same time [20]. Their results showed that the fabricated MZI sensor-based biochip could detect rabbit IgG and goat IgG simultaneously and the measured level of detection in terms of surface coverage is less than 0.3 pg/mm^2. Angelopoulou *et al.* developed an optofluidic chip combined with ten silicon MZI sensors and an advanced microfluidic module for simultaneous determination of four allergens, i.e., bovine milk protein, peanut protein, soy protein, and gliadin. It can complete analysis in 6.5 min, and its limits of detection for four allergens are 0.04 μg/mL, 1.0 μg/mL, 0.80 μg/mL and 0.10 μg/mL, respectively [21].

Polymer materials have advantages such as ease of manufacturing and modification as well as good biocompatibility, making them appealing for development of biomedical sensors and devices. For instance, Bruck *et al.* proposed a polymer MZI waveguide biochip, in which polyimide and Ormoclad were used to make core and cladding of polymer optical waveguide. Such a MZI waveguide sensor can measure streptavidin at the concentration of 0.1 μg/mL [22]. Paul *et al.* demonstrated a high-sensitivity SU-8 epoxy-based MZI biosensor, in which an extra ring resonator was introduced to enhance the sensitivity of the MZI optical biosensor via vernier effect. Such a sensor can achieve a sensitivity of above 17,000 nm/RIU in glucose solution measurement and its limit of detection is down to 1.1×10^{-6} RIU [23]. To fabricate high-quality optical waveguide sensors, one may use optical lithography [24], laser direct writing [25], or e-beam lithography technologies [26]. Although conventional optical lithography offers an efficient way to fabricate polymer optical waveguides, its process depends on a pre-prepared photomask and lacks grey-scale exposure ability. Laser direct writing and e-beam lithography technologies can overcome these technical bottlenecks to some extent but are commonly less efficient due to their inherent single-spot scanning nature.

In this paper, we present a polymer optical waveguide MZI sensor-integrated optofluidic biochip for label-free detection of disease biomarkers, which has become increasing important for the assessment of health, disease, or vaccination status in modern medical diagnostics, as shown in Fig. 1. With an own-developed digital ultraviolet lithography (DUL) technology [14, 27,28], an asymmetric MZI microsensor based on width-tailored optical waveguide is directly printed on a SiO$_2$/Si wafer for on-chip biosensing. A PDMS-based microfluidic layer is also fabricated by using DUL-based technology for packaging the optical waveguide chip to make an optofluidic chip. In the experiments, the fabricated optofluidic biochips showed a very high bulk sensitivity and can detect human immunoglobulin G (HIgG) at the concentration level of 1.78

pM. Moreover, it was demonstrated that the optofluidic chip can be repeatedly used multiple times and thus is promising to be developed towards reusable biodetection devices.
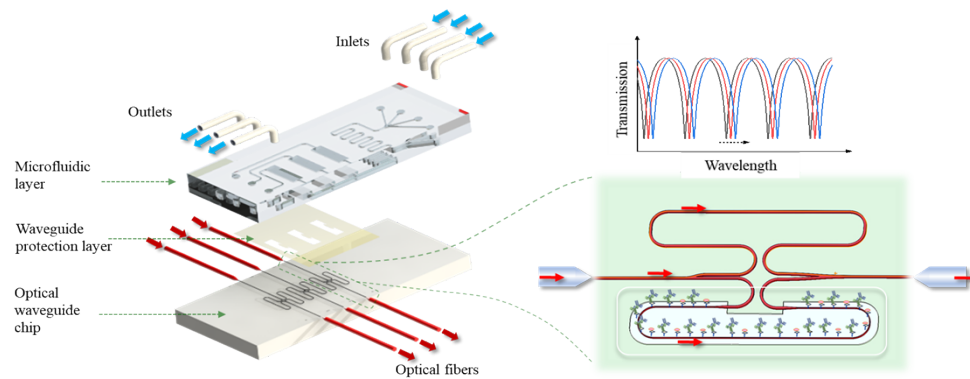

Fig. 1. Schematic of an optofluidic chip with multiple directly printed polymer optical waveguide MZ micro-interferometer sensors.

2. Methods and materials

2.1 Materials

SU-8 2050 and Omnicoat were purchased from Kayaku Advance Materials, Inc., USA. Ormoclad was molded from Micro Resist Technology GmbH, Germany. Ethanol, propylene glycol monomethyl ether acetate (PGMEA), (3-aminopropyl) triethoxysilane (APTES) and bovine serum albumin (BSA) were purchased from Sigma-Aldrich company, USA. Polydimethylsiloxane (PDMS) and its curing agent were obtained from Dow Corning, USA. Goat anti-human immunoglobulin G (IgG) and HIgG were purchased from Beijing Solarbio Science & Technology Co., Ltd., China.

2.2 Fabrication of SU-8 optical waveguide Mach-Zehnder interferometer sensors

The polymer optical waveguide sensors were fabricated by an own-developed DUL system, which was built with a high-power UV light-emitting diode (L10561-215, Hamamatsu Photonics, Japan), a high-speed digital micromirror device (DMD; DLP6500, Digital Light Innovations, USA), a nano-precision motorized stage (ANT130-XY, Aerotech Inc., USA) and a set of projection optics.

The designed waveguide was fabricated with a commercial SU-8 photoresist on a SiO₂/Si wafer. The fabrication process is shown in Fig. S2b (Supplement 1). To improve the adhesion between SU-8 and silicon wafer, an adhesion promoter called Omnicoat was applied before spin coating of SU-8. SU-8 was spun on the top of silicon wafer at the speed of 5000 rpm for 30 s. A soft bake was then conducted at 65 °C for 5 mins and 95 °C for 10 mins to evaporate solvent. After prebaking, a home-made DUL system was applied to DLI system project a grayscale pattern photoresist. The exposure process for a MZI pattern (22 mm × 4 mm) is about 20 minutes. A post bake was then carried out at 65 °C for 5 mins and dried out at 65 °C. The sample was 95 °C developed using PGMEA for 2 mins. Finally, a hard bake at 120 °C for 60 mins was applied to 120 °C for 60 mins. After both post-bake and hard-bake process for release the internal stress of SU-8 waveguide structure.

A cladding layer was fabricated by using another commercial photoresist Ormoclad. Plasma cleaning was conducted using PLUTO-T Plasma Cleaner (PLUTOVAC, Shanghai, China) with power of 200 W for 5 min. The air pressure and flow rate are 2.4 Pa and 100 mL/min, respectively. Then, Ormoclad is spun on the top of the fabricated SU-8 waveguide chip. The overlay exposure function of the DUL system was used to precisely expose the Ormoclad over optical waveguide to form a cladding layer, while leaving a window upon sensing arm for optofluidic biosensing. A transition zone with the width of ~ 90 μm were adopted during

function of the DUL system was used to precisely expose the Ormoclad over optical waveguide to form a cladding layer, while leaving a window upon sensing arm for optofluidic biosensing. A transition zone with the width of ~ 90 μm were adopted during exposure of each sub-pattern to alleviate the shrinkage problem of Ormoclad during exposure. After a post-bake at 130 °C for 15 min, the sample was developed by using methyl isobutyl ketone (MIBK). Finally, the optical waveguide chip was hard baked at 150 °C for 3 h.

2.3. Fabrication of the optofluidic chip by packaging the waveguide chip with a microfluidic layer

The microfluidic layer was fabricated by using a casting method. The mold of microchannels was also prepared with SU-8. Poly(dimethylsiloxane) (PDMS) monomer was mixed with a cross-linking agent in 10:1 ratio and then degassed for 30 min. Then, PDMS was poured upon the SU-8 mold and baked at 70 °C for 2 h to achieve completely cross-linking. Finally, the cured PDMS was peeled off from the SU-8 mould.

Both the PDMS layer and waveguide chip were first treated with plasma at the power of 200 W for 30 s. To prevent potential leakage between Ormoclad and substrate, some liquid PDMS was smeared around the edge of Ormoclad layer. The PDMS layer was then attached upon the waveguide chip with the help of a home-made alignment apparatus. Pressed with a clamp, the optofluidic chip was then baked in an oven at 70 °C for 3 h to enhance the bonding between the waveguide chip and PDMS microfluidic channel layer.

2.4. Measurement of the transmission spectra of optical waveguide MZI sensors

The spectral responses of the fabricated polymer optical waveguide chip were measured by using an end-fire coupling setup. Light was launched from an ASE light source (at C band, i.e., 1530 ~1560 nm) into the optical waveguide chip by using a lensed single-mode optical fibre (SMF). The transmitted light was coupled into optical fibre by using another lensed SMF and its spectra was measured by using an optical spectrum analyzer (AQ6374, Yokogawa Company, Japan).

2.5. Functionalization of optical waveguide MZI sensors for label-free biodetection

The surface of the fabricated MZI sensors was activated to hydrophilic by using oxygen plasma [24], when it was packaged with microfluidic layer. To functionalize MZI sensors, 4% APTES aqueous solution was first injected into the microchannel of optofluidic chip to salinize the sensing arm for about 20 mins. Then, the sensing window was flushed with Phosphate-buffered saline (PBS) buffer solution. Subsequently, 100 μg/mL goat anti-human IgG was injected to incubate the sensing arm at room temperature for about 30 min. After washing out the unbound detection antibody, 1% BSA solution was injected to block the nonspecific site. Finally, PBS buffer solution was injected to wash out loosely bounded molecules, the MZI biosensor is ready for HIgG detection.

3. Results

3.1. Directly printed polymer asymmetric MZI microsensors with width-tailored optical waveguide

The fabricated SU-8 waveguide MZI sensors are shown in Fig. 2(a)-(d). SU-8 ($n = 1.573$) [29], Ormoclad ($n = 1.52$) [30], and SiO$_2$ ($n = 1.45$) were chosen to make the core, cladding, and substrate of the optical waveguide, respectively. The size of the SU-8 waveguide except sensing arm is chosen to 2 μm (height) × 2.7 μm (width), as shown in the inset of Fig. 2(a), which can make the waveguide not only work under single mode condition but also possess a relatively weak evanescent field for suppressing the optical loss caused by the Ormoclad cladding fabricated by direct printing processes. The width of the optical waveguide of sensing arm is narrowed to 2.1

μm, as shown in the inset of Fig. 2(b), to enhance its evanescent field for a better sensitivity. According to the numerical simulation given in Fig. S1, the evanescent field of the fundamental guided mode of the designed SU-8 waveguide can enter external water environment about 744 nm, which is sufficient to cover most of biomarkers in biological detection applications.
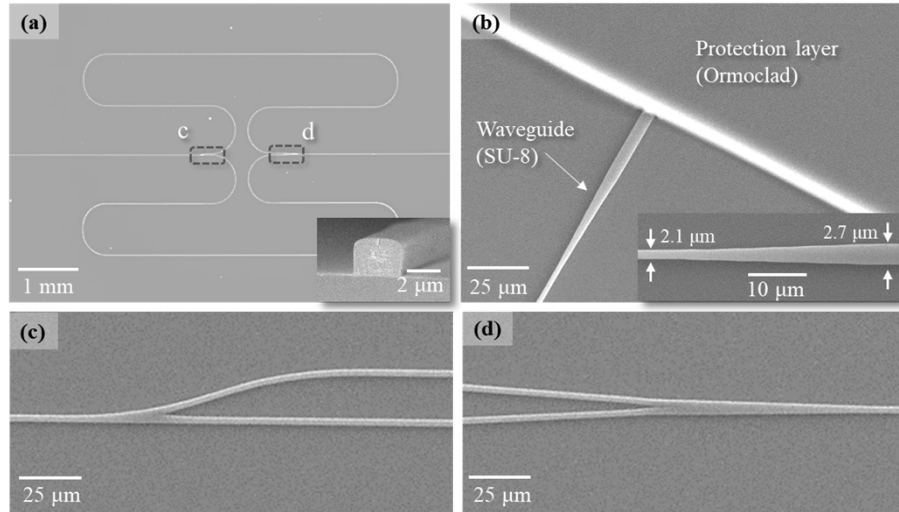

Fig. 2. (a) Optical microscope image of the MZI sensor, inset is interface of waveguide. (b) SEM image of waveguide covered by Ormoclad, inset is enlarge of the tapered waveguide (c) a 1:2 splitter, and (d) a 1:1 splitter.

To minimize the mode-mismatch induced optical propagation loss, an adiabatic taper with the length of 50 μm (Fig. 2(b)) is introduced between two different width waveguides. Since the powers of the light waves after transmitting through the reference and sensing arms will become different due to different optical losses between the two different waveguides. Since the powers of the light wave after first Y-split through the optical MZI has been specially designed with an asymmetric structure to compensate the light power difference. The two light waves propagating through the sensing and reference arms, respectively, will meet and interfere at the output Y-combiner.

When the sensing arm is immersed in a liquid with analytes, the effective refractive index of the optical modes of the sensing arm depends on the concentration of analyte. A change of analyte concentration will cause a variation of the effective refractive index and lead to a change of optical phase of the light wave propagating through the sensing arm. If the wavelength of a spectral dip in transmission spectrum is employed as an output signal, the wavelength shift $\Delta\lambda$ caused by a change of the refractive index in the working section of sensing arm, which can be given [31,32]:

$$\Delta\lambda = \frac{\lambda \tilde{L}_1 \Delta n_{e1}}{n_{g2}\bar{L}_1 + n_{g1}\tilde{L}_1 - n_{g2}L_2} \tag{1}$$

where $\tilde{L}_1$, Δn_{e1}, and n_{g1} are the length, the induced change of effective refractive index, the group refractive index of the 2.1-μm wide sensing arm, respectively; n_{g2} is the group refractive index of the 2.7-μm wide waveguide including the embedded part of sensing arm and the reference arm; $\bar{L}_1$ and L_2 are the lengths of the embedded part of sensing arm and the reference arm, respectively.

The measurement range of the waveguide MZI sensor depends on the free spectral range (FSR):

$$FSR = \frac{\lambda^2}{|n_{g2}\bar{L}_1 + n_{g1}\tilde{L}_1 - n_{g2}L_2|}. \tag{3}$$

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$$FSR = \frac{\lambda^2}{|n_{g2}\bar{L}_1 + n_{g1}\tilde{L}_1 - n_{g2}L_2|}. \tag{2}$$

If further consider the dependence of the effective refractive index of the working section of sensing arm on the refractive index of external medium, i.e., $\partial n_{e1}/\partial n_{ext}$, the bulk sensitivity S of the waveguide MZI sensor can be written as

$$S = \frac{FSR \cdot \tilde{L}_1}{\lambda} \cdot \frac{\partial n_{e1}}{\partial n_{ext}}, \tag{3}$$

where n_{ext} refers to the refractive index of external medium around the working section of sensing arm. In our design of MZI sensors, the length of the working section and embedded section of the sensing arm, i.e., $\tilde{L}_1$ and $\bar{L}_1$, and the length of reference arm L_2 are chosen to be 10.636 mm, 3.410 mm, and 13.918 mm, respectively. According to the numerical simulation, the group refractive indexes of the 2.1-µm wide sensing waveguide in water and the group refractive index of the 2.7-µm wide waveguide embedded in Ormoclad, i.e., n_{g1} and $n_{g2,}$ are 1.6028 and 1.5805, respectively. Moreover, it was calculated that a change of 6×10^{-4} in external refractive index caused an increase of 2.5×10^{-5} in the effective refractive index of the 2.1-µm wide sensing waveguide. Correspondingly, the wavelength shift of the spectral dip can be calculated from Eqn. (1) to be 0.936 nm. The sensitivity of the MZI sensor can be estimated by Eqn. (3) to be 1560 nm/RIU at the wavelength of 1550 nm.

3.2. Microfluidic layer and optical waveguide chip vertically integrated optofluidic chip

The optical waveguide chip before and after vertical integration with a microfluidic layer is shown in Fig. 3. Figure 3(a) shows the photo of a fabricated SU-8 optical waveguide incident with red light. It can be seen that a cladding layer has been printed along with optical waveguide and a sensing window has been opened for vertical integration of microfluidic layer for detecting analytes in liquid sample. Figure 3(b) shows a fully packaged optofluidic chip. The optofluidic chip includes four inlets, one serpentine mixer and three outlets which are designed for injection, mixing and collection of waste liquids, respectively. Fig. S3 shows the fabricated SU-8 mold. In our experiments, these four inlets are used to inject functionalization solution, target molecule solution, washing buffer solution, and an antibody strip buffer respectively.
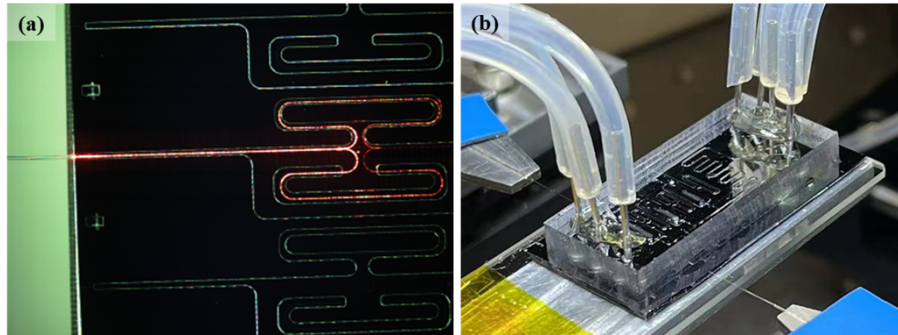

Fig. 3. (a) Photo of a fabricated SU-8 optical waveguide MZI sensor (inside with red light) (b) Photo of an optofluidic chip vertically integrated with a PDMS microfluidic layer upon an optical waveguide chip.

If further consider the dependence of the effective refractive index of the working section of sensing arm on the refractive index of external medium, i.e., $\partial n_{e1}/\partial n_{ext}$, the bulk sensitivity S of the waveguide MZI sensor can be written as

$$S = \frac{FSR \cdot \tilde{L}_1}{\lambda} \cdot \frac{\partial n_{e1}}{\partial n_{ext}}, \tag{4}$$

where n_{ext} refers to the refractive index of external medium around the working section of sensing arm. In our design of MZI sensors, the length of the working section and embedded section of the sensing arm, i.e., $\tilde{L}_1$ and $\bar{L}_1$, and the length of reference arm L_2 are chosen to be 10.636 mm, 3.410 mm, and 13.918 mm, respectively. According to the numerical simulation,

3.3. Transmission spectra of the fabricated MZI microsensors before and after packing with a microfluidic layer

The transmission spectra of the fabricated SU-8 optical waveguide MZI sensors before and after packing with microfluidic layer are shown in Fig. 4. The spectrum of MZI sensor before packaging is given in Fig. 4(a). It is not very flat in the wavelength range from 1530 nm to 1560 nm, which may result from the excitation of higher-order optical modes as the optical waveguide is designed to work at single-mode operation with Ormoclad cladding. For the waveguide of SiO_2/SU-8/air structure, the critical width for single mode operation is ~2.4 µm. After making a cladding of Ormoclad, the transmission spectrum of the MZI sensor becomes more regular and uniform as shown in Fig. 4(b). The FSR decreased from 7.3 nm to 4.2 nm. From Eqn. (2) and numerically calculated values of group refractive indexes, one can understand that such a decrease results from the change of n_{g2} from 1.6090 to 1.5805 (though its effective refractive index increased from 1.5213 to 1.5406), when its cladding layer is changed from air (whose refractive index is about 1.0) to Ormoclad (whose refractive index is about 1.52).
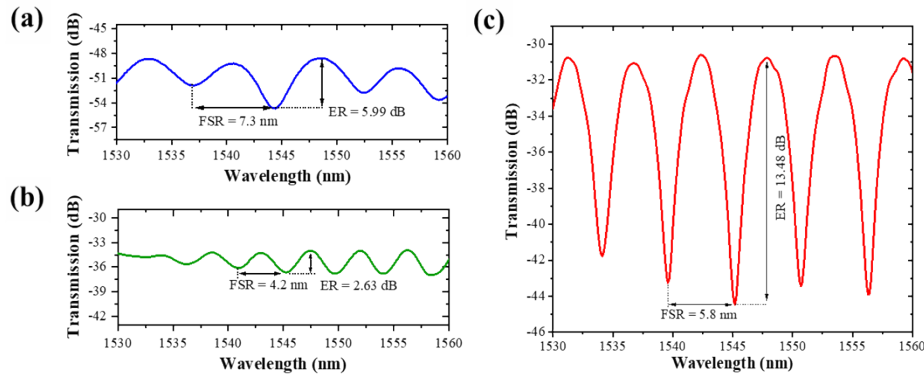

Fig. 4. Transmission spectra of the fabricated SU-8 waveguide MZI sensor. (a) Spectrum of the MZI sensor without cladding. (b) Spectrum of the MZI sensor after fabrication with Ormoclad cladding. (c) Spectrum of the MZI sensor in optofluidic chip after injection with water.

Figure 4(c) shows the measured transmission spectrum of the MZI sensor after packing with PDMS microfluidic layer and injecting water into the optofluidic chip. After injection of water into the sensing window, the FSR increased to 5.8 nm. From Eqn. (2) and numerically calculated values of group refractive indexes, one can understand that it resulted from a decrease of n_{g1} of the 2.1 µm wide waveguide from 1.6143 to 1.6028. Notably, the extinction ratio (ER) of the transmission spectrum increased from 2.63 dB to 13.48 dB. It is attributed to the specially designed Y splitter, which can compensate the light propagation loss in the sensing arm to make the light powers from the two arms to be fairly close and thereby achieve a balanced interference at the output. A more detailed comparison of the transmission spectra of MZI sensors, using different Y splitters, is given in Fig. S4. In Fig. S4(a), the fluidic Y splitter is a symmetric design. The arc radius of 1:4 Y splitter is smaller than that of 1:2 Y splitter. It contributes to higher bending loss and thus a higher splitting ratio of 1:4 Y splitter. Compared with the results achieved by using the Y splitters with the splitting ratio of 1:1 and 1:4, the transmission spectra of the MZI sensor with the Y splitter with the splitting ratio of 1:2 achieved highest extinction ratio.

Compared with the transmission spectra of the MZI sensor before and after fabrication of cladding, the optical power level of the transmission spectrum immersed in water has increased to some extent. It may be attributed to: 1) the eliminating of the excitation of high order modes after fabrication of Ormoclad cladding. As shown in the simulation result given in Fig. S5, the

order optical modes, such as TE_{21} and TM_{12} modes, occur only in the SU-8 waveguide with air cladding and disappear after changing the cladding from air to Ormoclad. 2) A better matching of optical waveguide modes at the interface around the edge of the sensing window after immersed in water. As the refractive index difference between Ormoclad and water is smaller than that between Ormoclad and air, the mode mismatching problem can thus be alleviated to depress optical loss. The simulation results in Fig. S6 revealed that the excess loss decreased from 0.329 dB to 0.066 dB when the cladding of the waveguide after the interface changes from air to water.

A long-time stability test of the fabricated polymer waveguide MZI sensor is shown in Fig. S7. Deionized (DI) water was injected into the sensing window of the packaged optofluidic chip in the test. The deviation of a peak wavelength of the transmission spectrum was measured for a long time over 2000 s. The standard deviation (SD) of the measured peak wavelengths is 30 pm.

3.4. Measurement of the bulk sensitivity of the fabricated MZI sensors

The bulk sensitivity of the fabricated MZI sensors was tested by using glucose solutions of different concentrations. A motorized syringe pump is used to inject and extract glucose solution into or out of the microfluidic channels. Figure 5(a) shows the measured wavelength shifts of the fabricated MZI sensor. It can be seen that the interference peak wavelength shifts to a longer wavelength with the increase of glucose concentration. Figure 5(b) presents the dependence of the wavelength shift of the MZI sensor on the external refractive indexes calculated by the concentrations of glucose solutions [33]. The inset shows the measured transmission spectra of the SU-8 waveguide MZI sensors in different glucose solutions. It reveals that the bulk sensitivity of the fabricated waveguide MZI sensor is 1695.95 nm/RIU, which is close to the estimated sensitivity, i.e., 1560 nm/RIU.
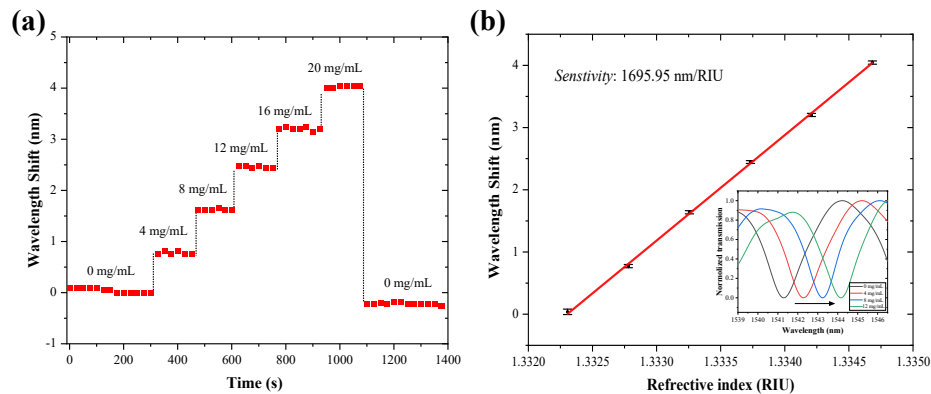

Fig. 5. Measured bulk sensitivity of the fabricated SU-8 waveguide MZI sensor. (a) Wavelength shift with respect to the concentration of glucose in water solution; (b) Wavelength shift with respect to the refractive index change. The inset shows the measured transmission spectra.

3.5. Highly specific detection of human Immunoglobulin G

The ability of the fabricated optofluidic chip in the detection of disease biomarkers was demonstrated by using the standard Human IgG, which is a predominant antibody in the blood and extracellular fluids and safeguards the human body against bacterial and viral infections [30]. The waveguide MZI sensors were functionalized as depicted in Fig. 6(a). The surface of SU-8 waveguide was activated to hydrophilic and then salinized with APTES and modified with goat anti-human IgG. Figure 6(b) shows the dynamic response of the MZI biosensor to a different solution concentration. Signal_start point, which the dash curve is the fitting curve of

the experiment data. It can be seen that the 90%-response time of the sensor is about 257 s, and the total wavelength shift is about 0.33 nm. The measured wavelength shifts of the MZI biosensors in the HIgG solutions of different concentrations, including 0 ng/mL, 1 ng/mL, 10 ng/mL, 100 ng/mL, 200 ng/mL, 500 ng/mL, and 1000 ng/mL, are shown in Fig. 6(c). The inset presents their corresponding transmission spectra. By using the triple of standard deviation, the noise-estimated limit of detection (LOD) is 267 pg/mL, corresponding to 1.78 pM. This value is comparable or exceeds most of same type sensors reported by other researchers [19,23,30].
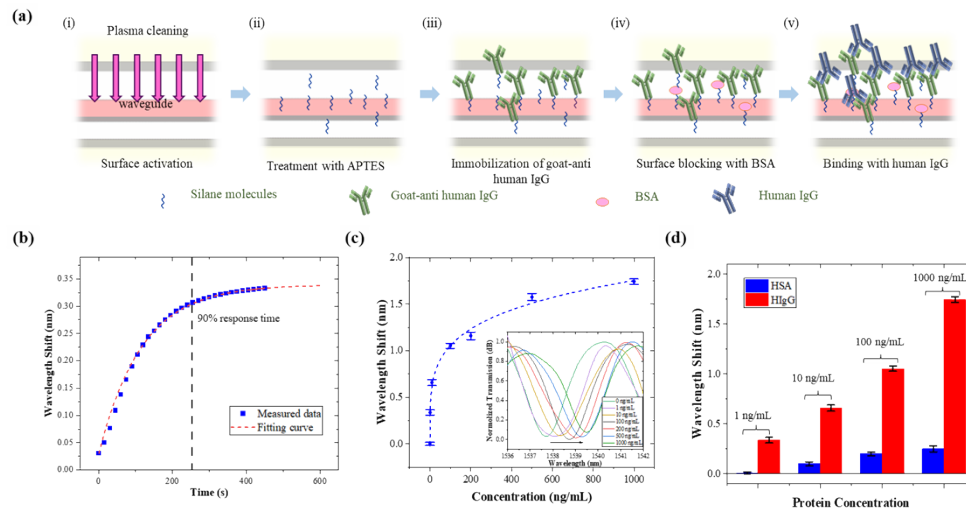

Fig. 6. (a) Schematic of the surface functionalization for detection of HIgG. (b) Dynamic response of the biosensor to 1 ng/mL target antibody solution. (c) Response of the biosensor in different concentrations of target antibody. (d) Comparison between the sensor's response to control protein HSA and target analyte HIgG.

The specificity of the MZI biosensor was tested by comparison of the biosensor's responses to the target analyte HIgG and the human serum albumin (HSA), serving as a negative control. As shown in Fig. 6(d), the measured responses of the biosensor to HSA at the concentration of 1 ng/mL, 10 ng/mL, 100 ng/mL, and 1000 ng/mL are 0.029, 0.152, 0.19, 0.143 times of these corresponding responses to HIgG at the same concentrations, which indicate a good selectivity of the MZI biosensor.

4. Discussion and conclusion

The polymer optical waveguide MZI sensor-based optofluidic biochip is a general label-free biosensing platform that can be applied to demonstrate the detection biomarker to Ash HIgG. This is widely used disease biomarker in clinic. Further considering that IgG molecules are relatively large (whose molecular weight is 150 kDa) and the binding of smaller protein biomarkers on a surface usually leads to a larger change of refractive index [34], one may anticipate that our MZI sensor-integrated optofluidic chip can detect a wide variety of protein biomarkers. It is also believed that similar processes can be extended for other biological analysis, such as the testing of nucleic acid or virus etc. [35].

Notably, the optofluidic chip can be repeatedly used in multiple measurements. Using an antibody stripping solution, the HIgG layer can be eluted from the sensor surface after one detection. Figure 7 shows a testing result for the repeated use of a MZI biosensor for 5 cycles. After a detection process, the MZI sensor was incubated in an antibody stripping solution for 30
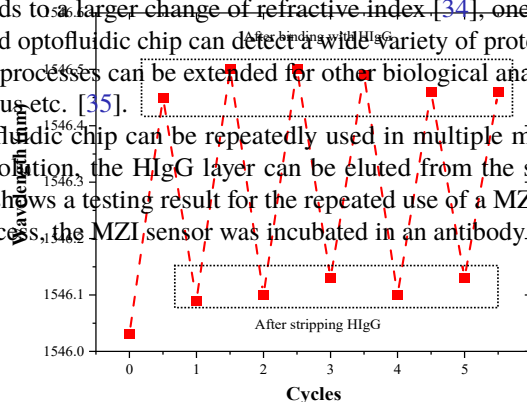

Fig. 7. Measured interference peak wavelengths of a fabricated optical MZI biosensor in 5 cycles of detection of HIgG.

to the target analyte HIgG and the human serum albumin (HSA), serving as a negative control. As shown in Fig. 6d, the measured responses of the biosensor to HSA at the concentration of 1 ng/mL, 10 ng/mL, 100 ng/mL, and 1000 ng/mL are 0.029, 0.152, 0.19, 0.143 times of these corresponding responses to HIgG at the same concentrations, which indicate a good selectivity of the MZI biosensor.

4. Discussion and conclusion

The polymer optical waveguide MZI sensor-based optofluidic biochip is a general label-free biosensing platform that can be applied to detect many kinds of diseases biomarkers. As HIgG is a widely used disease biomarker, we demonstrated the detection of HIgG to show the biodetection ability of the fabricated optofluidic chip. Further considering that IgG molecules are relatively large (whose molecular weight is 150 kDa) and the binding of smaller protein mins. The antibody stripping solution destroyed non-covalent bond only, and the lower layer of goat anti-human IgG was not removed because of its relatively stable binding with SU-8 surface via APTES. The MZI biosensor after stripping process can be reused to detect HIgG, and its sensitivity didn't show any significant change in 5 cycles of testing.
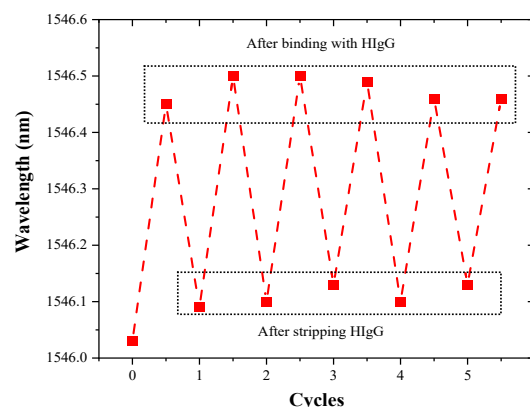

Fig. 7. Measured interference peak wavelengths of a fabricated optical MZI biosensor in 5 cycles of detection of HIgG.

In conclusion, we have presented an integrated optofluidic biochip with directly printed polymer optical waveguide MZI sensors. Asymmetric MZI sensors based on width-tailored waveguide have been designed and directly printed by using a digital UV lithography for high-sensitivity biosensing. After vertical integration with a microfluidic layer, an optofluidic chip has been demonstrated for on-chip biodetection. Experimental results showed that the bulk sensitivity of the on-chip integrated MZI sensors is as high as 1695.95 nm/RIU and it can detect HIgG at the concentration level of 1.78 pM. Such a small-size high-performance optofluidic chip with reusable MZI biosensors has great potential in the development of miniature point-of-care diagnostic instruments and devices.

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