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Silicon photonic chip-based biosensor for COVID-19 and flu detection with high sensitivity and specificity

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ABSTRACT

Since the end of 2021, Omicron, the new variant of SARS-CoV-2, has continued to spread as the predominant strain of COVID-19. Compared to previous variants, Omicron causes milder symptoms, which are similar to symptoms of other common respiratory infections, such as flu. In this work, we develop a silicon photonic chip-based biosensor for COVID-19 and flu detection using subwavelength grating micro-ring resonator. The biosensor realizes the detection of two pathogens with high sensitivity (1.31 fg/mL) and specificity. Besides, the microfluidic channel offers a promising solution for point-of-care detection.

Keywords: COVID-19, flu, biosensor, subwavelength grating, silicon photonics

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is continuously threatening human health.[1] Besides, the genetic variants of SARS-COV-2 are constantly emerging and may generate immune escape.[2] Since the winter of 2021, the Omicron variant has continued to spread worldwide as the new predominant strain of COVID-19. Compared with the Alpha or Delta subvariant, Omicron shows lower disease severity and relatively mild symptoms, but stronger infectious ability.[3] More importantly, the mild symptoms of Omicron make it difficult to distinguish from other common respiratory infections. Among these diseases, influenza shares many similar symptoms with COVID-19.[4] Considering different potential hazards of these two viruses, the timely identification of pathogen is significant for both patients and containing the epidemic.

In the past decades, optical biosensors bring new opportunities to biomedical detections due to series of advantages including high sensitivity, label-free detection, multiplexing capability, *etc*.[5] Additionally, the maturity of silicon photonics further promoted the development of optical biosensors. In this work, we develop a silicon photonic chip-based biosensor for COVID-19 detection using subwavelength grating (SWG) micro-ring resonator. To address the challenge brought by untypical symptoms of Omicron, the optical biosensor enables the concurrent detection of two potential pathogens (SARS-CoV-2 and influenza A H1N1in this study). The experimental results demonstrate an ultra-low limit of detection (LOD) with high specificity. Besides, a functional microfluidic channel is developed to provide a promising solution for point-of-care (POC) diagnosis.

2. DESIGN AND WORKING MECHANISM

2.1 Design of silicon photonic chip

Compared with conventional strip-waveguide micro-ring resonators, SWG resonators are constructed by periodic pillars with a period smaller than the operating wavelength. This structure shows good performance in biosensing scenarios because of the large effective sensing region increasing photon-matter interaction.[6] The resonant wavelength λ_{res} can be expressed as Eq (1).

$$\lambda_{res} = \frac{2\pi \cdot R \cdot n_{eff}}{m} \tag{1}$$

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Here, n_{eff} is the effective refractive index of SWG waveguide, R is the ring radius and m is mode order. The electric field intensity distribution of SWG resonators through finite difference time domain (FDTD) simulation is shown in Figure 1.(a)-(c). In this work, the antigen-antibody combination could change n_{eff}, resulting in the shift of resonate peaks.[7] The SWG resonators are fabricated on SOI wafer using E-beam lithography, and two sensing groups for the concurrent detection of two targets are placed on the chip (Figure 1.(d)&(e)).

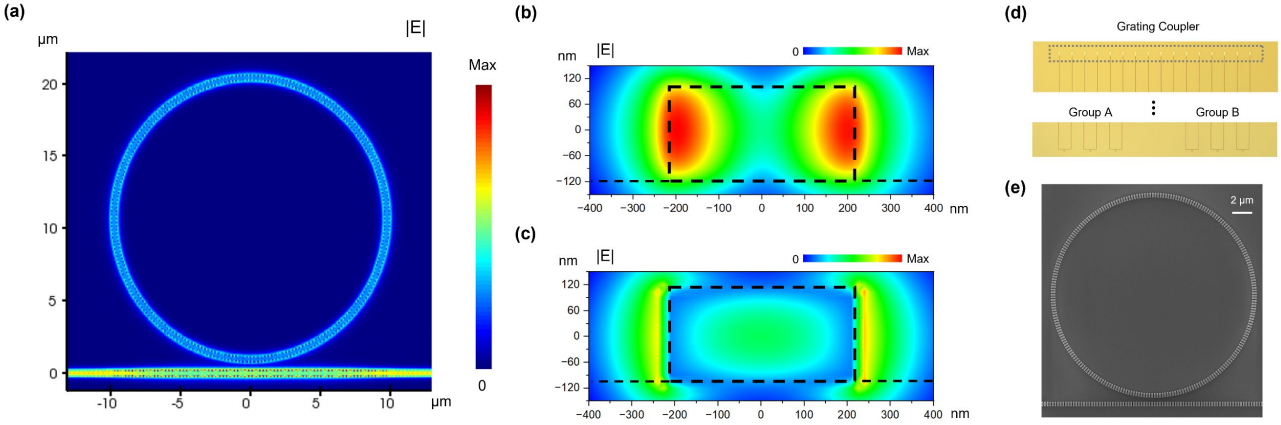

Figure 1 Design of SWG micro-ring resonators and electric field intensity distribution at different cross sections. (a) Electric field distribution in horizontal plane, while (b)&(c) correspond to the cross section in the middle of the gap and Si pillar. (d) Optical micrograph of chip layout. (e) SEM image of the SWG micro-ring resonator.

2.2 Functionalization of SWG resonator for concurrent detection

For the functionalization of device and following testing, we designed and fabricated a multipurpose microfluidic chip as shown in Figure 2.(a). This microfluidic chip has three ports that serve different functions (inlet/outlet) for functionalization and concurrent detection. Specifically, organosilane reagent (3-aminopropyl) triethoxysilane (APTES) and glutaraldehyde are introduced to the microfluidic chip in order via the middle port as the linker for further crosslink with antibody. After flowing through a Y-shaped splitter, the reagents reach two sensing groups. For antibody immobilization, the SARS-CoV-2 spike protein (SP) antibody and influenza A nucleoprotein (NP) antibody are pumped into the chip from two lateral ports (Figure .(b)), respectively, while the middle port works as the outlet.

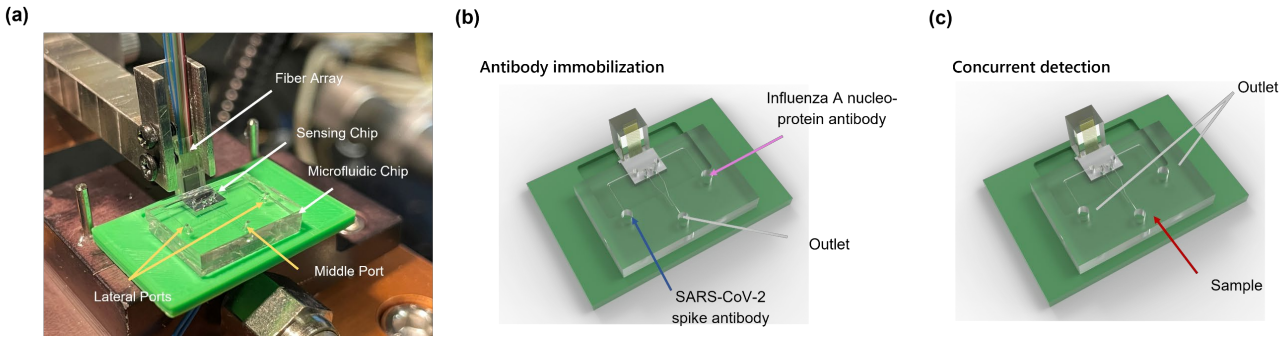

Figure 2 Diagram of system setup. (a) Photograph of the biosensing platform. (b) & (c) Schematic diagram of the functionalization and concurrent detection.

3. RESULTS AND DISCUSSIONS

To demonstrate the sensing performance of the optical biosensor, we first evaluated the quantitative relationship between peak shift and antigen concentration. The responses to different concentrations of SARS-CoV-2 antigen are shown in Figure 3. Testing results indicate that a concentration larger than 100 fg/mL, corresponding to 1.31 fM, could bring a significant redshift. For the concurrent detection, samples are introduced to the microfluidic chip through the middle port while lateral ports serve as outlets (Figure 2.(c)). The cross-reactivity testing results for SARS-CoV-2 SP and influenza NP indicate a significant difference between positive and negative responses (Table 1).

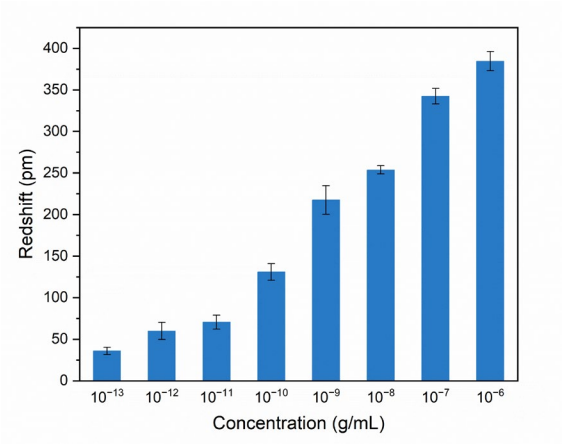

Figure 3. Concentration-dependent response of the SWG micro-ring resonator.

Table 1. The cross-reactivity testing results for SARS-CoV-2 SP and influenza NP (antigen concentration is 100 pg/mL).

Coating	SARS-CoV-2 SP antibody		Influenza A NP antibody	
Antigen	SP	NP	SP	NP
Sample #1	136.7	14.82	12.40	146.3
Sample #2	127.9	13.87	7.61	152.2
Sample #3	125.9	14.79	18.15	175.2
Results	(+)	(−)	(−)	(+)

CONCLUSIONS

This work reports a silicon photonic chip-based biosensor which realizes the on-chip concurrent detection of COVID-19 and flu. Quantitative detection and cross-reactivity testing results show an ultra-low LOD with high specificity. Besides, the microfluidic chip further improves the practicality and reliability in clinical diagnosis. Hence, the biosensor offers a promising solution to overcome challenges in the rapid diagnosis of COVID-19.

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